plant physiology asks and their solution will perhaps be aided by the isolation and the study of the components of the leaf dyestuff. These questions refer to the possibility of a chemical function of chlorophyll and to its nature.

BERLIN-DAHLEM, GERMANY.

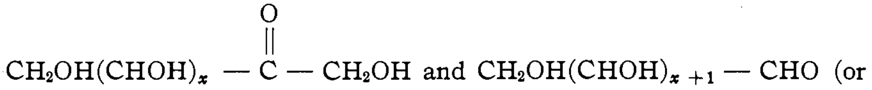
[CONTRIBUTION FROM THE KENT CHEMICAL LABORATORY OF THE UNIVERSITY OF CHICAGO.]

ON THE ESTERS, AS WELL AS THE MONOMOLECULAR β- AND γ-LACTONES, OF *d*-MANNONIC AND *d*-GLUCONIC ACIDS; ON ORTHO-BIS-*d*-GALACTONIC ACID, *d*-GALACTONIC γ-LACTONE AND ITS MONO-HYDRATE.

BY OSCAR F. HEDENBURG.

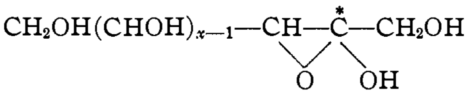
Received December 5, 1914.

A very condensed description of the properties and methods of preparation of the various compounds named in the above title has very recently been published by Nef,[1] who also discusses in detail the significance of the discovery of α-, β- and γ-lactones of the polyhydroxy acids, $C_nH_{2n}O_{n+1}$, in coming to a decision on the question of the constitution of the α- and β-modifications of aldose and ketose sugars, as well as of the α- and β-glucosides. He has reached the conclusion that the various crystalline forms of the simple sugars,[2] including also malt and milk sugars, are to be represented either by the free ketose or aldose structure,



$$CH_2OH(CHOH)_x - \overset{\overset{O}{\|}}{C} - CH_2OH \text{ and } CH_2OH(CHOH)_{x+1} - CHO$$

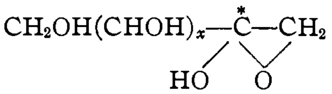
(or at times by a corresponding ketose or aldose monohydrate structure, analogous to chloral hydrate, etc.), or, by a monomolecular α-lactone formula,



$$CH_2OH(CHOH)_{x-1}-\underset{\diagdown\, O\, \diagup}{CH-\overset{*}{C}}\underset{\diagdown OH}{}-CH_2OH$$

2,3-α-Ketose lactone.

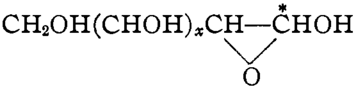
, or



$$CH_2OH(CHOH)_x-\underset{HO\diagup\;\diagdown O \diagup}{\overset{*}{C}-CH_2}$$

1,2-α-Ketose lactone.

and



$$CH_2OH(CHOH)_x\underset{\diagdown\, O\, \diagup}{CH-\overset{*}{C}HOH}$$

α-Aldose lactone.

Generally only one of these two, or, in the case of the ketoses, three forms,

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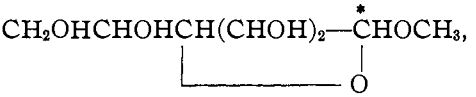
[1] *Ann.*, 403, 273-9, 306-331 (1914).

[2] In many cases the hydrazones, oximes, anilides and osazones of aldose and ketose sugars are known to show multarotation; this is unquestionably due to the existence of two or more analogous structural isomers, which have frequently been isolated, but have hitherto almost invariably been regarded as space isomers.
J. U. NEF.

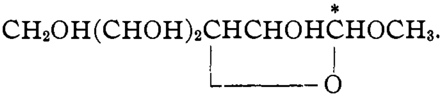
can be obtained pure by crystallization; the other modification, when isolated by Tanret's method for example, usually consists only of mixed crystals of which theoretically a limitless number are possible. Thus *α*-*d*-glucose, $[\alpha]_D^{20} = +104°$, m. p. 156°, must be represented by the *α*-lactone formula, whereas Tanret's *β*-*d*-glucose, $[\alpha]_D^{20} = +22.5°$, can not conceivably represent the pure aldehyde modification of *d*-glucose whose specific rotation must be slightly laevo, but consists of a mixture of about 80% of aldehyde sugar, contaminated with 20% of *α*-lactone. Crystallized *d*-mannose, $[\alpha]_D^{20} = -2°$, on the other hand, corresponds to the free aldehyde form, whereas the *α*-lactone modification, which exists to the extent of about 20% in an aqueous solution of *d*-mannose after 24 hrs. standing, $[\alpha]_D^{20} = +16°$, and which must undoubtedly possess $[\alpha]_D^{20} =$ over $+100°$, has not as yet been isolated in a pure condition. Crystallized *d*-fructose finally, whose melting point invariably ranges from 105°–115°, probably consists of a mixture of the two *α*-lactones, 2,3- and 1,2-*α*-*d*-fructose, etc., etc.

The so-called *α*- and *β*-glucosides, on the other hand, possess respectively, *γ*- and *β*-lactone structure, *e. g.*, *α*-methyl *d*-glucoside,



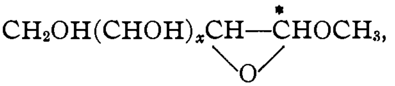
$$CH_2OHCHOHCH(CHOH)_2—\overset{*}{C}HOCH_3 \quad (\text{ring: } CH—O—\overset{*}{C})$$

and *β*-methyl *d*-glucoside,



$$CH_2OH(CHOH)_2CHCHOH\overset{*}{C}HOCH_3 \quad (\text{ring: } CH—O—\overset{*}{C})$$

It will be seen at once, therefore, that only the *α*-glucosides retain the *γ*-lactone structure hitherto ascribed in all the text books also to the *α*- and *β*-sugar modifications, as well as to the *β*-glucosides; they should therefore be renamed *γ*-glucosides in accord with their structure, especially as *α*-glucosides of the formula,



$$CH_2OH(CHOH)_xCH—\overset{*}{C}HOCH_3 \quad (\text{ring: } CH—O—\overset{*}{C})$$

are also possible theoretically, although representatives of this class have not yet actually been isolated.

The problem assigned to me by Dr. Nef, therefore, was to confirm and extend his observations on the preparation and properties of the various derivatives of *d*-mannonic, *d*-gluconic and *d*-galactonic acids named above, as well as to make a thorough search for other derivatives possibly overlooked by him and especially to analyse, titrate and to determine the molecular weights and physical constants of the new compounds obtained. Many of my results are to be found in Nef's paper in Liebig's Annalen; they are, however, given here in greater detail and many new observations are included.

Experimental Part.

I. On Ethyl *d*-Mannonate, and on *d*-Mannonic β- and γ-Lactones.

***d*-Mannonic β-Lactone.**—This is the normal and practically the only lactone formed from free *d*-mannonic acid, $[\alpha]_D^{20} = -1°$,[1] at ordinary temperatures; γ-lactone formation also takes place, although very slowly at lower temperatures, but far more rapidly as the temperature is raised. In order, therefore, to obtain the maximum yield of β-lactone an aqueous solution of *d*-mannonic acid should not be heated higher, nor longer, than absolutely necessary. Such a solution[2] is best prepared by adding the calculated amount of crystallized oxalic acid in water to an aqueous solution of calcium *d*-mannonate heated to 50°. The mixture is thereupon cooled within five minutes to about 20° and the calcium oxalate filtered off as rapidly as possible. The water must also be distilled off quickly from the filtrate at the lowest possible temperature and pressure. The residual gum may then be transformed into the β-lactone by prolonged heating under 20 mm. pressure at first at 50°, but finally up to 100°.

The β-lactone, which was used to determine constants and to perform various experiments (see below), was prepared from free *d*-mannonic acid obtained from barium *d*-mannonate by rapid treatment with dilute sulfuric acid at 95° to 98°. The salt was prepared by dissolving *d*-mannonic γ-lactone in a dilute solution of one and one-half times the calculated amount of crystallized barium hydroxide and heating for ten minutes on a boiling water bath. The calculated amount of sulfuric acid was then added to liberate mannonic acid; the solution was thereupon rapidly adjusted so that it contained only a trace of barium, filtered free from barium sulfate, cooled and distilled at 20 mm. pressure with the surrounding bath at 40–45° until no more moisture condensed in the neck of the flask. The resulting gum, a mixture of *d*-mannonic acid and β- and γ-lactones, is very soluble in absolute alcohol. Eight grams of γ-lactone were changed into barium *d*-mannonate by 21.28 g. barium hydroxide. The gum, obtained as described above, was kept in the flask about 15 hrs. longer and became partly crystalline. The gum that still remained dissolved readily, but the crystalline mass went into solution with considerable difficulty in 400 cc. of boiling absolute alcohol. After distilling off half of the solvent at ordinary pressure and cooling, 1.45 g. of pure β-lactone, melting at 161–162°, $[\alpha]_D^{20} = +111.85°$, came out in transparent, octahedral crystals. Mixed crystals of β- and γ-lactones, 3.66 g., melting from 134–150°, were obtained in four subsequent fractions on further concentration of the alcoholic filtrate.

Another experiment was carried out with 11 g. of γ-lactone in the same way, but here the adjustment for barium was made in one-half an hour,

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[1] *Ann.*, 403, 314 (1914).

[2] *Ibid.*, 403, 310 (1914).

i. e., more quickly than in the former experiment. The residual gum, after standing about 36 hrs. also became partly crystalline, and solution was effected with difficulty by 500 cc. of boiling absolute alcohol. After filtering off traces of barium salt, the solution was concentrated to about 300 cc. by distillation at 20 mm. pressure, and in the course of two days 4.48 g. of β-lactone, melting between 156° and 162°, separated out without seeding. The filtrate was concentrated to about 100 cc. and 1 g. of impure γ-lactone was obtained, which, recrystallized from 100 cc. of absolute alcohol, gave 0.65 g. melting at 149.5° with $[\alpha]_D^{20} = +57.05°$.

The following analytical results, molecular weight determination, specific rotation and other data were obtained with a preparation of pure β-lactone melting, after a second crystallization from absolute alcohol, between 161° and 162°. The β-lactone requires about 100 parts of boiling absolute alcohol for solution, from which, on standing at room temperatures, a very large amount crystallizes out unchanged in transparent, measurable octahedra. This lactone can be recrystallized from water, but this is not an advantageous process since an aqueous solution changes rapidly, even at 20°, to free *d*-mannonic acid.

0.2083 g. gave 0.3096 g. CO_2 and 0.1072 g. H_2O.

Calc. for $C_6H_{10}O_6$: C, 40.45; H, 5.62; found: C, 40.53; H, 5.72.

A titration was carried out as follows: the lactone was dissolved in an excess of 0.1 *N* KOH and the solution heated on a boiling water bath for 10 min. to form completely the potassium salt. The cooled solution was titrated back with 0.1 *N* H_2SO_4 (phenolphthalein as indicator) to excess, whereupon carbon dioxide was expelled by boiling. The solution, cooled again, was adjusted to the end point with 0.1 *N* KOH. 0.5051 g. used 28.26 cc. 0.1 *N* KOH instead of 28.36 cc. calculated for $C_6H_{10}O_6$.

A molecular weight determination was carried out according to the boiling point method of McCoy[1] with 0.3552 g. substance in freshly prepared absolute alcohol.[2]

Vol. of solution. Cc.	Rise in B. P.	Mol. wt. found.	Mol. wt. calc. for $C_6H_{10}O_6$.
25.60	0.107°	202.0	
28.50	0.102°	190.6	
33.30	0.096°	173.3	178
	Av.,	185.3	

The specific rotation of the β-lactone in 4% solution was found to be +111.85° six minutes after solution, for 0.4021 g. dissolved in 10.0456 g. of water gave +4.35° in a one decimeter tube. The specific gravity of the solution was considered 1.011, as were all subsequent 4% aqueous solutions. Observations were made with this tube kept at room temperature for 23 days to follow the changes in optical activity.

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[1] *Am. Chem. J.*, **23**, 353 (1900).

[2] The absolute alcohol used here and later was freshly prepared by redistillation over quick-lime. A middle fraction was used after standardization by determination of the molecular weight of benzoic acid.

TABLE I.

Time after solution.	Observed angle.	$[\alpha]_D$.
6 min.	+4.35°	+111.85°
1 hr. 40 min.	+3.95°	+101.54°
3 hr. 40 min.	+3.30°	+ 84.84°
5 hr. 30 min.	+2.53°	+ 65.03°
20 hr.	+1.18°	+ 30.28°
1 day 2 hr.	+1.15°	+ 29.57°
1 day 4 hr. 30 min.	+1.10°	+ 28.28°
1 day 20 hr.	+1.10°	+ 28.28°
2 days 2 hr.	+1.10°	+ 28.28°
2 days 21 hr.	+1.10°	+ 28.28°
3 days 4 hr.	+1.10°	+ 28.28°
4 days 20 hr.	+1.00°	+ 25.71°
5 days 21 hr.	+1.00°	+ 25.71°
6 days 20 hr.	+1.05°	+ 27.00°
15 days	+1.20°	+ 30.85°
23 days	+1.55°	+ 39.85°

When the specific rotation reached +28.28°, the solution evidently contained in equilibrium about 25% of β-lactone together with about 75% of free *d*-mannonic acid. Traces of γ-lactone were also present. At this point 70% of the original β-lactone can be recovered, either by evaporation of the aqueous solution over H_2SO_4 *in vacuo* or by rapid distillation at 20 mm. pressure with the bath at 40°. Thus a solution of 8.1 g. of β-lactone in 32.4 g. of water which stood for 24 hrs. was freed from water by distillation at 20 mm. pressure with the surrounding bath at 35–40°. Before all the water was removed crystals separated out; the crystalline residue was loosened and removed from the flask with 100 cc. of cold, absolute alcohol. The crystals thus obtained, 6.58 g., melted between 138° and 155° and gave $[\alpha]_D^{20} = +101.33°$, or, after 29 hrs. standing at ordinary temperatures, +32.18°; this showed that the mixed crystals contained about 90%, 5.9 g., of β-lactone. Furthermore, the alcoholic filtrate gave, after removing the solvent by distillation at 20 mm. pressure, 1.38 g. of solid residue, which yielded, on recrystallization from 25 cc. of warm, absolute alcohol (60°), 0.7 g. of mixed crystals melting between 132° and 142° with $[\alpha]_D^{20} = +77.1°$, and containing, therefore, about 40% of β-lactone (0.28 g.). 6.2 g. or 76.54% of the β-lactone was therefore recovered unchanged.

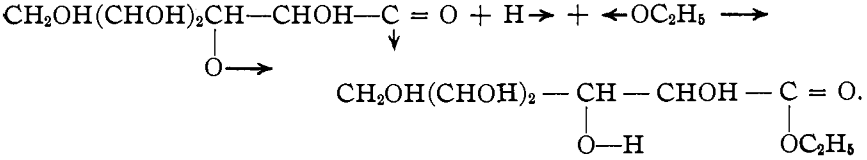
Judging from the optical activity of an aqueous solution of β-lactone at the end of 23 days (+39.85°), as shown in Table I, about 50% of *d*-mannonic γ-lactone must now have been present, since the specific rotation of pure γ-lactone is +51.8°, whereas equilibrium exists between *d*-mannonic acid and *d*-mannonic β-lactone at +28.28°. The abnormal γ-lactone is, therefore, slowly formed from free *d*-mannonic acid by loss of water, and since this reaction, according to observations on pure γ-lactone, is irreversible at 20°, the specific rotation should increase as shown in the table.

When solid *d*-mannonic β-lactone is heated to its melting point, γ-lactone formation also results, which must obviously be due to an intermediate formation of *d*-mannonic acid, produced by the presence of unavoidable traces of water. Thus, 0.3 g. β-lactone, heated in a small distilling flask in an oil bath kept at 156° for three-quarters of an hour, was transformed into 0.3 g. hard gum; this gave, when dissolved in 7.07 g. cold water, $\alpha = 1.3°$ in a one decimeter tube, whence $[\alpha]_D^{20} = +63.9°$; after 18 days' standing at 20°, the specific rotation had fallen to +45.7°. About 80% of the β-lactone must, therefore, have been transformed into γ-lactone.

The γ-lactone is also formed by loss of alcohol, when ethyl *d*-mannonate is heated for a short time at its melting point (cf. ethyl *d*-mannonate).

A fairly rapid transformation into γ-lactone also takes place, when an aqueous solution of β-lactone, or of *d*-mannonic acid is heated at 100°. Thus an approximately 4% aqueous solution of *d*-mannonic β-lactone (0.6244 g. in 14.4346 g. H_2O), when heated for one hour on a boiling water bath and cooled quickly with running water, gave at first a specific rotation of +48.43° ($\alpha = +2.03°$ in a 1 dc. tube); this fell, after standing $17^1/_2$ hrs. at room temperature, to +37.7°. In a second experiment, in which an aqueous solution containing 0.6172 g. β-lactone was heated for five hours on a boiling water bath, the specific rotation of the cold solution was found to be +48.68° at 20° (14.1991 g. H_2O; $\alpha = +2.05°$ in a 1 dc. tube); this changed to +45.83° only, after 18 hrs. standing at room temperature. On evaporating the solution over H_2SO_4 *in vacuo*, crystals, melting between 151° and 152°, and giving $[\alpha]_D^{20} = +52.19°$ (0.5665 g. in 13.2705 g. H_2O gave $\alpha = +2.15°$ in a 1 dc. tube), were obtained; the specific rotation fell to +49.02° after 51 hrs. The crystals were evidently almost pure γ-lactone. This explains why Nef[1] succeeded in obtaining practically pure γ-lactone by simply evaporating, with occasional stirring, an aqueous solution of free *d*-mannonic acid, of *d*-mannonic β-lactone, or of ethyl *d*-mannonate in the presence of a small amount of hydrogen chloride.

Ethyl *d*-Mannonate.—This substance is always formed by the addition of ethyl alcohol to the active molecules of *d*-mannonic β-lactone,



$$\text{CH}_2\text{OH(CHOH)}_2\underset{\underset{\text{O}\longrightarrow}{|}}{\text{C}}\text{H—CHOH—}\underset{\downarrow}{\text{C}} = \text{O} + \text{H}\rightarrow + \leftarrow\text{OC}_2\text{H}_5 \longrightarrow$$

$$\text{CH}_2\text{OH(CHOH)}_2 — \underset{\underset{\text{O—H}}{|}}{\text{C}}\text{H} — \text{CHOH} — \underset{\underset{\text{OC}_2\text{H}_5}{|}}{\text{C}} = \text{O}.$$

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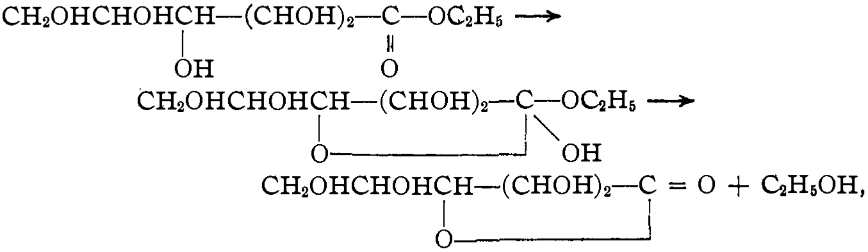
[1] *Ann.*, 403, 309 (1914).

Small amounts of hydrogen chloride or of free *d*-mannonic acid facilitate very much the addition of the reagent. Since, however, the ester is easily converted by intramolecular addition and subsequent loss of alcohol into *d*-mannonic γ-lactone,



$$\begin{array}{l}\mathrm{CH_2OHCHOHCH—(CHOH)_2—C—OC_2H_5} \longrightarrow \\ \qquad\qquad\qquad\ | \qquad\qquad\qquad\qquad \| \\ \qquad\qquad\quad\ \mathrm{OH} \qquad\qquad\qquad\ \ \mathrm{O} \\ \qquad\qquad\quad \mathrm{CH_2OHCHOHCH—(CHOH)_2—C—OC_2H_5} \longrightarrow \\ \qquad\qquad\qquad\qquad\qquad\ | \qquad\qquad\qquad\quad |\diagdown \\ \qquad\qquad\qquad\qquad\qquad \mathrm{O}\text{———————}\lrcorner\ \ \mathrm{OH} \\ \qquad\qquad\qquad\qquad\qquad\qquad \mathrm{CH_2OHCHOHCH—(CHOH)_2—C = O + C_2H_5OH,} \\ \qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\ | \qquad\qquad\qquad\quad | \\ \qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad \mathrm{O}\text{——————}\lrcorner \end{array}$$

a reaction which is also enormously accelerated by the presence of hydrogen chloride or of free *d*-mannonic acid, it is possible to prepare pure ethyl *d*-mannonate only under very definite conditions.

As a result of certain experiments (see below), from which mixed crystals of *d*-mannonic γ-lactone and of ethyl *d*-mannonate were obtained, a method for preparing the ethyl ester quantitatively from the β-lactone was developed as follows: 62 g. of the well-powdered β-lactone were covered in a stoppered flask with 200 cc. of cold absolute alcohol containing 1% of dry hydrogen chloride, and the mixture was thoroughly shaken. Within 25 minutes the compact β-lactone was replaced by a bulky mass of filamentous crystals. The mixture was allowed to stand, however, for 24 hrs., when the crystals were filtered off and thoroughly washed free from hydrogen chloride by cold absolute alcohol. 1.04 g. melting at 158–159° were obtained; on crystallizing a portion of these, 0.53 g., from 60 cc. of hot absolute alcohol, 0.38 g. of the pure, optically inactive product, melting at 160–161°, was recovered. No more ethyl ester could be obtained from the alcoholic filtrates containing hydrogen chloride by removal of the alcohol at reduced pressure, for the solid residue, 1.28 g., now gave, on rinsing with a small amount of absolute alcohol, 0.72 g. of insoluble crystals melting between 148° and 151° with $[\alpha]_D^{20} = +49.21°$. These evidently consisted of almost pure γ-lactone produced from the ester by decomposition by the hydrogen chloride.

A better yield was subsequently obtained by using 2.25 g. of β-lactone and only 100 cc. of cold 1% alcoholic hydrogen chloride; the crude, insoluble product, 2.12 g., melted between 155° and 157° and gave by crystallization from 200 cc. of absolute alcohol 1.49 g. of pure ester melting from 160–161°.

The ethyl ester can moreover only be obtained from *d*-mannonic γ-lactone by its preliminary conversion into free *d*-mannonic acid and β-lactone. The β-lactone then adds alcohol as described above. Thus 2 g. of the γ-lactone were dissolved in one and one-half times the calculated volume of normal sodium hydroxide solution, 16.86 cc., and the solution was warmed to form the sodium salt. Then, after cooling, an equivalent amount of normal hydrochloric acid was added; the water was distilled off at 20 mm. pressure with the bath at 40°. A gum containing sodium chloride was left, which weighed 3.41 g. and of which 3.04 g. dissolved in 80 cc. of hot absolute alcohol. Concentrated alcoholic hydrogen chloride was added to make the solution contain 1% of hydrogen chloride, and 0.74 g. of ester melting at 160–161° was obtained.

The following analysis, molecular weight determination and the data on the action of water and heat were obtained by the use of a pure preparation of ethyl *d*-mannonate melting at 160–161°:

0.1728 g. gave 0.2709 g. CO_2 and 0.1115 g. H_2O.

Calc. for $C_8H_{16}O_7$: C, 42.87; H, 7.14; found: C, 42.76; H, 7.17.

The molecular weight was determined with 0.5083 g. substance in boiling absolute alcohol by McCoy's method; the average of three readings (232, 243, 246) was 240 instead of 224 calculated for $C_8H_{16}O_7$.

Pure ethyl *d*-mannonate, which is very soluble in water, has no optical activity; but the solution becomes faintly dextrorotatory within five hours, due to hydrolysis of the ester, and to the subsequent change of free *d*-mannonic acid into β- and γ-lactones, *e. g.*, 0.4163 g. of substance in 10.0653 g. of water showed no activity in a one decimeter tube, but the Table II records a series of readings which show the changes wrought by the transformation of the ethyl ester.

TABLE II.

Time after solution.	Observed angle.	$[\alpha]_D$.
5 hrs. 10 min.	+0.15°	+ 3.53°
1 day	+0.22°	+ 5.48°
3 days	+0.52°	+12.95°
4 days	+0.62°	+15.44°
5 days	+0.65°	+16.16°
6 days	+0.70°	+17.44°
7 days	+0.75°	+18.68°
8 days	+0.80°	+19.93°
10 days	+0.85°	+21.17°
16 days	+1.08°	+26.90°
26 days	+1.15°	+28.65°

If the specific rotation at the end of 26 days be calculated on the basis of lactone produced by hydrolysis (0.4163 g. of ester gives 0.3308 g. of lactone), it becomes +35.74°, which is in fair agreement with the optical activity (+39.85°) of a solution of β-lactone, or of free *d*-mannonic acid, at the end of 23 days (see above).

It is evident from the data given, and this was also proved by special experiment, that the ester can be recovered unchanged from an aqueous solution, if the water be removed within an hour; thus, 0.3711 g. of ester in 8.9664 g. H_2O showed no optical activity; the solvent was distilled off at once at 20 mm. pressure with the bath at 40°. The residue was crystallized from 10 cc. of absolute alcohol and 0.24 g. of ester, melting at 160–161°, was recovered.

The ester is rapidly converted into γ-lactone by loss of ethyl alcohol, perhaps with intermediate formation of β-lactone (see above) when heated in a distilling flask under reduced pressure just above its melting point. One gram of ester, heated between 162° and 170° for about one-half an hour, lost 0.24 g. in weight. The stiff residual gum, 0.76 g. recrystallized from about 10 cc. of absolute alcohol, gave 0.37 g. *d*-mannonic γ-lactone which melted between 150° and 154° with $[\alpha]_D^{20} = +51.52°$. A second experiment with 1.2 g. ester, which was heated at 164° for 50 mins., gave 0.93 g. hard gum from which 0.63 g. *d*-mannonic γ-lactone, melting at 151–152° and with $[\alpha]_D^{20} = +48.25°$ was obtained.

Ethyl *d*-mannonate, which is optically inactive, and *d*-mannonic γ-lactone ($[\alpha]_D^{20} = +51.8°$) give a large number of mixed crystals melting from 135–155°, the specific rotations of which naturally fall between those of the pure substances and remain constant for some hours. For a long time Nef and I thought that a third monomolecular lactone of *d*-mannonic acid was present in these mixtures, but they all gave an iodoform test due to the presence of ethyl *d*-mannonate.

Thus, a solution of 0.5 g. of β-lactone in 100 cc. of absolute alcohol containing a small amount of dry hydrogen chloride was heated at about 75° under a reversed condenser for two hours. The alcohol was distilled off at 20 mm. pressure with the temperature of the surrounding bath between 30° and 35°; the residue was then crystallized from 30 cc. of absolute alcohol. The needles obtained, 0.2 g., melted at 139°, and gave $[\alpha]_D^{20} = +35.88°$ without change after 24 hrs. standing.

Again, 1 g. of β-lactone and 30 cc. of absolute alcohol, heated in a sealed tube at 120° for 5 hrs., gave 0.83 g. of concentric needles, melting between 140° and 142° with $[\alpha]_D^{20} = +45.63°$; the product was, therefore, mainly *d*-mannonic γ-lactone mixed with about 10% of ethyl ester.

A preparation consisting of mixed crystals of *d*-mannonic β- and γ-lactones (the melting point and specific rotation of which had not been determined) when treated with cold absolute alcohol containing a small amount of dry hydrogen chloride, soon deposited bulky, apparently homogeneous crystals melting at 140–141°, the specific rotation of which remained constant in aqueous solution at +24.8°.

Nef[1] and Lewis obtained many such mixed crystals when working with mixtures of *d*-mannonic acid and *d*-mannonic β- and γ-lactones both in the presence and absence of hydrogen chloride.

Finally it should be especially emphasized that pure *d*-mannonic γ-lac-

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[1] *Ann.*, 403, 310 (1914).

tone, treated in the cold or hot with alcoholic hydrogen chloride, gives no ethyl ester.

***d*-Mannonic γ-Lactone.**—This lactone was discovered by Fischer and Hirschberger,[1] but it was contaminated with β-lactone so that it melted over a range, 149–153°, and showed a high specific rotation, +53.81°, in 10% concentration. Nef[2] has shown that the pure γ-lactone melts sharply at 151° and gives $[\alpha]^{20}_{D} = +51.8°$ in 4% concentration; this lactone moreover remains unchanged in aqueous solution at 20° for a long time, whereas the far more strongly active β-lactone, $[\alpha]^{20}_{D} = +111.85°$, is rapidly hydrolyzed to mannonic acid (a gum very soluble in cold absolute alcohol, $[\alpha]^{20}_{D} = -1°$) to the extent of 75%, at which point the β-lactone exists in equilibrium at 20° with the free acid. Since the γ-lactone has repeatedly been analyzed and titrated, it was only necessary to make a molecular weight determination and thus prove that the substance is monomolecular. The determination was made with McCoy's boiling point apparatus, using absolute alcohol as the solvent, in which it is far more soluble than the β-lactone.

0.5391 g. of lactone gave 199 for the molecular weight instead of 178 calculated for $C_6H_{10}O_6$.

						Av.
Vol. of solution.	28.60	30.00	31.20	33.20	35.50	
Rise in B. P....	0.145°	0.141°	0.134°	0.130°	0.119°	
Mol. wt. found.	203	198	201	194	199	199

The γ-lactone reacts with water when heated in aqueous solution at 100°. *d*-Mannonic acid is first formed, from which the β-lactone is then produced; its presence can easily be proved since the specific rotation of the solution decreases in a few hours. The following experiments illustrate these changes: An approximately 4% solution of γ-lactone (0.5480 g. in 13.5908 g. H_2O), when heated for one hour on a boiling water bath and cooled quickly with running water, gave at first a specific rotation of +50.53° ($\alpha = +1.98°$ in a 1 dc. tube); this became +48.5° after 72 hrs. standing at room temperatures. Another experiment, in which an aqueous solution of γ-lactone was heated for five hours on a boiling water bath, gave on rapid cooling a specific rotation of +51.22° (0.5311 g. in 13.0843 g. H_2O gave $\alpha = +2.02°$ in a 1 dc. tube); this fell after 15 hrs. to +46.91°. The solution, evaporated over H_2SO_4 *in vacuo*, yielded a solid residue, 0.5374 g, melting between 132° and 148°; 0.4933 g. of this dissolved in 10.5960 g. H_2O gave a specific rotation of +59.14° ($\alpha = +2.66°$ in a 1 dc. tube); after 40 hrs. standing this had fallen to +46.69°. Evidently more β-lactone was formed from free *d*-mannonic acid, also at first present, which accounts for the higher specific rotation of the solid residue.

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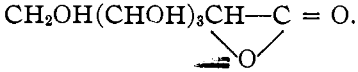
[1] *Ber.*, **22**, 3231 (1889).

[2] *Ann.*, 403, 316 (1914).

II. On Ethyl *d*-Gluconate and on *d*-Gluconic β- and γ-Lactones.

Nef presents with great precision in his Annalen paper[1]—the end result of years of experimental work—the most favorable conditions, A, for the conversion of free *d*-gluconic acid (a viscous syrup, $[\alpha]_D^{20} = -1.7°$, very soluble in cold absolute alcohol), or of *d*-gluconic β-lactone into ethyl *d*-gluconate (bulky, fibrous crystals, $[\alpha]_D^{20} = -1°$, melting between 60° and 65°); B, for the transformation of free *d*-gluconic acid or of ethyl *d*-gluconate into normal *d*-gluconic β-lactone (transparent prisms, $[\alpha]_D^{20} = +61.7°$, melting point 152°, and soluble in 100 parts of boiling absolute alcohol); and finally, C, for the conversion of any of these three substances at higher temperatures into the abnormal and more stable *d*-gluconic γ-lactone (heavy needles, melting from 134–136°, $[\alpha]_D^{20} = +67.8°$, and soluble in 14 parts of hot absolute alcohol). The situation in this series is complicated by the fact that here alone, among all the polyhydroxy acids $C_nH_{2n}O_{n+1}$ as yet studied, a very marked tendency to polymolecular anhydride formation is noticeable. This phenomenon is due, as Nef has shown, to an intermediate formation of *nascent* monomolecular *d*-gluconic α-lactone,[2]



$$CH_2OH(CHOH)_3CH{-}C = O.$$

The study of these polygluconic anhydrides, which are precipitated from aqueous solution by alcohol, is at present being continued in this laboratory and has been found to present great experimental difficulties; I have consequently limited myself mainly to a further study of the physical and chemical properties of ethyl *d*-gluconate, and of the monomolecular β- and γ-lactones of *d*-gluconic acid.

***d*-Gluconic β-Lactone.**—The new, normal β-lactone has been obtained both from free *d*-gluconic acid and from ethyl *d*-gluconate (see this).

Nef[2] has given precise directions whereby a yield of about 20% of β-lactone can be obtained from anhydrous calcium *d*-gluconate.

I prepared *d*-gluconic β-lactone from free *d*-gluconic acid by treatment of a warm (60°), aqueous solution of 10 g. of anhydrous calcium *d*-gluconate with 2.93 g. of crystallized oxalic acid in water. The solution of *d*-gluconic acid, cooled at once to 20° and filtered, was freed from water by distillation at 20 mm. pressure with the surrounding bath at 40°, until a syrup, containing about 10 g. of water, resulted, whereupon 100 cc. absolute alcohol were added to precipitate traces of calcium salt as well as polygluconic anhydrides. The residual gum, 8.18 g., obtained from the filtrate by removal of water and alcohol at reduced pressure, yielded, on dissolving in about 10 cc. warm absolute alcohol, 1.04 g. β-lactone (in two fractions) melting from 151–154°; this, recrystallized from 25 cc.

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[1] *Ann.*, 403, 322–331 (1914).

[2] *Ibid.*, 403, 322 (1914).

[3] *Ibid.*, 403, 323–325 (1914).

absolute alcohol, gave 0.75 g. pure β-lactone melting at 153° with $[\alpha]_D^{20}$ = 63.4° five minutes after solution.

The following constants and analyses were obtained with preparations of pure β-lactone:

0.1237 g. gave 0.1855 g. CO_2 and 0.0566 g. H_2O.

Calc. for $C_6H_{10}O_6$: C, 40.45; H, 5.92; found: C, 40.90; H, 5.13.

The titration was carried out as previously described. 0.4227 g. substance used 23.61 cc. 0.1 *N* KOH instead of 23.75 cc. calculated for $C_6H_{10}O_6$.

The molecular weight of β-lactone, determined by the boiling point method in McCoy's apparatus (see *d*-mannonic β-lactone) using absolute alcohol and 0.4801 g. substance, was found to be 199.3 instead of 178 calculated for $C_6H_{10}O_6$.

				Av.
Vol. of solution...........	33.2cc.	34.2cc.	35.0cc.	
Rise in B. P..............	0.112°	0.110°	0.108°	
Mol. wt. found............	201.0	199.0	198.0	199.3

Nef[1] found the specific rotation of *d*-gluconic β-lactone at 20° to be +61.7° twelve minutes after solution. The specific rotation was found by me to be +63.4° five minutes after solution (0.4288 g. dissolved in 9.4233 g. H_2O at 20° gave $\alpha = +2.79°$ in a 1 dc. tube). The changes in optical activity of this solution for nearly eight days (after which constancy ensued) are recorded in Table III.

TABLE III.

Time after solution.	Observed angle.	$[\alpha]_D$.	Time after solution.	Observed angle.	$[\alpha]_D$.
5 min.	+2.79°	+63.40°	46 min.	+1.64°	+37.25°
7 min.	+2.75°	+62.50°	59 min.	+1.27°	+29.13°
10 min.	+2.70°	+61.35°	1 hr. 16 min.	+0.98°	+22.37°
12 min.	+2.67°	+60.60°	1 hr. 30 min.	+0.76°	+17.27°
14 min.	+2.60°	+60.47°	1 hr. 45 min.	+0.67°	+15.23°
17 min.	+2.54°	+59.05°	2 hr. 20 min.	+0.50°	+11.36°
18½ min.	+2.50°	+58.13°	2 hr. 35 min.	+0.45°	+10.21°
19 min.	+2.47°	+57.44°	16 hr. 50 min.	+0.47°	+10.64°
22 min.	+2.35°	+53.40°	22 hr. 50 min.	+0.52°	+11.82°
24 min.	+2.30°	+52.26°	26 hr. 35 min.	+0.52°	+11.82°
26 min.	+2.25°	+51.13°	47 hr. 50 min.	+0.62°	+14.09°
35 min.	+1.97°	+44.77°	3 days 18 hr.	+0.76°	+17.27°
			7 days 21 hr.	+0.90°	+20.45°

From this table it is clear that *d*-gluconic β-lactone is converted in two and one-half hours at 20° to the extent of nearly 80% into free *d*-gluconic acid ($[\alpha]_D^{20}$ = —1.7°). It should be especially noticed that temporary equilibrium was maintained with $[\alpha]_D^{20} = +11°$ for 24 hrs.[2]

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[1] *Ann.*, 403, 325 (1914).

[2] According to Nef (*Ann.*, 403, 326 (1914)) aqueous solutions of β-lactone reach $[\alpha]_D^{20} = +9.94°$ after 2½ hrs. standing at 20°; $[\alpha]_D^{20} = +7.71°$ after 4½ hours; a *minimum* at $[\alpha]_D^{20} = +6.24°$ after 26 hrs.; $[\alpha]_D^{20} = +7.95°$ after 46 hrs.; $[\alpha]_D^{20}$ = +9.69° after 70 hrs.; and $[\alpha]_D^{20} = +9.94°$ after 114 hrs.

Dr. Nef suggests that the values for the specific rotation lower than +9.94° may be inaccurate due to fatigue of his research assistant's eyes.

Final equilibrium at 20° in 4% aqueous solutions of *d*-gluconic acid, as well as of β- and γ-lactones, is, however, only reached, when the specific rotation has become about +18° (see below). Such solutions, heated for five hours on a boiling water bath and then quickly cooled, give at first a specific rotation of +32° to +34°, which changes on long standing to about +18°.

Thus, a solution of 0.5748 g. β-lactone in 14.8255 g. H_2O, heated for one hour on a boiling water bath and then cooled rapidly, gave $[\alpha]_D^{20} = +28.89°$ ($\alpha = +1.09°$ in a 1 dc. tube); $[\alpha]_D^{20}$ fell to +25.17° after $2^3/_4$ hrs., and to +23.05° after 24 hrs. standing at room temperatures. In a second experiment a solution of 0.5075 g. β-lactone in 13.0649 g. H_2O, heated for five hours on a boiling water bath and cooled rapidly, gave $[\alpha]_D^{20} = +32.51°$ ($\alpha = +1.23°$ in a 1 dc. tube); $[\alpha]_D^{20}$ fell to +26.91° after $16^3/_4$ hrs. and to +17.72° after $15^1/_2$ days standing at room temperatures. This solution must have contained at first ($[\alpha]_D^{20} = +32.51°$) about 50% of β- and γ-lactones of which 8 to 12% was β-lactone, for an aqueous solution, originally containing pure *d*-gluconic γ-lactone (cf. Table V), gave, after standing $4^3/_4$ days at room temperatures, $[\alpha]_D^{20} = +33.98°$; this fell to +26.46° after 48 hrs. further standing at room temperatures

It is consequently obvious from the data presented that the situation here is entirely analogous to that observed in the case of free *d*-mannonic acid and its β-lactone. An aqueous solution of free *d*-gluconic acid (see below) or of *d*-gluconic β-lactone rapidly reaches an equilibrium with the specific rotation + 10° or +11°; since, however, abnormal γ-lactone formation also takes place, but extremely slowly at 20°, there is a gradual rise in the specific rotation of such solutions until a limit is reached with $[\alpha]_D^{20} = +18°$. There is in the present case no irreversible and complete transformation into γ-lactone, because *d*-gluconic γ-lactone is, in contrast to *d*-mannonic γ-lactone, slowly acted upon by water at 20°.

Ethyl *d*-Gluconate.—This ester crystallizes from absolute alcohol, in which it is very soluble, in bulky, fibrous needles; these contain, air-dried, much alcohol of crystallization and melt from 40–50°; after standing over H_2SO_4 *in vacuo*, they lose the alcohol and melt between 62° and 63°. I observed no optical activity in a 4% aqueous solution of the ester, whereas Nef[1] obtained $[\alpha]_D^{20} = -0.997°$.

The ester is formed by the addition of ethyl alcohol to the active molecules of *d*-gluconic β-lactone (cf. ethyl *d*-mannonate) in the presence of small quantities of the free *d*-gluconic acid or hydrogen chloride. In many experiments large amounts of ester were obtained by dissolving a residual gum, consisting of *d*-gluconic acid and of β- and γ-lactones, in boiling absolute alcohol, whereupon the alcohol was removed at reduced pressure, until a thin syrup remained; this would then, on standing, be spontaneously

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[1] *Ann.*, 403, 327 (1914).

transformed into a mass of crystals of γ-lactone and of ethyl ester, which could easily be separated by fractionation from absolute alcohol.

The ethyl ester was also obtained in the following definite way: A solution of free *d*-gluconic acid, obtained from 9.53 g. anhydrous calcium *d*-gluconate and 2.73 g. crystallized oxalic acid, was digested a few moments on a boiling water bath, cooled, and filtered free from calcium oxalate. The water was removed from the filtrate by distillation at 20 mm. pressure, with the surrounding bath at 40°, whereupon the residual gum, 7.13 g., was heated for five hours at 80°. A portion of this gum (5.21 g.) dissolved, on shaking, in 100 cc. of cold absolute alcohol; after concentration to about 25 cc., one drop of 17.25 *N* alcoholic hydrogen chloride was added to this solution, which was then warmed to 50° for about 3 mins., whereupon it was cooled by running water. After standing 20 hrs., 1.25 g. ethyl ester, melting (after drying over H_2SO_4 *in vacuo*) between 62° and 63°, separated out.

Analysis and physical constants of ethyl *d*-gluconate:

0.1997 g. gave 0.3123 g. CO_2 and 0.1267 g. H_2O.

Calc. for $C_8H_{16}O_7$: C, 42.83; H, 7.20; found: C, 42.65; H, 7.12.

The molecular weight of β-lactone, determined by the boiling point method in McCoy's apparatus (see above) using 0.5811 g. substance dissolved in absolute alcohol, was found to be 252 instead of 224 calculated for $C_8H_{16}O_7$.

Vol. of solution, cc..............	25.0	30.6	31.3	
Rise in B. P....................	0.141°	0.120°	0.115°	
Mol. wt. found..................	257	247	252	Av. 252

No optical activity was observed at first on dissolving 0.57 g. ethyl ester in 12.48 g. H_2O; the solution became optically active, however, on standing at room temperatures through hydrolysis of the ester and subsequent conversion of free *d*-gluconic acid into β- and γ-lactones.

Time after solution.	Observed angle.	$[\alpha]_D$.
6 days	+0.35°	+ 7.60°
10 days	+0.46°	+ 9.98°
17 days	+0.50°	+10.85°

If the specific rotation at the end of 17 days be calculated on the basis of lactone produced by hydrolysis (0.57 g. ester gives 0.453 g. lactone), it becomes +14.25°, which is in fairly close agreement with the region of equilibrium, +18°, reached by aqueous solutions of free *d*-gluconic acid and of *d*-gluconic β- and γ-lactones on long standing at ordinary temperatures.

The following further experiments with ethyl *d*-gluconate are interesting since they show that the β-lactone can be obtained from the ester to the extent of about 30% by simply heating in a distilling flask under 20 mm. pressure in a bath kept between 70° and 80° for 10 hrs.; a small amount of polygluconic anhydrides is also formed, as well as some γ-lactone. The γ-lactone could probably be obtained to the extent of 70% or more by raising the temperature of the surrounding bath to 130–140° during the experiment. Thus, after 3 g. of ethyl *d*-gluconate had been heated at 70–80° as described, with a loss in weight of 0.52 g., a partly crystalline mass remained in the distilling flask from which 1.03 g. crude β-lactone, melting from 140–152°, were obtained. In a second experiment 3.7 g. ester lost 0.55 g. in weight; the residual partly crystalline mass yielded 0.94 g. β-lactone melting from 152–153.5°.

***d*-Gluconic Acid.**—This acid, $C_6H_{12}O_7$, has been obtained only as a syrup ($[\alpha]_D^{20} = -1.7°$), very soluble in absolute alcohol, and is transformed in aqueous solution at ordinary temperatures mainly into β-lactone, but at 100° largely into γ-lactone; at all temperatures, however, equilibrium is established in aqueous solution with a definite percentage of these three components present.

In order to determine when equilibrium is reached in aqueous solutions at 20°, *d*-gluconic acid was prepared from a warm (60°) aqueous solution of 10 g. anhydrous calcium *d*-gluconate (corresponding to 9.19 g. $C_6H_{12}O_7$) by treatment with 2.93 g. crystallized oxalic acid in water also at 60°. Immediately after mixing, the solution of *d*-gluconic acid was cooled within one minute to 20°, filtered from calcium oxalate, and made up to 250 cc.; it gave $[\alpha]_D^{20} = +2.19°$ (calculated for $C_6H_{12}O_7$) forty-five minutes after cooling ($\alpha = +0.16°$ in a 2 dc. tube; c = 3.647). The following subsequent observations were made with the same tube kept at room temperatures. The calculations for the specific rotation are here, however, based on the theoretical amount of lactone, 8.28 g., obtainable from 10 g. anhydrous calcium *d*-gluconate. Equilibrium was finally reached with the specific rotation about +18°.

TABLE IV.

Time after cooling the solution.	Observed angle.	$[\alpha]_D$.
45 min.	+0.16°	+ 2.42°
2 hrs.	+0.45°	+ 6.80°
20 hrs.	+0.65°	+ 9.82°
1 day 23 hrs.	+0.65°	+ 9.82°
3 days	+0.77°	+11.63°
4 days	+0.81°	+12.24°
5 days	+0.96°	+14.50°
7 days	+1.05°	+15.85°
11 days	+1.17°	+17.67°

From Table IV it is evident that a condition of temporary equilibrium was maintained with the specific rotation at about +10° for 27 hrs.; this is in fairly close agreement with the region of temporary equilibrium (+11°), reached after an aqueous solution of *d*-gluconic β-lactone (see above) has stood for two and one-half hours at ordinary temperatures.

According to observations published by Schnelle and Tollens,[1] an

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[1] *Ann.*, **271**, 74 (1890); *Ber.*, **23**, 2991 (1890).

aqueous solution of free *d*-gluconic acid reaches equilibrium with the specific rotation between +10° and +12° after standing two or three weeks at room temperatures.

Equilibrium at 96–98° was found thus: a solution of *d*-gluconic acid, prepared from 10 g. anhydrous calcium *d*-gluconate (corresponding to 8.28 g. lactone), was heated for $13^1/_2$ hrs. on a boiling water bath; quickly cooled this gave $[\alpha]^{20}_{D} = +32.46°$ calculated on the basis of $C_6H_{10}O_6$, ($\alpha = +2.14°$ in a 2 dc. tube; $c = 3.312$); $[\alpha]^{20}_{D}$ fell to +25.52° after $15^1/_2$ hrs. and to +17.96° after 16 days' standing at room temperatures. *d*-Gluconic β-lactone as well as far more γ-lactone must have been present at the end of $13^1/_2$ hrs. heating.

***d*-Gluconic γ-Lactone.**—This abnormal lactone has been obtained by E. Fischer[1] in practically pure condition. He recrystallized the lactone twice from small amounts of water and found that it melted between 130° and 135°, and gave $[\alpha]^{20}_{D} = +68.2°$ in 8% concentration, or after 24 hrs. standing +64.13°. No β-lactone could therefore have been present. Schnelle and Tollens[2] describe a preparation, melting from 122° to 125°, which gave $[\alpha]^{20}_{D} = +61.59°$ ten minutes after solution, and eight minutes later +58.83°, in about 8% concentration; therefore a small amount of β-lactone was present. Nef[3] found the melting point of a preparation of pure γ-lactone, twice crystallized from 14 parts of absolute alcohol, to be 133–135° with $[\alpha]^{20}_{D} = +67.82°$ (in 4% concentration). I obtained γ-lactone, recrystallized from eight parts of absolute alcohol, melting from 134° to 136° with $[\alpha]^{20}_{D} = +67.52°$ (in 4% concentration).

Many experiments were carried out to determine the best conditions for obtaining the γ-lactone; the best of these with the results follow. When a solution of *d*-gluconic acid, of slightly less than 4% concentration, was heated for $13^1/_2$ hrs. on a boiling water bath (cf. *d*-gluconic acid), the specific rotation became +32.46°, indicating the presence of a large amount, perhaps 45 to 50%, of γ-lactone, besides a much smaller amount of β-lactone.

In another experiment the aqueous filtrate, obtained from 26.33 g. anhydrous calcium *d*-gluconate (corresponding to 21.8 g. lactone) by treatment with the calculated amount of crystallized oxalic acid, 7.115 g., was heated for only one hour on a boiling water bath and then allowed to reach room temperature by standing one hour longer, with final cooling at 20°. This filtrate made up to 640 cc. with water gave $[\alpha]^{20}_{D} = +16.99°$, calculated on the basis of $C_6H_{10}O_6$ ($\alpha = +1.21°$ in a 2 dc. tube; $c = 3.406$). The water was now removed from the solution 20 hrs. later by distillation at 20 mm. pressure with the surrounding bath at 50°, until no more mois-

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[1] *Ber.*, **23**, 2625 (1890).

[2] *Ann.*, **271**, 76 (1892).

[3] *Ibid.*, **403**, 330 (1914).

ture condensed in the neck of the flask, whereupon the gum, 21.3 g., gave $[\alpha]_D^{20} = +22.94°$, calculated on the basis of $C_6H_{10}O_6$ ($\alpha = +2.00°$ in a 2 dc. tube; c = 4.26); $[\alpha]_D^{20}$ fell to +17.77° after 50 hrs. standing at room temperatures. The amount of lactone in the gum was therefore very little more than that in solution before the above distillation. After removing the water again by distillation at 20 mm. pressure with the surrounding bath at 70°, the residual gum, heated two hours longer at 90°, now weighed 19.5 g. and gave $[\alpha]_D^{20} = +52.82°$, calculated on the basis of $C_6H_{10}O_6$, fifteen minutes after solution ($\alpha = +10.3°$ in a 2 dc. tube; c = 9.75); this fell to +28.72°, after standing 19 hrs. at room temperatures, showing that, besides a large amount of γ-lactone, much β-lactone was present.

These data make it perfectly clear that the most ideal way, in which to obtain a maximum yield of *d*-gluconic γ-lactone from anhydrous calcium *d*-gluconate, is to precipitate the calcium with the calculated amount of crystallized oxalic acid, and thereupon to heat the aqueous solution of free *d*-gluconic acid for 12 hrs. on a boiling water bath. At least 50% of the acid will be transformed into the β- and γ-lactones. The water must then be removed by distillation at 50 mm. pressure, while the temperature of the surrounding bath is kept between 90° and 100°. In this way at least 80% of γ-lactone should be obtained.

An attempt to prepare γ-lactone by heating a residual gum *in vacuo* to 130° proved successful. Under these conditions a larger amount than usual was produced. Thus, an aqueous solution of *d*-gluconic acid, prepared from 15 g. anhydrous calcium *d*-gluconate by treatment with 4.4 g. crystallized oxalic acid, was heated for one hour on a boiling water bath and filtered from calcium oxalate. The water was removed from the filtrate by distillation at 20 mm. pressure with the surrounding bath at 45°, whereupon the syrup was heated in an oil-bath at 130° for $4^1/_2$ hrs. The residual light brown gum, 11.58 g., was resolved by 200 cc. boiling absolute alcohol into two portions, A, 2.98 g. insoluble polygluconic anhydrides, and B, 8.6 g. soluble gum which dissolved in 50 cc. absolute alcohol yielded 1.98 g. crude γ-lactone, melting from 133° to 137°, with $[\alpha]_D^{20} = +67.05°$ (seven minutes after solution); this fell to +55.66° after five hours' standing at room temperatures. There was, therefore, a small amount of β-lactone present (cf. rate of change of β- and γ-lactones).

E. Fischer and others have analyzed *d*-gluconic γ-lactone; therefore only the following additional data on this substance were ascertained:

0.4761 g., dissolved in excess of 0.1 *N* KOH heated 10 mins. on a boiling water bath and titrated back with 0.1 *N* H_2SO_4, used 26.84 cc. 0.1 *N* KOH instead of 26.75 cc. calculated for $C_6H_{10}O_6$.

A molecular weight determination by the boiling point method with 0.5720 g. γ-lactone dissolved in absolute alcohol, using McCoy's apparatus (see above) gave 194 instead of 178 calculated for $C_6H_{10}O_6$.

Vol. of solution, cc.	27.3	28.4	29.5	30.8	
Rise in B. P.	0.169°	0.161°	0.154°	0.151°	
Mol. wt. found	193	195	196	191	Av. 194

The specific rotation of *d*-gluconic γ-lactone was found to be +67.52° at 20° nine minutes after solution (0.4190 g. in 9.8876 g. H_2O gave α = +2.78° in a 1 dc. tube). The following subsequent observations were made with the same tube kept at room temperatures:

TABLE V.

Time after solution.	Observed angle.	$[\alpha]_D$.
50 min.	+2.78°	+67.52°
18 hrs.	+2.42°	+58.75°
21 hrs.	+2.42°	+58.75°
2 days 18 hrs.	+1.83°	+44.43°
3 days 18 hrs.	+1.57°	+38.12°
4 days 18 hrs.	+1.40°	+33.98°
6 days 18 hrs.	+1.09°	+26.46°
7 days 18 hrs.	+0.98°	+23.79°
9 days 18 hrs.	+0.83°	+20.15°
10 days 22 hrs.	+0.78°	+18.94°
13 days 22 hrs.	+0.72°	+17.69°

Another experiment with 1.00015 g. γ-lactone dissolved in 24.0751 g. H_2O gave $[\alpha]_D^{20}$ = +66.91° twenty-five minutes after solution (α = +5.398° in a 2 dc. tube); this fell to +66.40° and to +58.35° after standing at room temperatures for $2^1/_4$ hrs. and 24 hrs. after solution, respectively.

d-Gluconic γ-lactone reacts rapidly with water at higher temperatures; such a solution, after heating 10 hrs. at 98°, reaches equilibrium at about +34°, as is evident from the following data: these are, moreover, in perfect agreement with the results of heating *d*-gluconic β-lactone and *d*-gluconic acid in aqueous solutions.

A solution of 0.8706 g. γ-lactone in 20.1144 g. H_2O, heated for one hour on a boiling water bath, gave, on rapid cooling to 20°, $[\alpha]_D^{20}$ = +40.53° (α = +1.7° in a 1 dc. tube); this fell to +37.92°, to +33.86° and to +18.09° after standing 1 hr., $14^1/_2$ hrs. and 19 days, respectively, at room temperatures. Another solution of 0.4441 g. γ-lactone in 10.1686 g. H_2O, heated for five hours on a boiling water bath and then cooled rapidly, gave $[\alpha]_D^{20}$ = +35.09° (α = +1.48° in a 1 dc. tube); this fell to +28.36° and to +25.76° after standing $1^1/_6$ hrs. and $20^1/_2$ hrs., respectively, at room temperatures. A third solution of 0.4239 g. γ-lactone in 9.7897 g. H_2O, heated for ten hours on a boiling water bath, gave, on rapid cooling to 20°, $[\alpha]_D^{20}$ = +34.84° ten minutes after cooling (α = +1.48° in a 1 dc. tube); this fell to +27.07° and to +18.12° after standing 18 hrs. and 17 days, respectively, at room temperatures.

The change in optical activity between +34.84° and +27.07° (during

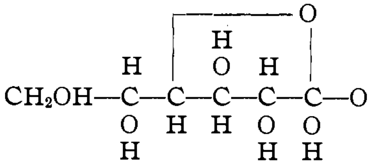
18 hrs.) is more rapid than the change, observed with an aqueous solution of pure *d*-gluconic γ-lactone (cf. Table V) at 20°, between +33.98° and +26.46° (during 48 hrs.); therefore considerable β-lactone must have been present.

Finally, Schnelle and Tollens[1] published long ago some observations on a crystalline lactone, obtained from free *d*-gluconic acid, to which they assign the composition $C_{12}H_{22}O_{11}$ or $C_{12}H_{20}O_{11}$. Their preparation melted between 110° and 115° and gave $[\alpha]_D^{20} = +39.07°$, or +14.84° after standing at 19° for 52 days. 1.017 g. substance lost 0.078 g. in weight assumed without proof to be water. It is now very obvious that their product simply consisted of mixed crystals of ethyl *d*-gluconate (about 57%) and *d*-gluconic γ-lactone. Nef, as well as I, has repeatedly obtained such low melting mixed crystals which could always be resolved into the two components by further recrystallization from alcohol.

III. Ortho-bis-*d*-Galactonic Acid, *d*-Galactonic γ-Lactone and Its Monohydrate.

All attempts to prepare an ester and a monomolecular β-lactone of *d*-galactonic acid, analogous to those in the *d*-mannonic acid and *d*-gluconic acid series, have failed, although some slight evidence of the existence of a β-lactone, rapidly decomposed by water has been obtained (see below) Kohn[2] has prepared ethyl *d*-galactonate in combination with calcium chloride.

Pure *d*-galactonic γ-lactone, opaque prismatic needles, melting between 108° and 11° with $[\alpha]_D^{20} = —76.97°$, has been prepared. This lactone is remarkable for the ease with which it adds water to form the very characteristic hydrate,



$$CH_2OH—\underset{\underset{H}{O}}{\overset{H}{C}}—\underset{H}{C}—\underset{H}{\overset{\overset{H}{O}}{C}}—\underset{\underset{H}{O}}{\overset{H}{C}}—\underset{\underset{H}{O}}{C}—OH$$

; large transparent prisms, melting at 66° with $[\alpha]_D^{20} = —70.1°$, analogous to chloral hydrate and bis-ortho oxalic acid. Both of these compounds are very soluble in water and in alcohol, but with some difficulty in ethyl acetate.

Free *d*-galactonic acid, on the other hand, is, in very marked contrast to *d*-mannonic and *d*-gluconic acids, a solid [melting between 140° and 141°, with $[\alpha]_D^{20}$ (calculated as $C_6H_{12}O_6$, see below) = —12.23°] practically insoluble in boiling absolute alcohol. It contains one-half a molecule of water of crystallization which can not be removed by prolonged drying over H_2SO_4 *in vacuo*. I therefore name it ortho-bis-*d*-galactonic acid and assign to it the bimolecular formula, $C_6H_{12}O_7.CH_2OH(CHOH)_4C(OH)_3$,

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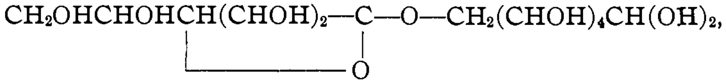
[1] *Ann.*, **271**, 79 (1892).

[2] *Monats.*, **16**, 334 (1895).

analogous to bis-ortho oxalic acid, or the very stable malt and milk sugar hydrates,



$$\mathrm{CH_2OHCHOH}\underbrace{\mathrm{CH(CHOH)_2{-}C}}_{\mathrm{O}}\mathrm{{-}O{-}CH_2(CHOH)_4CH(OH)_2},$$

etc. It is monomolecular in cold aqueous solutions, and titrates with alkali hydroxides, therefore, at once in the cold for free *d*-galactonic acid.

Ortho-bis-*d*-Galactonic Acid.—This acid has already been isolated in an impure condition (melting between 122° and 125°) over 30 years ago by Kiliani,[1] and his observations have been confirmed by Schnelle and Tollens[2] as well as by Fischer and Ruff.[3] Nef[4] succeeded in raising the melting point of the substance to 140–142° by crystallization from water with the addition of alcohol.

I prepared the pure acid in the following way: An aqueous solution of 97.2 g. calcium *d*-galactonate (containing 4 H_2O by analysis) was treated on a boiling water bath with the calculated amount of crystallized oxalic acid, 24.4 g., in water and, after five minutes' digestion, the mixture, cooled quickly with running water, was filtered free from calcium oxalate. When the filtrate had become concentrated by distillation at 20 mm. pressure with the surrounding bath never over 50°, crystals of ortho-bis-*d*-galactonic acid separated out in large amounts; 26.79 g. of crude acid, melting between 122° and 125°, were thus obtained in two crops. These were dissolved in 77 cc. water at 60° and the filtrate was then poured into 500 cc. absolute alcohol with subsequent addition of 200 cc. absolute alcohol; 17.48 g. crystal needles (melting at 140–141°, with $[\alpha]_D^{20}$ (calculated on the basis of $C_6H_{12}O_7$) = —12.23°) separated out on standing. The water-alcohol filtrate, concentrated to 50 cc. at reduced pressure, yielded, on addition of 100 cc. absolute alcohol, 4.17 g. of equally pure acid.[5]

The acid loses water with great difficulty for 0.9818 g., air-dry crystals, melting at 140–141°, kept over H_2SO_4 *in vacuo*, lost only 0.0041 g. H_2O after 20 days.

Six analyses of five prepartions of the substance were made; one preparation was crystallized from water alone, and the others from water and varying amounts of alcohol; the melting points of the acid obtained ranged, after drying over H_2SO_4 *in vacuo*, from 134–147°.

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[1] *Ber.*, 14, 651 (1881); *Ibid.*, 18, 1551 (1885).

[2] *Ann.*, 271, 82 (1892).

[3] *Ber.*, 33, 2146 (1900).

[4] *Ann.*, 403, 273–275 (1914).

[5] The mother liquor, still containing 5.1 g. substance, was united with the original aqueous filtrate from which 26.79 g. crude acid had been removed, and the combined solutions were worked up for *d*-galactonic γ-lactone and γ-lactone hydrate (see below).

	Gram.	M. p.	CO_2.	H_2O.	% C.	% H.
I	0.3168	140–1°	0.4051 g.	0.1837 g.	34.88	6.39
II	0.36375	140–1°	0.4680 g.	0.2143 g.	35.09	6.54
III	0.3199	147°	0.4105 g.	0.1837 g.	35.00	6.38
IV	0.3571	143–4°	0.4591 g.	0.2066 g.	35.06	6.43
V	0.3443	136–8°	0.4416 g.	0.1947 g.	34.98	6.35
VI	0.3235	134–6°	0.4125 g.	0.1850 g.	34.77	6.35
				Calc. for $C_{12}H_{26}O_{15}$	35.11	6.49

On titration with 0.1 *N* sodium hydroxide in the cold the substance behaved like a free acid; 0.4247 g. used 20.20 cc. 0.1 *N* NaOH (phenolphthalein) instead of 20.69 cc. calculated for $C_{12}H_{26}O_{15}$.

A molecular weight determination by the freezing point method proved that the acid, in cold aqueous solutions, is monomolecular, *i. e.*, such solutions contain either free meta *d*-galactonic acid or free ortho *d*-galactonic acid (molecular weights 196 and 214, respectively), or perhaps both. 1.1506 g. substance were used. The phenomenon of supercooling was considered in the usual way and the amount of liquid solvent, W′, was found by the formula

$$W' = W\left(1 - \frac{S.D}{L}\right),$$

in which W is the total solvent (24.879 g. H_2O), S is the specific heat of the solvent, L is the latent heat of fusion, and D is the supercooling.

D′.	W′.	Δ.	Mol. wt. found.[1]
0.184	24.84 g. H_2O	0.442°	194.9
1.674	24.12 g. H_2O	0.447°	198.4
1.663	24.38 g. H_2O	0.448°	195.9
		Average,	196.4

The molecular weight determination was not corrected for ionization of the acid; this would be too small to make much increase in the observed molecular weight.

There was for a long time doubt on the question as to whether the formula of the crystalline acid was $C_6H_{12}O_7.H_2O$ or $2C_6H_{12}O_7.H_2O$, *i. e.*, whether the substance was ortho-*d*-galactonic acid or ortho-bis-*d*-galactonic acid. This was finally settled in favor of the latter formula by the following experiment: 5.06 g. ortho-bis-*d*-galactonic acid, melting at 140–141°, were heated for two hours in a small distilling flask under 20 mm. pressure with the surrounding bath at 145°; the flask was connected with a small condenser, which was joined to a receiver cooled to —16°. A slow, continuous stream of dry air was passed through the molten mass by means of a capillary tube. The amount of ice, which accumulated in the receiver, was 0.62 g. or 12.35%, whereas 0.665 g., or 13.17%, is the

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[1] For preliminary practice the molecular weight of pure crystallized glucose by the freezing point method was found to be 176.7 instead of 180 for $C_6H_{12}O_6$.

theoretical amount of water, for $C_{12}H_{26}O_{15} = 3H_2O + 2C_6H_{10}O_6$. The molten distillate also gave no iodoform test, establishing therefore the absence of alcohol. Finally the residue in the distilling flask, 4.29 g., yielded by crystallization from absolute alcohol 2.62 g. *d*-galactonic γ-lactone, melting from 105° to 109°.

Since ortho-bis-*d*-galactonic acid exists only in the monomolecular form in aqueous solution, it should show exactly the same specific rotation as an acid just liberated from a salt. This is a fact. I found $[\alpha]_D^{20} =$ —12.23° (calculated on the basis of $C_6H_{12}O_7$) for the pure crystalline acid, melting at 140–141°, in a 4% aqueous solution. Schnelle and Tollens[1] found that the specific rotation of free *d*-galactonic acid, on liberation from its calcium salt by hydrochloric or oxalic acids, was —10.56° (calculated on the basis of $C_6H_{12}O_7$). Nef observed that the specific rotation of a 4% aqueous solution of a similarly liberated acid was —12.64°, six minutes after its preparation; this fell to —11.35° and rose again to —16.40°, after standing 8 hrs. and 22¹/₂ hrs., respectively, at ordinary temperatures.

The specific rotation of aqueous solutions of *d*-galactonic acid increase and reach a limit at about —50°, after standing about three weeks at ordinary temperatures, or in one hour at 100° (see below); this is due to a transformation of the acid mainly into the isomeric *d*-galactonic γ-lactone hydrate, melting at 66°, with $[\alpha]_D^{20} =$ —70.1° (see below). Since, however, this lactone hydrate is also slightly acted upon by water, even at 20°, aqueous solutions of γ-lactone hydrate, or of ortho-bis acid, finally always contain a mixture of three substances in equilibrium, namely, 70 to 80% of γ-lactone hydrate, 30 to 20% of free acid, besides traces of the γ-lactone (see below).

1.0383 g. of ortho-bis-*d*-galactonic acid (corresponding to 0.9927 g. $C_6H_{12}O_7$) dissolved in 25.0781 g. H_2O, gave $[\alpha]_D^{20} =$ —12.23°, six minutes after solution ($\alpha =$ —0.94° in a 2 dc. tube). The changes observed in the specific rotation of this solution on standing at ordinary temperatures follow:

TABLE VI.

Time after solution.	Observed angle.	$[\alpha]_D$ calculated on basis of $C_6H_{12}O_7$.
2 days 16 hrs.	—2.51°	—32.66°
3 days 19 hrs.	—2.85°	—37.08°
4 days 23 hrs.	—2.97°	—38.64°
5 days 22 hrs.	—3.16°	—41.12°
9 days 17 hrs.	—3.36°	—43.71°
10 days 17 hrs.	—3.46°	—45.02°
17 days 17 hrs.	—3.90°	—50.75°

Another observation on the specific rotation of a preparation of ortho-bis-*d*-galactonic acid, which had been kept one year, gave $[\alpha]_D^{20} =$ —13.32°

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[1] *Ann.*, **271**, 85 (1892).

(calculated on the basis of $C_6H_{12}O_7$) *i. e.*, 1.6143 g. ortho-bis-*d*-galactonic acid (corresponding to 1.544 g. $C_6H_{12}O_7$) dissolved in 36.1823 g. H_2O gave $\alpha = -1.10°$ in a 2 dc. tube fourteen minutes after solution. Subsequent changes in the optical activity of this solution are recorded in this table:

TABLE VII.

Time after solution.	Observed angle.	$[\alpha]_D$ calculated on the basis of $C_6H_{12}O_7$.
2 hrs. 25 min.	—0.95°	—11.50°
3 hrs. 25 min.	—0.89°	—10.78°
5 hrs. 40 min.	—0.89°	—10.78°
7 hrs. 25 min.	—0.89°	—10.78°
11 hrs. 20 min.	—0.97°	—11.75°
1 day	—1.22°	—14.78°
2 days	—1.53°	—18.53°
3 days 8 hrs.	—1.85°	—22.41°
18 days	—3.76°	—45.54°

The slight drop at first observed in the specific rotation of an aqueous solution of ortho-bis-*d*-galactonic acid (from —11.50° to —10.78°) possibly indicates the presence of a plus-rotating β-lactone, which is very unstable in aqueous solution (see below). Similar changes were invariably noticed in the case of freshly prepared aqueous solutions of *d*-galactonic acid, when set free from its salts by acids. Ten grams of calcium *d*-galactonate ($Ca(C_6H_{11}O_7)_2.4H_2O$ by analysis) for example were dissolved in 150 cc. H_2O and treated with 2.51 g. oxalic acid in water at 60°. After shaking a few seconds, the solution was cooled in one-half minute to 20° and filtered from calcium oxalate. The filtrate (containing by calculation 7.81 g. free *d*-galactonic acid, $C_6H_{12}O_7$) was made up to 250 cc. with water and gave $[\alpha]_D^{20} = -7.68°$ one hour after precipitation of the calcium oxalate ($\alpha = -0.48°$ in a 2 dc. tube). The following table gives the subsequent changes in the optical activity of this solution, kept at ordinary temperatures:

TABLE VIII.

Time after precipitation.	Observed angle.	$[\alpha]_D$ calculated on the basis of $C_6H_{12}O_7$.
3 hrs. 40 min.	—0.61°	— 9.76°
22 hrs. 15 min.	—1.33°	—21.29°
1 day 22 hrs. 40 min.	—1.90°	—30.40°
4 days 7 hrs.	—2.72°	—43.52°
19 days 6 hrs.	—3.20°	—51.20°
23 days 2 hrs.	—3.22°	—51.52°

An aqueous solution of 1.0803 g. ortho-bis-*d*-galactonic acid (corresponding to 1.033 g. $C_6H_{12}O_7$), dissolved in 26.2848 g. H_2O, heated for one hour on a boiling water bath and cooled quickly to 20°, gave $\alpha = -1.85°$ in a 1 dc. tube fifteen minutes after cooling; whence $[\alpha]_D^{20} = -48.51$ when calculated on the basis of lactone hydrate, $C_6H_{10}O_6.H_2O$. The following further changes occurred in the specific rotation of the solution on standing at ordinary temperatures. They show at first a notable rise in specific rotation and a subsequent fall back to —49.82°.

Time after cooling.	Observed angle.	$[\alpha]_D$ calculated on the basis of $C_6H_{12}O_7$.
2 hrs. 45 min.	—2.05°	—53.74°
20 hrs.	—2.10°	—55.05°
4 days	—2.05°	—53.74°
14 days	—1.90°	—49.82°

***d*-Galactonic γ-Lactone and Its Monohydrate.**—Schnelle and Tollens[1] were the first to obtain crystallized *d*-galactonic γ-lactone hydrate, $C_6H_{10}O_6.H_2O$, but they did not assign to it a structural formula. They gave the melting point, 66°, and found $[\alpha]_D^{20}$ = —65.6° five minutes after solution. According to later observations by Clowes and Tollens,[2] a preparation, crystallized from acetone, with the same melting point, 66°, gave $[\alpha]_D^{20}$ = —67.9°. After driving off water from the hydrate by a stream of warm air, a preparation of γ-lactone, still contaminated with hydrate, was obtained by them in the form of needles melting at 90° with $[\alpha]_D^{20}$ = —72.1°. A preparation, melting at 100°, obtained by Hlasiwetz and Barth[3] as early as 1862, also contained some unchanged hydrate, since *d*-galactonic γ-lactone is a very hygroscopic substance. Furthermore, it is obvious that the low specific rotations, obtained by Tollens and his co-laborers for the γ-lactone and its hydrate, were due to the presence of a small amount of ortho-bis-*d*-galactonic acid, since it is difficult to convert this substance completely into the γ-lactone. This can only be done, as Nef has repeatedly observed, by prolonged heating of residues at 20 mm. pressure in a distilling flask in a bath at 100°. By operating in this way he has, for example, repeatedly converted calcium *d*-galactonate, by treatment with oxalic acid, etc., to the extent of over 90% of the theory into pure *d*-galactonic γ-lactone, *i. e.*, by subsequently crystallizing the residual gums from *absolute* alcohol. It was, however, always necessary to reheat the gums left in the alcoholic filtrates at 100° and under 20 mm. pressure; and in fact at least three or four such operations were necessary in order to obtain a ninety per cent. yield of γ-lactone. Prepared[4] in this way, the γ-lactone crystallizes in needles, which melt between 108° and 111° and always give a specific rotation in the neighborhood of —77°, or of —70°, if calculated on the basis of γ-lactone hydrate, which is ob-

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[1] *Ann.*, **271**, 81 (1892).

[2] *Ibid.*, **310**, 166 (1900).

[3] *Ibid.*, **122**, 96 (1862).

[4] It is clear that the preparation of *d*-galactonic γ-lactone recently described by Ruff and Franz, *Ber.*, **35**, 948 (1902), possessing $[\alpha]_D^{20}$ = —77.61°, must be identical with my product; the high melting point given, 135°, is probably due to a typographical error.

viously the only natural basis (see below), since the latter substance is practically the only one present in aqueous solutions at 20°.

The best way of obtaining a pure preparation of *d*-galactonic γ-lactone hydrate is to place the powdered γ-lactone and the calculated amount of water side by side in dishes in a closed vessel; the water is completely absorbed after two days' standing, and the resulting addition product is thereupon crystallized from ethyl acetate (see below).

The following further experiments with *d*-galactonic γ-lactone, as well as with γ-lactone hydrate, are of especial interest since they confirm in a very decisive way many of the preceding statements.

The above mentioned aqueous, and aqueous-alcoholic, mother liquors, from which 17.48 g. and 4.17 g. pure ortho-bis-*d*-galactonic acid had separated out by crystallization (see footnote, p. 364), were now freed from alcohol and water by distillation at reduced pressure and the residue, about 50 g. in 500 cc. H_2O, was now heated at 40° for 25 hrs. The water was again removed by distillation at 20 mm. pressure with the surrounding bath at 40°, until no more moisture condensed in the neck of the flask. The residual gum, 49.2 g., dissolved in cold water and made up to 500 cc., gave $[\alpha]_D^{20} = -47.49°$ ($\alpha = -9.34°$ in a 2 dc. tube; $c = 9.84$). The water was now again removed by distillation at 20 mm. pressure with the bath at 40°. The residual gum, on digestion at 40° with 200 cc. absolute alcohol, left 5.15 g. crystalline material undissolved, which melted from 113° to 119°, and was insoluble in warm absolute alcohol. The filtrate, freed from alcohol by distillation at reduced pressure, gave a residue which was heated at 60° until bubbles ceased to appear in the melt. This gum was soon transformed on standing into a crystalline mass which, when carefully broken loose by a rod and removed from the flask with 25 cc. absolute alcohol, yielded 29.6 g. air-dry crude γ-lactone hydrate melting from 65° to 70° with $[\alpha]_D^{20} = -55.83°$ (calculated on the basis of $C_6H_{12}O_7$). A considerable portion of this, 19.8 g., when dissolved in 50 cc. of warm absolute alcohol, gave 8.07 g. mixed crystals melting from 66° to 85°; these, after drying three days over H_2SO_4 *in vacuo*, weighed 7.77 g., melted from 108° to 111°, and consisted therefore of practically pure γ-lactone.

Four grams of the finely powdered *d*-galactonic γ-lactone (melting from 108° to 111°) and the theoretical amount of water, 0.405 g., were placed side by side in dishes in an air-tight vessel. The water disapppeared within two days; and the solid now weighed 4.44 g. and melted between 65° and 70°, but, after standing for two days over H_2SO_4 *in vacuo*, again lost the combined water with a simultaneous rise in melting point up to 105° to 110°. The γ-lactone had, therefore, been transformed into the hydrate and again recovered unchanged. It is obvious from these data that the *d*-galactonic γ-lactone is a very hygroscopic substance, which can, therefore, be obtained pure only by crystallization from solvents containing no water; this explains why the melting point is found usually to range from 108° to 111°.

d-Galactonic γ-lactone is soluble in about 200 parts of boiling ethyl acetate and separates therefrom on standing in opaque needles. The γ-lactone hydrate crystallizes from this solvent in large transparent prisms.

1.48 g. mixed crystals of *d*-galactonic γ-lactone and hydrate were dissolved in 400 cc. boiling ethyl acetate; this, concentrated to 200 cc., yielded on standing 0.65 g. needles, melting from 90° to 105°; these, dried over H_2SO_4 *in vacuo* for three days, melted at 109–111° with $[\alpha]_D^{20}$ = —76.97° (calculated on the basis of $C_6H_{10}O_6$) consisting therefore of pure γ-lactone.

2.58 g. mixed crystals of γ-lactone and hydrate were dissolved in 350 cc. boiling ethyl acetate; this solution on standing yielded 1.5 g. large transparent prisms, melting at 65–67.5° (air-dried) with $[\alpha]_D^{20}$ = —70.1° (calculated on the basis of $C_6H_{10}O_6.H_2O$). This was pure *d*-galactonic γ-lactone hydrate. There must, therefore, be enough water in ordinary ethyl acetate to transform the γ-lactone into the hydrate. In a special experiment 0.5 g. *d*-galactonic γ-lactone, melting from 100° to 110°; dissolved in 75 cc. boiling ethyl acetate, gave, on concentration to two-thirds the original volume, a considerable amount of gum on standing; this slowly and completely became transformed into large transparent prisms of γ-lactone hydrate melting from 64°–67°.

Finally there are appended here data (physical, analytical, etc.) which were obtained with *d*-galactonic γ-lactone and its hydrate.

d-Galactonic γ-lactone.—0.5721 g. substance, heated 10 min. on a boiling water bath with an excess of 0.1 *N* KOH, cooled and titrated back with 0.1 *N* H_2SO_4, etc., used 32.01 cc. 0.1 *N* KOH (phenolphthalein) for neutralization instead of 32.12 cc. calculated for $C_6H_{10}O_6$.

A molecular weight determination with 0.5602 g. substance in boiling absolute alcohol using McCoy's apparatus (*Loc. cit.*) gave as the average molecular weight 192.3 instead of 178 calculated for $C_6H_{10}O_6$.

Vol. of solution, cc......	24.3	29.0	31.3	33.0	
Rise in B. P............	0.184°	0.156°	0.148°	0.137°	
Mol. wt. found..........	195	193	188	193	Av. 192.3

The specific rotation of pure γ-lactone was found to be —76.97°, or better —69.88°, when calculated on the basis of γ-lactone hydrate, since obviously this is practically the only substance present at first in a fresh aqueous solution, *i. e.*, 0.3464 g. substance and 9.0443 g. H_2O gave α = —2.87° in a 1 dc. tube eight minutes after solution. The solution then underwent the following changes on standing at ordinary temperatures:

TABLE IX.

Time after solution.	Observed angle.	$[\alpha]_D$ specific rotation for lactone hydrate.
20 hrs.	—2.79°	—67.92°
4 days $4^1/_2$ hrs.	—2.73°	—66.45°
9 days 1 hr.	—2.52°	—61.33°
13 days 19 hrs.	—2.41°	—58.65°
14 days 19 hrs.	—2.37°	—57.67°
21 days 19 hrs.	—2.25°	—54.77°
23 days 18 hrs.	—2.19°	—53.30°
28 days 18 hrs.	—2.18°	—53.07°
35 days 1 hr.	—2.03°	—49.41°
44 days 19 hrs.	—1.98°	—48.20°

***d*-Galactonic γ-Lactone Hydrate.**—0.6450 g. required 32.72 cc. 0.1 *N* KOH for neutralization by the usual method (see above) instead of 32.91 cc. calculated from $C_6H_{10}O_6.H_2O$.

The specific solution of the γ-lactone hydrate was found to be —70.1°, *i. e.*, 0.3906 g. substance and 9.7905 g. H_2O gave α = —2.72° in a 1 dc. tube ten minutes after solution. The solution then underwent the following changes at ordinary temperatures:

TABLE X.

Time after solution.	Observed angle.	$[\alpha]_D$.
$17^3/_4$ hrs.	—2.64°	—68.07°
2 days $17^1/_2$ hrs.	—2.63°	—67.77°
4 days 20 hrs.	—2.60°	—67.02°
7 days $1^1/_2$ hrs.	—2.47°	—63.67°
12 days 1 hr.	—2.32°	—59.80°
16 days 20 hrs.	—2.25°	—58.00°
24 days $20^1/_2$ hrs.	—2.20°	—56.70°
26 days 18 hrs.	—2.14°	—55.15°
31 days 18 hrs.	—2.08°	—53.68°
38 days 1 hr.	—1.98°	—51.10°
47 days 19 hrs.	—1.89°	—48.77°

When *d*-galactonic γ-lactone is heated in a boiling water bath in 4% aqueous solution, equilibrium is quickly reached with the specific rotation between —58° and —61°, if the calculation is made on the only natural basis of $C_6H_{12}O_7$, which is the empirical formula of *d*-galactonic γ-lactone hydrate, as well as of free *d*-galactonic acid. This is decidedly higher than the specific rotations, about —48.5° (see above), finally reached by aqueous solutions of ortho-bis-*d*-galactonic acid, as well as of *d*-galactonic γ-lactone and its hydrate, and proves, as in all other instances (cf. *d*-mannonic and *d*-gluconic series), that more lactone (or lactone hydrate) is present in aqueous solution at higher temperatures. Thus, (A) a solution of 0.5363 g. *d*-galactonic γ-lactone in 11.7732 g. H_2O, heated for one hour on a boiling water bath and cooled quickly, gave $[\alpha]_D^{20}$ = —60.42° *i. e.*, α = —2.93° in a 1 dc. tube. (B) A second experiment with 0.5769

g. γ-lactone in 13.4041 g. H_2O, heated for five hours on a boiling water bath and cooled quickly gave $[\alpha]_D^{20} = -58.79°$, *i. e.*, $\alpha = -2.75°$ in a 1 dc. tube; curiously enough the specific rotation rose after 16 hours' standing at room temperatures to —59.87°. (C) A third experiment with 0.5035 g. γ-lactone in 11.9932 g. H_2O, heated on a boiling water bath for seven hours and cooled quickly, gave $[\alpha]_D^{20} = -59.54°$, *i. e.*, $\alpha = -2.67°$ in a 1 dc. tube. Here again a curious rise and subsequent fall in specific rotation were observed on standing at ordinary temperatures.

Time after first reading.	Observed angle.	$[\alpha]_D$.
19 hrs.	—2.77°	—61.77°
6 days	—2.54°	—56.63°

It is clear from the data presented that aqueous solutions of ortho-bis-*d*-galactonic acid, or of *d*-galactonic γ-lactone or its hydrate, finally come to an equilibrium at 20° with $[\alpha]_D^{20} = -48.5°$; at 100°, on the other hand, equilibrium is quickly reached with $[\alpha]_D^{20} = -60°$. Such solutions contain 17 to 37% of free *d*-galactonic acid and 83 to 63% of *d*-galactonic γ-lactone hydrate (besides traces of γ-lactone) according to the temperature (between 20° and 100°) at which equilibrium occurs.

One might also draw the conclusion from the slight fluctuations at first noticed in the specific rotation of ortho-bis-*d*-galactonic acid, or of free *d*-galactonic acid when set free from its salts, as well as the curious fluctuations in specific rotation noticed after aqueous solutions of ortho-bis-*d*-galactonic acid and of *d*-galactonic γ-lactone have been heated at 100° and quickly cooled, that a faintly dextrorotatory *d*-galactonic β-lactone also exists in these solutions. All attempts, however, to isolate such a β-lactone, or even an ester of *d*-galactonic acid, were entirely fruitless.

I desire to express my gratitude to Dr. Nef for his painstaking instruction and constant aid in this work.

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

SYNTHESES IN THE DIPHENYLMETHANE SERIES.

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The work presented in this paper was undertaken with the idea of attempting to effect a synthesis of the hydrocarbon, fluorene, through the action of metals upon 2,2'-dibromodiphenylmethane. This latter substance was prepared by the elimination of the amino groups from 3,3'-diamino-6,6'-dibromodiphenylmethane, a compound which, in turn, had

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[1] The work described in this article formed part of a thesis submitted for the degree of Master of Science to the graduate school of the University of Illinois by E. A. Wildman.