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Benzylidenation of L-Sorbose[1-3]

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The acid-catalyzed benzylidenation of L-sorbose (I) was studied. The reaction by Reichstein's procedure gave a mixture of two diastereomeric 2,3:4,6-di-*O*-benzylidene-α-L-sorbofuranoses (III and IV), which were then successfully separated by preparative thin-layer chromatography. The use of slightly acidic conditions yielded 1,3:4,6-di-*O*-benzylidene-β-L-sorbofuranose (XI), 1,2:4,6-di-*O*-benzylidene-α- (XVII and XVIII) and -β-L-sorbofuranoses (XIX and XX), 1,2-*O*-benzylidene-α-L-sorbopyranoses (XXI and XXII), and 1,3-*O*-benzylidene-L-sorbose (XXIII). The absolute configurations at the acetal center of the five-membered benzylidene rings were assigned. A reaction sequence (I→(XXI, XXII⇄XXIII)→XI→IV→III) comparable with that of the ethylidenation of I was established.

1,2-*O*-Isopropylidene-α-L-sorbopyranose has been proposed as a key intermediate in the acetonation of L-sorbose (I) yielding 2,3:4,6-di-*O*-isopro-pylidene-α-L-sorbofuranose.[4] However, in the course of recent studies of the acetonation of I using weakly acidic conditions, we have isolated for the first time several types of isomers such as 1,3:4,6-di-*O*-isopropylidene-β-L-sorbofuranose,[5] and 1,3:4,6-di-*O*-isopropylidene-α-[6] and -β-L-sorbofuranoses.[5] The presence of these isomers suggests the complicated nature of the acetalation of I. More recently, ethylidenated L-sorboses corresponding to the acetonated ones have also been isolated from the ethylidenation of I under weakly acidic conditions, and a reaction sequence of the ethylidenation has been established as follows: I→[1,2-*O*-ethylidene-α-L-sorbopyranose ⇄ 1,3-*O*-ethylidene-α-L-sorbopyranose (1,3-*O*-acetal)] → 1,3:4,6-di-*O*-ethylidene-β-L-sorbofuranose (1,3:4,6-di-acetal) → 2,3:4,6-di-*O*-ethylidene-α-L-sorbofuranose.[2]

An important difference between the acetonation and the ethylidenation is that, with the former, a compound corresponding to the 1,3-*O*-acetal was not isolated, a fact probably explainable in terms of the Brown-Brewster-Schechter rule.[7] A pathway from the 1,3-*O*-acetal to the 1,3:4,6-di-*O*-acetal seemed to be required in the acetalations of I. The idea of the existence of this important pathway from a pyranose to a furanose would receive strong support if compounds of the 1,3-*O*-acetal type could be found in other acetalation reactions. From this point of view, we have described the benzylidenation of I with benzaldehyde. The structures of the products were determined by proton magnetic resonance (PMR) spectroscopic and chemical evidence. The PMR data are reported in Tables 1 and 2, and some of the spectra are shown in Figs. 1—4, which also indicate a clue to the elucidation of the diastereomeric configurations at the acetal centers of the products.

Reichstein and Grüssner[8] reported that the reaction of I with benzaldehyde in the presence of an acid gave a brown syrup. We could separate this syrup into two dibenzylidene-L-sorboses, III and IV, by preparative thin-layer chromatography. As the oxidation of the syrup mixture of III and IV afforded L-xylo-hexulosonic acid in good yield,[8] III and IV can be said to be diastereomeric 2,3:4,6-di-*O*-benzylidene-α-L-sorbofuranoses. The facts that III and IV reacted with trityl chloride-pyridine to yield tritylates (V and VI respectively) and with acetic anhydride-pyridine to give acetates (IIIa and IVa respectively) (see Figs. 1 and 2) supported their structures. The general characteristics of the PMR data of III and IV, especially the small coupling constants of $J_{3,4}$ (0.5 Hz),[5,9,10] leave no doubt that they have a furanose ring. As the phenyl group is equatorial in the chair con-

1) Sorboses XIV. For Part XIII, See Ref. 2.

2) T. Maeda, M. Kiyokawa and K. Tokuyama, This Bulletin, **42**, 492 (1969).

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

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

5) T. Maeda, This Bulletin, **40**, 2122 (1967).

6) K. Tokuyama and E. Honda, *ibid.*, **37**, 591 (1964).

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

8) T. Reichstein and A. Glüssner, *Helv. Chim. Acta*, **17**, 311 (1934).

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

10) J. D. Stevens and H. G. Fletcher, Jr., *J. Org. Chem.*, **33**, 1799 (1968).

Table 1. Chemical shifts in $CDCl_3$ (τ)[a]

Compound	H_1, $H_{1'}$	H_3	H_4	H_5	H_6, $H_{6'}$	Benzylic H of 1,3-dioxolane	Benzylic H of 1,3-dioxane	OAc	Aromatic H	Other H
III	~6.07[b]	5.27	5.41	~5.76[b]	~5.53,[b] ~5.97[b]	3.80	4.55		2.4—2.8	OH, 7.83
IIIa	5.34, 5.64 (5.15, 5.47)	5.32 (5.23)	5.40 (5.87)	5.75 (6.32)	5.52, 5.95 (5.79, 6.58)	3.80 (3.86)	4.55 (4.89)	8.12 (8.49)	2.5—2.7 (2.3—3.0)	
IV	~6.03[b]	5.30	5.50	5.77	5.57, 5.98	4.07	4.58		2.5—2.8	OH, 7.67
IVa	5.33, 5.61 (5.21, 5.46)	5.37 (5.34)	5.50 (5.88)	5.73 (6.07)	5.70, 5.97 (5.82, 6,59)	4.07 (4.09)	4.58 (4.91)	8.02 (8.40)	2.5—2.7 (2.3—2.9)	
V	6.26, 6.55	5.13	5.47	~5.78[b]	~5.63,[b] ~6.03[b]	3.80	4.67		2.3—2.9	
VIII	~6.12[b]	5.38	5.58	5.5	6.1[b]		4.56			OH, 7.93
IX	~5.61[b]	5.43	4.53	5.31	5.65, 5.87	3.77		7.89, 7.92, 8.00	2.62	
X	~5.58[b]	5.48	4.63	5.33	5.62, 5.88	4.07		7.87, 7.88, 7.95	2.5—2.6	
XI	5.71, 6.01	5.3			6.1[b]		4.47 4.53		2.5—2.8	OH, 5.98
XV	5.56, 6.09	5.67	4.62	5.15	5.7— 5.8[b]		4.53	7.92(6H)	2.5—2.8	OMe, 6.68
XVIIa	5.45, 5.78 (5.47, 5.77)	4.61 (4.50)	5.5	(6.17)	5.8,[b] 5.95 (5.80, 6.55)	4.04 (3.93)	4.55 (4.88)	8.01 (8.30)	2.5—2.7 (2.3—3.0)	
XVIIIa	5.53, 5.77 (5.50, 5.80)	4.76 (4.70)	5.5 (6.01)	(6.16)	5.8,[b] 5.92 (5.87, 6.63)	4.21 (4.07)	4.54 (4.90)	7.89 (8.23)	2.4—2.7 (2.2—3.0)	
XIXa	5.73, 5.90 (5.73, 5.85)	4.60 (4.42)	5.5 (5.93)	6.38	6.1[b] (5.73, 6.49)	3.80 (3.68)	4.60 (4.80)	7.94 (8.43)	2.6—2.8 (2.2—3.0)	
XXa	5.77, 5.95 (5.78, 6.15)	4.50 (4.40)	5.5 (6.00)	(6.43)	6.1[b] (5.74, 6.51)	3.97 (4.07)	4.56 (4.80)	7.89 (8.38)	2.2—2.8 (2.1—3.0)	
XXIa	5.82, 6.15 (5.92, 6.19)	4.87 (4.73)	4.47 (4.18)	4.98 (4.86)	6.1— 6.3[b] (6.2— 6.4)[b]	3.95 (3.96)		7.87, 7.98, 8.02 (8.25(6H), 8.42)	2.5—2.7 (2.4—3.0)	
XXIIa	5.95, 6.02 (5.88, 6.19)	4.82 (4.68)	4.45 (4.21)	4.95 (4.83)	6.0— 6.2[b] (6.1— 6.3)[b]	4.00 (4.08)		7.95, 7.98(6H) (8.27, 8.33, 8.35)	2.4—2.7 (2.3—3.0)	
XXIV	5.73, 6.07 (5.73, 6.25)	5.67 (5.82)	4.57 (4.58)	~5.2[b] (~5.3)[b]	5.5—5.8[b] (5.5—5.8)[b]		4.50 (4.73)	7.88, 7.95 (8.28, 8.31)	2.5—2.8 (2.3—2.9)	OH [c] OH [c]
XXV	5.9 — 6.5[b] (5.9 — 6.9)[b]		4.43 (4.58)	4.96 (~4.75)[b]	5.9— 6.5[b] (5.9— 6.9)[b]		4.43 (4.81)	7.95, 7.97 (8.27, 8.37)	2.5—2.8 (2.4—3.0)	OH [c] OH [c]
XXVI	5.31, 5.67 (5.15, 5.85)	5.17 5.29	4.57 (4.61)	~5.1[b] (~5.2)[b]	5.6— 5.8[b] (5.6— 5.8)[b]		4.37 (4.58)	7.92, 7.94(6H) (8.32(6H), 8.36)	2.5—2.7 (2.4—3.0)	
XXVII	5.62, 6.42	6.30	4.36	4.97	6.13, 6.40		4.45	7.97(6H)	2.5—2.8	OMe 6.64

a) Values in parentheses are those observed in C_6D_6.
b) Unresolved.
c) Obscured.

TABLE 2. COUPLING CONSTANTS (J, Hz)

Compound	$J_{1,1'}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$	Other J
III	a)	0.5	2.5	~2	~2	a)	
IIIa	(−)12.0	0.5	2.5	~2	2.0	(−)13.0	
IV	a)	0.5	2.5	~2	2.0	(−)13.0	
IVa	(−)12.0	0.5	2.5	~2	2.0	(−)13.0	
V	9.8	0.5	2.5	a)	a)	a)	
VIII	a)	0.5	2.5	a)	a)	a)	
IX	a)	0.5	3.6	5.0	7.0	(−)11.5	
X	a)	0.5	3.0	5.0	7.0	(−)11.5	
XI	(−)12.0	a)	a)	a)	a)	a)	
XV	(−)12.0	0.5	6.0	a)	a)	a)	$J_{1,3}\leq 0.5$
XVIIa	(−) 9.0	0.5	3.0	~2	2.0	(−)13.0	
XVIIIa	(−) 9.0	0.5	3.0	~2	2.0	(−)13.0	
XIXa	(−) 9.0	0.5	3.0	~2	2.0	(−)13.0	
XXa	(−) 9.0	0.5	3.0	~2	2.0	(−)13.0	
XXIa	(−) 9.2	9.6	9.6	a)	a)	a)	
XXIIa	(−) 9.3	9.6	9.3	a)	a)	a)	
XXIV	(−)12.0	0.5	4.5	a)	a)	a)	$J_{1,3}\leq 0.5$
XXV	a)	~9.5	~9.5	a)	a)	a)	
XXVI	(−)12.0	0.5	5.5	a)	a)	a)	$J_{1,3}\leq 0.5$
XXVII	(−)12.0	10.0	9.3	6.3	10.7	(−)10.7	

a) Not determinable.

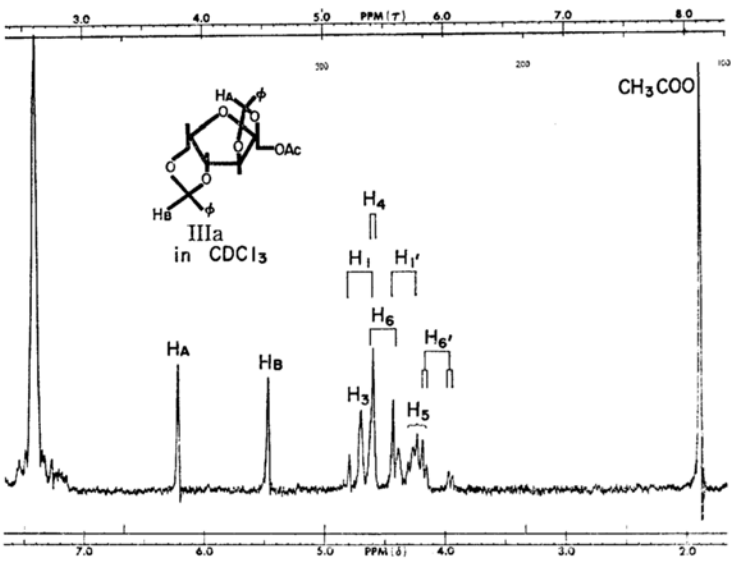


Fig. 1. PMR spectrum of IIIa in $CDCl_3$ at 60 MHz.

formation of the six-membered 4,6-*O*-benzylidene group, the diastereomerism between III and IV must be caused by the five-membered 2,3-*O*-benzylidene ring. The benzylic proton signals of III and IV in $CDCl_3$ appear at τ 3.80 and 4.55 and at τ 4.07 and 4.58 respectively. It is well known that a benzylic proton of 1,3-dioxolane resonates at a lower field than that of 1,3-dioxane.[11] The signals observed at τ 3.80 and 4.07 can be assigned to the benzylic protons of 2,3-*O*-benzylidenacetals. This assignment was supported by the benzylic proton signal (τ 4.56) of 4,6-*O*-benzylidene-2,3-*O*-isopropylidene-α-L-sorbofuranose (VIII), which was derived from 2,3-*O*-isopropylidene-α-L-sorbofuranose (VII)[12] and which was hydrolyzed to the starting material quantitatively.

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

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

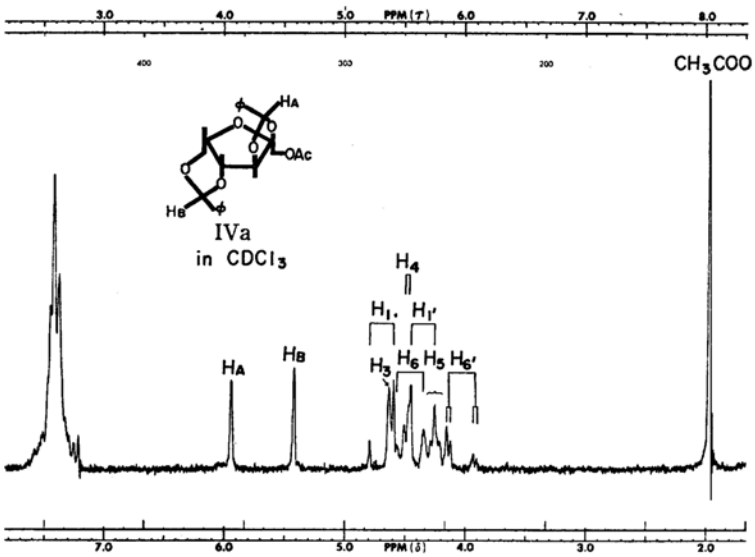


Fig. 2. PMR spectrum of IVa in $CDCl_3$ at 60 MHz.

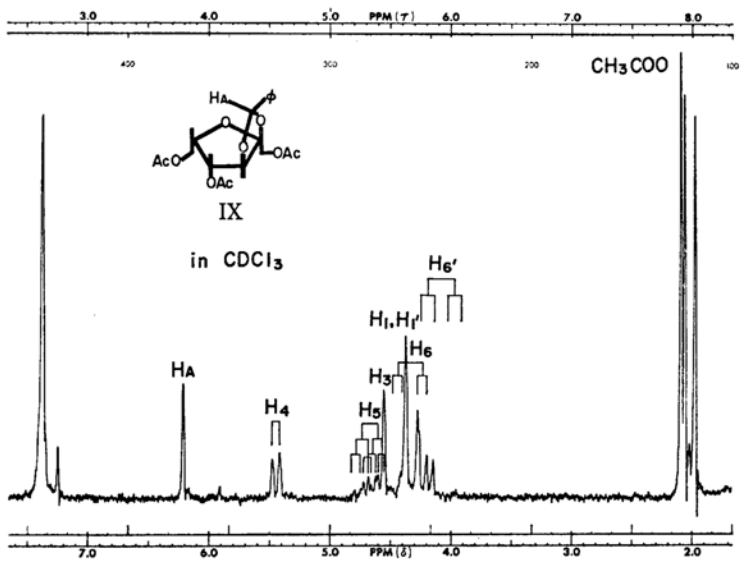


Fig. 3. PMR spectrum of IX in $CDCl_3$.

The selective removal of the 4,6-*O*-benzylidene rings of III and IV, followed by acetylation, yielded two 1,4,6-tri-*O*-acetyl-2,3-*O*-benzylidene-α-L-sorbofuranoses, IX and X respectively; in them the spectra of the lower-field benzylic protons of the parent compounds, III and IV, remained unchanged (see Figs. 3 and 4). Thus, it was unequivocally established that III and IV are, respectively, H-*endo* and H-*exo*[11,13] diastereomers at the acetal center of the 2,3-*O*-benzylidene ring. Since benzylic protons on dioxolane rings fused directly to five-membered cyclic systems are deshielded when in the *endo* position,[2,11,14] III and IV are assigned the H-*endo* and H-*exo* configurations respectively. Recently, Ferrier and Hatton[13] reported the assignment of diastereomeric 1,2 : 3,5-di-*O*-benzylidene-α-D-xylofuranoses on the basis of the difference in benzylic protons in the chemical shifts at τ 3.83 (H-*endo*) and 4.10 (H-*exo*); these values are in good agreement with our findings for sorbose derivatives (see Chart I).

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

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

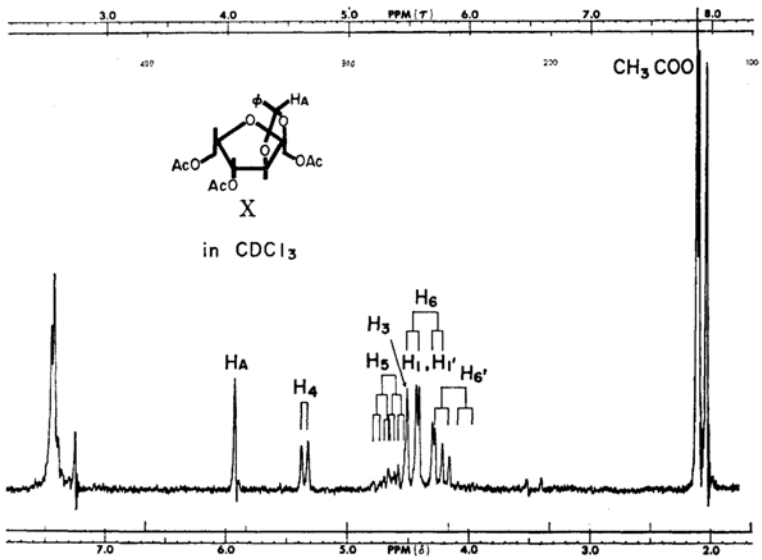
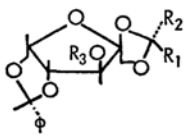
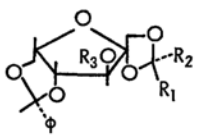
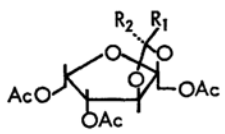


Fig. 4. PMR spectrum of X in $CDCl_3$ at 60 MHz.







XVII $R_1 = \phi$, $R_2 = R_3 = H$

XVIIa $R_1 = \phi$, $R_2 = H$, $R_3 = Ac$

XVIII $R_1 = H$, $R_2 = \phi$, $R_3 = H$

XVIIIa $R_1 = H$, $R_2 = \phi$, $R_3 = Ac$

XIX $R_1 = \phi$, $R_2 = R_3 = H$

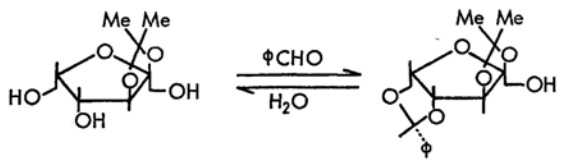
XIXa $R_1 = \phi$, $R_2 = H$, $R_3 = OAc$

XX $R_1 = H$, $R_2 = \phi$, $R_3 = H$

XXa $R_1 = H$, $R_2 = \phi$, $R_3 = Ac$

IX $R_1 = \phi$, $R_2 = H$

X $R_1 = H$, $R_2 = \phi$



VII VIII

Chart I

The use of a trace of *p*-toluenesulfonic acid as a catalyst afforded mainly another dibenzylidene derivative (XI), which reduces a Fehling solution. The methylation of XI with methyl iodide in the presence of silver oxide yielded methyl glycoside (XII), which was also obtainable by the acetal interchange reaction of methyl 1,3:4,6-di-*O*-isopropylidene-*β*-L-sorbofuranoside (XIII)[5] with a large excess of benzaldehyde. The debenzylidenation of XII with 60% acetic acid, followed by acetylation, afforded methyl 1,3,4,6-tetra-*O*-acetyl-*β*-L-sorbofuranoside (XIV)[9] and partially debenzylidenated sorbofuranoside (XV). The PMR spectra of XV, showing a pattern closely related to that of the methyl 4,6-di-*O*-acetyl-1,3-*O*-isopropylidene-*β*-L-sorbofuranoside (XVI)[9] obtained from XIII by a similar procedure, suggest that the structure of XV is methyl 4,6-di-*O*-acetyl-1,3-*O*-benzylidene-*β*-L-sorbofuranoside. Therefore, the structure of XI was determined to be 1,3:4,6-*O*-benzylidene-*β*-L-sorbofuranose. The benzylic proton singlets at τ 4.47 and 4.53 in $CDCl_3$, showing the presence of two 1,3-dioxanes, also supported the proposed structure. The absence of diastereomers in XI is quite natural, since it has only 1,3-dioxanes (see Chart II).

TABLE 3. THE ASSIGNMENT OF THE ANOMERIC AND DIASTEREOMERIC CONFIGURATIONS OF 1,2:4,6-DI-*O*-BENZYLIDENE-L-SORBOFURANOSES

Compound	$[\alpha]_D$	IR spectra OH (in CCl_4)	PMR spectra Benzylic H of 1,2-*O*-ring (in $CDCl_3$)	Configuration	
				Anomeric	Diastereomeric
XVII	−31.0	3558 cm^{-1}	τ 4.04	α	H-*endo*
XVIII	+34.7	3556	4.21	α	H-*exo*
XIX	+22.7	3629	3.80	β	H-*endo*
XX	+166.6	3630	3.97	β	H-*exo*

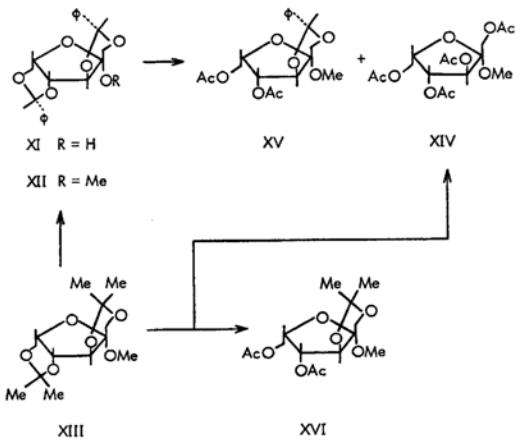


Chart II

When the benzylidenation reaction was carried out in dimethyl sulfoxide (DMSO), four non-reducing dibenzylidenated sorboses (XVII, XVIII, XIX, and XX) (see Table 3) and three mono-benzylidenated sorboses (the reducing XXIII and the non-reducing XXI and XXII) were isolated. The PMR spectra of their respective actates of XVII, XVIII, XIX, and XX, XVIIa, XVIIIa, XIXa, and XXa in C_6D_6[15] gave H_3 signals appearing at τ 4.40—4.73 in the AcO–CH region as somewhat broad singlets. The coupling constants of $J_{3,4}$ (0.5 Hz) furnished obvious evidence for their furanose structures.[9,10,13] Furthermore, two benzylic protons were observed at τ 3.80—4.21 (1,3-dioxolane) and τ 4.54—4.60 (1,3-dioxane) in each case. These results firmly established that XVII, XVIII, XIX, and XX are the anomeric and diastereomeric 1,2:4,6-di-*O*-benzylidene-L-sorbofuranoses.

Their anomeric configurations were substantiated by the use of the infrared spectra, where characteristic bands due to intramolecular hydrogen bonding between C_3–OH and C_2–O are sometimes present in α-anomers, but are always, absent in β-ones. Strong bands due to hydrogen bonding were observed in infinite dilute carbon tetrachloride solutions of XVII (3558 cm^{-1}) and XVIII (3556 cm^{-1}), but not in the cases of XIX (3629 cm^{-1}) and XX (3630 cm^{-1}). Therefore, XVII and XVIII were identified as α-anomers, and XIX and XX, as β-anomers. These identifications were in accord with the results of the optical rotation of the respective acetates XVIIa—XXa; the α-anomers (XVIIa and XVIIIa) showed negative signs of rotations, while the β-anomers (XIXa and XXa) showed positive signs, as was to be expected from the signs of the corresponding acetonated derivatives. The two α-anomers and β-anomers should differ only in stereochemistry at the acetal center of the 1,2-*O*-benzylidene ring. Model experiments indicated, for the H-*endo* configuration, the nearness of the benzylic proton of the 1,2-*O*-benzylidene ring to the ring oxygen of furanose and that of the acetoxy group of the α-anomer or H_3 of the β-anomer to the phenyl group of 1,2-*O*-benzylidene ring. Therefore, in the PMR spectra, benzylic proton signals should be deshielded,[11] and the acetoxy signal of the α-anomer,

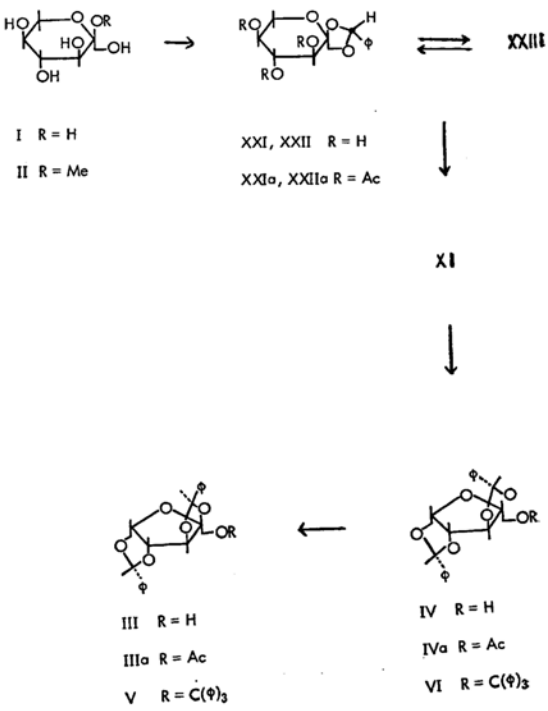


Chart III

15) The signals in C_6D_6 are more resolved than in $CDCl_3$.

and the H_3 signal of the β-anomer should be shielded,[16] when the position is H-*endo*. Table 1 obviously shows that, in each case, benzylic protons of the 1, 2-*O*-benzylidene rings of XVIIa and XIXa resonate at a field lower by 0.17 ppm than those of the corresponding anomers, XVIIIa and XXa respectively, while the acetoxyl of XVIIa and the H_3 of XIXa appear at a higher field than those of XVIIIa of XIXa appear at a higher field than those of XVIIIa and of XXa. Accordingly, XVIIa and XIXa were assigned the H-*endo* configuration, and XVIIIa and XXa, the H-*exo* (see Chart III).

The triacetates, XXIa and XXIIa, were very similar in IR and PMR spectra. The benzylic proton signals at τ 3.95 (XXIa) and 4.00 (XXIIa) (in $CDCl_3$)[16] fall into the range of 1,3-dioxolanes.[11,13,14] The coupling constants obtained, $J_{3,4}$, $J_{4,5}$, and $J_{5,6}$ are evidently the values of $J_{a,a}$, of pyranose in the 1C conformation.[17] Signals due to H_3, H_4, and H_5 appeared in the range of AcO–$\underset{|}{\overset{|}{C}}$H. The structures of XXI and XXII are, then, consistent with diastereomeric 1, 2-*O*-benzylidene-α-L-sorbopyranoses. They correspond to that of 1,2-*O*-isopyropylidene-α-L-sorbopyranose, which has been concluded to be the initial intermediate in the acetonation reaction of I.[4]

The acetylation of reducing monobenzylidene sorbose (XXIII) at an ordinary temperature gave three acetylated compounds, two reducing diacetates (XXIV and XXV) and one non-reducing triacetate (XXVI). These diacetates were methylated with methyl iodide in the presence of silver oxide to yield glycosides. The glycoside derived from XXIV was identified with XV, and the glycoside from XXV was identified with methyl 4,5-di-*O*-acetyl-1,3-*O*-benzylidene-α-L-sorbopyranoside (XXVII), which had been prepared by the benzylidenation[18] of methyl α-L-sorbopyranoside (II),[19] followed by acetylation. Therefore, the structure of XXIV and XXV were determined to be 4,6-di-*O*-acetyl-1,3-*O*-benzylidene-β-L-sorbofuranose and 4,5-di-*O*-acetyl-1,3-*O*-benzylidene-α-L-sorbopyranose respectively. These products showed that XXIII is 1,3-*O*-benzylidene-L-sorbose, an equilibrium mixture of 1,3-*O*-benzylidene-β-L-sorbofuranose (XXIIIf) and α-L-sorbopyranose (XXIIIp). The results of the optical rotationary dispersion (ORD) showing the absence of any carbonyl group (see Fig. 5), a value of optical rotation similar to those of XV and XXIV, and a small coupling constant of $J_{3,4}$ suggest that the structure of XXVI is 2,4,6-tri-*O*-acetyl-1,3-*O*-benzylidene-β-L-sorbofuranose.

The behavior of XXIII is very interesting. It may be considered to exist as the furanose (XXIIIf) in a crystalline state from its sharp melting point and its positive optical rotation in chloroform; however, it may be considered to be in an eqilibrium with the furanose (XXIIIf), a keto-form (XXIIIk) and the pyranose (XXIIIp) in solutions since the optical rotation, in pyridine, for instance, changes slowly with the time (see Chart IV).

During the course of these structure studies, an

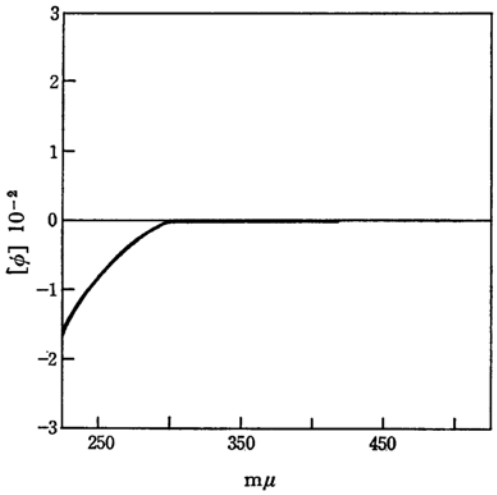


Fig. 5. The ORD curve for XXVI.

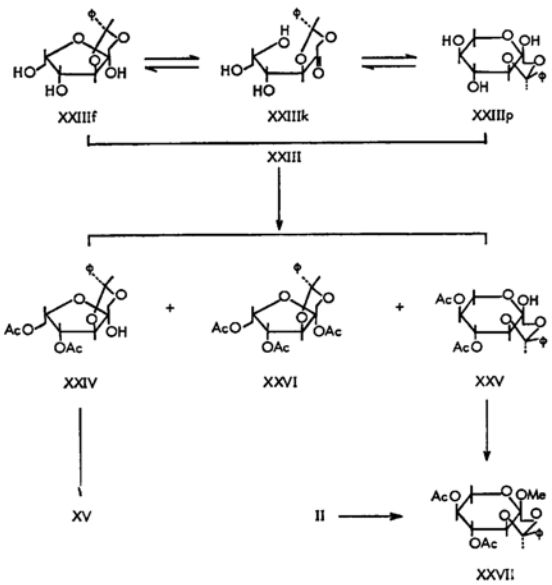


Chart IV

16) For example, see R. H. Bible, Jr., "Interpretation of NMR Spectra," Plenum Press, New York, N. Y. (1965).

17) 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. Heyns, *ibid.*, **100**, 2669 (1967).

18) D. Murphy, *J. Chem. Soc., C*, **1967**, 1732.

19) a) G. Arragon, *Compt. Rend.*, **199**, 1231 (1943). b) H. H. Schlubach and G. Graefe, *Ann.*, **532**, 211 (1937).

interesting transformation between III, IV and XI was observed. Under usual benzylidenation conditions, III and IV were the major products and the amounts of the others were negligibly small. The relative yields were checked by means of the PMR spectra using the benzylic proton singlets at τ 3.80 (III), 4.07 (IV), and 4.47 (XI) as the key signals; the results are reported in Table 4. Table 4 shows clearly that the reaction proceeds in the sequence of XI→IV→III. It has been suggested that the H-*exo* isomer is produced in a kinetic phase and that the H-*endo* isomer is preponderant at an equilibrium,[11,13] in the benzylidention of I, the H-*exo* isomer (IV) was also found as a kinetic product, indicating that the reaction occurred with the retention of the diastereomeric configuration at the acetal center in the step XI→IV.

As the monobenzylidenated compounds (XXI, XXII, and XXIII) were obtained under slightly acidic conditions, the benzylidenation of I can be said to proceed *via* a pathway, I→(XXI, XXII⇄XXIII)→XI→IV(H-*exo*)→III(H-*endo*), similar to that in the ethylidenation of I.[2] Since these types of ethylidenated and benzylidenated compounds correspond to the acetonated ones, the reaction pathway of the acetonation should be concluded to be the same as that above. A detailed discussion of this mechanism of the acetalation of I will be presented in following papers.

Experimental

All the melting points were recorded on a Kofler micro-stage apparatus and have been corrected.

The solvents used were removed under reduced pressure.

Thin-layer chromatography was carried out on a silica gel plate with benzene - ether (3:1 v/v, solvent A), ether - petroleum ether (5:1 v/v, solvent B; 2:1 v/v, solvent C; 1:1 v/v, solvent D; 1:2, solvent E), and chloroform - acetone (9:1 v/v, solvent F; 1:1, solvent G). Seliwanoff reagent[20] spray was used for detection; the R_f values are listed in Table 5. Preparative thin-layer chromatography was performed on silica gel with the same solvent systems as were used for detection, while the spots located with iodine vapor were extracted with either acetone or chloroform - methanol (9:1 v/v).

Table 4. Product-ratio (±5%) from the reaction of L-sorbose (I) (1.6 g) and benzaldehyde (40 ml) at 25°C for 6 hr in the presence of TsOH

Product	The acid concentration		
	0.1%	1.0%	10.0%
III	15.0	22.5	42.5
IV	35.0	55.0	52.5
XI	50.0	22.5	5.0

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

The evaporation of the solvents gave the materials.

The optical rotations were determined in chloroform containing 1% ethanol unless otherwise stated, and the concentrations have been recorded in percentages. The ORD curve of XXVI was obtained for the methanol solution on a Nippon-Bunko ORD/UV 5 spectrometer.

The PMR spectra were measured on a Varian A-60A spectrometer using 5% solutions of the samples in either $CDCl_3$ or C_6D_6, with TMS used as the internal standard. The results obtained from the analysis of the spectra of the compounds examined are listed in Tables 1 and 2. Some of the spectra are shown in Figs. 1—4.

The IR spectra measurements of XVII, XVIII, XIX, and XX were made using a Nippon-Bunko DS402G infrared spectrometer and a 3.5±0.5 mg/8 ml solution in a carbon tetrachloride solution (in a 20 mm cell).

Benzylidenation of L-Sorbose (I). a) Dry hydrogen chloride (0.75 g) was introduced into a mixture of L-sorbose (I) (2.0 g) and benzaldehyde (48 ml). The mixture was stirred at room temperature for 6 hr and then stored in a refrigerator overnight. The clear solution was diluted with ether and the solution was washed with aqueous sodium bicarbonate, and then with water, dried, and the solvent removed. The syrup thus obtained was dissolved in chloroform, and the chloroform solution was washed with a sodium hydrogen sulfite solution, and then with water, and dried. The evaporation of the solvent gave a syrup (3.4 g) whose thin-layer chromatogram showed the presence of III and IV. From the syrup, III (0.28 g) and IV (0.11 g) were separated in pure states by repeated PTC (first with the solvent A and then two times with the solvent C).

III: plates (174 mg), mp 129—131°C (recrystallized from benzene - petroleum ether), $[\alpha]_D^{24}$ −8.7° (*c* 0.722). Found: C, 67.46; H, 5.59%; mol wt, 341. Calcd for $C_{20}H_{20}O_6$: C, 67.40; H, 5.66%; mol wt, 356.

IV: Amorphous powder, mp <51°C, $[\alpha]_D^{23}$ −10.6° (*c* 0.993). Found: C, 67.14; H, 5.52%; mol wt, 366. Calcd for $C_{20}H_{20}O_6$: C, 67.40; H, 5.66%; mol wt, 356.

b) A mixture of L-sorbose (I) (1.00 g), benzaldehyde (24ml), and TsOH (0.24 g) was stirred at room temperature. After 20 hr, the solution was worked up by the above-described procedure. A syrup (1.86 g) containing III, IV and XI was thus obtained. XI (9.5 mg) was isolated as plates by PTC with the solvent C followed by recrystallization from ethanol, mp 164.6—167°C, $[\alpha]_D^{22}$ +48.8° (*c* 0.934). Found: C, 67.48; H, 5.79%; mol wt, 363. Calcd for $C_{20}H_{20}O_6$: C, 67.40; H, 5.66%; mol wt, 356.

c) To a solution of L-sorbose (I) (10 g) in DMSO (60 ml), there were added benzaldehyde (100 ml) and conc. sulfuric acid (0.5 g). After stirring at room temperature for 3 days, the solution was neutralized with 2N sodium bicarbonate, dried, and evaporated. A crystalline syrup (8.47 g) was obtained by the same work-up as above. (i) The addition of ethanol to the syrupy crystals thus obtained gave XI (2.9g). The evaporation of the ethanol from the mother liquor yielded a syrup (4.91g). From the syrup, XVII, XVIII, XIX and XX were isolated by PTC (first with the solvent A and then with the solvent D). The isolated materials were further purified by recrystallization.

XVII: Cubics, mp 113.7—114.7°C (recrystallized from ether - petroleum ether; yield, 12 mg), $[\alpha]_D^{22}$ −31.0° (*c* 0.813). Found: C, 67.56; H, 5.72%; mol wt, 350.

TABLE 5. R_f VALUES OF THE BENZYLIDENATED COMPOUNDS ON A SILICA GEL PLATE

Compound	Solvent system						
	A	B	C	D	E	F	G
III	0.43	—	0.57	0.34	0.19	—	—
IIIa	—	—	—	0.43	0.17	—	—
IV	0.48	—	0.65	0.38	—	—	—
IVa	—	—	—	0.59	—	—	—
V	—	—	—	0.51	0.37	—	—
VI	—	—	—	0.74	0.56	—	—
IX	—	—	0.60	—	—	—	—
X	—	—	—	0.26	—	—	—
XI	0.78	—	0.82	0.60	—	—	—
XII	—	—	—	0.73	0.60	—	—
XIV	—	—	0.46	—	—	—	—
XV	—	—	0.59	—	—	—	—
XVII	0.54	—	0.45	—	—	—	—
XVIIa	—	—	0.65	—	—	—	—
XVIII	0.41	—	0.36	—	—	—	—
XVIIIa	—	—	0.64	—	—	—	—
XIX	0.27	—	0.28	—	—	—	—
XIXa	—	—	0.38	—	—	—	—
XX	0.20	—	0.20	—	—	—	—
XXa	—	—	0.39	—	—	—	—
XXI, XXII	—	—	—	—	—	—	0.15—0.43
XXIa	—	—	—	0.45	—	—	—
XXIIa	—	—	—	0.55	—	—	—
XXIII	—	—	—	—	—	—	0.43—0.65
XXIV	—	0.38	—	—	—	0.36	—
XXV	—	0.60	—	—	—	0.36	—
XXVI	—	0.60	—	—	—	0.70	—

Calcd for $C_{20}H_{20}O_6$: C, 67.40; H, 5.66%; mol wt, 356.

XVIII: Needles, mp 121.5—125°C (recrystallized from ethanol), $[\alpha]_D^{22}$ +34.7° (*c* 0.864). Found: C, 67.61; H, 5.81%; mol wt, 357. Calcd for $C_{20}H_{20}O_6$: C, 67.40; H, 5.66%; mol wt, 356.

XIX: Needles, mp 186—196°C (recrystallized from chloroform), $[\alpha]_D^{24}$ +22.7° (*c* 0.343). Found: C, 67.22; H, 5.76%; mol wt, 353. Calcd for $C_{20}H_{20}O_6$: C, 67.40; H, 5.66%; mol wt, 356.

XX: Needles, mp 148—154°C (recrystallized from ethanolpetroleum ether), $[\alpha]_D^{24}$ +166.6° (*c* 0.393). Found: C, 67.30; H, 5.66%; mol wt, 337. Calcd for $C_{20}H_{20}O_6$: C, 67.40; H, 5.66%; mol wt, 356.

(ii) The syrup (6.15 g was used) was separated into XXIII (1.38 g) and a mixture syrup of XXI and XXII (1.27 g) by PTC with the solvent G.

XXIII: Cubics, mp 183.5—184.6°C (recrystallized from methanol; yield, 342 mg), $[\alpha]_D^{23}$ +30.5° (*c* 0.387, methanol); $[\alpha]_D^{23}$ +36.0→+20.2° after 24 hr (*c* 0.962, pyridine); $[\alpha]_D^{23}$ +20.4° (*c* 0.984, DMSO). Found: C, 58.13; H, 6.03%; mol wt, 244. Calcd for $C_{13}H_{16}O_6$: C, 58.20; H, 6.01%; mol wt, 268.

The latter mixture, a syrup (1.27 g), was treated with acetic anhydride (13 m*l*) in pyridine (13 m*l*) in the usual way, and the reaction mixture was poured into ice water. From the resulting syrup, the triacetates XXIa and XXIIa were isolated by PTC with the solvent C. The isolated materials were then further purified by recrystallization.

XXIa: Needles, mp 126—131.5°C (recrystallized from ether; yield, 487 mg), $[\alpha]_D^{22}$ −125.2° (*c* 0.956). Found: C, 57.53; H, 5.62%; mol wt, 405. Calcd for $C_{19}H_{22}O_9$: C, 57.86; H, 5.62%; mol wt, 394.

XXIIa: Needles, mp 111—115°C (recrystallized from ether; yield, 118 mg), $[\alpha]_D^{23}$ −89.2° (*c* 0.937). Found: C, 57.94; H, 5.53%; mol wt, 396. Calcd for $C_{19}H_{22}O_9$: C, 57.86; H, 5.62%; mol wt, 394.

d) A mixture of L-sorbose (I) (1.6 g), and benzaldehyde (40m*l*) containing 0.1, 1.0 and 10.0% (w/v%) TsOH respectively was stirred at 25°C in a thermostat for 6 hr. The solution was then worked up much as in a). The PMR spectra of the resulting syrup was measured without further purification. The values are listed in the Table 4.

Tritylation of III and IV. a) A solution of III (139 mg) in pyridine (0.4 m*l*) was treated with trityl chloride (115 mg) at room temperature. After 2 days, the product was poured onto ice water, and the resulting syrup, separated from water by decantation, was taken up with chloroform. The chloroform solution was then washed with 1N HCl and water. The concentration of the dried solution and the purification of the residue by PTC with the solvent E and by recrystallization from ether gave V (122 mg) as cubics, mp 166—168°C, $[\alpha]_D^{23}$ −8.6° (*c* 0.985). Found: C, 78.20; H, 5.73%; mol wt, 601. Calcd for $C_{39}H_{34}O_9$: C, 78.24; H, 5.72%; mol wt, 599.

b) Needles of VI (40 mg) were obtained from IV

(118 mg) by the same procedure as that above. It had a mp of 195—197°C; $[\alpha]_D^{24}$ −20.4° (*c* 0.992). Found: C, 78.51; H, 5.83%; mol wt, 623. Calcd for $C_{39}H_{34}O_6$: C, 78.24; H, 5.72%; mol wt 599.

Acetylations of III and IV. a) A sample of III (122 mg) was acetylated in a mixture of acetic anhydride (3.0 m*l*) and pyridine (3.0 m*l*) in a refrigerator for 6 hr. The mixture was then poured onto crushed ice and neutralized with an excess of sodium hydrogen carbonate. The solution was extracted with chloroform; the chloroform solution was washed with water, 2N HCl, and water, dried with anhydrous magnesium sulfate and evaporated to a syrup. IIIa (93 mg) was then isolated by PTC with the solvent C; $[\alpha]_D^{24}$ −17.9° (*c* 1.617). Found: C, 66.23; H, 5.75%; mol wt, 411. Calcd for $C_{22}H_{22}O_7$: C, 66.32; H, 5.57%; mol wt, 398.

b) IV (218mg) gave IVa (217mg) as a syrup, $[\alpha]_D^{24}$ −12.1° (*c* 0.810). Found: C, 64.58; H, 5.43%; mol wt, 410.[21] Calcd for $C_{22}H_{22}O_7$: C, 66.32; H, 5.57%; mol wt, 398.

Hydrolysis of III and IV. a) A sample of III (150 mg) was hydrolyzed with 60% acetic acid (15m*l*) at 70°C. After 1.5 hr, the solvent was removed by the addition of an excess of ethanol and by subsequent evaporation. The residual syrup (112 mg) was acetylated with acetic anhydride (1.5 m*l*) and pyridine (1.5 m*l*) in a manner similar to that used for IIIa. The purification of the product by PTC with the solvent C gave IX (83mg) as a syrup; $[\alpha]_D^{23}$ −1.6° (*c* 0.973). Found: C, 57.96; H, 5.68%; mol wt, 401. Calcd for $C_{19}H_{22}O_9$: C, 57.86; H, 5.62%; mol wt, 394.

b) X (152 mg) was obtained from IV (600 mg) by the same work-up as that used for IX. It was a syrup, $[\alpha]_D^{22}$ −15.6° (*c* 0.286). Found: C, 56.17; H, 5.71%; mol wt, 434.[21] Calcd for $C_{19}H_{22}O_9$: C, 57.86; H, 5.62%; mol wt, 394.

Preparation of VIII from VII. A solution of VII (1.10 g) and benzaldehyde (0.55 g) in dioxane (10 m*l*) containing TsOH (0.50 g) was allowed to stand overnight at room temperature. The crystals thus deposited were then fitered. Recrystallization from acetone gave needles (1.2 g) of VIII; mp 207—208°C; $[\alpha]_D^{24}$ −8.0° (*c* 0.747, acetone). Found: C, 62.46; H, 6.74%. Calcd for $C_{16}H_{20}O_6$: C, 62.32; H, 6.64%.

Hydrolysis of VIII. VIII (0.5 g) was treated with 60% acetic acid (5 m*l*) at 70°C for 1.5 hr to yield VII quantitatively.

Acetylation of XI. XI (0.10 g) was not acetylated with acetic anhydride - pyridine or acetic anhydride-sodium acetate at 60°C; XI was thus recovered almost quantitatively.

Methylation of XI. XI (0.78 g) in methyl iodide (50 g) was refluxed for 24 hr in the presence of silver oxide (3.75 g). The cooled solution was filtered, and the filtrate evaporated. The recrystallization of the residue (1.02 g) from ethanol - petroleum ether gave XII (0.55 g) as needles mp 114—116°C, $[\alpha]_D^{23}$ +56.3° (*c* 0.959). Found: C, 68.13; H, 6.03; OCH_3, 8.40%; mol wt, 367. Calcd for $C_{21}H_{22}O_6$: C, 68.09; H, 5.99; OCH_3, 8.40%; mol wt, 370.

Preparation of XII from XIII. A mixture of XIII (98.5 mg),[5] benzaldehyde (10 g), and TsOH (10 mg) was stirred at room temperature. After 7.0 hr, a 2N sodium bicarbonate solution (1 m*l*) was added to the solution, which was then extracted with benzene. The benzene solution was evaporated to give a syrup, which was then purified by PTC using the solvent E. Recrystallization from ethanol gave XII as needles (20.6 mg), mp 114—115.5°C, this substance was found to be identical with XII by a study of the IR spectra, and by thin-layer chromatograms and admixture tests.

Hydrolysis of XII. XII (660 mg) was treated with 60% acetic acid at 50°C for 50 min. The mixture was then diluted with ethanol and evaporated. The resulting syrup (0.55 g) was acetylated in a way similar to that used for IIIa. The syrup (638mg) thus produced was separated into XIV (51 mg) and XV (245 mg) by PTC with the solvent C. The isolated materials were then further purified by recrystallization.

XIV: Needles (15 mg), recrystallized from ether-*n*-hexane; this substance was identified with an authentic sample.[9]

XV: Needles, mp 87.5°C (recrystallized from ethanol; yield, 42mg); $[\alpha]_D^{21}$ +23.5° (*c* 0.970). Found: C, 58.58; H, 5.97%; mol wt, 364. Calcd for $C_{18}H_{22}O_8$: C, 59.01; H, 6.05%; mol wt, 366.

Acetylations of XVII, XVIII, XIX and XX. The acetates, XVIIa, XVIIIa, XIXa and XXa were obtained from XVII, XVIII, XIX and XX, respectively in the same manner as has been described for the preparation of IIIa.

XVIIa: Syrup; $[\alpha]_D^{22}$ −38.6° (*c* 1.083). Found: C, 66.44; H, 5.56%; mol wt, 411. Calcd for $C_{22}H_{22}O_7$: C, 66.32; H, 5.57%; mol wt, 398.

XVIIIa: Needles, mp 144.5—146°C (recrystallized from ethanol); $[\alpha]_D^{22}$ −28.6° (*c* 0.979). Found: C, 66.29; H, 5.55%; mol wt, 412. Calcd for $C_{22}H_{22}O_7$: C, 66.32; H, 5.57%; mol wt, 398.

XIXa: Syrup; $[\alpha]_D^{22}$ +34.4° (*c* 0.987). Found: C, 66.79; H, 5.40%; mol wt, 392. Calcd for $C_{22}H_{22}O_7$: C, 66.32; H, 5.57%; mol wt, 398.

XXa: Needles, mp 136.5—139°C (recrystallized from ether-petroleum ether); $[\alpha]_D^{22}$ +147.1° (*c* 0.961). Found: C, 66.34; H, 5.67%; mol wt, 410. Calcd for $C_{22}H_{22}O_7$: C, 66.32; H, 5.57%; mol wt, 398.

Acetylation of XXIII. a) To a cooled solution (−5—−6°C) of XXIII (387 mg) in pyridine (4 m*l*), acetic anhydride (4 m*l*) was added. After storage in a refrigerator for 16 hr, the mixture was worked up much as IIIa had been to give a syrup (530 mg). From the syrup, XXIV (107 mg) was isolated in a pure state by PTC with the solvent B. Another syrup (160 mg) was obtained which contained mixture of XXVI major and XXV minor.

XXIV: Syrup, $[\alpha]_D^{23}$ −3.3° (*c* 0.859). Found: C, 57.96; H, 5.77%; mol wt, 363. Calcd for $C_{17}H_{20}O_8$: C, 57.95; H, 5.72%; mol wt, 352.

b) XXIII (351mg) was acetylated at room temperature for 16 hr. The resulting syrup (686 mg) was then separated into XXV (39 mg) and XXVI (349 mg) by repeated PTC (first with the solvent B and then with the solvent F.).

XXV: Needles, mp 181—183.5°C (recrystallized from chloroform - petroleum ether; yield, 19 mg), $[\alpha]_D^{23}$ −47.6° (*c* 0.550). Found: C, 57.77; H, 5.76%; mol wt, 373. Calcd for $C_{17}H_{20}O_8$: C, 57.95; H, 5.72%; mol wt, 352.

XXVI: Cubics, mp 75—77°C (recrystallized from

21) It was difficult to analyze correctly, because of its hygroscopic nature. However, the interpretation of the PMR spectrum supported the formula given.

aqueous ethanol; yield, 290 mg); $[\alpha]_D^{24}$ −10.5° (*c* 0.703). Found: C, 58.02; H, 5.64%; mol wt, 402. Calcd for $C_{19}H_{22}O_9$: C, 57.86; H, 5.62%; mol wt, 394. The ORD curve is shown in Fig. 5.

Methylation of XXIV. XXIV (44 mg) was methylated in a way similar to that used for XI. The recrystallization of a crude products (46 mg) gave cubics (9 mg) of XV; mp 87—88°C.

Methylation of XXV. XXV (92.5 mg) was methylated by the same procedure as was used for XI. The recrystallization of the residue (81mg) gave XXVII (62 mg) as needles, mp 185—186°C; $[\alpha]_D^{23}$ −74.0° (*c* 0.995). Found: C, 59.09; H, 6.02%; mol wt, 364. Calcd for $C_{18}H_{22}O_8$: C, 59.01; H, 6.05%; mol wt, 366.

Preparation of XXVII from II. A mixture of II[19] (3.0 g), benzaldehyde (30 m*l*), and conc. sulfuric acid (0.15 g) was stirred at room temperature for 4 hr. The solution was then neutralized with a 2N K_2CO_3 solution and evaporated to a thick syrup. Methyl 1,3-*O*-benzylidene-α-L-sorbopyranoside[18] (202 mg) isolated as needles by PTC with the solvent *G* (R_f 0.47—0.58), followed by recrystallization from chloroform-ether. It had a mp of 187—188°C, and $[\alpha]_D^{23}$ −55.0° (*c* 0.936); Murphy[18] reported the values of mp 183—184°C and $[\alpha]_D$ −54.6° (*c* 1.06). The crystals (151 mg) were acetylated in the usual manner with acetic anhydride - pyridine. Needles (*c* 161 mg) of XXVII were obtained by recrystallization from ethanol; mp 186—186.5°C.

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