Anal. Calcd. for $C_{24}H_{24}O_8$: C, 65.44; H, 5.49. Found: C, 65.17; H, 5.62.

The substance gave a negative Fehling test and its infrared absorption spectrum indicated the absence of free hydroxyl groups.

Di-D-ribofuranose-1,5′:1′,5-dianhydride.—Two grams of the benzylidene derivative was reduced in the presence of palladium black, absolute ethanol being used as a solvent. When the theoretical quantity of hydrogen had been absorbed, the catalyst was removed and the solution concentrated *in vacuo* at 40° to yield 1.10 g. of crystalline residue. Recrystallization from ethanol–hexane gave the pure dianhydride melting at 230–232° and rotating +9.5° (H_2O, *c* 1.4). Jeanloz, Barker and Lock[8] reported m.p. 231–232° and $[\alpha]^{20}D$ +8.6° ± 0.5° in water (*c* 1.4).

Di-D-ribofuranose-1,5′:1′,5-dianhydride Tetraacetate.—A sample (250 mg.) of the anhydride was acetylated with acetic anhydride in pyridine in the usual manner to yield, from ethanol–pentane 405 mg. (99%) of crude product. Recrystallization from ethanol–pentane gave the pure ester melting at 171–172° and rotating +53.5° in chloroform (*c* 1.03). Mixed with a sample of the ester kindly provided by Dr. G. R. Barker, the material melted at 170–172°.

Acknowledgment.—We are indebted to the Institutes' Microanalytical Laboratory for elementary analyses performed under the direction of Dr. W. C. Alford.

BETHESDA, MARYLAND

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES, NATIONAL INSTITUTES OF HEALTH]

Sedoheptulose—Its Rotation, Reducing Power, Equilibrium with Sedoheptulosan in Acid Solution, and Crystalline Hexaacetate; Also Crystalline 2,7-Anhydro-β-D-*altro*-heptulofuranose

BY NELSON K. RICHTMYER AND JAMES W. PRATT

RECEIVED APRIL 27, 1956

Sedoheptulose (= D-*altro*-heptulose) has been purified by transformation to a crystalline hexaacetate and subsequent deacetylation; the liberated sugar showed $[\alpha]^{20}D$ +8.2° in water and had 80% of the reducing power of D-glucose toward the Hagedorn–Jensen–Hanes ferricyanide reagent. A reinvestigation of the equilibrium between sedoheptulose and sedoheptulosan (= 2,7-anhydro-β-D-*altro*-heptulopyranose) in dilute acid solution has shown that the amount of anhydride varies from 91% at 20° to 84.5% at 80°; loss of material due to the formation of dihydroxyethylfurfural was insignificant at 20–80° but became appreciable quickly at 100°. The new anhydride of sedoheptulose that was isolated first by Zill and Tolbert in 1954 has now been obtained in crystalline form (melting point 199–200°, $[\alpha]^{20}D$ +3.5° in water); its structure has been confirmed as 2,7-anhydro-β-D-*altro*-heptulofuranose.

Sedoheptulose (= D-*altro*-heptulose, I) was discovered in 1917 by LaForge and Hudson[1] in *Sedum spectabile* Bor. This seven-carbon ketone sugar was long considered a curiosity in nature; recently, however, it has become of great importance in biochemical studies, particularly because of its roles in the pentose phosphate pathway of carbohydrate metabolism, in the synthesis of other carbohydrates during photosynthesis,[2] and in the biosynthesis of shikimic acid (and hence of the benzene ring of the aromatic amino acids).[3] Although sedoheptulose can be identified readily through its crystalline anhydride, sedoheptulosan[1] (= 2,7-anhydro-β-D-*altro*-heptulopyranose,[4] IIa, IIb) and especially through sedoheptulosan tetrabenzoate,[5] the sugar itself has never been separated in crystalline form.[6] Furthermore, no derivative was known from which sedoheptulose could be recovered quantitatively. Consequently, no satisfactory data on either the specific rotation or the reducing power of sedoheptulose have been available.

We have now converted crystalline sedoheptulosan with acetic anhydride and pyridine to a sirupy tetraacetate ($[\alpha]^{20}D$ −110°). The acetolysis of this compound with acetic anhydride, in the presense of a small amount of perchloric acid as catalyst, led to the successful preparation of a crystalline sedoheptulose hexaacetate melting at 98–99.5° and showing $[\alpha]^{20}D$ +59.0° in chloroform. A comparison of its molecular rotation ($[M]^{20}D$ +27,300) with that of α-D-altropyranose pentacetate ($[M]^{20}D$ +24,600),[7] together with the fact that the ultraviolet spectrum of the new acetate shows no absorption band in the region of 280 mμ (indicating the absence of a ketone group[8]), is evidence that our hexaacetate is a cyclic form with the α-D-*altro* configuration and may be designated hexa-*O*-acetyl-α-D-*altro*-heptulopyranose. Cautious deacetylation of the hexaacetate yielded sedoheptulose whose rotation was determined as $[\alpha]^{20}D$

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

[2] See B. L. Horecker and A. H. Mehler, *Ann. Rev. Biochem.*, **24**, 229, 249 (1955), for pertinent references.

[3] See P. R. Srinivasan, M. Katagiri and D. B. Sprinson, THIS JOURNAL, **77**, 4943 (1955), for a recent paper and pertinent references.

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

[5] W. T. Haskins, R. M. Hann and C. S. Hudson, *ibid.*, **74**, 2198 (1952).

[6] Note, however, that L. Ujejski and E. R. Waygood [*Can. J. Chem.*, **33**, 687 (1955)] have reported "the beginnings of crystallization of sedoheptulose" although "complete crystallization of a large quantity of sedoheptulose was not obtained." Personal communications from those authors in March 1956 reveal that because of lack of material they were unable to obtain any physical data on their sedoheptulose.

[7] N. K. Richtmyer and C. S. Hudson, THIS JOURNAL, **63**, 1727 (1941). The corresponding rotations for α-D-*gluco*-heptulose hexaacetate and α-D-glucose pentaacetate are +40,200 and +39,700, respectively, and for α-D-*manno*-heptulose hexaacetate and α-D-mannose pentaacetate are +19,200 and +21,500, respectively. The molecular rotation of α-D-*manno*-heptulose hexaacetate has been calculated from a new value for its specific rotation, $[\alpha]^{20}D$ +41.5°, as determined recently by Mr. E. Zissis in this Laboratory.

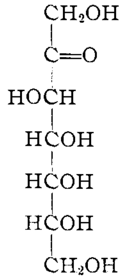
[8] *Cf.* Y. Khouvine and G. Arragon [*Compt. rend.*, **206**, 917 (1938)], who found that hexa-*O*-acetyl-*keto*-perseulose, of $[\alpha]^{20}_{578}$ +0.57° in chloroform, showed absorption at 280 mμ, whereas the hexaacetate of $[\alpha]^{20}_{578}$ −113.4° in chloroform showed no absorption at 280 mμ, could not be hydrogenated, and must therefore be a cyclic form. The corresponding cyclic α-L-galactopyranose pentaacetate shows $[\alpha]^{20}D$ −106.7°.

+8.2° in water. The reducing power of sedoheptulose, estimated by the Hanes modification of the Hagedorn and Jensen ferricyanide method,[9] was 80% that of D-glucose and 115% that of D-*manno*-heptulose.

LaForge and Hudson[1] concluded that both sedoheptulose and sedoheptulosan were transformed by heating with dilute acid to an equilibrium mixture that contained about 20% of the sugar and 80% of its anhydride. Zill and Tolbert,[10] following the earlier observations of Zill, Khym and Cheniae[11] and of Noggle,[12] showed that the equilibrium mixture contained two other components. One of these was formed in about 2% yield and they were able to isolate milligram amounts of it with the aid of thick-paper chromatography. They found that its solution was not appreciably oxidized by periodate, and when heated under acidic conditions it reverted to a mixture containing principally sedoheptulose and sedoheptulosan. At our suggestion, they proposed the 2,7-anhydro-β-D-*altro*-heptulofuranose structure (IIIa, IIIb) for the compound. The basis of this suggestion, as already explained by Zill and Tolbert,[10] lay in the knowledge that D-*glycero*-D-*gulo*-heptose forms two structurally different unimolecular non-reducing anhydrides in acid solution[13] and that 1,6-anhydro-β-D-glucofuranose (IV)[14] and 1,6-anhydro-α-D-galactofuranose,[15] obtained by the pyrolysis of starch and D-galactose, respectively, are resistant to oxidation by periodate and lead tetraacetate.[16]

Although the new anhydrosedoheptulose discovered by Zill and Tolbert[10] is formed to the extent of only 2%, we were able to isolate it readily by taking advantage of its unreactivity toward periodate. Thus, sedoheptulosan (II) was heated with dilute sulfuric acid and the sedoheptulose in the resulting mixture was then destroyed by heating with excess barium hydroxide; after neutralization, deionization and concentration, about 80% of the original sedoheptulosan was recovered in crystalline form. The small amount of sedoheptulosan (II) remaining in the mother liquor was oxidized with sodium metaperiodate followed by bromine and calcium carbonate; the aerated and filtered solution was deionized and concentrated and the new anhydride isolated in 2% yield. This second anhydrosedoheptulose melted at 199–200° and showed $[\alpha]^{20}D$ +3.5° in water in contrast to the values 155–156° and −146° reported[1,4b] for the original anhydrous sedoheptulosan (II). Our first isolation of the new anhydride was effected directly from old sedoheptulose–sedoheptulosan mother liquors by the same procedure, and the intermediate separation of pure sedoheptulosan (II) as a starting material is unnecessary.

Although formula III had been suggested earlier[10] as the most logical one for this new anhydride, structures V and VI could not be excluded without additional experimental evidence, for they also would be expected to resist oxidation by periodate. A glance at these three possibilities shows that III resembles the original sedoheptulosan (II) in that it contains only one CH_2OH group, whereas V and VI each contain two such groups. Accordingly, the tetratosylate of the new compound was prepared and found to be extremely resistant to exchange on heating with sodium iodide: even after 100 hours at 115° in 2,5-hexanedione, 90% of the tetratosylate was recovered. In this respect it behaves like tetra-*O*-tosyl-sedoheptulosan,[4,5] the primary tosyloxy group at C_1 of a substituted ketose being noted for its great lack of reactivity toward sodium iodide.[17] A primary tosyloxy group at C_7 in either V or VI, however, should exchange readily on treatment with sodium iodide. The presence of only one primary hydroxyl group in the new anhydride was confirmed by its reaction with excess triphenylchloromethane in pyridine solution. Like sedoheptulosan (II), it yielded only a monotrityl derivative; both V and VI, on the other hand, should form ditrityl derivatives. Thus, formulas V and VI cannot apply to the new sedoheptulose anhydride and the compound must be 2,7-anhydro-β-D-*altro*-heptulofuranose (III) as originally proposed.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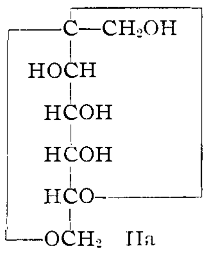
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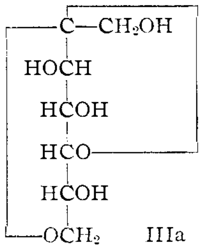
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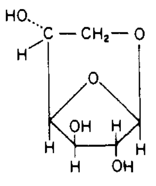

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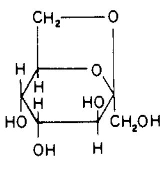
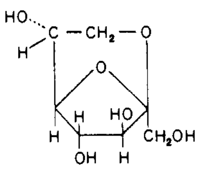


IIb



IIIb

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(9) C. S. Hanes, *Biochem. J.*, **23**, 99 (1929); H. C. Hagedorn and B. N. Jensen, *Biochem. Z.*, **135**, 46 (1923).

(10) L. P. Zill and N. E. Tolbert, This Journal, **76**, 2929 (1954).

(11) L. P. Zill, J. X. Khym and G. M. Cheniae, *ibid.*, **75**, 1339 (1953).

(12) G. R. Noggle, *Arch. Biochem. and Biophys.*, **43**, 238 (1953).

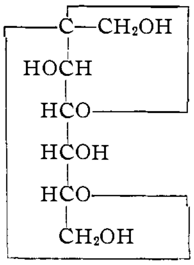
(13) L. C. Stewart and N. K. Richtmyer, This Journal, **77**, 424 (1955).

(14) R. J. Dimler, H. A. Davis and G. E. Hilbert, *ibid.*, **68**, 1377 (1946).

(15) R. M. Hann and C. S. Hudson, *ibid.*, **63**, 2241 (1941); B. H. Alexander, R. J. Dimler and C. L. Mehltretter, *ibid.*, **73**, 4658 (1951).

(16) For a review of the 1,6-anhydrohexofuranoses, including a discussion of the spatial relations involving the *trans*-1,2-diol in rigid ring compounds of this type, see R. J. Dimler, *Advances in Carbohydrate Chem.*, **7**, 37 (1952).

(17) See R. S. Tipson, *Advances in Carbohydrate Chem.*, **8**, 190, 196 (1953).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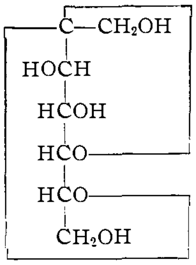
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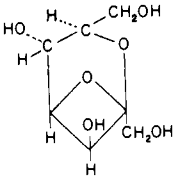
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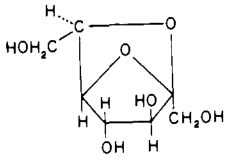
VIb

LaForge and Hudson[1] measured the change in reducing power when either crude sedoheptulose (I) or pure sedoheptulosan (II) was heated in dilute acid solution on the steam-bath and established the position of equilibrium at approximately 80:20 in favor of sedoheptulosan. Zill and Tolbert,[10] through modern chromatographic techniques, have shown that such solutions contain not only 2% of the new anhydride III but still a fourth component. This they were able to separate by thick-paper chromatography and identify, tentatively, as 5-(1,2-dihydroxyethyl)-2-furaldehyde (DHEF), because its ultraviolet absorption spectrum was almost identical with that of 5-(hydroxymethyl)-2-furaldehyde (HMF).[18] The destructive action of hot acids on pentoses and hexoses, particularly the hexuloses, is well known, and leads to furfural, hydroxymethylfurfural and other unsaturated compounds[19] that may subsequently polymerize to humin-like substances. In an attempt to minimize such reactions and to secure the maximum amount of sedoheptulosan (II) in the sedoheptulose–sedoheptulosan equilibrium mixture, we decided to study the transformation at lower temperatures. Preliminary experiments, in which the reaction was followed by the change in rotation only, showed that sedoheptulosan monohydrate ($II{\cdot}H_2O$) in 0.2 *N* hydrochloric acid at 100° formed a mixture that contained about 80% of $II{\cdot}H_2O$ after about 1–1.5 hours. This was not a true equilibrium, however, and further heating caused extensive destruction. When the temperature of the equilibrating reaction was kept at 80°, the amount of $II{\cdot}H_2O$ was about 84.5% and remained practically constant over the period 2–5 hours; additional heating caused only a very small loss by destruction. At 60°, the $II{\cdot}H_2O$ amounted to about 86.5% and showed no change over the period 10–86 hours.

In Table I are given data for sedoheptulose and dihydroxyethylfurfural as well as for sedoheptulosan hydrate in various solutions at approximate equilibrium in dilute hydrochloric acid. The first part of the table illustrates how the point of equilibrium shifts in the same solution when it is heated first at 40°, then at 60°, and finally at 80°; the next set of values shows the reverse shift as the temperature is lowered. The amount of DHEF formed at the lowest temperatures is extremely small and is only 0.1% in the equilibrium as established after 2 hours at 80°. Preliminary experiments in 0.2 *N* hydrochloric acid at 20° showed that equilibrium was reached in about 3 weeks; in 0.5 *N* acid and in *N* acid (see Table I), the same equilibrium was established in less than 10 days. In summary, we find that the equilibrium mixture contains about 91% of sedoheptulosan at 20°, 88.5% at 40°, 86.5% at 60°, and 84.5% at 80°.

TABLE I

THE EFFECT OF TEMPERATURE ON THE AMOUNTS OF SEDOHEPTULOSAN HYDRATE ($II{\cdot}H_2O$), SEDOHEPTULOSE (I) AND 5-(1,2-DIHYDROXYETHYL)-2-FURALDEHYDE (DHEF) IN THE EQUILIBRIUM MIXTURE IN 0.2 *N* HCl

Length of heating						
Hr.	Temp., °C.	$[\alpha]^{20}D$	% $II{\cdot}H_2O$[a]	% I[b]	% I + $II{\cdot}H_2O$	Mole % DHEF[c]
140	40	−117.7°	88.6	9.9	98.5	0.02
140	40 +					
40	60	−114.4	86.2	11.5	97.7	.17
140	40 +					
40	60 +					
4	80	−112.6	85.0	12.7	97.7	.33
4	80	−111.7	84.3	12.9	97.2	.22
4	80 +					
40	60	−114.5	86.3	11.1	97.4	.34
4	80 +					
40	60 +					
140	40	−116.9	88.0	10.1	98.1	.38
238	20 (0.5 *N* HCl)	−121.1	90.9	8.0	98.9	..
236	20 (1.0 *N* HCl)	−121.0	90.9	8.3	99.2	0.01
125	80	−104.0	78.9	13.1	92.0	3.89
1	100	−106.1	80.4	14.8	95.2	1.39
50	100	− 43.0	36.0	19.6	55.6	9.49[d]

[a] Calculated from the specific rotation on the assumption that the solution contained only sedoheptulose (I, $[\alpha]^{20}D$ +8.2°), and sedoheptulosan hydrate ($II{\cdot}H_2O$, $[\alpha]^{20}D$ −134°). The amount of new anhydride (III, $[\alpha]^{20}D$ +3.5°) is so small that its contribution to the total rotation may be neglected. [b] Determined by the ferricyanide method. [c] Calculated from the ultraviolet spectra—see Experimental. [d] This value represents only the DHEF in solution; two portions of solid, polymerized material had already been removed by filtration.

Table I includes also a summation of the percentages of I and $II{\cdot}H_2O$ as determined for each equilibrium mixture. Since these amounts do not total 100%, the difference, in each case where destruction is at a minimum, must represent principally the amount of the new 2,7-anhydro-β-D-*altro*-heptulofuranose (III), which has been set previously at about 2% in the "equilibrium mixture" formed after a short period of heating at 100°. Our figures seem to show a definite trend and indicate that in equilibrium at 20° probably less than 1% of the new anhydride is present, while at 80° the amount may be nearly 3%.

2,7-Di-*O*-acetyl-1,3,4,5-tetra-*O*-tosylsedoheptulose has been obtained by the acetolysis of tetra-*O*-tosylsedoheptulosan.

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(18) (a) M. L. Wolfrom, R. D. Schuetz and L. F. Cavalieri, THIS JOURNAL, **70**, 514 (1948); (b) B. Singh, G. R. Dean and S. M. Cantor, *ibid.*, **70**, 517 (1948); (c) J. H. Turner, P. A. Rebers, P. L. Barrick and R. H. Cotton, *Anal. Chem.*, **26**, 898 (1954).

(19) See, for example, F. A. H. Rice and L. Fishbein, THIS JOURNAL, **78**, 1005 (1956).

Experimental

Hexa-*O*-acetyl-α-D-*altro*-heptulopyranose.—The transformation of sedoheptulosan to sedoheptulose hexaacetate was effected in two stages because of the solubility relationships involved. First, the acetylation of sedoheptulosan with acetic anhydride and pyridine produced the sirupy **tetra-*O*-acetyl-2,7-anhydro-β-D-*altro*-heptulopyranose**; a reasonably pure sample, as determined by analysis, showed $[\alpha]^{20}D$ −110° in chloroform (*c* 1.7).

Anal. Calcd. for $C_{15}H_{20}O_{10}$: C, 50.0; H, 5.6; CH_3CO, 47.8. Found: C, 49.5; H, 5.9; CH_3CO, 45.1.

The second step—acetolysis of the sirupy sedoheptulosan tetraacetate—yielded, with acetic anhydride and sulfuric acid by the usual procedure, a product that could not be extracted from the aqueous sodium bicarbonate solution with chloroform and was presumed to contain an acidic sulfate group[20] that had been introduced during the opening of the 2,7-anhydride ring. Accordingly, the following modified procedure was adopted. A solution of 0.88 g. of sedoheptulosan tetraacetate in 25 ml. of acetic anhydride was cooled to 5° and 25 ml. of acetic anhydride containing 2 drops of 60% aqueous perchloric acid was added. The solution was allowed to stand at 5° for 6 days as the rotation, observed in a 4-dm. tube, changed from −5.93° (3.5 min.) to +4.13° (virtually constant). The solution was poured onto a mixture of ice and solid sodium bicarbonate and the product extracted with chloroform in the usual manner. Concentration of the washed and dried chloroform extract left a sirup that crystallized almost completely upon nucleation with seed crystals obtained by chromatographing the product from a preliminary acetolysis. The sedoheptulose hexaacetate was recrystallized first from ethanol–pentane and then by dissolving it in 5 parts of hot absolute ethanol, cooling slowly to room temperature, and finally adding, in small portions, a total of 25 parts of water. The clusters of white platelets melted at 98–99.5° and showed $[\alpha]^{20}D$ +59.0° in chloroform (*c* 1.2).

Anal. Calcd. for $C_{19}H_{26}O_{13}$: C, 49.35; H, 5.67; CH_3CO, 55.9. Found: C, 49.31; H, 5.83; CH_3CO, 55.8.

The Specific Rotation and Reducing Power of D-*altro*-Heptulose (I).—A solution of 1.504 g. of sedoheptulose hexaacetate in 20 ml. of cold 0.03 *N* methanolic barium methoxide was allowed to stand in the refrigerator for 18 hours. A white precipitate separated and was assumed to be a sedoheptulose–barium methoxide addition compound. The base was neutralized exactly by the addition of a predetermined quantity of standard aqueous hydrochloric acid. The resulting clear solution was concentrated carefully in a vacuum desiccator to a sirup that was dissolved in 10 ml. of water and the rotation of sedoheptulose (= D-*altro*-heptulose) found to be $[\alpha]^{20}D$ +8.2°.

The reducing power of sedoheptulose thus liberated from its acetate was estimated by the ferricyanide method.[9] Titrations showed that 1 mg. of sedoheptulose had the same reducing activity as 1.15 mg. of D-*manno*-heptulose, which is a convenient crystalline standard for heptulose studies; and that 1 mg. of D-glucose had the same reducing activity as 1.43 mg. of D-*manno*-heptulose. From these data we could calculate that, toward the ferricyanide reagent, 1 mg. of D-glucose is equivalent to 1.24 mg. of sedoheptulose; that sedoheptulose has 80% and D-*manno*-heptulose 70% of the reducing power of D-glucose, and that D-*manno*-heptulose has 87% of the reducing power of sedoheptulose. In a control experiment, D-glucose liberated from its α-pentaacetate in the manner described for sedoheptulose from its hexaacetate was found to have the same reducing power as pure crystalline D-glucose.

2,7-Anhydro-β-D-*altro*-heptulofuranose (III) from *Sedum spectabile*.—About 46,700 g. of *Sedum spectabile*, processed as described earlier,[4b] yielded 419 g. of anhydrous sedoheptulosan. The original mother liquor, however, was not treated again with acid but was heated instead with excess aqueous barium hydroxide in an open vessel for 20 hours to destroy any alkali-labile material, principally sedoheptulose. The hot solution was neutralized to phenolphthalein with solid carbon dioxide, cooled, filtered through carbon, deionized by passage through Amberlite IR-120 and Duolite A-4 ion-exchange resins, and concentrated to a sirup that weighed 175 g. Solution of this sirup in 150 ml. of hot methanol and subsequent cooling afforded an additional 80 g. of anhydrous sedoheptulosan. The new mother liquor was concentrated to a sirup weighing 93 g. It contained an estimated 18 g. of sedoheptulosan (from its rotation), plus other polyhydric substances such as D-mannitol and *myo*-inositol, both of which had been isolated in small amounts in previous years from *Sedum* mother liquors. These were oxidized by dissolving the sirup in 1 liter of water and adding aqueous sodium metaperiodate in portions until the solution contained an excess of oxidant even after standing overnight. A strong odor of formaldehyde was noted. Portions of calcium carbonate and bromine (totalling 600 g. and 80 ml., respectively) were added to the solution, which was shaken frequently, until it remained yellowish overnight. The excess bromine was removed by aeration, the mixture filtered, and the solution deionized and concentrated *in vacuo* to a sirup that weighed 6.5 g. and showed $[\alpha]^{20}D$ +4° in water (*c* 18). The product crystallized spontaneously after its concentrated methanol solution had been kept at −5° for several weeks. The 4.2 g. of new anhydride thus obtained represented about a 0.01% yield from *Sedum spectabile*. The compound was recrystallized several times from methanol, from which it separated as chunky prisms melting at 199–200° to a pale yellow liquid and showing $[\alpha]^{20}D$ +3.5° in water (*c* 7.7, *l* 4). On an ascending chromatogram on Whatman No. 1 filter paper, developed with 1-butanol–ethanol–water (4:1.1:1.9) and sprayed with orcinol–trichloroacetic acid reagent,[21] the 2,7-anhydro-β-D-*altro*-heptulofuranose (III) showed R_f 0.21 and sedoheptulosan (II) R_f 0.12; these values are practically identical with the 0.22 and 0.13 reported for the same compounds, respectively, by Zill and Tolbert,[10] but who used as developer 1-butanol–ethanol–water in the ratio 10:1:2.

Anal. Calcd. for $C_7H_{12}O_6$: C, 43.75; H, 6.30. Found: C, 43.88; H, 6.28.

2,7-Anhydro-β-D-*altro*-heptulofuranose (III) from Sedoheptulosan (II).—Nine hundred grams of sedoheptulosan monohydrate[4b] in 9 liters of 0.2 *N* sulfuric acid was heated for 2.5 hours, with the final temperature reaching 95°. The solution was neutralized and then heated with excess barium hydroxide, deionized, concentrated, and 750 g. of sedoheptulosan monohydrate recovered by crystallization of the sirupy residue from aqueous ethanol. The levorotatory mother liquor contained an estimated 18 g. of sedoheptulosan that was destroyed and removed by oxidation with sodium metaperiodate followed by bromine and calcium carbonate and subsequent deionization as described above. The final sirup from 900 g. of sedoheptulosan monohydrate weighed 19.5 g. and afforded 16.2 g. of crystalline 2,7-anhydro-β-D-*altro*-heptulofuranose (II); this yield of 2% is thus in excellent agreement with that reported from the ion-exchange procedure of Zill and Tolbert.[10]

Transformation of 2,7-Anhydro-β-D-*altro*-heptulofuranose (III) to 2,7-Anhydro-β-D-*altro*-heptulopyranose (II).—A solution containing 0.2007 g. of the new anhydride in 15 ml. of 0.2 *N* hydrochloric acid was heated for 5 hours in a boiling water-bath. The observed rotation was then $\alpha^{20}D$ −2.98° in a 2-dm. tube. Since an equal weight of sedoheptulosan under the same conditions showed $\alpha^{20}D$ −3.00°, it is apparent that the same equilibrium was reached from each anhydride. The solution derived from the new anhydride was neutralized to phenolphthalein with dilute aqueous sodium hydroxide, concentrated *in vacuo*, and the dry residue benzoylated in the usual manner. The product (0.35 g., 69%) separated from ethanol as lustrous, pointed plates typical of sedoheptulosan tetrabenzoate; this conclusion was confirmed by its rotation $[\alpha]^{20}D$ −188° in chloroform (*c* 0.8) and m.p. and mixed m.p. 165–166°, values that are identical with those reported by Haskins, Hann and Hudson.[5]

2,7-Anhydro-1,3,4,6-tetra-*O*-*p*-tolylsulfonyl-β-D-*altro*-heptulofuranose.—When a mixture of 0.5 g. of the new anhydride III and 6.0 g. of *p*-toluenesulfonyl chloride (12 molar equivalents) in 25 ml. of pyridine was allowed to stand for 4 days at room temperature and then poured onto ice, the gummy product became granular and filterable in a few hours. The yield was 2.1 g. (quantitative), m.p. 97–100°. Crystallization from methanol or from aqueous acetone gave clusters of short, fine needles that appeared granular, yet had a fluffy appearance. The material sintered at 171° and

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(20) *Cf.* the acetolysis of 1,4:3,6-dianhydro-2,5-di-*O*-benzyl-D-mannitol, in which a neutral sulfate appears to have been formed [R. Allerton and H. G. Fletcher, Jr., THIS JOURNAL, **76**, 1757 (1954)].

(21) A. Bevenue and K. T. Williams, *Arch. Biochem. and Biophys.*, **34**, 225 (1951).

melted at 175–176° to a viscous, milky liquid that became clear and colorless at 177°. From chloroform–ether the tetra-*O*-tosyl derivative separated as very fine, long, matted needles that filled the volume of liquid in the flask. This modification melted at 135–136°. The rotations of the two forms were identical, namely, $[\alpha]^{20}\text{D}$ +16.6° in chloroform (*c* 4).

Anal. Calcd. for $C_{35}H_{36}O_{14}S_4$: C, 51.97; H, 4.49; S, 15.85. Found (135–136° form): C, 52.02; H, 4.62; S, 15.58. (173–175° form): C, 51.97; H, 4.49; S, 15.71.

The tetratosylate was recovered quantitatively after being heated 4 hours with sodium iodide in boiling 2-butanone and 24 hours in 2,5-hexanedione at 100°. After 100 hours at 115° in 2,5-hexanedione a very small amount of sodium *p*-toluenesulfonate was noted, but 90% of the tetratosylate was recovered. Even after 96 hours at 130° in 2,5-hexanedione about 35% of the tetratosylate was recovered; however, nearly one equivalent of sodium *p*-toluenesulfonate also was obtained, presumably due to reaction of secondary tosyloxy groups with sodium iodide under such drastic conditions.

2,7-Anhydro-1-*O*-triphenylmethyl-β-D-*altro*-heptulofuranose.—One gram of the new anhydride III and 5.25 g. (3.6 molar equivalents) of triphenylchloromethane in 50 ml. of pyridine were kept for 48 hours at room temperature and the mixture was then poured, slowly and with stirring, into 2 liters of ice and water. After three days the granular product was filtered, washed with water, and dried. Extraction of the solid with 200 ml. of warm ether removed the triphenylcarbinol and left 0.91 g. of the desired trityl derivative; further quantities of the latter separated upon partial evaporation of the ether solution to furnish a total of 1.37 g. (61%). The trityl derivative was purified by two recrystallizations from acetone–pentane (clusters of stout prisms with pointed ends) and two recrystallizations from hot acetone by the addition of hot water (clusters of small plates). The melting point was about 209°, although values as low as 195° were observed when the temperature of the bath was raised slowly. The rotation was $[\alpha]^{20}\text{D}$ +28.7° in pyridine (*c* 2).

Anal. Calcd. for $C_{26}H_{26}O_6$: C, 71.87; H, 6.03. Found: C, 71.60; H, 6.21.

2,7-Anhydro-1-*O*-triphenylmethyl-β-D-*altro*-heptulopyranose.—One gram of sedoheptulosan (II) was tritylated in the same manner and at the same time as the new anhydride III. The crude product, after being extracted with ether, left 1.19 g. (53%) of trityl derivative melting at 165–170°. It separated from acetone–pentane and from acetone–water in clusters of diamond-shaped plates; after three recrystallizations from the former solvent pair it showed $[\alpha]^{20}\text{D}$ −51.0° in pyridine (*c* 2); the m.p. was about 178° or lower, depending on the rate of heating.

Anal. Calcd. for $C_{26}H_{26}O_6$: C, 71.87; H, 6.03. Found: C, 71.89; H, 6.16.

2,7-Anhydro-3,4,5-tri-*O*-benzoyl-1-*O*-triphenylmethyl-β-D-*altro*-heptulopyranose.—Before we discovered that both sedoheptulosan (II) and the new anhydride III yielded crystalline trityl derivatives readily, we attempted to acetylate and benzoylate their respective tritylation mixtures in pyridine. Of the four products, only the benzoate named above could be crystallized. Thus, 1 g. of sedoheptulosan, 3.5 g. of triphenylchloromethane and 50 ml. of pyridine were kept for 3 days at room temperature. To the colorless solution was then added 2.8 ml. of benzoyl chloride and the mixture kept 2 more days. The mixture was poured onto ice, and on the following day the product was extracted with chloroform. The extract was washed, dried, and concentrated in the usual manner. The resulting sirup was dissolved in carbon tetrachloride and 1.45 g. of triphenylcarbinol removed by crystallization. The mother liquor was concentrated to a sirup that crystallized when heated with methanol. Recrystallization from methanol afforded, in two crops, 1.45 g. (37%) of tritylsedoheptulosan tribenzoate melting at 182–183°. The mother liquor deposited 0.37 g. of sedoheptulosan tetrabenzoate. The trityl derivative, after additional recrystallizations from methanol, from which it separated as clusters of small flakes, melted at 184–185° and showed $[\alpha]^{20}\text{D}$ −206° in chloroform (*c* 1).

Anal. Calcd. for $C_{47}H_{38}O_9$: C, 75.59; H, 5.13. Found: C, 75.51; H, 5.20.

When the 2,7-anhydro-3,4,5-tri-*O*-benzoyl-1-*O*-triphenylmethyl-β-D-*altro*-heptulopyranose was crystallized from chloroform–pentane, it separated as transparent, chunky prisms that became chalky white as they lost solvent of crystallization on filtration and exposure to the air. In a second experiment, the crystals were filtered and washed with pentane, crushed, and weighed within ten minutes. The loss in weight at 20–25° was very rapid at first, and amounted to 10% in 2.75 hours, 11% in 3.5 hours, 12% in 5.25 hours, 13% in 7.5 hours, 16% in 27 hours, and 17% in 47 hours. At the end of 50 days the product had lost 20.5% of its originally recorded weight and was still losing very slowly. When heated in a melting point tube, it sintered and foamed at 90–100°, melted completely at 120°, resolidified at 130–140°, and remelted at 181–183°. On drying to constant weight at 100° in a high vacuum it lost an additional 3.8%. The total observed weight loss of 24.3%, together with some intermediate analyses and observations, suggest that the original, very unstable solvate may have contained one mole of chloroform and two moles of pentane (calcd. loss, 26.1%).

2,7-Di-*O*-acetyl-1,3,4,5-tetra-*O*-*p*-tolylsulfonyl-α-D-*altro*-heptulose.—A solution of 9 g. of tetra-*O*-tosylsedoheptulosan[5] in 95 ml. of acetic anhydride was chilled in an ice–salt mixture and 5 ml. of concentrated sulfuric acid added dropwise with stirring. The solution was allowed to warm slowly to room temperature and maintained there for a period of two weeks. The dark-brown, dextrorotatory solution was poured onto ice and the resulting crystalline mass separated by filtration. The diacetate was separated from unreacted starting material by fractional crystallization from acetone–methanol; it separated as water-white prisms with m.p. 145–146° dec. and $[\alpha]^{20}\text{D}$ +94.9° in chloroform (*c* 1.1).

Anal. Calcd. for $C_{39}H_{42}O_{17}S_4$: C, 51.42; H, 4.65; CH_3CO, 9.45. Found: C, 51.49; H, 4.90; CH_3CO, 9.50.

Determination of Position of Equilibrium between Sedoheptulose (I) and Sedoheptulosan Hydrate ($II \cdot H_2O$) in Dilute Acid Solution.—The test solutions in Table I, except for the last three examples, were 0.05 *M* in sedoheptulosan monohydrate; all others were about 0.07 *M*. The solutions, in glass-stoppered volumetric flasks, were heated either in a boiling water-bath or in an oven at the desired temperature. The solutions, after heating, were cooled rapidly to 20°, the volumes readjusted if necessary, and the rotations observed in a 4-dm. tube, usually. Aliquots were removed, neutralized to cresol red (*p*H 8), and diluted to the appropriate volume for determination of reducing sugar by the ferricyanide method.[9] The ultraviolet spectra were obtained with a Cary recording spectrophotometer, model 11. The spectra showed a major peak at about 285 mμ and a minor peak at about 230 mμ, values that are practically identical with those reported for HMF.[18] On the assumption that the molecular absorption coefficient of DHEF is about the same as that of HMF, namely, 16,500, the mole % of DHEF generated by the action of acid on sedoheptulose has been estimated as shown in the last column of Table I. We recognize that these values are only approximations, especially after the longer periods of heating at the higher temperatures, and that the recorded spectra are actually the composite spectra of DHEF, simpler aldehydes,[18,19] oxidation products[18c] and polymeric substances. However, these approximations do show the trend of the destructive action of the acid under the conditions of our experiments.

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