70.80; H, 7.80; N, 5.16. Found: C, 70.79; H, 7.85; N, 5.11.

General Procedure for Reaction of Hydroxylamine Derivatives and 2-Aryl-2-propanols. *O*-Benzyl-*N*-[1-methyl-1-[4-(benzyloxy)phenyl]ethyl]hydroxylamine (5a). Method A. 1-Methyl-1-[4-(benzyloxy)phenyl]ethanol (**3a**) (0.1 g, 0.41 mmol) and *O*-benzylhydroxylamine (**4a**) (0.1 g, 0.82 mmol) were dissolved in benzene (2 mL) and stirred under an argon atmosphere. To the reaction flask was added TFA (0.047 g, 0.41 mmol) via syringe, and the reaction mixture was allowed to stir at room temperature for 48 h. The reaction mixture was concentrated, and the residue was dissolved in Et_2O (50 mL). The organic layer was washed with saturated $NaHCO_3$ (25 mL) and brine (25 mL), dried over $MgSO_4$, filtered, and concentrated to afford a slightly yellow oil. Purification by column chromatography (silica gel, 3:1 hexane/ether) afforded 0.118 g (83%) of **5a** as a clear oil that solidified on prolonged standing to give a white power: mp 67–69 °C; ^1H NMR (300 MHz) (DMSO-d_6) δ 1.35 (s, 6 H), 4.53 (s, 2 H), 5.08 (s, 2 H), 6.85 (s, 1 H), 6.93 (m, 2 H), 7.19–7.48 (m, 12 H); IR ($CDCl_3$) 3060, 3030, 2980, 1610, 1510, 1460, 1010 cm^{-1}; MS *m/e* 348 $(M + H)^+$, 225, 164, 91. Anal. Calcd for $C_{23}H_{25}NO_2$: C, 79.51; H, 7.25; N, 4.03. Found: C, 79.70; H, 7.39; N, 4.01.

Method B. 1-Methyl-1-[4-(benzyloxy)phenyl]ethanol (**3a**) (0.2 g, 0.83 mmol) and *O*-benzylhydroxylamine (**4a**) (0.102 g, 0.83 mmol) were dissolved in methylene chloride (3 mL) and stirred under an argon atmosphere at 0 °C. To the reaction flask was added TFA (0.377 g, 3.31 mmol) via syringe, and the reaction mixture was allowed to stir at 0 °C for 1 h. The reaction mixture was concentrated, and the residue was partitioned between EtOAc (60 mL) and H_2O (30 mL). The organic layer was separated, dried ($MgSO_4$), and concentrated. The semicrystalline residue was triturated with Et_2O/hexane to afford 0.21 g of the trifluoroacetic acid salt of **5a** as a white powder. An additional 0.068 g precipitated from the filtrate to give a total of 0.28 g (79%): mp (EtOAc/hexane) 140–142 °C; ^1H NMR (300 MHz) (DMSO-d_6) δ 1.48 (s, 6 H), 4.70 (s, 2 H), 5.11 (s, 2 H), 6.85 (s, 2 H), 6.99 (m, 2 H), 7.20–7.50 (m, 12 H). Anal. Calcd for $C_{25}H_{26}F_3NO_4$: C, 65.07; H, 5.68; N, 3.04. Found: C, 65.09; H, 5.67; N, 3.02.

***O*-(*tert*-Butyldiphenylsilyl)-*N*-[1-methyl-1-[4-(benzyloxy)phenyl]ethyl]hydroxylamine (5b)** was prepared by method A from 1-methyl-1-[4-(benzyloxy)phenyl]ethanol (**3a**) (0.5 g, 2.06 mmol), *O*-(*tert*-butyldiphenylsilyl)hydroxylamine (**4b**) (1.12 g, 4.13 mmol), and TFA (0.236 g, 2.07 mmol) in benzene (2 mL) as a slightly yellow oil. Purification by column chromatography (silica gel, 97:3 hexane/ether) afforded 0.46 g (45%) of **5b** as a colorless oil: ^1H NMR (300 MHz) (DMSO-d_6) δ 1.10 (s, 9 H), 1.21 (b s, 6 H), 5.06 (s, 2 H), 6.06 (s, 1 H), 6.85 (m, 2 H), 7.18–7.48 (m, 13 H), 7.62 (m, 4 H); IR ($CDCl_3$) 3110, 2950, 2860, 1605, 1510, 1240, 1110 cm^{-1}; MS *m/e* 496 $(M + H)^+$, 225. Anal. Calcd for $C_{32}H_{37}NO_2Si$: C, 77.53; H, 7.52; N, 2.83. Found: C, 77.53; H, 7.53; N, 2.30.

***N*-[1-Methyl-1-[4-(benzyloxy)phenyl]ethyl]hydroxylamine (5c)** was prepared by method B from 1-methyl-1-[4-(benzyloxy)phenyl]ethanol (**3a**) (0.6 g, 2.48 mmol), *O*-(trimethylsilyl)-hydroxylamine (**4c**) (0.39 g, 3.7 mmol), and TFA (1.13 g, 10 mmol) in methylene chloride (3 mL). Neutralization, workup, and concentration gave a white solid. Purification by column chromatography (silica gel, 97:3 CH_2Cl_2/MeOH) afforded 0.434 g (68%) of **5c** as a white solid: mp (EtOAc/hexane) 122–124 °C; ^1H NMR (300 MHz) (DMSO-d_6) δ 1.30 (s, 6 H), 5.07 (s, 2 H), 5.56 (b s, 1 H), 6.90 (m, 2 H), 6.95 (b s, 1 H), 7.28–7.47 (m, 7 H); IR ($CDCl_3$) 3060, 3030, 2980, 1610, 1510, 1460, 1010 cm^{-1}; MS *m/e* 275 $(M + NH_4)^+$, 258 $(M + H)^+$, 225. Anal. Calcd for $C_{16}H_{19}NO_2$: C, 74.68; H, 7.44; N, 5.44. Found: C, 74.82; H, 7.59; N, 5.42.

***O*-Benzyl-*N*-[1-methyl-1-(4-butoxyphenyl)ethyl]-hydroxylamine (5d)** was prepared by method A from 1-methyl-1-(4-butoxyphenyl)ethanol (**3b**) (0.2 g, 1.0 mmol), *O*-benzylhydroxylamine (**4a**) (0.246 g, 2.0 mmol), and TFA (0.144 g, 1.0 mmol) in benzene (5 mL) as a slightly yellow oil. Purification by column chromatography (silica gel, 3:1 hexane/ether) afforded 0.27 g (86%) of **5d** as a colorless oil: ^1H NMR (300 MHz) (DMSO-d_6) δ 0.93 (t, 3 H, J = 7.5 Hz), 1.35 (s, 6 H), 1.43 (m, 2 H), 1.68 (m, 2 H), 3.93 (t, 2 H, J = 7.5 Hz), 4.53 (s, 2 H), 6.58 (s, 2 H), 6.83 (m, 2 H), 7.19–7.39 (m, 5 H), 7.49 (m, 2 H); IR (neat) 2960, 2930, 2870, 1610, 1510, 1245, 1180 cm^{-1}; MS *m/e* 314 $(M + H)^+$, 191, 135. Anal. Calcd for $C_{20}H_{27}NO_2$: C, 76.64; H, 8.68; N, 4.47. Found: C, 76.25; H, 8.62; N, 4.65.

Using method B, **5d** was prepared from 1-methyl-1-(4-butoxyphenyl)ethanol (**3b**) (0.1 g, 0.5 mmol), *O*-benzylhydroxylamine (**4a**) (0.084 g, 0.7 mmol), and TFA (0.216 g, 1.90 mmol) in methylene chloride (8 mL). The reaction mixture was concentrated, and the residue was purified by column chromatography (silica gel, 7:3 hexane/ether) to afford 0.18 g of the trifluoroacetic acid salt of **5d** as a white power (80%): mp (EtOAc/hexanes) 113–114 °C; ^1H NMR (300 MHz) ($CDCl_3$) δ 0.93 (t, 3 H, J = 7.5 Hz), 1.39 (m, 2 H), 1.64 (m, 2 H), 1.69 (s, 6 H), 3.68 (t, 2 H, J = 7.5 Hz), 4.67 (s, 2 H), 6.62 (b s, 1 H), 6.78 (m, 2 H), 7.23 (m, 2 H), 7.33 (m, 3 H), 7.47 (m, 2 H); IR ($CDCl_3$) 2960, 2875, 2760, 1675, 1520, 1260, 1190 cm^{-1}; MS *m/e* 331 $(M + NH4)^+$, 314 $(M + H)^+$, 225, 191, 91. Anal. Calcd for $C_{22}H_{28}F_3NO_4$: C, 61.82; H, 6.60; N, 3.28; F, 13.33. Found: C, 61.78; H, 6.76; N, 3.28; F, 13.83.

***O*-Benzyl-*N*-[1-methyl-1-(2-naphthyl)ethyl]hydroxylamine (5e)** was prepared by method A from 1-methyl-1-(2-naphthyl)ethanol (**3c**) (0.19 g, 1.0 mmol), *O*-benzylhydroxylamine (**4a**) (0.246 g, 2.0 mmol), and TFA (0.114 g, 1.0 mmol) in benzene (2 mL) as a slightly yellow oil. Purification by column chromatography (silica gel, 3:1 hexane/ether) afforded 0.143 g (49%) of **5e** as a colorless oil: ^1H NMR (300 MHz) (DMSO-d_6) δ 1.48 (s, 6 H), 4.55 (s, 2 H), 6.82 (s, 1 H) 7.16–7.31 (m, 5 H), 7.47 (m, 2 H), 7.75–7.95 (m, 5 H); MS *m/e* 496 $(M + H)^+$, 225. Anal. Calcd for $C_{20}H_{21}NO$: C, 82.44; H, 7.26; N, 4.81. Found: C, 82.51; H, 7.31; N, 4.82.

Registry No. **3a**, 94571-13-8; **3b**, 93308-49-7; **3c**, 20351-54-6; **4a**, 622-33-3; **4b**, 103587-51-5; **4c**, 22737-36-6; **5a**, 118684-93-8; **5a**·CF_3CO_2H, 118684-99-4; **5b**, 118684-94-9; **5c**, 118684-95-0; **5c**·CF_3CO_2H, 118684-98-3; **5d**, 115514-06-2; **5d**·CF_3CO_2H, 118684-97-2; **5e**, 118684-96-1; TFA, 76-05-1; hydroxylamine hydrochloride, 5470-11-1; *tert*-butylchlorodiphenylsilane, 58479-61-1.

Claisen Rearrangement of (*Z*)-3-Deoxy-3-*C*-[(hydroxymethyl)methylene]-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranose with Triethyl Orthopropionate[1]

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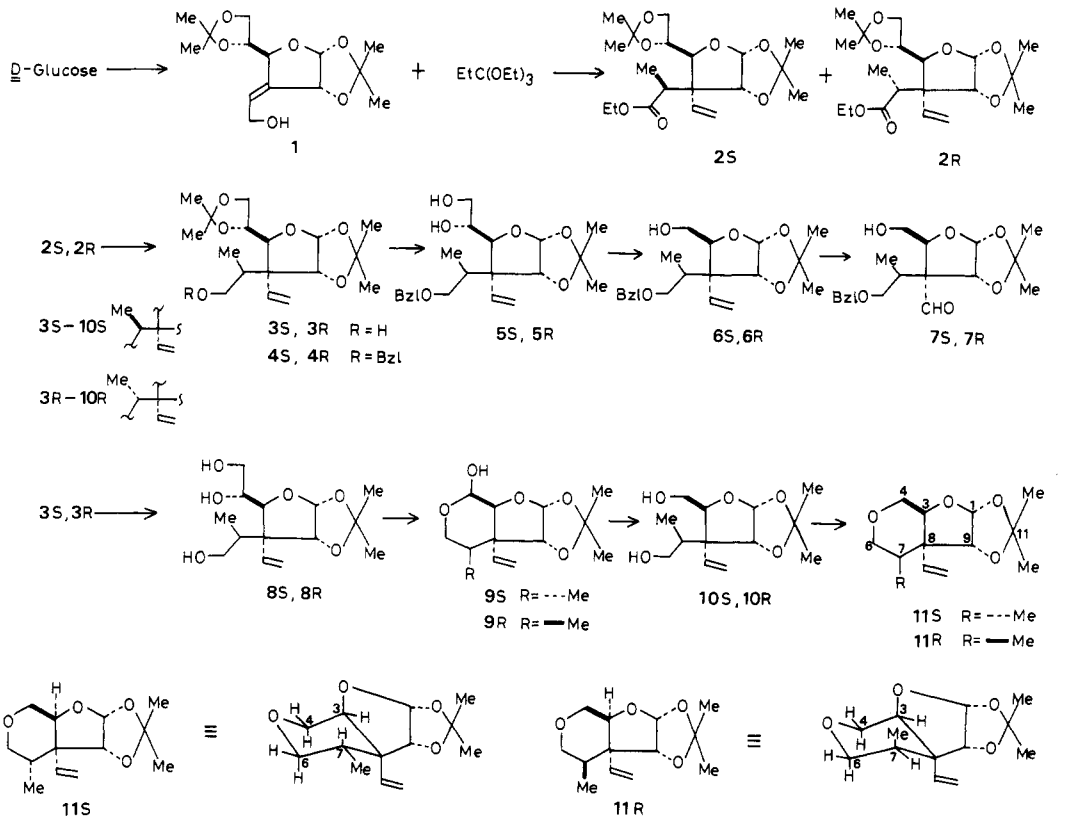
Recently, we reported the stereoselective quaternization at C-3 of some aldohexofuranoses by means of the ortho ester Claisen rearrangement of (*Z*)-3-deoxy-3-*C*-[(hydroxymethyl)methylene]-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-(1), -β-L-*lyxo*-, and -β-D-*arabino*-hexofuranose with triethyl orthoacetate.[2] These rearrangements proceed with high stereoselectivity to provide the corresponding 3-*C*-[(ethoxycarbonyl)methyl]-3-*C*-vinyl derivatives in moderate to high yields. For an extension of our interest in the Claisen rearrangement of carbohydrate-derived cyclic models, we describe herein the Claisen rearrangement of 1 with triethyl orthopropionate.

By heating 1 in triethyl orthopropionate at 135 °C in the presence of propanoic acid,[3] two products, **2S** and **2R**, were obtained in 65% and 16% yields, respectively, after recrystallization of the mixture followed by silica gel

(1) This work was presented at the 56th National Meeting of the Chemical Society of Japan, Tokyo, April 1–4, 1988. Abstract 1 IXB 29.
(2) Tadano, K.; Idogaki, Y.; Yamada, H.; Suami, T. *Chem. Lett.* **1985**, 1925; *J. Org. Chem.* **1987**, *52*, 1201.
(3) Johnson, W. S.; Werthemann, L.; Bartlett, W. R.; Brochsom, T. J.; Li, T.-t.; Faulkner, D. J.; Peterson, M. R. *J. Am. Chem. Soc.* **1970**, *92*, 741.

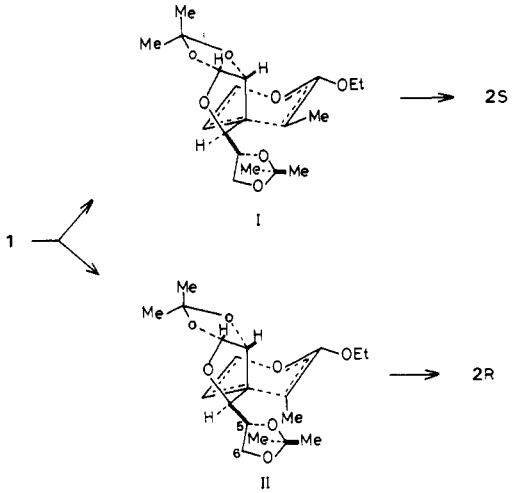
0022-3263/89/1954-1223$01.50/0

Scheme I



chromatography of the mother liquor (see Scheme I). Lithium aluminum hydride ($LiAlH_4$) reduction of **2S** and **2R** gave **3S** and **3R** in 95% and quantitative yields, respectively. The hydroxyl groups in **3S** and **3R** were protected as benzyl ethers giving **4S** (81%) and **4R** (93%). Selective deisopropylidenation of **4S** with 50% aqueous AcOH provided the monoisopropylidene derivative **5S** in 94% yield. Glycol cleavage of **5S** with $NaIO_4$ in aqueous MeOH followed by $LiAlH_4$ reduction gave **6S** in 54% yield. By the same reaction sequence, **4R** was converted into **6R** in an overall yield of 70%. Lemieux–Johnson oxidation[4] of **6S** gave **7S** possessing an aldehyde group in 36% yield. Analogously, **6R** was oxidized to the aldehyde **7R** in 41% yield. These results indicated that neither **7S** nor **7R** was a lactol and that the aldehyde group and the hydroxylmethyl group in **7S** and **7R** are in a trans relationship. Therefore, the configuration of the quaternary carbon in both **2S** and **2R** is *S*. This stereoselective rearrangement coincides with our previous results,[2] in which the rearrangement took place from the less hindered side (convex face) of bicyclic **1**.

The configurations of the newly introduced methyl groups adjacent to the ester functionality in **2S** and **2R** were determined as follows. Selective hydrolysis of **3S** and **3R** with 50% aqueous AcOH gave the monoisopropylidene derivatives **8S** and **8R** in 89% and 74% yields, respectively. Glycol cleavage of **8S** with $NaIO_4$ followed by $NaBH_4$ reduction of thus formed **9S** gave **10S** in 54% yield. A 63% overall yield of **10S** was achieved from **3S** when purification of **8S** was omitted. Analogously, **8R** was converted into **10R** in 88% yield. Treatment of **10S** with 3 molar equiv of *p*-toluenesulfonyl chloride (TsCl) in pyridine in the presence of 4-(dimethylamino)pyridine (DMAP) at 60 °C provided tricyclic compound **11S** in 74% yield. This conversion proceeds presumably via tosylation of one of the primary hydroxyl groups followed by spontaneous cyclization. Under analogous reaction conditions, **10R** was converted into the tricyclic **11R** in 69% yield. In the ^1H NMR (400 MHz) spectrum of **11S**, H-3 appeared at δ 4.14 as a singlet, indicating $J_{3,4_{eq}}$ and $J_{3,4_{ax}}$ are nearly 0 Hz. H-7 of **11S** appeared at δ 1.73 as a doublet of doublets of quartets with $J_{Me,7}$ = 7.3 Hz, $J_{6_{ax},7}$ = 11.2 Hz, and $J_{6_{eq},7}$ = 4.0 Hz, indicating that methyl group at C-7 is equatorially oriented as depicted. On the other hand, H-3 of **11R** appeared at δ 4.03 as a doublet with $J_{3,4_{ax}}$ = 1.9 Hz and $J_{3,4_{eq}}$ = 0 Hz, and H-7 appeared at δ 1.77 as a doublet of quartets with $J_{Me,7}$ = 7.3 Hz, $J_{6_{ax},7}$ = 1.0 Hz, and $J_{6_{eq},7}$ = 0 Hz, indicating that methyl group at C-7 is axially oriented. From these results, configurations of the newly



(4) Pappo, R.; Allen, D. S.; Lemieux, R. U.; Johnson, W. S. *J. Org. Chem.* **1956**, *21*, 478.

introduced chiral centers adjacent to the ester functionality are *S* for **2S** and *R* for **2R**. On the mechanism of the rearrangement of **1**, two chairlike transition states I and II are taken into consideration. Judging from the steric interaction, the transition state II is unfavorable by a likely repulsion generated between the methyl group in the ketene acetal moiety and the 5,6-isopropylidene moiety. On the basis of this assumption, the preferential formation of **2S** is reasonably explained.

Experimental Section

Reactions were carried out at room temperature unless otherwise described. Melting points are uncorrected. Specific rotations were measured by a JASCO DIP-4 polarimeter in a $CHCl_3$ solution in a 10-mm cell. Column chromatography was performed with silica gel (Katayama Chemicals, K070), and thin-layer chromatography (TLC) with glass plates coated with Kieselgel 60 GF_{254} (Merck). Preparative TLC (PTLC) was performed with glass plates (20 × 20 cm) coated with Kieselgel 60 PF_{254} (Merck), and compounds were extracted with $CHCl_3$. ^1H NMR spectra were recorded in $CDCl_3$ solutions at 90 MHz with a Varian EM-390 spectrometer and at 400 MHz with a JEOL JNM-GX 400 FT NMR spectrometer. High-resolution mass spectra were obtained by a Hitachi M-80 spectrometer.

N,N-Dimethylformamide (DMF) was dried over CaH_2 and then distilled. Pyridine was distilled over NaOH. Tetrahydrofuran (THF) was distilled over $LiAlH_4$ and then over Na/benzophenone.

Claisen Rearrangement of (*Z*)-3-Deoxy-3-*C*-[(hydroxymethyl)methylene]-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranose (1) with Triethyl Orthopropionate. (2*R*,3*R*,4*S*,5*S*)-4-[(1*S*)-1-(Ethoxycarbonyl)ethyl]-2,3-(isopropylidenedioxy)-5-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-4-vinyltetrahydrofuran (2S) and the 4-[(1*R*)-1-(Ethoxycarbonyl)ethyl] Isomer (2R).[5] A solution of **1**[2] (39.39 g, 138 mmol) in freshly distilled triethyl orthopropionate (300 mL) and propanoic acid (0.21 mL) was heated at 135 °C. An additional 0.05 mL of propanoic acid was added every 2 h, and the mixture was heated at this temperature for total 9 h while the formed ethanol was removed by distillation. The mixture was then concentrated in vacuo with an aid of toluene at 50 °C. The residue was chromatographed on silica gel (400 g, AcOEt/hexane, 1:20), and the fractions corresponding to R_f 0.56 and 0.49 (AcOEt/hexane, 1:5) were combined and concentrated in vacuo. The residue was crystallized from hexane to give **2S** (18.7 g) as cubics, mp 55.5–56 °C. The mother liquor was concentrated in vacuo, and the residue was chromatographed on silica gel (AcOEt/hexane, 1:40). Concentration of the fractions corresponding to R_f 0.56 (AcOEt/hexane, 1:5) gave **2R** (8.11 g, 16%) as a colorless oil. Concentration of the fractions corresponding to R_f 0.49 gave an additional **2S** (14.7 g, total 33.4 g, 65%): $[\alpha]^{26}_D$ +18.3° (*c* 0.91); IR ν_{max}^{neat} 2990, 1730, 1640 cm^{-1}; ^1H NMR (90 MHz) δ 1.28 (t, 3 H, *J* = 7 Hz, $COOCH_2CH_3$), 1.29 (d, 1 H, *J* = 7 Hz, CH_3 of the side chain at C-4), 1.31, 1.35, 1.47 (each s, 6 H, 3 H, 3 H, 2 $C(CH_3)_2$), 2.94 (q, 1 H, *J* = 7 Hz, $CHCH_3$ of the side chain at C-4), 3.82–4.32 (m, 3 H, H-5, H-1,2,2′ of the side chain at C-5), 4.09 (q, 2 H, *J* = 7 Hz, $COOCH_2CH_3$), 5.11 (dd, 1 H, *J* = 2 and 10 Hz, $CH=CH_2$), 5.21 (d, 1 H, *J* = 4 Hz, H-3), 5.27 (dd, 1 H, *J* = 2 and 18 Hz, $CH=CH_2$), 5.64 (d, 1 H, *J* = 4 Hz, H-2), 5.98 (dd, 1 H, *J* = 10 and 18 Hz, $CH=CH_2$). Anal. Calcd for $C_{19}H_{30}O_7$: C, 61.60; H, 8.16. Found: C, 61.69; H, 8.10. **2R**: $[\alpha]^{26}_D$ +14.8° (*c* 1.11); IR ν_{max}^{neat} 2990, 1730, 1640 cm^{-1}; ^1H NMR (90 MHz) δ 1.25 (t, 3 H, *J* = 7 Hz, $COOCH_2CH_3$), 1.30 (d, 3 H, *J* = 7 Hz, CH_3 of the side chain at C-4), 1.33, 1.38, 1.45 (each s, 6 H, 3 H, 3 H, 2 $C(CH_3)_2$), 2.81 (q, 1 H, *J* = 7 Hz, $CHCH_3$ of the side chain at C-4), 3.71–4.56 (m, 3 H, H-5, H-1,2,2′ of the side chain at C-5), 4.06 (q, 2 H, *J* = 7 Hz, $COOCH_2CH_3$), 4.76 (1 H, d, *J* = 4 Hz, H-3), 5.26 (dd, 1 H, *J* = 2 and 11 Hz, $CH=CH_2$), 5.39 (dd, 1 H, *J* = 2 and 18 Hz, $CH=CH_2$), 5.59 (d, 1 H, *J* = 4 Hz, H-2), 5.96 (dd, 1 H, *J* = 11 and 18 Hz, $CH=CH_2$); high-resolution mass spectrum calcd for $C_{18}H_{27}O_7$ *m/z* 355.1755, found, M − CH_3, 355.1757.

$LiAlH_4$ Reduction of 2S and 2R. (2*R*,3*R*,4*S*,5*S*)-4-[(1*S*)-1-(Hydroxymethyl)ethyl]-2,3-(isopropylidenedioxy)-5-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-4-vinyltetrahydrofuran (3S) and the 4-[(1*R*)-1-(Hydroxymethyl)ethyl] Isomer (3R). A solution of **2S** (15.0 g, 40.5 mmol) in THF (150 mL) was stirred with $LiAlH_4$ (2.77 g, 73.0 mmol) for 30 min. To the suspension was added water (80 mL), and the resulting solids were removed by filtration and washed with AcOEt. To the combined filtrate and washings was added water (200 mL), and this aqueous phase was then extracted with AcOEt (200 mL × 4). The combined extracts were dried (Na_2SO_4) and concentrated in vacuo. The residue was chromatographed on silica gel (140 g, AcOEt/hexane, 1:4), and the fractions corresponding to R_f 0.27 (AcOEt/hexane, 1:2) were concentrated in vacuo to give **3S** (12.7 g, 95%) as a colorless oil: $[\alpha]^{26}_D$ +45.6° (*c* 1.53); IR ν_{max}^{neat} 3460, 2990, 1640 cm^{-1}; ^1H NMR (90 MHz) δ 1.10 (d, 3 H, *J* = 6 Hz, $CHCH_3$ of the side chain at C-4), 1.30, 1.35, 1.39, 1.47 (each s, each 3 H, 2 $C(CH_3)_2$), 1.69–2.08 (m, 2 H, OH, $CHCH_3$ of the side chain at C-4), 3.41–4.26 (m, 6 H, H-5, H-1,2,2′ of the side chain at C-5, CH_2OH), 4.70 (d, 1 H, *J* = 3 Hz, H-3), 5.21 (dd, 1 H, *J* = 2 and 11 Hz, $CH=CH_2$), 5.36 (dd, 1 H, *J* = 2 and 19 Hz, $CH=CH_2$), 5.62 (d, 1 H, *J* = 3 Hz, H-2), 5.94 (dd, 1 H, *J* = 11 and 19 Hz, $CH=CH_2$); high-resolution mass spectrum, calcd for $C_{17}H_{29}O_6$ *m/z* 329.1963, found, M + H, 329.1967.

As with **2S**, **2R** (1.46 g, 3.95 mmol) was reduced with $LiAlH_4$ (196 mg, 5.16 mmol) to give **3R** (1.31 g, quantitatively) as a colorless oil: TLC R_f 0.13 (AcOEt/hexane, 1:3); $[\alpha]^{23}_D$ +36.5° (*c* 1.32); IR ν_{max}^{neat} 3500, 2990, 1640 cm^{-1}; ^1H NMR (90 MHz) δ 1.03 (d, 3 H, *J* = 6 Hz, $CHCH_3$ of the side chain at C-4), 1.29, 1.31, 1.37, 1.45 (each s, each 3 H, 2 $C(CH_3)_2$), 1.67–2.08 (m, 2 H, OH, $CHCH_3$ of the side chain at C-4), 3.40–4.22 (m, 6 H, H-5, H-1,2,2′ of the side chain at C-5, CH_2OH), 4.73 (d, 1 H, *J* = 4 Hz, H-3), 5.23 (dd, 1 H, *J* = 2 and 11 Hz, $CH=CH_2$), 5.34 (dd, 1 H, *J* = 2 and 18 Hz, $CH=CH_2$), 5.69 (d, 1 H, *J* = 4 Hz, H-2), 5.94 (dd, 1 H, *J* = 11 and 18 Hz, $CH=CH_2$); high-resolution mass spectrum calcd for $C_{16}H_{25}O_6$ *m/z* 313.1649, found, M − CH_3, 313.1652.

Benzylation of 3S and 3R. (2*R*,3*R*,4*S*,5*S*)-4-[(1*S*)-1-[(benzyloxy)methyl]ethyl]-2,3-(isopropylidenedioxy)-5-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-4-vinyltetrahydrofuran (4S) and the 4-[(1*R*)-1-[(Benzyloxy)methyl]ethyl] Isomer (4R). Sodium hydride (60% emulsion in mineral oil, 1.10 g, 45.8 mmol) was washed with hexane, dried, and suspended in DMF (25 mL). To the suspension was added a DMF (95 mL) solution of **3S** (3.76 g, 11.45 mmol) at 0 °C. The suspension was stirred for 1 h at 0 °C, and to it was added benzyl bromide (4.1 mL, 34.1 mmol). The mixture was stirred for 4.5 h at room temperature, and EtOH (5 mL) was added. After concentration of the mixture, the residue was diluted with water (200 mL). This aqueous solution was extracted with AcOEt (200 mL × 3), and the combined extracts were dried (Na_2SO_4) and concentrated in vacuo. The residue was chromatographed on silica gel (150 g, AcOEt/hexane, 1:40), and the fractions corresponding to R_f 0.51 (AcOEt/hexane, 1:5) were concentrated to give **4S** (3.85 g, 81%) as a colorless oil: $[\alpha]^{24}_D$ +47.0° (*c* 1.66); IR ν_{max}^{neat} 2990, 1640, 1500 cm^{-1}; ^1H NMR (90 MHz) δ 1.14 (d, 3 H, *J* = 6 Hz, $CHCH_3$ of the side chain at C-4), 1.31, 1.40, 1.47 (each s, 6 H, 3 H, 3 H, 2 $C(CH_3)_2$), 1.91–2.12 (m, 1 H, $CHCH_3$ of the side chain at C-4), 3.28–4.24 (m, 6 H, H-5, H-1,2,2′ of the side chain, CH_2OBzl), 4.46 (s, 2 H, $OCH_2C_6H_5$), 4.77 (d, 1 H, *J* = 4 Hz, H-3), 5.17 (dd, 1 H, *J* = 2 and 12 Hz, $CH=CH_2$), 5.31 (dd, 1 H, *J* = 2 and 18 Hz, $CH=CH_2$), 5.59 (d, 1 H, *J* = 4 Hz, H-2), 5.92 (dd, 1 H, *J* = 12 and 18 Hz, $CH=CH_2$), 7.33 (s, 5 H, $OCH_2C_6H_5$); high-resolution mass spectrum calcd for $C_{23}H_{31}O_6$ *m/z* 403.2119, found, M − CH_3, 403.2125.

As described above, **3R** (55 mg) was converted into **4R** (65 mg, 93%), a colorless oil: TLC R_f 0.54 (AcOEt/hexane, 1:5); $[\alpha]^{28}_D$ +37.0° (*c* 0.94); IR ν_{max}^{neat} 2990, 1640, 1490 cm^{-1}; ^1H NMR (90 MHz) δ 1.05 (d, 3 H, *J* = 6 Hz, $CHCH_3$ of the side chain at C-4), 1.25, 1.30, 1.37, 1.45 (each s, each 3 H, 2 $C(CH_3)_2$), 3.15–4.15 (m, 6 H, H-5, H-1,2,2′ of the side chain at C-5, CH_2OBzl), 4.49 (s, 2 H, $OCH_2C_6H_5$), 4.72 (d, 1 H, *J* = 4 Hz, H-3), 5.24 (dd, 1 H, *J* = 2 and 11 Hz, $CH=CH_2$), 5.30 (dd, 1 H, *J* = 2 and 18 Hz, $CH=CH_2$), 5.66 (d, 1 H, *J* = 4 Hz, H-2), 5.95 (dd, 1 H, *J* = 12 and 18

(5) Compounds **2S** (**2R**) to **10S** (**10R**) are named as pentasubstituted tetrahydrofurans (the tetrahydrofuran ring is numbered clockwise as the quaternary carbon is C-4). Compounds **11S** and **11R** are named as derivatives of 2,5,10,12-tetraoxatricyclo[7.3.0.0^{3,8}]dodecanes.

Hz, C*H*=CH_2), 7.36 (s, 5 H, $OCH_2C_6H_5$); high-resolution mass spectrum, calcd for $C_{24}H_{34}O_6$ m/z 418.2353, found, M, 418.2349.

Selective Deisopropylidenation of 4S and 4R. (2*R*,3*R*,4*S*,5*S*)-4-[(1*S*)-1-[(Benzyloxy)methyl]ethyl]-5-[(1*R*)-1,2-dihydroxyethyl]-2,3-(isopropylidenedioxy)-4-vinyltetrahydrofuran (5S) and the 4-[(1*R*)-1-[(Benzyloxy)methyl]ethyl] Isomer (5R). A solution of **4S** (303 mg, 0.72 mmol) in 50% aqueous AcOH (10 mL) was stirred at 35 °C for 15 h. The solution was concentrated in vacuo, and the residue was chromatographed on silica gel (AcOEt/hexane, 1:2). The fractions corresponding to R_f 0.14 (AcOEt/hexane, 1:3) were concentrated to give **5S** (257 mg, 94%) as a colorless oil: $[\alpha]^{21}_D$ +23.6° (*c* 1.44); IR ν_{max}^{neat} 3440, 2980, 1640, 1495 cm^{-1}; ^1H NMR (90 MHz) δ 1.10 (d, 3 H, *J* = 7 Hz, CHC*H*$_3$ of the side chain at C-4), 1.26, 1.46 (each s, each 3 H, C(CH_3)$_2$), 1.98–2.27 (m, 1 H, C*H*CH_3 of the side chain at C-4), 2.39–2.82 (br s, 2 H, 2 OH), 3.19–4.15 (m, 6 H, H-5, H-1,2,2′ of the side chain at C-5, C*H*$_2$OBzl), 4.74 (d, 1 H, *J* = 4 Hz, H-3), 5.17 (dd, *J* = 2 and 12 Hz, CH=C*H*$_2$), 5.29 (dd, 1 H, *J* = 2 and 18 Hz, CH=C*H*$_2$), 5.59 (d, 1 H, *J* = 4 Hz, H-2), 5.97 (dd, *J* = 12 and 18 Hz, C*H*=CH_2), 7.32 (s, 5 H, $OCH_2C_6H_5$); high-resolution mass spectrum calcd for $C_{21}H_{30}O_6$ m/z 378.2040, found, *M*, 378.2042.

Analogously, **4R** (49 mg) was converted into **5R** (38 mg, 85%), a colorless oil: TLC R_f 0.11 (AcOEt/hexane, 1:3); $[\alpha]^{29}_D$ +24.0° (*c* 0.94); IR ν_{max}^{neat} 3440, 2990, 1640, 1490 cm^{-1}; ^1H NMR (90 MHz) δ 1.12 (d, 3 H, *J* = 7 Hz, CHC*H*$_3$ of the side chain at C-4), 1.36, 1.46 (each s, each 3 H, C(CH_3)$_2$), 1.89–2.34 (m, 1 H, C*H*CH_3 of the side chain at C-4), 2.53–2.58 (m, 2 H, 2 OH), 3.28–4.15 (m, 6 H, H-5, H-1,2,2′ of the side chain at C-5, C*H*$_2$OBzl), 4.49 (s, 2 H, OC*H*$_2C_6H_5$), 4.66 (d, 1 H, *J* = 4 Hz, H-3), 5.28 (dd, 1 H, *J* = 2 and 10 Hz, CH=C*H*$_2$), 5.33 (dd, 1 H, *J* = 2 and 18 Hz, CH=C*H*$_2$), 5.68 (d, 1 H, *J* = 4 Hz, H-2), 6.06 (dd, 1 H, *J* = 12 and 18 Hz, C*H*=CH_2), 7.38 (s, 5 H, $OCH_2C_6H_5$); high-resolution mass spectrum calcd for $C_{20}H_{27}O_6$ m/z 363.1806, found, M − CH_3, 363.1807.

Glycol Cleavage of 5S and 5R and Successive $NaBH_4$ Reduction. (2*R*,3*R*,4*S*,5*S*)-4-[(1*S*)-1-[(Benzyloxy)methyl]ethyl]-5-(hydroxymethyl)-2,3-(isopropylidenedioxy)-4-vinyltetrahydrofuran (6S) and the 4-[(1*R*)-1-[(Benzyloxy)methyl]ethyl] Isomer (6R). To a solution of **5S** (129 mg, 0.34 mmol) in MeOH (10 mL) was added an aqueous solution (0.7 mL) of $NaIO_4$ (124 mg, 0.58 mmol), and the mixture was stirred for 30 min. The resulting solids were removed by filtration, and the filtrate was concentrated in vacuo. The residue was dissolved in water (20 mL) and extracted with AcOEt (20 mL × 3). The extracts were dried (Na_2SO_4) and concentrated. The residue was dissolved in THF (2 mL), and $LiAlH_4$ (26 mg, 0.69 mmol) was added. The reaction mixture was stirred for 90 min, and water (0.15 mL) was added to it. The resulting solids were removed by filtration, and the filtrate was concentrated in vacuo. The residue was dissolved in water (20 mL), extracted with AcOEt (20 mL × 4), and the combined extracts were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by PTLC (AcOEt/hexane, 1:1) to give **6S** (64 mg, 54%) as a colorless oil: TLC R_f 0.48 (AcOEt/hexane, 1:2); $[\alpha]^{27}_D$ +36.5° (*c* 1.36); IR ν_{max}^{neat} 3450, 2990, 1650 cm^{-1}; ^1H NMR (90 MHz) δ 1.11 (d, 3 H, *J* = 7 Hz, CHC*H*$_3$ of the side chain at C-4), 1.29, 1.49 (each s, each 3 H, C(CH_3)$_2$), 1.82–2.11 (m, 2 H, C*H*CH_3 of the side chain at C-4, OH), 3.39–4.37 (m, 5 H, H-5, H-1,1′ of the side chain at C-5, C*H*$_2$OBzl), 4.47 (s, 2 H, OC*H*$_2C_6H_5$), 4.72 (d, 1 H, *J* = 4 Hz, H-3), 5.09 (dd, 1 H, *J* = 2 and 20 Hz, CH=C*H*$_2$), 5.25 (dd, 1 H, *J* = 2 and 12 Hz, CH=C*H*$_2$), 5.77 (d, 1 H, *J* = 4 Hz, H-2), 6.05 (dd, 1 H, *J* = 12 and 20 Hz, C*H*=CH_2), 7.35 (s, 5 H, $OCH_2C_6H_5$); high-resolution mass spectrum calcd for $C_{19}H_{25}O_5$ m/z 333.1701, found, M − CH_3, 333.1703.

By the analogous procedure described for **5S**, **5R** (34 mg) was converted into **6R** (26 mg, 82%), a colorless oil: TLC R_f 0.11 (AcOEt/hexane, 1:3); $[\alpha]^{30}_D$ +21.9° (*c* 1.16); IR ν_{max}^{neat} 3470, 2990, 1640, 1490 cm^{-1}; ^1H NMR (90 MHz) δ 1.04 (d, 3 H, *J* = 7 Hz, CHC*H*$_3$ of the side chain at C-4), 1.30, 1.53 (each s, each 3 H, C(CH_3)$_2$), 1.82–2.13 (m, 2 H, C*H*CH_3 of the side chain at C-4, OH), 3.28–3.83 (m, 4 H, H-1,1′ of the side chain at C-5, C*H*$_2$OBzl), 4.37 (t, 1 H, *J* = 6 Hz, H-5), 4.50 (s, 2 H, OC*H*$_2C_6H_5$), 4.66 (d, 1 H, *J* = 4 Hz, H-3), 5.09 (dd, 1 H, *J* = 2 and 19 Hz, CH=C*H*$_2$), 5.26 (dd, 1 H, *J* = 2 and 12 Hz, CH=C*H*$_2$), 5.75 (d, 1 H, *J* = 4 Hz, H-2), 6.04 (dd, 1 H, *J* = 12 and 19 Hz, C*H*=CH_2), 7.38 (s, 5 H, $OCH_2C_6H_5$); high-resolution mass spectrum calcd for $C_{20}H_{28}O_5$ m/z 348.1945, found, M, 348.1960.

Lemieux–Johnson Oxidation of 6S and 6R. (2*R*,3*R*,4*R*,5*S*)-4-[(1*S*)-1-[(Benzyloxy)methyl]ethyl]-4-formyl-5-(hydroxymethyl)-2,3-(isopropylidenedioxy)tetrahydrofuran (7S) and the 4-[(1*R*)-1-[(Benzyloxy)methyl]ethyl] Isomer (7R). To a stirred solution of **6S** (31 mg, 0.09 mmol) in a mixture of water and MeOH (1:1, 2 mL) was added OsO_4 (0.05 M in 2-methyl-2-propanol, 0.10 mL, 0.005 mmol) in the dark. The reaction mixture was stirred for 30 min, and to it was added $NaIO_4$ (48 mg, 0.22 mmol). The mixture was then stirred for 19 h, and to it was then added $NaHSO_3$ (30 mg). The resultant mixture was then stirred for 30 min, diluted with water (10 mL), and extracted with Et_2O (15 mL × 3). The combined extracts were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by PTLC (AcOEt/hexane, 1:1) to give **6S** (11.5 mg, 36%) as a colorless oil: TLC R_f 0.32 (AcOEt/hexane, 1:1); $[\alpha]^{26}_D$ +7.2° (*c* 0.55); IR ν_{max}^{neat} 3460, 2930, 1720, 1490 cm^{-1}; ^1H NMR (90 MHz) δ 1.02 (d, 3 H, *J* = 7 Hz, CHC*H*$_3$ of the side chain at C-4), 1.33, 1.48 (each s, each 3 H, C(CH_3)$_2$), 2.26–2.47 (m, 1 H, C*H*CH_3 of the side chain at C-4), 2.68 (br, 1 H, OH), 3.48–3.56 (m, 2 H, H-1,1′ of the side chain at C-5), 3.82–3.98 (m, 2 H, C*H*$_2$OBzl), 4.30–4.40 (m, 1 H, H-5), 4.48 (s, 2 H, OC*H*$_2C_6H_5$), 5.04 (d, 1 H, *J* = 4 Hz, H-3), 5.76 (d, 1 H, *J* = 4 Hz, H-2), 7.32 (s, 5 H, $OCH_2C_6H_5$), 9.78 (s, 1 H, CHO).

As described for the preparation of **7S**, **6R** (31 mg) was converted into **7R** (13 mg, 41%), a colorless oil: TLC R_f 0.51 (AcOEt/hexane, 1:1); $[\alpha]^{27}_D$ +23.0° (*c* 0.63), IR ν_{max}^{neat} 3480, 2980, 1720, 1495 cm^{-1}; ^1H NMR (90 MHz) δ 1.15 (d, 3 H, *J* = 7 Hz, CHC*H*$_3$ of the side chain at C-4), 1.29, 1.48 (each s, each 3 H, C(CH_3)$_2$), 2.16–2.54 (m, 2 H, C*H*CH_3 of the side chain at C-4, OH), 3.46–3.90 (m, 4 H, H-1,1′ of the side chain at C-5, C*H*$_2$OBzl), 4.47 (s, 2 H, OC*H*$_2C_6H_5$), 5.02 (d, 1 H, *J* = 4 Hz, H-3), 5.74 (d, 1 H, *J* = 4 Hz, H-2), 7.32 (s, 5 H, $OCH_2C_6H_5$), 9.78 (s, 1 H, CHO).

Selective Deisopropylidenation of 3S and 3R. (2*R*,3*R*,4*S*,5*S*)-5-[(1R)-1,2-Dihydroxyethyl]-4-[(1*S*)-1-(hydroxymethyl)ethyl]-2,3-(isopropylidenedioxy)-4-vinyltetrahydrofuran (8S) and the 4-[(1*R*)-1-(Hydroxymethyl)ethyl] Isomer (8R). A solution of **3S** (100 mg, 0.30 mmol) in 50% aqueous AcOH (4 mL) was stirred for 9 h and then concentrated in vacuo. The residue was chromatographed on silica gel (EtOH/toluene, 1:15), and the fractions corresponding to R_f 0.38 (EtOH/toluene, 1:5) were concentrated in vacuo to give **8S** (78 mg, 89%), a colorless oil: $[\alpha]^{27}_D$ +31.9° (*c* 1.17); IR ν_{max}^{neat} 3400, 2990, 1640 cm^{-1}; ^1H NMR (90 MHz) δ 1.10 (d, 3 H, *J* = 7 Hz, CHC*H*$_3$ of the side chain at C-4), 1.35, 1.50 (each s, each 3 H, C(CH_3)$_2$), 1.91–2.11 (m, 2 H, C*H*CH_3 of the side chain at C-4, OH), 3.31–4.17 (m, 8 H, H-5, H-1,2,2′ of the side chain at C-5, 2 OH, C*H*$_2$OH at the side chain at C-4), 4.65 (d, 1 H, *J* = 4 Hz, H-3), 5.28 (dd, 1 H, *J* = 2 and 12 Hz, CH=C*H*$_2$), 5.37 (dd, 1 H, *J* = 2 and 19 Hz, CH=C*H*$_2$), 5.67 (d, 1 H, *J* = 4 Hz, H-2), 6.02 (dd, 1 H, *J* = 12 and 19 Hz, C*H*=CH_2); high-resolution mass spectrum, calcd for $C_{13}H_{21}O_6$ m/z 273.1336, found, M − CH_3, 273.1348.

Analogously as described above, **3R** (1.31 g) was converted into **8R** (838 mg, 74%), a colorless oil: TLC R_f 0.34 (EtOH/toluene, 1:5); $[\alpha]^{30}_D$ +29.3° (*c* 1.05); IR ν_{max}^{neat} 3400, 2990, 1635 cm^{-1}; ^1H NMR (90 MHz) δ 1.13 (d, 3 H, *J* = 7 Hz, CHC*H*$_3$ of the side chain at C-4), 1.27, 1.47 (each s, each 3 H, C(CH_3)$_2$), 2.10–2.22 (m, 1 H, C*H*CH_3 of the side chain at C-4), 3.23–4.02 (m, 9 H, H-5, H-1,2,2′ of the side chain at C-5, 3 OH, C*H*$_2$OH at the side chain at C-4), 4.56 (d, 1 H, *J* = 4 Hz, H-3), 5.26 (dd, 1 H, *J* = 2 and 11 Hz, CH=C*H*$_2$), 5.30 (dd, 1 H, *J* = 2 and 18 Hz, CH=C*H*$_2$), 5.69 (d, 1 H, *J* = 4 Hz, H-2), 5.98 (dd, 1 H, *J* = 11 and 18 Hz, C*H*=CH_2); high-resolution mass spectrum calcd for $C_{14}H_{25}O_6$ m/z 289.1630, found, M + H, 289.1649.

Glycol Cleavage of 8S and 8R and Successive $NaBH_4$ Reduction. (2*R*,3*R*,4*S*,5*S*)-5-(Hydroxymethyl)-4-[(1*S*)-1-(hydroxymethyl)ethyl]-2,3-(isopropylidenedioxy)-4-vinyltetrahydrofuran (10S) and the 4-[(1*R*)-1-(Hydroxymethyl)ethyl] Isomer (10R). To a stirred solution of **8S** (78 mg, 0.27 mmol) in MeOH (6 mL) was added an aqueous solution (0.4 mL) of $NaIO_4$ (70 mg, 0.33 mmol). The mixture was stirred for 30 min and concentrated in vacuo. The residue was partitioned between AcOEt (20 mL) and water (20 mL), the aqueous phase was extracted with AcOEt (20 mL × 4), and the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo to give

9S, which was reduced directly. To a solution of **9S** (59 mg) in EtOH (2 mL) was added $NaBH_4$ (88 mg, 2.3 mmol). The reaction mixture was refluxed for 20 h and then neutralized by addition of Amberlite IR-120 (H^+). The resin was removed by filtration, and the filtrate was concentrated in vacuo. The residue was chromatogaphed on silica gel (20 g, EtOH/toluene, 1:20), and the fractions corresponding to R_f 0.40 (EtOH/toluene, 1:5) were concentrated to give **10S** (38 mg, 54%), a colorless oil; **3S** (462 mg) was also converted into **10S** (201 mg, 63% yield from **3S**) when **8S** was not purified by silica gel chromatography. **10S**: $[a]^{23}_D$ +34.0° (*c* 0.81); IR ν_{max}^{neat} 3440, 2990, 1640 cm^{-1}; ^1H NMR (90 MHz) δ 1.10 (d, 3 H, J = 7 Hz, $CHCH_3$ of the side chain at C-4), 1.34, 1.53 (each s, each 3 H, $C(CH_3)_2$), 1.65–1.98 (m, 1 H, $CHCH_3$ of the side chain at C-4), 2.10–2.93 (m, 2 H, 2 OH), 3.48–4.23 (m, 5 H, H-5, CH_2OH at C-5, CH_2OH of the side chain at C-4), 4.62 (d, 1 H, J = 4 Hz, H-3), 5.11 (dd, 1 H, J = 2 and 18 Hz, $CH{=}CH_2$), 5.30 (dd, 1 H, J = 2 and 12 Hz, $CH{=}CH_2$), 5.82 (d, 1 H, J = 4 Hz, H-2), 6.01 (dd, 1 H, J = 12 and 18 Hz; $CH{=}CH_2$); high-resolution mass spectrum calcd for $C_{12}H_{19}O_5$ *m/z* 243.1232, found, M - CH_3, 243.1235.

Compound **8R** (838 mg, 2.9 mmol) was converted into **10R** via **9R** as described in the preparation of **10S**; **10R** (659 mg, 88%) was obtained as a colorless oil: TLC R_f 0.19 (EtOH/toluene, 1:5); $[\alpha]^{30}_D$ +23.1° (*c* 1.22); IR ν_{max}^{neat} 3400, 2990, 1650 cm^{-1}; ^1H NMR (90 MHz) δ 1.02 (d, 3 H, J = 7 Hz, $CHCH_3$ of the side chain at C-4), 1.33, 1.53 (each s, each 3 H, $C(CH_3)_2$), 1.83–2.06 (m, 1 H, $CHCH_3$ of the side chain at C-4), 2.32–2.64 (m, 2 H, 2 OH), 3.37–4.08 (m, 4 H, CH_2OH at C-5, CH_2OH of the side chain at C-4), 4.27 (dd, 1 H, J = 4 and 7 Hz, H-5), 4.66 (d, 1 H, J = 4 Hz, H-3), 5.10 (dd, 1 H, J = 2 and 18 Hz, $CH{=}CH_2$), 5.29 (dd, 1 H, J = 2 and 11 Hz, $CH{=}CH_2$), 5.84 (d, 1 H, J = 4 Hz, H-2), 6.05 (dd, 1 H, J = 11 and 18 Hz, $CH{=}CH_2$); high-resolution mass spectrum calcd for $C_{13}H_{23}O_5$ *m/z* 259.1544, found, M + H, 259.1575.

(1*R*,3*S*,7*S*,8*S*,9*R*)-7,11,11-Trimethyl-8-vinyl-2,5,10,12-tetraoxatricyclo[7.3.0.0^{3,8}]dodecane (11S). A solution of **10S** (201 mg, 0.78 mmol) in pyridine (10 mL) containing TsCl (444 mg, 2.33 mmol) and DMAP (56 mg, 0.46 mmol) was heated at 60 °C for 16 h. The solution was then concentrated in vacuo, and the residue was partitioned between AcOEt (50 mL) and water (30 mL). The aqueous phase was extracted with AcOEt (50 mL × 2), and the combined extracts were dried (Na_2SO_4) and concentrated in vacuo. The residue was chromatographed on silica gel (AcOEt/hexane, 1:10), and the fractions corresponding to R_f 0.30 (AcOEt/hexane, 1:5) were concentrated to give **11S** (138 mg, 74%) as needles: mp 62–63 °C; $[\alpha]^{30}_D$ +1.6° (*c* 1.20); IR ν_{max}^{neat} 2970, 1640 cm^{-1}; ^1H NMR (400 MHz) δ 0.86 (d, 3 H, J = 7.3 Hz, CH_3-7), 1.34, 1.50 (each s, each 3 H, 2 CH_3-11), 1.73 (ddq, 1 H, $J_{CH_3,7}$ = 7.3 Hz, $J_{6_{ax},7}$ = 11.2 Hz, $J_{6_{eq},7}$ = 4.0 Hz, H-7), 3.11 (t, 1 H, $J_{6_{ax},7} = J_{6_{ax},6_{eq}}$ = 11.2 Hz, H-6_{ax}), 3.56 (dd, 1 H, $J_{6_{eq},7}$ = 4.0 Hz, $J_{6_{eq},6_{ax}}$ = 11.2 Hz, H-6_{eq}), 3.72 (d, 1 H, $J_{3,4_{ax}}$ = 0 Hz, $J_{4_{ax},4_{eq}}$ = 11.8 Hz, H-4_{ax}), 4.14 (s, 1 H, $J_{3,4_{ax}} = J_{3,4_{eq}}$ = 0 Hz, H-3), 4.15 (d, 1 H, $J_{3,4_{eq}}$ = 0 Hz, $J_{4_{ax},4_{eq}}$ = 11.8 Hz, H-4_{eq}), 4.47 (d, 1 H, $J_{1,9}$ = 3.4 Hz, H-9), 5.16 (dd, 1 H, J = 1.0 and 18.1 Hz, $CH{=}CH_2$), 5.42 (d, 1 H, J = 11.2 Hz, $CH{=}CH_2$), 5.88 (dd, J = 11.2 and 18.1 Hz, $CH{=}CH_2$), 5.91 (d, 1 H, $J_{1,9}$ = 3.4 Hz, H-1); high-resolution mass spectrum calcd for $C_{13}H_{21}O_4$ *m/z* 241.1437, found, M + H, 241.1425. Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 65.13; H, 8.22.

(1*R*,3*S*,7*R*,8*S*,9*R*)-7,11,11-Trimethyl-8-vinyl-2,5,10,12-tetraoxatricyclo[7.3.0.0^{3,8}]dodecane (11R). By the procedure analogous to that described for the preparation of **11S**, **10R** (81 mg) was converted into **11R** (52 mg, 69%) as needles: mp 59–60 °C; TLC R_f 0.80 (EtOH/toluene, 1:5); $[\alpha]^{29}_D$ +111.3° (*c* 0.95); IR ν_{max}^{neat} 2960, 1635 cm^{-1}; ^1H NMR (400 MHz) δ 1.22 (d, 3 H, J = 7.3 Hz, CH_3-7), 1.33, 1.51 (each s, each 3 H, 2 CH_3-11), 1.77 (dq, 1 H, $J_{CH_3,7}$ = 7.3 Hz, $J_{6_{ax},7}$ = 1.0 Hz, $J_{6_{eq},7}$ = 0 Hz, H-7), 3.52 (d, 1 H, $J_{6_{eq},7}$ = 0 Hz, $J_{6_{ax},6_{eq}}$ = 10.7 Hz, H-6_{eq}), 3.60 (dd, 1 H, $J_{6_{ax},7}$ = 1.0 Hz, $J_{6_{ax},6_{eq}}$ = 10.7 Hz, H-6_{ax}), 3.62 (dd, 1 H, $J_{3,4_{ax}}$ = 1.9 Hz, $J_{4_{ax},4_{eq}}$ = 13.2 Hz, H-4_{ax}), 4.03 (d, 1 H, $J_{3,4_{ax}}$ = 1.9 Hz, $J_{3,4_{eq}}$ = 0 Hz, H-3), 4.13 (d, 1 H, $J_{3,4_{eq}}$ = 0 Hz, $J_{4_{eq},4_{ax}}$ = 13.2 Hz, H-4_{eq}), 4.49 (d, 1 H, $J_{1,9}$ = 3.4 Hz, H-9), 5.11 (d, 1 H, J = 17.5 Hz, $CH{=}CH_2$), 5.38 (d, 1 H, J = 11.7 Hz, $CH{=}CH_2$), 5.81 (d, 1 H, $J_{1,9}$ = 3.4 Hz, H-1), 5.83 (dd, 1 H, J = 11.7 Hz and 17.5 Hz, $CH{=}CH_2$); high-resolution mass spectrum calcd for $C_{13}H_{21}O_4$ *m/z* 241.1438, found, M + H, 241.1428. Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 65.12; H, 8.16.

Medium Effects as a Criterion for Reaction Mechanism. Application of the SWAG Procedures to the Mechanism of the Neutral Hydrolysis of [(*p*-Nitrophenyl)sulfonyl]methyl Perchlorate

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Introduction

According to the Savage–Wood additivity of group interactions (SWAG) procedure,[1,2] the thermodynamic properties of dilute aqueous solutions can be described in terms of pairwise solute–solute interaction parameters and, at the next level of sophistication, in terms of pairwise group interaction parameters. Recently we used these descriptions to quantify the effects of added cosolvents on the pseudo-first-order rate constants for the water-catalyzed hydrolysis of activated esters[3] and amides[4] in highly aqueous binary mixtures. In terms of the SWAG analysis, the effect of a cosolvent on the pseudo-first-order rate constant is expressed as:

$$\ln (k_{obsd}/k^0_{obsd}) = (2/RT)(1/m^0)^2(g_{A\leftrightarrow IS} - g_{A\leftrightarrow TS})m_A - n\phi m_A M_1 \quad (1)$$

where k_{obsd} is the rate constant in the water-rich aqueous solution (molality of cosolvent, m_A), k^0_{obsd} is the rate constant in water (m_A = 0), m^0 = 1 mol kg^{-1}, n is the order of the reaction with respect to water, ϕ is the practical osmotic coefficient and M_1 is the molar mass of water. The terms $g_{A\leftrightarrow IS}$ and $g_{A\leftrightarrow TS}$ are the pairwise cosolvent–initial state and cosolvent–transition state Gibbs energies of interaction. For chemical reactions, self-consistent sets of Gibbs energy interaction parameters were developed[3,4] describing interactions between functional groups (e.g. CH_2 and OH) in cosolvents and in key groups within both initial and transition states. The success of the analysis suggested the possibility of using the SWAG approach in studies of reaction mechanism. The present study is the first endeavor along these lines, using as a model reaction the water-catalyzed hydrolysis of [(*p*-nitrophenyl)sulfonyl]-methyl perchlorate (1).

Results and Discussion

Since the first synthesis of a covalent (arylsulfonyl)-methyl perchlorate,[5,6] considerable attention has been paid to the mechanism of the hydrolysis[5] and to medium effects on the hydrolytic process.[7-10] Hydrolysis does not proceed via nucleophilic displacement of the perchlorate moiety but involves general base catalysis via rate-determining deprotonation at the α-sulfonyl carbon atom. The transition state is symmetric as indicated by large, primary kinetic deuterium isotope effects ($k_H/k_D \approx 6$) and the Brønsted β value of 0.51. One mechanism for the water-catalyzed reaction is outlined in Scheme I. Medium effects on the hydrolysis induced by alcohols, 1,3- and 1,4-dioxane,[7-9] and electrolytes[10] have been interpreted pre-

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