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Ethylidenation of L-Sorbose[1-3]

Takashi MAEDA, Masumi KIYOKAWA and Kanji TOKUYAMA

Shionogi Research Laboratory, Shionogi & Co., Ltd., Fukushima-ku, Osaka

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The ethylidenation of L-sorbose (I) with acetaldehyde dimethylacetal in the presence of an acid was studied. When the reaction was interrupted at the initial stage, an equilibrium mixture of the two possible cyclic acetals, 1,2-*O*-(III) and 1,3-*O*-ethylidene-*α*-L-sorbopyranose (V), was obtained. When the reaction was allowed to proceed for longer periods of time, 1,3:4,6-di-*O*-ethylidene-*β*-L-sorbofuranose (IX) was mainly isolated; the transformation of this to two diastereoisomeric 2,3:4,6-di-*O*-ethylidene-*α*-L-sorbofuranoses (XV and XVIII) required the use of highly acidic conditions. A pathway of I→(III⇄V)→IX→(XV+XVIII) was tentatively proposed for the ethylidenation of I.

The acetonation of L-sorbose (I) yields 1,2-*O*-isopropylidene-*α*-L-sorbopyranose (II) as the initial product;[4,5] this is then converted into 2,3:4,6-di-*O*-isopropylidene-*α*-L-sorbofuranose (VII) exclusively.[6] Although the presence of an equilibrium between II and 1,3-*O*-isopropylidene-*α*-L-sorbopyranose (IV) at the initial stage of the reaction has reasonably been anticipated from the acetalation of glycerol,[7] IV could not be isolated. This discrepancy must be considered on stereochemical grounds. As has been pointed out by Brown, Brewster, and Schechter,[8] the formation of a six-membered *O*-isopropylidene ketal is inhibited because one of the two methyl groups is necessarily axial in the chair conformation for the six-membered ring. On the other hand, there is no axial methyl group in a six-membered ethylidene acetal, so that 1,3-*O*-ethylidene-*α*-L-sorbopyranose (V) can be expected to be isolated from the ethylidenation of I. The isolation of V may give important information regarding the complicated reaction mechanisms of the acetalation of I.[4,9,10] This paper will report on the ethylidenation of I with acetaldehyde dimethylacetal[11] in the presence of an acid. The products from this reaction were isolated by preparative thin-layer chromatography and were identified on the basis of chemical and proton magnetic resonance (PMR) spectroscopic evidence. The assignment of the PMR spectra shown in Tables 1 and 2 is based on the chemical shifts with reference to the corresponding acetonated compounds.[2,10,12]

The treatment of I with acetaldehyde dimethylacetal in the presence of *p*-toluenesulfonic acid at 40°C for 2.7 hr or under weaker conditions afforded one diethylidene compound (IX) and four monoethylidene compounds, the latter of which were purified as the acetates, IIIa, Va, VIa, and XIIIa. The Va acetate showed bands due to a hydroxyl group in its infrared spectrum. This hydroxyl group was considered to be a tertiary one, because no acetylation occurred with acetic anhydride in pyridine at ordinary temperatures, whereas reduction was observed with a Fehling solution. The methylation of Va with methyl iodide in the presence of silver oxide yielded VIa. This product, VIa, was also obtained by the ethylidenation of methyl *α*-L-sorbopyranoside (XXI),[13] followed by acetylation. Thus, the structures of Va and VIa were determined to be the 4,5-di-*O*-acetates of V and methyl 1,3-*O*-ethylidene-*α*-L-sorbopyranoside (VI). The PMR spectra of Va and VIa in chloroform-d

1) Sorboses. XIII. For Part XII, see Ref. 2.

2) T. Maeda, K. Tori, S. Satoh and K. Tokuyama, This Bulletin, **41**, 2495 (1968).

3) Some of results of this paper have appeared in a preliminary form. T. Maeda and K. Tokuyama, *Tetrahedron Letters*, **1968**, 3079.

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

5) J. R. Patil and J. L. Bose, *J. Indian Chem. Soc.*, **43**, 161 (1961).

6) T. Reichstein and A. Grüssner, *Helv. Chim. Acta*, **17**, 377 (1934).

7) a) R. V. Lemieux, "Molecular Rearrangements," Part 2, ed. by P. de Mayo, Interscience, New York (1964), p. 214. b) H. Hibbert and J. G. Morazain, *Can. J. Research*, **2**, 214 (1930). c) N. Baggett, J. M. Duxbury, A. B. Foster and J. M. Wegber, *Carbohyd. Res.*, **2**, 216 (1966). d) G. Stefanovic and D. Petrovic, *Tetrahedron Letters*, **1967**, 3153.

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

9) K. Tokuyama and E. Honda, This Bulletin, **37**, 591 (1964).

10) T. Maeda, *ibid.*, **40**, 2122 (1967).

11) The use of acetaldehyde was not feasible because of the formation of oxidoethylene derivatives.

12) L. D. Hall, *Adv. Carbohyd. Chem.*, **19**, 51 (1964).

13) H. H. Schlubach and G. Graef, *Ann.*, **532**, 211 (1937).

TABLE 1. CHEMICAL SHIFTS (τ) IN CHLOROFORM-d[a)]

Compound	H_1 and $H_{1'}$	H_3	H_4	H_5	H_6 and $H_{6'}$	$C\underline{H}_3$—CH(O)(O)	CH_3—$C\underline{H}$(O)(O)	Other signal
IIIa	6.00, 6.33 (6.03, 6.37)	4.95 (4.78)	4.52 (4.18)	~5.0 (~4.8)	~6.2 (~6.2)	8.55 (8.68)	4.70 (4.77)	$OCOC\underline{H}_3$: 7.93, 7.98, 8.00 (8.23, 8.30, 8.35)
Va	6.23, 6.42 (6.45,6.70)	6.52 (6.80)	4.58 (4.18)	5.02 (4.85)	5.97, 6.23 (6.00, 6.23)	8.62 (8.81)	5.25 (5.73)	$OCOC\underline{H}_3$: 7.95, 7.98 (8.25, 8.38)
VIa	5.83, 6.67	6.52	4.47 ~ 5.03		6.17, 6.45	8.63	5.27	$OCOC\underline{H}_3$: 7.95, $OC\underline{H}_3$: 6.67
VIII	5.93, 6.27	5.88	5.6 ~ 5.8		6.08	8.65, 8.67	5.28, 5.35	
XIa	5.73, 6.33 (5.50, 6.65)	5.97 (5.93)	4.73 (4.63)	~5.2 (5.18)	~5.8 (5.7~5.8)	8.67 (8.75)	5.37 (5.73)	$OCOC\underline{H}_3$: 7.93(6H), $OC\underline{H}_3$: 6.73 (8.30, 8.35) (6.98)
XIIIa	~5.59	4.76	5.6 ~ 6.2			8.68	5.37	$OCOC\underline{H}_3$: 7.89, 7.91
XV	~6.4 (~6.1)	5.53 (5.42)	5.70 (5.95)	6.00 (6.53)	5.75, 6.16 (6.00, 6.78)	8.63, 8.70 (8.78, 8.82)	4.57, 5.35 (4.77, 5.84)	O$\underline{H}$: 7.77 (7.78)
XVa	5.54, 5.75 (5.20, 5.51)	5.62 (5.46)	5.73 (6.08)	6.00 (6.49)	5.80, 6.16 (6.00, 6.73)	8.65, 8.70 (8.75, 8.80)	4.58, 5.37 (4.75, 5.82)	$OCOC\underline{H}_3$: 7.90 (8.31)
XVI	~5.7 (5.48, 5.56)	5.63 (5.52)	b) (~6.2)	6.03 (6.58)	b), 6.25 (~6.1, 6.85)	8.72, 8.80 (8.80, 8.88)	4.62, 5.42 (4.81, 5.90)	$ArC\underline{H}_3$: 7.57 (8.15)
XVII	6.38, 6.70 (6.15, 6.35)	5.40 (5.22)	5.57 (6.12)	6.05 (6.53)	5.85, 6.25 (6.02, 6.80)	8.65, 8.90 (8.55, 8.88)	4.52, 5.45 (4.67, 5.87)	
XVIII	~6.15 (~6.08)	5.56 (5.47)	b) b)	b) (6.06)	b), 6.12 (5.97, 6.72)	8.58, 8.70 (8.71, 8.79)	4.82, 5.35 (5.00, 5.83)	O$\underline{H}$: 7.72 (7.62)
XVIIIa	b) (5.32, 5.52)	5.67 (5.57)	5.5 ~ 6.0 (6.12)	(6.25)	6.13 (5.97, 6.73)	8.57, 8.70 (8.72, 8.80)	4.83, 5.37 (4.95, 5.83)	$OCOC\underline{H}_3$: 7.90 (8.33)
XIX	5.67, 5.80 (5.52, 5.60)	5.65 (5.55)	b) (~6.2)	5.82 (6.72)	b), 6.20 (~6.1, 6.80)	8.68, 8.78 (8.82, 8.87)	4.90, 5.42 (4.92, 5.90)	$ArC\underline{H}_3$: 7.57 (8.13)
XX	6.37, 6.67 (6.23, 6.30)	5.48 (5.28)	5.85 (6.10)	5.95 (~6.2)	5.85, 6.72 (5.98, 6.72)	8.58, 8.85 (8.70, 8.85)	4.60, 5.44 (4.70, 5.87)	

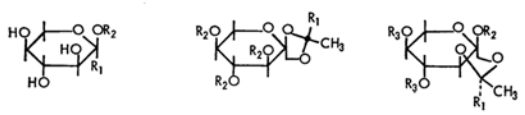
a) The values in parentheses were observed in benzene-d_6. b) Obscured.

TABLE 2. COUPLING CONSTANTS (Hz)

Compound	$J_{1,1'}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$	J_{CH_3CH}
IIIa	9.0	9.7	9	a)	a)	a)	5.0
Va	10.5	9.8	9.3	6.2	10.2	11.0	5.0
VIa	12.0	9.8	9	6.2	10.2	11.0	5.0
VIII	12.0	0.5	a)	a)	~2	13	5.0
XIa[b]	12.0	0.6	5.3	a)	a)	a)	5.0
XIIIa	a)	0.6	a)	a)	a)	a)	5.0
XV	a)	0.5	~2	~2	~2	12.8	5.0
XVa	11.8	0.5	~2	~2	~2	12.8	5.0
XVI	10.5	0.5	~2	~2	~2	12.8	5.0
XVII	9.6	0.5	2.5	~2	~2	12.8	5.0
XVIII	a)	0.5	a)	a)	~2	12.8	5.0
XVIIIa	11.8	0.5	~2	~2	~2	12.8	5.0
XIX	10.5	0.5	~2	~2	~2	12.8	5.0
XX	9.6	0.5	~2	~2	~2	12.8	5.0

a) not determinable. b) $J_{1,4}=0.8$

show a doublet due to H_3 at a higher filed (τ 6.52), a doublet-doublet due to H_4 (τ 4.47—4.58) and a multiplet due to H_4 (τ 5.02—5.03) at a lower field; the large coupling constants of $J_{3,4}$, $J_{4,5}$, and $J_{5,6}$, (9.3—10.2 Hz) are consistent with the proposed pyranose structures.[12,14,15]



I $R_1 = CH_2OH$, $R_2 = H$
XXI $R_1 = CH_2OH$, $R_2 = CH_3$
XXII $R_1 = CH_2OTs$, $R_2 = H$
XXIII $R_1 = COOCH_3$, $R_2 = H$

II $R_1 = CH_3$, $R_2 = H$
III $R_1 = R_2 = H$
IIIa $R_1 = H$, $R_2 = Ac$

IV $R_1 = CH_3$, $R_2 = R_3 = H$
V $R_1 = R_2 = R_3 = H$
Va $R_1 = R_2 = H$, $R_3 = Ac$
VI $R_1 = R_3 = H$, $R_2 = CH_3$
VIa $R_1 = H$, $R_2 = CH_3$, $R_3 = Ac$

Chart 1

The combined data of elemental analysis, optical rotation, and the infrared spectrum established that IIIa was the tri-*O*-acetate of monoethylidene-*α*-L-sorbose. The PMR spectrum in chloroform-d showed three three-proton singlets due to acetoxyls and signals due to H_3 (doublet), H_4 (doublet-doublet), and H_5 (multiplet) in the H–C–OAc region (τ 4.5—5.0). The large coupling constants of $J_{3,4}$ and $J_{4,5}$ (9—9.7 Hz) indicated its pyranose structure in the 1C conformation. Therefore, the structure of IIIa was determined to be the 3,4,5-tri-*O*-acetate of 1,2-*O*-ethylidene-*α*-L-sorbopyranose (III).

When the ethylidenation was allowed to continue for longer periods of time, the amount of diethylidene derivative (IX) increased at the expense of the monoethylidene compounds. The compound IX was considered to have a tertiary hydroxyl group for the same reasons as was Va. The methylation of IX with methyl iodide in the presence of silver oxide gave a glycoside (X), which was also isolated from the reaction mixture to a limited extent. The PMR spectrum of X in chloroform-d shows two one-proton quartets due to the methine protons of ethylidene groups at τ 5.27 and 5.28. Since the signal due to the methine proton of an ethylylidene ring in chloroform-d appeared at τ 4.70 for five-membered ring of IIIa and at τ 5.25—5.27 for the six-membered rings of Va and VIa, the ethylidene groups of X were assigned to those of six-membered rings. These data and their positive optical rotations apparently established that the structures of IX and X were 1,3:4,6-di-*O*-ethylidene-*β*-L-sorbofuranose, the ethylidene analog of 1,3:4,6-di-*O*-isopropylidene-*β*-L-sorbofuranose (VIII),[10] and methyl 1,3:4,6-di-*O*-ethylidene-*β*-L-sorbo-furanoside, respectively. The partial deacetalation of X with 60% acetic acid gave a monoethylidene sorboside (XI), which was then purified as a diacetate (XIa). The PMR spectrum of XIa in chloroform-d (see Fig. 1) shows singlets at τ 7.93 due to two acetyl methyls and at τ 6.73 due to one methoxy methyl, a doublet at τ 8.67 ($J=5.0$ Hz) due to one ethylidene methyl, and a quartet at τ 5.37 due to one methine proton of a six-membered ethylidene group. The patterns of the remaining protons are quite similar to those of methyl 1,3-

14) a) F. W. Lichtenthaler and H. K. Yahya, *Tetrahedron Letters*, **1965**, 1805. b) F. W. Lichtenthaler and H. K. Yahya, *Chem. Ber.*, **100**, 2389 (1967). c) H. Paulsen, H. Köster and K. Heynes, *ibid.*, **100**, 2669 (1967).

15) The evidence of PMR indicates that the favored conformations of Va and VIa are the 1C chair from.

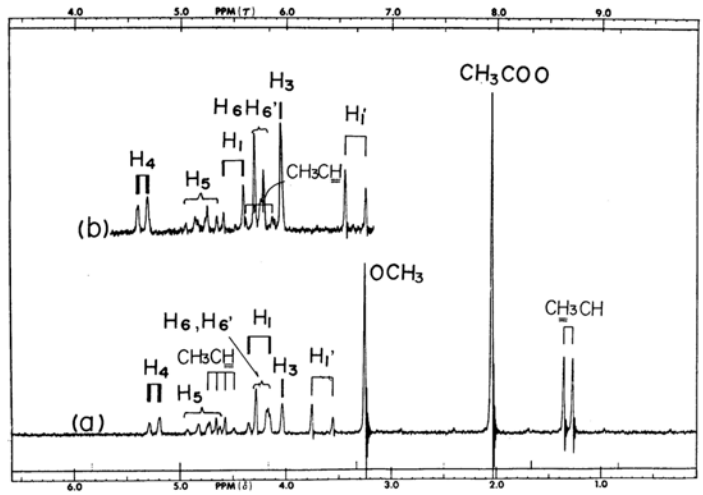
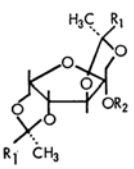


Fig. 1. PMR spectra of XIa in chloroform-d (a) and benzene-d_6 (b) at 60 MHz.

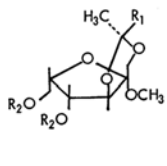
O-isopropylidene-4,6-di-*O*-acetyl-*β*-L-sorbofuranoside (XII), showing a remarkable low-field shift of H_4.[2] Therefore, XI was identified as methyl 1,3-*O*-ethylidene-*β*-L-sorbofuranoside; the formation of XI supports the structure of IX.



VIII $R_1 = CH_3$, $R_2 = H$

IX $R_1 = R_2 = H$

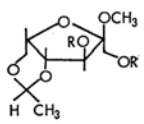
X $R_1 = H$, $R_2 = CH_3$



XI $R_1 = R_2 = H$

XIa $R_1 = H$, $R_2 = Ac$

XII $R_1 = CH_3$, $R_2 = Ac$



XIII R = H

XIIIa R = Ac

Chart 2

The exclusive formation of IX as compared to the predominant formation of VII from the acetonation of I under similar conditions is noteworthy. This fact suggests that IX is more stable than VIII in an acidic medium. This stability of IX can be attributed to the absence of an axial methyl group in the chair conformations of the *O*-ethylidene group.[8]

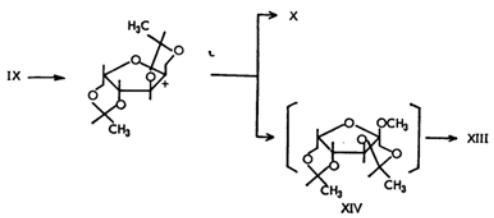
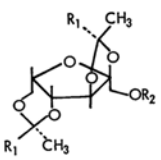


Chart 3

The negative value of optical rotation shows the anomeric configuration of XIIIa to be an *α*-anomer. The PMR spectrum of XIIIa in chloroform-d shows the presence of a six-membered ethylidene ring $\left(CH_3C\underline{H}<^{O}_{O}\ \tau\ 5.37\right)$; the signal due to H_3 is shifted downfield remarkably, while the signal due to H_4 is shifted upfield, in comparison with those observed in the spectrum of XIa. Therefore, the structure of XIII was determined to be methyl 4,6-*O*-ethylidene-*α*-L-sorbofuranoside.[2] The small coupling of $J_{3,4}$ (=0.6 Hz) also supports this furanose structure. The formation of X and XIII was proposed to be as follows: no isolation of 1,3:4,6-di-*O*-ethylidene-*α*-L-sorbofuranose results from its stereochemical instability.



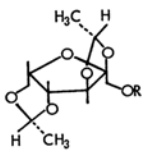
VII $R_1 = CH_3$, $R_2 = H$

XV $R_1 = R_2 = H$

XVa $R_1 = H$, $R_2 = Ac$

XVI $R_1 = H$, $R_2 = Ts$

XVII $R_1 = H$, $R_2 =$ trityl



XVIII R = H

XVIIIa R = Ac

XIX R = Ts

XX R = trityl

Chart 4

Drastic conditions were required for the formation of 2,3:4,6-di-*O*-ethylidene-*α*-L-sorbofuranose. When

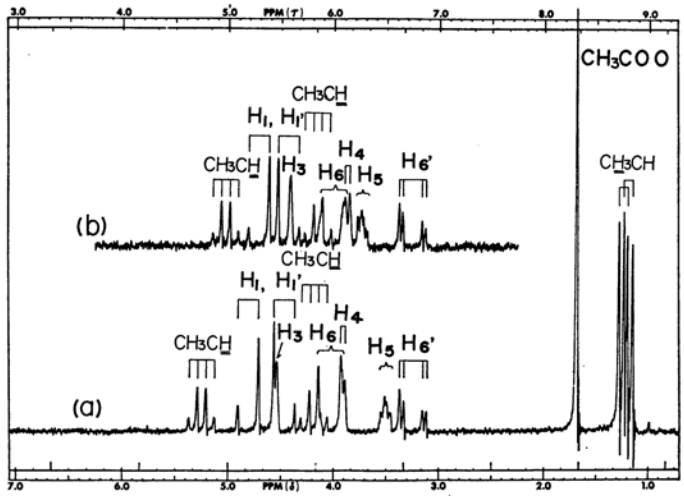


Fig. 2. PMR spectra of XV (a) and XVIII (b) in chloroform-d at 60 MHz.

I was treated with acetaldehyde dimethylacetal using a high concentration of sulfuric acid, a syrup was obtained which contained two isomers (XV and XVIII) with two ethylidene groups and negative optical rotations. Both derivatives, XV and XVIII, easily afforded acetates (XVa and XVIIIa), tosylates (XVI and XIX), and tritylates (XVII and XX respectively), and were both converted into methyl 2-keto-L-gulonate (XXIII) by Reichstein's procedure.[6] Further, XVI (or XIX) was identical with one of the two tosylates derived from the ethylidenation of 1-*O*-tosyl-L-sorbose (XXII).[16] These facts suggested the presence of a C_1-hydroxyl group in both isomers. The PMR spectra of the XVa and XVIIIa acetates (see Fig. 2) included the characteristic signals for a furanose structure, a somewhat broad singlet due to H_3 ($J_{3,4}$=0.5 Hz) and a doublet due to H_4 ($J_{4,5}$=5.8 Hz). Therefore, the structures of XV and XVIII were determined to be the diastereoisomers of 2,3:4,6-di-*O*-ethylidene-*α*-L-sorbofuranose, which differ only at the acetal center of the 2,3-*O*-ring since those methyl groups on the 1,3-dioxanes fused at the 4,6-position of furanose rings have been found to be equatorial in both isomers on the basis of non-bonded interactions[7a] and also on the basis of extensive studies of acetals.[17]

Ethylidene methine protons in chloroform-d appeared as quartets at τ 4.58 and 5.37 for XVa and at τ 4.83 and 5.37 for XVIIIa. Signals at a lower field were assignable to the protons on the dioxolane rings, as has been described above. Since the ethylidene methine proton on the dioxolane ring fused directly to the five-membered cyclic system is deshielded when *endo*,[17-19] XV (τ 4.58) and XVIII (τ 4.83) are assigned the H-*endo* and H-*exo* configurations[20,21] respectively.

As has been mentioned above, the expected 1,3-*O*-ethylidene pyranose V was successfully isolated; this suggested the presence of an equilibrium between 1,2-*O*-acetal (III) and 1,3-*O*-acetal (V) in the initial stage of the acetalation, much as in the acetalation of glycerol.[7] Further, the pathway of IX→(XV+XVIII) was also confirmed. Thus, the reaction pathway of I→(III⇄V)→IX→(XV+XVIII) for the ethylidenation of L-sorbose (I) was established; a detailed discussion of this will be presented elsewhere.

Experimental

Thin-layer chromatography was performed on silica gel using ether - *n*-hexane (2 : 1 v/v) as a solvent. The separated materials were developed with iodine. In the cases of preparative thin-layer chromatography (PTC), the developed zones were extracted with acetone. The evaporation of the acetone under reduced pressure gave the materials.

The PMR spectra were measured on a Varian A-60 spectrometer at 60 MHz in chloroform-d and/or benzene-d_6, using tetramethylsilane as the internal reference at

16) T. S. Gardner and J. Lee, *J. Org. Chem.*, **12**, 733 (1947).

17) N. A. Baggett, K. W. Buck, A. B. Foster and J. M. Webber, *J. Chem. Soc.*, **1965**, 3401, and earlier papers in this series.

18) F. Kametani and Y. Minoura, paper presented at the Annual Meeting of the Pharmaceutical Society of Japan, Tokyo, April, 1968.

19) R. J. Ferrier and L. R. Hatton, *Carbohyd. Res.*, **5**, 132 (1967).

20) The "H-*endo*" and "H-*exo*" diastereoisomers correspond to the R and S configurations respectively. See Ref. 21.

21) R. S. Cahn, C. K. Ingold and V. Prelog, *Angew. Chem. Internat. Edit.*, **5**, 385 (1966); *Experimentia*, **12**, 81 (1956); *J. Chem. Soc.*, **1951**, 612.

the ordinary probe temperature. All the melting points were measured on a Kofler block and were corrected. The optical rotations were determined in a 10 cm microtube in chloroform containing 1% ethanol, and the concentrations were recorded in percentages.

The solvents used were removed under reduced pressure below 40°C.

Ethylidenation of L-Sorbose (I). a) To a mixture of dry, finely-powdered L-sorbose (I) (15 g) and acetaldehyde dimethylacetal (50 ml), dioxane (50 ml) containing *p*-toluenesulfonic acid (TsOH) (1 g) was added. The suspended solution was vigorously stirred for 2.7 hr at 40°C, and then neutralized with potassium carbonate. After the removal of the unreacted L-sorbose (I) (7 g) and the excess potassium carbonate by filtration, the filtrate was concentrated to a yellow syrup (10.5 g). The chloroform solution (100 ml) of the syrup was washed with water (3×15 ml). From the chloroform layer, a di-*O*-ethylidene compound (IX) was isolated by a procedure (c) described below. The combined water was evaporated to a thick syrup (4.14 g). Without purification, the syrup was treated with acetic anhydride (20 ml) in pyridine (25 ml) at 0—5°C. After 3 hr, the solution was evaporated to give a syrup (4.7 g), from which IIIa (R_f 0.5—0.6, 0.27 g), VIa (R_f 0.44—0.51, 0.42 g), and XIIIa (R_f 0.39—0.49, 0.38 g) were then isolated by PTC. IIIa: syrup, $[\alpha]_D^{22}$ −45.7 (*c* 0.341). Found: C, 50.95; H, 6.02%. Calcd for $C_{14}H_{20}O_9$: C, 50.60; H, 6.07%. VIa: needles (recryst. from *n*-hexane), mp 93—94°C, $[\alpha]_D^{24}$ −58.4 (*c* 0.527). Found: C, 51.23; H, 6.59%. Calcd for $C_{13}H_{20}O_8$: C, 51.31; H, 6.63%. XIIIa: syrup, $[\alpha]_D^{23}$ −31.2 (*c* 1.020). Found: C, 51.30; H, 6.60%. Calcd for $C_{13}H_{20}O_8$: C, 51.31; H, 6.63%.

b) A solution of I (3.0 g) and acetaldehyde dimethylacetal (15 ml) in dimethylsulfoxide (15 ml) containing TsOH (0.3 g) was stirred at room temperature. After 3.3 hr, the solution was neutralized with ammonia water and then concentrated to a syrup (4.9 g). Without purification, the syrup was treated with acetic anhydride (20 ml) in pyridine (25 ml) at 0—5°C. After 3 hr, the solution was evaporated to give a syrup (3.9 g), from which IIIa (0.18 g), and Va (R_f 0.16—0.28, 0.16 g) were then isolated by PTC. Va: needles (recryst. from *n*-hexane, mp 140—142°C, $[\alpha]_D^{24}$ −24.7 (*c* 0.458). Found: C, 49.66; H, 6.19%. Calcd for $C_{12}H_{18}O_8$: C, 49.65; H, 6.25%.

c) A suspended solution of I (15 g) and acetaldehyde dimethylacetal (35 ml) in dioxane (50 ml) containing TsOH (1.0 g) was vigorously stirred at 40°C for 4.5 hr. The solution was made alkaline with potassium carbonate and then concentrated to a syrup (16.2 g), whose thin-layer chromatogram showed the presence of IX as the major product and X as the minor one. Several purifications of the syrup by PTC afforded IX (R_f 0.39—0.49, 2.5 g) and X (R_f 0.52—0.61, 0.52 g). IX: syrup, $[\alpha]_D^{24}$ +66.0 (*c* 1.006). Found: C, 51.48; H, 7.02%. Calcd for $C_{10}H_{16}O_6$: C, 51.72; H, 6.94%. X: syrup, $[\alpha]_D^{23}$ +68.1 (*c* 1.036). Found: C, 53.77; H, 7.35%. Calcd for $C_{11}H_{18}O_6$: C, 53.65; H, 7.37%.

d) A mixture of I (4.2 g), acetaldehyde dimethylacetal (30 ml), and sulfuric acid (6 g) was stirred at 30°C for 3 hr. The solution was neutralized with a a sodium carbonate solution and then concentrated to a syrup. The syrup was extracted with acetone, and the acetone removed. The chloroform solution of the residue was washed with water and dried, and the solvent removed. The purification of the residue (6.3 g) by PTC (R_f 0.14—0.27) gave crude crystals (3.9 g). The crystals were then treated with acetic anhydride (25 ml) in pyridine (25 ml) at 5°C. After standing overnight, the reaction mixture was poured over ice water and extracted with chloroform. The chloroform was washed with a sodium carbonate solution and then with water, and dried, after which the solvent was removed. From the residue, XVa (R_f 0.46—0.60, 1.28 g) and XVIIIa (R_f 0.38—0.49, 2.0 g) were isolated by PTC. XVa: plates (recryst. from *n*-hexane), mp 71—72°C, $[\alpha]_D^{20}$ −21.5 (*c* 0.783). Found: C, 52.33; H, 6.54%. Calcd for $C_{12}H_{18}O_7$: C, 52.55; H, 6.62%. XVIIIa; columns (recryst. from *n*-hexane), mp 53—54°C, $[\alpha]_D^{20}$ −24.0 (*c* 0.504). Found: C, 52.59; H, 6.46%. Calcd for $C_{12}H_{18}O_7$: C, 52.55; H, 6.62%.

Methyl 1,3-*O*-Ethylidene-4,6-di-*O*-acetyl-β-L-sorbofuranoside (XIa). A solution of X (1.19 g) in 60% acetic acid (50 ml) was heated at 95°C for 45 min. The solvent was removed twice by the addition of an excess of ethanol and by subsequent concentration. Without further purification, the residual syrup (1.04 g) was acetylated with acetic anhydride (20 ml) and pyridine (30 ml) in a refrigerator for 4 hr. The evaporation of the solvent gave a syrup (1.3 g), which was purified by PTC and then by recrystallization from *n*-hexane. XIa (197 mg) was obtained, mp 61—62°C, $[\alpha]_D^{24}$ +53.7 (*c* 0.536). Found: C, 51.50; H, 6.62%. Calcd for $C_{13}H_{20}O_8$: C, 51.31; H, 6.63%.

(R)-2,3:(R)-4,6-Di-*O*-ethylidene-α-L-sorbofuranose (XV). To a solution of XVa (0.7 g) in methanol (5 ml), 0.1 N methanolic sodium methoxide (150 ml) was added. After the mixture had stood at room temperature for 10 min, the solvent was removed, and then the mixture was extracted with chloroform. The chloroform was washed with water and dried, and the solvent was removed. The recrystallization of the residue from *n*-hexane gave needles (0.43 g), mp 58—59°C, $[\alpha]_D^{20}$ −8.5 (*c* 0.562). Found: C, 51.86; H, 6.96%. Calcd for $C_{10}H_{16}O_6$: C, 51.72; H, 6.94%.

(S)-2,3: (R)-4,6-Di-*O*-ethylidene-α-L-sorbofuranose (XVIII). A mixture of XVIIIa (1.55 g) in methanol (100 ml) and 0.1 N methanolic sodium methoxide (100 ml) was stirred at room temperature for 10 min. XVIII was then obtained in the above-described manner. XVIII: needles (recryst. from ethyl acetate and *n*-hexane), mp 82—83°C, $[\alpha]_D^{20}$ −9.5 (*c* 0.927). Found: C, 51.80; H, 6.85%. Calcd for $C_{10}H_{16}O_6$: C, 51.72; H, 6.94%.

Methyl 1,3-*O*-Ethylidene-4,5-di-*O*-acetyl-α-L-sorbopyranoside (VIa). a) A mixture of Va (0.15 g), methyl iodide (10.5 g), and silver oxide (1 g) was refluxed for 9 hr. The precipitates were removed by filtration, and the filtrate was concentrated to give a syrup. The syrup was purified by PTC (R_f 0.44—0.51), followed by recrystallization from *n*-hexane. VIa (0.1 g) was obtained.

b) A solution of methyl α-L-sorbopyranoside (XXI) (1.4 g), acetaldehyde dimethylacetal (28 ml), and TsOH (0.14 g) was stirred at room temperature. After 2 hr, the solution was neutralized with methanolic sodium methoxide. After the removal of the solvent, the residue was extracted with chloroform and the solvent removed. The residue was treated with acetic anhydride (20 ml) in pyridine (20 ml) at 5°C for 4 hr and then worked up by a procedure similar to that used in the ethylidena-

tion of I (a). VIa (0.1 g) was thus obtained.

Methyl 1,3:4,6-Di-*O*-ethylidene-*β*-L-sorbofuranoside (X). A mixture of IX (0.14 g), methyl iodide (14 g), and silver oxide (0.5 g) was refluxed for 4.7 hr. The precipitates were removed by filtration, and the filtrate was concentrated to give a syrup. The purification of the syrup by PTC (R_f 0.52—0.61) gave X (0.1 g).

1-*O*-Tosyl-(R)-2,3:(R)-4,6-di-*O*-ethylidene-*α*-L-sorbofuranose (XVI). A solution of XV (0.2 g) and tosyl chloride (0.5 g) in pyridine (3 m*l*) was kept overnight at room temperature. The solution was then poured over ice, extracted with chloroform which had been washed with a sodium bicarbonate solution and then with water, dried, and evaporated to dryness. The recrystallization of the residual syrup from methanol and water gave needles (0.26 g), mp 70—72°C (dec.), $[\alpha]_D^{24}$ −8.2 (*c* 0.970). Found: C, 52.84; H, 5.76; S, 8.26%. Calcd for $C_{17}H_{22}O_8S$: C, 52.85; H, 5.70; S, 8.29%.

1-*O*-Tosyl-(S)-2,3:(R)-4,6-di-*O*-ethylidene-*α*-L-sorbofuranose (XIX). A solution of XVIII (0.3 g) and tosyl chloride (0.5 g) in pyridine (3 m*l*) was worked up in a procedure similar to the above. XIX (0.35 g) was thus obtained as needles (recryst. from methanol and and water), mp 72.5—73°C, $[\alpha]_D^{24}$ −7.0 (*c* 0.814). Found: C, 53.15; H, 5.61; S, 8.49%. Calcd for $C_{17}H_{22}O_8S$: C, 52.85; H, 5.70; S, 8.29%.

Ethylidenation of 1-*O*-Tosyl-L-sorbose (XXII). A mixture of XXII (1.5 g) and acetaldehyde dimethylacetal (30 m*l*) was stirred at room temperature in the presence of sulfuric acid (2.2 g) for 3.7 hr and then neutralized with a sodium bicarbonate solution. The solvent was removed to give a syrup, which was then dissolved in chloroform, washed with water, and dried. The evaporation of the chloroform gave a syrup, from which XV (R_f 0.26—0.32, 0.56 g) and XVIII (R_f 0.39—0.45, 0.65 g) were isolated by PTC.

1-*O*-Trityl-(R)-2,3:(R)-4,6-di-*O*-ethylidene-*α*-L-sorbofuranose (XVII). To a solution of XV (0.3 g) in pyridine (6 m*l*), trityl chloride (1 g) was added. After standing at room temperature for 8 days, the solution was poured over ice and then extracted with chloroform. The chloroform was washed with a sodium carbonate solution, with hydrochloric acid, and then with water, and the solvent was removed. Crude crystals (1.25 g) were purified by PTC (R_f 0.41—0.49), followed by recrystallization from *n*-hexane. XVII was thus obtained as plates (0.09 g), mp 130—133°C, $[\alpha]_D^{24}$ −32.8 (*c* 2.903). Found: C, 73.69; H, 6.47%. Calcd for $C_{29}H_{30}O_6$: C, 73.40; H, 6.37%.

1-*O*-Trityl-(S)-2,3:(R)-4,6-di-*O*-ethylidene-*α*-L-sorbofuranose (XX) was obtained from XVIII (0.5 g), by a procedure similar to the above (PTC: R_f 0.54—0.59, 0.42 g). XX: columns (recryst. from *n*-hexane), mp 162—163°C, $[\alpha]_D^{23}$ −35.5 (*c* 0.738). Found: C, 73.43; H, 6.32%. Calcd for $C_{29}H_{30}O_6$: C, 73.40; H, 6.37%.

Oxidation of 2,3:4,6-di-*O*-ethylidene-*α*-L-sorbofuranoses (XV and XVIII). To a solution of a crude mixture of XV and XVIII (1.95 g) in water (24 m*l*) containing potassium hydroxide (1.11 g), a potassium permanganate (2.8 g) solution (31 m*l*) was added, batch by batch, over a 2.5-hr period. After the mixture had then been stirred at 25—26°C for 1.2 hr, the precipitates were removed by filtration, the filtrate was saturated with carbon dioxide, and then the water was removed. The residue was extracted with hot ethanol and the ethanol was concentrated to a powder, which was then dissolved in water (2 m*l*). The pH of the water was adjusted to 1.0 with hydrochloric acid under cooling. The acidic solution was extracted with ethyl acetate. The removal of the ethyl acetate gave a syrup; this solution in methanol (6 m*l*) containing one drop of hydrochloric acid was refluxed for 6 hr, and then the solvent was removed without heating to give methyl L-gulonate (XXIII) (0.04 g), mp 151—153°C. This was identical with an authentic sample.[6]

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