washed free of chloride ion. It was further purified by dissolving in an acetone–water mixture, filtering, precipitating in water, drying at 70° and finally at 116°.

Anal. Calcd. for $C_{10}H_9NO_3$: 5.23 cc. N sodium hydroxide per gram; N, 7.32. 0.5310 g. dissolved in 50 cc. of pyridine plus 50 cc. of water required 4.8 cc. of 0.5501 N sodium hydroxide, *i. e.*, 4.98 cc. of N sodium hydroxide per gram. Found: N, 7.28.

Analysis of Polyvinylamine Salts.—Table I presents the analyses of a few samples of polyvinylamine hydrochloride

TABLE II

	Water	Methanol	Ethanol	Acetone	Dioxane	Acetic acid	Pyridine	Dioxane + H₂O	Acetone + H₂O	10% NaOH
Polyvinylamine	+	+	+	−	0	+	0	0	0	0
Polyvinylamine hydrochloride	+	−	−	−	−	−	−	+	+	+
Polyvinylamine hydrobromide	+	−	−	−	−	−	−	+	+	+
Polyvinyl acetamide	+	+	+	−	−	+	⇌	+	+	+
Polyvinyl benzamide	−	+	+	−	−	+	+	+	+	−
Poly-N-vinyl urethan	−	+	+	+	−	+	+	+	+	−
Poly-N-vinyl-N'-phenylurea	−	−	−	−	−	+	⇌	+	+	−
Poly-N-vinyl-*p*-toluenesulfonamide	−	−	−	−	⇌	−	+	+	+	−
Polyvinyl phthalamic acid	−	−	−	−	−	−	−	−	−	+

Legend: +, soluble; −, insoluble; ⇌, swells; 0, not tested.

and polyvinylamine hydrobromide. It illustrates the degree of hydrolysis of the cyclic imide group to amino group. Column 3 shows the percentage by weight of amino nitrogen calculated from the halogen values of Column 1. Column 4 represents the percentage of the total nitrogen content which was present in the form of amino groups.

Solubility Table.—Table II lists some of the solubility properties at room temperature of the polymers described in this paper.

Summary

1. Polyvinyl phthalimide was treated with hydrazine to yield a polymer which is believed to be the hydrazine salt of polyvinylamine.

2. Reaction of the latter with acetic anhydride produced polyvinyl acetamide, whereas treatment with hydrohalide acids yielded polyvinylamine salts which were converted by alkalies to the free polymeric base.

3. The following related nitrogenous resins were prepared and characterized: polyvinylamine hydrochloride, polyvinylamine hydrobromide, poly-N-vinyl benzamide, poly-N-phenyl-*p*-toluenesulfonamide, poly-N-vinyl urethan, poly-N-vinylurea.

4. Polyvinylamine was found to be a relatively strong base forming stable carbonic acid salts.

The Controlled Sodium Amalgam Reduction of Aldonolactones and their Esters to Aldoses and an Improved Synthesis of D-Arabinose[1]

BY NATHAN SPERBER,[2,3] HAROLD E. ZAUGG[4] AND W. M. SANDSTROM

The sodium amalgam reduction of aldonolactones to aldoses, one of the most important reactions in carbohydrate chemistry, was discovered by Emil Fischer[5] in the course of his studies on the synthesis and structure proof of the aldoses. Fischer and Piloty[6] synthesized aldoses from the corresponding lactones by reduction with sodium amalgam and dilute sulfuric acid, for example, L-ribose from L-ribonolactone. Fischer[5,7] applied the cyanohydrin reaction to an aldose, obtained the next higher pair of epimeric acids which as lactones were reduced to the aldoses with sodium amalgam. Nef and co-workers[8] described a method whereby an aldose in the presence of air

and a strong base could be degraded one carbon atom to the salt of the lower aldonic acid. Hudson and Chernoff[9] employed the Nef procedure to prepare rhamnotetronic lactone from rhamnose. Spengler and Pfannenstiehl,[10] substituted oxygen for air in the Nef degradation and secured a 75% yield of potassium arabonate in the oxidation of glucose, as compared with the published yield of 36%. Isbell[11] prepared a number of aldonolactones by this method and Richtmyer, Hann and Hudson[12] have used this procedure in the degradation of perseulose and sedoheptulose.

A survey of the literature revealed that, although the procedure for the sodium amalgam reduction has been indicated broadly by Fischer and subsequent investigators, the conditions for securing maximum and reproducible yields are not as precise as is possible from modern methods of study. For example, Fischer[5] described the reduction of a lactone with a 10–15-fold quantity

(1) Paper No. 2297, Scientific Journal Series. Minnesota Agricultural Experiment Station.

(2) Abstracted from a thesis by Nathan Sperber, presented to the Graduate Faculty of the University of Minnesota, in partial fulfilment of the requirements for the Ph.D. degree. March, 1945.

(3) Present address: Schering Corporation. Bloomfield, New Jersey.

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(5) Fischer, *Ber.*, **22**, 2204 (1889); *ibid.*, **23**, 930 (1890).

(6) Fischer and Piloty, *ibid.*, **24**, 4214 (1891).

(7) Fischer, *ibid.*, **23**, 2611 (1890).

(8) Nef, Hedenburg and Glattfeld, THIS JOURNAL, **39**, 1638 (1917); Glattfeld, *Am. Chem. J.*, **50**, 135 (1913).

(9) Hudson and Chernoff, THIS JOURNAL, **40**, 1005 (1918).

(10) Spengler and Pfannenstiehl, *Z. Wirtschaftsgruppe Zuckerind. Tech. Tl.*, **85**, 546 (1935); German Patent 618,164 (1935).

(11) Isbell, *J. Research Natl. Bur. Standards*, **29**, 227 (1942).

(12) Richtmyer, Hann and Hudson, THIS JOURNAL, **61**, 340, 343 (1939).

of 2.5% sodium amalgam in the presence of sufficient sulfuric acid to keep the medium acid. In the preparation of ribose, Steiger[13] made several improvements on Fischer's method. She recommended the use of freshly prepared sodium amalgam and found congo paper a satisfactory indicator for the control of the acidity during the course of the reduction. The amalgam was added in one or two portions, rather than in small amounts; and the reaction was considered complete at the end of thirty minutes. Other investigators, however, have recommended longer periods of reaction. Isbell[14] has described a stainless steel apparatus for the reduction of gulonolactone wherein the pH of the reaction medium was kept at approximately 3 with the aid of indicator solutions or test papers.

Since no quantitative data on the reduction were available, a comprehensive study has been made of the effect of the ratio of aldonolactone to sodium amalgam, time of reaction, order of the addition of the reagents, particle size of the amalgam, temperature and pH of the reaction medium. A reaction vessel[15] for the electrometric control of the pH was devised in which 0.05–0.1 mole of the aldonolactone could be reduced under reproducible conditions. It was possible to determine the conditions which would give consistently high yields of aldose by measuring the amount of sugar produced and the acid consumed during the course of the reaction.

The application of these conditions to the reduction of arabonolactone and methyl arabonate[16] gave yields of 50–57% of crystalline arabinose. The crude sugar was free of ash, had a melting point of 155–156° and a specific rotation of −103.3°. These physical constants are substantially those reported for the once-recrystallized arabinose prepared by the method of Hockett and Hudson.[17] The crude arabinose was of sufficient purity for all synthetic purposes including the Amadori rearrangement.[18]

Table I contains the data on the reduction of 1–2 moles of methyl arabonate under varied conditions of pH, quantities of sodium amalgam, and temperature ranges.

Although D-arabinose has been synthesized by several methods, the Ruff[19] degradation as modified by Hockett and Hudson,[17] has been found to be convenient for large-scale preparation. Arabinose has also been secured from arabonolactone by sodium amalgam reduction. Neuberg and Collatz[20] prepared crystalline arabonolactone by

(13) Steiger, *Helv. Chim. Acta,* **19,** 189 (1936).

(14) Isbell, *J. Research Natl. Bur. Standards,* **5,** 741 (1930).

(15) Sperber and Briggs, *Ind. Eng. Chem., Anal. Ed.,* **18,** 74 (1946).

(16) Fischer reported that methyl aldonates as well as aldonolactones could be reduced with sodium amalgam, *Ber.,* **23,** 933 (1890).

(17) Hockett and Hudson, THIS JOURNAL, **56,** 1632 (1934).

(18) Amadori, *Atti. accad. Lincei* [6] **2,** 337 (1935); Weygand, *Ber.,* **73,** 1259 (1940).

(19) Ruff, *ibid.,* **31,** 1573 (1898); **32,** 553 (1899); see Wohl, *ibid.,* **26,** 730 (1893), and Weerman, *Rec. trav. chim.,* **37,** 16 (1918).

(20) Neuberg and Collatz, *Cellulosechem.,* **17,** 128 (1936).

the Spengler and Pfannenstiehl method[10] which gave, on reduction with sodium amalgam, arabinose in 30% yield. The method used in this investigation for the preparation of crystalline arabinose is a modification of and improvement on the procedures of Neuberg and Collatz[20] and of Fischer.[5]

Experimental

Materials

Sodium Amalgam.—The procedure of Fieser[21] was used employing three-fold quantities of reagents. The hot amalgam was poured on a sheet of transite board, broken up in a large earthenware mortar, screened through 4- and 8-mesh sieves and the fine powder discarded. The amalgam was stored in tightly sealed bottles and was analyzed for sodium content before use by titration of a ten gram sample with 0.1 *N* sulfuric acid. The recovered mercury was reused without distillation.

Aldonolactones and Methyl Aldonates.—(1) D-Galactono-γ-lactone, D-gluco-D-gulo-heptono-γ-lactone and D-gulono-γ-lactone were purchased from the Pfanstiehl Chemical Co., Waukegan, Ill.

(2) D-Glucono-γ-lactone was prepared from a commercial sample of D-glucono-δ-lactone according to the procedure of Isbell and Frush.[22]

(3) D-Arabono-γ-lactone: (a) Potassium D-Arabonate.—The procedure used was essentially that of Spengler and Pfannenstiehl.[10] It was found that if 50% methanol was used as solvent,[23] the product crystallized out and could be filtered directly. The two important factors in the reaction were found to be the presence of a large excess of finely dispersed oxygen and vigorous agitation of the solution. An alternative method which is more economical and suited to smaller scale laboratory preparation is the use of a high speed, horizontal, shaking machine enclosed in a thermostatically controlled cabinet which was kept at 30°. The use of a shaking machine has been described by both Spengler and Pfannenstiehl[10] and Richtmyer, Hann and Hudson.[12] The yield by either method was 70–75%.

Anal. Calcd. for C₅H₉O₆K: K, 19.15. Found: K, 19.05.

(b) **Calcium D-Arabonate Pentahydrate.**—To a solution of 516 g. of potassium arabonate in a minimum amount of hot water, there was added 220 g. of calcium acetate. Upon cooling, a mass of white needles of calcium arabonate pentahydrate was deposited. The product was washed with a small amount of ice water, ethanol and dried in the air, yield 80–90%.

(c) **Crystalline D-Arabonolactone.**—One hundred and twenty-four grams of calcium arabonate pentahydrate and 34 g. of oxalic acid monohydrate were dissolved in 500 ml. of hot water. The precipitated calcium oxalate was filtered with the aid of Norite. The combined filtrate and washings were concentrated *in vacuo* to a thin sirup and then evaporated to dryness in a casserole on a steam-bath. After heating for twenty-four hours, the sirup crystallized. The hard gummy lactone was pulverized in a mortar, triturated with cold acetone, filtered, washed with acetone and dried. The crude lactone (60 g.) was recrystallized from hot acetone, yield 46 g. (57.5%), m. p. 96–98°; [α]²⁰D +72° in water (*c* = 5,5 minutes). Upon concentrating the mother liquors, a crop of impure lactone was obtained which melted at 86–89°. The crude lactone could be converted to the pure product by repeating the lactonization process.

(d) **D-Arabonolactone Sirup.**—Although crystalline arabonolactone was required for the quantitative studies,

(21) Fieser, "Experiments in Organic Chemistry" 2nd. ed., D. C. Heath and Co., Boston. Mass., 1941. p. 418.

(22) Isbell and Frush. *J. Research Natl. Bur. Standards,* **11,** 649 (1933).

(23) We are indebted to Dr. D. L. Tabern for this procedure.

TABLE I

LARGE SCALE REDUCTION OF METHYL-D-ARABONATE AND D-ARABONO-γ-LACTONE BY SODIUM AMALGAM

Moles cpd. reduced	Lactone or ester	pH range	Temp. range, °C.	Time of reaction, hr.	% Na amalgam	G. atoms Na used	Yield, %	M. p. of product, °C.
1.3	L[a]	4–6	0–12	2	2.75	5.74	35[b]	155–156
1.0	L[c]	4–6	0–10	3.5	2.5	3.5	39[d]	153–156
1.0	L[a]	4.5–5.5	0–12	2.25	2.5	3.5	42[b]	152–154
1.0	L[c]	4–5	0–20	2.25	2.5	3.5	39[d]	145–148
1.0	L[a]	3.5–4	0–14	1.5	2.5	3.5	56[b]	150–152
1.0	L[c]	3.5–4	0–10	2	2.5	3.5	52[d]	144–146
1.0	E	3.5–4	2–9	1.5	2.5	3.5	57[e]	145–148
2.0	E	3.5–4	5–13	2.5	1.0	6.4	51[e]	144–148
1.0	E	3–3.5	3–10	1.25	1.0	3.5	59[e]	145–150
1.0	E	2.5–3	2–10	1.25	1.0	3.5	53[e]	144–148
1.0	E	2–2.5	2–9	1.25	1.0	3.5	55[e]	144–149

[a] Prepared from calcium arabonate. [b] Based on calcium arabonate. [c] Prepared from potassium arabonate. [d] Based on potassium arabonate. [e] Based on methyl arabonate.

arabonolactone sirup was satisfactory for the preparation of crystalline arabinose. The lactone sirup could be prepared from either calcium or potassium arabonate. In the calcium salt method, a stirred solution of 300 g. of calcium arabonate pentahydrate in 1.5 liters of hot water was treated with a warm, saturated solution containing 82 g. of oxalic acid monohydrate. After removal of the calcium oxalate, the filtrate and washings were concentrated *in vacuo* on the steam-bath and the sirup was heated for two to three hours to complete the lactonization process. In the potassium salt method, 204 g. of potassium arabonate in 300 ml. of water was cooled and with stirring 51.6 g. of cold, concentrated sulfuric acid dissolved in 60 ml. of water was added. After adding 600 ml. of hot ethanol, the mixture was cooled to 10° and filtered. The potassium sulfate obtained weighed 85 g. (theory requires 87 g.). The filtrate was concentrated to dryness *in vacuo* and the residual sirup heated on the steam-bath for two to three hours.

(e) **Methyl Arabonate: HCl Method.**—A rapid stream of anhydrous hydrogen chloride was passed into a suspension of 102 g. (0.5 mole) of potassium arabonate in 250 ml. of methanol for thirty to forty minutes. After saturation, the hot solution was allowed to stand for ten to fifteen minutes and filtered hot. The precipitated potassium chloride weighed 35 g. The product which crystallized from the filtrate on cooling was filtered, yield 80–90%. The material was pure enough for the reduction, although it was found to be contaminated with small amounts of chloride ion. For this reason, the sulfuric acid method was preferred. The data on the reduction are presented in Table I.

Sulfuric Acid Method.—To 400 ml. of methanol, there was added cautiously about half of a 108 g. (1.1 mole) portion of concentrated sulfuric acid. To this solution, 204 g. (1 mole) of potassium arabonate was added, followed by the remainder of the sulfuric aicd. The mixture was refluxed with stirring for thirty minutes. The potassium sulfate was filtered from the hot solution, the filtrate cooled and the product removed by filtration, yield 168 g. (94%). The material contained only a trace of sulfate ion. The melting point was approximately 140°. Böddener and Tollens[24] reported a melting point of 143° for the methyl ester of L-arabonic acid.

(4) L-Rhamnono-γ-lactone was prepared in 71% yield by the barium benzoate–bromine method of Jackson and Hudson,[25] m. p. 149–151°, [α]²⁰D −38.9° in water (c = 5, 5 minutes).

(5) D-Ribono-γ-lactone was prepared by the procedure of Steiger,[13] m. p. 76–77°, [α]²⁰D +18.4° in water (c = 5, 5 minutes).

(6) D-Mannono-γ-lactone was prepared from a solution

of calcium mannonate.[26] Since calcium mannonate has a tendency to form a gel, the isolation of the salt was avoided and the electrolytic oxidation mixture was converted directly to the gamma lactone by the procedure of Nelson and Cretcher.[27] The pure lactone was obtained in a yield of 60%, m. p. 151°, [α]²⁰D +51.1° in water (c = 5, 5 minutes), phenylhydrazide, m. p. 214°.

Apparatus.—The controlled sodium amalgam reduction experiments were carried out in the special reduction vessel previously described.[1b]

Procedure for the Small Scale Reduction.—A sample of 11 g. of crystalline arabonolactone, methyl arabonate or arabonolactone sirup dissolved in distilled water and diluted to exactly 200 ml., was reduced in the reduction vessel with a single 200-g. portion of 4–8 mesh, 2.5% sodium amalgam at pH 3–3.5 at 5–10°. The pH of the reaction medium was controlled by the addition of standard sulfuric acid from a buret and pH readings were taken every few seconds during the first two minutes of reaction. At three to five minute intervals, 5-ml. aliquot portions were removed from the chamber and later analyzed. The reduction was complete in eight minutes. The combined solutions from two identical experiments after separation from the mercury were filtered with the aid of carbon. The unreacted lactone was hydrolyzed with a few drops of normal sodium hydroxide solution until the red color of phenolphthalein persisted. Sufficient dilute sulfuric acid was added until the solution was acid to congo paper and it was concentrated *in vacuo* at 50° until crystals of sodium sulfate began to separate. The sodium sulfate was precipitated by the addition of methanol, the salt was washed with hot methanol, and the combined filtrate and washings concentrated *in vacuo* to a thick sirup. Twenty ml. of methanol was added, and the solution was allowed to stand overnight in the refrigerator. The crystalline arabinose after filtration was triturated with 10–15 ml. of warm glacial acetic acid, the mixture cooled, filtered and washed with methanol and ether. The arabinose was dried in a vacuum oven at 60°, yield 12.5 g. (56.3%), m. p. 155–156°, [α]²⁰D = −103.3° (c = 5, in water at equil.), ash content less than 0.1%. Upon recrystallization from methanol–water, the melting point was raised to 159°.

In other reduction experiments, the yields of arabinose varied from 50–56%. No difference in the yield or purity of product was observed when the crystalline lactone, lactone sirup or methyl arabonate was used. However, the two latter substances were preferable because of the ease of preparation.

Analysis of the Aldose Content.—The aldose contents of the various aliquot portions removed during the course

(24) Böddener and Tollens, *Ber.*, **43**, 1645 (1910).

(25) Jackson and Hudson, THIS JOURNAL, **52**, 1270 (1930).

(26) Isbell and Frush, *J. Research Natl. Bur. Standards*, **6**, 1145 (1931).

(27) Nelson and Cretcher, THIS JOURNAL, **52**, 403 (1930).

of the experiment were determined by the alkaline hypoiodite oxidation method of Goebel.[28] This method was chosen because the oxidation was stoichiometric and particularly suited to this study, since no other oxidizable substances were present. It was determined that the unreacted lactone and its salt did not interfere with the accuracy of the determination. The method was checked using standard samples of glucose and galactose under the conditions of the experiment and the results were accurate and reproducible.

Large Scale Preparation of D-Arabinose.—The larger scale experiments (1 mole) were carried out in a five-liter, three-necked flask fitted with a thermometer, dropping funnel and stainless steel stirrer. An outlet tube of maximum diameter extended two-thirds of the way down one of the side-necks. This outlet was connected to the inlet of a stainless steel centrifugal pump having an outlet attached by rubber tubing to the flow-cell tube. The flow-cell tube outlet was joined by rubber tubing to an inlet tube in the other side-neck of the reaction flask.

The flow-cell was made from an ordinary six-inch test-tube. The glass electrode was attached by means of a rubber stopper and connected to a pH meter by a short lead. The calomel cell was connected to the flow-cell by means of a rubber tube containing saturated potassium chloride. A glass bead large enough to prevent the flow of liquid was inserted inside the tube at the point of junction with the flow-cell.

Large Scale Reduction.—One mole of lactone or ester dissolved in 1500–2000 ml. of cold water (0–5°) was placed in a five-liter reaction flask cooled by an ice-salt-bath. The circulation pump was then started with priming and approximately one third of the total sodium amalgam to be used was added through the center neck of the flask. Stirring was started and the pH was kept in the desired range by the dropwise addition of cold 25% sulfuric acid through the dropping funnel. Complete reaction of the first portion of amalgam usually required from fifteen to thirty minutes and the temperature rose to 10–12°. In the more nearly neutral ranges, the pH was easily controlled. However, in the pH range of 2–3, proper control required considerable dexterity. In addition, the reaction was much more rapid, so that temperature control was more difficult. The solution was then cooled to 0–5° and a second portion of the amalgam was added.

After completion of the reaction, the liquid was separated from the mercury and made acid to congo paper with sulfuric acid. The solution was then warmed on the steam bath for one hour with an excess of powdered calcium carbonate and filtered hot through charcoal. The filtrate was concentrated *in vacuo* to a volume of about 500 ml. and 1300 ml. of hot methanol was added slowly with stirring.
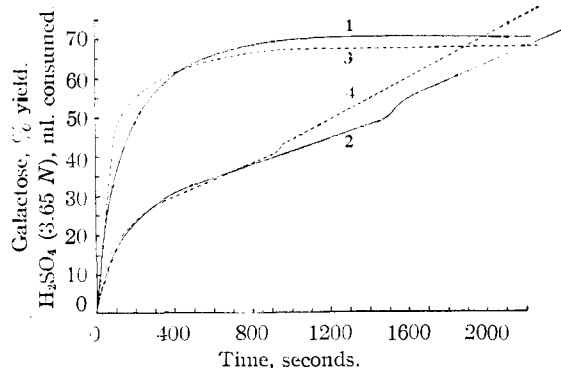

Fig. 1.—Effect of particle size of sodium amalgam on the yield of galactose: (1) galactose produced with 4-mesh Na–Hg, concn. 2.5%; (2) acid uptake for (1); (3) galactose produced with 8-mesh Na–Hg, concn. 2.5%; (4) acid uptake for (3).

(28) Goebel, *J. Biol. Chem.*, **72**, 801 (1927).

The precipitated salt was filtered and washed with 500 ml. of hot methanol. The combined filtrate and washings were concentrated *in vacuo* to a thick sirup which crystallized upon trituration with 250 ml. of warm (50–60°) glacial acetic acid. The mixture was cooled, filtered and the product washed with methanol and ether. The results of these experiments are reported in Table I. If desired, further purification can be effected by recrystallization from glacial acetic acid or aqueous methanol.

Optimum Experimental Conditions for Effecting the Sodium Amalgam Reduction.—D-Galactonolactone was chosen as the first test compound for determining the optimum conditions for carrying out the sodium amalgam reduction, since this lactone was readily available in crystalline anhydrous form and could be easily reduced.

Effect of Particle Size.—Eleven grams of galactonolactone in 200 ml. of solution was reduced at 2° with 250 g. of 2.5% sodium amalgam (4 mesh) added in one portion. The pH was kept at 4–5 by the addition of a small portion of 3.65 N sulfuric acid whenever the electrometer needle started to drift toward the upper limit of the pH range. At definite intervals, a 5-ml. aliquot portion of the solution was removed. Since the solution contained small air bubbles, the sugar analyses were not absolute and the values slightly low. However, analyses of runs, in which only one aliquot portion was removed at the end of the experiment, were in excellent agreement with the values obtained when several portions were removed during the course of the reduction.

The aliquots were treated with 0.1 N sodium hydroxide solution until the red color of phenolphthalein persisted, indicating the completion of the hydrolysis of the unreacted lactone. The solution was then analyzed for the aldose content. These data are presented in curve 1 of Fig. 1. Another experiment was performed in which 8 mesh sodium amalgam was used, all other conditions being the same. These data are presented in curve 3 of Fig. 1. Curves 2 and 4 of Fig. 1 represent the total acid consumed in the reduction of the lactone to the aldose. The acid consumed includes that required for the reduction of the lactone and the decomposition of the sodium amalgam.

Effect of pH.—The influence of the pH on the yield of aldose was studied by comparing the reduction of galactonolactone at three pH ranges: 4–5, 3–4 and 2–3. Above a pH of 5, it was found difficult to control the acidity; and as a result the solution became alkaline resulting in the formation of dulcitol. In these runs 11.0-g. samples of the lactone were reduced in the reduction vessel with 250 g. of amalgam. These data are presented in Fig. 2. Curves 2, 4 and 5 represent the acid uptake, while curves 1 and 3 follow the sugar formation. It was impossible to measure the sugar formation when the pH range was 2–3 because of the short reaction time.

Since there may be a small error caused by the presence of air bubbles in the aliquot sample, the experiments were repeated in the same pH ranges and the sugar formation was determined at the end of the reaction.

TABLE II

REDUCTION OF 10.0 G. OF GALACTONOLACTONE BY 2.5% SODIUM AMALGAM AT DIFFERENT pH RANGES

pH	Temp., °C.	Time reaction, min.	Sugar produced, %
4–5	5	17	65.0
3–4	8	15	82.4
2–3	12	8	78.4

Since it was observed that the reductions which were carried out in the pH range of 3–4 gave the best results, another lactone was reduced under the same conditions to determine whether the pH effect was evident. Both D-glucono-γ-lactone and D-galactono-γ-lactone were reduced with 200 g. of 2.5% sodium amalgam (4–8 mesh) at pH 3–3.5 and 4–5. These data are summarized in Table III.

Quantity of Sodium Amalgam Required.—A solution of 11 g. of galactonolactone in 200 ml. of water cooled to 0–2° was reduced with 250 g. of 2.5% sodium amalgam (4–8

TABLE III

REDUCTION OF GLUCONO- AND GALACTONOLACTONE AT
Two pH RANGES

pH	Gluconolactone glucose produced per cent.	Galactonolactone galactose produced per cent.
3-3.5	69.5	82.4
4-5	55.5	65.0

mesh) at pH 3-3.5. After five minutes a second portion of 150 g. of amalgam was added. The temperature rose to 8° and after ten minutes the reaction was complete. An analysis of the aldose content showed the presence of 9.05 g. of galactose (81.5%). The experiment was repeated using 250 g. of sodium amalgam added in portions of 150 and 100 g., respectively. The sugar content was 8.80 g. (79.0%). The third experiment using only 150 g. of sodium amalgam, added in one portion, yielded 8.73 g. of galactose (78.5%). The time of reaction was only six minutes.

Effect of Temperature.—The reduction of 11 g. of galactonolactone by 200 g. of 2.5% sodium amalgam (4–8 mesh) at pH 3-3.5 and 12° gave 8.74 g. (78.5%) of galactose. The time of reaction was only five minutes. A similar reduction at 15° caused no decrease in the yield, although the control of the pH was more difficult because of the rapid rate of reaction. An experiment at 20° met with failure because the control of the pH was not possible.

Effect of Addition of the Lactone Solution to the Amalgam.—To 200 ml. of distilled water, cooled to 0-2°, there was added 250 g. of 4–8 mesh 2.5% sodium amalgam. A cold solution (5°) of 11.0 g. of galactonolactone in 75 ml. of water was slowly dropped into the whirling amalgam over a period of three to five minutes. The lactone was reduced at pH 3-4 at a temperature below 10° and the reaction was complete in ten minutes, yield 9.12 g. (82%). The experiment was repeated under the same conditions, yield 9.12 g. (82%).

Reduction of Aldonolactones and Esters.—A number of aldonolactones and two esters were reduced with sodium amalgam at the optimum conditions which were determined in the previous experiments. The data are presented in Table IV.

TABLE IV

REDUCTION OF ALDONOLACTONES AND ESTERS

	Wt., g.	pH	Temp., °C.	Time of Rx. min.	Yield by I₂ titration, %
D-Galactono-	11.0	3-3.5	4	15	82.1
γ-lactone	10.0	3-4	8	15	82.4
D-Glucono-	11.0	3-3.5	7	11	69.5
γ-lactone	11.0	3-3.5	8	6	63.4
D-Gluco-D-	12.0	3-3.5	4	8	62.1
gulo-heptono-	12.0	3-3.5	4	8	58.4
γ-lactone	12.0	3-3.5	5	10	61.3
D-Arabono-γ-	11.0	3-3.5	8	8.5	73.5
lactone	11.0	3-3.5	9	8	75.0
D-Gulono-γ-	11.0	3-3.5	8	8	52.2
lactone	11.0	3-3.5	8	8.5	59.5
	11.0	3-3.5	8	9	58.6
D-Mannono-γ-	10.0	3-3.5	8	10.5	60.4
lactone	10.0	3-3.5	8	10	60.4
Methyl D-	11.0	3-3.5	7	9	73.9
arabonate	11.0	3-3.5	8	9	71.4
Methyl D-	11.0	3-3.5	5	8	83.7
galactonate	11.0	3-3.5	5	9	84.2

Discussion of the Results

The particle size and the age of the amalgam

have little effect on the yield of the aldose obtained. Both 4 and 8 mesh sodium amalgam gave approximately the same yields of aldose and the acid consumptions were almost identical. However, powdered sodium amalagam was unsatisfactory because the reaction was too rapid and could not readily be controlled under the conditions of the experiment.

The concentration of the lactone was of minor importance. Reversing the order of addition of the reagent gave yields of aldose almost identical with those obtained in the ordinary procedure. The hydrolysis of the lactone was a relatively small factor under the conditions of the experiment.

The pH of the reaction mixture was found to be the most important single factor in obtaining good results in the reduction. By plotting the acid consumed and the sugar formed against time, a series of curves was obtained. At the point where the sugar content was at a maximum, the rate of acid consumption became constant. The plateau in the sugar formation curve and the break in the acid uptake curve corresponded to the end of the reduction process; and when this point was reached only sodium amalgam was decomposed. At a pH of 4-5, the yield of aldose was at least 10% lower than that obtained at pH 3-4. At pH 4-5, the reaction was complete in fifteen minutes; at pH 3-4 in nine minutes; and at 2-3 in five minutes. The acid uptake at the point where the curve broke was a measure of the sodium required to complete the reduction. The average of a series of experiments was 2.39 atoms of sodium consumed per mole of galactonolactone. Since two atoms were required by theory, 20% additional sodium was expended in side reactions. In practice, 2.5-3 atoms of sodium per mole of lactone may be used. An excess of sodium will do no harm provided the pH is never allowed to reach the neutral or alkaline side. The data in Fig. 2 show that longer reaction times are of no value once the sugar content is at a maximum. At pH 3-4, the reduction was complete in ten minutes. Longer periods of reaction in the presence of excess sodium amalgam involved the decomposition of excess amalgam without altering the yield of sugar. In the literature, the time of reaction has varied from one half to several hours.

From the curves in Fig. 2, it may be noted that the major portion of the sugar is formed during the first three minutes of the reaction, after which the rate of reaction decreases to zero. The control of the pH is most important during this time. However, when congo paper, or other external indicator, is used, the pH control is least satisfactory during the initial period because of the rapid liberation of base. As a result, there are periods when the solution becomes basic which results in further reduction of the sugar. Steiger[13] has recommended that the acidity be kept at the point where congo paper is faint gray. Tests of
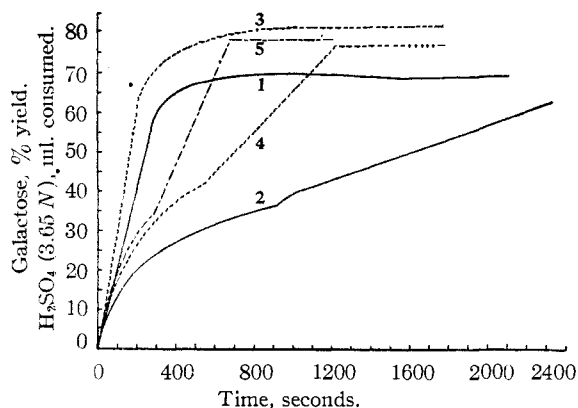
Fig. 2.—Effect of the pH of the reaction medium on the yield of galactose: (1) galactose yield, pH 4–5; (2) acid uptake for (1); (3) galactose yield, pH 3–4; (4) acid uptake for (3); (5) acid uptake pH 2–3.

various samples of congo paper against a glass electrode demonstrated that the transition point varied. If congo paper must be used, it is suggested that the pH of the solution be kept at the point where congo paper is medium purple (pH 3).

The pH range of 3–3.5 is most desirable because the sugar formation is quite rapid, but still easily regulated; and the yield of aldose is at a maximum. At pH 2–3, the yield is almost as high, but the pH control is more difficult because of the high rate of reaction. At pH 4–5, the yields are 10–15% lower and for this reason the higher ranges should be avoided.

The temperature of the reaction mixture is of minor importance. A temperature of 0–2° results in a lower rate of reaction without any particular advantages. This finding is in agreement with that of Steiger.[13] The results obtained in this study show that even a temperature of 15° is satisfactory provided that the pH can be maintained.

The sodium amalgam reduction under the conditions described in the experimental section has been found to be fairly reproducible for any given lactone. A number of lactones and two methyl esters were reduced (Table IV). By ap-

plying the optimum conditions for the sodium amalgam reduction to methyl arabonate and arabonolactone, it has been possible to prepare crystalline D-arabinose in 50–57% yields. The synthesis is facilitated by the availability of the starting ester or lactone and the ease of isolation of crystalline arabinose from the reaction mixture.

The reduction of a lactone or ester to an aldose can be considered to occur in two steps. In the first stage, the carbon atom of the polarized carbonyl group coördinates two electrons from the sodium atoms at the surface of the amalgam. Two protons from the surrounding medium replace the sodium ions and the aldose results. The sugar is removed from the surface of the amalgam and another lactone molecule comes into position for reduction. The layer of lactone molecules being reduced at the surface of the amalgam may prevent any extensive decomposition of the amalgam by the acid; and after the lactone has been reduced the destruction of the amalgam occurs.

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Summary

A study of the sodium amalgam reduction of aldonolactones and methyl aldonates showed that the maintenance of a pH range of 3–3.5 was the most important single factor in obtaining high and consistent yields of aldose. Other requirements were the use of 2.5–3 atoms of sodium per mole of lactone, the sodium being used as 2.5% amalgam in a particle size of 4–8 mesh. The reaction temperature should not exceed 15°.

The best yields of aldose obtained from the following lactones and esters were: D-galactono-γ-lactone and methyl D-galactonate, 82–84%; D-arabono-γ-lactone and methyl D-arabonate, 71–75%; D-glucono-γ-lactone, 70%; D-gluco-D-gulo-heptono-γ, D-gulono-γ and D-mannono-γ-lactones, 58–62%. Crystalline arabonolactone, methyl arabonate and arabonolactone sirup have been reduced to crystalline arabinose in 50–57% yields.