

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

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).

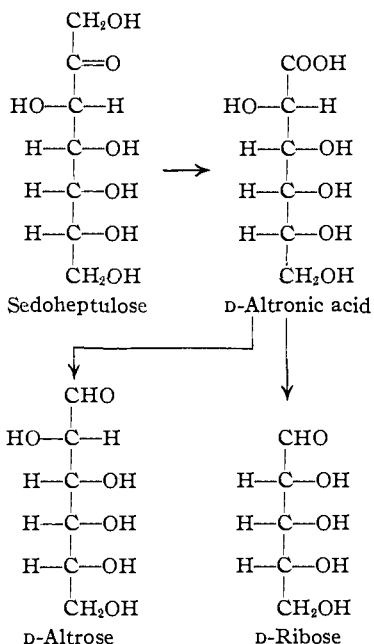
(9) Hudson, THIS JOURNAL, **60**, 1241 (1938).

(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).

with sodium amalgam¹³ should now furnish D-altrone in crystalline form;¹⁴ and the oxidation of calcium D-altronate by hydrogen peroxide and ferric acetate is already known to produce D-ribose.¹⁵



Experimental

Sedoheptulose Sirup.—About 5 kg. of fresh leaves and stalks of *Sedum spectabile* was forced through a food chopper, the finely ground product mixed with an equal volume of water, and the liquid separated with a small press. The press cake was disintegrated, covered with water and allowed to stand overnight, then pressed again, and the extracts combined. The solution was heated with activated carbon, filtered, and concentrated *in vacuo* to a thin sirup which was poured into 2 liters of warm 95% alcohol. The granular precipitate was removed by filtration, the alcohol distilled *in vacuo*, and the residue dissolved in 2 liters of water. A 50-cc. portion of 20% lead acetate solution was added, and a small precipitate removed. The solution was freed from lead with hydrogen sulfide and concentrated *in vacuo* to 107 g. of a very thick sirup. Diluted to 250 cc. with water, this "crude sedoheptulose solution" showed a rotation of -9.5 saccharimeter degrees in a 1-dm. tube. To estimate the amount of sedoheptulose present, 3 cc. of solution was diluted with 15 cc. of 5 *N* hydrochloric acid and water to make 25 cc.; overnight the solution attained a constant rotation of -9.2 saccharimeter degrees in a 1-dm. tube. On the assumption that sedoheptulose has zero rotation, and that the action of hydrochloric acid is to convert the sugar to an equilibrium mixture containing 80% of sedoheptulosan (an-

hydro-sedoheptose) of $[\alpha]^{20}_D -146^\circ$ in water,² we may estimate roughly that the original 107 g. of sirup contained 56 g. of sedoheptulose.

Oxidation of Sedoheptulose.—A 47-cc. portion of the crude sedoheptulose solution, estimated to contain 10.5 g. of sedoheptulose, was diluted with water to 150 cc., mixed with 150 cc. of 2 *N* potassium hydroxide, and shaken with oxygen. With a room temperature of 29° , it was desirable to dissipate some of the heat of oxidation by the use of an electric fan during the first fifteen minutes of shaking. In the first two hours 1500 cc. of oxygen was absorbed, in the next five hours 400 cc. of oxygen, and overnight an additional 200 cc. of oxygen, a total of 2100 cc. A second portion of sedoheptulose was oxidized in the same manner, and the combined pale yellow solutions concentrated *in vacuo* to a sirup. The cautious addition of 1 liter of methyl alcohol precipitated an oil and left the excess potassium hydroxide in solution. The oil was dissolved in water, clarified with activated carbon, and hydrochloric acid added until the solution turned congo red paper distinctly blue, indicating that all organic acids had been liberated. The solution was concentrated *in vacuo* to a semi-solid mass of sirup and potassium chloride; water was added, the solution concentrated, and the process repeated to expel the volatile acids, especially formic acid. The residue was heated finally *in vacuo* at 80° to bring about lactone formation, and then extracted several times with hot absolute alcohol. The extracts were concentrated, heated at 80° *in vacuo*, and this residue extracted with hot absolute alcohol to eliminate a little more potassium chloride. Evaporation of the alcohol *in vacuo* left a yellowish sirup.

TABLE I
MUTAROTATION OF CALCIUM D-ALTRONATE·3.5H₂O IN *N* HCl (c, 3) AT 20°

Time, min.	From sedoheptulose $[\alpha]^{20}_D$	From cellobiose ^a $[\alpha]^{20}_D$
5	+11.5	+11.7
10	13.8	14.0
15	15.9	15.7
20	17.3	17.5
30	19.6	20.1
45	21.9	22.4
60	23.1	23.2
90	24.2	24.3
Constant	24.8	24.8
Calcd. as lactone	34.4	34.4

^a Richtmyer and Hudson, THIS JOURNAL, 58, 2539 (1936).

Isolation of Calcium D-Altronate.—The lactone sirup was dissolved in 200 cc. of water and the solution heated with 15 g. of calcium carbonate for two hours on the steam-bath. The solids were removed by filtration through activated carbon and the colorless solution concentrated *in vacuo* to 100 cc. The cautious addition of ethyl alcohol and a seed crystal resulted in the separation of typical clusters of prismatic needles of calcium D-altronate. After eight hours the product was filtered, washed with dilute, then 95% alcohol, and dried *in vacuo* over granular calcium chloride. The weight was 4.8 g., plus 0.3 g. ob-

(13) Levene and Jacobs, *Ber.*, 43, 3143 (1910); Steiger and Reichstein, *Helv. Chim. Acta*, 19, 1011 (1936); cf. Austin and Humoller, THIS JOURNAL, 56, 1153 (1934), in the corresponding L-series.

(14) Richtmyer and Hudson, *ibid.*, 57, 1720 (1935).

(15) Richtmyer and Hudson, *ibid.*, 58, 2536 (1936).

tained from the mother liquor. One recrystallization yielded pure calcium D-altronate-3.5H₂O, which was identified by analyses, and by its mutarotation in *N* hydrochloric acid (Table I).

*Anal.*¹⁶ Calcd. for (C₈H₁₁O₇)₂Ca·3.5H₂O: Ca, 8.13; H₂O, 12.78. Found: Ca, 8.13; H₂O, 12.63.

One of the authors (N. K. R.) desires to thank the Chemical Foundation of New York for a Research Associateship.

(16) Through the kindness of Dr. W. T. Haskins of this Laboratory.

Summary

1. Sedoheptulose, the ketoheptose occurring in *Sedum spectabile*, Bor., has been degraded to D-altronic acid; this reaction confirms its formulation by Ettel as D-altroheptulose.

2. Sedoheptulose is suggested as a valuable starting point for the preparation of the rare sugars D-altrose and D-ribose, and their derivatives.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF ST. JOHN'S UNIVERSITY AND OF NEW YORK UNIVERSITY]

Condensations of Ketones with Phenols¹

BY MARTIN E. MCGREAL, VICTOR NIEDERL AND JOSEPH B. NIEDERL

The systematic investigation as to the condensations of carbonyl compounds with phenols by J. B. Niederl and co-workers² has been extended to the field of saturated ketones.

The purpose of this investigation was to establish whether the behavior of phenol and that of the ortho alkylated phenols with ketones are similar, regardless of the type of saturated ketone and of the reaction conditions employed (mole ratio, type of catalyzer, concentration, temperature and solvent). Representative ketones of the three main types, *i. e.*, saturated aliphatic, alicyclic and aromatic ketones were selected. Thus, of the saturated aliphatic ketones, methyl ethyl (I, II), methyl *n*-propyl (III) and methyl isobutyl ketone (IV, V); of the alicyclic types, cyclohexanone (VI, VII), 3- and 4-methylcyclohexanone (VIII, IX) and cyclopentanone (X), and of the aromatic series, acetophenone (XI, XII) and methyl *p*-tolyl ketone (XIII) were chosen for this investigation.

It was found that the condensation products were invariably the crystalline diphenylmethane type of compounds, regardless of the reaction conditions or of the mole ratios of reactants. Such findings, at first glance, would suggest a direct elimination of one molecule of water from one molecule of the ketone and two molecules of the phenol. However, mole for mole addition has been observed in the case of acetophenone,³

(1) Several parts are taken from the theses of Thomas Murphy and of Daniel Marino presented to the Graduate School of St. John's University in partial fulfillment of the requirements for the degree of Master of Science, June, 1938.

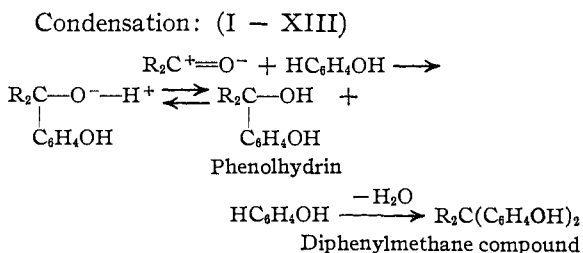
(2) J. B. Niederl, *THIS JOURNAL*, **50**, 2230 (1928); **51**, 2426 (1929); *Z. angew. Chem.*, **44**, 467 (1931); *Monatsh.*, **60**, 150 (1932); J. B. Niederl and co-workers, *ibid.*, **51**, 1038 (1929); *THIS JOURNAL*, **58**, 657 (1936); **59**, 1113 (1937).

(3) Zincke, *Ann.*, **363**, 275 (1908).

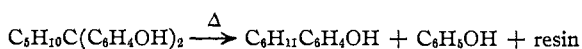
alloxan,⁴ and *d*-fructose.⁵ This would indicate that the first step in the condensation is an addition of the phenol to the carbonyl group, comparable to the addition of hydrocyanic acid, with the subsequent formation of a phenol-hydrin type of compound.⁶ In the next step one molecule of water is lost intermolecularly, *i. e.*, between one molecule of phenol-hydrin and one molecule of phenol with the subsequent formation of the crystalline diphenylmethane type of compounds. Thus, in this latter step, the ketones differ from the aldehydes, which lost water intramolecularly.

All the diphenolic condensation products obtained in the condensation of the alicyclic ketones (VI-X incl.) were subjected to pyrolysis and through disproportionation yielded in all cases the respective crystalline, alicyclic monophenol (VIA, VIIA, VIIIA, IXA and XA).

Schematically the reaction in both the condensation and the disproportionation may be presented as



Disproportionation: (VI - X)



(4) Boehringer, German Patent 107,720 (1900); **115**, 817 (1901).

(5) E. Fischer, *Ber.*, **27**, 1355 (1894); C. Counciler, *ibid.*, **28**, 24 (1895).

(6) J. B. Niederl and R. Maurmeyer, Rochester Meeting, Am. Chem. Soc., Sept., 1937.