Ortho Ester Claisen Rearrangements of Three 3-*C*-(Hydroxymethyl)methylene Derivatives of Hexofuranose: Stereoselective Introduction of a Quaternary Center on *C*-3 of D-*ribo*-, L-*lyxo*-, and D-*arabino*-Hexofuranoses

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Ortho ester Claisen rearrangements of (*E*)-3-deoxy-3-*C*-[(hydroxymethyl)methylene]-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranose (**3-*E***), -β-L-*lyxo*-hexofuranose (**12-*E***), and -β-D-*arabino*-hexofuranose (**33-*E***) proceeded with high stereoselectivity to provide the rearranged products **13**, **15**, and **34**, respectively, in acceptable yields. The rearrangements of the corresponding *Z* isomers **3-*Z***, **12-*Z***, and **33-*Z*** were also investigated. The stereochemistries of the newly introduced quaternary center on C-3 of compounds **13**, **15**, and **34** were established unambiguously by chemical modifications of each rearranged product.

Introduction of a quaternary center in an appropriate position of the carbon framework is a frequently encountered problem in organic synthesis, especially in natural product synthesis. For this crucial problem, several sophisticated solutions were reported in recent years.[1] Among these, the Claisen rearrangement approach is an effective and convenient strategy. In many cases, the rearrangement proceeds with high stereoselectivity. Ortho ester Claisen rearrangement, one of the variants of the Claisen rearrangement, is a useful procedure for simultaneous introduction of an (alkoxycarbonyl)methyl group and a vinyl group on the same carbon.[2] These functionalities are, in many cases, convertible to other functionalities by rather simple operations.

A number of elegant synthetic approaches to natural product synthesis have been achieved that employ readily available optically pure compounds such as carbohydrates, terpenes, and amino acids as chiral starting materials.[3] Fraser-Reid and coworkers recently reported the Claisen rearrangement ([3.3]-allyl vinyl ether type rearrangement) of some hexopyranose-derived compounds and achieved introduction of the quaternary centers on hexopyranoses,[4] realizing highly stereoselective introduction of the quaternary center by using six-membered cyclic models. Our own interest is in gaining stereoselectivity by studying the rearrangement of five-membered cyclic models, that is, some furanose models.

Here we describe the results of ortho ester Claisen rearrangements of three hexofuranose-derived substrates, all of which possess a (hydroxymethyl)methylene (an allyl alcohol) group on C-3. These substrates are (*E*)-3-*C*-(hydroxymethyl)methylene derivatives of the fully protected D-*ribo*-, L-*lyxo*-, and D-*arabino*-hexofuranose (**3-*E***, **12-*E***, and **33-*E***). Fortunately, these rearrangements proceeded smoothly and stereoselectively to provide the rearranged products **13**, **15**, and **34** in high to moderate yields. The factors involved in the stereoselectivities of the rearrangements are also discussed.[5,6]

Results and Discussion

Ortho Ester Claisen Rearrangements of 3-*E* and 12-*E* with Triethyl Orthoacetate. The substrates for the rearrangement, **3-*E*** and **12-*E***, were prepared as follows (Scheme I). The 3-ulose **1**, which was readily obtained by pyridinium chlorochromate (PCC) oxidation of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose, was subjected to Wittig olefination with [(ethoxycarbonyl)methylene]triphenylphosphorane as described in the literature.[7] The adducts **2-*E*** and **2-*Z*** were cleanly separated by chromatography on silica gel in 60% and 22% yields, respectively. Their geometrical structures were confirmed by comparing the ^{1}H NMR spectral data with reported data.[7] The 3-*C*-(ethoxycarbonyl)methylene derivatives **2-*E*** and **2-*Z*** were separately reduced to the 3-*C*-(hydroxymethyl)methylene derivatives **3-*E*** and **3-*Z*** by diisobutylaluminum hydride (DIBAL-H) reduction in 86% and 92% yields, respectively.

The L-lyxo isomer **12-*E***, as the other substrate, was prepared from the known 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose (**4**).[8] Although the configurational inversion at C-5 of **4** to the L-ido isomer by displacement of the corresponding 5,6-di-*O*-tosyl derivative with acetate anion in a S_N2 fashion was known in the literature,[9] we improved the overall yield from **4** to the known **7**[9] as follows. Compound **4** was treated with an excess amount of methanesulfonyl chloride (**4** to **5**), and the displacement of the 5,6-*O*-mesyl group with benzoate anion (sodium benzoate) in refluxing DMF afforded the L-ido derivative **6**, which was then saponificated with sodium methoxide. Consequently, 3-*O*-benzyl-1,2-*O*-isopropylidene-β-L-idofuranose **7** was obtained in 41% overall yield from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose in a five-step reaction. O-Isopropylidenation of **7** with 2,2-dimethoxypropane in the presence of camphorsulfonic acid (**7** to **8**[10]) followed by hydrogenolysis for cleavage of the benzyl group afforded the known **9**.[10] PCC oxidation of **9** gave the crystalline 3-ulose **10** in 95% yield. Inter-

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(2) Roads, S. J.; Raulins, N. R. *Org. React. (N.Y.)* **1975**, *22*, 1. Bennett, G. B. *Synthesis* **1977**, 589. Ziegler, F. E. *Acc. Chem. Res.* **1977**, *10*, 277.
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(10) Baggett, N.; Jeanloz, R. W. *J. Org. Chem.* **1963**, *28*, 1845.

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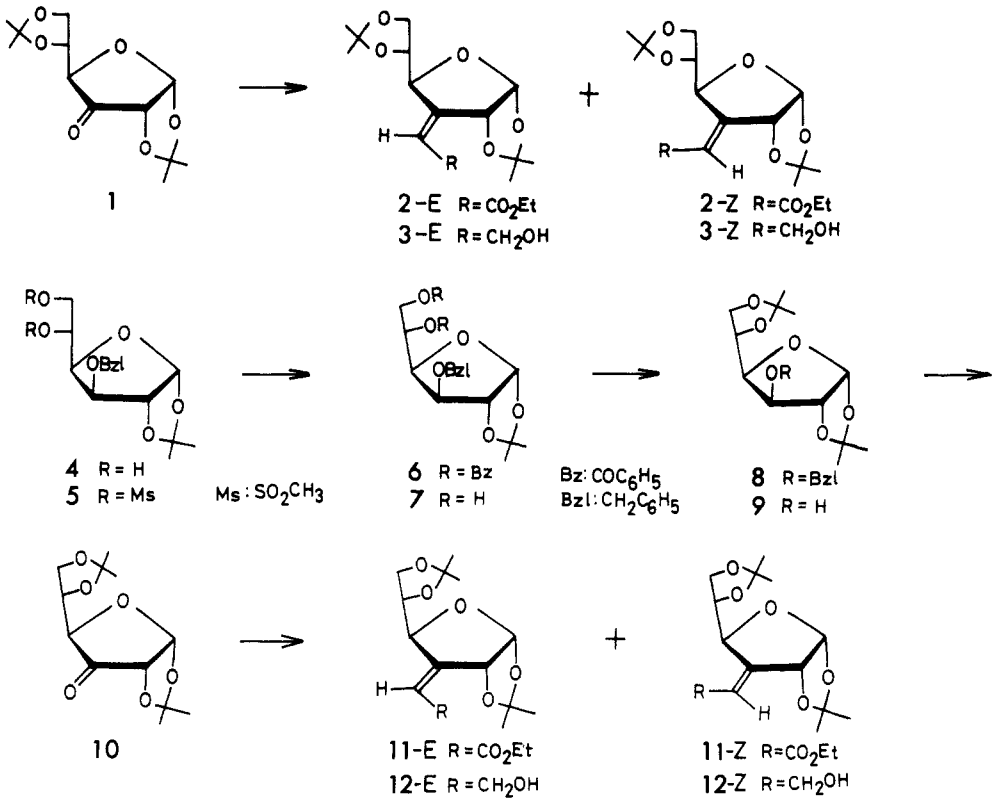
Scheme I



estingly, the Wittig olefination of **10** with [(ethoxycarbonyl)methylene]triphenylphosphorane in refluxing benzene gave no adduct, and **10** was recoverd quantitatively. On the other hand, the Horner–Emmons reaction of **10** with diethyl [(ethoxycarbonyl)methyl]phosphonate in the presence of sodium hydride in THF at 0 °C provided the desired 3-*C*-(ethoxycarbonyl)methylene derivatives, 11-***E*** and 11-***Z***, in 75% and 18% yields, respectively. In the ^{1}H NMR spectrum of 11-***E***, H-4 appeared at δ 4.84 as a broad singlet, and that of 11-***Z*** appeared at δ 5.04–5.20 as a multiplet in the ^{1}H NMR spectrum. The similar phenomenon that H-4 of an (*E*)-(ethoxycarbonyl)-methylene derivative revealed a small δ value in the ^{1}H NMR was observed in the case of 2-***E***. Therefore, the geometrical structures of 11-***E*** and 11-***Z*** were established. Reduction of 11-***E*** and 11-***Z*** with DIBAL-H afforded 3-*C*-(hydroxymethyl)methylene derivatives 12-***E*** and 12-***Z*** in 86% and 91% yields, respectively.

Ortho ester Claisen rearrangement of 3-***E***, according to the standard procedure reported by Johnson et al.[11] (heating at 135 °C for 9 h in a triethyl orthoacetate solution in the presence of a catalytic amount of propanoic acid), yielded a single rearranged product, **13**, in 64% yield (84% yield based on the consumed 3-***E***) in a 2-g-scale experiment (Scheme II). Presence of the newly introduced vinyl and (ethoxycarbonyl)methyl groups at C-3 was established by the ^{1}H NMR spectrum, and the configuration at C-3 was established as depicted by chemical modification (vide infra). Prolonged heating decreased the yield of **13**. In contrast to this result, the rearrangement of 3-***Z*** was troublesome. After 7 h of heating under the same conditions as in the case of 3-***E***, a mixture of **13** and the 3-epimer **14** was isolated in 16% yield and 65% of unreacted 3-***Z*** was recovered. The ratio of the inseparable mixture of **13** and **14** was estimated to be approximately 3:2 based on the ^{1}H NMR spectrum of the mixture, using the AB quartets centered at δ 2.60 for **13** and at δ 2.89 for **14**.

Ortho ester Claisen rearrangement of 12-***E*** proceeded smoothly under the same conditions to provide a single product **15** in 55% yield (79% yield based on the consumed 12-***E***). The structure determination at C-3 of **15** was achieved by chemical modification (vide infra). The rearrangement of 12-***Z*** gave an inseparable mixture of **15** and the 3-epimer **16** in a low yield (6%), and the unreacted 12-***Z*** was recovered in 79% yield. The approximate ratio of **15** and **16** was 3:1 based on the ^{1}H NMR spectrum (doublets for H-2 centered at δ 4.99 for **15** and at δ 4.80 for **16**).

Determination of the Stereochemistries of the Newly Introduced Quaternary Carbons in 13 and 15. While the results described above showed that stereoselective introduction of the C-3 quaternary centers had been achieved, the ^{1}H NMR spectra of the products could not be used for determining the configuration at C-3 of **13** and **15**, and we proceeded to establish them by chemical modification (Scheme III). By the reported procedure,[12] the rearranged product **13** was transformed to compound **19**. DIBAL-H reduction of **13** gave an approximately 1:2 mixture of **17** and **18**, which was oxidized with PCC to convert it to pure **18** in 63% yield. The formylmethyl group of **18** was then decarbonylated by thermolysis in refluxing benzonitrile in the presence of 10% palladium on charcoal to afford **19** in 76% yield. The *O*-isopropylidene group of the side chain in **19** was then selectively removed with 50% acetic acid (93%), and the primary hydroxyl group in the resulting **20** was preferentially protected by trimethylacetyl group, providing compound **21** in 83% yield. Ozonolysis of **21** and treatment with

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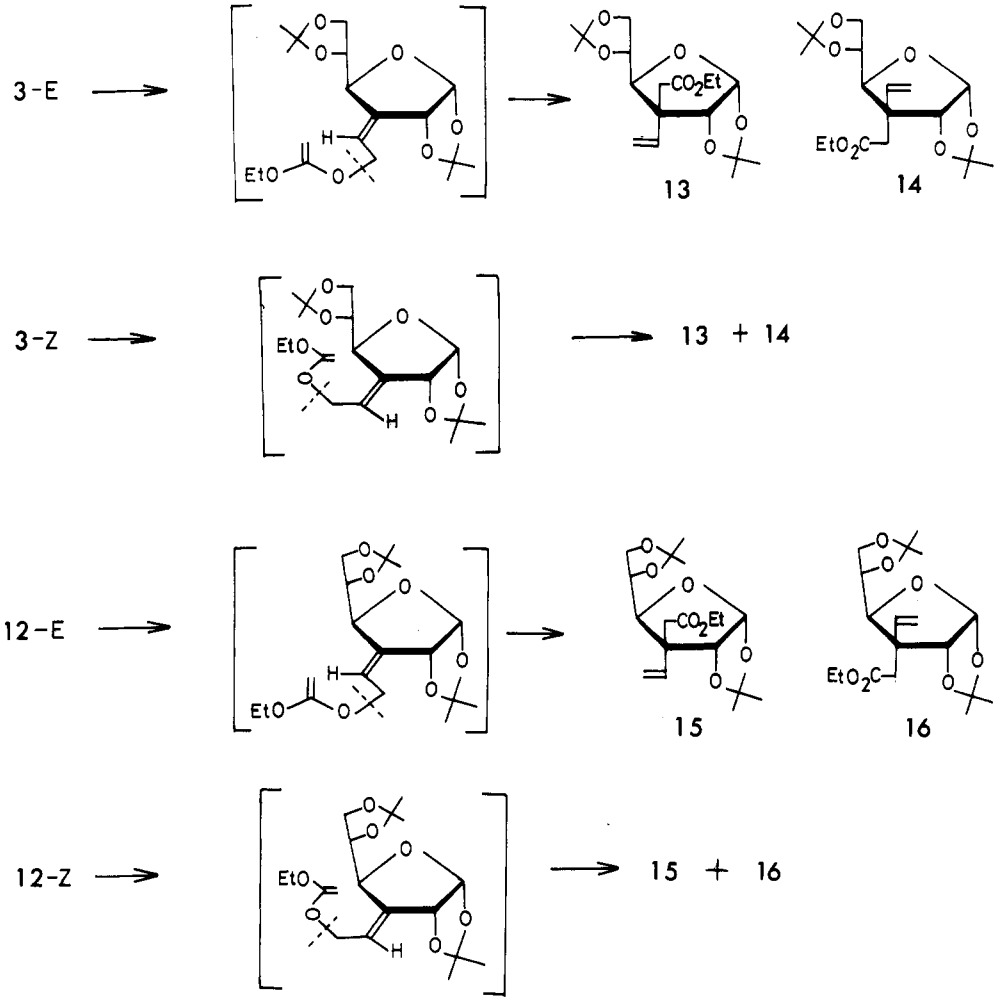
Scheme II



triphenylphosphine gave a 3-*C*-aldehyde (**22**) in 91% yield. The fact that no lactol formation occurred in compound **22** means that the aldehyde group, therefore the vinyl group in the rearranged product **13**, is located in a trans relationship to the C–C bond of the side chain. As can be seen by ozonolysis of compound **39** (vide infra), if the 3-*C*-aldehyde group is cis to the side chain, spotaneous lactol formation between the aldehyde and the C-5 hydroxyl group is expected to occur. The result of the ozonolysis of **21** demonstrates that the stereochemistry at C-3 of the rearranged product **13** is *R* as depicted.

The determination of the stereochemistry at C-3 in **15** was performed as follows. Employing the same reaction sequence as for **19** from **13**, the rearranged product **15** was transformed to compound **25** via compounds **23** and **24** (**23** in 91% yield, **24** in 85% yield, and **25** in 52% yield). On the other hand, compound **20** was per-O-mesylated to afford the di-*O*-mesyl derivative **26** in 90% yield. Treatment of **26** with excess sodium benzoate in refluxing DMF and purification of the products by silica gel chromatography afforded the di-*O*-benzoate **27** and the mono-*O*-benzoate **28** with inversion of the configurations at the chiral centers of the side chain in 43% and 11% yields, respectively. Both **27** and **28** were converted to compound **29** by treatment with sodium methoxide in 76% and 69% yields, respectively. O-Isopropylidenation of **29** in the usual manner gave compound **25**, which was identical with that derived from **15** in all respects (mp, $[\alpha]_D$, IR, and ^1H NMR). From this fact, it is concluded that the methyl group in **25**, therefore the (ethoxycarbonyl)methyl group in **15**, is cis to the C–C bond of the side chain and the stereochemistry at C-3 in **15** is *R*.

In sterically complicated compounds, Claisen rearrangements proceed in many cases from the less hindered side. In fact, the rearrangements of **3-*E*** and **12-*E*** occurred via attack from the β-side (from the side opposite to the neighboring 1,2-*O*-isopropylidene group) to provide **13** and **15**. In comparison of the transition states for α-side and β-side attack, a severe interaction between the 1,2-*O*-isopropylidene group and the ethoxy group in the chairlike transition model is expected in the case of α-attack. Therefore, attack from the β-face of the furanose ring seems to be preferred.

Ortho Ester Claisen Rearrangement of 33-*E* and the Stereochemistry of the Newly Introduced Quaternary Center of the Product 34. The rearrangements of **3-*E*** and **12-*E*** indicated that the configurations of the 1,2-*O*-isopropylidene groups in **3-*E*** and **12-*E*** seem to be important factors for stereocontrol of the rearrangement. To verify this assumption, we next chose compounds **33-*E*** and **33-*Z*** as substrates. Both of the 3-*C*-(hydroxymethyl)methylene derivatives of D-*arabino*-hexofuranose, **33-*E*** and **33-*Z***, possess 1,2-*O*-isopropylidene groups with configurations opposite to those of **3-*E*** and **12-*E***. The preparation of **33-*E*** and **33-*Z*** started from the known 1,2:5,6-di-*O*-isopropylidene-D-altrofuranose (**30**), which was obtained by the reported O-isopropylidenation[13] of D-altrose[14] (Scheme IV). PCC oxidation of **30** gave the 3-ulose **31**, which was directly subjected to Wittig olefination with

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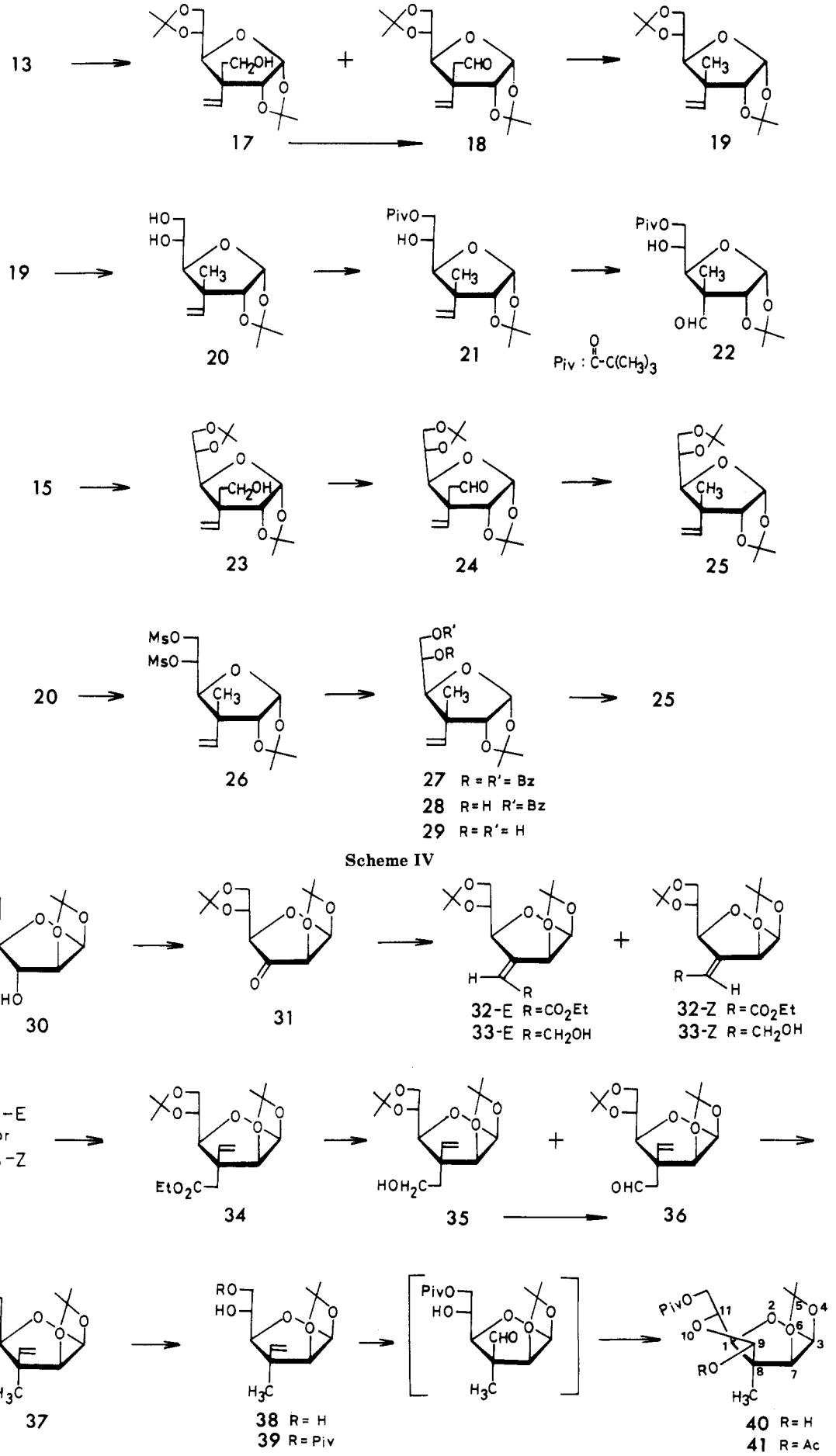
(14) Richtmyer, N. K. *Methods Carbohydr. Chem.* **1962**, *1*, 107.

Scheme III



Scheme IV

[(ethoxycarbonyl)methylene]triphenylphosphorane. After repeated chromatography of the Wittig adducts on silica gel, 3-*C*-(ethoxycarbonyl)methylene derivatives **32-*E*** and **32-*Z*** were isolated in 34% and 35% yields, respectively. The structures of **32-*E*** and **32-*Z*** were determined on the basis of their ^{1}H NMR spectra, and no preferential formation of the *E*-olefin **32-*E*** was observed in the Wittig reaction employing the stabilized ylide. DIBAL-H reduction of each **32-*E*** and **32-*Z*** afforded the 3-*C*-(hydroxymethyl)methylene derivatives, **33-*E*** and **33-*Z***, in 91% and 68% yields, respectively.

Ortho ester Claisen rearrangement of **33-*E*** under the usual conditions proceeded smoothly to provide a single rearranged product **34** in 63% yield. Interestingly, the rearrangement of **33-*Z*** under the same conditions proceeded somewhat slowly to afford **34** in 41% yield. Although the yields were not high, no other epimers at C-3 were detected.

The structure of **34** was established by the same chemical method as in the case of **13** and **15**. DIBAL-H reduction of **34** provided the (hydroxy)ethyl derivative **35** and the formylmethyl derivatives **36** in 19% and 73% yields, respectively. The conversion of **35** to **36** was achieved by PCC oxidation in 75% yield. Thermal decarbonylation of **36** in the presence of 10% palladium on charcoal gave compound **37** in 53% yield. Selective removal of the *O*-isopropylidene group on the side chain of **37** gave **38** in 93% yield. The primary hydroxyl group in **38** was protected as a trimethylacetyl ester, providing **39** in 90% yield. Ozonolysis of **39** and successive treatment with triphenylphosphine gave a lactol (**40**) in 75% yield. In the ^{1}H NMR spectrum of **40**, no aldehyde peak was detected. In addition, one proton singlet was observed at δ 6.41 in the ^{1}H NMR spectrum of the acetylation product (**41**) of **40**. The singlet was attributable to the proton on the acetylated lactol carbon. Although compounds **40** and **41** were diastereomerically pure, we could not determine the stereochemistries on the lactol carbons by spectral means. We tentatively assign them as *R* on the basis of speculation that the (*R*)-substituents suffer less steric hindrance by the *O*-isopropylidene group. Spontaneous lactol formation between the secondary hydroxyl group of the side chain and the aldehyde group formed by ozonolysis shows that the vinyl group in **39**, therefore that of the rearranged product **34**, is located on the same side on the furanose ring. The stereochemistry at C-3 of **34** is, therefore, *S*.

In conclusion, a substituent on the furanose that is syn to the hydroxymethyl group slows the rearrangement from the face of the furanose on which it resides. Furthermore, the *O*-isopropylidene group slows rearrangement from the face on which it resides, if it is syn or anti to the hydroxymethyl group, and this is probably because it effectively blocks the whole underside of the furanose ring.

Experimental Section

General Procedures. Evaporations were carried out under diminished pressure at below 40 °C (bath). Melting points were determined with a Mitamura Riken micro melting point apparatus and are uncorrected. Specific rotations were measured in a 1-dm tube with a JASCO DIP-4 polarimeter. Column chromatography was performed on Kieselgel 60 (Merck), and thin-layer chromatography (TLC) was performed on a glass plate coated with Kieselgel 60 GF_{254} (Merck) followed by detection by UV light and charring with sulfuric acid. Preparative TLC (PTLC) was performed on a glass plate (20 × 20 cm) coated with Kieselgel PF_{254} (Merck), and compounds were extracted with $CHCl_3$. IR spectra were recorded with a Hitachi Model 225 (KBr) or with a JASCO Model A-202 ($CHCl_3$) spectrometer. ^{1}H NMR spectra were recorded with a Varian EM-390 (90 MHz) spectrometer for solutions in $CDCl_3$ (internal Me_4Si). High-resolution mass spectra were obtained on a Hitachi Model M-80 spectrometer. Elemental analyses were performed by Mr. Akio Takahashi of the university, to whom our thanks are due.

Dichloromethane was distilled from CaH_2, pyridine was distilled from NaOH, benzene was distilled from $LiAlH_4$, triethyl orthoacetate was distilled without drying reagent, and both acetone and benzonitrile were distilled from K_2CO_3 (benzonitrile was distilled under diminished pressure).

Standard Procedure for Oxidation of the Primary and Secondary Alcohols. To a solution of the sugar in dry dichloromethane (15 mmol/100 mL) were added pyridinium chlorochromate (PCC) and molecular sieves (4A, powder). After completion of the reaction, ether was added. The ethereal mixture was applied on a silica gel column, and the column was eluted with ether. Fractions containing the oxidized product were evaporated. The aldehydes or ketones were subjected to the next step directly.

Standard Procedure for the Wittig Olefination or the Horner–Emmons Olefination of the 3-Uloses. The Wittig olefination was performed as follows. A solution of sugar in dry benzene (4 mmol/30 mL) with [(ethoxycarbonyl)methylene]triphenylphosphorane was refluxed. After completion of the reaction, the solvent was removed by evaporation. To the residue was added petroleum ether. After the mixture was stored at 5 °C overnight, the precipitated triphenylphosphine oxide was removed by filtration. The filtrate was evaporated, and the residue was chromatographed on a silica gel column to separate the *E* and *Z* isomers.

The Horner–Emmons olefination was performed as follows. To a suspension of sodium hydride (60% emulsion in mineral oil, washed with hexane several times) in dry THF (8.5 mmol of the sugar/20 mL) was added diethyl [(ethoxycarbonyl)methyl]-phosphonate (2 molar equiv). After the mixture was stirred for 30 min at 0 °C, a solution of the sugar (8.5 mmol/40 mL) was added. The mixture was stirred at ambient temperature for 1 h and diluted with water (500 mL). The aqueous solution was extracted with dichloromethane, and the extracts were dried (Na_2SO_4). After evaporation of the extracts, the residue was chromatographed on a silica column to separate the *E* and *Z* isomers.

Standard Procedure for Diisobutylaluminum Hydride (DIBAL-H) Reduction of Esters. To a solution of the sugar in dry dichloromethane (5 mmol/20 mL) was added DIBAL-H (Aldrich, 1.5 M solution in toluene, 3–4 mol as equiv) at −30 °C under argon atmosphere. The mixture was stirred at that temperature. After completion of the reaction, water (5 mmol of the sugar/10 mL) was added. The resulting solid was removed by filtration and washed with dichloromethane. The filtrate was diluted with water. This was extracted with dichloromethane. After drying (Na_2SO_4), the combined extracts were evaporated. The residue was chromatographed on a silica gel column to yield the allyl alcohol or the primary alcohol.

Standard Procedure for Ortho Ester Claisen Rearrangement of the Allyl Alcohols with Triethyl Orthoacetate. A solution of the allyl alcohol in triethyl orthoacetate (1.4–1.5 mmol/5 mL) in the presence of a catalytic amount of propanoic acid (pH 4.5) was heated at 135 °C with a distilled ethanol reservoir. After completion of the reaction (TLC monitoring), the mixture was evaporated by using a rotary pump. The residue was chromatographed on a silica gel column to afford the rearranged product.

Standard Procedure for Conversion of the Formylmethyl Groups to the Methyl Groups by Thermal Decarbonylation. A solution of the sugar in distilled benzonitrile (3.7 mmol/15 mL) was refluxed in the presence of 10% palladium on charcoal (50% weight of the sugar). After completion of the reaction (TLC monitoring), the catalyst was removed by filtration through a Celite pad. The filtrate was evaporated by using a rotary pump, and the residue was chromatographed on a silica gel column.

Standard Procedure for Ozonolysis of the Vinyl Groups. Into a solution of the sugar in dry dichloromethane (0.1 mmol/3 mL) was bubbled a stream of ozone (ca. 3% volume in O_2) at −78 °C until a pale blue color of the solution indicated excess ozone. To the solution was added triphenylphosphine (an equimolar amount), and the mixture was gradually warmed to ambient

temperature. After evaporation of the mixture, the residue was chromatographed on a silica gel column to afford the aldehyde or the lactol.

(*E*)- and (*Z*)-3-Deoxy-3-*C*-[(ethoxycarbonyl)methylene]-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranose (2-*E* and 2-*Z*). The Wittig olefination of 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose (**1**) with [(ethoxycarbonyl)methylene]triphenylphosphorane, according to the reported procedure,[7] gave **2-*E*** (60%) and **2-*Z*** (22%) after repeated chromatography on silica gel. In our case, compound **1** was prepared by PCC oxidation of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose followed by passage of the reaction mixture through a silica gel column (ether elution). **2-*E***: mp 67–69 °C (lit.[7] mp 69–71 °C); $[\alpha]^{24}_D$ +118.7° (*c* 1.26, $CHCl_3$) [lit.[7] $[\alpha]^{29}_D$ +114° (*c* 0.9, $CHCl_3$)]. **2-*Z***: $[\alpha]^{23}_D$ +207.6° (*c* 0.97, $CHCl_3$) [lit.[7] $[\alpha]^{26}_D$ +214° (*c* 0.6, $CHCl_3$)].

(*E*)-3-Deoxy-3-*C*-[(hydroxymethyl)methylene]-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranose (3-*E*). DIBAL-H reduction of **2-*E*** (6.48 g, 19.7 mmol) for 1.5 h and chromatographic purification on silica gel (200 g, ethyl acetate/hexane, 1:2) afforded **3-*E*** (4.85 g, 86%) as a colorless syrup: TLC R_f 0.18 (ethyl acetate/hexane, 1:2); $[\alpha]^{23}_D$ +112.7° (*c* 1.13, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3470, 3000, 2940, 2880, 1450, 1370, 1240, 1215, 1155, 1065 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.36, 1.40, 1.44, 1.50 (3 H × 4, each s, 2 × $C(CH_3)_2$), 1.97–2.30 (1 H, br s, OH), 3.83–4.16 (3 H, m, H-5,6,6′), 4.19–4.48 (2 H, m, C=CHCH_2OH), 4.51–4.77 (1 H, m, H-4), 5.15–5.30 (1 H, m, H-2), 5.85 (1 H, d, *J* = 5.5 Hz, H-1), 6.12 (1 H, dd, *J* = 2.5 and 6 Hz, C=C*H*CH_2OH). High-resolution mass spectrum, calcd for $C_{13}H_{19}O_6$: *m/z* 271.1179. Found: M − CH_3, 271.1170.

(*Z*)-3-Deoxy-3-*C*-[(hydroxymethyl)methylene]-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranose (3-*Z*). DIBAL-H reduction of **2-*Z*** (1.75 g, 5.34 mmol) for 3 h and chromatographic purification on silica gel (50 g, ethyl acetate/hexane, 1:2) afforded **3-*Z*** (1.40 g, 92%) as needles: TLC R_f 0.24 (ethyl acetate/hexane, 1:2); mp 93–94 °C; $[\alpha]^{24}_D$ +96.2° (*c* 1.00, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3400, 2980, 1455, 1370, 1325, 1240, 1210, 1150, 1080 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.44, 1.50, 1.56 (3 H, 6 H, 3 H, each s, 2 × $C(CH_3)_2$), 2.83–3.03 (1 H, br s, OH), 3.77–4.34 (5 H, m, H-5,6,6′, C=CHCH_2OH), 4.93–5.20 (2 H, m, H-2,4), 5.87 (1 H, d, *J* = 5 Hz, H-1), 6.12–6.37 (1 H, m, C=C*H*CH_2OH). High-resolution mass spectrum, calcd for $C_{14}H_{23}O_6$: *m/z* 287.1493. Found: M + H, 287.1497.

3-*O*-Benzyl-1,2-*O*-isopropylidene-β-L-idofuranose (7). To a stirred solution of the crude 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose (**4**) (19.7 g), which was prepared from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (15.2 g, 58 mmol) according to the literature,[8] in dry pyridine (200 mL) was added methanesulfonyl chloride (14.8 mL, 190 mmol) at 0 °C. After the mixture was stirred at ambient temperature for 3 h, it was evaporated with toluene. The residue was partitioned between dichloromethane (700 mL) and water (700 mL), and the aqueous layer was extracted with dichloromethane (700 mL). The combined organic layers were dried (Na_2SO_4) and evaporated to afford a crude 5,6-di-*O*-mesyl derivative (**5**) (TLC R_f 0.30; ethyl acetate/hexane, 1:2), which was subjected to the next step without purification: ^1H NMR ($CDCl_3$) δ 1.28, 1.46 (3 H × 2, each s, $C(CH_3)_2$), 2.97, 3.04 (3 H × 2, each s, 2 × OSO_2CH_3), 4.10 (1 H, d, *J* = 4 Hz, H-3), 4.29–4.74 (6 H, m, H-2,4,6,6′, OC$H_2C_6H_5$), 5.11–5.30 (1 H, m, H-5), 5.86 (1 H, d, *J* = 4 Hz, H-1), 7.35 (5 H, s, $OCH_2C_6H_5$).

A solution of the above crude **5** in dry DMF (400 mL) in the presence of sodium benzoate (dried at 70 °C in vacuo for 4 h, 46.2 g, 304 mmol) was gently refluxed for 6 h with vigorous stirring. After removal of the solvent by evaporation, the residue was partitioned between ethyl acetate (500 mL) and water (500 mL). The aqueous layer was extracted with ethyl acetate (500 mL × 2), and the combined organic layers were dried (Na_2SO_4) and then evaporated to afford a crude 5,6-di-*O*-benzoyl-3-*O*-benzyl-1,2-*O*-isopropylidene-α-L-idofuranose (**6**), which was saponificated directly. In a separate small-scale preparation, pure **6** was obtained by chromatographic purification on silica gel as a colorless syrup: TLC R_f 0.68 (ethyl acetate/hexane, 1:2); $[\alpha]^{23}_D$ −15.2° (*c* 1.12, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3010, 2950, 1725, 1605, 1585, 1500, 1455, 1380 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.33, 1.55 (3 H × 2, each s, $C(CH_3)_2$), 4.11 (1 H, d, *J* = 4 Hz, H-3), 4.82–4.40 (6 H, m, H-2,4,6,6′, OC$H_2C_6H_5$), 5.80–5.98 (1 H, m, H-5), 6.03 (1 H, d, *J* = 4.5 Hz, H-1), 7.35 (5 H, s, $OCH_2C_6H_5$), 7.27–8.22 (10 H, m, 2 × $OCOC_6H_5$).

To a stirred solution of the above crude **6** in dichloromethane (200 mL) was added sodium methoxide in methanol (1 M solution, 150 mL, 150 mmol) at 0 °C. After the solution was stirred at ambient temperature for 2 h, it was evaporated. The residue was dissolved in water (500 mL) and extracted with ethyl acetate (400 mL × 4). The extracts were dried (Na_2SO_4) and evaporated. The residue was chromatographed on silica gel (500 g, ethyl acetate/hexane, 1:2 to 2:1). Fractions corresponding to R_f 0.22 (ethyl acetate/hexane, 1:1) were evaporated to afford **7** (7.3 g, 41% yield from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose): mp 82–83 °C (lit.[9] mp 86–87 °C, lit.[10] mp 89–90 °C); $[\alpha]^{25}_D$ −53.1° (*c* 0.98, $CHCl_3$) [lit.[9] $[\alpha]^{25}_D$ −61° (*c* 0.26, $CHCl_3$), lit.[10] $[\alpha]^{15}_D$ −48° (*c* 0.59, $CHCl_3$)]; IR $\nu_{max}^{CHCl_3}$ 3420, 2980, 2930, 2880 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.29, 1.43 (3 H × 2, each s, $C(CH_3)_2$), 2.61, 3.15 (1 H × 2, each br s, 2 × OH), 3.55–3.60 (2 H, m, H-6,6′), 3.96–4.25 (3 H, m, H-3,4,5), 4.55 (1 H, d, *J* = 4 Hz, H-2), 4.63 (2 H, s, OC$H_2C_6H_5$), 5.95 (1 H, d, *J* = 4 Hz, H-1), 7.33 (5 H, s, $OCH_2C_6H_5$).

1,2:5,6-Di-*O*-isopropylidene-β-L-idofuranose (9). To a solution of **7** (6.54 g, 21 mmol) in dry DMF (65 mL) were added 2,2-dimethoxypropane (6.45 mL, 53 mmol) and camphorsulfonic acid (0.98 g, 4.2 mmol). After the mixture was stirred at ambient temperature for 1 h, it was neutralized by addition of saturated aqueous $NaHCO_3$ (6 mL) and evaporated. The residue was partitioned between ethyl acetate (200 mL) and water (400 mL), and the aqueous layer was extracted with ethyl acetate (200 mL × 3). The combined organic layers were dried (Na_2SO_4) and evaporated to afford a crude 3-*O*-benzyl-1,2:5,6-di-*O*-isopropylidene-β-L-idofuranose (**8**), which was de-O-benzylated without purification. In a small-scale experiment, the crude **8** was purified on PTLC (ethyl acetate/hexane, 1:4). **8**: TLC R_f 0.70 (ethyl acetate/hexane, 1:4); $[\alpha]^{25}_D$ −73.7° (*c* 1.15, $CHCl_3$) [lit.[10] $[\alpha]^{25}_D$ −74° (*c* 0.40, $CHCl_3$)]; IR $\nu_{max}^{CHCl_3}$ 2970, 2910, 1445, 1365 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.23, 1.28, 1.33, 1.41 (3 H × 4, each s, 2 × $C(CH_3)_2$), 3.33 (1 H, dd, *J* = 7 and 9 Hz, H-5), 3.75–4.66 (7 H, m, H-2,3,4,6,6′, OC$H_2C_6H_5$), 5.90 (1 H, d, *J* = 4 Hz, H-1), 7.61 (5 H, s, $OCH_2C_6H_5$).

A solution of the above crude **8** in ethanol (60 mL) was hydrogenolyzed in the presence of Raney nickel T-4 under 3.4 kg/cm^2 initial hydrogen pressure (Parr apparatus) for 2 days at ambient temperature. After removal of the catalyst through Celite-pad, the filtrate was evaporated. The residue was chromatographed on silica gel (180 g, ethyl acetate/hexane, 1:5 to 1:2). Fractions corresponding to R_f 0.23 (ethyl acetate/hexane, 1:2) were evaporated to afford **9** (3.94 g, 71%): mp 147.5–149 °C (lit.[10] mp 153–154 °C); $[\alpha]^{25}_D$ −27.8° (*c* 1.00, $CHCl_3$) [lit.[10] $[\alpha]^{23}_D$ −25° (*c* 0.55, acetone)]; IR ν_{max}^{KBr} 3440, 2995, 2980, 2940, 1375, 1250, 1220, 1165, 1080 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30, 1.38 (3 H × 2, each s, $C(CH_3)_2$), 1.46 (6 H, s, $C(CH_3)_2$), 1.61–2.06 (1 H, br, OH), 3.73–4.62 (6 H, m, H-2,3,4,5,6,6′), 5.95 (1 H, d, *J* = 4 Hz, H-1).

1,2:5,6-Di-*O*-isopropylidene-β-L-*lyxo*-hexofuranos-3-ulose (10). To a solution of **9** (3.94 g, 15 mmol) in dichloromethane (100 mL) were added PCC (19.6 g, 90 mmol) and molecular sieves (4A, powder, 13 g). The mixture was stirred at ambient temperature for 15 h, and then ether (80 mL) was added. This ethereal mixture was applied on a silica gel column (100 g), and the column was eluted with ether. Fractions corresponding to R_f 0.61 (ethyl acetate/hexane, 1:2) were evaporated to afford **10** (3.70 g, 95%) as needles: mp 64–66 °C; $[\alpha]^{26}_D$ +120.9° (*c* 0.90, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 2970, 2900, 1760, 1450, 1365, 1250, 1210, 1145, 1085, 1060 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.31, 1.42, 1.44 (3 H, 6 H, 3 H, each s, 2 × $C(CH_3)_2$), 3.97–4.43 (5 H, m, H-2,4,5,6,6′), 6.11 (1 H, d, *J* = 5 Hz, H-1).

(*E*)- and (*Z*)-3-Deoxy-3-*C*-[(ethoxycarbonyl)methylene]-1,2:5,6-di-*O*-isopropylidene-β-L-*lyxo*-hexofuranose (11-*E* and 11-*Z*). The Horner–Emmons olefination of **10** (2.19 g, 8.5 mmol) and chromatographic separation of the products on silica gel (60 g, ethyl acetate/hexane, 1:10 to 1:5) afforded **11-*Z*** [0.504 g, 18%; R_f 0.81 (ethyl acetate/hexane, 1:3)] as a colorless syrup and **11-*E*** (2.104 g, 75%; R_f 0.52) as a colorless syrup. **11-*E***: $[\alpha]^{23}_D$ +174.9° (*c* 1.39, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 2960, 2900, 2870, 1715, 1670, 1440, 1360, 1205, 1130, 1050 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30 (3 H, t, *J* = 6 Hz, $COOCH_2CH_3$), 1.32, 1.40, 1.45 (3 H, 6 H, 3 H, each s, 2 × $C(CH_3)_2$), 3.81–4.35 (3 H, m, H-5,6,6′), 4.27 (2 H, q, *J* = 6 Hz, $COOCH_2CH_3$), 4.84 (1 H, br s, H-4), 5.61–5.70 (1 H, m, H-2), 5.82–6.05 (2 H, m, H-1, C=C*H*COOEt).

High-resolution mass spectrum, calcd for $C_{16}H_{28}O_7$: m/z 329.1598. Found: M + H, 329.1587. **11-*Z***: $[\alpha]^{27}_D$ +220.7° (*c* 1.375, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 2950, 2900, 1705, 1675, 1450, 1365, 1210, 1150, 1110, 1080, 1030, 1010 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30 (3 H, t, J = 7 Hz, $COOCH_2CH_3$), 1.30, 1.43 (3 H, 9 H, each s, 2 × $C(CH_3)_2$), 3.97–4.50 (3 H, m, H-5,6,6'), 4.19 (2 H, q, J = 7 Hz, $COOCH_2CH_3$), 5.04–5.20 (1 H, m, H-4), 5.48–5.63 (1 H, br s, H-2), 5.97 (1 H, d, J = 5 Hz, H-1), 6.06 (1 H, t, J = 2 Hz, C=CHCOOEt). High-resolution mass spectrum, calcd for $C_{16}H_{28}O_7$: m/z 329.1598. Found: M + H, 329.1603.

(*E*)-3-Deoxy-3-*C*-[(hydroxymethyl)methylene]-1,2:5,6-di-*O*-isopropylidene-β-L-*lyxo*-hexofuranose (12-*E*). DIBAL-H reduction of 11-***E*** (3.30 g, 10 mmol) for 2.5 h and chromatographic purification of the product on silica gel (60 g, ethyl acetate/hexane, 1:3 to 1:2) afforded 12-***E*** (2.46 g, 86%): mp 79–80 °C; TLC R_f 0.18 (ethyl acetate/hexane, 1:2); $[\alpha]^{25}_D$ +172.1° (*c* 1.01, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3470, 2990, 2950, 2900, 1455, 1375, 1245, 1215, 1160, 1125, 1060, 1015 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32, 1.39, 1.43 (3 H, 6 H, 3 H, each s, 2 × $C(CH_3)_2$), 2.31 (1 H, br s, OH), 3.90–4.17 (3 H, m, H-5,6,6'), 4.35 (2 H, d, J = 6 Hz, C=CHCH_2OH), 4.72–4.75 (1 H, br s, H-4), 5.14–5.30 (1 H, m, H-2), 5.70–5.89 (1 H, m, C=CHCH$_2$OH), 5.93 (1 H, d, J = 5 Hz, H-1). Anal. Calcd for $C_{14}H_{22}O_6$: C, 58.72; H, 7.75. Found: C, 58.42; H, 7.64.

(*Z*)-3-Deoxy-3-*C*-[(hydroxymethyl)methylene]-1,2:5,6-*O*-isopropylidene-β-L-*lyxo*-hexofuranose (12-*Z*). DIBAL-H reduction of 11-***Z*** (494 mg, 1.5 mmol) and chromatographic purification (15 g, ethyl acetate/hexane, 1:3 to 1:2) afforded 12-***Z*** (389 mg, 91%) as a colorless syrup: TLC R_f 0.15 (ethyl acetate/hexane, 1:2); $[\alpha]^{25}_D$ +167.3° (*c* 1.12, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3460, 2970, 2930, 2900, 1630, 1450, 1370, 1235, 1210, 1150, 1115, 1075, 1060, 1010 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32, 1.38, 1.40 (3 H, 6 H, 3 H, each s, 2 × $C(CH_3)_2$), 1.97–2.21 (1 H, br s, OH), 3.90–4.35 (5 H, m, H-5,6,6', C=CHCH_2OH), 4.93–5.12 (2 H, m, H-2,4), 5.88 (1 H, d, J = 6 Hz, H-1), 5.90–6.08 (1 H, m, C=CHCH$_2$OH). High-resolution mass spectrum, calcd for $C_{14}H_{23}O_6$: m/z 287.1492. Found: M + H, 287.1479.

Ortho Ester Claisen Rearrangement of 3-*E*. (2*R*,3*R*,4*R*,5*S*)-4-[(Ethoxycarbonyl)methyl]-2,3-(isopropylidenedioxy)-5-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-4-vinyltetrahydrofuran (13).[15] Ortho ester Claisen rearrangement of 3-***E*** (2.076 g, 7.25 mmol) for 9 h of heating with addition of propanoic acid at an appropriate interval to maintain the pH at 4.5 and chromatographic purification of the product on silica gel (60 g, ethyl acetate/hexane, 1:10 to 1:2) afforded 13 (1.65 g, 64%, 84% based on the consumed 3-***E***) as a colorless syrup and the recovered 3-***E*** (24%). 13: TLC R_f 0.72 (ethyl acetate/hexane, 1:2); $[\alpha]^{28}_D$ +18.9° (*c* 1.04, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 2995, 1735, 1640, 1450, 1375, 1215, 1165, 1070, 1025 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30 (3 H, t, J = 7.5 Hz, $COOCH_2CH_3$), 1.38, 1.43, 1.58 (6 H, 3 H, 3 H, each s, 2 × $C(CH_3)_2$), 2.60 (2 H, AB q, J = 15 Hz, CH_2COOEt), 3.91–4.26 (4 H, m, H-5, H-1,2,2' of the side chain), 4.19 (2 H, q, J = 7.5 Hz, $COOCH_2CH_3$), 5.08 (1 H, d, J = 4.5 Hz, H-3), 5.18–5.48 (2 H, m, CH=CH_2), 5.82 (1 H, d, J = 4.5 Hz, H-2), 6.13 (1 H, dd, J = 18.5 and 11 Hz, CH=CH_2). High-resolution mass spectrum, calcd for $C_{18}H_{29}O_7$: m/z 357.1910. Found: M + H, 357.1900.

Ortho Ester Claisen Rearrangement of 3-*Z*. Mixture of 13 and the 4*S* Epimer (14).[15] Ortho ester Claisen rearrangement of 3-***Z*** (497 mg, 1.74 mmol) for 7 h afforded a mixture of 13 and 14 (102.5 mg, 16%) [R_f 0.72 (ethyl acetate/hexane, 1:2)], and the unreacted 3-***Z*** was recovered (321.5 mg, 65%). On the basis of the integration ratio of the mixture in the ^1H NMR spectrum, an approximate ratio of 13 and 14 was 3:2 [AB quartets centered at δ 2.60 for 13 (J = 15 Hz) and δ 2.89 for 14 (J = 16 Hz)].

Ortho Ester Claisen Rearrangement of 12-*E*. (2*R*,3*R*,4*R*,5*S*)-4-[(Ethoxycarbonyl)methyl]-2,3-(isopropylidenedioxy)-5-[(1*S*)-1,2-(isopropylidenedioxy)ethyl]-4-vinyltetrahydrofuran (15).[15] Ortho ester Claisen rearrangement of 12-***E*** (500 mg, 1.7 mmol) for 4.5 h and chromatographic purification of the product on silica gel (15 g, ethyl acetate/hexane, 1:15, then 1:3) afforded 15 (340 mg, 55%, 79% based on the consumed 12-***E***), and 154 mg (31%) of 12-***E*** was recovered. 15: TLC R_f 0.88 (ethyl acetate/hexane, 1:2); $[\alpha]^{26}_D$ +20.1° (*c* 1.45, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3000, 2960, 2900, 1735, 1640, 1450, 1375, 1350, 1250, 1215, 1190, 1165, 1100, 1075, 1020 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (3 H, t, J = 7.5 Hz, $COOCH_2CH_3$), 1.31, 1.35, 1.39, 1.51 (3 H × 4, each s, 2 × $C(CH_3)_2$), 2.57 (2 H, AB q, J = 15.5 Hz, CH_2COOEt), 3.74 (1 H, q, J = 8.5 Hz, H-2 of the side chain), 3.88–4.31 (3 H, m, H-5, H-1,2' of the side chain), 4.13 (2 H, q, J = 7.5 Hz, $COOCH_2CH_3$), 4.97 (1 H, d, J = 4 Hz, H-3), 5.09–5.40 (2 H, m, CH=CH_2), 5.89 (1 H, d, J = 4 Hz, H-2), 6.07 (1 H, dd, J = 18 and 10.5 Hz, CH=CH_2). High-resolution mass spectrum, calcd for $C_{18}H_{28}O_7$: m/z 356.1833. Found: M, 356.1809.

Ortho Ester Claisen Rearrangement of 12-*Z*. Mixture of 15 and the 4*S* Epimer (16).[15] Ortho ester Claisen rearrangement of 12-***Z*** (438 mg, 1.5 mmol) for 6 h and purification on silica gel (15 g, ethyl acetate/hexane, 1:15, then 1:3) afforded a mixture of 15 and 16 (33 mg, 6%), and the unreacted 12-***Z*** was recovered (347 mg, 79%). On the basis of the ^1H NMR spectrum, an approximate ratio of 15 and 16 was 3:1 (doublets of H-3 protons centered at δ 4.99 for 15 and δ 4.80 for 16).

(2*R*,3*R*,4*R*,5*S*)-4-(Formylmethyl)-2,3-(isopropylidenedioxy)-5-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-4-vinyltetrahydrofuran (18).[15] DIBAL-H reduction of 13 (954 mg, 2.68 mmol) for 3 h at −78 °C and extractive workup afforded an approximately 1:2 mixture of (2*R*,3*R*,4*R*,5*S*)-4-(2-hydroxyethyl)-2,3-(isopropylidenedioxy)-5-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-4-vinyltetrahydrofuran (17) and 18 as a colorless syrup. In a small-scale experiment, 17 and 18 were separated on silica gel (ethyl acetate/hexane, 1:15 to 1:5). 17: TLC R_f 0.30 (ethyl acetate/hexane, 1:2); $[\alpha]^{29}_D$ +44.7° (*c* 0.97, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3470, 2990, 2940, 2890, 1640, 1450, 1380, 1370, 1310, 1245, 1215, 1165, 1070 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30, 1.37, 1.49 (6 H, 3 H, 3 H, each s, 2 × $C(CH_3)_2$), 1.60–2.13 (3 H, m, CH_2CH_2OH, OH), 3.80 (2 H, t, J = 7 Hz, CH_2CH_2OH), 3.92–4.23 (4 H, H-5, H-1,2,2' of the side chain), 4.60 (1 H, d, J = 4 Hz, H-3), 5.11–5.42 (2 H, m, CH=CH_2), 5.76 (1 H, d, J = 4 Hz, H-2), 6.00 (1 H, dd, J = 18 and 10.5 Hz, CH=CH_2).

The mixture of 17 and 18 obtained above was oxidized with PCC. After repeated chromatography on silica gel [(1) 20 g, ether; (2) 24 g, ethyl acetate/hexane, 1:15], 529 mg (63%) of 18 was obtained as a colorless syrup. TLC R_f 0.59 (ethyl acetate/hexane, 1:15); $[\alpha]^{28}_D$ +23.4° (*c* 1.03, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 2995, 2945, 1720, 1640, 1380, 1375, 1310, 1250, 1125, 1165, 1070, 1020 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32, 1.38, 1.53 (6 H, 3 H, 3 H, each s, 2 × $C(CH_3)_2$), 2.59 (2 H, dq, J = 18 and 3 Hz, CH_2CHO), 3.81–4.25 (4 H, m, H-5, H-1,2,2' of the side chain), 4.55 (1 H, d, J = 4.5 Hz, H-3), 5.12–5.46 (2 H, m, CH=CH_2), 5.74 (1 H, d, J = 4.5 Hz, H-2), 6.12 (1 H, dd, J = 18 and 12 Hz, CH=CH_2), 9.92 (1 H, t, J = 3 Hz, CH_2CHO). High-resolution mass spectrum, calcd for $C_{16}H_{23}O_6$: m/z 311.1493. Found: M − H, 311.1487.

(2*R*,3*R*,4*R*,5*S*)-2,3-(Isopropylidenedioxy)-5-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-4-methyl-4-vinyltetrahydrofuran (19).[15] Thermal decarbonylation of 18 (534 mg, 1.71 mmol) for 30 min and chromatographic purification on silica gel (25 g, hexane, then ethyl acetate/hexane, 1:20) afforded 19 (371 mg, 76%) as a colorless syrup: $[\alpha]^{26}_D$ +67.5° (*c* 1.28, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 2990, 2940, 1640, 1450, 1370, 1245, 1215, 1165, 1070, 1015 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.05 (3 H, s, CH_3), 1.29, 1.37, 1.52 (6 H, 3 H, 3 H, each s, 2 × $C(CH_3)_2$), 3.88–4.10 (4 H, m, H-5, H-1,2,2' of the side chain), 4.14 (1 H, d, J = 4.5 Hz, H-3), 5.06–5.38 (2 H, m, CH=CH_2), 5.76 (1 H, d, J = 4.5 Hz, H-2), 6.04 (1 H, dd, J = 18 and 10.5 Hz, CH=CH_2). High-resolution mass spectrum, calcd for $C_{15}H_{25}O_5$: m/z 285.1699. Found: M + H, 285.1695.

When the preparation of 19 from 13 (1.65 g, 4.63 mmol) was performed without purification on silica gel of the intermediates 17 and 18, an improved overall yield was achieved (71%) [in this case, a silica gel chromatography of 18 (ether elution) was necessary].

(2*R*,3*R*,4*R*,5*S*)-5-[(1*R*)-1,2-Dihydroxyethyl]-2,3-(isopropylidenedioxy)-4-methyl-4-vinyltetrahydrofuran (20).[15] A solution of 19 (901 mg, 3.17 mmol) in 50% aqueous acetic acid (20 mL) was stirred at ambient temperature for 15 h and evaporated. The residue was chromatographed on silica gel (27 g, ethyl acetate/hexane, 1:2). Fractions corresponding to R_f 0.13 (ethyl

(15) For the accurate nomenclature, compounds 13–29 and 34–39 are regarded as tetrasubstituted tetrahydrofurans. The C-2, C-3, C-4, and C-5 of the tetrahydrofurans are corresponding to C-1, C-2, C-3, and C-4 of their carbohydrate precursors such as compounds 1–12 and 30–33. The C-5 and C-6 of the carbohydrate precursors are regarded as a side chain on C-5 of the tetrahydrofurans.

acetate/hexane, 1:2) were evaporated to afford **20** (720 mg, 93%) as a colorless syrup: $[\alpha]^{24}_D$ +100.0° (*c* 1.16, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3420, 2990, 2945, 1640, 1450, 1410, 1370, 1310, 1240, 1215, 1165, 1070 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10 (3 H, s, CH_3), 1.28, 1.52 (3 H × 2, each s, $C(CH_3)_2$), 1.91–2.52 (2 H, br, 2 × OH), 3.53–3.83 (3 H, m, H-5, H-2,2′ of the side chain), 3.90–4.05 (1 H, m, H-1 of the side chain), 4.09 (1 H, d, *J* = 4.5 Hz, H-3), 5.07–5.36 (2 H, m, CH=CH_2), 5.73 (1 H, d, *J* = 4.5 Hz, H-2), 6.10 (1 H, dd, *J* = 18 and 10.5 Hz, C*H*=CH_2). High-resolution mass spectrum, calcd for $C_{12}H_{21}O_5$: *m/z* 245.1388. Found: M + H, 245.1402.

(2*R*,3*R*,4*R*,5*S*)-5-[(1*R*)-1-Hydroxy-2-(trimethylacetoxy)ethyl]-2,3-(isopropylidenedioxy)-4-methyl-4-vinyltetrahydrofuran (21).[15] Compound **20** (32.6 mg, 0.13 mmol) in a mixture of dichloromethane (2 mL) and pyridine (0.2 mL) was trimethylacetylated with trimethylacetyl chloride (0.025 mL, 0.195 mmol) for 1.5 h at 0 °C. Dilution of the mixture with dichloromethane (8 mL), washing the solution with water (5 mL × 2), then drying the organic layer (Na_2SO_4), and evaporation of the organic layer afforded a crude **21**, which was purified on silica gel (1 g; ethyl acetate/hexane, 1:10) to afford a pure **21** (36.5 mg, 83%) as a colorless syrup: TLC R_f 0.51 (ethyl acetate/hexane, 1:2); $[\alpha]^{26}_D$ +73.6° (*c* 1.80, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3490, 2960, 1720, 1635, 1475, 1450, 1365, 1280, 1240, 1210, 1160, 1065 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.14 (3 H, s, CH_3), 1.23 (9 H, s, $OCOC(CH_3)_3$), 1.29, 1.52 (3 H × 2, each s, $C(CH_3)_2$), 1.90–2.31 (1 H, br, OH), 3.77–4.50 (4 H, m, H-5, H-1,2,2′ of the side chain), 4.13 (1 H, d, *J* = 4.5 Hz, H-3), 5.11–5.40 (2 H, m, CH=CH_2), 5.80 (1 H, d, *J* = 4.5 Hz, H-2), 6.15 (1 H, dd, *J* = 18.5 and 10.5 Hz, C*H*=CH_2). High-resolution mass spectrum, calcd for $C_{17}H_{29}O_6$: *m/z* 329.1962. Found: M + H, 329.1959.

(2*R*,3*R*,4*R*,5*S*)-5-[(1*R*)-1-Hydroxy-2-(trimethylacetoxy)ethyl]-4-formyl-2,3-(isopropylidenedioxy)-4-methyltetrahydrofuran (22).[15] Ozonolysis of **21** (34 mg, 0.1 mmol) and chromatographic purification of the product (1.2 g, ethyl acetate/hexane, 1:5) afforded **22** (31 mg, 91%) as a colorless syrup: $[\alpha]^{24}_D$ +80.8° (*c* 1.48, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3470, 2990, 2950, 2890, 1725, 1480, 1450, 1375, 1285, 1215, 1165, 1070, 1020 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.18 (3 H, s, CH_3), 1.27 (9 H, s, $OCOC(CH_3)_3$), 1.30, 1.55 (3 H × 2, each s, $C(CH_3)_2$), 2.65–3.04 (1 H, br, OH), 3.68–3.95 (1 H, m, H-1 of the side chain), 4.08–4.73 (3 H, m, H-5, H-2,2′ of the side chain), 4.50 (1 H, d, *J* = 4 Hz, H-3), 5.88 (1 H, d, *J* = 4 Hz, H-2), 9.75 (1 H, s, CHO). High-resolution mass spectrum, calcd for $C_{16}H_{26}O_7$: *m/z* 330.1677. Found: M, 330.1678.

(2*R*,3*R*,4*R*,5*S*)-4-(2-Hydroxyethyl)-2,3-(isopropylidenedioxy)-5-[(1*S*)-1,2-(isopropylidenedioxy)ethyl]-4-vinyltetrahydrofuran (23).[15] DIBAL-H reduction of **15** (1.984 g, 5.6 mmol) for 2 h at −30 °C and purification on silica gel (60 g, ethyl acetate/hexane, 1:2) afforded **23** (1.60 g, 91%): mp 85–87 °C; $[\alpha]^{26}_D$ +37.8° (*c* 0.92, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3500, 3000, 2950, 2900, 1640, 1460, 1420, 1375, 1320, 1250, 1220, 1165, 1065, 1015 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32, 1.36, 1.40, 1.53 (3 H × 4, each s, 2 × $C(CH_3)_2$), 1.67–2.04 (2 H, m, CH_2CH_2OH), 3.31–4.31 (7 H, m, H-5, H-1,2,2′ of the side chain, CH_2CH_2OH), 4.56 (1 H, d, *J* = 4 Hz, H-3), 5.05–5.45 (2 H, m, CH=CH_2), 5.90 (1 H, d, *J* = 4 Hz, H-2), 6.05 (1 H, dd, *J* = 18 and 12.5 Hz, C*H*=CH_2). Anal. Calcd for $C_{16}H_{26}O_6$: C, 61.13; H, 8.34. Found: C, 60.95; H, 8.33.

(2*R*,3*R*,4*R*,5*S*)-4-(Formylmethyl)-2,3-(isopropylidenedioxy)-5-[(1*S*)-1,2-(isopropylidenedioxy)ethyl]-4-vinyltetrahydrofuran (24).[15] To a stirred solution of **23** (1.38 g, 4.4 mmol) in benzene (14 mL) were added dimethyl sulfoxide (2.8 mL), pyridine (0.53 mL, 6.6 mmol), trifluoroacetic acid (0.51 mL, 6.6 mmol), and dicyclohexylcarbodiimide (7.26 g, 35 mmol). The mixture was stirred at ambient temperature for 2 h. The precipitated dicyclohexylurea was removed by filtration, and the filtrate was evaporated. The residue was triturated with chloroform, and the urea precipitate was removed. The filtrate was evaporated. This procedure was repeated until almost the urea was removed. The residue was chromatographed on silica gel (40 g, ethyl acetate/hexane, 1:3). Fractions corresponding to R_f 0.49 (ethyl acetate/hexane, 1:3) were evaporated to afford **24** (1.17 g, 85%) as a colorless syrup: $[\alpha]^{26}_D$ +37.2° (*c* 1.15, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3000, 2945, 2895, 1720, 1640, 1450, 1375, 1310, 1250, 1215, 1160, 1070, 1015 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30, 1.35, 1.40, 1.52 (3 H × 4, each s, 2 × $C(CH_3)_2$), 2.67 (2 H, d, *J* = 2.5 Hz, CH_2CHO), 3.70–4.31 (4 H, m, H-5, H-1,2,2′ of the side chain), 4.55 (1 H, d, *J* = 4 Hz, H-3), 5.05–5.47 (2 H, m, CH=CH_2), 5.77 (1 H, d, *J* = 4 Hz, H-2), 6.09 (1 H, dd, *J* = 18 and 11 Hz, C*H*=CH_2), 9.87 (1 H, t, *J* = 2.5 Hz, CH_2CHO). High-resolution mass spectrum, calcd for $C_{16}H_{24}O_6$: *m/z* 311.1492. Found: M − H, 311.1491.

(2*R*,3*R*,4*R*,5*S*)-2,3-(Isopropylidenedioxy)-5-[(1*S*)-1,2-(isopropylidenedioxy)ethyl]-4-methyl-4-vinyltetrahydrofuran (25).[15] Thermal decarbonylation of **24** (1.17 g, 3.7 mmol) for 1 h and purification on silica gel (50 g, ethyl acetate/hexane, 1:5) afforded **25** (558 mg, 52%): mp 87–88.5 °C; TLC R_f 0.75 (ethyl acetate/hexane, 1:2); $[\alpha]^{26}_D$ +54.8° (*c* 1.14, $CHCl_3$); IR ν_{max}^{KBr} 2980, 2930, 2880, 1640, 1450, 1420, 1380, 1370, 1310, 1285, 1250, 1215, 1160, 1060 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.04 (3 H, s, CH_3), 1.30, 1.35, 1.40, 1.55 (3 H × 4, each s, 2 × $C(CH_3)_2$), 3.38–3.64, 3.72–4.20 (4 H, m, H-5, H-1,2,2′ of the side chain), 4.10 (1 H, d, *J* = 4 Hz, H-3), 5.04–5.38 (2 H, m, CH=CH_2), 5.87 (1 H, d, *J* = 4 Hz, H-2), 6.06 (1 H, dd, *J* = 18 and 11 Hz, C*H*=CH_2). Anal. Calcd for $C_{15}H_{24}O_5$: C, 63.36; H, 8.51. Found: C, 63.35; H, 8.60.

(2*R*,3*R*,4*R*,5*S*)-2,3-(Isopropylidenedioxy)-5-[(1*R*)-1,2-bis[(methylsulfonyl)oxy]ethyl]-4-methyl-4-vinyltetrahydrofuran (26).[15] To a stirred solution of **20** (92 mg, 0.38 mmol) in pyridine (5 mL) was added methanesulfonyl chloride (0.11 mL, 1.52 mmol) at 0 °C. The mixture was stirred at ambient temperature for 1 h and evaporated. The residue was diluted with water (10 mL) and extracted with ethyl acetate (5 mL × 3). The extracts were dried (Na_2SO_4) and evaporated. The residue was chromatographed on silica gel (3 g, ethyl acetate/hexane, 1:2), and fractions corresponding to R_f 0.78 (ethyl acetate/hexane, 1:2) were evaporated to afford **26** (135 mg, 90%) as a colorless syrup: $[\alpha]^{25}_D$ +41.2° (*c* 1.20, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3030, 3000, 2950, 1640, 1450, 1410, 1355, 1240, 1220, 1175, 1070, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.17 (3 H, s, CH_3), 1.31, 1.55 (3 H × 2, each s, $C(CH_3)_2$), 3.05, 3.09 (3 H × 2, each s, 2 × OSO_2CH_3), 4.17 (1 H, d, *J* = 4 Hz, H-3), 4.27 (1 H, d, *J* = 8.5 Hz, H-5), 4.49, 4.52 (1 H × 2, each AB q, *J* = 11 Hz, H-2,2′ of the side chain), 4.77–4.98 (1 H, m, H-1 of the side chain), 5.12–5.42 (2 H, m, CH=CH_2), 5.78 (1 H, d, *J* = 4 Hz, H-2), 6.06 (1 H, dd, *J* = 16.5 and 11.5 Hz, C*H*=CH_2). High-resolution mass spectrum, calcd for $C_{14}H_{25}O_9S_2$: *m/z* 401.0939. Found: M + H, 401.0943.

(2*R*,3*R*,4*R*,5*S*)-5-[(1*S*)-1,2-Bis(benzoyloxy)ethyl]-2,3-(isopropylidenedioxy)-4-methyl-4-vinyltetrahydrofuran (27) and (2*R*,3*R*,4*R*,5*S*)-5-[(1*S*)-2-(Benzoyloxy)-1-hydroxyethyl]-2,3-(isopropylidenedioxy)-4-methyl-4-vinyltetrahydrofuran (28).[15] A solution of **26** (135 mg, 0.34 mmol) in DMF (5 mL) containing sodium benzoate (dried at 60 °C in vacuo for 6 h, 195 mg, 1.36 mmol) was gently refluxed for 5 h with vigorous stirring. The mixture was diluted with water (25 mL) and extracted with ethyl acetate (15 mL × 3). The extracts were dried (Na_2SO_4) and evaporated. The residue was chromatographed on silica gel (8 g, ethyl acetate/hexane, 1:30, 1:20, 1:15, then 1:5). Fractions corresponding to R_f 0.83 (ethyl acetate/hexane, 1:2) were evaporated to afford **27** (65 mg, 43%) as a waxy solid. Fractions corresponding to R_f 0.45 were evaporated to afford **28** (12 mg, 11%) as a colorless syrup. **27**: mp 130–133.5 °C; $[\alpha]^{26}_D$ +18.7° (*c* 1.26, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 2880, 1715, 1635, 1595, 1580, 1440, 1380, 1370, 1340, 1310, 1275, 1255, 1210, 1160, 1090, 1065, 1010 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.15 (3 H, s, CH_3), 1.30, 1.56 (3 H × 2, each s, $C(CH_3)_2$), 4.15 (1 H, d, *J* = 4 Hz, H-3), 4.20–4.71 (3 H, m, H-5 and H-2,2′ of the side chain), 5.16–5.46 (2 H, m, CH=CH_2), 5.51–5.75 (1 H, m, H-1 of the side chain), 5.88 (1 H, d, *J* = 4 Hz, H-2), 6.10 (1 H, dd, *J* = 18 and 11.5 Hz, C*H*=CH_2), 7.26–8.20 (10 H, m, 2 × $OCOC_6H_5$). High-resolution mass spectrum, calcd for $C_{26}H_{29}O_7$: *m/z* 453.1910. Found: M + H, 453.1900. **28**: $[\alpha]^{32}_D$ +42.9° (*c* 1.11, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3490, 3060, 2980, 2930, 1720, 1635, 1595, 1580, 1445, 1410, 1380, 1310, 1270, 1210, 1160, 1110, 1070 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.13 (3 H, s, CH_3), 1.32, 1.54 (3 H × 2, each s, $C(CH_3)_2$), 2.58–2.88 (1 H, m, OH), 4.19 (1 H, d, *J* = 5 Hz, H-3), 3.88–4.51 (4 H, m, H-5 and H-1,2,2′ of the side chain), 5.12–5.40 (2 H, m, CH=CH_2), 5.89 (1 H, d, *J* = 5 Hz, H-2), 5.98–6.22 (1 H, m, C*H*=CH_2), 7.31–8.18 (5 H, m, $OCOC_6H_5$).

(2*R*,3*R*,4*R*,5*S*)-5-[(1*S*)-1,2-Dihydroxyethyl]-2,3-(isopropylidenedioxy)-4-methyl-4-vinyltetrahydrofuran (29).[15] **From 27.** O-Debenzoylation of **27** (60 mg, 0.13 mmol) in dichloromethane (2 mL) with sodium methoxide (1 M solution in methanol, 0.45 mL, 0.45 mmol) for 2 h, extractive workup (ethyl acetate), and then purification on silica gel (3 g, ethyl acetate/hexane, 1:4, 1:2) afforded **29** (25 mg, 76%) as a colorless syrup: TLC R_f 0.28 (ethyl acetate/hexane, 3:1); $[\alpha]^{26}_D$ +69.9° (*c* 0.89,

$CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3510, 2975, 2920, 1635, 1445, 1410, 1370, 1310, 1240, 1210, 1160, 1075, 1010 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08 (3 H, s, CH_3), 1.30, 1.55 (3 H × 2, each s, $C(CH_3)_2$), 2.08–2.90 (2 H, br, 2 × OH), 3.40–3.84 (3 H, m, H-1,2,2′ of the side chain), 4.02 (1 H, d, J = 5.5 Hz, H-5), 4.14 (1 H, d, J = 4 Hz, H-3), 5.08–5.39 (2 H, m, CH=CH_2), 5.83 (1 H, d, J = 4 Hz, H-2), 6.05 (1 H, dd, J = 18 and 11.5 Hz, CH=CH_2). High-resolution mass spectrum, calcd for $C_{12}H_{21}O_5$: m/z 245.1388. Found: M + H, 245.1396.

From 28. Compound **28** was O-debenzoylated as described in the case of **27** to afford **29** (6 mg, 69%).

O-Isopropylidenation of Compound 29. A solution of **29** (29 mg, 0.12 mmol) in DMF (1 mL) containing 2,2-dimethoxypropane (0.036 mL, 0.30 mmol) and *d*-camphor-10-sulfonic acid (5.5 mg, 0.02 mmol) was stirred at ambient temperature for 30 min and then neutralized with a drop of saturated aqueous $NaHCO_3$. After evaporation of the mixture, the residue was diluted with water (10 mL) and extracted with ethyl acetate (5 mL × 3). The extracts were dried (Na_2SO_4) and evaporated. The residue was chromatographed on silica gel (2 g, ethyl acetate/hexane, 1:10), and fractions corresponding to R_f 0.75 (ethyl acetate/hexane, 1:2) were evaporated to afford **25** (29 mg, 86%). Compound **25** was identical with **25** derivatized from the Claisen rearrangement product **15** in all respects (mp, $[\alpha]_D$, IR, and ^1H NMR).

1,2:5,6-Di-*O*-isopropylidene-β-D-altrofuranose (30). This compound was prepared from D-altrose according to the reported procedure.[13] D-Altrose was also prepared on a 2-g scale from D-glucose by the reported method.[14] **30**: mp 84–85 °C (lit.[13] mp 87–88 °C); $[\alpha]^{23}_D$ +24.3° (*c* 1.03, acetone) [lit.[13] $[\alpha]_D$ +28.5° (*c* 0.4, acetone)]; ^1H NMR ($CDCl_3$) δ 1.30, 1.33, 1.40, 1.50 (3 H × 4, each s, 2 × $C(CH_3)_2$), 2.79–3.03 (1 H, br, OH), 3.70–4.50 (4 H, H-4,5,6,6′), 4.52 (1 H, d, J = 4.5 Hz, H-2), 5.85 (1 H, d, J = 4.5 Hz, H-1).

(*E*)- and (*Z*)-3-Deoxy-3-*C*-[(ethoxycarbonyl)methylene]-1,2:5,6-di-*O*-isopropylidene-β-D-*arabino*-hexofuranose (32-*E* and 32-*Z*). PCC (2.52 g, 11.7 mmol) oxidation of **30** (1.217 g, 4.68 mmol) in dichloromethane (30 mL) in the presence of molecular sieves (4A, powder, 4.5 g) for 16 h and passage of the mixture through silica gel (ether elution) gave 1,2:5,6-di-*O*-isopropylidene-β-D-*arabino*-hexofuranos-3-ulose (**31**) (880 mg) as a colorless syrup, which was subjected to Wittig olefination directly. Wittig reaction of **31** with [(ethoxycarbonyl)methylene]triphenylphosphorane (1.777 g, 5.11 mmol) in refluxing benzene (30 mL) for 2 h, removal of the triphenylphosphine oxide, and repeated chromatography of the crude products on silica gel [(1) 65 g, ethyl acetate/hexane, 1:20, 1:15, then 1:12; (2) 19 g, ethyl acetate/hexane, 1:20, then 1:10; (3) PTLC (ethyl acetate/hexane, 1:5)] afforded **32-*E*** (519 mg, 34% from **30**) and **32-*Z*** (544 mg, 35% from **30**). **32-*E***: TLC R_f 0.36 (ethyl acetate/hexane, 1:4); mp 64.5–68 °C; $[\alpha]^{24}_D$ −112.8° (*c* 1.19, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3000, 2950, 2900, 1725, 1680, 1480, 1450, 1375, 1345, 1300, 1255, 1220, 1160, 1140, 1095, 1055, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.31 (3 H, t, J = 7 Hz, $COOCH_2CH_3$), 1.32, 1.38, 1.43, 1.51 (3 H × 4, each s, 2 × $C(CH_3)_2$), 3.69–4.41 (4 H, m, H-4,5,6,6′), 4.21 (2 H, q, J = 7 Hz, $COOCH_2CH_3$), 5.65 (1 H, d, J = 4 Hz, H-2), 5.79 (1 H, d, J = 4 Hz, H-1), 6.12 (1 H, s, C=CHCOOEt). Anal. Calcd for $C_{16}H_{24}O_7$: C, 58.53; H, 7.37. Found: C, 58.54; H, 7.31.

32-*Z*: TLC R_f 0.30 (ethyl acetate/hexane, 1:4); mp 105.5–108 °C; $[\alpha]^{24}_D$ +44.7° (*c* 1.46, $CHCl_3$); IR ν_{max}^{KBr} 3000, 2995, 2990, 2940, 2905, 2900, 1720, 1715, 1480, 1455, 1385, 1375, 1350, 1340, 1320, 1290, 1280, 1270, 1260, 1255, 1230, 1210, 1160, 1125, 1100 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30 (3 H, t, J = 7 Hz, $COOCH_2CH_3$), 1.33, 1.40, 1.58 (6 H, 3 H, 3 H, each s, 2 × $C(CH_3)_2$), 4.00–4.59 (3 H, m, H-5,6,6′), 4.19 (2 H, q, J = 7 Hz, $COOCH_2CH_3$), 4.86 (1 H, d, J = 4 Hz, H-2), 5.40 (1 H, d, J = 7.5 Hz, H-4), 5.80 (1 H, d, J = 4 Hz, H-1), 6.11 (1 H, s, C=CHCOOEt). Anal. Calcd for $C_{16}H_{24}O_7$: C, 58.53; H, 7.37. Found: C, 58.54; H, 7.28.

(*E*)-3-Deoxy-3-*C*-[(hydroxymethyl)methylene]-1,2:5,6-di-*O*-isopropylidene-β-D-*arabino*-hexofuranose (33-*E*). DIBAL-H reduction of **32-*E*** (509 mg, 1.55 mmol) for 4 h and chromatographic purification on silica gel (20 g, ethyl acetate/hexane, 1:3, then 1:2) afforded **33-*E*** (402 mg, 91%) as a colorless syrup: TLC R_f 0.15 (ethyl acetate/hexane, 1:2); $[\alpha]^{26}_D$ −77.3° (*c* 1.19, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3370, 3000, 2950, 2890, 1450, 1375, 1245, 1215, 1060, 1045 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.35, 1.42, 1.50 (6 H, 3 H, 3 H, each s, 2 × $C(CH_3)_2$), 2.37–2.60 (1 H, br, OH), 3.93–4.45 (6 H, m, H-4,5,6,6′, C=CHCH_2OH), 5.17 (1 H, d, J = 4 Hz, H-2), 5.76 (1 H, d, J = 4 Hz, H-1), 6.03 (1 H, t, J = 6 Hz, C=CHCH_2OH). High-resolution mass spectrum, calcd for $C_{13}H_{19}O_6$: m/z 271.1180. Found: M − CH_3, 271.1179.

(*Z*)-3-Deoxy-3-*C*-[(hydroxymethyl)methylene]-1,2:5,6-di-*O*-isopropylidene-β-D-*arabino*-hexofuranose (33-*Z*). DIBAL-H reduction of **32-*Z*** (534 mg, 1.63 mmol) and extractive workup gave a TLC-homogeneous (R_f 0.14, ethyl acetate/hexane, 1:2) **33-*Z*** (316 mg, 68%) as a colorless syrup: $[\alpha]^{26}_D$ −48.0° (*c* 0.69, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3370, 3000, 2950, 2890, 1450, 1380, 1375, 1325, 1245, 1210, 1160, 1070 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.35, 1.40, 1.50, 1.56 (3 H × 4, each s, 2 × $C(CH_3)_2$), 2.86–3.10 (1 H, br, OH), 3.96–4.42 (5 H, m, H-5,6,6′, C=CHCH_2OH), 4.61–4.75 (1 H, m, H-4), 4.83 (1 H, d, J = 4 Hz, H-2), 5.70 (1 H, d, J = 4 Hz, H-1), 6.12 (1 H, t, J = 6 Hz, C=CHCH_2OH). High-resolution mass spectrum, calcd for $C_{13}H_{19}O_6$: m/z 271.1179. Found: M − CH_3, 271.1175.

Ortho Ester Claisen Rearrangement of 33-*E*. (2*S*,3*S*,4*S*,5*S*)-4-[(Ethoxycarbonyl)methyl]-2,3-(isopropylidenedioxy)-5-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-4-vinyltetrahydrofuran (34).[15] Ortho ester Claisen rearrangement of **33-*E*** (402 mg, 1.41 mmol) for 9 h and purification of the product on silica gel (20 g, ethyl acetate/hexane 1:15) afforded **34** (317 mg, 63%) as a colorless syrup: TLC R_f 0.68 (ethyl acetate/hexane, 1:2); $[\alpha]^{24}_D$ +4.1° (*c* 1.62, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 2990, 2940, 2870, 1730, 1635, 1475, 1450, 1415, 1370, 1340, 1310, 1285, 1245, 1210, 1160, 1065 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27 (3 H, t, J = 7 Hz, $COOCH_2CH_3$), 1.33, 1.38, 1.52 (6 H, 3 H, 3 H, each s, 2 × $C(CH_3)_2$), 2.55 (2 H, s, CH_2COOEt), 3.78–4.26 (3 H, m, H-1,2,2′ of the side chain), 4.15 (2 H, q, J = 7 Hz, $COOCH_2CH_3$), 4.41–4.68 (1 H, m, H-5), 4.77 (1 H, d, J = 4 Hz, H-3), 5.11–5.47 (2 H, m, CH=CH_2), 5.71 (1 H, d, J = 4 Hz, H-2), 6.22 (1 H, dd, J = 17 and 12 Hz, CH=CH_2). High-resolution mass spectrum, calcd for $C_{17}H_{25}O_7$: m/z 341.1598. Found: M − CH_3, 341.1594.

Ortho Ester Claisen Rearrangement of 33-*Z*. Ortho ester Claisen rearrangement of **33-*Z*** (316 mg, 1.11 mmol) for 13 h and chromatographic purification on silica gel afforded **34** (160 mg, 41%), which was identical with the rearranged product from **33-*E*** in all respects (TLC, $[\alpha]_D$, IR, and ^1H NMR).

(2*S*,3*S*,4*S*,5*S*)-4-(2-Hydroxyethyl)-2,3-(isopropylidenedioxy)-5-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-4-vinyltetrahydrofuran (35) and (2*S*,3*S*,4*S*,5*S*)-4-(Formylmethyl)-2,3-(isopropylidenedioxy)-5-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-4-vinyltetrahydrofuran (36).[15] DIBAL-H reduction of **34** (302 mg) at −78 °C for 2 h and chromatographic purification on silica gel (15 g, ethyl acetate/hexane, 1:8, then 1:3) afforded **35** (52 mg, 19%) as a colorless syrup and **36** (193 mg, 73%) as a colorless syrup. **35**: TLC R_f 0.17 (ethyl acetate/hexane, 1:2); $[\alpha]^{22}_D$ −3.4° (*c* 1.00, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3450, 2970, 2920, 2870, 1630, 1445, 1370, 1245, 1205, 1160, 1060 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.29, 1.33, 1.38, 1.53 (3 H × 4, each s, 2 × $C(CH_3)_2$), 1.73–2.07 (3 H, m, CH_2CH_2OH), 3.71–4.19 (5 H, m, H-5, H-2,2′ of the side chain, CH_2CH_2OH), 4.45–4.73 (1 H, m, H-1 of the side chain), 4.55 (1 H, d, J = 4 Hz, H-3), 5.19–5.58 (2 H, m, CH=CH_2), 5.80 (1 H, d, J = 4 HZ, H-2), 6.21 (1 H, J = 18 and 12 Hz, CH=CH_2). High-resolution mass spectrum, calcd for $C_{15}H_{23}O_6$: m/z 299.1493. Found: M − CH_3, 299.1492. **36**: TLC R_f 0.50 (ethyl acetate/hexane, 1:2); $[\alpha]^{22}_D$ −4.9° (*c* 1.83, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 2970, 2925, 2870, 1720, 1635, 1445, 1370, 1245, 1205, 1155, 1060 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.29, 1.32, 1.37, 1.53 (3 H × 4, each s, 2 × $C(CH_3)_2$), 2.61 (2 H, d, J = 2 Hz, CH_2CHO), 3.79–4.21 (3 H, m, H-5, H-2,2′ of the side chain), 4.44–4.73 (1 H, m, H-1 of the side chain), 4.49 (1 H, d, J = 4 Hz, H-3), 5.12–5.53 (2 H, m, CH=CH_2), 5.77 (1 H, d, J = 4 Hz, H-2), 6.34 (1 H, dd, J = 18 and 12 Hz, CH=CH_2), 9.80 (1 H, t, J = 2 Hz, CH_2CHO). High-resolution mass spectrum, calcd for $C_{15}H_{21}O_6$: m/z 297.1336. Found: M − CH_3, 297.1328.

PCC (2 molar equiv) oxidation of **35** (48 mg, 0.15 mmol) and a short silica gel column purification of the mixture (ether elution) gave **36** (36 mg, 75%).

(2*S*,3*S*,4*S*,5*S*)-2,3-(Isopropylidenedioxy)-5-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-4-methyl-4-vinyltetrahydrofuran (37).[15] Thermal decarbonylation of **36** (227 mg, 0.73 mmol) for 30 min and silica gel chromatography (12 g, hexane, then ethyl acetate/hexane, 1:30) of the reaction product afforded **37** (111 mg, 53%) as a colorless syrup: TLC R_f 0.51 (ethyl acetate/hexane, 1:4); $[\alpha]^{21}_D$ −9.8° (*c* 1.65, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 2990, 2940, 2880,

1640, 1450, 1415, 1370, 1310, 1285, 1245, 1210, 1160, 1060 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.21 (3 H, s, CH_3), 1.27, 1.35, 1.53 (3 H, 6 H, 3 H, each s, 2 × $C(CH_3)_2$), 3.60 (1 H, d, J = 9 Hz, H-5), 3.78–4.12 (2 H, m, H-2,2′ of the side chain), 4.19 (1 H, d, J = 4 Hz, H-3), 4.62 (1 H, m, H-1 of the side chain), 5.11–5.37 (2 H, m, CH=CH_2), 5.78 (1 H, d, J = 4 Hz, H-2), 6.30 (1 H, ddd, J = 17, 11 and 2 Hz, CH=CH_2). High-resolution mass spectrum, calcd for $C_{14}H_{21}O_5$: m/z 269.1387. Found: M - CH_3, 269.1381.

(2*S*,3*S*,4*S*,5*S*)-5-[(1*R*)-1,2-Dihydroxyethyl]-2,3-(isopropylidenedioxy)-4-methyl-4-vinyltetrahydrofuran (38).[15] A solution of **37** (99 mg, 0.35 mmol) in 50% aqueous trifluoroacetic acid (2 mL) was stirred at ambient temperature for 6 h and evaporated. The residue was chromatographed on silica gel (3 g, ethyl acetate/hexane, 1:3, then 1:2) to afford **38** (79 mg, 93%) as a colorless syrup: $[\alpha]^{22}_D$ -14.6° (c 1.41, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3440, 2990, 2950, 2880, 1640, 1450, 1420, 1375, 1320, 1295, 1250, 1210, 1160, 1140, 1060 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.24 (3 H, s, CH_3), 1.28, 1.53 (3 H × 2, each s, $C(CH_3)_2$), 2.47–2.82 (2 H, m, 2 × OH), 3.60 (1 H, d, J = 10 Hz, H-5), 3.69–3.84 (2 H, m, H-2,2′ of the side chain), 4.20 (1 H, d, J = 4 Hz, H-3), 4.09–4.34 (1 H, m, H-1 of the side chain), 5.22–5.50 (2 H, m, CH=CH_2), 5.85 (1 H, d, J = 4 Hz, H-2), 6.40 (1 H, dd, J = 18 and 11 Hz, CH=CH_2). High-resolution mass spectrum, calcd for $C_{11}H_{17}O_5$: m/z 229.1074. Found: M - CH_3, 299.1073.

(2*S*,3*S*,4*S*,5*S*)-5-[(1*R*)-1-Hydroxy-2-(trimethylacetoxy)ethyl]-2,3-(isopropylidenedioxy)-4-methyl-4-vinyltetrahydrofuran (39).[15] Trimethylacetylation of **38** (77 mg, 0.32 mmol) in dichloromethane (3 mL), pyridine (0.3 mL), and triethylamine (0.04 mL) with trimethylacetyl chloride (0.098 mL, 0.8 mmol) for 17 h, then extractive workup (dichloromethane), and chromatographic purification (3 g, ethyl acetate/hexane, 1:10) afforded **39** (93 mg, 90%) as a colorless syrup: TLC R_f 0.57 (ethyl acetate/hexane, 1:10); $[\alpha]^{23}_D$ +4.5° (c 1.39, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3510, 2970, 2940, 2910, 2870, 1725, 1635, 1480, 1455, 1415, 1395, 1370, 1325, 1280, 1265, 1245, 1210 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.21 (3 H, s, $OCOC(CH_3)_3$), 1.22 (3 H, s, CH_3), 1.28, 1.52 (3 H × 2, each s, $C(CH_3)_2$), 2.18–2.33 (1 H, br, OH), 3.55 (1 H, d, J = 9 Hz, H-5), 4.18 (1 H, d, J = 4 Hz, H-3), 4.27–4.54 (3 H, m, H-1,2,2′ of the side chain), 5.18–5.44 (2 H, m, CH=CH_2), 5.81 (1 H, d, J = 4 Hz, H-2), 6.38 (1 H, dd, J = 19 and 11 Hz, CH=CH_2). High-resolution mass spectrum, calcd for $C_{16}H_{25}O_6$: m/z 313.1649. Found: M - CH_3, 313.1649.

(1*S*,3*S*,7*S*,8*S*,9*R*,11*R*)-9-Hydroxy-5,5,8-trimethyl-11-[(trimethylacetoxy)methyl]-2,4,6,10-tetraoxatricyclo-[6.3.0^{1,8}.0^{3,7}]undecane (40). Ozonolysis of **39** (38.5 mg, 0.12 mmol), triphenylphosphine treatment, and chromatographic purification of the product (3 g, ethyl acetate/hexane, 1:2) afforded **40** (29.2 mg, 75%) as a colorless syrup: TLC R_f 0.43 (ethyl acetate/hexane, 1:10, then 1:5); $[\alpha]^{21}_D$ -25.8° (c 1.42, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3450, 2970, 2930, 2800, 1725, 1470, 1380, 1370, 1280, 1240, 1210, 1160, 1090, 1050 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.22 (12 H, s, CH_3 and $OCOC(CH_3)_3$), 1.30, 1.54 (3 H × 2, each s, $C(CH_3)_2$), 1.83–1.97 (1 H, m, OH), 3.40 (1 H, d, J = 4 Hz, H-1), 4.10–4.42 (4 H, m, H-7,11, $CH_2OCOC(CH_3)_3$), 5.50 (1 H, d, J = 4 Hz, H-9), 5.95 (1 H, d, J = 4 Hz, H-3). High-resolution mass spectrum, calcd for $C_{15}H_{23}O_7$: m/z 315.1442. Found: M - CH_3, 315.1433.

(1*S*,3*S*,7*S*,8*S*,9*R*,11*R*)-9-Acetoxy-5,5,8-trimethyl-11-[(trimethylacetoxy)methyl]-2,4,6,10-tetraoxatricyclo-[6.3.0^{1,8}.0^{3,7}]undecane (41). Acetylation of **40** (10.1 mg, 0.03 mmol) with acetic anhydride (0.5 mL) in pyridine (0.5 mL) for 3 h and chromatographic purification on silica gel (1 g, ethyl acetate/hexane, 1:2) afforded **41** (11.6 mg, quantitatively): TLC R_f 0.50 (ethyl acetate/hexane, 1:2); mp 111.5–113 °C; $[\alpha]^{21.5}_D$ -77.1° (c 0.70, $CHCl_3$); IR ν_{max}^{KBr} 2980, 2960, 2935, 1745, 1730, 1480, 1460, 1400, 1385, 1375, 1360, 1290, 1270, 1250, 1240, 1210, 1170, 1145, 1100, 1090 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.20 (3 H, s, CH_3), 1.21 (9 H, s, $C(CH_3)_3$), 1.31, 1.54 (3 H × 2, each s, $C(CH_3)_2$), 2.06 (3 H, s, $OCOCH_3$), 4.00–4.50 (5 H, m, H-1,7,11, $CH_2OCOC(CH_3)_3$), 5.93 (1 H, d, J = 4 Hz, H-3), 6.41 (1 H, s, H-9). Anal. Calcd for $C_{18}H_{28}O_8$: C, 58.05; H, 7.58. Found: C, 57.79; H, 7.44.

Rotational Barriers of Bis(2,6-disubstituted-aryl) Ketones and Bis(2,6-disubstituted-aryl)methanes and -ethanes and Their Mono- and Bis(tricarbonylchromium) Complexes†

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Bis(2,6-dialkylphenyl)methanes and -ethanes and bis(2,6-dialkylphenyl) ketones and their mono- and bis(tricarbonylchromium) complexes have been prepared and their variable-temperature NMR spectra recorded. Monocomplexation increases the isomerization barrier of bis(2-ethyl-6-methylphenyl) ketone (**2**) from 51.4 kJ/mol to 83.2/84.4 kJ/mol but does not significantly change the corresponding barriers for bis(2-ethyl-6-methylphenyl)methane (**1**) and 1,1-bis(2-ethyl-6-methylphenyl)ethane (**3**). The barriers of the bis complexes are found to be almost the same as those of the mono complexes. Monocomplexation of bis(2-*tert*-butyl-4,6-dimethylphenyl) ketone (**5**) yields two diastereomers which are stable at room temperature and separable by chromatography. The NMR spectra and possible isomerization pathways of ligands and complexes are discussed.

Compounds with two aryl rings attached to a central unit X, Ar_2X, are the simplest representatives of polyaryl compounds which may undergo correlated rotation,[1,2] the rotation of one ring thus causing rotation of the other. A previous study[3] has shown that in diaryl compounds Ar_2X, depending on the relative size of the aryl rings, the lowest energy pathway for isomerization can be either correlated rotation[4] of the aryl rings or topomerization involving nonflip mechanisms. Variable-temperature proton NMR spectroscopy indicates that the latter mechanism applies for 1-mesityl-1-phenylethane[6,7] and 2,4,6-triisopropyl-

† For a preliminary account of parts of this work, see: Schlögl, K. *J. Organomet. Chem.* **1986**, *300*, 219.

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