tation in an aqueous solution. An optical-crystallographic examination of the compound by Mr. Keenan showed that *in ordinary light* the refractive indices were $n_\alpha = 1.552$, n_β indeterminate and $n_\gamma = 1.555$, both ±0.002; *in parallel polarized light* (*crossed nicols*) the birefringence is weak and low order polarization colors are usually seen; no interference figures were observed *in convergent polarized light.* The differences in these optical-crystallographic properties from those of L-gluco-L-ido-heptitol indicate that the substance which is here described is a true racemate.

Anal. Calcd. for $C_7H_{16}O_7$: C, 39.60; H, 7.60. Found: C, 39.66; H, 7.72.

Summary

L-Glucoheptulose has been prepared in high yield through the biochemical oxidation of α-glucoheptitol with *Acetobacter suboxydans.* The phenylosazone of the ketose has been shown to possess a specific rotation equal in magnitude, but opposite in sign, to that of D-glucoheptose phenylosazone. Catalytic reduction of L-glucoheptulose by hydrogen and Raney nickel produces L-gluco-L-gulo-heptitol and L-gluco-L-ido-heptitol and thus provides supporting evidence for the accepted configuration of the ketose. New substances which have been described are D,L-glucoheptulose, L-gluco-L-ido-heptitol (L-β-glucoheptitol), L-gluco-L-ido-heptitol heptabenzoate, racemic gluco-ido-heptitol heptabenzoate, and racemic gluco-ido-heptitol.

BETHESDA, MD. RECEIVED APRIL 13, 1942

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

The Oxidative Degradation of L-Glucoheptulose

BY NELSON K. RICHTMYER AND C. S. HUDSON

In an earlier communication from this Laboratory[1] we reported the isolation of potassium L-galactonate in a 45% yield from the degradation of perseulose (L-galaheptulose) in alkaline solution by oxygen, according to the procedure developed by Spengler and Pfannenstiel.[2] Having available a considerable amount of L-glucoheptulose from another research,[3] we had planned to degrade it in similar fashion to potassium L-gluconate, and thus to obtain, by reduction of the lactone, the difficultly accessible L-glucose.[4] Unfortunately for our purpose the oxidation could not be controlled sufficiently to yield L-gluconic acid as the principal degradation product. Instead there was formed one of those complex mixtures of acids such as have been obtained, by a succession of enolizations and cleavages, from the oxidation of other sugars in alkaline solution by air.[5]

When the oxidation of L-glucoheptulose was carried out in the manner described previously for L-galaheptulose, the first product to be isolated was the readily crystallized potassium L-arabonate, in a yield of 31%. It was identified by its rotation[6] of +5.2° in water as compared to −5.0° for potassium D-arabonate, and by conversion to the benzimidazole derivative described by Moore and Link.[7] The remainder of the oxidation products was converted to a mixture of brucine salts. Crystallized from water, the least soluble fraction, about 14% of the theoretical yield, consisted of approximately equal amounts of the brucine salts of L-gluconic and L-erythronic acids. Brucine L-gluconate was identified by comparison of its constants with those recorded in the literature, by conversion to potassium L-gluconate rotating −11.3° in water as compared to +11.3° for potassium D-gluconate, and by conversion to 2-[L-*gluco*-pentahydroxyamyl]-benzimidazole. This last-named compound has the same melting point as the D-derivative described by Moore and Link,[8] while the rotation, −9.0° in citric acid solution, is about equal in magnitude but is opposite in sign to that recorded for its better-known antipode.

Brucine L-erythronate was identified by analy-

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[1] Richtmyer, Hann and Hudson, THIS JOURNAL, **61**, 340 (1939).

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

[3] Maclay, Hann and Hudson, THIS JOURNAL, **64**, 1606 (1942).

[4] Fischer, *Ber.*, **23**, 2618 (1890); for the crystalline L-gluconolactone, see Kiliani, *ibid.*, **58**, 2349 (1925); Upson, Sands and Whitnah, THIS JOURNAL, **50**, 519 (1928). Although L-glucose has been reported to occur in *Grindelia robusta* [Power and Tutin, *Pub. Wellcome Chem. Research Lab.*, **57**, 1 (1905)], in capsularin, a glycoside from jute (*Corchorus capsularis*) [Saha and Choudhury, *J. Chem. Soc.*, **121**, 1044 (1922)], and collagen [Beek, THIS JOURNAL, **63**, 1483 (1941); *J. Research Natl. Bur. Standards*, **27**, 507 (1941)], the evidence is not conclusive in any case.

[5] See, for example, the degradation of D-glucose [Power and Upson, THIS JOURNAL, **48**, 195 (1926)].

[6] Throughout the article the rotations are specific rotations at 20° for sodium light; *c* designates concentration in grams per 100 cc. of solution, and *l* the length of the tube in decimeters.

[7] Moore and Link, *J. Biol. Chem.*, **133**, 300 (1940).

[8] Moore and Link, ref. 7; see also Haskins and Hudson, THIS JOURNAL, **61**, 1267 (1939).

sis, melting point and rotation, and by conversion to the known, crystalline L-erythronolactone. The latter was characterized further by preparing from it 2-[L-*erythro*-trihydroxypropyl]-benzimidazole, which has the same melting point as 2-[D-*erythro*-trihydroxypropyl]-benzimidazole prepared from D-erythronolactone; the rotations are similar in magnitude, but are opposite in sign.

The more soluble fractions of the brucine salts contained some additional brucine L-gluconate, but carbon and hydrogen analyses indicated that the rest of the material consisted chiefly of the brucine salts of hydroxy acids containing only two or three carbon atoms.

While the oxidative degradation of L-galaheptulose to L-galactonic acid had been satisfactory in regard to yield, the degradation of L-glucoheptulose was disappointing because the principal product isolated was L-arabonic acid. However, such a two-carbon atom degradation would be very useful if the oxidation of sedoheptulose should be found to produce D-ribonic acid in considerable amount in addition to the small yield of D-altronic acid already reported.[9]

The degradation of L-glucoheptulose to L-gluconic acid derivatives, as reported above, completes a series of reactions by which D-glucose has been transformed to its mirror-image, L-glucose, as follows: D-glucose → D-gluco-D-gulo-heptose (= D-α-glucoheptose)[10] → D-gluco-D-gulo-heptitol (= L-gluco-L-gulo-heptitol = α-glucoheptitol)[10] → L-glucoheptulose[11] → L-gluconic acid → L-glucose.[12]

Experimental Part

Oxidation of L-Glucoheptulose; Isolation of Potassium L-Arabonate.—A solution of 21 g. of L-glucoheptulose (0.1 mole) in 100 cc. of water was added to 150 cc. of 2 *N* aqueous potassium hydroxide (0.3 mole) and the mixture was shaken vigorously with oxygen at 20–25°. After twenty-four hours the oxygen consumption had ceased at about 3000 cc., measured at room temperature. A product was isolated, as in the oxidation of perseulose, by concentration, precipitation with methyl alcohol, and crystallization from water by the addition of methyl alcohol. It was identified as potassium L-arabonate,[13] and was obtained in a 31% yield (average).

Anal. Calcd. for $C_5H_9O_6K$: K, 19.15. Found: K, 19.20.

A thrice recrystallized sample rotated[6] +5.2 ± 0.1° in water (*c*, 5; *l*, 4). For comparison, a specimen of potassium D-arabonate was crystallized to constant rotation and showed −5.0 ± 0.1° in water (*c*, 5; *l*, 4). Both D- and L-salts melted about 220° with decomposition. The potassium L-arabonate was characterized further by conversion to 2-[L-*arabo*-tetrahydroxybutyl]-benzimidazole by the procedure of Moore and Link.[7] This derivative melted at 235° (decomp.) and rotated +49.7 ± 0.2° in 5% citric acid solution (*c*, 2), in good agreement with the data reported by those authors.

Isolation of L-Gluconic Acid Derivatives.—After 145 g. of potassium L-arabonate had been separated from the products obtained by the oxidation of 478 g. of L-glucoheptulose, the mother liquor was acidified with hydrochloric acid until all the organic acids had been liberated. The solution was concentrated *in vacuo* to a thin sirup which was diluted with methyl alcohol and most of the potassium chloride was removed by filtration. The filtrate was concentrated to a thick sirup which was heated *in vacuo* for two hours at 70°, and the lactones and acids were extracted from the remainder of the potassium chloride with hot absolute alcohol. The alcohol was removed by distillation, and the residue was heated for several hours with 1500 cc. of water and 60 g. of calcium carbonate. Excess carbonate and any calcium oxalate were removed by filtration. Inasmuch as no crystalline calcium salt could be obtained by concentrating the aqueous solution, the calcium ions were removed by the addition of an equivalent amount of oxalic acid, as determined by analysis of an aliquot portion, and the organic acids were then converted to brucine salts in the usual manner. Upon concentration of the aqueous solution of the brucine salts, there were obtained several crops of crystals, totaling 181 g. An attempt to purify this material showed that it consisted of about equal amounts of the brucine salts of L-gluconic and L-erythronic acids which could be separated, partially, by a series of extractions and crystallizations with methyl alcohol. In this way we were able to isolate **brucine L-gluconate** in clusters of elongated, more or less rectangular, plates which were solvent-free after being dried in the air at room temperature. The rotation, −28.6° in water (*c*, 4), is higher than −25.4° in water (*c*, 4), the only value recorded previously, by Upson, Sands and Whitnah.[14] The melting point, 180° with evolution of gas, is in agreement with that of those authors, but is higher than the value 167–168° reported by Kiliani.[14]

Anal. Calcd. for $C_{29}H_{38}N_2O_{11}$: C, 58.97; H, 6.49. Found: C, 59.36; H, 6.59.

A portion of the brucine L-gluconate was converted to barium L-gluconate by treatment with barium hydroxide in the usual manner. Although barium L-gluconate has been obtained in crystalline form by Kiliani,[14] our product was amorphous. By reacting with an equivalent amount of potassium sulfate, the barium salt was converted to a crystalline potassium salt. **Potassium L-gluconate,** twice recrystallized from water by the addition of methyl alcohol, separated in clusters of flattened, acicular prisms. It melted about 185° with decomposition, and rotated −11.3 ± 0.2° in water (*c*, 4; *l*, 4).

Anal. Calcd. for $C_6H_{11}O_7K$: K, 16.69. Found: K, 16.82, 16.62.

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[9] Richtmyer, Hann and Hudson, THIS JOURNAL, **61**, 343 (1939).

[10] Fischer, *Ann.*, **270**, 64 (1892).

[11] Bertrand and Nitzberg, *Compt. rend.*, **186**, 925 (1928).

[12] Fischer, ref. 4.

[13] First prepared by Kiliani, *Ber.*, **21**, 3009 (1888); neither m. p. nor rotation was reported.

[14] Upson, Sands and Whitnah, THIS JOURNAL, **50**, 519 (1928); *cf.* Kiliani, *Ber.*, **55**, 100 (1922); **58**, 2349 (1925).

Potassium D-gluconate, prepared for comparison and thrice recrystallized as similar acicular prisms, melted at 185° (decomp.), and rotated +11.3 ± 0.2° in water (*c*, 4; *l*, 4). This value is higher than the value +10.3° reported by May, Weisberg and Herrick[15] but lower than the +13.0° reported by Nilkantum.[16]

Final identification of L-gluconic acid was obtained by converting it to **2-[L-*gluco*-pentahydroxyamyl]-benzimidazole** by the procedure of Moore and Link.[7] This compound, after four recrystallizations as colorless needles from water, melted about 215° with decomposition, and rotated −9.0 ± 0.2° in 5% citric acid solution (*c*, 2; *l*, 4). Although optical enantiomorphs should have equal and opposite rotations, according to the classical views of stereochemistry,[17] this rotation is slightly lower in magnitude than the value +9.6° reported by Moore and Link, and +9.5 ± 0.2° as confirmed by our own measurements for the D-antipode; this is due perhaps to the presence of a very small amount of the dextrorotatory (+49.7°), rather insoluble L-*arabo*-benzimidazole which might accompany the L-*gluco* derivative as an impurity.

Anal. Calcd. for $C_{12}H_{16}N_2O_5$: C, 53.72; H, 6.02. Found: C, 53.72; H, 6.04.

Isolation of L-Erythronic Acid Derivatives.—Besides brucine L-gluconate we were able to isolate, from the less soluble brucine salts, **brucine L-erythronate.** This salt crystallized from methyl alcohol as small, colorless prisms with many faces. The air-dried product contained about 0.9% of water which it lost in a desiccator but regained upon subsequent exposure to the air. It melted about 210° with vigorous decomposition. The rotation, on a solvent-free basis, was −31.6° in water (*c*, 4), or slightly higher than the value −28.4° in water (*c*, 4) reported by Ruff.[18]

Anal. Calcd. for $C_{27}H_{34}N_2O_9$: C, 61.12; H, 6.46. Found, on sample dried at 100° *in vacuo:* C, 61.08; H, 6.42.

The conversion of brucine L-erythronate to **L-erythronolactone** was accomplished by standard procedures. The lactone crystallized from ethyl acetate as elongated, flattened prisms, which appeared to consist of bundles of tough, flexible needles. The m. p. 102–103° and the rotation +73.0° in water (*c*, 4) are in agreement with the data of Glattfeld and Forbrich.[19]

Benzimidazole derivatives were prepared from both D- and L-erythronolactones by the procedure of Moore and Link.[7] The compounds were recrystallized from 12 parts of hot water, as colorless, prismatic needles melting at 177–178°. A thrice-recrystallized sample of **2-[D-*erythro*-trihydroxypropyl]-benzimidazole** rotated +9.0 ± 0.2° in 5% citric acid solution (*c*, 2; *l*, 4), and the twice recrystallized **2-[L-*erythro*-trihydroxypropyl]-benzimidazole** rotated −8.3 ± 0.2° under identical conditions. The L-form may be contaminated with a very small amount of the L-*arabo*-benzimidazole which would lower the rotation.

Anal. Calcd. for $C_{10}H_{12}N_2O_3$: C, 57.68; H, 5.81. Found: (D-form) C, 57.73; H, 5.76; (L-form) C, 57.58; H, 5.78.

One of the authors (N. K. R.) desires to thank the Chemical Foundation of New York for a Research Associateship. The authors express their indebtedness to Dr. W. Dayton Maclay and Dr. Raymond M. Hann for their generous gift of L-glucoheptulose, and to Dr. Arthur T. Ness for carrying out the micro-analyses.

Summary

1. L-Glucoheptulose has been degraded in alkaline solution by oxygen to potassium L-arabonate in a 31% yield. Smaller amounts of L-gluconic and L-erythronic acids were isolated and identified by means of their salts and other derivatives.

2. The D- and L-forms of 2-[*erythro*-trihydroxypropyl]-benzimidazole have been described.

3. The transformation of D-glucose to L-glucose has now been completed by the step involving the degradation of L-glucoheptulose to L-gluconic acid.

BETHESDA, MD. RECEIVED APRIL 13, 1942

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[15] May, Weisberg and Herrick, *J. Wash. Acad. Sci.*, **19**, 443 (1929).

[16] Nilkantum, *J. Sci. Tech.* (India), **2**, 39 (1936); *C. A.*, **32**, 1402 (1938).

[17] This has been verified in the case of the *arabo* and *galacto* pairs of benzimidazoles; see Richtmyer and Hudson, THIS JOURNAL, **64**, 1612 (1942).

[18] Ruff, *Ber.*, **34**, 1369 (1901); see also Nef, Hedenburg and Glattfeld, THIS JOURNAL, **39**, 1638 (1917).

[19] Glattfeld and Forbrich, *ibid.*, **56**, 1209 (1934); *cf.* Ruff, ref. 18.