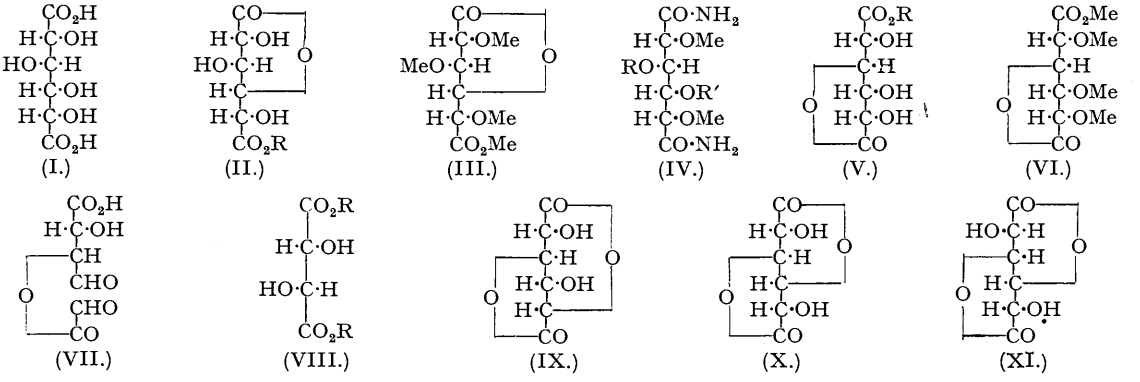
173. *Lactones of Glucosaccharic Acid. Part III. Mono- and Di-lactones.*

By F. Smith.

Sohst and Tollens's saccharolactone (*Annalen*, 1888, **245**, 1, 19), now obtained directly from potassium hydrogen saccharate, is a mixture of glucosaccharo-1 : 4-lactone (II; R = H) and glucosaccharo-3 : 6-lactone (V; R = H). These two monolactones have been separated and their structures proved by conversion into known crystalline derivatives. They have been transformed respectively into the dilactones (X) and (IX), both of which reduce Fehling's solution.

In a previous communication (this vol., p. 571) evidence was put forward which indicated that the so-called saccharolactone (m. p. 133°) of Sohst and Tollens, originally assumed to be a 3 : 6-monolactone (V; R = H), is a mixture of this with a 1 : 4-monolactone (II; R = H). Confirmation of this view was effected by the separation and identification of these two monolactones.

The syrupy mixture of the monolactones of glucosaccharic acid which gradually crystallises on keeping in air at room temperature was extracted with cold acetone. This procedure removed the 1 : 4-lactone, leaving the 3 : 6-lactone. Pure specimens of the latter show m. p. 149°, $[\alpha]_D$ +45° (Sohst and Tollens, *loc. cit.*; Rehorst and Scholz, *Ber.*, 1936, **69**, 524, record m. p. 130—132°, $[\alpha]_D$ +38° for this substance). The saccharo-1 : 4-lactone can be separated from the acetone extract as a crystalline monohydrate, m. p. 98°, $[\alpha]_D$ +32·5° (cf. Reichstein, *Helv. Chim. Acta*, 1939, **22**, 4).



The structure (II; R = H) assigned to this monohydrate (m. p. 98°) is based upon the following facts: The monolactone showed relatively slow mutarotation in aqueous solution, typical of the γ-lactones in the glucose series. Reduction of (II; R = H) with sodium amalgam affords glucuronic acid (Fischer and Piloty, *Ber.*, 1891, **24**, 522; Reichstein, *loc. cit.*), and since it is the carbonyl group of the lactone ring and not that of the carboxyl group which is transformed into the reducing group of glucuronic acid, then in the monolactone (II; R = H) it must be C_1 and not C_6 which is engaged in the lactone ring. This monolactone does not react with periodic acid under conditions which easily effect disruption of the carbon chain of the glucosaccharo-3 : 6-lactone (see below). This suggests that (II; R = H) does not contain adjacent *cis*-hydroxyl groups. Titration of (II; R = H) with an ethereal solution of diazomethane yielded a crystalline methyl ester (II; R = Me); when this was treated with silver oxide and methyl iodide it afforded crystalline 2 : 3 : 5-trimethyl glucosaccharo-1 : 4-lactone 6-methyl ester (III). The latter, obtainable also by direct methylation of the monolactone (II; R = H) with silver oxide and methyl iodide, was further characterised by its conversion into the corresponding diamide (IV; R = Me, R′ = H). Both the ester (III) and this amide were identical with specimens previously prepared by methylation of the crude mixture of monolactones (II; R = H) and (V; R = H), and with specimens prepared synthetically from glucose (Smith, this vol., p. 571). The structure (II; R = H) given to the glucosaccharo-1 : 4-lactone monohydrate is therefore correct.

The monolactone (m. p. 149°) to which was assigned the structure (V; R = H) behaves like the 1 : 4-monolactone in that it exhibits slow mutarotation in aqueous solution, thus indicating the presence of a γ- and not a δ-lactone ring. Reduction of (V; R = H) in neutral or slightly acid solution has been shown to give rise to

guluronic acid (Reichstein, *loc. cit.*), a fact which proves that the carboxyl group at C_6 must be engaged in the lactone ring. Titration of (V; R = H) with an ethereal solution of diazomethane causes rapid esterification of the carboxyl group and there is formed the crystalline glucosaccharolactone methyl ester (V; R = Me) (cf. Reeves, *J. Amer. Chem. Soc.*, 1939, **61**, 664). This ester, like the glucosaccharo-1 : 4-lactone 6-methyl ester, reduces boiling Fehling's solution. [The explanation of the reducing activity of these ester lactones and that shown by the two dilactones (IX) and (X) will be advanced in a subsequent communication.] Methylation of (V; R = Me) with silver oxide and methyl iodide gives the trimethyl glucosaccharolactone methyl ester (VI), which is converted into the known diamide (IV; R = H, R′ = Me) of 2 : 4 : 5-trimethyl glucosaccharic acid identical with that previously prepared from the mixture of monolactones of saccharic acid (Smith, *loc. cit.*). Confirmation of the structure assigned to the monolactone (m. p. 149°) was forthcoming from an examination of its reactions with periodic acid (Malaprade, *Bull. Soc. chim.*, 1928, **43**, 683; 1934, **1**, 833; Herrissey, Fleury, and Joly, *J. Pharm. Chim.*, 1934, **20**, 149; Schmidt and Gunthert, *Ber.*, 1938, **71**, 493; Reeves, *loc. cit.*). This reagent effects scission of the carbon chain between C_4 and C_5 to give the dialdehyde (VII), which is readily oxidised by bromine to oxalic acid and dihydroxy-*l*-threosuccinic acid (*d*-tartaric acid) (VIII; R = H), identified in the form of its crystalline methyl ester (VIII; R = Me).

Inspection of the structures (II; R = H) and (V; R = H) allocated to the two monolactones of glucosaccharic acid shows that each should be capable of giving rise to a dilactone. This proved to be the case: when the 3 : 6-lactone is subjected to prolonged heating in a vacuum it melts gradually, water is eliminated, and a dilactone (m. p. 135°) believed to have the structure (IX) crystallises spontaneously. This dilactone exhibits relatively rapid mutarotation in aqueous solution ($[\alpha]_D$ +166° changing in 22 hours to +44°). The specific rotation of an aqueous solution of the dilactone at equilibrium is almost identical with that of a freshly prepared solution of the 3 : 6-lactone. This fact, together with the observation that removal of the solvent from the equilibrium solution at a low temperature affords the original saccharolactone (V; R = H), shows that the dilactone contains the 3 : 6-γ-lactone ring. The relatively rapid mutarotation of the dilactone suggests, but does not prove, that its second lactone ring is of the δ-type and that it engages C_1 and C_5 (see below). Hence the formula (IX) was tentatively assigned to this dilactone (cf. Rehorst and Scholz, *Ber.*, 1936, **69**, 524).

Similarly, it has been demonstrated that when the monohydrate of saccharo-1 : 4-lactone (II; R = H) is heated in a vacuum above its m. p. the water of crystallisation is first eliminated and a second ring is introduced into the molecule. The stereochemical arrangement of the hydroxyl groups at C_2 and C_3 is such as to allow of the formation of a lactone ring only between the hydroxyl group at C_3 and the carboxyl group at C_6. The formation of a δ-lactone ring between C_6 and C_2 of (II; R = H) would involve so much strain that such a possibility can be ruled out. The only possible configuration for this dilactone is therefore (X), in which both the lactone rings are of the γ-type. This new glucosaccharodilactone thus has a configuration analogous to that assigned to mannosaccharodilactone (XI), which likewise possesses two γ-lactone rings (Schmidt and Kraft, *Ber.*, 1941, **74**, 33; Heslop and Smith, this vol., p. 574). Support for the presence of the 3 : 6-lactone ring in (X) is provided by the fact that evaporation of an aqueous solution of the dilactone, which has mutarotated and reached equilibrium, gives glucosaccharo-3 : 6-lactone (V; R = H). The introduction of the 3 : 6-lactone ring in the conversion of the monolactone (II; R = H) ($[\alpha]_D$ +32·5° for the monohydrate) into the dilactone (X) ($[\alpha]_D$ +144°) is also borne out by the fact that the formation of the dilactone is accompanied by an enhancement of the rotation in the positive direction. If the second lactone ring in (X) were of the δ-type, joining C_6 to C_2, its formation would be expected to be accompanied by a rotational change in the negative sense. Since the two dilactones, derived from the 3 : 6- and the 1 : 4-glucosaccharolactone respectively, are different, it follows that the second ring introduced into the 3 : 6-monolactone in the formation of the corresponding dilactone must engage C_1 and C_5, for if it involved C_1 and C_4 then it would be identical with the dilactone obtained from saccharo-1 : 4-lactone.

It is noteworthy that the dilactone (IX) derived from glucosaccharo-3 : 6-lactone (V; R = H) is given a formula in which one lactone ring is of the δ-type, chiefly because it shows rapid mutarotation in aqueous solution. On the other hand, the dilactone obtained from glucosaccharo-1 : 4-lactone (II; R = H), and given the structure (X) because of stereochemical considerations and the fact that (X) has a higher positive rotation than (II; R = H), also shows relatively rapid mutarotation. This similarity of the mutarotation of these two dilactones is difficult to reconcile with the structure (X) given to the dilactone, especially when one considers that mannosaccharodilactone (XI), which has two γ-lactone rings (Schmidt and Kraft, *Ber.*, 1941, **74**, 33), shows very slow mutarotation. The apparent anomaly may be partly due to the strain in such dicyclic systems caused by the interlocking rings (see Haworth, Jackson, and Smith, J., 1940, 620; Haworth, Owen, and Smith, J., 1941, 88), and partly to the spatial configuration of the other groups in the molecules, *e.g.*, the hydroxyl group at C_2. Until conditions permit further studies to be made of derivatives of these dilactones of saccharic acid and other dilactones, formulæ (IX) and (X) are put forward tentatively.

Experimental.

Glucosaccharo-3 : 6-lactone (V; R = H) *and Glucosaccharo-1 : 4-lactone* (II; R = H).—A solution of potassium hydrogen saccharate (68 g.), obtained from glucose by oxidation with nitric acid, in water (100 c.c.), was treated with 5N-sulphuric acid (55 c.c., 1 equiv.). The solution was evaporated to dryness under diminished pressure at 50—60°, the residue extracted with methyl alcohol at room temperature, and the extract filtered. The filtrate was concentrated to small bulk under reduced pressure, and the concentrate, while still containing some methyl alcohol, set aside in a dish at room temperature. After 1—2 weeks the resulting crystalline mass was triturated with acetone, the residue collected,

and washed with acetone. The residue (25 g.) of saccharo-3 : 6-lactone (V; R = H) recrystallised from acetone–light petroleum; when pure, it has m. p. 149°, $[\alpha]_D^{20°}$ +45° in water (*c*, 0·9); +44° (5 days); +39·5° (15 days); +32·4° (60 days) (Found: C, 37·8; H, 4·3. Calc. for $C_6H_8O_7$: C, 37·5; H, 4·2%).

Concentration of the above acetone filtrate gave a syrup, from which a further yield of saccharo-3 : 6-lactone was obtained. Reconcentration of the acetone mother-liquors to a small volume, followed by transference to an open dish from which the residual acetone slowly evaporated, gave large crystals of saccharo-1 : 4-lactone. These were removed, washed with a little ice-cold acetone, and then recrystallised from acetone–ethyl acetate, or better, from acetone alone. The saccharo-1 : 4-lactone monohydrate thus obtained had m. p. 98° (sintering at 85°), $[\alpha]_D^{20°}$ +34° (initial value in water, *c*, 1·5); +33° (1 day); +20° (22 days). Further crops of the monohydrate were obtained from the mother-liquors (Found: C, 34·9; H, 4·8. Calc. for $C_6H_8O_7,H_2O$: C, 34·3; H, 4·8%).

Glucosaccharo-1 : 4-*lactone* 6-*Methyl Ester* (II; R = Me).—A solution of the lactone (0·2 g.) in acetone (10 c.c.) was cooled in ice and titrated with an ice-cold ethereal solution of diazomethane until the latter was in slight excess as indicated by the persistence of a yellow colour. Immediate evaporation of the solvent under diminished pressure at 30—35° afforded the crystalline 6-methyl ester in almost quantitative yield, m. p. 165° (after recrystallisation from ethyl alcohol). The crystals dissolve in water to give a neutral solution showing $[\alpha]_D^{18°}$ +24° in water (*c*, 0·5), but on keeping, the aqueous solution becomes slightly acid to litmus and Congo-red paper. The methyl ester reduces Fehling's solution on boiling (Found: C, 41·0; H, 5·0; OMe, 15·2. Calc. for $C_7H_{10}O_7$: C, 40·8; H, 4·9; OMe, 15·05%).

Methylation of the Methyl Ester (II; R = Me).—A solution of this ester (0·9 g.) in the minimum amount of acetone was allowed to react with methyl iodide (5 c.c.) and silver oxide (4 g.) during 8 hours at 45—50°; the silver oxide was added in small amounts within 4 hours of the commencement of the methylation. The solution was filtered, and the residue washed well with hot acetone. Removal of the solvent afforded a syrup which was not completely soluble in methyl iodide. The product was therefore subjected to another treatment with silver oxide and methyl iodide in the presence of acetone. The product, isolated in the same manner, was then completely soluble in methyl iodide, and two additional similar methylations effected complete methylation. The product, isolated by means of acetone, crystallised spontaneously. Trituration of the crystalline material with ethyl alcohol–ether, followed by filtration and recrystallisation from ethyl alcohol, gave 2 : 5-dimethyl Δ^4-glucosaccharo-3 : 6-lactone 1-methyl ester (0·3 g.), m. p. 87°, $[\alpha]_D^{20°}$ +91·5° in water (*c*, 1·4).

Removal of the solvent from the mother-liquors gave a syrupy residue which upon distillation under 0·04 mm. (bath temps.) yielded: Fraction (I) (0·05 g.), b. p. 100°, $n_D^{19°}$ 1·4440; fraction (II) (0·49 g.), b. p. 135—145°, $n_D^{19°}$ 1·4550—1·4595; fraction (III) (0·11 g.), b. p. >145°, $n_D^{19°}$ 1·4640. Fraction (I) was mainly methylated tartaric acid, but fraction (III) proved to be almost pure 2 : 5-dimethyl Δ^4-glucosaccharo-3 : 6-lactone 1-methyl ester, m. p. and mixed m. p. 87° (after recrystallisation from ethyl alcohol). Fraction (II) also crystallised, and trituration with ether afforded 2 : 5-dimethyl Δ^4-glucosaccharolactone methyl ester (0·2 g.), and from the mother-liquors of this fraction a syrup was obtained which readily crystallised upon nucleation with a synthetic specimen of 2 : 3 : 5-trimethyl saccharolactone methyl ester. After recrystallisation from acetone–ether the 2 : 3 : 5-trimethyl glucosaccharolactone 6-methyl ester had m. p. 79° alone or in admixture with an authentic specimen; $[\alpha]_D^{20°}$ −12° in water (*c*, 3·0) (Found: C, 48·4; H, 6·9; OMe, 49·2. Calc. for $C_{10}H_{16}O_7$: C, 48·4; H, 6·45; OMe, 50·0%).

Methylation of Glucosaccharo-1 : 4-*lactone* (II; R = H).—A solution of glucosaccharo-1 : 4-lactone monohydrate (0·25 g.) in acetone (2 c.c.) was boiled for 8 hours under reflux with methyl iodide (3 c.c.) in the presence of silver oxide (*ca.* 2 g.), the latter being added in small portions during the first 4 hours. The product, after isolation by means of acetone, was soluble in methyl iodide and so was given two more methylations as before but without addition of acetone. Distillation of the syrupy product gave a fairly mobile, colourless oil (0·22 g.), b. p. 140°/0·02 mm., $n_D^{17°}$ 1·4520. The distillate crystallised immediately upon nucleation with a crystal of 2 : 3 : 5-trimethyl glucosaccharolactone methyl ester, and after recrystallisation from ethyl alcohol–ether–light petroleum, the 2 : 3 : 5-trimethyl glucosaccharolactone methyl ester had m. p. and mixed m. p. 79° (Found: OMe, 49·5%). 0·02 G. of distillate, b. p. (bath temp.) approx. 160°/0·02 mm., was collected after this ester, and readily crystallised on nucleation with a specimen of 2 : 5-dimethyl Δ^4-glucosaccharolactone methyl ester; after recrystallisation from ethyl alcohol–ether, it had m. p. and mixed m. p. 87°.

2 : 3 : 5-*Trimethyl Glucosaccharic Acid Diamide* (IV; R = Me, R′ = H).—A solution of 2 : 3 : 5-trimethyl saccharolactone methyl ester (0·1 g.) in dry methyl alcohol (2 c.c.) was cooled in ice, saturated with dry ammonia, and kept for 2 days at −5°; removal of the excess of the solvent in a vacuum at room temperature then yielded crystalline 2 : 3 : 5-trimethyl glucosaccharic acid diamide, m. p. 213°, $[\alpha]_D^{17°}$ +18·5 in water (*c*, 2·0) (after crystallisation from ethyl alcohol–ether). This diamide showed a negative Weerman reaction (tested on 20 mg.).

Treatment of Glucosaccharo-1 : 4-*lactone* (II; R = H) *with Periodic Acid.*—A solution of the lactone monohydrate (1 g.) in water (10 c.c.) was treated with periodic acid (1·14 g.) (80% pure) in water (15 c.c.) for 1 hour at room temperature. Hydriodic acid (39 c.c.; 0·62N) and sulphuric acid (5 c.c.; 1·05N) were then stirred in, the iodine precipitated was filtered off, and that remaining in solution was extracted with chloroform. The solution, after evaporation under diminished pressure for a short time to remove chloroform, showed no reducing activity towards Fehling's solution. The solution was neutralised with dilute potassium hydroxide, evaporated to 20—30 c.c., and treated with a slight excess of glacial acetic acid. The precipitate of potassium hydrogen saccharate was filtered off, and washed with ice-cold water; yield 0·8 g.

Glucosaccharo-3 : 6-*lactone* 1-*Methyl Ester* (V; R = Me).—A solution of the lactone (4·26 g.) in acetone (200 c.c.) was cooled in ice and titrated with an ice-cold ethereal solution of diazomethane until a permanent yellow colour persisted. The esterification proceeded smoothly and rapidly, and was accompanied by the brisk evolution of nitrogen. Removal of the excess of the solvent and diazomethane by distillation in a vacuum at 25—30° gave a crystalline residue, which was crystallised from ethyl alcohol. The glucosaccharo-3 : 6-lactone 1-methyl ester thus produced (3·0 g.) had m. p. 115°, $[\alpha]_D^{18}$ +30° in water (*c*, 1·0) (Found: C, 41·0; H, 5·0; OMe, 15·0; equiv., 102. Calc. for $C_7H_{10}O_7$: C, 40·8; H, 4·9; OMe, 15·05%; equiv., 103). It can be kept unchanged in a sealed tube, but is extremely sensitive to traces of moisture which hydrolyse it with elimination of the ester methoxyl group. Hence, when an aqueous solution of the ester had been kept for 5 weeks at room temperature, removal of the water at room temperature in a vacuum gave crystalline glucosaccharo-3 : 6-lactone, m. p. and mixed m. p. 149° (after recrystallisation from methyl alcohol–acetone) (Found: OMe, nil). Glucosaccharo-3 : 6-lactone 1-methyl ester reduces boiling Fehling's solution actively, especially if the crystalline ester is added to the hot Fehling's solution.

Methylation. A solution of the glucosaccharolactone methyl ester (2·9 g.) in the minimum volume of acetone was boiled under reflux with methyl iodide (5 c.c.) and silver oxide (5 g.) for 8 hours. The silver oxide was added in small quantities during the first 4 hours of the reaction. The syrupy product, isolated by means of acetone, was not completely soluble in methyl iodide. After a second methylation carried out under the same conditions complete solution in methyl iodide was attained. Thereafter the product was given three more methylations with methyl iodide (8 c.c.) and silver oxide (5 g.) at 40—45° during 8 hours. This procedure afforded a mixture of syrup and crystals which was triturated with ether–ethyl alcohol and filtered. These crystals, 2 : 5-dimethyl Δ^4-glucosaccharo-3 : 6-lactone 1-methyl ester (0·7 g.), had m. p. and mixed m. p. 87°, $[\alpha]_D^{20°}$ +94° in water (*c*. 2·0) (after recrystallisation from ethyl alcohol). The

syrup obtained from the mother-liquors was distilled under 0·03 mm. (bath temps.), giving: Fraction I (0·87 g.), b. p. 138°, $n_D^{20°}$ 1·4568; fraction II (0·99 g.), b. p. 150—155°, $n_D^{20°}$ 1·4645; fraction III (0·1 g.), b. p. 155—200°, $n_D^{20°}$ 1·4690. Fractions II and III crystallised almost completely upon nucleation with 2 : 5-dimethyl Δ^4-glucosaccharo-3 : 6-lactone methyl ester, and after recrystallisation from ethyl alcohol the crystals had m. p. and mixed m. p. 87°.

Fraction I gave 2 : 5-dimethyl Δ^4-glucosaccharolactone methyl ester (0·2 g.), m. p. 87° (after crystallisation from ethyl alcohol). The syrup obtained from the mother-liquors of this fraction failed to crystallise. Treatment of a portion (0·1 g.) of the syrup with methyl-alcoholic ammonia for 3 days at −5°, followed by removal of the excess of the solvent, furnished crystalline 2 : 4 : 5-trimethyl glucosaccharic acid diamide (IV; R = H, R′ = Me), m. p. 195°, $[\alpha]_D^{20°}$ +22° in water (*c*, 0·9) (after recrystallisation from water) (Found: C, 43·2; H, 7·4; N, 11·05; OMe, 37·7. Calc. for $C_9H_{18}O_6N_2$: C, 43·2; H, 7·2; N, 11·2; OMe, 37·2%). A Weerman test carried out upon this diamide (20 mg.), according to the conditions previously employed, was negative. A control test upon gluconamide (20 mg.) readily gave hydrazodicarbonamide (10 mg.), m. p. and mixed m. p. 258° (decomp.). As a further control, a Weerman test was carried out upon the diamide of 2 : 4-dimethyl mucic acid; this was positive (see Smith, J., 1939, 1724).

Treatment of Glucosaccharo-3 : 6-*lactone with Periodic Acid.*—To a solution of the lactone (1 g., m. p. 149°) in water (20 c.c.) cooled in ice, was added an ice-cold solution of periodic acid (1 g.; 1 mol.) in water (10 c.c.). After 10 minutes at 0°, the reaction mixture was treated with hydriodic acid (2·0 c.c., 5 mols.) followed by N-sulphuric acid (6 c.c.). The solution was worked up as in the oxidation of (II; R = H), and the resulting aqueous solution, which reduced Fehling's solution actively on warming, was heated for 10 minutes at 70°, neutralised with barium carbonate, and filtered. The filtrate was evaporated under diminished pressure to 10 c.c., treated with bromine (0·8 c.c.) in the presence of excess barium carbonate for 2 days, and the excess of bromine removed by aeration; the solution now no longer reduced boiling Fehling's solution. Barium hydroxide solution (0·3N) was added until the solution was just alkaline to phenolphthalein in order to precipitate the barium oxalate and tartrate, and complete precipitation of the latter effected by addition of methyl alcohol (2 vols.). The insoluble barium salts were filtered off, washed with methyl alcohol to remove barium bromide, dried in a vacuum over phosphoric oxide, and boiled for 8 hours with 1% methyl-alcoholic hydrogen chloride (250 c.c.). The solution was cooled, neutralised with barium carbonate, filtered, and evaporated to dryness under diminished pressure, whereby the methyl oxalate was volatilised. The syrupy residue, after purification by extraction with ether to eliminate some inorganic impurity, readily crystallised upon nucleation with methyl dimethoxy *l*-threo-succinate (methyl dimethyl *d*-tartrate), and after recrystallisation from ether the methyl ester (0·56 g.) had m. p. and mixed m. p. 48°, $[\alpha]_D^{20°}$ +19° in water (*c*, 2·0) (Found: OMe, 34·6. Calc. for $C_6H_{10}O_6$: OMe, 34·8%).

Glucosaccharo-1 : 5-3 : 6-*dilactone* (IX).—Finely powdered glucosaccharo-3 : 6-lactone (m. p. 149°) (1 g.) contained in a test-tube was inserted in a Fischer dryer and heated in a vacuum at 100°. After 2—3 hours the lactone gradually melted and there was a slow evolution of bubbles from the colourless, stiff syrup. The heating was continued until no more bubbles were evolved, and while at this temperature the syrup crystallised spontaneously. When crystallisation was complete, the heating was stopped, and the product was crystallised from acetone–light petroleum. The glucosaccharo-1 : 5-3 : 6-dilactone was obtained as colourless needles, m. p. 133° (Found: C, 41·6; H, 3·9. Calc. for $C_6H_6O_6$: C, 41·4; H, 3·45%); $[\alpha]_D^{20°}$ +167° in water (*c*, 1·0) (initial value); +126° (2 hrs.); +113·5° (2½ hrs.) +87·5° (5 hrs.); +75° (7½ hrs.); +66° (10 hrs.); +53·5° (15 hrs.); +44·5° (21½ hrs.); +43·5° (90 hrs.) (constant for 10 hrs.). This dilactone reduces boiling Fehling's solution actively, and its freshly prepared aqueous solution is acid to litmus.

Evaporation in a vacuum at room temperature of an aqueous solution of the dilactone (25 mg.) after the rotation had reached the equilibrium value gave a colourless, thin syrup, and while containing some water this syrup was nucleated with a crystal of saccharo-3 : 6-lactone. The last traces of water were eliminated by evaporation in a vacuum over phosphoric oxide. The residue was triturated with acetone, and pure glucosaccharo-3 : 6-lactone, m. p. and mixed m. p. 149°, remained.

Glucosaccharo-1 : 4-3 : 6-*dilactone* (X).—Finely ground glucosaccharo-1 : 4-lactone monohydrate (1 g.) was heated for 2 hours at 60° in a vacuum. The m. p. (originally 98°) gradually rose until after 3 hours it was 115—125°. This product evidently contained some dilactone, because it reduced boiling Fehling's solution slightly and showed $[\alpha]_D^{18°}$ +60° in water (*c*, 1·5) (initial value), changing in 1 day to +38°; when a small portion of it was melted, it displayed immediately an increase in reducing activity towards boiling Fehling's solution. The product was then further heated at 100° in a vacuum; it gradually melted, and after 18 hours lactonisation appeared to be complete. The glucosaccharo-1 : 4-3 : 6-dilactone, which was a pale yellow glass, failed to crystallise. An aqueous solution of it reacted acid to Congo-red paper and showed $[\alpha]_D^{18°}$ +155° in water (*c*, 2·0) (initial value); +135° (1 hr.); +117·5° (2 hrs.); +102·5° (3 hrs.); +92·5° (4 hrs.); +83° (5 hrs.); +70° (7 hrs.); +65° (8 hrs.); +58° (10 hrs.); +54° (12 hrs.); +51° (14 hrs.); +47·5° (20 hrs.); +43·5° (32 hrs.); subsequently there was a gradual decrease in rotation to *ca.* $[\alpha]_D^{18°}$ +31·5° (7 days). The dilactone reduces Fehling's solution actively (Found: C, 41·5; H, 3·9. Calc. for $C_6H_6O_6$: C, 41·4; H, 3·5%).

Evaporation in a vacuum of an aqueous solution of this dilactone which had reached equilibrium gave a syrup which, whilst still containing a little water, readily crystallised upon nucleation with a specimen of glucosaccharo-3 : 6-lactone. Trituration with acetone followed by filtration gave glucosaccharo-3 : 6-lactone, m. p. and mixed m. p. 148°. Removal of the acetone from the mother-liquors gave a syrup which slowly crystallised on exposure to air. After trituration with ethyl acetate–acetone, these crystals of glucosaccharo-1 : 4-lactone monohydrate had m. p. 88°.

Treatment of Glucosaccharo-1 : 4-3 : 6-*dilactone with Silver Oxide and Methyl Iodide.*—The syrupy dilactone (0·54 g.), prepared as above, was dissolved in dry acetone (5 c.c.) and heated with methyl iodide (5 c.c.) and silver oxide (3—4 g.), the latter being added in small portions during the first 5 hours. After 8 hours the mixture was extracted with hot acetone; the solution was filtered and evaporated to dryness under diminished pressure, and the syrupy product given 3 more treatments with silver oxide and methyl iodide (no acetone used). After this procedure the product crystallised spontaneously. Trituration with ethyl alcohol–ether to remove adhering syrup, followed by crystallisation of the product from ethyl alcohol, gave 2 : 5-dimethyl Δ^4-glucosaccharo-3 : 6-lactone 1-methyl ester, m. p. and mixed m. p. 89°, $[\alpha]_D^{18°}$ +92° in water (*c*, 1·4) (Found: C, 50·2; H, 5·65; OMe, 42·7. Calc. for $C_9H_{12}O_6$: C, 50·0; H, 5·6; OMe, 43·0%). Distillation of the syrup obtained from the mother-liquors gave a colourless liquid (0·3 g.), b. p. (bath temp.) 148—168°/0·04 mm., $n_D^{19°}$ 1·4744, from which a further 0·12 g. of 2 : 5-dimethyl glucosaccharo-3 : 6-lactone 1-methyl ester was separated. Treatment of the syrup obtained (0·18 g.) from the mother-liquors, after the removal of crystals (0·12 g.), with methyl-alcoholic ammonia gave a diamide (10 mg.), m. p. 202°, $[\alpha]_D^{20°}$ +19° in water (*c*, 2·0) (after recrystallisation from ethyl alcohol) (Found: C, 44·4; H, 6·9; N, 11·8; OMe, 37·5. Calc. for $C_9H_{18}O_6N_2$: C, 43·2; H, 7·2; N, 11·2; OMe, 37·2%). This amide (as yet unidentified) gave no depression of the m. p. when mixed with an amide obtained in small yield from a corresponding fraction of methylated glucosaccharo-1 : 5-3 : 6-dilactone.

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