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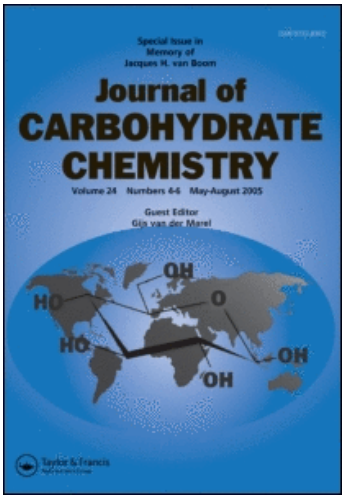

Journal of Carbohydrate Chemistry

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Kin-ichi Tadano[a]; Yoshiaki Isshiki[a]; Toshihito Kumagai[a]; Seiichiro Ogawa[a]
[a] Department of Applied Chemistry, Faculty of Science and Technology, Keio University, Yokohama, Japan

To cite this Article Tadano, Kin-ichi , Isshiki, Yoshiaki , Kumagai, Toshihito and Ogawa, Seiichiro(1993) 'Off-Template Claisen Rearrangement of a D-Glucose-Derived Bicyclic Substrate', Journal of Carbohydrate Chemistry, 12: 1, 1 — 11
To link to this Article: DOI: 10.1080/07328309308018536
URL: http://dx.doi.org/10.1080/07328309308018536

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J. CARBOHYDRATE CHEMISTRY, 12(1), 1-11 (1993)

OFF-TEMPLATE CLAISEN REARRANGEMENT OF A D-GLUCOSE-DERIVED BICYCLIC SUBSTRATE

Kin-ichi Tadano,* Yoshiaki Isshiki, Toshihito Kumagai, and Seiichiro Ogawa

Department of Applied Chemistry, Faculty of Science and Technology,
Keio University, Hiyoshi, Kohoku-ku, Yokohama 223, Japan

Received April 4, 1992 - Final Form August 24, 1992

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ABSTRACT

The Claisen rearrangement of branched-chain furanose **5**, which has an allylic alcohol function as a side chain, by heating in triethyl orthoacetate afforded a diastereomeric mixture **6** of the rearrangement products. The ratio of the products was estimated to be nearly 3:1 based on the ^{1}H NMR analysis. The configuration at the newly introduced chiral center in each product was established by chemical conversion of the mixture **6** to tricyclic products **13R** and **13S**. The preferential formation of the rearrangement product having *R*-configuration at the newly formed chiral center was rationalized by consideration of the chair-like transition states.

INTRODUCTION

Claisen rearrangements which enable stereoselective introduction of a carbon-carbon bond into the skeletal or side chain carbons of hexoses or pentoses extend the utility of carbohydrates as versatile synthons.[1] As an example of a stereoselective Claisen rearrangement realized by using a D-glucose-derived substrate, we reported the orthoester Claisen (Johnson-variant) rearrangement of the allylic alcohol **1** with triethyl orthoacetate.[2] The rearrangement product **2**, which was obtained as a single product in high yield, includes an asymmetric quaternary carbon atom at C-3 of the D-

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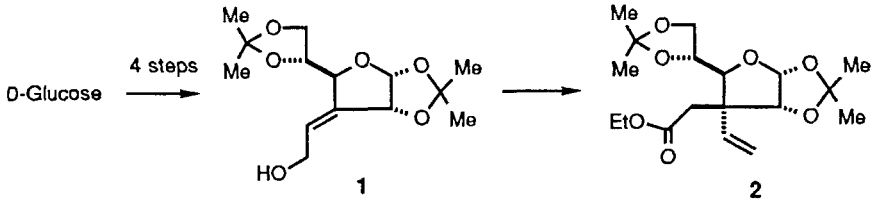
glucofuranose skeleton. It should be appreciated that compound **2** served as a key intermediate for stereoselective and enantiospecific total synthesis of some natural products.[3] In the course of our ongoing interest in the Claisen rearrangement of carbohydrate-derived substrates,[4] we have investigated the orthoester Claisen rearrangement of **5**, an analog of **2**. In this case, a new chiral center was introduced into the side chain of the furanose ring, a so-called off-template site. The rearrangement products have a new tertiary chiral carbon bonded to an existing chiral quaternary carbon. We describe herein the Claisen rearrangement of **5** and the stereochemical establishment of the rearrangement products.



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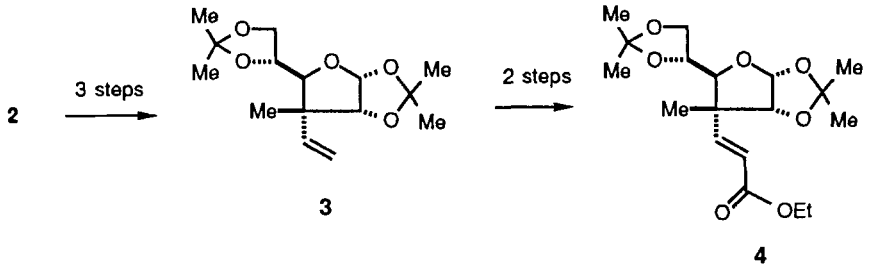
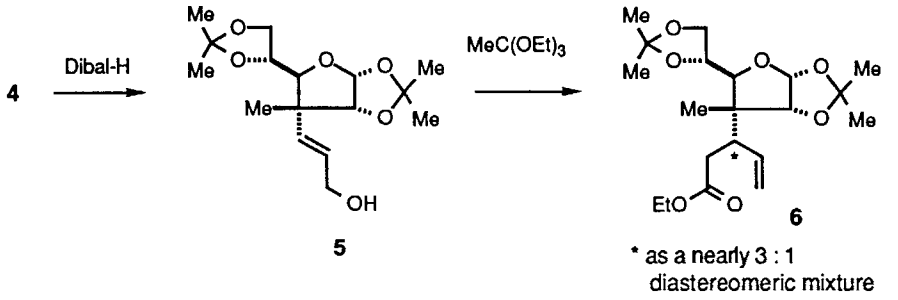
RESULTS AND DISCUSSION

The allylic alcohol **5** was efficiently prepared from the known α,β-unsaturated ester **4**,[5] which in turn was derived from the Claisen rearrangement product **3**[2] through ozonolysis followed by Wittig olefination. Diisobutylaluminum hydride (Dibal-H) reduction of **4** gave the allylic alcohol **5** quantitatively.[5]



The Claisen rearrangement of **5** under reaction conditions analogous to those used for **1** gave a nearly 3:1 diastereomeric mixture **6**, as estimated by ^{1}H NMR analysis, in 87% yield. However, separation of the products in the mixture at this stage was difficult. The configuration at the chiral center in the side chain of each isomer of the mixture **6** was established as follows.



Reduction of the ester function of the diastereomeric mixture **6** followed by protection of the new primary hydroxyl group of **7** as a benzyl ether gave **8** in an overall yield of 83%. The 5,6-*O*-isopropylidene group of **8** was removed selectively by mild acid hydrolysis using 60% AcOH to give **9** in 85% yield. Glycol cleavage of the resulting diol **9** by sodium periodate ($NaIO_4$) oxidation followed by $NaBH_4$ reduction of the aldehyde formed provided **10** in high yield. The vinyl group of **10** was then converted to a hydroxymethyl group as follows. Dihydroxylation of **10** using osmium tetraoxide-mediated oxidation under Kelly's conditions[6] gave a diastereomeric mixture of triols **11** in 59% yield. Compound **10** was recovered in 18% yield. The diastereomeric ratio of **11** was estimated to be nearly 3:1 based on the ^1H NMR analysis. Cleavage of the diol function of **11** followed by $NaBH_4$ reduction gave a diastereomeric mixture of **12R** and **12S**. Fortunately, the mixture was easily separated by chromatography on silica gel to give **12R** and **12S** in 60% and 18% yields, respectively. Finally, diastereomers **12R** and **12S** were each treated with an excess of mesyl chloride resulting in the formation of a mixture of mono- and dimesyl esters which, without separation, was subjected to a base (NaH) mediated intramolecular etherification. Tricyclic products **13R** and **13S** were obtained in 49% and 45% yields, respectively. The dimesyl esters of **12R** and **12S**, which did not undergo the tetrahydropyran formation, were isolated in a yield of 34% (from **12R**) and 26% (from **12S**), respectively. We could not find suitable conditions to form the monomesylate exclusively. In the ^1H NMR spectrum of **13R**, the *H*-3 signal appeared at δ 3.97 as a doublet of doublets having $J_{3,4ax}$=10.3 Hz and $J_{3,4eq}$=3.9 Hz and the signal *H*-6 axial appeared at δ 3.30 as a triplet having $J_{6ax,7}=J_{6ax,6eq}$=11.7 Hz. These observations indicated that the configuration at *C*-7 of **13R** is *R*. Hence, the configurations of new tertiary chiral carbons in the Claisen rearrangement products **6** were established to be *S* for the major product and *R* for the minor product.

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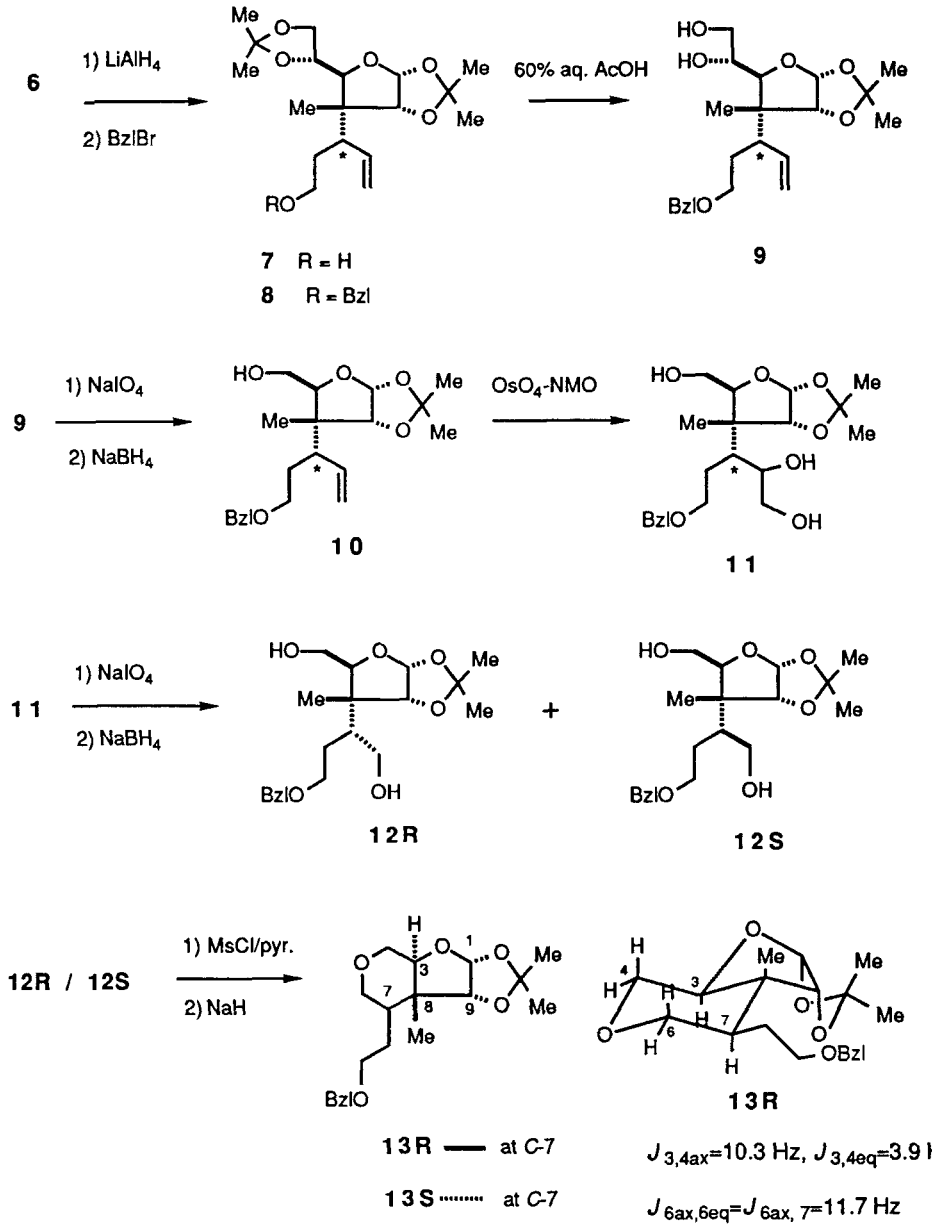

The preferential formation of **6S** can be explained using the following transition state argument. In mixing the allylic alcohol **5** with triethyl orthoacetate in the presence of a catalytic amount of propionic acid, the alcohol was converted into the

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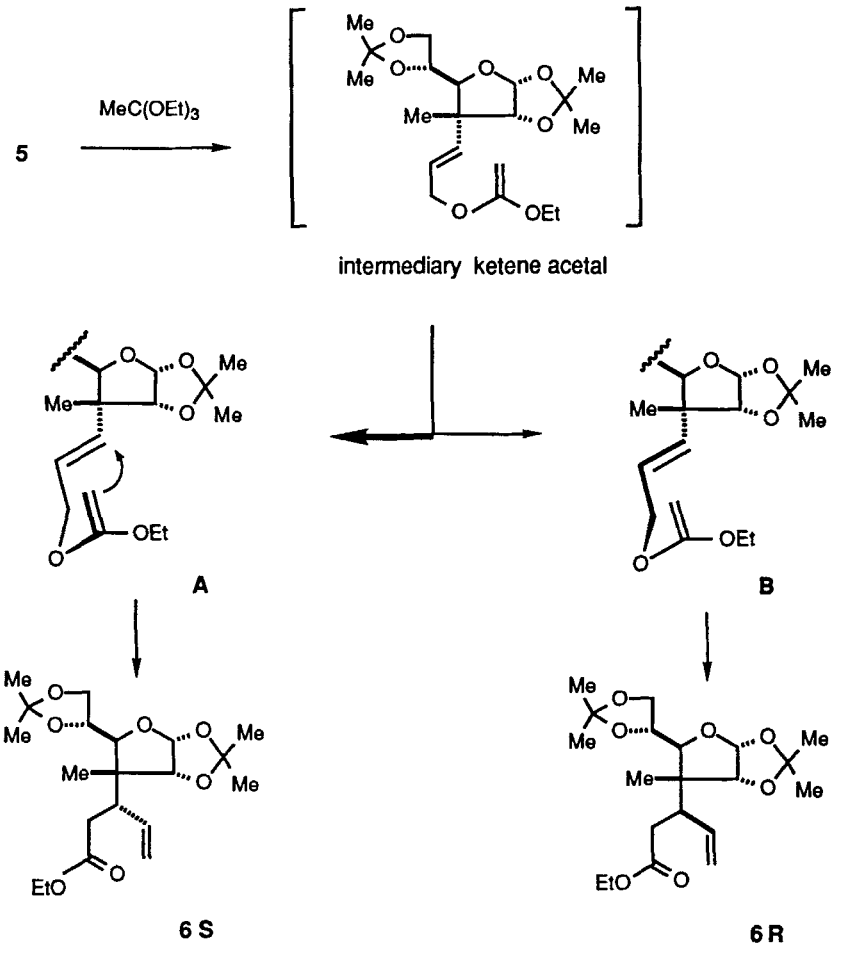
corresponding allyl ethyl ketene acetal as an intermediate. It is likely that the allylic double bond of the ketene acetal was turned away from the 1,2-*O*-isopropylidene group owing to an unfavorable interaction. This intermediate underwent a [3,3] sigmatropic rearrangement to provide two possible products **6S** and **6R**. The two chair-like transition states **A** and **B** are shown below. It is apparent that the transition state **A**, wherein attack of the ketene acetal occurs away from the furanose ring, is relatively free of non-bonded interactions from the 1,2-*O*- isopropylidene group. In contrast, in the transition state **B** the ketene acetal part is forced into the sterically crowded underside of the bicyclic system. Consequently, **6S** may be formed preferentially. In the case of **5**, the presence of the 1,2-*O*-isopropylidene group strongly affects the stereochemical outcome of the rearrangement as in our previous reports.[2]



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EXPERIMENTAL

General Procedures. Reactions were carried out at room temperature unless stated otherwise. Solvents were removed by concentration *in vacuo* using an evaporator at 30-40 °C. Melting points are uncorrected. Specific rotations were measured with a JASCO DIP-370 polarimeter using a 10-mm cell. Crude products were purified by chromatography using silica gel K060 (Katayama Chemicals). Thin layer chromatography (TLC) was performed with plates coated with Kieselgel 60 GF_{254} (Merck). ^1H NMR spectra were recorded in $CDCl_3$ solution with a JEOL JNM-EX 90 (90 MHz) or JEOL-GX 400 (400 MHz) FT spectrometer. Infrared (IR) spectra (neat) were recorded with a JASCO A-202 spectrometer. High resolution mass spectra (HRMS) were taken with a Hitachi M-80 mass spectrometer. Dichloromethane (CH_2Cl_2) and benzene were distilled after drying over CaH_2. *N,N*-Dimethylformamide (DMF) was distilled under reduced pressure after drying over CaH_2. Pyridine was distilled in the presence of NaOH. Tetrahydrofuran (THF) was distilled from $LiAlH_4$ and then from sodium/benzophenone. Triethyl orthoacetate and propionic acid were distilled under reduced pressure.

Mixture of (3*R*)-3-Deoxy-3-*C*-[(3*RS*)-4-ethoxycarbonyl-1-penten-3-yl]-1,2:5,6-di-*O*-isopropylidene-3-*C*-methyl-α-D-allofuranose (6). To a solution of **5** (2.59 g, 8.24 mmol) in triethyl orthoacetate (10 mL) was added propionic acid (0.025 mL). The mixture was heated at 135 °C with stirring. A reservoir (20 mL flask) was connected to the reaction equipment for collection of distilled EtOH. After 4 h, 0.025 mL of propionic acid was added. Heating was continued for a total of 9 h. After being cooled to room temperature, the solvent was removed by evaporation with toluene. The residue was chromatographed on silica gel (EtOAc/hexane, 1:15) to provide 2.76 g (87%) of an inseparable isomeric mixture **6** as a colorless oil: TLC, R_f 0.40 (EtOAc/hexane, 1:3); IR 2980, 2950, 1730, 1640, 1460, 1380, 1250 cm^{-1}; ^1H NMR (400 MHz) δ 0.94 (s, 3/4 x 3H), 0.96 (s, 1/4 x 3H), 1.22 (t, *J*=7.3 Hz, 3/4 x 3H), 1.24 (t, *J*=7.3 Hz, 1/4 x 3H), 1.29, 1.34, 1.41, 1.54 (4 s, each 3/4 x 3H), 1.29, 1.34, 1.38, 1.53 (4 s, each 1/4 x 3H), 2.46 (dd, *J*=14.1, 11.2 Hz, 1/4 x 1H), 2.67 (dd, *J*=14.1, 11.7 Hz, 3/4 x 1H), 2.78-2.90 (m, 2H), 3.82-4.19 (m, 6H), 4.16 (d, *J*=3.4 Hz, 1/4 x 1H), 4.18 (d, *J*=3.4 Hz, 3/4 x 1H), 5.04-5.17 (m, 2H), 5.67 (d, *J*=3.4 Hz, 1H), 5.84 (ddd, *J*=16.6, 10.25, 9.8 Hz, 3/4 x 1H), 5.99-6.09 (m, 1/4 x 1H).

Anal. Calcd for $C_{20}H_{32}O_7$: C,62.48; H, 8.39. Found: C, 62.23; H, 8.16.

Mixture of (3*R*)-3-Deoxy-3-*C*-[(3*RS*)-5-hydroxy-1-penten-3-yl]-1,2:5,6-di-*O*-isopropylidene-3-*C*-methyl-α-D-allofuranose (7). To a cooled (0 °C) solution of **6** (296 mg, 0.77 mmol) in THF (6 mL) was added $LiAlH_4$ (59

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mg, 1.54 mmol). The mixture was stirred at room temperature for 35 min and quenched with H_2O (0.5 mL). The resulting gels were removed by filtration and washed well with EtOAc. The combined filtrate and washings were concentrated. The residue was chromatographed on silica gel (EtOAc/hexane, 1:4) to provide an inseparable isomeric mixture **7** (250 mg, 95%) as a colorless oil: TLC, R_f 0.39 (EtOAc/hexane, 1:1); IR 3450, 2980, 2950, 1640, 1460, 1370, 1220 cm^{-1}; ^1H NMR (90 MHz) δ 0.87 (s, 3/4 x 3H), 0.97 (s, 1/4 x 3H), 1.28, 1.33, 1.42, 1.54 (4 s, 4 x 3H), 1.6-2.6 (m 4H), 3.4-4.3 (m, 7H), 4.9-5.3 (m, 2H), 5.71 (d, *J*=3.5 Hz, 1H), 5.6-6.3 (m, 1H).

Anal. Calcd for $C_{18}H_{30}O_6$: C, 63.14; H, 8.83. Found: C, 62.89; H, 8.72.

Mixture of (3*R*)-3-Deoxy-3-*C*-[(3*RS*)-5-(benzyloxy)-1-penten-3-yl]-1,2:5,6-di-*O*-isopropylidene-3-*C*-methyl-α-D-allofuranose (8). To a cooled (0 °C) solution of **7** (250 mg, 0.73 mmol) in DMF (5 mL) was added NaH (commercial reagent in mineral oil, washed well with hexane, dried, and weighed, 88 mg, 3.67 mmol). After being stirred for 1 h, benzyl bromide (0.35 mL, 2.94 mmol) was added to the mixture. The mixture was stirred at room temperature for a total of 5 h while NaH (32 mg, 9 mg) was added after 2 and 4 h and benzyl bromide (0.17 mL) was added after 4 h. The mixture was quenched with EtOH (0.3 mL), diluted with H_2O (40 mL) and extracted with CH_2Cl_2 (30 mL x 3). The combined extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed on silica gel (EtOAc/hexane, 1:12) to provide an inseparable isomeric mixture **8** (275 mg, 87%) as a colorless oil: TLC, R_f 0.62 (EtOAc/hexane, 1:3); IR 2990, 2940, 2880, 1640, 1450, 1370, 1250 cm^{-1}; ^1H NMR (90 MHz) δ 0.80 (s, 3/4 x 3H), 0.97 (s, 1/4 x 3H), 1.28, 1.30, 1.48, 1.52 (4 s, 4 x 3H), 1.6-2.2 (m, 2H), 2.40 (ddd, *J*=11, 9, 2 Hz, 1H), 3.3-4.3 (m, 7H), 4.47 (d, *J*=2.5 Hz, 2H), 4.9-5.25 (m, 2H), 5.5-6.2 (m, 1H), 5.68 (d, *J*=4 Hz, 1H), 7.3-7.4 (m, 5H).

Anal. Calcd for $C_{25}H_{36}O_6$: C, 69.42; H, 8.39. Found: C, 69.38; H, 8.26.

Mixture of (3*R*)-3-Deoxy-3-*C*-[(3*RS*)-5-(benzyloxy)-1-penten-3-yl]-1,2-*O*-isopropylidene-3-*C*-methyl-α-D-allofuranose (9). A solution of **8** (275 mg, 0.64 mmol) in 60% acetic acid (5.5 mL) was stirred for 18 h, and concentrated after addition of toluene. The residue was chromatographed on silica gel (EtOAc/hexane, 1:3) to provide an inseparable isomeric mixture **9** (213 mg, 85%) as a colorless oil: TLC, R_f 0.19 (EtOAc/hexane, 2:3); IR 3430, 3080, 3030, 2980, 2950, 1640, 1500, 1460, 1380, 1320, 1230 cm^{-1}; ^1H NMR (90 MHz) δ 0.95 (s, 3/4 x 3H), 1.05 (s, 1/4 x 3H), 1.30, 1.55 (2 s, 2 x 3H), 1.7-2.8 (m, 5H), 3.3-3.8, 4.05-4.2 (2 m, 5H, 2H), 4.47 (d, *J*=2 Hz, 2H), 4.95-5.2 (m, 2H), 5.70 (d, *J*=4 Hz, 1H), 5.6-6.1 (m, 1H), 7.3-7.4 (m, 5H).

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Mixture of (3*R*)-3-Deoxy-3-*C*-[(3*RS*)-5-(benzyloxy)-1-penten-3-yl]-1,2-*O*-isopropylidene-3-*C*-methyl-α-D-ribofuranose (10). To a stirred solution of **9** (208 mg, 0.53 mmol) in MeOH (4 mL) was added a solution of $NaIO_4$ (227 mg, 1.06 mmol) in H_2O (0.3 mL) at 0 °C. After being stirred for 30 min, the resulting white precipitates were removed by filtration and washed well with EtOAc. The combined filtrate and washings were concentrated. The residue was partitioned between EtOAc (30 mL) and H_2O (40 mL). The aqueous phase was extracted with EtOAc (30 mL x 2). The combined organic phases were dried (Na_2SO_4) and concentrated.

The residual oily product was dissolved in MeOH (4 mL) and $NaBH_4$ (102 mg, 2.70 mmol) was added at 0 °C. The mixture was stirred for 20 min, and then made neutral with Amberlite IR-120 (H^+). The resin was removed by filtration, and the filtrate was concentrated. The residue was chromatographed on silica gel (EtOAc/hexane, 1:4) to provide an inseparable isomeric mixture **10** (162 mg, 84%) as a colorless oil: TLC, R_f 0.36 (EtOAc/hexane, 1:1); IR 3470, 3080, 3030, 2980, 2940, 2880, 1640, 1500, 1460, 1380, 1220 cm^{-1}; ^1H NMR (400 MHz) δ 0.84 (s, 3/4 x 3H), 0.87 (s, 1/4 x 3H), 1.31, 1.53 (2 s, each 3/4 x 3H), 1.28, 1.53 (2 s, each 1/4 x 3H), 1.50-2.00 (m, 3H), 2.32 (td, *J*=9.8, 2.8 Hz, 1/4 x 1H), 2.56 (td, *J*=9.8, 2.8 Hz, 3/4 x 1H), 3.35-3.87 (m, 4H), 4.04 (dd, *J*=8.3, 2.4 Hz, 3/4 x 1H), 4.18 (d, *J*=3.4 Hz, 1/4 x 1H), 4.22 (d, *J*=3.4 Hz, 3/4 x 1H), 4.44, 4.53 (ABq, *J*=11.7 Hz, 2H), 4.95-5.15 (m, 2H), 5.62 (dt, *J*=16.6, 10.3 Hz, 3/4 x 1H), 5.73 (d, *J*=3.4 Hz, 1/4 x 1H), 5.78 (d, *J*=3.4 Hz, 3/4 x 1H), 5.89 (dt, *J*=16.6, 10.3 Hz, 1/4 x 1H), 7.26-7.35 (m, 5H).

Anal. Calcd for $C_{21}H_{30}O_5$: C, 69.59; H, 8.34. Found: C, 69.36; H, 8.17.

(3*R*)-3-Deoxy-3-*C*-[(2*R*) and (2*S*)-4-(benzyloxy)-1-hydroxybut-2-yl]-1,2-*O*-isopropylidene-3-*C*-methyl-α-D-ribofuranoses (12R) and (12S). To a solution of **10** (50.9 mg, 0.14 mmol) in acetone (1 mL) were added OsO_4 (0.05 M solution in *t*-BuOH, 0.14 mL, 0.007 mmol) and a solution of *N*-methylmorpholine *N*-oxide (NMO) (42.8 mg, 0.365 mmol) in H_2O (0.1 mL). The mixture was stirred for 9 days in the dark, while 0.28 mL of OsO_4 in *t*-BuOH and 24.6 mg of NMO were added after 5 and 8 days. To the mixture were added saturated aq $NaHSO_3$ (1.5 mL) and H_2O (15 mL). This was extracted with EtOAc (15 mL x 3). The combined organic phases were dried (Na_2SO_4) and concentrated. The residue was chromatographed on silica gel (acetone/hexane, 1:6) to provide an inseparable isomeric mixture **11** (33.0 mg, 59%) and unchanged **10** (9.0 mg, 18%). **11**: TLC, R_f 0.52 (EtOH/toluene, 1:5); IR 3420, 2980, 2950, 2880, 1500, 1460, 1380, 1220 cm^{-1}; ^1H NMR (90 MHz) δ 0.88 (s, 3/4 x 3H), 0.92 (s, 1/4 x 3H), 1.25, 1.48 (2 s, each 3/4 x

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3H), 1.29, 1.52 (2 s, each 1/4 x 3H), 1.6-2.5 (m, 6H), 3.3-4.4 (m, 9H), 4.52 (s, 2H), 5.73 (d, *J*=3.5 Hz, 1H), 7.2-7.5 (m, 5H).

To a stirred solution of **11** (30.2 mg, 0.076 mmol) in MeOH (0.6 mL) was added a solution of $NaIO_4$ (33.0 mg, 0.16 mmol) in H_2O (0.2 mL). After being stirred for 30 min, the resulting precipitates were removed by filtration. The combined filtrate and washings (EtOAc) were concentrated. The residue was partitioned between EtOAc (12 mL) and H_2O (12 mL). The aqueous phase was extracted with EtOAc (12 mL x 2). The combined organic phases were dried (Na_2SO_4) and concentrated to leave an oil (32 mg), which was used in the next step without purification.

The residue was dissolved in MeOH (0.6 mL) and $NaBH_4$ (15.0 mg, 0.38 mmol) was added. The mixture was stirred for 30 min, and made neutral with Amberlite IR-120 (H^+). The resin was removed by filtration, and the filtrate and washings (MeOH) were combined and concentrated. The residue was purified by preparative TLC (EtOH/toluene, 1:8) to provide **12R** (16.7 mg, 60%) and **12S** (5.0 mg, 18%). **12R**, a colorless oil, had $[\alpha]_D^{23}$ +18.2° (*c* 0.70, $CHCl_3$); TLC, R_f 0.42 (EtOH/toluene, 1:7); IR 3420, 2980, 2950, 2860, 1500, 1460, 1220 cm^{-1}; ^1H NMR (400 MHz) δ 0.87 (s, 3H), 1.28, 1.49 (2 s, 2 x 3H), 1.70-1.95, 2.00-2.05 (2 m, 2H, 1H), 2.32, 3.13 (br s, 2 x 1H), 3.53-3.74 (m, 5H), 3.84 (dd, *J*=12.0, 2.7 Hz, 1H), 4.18 (dd, *J*=8.8, 2.7 Hz, 1H), 4.19 (d, *J*=3.4 Hz, 1H), 4.52, 4.55 (ABq, *J*=11.7 Hz, 2H), 5.76 (d, *J*=3.4 Hz, 1H), 7.26-7.36 (m, 5H). **12S**, a colorless oil, had $[\alpha]_D^{24}$ +12.7° (*c* 0.40, $CHCl_3$); TLC, R_f 0.47 (EtOH/toluene, 1:7); IR 3420, 2940, 1500, 1460, 1380, 1220 cm^{-1}; ^1H NMR (400 MHz) δ 0.91 (s, 3H), 1.31, 1.55 (2 s, 2 x 3H), 1.25, 1.62 (2 br s, 2 x 1H), 1.75-1.80 (m, 2H), 1.92-1.94 (m, 1H), 3.56-3.61 (m, 2H), 3.65-3.79 (m, 4H), 4.23 (dd, *J*=5.8, 4.4 Hz, 1H), 4.26 (d, *J*=3.4 Hz, 1H), 4.51, 4.54 (ABq, *J*=11.7 Hz, 2H), 5.77 (d, *J*=3.4 Hz, 1H), 7.26-7.36 (m, 5H).

(1*R*,3*S*,7*R*,8*R*,9*R*)-7-(2-Benzyloxy)ethyl-8,11,11-trimethyl-2,5,10,12-tetraoxatricyclo[7.3.0.0^{3,8}]dodecane (13R) and its 7*S* isomer (13S). To a stirred solution of **12R** (10.9 mg, 0.03 mmol) in pyridine (0.2 mL) were added mesyl chloride (MsCl) (2.3 μL, 0.03 mmol) and 4-dimethylaminopyridine (1.9 mg). The mixture was stirred for 5 h while MsCl (0.5, 0.9, and 0.9 μL, total 2.0 mol. eq) was added after 2h, 3h, and 4 h. The mixture was diluted with H_2O (8 mL) and extracted with CH_2Cl_2 (8 mL x 3). The combined extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed on short silica gel column (EtOAc/hexane, 1:2) to provide a mixture of mono- and dimesylates (12.6 mg) as a colorless oil, which was used without separation.

The mixture (12.6 mg) was dissolved in DMF (0.3 mL) and NaH (2.9 mg, 0.12 mmol) was added. The mixture was stirred for 3.5 h while NaH (1.3 mg and 0.6 mg)

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was added after 1.5 h and 3 h. The mixture was quenched with EtOH (0.1 mL), diluted with H_2O (8 mL), and extracted with CH_2Cl_2 (8 mL x 3). The combined extracts were dried (Na_2SO_4) and concentrated. The residue was purified by PTLC (EtOAc/hexane, 1:2) to provide **13R** (5.0 mg, 49%) and the dimesyl ester of **12R** (5.2 mg, 34%). **13R**, a colorless oil, had $[\alpha]_D^{23}$ +40.4° (c 0.25, $CHCl_3$); TLC, R_f 0.52 (EtOH/toluene, 1:8); IR 2980, 2940, 2860, 1500, 1450, 1380, 1300, 1260 cm^{-1}; ^1H NMR (400 MHz) δ 0.83 (s, 3H), 1.31, 1.53 (2 s, 2 x 3H), 1.43 (ddd, *J*=13.7, 8.3, 6.8 Hz, 1H), 1.70 (ddd, *J*=13.7, 8.3, 6.8 Hz, 1H), 2.19-2.27 (m, 1H), 3.30 (t, *J*=11.2 Hz, 1H), 3.48-3.55 (m, 2H), 3.56 (t, *J*=11.2 Hz, 1H), 3.78 (dd, *J*=11.2, 4.4 Hz, 2H), 3.97 (dd, *J*=10.3, 3.9 Hz, 1H), 4.27 (d, *J*=3.4 Hz, 1H), 4.47, 4.52 (ABq, *J*=11.7 Hz, 2H), 5.78 (d, *J*=3.4 Hz, 1H), 7.26-7.35 (m, 5H). HRMS. Calcd for $C_{20}H_{27}O_5$ (M^+-H): *m/z* 347.1856. Found: *m/z* 347.1842.

Analogously, **12S** (8.0 mg) was converted into **13S** (3.4 mg, 45%). The dimesylate of **12S** (3.0 mg, 26%) was also obtained. **13S**, white crystals, had mp 59-60 °C and $[\alpha]_D^{23}$ +6.9° (*c* 0.15, $CHCl_3$); TLC, R_f 0.71 (EtOH/toluene, 1:8); IR ($CHCl_3$) 3050, 2800, 2750, 1450, 1370 cm^{-1}; ^1H NMR (400 MHz) δ 0.99 (s, 3H), 1.29, 1.52 (2 s, 2 x 3H), 1.79 (ddd, *J*=14.9, 10.0, 5.1 Hz, 1H), 2.00-2.04 (m, 1H), 2.41-2.48 (m, 1H), 3.50-3.54 (m, 2H), 3.57 (t, *J*=10.7 Hz, 1H), 3.68 (s, 2H), 4.02 (dd, *J*=10.3, 4.9 Hz, 1H), 4.15 (dd, *J*=10.7, 4.9 Hz, 1H), 4.35 (d, *J*=3.4 Hz, 1H), 4.49 (s, 2H), 5.73 (d, *J*=3.4 Hz, 1H), 7.26-7.35 (m, 5H). HRMS. Calcd for $C_{19}H_{25}O_5$ (M^+-CH_3): *m/z* 333.1700. Found: *m/z* 333.1697.

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