An Effective Method for the Preparation of Chiral Polyoxy 8-Membered Ring Enone Corresponding to the B Ring of Taxol

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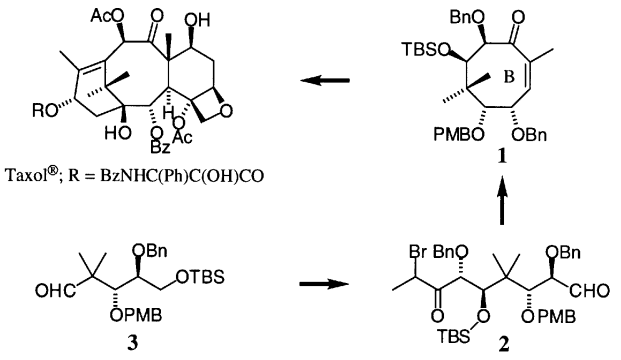
An effective method for the preparation of 8-membered ring enone, (4*S*,5*R*,7*R*,8*R*)-4,8-bis(benzyloxy)-7-(*t*-butyldimethylsiloxy)-5-(4-methoxybenzyloxy)-2,6,6-trimethylcyclooct-2-enone (**1**), in sufficient quantities was developed. Optically active trioxy aldehyde, (3*R*,4*S*)-4-benzyloxy-5-(*t*-butyldimethylsiloxy)-3-(4-methoxybenzyloxy)-2,2-dimethylpentanal (**3**), was prepared first by diastereoselective dihydroxylation of (2*R*,4*S*)-2-(4-methoxyphenyl)-5,5-dimethyl-4-vinyl-1,3-dioxane derived from D-pantolactone. Next, 8-chloro-7-oxoaldehyde, (2*R*,3*R*,5*R*,6*R*)-2,6-bis(benzyloxy)-5-(*t*-butyldimethylsiloxy)-8-chloro-3-(4-methoxybenzyloxy)-4,4-dimethyl-7-oxononanal (**30**), was newly synthesized by the following reactions: i) $MgBr_2$•OEt_2-mediated diastereoselective aldol reaction of the aldehyde **3** with (*Z*)-2-benzyloxy-1-methoxy-1-(trimethylsiloxy)ethene and ii) reaction of methyl (2*R*,3*R*,5*R*,6*S*)-2,6-bis(benzyloxy)-3,7-bis(*t*-butyldimethylsiloxy)-5-(4-methoxybenzyloxy)-4,4-dimethylheptanoate with 1,1-dichloroethyllithium, followed by successive reductive dehalogenation of thus formed 1,1-dichloroethyl ketone with 1,1-dichloroethyllithium. Then, the chiral 8-chloro-7-oxoaldehyde **30** was converted to the 8-membered ring enone **1** by SmI_2-mediated aldol cyclization.

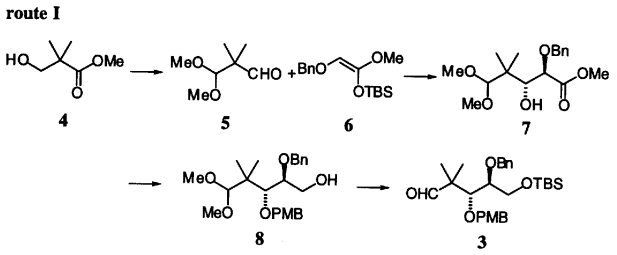
Syntheses of Taxol and its analogues were recently reported from our laboratory.[1] These synthetic strategies were to first construct the basic frameworks of taxoids from optically active polyoxy 8-membered ring enone **1** corresponding to the B ring of Taxol (Scheme 1).

In the previous papers, two routes for the synthesis of trioxy aldehyde **3** via the following key steps were reported: namely, i) enantioselective aldol reaction of 3,3-dimethoxy-2,2-dimethylpropanal (**5**) with ketene *t*-butyldimethylsilyl acetal **6** using tin(II) trifluoromethanesulfonate coordinated with chiral diamine (Scheme 2) and ii) diastereoselective aldol reaction between optically active dioxy aldehyde **10** derived from L-serine and lithium enolate prepared from methyl isobutyrate (Scheme 3).

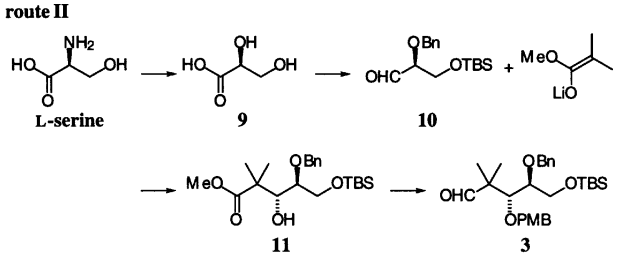
In the above routes, however, much still remains to be improved in preparing sufficient quantities of aldehyde **3**, because **route I** requires the reaction to be performed carefully at low



Scheme 1.



Scheme 2. Reagents and conditions.[1a]



Scheme 3. Reagents and conditions.[1a]

temperature by using a stoichiometric amount of chiral diamine. In **route II**, racemization of α-position of the carbonyl group takes place slowly when dioxy aldehyde **10** is prepared on a scale over 10 g. The ee of aldol adduct formed from **10** and methyl isobutylate ranges between 78–95%. Therefore, the third route was planned in anticipation of the key intermediate, aldehyde **12**, to resist racemization, since this compound contained a stable 6-membered ring in chair form with three equatorial functionalities. By theoretical calculation at RHF/6-31G*//PM3 level,[2] it was shown that **12** is more stable than ***epi***-

12, as shown in Fig. 1.

The aldehyde **12** might be prepared from commercially available D-pantolactone, and it might be further converted to the optically active key intermediate **3** by one-carbon elongation and successive dihydroxylation onto the double bond of **13** (Scheme 4).

Further, the improvement of each step involved in the multistep procedure of synthesizing 8-membered ring enone **1** from aldehyde **3** was also desired.

In this paper, we would like to report an effective method for the preparation of optically active trioxy aldehyde **3** starting from D-pantolactone and for the preparation of 8-membered ring enone **1** from **3** according to the following procedure:[3] i.e. an improved diastereoselective aldol reaction of the above aldehyde **3** with ketene trimethylsilyl acetal **21**, and successive formation of 1,1-dichloroethyl ketone **29** from ester **23**, followed by partial dehalogenation of **29** to form 1-chloroethyl ketone **28**, and facile 8-membered ring formation by treating 8-chloro-7-oxoaldehyde **30** with SmI_2.

Results and Discussion

At first, D-pantolactone was reduced with $LiAlH_4$ in THF to give the corresponding optically active triol **14** in good yield. The triol was successively converted to *p*-methoxybenzylidene acetal under thermodynamic conditions by using camphorsulfonic acid (CSA), and a 6-membered ring acetal **15c** was obtained exclusively, as shown in Scheme 5.[4]

The relative energy of each stable structure of *p*-methoxybenzylidene acetals **15a–15d** which are produced from triol **14** is shown in Fig. 2.[2] It was suggested that the 6-membered ring acetals **15c** and **15d** are more stable than the 5-membered ring acetals **15a** and **15b**, and the structure of **15c** containing three equatorial substituents is more favorable compared to that of **15d** containing two equatorial ones.

The alcohol **15c** was oxidized under Swern's conditions to afford the desired aldehyde **12**. The Wittig reaction of **12** furnished olefin **13**, which has a five-carbon backbone corresponding to that of trioxy aldehyde **3**. Dihydroxylation of the double bond of **13** smoothly proceeded to yield *anti*-diol **16** with high diastereoselectivity (99%, *anti*/*syn* = 24/1) by using a catalytic amount of OsO_4 in the presence of *N*-methylmorpholine *N*-oxide (NMO) in acetone and water. When this reaction was carried out in the presence of AD-mix-α, a mixture of diols was obtained in 44% yield with lower stereoselectivity (*anti*/*syn* = 15/1), while the presence of AD-mix-β afforded the corresponding *anti*-diol **16** stereoselectively in moderate yield (51%, *anti*/*syn* = 33/1). Similar to the recently proposed mechanism of diastereoselective dihydroxylation,[5] *anti*-diol **16** should be formed by the α-side attack of OsO_4 on **13**α as shown in Fig. 3, though the model **13**β is more stable than the model **13**α according to the conformational analysis of **13**.

In order to discuss the selectivity in detail, MMFF-transition state combined model was employed.[6] Based on the calculation at B3LYP/LACVP*(6-31G*)//B3LYP/LACVP*(6-31G*) level, an earlier structure of transition state for dihydroxylation of propene was predicted (Fig. 4).[2,7] As shown in Fig. 5, structures for the osmate formation of **13** via **path A–D** were optimized with MMFF including constraints obtained in TS for

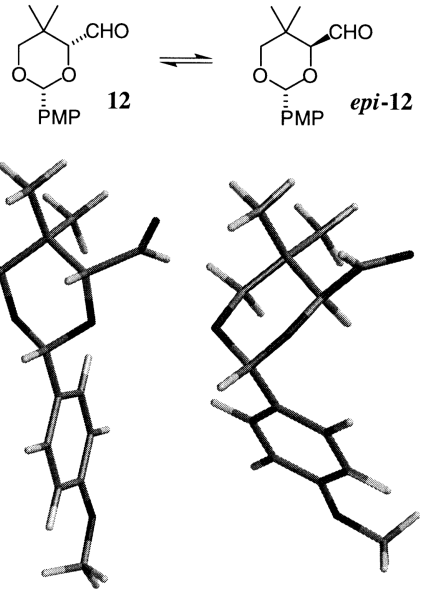
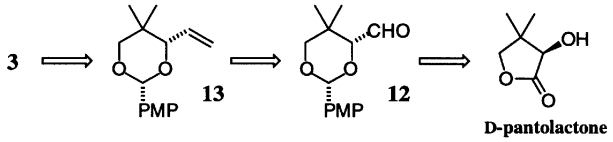
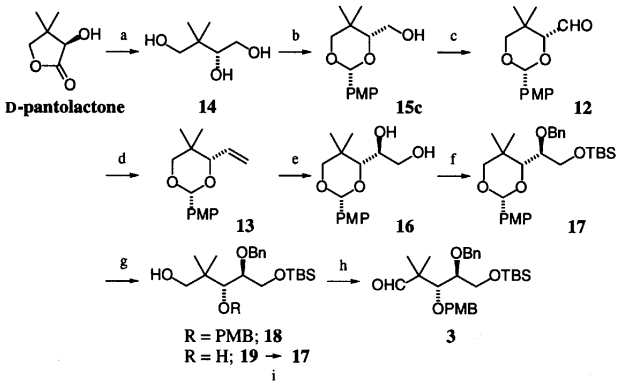


Fig. 1. Relative energy of the most stable structure concerning **12** and ***epi*-12** was presented. Relative energy of each conformer was estimated by molecular orbital calculation (RHF/6-31G*//PM3) after generating all conformations with MMFF.



Scheme 4.



Scheme 5. Reagents and conditions: a) $LiAlH_4$, THF, 0 °C, b) $PMPCH(OMe)_2$, CSA, CH_2Cl_2, rt (92%, 2 steps); c) DMSO, $(COCl)_2$, Et_3N, CH_2Cl_2, −78 °C to rt; d) $Ph_3P^+CH_3Br^-$, ^{n}BuLi, THF, −15 °C to rt (86%, 2 steps); e) OsO_4, NMO, acetone, H_2O, ^{t}BuOH, rt (99%, *anti*/*syn* = 24/1); f) TBSCl, imidazole, DMF, 0 °C (quant.); BnBr, NaH, THF, DMF, rt (96%); g) BH_3·SMe_2, toluene, reflux (85% of **18** plus 11% of **19**); h) DMSO, $(COCl)_2$, Et_3N, CH_2Cl_2, −78 °C to rt (96%);[1a] i) $PMPCH(OMe)_2$, CSA, CH_2Cl_2, 0 °C (90%).

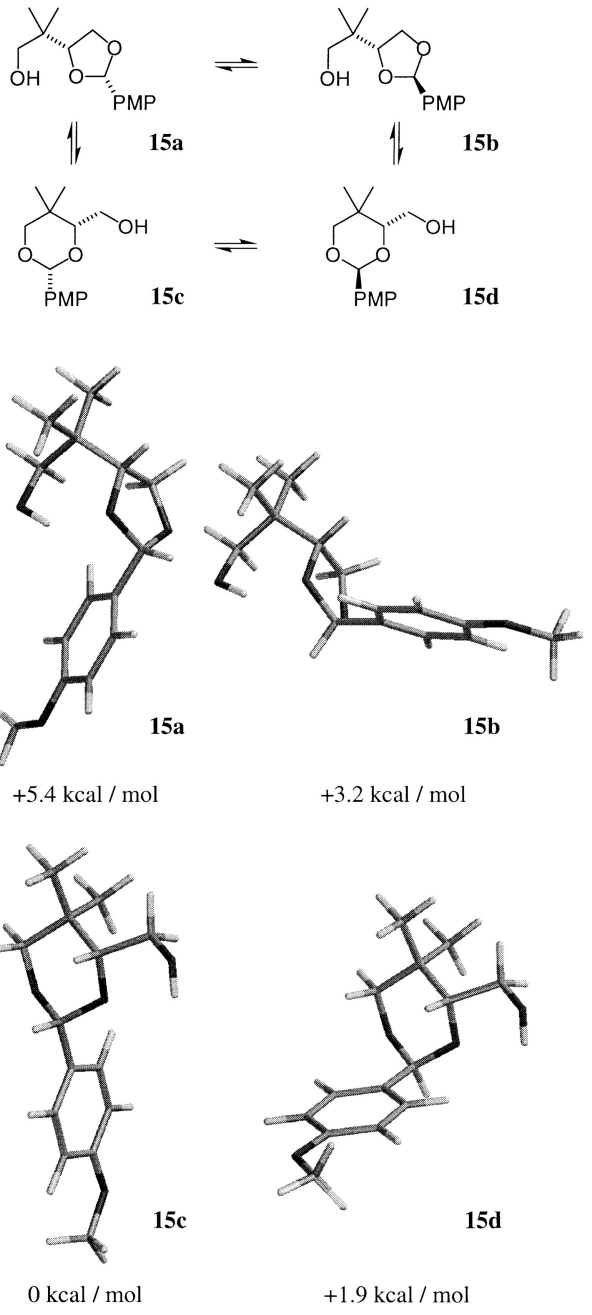


Fig. 2. Relative energy of the most stable structure concerning **15a–15d** was presented. Relative energy of each conformer was estimated by molecular orbital calculation (RHF/6-31G*//PM3) after generating all conformations with MMFF.

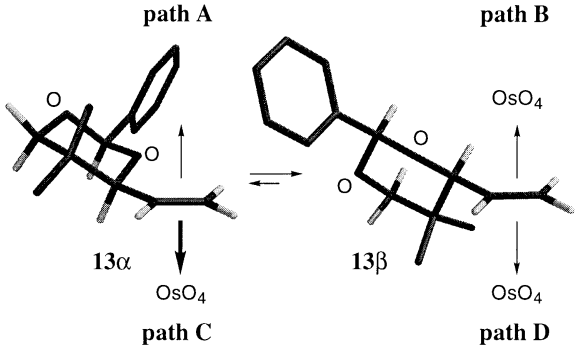


Fig. 3. Stable conformations of olefin **13** where some atoms have been omitted for clarity.

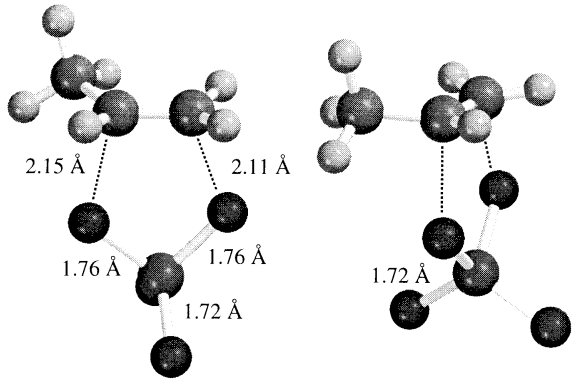


Fig. 4. Transition state forming osmate from propene estimated by molecular orbital calculation (B3LYP/LACVP* (6-31G*)//B3LYP/LACVP* (6-31G*)).

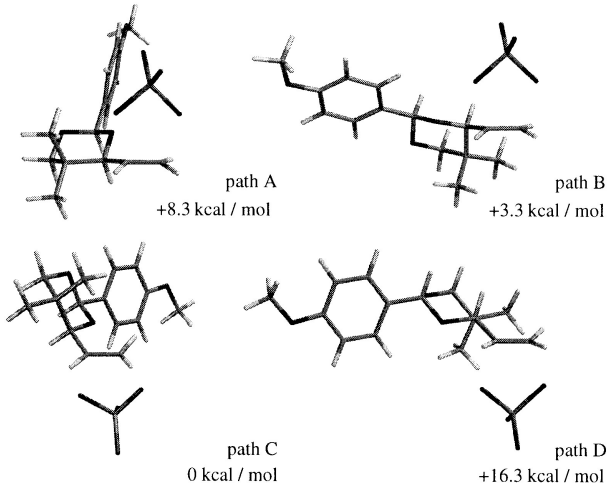
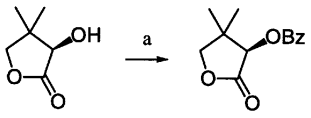


Fig. 5. Transition states forming osmate from **13** via **path A–D**. Optimized structures were given by MMFF-transition state combined model. Relative energy was estimated by calculation with MMFF according to MMFF-transition state combined model.

propene (rigid TS model).[2] Though the relative activation energy for the formation of *syn*-diol via **path A** and **path B** was lower compared to that of forming desired *anti*-diol **16** via **path D**, the relative activation energy for the formation of **16** via **path C** was lowest among them. Therefore, it was confirmed that α-side attack of OsO_4 to conformer **13**α in **path C** induced the excellent diastereoselectivity of dihydroxylation.

Successive regioselective protection of the primary and secondary hydroxyl groups of **16** afforded *p*-methoxybenzylidene acetal **17** in quite high yield. A small amount of stereoisomer of **17** was separated at this stage and HPLC analysis revealed that the optical purity of **17** was 96% ee. The optical purity of D-pantolactone was determined after it had been converted to its benzoate **20** (99% ee), as shown in Scheme 6. The intermedi-



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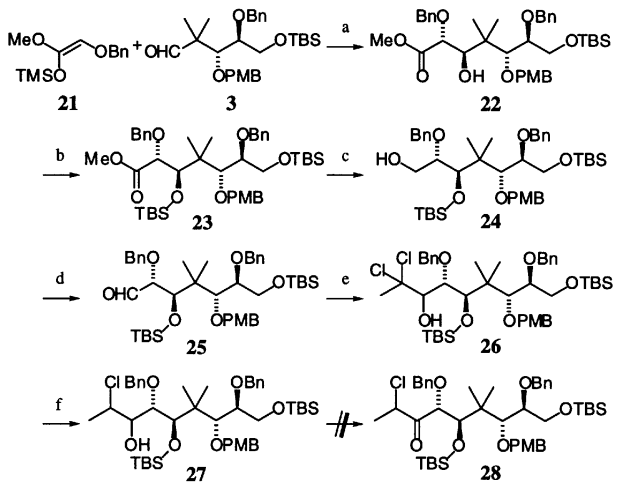
Scheme 6. Reagents and conditions: a) BzCl, DMAP, Et_3N, CH_2Cl_2, 0 °C (quant.).

ate **12** slightly racemizes during the operation; however, it was confirmed that the optical purity of **17** was excellently preserved even in large scale synthesis of the intermediates (e.g. treating 20–100 g of alcohol **15c**).

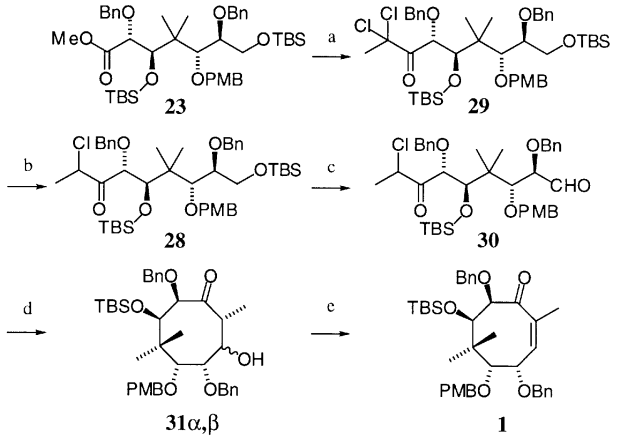
Then regioselective reductive cleavage of the acetal function was carried out with a stoichiometric amount of BH_3•SMe_2, and the desired primary alcohol **18** was exclusively obtained. When diisobutylaluminum hydride (DIBAL) was employed in the above reductive cleavage, an undesirable secondary alcohol resulted as a major product. Diol **19** formed along with **18** was re-used after having been treated with *p*-methoxybenzaldehyde dimethyl acetal and CSA. The primary alcohol **18** was oxidized under Swern's conditions to produce aimed aldehyde **3** in quite high yield. Thus, a new route for the preparation of optically active trioxy aldehyde **3** in sufficient quantities which started from D-pantolactone was established. This synthetic procedure gave **3** in 67% total yield from D-pantolactone by combining yield of **3** from **18** and that of separately produced **3** from **19**, while the total yield of **3** from L-serine was 39%.

Next, the synthesis of 8-membered ring enone **1** in sufficient quantities from the trioxy aldehyde **3** was studied (Schemes 7 and 8). The aldol reaction of **3** with ketene trimethylsilyl acetal **21**,[8] a reactive nucleophile, instead of previously reported ketene *t*-butyldimethylsilyl acetal **6**, was tried in the presence of 3 molar amounts of $MgBr_2$•OEt_2. This addition reaction proceeded smoothly at –19 °C, and the desired 2,3,5-*anti*,*anti*-aldol **22** was obtained in better yield (87%) compared to the case



21 **3** **22** **23** **24** **25** **26** **27** **28**

Scheme 7. Reagents and conditions: a) $MgBr_2$•OEt_2, toluene, –19 °C (87%); b) TBSOTf, 2,6-lutidine, CH_2Cl_2, 0 °C (quant.);[1a] c) DIBAL, toluene, –78 °C;[1a] d) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, –78 °C to rt (94%, 2 steps);[1a] e) CH_3CHCl_2, ^{n}BuLi, Et_2O, THF, –100 °C to –78 °C (51%); f) ^{n}Bu_3SnH, benzene, reflux (38%).



23 **29** **28** **30** **31**α,β **1**

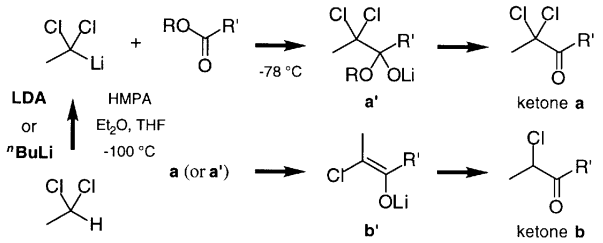
Scheme 8. Reagents and conditions: a) CH_3CHCl_2, ^{n}BuLi, Et_2O, THF, –100 °C to –78 °C (78%); b) ^{n}Bu_3SnH, benzene, reflux (90%); c) 1 M HCl, THF, rt (93%); DMSO, $(COCl)_2$, Et_3N, CH_2Cl_2, –78 °C to rt (92%); d) SmI_2, THF, –23 °C (65%); g) Ac_2O, DMAP, pyridine, rt; DBU, benzene, 60 °C (82%, 2 steps).[1a]

of using **6** as a nucleophile (63%). After converting the aldol **22** to silyl ether **23**, successive reduction and oxidation gave the corresponding pentaoxy aldehyde **25**. In the beginning, conversion of **25** to chloro alcohol **27** was planned by treating 1-chloroethyllithium generated from 1-bromo-1-chloroethane with ^{n}BuLi; however, 1-bromo-1-chloroethane was not easily available. Then, dichloro alcohol **26** was synthesized by reaction of **25** with 1,1-dichloroethyllithium[9–12] generated from 1,1-dichloroethane and ^{n}BuLi instead of 1-chloroethyllithium. When ^{n}Bu_3SnH was used as a reductant, partial dehalogenation of **26** proceeded to give **27** in moderate yield. However, successive oxidations of thus formed alcohol with several reagents did not proceed at all, probably because of steric hindrance around the secondary hydroxyl group.

Then, reaction of ester **23** with 1,1-dichloroethyllithium was tried.[3,11] When the ester in a mixed solvent of Et_2O and THF was treated with 1,1-dichloroethyllithium prepared from 1,1-dichloroethane and a solution of ^{n}BuLi in hexane at –100 °C, the desired 1,1-dichloroethyl ketone **29** was exclusively formed in good yield. Complete dehalogenation of 1,1-dichloroethyl ketone **29** gave the corresponding ethyl ketone by using ^{n}Bu_3SnH and AIBN combined system. On the other hand, partial dehalogenation of **29** afforded 1-chloroethyl ketone **28** in high yield by using ^{n}Bu_3SnH alone. After the removal of TBS group at C9 of **28**, 8-chloro-7-oxoaldehyde **30**, a precursor of 8-membered ring compound, was obtained by Swern oxidation. Similar to the case of 8-bromo-7-oxoaldehyde **2** mentioned in the previous paper, intramolecular aldol reaction of **30** also proceeded smoothly to produce a diastereomeric mixture of 8-membered ring aldols **31**α,β in good yield (**31**α/**31**β = 83/17).[1a,13] The above results suggested that the same samarium enolate was formed from both precursors, 1-bromoethyl ketone and 1-chloroethyl ketone, and stable conformation of the enolate anion favored cyclization to afford the desired 8-membered ring compounds.[1a] Eight-membered ring enone **1** was obtained in high yield from **31**α,β via the corresponding

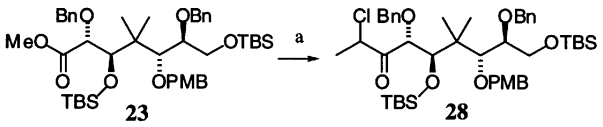
acetates on treatment with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU).

Finally, improved synthesis of 1-chloroethyl ketone **28** from the ester **23** was studied.[11] The reaction giving 1-chloroethyl ketones from alkyl carboxylates was assumed to proceed stepwise, as shown in Scheme 9:[11] that is, i) reaction of alkyl carboxylates with 1,1-dichloroethyllithium to form ketones **a**, and ii) successive dehalogenation of thus formed ketones **a** by reduction with excess 1,1-dichloroethyllithium, affording ketones **b** via lithium enolates **b′**.



Scheme 9.

Expectedly, 1-chloroethyl ketone **28** was directly obtained in 91% yield when **23** was treated with an excess amount of 1,1-dichloroethyllithium generated from 1,1-dichloroethane and ^{n}BuLi (30 molar amounts) in the presence of HMPA, as shown in Scheme 10.



Scheme 10. Reagents and conditions: a) CH_3CHCl_2, ^{n}BuLi, Et_2O, THF, HMPA, −100 °C to −78 °C (91%).

Thus, an effective method for the preparation of 8-membered ring enone **1**, a key intermediate of Taxol synthesis, that started from D-pantolactone was accomplished by the following successive reactions: that is, diastereoselective dihydroxylation of olefin **13**, regioselective cleavage of *p*-methoxybenzylidene acetal **17**, diastereoselective aldol reaction of **3** with ketene trimethylsilyl acetal **21**, conversion of the ester **23** to 1-chloroethyl ketone **28**, and 8-membered ring formation by aldol-type cyclization of 8-chloro-7-oxoaldehyde **30** with SmI_2.

Experimental

General. All melting points were measured on a Yanaco MP-S3 micro melting point apparatus. Infrared spectra were recorded on a Horiba FT-300 infrared spectrometer. Proton and ^{13}C NMR spectra were recorded on a JEOL JNM-EX270L, a JEOL JNM-LA400 or a JEOL JNM-LA500 spectrometer with chloroform (in chloroform-*d*) or benzene (in benzene-d_6) as an internal standard. High-resolution mass spectra were recorded on a JEOL JMS-SX102A or a JEOL JMS-AX505HA instrument using 4-nitrobenzyl alcohol as a matrix. High performance liquid chromatography was carried out using a Hitachi LC-Organizer, L-4000 UV Detector, L-6200 Intelligent Pump, and D-2500 Chromato-Integrator. Column chromatography was performed on Silica gel 60 (Merck). Thin layer chromatography was performed on Wakogel B-5F.

All reactions were carried out under an argon atmosphere in dried glassware, unless otherwise noted. Dichloromethane was distilled from diphosphorus pentaoxide, then calcium hydride, and dried over MS 4Å; benzene and toluene were distilled from diphosphorus pentaoxide, and dried over MS 4Å; DMF, HMPA, and DMSO were distilled from calcium hydride, and dried over MS 4Å; and THF and diethyl ether were distilled from sodium/benzophenone immediately prior to use. Lithium aluminum hydride was purchased from Yoneyama Yakuhin Kogyo Co., Ltd. *t*-Butylchlorodimethylsilane was purchased from Shin-Etsu Chemical Co., Ltd. Other reagents were purchased from Tokyo Kasei Kogyo Co., Ltd., Kokusan Chemical Co., Ltd., Kanto Chemical Co., Inc. or Aldrich Chemical Co., Inc., and were used without further purification unless otherwise noted.

Experimental details for compounds **1–11**, **18**, **22–25** and **31** were described in Ref. 1a.

(2*R*)-3,3-Dimethylbutane-1,2,4-triol (14). To a suspension of lithium aluminum hydride (29.2 g, 771 mmol) in THF (500 mL) at 0 °C was added a solution of D-pantolactone (50.0 g, 380 mmol) in THF (100 mL). After the reaction mixture was stirred for 4 h at room temperature, solid sodium sulfate decahydrate was gradually added. The pH of the mixture was adjusted to 3 with sulfuric acid (50 wt%) and then it was neutralized with solid sodium hydrogencarbonate. The crude product was filtered through a short pad of Celite with ethyl acetate and the filtrate was concentrated by evaporation of the solvent to afford triol **14** (51.0 g) as a colorless oil. This was used in next step without further purification. For detailed analysis of **14**, it can be purified by thin layer chromatography (hexane/AcOEt = 1/2). $[\alpha]_D^{25} = -14.6°$ (*c* 1.62, EtOH). IR (neat) 3390, 3340 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 4.02 (br s, 3H, OH), 3.67 (dd, *J* = 16.8, 7.9 Hz, 1H, 1-H), 3.55 (dd, *J* = 16.8, 7.9 Hz, 1H, 1-H), 3.54 (t, *J* = 7.9 Hz, 1H, 2-H), 3.44 (d, *J* = 10.8 Hz, 1H, 4-H), 3.38 (d, *J* = 10.8 Hz, 1H, 4-H), 0.95 (s, 3H, 3-Me), 0.93 (s, 3H, 3-Me). ^{13}C NMR ($CDCl_3$) δ 77.9 (2), 70.3 (4), 62.8 (1), 37.7 (3), 22.6 (Me), 19.6 (Me). HRMS(ESI) Found: *m*/*z* 157.0848. Calcd for $C_6H_{14}O_3Na$ $[M + Na]^+$: 157.0841.

[(2*R*,4*R*)-2-(4-Methoxyphenyl)-5,5-dimethyl-1,3-dioxan-4-yl]methanol (15c). To a solution of mixture of triol **14** (51.0 g, 380 mmol) and 4-methoxybenzaldehyde dimethyl acetal (69.2 g, 380 mmol) in dichloromethane (300 mL) at room temperature was added camphorsulfonic acid (4.41 g, 19.0 mmol). The reaction mixture was stirred for 2 h at room temperature and then triethylamine (5.25 mL, 37.7 mmol) was added. After evaporation of the solvent, the crude product was purified by column chromatography (hexane/AcOEt = 6/1) to afford alcohol **15c** (88.1 g, 92%, 2 steps) as a colorless oil. $[\alpha]_D^{18} = -25.3°$ (*c* 1.15, benzene). IR (neat) 3470 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 7.43 (d, *J* = 8.6 Hz, 2H, Ph), 6.90 (d, *J* = 8.6 Hz, 2H, Ph), 5.44 (s, 1H, 2′-H), 3.79 (s, 3H, MeO), 3.67–3.56 (m, 5H, 1-H, 4′-H, 6′-H), 1.12 (s, 3H, 5′-Me), 0.82 (s, 3H, 5′-Me). ^{13}C NMR ($CDCl_3$) δ 160.0 (PMP), 130.8 (PMP), 127.5 (PMP), 113.6 (PMP), 101.9 (2′), 85.8 (4′), 78.8 (6′), 61.4 (1), 55.2 (MeO), 31.4 (5′), 21.3 (Me), 19.0 (Me). HRMS(FAB) Found: *m*/*z* 253.1438. Calcd for $C_{14}H_{21}O_4$ $[M + H]^+$: 253.1440.

(2*R*,4*R*)-2-(4-Methoxyphenyl)-5,5-dimethyl-1,3-dioxane-4-carbaldehyde (12). To a solution of DMSO (12.3 mL, 173 mmol) in dichloromethane (150 mL) at –78 °C was added oxalyl chloride (11.3 mL, 130 mmol). The reaction mixture was stirred for 15 min at –78 °C and then a solution of alcohol **15c** (21.9 g, 86.6 mmol) in dichloromethane (80 mL) was added. After the reaction mixture was stirred for 30 min, triethylamine (60.1 mL, 433 mmol) was added. The reaction mixture was allowed to warm to room temperature and then water was added. The mixture was extracted with dichloromethane, and the organic layer was washed with water, saturated aqueous sodium hydrogencarbonate and

brine, and then dried over sodium sulfate. After filtration of the mixture and evaporation of the solvent, the crude product was filtered through a short pad of sodium sulfate with diethyl ether and the filtrate was concentrated by evaporation of the solvent to afford aldehyde **12** (21.2 g) as a colorless oil. This was used in next step without further purification. For detailed analysis of **12**, it can be purified by column chromatography (hexane/AcOEt = 1/1). A white solid was obtained when a small amount of pure **12** was stored in a refrigerator. Mp 56–57 °C. $[\alpha]_D^{23}$ = +35.2° (*c* 0.833, benzene). IR (neat) 1740 cm^{-1}. ^1H NMR ($CDCl_3$) δ 9.55 (s, 1H, CHO), 7.38 (d, *J* = 8.6 Hz, 2H, Ph), 6.82 (d, *J* = 8.6 Hz, 2H, Ph), 5.40 (s, 1H, 2-H), 3.83 (s, 1H, 4-H), 3.71 (s, 3H, MeO), 3.60 (d, *J* = 11.3 Hz, 1H, 6-H), 3.54 (d, *J* = 11.3 Hz, 1H, 6-H), 1.13 (s, 3H, 5-Me), 0.90 (s, 3H, 5-Me). ^{13}C NMR ($CDCl_3$) δ 201.7 (CHO), 160.3 (PMP), 130.2 (PMP), 127.6 (PMP), 113.8 (PMP), 101.4 (2), 87.3 (4), 78.5 (6), 55.3 (MeO), 33.4 (5), 20.9 (Me), 19.2 (Me). HRMS(FAB) Found: *m*/*z* 251.1278. Calcd for $C_{14}H_{19}O_4$ $[M + H]^+$: 251.1283.

(2*R*,4*S*)-2-(4-Methoxyphenyl)-5,5-dimethyl-4-vinyl-1,3-dioxane (13). To a suspension of methyltriphenylphosphonium bromide (60.5 g, 169 mmol) in THF (400 mL) at –15 °C was added a solution of butyllithium in hexane (1.6 M, 79.4 mL, 127 mmol) (1 M = 1 mol dm^{-3}). After the reaction mixture was stirred for 1 h at –15 °C, a solution of aldehyde **12** (21.2 g, 84.7 mmol) in THF (80 mL) was added. The reaction mixture was stirred for 12 h at room temperature and then water was added. The mixture was extracted with ethyl acetate, and the organic layer was washed with water and brine, and then dried over sodium sulfate. After filtration of the mixture and evaporation of the solvent, the crude product was purified by column chromatography (hexane/AcOEt = 20/1) to afford olefin **13** (18.5 g, 86%, 2 steps) as a colorless oil. $[\alpha]_D^{19}$ = –61.3° (*c* 0.333, benzene). IR (neat) 1740, 1610, 1390, 1250, 1110 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.46 (d, *J* = 8.9 Hz, 2H, Ph), 6.90 (d, *J* = 8.9 Hz, 2H, Ph), 5.87 (ddd, *J* = 17.1, 10.7, 6.4 Hz, 1H, 1′-H), 5.50 (s, 1H, 2-H), 5.32 (dd, *J* = 17.1, 1.8 Hz, 1H, 2′-H), 5.25 (ddd, *J* = 10.7, 1.8, 1.2 Hz, 1H, 2′-H), 4.02 (d, *J* = 6.4 Hz, 1H, 4-H), 3.80 (s, 3H, MeO), 3.75 (d, *J* = 11.1 Hz, 1H, 6-H), 3.64 (d, *J* = 11.1 Hz, 1H, 6-H), 1.14 (s, 3H, 5-Me), 0.80 (s, 3H, 5-Me). ^{13}C NMR ($CDCl_3$) δ 159.9 (PMP), 133.8 (1′), 131.2 (PMP), 127.5 (PMP), 117.6 (2′), 113.6 (PMP), 101.6 (2), 86.1 (4), 78.5 (6), 55.3 (MeO), 32.9 (5), 21.4 (Me), 18.8 (Me). HRMS(FAB) Found: *m*/*z* 249.1495. Calcd for $C_{15}H_{21}O_3$ $[M + H]^+$: 249.1491.

(1*S*)-1-[(2*R*,4*R*)-2-(4-Methoxyphenyl)-5,5-dimethyl-1,3-dioxan-4-yl]ethane-1,2-diol (16). To a solution of olefin **13** (46.8 g, 188 mmol) in acetone (380 mL) and water (62 mL) at room temperature were added a solution of *N*-methylmorpholine *N*-oxide in water (50 wt%, 66.1 g, 282 mmol) and a solution of osmium tetraoxide in *t*-butyl alcohol (0.02 M, 18.8 mL, 0.376 mmol). The reaction mixture was stirred for 3 days at room temperature and then saturated aqueous sodium sulfite (160 mL) was added. The mixture was extracted with ethyl acetate, and the organic layer was washed with brine and dried over sodium sulfate. After filtration of the mixture and evaporation of the solvent, the crude product was purified by column chromatography (hexane/AcOEt = 2/1) to afford diol **16** (52.7 g, 99%, *anti*/*syn* = 24/1) as a colorless oil. A white solid was obtained when a small amount of this compound was stored in a refrigerator. Mp 52–54 °C. $[\alpha]_D^{19}$ = –66.0° (*c* 1.21, benzene). IR (neat) 3390 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.38 (d, *J* = 8.5 Hz, 2H, Ph), 6.89 (d, *J* = 8.5 Hz, 2H, Ph), 5.41 (s, 1H, 2′-H), 3.84–3.78 (m, 3H, 1-H, 2-H), 3.81 (s, 3H, MeO), 3.67 (d, *J* = 5.8 Hz, 1H, 4′-H), 3.67 (d, *J* = 11.3 Hz, 1H, 6′-H), 3.61 (d, *J* = 11.3 Hz, 1H, 6′-H), 1.23 (s, 3H, 5′-Me), 0.96 (s, 3H, 5′-Me). ^{13}C NMR ($CDCl_3$) δ 160.0 (PMP), 130.8 (PMP), 127.3 (PMP), 113.7 (PMP), 101.7 (2′), 86.3 (4′), 79.3 (6′), 70.9 (1), 64.4 (2), 55.3 (MeO), 32.5 (5′), 22.2 (Me), 19.2 (Me). HRMS(FAB) Found: *m*/*z* 283.1531. Calcd for $C_{15}H_{23}O_5$ $[M + H]^+$: 283.1545.

(1*S*)-2-(*t*-Butyldimethylsiloxy)-1-[(2*R*,4*R*)-2-(4-methoxyphenyl)-5,5-dimethyl-1,3-dioxan-4-yl)]ethanol. To a solution of diol **16** (8.63 g, 30.6 mmol) and imidazole (2.50 g, 36.7 mmol) in DMF (120 mL) at 0 °C was added *t*-butylchlorodimethylsilane (4.61 g, 30.6 mmol) in DMF (15 mL). The reaction mixture was stirred for 1 h at 0 °C and then saturated aqueous sodium hydrogencarbonate was added. The mixture was extracted with ethyl acetate, and the organic layer was washed with brine and dried over sodium sulfate. After filtration of the mixture and evaporation of the solvent, the crude product was purified by column chromatography (hexane/AcOEt = 8/1) to afford (1*S*)-2-(*t*-butyldimethylsiloxy)-1-[(2*R*,4*R*)-2-(4-methoxyphenyl)-5,5-dimethyl-1,3-dioxan-4-yl)]ethanol (12.0 g, quant.) as a colorless oil. $[\alpha]_D^{20}$ = –44.6° (*c* 1.87, benzene). IR (neat) 3570 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.38 (d, *J* = 8.7 Hz, 2H, Ph), 6.89 (d, *J* = 8.7 Hz, 2H, Ph), 5.36 (s, 1H, 2′-H), 3.81 (s, 3H, MeO), 3.78–3.71 (m, 3H, 1-H, 2-H), 3.66 (d, *J* = 11.1 Hz, 1H, 6′-H), 3.59 (d, *J* = 11.1 Hz, 1H, 6′-H), 3.51 (d, *J* = 7.9 Hz, 1H, 4′-H), 2.57 (br s, 1H, OH), 1.24 (s, 3H, 5′-Me), 0.99 (s, 3H, 5′-Me), 0.91 (s, 9H, TBS), 0.07 (s, 6H, TBS). ^{13}C NMR ($CDCl_3$) δ 159.9 (PMP), 131.1 (PMP), 127.3 (PMP), 113.5 (PMP), 101.3 (2′), 83.6 (4′), 79.3 (6′), 71.1 (1), 64.0 (2), 55.3 (MeO), 32.4 (5′), 25.9 (TBS), 22.5 (Me), 18.9 (Me), 18.3 (TBS), –5.3 (TBS), –5.4 (TBS). HRMS(FAB) Found: *m*/*z* 397.2414. Calcd for $C_{21}H_{37}O_5Si$ $[M + H]^+$: 397.2410.

(2*R*,4*R*)-2-(4-Methoxyphenyl)-5,5-dimethyl-4-[(1*S*)-1-benzyloxy-2-(*t*-butyldimethylsiloxy)ethyl]-1,3-dioxane (17). To a suspension of sodium hydride (55% in oil, 1.58 g, 36.3 mmol, washed with pentane prior to use) in THF (90 mL) at 0 °C was added a solution of (1*S*)-2-(*t*-butyldimethylsiloxy)-1-[(2*R*,4*R*)-2-(4-methoxyphenyl)-5,5-dimethyl-1,3-dioxan-4-yl)]ethanol (11.2 g, 30.1 mmol) in THF (60 mL). After the reaction mixture was stirred for 15 min at 0 °C, benzyl bromide (4.7 mL, 39.5 mmol) and DMF (15 mL) were successively added. The reaction mixture was stirred for 18 h at room temperature and then saturated aqueous ammonium chloride (80 mL) was added. The mixture was extracted with ethyl acetate, and the organic layer was washed with brine and dried over sodium sulfate. After filtration of the mixture and evaporation of the solvent, the crude product was purified by column chromatography (hexane/AcOEt = 20/1) to afford acetal **17** (14.9 g, 96%) as a colorless oil. $[\alpha]_D^{17}$ = –25.6° (*c* 0.500, benzene). IR (neat) 2940, 2860, 1250, 1110 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.44–7.35 (m, 7H, Ph), 6.92 (d, *J* = 8.9 Hz, 2H, Ph), 5.41 (s, 1H, 2-H), 4.89 (d, *J* = 11.5 Hz, 1H, Bn), 4.62 (d, *J* = 11.5 Hz, 1H, Bn), 4.02 (dd, *J* = 11.2, 2.0 Hz, 1H, 2′-H), 3.85 (dd, *J* = 11.2, 5.6 Hz, 1H, 2′-H), 3.82 (s, 3H, MeO), 3.76 (d, *J* = 7.0 Hz, 1H, 4-H), 3.66 (ddd, *J* = 7.0, 5.6, 2.0 Hz, 1H, 1′-H), 3.66 (d, *J* = 11.3 Hz, 1H, 6-H), 3.61 (d, *J* = 11.3 Hz, 1H, 6-H), 1.21 (s, 3H, 5-Me), 0.95 (s, 9H, TBS), 0.92 (s, 3H, 5-Me), 0.08 (s, 6H, TBS). ^{13}C NMR ($CDCl_3$) δ 159.8 (PMP), 138.6 (Ph), 131.2 (Ph), 128.2 (Ph), 128.2 (Ph), 127.9 (Ph), 127.4 (Ph), 113.4 (PMP), 101.4 (2), 83.2 (4), 80.0 (1′), 79.2 (6), 72.0 (Bn), 63.2 (2′), 55.2 (MeO), 32.4 (5), 25.9 (TBS), 22.5 (Me), 19.2 (Me), 18.3 (TBS), –5.4 (TBS), –5.4 (TBS). HPLC (CHIRALCEL OD, hexane/^{i}PrOH = 300/1, flow rate = 0.6 mL min^{-1}) t_R = 18.6 min (98.0%), t_R = 25.5 min (2.0%). HRMS(FAB) Found: *m*/*z* 487.2874. Calcd for $C_{28}H_{43}O_5Si$ $[M + H]^+$: 487.2880.

(3*R*,4*S*)-4-Benzyloxy-5-(*t*-butyldimethylsiloxy)-3-(4-methoxybenzyloxy)-2,2-dimethylpentan-1-ol (18). To a solution of borane–dimethyl sulfide complex (15.4 mL, 162 mmol) in toluene

(300 mL) at reflux over a period of 5 min was added a solution of acetal **17** (52.6 g, 108 mmol) in toluene (50 mL). The reaction mixture was refluxed for 30 min and then methanol and saturated aqueous sodium hydrogencarbonate were successively added at 0 °C. The mixture was extracted with ethyl acetate, and the organic layer was washed with brine and dried over sodium sulfate. After filtration of the mixture and evaporation of the solvent, the crude product was purified by column chromatography (hexane/AcOEt = 8/1) to afford alcohol **18** (45.0 g, 85%) and diol **19** (4.10 g, 11%) as colorless oils.

(3*R*,4*R*)-4-Benzyloxy-5-(*t*-butyldimethylsiloxy)-2,2-dimethylpentane-1,3-diol (19). $[\alpha]_D^{22}$ = +7.8° (*c* 0.493, benzene). IR (neat) 3440 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 7.33–7.27 (m, 5H, Ph), 4.63 (d, *J* = 11.3 Hz, 1H, Bn), 4.49 (d, *J* = 11.3 Hz, 1H, Bn), 3.98 (dd, *J* = 11.3, 4.3 Hz, 1H, 5-H), 3.85 (dd, *J* = 11.3, 3.5 Hz, 1H, 5-H), 3.77 (d, *J* = 6.4 Hz, 1H, 3-H), 3.56 (br s, 1H, OH), 3.53 (ddd, *J* = 6.4, 4.3, 3.5 Hz, 1H, 4-H), 3.50 (d, *J* = 11.3 Hz, 1H, 1-H), 3.37 (d, *J* = 11.3 Hz, 1H, 1-H), 1.02 (s, 3H, 2-Me), 0.90 (s, 9H, TBS), 0.89 (s, 3H, 2-Me), 0.09 (s, 6H, TBS). ^{13}C NMR ($CDCl_3$) δ 137.8 (Ph), 128.5 (Ph), 127.9 (Ph), 127.9 (Ph), 79.9 (3), 79.3 (4), 72.3 (1), 71.6 (Bn), 63.1 (5), 38.6 (2), 25.8 (TBS), 21.5 (Me), 20.4 (Me), 18.0 (TBS), –5.4 (TBS), –5.6 (TBS). HRMS(FAB) Found: *m*/*z* 369.2460. Calcd for $C_{20}H_{37}O_4Si$ [M + H]$^+$: 369.2461.

(2*R*,4*R*)-2-(4-Methoxyphenyl)-5,5-dimethyl-4-[(1*S*)-1-benzyloxy-2-(*t*-butyldimethylsiloxy)ethyl]-1,3-dioxane (17) (from diol **19**). To a solution of a mixture of diol **19** (1.90 g, 5.16 mmol) and 4-methoxybenzaldehyde dimethyl acetal (941 mg, 5.16 mmol) in dichloromethane (42 mL) at 0 °C was added camphorsulfonic acid (72.9 mg, 0.258 mmol). The reaction mixture was stirred for 1.5 h at 0 °C and then saturated aqueous sodium hydrogencarbonate was added. The mixture was extracted with dichloromethane, and the organic layer was washed with water and brine, and then dried over sodium sulfate. After evaporation of the solvent, the crude product was purified by column chromatography (hexane/AcOEt = 25/1) to afford acetal **17** (2.25 g, 90%) as a colorless oil.

(2*R*)-2-Benzyloxy-3,3-dimethyl-4-butanolide (20). To a solution of a mixture of D-pantolactone (50.7 mg, 0.39 mmol), DMAP (4.7 mg, 0.039 mmol) and triethylamine (0.11 mL, 0.78 mmol) in dichloromethane (2.0 mL) at 0 °C was added benzoyl chloride (0.065 mL, 0.57 mmol). The reaction mixture was stirred for 30 min at 0 °C and then saturated aqueous sodium hydrogencarbonate was added. The mixture was extracted with dichloromethane, and the organic layer was washed with water and brine, and then dried over sodium sulfate. After filtration of the mixture and evaporation of the solvent, the crude product was purified by thin layer chromatography (hexane/AcOEt = 2/1) to afford benzoate **20** (91.6 mg, quant.) as a colorless oil. $[\alpha]_D^{23}$ = –11.8° (*c* 2.98, benzene). IR (neat) 1810, 1730 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 8.09 (dd, *J* = 7.3, 1.2 Hz, 2H, Bz), 7.60 (tt, *J* = 7.3, 1.2 Hz, 1H, Bz), 7.46 (ddd, *J* = 7.3, 7,3, 1.2 Hz, 2H, Bz), 5.62 (s, 1H, 2-H), 4.12 (d, *J* = 9.2 Hz, 1H, 4-H), 4.09 (d, *J* = 9.2 Hz, 1H, 4-H), 1.27 (s, 3H, 3-Me), 1.22 (s, 3H, 3-Me). ^{13}C NMR ($CDCl_3$) δ 172.3 (1), 165.3 (Bz), 133.7 (Ph), 129.9 (Ph), 128.7 (Ph), 128.5 (Ph), 76.2 (4), 75.4 (2), 40.5 (3), 23.0 (Me), 19.9 (Me). HPLC (CHIRALCEL OD, hexane/^{i}PrOH = 20/1, flow rate = 1.0 mL min^{-1}) t_R = 14.4 min (99.5%), t_R = 17.9 min (0.5%). HRMS(FAB) Found: *m*/*z* 235.0972. Calcd for $C_{13}H_{15}O_4$ [M + H]$^+$: 235.0970.

(*Z*)-2-Benzyloxy-1-methoxy-1-(trimethylsiloxy)ethene (21).[8] To a solution of hexamethyldisilazane (16.0 g, 99.8 mmol) in THF (90 mL) at 0 °C was added a solution of butyllithium in hexane (1.59 M, 57.6 mL, 91.6 mmol). After the reaction mixture was stirred for 10 min at 0 °C, a solution of methyl benzyloxyacetate[1a] (15.0 g, 83.3 mmol) in THF (20 mL) and a solution of chlorotrimethylsilane (9.95 g, 91.6 mmol) in THF (10 mL) were added at –78 °C. The reaction mixture was allowed to warm to room temperature and then it was concentrated by evaporation of the solvent. Petroleum ether (150 mL) was added to the residue, and the suspension was filtered through a short pad of Celite under argon atmosphere. After evaporation of the solvent, the crude product was purified by distillation to afford ketene trimethylsilyl acetal **21** (17.5 g, 83%) as a colorless oil. Bp 98 °C / 1.0 mmHg. IR (neat) 2900, 1690, 1220, 850 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 7.29–7.21 (m, 5H, Ph), 5.32 (s, 1H, 2-H), 4.57 (s, 2H, Bn), 3.37 (s, 3H, MeO), 0.16 (s, 9H, TMS). ^{13}C NMR ($CDCl_3$) δ 150.2 (1), 137.4 (Ph), 127.8 (Ph), 127.3 (Ph), 127.2 (Ph), 109.9 (2), 74.1 (Bn), 55.3 (MeO), –0.2 (TMS).

Methyl (2*R*,3*R*,5*R*,6*S*)-2,6-bis(benzyloxy)-7-(*t*-butyldimethylsiloxy)-3-hydroxy-5-(4-methoxybenzyloxy)-4,4-dimethylheptanoate (22). To a suspension of magnesium bromide-diethyl ether complex (12.9 g, 49.9 mmol) in toluene (100 mL) at –19 °C were successively added a solution of ketene trimethylsilyl acetal **21** (6.30 g, 24.9 mmol) in toluene (30 mL) and a solution of aldehyde **3** (8.10 g, 16.6 mmol) in toluene (30 mL). The reaction mixture was stirred for 1 h at –19 °C and then triethylamine (23 mL) and saturated aqueous sodium hydrogencarbonate were successively added. The mixture was extracted with diethyl ether, the organic layer was washed with brine and dried over sodium sulfate. After filtration of the mixture and evaporation of the solvent, the crude product was purified by column chromatography (hexane/AcOEt = 9/1) to afford aldol **22** (9.60 g, 87%) as a colorless oil.

(4*R*,5*R*,7*R*,8*S*)-4,8-Bis(benzyloxy)-5,9-bis(*t*-butyldimethylsiloxy)-2,2-dichloro-7-(4-methoxybenzyloxy)-6,6-dimethylnonan-3-ol (26). To a solution of butyllithium in hexane (1.54 M, 0.26 mL, 0.39 mmol) diluted with THF (1.8 mL) at –100 °C was added 1,1-dichloroethane (0.04 mL, 0.49 mmol). After the reaction mixture was stirred for 30 min, a solution of aldehyde **25** (10.0 mg, 0.0133 mmol) in THF (1.0 mL) was added at –100 °C. The reaction mixture was stirred for 1 h at –78 °C and then saturated aqueous ammonium chloride (1.5 mL) was added. The mixture was extracted with diethyl ether, and the organic layer was washed with brine and dried over sodium sulfate. After filtration of the mixture and evaporation of the solvent, the crude product was purified by thin layer chromatography (hexane/AcOEt = 7/1) to afford 2,2-dichloroalkan-3-ol **26** (5.8 mg, 51%) and recovered aldehyde **25** (1.8 mg, 18%) as colorless oils. **2,2-Dichloroalkan-3-ol 26.** $[\alpha]_D^{22}$ = +35.7° (*c* 3.25, benzene). IR (neat) 3490 cm^{-1}. ^{1}H NMR (C_6D_6) δ 7.45 (d, *J* = 6.9 Hz, 2H, Ph), 7.37 (d, *J* = 8.6 Hz, 2H, Ph), 7.28–7.10 (m, 8H, Ph), 6.88 (d, *J* = 8.6 Hz, 2H, Ph), 4.95 (d, *J* = 10.2 Hz, 1H, Bn), 4.86 (d, *J* = 10.9 Hz, 1H, Bn), 4.80 (d, *J* = 10.9 Hz, 1H, Bn), 4.78 (d, *J* = 11.5 Hz, 1H, Bn), 4.73 (d, *J* = 10.2 Hz, 1H, Bn), 4.63 (s, 1H, 5-H), 4.57 (s, 1H, 4-H), 4.52 (d, *J* = 11.5 Hz, 1H, Bn), 4.48 (d, *J* = 9.6 Hz, 1H, 3-H), 4.30 (d, *J* = 6.3 Hz, 1H, 7-H), 4.25 (d, *J* = 9.6 Hz, 1H, OH), 4.12 (dd, *J* = 11.2, 1.8 Hz, 1H, 9-H), 4.04 (dd, *J* = 11.2, 3.6 Hz, 1H, 9-H), 3.77 (ddd, *J* = 6.3, 3.6, 1.8 Hz, 1H, 8-H), 3.34 (s, 3H, MeO), 2.30 (s, 3H, 1-H), 1.57 (s, 3H, 6-Me), 1.34 (s, 3H, 6-Me), 1.13 (s, 9H, TBS), 1.06 (s, 9H, TBS), 0.23 (s, 3H, TBS), 0.18 (s, 3H, TBS), 0.15 (s, 3H, TBS), 0.14 (s, 3H, TBS). ^{13}C NMR (C_6D_6) δ 159.7 (PMP), 138.7 (Ph), 138.1 (Ph), 131.4 (Ph), 129.2 (Ph), 128.7 (Ph), 128.6 (Ph), 128.5 (Ph), 127.9 (Ph), 127.3 (Ph), 127.0 (Ph), 114.1 (PMP), 94.4 (2), 83.0 (8), 81.2 (7), 79.5 (5), 79.1 (4), 77.3 (3), 74.4 (PMB), 73.8 (Bn), 72.5 (Bn), 63.0 (9), 54.8 (MeO), 45.0 (6), 34.6 (1), 26.7

(TBS), 26.2 (TBS), 22.3 (Me), 19.8 (Me), 18.8 (TBS), 18.5 (TBS), –2.4 (TBS), –2.4 (TBS), –4.3 (TBS), –4.3 (TBS). HRMS(FAB) Found: *m*/*z* 871.3931. Calcd for $C_{45}H_{70}O_7Cl_2Si_2Na$ [M + Na]$^+$: 871.3935.

(4*R*,5*R*,7*R*,8*S*)-4,8-Bis(benzyloxy)-5,9-bis(*t*-butyldimethylsiloxy)-2-chloro-7-(4-methoxybenzyloxy)-6,6-dimethylnonan-3-ol (27). To a solution of 2,2-dichloroalkan-3-ol **26** (6.0 mg, 0.0071 mmol) in benzene (0.5 mL) at room temperature were successively added tributyltin hydride (0.0074 mL, 0.028 mmol) and 2,2′-azobisisobutyronitrile (0.12 mg, 0.00071 mmol). The reaction mixture was refluxed for 5 h. After evaporation of the solvent, the crude product was purified by thin layer chromatography (hexane/AcOEt = 7/1) to afford 2-chloroalkan-3-ol **27** (2.2 mg, 38%) as a colorless oil. $[\alpha]_D^{23} = -5.7°$ (*c* 1.01, benzene). IR (neat) 3460 cm^{-1}. ^{1}H NMR (C_6D_6) δ 7.48 (d, *J* = 7.3 Hz, 2H, Ph), 7.39 (d, *J* = 8.6 Hz, 2H, Ph), 7.29–7.09 (m, 8H, Ph), 6.90 (d, *J* = 8.6 Hz, 2H, Ph), 4.90 (d, *J* = 1.7 Hz, 1H, OH), 4.87 (d, *J* = 11.4 Hz, 1H, Bn), 4.86 (d, *J* = 10.6 Hz, 1H, Bn), 4.73 (d, *J* = 10.6 Hz, 1H, Bn), 4.73 (d, *J* = 1.8 Hz, 1H, 5-H), 4.56 (dq, *J* = 9.2, 6.6 Hz, 1H, 2-H), 4.55 (d, *J* = 10.2 Hz, 1H, Bn), 4.50 (d, *J* = 11.4 Hz, 1H, Bn), 4.45 (d, *J* = 10.2 Hz, 1H, Bn), 4.39 (br s, 1H, 4-H), 4.29 (br d, *J* = 9.2 Hz, 1H, 3-H), 4.18 (dd, *J* = 11.6, 2.0 Hz, 1H, 9-H), 4.08 (dd, *J* = 11.6, 4.5 Hz, 1H, 9-H), 4.00 (d, *J* = 5.9 Hz, 1H, 7-H), 3.79 (ddd, *J* = 5.9, 4.5, 2.0 Hz, 1H, 8-H), 3.35 (s, 3H, MeO), 1.78 (d, *J* = 6.6 Hz, 3H, 1-H), 1.49 (s, 3H, 6-Me), 1.33 (s, 3H, 6-Me), 1.08 (s, 9H, TBS), 1.02 (s, 9H, TBS), 0.24 (s, 3H, TBS), 0.17 (s, 3H, TBS), 0.17 (s, 3H, TBS), 0.15 (s, 3H, TBS). ^{13}C NMR (C_6D_6) δ 160.2 (PMP), 139.5 (Ph), 139.5 (Ph), 131.1 (Ph), 129.4 (Ph), 128.8 (Ph), 128.8 (Ph), 128.7 (Ph), 127.8 (Ph), 127.8 (Ph), 127.5 (Ph), 114.1 (PMP), 83.0 (8), 81.5 (7), 80.0 (5), 78.9 (4), 76.8 (3), 74.6 (PMB), 73.6 (Bn), 73.0 (Bn), 64.2 (9), 58.0 (2), 54.7 (MeO), 44.0 (6), 26.5 (TBS), 26.2 (TBS), 22.5 (1), 21.9 (Me), 19.9 (Me), 19.0 (TBS), 18.5 (TBS), –3.1 (TBS), –4.7 (TBS), –5.1 (TBS), –5.1 (TBS). HRMS(FAB) Found: *m*/*z* 837.4325. Calcd for $C_{45}H_{71}O_7ClSi_2Na$ [M + Na]$^+$: 837.4325.

(4*R*,5*R*,7*R*,8*S*)-4,8-Bis(benzyloxy)-5,9-bis(*t*-butyldimethylsiloxy)-2,2-dichloro-7-(4-methoxybenzyloxy)-6,6-dimethylnonan-3-one (29). To a solution of butyllithium in hexane (1.54 M, 0.76 mL, 1.17 mmol) diluted with diethyl ether (1.9 mL) and THF (1.5 mL) at –100 °C was added 1,1-dichloroethane (0.12 mL, 1.46 mmol). After the reaction mixture was stirred for 30 min, a solution of ester **23** (30.0 mg, 0.0384 mmol) in diethyl ether (0.5 mL) was added at –100 °C. The reaction mixture was stirred for 1 h at –78 °C and then saturated aqueous ammonium chloride (2.0 mL) was added. The mixture was extracted with diethyl ether, and the organic layer was washed with brine and dried over sodium sulfate. After filtration of the mixture and evaporation of the solvent, the crude product was purified by thin layer chromatography (hexane/AcOEt = 4/1) to afford 1,1-dichloroethyl ketone **29** (25.3 mg, 78%) as a colorless oil. $[\alpha]_D^{23} = -17.0°$ (*c* 1.25, benzene). IR (neat) 1740 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 7.35–7.22 (m, 12H, Ph), 6.83 (d, *J* = 8.9 Hz, 2H, Ph), 4.99 (d, *J* = 2.0 Hz, 1H, 4-H), 4.86 (d, *J* = 2.0 Hz, 1H, 5-H), 4.72 (d, *J* = 11.9 Hz, 1H, Bn), 4.71 (d, *J* = 9.9 Hz, 1H, Bn), 4.61 (d, *J* = 11.2 Hz, 1H, Bn), 4.58 (d, *J* = 9.9 Hz, 1H, Bn), 4.51 (d, *J* = 11.2 Hz, 1H, Bn), 4.47 (d, *J* = 11.9 Hz, 1H, Bn), 3.95 (dd, *J* = 11.2, 1.7 Hz, 1H, 9-H), 3.82 (d, *J* = 6.7 Hz, 1H, 7-H), 3.78 (dd, *J* = 11.2, 3.7 Hz, 9-H), 3.78 (s, 3H, MeO), 3.70 (ddd, *J* = 6.7, 3.7, 1.7 Hz, 1H, 8-H), 2.16 (s, 3H, 1-H), 1.09 (s, 3H, 6-Me), 0.98 (s, 3H, 6-Me), 0.93 (s, 9H, TBS), 0.86 (s, 9H, TBS), 0.08 (s, 3H, TBS), 0.02 (s, 3H, TBS), 0.01 (s, 3H, TBS), 0.00 (s, 3H, TBS). ^{13}C NMR ($CDCl_3$) δ 195.6 (3), 158.8 (PMP), 138.9 (Ph), 137.7 (Ph), 131.2 (Ph), 128.7 (Ph), 128.2 (Ph), 128.2 (Ph), 127.8 (Ph), 127.7 (Ph), 127.6 (Ph), 127.3 (Ph), 113.6 (PMP), 85.6 (4), 84.6 (2), 83.7 (7), 82.3 (8), 76.0 (5), 73.4 (PMB), 73.3 (Bn), 72.3 (Bn), 65.3 (9), 55.3 (MeO), 45.0 (6), 33.5 (1), 26.2 (TBS), 26.0 (TBS), 21.0 (Me), 19.2 (Me), 18.6 (TBS), 18.2 (TBS), –2.8 (TBS), –4.5 (TBS), –5.3 (TBS), –5.3 (TBS). HRMS(FAB) Found: *m*/*z* 869.3805. Calcd for $C_{45}H_{68}Cl_2O_7Si_2Na$ [M + Na]$^+$: 869.3778.

(4*R*,5*R*,7*R*,8*S*)-4,8-Bis(benzyloxy)-5,9-bis(*t*-butyldimethylsiloxy)-2-chloro-7-(4-methoxybenzyloxy)-6,6-dimethylnonan-3-one (28) (from 1,1-dichloroethyl ketone **29**)**.** To a solution of 1,1-dichloroethyl ketone **29** (50.0 mg, 0.0590 mmol) in benzene (5.0 mL) at room temperature was added tributyltin hydride (0.062 mL, 0.24 mmol). The reaction mixture was refluxed for 30 min. After evaporation of the solvent, the crude product was purified by thin layer chromatography (hexane/AcOEt = 7/1) to afford 1-chloroethyl ketone **28** (43.3 mg, 90%) as a colorless oil. $[\alpha]_D^{15} = +22.1°$ (*c* 1.00, benzene). IR (neat) 1720 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 7.27–7.16 (m, 10H, Ph), 7.08–7.04 (m, 2H, Ph), 6.79 (d, *J* = 8.6 Hz, 2H, Ph), 4.95 (q, *J* = 6.6 Hz, 1H, 2-H), 4.61 (d, *J* = 11.2 Hz, 1H, Bn), 4.57 (d, *J* = 10.8 Hz, Bn), 4.52 (d, *J* = 10.8 Hz, Bn), 4.43 (d, *J* = 9.9 Hz, 1H, Bn), 4.35 (d, *J* = 1.8 Hz, 1H, 4-H), 4.34 (d, *J* = 1.8 Hz, 1H, 5-H), 4.33 (d, *J* = 11.2 Hz, 1H, Bn), 4.22 (d, *J* = 9.9 Hz, 1H, Bn), 4.10 (d, *J* = 6.9 Hz, 1H, 7-H), 3.95 (dd, *J* = 11.2, 1.7 Hz, 1H, 9-H), 3.75 (dd, *J* = 11.2, 3.8 Hz, 1H, 9-H), 3.71 (s, 3H, MeO), 3.47 (ddd, *J* = 6.9, 3.8, 1.7 Hz, 1H, 8-H), 1.46 (d, *J* = 6.6 Hz, 3H, 1-H), 0.94 (s, 3H, 6-Me), 0.85 (s, 9H, TBS), 0.81 (s, 3H, 6-Me), 0.79 (s, 9H, TBS), 0.01 (s, 6H, TBS), 0.00 (s, 6H, TBS). ^{13}C NMR ($CDCl_3$) δ 208.7 (3), 158.9 (PMP), 138.2 (Ph), 137.4 (Ph), 131.2 (Ph), 128.9 (Ph), 128.4 (Ph), 128.3 (Ph), 128.2 (Ph), 128.1 (Ph), 128.0 (Ph), 127.7 (Ph), 113.7 (PMP), 86.0 (4), 82.1 (8), 81.0 (7), 80.0 (5), 74.0 (PMB), 74.0 (Bn), 72.0 (Bn), 61.7 (9), 55.3 (MeO), 51.2 (2), 44.1 (6), 26.4 (TBS), 25.9 (TBS), 21.7 (Me), 19.3 (1), 18.7 (Me), 18.7 (TBS), 18.2 (TBS), –2.9 (TBS), –2.9 (TBS), –5.1 (TBS), –5.1 (TBS). HRMS(FAB) Found: *m*/*z* 835.4158. Calcd for $C_{45}H_{69}ClO_7Si_2Na$ [M + Na]$^+$: 835.4168.

(4*R*,5*R*,7*R*,8*S*)-4,8-Bis(benzyloxy)-5,9-bis(*t*-butyldimethylsiloxy)-2-chloro-7-(4-methoxybenzyloxy)-6,6-dimethylnonan-3-one (28) (from ester **23**)**.** To a solution of HMPA (6.90 mL, 39.7 mmol) in diethyl ether (26 mL) and THF (20 mL) at 0 °C was added a solution of butyllithium in hexane (1.53 M, 25 mL, 38.4 mmol). The reaction mixture was cooled down to –100 °C and then 1,1-dichloroethane (4.0 mL, 48.0 mmol) was added. After the reaction mixture was stirred for 30 min, a solution of ester **23** (1.00 g, 1.28 mmol) in diethyl ether (5.0 mL) was added at –100 °C. The reaction mixture was stirred for 1 h at –78 °C and then saturated aqueous ammonium chloride (27 mL) was added. The mixture was extracted with diethyl ether, and the organic layer was washed with water and brine, and then dried over sodium sulfate. After filtration of the mixture and evaporation of the solvent, the crude product was purified by column chromatography (hexane/AcOEt = 19/1) to afford 1-chloroethyl ketone **28** (946 mg, 91%) as a colorless oil.

(4*R*,5*R*,7*R*,8*S*)-4,8-Bis(benzyloxy)-5-(*t*-butyldimethylsiloxy)-2-chloro-9-hydroxy-7-(4-methoxybenzyloxy)-6,6-dimethylnonan-3-one. To a solution of 1-chloroethyl ketone **28** (187 mg, 0.230 mmol) in THF (21 mL) at 0 °C was added hydrochloric acid (1.0 M, 13.8 mL, 13.8 mmol). After the reaction mixture was stirred for 12 h at room temperature, it was diluted with hexane (15 mL). The reaction mixture was cooled down to 0 °C and then aqueous sodium hydrogencarbonate was slowly added. The mixture was extracted with diethyl ether, and the organic layer was washed with saturated aqueous sodium hydrogencarbonate and brine, and then dried over sodium sulfate. After filtration of the

mixture and evaporation of the solvent, the crude product was purified by thin layer chromatography (hexane/AcOEt = 2/1) to afford (4*R*,5*R*,7*R*,8*S*)-4,8-bis(benzyloxy)-5-(*t*-butyldimethylsiloxy)-2-chloro-9-hydroxy-7-(4-methoxybenzyloxy)-6,6-dimethylnonan-3-one (150 mg, 93%) as a colorless oil. $[\alpha]_D^{20}$ = +16.8° (*c* 1.04, benzene). IR (neat) 3600, 1720 cm^{-1}. ^{1}H NMR (C_6D_6) δ 7.33–6.99 (m, 12H, Ph), 6.77 (d, *J* = 8.2 Hz, 2H, Ph), 5.08 (q, *J* = 6.8 Hz, 1H, 2-H), 4.85 (d, *J* = 10.9 Hz, 1H, Bn), 4.69 (d, *J* = 10.9 Hz, 1H, Bn), 4.57 (d, *J* = 10.2 Hz, 1H, Bn), 4.58 (d, *J* = 1.1 Hz, 1H, 5-H), 4.52 (d, *J* = 1.1 Hz, 1H, 4-H), 4.46 (d, *J* = 10.2 Hz, 1H, Bn), 4.32 (d, *J* = 11.5 Hz, 1H, Bn), 4.24 (d, *J* = 11.5 Hz, 1H, Bn), 4.10 (d, *J* = 5.9 Hz, 1H, 7-H), 3.75 (br s, 2H, 9-H), 3.50 (br dt, *J* = 5.9, 2.8 Hz, 1H, 8-H), 3.22 (s, 3H, MeO), 1.88 (br s, 1H, OH), 1.47 (d, *J* = 6.8 Hz, 3H, 1-H), 1.10 (s, 3H, 6-Me), 0.98 (s, 3H, 6-Me), 0.89 (s, 9H, TBS), 0.02 (s, 3H, TBS), 0.00 (s, 3H, TBS). ^{13}C NMR (C_6D_6) δ 207.0 (3), 159.7 (PMP), 138.5 (Ph), 137.8 (Ph), 131.1 (Ph), 129.4 (Ph), 128.8 (Ph), 128.7 (Ph), 128.5 (Ph), 128.5 (Ph), 128.1 (Ph), 128.1 (Ph), 114.1 (PMP), 86.7 (4), 82.3 (7), 81.5 (8), 79.7 (5), 75.0 (PMB), 74.8 (Bn), 71.7 (Bn), 61.4 (9), 54.7 (MeO), 51.8 (2), 44.5 (6), 26.5 (TBS), 21.8 (Me), 19.3 (1), 19.3 (Me), 18.8 (TBS), –2.6 (TBS), –4.9 (TBS). HRMS(FAB) Found: *m*/*z* 721.3330. Calcd for $C_{39}H_{55}ClO_7SiNa$ $[M + Na]^+$: 721.3303.

(2*R*,3*R*,5*R*,6*R*)-2,6-Bis(benzyloxy)-5-(*t*-butyldimethylsiloxy)-8-chloro-3-(4-methoxybenzyloxy)-4,4-dimethyl-7-oxononanal (30). To a solution of oxalyl chloride (28.9 mg, 0.228 mmol) in dichloromethane (1.7 mL) at –78 °C was added a solution of DMSO (29.5 mg, 0.376 mmol) in dichloromethane (2.0 mL). The reaction mixture was stirred for 30 min at –78 °C and then a solution of (4*R*,5*R*,7*R*,8*S*)-4,8-bis(benzyloxy)-5-(*t*-butyldimethylsiloxy)-2-chloro-9-hydroxy-7-(4-methoxybenzyloxy)-6,6-dimethylnonan-3-one (40.0 mg, 0.0572 mmol) in dichloromethane (2.0 mL) was added. After the reaction mixture was stirred for 30 min, triethylamine (0.130 mL, 0.946 mmol) was added. The reaction mixture was allowed to warm to room temperature and then saturated aqueous ammonium chloride (3.0 mL) was added. The mixture was extracted with dichloromethane, and the organic layer was washed with brine and dried over sodium sulfate. After filtration of the mixture and evaporation of the solvent, the crude product was purified by thin layer chromatography (hexane/AcOEt = 3/1) to afford aldehyde **30** (36.6 mg, 92%) as a colorless oil. $[\alpha]_D^{18}$ = +23.7° (*c* 1.00, benzene). IR (neat) 1730, 1610 cm^{-1}. ^{1}H NMR (C_6D_6) δ 9.59 (s, 1H, 1-H), 7.32–6.76 (m, 14H, Ph), 4.96 (q, *J* = 6.6 Hz, 1H, 8-H), 4.72 (d, *J* = 1.7 Hz, 1H, 5-H), 4.71 (d, *J* = 10.1 Hz, 1H, Bn), 4.60 (d, *J* = 11.1 Hz, 1H, Bn), 4.59 (d, *J* = 10.1 Hz, 1H, Bn), 4.47 (d, *J* = 11.1 Hz, 1H, Bn), 4.49 (d, *J* = 1.7 Hz, 1H, 6-H), 4.40 (d, *J* = 11.9 Hz, 1H, Bn), 4.13 (d, *J* = 11.9 Hz, 1H, Bn), 3.96 (br dd, *J* = 3.0, 1.0 Hz, 1H, 2-H), 3.93 (d, *J* = 1.0 Hz, 1H, 3-H), 3.19 (s, 3H, MeO), 1.32 (d, *J* = 6.6 Hz, 3H, 9-H), 1.09 (s, 3H, 4-Me), 0.97 (s, 3H, 4-Me), 0.90 (s, 9H, TBS), 0.03 (s, 3H, TBS), 0.00 (s, 3H, TBS). ^{13}C NMR (C_6D_6) δ 205.2 (7), 200.8 (1), 159.8 (PMP), 137.9 (Ph), 137.8 (Ph), 130.6 (Ph), 129.2 (Ph), 129.2 (Ph), 128.7 (Ph), 128.7 (Ph), 128.5 (Ph), 128.1 (Ph), 128.1 (Ph), 114.2 (PMP), 87.3 (6), 85.2 (2), 84.4 (3), 78.6 (5), 75.7 (PMB), 73.3 (Bn), 72.8 (Bn), 54.7 (MeO), 51.6 (8), 44.5 (4), 26.4 (TBS), 21.0 (Me), 19.4 (Me), 18.9 (9), 18.6 (TBS), –2.8 (TBS), –4.9 (TBS). HRMS(FAB) Found: *m*/*z* 719.3171. Calcd for $C_{39}H_{53}ClO_7SiNa$ $[M + Na]^+$: 719.3146.

(2*R*,3*R*,5*R*,6*S*,7*R*,8*R*)-2,6-Bis(benzyloxy)-3-(*t*-butyldimethylsilsiloxy)-7-hydroxy-5-(4-methoxybenzyloxy)-4,4,8-trimethylcyclooctanone (31α) and (2*R*,3*R*,5*R*,6*S*,7*S*,8*R*)-2,6-Bis(benzyloxy)-3-(*t*-butyldimethylsilsiloxy)-7-hydroxy-5-(4-methoxybenzyloxy)-4,4,8-trimethylcyclooctanone (31β). To a solution of aldehyde **30** (50.0 mg, 0.0717 mmol) in THF (25 mL) at –23 °C was added a solution of samarium(II) iodide in THF (0.1 M, 2.87 mL, 0.287 mmol). The reaction mixture was stirred for 20 min at –23 °C and then saturated aqueous ammonium chloride was added. The mixture was filtered through a short pad of silica gel and then the filtrate was extracted with diethyl ether. The organic layer was washed with water and brine, and then dried over sodium sulfate. After filtration of the mixture and evaporation of the solvent, the crude product was purified by column chromatography (hexane/AcOEt = 2/1) to afford a mixture of aldols **31** (α/β = 83/17, 30.8 mg, 65%) as a colorless oil.

(4*S*,5*R*,7*R*,8*R*)-4,8-Bis(benzyloxy)-7-(*t*-butyldimethylsiloxy)-5-(4-methoxybenzyloxy)-2,6,6-trimethylcyclooct-2-enone (1). To a solution of mixture of aldols **31** (395 mg, 0.596 mmol) in pyridine (8.57 mL) at 0 °C were added acetic anhydride (1.70 mL, 1.84 mmol) and DMAP (7.3 mg, 0.060 mmol). The reaction mixture was stirred for 1 h at room temperature and then ethanol (2 mL), hexane (4 mL) and phosphate buffer (5 mL, pH = 7) were successively added at 0 °C. The mixture was extracted with ethyl acetate, and organic layer was washed with saturated aqueous copper(II) sulfate, saturated aqueous sodium hydrogencarbonate and brine, and finally dried over sodium sulfate. The crude product was filtered and the filtrate was concentrated by evaporation of the solvent to afford a mixture of (2*R*,3*R*,5*R*,6*R*,7S,8*R*)-7-acetoxy-2,6-bis(benzyloxy)-3-(*t*-butyldimethylsiloxy)-5-(4-methoxybenzyloxy)-4,4,8-trimethylcyclooctanone and (2*R*,3*R*,5*R*,6*R*,7*R*,8*R*)-7-acetoxy-2,6-bis(benzyloxy)-3-(*t*-butyldimethylsiloxy)-5-(4-methoxybenzyloxy)-4,4,8-trimethylcyclooctanone as a colorless oil. This was used in next step without further purification.

To a solution of mixture of (2*R*,3*R*,5*R*,6*R*,7*S*,8*R*)-7-acetoxy-2,6-bis(benzyloxy)-3-(*t*-butyldimethylsiloxy)-5-(4-methoxybenzyloxy)-4,4,8-trimethylcyclooctanone and (2*R*,3*R*,5*R*,6*R*,7*R*,8*R*)-7-acetoxy-2,6-bis(benzyloxy)-3-(*t*-butyldimethylsiloxy)-5-(4-methoxybenzyloxy)-4,4,8-trimethylcyclooctanone in benzene (8 mL) at room temperature was added a solution of DBU (1.37 g, 9.00 mmol) in benzene (4 mL). The reaction mixture was stirred for 1 h at 60 °C and then phosphate buffer (6 mL, pH = 7) was added at room temperature. The mixture was extracted with ethyl acetate, and organic layer was washed with brine and dried over sodium sulfate. After filtration of the mixture and evaporation of the solvent, the crude product was purified by column chromatography (hexane/AcOEt = 19/1) to afford enone **1** (316 mg, 82%, 2 steps) as a colorless oil.

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References

1 a) T. Mukaiyama, I. Shiina, H. Iwadare, M. Saitoh, T. Nishimura, N. Ohkawa, H. Sakoh, K. Nishimura, Y. Tani, M. Hasegawa, K. Yamada, and K. Saitoh, *Chem. Eur. J.*, **5**, 121 (1999), and references cited therein; b) I. Shiina, T. Nishimura, N. Ohkawa, H. Sakoh, K. Nishimura, K. Saitoh, and T. Mukaiyama, *Chem. Lett.*, **1997**, 419; c) H. Iwadare, H. Sakoh, H. Arai, I. Shiina, and T. Mukaiyama, *Chem. Lett.*, **1999**, 817.

2 All calculations were performed with the program package *SPARTAN* 5.0.3 of Wavefunction, Inc. (http://www.wavefun.com) or *TITAN* 1.0.1 of Schrödinger, Inc. (http://www.schrodinger.com)

and Wavefunction, Inc.

3 I. Shiina, J. Shibata, Y. Imai, R. Ibuka, H. Fujisawa, I. Hachiya, and T. Mukaiyama, *Chem. Lett.*, **1999**, 1145.

4 P. Lavallée, R. Ruel, L. Grenier, and M. Bissonnette, *Tetrahedron Lett.*, **27**, 679 (1986).

5 For a review, see: J. K. Cha and N.-S. Kim, *Chem. Rev.*, **95**, 1761 (1995). See a case of nucleophilic addition of allylic group to electrophile: K. N. Houk, M. N. Paddon-Row, N. G. Rondan, Y.-D. Wu, F. K. Brown, D. C. Spellmeyer, J. T. Metz, Y. Li, and R. J. Loncharich, *Science*, **231**, 1108 (1986). See cases of *E*-alkenes: E. Vedejs and C. K. McClure, *J. Am. Chem. Soc.*, **108**, 1094 (1986).

6 For a review, see: J. E. Eksterowicz and K. N. Houk, *Chem. Rev.*, **93**, 2439 (1993). Houk et al. utilized MM-transition state combined model (rigid TS model) for understanding the stereoselectivity of asymmetric dihydroxylation. They constructed the MM2 transition-structure model based on geometrical information from X-ray and *ab initio* structure of osmates and amine–OsO_4 complexes. See, Y.-D. Wu, Y. Wang, and K. N. Houk, *J. Org. Chem.*, **57**, 1362 (1992).

7 U. Pidun, C. Boehme, and G. Frenking, *Angew., Chem. Int. Ed. Engl.*, **35**, 2817 (1996); S. Dapprich, G. Ujaque, F. Maseras, A. Lledós, D. G. Musaev, and K. Morokuma, *J. Am. Chem. Soc.*, **118**, 11660 (1996); M. Torrent, L. Deng, M. Duran, M. Sola, and T. Ziegler, *Organometallics*, **16**, 13 (1997); A. J. DelMonte, J. Haller, K. N. Houk, K. B. Sharpless, D. A. Singleton, T. Strassner, and A. A. Thomas, *J. Am. Chem. Soc.*, **119**, 9907 (1997).

8 B. D. Gray and J. D. White, *J. Chem. Soc., Chem. Commun.*, **1985**, 20.

9 For a review, see: G. Cainelli, A. U. Ronchi, F. Bertini, P. Grasselli, and G. Zubiani, *Tetrahedron*, **27**, 6109 (1971); G. Köbrich, *Angew., Chem. Int. Ed. Engl.*, **11**, 473 (1972).

10 J. Villieras, P. Perriot, and J. F. Normant, *Bull. Soc. Chim. Fr.*, **1977**, 765; J. Villiéras and M. Rambaud, *C. R. Acad. Sci., Ser. C*, **291**, 105 (1980); M. Larchevéque and Y. Petit, *Synthesis*, **1986**, 60.

11 I. Shiina, Y. Imai, A. Kagayama, and T. Mukaiyama, *Chem. Lett.*, **2000**, 190.

12 I. Shiina, Y. Imai, M. Suzuki, M. Yanagisawa, and T. Mukaiyama, *Chem. Lett.*, **2000**, 1062.

13 I. Shiina, K. Uoto, N. Mori, T. Kosugi, and T. Mukaiyama, *Chem. Lett.*, **1995**, 181; M. Inoue, M. Sasaki, and K. Tachibana, *Tetrahedron Lett.*, **38**, 1611 (1997); M. Inoue, M. Sasaki, and K. Tachibana, *Angew. Chem., Int. Ed. Engl.*, **37**, 965 (1998).