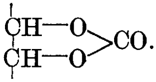
XXIII.—*Sugar Carbonates. Part IV. The Dicarbonates of Glucose, Fructose, Mannose, Galactose, and Arabinose.*

By WALTER NORMAN HAWORTH and CHARLES RAYMOND PORTER.

A SERIES of new crystalline derivatives of sugars has been prepared containing two carbonate residues of the type



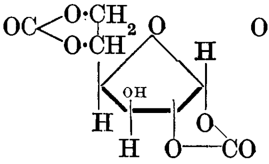
$$\begin{matrix}|\\ CH-O\\ |\\ CH-O\\ |\end{matrix}\!\!>CO.$$

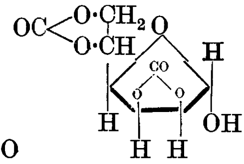
Hitherto the attempts to prepare these substances have led either to the introduction of only one such residue or to the formation of sugar carbonates containing also carbonic ester groups. The present results have been obtained by the condensation of various sugars with carbonyl chloride in pyridine solution. Accompanying the crystalline dicarbonate there is usually an amorphous by-product of higher molecular weight which appears to be a polysaccharide derivative. The latter reaction has not been studied in detail.

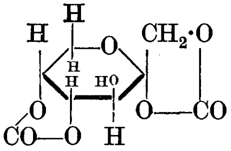
The dicarbonates of the sugars are well-defined and easily characterised products which resemble closely the diacetone derivatives of the sugars. For instance, they are hydrolysed by dilute acids to the parent sugars; this change, however, does not proceed nearly so readily as with the sugar-acetones. On the other hand, the sugar carbonates are instantly attacked by alkali even in the cold. It is these properties that suggested the utilisation of the dicarbonates in synthetic operations such as those recently described (J., 1929, 2796).

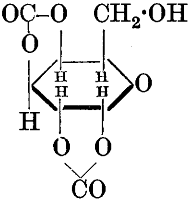
The specific rotations of the dicarbonates derived from glucose, fructose, and mannose are analogous to those of the corresponding diacetone derivatives, but arabinose dicarbonate, $[\alpha]_{5780} + 61{\cdot}3^\circ$, and galactose dicarbonate, $[\alpha]_{5780} - 86{\cdot}5^\circ$, have higher rotations than arabinose-diacetone and galactose-diacetone, $[\alpha]_{5780} \pm 1^\circ$ and $- 56^\circ$ respectively (in aqueous acetone). These variations appear to be due to differences of conformation rather than of structure.

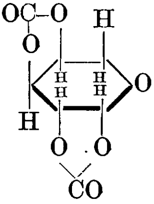
The constitutional formulæ suggested are indicated below and are based on the similarity in properties to the diacetones, the constitutional formulæ of which have been elucidated.


Glucose dicarbonate.


Mannose dicarbonate.


α-Fructose dicarbonate.


Galactose dicarbonate.


Arabinose dicarbonate.

Evidence of the constitution here assigned to mannose dicarbonate is furnished by the fact that this substance gives rise to a crystalline anilide and a crystalline methylmannoside dicarbonate which does not reduce Fehling's solution. This interesting mannoside will form the subject of a further communication.

The behaviour of the glucose dicarbonate, including its relationship to glucose-acetone carbonate (*loc. cit.*), provides support for the constitution which is here assigned.

EXPERIMENTAL.

Glucose Dicarbonate.—In the first attempts to condense carbonyl chloride with glucose the sugar was dissolved in pyridine, cooled in ice, and vigorously stirred while a 20% solution of carbonyl chloride in toluene was added drop by drop. The addition caused the precipitation of a yellow crystalline solid (possibly the addition compound of carbonyl chloride and pyridine), and the removal of the reagent in this form was probably the reason for the minute amount of sugar carbonate formed in this way.

In subsequent experiments gaseous carbonyl chloride, obtained from a cylinder of the compressed gas, was passed into the solution of the sugar in pyridine. At the end of the reaction the mixture was treated with ice, to decompose the carbonyl chloride–pyridine complex, and the liquid was filtered. When the reaction was arrested after about an hour, an almost clear solution was obtained, but if the reagents had been in contact for several hours, or if a very rapid current of carbonyl chloride had been passed, or the temperature allowed to rise, a considerable amount of an insoluble amorphous condensation product (A) was formed, which was removed by filtration.

The aqueous filtrate contained pyridine, pyridine hydrochloride, glucose dicarbonate, and glucose. The pyridine and its hydrochloride were removed together by adding an excess of barium carbonate and evaporating the solution to a small bulk at 30—35° under reduced pressure. The glucose dicarbonate was sparingly soluble in water and was extracted with ethyl acetate in a mechanical extractor. Another and somewhat more rapid method of separating the sugar carbonate from the original mixture consisted in treatment of the latter with excess of barium carbonate and repeated extraction with ethyl acetate : the whole of the pyridine was thus removed, and with it the sugar carbonate, which was much more soluble in pyridine than in ethyl acetate. The latter solvent was eliminated by distillation at 40—50° under diminished pressure. The residual pyridine solution was evaporated at the ordinary temperature in a vacuum desiccator containing sulphuric acid. The residue was a viscid liquid or glassy solid, which became crystalline on trituration with alcohol. In this method, some unchanged glucose as well as the glucose carbonate was extracted by the pyridine.

In a typical preparation, carbonyl chloride was passed for 1 hour, from a delivery tube with a bell-shaped orifice in order to prevent stoppages, into an ice-cooled, vigorously stirred solution of 18 g. of glucose in about 50 c.c. of pyridine. The product was treated with ice-water, filtered, and extracted with ethyl acetate. During the extraction, sufficient barium carbonate was added to neutralise the hydrochloric acid liberated by the removal of pyridine from the solution of its hydrochloride. Evaporation of the solvents from this extract left a viscid mass which deposited crystals on treatment with alcohol. Further crops of crystals were deposited on concentration of the alcoholic solution, and finally a viscid residue remained which yielded no further crystalline material (yield, 1 g.).

An attempt was also made to prepare a glucose carbonate by passing carbonyl chloride into a thoroughly stirred, concentrated aqueous solution of glucose cooled in ice and salt. The hydrochloric acid and excess of carbonyl chloride were then removed by the addition of silver carbonate, and the solution was evaporated at a low temperature. The product crystallised and appeared to be mainly unchanged glucose; a very small amount of glucose carbonate was, however, detected.

The amorphous product A (see above) was insoluble in the usual organic solvents except pyridine, but was soluble in a mixture of acetone and water. It gave a precipitate of barium carbonate when warmed with barium hydroxide solution, and reduced Fehling's solution. On treatment with dilute alkali it dissolved, a polysaccharide being probably formed.

Glucose dicarbonate is sparingly soluble in most solvents, the decreasing order of solubility being pyridine, acetone (about 1·5% in cold), ethyl acetate, alcohol (about 0·4% when boiling), water, and chloroform. It crystallises well from alcohol, being about four times as soluble in the hot as in the cold, yielding needles or lustrous flakes, m. p. 224° (efferv.; sintering at 200°).

Glucose dicarbonate is hydrolysed rapidly by dilute alkalis, but is not readily decomposed by dilute acids in the cold. When it is warmed with aqueous barium hydroxide solution, a precipitate of barium carbonate is formed. The alkali present in Fehling's solution is sufficient to effect hydrolysis, followed by reduction. The dicarbonate has $[\alpha]_D - 29°$ ($c = 1·0$ in acetone containing 25% of water). No change in this value was observed, even after the addition of a drop of aqueous hydrochloric acid (Found: C, 41·5; H, 3·6; CO_2, 37·5; *M*, ebullioscopic in acetone, 239. $C_8H_8O_8$ requires C, 41·4; H, 3·5; CO_2, 37·9%; *M*, 232).

Galactose Dicarbonate.—This compound was prepared in the same manner as glucose dicarbonate. Several variations of the method of extraction were tried, but the process ultimately adopted for the glucose analogue was found to be the most effective.

In general, *galactose dicarbonate* is similar in its properties to glucose dicarbonate. It is, however, somewhat more soluble in water, from which it crystallises well in long needles, m. p. 212° (efferv.; slight sintering at 190°); $[\alpha]_{5780}^{21·5°} - 86·5°$ in acetone containing 25% of water ($c = 0·6$). The addition of a trace of hydrochloric acid did not alter the rotation in 22 hours (Found: C, 41·7; H, 3·7. $C_8H_8O_8$ requires C, 41·4; H, 3·5%).

Mannose Dicarbonate.—This preparation proceeded rather more readily than in the previous examples, and the product was more easily extracted.

In a typical preparation, 6 g. of mannose were dissolved in 20 c.c. of pyridine, the solution was cooled in an ice-bath and vigorously stirred, and a fairly rapid current of carbonyl chloride was passed for about ¾ hour. Ice-water was then added, and 1·5 g. of an amorphous carbonate, probably a polysaccharide carbonate, were collected. The filtrate was treated with an excess of barium carbonate and evaporated to small bulk under diminished pressure at 30—35°. After removal of the pyridine by this process, the solution was filtered and extracted with ethyl acetate in the mechanical extractor. Yield, 0·5 g.

Mannose dicarbonate crystallised well from water in lustrous flakes or needles, m. p. 122—123° (efferv.; slight sintering at 118°).

It gave a precipitate with barium hydroxide solution, and reduced Fehling's solution suddenly, on heating (Found: C, 41·4; H, 3·6; CO_2, 36·7. $C_8H_8O_8$ requires C, 41·4; H, 3·5; CO_2, 37·9%). $[\alpha]^{21^\circ}_{5780}$ + 26°; $[\alpha]^{21^\circ}_{5461}$ + 28·5° in dry acetone ($c = 1·0$). The substance showed no appreciable mutarotation in this solvent even after the addition of a trace of hydrochloric acid.

The *anilide* of mannose dicarbonate was prepared by heating mannose dicarbonate and aniline (2 mols.) in alcoholic solution for 2 hours. The solution was then allowed to evaporate at the ordinary temperature. The residue, after being triturated with several solvents, crystallised from ethyl acetate, containing dry ether, in hard white prisms, m. p. 174—175°. The substance was sparingly soluble in alcohol or ethyl acetate and slowly became discoloured on exposure to the air. $[\alpha]^{20^\circ}_{5780}$ − 70° (after 5 minutes); −32° (after 18 hours) in ethyl alcohol ($c = 0·2$); $[\alpha]^{18^\circ}_{D}$ − 83° in methyl alcohol ($c = 0·1$) (Found: C, 54·85; H, 4·5; N, 4·65. $C_{14}H_{13}O_7N$ requires C, 54·7; H, 4·25; N, 4·55%).

Fructose Dicarbonate.—Fructose (10 g.) was dissolved in 25 c.c. of pyridine and cooled in ice and vigorously stirred. A fairly rapid current of carbonyl chloride was admitted during ¾ hour; ice-water was then added, and an amorphous fructose carbonate derivative removed by filtration. After addition of excess of barium carbonate, the filtrate was extracted with ethyl acetate, first by hand and then mechanically. The ethyl acetate was distilled at 40—50° under slightly reduced pressure and the pyridine was evaporated from the residue at the ordinary temperature in a vacuum desiccator containing sulphuric acid. When only a trace of pyridine remained, a little water was added, which caused the fructose dicarbonate to become crystalline (yield, 1 g.).

The aqueous solution remaining after the extraction with ethyl acetate was evaporated to dryness at 30—35°, and the finely powdered residue extracted repeatedly with boiling acetone in the hope of isolating an isomeric fructose dicarbonate. Only a small amount of a syrupy product was extracted and this yielded a further amount of the same fructose dicarbonate.

Fructose dicarbonate has solubilities intermediate between those of the corresponding derivatives of glucose and mannose, being quite easily soluble in acetone and alcohol. It crystallised well from water, separating in hard prisms if not quite pure, but when pure it was obtained in clusters of needles. It contained ½ mol. of water of crystallisation, which was not removed in a vacuum over sulphuric acid at the ordinary temperature, but was eliminated in a vacuum at 90°. M. p. 173—174°; effervescence occurred at this temperature after a few seconds. The rotation was similar to that of the α-form of fructose diacetone, and mutarotation was not observed on the addition of a trace of hydrochloric acid. $[\alpha]_{5780}^{16^\circ}$ −143° and $[\alpha]_{5461}^{16^\circ}$ − 159° (in 50% aqueous acetone, $c = 1{\cdot}14$) (Found: C, 40·1; H, 3·95; CO_2, 36·4; H_2O, 3·4. $C_8H_8O_8,\frac{1}{2}H_2O$ requires C, 39·9; H, 3·75; CO_2, 36·5; H_2O, 3·7%).

The amorphous substance which was collected after the addition of ice-water to the pyridine solution in the above reaction appeared to be insoluble in most liquids except pyridine, but was soluble in acetone containing a little water. The acetone was allowed to evaporate from such a solution and the precipitated solid was removed. The aqueous filtrate left only a small amount of glassy residue on evaporation. The precipitated solid was washed with water and was then almost completely soluble in dry acetone. It was extracted with this solvent, and the solution allowed to evaporate; the vitreous residue became opaque on trituration with water. It reduced Fehling's solution, and gave a precipitate when warmed with barium hydroxide solution. The product decomposed without melting between 150° and 180°. $[\alpha]_{5780}^{16^\circ}$ −58° ($c = 1{\cdot}29$ in acetone) (Found: CO_2, 37·7%; M, ebullioscopic in acetone, 780, 765). This molecular weight is intermediate between those required by three (660) and four (874) fructose dicarbonate residues joined by loss of water. The carbonate values required by these substances are 40·0 and 40·3% respectively.

A further attempt was made to separate the obviously complex mixture by fractional precipitation from acetone solution by the addition of ether. By this process four fractions were collected, the rotations of which did not vary greatly [(1) $[\alpha]_{5780}$ − 64°; (2) $[\alpha]_{5780}$ − 58·5°; (3) $[\alpha]_{5780}$ − 63°; (4) $[\alpha]_{5780}$ − 65°], and, although the solubilities of the fractions differed considerably, pure substances were not obtained. The examination of this mixture is therefore held over until larger quantities are available.

Arabinose Dicarbonate.—The reaction of arabinose with carbonyl chloride in pyridine did not proceed so quickly as was the case with the other sugars. The gas was passed for 2 hours into a cooled and vigorously stirred solution of 10 g. of arabinose in 30 c.c. of pyridine. The product was an extremely thick paste, and stirring was impracticable. Ice-water was added, and the clear solution extracted with ethyl acetate, barium carbonate being added to keep the solution neutral. After removal of the solvent from the extracts as in previous cases, a viscid syrup remained which deposited crystals on treatment with water. The filtrate from this solid deposited more crystalline material after being kept for some weeks (yield, 2 g.).

Arabinose dicarbonate is slightly soluble in chloroform, but rather more soluble in ethyl acetate, alcohol, water, and acetone. It crystallises well from water (solubility in hot water, 1 part in 140 parts). It separated in short hard prisms when not quite pure, and in longer crystals when pure. M. p. 200—202° (efferv.). It gave a precipitate with barium hydroxide and reduced Fehling's solution.

When heated to 160° in a vacuum, this dicarbonate very slowly sublimes, and at a slightly higher temperature, *e.g.*, 180—190°, can be economically purified by this procedure. This behaviour is in marked contrast to that of the dicarbonates of the hexoses, which appeared to possess a negligible vapour pressure and decomposed on prolonged heating.

Arabinose dicarbonate did not exhibit mutarotation in aqueous acetone, even after the addition of a trace of hydrochloric acid. $[\alpha]_{5780}^{25^\circ} + 61{\cdot}3^\circ$; $[\alpha]_{5461}^{25^\circ} + 66{\cdot}0^\circ$ (in acetone containing 33% of water, $c = 1{\cdot}3$) (Found: C, 41·7; H, 3·1; CO_2, 41·6. $C_7H_6O_7$ requires C, 41·6; H, 3·0; CO_2, 43·5%).

The authors are grateful to the Government Grant Committee of the Royal Society for a contribution towards the cost of materials.

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[*Received, November* 18*th*, 1929.]