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Studies on the D-Glucosaccharinic Acids

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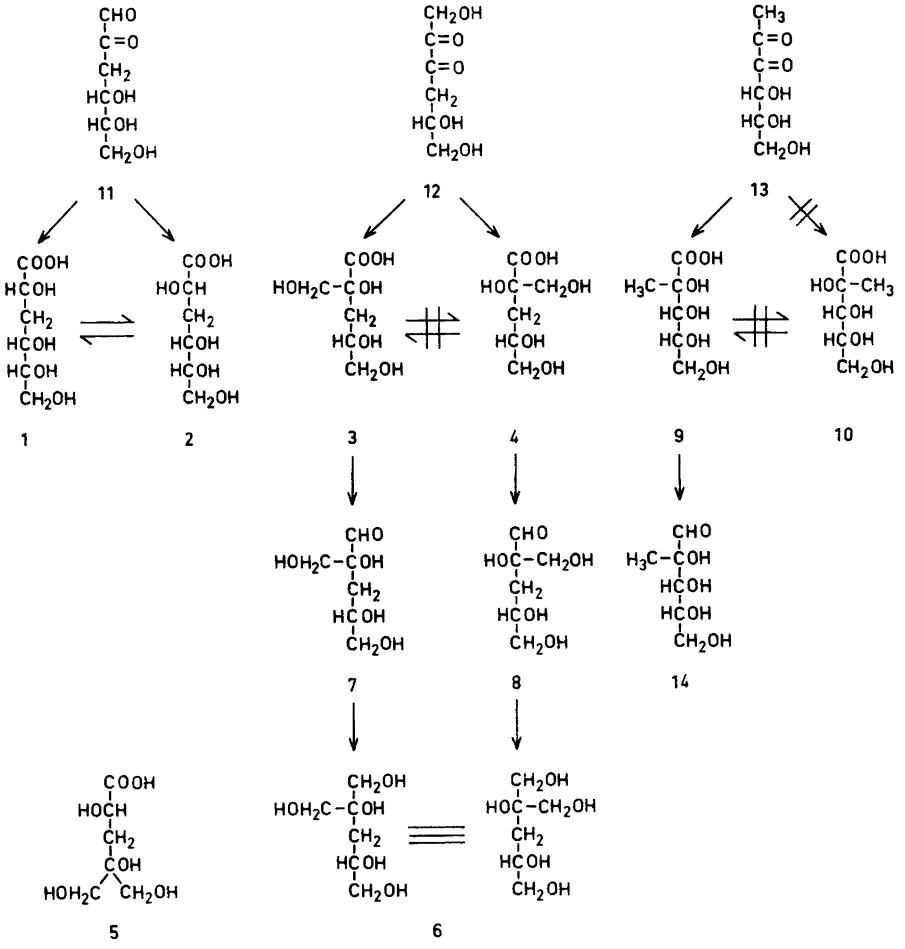
The six-carbon saccharinic acids obtained from D-glucose, D-mannose and D-fructose derivatives have been investigated. The new "*β*"-D-glucoisosaccharinic acid has been isolated and characterised. This acid is formed together with comparable amounts of "*α*"-D-glucoisosaccharinic acid on alkaline degradation of 4-*O*-substituted D-glucoses. "*β*"-L-Glucosaccharinic acid has been synthesised and it has been demonstrated that only the "*α*"- and no "*β*"-D-glucosaccharinic acid is formed on alkaline degradation of 1-*O*-substituted D-fructoses. The 1,4-lactones of the acids have been reduced to the corresponding sugars. The 1,4-lactones of the six acids have been separated as their trimethylsilyl ethers by gas-liquid chromatography.

The so called saccharinic acids are formed by alkaline-rearrangements of reducing sugars, and their formation and chemistry have been reviewed previously.[1,2] Three types of six-carbon saccharinic acids, D-glucosaccharinic, D-glucometasaccharinic and D-glucoisosaccharinic acids are formed from the sugars D-glucose, D-mannose and D-fructose and from derivatives of these sugars. The final step in their formation involves a benzilic acid type of rearrangement of a dicarbonyl compound, during which a new asymmetric centre is formed. There are therefore two possible isomers of each type, designated "*α*"- and "*β*"-. In the present paper studies on the formation of these acids, with special reference to the proportions of "*α*"- and "*β*"-isomers formed and studies on the reductions of saccharinolactones to reducing sugars are reported.

The "*α*"- and "*β*"-D-glucometasaccharinic acids, 3-deoxy-D-*ribo*-hexonic acid (1) and 3-deoxy-D-*arabino*-hexonic acid (2) are formed in good yields by alkaline degradation of 3-*O*-substituted D-glucoses. An equilibrium between the lactones is established on heating.[3,4] The lactones have been reduced to 3-deoxy-D-*ribo*-hexose and 3-deoxy-D-*arabino*-hexose, respectively.[5] The observations that the best yields of sugar are obtained when the D-*ribo*-lactone is reduced with borohydride and the D-*arabino*-lactone with sodium amalgam were confirmed.

The "*α*"-D-glucoisosaccharinic acid, 3-deoxy-2-*C*-hydroxymethyl-(D-*erythro* or D-*threo*)-pentonic acid (3 or 4) is formed by alkaline treatment of 4-*O*-

substituted D-glucoses. It is readily converted to its crystalline calcium salt and its 1,4-lactone. There are indications in the literature [1] that the epimeric "β"-acid is also formed, but it has not been characterised. In two recent communications Whistler and BeMiller [6] and Whistler and Medcalf [7] report the isolation of "β"-D-glucoisosaccharinic acid by alkaline treatment of guaran and lactose and by treatment of lactose in liquid ammonia. Their acid, which gives a crystalline benzoate, has, however, some properties which are not in agreement with the known structures of 3 and 4. In contrast to the "α"-acid and other γ-hydroxy-carboxylic acids it does not lactonise. It is reported to be a very much weaker acid than the "α"-form. Furthermore the proportions of "α"- and "β"-acids appeared to be dependent upon the nature of the starting material, in disagreement with the generally accepted mechanism involving a 4-deoxy-2,3-hexodiulose (12) as an intermediate.



We subjected lactose to alkaline treatment and isolated the "*α*"-glucoisosaccharinic acid as its calcium salt. The lactone mixture obtained from the mother liquors was fractionated on a cellulose column. One of the fractions, which was chromatographically homogeneous, had the same R_F-value as the 1,4-lactone of "*α*"-D-glucoisosaccharinic acid, but did not crystallise. After benzoylation of this fraction, thin-layer chromatography revealed the presence of two components, one of which had the same mobility as the tri-*O*-benzoate (m.p. 120.5—121.5°, $[\alpha]_D$ + 46.6°) of "*α*"-D-glucoisosaccharinolactone. The substance giving the other spot was isolated by preparative thin-layer chromatography and obtained crystalline (m.p. 113.5—114.5°, $[\alpha]_D$ + 42.5°). Further quantities of this substance were obtained by fractional crystallisation of the benzoate mixture. The substance analysed as a tri-*O*-benzoate of a six-carbon saccharinolactone and gave a strong absorption at 1779 cm^{-1}, characteristic of 1,4-lactones. The free lactone was prepared from the benzoate. It was amorphous, $[\alpha]_D$ + 28°, and paper chromatographically hardly distinguishable from the "*α*"-lactone. This lactone and the "*α*"-lactone were reduced by borohydride to the corresponding alditols. These, which were amorphous and had $[\alpha]_D$ −13° and −12°, respectively, were indistinguishable by paper chromatography, paper electrophoresis in borate buffer, and gas-liquid chromatography of their trimethylsilyl ethers.[8,9] Their IR spectra, and more significantly, their NMR spectra were superimposable, showing that the two substances are identical. The lactones of the two possible D-glucoisosaccharinic acids, and also the lactone of 3-deoxy-4-*C*-hydroxymethyl-L-*glycero*-pentonic acid (5) should all give the same alditol, 3-deoxy-2-*C*-hydroxymethyl-D-*glycero*-pentitol (6). There appears to be no possible route for the formation of the last mentioned acid (5) from lactose, and furthermore, the acid was not epimerised by alkaline treatment, (see below) indicating the absence of a hydrogen atom *α*- to the carboxyl group. The new acid is therefore the "*β*"-D-glucoisosaccharinic acid (4 or 3). The optical rotations of the two D-glucoisosaccharinolactones and of their benzoates do not allow any conclusions to be drawn about their configurations at C-2, which remain unsettled. The "*α*"- and "*β*"-lactones were readily separated as their trimethylsilyl ethers by gas-liquid chromatography (see Table 1). By this technique it was proved that the two corresponding acids are formed in approximately equal amounts on alkaline degradation of 4-*O*-methyl-D-glucose, maltose, lactose or guaran, and that the acids and their lactones are not epimerised on alkaline treatment or distillation. The results of Whistler and coworkers [6,7] concerning the *β*-D-glucoisosaccharinic acid cannot be explained.

The sugars (7,8) corresponding to the two D-glucoisosaccharinic acids were prepared by reduction of the lactones, and it was found for both that reduction with borohydride was better than that with sodium amalgam. The sugars were chromatographically pure but were amorphous. The reduction of the "*α*"-lactone has been studied earlier.[10]

"*α*"-D-Glucosaccharinic acid is generally prepared by alkaline treatment of D-fructose or 1-*O*-substituted D-fructoses. It has recently been proved to be 2-*C*-methyl-D-*ribo*-pentonic acid (9).[11] In agreement with this structure its 1,4-lactone had a high mobility on paper electrophoresis in sulphonated phenylboronic acid,[12] characteristic for *cis*-diol groupings in fivemembered

rings. The corresponding lactone with the L-*arabino*-structure (see below) did not migrate. The "*α*"-lactone was further characterised as its tri-*O*-benzoate. The epimeric "*β*"-D-glucosaccharinic acid, 2-*C*-methyl-D-*arabino*-pentonic acid (10), has not been described. We prepared the L-isomer of this acid, and the amorphous 1,4-lactone, by bromine oxidation of the synthetic sugar 2-*C*-methyl-L-arabinose.[13] The two lactones were separated as their trimethylsilyl ethers by gas-liquid chromatography (Table 1). The lactone mixture obtained from either D-fructose or 1-*O*-benzyl-D-fructose by alkaline treatment, isolation of the acids and lactonisation was investigated by the same method. Not even traces of a substance, with the same retention time as the 1,4-lactone of 2-*C*-methyl-L-*arabino*-pentonic acid were observed, indicating that the "*β*"-glucosaccharinic acid had not been formed. As expected, neither of the glucosaccharinic acids was isomerised on alkaline treatment or heating. The dicarbonyl intermediates in the formation of D-glucometasaccharinic acid, D-glucoisosaccharinic acid and D-glucosaccharinic acid have the structures of 11, 12, and 13, respectively. It is only in 13 that the asymmetric centre formed during the rearrangement is adjacent to an asymmetrically substituted carbon atom. It seems reasonable, therefore, that the two former should give comparable amounts of two isomeric acids but that the rearrangement of the latter should be sterically controlled to a higher degree. It is remarkable, however, that only one of the acids, that with the D-*ribo*-configuration, is formed.

2-*C*-Methyl-D-ribose (14), chromatographically indistinguishable from its L-isomer,[14] was prepared by sodium amalgam reduction of the "*α*"-D-glucosaccharinilactone and was characterised as its toluene-*p*-sulphonylhydrazone. The borohydride reduction was less successful. The reduction of this substance has been studied earlier.[15-17]

1-*O*-Toluene-*p*-sulphonyl-D-fructose was treated with alkali. It was hoped that the tosyl group would facilitate the elimination at C-1, yielding either 1-deoxy-D-*glycero*-2,3-hexodiulose (13) or some degraded or rearranged product. The substance was however rapidly hydrolysed to D-fructose.

The separation of the 1,4-lactones of the six saccharinic acids, as their trimethylsilyl ethers, was accomplished by gas-liquid chromatography. The method seems to be of general value for work in this and related fields. The chromatographic properties of the lactones are given in Table 1.

Table 1. Chromatographic properties of saccharino-1,4-lactones.

1,4-Lactone	Gas-liquid chromatography retention time (min)	Paper chromatography R_F-values		
		Solvent A	Solvent C	Solvent D
"α"-D-glucometasaccharino-	19.2	0.57	0.50	0.39
"β"-D-glucometasaccharino-	22.9	0.53	0.42	0.30
"α"-D-glucoisosaccharino-	9.5	0.59	0.52	0.41
"β"-D-glucoisosaccharino-	10.8	0.57	0.50	0.39
"α"-D-glucosaccharino-	6.2	0.68	0.61	0.60
"β"-L-glucosaccharino-	7.3	0.65	0.61	0.55

EXPERIMENTAL

Concentrations were carried out under reduced pressure below 45°. Melting points are corrected.

The solvent systems used for paper chromatography and buffers used for paper electrophoresis (on Whatman No. 1 papers) were: A. Ethyl acetate-acetic acid-water, 3:1:1, B. ethyl acetate-pyridine-water, 8:2:1, C. butanol-ethanol-water, 10:3:5, D. butanone, saturated with water, E. 0.1 M borate, pH 10, and F. 0.1 M sulphonated phenylboronic acid, pH 6.5.

Thin-layer chromatography was carried out on "Kieselgel HF_{254} nach Stahl" using ethyl acetate-light petroleum (b.p. 40—60°), 1:5, as solvent.

Gas-liquid chromatography of trimethylsilyl ethers, prepared according to Sweeley and coworkers,[9] was carried out on a butanediol-succinate column at 160°.

Conventional spraying agents for acids, lactones, polyols and carbonyl compounds were used.

D-Glucoisosaccharinic acids

Isolation from lactose. Lactose was treated with aqueous calcium hydroxide and the calcium salt of the "α"-D-glucoisosaccharinic acid isolated.[18] The 1,4-lactone, m.p. 94—95°, $[\alpha]_D^{22}$ + 62.7° (*c* 0.9, water), was prepared from this salt. The mother liquors from the calcium salt were passed down a column of Dowex 50 (H^+) and concentrated to a syrup. A paper chromatographic investigation of this syrup revealed the presence of three main components giving lactone reactions. Part of the syrup (8.5 g) was fractionated on a cellulose column (5 × 105 cm) using solvent system D. Three top fractions (*a* 0.79 g, *b* 0.48 g, and *c* 0.92 g) each containing essentially pure lactones were obtained. Fraction *c* (the last eluted of the three), crystallised from ethanol and showed m.p. 143.5—145.0°, $[\alpha]_D^{22}$—47.4° (*c* 1, water). These values are in good agreement with those reported for "α"-D-galactometasaccharino-1,4-lactone.[19] Nef[20] showed that this lactone when heated in a sealed tube to 200° was partially converted to the "β"-isomer. After a similar treatment of the substance isolated from fraction *c* a second spot appeared on the paper chromatograms, indistinguishable from that given by fraction *b*. The same mixture was also obtained from fraction *b* which consequently should be the "β"-D-galactometasaccharino-1,4-lactone.

Fraction *a* was chromatographically indistinguishable from "α"-D-isosaccharino-1,4-lactone. Gas-liquid chromatography of the trimethylsilylated fraction gave two peaks, one of which corresponded to the "α"-lactone. The lactone mixture in fraction *a* was benzoylated as described for "α"-D-glucoisosaccharino-1,4-lactone.[6] Thin-layer chromatography revealed the presence of two components, one of which was indistinguishable from the "α"-lactone benzoate. Part of the benzoate mixture (250 mg) was fractionated on several thin layer chromatography plates (1 mm thickness). A slower component (170 mg), a mixed fraction (30 mg) and pure "α"-lactone tribenzoate (40 mg) were obtained. The former component crystallised and after recrystallisation from methanol showed m.p. 113.5—114.5° and $[\alpha]^{22}$: (*c* 1, in chloroform): + 42.5° (589 mμ), + 44.4° (578 mμ), + 50.8° (546 mμ), + 88.1° (436 mμ), and + 144.1° (364 mμ). [The corresponding values for the "α"-derivative were m.p. 120.5—121.5° and $[\alpha]^{22}$ (*c* 1, chloroform): + 46.6° (589 mμ), + 48.6° (578 mμ), + 55.2° (546 mμ), + 91.8° (436 mμ), and + 138.8° (364 mμ).] In the IR (KBr) a strong absorption at 1779 cm^{-1} (1,4-lactone) was obtained, but no hydroxyl absorption. (Found: C 68.7; H 4.67. $C_{27}H_{22}O_8$ requires: C 68.3; H 4.67).

Further amounts of crystalline "β"-benzoate were obtained by seeding the benzoylated *a*-fraction. The crystals contained some "α"-benzoate, which could be removed by recrystallisation from methanol.

The "β"-benzoate (0.45 g) was suspended in 60 % aqueous ethanol (40 ml) and 0.2 M sodium ethoxide in ethanol (40 ml) added with stirring. The mixture, which soon became clear, was kept overnight at room temperature; water (100 ml) and Dowex 50 (H^+) resin (25 ml) were added, the mixture stirred for 1 h, filtered and concentrated to about 50 ml. The solution was then extracted with ether (6 × 15 ml), concentrated to dryness and kept for 3 h at 55° to complete lactonisation. The colourless syrup (0.16 g) gave a single peak when investigated by gas-liquid chromatography as above. Part of

the product was further purified by preparative paper chromatography (solvent D) and showed $[\alpha]^{22}$ (*c* 1, water): + 28° (589 mμ), + 30° (578 mμ), + 35° (546 mμ), + 65° (436 mμ), and + 107 (364 mμ). The corresponding values for the crystalline "α"-lactone were: + 62.7°, + 65.4°, + 74.1°, + 121.8°, and + 181.8°.

Reduction of glucoisosaccharino-1,4-lactone to the pentitol. "α"-D-Glucoisosaccharino-1,4-lactone (0.17 g) was reduced to the alditol using sodium borohydride in the presence of cation exchange resin.[21] The pentitol (0.19 g) was purified by preparative paper chromatography (solvent B) and was obtained as a colourless syrup; R_F-values 0.20 (solvent B) and 0.34 (solvent C), respectively, and M_G 0.69 (buffer E). It was homogeneous by gas-liquid chromatography (as trimethylsilyl ether) and showed $[\alpha]_D^{22} - 12°$ (*c* 0.5, water).

"β"-D-Glucoisosaccharino-1,4-lactone was reduced in the same manner, yielding a pentitol, $[\alpha]_D^{22} - 13°$ (*c* 0.4, water). This was indistinguishable from the pentitol prepared from the "α"-lactone by paper chromatography, gas-liquid chromatography, and paper electrophoresis in borate buffer. Their IR-spectra (KBr) were superimposable as well as their NMR spectra, which were consistent with the postulated structure (6).

Formation of D-glucoisosaccharinic acid from maltose, 4-O-methyl-D-glucose and guaran. Maltose was treated with aqueous calcium hydroxide and the mixture worked up as described by Corbett and Kenner.[22] After removal of the crystalline calcium salt of "α"-D-glucoisosaccharinic acid and neutral components, the material was converted to the calcium salts. It was not possible by crystallisation or fractional precipitation of an aqueous solution with ethanol to obtain the pure salt of the "β"-acid. It was shown, however, by converting the salts to the lactones and investigating their trimethylsilyl ethers by gas-liquid chromatography, that the fractions precipitated at higher alcohol concentrations were enriched with the "β"-epimer.

4-*O*-Methyl-D-glucose was treated with aqueous calcium hydroxide as described previously.[23] The product was converted to the lactones, which were shown by gas-liquid chromatography to be the "α"- and "β"-D-glucoisosaccharino-1,4-lactones, with a slight predominance of the latter.

Guaran was subjected to partial hydrolysis followed by treatment with aqueous calcium hydroxide essentially as described by Whistler and BeMiller.[6] The isosaccharinolactone fraction was isolated and on analyses by gas-liquid chromatography comparable amounts of "α"- and "β"-D-glucoisosaccharino-1,4-lactones were found to be present.

Reduction of "α"- and "β"-D-glucoisosaccharino-1,4-lactones to reducing sugars. Sodium borohydride (0.70 g) in water (20 ml) was added to a stirred solution of "α"-D-glucosaccharino-1,4-lactone in water (30 ml) containing 50 % aqueous acetic acid (0.4 ml). The mixture was cooled externally with ice, and the pH kept at about 4 by addition of 50 % aqueous acetic acid. After 30 min excess of acetic acid was added, the solution passed through a column of Dowex 50 (H^+) resin, evaporated to dryness, and distilled with methanol three times to remove boric acid. The syrup, which gave an intense spot for reducing sugar and weak spots for acid, lactone and the pentitol was dissolved in water (100 ml), warmed to 50° and solid sodium carbonate added until a constant pH-value of 8 was reached. After 3 h, Dowex 50 (H^+) and Dowex 3 (free base) resins were added and the mixture stirred for 2 h, filtered, and concentrated to a syrup (0.72 g). Part of the product was further purified by preparative paper chromatography (solvent B) and the amorphous chromatographically pure sugar had $[\alpha]_D^{22} - 22°$ (*c* 1, water); R_F-values 0.29 (solvent B) and 0.35 (solvent C), respectively, and M_G 0.76 (buffer E).

The epimeric sugar from "β"-D-glucoisosaccharino-1,4-lactone was prepared analogously and had $[\alpha]_D^{22}$ + 3° (*c* 0.8, water); R_F-values 0.27 (solvent B) and 0.35 (solvent C), respectively, and M_G 0.76 (buffer E). Both sugars gave a pink colour reaction with *p*-anisidine hydrogen chloride.

The effect of heat and alkali on the lactones and acids. The "α"-lactone was distilled in a Pyrex tube under reduced pressure (0.5 mm Hg) and a bath temperature of 200° and kept at that temperature for 20 min. No "β"-lactone was formed under these conditions. Similarly the "β"-lactone was unchanged by the same treatment.

The lactone was dissolved in 7 % aqueous sodium hydroxide, kept at 97° for 4 h and recovered. Small amounts of degradation products had been formed, but no epimerisation was observed for either the "α"- or the "β"-lactone.

D-Glucosaccharinic acids

"α"-D-*Glucosaccharino-1,4-lactone.* This lactone was prepared from D-fructose as previously described.[24] The lactone mixture in the mother liquors of the crystalline "α"-lactone was investigated by paper chromatography and gas-liquid chromatography. The "α"-lactone and several minor components were found to be present. None of these, however, had the same R_F-value or retention time as the "β"-L-glucosaccharino-1,4-lactone (see below).

1-*O*-Benzyl-D-fructose (0.1 g) was treated with aqueous calcium hydroxide for 17 days as described by Kenner and Richards for the 1-*O*-methyl derivative.[26] After removal of cations and concentration the "α"-lactone crystallised. No "β"-epimer could be detected in the mother liquors.

When 1-*O*-toluene-*p*-sulphonyl-D-fructose was treated with saturated aqueous calcium hydroxide at room temperature, most of the starting material disappeared during the first hour. Fructose was the only product detected.

The tribenzoate of the "α"-D-glucosaccharino-1,4-lactone was prepared as described for the corresponding derivative of "α"-D-isosaccharino-1,4-lactone.[6] It was recrystallised from ethanol as fine needles; m.p. 141.5—142°, and had $[\alpha]_D^{22}$ + 124.6° (*c* 1, chloroform). (Found: C 67.7; H 4.46. $C_{27}H_{22}O_8$ requires: C 68.3; H 4.67). In IR (KBr) a strong absorption at 1780 cm^{-1} (1,4-lactone) was obtained but no hydroxyl absorption.

β-L-*Glucosaccharino-1,4-lactone.* Methyl 2-*C*-methyl-L-*arabino*-pyranoside[13] (1.00 g) in water (50 ml) containing Dowex 50 (H^+) resin was boiled under reflux for 3 h, filtered and concentrated to a syrup (0.90 g). The sugar, 2-*C*-methyl-L-arabinose was chromatographically pure but did not crystallise; $[\alpha]_D^{23}$ −2° (*c* 0.8, water); R_F-values 0.38 (solvent B) and 0.40 (solvent C), respectively, and M_G 0.80 (buffer E). It gave a reddishbrown colour reaction with *p*-anisidine hydrogen chloride.

The sugar (0.43 g) was oxidised with bromine as described by Isbell[26] for the preparation of aldonic acids, to give a colourless syrup (0.39 g). The substance, $[\alpha]_D^{23}$ −106° (*c* 0.6, water), did not crystallise, but was pure as revealed by paper chromatography and gas-liquid chromatography. It showed a strong absorption in IR (KBr) at 1760 cm^{-1}, indicative of a 1,4-lactone. It did not migrate on electrophoresis using buffer F at *ca.* 10° in contrast to "α"-D-glucosaccharino-1,4-lactone which moved fairly rapidly.

2-C-*Methyl*-D-*ribose.* 2 % Sodium amalgam (35 g) was added in three portions over a period of 10 min to a vigorously shaken solution of "α"-D-glucosaccharino-1,4-lactone (1.00 g) in aqueous 2 M sodium hydrogen oxalate (30 ml, pH 3) at 3—5°. During the reaction the pH increased from 3 to 4. After 20 min the solution was filtered. A paper chromatographic examination revealed the presence of a reducing sugar together with small amounts of glyoxylic acid (presumably arising from the oxalic acid) and unreacted lactone. The solution was warmed to 50° and sodium carbonate added until a constant pH of 8 was obtained. It was then deionised by stirring with a mixture of Dowex 50 (H^+) and Dowex 3 (free base) resins. The solution was filtered, concentrated to low volume, treated with charcoal and concentrated to dryness yielding a colourless syrup (0.57 g), which did not crystallise. The sugar, which contained only traces of impurities, was further purified by preparative paper chromatography (solvent C). It showed $[\alpha]_D^{23}$ −12° (*c* 0.9, water); R_F-values 0.41 (solvent B) and 0.40 (solvent C), respectively, and M_G 0.73 (buffer E). It was chromatographically indistinguishable from its enantiomer, obtained by acid hydrolysis of methyl 2-*C*-methyl-β-L-*ribo*-pyranoside.[14] 2-*C*-Methyl-ribose and 2-*C*-methyl-arabinose are well separated by paper chromatography in butanol-ethanol-water (4:1:5), containing 5 % phenylboronic acid,[27] in which their R_F-values are 0.82 and 0.43, respectively. 2-*C*-Methyl-D-ribose was characterised as its toluene-*p*-sulphonylhydrazone, prepared as described previously[28] for other sugars and recrystallised from ethanol: m.p. 169.5—170.0° and $[\alpha]_D^{22}$ + 1.8° (*c* 0.5, pyridine). (Found: C 47.8; H 6.41; S 9.65. $C_{13}H_{20}N_2O_6S$ requires: C 47.0; H 6.07; S 9.63).

Part of the 2-*C*-methyl-D-ribose was oxidised with bromine to give the "α"-glucosaccharino-1,4-lactone, m.p. 163.5—164.0°. The reduction of the "α"-D-glucosaccharino-1,4-lactone with borohydride, as described above for the reduction of the D-glucoisosaccharinic acids, proved to be inefficient.

The effect of heat and alkali on "α"-D-*glucosaccharino-1,4-lactone.* "α"-D-Glucosaccharino-1,4-lactone was subjected to the same thermal and alkaline treatment as described

above for the D-glucoisosaccharino-lactones. No trace of the "β"-epimer could be detected after either treatment.

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REFERENCES

1. Sowden, J. C. *Advan. Carbohydrate Chem.* **12** (1957) 35.
2. Whistler, R. L. and BeMiller, J. N. *Advan. Carbohydrate Chem.* **13** (1958) 289.
3. Kenner, J. and Richards, G. N. *J. Chem. Soc.* **1954** 278.
4. Lindberg, B. and Theander, O. *Svensk Papperstid.* **65** (1962) 509.
5. Wood, Jr., H. B. and Fletcher, Jr., H. G. *J. Org. Chem.* **26** (1961) 1969.
6. Whistler, R. L. and BeMiller, J. N. *J. Org. Chem.* **26** (1961) 2886.
7. Whistler, R. L. and Medcalf, D. G. *J. Org. Chem.* **27** (1962) 3560.
8. Hedgley, E. J. and Overend, W. G. *Chem. Ind. (London)* **1960** 378.
9. Sweeley, C. C., Bentley, R., Makita, M. and Wells, W. W. *J. Am. Chem. Soc.* **85** (1963) 2497.
10. Schorigin, P. and Makarowa-Semljanskaja, N. N. *Ber.* **66** (1933) 387.
11. Foster, A. B., Inch, T. D., Lehman, J. and Webber, J. M. *J. Chem. Soc.* **1964** 948.
12. Garegg, P. J. and Lindberg, B. *Acta Chem. Scand.* **15** (1961) 1913.
13. Wall, H. M. *M. Sc. Thesis, University of London* (1964).
14. Rafferty, G. A. (Mrs), *M. Sc. Thesis, University of London* (1964).
15. Scheibler, C. *Ber.* **16** (1883) 3010.
16. Fischer, E. *Ber.* **22** (1889) 2204.
17. Votoček, E. *Collection Czech. Chem. Commun.* **2** (1930) 158.
18. Whistler, R. L. and BeMiller, J. N. In *Methods in Carbohydrate Chem.* Academic Press, New York and London 1963, part II, p. 477.
19. Sowden, J. C., Blair, M. G. and Kuenne, D. J. *J. Am. Chem. Soc.* **79** (1957) 6450.
20. Nef, J. V. *Ann.* **376** (1910) 1.
21. Wolfrom, M. L. and Thompson, A. In *Methods in Carbohydrate Chem.* Academic Press, New York and London 1963, part II, p. 66.
22. Corbett, W. M. and Kenner, J. *J. Chem. Soc.* **1954** 1789.
23. Kenner, J. and Richards, G. N. *J. Chem. Soc.* **1955** 1810.
24. Whistler, R. L. and BeMiller, J. N. In *Methods in Carbohydrate Chem.* Academic Press, New York and London 1963, part II, p. 484.
25. Kenner, J. and Richards, G. N. *J. Chem. Soc.* **1954** 1784.
26. Isbell, H. S. In *Methods in Carbohydrate Chem.* Academic Press, New York and London 1963, part II, p. 13.
27. Ferrier, R. J., Overend, W. G., Rafferty, G. A. (Mrs), Wall, H. M. and Williams, N. R. *Proc. Chem. Soc. (London)* **1963** 133.
28. Helferich, B. and Schirp, H. *Chem. Ber.* **86** (1953) 547.

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