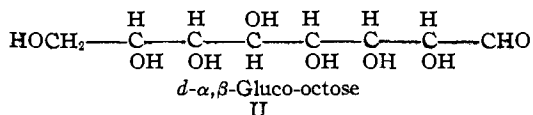
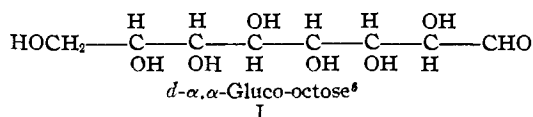


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The Amides and Phenylhydrazides of Two Epimeric (α,α and α,β) *d*-Gluco-octonic Acids¹By R. C. HOCKETT² AND C. S. HUDSON

By the cyanohydrin synthesis, Philippe³ prepared from *d*- α,α -glucononose two glucooctic acids and found the specific rotations of their lactones to be -35 and -40° , respectively. The levorotation of these presumably γ -lactones indicates that the lactone ring is on the left of the sugar chain in the conventional projection formula, and this determination of the position of the hydroxyl group on the γ -carbon proves the configuration of *d*- α,α -gluco-octose⁴ (I) and its epimeric *d*- α,β -gluco-octose⁵ (II). This paper reports confirmatory evidence concerning these configurations adduced from the amide and phenylhydrazide rules.



Earlier investigations⁷ of a number of aldonic acid amides led to the statement of several generalizations: (1) the alpha carbon atom is responsible for so large a proportion of the optical rotation that its value predominates over the combined influences of the other asymmetric carbon atoms, whose effect decreases with the distance from the functional group; (2) when the hydroxyl group is on the right of the alpha carbon atom, in the conventional projection formula, the amide gives a dextrorotation, and when on the left, a levorotation; (3) the molecular rotations of corresponding carbon atoms in the five, six and seven carbon series are almost the same numerically.

(1) Publication authorized by the Surgeon General, U. S. Public Health Service. Presented before the Organic Chemistry Division of the American Chemical Society in Buffalo, N. Y., Sept., 1931.

(2) National Research Fellow, Oct., 1929–April, 1931.

(3) Philippe, *Ann. chim. phys.*, [8] **26**, 369 (1912).

(4) Hudson, *This Journal*, **39**, 463 (1917).

(5) Fischer, *Ann.*, **270**, 90 (1892).

(6) The designations α,α and α,β were made by Fischer and Philippe; they refer to the chronological order of isolation and bear no relation to configuration. The full configurations were not known by those workers.

(7) Hudson, *This Journal*, (a) **39**, 465 (1917); (b) **40**, 813 (1918); (c) Hudson and Komatsu, **41**, 1141 (1919).

In support of the configuration deduced by application of the lactone rule, and in agreement with the first two amide generalizations, *d*- α,α -gluco-octonic amide has now been found to rotate -24.4° ⁸ and its epimer $+12.1^\circ$. Evaluation of the molecular rotation of the alpha carbon atom from these rotations by the superposition principle gives $+46.49(10)^2$ as compared with $44.5(10)^2$, $47.25(10)^2$ and $45.85(10)^2$, respectively, for the five-, six- and seven-carbon series, indicating that the third generalization may be extended to the eight-carbon series. Assuming that such is the case the rotations of the gluco-octonic amides may be calculated by using for the individual carbon atoms the values previously found in the hexonic series,^{7c} the rotations of the epsilon and zeta carbon atoms being considered negligible under the latter part of generalization (1). The calculated specific rotations, -23.1° for the *d*- α,α -gluco-octonic amide and $+13.9^\circ$ for its epimer, are near the observed values.

The phenylhydrazides of these two acids also have been measured and found to rotate in the directions to be expected from the phenylhydrazide rule of rotation.

The configuration for *d*- α,α -gluco-octose that is shown by the lactone, amide and phenylhydrazide rules leads to the inference that the corresponding *d*- α,α -gluco-octitol will prove to be identical with an octitol that should be obtainable by the application of the cyanohydrin reaction to the known *d*- β -galactose.

Appreciation is expressed to Dr. R. T. K. Cornell and Mr. W. D. Chase for performing the microchemical analyses required in this study.

Experimental

d- α,α -Gluco-octonic Lactone.—To an ice-cold solution of 100 g. of *d*- α -glucoheptose in 600 cc. of water, a solution of 57 g. of calcium chloride dihydrate in 80 cc. of water, and one of 35 g. of sodium cyanide in 80 cc. of water were added successively. After standing overnight in the refrigerator, the solution was treated with 40 g. of calcium

(8) All rotations, unless otherwise stated, are constant specific rotations at 20° in water for sodium light, c is concentration in grams in 100 cc. of solution, and l is the tube length in decimeters.

oxide, the mixture of basic calcium salts which separated was heated for three hours on the water-bath to complete the hydrolysis of nitriles and amides, and the precipitated salts were filtered and washed free of chlorides with saturated lime water. The precipitate was mixed with a solution of 50 cc. of concentrated sulfuric acid in 310 cc. of water, the calcium sulfate was filtered off, and the filtrate was analyzed for calcium and sulfate ions. Additional acid was added to balance the calcium, the solution was concentrated to 250 cc., an equal volume of alcohol was added and the residual calcium sulfate removed. The alcohol-free filtrate was neutralized to phenolphthalein with barium hydroxide, and upon concentration to a small volume the barium salt of *d*- α , α -gluco-octonic acid was obtained crystalline in a yield of 75 g., equivalent to 59.8 g. of the acid or about 50% of the theoretical yield. The lactone was obtained readily by quantitative decomposition of the pure barium salt with sulfuric acid. Recrystallized to constant properties by solution in a minimum volume of hot water and addition of four volumes of ethyl or methyl alcohol the anhydrous lactone separated in clear needles melting at 151–152° (corr.) and having a specific rotation of +53.7° (*c*, 1.65; *l*, 2) in water. Fischer found a rotation of +45.9° and a melting point of 145–147° (uncorr.), while Philippe reported +48.8° and 165–166°.

d- α , β -Gluco-octonic Lactone.—The sirup remaining from the crystallization of barium *d*- α , α -gluco-octonate yielded 34 g. (29%) of *d*- α , β -gluco-octonic lactone upon quantitative decomposition with sulfuric acid. The total yield of lactones was 79%, the proportion of the α , β -isomer being much greater than that reported by Fischer, probably due to the use of calcium cyanide instead of hydrocyanic acid in the synthesis. This lactone was recrystallized from 60% alcohol and obtained as short prisms which melted at 185.5–186° (corr.) and rotated +24.6° in water (*c*, 3.24; *l*, 2). Fischer found +23.6° for the rotation and a melting point of 186–188° (uncorr.), while Philippe reports +24.1° and 195–197° for these constants.

d- α , α -Gluco-octonic Acid Phenylhydrazide.—A solution of 3 g. of *d*- α , α -gluco-octonic lactone in 10 cc. of water was warmed with 1.36 g. of phenylhydrazine for one hour, the separated phenylhydrazide was filtered and recrystallized from aqueous alcohol, being obtained in rosetts of needles. The substance decomposes at 190.5–194° (corr.) and rotates –17.8° (*c*, 0.40; *l*, 2) in water.

Anal. Calcd. for $C_{14}H_{22}O_8N_2$: C, 48.5; H, 6.4; N, 8.1. Found: C, 48.7; H, 6.5; N, 8.0.

d- α , β -Gluco-octonic Acid Phenylhydrazide.—This phenylhydrazide was prepared similarly but, because of its greater solubility in water, was recrystallized from 90% alcohol, being obtained in cottony masses of long needles. The compound melts at 162.5–164.5° (corr.) and rotates +25.9° (*c*, 1.52; *l*, 4) in water.

Anal. Calcd. for $C_{14}H_{22}O_8N_2$: C, 48.5; H, 6.4; N, 8.1. Found: C, 48.8; H, 6.4; N, 8.1.

d- α , α -Gluco-octonic Amide.—A suspension of the *d*- α , α -gluco-octonic lactone in absolute alcohol was saturated with ammonia gas, agitated for five hours at room temperature and refrigerated overnight. The amide was separated and recrystallized from minimum volumes of tepid water by addition of absolute alcohol, being obtained as well formed rectangular plates which melted at 160.5–161.5° (corr.) and rotated –24.4° (*c*, 3.88; *l*, 4) in water.

Anal. Calcd. for $C_8H_{17}O_8N$: C, 37.6; H, 6.7; N, 5.5. Found: C, 37.6; H, 6.6; N, 5.4.

d- α , β -Gluco-octonic Amide.—The method of preparation was identical with that just described for the other isomer. Because of its higher solubility in water, very little of the solvent was used to dissolve it in the cold and ten or twelve volumes of absolute alcohol were added just to turbidity; the amide separated as small well formed prisms. The compound melted at 125.5–126.5° (corr.) and rotated +12.1° (*c*, 3.30; *l*, 2) in water.

Anal. Calcd. for $C_8H_{17}O_8N$: C, 37.6; H, 6.7; N, 5.5. Found: C, 37.8; H, 6.9; N, 5.4.

Summary

The preparation and study of the amides and phenylhydrazides of *d*- α , α - and *d*- α , β -gluco-octonic acids confirm the configurations previously assigned these acids and the corresponding octoses through application of the lactone rule to the rotation of the glucoconic lactones of Philippe.

Three generalizations concerning the relation between rotation and configuration among aldonic acid amides of the five, six and seven carbon series have been tested and found valid in the eight-carbon series.

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