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Acetonated Sorbofuranoses and Their Favored Conformations as Determined by Proton Magnetic Resonance Spectroscopy[1]

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A series of L-sorbofuranose derivatives have been studied by PMR spectroscopy in order to determine their favored conformations from the coupling constants obtained by applying the spin-decoupling techniques and the solvent effects of benzene at 100 MHz. The coupling constants $J_{3,4}$, have disclosed that the furanose ring of methyl 1,3,4,6-tetra-*O*-acetyl-α-L-sorbofuranoside (IIa) in solutions has a conformation close to a C_3-*endo*-C_4-*exo* half-chair, while that of its β-anomer (IVa) has a C_3-*exo*-C_4-*endo* half-chair conformation. Their conformations are unchanged over the temperature range of 32—74°C, but they are affected by the introduction of a 4,6-*O*- or 2,3-*O*-isopropylidene group, either of which locks the furanose ring to a C_3-*exo*-C_4-*endo* half-chair conformation. This effect is thought to play an important role in the exclusive formation of 2,3 : 4,6-di-*O*-isopropylidene-α-L-sorbofuranose (XII) during the acetonation of L-sorbose.

The acetonation of L-sorbose yields 2,3 : 4,6-di-*O*-isopropylidene-α-L-sorbofuranose (XII) exclusively.[2] Recent investigations of the reaction using acetone dimethyl ketal have shown the isolation of many kinds of acetonated sorbofuranoses as intermediates,[3,4] whose relative yields are much influenced by the reaction conditions employed; *e. g.*, they were hardly detectable under usual acetonation conditions.[5-7] The results have suggested that conformational factors play an important role in the reaction; accordingly, we were prompted to study the ring conformations of L-sorbofuranoses by mean of proton magnetic resonance (PMR) spectroscopy, as it has proved to be a powerful tool for this purpose. The present conformational study may provide important information about the differences in the stability of many intermediate L-sorbofuranoses.

Experimental

All the meting points were recorded on a Kofler microstage and have been corrected. The optical rotations were measured in acetone solutions unless otherwise stated, and the concentrations are recorded in percentages. The thin-layer chromatography (TLC) was carried out on a silica-gel plate with acetone-chloroform (1 : 9 v/v) (Solvent A) and with ether-petroleum ether (2 : 1 v/v) (Solvent B). The separated materials were developed with a Seliwanoff reagent[8] and then heated in an oven. The preparative thin-layer chromatography (PTC) was performed on silica gel with the same solvent systems for detection, and the spots developed with iodine vapor were extracted with acetone. The evaporation of the acetone under reduced pressure yielded the materials.

Isolation of Methyl 4,6-*O*-Isopropylidene-α-L-sorbofuranoside (I). This substance was prepared essentially according to a previously-reported procedure.[4] L-Sorbose (40 g) was refluxed in acetone dimethyl ketal (100 m*l*)[9] containing *p*-toluenesulfonic acid (500 mg) for 2 hr. The solution was then neutralized with a slight excess of methanolic sodium methoxide. After the removal of the solvent, the residual syrup was extracted with benzene (200 m*l*); thin-layer chromatograms showed the presence of methyl 1,3 : 4,6-di-*O*-isopropylidene-β-L-sorbofuranoside (III)[4] and 2,3 : 4,6-di-*O*-isopropylidene-α-L-sorbofuranose (XII)[2] as the major products, and of 1,2-*O*-isopropylidene-α-L-sorbopyranose,[10] 2,3-*O*-isopropylidene-α- (XI),[11] 1,2 : 4,6-di-*O*-isopropylidene-α-(VIII),[3,4] and -β- (X),[4] 1,3 : 4,6-di-*O*-isopropylidene-β- (VI),[4] 1-*O*-α-methoxyisopropyl-2,3 : 4,6-di-*O*-isopropylidene-α-L-sorbofuranose,[4] and I as the minor products. The benzene solution was then extracted with water (50 m*l* × 3). The aqueous layer was saturated with sodium chloride

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[1] Sorboses. XII. Part XI: M. Katsuhara, S. Wakahara and K. Tokuyama, This Bulletin, **41**, 1208 (1968).

[2] T. Reichstein and G. Grüssner, *Helv. Chim. Acta*, **17**, 311 (1934).

[3] K. Tokuyama and E. Honda, This Bulletin, **37**, 591 (1964).

[4] T. Maeda, *ibid.*, **40**, 2212 (1967).

[5] K. Tokuyama, E. Honda and N. Hōki, *J. Org. Chem.*, **29**, 133 (1964).

[6] D. C. DeJongh and K. Biemann, *J. Am. Chem. Soc.*, **86**, 67 (1964).

[7] J. R. Patil and J. L. Bose, *J. Indian Chem. Soc.*, **43**, 161 (1966).

[8] A. Anno and N. Seno, "Jikken Kagaku Kōza," Bd. 23, ed. by Chem. Soc. Japan, Maruzen, Tokyo (1957), p. 374.

[9] J. H. Brown, Jr., and N. B. Lorett, U. S. Pat. 2827494 (1958).

[10] H. Ohle, *Ber.*, **71**, 762 (1938).

[11] T, I. Temnikova and V. V. Sklyarava, *Zh. Prikl. Khim.*, **21**, 1131 (1954); *Chem. Abstr.*, **49**, 2952 (1955).

and extracted with chloroform (200 m*l*×3), and the solvent removed. From the residue (10.6 g), I (2.1 g) was separated by PTC (R_f, 0.1—0.15, Solvent A) as a crystalline syrup. Two successive recrystallizations from ether gave I as colorless needles, mp 108—109°C $[\alpha]_D^{25}$ −65.0 (*c* 1.024). Found: C, 51.47; H, 7.82; OCH_3, 13.19%. Calcd for $C_{10}H_{18}O_6$: C, 51.27; H, 7.75; OCH_3, 13.25%.

Hydrolysis of I. I (1.0 g) was treated with 60% acetic acid (10 m*l*) at 50°C. After 1.5 hr, the solvent was evaporated to dryness, giving L-sorbose (0.5 g).

Methyl 1,3-Di-*O*-acetyl-4,6-*O*-isopropylidene-*α*-L-sorbofuranoside (Ia). A mixture of I (100 mg), acetic anhydride (1 m*l*), and pyridine (1 m*l*) was kept overnight in a refrigerator, and then evaporated to dryness. The recrystallization of the residue from ether gave Ia as colorless needles (51 mg), mp 104—105°C, $[\alpha]_D^{25}$ −63.9 (*c* 0.549). Found: C, 52.53; H, 6.93%. Calcd for $C_{14}H_{22}O_8$: C, 52.82; H, 6.97%.

Methyl 1,3,4,5-Tetra-*O*-acetyl-*α*-L-sorbofuranoside (IIa). A solution of Ia (310 mg) in 60% acetic acid (2 m*l*) was allowed to stand at room temperature for 2 hr. The solvent was then removed twice by the addition of an excess of ethanol, and by concentration. Without further purification, the residual syrup was acetylated with acetic anhydride (2 m*l*) and pyridine (2 m*l*) in a refrigerator for 4 hr. The evaporation of the solvent gave a syrup (315 mg); this syrup was subsequently purified by PTC with Solvent B. IIa was obtained as a syrup, $[\alpha]_D^{22}$ −66.1 (*c* 0.672). Found: C, 50.03; H, 6.24%; mol wt, 363. Calcd for $C_{15}H_{22}O_{10}$: C, 49.72; H, 6.12%; mol wt, 362.

Hydrolysis of Methyl 1,3:4,6-di-*O*-isopropylidene-*β*-L-sorbofuranoside (III). A solution of III[3] (1.42 g) in 60% acetic acid (20 m*l*) was allowed to stand at room temperature. After 1 hr, the solution was worked-up by a procedure similar to the above. The thin-layer chromatograms of the obtained syrup (1.56 g) showed the presence of methyl 1,3,4,6-tetra-*O*-acetyl-*β*-L-sorbofuranoside (IVa) and methyl 1,3-*O*-isopropylidene-4,6-di-*O*-acetyl-*β*-L-sorbofuranoside (Va); IVa (285 mg, R_f 0.38—0.46) and Va (0.60 g, R_f 0.50—0.65) were isolated by PTC with Solvent B. IVa: colorless needles (95 mg), mp 49—50°C (recrystallized from *n*-hexane), $[\alpha]_D^{24}$ +34.7 (*c* 0.773, chloroform). Found: C, 49.53; H, 6.18%. Calcd for $C_{15}H_{22}O_{10}$: C, 49.72; H, 6.12%. Va: syrup, $[\alpha]_D^{25}$ +34.9 (*c* 0.815). Found: C, 53.02; H, 7.20%. Calcd for $C_{14}H_{22}O_8$: C, 52.82; H, 6.97%.

1,2-*O*-Isopropylidene-3,4,6-tri-*O*-acetyl-*α*-L-sorbofuranose (VIIa). 1,2 : 4,6-Di-*O*-isopropylidene-*α*-L-sorbofuranose (VIII)[3,4] (60 mg) was treated with 60% acetic acid (1.2 m*l*) at 40°C for 80 min. The solution was then evaporated to dryness and extracted with chloroform. The removal of the solvent gave a hygroscopic syrup (36.5 mg), which was immediately acetylated with a mixture of acetic anhydride (1 m*l*) and pyridine (1 m*l*) at room temperature. After 4 hr, the evaporation of the solution gave VIIa as a syrup, $[\alpha]_D^{23}$ −67.3 (*c* 0.989). Found: C, 52.06; H, 6.68%. Calcd for $C_{15}H_{22}O_9$: C, 52.02; H, 6.40%.

1,2-*O*-Isopropylidene-3,4,6-tri-*O*-acetyl-*β*-L-sorbofuranose (IXa). IXa (230 mg) was prepared from 1,2 : 4,6-di-isopropylidene-*β*-L-sorbofuanose (X)[4] (500 mg) in a manner similar to the above. IXa: syrup, $[\alpha]_D^{23}$ +45.6 (*c* 1.128). Found: C, 51.85; H, 6.41%. Calcd for $C_{15}H_{22}O_9$: C, 52.02; H, 6.40%.

PMR Spectra Measurements. The PMR spectra were recorded on a Varian HA-100 spectrometer by using about 5% (w/v) solutions of the samples in chloroform-d ($CDCl_3$) and/or benzene-d_6 (C_6D_6). The spectrometer was operated at 100 MHz in the frequency-swept and internal TMS-locked mode. Spin-decoupling experiments were carried out by using two Hewlett-Packard HP-200ABR audiooscillators. The spectral charts were calibrated by direct readings of the resonance frequencies by means of a Hewlett-Packard HP-5212A electronic counter. The accuracies of the chemical shifts and coupling constants described are within ±0.02 and ±0.2 Hz, respectively.

Results and Discussion

Sorbofuranosides. *a) Preparation.* Methyl 1,3,4,6-tetra-*O*-acetyl-*α*- (IIa) and -*β*-L-sorbofuranoside (IVa) could be obtained from methyl 4,6-*O*-isopropylidene-*α*- (I) and 1,3:4,6-di-*O*-isopropylidene-*α*-L-sorbofuranoside (III)[4] respectively. The former starting material, I, was newly isolated as a minor product from the acetonation of L-sorbose with acetone dimethyl ketal. The combined data on the elemental analysis and the mild hydrolysis yielding L-sorbose showed that I is a methyl monoacetonated sorboside. I gave a diacetate (Ia) with acetic anhydride and pyridine at an ordinary temperature. The deacetonation of Ia with 60% acetic acid, followed by acetylation, afforded a new glycoside tetraacetate, one which was not identical with the known methyl 1,3,4,5-tetra-*O*-acetyl-*α*-[12] or -*β*-L-sorbopyranoside.[12] On the basis of the negative sign of its optical rotation, the tetraacetate was identified as the desired *α*-furanoside IIa. Consequently, the structure of I should be either methyl 1,3- or 4,6-*O*-isopropylidene-*α*-L-sorbofuranoside. *β*-Furanoside IVa was successfully obtained by the deacetonation of III, followed by acetylation. In this case, a partially-deacetonated sorboside (Va) was also isolated as a diacetate; this should be either the diacetate of methyl 1,3- or 4,6-*O*-isopropylidene-*β*-L-sorbofuranoside. The determination of the I and Va structures, which are 4,6- and 1,3-*O*-isopropylidene derivatives, respectively, leaned heavily on their PMR spectral interpretations, as will be described below.

b) Conformations. The conformations of the sorbofuranosides IIa and IVa were establsihed by means of PMR spectroscopy. In their PMR spectra, singlets due to *O*-acetyl, *O*-methyl, and *O*-isopropylidene protons are easily assigned. Methylene protons at C_1 (H_1, $H_{1'}$) usually appear as an AB-type quartet, and those at C_6 (H_6, $H_{6'}$), as the AB part of an ABX system, being coupled to H_5. The remaining ring protons, H_3, H_4, and H_5, can be expected to appear as a doublet, a quartet,

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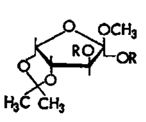
[12] H. H. Schulbach and G. Graefe, *Ann.*, **532**, 211 (1937).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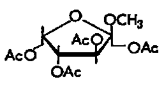
Ia R = Ac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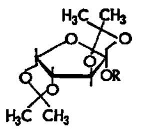
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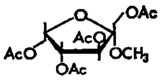
VI R = H

VIa R = Ac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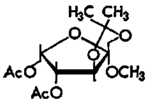
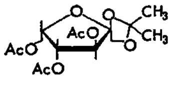

Va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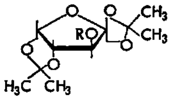
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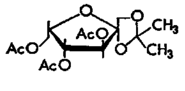
VIIIa R = Ac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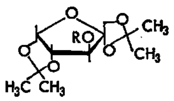
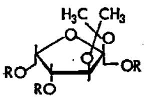
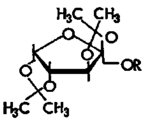

X R = H

Xa R = Ac


XI R = H

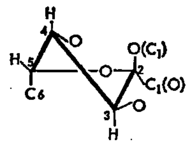
XIa R = Ac


XII R = H

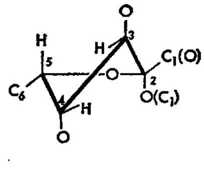
XIIa R = Ac

and a multiplet respectively, according to the first-order approximation. However, H_6, $H_{6'}$, H_5, H_4, and H_3 constitute an ABXYZ spin system, the signals of which can appear as a second-order pattern, depending on the $\Delta\nu_{ij}/J_{ij}$ values, where $\Delta\nu_{ij}$ is the difference in chemicals shifts (in Hz) between two interacting protons. Spin-decoupling experiments and the solvent effects of benzene¹³⁾ were mainly used to obtain the chemical shifts and coupling constants by means of the first-order approximation. However, in the present study, second-order patterns were sometimes analyzed by the usual procedure.¹⁴⁾

The spectrum of IIa in $CDCl_3$ (Fig. 1a) shows a doublet at τ 4.58 due to H_3 and a doublet of doublets at τ 4.50 due to H_4 ($J_{3,4}=5.8$ and $J_{4,5}=6.0$ Hz). Double irradiation at the resonance frequency of a multiplet due to the H_5 centered at τ 5.50 changes the signal due to H_4 into a doublet, from the spacing of which the $J_{3,4}$ value (5.8 Hz) was confirmed (Fig. 1b). Reverse double-irradiation at the center of the resonance frequencies of H_3 and H_4 causes a collapse of the H_5-multiplet into a triplet, but it does not change the AB-type quartet due to H_1 and $H_{1'}$ at τ 5.71 and 5.78 ($J_{1,1'}=(-)12.2$ Hz); the AB-type quartet is further split into doublets by the coupling to H_5 at τ 5.75 (H_6) and 5.88 ($H_{6'}$) ($J_{5,6}=5.0$, $J_{5,6'}=5.1$, and $J_{6,6'}=(-)11.8$ Hz). Similar decoupling experiments on the spectrum in C_6D_6 also support the above assignments. The J values are unchanged by the alteration in the solvent.



C_3-endo C_4-exo (A)



C_3-exo-C_4-endo (B)

The spectrum of IVa in C_6D_6 (Fig. 2a) shows a doublet at τ 4.28 due to H_3 ($J_{3,4}=2.5$ Hz) and a doublet of doublets at τ 4.58 arising from H_4 ($J_{4,5}=5.8$ Hz). Singnals appearing as the AB part of an ABX system at τ 5.68 (H_6) and 5.76 ($H_{6'}$) are due to C_6-methylene protons ($J_{5,6}=5.3$, $J_{5,6'}=7.2$, and $J_{6,6'}=(-)11.8$ Hz). On the double irradiation of H_4, a change in the shape of the H_5-multiplet centered at τ 5.45 was observed (Fig. 2b). The decoupling of H_5 changes the H_4-signal into a doublet. The observation of the spectrum in $CDCl_3$, including spin-decoupling experiments, also supports these assignments.

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13) See, for example, J. Ronayne and D. H. Williams, *J. Chem. Soc.*, *(B)*, **1967**, 540, and the reference cited therein.

14) J. W. Emsley, J. Feeney and L. H. Sutcliffe, "Highresolution Nuclear Magnetic Resonance Spectroscopy," Pergamon Press, London (1965), Chaptor 8.

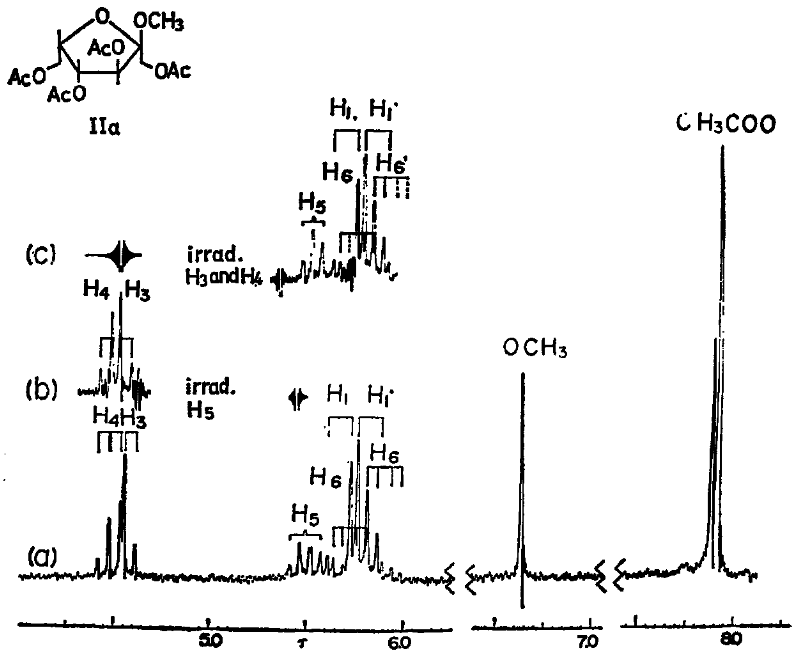

Fig. 1. PMR spectra of IIa in chloroform-d at 100 MHz.

a) Normal spectrum, b) and c) PMDR spectra

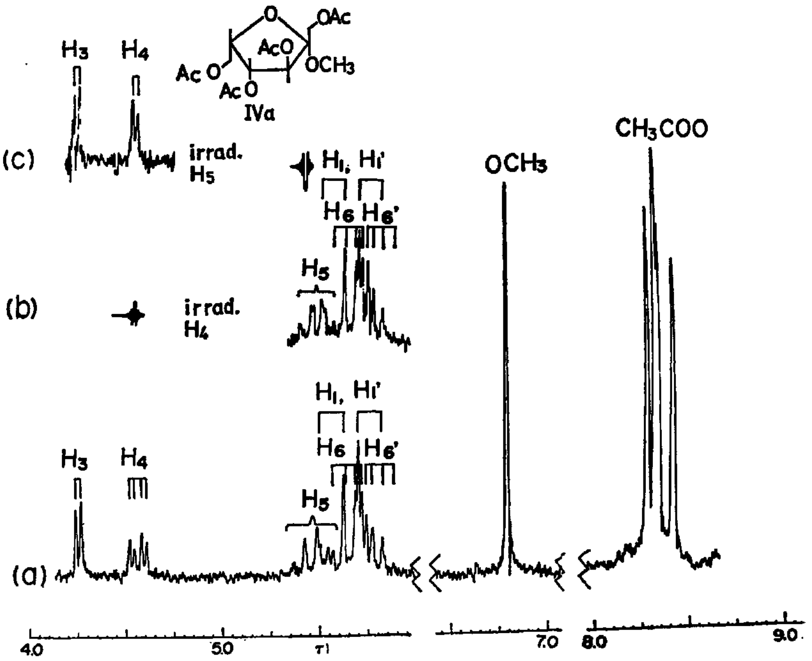

Fig. 2. PMR spectra of IVa in benzene-d_6 at 100 MHz.

a) Normal spectrum, b) and c) PMDR spectra

Table 1. Chemical shifts (τ) in $CDCl_3$ at 32°C[a]

Compound	H_1 and $H_{1'}$	H_3	H_4	H_5	H_6 and $H_{6'}$	CH_3-$\overset{\mid}{\underset{\mid}{C}}$-	CH_3COO	Other H
IIa	5.71, 5.78	4.58	4.50	5.50	5.75, 588		7.89 7.92(9H)	OCH_3 6.63
	(5.54, 5.71)	(4.28)	(4.24)	(5.61)	(5.8—6.0)		(8.23, 8.27 8.28, 8.32)	OCH_3 (6.89)
IVa	5.62, 5.90	~4.6	~4.7	~5.4	5.7—5.8		7.93(9H), 7.98	OCH_3 6.70
	(5.57, 5.75)	(4.28)	(4.58)	(5.45)	(5.68, 5.76)		(8.27, 8.32, 8.34, 8.41)	OCH_3 6.78
VIa	5.61, 5.99	5.28	5.60	5.88	5.98, 6.06	8.40, 8,63(9H)	7.93	
Ia	~5.64	4.73	5.62	~5.9	5.9—6.1	8.60(6H)	7.89	OCH_3 6.64
	(~5.41)	(4.36)	(5.82)	(~6.2)	(6.3—6.5)	(8.65, 8.88)	(8.17, 8.23)	OCH_3 (6.77)
Va	~6.12	5.88	4.75	5.30	5.6—5.7	8.57, 8.62	7.92, 7.93	OCH_3 6.70
	(6.17, 6.23)	(5.72)	(4.60)	(~5.3)	(~5.7)	(8.66, 8.78)	(8.27, 8.35)	OCH_3 (6.90)
VIIa	5.80, 5.91	4.77	4.50	5.47	5.76, 5.86	8.51, 8.63	7.89, 7.93(6H)	
VIIIa	5.70, 5.81	4.83	5.67	5.84	5.96, 6.04	(8.50, 8.58 8.63, 8.65)	7.88	
	(5.62, 5.70)	(4.65)	(5.92)	(6.12)	(6.22, 6.46)	(8.45, 8.62 8.71, 8.92)	(8.19)	
VIII	5.73, 5.89	5.96	5.88	6.04	6.20, 6.48	8.44, 8.71(6H), 8.92		OH 7.12
IXa	5.97	4.6—4.8		~5.5	6.6—6.8	8.53, 8.62	7.88(6H), 7.94	
	(5.95)	(4.38)	(4.56)	(5.3—5.8)		(8.50, 8.67)	(8.27, 8.38 8.45)	
Xa	~5.98	4.76	5.7—5.8		~6.1	8.50, 8.62(6H) 8.64	7.91	
	(5.85, 5.91)	(4.47)	(5.8—6.0)		~6.2	(8.44, 8.59, 8.65, 8.81)	(8.44)	
XIa	5.65, 5.75	5.58	4.73	5.41	5.73, 5.85	8.47, 8.64	7.91, 7.92 7.95	
XIIa	5.45, 5.85	5.58	5.68	5.7—5.9, 6.00		8.52, 8.57 8.63(6H)	7.90	
	(5.17, 5.61)	(5.48)	(5.8)	(6.1—6.2) (6.42)		(8.53, 8.68 8.69, 8.92)	(8.31)	
XII	~6.2	5.48	5.63	5.8—5.9		8.50(6H) 8.57, 8.63		OH 7.43

a) Values in parentheses are those observed in C_6D_6.

Since the only available J values for the conformational studies of ketofuranoses are $J_{3,4}$ and $J_{4,5}$, it seems rather difficult to distinguish rigorously their furanose-ring conformations from possible C_s (envelope) and C_2 (half-chair) conformations. However, it has been suggested that cyclopentane derivatives containing one hetero-atom (*e. g.*, tetrahydrofuran, tetrahydrothiophene, and pyrrolidine) exist in the half-chair conformation (C_2) with the hetero-atom located on the axis of symmetry.[15] In the case of L-sorbofuranoses, there are only two possible C_2-conformations, *i. e.*, a C_3-*endo*-C_4-*exo* (A) and a C_3-*exo*-C_4-*endo* half-chair (B).[16] By using Dreiding models, the

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[15] J. E. Kilpatrick, K. S. Pitzer and R. Spitzer, *J. Am. Chem. Soc.*, **69**, 2483 (1947); K. S. Pitzer and W. E. Donath, *ibid.*, **81**, 3213 (1959).

[16] "*Endo*" means that the atom is located on the same side of the plane defined by the C_2–O–C_5 ring atom as the C_5–C_6 bond, while "*exo*" means that they are found on opposite side.

TABLE 2. COUPLING CONSTANTS (J, Hz)

Compound	$J_{1,1'}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$
IIa	(−)12.2	5.8	6.0	5.0	5.1	(−)11.8
IVa	(−)12.2	2.5	5.8	5.3	7.2	(−)11.8
VIa	(−)12.5	0.5	4.0	4.0	4.0	(−)12.8
Ia	a)	1.5	4.0	a)	a)	a)
Va	(−)12.2	0.6	5.3	a)	a)	a)
VIIa	(−)9.0	5.3	6.2	5.2	4.8	(−)11.8
VIIIa	(−)9.0	1.5	3.0	2.8	3.0	(−)13.0
VIII	(−)9.0	1.5	3.0	2.8	3.0	(−)13.0
IXa	a)	2.5	5.8	a)	a)	a)
Xa	(−)9.0	0.3	a)	a)	a)	a)
XIa	(−)12.0	0.5	3.0	5.0	7.2	(−)11.0
XIIa	(−)12.0	0.5	2.3	a)	2.8	(−)13.8
XII	(−)12.0	0.5	2.3	a)	3.0	(−)13.8

a) Not determinable.

dihedral angles between H_3 and H_4 in the A and B conformers are found to be about 150—160° and 90—110°, respectively, whereas the angles between H_4 and H_5 are measured to be about 10—30° in both the conformers. Therefore, only the $J_{3,4}$ values in the compounds examined can be used for determining their conformations, for the dihedral angles between H_3 and H_4 in the two conformers should lead to obviously different $J_{3,4}$ values according to the Karplus equation, even though it is used in a very qualitative sense.[17] The $J_{3,4}$ values can thus be expected to be in the range of 5—6 Hz for the A conformer and in the range of 0—2.5 Hz for the B conformer.

On the basis of the $J_{3,4}$ values determined above, the conformation of IIa was concluded to be one close to C_3-*endo*-C_4-*exo* half-chair ($J_{3,4}$=5.8 Hz), and that of IVa, one close to C_3-*exo*-C_4-*endo* half-chair ($J_{3,4}$=2.5 Hz). Both conformations can satisfy the operation of the anomeric effect of the OCH_3 group and probably, the reverse anomeric effect of the CH_2OAc group[18] at the C_2 atom. The C_3-*exo*-C_4-*endo* half-chair conformation of the β-D-fructofuranose moiety of sucrose, as determined by neutron diffraction,[19] also supported the above conclusion.

The spectra of IIa and IVa in $CDCl_3$ are unchanged in chemical shifts and coupling constants over the temperature range of 32—74°C. The results show that they exist in fixed conformations in this temperature range.

Conformations of Acetonated Derivatives. The assignments of the spectra of acetonated sorbofuranoses were established in a manner similar to those described above. The data obtained are listed in Tables 1 and 2, while some of the spectra are shown in Figs. 3—6.

At the outset we investigated the conformation of the acetate (VIa) of 1,3:4,6-di-*O*-isopropylidene-β-L-sorbofuranose (VI),[4] which has two 1,3-dioxane rings. An examination of Dreiding models suggests that when the furanose-ring conformation is C_3-*exo*-C_4-*endo* half-chair, the 1,3-*O*- and 4,6-*O*-isopropylidene rings can be formed without severe non-bonded interactions, whereas when the ring has a C_3-*endo*-C_4-*exo* half-chair conformation, there are strong interactions between axial methyl groups at 1,3-dioxanes and either H_3 or H_4. As expected, the characteristic value for $J_{3,4}$ (0.5 Hz) in VIa indicates that its most favored conformation is C_3-*exo*-C_4-*endo* half-chair, where the dihedral angles are slightly contracted compared with the corresponding angles in IVa.

The determination of the spectra of the two monoisopropylidene derivatives containing one 1,3-dioxane ring, Ia and Va, provided important information. The fact that the signals due to H_3 and C_1-methylene protons are remarkably shifted downfield in the spectrum of Ia in comparison with those observed in the spectrum of VIa, confirmed the structure of I to be methyl 4,6-*O*-isopropylidene-α-L-sorbofuranoside. Similar lower-field shifts of the signals due to H_4 and C_6-methylene protons confirmed the structure of Va to be methyl 1,3-*O*-isopropylidene-4,6-di-*O*-acetyl-β-L-sorbofuranoside. The small values for $J_{3,4}$ (1.5 Hz in Ia and 0.6 Hz in Va) indicate that both monoisopropylidene furanoses also exist in a C_3-*exo*-C_4-*endo* half-chair conformation. It should be noted that the conformation of Ia is a C_3-*exo*-C_4-*endo* half-chair. This fact suggests that the restrictive influence of the 4,6-*O*-isopropylidene ring is stronger than that of the anomeric effect in the opposite direction; the 4,6-*O*-isopropylidene ring locks the

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[17] For instance, see N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, San Francisco (1964), Chapter 6.

[18] R. U. Lemieux and A. R. Morgan, *Can. J. Chem.*, **43**, 2205 (1965).

[19] M. S. Sundaralingam, *J. Am. Chem. Soc.*, **87**, 599 (1965).

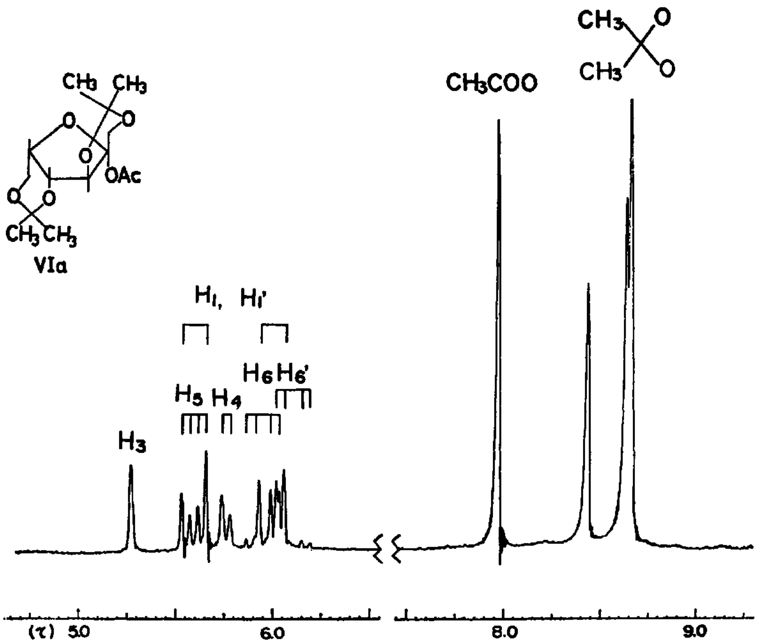

Fig. 3. PMR spectrum of VIa in chloroform-d at 100 MHz.

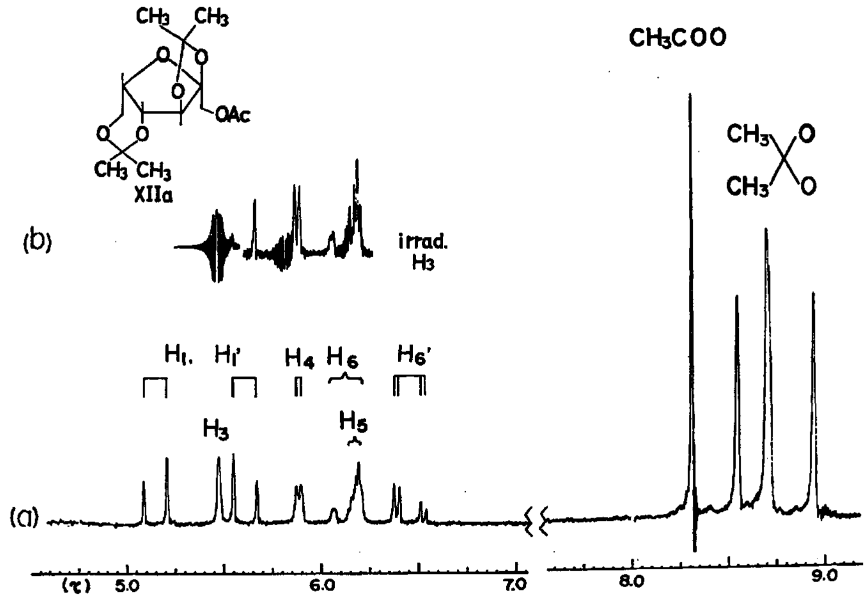

Fig. 4. PMR spectra of XIIa in benzene-d$_6$ at 100 MHz.
a) Normal spectrum, b) PMDR spectrum

furanose-ring to a C$_3$-*exo*-C$_4$-*endo* conformation.

This effect is also observed in other 4,6-*O*-isopropylidene-sorbofuranoses: 1,2 :4,6-di-*O*-isopropylidene-α-L-sorbofuranose (VIII),[3,4] the acetate of VIII (VIIIa),[4] the acetate (Xa) of 1,2 : 4,6-di-*O*-isopropylidene-β-L-sorbofuranose (X),[4] XII, and the acetate of XII (XIIa).[4] The furanose-ring conformations of such furanoses were found from the small values for $J_{3,4}$ (0.3—1.5 Hz) to be C$_3$-*exo*-C$_4$-*endo* half-chairs.

The conformation of the acetate (XIa)[4] of 2,3-*O*-isopropylidene-α-L-sorbofuranose (XI),[11] the unlocked derivative of XII, seems interesting because a C$_3$-*endo*-C$_4$-*exo* half-chair conformation seems likely

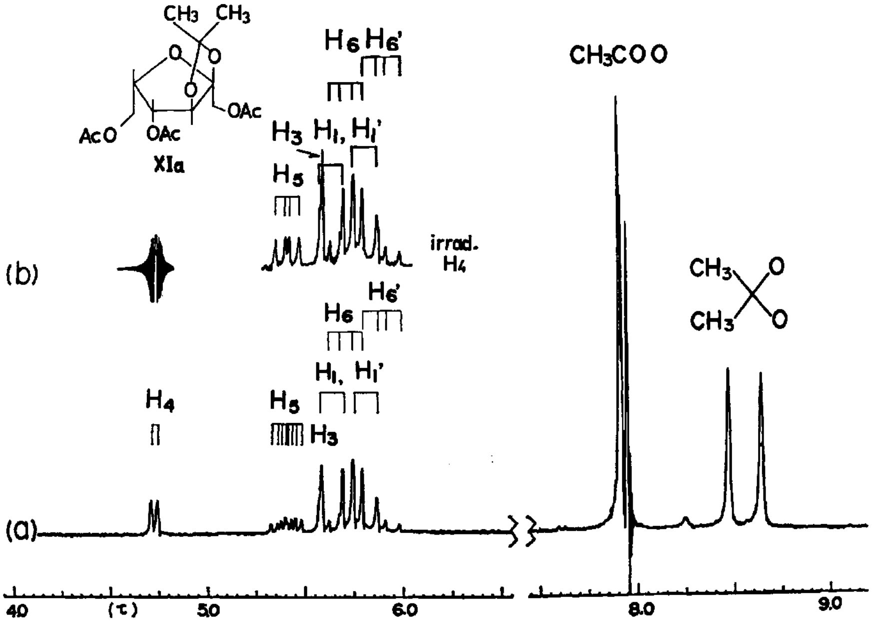

Fig. 5. PMR spectra of XIa in chloroform-d at 100 MHz.
a) Normal spectrum, b) PMDR spectrum

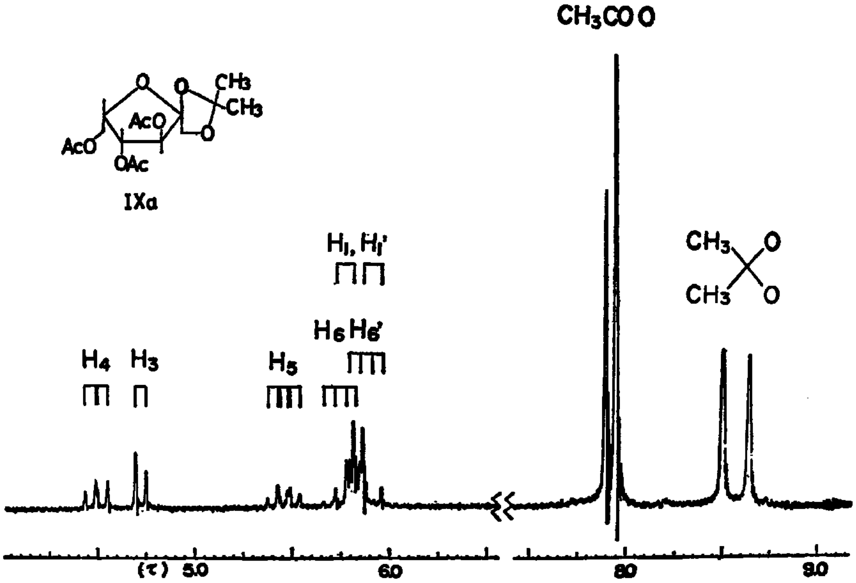

Fig. 6. PMR spectrum of IXa in chloroform-d at 100 MHz.

in view of the non-bonded interaction and the anomeric effect. However, the small $J_{3,4}$ value established that XIa adopts a similar conformation to XII. A similar situation has been found in the conformation of 1,2-*O*-isopropylidene-α-D-glucofuranose derivatives ($J_{2,3}$=0.5 Hz).[20,21] Therefore, the 2,3-*O*-isopropylidene ring was concluded to lock the furanose-ring conformation in the same direction as does the 4,6-*O*-isopropylidene ring.

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[20] Recently, the value of 0.5 Hz for $J_{2,3}$ in 1,2-*O*-benzylidene-α-D-xylofuranose was reported by R. J. Ferrier and L. R. Hotton, *Carbohyd. Res.*, **5**, 132 (1967).

[21] R. J. Abraham, K. A. McLauchlan, L. D. Hall and L. Hough, *Chem. Ind.*, **1962**, 213; R. H. Abraham, L. D. Hall, L. Hough and K. A. McLauchlan, *J. Chem. Soc.*, **1962**, 3699.

In order to compare it with the above results, the effect of a 1,2-*O*-isopropylidene ring was studied in a similar manner by using 1,2-*O*-isopropylidene-3,4,6-tri-*O*-acetyl-α- (VIIa) and β-L-sorbofuranose (IXa), derived from VIII and X, respectively. As can be seen from Table 2, the *J* values in VIIa are in substantial agreement with those in IIa; the α-anomer VIIa has the same conformation as the α-furanoside IIa. Similarly, the *J* values provided evidence that the β-anomer IXa has the same conformation as the β-furanoside IVa. Thus, the 1,2-*O*-isopropylidene ring orients the furanose ring in the same direction as does the influence of the anomeric effect of the OCH_3 group.

Under usual reaction conditions, the acetonation of L-sorbose affords XII exclusively.(2) DeJongh and Biemann(6) suggested that the reason why VIII and X were not found might be the steric interference between the 1,3-dioxane and the 1,3-dioxolane. However, such interactions in VIII and X, if they do exist, are believed to be essentially of a degree similar to those in XII, because the VIII and X isolated by us have a similar conformation to XII. Since both the isopropylidene rings of XII lock its furanose ring in the same direction, the furanose ring of XII is thought to be stable. Both the isopropylidene rings of X similarly lock the furanose ring in the same direction. However, the difference in $J_{3,4}$ values between IXa (2.5 Hz) and Xa (0.3 Hz) suggests that there are some other factors governing the small instability in the X molecule. On the other hand, the 1,2-*O*-isopropylidene ring of VIII tends to destabilize to some extent the furanose-ring conformation restricted by the 4,6-*O*-isopropylidene ring. Therefore, a spiro-1,3-dioxolane ring at the 1,2-position of a furanose is considered to be less stable than a fused-1,3-dioxolane ring at the 2,3-position. A similar example has been reported in the acetonation of D-fructose; 2,3:4,6-di-*O*-isopropylidene-β-D-fructopyranose is formed as a final product *via* 1,2:4,5-di-*O*-isopropylidene-β-D-fructopyranose.(22)

Finally, the fact that VI has a lower stability than XII, can be reasonably explained by the lower stability of the 1,3-*O*-isopropylidene (1,3-dioxane) ring than that of the 2,3-*O*-isopropylidene ring (1,3-dioxolane), according to the Brown-Brewster-Schechter rule.(23)

On the basis of the conformational data presented above, it can be concluded that 2,3-*O*-isopropylidene derivatives are more stable than 1,2- or 1,3-*O*-isopropylidene derivatives in sorbofuranoses locked by the 4,6-*O*-isopropylidene ring. This conclusion accords well with the predominant formation of XII in the acetonation of L-sorbose under strongly acid conditions. The effect of the 4,6-*O*-isopropylidene group must play an important role in the acetonation, a mechanism for which will be proposed in future papers.

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22) E. Fisher, *Ber.*, **28**, 1164 (1895); J. C. Irvine and C. S. Garrett, *J. Chem. Soc.*, **97**, 1277 (1910); W. L. Glen, G. S. Myers and G. A. Grant, *ibid.*, **1951**, 2568; H, Ohle and I. Koller, *Ber.*, **57**, 1566 (1924).

23) H. C. Brown, J. H. Brewster and H. Shechter, *J. Am. Chem. Soc.*, **76**, 467 (1954).