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Acid-Catalyzed Isomerization of 1,3,4,5-Tetra-O-acetyl-2deoxy-L-sorbopyranos-2,3-ene¹⁾

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An acid-catalyzed reaction in acetic anhydride was found to isomerize 1,3,4,5-tetra-O-acetyl-2-deoxyl-L-sorbopyranos-2,3-ene (V) to four new unsaturated compounds. When the reaction was allowed to continue for a longer period, they underwent polymerization, but did not afford 2-hydroxyacetylfuran acetate (XXVIb). The reaction in acetic acid containing water was shown to mainly convert V into XXVIb. This reaction pathway was thought to be different from the above.

Dehydrochlorination of 1,3,4,5-tetra-O-acetyl- α -L-sorbopyranosyl chloride (IV),^{2,8)} derived from L-sorbose (I), through the agency of mercuric cyanide,4,5) yields 1,3,4,5-tetra-O-acetyl-2-deoxy-Lsorbopyranos-2,3-ene (V). This communication is concerned with isomerizations of this unsaturated compound.

The isomerizations and other reactions of acylated aldo-1-enoses have recently received considerable attention.^{6,7)} The facile dissociation of the C₈-substituent in these compounds is readily understood as resulting from activation of the C₈-position toward carbonium ion formation by the allylic double bond.8) The activation is especially strong for 1-enose structures since the ring oxygen can participate in charge

¹⁾ Sorboses. Part XI. For Part X, see T. Maeda, B. B. L. L. Schubach and G. Graefe, Ann., 532, 211 (1937).
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⁴⁾ R. U. Lemieux and D. R. Linback, Can. J. Chem., 43, 94 (1965).

⁵⁾ B. Coxon, Tetrahedron, 22, 228 (1966).

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^{(1963),} p. 384. 8) H. S. Isbell, J. Res. Natl. Bur. Stand., A32, 45 (1944).





delocalization.⁹⁻¹⁸⁾ It was anticipated that V would undergo similar isomerization, which pathway may provide interesting information regarding the acidcatalyzed degradation of ketohexose to 2-hydroxyacetylfuran (XXVIa)14,15) through 2,3-enolization with the elimination of the hydroxyl group at the allylic C₄-position.^{16,17)}

The structure of V was confirmed by methoxymercuration¹⁸⁾ and NMR spectroscopy. NMR data obtained by 1st-order approximation are reported in

10) R. J. Ferrier, ibid., 1964, 5443.

D. M. Cement and R. J. Ferrier, ibid., 1966, 11)2830.

- R. U. Lemieux, D. R. Linback, M. L. Wolfrom, 12) F. B. Moody, E. G. Wallace and F. Komitsky, Jr., J. Org. Chem., 30, 1092 (1965).
 R. K. Ness and H. G. Fletcher, Jr., *ibid.*, 28, 435
- (1963).

C. J. Moye, Australian J. Chem., 19, 2317 (1966) R. E. Miller and S. M. Cantor, J. Am. Chem. 14) 15) R. E. Miller Soc., 74, 5236 (1956).

16) E. F. L. J. Anet, Chem. & Ind., 1962, 262.

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18) K. Tokuyama, E. Tsujino and M. Kiyokawa, This Bulletin, 38, 1344 (1965).

Tables 1 and 2. The methoxymercuration of V gave a mercurichloride (VI). Reductive demercuration of VI with sodium borohydride in the presence of pyridine was accompanied by deacetylation, and yielded a methyl glycoside, which was isolated as a tetraacetate (VII).¹⁹⁾ Despite its large positive value of optical rotation, VII was not identical with methyl 1,3,4,5-tetra-O-acetyl- β -L-sorbopyranoside Thus, VII was concluded to be methyl (Xb).⁸⁾ 1,3,4,5-tetra-O-acetyl- β -L-tagatopyranoside.^{20,21)} The formation of the tagatopyranoside (VII) supports the structure of V, because another possible isomer VIII from the dehydrochlorination of IV should yield X via IX.

The NMR spectrum of V in chloroform-d (Fig. 1a) showed four singlets at about τ 7.9 due to acetoxyls, a somewhat broad singlet at $\tau 5.39$ due to H_1 (see also Fig. 1h) and signals due to H_6 , $H_{6'}$, H₅, and H₄ as an ABXY pattern. This assignment

21) C. V. Holland, D. Horton and J. S. Jewell, J. Org. Chem., 32, 1818 (1967).

R. J. Ferrier and G. H. Sankey, J. Chem. Soc. (C), 9) 1966, 2339, 2345.

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The evidence of NMR indicates that the favorable 20) conformation of VII in chloroform-d is the Cl chair form. See Ref. 21.

TABLE	1.	CHEMICAL	SHIFTS	$(\tau)^{a}$
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Compound	H ₆	H _{6'}	H ₅	H4	H_3	H_1 and H_1'	CH ₃ COO	Other signal
IIIa	6.00	6.29	4.88	4.46	4.73	5.32, 5.43	7.93, 7.96(2) 8.00	COOCH ₃ 6.19
Шь	5.93	6.38	4.90	4.46	4.74	5.32, 5.45	7.93, 7.96(2) 8.00	COOC <u>H</u> 2CH ₃ 5.70 COOCH2CH3 8.66
IV	5.88	6.08	4.92	4.44	4.72	5.57, 5.77		
V	5.72	5.97	5.04	4.61		5.39	7.89, 7.91 7.95(2)	
VI	5.92	6.22	5.08	4.41		5.46, 6.16	7.77, 7.80 7.92(2)	OC <u>H</u> ₃ 6.59
VII	5.89	6.23	5.09	4.70	4.59	5.76, 5.82	7.87, 7.92 7.91, 7.94	\mathbf{OCH}_{3}
XII ^{b)}	6.00	6.24	4.85	4.17	_	2.67°)	8.27, 8.31 8.33	
XIV	5.67	5.95	5.04	4.55		2.55°)	7.86, 7.90(2) 7.91, 7.94	
XV	5.23	5.38	2.88	3.70		2.92°)	7.88, 7.93 7.95	
XXb)	$\sim 5.51 \\ \sim 6.14$		$\substack{2.94\\3.92}$	3.89 4.12		5.56 5.39	7.94 8.32	$\begin{array}{c} \text{OC}\underline{H}_3 & 6.58 \\ \text{OC}\underline{H}_3 & 6.94 \end{array}$
XXI	6.07	6.56	4.78	5.50	4.52	5.90	7.86, 7.91 7.95	OC <u>H</u> ₃ 6.71
XXII	5.80	6.23	4.83	5.58	4.65	5.79	7.85(2) 7.88	OC <u>H</u> 3 6.63
XXIV	5.61	5.94	4.96	4.79	4.06	0.74 ^{c,d})	7.91, 7.94	

a) In chloroform-d (unless otherwise stated). b) In benzene-d₆. c) One proton.

d) Aldehyde proton.

Compound	$J_{6,6'}$	$J_{5,6}$	$J_{5,6'}$	J4,6	$J_{4,6'}$	J4,5	$J_{8,5}$	$J_{3,4}$	$J_{1,4}$	$J_{1,1'}$
IIIa	11.2	5.8	11.2	_		9.7	1.5	8.4	—	11.8
IIIbc)	10.4	5.7	10.4	_		10.1	1.0	8.3		11.5
IV	10.6	5.3	10.6			9.0	1.0	9.0	_	12.3
v	12.3	2.4	1.5	1.3	_	2.7		—	0.5	0
VI	13.2	2.4	1.3		1.3	3.7				12.0
VII	13.1	2.1	1.3		1.3	3.8		3.8	_	11.8
XII _P)	12.1	2.2	2.8	0.7		6.2	_		0.7	
XIV	12.5	2.7	1.8	1.5		2.7		_		
XV	18.4	2.4	3.6	2.4	1.8	11.0				-
XX	d)	2.4	3.4	2.0	2.0	10.5				d)
XXI	10.3	5.7	10.3			10.8		3.1		d)
XXII	13.2	3.0	1.6		1.6	3.0		4.4		d)
XXIV	12.4	3.0	2.0	1.7		3.0	1.4	5.0	—	—

TABLE 2. COUPLING CONSTANTS (CDS)^{a)}

a) In chloroform-d unless otherwise stated. b) In benzene-d₆. c) COOCH₂CH₃: J_{CH_2} , $_{CH_3}$ =7.0. d) Obscured.

was confirmed by decoupling experiments (Fig. 1b—1g). Double irradiation at the center of resonance frequencies of H_6 and $H_{6'}$ (Fig. 1b) changed the 8-line multiplet of H_5 into a doublet $(J_{4,5} 2.7 \text{ cps})$ and the 8-line multiplet of H_4 into a somewhat broad doublet. By double irradiation on $H_{6'}$, the H_5 signal collapsed to a doublet-doublet $(J_{5,6} 2.4 \text{ cps})$, but no changes in the H_4 signal were

observed (Fig. 1c). By double irradiation on $[H_6$, the H₅ signal collapsed to a doublet-doublet and the H₄ signal to a somewhat broad doublet (Fig. 1d). Conversely, decouplings of H₄ (Fig. 1f) and H₅ (Fig. 1g) resulted in changes of the signals of H₅ and H₆ ($J_{5,6'}$ 1.5 cps) and of those of H₄, H₆ and H_{6'} ($J_{6,6'}$ 12.3 cps and $J_{4,6}$ 1.3 cps), respectively. Decoupling of H₁ (Fig. 1e) made the broad signal





of H₄ relatively sharper, showing the presence of homoallylic coupling between C_4 and C_1 protons. These observations provided evidence for the structure of V. Applying the Karplus correlation²²⁾ for the coupling constants obtained and the "W-letter" rule²⁸⁾ for the long-range spin coupling between H_4 and H_6 , we reached the conclusion that V should exist in H1 conformation.24)

It was found that the treatment of V in acetic anhydride containing p-toluenesulfonic acid (TsOH) resulted in rapid formation of a mixture of at least four products (A, B, C, and D) in the thin-layer chromatograms. When the reaction was interrupted at the initial stages, the product A was mainly

isolated. On the other hand, when the reaction was allowed to proceed for 48 hr, products B and C were detected as major products. These products could be resolved by preparative thin-layer chromatography using several solvent systems. The structures established for the new compounds described above were confirmed by the application of NMR spectroscopy with the use of spin decoupling to assign the origins of the signals. The assignment was also based on the chemical shifts with reference to those of V.

As it is expected that the reaction of V under acidic conditions undergoes allylic displacement of the C4-ester grouping and the formation of a 3,4-unsaturated compound (XI),8-13) the structure of compound A was thought to be XI or its derivative. The analytical data and the integration of an NMR spectrum determined it as a triacetate C12H14- O_7 , which was thought to be derived from XI by the elimination of one mole of acetic acid. The elimination may occur at the 1,2- or 5,6-position. Thus, the

²²⁾ M. Karplus, J. Chem. Phys., **30**, 11(1959); J. Am. Chem. Soc., **85**, 2870 (1963).

²³⁾ N. S. Bhacca and D. H. Williams, "Application of NMR Spectroscopy in Organic Chemistry," Holden-Day Inc., San Francisco (1964), p. 115. 24) R. J. Ferrier and W. G. Overend, Quart. Rev., 13,

^{265 (1959).}



structure is proposed to be XII or XIII. The UV and IR spectra showed the characteristic bands due to a conjugated diene and the NMR spectrum (Fig. 2) revealed the presence of C_6 -methylene protons and an olefinic C1-proton. The results clearly support the structure of XII. Figure 2a shows the assignment of the NMR spectrum in benzene-d₆. The rough, 1-proton singlet at $\tau 2.67$ should arise from the olefinic H_1 . Its lower chemical shift is understandable in view of acetoxy substituent on the ethylenic group. The signals of the other protons $(H_6, H_{6'}, H_5 \text{ and } H_4)$ appear as the pattern of ABXY system, an AB quartet at $\tau 6.00$ (H₆) and 6.24 (H_{6'}), an 8-line multiplet (X part) at τ 4.85 (H₅) and a 6-line multiplet (Y part) at τ 4.17 (H₄). On double irradiation at the C₆-methylene position, the H₅ multiplet collapsed to a sharp doublet $(J_{4.5})$ 6.2 cps) and the H_4 multiplet to a doublet-doublet (Fig. 2b), showing the presence of long-range coupling between H_1 and H_4 ($J_{1,4}$ 0.7 cps). Double irradiation at the H₆ position caused the H₄ multiplet to collapse to a doublet-doublet (Fig. 2c), but double irradiation at the $H_{6'}$ position did not cause any changes of the H₄ signal (Fig. 2d). These decoupling experiments confirmed the above-described assignment (Fig. 2a), which is consistent with structure XII.

The reaction of XII with hydrogen bromide in benzene followed by glycosidation with methanol gave three pyranosides XX, XXI and XXII as major products. XX gave analytical data corresponding to methyl glycoside monoacetate, C9H12-O5, and its IR and UV spectra revealed bands due to an α , β -unsaturated ketone. The NMR spectrum in chloroform-d (Fig. 3) showed two singlets at τ 7.94 due to one acetyl methyl and at τ 6.58 due to one methoxy methyl, 2-proton singlet at $\tau 5.56$ due to C1-protons and an AB type quartet of ABXY system due to C₆-protons at about τ 5.5. The above-described data established the structure XX. The remaining two 1-proton multiplets at τ 2.94 and 3.89 due to olefinic protons were assignable to H_5 and H_4 , which are coupled to each other (J 10.5 cps), and the latter showed allylic coupling with C6-methylene protons. These observations provided further proof for the structure XX. Evidence bearing on the anomeric configuration of XX was not obtained.

Analytical data and optical rotation showed that XXI was a methyl bromo-tri-O-acetyl- α -L-glycoside, C₁₃H₁₉O₈Br. The NMR spectrum showed a 2-proton singlet at τ 5.90 due to C₁-protons, an AB type quartet of ABX system at τ 6.07 (H₆) and 6.56 (H_{6'}) due to C₆-protons, an 8-line multiplet at τ 4.78 due to H₅, a doublet-doublet at τ 5.50 due to H₄ and a doublet at τ 4.52 due to H₈. The relatively lower chemical shifts of H₈ and H₅ than H₄ determined the position of the bromine to be at the C₄-position. The coupling constants (J_{8,4} 3.1 cps and J_{4,5} 10.8 cps) suggest that the relationship of H₈ and H₄ should be *cis* (equatorial-axial) and that of H₄ and H₅ be trans May, 1968]



Fig. 1. NMR spectra of V in chloroform-d at 100 Mc.

(axial-axial).²⁵⁾ Therefore, the structure of XXI was clearly determined as methyl 1,3,5-tri-O-acetyl-4bromo-4-deoxy- α -L-tagatopyranoside.^{26,27)}

Treatment of XXII with hydrogen chloride in benzene followed by glycosidation with methanol gave XXI. Thus, it was determined to be the β anomer of XXI.

The reaction process of the formation of these pyranosides is considered as shown in Chart 3. The 1,4-addition of hydrogen bromide to XII afforded XVI, which was then converted into XVII by an allylic displacement reaction with hydrogen bromide. Two reaction pathways can exist for the further reaction of XVII. The first is the addition of hydrcgen bromide to the 3,4-double bond yielding XIX which is transformed to glycosides XXI and XXII. The preferable formation of tagatopyranosides is thought to be caused by the anchimeric effect of the acetoxy group at the C5-position.28,29) The second is the formation of XVIII, which may be formulated

²⁵⁾ R. H. Bible, "Interpretation of NMR Spectra,"
Plenum Press, New York (1965), p. 35.
26) The evidence of NMR indicates that the favored

conformation of XXI is the 1C chair form. See, Ref.

<sup>27.
27)</sup> F. W. Lichtenthaler and H. K. Yahya, *Tetrahedron*

²⁸⁾ Formation of 4,5-acetonium ion²⁹⁾ may be thought on the protonation of XVII. In this ion form, the \tilde{C}_{3} -acetoxy group might be expected to predominantly be trans to 4,5-acetonium group. 29) H. Paulsen, W. P. Trautwein, F. G. Espinosa and

K. Heynes, Tetrahedron Letters, 1966, 4131.



Fig. 2. NMR spectra of XII in benzene-d₆ at 100Mc.

as an elimination of the acetoxy group of the C_5 position to form an allylic cation, followed by loss of a C_8 -acetyl cation. XVIII is converted into XX by methanolysis.

The same results were obtained in the treatment of V under the same reaction conditions, in which the formation of XVII is very probable. Therefore, the above pathway and, consequently, the structure XII were confirmed.

The compound B had the correct analysis for XII plus one mole of acetic anhydride and had a conjugate diene absorption in the infrared. It was also derived from the acid treatment of XII in acetic anhydride. Therefore, its structure should be XIV, which is the ring-open form of XII. The fact that the NMR data in chloroform-d are quite similar to those of XII supported this structure. The spectrum

(Fig. 4a) contained singlets at about τ 7.9 due to five acetoxyls, a noisy singlet at τ 2.55 due to olefinic H₁, an AB type quartet of ABXY system at $\tau 5.67$ (H₆) and 5.95 ($H_{6'}$) due to C₆-protons, a 6-line multiplet at $\tau 5.04$ due to H₅ (X part) and a doublet-doublet at τ 4.55 due to H₄ (Y part). Double irradiation at the H₄ position (Fig. 4b) caused the collapse of the H_5 and H_6 signals to doublet-doublets ($J_{5.6'}$ 1.8 and $J_{5,6}$ 2.7 cps), while double irradiation at the H₅ position caused the collapse of the H_4 , H_6 and $H_{6'}$ signals to a somewhat broad doublet, a doublet-doublet $(J_{4,6} \ 1.5 \ \text{cps})$ and a doublet $(J_{6,6'} \ 12.5 \ \text{cps})$, respectively (Fig. 4c). The somewhat broad signals of H_4 and H1 imply the presence of weak long-range spin coupling between them. Thus, the structure XIV was established.

The combined data of chemical analysis, the UV



Fig. 3. NMR spectrum of XX in chloroform-d at 60Mc.

and IR spectra established that compound C was a conjugate ketone compound with an elementary composition corresponding to that of XIV minus one mole of acetic anhydride. It was also derived from the acid-treatment of XIV. As elimination of the acetoxy group at allylic C5-position and an acetyl group at the C₈-position of XIV are reasonably expected,^{30,81}) its structure was concluded to be XV. In chloroform-d, XV displayed a well-resolved spectrum (Fig. 5) with three acetoxyl singlets at about τ 7.9, a singlet at τ 2.92 due to H₁ and an ABXY pattern of a 8-line multiplet at τ 3.70 (Y part), an 8-line multiplet at $\tau 2.88$ (X part) and an AB quartet at τ 5.23 and 5.38 due respective to olefinic H₄ and H₅, which are coupled to each other, and to methylene H_6 and $H_{6'}$. The double irradiation at the center of resonance of H₅ (Fig. 5b) changed the signals of H_4 , H_6 and $H_{6'}$ into doublet-doublet. On double irradiation on C_6 protons (Fig. 5c), the signals of H_4

and H_5 collapsed into doublets ($J_{4,5}$ 11.0 cps), showing the presence of allylic coupling between C4 and C_6 protons. These irradiation experiments supported the structure XV.

The formation of the compound D was also observed at the initial stage of the reaction of V as a minor product. The analytical data corresponded to a diacetate, C10H12O6, showing IR bands due to an α,β -unsaturated aldehyde. Thus, this was tentatively assigned to XXIV. The NMR spectrum (Fig. 6a) showed unequivocally the presence of an aldehyde at $\tau 0.74$. An AB quartet due to C₆-methylene at τ 5.61 and 5.94, multiplet at τ 4.96 due to H₅ and at $\tau 4.79$ due to H₄ and a doublet-doublet at τ 4.06 due to H₈ are also easily analyzed as an ABXY pattern. The chemical shifts show that H₈ should be an olefinic proton and acetoxy groups should be at the C4- and C5-positions. Therefore, the structure of compound D was determined to be XXIV. Double irradiation at H₈ (Fig. 6b), giving a pattern similar to that of V (Fig. 1), also supported the structure.

³⁰⁾ E. F. L. J. Anet, Chem. & Ind., 1963, 1035.
31) E. F. L. J. Anet, see Ref. 14, p. 195.



Fig. 4. NMR spectra of XIV in chloroform-d at 100Mc.

Thin-layer chromatographic studies on the abovedescribed degradation of V in acetic anhydride showed that the initial products were primarily XII and a minor amount of XXIV. When the reaction was allowed to continue for longer periods of time, the amounts of XIV and XV increased at the expense of XII. Under similar acidic conditions, the conversion of XIV into XV was also observed, however, the reverse reactions XV \rightarrow XIV and XIV \rightarrow XII were not observed. Consequently, the reaction process of the degradation of V is concluded to proceed *via* a pathway of $V\rightarrow$ (XI) \rightarrow XII \rightarrow XIV \rightarrow XV as shown in Chart 2.⁸² No isolation of XI must be caused by its instability.⁸⁸

It is quite natural to consider that the precursor of XXIV should be a 1,2-ene derivative, VIII or its epimer XXIII. The elimination of a protonated C_3 acetoxy group of VIII or XXIII, followed by the loss of C_1 acetyl cation yielded XXIV. For the formation of VIII or XXIII, two possible pathways can be proposed. One is the 3,4 addition of acetic acid to XII and the other is the rearrangement of the 2,3-double bond of V into 1,2-position; however, the latter is favorable, since thin-layer chromatographic data elucidated no formation of XXIV by acid-treatment of XII in acetic anhydride or in acetic acid.

Anet's mechanism for the acid-catalyzed degradation of hexose to furans proposed that a key intermediate is an unsaturated osone such as XXV which may be converted into XXVIa. As the deacetylated form of XV is quite similar to XXV, it is expected that XV may also be converted into XXVI. However, the possibility of the above-described intermediates XII, XIV and XV being the precursor of furans is excluded, since heating them in an acetic anhydride medium only gave polymeric substances.

The treatment of V in acetic anhydride also did not afford furans even under stronger conditions, however, treatment in acetic acid yielded XXVIb. Since the UV absorption spectrum of XXVIb gave an absorption maximum at 272 m μ , it was felt that furan formation could be followed by observing the appearance of this peak. Solutions were made of V (1%) in acetic acid containing different concentrations of water and the absorbance of each solution at 272 m μ was recorded after heating at 95°C for 4.5 hr. The results, as shown in Fig. 7, revealed that the formation of XXVIb tended to increase with increasing addition of water. Although XII was detected at the initial stages of these reactions, it yielded

³²⁾ This pathway via XI was thought to be more favorable than a pathway of $V \rightarrow XII \rightarrow XIV \rightarrow XV$, since the formation of XX (XVII) was observed in the reaction of V with hydrogen bromide.

³³⁾ It was supposed that the two large substituents, of the C_2 position, OAc and CH₂OAc, make the molecule unstable.

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only traces of XXVIb under the same reaction conditions. Intermediates XIV and XV were hardly detected in the reaction mixtures and did not afford XXVIb in acetic acid-water. On the other hand, heating of another type of osone, XX, easily gave XXVIb. Therefore, the reaction process of the degradation of V to XXVIb is assumed to be as follows: $V \rightarrow XI \rightarrow XXVII \rightarrow XXVIII \rightarrow XXVIb$ (see Chart 2). Attempts were made to isolate unknown osone XXVII from an acetic acid solution of V, but a complex mixture of products were isolated. By preparative thin-layer chromatography of the mixture, a compound showing IR and UV bands due to conjugate ketone and a quite similar pattern of NMR spectrum to XX was isolated, and was easily converted into XXVIb. Therefore, this thought to be XXVII, however, an adequate amount for determination of its correct structure was not obtained.84-86)

It was somewhat surprising that the presence of water is very important for the degradation of V; it degradates to form polymeric substances under an-



Fig. 7. The formation of XXVIb from V (at 95°C for 4.5hr).

- a) acetic acid only (without V) -
- b) in acetic acid ----
- c) in acetic acid containing 10% of water ----
- d) in acetic acid containing 50% of water ----
- e) in acetic acid containing 90% of water ----

hydrous conditions and to form furan XXVIb by aqueous treatment.

Experimental

Melting points were determined on a Kofler block. The NMR spectra were measured on a Varian A-60 spectrometer at 60 Mc at room temperature using tetramethylsilane (TMS) as internal reference. Spectra at 100 Mc were obtained at room temperature from Varian HA-100 instrument internally locked on TMS in the frequency-sweep mode of operation. NMR data obtained by 1st-order approximation were summarized in Tables 1 and 2.

Thin-layer chromatography was performed on a silica gel plate. The solvent-systems used were ether-petroleum ether (3: 1, v/v, solvent A, 2: 1, v/v, solvent B and 1: 2, v/v, solvent C), benzene-ether (3: 1, v/v, solvent D), chloroform-acetone (60: 1, v/v, solvent E) and ethyl acetate-petroleum ether (2: 3, v/v, solvent F). The separated materials were developed with either iodine vapor or 0.2% resorcinol in 10% ethanolic phosphoric acid, and then heated in an oven.^{\$70} In the cases of preparative thin-layer chromatography, the developed zones were extracted with acetone unless otherwise stated. The evaporation of the acetone under reduced pressure gave the materials.

The optical rotations were determined in a 10cm microtube in chloroform containing 1% of ethanol, and concentrations were recorded in percentage. The UV spectra were measured in ethanol.

1,3,4,5-Tetra-O-acetyl-2-O-carbomethoxy- α -L-sorbopyranose (IIIa). A mixture of II (10 g),⁸⁰ dimethyl pyrocarbonate (8 ml)^{89.40} and potassium carbonate (0.1 g) was warmed at 50—60°C for 1.5 hr with stirring. The reaction mixture was filtered and washed with ether. The washings and the filtrate were combined and then evaporated under reduced pressure. The residue was recrystallized from ether to give colorless columns (6.9 g), mp 117—117.5°C, $[\alpha]_D^{22} - 63.2^\circ$ (c 1.038).

Found: C, 47.59; H, 5.58%. Calcd for $C_{16}H_{22}O_{12}$: C, 47.29; H, 5.46%.

1,3,4,5-Tetra-O-acetyl-2-O-carboethoxy- α -L-sorbopyranose (IIIb). A mixture of II (30 g), diethyl pyrocarbonate (23 ml) and potassium carbonate (0.3 g) was warmed at 50–55°C for 0.5 hr with stirring. IIIb (38.9 g) was obtained in a manner similar to IIIa. IIIb had mp 96–97°C, $[\alpha]_{12}^{22}$ –69.7° (c 1.116).

Found: C, 48.73; H, 5.92%. Calcd for $C_{17}H_{24}O_{12}$: C, 48.57; H, 5.76%.

1,3,4,5-Tetra-O-acetyl-a-L-sorbopyranosyl Chloride (**IV**). A solution of IIIb (30 g) in acetic acid (600 ml) saturated with anhydrous hydrogen chloride was kept at $0-5^{\circ}$ C for 3.5 hr. The solution was added to chloroform (500 ml) and washed with ice-water, saturated aqueous sodium bicarbonate and ice-water,

39) Kindly supplied by Dr. Shinzaburo Sumimoto of this Laboratory. S. Sumimoto, Japanese Pat. 42-19818 (1967).

40) M. Fujimoto, Japanese Pat. 42-12272 (1967).

³⁴⁾ Another new compound was isolated, which gave analytical data corresponding to $C_{12}H_{14}O_7$. Its NMR spectrum in chloroform-d at 60 Mc revealed three 3-proton singlets at τ 7.73, 7.92 and 7.94 due to acetoxyls, one 1-proton singlet at τ 3.51 and two 2-proton singlets at τ 4.99 and 5.01. Therefore, the structure was tentatively assigned to be 2,5-diacetoxymethyl-3-acetoxyfuran. Although further evidence seems to be required, a related experiment that D-glucal smoothly yielded 2-methoxymethyl-5-hydroxymethylfuran with methanolic hydrochloric acid seems support this structure (see Refs. 35 and 36).

and 36). 35) F. Shafizadeh and M. Stacey, J. Chem. Soc., 1952, 3608.

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and dired. Removal of the solvent gave a crude chloride (24.5 g) which was purified by silica gel chromatography with benzene. From 1.55 g of the crude syrup, using 30 g of silica gel, a colorless syrup (0.36 g) was obtained. The recrystallization of the syrup from ether and petroleum ether gave pure IV (0.15 g), mp 67.5–69.5°C, which was identical with an authentic sample.^{2,3)} IV was also prepared from IIIa in a similar way.

1,3,4,5-Tetra-O-acetyl-2-deoxy-L-sorbopyranos-2,3-ene (V). To a suspension of mercuric cyanide (19.9 g) in dry benzene (400 ml), a dry benzene solution (100 ml) of crude IV (24.5 g) was added. Traces of water were removed by azeotropic distillation with benzene (ca. 20 ml). After it had been refluxed for 8 hr with stirring, the reaction mixture was filtered and the filtrate was evaporated. The residue was extracted with chloroform (500 ml) and the chloroform was washed with 30% potassium iodide solution and then water and dried. Removal of the chloroform gave a dark brown syrup (18 g). The purification of the syrup on alumina column chromatography (135 g of alumina was used) with benzene gave V as a colorless syrup (13.7 g), $[\alpha]_{\rm B}^{22}$ +217.6° (c. 1.032).

Found: C, 50.95; H, 5.51%. Calcd for $C_{14}H_{18}O_9$: C, 50.91; H, 5.49%. UV_{max} 209 m μ (ε 8800).

Methyl 1,3,4,5-Tetra-O-acetyl-3-C-chloromercuri- β -L-tagatopyranoside (VI). To a solution of mercuric acetate (1.05 g) in absolute methanol (20 ml), V (1.0 g) was added. After the mixture had stood overnight at room temperature, the solvent was removed and extracted with chloroform. The chloroform solution was shaken with saturated aqueous sodium chloride (100 ml \times 2), washed with saturated aqueous sodium bicarbonate and water, dried and the solvent removed. The syrup (1.07 g) which was obtained was purified by preparative thin-layer chromatography (solvent A, R_f , 0.20). The purified syrup (0.21 g) was recrystallized from ethanol to give colorless columns (0.12 g), mp 184—189°C, $[\alpha]_{\rm D}^{23}$ $+71.1^{\circ}$ (c 1.017).

Found: C, 30.72; H, 3.62; Hg, 32.96%; mol wt, 588. Calcd for $C_{15}H_{21}O_{10}HgCl$: C, 30.16; H, 3.54; Hg, 33.58%; mol wt, 597.385.

Methyl 1,3,4,5-Tetra-O-acetyl-B-L-tagatopyranoside (VII). Sodium borohydride (50 mg) was added as a solid in five portions, at intervals, to a pyridine solution (5 ml) of VI (0.7 g). After being kept at room temperature for 2.5 hr, the reaction mixture was filtered and washed with pyridine (5 ml). Acetic anhydride (10 ml) was added to a combined solution of the filtrate and the washings. The solution was allowed to stand overnight at room temperature, and then poured onto ice, made alkaline with sodium carbonate, and extracted with chloroform. The extract was washed with 5% sulfuric acid, water and dried, after which the solvent was removed under reduced pressure. The purification of the residue by preparative thin-layer chromatography (solvent A, R_f 0.38, extracted with chloroform) gave crude crystals (205 mg). Recrystallization of the crystals from ether and petroleum ether gave colorless columns

(83 mg), mp 87–87.5°C, $[\alpha]_{12}^{22}$ +104.2° (c 0.947). Found: C, 49.67; H, 6.12%. Calcd for $C_{15}H_{22}O_{10}$: C, 49.72; H, 6.12%.

Acid-catalyzed Isomerization of V in Acetic Anhydride.⁴¹⁾ A solution of V (6.68 g) in acetic anhydride (67 ml) containing 1% of TsOH was kept at 30°C for 24-48 hr (for 24 hr to obtain XII as a major product

and for 48 hr to obtain XIV and XV as major products). The solution was then poured into ice-water (800 ml) under vigorous stirring, made alkaline with sodium bicarbonate and extracted with chloroform. The extract was washed with 5% aqueous sodium bicarbonate and water. The syrup (5.8 g) obtained on solvent removal from the dried extract was fractionated by preparative thin-layer chromatography. (i) From the syrup (3.6 g)obtained from the reaction for 24 hr, XII (0.40 g) was isolated as a syrup in a pure state by repeated preparative thin-layer chromatography (solvent D, R_f 0.65, extracted with ether). (ii) From the syrup obtained from the reaction for 48 hr, XIV, XV and XXIV were fractionated by thin-layer chromatography (solvent F, $R_f 0.29$ (XIV), 0.22 (XV), 0.4-0.7 (XXIV)). From the syrup (14.29 g), these were obtained in a crude state in the ratio of XIV (0.36 g), XV (0.46 g), and XXIV (0.94 g). XIV was recrystallized from ether (yield, 51 mg), and XV from ethanol (yield, 71 mg). XXIV was purified by repeated thin-layer chromatography (solvent E, R_f 0.61) (yield, 65.5 mg).

XII: Syrup $[\alpha]_{2}^{**}$ -88.0° (c 0.980). Found: C, 53.72; H, 5.73%; mol wt, 281. Calcd for $C_{12}H_{14}O_7$: C, 53.33; H, 5.22%; mol wt, 270.23. UV_{max} 261 mµ (ε 16100). IR_{film} 1635 cm⁻¹ (conj. C=C).

XIV: Colorless columns, mp 110–111.5°C, $[\alpha]_{12}^{12}$ +198.8° (c 0.997). Found: C, 49,44; H, 5.23%; mol wt, 387. Calcd for C₁₆H₂₀O₁₀·H₂O: C, 49.23; H, 5.68%; mol wt, 390.34. UV_{max} 213 m μ (ϵ 8970).

XV: Colorless columns, mp 111.5—113°C. Found: C, 51.43; H, 5.16%; mol wt, 298. Calcd for $C_{12}H_{14}O_7$. $\frac{1}{2}H_2O$: C, 51.61; H, 5.41%; mol wt, 279.24. UV_{max} 230 mµ (ε 7280). IR_{CHC13} 1630, 1700 cm⁻¹(C=C-C=O).

XXIV: Syrup, $[\alpha]_{12}^{22} + 236.8^{\circ}$ (c 0.641). Found: C, 52.53; H, 5.55%. Calcd for C₁₀H₁₂O₆: C, 52.63; H, 5.30%. UV_{max} 253 m μ (ε 6390). IR_{f11m} 1640, H

 1705 cm^{-1} (C=C-C=O).

Reaction of XII with Hydrogen Bromide in Dry Benzene. A solution of XII (1.15 g) in dry benzene (21 ml) containing hydrogen bromide (2.34 g) was kept at $0-5^{\circ}$ C for 1.5 hr. Evaporation of benzene under reduced pressure gave a dark red syrup, which was dissolved in methanol (8.4 ml) containing silver carbonate (1.53 g) and kept overnight at room temperature. The solution was filtered and evaporation of the filtrate gave a brown syrup. From the syrup, XX, XXI and XXII were isolated by preparative thin-layer chromatography (solvent B, R_f , 0.71 (XX), 0.93 (XXI), 0.85 (XXII), extracted with chloroform). Isolated materials were further purified by recrystallization or by preparative thin-layer chromatography.

XX: Syrup (purified by repeated preparative thinlayer chromatography, solvent D, R_f 0.50, yield, 0.1 g), $[\alpha]_{D}^{2*} + 66.6^{\circ}$ (c 0.695). Found: C, 52.90; H, 5.97%. Calcd for C₉H₁₂O₅: C, 53.99; H, 6.04%. UV_{max} 226 m μ (ε 6800). IR_{film} 1635, 1690 cm⁻¹ (C=C-C=O).

XXI: Colorless columns, mp 136—138°C (recrystallized from ether and petroleum ether, yield, 10 mg), $[\alpha]_{12}^{32}$ -30.9° (c 1.045). Found: C, 40.88; H, 5.01; Br, 20.93%. Calcd for C₁₈H₁₉O₈ Br: C, 40.74; H, 5.00; Br, 20.86%.

⁴¹⁾ Products isolated from the reaction were rather unstable and should be stored in a refrigerator under strictly anhydrous conditions.

XXII:⁴²⁾ Syrup (purified by repeated preparative thin-layer chromatography, solvent B, R_f 0.85, yield, 0.03 g), $[\alpha]_{13}^{23}$ +51.3° (c 0.825). Found: C, 41.42; H, 5.10; Br, 20.82%. Calcd for C₁₈H₁₉O₈ Br: C, 40.74; H, 5.00; Br, 20.86%.

Reaction of V with Hydrogen Bromide in Dry Benzene. When the above reaction was carried out by using V as the starting material, the same result was obtained.

Conversion of XXII into XXI. When the above reaction was carried out by using XXII as the starting material (instead of hydrogen bromide, hydrogen chloride was used), the formation of XXI was confirmed by thin-layer chromatography.

Acid-catalyzed Isomerization of XII. A solution of XII (0.25 g) in acetic anhydride (3 ml) containing 1% of TsOH was kept at 40—50°C for 7 hr. When the solution was worked up in a way similar to the acidcatalyzed isomerization of V, a crude syrup (0.18 g) was obtained from which XIV (38 mg) and XV (15 mg) were obtainable.

Acid-catalyzed Isomerization of XIV. A solution of XIV (15 mg) in acetic anhydride (0.3 ml) containing 1% of TsOH was kept at 50°C for 8 hr. The formation of XV was confirmed by thin-layer chromatography (solvent F, R_f 0.40).

Isomerization of V in Acetic Acid. (i) A solution of V (2.0 g) in acetic acid-water (1:1, v/v) was kept at 95°C for 4.5 hr. The syrup obtained on solvent removal under reduced pressure was purified by repeated pre-

42) The NMR data show that the favorable conformation of XXII is Cl chair form. parative thin-layer chromatography (solvent D, R_f 0.70). XXVIb (0.36 g) was obtained and was identical to an authentic sample.⁴⁹ (ii) A solution of V (0.54 g) in acetic acid was kept at 95°C for 6 hr. The solution was worked up in a way similar to the above. XXVIb (0.07 g) was obtained. 2,4-Dinitrophenylhydrazone of XXVIb was prepared in a usual way as red needles, mp 142.5—147°C (recrystallized from ethanol). Found: C, 48.42; H, 3.57; N, 15.89%, mol wt, 357. Calcd for C₁₄H₁₇O₇N₄: C, 48.28; H, 3.47; N, 16.09%; mol wt, 348.27.

Isomerization of XII in Acetic Acid. A solution of XII (0.13 g) in acetic acid-water (1: 1, v/v) (2 ml) was kept at 95°C for 2 hr. A syrup was obtained on solvent removal under reduced pressure. From the syrup, traces of XXVIb were isolated by repeated thinlayer chromatography (solvent D, R_f 0.70 and solvent C, R_f 0.28).

Isomerization of XX in Acetic Acid. A solution of XX (40 mg) in acetic acid-water (1: 1, v/v) (1.5 ml) was kept at 95°C for 6 hr. Evaporation of the solvent gave a syrup (20 mg), the thin-layer chromatography of which indicated XXVIb as a major component and XX as a minor one (the ratio was about 2: 1).

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⁴³⁾ Synthesized by Schubert's method. H. Schubert, E. Hagen and G. Lehrmann, J. Prakt., 17, 173 (1962).