stirred for 40 min under reflux. The solution was coevaporated with methanol, and the product was purified by a silica gel preparative TLC (10:1 (v/v) dichloromethane–methanol) to give 3.0 mg (62%) of **2** as white crystals: R_f on TLC 0.40 (10:1 (v/v) dichloromethane–methanol); $[\alpha]^{21}_D$ −8° (c 0.23, methanol); IR (KBr) 3430, 1710 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 9.93 (s, 1 H, H-6), 5.76 (s, 1 H, H-1′), 4.65 (m, 1 H, H-5′), 4.61 (dd, 1 H, J = 3 Hz, 12 Hz, H-7′), 4.31 (d, 1 H, J = 4.5 Hz, H-2′), 4.11 (dd, 1 H, J = 2 Hz, 10 Hz, H-4′), 3.94 (dd, 1 H, J = 10 Hz, 4.5 Hz, H-3′), 3.86, 3.78 (each s, each 3 H, methyl ester × 2), 2.22 (dt, 1 H, J = 15 Hz, 3 Hz, H-6′e), 1.83 (ddd, 1 H, J = 15 Hz, 13 Hz, 3 Hz, H-6′a); MS calcd for $C_{15}H_{18}N_2O_{10}$ m/z 386.26, found (M + 1) 387.

Acknowledgment. We express our sincere thanks to Masazumi Kameda for recording the IR spectra and Akio Takahashi for his elemental analyses. We also thank Dr. Kin-ichi Tadano (Department of Chemistry, Faculty of Science and Technology, Keio University), Shigeko Miki, and Masayuki Ito (Meiji Seika Kaisha, Ltd.) for measurement of the mass spectra. We also thank Prof. S. Danishefsky (Yale University) for providing us the ^1H NMR spectrum of an authentic sample of **2**.

Registry No. **1**, 55728-21-7; **2**, 101696-63-3; **3**, 106180-08-9; **4**, 15186-48-8; **6a**, 111689-96-4; **6b**, 111717-87-4; **7**, 111689-97-5; **8**, 111689-98-6; **9a**, 111689-99-7; **9b**, 111690-00-7; **10a**, 111690-01-8; **10b**, 111690-02-9; **11a**, 111690-03-0; **11b**, 111690-04-1; **12a**, 111690-05-2; **12b**, 111690-06-3; **13a**, 111690-07-4; **13b**, 111717-88-5; **14a**, 111690-08-5; **14b**, 111690-09-6; **15a**, 111690-10-9; **15b**, 111690-11-0; **16**, 111690-12-1; **17a**, 111690-13-2; **17b**, 111690-14-3; **18**, 111690-15-4; **19**, 111690-16-5; **20**, 111690-17-6; **21**, 111690-18-7; **22**, 111690-19-8; **23**, 111690-20-1; methyl 2,4-dihydroxypyrimidine-5-carboxylate, 42821-92-1.

Synthesis and Structural Revision of (7*E*)- and (7*Z*)-Punaglandin 4[1]

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A convergent synthesis of antineoplastic (7*E*)- and (7*Z*)-punaglandin 4 is described, dictating revision of the originally postulated structures, **1** and **2**, to the stereoisomers, **3** and **4**, respectively. Condensation of (*R*)-3-chloro-4-(*tert*-butyldimethylsiloxy)-2-cyclopentenone (**5**) and the organolithium derivative generated from 3-(trimethylstannyl)-1,2-octadiene (**27**) and methyllithium gives after desilylation the crystalline acetylenic diol **28**. Partial hydrogenation of the triple bond using Lindlar catalyst followed by oxidation of the secondary alcohol with pyridinium dichromate affords the hydroxy enone **31**. The whole punaglandin skeleton is constructed by aldol condensation of the silyl-protected hydroxycyclopentenone **32** and (2*R*,3*S*)-2,3-diacetoxy-6-carbomethoxyhexanal (**7**). Dehydration of the resulting aldol followed by removal of the silyl protective group leads to a mixture of **3** and **4**, identical with the naturally occuring sample in all respects. The enantiomers and some other stereoisomers exhibit similar inhibitory effects on L1210 leukemia cell proliferation.

Prostaglandin (PG) chemistry has now entered a new stage by adding newly discovered antineoplastic activity[2] to their properties as powerful local hormones maintaining the homeostasis of the human body. Punaglandins (PUGs), PUG 1–PUG 4, are halogenated eicosanoids first isolated from a Hawaiian octacoral, *Telesto riisei*.[3] PUG 1 and 2 are chlorinated cyclopentenone derivatives having the functionalized seven-carbon and unsaturated eight-carbon side chains. PUG 3 and 4 formally result from elimination of acetic acid from PUG 1 and 2, respectively, and possess the cross-conjugated dienone structures. Both 7*E* and 7*Z* isomers are natural products. PUG 3 and 4 among others have received particular attention because of the potent inhibitory effect on L1210 leukemia cell proliferation.[4] Their potency of IC_{50} 0.02 μg/mL[4] is 10- to 15-fold greater than that of the corresponding non-chlorinated compounds such as clavulone[5] (or claviridenone[6]), PGJ_2,[7] Δ^{12}-PGJ_2,[8] or Δ^7-PGA_1.[9] The relative configurations of these important materials have been postulated[3] on the basis of spectroscopic data and an assumed mechanism of chemical transformation, and the absolute configurations have been suggested by assuming stereochemical analogy of C-12 oxygenation with the related octacoral-derived clavulones[5] (or claviridenones[6]). However, because these grounds seemed not sufficiently

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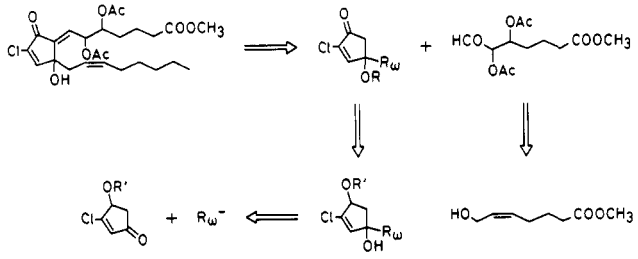
[‡] University of Hawaii at Manoa.

(1) Prostaglandin synthesis 15. Part 14: Suzuki, M.; Koyano, H.; Noyori, R. *J. Org. Chem.* **1987**, *52*, 5583.
(2) (a) Prasad, K. N. *Nature (London), New Biol.* **1972**, *236*, 49. (b) Santoro, M. G.; Philpott, G. W.; Jaffe, B. M. *Nature (London)* **1976**, *263*, 777. (c) Honn, K. V.; Dunn, J. R., II; Morgan, L. R.; Bienkowski, M.; Marnett, L. J. *Biochem. Biophys. Res. Commun.* **1979**, *87*, 795. (d) Fukushima, M.; Kato, T.; Ueda, R.; Ota, K.; Narumiya, S.; Hayaishi, O. *Ibid.* **1982**, *105*, 956.
(3) Baker, B. J.; Okuda, R. K.; Yu, P. T. K.; Scheuer, P. J. *J. Am. Chem. Soc.* **1985**, *107*, 2976.
(4) Fukushima, M.; Kato, T. *Advances in Prostaglandin, Thromboxane, and Leukotriene Research*; Hayaishi, O., Yamamoto, S., Eds; Raven: New York, 1985; Vol. 15, p 415.
(5) Kikuchi, H.; Tsukitani, Y.; Iguchi, K.; Yamada, Y. *Tetrahedron Lett.* **1982**, *23*, 5171.
(6) Kobayashi, M.; Yasuzawa, T.; Yoshihara, M.; Akutsu, H.; Kyogoku, Y.; Kitagawa, I. *Tetrahedron Lett.* **1982**, *23*, 5331.
(7) Fukushima, M.; Kato, T.; Ohta, K.; Arai, Y.; Narumiya, S.; Hayaishi, O. *Biochem. Biophys. Res. Commun.* **1982**, *109*, 626.
(8) (a) Fukushima, M.; Kato, T. *Icosanoids and Cancer*; Thaler-Dao, H., de Paulet, A. C., Paoletti, R., Eds.; Raven: New York, 1984, p 277. (b) Kikawa, Y.; Narumiya, S.; Fukushima, M.; Wakatsuka, H.; Hayaishi, O. *Proc. Natl. Acad. Sci. U.S.A.* **1984**, *81*, 1317. (c) Kato, T.; Fukushima, M.; Kurozumi, S.; Noyori, R. *Cancer Res.* **1986**, *46*, 3538.
(9) Sugiura, S.; Toru, T.; Tanaka, T.; Hazato, A.; Okamura, N.; Bannai, K.; Manabe, K.; Kurozumi, S.; Noyori, R. *Chem. Pharm. Bull.* **1984**, *32*, 4658. See also ref 8c.

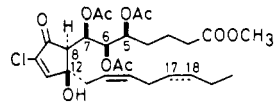
0022-3263/88/1953-0286$01.50/0

Scheme I. Retrosynthesis of Punaglandin 4

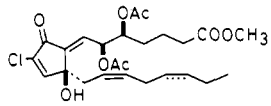


firm,[10] we were intrigued to elucidate these structures by an unambiguous chemical synthesis using stereo-defined building blocks. The following stereoauthentic synthesis of (7E)- and (7Z)-PUG 4 dictates the structural revision from the original formulas, **1** and **2**, to the stereoisomers, **3** and **4**, respectively.[11,12]

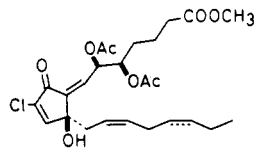
Original structures:



PUG 1: 17,18-unsaturated
PUG 2: 17,18-saturated

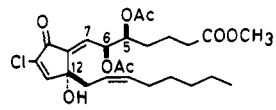


(7E)-PUG 3: 17,18-unsaturated
1, (7E)-PUG 4: 17,18-saturated

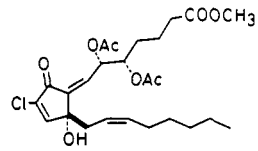


(7Z)-PUG 3: 17,18-unsaturated
2, (7Z)-PUG 4: 17,18-saturated

Revised structures:



3, (7E)-PUG 4

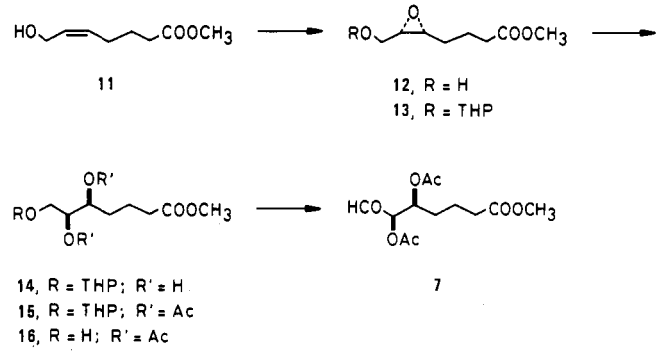


4, (7Z)-PUG 4

Results and Discussion

Our retro-synthetic analysis of PUG 4 is described in Scheme I. PUG 4 having a 5-alkylidene-2-cyclopentenone structure can be simplified into a chlorinated cyclopentenone and an α side chain aldehyde moiety equivalent to a retro-aldol condensation. The cyclopentenone moiety is further transformed, via a cyclopentenediol, ultimately to 4-hydroxy-2-cyclopentenone and the ω side chain component. All chiral building blocks are available in optically pure forms. (4R)- and (4S)-cyclopentenones **5** and **6** can be prepared from 2,4,6-trichlorophenol in four steps including optical resolution,[13] and the diacetoxy aldehyde having the 2R,3S, 2S,3R, 2S,3S, and 2R,3R configurations, **7–10**, can be obtained by Sharpless asymmetric epoxidation of allylic alcohols[14] as the key step or by structural modification of certain carbohydrates.[12,15] Thus, this convergent sequence is highly flexible and allows selective synthesis of the eight possible stereisomers of PUG 4 by combining the appropriate stereodefined chiral units.

Scheme II. Synthesis of 2R,3S-α Side Chain Aldehyde 7



The synthesis of the 2R,3S α side chain aldehyde **7** is described in Scheme II. The two adjacent stereogenic centers were created in a stereoselective manner by combination of the Sharpless asymmetric epoxidation of allylic alcohols[14] and the neighboring group participated ring opening of the epoxide. Thus treatment of the (Z)-allylic alcohol **11**[16] with *tert*-butyl hydroperoxide in the presence of titanium tetraisopropoxide and L-(+)-diethyl tartrate[14] gave the epoxide **12** in 57% yield with an enantiomeric excess of 95%. The absolute configuration of **12** was defined by comparison of the sign of rotation of **12** with that of the authentic epoxy alcohol[17] obtained from 2-deoxy-D-ribose. After protection of the hydroxyl group of **12** by treatment with dihydropyran and pyridinium *p*-toluenesulfonate (94% yield), the epoxy ester **13** was exposed to

(10) In the original paper,[3] the relative configurations of **1** and **5** (or **2** and **6**) are not correlated each other. The structures of **1** (or **2**) and **a** are not identical but diastereomeric of each other. If **1** or **2** were correct, the stereochemistry at C(5) and C(6) must be reversed. On the other hand, kinetically controlled E2 elimination of acetic acid from **a** (seemingly the most comfortable conformation) leads to **5** or **6**, consistent with the observed Z/E stereoselectivity. Then the configurations of C(5) to C(7) of **1** and **2** should be reversed. It should be added, however, that possible E1cB elimination of acetic acid from **1** or **2** could produce the thermodynamically favorable 7Z isomers predominantly. Notably, in nature (7E)-PUG 3 and 4 occur predominantly over the 7Z isomers (ca. 10:1), whereas pyridine-induced elimination of acetic acid from PUG 1 and 2 gives the 7Z isomers as the major products.

(11) Preliminary report: Suzuki, M.; Morita, Y.; Yanagisawa, A.; Noyori, R.; Baker, B. J.; Scheuer, P. J. *J. Am. Chem. Soc.* **1986**, *108*, 5021.

(12) The same conclusion was derived by: Nagaoka, H.; Miyaoka, H.; Miyakoshi, T.; Yamada, Y. *J. Am. Chem. Soc.* **1986**, *108*, 5019.

(13) (a) Gill, M.; Rickards, R. W. *Tetrahedron Lett.* **1979**, 1539; (b) *J. Chem. Soc., Chem. Commun.* **1979**, 121.

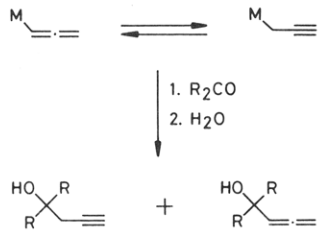
(14) (a) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974. (b) Rossiter, B. E.; Katsuki, T.; Sharpless, K. B. *Ibid.* **1981**, *103*, 464. See also a review: Pfenninger, A. *Synthesis* **1986**, 89.

(15) (a) Corey, E. J.; Goto, G. *Tetrahedron Lett.* **1980**, *21*, 3463. (b) Morris, J.; Wishka, D. G. *Ibid.* **1986**, *27*, 803. See also ref 17, 21, and 23.

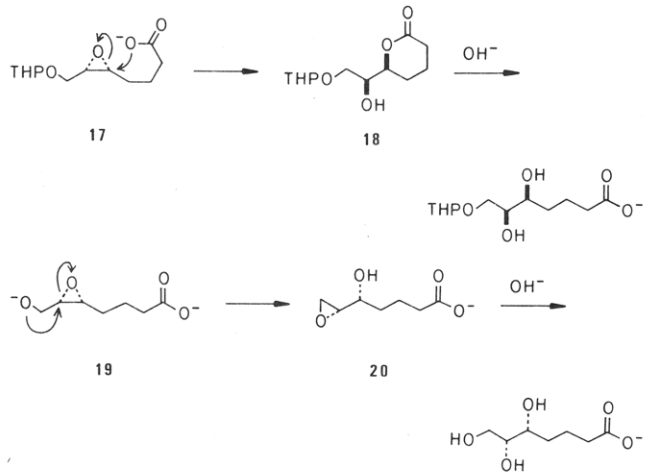
(16) Martel, J. Japanese Patent 46-28153, 1971; Japan Kokai 46-5625, 1971.

(17) (a) Rokach, J.; Zamboni, R.; Lau, C.-K.; Guindon, Y. *Tetrahedron Lett.* **1981**, *22*, 2759. (b) Rokach, J.; Lau, C.-K.; Zamboni, R.; Guindon, Y. *Ibid.* **1981**, *22*, 2763.

Scheme III. Reaction of Allenyl or Propargyl Metals with Carbonyl Compounds



0.5 N sodium hydroxide in a 5:1 water–*tert*-butyl alcohol mixture, causing saponification and opening of the epoxy ring; this was followed by reesterification of the carboxylic acid with diazomethane to the diol **14** in 82% overall yield. The absolute configuration was proved by comparison of the rotation of the 2*S*,3*S* triol obtained by acid hydrolysis of **14** with that of the authentic 2*R*,3*R* enantiomer[17] derived from 2-deoxy-D-ribose. Diol **14** was acetylated under standard conditions, leading to **15** (96% yield), followed by deprotection of the THP group to the acetylated alcohol **16** in 90% yield. The enantiomeric excess was assayed by 500-MHz ^{1}H NMR analysis of the corresponding MTPA ester[18] to be 94%. Finally, Moffat oxidation of **16** afforded aldehyde **7** having 2*R*,3*S* configuration in 75% yield. It should be added that the two-step conversion of **13** to **14** proceeded stereospecifically with inversion of configuration at C-3 of the epoxy THP ether via δ-lactone **18** formed by the carboxylate-aided epoxide ring opening of **17**.[19] When this conversion was conducted by using the epoxy alcohol **12** without THP protection, the enantiomeric purity dropped from 94% to 89% because of the competing Payne rearrangement, **19** → **20**,[20] leading to the enantiomeric product.



The synthesis of 2*S*,3*R* aldehyde **8**, the antipode of **7**, was also conducted by the same procedures using D-(−)-diethyl tartrate as the chiral source in the asymmetric epoxidation step. The synthesis of 2*S*,3*S* aldehyde **9** was accomplished in four steps from **21**. The primary alcohol of the starting triol **21**[21] was selectively silylated with *tert*-butyldiphenylsilyl chloride[22] in the presence of imidazole in DMF, giving **22** (74% yield). After acetylation of the hydroxy groups leading to **23** (63% yield), desilylation with hydrogen fluoride–pyridine in acetonitrile led to the diacetate **24** in 94% yield. Finally, Moffat oxidation of **24** gave aldehyde **9** having 2*S*,3*S* configuration in 66% yield. 2*R*,3*R* aldehyde **10** can be prepared from **25**[23] by a similar reaction sequence from **12** to **7**.

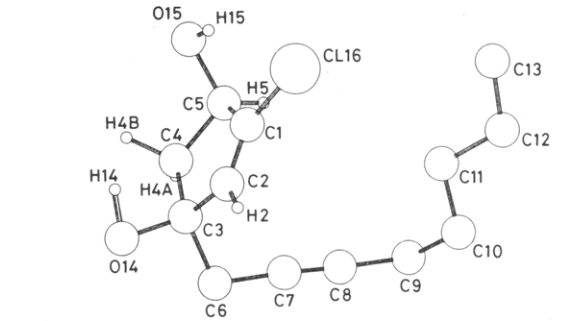


Figure 1. Structure of **28** by X-ray crystallographic analysis.

21, R = R' = H
22, R = Si(C$_6$H$_5$)$_2$-*t*-C$_4$H$_9$; R' = H
23, R = Si(C$_6$H$_5$)$_2$-*t*-C$_4$H$_9$; R' = Ac
24, R = H; R' = Ac

25

Selective propargylation of ketones required in Scheme I is not easy. Allenic and propargylic metal compounds, in many cases, undergo rapid equilibration and the nucleophilic reaction with carbonyl compounds often gives a mixture of the propargylic and allenic adducts (Scheme III). The selectivity is governed by the equilibrium concentration and relative reactivities of the organometallic nucleophiles and is high dependent on the nature of the substituents and the metallic species.[24] We found that organolithium reagents formed from allenyltin compounds and methyllithium give the adducts favoring the propargylic adducts. Thus the lower side chain precursor **27**[25] was synthesized in 74% yield by the reaction of 3-chloro-1-(trimethylstannyl)propyne (**26**)[27] and pentylmagnesium bromide in the presence of a catalytic amount of copper(I) cyanide.

Naturally occurring (7*E*)- and (7*Z*)-PUG 4 were synthesized in the following way. Reaction of optically pure (4*R*)-cyclopentenone **5**[13] and 1 equiv of allenyltin **27** with

(18) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

(19) Possibility of direct nucleophilic displacement by hydroxide ion at C-3 of the epoxy THP ether could not be excluded, but such a mechanism is unlikely in view of the high degree of retention of enantiomeric purity during the **13** to **14** transformation (95% to 94% ee).

(20) Katsuki, T.; Lee, A. W. M.; Ma, P.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Tuddenham, D.; Walker, F. J. *J. Org. Chem.* **1982**, *47*, 1373.

(21) Corey, E. J.; Marfat, A.; Munroe, J.; Kim, K. S.; Hopkins, P. B.; Brion, F. *Tetrahedron Lett.* **1981**, *22*, 1077.

(22) Hanessian, S.; Lavallee, P. *Can. J. Chem.* **1975**, *53*, 2975.

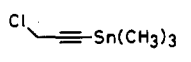
(23) Corey, E. J.; Clark, D. A.; Goto, G.; Marfat, A.; Mioskowski, C.; Samuelsson, B.; Hammarström, S. *J. Am. Chem. Soc.* **1980**, *102*, 1436; Cohen, N.; Banner, B. L.; Lopresti, R. J.; Wong, F.; Rosenberger, M.; Liu, Y.-Y.; Thom, E.; Liebman, A. A. *Ibid.* **1983**, *105*, 3661.

(24) Reviews: (a) Klein, J. *The Chemistry of the Carbon–Carbon Triple Bond*; Patai, S., Ed.; Wiley: New York, 1978; Part 1, Chapter 9. (b) Moreau, J.-L. *The Chemistry of Ketenes, Allenes, and Related Compounds*; Patai, S., Ed.; Wiley: New York, 1980; Part 1, Chapter 10. (c) Huntsman, W. D., in ref 24b, Part 2, Chapter 15. (d) Epsztein, R. *Comprehensive Carbanion Chemistry*; Buncel, E., Durst, T., Eds.; Elsevier: New York, 1984; Part B, Chapter 3.

(25) 3-(Tributylstannyl)-1,2-octadiene was also prepared in 37% yield by reacting 3-chloro-1-(tributylstannyl)propyne with a tributylphosphine complexed pentylcopper reagent.[26] This stannyl compound gave the similar results as **27** in the reaction with **5**.

(26) Suzuki, M.; Suzuki, T.; Kawagishi, T.; Morita, Y.; Noyori, R. *Isr. J. Chem.* **1984**, *24*, 118.

(27) (a) Pestunovich, V. A.; Tsetlina, E. O.; Voronkov, M. G.; Liepins, E.; Bogoradovskii, E. T.; Zavgorodnii, V. S.; Maksimov, V. L.; Petrov, A. A. *Dokl. Akad. Nauk SSSR* **1978**, *243*, 149. (b) Bogoradovskii, E. T.; Cherkasov, V. N.; Zavgorodnii, V. S.; Rogozev, B. I.; Petrov, A. A. *Zh. Obshch. Khim.* **1980**, *50*, 2031. (c) Razuvaev, G. A.; Egorochkin, A. N.; Skobeleva, S. E.; Kuznetsov, V. A.; Lopatin, M. A. *J. Organomet. Chem.* **1981**, *222*, 55.



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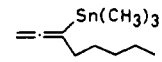
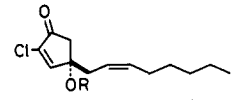


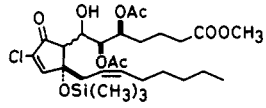
27

the aid of methyllithium at −78 °C, followed by desilylation with tetrabutylammonium fluoride[28] gave the crystalline acetylenic diol **28** in 42% yield, together with the undesired allenic condensation product (22%).[29] The IR spectrum of the monoacetylated derivative **29** in dilute (4.0×10^{-3} M) carbon tetrachloride solution revealed the O–H stretch band at 3520 cm^{-1}, indicating the presence of intramolecular hydrogen bonding, consistent with the cis diol structure. Definitive stereochemical determination of **28** was conducted by X-ray crystallographic analysis (Figure 1). The *Z* structure of the ω side chain was then introduced by hydrogenation of the acetylenic bond over Lindlar catalyst, furnishing **30** in 98% yield; subsequent oxidation of the secondary alcohol with pyridinium dichromate afforded the hydroxy enone **31** in 91% yield. Thus, in going from **5** to **31**, chirality of the hydroxylated carbon was transferred cleanly in a 1,3-manner. Silylation of **31** with trimethylsilyl triflate and diisopropylethylamine gave **32** in 86% yield. The whole PUG skeleton was constructed by aldol condensation of the cyclopentenone **32** and the 2*R*,3*S* aldehyde **7**. The enolate of **32** was generated with lithium diisopropylamide at −78 °C in THF, followed by the addition of aldehyde **7** (3 equiv), which afforded the condensation product **33** in 58% yield (95% yield, corrected for 39% recovery of starting enone). Dehy-

28, R = H; R' = $CH_2C{\equiv}C\text{-}n\text{-}C_5H_{11}$
29, R = CH_3CO; R' = $CH_2C{\equiv}C\text{-}n\text{-}C_5H_{11}$
30, R = H; R' = (*Z*)-$CH_2CH{=}CH\text{-}n\text{-}C_5H_{11}$



31, R = H
32, R = $Si(CH_3)_3$



33

dration of the aldol product **33** with acetic anhydride and 4-(dimethylamino)pyridine and subsequent hydrolytic desilylation gave a 2:5 mixture of **3** and **4** having 5*S*,6*S*,12*R* configuration in 41% yield. Irradiation of pure **3** and **4** with a Pyrex 25-W fluorescent lamp at 20 °C in benzene led to a 7:3 photoequilibrated mixture of **3** and **4**. These geometrical isomers were readily separated by silica gel column chromatography. All spectral data and chromatographic behavior of **3** and **4** were identical with those of naturally occurring (7*E*)- and (7*Z*)-PUG 4, respectively. The enantiomers of these compounds, **34** and **2**, having opposite CD curves, were synthesized by the same sequence using **6** and **8** as chiral starting materials.[11]

In a like manner, we prepared three other stereoisomers for each of (7*E*)- and (7*Z*)-PUG 4 from the appropriate chiral cyclopentenones and side chain units. These include all possible four diastereomers with respect to C-5, C-6, and C-12 relative configurations. The spectral data and chromatographic behavior of (7*E*)- and (7*Z*)-PUG 4 and their synthetic stereoisomers were carefully compared. The results are summarized in Table I. The chemical shifts at C(7)H and C(6)H and the coupling constants, J_{6-7} and J_{5-6}, observed on 500-MHz ^1H NMR spectra are subtly but distinctly differentiated for the four kinds of diastereomers, reconfirming the relative configuration of PUG 4.

Thus we can now conclude that (7*E*)- and (7*Z*)-PUG 4 have 5*S*,6*S*,12*R* configuration.[12] The 17,18-dehydro derivatives, (7*E*)- and (7*Z*)-PUG 3, must have the same stereochemistry.[12] Most significantly, *R* configuration at C-12 in PUG 3 and 4 is the opposite of the *S* stereochemistry (*ent*-prostanoids structure) of the closely related marine eicosanoids, clavulones[5] or claviridenones.[6] Recently isolated chlorovulones also possess the 12*R* configuration.[33,34] PUG 3 and 4 are derived from PUG 1 and 2, respectively, by elimination of acetic acid.[3] The trans relationship of the two side chains in PUG 1 and 2 dictates *R* configuration at C-8.[3] At present, however, we shall refrain from postulating the remaining C-7 configuration of PUG 1 and 2 by NMR analysis.

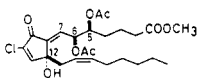
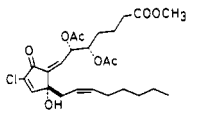
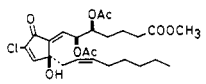
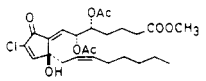
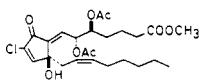
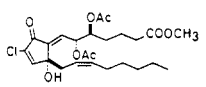
Finally, it should be noted that antineoplastic activities for L1210 tumor cell proliferation are not influenced greatly by stereochemical modifications of the PUG structure as indicated in Table I.[35] Presence of the chlorinated cross-conjugated dienone moiety is significant, but the degree of potency is not much affected by the relative or absolute configurations.

Experimental Section

General Remarks. (a) Spectrometer. IR spectra were obtained with a JASCO IRA-1 or IR-810 spectrometer. NMR spectra were determined on a JEOL FX-90Q, GX-270, or GX-500 spectrometer. Chemical shifts are reported relative to tetramethylsilane, $\delta = 0$. High-resolution mass spectra (HRMS) were recorded with a JEOL TMS-DX 300 spectrometer. Optical rotation was measured on a JASCO DIP-181 polarimeter. CD spectra were obtained with a JASCO J-500E spectrometer. Melting points were measured on a YANACO micro-melting point apparatus and were uncorrected. A Rigaku automated four-cycle diffractometer, AFC-5, was used for X-ray crystallographic analysis with graphite monochromated Cu radiation (Cu $K\alpha$ = 1.54051 Å). HPLC was conducted on Shimadzu SPD-6A, LC-6A, or C-R3A instrument using Yamamura Chemical YMC packed columns, A-002-3 and A-003-3, connected in series: solvent, 1:1 hexane/ether; flow rate, 1.0 mL/min; pressure, 140 kg/cm^2; detection, UV (254 nm). Bulb-to-bulb short-path distillation was performed by using a Büchi Kugelrohrofen. The cited temperatures for these distillations refer to the oven temperature and therefore are not true boiling points.

(28) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.
(29) Reaction of racemic 3-chloro-4-hydroxy-2-cyclopentenone and the reagent (5 equiv) generated by mixing of 1-bromo-2-octyne and activated zinc powder[30] gave the racemic **28** (46%, cis diol/trans diol = 10:1) and the allenic condensation product (32%). The reaction of racemic **5** and the same reagent (2 equiv) afforded the racemic **28** (56%, cis diol/trans diol = 1.2:1) and the allenyl compound (29%) after treatment with tetrabutylammonium fluoride. 3-(Dimethylphenylsilyl)-1,2-octadiene[31] did not react with racemic **5** in the presence of $TiCl_4$ at −78 to 25 °C in dichloromethane. 3-(Dipentylboryl)-1,2-octadiene[32] reacted with racemic **5** to give after desilylation a 1:1 mixture of racemic **28** and the allenyl compound in 20% yield.
(30) (a) Moreau, J.-L. *Bull. Soc. Chim. Fr.* **1975**, 1248. (b) Daniels, R. G.; Paquettte, L. A. *Tetrahedron Lett.* **1981**, *22*, 1579. See also: (c) Kosugi, H.; Konta, H.; Uda, H. *Abstr. Annu. Meet. Jpn. Chem. Soc. (Kyoto), 52nd*, **1986**, 1073. (d) Watanabe, Y.; Kosugi, H.; Uda, H. *Abstr. Annu. Meet. Jpn. Chem. Soc. (Tokyo), 54th* **1987**, 1122.
(31) (a) Danheiser, R. L.; Carini, D. J.; Fink, D. M.; Basak, A. *Tetrahedron* **1983**, *39*, 935. (b) Danheiser, R. L.; Carini, D. J.; Kwasigroch, C. A. *J. Org. Chem.* **1986**, *51*, 3870.
(32) Zweifel, G.; Backlund, S. J.; Leung, T. *J. Am. Chem. Soc.* **1978**, *100*, 5561.
(33) Nagaoka, H.; Iguchi, K.; Miyakoshi, T.; Yamada, N.; Yamada, Y. *Tetrahedron Lett.* **1986**, *27*, 223.
(34) For the biosynthetic pathway see: (a) Corey, E. J. *Experientia* **1983**, *39*, 1084. (b) Corey, E. J.; d'Alarcao, M.; Matsuda, S. P. T.; Lansbury, P. T., Jr. *J. Am. Chem. Soc.* **1987**, *109*, 289.
(35) The biological assay was conducted by Dr. M. Fukushima at Aichi Cancer Center.

Table I. Spectral Data, Chromatographic Behavior, and Antineoplastic Activities of (7*E*)- and (7*Z*)-PUG 4 and Their Stereoisomers

		^{1}H NMR[a] δ		^{1}H NMR[a] *J*, Hz[b]				inhibitory effect of the growth of L1210 tumor cells,
		C(7)H	C(6)H	6–7	5–6	CD spectrum,[c] Δε	HPLC[d] t_R, min	IC_{50},[e] μg/mL[f]
 3, (7*E*)-PUG 4 5*S*, 6*S*, 12*R*	natural	6.37	6.04	9.2	4.3	−5.0	17.34	0.07 (0.02)[g]
	synthetic	6.38	6.04	9.2	4.4	−5.8	17.34	0.07
 4, (7*Z*)-PUG 4 5*S*, 6*S*, 12*R*	natural	6.10	6.36	7.8	3.7	−4.8	32.04	0.06
	synthetic	6.10	6.35	7.9	3.5	−5.4	32.04	0.06
 1, 5*S*, 6*S*, 12*S*		6.32	5.69	10.4	4.3		17.86	0.05
7*Z* isomer of 1 (**35**)		6.07	6.62	7.9	4.4		33.74	0.035
 **34**, 5*R*, 6*R*, 12*S*		6.37	6.04	9.2	4.4	+5.5	17.34	0.1
7*Z* isomer of **34** (**2**)		6.10	6.36	7.8	3.7	+4.1	32.04	0.035
 **36**, 5*S*, 6*R*, 12*S*		6.53	6.24	9.5	2.6		17.57	0.05
7*Z* isomer of **36** (**37**)		6.18	6.48	8.9	3.5		29.29	0.02
 **38**, 5*S*, 6*R*, 12*R*		6.31	5.77	10.3	4.9		18.61	0.05
7*Z* isomer of **38** (**39**)		6.23	6.68	9.2	4.0		30.09	0.035

[a] Measured by a 500-MHz NMR machine. [b] Digital resolution was 0.3 Hz. [c] Values at 250 nm for 7*E* isomers and at 268 nm for 7*Z* isomers in methanol as solvent. [d] Conducted using Yamamura Chemical YMC packed columns, A-002-3 and A-003-3, connected in series with 1:1 hexane/ether as solvent; flow rate, 1.0 mL/min. Peaks were detected by UV (254 nm) lamp. [e] Concentration corresponding to 50% suppression of tumor cell growth. [f] All samples were investigated under same physiological conditions. [g] Reported values in ref 4.

(b) Chromatography. R_f values on TLC were recorded on E. Merck precoated (0.25 mm) silica gel 60 F_{254} plates. The plates were sprayed with a solution of 2% *p*-anisaldehyde in 5% ethanolic sulfuric acid and then heated until the spots became clearly visible. Column chromatography was conducted with silica gel (E. Merck, 7734 70–230 mesh or Fuji Devison, BW-80, 80–200 mesh) and Florisil (Nakarai, M7P4145). Celite (Manville) was used for filtration.

(c) Solvent. Dry ether, THF, and benzene were distilled over sodium–benzophenone ketyl under argon atmosphere. Dry CH_2Cl_2 was distilled over P_2O_5. Dry DMF, CH_3CN, and DMSO were distilled over CaH_2.

(d) Substrates and Reagents. (*Z*)-6-Carbomethoxy-2-hexen-1-ol (**11**) was prepared according to the method of Martel.[16] Methyl (5*S*,6*R*)-5,6,7-trihydroxyheptanoate (**21**)[21] was synthesized according to the method of Rokach.[17] (*R*)-3-Chloro-4-(*tert*-butyldimethylsiloxy)-2-cyclopentenone (**5**) and (*S*)-3-chloro-4-(*tert*-butyldimethylsiloxy)-2-cyclopentenone (**6**) were synthesized by the Rickards method.[13] 3-Chloro-1-(trimethylstannyl)propyne (**26**),[27] bp 50–60 °C [0.3 mmHg (Kugelrohr)], was synthesized by trimethylstannylation of propargyl chloride with the aid of CH_3Li (1.08 M ether solution).[36] n-$C_5H_{11}MgBr$ (1.80 M THF solution) was synthesized from pentyl bromide and magnesium turnings.[37] Molarity of alkyllithiums was determined by titration.[38] Pyridinium *p*-toluenesulfonate (PPTS) was purchased from Aldrich. Diazomethane was generated by mixing *N*-nitrosomethylurea and 30% aqueous KOH in ether at 0 °C. (+)-α-Methoxy-α-(trifluoromethyl)phenylacetyl chloride (MTPA chloride) was prepared by Mosher's method.[18] HF–pyridine (Aldrich) was used for desilylation reactions. Ti(O-*i*-$C_3H_7)_4$ (Aldrich) and *tert*-butyl hydroperoxide (TBHP, 2.89 M toluene solution)[39] were used for the Sharpless asymmetric epoxidation procedure. Lindlar catalyst (Nippon Engelhard, Lot No. 29) was used for hydrogenation. pH 7.4 phosphate buffer (0.1 M solution, Nakarai) was used for workup procedures. Reactions with organometallic reagents were conducted under argon atmosphere. The apparatus (ampule, test tube, and flask) for such reactions was evacuated by heating with a heat gun under high vaccum and then filled with argon. A solution of lithium diisopropylamide (LDA) in THF was prepared by mixing equimolar amounts of diisopropylamine and n-C_4H_9Li in THF at 0 °C for 2 h, yielding a solution of LDA in THF.

Methyl (5*R*,6*S*)-5,6-Epoxy-7-hydroxyheptanoate (12). Dry CH_2Cl_2 (150 mL) was placed in a 500-mL round-bottomed flask

(36) Ruitenberg, K.; Westmijze, H.; Kleijn, H.; Vermeer, P. *J. Organomet. Chem.* **1984**, *277*, 227.

(37) Kharasch, M. S.; Reinmuth, O. *Grignard Reactions of Nonmetallic Substances*; Prentice-Hall: New York, 1954.

(38) Kofron, W. G.; Baclawski, L. M. *J. Org. Chem.* **1976**, *41*, 1879.

(39) (a) Sharpless, K. B.; Verhoeven, T. R. *Aldrichimica Acta* **1979**, *12*, 63. (b) Hill, J. G.; Sharpless, K. B.; Exon, C. M.; Regenye, R. *Org. Synth.* **1984**, *63*, 66.

and cooled to −50 °C. To this was added $Ti(O\text{-}i\text{-}C_3H_7)_4$ (5.28 mL, 1.8×10^{-2} mol) and a solution of L-(+)-diethyl tartrate (3.66 g, 1.8×10^{-2} mol) in dry CH_2Cl_2 (8 mL) with stirring. After the reaction was stirred at −50 °C for 5 min, a solution of (Z)-6-carbomethoxy-2-hexen-1-ol (**11**, 2.81 g, 1.8×10^{-2} mol) in dry CH_2Cl_2 (8 mL) and TBHP (12.5 mL, 3.6×10^{-2} mol) was added. After being stirred at −50 °C for 30 min, this mixture was warmed up to −20 °C and stirred for 8 h at this temperature. After addition of dimethyl sulfide (5.6 mL, 7.6×10^{-2} mol), this mixture was poured into 5% aqueous NaF (400 mL). After being stirred at 20 °C for 10 min, the mixture was filtered through Celite, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (200 mL × 2). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residual oil was subjected to silica gel column chromatography (300 g) with a 1:1 mixture of hexane and ethyl acetate as eluant yielding the epoxide **12** (1.796 g, 57%, 1.0×10^{-2} mol) as a colorless oil: TLC R_f 0.14 (1:1 hexane/ethyl acetate); IR ($CHCl_3$) 3600–3200, 2930, 1735 cm^{-1}; $[\alpha]^{14}D$ −2.5° (*c* 1.74, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.4–2.1 (m, 4, 2 CH_2), 2.23 (br s, 1, OH), 2.41 (t, 2, J = 6.6 Hz, CH_2CO), 2.9–3.3 (m, 2, 2 CHO), 3.69 (s, 3, OCH_3), 3.5–4.7 (m, 2, CH_2O); MS, m/z 175 (M^+ + H), 143, 125; HRMS, m/z calcd for $C_8H_{15}O_4$ (M^+ + H) 175.0970, found 175.0938.

Antipode of **12** was prepared under the same reaction conditions using D-(−)-diethyl tartrate as a chiral source: $[\alpha]^{21}D$ +2.5° (*c* 1.04, $CHCl_3$).

Methyl (5*R*,6*S*)-5,6-Epoxy-7-[(tetrahydropyran-2-yl)-oxy]heptanoate (13). The epoxy alcohol **12** (25.2 mg, 1.45×10^{-4} mol) was placed in a 5-mL test tube and dissolved in dry CH_2Cl_2 (1 mL). After the reaction was cooled to 0 °C, 2,3-dihydropyran (0.13 mL, 1.45×10^{-3} mol) and PPTS (18.2 mg, 7.25×10^{-5} mol) were added. The reaction mixture was stirred at 16 °C for 14.5 h, poured into water (2 mL), and vigorously shaken. After separation of the organic layer, the aqueous layer was extracted with CH_2Cl_2 (5 mL × 2). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residual oil was subjected to silica gel column chromatography (4 g) with a 10:1 to 5:1 mixture of hexane and ethyl acetate as eluant, yielding THP ether **13** (35.3 mg, 94%, 1.73×10^{-4} mol) as a colorless oil: TLC R_f 0.52 (1:1 hexane/ethyl acetate); IR ($CHCl_3$) 2920, 1735 cm^{-1}; $[\alpha]^{14}D$ −1.2° (*c* 1.77, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.4–2.0 (m, 10, 5 CH_2), 2.40 (t, 2, J = 6.8 Hz, CH_2CO), 2.9–3.3 (m, 2, 2 CHO), 3.67 (s, 3, OCH_3), 3.4–4.0 (m, 4, 2 CH_2O), 4.66 (m, 1, OCHO); MS, m/z 259 (M^+ + H), 156, 143; HRMS, m/z calcd for $C_{13}H_{23}O_5$ (M^+ + H) 259.1546, found 259.1547.

Antipode of **13** was prepared under the same reaction conditions from the antipode of **12**: $[\alpha]^{11}D$ + 1.0° (*c* 1.39, $CHCl_3$).

Methyl (5*S*,6*S*)-5,6,7-Trihydroxyheptanoate. Diol **14** (97.3 mg, 3.52×10^{-4} mol) was placed in a 10-mL round-bottomed flask and dissolved in CH_3OH (1 mL), and a 1 N HCl solution (1 mL) was added. After being stirred at 18 °C for 2 h, the reaction mixture was concentrated under reduced pressure. After dilution of the residual oil with CH_3OH (2 mL), a solution of diazomethane in ether was added until the polar spot on TLC disappeared; then the mixture was concentrated under reduced pressure. The residual oil was subjected to silica gel column chromatography (10 g) with a 1:5 mixture of CH_3OH and ethyl acetate as eluant, yielding the title triol[17] (51.2 mg, 76%, 2.66×10^{-4} mol) as a colorless oil: TLC R_f 0.51 (1:5 CH_3OH/ethyl acetate); IR ($CHCl_3$) 3700–3100, 1730 cm^{-1}; $[\alpha]^{20}D$ −10.7° (*c* 2.56, $CDCl_3$);[17] ^1H NMR ($CDCl_3$) δ 1.4–2.0 (m, 4, 2 CH_2), 2.38 (t, 2, J = 6.8 Hz, CH_2CO), 3.0–4.0 (m, 7, 2 CHO, CH_2O, and 3 OH), 3.68 (s, 3, OCH_3); MS, m/z 193 (M^+ + H), 175, 161, 143; HRMS, m/z calcd for $C_8H_{17}O_5$ (M^+ + H) 193.1076, found 193.1091.

The same triol was also obtained from **16**. Alcohol **16** (11.2 mg, 4.05×10^{-5} mol) was placed in a 5-mL test tube and dissolved in CH_3OH (0.5 mL). CH_3ONa/CH_3OH solution (0.2 mL, 5.00×10^{-4} mol) was added to the reaction mixture at 12 °C. After being stirred at 12 °C for 1.5 h, the reaction mixture was concentrated under reduced pressure. The residual oil was subjected to silica gel column chromatography (1 g) with a 5:1 mixture of hexane and ethyl acetate as eluant, yielding the title triol (2.1 mg, 27%, 1.09×10^{-5} mol).

Direct ring opening of alcohol **12** also afforded the same triol, but the enantiomeric purity of the product decreased to some extent (95% to 89% ee). Epoxy alcohol **12** (1.44 g, 8.26×10^{-3} mol) was placed in a 200-mL round-bottomed flask, and to it was added a solution of NaOH (2 g, 5.0×10^{-2} mol) in a 5:1 mixture of H_2O and $t\text{-}C_4H_9OH$ (100 mL). After being stirred at 60 °C for 13 h, the mixture was neutralized with 1 N HCl solution (50 mL). The mixture was concentrated under reduced pressure. After dilution of the residual material with CH_3OH (50 mL), a solution of diazomethane in ether was added until the polar spot on TLC disappeared; then the mixture was concentrated under reduced pressure. The residual oil was subjected to silica gel column chromatography (50 g) with a 1:10 mixture of CH_3OH and ethyl acetate as eluant, yielding the title triol (1.04 g, 66%, 5.41×10^{-3} mol). Decreased optical purities (89% ee) were determined by applying Mosher's MTPA method[18] after conversion to methyl (5*S*,6*S*)-7-hydroxy-5,6-*O*-isopropylidene-5,6-dihydroxyheptanoate by sequential combination of the three operations: selective silylation of the primary hydroxyl group[22] (98%), conversion to the acetonide[40] (73%), and selective desilylation[28] (98%).

Methyl (5*S*,6*S*)-5,6-Dihydroxy-7-[(tetrahydropyran-2-yl)oxy]heptanoate (14). Epoxide **13** (515.5 mg, 2.00×10^{-3} mol) was placed in a 50-mL round-bottomed flask. To this was added a solution of NaOH (400 mg, 1.00×10^{-2} mol) in a 5:1 mixture (20 mL) of H_2O and $t\text{-}C_4H_9OH$. After being stirred at 60 °C for 40 min, the reaction mixture was neutralized with 1 N HCl solution (10 mL); then the mixture was concentrated under reduced pressure. After dilution with CH_3OH (10 mL), a solution of diazomethane in ether was added until the polar spot on TLC disappeared; then the mixture was concentrated under reduced pressure. The residual oil was subjected to silica gel column chromatography (25 g) with a 1:10 to 1:5 mixture of CH_3OH and ethyl acetate as eluant, yielding diol **14** (451.9 mg, 82%, 1.64×10^{-3} mol) as a colorless oil: TLC R_f 0.66 (1:5 CH_3OH/ethyl acetate); IR ($CHCl_3$) 3600–3200, 1735 cm^{-1}; $[\alpha]^{14}D$ −9.6° (*c* 0.78, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.4–2.1 (m, 12, 5 CH_2 and 2 OH), 2.37 (t, 2, J = 7.0 Hz, CH_2CO), 3.4–4.2 (m, 9, 2 CHO, 2 CH_2O, and OCH_3), 4.55 (br, s, 1, OCHO); MS, m/z 277 (M^+ + H), 215, 203, 193; HRMS, m/z calcd for $C_{13}H_{25}O_6$ (M^+ + H) 277.1651, found 277.1665.

Antipode of **14** was prepared under the same reaction conditions from the antipode of **13**: $[\alpha]^{12}D$ +9.2° (*c* 0.22, $CHCl_3$).

Methyl (5*S*,6*S*)-5,6-Diacetoxy-7-[(tetrahydropyran-2-yl)oxy]heptanoate (15). Diol **14** (129.1 mg, 4.67×10^{-4} mol) was placed in a 10-mL round-bottomed flask and dissolved in dry CH_2Cl_2 (2 mL). After the mixture was cooled to 0 °C, acetic anhydride (0.114 mL, 1.17×10^{-3} mol) and 4-(dimethylamino)-pyridine (DMAP) (171.2 mg, 1.40×10^{-3} mol) were added. After removal of the ice bath, the mixture was stirred at 18 °C for 20 min. The mixture was poured into saturated aqueous NH_4Cl solution (20 mL) and extracted with CH_2Cl_2 (20 mL × 3). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residual oil was subjected to silica gel column chromatography (12 g) with a 5:1 mixture of hexane and ethyl acetate as eluant, yielding the diacetate **15** (161.6 mg, 96%, 4.48×10^{-4} mol) as a yellow oil: TLC R_f 0.46 (1:1 hexane/ethyl acetate); IR ($CHCl_3$) 1740 cm^{-1}; $[\alpha]^{12}D$ −15.4° (*c* 0.36, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.4–1.9 (m, 10, 5 CH_2), 2.07 (s, 3, CH_3CO), 2.10 (s, 3, CH_3CO), 2.2–2.4 (m, 2, CH_2CO), 3.4–4.0 (m, 4, 2 CH_2O), 3.66 (s, 3, OCH_3), 4.58 (br s, 1, OCHO), 5.16 (m, 2, 2 CHO); MS, m/z 361 (M^+ + H), 329, 277, 259, 245, 217, 199; HRMS, m/z calcd for $C_{17}H_{29}O_8$ (M^+ + H) 361.1862, found 361.1852.

Antipode of **15** was prepared under the same reaction conditions from the antipode of **14**: $[\alpha]^{12}D$ +14.1° (*c* 0.24, $CHCl_3$).

Methyl (5*S*,6*S*)-5,6-Diacetoxy-7-hydroxyheptanoate (16). Diacetate **15** (116.5 mg, 3.23×10^{-4} mol) was placed in a 30-mL round-bottomed flask and dissolved in CH_3OH (10 mL). To this was added PPTS (16.6 mg, 6.47×10^{-5} mol) at 50 °C, and then the mixture was stirred at 50 °C for 2.5 h. After cooling to room temperature, the reaction mixture was concentrated under reduced pressure. The residual oil was subjected to silica gel column chromatography (10 g) with a 1:1 mixture of hexane and ethyl acetate as eluant, yielding alcohol **16** (78.1 mg, 88%, 2.83×10^{-4}

(40) Greene, T. W. *Protective Groups in Organic Synthesis*; Wiley: New York, 1981.

mol) as a colorless oil: TLC R_f 0.20 (1:1 hexane/ethyl acetate); IR ($CHCl_3$) 3700–3200, 1730 cm^{-1}; $[\alpha]^{14}_D$ –26.3° (*c* 0.56, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.5–1.7 (m, 4, 2 CH_2), 2.11 (s, 6, 2 CH_3CO), 2.2–2.8 (m, 3, CH_2 and OH), 3.67 (s, 3, OCH_3), 3.6–4.5 (m, 2, CH_2O), 4.9–5.3 (m, 2, 2 CHO); MS, *m/z* 277 (M^+ + H), 259, 245, 217; HRMS, *m/z* calcd for $C_{12}H_{21}O_7$ (M^+ + H) 277.1288, found 277.1260.

Antipode of **16** was prepared under the same reaction conditions from the antipode of **15**: $[\alpha]^{12}_D$ +24.7° (*c* 0.32, $CHCl_3$).

Methyl (5*S*,6*R*)-5,6-Diacetoxy-6-formylheptanoate (7). Alcohol **16** (385.2 mg, 1.39 × 10^{-3} mol) was placed in a 20-mL round-bottomed flask and dissolved in dry benzene (4 mL). To this was added successively dry DMSO (4.64 mL, 6.54 × 10^{-2} mol), pyridine (0.113 mL, 1.39 × 10^{-3} mol), trifluoroacetic acid (0.054 mL, 6.97 × 10^{-4} mol), and 1,3-dicyclohexylcarbodiimide (863 mg, 4.18 × 10^{-3} mol). The mixture was stirred at 22 °C for 3 h, and benzene (10 mL) was added. The precipitated crystalline dicyclohexylurea was removed by filtration and washed with benzene. The combined filtrates were washed with water (20 mL × 3). The organic layer was separated, and the aqueous layer was extracted with benzene (10 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residual oil was subjected to column chromatography (Florisil, 80 g) with a 2:1 mixture of hexane and ethyl acetate as eluant, furnishing aldehyde **7** (284.9 mg, 75%, 1.04 × 10^{-3} mol) as a colorless oil: TLC R_f 0.21 (1:1 hexane/ethyl acetate); IR (C_6H_6) 2900, 1740 cm^{-1}; $[\alpha]^{23}_D$ –22.4° (*c* 0.36, C_6H_6); ^1H NMR ($CDCl_3$) δ 1.4–2.5 (m, 12, 2 CH_2, 2 CH_3CO, and CH_2CO), 3.70 (s, 3, OCH_3), 4.8–5.6 (m, 2, 2 CHO), 9.53 (s, 1, HCO); MS, *m/z* 275 (M^+ + H), 243, 215, 201; HRMS, *m/z* calcd for $C_{12}H_{19}O_7$ (M^+ + H) 275.1131, found 275.1125.

Compound **8** was prepared under the same reaction conditions from the antipode of **16**: $[\alpha]^{22}_D$ +21.8° (*c* 0.97, C_6H_6).

Methyl (5*S*,6*R*)-5,6-Dihydroxy-7-(*tert*-butyldiphenylsiloxy)heptanoate (22). Triol **21** (276.1 mg, 1.44 × 10^{-3} mol) was placed in a 10-mL test tube and dissolved in dry DMF (4 mL). After the reaction was cooled to 0 °C, imidazole (195.6 mg, 2.87 × 10^{-3} mol) and *tert*-butyldiphenylsilyl chloride (0.381 mL, 1.44 × 10^{-3} mol) were added. After removal of the ice bath, the mixture was stirred at 15 °C for 20 min and then directly subjected to silica gel column chromatography (30 g) with a 2:1 mixture of hexane and ethyl acetate as eluant, yielding monosilylated ether **22** (460.9 mg, 74%, 1.07 × 10^{-3} mol) as a colorless oil: TLC R_f 0.45 (1:1 hexane/ethyl acetate); IR (neat) 3600–3100, 1740 cm^{-1}; $[\alpha]^{13}_D$ –0.02° (*c* 1.32, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.07 (s, 9, Si-*t*-C_4H_9), 1.2–2.1 (m, 4, 2 CH_2), 2.34 (t, 2, *J* = 7.3 Hz, CH_2CO), 2.2–3.0 (m, 2, 2 OH), 3.65 (s, 3, OCH_3), 3.5–3.9 (m, 4, 2 CHO and CH_2O), 7.3–7.8 (m, 10, aromatic); MS, *m/z* 431 (M^+ + H), 371, 355, 323; HRMS, *m/z* calcd for $C_{24}H_{35}O_5Si$ (M^+ + H) 431.2254, found 431.2203.

Methyl (5*S*,6*R*)-5,6-Diacetoxy-7-(*tert*-butyldiphenylsiloxy)heptanoate (23). Diol **22** (289.6 mg, 6.73 × 10^{-4} mol) was placed in a 10-mL test tube and dissolved in CH_2Cl_2 (3 mL). After the reaction was cooled to 0 °C, acetic anhydride (0.165 mL, 1.68 × 10^{-3} mol) and DMAP (246.5 mg, 2.02 × 10^{-3} mol) were added. After removal of the ice bath, the mixture was stirred at 16 °C for 30 min. The mixture was poured into saturated aqueous NH_4Cl solution (5 mL) and extracted with CH_2Cl_2 (5 mL × 3). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residual oil was subjected to silica gel column chromatography (15 g) with a 5:1 mixture of hexane and ethyl acetate as eluant, yielding diacetate **23** (216.8 mg, 63%, 4.21 × 10^{-4} mol) as a colorless oil: TLC R_f 0.69 (1:1 hexane/ethyl acetate); IR ($CHCl_3$) 1740 cm^{-1}; $[\alpha]^{14}_D$ –8.9° (*c* 0.71, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.04 (s, 9, Si-*t*-C_4H_9), 1.5–1.8 (m, 4, 2 CH_2), 1.99 (s, 3, $COCH_3$), 2.02 (s, 3, $COCH_3$), 2.32 (m, 2, 2 CHO), 365 (s, 3, OCH_3), 3.74 (d, 2, *J* = 5.5 Hz, CH_2O), 5.18 (m, 2, 2 CHO), 7.4–7.8 (m, 10, aromatic); MS, *m/z* 515 (M^+ + H), 483, 457, 395; HRMS, *m/z* calcd for $C_{28}H_{39}O_7Si$ (M^+ + H) 515.2465, found 515.2483.

Methyl (5*S*,6*R*)-5,6-Diacetoxy-7-hydroxyheptanoate (24). Silyl ether **23** (414.4 mg, 8.05 × 10^{-4} mol) was placed in a 50-mL round-bottomed flask and dissolved in dry CH_3CN (10 mL). After the reaction was cooled to 0 °C, HF–pyridine (2.5 mL) was added. After removal of the ice bath, the mixture was stirred at 20 °C for 15.5 h. The mixture was poured into a mixture of saturated aqueous KF solution (25 mL), saturated aqueous $NaHCO_3$ solution (50 mL), and ether (60 mL). After extraction with ether (50 mL × 3), the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residual oil was subjected to silica gel column chromatography (40 g) with a 1:1 mixture of hexane and ethyl acetate as eluant, yielding alcohol **24** (210.0 mg, 94%, 7.60 × 10^{-4} mol) as a colorless oil. TLC R_f 0.20 (1:1 hexane/ethyl acetate); IR ($CHCl_3$) 3680–3260, 1740 cm^{-1}; $[\alpha]^{14}_D$ –5.3° (*c* 1.03, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.6–2.5 (m, 3, CH_2CO and OH), 3.67 (s, 3, OCH_3), 3.6–3.8 (m, 2, CH_2OH), 4.9–5.3 (m, 2, 2 CHO); MS, *m/z* 277 (M^+ + H), 245, 201, 173; HRMS, *m/z* calcd for $C_{12}H_{21}O_7$ (M^+ + H) 277.1287, found 277.1311.

Methyl (5*S*,6*S*)-5,6-Diacetoxy-6-formylheptanoate (9). Alcohol **24** (95.3 mg, 3.45 × 10^{-4} mol) was placed in a 10-mL test tube and dissolved in dry benzene (1 mL). To this was added successively dry DMSO (1.15 mL, 1.63 × 10^{-2} mol), pyridine (0.0279 mL, 3.45 × 10^{-4} mol), trifluoroacetic acid (0.0133 mL, 1.72 × 10^{-4} mol), and 1,3-dicyclohexylcarbodiimide (213.5 mg, 1.03 × 10^{-3} mol). The mixture was stirred at 25 °C for 1 h. Benzene (3 mL) was added, and the precipitated dicyclohexylurea was removed by filtration and washed with benzene. The combined filtrates were washed with water (6 mL × 3). The organic layer was separated and the aqueous layer was extracted with benzene (5 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residual oil was subjected to column chromatography (Florisil, 20 g) with a 2:1 mixture of hexane and ethyl acetate as eluant, yielding aldehyde **9** (62.7 mg, 66%, 2.29 × 10^{-4} mol) as a colorless oil: TLC R_f 0.22 (1:1 hexane/ethyl acetate); IR ($CHCl_3$) 1740 cm^{-1}; $[\alpha]^{23}_D$ –1.0° (*c* 0.81, C_6H_6); ^1H NMR ($CDCl_3$) δ 1.5–1.9 (m, 4, 2 CH_2), 2.07 (s, 3, $COCH_3$), 2.19 (s, 3, $COCH_3$), 2.2–2.5 (m, 2, CH_2CO), 3.67 (s, 3, OCH_3), 4.8–5.4 (m, 2, 2 CHO), 9.52 (s, 1, HCO); MS, *m/z* 275 (M^+ + H), 245, 201, 173; HRMS, *m/z* calcd for $C_{12}H_{19}O_7$ (M^+ + H) 275.1131, found 275.1147.

3-(Trimethylstannyl)-1,2-octadiene (27). Copper(I) cyanide (4.7 mg, 0.52 × 10^{-4} mol) and dry THF (6 mL) were placed in a 40-mL ampule under argon atmosphere. After the reaction was cooled to –25 °C, *n*-$C_5H_{11}MgBr$ (0.80 mL, 1.44 × 10^{-3} mol) was added, and the mixture was stirred 10 min at this temperature. To this was added a solution of 3-chloro-1-(trimethylstannyl)-propyne (**26**, 341.9 mg, 1.44 × 10^{-3} mol) in THF (3 mL) over a period of 5 min at –25 °C. After being stirred at –25 to –18 °C for 15 min, the mixture was poured into saturated aqueous NH_4Cl solution (8 mL) and extracted with hexane (5 mL). The organic extract was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Bulb-to-bulb short-path distillation [38–48 °C (0.3 mmHg)] gave **27** (290.0 mg, 74%, 1.06 × 10^{-3} mol) as a colorless oil. TLC R_f 0.66 (hexane); IR ($CHCl_3$) 1920 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.18 (s, 9, $^2J(^{117}Sn-^1H)$ = 52.3 Hz, $^2J(^{119}Sn-^1H)$ = 54.9 Hz, $Sn(CH_3)_3$), 0.7–1.1 (br t, 3, CH_3), 1.1–1.6 (br, 6, 3 CH_2), 2.0–2.3 (br, 2, CH_2), 4.17 (t, 2, *J* = 3.0 Hz, allenyl); MS, *m/z* 274 (M^+), 259, 165, 109; HRMS, *m/z* calcd for $C_{11}H_{22}Sn$ 274.0744 (Sn = 119.9022), found 274.0744.

(3*S*,5*R*)-1-Chloro-3,5-dihydroxy-3-(2-octynyl)cyclopentene (28). 3-(Trimethylstannyl)-1,2-octadiene (**27**) (327.6 mg, 1.20 × 10^{-3} mol) was placed in a 40-mL ampule and dissolved in dry THF (6 mL) under argon atmosphere. After the reaction was cooled to –78 °C, CH_3Li (1.11 mL, 1.20 × 10^{-3} mol) was added, and the mixture was stirred at –78 °C for 30 min. To this was added a solution of enone **5** (271 mg, 1.10 × 10^{-3} mol) in ether (5 mL) over a period of 10 min at –78 °C. After being stirred at –78 °C for 30 min, the mixture was poured into saturated aqueous NH_4Cl solution and extracted with ether (15 mL × 2). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. After purification of the residual oil [TLC R_f 0.36 (5:1 hexane/ethyl acetate)] by silica gel column chromatography (10 g) with a 20:1 mixture of hexane and ethyl acetate as eluant, the oily material was dissolved in dry THF (8 mL) and cooled to 0 °C. To this was added tetrabutylammonium fluoride (1.0 M THF solution, 3.20 mL, 3.20 × 10^{-3} mol) at this temperature, and the mixture was stirred for 13 h at room temperature. The mixture was poured into saturated aqueous NaCl solution, followed by extraction with ethyl acetate (15 mL × 2). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. After passage of the residual

oil through a short silica gel column with a 2:1 mixture of hexane and ethyl acetate as eluant, the semipurified material was subjected to silica gel column chromatography (15 g) with a 5:1 mixture of hexane and ethyl acetate as eluant, yielding acetylenic diol **28** (112 mg, 42%, 4.61×10^{-4} mol) as a white solid and its allenyl isomer (58.7 mg, 22%, 2.42×10^{-4} mol) as an oil. Acetylenic diol **28**: mp 89–90 °C; TLC R_f 0.35 (1:1 hexane/ethyl acetate); IR ($CHCl_3$) 3600–3200, 1630 cm^{-1}; $[\alpha]^{15}_D$ +62.6° (*c* 0.13, $CHCl_3$); ^1H NMR ($CDCl_3$, 270 MHz) δ 0.90 (t, 3, J = 6.9 Hz, CH_3), 1.2–1.7 (m, 6, 3 CH_2), 1.96 (dd, 1, J = 14.2 and 3.6 Hz, a proton of CH_2), 2.1–2.3 (m, 3, CH_2 and OH), 2.44 (s, 1, OH), 2.49 (t, 2, J = 1.8 Hz, CH_2), 2.65 (dd, 1, J = 13.9 and 7.3 Hz, a proton of CH_2) 4.5–4.6 (m, 1, CHO), 5.94 (s, 1, vinyl); MS, m/z 242 (M^+), 225, 207, 189; HRMS, m/z calcd for $C_{13}H_{19}O_2Cl$ 242.1074, found 242.1110. The stereostructure of **28** was solved by X-ray crystallographic analysis using the Monte Carlo direct method[41] with the aid of MULTAN78 program system;[42] 1042 non-zero unique reflections were collected for the analysis and refined by the full-matrix least-squares program with the analytical absorption correction.[43] Non-H atoms were assigned by anisotropic temperature factors. All H atoms (except for some H atoms) located from difference Fourier map and refined with the equivalent isotropic temperature factors to that for the bonded carbon atoms. Function minimized by refinement was used $\sum(|F_o| - |F_c|)^2/\sum|F_o|^2$, $R = 0.082$, $R_w = 0.077$, where $R_w = \{\sum(|F_o| - |F_c|)^2/\sum|F_o|^2\}^{1/2}$. Atomic scattering factors were taken from *International Tables for X-ray Crystallography*.[44] All calculations made on a FACOM M-382 computer at the Computer Center of Nagoya University. Crystal data: molecular formula $C_{13}H_{19}O_2Cl$; M_r = 242.11; crystal size, 0.70 × 0.05 × 0.03 mm^3; space group, $P2_1$; cell dimensions, a = 16.910 (6) Å, b = 6.899 (2) Å, c = 5.941 (1) Å, α = 89.96 (2)°, β = 88.21 (2)°, γ = 89.91 (3)°; V = 692.7 (3) $Å^3$; Z = 2; ρ_{obsd} = 1.140 g cm^{-3}; ρ_{calcd} = 1.164 g cm^{-3}. Intensities were collected, $2\theta_{max}$ = 126°.

The antipode of **28** was synthesized by a similar procedure from **6**: $[\alpha]^{11}_D$ −56.4° (*c* 0.14, $CHCl_3$).

(3*S*,5*R*)-1-Chloro-3-acetoxy-5-hydroxy-3-(2-octynyl)-cyclopentene (29). (3*S*,5*R*)-1-Chloro-3-hydroxy-5-(*tert*-butyldimethylsiloxy)-3-(2-octynyl)cyclopentene (8.7 mg, 2.44×10^{-5} mol), the intermediate for the synthesis of **28** from **5** by propargylation, was placed in a 5-mL test tube and dissolved in dry CH_2Cl_2 (0.5 mL). After cooling to 0 °C, acetic anhydride (3.6 μL, 3.66×10^{-5} mol) and DMAP (8.9 mg, 7.31×10^{-5} mol) were added, and the mixture was stirred at 21 °C for 10 days. This mixture was diluted with CH_2Cl_2 and washed with water. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. After the residual oil was subjected to silica gel chromatography (1 g) with a 20:1 mixture of hexane and ethyl acetate as eluant, the resulting product [TLC R_f 0.53 (5:1 hexane/ethyl acetate)] was placed in a 5-mL round-bottomed flask and dissolved in dry CH_3CN (0.6 mL). After the reaction was cooled to 0 °C, HF–pyridine (0.8 mL) was added, and the mixture was stirred at 16 °C for 21 h. This mixture was poured into the mixture of saturated aqueous KF solution (8 mL) , saturated aqueous $NaHCO_3$ solution (16 mL), and ether (20 mL) and then extracted with ether (10 mL × 3). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residual oil was subjected to silica gel column chromatography (1 g) with a 1:1 mixture of hexane and ethyl acetate as eluant, yielding acetate **29** (6.4 mg, 92%, 2.25×10^{-5} mol) as a colorless oil: TLC R_f 0.27 (3:1 hexane/ethyl acetate); IR (CCl_4) 3600, 3520, 1740, 1630 cm^{-1}; IR (CCl_4, 4.0×10^{-3} M) 3600, 3520 cm^{-1}; $[\alpha]^{11}_D$ −28.2° (*c* 0.25, $CHCl_3$); ^1H NMR ($CDCl_3$, 270 MHz) δ 0.90 (t, 3, J = 7.1 Hz, CH_3), 1.2–1.6 (m, 6, 3 CH_2), 2.03 (s, 3, $COCH_3$), 2.1–2.9 (m, 6, 3 CH_2) 3.24 (d, 1, J = 9.2 Hz, OH), 4.51 (ddd, 1, J = 9.2, 7.8, and 2.5 Hz, CHO), 5.96 (s, 1, vinyl); MS, m/z 224 ($M^+ - C_2H_4O_2$), 206, 189; HRMS, m/z calcd for $C_{13}H_{17}OCl$ ($M^+ - C_2H_4O_2$) 224.0969, found 224.0984.

(3*S*,5*R*)-1-Chloro-3,5-dihydroxy-3-((*Z*)-2-octenyl)cyclopentene (30). Acetylenic diol **28** (22.9 mg, 9.43×10^{-5} mol) was placed in a 10-mL round-bottomed flask, and then CH_3OH (1.5 mL) and Lindlar catalyst (5 mg) were added. The mixture was stirred under H_2 gas (1 atm) at 24 °C for 72 h. The mixture was filtered through a short Celite column and washed with ether, and the filtrates were concentrated under reduced pressure. The residual oil was subjected to silica gel column chromatography (2 g) with a 3:1 mixture of hexane and ethyl acetate as eluant, yielding olefinic diol **30** (22.5 mg, 98%, 9.19×10^{-5} mol) as a white solid: mp 44–45 °C; TLC R_f 0.37 (1:1 hexane/ethyl acetate); IR ($CHCl_3$) 3600–3200, 1630 cm^{-1}; $[\alpha]^{11}_D$ +22.8° (*c* 0.19, $CHCl_3$); ^1H NMR ($CDCl_3$, 270 MHz) δ 0.89 (t, 3, J = 6.8 Hz, CH_3), 1.15–1.45 (m, 6, 3 CH_2), 1.88 (dd, 1, J = 14.2 and 3.3 Hz, a proton of CH_2), 1.95–2.10 (m, 2, CH_2), 2.30–2.45 (m, 2, CH_2), 2.55 (dd, 1, J = 14.2 and 7.4 Hz, a proton of CH_2), 2.95–3.40 (br, 2, 2 OH), 4.35–4.55 (br, 1, CHO), 5.25–5.65 (m, 2, 2 vinyl), 5.87 (s, 1, vinyl); MS, m/z 244 (M^+), 226, 208. HRMS, m/z calcd for $C_{13}H_{19}OCl$ ($M^+ - H_2O$) 226.1124, found 226.1115.

The antipode of **30** was synthesized by a similar procedure using the 3*R*,5*S* isomer of **28**: $[\alpha]^{21}_D$ −23.0° (*c* 0.13, $CHCl_3$).

(4*S*)-2-Chloro-4-hydroxy-4-((*Z*)-2-octenyl)-2-cyclopentenone (31). Diol **30** (21.0 mg, 8.58×10^{-5} mol) was placed in a 10-mL test tube and dissolved in dry DMF (2.5 mL). After the reaction was cooled to 0 °C, pyridinium dichromate (64 mg, 1.7×10^{-4} mol) was added, and the mixture was stirred at 28 °C for 24 h. The reaction mixture was filtered through a short Celite column and washed with ether. The filtrates were concentrated under reduced pressure and subjected to silica gel column chromatography (4 g) with a 10:1 mixture of hexane and ethyl acetate as eluant, yielding hydroxy enone **31** (19.0 mg, 91%, 7.83×10^{-5} mol) as a colorless oil. TLC R_f 0.59 (1:1 hexane/ethyl acetate); IR ($CHCl_3$) 3600–3200, 1730, 1670 cm^{-1}; $[\alpha]^{15}_D$ +59.9° (*c* 0.18, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.7–1.1 (br t, 3, CH_3), 1.1–1.6 (m, 6, 3 CH_2), 1.9–2.3 (m, 3, CH_2 and OH), 2.54 (d, 2, J = 7.0 Hz, CH_2), 2.54 (d, 1, J = 18.5 Hz, a proton of CH_2CO), 2.77 (d, 1, J = 18.5 Hz, a proton of CH_2CO), 5.2–5.9 (m, 2, vinyl), 7.34 (s, 1, vinyl); MS, m/z 242 (M^+), 224, 203, 131; HRMS, m/z calcd for $C_{13}H_{17}OCl$ ($M^+ - H_2O$) 224.0968, found 224.0961.

The antipode of **31** was synthesized by a similar procedure using the 4*R* isomer of **30**: $[\alpha]^{25}_D$ −57.6° (*c* 0.25, $CHCl_3$).

(4*S*)-2-Chloro-4-(trimethylsiloxy)-4-((*Z*)-2-octenyl)-2-cyclopentenone (32). Alcohol **31** (118.0 mg, 4.86×10^{-4} mol) was placed in a 20-mL round-bottomed flask and dissolved in dry CH_2Cl_2 (8 mL). After the reaction was cooled to 0 °C, diisopropylethylamine (0.42 mL, 2.43×10^{-3} mol) and trimethylsilyl triflate (0.12 mL, 6.21×10^{-4} mol) were successively added. After stirring at 0 °C for 30 min, the mixture was diluted with CH_2Cl_2 (5 mL) and extracted with CH_2Cl_2 (10 mL × 2). The organic extracts were washed with water (5 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residual oil was subjected to silica gel column chromatography (5 g) with a 100:1 mixture of hexane and ethyl acetate as eluant, yielding silyl ether **32** (131.0 mg, 86%, 4.16×10^{-4} mol) as a colorless oil: TLC R_f 0.61 (5:1 hexane/ethyl acetate); IR ($CHCl_3$) 1730, 1605 cm^{-1}; $[\alpha]^{12}_D$ +23.7° (*c* 1.14, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.13 (s, 9, $Si(CH_3)_3$), 0.7–1.1 (br t, 3, CH_3), 1.1–1.6 (m, 6, 3 CH_2), 1.8–2.2 (m, 2, CH_2), 2.50 (d, 2, J = 6.4 Hz, CH_2), 2.50 (d, 1, J = 18.5 Hz, a proton of CH_2CO), 2.73 (d, 1, J = 18.5 Hz, a proton of CH_2CO), 5.2–5.9 (m, 2, vinyl), 7.32 (s, 1, vinyl); MS, m/z 314 (M^+), 299, 260, 245, 225, 203; HRMS, m/z calcd for $C_{16}H_{27}O_2ClSi$ 314.1469, found 314.1502.

The antipode of **32** was synthesized by a similar procedure using the 4*R* isomer of **31**: $[\alpha]^{23}_D$ −20.9° (*c* 0.31, $CHCl_3$).

(4*S*)-2-Chloro-4-(trimethylsiloxy)-4-((*Z*)-2-octenyl)-5-((2*S*,3*S*)-6-carbomethoxy-2,3-diacetoxy-1-hydroxyhexyl)-2-cyclopentenone (33). Enone **32** (22.5 mg, 7.14×10^{-5} mol) was placed in a 10-mL ampule and dissolved in dry THF (0.6 mL) under argon atmosphere. After the reaction was cooled to −78 °C, a solution of LDA (0.40 M THF solution, 0.18 mL, 7.0×10^{-5} mol) was added at −78 °C with stirring, and the mixture was stirred for 10 min. To this was added a solution of aldehyde **7** (56.5 mg, 2.06×10^{-4} mol) in THF (0.3 mL) at −78 °C. After being stirred at the same temperature for 20 min, the mixture was poured into a pH 7.4 phosphate buffer (1.5 mL) and extracted with ether (10 mL × 2). The combined organic extracts were dried over Na_2SO_4,

(41) Furusaki, A. *Acta Crystallogr., Sect. A* **1979**, *A35*, 220.
(42) Main, P.; Hull, S. E.; Lessinger, L.; Germain, G.; Declercq, J. P.; Woolfson, M. M. MULTAN78; Universities of York, England, and Louvain, Belguim, 1978.
(43) Katayama, C.; Sakabe, N.; Sakabe, K. *Acta Crystallogr., Sect. A* **1972**, *A28*, S207.
(44) *International Tables for X-ray Crystallography*; Kynoch: Birmingham, England, 1974; Vol. IV.

filtered, and concentrated under reduced pressure. The residual oil was subjected to silica gel column chromatography (3 g) with a 20:1 to 5:1 mixture of hexane and ethyl acetate as eluant, yielding the aldol product **33** (24.2 mg, 58%, 4.11×10^{-5} mol) as a yellow oil, together with starting enone **32** (8.7 mg, 39%, 2.76×10^{-5} mol): TLC R_f 0.37 and 0.30 (2:1 hexane/ethyl acetate); IR ($CHCl_3$) 3600–3200, 1735, 1605 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 0.04 and 0.20 (s each, 9, $Si(CH_3)_3$), 0.89 (t, 3, J = 6.9 Hz, CH_3), 1.1–1.4 (m, 6, 3 CH_2), 1.5–1.8 (m, 4, 2 CH_2), 2.05, 2.08, 2.12, and 2.14 (s each, 6, 2 $COCH_3$), 1.9–2.0 (br, 2, CH_2), 2.2–2.9 (m, 6, 2 CH_2, CH, and OH), 3.65 and 3.66 (s each, 3, OCH_3), 4.1–4.3 (m, 1, CHO), 5.1–5.8 (m, 4, two vinyl and 2 C*H*OCOCH_3), 7.29 and 7.31 (s each, 1, vinyl).

(4*R*)-2-Chloro-4-(trimethylsiloxy)-4-((*Z*)-2-octenyl)-5-((2*S*,3*S*)-6-carbomethoxy-2,3-diacetoxy-1-hydroxyhexyl)-2-cyclopentenone: yield, 51% and 32% recovery of the antipode of **32**; TLC R_f 0.36 and 0.29 (2:1 hexane/ethyl acetate); ^1H NMR ($CDCl_3$, 270 MHz) δ 0.12, 0.16, 0.20, and 0.22 (s each, 9, $Si(CH_3)_3$), 0.89 (t, 3, J = 6.9 Hz, CH_3), 1.2–1.4 (m, 6, 3 CH_2), 1.5–1.8 (m, 4, 2 CH_2), 1.9–2.1 (m, 2, CH_2), 2.05, 2.09, 2.12, and 2.13 (s each, 6, 2 $COCH_3$), 2.3–3.2 (m, 6, 2 CH_2, CH, and OH), 3.66 (s, 3, OCH_3), 3.9–4.5 (m, 1, CHO), 5.0–5.9 (m, 4, two vinyl and 2 C*H*OCOCH_3), 7.30, 7.32, and 7.34 (s each, 1, vinyl).

(4*R*)-2-Chloro-4-(trimethylsiloxy)-4-((*Z*)-2-octenyl)-5-((2*R*,3*R*)-6-carbomethoxy-2,3-diacetoxy-1-hydroxyhexyl)-2-cyclopentenone: yield, 61% and 32% recovery of the antipode of **32**; TLC R_f 0.37 and 0.30 (2:1 hexane/ethyl acetate). less polar material on TLC: ^1H NMR ($CDCl_3$, 500 MHz) δ 0.05 and 0.21 (s each, 9, $Si(CH_3)_3$), 0.7–1.1 (br t, 3, CH_3), 1.1–1.5 (m, 6, 3 CH_2), 1.5–1.8 (m, 4, 2 CH_2), 2.06, 2.09, 2.13, and 2.15 (s each, 6, 2 $COCH_3$), 1.9–2.0 (br, 2, CH_2), 2.2–2.8 (m, 6, 2 CH_2, CH, and OH), 3.67 (s, 3, OCH_3), 4.1–4.4 (m, 1, CHO), 5.1–5.9 (m, 4, 2 vinyl and 2 C*H*OCOCH_3), 7.29 and 7.32 (s each, 1, vinyl). More polar material on TLC: ^1H NMR ($CDCl_3$, 500 MHz) δ 0.15 and 0.18 (s each, 9, $Si(CH_3)_3$), 0.7–1.1 (br t, CH_3), 1.1–1.5 (m, 6, 3 CH_2), 1.5–1.9 (m, 4, 2 CH_2), 1.9–3.0 (m, 14, 2 $COCH_3$, 3 CH_2, CH, and OH), 3.66 (s, 3, OCH_3), 3.7–4.1 (br, 1, CHO), 4.8–5.8 (m, 4, 2 vinyl and 2 C*H*OCOCH_3), 7.31 (s, 1, vinyl).

(4*R*)-2-Chloro-4-(trimethylsiloxy)-4-((*Z*)-2-octenyl)-5-((2*R*,3*S*)-6-carbomethoxy-2,3-diacetoxy-1-hydroxyhexyl)-2-cyclopentenone: yield, 22% and 68% recovery of the antipode of **32**; TLC R_f 0.35 and 0.27 (2:1 hexane/ethyl acetate); ^1H NMR ($CDCl_3$, 270 MHz) δ 0.08, 0.14, 0.18, and 0.21 (s each, 9, $Si(CH_3)_3$), 0.89 (t, 3, J = 6.9 Hz, CH_3), 1.1–1.4 (m, 6, 3 CH_2), 1.5–1.8 (m, 4, 2 CH_2), 1.9–2.1 (m, 2, CH_2), 2.02, 2.04, 2.09, and 2.20 (s each, 6, 2 $COCH_3$), 2.3–3.3 (m, 6, 2 CH_2, CH, and OH), 3.66, 3.67, and 3.68 (s each, 3, OCH_3), 3.9–4.4 (m, 1, CHO), 5.1–5.8 (m, 4, 2 vinyl and 2 C*H*OCOCH_3), 7.35, 7.36, and 7.45 (s each, 1, vinyl).

(4*S*)-2-Chloro-4-(trimethylsiloxy)-4-((*Z*)-2-octenyl)-5-((2*R*,3*S*)-6-carbomethoxy-2,3-diacetoxy-1-hydroxyhexyl)-2-cyclopentenone: yield, 44% and 41% recovery of **32**; TLC R_f 0.40 and 0.37 (2:1 hexane/ethyl acetate); ^1H NMR ($CDCl_3$) δ 0.12, 0.16, 0.23, and 0.26 (s each, 9, $Si(CH_3)_3$), 0.89 (t, 3, J = 5.5 Hz, CH_3), 1.1–1.5 (m, 6, 3 CH_2), 1.5–1.9 (m, 4, 2 CH_2), 2.01, 2.04, and 2.06 (s each, 6, 2 $COCH_3$), 1.9–3.0 (m, 8, 3 CH_2, CH, and OH), 3.67 (s, 3, OCH_3), 4.4–4.6 (m, 1, CHO), 5.1–5.8 (m, 4, two vinyl and 2 C*H*OCOCH_3), 7.29, 7.32, and 7.44 (s each, 1, vinyl).

(7*E*)-PUG 4 (3) and (7*Z*)-PUG 4 (4). Hydroxy enone **33** (19.8 mg, 3.36×10^{-5} mol) was placed in a 10-mL round-bottomed flask and dissolved in dry CH_2Cl_2 (1 mL). After the mixture was cooled to 0 °C, acetic anhydride (0.034 mL, 3.36×10^{-4} mol) and DMAP (83.0 mg, 6.72×10^{-4} mol) were added. The mixture was stirred at 4 °C for 28 h; then the mixture was diluted with CH_2Cl_2 (2 mL) and washed with H_2O (2 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residual oil was subjected to silica gel column chromatography (5 g) with a 10:1 mixture of hexane and ethyl acetate as eluant, yielding dehydrated products (8.3 mg, 43%, 1.45×10^{-5} mol) as a colorless oil: TLC R_f 0.53 (2:1 hexane/ethyl acetate); ^1H NMR ($CDCl_3$) δ 0.02 and 0.16 (s each, 9, $Si(CH_3)_3$), 0.7–1.1 (br t, 3, CH_3), 1.1–1.8 (m, 10, 5 CH_2), 1.8–2.1 (m, 2, CH_2), 2.04, 2.09, and 2.12 (s each, 6, 2 $COCH_3$), 2.1–3.0 (m, 4, 2 CH_2), 3.66 (s, 3, OCH_3), 5.1–5.8 (m, 3, CHO and two vinyl), 5.9–6.2 (m, 1, CHO and vinyl), 6.4–6.7 (m, 1, CHO and vinyl), 7.18 and 7.28 (s each, 1, vinyl).

The dehydrated products from above (8.3 mg, 1.45×10^{-5} mol) were placed in a 10-mL round-bottomed flask, followed by the addition of a 6:3:1 mixture of CH_3COOH–H_2O–THF (0.5 mL) at 0 °C. After warming to 16 °C, the mixture was stirred at this temperature for 6 h. The mixture was diluted with ether (2 mL), cooled to 0 °C, and neutralized with saturated aqueous $NaHCO_3$ solution. The organic layer was separated and aqueous layer was extracted with ether (3 mL × 2). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residual oil was subjected to silica gel column chromatography (3 g) with a 5:1 mixture of hexane and ethyl acetate as eluant, yielding (7*E*)-PUG 4 (**3**) (2.0 mg, 28%, 4.01×10^{-6} mol) as a colorless oil and (7*Z*)-PUG 4 (**4**) (4.9 mg, 68%, 9.82×10^{-6} mol) as a colorless oil. (7*E*)-PUG 4 (**3**): HPLC t_R 17.34 min; CD (CH_3OH) λ_{max} 250 nm ($\Delta\epsilon$ −5.8); ^1H NMR ($CDCl_3$, 500 MHz) δ 0.89 (t, 3, J = 7.0 Hz, CH_3), 1.20–1.40 (m, 6, 3 CH_2), 1.60–1.75 (m, 4, 2 CH_2), 1.97–2.02 (m, 2, C(16)H_2), 2.06 (s, 3, $COCH_3$), 2.13 (s, 3, $COCH_3$), 2.29–2.35 (m, 2, C(2)H_2), 2.68 (dd, 1, J = 14.4 and 7.0 Hz, a proton of C(13)H_2), 3.01 (dd, 1, J = 14.2 and 8.4 Hz, a proton of C(13)H_2), 3.66 (s, 3, OCH_3), 5.23–5.29 (m, 1, C(5)H), 5.29–5.32 (m, 1, C(14)H), 5.57 (dt, 1, J = 11.0 and 7.0 Hz, C(15)H), 6.04 (dd, 1, J = 9.0 and 4.4 Hz, C(6)H), 6.38 (d, 1, J = 9.2 Hz, C(7)H), 7.29 (s, 1, C(11)H); HRMS, m/z calcd for $C_{25}H_{35}O_8Cl$ 498.2020 found 498.2030. Natural (7*E*)-PUG 4 showed CD (CH_3OH) λ_{max} 250 nm ($\Delta\epsilon$ −5.0). (7*Z*)-PUG 4 (**4**): HPLC t_R 32.04 min; CD (CH_3OH) λ_{max} 268 nm ($\Delta\epsilon$ −5.4); ^1H NMR ($CDCl_3$, 500 MHz) δ 0.89 (t, 3, J = 7.0 Hz, CH_3), 1.20–1.40 (m, 6, 3 CH_2), 1.60–1.75 (m, 4, 2 CH_2), 1.97–2.01 (m, 2, C(16)H_2), 2.05 (s, 3, $COCH_3$), 2.12 (s, 3, $COCH_3$), 2.35 (t, 2, J = 6.7 Hz, C(2)H_2), 2.45 (dd, 1, J = 14.4 and 7.3 Hz, a proton of C(13)H_2), 2.58 (dd, 1, J = 14.6 and 7.9 Hz, a proton of C(13)H_2), 3.67 (s, 3, OCH_3), 5.20–5.24 (m, 1, C(5)H), 5.24–5.29 (m, 1, C(14)H), 5.60 (dt, 1, J = 11.0 and 7.3 Hz, C(15)H), 6.10 (d, 1, J = 7.9 Hz, C(7)H), 6.35 (dd, 1, J = 7.8 and 3.5 Hz. C(6)H), 7.22 (s, 1, C(11)H); HRMS, m/z calcd for $C_{17}H_{20}O_8Cl$ ($M^+ - C_8H_{15}$) 387.0847, found 387.0824. Natural (7*Z*)-PUG 4 showed CD (CH_3OH) λ_{max} 268 nm ($\Delta\epsilon$ −4.8).

12-*epi*-(7*E*)-PUG 4 (1). Overall yield from the corresponding aldol product was 12%: HPLC t_R 17.86 min; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.90 (t, 3, J = 7.0 Hz, CH_3), 1.20–1.40 (m, 6, 3 CH_2), 1.60–1.80 (m, 4, 2 CH_2), 1.95–2.03 (m, 2, C(16)H_2), 2.11 (s, 6, 2 $COCH_3$), 2.34–2.36 (m, 2, C(2)H_2), 2.48 (dd, 1, J = 14.3 and 7.3 Hz, a proton of C(13)H_2), 2.76 (dd, 1, J = 14.3 and 7.3 Hz, a proton of C(13)H_2), 3.68 (s, 3, OCH_3), 5.15–5.32 (m, 2, C(5)H and C(14)H), 5.57 (dt, 1, J = 11.0 and 7.3 Hz, C(15)H), 5.69 (dd, 1, J = 10.4 and 4.3 Hz, C(6)H), 6.32 (d, 1, J = 10.4 Hz, C(7)H), 7.31 (s, 1, C(11)H); HRMS, m/z calcd for $C_{25}H_{35}O_8Cl$ 498.2020, found 498.1989.

12-*epi*-(7*Z*)-PUG 4 (35). Overall yield from the corresponding aldol product was 26%: HPLC t_R 33.74 min; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.90 (t, 3, J = 7.0 Hz, CH_3), 1.20–1.40 (m, 6, 3 CH_2), 1.60–1.80 (m, 4, 2 CH_2), 1.95–2.02 (m, 2, C(16)H_2), 2.06 (s, 3, $COCH_3$), 2.11 (s, 3, $COCH_3$), 2.30–2.40 (m, 2, C(2)H_2), 2.53 (dd, 1, J = 15.3 and 7.9 Hz, a proton of C(13)H_2), 2.66 (dd, 1, J = 14.5 and 7.8 Hz, a proton of C(13)H_2), 3.64 (s, 3, OCH_3), 5.20–5.40 (m, 2, C(5)H and C(14)H), 5.55–5.67 (m, 1, C(15)H), 6.07 (d, 1, J = 7.9 Hz, C(7)H), 6.62 (dd, 1, J = 8.1 and 4.4 Hz, C(6)H), 7.23 (s, 1, C(11)H); HRMS, m/z calcd for $C_{25}H_{35}O_8Cl$ 498.2020, found 498.2065.

***ent*-(7*E*)-PUG 4 (34).** Overall yield from the corresponding aldol product was 8%: HPLC t_R 17.34 min; CD (CH_3OH) λ_{max} 250 nm ($\Delta\epsilon$ +5.5); ^1H NMR ($CDCl_3$, 500 MHz) δ 0.9 (t, 3, J = 7.0 Hz, CH_3), 1.2–1.4 (m, 6, 3 CH_2), 1.6–1.7 (m, 4, 2 CH_2), 1.95–2.02 (m, 2, C(16) H_2), 2.05 (s, 3, $COCH_3$), 2.12 (s, 3, $COCH_3$), 2.27–2.30 (m, 2, C(2)H_2), 2.67 (dd, 1, J = 14.2 and 6.7 Hz, a proton of C(13)H_2), 3.01 (dd, 1, J = 14.0 and 8.6 Hz, a proton of C(13)H_2), 3.66 (s, 3, OCH_3), 5.26–5.35 (m, 2, C(5)H and C(14)H), 5.54–5.57 (dt, 1, C(15)H), 6.04 (dd, 1, J = 9.0 and 4.4 Hz, C(6)H), 6.37 (d, 1, J = 9.2 Hz, C(7)H), 7.28 (s, 1, C(11)H); HRMS, m/z calcd for $C_{25}H_{33}O_7Cl$ ($M^+ - H_2O$) 480.1915, found 480.1919.

***ent*-(7*Z*)-PUG 4 (2).** Overall yield from the corresponding aldol product was 22%: HPLC t_R 32.04 min; CD (CH_3OH) λ_{max} 268 nm ($\Delta\epsilon$ +4.1); ^1H NMR ($CDCl_3$, 500 MHz) δ 0.89 (t, 3, J = 7.0 Hz, CH_3), 1.20–1.35 (m, 6, 3 CH_2), 1.65–1.72 (m, 4, 2 CH_2), 1.99 (dt, 2, J = 9.5 and 5.5 Hz, C(16)H_2), 2.05 (s, 3, $COCH_3$), 2.11 (s, 3, $COCH_3$), 2.35 (t, 2, J = 7.0 Hz, C(2)H_2), 2.46 (dd, 1, J = 14.3 and 7.3 Hz, a proton of C(13)H_2), 2.58 (dd, 1, J = 14.5 and 7.8 Hz, a proton of C(13)H_2), 3.66 (s, 3, OCH_3), 5.20–5.24 (m, 1, C(5)H), 5.24–5.29 (m, 1, C(14)H), 5.60 (dt, 1, J = 10.7 and 7.6 Hz, C(15)H),

6.10 (d, 1, J = 7.8 Hz, C(7)H), 6.36 (dd, 1, J = 7.8 and 3.7 Hz, C(6)H), 7.22 (s, 1, C(11)H); HRMS, m/z calcd for $C_{25}H_{35}O_8Cl$ 498.2020, found 498.1985.

6-*epi*-12-*epi*-(7*E*)-PUG 4 (36). Overall yield from the corresponding aldol product was 10%: HPLC t_R 17.57 min; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.90 (t, 3, CH_3), 1.20–1.40 (m, 6, 3 CH_2), 1.60–1.70 (m, 4, 2 CH_2), 1.95–2.02 (m, 2, C(16)H_2), 2.08 (s, 3, $COCH_3$), 2.10 (s, 3, $COCH_3$), 2.27–2.33 (m, 2, CH_2), 2.66 (dd, 1, J = 13.9 and 8.0 Hz, a proton of C(13)H_2), 2.90 (dd, 1, J = 13.9 and 9.0 Hz, a proton of C(13)H_2), 3.64 (s, 3, OCH_3), 5.30–5.48 (m, 2, C(5)H and C(14)H), 5.52–5.58 (dt, 1, C(15)H), 6.24 (dd, 1, J = 9.5 and 2.6 Hz, C(6)H), 6.53 (d, 1, J = 9.5 Hz, C(7)H), 7.30 (s, 1, C(11)H); HRMS, m/z calcd for $C_{25}H_{33}O_7Cl$ ($M^+ - H_2O$) 480.1915, found 480.1885.

6-*epi*-12-*epi*-(7*Z*)-PUG 4 (37). Overall yield from the corresponding aldol product was 24%. HPLC t_R 29.29 min; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.90 (t, 3, CH_3), 1.20–1.40 (m, 6, 3 CH_2), 1.60–1.70 (m, 4, 2 CH_2), 1.95–2.02 (m, 2, C(16)H_2), 2.03 (s, 3, $COCH_3$), 2.08 (s, 3, $COCH_3$), 2.27–2.30 (m, 2, CH_2), 2.56 (dd, 1, J = 14.7 and 8.2 Hz, a proton of C(13)H_2), 2.63 (dd, 1, J = 13.9 and 7.8 Hz, a proton of C(13)H_2), 3.65 (s, 3, OCH_3), 5.25–5.45 (m, 2, C(5)H and C(14)H), 5.61 (dt, 1, J = 11.0 and 7.3 Hz, C(15)H), 6.18 (d, 1, J = 8.9 Hz, C(7)H), 6.48 (dd, 1, J = 8.9 and 3.5 Hz, C(6)H), 7.23 (s, 1, C(11)H); HRMS, m/z calcd for $C_{25}H_{35}O_8Cl$ 498.2020, found 498.2078.

6-*epi*-(7*E*)-PUG 4 (38). Overall yield from the corresponding aldol product was 8%: HPLC t_R 18.61 min; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.89 (t, 3, J = 7.0 Hz, CH_3), 1.20–1.40 (m, 6, 3 CH_2), 1.50–1.70 (m, 4, 2 CH_2), 1.96–2.02 (m, 2, C(16)H_2), 2.08 (s, 3, $COCH_3$), 2.10 (s, 3, $COCH_3$), 2.32–2.37 (m, 2, C(2)H_2), 2.57 (dd, 1, J = 14.0 and 6.7 Hz, a proton of C(13)H_2), 2.88 (dd, 1, J = 14.0 and 7.9 Hz, a proton of C(13)H_2), 3.68 (s, 3, OCH_3), 5.08–5.12 (m, 1, C(5)H), 5.22–5.26 (m, 1, C(14)H), 5.54–5.57 (m, 1, C(15)H), 5.77 (dd, 1, J = 10.3 and 4.9 Hz, C(6)H), 6.31 (d, 1, J = 10.3 Hz, C(7)H), 7.33 (s, 1, C(11)H); HRMS, m/z calcd for $C_{25}H_{35}O_8Cl$ 498.2020, found 498.1988.

6-*epi*-(7*Z*)-PUG 4 (39). Overall yield from the corresponding aldol product was 36%: HPLC t_R 30.09 min; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.89 (t, 3, J = 7.0 Hz, CH_3), 1.20–1.40 (m, 6, 3 CH_2), 1.60–1.80 (m, 4, 2 CH_2), 1.98–2.02 (m, 2, C(16)H_2), 2.06 (s, 3, $COCH_3$), 2.07 (s, 3, $COCH_3$), 2.30–2.40 (m, 2, C(2)H_2), 2.57 (dd, 1, J = 14.4 and 7.6 Hz, a proton of C(13)H_2), 2.70 (dd, 1, J = 14.4 and 7.3 Hz, a proton of C(13)H_2), 3.67 (s, 3, OCH_3), 5.20–5.37 (m, 2, C(5)H and C(14)H), 5.66 (dt, 1, J = 10.7 and 7.5 Hz, C(15)H), 6.23 (d, 1, J = 9.2 Hz, C(7)H), 6.68 (dd, 1, J = 9.2 and 4.0 Hz, C(6)H), 7.25 (s, 1, C(11)H); HRMS, m/z calcd for $C_{25}H_{33}O_7Cl$ ($M^+ - H_2O$) 480.1915, found 480.1914.

Photoisomerization of (7*E*)-PUG 4 (3) and (7*Z*)-PUG 4 (4). A solution of (7*E*)-PUG 4 (**3**) or (7*Z*)-PUG 4 (**4**) (0.82 mg, 0.59 mg each) in benzene (0.7 mL, 0.5 mL each) in a Pyrex tube was irradiated with a fluorescent lamp (25 W) at 20 °C. The reactions of **3** and **4** were monitored by HPLC analysis (t_R 17.34 min for **3**; t_R 32.04 min for **4**). From both compounds photoequilibration (the ratio of **3**/**4** = 7:3) was established after 60 h.

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Registry No. **1**, 105927-56-8; **2**, 103384-66-3; **3**, 96055-66-2; **3** ($Si(CH_3)_3$ ether), 103529-69-7; **4**, 96055-68-4; **4** ($Si(CH_3)_3$ ether), 103476-02-4; **5**, 72034-82-3; (±)-**5**, 75598-96-8; (±)-**5** (desilyl deriv), 85994-98-5; **6**, 71268-69-4; **7**, 103384-40-3; **8**, 103384-51-6; **9**, 103384-55-0; **11**, 64244-45-7; **12**, 79356-66-4; *ent*-**12**, 77519-23-4; **13**, 103384-35-6; *ent*-**13**, 103475-95-2; **14**, 103384-37-8; *ent*-**14**, 103475-97-4; **14** (triol), 103384-42-5; **15**, 103384-38-9; *ent*-**15**, 103475-98-5; **16**, 103384-39-0; *ent*-**16**, 103384-50-5; **21**, 78606-80-1; **22**, 103384-52-7; **23**, 103384-53-8; **24**, 103384-54-9; **26**, 69165-98-6; **27**, 111847-83-7; **28**, 103476-03-5; **28** (5-$Si(CH_3)_2C_4H_9$-*t* ether), 103475-94-1; **28** (allene), 103384-57-2; *ent*-**28**, 103384-56-1; (±)-**28**, 111901-60-1; (±)-*trans*-**28**, 111901-61-2; **29**, 111822-75-4; **29** (5-$Si(CH_3)_2C_4H_9$-*t* ether), 111822-74-3; **30**, 103476-01-3; *ent*-**30**, 103384-44-7; **31**, 103384-59-4; *ent*-**31**, 103384-45-8; **32**, 103384-60-7; *ent*-**32**, 103384-46-9; **33**, 111901-56-5; *ent*-**33**, 103384-61-8; (6*R*)-**33**, 111901-58-7; (12*R*)-**33**, 103384-47-0; (6*R*,12*R*)-**33**, 111901-57-6; **34**, 103384-65-2; **35**, 105927-55-7; **36**, 103384-67-4; **37**, 103384-68-5; **38**, 103531-36-8; **39**, 111901-59-8; *n*-$C_5H_{11}MgBr$, 693-25-4; $BrCH_2C{\equiv}CC_5H_{11}$-*n*, 18495-27-7.