with basic reagents.[8] That the configurations about the >C=N— bond were not disturbed during conversion to the acetates was shown by the absorption curves for these compounds (Fig. 3). The data obtained for the three pairs of isomers are given in Table I.

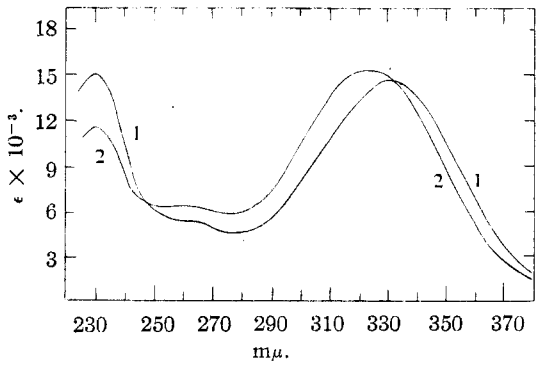


Fig. 3.—Ultraviolet absorption spectra of the 5-nitrofuraldoxime acetates: curve 1, *syn;* curve 2, *anti;* determinations in water, c = 10.2 mg./l.

Experimental

Furaldoxime.—The isomers were prepared by the method of Brady and Goldstein[9]: α-form (*anti*), m. p. 90–91°; β-form (*syn*), m. p. 75–76°.

5-Nitrofuraldoximes.—These were prepared according to the directions of Gilman and Wright[5]: α-form, m. p. 159–161°; β-form, m. p. 121°.

5-Nitrofuraldoxime Acetates.—The oximes were dissolved in warm acetic anhydride in which they were readily soluble. Sufficient water was then added to hydrolyze the excess acetic anhydride, and the products were allowed to crystallize from the warm liquors. Each was then recrystallized from dilute methanol: α-form, light yellow powder, m. p. 107–109°; β-form, colorless needles, m. p. 169–170°.

Anal. Calcd. for $C_7H_6N_2O_5$: C, 42.4; H, 3.03. Found: (α) C, 42.5; H, 2.94; (β) C, 42.9; H, 3.35.

Treatment of the Oxime Acetates with Pyridine.—The α-oxime acetate was dissolved in warm pyridine, and the mixture was then diluted with an equal volume of water and refrigerated. The solid which separated was crystallized from dilute methanol; colorless needles, m. p. 63–65° alone and when mixed with an authentic specimen of 5-nitrofuronitrile. Under identical conditions, the β-oxime acetate was recovered unchanged; m. p. and mixed m. p. 169–170°.

5-Nitrofuronitrile.—This was prepared according to the procedure used by Williams[10] for the tetrahydro compound. The product was not distilled, but was twice crystallized from dilute methanol; yield 78%, colorless needles, m. p. 63–65°.

Anal. Calcd. for $C_5H_2N_2O_3$: C, 43.5; H, 1.45. Found: C, 43.6; H, 1.70.

Absorption Spectra.—Spectral data were taken, using aqueous solutions, in the region 220–400 mμ, on a Beckmann Model D Quartz Spectrophotometer with a hydrogen source. $\text{Log}_{10} I_0/I$ was read directly from the instrument, and the extinction coefficients were then calculated from the concentrations of the solutions.

Summary

Isomerism about the >C=N— bond in the furaldoximes is reflected by consistent differences in the ultraviolet absorption spectra of these compounds.

On this basis configurations have been assigned to the 5-nitrofuraldoximes and their acetates, and the validity of the method was checked by an accepted chemical procedure.

(8) Gilman, "Organic Chemistry," Vol. I, 2nd ed., John Wiley and Sons, New York, N. Y., 1943, p. 468.

(9) Brady and Goldstein, *J. Chem. Soc.*, 1959 (1927).

(10) Williams, *Ber.*, **60**, 2509 (1927).

NORWICH, N. Y. RECEIVED MARCH 12, 1946

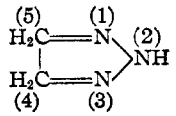
[CONTRIBUTION FROM THE CHEMISTRY LABORATORY, NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE]

The Action of Copper Sulfate on the Phenylosazones of the Sugars. III. The D-, L- and D,L-Arabinose Phenylosotriazoles[1]

BY W. T. HASKINS, RAYMOND M. HANN AND C. S. HUDSON

In the previous articles[2] concerning the transformation of sugar phenylosazones to the corresponding phenylosotriazoles through the action of copper sulfate, no mention was made of the behavior of arabinose phenylosazone because the corresponding arabinose phenylosotriazole was not obtained in crystalline condition. Lately we have found that arabinose phenylosazone can be purified so that its melting point (171–172°, with decomposition) is approximately ten degrees higher than the values that have been reported by previous investigators.[3] The mutarotations of the purified L-arabinose phenylosazone were $[\alpha]^{20}D$ + 60.5° → + 31.0° (forty-eight hours, constant value) in a mixture of four parts by volume of pyridine and six parts of absolute alcohol, and +33.3° → +20.4° (twenty-four hours, constant

(1) We named the first member of this group of sugar derivatives *phenyl-D-glucosotriazole.* However, it now seems preferable to change the name to read D-*glucose phenylosotriazole* in order that the form may be similar to that of D-*glucose phenylosazone,* which has come into general use. The substance which has the formula



was named by its discoverer, von Pechmann, [*Ann.*, **262**, 265 (1891)] *osotriazole;* it has subsequently been assigned the indicated numbering and the systematic name *2,1,3-triazole* [*C. A.*, **39**, 6541 (1945)]. The systematic name of D-glucose phenylosotriazole is accordingly 2-phenyl-4-(D-*arabino*-tetrahydroxybutyl)-2,1,3-triazole and that of D-arabinose phenylosotriazole 2-phenyl-4-(D-*erythro*-trihydroxypropyl)-2,1,3-triazole.

This paper was presented in part at a meeting of the Washington Section of the American Chemical Society, May 9, 1946.

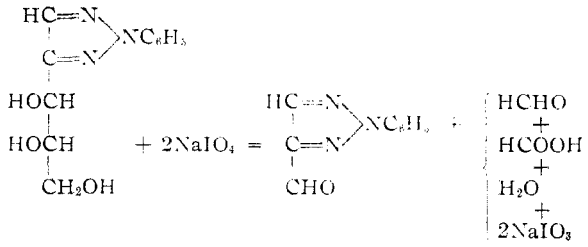
(2) (I) Hann and Hudson, THIS JOURNAL, **66**, 735 (1944); (II) Haskins, Hann and Hudson, *ibid.*, **67**, 939 (1945).

(3) Kiliani, *Ber.*, **20**, 339 (1887); Ruff, *ibid.*, **31**, 1573 (1898); Levene and LaForge, *J. Biol. Chem.*, **20**, 429 (1915).

value) in methyl cellosolve solution. The corresponding values for the D-arabinose phenylosazone were of equal magnitude but opposite in sign. Levene and LaForge[3] reported that their L-arabinose phenylosazone mutarotated $[\alpha]^{20}D$ + 55° → + 30° (eighteen hours, not stated to be constant) in a mixture of four parts of pyridine and six parts of absolute alcohol, and Neuberg[4] reported a specific rotation of +58° for the substance in the same proportions of pyridine and alcohol, a value which presumably referred to a freshly prepared solution. When arabinose phenylosazone is prepared in the usual way with water as the reaction medium the product separates from the hot solution as a reddish oil which crystallizes on cooling to form an orange-colored mass; this crude product darkens upon drying and over a period of a few days becomes nearly black; recrystallization of this crude phenylosazone is difficult and the recrystallized material also becomes progressively darker with age. By using the monomethyl ether of ethylene glycol (methyl cellosolve) as solvent in the reaction, the precipitation of the phenylosazone as an oil is avoided and the crude product, which is obtained by pouring the reaction mixture into water, is easily recrystallized to give a pure, yellow arabinose phenylosazone which does not darken with reasonable age. If such purified arabinose phenylosazone be used in the reaction with copper sulfate there is no difficulty in obtaining the crystalline phenylosotriazole of either D- or L-arabinose.

Both enantiomorphs of arabinose phenylosotriazole exhibit dimorphism. There is a compact prism form which melts at 80–81° and a fine acicular modification of melting point 69–70°; these forms possess the same rotation and they are interconvertible by crystallization from solution. The two forms often crystallize together and then the stable prisms slowly increase as the metastable needle form gradually disappears. The needle form of D-arabinose phenylosotriazole is unstable at room temperature even in the dry state and spontaneously changes to the stable prism form; thus the melting point of the crystals upon standing at 25° for three months rose from 69–70° to 80–81°. Such behavior has not been observed with the needle form of L-arabinose phenylosotriazole and its melting point has remained constant for several months, but we anticipate that it will eventually rise. When a solution of equal amounts of the D- and L-arabinose phenylosotriazoles is allowed to crystallize, fine needles of the D,L-form (m.p. 74–75°) separate.

The oxidation of L-arabinose phenylosotriazole by a moderate excess of an aqueous solution of sodium metaperiodate reduces two molecular equivalents of the oxidant to sodium iodate and produces one molecular equivalent each of formaldehyde, formic acid, and the aldehyde 2-phenyl-4-formyl-2,1,3-triazole (II). This aldehyde is insoluble in water and crystallizes in 91% yield from the solution. The formaldehyde was isolated as the dimedone compound and the formic acid was measured by titration; the yields of each were nearly theoretical. These data, which were obtainable from less than 0.4 g. of arabinose phenylosotriazole, show that the structure of L-arabinose phenylosotriazole is I and that it is oxidized according to the equation



(I) L-Arabinose phenylosotriazole

(II) 2-Phenyl-4-formyl-2,1,3-triazole

The tribenzoates of the D- and L-forms of arabinose phenylosotriazole crystallize readily. A mixture of equal parts of these enantiomorphs crystallizes as a true racemate melting 10° higher than the crystals of its components. The analogous triacetates were also obtained in crystalline form.

We are indebted to Mr. Charles A. Kinser of the National Institute of Health for performing the microchemical analyses.

Experimental

D-Arabinose Phenylosazone.—A mixture of 25 g. of D-arabinose ($[\alpha]_D$ −104°), 32.5 cc. of glacial acetic acid and 100 cc. of methyl cellosolve was heated to 80° on the steam-bath and 65 cc. of phenylhydrazine was added. Solution of the sugar took place rapidly and, after an additional hour on the steam-bath, the solution was poured with stirring into 1600 cc. of water. The voluminous yellow precipitate was collected on a suction filter and washed with two 50-cc. portions of 10% acetic acid and four 100-cc. portions of water; the cake was sucked as dry as possible and without delay dissolved in 100 cc. of boiling alcohol. Upon cooling the solution the phenylosazone crystallized in nearly pure condition as tufts of fine yellow needles which were recovered by filtration and washed with three 25-cc. portions of ice-cold alcohol (yield, 23 g.; 42%). The phenylosazone was again recrystallized from five parts of alcohol; the pure substance did not darken on standing at room temperature for several weeks. It melted with decomposition at 171–172°; its rotation was $[\alpha]^{20}D$ −60.7° → −30.4° (forty-eight hours, constant value) in a mixture of four parts (by volume) of pyridine and six parts of absolute alcohol (*c*, 0.84), and −33.6° → −19.8° (twenty-four hours, constant value) in methyl cellosolve (*c*, 0.88).

Anal. Calcd. for $C_{17}H_{20}N_4O_3$: C, 62.18; H, 6.14; N, 17.06. Found: C, 62.35; H, 5.98; N, 17.21.

L-Arabinose Phenylosazone.—The L-arabinose phenylosazone was obtained in a yield of 20 g. (36%) upon treatment of 25 g. of L-arabinose by the method employed for the preparation of its enantiomorph. It was purified by recrystallization from five parts of alcohol and it formed clusters of fine yellow needles which melted with decomposition at 171–172° and rotated $[\alpha]^{20}D$ +60.5° → +31.0° (forty-eight hours, constant value) in a mixture of four parts of pyridine and six parts of absolute alcohol (*c*, 0.88)

(4) Neuberg, *Ber.*, **32**, 3386 (1900).

and +33.3° → +20.4° (twenty-four hours, constant value) in methyl cellosolve (*c*, 0.92).

Anal. Calcd. for $C_{17}H_{20}N_4O_3$: C, 62.18; H, 6.14; N, 17.06. Found: C, 62.16; H, 6.08; N, 16.80.

L-Arabinose Phenylosotriazole.—A suspension of 10 g. of L-arabinose phenylosazone in 1000 cc. of water was heated to boiling and a solution of 8.35 g. (1.1 molecular equivalents) of copper sulfate pentahydrate in 100 cc. of boiling water was added; a cherry-red color developed at once and during continued boiling under reflux the color faded to green after fifteen minutes, at which time all of the osazone had dissolved and a fine red precipitate had deposited from the solution. Refluxing was continued for an additional fifteen minutes and the cooled solution was filtered; the copper still present in the solution was removed as sulfide and the filtrate, after neutralization with 10 g. of barium carbonate, was concentrated *in vacuo* to a sirup which was dried by three successive evaporations with absolute alcohol. A solution of the sirup in 25 cc. of warm chloroform was filtered to remove a small amount of insoluble material and diluted with a mixture of 15 cc. of ether and 15 cc. of hexane; upon scratching, the reaction product crystallized readily (6.5 g., m. p. 60–70°). The dark-colored crude osotriazole was extracted with five 50-cc. portions of boiling ether and the filtered extracts were evaporated to 50 cc., 10 cc. of chloroform was added to prevent clouding, and the osotriazole crystallized spontaneously as needles on cooling the solution (4.7 g., m. p. 68–69°). Concentration of the mother liquor gave an additional 0.5 g. (m. p. 67–68°) of material, making the total yield 5.2 g. (72%). The product crystallized from its solution in ten parts of chloroform by the addition of four parts of hexane as clusters of fine needles melting at 69–70° and rotating $[\alpha]^{20}D$ −22.8° in aqueous solution (*c*, 0.92) and −25.8° in pyridine solution (*c*, 0.85). A second modification of the compound in the form of short thick prisms melting at 80–81° and showing the same rotation was obtained by heating the needle form slightly above its melting point for several days in an oven. Both forms of the compound are very soluble in water, alcohol, acetone, and pyridine, moderately soluble in ether and nearly insoluble in petroleum ether.

Anal. Calcd. for $C_{11}H_{13}N_3O_3$: C, 56.16; H, 5.57. Found: C, 56.20; H, 5.47.

D-Arabinose Phenylosotriazole.—D-Arabinose phenylosazone was converted to the corresponding osotriazole by the same procedure that has been described for the L-derivative. The yield of the crude product was 5.6 g. and, after extraction with ether, 4.9 g. (68%) of nearly pure material was obtained. Upon recrystallization from ten parts of chloroform by the addition of four parts of hexane, the substance crystallized in two forms, namely, long fine needles and short thick prisms. The mixture, upon standing several days at 5°, was gradually converted completely to the prism form, which melted at 80–81° and rotated $[\alpha]^{20}D$ +23.1° in aqueous solution (*c*, 0.80) and +26.0° in pyridine solution (*c*, 0.81). The needle form, which was obtained by seeding a chloroform–hexane solution of the prism form with the needles, melted at 69–70° and showed the same rotation as the prism form. The solubilities of the needle and prism dimorphs are the same as those of the corresponding modifications of the L-enantiomorph.

Anal. Calcd. for $C_{11}H_{13}N_3O_3$: C, 56.16; H, 5.57. Found: C, 56.36; H, 5.54.

D,L-Arabinose Phenylosotriazole.—A solution of 0.50 g. of D-arabinose phenylosotriazole and 0.50 g. of L-arabinose phenylosotriazole in 10 cc. of warm chloroform, upon the addition of 5 cc. of hexane, crystallized as needles having the same general appearance as the needles of the component enantiomorphs. The D,L-crystals melted at 74–75° and showed no rotation in aqueous solution. The solubility of the D,L-crystals was not prominently different from that of its components.

Anal. Calcd. for $C_{11}H_{13}N_3O_3$: C, 56.16; H, 5.57. Found: C, 56.17; H, 5.47.

Sodium Metaperiodate Oxidation of L-Arabinose Phenylosotriazole.—To a solution of 0.3735 g. of L-arabinose phenylosotriazole in 10 cc. of water was added 7.44 cc. (2.5 molecular equivalents) of 0.534 *M* sodium metaperiodate solution. In a short time a crystalline precipitate formed and after two hours it was removed by filtration and washed with cold water; the filtrate and washings were diluted to 50 cc. and reserved for analysis as described in the following paragraph. The crystals melted at 68–69° and showed no depression of this value when mixed with an authentic sample of 2-phenyl-4-formyl-2,1,3-triazole previously prepared by the oxidation of D-glucose phenylosotriazole[2]; the yield was 0.25 g., which corresponds to 0.91 mole per mole of L-arabinose phenylosotriazole. The filtrate from the crystalline aldehyde was analyzed for other oxidation products and found to contain 0.99 molecular equivalents of formic acid and 1.03 molecular equivalents of formaldehyde; since 2.04 molecular equivalents of the oxidant were reduced, the oxidation by periodate follows the equation that has been recorded.

L-Arabinose Phenylosotriazole Tribenzoate.—The benzoylation of 1.0 g. of L-arabinose phenylosotriazole in pyridine solution with benzoyl chloride in the usual way gave a quantitative yield (2.3 g.) of the tribenzoate; it was recrystallized from ten parts of absolute alcohol, forming clusters of fine needles which melted at 114–115° and rotated $[\alpha]^{20}D$ −6.8° in chloroform solution (*c*, 0.82). It is soluble in acetone, ether, chloroform and pyridine and nearly insoluble in water and petroleum ether.

Anal. Calcd. for $C_{32}H_{25}N_3O_6$: C, 70.19; H, 4.60; C_6H_5CO, 57.6. Found: C, 69.93; H, 4.52; C_6H_5CO, 57.4.

D-Arabinose Phenylosotriazole Tribenzoate.—The tribenzoate of D-arabinose phenylosotriazole was prepared from 1.0 g. of the D-form of the phenylosotriazole in the same way as its enantiomorph. The yield was quantitative (2.3 g.) and upon recrystallization from ten parts of absolute alcohol it also formed clusters of fine needles which melted at 114–115° and rotated $[\alpha]^{20}D$ +6.9° in chloroform solution (*c*, 0.83). The solubility of the substance was the same as that of the L-form previously described.

Anal. Calcd. for $C_{32}H_{25}N_3O_6$: C, 70.19; H, 4.60; C_6H_5CO, 57.6. Found: C, 70.37; H, 4.65; C_6H_5CO, 57.7.

D,L-Arabinose Phenylosotriazole Tribenzoate.—A solution of 0.50 g. of D-arabinose phenylosotriazole tribenzoate and 0.50 g. of L-arabinose phenylosotriazole tribenzoate in 10 cc. of hot absolute alcohol upon cooling deposited 0.95 g. of short prismatic needles of different appearance from the fine needles of its components. The racemate melted at 125–126° and exhibited no rotation in chloroform solution (*c*, 0.85). Its solubility is qualitatively the same as that of its components.

Anal. Calcd. for $C_{32}H_{25}N_3O_6$: C, 70.19; H, 4.60; C_6H_5CO, 57.6. Found: C, 70.20; H, 4.60; C_6H_5CO, 57.5.

D-Arabinose Phenylosotriazole Triacetate.—The acetylation of 1.0 g. of D-arabinose phenylosotriazole with a mixture of pyridine and acetic anhydride yielded a sirupy product, which crystallized from ether–hexane solution after standing two months at −5°. The 1.1 g. (73%) of material obtained was recrystallized from a mixture of five parts of ether and ten parts of hexane; it formed clusters of prisms melting at 63–64° and rotating $[\alpha]^{20}D$ +68.0° in chloroform solution (*c*, 0.83). It is soluble in alcohol, ether, acetone and pyridine and nearly insoluble in petroleum ether and water.

Anal. Calcd. for $C_{17}H_{19}N_3O_6$: C, 56.50; H, 5.30; CH_3CO, 35.7. Found: C, 56.72; H, 5.26; CH_3CO, 35.7.

L-Arabinose Phenylosotriazole Triacetate.—The acetylation of 1.0 g. of L-arabinose phenylosotriazole with acetic anhydride in pyridine solution in the usual way yielded a sirup which crystallized from ether–hexane solution after standing for several weeks at −5° (1.1 g., 73%). The compound crystallized from a mixture of five parts of ether and ten parts of hexane as prisms of the same appearance as those of the D-form; its melting point is 63–64° and

its rotation $[\alpha]^{20}D$ is $-68.0°$ in chloroform solution (*c*, 0.85); its solubility is the same as that previoulsy described for its enantiomorph.

Anal. Calcd. for $C_{17}H_{19}N_3O_6$: C, 56.50; H, 5.30; CH_3CO, 35.7. Found: C, 56.60; H, 5.32; CH_3CO, 35.8.

D,L-Arabinose Phenylosotriazole Triacetate.—A solution of 0.40 g. of D-arabinose phenylosotriazole triacetate and 0.40 g. of L-arabinose phenylosotriazole triacetate in 4 cc. of ether and 10 cc. of hexane, upon standing at 5° for several days, crystallized as prisms of the same general appearance as those of its component enantiomorphs; the substance melted at 48–50° and had no rotation in chloroform solution. Its solubility was qualitatively the same as that of its components.

Anal. Calcd. for $C_{17}H_{19}N_3O_6$: C, 56.50; H, 5.30; CH_3CO, 35.7. Found: C, 56.49; H, 5.15; CH_3CO, 35.6.

Summary

The preparation of the D- and L-arabinose phenylosazones has been improved and it is found that the pure substances melt about ten degrees higher than has been reported previously. The D-, L- and D,L-arabinose phenylosotriazoles and their corresponding triacetates and tribenzoates are described.

BETHESDA, MARYLAND RECEIVED MAY 15, 1946

[CONTRIBUTION FROM THE CHEMISTRY LABORATORY, NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE

The 3,5-Benzylidene and 3,5-Methylene Acetals of Gluco-*gulo*-heptitol

BY RAYMOND M. HANN, A. T. NESS AND C. S. HUDSON[1]

When Emil Fischer[2] discovered gluco-*gulo*-heptitol ("α-glucoheptitol") he proved its meso configuration (I) by showing that it, and also the corresponding pentahydroxypimelic acid, exhibit no optical rotation. The seven hydroxyl groups of its molecule could conceivably react with benzaldehyde to yield variously constituted benzylidene cyclic acetals, and the maximum condensation would produce a tribenzylidene acetal. A tribenzylidene acetal of the hexitol mannitol, representing maximum condensation, was known. Fischer found that gluco-*gulo*-heptitol condenses readily with benzaldehyde in the presence of mineral acids to yield a crystalline acetal but the derivative proved to have the unusual constitution of a monobenzylidene heptitol. Apparently the cause of the striking difference in the behavior of mannitol and gluco-*gulo*-heptitol was to be attributed to steric influences but it was not possible at that early period to specify in more precise terms the character of these influences because even the structures of such acetals were not then known, nor could the structures be ascertained by any of the experimental methods that were then in use. In recent years the structures of a considerable number of such benzylidene and methylene cyclic acetals have been determined through new methods of experimentation; the extensive new data led recently to some generalizations[3] by which the structure of favored benzylidene and methylene acetals of polyhydric alcohols may be predicted from the configuration of the alcohol. These generalizations have been found to apply in the pentitol and hexitol series and in the case of such 6-desoxy-hexitols as rhamnitol[4] and epirhamnitol.[5] Regarding their possible application to heptitols and higher polyhydric alcohols it was stated[3] that "we defer application of the generalizations to such alcohols until more experimental data are available for guidance." In the present article proofs are presented for the structure of the monobenzylidene-gluco-*gulo*-heptitol of Fischer and for that of a corresponding monomethylene-gluco-*gulo*-heptitol which we have prepared; the structures of these acetals agree with the generalizations, as will be explained later.

(1) Presented at the Atlantic City meeting of the American Chemical Society, April 10, 1946.

(2) E. Fischer, *Ann.*, **270**, 64 (1892); *Ber.*, **27**, 1524 (1894).

(3) Hann and Hudson, THIS JOURNAL, **66**, 1909 (1944).

(4) Haskins, Hann and Hudson, THIS JOURNAL, **67**, 1800 (1945).

(5) Ness, Hann and Hudson, *ibid.*, **66**, 1235 (1944).

Proof of the Structure of 3,5-Benzylidene-gluco-*gulo*-heptitol

The oxidation of Fischer's benzylidene-gluco-*gulo*-heptitol (m. p. 218°) in aqueous solution by excess sodium metaperiodate reduces two equivalents of periodate to iodate without the formation of any acidity; formaldehyde can be detected by its odor but its accurate estimation with dimedon was not carried out because it was found that this reagent likewise forms a crystalline precipitate with the other oxidation product, which proved later to be 2,4-benzylidene-*xylo*-trihydroxy-glutardialdehyde (III). However, the preliminary oxidation data, showing no formic acid, some formaldehyde, and the reduction of two equivalents of periodate, limited the structure of the acetal at this early stage of the work to that of 3,5- or 2,5-benzylidene-gluco-*gulo*-heptitol. Decision in favor of the 3,5 structure was obtained through the isolation of a crystalline dioxime and a crystalline disemicarbazone, the analyses of which showed the presence of a substituted glutardialdehyde (III). This substituted dialdehyde was reduced with hydrogen and Raney nickel to crystalline 2,4-benzylidene-xylitol (IV), from which xylitol was obtained after acid hydrolysis. The same 2,4-benzylidene-xylitol was also prepared from the known 2,4-benzylidene-D-sorbitol (V), in confirmation of the structure of 3,5-benzylidene-gluco-*gulo*-heptitol.

The $H\cdot\dot{C}\cdot C_6H_5$ grouping in the structure of such benzylidene cyclic acetals can have two ar-