quots of this solution were carefully sealed in test-tubes (18 × 150 cm.) which were weighted and placed in an oil-bath at 119.71 ± 0.08°. As the reaction progressed, samples were removed and placed in an ice-bath. After careful washing, the sample tubes were then opened in erlenmeyer flasks and titrated for chloride ion content by the Volhard method. The rate constants were determined in the manner described previously. A correction was applied to the rate constants for volume expansion, as the reaction temperature was much higher than that at which the solutions were made up for the kinetic run.

Because of the peculiar solvent and high temperatures used, coefficient of expansion data were not available; so a special method was developed for measuring volume expansion. Twenty-five milliliters of a 50% (by vol.) solution of dioxane in 92.6% (by wt.) ethanol were sealed in a Kimble glass buret. The height of the liquid in the buret at 22.5° was determined by reading the buret markings. The buret was then completely immersed in the oil-bath at the temperature used for the kinetic run and, after equilibrating, the new height of the liquid in the buret was observed. The difference in level between that at 22.5° and that at the temperature of the kinetic run represents the volume expansion for 25 ml. of the solution. Of course, this increase in volume had to be corrected for the expansion of Kimble glass.

The correction factor, C, by which the rate constant is multiplied is given by the equation

$$C = (V + \Delta V + A)/V$$

where V is 25 ml., ΔV is the observed volume expansion and A is a correction factor for the expansion of Kimble glass. The factor A may be determined from the equation

$$A = nl\pi d^2/4[(l + \alpha\Delta T)^3 - l]$$

where n is the distance in centimeters between milliliter buret markings, l is the buret reading at the temperature of the kinetic run, d is the inside diameter of the buret at 22.5°, α^{15} is the linear coefficient of expansion of Kimble glass, and ΔT is the difference between the temperature of the kinetic run and 22.5°. Correction factors are given in Table III.

TABLE III

CORRECTION FACTORS

V = 25 ml. at 22.5°

T, °C.	ΔV, ml.	A, ml.	C
90.68	2.10	0.05	1.086
101.88	2.50	.06	1.102
109.56	2.80	.06	1.114
119.71	3.17	.07	1.130
128.88	3.47	.08	1.142

(15) α = 0.0000092 cm./cm./°C.

BOULDER, COLORADO RECEIVED AUGUST 10, 1951

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE OHIO STATE UNIVERSITY]

Synthesis of Sedoheptulose (D-Altroheptulose)[1]

BY M. L. WOLFROM, J. M. BERKEBILE AND A. THOMPSON

Sedoheptulose, as its 2,7-anhydropyranose form, has been synthesized from D-altronic acid. This further verifies its structure as D-altroheptulose.

Sedoheptulose, originally designated sedoheptose, was isolated from the common garden plant *Sedum spectabile* by LaForge and Hudson[2] as its characteristic anhydro form designated sedoheptulosan. The structure of the basic sugar unit was established as D-altroheptulose by Ettel[3] and sedoheptulosan was later demonstrated[4] to be 2,7-anhydro-D-altroheptulopyranose. Recently it has been shown that phosphorylated sedoheptulose is an apparent intermediate in plant photosynthesis.[5] We report herein a synthesis of this ketoheptose from D-altronic acid by a procedure which verifies its structure as D-altroheptulose. All intermediates were unfortunately not crystallizable but the inherent and unusual ease of crystallization of the final product, the anhydro sugar, allowed the synthesis to be completed successfully.

Experimental

Sedoheptulosan from Cadmium D-Altronate.—Following the general procedure of Ladenburg and co-workers[6] for the preparation of fully acetylated aldonic acids, 60 g. of the crystalline cadmium salt of D-altronic acid[7] was added under mechanical stirring to 350 ml. of acetic anhydride. This reaction mixture was cooled to 10° and dry hydrogen chloride gas was passed slowly through the agitated slurry. After 15–20 min. the temperature of the solution rose rapidly and then slowly subsided. When a constant temperature was reached, a water-bath was substituted for the ice-bath, the stirring of the solution and the passage of hydrogen chloride being continued. Concluding 1 hr. at 50°, this acetylation mixture was allowed to stand for 12 hr. at room temperature. The solution was concentrated under reduced pressure at 50–60° until a thick slurry resulted. The cooled residue was treated with 500 ml. of ice and water to hydrolyze the acetic anhydride and to dissolve the cadmium salts. This solution was thrice extracted with chloroform and the combined extracts were washed once with water, dried over Na_2SO_4, decolorized with charcoal and concentrated under reduced pressure to a sirupy D-altronic acid pentaacetate which resisted crystallization.

An amount of 25 g. of the above product was dissolved in 200 ml. of toluene, 25 g. of purified[8] thionyl chloride added, and the solution brought to reflux. After 2 hr. of gentle reflux, the excess thionyl chloride and toluene were removed under reduced pressure to yield a sirupy D-altronyl chloride pentaacetate which resisted crystallization.

An amount of 20 g. of the above sirupy product dissolved in 100 ml. of abs. ether was added slowly to 200 ml. of abs. ether containing 6.0 g. of diazomethane. The solution stood at room temperature for several hours and was then kept at ice-box temperature for 24 hr. Solvent removal yielded a sirupy 1-diazo-1-desoxy-*keto*-D-altroheptulose pentaacetate which resisted crystallization. One gram of this preparation was dissolved in 10 ml. of benzene and chromatographed on a 230 × 35 mm. (i.d.)[9] column of Magnesol[10]–Celite[10] (5:1 by wt.) by development with 600 ml. of benzene–ethanol (100:1 by vol.). An alkaline permanganate streak[10] indicated one main zone near the bottom of the

(1) Paper No. 14 in the series entitled "The Action of Diazomethane upon Acyclic Sugar Derivatives"; previous communication, M. L. Wolfrom and H. B. Wood, THIS JOURNAL, **73**, 730 (1951).

(2) F. B. LaForge and C. S. Hudson, *J. Biol. Chem.*, **30**, 61 (1917).

(3) V. Ettel, *Collection Czechoslov. Chem. Communs.*, **4**, 504, 513 (1932).

(4) J. W. Pratt, N. K. Richtmyer and C. S. Hudson, THIS JOURNAL, **73**, 1876 (1951); *ibid.*, **74**, 2200 (1952).

(5) A. A. Benson, J. A. Bassham and M. Calvin, *ibid.*, **73**, 2970 (1951).

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

(7) P. P. Regna and B. P. Caldwell, *ibid.*, **66**, 244 (1944).

(8) J. W. E. Glattfeld and B. P. Kribben, *ibid.*, **61**, 1720 (1939).

(9) Adsorbent dimensions.

(10) W. H. McNeely, W. W. Binkley and M. L. Wolfrom, THIS JOURNAL, **67**, 527 (1945).

column. Elution of this zone with acetone and separation of the pale yellow acetate by evaporation of the solvent, resulted in a sirup which still failed to crystallize.

An amount of 10 g. of the above crude sirup, dissolved in 150 ml. of glacial acetic acid containing 0.01 g. of cupric acetate, was heated at reflux for 20 min. One hundred ml. of solvent was removed under reduced pressure and the residual solution was treated with decolorizing charcoal. This solution of crude *keto*-D-altroheptulose hexaacetate was diluted to 750 ml. with *N* HCl and refluxed for 3 hr. After treatment with decolorizing charcoal the solvent was removed under reduced pressure and the resultant sirup was dissolved in 50 ml. of 80% ethanol. The large crystals of sedoheptulosan monohydrate[4,11] that formed on slow evaporation of the solution at room temperature were recrystallized from hot 80% ethanol; yield 2.0 g., m.p. 100–102° with sintering at 90–92° unchanged on admixture with an authentic specimen[12] of like melting point behavior. X-Ray powder diffraction data (identical with those of an authentic specimen): 7.83[13]–4,[14] 6.15–3, 5.37–3, 4.95–1, 4.41–3, 4.11–3, 3.47–2, 3.32–5, 2.95–5, 2.61–5, 2.53–5, 2.46–5, 2.35–4, 2.20–5, 2.12–5.

Crystallization of the monohydrate from hot abs. methanol yielded the anhydrous form; m.p. 155°, $[\alpha]^{26}D$ −145° (*c* 4, water) in agreement with those (155° and −146°) cited by LaForge and Hudson.[2] X-Ray diffraction data[13,14]: 6.15–2, 5.61–1, 5.01–1, 4.23–5, 3.93–2, 3.44–4, 3.22–5, 3.20–5, 2.77–4, 2.56–5, 2.48–5.

(11) Laura C. Stewart, N. K. Richtmyer and C. S. Hudson, THIS JOURNAL, **71**, 3533, footnote 21 (1949).

(12) We are indebted to Dr. N. K. Richtmyer of the National Institutes of Health, Bethesda, Maryland, for an authentic sample of sedoheptulosan monohydrate.

(13) Interplanar spacing, Å.; λ, 1.5418 Å.; film exposure, 1.8 hr. Acknowledgment is made to Prof. P. M. Harris and Messrs. A. Mishkin and H. B. Wood for assistance in obtaining these data.

(14) Relative intensity, estimated visually; 1 = strongest line.

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[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES, NATIONAL INSTITUTES OF HEALTH, PUBLIC HEALTH SERVICE, FEDERAL SECURITY AGENCY]

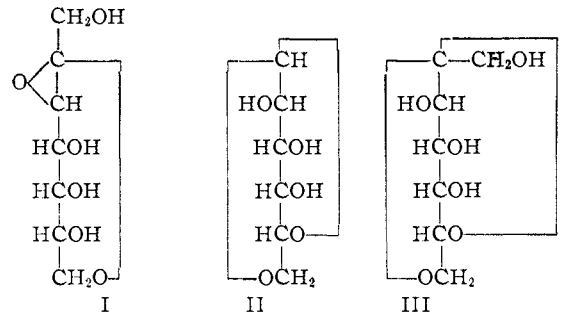
Some Reactions and Derivatives of Sedoheptulosan

BY W. T. HASKINS,[1] RAYMOND M. HANN[2] AND C. S. HUDSON

The behavior of sedoheptulosan and of tetramethylsedoheptulosan toward periodate oxidation has been studied; the molecular weight of sedoheptulosan and the position of the equilibrium between sedoheptulose and sedoheptulosan in acid have been confirmed; and crystalline isopropylidene, dimethylene, tetratosyl and tetrabenzoyl derivatives of sedoheptulosan have been described.

The experiments described in this paper were carried out several years ago and although they did not distinguish between the two most probable formulas for sedoheptulosan they did furnish valuable information leading to the definitive proofs of structure for that compound that are elaborated in the following paper.[3]

In 1938 one of us,[4] assuming the correctness of the experimental observations that had been reported from other laboratories, showed that sedoheptulosan must be regarded as possessing the unusual structure I, with one of its rings having an ethylene oxide form and the other a septanoid form. Shortly afterwards it was found[5] that D-altrosan, which is formed under acidic conditions from D-altrose in the same way that sedoheptulosan is formed from sedoheptulose (= D-altroheptulose), has a 1,6-anhydro ring and a normal pyranose ring as shown in formula II. Accordingly, it seemed desirable either to obtain a confirmatory proof of structure I for sedoheptulosan or to secure evidence of its possible formulation as III, analogous to that of D-altrosan (II). To this end we subjected sedoheptulosan to periodate oxidation[6]; the consumption of two molecular equivalents of oxidant and the liberation of one molecular equivalent of formic acid and no formaldehyde was in agreement with either I or III. Further oxidation of the dialdehyde with bromine water yielded a dibasic acid whose crystalline calcium salt had the composition $C_6H_6CaO_7 \cdot 3H_2O$. Unfortunately, neither the dialdehyde nor the dibasic acid appeared to be hydrolyzable to fragments whose identification would enable us to decide between formulas I and III for sedoheptulosan.



I II III

Other experiments described below have confirmed the monomeric molecular weight of sedoheptulosan and the position of its equilibrium with sedoheptulose under acidic conditions as first announced by its discoverers, LaForge and Hudson,[7] many years ago. Crystalline isopropylidene, dimethylene, tetratosyl and tetrabenzoyl derivatives of sedoheptulosan have been prepared and characterized.

Experimental

Oxidation of Sedoheptulosan by Periodic Acid Followed by Hypobromite.—The reaction of sedoheptulosan with sodium periodate will be discussed in the following paper.[3] For its reaction with periodic acid, 7.7 g. of sedoheptulosan in 300 ml. of water was mixed with 134 ml. (2.1 molecular equivalents) of 0.628 *M* periodic acid. After standing at 25° for 1 hour the reaction mixture was neutralized to phenolphthalein by the addition of aqueous calcium hydroxide.

(1) National Microbiological Institute, National Institutes of Health.

(2) Deceased April 30, 1949.

(3) J. W. Pratt, N. K. Richtmyer and C. S. Hudson, THIS JOURNAL, **74**, 2200 (1952); see also *ibid.*, **73**, 1876 (1951).

(4) C. S. Hudson, *ibid.*, **60**, 1241 (1938).

(5) N. K. Richtmyer and C. S. Hudson, *ibid.*, **62**, 961 (1940).

(6) A preliminary announcement of this reaction was reported by N. K. Richtmyer, *Advances in Carbohydrate Chem.*, **1**, 52 (1945).

(7) F. B. LaForge and C. S. Hudson, *J. Biol. Chem.*, **30**, 61 (1917).