JOURNAL OF THE
AMERICAN CHEMICAL SOCIETY

VOLUME 60 SEPTEMBER 7, 1938 NUMBER 9

[CONTRIBUTION FROM THE KENT AND GEORGE HERBERT JONES CHEMICAL LABORATORIES, UNIVERSITY OF CHICAGO]

The Catalytic Dehydrogenation of Sugar Alcohols[1]

BY J. W. E. GLATTFELD AND SOLOMON GERSHON

The preparation of aldoses by the oxidation of the corresponding sugar alcohols has been accomplished with varying degrees of success by several investigators. The published methods have not given encouraging results when applied to the preparation of some of the rare and more expensive aldoses. *l*-Galactose and *dl*-erythrose are sugars which might be made available for study if a method for accomplishing the dehydrogenation of the alcohols in a sufficiently convenient and inexpensive manner could be devised. A catalytic dehydrogenation process in which platinum is the catalyst was considered to have possibilities in this direction and the dehydrogenation of mannitol and dulcitol was attempted to test it.

Dehydrogenation of mannitol should give but one aldohexose, *d*-mannose, and one 2-ketohexose, *d*-fructose. This consideration together with the fact that the phenylhydrazone of mannose is particularly easy to separate in good yield makes mannitol an ideal alcohol for study. Fischer[2] treated mannitol with dilute nitric acid and isolated mannose phenylhydrazone and phenylglucosazone. Since then the presence of aldoses and ketoses in solutions obtained by oxidative treatment of hexitols has been verified on numerous occasions. In the case of dulcitol the aldohexoses and 2-ketohexoses theoretically possible as dehydrogenation products are *d*-galactose, *l*-galactose, *d*-tagatose, and *l*-tagatose.

(1) This article is condensed from a dissertation which was presented by Solomon Gershon in partial fulfilment of the requirements for the degree of Doctor of Philosophy in the University of Chicago.

(2) E. Fischer, *Ber.*, **20**, 832 (1887).

With the possibilities outlined above in mind, the catalytic dehydrogenation of the two hexitols by the use of platinic oxide monohydrate as the catalyst source was undertaken. The course of the reaction and the effect of changes in the possible variants were studied first. Mannitol was used exclusively as the alcohol in this study; the data obtained are reported below under the head "Dehydrogenation Study." Procedures for the isolation of the aldoses produced from the alcohols were then investigated; the data here accumulated are reported under the head "Isolation Study." Finally the experimental work which yielded the data discussed under these two heads is reported under the head "Experimental Part."

Dehydrogenation Study

The preliminary data on the course of the reaction were obtained by analysis of the dehydrogenated mannitol solutions for total reducing material (Benedict titration), for aldose content (iodometric titration), and for acid content (titration with alkali). In order to determine the extent of oxidation of the primary products of hexitol dehydrogenation and the nature of their oxidation products, *d*-mannose and *d*-fructose were subjected to catalytic oxidation under the conditions that prevailed during the oxidation of mannitol. The data accumulated are given in Table I. In each case the dehydrogenation was carried out on a sample of 10 g. of substance in 200 cc. of water solution.

Dehydrogenation of *d*-Mannose.—The data in Table I indicate that *d*-mannonic acid was the

TABLE I

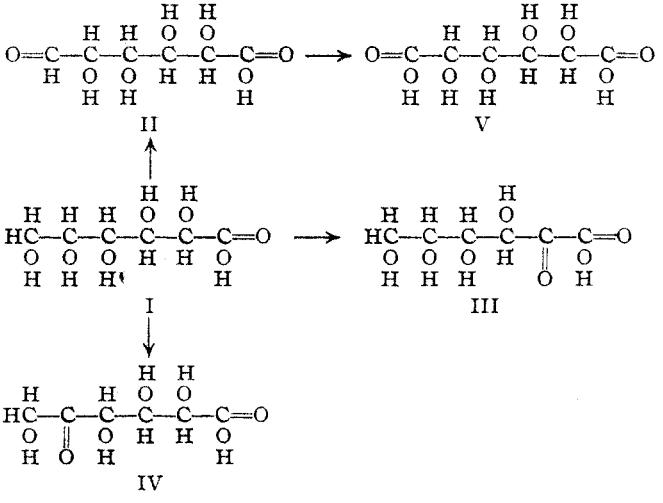
CATALYTIC DEHYDROGENATION OF *d*-MANNOSE AND *d*-FRUCTOSE

Time, hrs.	A Total red. power (calcd. as hexose) (Benedict titr.), %	100 − A Loss in total red. power, %	B Mat. oxid. to acid (calcd. as hexonic acid) (alkali titr.), %	C Aldose present (iod. titr.), %	$\frac{C}{A} \times 100$ Red. mat. present as aldose, %	D Mat. oxid. to osone (iod. titr.), %	B + D, %
			d-Mannose				
0	100.0	0.0	0.0	100.0	100.0		
12	67.2	32.8	33.8	66.7	99.2		
24	50.0	50.0	68.9	51.5	103.0		
36	43.5	56.5	90.1	49.3	113.3		
48	35.2	64.8	103.6	41.7	118.4		
60	25.0	75.0	115.7	29.1	116.4		
72	14.0	86.0	122.3	....	....		
			d-Fructose				
0	100.0	0.0	0.0[a]			0.0	0.0
12	93.7	6.3	18.4			14.6	33.0
24	93.7	6.3	18.5			20.3	38.8
36	90.7	9.3	21.5			26.5	48.0
48	90.7	9.3	23.8			30.3	54.1
60	90.3	9.7	30.0			32.1	62.1
72	88.3	11.7	30.0			34.7	64.7

[a] This column calcd. as 2-ketohexonic acid.

only oxidation product of *d*-mannose in the early stages of the oxidation (the loss in reducing power 32.8%, twelve hours oxidation, coincided fairly well with the gain in hexonic acid content, 33.8%). Furthermore, the only reducing material present during this period was unchanged *d*-mannose (the amount of aldohexose present, as determined by iodometric titration, coincided with the total amount of reducing material present as determined by Benedict titration). As the dehydrogenation proceeded, however, the situation became more complex. A consideration of all the facts supports the conclusions that the second step in the oxidation process was the formation of *d*-mannuronic acid from *d*-mannonic acid and the third step the formation of *d*-mannosaccharic acid from *d*-mannuronic acid. The discussion below provides the basis for these conclusions.

A few of the theoretically possible primary oxidation products of *d*-mannonic acid (I) are indicated by the given formulas. *d*-Mannuronic acid (II) is a reducing alduronic acid. 2-Keto-*d*-mannonic acid (III) and 5-keto-*d*-mannonic acid (IV) are reducing keturonic acids. *d*-Mannuronic acid reduces both Benedict's solution and iodine solution whereas the two keturonic acids reduce the former but the latter only slightly, if at all. The reducing power of alduronic acids as measured by Benedict's solution is generally less than that of an equivalent weight of aldohexose[3] whereas the amount of iodine consumed in the two cases is the same. Hence, if alduronic acid were present with *d*-mannose an iodometric analysis would show more aldose, calculated as *d*-mannose, than would be indicated by a total reduction method. If keturonic acids were present with *d*-mannose, the iodometric analysis would show less aldose than would be obtained by a total reduction method. The per cent. aldose actually found by iodometric titration in the solution of *d*-mannose which had been oxidized for twenty-four hours or more



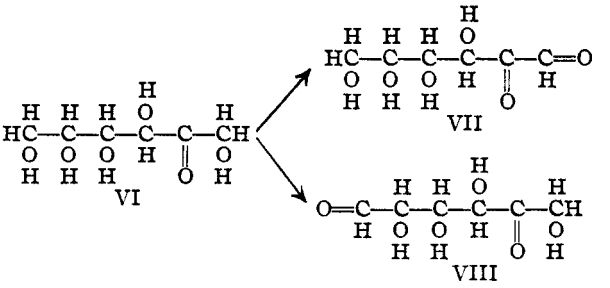
(3) H. Ohle and R. Wolter, *Ber.*, **68**, 843 (1930); F. Ehrlich and R. Guttmann, *ibid.*, **67**, 573 (1934); W. F. Goebel and F. H. Babers, *J. Biol. Chem.*, **100**, 573 (1933); Z. I. Kertesz, *ibid.*, **108**, 127 (1935)

was greater than that found by Benedict's titration (Table I). This is best explained on the assumption that *d*-mannonic acid was being oxidized to *d*-mannuronic acid. Undoubtedly some keto-mannonic acid was also formed but the amount must have been small. That *d*-mannuronic acid (II) was further oxidized to *d*-mannosaccharic acid (V) was shown by the isolation of the monohydrate of calcium *d*-mannosaccharate.

Nelson and Cretcher[4] have reported that *d*-mannuronic acid lactone reacts to some extent with alkaline iodine solutions to produce iodoform. The odor of iodoform was detected in some of the iodometric titrations carried out but no precipitation of iodoform occurred in the dilute solutions titrated. The consumption of iodine in iodoform formation would result in high values for the calculated amounts of aldose present and thus would nullify to some extent the argument presented for *d*-mannuronic acid formation. The authors, however, believe the amount of iodine consumed in iodoform formation in the dilute solutions titrated to have been so small as not to affect the reasoning to any appreciable extent. That iodoform was formed was proved by treatment of the undiluted dehydrogenated mannitol solutions with alkaline iodine solution; iodoform precipitated and was identified by melting point.

Hexoses, at elevated temperatures and in acid solution, give levulinic acid which is known to react with alkaline iodine solution to give iodoform. *d*-Glucose, *d*-mannose, *d*-galactose, and *d*-fructose were heated for twenty-four hours in a *d*-galactonic acid–lactone solution under conditions which prevailed in the hexitol oxidations. Benedict and iodometric titrations were made on the solutions before and after such treatment. No marked difference in results was observed. Levulinic acid apparently was not generated and could not, therefore, have been the source of the iodoform in the iodometric analyses.

Dehydrogenation of *d*-Fructose.—The possible six-carbon atom aldehydes that could be formed from *d*-fructose (VI) are indicated below (VII and VIII). The aldehydes as well as the corresponding acids produced by their oxidation are reducing substances. Even after seventy-two hours of oxidation the *d*-fructose solution retained 88.3% of its original reducing power. Analysis of this solution showed a 34.7% aldehyde and a 30.0% acid content. Thus 35.3% of the *d*-fructose was left unoxidized. When this solution was treated with phenylhydrazine in the cold an abundant yellow precipitate, identified as *d*-glucosazone, formed in a few minutes. The speed with which the precipitate formed indicated its source was *d*-glucosone (VII) and not *d*-fructose (VI). A 2% solution of *d*-fructose and phenylhydrazine did not produce a precipitate for twenty-five minutes while a 5% solution required ten to fifteen minutes.



VI VII VIII

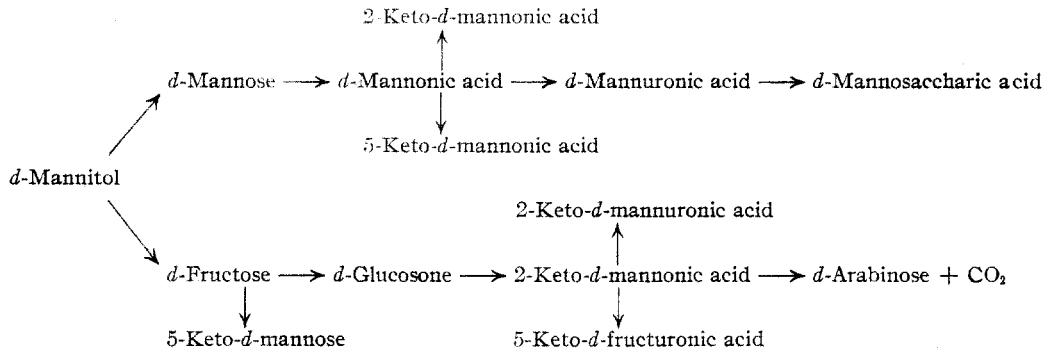
Dehydrogenation of Mannitol.—The facts and conclusions recorded above aid in arriving at an interpretation of the data for the dehydrogenation of mannitol presented in Tables II and III. These data and some additional facts presented below indicate a course of reaction represented by the following scheme chart.

The first point to be noted is that the passage of air through a mannitol solution at 80–90° for thirty-five hours had practically no effect on the mannitol (Table II, 1). When platinic oxide monohydrate was added to a mannitol solution at 80–90° the mannitol was oxidized and the platinic oxide reduced to platinum (2, 3). The reaction between the oxide and mannitol was stoichiometric (4) (see Experimental Part). The passage of air through a mannitol solution which contained catalyst resulted in a dehydrogenation of the mannitol beyond the stoichiometric point. This indicates a catalytic effect of the platinum formed (5–8, etc.). Spent catalyst alone, *i. e.*, the platinum formed from the oxide in previous experiments, was without effect on mannitol (9). In the presence of air, however, the spent catalyst was a catalytic agent (10).

Experiments intended to compare oxygen with air as the oxidizing agent indicated the latter to be more efficient (11, 12). This was due to the fact that the oxide was reduced to platinum much more slowly in the presence of oxygen than in air

(4) W. F. Nelson and L. H. Cretcher, THIS JOURNAL, **52**, 2130 (1930).

SOME POSSIBLE OXIDATION PRODUCTS OF *d*-MANNITOL



which of course delayed the catalytic effect of the platinum. When time was allowed for the complete reduction of the oxide before the use of oxygen or air the former was more efficient. In such cases the time of reaction with oxygen was only 40–45% of that when air was used. Fifty grams of mannitol in 350 cc. of solution required the use of air for ninety-six hours in order to obtain maximum yields of mannose, whereas only fifty-five to sixty hours was required with oxygen. Twenty-five grams of mannitol in 200 cc. of solution required fifty-five hours with air but only thirty-two hours with oxygen.

The addition of the oxide in portions had no advantage. The addition of the entire amount of oxide at the start produced slightly better results because of longer contact between all of the catalyst and the solution (13b, 14). The amount of catalyst for best results depends somewhat on the amount of mannitol to be oxidized and the volume of solution (6, 7). Fifteen to 50 grams of mannitol in a 200–400 cc. volume can be dehydrogenated

TABLE II

DEHYDROGENATION OF MANNITOL

Expt.	Temp.,[a] °C.	Catalyst, g.	Mannitol in 200 cc. soln., g.	Time, hours	Conditions[b]	A, oxid. to red. mat. (calcd. as *d*-mannose) (Benedict titr.), %	B, oxid. to acid (calcd. as hexonic acid) (alkali titr.), %	A + B, %
1	80–90	0.0	5.0	35[e]	Air[c]	0.0	0.1	0.1
2	80–90	1.0	5.0	35[e]	No air	11.0		
3	80–90	0.5	5.0	35[e]	No air	9.8		
4	75	1.011	5.0	24	No air	19.1	6.7	25.8
5	80–90	1.0	5.0	35[e]	Air	41.8		
6	80–90	1.0	5.0	31[e]	Air	64.5		
7	80–90	0.5	5.0	31[e]	Air	49.1		
8	85	1.0	2.5	24	Air	37.6	65.5	103.1
9	80–90	1.0 spent	5.0	31[e]	No air	0.0		
10	80–90	1.0 catalyst	5.0	31[e]	Air	32.6		
11	60	1.0	2.5	46	Air	32.6	86.0	118.6
12	60	1.0	100 cc.	46	Oxygen	14.2	31.4	45.6
13[a]	85	4.0	5.0	2	Air, 8.6 l.	28.8	21.1	49.9
13[b]	85	4.0	5.0	8	Air, 30.0 l.	34.4	24.6	59.0
14	85	4.0[d]	5.0	8	Air, 30.0 l.	31.6	17.0	48.6
					O_2, lb. R. p. m.			
15	27	1.0	2.5	24	30 185	5.8	1.4	7.2
16	80	1.0	2.5	24	30 185	28.0	29.9	57.9
17	80	1.0	2.5	12	25 300	20.1	9.4	29.5
18	75	0.84	2.5	32[e]	10 300	20.8	11.6	32.4
19[a]	63	1.0	2.5	45	23 air 245	18.6	7.3	25.9
19[b]	63	1.0	100 cc.	86	23 air 245	28.0	10.0	38.0

[a] Thermometer in the oil-bath for all cases except when pressure was used; in pressure work the temperature of the solution is recorded. [b] In all experiments in which air was used the air was started immediately after the catalyst was added. [c] Active bubbling of air through the solution to maintain an excess at all times. [d] Catalyst added in 1-g. portions every two hours. [e] Intermittent heating, eight hours per day.

satisfactorily with 2 g. of platinic oxide monohydrate.

The length of time required to reduce the oxide to platinum, as determined by change of color from brown to black, was dependent on the temperature and concentration of material being oxidized; the higher the temperature and the more concentrated the solution, the faster the reduction. Two grams of platinic oxide monohydrate was not reduced by 5 g. of mannitol in 200 cc. of solution after twenty-four hours of stirring at 30° whereas only forty-five minutes was required at 75°. Twenty-five grams of mannitol in 200 cc. of solution reduced 2 g. of oxide in twenty to twenty-five minutes at 80° while 15 g. required thirty to thirty-five minutes.

The optimum temperature for the catalytic dehydrogenation was 80–85° (thermometer in bath). Higher temperatures caused excessive caramelization and decomposition whereas lower temperatures necessitated longer reaction periods.

The effectiveness of the catalyst was not altered by varying its temperature of preparation. Platinic oxide monohydrate samples prepared at 400, 485, 535, and 600° all proved equally effective.

The use of oxygen or air at increased pressures, without first allowing time for the reduction of the oxide to platinum black, was less effective than oxidation at atmospheric pressure (15–19). In most cases the oxide was not reduced after twenty-four hours of agitation at the increased pressure. If sufficient time was allowed for the reduction of the oxide and pressure then applied, dehydrogenation proceeded much faster at the increased pressures than by simply bubbling oxygen or air through the solution (see Experimental Part and Table IV).

After the preliminary work discussed above, an extended study of dehydrogenation with platinum oxide and air at atmospheric pressure was made. From the data of Table III it is seen that during the first twenty-four hours mannitol was oxidized to about equal amounts of *d*-mannose and other reducing material. During the first thirty-six hours the percentage mannitol oxidized to reducing material exceeded the percentage mannitol oxidized to acid. As the concentration of the sugars increased the rate of acid formation increased, and the iodometric aldose titrations indicated increasing amounts of aldehyde. A faint iodoform odor was perceptible in the iodometric titrations of the sixty and seventy-two hour samples. Iodoform crystals were deposited when the undiluted seventy-two hour sample was treated with sodium carbonate and iodine. All oxidized mannitol solutions gave positive ketose tests and the twenty-four hour sample as well as the subsequent samples gave positive naphthoresorcin tests indicative of uronic acids.

The maximum value obtained for percentage mannitol oxidized to reducing substances, calculated as *d*-mannose, was 64.7% [Table III, (1)]. In pressure dehydrogenations the maximum value obtained was 67.7% [Table IV, (7)]. These values are higher than any previously reported value and demonstrate the possibilities of the catalytic dehydrogenation of sugar alcohols when properly controlled.

TABLE III

CATALYTIC DEHYDROGENATION OF HEXITOLS

Hexitol (15 g. in 200 cc. sol.)	Time, hrs.	A Oxid. to red. material (calcd. as aldohexose) (Benedict titr.), %	B Oxid. to acid (calcd. as hexonic acid) (alkali titr.), %	C Oxid. to aldose (iod. titr.), %	$\frac{C}{A} \times 100$ Red. mat. present as aldose, %	A + B, %
(1)Mannitol	0	0.0	0.0	0.0	0.0	0.0
	12	21.6	15.7	10.7	49.5	37.3
	24	35.9	29.8	23.1	64.3	65.7
	36	57.3	49.3	46.8	81.7	106.6
	48	64.7	76.0	59.5	92.0	140.7
	60	58.8	111.7	65.3	111.0	170.5
	72	43.5	165.0	55.4	127.4	208.5
(2)Dulcitol	0	0.0	0.0	0.0	0.0	0.0
	12	12.4	9.2	8.5	68.5	21.6
	24	19.4	24.6	13.5	69.6	44.0
	36	40.0	42.8	34.8	87.0	82.8
	48	55.2	61.6	55.2	100.0	116.8
	60	42.3	84.0	46.5	109.9	126.3
	72	29.2	104.4	31.0	106.1	133.6

Isolation Study

Mannitol.—It is apparent from the data of Table III (1) that the percentage mannitol oxidized to reducing material is in itself not a sufficient criterion of best condition for aldose isolation. A thirty-six hour sample showed 57.3% oxidation whereas a sixty-hour sample showed 58.8% oxidation to reducing material, yet the latter was contaminated with over twice as much acid as the former. Analysis of a solution might indicate 30–40% oxidation to reducing material and yet the solution might contain very little *d*-mannose, the reduction being due mainly to uronic acids. Such a solution would not be suitable for *d*-mannose isolation. The best criterion for isolation of *d*-mannose was found to be that point at which the solution showed 55–60% oxidation to reducing material and about 50% oxidation to acid.

The best yield of mannose from mannitol oxidation found recorded in the literature was that of Fenton and Jackson[5] who used hydrogen peroxide with ferrous catalyst and obtained a 42% yield of mannose as crude orange-colored phenylhydrazone. In the catalytic dehydrogenation of mannitol reported in this paper a 35.3% yield of mannose was obtained as white phenylhydrazone, which when decomposed according to the method of Herzfeld,[6] yielded a sirup which contained *d*-mannose equivalent to a 92% yield, from which in turn crystalline *d*-mannose in 50% yield was obtained calculated from the phenylhydrazone. Calculated from the mannitol the yield of *d*-mannose sirup was 32.5%, and of crystalline *d*-mannose 17.6%. The mannose was also isolated as α-methyl-*d*-mannoside, from the oxidized mannitol solutions from which the acids had been removed, in 19.9% yield and from solutions from which the acids had not been removed in 10.5% yield. The mannoside can be converted to crystalline *d*-mannose in 70% yield.[7]

After removal of the acids and of the *d*-mannose, phenylglucosazone was isolated. This was indicative of the presence of *d*-fructose. The Seliwanoff[8] ketose tests and the results of the iodometric analyses were also evidence for the presence of ketose. Calcium salts were isolated at various times from the reducing solutions. Analysis of one salt indicated it to be the monohydrate of calcium *d*-mannonate and that of another the monohydrate of calcium *d*-mannosaccharate (see below).

Dulcitol.—The analytical results obtained in the catalytic dehydrogenation of dulcitol are presented in Table III (2). The products of the reaction are of the same type as found with mannitol. Thus *dl*-galactose, *dl*-tagatose, *dl*-galactonic acid, *dl*-galactosone, 2-keto-*dl*-galactonic acid, *dl*-galacturonic acid, and mucic acid are present in the reaction solution.

The best yield of *dl*-galactose reported in the literature is that of Neuberg and Wohlegemuth[9] who used 3% hydrogen peroxide in the presence of ferrous sulfate to oxidize the dulcitol and obtained a solution which contained 40% reducing sugars. From this these authors obtained *dl*-galactose in 10% yield by direct isolation and in about 30% yield when they used phenylhydrazine. In the catalytic dehydrogenation of dulcitol herewith reported a 30% yield of *dl*-galactose, isolated as the phenylhydrazone, was obtained. Crystalline *dl*-galactose was isolated from the phenylhydrazone in 52% yield. The yield of crystalline *dl*-galactose obtained was 15.5% based on the dulcitol.

E. Votocek and co-workers[10] have reported the quantitative precipitation of *d*-galactose as 2,4-dibromophenylhydrazone monohydrate from aqueous acetic acid solution. With this fact in mind, a dulcitol solution was subjected to catalytic dehydrogenation until it showed about 50% oxidation to reducing material. *dl*-Galactose was isolated in 23.5% yield as a pink anhydrous 2,4-dibromophenylhydrazone.

dl-2,4-Dibromophenylgalactosazone and *dl*-phenylgalactosazone were isolated from the filtrates obtained after removal of the corresponding hydrazones. Mucic acid also was isolated. Two barium salts were isolated and analyzed for barium. One contained 26.42% barium, the other 34.93% barium. Barium *dl*-galactonate contains 26.03% and the dihydrate of barium mucate contains 35.80% barium.

The salts isolated from the various reducing solutions cannot be considered pure substances even with satisfactory analyses. Barium *dl*-

(5) H. J. H. Fenton and H. Jackson, *J. Chem. Soc.*, **75**, 1 (1899).

(6) A. Herzfeld, *Ber.*, **28**, 442 (1895); E. Abderhalden, "Handbuch der biochemischen Arbeitsmethoden," Urban and Schwarzenberg, Berlin, Vol. II, 1909, p. 74.

(7) C. S. Hudson and E. L. Jackson, THIS JOURNAL, **56**, 958 (1934).

(8) T. Seliwanoff, *Ber.*, **20**, 181 (1887); E. Abderhalden, ref 6, p. 109.

(9) C. Neuberg and J. Wohlegemuth, *Z. physiol. Chem.*, **36**, 221 (1902).

(10) E. Votocek, V. Ettel and B. Koppova, *Bull. soc. chim.*, [4] **39**, 278 (1926).

galactonate contains 26.03% barium whereas barium *dl*-galacturonate contains 26.24%. The isolated barium salt which contained 26.42% barium did contain some of the barium *dl*-galacturonate. Its solution reduced Benedict's solution and gave a faint naphthoresorcin test.

Experimental Part

Reagents and Procedures.—(1) The platinic oxide monohydrate was prepared by the method of Adams, Voorhees, and Shriner[11] as modified by Schimpff[12] for larger amounts of catalyst. (2) The mannitol, dulcitol, and *d*-galactose were products of the Kahlbaum Chemical Company. (3) The *d*-glucose, *d*-fructose, and *d*-mannose were products of Pfanstiehl Chemical Company. (4) 2,4-Dibromophenylhydrazine was prepared from β-acetylphenylhydrazine by the method of Humphries and Evans.[13] The β-acetylphenylhydrazine was prepared by the method of A. Kaufmann.[14] (5) The naphthoresorcin was manufactured by the Eastman Kodak Company.

All iodometric analyses were made by the method developed by Cajori.[15] In all cases in which alcoholic solutions were to be analyzed, the alcohol was first removed by evaporation of the sample to a thick sirup *in vacuo* at 60–70°. Water was then added and the evaporation repeated. Iodoform formation due to the presence of the alcohol thus was avoided.

The acidimetric analyses were performed as follows. An excess of 0.1 *N* sodium hydroxide solution was added to the sample to be analyzed (phenolphthalein indicator). The solution was heated on a steam-bath for three minutes, after which time the solution still retained the pink color. An excess of 0.1 *N* hydrochloric acid was then added and the three-minute heating was repeated. The solution was then cooled and the excess acid determined by titration with standard alkali.

Tollens' naphthoresorcin[16] test for glycuronic acids was performed according to the modification of Neuberg and Kobel.[17]

1. Dehydrogenation of Mannitol

Preliminary Dehydrogenation Work.—All of the preliminary work was performed with mannitol. In all but the pressure work the solution of mannitol was made in a 500-cc. three-necked flask fitted with a mercury-seal stirrer, an efficient condenser, and an air inlet tube. The flask was immersed in a paraffin oil-bath which was heated on an electric hot plate. The temperature of the oil-bath was regulated by means of a rheostat. The conditions desired (recorded in Table II) were maintained by suitable adjustment of the rheostat, air flow, or other variables. In all cases in which the volume of air used is recorded a gasometer was used. In all cases, the air or oxygen was passed through concentrated sulfuric acid and then through a long calcium chloride tube before entrance into the reaction flask. The reaction solutions were filtered to remove platinum and then analyzed.

In the case of the test runs for which the data are presented in Table III the solutions were analyzed every twelve hours. All samples showed positive ketose tests. All samples beyond the twelve-hour sample showed positive naphthoresorcin tests.

All work performed under pressures greater than atmospheric was carried out in the hydrogenation apparatus manufactured by the Burgess-Parr Company of Moline, Illinois. The tank was filled with oxygen or air at the pressure desired. The pressure bottle was wired to maintain the reaction mixture at desired temperatures.

Stoichiometric Relationship between Catalyst and Hexitol.—Five grams of mannitol was dissolved in 200 cc. of boiled water at 75° in a three-necked flask fitted with a mercury-seal stirrer and condenser. The platinic oxide monohydrate (1.011 g.) was added with stirring. The oxide was reduced but did not settle readily after eight hours of stirring at 75°. The stirring at 75° was continued overnight, after which time the platinum settled readily and left a colorless solution. The platinum was removed by filtration and the filtrate was analyzed for total reducing material, aldose, and acid. The amount of mannitol oxidized to reducing material (calculated as *d*-mannose) was 0.953 g. (62.3% of the reducing material was aldose). This would require 0.642 g. of the platinic oxide monohydrate. The amount of mannitol oxidized to acid (calculated as monobasic acid) was 0.335 g. which would require 0.451 g. of the oxide. A total of 1.093 g. of oxide is thus theoretically necessary. This value is 0.082 g. in excess of the amount of oxide actually used and is slightly in excess of the amount accountable for by experimental error. The simplifications made in the calculation of the per cent. mannitol oxidized, however, would tend to make such small differences. There can be no doubt that the reaction is stoichiometric.

Preparation of the Phenylhydrazone of *d*-Mannose.—Fifty grams of mannitol was dissolved in 350 cc. of hot distilled water in a three-necked flask fitted with a mercury-seal stirrer, an efficient condenser, and an air-inlet tube. The flask was immersed in an oil-bath maintained at 80–85° throughout the dehydrogenation. Two grams of platinic oxide monohydrate was added. Stirring was begun and allowed to continue for thirty minutes. Oxygen was then passed through the solution rapidly enough to keep the catalyst uniformly suspended. The stirring and passage of oxygen was maintained for sixty hours (when air was used, ninety-six to one hundred hours was necessary). The platinum was allowed to settle (about ten minutes) and the solution was filtered. The filtrate and washings were concentrated to about 200 cc. at 55–60° under reduced pressure. A filtered solution of 40 g. of phenylhydrazine hydrochloride and 60 g. of sodium acetate trihydrate in 300 cc. of water (made by the application of gentle heat) was then added slowly and with stirring to the concentrated solution. A precipitate began to form in about one minute. The mixture was allowed to stand for one and one-half hours with occasional stirring. The yellow precipitate was separated by filtration and washed

(11) Adams, Voorhees and Shriner, "Organic Syntheses," 1928, John Wiley and Sons, Inc., New York City, Vol. VIII, p. 98.

(12) G. W. Schimpff, Ph.D. dissertation, Dept. of Chemistry, University of Chicago, 1935.

(13) J. E. Humphries and R. Evans, *J. Chem. Soc.*, **127**, 1676 (1925).

(14) A. Kaufmann, *Ber.*, **42**, 3480 (1909).

(15) F. A. Cajori, *J. Biol. Chem.*, **54**, 617 (1922).

(16) B. Tollens, *Ber.*, **41**, 1788 (1908).

(17) Neuberg and Kobel, *Biochem. Z.*, **243**, 435 (1931).

with water. After it had been drained free of excess water on a Büchner funnel the precipitate was heated in about 700 cc. of acetone until the acetone boiled. The mixture was then cooled, subjected to filtration, and the solid washed with cold acetone. The phenylhydrazone of *d*-mannose was left as a fine white powder which weighed twenty-six grams. This corresponded to a 35.3% yield. The product melted with decomposition at 195–196° (corr.) and was found to be suitable for *d*-mannose isolation.

A portion of the phenylhydrazone was recrystallized twice from 95% alcohol, dried in a vacuum desiccator, and analyzed for carbon, hydrogen, and nitrogen with the results recorded below.

Anal. Calcd. for $C_{12}H_{18}O_5N_2$: C, 53.30; H, 6.71; N, 10.37. Found: C, 53.37; H, 6.53; N, 10.17.

Isolation of *d*-Mannose from Phenylhydrazone.—Twenty-five grams of the phenylhydrazone of *d*-mannose was added in small portions to a mixture of 20 g. of benzaldehyde, 25 cc. of alcohol, and 25 cc. of water which was kept hot on a steam-bath. The mixture was then refluxed for thirty minutes during which time 35 cc. of water was added. The mixture was cooled and subjected to filtration. The precipitate was triturated with small amounts of water and again separated by filtration. It was identified, after recrystallization from dilute alcohol, as the phenylhydrazone of benzaldehyde (m. p. 154.5°). The combined filtrates from the benzaldehyde phenylhydrazone were extracted with ether; the separated aqueous layer was heated with charcoal and filtered. The solution thus obtained had a volume of 225 cc. and a rotation of +2.00°. This indicates the presence of 15.2 g. of *d*-mannose (theoretical yield, 16.6 g.). The solution was evaporated to a sirup at reduced pressure and at 50°. The sirup weighed 16.5 g. and contained 91.7% mannose (Benedict titration). An optical rotation analysis showed the sirup to be 93.0% mannose.

A mixture of the sirup and 35 cc. of glacial acetic acid was warmed to 60° and maintained at 60° for one hour in order to effect complete solution of the sirup in the acid. The solution was allowed to cool slowly to room temperature and stored for one day, during which time crystals appeared. The mixture was then stored in the refrigerator for four days. The crystalline *d*-mannose was removed by filtration and washed with two 5-cc. portions of glacial acetic acid, followed by small volumes of alcohol and ether. The crystals were dried to constant weight in a vacuum desiccator which contained sodium hydroxide. The crystals then melted at 130–131° (corr.) and weighed 7.0 g. This corresponded to a 50% yield of *d*-mannose. The specific rotation of the *d*-mannose was +14.9°. From the acetic acid filtrates 3.5 g. of a white sirupy mannose was precipitated by the addition of ether.

Isolation of α-Methyl-*d*-mannoside.—Fifty grams of mannitol dissolved in 350 cc. of water was oxidized with oxygen at 80–85° for fifty-five hours in the presence of 2 g. of platinic oxide monohydrate. The solution was filtered to remove platinum; the acids were removed from the filtrate with barium carbonate as described under the head "Isolation of Calcium and Barium Salts" below.

The combined alcohol filtrates obtained after the removal of the acids as barium salts were evaporated to a thick sirup *in vacuo* at 55°. The residue was kept at reduced pressure and 55° for one hour and then *in vacuo* overnight. It was then treated with 150 cc. of a 2% solution of hydrogen chloride in anhydrous methyl alcohol (acetone free). The mixture was gently refluxed for two hours on a steam-bath. Agitation was necessary during the first ten minutes to assist in the solution of the sirup. The solution was cooled somewhat, treated with 3–4 g. of charcoal, and then refluxed for thirty minutes. The solution was filtered hot. Small portions (a total of 20 cc.) of hot anhydrous methyl alcohol were used to complete the transfer. The filtrate was placed in the refrigerator for fifty hours. The crystalline mannoside was then removed by filtration and washed with a little cold absolute methyl alcohol followed by a little dry acetone. The air-dried α-methyl-*d*-mannoside melted at 189–191° (corr.), did not reduce Benedict's solution, and had a specific rotation of +79.0° at 20°. A 16.5% yield (8.8 g.) was obtained by this procedure. The filtrate was concentrated to 40 cc. at 35° *in vacuo* and placed in the refrigerator for four days. One and eight-tenths grams of crystals (m. p. 185–187°, corr.) was obtained, making a total yield of 19.9% (10.6 g.).

Isolation of Calcium and Barium Salts.—The following general procedure was used for the isolation of the calcium or barium salts from the solutions obtained by the oxidation of 25 g. of each of the oxidized hexitols. The platinum was first removed by filtration. The filtrate was treated with excess calcium or barium carbonate and the mixture maintained at 80° (thermometer in oil-bath) for one to two hours. Frequent or continuous stirring was employed throughout this heating. The excess carbonate was removed by filtration and the filtrate was concentrated at 55–60° *in vacuo* to a volume of about 50 cc. Three hundred cc. of hot alcohol was then added slowly and the mixture thoroughly shaken. The mixture was cooled and the supernatant liquid filtered. The residual gummy barium or calcium salts were treated with 25 cc. of hot water and the mixture again treated with 150 cc. of hot alcohol. After one hour the solution was again decanted through the filter. The barium or calcium salts were left behind in the form of a gum. The combined alcoholic solutions were used for aldose and osazone isolations (see below). The calcium or barium salt gums were dissolved in hot water, treated with charcoal, and the solutions filtered. Hot alcohol was added in small amounts to the hot filtrates until a permanent turbidity occurred. The solutions were then cooled and allowed to stand overnight. The salts which had crystallized out were separated from the solution by filtration, washed with 60–80% alcohol, and dried in a desiccator. The dried salts were then recrystallized by solution in hot water followed by reprecipitation with alcohol as described above. The salts thus obtained were dried in a vacuum desiccator.

Two calcium salts were thus isolated from twenty-five grams of mannitol which had been subjected to oxidation for forty-eight hours. During the recrystallization process the major portion of the calcium salt precipitated from the aqueous alcohol solution as an amorphous white solid. The filtrate from this solid deposited more salt on standing. The first salt contained 9.06% while the second contained 14.80% calcium. Calcium *d*-mannonate monohydrate contains 8.94% calcium, while calcium *d*-mannosaccharate

TABLE IV

PRESSURE DEHYDROGENATION

In all cases 25 g. of mannitol was dissolved in 200 cc. of water except in experiment 6 where 15 g. was dissolved in 100 cc. of water; the shaker was regulated at 300 rev. per min. In all cases thirty minutes of shaking at atmospheric pressure was used after each addition of catalyst. The temperature was 83°.

Expt.	Initial oxy. press., lb.	Catalyst added, g.	Time, hrs.	Press. decr., lb.	Oxid. to reducing material (calcd. as *d*-mannose) (Benedict titr.) %	Oxid. to acid (calcd. as hexonic acid) (alkali titr.) %	Yield of *d*-mannose as phenylhydrazone, %
1	40	2.0	2.0	4.6			
			5.0[a]	0.0	32.3	31.6	16.8
2a	42	2.0	2.0	5.0			
b	42	1.0	1.0	2.0	35.1	53.0	14.0
3a	42	2.0	1.0	4.8			
b	42	1.0	1.0	2.2	49.4	56.2	20.7
4a	42	2.0	1.0	4.3			
b	42	2.0	0.5	2.1	41.3	59.2	16.4
5a	42	2.0	1.0	5.5			
b	42	1.0	1.0	2.2			
c	42	1.0	1.0	1.5	44.4	73.4	5.6
6	40	2.0	2.5	4.6	39.0	56.6	11.4
7	42	2.0	2.5[b]	5.0			
			3.5 hot				
			2.5 cold				
			4.0 hot	3.0			
			22.0 hot and cold	0.2	67.7	58.3	25.4

[a] The hours listed are in addition to those listed in the same experiment. [b] The hours listed in this case are only approximate; the wire connected to the bottle snapped off twice while shaking, thus allowing the bottle to cool.

monohydrate contains 15.05% calcium. Fischer and Hirschberger[18] prepared a hydrated calcium *d*-mannonate which contained 8.78% calcium.

Isolation of Phenylglucosazone from an Oxidized Mannitol Solution.—The aqueous alcohol solution from which the calcium salts had been removed was treated with a filtered solution of 20 g. of phenylhydrazine hydrochloride and 30 g. of sodium acetate trihydrate in 150 cc. of water. The mixture was allowed to stand for one and one-half hours and then subjected to filtration. The filtrate was reserved for the isolation of glucosazone. The precipitate was washed with water, heated with 200 cc. of acetone until the latter boiled, the mixture cooled, subjected to filtration, the precipitate washed with acetone, and dried. This yield of phenylhydrazone of *d*-mannose was 20%.

The filtrate saved for glucosazone isolation was treated with 10 g. of phenylhydrazine in 10 cc. of 50% acetic acid and the solution heated on a steam-bath for two hours. The mixture was cooled and subjected to filtration. The precipitate was washed with water followed by alcohol, and dried. A yield of 9.5% glucosazone was obtained. The melting point was 206–207° (corr.). The product was recrystallized from 65% alcohol, dried, and analyzed for nitrogen.

Anal. Calcd. for $C_{18}H_{22}O_4N_4$: N, 15.64. Found: N, 15.53.

Pressure Dehydrogenations.—Twenty-five grams of mannitol was dissolved in 200 cc. of hot water in a pressure bottle. The bottle was wired and by regulation of the current a temperature of 83° was maintained. Two grams of platinic oxide monohydrate was added and the bottle shaken at 300 revolutions per minute and at atmospheric pressure for thirty minutes, when the catalyst was black. The bottle was carefully evacuated until the solution began to boil and then filled with oxygen at 42 lb. (3 atm.) pressure. The evacuation and filling were repeated three times. After the third filling, shaking was started and maintained for one hour. The pressure decreased 4.8 lb. (0.3 atm.). After one hour of agitation at the increased pressure, the catalyst activity ceased and the use of oxygen by the mannitol stopped. One gram of platinic oxide was added after the pressure had been released, the mixture was shaken at atmospheric pressure for thirty minutes followed by evacuation and filling with oxygen at 42 lb. (3 atm.) pressure as described. This time there was a decrease of 2.2 lb. (0.15 atm.) in one hour. (It is to be noted that the catalyst was added in several portions during the pressure dehydrogenations rather than in one portion as was more desirable in atmospheric pressure dehydrogenations. The cessation of catalyst activity at the increased pressures makes such a procedure necessary.) The solution was cooled for about thirty minutes and then the pressure was released and the solution filtered. The small amount of colloidal platinum was removed from the filtrate by the use of charcoal. Analysis of the filtrate from the charcoal showed that 49.4% of the mannitol had been oxidized to reducing material, calculated as *d*-mannose, and that 56.2% had been oxidized to acids, calculated as hexonic acid. The *d*-mannose was isolated as the phenylhydrazone in 20.7% yield from this solution. Table IV lists the data for other experiments with different conditions.

The main disadvantage of pressure dehydrogenations is the tendency for the oxidation to proceed beyond the aldose in the later stages of the oxidation, thus building up high concentrations of acid at the expense of aldose. As a re-

(18) Fischer and Hirschberger, *Ber.*, **22**, 3219 (1889).

sult, the yields obtained by pressure dehydrogenation were lower than those obtained at atmospheric pressure.

2. Dehydrogenation of Dulcitol

Isolation of Mucic Acid.—The data for the results obtained in a test run in which 15 g. of dulcitol in 200 cc. of water at 80° and 2.0 g. of platinic oxide monohydrate were used, are presented in Table III (2). The solution which remained after the seventy-two hour sample had been removed deposited a crystalline substance that was identified as mucic acid by its melting point (213°, corr.) and that of its diphenylhydrazide[19] (241°, corr.).

Isolation of *dl*-Galactose with 2,4-Dibromophenylhydrazine.—Fifteen grams of dulcitol in 200 cc. of water at 80° was treated with 2.0 g. of platinic oxide monohydrate and the procedure described in the case of mannitol carried out. After thirty minutes, air was passed through the solution for forty-four hours. This solution gave positive ketose and naphthoresorcin tests and showed that 47.2% of the dulcitol had been oxidized to reducing material (calculated as *dl*-galactose) and that 48.8% had been oxidized to acid (calculated as *dl*-galactonic acid). Iodometric analysis showed that 90% of the reducing material was aldose. The solution was filtered to remove platinum and the filtrate concentrated *in vacuo* at 50° to about 35 cc. A filtered solution of 20 g. of 2,4-dibromophenylhydrazine in 140 cc. of 50% acetic acid (prepared by gentle warming) was added slowly to this concentrate. The mixture was filtered rapidly to remove a small amount of red oil which formed and the filtrate allowed to stand for three hours at room temperature. The mixture was stirred several times during this period. The precipitate was removed by filtration, washed with 100 cc. of 5% acetic acid, 25 cc. of diluted alcohol, and finally with ether. The filtrate was saved for osazone isolation. The 2,4-dibromophenylhydrazone of *dl*-galactose thus obtained was faintly pink and melted at 151–152° (corr.). The yield was 23.5%. Three recrystallizations from dilute alcohol raised the melting point to 171–172° (corr.). Charcoal was used in each recrystallization. The pure 2,4-dibromophenylhydrazone was white. It was dried at room temperature over magnesium perchlorate for two days at 20 mm. pressure and was then analyzed for nitrogen.

Anal. Calcd. for $C_{12}H_{16}O_5N_2Br_2$: N, 6.55. Found: N, 6.64.

The 2,4-dibromophenylhydrazone of *dl*-galactose was decomposed with benzaldehyde by the method of Herzfeld and yielded the 2,4-dibromophenylhydrazone of benzaldehyde and *dl*-galactose. The former melted at 103° (corr.) after several recrystallizations from dilute alcohol while the latter melted at 142–144° (corr.).

Isolation of the 2,4-Dibromophenylosazone of *dl*-Galactose.—The filtrate saved for osazone isolation was heated for two hours on a steam-bath. A black oil settled out. The mixture was cooled and about 4 g. of solid crystallized out. This was separated from the oil which remained on the bottom of the flask and was recrystallized from dilute alcohol. It was identified as the 2,4-dibromophenylhydrazide of acetic acid by its melting point, 147° (corr.).

The oil was dissolved in boiling 60% alcohol and the solution treated with charcoal, filtered, and cooled. It deposited 4 g. of a yellow precipitate which decomposed at 145–149° (corr.). This was recrystallized from dilute alcohol to which charcoal had been added and thoroughly dried over phosphorus pentoxide. The compound decomposed at 152–153° (corr.).

Anal. Calcd. for $C_{18}H_{18}O_4N_4Br_4$: N, 8.32. Found: N, 8.37.

Isolation of *dl*-Galactose with Phenylhydrazine.—Twenty-five grams of dulcitol was dissolved in 350 cc. of hot water in a three-necked flask fitted as described for mannitol. Two grams of platinic oxide monohydrate was added when the solution had reached 80°. The mixture was stirred for one hour after which air was bubbled through the solution for seventy hours. The solution then showed 60.3% of the dulcitol to have been oxidized to reducing material (calculated as *dl*-galactose) and 56.0% to acid. The solution gave positive ketose and naphthoresorcin tests. The platinum was removed by filtration and the acids were removed as barium salts by the general method described.

The alcoholic filtrate from the precipitated barium salts was concentrated at 40–50° at reduced pressure to a thin sirup which was treated with 9 g. of distilled phenylhydrazine in an equal volume of 50% acetic acid. The mixture was warmed gently a few minutes on a steam-bath, stoppered, and set aside in a dark place at room temperature for twenty-four hours. The yellow precipitate was separated by filtration and washed with a small amount of 50% alcohol. The filtrate was saved for the isolation of the *dl*-osazone. The precipitate was washed further with absolute alcohol and ether and dried. It decomposed at 144–148° (corr.). The yield of this impure phenylhydrazone was 30%. Recrystallization of the phenylhydrazone resulted in considerable loss because of solubility and because of the formation of osazone. It was therefore used without purification for the isolation of *dl*-galactose.

The crude phenylhydrazone was treated with 300 cc. of water and 12 g. of benzaldehyde. The mixture was kept on a steam-bath for thirty minutes, cooled, and subjected to filtration. The filtrate was extracted with ether several times and the separated aqueous solution was decolorized with charcoal. The solution was optically inactive. It was concentrated at 50–55° at reduced pressure to a thick sirup which weighed 5.3 g. The sirup was dissolved in hot alcohol and the solution deposited 3.8 g. of *dl*-galactose crystals, a 15.5% yield calculated from dulcitol used. The crystals were dried in vacuum over calcium chloride at 15 mm. pressure for two days. The melting point was 145° (corr.). Oxidation with nitric acid yielded mucic acid. Analysis by Benedict titration showed the material to be 98.6% *dl*-galactose. Iodometric analysis showed it to be 99.2% *dl*-galactose.

Isolation of *dl*-Phenylgalactosazone.—The filtrate set aside for osazone isolation was treated with a filtered solution of 20 g. of phenylhydrazine hydrochloride and 30 g. of sodium acetate trihydrate in 100 cc. of water. The mixture was heated on the steam-bath for one and one-half hours, cooled, and subjected to filtration. The precipitate was washed with absolute alcohol and then with ether. The dry *dl*-osazone weighed 3.5 g. indicating a 7.3% yield. It decomposed at 207° (corr.). It was recrystallized from

(19) C. Bülow, *Ann.*, **236**, 194 (1886).

alcohol and dried *in vacuo* over calcium chloride. The compound decomposed at 208–209° (corr.).

Anal. Calcd. for $C_{18}H_{22}O_4N_4$: N, 15.64. Found: N, 15.71.

Isolation of Barium Salts.—The gummy barium salt obtained in a sixty-hour oxidation of 25 g. of dulcitol was heated with charcoal and hot water which dissolved all but 0.5 g. of material. The solution was filtered and concentrated at reduced pressure and 55° to a thin sirup. Alcohol was added very slowly to precipitate the barium salt and the mixture then warmed on a steam-bath for one hour. The mixture was cooled and subjected to filtration. The precipitate was washed with alcohol and with ether. It was dried in a vacuum desiccator for one hour, followed by two hours in an oven at 100°.

Anal. Calcd. for barium *dl*-galactonate: Ba, 26.03; for barium *dl*-galacturonate, 26.24. Found: Ba, 26.43, 26.40.

The barium salt obtained by an identical procedure in a seventy-two hour oxidation contained 34.93% barium; calculated for barium mucate dihydrate, 35.80%. Neither salt decomposed at 250° and both gave naphthoresorcin tests.

Summary

A convenient method for the catalytic dehydrogenation of sugar alcohols was developed. Mannitol and dulcitol were the hexitols studied. The advantage of the method lies in the ease of controlling the amount of hexitol dehydrogenated. The results obtained indicate that the method is most satisfactory for aldose isolation in the case of alcohols which yield but one aldose or a *dl*-aldose when dehydrogenated.

Platinic oxide monohydrate was used as the source of the platinum catalyst. The oxide acts first as an oxidizing agent.

The effect of change in the possible variants was studied.

The course of the reaction was determined by a combination of isolation of products and analytical procedures. Mannitol was oxidized to *d*-mannose and *d*-fructose. *d*-Mannose was oxidized, in the main, to *d*-mannonic acid, *d*-mannuronic acid, and finally to *d*-mannosaccharic acid. The *d*-fructose was oxidized, in the main, to *d*-glucosone and 2-keto-*d*-mannonic acid. Other products were also formed in small amounts. The products with dulcitol were similar in nature.

d-Mannose was conveniently prepared by the catalytic dehydrogenation of mannitol. The *d*-mannose was isolated from the reaction mixtures as the phenylhydrazone and as the α-methyl-*d*-mannoside.

dl-Galactose was prepared similarly from dulcitol.

The catalytic dehydrogenation method gives promise of being satisfactory for the preparation of sugars like *dl*-erythrose from the alcohol, erythritol.

CHICAGO, ILLINOIS RECEIVED JUNE 21, 1938

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

The Reductive Alkylation of Aniline

BY WILLIAM S. EMERSON AND PHILIP M. WALTERS

Although the reductive alkylation of amines is a well-known reaction,[1] it has found little application with primary aromatic amines. Clarke, Gillespie and Weisshaus,[1a] using formic acid as their reducing agent, methylated tribromoaniline with formaldehyde to give 77% of N,N-dimethyltribromoaniline. However, they obtained only polymers when aniline was used. While Skita and Keil[2] were able to prepare cyclohexylaniline from aniline and cyclohexanone in the presence of platinum and hydrogen, they did not mention their yield. Wallach[3] obtained di-*n*-amylaniline by heating valeraldehyde with phenylammonium formate, but he also gave no yield. The patent literature[4] contains references to the reductive alkylation of primary aromatic amines. In view of the importance of the reaction as a synthetic method, we felt that its possibilities with primary aromatic amines should be investigated.

The mechanism of the reaction is probably the following

(1) (a) Clarke, Gillespie and Weisshaus, THIS JOURNAL, **55**, 4571 (1933); (b) Skita, Keil and Havemann, *Ber.*, **66**, 1400 (1933); (c) Forsee and Pollard, THIS JOURNAL, **57**, 1788 (1935).

(2) Skita and Keil, *Ber.*, **61**, 1682 (1928).

(3) Wallach, *Ann.*, **343**, 54 (1935).

(4) German Patents 376,013, 491,856, 503,113.