

Reactions between D-Glucosone and Alkali

BENGT LINDBERG and OLOF THEANDER

*Träkemiska avdelningen, Svenska Träforskningsinstitutet, Stockholm Ö, Sweden and
Institutionen för Organisk kemi, Stockholms Universitet, Stockholm, Sweden*

D-Glucosone (D-*arabino*-hexosulose), on treatment with alkali, gives a mixture of acids, consisting largely of mannonic, gluconic, arabinonic, ribonic and erythronic acids. The stereoselective rearrangement into mannonic acids is the main reaction with calcium hydroxide and the cleavage yielding arabinonic acid is the main reaction with sodium hydroxide. The similarity in reaction products obtained when glucose is treated with aqueous sodium polysulphide and when glucosone is treated with aqueous sodium hydroxide strongly supports the hypothesis that glucosone is an intermediate in the former reaction.

Studies on the reactions between D-glucose and aqueous sodium polysulphide were reported in a previous paper.¹ In addition to the saccharinic acids, also formed on treatment of glucose with aqueous sodium hydroxide, the formation of four aldonic acids, mannonic, arabinonic, ribonic, and erythronic acids, was observed. Gluconic acid was not detected in the reaction product. Similar results were obtained when cellobiose or hydrocellulose was subjected to the same treatment and hydrolysed.² In the latter experiments, the formation of small amounts of gluconic acid was also observed.

As the predominant hexonic acid was mannonic acid and not gluconic acid, the formation of gluconic acid as the primary oxidation product seemed to be ruled out. It also seemed improbable that mannose, which should be present at low concentration in equilibrium with glucose in the alkaline solution, could be oxidised so much more readily that mannonic acid became the major product. We therefore suggested¹ that the primary oxidation product might be D-glucosone (D-*arabino*-hexosulose) and that the latter was subsequently rearranged by a benzylic acid type of rearrangement, to give mainly D-mannonic acid. A similar, stereoselective rearrangement was recently observed.³ 1-Deoxy-D-*erythro*-2,3-hexodiulose on alkaline treatment yielded predominantly "α"-glucosaccharinic acid (2-C-methyl-D-ribonic acid) and only traces of "β"-glucosaccharinic acid (2-C-methyl-D-arabinonic acid).

The reactions between D-glucosone, and other osones, with alkali have been little studied. It has, however, been reported⁴ that D-glucosone and its tetra-

Table 1. Relative proportions of the aldonic acids formed on alkaline treatment of D-glucosone.

Acid	Treatment with NaOH	Treatment with Ca(OH) ₂
Mannonic	14	53
Gluconic	3	8
Arabinonic	59	29
Ribonic	4	5
Erythronic	20	5

acetate yield kojic acid on treatment with alkali. In the present paper studies on the products obtained by the treatment of D-glucosone with aqueous sodium hydroxide and aqueous calcium hydroxide are reported.

The treatment of D-glucosone with 0.04 M aqueous sodium hydroxide for 2 h at 50° caused complete consumption of the starting material and the appearance of the four pentoses, arabinose, ribose, xylose and, in traces only, lyxose, as demonstrated by paper chromatography and electrophoresis. Cleavage between carbon 1 and 2 in glucosone could yield arabinose and the formation of the other pentoses must be due to isomerisation before or after this cleavage. Several acids were also formed and these were the only reaction products when the alkaline treatment was carried out at 100° for 5 h. The acids, as their lactones, were identified by paper chromatography and by gas-liquid chromatography of their trimethylsilyl ethers.⁵ The relative proportions of the acids were determined by the latter method (Table 1). A considerable amount of mannonic acid but a relatively small amount of gluconic acid was found. Kojic acid, which gives a typical colour reaction with ferric chloride, was detected in traces only.

When D-glucosone was treated with 0.02 M aqueous calcium hydroxide for 5 h at 100°, the same acids were obtained, but in different proportions (Table 1). With this reagent mannonic acid was formed in the highest yield, followed

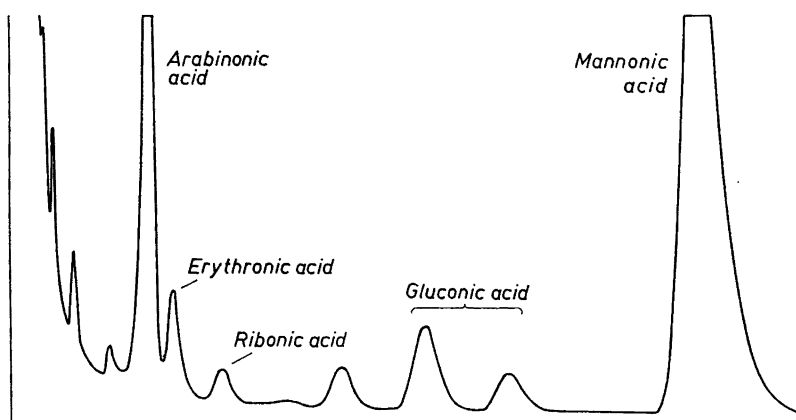


Fig. 1. Gas-liquid chromatography of lactones (as their trimethylsilyl ethers) from treatment of D-glucosone with aqueous calcium hydroxide.

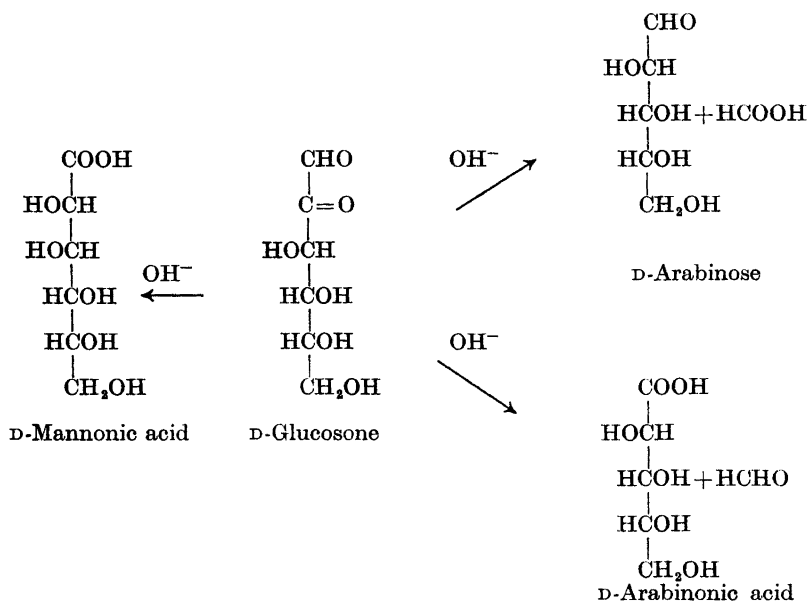
by arabinonic acid. In addition to the acids listed in Table 1 the formation of small amounts of some other acids was also observed, both after the sodium and the calcium hydroxide (Fig. 1) treatment. Those with the low retention times are probably C₄- and C₅-saccharinic acids. A peak before the gluconolactone peaks might be due to an unidentified higher acid.

It has been observed with other α -dicarbonyl sugars that treatment with calcium hydroxide favours the benzilic acid type of rearrangement whereas treatment with sodium hydroxide favours the hydrolytic cleavage between the carbonyl groups.⁶ The same behaviour has now been demonstrated for glucosone. The cleavage seems to proceed in two ways, giving either formic acid and arabinose or formaldehyde and arabinonic acid (Fig. 2).

The formation of ribonic acid indicates that some isomerisation of glucosone may precede the cleavage. Treatment of glucose with polysulphide gives a yield of ribonic acid which is of the same high order of magnitude as that of arabinonic acid. Thus it is probable that the ribonic acid formed under these conditions arises largely from pentoses which are produced by cleavage of glucosone, *via* oxidation to D-erythro-pentosulose and alkaline rearrangement. It has previously¹ been demonstrated that gluconic acid is not significantly epimerised in alkaline solution at 100°. It seems likely that the same should be true for arabinonic acid.

Erythronic acid may be formed by cleavage of a 2,3-hexodiulose, also formed by the isomerisation of glucosone. The polysulphide treatment of glucose¹ may, however, give rise to the hexodiulose directly by oxidation.

Fig. 2. Main reaction of D-glucosone in alkaline solution.



It is also possible that erythronic acid is formed by cleavage of *D-erythro*-pentosulose.

Some saccharinic acids may derive from the pentoses formed by cleavage of glucosone or its isomerisation products. The benzilic acid type of rearrangement of glucosone is, as anticipated, stereoselective giving mannonic acid as the major and gluconic acid as the minor reaction product. In both this example and that reported previously,³ where a stereoselective rearrangement of an α -dicarbonyl sugar has taken place, there is an asymmetrical carbon atom adjacent to the dicarbonyl grouping, which probably directs the reaction. The main reactions which *D*-glucosone undergoes in alkaline solution are summarised in Fig. 2.

Strong support for the hypothesis that *D*-glucosone is the primary oxidation product in the treatment of *D*-glucose with sodium polysulphide is thus provided by the facts that the same aldonic acids are formed from both polysulphide oxidation of *D*-glucose and alkaline treatment of *D*-glucosone, and that considerably more mannonic than gluconic acid is formed in both reactions.

It is also likely that osones are intermediates in other reactions when reducing sugars, including polysaccharides having reducing endgroups, are treated with oxidants under alkaline conditions. Some examples are the formation of *D*-arabinonic⁷ and *D*-erythronic acid⁸ on treatment of *D*-glucose and *D*-ribose, respectively, with oxygen in alkaline solution. The possibility of osone-intermediates was already suggested by Nef⁹ in order to explain the products obtained on oxidation of sugars with Fehling's solution.

EXPERIMENTAL

General methods. Solutions were concentrated by evaporation under reduced pressure, at a temperature not exceeding 45°.

Paper chromatograms were run on Whatman No. 1 filter papers using the following systems (v/v): A. Ethyl acetate-acetic acid-water, 3:1:1, B. Ethyl acetate-pyridine-water, 8:2:1, and C. Butanone, saturated with water.

Paper electrophoresis was carried out on Whatman No. 1 filter papers in 0.1 M hydrogen sulphite, pH 4.7 at 50°. Conventional spray reagents for polyols, acids, lactones, and reducing sugars were used.

Gas-liquid chromatography of lactones, as their trimethylsilyl derivatives,⁵ was performed on a Perkin-Elmer 820 instrument, using a butan-1,4-diol succinate column at 160°. The response factors for the different lactones were determined using mixtures of authentic samples.

D-Glucosone (*D-arabino*-hexosulose) was prepared by removal of the phenylhydrazine residues in *D-arabino*-hexose phenylosazone.¹¹ The compound gave double spots with tailing between on paper chromatography but a single, compact spot on paper electrophoresis.

Alkaline treatment of D-glucosone. A solution of *D*-glucosone (50 mg) in 0.04 M sodium hydroxide (25 ml) was heated at 50° for 2 h (small scale experiments had shown that no starting material remained after that time). Subsequently the solution was treated with Dowex-50 (H⁺) and concentrated. The resulting syrup was examined by paper chromatography, paper electrophoresis, and gas-liquid chromatography (after trimethylsilylation). The following compounds: arabinose, ribose, xylose, lyxose, manno-, glucono-, arabino- and erythro-1,4-lactones, and glucono-1,5-lactone, were observed to be chromatographically and electrophoretically (shown for the pentoses) indistinguishable from authentic samples.

A solution of D-glucosone (50 mg) in 0.04 M aqueous sodium hydroxide (70 ml) was heated at 100° for 5 h and worked up and investigated as above. No free sugars but the same lactones as above were observed. A quantitative analysis of the lactones, by gas-liquid chromatography gave the relative proportions recorded in Table 1.

A solution of D-glucosone (50 mg) in 0.02 M aqueous calcium hydroxide (70 ml) was heated at 100° for 5 h and worked up and investigated as above. No free sugars but the same lactones, although in different proportions, were observed (Table 1; see also Fig. 1).

REFERENCES

1. Abenius, P. H., Ishizu, A., Lindberg, B. and Theander, O. *Svensk Papperstid.* **70** (1967) 612.
2. Ahlgren, P., Ishizu, A., Szabo, I. and Theander, O. *Svensk Papperstid.* **71** (1968) 355.
3. Ishizu, A., Lindberg, B. and Theander, O. *Carbohydr. Res.* **5** (1967) 329.
4. Bayne, S. and Fewster, J. A. *Advan. Carbohydrate Chem.* **11** (1956) 43.
5. Sweely, C. C., Bentley, R., Makita, M. and Wells, W. W. *J. Am. Chem. Soc.* **85** (1963) 2497.
6. Theander, O. *Advan. Carbohydrate Chem.* **17** (1962) 223.
7. Spengler, O. and Pfannenstiel, A. *Z. Wirtschaftsgruppe in Zuckerind.* **85** (1935) 546.
8. Hardegger, E., Kreis, K. and El Khadem, H. *Helv. Chim. Acta* **34** (1951) 2343.
9. Nef, J. U. *Ann.* **357** (1907) 214.
10. Theander, O. *Acta Chem. Scand.* **11** (1957) 717.
11. Bayne, S. *Methods Carbohydrate Chem.* **2** (1963) 421.

Received January 23, 1968.