BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 45, 3692—3698 (1972)

The Acid-catalyzed Degradation of Methyl 2,3,4,5-Tetra-*O*-acetyl-α-L-xylo-2-hexulopyranosonate. A Model for the Degradation of L-xylo-Hexulosonic Acid[1]

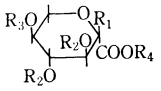
Kazuaki GOSHIMA, Norihide MAEZONO, and Kanji TOKUYAMA

Shionogi Research Laboratory, Shionogi & Co., Ltd., Fukushima-ku, Osaka, 553

(Received April 15, 1972)

The degradation reaction of L-xylo-hexulosonic acid (**1**) was studied, using methyl 2,3,4,5-tetra-*O*-acetyl-L-xylo-2-hexulopyranosonate (**11**) as a model compound. The degradation of **11** proceeded *via* two pathways, **11**→α,β-unsaturated ketone compound→a furan compound (path a) and **11**→a dihydropyrone compound→further decomposed products (not furans) (path b). The major pathway was path a in benzene and path b in water. The results supported the idea that the acid-catalyzed degradation of L-ascorbic acid (**2**) to furans would not proceed *via* **1**, but directly.

In spite of the long-standing interest in the degradation of L-ascorbic acid (**2**) in acidic solutions, the mechanism for the degradation under anaerobic conditions is still not well understood.[2-6] The reaction may be summarized in two major pathways. One involves the pathway of **2**→L-xylo-hexulosonic acid (**1**)→2-furaldehyde (**3**); the other involves the alternative one of **1**→**2**→**3**. The latter one seemed to have been established by kinetic studies,[5,6] whose validities were confirmed over wide ranges of acid concentration by our reinvestigation.[7] The former pathway, however, has recently received renewed attention because of the isolation of a new intermediate.[4] In this paper, we will attempt to study the behavior of **1** in acidic media when the conversion of **1** into **2** is inhibited. For this purpose, methyl 2,3,4,5-tetra-*O*-acetyl-α-L-xylo-hexulopyranosonate (**11**) was prepared as a starting material. If the pathway of **2**→**1**→**3** is probable, **11** can be converted into furan compounds.



1: R_1=OH, R_2=R_3=R_4=H
4: R_1=OH, R_2=R_3=H, R_4=Me
5: R_1=OH, R_2=R_3=Ac, R_4=Me
6: R_1=OAc, R_2=Ac, R_3=H, R_4=Me
7: R_1=Br, R_2=R_3=Ac, R_4=Me
11: R_1=OAc, R_2=R_3=Ac, R_4=Me

33 **34**

Chart 1.

The acetylation of methyl L-xylo-hexulosonate (**4**)[8] gave a triacetate (**5**), which was converted into the desired **11** by further acetylation. The pyranose

1) Sorboses. Part 21. For Part 20, see Ref. 7. A part of this paper was reported in preliminary forms: K. Goshima and K. Tokuyama, *Tetrahedron Lett.*, **1969**, 2383; K. Goshima, N. Maezono, and K. Tokuyama, *Carbohyd. Res.*, **17**, 245 (1971).

2) S. Kamiya, *Nippon Nogei Kagaku Kaishi*, **33**, 398, 402 (1959); **34**, 13 (1960).

3) A. Cier, C. Nofre, and B. Drevon, *Bull. Soc. Chim. Fr.*, **1959**, 74.

4) T. Kurata and Y. Sakurai, *Agr. Biol. Chem.*, **31**, 179 (1967).

5) P. P. Regna and B. P. Caldwell, *J. Amer. Chem. Soc.*, **66**, 246 (1944).

6) R. Yamamoto and E. Yamamoto, *Yakuzaigaku*, **25**, 42 (1965).

7) K. Tokuyama, K. Goshima, N. Maezono, and T. Maeda, *Tetrahedron Lett.*, **1971**, 2503.

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

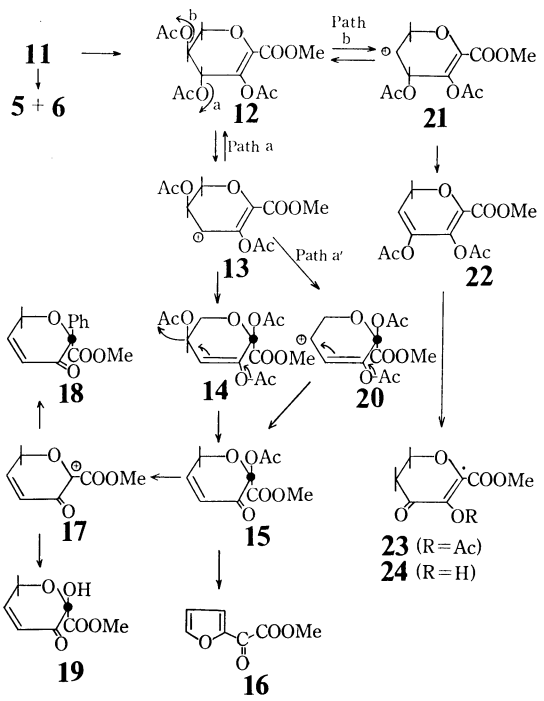


Chart 2.

structure of **11** was confirmed by the large coupling constants among ring-protons in the NMR spectrum.[9]

The heating of **11** in acetic acid-water (1 : 9, v/v) on a boiling-water bath gave no furan compounds. After 7 hr, four products, **5** and three unknown ones, were isolated by preparative thin-layer chromatography, along with the recovery of **11** to some extent. The elemental analysis of unknown products suggested them to be partially hydrolyzed derivatives of **11**; that is, one seemed to be the triacetate of **4** (**6**) and the others, to be diacetates. With **6**, the signals in the NMR spectrum were quite similar to those of **11**, but the multiplet due to H_5 shifted upfield. Therefore, the structure was determined to be methyl 2,3,4-tri-*O*-acetyl-L-xylo-hexulopyranosonate. The structures of diacetates were not determined, but the fact that the acetylation of them gave **11** suggested that they were hydrolyzed products of **11**. The results apparently showed that, in aqueous media, the degradation of **11** proceeded much slower than its hydrolysis; the studies under anhydrous conditions were clearly called for.

When **11** in dry benzene was treated with boron trifluoride-etherate, the reaction smoothly proceeded at a reflux temperature. The preparative thin-layer chromatography of the product gave three compounds **15**, **16**, and **18**, though trace amounts of other components were not isolated in pure states. The UV and IR spectra of **15** and **18** revealed bands indicative of α,β-unsaturated ketone and ester groups. The NMR spectra for ring-protons appeared as an ABXY system, which were similar to those previously reported for 1-*O*-acetyl-2-*O*-methyl-4,5-dideoxy-2,3-hexodiulopyranos-4,5-ene (**34**).[10] The spectra also suggested the presence of one acetoxyl group in **15** and one phenyl group in **18**. Therefore, **15** and **18** were identified as methyl 2-*O*-acetyl-4,5-dideoxy- and methyl 2-*C*-phenyl-2,4,5-trideoxy-2,3-hexodiulopyranosonate-4,5-ene respectively. Both compounds were racemates from optical rotations. The mass spectrum of **16** was identical with that of **3** except for the molecular ion peak (M^+)[11] and the IR spectrum showed the presence of ketone and ester groups. The structure of **16** was thus determined to be 2-methoxalylfuran. This structure was also supported by the NMR and UV spectra.

As **15** corresponded to the intermediates in the degradation of hexoses,[12] the degradation of **11** must proceed *via* the pathway of **11**→**15**→**16**. This idea was supported by the fact that the treatment of **15** in benzene containing boron trifluoride-etherate or in acetic acid-water gave **16**. As a small amount of **18** was also detected in the reaction of **15**, **18** must be formed *via* the pathway of **15**⇄**17**→**18**. The use of 1,2-dimethoxyethane as a solvent instead of benzene inhibited the formation of **18** and retarded the degradation rate. No further degradation of **18** was observed under the reaction conditions employed.

To elucidate the earlier stages of the degradation reaction in benzene, the reaction was performed under milder conditions. When **11** was treated at 60°C, the formation of **15** and a new compound was initially observed. The structure of the new compound was identified as the racemate of methyl 3,4,5-tri-*O*-acetyl-2-deoxy-L-threo-hexulopyranosonate-2,3-ene (**12**) by a comparison of its NMR and IR spectra with those of an authentic sample of **12**. The sample was prepared by a procedure similar to the preparation of 1,3,4,5-tetra-*O*-acetyl-2-deoxy-L-threo-hexulopyranos-2,3-ene (**33**)[10] to be described below. The acetobromination[13] of **4** gave a 2-bromo compound (**7**), while the dehydrobromination of **7** with mercuric cyanide in toluene yielded **12**, whose structure was confirmed by spectral data. Signals due to the ring protons of **12** appeared in an ABXY system quite similar to that of **33** in the NMR spectrum[10] and the characteristic band due to a double bond appeared in the IR. As the transformation of **33** to **34** under acidic conditions had already been established, the major pathway of the degradation of **11** was proposed to be **11**→**12**→**15**→**16**.

If the suggested pathway is reliable, the reaction rate (k_2) of **12**→**15** should be larger than that (k_1) of **11**→**12**, since the yield of **12** was very poor. Expectedly, the k_2/k_1 ratio given from the kinetic measurement of both reactions by following the decreases in the respective starting materials polarimetrically was about 15; consequently, it supported the pathway.

The fact that **11** was first isomerized to **12** prompted

9) T. Maeda, K. Tori, S. Satoh, and K. Tokuyama, This Bulletin, **41**, 2495 (1968); **42**, 2635 (1969).

10) M. Katsuhara, S. Wakahara, and K. Tokuyama, *ibid.*, **41**, 1208 (1968).

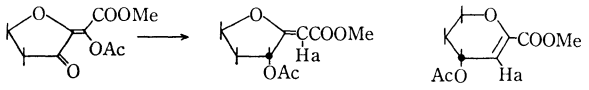
11) K. Heyns, R. Stute, and H. Scharmann, *Tetrahedron*, **22**, 2223 (1966).

12) E. F. L. J. Anet, *Adv. Carbohydrate Chem.*, **19**, 181, (1964).

13) R. U. Lemieux, "Methods in Carbohydrate Chemistry," Vol. 2, ed. by R. L. Whistler and M. L. Wolfrom, Academic Press, New York (1963), p. 221.

us to study the reaction of **12** as a starting material. First of all, reactions in benzene were examined. The treatment of **12** in boiling benzene containing boron trifluoride-etherate showed a tlc similar to that of the reaction of **11** under similar conditions. From the product, three major products, **15**, **18**, and **16**, and two minor ones were isolated. When the reaction was allowed to continue for longer periods of times, the amounts of **16** and **18** increased at the expense of **15**. This result also supported the existence of the above pathway of **12**→**15**→**16**.

The two minor products were identified, by a comparison of the tlc, as the minor components detected in the above-described reaction of **11** in benzene. One of them was also obtained by the mild hydrolysis of **15** and showed the characteristic bands due to hydroxyl and ester groups in the IR spectrum. Therefore, it was determined to be methyl 4,5-dideoxy-2,3-hexodiulopyranosonate-4,5-ene (**19**), which satisfied the NMR spectrum, too. As the mild hydrolysis of **15** yielded **19**, **19** must be formed by the hydrolysis of **15** during the reaction and/or preparative thin-layer chromatography.

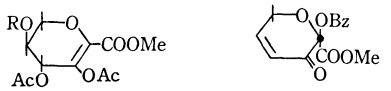


8 **10** **9**

Chart 3.

The other minor product showed the characteristic bands due to three kinds of carbonyl groups and a conjugate double bond in the IR spectrum. The NMR spectrum showed two 3-proton singlets due to one carbomethoxy and one acetoxyl and two 2-proton triplets, which constitute an A_2X_2 system. These spectral data suggested that this compound was a six-membered ring compound (**23**) or a five-membered ring one (**8**). The reduction of the compound with sodium borohydride in pyridine, followed by acetylation, gave a monoacetate. The combined data of spectral and elemental analyses, which showed the presence of one acetoxyl, one carbomethoxy and a double bond, suggested that the monoacetate was **9** or **10**. The signal due to Ha (see Chart 3) appeared as a doublet (J=5 Hz). As the Ha signal of **9** should appear as a doublet, and that of **10** as a singlet, the monoacetate was determined to be **9**; consequently, the parent compound must be **23**. The spectral data of analogus compounds also supported this conclusion.[14,15] The formation of **23** was very interesting. Although kojic acid and maltol are formed *via* enolone intermediates,[16] **23** was not derived from an enolone compound, **15**, and was not converted into furan derivatives on further acid treatments.

Chart 2 shows a summarized pathway of the reaction of **11**, which involves an initial 4→2 migration[10,17] of the acetoxyl group at C_4 of **12** (**11**→**12**→**13**→**14**→**15**→**16**, path a) and an initial elmination of the acetoxyl group at C_5 of **12** (**11**→**12**→**21**→**22**→**23**, path b). The racemization of **12** during the reaction supported the presence of the equilibrium among **12**, **13**, and **21**. In path a, the possibility of the 5→2 migration of the acetoxyl group (**11**→**12**→**13**→**20**→**15**→**16**, path a′) could not be excluded, judging from the facts described below.



25: R=H
26: R=Bz

27

Chart 4.

The partial deacetylation of **12** under milder conditions, followed by benzoylation, gave 5-benzoate (**26**). The fact that the H_5 signal of a partially-deacetylated compound (**25**) appeared more in upfield than that of **12** supported the structures of **25** and **26**. The reaction of **26** under conditions similar to the above reaction afforded **15**, **16**, **18**, and **27**. The new product, **27**, was identified as the benzoyl analog of **15** by spectral and elemental analyses, and its formation suggested the existence of the 5→2 migration (path a′).

It was difficult to study the degradation of **11** in aqueous media, since the hydrolysis of **11** was more rapid than the degradation. On the other hand, as **12** was established to be the initial intermediate in benzene, the reaction of **12** in acetic acid-water was carried out.

When **12** in water containing 10% acetic acid was heated on a boiling-water bath for 6 hr, multispots were detected in the tlc. From the chloroform extract of the product, three major components, **23**, **24**, and **25**, were isolated. Proof of the structure of the unknown compound, **24**, was provided by acetylation, which gave **23**. Among many minor components, **3** and **16** were successfully isolated. The water layer was evaporated to dryness. When the residue was dissolved in pyridine, the pyridine salt of oxalic acid was precipitated. After the removal of the salt by filtration, the pyridine solution was acetylated with acetic anhydride. The tlc of the product also showed many spots, from which relatively major component, **23**, and two unknown compounds, were isolated in pure states. The compound **23** isolated must naturally exist as **24** in the reaction medium. The NMR spectrum of the one of the unknown compounds showed one 3-proton singlet due to acetoxyl, one 1-proton singlet at a lower field and two 2-proton triplets, which constitute an A_2X_2 system. Therefore, its structure was identified as **32**. This structure was also supported by the UV and IR spectra. The other compound showed the characteristic band due to a carbonyl group in the IR spectrum, but no absorption

14) S. Gelin and R. Gelin, *Bull. Chim. Soc. Fr.*, **1969**, 1383.
15) K. Nakanishi, M. Nagao, and K. Okada, *Yakugaku Zasshi*, **88**, 1944 (1968).
16) F. W. Lichtenthaler and P. Heidel, *Angew. Chem. Int. Ed. Engl.*, **8**, 978 (1969).
17) R. J. Ferrier and N. Parasad, *J. Chem. Soc., C*, **1969**, 570.

maximum in the UV. The NMR spectrum showed two 3-proton singlet due to acetoxyl groups, one 2-proton singlet, and two 2-proton triplets of A_2X_2 system. Its structure was thus determined to be the acetate of 3-deoxy-tetroulose (**30**).

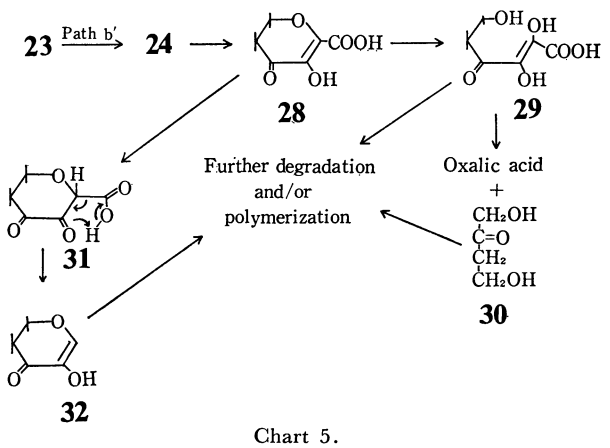


Chart 5.

Only a limited amount of 2-furaldehyde (**3**) was obtained from the degradation of **12** in water, contrary to that in benzene. The degradation in water must proceed mostly *via* path b (Chart 2), followed *via* path b′ (Chart 5). Some minor products were isolated, but their structures could not be determined. They must be further decomposed and/or polymerized products of the various intermediates shown in Chart 5. The possibility of path b′ was experimentally established; the treatment of **23** in acetic acid–water afforded oxalic acid, **30**, and **32**.

It is surprising that the pathway forming furans is not a major one in an aqueous solution. This fact suggested that **1** is not a probable intermediate in the acid-catalyzed degradation of **2**, as the kinetic data have previously presented.[5-7]

Experimental

All the melting points were recorded on a Kofler block and are uncorrected. The NMR spectra were taken in chloroform-*d* with a Varian A-60-A spectrometer using tetramethylsilane as the internal standard. The chemical shifts and coupling constants are expressed in τ unit and Hz respectively. The multiplicities of the signals are abbreviated as follows: s=singlet, d=doublet, t=triplet, q=quartet, and m=multiplet. The UV spectra were observed in 95% ethanol unless otherwise stated, and they are shown in nm. The IR spectra are expressed in cm^{-1}. The optical rotations were determined in a 10-cm microtube in chloroform containing 1% of ethanol, and the concentrations were recorded in percentages. Preparative thin-layer chromatography (ptc) and tlc were performed on a silica-gel plate. The solvent-systems (v/v) used were acetone and benzene (7 : 15, solvent A_1, and 1 : 4, solvent A_2), acetone and chloroform (1 : 9, solvent B), acetone and petroleum ether (1 : 3, solvent C), ether and benzene (7 : 15, solvent D_1, 1 : 3, solvent D_2, and 1 : 7, solvent D_3), ether and petroleum ether (4 : 1, solvent E_1, 7 : 3, solvent E_2, 3 : 2, solvent E_3, 1 : 1, solvent E_4, 2 : 3, solvent E_5, and 1 : 2, solvent E_6), and ether and chloroform (3 : 35, solvent F). The separated materials were developed with iodine vapor and the developed zones were extracted with acetone. Fraction 1 showed the fastest-moving components.

The evaporation of solvents used was carried out under reduced pressure.

*Methyl 3,4,5-Tri-*O*-acetyl-L-xylo-hexulopyranosonate (**5**).* To a solution of methyl L-xylo-hexulosonate (**4**)[8] (15 g) in pyridine (150 m*l*), we added, drop by drop, acetic anhydride (15 g) at −50°C. After stirring at the same temperature for 4 hr, the solution was evaporated to dryness. The residue was washed with petroleum ether and then recrystalized from ether, and then from a mixture of ethyl acetate and petroleum ether. The yield was 5.6 g, mp 109.6—112°C. $[\alpha]_D^{25.0}$ −27°(0.995). Found: C, 46.84; H, 5.47%; mol wt, 338. Calcd for $C_{13}H_{18}O_{10}$: C, 46.71; H, 5.43%; mol wt, 334.27.

*Methyl 2,3,4,5-Tetra-*O*-acetyl-α-L-xylo-hexulopyranosonate (**11**).* *(1) Synthesis*: A mixture of **5** (0.4 g), acetic anhydride (6 m*l*), and sodium acetate (0.4 g) was stirred at 70°C for 4 hr. The mixture was poured onto ice water, neutralized with sodium bicarbonate, and then extracted with chloroform. The chloroform solution was washed with water, and the chloroform was evaporated. The recrystallization of the residue from ether gave colorless columns; (0.32 g), mp 118—119°C. $[\alpha]_D^{25}$ −73.9° (0.973). NMR H_3, 4.48^d, ($J_{3,4}$ 10), H_4, 4.45^q ($J_{4,5}$ 9.0), H_5, 4.89^m ($J_{5,6}$, 6.0, $J_{5,6'}$, 10.5), H_6, 5.88^m ($J_{6,6'}$, 11.5) $H_{6'}$, 6.46^m. Found: C, 47.92; H, 5.37%; mol wt, 380. Calcd for $C_{15}H_{20}O_{11}$: C, 47.89; H, 5.36%; mol wt, 376.31.

(2) Reaction with Acetic Acid-water: A solution of **11** (2.0 g) in acetic acid-water (1 : 9, v/v) was heated for 7 hr on a boiling-water bath and then evaporated to dryness. The residual syrup was fractionated by ptc (solvent A_1). From Fraction 1, **11** (102 mg) was recovered. From Fractions 2, 3, and 4, **5** (53 mg), methyl 2,3,4-tri-*O*-acetyl-α-L-xylo-hexulopyranosonate (**6**) (328 mg) and a diacetate of **4** (92 mg) were obtained respectively. From Fraction 5 (the slowest-moving component), another diacetate of **4** (342 mg) was isolated. The acetylation of both the diacetates in a procedure similar to **5** gave **11**. **6**: mp 198—200°C. $[\alpha]_D^{25.0}$ −72.7° (1.019). NMR($CDCl_3$): H_5, 6.1^m. Found: C, 46.95; H, 5.43%. Calcd for $C_{13}H_{18}O_{10}$: C, 46.71; H, 5.43%. Fraction 4 (a diacetate of **4**); Found: C, 45.02; H, 5.48%. Calcd for $C_{11}H_{16}O_9$: C, 45.21; H, 5.52%. Fraction 5 (a diacetate of **4**); Found: C, 45.22; H, 5.66%. Calcd for $C_{11}H_{16}O_9$: C, 45.21; H, 5.52%.

(3) Reaction in Benzene Containing Boron Trifluoride-etherate: (a) A solution of **11** (0.5 g) in dry benzene (5 ml) containing boron trifluoride-etherate (0.25 ml) was refluxed for 3 hr and then evaporated to dryness. The residual syrup was fractionated to two components by ptc (solvent D_1). The further ptc (solvent E_5) of the fast-moving component gave faster-moving 2-methoxalyfuran (**16**) (40 mg) and slower-moving **18** (4.5 mg). The purification of the slow-moving component by ptc (solvent D_1), followed by recrystallization from methanol, afforded **15** (41 mg). **15**: mp 95—96°C. $[\alpha]_{D,436}^{25.2}$ 0°. UV 226 (ε 9.8×10^3), 335 (ε 7.3×10). IR(KBr) 1762, 1700, 1629 (C=C, C=O). NMR H_4, 3.75^m ($J_{4,5}$ 10.5, $J_{4,6}=J_{4,6'}$, 2), H_5, 2.88^m ($J_{5,6}=J_{5,6'}$, 3), $H_{6,6'}$, 5.37^m. Found: C, 50.65; H, 4.57%. Calcd for $C_9H_{10}O_6$: C, 50.47; H, 4.71%. **16**: mp 42—42.5°C (recryst. from ether and petroleum ether). UV 233 (ε 2.2×10^3), 291.5 (ε 1.2×10^4). IR(KBr) 1740, 1667 (C=C), 1557, 885 (furan).[18] NMR H_3, H_5, 2.2—2.35^m, H_4, 3.37^m ($J_{3,5}$ 3.5, $J_{3,4}$ 1.5). Found: C, 54.59; H, 3.97%. Calcd for $C_7H_6O_4$: C, 54.55; H, 3.92%. **18**: syrup. $[\alpha]_D^{25.1}$ +2.0° (1.001). UV 296 (ε

18) A. R. Katritzky and L. M. Logowsky, *J. Chem. Soc.*, **1959**, 657.

3.5×10^2). IR(film) 1745, 1685, 1627 (C=O, C=C), 1548 (phenyl). NMR H_4, 3.78^m ($J_{4,5}$ 10.5, $J_{4,6}=J_{4,6'}$ 2.0), H_5, 3.03 ($J_{5,6}=J_{5,6'}$ 3.0) $H_{6,6'}$, 5.35^m, 5.60^m ($J_{6,6'}$ 19.5). Phenyl group (5H), 2.45—2.73^m. Found: C, 67.29; H, 5.45%; mol wt 243. Calcd for $C_{13}H_{12}O_4$: C, 67.23; H, 5.21%; mol wt 232.

(b) A solution of **11** (1.0 g) in dry benzene (10 m*l*) containing boron trifluoride-etherate (0.05 ml) was kept at 60°C for 10 hr, and then the solvent was removed. The residual syrup was fractionated by ptc (solvent E_1). Fractions 1, 2, 3 (a syrup, 101 mg), and **4** (a crystalline syrup, 692 mg) were obtained, but Fractions 1 and 2 could not be examined because of very limited amounts. The recrystallization of Fraction 3 gave **12** (5 mg), which was identified by a comparison of its IR and NMR spectra with those of an authentic sample (see below). However, the value of optical rotation was very small. [$[\alpha]^{25.0}$ 8° (1.00)]. The preparative thin-layer chromatography of Fraction 4 (solvent E_1) afforded **11** (529 mg) and **15** (40 mg).

Reaction of ***15****.* *(1) In the presence of Boron Trifluoride-etherate*: (a) A solution of **15** (20 mg) in dry benzene (0.5 m*l*) containing boron trifluoride-etherate (0.025 m*l*) was refluxed for 30 min and then evaporated to dryness. Preparative thin-layer chromatography (solvent E_1) of the residual syrup gave **16** (9 mg) and **18** (3 mg). (b) A solution of **15** (100 mg) in 1,2-dimethoxyethane (1 m*l*) containing boron trifluoride-etherate (0.05 m*l*) was stirred at 80°C for 20 hr and then evaporated to dryness. From the residue, a large part of the starting material was recovered, and **16** (36 mg) was isolated by ptc (solvent E_2).

(2) In Acetic Acid-water: A mixture of **15** (450 mg), acetic acid (0.5 m*l*) and water (4.5 m*l*) was heated on a boiling-water bath for 2 hr and then extracted with chloroform. The chloroform layer was evaporated to dryness and fractionated by ptc (solvent E_4). Forty-one miligrams of **16** and 7 mg of **15** were obtained. The water layer was also evaporated to dryness. The treatment of the residue with diazomethane, followed by purification by ptc (solvent E_4), gave **16** (26 mg).

(3) Hydrolysis: A solution of **15** (260 mg) in a mixture of methanol (2 m*l*), chloroform (2 m*l*) and one drop of hydrochloric acid was left to stand for 2 days at room temperature, and then the solvent was removed. The purification of the residue by ptc (solvent A_2) gave **19** (61 mg).

*Methyl 2-Deoxy-2-bromo-3,4,5-tri-*O*-acetyl-*L*-xylo-hexulopyranosonate (****7****).* Acetic anhydride (260 m*l*) was cooled in an ice and water mixture, and then 60% perchloric acid (1.6 m*l*) was added, drop by drop. The solution was warmed to room temperature and **4** (64.5 g) was added to the stirred mixture at such a rate, over an about 30-min period, that the reaction temperature was kept between 30 and 40°C. The solution was then stirred at 0°C for 6 hr. Red phosphorus (19.4 g) was added slowly, and then bromine (116 g) was added at such a rate as to keep the reaction temperature below 20°C. Water (26 m*l*) was added, drop by drop, the continuously stirred and cooled mixture over an about 30-min period to pervent the temperature from rising above 20°C. The reaction mixture was kept for 10 hr at room temperature. Chloroform (60 m*l*) was added, and the mixture was filtered. The chloroform layer was washed with water, a saturated sodium bicarbonate solution and then water, subsequently it was dried, and the chloroform was removed. The recrystallization of the residue from ether gave needles of **7** (51 g), mp 107—109°C. $[\alpha]_D^{24.0}$ −134.8°(0.994). Found: C, 39.46; H, 4.35; Br, 20.41%; mol wt 400. Calcd for $C_{13}H_{17}O_9Br$: C, 39.28; H, 4.29; Br, 19.89%; mol wt 397.19.

*Methyl 3,4,5-Tri-*O*-acetyl-2-deoxy-*L*-threo-hexulopyranosonate-2,3-ene (****12****).* *(1) Synthesis*: To a suspension of mercuric cyanide (13.7 g) in dry toluene (300 m*l*), a dry toluene solution (100 m*l*) of **7** (21 g) was added. Traces of water were removed by azeotropic distillation with toluene. After it had been refluxed for 10.5 hr with stirring, the reaction mixture was filtered and the filtrate was evaporated. The residue was extracted with chloroform (500 m*l*) and the chloroform was washed with a 30% potassium iodide solution and then water and dried. The subsequent removal of the chloroform gave a brown syrup. The repeated recrystallization of the syrup from ether gave needles of **12** (8 g), mp 109—111°C. $[\alpha]_D^{21.0}$ +236.9° (0.966). UV 243 (ε 7.6×10^3). IR(KBr) 1780—1720, 1655 (C=O, C=C). NMR H_4, 4.58^m, 5.02^m, H_6 5.60^m, $H_{6'}$ 5.97^m. Found: C, 49.41; H, 5.14%; mol wt 315. Calcd for $C_{13}H_{16}O_9$: C, 49.37; H, 5.10%; mol wt 316.26.

(2) Reaction in Benzene Containing Boron Trifluoride-etherate: A solution of **12** (1.0 g) in dry benzene (10 m*l*) containing boron trifluoride-etherate (0.5 m*l*) was refluxed with stirring, and then the solvent was removed. The residue was fractionated by ptc (solvent D_1). Fractions 1, 2, 3, 4, and 5 corresponded to **16**, **18**, **23**, **15**, and **19** respectively. The yields in mg are shown below:

Product	Reaction time			
	1 hr	3 hr	5 hr	13 hr[a]
15	194	157	27	56
18	31	32	41	—
16	22	47	131	115
23	54	46	22	32
19	trace	trace	trace	trace

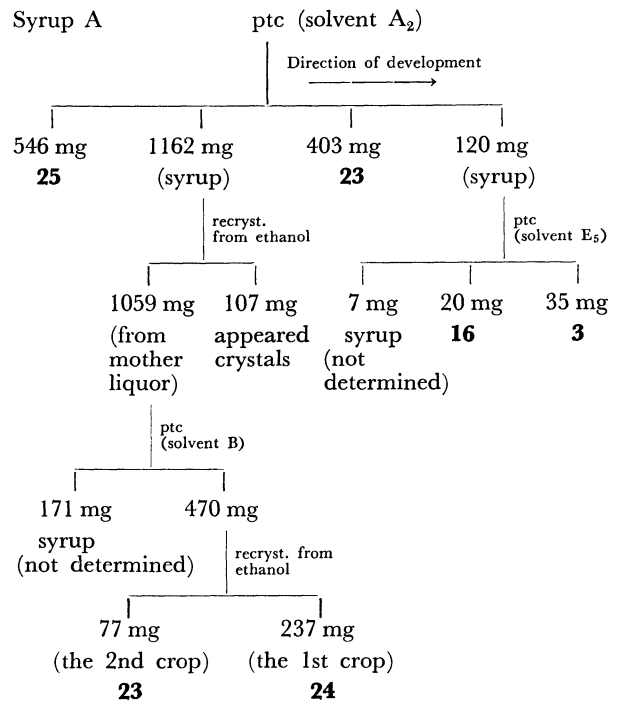
a) As a solvent, 1,2-dimethoxyethane was used instead of benzene.

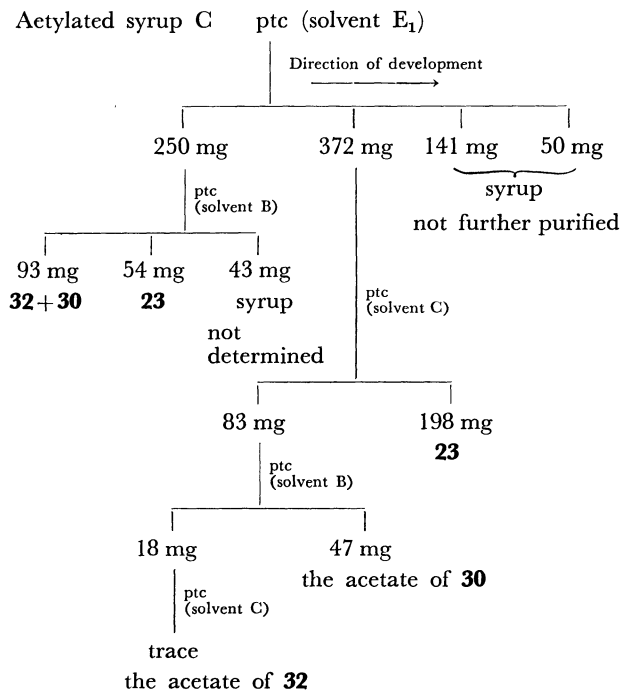
19: mp 48.49°C. $[\alpha]_D^{21.5}$ 0° (1.275). UV 226 (ε 9.9×10^3). IR(KBr) 3450 (OH), 1775, 1688, 1623 (C=O, C=C). NMR H_4, 3.75^m ($J_{4,5}$ 10.5, $J_{4,6}=J_{4,6'}$ 2), H_5 2.85^m ($J_{5,6}=J_{5,6'}$ 3), $J_{6,6'}$ 5.55^m, 5.25 ($J_{6,6'}$ −19). Found: C, 48.96; H, 4.66%. Calcd for $C_7H_8O_5$: C, 48.84; H, 4.68%. **23**: mp 149—150°C (recryst. from methanol). UV 285 (ε 8.1×10^3), IR(nujol) 1765, 1739, 1689, 1620 (C=O, C=C). NMR $H_{5,5'}$, 5.22^t ($J_{5,6}$ 7), $H_{6,6'}$, 5.22^t. Found: C, 50.71; H, 4.77%; mol wt 218. Calcd for $C_9H_{10}O_6$: C, 50.47; H, 4.71%; mol wt 214.17.

(3) Reaction in Acetic Acid-Water: A solution of **12** (18 g) in acetic acid (18 m*l*) and water (162 m*l*) was heated on a boiling-water bath for 6 hr, and then, after cooling, extracted with chloroform (50 m*l*×4). The aqueous layer was evaporated to dryness. A syrup (5.9 g) was thus obtained (syrup C). The chloroform layer was washed with a 5% sodium carbonate solution (60 m*l*×2) and water, and dried, and then the chloroform was removed. An yellow syrup, (2.7 g) was thus obtained (syrup A). The sodium carbonate solution was made acid to pH 2 with hydrochloric acid, and extracted with chloroform, and then the chloroform was removed. Another syrup (520 mg) was thus obtained (syrup B). Syrup A was fractionated by ptc as follows:

The syrup B was purified by ptc (solvent B). Fifty-five milligrams of **24** were obtained.

The syrup C (2.0 g) was dissolved in dry pyridine (10 m*l*), and the pyridine salt of oxalic acid thus precipitated (424 mg) was collected by filtration. To the filtrate, we added acetic anhydride (10 m*l*). The solution was kept at room temperature for 2 days and then evaporated to dryness. The residue (2.4 g) was fractionated by ptc as follows:





24: mp 78—79°C. UV 325 (ε 8.3×10^3). Found: C, 48.65; H, 4.65%; mol wt 182. Calcd for $C_7H_8O_5$: C, 48.84; H, 4.68%; mol wt 172.13. **32** (acetate): syrup. UV(MeOH) 267 (ε 7.9×10^3). IR(film) 1760, 1670, 1620 (C=O, C=C). NMR H_1 2.62^s, $H_{4,4'}$ 7.31^q, $H_{5,5'}$ 5.47, CH_3-COO 7.81^s (Satisfactory elementary analysis was not obtained). **30** (acetate): syrup. IR(film) 745 (OAc). NMR H_1 5.32^s, $H_{3,4}$ 7.25^t, 5.65^t, CH_3COO 7.85^s, 8.00. Found: C, 51.14; H, 6.35%. Calcd for $C_8H_{12}O_5$: C, 51.66; H, 6.43%.

Reduction of ***23***. To a solution of **23** (3.0 g) in pyridine (70 m*l*) we added finely powdered sodium borohydride (0.8 g) at 0°C under cooling. The solution was allowed to stand for 3 days in a refrigerator, made acidic with acetic acid and then evaporated to dryness. The residue was added to a mixture of acetic anhydride (75 m*l*) and pyridine (75 m*l*), left to stand in a refrigerator for 4 hr, and then evaporated to dryness. The residue was purified by ptc (R_f 0.75, solvent D_2), followed by ptc (R_f 0.31, solvent E_6). Eighty-one grams of **9** were thus obtained as a syrup. UV 240 (7.4×10^3). IR(KBr) 1740, 1640 (C=O, C=C). NMR ACO 7.95^s, COOMe 6.19, H_3 (Ha) 3.89^d ($J_{3,4}$ 5.0), H_4 4.75^m, $H_{5,5'}$ 7.43—8.17^m, $H_{6,6'}$ 5.46—6.14^m. Found: C, 53.40; H, 6.10%; mol wt 210. Calcd for $C_9H_{12}O_5$: C, 53.99; H, 6.04%; mol wt 200.12.

Reaction of ***23*** *in Acetic Acid–Water.* (1) A mixture of **23** (500 mg), acetic acid (0.5 m*l*), and water (4.5 m*l*) was heated on a boiling-water bath. After 3 hr, the reaction mixture was worked up in a manner similar to the one described above. The acetate of **30** (31 mg) was obtained.

(2) A mixture of **23** (2.5 g), acetic acid (2.5 ml) and water was heated on a boiling-water bath for 6 hr, and then worked up in a manner similar to the one described above. The pyridine salt of oxalic acid (10 mg), the acetate of **30** (15 mg), **24** (248 mg), and a mixture of the acetates of **30** and **32** (28 mg) were obtained.

*Methyl 3,4-Di-*O*-acetyl-*L*-*threo*-hexulopyranosonate-2,3-ene (****25****).* To a solution of **12** (4.0 g) in a mixture of dioxane (10 m*l*) and methanol (400 m*l*), we added a solution of potassium carbonate (2.0 g) in water (10 m*l*) below 5°C. After stirring for 30 min, the solution was neutralized by Amberlite IR 120 and then evaporated to dryness. The purification of the residue by ptc (solvent A_2) gave **25** (syrup, 0.68 g). $[\alpha]_D^{22}+222.1°$ (0.592). UV 247.5 (ε 1.47×10^4). IR(CCl_4) 3500 (OH). 1780, 1750, 1675 (C=O, C=C). NMR H_4 5.65^m, H_5 5.9—6.2^m. Found: C, 47.88; H, 5.35%; mol wt 295. Calcd for $C_{11}H_{14}O_8$: C, 48.14; H, 5.15%; mol wt, 274.32.

*Methyl 3,4-Di-*O*-acetyl-5-*O*-benzoyl-*L*-threo-hexulopyranosonate-2,3-ene (****26****).* *(1) Synthesis*: To a solution of **24** (1.0 g) in pyridine (10 ml), we added freshly distilled benzoyl chloride (1.0 g) under cooling, and then the mixture was left to stand overnight in a refrigerator. The solution was poured into water and extracted with chloroform. The chloroform was washed with 5% hydrochloric acid, a 5% sodium carbonate solution and then water, and dried, and the solvent was removed. The residual syrup was purified by ptc (solvent D_3). One gram of **26** was thus obtained, mp 120—121.5°C. $[\alpha]_D^{25.6}+256.7°$ (0.379). UV 233.5 (ε 2.0×10^4), 282 (ε 9.4×10^2). IR(KBr) 1777, 1743, 1727, (C=O, C=C). 1600 (phenyl). NMR H_4 4.41^m, H_5 4.75^m ($J_{4,5}$ 2.5), H_6 5.42^m ($J_{5,6}$ 3.0, $J_{4,6}$ 1.5), $H_{6'}$ 5.86^m ($J_{5,6}=J_{4,6}$ 1.5). Found: C, 57.29; H, 4.92%. Calcd for $C_{18}H_{18}O_9$: C, 57.14; H, 4.80%.

(2) Reaction in Benzene Containing Boron Trifluoride-etherate: A solution of **26** (750 mg) in dry benzene (7.5 m*l*) containing boron trifluoride-etherate (0.4 m*l*) was refluxed for 1 hr and then evaporated to dryness. The residue was fractionated into two fractions by ptc (solvent D_3). The slow-moving compound (270 mg) was **15**. The fast-moving fraction was further fractionated to two fractions and benzoic acid by ptc (solvent F). The fast-moving fraction (18 mg) contained **16** and **18**, and the slow-moving one, **27**. **27**: syrup. $[\alpha]_D^{25.6}$ 0.° UV 232.5 (ε 2.1×10^4), 276 (ε 1.2×10^3). IR (CCl_4) 1778, 1747, 1626 (C=O, C=C). Found: C, 60.99; H, 4.55%. Calcd for $C_{14}H_{12}O_6$: C, 60.87; H, 4.38%.

*Methyl 2-*O*-Benzoyl-4,5-dideoxy-2,3-hexodiulopyranosonate-4,5-ene (****27****).* To a solution of **19** (0.1 g) in pyridine (1 ml) we added benzoyl chloride (0.1 g), and then the mixture was left overnight in a refrigerator. The solution was poured into water and extracted with chloroform. The chloroform

was washed with 5% hydrochloric acid, a 5% sodium carbonate solution and then water; subsequently it was dried, and the solvent was removed. The residue was purified by ptc (solvent E_3), Pure **27** (0.1 g) was thus obtained.

*The Decrease Rates of **11** and **12**.* Kinetic measurements were made polarimetrically. About 0.025 mol of **11** (or **12**) was dissolved in an appropriate volume of benzene in a 250-m*l* volumetric flask at 50°C. Boron trifluoride-etherate (1 m*l*) was added to the solution, and the flask was filled exactly to the mark with benzene at 50°C. Samples (2 m*l*) was quickly transfered to a 5-m*l* volumetric flask containing triethylamine (0.1 m*l*); the flask was filled exactly with methanol at 25° for an optical rotation determination at 578 nm. The decreases in optical activities obeyed first-order kinetics. k_1 (decrease of **11**): 2.9×10^{-5} sec^{-1}; k_2 (decrease of **12**): 4.4×10^{-4} sec^{-1}.