The material from zone 3 (76 mg.) was found to contain further amounts (50 mg.) of glycerol triacetate, identified by micro b. p. A negative Scherer[27] inositol test was obtained on the residue left in zone 3 after removal of the glycerol triacetate.

Identification of Inositol in Cane Juice.—The cane juice (1500 g.) was concentrated to *ca.* 1300 g. under reduced pressure in sterilized equipment to remove toluene and brought to its original volume with sterilized distilled water. It was fermented as described above for the cane blackstrap molasses, employing the same amount of yeast. It was deionized, without dilution, in the same manner (soln. ash changed from 0.31% to 0.014%) and the non-fermented residue isolated; yield *ca.* 10 g. of a dark amber colored, hygroscopic sirup with little odor and a bitter taste. The reducing sugar content (modified Scales method) of this residue was found to be 0.1 (calcd. as % of original cane juice). This material was acetylated as described above for cane blackstrap molasses; yield 1.0 g. of Fraction A′ (corresponding to A; an amorphous, dark-colored solid that was partially soluble in acetone but only slightly soluble in chloroform or benzene) and 20.9 g. of chloroform extracted material (golden yellow sirup). The glycerol triacetate (14.6 g.) was removed as described above and a portion (1 g.) of the residual sirup (total amount, 6.0 g., Fraction B′, corresponding to B) was dissolved in 5 cc. of benzene and added at the top of a column (35 mm. in diameter and 230 mm. long) containing 45 g. of 5/1 (by wt.) "Magnesol"[28]/"Celite."[25] The chromatogram was developed with 1350 cc. of 500/1 (by vol.) benzene/ethanol. A well-defined zone about half way down the column was located, isolated and eluted as described above; yield 50 mg. of a golden yellow sirup. This sirup yielded crystals from hot ethanol (abs.); yield 17 mg., m. p. 214–215°, unchanged on admixture with an authentic specimen of inositol hexaacetate, Molisch (−), Fehling (−), Scherer[27] inositol test (+). This crystalline material, in relation to the previously described work with cane blackstrap molasses, was considered to be adequately identified as inositol hexaacetate.

Investigation of the Non-fermented Residue from the Fermentation of Pure Sucrose.—A solution of sucrose (225 g.) in 1500 g. of sterile water was fermented in sterilized equipment with 45 g. of yeast for five days at 30° as described above for the fermentation of cane blackstrap molasses. The resultant solution was deionized in the same manner and the non-fermented residue isolated; yield *ca.* 10 g. of a light yellow sirup with a bitter taste and little odor. This sirup was acetylated as described previously; yield: Fraction A″, 0.8 g. of a dark brown solid with a fatty odor; Fraction B″, 25.1 g. Fraction B″ yielded 18.8 g. of glycerol triacetate and 5.9 g. of residual sirup, a portion (400 mg.) of which was chromatographed as described above. Only an additional quantity of glycerol triacetate was found present.

Dephosphorylation of Phytin During Yeast Fermentation.—An amount of 89.5 mg. of calcium phytate[28] of 17% inositol content, determined by the method of Heubner and Stadler[6] as modified by Earley,[7] and which contained no free inositol by the Beadle procedure,[5] was added to 100 cc. of an aqueous solution of D-glucose (15 g.) and fermented with 3 g. of baker's yeast (Fleischmann, starch-free) for three days at 30°. The yeast was removed by centrifugation and the centrifugate was diluted to 1000 cc. and analyzed for its free inositol content by the method of Beadle[5]; found an amount of free inositol corresponding to a phytin hydrolysis of 68%.

Acknowledgment.—Acknowledgment is made to Dr. R. C. Hockett, Scientific Director of the Sugar Research Foundation, for his counsel. Advice was also rendered by Professor G. L. Stahly of the department of bacteriology of The Ohio State University.

Summary

1. Inositol (m. p. 225°) has been isolated from sugar cane juice (as inositol hexaacetate) and from cane blackstrap molasses.

2. The presence of phytin in cane molasses has been detected by biochemical methods.

3. D-Mannitol has been isolated in small amount from a normal sample of cane molasses but was found to be absent in normal cane juice.

4. D-Glucose (as β-D-glucose pentaacetate) was isolated from cane molasses.

5. It was demonstrated that a commercial sample of baker's yeast was able to dephosphorylate phytin.

6. A method of deacetylation employing ion exchange resins has been established.

(28) We are indebted for this material to the Corn Products Refining Company, Argo, Illinois.

COLUMBUS, OHIO RECEIVED JUNE 28, 1945

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

The Action of Diazomethane upon Acyclic Sugar Derivatives. VII.[1] D-Psicose[2]

BY M. L. WOLFROM, A. THOMPSON[3] AND EVAN F. EVANS[4]

In continuation of our studies on the action of diazomethane upon acyclic sugar derivatives, we have synthesized 1-diazo-1-desoxy-*keto*-D-psicose tetraacetate (II) from D-ribonyl chloride tetraacetate (I). D-Ribonic acid tetraacetate has been recorded by Pasternack and Brown[5] and by Ladenburg and co-workers.[6] The latter synthesized it by the direct acetylation of salts of ribonic acid and the former synthesized it through the acetylated amide according to the general procedure of Hurd and Sowden.[7] Chloroform is the solvent of choice for recording the rotations of sugar acetates and we record herein a number of new rotations of D-ribonic acid derivatives in this solvent. Methyl D-ribonate tetraacetate was synthesized in this work and an improved

(1) Previous publication in this series: M. L. Wolfrom, S. M. Olin and E. F. Evans, THIS JOURNAL, 66, 204 (1944).

(2) Presented in part before the Division of Sugar Chemistry and Technology at the 106th meeting of the American Chemical Society, Pittsburgh, Pennsylvania, September 7, 1943.

(3) Research Foundation Associate of the Graduate School.

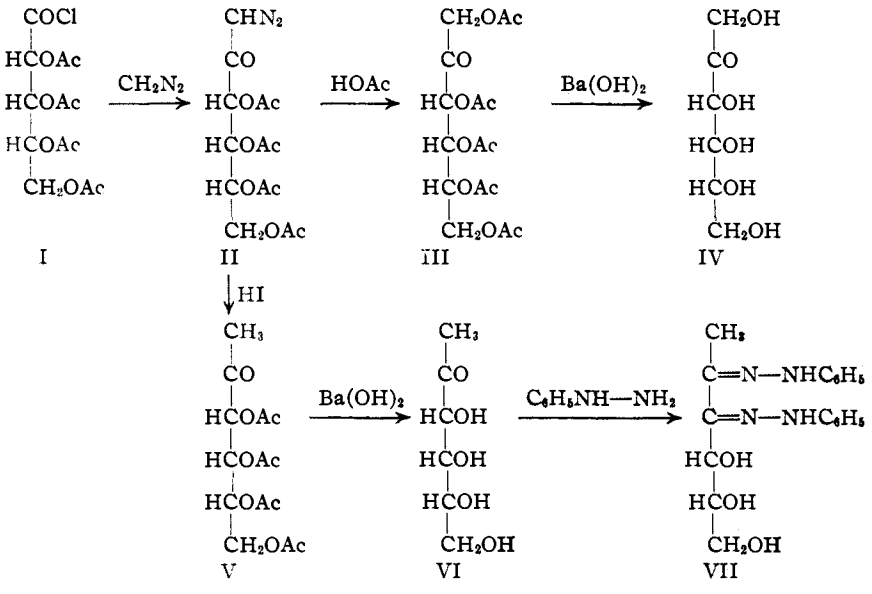
(4) Allied Chemical and Dye Corporation Fellow, 1942–1943.

(5) R. Pasternack and E. V. Brown, U. S. Patent 2,237,263 (1941).

(6) K. Ladenburg, M. Tishler, J. W. Wellman and R. D. Babson, THIS JOURNAL, 66, 1217 (1944).

(7) C. D. Hurd and J. C. Sowden, *ibid.*, 60, 235 (1938).

procedure for the preparation of D-ribonyl chloride tetraacetate[5] is reported.



Reaction of II with acetic acid yielded *keto*-D-psicose pentaacetate (III) in crystalline form. This is the first acetate to be recorded for this very rare sugar. The ease (speed and absence of obscure by-products) of the reaction of II with acids varies directly with the strength of the acid. Since acetic acid is not a very strong acid, the yields on this step were not always satisfactory. We found that catalysis by cupric ion or finely divided copper was beneficial for this step, tending to make the yields higher and less variable. Reaction of II with hydriodic acid according to the general procedure of Wolfrom and Brown,[8] led to the synthesis of the crystalline 1-desoxy-*keto*-D-psicose tetraacetate (V).

keto-Acetates are very sensitive to alkali and are difficult to saponify. The deacetylation procedure of Hudson and Brauns[9] is excellent when the product crystallizes but when the product is amorphous it is difficult to obtain it in ash-free condition, at least with laboratory reagents of the usual purity. Deacetylation of the *keto*-acetates III and V was carried out with barium hydroxide at low temperatures according to the general procedure of Hudson and Brauns but most of the barium ion was then removed as barium oxalate and the remaining ions were removed with ion exchange resins. A similar saponification method differing in detail but employing ion exchange resins, had been reported by Binkley, Blair and Wolfrom.[10] The two ketoses, D-psicose and 1-desoxy-D-psicose, while unfortunately amorphous, were thus prepared in an ash-free state. D-Psicose was characterized as its phenylosazone and phenyl osotriazole.[11] The latter is by far the preferable derivative since the decomposition point of the phenylosazone is extremely unreliable. 1-Desoxy-D-psicose was characterized as its phenylosazone (VII), an interesting derivative since it is a 2,3-osazone. It formed readily and the question arises whether an osazone formed from a ketohexose may not be a mixture of the 1,2 and 2,3 derivatives. This would help to explain the difficulty encountered by us in purifying D-allose phenylosazone when synthesized from D-psicose.

Lobry de Bruyn and Alberda van Ekenstein[12] noted that in the alkaline interconversion of D-glucose and D-fructose, the latter was accompanied by another ketose which they characterized as its phenylosazone and named pseudofructose. Later work has shown that this interconversion is accompanied by the formation of another ketose derived from the 2,3-enediol, in this case the ketose of the D-allose, D-altrose series. Zerban and Sattler[13] have indeed isolated amorphous D-psicose (characterized as its crystalline phenylosazone) from cane molasses distillery residues wherein it undoubtedly originated from the action of the processing alkali (lime defecation) on the reducing sugars present in the cane. Steiger and Reichstein[14] have also synthesized amorphous D-psicose by the pyridine interconversion of D-allose. They characterized the substance as its crystalline phenylosazone and crystalline diisopropylidene derivative. Previously they had synthesized amorphous L-psicose[15] by the action of *Acetobacter xylinum* on allitol.

The use of the trivial term psicose, a contraction of pseudo-fructose suggested by Ohle and Just,[16] is supported by the fact that the names of the other ketohexoses, fructose, sorbose and tagatose bear no generic relation to those of the aldohexoses of the same configuration and it would appear suitable to complete the names of the four D-ketohexoses with a fourth trivial name. The term allulose which has also been applied[13] to this sugar, is loosely formulated. The suffix -ulose,

(8) M. L. Wolfrom and R. L. Brown, THIS JOURNAL, **65**, 1516 (1943).

(9) C. S. Hudson and D. H. Brauns, *ibid.*, **38**, 1216 (1916).

(10) W. W. Binkley, Mary G. Blair and M. L. Wolfrom, *ibid.*, **67**, 1789 (1945).

(11) W. T. Haskins, R. M. Hann and C. S. Hudson, *ibid.*, **67**, 939 (1945).

(12) C. A. Lobry de Bruyn and W. Alberda van Ekenstein, *Rec. trav. chim.*, **16**, 257, 274 (1897).

(13) F. W. Zerban and L. Sattler, THIS JOURNAL, **64**, 1740 (1942); *Ind. Eng. Chem.*, **34**, 1180 (1942).

(14) Marguerite Steiger and T. Reichstein, *Helv. Chim. Acta*, **19**, 184 (1936).

(15) Marguerite Steiger and T. Reichstein, *ibid.*, **18**, 790 (1935).

(16) H. Ohle and F. Just, *Ber.*, **68B**, 601 (1935).

indicating a ketose[17] (*cf.* levulose) is best used in combination with a generic term containing the stereochemical name of the aldose having one less carbon atom followed by a term indicative of the carbon content of the ketose. An example is the established name D-glucoheptulose. Such a name is definitive and non-ambiguous. The systematic name for D-psicose would then be D-ribohexulose. The D-series of the ketoses with their accompanying systematic and trivial (for the ketohexoses only) names is shown in Fig. 1.

We include in this report the synthesis of the 1-chloro-, 1-bromo- and 1-iodo-*keto*-D-psicose tetraacetates. The latter two were desired in order to determine whether they could be used in an improved route to the synthesis of *keto*-D-psicose tetraacetate, an objective which was not realized. These derivatives form another group of acetylated 1-halo-*keto*-acetates, a number of which have already been reported from this Laboratory.[8] The molecular rotations of the three derivatives, Cl:Br:I = −9,500:−6,200:+3,100, change in the same dextro direction as do those of D-fructose. Those of the D-glucoheptulose series[8] change in the levo direction when arranged in this same order.

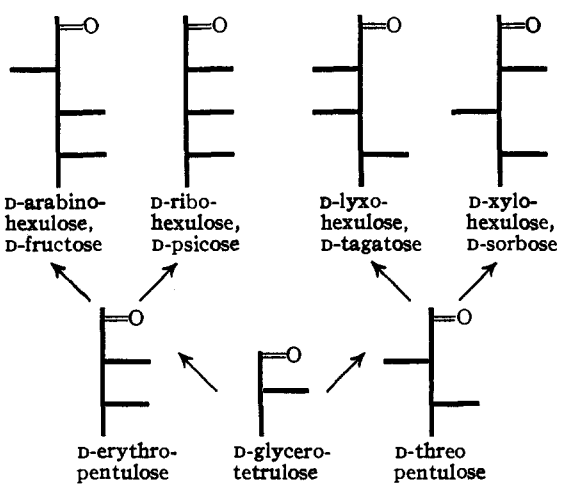


Fig. 1.—D-Series of the ketoses.

Experimental

Preparation of D-Ribonyl Chloride Tetraacetate (I) from D-Ribono-γ-lactone.—D-Ribonamide was prepared from D-ribono-γ-lactone according to the general procedure of Glattfeld and MacMillan[18]; m. p. 136–137°, $[\alpha]^{20}D$ +16.5° (*c* 3, H_2O), in agreement with the constants (m. p. 138–139°, dec.) cited by Tishler and Wellman,[19] by Pasternack and Brown[5] (m. p. 136–137°; $[\alpha]^{20}D$ +16°, H_2O) and by Hudson and Komatsu[20] (m. p. 137–138°; $[\alpha]^{20}D$ −16.4°, H_2O, for the enantiomorph). Acetylation yielded D-ribonamide tetraacetate[5,19]; m. p. 123–124°, $[\alpha]^{20}D$ −35.5° (*c* 3, abs. $CHCl_3$). Deamination of the acetylated amide produced D-ribonic acid tetraacetate[5,6]; m. p. 138–139°, $[\alpha]^{17}D$ −24.4° (*c* 2.3, abs. $CHCl_3$).

(17) G. Bertrand, *Ann. chim. phys.*, [8] **3**, 181 (1904).

(18) J. W. E. Glattfeld and D. MacMillan, THIS JOURNAL, **56**, 2481 (1934).

(19) M. Tishler and J. W. Wellman, U. S. Patent 2,261,608 (1941).

(20) C. S. Hudson and S. Komatsu, THIS JOURNAL, **41**, 1141 (1919); *cf.* R. A. Weermann, *Rec. trav. chim.*, **37**, 16 (1918).

D-Ribonic acid tetraacetate (1.2 g.), suspended in 10 cc. of anhydrous ether, was treated with 0.79 g. (1.1 moles) of phosphorus pentachloride and the mixture shaken mechanically for several hours. The resulting clear solution was diluted to 50 cc. with petroleum ether and from this D-ribonyl chloride tetraacetate separated on cooling; yield 1.19 g. (92%), m. p. 74–76°, $[\alpha]^{22}D$ −43° (*c* 3, abs. $CHCl_3$). Pasternack and Brown[5] recorded only the melting point (75°) for this compound.

Methyl D-Ribonate Tetraacetate.—A solution of diazomethane in ether was added to a solution of D-ribonic acid tetraacetate (2.0 g.) in acetone–ether (25 cc., 1:8) until a slight, permanent yellow color was obtained. Upon the addition of petroleum ether, methyl D-ribonate tetraacetate separated in crystalline form; yield 2.0 g. (96%), m. p. 87–89°. Pure material was obtained on recrystallization from methanol–ether by the addition of petroleum ether; m. p. 89–90°, $[\alpha]^{22}D$ −13.0° (*c* 3, MeOH).

Anal. Calcd. for $C_4H_5O_4(COOCH_3)(CH_3CO)_4$: C, 48.27; H, 5.79; saponification value (5 equiv.), 14.36 cc. 0.1 *N* NaOH per 100 mg. Found: C, 48.28; H, 5.73; saponification value, 14.40 cc.

1-Diazo-1-desoxy-*keto*-D-psicose Tetraacetate (II).—To a solution of 7.8 g. of D-ribonyl chloride tetraacetate in dry ether (110 cc.) was added slowly an ethereal solution (130 cc.) of diazomethane (2.33 g.). After standing for several hours, decolorizing carbon was added and the mixture filtered. Petroleum ether was added to the filtrate just short of opalescence and upon cooling 1-diazo-1-desoxy-*keto*-D-psicose tetraacetate crystallized; yield 6.4 g. (81%), m. p. 68–72°. Three recrystallizations from acetone–ether–petroleum ether yielded pure material; m. p. 73–75°, $[\alpha]^{23}D$ +2.0° (*c* 3, abs. $CHCl_3$).

The compound was colored light yellow. It was soluble in acetone, ether and chloroform; moderately so in ethanol; and was insoluble in petroleum ether and water. It reduced Fehling solution and evolved nitrogen when treated with acids.

Anal. Calcd. for $C_{14}H_{18}O_9N_2$: C, 46.93; H, 5.06; N, 7.82. Found: C, 46.79; H, 5.05; N, 7.60.

The D-ribonyl chloride tetraacetate must be freshly prepared, as otherwise the product is frequently contaminated with methyl D-ribonate tetraacetate.

***keto*-D-Psicose Pentaacetate (III).**—Twenty grams of 1-diazo-1-desoxy-*keto*-D-psicose tetraacetate was dissolved in 200 cc. of acetic acid (99.9%) and 0.3 g. of cupric acetate added. A like amount of finely divided copper (copper bronze) may be substituted for the cupric acetate. On heating to 70–80° a rapid evolution of gas occurred. The solution was finally refluxed for three minutes, cooled, poured into 400 cc. of cold water and the solution extracted with chloroform. The chloroform extract was washed with water, dried and concentrated to a sirup. The sirup was triturated with several portions of petroleum ether to remove residual chloroform, dissolved in ethanol (40 cc.) and water added to incipient opalescence. Crystallization resulted on standing at ice-box temperature; yield 10.1 g., m. p. 55°. Pure material was obtained on recrystallization from ether–petroleum ether and then from methanol–ether–petroleum ether; m. p. 63–65°, $[\alpha]^{20}D$ −21.5° (*c* 3, abs. $CHCl_3$).

keto-D-Psicose pentaacetate crystallized in beautiful, white elongated prisms. It was readily soluble in acetone, chloroform and ether, moderately so in ethanol, and was insoluble in petroleum ether and water. It reduced hot Fehling solution and gave the Pacsu[21] *keto*-acetate test, a useful color test by means of which a *keto*-acetate may be distinguished from an *aldehydo*-acetate or from a sugar acetate of cyclic structure. Negative tests were, however, exhibited by the 1-halo-*keto*-D-psicose tetraacetates described below. An absorption spectrum analysis[22] of the substance in chloroform (U. S. P.) solution (0.0128 molar)

(21) E. Pacsu and F. V. Rich, THIS JOURNAL, **55**, 3018 (1933); F. B. Cramer and E. Pacsu, *ibid.*, **59**, 1467 (1937).

(22) We are indebted to Professor W. R. Brode and Mr. B. Wildi of this Laboratory for this analysis.

revealed an absorption maximum at 2720 Å. (log. $\epsilon_{max.}$ = 0.77; cell thickness, 1 cm.; Beckman quartz spectrophotometer).

Anal. Calcd. for $C_{16}H_{22}O_{11}$: C, 49.23; H, 5.68. Found: C, 49.17; H, 5.59.

D-Psicose (IV) from *keto*-D-Psicose Pentaacetate (III).—To a solution, cooled to 0°, of 20 g. of barium hydrate octahydrate in 200 cc. of water, there was added 15 g. of powdered *keto*-D-psicose pentaacetate. The mixture was maintained at 0° and shaken occasionally until the acetate had dissolved, which required about thirty minutes. The solution was kept at 0° for ninety minutes longer. Approximately 95% of the barium ion was removed by precipitation with the calculated amount of oxalic acid with subsequent filtration of the barium oxalate formed. The filtrate was passed at the rate of 1 liter per thirty minutes over 200 g. of cation exchange resin (Amberlite I R-100[23]) packed in a glass tube 30 mm. in diameter and 620 mm. long. The effluent was then passed at the same rate over a like amount of anion acceptor resin (Amberlite I R-4[23]). This treatment removed the acetate, oxalate and the remaining barium ions. The resulting solution (*ca.* 1500 cc. with the rinse waters from the columns) was concentrated under reduced pressure to a sirup which was dried by ethanol distillation under reduced pressure; yield 2.1 g., $[\alpha]^{25}D$ +4.7° (*c* 4.3, H_2O, 2-dm. tube, no detectable mutarotation). Steiger and Reichstein[14] recorded the value +3.1° for the product regenerated from the crystalline diisopropylidene compound.

The amorphous product was soluble in water, methanol and ethanol but was insoluble in acetone. It reduced hot Fehling solution and possessed a sweet taste.

Anal. Calcd. for $C_6H_{12}O_6$: C, 40.00; H, 6.72. Found: C, 40.16; H, 6.92; ash, absent.

The D-psicose sirup was further characterized as its phenylosazone of m. p. *ca.* 162–163° (dec.) and $[\alpha]^{20}D$ −78.1° (0.25 hr.), −81.4° (3 hrs.), −67.1° (22 hrs.) (*c* 5, pyridine) and more precisely by the preparation of phenyl D-altrosotriazole of m. p. 132–134° from this phenylosazone according to the procedure of Haskins, Hann and Hudson,[11] who record the m. p. 134–135° for this substance. The pyridine rotation cited for the phenylosazone is in agreement (opposite sign) with that reported by Steiger and Reichstein[15] for the enantiomorph; our decomposition point is lower than generally recorded although it is in good agreement with the value cited by Austin and Humoller.[24]

1-Desoxy-*keto*-D-Psicose Tetraacetate (V).—1-Diazo-1-desoxy-*keto*-D-psicose tetraacetate (4.8 g.), dissolved in 100 cc. of chloroform, was shaken in a separatory funnel with 20 cc. of 47% aqueous hydriodic acid. After cessation of nitrogen evolution, water was added and the separated chloroform layer was washed successively with a dilute aqueous solution of sodium thiosulfate (until free of iodine) and with water. The sirup obtained on solvent removal from the dried chloroform solution was crystallized by trituration with petroleum ether; yield 3.08 g., m. p. 71–75°. Pure material was obtained on recrystallization from methanol-ether-petroleum ether; m. p. 75–77°, $[\alpha]^{28}D$ −47° (*c* 3, abs. $CHCl_3$). The compound reduced hot Fehling solution and gave a positive Pacsu[21] *keto*-acetate test. It exhibited solubilities similar to those of *keto*-D-psicose pentaacetate.

Anal. Calcd. for $C_{14}H_{20}O_9$: C, 50.59; H, 6.07. Found: C, 50.2; H, 5.95.

1-Desoxy-D-psicose (VI).—1-Desoxy-*keto*-D-psicose tetraacetate (5 g.) was deacetylated as described above for *keto*-D-psicose pentaacetate and the amorphous product was isolated in the same manner; yield 1.8 g., $[\alpha]^{30}D$ +1.5° (*c* 5, H_2O, 2-dm. tube, no detectable mutarotation).

The substance was soluble in water, ethanol and acetone. It reduced hot Fehling solution and gave a positive iodoform test.

(23) A product of the Resinous Products and Chemical Co., Philadelphia, Pennsylvania.

(24) W. C. Austin and F. L. Humoller, THIS JOURNAL, **56**, 1153 (1936).

Anal. Calcd. for $C_6H_{12}O_6$: C, 43.89; H, 7.37. Found: C, 44.36; H, 7.63; ash, absent.

1-Desoxy-D-psicose Phenylosazone (VII).—This substance was synthesized in the customary manner and was purified by recrystallization from ethanol-water; m. p. 128–130° (dec.), $[\alpha]^{20}D$ +52° → +80° (6 hr.) → +75.7° (24 hr.), (*c* 2.3, pyridine).

Anal. Calcd. for $C_{18}H_{22}O_3N_4$: C, 63.19; H, 6.46; N, 16.32. Found: C, 62.87; H, 6.35; N, 15.92.

1-Chloro-*keto*-D-psicose Tetraacetate.—Dry hydrogen chloride gas was passed into a suspension of 5.0 g. of 1-diazo-1-desoxy-*keto*-D-psicose tetraacetate in 25 cc. of dry ether until the evolution of nitrogen ceased. The product crystallized from the reaction mixture and crystallization was completed by the addition of petroleum ether and standing at ice-box temperature; yield 4.7 g., m. p. 78–80°. Pure material was obtained on further crystallization from ethanol; m. p. 89–91°, $[\alpha]^{30}D$ −26.0° (*c* 4.5, abs. $CHCl_3$).

Anal. Calcd. for $C_{14}H_{19}O_9Cl$: C, 45.83; H, 5.22; Cl, 9.66; saponification value (5 equiv.), 13.63 cc. 0.1 *N* NaOH per 100 mg. Found: C, 45.85; H, 5.20; Cl, 9.65; saponification value, 13.65 cc.

1-Bromo-*keto*-D-psicose Tetraacetate.—1-Diazo-1-desoxy-*keto*-D-psicose tetraacetate (9 g.) was treated as described above for the synthesis of the corresponding chloro compound except that hydrogen bromide was substituted for the hydrogen chloride; yield 8.5 g., m. p. 70–75°. Pure material was obtained on further crystallization from ethanol; m. p. 77–79°, $[\alpha]^{25}D$ −15.1° (*c* 4.6, abs. $CHCl_3$).

Anal. Calcd. for $C_{14}H_{19}O_9Br$: C, 40.89; H, 4.65; Br, 19.43; saponification value (5 equiv.), 12.15 cc. 0.1 *N* NaOH per 100 mg. Found: C, 41.24; H, 4.72; Br, 19.1; saponification value, 12.28 cc.

Experiments designed to improve the ease of preparation of *keto*-D-psicose pentaacetate by treating 1-bromo-*keto*-D-psicose tetraacetate with silver acetate under various conditions or by heating the bromo derivative with acetic anhydride and potassium acetate, were not successful. Similar negative results were obtained on employing the chloro derivative and the iodo derivative (described below).

1-Iodo-*keto*-D-psicose Tetraacetate.—To a solution of 4.8 g. of 1-chloro-*keto*-D-psicose tetraacetate in 25 cc. of acetone, cooled to 5°, was added a solution of 4.8 g. of sodium iodide in 35 cc. of acetone. The mixture was maintained at 5° for three hours and then filtered. The residue obtained on solvent removal under reduced pressure was dissolved in chloroform and washed successively with dilute aqueous sodium thiosulfate and water. The sirup obtained on solvent removal from the dried chloroform solution was crystallized from a small volume of ethanol by the addition of water; yield 4.1 g., m. p. 61–63°. Pure material was obtained on further crystallization from ethanol; m. p. 64–65°, $[\alpha]^{25}D$ +6.8° (*c* 5, abs. $CHCl_3$).

Anal. Calcd. for $C_{14}H_{19}O_9I$: C, 36.69; H, 4.17; I, 27.70; saponification value (5 equiv.) 10.91 cc. 0.1 *N* NaOH per 100 mg. Found: C, 36.77; H, 4.09; I, 27.77; saponification value, 11.07 cc.

Acknowledgment.—We are pleased to acknowledge the assistance of Mr. Hershel Ullman (N. Y. A. Project O. S. U. 161) and of Mr. J. Jay Van Voorhis in a portion of this work. We are also indebted to Dr. H. M. Wuest of Hoffmann-La Roche, Inc., Nutley, New Jersey, for the generous gift of a supply of D-ribonolactone. One of us (A. T.) acknowledges a stipend from the funds of The Ohio State University Research Foundation administered by the Graduate School.

Summary

1. Chloroform rotations are recorded for D-

ribonic acid tetraacetate, its amide, chloride and methyl ester. The latter is recorded for the first time and improved directions for the preparation of the chloride are cited.

2. Reaction of D-ribonyl chloride tetraacetate with diazomethane yielded 1-diazo-1-desoxy-*keto*-D-psicose tetraacetate (II).

3. *keto*-D-Psicose pentaacetate and 1-desoxy-*keto*-D-psicose tetraacetate have been synthesized from II.

4. D-Psicose has been prepared in amorphous form from its *keto*-acetate and characterized as its crystalline phenylosazone and phenyl osotriazole. 1-Desoxy-D-psicose (amorphous) likewise has been synthesized from its *keto*-acetate and characterized as its crystalline phenylosazone.

5. The 1-chloro-, 1-bromo- and 1-iodo- derivatives of *keto*-D-psicose tetraacetate have been synthesized.

6. A systematic nomenclature for ketoses is proposed.

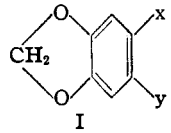
COLUMBUS, OHIO RECEIVED AUGUST 20, 1945

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

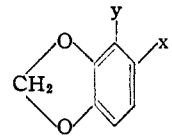
Orientation in the 1,3-Benzodioxole Series

BY RICHARD T. ARNOLD AND NEWMAN BORTNICK[1]

The unusual tendency for direct nuclear substitution to occur almost exclusively at the para positions in 1,3-benzodioxole to give 5,6-disubstituted-1,3-benzodioxoles (type I below) is well known.[2]



I



II

As a result of this preferred orientation, compounds related to type II are not readily accessible and are generally prepared by indirect methods.

In an earlier publication[3] dealing with the synthesis of comparable isomeric pairs in the veratrole series, it was shown that the Claisen thermal rearrangement of allyl phenyl ethers could be used for the synthesis of compounds related to substances I and II (x = hydroxyl; y = allyl) from a common intermediate (III). We have now proved that the procedure employed in the veratrole series[3] can be applied with equal success to the synthesis of 1,3-benzodioxoles as outlined in the reaction diagram (p. 1798).

Some interest has been shown in the possible analgesic action of the acetoxy acids ("aspirins") in the veratrole and 1,3-benzodioxole series.[5] These substances have been prepared by careful oxidation of the corresponding acetoxyaldehydes[2,4] although attempts to acetylate the hydroxy acids directly in the usual manner have been unsuccessful.[2,5]

Incidental to the main study reported in this paper, we have been able to show that the failures mentioned above are due to the remarkable rapidity with which the acetoxy acids undergo hydrolysis and not due to the inability of effecting the acetylation of the hydroxy acids. When the acetylation is brought about by acetic anhydride, good yields of the acetoxy acids are obtained if the excess acetic anhydride is hydrolyzed at low temperatures as described in the experimental section.

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(1) Sharp and Dohme Fellow, 1942–1944.
(2) Arnold and Bordwell, THIS JOURNAL, **64**, 2983 (1942).
(3) Arnold and Bortnick, *ibid.*, **67**, 806 (1945).
(4) Robertson and Head, *J. Chem. Soc.*, 2434 (1930).
(5) Bogert and Elder, THIS JOURNAL, **51**, 534 (1929).

Experimental

6-Carbomethoxy-5-allyloxy-1,3-benzodioxole.—Allylation of 6-carbomethoxy-5-hydroxy-1,3-benzodioxole was effected with allyl bromide and potassium carbonate in acetone solution in a manner identical to that used in the veratrole series[3]; yield 96.5%; m. p. 73–73.5°. A mixture of ether and petroleum ether (b. p. 28–38°) was used as solvent in the recrystallization.

Anal. Calcd. for $C_{12}H_{12}O_5$: C, 61.06; H, 5.13. Found: C, 61.29; H, 5.33.

4-Allyl-5-hydroxy-6-carbomethoxy-1,3-benzodioxole.—The above allyloxy ester (20 g.) was heated at 180–215° for five hours in a nitrogen atmosphere. The product was distilled in a sausage flask at reduced pressure (16 mm.); yield 16.5 g.; m. p. 51–55°. Three recrystallizations from dilute methanol gave the analytical sample; m. p. 54–56°.

Anal. Calcd. for $C_{12}H_{12}O_5$: C, 61.06; H, 5.13. Found: C, 61.19; H, 5.45.

Saponification of this ester with dilute potassium hydroxide gave 5-allyl-6-hydroxypiperonylic acid; m. p. 169–170° (dec.).

Anal. Calcd. for $C_{11}H_{10}O_5$: C, 59.50; H, 4.55. Found: C, 59.45; H, 4.45.

4-Propyl-5-hydroxy-1,3-benzodioxole-6-carboxylic Acid.—When 4-allyl-5-hydroxy-6-carbomethoxy-1,3-benzodioxole (15 g.) was dissolved in methanol (100 cc.) and shaken with hydrogen at forty pounds pressure in the presence of Adams catalyst (100 mg.), the theoretical uptake of hydrogen required only four minutes. The precipitated propyl ester was redissolved by warming the solution. After removing the catalyst on a filter, the filtrate was boiled with excess potassium hydroxide (10%). During this time the methanol was slowly removed by distillation. Acidification and crystallization of the product from dilute acetic acid gave 12 g. of pure product; m. p. 168–169° (dec.).

Anal. Calcd. for $C_{11}H_{12}O_5$: C, 58.97; H, 5.40. Found: C, 58.78; H, 5.33.