

peatedly recrystallized from 50% alcohol, finally being obtained in fine needles melting at 138° (corr.).

(2) An ice cold solution of 1.0 g. of pure racemic galuco-heptitol heptaacetate in 70 cc. of methyl alcohol was deacetylated by addition of 2 cc. of 1.35 *N* barium methy- late. The next morning the barium was precipitated by addition of 27 cc. of 0.1 *N* sulfuric acid, and the filtered solution concentrated to a dry sirup. The sirup was dissolved in 10 cc. of hot alcohol and the solution when cooled deposited the racemate in rosets of very fine needles, differing greatly in crystalline appearance from the active forms. One recrystallization from 5 parts of 90% alcohol gave a pure product melting at 138° (corr.): yield 0.4 g. (quantitative). Because of the difficulty of removing small amounts of active component, the deacetylation of the pure racemic alcohol heptaacetate is definitely superior as a preparative method for this substance.

Anal. Calcd. for $C_7H_{16}O_7$: C, 39.60; H, 7.60. Found: C, 39.46; H, 7.77.

Summary

Perseulose phenylosazone and the phenyl- osazone that is common to D-gala-L-gluco- and D-gala-L-manno-heptose are found to be enan- tiomorphic forms, and the same is true of the pen- taacetates of these osazones. The reduction of perseulose by hydrogen and Raney nickel yields D-manno-D-gala- and L-gala-D-gluco-heptitol. These data supply two independent conclusive proofs that perseulose is L-galaheptulose, as was surmised some years ago by La Forge.

WASHINGTON, D. C.

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[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE]

The Oxidative Degradation of Perseulose to L-Galactonic Acid¹

BY NELSON K. RICHTMYER, RAYMOND M. HANN AND C. S. HUDSON

Kiliani and Sanda² observed that the oxygen of the air reacted with alkaline solutions of re- ducing sugars, and suggested that many inter- esting compounds would be found among the products of such reactions. The classical re- searches of Nef confirmed this prediction. Nef and his collaborators³ studied the effect of passing very rapid streams of air through alkaline solu- tions of D-glucose, D-fructose and D-galactose. Among the numerous products isolated were D- arabanolactone from glucose and fructose, and D-lyxonolactone in 22% yield from galactose. These substances had been formed by cleavage of the hexose molecule between the first and second carbon atoms, the fragments appearing as formic acid and a pentonic acid which could be identified through its crystalline derivatives. Since D- glucose and D-fructose each yielded D-arabonic acid, it was apparent that the oxidation and cleavage involved the 1,2-enediol common to those sugars and formed readily from them under the influence of the caustic alkali. Nef, Hedenburg and Glattfeld,⁴ applying this reaction in a study

of the alkaline oxidation of pentoses with air, ob- tained D-threonic acid phenylhydrazide from D- xylose, and L-erythronolactone in 36% yield from L-arabinose. Hudson and Chernoff⁵ oxidized rhamnose to L-rhamnotetronolactone, and Clark⁶ oxidized fucose to L-fucotetronolactone, both reactions being of importance in studies of the configurations of the respective methylpentoses.

In 1935, Spengler and Pfannenstiel⁷ oxidized a number of reducing sugars under conditions simi- lar to those of Nef, but instead of air they used pure oxygen. The results were startling in that the yields of aldonic acid having one less carbon atom than the original aldehyde or ketone sugar rose to 60-75% of the theoretical. The further application of this oxidation with pure oxygen in alkaline solution furnished Neuberg and Collatz⁸ with a 90% yield of D-arabonic acid-5-phosphoric acid from D-fructose-6-phosphoric acid.

Having available a considerable quantity of perseulose from previous researches in this Lab- oratory⁹ we decided to seek still further confirma- tion of its formulation as L-galaheptulose¹⁰ by applying to it the procedure of Spengler and

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(2) Kiliani and Sanda, *Ber.*, **26**, 1650, 1654 (1893).

(3) Nef (and Lucas), *Ann.*, **376**, 55 Note (1910); Spoehr (and Rosario), *Am. Chem. J.*, **43**, 240 (1910); Glattfeld, *ibid.*, **50**, 152 (1913); Nef, *Ann.*, **403**, 204 (1914). Cf. also Framm, *Arch. ges. Physiol.* (Pflügers), **64**, 575 (1896); Schade, *Z. physik. Chem.*, **57**, 1 (1906); Buchner, Meisenheimer and Schade, *Ber.*, **39**, 4217 (1906).

(4) Nef, Hedenburg and Glattfeld, *This Journal*, **39**, 1638 (1917).

(5) Hudson and Chernoff, *ibid.*, **40**, 1005 (1918).

(6) E. P. Clark, *J. Biol. Chem.*, **54**, 70 (1922).

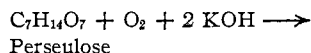
(7) Spengler and Pfannenstiel, *Z. Wirtschaftsgruppe Zuckerind.*, **85**, Tech. Tl. 547 (1935).

(8) Neuberg and Collatz, *Cellulosechem.*, **17**, 125 (1936).

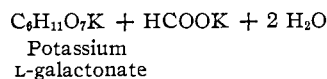
(9) Hann, Tilden and Hudson, *This Journal*, **60**, 1201 (1938); Tilden, forthcoming publication.

(10) La Forge, *J. Biol. Chem.*, **28**, 511 (1917); Hann and Hudson, *This Journal*, **61**, 336 (1939).

Pfannenstiel. Oxidation in alkaline solution by oxygen should yield L-galactonic acid according to the equation



Perseulose



The oxidation of the ketoheptose proceeded smoothly and the crystalline potassium salt of a hexonic acid was obtained readily in a yield of 45%. Identification as the L-galactonate was effected by comparing it with its optical antipode prepared from D-galactonolactone. Potassium D-galactonate monohydrate rotated¹¹ $+3.11 \pm 0.1^\circ$ in water, while potassium L-galactonate monohydrate rotated $-2.95 \pm 0.1^\circ$; the magnitude of the rotation of the salts considered as anhydrous is thus 3.26° , the D-salt rotating to the right and the L-salt to the left. Dissolved in an excess of *N* hydrochloric acid the two salts were converted to the corresponding galactonic acids which then mutarotated as shown in Table I. The rates of mutarotation at 20° were practically identical, and the final rotations, calculated as lactone, were -61.0° and $+61.2^\circ$ for the D- and L-forms, respectively. The crystalline lead salts of the enantiomorphs were prepared from the potassium salts, and further comparisons made. Lead D-galactonate in water was found to rotate $-12.9 \pm 1.1^\circ$ as previously noted by Isbell,¹² the new lead L-galactonate rotated $+13.6 \pm 1.1^\circ$. Values for the mutarotation of the lead salts dissolved in *N* nitric acid are shown in Table I, the final rotations, calculated as lactone, being -61.2 and $+61.2^\circ$ for the D- and L-forms, respectively.

TABLE I
MUTAROTATION OF GALACTONATES, CALCULATED AS LACTONE. TEMP. 20°

Time, min.	Potassium galactonate · H ₂ O in <i>N</i> HCl (<i>c</i> , 4)		Lead galactonate in <i>N</i> HNO ₃ (<i>c</i> , 4)	
	D-	L-	D-	L-
5	-12.2	+12.2	-15.8	+14.2
15	20.1	20.3	23.3	21.8
30	29.8	30.1	31.8	30.5
45	36.6	37.2	38.0	36.8
60	41.5	42.4	42.8	42.4
90	49.1	49.4	49.2	50.0
120	54.9	53.8	54.4	54.4
240	60.8	60.9	60.9	60.9
Final	61.0	61.2	61.2	61.2

(11) Throughout the article the rotations are specific rotations at 20° for sodium light.

(12) Isbell, *J. Research Natl. Bur. Standards*, **14**, 314 (1935).

Finally, the γ -lactone of L-galactonic acid was prepared, from both the potassium and the lead L-galactonates. L-Galactonolactone was first obtained, but not crystallized, by Fischer and Hertz.¹³ A crystalline lactone with $[\alpha]_D +65.3^\circ$ was reported by Smoleński and Złotnik,¹⁴ but no melting point was given. Later, Glatthaar and Reichstein¹⁵ prepared L-galactonolactone melting at 94° ; they added, however, that one sample melted at 128° . No rotations were given. Fukunaga and Kubota¹⁶ reported that their lactone crystallized in small needles melting at $109.5-111^\circ$, with $[\alpha]^{18}_D +77^\circ$. Our L-galactonolactone crystallized from absolute alcohol in large prisms, melted at 134° , and rotated $+78.4 \pm 0.5^\circ$ in water.

A survey of the literature concerning the enantiomorphous D-galactonolactone reveals that this lactone crystallizes in needles of an anhydrous form melting at 112° and rotating -77.8° ;¹⁷ the substance is hygroscopic, and readily forms a monohydrate which crystallizes in prisms melting at 66° . Ruff and Franz,¹⁸ however, reported an anhydrous lactone which melted at $133-135^\circ$, and rotated -77.6° , in good agreement with the melting point 134° and rotation $+78.4^\circ$ found by us for the γ -lactone of L-galactonic acid. These high-melting, anhydrous forms appeared to be unusual until we happened to examine a sample of commercial γ -D-galactonolactone which had been received recently.¹⁹ Much to our surprise we found that it also melted at $133-134^\circ$. Thus the 134° lactone appears to be the most stable of the three forms; it is not hygroscopic and could even be recrystallized from water at room temperature, in large transparent prisms, without forming the hydrate.

These results prove conclusively that the oxidation of perseulose yields L-galactonic acid, and hence that the ketose is L-galaheptulose. It thus appears that perseulose from perseitol is a satisfactory source for the preparation of L-galactonolactone, which upon reduction with sodium amalgam yields the very rare sugar L-galactose.²⁰

(13) Fischer and Hertz, *Ber.*, **25**, 1258 (1892).

(14) Smoleński and Złotnik, *Bull. intern. acad. polonaise, Classe sci. math. nat.*, **B**, 293 (1934).

(15) Glatthaar and Reichstein, *Helv. Chim. Acta*, **20**, 1537 (1937).

(16) Fukunaga and Kubota, *Bull. Chem. Soc. Japan*, **13**, 272 (1938).

(17) Data of Lowry and Krieble, *Z. physik. Chem.*, Bodenstein Festband, 884 (1931); cf. especially Hedenburg, *THIS JOURNAL*, **37**, 368 (1915).

(18) Ruff and Franz, *Ber.*, **35**, 948 (1902).

(19) From Pfanstiehl Chemical Co., Waukegan, Illinois.

(20) Glatthaar and Reichstein, Ref. 15; cf. Iwadare and Kubota, *Sci. Papers Inst. Phys. Chem. Res. (Tokyo)*, **34**, 183 (1938).

Furthermore, the degradation of calcium L-galactonate by the method of Ruff,²¹ or of L-galactonamide by the method of Weerman,²² yields L-lyxose, an even rarer sugar. In similar fashion, the oxidation of other aldoses and ketoses with oxygen should furnish valuable proof of structure and configuration, and also provide new sources for certain rare sugars and their derivatives.

Experimental

Potassium L-Galactonate Monohydrate from Perseulose.—A solution of 21.9 g. (0.1 mole) of perseulose hemihydrate in 150 cc. of water was added to 150 cc. (0.3 mole) of 2 *N* potassium hydroxide in a bottle placed on a mechanical shaker. The air in the system was displaced by oxygen from a measuring reservoir, and vigorous shaking begun. Oxidation proceeded readily, the rate depending upon the temperature; at 23°, seven hours was required for the absorption of 2400 cc. of oxygen (0.1 mole), while at 27° only three hours was necessary. At higher temperatures or with larger amounts of material, cooling with an electric fan was employed to moderate the exothermic reaction. Shaking was continued overnight, the reaction stopping after about 3000 cc. of oxygen had been absorbed. The colorless reaction mixture was concentrated *in vacuo* to a thin sirup, then diluted slowly with 750 cc. of methyl alcohol to precipitate a thick oil and leave the excess potassium hydroxide in solution. The oil was dissolved in water, the solution clarified with carbon and concentrated, and crystals obtained by the addition of methyl alcohol. The product weighed 11.5 g. (46%) and could be recrystallized from water-methyl alcohol without appreciable loss. It appeared originally in thin, rectangular plates, later in clusters of prisms; either form can be obtained by inoculation as desired. The prismatic form, however, is the stable form in contact with dilute methyl alcohol at room temperature, the plates being transformed to prisms overnight in the presence of a crystal of the latter type. Potassium L-galactonate monohydrate rotates -2.95° in water (*c*, 5; 4-dm. tube); it mutarotates in *N* hydrochloric acid as shown in Table I.

Anal. Calcd. for $C_6H_{11}O_7K \cdot H_2O$: K, 15.50; H_2O , 7.14. Found (plates): K, 15.56; H_2O (100° *in vacuo*), 7.00. Found (prisms): K, 15.68; H_2O , 7.05.

Potassium D-Galactonate Monohydrate.—A sample of commercial γ -D-galactonolactone was neutralized with potassium hydroxide, the solution concentrated *in vacuo*, and the product crystallized from water by the addition of methyl alcohol. This compound in the D-series was obtained as thin, rectangular plates only, the prismatic form not appearing during the recrystallizations. Potassium D-galactonate monohydrate rotates $+3.11^\circ$ in water (*c*, 5; 4-dm. tube), and mutarotates in *N* hydrochloric acid as shown in Table I.

Anal. Calcd. for $C_6H_{11}O_7K \cdot H_2O$: K, 15.50; H_2O , 7.14. Found: K, 15.48; H_2O , 7.23.

(21) Van Ekenstein and Blanksma, *Chem. Weekblad*, 11, 189 (1914).

(22) Ault, Baird, Carrington, Haworth, Herbert, Hirst, Percival, Smith and Stacy, *J. Chem. Soc.*, 1422 (1933).

Lead L-Galactonate.—To 53.7 g. of potassium L-galactonate hydrate in 150 cc. of water was added 44.4 g. of lead acetate trihydrate in 150 cc. of water, and the mixture inoculated with a crystal obtained previously in a preliminary experiment. The product was allowed to crystallize at room temperature, then in the ice box overnight; filtered, washed with cold water, and dried *in vacuo* over calcium chloride it weighed 54.2 g. (85% yield). For analysis, 4 g. was recrystallized from 100 cc. of hot water. Lead L-galactonate separates in clusters of rhombic plates. It rotates $+13.6^\circ$ in water (*c*, 0.4; 4-dm. tube), and mutarotates in *N* nitric acid as shown in Table I.

Anal. Calcd. for $C_{12}H_{22}O_{14}Pb$: Pb, 34.68. Found: Pb, 34.71.

Lead D-Galactonate.—This salt in the D-series was prepared from calcium D-galactonate and lead nitrate according to Isbell,¹² and also from potassium D-galactonate and lead acetate as described above for the L-salt. The rotation of -12.9° in water (*c*, 0.4; 4-dm. tube) agrees with the value previously recorded; the mutarotation in *N* nitric acid is shown in Table I.

γ -L-Galactonolactone.—The lactone was obtained from both the lead and potassium salts. Thus, 50.6 g. of lead L-galactonate was dissolved in 1500 cc. of hot water, the lead precipitated with hydrogen sulfide, and the filtered solution concentrated *in vacuo* until a mass of acicular prisms, presumably L-galactonic acid, appeared. The solution was warmed to dissolve the crystals, and concentration continued; the thick sirup was heated for one hour *in vacuo* at 80°, dissolved in hot absolute alcohol, concentrated and heated two additional hours *in vacuo* at 80°. The lactone was dissolved in hot absolute alcohol and crystallized after inoculation with crystals obtained by rubbing with ethyl acetate a small sample which had been heated for two hours in the oven at 102°. Again, 70.4 g. of potassium L-galactonate hydrate was treated with 300 cc. of *N* hydrochloric acid, the solution concentrated *in vacuo* at 85° and the residue dissolved in water; these last two processes were repeated several times to effect lactonization and to remove the slight excess of hydrochloric acid. The final lactone sirup was extracted from the potassium chloride with hot absolute alcohol and the crystalline lactone isolated in the usual manner. The yield from either lead or potassium salt was over 90%. The γ -lactone of L-galactonic acid, recrystallized from absolute alcohol, was obtained in large prisms melting at 134°, with preliminary sintering about 128°. It rotated $+78.4^\circ$ in water (*c*, 4; readings taken 4 to 8 minutes after solvent was added).

Anal. Calcd. for $C_6H_{10}O_6$: C, 40.45; H, 5.66. Found: C, 40.50; H, 5.75.

One of the authors (N. K. R.) desires to thank the Chemical Foundation of New York for a Research Associateship. The authors also express their indebtedness to Dr. W. T. Haskins for carrying out the microanalyses.

Summary

Perseulose has been degraded in alkaline solution by oxygen to L-galactonic acid. The reac-

tion confirms the formulation of perseulose as L-galaheptulose.

The potassium and lead L-galactonates have been compared with their D-antipodes.

γ -L-Galactonolactone has been obtained in an anhydrous modification which melts at 134°. This compound appears to be more stable than the 66° monohydrate and the 112° anhydrous forms expected from analogy with γ -D-galactonolactone.

The further application of this oxidative degradation is suggested for the determination of structure and configuration of reducing sugars, and for the preparation of certain of the rarer sugars and their derivatives; another example of such an application is described in the following article.²³

(23) Richtmyer, Hann and Hudson, THIS JOURNAL, 61, 343 (1939).
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The Oxidative Degradation of Sedoheptulose to D-Altronic Acid¹

BY NELSON K. RICHTMYER, RAYMOND M. HANN AND C. S. HUDSON

Sedoheptulose, originally designated sedoheptose, was first discovered by La Forge and Hudson² in *Sedum spectabile*, Bor.; its presence in *S. acre*, Linn., in *S. boloniense*, Lois., and in *S. reflexum*, Linn., has been noted recently by Proner.³ The sugar occurs to the extent of 1% or more in the stems and leaves of *Sedum spectabile*, a succulent, hardy, perennial herb of the easiest cultivation. The sugar is readily obtainable in sirupy form from the plant, although so far it has not been crystallized. We are undertaking new studies of it and its derivatives and present herewith the first results.

The reduction of sedoheptulose with sodium amalgam furnished its discoverers with two heptitols which they named α - and β -sedoheptitol. The α -sedoheptitol was found⁴ to be identical with volemitol from *Lactarius volemus*, Fr.,⁵ and volemitol was subsequently identified⁶ as D- β -mannoheptitol (D-manno-D-talo-heptitol)⁷ of known configuration. The β -sedoheptitol was shown⁸ to be the enantiomorph of the known D- β -guloheptitol (D-gulo-L-talo-heptitol), and hence must be L- β -guloheptitol (L-gulo-D-talo-heptitol). From this evidence Ettel concluded that sedoheptulose could be formulated only as D-altroheptulose.

In the presence of mineral acids, sedoheptulose is transformed to a crystalline anhydride, sedoheptulosan. Hudson⁹ has shown recently that this compound must contain the unusual combination of an ethylene oxide and a septanoid ring. The evidence for such a structure rests upon the methylation studies by Hibbert and Anderson,¹⁰ and upon the configuration assigned to the parent sugar by Ettel. Independent proof for the D-altroheptulose configuration is now presented.

The oxidative degradation of reducing sugars in alkaline solution by pure oxygen has been developed by Spengler and Pfannenstiel¹¹ into a reaction useful for the preparation of aldonic acids containing one less carbon atom than the original sugar. In the preceding communication¹² we have demonstrated that perseulose (L-galaheptulose) may be degraded successfully to L-galactonic acid. In similar fashion, we now find that the oxidation of sedoheptulose produces D-altronic acid, which may be isolated in the form of its characteristic calcium salt. This reaction furnishes conclusive proof that sedoheptulose is indeed D-altroheptulose.

Aside from its value in confirming the structure of sedoheptulose, the oxidative degradation of the sugar of *Sedum spectabile* offers itself as a convenient step in the preparation of the rare sugars D-altrose and D-ribose, and their derivatives. Thus, the reduction of D-altronolactone

(1) Publication authorized by the Surgeon General, U. S. Public Health Service. Presented in part before the Divisions of Organic Chemistry and of Sugar Chemistry and Technology, at the Milwaukee meeting of the American Chemical Society, Sept. 5-9, 1938.

(2) La Forge and Hudson, *J. Biol. Chem.*, **30**, 61 (1917).

(3) Proner, *Bull. sci. pharmacol.*, **43**, 7 (1936); *Wiadomosci Farm.*, **62**, 742 (1935).

(4) La Forge, *J. Biol. Chem.*, **42**, 375 (1920); La Forge and Hudson, *ibid.*, **79**, 1 (1928).

(5) Bourquelot, *Bull. soc. mycologique France*, **5**, 132 (1889).

(6) Ettel, *Coll. Czechoslov. Chem. Commun.*, **4**, 504 (1932).

(7) Hudson, THIS JOURNAL, **60**, 1537 (1938).

(8) Ettel, *Coll. Czechoslov. Chem. Commun.*, **4**, 513 (1932).

(9) Hudson, THIS JOURNAL, **60**, 1241 (1938).

(10) Hibbert and Anderson, *Can. J. Research*, **3**, 306 (1930).

(11) Spengler and Pfannenstiel, *Z. Wirtschaftsgruppe Zuckerind.*, **85**, Tech. Tl. 547 (1935).

(12) Richtmyer, Hann and Hudson, THIS JOURNAL, **61**, 340 (1939).