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

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[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).

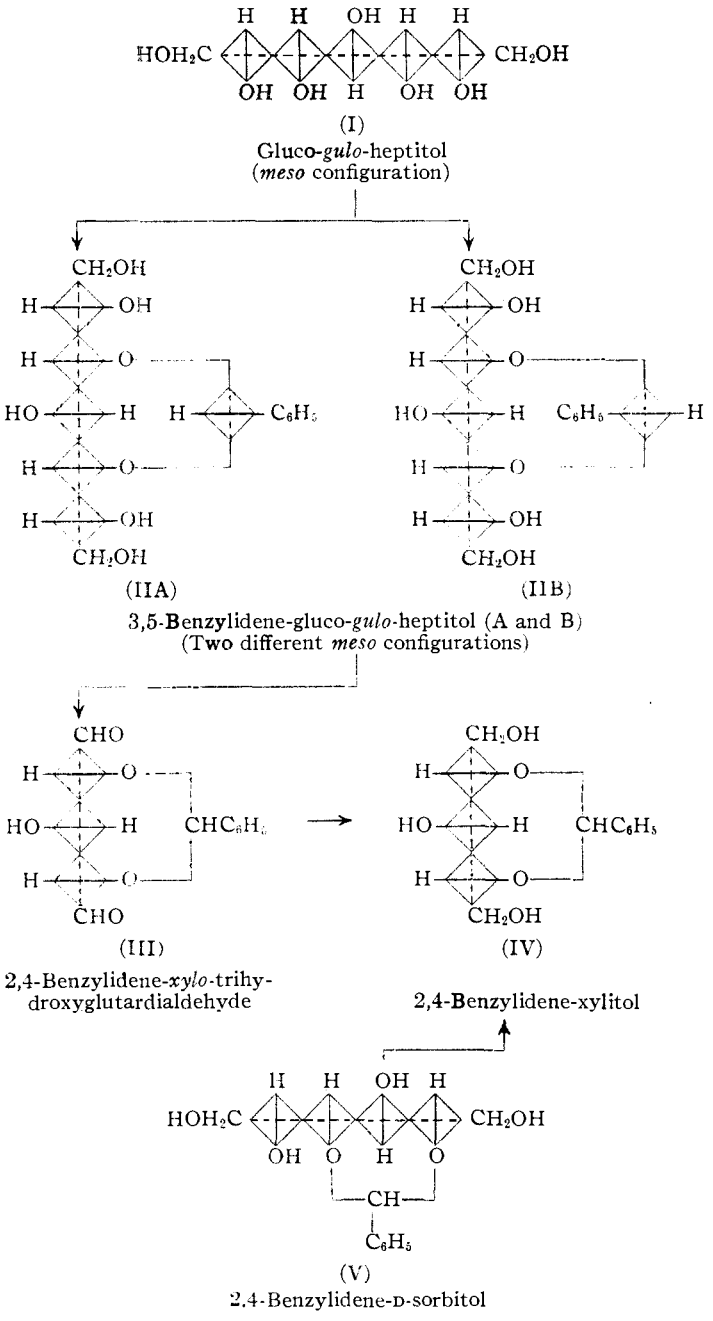
(4) Haskins, Hann and Hudson, THIS JOURNAL, **67**, 1800 (1945).

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

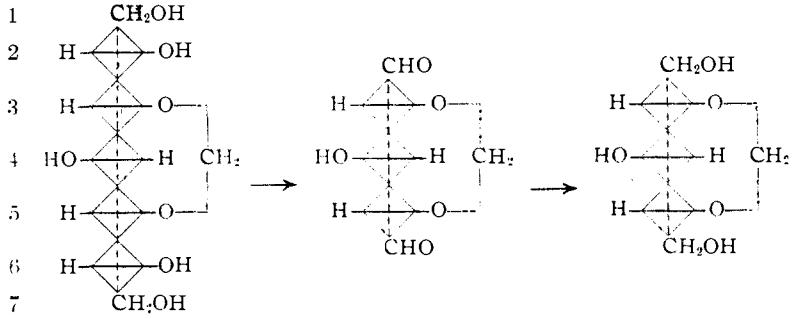



rangements, as was first indicated by Fischer[2] for the general case and as is shown in the formulas (IIA and IIB) for the particular case from the gluco-*gulo*-heptitol series. Since the benzylidene attachments are to the carbon atoms 3 and 5, IIA and IIB represent the configurations of two *meso* substances which are different from each other and which should show, for example, different melting points. There is no way known at present for distinguishing between IIA and IIB as the configurational formula for Fischer's 3,5-benzylidene-gluco-*gulo*-heptitol (m. p. 218°).

In Fischer's article he records that in some of the experiments he obtained a labile acetal of m. p. 155–156° which passed with extraordinary ease to the higher-melting stable isomer during recrystallization from alcohol. He suggested the possibility that the two crystalline substances might be isomers which differ in configuration through different arrangements for the acetal carbon atom of the benzylidene group. Now that the structure of the stable acetal is known to be that of 3,5-benzylidene-gluco-*gulo*-heptitol, Fischer's suggestion can be specified precisely as implying that the two crystalline substances which show the different melting points have the configurations IIA and IIB and that one of these configurations is so labile that it changes immediately to the other when the lower-melting substance is recrystallized from alcohol. It does not seem possible to decide from existing data whether Fischer's detection of two isomers of different melting points indicates dimorphism of a single substance such as IIA, or the case of a labile structure of IIB changing easily to a more stable IIA isomer. Later studies of such a question in the case of 1,3-benzylidene-glycerol,[6] and especially concerning 1,3-*p*-nitrobenzylidene-glycerol,[7] appear to make it probable that one of the isomers IIA and IIB can be so much more stable than the other that a spontaneous rearrangement can occur even in the pure crystalline state and that the change is indicated by an observed rise in the melting point of the crystals with age. Hibbert and Carter's freshly prepared 1,3-*p*-nitrobenzylidene-glycerol melted at 88°, but on aging the compound a few days the melting point rose to 98°. When the higher-melting substance was recrystallized the product melted at 88° and the change in the solid state on aging occurred again. The evidence against the view of dimorphism in this case is that the benzoylation of the 88° substance yielded solely a stable benzoate of m. p. 204° but the benzoylation of the 98° substance yielded a mixture of this benzoate with a stable isomer of m. p. 159°. This evidence and supporting observations on analogous derivatives led Hibbert and Carter to conclude that 1,3-*p*-nitrobenzylidene-glycerol appears to consist of a mixture of two geometrical isomers. The possibility that the benzylidene

(6) Irvine, Macdonald and Souter, *J. Chem. Soc.*, **107**, 344 (1915).
(7) Hibbert and Carter, THIS JOURNAL, **50**, 3376 (1928).

acetals which are studied in the present article may possess lability with respect to the arrangements on the benzylidene carbon atom of the ring leaves the question open as to whether the benzylidene grouping has the same configuration throughout this series of related acetals; accordingly, the grouping is left in the indeterminate form $\dot{C}H\cdot C_6H_5$ in the formulas.



(VI) 3,5-Methylene-gluco-*gulo*-heptitol (*meso*)

(VII) 2,4-Methylene-*xylo*-trihydroxy-glutardialdehyde (not isolated)

(VIII) 2,4-Methylene-xylitol (*meso*)

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

The condensation of gluco-*gulo*-heptitol with formaldehyde in aqueous hydrochloric acid yields a crystalline acetal which proves to be 3,5-methylene-gluco-*gulo*-heptitol, a *meso* structure, the formula for which is VI. The oxidation of this acetal by periodic acid evidently produces 2,4-methylene-*xylo*-trihydroxy-glutardialdehyde (VII), a *meso* substance which was not isolated; the reduction of a solution of VII yields the known 2,4-methylene-xylitol (VIII),[8] which is also a *meso* substance.

Now that the structural formulas of the benzylidene and methylene acetals of gluco-*gulo*-heptitol have become known, one may inquire whether they conform with the generalizations[3] that have been mentioned in the early part of this article. Inspecting first the positions of the secondary hydroxyl groups of formula I it is seen that those of $\beta$ position which are attached to the carbon atom pairs numbered 2,4 and 4,6, are *trans* in configuration and are thus in unfavorable arrangement[3]; on the other hand, the members of the pair at 3,5 are $\beta$ in position and *cis* in configuration, which is a favorable arrangement. The secondary hydroxyls which are $\gamma$ in position are *cis* in configuration in all cases and therefore represent unfavorable arrangements. Considering next the acetal forms that would involve a primary hydroxyl, which in previous work have been found to be weaker ring types than those involving two secondary hydroxyls, a 1,3 or 5,7 acetal conflicts with the 3,5 acetal. The generalizations thus apply to these first examples from the heptitol series and they indicate that these unusual *mono*-acetals are indeed the types that are to be expected for gluco-*gulo*-heptitol.

## Experimental

### 3,5-Benzylidene-gluco-*gulo*-heptitol and Derivatives

**3,5-Benzylidene-gluco-*gulo*-heptitol** (II).—A solution of 20 g. of gluco-*gulo*-heptitol in 40 ml. of concentrated hydrochloric acid was cooled to 0° and 19 ml. of benzaldehyde was added and brought into solution by agitation. The magma of crystals which deposited upon allowing the reaction mixture to stand at 5° overnight was transferred to an evaporating dish and placed in an evacuated desiccator containing moist sodium hydroxide pellets. After four days the crystals were triturated successively with ether to remove excess benzaldehyde and 5% aqueous sodium hydroxide to remove residual acid, and then filtered on a Büchner funnel and washed with water, alcohol and ether. The product, 26.1 g. (92%), was recrystallized from 1300 ml. of boiling ethanol and yielded 22.1 g. (78%) of the stable form of 3,5-benzylidene-gluco-*gulo*-heptitol in the form of fine needles melting at 216–217° (cor.). Fischer[2] reported a melting point of 214° (uncor.) and 218° (cor.) for this stable form of the acetal.

**Sodium Periodate Oxidation of 3,5-Benzylidene-gluco-*gulo*-heptitol.**—A solution of 0.1553 g. of 3,5-benzylidene-gluco-*gulo*-heptitol in 30 ml. of water was cooled to 5° and 5 ml. (4.20 molecular equivalents) of 0.434 *M* aqueous sodium periodate solution was added; the mixture was allowed to warm to 25° and the volume was adjusted to 50 ml. with water. Analysis of 5-ml. aliquots at the expiration of forty-five minutes, two, twenty-two and one hundred hours indicated that 1.96, 1.99, 2.03 and 2.37 molecular equivalents, respectively, of sodium periodate had been consumed. Titration of a 5-ml. aliquot at the end of two hours with 0.1 *N* sodium hydroxide indicated that no acid had been formed. At the expiration of twenty-two hours the solution had a definite odor of formaldehyde; at one hundred hours it was straw-colored and possessed an odor of benzaldehyde.

The consumption of two molecular equivalents of periodate with the production of formaldehyde but without the generation of acid limits the structure of benzylidene-gluco-*gulo*-heptitol to that of 2,5 or 3,5-benzylidene-gluco-*gulo*-heptitol.

**2,4-Benzylidene-*xylo*-trihydroxy-glutardialdehyde** (III).—Ten grams of powdered 3,5-benzylidene-gluco-*gulo*-heptitol was added to an ice-cold solution of 15 g. (theory, 14.3 g.) of sodium periodate in 300 ml. of water; the reaction mixture was allowed to come to room temperature (25°) and shaken occasionally to aid solution of the acetal, which was usually complete in two hours. After three hours a solution of 9.5 g. (theory, 8.5 g.) of barium chloride dihydrate in 25 ml. of water was added to the clear solution, and the precipitated barium salts were removed by filtration. The filtrate was concentrated *in vacuo* to dryness, and the residue further dried by successive addition and evaporation of two 50-ml. volumes of absolute alcohol. The residue was extracted with 100 ml. of hot absolute methanol, and the filtered extract was concentrated *in vacuo* to dryness, yielding 9 g. (theory, 8 g.) of a frothy, glassy product. This material was used for the preparation of derivatives.

**2,4-Benzylidene-*xylo*-trihydroxy-glutardialdehyde dioxime.**—To a solution of 1 g. of the dialdehyde in 20 ml. of methanol was added a solution of 1 g. of hydroxylamine hydrochloride and 1.5 g. of sodium acetate trihydrate in 5 ml. of water and the mixture was heated under a reflux condenser for one hour. The product (0.65 g., 58%) which deposited from the solution on concentration to about one-third its volume was recrystallized twice from 40 parts of 50% aqueous methanol and yielded 0.40 g. of

(8) Hann, Ness and Hudson, THIS JOURNAL, **66**, 673 (1944).

the pure dioxime which crystallized as long, fine needles melting at 210–211° (cor.). The substance was insoluble in hot and cold water, cold methanol and ethanol, chloroform and benzene, and soluble in warm alcohols, acetone and glacial acetic acid.

*Anal.* Calcd. for $C_{12}H_{14}O_5N_2$: C, 54.13; H, 5.30; N, 10.52. Found: C, 54.25; H, 5.42; N, 10.63.

**2,4-Benzylidene-*xylo*-trihydroxy-glutardialdehyde disemicarbazone.**—A solution of 1 g. of dialdehyde in 10 ml. of methanol was mixed with a solution of 1.2 g. of semicarbazide hydrochloride and 1.5 g. of sodium acetate trihydrate in 5 ml. of water. No precipitation of product took place on standing overnight at room temperature; the solution was concentrated to about one-half of its volume by means of an air-current at 25° and a fine crystalline precipitate gradually separated. Ten milliliters of water was added and after standing one hour at 0°, the mixture was filtered, yielding 0.8 g. (54%) of product melting at 212–213° with decomposition. Two recrystallizations from 30 parts of 50% aqueous methanol gave 0.6 g. of pure product as small needles melting at 225–226° (cor.) with decomposition. The compound was insoluble in hot methanol, benzene, chloroform and hot or cold acetone, but it was readily soluble in hot glacial acetic acid or 20 parts of hot water.

*Anal.* Calcd. for $C_{14}H_{18}O_5N_6$: C, 47.99; H, 5.18; N, 23.99. Found: C, 48.04; H, 5.05; N, 23.94.

**2,4-Benzylidene-xylitol (IV) from 3,5-Benzylidene-gluco-*gulo*-heptitol (II).**—Ten grams of powdered 3,5-benzylidene-gluco-*gulo*-heptitol was added to 240 ml. (theory, 240 ml.) of ice-cold 0.278 *M* sodium periodate solution and the mixture was allowed to stand for two hours at room temperature with frequent shaking. To the clear solution, a solution of 9 g. (10% excess) of barium chloride dihydrate in 25 ml. of water was added and, after standing at 0° for one hour, the precipitated barium salts were removed by filtration. The filtrate, which was strongly reducing to Fehling solution, was agitated overnight (sixteen hours) at room temperature in a bomb with Raney nickel and hydrogen under a pressure of 100 atmospheres. The catalyst was removed by filtration and the non-reducing filtrate was concentrated *in vacuo* to dryness; the residue was extracted with 75 ml. of hot absolute alcohol and the extract was concentrated *in vacuo* to dryness, yielding 8 g. (theory, 8 g.) of a crystalline residue. Recrystallization from 8 parts of water yielded 5.3 g. (66%) of 2,4-benzylidene-xylitol in the form of fine needles melting at 143–144° (cor.). The substance is soluble in methanol and ethanol, moderately soluble in acetone and water, and insoluble in chloroform and benzene.

*Anal.* Calcd. for $C_{12}H_{16}O_5$: C, 59.99; H, 6.71. Found: C, 59.90; H, 6.82.

**2,4-Benzylidene-xylitol from 2,4-Benzylidene-D-sorbitol.**—To a suspension of 13.5 g. of powdered 2,4-benzylidene-D-sorbitol[9] in 50 ml. of water and 10 ml. of ethanol was added 90 ml. (theory, 85 ml.) of a 0.588 *M* sodium periodate solution; after standing two hours at room temperature, when the solution of the acetal was complete, a solution of 7.0 g. (theory, 6.5 g.) of barium chloride dihydrate in 25 ml. of water was added to the reaction mixture, and the precipitated barium salts were removed by filtration. The filtrate was agitated in a bomb overnight at 25° with Raney nickel and hydrogen under a pressure of 86 atmospheres. After filtration to remove the catalyst, the solution was concentrated *in vacuo* to dryness; the residue was extracted with 75 ml. of hot absolute alcohol. As it cooled, the extract became filled with fine needles and after standing overnight in the refrigerator they were separated by filtration and yielded 3.3 g. (theory, 12 g.) of 2,4-benzylidene-xylitol melting at 143–144°; a mixed melting point with 2,4-benzylidene-xylitol prepared from 3,5-benzylidene-gluco-*gulo*-heptitol showed no depression. The alcohol filtrate was evaporated to dryness and the residue was recrystallized from 30 ml. of water and yielded 3.6 g. of product melting at 142–144°, making the total yield of pure compound 6.9 g. or 58%.

**Xylitol from the Hydrolysis of 2,4-Benzylidene-xylitol.**—A mixture of 3 g. of 2,4-benzylidene-xylitol, 25 ml. of water and 5 ml. of glacial acetic acid was refluxed for three hours and then was concentrated *in vacuo* to dryness. The residual sirup (1.5 g.; theory, 1.9 g.) was dissolved in 10 ml. of hot 95% ethanol, filtered through carbon and the filtrate was seeded with xylitol. The crystalline product (1.2 g.) was recrystallized from 10 parts of ethanol and gave 1.0 g. of pure xylitol as small prisms melting at 93–94°; a mixed melting point with authentic xylitol (m. p. 93–94°) showed no depression. Upon acetylation in pyridine solution with acetic anhydride it was converted to the known xylitol pentaacetate (m. p. 63–64°).

*Anal.* Calcd. for $C_5H_{12}O_5$: C, 39.47; H, 7.95. Found: C, 39.35; H, 7.99.

**Triacetyl-2,4-benzylidene-xylitol.**—A mixture of 1.0 g. of 2,4-benzylidene-xylitol, 10 ml. of pyridine and 5 ml. of acetic anhydride was allowed to stand for forty-eight hours at room temperature and then was poured into 200 ml. of ice and water; the triacetyl-2,4-benzylidene-xylitol (1.5 g., m. p. 93–95°) which precipitated was recrystallized from 8 parts of alcohol and yielded 1.3 g. of pure compound melting at 94–95° (cor.). The substance is soluble in warm alcohol, acetone, benzene, chloroform and glacial acetic acid and insoluble in water and cold alcohols.

*Anal.* Calcd. for $C_{18}H_{22}O_8$: C, 59.01; H, 6.05; $CH_3CO$, 35.2. Found: C, 58.94; H, 6.19; $CH_3CO$, 35.1.

**Dibenzoyl-2,4-benzylidene-xylitol.**—This compound is the only product as yet isolated in several attempts to prepare tribenzoyl-2,4-benzylidene-xylitol. To an ice-cold solution of 0.5 g. of 2,4-benzylidene-xylitol in 10 ml. of pyridine was added dropwise 1.5 ml. (100% excess) of benzoyl chloride. After standing at room temperature for forty-four hours, the rose-colored slurry was poured into 300 ml. of ice and water; the gummy precipitate gradually crystallized and was filtered, washed well and dried. The product (0.8 g.) was twice recrystallized from 15 parts of ethanol and yielded 0.3 g. of a compound which formed slender rods melting at 148–149° (cor.) having the composition of a dibenzoyl-2,4-benzylidene-xylitol. The substance is soluble in chloroform, acetone and hot alcohols and insoluble in water and cold alcohols.

*Anal.* Calcd. for $C_{26}H_{24}O_7$: C, 69.63; H, 5.39; $C_6H_5CO$, 46.9. Found: C, 69.61; H, 5.37; $C_6H_5CO$, 46.5

**Tritosyl-2,4-benzylidene-xylitol.**—To a cold solution of 1.0 g. of 2,4-benzylidene-xylitol in 10 ml. of pyridine an ice-cold solution of 3 g. (4 molecular equivalents) of *p*-toluenesulfonyl chloride in 5 ml. of pyridine was added dropwise. After standing at room temperature for forty-eight hours, the mixture was poured into 250 ml. of ice and water; the separated product (2.9 g., quantitative) was recrystallized by solution in 5 parts of chloroform and addition of 20 parts of ethanol, whereupon long prismatic rods rapidly deposited. The pure compound melts at 157–158° (cor.); it is insoluble in water and in hot 95% ethanol, and soluble in chloroform, acetone, benzene and warm glacial acetic acid.

*Anal.* Calcd. for $C_{33}H_{34}O_{11}S_3$: C, 56.39; H, 4.88; S, 13.69. Found: C, 56.35; H, 4.94; S, 13.58.

### 3,5-Methylene-gluco-*gulo*-heptitol and Derivatives

**3,5-Methylene-gluco-*gulo*-heptitol.** A solution of 20.0 g. of gluco-*gulo*-heptitol in a mixture of 50 ml. of concentrated hydrochloric acid and 50 ml. of 37% aqueous formaldehyde was placed in an evacuated desiccator containing small beakers of concentrated sulfuric acid and solid sodium hydroxide and allowed to evaporate at 25° to a thin sirup. The sirup was diluted with 20 ml. of absolute alcohol and the evaporation was continued; this process was repeated four times. Crystallization of the acetal occurred after the second evaporation and progressed with each addition and evaporation of alcohol. The magma so obtained was thinned with 10 ml. of absolute alcohol and the acetal was separated by filtration. The reaction product

(9) L. von Vargha, *Ber.*, **68**, 18 (1935).

(18.3 g., 87%), which was nearly pure, was recrystallized from 40 parts of alcohol and gave 15.4 g. (73%) of pure 3,5-methylene-gluco-*gulo*-heptitol. The acetal formed elongated plates which melted at 184–185°. An aqueous solution of the compound is optically inactive, as would be expected. It is soluble in hot methanol and dioxane, cold water and pyridine and nearly insoluble in acetone, chloroform, ethyl acetate, benzene, ether and petroleum ether.

*Anal.* Calcd. for $C_8H_{16}O_7$: C, 42.85; H, 7.19. Found: C, 42.82; H, 7.14.

**Pentaacetyl-3,5-methylene-gluco-*gulo*-heptitol.**—A solution of 1.0 g. of 3,5-methylene-gluco-*gulo*-heptitol in a mixture of 10 ml. of pyridine and 10 ml. of acetic anhydride was allowed to stand at room temperature for forty-eight hours and then poured upon crushed ice. The precipitated acetyl derivative (1.7 g., 89%) was recrystallized from 10 parts of alcohol and it formed quadrilateral platelets which melted at 173–174°. The compound, as is to be expected, showed no rotation in chloroform solution (*c*, 1.05); it is soluble in cold chloroform, acetone and pyridine and in warm methanol and ethanol, ethyl acetate and benzene and insoluble in water and petroleum ether.

*Anal.* Calcd. for $C_{18}H_{26}O_{12}$: C, 49.77; H, 6.03; $CH_3CO$, 49.5. Found: C, 49.75; H, 5.95; $CH_3CO$, 49.2.

**Pentabenzoyl-3,5-methylene-gluco-*gulo*-heptitol.**—A suspension of 0.5 g. of the 3,5-monomethylene-gluco-*gulo*-heptitol in 10 ml. of pyridine was agitated at room temperature with 1.4 ml. (5.5 molecular equivalents) of benzoyl chloride. The acetal dissolved and shortly thereafter a precipitate of pyridine hydrochloride deposited. The mixture was allowed to stand at 25° for sixty hours and then was poured upon crushed ice. The solid reaction product was recrystallized from 110 parts of alcohol as fan-like clusters of small needles. The compound is readily soluble in cold acetone, ethyl acetate, chloroform, benzene, dioxane and warm methanol and ethanol; it is nearly insoluble in water, ether and petroleum ether. The compound, which is optically inactive by reason of its *meso* structure, melts at 179–180°. The yield was 1.1 g. (65%).

*Anal.* Calcd. for $C_{43}H_{36}O_{12}$: C, 69.34; H, 4.87; $C_6H_5CO$, 70.6. Found: C, 69.53; H, 5.06; $C_6H_5CO$, 70.4.

**Tri- and Tetra-tosyl-3,5-methylene-gluco-*gulo*-heptitols.**—A solution of 2.0 g. of 3,5-methylene-gluco-*gulo*-heptitol and 9.4 g. of *p*-toluenesulfonyl chloride in 40 ml. of pyridine was allowed to stand at 25° for six days. The precipitate which formed on pouring the reaction mixture into 300 ml. of ice-cold water was triturated repeatedly with water and after five days it partly crystallized. The product (7.6 g.) was recrystallized from 15 parts of alcohol and yielded 1.25 g. of a mixture of crystals melting at 149–154°; no other crystalline material could be obtained. Fractional recrystallization of the mixture from 75 parts of alcohol gave 0.6 g. of a fraction melting at 145–151°, and 0.23 g. of a second fraction melting at 153–154°. The first fraction was recrystallized from 166 parts of methanol and yielded 0.4 g. (5%) of tetratosyl-3,5-methylene-gluco-*gulo*-heptitol melting at 161–162° and crystallizing in the form of elongated narrow plates; further recrystallization did not change the melting point. The substance is soluble in cold acetone, chloroform and ethyl acetate and in warm methanol, acetic acid and methyl cellosolve.

*Anal.* Calcd. for $C_{36}H_{40}O_{15}S_4$: C, 51.42; H, 4.79; S, 15.25. Found: C, 51.15; H, 4.71; S, 15.37.

The second fraction of 0.23 g. (7%) was recrystallized from 90 parts of absolute alcohol; it formed glistening platelets, distinctly different in appearance from the tetratosyl derivative; its melting point remained 153–154°. Analysis showed it to be a tritosyl-3,5-methylene-gluco-*gulo*-heptitol. The compound is soluble in cold acetone and chloroform, and in warm acetic acid, ethyl acetate and methyl cellosolve and nearly insoluble in cold or warm methanol and water.

*Anal.* Calcd. for $C_{29}H_{34}O_{13}S_3$: C, 50.72; H, 4.99; S, 14.00. Found: C, 50.87; H, 4.85; S, 14.08.

**Pentatosyl-3,5-methylene-gluco-*gulo*-heptitol.**—A solution of 1.0 g. of 3,5-methylene-gluco-*gulo*-heptitol and 4.7 g. (5.5 molecular equivalents) of *p*-toluenesulfonyl chloride in 10 ml. of pyridine was heated on the steam-bath for ninety minutes. The pyridine was evaporated by an air current and the sirup which remained was extracted with cold water and then dissolved in 10 ml. of hot ethyl acetate. The precipitate which deposited on cooling was recrystallized four times from ethyl acetate to free it from partially tosylated derivatives and gave 0.37 g. (8%) of pure pentatosyl-3,5-methylene-gluco-*gulo*-heptitol. The compound was obtained as microcrystalline granules which melted at 211–212°; it is soluble in cold acetic acid and methanol and warm chloroform, and nearly insoluble in warm acetone and methyl cellosolve.

*Anal.* Calcd. for $C_{43}H_{46}O_{17}S_5$: C, 51.90; H, 4.66; S, 16.11. Found: C, 51.89; H, 4.85; S, 15.97.

**Pentaphenylcarbamyl-3,5-methylene-gluco-*gulo*-heptitol.**—A solution of 1.0 g. of 3,5-methylene-gluco-*gulo*-heptitol and 2.9 g. (5.5 molecular equivalents) of phenyl isocyanate in 25 ml. of pyridine was refluxed for two hours. The precipitate (2.8 g., 78%; m. p. 245–247°) which separated on evaporation of the pyridine was recrystallized by solution in 10 parts of pyridine and the addition of 20 parts of methanol. The phenylcarbamate crystallizes in tiny, irregularly shaped granules which melt at 246–247°; it is soluble in pyridine, dioxane and hot methyl cellosolve and nearly insoluble in cold or hot acetone, methanol, ethanol and acetic acid.

*Anal.* Calcd. for $C_{43}H_{41}O_{12}N_5$: C, 62.99; H, 5.04; N, 8.54. Found: C, 62.82; H, 5.05; N, 8.43.

**Sodium Periodate Oxidation of 3,5-Methylene-gluco-*gulo*-heptitol.**—A solution of 0.1229 g. of 3,5-methylene-gluco-*gulo*-heptitol in 10 ml. of water was cooled to 5° and 5 ml. (3.96 molecular equivalents) of 0.434 *M* aqueous sodium periodate solution was added; the solution was then allowed to warm to 20° and the volume was adjusted to 25 ml. with water. Analysis of 5-ml. aliquots at the expiration of thirty minutes, four and twenty-four hours, and eight days indicated that 1.92, 1.91, 2.00 and 2.05 molecular equivalents, respectively, of sodium periodate had been consumed. No acidic compound was produced as a result of the oxidation. An aliquot of the oxidized solution (equal to 0.0460 g. of acetal) was poured into 200 ml. of 0.4% dimedon solution and the mixture, upon preservation at 5° for forty-eight hours, deposited 0.1220 g. of formal-dimedon, or 2.03 molecular equivalents for each equivalent of acetal oxidized. These analyses prove that methylene-gluco-*gulo*-heptitol contains two terminal glycol groups as parts of its structure. The absence of formic acid as an oxidation product shows that the secondary alcoholic groups which are adjacent to these terminal glycol groups are concerned in the acetal formation and the structure of the acetal is therefore limited to that of 3,5-methylene-gluco-*gulo*-heptitol. Such a structure conforms with the reduction of two equivalents of sodium periodate.

**2,4-Methylene-xylitol from 3,5-Methylene-gluco-*gulo*-heptitol.**—To a cold solution of 4.5 g. (0.02 mole) of 3,5-methylene-gluco-*gulo*-heptitol in 50 ml. of water an aqueous solution of 8.6 g. (0.04 mole) of sodium periodate in 100 ml. of water was added in 25-ml. portions at five-minute intervals. The mixture was allowed to stand for one hour at 25° and, after the addition of a solution of 4.9 g. (0.02 mole) of barium chloride dihydrate in 100 ml. of water, it was cooled to 5° and allowed to stand for two hours more. The precipitated barium salts were separated by filtration and the filtrate (which was reducing to Fehling solution) was agitated in a bomb with Raney nickel and hydrogen under a pressure of 66 atmospheres at 100° for six hours. The catalyst was separated by filtration and the filtrate, which was non-reducing to Fehling solution, was concentrated *in vacuo* to dryness; the residue was extracted with 25 ml. of cold methanol and the extract was again concentrated *in vacuo* to dryness and the crystalline residue (3.5 g.) was recrystallized from hot absolute alcohol. The reaction product, which crystallized as clusters of elongated prisms, melted at 108–109° in agreement with the known value for 2,4-methylene-xylitol; a mixed melt-

ing point determination with authentic 2,4-methylene-xylitol caused no depression of this value. The yield was 2.8 g. (88%). The series of reactions constitutes a definitive proof that monomethylene-gluco-*gulo*-heptitol is 3,5-methylene-gluco-*gulo*-heptitol.

Although the expected dialdehydo oxidation product from 3,5-methylene-gluco-*gulo*-heptitol could not be crystallized, it was isolated in a separate experiment in the form of its di(phenylhydrazone). The latter compound crystallized from 30 parts of alcohol as small, light yellow plates which melted with decomposition at 188–190°.

*Anal.* Calcd. for $C_{18}H_{20}O_3N_4$: C, 63.51; H, 5.92; N, 16.46. Found: C, 63.23; H, 6.10; N, 16.56.

## Summary

Proof is presented that the monobenzylidene-gluco-*gulo*-heptitol (m. p. 218°) which Emil Fischer discovered is the 3,5-benzylidene acetal. The condensation of gluco-*gulo*-heptitol with formaldehyde also gives a high yield of a monoacetal which proves to be 3,5-monomethylene-gluco-*gulo*-heptitol. These 3,5-monoacetals are those to be expected from generalizations relating the configuration of polyhydric alcohols and the structure of their derived benzylidene and methylene acetals.

Crystalline 2,4-benzylidene-xylitol and a number of its derivatives have been described.

BETHESDA, MARYLAND RECEIVED MAY 9, 1946

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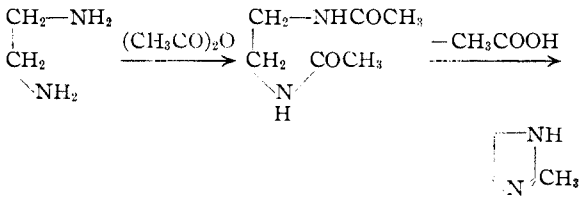
[CONTRIBUTION FROM THE STERLING-WINTHROP RESEARCH INSTITUTE]

# The Preparation of Some Monoalkyl- and Symmetrical Dialkylethylenediamines

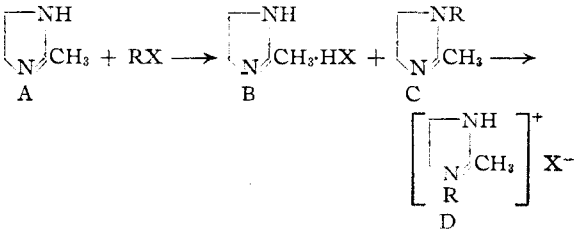
BY JOHN A. KING AND FREEMAN H. MCMILLAN

It was hoped that a convenient preparation of monoalkylethylenediamines[1,1a] could be realized by making use of the fairly readily available 2-methylimidazoline. Following the observation of Ladenburg[2] that 2-methylimidazoline methylated easily, and the finding by Aspinall[3] that 2-substituted imidazolines could be hydrolyzed to ethylenediamine without great difficulty, it seemed reasonable to assume that the preparation of 1-alkyl-2-methylimidazolines and their hydrolysis to monoalkylethylenediamines should afford a satisfactory source of such diamines. In the present work only moderate success was attained by this method.

Commercial (70%) ethylenediamine was converted in essentially quantitative yield to the symmetrical diacetyl derivative[4] with acetic anhydride. By a procedure based on Chitwood and Reid's[5] modification of Ladenburg's original preparation of the material, symmetrical diacetylethylenediamine was pyrolyzed over magnesium powder to give 2-methylimidazoline in yields ranging from 86 to 94%. This represents some improvement over previously reported yields for this reaction.[6]



The alkylation reaction proved to be much more complex than had been anticipated; in addition to the desired product (C) there was



formed the quaternary ammonium salt (D), as well as the hydrohalide salt (B) of the starting material (A).

In an effort to prevent the formation of the hydrohalide of the initial imidazoline, which removed the starting material from participation in any addition reaction, some of the reactions were run in the presence of potassium carbonate to neutralize the halogen acid as soon as it was formed. However, only quaternary products were formed.

The results obtained are summarized in Table I.

Our alkylation data are in general agreement with the very recently available results of Kyrides[6] who obtained 30 to 40% yields (based on halide used) of 1-higher alkyl-2-lower alkyl imidazolines by alkylation of 2-substituted imidazolines with only one-half mole of alkyl halide in an hydrocarbon solvent. He did not hydrolyze the imidazolines to ethylenediamines or report any investigation of higher alkylation products.

(1) A literature review of the preparation of monoalkylethylenediamines has been given by Aspinall, THIS JOURNAL, **63**, 852 (1941). Bloom, Breslow and Hauser, *ibid.*, **67**, 539 (1945), have recently reported the preparation of isoamylethylenediamine in 20% yield by sodium and alcohol reduction of isoamylaminoacetonitrile; while still more recently Linsker and Evans, *ibid.*, **67**, 1581 (1945), have reported the preparation of higher monoalkylethylenediamines in 83 to 98% yield by direct alkylation. The present work was completed before the appearance of the last paper cited.

(1a) Pearson, Jones and Cope, *ibid.*, **68**, 1225 (1946), have very recently described the preparation of cyclohexylethylenediamine and isopropylethylenediamine.

(2) Ladenburg, *Ber.*, **27**, 2957 (1894).

(3) Aspinall, *J. Org. Chem.*, **6**, 895 (1941).

(4) Hofmann, *Ber.*, **21**, 2332 (1888).

(5) Chitwood and Reid, THIS JOURNAL, **57**, 2424 (1935).

(6) Kyrides, U. S. Patent 2,392,326, prepared this and other lower alkyl 2-substituted imidazolines in substantially lower yields by calcium oxide cyclization of monoacylethylenediamines.