Stereoselective Ring-Opening of Acetylated Pyranose-1,2-(ethyl orthoacetates)

Setsuo SAITO,*[a] Shigeya SUMITA,[b] Koki ICHINOSE,[a] and Yasuhiko KANDA[a]

Faculty of Pharmaceutical Sciences, Josai University,[a] Keyakidai 1-1, Sakado, Saitama 350-02, Japan and Shiratori Pharmaceutical Co. Ltd.,[b] Tsudanuma 6-11-24, Narashino, Chiba 275, Japan. Received July 23, 1992

When acetylated pyranose-1,2-(ethyl orthoacetates) were hydrolyzed in acidic solvents, the ring-opening of the orthoacetate rings was influenced by the axial or equatorial OAc group at C-4 on the pyranoses; on acid-catalyzed hydrolysis, 3,4,6-tri-*O*-acetyl-α-D-galactopyranose- (8) and methyl 3,4-di-*O*-acetyl-α-D-galacturonatopyranose-1,2-(ethyl orthoacetate) (16) having an axial OAc group at C-4 on the pyranose rings gave 1,3,4,6-tetra-*O*-acetyl-α-D-galactopyranose (9) and methyl 1,3,4-tri-*O*-acetyl-α-D-galacturonatopyranose (23), respectively, whereas 3,4,6-tri-*O*-acetyl-α-D-glucopyranose- (10) and methyl 3,4-di-*O*-acetyl-α-D-glucuronatopyranose-1,2-(ethyl orthoacetate) (22) having an equatorial OAc group at C-4 on the pyranose rings gave 2,3,4,6-tetra-*O*-acetyl-D-glucopyranose (11) and methyl 2,3,4-tri-*O*-acetyl-D-glucuronatopyranose (24), respectively. On the acid-catalyzed hydrolysis, 3,4-di-*O*-acetyl-β-L-arabinopyranose-1,2-(ethyl orthoacetate) (34) having an axial OAc group at C-4 on the pyranose ring gave a mixture of 1,3,4-tri-*O*-acetyl-β-L- (35) and 2,3,4-tri-*O*-acetyl-L-arabinopyranose (36). These selectivities of ring-opening of the 1,2-(orthoacetates) were considered to have resulted from the differences of the conformers of the 1,2-(orthoacids) intermediates derived from the 1,2-(orthoacetates) and the orientation of the acetyl groups at C-4 on the pyranose rings.

Keywords pyranose-1,2-(ethyl orthoacetate); acid-catalyzed hydrolysis; 1,2-(orthoacid) intermediate; stereoselectivity; half-chair conformer; axial acetyl group

Acetylated pyranose-1,2-(alkyl orthoacetates)[1-6] have been utilized as starting materials for synthesis of various *O*-glycosides[4] and oligosaccharides[7] as well as acetylated pyranose bromides.[8] The 1,2-(alkyl orthoacetates) undergo alkaline-[1,5,9] and acid-catalyzed hydrolyses,[1,6,10] resulting in the opening of the orthoacetate rings to give 2-*O*-acetyl-pyranoses. It is known that the ring-opening of the orthoacetates in alkaline hydrolysis is caused by a direct nucleophilic attack on the anomeric carbon atom by hydroxyl ion (OH^-), whereas that in acid-catalyzed hydrolysis proceeds *via* unstable orthoacid intermediates derived from the orthoacetates. In this paper, we will report the stereoselective ring-openings of the acetylated pyranose-1,2-(ethyl orthoacetates) on acid-catalyzed hydrolysis.

A few reports have appeared on stereoselective ring-openings of the 1,2-(alkyl orthoacetates). Franks and Montgomery[11] examined the acid-catalyzed hydrolysis of β-D-mannopyranose-1,2-(benzyl orthoacetate) (**1**) to give 2-*O*-acetyl-D-mannopyranose (**2**)[12] by using 3,4,6-tri-*O*-benzyl-β-D-mannopyranose-1,2-(ethyl orthoacetate) (**3**) as a model substrate for the hydrolysis instead of **1**; the reaction of **3** with methanol in the presence of a catalytic amount of *p*-toluenesulfonic acid (*p*-TsOH) gave a product (**5**) having a 2-*O*-axial ester group. From this experimental result, they proposed a dioxolenium intermediate (**4**) which was attacked by methanol at the anomeric carbon from the α-side (less steric hindrance) of the pyranose ring (Fig. 1).

King and Allbutt[13] explained the ring-opening of the 1,2-(alkyl orthoacetate) ring on the basis of the result of hydrolysis of 9β,10α-decalin-2β,3β-diyl-(ethyl orthoacetate) (**6**) with 20% H_2O in acetic acid to give 3β-hydroxy-9β,10α-decalin-2β-yl acetate (**7**) as follows. When the two conformers **6a** and **6b** for **6** are compared (Fig. 2), the *endo* methyl group on the orthoacetate ring and 4β-hydrogen on the decalin ring in **6b** come close to each other, resulting in steric hindrance, so that the conformer **6a** is more stable than **6b**. In the conformer **6a**, the *exo* electrons of the axial

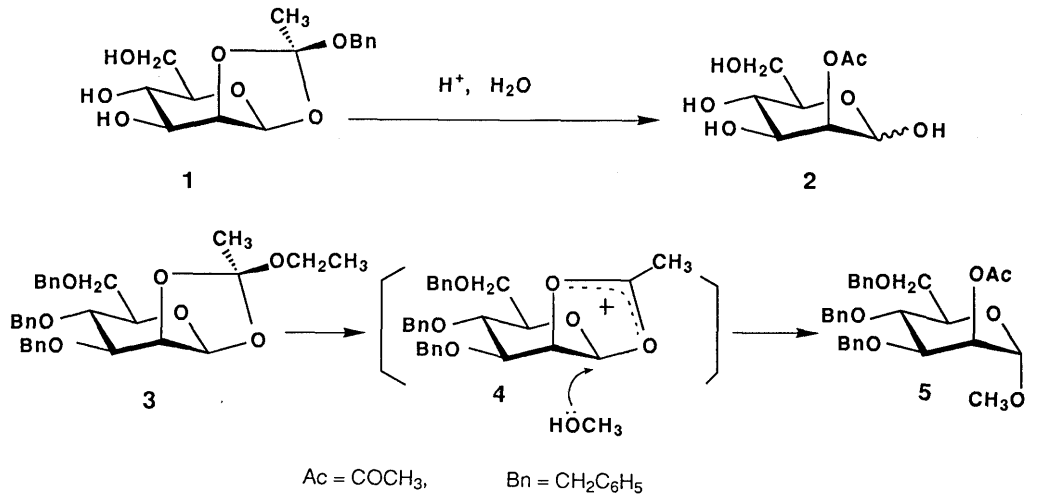


Fig. 1

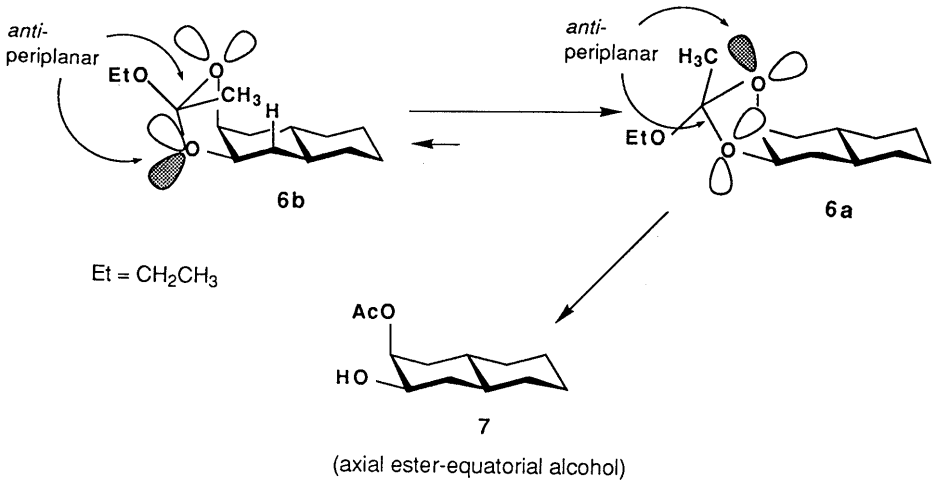


Fig. 2

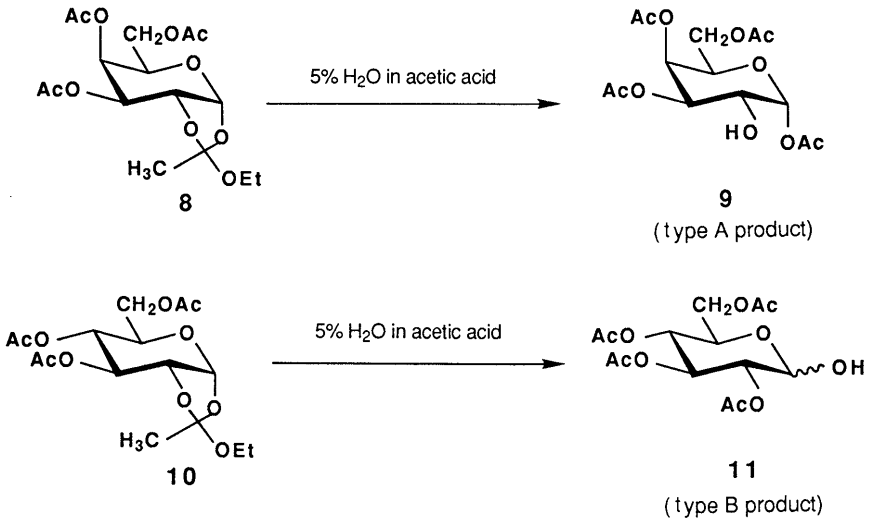


Fig. 3

oxygen in the orthoacetate ring can comparatively readily become *anti*-periplanar to the C–O bond, where C is the carbon in the orthoacetate ring and O is the equatorial oxygen on the decalin ring. The *anti*-periplanarity might make the cleavage of the C–O bond easier according to the orbital orientation theory proposed by Deslongchamps *et al.*,[14] to give an axial ester–equatorial alcohol **7**. Lemieux and Driguez[15] reported that the hydrolysis of 3,4,6-tri-*O*-acetyl-α-D-galactopyranose-1,2-(ethyl orthoacetate) (**8**) with 5% H_2O in acetic acid gave quantitatively 1,3,4,6-tetra-*O*-acetyl-α-D-galactopyranose (**9**) (type A product, formed through cleavage of the C–O(2) bond, where C is the carbon on the orthoacetate ring and O(2) is the oxygen at C-2 on the pyranose ring) (Fig. 3). They explained the ring-opening of **8** to **9** as follows; the strain of the strongly distorted half-chair pyranose ring of **8** was relieved by the stretching and eventual cleavage of the C–O(2) bond of the orthoacetate ring, giving **9**.

During our investigation of the synthesis of glycyrrhetic acid glycosides having β(1→2)-linked disaccharides[16] derived from various acetylated pyranose-1,2-(ethyl orthoacetates) as starting materials, it was found that the hydrolysis of 3,4,6-tri-*O*-acetyl-α-D-glucopyranose-1,2-(ethyl orthoacetate) (**10**)[3] under the same reaction conditions as those of Lemieux and Driguez gave quantitatively 2,3,4,6-tetra-*O*-acetyl-D-glucopyranose (**11**) (type B product formed through cleavage of the C–O(1) bond, where C is the carbon on the orthoacetate ring and O(1) is the anomeric oxygen on the pyranose) (Fig. 3). The ^{1}H-NMR spectrum of **11** exhibited two anomeric protons due to β- and α-anomers at δ 4.82 (d, J=9.0 Hz) and 5.47 (d, J=4.0 Hz) with the integration ratio of 3 : 1. Other protons could not be assigned completely because of signal overlapping due to a mixture of α- and β-anomers. Each anomeric proton signal was shifted to higher field than the corresponding ones of α- (**13**)[17] and β-D-glucopyranose peracetate (**14**),[18] observed at δ 6.33 (d, J=3.7 Hz) and 5.13 (d, J=8.1 Hz) (see the experimental section), respectively. According to King and Allbutt[13] and Lemieux and Driguez,[15] the ring-opening of the orthoacetate ring of **10** should give the type A product, 1,3,4,6-tetra-*O*-acetyl-α-D-glucopyranose **12**, because the steric circumstances around the orthoacetate ring fused to the pyranose ring of **10** are almost the same as in **8**. In practice, however, the reaction of **10** with 5% H_2O in acetic acid gave the type B product **11**. Moreover, although the mechanism proposed by Franks and Montgomery[11] could explain the ring-opening of **10** to **11**, it could not account

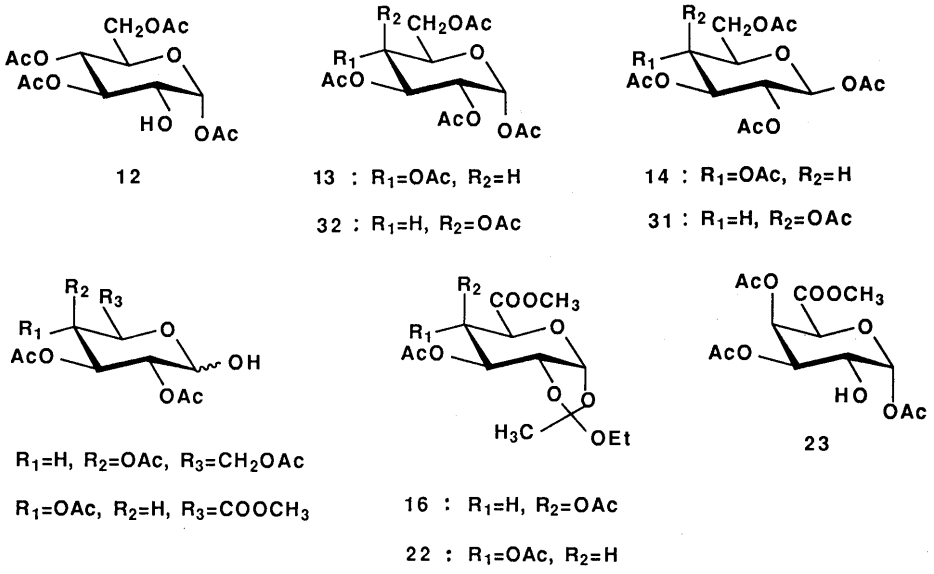


Chart 1

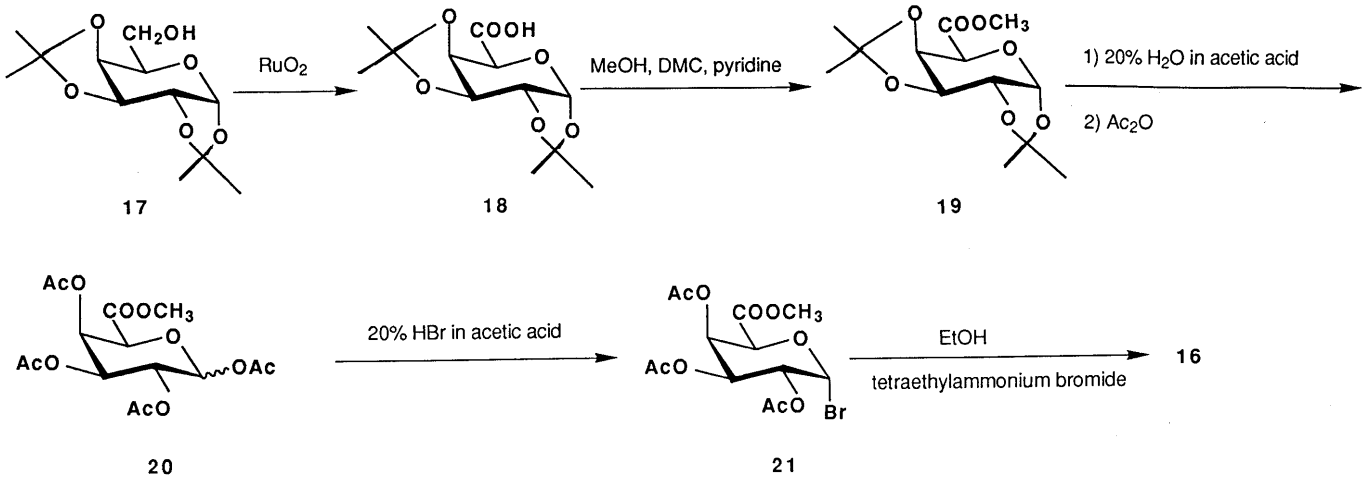


Fig. 4

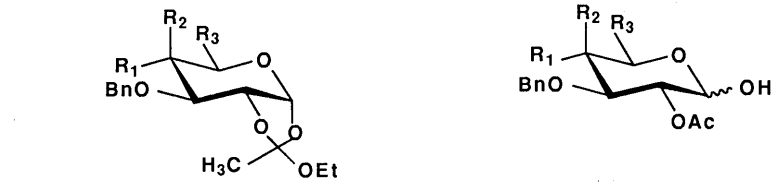


Chart 2

for that of **8** to give **9**. If the ring-opening of the orthoacetate ring of **8** proceeds *via* a cation intermediate such as **4** in Fig. 1, the type B product, 2,3,4,6-tetra-*O*-acetyl-D-galactopyranose (**15**), should be obtained on hydrolysis in 5% H_2O in acetic acid, whereas **8** gave quantitatively the type A product **9**.

The structural difference between **8** and **10** is that the former bears an axial OAc group at C-4 on the pyranose ring and the latter an equatorial one. As it was thought that this difference influences the ring-openings of the orthoacetate rings in **8** and **10**, hydrolysis with 5% H_2O in acetic acid of 1,2-(ethyl orthoacetates) **16** having an axial OAc group at C-4 on the pyranose ring [synthesized from 1,2;3,4-di-*O*-isopropylidene-α-D-galactopyranose (**17**)[19] (Fig. 4)] and **22** having an equatorial one were further investigated. Compound **16** gave quantitatively the type A product (**23**), while compound **22** gave the type B product (**24**). The electron impact mass spectra (EI-MS) of **23** and

TABLE I. ^{1}H-NMR Spectral Data for Pyranose-1,2-(ethyl orthoacetates) **8**, **10**, **16**, **22** and **34**[a]

	8	10	16	22	34
H-1	5.80 (d, 4.4)	5.73 (d, 5.1)	5.93 (d, 4.0)	5.86 (d, 4.8)	5.56 (d, 4.0)
H-2	4.32 (dd, 6.6, 4.4)	4.34 (ddd, 5.1, 2.8, 1.1)	4.39 (dd, 6.1, 4.0)	4.32 (ddd, 4.8, 2.9, 1.1)	4.29 (dd, 4.8, 4.0)
H-3	5.06 (dd, 6.6, 3.3)	5.20 (dd, 2.8, 2.8)	5.07 (dd, 6.1, 2.9)	5.24 (dd, 2.9, 2.6)	5.29 (dd, 4.8, 3.7)
H-4	5.43 (dd, 3.3, 2.2)	4.92 (ddd, 9.5, 2.8, 1.1)	5.77 (dd, 4.6, 2.9)	5.15 (ddd, 7.3, 2.6, 1.1)	5.25 (ddd, 5.1, 4.8, 3.7)
H-5	4.33 (dd, 6.6, 2.2)	3.96 (ddd, 9.5, 5.1, 3.3)	4.77 (d, 4.6)	4.31 (d, 7.3)	4.05 (dd, 12.1, 4.8)
H-5′	—	—	—	—	3.73 (dd, 12.1, 5.1)
H-6	4.17 (dd, 11.4, 6.6)	4.80 (dd, 9.2, 3.3)	—	—	—
H-6′	4.11 (d, 11.4, 6.6)	4.24 (dd, 9.2, 5.1)	—	—	—
CH_3	1.67	1.74	1.70	1.75	1.69
CH_2CH_3	1.19 (t, 7.3)	1.20 (t, 7.0)	1.21 (t, 7.3)	1.29 (t, 7.3)	1.20 (t, 7.3)
CH_2CH_3	3.56 (q, 7.3)	3.55 (q, 7.0)	3.53 (q, 7.3)	3.55 (q, 7.3)	3.58 (q, 7.3)
OCH_3	—	—	3.75	3.75	—
Ac	2.06, 2.07, 2.11	2.11, 2.12, 2.13	2.06, 2.08	2.09, 2.12	2.09, 2.12, 2.18

a) Multiplicities and coupling constants (J in Hz) are given in parentheses. The signal assignments were based on decoupling and ^{1}H–^{1}H-correlation spectroscopy (COSY) methods.

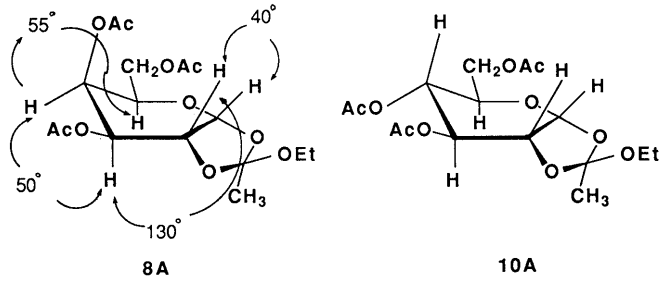


Fig. 5

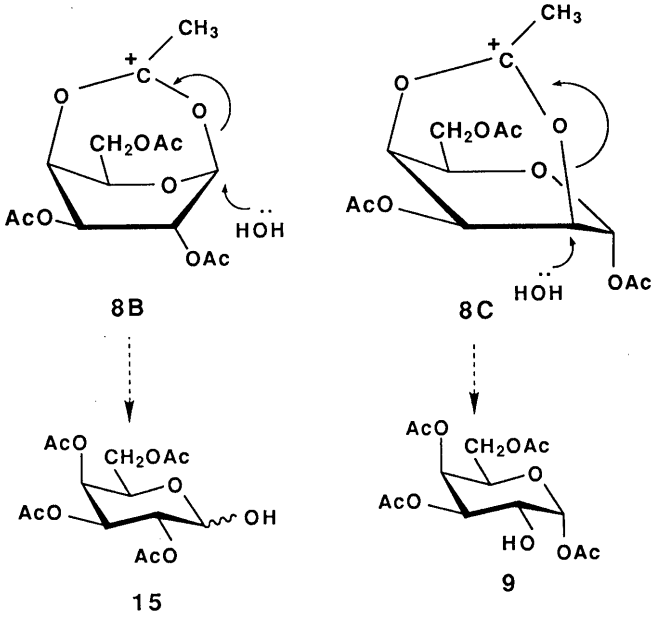
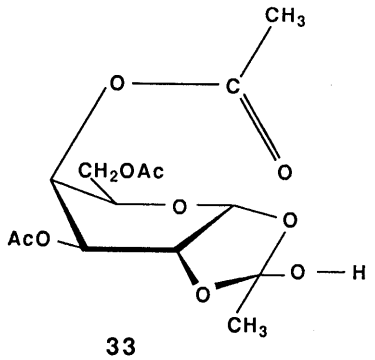


Fig. 6

24 showed molecular ion peaks at m/z 334. In the ^{1}H-NMR spectrum of **23**, the anomeric and H-2 protons were observed at δ 6.46 (d, J=4.0 Hz) and 4.25 (dd, J=10.6, 4.0 Hz), respectively, suggesting that the substituents at C-1 and 2 are OAc and OH groups in axial and equatorial orientations, respectively. On the other hand, in the ^{1}H-NMR spectrum of **24**, the anomeric and H-2 protons were observed at δ 5.53 (d, J=3.7 Hz) and 4.89 (dd, J=10.3, 3.7 Hz), respectively, and the spectrum showed that compound **24** mostly existed as the α-isomer (more than 97%). Furthermore, as we reported in the previous paper,[16] benzylated pyranose-1,2-(ethyl orthoacetates) **25**—**27** gave only the type B products **28**—**30** upon hydrolysis in 5% H_2O in acetic acid.

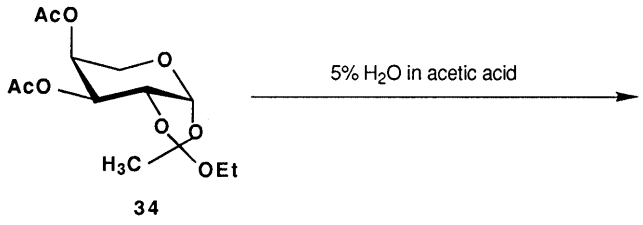
The ^{1}H-NMR spectral data for acetylated pyranose-1,2-(ethyl orthoacetates) studied this time are listed in Table I. From the values of the coupling constants, compounds **8** and **10** are considered to take the half-chair conformers **8A** and **10A**, respectively, as shown in Fig. 5. In those conformers, the carbonyl oxygen of the axial acetyl group at C-4 in **8A** can lie close to C-1 or C-2 on the pyranose ring, resulting in formation of intermediates **8B** and **8C**, respectively, while that of the equatorial acetyl group in **10A** can not (Fig. 6). As the product obtained by the hydrolysis of **8** was **9**, the ring-opening of the orthoacetate ring of **8** seemed to proceed *via* the intermediate **8C**; C-2 seemed to be attacked by an H_2O molecule from the α-side, resulting in opening of the dioxolenium cation ring to give **9**. In order to examine the mechanism of the ring-opening, **8** was treated with acetic acid, but the product was the β-pyranose peracetate **31**, not the α-pyranose peracetate **32**, consequently eliminating the mechanism of ring-opening *via* intermediates **8B** and **8C**.

Hydrolyses of **8** and **10** with 10% H_2O in MeOH in the presence of a catalytic amount of *p*-TsOH quantitatively gave **9** and **11**, respectively, as in the case of using 5% H_2O in acetic acid. These results suggest that, as proposed by Pacsu,[1] the ring-openings of 1,2-(orthoacetates) on acid-catalyzed hydrolysis in H_2O-containing solvents proceed *via* unstable 1,2-(orthoacids) as intermediates. We will now consider the orthoacid intermediate (**33**) which might be derived from **8** (Fig. 7). In the ring-opening of the orthoacetate ring, protonation at O(1) or O(2) of **33** might occur first. In the molecular stereomodel of **33**, the acetyl carbonyl group at C-4 on the pyranose can come closer to O(1) than to O(2), so that the protonation at O(1) may be prevented, resulting in preferential formation of an intermediate protonated at O(2) of **33**, from which **9** is derived through cleavage of the C–O(2) bond. Therefore, on acid-catalyzed hydrolysis, acetylated pyranose-1,2-(alkyl orthoacetates) having an axial OAc group at C-4 on the pyranoses give type A products. On the other hand, in the orthoacid intermediates derived from 1,2-(alkyl orthoace-



33

Fig. 7



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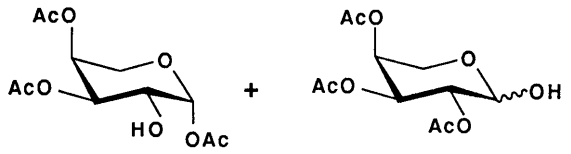
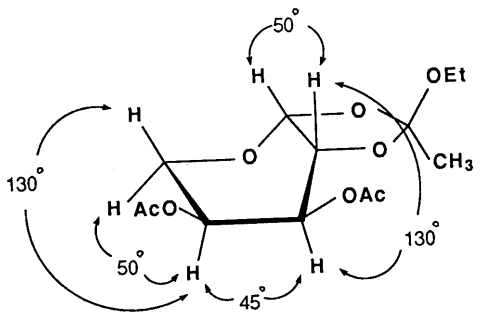


35 36

Fig. 8



37

Fig. 9

tates) in which the equatorial OAc group is present at C-4 on the pyranoses, the protonation at O(1) is not prevented, and as the electronegativity of the anomeric carbon is greater than that of C-2, the cleavage of the C–O(1) bond occurs preferentially to give the type B products.

However, in spite of having an axial OAc group at C-4 on the pyranose ring, 3,4-di-*O*-acetyl-*β*-L-arabinopyranose-1,2-(ethyl orthoacetate) (**34**) gave a mixture of type A product, 1,3,4-tri-*O*-acetyl-*β*-L-arabinopyranose (**35**), and type B product, 2,3,4-tri-*O*-acetyl-L-arabinopyranose (**36**) (Fig. 8). In the ^{1}H-NMR spectrum of the mixture, the anomeric protons of **35** and *β*- and *α*-anomers of **36** were observed at δ 6.26 (d, J=4.0 Hz), 5.47 (d, J=3.3 Hz) and 4.64 (d, J=7.0 Hz) with the integration ratio of 1 : 2.4 : 1.6, respectively, though other protons on the pyranoses could not be assigned because of overlapping of the signals. In this case, from the coupling constants in the ^{1}H-NMR spectrum (Table I), compound **34** is considered to take a boat conformer (**37**), as shown in Fig. 9. In the conformer **37**, the quasi-axial OAc group at C-4 on the pyranose ring is further from the anomeric carbon than is the case in **8A**, so that the participation of the carbonyl oxygen of the acetyl group is expected to decrease. This is why the ring-opening giving the type B product **36** predominates over that giving the type A product **35**.

Experimental

Materials 1,2-(Ethyl orthoacetates) **8**, **10** and **22** were prepared according to the published procedure.[2-4,16] 2-Chloro-1,3-dimethylimidazolinium chloride (DMC) was kindly provided by Shiratori Pharmaceutical Co., Ltd. Other chemicals and solvents were of reagent grade, and were obtained from commercial sources.

Measurements The TLC was done on Kieselgel HF_{254} plates (Merck), and spots were detected by spraying the plates with dilute H_2SO_4 followed by heating at 80 °C for 10 min. Column chromatography was carried out on Wakogel C-200. Melting points were determined on a Yanagimoto micro melting point apparatus, and are given as uncorrected values. ^{1}H-NMR spectra were obtained with a JEOL JNM-GX NMR spectrometer at 270 MHz, and chemical shifts are given in ppm with tetramethylsilane as an internal standard. EI-MS were recorded on a JEOL JMS-DX 300 mass spectrometer.

Hydrolysis of 10 in 5% H_2O in Acetic Acid Compound **10** (6 g) was dissolved in 5% H_2O in acetic acid (15 ml) and the solution was allowed to stand for 15 min at room temperature. The reaction mixture was poured into ice-water (50 ml) and extracted with CH_2Cl_2 (30 ml × 3). The combined organic extracts were successively washed with $NaHCO_3$-saturated aqueous solution and water, dried over $MgSO_4$, and filtered. The filtrate was evaporated to give **11** (5.1 g, 91.9%). EI-MS *m/z* (rel. intensity): 331 (2, $M^+ - OH$), 242 (6), 200 (23), 199 (8), 186 (6), 169 (7), 157 (75), 145 (19), 140 (33), 139 (8), 126 (30), 115 (74), 103 (24), 102 (20), 98 (100). The ^{1}H-NMR spectrum ($CDCl_3$) shows two anomeric protons due to *β*- and *α*-anomers at δ 4.82 (d, J=9.0 Hz) and 5.47 (d, J=4.0 Hz) with the integration ratio of 3 : 1, respectively. Other protons could not be assigned because of signal overlapping. *Anal.* Calcd for $C_{14}H_{20}O_{10}$: C, 48.28; H, 5.79. Found: C, 48.12; H, 5.83.

Preparation of 18 A solution of **17** (10 g) in acetone (40 ml) was added dropwise to a solution of KIO_4 (24 g), ruthenium dioxide (34 mg) in H_2O (80 ml) and acetone (40 ml) at room temperature. The reaction mixture was further stirred for 2.5 h, then extracted with CH_2Cl_2 (60 ml × 3). The combined organic extracts were washed with H_2O, dried over $MgSO_4$, and filtered. The filtrate was evaporated to give compound **18** (mp 153—155 °C, 5.3 g, 50%, after recrystallization from ether–*n*-hexane). EI-MS *m/z* (rel. intensity): 259 (3, $M^+ - CH_3$), 201 (39), 159 (12), 141 (26), 114 (6), 113 (60), 101 (15), 100 (50). ^{1}H-NMR spectrum ($CDCl_3$) δ: 8.61 (br s, COOH), 5.66 (d, J=4.8 Hz, H-1), 4.70 (dd, J=7.7, 2.6 Hz, H-3), 4.63 (dd, J=7.7, 2.6 Hz, H-4), 4.47 (d, J=2.6 Hz, H-5), 4.40 (dd, J=4.8, 2.6 Hz, H-2), 1.54, 1.47, 1.36, 1.35 (each s, CH_3). *Anal.* Calcd for $C_{12}H_{18}O_7$: C, 52.55; H, 6.62. Found: C, 52.35; H, 6.69.

Preparation of 19 DMC (10 g), pyridine (5 ml) and methanol (10 ml) were added to a solution of **18** (1.5 g) in CH_2Cl_2 (100 ml), then the mixture was stirred for 20 h, poured into ice-water (300 ml) and extracted with CH_2Cl_2 (100 ml × 3). The combined organic extracts were successively washed with 5% HCl, $NaHCO_3$-saturated aqueous solution and water, dried over $MgSO_4$, and filtered. The filtrate was evaporated to give a residue, which was subjected to column chromatography (benzene–acetone, gradient up to 5%) to give **19** (1.3 g, 81.8%). EI-MS *m/z* (rel. intensity): 273 (2, $M^+ - CH_3$), 215 (21), 171 (14), 155 (8), 143 (14), 141 (38), 129 (6), 127 (49), 114 (38), 113 (66). ^{1}H-NMR spectrum ($CDCl_3$) δ: 5.66 (d, J=4.8 Hz, H-1), 4.67 (dd, J=7.7, 2.6 Hz, H-3), 4.58 (dd, J=7.7, 2.6 Hz, H-4), 4.45 (d, J=2.6 Hz, H-5), 4.38 (dd, J=4.8, 2.6 Hz, H-2), 3.82 (s, OCH_3), 1.54, 1.45, 1.35, 1.34 (each s, Ac). *Anal.* Calcd for $C_{13}H_{21}O_7$: C, 54.16; H, 6.99. Found: C, 54.02; H, 7.03.

Preparation of 20 Compound **19** (1.3 g) was dissolved in 20% H_2O in acetic acid (50 ml) and the solution was refluxed at 100 °C for 12 h. After cooling of the mixture, acetic anhydride (50 ml) was added and the whole was allowed to stand overnight at room temperature. The reaction mixture

was coevaporated with toluene (100 ml × 5) to give a residue, which was subjected to column chromatography (benzene–acetone, gradient up to 5%) to give **20** (1.2 g, 70.9%). EI-MS *m/z* (rel. intensity): 345 (trace, $M^+ - OCH_3$), 317 (16), 246 (9), 245 (71), 243 (9), 228 (12), 215 (23), 214 (23), 203 (28), 197 (33), 186 (20), 182 (8), 174 (16), 172 (13), 169 (11), 158 (8), 157 (47), 155 (50), 144 (83), 143 (100). *Anal.* Calcd for $C_{15}H_{20}O_{11}$: C, 47.88; H, 5.36. Found: C, 47.68; H, 5.40.

Preparation of 21 A solution of 20% HBr in acetic acid (10 ml) was added to a solution of **20** (1.2 g) in acetic acid (5 ml) under stirring at 0 °C. The reaction mixture was further stirred for 2 h at 0 °C and poured into ice-water (200 ml). The mixture was extracted with CH_2Cl_2 (100 ml × 3). The combined organic extracts were successively washed with water, $NaHCO_3$-saturated aqueous solution and water, dried over $MgSO_4$, and filtered. The filtrate was evaporated to give a residue which was subjected to column chromatography (benzene–acetone, gradient up to 2%) to give **21** (mp 132—133 °C, 785 mg, 62%, after recrystallization from ether–petroleum ether). EI-MS *m/z* (rel. intensity): 354 (trace, $M^+ - COCH_3$), 317 (trace, $M^+ - Br$), 232 (6), 215 (10), 197 (11), 190 (7), 173 (8), 172 (7), 156 (9), 155 (100). ^{1}H-NMR spectrum ($CDCl_3$) δ: 6.77 (d, J=4.0 Hz, H-1), 5.88 (dd, J=3.3, 1.4 Hz, H-4), 5.45 (dd, J=10.6, 3.3 Hz, H-3), 5.10 (dd, J=10.6, 4.0 Hz, H-2), 4.88 (d, J=1.4 Hz, H-5), 3.78 (s, OCH_3), 2.12, 2.12, 2.03 (each s, Ac). *Anal.* Calcd for $C_{13}H_{17}BrO_9$: C, 39.31; H, 4.31. Found: C, 39.15; H, 4.44.

Preparation of 16 A solution of **21** (250 mg), tetraethyl ammonium bromide (50 mg) and dry ethanol (0.07 ml) in γ-collidine (5 ml) was warmed at 50 °C overnight. The reaction mixture was filtered. The filtrate was poured into ice-water (20 ml) and extracted with CH_2Cl_2 (20 ml × 3). The combined organic extracts were successively washed with 5% HCl, $NaHCO_3$-saturated aqueous solution and water, dried over $MgSO_4$, and filtered. The filtrate was evaporated to give a residue, which was subjected to column chromatography (benzene–acetone, gradient up to 2%) to give **16** (200 mg, 87.6%). EI-MS *m/z* (rel. intensity): 317 (trace, $M^+ - OEt$), 303 (8), 275 (11), 245 (6), 232 (27), 231 (10), 215 (22), 197 (11), 190 (22), 185 (6), 173 (28), 172 (19), 157 (18), 155 (100). ^{1}H-NMR spectrum: see Table I. *Anal.* Calcd for $C_{15}H_{22}O_{10}$: C, 49.72, H, 6.12. Found: C, 49.68; H, 6.18.

Hydrolysis of 16 in 5% H_2O in Acetic Acid Compound **16** (200 mg) was dissolved in 5% H_2O in acetic acid (2 ml) and the solution was allowed to stand for 15 min, then treated as described for the hydrolysis of **10** to give **23** (170 mg, 91.8%). EI-MS *m/z* (rel. intensity): 334 (3, M^+), 317 (5, $M^+ - OH$), 275 (11), 245 (6), 232 (27), 215 (25), 197 (12), 190 (22), 185 (6), 173 (28), 172 (18), 157 (18), 155 (100). ^{1}H-NMR ($CDCl_3$) δ: 6.46 (d, J=4.0 Hz, H-1), 5.75 (dd, J=3.3, 1.5 Hz, H-4), 5.24 (dd, J=10.6, 3.3 Hz, H-3), 4.69 (d, J=1.5 Hz, H-5), 4.25 (dd, J=10.6, 4.0 Hz, H-2), 3.75 (s, OCH_3), 2.17, 2.11, 2.08 (each s, Ac). *Anal.* Calcd for $C_{13}H_{18}O_{10}$: C, 46.71; H, 5.43. Found: C, 46.63; H, 5.51.

Hydrolysis of 22 in 5% H_2O in Acetic Acid Compound **22** (5.5 g) was dissolved in 5% H_2O in acetic acid (10 ml) and the solution was allowed to stand for 15 min at room temperature, then treated as described for the hydrolysis of **10** to give **24** (4.6 g, 90.6%). EI-MS *m/z* (rel. intensity): 334 (trace, M^+), 317 (3, $M^+ - OH$), 275 (15), 274 (8), 245 (9), 232 (32), 215 (30), 197 (15), 190 (16), 185 (8), 173 (25), 172 (14), 157 (26), 155 (100). ^{1}H-NMR spectrum ($CDCl_3$) δ: 5.57 (dd, J=10.3, 9.5 Hz, H-3), 5.53 (d, J=3.7 Hz, H-1), 5.17 (dd, J=10.3, 9.5 Hz, H-4), 4.89 (dd, J=10.3, 3.7 Hz, H-2), 4.59 (d, J=10.3 Hz, H-5), 3.75 (s, OCH_3), 2.09, 2.05, 2.04 (each s, Ac). *Anal.* Calcd for $C_{13}H_{18}O_{10}$: C, 46.71; H, 5.43. Found: C, 46.66; H, 5.45.

Hydrolysis of 8 in 10% H_2O in MeOH Containing *p*-TsOH Compound **8** (1 g) was dissolved in 10% H_2O in MeOH (10 ml), then a solution of *p*-TsOH (20 mg) in CH_2Cl_2 (1 ml) was added. The mixture was allowed to stand for 15 min at room temperature, then poured into ice-water (50 ml) and extracted with CH_2Cl_2 (30 ml × 3). The combined organic extracts were successively washed with $NaHCO_3$-saturated aqueous solution and water, dried over $MgSO_4$, and filtered. The filtrate was evaporated to give **9** (840 mg, 90.8%).

Hydrolysis of 10 in 10% H_2O in MeOH Containing *p*-TsOH Compound **10** (1 g) was dissolved in 10% H_2O in MeOH (10 ml), then a solution of *p*-TsOH (20 mg) in CH_2Cl_2 (1 ml) was added. The mixture was treated as described above to give **11** (830 mg, 89.7%).

^{1}H-NMR Spectra of 13 and 14 Compounds **13** and **14** were prepared according to the published procedures.[17,18] ^{1}H-NMR spectrum of **13** ($CDCl_3$) δ: 6.33 (d, J=3.7 Hz, H-1), 5.47 (dd, J=9.5, 9.5 Hz, H-3), 5.12 (dd, J=9.9, 9.5 Hz, H-4), 5.10 (dd, J=9.5, 3.7 Hz, H-2), 4.27 (dd, J=11.7, 3.7 Hz, H-6), 4.13 (ddd, J=9.9, 3.7, 2.2 Hz, H-5), 4.06 (dd, J=11.7, 2.2 Hz, H-6'), 2.18, 2.10, 2.04, 2.02, 2.02 (each s, Ac). ^{1}H-NMR spectrum of **14** ($CDCl_3$) δ: 5.73 (d, J=8.1 Hz, H-1), 5.26 (dd, J=9.5, 9.5 Hz, H-4), 5.13 (dd, J=9.0, 8.1 Hz, H-2), 5.12 (dd, J=9.5, 9.0 Hz, H-3), 4.30 (dd, J=12.5, 4.4 Hz, H-6), 4.11 (dd, J=12.5, 2.2 Hz, H-6'), 3.88 (ddd, J=9.5, 4.4, 2.2 Hz, H-5), 2.12, 2.09, 2.04, 2.04, 2.02 (each s, Ac).

Treatment of 8 with Acetic Acid Compound **8** (100 mg) was dissolved in acetic acid (2 ml) and the solution was allowed to stand for 1 h. The reaction mixture was poured into ice-water (50 ml) and extracted with CH_2Cl_2 (30 ml × 3). The combined organic extracts were successively washed with water, $NaHCO_3$-saturated aqueous solution and water, dried over $MgSO_4$, and filtered. The filtrate was evaporated to give **31** (96 mg 92.6%, mp 138—139 °C, after recrystallization from ether–petroleum ether). EI-MS *m/z* (rel. intensity): 331 (2, $M^+ - OAc$), 242 (24), 200 (27), 199 (11), 182 (6), 169 (9), 157 (63), 145 (19), 140 (30), 126 (12), 115 (100). ^{1}H-NMR spectrum ($CDCl_3$) δ: 5.71 (d, J=8.2 Hz, H-1), 5.43 (d, J=3.4 Hz, H-4), 5.33 (dd, J=10.4, 8.2 Hz, H-2), 5.09 (dd, J=10.4, 3.4 Hz, H-3), 4.15 (dd, J=10.8, 7.8 Hz, H-6), 4.11 (dd, J=10.8, 7.8 Hz, H-6'), 4.07 (dd, J=7.8, 7.8 Hz, H-5), 2.17, 2.13, 2.05, 2.05, 2.00 (each s, Ac). *Anal.* Calcd for $C_{16}H_{22}O_{11}$: C, 49.23; H, 5.68. Found: C, 49.21; H, 5.70.

Preparation of 34 A solution of 2,3,4-tri-*O*-acetyl-β-L-arabinopyranosyl bromide (1 g),[20] tetraethyl ammonium bromide (240 mg) and dry ethanol (0.4 ml) was warmed at 50 °C overnight. The reaction mixture was treated according to the preparative method for **16** to give a residue, which was subjected to column chromatography (benzene–acetone, gradient up to 1%) to obtain **34** (580 mg, 63.7%). EI-MS *m/z* (rel. intensity): 289 (trace, $M^+ - CH_3$), 259 (trace, $M^+ - OEt$), 245 (10), 217 (16), 174 (16), 170 (52), 157 (53), 139 (34), 131 (9), 128 (79), 115 (84), 103 (23), 97 (63), 89 (18), 85 (56), 68 (100). *Anal.* Calcd for $C_{13}H_{20}O_8$: C, 51.31; H, 6.62. Found: C, 51.29; H, 6.63.

Hydrolysis of 34 in 5% H_2O in Acetic Acid Compound **34** (580 mg) was dissolved in 5% H_2O in acetic acid (5 ml) and the solution was allowed to stand for 15 min at room temperature, then treated as described for the hydrolysis of **10** to give a mixture (480 mg, 91.2%) of **35** and **36**. EI-MS *m/z* (rel. intensity): 276 (3, M^+), 259 (3, $M^+ - OH$), 157 (8), 128 (22), 115 (29), 103 (10), 97 (16), 96 (30), 86 (23), 85 (66), 73 (14), 68 (60), 60 (100). The mixture showed three anomeric protons due to **35** and β- and α-anomers of **36** at δ 6.26 (d, J=4.0 Hz), 5.47 (d, J=3.3 Hz), 4.64 (d, J=7.0 Hz) with the integration ratio of 1:2.4:1.6, respectively, in the ^{1}H-NMR spectrum.

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