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Intramolecular Aldol Condensation Applied to D-Glucose-derived δ-Ketoaldehydes : Access to Enantiomerically Pure Six-membered Carbocycles

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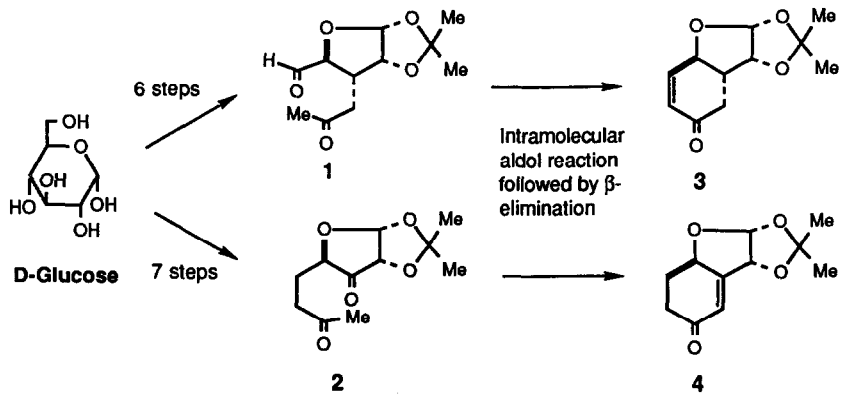
ABSTRACT: An enantiomerically pure δ-ketoaldehyde **10**, efficiently prepared from D-glucose, was subjected to an intramolecular aldol condensation. By using DBU as a base, the expecting aldol reaction took place smoothly giving the aldol **11** stereoselectively. Further functionalization of **11** provided tri-*C*-substituted cyclohexanediols **26** and **27**, *via* the functionalized cyclohexenone **15**.

We have reported recently the intramolecular aldol condensation approaches for preparation of enantiomerically pure highly functionalized six- or five-membered carbocycles. The representative achievements are summarized in Scheme 1. The substrates **1** and **2**, both were readily prepared from D-glucose, underwent intramolecular aldol reaction smoothly resulting in the formation of enones **3**[1,2] and **4**[3] after β-elimination of the initially formed aldols. The enone **3** was evidenced to be a versatile building block through enantiospecific synthesis of a variety of pseudo-sugars (carbocyclic analogues of aldopyranoses),[1,2,4] and synthesis of the key intermediate for paniculide B total synthesis.[5] As part of our continuous interest in these areas, we report here an intramolecular aldol condensation applied to another carbohydrate-derived substrate **10**. The present work provides a reliable route to highly functionalized six-membered carbocycles such as **11**, **15**, **26**, and **27**. The enantio-

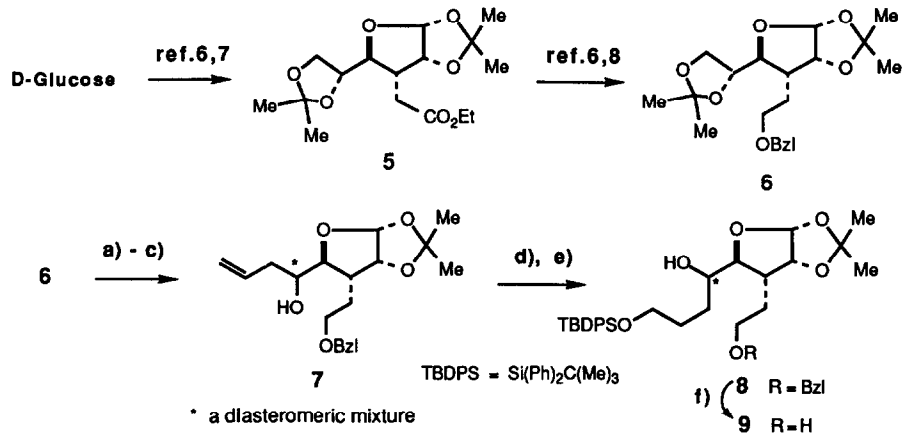


Scheme 1

merically pure cyclohexanediols **26** and **27** equipping with differentially utilizable three carbon functionalities may serve as versatile building blocks, such as polypropionate equivalents.

RESULTS AND DISCUSSION

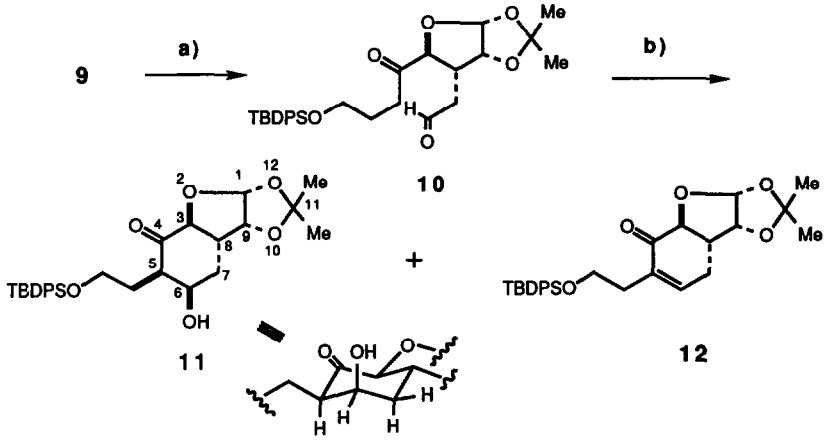
The preparation of the substrate **10** and the intramolecular aldol reaction of **10** are illustrated in Schemes 2 and 3. The starting material **6** is readily available from D-glucose according to a slight modification of the reported procedures.[6-8] Namely, the carbon elongation at *C*-3 of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuran-3-ulose with $Ph_3P{=}CHCO_2Et$ followed by the catalytic hydrogenation (Raney Ni T-4) of the resulting 3-*C*-unsaturated ester provided stereoselectively the branched D-allofuranose derivative **5** (Scheme 2). $LiAlH_4$ reduction of **5** followed by protection of so formed primary alcohol afforded the benzyl ether **6**. Acid hydrolysis of **6** for removal of the side chain acetal, glycol cleavage of so formed diol by $NaIO_4$-oxidation, nucleophilic addition with allylmagnesium chloride to the resulting aldehydo group gave a diastereomeric mixture of homoallylic alcohols, **7**, in a combined yield of 85% from **6**. The Grignard reaction proceeded without notable stereoselectivity. The diastereomeric ratio of **7** was estimated to be nearly 1:1 based on isolated amounts of the diastereomers after separation by column chromatography on silica gel. We did not necessitate to improve the selectivity since both hydroxyl groups would be oxidized to keto function in a later stage. Hydroboration of the double bond in **7** with BH_3•THF, oxidative work-up to a hydroxyl group by treating with alkaline aq H_2O_2, followed by preferential protection , provided a mono silyl ether **8** in 74% yield. The benzyl group of **8** was then removed under Pearlman-Hanessian conditions[9] to provide **9**. Swern oxidation[10] of the diol **9** gave the δ-ketoaldehyde **10**, the substrate for the intramolecular aldol reaction (Scheme 3). Other oxidation procedures (PCC,[11] Collins,[12] or Pfitzner-Moffatt[13]) were less effective and gave a complex mixture. Similarly in the case of our previous substrates,[1-3] the aldol reaction of **10** was achieved successfully by heating a solution of it in benzene in the presence of a catalytic amount of diazabicyclo-[5.4.0]undec-7-ene (DBU). The aldol product **11** was isolated as a single isomer in 64% yield from **9**. In addition, the β-elimination product **12** was obtained in 3%



a) 50% aqueous AcOH; b) $NaIO_4$ / aq. MeOH; c) $CH_2{=}CHCH_2MgCl$ / THF / 0 °C to rt (85% combined yield for two diastereomers) ; d) BH_3•THF / THF / 0 °C, then 30% aq H_2O_2 / aq. NaOH ; e) TBDPSCl / imidazole / DMF (74% yield from **7**) ; f) H_2 / 20% $Pd(OH)_2$ in charcoal / EtOH / reflux (85%).

Scheme 2

yield. Stereochemical assignment of the aldol **11** was based on the ^{1}H NMR (400 MHz) analysis, in which *H*-6 appeared at δ 4.55 as a quartet with *J* =2.7 Hz by irradiation of a singlet at δ 3.15 attributable to the OH proton. NOEDS experiments of **11** supported this structure determination. Enhancements of the signals due to *H*-6 (5.9%) and due to *H*-3 at δ 4.33 (13.0%) were observed when the signal due to *H*-5 at δ 2.62 was irradiated, whereas an enhancemant of *H*-5 (6.4%) was observed by irradiation of *H*-6. The predominant formation of the cis-aldol **11** can be rationalized by adopting the well known argument that an enolate attack to a carbonyl group occurs favorably when the C-O double bond exists axially in the chair-like transition state. This stereoelectronic effect had been reported by Seebach.[14,15] As concerns the stereochemistry of the substituent at *C*-5, axial orientation is unlikely since a bulky substituent tends to be disposed equatorially under the epimerizable reaction conditions. Incidentally, less than 10% yield of the *C*-5 epimer of **11** was once isolated in 1 g scale experiment. We found that the 5-epimer rapidly epimerized to **11** during chromatographic purification on silica gel. In a 6.2 g scale experiment, the 5-epimer, which was detected in the reaction mixture, completely epimerized when the mixture was passed through silica gel. On the other hand, the formation of **12** was a consequence of the β-elimination of the aldol **11**. The hydroxyl group and the proton at *C*-5 of **11** dispose antiperiplanarly. This alignment, which satisfies a stereoelectronic demand,[15] accelerates the β-elimination.

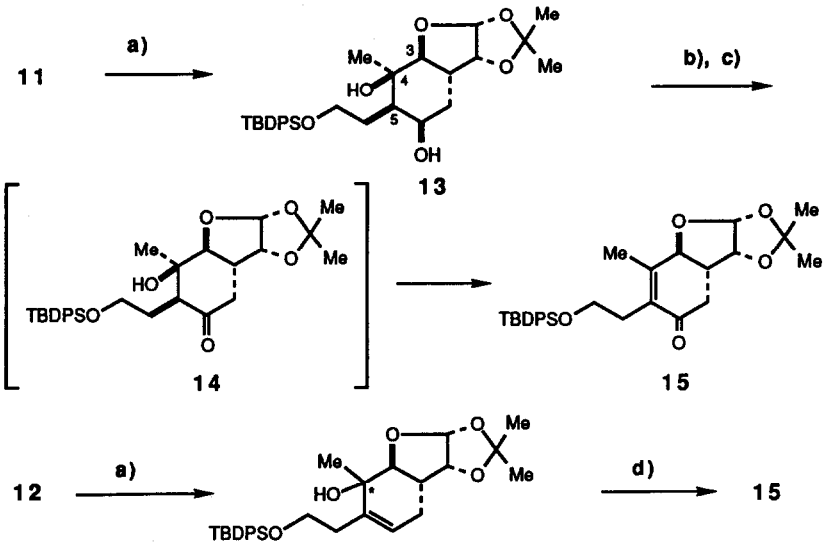


a) Swern oxidation ; b) DBU / benzene / reflux (64% yield from **9**).

Scheme 3

Having established a reliable route for access to the six-membered carbocycle **11**, we interested in further functionalization of **11**. Introduction of a carbon functionality to *C*-4 of **11** was next investigated. Methyl group was a choise for this purpose since the methylated product, a tri-*C*-alkylated derivative of cyclohexanediol, can be regarded as a synthetic equivalent of polypropionates. An alternating methyl and hydroxyl groups is hidden in the product. Nucleophilic attack at *C*-4 carbonyl group of **11** using MeMgBr proceeded stereoselectively (Scheme 4). Crystalline adduct **13** obtained was diastereomerically pure. The configuration of the newly introduced stereogenic center was determined to be as depicted by NOEDS experiments of **13**. When the methyl group at δ 1.27 was irradiated, enhancements of the signals due to *H*-3 at δ 3.45 (7.1%) and *H*-5 at δ 2.08 (6.0%) were observed. Whereas, 3.3% enhancement of the signal due to the *C*-4 methyl group was observed by irradiation of the signals due to *H*-3. The Grignard reagent favorably attacked from the less

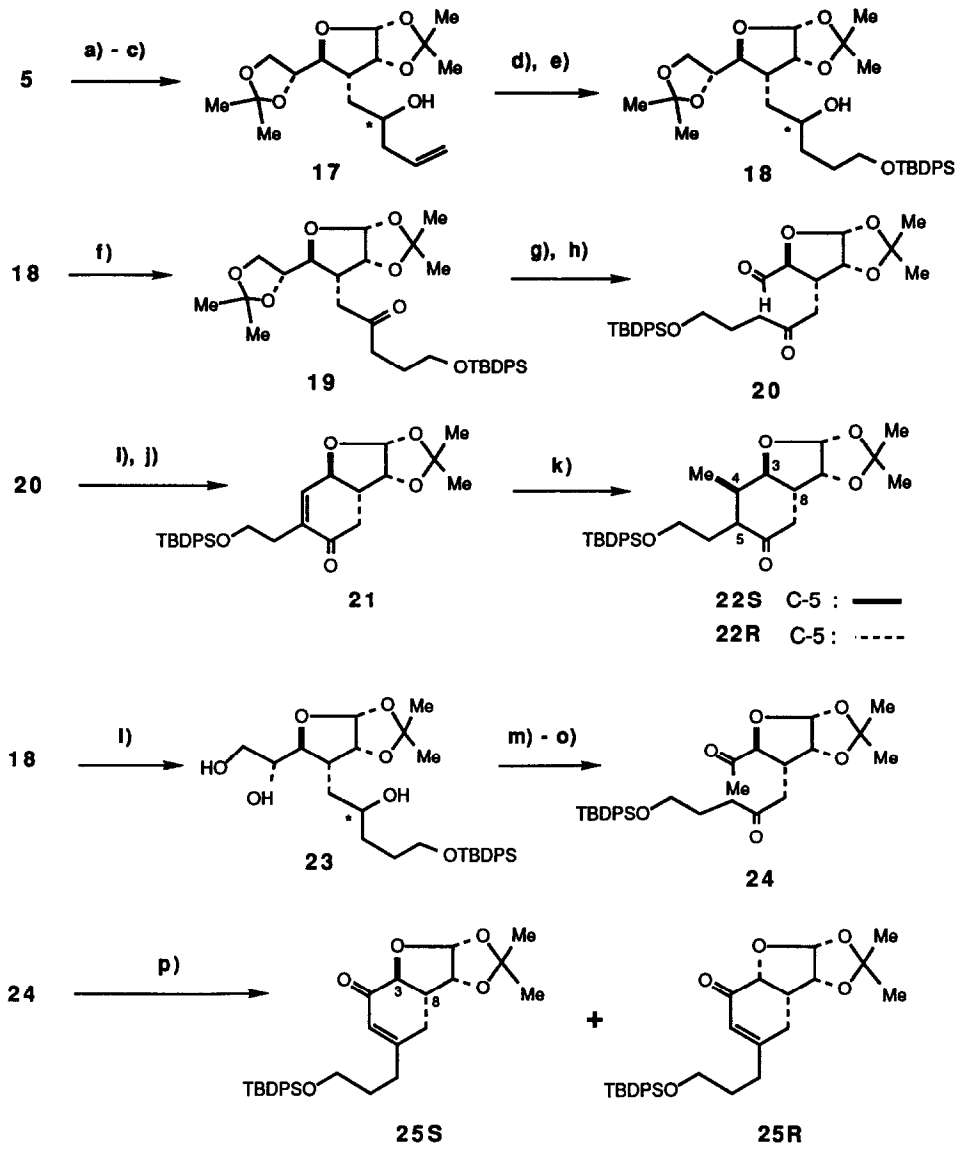
hindered equatorial direction, introducing an α-oriented methyl group. Swern oxidation[10] of **13** followed by β-elimination of so formed *C*-6 keto derivative **14** under mesylation conditions provided a 2,3,5-tri-*C*-alkylated cyclohex-2-enone-4-ol **15** in 56% overall yield from **11**. Compound **15** was also prepared from the β-elimination product **12** as follows albeit less effectively. Treatment of **12** with MeMgBr gave a nearly 3:1 separable mixture of two diastereomers, i. e. **16**, in 94% combined yield. The structure of each diastereomer was not determined. Each isomer was then subjected to PCC oxidation affording **15** in 53% or 28% yield. In either case, formation of several unidentified products was accompanied.



a) MeMgBr / THF / 0 °C; b) Swern oxidation ; c) $MeSO_2Cl$ / pyridine / 70 °C (56% yield from **11**) ; d) PCC / MS / CH_2Cl_2 .

Scheme 4

Prior to the establishment of the efficient route to **15**, we investigated other intramolecular aldol cyclization approaches for preparation of the structurally related six-membered carbocycles (Scheme 5). Two substrates **20** and **24** were prepared successfully from **5** through a three carbon elongation of the side chain at *C*-3 (**5** to **17**), functional group transformation of the side chain at C-*3* (**17** to **19**), introduction of a carbonyl functionality at *C*-4 (**19** to **20**) or (**18** to **24**). DBU-catalyzed intramolecular aldol cyclization of the δ-ketoaldehyde **20** proceeded smoothly, after β-elimination of the aldol by treating with acetic anhydride in pyridine, to provide the enone **21** efficiently. 1,4-Conjugate addition of a methyl anion to **21** using Me_2CuLi proceeded without specified stereoselectivity, giving an inseparable diastereomeric mixture of **22S** and **22R** in 79% combined yield. The ratio of **22S** and **22R** was determined to be nearly 1:2 based on ^1H NMR analysis. The methyl groups of **22S** and **22R** dispose both axially, being evidenced by the doublet of doublets due to *H*-4 having $J_{3,8}$ =11.4 Hz and $J_{3,4}$=5.1 Hz for **22R**, and that having $J_{3,8}$=11.4 Hz and $J_{3,4}$=4.4 Hz for **22S**. By treating the mixture of **22S** and **22R** with MeONa (0.4 mol eq) at rt, the ratio of **22S** and **22R** was changed to 5:1 as a



a) $LiAlH_4$ / THF; b) PCC / MS / CH_2Cl_2 (67% from 5); c) allylmagnesium chloride / THF / 0 °C to rt (87%); d) BH_3•THF / THF / 0 °C; then 35% H_2O_2 / aq NaOH ; e) TBDPSCl / imidazole /DMF (88% from 17); f) PCC / MS / CH_2Cl_2 (98%); g) AcOH:H_2O:THF (6:1:1) (68%); h) $NaIO_4$ / aq MeOH; i) DBU / benzene / reflux ; j) Ac_2O / pyridine (77% for 3 steps); k) Me_2CuLi / THF / 0 °C (79% combined yield for the mixture of 22S and 22R); l) AcOH:H_2O:THF (6:1:1) (77%); m) $NaIO_4$ / aq MeOH; n) MeMgBr / THF / reflux ; o) PCC / MS / CH_2Cl_2 (78.5% from 23); p) potassium *tert*-butoxide (1.7 mol eq) / benzene / reflux (17% for 25S, 13% for 25R), or potassium *tert*-butoxide (0.6 mol eq) / THF / 0 °C; then MsCl /pyridine / DMAP / 70 °C (25% for 15).

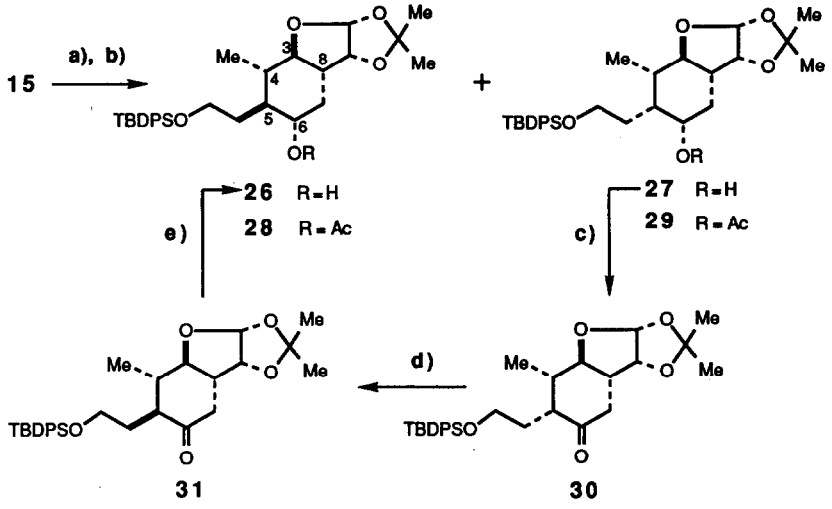
Scheme 5

consequence of thermodynamic controlled epimerizarion to **22S**. In compound **22S**, the bulky substituent at *C*-5 is disposed equatorially. Unfortunately we could not find practical regioselective deprotonation conditions to introduce a double bond between *C*-4 and 5 of the mixture of **22S** and **22R**. Enolate genenation (LDA-THF-0 °C) of the mixture of **22R** and **22S**, selenenylation (PhSeCl) followed by oxidative treatment with H_2O_2 resulted in the formation of a complex mixture. We did not explore other procedures enabling the practical transformation of **22S** and **22R** into **15**.

On the other hand, the aldol condensation of the δ-diketone **24** occurred by treating a solution of **24** in benzene with potassium *tert*-butoxide, giving two cyclohexenones **25S** and **25R** in yields of 17% and 13%, respectively, which were accompanied by several unidentified byproducts. The aldol condensation products **25S** and **25R** were characterized by their ^{1}H NMR spectra, in which the signal due to *H*-3 of **25S** appeared at δ 4.39 as a doublet having $J_{3,8}$=12.4 Hz and that of **25R** at δ 4.39 as a doublet having $J_{3,8}$=8.8 Hz. Furthermore, NOEDS experiments of **25R** supported its cis ring juncture, in which 7.2% enhancement of the signal due to *H*-8 was observed when the signal due to *H*-3 was irradiated. Unfortunately, the regiochemistry of the aldol cyclization of **24** was undesirable for our purpose. The aldol condensation of **24** carried out using the same base but in THF at 0 °C, which provided the alternative aldol as a single diastereomer albeit in 31% yield, was interesting. Although we could not compare directly this aldol product to an authentic sample, the aldol product was likely to be **14**. Under these conditions, compound **24** was recovered in 13%. β-Elimination of so obtained **14** under the same conditions described above (Scheme 4) provided the enone **15** in 80% yield. We have no reasonable account for this solvent effect on the regioselectivity of the cyclization. Because of the low yield of **14** from **24**, we concluded that the route to **15** from **17** seems to be less effective, comparing to the route from **7**.

With the highly functionalized six-membered carbocycle **15** in hand, we next examined the stereoselectivity on hydrogenation of **15**. Under atmospheric hydrogenation conditions in the presence of Raney Ni, no addition of hydrogen to the tetrasubstituted olefin was observed. The hydrogen addition eventually became possible under medium hydrogen pressure using a Parr apparatus that completed after 32 h in a 2.16 g scale. Rather surprisingly, addition of hydrogen to the carbonyl group also took place under these conditions, resulting in the formation of two cyclohexanols **26** and **27** in 59% and 25.5% yields, respectively (Scheme 6). The structures of **26** and **27** were determined by ^{1}H NMR (400 MHz) analysis of the respective acetates **28** and **29**. Each methyl group in **28** or **29** exists equatorially, being evidenced by $J_{3,4}$= $J_{3,8}$=10.0 Hz for either acetate. The stereochemical assignment of **29** was further supported by NOEDS experiments, in which 6.8% enhancement of the signal due to *H*-5 at δ 2.00-2.04 was observed when the signal due to *H*-6 at δ 4.89 was irradiated. These structural features of **26** and **27** imply that hydrogenation to the double bond of **15** occurred exclusively from β-site of the cyclohexenone ring. Furthermore, prior to addition of hydrogen to the carbonyl group of the intermediate **30**, epimerization of the α-carbon (*C*-5) of the carbonyl group occurred, increasing the proportion of the thermodynamically more stable **31** in which the bulky side chain at C-5 is disposed equatorially. Change of the catalyst to 10% Pd on charcoal or PtO_2 (under medium hydrogen pressure) did not effect on depression of the epimerization. Subsequent hydrogen addition to the carbonyl groups of the epimeric mixture again occurred preferentially from the β-site. From these observations, we expected that stereochemical inversion of **27** to **26** would occur feasibly. To confirm this, the diastereomer **27** was oxidized with PCC giving the cyclohexanone **30**, which was then treated with base (MeONa-in MeOH). The epimerization of **30** to **31** occurred almost completely at rt in one day. The carbonyl group of the *C*-5 epimer **31**

so formed was then reduced with $NaBH_4$, giving **26** stereoselectively in 81% yield from **27**. Unepimerized **27** was recovered in 4% yield. These experiments validated that the facile epimerization at *C*-5 of **30** occurred during the hydrogenation of **15**.



a) H_2 (55 psi) / Raney-Ni / EtOH (59% yield for **26**, 25.5% for **27**) ; b) Ac_2O / pyridine ; c) PCC / MS / CH_2Cl_2; d) MeONa / MeOH ; e) $NaBH_4$ / MeOH (81% yield from **27**).

Scheme 6

In summary, we could find an efficient route for access to enantiomerically pure and densely functionalized six-membered carbocycles such as **11**, **15**, and **26**. The stereochemical insight of the intramolecular aldol condensation achieved with the substrate **10** is also discussed. To investigate the addition of a variety of nucleophiles to the carbonyl group in aldol product **11** or to the double bond in the cyclohexenones **12** and **15** will widen the applicability of these carbocycles as versatile building blocks.

EXPERIMENTAL

Melting points are uncorrected. Specific rotations were measured using a JASCO Model DIP-4 polarimeter in a 10 mm cell. IR spectra (neat) were recorded using a JASCO Model A-202 spectrometer. ^1H NMR spectra were recorded using a Varian EM-390 (90 MHz), JEOL EX-90 (90 MHz), JEOL GX-270 (270 MHz) or JEOL JNM-GX 400 FT spectrometer (400 MHz) in $CDCl_3$ solution with tetramethysilane as an internal standard. High-resolution mass spectra (HRMS) were taken using a Hitachi M-80 mass spectrometer. Microanalyses were carried out by staffs of the Analytical Center in our university.

Thin-layer chromatography (TLC) was performed with a glass plate coated Kieselgel 60 GF_{254} (Merck). Crude reaction mixtures or extractive materials were chromatographed on silicagel 60 K070 (Katayama Chemicals). Preparative TLC were performed using a glass plate (200 x 200 mm) coated Kieselgel 60 PF_{254} (Merck).

Unless otherwise specified, reactions were carried out at room temperature (rt). Reagents and solvents were removed by concentration in vacuo, using an evaporator with bath at 35-45 °C.

Solvents were dried (drying reagent in parenthesis) and distilled prior to use: tetrahydrofuran=THF ($LiAlH_4$, then Na/benzophenone ketyl), *N,N*-dimethylformamide=DMF ($MgSO_4$), CH_2Cl_2 (CaH_2), dimethyl sulfoxide= DMSO (CaH_2), oxalyl chloride (CaH_2 then distilled under an Ar), triethylamine ($CaSO_4$), benzene (CaH_2), and pyridine (NaOH).

3-*C*-(2-Benzyloxyethyl)-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (6). This compound was prepared from the known ester **5**[8] according to the reported procedure with slight modification. Benzylation of the $LiAlH_4$ reduction product of **5** was executed with benzyl bromide in the presence of NaH in our case. **6** as a colorless oil: $[\alpha]_D^{19.5}$ +50.7° (*c* 0.86, $CHCl_3$), [lit.[8] $[\alpha]_D^{24}$ +54.6 ° (*c* 1.0, $CHCl_3$)]. ^1H NMR spectrum of **6** was coincident with the reported data.[8] Anal. Calcd for $C_{21}H_{30}O_6$: C, 66.65; H, 7.99. Found: C, 66.83; H, 7.77.

Mixture of 3-*C*-[(2-Benzyloxy)ethyl]-3,6-dideoxy-1,2-*O*-isopropylidene-6-*C*-vinyl-α-D-allo- and -β-L-talofuranose (7). A solution of **6** (20.20 g, 53.4 mmol) in 50% aqueous acetic acid (400 mL) was stirred for 12 h, and the solution was concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:2 then 3:1), giving 16.10 g of 5,6-diol as a colorless oil: TLC R_f 0.47 (EtOH/toluene, 1:5); $[\alpha]_D^{25}$ +47.9 ° (*c* 0.90, $CHCl_3$); IR 3420, 2990, 2940, 2880, 1455, 1380, 1370, 1310, 1245 cm^{-1}; ^1H NMR (90 MHz) δ 1.27, 1.47 (2 s, 3H x 2), 1.8-2.2 (m, 3H), 2.65-2.9 (br, 1H), 3.3-3.6 (br, 1H), 3.65-4.0 (m, 6H), 4.53 (s, 2H), 4.55 (t, *J* =4 Hz, 1H), 5.69 (d, *J* =4 Hz, 1H), 7.35 (s, 5H).

To a stirred solution of the 5,6-diol (16.10 g) in MeOH (400 mL) was added dropwise aq $NaIO_4$ (12.32 g, 57.6 mmol in H_2O 85 mL). The mixture was stirred for 40 min, and the resulting white precipitates were removed by filtration and washed well with MeOH. The filtrate and washings were combined and concentrated in vacuo to *ca.* 30 mL volume. It was diluted with 3% aq NaCl (300 mL), and the whole was extracted with CH_2Cl_2 (500 mL x 3). The combined extracts were dried (Na_2SO_4) and concentrated in vacuo, leaving 14.90 g of 5-aldehyde derivative as a colorless oil, which was used directly for the next Grignard reaction: TLC R_f 0.58 (EtOAc/hexane, 2:3); IR 2990, 2940, 2860, 1730, 1495, 1450, 1380, 1370, 1240 cm^{-1}; ^1H NMR (90 MHz) δ 1.33, 1.51 (2 s, 3H x 2), 1.7-2.4 (m, 3H), 3.54 (t, *J* =7 Hz, 2H), 4.07 (dd, *J* =3, 13 Hz, 1H), 4.47 (s, 2H), 4.60 (t, *J* =4 Hz, 1H), 5.85 (d, *J* =4 Hz, 1H), 7.33 (s, 5H), 9.60 (d, *J* =3 Hz, 1H).

The following reaction was carried out under Ar. To a cold (0 °C) stirred solution of the 5-aldehyde (14.90 g) in THF (400 mL) was added dropwise allylmagnesium chloride (2.0 M solution in THF, 107.5 mL, 215 mmol). The mixture was stirred at rt for 1 h, then was quenched with 10% aq NH_4Cl (400 mL). This was diluted with H_2O (100 mL), then it was extracted with EtOAc (500 mL x 3). The combined extracts were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:8 then 1:4), giving a diastereomeric mixture of **7** (15.73 g, 85% from **6**) as a colorless oil. In a separate experiment using 176 mg of **6**, the mixture of **7** was cleanly separated by chromatography on silica gel. Two diastereomers, 71 mg (44%) and 73 mg (45%), were obtained. The former compound having R_f 0.55 (EtOAc/hexane, 1:2): $[\alpha]_D^{19}$ +59.5° (*c* 1.10, $CHCl_3$); IR 3450, 2985, 2940, 2860, 1640, 1495, 1450, 1380, 1370, 1240 cm^{-1}; ^1H NMR (90 MHz) δ 1.30, 1.47 (2 s, 3H x 2), 1.8-2.45 (m, 6H), 3.5-3.9 (m, 4H), 4.48 (t, *J* =4 Hz, 1H), 4.52 (s, 2H), 5.0-5.1 (m, 2H), 5.8-6.15 (m, 1H), 5.71 (d, *J* =4 Hz,1H), 7.33 (s, 5H). Anal. Calcd for $C_{20}H_{28}O_5$: C, 68.94; H, 8.10. Found: C, 68.84; H, 7.94. The latter compound having R_f 0.46

(EtOAc/hexane, 1:2): $[\alpha]_D^{19}$ +39.5° (*c* 1.02, $CHCl_3$); IR 3470, 2990, 2940, 2860, 1640, 1450, 1380, 1370, 1240 cm^{-1}; ^1H NMR (90 MHz) δ 1.30, 1.48 (2 s, 3H x 2), 1.6-2.5 (m, 6H), 3.5-3.9 (m, 4H), 4.53 (s, 2H), 4.57 (t, *J* =4 Hz, 1H), 5.0-5.2 (m, 2H), 5.75-6.15 (m, 1H), 5.85 (d, *J* =4 Hz, 1H), 7.35 (s, 5H). Anal. Calcd for $C_{20}H_{28}O_5$: C, 68.94; H, 8.10. Found: C, 68.62; H, 7.90.

Mixture of 3-*C*-[(2-Benzyloxy)ethyl]-3,6,7-trideoxy-1,2-*O*-isopropylidene-8-*O*-(*tert*-butyldiphenylsilyl)-α-D-*allo*- and -β-L-*talo*-octofuranose (8). The following reaction was carried out under Ar. To a cold (0 °C) stirred solution of the nearly 1:1 mixture of **7** (15.73 g, 45.15 mmol) in THF (300 mL) was added dropwise BH_3•THF (1.0 M solution in THF, 105.5 mL, 105.5 mmol). After the mixture was stirred at 0 °C for 4 h, H_2O (105 mL) and 3 N aq NaOH (105 mL) were added. The mixture was stirred for 15 min at rt, then 30% aq H_2O_2 (105 mL) was added. After being stirred for 40 min, the mixture was quenched with saturated aq Na_2SO_3 (130 mL), then it was diluted with H_2O (100 mL). This was extracted with AcOEt (500 mL x 5). The combined extracts were dried (Na_2SO_4) and concentrated in vacuo. The residue was passed through a short column of silica gel (EtOAc/hexane, 1:3 then 3:1), giving a mixture of α-D-*allo*- and -β-L-*talo*-octofuranose derivatives (15.12 g) as a colorless oil [TLC R_f 0.20 and 0.15 (EtOAc/hexane, 3:1)], which was silylated without separation.

To a stirred solution of the mixture obtained (15.12 g) in DMF (230 mL) were added imidazole (5.65 g, 83.0 mmol) and *tert*-butylchlorodiphenylsilane (8.58 mL, 33.0 mmol). After the mixture was stirred for 3.5 h, the silylating reagent (4.29 mL, 16.5 mmol) and imidazole (2.81 g, 41.3 mmol) were added. The mixture was stirred for 2 h, then it was diluted with EtOAc(1 L). The whole was washed with H_2O (600 mL x 3). The organic layer was drawn off, dried (Na_2SO_4) and concentrated in vacuo with aid of coevaporation with toluene. The residue was purofoed by column chromatography on silica gel (EtOAc/hexane, 1:8 then 1:6), giving 20.15 g (74% from **7**) of the mixture of **8** as a colorless oil. Each pure diastereomer was obtained by partial separation of the mixture by chromatography. One isomer having R_f 0.70 (EtOH/toluene, 1:8): $[\alpha]_D^{24}$ +30.5° (*c* 1.05, $CHCl_3$); IR 3450, 2950, 2930, 2855, 1590, 1470, 1455, 1425, 1380, 1370, 1360, 1240 cm^{-1}; ^1H NMR (90 MHz) δ 1.05 (s, 9H), 1.29, 1.48 (2 s, 3H x 2), 1.55-2.3 (m, 7H), 2.61 (d, *J* =5 Hz, 1H), 3.5-3.9 (m, 6H), 4.50 (s, 2H), 4.55 (t, *J* =4 Hz, 1H), 5.69 (d, *J* =4 Hz, 1H), 7.2-7.5, 7.55-7.8 (2 m, 6H, 4H), 7.32 (s, 5H). Anal. Calcd for $C_{36}H_{48}O_6Si$: C, 71.49; H, 8.00. Found: C, 71.21; H, 7.91. Another isomer having R_f 0.67 (EtOH/toluene, 1:8): $[\alpha]_D^{24}$ +17.6° (*c* 1.15, $CHCl_3$); IR 3460, 2950, 2935, 2860, 1590, 1475, 1455, 1430, 1380, 1370, 1360, 1220 cm^{-1}; ^1H NMR (90 MHz) δ 1.05 (s, 9H), 1.30, 1.47 (2 s, 3H x 2), 1.6-2.35 (m, 8H), 3.4-3.8 (m, 6H), 4.49 (s, 2H), 4.55 (t, *J* =4 Hz, 1H), 5.71 (d, *J* =4 Hz, 1H), 7.2-7.4, 7.6-7.8 (2 m, 6H, 4H), 7.32 (s, 5H). Anal. Calcd for $C_{36}H_{48}O_6Si$: C, 71.49; H, 8.00. Found: C, 71.29; H, 7.95.

Mixture of 3,6,7-Trideoxy-3-*C*-(2-hydroxyethyl)-1,2-*O*-isopropylidene-8-*O*-(*tert*-butyldiphenylsilyl)-α-D-*allo*- and -β-L-*talo*-octofuranose (9). The 1:1 diastereomeric mixture of **8** (8.91 g, 14.7 mmol) was dissolved in EtOH (100 mL), and freshly distilled cyclohexene (150 mL) and 20% $Pd(OH)_2$ on charcoal (1.50 g) were added. The mixture was heated under reflux for 4 h, then the catalyst was removed by filtration through a pad of Celite and washed well with EtOH. The combined filtrate and washings were concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:6 then 3:2), giving the mixture of **9** (6.44 g, 85%) as a colorless oil. The starting material was also recovered (0.67 g, 7.5%). The two diastereomers of **9** could be separated partially by chromatography on silica gel. The less polar compound: R_f 0.40 (EtOH/toluene, 1:8); $[\alpha]_D^{24}$ +17.7° (*c* 0.89, $CHCl_3$); IR 3400, 2960, 2940, 2860,

1590, 1470, 1460, 1425, 1380, 1370, 1240 cm^{-1}; ^1H NMR (90 MHz) δ 1.05 (s, 9H), 1.33, 1.51 (2 s, 3H x 2), 1.2-2.4 (m, 8H), 2.6-3.1 (br, 1H), 3.6-4.0 (m, 6H), 4.70 (t, *J* =4 Hz, 1H), 5.77 (d, *J* =4 Hz, 1H), 7.3-7.5, 7.6-7.7 (2 m, 6H, 4H). The polar compound: R_f 0.37 (EtOH/toluene, 1:8)]: $[\alpha]_D^{24}$ +13.9° (*c* 0.87, $CHCl_3$); IR 3390, 2960, 2940, 2860, 1590, 1470, 1460, 1425, 1380, 1370, 1240 cm^{-1}; ^1H NMR (90 MHz) δ 1.05 (s, 9H), 1.33, 1.50 (2 s, 3H x 2), 1.2-2.45 (m, 9H), 3.45-3.9 (m, 6H), 4.69 (t, *J* =4 Hz, 1H), 5.79 (d, *J* =4 Hz, 1H), 7.3-7.45, 7.6-7.7 (2 m, 6H, 4H).

(1*R*,3*S*,5*R*,6*R*,8*R*,9*R*)-6-Hydroxy-11,11-dimethyl-5-[2-(*tert*-butyldiphenylsilyloxy)-ethyl]-2,10,12-trioxatricyclo[7.3.0.0^{3,8}]dodecan-4-one (11) and (1*R*,3*S*,8*R*,9*R*)-11,11-Dimethyl-5-[2-(*tert*-butyldiphenylsilyloxy)ethyl]-2,10,12-trioxatricyclo[7.3.0.0^{3,8}]dodec-5-en-4-one (12). The following reaction was carried out under Ar. To a cold (-78 °C) stirred mixture of CH_2Cl_2 (250 mL) and DMSO (5.10 mL, 71.9 mmol) was added freshly distilled oxalyl chloride (5.22 ml, 59.8 mmol). This was stirred at -78 °C for 20 min, and a solution of the 1:1 mixture of **9** (6.16 g, 12.0 mmol) in CH_2Cl_2 (three portions, 10 mL x 3) was added dropwise. After the mixture was stirred at -78 °C for 2 h, (*i*-Pr)$_2$NEt (20.9 mL, 119.7 mmol) was added. The mixture was allowed to warm to rt gradually, and then stirred for 10 min. The mixture was diluted with H_2O (200 mL), then it was extracted with CH_2Cl_2 (400 mL x 3). The combined extracts were dried (Na_2SO_4) and concentrated in vacuo. The residue was passed through a short column of silica gel (EtOAc/hexane, 1:10), giving **10** (5.48 g) as a pale yellow oil. **10**: TLC R_f 0.62 (EtOH/toluene, 1:10); IR 2960, 2940, 2900, 2860, 1720, 1590, 1475, 1460, 1430, 1380, 1370, 1250 cm^{-1}; ^1H NMR (90 MHz) δ 1.05 (s, 9H), 1.31, 1.47 (2 s, 3H x 2), 1.6-2.5 (m, 3H), 2.6-2.95 (m, 4H), 3.65 (t, *J* =7 Hz, 2H), 4.05 (d, *J* =11 Hz, 1H), 4.79 (t, *J* =4 Hz, 1H), 5.89 (d, *J* =4 Hz, 1H), 7.3-7.45, 7.6-7.75 (2 m, 6H, 4H), 9.78 (s, 1H).

A solution of **10** (5.48 g) in benzene (280 mL) was heated under reflux in the presence of DBU (0.096 mL, 0.64 mmol). Each 0.032 mL of DBU was added after 2, 15, and 24 h, and the mixture was heated for 33 h in total. After being cooled to rt, the mixture was neutralized by adding acetic acid (5 v/v % in benzene) and then concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:4 to 2/3), giving **11** (3.90 g, 64%) and **12** (0.17 g, 3%). The δ-ketoaldehyde **10** (0.23 g) was recovered. **11** as a colorless oil: TLC R_f 0.12 (EtOAc/hexane, 1:2); $[\alpha]_D^{24}$ -38.7° (*c* 1.03, $CHCl_3$); IR 3500, 2960, 2940, 2860, 1740, 1590, 1475, 1460, 1430, 1380, 1370, 1305, 1255 cm^{-1}; ^1H NMR (400 MHz) δ 1.05 (s, 9H), 1.36, 1.54 (2 s, 3H x 2), 1.92-2.05 (m, 3H), 2.23 (dt, *J* =13.7, 2.9 Hz, 1H), 2.48 (tt, *J* =12.5, 3.4 Hz, 1H), 2.62 (br s, 1H), 3.15 (br s, 1H), 3.69 (ddd, *J* =3.4, 8.3, 11.8 Hz, 1H), 3.91 (ddd, *J* =3.9, 6.3, 10.3 Hz, 1H), 4.33 (dd, *J* = 1.0, 12.0 Hz, 1H), 4.55 (triplet like, *J* =2.7 Hz, 1H), 4.68 (t, *J* =3.5 Hz, 1H), 5.90 (d, *J* =3.5 Hz, 1H), 7.38-7.46, 7.62-7.66 (2 m, 6H, 4H). Anal. Calcd for $C_{29}H_{38}O_6Si$: C, 68.20; H, 7.51. Found: C, 67.80; H, 7.33. **12** as a colorless oil: TLC R_f 0.49 (EtOAc/hexane, 1:2); IR 2960, 2940, 2860, 1700, 1620, 1590, 1475, 1460, 1430, 1380, 1370, 1300, 1255 cm^{-1}; ^1H NMR (90 MHz) δ 1.02 (s, 9H), 1.30, 1.48 (2 s, 3H x 2), 1.45-2.8 (m, 5H), 3.71 (t, *J* =7 Hz, 2H), 4.35 (d, *J* =12 Hz, 1H), 4.60 (t, *J* =4 Hz, 1H), 5.83 (d, *J* =4 Hz, 1H), 6.55-6.7 (m, 1H), 7.3-7.4, 7.5-7.8 (2 m, 6H, 4H).

(1*R*,3*S*,8*R*,9*R*)-4,11,11-Trimethyl-5-[2-(*tert*-butyldiphenylsilyloxy)ethyl]-2,10,12-trioxa-tricyclo[7.3.0.0^{3,8}]dodec-4-en-6-one (15). From 11. The following reactions were carried out under Ar. To a cold (-15 °C) stirred solution of **11** (3.90 g, 7.64 mmol) in THF (300 mL) was added MeMgBr (2.0 M solution in THF, 22.9 mL, 46.0 mmol). After being stirred at rt for 1 h, the mixture was quenched by

adding 10% aq NH_4Cl (150 mL) at 0 °C, then it was diluted with H_2O (150 mL). The aqueous solution was extracted with EtOAc (600 mL x 3). The combined extracts were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:5 then 1:2), giving **13** (3.29 g) as white crystals, mp 92.5-94.0 °C: TLC R_f 0.37 (EtOAc/hexane, 1:1); $[\alpha]_D^{22.5}$ -5.3° (*c* 1.11, $CHCl_3$); IR 3420, 2960, 2940, 2840, 1590, 1470, 1425, 1380, 1370, 1255 cm^{-1}; ^1H NMR (400 MHz) δ 1.05 (s, 9H), 1.27 (s, 3H), 1.35, 1.53 (2 s, 3H x 2), 1.40-1.50, 1.55-1.63 (2 m, 1H x 2), 1.91-2.05 (m, 2H), 2.08 (dt, *J* =13.2, 3.2 Hz, 1H), 2.17-2.23 (m, 1H), 2.76 (s, 1H), 3.45 (d, *J* =10.7 Hz, 1H), 3.58 (d, *J* =7.3 Hz, 1H), 3.78-3.86 (m, 2H), 4.01-4.04 (m, 1H), 4.64 (t, *J* =3.9 Hz, 1H), 5.86 (d, *J* =3.9 Hz, 1H), 7.37-7.46, 7.64-7.69 (2 m, 6H, 4H). Anal. Calcd for $C_{30}H_{42}O_6Si$: C, 68.41; H, 8.04. Found: C, 68.33; H, 7.95.

To a cold (-78 °C) stirred mixture of CH_2Cl_2 (120 mL) and DMSO (4.43 mL, 62.4 mmol) was added freshly distilled oxalyl chloride (4.42 mL, 50.7 mmol). The mixture was stirred at -78 °C for 20 min, then a solution of **13** (3.29 g) in CH_2Cl_2 (5 mL x 5) was added portionwise. The mixture was stirred at -78 °C for 2 h, then Et_3N (43.5 mL, 312 mmol) was added. The mixture was allowed to warm to rt gradually, then it was stirred for 10 min. The mixture was diluted with H_2O (300 mL) and extracted with CH_2Cl_2 (600 mL x 3). The combined extracts were dried (Na_2SO_4) and concentrated in vacuo to *ca.* one-half volume. The white needles that appeared were removed by filtration and washed well with EtOAc. The filtrate and washings were combined and concentrated in vacuo, leaving a crude mixture of **14** and **15** (4.42 g) as a pale yellow oil, which was used without separation [TLC R_f 0.17 for **14** and 0.60 for **15** (EtOAc/hexane, 1:3)].

To a stirred solution of the mixture of **14** and **15** (4.42 g) in pyridine (70 mL) was added dropwise $MeSO_2Cl$ (0.24 mL, 3.12 mmol). The mixture was heated at 70 °C for 5 h, then it was diluted with H_2O (300 mL). The whole was extracted with CH_2Cl_2 (600 mL x 3). The combined extracts were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:8 then 1:4), giving **15** (2.16 g, 56% from **11**) as a colorless oil: $[\alpha]_D^{24}$ -20.4 ° (*c* 1.23, $CHCl_3$); IR 2970, 2940, 2860, 1670, 1620, 1590, 1470, 1430, 1380, 1370, 1300, 1260, 1250 cm^{-1}; ^1H NMR (400 MHz) δ 1.02 (s, 9H), 1.34, 1.53 (2 s, 3H x 2), 1.87-1.96 (m, 1H), 2.00 (d, *J* =1.5 Hz, 3H), 2.43 (dd, *J* =14.2, 17.1 Hz, 1H), 2.51 (apparently quintet, *J* =6.4 Hz, 1H), 2.63-2.69 (m, 2H), 3.63 (t, *J* =6.8 Hz, 2H), 4.43 (d, *J* =10.8 Hz, 1H), 4.62 (t, *J* =3.7 Hz, 1H), 5.87 (d, *J* =3.7 Hz, 1H), 7.36-7.43, 7.62-7.67 (2 m, 6H, 4H). Anal. Calcd for $C_{30}H_{38}O_5Si$: C, 71.11; H, 7.56. Found: C, 71.30; H, 7.82.

From 12. The following reaction was carried out under Ar. To a cold (0 °C) stirred solution of **12** (76.9 mg, 0.16 mmol) in THF (2.0 mL) was added dropwise MeMgBr (2.0 M solution in THF, 0.24 mL, 0.48 mmol). The mixture was stirred at rt for 2 h and quenched with 10% aq NH_4Cl (3 mL). It was diluted with H_2O (12 mL), then it was extracted with CH_2Cl_2 (30 mL x 3). The combined extracts were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by column chromatography on silica gel followed by preparative TLC (EtOAc/hexane, 1:7), giving two diastereomers of **16**. The less polar compound having R_f 0.38 (EtOAc/hexane, 1:4) (56.0 mg, 70.5%) as a colorless oil: ^1H NMR (90 MHz) δ 1.04 (s, 9H), 1.22 (s, 3H), 1.32, 1.47 (2 s, 3H x 2), 1.55-2.7 (m, 5H), 3.20 (s, 1H), 3.6-3.8 (m, 2H), 3.92 (d, *J* =12 Hz, 1H), 4.58 (t, *J* =4 Hz, 1H), 5.39 (t, *J* =5 Hz, 1H), 5.87 (d, *J* =4 Hz, 1H), 7.3-7.45, 7.55-7.8 (2 m, 6H, 4H). The polar compound having R_f 0.25 (EtOAc/hexane, 1:4) (18.3 mg, 23%) as a colorless oil: ^1H NMR (90 MHz) δ 1.04 (s, 9H), 1.28 (s, 3H), 1.34, 1.48 (2 s, 3H x 2), 2.1-2.6 (m, 5H), 2.80 (s, 1H), 3.55-3.8 (m, 2H), 3.82 (dd, *J* =1, 10 Hz, 1H), 4.62 (t, *J* =4 Hz, 1H), 5.52 (t, *J* =5 Hz, 1H), 5.91 (d, *J* =4 Hz, 1H), 7.3-7.45, 7.6-7.75 (2 m, 6H, 4H).

To a stirred solution of **16** having R_f 0.38 (54.0 mg, 0.11 mmol) in CH_2Cl_2 (1 mL) were added PCC (91.5 mg, 0.43 mmol) and powdered molecular sieve 4A (153 mg). The mixture was stirred for 7.5 h, and the whole was passed though a short column of silica gel (2 g). The column was eluted with excess Et_2O, and the eluate was concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:5) to provide **15** (28.7 mg, 53%).

Analogously, **16** having R_f 0.25 (18.3 mg) was converted to **15** (5.1 mg, 28%).

Diastereomeric Mixture of 3-Deoxy-3-*C*-(2-hydroxypent-4-enyl)-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (17). According to the reported procedure ($LiAlH_4$-THF),[8] compound **5** [3.08 g, (9.3 mmol)] was converted to the primary alcohol quantitatively (2.82 g). To a stirred suspension of PCC (4.02 g, 18.6 mmol) and powdered molecular sieve 4A (2.36 g) in CH_2Cl_2 (40 mL) was added dropwise a solution of thus obtained primary alcohol derivative (2.82 g) in CH_2Cl_2 (20 mL). The mixture was stirred for 45 min, and concentrated in vacuo. The residue was passed through a short column of silica gel. The column was eluted with excess Et_2O. The eluate was concentrated in vacuo to provide an aldehyde derivative (1.79 g, 67% from **5**): ^{1}H NMR (270 MHz) δ 1.29, 1.33, 1.42, 1.49 (4 s, 3H x 4), 2.37 (tt, J =9.3, 4.4 Hz, 1H), 2.86 (dd, J =19.0, 9.3 Hz, 1H), 2.99 (dd, J =19.0, 4.4 Hz, 1H), 3.67-4.15 (m, 4H), 4.82 (t, J =4.4 Hz, 1H), 5.79 (d, J =4.4 Hz, 1H), 9.81 (s, 1H).

The following reaction was carried out under Ar. To a cold (0 °C) stirred solution of thus obtained aldehyde (1.79 g, 6.25 mmol) in THF (30 mL) was added dropwise allylmagnesium chloride (2.0 M solution in THF, 9.4 mL, 19.0 mmol). The mixture was stirred at rt for 45 min, then it was quenched with saturated aq NH_4Cl (5 mL) and diluted with CH_2Cl_2 (150 mL). The whole was washed with 0.2 M aqueous HCl (150 mL). The aqueous phase was extracted with CH_2Cl_2 (50 mL x 2). The combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:3), giving the diastereomeric mixture of **17** (1.78 g, 87%) as a colorless oil: ^{1}H NMR (270 MHz) δ 1.32, 1.32, 1.41, 1.51 (4 s, each 5/11 x 3H), 1.35, 1.35, 1.42, 1.51 (4 s, each 6/11 x 3H), 1.71-2.06 (m, 3H), 2.14-2.39 (m, 3H), 3.73-4.13 (m, 5H), 4.71 (t, J =4.0 Hz, 6/11 x 1H), 4.75 (t, J =4.0 Hz, 5/11 x 1H), 5.11-5.20 (m, 2H), 5.76 (d, J =4.0 Hz, 6/11 x 1H), 5.77 (d, J =4.0 Hz, 5/11 x 1H), 5.81-5.94 (m, 1H).

Diastereomeric Mixture of 3-Deoxy-3-*C*-[2-hydroxy-5-[(*tert*-butyldiphenylsilyl)oxy]pentyl]-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (18). The following reaction was carried out under Ar. To a cold (0 °C) stirred solution of the mixture of **17** (1.78 g, 5.42 mmol) in THF (30 mL) was added dropwise BH_3•THF (1.0 M solution in THF, 19.0 mL, 19.0 mmol). The mixture was stirred at 0 °C for 3 h, then H_2O (20 mL), 3M aq NaOH (20 mL) and 35% aq H_2O_2 (20 mL) were added, successively. The mixture was stirred for 30 min then saturated aq Na_2SO_3 (30 mL) was added. The mixture was stirred for 30 min, then it was diluted with H_2O (100 mL). The whole was extracted with CH_2Cl_2 (100 mL x 3). The combined extracts were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by column chromatography on silica gel (acetone/toluene, 1:2) to provide a diastereomeric mixture of the diol derivative (1.95 g), which was used without separation, as a colorless oil: ^{1}H NMR (270 MHz) δ 1.32, 1.33, 1.42, 1.51 (4 s, each 5/11 x 3H), 1.35, 1.35, 1.42, 1.51 (4 s, each 6/11 x 3H), 1.54-2.23 (m, 7H), 2.63-2.94 (br, 2H), 3.61-3.83, 3.92-4.16 (m, 7H), 4.72 (t, J =3.9 Hz, 6/11 x 1H), 4.75 (t, J =3.9 Hz, 5/11 x 1H), 5.76 (d, J =3.9 Hz, 6/11 x 1H), 5.77 (d, J =3.9 Hz, 5/11 x 1H).

To a stirred solution of the diol (1.95 g) in DMF (40 mL) were added imidazole (817 mg, 12.0 mmol) and *tert*-butylchlorodiphenylsilane (1.55 mL, 6.0 mmol). The mixture was stirred for 3 h then diluted with EtOAc (250 mL). The whole was washed with H_2O (100 mL x 3). The organic phase was drawn off and dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:3), giving a diastereomeric mixture of **18** (2.79 g, 88% from **17**) as a colorless oil. In a small scale experiment, the diastereomers (nearly 6:5 ratio) were separated by repeated column chromatography on silica gel. The less polar compound having R_f 0.75 (EtOH/toluene, 1:6): $[\alpha]_D^{24.5}$ +21.9° (*c* 1.24, $CHCl_3$); IR 3500, 3070, 2990, 2930, 2850, 1585, 1470, 1455, 1450, 1425, 1375, 1365, 1300, 1240 cm^{-1}; ^1H NMR (90 MHz) δ 1.03 (s, 9H), 1.30, 1.39, 1.48 (3 s, 6H, 3H, 3H), 1.5-2.3 (m, 7H), 2.3-2.6 (br, 1H), 3,5-4.1 (m, 7H), 4.66 (t, *J* =4 Hz, 1H), 5.71 (d, *J* =4 Hz, 1H), 7.3-7.55, 7.6-7.75 (2 m, total 10H). HRMS; Calcd for $C_{32}H_{45}O_7Si$ (M^+-CH_3): *m/z* 569.2931. Found: *m/z* 569.2929. The polar compound R_f 0.70 (EtOH/toluene, 1:6): $[\alpha]_D^{22.5}$ +31.4° (*c* 0.92, $CHCl_3$); IR 3470, 3080, 2990, 2940, 2860, 1590, 1475, 1465, 1455, 1430, 1380, 1375, 1310, 1240 cm^{-1}; ^1H NMR (90 MHz) δ 1.07 (s, 9H), 1.32, 1.33, 1.42, 1.50 (4 s, 3H x 4), 1.5-2.4 (m, 7H), 2.3-2.6 (br, 1H), 3.6-4.2 (m, 7H), 4.69 (t, *J* =4 Hz, 1H), 5.73 (d, *J* =4 Hz, 1H), 7.3-7.5, 7.6-7.75 (2 m, total 10H). HRMS; Calcd for $C_{32}H_{45}O_7Si$ (M^+-CH_3): *m/z* 569.2932. Found: *m/z* 569.2935.

3-Deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-[2-oxo-5-[(*tert*-butyldiphenylsilyl)oxy]pentyl]-α-D-allofuranose (19). To a stirred suspension of PCC (634 mg, 2.9 mmol) and powdered molecular sieve 4A (370 mg) in CH_2Cl_2 (10 mL) was added a solution of the mixture of **18** (841 mg, 1.44 mmol) in CH_2Cl_2 (5 mL). The mixture was stirred for 1 h and the solvent was removed by concentration in vacuo. The residue was passed through a short column of silica gel. The column was eluted with excess Et_2O. The eluate was concentrated in vacuo to provide **19** (824.5 mg, 98%) as a pale yellow oil. Analytical sample was obtained by purification on preparative TLC (EtOAc/hexane, 1:3): TLC R_f 0.71 (EtOAc/hexane, 1:2); $[\alpha]_D^{23}$ +46.6° (*c* 0.69, $CHCl_3$); IR 3070, 2990, 2950, 2860, 1720, 1590, 1475, 1460, 1430, 1410, 1380, 1330, 1305, 1250 cm^{-1}; ^1H NMR (270 MHz) δ 1.05 (s, 9H), 1.27, 1.31, 1.41, 1.48 (4 s, 3H x 4), 1.85 (quint., *J* =7.0 Hz, 2H), 2.31-2.42 (m, 1H), 2.57 (t, *J* =7.0 Hz, 2H), 2.78 (dd, *J* =18.1, 8.6 Hz, 1H), 2.87 (dd, *J* =18.1, 4.9 Hz, 1H), 3.65-3.71, 3.90-3.98, 4.05-4.11 (3 m, total 6H), 4.76 (t, *J* =4.0 Hz, 1H), 5.76 (d, *J* =4.0 Hz, 1H), 7.34-7.43, 7.64-7.68 (2 m, total 10H). Anal. Calcd for $C_{33}H_{46}O_7Si$: C, 68.01; H, 7.96. Found: C, 68.08; H, 7.90.

3-Deoxy-1,2-*O*-isopropylidene-3-*C*-[[2-oxo-5-(*tert*-butyldiphenylsilyl)oxy]pentyl]-α-D-1,4-dialdo-ribofuranose (20). Compound **19** (811 mg, 1.39 mmol) was dissolved in a mixture of AcOH:H_2O:THF (v/v, 6:1:1, 20 mL), and it was stirred for 15 h. Then the solvents were removed by concentration in vacuo. The residue was purified by column chromatography on silica gel (acetone/toluene, 1:7), giving the 5,6-diol (425.5 mg, 56%) and the de-*O*-silylated product existing as a hemiketal form (34 mg, 8%). Compound **19** was also recovered (200.5 mg, 25%), which was hydrolyzed repeatedly. Total 511 mg (68%) of the 5,6-diol, 41 mg (10%) of the de-*O*-silylated product were obtained after one-recycle. 22 mg (3%) of **19** was recovered. The 5,6-diol: TLC R_f 0.37 (acetone/toluene, 1:3); $[\alpha]_D^{20}$ +68.4° (*c* 0.51, $CHCl_3$); IR 3440, 3080, 2970, 2940, 2860, 1715, 1590, 1475, 1460, 1430, 1410, 1380, 1370, 1330, 1310, 1250 cm^{-1}; ^1H NMR (270 MHz) δ 1.05 (s, 9H), 1.27, 1.48 (2 s, 3H x 2), 1.84 (quint., *J* =7.0 Hz, 2H), 2.13-2.17 (m, 1H), 2.35-2.48 (m, 1H), 2.57 (t, *J* =7.0 Hz, 2H), 2.63-2.65 (m, 1H), 2.78 (dd, *J* =18.7, 5.0 Hz, 1H), 2.88 (dd, *J* =18.7, 8.4 Hz, 1H), 3.61-3.85 (m, 6H), 4.73 (t, *J* =4.2 Hz, 1H), 5.77 (d, *J* =4.2 Hz, 1H), 7.34-7.43, 7.63-7.66 (2 m, total 10H). De-*O*-silylated product as a single diastereomer on the hemiketal carbon, of which stereochemistry

was not determined: TLC R_f 0.44 (acetone/toluene, 1:3); IR 3480, 2990, 2960, 2940, 1460, 1440, 1380, 1370, 1340, 1300, 1260 cm^{-1}; ^1H NMR (270 MHz) δ 1.33, 1.52 (2 s, 3H x 2), 1.71-2.16 (m, 8H), 3.50-3.94 (m, 6H), 4.62 (t, *J* =3.5 Hz, 1H), 5.84 (d, *J* =3.5 Hz, 1H).

To a stirred solution of the 5,6-diol (497 mg, 0.92 mmol) in MeOH (7 mL) was added dropwise aq $NaIO_4$ (312 mg, 1.46 mmol in H_2O 3 mL). The mixture was stirred for 1 h, and the white precipitates that formed were removed by filtration and washed well with MeOH. The combined filtrate and washings were concentrated in vacuo. The residue was partitioned between CH_2Cl_2 (40 mL) and H_2O (40 mL). The aqueous phase was extracted with CH_2Cl_2 (40 mL x 2). The combined organic phases were dried (Na_2SO_4) and concentrated in vacuo to provide a crude **20** (498 mg), which included the aldol condensation product in some contents. This mixture was used directly.

(1*R*,3*S*,8*R*,9*R*)-11,11-Dimethyl-5-[2-(*tert*-butyldiphenylsilyloxy)ethyl]-2,10,12-trioxatricyclo[7.3.0.0^{3,8}]dodec-4-en-6-one (21). A solution of the crude **20** (498 mg) in benzene (20 mL) was refluxed for 15 h in the presence of DBU (34 μL, 0.23 mmol). The mixture was concentrated in vacuo. The residue was dissolved in pyridine (5 mL) and acetic anhydride (5 mL) was added. It was stirred for 6 h and concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:8), giving **21** (346 mg, 77% from the 5,6-diol for 3 steps) as a colorless oil: TLC R_f 0.73 (EtOAc/hexane, 1:2); $[\alpha]_D^{24.5}$ -24.1° (*c* 1.25, $CHCl_3$); IR 3070, 2960, 2930, 2860, 1675, 1585, 1470, 1460, 1420, 1380, 1355, 1340, 1295 cm^{-1}; ^1H NMR (270 MHz) δ 1.03 (s, 9H), 1.35, 1.54 (2 s, 3H x 2), 1.97 (dddd, *J* =13.9, 10.1, 4.0, 3.7 Hz, 1H), 2.44 (t, *J* =6.2 Hz, 2H), 2.46 (dd, *J* =17.0, 13.9 Hz, 1H), 2.70 (dd, *J* =17.0, 4.0 Hz, 1H), 3.70 (dt, *J*=10.3, 6.2 Hz, 1H), 3.74 (dt, *J* =10.3, 6.2 Hz, 1H), 4.53 (d, *J* =10.1 Hz, 1H), 4.63 (t, *J* =3.7 Hz, 1H), 5.91 (d, *J* =3.7 Hz, 1H), 7.07 (s, 1H), 7.33-7.44, 7.60-7.64 (2 m, total 10H). HRMS; Calcd for $C_{29}H_{36}O_5Si$ (M^+): *m/z* 492.2329. Found: *m/z* 492.2310.

Mixture of (1*R*,3*R*,4*R*,5*S*,8*R*,9*R*)- (22S) and (1*R*,3*R*,4*R*,5*R*,8*R*,9*R*)- (22R) 4,11,11-Trimethyl-5-[2-(*tert*-butyldiphenylsilyl)oxyethyl]-2,10,12-trioxatricyclo[7.3.0.0^{3,8}]dodecan-6-one (22S and 22R). The following reaction was carried out under Ar. To a cold (0 °C) stirred suspension of CuI (dried in vacuo, 28.2 mg, 0.15 mmol) in THF (0.5 mL) was added MeLi (1.12 M solution in Et_2O, 0.26 mL, 0.29 mmol). The mixture was stirred for 5 min at 0 °C, then a solution of **21** (35.9 mg, 0.073 mmol) in THF (0.5 mL) was added. The whole was stirred for 30 min at 0 °C then quenched by adding saturated aq NH_4Cl (3 drops). It was diluted with CH_2Cl_2 (15 mL), and the whole was washed with H_2O (15 mL). The aqueous phase was extracted with CH_2Cl_2 (5 mL x 3). The combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:10), giving an inseparable mixture of **22S** and **22R** (29.2 mg, 79%) as a colorless oil. The ratio of **22S** and **22R** was estimated to be nearly 1:2 based on its ^1H NMR analysis. For the mixture of **22S** and **22R**: IR 2960, 2940, 2860, 1710, 1590, 1470, 1460, 1430, 1380, 1370, 1210 cm^{-1}; ^1H NMR (270 MHz) δ 0.72 (d, *J*=7.0 Hz, 1/3 x 3H), 0.98 (d, *J* =7.0 Hz, 2/3 x 3H), 1.04 (s, 9H), 1.34, 1.54 (2 s, each 2/3 x 3H), 1.35, 1.59 (2 s, each 1/3 x 3H), 1.35-2.16 (m, 3H), 2.32-2.72 (m, 4H), 3.58-3.76 (m, 2H), 4.23 (dd, *J* =11.4, 5.1 Hz, 2/3 x 1H), 4.24 (dd, *J* =11.4, 4.4 Hz, 1/3 x 1H), 4.55 (t, *J* =3.6 Hz, 1/3 x 1H), 4.56 (t, *J*=3.6 Hz, 2/3 x 1H), 5.88 (d, *J* =3.6 Hz, 1/3 x 1H), 5.89 (d, *J* =3.6 Hz, 2/3 x 1H), 7.34-7.43, 7.62-7.66 (2 m, 10H). Anal. Calcd for $C_{30}H_{40}O_5Si$: C, 70.83; H, 7.93. Found: C, 70.60; H, 7.76.

Epimerization of the Mixture of 22S and 22R. A solution of the mixture of **22S** and **22R** (29.2 mg, 0.057 mmol) in MeOH (1 mL) was stirred for 7 h in the presence of MeONa (1.0 M in MeOH, 25 μL, 0.025 mmol). The mixture was neutralized by adding Amberlite IR-120 (H^+). The resin was removed by filtration, washed well with MeOH. The combined filtrate and washings were concentrated in vacuo. The residue was purified by column chromatography on silica gel, giving a nealy 5:1 mixture of **22S** and **22R** (270 MHz ^1H NMR analysis) (27.9 mg, 96%). When the mixture was further treated with MeONa, the ratio of **22S** and **22R** did not change.

Diastereomeric Mixture of 3-Deoxy-3-*C*-[2-hydroxy-5-[(*tert*-butyldiphenylsilyl)oxy]pentyl]-1,2-O-isopropylidene-α-D-allofuranose (23). Compound **18** (1.05 g, 1.80 mmol) was dissolved in a mixture of AcOH:H_2O:THF (v/v, 6:1:1, 20 mL). The solution was stirred for 15 h, and the solvents were removed by concentration in vacuo. The residue was purified by column chromatography on silica gel (acetone/toluene, 1:3), giving a diastereomeric mixture of **23** (628.5 mg, 64%) as a colorless oil. Compound **18** (211 mg, 20%) was recovered, and was hydrolyzed again. After one-recycle, total 752 mg (77%) of **23** was obtained. **23**: TLC R_f 0.50 (EtOH/toluene, 1:5); IR 3400, 2940, 2860, 1590, 1470, 1430, 1380, 1370, 1220 cm^{-1}; ^1H NMR (270 MHz) δ 1.06 (s, 9H), 1.32, 1.51 (2 s, 3H x 2), 1.51-2.43 (m, 8H), 3.37-3.96 (m, 9H), 4.66 (t, J =4.2 Hz, 1H), 5.76 (d, J =4.2 Hz, 1H), 7.34-7.44, 7.65-7.68 (2 m, 10H).

3,6-Dideoxy-1,2-*O*-isopropylidene-3-*C*-[2-oxo-5-[(*tert*-butyldiphenylsilyl)oxy]pentyl]-α-D-allofuran-5-ulose (24). To a stirred solution of the mixture of **23** (738 mg, 1.35 mmol) in MeOH (10 mL) was added dropwise aq $NaIO_4$ (445.5 mg, 2.08 mmol in H_2O 4 mL). The mixture was stirred for 1 h and the white precipitates that formed were removed by filtration and washed well with MeOH. The combined filtrate and washings were concentrated in vacuo. The residue was partioned between CH_2Cl_2 (40 mL) and H_2O (40 mL). The aqueous phase was extracted with CH_2Cl_2 (10 mL x 3). The combined organic phases were dried (Na_2SO_4) and concentrated in vacuo to provide a crude 5-aldehyde (681 mg), which was used directly, as a colorless oil: TLC, Rf 0.65 (EtOH/toluene, 1:5); IR 3420, 2930, 2850, 1730, 1580, 1470, 1420, 1380, 1370, 1210 cm^{-1}; ^1H NMR (270 MHz) δ 1.04 (s, 9H), 1.33, 1.52 (2 s, 3H x 2), 1.40-2.36 (m, 7H), 2.53-3.00 (m, 1H), 3.40-4.14 (m, 4H), 4.56-5.49 (m, 2H), 5.76-5.93 (m, 1H), 7.34-7.42, 7.65-7.67 (2 m, total 10H).

The following reaction was carried out under Ar. To a stirred and refluxing solution of the 5-aldehyde (681 mg) in THF (10 mL) was added dropwise MeMgBr (0.95 M solution in THF, 11.0 mL, 10.0 mmol). The mixture was refluxed for 30 min, then quenched by adding saturated aq NH_4Cl (1 mL). It was diluted with CH_2Cl_2 (40 mL) and the whole was washed with 1M aq HCl (40 mL). The aqueous phase was extracted with CH_2Cl_2 (15 mL x 3). The combined organic phases were dried (Na_2SO_4) and concentrated in vacuo to provide crude methyl alcohol as a distereomeric mixture (731 mg), which was used directly, as a colorless oil: IR 3380, 2940, 2860, 1590, 1470, 1430, 1380, 1370, 1220 cm^{-1}; ^1H NMR (270 MHz) δ 1.05 (s, 9H), 1.32, 1.51 (2 s, 3H x 2), 1.21-1.34 (m, 3H), 1.51-2.39 (m, 7H), 2.78 (br, 1H), 3.67-3.96 (m, 6H), 4.67-4.74 (m, 1H), 5.77 (d, J =3.7 Hz, 1/2 x 1H), 5.79 (d, J =3.7 Hz, 1/2 x 1H), 7.36-7.47, 7.65-7.68 (2 m, total 10H).

To a stirred suspension of PCC (1.16 g, 5.38 mmol) and powdered molecular sieve 4A (0.75 g) in CH_2Cl_2 (10 mL) was added dropwise a solution of the methyl alcohol (731 mg) in CH_2Cl_2 (5 mL). The mixture was stirred for 4 h, then the whole was passed through a short column of silica gel. The column was eluted with excess Et_2O. The eluate was concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:8), giving **24** (558 mg, 78.5% from **23**) as a colorless oil: TLC R_f 0.52

(EtOAc/hexane, 1:4); $[\alpha]_D^{23}$ +20.3° (*c* 1.03, $CHCl_3$); IR 2960, 2940, 2900, 2860, 1720, 1580, 1470, 1420, 1380, 1370, 1230 cm^{-1}; ^1H NMR (270 MHz) δ 1.04 (s, 9H), 1.29, 1.47 (2 s, 3H x 2), 1.83 (quint., *J* =6.7 Hz, 2H), 2.23 (s, 3H), 2.35-2.46 (m, 1H), 2.55 (t, *J* =6.7 Hz, 2H), 2.71 (dd, *J* =18.3, 4.0 Hz, 1H), 2.86 (dd, *J* =18.3, 9.7 Hz, 1H), 3.66 (t, *J* =6.7 Hz, 2H), 4.05 (d, *J* =11.0 Hz, 1H), 4.79 (t, *J* =3.8 Hz, 1H), 5.93 (d, *J* =3.8 Hz, 1H), 7.34-7.45, 7.63-7.67 (2 m, total 10H). Anal. Calcd for $C_{30}H_{40}O_6Si$: C, 68.67; H, 7.68. Found: C, 68.70; H, 7.72.

(1*R*,3*S*,8*R*,9*R*)- (25S) and (1*R*,3*R*,8*R*,9*R*)- (25R) 11,11-Dimethyl-6-[3-(*tert*-butyldiphenylsilyloxy)propyl]-2,10,12-trioxatricyclo[7.3.0.0^{3,8}]dodec-5-en-4-one. Compound **24** (104 mg, 0.20 mmol) was dissolved in benzene (8 mL), and the solution was refluxed for 2 h in the presence of potassium *tert*-butoxide (37 mg, 0.33 mmol). It was diluted with AcOEt (20 mL), and the whole was washed with 1M aq HCl (10 mL), saturated aq $NaHCO_3$ (10 mL), and saturated brine (10 mL), successively. The organic phase was dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:8, 1:3, then 1:1), giving **25S** (17 mg, 17%), **25R** (13 mg, 13%), and an inseparable mixture of unidentified products (11 mg). **25S** as a colorless oil: TLC R_f 0.55 (EtOAc/hexane, 1:1); $[\alpha]_D^{22}$ -57.3° (*c* 1.22, $CHCl_3$); IR 2950, 2930, 2850, 1700, 1610, 1580, 1470, 1380, 1370, 1210 cm^{-1}; ^1H NMR (270 MHz) δ 1.05 (s, 9H), 1.36, 1.53 (2 s, 3H x 2), 1.70-1.80 (m, 2H), 2.12-2.24 (m, 1H), 2.33-2.39 (m, 2H), 2.47 (dd, *J* =18.0, 4.4 Hz, 1H), 2.65 (ddd, *J* =18.0, 11.4, 2.2 Hz, 1H), 3.65 (td, *J* =6.0, 10.3 Hz, 1H), 3.74 (dt, *J* =6.0, 10.3 Hz, 1H), 4.39 (d, *J* =12.4 Hz, 1H), 4.66 (t, *J* =3.5 Hz, 1H), 5.82 (br s, 1H), 5.91 (d, *J* =3.5 Hz, 1H), 7.35-7.43, 7.63-7.66 (2 m, total 10H). HRMS; Calcd for $C_{26}H_{29}O_5Si$ [M^+-$C(CH_3)_3$]: *m/z* 449.1783. Found: *m/z* 449.1783. **25R** as a colorless oil: TLC R_f 0.12 (EtOAc/hexane, 1:1); $[\alpha]_D^{20}$ -3.9 ° (*c* 0.78, $CHCl_3$); IR 2960, 2940, 2860, 1680, 1640, 1590, 1470, 1430, 1380, 1370, 1260 cm^{-1}; ^1H NMR (270 MHz) δ 1.05 (s, 9H), 1.20, 1.24 (2 s, 3H x 2), 1.76 (quint., *J* =6.7 Hz, 2H), 2.28-2.36 (m, 2H), 2.65-2.66 (m, 2H), 2.77-2.82 (m, 1H), 3.69 (t, *J* =6.7 Hz, 2H), 4.39 (d, *J* =8.8 Hz, 1H), 4.60 (t, *J* =4.2 Hz, 1H), 5.83 (d, *J* =4.2 Hz, 1H), 5.92 (br s, 1H), 7.35-7.43, 7.63-7.67 (2 m, total 10H). HRMS; Calcd for $C_{26}H_{29}O_5Si$ [M^+-$C(CH_3)_3$]: *m/z* 449.1782. Found: *m/z* 449.1772.

Cyclization of 24 by using potassium *tert*-butoxide in THF. Formation of 15 *via* 14. Compound **24** (33.5 mg, 64 μmol) was dissolved in THF (3 mL) and the solution was stirred at 0 °C for 30 min in the presence of potassium *tert*-butoxide (4.5 mg, 40 μmol). Then the mixture was quenched by adding saturated aq NH_4Cl (3 drops). It was diluted with CH_2Cl_2 (15 mL) and washed with 1M aq HCl (15 mL). The aqueous phase was extracted with CH_2Cl_2 (5 mL x 3). The combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:8, 1:3, then 1:2), giving **14** (10 mg, 31%), an inseparable unidentified mixture (10 mg), and recovered **24** (4 mg).

To a stirred solution of **14** (10 mg) in pyridine (1 mL) were added $MeSO_2Cl$ (10 μL) and 4-dimethylaminopyridine (1.3 mg). The mixture was stirred for 15 h at 70 °C, then diluted with EtOAc (20 mL). It was washed with 1 M aq HCl (10 mL), saturated aq $NaHCO_3$ (10 mL), and saturated brine (10 mL), successively. The organic phase was dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by column chromatgraphy on silica gel to provide **15** (8 mg, 80%).

(1*R*,3*R*,4*S*,5*S*,6*S*,8*R*,9*R*)-6-Hydroxy-4,11,11-trimethyl-5-[2-(*tert*-butyldiphenylsilyloxy)ethyl]-2,10,12-trioxatricyclo[7.3.0.0^{3,8}]dodecane (26) and the 5*R* Diastereomer (27).

Compound **15** (2.16 g, 4.27 mmol) was dissolved in EtOH (5 mL) and it was hydrogenated for 32 h in the presence of Raney Ni T-4 using a Parr apparatus under 55 psi initial hydrogen pressure. The catalyst was removed by filtration through a pad of Celite and washed well with EtOH. The combined filtrate and washings were concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:7 then 1:4), giving **26** (1.29 g, 59%) and **27** (0.556 g, 25.5%). **26** as a colorless oil: TLC R_f 0.32 (EtOAc/hexane, 1:3); $[\alpha]_D^{28}$ +9.7° (*c* 0.94, $CHCl_3$); IR 3430, 2970, 2940, 2890, 2860, 1590, 1470, 1425, 1380, 1370, 1240 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.98 (d, *J* =5.9 Hz, 3H), 1.06 (s, 9H), 1.33, 1.53 (2 s, 3H x 2), 1.33-1.53 (m, 4H), 1.67-1.75 (m, 1H), 1.89-1.94 (m, 1H), 2.15-2.20 (m, 1H), 3.30 (t, *J* =10.3 Hz, 1H), 3.49-3.55 (m, 1H), 3.63 (td, *J* =9.6, 3.7 Hz, 1H), 3.75-3.82 (m, 2H), 4.57 (t, *J* =3.7 Hz, 1H), 5.81 (d, *J* =3.7 Hz, 1H), 7.40-7.44, 7.66-7.69 (2 m, 6H, 4H). Anal. Calcd for $C_{30}H_{42}O_5Si$: C, 70.55; H, 8.29. Found: C, 70.35; H, 8.23. **27** as a colorless oil: TLC R_f 0.22 (EtOAc/hexane, 1:3); $[\alpha]_D^{28}$ -6.3° (*c* 1.34, $CHCl_3$); IR 3430, 2970, 2940, 2890, 2860, 1585, 1470, 1425, 1380, 1370, 1260 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.00 (d, *J* =6.8 Hz, 3H), 1.06 (s, 9H), 1.32, 1.51 (2 s, 3H x 2), 1.25-1.44 (m, 4H), 1.51-1.68 (m, 1H), 1.73-1.86 (m, 2H), 1.96-2.04 (m, 1H), 2.05-2.13 (m, 1H), 3.36 (t, *J* =10.7 Hz, 1H), 3.47 (td, *J* =10.0, 3.4 Hz, 1H), 3.74-3.89 (m, 3H), 4.55 (t, *J* =3.7 Hz, 1H), 5.80 (d, *J* =3.7 Hz, 1H), 7.38-7.45, 7.66-7.69 (2 m, 6H, 4H). Anal. Calcd for $C_{30}H_{42}O_5Si$: C, 70.55; H, 8.29. Found: C, 70.13; H, 8.02.

The 6-Acetates (28) and (29) of 26 and 27. Compound **26** (3.5 mg) was treated with acetic anhydride (0.2 mL) in pyridine (0.4 mL) for 2.5 h. The reagents were removed by concentration in vacuo, and the residue was purified by preparative TLC (EtOAc/hexane, 1:2), giving **28** (3.6 mg, 95%) as a colorless oil: TLC R_f 0.67 (EtOAc/hexane, 1:2); IR 2960, 2940, 2880, 2860, 1735, 1590, 1470, 1455, 1425, 1380, 1370, 1240 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.02 (d, *J* =6.4 Hz, 3H), 1.04 (s, 9H), 1.30, 1.50 (2 s, 3H x 2), 1.30-1.50, 1.62-1.69, 1.77-1.86 (3 m, 4H, 1H, 1H), 1.89 (s, 3H), 2.20 (dd, *J* =4.8, 8.8 Hz, 1H), 3.26 (t, *J* =10.0 Hz, 1H), 3.60-3.71 (m, 2H), 4.52 (t, *J* =3.8 Hz, 1H), 4.63 (td, *J* =10.3, 4.8 Hz, 1H), 5.81 (d, *J* =3.8 Hz, 1H), 7.35-7.42, 7.64-7.66 (2 m, 6H, 4H).

Analogously as described for **26**, **27** (2.3 mg) was acetylated to give **29** (1.9 mg, 76%) as a colorless oil: TLC R_f 0.63 (EtOAc/hexane, 1:2); IR 2970, 2940, 2890, 2860, 1740, 1590, 1475, 1425, 1380, 1240 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.03 (d, *J* =6.4 Hz, 3H), 1.04 (s, 9H), 1.32, 1.52 (2 s, 3H x 2), 1.17-1.58, (m, 2H), 1.32-1.43 (m, 1H), 1.66-1.85 (m, 2H), 1.78 (s, 3H), 1.92 (dt, *J* =12.7, 3.7 Hz, 1H), 2.00-2.04 (m, 1H), 3.40 (t, *J* =10.0 Hz, 1H), 3.52 (dt, *J* =9.8, 7.7 Hz, 1H), 3.65-3.71 (m, 1H), 4.53 (t, *J* =3.8 Hz, 1H), 4.89 (dt, *J* =11.7, 4.8 Hz, 1H), 5.81 (d, *J* =3.8 Hz, 1H), 7.36-7.42, 7.64-7.68 (2 m, 6H, 4H).

Conversion of 27 to 26 *via* PCC-oxidation, epimerization followed by $NaBH_4$-reduction.

To a stirred solution of **27** (714 mg, 1.40 mmol) in CH_2Cl_2 (10 mL) were added PCC (1.062 g, 4.93 mmol) and powdered molecular sieve 4A (1.23 g). The mixture was stirred for 4 h, then Et_2O (5 mL) was added. The insoluble materials were removed by passing through a short silica gel column (10 g). The column was eluted with excess Et_2O and the eluate was concentrated in vacuo, giving **30** (688 mg) as a colorless oil: TLC R_f 0.49 (EtOAc/hexane, 1:4); IR 2970, 2940, 2890, 2860, 1715, 1590, 1470, 1425, 1380, 1370, 1300, 1260 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.04 (s, 9H), 1.06 (d, *J* =6.3 Hz, 3H), 1.34, 1.55 (2 s, 3H x 2), 1.62-1.88 (m, 3H), 2.11 (dt, *J* =10.9, 6.6 Hz, 1H), 2.36 (ddd, *J* =14.3, 4.3, 1.1 Hz, 1H), 2.53-2.58 (m, 1H), 2.66 (t, *J* =14.2 Hz,

1H), 3.59 (t, J =6.6 Hz, 2H), 3.79 (t, J =10.0 Hz, 1H), 4.55 (t, J =3.7 Hz, 1H), 5.88 (d, J =3.7 Hz, 1H), 7.36-7.42, 7.63-7.66 (2 m, 6H, 4H).

Compound **30** (688 mg) was dissolved in MeOH (14 mL), and it was stirred in the presence of MeONa (1 M solution in MeOH, 0.27 mL) for 21 h. The solution was neutralized by adding Amberlite-120 (H^+). The resin was removed. The filtrate and washings (MeOH) were combined and concentrated in vacuo, giving **31** (698 mg) as a colorless oil, which was contaminated by a trace amount of **30** (400 MHz ^{1}H NMR analysis). **31**: TLC R_f 0.51 (EtOAc/hexane, 1:4); IR 2970, 2940, 2890, 2860, 1710, 1590, 1460, 1425, 1380, 1370, 1300, 1260 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.04 (s, 9H), 1.15 (d, J =6.3 Hz, 3H), 1.34, 1.58 (2 s, 3H x 2), 1.61-1.71, 1.77-1.85, 1.89-1.98, 1.96-2.04 (4 m, 1H x 4), 2.44 (t, J =14.0 Hz, 1H), 2.50 (dd, J =14.0, 4.9 Hz, 1H), 3.61-3.67 (m, 1H), 3.67 (t, J =10.5 Hz, 1H), 3.74-3.80 (m, 1H), 4.54 (t, J =3.7 Hz, 1H), 5.87 (d, J =3.7 Hz, 1H), 7.35-7.44, 7.62-7.65 (2 m, 6H, 4H).

To a stirred solution of **31** (698 mg) in MeOH (14 mL) was added $NaBH_4$ (27.0 mg, 0.72 mmol) portionwise. The mixture was stirred for 40 min and neutralized by adding Amberlite-120 (H^+). After removal of the resin by filtration, the filtrate and washings were combined and concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:6 then 1/4) to provide **26** (578 mg, 81% from **27**). The starting compound **27** was recovered (30.6 mg, 4%).

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