TOTAL SYNTHESIS OF (-)-DACTYLYNES

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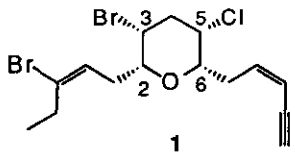
Abstract-The first total synthesis of (-)-dactylyne (**1**) and (-)-isodactylyne (**2**), which have been isolated from sea hare, is described in detail. Critical steps in the synthesis include a stereoselective construction as well as an intramolecular ring closure of **32**, and the effective double elongation reactions (**59** → **63** and **64**, **67** → **68**, and **70** → **71**).

In 1975 and 1976, Schmitz *et al.* have isolated dactylyne (**1**) and isodactylyne (**2**) from the digestive tract of the sea hare *Aplysia dactylomela*.[1,2] The structure of **1** including its absolute stereochemistry has been decided using spectroscopic and X-ray crystallographic techniques.[1] The structure of **2** was elucidated on the basis of spectral comparison with **1**.[2] The absolute configurations at C-2, C-3, C-5, and C-6 are *R*, *R*, *S*, and *S*, respectively. These products are structurally characterized by unbranched 15 carbon skeletons containing tetrahydropyran rings with all *cis*-oriented four substituents, which consist of (2*E*)-3-bromo-2 pentenyl, and pentenynyl groups at C-2 and C-6, and diaxial bromine and chlorine atoms at C-3 and C-5, respectively, as revealed in **1A** and **2A**. Both of them possess central nervous depressant activities evidenced by a potentiation of pentobarbital hypnosis and have nontoxic characters.[3-5] These unique structures, high biological potencies, and relative nontoxic natures make these natural products attractive synthetic targets. After many failure to replace the hydroxyl groups by halogen atoms, we have thought to be impossible to construct all *cis*-substituted tetrahydropyran systems with halogen atoms, such as dactylynes (**1** and **2**) and dactomelynes (**3** and **4**),[6] from the corresponding hydroxyl groups. Our alternate



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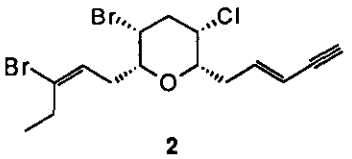

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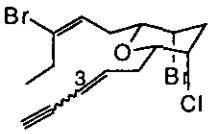
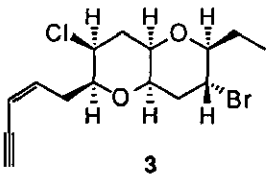


1A, 3*Z*
2A, 3*E*



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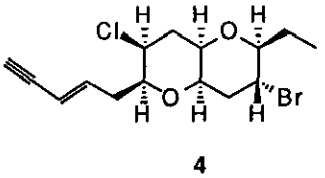

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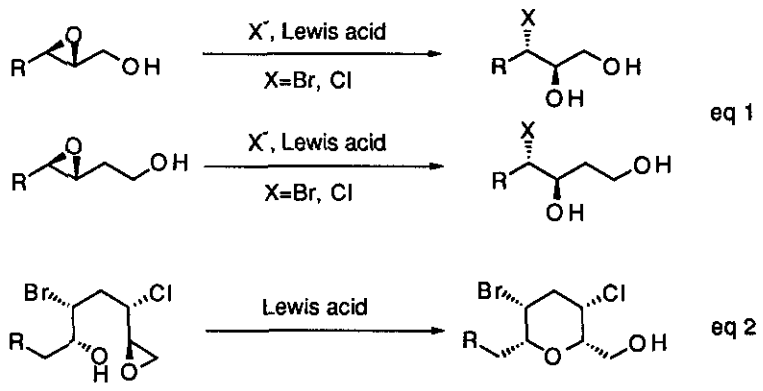
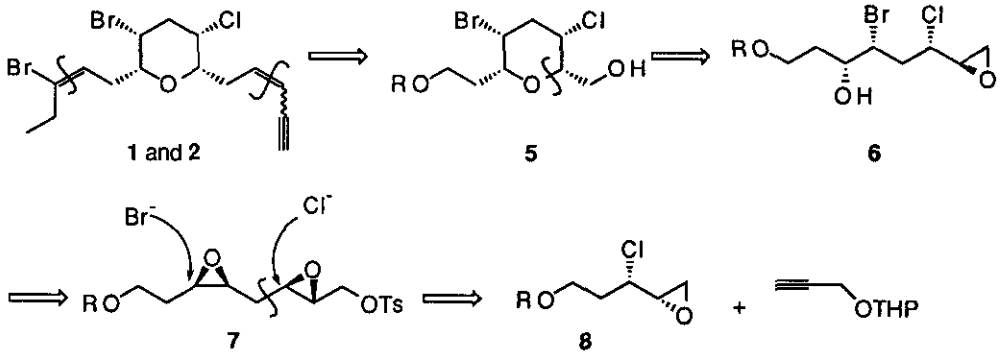
strategy contains two critical reactions: the first is to construct an acyclic framework containing bromine and chlorine atoms with correct stereochemistries by the ring-opening reactions of epoxy alcohols with



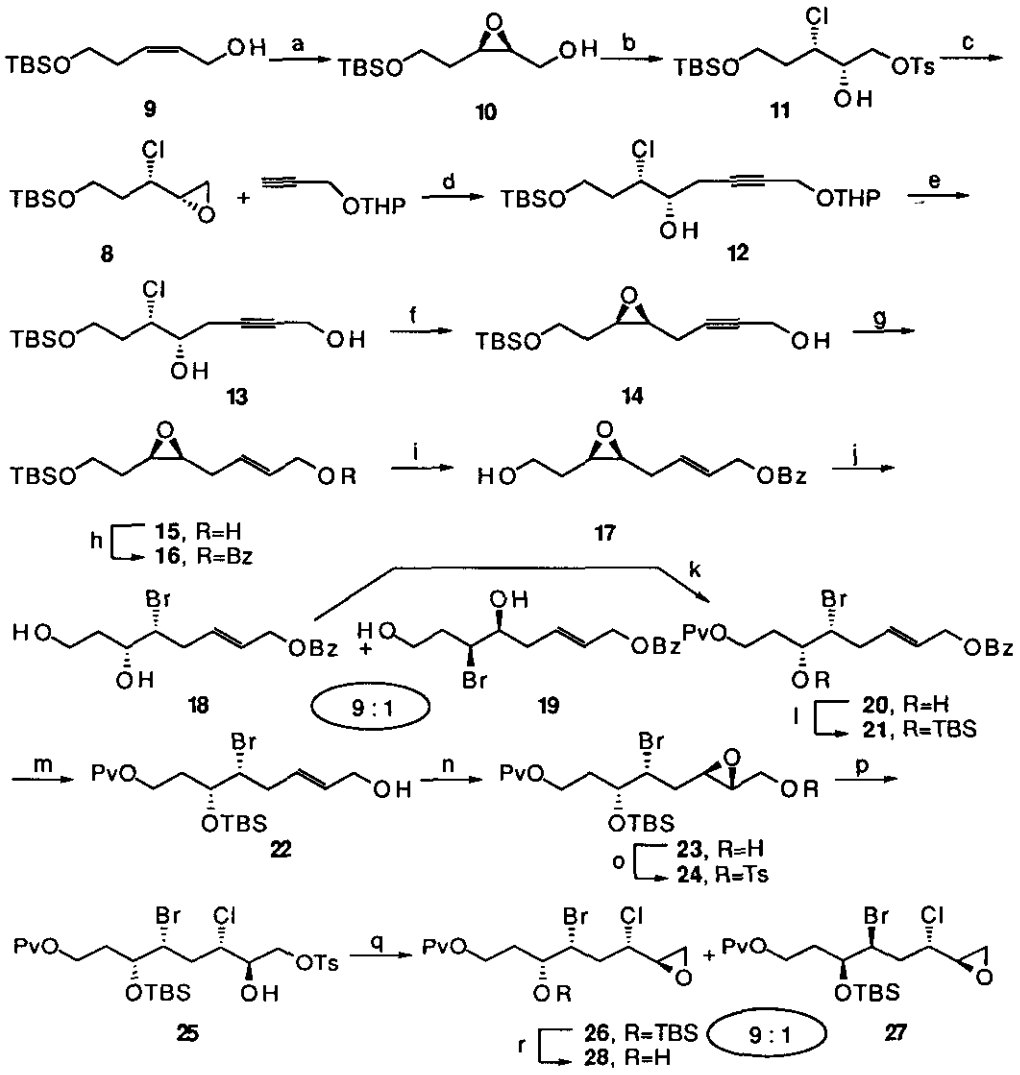
halogeno-nucleophiles (eq. 1), and the second is to construct an all cis-substituted tetrahydropyran ring *via* intramolecular cyclization of the epoxy alcohol (eq. 2). According to this strategy, we accomplished recently the first total synthesis of dactylynes (**1** and **2**).[7] We describe here the detail of the synthesis.
We chose the retrosynthetic route for dactylynes (**1** and **2**) as shown in Scheme 1. Compounds (**1** and **2**) were disconnected to an all *cis*-substituted tetrahydropyran framework (**5**) in the indicated bonds by employing the double Wittig reactions and the simple functional group manipulations. Then, disconnection of the C-O bond in **5** led to an acyclic halogenated epoxy alcohol (**6**), which would be derived from an equivalent of the bisepoxide (**7**) by use of the epoxy-opening methods developed by us.[8~10] The epoxide (**7**) was further disconnected to a chiral C-5 unit (**8**) and propargyl alcohol THP-ether on the basis of the coupling reaction of acetylide to a terminal epoxide.

Scheme 1.



The C-5 unit (**8**) has been prepared on a large scale in a few steps from the readily available (2Z)-5-*t*-butyldimethylsilyloxy-2-penten-1-ol (**9**)[11] (Scheme 2). With the chiral terminal epoxide (**8**) in hand, our synthesis was commenced from coupling reaction of **8** with propargyl alcohol THP-ether according to the Yamaguchi method[12] (Scheme 2). Thus, the latter ether was treated with BuLi and $BF_3 \cdot OEt_2$ to afford alkynylborane complex, which was treated rapidly *in situ* with **8** at -78 °C to give the β-hydroxyacetylene (**12**) in 98% yield based on the recovered **8** (19%). The THP group in **12** was detached with Et_2AlCl in CH_2Cl_2[13] to furnish the propargyl alcohol (**13**), which was converted to the *cis*-epoxide (**14**) on treatment with K_2CO_3 in MeOH in 97% yield for two steps. The triple bond in **14** was reduced with Red-Al®[14] to *trans*-olefin (**15**) and the hydroxyl group of **15** was protected with PhCOCl in a usual manner, followed by detaching the TBS group with TBAF to afford the 3,4-epoxy alcohol (**17**) *via* **16** in an 86% combined yield from **14**. Further transformation of **17** into the bromohydrin (**18**) was performed efficiently with titanium-mediated epoxy-opening process.[8] Thus, when compound (**17**) was allowed to react with $Et_2NH \cdot HBr$ in the presence of $Ti(O\text{-}i\text{-}Pr)_4$ in CH_2Cl_2, the ring-opening reaction of the oxirane proceeded

Scheme 2.



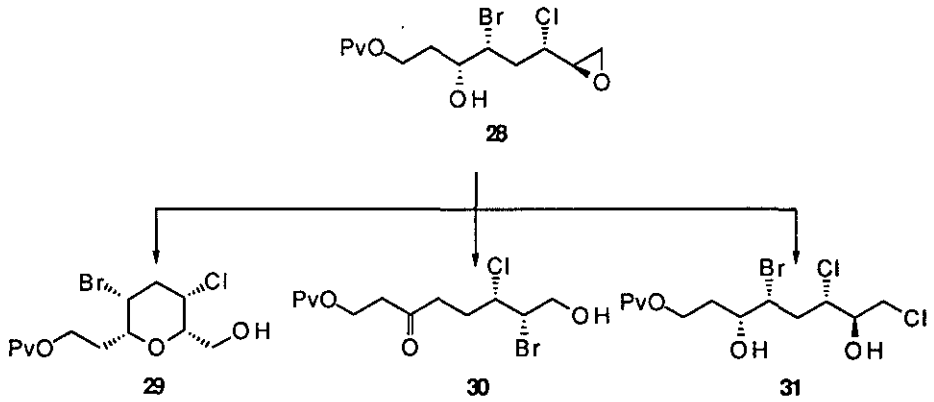
Reagents and conditions: a) L-(+)-DET, Ti(O-*i*-Pr)$_4$, TBHP, 4A-MS, CH_2Cl_2, -20 °C, 16 h, 97%, 87%ee; b) TsCl, TEA, DMAP, CH_2Cl_2, 0 °C, 5 h, 100%; Et_2AlCl (1.1 eq.), CH_2Cl_2, -20 → -10 °C, 5 h, 100%; c) K_2CO_3, MeOH, 0 °C, 1 h, 91%; d) BuLi, BF_3-OEt_2, THF, -78 °C, 45 min, 79%; e) Et_2AlCl, CH_2Cl_2, 0 → 25 °C, 4 h, 100%; f) K_2CO_3, MeOH, 25 °C, 3 h, 97%; g) Red-Al®, ether, 0 → 25 °C, 5 h, 98%; h) PhCOCl, TEA, DMAP, CH_2Cl_2, -40 °C, 2 h, 97%; i) TBAF, THF, 0 °C, 4 h → 20 °C, 2 h, 90%; j) Ti(O-*i*-Pr)$_4$ (1.5 eq.), Et_2NH·HBr (4.0 eq.), CH_2Cl_2, 25 °C, 12 h, 76%; k) PvCl, Py, -20 °C, 2 h → -10 °C, 12 h, 70%; l) TBSOTf, 2,6-lutidine, CH_2Cl_2, -20 °C, 4 h, 96%; m) K_2CO_3, MeOH, 20 °C, 80 min, 96%; n) D-(-)-DET, Ti(O-*i*-Pr)$_4$, TBHP, 4A-MS, CH_2Cl_2, -20 °C, 10 h, 99%; o) TsCl, TEA, DMAP, CH_2Cl_2, 0 °C, 12 h, 100%; p) Et_2AlCl, CH_2Cl_2, 20 °C, 13 h, 97%; q) K_2CO_3, MeOH, 20 °C, 1 h, 93%; r) TBAF-HF (pH≈3), THF, 20 °C, 20 h, 97%.

regioselectively leading to a 9:1 separable mixture of the C-4 (**18**) and C-3 opening products (**19**) in a 76% combined yield. Next, the transformation of **18** to halogenated terminal epoxide (**28**) was carried out (Scheme 2). The separated diol (**18**) was converted to **21** by selective esterification of the primary hydroxyl group with PvCl, followed by protection of the secondary hydroxyl group in **20** as the silyl ether in a usual manner. The benzoyl group of **21** was then detached by methanolysis with K_2CO_3 in anhydrous

MeOH, with no effect on the co-existing pivaloyl group, giving **22**. This was submitted to Sharpless asymmetric epoxidation[15] with D-(-)-DET as an auxiliary to afford the desired product (**23**) as a sole product. Toluenesulfonylation of **23** with a standard method gave the corresponding epoxy sulfonate (**24**). When **24** was treated with Et_2AlCl in CH_2Cl_2 for 10 h,[10] the ring-opening reaction proceeded smoothly to provide exclusively the desired product (**25**). Then, exposure of **25** to K_2CO_3 in MeOH resulted in regioselective oxirane formation to afford the terminal epoxides (**26** and **27**) in 93% yield. The diastereoisomer **27**, arisen from the contaminated antipode of the C-5 unit (**8**) used in the first step, was easily removed by flash chromatography. The attempted desilylation of **26** with aqueous 5% HF in MeCN resulted in the decomposition of the epoxide to give a mixture. When only TBAF was used as a desilylating agent, debromination occurred preferentially to afford a bisepoxide in 92% yield. Deprotection of the TBS group of **26** to the 6-hydroxy-1, 2-epoxide (**28**) was performed with a mixture of TBAF-HF (pH≈3) in THF, prepared from TBAF (1.0 M solution in THF) and 38% HF in water in a ratio of 12:1, in 93% yield.

With the intermediate (**28**) at hand, attention was then focused on the construction of all *cis*-substituted tetrahydropyran ring (**29**) *via* an intramolecular cyclization of **28** (Scheme 3). When protic acids, such as PPTS, PTS, CSA, and TFA, were used as cyclization activators, the reaction did not occur with either recovery or decomposition of the starting **28**, no trace of cyclized product being obtained. Lewis acids were then examined. Unfortunately, **28** could not be induced to cyclize under various attempted conditions. Interestingly, when **28** was treated with $BF_3{\cdot}OEt_2$ (2 eq.) in CH_2Cl_2 at -20 °C for 0.5 h or $Ti(O\text{-}i\text{-}Pr)_4$ (2 eq.) in PhH at 80 °C for 24 h, the rearrangement reaction proceeded preferentially to give the ketone (**30**)[16] in 70% or 65% yield, while **28** was transformed into dichlorohydrin(**31**)[17]on reaction with $TiCl_4$ (2 eq.) in CH_2Cl_2 at -20 °C for 1 h. These results might reflect that **28** would exist mainly as the conformer (**28B**) in the solution, instead of **28A**, because there would be a serious diaxial repulsive interaction between two halogen atoms in the latter (Figure 1). Thus, **30** would be formed from the preferentially existed conformer (**28B**). The structure of **30** was determined by ^{13}C- and ^1H-nmr, FAB-ms, and elemental analysis. The stereochemistry at C-2 in **30** was assigned to be an *S* configuration on the assumption that the bromine atom would be rearranged in an S_N2 fashion *via* a five-membered ring transition state. The assignment was proven by an NOE experiment on its analogue (**54**). These results led us to revise the isolated terminal epoxide to 2, 3-epoxy-1-ol type expecting regulation of regioselective opening at C-3 position, because the intramolecular cyclization would be favored in the 2, 3-epoxy-1-ol type due to the stronger coordination to some Lewis acids.[18] Accordingly, we anticipated that compound (**32**) would be the more efficient synthetic precursor for **1** and **2** (Scheme 4). The compound could be prepared from the reaction of epoxy alcohol derivative (**33**) with some chloro-nucleophile according to our procedure.[9] Its precursor (**34**) would be formed by coupling of **8** with the chiral acetylene (**36**). Detached **35** has been prepared from D-(-)-tartaric acid by Yadav *et al.*[19] Therefore, the synthetic study of **1** and **2** started from the coupling reaction of these two compounds.

Scheme 3.



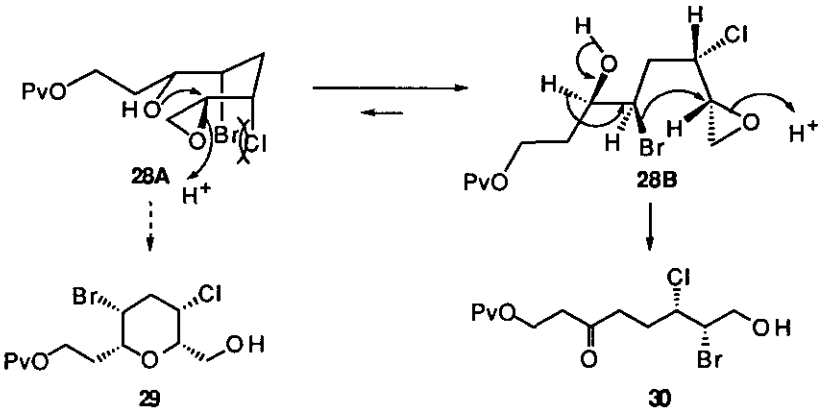
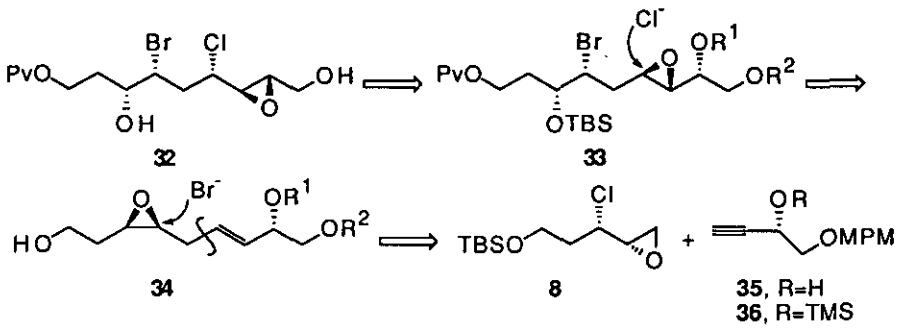


Figure 1. Why didn't **28** lead to formation of the cyclized compound (**29**)?

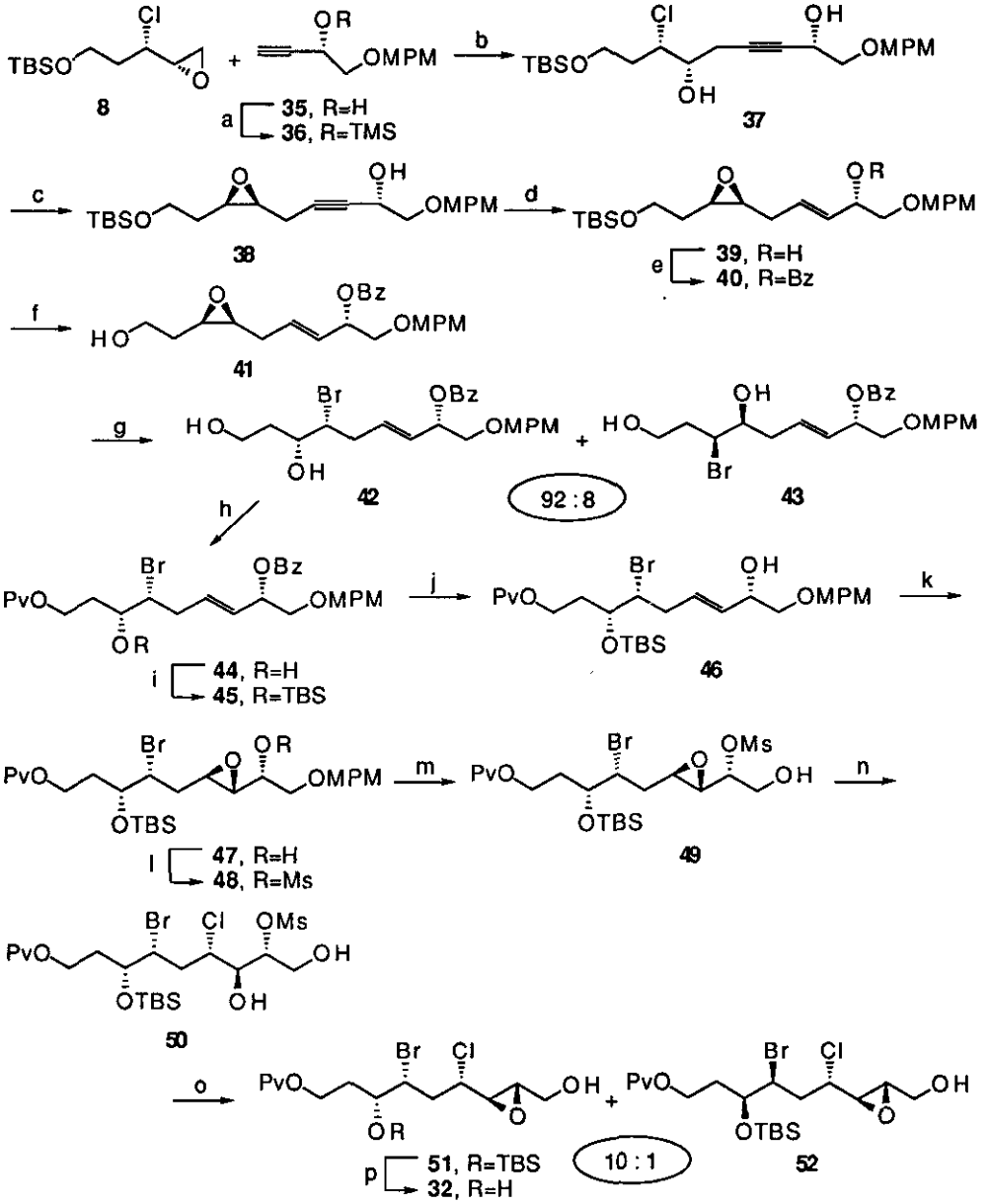
Scheme 4.



Protection of the OH group in **35** with TMSCl gave the unstable silyl ether (**36**), which was directly used in the next step without purification (Scheme 5). According to the Yamaguchi method,[12] compound (**36**) was treated with BuLi and BF_3·OEt_2 in THF to afford an alkynylborane complex, which reacted *in situ* with the epoxide (**8**) to yield, after an AcOH work-up, the chlorohydrin alcohol (**37**) in 98% yield. Exposure of **37** to K_2CO_3 in MeOH led to the epoxide (**38**) in 98% yield. The triple bond of **38** was reduced with Red-Al®[14] in ether affording allylic alcohol (**39**) in 98% yield. The alcohol (**39**) was converted to the benzoyl ester (**40**), which was treated with TBAF in THF to furnish the *cis*-3, 4-epoxy alcohol (**41**) in 95% yield. When compound (**41**) was treated with Et_2NH·HBr and Ti(O-*i*-Pr)$_4$ in CH_2Cl_2 at 25 °C for 12 h, the ring-opening reaction of the oxirane proceeded regioselectively to yield a 92:8 separable mixture of C-4 opening (**42**) and C-3 opening products (**43**) in a 78% combined yield. Elaboration of **42** to the requisite 2, 3-epoxy alcohol methanesulfonate (**48**) was accomplished in five steps. Thus, the primary hydroxyl group of **42** was esterified with PvCl and Py in CH_2Cl_2 to give the pivaloate (**44**), of which the secondary alcohol was protected as a silyl ether to afford **45**. The benzoyl group of **45** was saponified with K_2CO_3 in a mixture of MeOH-water (20:1) to yield the allylic alcohol (**46**) in 91% yield. Compound (**46**) was submitted to Sharpless asymmetric epoxidation[15] using D-(-)-DIPT to give β-epoxide (**47**) as a sole product in 97% yield. Methanesulfonylation of **47** produced the sulfonate (**48**) quantitatively, which was detached with DDQ to give an alcohol (**49**) in 94% yield. When **49** was treated with 3.0 eq.of Et_2AlCl in CH_2Cl_2-hexane (3:1) at 0 °C for 3 h, the ring-opening reaction of the oxirane proceeded smoothly to provide exclusively the desired chlorohydrin (**50**) in 90~100% yield. Then, exposure of **50** to K_2CO_3 in MeOH resulted in regioselective oxirane formation to furnish the 2, 3-epoxy alcohol (**51**, 87% and **52**, 8.7%), without the loss of the chlorine atom. Compound (**52**), arisen from the antipode of C-5

segment (**8**), could be easily removed from the main product by flash chromatography. Detachment of TBS group from **51** under the mild conditions provided the requisite 7-hydroxy-2, 3-epoxy alcohol (**32**).

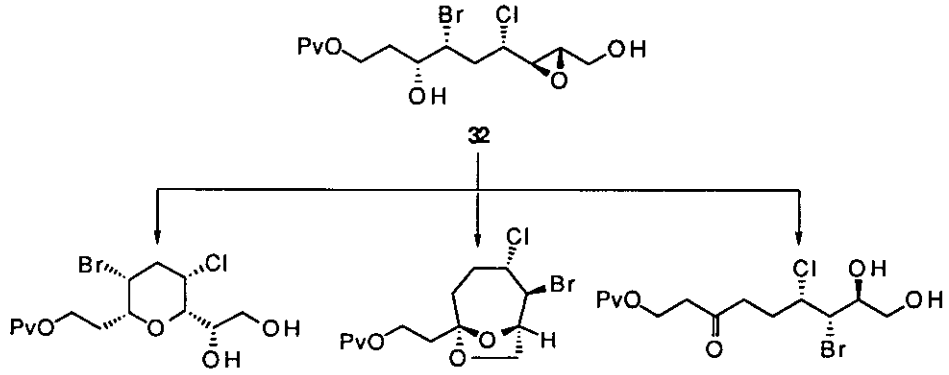
Scheme 5.



Reagents and conditions: a) TMSCl, TEA, CH_2Cl_2, -15 °C, 30 min, 95%; b) BuLi, $BF_3{\cdot}OEt_2$, THF, -78 °C, 1.5 h; 20% AcOH, -78 → 20 °C, 2 h, 98%; c) K_2CO_3, MeOH, 23 °C, 6 h, 98%; d) Red-Al®, ether, 0 °C, 1 h, 98%; e) PhCOCl, TEA, DMAP, CH_2Cl_2, 0 °C, 3 h, 98%; f) TBAF, THF, -10 °C, 3 h, 97%; g) Ti(O-*i*-Pr)$_4$, $Et_2NH{\cdot}HBr$, CH_2Cl_2, 25 °C, 12 h, 78%; h) PvCl, Py, CH_2Cl_2, 0 °C, 12 h, 97%; i) TBSOTf, TEA, DMAP, CH_2Cl_2, -20 °C, 4 h, 97%; j) K_2CO_3, MeOH-H_2O (20:1), 20 °C, 3 h, 91%; k) D-(-)-DIPT, Ti(O-*i*-Pr)$_4$, TBHP, 4A-MS, CH_2Cl_2, -20 °C, 72 h, 97%; l) MsCl, TEA, DMAP, CH_2Cl_2, -40 °C, 1 h, 100%; m) DDQ, CH_2Cl_2-H_2O (18:1), 23 °C, 4 h, 94%; n) Et_2AlCl (3.0 eq.), CH_2Cl_2-hexane (3:1), 0 °C, 3 h, 90~100%; o) K_2CO_3, MeOH, 20 °C, 1 h, 96%; p) TBAF-HF, THF, 20 °C, 28 h, 89%.

The intramolecular cyclization reaction of the 2, 3-epoxy alcohol (**32**) was then examined. Table 1 summarizes some of the attempted conditions and results. Initial reaction of **32** with $Ti(O\text{-}i\text{-}Pr)_4$ (0.25 eq.) and 4A-MS in toluene at 105 °C for 3 h gave rise to the desired cyclized product (**53**), though in a low yield (16%). Next, employment of a soft Lewis acid, $Sn(OTf)_2$, in CH_2Cl_2 at 20 °C led to **53** in 26% yield along with 50% of a bicyclic product (**54**). However, when rather non-polar solvents, such as PhH or toluene, were used, the other by-product (**55**) was produced besides **54**. Next, treatment of **32** with $Zn(OTf)_2$ in refluxed PhH yielded **53** in 13% yield, along with 42% of **54**. Fortunately, when a two-necked flask equipped with a reflux condenser and a septum (Aldrich, Z10, 076-5) (not a glass stopper) was used, the reaction with $Zn(OTf)_2$ in PhH under reflux gave rise to only the desired product (**53**) in 38% yield (in a 74% corrected yield based on the recovered starting material). The details of the effect of the septum on the reaction is not yet clear. The structure of **54** including its stereochemistry was established by ^{1}H-nmr and HR-ms spectroscopic analysis[20] combined with an NOE experiment (Figure 2). The ketone (**55**) was confirmed from its ^{1}H-nmr spectrum and finally by the chemical transformation into **54** with $Sn(OTf)_2$ (1.0 eq.) in CH_2Cl_2 at 20 °C for 12 h (72% yield).[21]

Table 1. Intramolecular Cyclization of the Epoxy Alcohol (**32**).



	53	**54**	**55**
$Ti(O\text{-}i\text{-}Pr)_4$ (0.25 eq.) toluene, 4A-MS, 105 °C, 3 h	16%	—	—
$Sn(OTf)_2$ (1.0 eq.) CH_2Cl_2, 20 °C, 2 h	26%	50%	—
$Sn(OTf)_2$ (1.1 eq.) PhH, 20 °C, 2 h	34%	30%	24%
$Sn(OTf)_2$ (1.1 eq.) toluene, 20 °C, 6 h	30%	18%	32%
$Zn(OTf)_2$ (1.1 eq.) PhH, reflux, 8 h	13%	42%	—
$Zn(OTf)_2$ (1.1 eq.)[a] PhH, reflux, 15 h	38% (74%)[b]	—	—

a) The septum (Aldrich, Z-10,076-5) was used. b) The value in parenthesis denotes the corrected yield based on the recovered starting material.

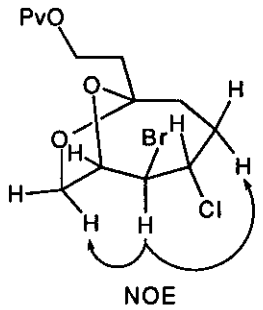
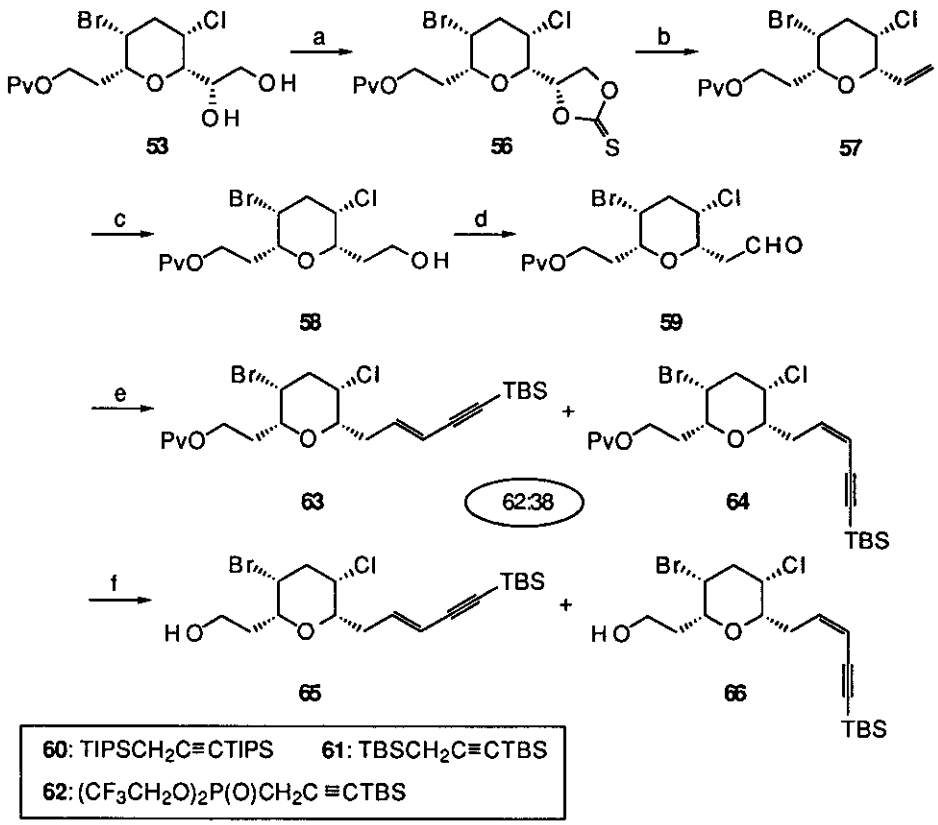


Figure 2. The NOE experiment of **54**.

With the ring closed product at hand, attention was then paid to elaborate the enyne functionality, so that **53** was transformed into aldehyde(**59**) in four steps (Scheme 6). Firstly, the vicinal diol part of **53** was converted to the vinyl derivative (**57**) by the modified Corey procedure.[22] Conversion of the diol to the corresponding thiocarbonate (**56**) was accomplished with $CSCl_2$ in the presence of DMAP in 82% yield.

Scheme 6.



Reagents and conditions: a) $CSCl_2$, DMAP, CH_2Cl_2, 0 °C, 1 h, 82%; b) 1,3-dimethyl-2-phenyl-1,3-diazaphospholidine, toluene, 20 °C, 2 h, 97%; c) 9-BBN, THF, 20 °C, 2 h; 5% NaOH, H_2O_2, 20 °C, 1 h, 96%; d) $(COCl)_2$, DMSO, TEA, -78 → 20 °C, 1.5 h, 89%; e) **62** (1.5 eq.), $KN(TMS)_2$ (1.2 eq.), 18-crown-6 (1.4 eq.), THF, -78 °C, 45 min, 85%; f) DIBAH, CH_2Cl_2, -78 → -40 °C, 1 h, 61% (**65**) and 38% (**66**).

Then, treatment of **56** with 1,3-dimethyl-2-phenyl-1,3-diazaphospholidine in dry toluene afforded the terminal olefin (**57**) in 97% yield.[23] Hydroboration of the vinyl function in **57** with 9-BBN in THF, followed by oxidative work-up, produced the alcohol (**58**) in 96% yield. Finally, Swern oxidation[24] of **58** furnished the aldehyde (**59**) in 89% yield. For the next sequence, the rather mild conditions were needed to elongate the enyne unit to the aldehyde (**59**), since the compound would be unstable under basic conditions due to the liable elimination of the axially situated halogen atoms, particularly the bromine atom. The initial Wittig reaction with the Corey reagent (**60**)[25] gave an unknown mixture, which showed no enyne protons (δ5.5-6.2 ppm) on the ^{1}H-nmr of the crude mixture. Next, modification of the Corey method using compound **61** led to formation of a 1:1 mixture of (*E*)- (**63**) and (*Z*)-olefins (**64**) in only a 19% combined yield. Therefore, a Horner-Wittig-type reagent (**62**)[26] was newly prepared for this transformation, because **62** was expected to show a higher reactivity rather than the Corey reagent. Indeed, the aldehyde (**59**), when treated with the K-salt of **62** in the presence of 18-crown-6 in THF, gave rise to a 62:38 mixture of (*E*)- and (*Z*)-enynes (**63** and **64**) in an 85% combined yield. The mixture was then converted to the corresponding alcohols (**65** and **66**) on DIBAH reduction in 99% yield, which were easily separated by flash chromatography.

The final critical stage of the synthesis was how to construct efficiently the left double bond containing a bromine atom. The synthesis of (-)-**2** was completed in three steps as revealed in Scheme 7. Thus, Swern oxidation[24] of (*E*)-olefin alcohol (**65**) afforded the aldehyde (**67**) in a quantitative yield, which, on reaction with the Smithers reagent ($Ph_3P^+CBr_2EtBr^-$)[27] in the presence of BuLi in THF, afforded a 1:1 mixture of the (*E*)-olefin (**68**) and its (*Z*)-isomer (**69**) in 23% yield. After many invalid attempts, we found that addition of DMSO raised greatly the yield and enhanced the geometrical selectivity. Treatment of **67** with the above Wittig reagent and BuLi in the mixture of THF-DMSO (5:1) provided an 83:17 mixture of **68** and **69** in an 87% combined yield. The pure (*E*)-olefin (**68**) was obtained by separating the mixture with hplc. Finally, **68** was detached with a mixture of TBAF-HF in THF to give a colorless oil in 79% yield. This material was identical with the natural isodactylyne (-)-(**2**) in all respects (tlc behavior, specific rotation, ir, ^{1}H-nmr, and ms). On the other hand, the (-)-dactylyne synthesis was accomplished from the (*Z*)-olefin alcohol (**66**) in the same manner as mentioned above. Thus, the alcohol (**66**) was oxidized to aldehyde (**70**) by the Swern method[24] in 95% yield, which was transformed into an 82:18 mixture of (*E*)-vinyl bromide (**71**) and its (*Z*)-isomer (**72**) in a 67% total yield. Similarly, desilylation of the separated compound (**71**) gave rise to dienyne as white crystals, mp 62.5-63.2 °C, which was identical with (-)-dactylyne (**1**) by comparison with their mps, specific rotations, as well as ir, ^{1}H-nmr, and ms spectra. In this way, the first total synthesis of (-)-dactylyne (**1**) and (-)-isodactylyne (**2**) was achieved from **8** *via* the key intermediate (**53**) in 25 steps. The overall yields toward **1** and **2** amounted to 14% and 15%, respectively, from the initial coupling reaction.

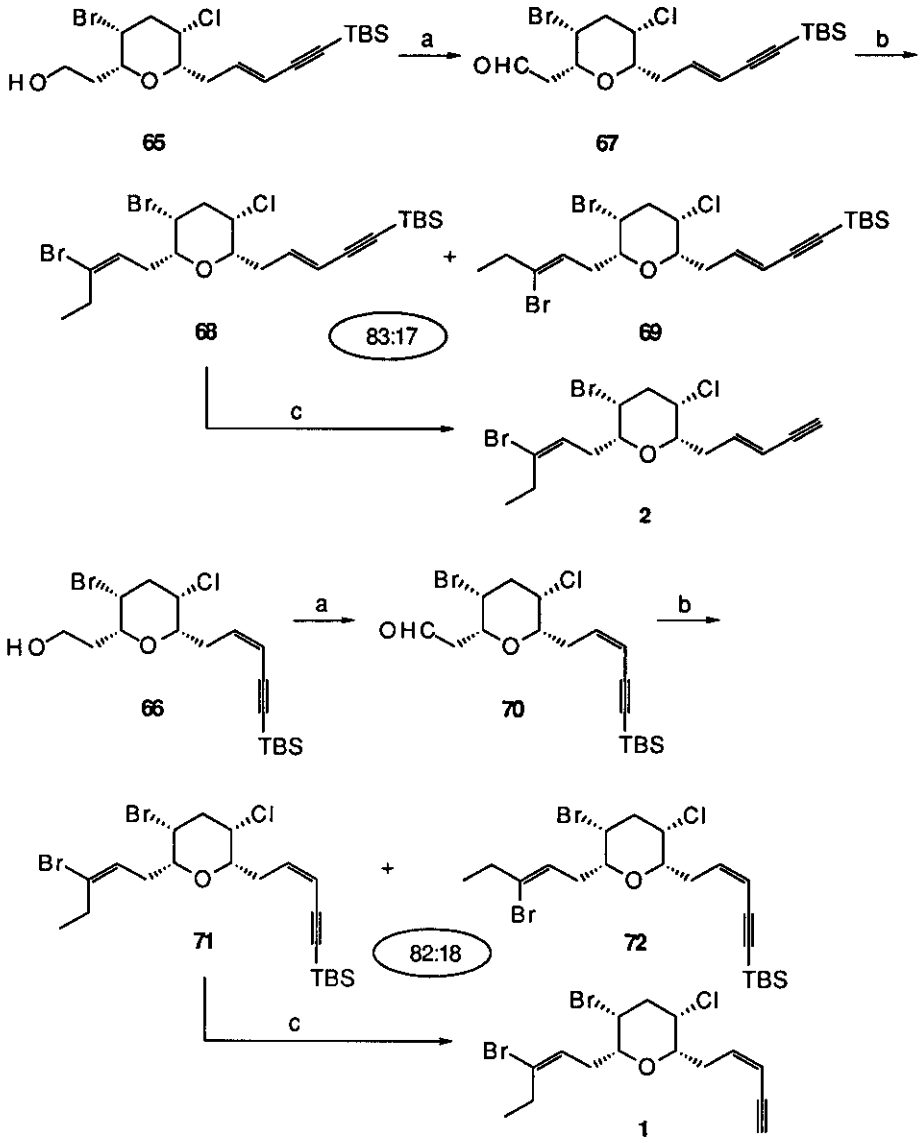
EXPERIMENTAL

Solvents and reagents were dried and distilled before use. Ether, THF, and toluene were distilled from sodium benzophenone ketyl. MeCN, CH_2Cl_2, Py, and Et_3N (TEA) were distilled from CaH_2. DMSO and HMPA were distilled under reduced pressure from CaH_2. EtOH and MeOH were distilled from their magnesium alkoxides. Molecular sieves 4Å (4A-MS) were powdered finely and activated at 180 °C for 5 h *in vacuo*. Normal reagent-grade solvents were used for flash chromatography and extraction.

All reacions were monitored by tlc with precoated SiO_2 plates (E. Merck, silica gel 60 F_{254} Art. 5554). Visualization was achieved *via* uv light and a 5.6% ethanolic *p*-anisaldehyde solution containing 5.6% of concentrated H_2SO_4-heat. For flash chromatography was utilized SiO_2 (E. Merck, silica gel 60, 70-230 mesh ASTM, Art. 7734). Preparative hplc was run with a Waters Associates 6000A liquid chromatography, equipped with a JASCO UVIDEC-100 UV spectrophotometer.

Melting points were determined in open capillary tubes and uncorrected. Ir spectra were obtained on a Hitachi model 270-30 infrared spectrophotometer in neat state or in $CHCl_3$ solution. The ^{1}H-nmr spectra were recorded on a JEOL model GX-400 (400 MHz) spectrometer in $CDCl_3$. The ^{13}C-nmr spectra were

Scheme 7.



Reagents and conditions: a) $(COCl)_2$, DMSO, TEA, CH_2Cl_2, -78 → 20 °C, 1.5 h, 100% (**67**) or 95% (**70**); b) $Ph_3P^+CBr_2EtBr^-$ (1.5 eq.), BuLi (1.5 eq.), THF-DMSO (5:1), -78 °C, 45 min, 87% (**68+69**) or 67% (**71+72**); c) TBAF-HF (pH≈4.5), THF, -5 °C, 1 h and -5 → 0 °C, 1 h, 79% (**2**) or 82% (**1**).

measured on a JEOL model GX-400 (100 MHz) spectrometer in $CDCl_3$. Chemical shifts (δ) are reported with tetramethylsilane (δ=0.00 ppm) or $CHCl_3$ (δ=7.26 ppm) as internal standards. Splitting patterns are designated as "s, d, t, q, m, and br"; these symbols indicate "singlet, doublet, triplet, quartet, multiplet, and broad", respectively. Optical rotations were recorded on JASCO model DIP-360 digital polarimeter using $CHCl_3$ as solvent. Low- and high-resolution mass spectra (LR-ms and HR-ms) were obtained on a JEOL model JMS-HX-110 mass spectrometer under fast atom bombardment (FAB) conditions. Elemental analyses for C and H were performed on YANACO model CHN corder MT-3 and those for halogens and S were carried out by Shoniger flask combustion method.

All reactions were carried out under anhydrous conditions and argon atmosphere, unless otherwise noted.

(2*S*,3*S*)-5-*t*-Butyldimethylsilyloxy-3-chloro-1,2-epoxypentane (**8**).

To a stirred mixture of L-(+)-DET (8.6 ml, 0.05 mol) and 4A-MS (18.0 g) in dry CH_2Cl_2 (1450 ml) at -20 °C was added Ti(O-*i*-Pr)$_4$ (10.7 ml, 0.04 mol). After 30 min, TBHP (4.81 M solution in CH_2Cl_2, 150 ml, 0.72 mol) was added and the resulting mixture was stirred at -20 °C for 30 min. (2*Z*)-5-*t*-butyldimethylsilyloxy-2-penten-1-ol (**9**)[11] (77.80 g, 0.360 mol) in CH_2Cl_2 (150 ml) was then added dropwise and the reaction mixture was stored in refrigerator at -20 °C for 16 h. After warmed to room temperature, the mixture was poured onto a cooled (0 °C) solution of tartaric acid (72.0 g) and $FeSO_4 \cdot 7H_2O$ (120.0 g) in deionized water (360 ml) and the contents were vigorously stirred at 0 °C for 30 min. The organic layer was separated and the water layer was extracted with $CHCl_3$ (100 ml). The combined organic layers were washed with water (2 × 300 ml), aqueous 5% $NaHCO_3$ (300 ml), and brine (300 ml), dried over Na_2SO_4, and concentrated *in vacuo*. Flash chromatography of the residue (SiO_2, 20% → 25% EtOAc in hexane) gave the epoxy alcohol (**10**, 79.73 g, 97%, 87%ee, determined by ^{1}H-nmr analysis of its Mosher ester). **10**: a colorless oil; $[\alpha]_D^{25}$ +10.6° (c=2.13, $CHCl_3$); ir (neat), 3450, 2932, 2854, 1475, 1257, 1101, 1058, 935, 837, and 777 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ3.89-3.82 (2H, m), 3.78 (1H, dt, J=3.4 and 10.3 Hz), 3.60 (1H, ddd, J=3.9, 6.8, and 12.2 Hz), 3.21 (1H, ddd, J=4.4, 4.9, and 6.8 Hz), 3.06 (1H, dt, J=8.8 and 4.4 Hz), 2.79 (1H, dd, J=3.9 and 8.3 Hz), 1.99 (1H, ddt, J=4.4, 14.2, and 3.4 Hz), 1.74 (1H, dddd, J=4.9, 8.8, 10.3, and 14.2 Hz), 0.91 (9H, s), and 0.10 (6H, s); LR-FAB-ms, m/z 233, 214, 145, 131, 101, and 75 (base). *Anal.* Calcd for $C_{11}H_{24}O_3Si$: C, 56.75; H, 10.51. Found: C, 56.78; H, 10.49.

TsCl (19.60 g, 102.8 mmol) was added in portions to a stirred solution of **10** (22.76 g, 97.9 mmol), TEA (16.4 ml, 117.5 mmol), and DMAP (0.6 mg, 4.9 mmol) in CH_2Cl_2 (400 ml) at 0 °C. After stirred at the same temperature for 5 h, the reaction mixture was washed with 5% HCl (2 × 100 ml), aqueous 5% $NaHCO_3$ (100 ml), and brine (100 ml), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, 15% EtOAc in hexane) to give the epoxy sulfonate (37.85 g, 100%). A colorless oil; $[\alpha]_D^{25}$ -15.3° (c=1.77, $CHCl_3$); ir (neat), 2963, 2931, 1600, 1465, 1368, 1285, 1255, 1160, 1097, 1044, 978, 837, and 777 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ7.79 (2H, d, J=8.3 Hz), 7.34 (2H, d, J=8.3 Hz), 4.25 (1H, dd, J=4.4 and 11.2 Hz), 4.01 (1H, dd, J=6.8 and 11.2 Hz), 3.74-3.67 (2H, m), 3.17 (1H, dt, J=4.4 and 3.9 Hz), 3.11 (1H, dt, J=6.8 and 4.4 Hz), 2.44 (3H, s), 1.68-1.60 (2H, m), 0.86 (9H,s), and 0.03 (6H, s); LR-FAB-ms, m/z 387, 223, 131, 105, and 75 (base). *Anal.* Calcd for $C_{18}H_{30}O_5SSi$: C, 55.93; H, 7.82; S, 8.29. Found: C, 55.88; H, 7.88; S, 8.24.

Et_2AlCl (0.94 M solution in hexane, 61 ml, 57.4 mmol) was added slowly to a stirred solution of the epoxy sulfonate (20.17 g, 52.2 mmol) in CH_2Cl_2 (180 ml) at -20 °C. After stirred at -20 → -10 °C for 5 h, the reaction was quenched with aqueous tartaric acid (120 ml) and the mixture was diluted with ether (500 ml). The separated organic layers were washed with 5% HCl (2 × 150 ml), aqueous 5% $NaHCO_3$ (150 ml), and brine (150 ml), dried over Na_2SO_4, and concentrated *in vacuo* to afford the C-3 opening product (**11**, 22.61g, 100%), which was used directly for next step without purification. An analytical sample was obtained by flash chromatography of the crude residue (SiO_2, 20% EtOAc in hexane). **11**: a colorless oil; $[\alpha]_D^{25}$ -23.8° (c=2.44, $CHCl_3$); ir (neat), 3508, 2958, 1602, 1480, 1442, 1286, 1265, 1155, 1098, 1032, 976, 841, and 777 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ7.80 (2H, d, J=8.3 Hz), 7.35 (2H, d, J=8.3 Hz), 4.28 (1H, ddd, J=2.4, 5.4, and 7.3 Hz), 4.13 (1H, dd, J=6.4 and 9.8 Hz), 4.08 (1H, dd, J=5.9 and 9.8 Hz), 4.00 (1H, ddt, J=2.4, 6.4, and 5.9 Hz), 2.83 (1H, ddd, J=4.4, 5.9, and 10.7 Hz), 3.72 (1H, ddd, J=4.0, 6.8, and 10.7 Hz), 3.15 (1H, d, J=5.9 Hz), 2.45 (3H, s), 2.08-1.94 (2H, m), 0.89 (9H, s), 0.07 (3H, s), and 0.07 (3H, s); LR-FAB-ms, m/z 425, 423, 367, 365, 293, 291, 131, 105, and 75 (base). *Anal.* Calcd for $C_{18}H_{31}O_5ClSSi$: C, 51.07; H, 7.44; Cl, 8.26; S, 7.41. Found: C, 50.89; H, 7.58; Cl, 8.19; S, 7.35.

A mixture of the crude chlorohydrin (**11**, 19.60 g, 46.3 mmol) and K_2CO_3 (7.68 g, 55.6 mmol) in MeOH

(154 ml) was stirred at 0 °C for 1 h. The mixture was diluted with ether (500 ml), washed with water (4 × 150 ml), and brine (150 ml), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, 10% EtOAc in hexane) to furnish the terminal epoxide (**8**, 10.60 g, 91%). **8**: a colorless oil; $[\alpha]_D^{25}$ -12.5° (c=0.56, $CHCl_3$); ir (neat), 2932, 2854, 1473, 1393, 1257, 1193, 1104, 1006, 960, 924, 876, 837, 777, and 681 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ3.86 (1H, ddd, J=4.4, 7.3, and 9.3 Hz), 3.80 (2H, dd, J=4.4 and 7.3 Hz), 3.19 (1H, ddd, J=2.7, 3.9, and 7.3 Hz), 2.90 (1H, dd, J=3.9 and 4.4 Hz), 2.74 (1H, dd, J=2.7 and 4.4 Hz), 2.10-2.00 (1H, m), 1.92 (1H , ddt, J=9.3, 14.2, and 4.4 Hz), 0.89 (9H, s), 0.061 (3H, s), and 0.058 (3H, s); LR-FAB-ms, m/z 253, 251, 195, 193, 165, 163, 95, 93, and 57 (base). *Anal.* Calcd for $C_{11}H_{23}O_2ClSi$: C, 52.67; H, 9.24; Cl, 14.13. Found: C, 52.61; H, 9.31; Cl, 14.08.

(5*S*,6*S*)-8-*t*-Butyldimethylsilyloxy-6-chloro-1-tetrahydropyranyloxy-2-octyn-5-ol (**12**).

BuLi (1.57 M solution in hexane, 87 ml, 136.0 mmol) was added dropwise at -78 °C to a solution of propargyl alcohol THP-ether (19.06 g, 136 mmol) in THF (450 ml) and stirred for 15 min, and then $BF_3{\cdot}OEt_2$ (16.7 ml, 136 mmol) was added dropwise. After 15 min, the epoxide (**8**) (17.05 g, 68 mmol) in THF (50 ml) was introduced by cannula and stirring was continued at the same temperature for an additional 45 min. The reaction mixture was poured onto an aqueous 5% $NaHCO_3$ solution (200 ml) and the water layers were extracted with ether (3 × 100 ml). The combined organic layers were washed with brine (200 ml), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was then subjected to flash chromatography (SiO_2, 17% → 25% EtOAc in hexane) to afford the chlorohydrin (**12**, 21.04 g, 79%) and the recovered starting epoxide (**10**, 3.28 g, 19%). **12**: a pale yellow oil; $[\alpha]_D^{25}$ -5.0° (c=2.53, $CHCl_3$); ir (neat), 3435, 2958, 2926, 1480, 1287, 1257, 1150, 1092, 1026, 975, 834, and 777 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ4.78 (1H, t, J=3.4 Hz), 4.43 (1H, m), 4.22 (2H, ABX pattern, J_{AB}=15.5 Hz), 3.90-3.74 (3H, m), 3.53 (2H, m), 2.85 (1H, br s), 2.61 (2H, dt, J=6.4 and 2.4 Hz), 2.12-1.96 (6H, m), 1.90-1.46 (6H, m), 0.90 (9H, s), 0.080 (3H, s), and 0.075 (3H, s); LR-FAB-ms, m/z 393, 391, 335, 333, 253, 251, 233, 231, 101, 95, and 75 (base). *Anal.* Calcd for $C_{19}H_{35}O_4ClSi$: C, 58.36; H, 9.02; Cl, 9.07. Found: C, 58.34; H, 9.07; Cl, 9.03.

(5*S*,6*S*)-8-*t*-Butyldimethylsilyloxy-5,6-epoxy-2-octyn-1-ol (**14**).

Et_2AlCl (1.0 M solution in hexane, 161.0 ml, 161.0 mmol) was added to a stirred solution of **12** (21.04 g, 53.8 mmol) in CH_2Cl_2 (400 ml) and stirring was continued at 0 → 5 °C for 3 h and at 25 °C for an additional 1 h. The reaction mixture was re-cooled to 0 °C, quenched with aqueous 5% $NaHCO_3$ (30 ml), poured onto a solution of tartaric acid (240 g) in water (1200 ml) and then stirred at 0 °C for 10 min. The organic layer was separated and the aqueous layer was extracted with $CHCl_3$ (3 × 150 ml). The combined organic layers were washed with aqueous 5% NH_4Cl (150 ml) and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a pale yellow oil (**13**, 17.61 g).
A mixture of the crude oil (**13**, 17.61 g, 53.8 mmol) obtained above and K_2CO_3 (13.2 g, 88.5 mmol) in MeOH (88 ml) was stirred at 25 °C for 3 h. The reaction mixture was diluted with ether (350 ml), washed with water (3 × 80 ml) and brine (100 ml), dried over Na_2SO_4, and concentrated *in vacuo*. The obtained crude product was purified by flash chromatography (SiO_2, 20% EtOAc in hexane) to yield the epoxy alcohol (**14**, 14.13 g, 97%). **14**: a colorless oil; $[\alpha]_D^{25}$ +23.1° (c=1.97, $CHCl_3$); ir (neat), 3424, 2932, 2854, 1471, 1391, 1257, 1101, 1003, 958, 837, and 777 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ4.26 (2H, dt, J=5.9 and 2.0 Hz), 3.80 (2H, ABX pattern), 3.15 (2H, m), 2.57 (1H, ddd, J=5.9, 17.1, and 2.0 Hz), 2.39 (1H, ddt, J=5.9, 17.1, and 2.0 Hz), 1.85-1.63 (3H, m), 0.90 (9H, s), and 0.07 (6H, s); LR-FAB-ms, m/z 271, 253, 213, 195, 131, 105, and 75 (base). *Anal.* Calcd for $C_{14}H_{26}O_3Si$: C, 62.18; H, 9.69. Found: C, 62.16; H, 9.74.

(5*S*,6*R*)-(2*E*)-8-*t*-Butyldimethylsilyloxy-5,6-epoxy-2-octen-1-ol (**15**).

To a stirred solution of **14** (14.13 g, 52.2 mmol) in ether (600 ml) at 0 °C was added dropwise Red-Al® (3.46 M solution in toluene, 18 ml, 62.6 mmol), and stirring was continued at 0 → 25 °C for 5 h. The reaction mixture was mixed carefully with an aqueous 20% tartaric acid solution at 0 °C, followed by washing with aqueous 20% tartaric acid (3 × 100 ml), $NaHCO_3$ (100 ml), and brine (100 ml). Drying over Na_2SO_4, concentrating *in vacuo*, and purifying by flash chromatography of the resulting residue (SiO_2, 25% → 33% EtOAc in hexane) afforded the allylic alcohol (**15**, 14.21 g, 98%). **15**: a colorless oil; $[\alpha]_D^{25}$ +7.3° (c=2.26, $CHCl_3$); ir (neat), 3503, 2932, 2854, 1467, 1302, 1251, 1170, 1101, 1035, 837, and 777 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ5.78 (2H, m), 4.13 (2H, d, J=3.9 Hz), 3.80 (2H, t, J=5.5 Hz), 3.10 (1H, dt, J=4.4 and 6.4 Hz), 3.03 (1H, dt, J=4.4 and 6.4 Hz), 2.30 (2H, m), 1.81 (1H, m), 1.70 (1H, m), 1.60 (1H, br s), 0.90 (9H, s), and 0.07 (6H, s); LR-FAB-ms, m/z 273, 255, 215, 131, 105, and 75 (base). *Anal.* Calcd for $C_{14}H_{28}O_3Si$: C, 61.72; H, 10.36. Found: C, 61.71; H, 10.39.

(5*S*,6*R*)-(2*E*)-8-*t*-Butyldimethylsilyloxy-5,6-epoxy-2-octen-1-ol 1-Benzoate (**16**).

PhCOCl (6.2 ml, 53.2 mmol) was added slowly to a stirred solution of **15** (9.65 g, 35.4 mmol), DMAP (0.22 g, 1.8 mmol), and TEA (8.9 ml, 63.8 mmol) in CH_2Cl_2 (150 ml) at -40 °C. After stirring for 2 h, the reaction mixture was diluted with $CHCl_3$ (150 ml), washed with 5% HCl (2 × 80 ml), aqueous 5% $NaHCO_3$ (80 ml), and brine (100 ml), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, 10% EtOAc in hexane) to yield the benzoate (**16**, 13.00 g, 97%). **16**: a colorless oil; $[\alpha]_D^{25}$ +2.8° (c=1.18, $CHCl_3$); ir (neat), 2956, 1725, 1455, 1272, 1257, 1101, 834, 777 and 711 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ8.05 (2H, d, J=7.3 Hz), 7.56 (1H, t, J=7.3 Hz), 7.44 (2H, t, J=7.3 Hz), 5.93 (1H, ddd, J=5.9, 6.4, and 15.4 Hz), 5.85 (1H, dt, J=15.4 and 5.9 Hz), 4.80 (2H, ABX pattern), 3.80 (2H, m), 3.12 (1H, ddd, J=4.4, 4.9, and 7.3 Hz), 3.04 (1H, ddd, J=4.4, 6.4, and 6.4 Hz), 2.33 (2H, m), 1.82 (1H, m), 1.71 (1H, m), 0.90 (9H, s), 0.07 (6H, s); LR-FAB-ms, m/z 377, 319, 255, 197, 179, 105 (base), and 73. *Anal.* Calcd for $C_{21}H_{32}O_4Si$: C, 66.98; H, 8.56. Found: C, 66.93; H, 8.60.

(5*S*,6*R*)-(2*E*)-1-Benzoyloxy-5,6-epoxy-2-octen-8-ol (**17**).

To a solution of **16** (12.96 g, 34.4 mmol) in THF (42 ml) was added TBAF (1.0 *M* solution in THF, 41.3 ml, 41.3 mmol) at 0 °C, and stirred at 0 °C for 4 h, and then at 20 °C for 2 h. The reaction mixture was diluted with ether (250 ml), washed with water (2 × 80 ml) and brine (2 × 100 ml), dried over Na_2SO_4, and concentrated *in vacuo*. The resulting residue was purified with flash chromatography (SiO_2, 50% EtOAc in hexane) to give **17** (8.09 g, 90%). **17**: a colorless oil; $[\alpha]_D^{25}$ +11.2° (c=1.91, $CHCl_3$); ir (neat), 3485, 2998, 1722, 1618, 1597, 1455, 1272, 1113, and 711 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ8.05 (2H, d, J=7.3 Hz), 7.56 (1H, t, J=7.3 Hz), 7.44 (2H, t, J=7.3 Hz), 5.92 (1H, dt, J=15.6 and 6.4 Hz), 5.86 (1H, dt, J=15.6 and 5.9 Hz), 4.81 (2H, d, J=6.4 Hz), 3.87 (2H, m), 3.15 (1H, dt, J=7.8 snf 4.4 Hz), 3.06 (1H, dt, J=4.4 and 6.4 Hz), 2.45-2.28 (2H, m), 1.88 (1H, m), 1.74 (1H, m), and 1.60 (1H, br s); LR-FAB-ms, m/z 263, 186, 105 (base), and 73. *Anal.* Calcd for $C_{15}H_{18}O_4$: C, 68.69; H, 6.92. Found: C, 68.53; H, 7.02.

(5*R*,6*R*)-(2*E*)-Benzoyloxy-5-bromo-2-octene-6,8-diol (**18**).

A flame dried 500 ml three-necked round-bottomed flask, equipped with a magnetic stirbar, an argon inlet, and a rubber septum, containing Et_2NH·HBr (18.89 g, 122.6 mmol), was heated under reduced pressure (0.02 mmHg) at 160 °C for 2 h. After cooling to room temperature, CH_2Cl_2 (120 ml) and $Ti(O\text{-}i\text{-}Pr)_4$ (13.7 ml, 46.0 mmol) were introduced successively *via* syringe through the septum and stirred at 25 °C for 30 min under an argon atmosphere. The 3,4-epoxy-1-ol (**17**, 8.04 g, 30.6 mmol) in CH_2Cl_2 (40 ml) was then added and stirring was continued at 25 °C for 12 h. The reaction was quenched with

saturated aqueous tartaric acid (260 ml). The resulting mixture was diluted with EtOAc (450 ml) and vigorously stirred until it became two phases clearly. The separated organic layers were washed with 10% HCl (2 × 80 ml), aqueous 5% Na_2CO_3 (100 ml), and brine (100 ml), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was subjected to flash chromatography (SiO_2, 50% → 60% EtOAc in hexane) to afford the desired 4-bromo-1,3-diol (**18**, more polar, 7.25 g, 70%) and its regioisomer, 3-bromo-1,4-diol (**19**, less polar, 0.64 g, 7%). **18**: a pale yellow oil; $[\alpha]_D^{25}$ +13.5° (c=1.85, $CHCl_3$); ir (neat), 3600, 3050, 2920, 1716, 1610, 1455, 1374, 1275, 1116, 975, and 777 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ8.04 (2H, d, J=7.3 Hz), 7.57 (1H, t, J=7.3 Hz), 7.44 (2H, t, J=7.3 Hz), 5.91 (1H, dt, J=15.6 and 6.4 Hz), 5.84 (1H, dt, J=15.6 and 5.9 Hz), 4.81 (2H, d, J=5.9 Hz), 4.08 (1H, ddd, J=3.4, 5.4, and 8.3 Hz), 3.92-3.81 (3H, m), 2.81 (1H, ddd, J=5.4, 6.4, and 15.1 Hz), 2.71 (1H, ddd, J=6.4, 8.3, and 15.1 Hz), 2.56 (1H, br s), 1.93-1.76 (2H, m), and 1.63 (1H, br s); LR-FAB-ms, m/z 345, 343, 239, 237, 191, 179, 177, 140, 122, 105 (base), and 87. *Anal.* Calcd for $C_{15}H_{19}O_4Br$: C, 52.49; H,5.58; Br, 23.28. Found: C, 52.46; H, 5.60; Br, 23.22.

(5*R*,6*R*)-(2*E*)-1-Benzoyloxy-5-bromo-2-octene-6,8-diol 8-Pivaloate (**20**).

To a stirred aolution of **18** (7.98 g, 23.2 mmol) in Py (18.8 ml, 232.0 mmol) was added slowly PvCl (3.4 ml, 27.9 mmol) at -20 °C and stirring was continued at -20 °C for 2 h and at -10 °C for an additional 10 h. The reaction mixture was poured onto a cooled (0 °C) 5% HCl solution (150 ml) and extracted with ether (4 × 200 ml). The combined extracts were washed with water (100 ml), aqueous 5% $NaHCO_3$ (150 ml), and brine (150 ml), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, 25% EtOAc in hexane) yielding the pivaloate (**20**, 6.32 g, 70%). **20**: a colorless oil; $[\alpha]_D^{25}$ +22.6° (c=3.40, $CHCl_3$); ir (neat), 3508, 2968, 1725, 1605, 1482, 1455, 1383, 1275, 1161, 1116, 1071, 1026, 975, and 756 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ8.04 (2H, d, J=7.3 Hz), 7.55 (1H, t, J=7.3 Hz), 7.43 (2H, t, J=7.3 Hz), 5.87 (1H, dt, J=15.1 and 5.9 Hz), 5.84 (1H, dt, J=15.1 and 5.4 Hz), 4.78 (2H, ABX pattern), 4.26 (1H, ddd, J=6.4, 7.3, and 11.2 Hz), 4.19 (1H, ddd, J=5.9, 5.9, and 11.2 Hz), 4.06 (1H, ddd, J=2.9, 5.9, and 8.3 Hz), 3.66 (1H, m), 2.80 (1H, dt, J=14.6 and 5.9 Hz), 2.74 (1H, ddd, J=5.9, 8.3, and 14.6 Hz), 2.31 (1H, d, J=7.8 Hz), 1.91 (2H, m), and 1.17 (9H, s); LR-FAB-ms, m/z 429, 427, 411, 409, 307, 305 (base), 205, 203, 105, and 57. *Anal.* Calcd for $C_{20}H_{27}O_5Br$: C, 56.21; H, 6.37; Br, 18.70. Found: C, 56.08; H, 6.48; Br, 18.79.

(5*R*,6*R*)-(2*E*)-1-Benzoyloxy-5-bromo-6-*t*-butyldimethylsilyloxy-2-octen-8-ol 8-Pivaloate (**21**).

To a stirred mixture of **20** (6.25 g, 14.6 mmol) and 2, 6-lutidine (6.8 ml, 58.4 mmol) in CH_2Cl_2 (80 ml) at -20 °C was added dropwise TBSOTf (8.4 ml, 36.5 mmol). After stirred at this temperature for 4 h, the reaction mixture was poured onto a cooled (0 °C) 5% HCl solution (100 ml) and extracted with $CHCl_3$ (3 × 100 ml). The combined extracts were washed with water (2 × 100 ml), aqueous 5% $NaHCO_3$ (100 ml), and brine (100 ml), dried over Na_2SO_4, and concentrated *in vacuo*. Flash chromatography of the resulted residue (SiO_2, 10% EtOAc in hexane) afforded **21** (7.56 g, 96%). **21**: a colorless oil; $[\alpha]_D^{25}$ +30.9° (c=0.89, $CHCl_3$); ir (neat), 2962, 2860, 1725, 1458, 1368, 1272, 1155, 1110, 1008, 975, 939, 837, 777, and 771 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ8.05 (2H, d, J=7.8 Hz), 7.55 (1H, t, J=7.8 Hz), 7.43 (2H, t, J=7.8 Hz), 5.90 (1H, ddd, J=6.3, 6.8, and 15.6 Hz), 5.81 (1H, ddd, J=5.9, 6.4, and 15.6 Hz), 4.79 (2H, ABX pattern), 4.26 (1H, dt, J=11.2 and 5.4 Hz), 4.04-3.97 (2H, m), 3.93 (1H, dt, J=10.3 and 3.4 Hz), 2.83 (1H, ddd, J=3.3, 5.9, and 14.9 Hz), 2.48 (1H, ddd, J=6.3, 9.6, and 14.9 Hz), 2.20 (1H, m), 1.70 (1H, ddt, J=8.9, 14.2, and 4.9 Hz), 1.20 (9H, s), 0.90 (9H, s), and 0.08 (6H, s); LR-FAB-ms, m/z 543, 541, 485, 483, 421, 419, 319, 317, 205, 203, 187, 185, 179, 171, 159, 105 (base), 73, and 57. *Anal.* Calcd for $C_{26}H_{41}O_5BrSi$: C, 57.66; H, 7.63; Br, 14.75. Found: C, 57.73; H, 7.74; Br, 14.76.

(5*R*,6*R*)-(2*E*)-5-Bromo-6-*t*-butyldimethylsilyloxy-2-octene-1,8-diol 8-Pivaloate (**22**).

A mixture of **21** (4.96 g, 9.2 mmol), and K_2CO_3 (0.633 g, 4.6 mmol) in MeOH (46 ml) was stirred at 20 °C for 80 min. The reaction mixture was diluted with ether (250 ml), washed with water (2 × 50 ml), and brine (2 × 80 ml), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was subjected to flash chromatography (SiO_2, 13% → 25% EtOAc in hexane) to furnish the allylic alcohol (**22**, 5.49 g, 96%). **22**: a colorless oil; $[\alpha]_D^{25}$ +38.0° (c=1.19, $CHCl_3$); ir (neat), 3454, 2962, 1734, 1482, 1254, 1155, 837, and 777 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ5.37 (2H, m), 4.26 (1H, dt, J=11.2 and 5.4 Hz), 4.12 (2H, br s), 4.03-3.96 (2H, m), 3.90 (1H, dt, J=10.3 and 3.4 Hz), 2.79 (1H, br d, J=14 Hz), 2.42 (1H, m), 2.20 (1H, dddd, J=3.4, 5.9, 9.3 and 14.2 Hz), 1.69 (1H, dddd, J=4.4, 4.9, 8.8, and 14.2 Hz), 1.48 (1H, br s), 1.20 (9H, s), 0.90 (9H, s), and 0.08 (6H, s); LR-FAB-ms, m/z 439, 437, 421, 419, 381, 379, 319, 317, 255, 237, 187, 185, 171, 159, 137, 105, 73 (base), and 57. *Anal.* Calcd for $C_{19}H_{37}O_4BrSi$: C, 52.16; H, 8.52; Br, 18.26. Found: C, 52.10; H, 8.62; Br, 18.14.

(2*R*,3*R*,5*R*,6*R*)-5-Bromo-6-*t*-butyldimethylsilyloxy-2,3-epoxyoctane-1,8-diol 8-Pivaloate (**23**).

To a stirred mixture of D-(-)-DET (298 μl, 1.74 mmol) and 4A-MS (1.24 g) in dry CH_2Cl_2 (80 ml) at -20 °C was added Ti(O-*i*-Pr)$_4$ (370 μl, 1.24 mmol). After 30 min, TBHP (4.81 M solution in CH_2Cl_2, 5.2 ml, 24.8 mmol) was added and the resulting mixture was stirred at -20 °C for 30 min. The allylic alcohol (**22**, 5.45 g, 12.4 mmol) in CH_2Cl_2 (20 ml) was then added dropwise and the reaction mixture was stored in refrigerator at -20 °C for 10 h. After warmed to room temperature, the mixture was poured onto a cooled (0 °C) solution of tartaric acid (2.23 g) in water (50 ml) and the mixture were vigorously stirred at 0 °C for 30 min, diluted with ether (300 ml), washed with water (2 × 100 ml), aqueous 5% $NaHCO_3$ (100 ml), and brine (100 ml), dried over Na_2SO_4, and concentrated *in vacuo* to give a viscous oil. Careful flash chromatography of the residue (SiO_2, 20% → 33% EtOAc in hexane) afforded the β-epoxy alcohol (**23**, 5.54 g, 99%) as a single product. **23**: a colorless oil; $[\alpha]_D^{25}$ +51.8° (c=0.95, $CHCl_3$); ir (neat), 3454, 2956, 1731, 1479, 1287, 1257, 1158, 1095, 837, and 777 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ4.27 (1H, dt, J=11.2 and 5.4 Hz), 4.03-3.92 (3H, m), 3.69 (1H, ddd, J=3.9, 7.3, and 12.7 Hz), 3.16 (1H, ddd, J=2.4, 4.4, and 6.4 Hz), 3.02 (1H, dt, J=3.9 and 2.4 Hz), 2.20 (1H, m), 2.15 (1H, ddd, J=2.4, 6.8, and 14.7 Hz), 1.96 (1H, ddd, J=4.9, 11.2, and 14.7 Hz), 1.71-1.60 (2H, m), 1.21 (9H, s), 0.89 (9H, s), 0.09 (3H, s), and 0.08 (3H, s); LR-FAB-ms, m/z 455, 453, 397, 395, 353, 351, 323, 321, 295, 293, 221, 219, 171, 159, 73 (base), and 57. *Anal.* Calcd for $C_{19}H_{37}O_5BrSi$: C, 50.32; H, 8.22; Br, 17.62. Found: C, 50.21; H, 8.26; Br, 17.71.

(2*R*,3*R*,5*R*,6*R*)-5-Bromo-6-*t*-butyldimethylsilyloxy-2,3-epoxy-1-*p*-toluenesulfonyloxyoctan-8-ol 8-Pivaloate (**24**).

To a stirred solution of **23** (3.58 g, 7.9 mmol), TEA (1.7 ml, 12.0 mmol), and DMAP (48 mg, 0.4 mmol) in CH_2Cl_2 (80 ml) at 0 °C was added TsCl (1.81 g, 9.5 mmol) in one portion. After stirred at the same temperature for 12 h, the reaction mixture was diluted with $CHCl_3$ (150 ml), washed with 5% HCl (60 ml), aqueous 5% $NaHCO_3$ (60 ml), and brine (60 ml). Drying over Na_2SO_4, concentration *in vacuo*, and purification of the residue by flash chromatography (SiO_2, 12% → 25% EtOAc in hexane) gave the epoxy sulfonate (**24**, 4.81 g, 100%). **24**: a colorless oil; $[\alpha]_D^{25}$ +43.8° (c=1.00, $CHCl_3$); ir (neat), 2962, 1731, 1602, 1467, 1368, 1287, 1257, 1155, 1098, 1044, 978, 837, and 777 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ7.78 (2H, d, J=8.3 Hz), 7.34 (2H, d, J=8.3 Hz), 4.24 (2H, m), 4.05 (1H, dt, J=11.2 and 2.9 Hz), 3.96 (3H, m), 3.03 (1H, ddd, J=2.0, 4.4, and 5.9 Hz), 2.97 (1H, ddd, J=2.0, 4.9, and 6.8 Hz), 2.47 (3H, s), 2.16 (1H, m), 2.01 (1H, ddd, J=2.9, 6.8, and 14.7 Hz), 1.92 (1H, ddd, J=4.4, 11.2, and 14.7 Hz), 1.59 (1H, ddt, J=9.3, 14.2, and 4.9 Hz), 1.18 (9H, s), 0.85 (9H, s), 0.05 (3H, s), and 0.04 (3H, s); LR-FAB-ms, m/z 609, 607, 551, 549, 507, 505, 449, 447, 375, 373, 335, 333, 277, 275, 229 (base), 203, 201, 171, 159, 73, and 57. *Anal.* Calcd for $C_{26}H_{43}O_7BrSSi$: C, 51.39; H, 7.13; Br, 13.15; S, 5.28. Found: C, 51.33; H, 7.24; Br, 13.14; S,

5.39.

(2*R*,3*S*,5*R*,6*R*)-5-Bromo-6-*t*-butyldimethylsilyloxy-3-chloro-1-*p*-toluenesulfonyloxyoctane-2, 8-diol 8-Pivaloate (**25**).

Et_2AlCl (1.0M solution in hexane, 11.9 ml, 11.9 mmol) was added dropwise to a stirred solution of **24** (4.80 g, 7.9 mmol) in CH_2Cl_2 (35 ml) at -20 °C. The reaction mixture was allowed to warm to room temperature during the 6 h period and to stir for an additional 7 h, quenched with aqueous tartaric acid (40 ml) and then diluted with ether (200 ml). After stirred for 30 min, the organic layer was separated and washed with 5% HCl (2 × 80 ml), aqueous 5% $NaHCO_3$ (80 ml), and brine (80 ml). Drying over Na_2SO_4, concentrationg *in vacuo*, and purification of the residue by flash chromatography (SiO_2, 20% → 25% EtOAc in hexane) afforded the chlorohydrin (**25**, 4.48 g, 94%). **25**:a colorless oil; $[\alpha]_D^{25}$ +67.2° (c=1.56, $CHCl_3$); ir (neat), 3481, 2975, 2870, 1731, 1600, 1465, 1368, 1287, 1255, 1155, 1098, 978, 840, and 777 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ7.81 (2H, d, J=8.3 Hz), 7.37 (2H, d, J=8.3 Hz), 4.34 (1H, m), 4.33 (1H, dd, J=2.9 and 10.7 Hz), 4.26 (1H, dt, J=11.2 and 5.4 Hz), 4.19 (1H, dt, J=10.7 and 5.9 Hz), 4.13 (1H, dt, J=11.2 and 7.3 Hz), 4.02-3.92 (3H, m), 2.71 (1H, ddd, J=3.9, 5.9, and 15.6 Hz), 2.68 (1H, d, J=6.4 Hz), 2.46 (3H, s), 2.28 (1H, dt, J=15.6 and 7.3 Hz), 2.18 (1H, m), 1.66 (1H, ddt, J=8.8, 14.2, and 4.9 Hz), 1.20 (9H, s), 0.89 (9H, s), 0.10 (3H, s), and 0.08 (3H, s); LR-FAB-ms, m/z 647, 645, 643, 589, 587, 585, 545, 543, 541, 413, 411, 409, 229 (base), 159, 73, and 57. *Anal.* Calcd for $C_{26}H_{44}O_7BrClSSi$: C, 48.48; H, 6.88; Br, 12.40; Cl, 5.50. Found: C, 48.47; H, 6.92; Br, 12.37; Cl, 5.42.

(2*S*,3*R*,5*R*,6*R*)-5-Bromo-6-*t*-butyldimethylsilyloxy-3-chloro-1,2-epoxyoctan-8-ol 8-Pivaloate (**26**).

A mixture of **25** (3.55 g, 5.5 mmol) and K_2CO_3 (0.76 g, 5.5 mmol) in anhydrous MeOH (28 ml) was stirred at 20 °C for 1 h. The mixture was diluted with ether (150 ml), washed with water (2 × 50 ml) and brine (80 ml), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was subjected to flash chromatography (SiO_2, 5% EtOAc in hexane) to furnish the desired terminal epoxide (**26**, less polar, Rf=0.27, SiO_2, 9% EtOAc in hexane, 2.08 g, 80%) and its (5*S*,6*S*)-diastereoisomer (**27**, more polar, Rf=0.18, above conditions, 0.19 g, 7%) arisen from the antipode of the C-5 unit (**8**). **26**: a colorless oil; $[\alpha]_D^{25}$ +56.2° (c=0.92, $CHCl_3$); ir (neat), 2960, 1729, 1480, 1440, 1287, 1265, 1203, 1117, 1097, 840, and 777 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ4.30 (2H, m), 4.00 (2H, m), 3.72 (1H, dt, J=5.4 and 8.3 Hz), 3.06 (1H, ddd, J=2.4, 3.9, and 8.3 Hz), 2.87 (1H, dd, J=3.9 and 4.4 Hz), 2.70 (1H, ddd, J=4.8, 8.3, and 15.1 Hz), 2.65 (1H, dd, J=2.4 and 4.4 Hz), 2.33 (1H, ddd, J=5.4, 9.8, and 15.1 Hz), 2.22 (1H, dddd, J=2.9, 5.9, 9.3, and 14.2 Hz), 1.69 (1H, ddt, J=9.3, 14.2, and 4.9 Hz), 1.21 (9H, s), 0.91 (9H, s), 0.12 (3H, s), and 0.09 (3H, s); LR-FAB-ms, m/z 475, 473, 471, 459, 457, 455, 417, 415, 413, 373, 371, 369, 343, 341, 339, 171, 165, 159, 85, 73, and 57 (base). *Anal.* Calcd for $C_{19}H_{36}O_4BrClSi$: C, 48.36; H, 7.69; Br, 16.93; Cl, 7.51. Found: C, 48.33; H, 7.79; Br, 16.69; Cl, 7.40.
27: a pale yellow oil; ^{1}H-nmr ($CDCl_3$), δ4.31-4.26 (2H, m), 4.05-3.97 (2H, m), 3.80 (1H, ddd, J=3.9, 7.3, and 9.8 Hz), 3.16 (1H, ddd, J=2.4, 3.9, and 7.3 Hz), 2.91 (1H, dd, J=3.9 and 4.4 Hz), 2.75 (1H, dd, J=2.4 and 4.4 Hz), 2.33-2.19 (3H, m), 1.67 (1H, ddt, J=9.3, 14.2, and 4.9 Hz), 1.21 (9H, s), 0.91 (9H, s), 0.12 (3H, s), and 0.09 (3H, s).

(2*R*,3*S*,5*R*,6*R*)-5-Bromo-3-chloro-1, 2-epoxyoctane-6,8-diol 8-Pivaloate (**28**).

A mixture of TBAF-HF (pH≈3, 1.5 ml, *ca.* 1.5 mmol of F^-) prepared from 1.0 M solution of TBAF in THF and 48% HF in a ratio of 1:1 was added to a solution of **26** (376 mg, 0.79 mmol) in THF (1.5 ml) at 20 °C and stirred at 20 °C for 20 h. The mixture was diluted with EtOAc (50 ml), washed with water (2 × 20 ml) and brine (30 ml), dried over Na_2SO_4, and concentrated *in vacuo*. The resulting residue was purified by flash chromatography (SiO_2, 33% EtOAc in hexane) to yield the epoxy alcohol (**28**, 263 mg,

93%) along with the starting material (**26**, 18 mg, 5%). **28**: a colorless oil; $[\alpha]_D^{25}$ +8.7° (c=0.48, $CHCl_3$); ir (neat), 3508, 2958, 1726, 1480, 1442, 1286, 1265, 1201, 1092, 841, and 777 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ4.38 (1H, ddd, J=2.4, 6.4, and 7.8 Hz), 4.30 (1H, ddd, J=5.4, 7.8, and 11.2 Hz), 4.20 (1H, ddd, J=5.4, 5.9, and 11.2 Hz), 3.72 (1H, ddd, J=6.8, 7.3, and 7.8 Hz), 3.66 (1H, m), 3.12 (1H, ddd, J=2.4, 3.9, and 7.8 Hz), 2.88 (1H, dd, J=3.9 and 4.4 Hz), 2.71 (1H, dd, J=2.4 and 4.4 Hz), 2.68 (1H, ddd, J=6.4, 6.8, and 14.7 Hz), 2.53 (1H, ddd, J=7.3, 7.8, and 14.7 Hz), 2.18 (1H, d, J=8.3 Hz), 1.94 (2H, m), and 1.20 (9H, s); LR-FAB-ms, m/z 361, 359, 357, 343, 341, 339, 259, 257, 255, 211, 175, 85 (base), 73, and 57. *Anal.* Calcd for $C_{13}H_{22}O_4BrCl$: 43.66; H, 6.20; Br, 22.33; Cl, 9.91. Found: C, 43.62; H, 6.17; Br, 21.93; Cl, 9.73.

(2*S*,6*S*,7*S*)-9-*t*-Butyldimethylsilyloxy-7-chloro-1-*p*-methoxyphenylmethoxynon-3-yne-2,6-diol (**37**).

TMSCl (8.3 ml, 65.9 mmol) was added dropwise to a stirred mixture of the alcohol (**35**, 9.06 g, 43.9 mmol) and TEA (12.2 ml, 87.8 mmol) in CH_2Cl_2 (130 ml) at -15 °C. After stirred for 30 min, the mixture was diluted with EtOAc (500 ml), washed with brine (2 × 150 ml), dried over Na_2SO_4, and concentrated *in vacuo* to yield a pale yellow oil. The crude product (**36**) was used directly for the next step, because it was unstable to purify with flash chromatography.
BuLi (1.66 M solution in hexane, 18 ml, 30.0 mmol) was added dropwise at -78 °C to a solution of the acetylene (**36**, 8.35 g, 30.0 mmol) in THF (100 ml) and the mixture was stirred at -78 °C for 15 min. Then, $BF_3{\cdot}OEt_2$ (3.7 ml, 30.0 mmol) was added dropwise, and the solution was stirred for 15 min. Epoxide (**8**) (5.17 g, 20 mmol) in THF (50 ml) was introduced by cannula and stirring was continued at the same temperature for an additional 1.5 h. Then 20% aqueous AcOH (30 ml) was added to quench the reaction and remove the TMS-group. The cooling bath was removed, and the resulting mixture was stirred for 2 h and diluted with EtOAc (500 ml). The mixture was washed with water (100 ml), aqueous 5% $NaHCO_3$ (100 ml), and brine (100 ml), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was subjected to flash chromatography (SiO_2, 25% → 50% EtOAc in hexane) to afford the diol (**37**, 8.95 g, 98%). **37**: a colorless oil; $[\alpha]_D^{25}$ -1.1° (c=5.22, $CHCl_3$); ir (neat), 3432, 2932, 2860, 1614, 1516, 1466, 1376, 1340, 1250, 1104, 1042, 834, and 778 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ7.26 (2H, d, J=8.8 Hz), 6.89 (2H, d, J=8.8 Hz), 4.59-4.49 (3H, m), 4.38 (1H, ddd, J=2.4, 4.9, and 7.8 Hz), 3.89-3.73 (3H, m), 3.81 (3H, s), 3.59 (1H, dd, J=3.4 and 9.8 Hz), 3.50 (1H, dd, J=7.9 and 9.8 Hz), 2.87 (1H, d, J=6.8 Hz), 2.59 (2H, m), 0.89 (9H, s), 0.08 (3H, s), and 0.07 (3H, s); HR-FAB-ms, Calcd for $C_{23}H_{36}O_5ClSi$ (M-H), 455.2021. Found, m/z 455.2004. Calcd for $C_{23}H_{36}O_5{}^{37}ClSi$ (M-H), 457.1991. Found, 457.1987.

(2*S*,6*S*,7*R*)-9-*t*-Butyldimethylsilyloxy-6,7-epoxy-1-*p*-methoxyphenylmethoxynon-3-yn-2-ol (**38**).

A mixture of the diol (**37**, 24.17 g, 52.9 mmol), K_2CO_3 (8.77 g, 63.5 mmol), and MeOH (159 ml) was stirred at 23 °C for 6 h. The reaction mixture was diluted with ether (700 ml), washed with water (3 × 70 ml) and brine (100 ml), dried over Na_2SO_4, and concentrated *in vacuo*. The resulting crude oil was subjected to flash chromatography (SiO_2, 25% EtOAc in hexane) to furnish the epoxy alcohol (**38**, 25.04 g, 98% yield). **38**: a colorless oil; $[\alpha]_D^{25}$ +16.5° (c=2.03, $CHCl_3$); IR (neat), 3454, 2932, 2860, 1640, 1515, 1467, 1320, 1251, 1176, 1104, 1035, 834, and 777 cm^{-1}; ^{1}H-NMR ($CDCl_3$), δ7.27 (2H, d, J=8.8 Hz), 6.89 (2H, d, J=8.8 Hz), 4.56-4.50 (3H, m), 3.81 (3H, s), 3.81-3.77 (2H, m), 3.60 (1H, dd, J=3.4 and 9.8 Hz), 3.51 (1H, dd, J=7.8 and 9.8 Hz), 3.17-3.08 (2H, m), 2.55 (1H, ddd, J=2.0, 6.4, and 17.1 Hz), 2.47 (1H, ddd, J=2.0, 6.4, and 17.1 Hz), 2.45 (1H, d, J=4.4 Hz), 1.84-1.76 (1H, m), 1.72-1.64 (1H, m), 0.90 (9H, s), and 0.06 (6H, s); HR-FAB-ms, Calcd for $C_{23}H_{35}O_5Si$ (M-H), 419.2254. Found, m/z 419.2264.

(2*S*,6*S*,7*R*)-(3*E*)-9-t-Butyldimethylsilyloxy-6,7-epoxy-1-*p*-methoxyphenylmethoxynon-3-en-2-ol (**39**).

To a stirred solution of **38** (16.83 g, 40.0 mmol) in ether (250 ml) at 0 °C was added dropwise Red-Al®

(3.46 M solution in toluene, 13.9 ml, 48 mmol), and stirring was continued at the same temperature for 1 h. The reaction was quenched carefully with an aqueous tartaric acid solution at 0 °C, followed by dilution of the mixture with ether (400 ml). The mixture was washed with aqueous tartaric acid (3 × 80 ml), water (80 ml), aqueous 5% $NaHCO_3$ (80 ml), and brine (100 ml), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by flash chromatography (33% EtOAc in hexane) to give the allylic alcohol (**39**, 16.57 g, 98%). **39**: a colorless oil; $[\alpha]_D^{25}$ +9.0° (c=1.97, $CHCl_3$); ir (neat), 3472, 2932, 2854, 1614, 1515, 1467, 1302, 1251, 1176, 1101, 1035, 834, and 777 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ7.26 (2H, d, J=8.8 Hz), 6.89 (2H, d, J=8.8 Hz), 5.83 (1H, ddt, J=1.0, 15.6, and 6.8 Hz), 5.58 (1H, dd, J=6.4 and 15.6 Hz), 4.50 (2H, AB pattern, J_{AB}=12.2 Hz), 4.32 (1H, m), 3.97 (2H, m), 3.81 (3H, s), 3.49 (1H, dd, J=3.4 and 9.8 Hz), 3.33 (1H, dd, J=8.3 and 9.8 Hz), 3.09 (1H, ddd, J=4.4, 4.5, and 6.8 Hz), 3.00 (1H, ddd, J=4.4, 5.9, and 6.3 Hz), 2.47 (1H, s), 2.34-2.21 (2H, m), 1.80 (1H, dddd, J=5.4, 6.4, 7.3, and 14.2 Hz), 1.67 (1H, ddt, J=6.8, 14.2, and 5.9 Hz), 0.90 (9H, s), and 0.06 (6H, s); HR-FAB-ms, Calcd for $C_{23}H_{39}O_5Si$ (M+H), 423.2567. Found, m/z 423.2583.

(2*S*,6*S*,7*R*)-(3*E*)-9-*t*-Butyldimethylsilyloxy-6,7-epoxy-1-*p*-methoxyphenylmethoxynon-3-en-2-ol 2-Benzoate (**40**).

PhCOCl (8.3 ml, 71.5 mmol) was added dropwise at 0 °C to a stirred solution of the alcohol (**39**, 25.19 g, 59.6 mmol), DMAP (0.36 g, 3.0 mmol), and TEA (12.5 ml, 89.4 mmol) in dry CH_2Cl_2 (380 ml). After stirring for 3 h, the reaction mixture was diluted with ether (600 ml), followed by washing with 5% HCl (2 × 100 ml), aqueous 5% $NaHCO_3$ (100 ml), water (100 ml), and brine (100 ml). Drying over Na_2SO_4, concentration *in vacuo*, and flash chromatography (SiO_2, 17% EtOAc in hexane) gave the benzoate (**40**, 30.70 g, 98%). **40**: a colorless oil; $[\alpha]_D^{25}$ -3.5° (c=1.72, $CHCl_3$); ir (neat), 2956, 2860, 1725, 1614, 1515, 1455, 1251, 1176, 1101, 1035, 834, 777, and 714 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ8.06 (2H, d, J=7.3 Hz), 7.56 (1H, t, J=7.3 Hz), 7.44 (2H, t, J=7.3 Hz), 7.24 (2H, d, J=8.8 Hz), 6.84 (2H, d, J=8.8 Hz), 5.92 (1H, m), 5.72 (2H, m), 4.52 (2H, AB pattern, J_{AB}=11.7 Hz), 3.79 (3H, s), 3.77 (2H, m), 3.69 (1H, dd, J=6.4 and 10.7 Hz), 3.64 (1H, dd, J=3.9 and 10.7 Hz), 3.09 (1H, ddd, J=4.4, 4.9, and 7.3 Hz), 3.00 (1H, ddd, J=4.4, 6.4, and 6.4 Hz), 2.30 (2H, m), 1.78 (1H, dddd, J=4.9, 6.8, 7.3, and 14.2 Hz), 1.66 (1H, ddt, J=7.3, 14.2, and 5.4 Hz), 0.89 (9H, s), and 0.05 (6H, s); HR-FAB-ms, Calcd for $C_{30}H_{43}O_6Si$ (M+H), 527.2829. Found, m/z 527.2875.

(2*S*,6*S*,7*R*)-(3*E*)-6, 7-Epoxy-1-*p*-methoxyphenylmethoxynon-3-ene-2, 9-diol 2-Benzoate (**41**).

A mixture of **40** (29.26 g, 55.5 mmol), TBAF (1.0 M solution in THF, 83.3 ml, 83.3 mmol), and THF (300 ml) was stirred at -10 °C for 3 h. Dilution with EtOAc (600 ml), followed by washing with water (2 × 150 ml), and brine (3 × 150 ml), drying over Na_2SO_4, and solvent removal gave a crude oil. The crude product was subjected to flash chromatography (SiO_2, 60% → 70% EtOAc in hexane) to furnish the 3,4-epoxy-1-ol (**41**, 22.18 g, 97%). **41**: a colorless oil; $[\alpha]_D^{25}$ +1.2° (c=0.98, $CHCl_3$); ir (neat), 3472, 2956, 1722, 1614, 1515, 1455, 1272, 1176, 1101, 1071, 1035, 975, 815, 756, and 714 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ8.06 (2H, d, J=7.3 Hz), 7.57 (1H, t, J=7.3 Hz), 7.44 (2H, t, J=7.3 Hz), 7.24 (2H, d, J=8.8 Hz), 6.85 (2H, d, J=8.8 Hz), 5.91 (1H, dt, J=14.7 and 6.4 Hz), 5.72 (1H, dd, J=6.4 and 14.7 Hz), 5.69 (1H, m), 4.53 (2H, AB pattern, J_{AB}=11.7 Hz), 3.81 (2H, m), 3.79 (3H, s), 3.70 (1H, dd, J=6.4 and 10.7 Hz), 3.65 (1H, dd, J=4.4 and 10.7 Hz), 3.11 (1H, ddd, J=4.4, 4.9, and 7.3 Hz), 3.03 (1H, ddd, J=4.4, 6.4, and 6.4 Hz), 2.41 (1H, ddd, J=6.4, 6.4, and 15.5 Hz), 2.25 (1H, ddd, J=6.4, 6.4, and 15.5 Hz), and 1.88-1.67 (3H, m); HR-FAB-ms, Calcd for $C_{24}H_{29}O_6$ (M+H), 413.1964. Found, m/z 413.1980.

(2*S*,6*R*,7*R*)-(3*E*)-2-Benzoyloxy-6-bromo-1-*p*-methoxyphenylmethoxynon-3-ene-7,9-diol (**42**).

A flame dried 1-l three-necked round-bottomed flask, equipped with a magnetic stirbar, an argon inlet,

and rubber septum, containing Et_2NH·HBr (26.59 g, 172.6 mmol) was heated to 160 °C with stirring under reduced pressure (0.01 mmHg) for 2 h. After cooling the mixture to 25 °C, a solution of $Ti(O\text{-}i\text{-}Pr)_4$ (19.3 ml, 64.7 mmol) in CH_2Cl_2 (400 ml) was introduced *via* cannula through the septum and the mixture was stirred at 25 °C for 30 min under an argon atmosphere. The 3,4-epoxy-1-ol (**41**, 17.8 g, 43.1 mmol) dissolved in CH_2Cl_2 (32 ml) was then added and stirring was continued at 25 °C for 12 h. The reaction mixture was then mixed with saturated aqueous tartaric acid (250 ml), diluted with EtOAc (900 ml), and the resulting mixture was vigorously stirred until it became two phases clearly. The separated organic layer was washed with 10% HCl (2 × 100 ml), aqueous 5% $NaHCO_3$ (100 ml), dried over Na_2SO_4, and concentrated *in vacuo* to afford a viscous oil. The residue was subjected to flash chromatography (SiO_2, 60% → 70% EtOAc in hexane) to give the 4-bromo-1,3-diol (**42**, 15.11 g, 71%) along with the regioisomeric 3-bromo-1,4-diol (**43**, 1.42 g, 6.6%). **42**: a colorless oil; $[\alpha]_D^{25}$ -0.1° (c=1.65, $CHCl_3$); ir (neat), 3046, 2948, 1725, 1614, 1515, 1455, 1374, 1248, 1176, 1110, 1041, and 714 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ8.05 (2H, d, J=7.3 Hz), 7.56 (1H, t, J=7.3 Hz), 7.44 (2H, t, J=7.3 Hz), 7.24 (2H, d, J=8.8 Hz), 6.85 (2H, d, J=8.8 Hz), 5.91 (1H, ddd, J=6.4, 7.3, and 15.1 Hz), 5.72 (1H, dd, J=6.4 and 15.1 Hz), 5.66 (1H, m), 4.53 (2H, AB pattern, J_{AB}=11.7 Hz), 4.03 (1H, ddd, J=3.9, 5.4, and 7.8 Hz), 3.80 (3H, m), 3.79 (3H, s), 3.70 (1H, dd, J=6.4 and 10.8 Hz), 3.65 (1H, dd, J=4.4 and 10.8 Hz), 2.77 (1H, ddd, J=5.4, 6.4, and 14.7 Hz), 2.8 (1H, ddd, J=7.3, 7.8, and 14.7 Hz), 2.53 (1H, br s), 1.89-1.80 (1H, m), 1.78-1.71 (1H, m), and 1.62 (1H, br s); HR-FAB-ms, Calcd for $C_{24}H_{28}O_6Br$ (M-H), 491.1069. Found, m/z 493.1091. Calcd for $C_{24}H_{28}O_6{}^{81}Br$ (M-H), 493.1049. Found, 491.1079.
Regioisomer (**43**): a pale yellow oil; ir (neat), 3080, 2950, 1725, 1614, 1515, 1368, 1272, 1176, 1108, 1038, 772, and 712 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ8.04 (2H, d, J=7.3 Hz), 7.56 (1H, t, J=7.3 Hz), 7.44 (2H, t, J=7.3 Hz), 7.25 (2H, d, J=8.8 Hz), 6.85 (2H, d, J=8.8 Hz), 5.85 (1H, dt, J=15.1 and 7.3 Hz), 5.71 (1H, dd, J=6.8 and 15.1 Hz), 5.63 (1H, ddd, J=4.4, 6.4, and 6.8 Hz), 4.52 (2H, AB pattern, J_{AB}=11.9 Hz), 4.39 (1H, dt, J=2.4 and 6.4 Hz), 3.85-3.72 (3H, m), 3.79 (3H, s), 3.70 (1H, dd, J=6.4 and 10.7 Hz), 3.64 (1H, dd, J=4.4 and 10.7 Hz), 3.59 (1H, t, J=5.9 Hz), 2.40 (2H, m), 2.22 (2H, m), and 1.83 (1H, br s).

(2*S*,6*R*,7*R*)-(3*E*)-Benzoyloxy-6-bromo-1-*p*-methoxyphenylmethoxynon-3-ene-7,9-diol 9-Pivaloate (**44**).

PvCl (4.0 ml, 32.5 mmol) was added dropwise to a stirred mixture of **42** (13.35 g, 27.0 mmol) and Py (3.3 ml) in dry CH_2Cl_2 (134 ml) at 0 °C. After stirring at 0 °C for 12 h, the reaction mixture was diluted with ether (300 ml), followed by washing with 5% HCl (60 ml), aqueous 5% $NaHCO_3$ (60 ml), and brine (60 ml). Drying over Na_2SO_4, concentration *in vacuo*, and flash chromatography (SiO_2, 20% →33% EtOAc in hexane) gave the pivaloate (**44**, 15.26 g, 98%). **44**: a colorless oil; $[\alpha]_D^{25}$ +6.3° (c=2.02, $CHCl_3$); ir (neat), 3508, 2968, 1722, 1614, 1514, 1480, 1366, 1247, 1162, 1114, 1036, 947, 822, 756, and 714 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ8.05 (2H, d, J=7.3 Hz), 7.57 (1H, t, J=7.3 Hz), 7.44 (2H, t, J=7.3 Hz), 7.24 (2H, d, J=8.8 Hz), 6.85 (2H, d, J=8.8 Hz), 5.89 (1H, ddd, J=6.8, 7.3, and 14.7 Hz), 5.72 (1H, dd, J=6.4 and 14.7 Hz), 5.69 (1H, m), 4.52 (2H, AB pattern, J_{AB}=11.7 Hz), 4.24 (1H, ddd, J=5.9, 7.3, and 11.2 Hz), 4.18 (1H, dt, J=11.2 and 5.9 Hz), 4.03 (1H, ddd, J=2.9, 5.9, and 7.9 Hz), 3.79 (3H, s), 3.69 (1H, dd, J=6.4 and 10.7 Hz), 3.64 (1H, dd, J=4.4 and 10.7 Hz), 3.62 (1H, m), 2.74 (2H, ABX pattern, J_{AB}=15.0 Hz), 2.16 (1H, d, J=7.8 Hz), 1.88 (2H, m), and 1.17 (9H, s); HR-FAB-ms, Calcd for $C_{29}H_{36}O_7Br$ (M-H), 575.1645. Found, m/z 575.1658. Calcd for $C_{29}H_{36}O_7{}^{81}Br$ (M-H), 577.1624. Found, 557.1649.

(2*S*,6*R*,7*R*)-(3*E*)-2-Benzoyloxy-6-bromo-7-*t*-butyldimethylsilyloxy-1-*p*-methoxyphenylmethoxynon-3-en-9-ol 9-Pivaloate (**45**).

TBSOTf (7.3 ml, 3.17 mmol) was added dropwise to a stirred mixture of **44** (15.26 g, 26.4 mmol), TEA (5.5 ml, 39.6 mmol), and DMAP (0.16 g, 1.3 mmol) in CH_2Cl_2 (153 ml) at -20 °C. After stirring for 4 h, the reaction mixture was diluted with ether (600 ml), followed by washing with 5% HCl (2 × 100 ml), aqueous 5% $NaHCO_3$ (100 ml), and brine (100 ml). Drying over Na_2SO_4, concentration *in vacuo*, and

flash chromatography (SiO_2, 12% → 16% EtOAc in hexane) afforded the silyl ether (**45**, 17.70 g, 97%). **45**: a colorless oil; $[\alpha]_D^{25}$ +19° (c=1.02, $CHCl_3$); ir (neat), 2956, 2860, 1731, 1614, 1515, 1467, 1365, 1251, 1155, 1098, 1038, 969, 837, 777, and 711 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ8.06 (2H, d, J=7.3 Hz), 7.56 (1H, t, J=7.3 Hz), 7.44 (2H, t, J=7.3 Hz). 7.24 (2H, d, J=8.8 Hz), 6.84 (2H, d, J=8.8 Hz), 5.90 (1H, m), 5.70 (2H, m), 4.55 (1H, d, J=11.7 Hz), 4.50 (1H, d, J=11.7 Hz), 4.23 (1H, dt, J=10.7 and 5.4 Hz), 4.03-3.94 (2H, m), 3.88 (1H, ddd, J=2.9, 3.4, and 10.3 Hz), 3.79 (3H, s), 3.67 (2H, ABX pattern, J_{AX}=6.4, J_{BX}=3.9, J_{AB}=10.8 Hz), 2.78 (1H, ddd, J=2.7, 6.8, and 15.1 Hz), 2.45 (1H, ddd, J=6.8, 10.3, and 15.1 Hz), 2.17 (1H, m), 1.68 (1H, ddt, J=9.3, 13.7, and 4.9 Hz), 1.19 (9H, s), 0.88 (9H, s), 0.064 (3H, s), and 0.058 (3H, s); HR-FAB-ms, Calcd for $C_{35}H_{50}O_7BrSi$ (M-H), 689.2509. Found, m/z 689.2535. Calcd for $C_{35}H_{50}O_7{}^{81}BrSi$ (M-H), 691.2488. Found, 691.2454.

(2*S*,6*R*,7*R*)-(3*E*)-6-Bromo-7-*t*-butyldimethylsilyloxy-1-*p*-methoxyphenylmethoxynon-3-ene-2,9-diol 9-Pivaloate (**46**).

A mixture of **45** (13.18 g, 19.0 mmol), K_2CO_3 (3.95 g, 28.5 mmol), and MeOH-water (20:1, 143 ml) was stirred at 25 °C for 3 h. The reaction mixture was diluted with ether-EtOAc (1:1, 500 ml), washed with water (2 × 80 ml) and brine (80 ml), dried over Na_2SO_4, and concentrated *in vacuo*. The resulting residue was subjected to flash chromatography (SiO_2, 20% → 50% EtOAc in hexane) to furnish **46** (10.15 g, 91%). **46**: a colorless oil; $[\alpha]_D^{25}$ +31.9° (c=1.55, $CHCl_3$); ir (neat), 3487, 2956, 2860, 1371, 1614, 1515, 1467, 1284, 1251, 1158, 1095, 1038, 837, 777, and 756 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ7.26 (2H, d, J=8.8 Hz), 6.89 (2H, d, J=8.8 Hz), 5.81 (1H, dt, J=15.1 and 6.8 Hz), 5.55 (1H, dd, J=5.9 and 15.1 Hz), 4.50 (2H, AB pattern, J_{AB}=11.7 Hz), 4.32 (1H, m), 4.26 (1H, dt, J=11.3 and 5.4 Hz), 4.03-3.96 (2H, m), 3.89 (1H, ddd, J=2.9, 3.4, and 10.8 Hz), 3.81 (3H, s), 3.50 (1H, dd, J=3.4 and 9.8 Hz), 3.34 (1H, dd, H=8.3 and 9.8 Hz), 2.77 (1H, ddd, J=2.9, 6.4, and 15.1 Hz), 2.42 (1H, d, J=2.9 Hz), 2.45-2.37 (1H, m), 2.19 (1H, m), 1.69 (1H, ddt, J=9.3, 14.2, and 4.9 Hz), 1.20 (9H, s), 0.89 (9H, s), 0.08 (3H, s), and 0.07 (3H, s); HR-FAB-ms, Calcd for $C_{28}H_{46}O_6BrSi$ (M-H), 585.2247. Found, m/z 585.2257. Calcd for $C_{28}H_{46}O_6{}^{81}BrSi$ (M-H), 587.2227. Found, 587.2224.

(2*R*,3*S*,4*R*,6*R*,7*R*)-6-Bromo-7-*t*-butyldimethylsilyloxy-3,4-epoxy-1-*p*-methoxyphenylmethoxynonane-2,9-diol 9-Pivaloate (**47**).

Ti(O-*i*-Pr)$_4$ (8.2 ml, 27.6 mmol) was added to a stirred mixture of D-(-)-DIPT (8.2 ml, 38.6 mmol) and 4A-MS (4.9 g) in dry CH_2Cl_2 (130 ml) at -20 °C. After 30 min, TBHP (5.6 M solution in CH_2Cl_2, 10.0 ml, 55.1 mmol) was added and the resulting mixture was stirred at -20 °C for 30 min. The allylic alcohol (**46**, 16.20 g, 27.6 mmol) dissolved in CH_2Cl_2 (50 ml) was then added dropwise and the reaction mixture was stored in refrigerator at -20 °C for 72 h. After warming to room temperature, the reaction mixture was poured onto a cooled (0 °C) solution of $FeSO_4 \cdot 7H_2O$ (10 g) and tartaric acid (50 g) in water (120 ml), and the mixture was vigorously stirred at 0 °C for 30 min. Dilution with ether-EtOAc (1:1, 700 ml), washing with water (2 × 200 ml), aqueous 5% $NaHCO_3$ (200 ml), and brine (200 ml), drying over Na_2SO_4, and concentration *in vacuo* gave a viscous residue. Careful chromatography of the residue (SiO_2, 20% → 50% EtOAc in hexane) afforded the epoxy alcohol (**47**, 16.10 g, 97%) as a single product. **47**: a colorlss oil; $[\alpha]_D^{25}$ +27.9° (c=2.23, $CHCl_3$); ir (neat), 3470, 2956, 2860, 1730, 1614, 1515, 1465, 1365, 1283, 1250, 1150, 1095, 1030, 835, 777, and 731 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ7.26 (2H, d, J=8.8 Hz), 6.88 (2H, d, J=8.8 Hz), 4.51 (2H, AB pattern, J_{AB}=11.7 Hz), 4.26 (1H, dt, J=11.2 and 5.4 Hz), 4.11 (1H, dt, J=11.2 and 2.9 Hz), 4.03-3.95 (2H, m), 3.84 (1H, m), 3.81 (3H, s), 3.63 (1H, dd, J=3.9 and 9.8 Hz), 3.57 (1H, dd, J=5.9 and 9.8 Hz), 3.19 (1H, ddd, J=2.0, 4.9, and 6.8 Hz), 2.93 (1H, dd, J=2.0 and 4.4 Hz), 2.34 (1H, d, J=3.4 Hz), 2.20 (1H, m), 2.10 (1H, ddd, J=2.4, 6.8, and 14.7 Hz), 1.98 (1H, ddd, J=4.9, 11.2, and 14.7 Hz), 1.67-1.59 (1H, m), 1.21 (9H, s), 0.89 (9H, s), 0.083 (3H, s), and 0.077 (3H, s); HR-FAB-ms,

Calcd for $C_{28}H_{46}O_7BrSi$ (M-H), 601.2196. Found, m/z601.2191. Calcd for $C_{28}H_{46}O_7{}^{81}BrSi$ (M-H), 603.2176. Found, 603.2205.

(2*R*,3*S*,4*R*,6*R*,7*R*)-6-Bromo-7-*t*-butyldimethylsilyloxy-3,4-epoxy-2-methanesulfonyloxy-1-*p*-methoxyphenylmethoxynonan-9-ol 9-Pivaloate (**48**).

MsCl (3.1 ml, 40.0 mmol) was added to a stirred solution of **47** (16.08 g, 26.6 mmol), TEA (9.3 ml, 66.6 mmol), and DMAP (163 mg, 1.3 mmol) in CH_2Cl_2 (266 ml) at -40 °C. After stirring for 1 h, the reaction mixture was diluted with $CHCl_3$ (250 ml), followed by washing with 10% HCl (80 ml), aqueous 5% $NaHCO_3$ (80 ml), and brine (80 ml). Drying over Na_2SO_4, concentration *in vacuo*, and purification by flash chromatography (SiO_2, 25% EtOAc in hexane) gave the epoxy methanesulfonate (**48**, 18.17 g, 100%). **48**: a colorless oil; $[\alpha]_D{}^{25}$ +34.2° (c=1.98, $CHCl_3$); ir (neat), 2956, 2860, 1728, 1614, 1515, 1482, 1465, 1284, 1154, 1095, 1034, 837, 777, and 734 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ7.25 (2H, d, J=9.0 Hz), 6.88 (2H, d, J=9.0 Hz), 4.66 (1H, q, J=4.9 Hz), 4.51 (2H, AB pattern, J_{AB}=11.3 Hz), 4.26 (1H, ddd, J=4.9, 5.9, and 11.2 Hz), 4.09 (1H, dt, J=11.2 and 2.9 Hz), 4.03-3.96 (2H, m), 3.81 (3H, s), 3.72 (2H, ABX pattern), 3.23 (1H, ddd, J=2.0, 4.9, and 6.8 Hz), 3.04 (3H, s), 3.03 (1H, dd, J=2.0 and 4.9 Hz), 2.19 (1H, m), 2.11 (1H, ddd, J=2.4, 6.8, and 15.1 Hz), 1.97 (1H, ddd, J=4.9, 11.2, and 15.1 Hz), 1.61 (1H, ddt, J=8.8, 13.7, and 4.9 Hz), 1.21 (9H, s), 0.88 (9H, s), 0.082 (3H, s), and 0.077 (3H, s); HR-FAB-ms, Calcd for $C_{29}H_{48}O_9BrSSi$ (M-H), 679.1972. Found, m/z 679.2017. Calcd for $C_{29}H_{48}O_9{}^{81}BrSSi$ (M-H), 681.1952. Found, 681.2018.

(2*R*,3*S*,4*R*,6*R*,7*R*)-6-Bromo-7-*t*-butyldimethylsilyloxy-3,4-epoxy-2-methanesulfonyloxynonane-1,9-diol 9-Pivaloate (**49**).

A mixture of the *p*-methoxyphenylmethyl ether (**48**, 16.91 g, 24.8 mmol) and DDQ (11.26 g, 49.6 mmol) in CH_2Cl_2-water (18:1, 169 ml) was stirred at 23 °C for 4 h. The mixture was diluted with ether (600 ml), washed with cold (0 °C) 1M NaOH solution (3 × 700 ml), aqueous 5% NH_4Cl (100 ml), and brine (100 ml), dried over Na_2SO_4, and concentrated *in vacuo*. The resulting residue was subjected to flash chromatography (SiO_2, 33% → 50% EtOAc in hexane) to furnish the epoxy alcohol (**49**, 14.38 g, 94%). **49**: a colorless oil; $[\alpha]_D{}^{25}$ +42.9° (c=2.24, $CHCl_3$); ir (neat), 3538, 2962, 2860, 1731, 1482, 1302, 1287, 1260, 1176, 1092, 1047, 927, 837, and 777 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ4.65 (1H, ddd, J=3.4, 4.4, and 5.9 Hz), 4.27 (1H, dt, J=11.2 and 5.4 Hz), 4.11 (1H, dt, J=11.2 and 2.9 Hz), 4.03-3.94 (3H, m), 3.90 (1H, dt, J=12.7 and 5.9 Hz), 3.24 (1H, ddd, J=2.0, 4.9, and 6.4 Hz), 3.12 (3H, s), 3.07 (1H, dd, J=2.0 and 4.4 Hz), 2.24-2.13 (2H, m), 2.06 (1H, t, J=6.4 Hz, OH), 1.98 (1H, ddd, J=4.9, 11.5, and 14.7 Hz), 1.62 (1H, m), 1.21 (9H, s), 0.89 (9H, s), 0.09 (3H, s), and 0.08 (3H, s); HR-FAB-ms, Calcd for $C_{21}H_{42}O_8BrSSi$ (M+H), 561.1553. Found, m/z 561.1533. Calcd for $C_{21}H_{42}O_8{}^{81}BrSSi$ (M+H), 563.1533. Found, 563.1561.

(2*R*,3*R*,4*S*,6*R*,7*R*)-6-Bromo-7-*t*-butyldimethylsilyloxy-4-chloro-2-methanesulfonyloxynonane-1,3,9-triol 9-Pivaloate (**50**).

Et_2AlCl (0.94 M solution in hexane, 62.5 ml, 58.8 mmol) was added dropwise to a stirred solution of **49** (11.00 g, 19.6 mmol) in CH_2Cl_2 (196 ml) at 0 °C. After stirring at 0 °C for 3 h, the reaction was quenched carefully by addition of an aqueous tartaric acid solution (50 ml) and the mixture was vigorously stirred at 0 °C for 20 min. The mixture was diluted with ether (600 ml), washed with 10% aqueous tartaric acid solution (2 × 200 ml), water (200 ml), aqueous 5% $NaHCO_3$ (200 ml), and brine (100 ml), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was subjected to flash chromatography (SiO_2, 40% EtOAc in hexane) to give the chlorohydrin (**50**, 10.78 g, 93%) as a single product. **50**: a colorless oil; $[\alpha]_D{}^{25}$ +17.6° (c=1.82, $CHCl_3$); ir (neat), 3508, 2962, 2860, 1725, 1467, 1362, 1287, 1260, 1173, 1086, 1005, 936, 837, and 759 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ5.04 (1H, q, J=3.9 Hz), 4.40 (1H, dt, J=2.9 and

6.8 Hz), 4.27 (1H, dt, J=11.2 and 5.4 Hz), 4.23 (1H, ddd, J=4.9, 7.3, and 8.8 Hz), 4.16-3.95 (5H, m), 3.46 (1H, d, J=6.4 Hz), 3.16 (3H, s), 2.81 (1H, ddd, J=4.9, 6.8, and 15.1 Hz), 2.60 (1H, t, J=5.4 Hz), 2.34 (1H, dt, J=15.1 and 7.3 Hz), 2.20 (1H, m), 1.75 (1H, ddt, J=13.7, 8.3, and 5.4 Hz), 1.20 (9H, s), 0.91 (9H, s), 0.13 (3H, s), and 0.09 (3H, s); HR-FAB-ms, Calcd for $C_{21}H_{43}O_8BrClSSi$ (M+H), 597.1320. Found, m/z 597.1323. Calcd for $C_{21}H_{43}O_8{}^{81}BrClSSi$ (M+H), 599.1300 and for $C_{21}H_{43}O_8Br^{37}ClSSi$ (M+H), 599.1290. Found, 599.1289. Calcd for $C_{21}H_{43}O_8{}^{81}Br^{37}ClSSi$ (M+H), 601.1271. Found, 601.1277.

(2*S*,3*R*,4*S*,6*R*,7*R*)-6-Bromo-7-*t*-butyldimethylsilyloxy-4-chloro-2,3-epoxynonane-1,9-diol 9-Pivaloate (**51**).

A mixture of chlorohydrin (**50**, 13.29 g, 22.2 mmol) and K_2CO_3 (3.69 g, 16.7 mmol) in anhydrous MeOH (133 ml) was stirred at 20 °C for 1 h. The reaction mixture was diluted with ether (600 ml), washed with water (3 × 100 ml) and brine (100 ml), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was subjected to chromatography (SiO_2, 17% → 25% EtOAc in hexane) to furnish the epoxy alcohol (**51**, 9.75 g, 87.4%) along with its diastereoisomer (**52**, 0.97 g, 8.7%) arisen from the antipode of the C-5 unit (**8**). The total yield of the epoxidation reaction amounted to 96%. **51**: Rf=0.30 (25% EtOAc in hexane, SiO_2); a colorless oil; $[\alpha]_D^{25}$ +33.4° (c=2.15, $CHCl_3$); ir (neat), 3520, 2960, 2932, 2860, 1726, 1482, 1464, 1376, 1286, 1256, 1162, 1088, 1046, and 838 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ4.29 (2H, m), 4.03-3.96 (2H, m), 3.96 (1H, ddd, J=2.0, 5.4, and 13.2 Hz), 3.84 (1H, dt, J=5.4 and 8.3 Hz), 3.71 (1H, ddd, J=3.9, 7.8, and 13.2 Hz), 3.15 (1H, dd, J=1.9 and 8.3 Hz), 3.12 (1H, dt, J=3.9 and 2.0 Hz), 2.67 (1H, ddd, J=3.9, 8.3, and 14.7 Hz), 2.34 (1H, ddd, J=5.4, 9.8, and 14.7 Hz), 2.22 (1H, dddd, J=3.4, 5.96, 8.8, and 14.2 Hz), 1.69 (1H, ddt, J=9.3, 14.2, and 4.9 Hz), 1.60 (1H, dd, J=5.4 and 7.8 Hz), 1.21 (9H, s), 0.91 (9H, s), 0.12 (3H, s), and 0.09 (3H, s); HR-FAB-ms, Calcd for $C_{20}H_{39}O_5BrClSi$ (M+H), 501.1439. Found, m/z 501.1426. Calcd for $C_{20}H_{39}O_5{}^{81}BrClSi$ (M+H), 503.1418 and for $C_{20}H_{39}O_5Br^{37}ClSi$ (M+H), 503.1409. Found, 503.1407. Calcd for $C_{20}H_{39}O_5{}^{81}Br^{37}ClSi$ (M+H), 505.1389. Found, 505.1408.
Diastereoisomer (**52**): Rf=0.20 (SiO_2, 25% EtOAc in hexane); a colorless oil; ir (neat), 3538, 2962, 2860, 1731, 1482, 1362, 1287, 1266, 1170, 1090, 1045, and 925 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ4.27 (2H, m), 4.40-3.93 (3H, m), 3.81 (1H, ddd, J=3.4, 7.3, and 10.3 Hz), 3.71 (1H, m), 3.23 (1H, dd, J=2.0 and 7.3 Hz), 3.17 (1H, dt, J=3.9 and 2.0 Hz), 2.32-2.20 (3H, m), 1.82 (1H, br s), 1.67 (1H, ddt, J=9.3, 11.3, and 4.9 Hz), 1.20 (9H, s), 0.90 (9H, s), 0.11 (3H, s), and 0.08 (3H, s).

(2*S*,3*R*,4*S*,6*R*,7*R*)-6-Bromo-4-chloro-2,3-epoxynonane-1,7,9-triol 9-Pivaloate (**32**).

A mixture of TBAF-HF (pH≈4, 7.2 ml, *ca.* 7.2 mmol of F^-) prepared from a 1.0 M solution of TBAF in THF and 48% HF in a ratio of 12: 1 was added to a solution of the silyl ether (**51**, 1.45 g, 2.9 mmol) in THF (7.2 ml) at 20 °C and stirred for 28 h. The reaction mixture was diluted with EtOAc (150 ml), washed with water (2 × 30 ml), aqueous 5% $NaHCO_3$ (30 ml), and brine (30 ml), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was subjected to flash chromatography (SiO_2, 50% EtOAc in hexane) to give the epoxy diol (**32**, 1.00 g, 89%) along with the starting material (**51**, 0.15 g, 10%). **32**: a colorless oil; $[\alpha]_D^{25}$ +2.5° (c=5.10, $CHCl_3$); ir (neat), 3464, 2976, 2872, 1724, 1482, 1464, 1400, 1286, 1160, 1038, 938, 902, and 772 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ4.46 (1H, ddd, J=2.4, 6.4, and 7.8 Hz), 4.30 (1H, ddd, 5.4, 7.8, and 11.2 Hz), 4.21 (1H, ddd, J=5.4, 5.9, and 11.2 Hz), 3.96 (1H, dd, J=2.0 and 13.2 Hz), 3.83 (1H, dt, J=6.8 and 7.3 Hz), 3.73 (1H, dd, J=3.4 and 13.2 Hz), 3.66 (1H, m), 3.21 (1H, dd, J=2.0 and 7.3 Hz), 3.16 (1H, dt, J=3.4 and 2.0 Hz), 2.65 (1H, ddd, J=6.4, 6.8, and 14.7 Hz), 2.52 (1H, ddd, J=7.3, 7.8, and 14.7 Hz), 2.29 (1H, d, J=6.8 Hz), 1.94 (2H, m), 1.74 (1H, br s), and 1.20 (9H, s); HR-FAB-ms, Calcd for $C_{14}H_{25}O_5BrCl$ (M+H), 387.0574. Found, m/z 387.0560. Calcd for $C_{14}H_{25}O_5{}^{81}BrCl$ (M+H), 389.0553 and for $C_{14}H_{25}O_5Br^{37}Cl$ (M+H), 389.0544. Found 389.0528. Calcd for $C_{14}H_{25}O_5{}^{81}Br^{37}Cl$ (M+H), 391.0524. Found, 391.0548.

Intramolecular Cyclization of **32** to (2*R*,3*R*,5*S*,1'*S*)-3-bromo-5-chloro-6-(1',2'-dihydroxyethyl)-2-(2'-pivaloyloxyethyl)tetrahydropyran (**53**).

The 2,3-epoxy alcohol (**32**, 340 mg, 0.88 mmol) in PhH (44 ml) was added to a 100- ml two-necked round-bottomed flask, equipped with a magnetic stirbar, a reflux condenser, and a rubber septum (Aldrich, Z 10, 076-5), containing $Zn(OTf)_2$ (351 mg, 0.96 mmol). The reaction mixture was refluxed under an argon atmosphere for 15 h. After cooling to room temperature, the mixture was diluted with EtOAc (150 ml), washed with 5% HCl (3 × 30 ml), aqueous 5% $NaHCO_3$ (50 ml), and brine (50 ml). Drying over Na_2SO_4 and removal of solvents *in vacuo* afforded a viscous oil, which was subjected to flash chromatography (SiO_2, 60% EtOAc in hexane) to furnish the tetrahydropyran (**53**, 129 mg, 38%) and the starting epoxy alcohol (**32**, 165 mg, 49%). **53**: a pale yellow oil; $[\alpha]_D^{25}$ +3.8° (c=3.0, $CHCl_3$); ir ($CHCl_3$), 3532, 3010, 2974, 1719, 1482, 1464, 1452, 1368, 1287, 1170, 1095, 1047, 942, and 918 cm^{-1}; ^{1}H-nmr ($CHCl_3$), δ4.66 (1H, dt, J=3.4 and 10.7 Hz), 4.49 (1H, dt, J=4.9 and 2.0 Hz), 4.14 (1H. dt. J=4.9 and 2.0 Hz), 4.04-3.94 (3H, m), 3.81 (1H, dd, J=2.0 and 11.2 Hz), 3.56 (1H, dd, J=2.0 and 8.8 Hz), 3.31 (1H, dt, J=9.8 and 2.0 Hz), 2.89 (1H, dt, J=16.6 and 2.0 Hz), 2.75 (1H, br s), 2.72 (1H, dt, J=16.6 and 4.9 Hz), 2.34 (1H, br s), 2.18 (1H, ddt, J=9.8, 14.6, and 3.4 Hz), 1.79 (1H, dddd, J=2.0, 4.9, 10.7, and 14.6 Hz), and 1.20 (9H, s); HR-FAB-ms, Calcd for $C_{14}H_{25}O_5BrCl$ (M+H), 387.0574. Found, m/z 387.0565. Calcd for $C_{14}H_{25}O_5{}^{81}BrCl$ (M+H), 389.0553 and for $C_{14}H_{25}O_5Br^{37}Cl$ (M+H), 389.0544. Found, 389.0553. Calcd for $C_{14}H_{25}O_5{}^{81}Br^{37}Cl$ (M+H), 391.0542. Found, 391.0588.

(2*R*,3*R*,5*S*,6*S*,1'*S*)-3-Bromo-5-chloro-2-(2'-pivaloyloxyethyl)-6-(2'-thio-1',3'-dioxolan-4'-yl)-tetrahydropyran (**56**).

$CSCl_2$ (163 µl, 2.14 mmol) was added to a stirred solution of diol(**54**)(414 mg, 1.07 mmol) and DMAP (533 mg, 4.28 mmol) in CH_2Cl_2 (11 ml) at 0 °C and the contents were stirred at 0 °C for 1 h. SiO_2 (3 g) was added and the mixture was allowed to warm to room temperature. SiO_2 was filtrated out of the mixture and washed thoroughly with CH_2Cl_2, and then the solvent was removed *in vacuo*. The residue was purified by flash chromatography (SiO_2, 33% EtOAc in hexane) to afford the thiocarbonate (**56**, 376 mg, 82%). **56**: a pale yellow oil; $[\alpha]_D^{25}$ -6.7° (c=1.00, $CHCl_3$); ir ($CHCl_3$), 2980, 1725, 1482, 1428, 1371, 1311, 1164, 1098, 1038, 987, and 948 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ5.63 (1H, ddd, J=5.4, 6.4, and 8.3 Hz), 4.95 (1H, dd, J=5.4 and 9.3 Hz), 4.77 (1H, dd, J=8.3 and 9.3 Hz), 4.34 (1H, dt, J=4.4 and 2.4 Hz), 4.22 (1H, ddd, J=4.9, 8.3, and 11.2 Hz), 4.19 (1H, dt, J=4.4 and 2.4 Hz), 4.14 (1H, dt, J=11.2 and 5.4 Hz), 3.98 (1H, dd, J=2.4 and 5.4 Hz), 3.54 (1H, ddd, J=2.4, 4.4, and 8.8 Hz), 2.86 (1H, dt, J=16.6 and 2.4 Hz), 2.79 (1H, dt, J=16.6 and 4.4 Hz), 2.18 (1H, dddd, J=4.9, 5.4, 8.8, and 14.7 Hz), 1.91 (1H, dddd, J=4.4, 5.4, 8.3, and 14.7 Hz), and 1.20 (9H, s); HR-FAB-ms, Calcd for $C_{15}H_{23}O_5BrClS$ (M+H), 429.0138. Found, m/z 429.0163. Calcd for $C_{15}H_{23}O_5{}^{81}BrClS$ (M+H), 431.0188 and for $C_{15}H_{23}O_5Br^{37}ClS$ (M+H), 431.0109. Found, 431.0118. Calcd for $C_{15}H_{23}O_5{}^{81}Br^{37}ClS$ (M+H), 433.0089. Found, 433.0094.

(2*R*,3*R*,5*S*,6*S*)-3-Bromo-5-chloro-2-(2'-pivaloyloxyethyl)-6-vinyltetrahydropyran (**57**).

1,3-Dimethyl-2-phenyl-1,3-diazaphospholidine (1014 mg, 5.22 mmol) was added to a stirred solution of thiocarbonate (**56**, 376 mg, 0.87 mmol) in toluene (10 ml) and stirring was continued at 20 °C for 2 h. After removal of toluene *in vacuo*, the residue was directly adsorbed by flash chromatography (SiO_2, 25% EtOAc in hexane) to give a mixture of the desired product (**57**) and 1,3-dimethyl-2-phenyl-2-thioxo-1,3-diazaphospholidine (488 mg containing 298 mg of **57**, 97%) in a 1:1 of molar ratio. The mixture was directly used for the next step without further purification.

An analytical sample of **57** was obtained by further purification of the mixture by hplc (Unisil Q, 10.7 × 250 mm; 80% hexane-17% CH_2Cl_2-3% MeCN; 4.0 ml/min flow; detected by uv at 228 nm). **57**: t_R=11.1 min (above conditions); white crystals, mp 67-68 °C (recrystallized from ether-hexane); $[\alpha]_D^{25}$ +18.6°

(c=2.85, $CHCl_3$); ir ($CHCl_3$), 2932, 2854, 1725, 1464, 1380, 1287, 1155, 1104, 1062, 1032, 981, and 720 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ5.94 (1H, ddd, J=5.1, 10.6, and 17.2 Hz), 5.37 (1H, dt, J=17.2 and 1.5 Hz), 5.30 (1H, dt, J=10.6 and 1.5 Hz), 4.27-4.15 (5H, m), 3.55 (1H, ddd, J=2.0, 4.4, and 8.4 Hz), 2.85 (1H, dt, J=16.5 and 2.0 Hz), 2.78 (1H, dt, J=16.5 and 4.4 Hz), 2.25 (1H, ddt, J=8.4, 14.7, and 5.5 Hz), 1.92 (1H, dddd, J=4.4, 6.6, 7.7, and 14.7 Hz), and 1.19 (9H, s); HR-FAB-ms, Calcd for $C_{14}H_{23}O_3BrCl$ (M+H), 353.0519. Found, m/z 353.0528. Calcd for $C_{14}H_{23}O_3{}^{81}BrCl$ (M+H), 355.0499, and for $C_{14}H_{23}O_3Br^{37}Cl$ (M+H), 355.0489. Found, 355.0476. Calcd for $C_{14}H_{23}O_3{}^{81}Br^{37}Cl$ (M+H), 357.0469. Found, 357.0491.

(2*R*,3*R*,5*S*,6*S*)-3-Bromo-5-chloro-6-(2'-hydroxyethyl)-2-(2'-pivaloyloxyethyl)tetrahydropyran (**58**).

9-BBN (0.5 M solution in THF, 6.7 ml, 3.36 mmol) was added dropwise to a stirred solution of the terminal olefin (**57**, 298 mg, 0.84 mmol) in THF (6.7 ml) at 0 °C. After 30 min, the cooling bath was removed and the mixture was stirred for 2 h. The homogenous solution was re-cooled to 0 °C, and the borane was oxidized by slow addition of a solution of 5% NaOH (4.0 ml, 5.04 mmol) and H_2O_2 (35% solution in water, 4.0 ml, 40 mmol). After 30 min, the heterogenous solution was allowed to warm to room temperature and continued to stir for 1 h. Then, the mixture was diluted with water (30 ml), extracted with $CHCl_3$ (3 × 60 ml), washed with water (50 ml), 5% HCl (50 ml), aqueous 5% $NaHCO_3$ (50ml), and brine (50 ml), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, 30% → 50% EtOAc in hexane) to furnish the alcohol (**58**, 301 mg, 96%). **58**: a colorless oil; $[\alpha]_D^{25}$ -10.7° (c=2.20, $CHCl_3$); ir (neat), 3448, 2968, 1275, 1482, 1425, 1401, 1368, 1323, 1287, 1164, 1089, 1059, 936, 909, 956, and 666 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ4.60 (1H, ddd, J=3.9, 9.8, and 11.2 Hz), 4.15 (1H, dt, J=4.4 and 2.0 Hz), 4.02 (1H, ddd, J=4.4, 4.4, and 11.2 Hz), 3.95 (1H, ddd, J=3.4, 9.8, and 11.2 Hz), 3.86 (1H, ddd, J=2.0, 3.4, and 9.8 Hz), 3.76 (1H, dt, J=11.2 and 4.9 Hz), 3.37 (1H, ddd, J=2.0, 3.4, and 9.8 Hz), 2.84 (1H, dt, J=16.6 and 2.0 Hz), 2.75 (1H, dt, J=16.6 and 4.4 Hz), 2.50-2.26 (1H, br s), 2.20 (1H, dddd, J=3.9, 4.4, 9.8, and 14.7 Hz), 2.13 (1H, dddd, J=3.4, 4.4, 9.8, and 14.7 Hz), 1.82 (1H, dddd, J=3.4, 4.9, 9.8, and 14.7 Hz), 1.74 (1H, dddd, J=3.4, 4.9, 9.8, and 14.7 Hz), and 1.20 (9H, s); HR-FAB-ms, Calcd for $C_{14}H_{25}O_4BrCl$ (M+H), 371.0625. Found, m/z 371.0620. Calcd for $C_{14}H_{25}O_4{}^{81}BrCl$ (M+H), 373.0604 and for $C_{14}H_{25}O_4Br^{37}Cl$ (M+H), 373.0595. Found, 373.0598. Calcd for $C_{14}H_{25}O_4{}^{81}Br^{37}Cl$ (M+H), 375.0575. Found, 375.0577.

(2*R*,3*R*,5*S*,6*S*)-3-Bromo-5-chloro-6-(2'-oxoethyl)-2-(2'-pivaloyloxyethyl)tetrahydropyran (**59**).

$(COCl)_2$ (353 µl, 4.05 mmol) was slowly added to a cooled (-78 °C) and a stirred solution of DMSO (430 µl, 6.08 mmol) in dry CH_2Cl_2 (5 ml). After stirring of the mixture for 15 min, alcohol (**58**, 301 mg, 0.81 mmol) in CH_2Cl_2 (5 ml) was introduced by cannula and the container was washed into the reaction flask with the same solvent (5 ml), and stirring was continued at -78 °C for 15 min. TEA (1.1 ml, 8.1 mmol) was then dropwise added at -78 °C and the reaction mixture was allowed to warm to room temperature during a period of 1 h, stirred for an additional 30 min, and then poured onto a mixture of water (50 ml) and EtOAc (100 ml). The separated organic phase was washed with water (2 × 30 ml) and brine (30 ml), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, 33% EtOAc in hexane) to afford the aldehyde (**59**, 267 mg, 89%). **59**: a pale yellow oil; $[\alpha]_D^{25}$ +8.7° (c=2.25, $CHCl_3$); ir ($CHCl_3$), 2968, 2868, 1728, 1482, 1464, 1428, 1398, 1365, 1323, 1287, 1212, 1164, 1089, 1038, and 756 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ9.80 (1H, s), 4.25 (1H, dt, J=4.4 and 2.0 Hz), 4.22-4.11 (4H, m), 3.53 (1H, ddd, J=2.0, 4.4, and 8.8 Hz), 3.04 (1H, dd, J=7.3 and 18.1 Hz), 2.88 (1H, dd, J=5.9 and 18.1 Hz), 2.86 (1H, dt, J=16.6 and 2.0 Hz), 2.79 (1H, dt, J=16.6 and 4.4 Hz), 2.16 (1H, ddt, J=8.8, 14.2, and 5.4 Hz), 1.86 (1H, dddd, J=4.4, 6.4, 8.3, and 14.2 Hz), and 1.20 (9H, s); HR-FAB-ms, Calcd for $C_{14}H_{23}O_4BrCl$ (M+H), 369.0468. Found, m/z 369.0491. Calcd for $C_{14}H_{23}O_4{}^{81}BrCl$ (M+H), 371.0488 and for $C_{14}H_{23}O_4Br^{37}Cl$ (M+H), 371.0439. Found, 371.0461. Calcd for $C_{14}H_{23}O_4{}^{81}Br^{37}Cl$ (M+H), 373.0418. Found, 373.0438.

(2*R*,3*R*,5*S*,6*S*)-3-Bromo-6-[(2'*E*)-5'-*t*-butyldimethylsilyl-2'-pentenynyl]-5-chloro-2-(2'-pivaloyloxyethyl)-tetrahydropyran (**63**) and (2*R*,3*R*,5*S*,6*S*)-3-Bromo-6-[(2'*Z*)-5'-*t*-butyldimethylsilyl-2'-pentenynyl]-5-chloro-2-(2'-pivaloyloxyethyl)tetrahydropyran (**64**).

KHMDS (0.5 M solution in toluene, 1.66 ml, 0.83 mmol) was added dropwise to a suspension of phosphate (**62**, 385 mg, 0.97 mmol) and 18-crown-6 (255 mg, 0.97 mmol) in THF (7 ml) at -78 °C. The white suspension was soon turned to a pale yellow and clean solution, and stirred at the same temperature for 5 min. The aldehyde (**59**, 255 ml, 0.69 mmol) in THF (4 ml) was added dropwise by cannula and the container was washed with THF (3 ml) into the reaction flask. After stirring at -78 °C for 45 min, the reaction mixture was mixed with water (10 ml) and diluted with EtOAc (100 ml), and allowed to warm to room temperature. The mixture was washed with 5% HCl (30 ml), aqueous 5% $NaHCO_3$ (30 ml), and brine (30 ml), dried over Na_2SO_4, and concentrated *in vacuo*. The resulting residue was subjected to flash chromatography (SiO_2, 15% EtOAc in hexane) to give a mixture of the *E*-isomer (**63**) and the *Z*-isomer (**64**) (296 mg, 85%) in a ratio of 62:38. This mixture was used directly for the next step without further purification.

Analytical samples of **63** and **64** were obtained by further separation of the geometric isomers by hplc (Unisil Q 10.7 × 250 mm; 9% EtOAc in hexane; 4.0 ml/min flow; detected by uv at 254 nm).

E-isomer (**63**): t_R=12.2 min (above conditions); white crystals, mp 117-119 °C (recrystallized from ether-hexane); $[\alpha]_D^{25}$ +34.3° (c=1.90, $CHCl_3$); ir ($CHCl_3$), 3014, 2962, 2930, 2858, 1725, 1482, 1287, 1254, 1167, 1083, 960, and 825 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ6.12 (1H, ddd, J=6.8, 8.3, and 14.7 Hz), 5.86 (1H, dt, J=14.7 and 1.5 Hz), 4.20 (2H, ABX_2 pattern), 4.16 (1H, dt, J=4.4 and 2.0 Hz), 4.11 (1H, dt, J=4.4 and 2.0 Hz), 3.58 (1H, dt, J=6.8 and 2.0 Hz), 3.47 (1H, ddd, J=2.0, 4.4, and 8.3 Hz), 2.85 (1H, dt, J=16.6 and 2.0 Hz), 2.70 (1H, dt, J=16.6 and 4.4 Hz), 2.61 (1H, dddd, J=1.5, 6.8, 8.3, and 14.2 Hz), 2.49 (1H, ddt, J=1.5, 14.2, and 6.8 Hz), 2.19 (1H, ddt, J=8.3, 14.7, and 5.4 Hz), 1.89 (1H, ddt, J=4.4, 14.7, and 7.3 Hz), 1.12 (9H, s), 0.94 (9H, s), and 0.11 (6H, s); HR-FAB-ms, Calcd for $C_{23}H_{39}O_3BrClSi$ (M+H), 505.1540. Found, m/z 505.1522. Calcd for $C_{23}H_{39}O_3{}^{81}BrClSi$ (M+H), 507.1520 and for $C_{23}H_{39}O_3Br^{37}ClSi$ (M+H), 507.1511. Found, 507.1532. Calcd for $C_{23}H_{39}O_3{}^{81}Br^{37}ClSi$ (M+H), 509.1491. Found, 509.1519.

Z-isomer (**64**): t_R=12.9 min (above conditions); a colorless oil; $[\alpha]_D^{25}$ +2.6° (c=1.20, $CHCl_3$); ir ($CHCl_3$), 3010, 2962, 2936, 2834, 1725, 1482, 1287, 1254, 1167, 1083, 960, 840, and 828 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ6.05 (1H, ddd, J=6.4, 8.3, and 10.8 Hz), 5.62 (1H, d, J=10.8 Hz), 4.20 (2H, m), 4.16 (1H, dt, J=4.4 and 2.0 Hz), 4.09 (1H, dt, J=4.4 and 2.0 Hz), 3.68 (1H, ddd, J=2.0, 5.9, and 8.3 Hz), 3.47 (1H, ddd, J=2.0, 3.9, and 8.8 Hz), 2.85 (1H, dt, J=16.6 and 2.0 Hz), 2.83 (1H, m), 2.71 (1H, dt, J=16.6 and 4.4 Hz), 2.69 (1H, m), 2.20 (1H, ddt, J=8.8, 14.7, and 5.4 Hz), 1.87 (1H, dddd, J=3.9, 6.4, 8.3, and 14.7 Hz), 1.19 (9H, s), 0.95 (9H, s), and 0.13 (6H, s); HR-FAB-ms, Calcd for $C_{23}H_{39}O_3BrClSi$ (M+H), 505.1540. Found m/z 505.1532. Calcd for $C_{23}H_{39}O_3{}^{81}BrClSi$ (M+H), 507.1520 and for $C_{23}H_{39}O_3Br^{37}ClSi$ (M+H), 507.1511. Found, 507.1521. Calcd for $C_{23}H_{39}O_3{}^{81}Br^{37}ClSi$ (M+H), 509.1491. Found, 509.1474.

(2*R*,3*R*,5S,6S)-3-Bromo-6-[(2'*E*)-5'-*t*-butyldimethylsilyl-2'-pentenynyl]-5-chloro-2-(2'-hydroxyethyl)-tetrahydropyran (**65**) and (2*R*,3*R*,5*S*,6*S*)-3-Bromo-6-[(2'*Z*)-5'-*t*-butyldimethylsilyl-2'-pentenynyl]-5-chloro-2-(2'-hydroxyethyl)tetrahydropyran (**66**).

DIBAH (0.95 M solution in hexane, 2.4 ml, 2.28 mmol) was added to a stirred solution of pivaloates (**63**, *E*-isomer and **64**, *Z*-isomer) (290 mg, 0.57 mmol) in CH_2Cl_2 at -78 °C and stirring was continued at -78 °C → 40 °C for 1 h. The solution was diluted with EtOAc (100 ml), washed with 5% HCl (2 × 20 ml), aqueous 5% $NaHCO_3$ (30 ml), and brine (30 ml), dried over Na_2SO_4, and concentrated *in vacuo*. Flash chromatography (SiO_2, 33% → 50% EtOAc in hexane) of the residue afforded the *E*-isomer (**65**, less polar, Rf=0.37, SiO_2, 50% EtOAc in hexane, 147 mg, 61%) and the *Z*-isomer (**66**, more polar, Rf=0.22, above conditions, 91 mg, 38%).

E-isomer (**65**): white crystals, mp 100-102 °C (recrystallized from ether-hexane); $[\alpha]_D^{25}$ +29.1° (c=2.16,

$CHCl_3$); ir ($CHCl_3$), 3634, 3010, 2962, 2932, 2890, 2854, 2134, 1473, 1425, 1362, 1323, 1254, 1080, 1011, 960, 903, 840, and 828 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ6.13 (1H, ddd, J=6.8, 7.8, and 16.1 Hz), 5.69 (1H, dt, J=16.1 and 1.5 Hz), 4.19 (1H, dt, J=4.4 and 2.0 Hz), 4.12 (1H, dt, J=4.4 and 2.0 Hz), 3.87-3.76 (2H, m), 3.68-3.63 (2H, m), 2.84 (1H, dt, J=19.6 and 2.0 Hz), 2.71 (1H, dt, J=16.6 and 4.4 Hz), 2.61 (1H, dddd, J=1.5, 6.8, 7.3, and 14.2 Hz), 2.49 (1H, dddd, J=1.5, 6.8, 7.8, and 14.2 Hz), 2.14 (1H, dddd, J=4.4, 6.4, 8.8, and 14.7 Hz), 1.75 (1H, dddd, J=4.4, 4.9, 7.3, and 14.7 Hz), 1.64 (1H, br s), 0.94 (9H, s), and 0.12 (6H, s); HR-FAB-ms, Calcd for $C_{18}H_{31}O_2BrClSi$ (M+H), 421.0965. Found, m/z 421.0958. Calcd for $C_{18}H_{31}O_2{}^{81}BrClSi$ (M+H), 423.0945 and for $C_{18}H_{31}O_2Br{}^{37}ClSi$ (M+H), 423.0936. Found, 423.0959. Calcd for $C_{18}H_{31}O_2{}^{81}Br{}^{37}ClSi$ (M+H), 425.0915. Found, 425.0934.

Z-isomer (**66**): a colorless oil; $[\alpha]_D{}^{25}$ +7.4° (c=1.09, $CHCl_3$); ir ($CHCl_3$), 3650, 3012, 2964, 2932, 2894, 2860, 2130, 1473, 1427, 1365, 1258, 1078, 1010, 960, 908, 840, and 828 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ6.03 (1H, ddd, J=6.8, 7.8, and 10.8 Hz), 5.64 (1H, dt, J=10.8 and 1.5 Hz), 4.18 (1H, dt, J=4.4 and 2.0 Hz), 4.10 (1H, dt, J=4.4 and 2.0 Hz), 3.85-3.79 (2H, ABX_2 pattern), 3.76 (1H, ddd, J=2.0, 5.9, and 8.3 Hz), 3.65 (1H, ddd, J=2.0, 3.9, and 8.8 Hz), 2.90-2.81 (1H, m), 2.84 (1H, dt, J=16.6 and 2.0 Hz), 2.72 (1H, dt, J=16.6 and 4.4 Hz), 2.66 (1H, m), 2.16 (1H, dddd, J=4.9, 6.4, 8.8, and 14.7 Hz), 1.78 (1H, s), 1.73 (1H, dddd, J=3.9, 4.9, 6.8, and 14.7 Hz), 0.96 (9H, s), and 0.14 (6H, s); HR-FAB-MS, Calcd for $C_{18}H_{31}O_2BrClSi$ (M+H), 421.0965. Found, m/z 421.0963. Calcd for $C_{18}H_{31}O_2{}^{81}BrClSi$ (M+H), 423.0945 and for $C_{18}H_{31}O_2Br{}^{37}ClSi$ (M+H), 423.0936. Found, 423.0967. Calcd for $C_{18}H_{31}O_2{}^{81}Br{}^{37}ClSi$ (M+H), 425.0915. Found, 425.0934.

(2*R*,3*R*,5*S*,6*S*)-3-Bromo-6-[(2'*E*)-5-*t*-butyldimethylsilyl-2'-pentenynyl]-5-chloro-2-(2'-oxoethyl)tetrahydropyran (**67**).

$(COCl)_2$ (91 μl, 1.05 mmol) was added to a cooled (-78 °C) and stirred solution of DMSO (110 μl, 1.58 mmol) in dry CH_2Cl_2 (5 ml). After stirring for 15 min, alcohol (**65**, 90 mg, 0.21 mmol) in CH_2Cl_2 (3 ml) was added by cannula and the container was washed with the same solvent (2 ml) into the reaction flask, and stirring was continued at -78 °C for 15 min. TEA (293 μl, 2.10 mmol) was then dropwise added at -78 °C and the reaction mixture was allowed to warm to room temperature during a 1 h period, stirred for an additional 30 min, and then poured onto a mixture of water (30 ml) and EtOAc (100 ml). The separated organic phase was washed with water (2 × 30 ml) and brine (30 ml), dried over Na_2SO_4, and concentrated *in vacuo*. Flash chromatography (SiO_2, 25% EtOAc in hexane) of the residue gave the aldehyde (**67**, 88 mg, 100%). **67**: a pale yellow oil; $[\alpha]_D{}^{25}$ +23.5° (c=2.50, $CHCl_3$); ir ($CHCl_3$), 3010, 2932, 2854, 2152, 1728, 1473, 1425, 1362, 1323, 1254, 1080, 1008, 960, 840, and 825 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ9.80 (1H, s), 6.10 (1H, ddd, J=3.8, 8.3, and 16.1 Hz), 5.67 (1H, dt, J=16.1 and 1.5 Hz), 4.31 (1H, dt, J=4.4 and 2.0 Hz), 4.12 (1H, dt, J=4.4 and 2.0 Hz), 3.97 (1H, dt, J=2.0 and 6.4 Hz), 3.66 (1H, dt, J=2.0 and 6.8 Hz), 3.02 (1H, ddd, J=1.0, 6.4, and 18.6 Hz), 2.88 (1H, ddd, J=1.0, 6.4, and 18.6 Hz), 2.83 (1H, dt, J=16.6 and 2.0 Hz), 2.74 (1H, dt, J=16.6 and 4.4 Hz), 2.58 (1H, ddt, J=1.5, 14.7, and 6.8 Hz), 2.46 (1H, dddd, J=1.5, 6.8, 8.3, and 14.7 Hz), 0.94 (9H, s), and 0.12 (6H, s); HR-FAB-ms, Calcd for $C_{18}H_{29}O_2BrClSi$ (M+H), 419.0809. Found, m/z 419.0826. Calcd for $C_{18}H_{29}O_2{}^{81}BrClSi$ (M+H), 421.0788 and for $C_{18}H_{29}O_2Br{}^{37}ClSi$ (M+H), 421.0779. Found, 421.0787. Calcd for $C_{18}H_{29}O_2{}^{81}Br{}^{37}ClSi$ (M+H), 423.0759. Found, 423.0790.

(2*R*,3*R*,5*S*,6*S*)-3-Bromo-2-[(2'*E*)-3'-Bromo-2'-pentenyl]-6-[(2'*E*)-5'-*t*-butyldimethylsilyl-2'-pentenynyl]-5-chlorotetrahydropyran (**68**) and (2*R*,3*R*,5*S*,6*S*)-3-Bromo-2-[(2'*Z*)-3'-bromo-2'-pentenyl]-6-[(2'*E*)-5'-*t*-butyldimethylsilyl-2'-pentenynyl]-5-chlorotetrahydropyran (**69**).

BuLi (1.64 M solution in hexane, 192 μl, 0.32 mmol) was added to a stirred suspension of $Ph_3P^+CBr_2EtBr^-$ (174 mg, 0.32 mmol) in THF (2.0 ml) at -78 °C. After stirring for 30 min at -78 °C, a solution of **67** (88 ml, 0.21 mmol) in a mixed solvent of THF (1.0 ml) and DMSO (0.8 ml) was added by cannula at the

same temperature, and the container was washed with THF (1.0 ml) into the reaction flask. After stirred at -78 °C for 45 min, the reaction mixture was poured onto cooled (0 °C) water (20 ml), and extracted with EtOAc (3 × 3 ml). The combined extracts were washed with 5% HCl (20 ml), aqueous 5% $NaHCO_3$ (20 ml), and brine (30 ml), dried over Na_2SO_4, and concentrated *in vacuo*. Short flash chromatography (SiO_2, 14% EtOAc in hexane) of the residue afforded a mixture of the *E*- and the *Z*-bromo-olefins (**68** and **69**, 96 mg, an 87% combined yield). The *E*/*Z* ratio was estimated to be 83:17 by the ^{1}H-nmr method. Further purification by hplc (Unisil Q, 10.7 × 250 mm; 14% EtOAc in hexane; 4 ml/min flow ; detected by uv at 254 nm) provided the pure *E*-isomer (**68**, 69 mg) and the *Z*-isomer (**69**, 15 mg). **68**: t_R=7.2 min (under above conditions); a pale yellow oil; $[\alpha]_D^{25}$ -1.0° (c=0.84, $CHCl_3$); ir ($CHCl_3$), 3010, 2932, 2854, 2152, 1467, 1377, 1254, 1080, 1047, 963, 885, 840, and 828 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ6.13 (1H, ddd, J=6.8, 8.3, and 15.6 Hz), 5.78 (1H, dd, J=7.8 and 8.3 Hz), 5.68 (1H, branched d, J=15.6 Hz), 4.15 (1H, ddd, J=1.5, 2.0, and 4.4 Hz), 4.10 (1H, ddd, J=1.5, 2.0, and 4.4 Hz), 3.60 (1H, dt, J=1.5 and 6.8 Hz), 3.32 (1H, dt, J=1.5 and 4.8 Hz), 2.83 (1H, dt, J=16.6 and 2.0 Hz), 2.67 (1H, dt, J=16.6 and 4.4 Hz), 2.60 (1H, dddd, J=1.5, 6.8, 7.3, and 14.2 Hz), 2.55-2.44 (2H, m), centered at 2.50 (2H, q, J=7.3 Hz), 2.37 (1H, ddd, J=6.8, 8.3, and 14.7 Hz), 1.12 (3H, t, J=7.3 Hz), 1.12 (3H, t, J=7.3 Hz), 0.94 (9H, s), and 0.12 (6H, s); HR-FAB-ms, Calcd for $C_{21}H_{34}OBr_2ClSi$ (M+H), 523.0434. Found, m/z 523.0417. Calcd for $C_{21}H_{34}OBr^{81}BrClSi$ (M+H), 525.0414 and for $C_{21}H_{34}OBr_2{}^{37}ClSi$ (M+H), 525.0405. Found, 525.0397. Calcd for $C_{21}H_{37}O^{81}Br_2ClSi$ (M+H), 527.0393 and for $C_{21}H_{34}OBr^{81}Br^{37}ClSi$ (M+H), 527.0384. Found, 527.0405. Calcd for $C_{21}H_{34}O^{81}Br_2{}^{37}ClSi$ (M+H), 529.0364. Found, 529.0401.
Z-isomer (**69**): t_R=6.6 min (under above conditions); a pale yellow oil; ir ($CHCl_3$), 3010, 2932, 2854, 2150, 1467, 1375, 1253, 1082, 965, 857, and 840 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ6.15 (1H, ddd, J=6.8, 8.3, and 15.6 Hz), 5.78 (1H, dd, J=6.4 and 7.8 Hz), 5.68 (1H, dt, J=15.6 and 1.5 Hz), 4.15 (1H, dt, J=4.6 and 2.0 Hz), 4.09 (1H, dt, J=4.6 and 2.0 Hz), 3.61 (1H, ddd, J=2.0, 5.9, and 7.8 Hz), 3.42 (1H, ddd, J=2.0, 5.4, and 8.3 Hz), 2.82 (1H, dt, J=16.1 amd 2.0 Hz), 2.69 (1H, dt, J=16.1 and 4.6 Hz), 2.69-2.60 (2H, m), 2.51-2.40 (4H, m), 1.12 (3H, t, J=7.3 Hz), 0.94 (9H, s), and 0.11 (6H, s).

Isodactylyne (**2**).

A mixture of TBAF-HF (pH=4.5, 35μl, ca. 35 μmol of F$^-$) prepared from a 1.0 M solution of TBAF in THF and 48% HF in a ratio of 13:1 was added to a solution of **68** (15 mg, 28 μmol) in THF (1.2 ml) at -5 °C and stirring was continued at -5 °C for 1 h, and at -5 → 0 °C for an additional 1 h. The reaction mixture was diluted with EtOAc (50 ml), washed with water (15 ml) and brine (20 ml), dried over Na_2SO_4, and concentrated in *vacuo*. The residue was purified by hplc (Unisil Q, 10.7 × 250 mm; 80% hexane-17% CH_2Cl_2-3% MeCN; 4ml/min flow; detected by uv at 228 nm) to yield a pure material (9 mg, 79%) which was identical with isodactylyne by comparison of their specific rotations and ^{1}H-nmr spectra. **2**: t_R=8.1 min (under above conditions); Rf=0.46 (1:1 of PhH-hexane, SiO_2)[lit.[2] Rf=0.46 (1:1 of PhH-hexane, SiO_2)][2]; a colorless oil; $[\alpha]_D^{25}$ -8.2° (c=1.80, $CHCl_3$) [lit.[2] $[\alpha]_D^{25}$ -8.06° (c=0.797, $CHCl_3$)]; ir ($CHCl_3$), 3304, 3010, 2974, 2932, 2836, 1464, 1428, 1353, 1323, 1263, 1086, 1017, 963, 885, 645, and 615 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ6.20 (1H, ddd, J=6.8, 8.3, and 16.1 Hz), 5.78 (1H, dd, J=6.8 and 8.8 Hz), 5.64 (1H, ddt, J=2.4, 16.1, and 2.0 Hz), 4.15 (1H, dt, J=4.4 and 2.0 Hz), 4.15 (1H, dt, J=4.4 and 2.0 Hz), 4.09 (1H, dt, J=4.4 and 2.0 Hz), 3.61 (1H, dt, J=2.0 and 6.8 Hz), 3.33 (1H, dt, J=2.0 and 6.8 Hz), 2.84 (1H, d, J=2.4 Hz), 2.83 (1H, dt, J=16.6 and 2.0 Hz), 2.67 (1H, dt, J=16.6 and 4.4 Hz), 2.64 (1H, m), 2.55-2.45 (4H, m), 2.40 (1H, ddd, J=6.8, 8.3, and 14.7 Hz), and 1.12 (3H, t, J=7.3 Hz); HR-FAB-ms, Calcd for $C_{15}H_{20}OBr_2Cl$ (M+H), 408.9569. Found, m/z 408.9549. Calcd for $C_{15}H_{20}OBr^{81}BrCl$ (M+H), 410.9549 and for $C_{15}H_{20}OBr_2{}^{37}Cl$ (M+H), 410.9540. Found, 410.9569. Calcd for $C_{15}H_{20}O^{81}Br_2Cl$ (M+H), 412.9529 and for $C_{15}H_{20}OBr^{81}Br^{37}Cl$ (M+H), 412.9520. Found, 412.9531. Calcd for $C_{15}H_{20}O^{81}Br_2{}^{37}Cl$ (M+H), 414.9499. Found, 414.9478.

(2*R*,3*R*,5*S*,6*S*)-3-Bromo-6-[(2'*Z*)-5'-*t*-butyldimethylsilyl-2'-pentenynyl]-5-chloro-2-(2'-oxoethyl)tetrahydropyran (**70**).

$(COCl)_2$ (110 µl, 1.25 mmol) was added to a cooled (-78 °C) and stirred solution of DMSO (133 µl, 1.88 mmol) in dry CH_2Cl_2 (5 ml) and the mixture was stirred for 15 min. The alcohol (**66**, 106 mg, 0.25 mmol) in CH_2Cl_2 (3 ml) was then introduced by cannula and the container was washed with the same solvent (2 ml) into the reaction flask, and stirring was continued at -78 °C for 15 min. TEA (350 µl, 2.50 mmol) was added at -78 °C and the reaction mixture was allowed to warm to room temperature during a period of 1 h, stirred for an additional 30 min and then poured onto a mixture of water (30 ml) and EtOAc (100 ml). The separated organic layers were washed with water (2 × 30 ml) and brine (30 ml), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was subjected to flash chromatography (SiO_2, 33% EtOAc in hexane) to furnish the aldehyde (**70**, 100 mg, 95%). **70**: a pale yellow oil; $[\alpha]_D^{25}$ +9.7° (c=3.68, $CHCl_3$); ir ($CHCl_3$), 3010, 2932, 2854, 1726, 1471, 1423, 1362, 1324, 1252, 1080, 1008, 958, 838, and 825 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ9.80 (1H, s), 6.00 (1H, ddd, J=6.8, 8.3, and 10.7 Hz), 5.62 (1H, d, J=10.7 Hz), 4.30 (1H, dt, J=4.4 and 2.0 Hz), 4.10 (1H, dt, J=4.4 and 2.0 Hz), 3.97 (1H, ddd, J=2.0, 5.9, and 6.8 Hz), 3.76 (1H, ddd, J=2.0, 5.9, and 7.8 Hz), 3.02 (1H, ddd, J=1.0, 6.8, and 18.1 Hz), 2.87-2.77 (3H, m), 2.76 (1H, dt, J=16.1 and 4.4 Hz), 2.68 (1H, dddd, J=1.0, 5.8, 7.8, and 14.7 Hz), 0.95 (9H, s), and 0.13 (6H, s); HR-FAB-ms, Calcd for $C_{18}H_{29}O_2BrClSi$ (M+H), 419.0809. Found, m/z 419.0820. Calcd for $C_{18}H_{29}O_2{}^{81}BrClSi$ (M+H), 421.0788 and for $C_{18}H_{29}O_2Br^{37}ClSi$ (M+H), 421.0779. Found, 421.0788. Calcd for $C_{18}H_{29}O_2{}^{81}Br^{37}ClSi$ (M+H), 423.0759. Found, 423.0741.

(2*R*,3*R*,5*S*,6*S*)-3-Bromo-2-[(2'*E*)-3'-bromo-2'-pentenyl]-6-[(2'*Z*)-5'-*t*-butyldimethylsilyl-2'-pentenynyl]-5-chlorotetrahydropyran (**71**) and (2*R*,3*R*,5*S*,6*S*)-3-Bromo-2-[(2'*Z*)-3'-bromo-2'-pentenyl]-6-[(2'*Z*)-5'-*t*-butyldimethylsilyl-2'-pentenynyl]-5-chlorotetrahydropyran (**72**).

BuLi (1.64 M solution in hexane, 75 µl, 0.12 mmol) was added to a stirred suspension of $Ph_3P^+CBr_2EtBr^-$ (72 mg, 0.13 mmol) in THF (0.75 ml) at -78 °C and the mixture was stirred for 45 min at the same temperature. Aldehyde (**70**, 37 mg, 0.09 mmol) in a mixed solvent of THF (0.75 ml) and DMSO (0.5 ml) was added by cannula at -78 °C and the container was washed with THF (1.0 ml) into the reaction flask. After stirred at the same temperature for 45 min, the reaction mixture was poured onto cooled (0 °C) water (20 ml), and then extracted with EtOAc (3 × 30 ml). The combined extracts were washed with 5% HCl (20 ml), aqueous 5% $NaHCO_3$ (20 ml), and brine (30 ml), dried over Na_2SO_4, and concentrated *in vacuo*. Short flash chromatography (SiO_2, 13% → 25% EtOAc in hexane) of the residue afforded a mixture of the *E*- and *Z*-bromoolefins (**71** and **72**, 31 mg, a 67% combined yield) along with the starting **70** (6 mg, 17%). The ratio of *E*/*Z* was estimated to be an 82:18 by the ^{1}H-nmr spectrum. Further purification by hplc (Unisil Q, 10.7 × 250 mm; 13% EtOAc in hexane; 4 ml/min flow; detected by uv at 254 nm) provided the pure *E*-isomer (**71**, 23 mg) and the *Z*-isomer (**72**, 5 mg). **71**: t_R =7.5 min (under above conditions); a colorless oil ; $[\alpha]_D^{25}$ -14.2° (c=1.40, $CHCl_3$); ir ($CHCl_3$), 3010, 2932, 2854, 2142, 1467, 1426, 1362, 1321, 1254, 1080, 1008, 912, 885, 846, and 825 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ6.03 (1H, ddd, J=6.8, 8.3, and 10.7 Hz), 5.78 (1H, dd, J=7.3 and 8.3 Hz), 5.64 (1H, d, J=10.6 Hz), 4.15 (1H, dt, J=4.4 and 2.0 Hz), 4.08 (1H, dt, J=4.4 and 2.0 Hz), 3.71 (1H, ddd, J=2.0, 5.9, and 6.4 Hz), 3.32 (1H, dt, J=2.0 and 6.8 Hz), 2.87-2.80 (2H, m), 2.73-2.64 (2H, m), 2.55-2.47 (3H, m), 2.38 (1H, ddd, J=6.4, 8.3, and 14.7 Hz), 1.12 (3H, t, J=7.3 Hz), 0.96 (9H, s), and 0.14 (6H, s); HR-FAB-ms, Calcd for $C_{21}H_{34}OBr_2ClSi$ (M+H), 523.0434. Found, m/z 523.0461. Calcd for $C_{21}H_{34}OBr^{81}BrClSi$ (M+H), 525.0414 and for $C_{21}H_{34}OBr_2{}^{37}ClSi$ (M+H), 525.0405. Found, 525.0397. Calcd for $C_{21}H_{34}O^{81}Br_2ClSi$ (M+H), 527.0393 and for $C_{21}H_{34}OBr^{81}Br^{37}ClSi$ (M+H), 527.0384. Found, 527.0398. Calcd for $C_{21}H_{34}O^{81}Br_2{}^{37}ClSi$ (M+H), 529.0364. Found, 529.0374.

Z-isomer (**72**): t_R=7.2 min (under above conditions); a colorless oil ; ir ($CHCl_3$), 3010, 2932, 2854, 2146,

1465, 1373, 1251, 1080, 965, 885, and 840 cm^{-1} ; ^{1}H-nmr ($CDCl_3$), δ6.05 (1H, ddd, J=6.8, 7.8, and 10.7 Hz), 5.77 (1H, dd, J=6.4 and 7.3 Hz), 5.63 (1H, d, J=10.7 Hz), 4.15 (1H, dt, J=4.4 and 2.0 Hz), 4.08 (1H, dt, J=4.4 and 2.0 Hz), 3.71 (1H, ddd, J=2.0, 5.9, and 6.4 Hz), 3.42 (1H, ddd, J=2.0, 5.9, and 7.8 Hz), 2.86-2.81 (2H, m), 2.73-2.63 (3H, m), 2.50-2.42 (3H, m), 1.12 (3H, t, J=7.3 Hz), 0.96 (9H, s), and 0.13 (6H, s).

Dactylyne (**1**).

A mixture of TBAF-HF (pH≈4.5, 46 μl, ca. 46 μmol of F^-) prepared from a 1.0 M solution of TBAF in THF and 48% HF in a ratio of 13:1 was added to a solution of **71** (20 mg, 38 μmol) in THF (1.2 ml) at -5 °C and stirring was continued at -5 °C for 1 h and at -5 → 0 °C for an additional 1 h. The reaction mixture was diluted with EtOAc (50 ml), washed with water (15 ml) and brine (20 ml), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by hplc (Unisil Q, 10.7 × 250 mm; 80% hexane-17% CH_2Cl_2-3% MeCN; 4 ml/min flow; detected by uv at 228 nm) to yield a pure material (13 mg, 82%), which was identical with dactylyne by comparison of their specific rotations, mps, and ^{1}H-nmr spectra. **1**: t_R=7.4 min (above conditions); Rf=0.57 (1:1 of PhH-hexane, SiO_2) [lit.[1] Rf=0.57 (1:1 of PhH-hexane, SiO_2)]; white crystals, mp 62.5-63.2 °C (recrystallized from ether-hexane) (lit.[1] mp 62.2-63.3°C); $[\alpha]_D^{25}$ -37.6° (c=2.10, $CHCl_3$) [lit.[1] $[\alpha]_D^{25}$ -36° (c=15.2, $CHCl_3$)]; ir ($CHCl_3$), 3304, 3010, 2980, 2830, 1428, 1356, 1323, 1083, 885, 786, 750, 645, and 615 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ6.10 (1H, dddd, J=1.0, 7.3, 7.3, and 10.3 Hz), 5.79 (1H, dd, J=7.3 and 8.3 Hz), 5.60 (1H, ddt, J=1.0, 10.3, and 2.0 Hz), 4.15 (1H, dt, J=4.9 and 2.0 Hz), 4.11 (1H, dt, J=4.9 and 2.0 Hz), 3.68 (1H, ddd, J=2.0, 5.9, and 7.8 Hz), 3.34 (1H, ddd, J=2.0, 6.4, and 6.8 Hz), 3.14 (1H, d, J=2.0 Hz), 2.83 (1H, dt, J=16.6 and 2.0 Hz), 2.82 (1H, m), 2.72 (1H, m), 2.71 (1H, dt, J=16.6 and 4.9 Hz), 2.56-2.47 (3H, m), 2.39 (1H, ddd, J=6.4, 8.3, and 14.7 Hz), and 1.12 (3H, t, J=7.3 Hz); HR-FAB-ms, Calcd for $C_{15}H_{20}OBr_2Cl$ (M+H), 408.9569. Found, m/z 408.9565. Calcd for $C_{15}H_{20}OBr^{81}BrCl$ (M+H), 410.9549 and for $C_{15}H_{20}OBr_2{}^{37}Cl$ (M+H), 410.9540. Found, 410.9530. Calcd for $C_{15}H_{20}O^{81}Br_2Cl$ (M+H), 412.9529 and for $C_{15}H_{20}OBr^{81}Br^{37}Cl$ (M+H), 412.9520. Found, 412.9506. Calcd for $C_{15}H_{20}O^{81}Br_2{}^{37}Cl$ (M+H), 414.9499. Found, 414.9496.

REFERENCES AND NOTES

1. F. J. McDonald, D. C. Campbell, D. J. Vanderah, F. J. Schmitz, D. M. Washecheck, J. E. Burks, and D. van der Helms, *J. Org. Chem.*, 1975, **40**, 665.
2. D. J. Vanderah and F. J. Schmitz, *J. Org. Chem.*, 1976, **41**, 3480.
3. P. N. Kaul and S. K. Kulkarni, *J. Pharm. Sci.*, 1978, **67**, 1293.
4. P. N. Kaul and S. K. Kulkarni, *Pharmacologist*, 1976, **19**, 166.
5. P. N. Kaul and S. K. Kulkarni, and E. Kurosawa, *J. Pharm. Pharmac.*, 1978, **30**, 589.
6. Y. Goopichand, F. J. Schmitz, J. Shelly, A. Rahman, and D. van der Helm, *J. Org. Chem.*, 1981, **46**, 5192.
7. L.-x. Gao and A. Murai, *Tetrahedron Lett.*, 1992, **33**, 4349.
8. L.-x. Gao and A. Murai, *Chem. Lett.*, **1989**, 357.
9. L.-x. Gao and A. Murai, *Chem. Lett.*, **1991**, 1503.
10. L.-x. Gao, H. Saitoh, F. Feng, and A. Murai, *Chem. Lett.*, **1991**, 1787.
11. S. Takano, T. Sugihara, and K. Ogasawara, *Tetrahedron Lett.*, 1991, **32**, 2797.
12. M. Yamaguchi and I. Hirao, *Tetrahedron Lett.*, 1983, **24**, 391.
13. Y. Ogawa and M. Shibasaki, *Tetrahedron Lett.*, 1984, **25**, 663.
14. S. E. Denmark and T. K. Jones, *J. Org. Chem.*, 1982, **47**, 4595.
15. Y. Gao, R. M. Hanson, J. M. Klander, S. Y. Ko, H. Masamune, and K. B. Sharpless, *J. Am. Chem. Soc.*, 1987, **109**, 5765.
16. (2*S*,3*S*)-2-Bromo-3-chloro-6-oxooctane-1,8-diol 8-Pivaloate (**30**): a colorless oil; ir ($CHCl_3$), 3550,

2980, 1725, 1287, and 1181cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ4.43 (2H, t, J=6.4 Hz), 4.31-4.24 (2H, m), 3.96 (2H, d, J=6.8 Hz), 2.75 (2H, t, J=6.4 Hz), 2.71 (2H, t, J=7.3 Hz), 2.22 (1H, ddt, J=2.9, 14.6, and 7.3 Hz), 2.09 (1H, m), 2.20-1.90 (1H, br s), and 1.17 (9H, s); ^{13}C-nmr ($CDCl_3$), δ206.6 (C-6), 178.5 (COO), 64.7 (C-8), 61.1 (C-2), 59.5 (C-1), 59.4 (C-3), 41.8 (C-7), 39.7 (C-5), 38.8 (Me_3C), 30.2 (C-4), and 27.2 (3 × Me); LR-FAB-ms, m/z 407, 405, 403, 361, 359, 357, 343, 341, 339, 251, 249, 247, 241, 239, 231, 186, 85, and 57 (base). *Anal.* Calcd for $C_{13}H_{22}O_4BrCl$: C, 43.52; H, 6.26; Br, 22.18; Cl, 9.83. Found:C, 43.66; H, 6.20; Br, 22.34; Cl, 9.91.

17. (2*R*,3*S*,5*R*,6*R*)-5-Bromo-1,3-dichlorooctane-2,6,8-triol 8-Pivaloate (**31**): a colorless oil; ir ($CHCl_3$), 3481, 2975, 1726, 1480, 1462, 1375, 1279, 1250, 1044, and 902 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ4.42 (1H, ddd, J=2.0, 5.9, and 8.8 Hz), 4.31 (1H, ddd, J=4.9, 8.3, and 11.2 Hz), 4.20 (1H, dt, J=11.2 and 5.4 Hz), 4.11 (1H, ddd, J=4.4, 7.3, and 9.3 Hz), 3.94 (1H, m), 3.85 (2H, ABX pattern, J_{AX}=3.9, J_{BX}=4.9, and J_{AB}=11.2 Hz), 3.68 (1H, m), 2.86 (1H, ddd, J=4.4, 8.8, and 14.7 Hz), 2.57 (1H, d, J=6.8 Hz), 2.41 (1H, ddd, J=5.9, 9.3, and 14.7 Hz), 2.20 (1H, d, J=8.8 Hz), 2.03-1.87 (2H, m), and 1.21 (9H, s); LR-FAB-ms, m/z 399, 397, 395, 393, 381, 379, 377, 375, 279, 277, 275, 273, 261, 259, 257, 255, 85, 73, and 57 (base). *Anal.* Calcd for $C_{13}H_{22}O_4BrCl$: C, 39.62; H, 5.88; Br, 20.27; Cl, 17.99. Found: C, 39.61; H, 5.94; Br, 20.21; Cl, 17.96.

18 Cf. M. Hashimoto, T. Kan, K. Nozaki, M. Yanagiya, H. Shirahama, and T. Matsumoto, *J. Org. Chem.*, 1990, **55**, 5088.

19. J. S. Yadav, M. C. Chander, and B. V. Joshi, *Tetrahedron Lett.*, 1988, **29**, 2737.

20. (1*R*,4*S*,5*S*,6*S*)-5-Bromo-4-chloro-1-(2'-pivaloyloxyethyl)-8,9-dioxabicyclo[4.2.1]nonane (**54**): a pale yellow oil; ir (neat), 2972, 2952, 1726, 1482, 1462, 1400, 1368, 1286, 1160, 1088, 1062, 1036, 892, 754, and 674 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ4.52 (1H, dd, J=2.9 and 7.8 Hz), 4.29 (1H, dt, J=11.2 and 6.8 Hz), 4.17-4.11 (2H, m), 3.69 (1H, d, J=7.8 Hz), 3.42 (1H, dd, J=7.8 and 8.3 Hz), 3.24 (1H, dd, J=2.9 and 8.3 Hz), 1.92-1.78 (3H, m), 1.69 (1H, ddt, J=3.4, 15.1, and 11.2 Hz), 1.46 (1H, ddd, J=3.4, 5.4, and 14.7 Hz), and 1.21 (1H, ddd, J=3.9, 10.2, and 14.7 Hz); HR-FAB-ms, Calcd for $C_{14}H_{23}O_4BrCl$ (M+H), 369.0468. Found, m/z 369.0455. Calcd for $C_{14}H_{23}O_4{}^{81}BrCl$ (M+H), 371.0488 and for $C_{14}H_{23}O_4Br^{37}Cl$ (M+H), 371.0439. Found, 371.0461. Calcd for $C_{14}H_{23}O_4{}^{81}Br^{37}Cl$ (M+H), 373.0418. Found, 373.0434.

21. (2*S*,3*S*,4*S*)-3-Bromo-4-chloro-7-oxononane-1,2,9-triol 9-Pivaloate (**55**): a pale yellow oil; ir ($CHCl_3$), 3553, 2960, 2932, 1726, 1464, 1285, and 1179 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ4.49 (1H, ddd, J=2.0, 3.4, and 9.3 Hz), 4.33 (2H, m), 4.18 (1H, dd, J=2.0 and 9.3 Hz), 4.05-3.90 (3H, m), 2.82-2.70 (5H, m), 2.19 (1H, ddt, J=10.3, 14.7, and 6.4 Hz), 2.09 (1H, ddt, J=3.9, 14.7, and 7.3 Hz), 2.04 (1H, s), and 1.17 (9H, s).

22. E. J. Corey and P. B. Hopkins, *Tetrahedron Lett.*, 1982, **23**, 1979.

23. Cf. M. K. Das and J. J. Zuckerman, *Inorg. Chem.*, 1971, **10**, 1028.

24. S. L. Huang, A. G. Mancuso, and D. Swern, *J. Org. Chem.*, 1978, **63**, 2480.

25. E. J. Corey and C. Rucker, *Tetrahedron Lett.*, 1982, **23**, 719.

26. The new Horner-Wittig-type reagent (**62**) was prepared as follows: readily available propargyl alcohol THP-ether was converted to 3-*tert*-butyldimethylsilyl-2-propyn-1-ol in a two-step process [(i) BuLi, TBSCl, THF, 20 °C, 2 h ; (ii) PTS, MeOH, 20 °C, 1 h] in a 90% total yield. The alcohol was treated with NBS and Me_2S in CH_2Cl_2 at 20 °C for 7 h to yield the corresponding bromo derivative in 86% yield, which gave rise to **62** in 11% yield on reaction with tris(2,2,2-trifluoro-ethyl)phosphite at 130 °C (neat) for 48 h. **62**: bp 86-87 °C/0.05 mmHg; ir (neat), 2938, 2896, 2860, 2182, 1467, 1422, 1269, 1188, 1074, 966, 885, 840, 825, 810, and 777 cm^{-1}; ^{1}H-nmr ($CDCl_3$), δ4.52-3.97 (4H, m), 2.99 (2H, d, J=23.1 Hz), 0.92 (9H, s), and 0.08 (6H, s).

27. R. H. Smithers, *J. Org. Chem.*, 1978, **43**, 2833.

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