δ-Dicarbonyl Sugars. 5. A Novel Synthesis of a Branched-Chain Cyclitol[1]

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The cyclization of tri-*O*-acetyl-1,7-dideoxy-1,7-bis(diazo)-*xylo*-2,6-heptodiulose (**5**), in acetic acid solution, to DL-3-*C*-acetoxymethyl-2,4,5,6-tetra-*O*-acetyl-2,3,4,6/5-pentahydroxycyclohexanone (**8**) is described. This conversion, considered to take place by way of a carbene, represents a new synthesis of the cyclitol ring system. The reactive diketone (**5**) was prepared by a diazomethane chain extension sequence originating with D-xylose (**1**). Reduction of the keto carbonyl of **8** followed by the acetylation of the resulting products gave DL-2-*C*-acetoxymethyl-1,3,4,5,6-penta-*O*-acetyl-*epi*-inositol (**12**). A minor product from the decomposition of **5** was identified as penta-*O*-acetyl-*xylo*-2,6-heptodiulose (**9**).

The biosynthetic pathways that lead to the carbocyclic ring system as it is found in the cyclitols[3] are thought to involve enzyme-catalyzed aldol condensations of appropriate δ-dicarbonyl monosaccharides. We have recently discovered that some synthetically prepared derivatives of this class of carbohydrates can be chemically induced to undergo these same ring closures.[1,4] This paper describes a new route to the acetylated hydroxymethylcyclitol DL-2-*C*-acetoxymethyl-1,3,4,5,6-penta-*O*-acetyl-*epi*-inositol (**12**) by way of an unusual cyclization of a bisdiazo ketone (**5**) derived from *xylo*-2,6-heptodiulose.

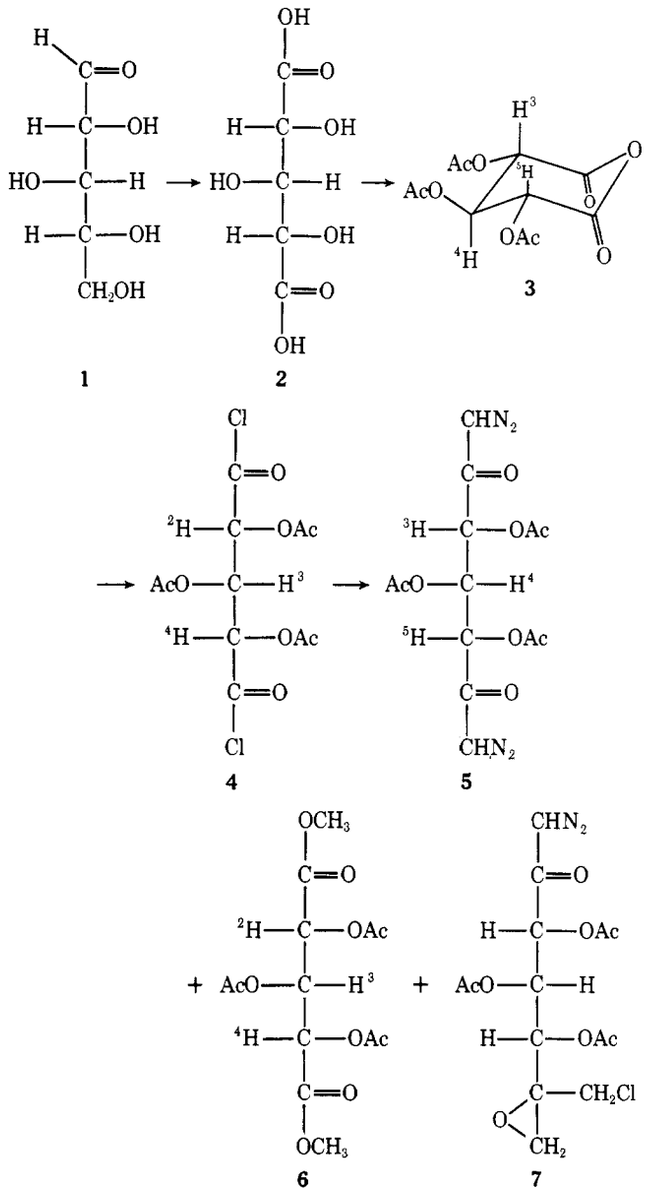
Results and Discussion

The bisdiazo ketone **5** was prepared by a standard diazomethane chain extension sequence beginning with D-xylose (**1**) (Scheme I). In order to obtain satisfactory yields of xylaric acid (**2**) and tri-*O*-acetylxylaric anhydride (**3**), it was necessary to modify the Wolfrom and Usdin procedure for the synthesis of these compounds.[5] When the oxidation of D-xylose with nitric acid was completed, excess oxidizing agent was destroyed with 2-propanol and crystalline xylaric acid was obtained in 44% yield. Deletion of the 2-propanol addition step in the workup procedure resulted in the isolation of a syrup that did not crystallize and eventually decomposed. When the anhydride **3** was prepared by refluxing zinc xylarate in acetyl chloride,[5] the average yield of the product from the reaction was only 30%. Furthermore, the anhydride obtained in this way gradually underwent an irreversible phase change to an oil. However, stable **3** was synthesized in reasonable yield (70–80%) by treating **2** with acetic anhydride that contained a catalytic amount of sulfuric acid.

Syrupy tri-*O*-acetylxylaryl dichloride (**4**),[6] prepared by refluxing the half sodium salt of **2** triacetate with thionyl chloride, was treated with an ether solution of diazomethane and tri-*O*-acetyl-1,7-dideoxy-1,7-bis(diazo)-*xylo*-2,6-heptodiulose (**5**) crystallized as yellow needles directly from the reaction mixture (68%). Thin-layer chromatography of the mother liquors showed a three-component mixture. Silica gel column chromatography of this residue gave first dimethyl tri-*O*-acetylxylarate (**6**). Next off the column was a mixture (ca. 40% of the material from the column) of **7** and an unidentified compound. The characterization of **7** is described in the following paper (ref 18). The third component, **5**, was also isolated (5%).

The bisdiazo ketone **5**, when dissolved in acetic acid that contained cupric acetate, rapidly decomposed (5 min) at 70 °C to give **8** (32%), which crystallized directly from the reaction mixture (Scheme II). The conversion was also accomplished without the presence of copper ion, but required a higher temperature (80–90 °C), and a significantly longer reaction time (10 h).

Scheme I



A first-order analysis of the ^1H NMR spectrum of **8** (Figure 1) clearly showed large coupling (J = 10.0 Hz) between H-5, H-6, and H-4, H-5, thus establishing the consecutive anti relationship of these three ring protons. Propanic long-range coupling in the molecule was evidenced by small splitting of the H-4 doublet and broadening of the H-2 singlet. The value

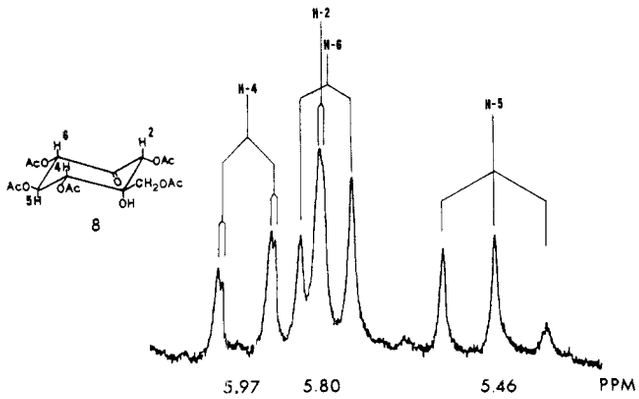


Figure 1. 90-MHz ^1H NMR spectrum of **8** in Me_2SO-d_6 (ring proton region).

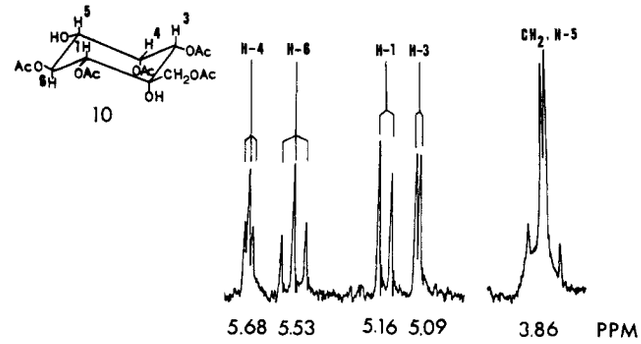
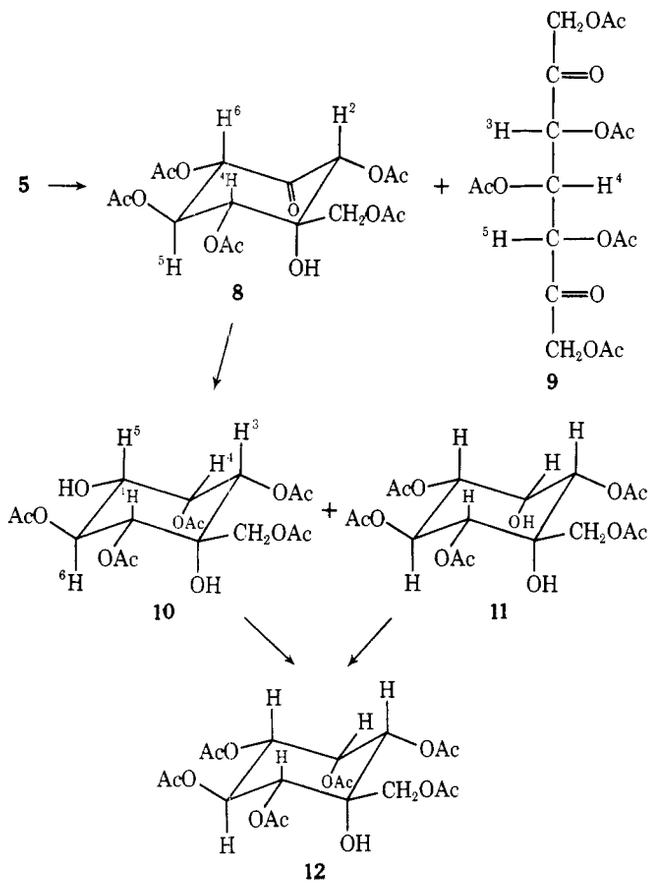


Figure 2. 220-MHz ^1H NMR spectrum of **10** in $CDCl_3$ (ring proton region).

Scheme II



of the coupling (J = 0.8 Hz) falls within the normal range of propanic coupling (−0.3–0.9 Hz) for 1,3-diaxially oriented protons.[7] Excellent agreement between the observed spectrum and the theoretical spectrum served to confirm these assignments.[8]

Two isomeric crystalline cyclitol pentaacetates (**10** and **11**) were obtained after the keto carbonyl of **8** was reduced by catalytic hydrogenation in acetic acid. The minor product (**10**) in the mixture was presumably formed from the major product (**11**) by an acid-catalyzed acetyl migration to the hydroxy group generated in the reduction step. The stereochemistry at four of the ring carbons of **10**, C-1, C-4, C-5, and C-6, was deduced after analysis of the 220-MHz ^1H NMR spectrum of the compound (Figure 2). However, the stereochemistry at C-3 is not discernible from the H-3, H-4 coupling, since the two protons are gauche when H-3 is axial or equatorial. The coupling constants assigned to the ring protons of **10** were unchanged in the ^1H NMR spectrum of **11**, the major product from the reduction of **8** (Table I).

Acetylation of **10** and **11** gave the cyclitol hexaacetate, DL-2-*C*-acetoxymethyl-1,3,4,5,6-penta-*O*-acetyl-*epi*-inositol (**12**). The splitting of the ring proton signals in the ^1H NMR spectrum of **12** was in accord with the assigned stereochemistry for **10** and **11**. The problem of ascertaining the stereochemistry at the remaining two ring carbons common to **8**, **10**, **11**, and **12** was resolved by an x-ray crystallographic structure determination of **10**.[9] The x-ray study revealed that the tertiary hydroxyl group of **10** is axial and both vicinal acetoxy groups equatorial. The ^1H NMR derived stereochemical assignments for the four previously discussed ring protons were found to be correct. The free cyclitol derived from **12**, 2-hydroxymethyl-*epi*-inositol, has been prepared in crystalline form,[10] and most recently by deacetylation of **12**.[11]

The mother liquors from the cyclization of **5**, about 60% of the material in the reaction mixture, were chromatographed on a column of silica gel to give ca. 5% of a single crystalline compound, the acyclic pentaacetate **9**. The poor recovery of material from the column was due largely to extensive decomposition of unidentified compounds in the mixture on the silica gel. However, TLC showed that even at best **9** was a minor component in the original reaction mixture.

Prompted by the successful cyclization of **5**, we sought to gain additional insight into the requirements for this type of ring closure. Two modifications in the structure of the bisdiazo ketone were considered to be the most important for the study: (1) removal of the bulky acetoxy groups from the molecule to see if these groups were responsible for a conformation favorable for cyclic product formation, and (2) changing the type of carbonyl group which was affected in the cyclization. The first modification was realized with 1,7-bis(diazo)heptane-2,6-dione[12] (**15**), while methyl tri-*O*-acetyl-6-deoxy-6-diazo-DL-*xylo*-5-hexulosonate (**14**) satisfied the structural requirement prescribed by the second modification. The preparation of **14** was accomplished in several steps beginning with the anhydride **3**. The first step in the sequence, the methanolysis of **3**, gave the methyl ester **13** and the dimethyl ester **6** in almost equal amounts (Scheme III).

The cupric acetate catalyzed decomposition of **15** in acetic acid at 70 °C gave, as the only identifiable product, the crystalline acyclic diacetate **16** (74%) (Scheme III). The attempted cyclization of **14** in acetic acid yielded a mixture which TLC showed to be composed of a major product and at least two slower moving minor products. The principal product was isolated by silica gel column chromatography (39%) and spectral data and elemental analysis confirmed that the compound was methyl tetra-*O*-acetyl-DL-*xylo*-5-hexulosonate (**17**)[13] (Scheme III). The minor products from the column chromatographic separation were not obtained pure enough or in large enough quantities for identification. The apparent reluctance of either **14** or **15** to cyclize under the conditions

Table I. Proton Magnetic Resonance Chemical Shifts and Coupling Constants for Compounds 2–6 and 8–17

Compd[a-c]	Registry no.	Solvent	H_1, δ	H_2, δ	H_3, δ	H_4, δ	H_5, δ	H_6, δ	Other δ	$J_{2,3'}$, Hz	$J_{3,4'}$, Hz	$J_{4,5'}$, Hz	$J_{5,6'}$, Hz	$J_{1,6'}$, Hz
2	10158-64-2	Me_2SO-d_6		4.05, d	3.89, t	4.05, d				4.38	4.38			
		D_2O[21]		3.96, d	3.72, t	3.96, d				4.14	4.14			
3	63181-58-8	Me_2SO-d_6			6.20	6.05	6.20			11.0	11.0			
4	63181-59-9	$CDCl_3$		5.60, d	5.85, d	5.60, d				5.0	5.0			
5	38910-01-9	$CDCl_3$	5.51		5.37, d	5.73, t	5.37, d				5.03	5.03		
6	63181-60-2	$CDCl_3$		5.36, d	5.71, t	5.36, d				4.61	4.61			
8	63229-94-7	Me_2SO-d_6		5.82		5.97, dd	5.46, t	5.80, d	3.90 (s, 2, CH_2)			10.0	10.0	
9	38877-05-3	$CDCl_3$			5.46, d	5.74, t	5.46, d				4.33	4.33		
10	43068-08-2	$CDCl_3$	5.16, d		5.09, d	5.68, t	3.86, m	5.53, t			3.5	3.5	10.0	10.0
11	63229-95-8	$CDCl_3$	5.18, d		4.95, d	3.88, m	5.04, dd	5.68, t			3.5	3.5	10.0	10.0
12	52795-30-9	$CDCl_3$	5.23		5.16	5.69	5.15	5.71			3.63	3.12	10.17	10.44
13	63181-61-3	$CDCl_3$		5.44, d	5.73, t	5.44, d				4.57	4.57			
14	63181-63-5	$CDCl_3$		5.34, d	5.80, t	5.44, d		5.58		5.01	6.84			
15	27475-07-6	$CDCl_3$	5.30		2.40, t	2.00, m	2.40, t				7.0	7.0		
16	63181-64-6	$CDCl_3$			2.20, t	2.04, m	2.20, t				7.0	7.0		
17	63229-96-9	$CDCl_3$		5.13	5.47	5.70				4.47	4.55			

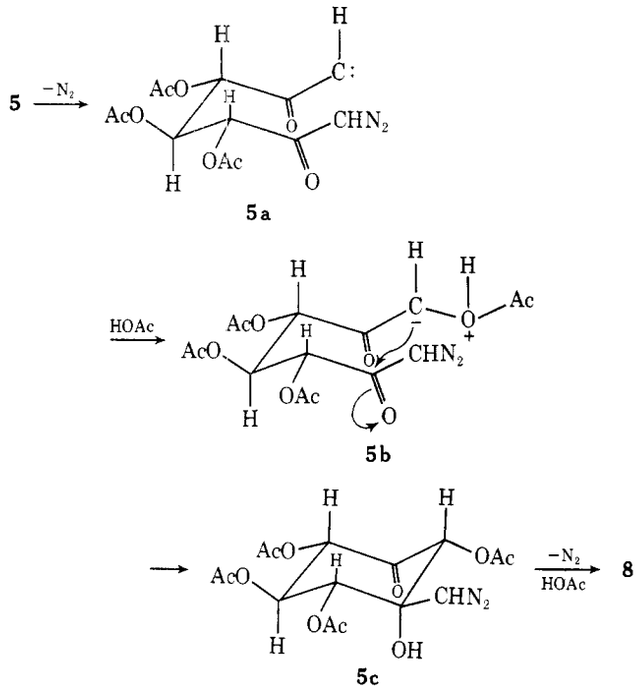
[a] The spectra of compounds 2, 3, 4, 5, 6, 8, 9, 12, 13, 14, and 17 were computer analyzed by LAOCOON III program (see ref 8). All parameters sets have a rms error less than 0.2 Hz. [b] The spectra of compounds 14–16 were recorded at 60 MHz; the spectra of compounds 9–12 at 220 MHz, and the remaining spectra at 90 MHz. [c] The measured values of the coupling constnats of compounds 2, 4, 5, 6, 9, 13, 14 and 17 lie between 4.33 and 5.01 Hz and indicate that the sickle conformer is the major conformer of these acyclic xylo derivatives (see ref 15 and 16).

Scheme III

whereby **5** was converted to the cyclose 8 (Scheme IV) suggests that a proper combination of backbone substitution and carbonyl reactivity is necessary for ring closure to occur.

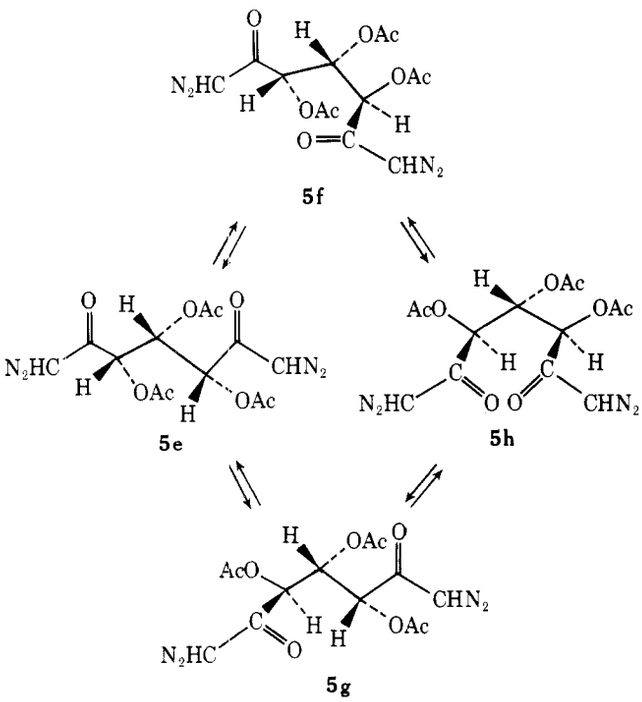
Mechanistic Considerations. The thermal decomposition of a diazo ketone in an aprotic solvent generally gives a carbene, whereas diazonium and carbonium ions are the favored products when the decomposition is carried out in a protic solvent, particularly in the presence of added mineral acid.[14] However, Yamamoto and Moritani reported that decomposition of diethyl diazosuccinate in the protic solvent acetic acid to the corresponding carbene accounted for 66% of the olefinic products, diethyl fumarate and diethyl maleate.[15] In the less acidic solvents ethanol and cyclohexanol, even higher percentages of olefin were produced by the carbene pathway. The mechanism we propose for the formation of the cyclose 8 in acetic acid from the bisdiazo ketone **5** also involes a carbene (**5a**). The reaction between this electrophilic intermediate and the solvent, acetic acid, may then give the ylide **5b**, which can convert to the acyclic pentaacetate **9**, or by a simple intramolecular aldol condensation to **5c**, a precursor of **8**. A similar but less probable scheme would be initiated by the generation of a dicarbene directly from **5**.

Scheme IV



In the ^1H NMR spectrum of **5**, the value of the observed coupling constant between H-4 and equivalent H-3 and H-5 ($J_{3,4} = J_{4,5} = 5.0$ Hz) is intermediate between the predicted value for a consecutive gauche arrangement ($J \simeq 3$–4 Hz) and a consecutive anti arrangement ($J \simeq 7$–10 Hz) of the three protons. In considering some idealized conformational possibilities for **5** (Scheme V), the smaller value of the coupling

Scheme V



constant would account for a planar zigzag arrangement of protons and bulky acetoxy groups (**5e**) while a U conformation (**5h**)[16] would fit the larger value of J. The destablizing 1,3 interactions between the eclipsed acetoxy groups in the zigzag conformation can be relieved by rotating either C-3 or C-5 120°. The resulting enantiomeric sickle conformations, **5f** and **5g**, can then be converted directly to the U conformation by rotating previously undisturbed C-5 or C-3 120°.

The low yield conversion of **5** to the acyclic pentaacetate **9** rules against a high percentage of zigzag conformation **5e** being in the reaction mixture at the temperature (70 °C) that **5** decomposed. This conclusion is also based on the assumption that the distribution of the active carbene conformational isomers is essentially the same as that of the precursor bisdiazo ketone conformations. The fact that the substitued bisdiazo ketone **5** produces the cyclic product **8** under the same conditions whereby the unsubstituted bisdiazo ketone **15** gives the acyclic diacetate (**16**) serves to underline the importance of the U conformation (**5h**) for **5** in acetic acid solution. It should be pointed out that in inert solvents the copper-catalyzed decomposition of **15** does give a cyclic product (15–32%), cyclohept-2-ene-1,4-dione,[17] presumably by a dicarbene coupling. However, we found no evidence that either **5** or **15** underwent this kind of ring closure in acetic acid. If such a product was formed from **5** it must have decomposed in the silica gel column chromatographic purification of **9**.

The methyl ester–diazo ketone **14**, since it is structurally akin to **5**, should be conformationally disposed to cyclize. The absence of cyclic products in the decomposition mixture from **14** may simply mean that the methyl ester carbonyl carbon is not electrophilic enough to react with the anionic portion of the ylide, a step that gives the carbocyclic ring. Instead, the ylide is preferentially converted to the final acyclic product **17**.

Experimental Section

General Methods. Melting points were obtained with a Fischer-Johns melting point apparatus and are uncorrected. The ^1H NMR spectra were recorded at 60, 90, or 220 MHz with tetramethylsilane as the internal standard. The IR spectra were obtained with a Perkin-Elmer Model 337 grating infrared spectrophotometer. Thin-layer chromatography was performed on plates coated with silica gel GF-254 (E. Merck, Darmstadt) and the components were detected by spraying with 20% sulfuric acid. Column chromatography was carried out with columns of silica gel (0.05–0.20 mm; E. Merck). All chromatographic solvent systems employed are given as volume to volume ratios and column dimensions are given as length and outside diameter. Mass spectra were recorded with an LKB-9000 combined gas chromatograph–mass spectrometer or a Hitachi-Perkin Elmer Model RMU-7 double focusing mass spectrophotometer. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. 37921.

Xylaric Acid (2). A solution of D-xylose (**1**, 101 g) in water (78 mL) was charged to a 1-L round-bottom flask equipped with a reflux condenser and magnetic stirrer. Concentrated nitric acid (70%, 203 mL) was added to the flask and the solution was carefully heated until evolution of nitric oxide began (ca. 60 °C). The reaction mixture was immediately transferred to an ice bath until the gas evolution subsided. The flask was then allowed to stand at room temperature for 15 min. The temperature of the solution was maintained at 60 °C for 2 h, and then gradually raised to 90 °C over 30 min. After keeping the reaction mixture at 90 °C for 10 min, the solution was cooled to 60 °C, and 2-propanol (200 mL) was added with stirring in 20-mL portions to destroy excess nitric acid. The solution was diluted with water (100 mL), then with concentrated HCl (10 mL), and warmed at 60–70 °C for 30 min. The yellowish-green solution was concentrated in vacuo at 50 °C until it became a syrup or semicrystalline mass. This material was then taken up in 2-propanol (100 mL), the solution refluxed for 30 min, and then concentrated in vacuo at 50 °C to yield a tacky semicrystalline product. The tacky product was freed of some residual water by freeze drying for 30 min and the resulting crystalline mass was then broken up and washed with cold acetone (50 mL). The suspension was filtered and washed several times with cold acetone to give 53 g (44%) of **2**; mp 145–147 °C (lit.[5] 150–151 °C).

Tri-*O*-acetylxylaric Anhydride (3). A solution of xylaric acid (**2**, 18 g) in acetic anhydride (60 mL) and concentrated sulfuric acid (0.10 mL) was kept at 60 °C for 3 h. The solution was concentrated in vacuo at 70 °C to give a white solid product, which was washed with chloroform (50 mL) and recrystallized from ethyl acetate to give 21 g (73%) of **3**; mp 162–164 °C (lit.[5] 146–147 °C); IR (KBr) 1760 cm^{-1} (broad C=O).

Tri-*O*-acetylxylaryl Dichloride (4). Sodium bicarbonate (3 g, 0.035 mol) was slowly added to a solution of tri-*O*-acetyl xylaric an-

hydride (**3**, 10 g, 0.035 mol) in water (30 mL). The aqueous solution was decolorized with carbon, the suspension filtered, and the filtrate concentrated in vacuo at 50 °C to give a colorless oil that crystallized overnight. The crystalline mass was washed with acetone and the mixture filtered to yield sodium hydrogen tri-*O*-acetylxylarate (11.0 g, 97%). After the salt was dried at ca. 0.10 mmHg for 2 h at 80 °C, it was added to thionyl chloride (40 mL) and the suspension refluxed for 2 h. Excess thionyl chloride was removed in vacuo to give a syrup which was stirred in benzene (50 mL) or ether (15 mL) and then filtered. The filtrate was decolorized with charcoal and concentrated in vacuo to yield crude tri-*O*-acetylxylaryl dichloride (**4**, 11.0 g): IR (neat) no O–H stretching vibrations, 1760 cm^{-1} (C=O). The acid dichloride was used in the preparation of **5** without further purification.

Tri-*O*-acetyl-1,7-dideoxy-1,7-bisdiazo-*xylo*-2,6-heptodiulose (5). A solution of the acid chloride **4** (10.0 g, 0.03 mol) in anhydrous ether (30 mL) was slowly added to a cold (dry ice–acetone bath) stirred solution of diazomethane (0.30 mol) in ether (275 mL). The ether solution was allowed to warm to 0 °C and after 30 min was cooled again (dry ice–acetone bath) with stirring for 1 h. The product was isolated by carefully filtering the mixture under the hood. A solution of the yellow compound in acetone (2 mL) was slowly added to boiling ether (200 mL), the ether solution was concentrated to half volume and upon standing yielded 7.0 g (68%) of the bisdiazo ketone **5**: mp 118–120 °C; IR(KBr) 2100 (C=N=N), 1740 (ester C=O), and 1640 cm^{-1} (N=N).

Anal. Calcd for $C_{13}H_{14}N_4O_8$ (354.28): C, 44.08; H, 3.98; N, 15.81. Found: C, 44.02; H, 4.05; N, 15.89.

The mother liquors were cooled to between −50 and −20 °C in a dry ice–acetone bath and glacial acetic acid was added until no more nitrogen evolved. The solution was freed of acetic acid by azeotropic distillation with benzene in vacuo. The residual syrup was dried in vacuo (ca. 1 mmHg) for 5 h. A TLC analysis (dichloromethane–ether, 4:1) showed that the oil was composed of three products having R_f values of 0.90, 0.75, and 0.60, respectively. The syrup (3.8 g) was dissolved in a minimum amount of dichloromethane–ether (8.5:1.5) and chromatographed on silica gel (250 g in a 30 × 460 mm column) with the same solvent. The fastest moving component of the mixture was identified as dimethyl tri-*O*-acetylxylarate (**6**, 0.15 g): mp 60–62 °C; IR(KBr) 1750 cm^{-1} (C=O).

Anal. Calcd for $C_{13}H_{18}O_{10}$ (334.29): C, 46.71; H, 5.43. Found: C, 46.93; H, 5.33.

The second component (1.30 g), R_f 0.75, was isolated as an oil. From the oil, 0.55 g of 3,4,5,-tri-*O*-acetyl-6,7-anhydro-6-chloromethyl-1-deoxy-1-diazo-DL-*ido*-2-heptulose (**7**) was obtained.[18] The slowest moving component was the bisdiazo ketone **5**. The 0.62 g of this material was combined with the first crop of crystalline **5**, making its overall yield 73%.

Decomposition of 5 with Acetic Acid. A solution of **5** (3 g) in acetic acid (15 mL) containing cupric acetate (10 mg) was slowly heated until the evolution of nitrogen began (bath temperature 70 °C). The temperature was maintained at 70 °C for 5 min and the reaction mixture afforded 1.15 g (32%) of DL-3-*C*-acetoxymethyl-2,4,5,6-tetra-*O*-acetyl-2,3,4,6/5-pentahydroxycyclohexanone (**8**). The white solid, which gave a positive Scherer's test for a cyclitol,[19] was recrystallized from acetic acid as colorless plates: mp 240–242 °C; IR (KBr) 3320 (O–H) and 1725 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* (rel intensity) 376 (16), 358 (27), 345 (49), 316 (16), 196 (34), 154 (36).

Anal. Calcd for $C_{17}H_{22}O_{12}$ (418.36): C, 48.81; H, 5.30. Found: C, 48.76; H, 5.47.

Isolation of Penta-*O*-acetyl-*xylo*-2,6-heptodiulose (9) by Column Chromatography. The mother liquor from the reaction of **5** with acetic acid was freeze-dried to give a reddish-brown oil (1.8 g). Thin-layer chromatography (ether) of the oil showed considerable streaking with an intensified spot at R_f 0.60. The mixture was chromatographed on silica gel (90 g in a 25 × 370 mm column) by eluting with ether. The fractions composed mostly of the material of R_f 0.60 were combined and concentrated to give a light yellow oil (0.83 g). A solution of the oil in ether (10 mL), after standing overnight, yielded 0.20 g (5%) of penta-*O*-acetyl-*xylo*-2,6-heptodiulose (**9**): mp 90–92 °C; IR (KBr) no O-H stretching vibrations, 1750 cm^{-1} (C=O).

Anal. Calcd for $C_{17}H_{22}O_{12}$ (418.36): C, 48.81; H, 5.30. Found: C, 48.83; H, 5.44.

Catalytic Hydrogenation of 8. A solution of **8** (0.40 g) in acetic acid (15 mL) was stirred at 50 °C for 25 h with hydrogen at atmospheric pressure and freshly prepared platinum generated from platinum oxide (0.40 g). The suspension was filtered and the filtrate concentrated in vacuo to give a colorless syrup which, by TLC (acetone–hexane, 1:1), was shown to consist of a major product, R_f 0.66, and a minor product, R_f 0.52. The syrup was dissolved in hot ethanol (5 mL) and ether (15 mL) was then added. The first crop of crystals (0.030 g, 7%) obtained from the mixture was the minor product, DL-2-*C*-acetoxymethyl-1,3,4,6-tetra-*O*-acetyl-*epi*-inositol (**10**): mp 209–211 °C; IR (KBr) 3460 (O–H) and 1725 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* (rel intensity) 402 (53), 347 (100), 300 (56), 288 (100), 269 (93), 245 (100), 241 (100).

Anal. Calcd for $C_{17}H_{24}O_{12}$ (420.38): C, 48.57; H, 5.75. Found: C, 48.38; H, 5.77.

A second crop of crystals (0.24 g, 60%) proved to be the major product DL-2-*C*-acetoxymethyl-1,3,5,6-tetra-*O*-acetyl-*epi*-inositol (**11**): mp 160–162 °C; IR (KBr) 3400 (O–H) and 1740 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* (rel intensity) 361 (21), 329 (32), 287 (87), 227 (98), 185 (100), 167 (62), 143 (66), 125 (100).

Anal. Calcd for $C_{17}H_{24}O_{12}$ (420.38): C, 48.57; H, 5.75. Found: C, 48.20; H, 6.03.

Acetylation of the Reduction Mixture Obtained from 8. A solution of the solid mixture (0.10 g) obtained from the hydrogenation of **8** in acetic anhydride (4 mL) and pyridine (1 mL) was kept at room temperature for 8 h and then concentrated in vacuo to give a single crystalline compound. The product, DL-2-*C*-acetoxymethyl-1,3,4,5,6-penta-*O*-acetyl-*epi*-inositol (**12**), was recrystallized from ethanol and 0.08 g (73%) was obtained: mp 189–191 °C; IR (KBr) 3480 (O–H) and 1740 cm^{-1} (C=O).

Anal. Calcd for $C_{19}H_{26}O_{13}$ (462.42): C, 49.36; H, 5.67. Found: C, 49.11; H, 5.90.

By the same procedure, **10** and **11** were each separately converted to the same hexaacetate **12**.

Methyl Hydrogen Tri-*O*-acetylxylarate (13). A solution of **3** (14 g) in dry methanol (100 mL) was refluxed 40 h and the reaction mixture concentrated to give a colorless oil. The oil was dissolved in water (50 mL) and a white solid formed when the aqueous solution was neutralized with sodium bicarbonate. The solid was removed by filtration and recrystallized from ether to give dimethyl tri-*O*-acetylxylarate (**6**, 3 g, 24%). The aqueous filtrate from the original reaction mixture was extracted with three 50-mL portions of chloroform. The water layer was made acidic by treating it with an acid form cation-exchange resin (8 mL, amberlite IR-120 H^+, 20–50 mesh), the resin was removed by filtration, and the filtrate was extracted with three 50-mL portions of chloroform. The combined chloroform extracts were concentrated to give a white solid, which, when recrystallized from ether, gave **13** (4.0 g, 26%): mp 125–127 °C; IR (KBr) 3000 (broad O–H), and 1725 cm^{-1} (C=O).

Anal. Calcd for $C_{12}H_{16}O_{10}$ (320.26): C, 45.01; H, 5.04. Found: C, 44.78; H, 5.10.

Methyl Tri-*O*-acetyl-6-deoxy-6-diazo-DL-*xylo*-5-hexulosonate (14). Sodium bicarbonate (0.40 g, 0.0054 mol) was slowly added to an aqueous solution (10 mL) of methyl hydrogen tri-*O*-acetylxylarate (**13**, 1.75 g, 0.0054 mol). The solution was concentrated in vacuo to a syrup, which was dried at room temperature and 0.10 mmHg for 2 h. The glassy solid was added to thionyl chloride (10 mL) and the mixture refluxed for 3 h. Additional thionyl chloride (15 mL in three 5-mL portions) was added during the refluxing period. The excess thionyl chloride was removed in vacuo, and the bulk of the gelatinous mass was dissolved in dry ether (50 mL). Residual inorganic salts were removed by filtration and the filtrate was concentrated in vacuo to give the crude syrupy acid chloride (1.5 g, 0.0044 mol, 82%). A solution of the acid chloride in dry ether (10 mL) was slowly added to a cold (dry ice–acetone bath) solution of diazomethane (1 g, 0.022 mol) in dry ether (50 mL). The reaction mixture was kept cold for 1 h and then concentrated under the hood to give a greenish-yellow oil. Thin layer chromatography (dichoromethane–ether, 4:1) of the mixture showed two products with R_f values 0.90 and 0.75, respectively. The oil (1.5 g) was chromatographed on silica gel (75 g in a 25 × 370 mm column) with dichoromethane–ether, 4:1, as the eluent. The major component, R_f 0.75, was isolated in chromatographically pure form as a light yellow oil (0.80 g, 53%) and identified as methyl tri-*O*-acetyl-6-deoxy-6-diazo-DL-*xylo*-5-hexulosonate (**14**): IR (neat) 2110 (C=N=N), 1740 (C=O), and 1640 cm^{-1} (N=N).

Anal. Calcd for $C_{13}H_{16}N_2O_9$ (344.28): C, 45.35; H, 4.68; N, 8.14. Found: C, 45.21; H, 4.68; N, 7.99.

1,7-Bisdiazoheptane-2,6-dione (15). Glutaryl dichloride was prepared by the method of Marvel and Casey.[20] A solution of dichloride (5.1 g, 0.03 mol) in anhydrous ether (30 mL) was slowly added to a cold solution (dry ice–acetone bath) of diazomethane (0.30 mol). After standing 1 h in the cold, the yellow precipitate was removed by filtration and recrystallized from ether to give 1,7-bis(diazo)heptane-2,6-dione (**15**) as yellow needles (4 g, 74%): mp 62–64 °C (lit.[17] 63–65 °C).

Decomposition of 14 in Acetic Acid. A solution of methyl tri-*O*-acetyl-6-deoxy-6-diazo-DL-*xylo*-5-hexulosonate (**14**, 0.75 g) and

cupric acetate (10 mg) in acetic acid (5 mL) was slowly heated until the evolution of nitrogen began (ca. 65 °C). The temperature was maintained at 65 °C for an additional 5 min and then the solvent was removed by freeze-drying. Thin layer chromatography (dichloromethane–ether, 4:1) of the oily product revealed a distinct spot at R_f 0.75, but with considerable streaking below it. The mixture (0.80 g) was chromatographed on silica gel (40 g in a 20 × 370 mm column) using dichloromethane–ether, 4:1, as the eluent. The major product, isolated in chromatographically pure form, was the one of R_f 0.75 (**17**, 0.32 g, 39%), which on standing for a month crystallized: mp 87–89 °C (lit.[13] 59–61 °C); IR (KBr) 1780 cm^{-1} (C=O).

Anal. Calcd for $C_{15}H_{20}O_{11}$ (376.32): C, 47.87; H, 5.35. Found: C, 48.05; H, 5.50.

Decomposition of 15 in Acetic Acid. A solution of **15** (1.0 g) and cupric acetate (10 mg) in acetic acid (5 mL) was slowly heated until the evolution of nitrogen began (bath temperature 70 °C). The temperature was maintained at 70 °C for 5 min and the solution was concentrated in vacuo to give a white solid. The solid was recrystallized from ether to give the acyclic diketone **16** (1.0 g, 74%): mp 85–87 °C.

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Registry No.—**1**, 58-86-6; **13** acid chloride, 63181-62-4; sodium hydrogen tri-*O*-acetylxylarate, 63181-65-7; diazomethane, 334-88-3; glutaryl dichloride, 2873-74-7.

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δ-Dicarbonyl Sugars. 6. Preparation of an Unusual Trihaloheptulose from Xylaric Acid

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The formation of 3,4,5-tri-*O*-acetyl-6,7-anhydro-6-chloromethyl-1-deoxy-1-diazo-DL-*ido*-2-heptulose (**3**) as a by-product of the reaction of tri-*O*-acetylxylaryl dichloride (**1**) with diazomethane is described. Treatment of **3** with hydrogen bromide yielded 3,4,5-tri-*O*-acetyl-1,7-dibromo-6-chloromethyl-1,7-dideoxy-α-DL-*ido*-heptopyranos-2-ulose (**5**), which reacted with sodium azide to give a mixture of 3,4,5-tri-*O*-acetyl-2,7-anhydro-1-bromo-6-chloromethyl-1-deoxy-α-DL-*ido*-heptopyranos-2-ulose (**6**) and the 1-azido derivative **7**. The structure of **5** was determined by an x-ray crystallographic analysis.

In an earlier publication from this laboratory,[3] the acetate-induced cyclization of tri-*O*-acetyl-1,7-dibromo-1,7-dideoxy-*xylo*-2,6,-heptodiulose (**4**) was described.[4] This dibromide was prepared by treating crystalline tri-*O*-acetyl-1,7-bisdiazo-1,7-dideoxy-*xylo*-2,6-heptodiulose (**2**) with hydrogen bromide (Scheme I). On the basis of TLC it was deemed that the mother liquors of the reaction mixture that gave **2** were rich in this compound and when treated with hydrogen bromide would give additional **4**. When the crude product from this reaction failed to crystallize, the reaction mixture was treated with sodium azide to see if any bromide displacement might occur. This reaction yielded a crystalline compound whose IR spectrum had a moderately sized absorption due to an azido group, a strong carbonyl absorption, but no hydroxyl peak. Deacetylation gave a crystalline solid whose IR spectrum had the azide peak, a strong hydroxyl peak, but no carbonyl absorption. Reacetylation gave back the precursor acetate.

In order to discover the origin of the acetylated azido compound, a reexamination of the diazomethylation mother liquors was necessary. Column chromatographic purification of a sample of the mother liquors after crystallization of **2** af-