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CHEMICAL REACTIONS OF THE CHLORITES WITH CARBOHYDRATES [1]

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ABSTRACT

Interest in the chemistry of the chlorites has recently been stimulated by the commercial production of sodium chlorite. Until just a few months ago the literature afforded only meager information about the general chemistry of the chlorites, and knowledge of their chemical behavior with the carbohydrates was limited to the fact that sodium chlorite bleaches the objectionable colored substances in paper and cotton textile materials without weakening the cellulose fibers. A reagent possessing the desirable properties of sodium chlorite should find extensive use in the field of carbohydrate chemistry. To provide a guide for the application of the reagent and to determine how the characteristic groups and structures occurring in the carbohydrates react with chlorites, the authors undertook a systematic investigation of the reactions of chlorites with carbohydrate material of diverse character.

This investigation has shown that at room temperature the nonreducing disaccharide, sucrose, is completely inert to chlorites under all conditions which do not involve acid hydrolysis, and that the ketoses, the polyhydroxy alcohols, and the aldonic acids are attacked only after treatment with chlorites for many days. In marked contrast to the glycosides, polyhydroxy alcohols, aldonic acids, and ketoses, the aldoses are oxidized readily and give the corresponding aldonic acids. The aldopentoses are oxidized more rapidly than the aldohexoses, and the monosaccharides more rapidly than the disaccharides. The reaction is slow in neutral solution but rapid in acid solution. Quantitative measurements under various conditions have revealed that chlorous acid is the oxidant and that the reaction corresponds in large measure to the following equation:

$$\underset{\text{(Aldose)}}{\mathrm{RCHO}}+3\mathrm{HClO_2}\longrightarrow\underset{\text{(Aldonic acid)}}{\mathrm{RCOOH}}+2\mathrm{ClO_2}+\mathrm{HCl}+\mathrm{H_2O}.$$

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[1] This paper was presented before the Division of Sugar Chemistry and Technology of the American Chemical Society at St. Louis, April 10, 1941.

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I. APPLICATION OF CHLORITES IN THE CARBOHYDRATE FIELD

Recently sodium chlorite has become commercially available and it has been advocated as a very useful bleaching agent for wood pulp and cotton textile materials [1].[3] The new reagent appears to oxidize and bleach the objectionable colored substances without materially altering or injuring the cellulose fibers. Aside from the bleaching action on cellulose very little was heretofore known concerning the reactions of chlorites with carbohydrate materials.[4]

The carbohydrates contain several characteristic groups which exhibit specific reactions with various oxidizing agents. Chlorine, bromine, hypochlorite, hypobromite, and hypoiodite react readily with aldoses to give the sugar acids or their lactones. On prolonged treatment with these reagents, the oxidation proceeds further and gives rise to lower acids, together with ketonic and dibasic acids. Oxidation of the ketonic group usually results in the cleavage of the carbon chain and the formation of lower acids. On oxidation with cupric acetate or phenylhydrazine, the sugars yield osones. Hydrogen peroxide, in the presence of iron salts, oxidizes the aldonic acids to the next lower sugars. Other reagents, such as periodic acid or lead tetraacetate, cause cleavage of the carbon chain and give dialdehydes. These examples clearly show that extensive generalization concerning the behavior of oxidizing agents with the carbohydrates cannot be made and that, in advance of this experimental study, the reactions of the new reagent could not be predicted.

In order to determine the behavior of chlorites with each of the constituent parts of a typical carbohydrate, a number of simple sugars and sugar derivatives were treated with chlorites in solutions of different acidity and the progress of the reactions was followed by determination of the optical rotation, acidity, and the amount of reducing sugar and chlorite. In these experiments, sucrose, methyl α-*d*-glucoside, mannitol, sodium gluconate, levulose, lactose, glucose, and arabinose were used to represent nonreducing disaccharides, the pyranosides, the open-chain polyhydroxy alcohols, aldonic acids, the ketoses, the reducing disaccharides, the aldohexoses, and the pentoses, respectively. These substances contain nearly all of the structural groups characteristic of the carbohydrates which might be used in conjunction with the new reagent.

Our results reveal that the glycosidic linkages in sucrose and in methyl α-*d*-glucopyranoside are not altered by chlorites, except in the presence of acid, which causes the well-known acid hydrolysis. Even after treatment for 105 days, neutral and alkaline sucrose solutions containing chlorites gave no indication of oxidation (see table 1). During the first 14 days samples of sodium gluconate and magnesium xylonate were not appreciably affected by chlorites; but on longer treatment small changes were observed. These observations clearly show the inertness of the carboxylic and the alcoholic groups of the carbohydrates to oxidation by chlorites. Levulose (table 2) was not appreciably affected by chlorites in the course of several days, but in 21 days some oxidation had occurred, as shown by a slight decrease in

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[3] Figures in brackets indicate the literature references at the end of this paper.

[4] In 1939 M. C. Taylor, in conversation with one of us (Isbell), mentioned the production of sodium chlorite by the Mathieson Alkali Works and offered to supply some of the salt for investigation in the carbohydrate field. Shortly thereafter a sample, originally donated by the Mathieson Alkali Works, Inc., was obtained through the courtesy of A. L. Pitman, of the Bureau of Agricultural Chemistry and Engineering, U. S. Department of Agriculture.

reducing power. In marked contrast to the nonreducing carbohydrates and the ketoses, the aldoses are oxidized readily (tables 3 and 4). In subsequent paragraphs it will be shown that each aldose is oxidized to the corresponding aldonic acid and that the oxidation reaction provides a means for investigating the chemistry of chlorous acid.

TABLE 1.—*Behavior of nonreducing carbohydrates with chlorites in aqueous solutions at 20° C*

Time (days)	Sodium chlorite (5 g of $NaClO_2$ in 100 ml) pH=8.7[a]		Sodium chlorite+sodium bicarbonate (5 g of $NaClO_2$+5 g of $NaHCO_3$ in 100 ml) pH=8.9[a]		Calcium chlorite (4.3 g of $Ca(ClO_2)_2$ in 100 ml) pH=7.2[a]		Sodium chlorite+sodium carbonate (4.8 g of $NaClO_2$+5.3 g of Na_2CO_3 in 100 ml) pH=10.1[a]		Calcium chlorite+calcium carbonate (4.3 g of $Ca(ClO_2)_2$ in 100 ml+$CaCO_3$) pH=7.5[a]		Sodium chlorite in acid solution[b] (5 g of $NaClO_2$+0.028 mole of H_3PO_4 in 100 ml) pH=2.2[a]	
	Optical rotation 2-dm tube (°S)	Titer[c] (ml 0.1 *N* $NaHSO_3$/ml)	Optical rotation 2-dm tube (°S)	Titer[c] (ml 0.1 *N* $NaHSO_3$/ml)	Optical rotation 2-dm tube (°S)	Titer[c] (ml 0.1 *N* $NaHSO_3$/ml)	Optical rotation 2-dm tube (°S)	Titer[c] (ml 0.1 *N* $NaHSO_3$/ml)	Optical rotation 2-dm tube (°S)	Titer[c] (ml 0.1 *N* $NaHSO_3$/ml)	Optical rotation 2-dm tube (°S)	Titer[c] (ml 0.1 *N* $NaHSO_3$/ml)
Sucrose (10 g of $C_{12}H_{22}O_{11}$ per 100 ml)												
0	+38.20	22.0	+37.80	22.0	+38.5	19.4	+36.50	21.4	+38.40	19.4	+36.40	[d] 22.2
1	+38.20	22.0	+37.80	22.0			36.70				+35.70	12.1
7	+38.20	21.9	+37.85	21.8	+38.35	19.1	+36.55	21.6	+38.70	19.1	+30.10	9.2
14	+38.17	21.9	+37.80	21.5			+36.65	21.4				
21	+38.35	21.8	+37.95	21.4	+38.30	19.6			+39.50	19.9		
49	+38.45	21.4	+37.70	21.3	+38.40	18.5			[e] +40.45	18.4		
105	[e] +39.60	18.9	+37.75	21.0								
Methyl *α-d*-glucopyranoside (10 g of $CH_3OC_6H_{11}O_5$ per 100 ml)												
0	+90.10	22.0	+90.40	22.0							+90.00	[d] 22.2
1	+90.10	22.0		22.0							+89.85	12.3
7	+90.20		+90.15	21.8							+89.75	9.2
49	+90.45	21.9	+90.15	21.3								
Mannitol (10 g of $C_6H_{14}O_6$ per 100 ml)												
0	Inactive	22.0	Inactive	22.0								
7		21.5		21.4								
14		[f] 20.5		20.8								
49		16.9		20.1								
Sodium gluconate (12 g of $NaC_6H_{11}O_7$ per 100 ml)												
0	+8.00	22.0										
14	[f] +8.00	21.5										
21	+7.63	20.6										
49	+7.10	19.2										
Magnesium xylonate (11.4 g of $Mg(C_5H_9O_6)_2.5H_2O$ per 100 ml)												
0	+8.80	22.0										
14	+8.80	21.8										
21	+8.60	21.7										

[a] The pH values were measured at the beginning of the experiment.

[b] The samples were kept in sealed glass tubes.

[c] The values under this heading were obtained by titrating with $NaHSO_3$ solution the iodine liberated by treatment of the solution with potassium iodide and acetic acid, and they correspond to the sum of the chlorite, chlorous acid, and chlorine dioxide which remain in solution. Under the experimental conditions employed part of the chlorine dioxide escaped during the manipulations.

[d] The initial drop in the "titer" was caused by the loss of chlorine dioxide gas during the preparation of the samples. The "titer" at zero time was calculated from the amount of sodium chloride originally added. A control experiment run in the absence of any carbohydrate, using sodium chlorite, phosphoric acid and water in the proper proportions, gave the following results:

Time in days	0	1	3	5	7
"Titer" ml 0.1 *N* $NaHSO_3$/ml	(22.1)	12.2	10.9	10.6	9.6

[e] The slight rise in optical rotation was caused by slight evaporation of the solution over the long period of time.

[f] At this time the solution turned slightly yellow, which is evidence of the formation of ClO_2.

TABLE 2.—*Behavior of levulose with chlorites in aqueous solution at 20° C*

Time (days)	Sodium chlorite (5 g of $NaClO_2$ in 100 ml). pH=8.7 [a]			Sodium chlorite+sodium bicarbonate 5 g of $NaClO_2$+5 g of $NaHCO_3$ in 100 ml). pH=8.9 [a]			Calcium chlorite (4.3 g of $Ca(ClO_2)_2$ in 100 ml). pH=7.2 [a]			Calcium chlorite+calcium carbonate (4.3 g of $Ca(ClO_2)_2$+$CaCO_3$). pH=7.5 [a]			Sodium chlorite in acid solution [b] (5 g of $NaClO_2$+0.028 mole H_3PO_4 in 100 ml). pH=2.2 [a]		
	Optical rotation 2-dm tube (°S)	Reducing sugar (mg/ml)	Titer [c] (ml 0.1 *N* $NaHSO_3$/ml)	Optical rotation 2-dm tube (°S)	Reducing sugar (mg/ml)	Titer [c] (ml 0.1 *N* $NaHSO_3$/ml)	Optical rotation 2-dm tube (°S)	Reducing sugar (mg/ml)	Titer [c] (ml 0.1 *N* $NaHSO_3$/ml)	Optical rotation 2-dm tube (°S)	Reducing sugar (mg/ml)	Titer [c] (ml 0.1 *N* $NaHSO_3$/ml)	Optical rotation 2-dm tube (°S)	Reducing sugar (mg/ml)	Titer [c] (ml 0.1 *N* NaHSO/ml)
0	−54. 51	101. 7	22. 1	−54. 60	100. 0	21. 8	−55. 40	103. 3	19. 4	−55. 25	103. 3	19. 4	−53. 95	98. 0	[d] 22. 2
1	−54. 20	101. 7	21. 7	−54. 50	--------	21. 1	−55. 45	--------	19. 4	−55. 15	--------	19. 4	−54. 05	97. 6	11. 7
3	−54. 05	99. 6	21. 2	−54. 55	99. 6	20. 0	--------	102. 2	--------	--------	--------	--------	−53. 85	96. 0	10. 8
7	−53. 60	98. 5	20. 6	−53. 60	99. 1	18. 5	−55. 20	102. 2	19. 0	−55. 30	102. 2	19. 0	−53. 45	96. 0	9. 1
14	−53. 50	101. 2	20. 9	−52. 35	98. 0	17. 6	−54. 45	102. 2	19. 1	−54. 60	102. 2	19. 2	--------	--------	--------
21	−53. 30	100. 0	20. 5	−51. 10	95. 8	16. 0	−53. 95	99. 0	18. 4	−54. 20	99. 0	18. 9	--------	--------	--------

[a b c d] See corresponding footnotes, table 1.

TABLE 3.—*Reactions of aldoses with chlorites in aqueous solutions at 20° C*

Time (days)	Sodium chlorite (5 g of $NaClO_2$ in 100 ml) pH=8.7 [a]			Sodium chlorite+sodium bicarbonate [b] (5 g of $NaClO_2$+5 g of $NaHCO_3$ in 100 ml) pH=8.9 [a]			Calcium chlorite (4.3 g of $Ca(ClO_2)_2$ in 100 ml) pH=7.2 [a]			Calcium chlorite+calcium carbonate (4.3 g of $Ca(ClO_2)_2$+$CaCO_3$ in 100 ml) pH=7.5 [a]			Sodium chlorite in acid solution [b] (5 g of $NaClO_2$+0.028 mole H_3PO_4 in 100 ml) pH=2.2 [a]		
	Optical rotation 2-dm tube (°S)	Reducing sugar (mg/ml)	Titer [c] (ml 0.1 *N* $NaHSO_3$/ml)	Optical rotation 2-dm tube (°S)	Reducing sugar (mg/ml)	Titer [c] (ml 0.1 *N* $NaHSO_3$/ml)	Optical rotation 2-dm tube (°S)	Reducing sugar (mg/ml)	Titer [c] (ml 0.1 *N* $NaHSO_3$/ml)	Optical rotation 2-dm tube(°S)	Reducing sugar (mg/ml)	Titer [c] (ml 0.1 N $NaHSO_3$/ml)	Optical rotation 2-dm tube (°S)	Reducing sugar (mg/ml)	Titer [c] (ml 0.1 *N* $NaHSO_3$/ml)
d-Glucose (10 g of $C_6H_{12}O_6$ in 100 ml)															
0	+30. 36	99. 2	22. 1	+30. 02	99. 8	22. 0	+30. 50	104. 2	19. 6	+30. 50	100. 8	19. 6	+30. 50	99. 4	[d] 22. 2
1	+30. 15	101. 5	22. 0	+29. 70	--------	21. 7	+30. 65	--------	--------	+30. 10	--------	19. 1	+21. 90	70. 3	14. 0
2	+29. 90	--------	21. 6	--------	100. 0	--------	*+28. 90	97. 5	18. 0	*+29. 05	98. 0	18. 3	+21. 05	69. 9	12. 9
4	*+28. 43	98. 4	20. 3	+29. 20	--------	21. 0	+25. 45	87. 6	13. 7	+25. 95	91. 7	14. 9	+20. 05	69. 0	10. 2
7	+22. 95	76. 6	9. 7	+29. 00	100. 0	20. 5	+21. 55	74. 6	8. 0	+22. 10	76. 3	8. 7	+19. 45	67. 6	8. 4
14	+18. 25	68. 1	2. 7	+28. 35	97. 0	20. 6	+18. 98	71. 5	5. 3	+16. 80	66. 0	2. 9	--------	--------	--------
21	+17. 45	67. 6	0. 9	+27. 90	97. 0	20. 3	+18. 00	69. 5	3. 7	+14. 73	61. 8	0. 9	--------	--------	--------

l-Arabinose (8.3 g of $C_5H_{10}O_5$ in 100 ml)

0	**+50.00	83.2	21.8	+50.00	83.2	21.8	**+50.00	83.2	19.3	**+50.00	83.2	19.3	+50.00	83.2	[d] 22.2
1	+29.35	51.1	10.9	*+38.43	65.3	14.5	+33.00	57.5	10.6	+33.15	57.8	10.1	+29.50	51.4	12.6
2	+26.20	46.9	8.1	+28.45	48.0	6.6	+28.70	51.1	8.3	+28.25	50.0	6.5	---	---	---
3	+25.55	46.4	6.1	+24.60	41.4	3.4	+28.25	50.5	5.8	+26.70	47.6	5.0	+26.00	50.3	8.1
5	+24.50	44.7	3.8	+22.15	37.0	1.2	+27.45	48.8	4.1	+24.75	45.0	3.8	+21.35	46.3	6.4
7	+23.85	44.0	1.7	+21.40	34.4	0.5	+26.90	48.2	1.8	+23.50	42.3	2.8	+18.90	45.5	4.8

d-Xylose (8.3 g of $C_5H_{10}O_5$ in 100 ml)

0	+9.39	83.2	21.9	+9.45	82.6	22.0	+9.68	84.2	19.3	+9.68	84.2	19.3	+9.40	83.2	[d] 22.2
1	*+9.05	72.1	17.8	*+9.25	74.7	18.4	*+8.70	61.9	11.9	*+8.90	59.7	10.1	+6.35	53.0	12.9
2	+9.55	50.1	10.2	+9.32	56.1	9.9	+8.50	53.4	7.9	+8.63	52.9	6.3	---	---	---
3	+9.10	48.8	8.0	---	---	4.6	---	---	---	---	---	---	+6.45	52.0	9.5
4	+8.65	48.1	6.2	+9.10	43.8	4.6	+7.80	52.6	7.0	+8.0	50.3	4.5	+6.90	50.0	8.2
7	+8.05	47.2	2.6	+9.00	37.4	1.6	+7.18	50.0	5.4	+7.25	46.0	3.3	+8.35	48.7	5.6
14	+7.75	46.7	0.5	+8.80	34.4	0.7	+6.75	49.0	2.7	+6.25	42.2	1.2	---	---	---

Lactose (10 g of $C_{12}H_{22}O_{11}$ in 100 ml)

0	+32.10	98.0	22.1	+32.38	100.0	22.1	---	100.0	19.5	---	100.0	19.5	---	---	---
1	+31.90	99.7	22.0	+32.05	99.1	21.7	+32.60	---	---	+32.45	---	19.4	---	---	---
3	+31.80	99.9	21.6	+31.30	96.5	21.0	*+31.40	95.0	18.3	*+31.70	96.0	19.0	---	---	---
7	*+29.85	92.5	20.0	+30.30	94.0	20.1	+29.25	82.9	15.8	+29.95	87.4	17.0	---	---	---
14	+24.75	62.2	12.0	+29.15	90.3	20.0	+25.65	61.4	9.1	+26.40	64.0	10.8	---	---	---
21	+21.15	46.8	4.3	+28.90	89.3	19.9	+23.85	51.4	4.7	+24.25	53.2	6.0	---	---	---

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[a],[b],[c],[d],* See corresponding footnotes, table 1.

** Color appeared in the solution after 1 hour.

TABLE 4.—*Oxidation of glucose at 20° C by chlorous acid in solutions of different acidities*

Saturated benzoic acid			0.56 *M* acetic acid			0.19 *M* phosphoric acid			0.56 *M* phosphoric acid		
0.056 mole *d*-glucose +0.056 mole sodium chlorite in 100 ml solution saturated with benzoic acid at 20° C.			0.056 mole *d*-glucose +0.056 mole sodium chlorite +0.056 mole acetic acid in 100 ml solution at 20° C.			0.056 mole *d*-glucose +0.056 mole sodium chlorite +0.019 mole phosphoric acid in 100 ml solution at 20° C.			0.056 mole *d*-glucose +0.056 mole sodium chlorite +0.056 mole phosphoric acid in 100 ml solution at 20° C.		
Time (min)	Optical rotation 2-dm tube (° S)	pH	Time (min)	Optical rotation 2-dm tube (° S)	pH	Time (min)	Optical rotation 2-dm tube (° S)	pH	Time (min)	Optical rotation 2-dm tube (° S)	pH
6.2	+29.35	4.2	5.3	+28.30	3.7	6.1	+25.74	3.2	5.9	+20.80	2.1
28.0	+27.89	4.6	15.3	+25.84	4.1	22.8	+25.00	4.0	15.0	+21.34	2.1
64.0	+26.87	4.7	30.3	+24.64	4.3	30.1	+24.68	4.1	24.8	+21.87	2.2
122.4	+25.78	4.8	133.0	+22.98	4.3	129.3	+24.50	4.8	178.4	+22.96	2.2
1,275.0	+21.97	4.9	1,394.0	+21.43	4.2	1,440.0	+21.78	3.8	1,414.0	+22.86	2.0
Sugar oxidized, 31.5 percent [a]			Sugar oxidized, 29.9 percent [a]			Sugar oxidized, 28.3 percent [a]			Sugar oxidized, 27.2 percent [a]		

[a] The percentage of oxidation was calculated from the reducing-sugar content at the time of the last sample.

II. OXIDATION OF ALDOSES WITH CHLORITES IN NEUTRAL AND ACID SOLUTION

The present investigation has revealed that under suitable conditions the aldoses are oxidized to aldonic acids by chlorites and that during the course of the reaction chloride, chlorine dioxide, and chlorate are produced. Inasmuch as the oxidation is slow in neutral and in alkaline solutions as compared with the oxidation in acid solutions, it appears that chlorous acid, or some substance derived therefrom, is the oxidant. Since chlorous acid decomposes spontaneously into chloride, chlorine dioxide, and chlorate, [2] these substances must be considered as possible oxidants in the aldose reaction. Previously Schmidt and Graumann [3] reported that several simple carbohydrates, including glucose, arabinose, levulose, and sucrose, were inactive in respect to aqueous chlorine dioxide. We have found (table 5) that the aldoses are oxidized slowly by chlorine dioxide and that in the absence of a buffer, sucrose is hydrolyzed. Nevertheless, the oxidation of aldoses by chlorine dioxide is very slow, and consequently, chlorine dioxide cannot be responsible for the rapid oxidation observed in solutions containing chlorous acid.

Other measurements (table 6) have shown that the aldoses are not oxidized by chloric acid or by chlorates and that neither of these substances can be the oxidant. Thus none of the products that are ordinarily formed during the decomposition of chlorous acid are particularly reactive, and it seems probable that the oxidation of the aldoses is effected by chlorous acid.

TABLE 5.—*Carbohydrates treated with chlorine dioxide in aqueous solution* [a] *at 20° C*

Time (days)	*l*-Arabinose (8.3 g of $C_5H_{10}O_5$ in 100 ml)			*d*-Glucose (10 g of $C_6H_{12}O_6$ in 100 ml)			Levulose (10 g of $C_6H_{12}O_6$ in 100 ml)			Sucrose (10 g of $C_{12}H_{22}O_{11}$ in 100 ml)	
	Optical rotation 2-dm tube (°S)	Reducing sugar (mg/ml)	Titer (ml 0.1 *N* $NaHSO_3$/ml)	Optical rotation 2-dm tube (°S)	Reducing sugar (mg/ml)	Titer (ml 0.1 *N* $NaHSO_3$/ml)	Optical rotation 2-dm tube (°S)	Reducing sugar (mg/ml)	Titer (ml 0.1 *N* $NaHSO_3$/ml)	Optical rotation 2-dm tube (°S)	Titer (ml 0.1 *N* $NaHSO_3$/ml)
0	+49.35	83.6	------	+30.93	100.8	------	−53.55	100.2	------	[b]+38.40	------
2	+47.50	80.8	14.2	+30.45	100.3	15.5	−53.20	100.2	13.7	+33.28	15.2
4	+46.00	79.1	10.1	+29.40	96.1	13.5	−51.42	99.0	14.3	+21.40	15.5
7	+43.00	76.3	8.8	+28.70	92.9	8.7	−52.10	99.0	12.1	+3.90	13.9

[a] The solutions contained approximately 3.3 g of ClO_2 per 100 ml and were kept in sealed glass tubes in the dark.

[b] The marked change in optical rotation is the result of inversion caused by acid formed from the chlorine dioxide.

TABLE 6.—*Carbohydrates treated with chlorates in neutral and in acid solutions* [a]

Time (days)	*d*-Glucose (10 g in 100 ml)			Levulose (10 g in 100 ml)			Sucrose (10 g in 100 ml)			*l*-Arabinose (8.3 g in 100 ml)	
	0.15 *M* $KClO_3$	0.15 *M* $KClO_3$, 0.56 *M* with acetic acid	0.15 *M* $KClO_3$, 0.56 *M* with phosphoric acid	0.15 *M* $KClO_3$	0.15 *M* $KClO_3$, 0.56 *M* with acetic acid	0.15 *M* $KClO_3$, 0.56 *M* with phosphoric acid	0.15 *M* $KClO_3$ —	0.15 *M* $KClO_3$, 0.56 *M* with acetic acid	0.15 *M* $KClO_3$, 0.56 *M* with phosphoric acid	0.15 *M* $KClO_3$	0.15 *M* $KClO_3$ 0.56 *M* with acetic acid
	°*S*	°*S*	°*S*	°*S*	°*S*	°*S*	°*S*	°*S*	°*S*	°*S*	°*S*
0	------	------	+30.50	------	------	------	+38.40	+38.30	+38.15	+49.50	+49.50
1	+30.50	+30.65	------	−54.35	−54.35	−55.00	------	------	------	------	------
7	+30.45	+30.65	+30.45	−54.36	−54.10	−54.80	+38.40	+29.50	−12.55	+49.15	+49.25
14	+30.40	+30.60	+30.45	−54.50	−54.35	−54.65	+38.50	+21.75	[b]−13.20	+49.40	+49.25

[a] Optical rotations in °*S*, read in a 2-dm tube, at 20° C.

[b] The optical rotation of a similar solution containing 10 g of completely hydrolyzed sucrose is calculated to be approximately −12.2°.

Investigation of the quantitative aspects of the reactions of the chlorites with the carbohydrates has been greatly complicated by the instability of chlorous acid. When one equivalent of a mineral acid is added to a cold aqueous solution containing sodium chlorite, the solution develops a yellow color which soon turns to reddish brown; on further standing, a yellow gas, presumably chlorine dioxide, is evolved and the solution becomes light yellow. Very little is known concerning the intermediate compounds necessary to explain these color changes. When an aqueous solution containing a chlorite and an aldose is acidified, the color changes previously noted for the chlorite alone are observed in somewhat more rapid sequence. An examination of the reaction in detail reveals that the oxidation of the aldose proceeds rapidly at first and then more slowly. After the initial rapid reaction the dark color, probably due to chlorous acid, disappears and the oxidation of the sugar virtually ceases, even though the solution contains both chlorine dioxide and chloric acid. The rapid initial oxidation reaction proceeds more rapidly in strongly acid solution than in less acid solution. Thus, as shown by the results given in table 4, when glucose is treated with sodium chlorite and phosphoric acid at pH 2.1, the reaction is substantially complete in 6 minutes, but at pH 4.2 the oxidation reaction continues over a period of several hours. Although the rate of reaction increases markedly with increasing acidity, the amount of oxidation produced by a given quantity of chlorite decreases slightly with increasing acidity. The smaller quantity of sugar oxidized in the more strongly acid solutions suggests that part of the chlorous acid undergoes a competitive side reaction and that the distribution of the chlorous acid between the competitive reaction and the carbohydrate reaction is influenced by the acidity. The existence of a competitive side reaction is in accord with the well-known decomposition of chlorous acid in acid solution.

According to the work of Taylor, White, Vincent, and Cunningham [1], the reaction of sodium chlorite with acetic acid at pH 2.5 produces chlorine dioxide and chloric and hydrochloric acids. When the solution is aerated to remove the chlorine dioxide as it is formed, the final products may be represented approximately by reaction I; but as suggested by Taylor, White, Vincent, and Cunningham, the chlorine dioxide and the chloric acid might be formed by separate reactions. Under suitable conditions chloric acid may be produced from chlorous acid by reaction II, or from chlorine dioxide by reaction III. In the presence of reducing agents, such as the aldoses, chlorous acid might be completely reduced to chloride (reaction IV), or it might be partially reduced and partially oxidized to give chloride and chlorine dioxide (reaction V). Since reactions I to V may take place simultaneously, interpretation of the oxidation process is a highly complicated problem.

$$4HClO_2 \longrightarrow HClO_3 + HCl + 2ClO_2 + H_2O \qquad \text{(I)}$$

$$3HClO_2 \longrightarrow HCl + 2HClO_3 \qquad \text{(II)}$$

$$2ClO_2 + H_2O \longrightarrow HClO_2 + HClO_3 \qquad \text{(III)}$$

$$\underset{\text{(Aldose)}}{2RCHO} + HClO_2 \longrightarrow \underset{\text{(Aldonic acid)}}{2RCOOH} + HCl \qquad \text{(IV)}$$

$$\underset{\text{(Aldose)}}{RCHO} + 3HClO_2 \longrightarrow \underset{\text{(Aldonic acid)}}{RCOOH} + HCl + 2ClO_2 + H_2O \qquad \text{(V)}$$

A better understanding of the course of the oxidation reaction can be derived from consideration of the quantitative relationships between the amounts of sugar oxidized and the reaction products. A summary of the results obtained by the treatment of glucose (1) with 3 moles of chlorous acid at 0° C, (2) with 1 mole of chlorous acid at 20° C, and (3) with one-half mole of calcium chlorite in a solution buffered with calcium carbonate, is given in table 7. In each case the reaction products correspond roughly to those required by the reaction of equation V. In the first experiment 1 mole of glucose consumed 3.83 moles of chlorous acid and gave in addition to gluconic acid, 1.35 moles of chloride, 0.47 mole of chlorate, and 2.01 moles of chlorine dioxide. According to reaction IV 1 mole of glucose would produce only 0.5 mole of chloride, while reaction V would result in the formation of 1 mole of chloride. Since more than 1 mole of chloride was isolated, it appears that reaction IV can be regarded as of little importance under the conditions of this experiment.

TABLE 7.—*Quantitative study of the products formed by the oxidation of glucose with chlorites in acid and in neutral solutions*

Constituents	I 0.0555 mole of glucose+0.1516 mole of $NaClO_2$+0.168 mole of acetic acid in 100 ml at 0° C for 24 hours	II 0.0555 mole of glucose+0.0531 mole of $NaClO_2$+0.056 mole of acetic acid in 100 ml at 20° C for 24 hours	III 0.0555 mole of glucose+0.0248 mole of $Ca(ClO_2)_2$ in 100 ml+$CaCO_3$ at 20° C for 7 days
	Moles	*Moles*	*Moles*
Chlorous acid consumed per mole of glucose oxidized	3.83	3.19	2.59
Chloride formed per mole of glucose oxidized	1.35	1.24	1.24
Chlorate formed per mole of glucose oxidized	.47	.14	.51
Chlorine dioxide lost per mole of glucose oxidized	2.01	1.82	.85
Oxalic acid formed per mole of glucose oxidized	none	none	.01

The utilization of more than 3 moles of chlorous acid per mole of glucose shows that the oxidation proceeds beyond the gluconic acid stage, or else that part of the chlorous acid was decomposed either by reaction I or by reaction II. The production of only 2 moles of chlorine dioxide per mole of sugar indicates that the excess of chlorous acid probably did not undergo reaction I, while the excess of chloride and chlorate found suggests that part of the chlorous acid was converted to chlorate and chloride by reaction II. It appears that in highly acid solutions the oxidation of glucose follows reaction V with small deviations, which may be explained by competitive reaction II. Chlorites in aqueous solution in the absence of reducing agents are stable for long periods of time. Hence the conversion of chlorous acid to chloric acid by reaction II does not take place readily in neutral solution, and under such conditions one might anticipate that very little of the chlorous acid would undergo decomposition. As a matter of fact, when the oxidation was conducted in neutral solution (experiment III) 1 mole of glucose reduced 2.59 moles of chlorite and gave in addition to gluconic acid, 1.24 moles of chloride, 0.51 mole of chlorate, 0.85 mole of chlorine dioxide, and 0.01 mole of oxalate. The quantity of chlorine dioxide separated in this experiment is much less than that required by reaction V. This discrepancy finds explanation in the chemistry of chlorine dioxide. Other experiments have shown that chlorine dioxide in aqueous solution in the presence of calcium carbonate is slowly decomposed according to reaction III. By this reaction 1 mole of chlorous acid and 1 mole of chlorate are formed from 2 moles of chlorine dioxide. Hence, if we assume that the chlorate found in the experiment under discussion is a measure of the amount of chlorine dioxide which had been hydrolyzed, we may calculate that the 0.51 mole of chlorate (determined by analysis) was derived from 1.02 moles of chlorine dioxide. By adding this quantity to that found experimentally, we may calculate that 1.87 moles of chlorine dioxide were produced. This compares favorably with the 2 moles required by reaction V. Furthermore, the hydrolysis of the chlorine dioxide would have produced 0.51 mole of chlorous acid, which would have been used in oxidation and would make the total chlorous acid used 3.10 moles in comparison with 3 moles required by reaction V. Thus the results in neutral solution may be explained by reaction V in conjunction with reaction III. The presence of a small quantity of oxalic acid among the oxidation products shows that part of the sugar is oxidized beyond the aldonic acid stage, and this may account for the production of slightly more than 1 mole of chloride. Similar studies with *l*-arabinose and lactose revealed that in each case calcium aldonate, calcium oxalate, chloride, chlorine dioxide, and chlorate are produced. By comparison of the results obtained in neutral solution with those obtained in acid solutions, it will be noted that the reactions differ mainly in the reaction rates and in the relative importance of the side reactions II and III. In highly acid solutions reaction II is important, while in neutral and in slightly alkaline solutions reaction III is important.

The oxidation of aldoses with chlorites, even in neutral solution, appears to depend in large measure on the presence of chlorous acid. When an aldose is treated with a chlorite in neutral or slightly alkaline solution, considerable time elapses before a relatively rapid reaction begins. Ordinarily the oxidation does not become pronounced until after the lapse of several days, at which time the formation of chlorine dioxide is shown by the evolution of a yellow gas. The length of the induction period varies erratically with different sugars and with different samples of sodium chlorite. The end of the induction period is marked by the appearance of the yellow color caused by chlorine dioxide, and is accompanied by a significant increase in acidity. These observations confirm our conclusion that the oxidizing agent is chlorous acid. Presumably during the induction period the rate of reaction is slowly accelerated by the formation of chlorous acid, which oxidizes the carbohydrate and forms acids which in turn liberate additional chlorous acid and thus further increase the rate of oxidation.

Reference to table 3 shows that oxidations utilizing calcium chlorite exhibit a shorter induction period than those using sodium chlorite, either alone or in conjunction with sodium bicarbonate. Inasmuch as a freshly prepared aqueous solution of calcium chlorite is pale yellow and has the odor of chlorine dioxide. it must contain some free chlorous acid. In the concentrations employed in this investigation, solutions containing calcium chlorite have an initial pH of about 7.5. In table 8 it is shown that the rate of oxidation increases very rapidly as the pH of the solution falls below 8.

TABLE 8.—*Oxidation of pentoses with sodium chlorite in the presence of sodium bicarbonate*

Time (days)	*d*-Xylose				*l*-Arabinose			
	8.3 g of *d*-xylose+4.83 g of sodium chlorite+50 ml of sodium bicarbonate solution (saturated at 20°C) per 100 ml of solution				8.3 g of *l*-arabinose+4.83 g of sodium chlorite+50 ml of sodium bicarbonate solution (saturated at 20°C) per 100 ml of solution			
	Optical rotation 2-dm tube (°S)	Reducing sugar (mg/ml)	Sodium chlorite [a] (mg/ml)	pH	Optical rotation 2-dm tube (°S)	Reducing sugar (mg/ml)	Sodium chlorite [a] (mg/ml)	pH
0	+9.30	83.3	48.3	8.9	+49.85	83.3	48.3	8.9
3	+9.20	79.2	45.0	8.7	+46.95	78.0	44.4	8.7
7	+9.15	73.5	41.7	8.5	*+29.10	47.7	17.6	7.0
9	*+8.95	59.4	29.2	7.1	+21.70	33.0	5.1	7.1
11	+8.75	40.1	11.1	7.1	+20.30	32.6	3.1	7.6

[a] Any chlorine dioxide in the sample was removed by aeration with nitrogen, and the chlorite was determined by titration of the iodine liberated from potassium iodide in acetic acid solution.

* Indicates first appearance of yellow color in the solution.

It is of further interest to note the changes in acidity which accompany and follow the treatment of carbohydrates with chlorous acid. Samples of various sugars were permitted to react with sodium chlorite and phosphoric acid in sealed tubes, and at intervals the tubes were opened and the acidity was measured with a glass electrode. It will be observed from the data given in table 9 that in the absence of any carbohydrate or in the presence of sucrose or methyl α-*d*-glucoside, the acidity decreases from about pH 2.2 to about pH 2.8 and then increases to about pH 2.3. The initial decrease in acidity is caused by the formation of chlorine dioxide (reaction I), and the subsequent increase in acidity is caused by the slow hydrolysis of the chlorine dioxide with the formation of hydrochloric and chloric acids (reaction III). Presumably, in a closed system an equilibrium would be established between the chlorine dioxide, and the hydrochloric, chloric, and chlorous acids. In the experiments in which glucose, arabinose, and xylose were oxidized by chlorous acid, the acidity decreased rapidly to a minimum and then increased slowly. The initial decrease in acidity parallels the formation of chlorine dioxide and the rapid oxidation of the sugar, according to reaction V. The subsequent increase in acidity is presumably caused by the slow hydrolysis of the chlorine dioxide (reaction III). In this connection, it will be recalled that these experiments were conducted in closed tubes to prevent the loss of chlorine dioxide. After standing for 7 days, the acidity of the solutions containing oxidizable sugars was greater than the acidity of the solutions not containing easily oxidizable carbohydrates. The higher acidity found in the solutions containing oxidizable sugars arose from the formation of a larger quantity of hydrochloric acid and from the presence of aldonic acids formed in the course of the reaction. These remarks suffice to explain the observations, but it might be mentioned that part of the change in acidity may have arisen from the formation of sugar acid lactones and their subsequent hydrolysis.

TABLE 9.—*Changes in the acidity of carbohydrate solutions containing aqueous chlorous acid* [a]

Time (days)	Control (no sugar)	*d*-Glucose (10 g in 100 ml)	Levulose (10 g in 100 ml)	*l*-Arabinose (8.3 g in 100 ml)	*d*-Xylose (8.3 g in 100 ml)	Sucrose (10 g in 100 ml)	Methyl α-*d*-glucoside (10 g in 100 ml)
	pH	pH	pH	pH	pH	pH	pH
0	2.2	[b]	2.1	[b]	[b]	2.2	2.2
0.007		2.7		3.4	3.3		
0.021		3.4					
0.125	2.6	3.4		3.3		2.9	2.7
1	2.8						
3	2.7		2.6	2.0	2.2	2.7	2.7
5	2.6	2.1	2.3	1.8	1.8	2.4	2.4
7	2.4	2.0	2.2	1.7	1.6	2.2	2.3

[a] The chlorous acid was prepared from equal volumes of 1 *M* sodium chlorite and 0.5 *M* phosphoric acid. The samples were kept at 20° C in sealed glass tubes.

[b] This substance gave a rapid, exothermic reaction. The acidity at the beginning is presumably the same (pH 2.2) as that of the control experiment conducted in the absence of carbohydrate.

At the beginning of this investigation, it was thought likely that the ring modifications of the aldoses might be oxidized directly to lactones in a manner analogous to that previously observed in the oxidation of the aldoses with bromine water [4, 5]. Unfortunately, the oxidation with chlorous acid in neutral solution is so slow that equilibrium between the delta lactones and the acids is established as the reaction proceeds, and although the oxidation in strongly acid solution is fairly rapid, the delta lactone under these conditions is also split rapidly. Thus, our measurements (changes in pH and in optical rotation) do not give information concerning the character of the oxidation product.

Inasmuch as the reducing sugars in solution contain a number of isomeric modifications in dynamic equilibrium, it is of interest to ascertain, if possible, the relative rates of reaction for the separate modifications. Preliminary information on this subject was obtained by the oxidation of alpha and beta glucose under such conditions that the interconversion of the alpha and beta isomers is slow in comparison with the oxidation reaction. The sugar was mixed with a solution containing sodium chlorite and acetic acid at 0° C, and the oxidation was followed by optical rotation measurements made on samples of the solution taken from time to time. The oxidation reaction in the samples was stopped by the addition of sodium bisulfite, and the optical rotation of the sample was read after equilibrium was established. The results so obtained are recorded in figure 1.

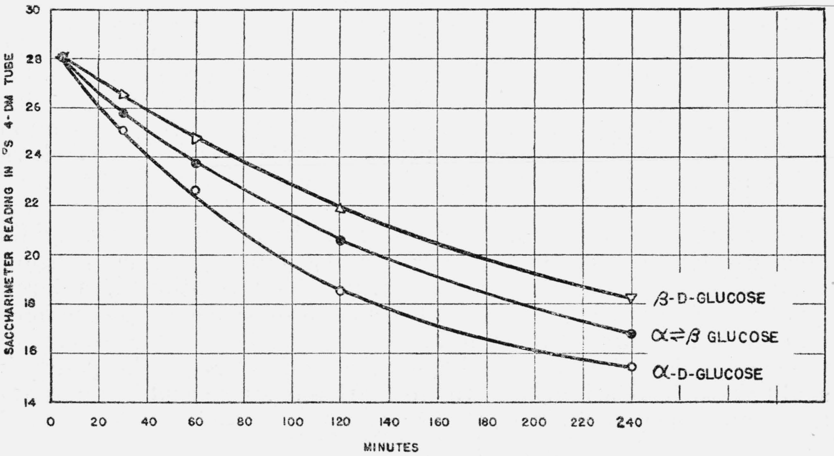

FIGURE 1.— *The oxidation of the alpha and beta modifications of d-glucose by chlorous acid at 0° C.*

The reaction solutions were prepared at 0° C from 0.056 mole of the sugar, 0.167 mole of sodium chlorite, and 0.167 mole of acetic acid in sufficient water to give 100 ml at 0° C. At intervals 12-ml samples were removed and added to equal volumes of 3*M* sodium bisulfite solution at 0° C. The temperature was allowed to rise to 20° C, and after 24 hours the optical rotation of the sample was read in a 4-dm tube.

A comparison of the curves given in figure 1 shows that *α-d*-glucose is oxidized by chlorous acid slightly more rapidly than *β-d*-glucose. The relationship is the opposite of that found by one of us for the oxidation of the *α*- and *β*-aldoses with bromine water [5, 6], in which case it will be recalled that *β-d*-glucose is oxidized approximately 50 times as fast as *α-d*-glucose. As might be expected, the curve obtained for the data representing the oxidation of glucose in the equilibrium solution lies between the curves representing the oxidation of the alpha and beta isomers. A difference in the rates of oxidation for the alpha and beta isomers also explains the small rise in optical rotation observed during the oxidation of xylose (see table 3).

III. EXPERIMENTAL DETAILS

1. REACTIONS OF CARBOHYDRATES WITH CHLORITE SOLUTIONS

In order to obtain information as to which carbohydrate groups are reactive and as to the conditions which are suitable for a more detailed investigation, certain typical sugars and sugar derivatives were treated with chlorites under a variety of conditions and the reactions were followed by determinations of optical rotation and of reducing power, and by titration of the oxidizing agent. The results of these measurements are reported in tables 1, 2, and 3. In the reactions utilizing sodium chlorite, calcium chlorite, and calcium chlorite with calcium carbonate, the sugar or its derivative was dissolved in water and allowed to come to equilibrium, after which 50 ml of the chlorite solution was added and the volume made to 100 ml. The sodium chlorite solution was approximately 1.1 *M*, while the calcium chlorite was about 0.5 *M*. In the reactions in which sodium chlorite was used in conjunction with sodium bicarbonate, the sugar or sugar derivative was dissolved in 25 ml of sodium bicarbonate solution (saturated at 20° C) and allowed to come to equilibrium. Then 50 ml of 1.1 *M* sodium chlorite solution was added and the solution was made to 100 ml by the addition of saturated sodium bicarbonate solution. In the reactions using calcium chlorite in the presence of calcium carbonate, 100 ml of the sugar-calcium chlorite solution was poured into a bottle containing 10 g of precipitated calcium carbonate, which was kept in suspension by frequent shaking. On account of the large amount of gas liberated, the oxidations with chlorous acid were conducted in a slightly different manner and will be described in a subsequent paragraph. The solutions containing the reacting mixtures were kept in a room maintained at 20° C, from which sunlight was excluded. From time to time samples were taken and analyzed in the following manner:

Ten milliliters of the solution undergoing oxidation was transferred to a 2-dm polariscope tube and the optical rotation was read. Then 5 ml of the solution was removed from the polariscope tube and diluted to 25 ml. The solution remaining in the tube was used for the measurement of pH with a conventional pH meter, using a glass electrode. A 10-ml sample of the diluted solution was then slowly added to a solution prepared from 15 ml of 10-percent potassium iodide and 15 ml of 30-percent acetic acid. The iodine liberated was titrated in a 100-ml sugar flask with a 0.2 *N* sodium bisulfite solution [5] standardized at frequent intervals with potassium dichromate solution. The titration is a measure of the quantity of chlorite and chlorine dioxide in the solution [7]. The solution from the sodium bisulfite titration was cooled in ice water and neutralized to phenolphthalein with 30-percent sodium hydroxide solution, and ultimately made up to 100 ml at 20° C. From this neutral solution, samples of 5 or 10 ml were taken for the determination of reducing-sugar values by means of the modified Scales procedure and the factors determined by Isbell, Pigman, and Frush [8].

The measurements utilizing chlorous acid were conducted in sealed tubes using essentially the same proportions of sugar and oxidant as

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[5] Sodium thiosulfate could not be employed for this titration because the tetrathionate formed from sodium thiosulfate interferes in the subsequent determination of reducing sugar.

were employed in the measurements using chlorites. The sugar or sugar derivative and phosphoric acid were placed in the tube, prepared for sealing. After the tube and contents were cooled in ice water, the required quantity (10 ml) of 1 *M* sodium chlorite solution was added and the tube was sealed at once. The tubes were kept for about 15 minutes in cold water and were then placed in a dark room at 20° C and allowed to stand until opened for analysis. A number of tubes were made up for each reaction mixture, and at stated intervals the tubes were opened and the contents were analyzed. Immediately after opening a tube, 5 ml of the solution was removed and diluted to 25 ml for the determination of the oxidant and the reducing sugar by the procedure described in the preceding paragraph. The solution remaining in the tube was used for the determination of optical rotation and pH. Some of the reactions were very rapid, and it was necessary to estimate the constants at zero time by indirect methods. The initial pH values of the highly reactive sugars were postulated to be the same as those given by sucrose under like conditions; the values for the initial optical rotations and the reducing sugars were determined by measurements on samples of the sugar containing phosphoric acid diluted with water, instead of with the sodium chlorite solution. The initial bisulfite titration was estimated by titration of a solution containing sodium chlorite and water diluted as described for the samples containing the sugars.

In the experiments reported in tables 1 to 4 approximately 0.056 mole of the carbohydrate was treated with 0.056 mole of chlorite in 100 ml. This proportion of chlorite is only one-third of that required for the oxidation of the aldoses by reaction V. Experiments using the theoretical quantity of chlorite have shown that the reactions are essentially the same as those in which only one-third the theoretical amount of chlorite was used.

2. ACTION OF CHLORINE DIOXIDE ON SUGARS

Chlorine dioxide was generated in an all-glass apparatus from a mixture of 25 g of potassium chlorate and 20 g of oxalic acid dihydrate, to which 80 ml of a cold solution of sulfuric acid (made from 40 ml of concentrated sulfuric acid and 90 ml of water) was added [3,9]. The mixture was well shaken and then warmed to 58° C in a water bath to initiate reaction and was kept at 50° to 58° C during the reaction. The chlorine dioxide gas was passed through water to wash it before it was absorbed in 250 ml of water kept at 0° C by an ice bath. The reaction was complete in about 1 hour and gave about 8 g of chlorine dioxide in solution.

The measurements recorded in table 5 were conducted in the following manner: Ten-gram samples of glucose, fructose, and sucrose, and an 8.325-g sample of *l*-arabinose were made up to 50 ml with water. Ten milliliters of these solutions were introduced into tubes prepared for sealing, and the tubes and contents cooled to 0° C. Ten milliliters of the previously prepared ice-cold chlorine dioxide solution was then added to each tube while cooling was continued, and the tube was sealed and kept in the dark at 20° C. At stated intervals the solutions were sampled, the optical rotations and the reducing-sugar content were determined, and the sodium bisulfite titration was performed in the manner described for the reactions using chlorous acid.

3. ANALYSIS OF OXIDATION PRODUCTS FOR CHLORIDE, CHLORITE, CHLORATE, AND CHLORINE DIOXIDE

The investigations in which the reactions were followed by the amount of oxidation were supplemented by experiments in which the degradation products of the oxidant were determined. In these experiments, the quantity of chlorite consumed in the reaction was calculated from the difference between the amount added and that remaining in the sample. The latter was determined by titration in acetic acid solution with thiosulfate according to the method described in reference [7]. Before titration the chlorine dioxide was removed by passing nitrogen through the solution. Chloride was determined as silver chloride in the conventional manner, and the "total chlorine content" of the solution after removal of the chlorine dioxide was determined by reducing all the chlorine compounds to chloride by heating with zinc according to the method described on page 408 of reference [10]. The total chlorine content of the solution consists of the chloride, chlorite, and chlorate chlorine, and hence the chlorate chlorine was obtained by subtracting the chloride and chlorite chlorine from the total. The amount of chlorine dioxide was calculated from the difference between the chlorine originally added as chlorite and the chlorine content determined after removing the chlorine dioxide by volatilization. This calculation is based on the assumption that the only volatile product containing chlorine is chlorine dioxide. The results obtained by these methods are given in tables 7 and 10 and are discussed on page 132.

TABLE 10.—*Products formed by the oxidation of d-glucose with chlorites in acid and in neutral solutions*

Constituents	I 0.0555 mole of *d*-glucose+ 0.1516 mole of $NaClO_2$+0.168 mole of acetic acid in 100 ml at 0° C for 24 hours	II 0.0555 mole of *d*-glucose+ 0.0531 mole of $NaClO_2$+0.056 mole of acetic acid in 100 ml at 20° C for 24 hours	III 0.0555 mole of *d*-glucose+ 0.0248 mole of $Ca(ClO_2)_2$ in 100 ml+CaCO at 20° C for 7 days
	Moles	*Moles*	*Moles*
Chlorite (initial)	0.1516	0.0531	0.0495
Chlorite unreacted	.0000	.0001	.0081
Chlorous acid consumed	.1516	.0530	.0414
Glucose oxidized	.0396	.0166	.0160
Total chlorine in nonvolatile products	.0721	.0230	.0359
Chloride formed in reaction	.0533	.0206	.0197
Chloride plus chlorate, formed	.0721	.0229	.0278
Chlorate, formed	.0187	.0023	.0081
Chlorine dioxide lost	.0796	.0301	.0136

4. ISOLATION OF THE OXIDATION PRODUCTS

(a) OXIDATION OF *d*-GLUCOSE IN NEUTRAL SOLUTION

Twenty-five grams of *d*-glucose and 12 g of calcium chlorite were dissolved in water and made to a volume of 250 ml. This solution was mixed in a glass-stoppered flask with 25 g of precipitated calcium carbonate and allowed to stand at 20° C in the dark with occasional shaking. In the course of 7 days, the glucose content dropped from 100 mg/ml to 66 mg/ml and the pH changed from 7.2 to 5.9. On the 7th, 9th, and 15th days, 6-g portions of calcium chlorite were added.

On the 16th day the glucose content was 32 mg/ml; at this time the solution was placed in a distillation flask and the chlorine dioxide was removed by volatilization in vacuo at room temperature. The solution containing calcium carbonate and calcium oxalate in suspension was filtered and the insoluble residue washed with hot water.

The calcium carbonate residue was dried, and the amount of calcium oxalate was determined by titration in sulfuric acid solution with potassium permanganate. The titration showed the presence of 0.492 g of calcium oxalate in the residue. This corresponds to 1 molecule of oxalic acid for each 24.6 molecules of glucose oxidized.

The solution, containing the soluble products from the oxidation described above, was added slowly to 50 g of lime in 150 ml of water. The resultant mixture was heated to 50° C, filtered, and the insoluble basic calcium salts were washed with saturated limewater. The basic salts were then suspended in water and treated with carbon dioxide until neutral to phenolphthalein. The carbonated solution was heated to boiling, filtered, and concentrated *in vacuo* to a thin sirup; sufficient alcohol was added to saturate the solution, which was then seeded with calcium gluconate. After 24 hours the product was removed by filtration, washed with 75-percent aqueous alcohol, and air-dried. The crystals weighed 3.5 g and gave $[\alpha]_D^{20}=+8.5$ (water; *c*,[6] 3). Calcium gluconate has a specific rotation of +8.5 [11]. The mother liquor gave a small second crop of crystalline calcium gluconate, but the residue could not be brought to crystallization.

(b) OXIDATION OF *l*-ARABINOSE IN NEUTRAL SOLUTION

Twenty-one grams of *l*-arabinose and 12 g of calcium chlorite were dissolved in water and the volume was made to 250 ml. The solution was mixed in a glass-stoppered flask with 25 g of precipitated calcium carbonate and allowed to stand at 20° C in the dark with occasional stirring. After 2 days the sugar content had dropped from 83.24 to 44.40 mg/ml and the pH had changed from 7.5 to 5.5. On the 2d and 5th days, 6-gram portions of calcium chlorite were added. On the 6th day, when the sugar content had dropped to 6 mg/ml and considerable calcium arabonate had crystallized from solution, the chlorine dioxide was removed by volatilization at room temperature and the residual calcium salts were collected on a filter and washed with water. The calcium arabonate in the filtrate was separated by precipitation with 50 g of hydrated lime. The basic salt was collected on a filter and washed with limewater. Then the basic salt was suspended in water and carbonated until neutral to phenolphthalein. The mixture was heated to boiling, and the calcium carbonate was removed by filtration and washed with hot water. The filtrate and washings were concentrated *in vacuo* until crystallization began, when 3 volumes of 50-percent aqueous methyl alcohol was added. On standing, 3.4 g of crystalline calcium arabonate separated. The air-dried salt gave $[\alpha]_D^{20}=+2.81$ (water; *c*, 2.3) and contained 8.66 percent of calcium. Calcium arabonate, $Ca(C_5H_9O_6)_2.5H_2O$, gives $[\alpha]_D^{20}=+2.97$ [12] and has a calcium content of 8.69 percent. The larger part of the calcium arabonate was extracted from the calcium carbonate residue separated from the original reaction mixture. This material was extracted with boiling water and the water solution was evaporated

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[6] Throughout this article *c* designates the concentration of the optically active substance in grams per 100 ml of solution.

and brought to crystallization. The first crystals weighed 3.63 g, gave $[\alpha]_D^{20}=+2.85$ (water; *c*, 2.3), and contained 8.90 percent of calcium. The second crop of crystals weighed 5.84 g, gave $[\alpha]_D^{20}=+3.16$ (water; *c*, 2.3), and contained 8.58 percent of calcium. The total quantity of calcium arabonate separated was 12.88 g. As final proof of the identification of this material, it was converted into crystalline *l*-arabonic acid, which was found to melt at 112° to 114° C in agreement with the recorded value [13].

Part of the insoluble calcium carbonate residue after extraction of the calcium arabonate was dissolved in sulfuric acid and titrated with potassium permanganate. The titration showed a total of 0.767 g of calcium oxalate in the residue. This corresponds to 1 mole of oxalic acid for each 21.6 moles of arabinose oxidized. The identity of the salt was established by the isolation of crystalline oxalic acid from the residue.

(c) OXIDATION OF LACTOSE IN NEUTRAL SOLUTION

Forty-eight grams of anhydrous lactose and 12 g of calcium chlorite were dissolved and made up to 250 ml with water. This solution was mixed with 25 g of precipitated calcium carbonate in a glass-stoppered flask and allowed to stand at 20° C in the dark with occasional shaking. After 2 days the solution was yellow with chlorine dioxide gas. By the 5th day the color of the solution had diminished considerably and 12 g of calcium chlorite was added. Likewise, on the 7th day 12 g of calcium chlorite was added. On the 10th day the chlorine dioxide was removed from the mixture at 20° C *in vacuo* and the solution was filtered. It was found that the reducing sugar had changed from 192 to 70.20 mg/ml, and the pH from 7.5 to 5.4. The unreacted calcium chlorite in the total solution was about 0.5 g. The insoluble residue, which consisted of a mixture of calcium carbonate and calcium oxalate, was extracted with hot water and dried. The calcium oxalate present, determined by permanganate titration in sulfuric acid solution, was 0.124 g. This corresponds to 1 mole of oxalic acid for each 88 moles of lactose oxidized. The filtrate was treated with 50 g of freshly hydrated lime. The resultant mixture was warmed to 50° C, and the insoluble basic salts were removed and washed with saturated limewater. The basic salts, suspended in water, were carbonated until neutral to phenolphthalein. The mixture was heated to boiling and filtered, and 30 g of $CaBr_2\ 6H_20$ (1.1 *M* equivalents) was added. The solution was concentrated *in vacuo* to a thick syrup, and crystallization was initiated by saturating the solution with alcohol and seeding with calcium lactobionate–calcium bromide crystals. After 24 hours at 4° C the crystals were removed, washed with 50-percent aqueous alcohol, and dried at 50° C. Weight, 8.31 g; $[\alpha]_D^{20}=+18.8$ (water; *c*, 7.3). Calcium lactobionate–calcium bromide $(Ca(C_{12}H_{21}O_{12})_2\ CaBr_2 \cdot 6H_2O)$ gives $[\alpha]_D^{20}=+18.7$ [14].

IV. REFERENCES

[1] M. C. Taylor, J. F. White, G. P. Vincent, and G. L. Cunningham, Ind. Eng. Chem. **32,** 899 (1940).
[2] J. W. Mellor, A Comprehensive Treatise on Inorganic and Theoretical Chemistry, vol. II, p. 281 (Longmans, Green and Co., London, 1922).
[3] E. Schmidt and E. Graumann, Ber. deut. chem. Ges. **54,** 1860 (1921).
[4] H. S. Isbell and C. S. Hudson, BS J. Research **8,** 327 (1932) RP418.
[5] H. S. Isbell, BS J. Research **8,** 615 (1932) RP441.

[6] H. S. Isbell and W. W. Pigman, BS J. Research **10,** 337 (1933) RP534; **18,** 141 (1937) RP969.
[7] D. T. Jackson and J. L. Parsons, Ind. Eng. Chem., Anal. Ed. **9,** 14 (1937).
[8] H. S. Isbell, W. W. Pigman, and H. L. Frush, J. Research NBS **24,** 241 (1940) RP1282.
[9] E. Schmidt, E. Geisler, P. Arndt, and F. Ihlov, Ber. deut. chem. Ges. **56,** 23 (1923).
[10] F. P. Treadwell and W. T. Hall, Analytical Chemistry, vol. II, p. 408 (John Wiley & Sons, Inc., New York, N. Y., 1935).
[11] C. S. Hudson and H. S. Isbell, BS J. Research **3,** 59 (1929) RP82.
[12] H. S. Isbell, J. Research NBS **14,** 307 (1935) RP770.
[13] H. S. Isbell and H. L. Frusch, BS J. Research **11,** 662 (1933) RP613.
[14] H. S. Isbell, J. Research NBS **17,** 333 (1937) RP914.

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