Claisen Rearrangements of 5,6-Dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*- and α-D-*ribo*-hept-5-eno-1,4-furanoses with Triethyl Orthoacetate[1)]

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The (*E*)- and (*Z*)-isomers (**2E** and **2Z**) of 3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hept-5-eno-1,4-furanose were subjected to Claisen rearrangement with triethyl orthoacetate. Possible two diastereomers were obtained as a 1 to 1 mixture from both of **2Z** and **2E**, and also from their 3-hydroxy or 3-siloxy derivatives. On the other hand, the rearrangement of the corresponding D-ribo derivative (**13Z**) and its 3-*O*-(*t*-butyldiphenylsilyl) derivative proceeded with a high level of diastereoselectivity. By contrast, the (*E*)-isomer of **13Z** showed no significant stereoselectivity, resulting in the formation of a diastereomeric mixture. The configurations of the introduced stereogenic centers by the rearrangements were unambiguously established by chemical transformations.

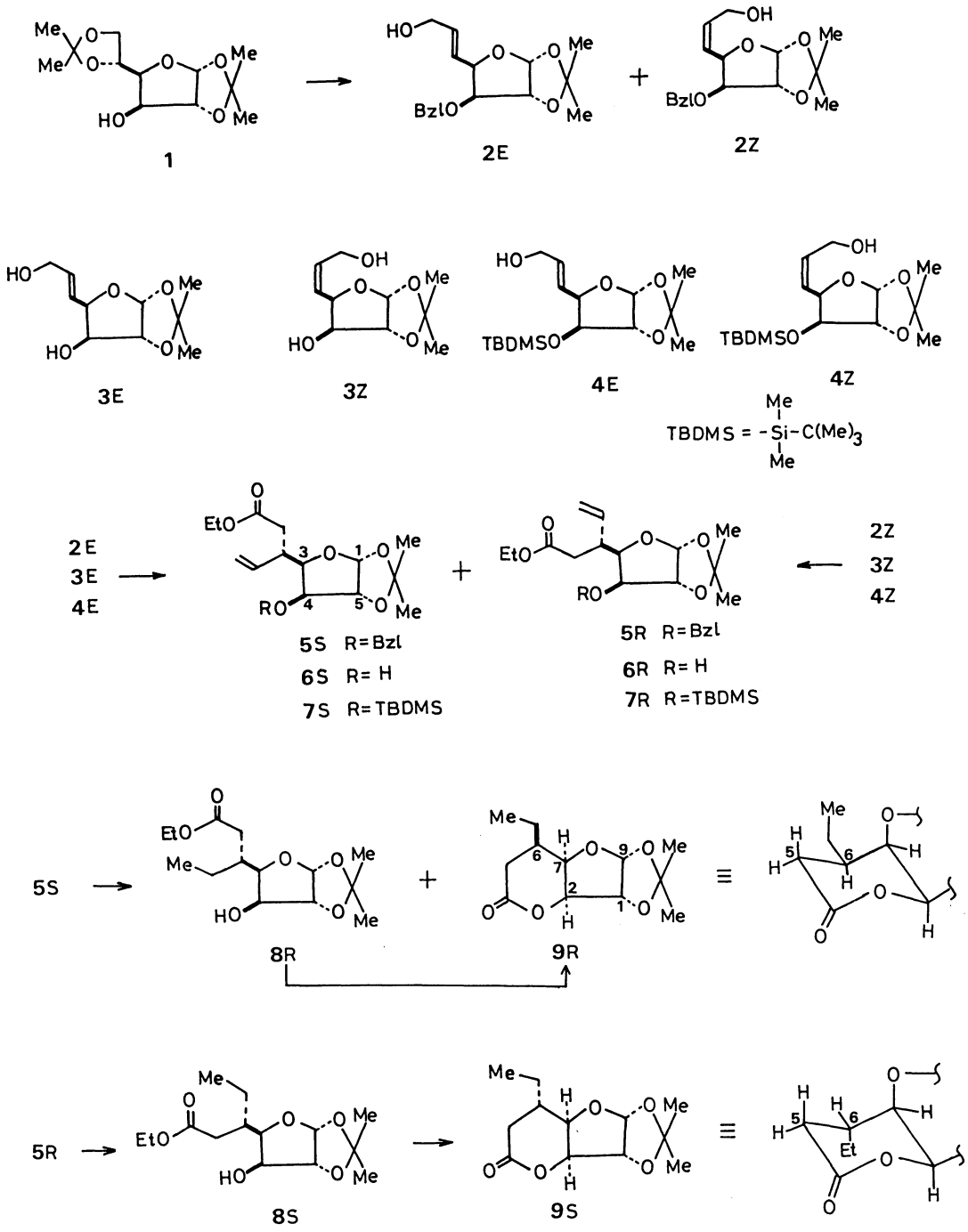
Recent extensive studies on [3.3] sigmatropic rearrangements represented by the Claisen-type rearrangement, as one of the promising protocol for stereoselective carbon-carbon bond forming reactions, widen their values through simple access to complex carbon frameworks found in natural products.[2)] In these several years, we focus our efforts on investigation of the ortho ester Claisen (Johnson-Claisen type) rearrangement of the carbohydrate-derived substrates.[3)] As a result, some versatile chiral building blocks, especially for natural products synthesis, are now available.[4)] In the course of pursuit of versatile chirons,[5)] herein, we report the Claisen rearrangement of two 5,6-dideoxyhept-5-eno-1,4-furanoses and some of their derivatives with triethyl orthoacetate. In the present work, the allyl alcohol part of each substrate is involved in the side chain on the furanose ring. These steric environments make the prediction of the stereochemical outcome of the rearrangement more difficult, in comparing with our previous results[3)] obtained by the rearrangements of 3-deoxy-3-*C*-[3-hydroxy-1-propenyl]hexofuranoses with triethyl orthoesters.

Results and Discussion

Rearrangement of Derivatives of 5,6-Dideoxy-α-D-*xylo*-hept-5-eno-1,4-furanose. We pursued first the Claisen rearrangement of some derivatives of 5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hept-5-eno-1,4-furanose, namely, *E* and *Z* isomers of **2**, **3**, and **4**. The allyl alcohols **2E** and **2Z** were prepared from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**1**) according to the known procedure.[6)] Compounds **3E** and **3Z** were prepared from **1** by standard functional group manipulation, namely, 1) selective removal of the 5,6-isopropylidene acetal by acid hydrolysis, 2) glycol cleavage with sodium periodate ($NaIO_4$), 3) Wittig olefination with (ethoxycarbonylmethylene)-triphenylphosphorane,[7)] followed by 4) diisobutylaluminum hydride (Dibal-H) reduction.[8)] The *O*-silyl derivatives **4E** and **4Z** were prepared from the 3-*O*-(*t*-butyldimethylsilyl) derivative of **1** by the analogous reaction sequence used for the preparation of **3**. In the preparation of **4**, acid hydrolysis (60% aqueous AcOH) of 3-*O*-(*t*-butyldimethylsilyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose was troublesome, and the desired mono isopropylidene derivative was obtained in 12% yield along with substantial amount of 1,2-*O*-isopropylidene-α-D-glucofuranose. We did not optimize the reaction conditions.

The Claisen rearrangement of **2E** with triethyl orthoacetate was performed according to the original procedure.[9)] By repeated silica-gel chromatography of the reaction mixture, two rearrangement products **5S** and **5R** were obtained in 42% and 40% yields, respectively. The unreacted **2E** was also recovered in 8% yield. The *Z* isomer **2Z** was exposed to the same reaction conditions, resulting in the non-stereoselective formation of **5S** (35%) and **5R** (29%) along with recovery of **2Z** (13%). Establishment of the introduced stereogenic centers in diastereomers **5S** and **5R** was achieved by chemical transformation (vide infra). The rearrangements were also explored for **3** and **4**. None of **3E**, **3Z**, **4E**, or **4Z** provided the rearrangement product stereoselectively. In the case of **3E**, two diastereomers **6S** and **6R** were obtained in an approximately 1:1.4 ratio.[10)] Besides, the *Z* isomer **3Z** gave two products in an approximately 1:1 ratio. The silyl ether **4E** gave an approximately 1.4:1 ratio of **7S** and **7R** in a combined yield of 79%,[11)] while the *Z*-isomer **4Z** provided a 55% combined yield of the diastereomeric mixture in an approximately 2:1 ratio with a slightly improved formation of **7S**.

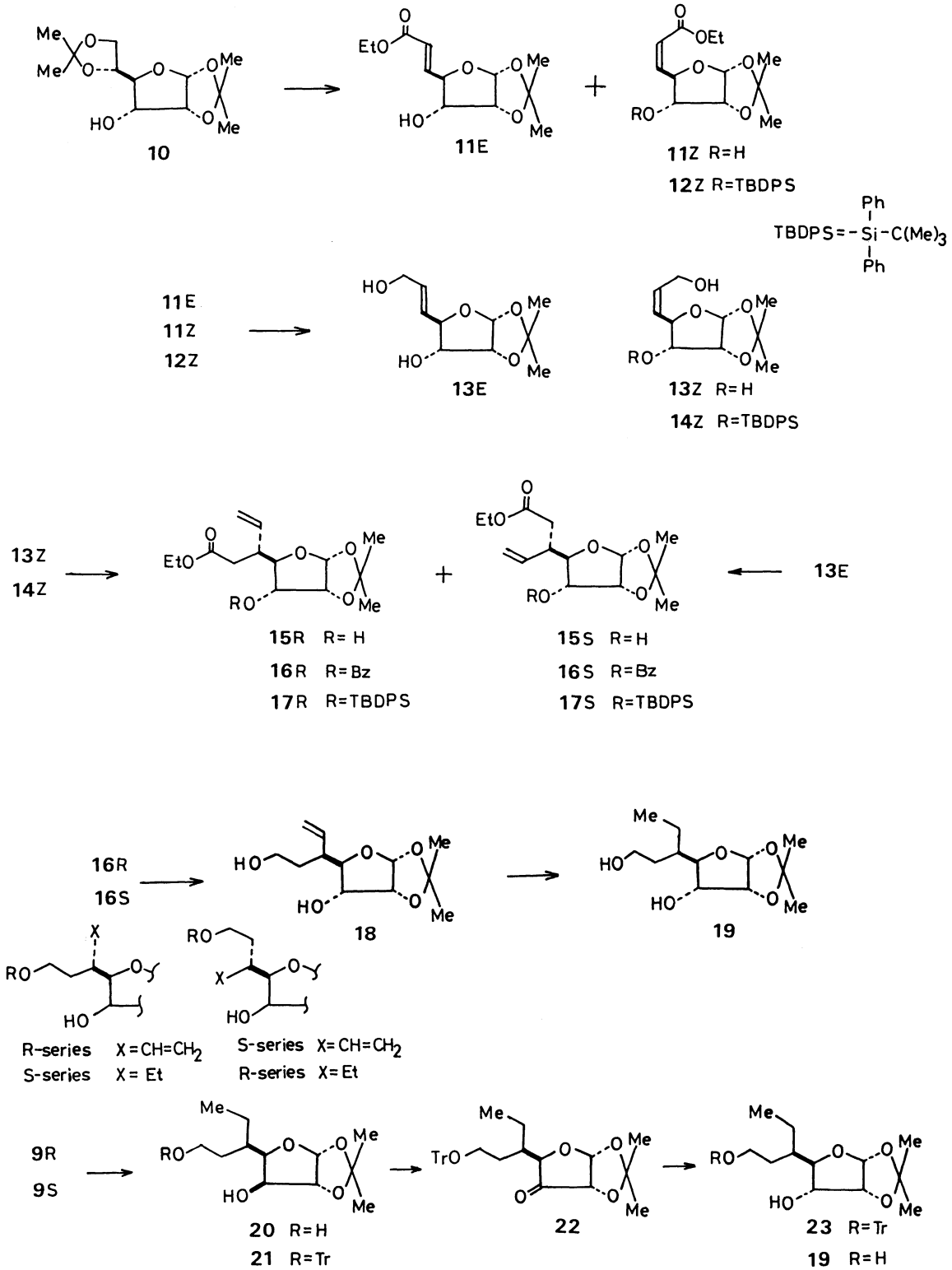
The newly introduced stereogenic centers in **5S** and **5R** were determined by the following transformations. The product with *S*-configuration **5S** was treated with cyclohexene in the presence of $Pd(OH)_2$ on charcoal resulting in the formation of a mixture of **8R** and **9R**. Under these reaction conditions, debenzylation and



saturation of the double bond took place. δ-Lactonization of **8R** to **9R** was promoted by passage of the mixture through silica gel. The mixture of **8R** and **9R** was treated with silica gel for completion of lactonization. Finally, the tricyclic δ-lactone **9R** was obtained in an overall yield of 66.5%. Analogously, the *R*-diastereomer **5R** was converted into **8S**. Interestingly, no lactonization was observed in this case. Acid (*p*-TsOH) catalyzed lactonization of **8S** smoothly gave the lactone **9S** in 61% from **5R**. Both of ^{1}H NMR spectra (400 MHz) of the tricyclic δ-lactones **9R** and **9S** clarified their structures. The conformations of **9R** and **9S** were also confirmed as depicted. In the ^{1}H NMR spectrum of **9R**, H-5_{ax} and 5_{eq} appeared at δ 2.40 and 2.53 with $J_{5ax,6}$=12.8 Hz, $J_{5eq,5ax}$=17.5 Hz and with $J_{5eq,6}$=5.3 Hz, $J_{5eq,5ax}$=17.5 Hz, respectively. On the other hand, those of **9S** appeared at δ 2.27 and 2.70 with $J_{5ax,6}$=6.8 Hz, $J_{5eq,5ax}$=16.6 Hz, and with $J_{5eq,6}$=5.4 Hz, $J_{5eq,5ax}$=16.6 Hz, respectively. These results indicate that the ethyl groups in **9R** and **9S** are equatorial- and axial-orientations, respectively. Therefore, configurations of the newly introduced stereogenic centers in **5S** and **5R** were unequivocally established.

Rearrangement of Derivatives of 5,6-Dideoxy-α-D-*ribo*-hept-5-eno-1,4-furanose. For pursuit of improving the stereoselectivity, we next executed the rearran-

gement of derivatives of 5,6-dideoxy-α-D-*ribo*-hept-5-eno-1,4-furanose, **13** and **14**. The standard procedures from the known 1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (**10**)[12] provided efficiently the substrates **13** and **14**. Namely, selective removal of the 5,6-isopropylidene acetal in **10** by acid hydrolysis, glycol cleavage of the 5,6-diol with $NaIO_4$ followed by Wittig reaction with (ethoxycarbonylmethylene)triphenylphosphorane resulted in the formation of α,β-unsaturated esters **11E** and **11Z**, which were readily separated by silica-gel chromatography, in 43% and 31% yields from **10**, respectively.[13] Dibal-H reduction of **11E** and **11Z** provided the allyl alcohols **13E** and **13Z** effectively. Besides, silylation of the *Z*-isomer **11Z** with *t*-butyldiphenylchlorosilane gave the silyl ether **12Z** quantitatively. Silylation was carried



out for *Z*-isomer **11Z** by reason that the rearrangement of the *Z*-isomer **13Z** proceeded with significant stereoselectivity (vide infra). Reduction of **12Z** gave the other substrate **14Z**.

The Claisen rearrangement of **13Z** with triethyl orthoacetate gave an inseparable mixture of **15R** and **15S** in a combined yield of 72%. To determine the ratio of **15R** and **15S** accurately, the mixture was converted into the benzoates **16R** and **16S**, which were readily separated by silica-gel chromatography. From the yields of **16R** and **16S**, the ratio of the rearrangement products **15R** and **15S** was determined to be 11 : 70. On the other hand, *E*-isomer **13E** provided a mixture of **15R** and **15S** in a combined yield of 71% with an approximately 1 : 1.3 ratio. *E*-Isomer **13E** showed no significant stereoselectivity. Furthermore, the rearrangement of the silylated derivative **14Z** proceeded with an improved stereoselectivity to afford an inseparable mixture of **17R** and **17S** in a combined yield of 48%. The ratio (approximately 1 : 8) of **17R** and **17S** was determined by conversion of the mixture into separable **16R** and **16S** by desilylation followed by benzoylation.

The stereochemical assignment of the introduced stereogenic centers in **15R** and **15S** was achieved as follows. Both benzoates **16R** and **16S** were converted into **19S** and **19R** via vinyl-alcohols **18R** and **18S** by $LiAlH_4$ reduction of the ester groups followed by hydrogenation of the vinyl groups. On the other hand, the stereochemically defined δ-lactones **9R** and **9S** were converted into diols **20R** and **20S** by $LiAlH_4$ reduction. Tritylation of **20R** and **20S** under the standard conditions gave mono-trityl ethers **21R** and **21S** quantitatively. Pyridinium chlorochromate (PCC) oxidation[14] of **21R** and **21S** and subsequent $NaBH_4$ reduction of the 3-uloses **22R** and **22S** provided **23R** and **23S**, respectively. As anticipated, the hydride attacks to **22R** and **22S** took place exclusively from the less hindered convex-face to give **23R** and **23S**. Exposure of **23R** to *p*-toluenesulfonic acid provided the detritylated product, which was found to be identical with **19R** by direct comparison (mp, IR, and ^1H NMR). The detritylated product of **23S** was identical with **19S** in all respects. Therefore, the structures of **15R** and **15S** were established.

One of the stereocontrolling factors in the Claisen rearrangement is, in general, a steric environment surrounding the six membered transition state that consists of the intermediary allylic ketene acetal. As concerns the stereochemical outcome of the aforementioned ortho ester Claisen rearrangements, it is most likely that the C-3 substituent of each substrate interacts with the intermediary allylic ketene acetal moiety. It was forecasted that the interactions occurred between the C-3 substituents in **2**, **3**, and **4** and each of the intermediary ketene acetal moiety were more severe than those occurred in the case of substrates **13** and **14**. Unexpectedly, the results of the present work revealed that the C-3 substituent in **2**, **3**, or **4** was not likely to work as a stereocontrolling factor, irrespective of its bulkiness or of the allylic geometry. On the contrary, the C-3 substituents of *ribo*-type substrates possessing *Z*-allyl alcohol part, i.e. **13Z** and **14Z**, seem to contribute largely for outcome of the high-stereoselectivity in their rearrangement reactions. In the case of **13Z** and **14Z**, the transition state (A) shown in Fig. 1, which leads the formation of the major *S*-rearrangement product, seems to be favorable than the alternative transition state (B). This assumption is based on that nonbonded interaction between the C-3 substituent and the ethoxy group in the ketene acetal moiety is not negligible in the case of transition state (B). Furthermore, the influence of this interaction on the stereoselectivity of the rearrangement would be proportional to the bulkiness of the C-3 substituent. In fact, the stereoselectivity was slightly improved when a hydroxy group (i.e. **13Z**) was substituted by a (*t*-butyldiphenylsilyl)oxy group (i.e. **14Z**). Speculation of the transtion state, made by using Dreiding models, also reveals that high-stereoselective formation of either diastereomer is not expected for **13E**. No preferential transition state is considered in this case. Although we have no valid evidence for these explanations, the Claisen rearrangement protocol demonstrated in the present work is a practical access to highly functionalized enantiomerically pure building blocks.

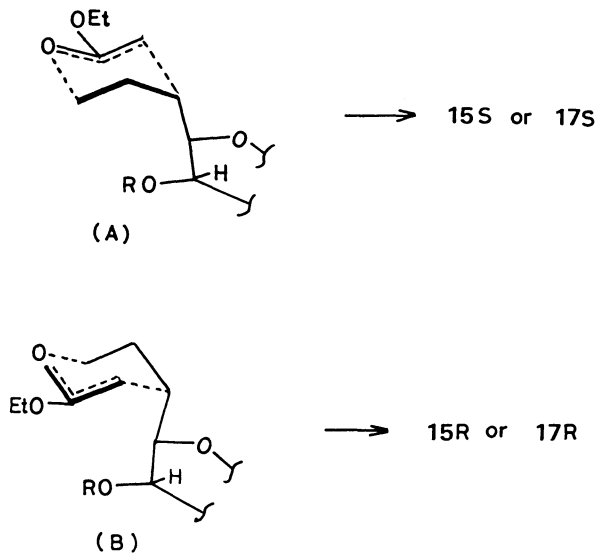


Fig. 1.

Experimental[15]

***E* and *Z* Isomers of 3-*O*-Benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hept-5-eno-1,4-furanose (2E and 2Z).** These compounds were prepared according to the reported procedure.[6] **2E**: TLC R_f 0.15 (AcOEt/hexane 1 : 3); $[\alpha]_D^{27}$ −60.9° (*c* 1.22, $CHCl_3$). **2Z**: TLC R_f 0.19 (AcOEt/hexane 1 : 3); $[\alpha]_D^{28}$−92.9° (*c* 1.10, $CHCl_3$).

***E* and *Z* Isomers of 5,6-Dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hept-5-eno-1,4-furanose (3E and 3Z).** 1,2-*O*-Isopropylidene-α-D-glucofuranose (2.39 g), which was obtained by hydrolysis of **1** with 80% aqueous AcOH, was subjected to $NaIO_4$ oxidation (3.0 g in aqueous MeOH, 3 : 5 v/v, 64 ml). The reaction mixture was filtered, and the filtrate was concentrated in vacuo to give an aldehyde, which was used without purification. The aldehyde was dissolved in benzene (50 ml) and (ethoxycarbonylmethylene)triphenylphosphorane (5.0 g) was added. The mixture was stirred for 45 min, and concentrated in vacuo. The residue was chromatographed on silica gel (EtOAc/hexane 1 : 4) to give a mixture of *E*- and *Z*- α,β-unsaturated esters and *Z*-δ-lactone (2.44 g). Dibal-H (1.5 mol dm^{-3} solution in $PhCH_3$, 19 ml) reduction of the mixture in CH_2Cl_2 (40 ml) at −60 °C, and silica-gel chromatographic purification of the reaction mixture (AcOEt/hexane 1 : 1) gave **3E** (509 mg, 22%), **3Z** (356 mg, 15%), and a diastereomeric mixture of the hemiacetals derived from *Z*-δ-lactone (584 mg, 25%). **3E**: mp 70—71.5 °C, TLC R_f 0.43 (AcOEt); $[\alpha]_D^{87}$ −54.1° (*c* 1.53, $CHCl_3$); IR (KBr) ν_{max} 3410, 3230, 2965, 2865, 1630, 1375 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=1.32, 1.50 (3H each, 2 s), 3.50, 3.67 (1H each, 2 br s), 4.08 (1H, d, *J*=2.4 Hz), 4.16 (2H, br s), 4.54 (1H, d, *J*=3.7 Hz), 4.68 (1H, dd, *J*=1.0 and 4.8 Hz), 5.78 (1H, ddt, *J*=15.6, 4.8, and 1.0 Hz), 5.94 (1H, d, *J*=3.7 Hz), 6.05 (1H, ddt, *J*=15.6, 4.9, and 1.0 Hz). Found: C, 55.49; H, 7.19%. Calcd for $C_{10}H_{16}O_5$: C, 55.55; H, 7.46%. **3Z:** mp 90.5—92 °C, TLC R_f 0.51 (AcOEt); IR (KBr) ν_{max} 3435, 2990, 2855, 1640, 1460 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=1.33, 1.51 (3H each, 2 s), 2.98, 3.20 (1H each, 2 s), 4.12—4.19 (2H, m), 4.30 (1H, dd, *J*=6.8 and 13.1 Hz), 4.57 (1H, d, *J*=3.9 Hz), 4.93 (1H, d, *J*=6.4 Hz), 5.65 (1H, dd, *J*=6.4 and 11.5 Hz), 5.91—5.98 (2H, m). Found: C, 55.54; H, 7.22%. Calcd for $C_{10}H_{16}O_5$: C, 55.55; H, 7.46%.

***E* and *Z* Isomers of 3-*O*-(*t*-Butyldimethylsilyl)-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hept-5-eno-1,4-furanose (4E and 4Z).** Compound **1** (5.00 g) was silylated with *t*-butylchlorodimethylsilane (4.36 g) in DMF (80 ml) in the presence of imidazole (1.23 g). Extractive work-up and chromatographic purification on silica gel gave the 3-*O*-silyl derivative (6.78 g, 94%) as a colorless oil, TLC R_f 0.18 (AcOEt/hexane 1:30): ^1H NMR (90 MHz, $CDCl_3$) δ=0.13, 0.14 (3H each, 2 s), 0.91 (9H, s), 1.32, 1.40, 1.49 (3H, 3H, 6H, 3 s), 4.04—4.26 (5H, m), 4.34 (1H, d, *J*=3.5 Hz), 5.87 (1H, d, *J*=3.5 Hz).

The 3-*O*-silyl derivative (6.77 g) was hydrolyzed with 60% aqueous AcOH (160 ml) and 1,4-dioxane (10 ml) for 30 min at room temperature. The mixture was concentrated in vacuo, and the residue was chromatographed on silica gel (EtOH/$PhCH_3$ 1:20) to give 3-*O*-(*t*-butyldimethylsilyl)-1,2-*O*-isopropylidene-α-D-glucofuranose (721 mg, 12%) as a colorless oil. This mono-isopropylidene derivative (721 mg) was dissolved in MeOH (26 ml) and $NaIO_4$ (534 mg) in H_2O (4.4 ml) was added. After stirring for 1.5 h, the mixture was filtered. The filtrate was concentrated in vacuo. The residue was dissolved in benzene (25 ml), (ethoxycarbonylmethylene)triphenylphosphorane (1.49 g) was added. The mixture was stirred for 1 h, concentrated in vacuo. The residue was triturated with petroleum ether. The precipitated triphenylphosphine oxide was removed, and the filtrate was concentrated in vacuo. The residue was chromatographed on silica gel (AcOEt/hexane 1 : 60) to give the *E*-α,β-unsaturated ester [407 mg, 51%, TLC R_f 0.59 (EtOH/$PhCH_3$ 1 : 30)] and the *Z*-α,β-unsaturated ester [346 mg, R_f 0.72 (EtOH/$PhCH_3$ 1 : 30)]. Each α,β-unsaturated ester was reduced with Dibal-H at −60 °C. After chromatographic purification of the reaction mixture on silica gel, **4E** (99%) and **4Z** (88%) were obtained. **4E**, TLC R_f 0.26 (AcOEt/hexane 1:3): $[\alpha]_D^{26}$ −42.4° (*c* 0.90, $CHCl_3$); IR (neat) ν_{max} 3425, 2925, 2850, 1470, 1460 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ=0.06, 0.09 (3H each, 2 s), 0.90 (9H, s), 1.33, 1.55 (3H each, 2 s), 4.09 (1H, d, *J*=2.9 Hz), 4.15, 4.19 (1H each, 2 s), 4.39 (1H, d, *J*=3.7 Hz), 4.61 (1H, dd, *J*=2.9 and 6.4 Hz), 5.81—5.94 (2H, m), 5.92 (1H, d, *J*=3.7 Hz). Found: C, 57.76; H, 8.83%. Calcd for $C_{16}H_{30}O_5Si$: C, 58.15; H, 9.15%. **4Z**, TLC R_f 0.21 (AcOEt/hexane 1 : 5): $[\alpha]_D^{25}$ −63.6° (*c* 1.28, $CHCl_3$); IR (neat) ν_{max} 3460, 2950, 2880, 1480, 1470 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ=0.07, 0.09 (3H each, 2 s), 0.89 (9H, s), 1.33, 1.51 (3H each, 2 s), 1.93 (1H, s), 4.08 (1H, d, *J*=2.9 Hz), 4.19—4.31 (2H, m), 4.40 (1H, d, *J*=3.6 Hz), 4.91 (1H, dd, *J*=2.9 and 7.4 Hz), 5.51—6.05 (2H, m), 5.93 (1H, d, *J*=3.6 Hz). Found: C, 57.90; H, 8.84%. Calcd for $C_{16}H_{30}O_5Si$: C, 58.15; H, 9.15%.

(1*R*,3*R*,4*S*,5*R*)-4-Benzyloxy-3-[(1*S*)- and (1*R*)-1-(ethoxycarbonyl)methyl-2-propenyl]-7,7-dimethyl-2,6,8-trioxabicyclo[3.3.0]octanes (5S and 5R). From 2E. The reaction was carried out under an argon atmosphere. A solution of **2E** (1.82 g, 5.9 mmol) in freshly distilled triethyl orthoacetate (20 ml) was heated in the presence of 0.013 ml of distilled propionic acid at 135 °C for 5 h. The reaction mixture was then concentrated in vacuo with an aid of $PhCH_3$. The residue was repeatedly chromatographed on silica gel (AcOEt/hexane 1 : 15). The rearrangement products **5S** (940 mg, 42%) and **5R** (901 mg, 40%) were obtained and **2E** (138 mg, 8%) was recovered. **5S**: mp 56—58 °C, R_f 0.21 (AcOEt/hexane 1 : 10); $[\alpha]_D^{28}$ −33.9° (*c* 0.83, $CHCl_3$); IR (neat) ν_{max} 3010, 2960, 2900, 1740, 1650, 1510, 1465, 1380, 1265, 1225 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=1.22 (3H, t, *J*=7.3 Hz), 1.31, 1.49 (3H each, 2 s), 2.39 (1H, dd, *J*=10.3 and 15.4 Hz), 2.81 (1H, dd, *J*=4.2 and 15.4 Hz), 3.17 (1H,dddd, *J*=4.2, 7.6, and 10.3 Hz), 3.82 (1H, d, *J*=3.0 Hz), 4.03 (1H, dd, *J*=3.0 and 10.3 Hz), 4.10 (2H, q, *J*=7.3 Hz), 4.47, 4.63 (2H each, 2 d, *J*=11.5 Hz), 4.58 (1H, d, *J*=3.9 Hz), 5.06 (1H, dd, *J*=1.5 and 10.3 Hz), 5.14 (1H, dd, *J*=1.5 and 18.8 Hz), 5.67 (1H, ddd, *J*=7.6, 10.3, and 18.8 Hz), 5.90 (1H, d, *J*=3.9 Hz), 7.28—7.37 (5H, m). Found: C, 66.88; H, 7.36%. Calcd for $C_{21}H_{28}O_6$: C, 67.00; H, 7.50%. **5R:** mp 47.5—49 °C, TLC R_f 0.19 (AcOEt/hexane 1 : 10); $[\alpha]_D^{28}$ −27.1° (*c* 0.98, $CHCl_3$); IR (neat) ν_{max} 2990, 2940, 1735, 1650, 1500, 1460, 1375, 1260 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=1.24 (3H, t, *J*=7.3 Hz), 1.32, 1.48 (3H each, 2 s), 2.16—2.28 (2H, m), 3.07—3.15 (1H, m), 3.85 (1H, d, *J*=3.3 Hz), 4.05 (1H, dd, *J*=3.3 and 9.5 Hz), 4.08 (2H, q, *J*=7.3 Hz), 4.46, 4.73 (2H each, 2 d, *J*=11.7 Hz), 4.64 (1H, d, *J*=3.9 Hz), 5.11 (1H, dd, *J*=1.5 and 10.3 Hz), 5.17 (1H, dd, *J*=1.5 and 17.1 Hz), 5.81 (1H, ddd, *J*=7.8, 10.3, and 17.1 Hz), 5.93 (1H, d, *J*=3.9 Hz), 7.30—7.37 (5H, m). Found: C, 66.78; H, 7.27%. Calcd for $C_{21}H_{28}O_6$: C, 67.00; H, 7.50%.

From 2Z. Compoud **2Z** (1.59 g) was subjected to the Claisen rearrangement under the same reaction conditions as above. Silica-gel chromatography of the reaction mixture gave 675 mg (35%) of **5S** and 563 mg (29%) of **5R**, and 202 mg (13%) of **2Z** was also recovered.

Claisen Rearrangement of 3E and 3Z and Successive $LiAlH_4$ Reduction of the Products. From 3E. Compound **3E** (550 mg) was heated at 135 °C in triethyl orthoacetate (5 ml) in the presence of catalytic propionic acid for 5.5 h.

The reaction mixture was concentrated in vacuo, and the residue was chromatographed on silica gel (AcOEt/hexane 1 : 6) to give a mixture of **6S**, **6R**, and their δ-lactone derivatives (472 mg). This mixture (472 mg) was reduced with $LiAlH_4$ (116 mg) in THF (24 ml) for 1 h. The mixture was quenched with H_2O, filtered, and the filtrate was concentrated in vacuo. The residue was chromatographed on silica gel (AcOEt/hexane 1 : 1) to give a diol derived from **6S** (144 mg, 23% from **3E**), a diol derived from **6R** (209 mg, 34%), and a mixture of them (21 mg, 3%). Diol derived from **6S**, TLC R_f 0.59 (AcOEt): $[\alpha]_D^{26}$+12.1° (*c* 1.99, $CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ=1.30, 1.49 (3H each, 2 s), 1.56—2.21 (2H, m), 2.49—2.86 (1H, m), 3.00 (2H, br s), 3.58—4.05 (5H, m), 4.49 (1H, d, *J*=4.0 Hz), 5.15 (1H, dd, *J*=2.7 and 8.4 Hz), 5.22 (1H, dd, *J*=2.7 and 17.8 Hz), 5.65 (1H, dd, *J*=8.4 and 17.8 Hz), 5.89 (1H, d, *J*=4.0 Hz). Diol derived from **6R**, TLC R_f 0.46 (AcOEt): $[\alpha]_D^{26}$=−32.9° (*c* 1.96, $CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ=1.30, 1.48 (3H each, 2 s), 1.42—1.87 (2H, m), 2.44—2.79 (1H, m), 3.34 (2H, br s), 3.47—4.18 (4H, m), 4.50 (1H, d, *J*=3.8 Hz), 5.07—5.24 (2H, m), 5.71 (1H, dd, *J*=9.2 and 17.8 Hz), 5.89 (1H, d, *J*=3.8 Hz).

From 3Z. Rearrangement of **3Z** (327 mg), and successive $LiAlH_4$ reduction of the products as described for **3E** resulted in formation of an approximately 1 : 1 mixture of the diols derived from **6S** and **6R** (103.5 mg, 28% from **3Z**). The ratio was estimated based on the ^1H NMR (400 MHz) spectral analysis, though the diastereomers were not separated.

(1*R*,3*R*,4*S*,5*R*)-4-(*t*-Butyldimethylsilyloxy)-3-[(1*S*)- and (1*R*)-1-(ethoxycarbonyl)methyl-2-propenyl]-7,7-dimethyl-2,5,8-trioxabicyclo[3.3.0]octanes (7S and 7R). From 4E. Compound **4E** (376 mg) was heated in triethyl orthoacetate (12 ml) at 135 °C in the presence of catalytic amount of propionic acid for 5 h. Concentration of the reaction mixture, and chromatographic purification of the residue on silica gel (AcOEt/hexane 1 : 25) gave **7S** (202 mg, 44%), **7R** (142 mg, 31%), and a mixture of **7S** and **7R** (16 mg, 4%). **7S:** TLC R_f 0.55 (AcOEt/hexane 1 : 5); $[\alpha]_D^{28}$−27.4° (*c* 1.23, $CHCl_3$); IR (neat) ν_{max} 2990, 2960, 2840, 1740, 1470 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ=0.08, 0.14 (3H each, 2 s), 0.92 (9H, s), 1.22 (3H, t, *J*=7.2 Hz), 1.31, 1.48 (3H each, 2 s), 2.22—2.78 (2H, m), 2.92—3.25 (1H, m), 3.92—4.11 (2H, m), 4.10 (2H, q, *J*=7.2 Hz), 4.36 (1H, d, *J*=3.7 Hz), 5.04—5.07 (1H, m), 5.15—5.17 (1H, m), 5.23—5.26 (1H, m), 5.85 (1H, d, *J*=3.7 Hz). **7R:** TLC R_f 0.48 (AcOEt/hexane 1 : 5); $[\alpha]_D^{28}$−17.5° (*c* 1.27, $CHCl_3$); IR (neat) ν_{max} 2990, 2960, 2860, 1740, 1640, 1470 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ=0.13, 0.16 (3H each, 2 s), 0.92 (9H, s), 1.23 (3H, t, *J*=7.1 Hz), 1.30, 1.47 (3H each, 2 s), 2.27—2.40 (2H, m), 2.84—3.21 (1H, m), 3.94—4.13 (2H, m), 4.11 (2H, q, *J*=7.1 Hz), 4.37 (1H, d, *J*=3.7 Hz), 5.05—5.06 (1H, m), 5.18—5.24 (1H, m), 5.67—5.78 (1H, m), 5.88 (1H, d, *J*=3.7 Hz).

From 4Z. As described above, compound **4Z** (114 mg) was subjected to the Claisen rearrangement to give **7S** (44 mg, 32%), **7R** (22 mg, 16%), and a mixture of **7S** and **7R** (9.5 mg, 7%).

(1*R*,2*S*,6*R*,7*R*,9*R*)-6-Ethyl-11,11-dimethyl-3,8,10,12-tetraoxatricyclo[7.3.0.0^{2,7}]dodecan-4-one (9R). A solution of **5S** (88 mg, 0.23 mmol) in a mixture of EtOH (3 ml) and freshly distilled cyclohexene (5 ml) was refluxed for 3 h in the presence of 20% $Pd(OH)_2$ on charcoal (133 mg). The catalyst was removed by filtration, washed with EtOH. The combined filtrate and washings were concentrated in vacuo. The residue was chromatographed on silica gel (AcOEt/hexane 1 : 5) to give **9R** (25 mg, 44%) and a mixture of the hydroxy ester **8R** and **9R** (37 mg). The mixture of **8R** and **9R** (37 mg) was dissolved in AcOEt/hexane (1/5 v/v 1.5 ml), then silica gel (0.2 g) was added. The mixture was kept standing at room temperature for 3.5 d. Then, the silica gel was removed by filtration, washed with AcOEt. The combined filtrate and washings were concentrated in vacuo. The residue was chromatographed on silica gel to give **9R** (12.5 mg, total 37.5 mg, 66.5%) as a colorless oil. **9R:** TLC R_f 0.61 (AcOEt/hexane 1 : 2); $[\alpha]_D^{25}$−8.8° (*c* 0.85, $CHCl_3$); IR (neat) ν_{max} 2970, 2950, 2890, 1745, 1460, 1375, 1300, 1220 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=0.99 (3H, t, *J*=7.5 Hz), 1.34, 1.52 (3H each, 2 s), 1.44—1.68 (2H, m), 1.97—2.06 (1H, m), 2.40 (1H, dd, *J*=12.8 and 17.5 Hz), 2.53 (1H, dd, *J*=5.3 and 17.5 Hz), 4.42 (1H, dd, *J*=2.0 Hz), 4.68 (1H, d, *J*=3.7 Hz), 4.70 (1H, d, *J*=2.0 Hz), 5.92 (1H, d, *J*=3.7 Hz). Found: C, 59.36; H, 7.26%. Calcd for $C_{12}H_{18}O_5$: C, 59.49; H, 7.49%.

(1*R*,2*S*,6*S*,7*R*,9*R*)-6-Ethyl-11,11-dimethyl-3,8,10,12-tetraoxatricyclo[7.3.0.0^{2,7}]dodecan-4-one (9S). As desdribed for the preparation of **9R**, 119 mg (0.32 mmol) of **5R** was analogously converted into crude **8S** (99.5 mg), which was lactonized directly. The crude **8S** (99.5 mg) was dissolved in benzene (3 ml) and *p*-TsOH (monohydrate, 15 mg) was added. The mixture was stirred at room temperature for 3 h, and saturated aqueous $NaHCO_3$ (2 ml) was added. This was diluted with benzene (15 ml) and washed with H_2O (10 ml×3). The organic phase was dried (Na_2SO_4) and concentrated in vacuo. The residue was chromatographed on silica gel (AcOEt/hexane 1 : 8) to give **9S** (47 mg, 61%), mp 69—70 °C, TLC R_f 0.69 (AcOEt/hexane 1 : 2); $[\alpha]_D^{24}$+28.8° (*c* 1.21, $CHCl_3$); IR (neat) ν_{max} 2970, 2940, 2870, 1730, 1460, 1370, 1250 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=1.03 (3H, t, *J*=7.3 Hz), 1.34, 1.52 (3H each, 2 s), 1.36—1.60 (2H, m), 2.09—2.17 (1H, m), 2.27 (1H, dd, *J*=6.8 and 16.6 Hz), 2.70 (1H, dd, *J*=5.4 and 16.6 Hz), 4.30 (1H, dd, *J*=3.4 Hz), 4.66 (1H, d, *J*=3.4 Hz), 4.73 (1H, d, *J*=3.4 Hz), 5.95 (1H, d, *J*=3.4 Hz). Found: 59.54; H, 7.29%. Calcd for $C_{12}H_{18}O_5$: C, 59.49; H, 7.49%.

***E* and *Z* Isomers of Ethyl 5,6-Dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hept-5-eno-1,4-furanuronates (11E and 11Z).** A solution of **10**[12] (4.02g, 15.4 mmol) in 60% aqueous AcOH (80 ml) was stirred for 14 h and concentrated in vacuo. The residue [R_f 0.22 (EtOH/$PhCH_3$ 1 : 5)] was dissolved in MeOH (80 ml), and an aqueous solution (15 ml) of $NaIO_4$ (4.01 g, 18.7 mmol) was added. After being stirred for 1 h, insoluble solids were removed. The filtrate was concentrated in vacuo. The residue was triturated with CH_2Cl_2, and insoluble solids were removed. The filtrate was concentrated in vacuo. The residue [R_f 0.52 (EtOH/$PhCH_3$ 1 : 5)] was dissolved in benzene (80 ml) and (ethoxycarbonylmethylene) triphenylphosphorane (8.07 g, 23.2 mmol) was added. The mixture was stirred at room temperature for 1 h and concentrated in vacuo. The residue was triturated with petroleum ether, and insoluble triphenylphosphine oxide was removed. The filtrate was concentrated in vacuo. The residue was chromatographed on silica gel (AcOEt/hexane 1 : 4) to give 1.72 g (43%) of **11E** and 1.24 g (31%) of **11Z** (73 mg of the mixture was also obtained). **11E:** mp 51—52 °C, TLC R_f 0.54 (EtOH/$PhCH_3$ 1 : 5); $[\alpha]_D^{27}$ +33.3° (*c* 1.18, $CHCl_3$); IR (KBr) ν_{max} 3470, 2985, 2950, 1720, 1645, 1465, 1445, 1425, 1385 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ=1.29

(3H, t, J=7.1 Hz), 1,38, 1.58 (3H each, 2 s), 2.61 (1H, d, J=10.8 Hz), 4.18 (2H, q, J=7.1 Hz), 3.71—4.42 (2H, m), 4.60 (1H, dd, J=4.2 Hz), 5.86 (1H, d, J=4.2 Hz), 6.13 (1H, dd, J=1.5 and 15.8 Hz), 7.00 (1H, dd, J=4.5 and 15.8 Hz). Found: C, 55.80; H, 6.72%. Calcd for $C_{12}H_{18}O_6$: C, 55.81; H, 7.02%. **11Z:** mp 103—105 °C, TLC R_f 0.58 (EtOH/$PhCH_3$ 1 : 5); $[\alpha]_D^{28}$ −23.0° (c 1.08, $CHCl_3$); IR (KBr) ν_{max} 3480, 2980, 1720, 1655, 1220 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ=1.29 (3H, t, J=7.0 Hz), 1.38, 1.62 (3H each, 2 s), 3.41 (1H, d, J=9.0 Hz), 3.75 (1H, ddd, J=4.3, 9.0, and 9.0 Hz), 4.19 (2H, q, J=7.0 Hz), 4.60 (1H, dd, J=4.3 Hz), 5.49 (1H, dd, J=7.1 and 9.0 Hz), 5.80 (1H, d, J=4.3 Hz), 5.99 (1H, d, J=11.8 Hz), 6.22 (1H, dd, J=7.1 and 11.8 Hz). Found: C, 55.95; H, 6.79%. Calcd for $C_{12}H_{18}O_6$: C, 55.81; H, 7.02%.

***Z* Isomer of Ethyl 3-*O*-(*t*-Butyldiphenylsilyl)-5,6-dideoxy-1,2-isopropylidene-α-D-*ribo*-hept-5-eno-1,4-furanuronate (12Z).** A mixture of **11Z** (326 mg, 1.3 mmol), *t*-butylchlorodiphenylsilane (0.66 ml, 2.5 mmol), and imidazole (341 mg) in DMF (6 ml) was stirred at room temperature for 7 h. The mixture was diluted with CH_2Cl_2 (30 ml), wahsed with dilute HCl (30 ml), saturated aqueous $NaHCO_3$ (30 ml), and H_2O (30 ml) successively. The organic phase was dried (Na_2SO_4) and concentrated in vacuo. The residue was chromatographed on silica gel (AcOEt/hexane 1 : 15) to give **12Z** (614 mg, 98%) as a colorless oil: TLC R_f 0.58 (AcOEt/hexane 1 : 4); $[\alpha]_D^{21}$ −30.8° (c 0.96, $CHCl_3$); IR (neat) ν_{max} 2985, 2955, 1720, 1650, 1470, 1425, 1380, 1370 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ=1.04 (9H, s), 1.26, 1.65 (3H each, 2 s), 1.32 (3H, t, J=7.0 Hz), 3.64 (1H, dd, J=4.0 and 8.2 Hz), 3.98 (1H, dd, J=4.0 Hz), 4.20 (2H, q, J=7.0 Hz), 5.55 (1H, d, J=4.0 Hz), 5.68—6.01 (3H, m), 7.29—7.82 (10H, m). Found: C, 67.79; H, 7.10%. Calcd for $C_{28}H_{36}O_6Si$: C, 67.71; H, 7.31%.

***E* and *Z* Isomers of 5,6-Dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hept-5-eno-1,4-furanoses (13E and 13Z).** The reaction was carried out under an argon atmosphere. To a solution of **11E** (777 mg, 3.0 mmol) in CH_2Cl_2 (15 ml) was injected Dibal-H (1.5 mol dm^{-3} solution in $PhCH_3$, 7.9 ml, 11.9 mmol) at −78 °C. After being stirred for 90 min, the mixture was quenched with H_2O (0.5 ml). Insoluble solids were removed, washed well with CH_2Cl_2. The combined filtrate and washings were concentrated in vacuo. The residue was chromatographed on silica gel (EtOH/$PhCH_3$ 1 : 15) to give **13E** (514 mg, 79%) as a colorless oil: TLC R_f 0.29 (EtOH/$PhCH_3$ 1 : 5); $[\alpha]_D^{27}$ +31.1° (c 1.29, $CHCl_3$); IR (neat) ν_{max} 3400, 2990, 1645, 1375, 1215 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ=1.33, 1.54 (3H each, 2 s), 2.4—2.7, 2.8—3.0 (1H each, 2 m), 3.52—3.78 (1H, m), 4.07—4.35 (3H, m), 4.53 (1H, dd, J=4.4 Hz), 5.53—5.79 (2H, m), 6.06 (1H, ddd, J=15.6, 4.6, and 4.6 Hz). Found: C, 55.18; H, 7.30%. Calcd for $C_{10}H_{16}O_5$: C, 55.55; H, 7.46%.

As described above, 720 mg of **11Z** was analogously converted into 568 mg (94%) of **13Z**, mp 105—106 °C: TLC R_f 0.34 (EtOH/$PhCH_3$ 1 : 5); $[\alpha]_D^{27}$ +56.6° (c 0.86, $CHCl_3$); IR (KBr) ν_{max} 3420, 2995, 1430, 1385, 1250 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ=1.36, 1.57 (3H each, 2 s), 2.5—2.8, 3.1—3.3 (1H each, 2 m), 3.51—3.75 (1H, m), 4.12—4.19 (2H, m), 4.52—4.70 (2H, m), 5.46—5.67 (1H, m), 5.82 (1H, d, J=4.0 Hz), 5.91—6.12 (1H, m). Found: C, 55.51; H, 7.27%. Calcd for $C_{10}H_{16}O_5$: C, 55.55; H, 7.46%.

***Z*-Isomer of 3-*O*-(*t*-Butyldiphenylsilyl)-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hept-5-eno-1,4-furanose (14Z).** Compound **12Z** (461 mg, 0.93 mmol) was treated with 5 mol equiv of Dibal-H as described for the preparation of **13E** and **13Z**. By chromatographic purification of the reaction mixture on silica gel, 419 mg (99%) of **14Z** was obtained, mp 92.5—93.5 °C: TLC R_f 0.52 (AcOEt/hexane 1 : 3); $[\alpha]_D^{21}$ +4.7° (c 1.33, $CHCl_3$); IR (neat) ν_{max} 3440, 2960, 2900, 1590, 1460, 1430, 1380, 1375, 1250 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=1.07 (9H, s), 1.21, 1.60 (3H each, 2 s), 1.79 (1H, d, J=6.1 Hz), 3.65 (1H, dd, J=4.1 and 8.8 Hz), 3.76 (1H, dd, J=4.1 Hz), 4.18—4.25, 4.32—4.38 (2H, m), 4.84 (1H, dd, J=8.8 Hz), 5.36—5.41 (1H, m), 5.50 (1H, d, J=4.1 Hz), 5.89—5.95 (1H, m), 7.35—7.77 (10H, m). Found: C, 68.35; H, 7.20%. Calcd for $C_{26}H_{34}O_5Si$: C, 68.69; H, 7.53%.

(1*R*,3*R*,4*R*,5*R*)-3-[(1*R*)- and (1*S*)-1-(Ethoxycarbonyl)methyl-2-propenyl]-4-hydroxy-7,7-dimethyl-2,6,8-trioxabicyclo-[3.3.0]octanes (15R and 15S). A solution of **13E** (1.32 g, 6.1 mmol) in freshly distilled triethyl orthoacetate (10 ml) was heated at 135 °C for 6.5 h in the presence of catalytic propionic acid. The reaction mixture was concentrated in vacuo. The residue was chromatographed on silica gel (AcOEt/hexane 1 : 5) to give an inseparable mixture of **15R** and **15S** (1.25 g, 71% of combined yield) [TLC R_f 0.58 (EtOH/$PhCH_3$ 1:5)] as a colorless oil.

Analogously, the *Z*-isomer **13Z** (1.18 g) was heated at 135 °C in triethyl orthoacetate (20 ml) in the presence of catalytic propionic acid for 14 h. Concentration of the reaction mixture in vacuo and chromatographic purification of the residue gave the mixture of **15R** and **15S** (1.12 g, 72% of combined yield).

Benzoates 16R and 16S. From the Mixture 15R and 15S Obtained from 13E. The mixture (63 mg, 0.22 mmol) was benzoylated with benzoyl chloride (0.05 ml, 0.43 mmol) in pyridine (2 ml). After being stirred for 30 min, the mixture was concentrated in vacuo. The residue was partitioned between CH_2Cl_2 (20 ml) and H_2O (20 ml). The aqueous phase was extracted with CH_2Cl_2 (20 ml×2). The combined organic phases were dried (Na_2SO_4) and concentrated. The residue was chromatographed on silica gel (Et_2O/hexane 1 : 8) to give 41 mg (48%) of **16S**, 31 mg (36%) of **16R**, and 12 mg (14%) of an approximately 1 : 1 mixture of **16R** and **16S**. **16R:** a colorless oil, TLC R_f 0.20 (Et_2O/hexane 1 : 6); $[\alpha]_D^{23}$ +96.0° (c 0.83, $CHCl_3$); IR (neat) ν_{max} 2990, 1725, 1640, 1600, 1450, 1275 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=1.21 (3H, t, J=7.1 Hz), 1.31, 1.52 (3H each, 2 s), 2.54 (1H, dd, J=8.8 and 15.6 Hz), 2.63 (1H, dd, J=5.9 and 15.6 Hz), 2.91 (1H, dddd, J=3.7, 5.9, 8.8, and 8.8 Hz), 4.10 (2H, q, J=7.1 Hz), 4.35 (1H, dd, J=3.7 and 9.0 Hz), 4.81 (1H, dd, J=4.9 and 9.0 Hz), 4.91 (1H, dd, J=3.9 and 4.9 Hz), 4.93—5.18 (2H, m), 5.75 (1H, ddd, J=8.8, 10.3, and 17.1 Hz), 5.82 (1H, d, J=3.9 Hz), 7.45—8.08 (5H, m). Found: C, 64.87; H, 6.83%. Calcd for $C_{21}H_{26}O_7$: C, 64.60; H, 6.71%. **16S:** a colorless oil; TLC R_f 0.14 (Et_2O/hexane 1 : 6); $[\alpha]_D^{25}$ +103.9° (c 1.08, $CHCl_3$); IR (neat) ν_{max} 2990, 1725, 1640, 1600, 1450, 1375, 1275 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ=1.23 (3H, t, J=7.1 Hz), 1.31, 1.53 (3H each, 2 s), 2.42 (1H, dd, J=8.8 and 15.1 Hz), 2.71 (1H, dd, J=4.9 and 15.1 Hz), 2.87 (1H, dddd, J=4.9, 7.3, 8.3, and 8.8 Hz), 4.11 (2H, q, J=7.1 Hz), 4.27 (1H, dd, J=7.3 and 8.8 Hz), 4.79 (1H, dd, J=5.2 and 8.8 Hz), 4.92 (1H, dd, J=3.9 and 5.2 Hz), 5.03 (1H, dd, J=1.0 and 10.3 Hz), 5.14 (1H, dd, J=1.0 and 17.1 Hz), 5.76 (1H, ddd, J=8.3, 10.3 and 17.1 Hz), 5.85 (1H, d, J=3.9 Hz), 7.44—8.05 (5H, m). Found: C, 64.79; H, 6.71%. Calcd for $C_{21}H_{26}O_7$: C, 64.60; H, 6.71%.

From the Mixture Obtained from 13Z. The mixture of **15R** and **15S** (491 mg) was benzoylated as described above.

Extractive work-up and silica-gel chromatography of the extracts gave **16R** (76 mg, 11%) and **16S** (466 mg, 70%), which were identical with those obtained above (TLC, IR, and ^{1}H NMR).

Claisen Rearrangement of 14Z and Separation of the Diastereomers as the Benzoates 16R and 16S. Compound **14Z** (211 mg, 0.46 mmol) was heated at 135 °C in triethyl orthoacetate (4 ml) in the presence of catalytic propionic acid for 15 h. Then, the reaction mixture was concentrated in vacuo. The residue was chromatographed on silica gel (AcOEt/hexane 1 : 20) to give an inseparable mixture of **17R** and **17S** (118 mg) as a colorless oil [R_f 0.60 (AcOEt/hexane 1 : 3)].

The mixture (118 mg) was dissolved in THF (3 ml) and tetrabutylammonium fluoride (1.0 mol dm^{-3} solution in THF, 0.49 ml) was added. The mixture was stirred at room temperature for 1 h and concentrated in vacuo. The residue was chromatographed on silica gel (AcOEt/hexane 1 : 5) to give an inseparable mixture of **15R** and **15S** (54 mg).

The mixture (54 mg) was benzolylated as described above. Silica-gel chromatography of the reaction mixture gave 7.8 mg (4.3% yield from **14Z**) of **16R** and 58.2 mg (32.1%) of **16S**.

(1*R*,3*R*,4*R*,5*R*)-4-Hydroxy-3-[(1*R*)- and (1*S*)-1-(2-hydroxyethyl)-2-propenyl]-7,7-dimethyl-2,6,8-trioxabicyclo[3.3.0]-octanes (18R and 18S). A solution of **16R** (30 mg, 0.07 mmol) in THF (2 ml) was stirred in the presence of $LiAlH_4$ (10 mg, 0.27 mmol) for 1 h. To the mixture was added H_2O (0.02 ml). The resulting solids were removed by filtration. The filtrate was concentrated in vacuo. The residue was chromatographed on silica gel (EtOH/$PhCH_3$ 1 : 15) to give **18R** (17 mg, 92%) as a colorless oil: TLC R_f 0.42 (EtOH/$PhCH_3$ 1 : 5); $[\alpha]_D^{23}$ +6.3° (*c* 1.0, $CHCl_3$); IR (neat) ν_{max} 3390, 2940, 1640, 1500, 1455, 1375, 1315, 1220 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ=1.34, 1.55 (3H each, 2 s), 1.62—2.12 (3H, m), 2.37—2.70 (2H, m), 3.46—3.82 (4H, m), 4.49 (1H, dd, *J*=4.3 Hz), 5.02—5.27 (2H, m), 5.74 (1H, d, *J*=4.3 Hz), 5.48—5.93 (1H, m). Found: C, 58.73; H, 8.05%. Calcd for $C_{12}H_{20}O_5$: C, 59.00; H, 8.25%.

Analogously, *S*-diastereomer **16S** (40 mg) was reduced with 3.0 mol equiv of $LiAlH_4$. Silica-gel chromatography of the reaction mixture gave **18S** (23 mg, 92%) as a colorless oil: TLC R_f 0.42 (EtOH/$PhCH_3$ 1 : 5); $[\alpha]_D^{25}$ +53.7° (*c* 1.07, $CHCl_3$); IR (neat) ν_{max} 3390, 2940, 1640, 1455, 1380, 1375, 1240 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ=1.35, 1.56 (3H each, 2 s), 1.63—2.12 (3H, m), 2.28—2.64 (2H, m), 3.42—3.94 (4H, m), 4.53 (1H, dd, *J*=4.1 Hz), 5.02—5.31 (2H, m), 5.65 (1H, d, *J*=4.1 Hz), 5.57—6.00 (1H, m). Found: C, 58.64; H, 8.02%. Calcd for $C_{12}H_{20}O_5$: C, 59.00; H, 8.25%.

(1*R*,3*R*,4*R*,5*R*)-4-Hydroxy-3-[(1*S*)- and (1*R*)-1-ethyl-3-hydroxypropyl]-7,7-dimethyl-2,6,8-trioxabicyclo[3.3.0]octanes (19S and 19R). A solution of **18R** (17 mg, 0.07 mmol) in EtOH (2 ml) was hydrogenated under atmospheric hydrogen gas in the presence of Raney nickel T-4 for 3 h. The catalyst was removed through a Celite pad, washed with EtOH. The filtrate and washings were combined and concentrated in vacuo. The residue was chromatographed on silica gel (EtOH/$PhCH_3$ 1 : 20) to give **19S** (16 mg, 91%) as white crystals, mp 47.5—48.5 °C: TLC R_f 0.43 (EtOH/$PhCH_3$ 1 : 5); $[\alpha]_D^{25}$ +25.0° (*c* 0.76, $CHCl_3$); IR (KBr) ν_{max} 3295, 2980, 2965, 2930, 2870, 1460, 1380, 1370, 1325, 1245, 1235 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=0.93 (3H, t, *J*=7.6 Hz), 1.37, 1.57 (3H each, 2 s), 1.38—1.85 (5H, m), 2.20 (1H, br s), 2.75 (1H, d, *J*=8.3 Hz), 3.63—3.83 (4H, m), 4.56 (1H, dd, *J*=4.2 Hz), 5.77 (1H, d, *J*=4.2 Hz). Found: C, 58.29; H, 8.71%. Calcd for $C_{12}H_{22}O_5$: C, 58.52; H, 9.00%.

Analogously, compound **18S** (23 mg) was hydrogenated to give **19R** (19.5 mg, 83%) as white crystals, mp 79.5—81 °C: TLC R_f 0.43 (EtOH/$PhCH_3$ 1 : 5); $[\alpha]_D^{23}$ +26.0° (*c* 0.95, $CHCl_3$); IR (KBr) ν_{max} 3425, 2985, 2975, 2955, 2940, 1460, 1380, 1370, 1320 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=0.95 (3H, t, *J*=7.3 Hz), 1.37, 1.57 (3H each, 2 s), 1.38—1.72 (5H, m), 2.24 (1H, br s), 2.65 (1H, d, *J*=9.8 Hz), 3.62—3.83 (4H, m), 4.56 (1H, dd, *J*=3.9 and 4.9 Hz), 5.78 (1H, d, *J*=3.9 Hz). Found: C, 58.34; H, 8.73%. Calcd for $C_{12}H_{22}O_5$: C, 58.52; H, 9.00%.

(1*R*,3*R*,4*S*,5*R*)-4-Hydroxy-3-[(1*R*)- and (1*S*)-1-ethyl-3-hydroxypropyl]-7,7-dimethyl-2,6,8-trioxabicyclo[3.3.0]octanes (20R and 20S). A solution of **9R** (99 mg, 0.41 mmol) in THF (2 ml) was stirred with $LiAlH_4$ (38.5 mg, 1.0 mmol) for 1 h. The mixture was quenched with H_2O (0.1 ml). The resulting solids were removed, washed with CH_2Cl_2. The combined filtrate and washings were concentrated in vacuo. The residue was chromatographed on silica gel (AcOEt/hexane 1 : 1) to give **20R** (88 mg, 87%) as a colorless oil: TLC R_f 0.26 (AcOEt/hexane 1 : 1); $[\alpha]_D^{27}$ −21.8° (*c* 0.61, $CHCl_3$); IR (neat) ν_{max} 3400, 2960, 2940, 2880, 1460, 1380, 1250, 1220 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=0.95 (3H, t, *J*=7.5 Hz), 1.31, 1.49 (3H each, 2 s), 1.25—1.89 (5H, m), 2.71 (2H, br s), 3.63—3.69, 3.76—3.82 (1H each, 2 m), 3.93 (1H, dd, *J*=2.4 and 9.8 Hz), 4.11 (1H, d, *J*=2.4 Hz), 4.50 (1H, d, *J*=3.9 Hz), 5.90 (1H, d, *J*=3.9 Hz). Found: C, 58.85; H, 8.78%. Calcd for $C_{12}H_{22}O_5$: C, 58.52; H, 9.00%.

Analogously, 14.5 mg of **9S** was reduced with $LiAlH_4$ to give 12 mg (84%) of **20S** as a colorless oil: TLC R_f 0.55 (AcOEt); $[\alpha]_D^{26}$ −15.6° (*c* 0.61, $CHCl_3$); IR (neat) ν_{max} 3380, 2960, 2940, 2880, 1460, 1370, 1250, 1210 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=0.93 (3H, t, *J*=7.5 Hz), 1.32, 1.49 (3H each, 2 s), 1.40—1.91 (5H, m), 2.84 (1H, br s), 3.62—3.68, 3.79—3.84 (1H each, 2 m), 3.89 (1H, dd, *J*=2.0 and 11.0 Hz), 4.18 (1H, d, *J*=2.0 Hz), 4.38 (1H, br s), 4.51 (1H, d, *J*=3.7 Hz), 5.90 (1H, d, *J*=3.7 Hz). Found: C, 58.22; H, 8.73%. Calcd for $C_{12}H_{22}O_5$: C, 58.52; H, 9.00%.

Conversion of 20R into 19R via 21R, 22R, and 23R. To a solution of **20R** (20 mg, 0.08 mmol) in pyridine (1 ml) were added trityl chloride (52 mg, 0.19 mmol) and 4-dimethylaminopyridine (5 mg). After being heated at 65 °C for 3.5 h, the mixture was concentrated in vacuo. The residue was partitioned between CH_2Cl_2 (20 ml) and saturated aqueous $NaHCO_3$ (10 ml). The aqueous phase was extracted with CH_2Cl_2 (20 ml). The combined organic phases were dried (Na_2SO_4) and concentrated. The residue was chromatographed on silica gel (AcOEt/hexane 1 : 10) to give **21R** (39 mg, 98%) as a colorless oil: TLC R_f 0.51 (AcOEt/hexane 1 : 2); $[\alpha]_D^{24}$ −11.1° (*c* 1.19, $CHCl_3$); IR (KBr) ν_{max} 3470, 2970, 2940, 2880, 1600, 1490, 1450, 1380, 1220 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ=0.84 (3H, t, *J*=7.2 Hz), 1.24, 1.38 (3H each, 2 s), 1.10—2.10 (6H, m), 3.06—3.25 (2H, m), 3.83 (1H, dd, *J*=2.8 and 9.2 Hz), 4.04 (1H, d, *J*=2.8 Hz), 4.43 (1H, d, *J*=4.1 Hz), 5.79 (1H, d, *J*=4.1 Hz), 7.17—7.49 (15 H, m).

To a solution of **21R** (48 mg, 0.10 mmol) in CH_2Cl_2 (1 ml) were added anhydrous sodium acetate (17 mg), PCC (221 mg, 1.0 mmol), and molecular sieves (4A, powder, 143 mg). The mixture was stirred for 8 h, and charged on silica-gel column (8 g). The column was eluted with Et_2O containing 1% of triethylamine to give 47 mg of **22R** as a colorless oil: TLC R_f 0.80 (AcOEt/hexane 1 : 2); ^{1}H NMR (90 MHz,

$CDCl_3$) δ=0.85 (3H, t, J=7.5 Hz), 1.34, 1.40 (3H each, 2 s), 1.24—2.01 (5H, m), 2.90—3.20 (2H, m), 4.06 (1H, d, J=3.9 Hz), 4.30—4.36 (1H, m), 5.89 (1H, d, J=3.9 Hz), 7.15—7.46 (15H, m).

The crude **22R** (47 mg) was dissolved in EtOH (1 ml), and $NaBH_4$ (10 mg) was added. After being stirred for 50 min, the mixture was neutralized by addition of 50% aqueous AcOH and concentrated in vacuo. The residue was chromatographed on silica gel (AcOEt/hexane 1 : 5 containing 1% of triethylamine) to give **23R** (35 mg, 72% from **21R**) as a colorless oil: TLC R_f 0.59 (AcOEt/hexane 1 : 2); $[\alpha]_D^{20}$ +64.7° (c 1.68, $CHCl_3$); IR (neat) ν_{max} 3500, 2960, 2930, 2870, 1595, 1490, 1450, 1380, 1370, 1215 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ=0.84 (3H, t, J=7.0 Hz), 1.34, 1.50 (3H each, 2 s), 1.05—2.34 (6H, m), 2.92—3.28 (2H, m), 3.52—3.81 (2H, m), 4.45 (1H, dd, J=4.4 Hz), 5.69 (1H, d, J=4.4 Hz), 7.16—7.49 (15H, m).

A solution of **23R** (28 mg, 0.06 mmol) in MeOH (1 ml) was stirred in the presence of p-toluenesulfonic acid (monohydrate, 10 mg) for 30 min at room temperature. Then, saturated aqueous $NaHCO_3$ (15 ml) was added. This was extracted with CH_2Cl_2 (20 ml×5). The combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The residue was chromatographed on silica gel (EtOH/$PhCH_3$ 1 : 15) to give **19R** (11 mg, 75%), which was identical with that obtained from **16S** in respects of TLC, mp, $[\alpha]_D$, IR and ^1H NMR.

Conversion of 20S into 19S via 21S, 22S, and 23S. Compound **20S** was converted into **19S** via **21S**, **22S**, and **23S** by the analogous reaction sequence described for **20R**. **21S** (91%): mp 179—180 °C, TLC R_f 0.49 (AcOEt/hexane 1 : 2); $[\alpha]_D^{24}$ +5.8° (c 0.94, $CHCl_3$); IR (KBr) ν_{max} 3440, 2980, 2950, 1620, 1480, 1460, 1380, 1220 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ=0.86 (3H, t, J=7.5 Hz), 1.29, 1.45 (3H each, 2 s), 1.50—2.03 (5H, m), 2.61 (1H, br s), 3.21 (2H, dd, J=6.2 Hz), 3.85 (1H, dd, J=2.4 and 10.8 Hz), 4.05 (1H, br s), 4.47 (1H, d, J=4.1 Hz), 5.85 (1H, d, J=4.1 Hz), 7.18—7.49 (15H, m). **22S:** a colorless oil, TLC R_f 0.80 (AcOEt/hexane 1 : 2); ^1H NMR (90 MHz, $CDCl_3$) δ=0.83 (3H, t, J=7.7 Hz), 1.39, 1.58 (3H each, 2 s), 1.13—2.25 (5H, m), 3.14 (2H, dd, J=6.2 Hz), 4.19—4.37 (2H, m), 5.96 (1H, d, J=4.5 Hz), 7.20—7.58 (15H, m). **23S** (97% from **21S**): mp 96.5—97.5 °C, TLC R_f 0.62 (AcOEt/hexane 1 : 2); $[\alpha]_D^{21}$ +20.6° (c 1.00, $CHCl_3$); IR (KBr) ν_{max} 3540, 2980, 2960, 1480, 1450, 1400, 1380, 1315, 1260 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ=0.85 (3H, t, J=7.0 Hz), 1.34, 1.46 (3H each, 2 s), 1.25—2.40 (6H, m), 3.06—3.20 (2H, m), 3.55—3.79 (2H, m), 4.48 (1H, dd, J=4.0 Hz), 5.70 (1H, d, J=4.0 Hz), 7.17—7.50 (15H, m).

Compound **19S** obtained by p-TsOH hydrolysis of **23S** in 58% yield was identical with that obtained from **16R**.

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7) Under the standard reaction conditions (benzene as a solvent at room temperature for 45 min), the formation of three products was detected. These were E- and Z-α,β-unsaturated esters and the δ-lactone derivative derived from the Z-Wittig adduct.

8) Dibal-H reduction of mixture of the E- and Z-α,β-unsaturated esters and the α,β-unsaturated δ-lactone gave the E- and Z-allyl alcohols and a hemiacetal derived from the δ-lactone in 22%, 15%, and 25% yields from **1**, respectively.

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10) The ratio and stereochemistries of the rearrangement products **6R** and **6S** were determined as follows. The mixture of the rearrangement product was reduced with $LiAlH_4$. The resulting two diols with S- and R-configurations were completely separated by repeated chromatography on silica gel. The ratio of **6S** and **6R** was estimated based on the yields of these diol derivatives. The double bond in each of the diol was then hydrogenated to afford **20R** or **20S**, which were compared with those prepared from structurally defined **9R** and **9S**.

11) The stereochemistries of **7S** and **7R** were confirmed by transformation of them into the diols, which were independently derived from the mixture of **6S** and **6R** (see, Ref. 10), by desilylation follwed by $LiAlH_4$ reduction.

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