The alkylnitroguanidines are colorless, crystalline solids, moderately soluble in alcohol, insoluble or slightly soluble in cold water, more soluble in hot, and insoluble or slightly soluble in ether. Benzylnitroguanidine is the least soluble, requiring about 1050 parts of cold water and about 200 parts of boiling water for solution, and is sparingly soluble even in hot alcohol. It chars with concd. sulfuric acid. The others dissolve readily in concd. sulfuric acid, give a blue color with a solution of diphenylamine in that substance, and give up their nitro group nitrogen quantitatively in the nitrometer. They decompose slowly when boiled in aqueous solution.

CAMBRIDGE 39, MASSACHUSETTS

[CONTRIBUTION FROM THE KENT CHEMICAL LABORATORY, UNIVERSITY OF CHICAGO]

THE CATALYTIC REDUCTION OF *d*-GLUCONIC ACID TO *d*-GLUCOSE

BY J. W. E. GLATTFELD AND EDNA H. SHAVER[1]

RECEIVED JUNE 18, 1927 PUBLISHED SEPTEMBER 2, 1927

The work reported below is an outgrowth of the efforts that are being made in this Laboratory to prepare and study the C_4-saccharinic acids.[2] This preparation work has now progressed to such an extent that the possibility of extending it to the C_5-saccharinic acids is being considered. This extension would involve as one step the reduction of the C_4-acids to the corresponding aldehydes. The realization of the extension depends, in large measure, on the possibility of discovering a practical procedure for this reduction. Of possible reduction methods the catalytic hydrogenation of the acids in the presence of oxides of platinum seemed to hold promise and the work reported below was done to test it. In order to conserve material, the easily obtained *d*-gluconic acid was used instead of the C_4-saccharinic acids for this preliminary study.

W. E. Cake[3] has recently stated that glucose in neutral solution is not reduced by hydrogen in the presence of platinum black. It occurred to us, therefore, that if the reduction of the aldonic acids could be effected by hydrogen in the presence of platinum oxides in neutral or slightly acid solution (that is, with no added acid or very little), the yield of aldoses

---

[1] The dissertation of which this paper is a condensation was presented by Edna H. Shaver in partial fulfilment of the requirements for the degree of Doctor of Philosophy, in the University of Chicago. Some of the material reported in this paper was presented at the meeting of the Midwest Sections of the American Chemical Society in Chicago, May 27–28, 1927.

[2] (a) Glattfeld and Miller, THIS JOURNAL, **42**, 2314 (1920). (b) Glattfeld and Sander, *ibid.*, **43**, 2675 (1921). (c) Glattfeld and Sherman, *ibid.*, **47**, 1742 (1925). (d) Glattfeld and Woodruff, *ibid.*, **49**, 2309 (1927).

[3] Cake, THIS JOURNAL, **44**, 861 (1922).

might be very good because of the fact that the aldoses might not be reduced under these conditions to alcohols.

It was found to be possible to reduce *d*-gluconic acid to *d*-glucose in 14–28% yield (measured as osazone) by this method. A few experiments were tried with mannonic acid and with galactonic acid. With mannonic acid under what seemed to be the same conditions that had proved favorable for the reduction of gluconic acid to glucose, a yield of only 0–2% of mannose (as osazone) was obtained. Galactonic acid in water solution was reduced to dulcitol in 30–45% yield. The conclusion is therefore reached that different aldonic acids require different experimental conditions for successful reduction to the aldoses and, therefore, that the method may prove to be of some value in individual cases with the C_4-saccharinic acids.

Experimental Part

Materials and Apparatus.—The calcium gluconate used as starting material was made by the oxidation of glucose by means of bromine. The purified product showed only a trace of bromide ion, and did not reduce Fehling's solution; analysis for calcium showed it to be practically pure (calcd. for $C_{12}H_{22}O_{14}Ca$: Ca, 9.31. Found: 9.28, 9.23). The catalyst was prepared by the method of Vorhees and Adams[4] except that about 0.2 g. of ferrous sulfate per 3 g. of platinum[5] was added with the sodium nitrate to the chloroplatinic acid solution. The hydrogen used came from a commercial tank of the gas; it was used without purification. The hydrogenating apparatus was that described by Skita[6] and modified by Vorhees and Adams.[4]

The Procedure.—The sample of calcium gluconate (6.2 g., Col. 2 of table below) was dissolved in about 10 parts of water and such an amount of a sulfuric acid solution (sp. gr. 1.525), (Col. 3) added as to leave the solution finally in the desired condition of acidity with respect to sulfuric acid (Col. 4). The filtrate from the calcium sulfate was concentrated on the water-bath, made up to volume (25 cc.) and the specific rotation determined (Col. 5). The solution was transferred to the reaction bottle, 1 g. of catalyst added and the hydrogenation started. The air was not removed from the reaction bottle before admission of hydrogen.[7] The bottle was shaken vigorously by a mechanical device for three hours; then another 1g. portion of catalyst was added and the shaking continued for two hours when another 1g. portion of catalyst was introduced and the hydrogenation continued for another two-hour period. The pressure in the reaction bottle slowly dropped during the seven-hour period from 17 pounds to 10. The reaction mixture was then filtered, the volume of the filtrate measured and the specific rotation determined (Col. 6).

Glucosazone.—The reduced reaction solution (from 6.2 g. of calcium gluconate) was made neutral to litmus with sodium hydroxide, and 6 cc. of phenylhydrazine and 4 cc. of glacial acetic acid were added. The customary procedure for osazone formation yielded 4.2 g. of air-dry crystals which were treated with 50 cc. of water. The mixture was heated to boiling and subjected to filtration while hot. The filtrate deposited crystals (Col. 7)

---

[4] Vorhees with Adams, THIS JOURNAL, **44**, 1402 (1922).

[5] Carothers and Adams, *ibid.*, **45**, 1071 (1923).

[6] Skita, *Ber.*, **45**, 3594 (1912).

[7] Because of the small volume of air in the bottle this seemed a safe procedure in this case; if a large reaction vessel is used the air should be removed before admission of hydrogen because of the possibility of explosion.

which were shown to be the phenylhydrazide of gluconic acid. The material insoluble in the 50 cc. of hot water (Col. 8) was shown to be glucosazone. It was twice recrystallized from 30% alcohol and then melted at 207°, as did also a mixture of this compound with known glucosazone. This fact, together with the analysis of samples (calcd. for $C_{18}H_{22}O_4N_4$: H, 6.19; C, 60.29. Found: 6.19, 6.15, 60.19, 60.23) should be conclusive evidence of the identity of the compound.

This procedure was carried out many times. The table below summarizes the data from six experiments which are fairly representative of the results obtained.

TABLE I

REDUCTION OF *d*-GLUCONIC ACID UNDER 10–17 POUNDS' PRESSURE

Expt. No.	Calcium gluconate, g.	H_2SO_4, cc. (sp. gr. 1.525)	Theoretical H_2SO_4 if all calcium pptd.	Sp. rot. before reduction	Sp. rot. after reduction	Gluconic phenylhydrazide, g.	Glucosazone, g.	Yield of hydrazide, %	Yield of osazone, %
1	6.2	1.5	0	+12.8	+23.5	2.0	2.1	24.3	20.3
2	6.2	1.5	0	+12.8	+23.5	2.4	2.1	29.1	20.3
3	6.2	1.5	0	+12.8	...	2.5	2.9	30.3	28.1
4	6.2	1.4	Incomplete precipitation	+12.8	+23.8	2.6	2.6	31.5	25.1
5	6.2	1.3	Incomplete precipitation	...	+22.5	2.6	2.6	31.5	25.1
6	6.2	2.0	0.4	...	...	3.2	1.5	38.8	14.5

Glucose Oxime.—The gluconic acid obtained from 6.2 g. of calcium gluconate by the addition of the theoretical amount of sulfuric acid was hydrogenated as described above. The filtrate from the catalyst was neutralized with sodium hydroxide and yielded with hydroxylamine 0.15 g. of crystals, m. p. 137°; the melting point of a mixture with known glucose oxime was also 137°.

Isolation and Identification of Glucose

For the isolation of glucose, the filtrate from the catalyst was heated at 100° for half an hour with excess calcium carbonate. The filtrate from the carbonate was concentrated under reduced pressure to a sirup which was repeatedly extracted with boiling absolute alcohol. The alcoholic solution was concentrated under reduced pressure to a sirup, the sirup dissolved in water, the solution again treated with calcium carbonate and the procedure just outlined carried out once more. The alcoholic solution this time was treated with a small amount of ether and allowed to stand for several days with occasional addition of small amounts of ether until such addition caused no further cloudiness. Warty aggregates of crystals appeared on the sides of the test-tubes. The crystals from a large number of such experiments were combined and studied.

Melting Point.—Repeated solution of the crude crystals (m. p. 140°) in absolute alcohol and precipitation with ether yielded crystals which melted at 146°; this melting point could not be raised. A mixture of the purified crystals with anhydrous glucose (m. p. 146°) also melted at 146°.

Rotation.—Four-tenths of a gram of crystals of m. p. 146° in 10 cc. of water solution gave α in a 1-dcm. tube, 20 minutes after solution,

+2.45°; 2 hours after solution, +2.14; 24 hours after solution, +2.08 with no further change in rotation. The corresponding specific rotations are +61.2, +53.5, +52.0. (The equilibrium specific rotation of glucose is +52.6.)

Titration.—Four cc. of the solution used for rotation was made up to 50 cc.; 14.8 cc. of this solution was required for the complete precipitation of the copper in 10 cc. of Fehling's solution of such strength that 10 cc. was equivalent to 0.047 g. of glucose; purity of sample, 99.2%.

Anal. Samples of m. p. 146° were analyzed after repeated purifications by means of solution in absolute alcohol and precipitation with ether. Calcd. for $C_6H_{12}O_6$: H, 6.72; C, 39.97. Found: 6.30, 6.21, 6.18, 6.24, 38.78, 38.87, 38.64, 39.10.

The combustion data were very puzzling in the light of the very good agreement of all other data with those for pure *d*-glucose. The conclusion was finally reached that the impurity present must be an inorganic compound which clung tenaciously to the glucose crystals through all purifications. A sample of 0.4459 g. (m. p. 146°) was ignited, therefore, and found to leave a glassy residue of 0.0100 g. If the impurity were absolutely free from carbon, this small amount of residue might adequately account for the low results of combustion.

Glucosazone from Crystalline Product.—In view of the unsatisfactory combustion results, a characteristic glucose derivative from the crystalline product of the hydrogenation was prepared. From 0.34 g. of crude crystals (m. p. 140°), there was obtained 0.29 g. of crude osazone which, after one recrystallization from 30% alcohol, melted at 207°. This melting point was not lowered by addition of crystals of known glucosazone of m. p. 207°. Furthermore, the analysis of this product gave figures that indicated it to be glucosazone (calcd. for $C_{18}H_{22}O_4N_4$: H, 6.19; C, 60.29. Found: 6.51, 6.34, 60.42, 60.40.).

Summary

The results of a study of the catalytic reduction of *d*-gluconic acid to *d*-glucose in water solution under 10–17 pounds' pressure and in the presence of a platinum oxide catalyst are reported. From the reaction mixture, there was isolated (a) glucosazone in 14–28% yield, (b) glucose oxime and (c) crystalline *d*-glucose.

CHICAGO, ILLINOIS