5,6-Dimethoxy-2-benzylaminoindanol-1 Hydrochloride.—Four and ninety-one hundredths grams (0.02 mole) of the primary aminoalcohol hydrochloride, 2.12 g. (0.02 mole) of freshly distilled benzaldehyde and 2.12 g. (0.02 mole) of sodium carbonate were added to a suspension of freshly reduced Adams platinum catalyst in absolute ethanol and the mixture subjected to hydrogenation at three atmospheres pressure. The calculated uptake of hydrogen occurred in thirty minutes after which the suspension was warmed, filtered from the catalyst and the filtrate poured into chilled ethereal hydrogen chloride. After chilling, the white precipitate was collected and recrystallized several times from absolute alcohol. The pure white, crystalline product melted at 181.5° (dec.).

Anal. Calcd. for $C_{18}H_{22}O_3NCl$: C, 64.37; H, 6.60; N, 4.17. Found: C, 64.36; H, 6.58; N, 4.41.

In some cases starting material was isolated by the addition of ether to the alcohol filtrate from the main product.

5,6-Dimethoxy-2-isopropylaminoindanol-1 Hydrochloride.—By a procedure similar to that described above but using acetone, there was obtained a product which, after several recrystallizations from absolute alcohol, amounted to 2.3 g. and melted at 190° (dec.).

Anal. Calcd. for $C_{14}H_{22}O_3NCl$: C, 58.43; H, 7.71; N, 4.87. Found: C, 58.54; H, 7.66; N, 5.05.

5,6-Dimethoxy-2-dimethylaminoindanol-1 Hydrochloride.—By a procedure analogous to that described above but using one mole of formaldehyde there was obtained no monomethylamine, but only the dimethylaminoindanol hydrochloride, melting at 172° (dec.).

Anal. Calcd. for $C_{13}H_{20}O_3NCl$: C, 57.03; H, 7.36; N, 5.12. Found: C, 56.87; H, 7.46; N, 5.58.

Summary

A series of thirty-six aminoindanones, aminoindanols and N-substituted aminoindanols containing one or more hydroxyl, methoxyl or methylenedioxy groups in the aromatic ring, have been synthesized. The nitrogen substituents were hydrogen, dimethyl, isopropyl and benzyl; the benzylaminoindanols were prepared through the intermediate oxazolidines and were in some cases isolated in two racemic forms.

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[CONTRIBUTION FROM THE STERLING CHEMISTRY LABORATORY, YALE UNIVERSITY]

The Structures of Some Isopropylidene-*aldehydo*-L-arabinose Derivatives

BY JAMES ENGLISH, JR., AND PAUL H. GRISWOLD, JR.[1]

In a previous paper[2] the positions of the isopropylidene groups in di-isopropylidene-*aldehydo*-L-arabinose and the products of its reaction with Grignard reagents were left indeterminate. An extension of our work on C-substituted pentitols has disclosed evidence leading to the establishment of the structures of these arabinose derivatives in both the D- and L- series.

The triacetone mannitol of Fischer[3] has been shown by Wiggins[4] to be 1,2:3,4:5,6-triacetone mannitol. A graded hydrolysis of this substance[4,5] has been found to yield a diacetone mannitol which Wiggins has converted to an *aldehydo*-diacetone-D-arabinose by lead tetraacetate oxidation. In view of the earlier work of Brigl and Grüner[6] and of Baer and H. O. L. Fischer[7] the structure of this arabinose derivative may be considered established beyond reasonable doubt as 2,3:4,5-diacetone-*aldehydo*-D-arabinose.

2,3:4,5-Di-isopropylidene-*aldehydo*-D-arabinose prepared by the method of Wiggins, or better by periodate oxidation of the same starting material, was treated with cyclohexylmagnesium chloride to form a crystalline di-isopropylidene-1-C-cyclohexylpentitol. This substance was found to be the enantiomorph of the di-isopropylidene-1-C-cyclohexylpentitol previously prepared in this Laboratory[2] from di-isopropylidene-*aldehydo*-L-arabinose. On recrystallizing an equimolar mixture of the two enantiomorphs there resulted a di-isopropylidene-D,L-1-C-cyclohexylpentitol which gave a depression in mixed melting points with both isomers.

In the preparation of di-isopropylidene-L-arabinose diethyl mercaptal the intermediate monoisopropylidene derivative was obtained in a manner analogous to that reported by Gätzi and Reichstein[8] for the D-isomer. Since this substance can be converted into the di-isopropylidene derivative[8] by excess acetone it is evident that the isopropylidene group in this case must be on either the 2,3 or the 4,5 carbon atoms. A lead tetraacetate oxidation of monoisopropylidene-L-arabinose diethyl mercaptal followed by removal of the mercaptal and isopropylidene groups, led to a mixture from which glyoxal was identified as its nitrophenylhydrazone and dinitrophenylhydrazone. This established the structure of this substance as 4,5-isopropylidene-L-arabinose diethyl mercaptal, since no other monoisopropylidene derivative would be expected to yield glyoxal.

Hence it may be concluded that the positions of the isopropylidene groups in this series are as shown in the reaction scheme below.

It is worthy of note that in both the D- and L-series the ratio of the two stereoisomeric pentitols obtained in the reaction of *aldehydo*-di-isopropylidene arabinose with cyclohexylmagnesium chloride is far from unity. In one case as much as

(1) Taken from the thesis presented by Paul H. Griswold, Jr., to the Graduate School of Yale University in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) J. English, Jr., and P. H. Griswold, Jr., THIS JOURNAL, **67**, 2039 (1945).

(3) E. Fischer, *Ber.*, **28**, 1167 (1895).

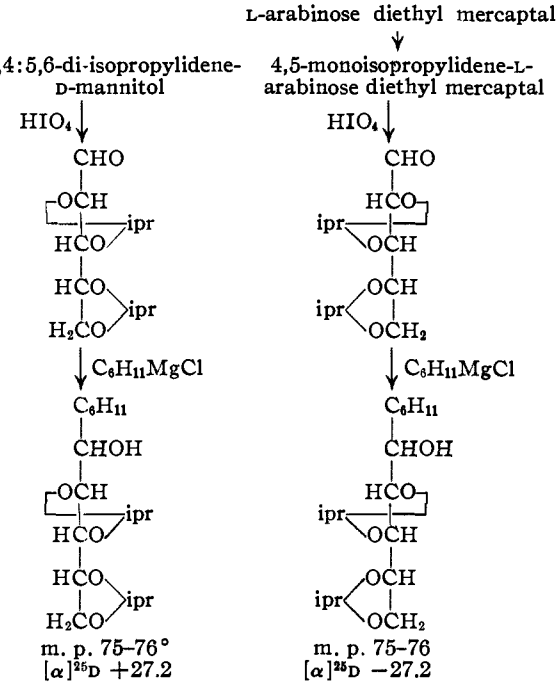
(4) Wiggins, *J. Chem. Soc.*, 13 (1946).

(5) Irvine and Patterson, *ibid.*, 898 (1914).

(6) Brigl and Grüner, *Ber.*, **66**, 931 (1933).

(7) H. O. L. Fischer and Baer, *Helv. Chim. Acta*, **17**, 622 (1943).

(8) Gätzi and Reichstein, *ibid.*, **21**, 914 (1938).



80% of the total 1-C-cyclohexylpentitol was obtained as a pure isomer, crystallized to constant rotation, and it has not yet been possible to isolate any of the other anomer in pure form.

Experimental[9]

2,3:4,5-Di-isopropylidene-*aldehydo*-D-arabinose.—This substance was prepared by oxidation of 3,4:5,6-di-isopropylidene-D-mannitol by the method of Wiggins[4] with a yield of 19%. Improved yields were obtained as follows.

In a well-stirred and cooled flask was placed a solution of 31.4 g. of 3,4:5,6-di-isopropylidene-D-mannitol dissolved in 100 cc. of water. A solution of 28.8 g. of sodium periodate in 450 cc. of water was added, maintaining the temperature at 0–5°. The reaction mixture was allowed to remain at this temperature for thirty minutes, then saturated with salt and extracted with ten 100-cc. portions of chloroform. After drying over sodium sulfate, removing the solvent at room temperature and distillation, there was obtained 24.6 g. (89%) of colorless sirupy 2,3:4,5-di-isopropylidene-*aldehydo*-D-arabinose, b. p. 60–65° (0.08 mm.). This compound was found to be unstable as shown by a change in rotation with time from an initial $[\alpha]^{22}D$ −18.2° in chloroform (*c*, 13.5) to $[\alpha]^{25}D$ +16 after standing for two months. Accordingly the fresh preparations were used immediately for subsequent operations.

1-C-Cyclohexyl-2,3:4,5-di-isopropylidene-D-arabitol.[10] —To a solution of cyclohexylmagnesium chloride prepared from 33.4 g. of chlorocyclohexane and 7.69 g. dry magnesium in 100 cc. dry ether was added 22.5 g. of 2,3:4,5-di-isopropylidene-*aldehydo*-D-arabinose in 100 cc. of ether. The reaction mixture was refluxed for fifteen minutes, cooled in ice, and decomposed with saturated ammonium chloride solution. After ether extraction, drying over sodium sulfate and removal of solvent at low temperatures there remained a solid that was recrystallized from petroleum ether (30–60° b. p.). The yield was 18 g. of 1-C-cyclohexyl-2,3:4,5-di-isopropylidene-D-arabitol after recrystallization to a constant melting point 75–76° and constant rotation $[\alpha]^{25}D$ +27.2 in pyridine (*c*, 2.8). *Anal.* Calcd. for $C_{17}H_{30}O_5$: C, 64.94; H, 9.62. Found: C, 64.96; H, 9.60.

1-C-Cyclohexyl-2,3:4,5-di-isopropylidene-D,L-arabitol. —This substance was prepared by mixing saturated hot petroleum ether solutions of the two enantiomorphs. On cooling the D,L-form separated as large prisms with a melting point 90° which could not be altered by further recrystallization. Mixed melting points with both the D- and L-forms were depressed. *Anal.* Calcd. for $C_{17}H_{30}O$: C, 64.94; H, 9.62. Found: C, 65.05; H, 9.83.

1-C-Cyclohexyl-D-arabitol was prepared by the hydrolysis of its di-isopropylidene derivative as already described for its enantiomorph.[2] After recrystallization from ethanol to constant properties a crystalline product, m. p. 148°, $[\alpha]^{24}D$ −12.6° in pyridine (*c*, 5.2), was obtained. On drying at 60° prior to analysis it was observed that the rotation had changed to $[\alpha]^{24}D$ −15.0° in pyridine (*c*, 4.4). This same phenomenon was then observed with the previously reported L-isomer which was found to change to $[\alpha]^{25}D$ + 15.0°. The loss of weight corresponded to the loss of one molecule of ethanol of crystallization in each case. Since the solvent is reasily lost even in the melting point tube without much change in crystal structure the melting points of both the alcoholate and the free pentitol are apparently the same.

Anal. Calcd. for $C_{11}H_{22}O_5 \cdot C_2H_5OH$: C, 55.68; H, 10.06. Found: C, 55.75; H, 10.37. Calcd. for $C_{11}H_{22}O_5$: C, 56.34; H, 9.47. Found: C, 56.24; H, 9.33. 7.616 g. alcoholate lost 0.848 g. at 60°. Calcd. for $C_{11}H_{22}O_5 \cdot C_2H_5OH$: 0.8478 g.

4,5-Monoisopropylidene-L-arabinose Diethyl Mercaptal.—Thirty grams of L-arabinose diethyl mercaptal was shaken with 600 cc. of dry acetone and 150 g. of anhydrous copper sulfate for three days. Some sodium carbonate was added to insure freedom from acidity, the solution filtered and evaporated at room temperature. There was obtained 29 g. of crude product (m. p. 72°) which was recrystallized from ether–petroleum ether to yield pure 4,5-minoisopropylidene-L-arabinose, m. p. 75.6° and $[\alpha]^{23}D$ +7.6° in methanol (*c*, 8.5). Gätzi and Reichstein[8] reported the same melting point and $[\alpha]^{19}D$ −7.4° in methanol for the D-form.

Anal. Calcd. for $C_{12}H_{24}O_4S_2$: C, 48.7; H, 8.2; Found: C, 49.0; H, 8.3.

Lead Tetraacetate Oxidation of 4,5-Isopropylidene-L-arabinose Diethyl Mercaptal.—A fine suspension of 15 g. of lead tetraacetate in 400 cc. of benzene was stirred vigorously at room temperature with 10 g. of 4,5-di-isopropylidene-L-arabinose diethyl mercaptal. In ten minutes all the oxidizing agent had been consumed. The mixture was filtered and the benzene removed through a fractionating column. The residue distilled at 48–52° (14 mm.). After heating with 4 *N* sulfuric acid for ten minutes the distillate yielded a crystalline *p*-nitrophenylhydrazone. After recrystallization from nitrobenzene, pure glyoxal *p*-nitrophenylhydrazone m. p. 306° (dec.) was obtained. *Anal.* Calcd. for $C_{14}H_{12}O_4N_6$: N, 26.5. Found: N, 25.9. The dinitrophenylhydrazone m. p. 321° (dec.) was also prepared. *Anal.* Calcd. for $C_{14}H_{10}O_8N$: N, 26.8. Found: N, 27.0.

1-C-Cyclohexyl-1,2,3,4-tetraacetyl-5-trityl-D-arabitol was prepared in the same manner as already reported for the enantiomorphous pentitol. There was obtained an 82% yield of pure material, m. p. 134°, $[\alpha]^{25}D$ +15° pyridine (*c*, 27.2). *Anal.* Calcd. for $C_{38}H_{44}O_9$: C, 70.79; H, 6.88. Found: C, 70.80; H, 6.97.

Summary

The position of the isopropylidene groups in 2,3:4,5-di-isopropylidene-D- and L-arabinose diethyl mercaptal and related compounds has been

(9) All melting points are corrected.

(10) These pentitols are referred to as arabitols to distinguish them from the corresponding derivatives prepared from other aldehydo sugars. It is recognized that proper nomenclature must await the establishment of the configuration of the new asymmetric carbon atoms in this series.

established by conversion through D- and L-di-isopropylidene-*aldehydo*-arabinose to enantiomorphous, crystalline, 1-C-cyclohexylarabitols. These substances have all been related to 3,4:5,6-di-isopropylidene-D-mannitol of known structure.

The position of the isopropylidene group in 4,5-isopropylidene-L-arabinose diethyl mercaptal has been established by lead tetraacetate oxidation.

1-C-Cyclohexyl-1,2,3,4-tetraacetyl-5-trityl-D-arabitol has been prepared.

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1-Thiosorbitol

BY M. W. FARLOW, MADISON HUNT,[1] C. M. LANGKAMMERER, WILBUR A. LAZIER,[2] W. J. PEPPEL[3] AND F. K. SIGNAIGO[4]

The deactivation or poisoning of hydrogenation catalysts by even small amounts of sulfur, hydrogen sulfide, or sulfur-containing organic compounds is a familiar phenomenon of hydrogenation chemistry. Accordingly, the discovery in this laboratory[5] that catalysts, such as cobalt polysulfide, function effectively in the conversion of aldehydes, ketones, and nitriles to thiols by hydrogenation in the presence of sulfur or hydrogen sulfide represents an important advance in this field.

Among the aldehydes and ketones to which this reaction can be applied, sugars are of especial interest since their hydrogenation in the presence of hydrogen sulfide has made available for study a variety of new polyhydroxyalkane monothiols. This paper describes the preparation, properties, and more interesting chemical reactions of 1-thiosorbitol[6] which is derived from D-glucose.

The preparation of thiosorbitol from D-glucose by hydrogenation in the presence of sulfur can be represented by the equations

$$H_2 + S \xrightarrow{\text{catalyst}} H_2S$$

$$CH_2OH\overset{\frown O \frown}{CH(CHOH)_3CHOH} + H_2S \longrightarrow \left[CH_2OH\overset{\frown O \frown}{CH(CHOH)_3CHSH}\right] + H_2O$$

$$\left[CH_2OH\overset{\frown O \frown}{CH(CHOH)_3CHSH}\right] + H_2 \xrightarrow{\text{catalyst}} CH_2OH(CHOH)_4CH_2SH$$

This mechanism is supported by the following facts: (1) thioketones and thioaldehydes readily hydrogenate to thiols under the conditions used here; (2) aldehydes and ketones have not undergone hydrogenation to alcohols under the conditions and with the catalysts used here; and (3) alcohols and hydrogen sulfide have not yielded thiols under these conditions. The reactions indicated have been carried out conveniently in pressure equipment using an aqueous reaction medium, free sulfur, and commercial dextrose. At 125–150° and a hydrogen pressure of 1000–1500 lb./sq. in. the reaction is complete in three to four hours. There is obtained a good yield of crude thiosorbitol sirup from which highly purified thiosorbitol can be isolated by several procedures. The preferred method for the isolation of thiosorbitol involves preparation and separation of the cuprous salt which is suspended in ethanol and treated with hydrogen sulfide to regenerate the free thiol. The aqueous solution is evaporated to dryness, and white crystalline 1-thiosorbitol, m. p. 92–93°, is recovered in 25–30% over-all yields by crystallization at low temperatures from alcohol. Nearly pure varieties of thiosorbitol can be obtained by direct crystallization of concentrated crude sirup from ethanol or by oxidation to the corresponding disulfide, which is recrystallized and subsequently cleaved by catalytic reduction in the presence of sulfactive catalysts. Crude thiosorbitol sirup contains organic sulfur compounds which are not thiols. Some of these products are thought to be the result of side reactions involving thioacetal formation or dehydration of thiosorbitol to cyclic sulfides. Low molecular weight cleavage products are also present in crude sirup. Removal of these prior to the above purification procedure is best accomplished by steam distillation or by extracting the aqueous reaction medium with an immiscible organic solvent.

1-Thiosorbitol is a white, crystalline, water-soluble compound showing the reactions characteristic of aliphatic mercaptans and of polyhydric alcohols. For example, oxidation with iodine in hot absolute alcohol gives the corresponding disulfide in excellent yields. The hexaacetate can be prepared by treatment of thiosorbitol with fused sodium acetate and acetic anhydride at 100°. The corresponding benzoate was obtained as a sirup.

Reaction of 1-thiosorbitol in alkaline dioxane with *n*-dodecyl bromide yields *n*-dodecyl 2,3,4,5,6-pentahydroxyhexyl sulfide.

Perhaps the most unusual property of 1-thiosorbitol is its ability to form water soluble salts with a

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(5) Signaigo, U. S. 2,230,390, Feb. 4, 1941; Farlow and Signaigo, U. S. 2,402,613, June 25, 1946.

(6) Lazier and Signaigo, U. S. 2,402,640, June 25, 1946.