XCVI.—*Some Compounds of Guanidine with Sugars.* *Part I.*

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THE action of ammonia on sugars has been investigated by Lobry de Bruyn in conjunction with van Leent and Alberda van Ekenstein (*Rec. trav. chim.*, 1893, **12**, 286; 1894, **13**, 218; 1895, **14**, 98 and 134). They showed that ammonia reacted slowly with sugars in methyl-alcoholic solution to give "osamines," for example, $C_6H_{13}O_5N$, or in the case of lactose a simple addition product of the carbohydrate with ammonia was formed.

Compounds of lime and lead monoxide with mono- and disaccharides are well-known substances.

Several years ago one of us in investigating the action of organic bases on glucosone tried the action of guanidine on it. On mixing alcoholic solutions of the two substances, a white, amorphous precipitate was obtained which seemed to contain two molecules of guanidine with one molecule of glucosone.

On addition of an alcoholic solution of guanidine, prepared from guanidine carbonate, to alcoholic solutions of dextrose, lævulose, or mannose, white, microcrystalline precipitates were obtained which were extremely hygroscopic. Alcoholic solutions of galactose, rhamnose, arabinose, or maltose gave with guanidine similar precipitates.

Dextrose guanidine had been obtained by Herzfeld (*Zeitsch. Ver. deut. Zuckerind.*, 1895, **45**, 853), but not in a pure state, and

further investigation of these guanidine compounds seemed to be of interest.

The guanidine used in the preparation of guanidine sugar compounds was obtained from the carbonate by treatment with less than the calculated quantity of barium hydroxide; after filtration from barium carbonate, the aqueous solution of guanidine was concentrated under reduced pressure at 40° to a thick syrup; the syrup was dissolved in absolute alcohol, filtered from guanidine carbonate, and allowed to flow drop by drop into a solution of a sugar in 98 per cent. ethyl alcohol. In almost every case the guanidine compound separated as a white, minutely crystalline substance. After a few hours the precipitate was filtered off, washed with absolute alcohol, afterwards with dry ether, and dried in a vacuum over phosphoric oxide. The yield was generally excellent. In one experiment 18 grams of dextrose dissolved in 1500 c.c. of 98 per cent. alcohol gave nearly 22 grams of the compound, this being the calculated amount for dextrose guanidine of the formula $3C_6H_{12}O_6, 2CH_5N_3$. From 18 grams of lævulose 13 grams of lævulose guanidine were obtained. A portion of the lævulose guanidine is generally precipitated immediately, and the remainder separates after several hours.

The compounds of guanidine with mannose, lævulose, and dextrose are very hygroscopic; they are insoluble in all solvents except methyl alcohol or water, but from these solvents it is impossible to obtain them in a crystalline form owing to secondary changes in the solutions, which will be referred to later. The substances were analysed as precipitated, constancy of composition on analysis of several samples prepared by using varying quantities of guanidine being the only possible guarantee of their purity.

Dextrose guanidine:

0.1948 gave 0.2613 CO_2 and 0.129 H_2O . C = 36.59; H = 7.35.

0.1748 „ 19 c.c. moist nitrogen at 15° and 767 mm. N = 12.57.

0.8995, prepared by using a large excess of guanidine, required 24.7 c.c. $N/10$ HCl. $CN_3H_5 = 17.97$.

1.335 dissolved in 20 c.c. N -hydrochloric acid required 41 c.c. $N/10$ sodium hydroxide for neutralisation. $CN_3H_5 = 18.0$.

1.051 gave 0.8494 guanidine picrate. $CN_3H_5 = 17.5$.

$3C_6H_{12}O_6, 2CH_5N_3$ requires C = 36.47; H = 6.99; N = 12.76;
 $CH_5N_3 = 17.9$ per cent.

Picric acid can be used to estimate the guanidine, if the correction for the solubility of guanidine picrate in water (Emich, *Monatsh.*, 1892, 12, 24) is introduced.

Lævulose guanidine:

0.1757 gave 0.2378 CO_2 and 0.1173 H_2O . C = 36.9; H = 7.41.

3 x 2

0.1500 gave 16.6 c.c. moist nitrogen at 14° and 755 mm. $N = 12.92$.

0.7890 dissolved in 10 c.c. *N*-hydrochloric acid required 76.4 c.c. *N*/10 sodium hydroxide. $CH_5N_3 = 17.6$.

$3C_6H_{12}O_6, 2CH_5N_3$ requires $C = 36.47$. $H = 6.99$; $N = 12.76$;
 $CH_5N_3 = 17.9$ per cent.

Mannose guanidine :

0.1725 gave 0.2300 CO_2 and 0.1117 H_2O . $C = 36.36$; $H = 7.19$.

0.1885 „ 21.5 c.c. moist nitrogen at 17° and 756 mm. $N = 13.16$.

0.3516 required 10.6 c.c. *N*/10 hydrochloric acid. $CH_5N_3 = 17.78$.

$3C_6H_{12}O_6, 2CH_5N_3$ requires $C = 36.47$. $H = 6.99$; $N = 12.76$;
 $CN_3H_5 = 17.9$ per cent.

These compounds on being heated for some time to about 50° in a vacuum over phosphoric oxide become yellow, but they can be dried at 40° without change in composition. They have no sharp melting points; below 100° they fuse with effervescence; dextrose guanidine at 94°, lævulose guanidine at 90°, mannose guanidine at 80°. When dextrose guanidine was heated to 100° for several hours, the alkaline reaction disappeared, and the substance no longer reduced Fehling's solution, but it gave phenylglucosazone when warmed with phenylhydrazine acetate. The residue on analysis contained $C = 40.9$; $H = 6.5$, and $N = 14.7$. $3C_6H_{12}O_6, 2CH_5N_3 - 4H_2O$ requires $C = 40.95$; $H = 6.48$; $N = 14.3$ per cent. We have not investigated this substance further.

From the heat of neutralisation of guanidine by nitric acid (Matignon, *Ann. Chim. Phys.*, 1893, [vi], 28, 88), namely, 14.12 C per gram-molecule, and the electrical conductivity as determined by Ostwald (*J. pr. Chem.*, 1886, [ii], 33, 367), guanidine is a stronger base than tetramethylammonium hydroxide, and very nearly as strong as caustic soda and baryta. This conclusion we have confirmed by applying three other methods, (a) by observing the velocity of the fall in angle of a hyoscyamine solution in the presence of guanidine (Witt and Bredig, *Ber.*, 1888, 21, 2777); (b) by measuring the velocity of saponification of ethyl acetate by the free base; (c) by measuring the depression of the freezing point of an aqueous solution of guanidine. In these experiments the influence of the guanidine was compared with that of sodium hydroxide or baryta of equivalent strength.

(a). Hyoseyamine + *N*-sodium hydroxide.
 $t=20^{\circ}$.

Mins.	$[\alpha]_D^{20}$	$K = 1/\log \frac{[\alpha]_0^p - [\alpha]_{\infty}^p}{[\alpha]_t^p - [\alpha]_{\infty}^p}$
0	-20.32°	—
5½	17.94	0.0114
8½	17.14	0.0096
13½	15.45	0.0103
21½	12.97	0.0102
28½	11.19	0.0103
39½	9.32	0.0100
50	7.64	0.0101
64	6.48	0.0098
∞	1.86	0.0103 mean

Hyoseyamine + *N*-guanidine solution.
 $t=20^{\circ}$.

Mins.	$[\alpha]_D^{20}$	$K = 1/\log \frac{[\alpha]_0^p - [\alpha]_{\infty}^p}{[\alpha]_t^p - [\alpha]_{\infty}^p}$
0	-20.32°	—
8	17.79	0.0080
9	17.28	0.0087
10	17.11	0.0083
16½	15.18	0.0086
27	13.34	0.0076
35	11.74	0.0078
45	10.06	0.0078
∞	1.86	0.0081 mean

Sodium hydroxide : guanidine = 1 : 0.78.

In two other experiments the $[\alpha]_D$ values for sodium hydroxide and guanidine with hyoseyamine were found to be practically the same, and the ratios were 1 : 0.72. Experiments using 2*N*-solutions of the bases gave the ratio 1 : 0.76.

(b) Velocity of saponification of ethyl acetate by sodium hydroxide, baryta, and guanidine.

 a = c.c. of *N*/20-alkali originally present. x = c.c. of *N*/20-alkali disappeared.*N*/20 Sodium hydroxide and *N*/20 ethyl acetate, $t=20^{\circ}$.

Mins.	$a - x$	x	ak
0	25.0	0.0	—
3	18.3	6.7	0.121
6	15.0	10.0	0.111
9	12.0	13.0	0.120
12	10.7	14.3	0.111
15	9.5	15.5	0.109
18	8.55	16.45	0.107
21	7.65	17.35	0.108
24	6.9	18.1	0.109

Mean 0.112

N/20 Guanidine and *N*/20 ethyl acetate, $t=20^{\circ}$.

Mins.	$a - x$	x	ak
0	25.0	0.0	—
3	19.5	5.5	0.0940
6	15.65	9.35	0.0995
9	13.3	11.7	0.0985
12	11.65	13.35	0.0955
15	10.3	14.7	0.0951
18	9.3	15.7	0.0938
21	8.4	16.6	0.0941
24	7.9	17.1	0.0902

Mean 0.0951

Several determinations of the velocity of saponification of ethyl acetate were made, and the ratios of strengths of sodium hydroxide or baryta and guanidine were : Sodium hydroxide : guanidine = 1 : 0.85 ; baryta : guanidine = 1 : 0.926.

(c) *Depression of the Freezing Point of an Aqueous Solution of Guanidine.*—The guanidine solution was prepared by the action of baryta water on an aqueous solution of purified guanidine sulphate of correctly equivalent strength. The caustic soda was the same as that used in the two previous methods.

The depression of the freezing point for a *N*/2 guanidine solution was found to be -1.67° (mean of four determinations, each with fresh

samples of guanidine prepared from three different samples of guanidine sulphate).

The depression of the freezing point for a $N/2$ sodium hydroxide solution was -1.838° (mean of several determinations of separate and new solutions of freshly prepared $N/2$ sodium hydroxide).

If the $N/2$ sodium hydroxide be considered as containing completely dissociated molecules, the strength of guanidine as a base compared with sodium hydroxide will be $\frac{1.67 - 0.919}{0.919} = 0.81$.

This agrees fairly well with the results obtained by the hyoscyamine and saponification methods.

The Properties of Aqueous Solutions of the Compounds of Guanidine with Sugars.

Since the compounds of guanidine with sugars are decomposed by water, it seemed of interest to investigate whether they were completely resolved into their components in aqueous solution or not. We have determined the freezing points for aqueous solutions of dextrose and guanidine mixed in the proportions of three to two, and the freezing points of similar solutions of fructose and guanidine.

The following table gives the results of a number of determinations:

Depression of Freezing Points.

$N/2$ -Guanidine.	$N/2$ -Caustic soda.	$N/2$ -Dextrose.	$N/2$ -Lævulose.	3 c.c. $N/2$ -Dextrose, 2 c.c.	3 c.c. $N/2$ -Lævulose, 2 c.c.	Calculated depression.
				$N/2$ -guanidine.	$N/2$ -guanidine.	
-1.67°	—	-1.01°	—	-0.93°	—	-1.274°
-1.67	—	—	-1.02°	—	-0.97°	-1.28
				3 c.c. $N/2$ -Glucose, 2 c.c.	3 c.c. $N/2$ -Fructose, 2 c.c.	
				$N/2$ -Caustic soda.	$N/2$ -Caustic soda.	
—	-1.838°	-1.01°	—	-0.89°	—	-1.341°
—	-1.838	—	-1.02°	—	-0.95°	-1.347

The calculated depression is obtained by taking the sum of $\frac{2}{5} \times 1.67^\circ + \frac{3}{5} \times 1.01^\circ = 1.274^\circ$ for dextrose guanidine, and similarly for the other compounds. From these data it is evident that guanidine forms a compound with dextrose or lævulose in aqueous solution.

H. Euler (*Ber.*, 1905, **38**, 2551; 1906, **39**, 350) came to similar conclusions as to the acidic nature of aldehydes from the study of the

freezing points of normal and semi-normal solutions of sodium hydroxide, dextrose, formaldehyde, and acetaldehyde.

From the freezing points of aqueous solutions of guanidine dextrose and lævulose compounds, the molecular weights were found to be 122 and 118.6 respectively. The calculated molecular weight of the solid compound is 658. Complete dissociation in solution would furnish per molecule 7 parts, namely: 3 dextrose, 2 (CN₃H₅H), and 2 (OH)', but guanidine is only dissociated to the extent of 80 per cent., therefore the calculated molecular weight of the compounds in solution will be $\frac{658 \times 100}{7 \times 80} = 117.5$. The observed values agree exceedingly well with this number.

In aqueous solution the compounds show decided mutarotation to an equilibrium value. It was found that the initial specific rotation was dependent on the age of the specimen examined, although the composition remained unaltered. It is thought that the solid substance undergoes slow isomeric change on standing in a vacuum. In the case of dextrose guanidine a freshly prepared specimen has a specific rotation $[\alpha]_D + 31.47^\circ$, whilst older specimens have $[\alpha]_D + 29^\circ$ and even $+ 22.95^\circ$. A freshly prepared mannose guanidine has $[\alpha]_D + 10.03^\circ$, the same specimen several days later $[\alpha]_D + 8.81$. In the case of lævulose guanidine, the initial specific rotation varies between $[\alpha]_D - 62.21^\circ$, $[\alpha]_D - 53.3^\circ$, and $[\alpha]_D - 38.84^\circ$. The influence of concentration and temperature and the slow isomeric change which sets in when an aqueous solution is examined make an absolute uniformity of values impossible.

The gradual isomeric change of one sugar into another by the action of free alkali was first investigated by Lobry de Bruyn and Alberda van Ekenstein (*Rec. trav. chim.*, 1895, 14, 18). They showed a partial reciprocal transformation of dextrose into lævulose and mannose in which lævulose was the intermediate substance in the change according to the scheme:

Acids, probably saccharinic and other sugars, for example ψ -lævulose and glucose, were formed (*loc. cit.*, 1897, 16, 262). By boiling a 20 per cent. aqueous solution of dextrose with 2½ per cent. aqueous caustic potash for five minutes, the composition of the mixture of sugars was given as 49 per cent. dextrose, 5 per cent. mannose, and 28 per cent. lævulose. The percentage of lævulose was considered to be too high owing to the presence of isomeric ketoses. At the ordinary temperature an aqueous solution of 10 per cent. dextrose containing 2.8 per cent. aqueous caustic potash had its rotatory power

changed in 117 hours from $+42^\circ$ to -3.5° with the disappearance of 60 per cent. of the alkali.

In the presence of lime the fall in the rotatory power at the ordinary temperature was more rapid and no mannose was formed. The mechanism of the change was explained by the combination of a molecule of water with the aldehydic or ketonic groups of the sugar

and subsequent loss of water to form the group $\begin{array}{c} \text{O} \\ \diagup \quad \diagdown \\ \cdot\text{CH}\cdot\text{CH}\cdot\text{OH} \end{array}$, which

is probably capable of existing in two forms. This complex is converted by intramolecular transposition partly into lævulose

mannose $\cdot\text{CH}(\text{OH})\cdot\text{CHO}$, and an acid $\cdot\text{CH}_2\cdot\text{CO}_2\text{H}$, which is an intermediate substance in the formation of saccharinic acid,

That lævulose is actually the intermediate substance was stated by Lobry de Bruyn to be borne out by the fact that in the action of alkalis on mannose the rotatory power becomes negative and then rises to zero owing to the increase in the amount of dextrose (*Rec. trav. chim.*, 1895, 14, 221).*

Wohl (*Ber.*, 1900, 33, 3093) considers that dextrose, lævulose, and mannose in alkaline solution produce a common enolic substance, $\cdot\text{CH}(\text{OH})\cdot\text{C}(\text{OH})\cdot\text{CH}(\text{OH})\cdot$. The change of these sugars into their intermediate substance proceeds at different rates, and since it is accompanied by secondary transformations no strict equilibrium can be expected. The formation of other ketoses such as glucose might be ascribed to lævulose possessing a second enolic form, for example, $\cdot\text{C}(\text{OH})\cdot\text{C}(\text{OH})\cdot\text{CH}_2\cdot\text{OH}$.

In the review on the work on "Dynamic Isomerism," by Lowry (*British Assoc. Reports*, 1904), dextrose is stated to exist in four isodynamic modifications, of which the stereoisomeric α and β (hydrogen) glucosides are the dominant forms, the aldehyde the minor constituent, and the enolic form is present only in traces. Owing to the moderate proportion of aldoglucose present, equilibrium is rapidly established between α - and β -glucosides. Dextrose, lævulose, and mannose have a common enolic form, and the slow rate at which equilibrium is established between the three sugars in the presence of considerable quantities of alkali is an indication of the minute proportion of the enolic form in the mixture. The relationships between the three sugars allowing the existence of no less than 10 isomeric forms may be shown as follows :

* We have not noticed such a change in the rotation angle, and we consider that Lobry de Bruyn's observations are due to the high temperature coefficient of the rotation angle of lævulose and do not represent the formation of more dextrose.

α - and β -glucoside

α - and β -mannoside

aldodextrose

aldomannose

enolic form dextrose, mannose, and lævulose

ketolævulose

α - and β -fructoside

It is evident that the latter view is merely a modification of Wohl's suggestion on the lines of the generally accepted view of the structure of glucosides.

To investigate the velocity of a reaction in which the existence of at least ten isomeric forms is to be considered is not a very hopeful task. A sugar solution in the presence of an alkali might involve the consideration of all the ten forms, but in the decomposition of a solid compound of a sugar with an alkali one would be led to suppose the presence initially of only one form in preponderating quantity.

The influence of alkalis on the birotation of dextrose was shown by Trey to be a very rapidly acting one (*Zeitsch. physikal. Chem.*, 1895, 18, 193; and 1896, 22, 424), the normal value $[\alpha]_D + 52^\circ$ being attained in fifteen minutes by addition of 0.2 gram of caustic soda to a 2.25 per cent. solution of dextrose anhydride; in sixty-five days the $[\alpha]_D$ had fallen off to $+0.44^\circ$. Osaka (*loc. cit.*, 1901, 35, 661) has shown that the drop in angle is strictly proportional to the concentration of the hydroxyl ions and is a reaction of the first order, the constant of which at 20° is 0.0104. Moreover, the proportionality is so close that the dissociation constants of weak bases can be determined.

Osaka obtained his velocity constant by using the expression :

$$K = \frac{1}{t} \log \frac{\alpha_0 - \alpha_\infty}{\alpha_t - \alpha_\infty}$$

From Trey's numbers no attempt was made to establish a relationship between the values for rotation powers after the ordinary birotation had stopped. The change was slow and the products were probably many.

In the action of water on dextrose-, lævulose-, and mannose-

guanidine, the change is slow at the ordinary temperature, but at 37° the rate is conveniently rapid, and in about six hours a constant angle is obtained. The conclusion that can be drawn from the values of the rotatory powers is that a satisfactory constant can be obtained, the value of which is given by the expression :

$$K_1 + K_2 = \frac{1}{t} \log \frac{[\alpha]_0^D - [\alpha]_\infty^D}{[\alpha]_t^D - [\alpha]_\infty^D}.$$

Dextrose Guanidine.

Experiment 1.— $t=37^\circ$. $c=5.445$.			Experiment 2.— $t=37\frac{1}{2}$. $c=6.115$.		
Mins.	$[\alpha]_0^D$.	$k_1 + k_2$.	Mins.	$[\alpha]_0^D$.	$k_1 + k_2$.
0	+26.54°	—	0	+31.96°	—
10	24.33	0.00367	10	28.78	0.00447
20	22.31	0.00366	20	26.00	0.00439
30	20.38	0.00371	30	23.46	0.00438
40	18.36	0.00387	40	21.42	0.00425
50	17.00	0.00374	50	19.37	0.00416
60	15.51	0.00375	60	17.74	0.00416
85	12.12	0.00384	80	14.47	0.00419
100	10.62	0.00380	100	11.86	0.00418
120	8.72	0.00384	120	9.64	0.00419
∞	-0.72	Mean 0.00376	150	7.03	0.00421
			180	5.07	0.00423
			∞	-0.57	Mean 0.00425

Experiment 3.—At room temperature. $C=6.426$.

Mins.	$[\alpha]_0^D$.	$k_1 + k_2$.
0	+28.91°	—
1635	16.34	0.000126
2730	10.13	0.000131
4500	4.04	0.000134
5700	0.0	0.000157
6780	-1.55	0.000161
∞	-4.20	Mean 0.000142

Experiment 3.—A six days' old preparation. A little ammonia was added to the alcoholic solution of dextrose, in order to establish equilibrium between the α - and β -isomerides before guanidine was added, and the precipitate was left overnight in contact with alcohol before it was filtered off.

The initial value of the specific rotation varies with the age of the sample. When freshly prepared the $[\alpha]_0^D$ of dextrose guanidine is +33.52° at 37°; two months afterwards a solution of the same sample showed a specific rotation of 26.54°. The value of the velocity constant is independent of the age of the preparation.

*Lævulose Guanidine.*Experiment 1.— $t = 36\frac{1}{2}^{\circ}$, $c = 6.263$.

Mins.	$[\alpha]_D$	$k_1 - k_2$
0	-41.35°	—
10	38.32	0.00337
30	33.21	0.00324
44	28.42	0.00378
82	21.40	0.00357
105	17.64	0.00362
166	12.21	0.00330
212	7.98	0.00352
∞	0.72	Mean 0.00349

Experiment 2.— $t = 37^{\circ}$, $c = 6.3735$.

Mins.	$[\alpha]_D$	$k_1 + k_2$
0	-23.85°	—
10	21.81	0.00401
20	20.29	0.00363
30	18.61	0.00372
40	17.08	0.00376
50	15.72	0.00376
60	14.51	0.00373
80	12.16	0.00382
100	10.43	0.00377
120	8.94	0.00376
140	7.92	0.00362
—	0.72	Mean 0.00376

Experiment 3.—At room temperature. $C = 6.033$.

Mins.	$[\alpha]_D$	$k_1 + k_2$
0	-50.62°	—
980	43.93	0.000069
5250	15.41	0.000118
5680	13.92	0.000120
6780	11.6	0.000118
7140	10.4	0.000123
8125	7.79	0.000135
∞	4.34	Mean 0.000120

The lævulose guanidine used in Experiment 3 was precipitated from its ethyl alcohol solution by means of ether.

The initial value of the specific rotation of lævulose guanidine varies with the age of the sample. When freshly prepared the $[\alpha]_D$ is -50.62° . The value of the velocity constant is independent of the age of the preparation.

*Mannose Guanidine.*Experiment 1.— $t = 37.25^{\circ}$, $c = 6.9292$.

Mins.	$[\alpha]_D$	$k_1 + k_2$
0	$+10.03^{\circ}$	—
60	6.38	0.00360
120	4.40	0.00336
180	3.03	0.00336
240	2.16	0.00337
300	1.44	0.00366
∞	-0.72	Mean 0.00347

Experiment 2.— $t = 37.25^{\circ}$, $c = 10.391$.

Mins.	$[\alpha]_D$	$k_1 + k_2$
0	$+8.81^{\circ}$	—
10	7.99	0.00391
20	7.27	0.00383
30	6.69	0.00364
40	6.16	0.00354
60	5.24	0.00339
80	4.38	0.00339
100	3.75	0.00329
120	3.32	0.00310
150	2.41	0.00322
∞	-0.72	Mean 0.00348

It will be seen that the values of the constants for dextrose-, laevulose- and mannose-guanidine are equal at the same temperature. The variation of a degree in temperature exercises a marked influence on the value of the constant.

At 34.25° the mean value of the velocity constant for dextrose guanidine was 0.00296; at 38° it was 0.00501.

At 36.5° the value of the velocity constant for laevulose guanidine was 0.00349; at 34.25° it was 0.00286.

The reason that the value of $k_1 + k_2$ in the case of mannose is equal to the corresponding values of $k_1 + k_2$ for laevulose- and dextrose-guanidine respectively will be explained later.

The value of $[\alpha]_D$ is taken to be the same in all cases, since the actually observed values for dextrose guanidine were: $[\alpha]_D^{37.5^\circ} - 0.986^\circ$; $[\alpha]_D^{37^\circ} - 4.97^\circ$; $[\alpha]_D^{35^\circ} - 4.32^\circ$; laevulose guanidine, $[\alpha]_D^{37.5^\circ} - 1.6^\circ$; $[\alpha]_D^{37^\circ} - 1.77^\circ$; $[\alpha]_D^{35^\circ} - 4.34^\circ$; mannose guanidine, $[\alpha]_D^{37.5^\circ} - 0.652^\circ$; $[\alpha]_D^{37^\circ} - 0.72^\circ$; $[\alpha]_D^{35^\circ} - 3.69^\circ$; $[\alpha]_D^{30^\circ} - 3.55^\circ$.

The final specific rotation at the ordinary temperature is nearly -4.3° . The laevulose guanidine shows too high a laevorotatory value, but it must be remembered with small rotation angles an error of 0.02° makes a difference of 0.2° in the value of the $[\alpha]_D$.

At the ordinary temperature the velocity of transformation (compare Experiment 3) is much slower. More than 150 hours were required before equilibrium was established in the case of dextrose- and laevulose-guanidine. The time limit at the ordinary temperature was only roughly determined, since the presence of laevulose introduces a relatively large temperature coefficient.

For the experiments at room temperature the values of $k_1 + k_2$ are as good as can be expected, since it is difficult to maintain a constant temperature of 17—18° during the summer, when these experiments were performed; and the agreement between the $[\alpha]_D$ values is satisfactory. There is not the least difficulty in observing the equilibrium rotation of the guanidine sugar solutions. They change colour very slowly and show only a pale yellow colour even after being heated for ten hours at 40°; moreover, the solutions remain perfectly clear. In the presence of caustic alkalis sugar solutions darken rapidly, and in a few hours become almost opaque.

The action of methyl alcohol on laevulose guanidine is apparently similar to that of water. The initial specific rotation was $[\alpha]_D - 29.73^\circ$, at the ordinary temperature falling to $[\alpha]_D - 4.31^\circ$ in one hundred and forty-eight hours.

In order to examine the chemical changes which occurred during the mutarotation, aqueous solutions of guanidine sugar compounds were warmed to 40° until the equilibrium angle was reached. The products of the reaction were then investigated, following the

directions given by Lobry de Bruyn (*Rev. trav. chim.*, 1895, 14, 205).

Dextrose guanidine was found to yield 4.26 per cent. of mannose, identified by its hydrazone, and lævulose, identified by the resorcinol test; moreover, a lime compound was isolated, from which a strongly lævorotatory sugar solution was obtained, possessing the properties of lævulose.

The presence of unchanged dextrose was proved by the isolation of acid potassium saccharate:

0.1619 gave 0.0576 K_2SO_4 . $K = 15.95$.

$C_6H_9O_8K$ requires $K = 15.72$ per cent.

The difficulty of removing guanidine salts rendered fermentation experiments, to test for the presence of ψ -lævulose, inconclusive.

Lævulose guanidine dissolved in water was found to give 6.1 per cent. of mannose and dextrose, identified by isolation and analysis of potassium hydrogen saccharate:

0.1475 gave 0.0515 K_2SO_4 . $K = 15.65$.

$C_6H_9O_8K$ requires $K = 15.72$ per cent.

The investigation of the products of the action of water on mannose guanidine was not attempted. It is evident that they would be the same as were obtained by Lobry de Bruyn from the action of alkalis on mannose, but the amount of mannose remaining, when the equilibrium angle was reached, was determined, and this was found to be 33.8 per cent.

Lobry de Bruyn showed that, in addition to sugars, acids were formed, corresponding to a disappearance of 60 per cent. of alkali, when alkaline solutions of dextrose, lævulose, and mannose were heated to 100°. These may be saccharinic, acetic, formic, and lactic acids (H. Shade, *Zeitsch. physikal. Chem.*, 1906, 57, 46). It was necessary to prove that the formation of these acids did not interfere with the constant determined by the change in optical angle, because saccharinic acid yields a sodium salt having $[\alpha]_D - 17.2^\circ$ (Scheibler, *Ber.*, 1880, 13, 2212).

Very small values for the velocity of disappearance of guanidine were obtained by titrating the solutions with *N*/10 hydrochloric acid, at definite intervals of time, using phenolphthalein or litmus as indicator.*

* From the strength of guanidine as a base, it is permissible to use phenolphthalein for the purpose.

Dextrose guanidine. $t=37.25^\circ$. $c=5.0258$.				Lævulose guanidine. $t=36.5^\circ$. $c=4.278$.			
Mins.		C.c.		Mins.		C.c.	
[α] _D ^{37.5} . $N/10\text{-HCl}$. $K=1/t\log x_0/x_t$.				[α] _D ^{36.5} . $N/10\text{-HCl}$. $K=1/t\log x_0/x_t$.			
0	+33.52°	27.2	—	0	-47.80°	33.7	—
60	19.49	26.8	0.000172	60	32.37	32.1	0.000352
120	11.34	26.2	0.000135	120	22.08	30.8	0.000325
180	6.57	25.8	0.000127	180	15.42	30.4	0.000248
240	3.97	25.0	0.000152	270	8.99	28.4	0.000275
300	2.28	23.8	0.000193	360	5.96	27.55	0.000243
390	+0.99	21.6	Mean 0.000156	480	3.42	25.85	0.000240
∞	+0.99	9.7	—	600	—	24.05	0.000244
∞ [α] _D ³⁷ = -3.77°.				1440	—	13.45	0.000277
x_0 = c.c. $N/10\text{-HCl}$ used at t_0 .				Mean 0.000275			
x_t = ,, ,, t							

The action will be unimolecular if saccharinic acid,
 $\text{CH}_2(\text{OH})\cdot\text{CH}(\text{OH})\cdot\text{CH}(\text{OH})\cdot\text{CMe}(\text{OH})\cdot\text{CO}_2\text{H}$
 (Lippmann, *Chemie der Zuckerarten*, 1904, 335), or an acid,
 $\text{CMe}(\text{OH})\cdot\text{CO}\cdot\text{CH}_2\cdot\text{CH}(\text{OH})\cdot\text{CO}_2\text{H}$,
 be formed. The formation of lactic acid from glucose has been represented by Wohl and other authors by the following scheme :

(*loc. cit.*, 1890). The production of acetaldehyde and formic acid from dextrose is represented by Schade (*Zeitsch. physikal. Chem.*, 1906, **57**, 30) by supposing that an intermediate substance,

is first formed, and this by the action of hydrogen and hydroxyl ions furnishes molecules of formic acid and acetaldehyde.*

* Buchner, Meisenheimer, and Schade (*Ber.*, 1906, **39**, 4217) state that the conclusions arrived at by Schade can no longer be maintained. The yield of formic acid is greater and, in addition, glycollic acid and trihydroxybutyric acid are formed. The authors consider that glyceraldehyde is first formed; this under normal conditions would be transformed into methylglyoxal and so into lactic acid.

The "acetaldehyde" appears to have been furfuraldehyde and is produced in very small quantity.

Mannose guanidine. $t = 37.25^\circ$. $c = 6.9292$.

Mins.	$[\alpha]_D^{37.4^\circ}$	C.c. N/10-HCl.	$K = 1/t \log x_0/x_t$
0	$+10.03^\circ$	35.3	—
60	6.38	34.8	0.000132
120	4.40	34.4	0.000093
180	3.03	33.4	0.000133
240	2.16	33.05	0.000119
300	1.23	32.7	0.000111
* 420 at $37\frac{1}{4}$	0.53	29.8	0.000175
540 „	0.36	27.1	(0.000212)
* $[\alpha]_D^{12} =$	-2.88	—	—
780	-0.72	23.2	(0.000233)
1020	-0.72	16.4	(0.000326)
$[\alpha]_D^{11^\circ} =$	-3.96	—	Mean... 0.000127

* Overnight at the ordinary temperature.

It is to be noticed that the value of the velocity constant for the disappearance of alkali is so small that it will not interfere with the value of the constant obtained from the rotation angle. It is evident that the constant obtained by Rimbach (*Zeitsch. physikal. Chem.*, 1905, 51, 473) from the change in the rotation angle, on the assumption that only sodium saccharinate is formed by the action of caustic soda on dextrose, is not in agreement with the above numbers. He stated that the change could be represented by the equation

The equation was then bimolecular if in $K = \left(\frac{1}{A-x} - \frac{1}{A-x_0} \right) \frac{1}{t-t_0}$ (x = grams of dextrose transformed) t_0 and x_0 are taken ten to thirty minutes after mixing the solutions of alkali and sugar. This selection of the initial times and corresponding values of x_0 seems unnecessary; for example, at 20° thirty minutes after the commencement of the reaction, at 25° ten minutes, at 30° thirty minutes, and at 40° fifteen minutes are taken as the initial times. An explanation is possible if it is assumed that a compound of caustic soda and dextrose is first formed. The $[\alpha]_D$ of dextrose in sodium glucosate in water is 42.5° , whilst 42.5° is the $[\alpha]_D$ of the mixture of caustic soda and dextrose after thirty minutes given in Rimbach and Weber's paper. The amount of sodium saccharinate obtainable from 1 gram of dextrose was taken at 1.123 grams and its $[\alpha]_D = 17.2^\circ$ (*loc. cit.*, 481). The constants obtained, 0.00389 at 20° , 0.01902 at 30° , are much higher than the constants obtained by us from optical measurements. Rimbach and Weber worked with stronger alkaline solutions than ours, but their experimental data will give a satisfactory constant if calculated on the formula adopted by us.

Saccharinic acid is undoubtedly a product, but lactic and other acids ought not to be left out of consideration.

Further evidence in support of these small velocity constants for

the disappearance of alkali will be brought forward in considering the results of the investigation of the compounds of dextrose, lævulose, and mannose with caustic potash and soda.

It was found that when the rotation had reached a constant value the alkalinity continued to decrease until at length it became zero, but several days elapsed before the solution lost its alkalinity. The percentages of free guanidine present at optical equilibrium are for the dextrose, lævulose, and mannose compounds, 11.2 and 10.9, 12.3, 10.1 respectively, having fallen from 17.9; but these numbers are really much too low, as the alkalinity at 37.25° falls only 10–12 per cent. of its value during the first five hours, and in our experiments the solutions were kept after the first five hours at the ordinary temperature overnight, and the optical angle determined next day. It will be shown in the case of the compounds of dextrose and lævulose with caustic alkalis that the loss in alkalinity during five hours at 37.25° is about 15 per cent. of its original value. From the values of the constants calculated on the supposition that a six-carbon-atom acid is formed, it is found that the sugars yield more than one acid, or that saccharinic acid is not the sole product of the change. Moreover, when the alkaline solutions have become neutral a quarter to one-third of the sugar has disappeared, whereas for the production of a six-carbon-atom acid two-thirds ought to have disappeared.

The rates of formation and disappearance of mannose were studied separately. In one series of experiments it was found that 4–6 per cent. of mannose was formed when optical equilibrium had been attained by aqueous solutions of dextrose- and lævulose-guanidine.

In another series of experiments the changes in optical activity, the amounts of mannose hydrazone produced, as well as the weights of phenylglucosazone precipitated after the removal of mannose hydrazone, were determined in one and the same solution of mannose guanidine.

Hours.	$[\alpha]_D^{37.25}$	Mannose found from hydrazone.	Mannose calcu- lated.	Constant for disappearance of mannose $K = 1/t \log \frac{M_0 - M_\infty}{M_t - M_\infty}$	Per cent.	Per cent.
					osazone on original weight of sugar present.	calculated on the as- sumption that 1 gram osazone = 1.12 grams mixed sugars.
0	+10.03°	100	—	—	—	—
1	6.38	89.3	85.3	0.000865	12.12	16.32
2	4.40	76.5	77.4	0.000103	18.28	23.46
3	3.03	70.24	71.9	0.000907	24.70	33.64
4	2.16	67.3	68.4	0.000764	32.71	44.53
5	1.23	65.3	64.7	0.000752	35.21	47.85
*7	-0.72	50.9	56.8	0.000848	49.17	66.94
*13	0.72	33.8	—	Mean 0.000861	55.12	75.05
23½	0.63	15.17	—		33.62	51.35
69	0.63	8.56	—		26.14	35.60

* Overnight at the ordinary temperature.

M_0 , M_t , M_∞ = quantities of mannose present at t_0 , t , and t_∞ respectively.

It has been pointed out by Neuberg that the presence of salts of nitrogen bases retards the formation of osazones, but guanidine salts do not prevent the complete precipitation of mannose hydrazone, as may be shown by the following experiment. 0.2144 Gram of guanidine carbonate was dissolved in a 3.153 per cent. aqueous solution of mannose. On treatment with phenylhydrazine acetate at 0°, 0.9407 gram of mannose hydrazone was obtained. Percentage of mannose hydrazone precipitated = 99.4.

These numbers show that as the mannose decreases the amount of osazone increases up to a maximum and then diminishes; the percentages of dextrose and lævulose are only very approximately accurate, because they are calculated on the assumption that 1 gram of osazone = 1.12 grams of sugar; moreover, the influence of guanidine in the precipitation of the osazone may be appreciable, nevertheless the errors will be of a constant nature and will not interfere with the order of the change. The phenylglucosazone precipitated, after having been washed with ether, decomposed at 199° instead of 205°, so that it was not quite pure.

It is remarkable that when dextrose and lævulose reach optical equilibrium 5 per cent. of mannose is present, but when mannose has reached optical equilibrium only 50 per cent. of the mannose has been transformed.

The velocity constant for the disappearance of mannose, on the assumption that 5 per cent. is the true value of concentration of the mannose when the change is complete, is much smaller than that obtained from the rotation values of dextrose, lævulose, and mannose, and yet the rate of change in rotation angle for mannose is the same as for the two preceding sugars. We have endeavoured to explain this by the following hypothesis:

It has been shown that if $k_1 + k_2 = \frac{1}{t} \log \frac{A_0^D - A_\infty^D}{A_t^D - A_\infty^D}$, then $k_1 + k_2 = 0.0036$ for dextrose- and lævulose-guanidine respectively.

The equilibrium constant $K = \frac{k_2}{k_1}$ is equal to the ratio of the masses of dextrose and lævulose in equilibrium. Expressing this in terms of the specific optical rotations:

$$K = \frac{k_2}{k_1} = \frac{\text{specific rotation of lævulose guanidine} - \text{constant } [\alpha]^D}{\text{constant } [\alpha]_D - [\alpha]_D \text{ of dextrose guanidine}} = \frac{-48.54^\circ - (-0.72^\circ)}{-0.72^\circ - 32.15^\circ} = 1.45$$

(Hudson, *Zeitsch. physikal. Chem.*, 1903, 44, 491).

Since $k_1 + k_2 = 0.0036$

$$k_2 = 0.0021. \quad k_1 = 0.0015.$$

Therefore the velocity constant $G \rightarrow F = k_1 = 0.0015$ and the velocity constant $F \rightarrow G = k_2 = 0.0021$.

In obtaining the value of these constants, the formation of any mannose has not been taken into account, because that sugar cannot be detected in solutions of dextrose- and lævulose-guanidine, nor in dextrose- and lævulose-soda solutions until the optical equilibrium has been nearly reached. It will be shown later that at the constant specific rotation 58 per cent. of dextrose and 42 per cent. of lævulose are present in the solution. From these numbers and the value of $k_1 + k_2 = 0.0036$, it follows that $k_1 = 0.0015$ and $k_2 = 0.0021$, since if A_1 = amount of dextrose at the beginning of the experiment, A_2 that of lævulose in the reverse reaction, and x gram molecules of dextrose be transformed after time t into lævulose :

$$\frac{dx_1}{dt} = k_1(A_1 - x) \quad \frac{dx_2}{dt} = k_2(A_2 + x).$$

At equilibrium :

$$\frac{dx}{dt} = k_1(A_1 - x) - k_2(A_2 + x) = 0$$

$$\frac{k_1}{k_2} = \frac{A_2 + x}{A_1 - x}$$

Suppose 100 per cent. of dextrose present at the commencement of the experiment, at equilibrium 58 per cent. would be present and 42 per cent. transformed ; therefore :

$$x = 42$$

$$\frac{k_1}{k_2} = \frac{0 + 42}{100 - 42} = \frac{42}{58}$$

$$k_1 + k_2 = 0.0036.$$

$$k_1 = 0.0015 \text{ and } k_2 = 0.0021.$$

It is possible to calculate what will be the amount of mannose present at any time t during the change which the mannose-guanidine undergoes in aqueous solution. It must be assumed that the transformation of dextrose, lævulose, and mannose may be represented by the following scheme :

X = an intermediate substance the concentration of which at any time is negligible (Jungius, *Zeitsch. physikal. Chem.*, 1905, 52, 99).

If mannose-guanidine be transformed at any moment into lævulose- and dextrose-guanidine in the proportions of 0.0021 and 0.0015, since the values of the $[\alpha]_D$ of lævulose- and dextrose-guanidine are respectively -48.54° and $+32.15^\circ$, the $[\alpha]_D$ of the mixture would be -14.9° . Because $\frac{21}{36} \times -48.54 - \frac{15}{36} \times 32.15 = -14.9^\circ$ must be

the rotation angle of the mixture of dextrose and lævulose formed from mannose. Consequently, at every moment the mannose guanidine $[\alpha]_D + 10.03^\circ$ is being transformed into a mixture with $[\alpha]_D - 14.9^\circ$. After one hour the $[\alpha]_D$ was found to be $+6.38^\circ$; therefore the percentage of mannose remaining at that time is :

$$\frac{6.38 - (-14.9) \times 100}{10.03 - (-14.9)} = 85.3.$$

It is assumed that the fall in the angle is proportional to the amount of mannose transformed.

The calculated values agree very fairly with the experimental percentages of mannose obtained from its hydrazone (see p. 1024). Special precautions were taken in the estimation of the hydrazones. Bourquelot and Hérissé's directions (*Compt. rend.*, 1899, 129, 339) were followed as to the quantities to be used, and in every case the hydrazone was precipitated at 0° , and kept at that temperature for two hours before it was filtered off. It was found that no osazone was precipitated under these conditions, and the presence of lævulose did not interfere with the estimation. The hydrazone was collected on a weighed filter paper, washed with cold water and ether, and dried at 100° :

0.4955 mannose gave 0.7305 hydrazone, mannose = 98.28 per cent.

0.7275 „ mixed with 0.3272 lævulose gave 1.0785 hydrazone, mannose = 98.9 per cent.

0.4045 mannose mixed with 1.2985 lævulose gave 0.6005 hydrazone, mannose = 98.1 per cent.

The agreement in the results is well within the experimental error of the determination.

At first it was thought that the passage of mannose into dextrose could be represented by the scheme :

When dextrose and lævulose are in equilibrium, the specific rotation of the mixture is -1° , and the proportions of the two sugars are nearly 58:42. The value of $k_1 + k_2$, obtained from the change in the rotation angle of mannose guanidine, is 0.0036, and the value of k_1 , obtained from the weights of mannose hydrazone, is 0.00086. Therefore the value of $k_2 = 0.00274$, and this represents the velocity constant of the change $X \rightarrow M$; but as mannose cannot be detected in guanidine-dextrose and -lævulose solutions until equilibrium in optical activity has been established, it follows that $X \rightarrow M$ must have an extremely small velocity. The scheme thus described is not in keeping with the experimental facts.

Another representation would be that put forward by Lobry de Bruyn, namely :

If this were so, starting with mannose guanidine it would be expected that the lævulose would always be in slight excess until the equilibrium between lævulose and dextrose had been established. From results obtained from an investigation of mannose-soda, it would appear that lævulose is always in excess until after the equilibrium angle is reached. As the mannose continues to disappear, the dextrose increases until 5 per cent. of mannose is left, together with 51.5 per cent. of dextrose and 43.5 per cent. of lævulose. It must be noticed that these are the quantities of the three sugars present when optical equilibrium has been reached in the case of dextrose- and lævulose-guanidine.

In the representation described on p. 1026,

it is assumed that mannose gives rise to a mixture of lævulose and dextrose, the former being in the predominant quantity. The $[\alpha]_D$ of the mixture is -14.9° , and it contains 58 per cent. of lævulose and 42 per cent. of dextrose. If mannose passes to both lævulose and dextrose, the proportions of lævulose and dextrose will be by Wegscheider's test for side reactions independent of the time and constant. From experiments with solutions of mannose-soda it has been found that the ratio of fructose and glucose formed is 54:46 up to the tenth hour of the change. On the assumption of such a side reaction the quantities of mannose present in solutions of mannose-soda have been calculated with fair accuracy. The equality of the velocity constants of the guanidine compound of the three sugars can be explained by considering the final equilibrium angle (-0.72°) and the angles observed from time to time. Actually the mannose passes with a velocity constant of 0.00086 into a mixture of dextrose and lævulose with a calculated $[\alpha]_D -14.8^\circ$. This mixture passes into an equilibrium mixture $[\alpha]_D -0.72^\circ$ with a more rapid velocity. At every moment of the change, lævulose and dextrose, in the proportions of 58 to 42, are being formed, and this mixture then passes to an equilibrium mixture $[\alpha]_D -0.72^\circ$ of lævulose and dextrose in the proportions of 42:58. At every moment, from one part of mannose, 0.0005 part of lævulose and 0.00036 part of dextrose are being formed. These change into an equilibrium mixture of 0.0005 part of dextrose and 0.00036 part of lævulose, so that while 58 parts of lævulose are formed at the same time as 42 parts dextrose, the 58 parts of lævulose

pass to 58 parts dextrose in the same time that 42 parts dextrose furnish 42 of lvulose. The reason why the $[\alpha]_D - 0.72^\circ$ is reached while 50—51 per cent. of mannose is present is that the remaining mannose guanidine, with $[\alpha]_D 10.03 \times 0.57 = 5.7$, is in contact with a mixture with an $[\alpha]_D$ of $-14.9 \times 0.43 = -6.4$; therefore the total $[\alpha]_D$ is -0.7° , that is, the equilibrium $[\alpha]_D$. The change of mannose into lvulose and dextrose continues, but cannot be followed by the polarimeter.

Mannose passes to lvulose and dextrose, and these attain an equilibrium mixture with $[\alpha]_D - 0.72^\circ$. Actually the change followed optically is equivalent to

$M \rightarrow$ equilibrium mixture of dextrose and lvulose $[\alpha]_D - 0.72^\circ$.

Such a change would be represented by $K_1 = \frac{1}{t} \log \frac{a_0 - a_\infty}{a_t - a_\infty}$ and the constant would be the same as in the case of lvulose and dextrose.

In the later stages of the change disturbing factors are more marked; the intermediate substance X , the concentration of which may be considered small, owing to its relatively rapid change into dextrose and lvulose, furnishes acids at the expense of the sugars. There would seem to be a limit at which X yields dextrose or lvulose; when this is reached X continues to give rise to acids, causing a disappearance of the sugars until the hydroxyl ions disappear and the reaction stops. It will be shown in a later communication that from the determination of the reducing power of alkaline sugar solutions after optical equilibrium is reached the alkalinity goes on decreasing, and the dextrose and lvulose disappear, but the ratio of the amounts of dextrose to lvulose remains constant. Moreover, it has been shown that the yield of glucosazone after reaching a maximum diminishes, and in the case of mannose guanidine the sugar decreases uniformly until 8 per cent. of it is left.

An attempt was made to determine the velocity of change of the reducing power during the mutarotation of dextrose guanidine. Owing to the presence of the nitrogenous base, Pavy's method was alone available. The modification described by Peska (*Chem. Zeit. Rep.*, 1895, 257) was employed. The lvulose formed was destroyed by treatment with hydrochloric acid according to Sieben's method (*Zeitsch. anal. Chem.*, 1885, 24, 137). During the estimation a difficulty was encountered owing to the presence of the guanidine: on warming the Pavy's solution to 80° and adding the sugar solution, a turbidity appeared which made the disappearance of the blue colour of the solution rather difficult to detect. Nevertheless very fairly concordant results were obtained. The following table shows the values obtained:

(a) One hundred c.c. of Pavy's solution required 20.3 c.c. of a 4 per cent. dextrose solution. Therefore 100 c.c. Pavy's solution = 0.0802 gram dextrose.

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(b) One hundred c.c. of Pavy's solution required 22.5 c.c. of a 4 per cent. lævulose solution. Therefore 100 c.c. Pavy's solution = 0.09 gram lævulose.

(c) One hundred c.c. of Pavy's solution was titrated with 20 c.c. of a 5.0258 per cent. solution of dextrose guanidine diluted to 200 c.c.

(d) Ten c.c. of a 5.0258 per cent. solution of dextrose guanidine were heated for three hours to 100° with 6 *N*-hydrochloric acid according to the directions given by Muller (*Chem. Zeit.*, 1888, 12, 240). After neutralisation the volume was made up to 100 c.c., and 100 c.c. of Pavy's solution were used for the titration.

Hours.	$[\alpha]_D^{37.5}$	c. c.c. dextrose guanidine solution required for 100 c.c. Pavy's solution 20.2 c.c. were found to contain 0.0802 gram dextrose, calc. = 0.0830 or 0.410 gram in 100 c.c.	d. c.c. after boiling with HCl, required for 100 c.c. of Pavy's solution.	F : G = (d - c) : c.	Per cent. lævulose in mixture of dextrose and lævulose.
0	+33.52°	20.2	21.0	0.039	3.7
1	19.49	20.4	24.5	0.20	16.7
2	11.34	20.8	27.8	0.336	25.2
3	6.57	21.2	32.1	0.514	34
4	3.97	21.4	34.55	0.64	41
5	2.28	21.7	36.3	0.67	40
6	0.99	21.8	38.4	0.76	43
13*	0.99	26.7	42.5	0.59	37

* And 35 hours at the ordinary temperature.

A similar experiment was performed with lævulose guanidine.

(a) Twenty c.c. of a 4.275 per cent. solution of lævulose guanidine were diluted to 200 c.c., and 100 c.c. of Pavy's solution were used for the titration.

(b) Ten c.c. of a 4.275 per cent. solution were heated for three hours with 6 *N*-hydrochloric acid, neutralised, and made up to 100 c.c., and 100 c.c. of Pavy's solution were used for the titration.

Hours.	$[\alpha]_D^{36}$	a. c.c. lævulose guanidine solution required for 100 c.c. of Pavy's solution.	b. c.c. after boiling with HCl, required for 100 c.c. of Pavy's solution.	F : G = (b - a) : a.	Per cent. lævulose in mixture of dextrose and lævulose present.
0	-47.80°	24.0	—	—	—
1	32.37	24.0	96.6	3.0	75
2	22.08	24.05	60.2	1.5	60
3	15.42	24.2	53.2	1.17	54
4½	8.99	24.75	49.2	0.98	49
6	5.96	25.0	47.75	0.91	47
8	3.42	25.35	47.0	0.85	46
10	—	26.4	46.75	0.77	43
24	—	29.15	48.75	0.67	40

In spite of the difference of the reducing powers of dextrose and lævulose, the numbers in column *a* have been taken as proportional to the amounts of lævulose and dextrose respectively. The difference is not great and will affect the percentages of lævulose only slightly, especially when the unavoidable experimental errors in the values in column *b* are considered.

The reducing power of the solutions does not change appreciably, and the small increase in the number of c.c. may be accounted for by the inferior reducing powers of the acids which are slowly produced.

In the case of dextrose guanidine, after the sixth hour, the ratio of dextrose to lævulose, or ketohexose, remains constant, or nearly so, and although the dextrose is disappearing, the lævulose is disappearing at the same rate. In the case of lævulose guanidine, the experiment was performed at a somewhat lower temperature; for example, 36° instead of 37·25°; consequently the velocity of transformation was slower, and it was not until the tenth hour that the ratio of dextrose to lævulose became constant. This constancy of the ratio of dextrose to lævulose when optical equilibrium has been obtained has been confirmed in the action of water on dextrose-soda and lævulose-soda.

The calculated proportions of dextrose and lævulose present when $[\alpha]_D = -1^\circ$ are 58 per cent. and 42 per cent. respectively; the proportions found experimentally, 57—60 and 40—43 per cent. respectively, are in very fair agreement with these numbers.

The conclusions to be drawn from the mutarotation of solutions of dextrose-, lævulose-, and mannose-guanidine are:

(1) The fall in angle to a constant minimum represents in the case of dextrose- and lævulose-guanidine an apparent equilibrium between dextrose and lævulose through an intermediate substance *X*, the concentration of which at any moment is very small:

(2) The fall in angle to a constant minimum in the case of mannose guanidine represents the formation of lævulose and dextrose according to the scheme:

(3) The velocity constant for the transformation of dextrose to lævulose = 0·0015.

The velocity constant for the transformation of lævulose to dextrose = 0·0021.

The velocity constant for the transformation of mannose to lævulose and dextrose = 0·00086.

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The velocity constant for the transformation of mannose to lævulose = 0·0005.

The velocity constant for the transformation of mannose to dextrose = 0·00036.

The velocity of the reverse change of lævulose and dextrose into mannose is very small. (The velocity constants were determined at 37°.)

(4) There is a continual slow disappearance of X to form acids, accompanied by disappearance of dextrose and lævulose in constant proportion, and by the disappearance of mannose according to the scheme :

(5) The velocity constant for the disappearance of alkali in lævulose guanidine = 0·000275.

The velocity constant for the disappearance of alkali in dextrose guanidine = 0·000156.

The velocity constant for the disappearance of alkali in mannose guanidine = 0·000127.

The difference in the first two velocity constants is too large ; probably it may be due to experimental errors, but if the concentration of X at any moment is not always negligibly small, part of X may change to acids instead of to a sugar.

These conclusions are similar in substance to those put forward by Wohl from the study of the results of the chemical changes observed by Lobry de Bruyn.

In our investigations attempts have been made to follow the course of the chemical changes by quantitative methods, and to avail ourselves of as many independent methods as we could use to determine the values of the constants involved.

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