Carbohydrate Research, 141 (1985) 319–322
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

Note

Cleavage of the intermediate hydroperoxides in the oxidation of D-glucose and D-fructose with oxygen

TAPANI VUORINEN
Laboratory of Wood Chemistry, Helsinki University of Technology, SF-02150 Espoo 15 (Finland)
(Received June 30th, 1984; accepted for publication in revised form, January 28th, 1985)

In an alkaline solution, D-glucose and D-fructose are interconverted *via* their 1,2-enolates. When the enolates are oxidized *in situ* with oxygen, D-arabinonic and formic acids are mainly formed. Although it has been shown that these products are formed *via* an intermediate that is a reversible addition product of D-*arabino*-hexos-2-ulose and hydrogen peroxide[1], it has not been known whether the cleavage goes directly through the hydroperoxide form or *via* a dioxetane structure[2]. To resolve this question, D-glucose and D-fructose have here been oxidized with ^{18}O-enriched oxygen, and the introduction of ^{18}O into the products determined. In addition, the formation of some minor products is discussed.

In Table I, the molar amounts of the hydroxy carboxylic acids identified are expressed in relation to D-arabinonic acid, so that the relative amounts of those products that are formed *via* the 1,2-enolates are roughly independent of the

TABLE I

THE RELATIVE YIELDS OF THE OXIDATION PRODUCTS OF D-GLUCOSE AND D-FRUCTOSE (mol/mol OF D-ARABINONIC ACID)

Product	D-*Glucose*	D-*Fructose*
Lactic acid	0.057	0.043
Glycolic acid	0.173	0.334
Oxalic acid	0.056	0.042
Glyceric acid	0.080	0.189
Tartronic acid	0.041	0.032
2-Deoxytetronic acid	0.016	0.015
Erythronic acid	0.072	0.066
2-Deoxy-*erythro*-pentonic acid	0.011	0.008
Ribonic acid	0.014	0.014
Arabinonic acid	1.000	1.000
Mannonic acid	0.016	0.016
Gluconic acid	0.009	0.003

0008-6215/85/$ 03.30

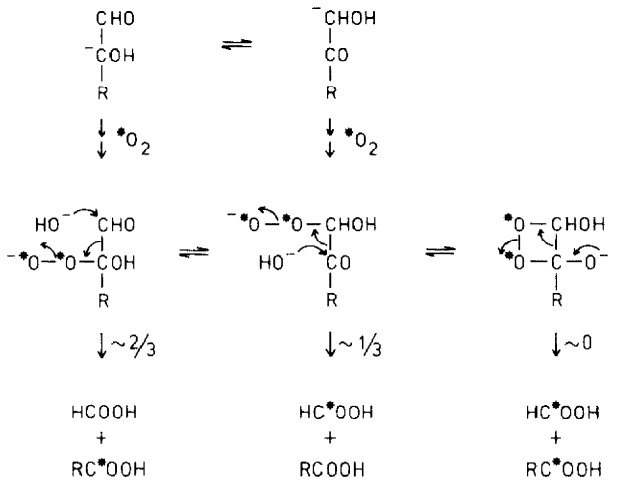
TABLE II

INTRODUCTION OF OXYGEN INTO THE OXIDATION PRODUCTS OF D-GLUCOSE AND D-FRUCTOSE (EQUIV O)

Product	D-*Glucose*	D-*Fructose*
Formic acid	0.35	0.35
Glycolic acid	0.23	0.40
Glyceric acid	0.30	0.24
Erythronic acid	0.71	0.71
2-Deoxy-*erythro*-pentonic acid	0.63	—
Arabinonic acid	0.68	0.68
Mannonic acid	0.00	0.00
Gluconic acid	0.40	—

starting material. The equivalents of oxygen atoms of molecular oxygen introduced into the products are shown in Table II. The same units are used throughout the paper.

If the cleavage of D-*arabino*-hexos-2-ulose went through the dioxetane structure, one equivalent of oxygen would be introduced both in D-arabinonic and formic acids (see Scheme 1). It was, however, found that the amount of oxygen introduced was half of that, or ~2/3 equivalent in D-arabinonic acid and 1/3 equivalent in formic acid. Accordingly, it may be deduced that the cleavage goes directly



Scheme 1

via the C-1 and C-2 hydroperoxides in the ratio of ~1:2 (^{18}O remains on the carbon atom to which the hydroperoxyl group is attached), and half of the consumed, ^{18}O-enriched oxygen is liberated as water. The cleavage of 3-deoxy-D-*erythro*-hexos-2-ulose, which is formed from the 1,2-enolate after β-elimination of hydroxyl ion, goes through the C-1 and C-2 hydroperoxides in almost the same ratio, as is indicated by the amount of oxygen incorporated into 2-deoxy-D-*erythro*-pentonic acid.

TABLE III

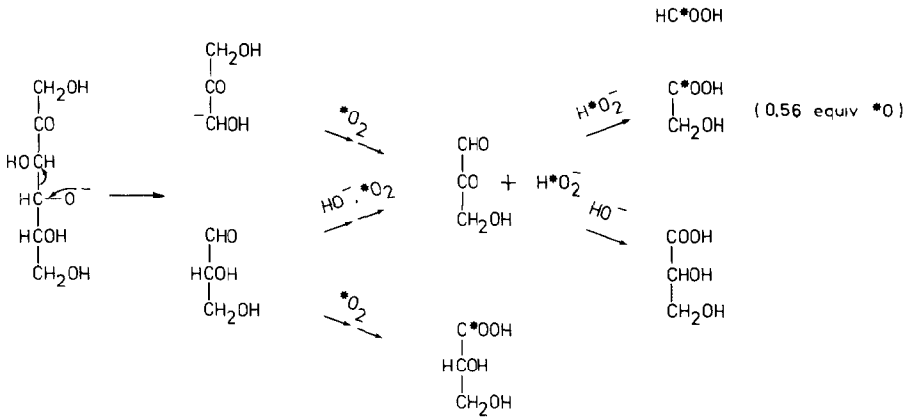
INTRODUCTION OF OXYGEN (EQUIV. O) INTO GLYCOLIC AND GLYCERIC ACIDS (YIELDS IN mol/mol OF D-ARABINONIC ACID) ACCORDING TO THEIR ORIGIN

Origin	*Product*	*Yield*	*Oxygen*
Reversed-aldol cleavage of D-fructose	Glycolic acid	0.196	0.56
	Glyceric acid	0.133	0.21
D-*arabino*-Hexos-2-ulose	Glycolic acid	0.138	0.20
	Glyceric acid	0.056	0.31

D-Erythronic acid was formed in equal amounts from D-glucose and D-fructose, which shows that its formation does not involve the oxidation of the 2,3-enolate of D-fructose, as had earlier been supposed[2]. The content of ^{18}O in D-erythronic acid was, however, high, indicating that D-erythronic acid is formed *via* cleavage of a hydroperoxide.

The yields and the contents of ^{18}O of glycolic and glyceric acids depended on the starting material, and therefore, new values were calculated according to whether the acids originated from the intermediate D-*arabino*-hexos-2-ulose or from the products of the reversed-aldol cleavage of D-fructose (the figures were corrected for isomerization; under the present conditions, ~15 and 1.5% of D-glucose and D-fructose, respectively, were converted into each other) (see Table III).

After the reversed-aldol cleavage, D-fructose gives glyceraldehyde and the enolate of 1,3-dihydroxy-2-propanone, which are oxidized by oxygen to (hydroxymethyl)glyoxal and hydrogen peroxide (see Scheme 2). The high content of ^{18}O in the glycolic acid indicated that it is mainly formed *via* cleavage of the addition product of (hydroxymethyl)glyoxal and hydrogen peroxide. Glyceric acid was mainly formed after a benzilic acid type of rearrangement of (hydroxymethyl)-glyoxal, and no ^{18}O was incorporated in that case, as it was neither in the rearrangement of D-*arabino*-hexos-2-ulose to D-mannonic acid. The small amount of



Scheme 2

oxygen introduced into glyceric acid probably resulted from the direct oxidation of glyceraldehyde to glyceric acid; this is supported by the fact that a significant amount of ^{18}O was introduced into D-gluconic acid. In separate experiments, it was also shown that the yield of D-gluconic acid was increased markedly when the pressure of oxygen was increased, verifying that the aldehydo groups are, to some extent, oxidized by oxygen without enolization.

The formation of glyceric acid, and part of glycolic acid, from D-*arabino*-hexos-2-ulose undoubtedly involves a reversed-aldol cleavage, and oxidation of the resulting glyceraldehyde [the other product, the enolate of (hydroxymethyl)-glyoxal, is probably a significant source of oxalic and tartronic acids]. However, because the content of ^{18}O of glycolic acid was very low, a large part of it must ultimately be formed *via* rearrangement of glyoxal.

EXPERIMENTAL

To a sealed vial (50 mL) provided with a septum was added M sodium hydroxide in 44% (w/w) ethanol (4 mL), the vial was carefully deaerated by successive evacuations and replacements with nitrogen, and finally filled at atmospheric pressure with oxygen which contained 54.7% of ^{18}O. The reaction was started by adding M D-glucose or D-fructose (200 μL). The vial was shaken vigorously for 42 h at 21°. The oxidation products were converted into the ammonium or tetrabutylammonium salts. The ammonium salts were per(trimethylsilyl)ated[3], and the tetrabutylammonium salts esterified with benzyl bromide[4].

The per(trimethylsilyl)ated hydroxy carboxylic acids and benzyl formate were analyzed with a Hewlett–Packard 5880 A gas chromatograph equipped with a flame-ionization detector, and with a Hewlett–Packard 5992 quadrupole mass spectrometer, both equipped with an OV-101-coated fused-silica capillary column. The amount of ^{18}O introduced into the reaction products was calculated from the relative intensities of the peaks at *m/z* 136/138 (formic acid), 205/207 (glycolic acid), 292/294 (glyceric, erythronic, arabinonic, gluconic, and mannonic acids), or 233/235 and 335/337 (2-deoxy-*erythro*-pentonic acid)[5].

ACKNOWLEDGMENTS

Thanks are expressed to Professor Eero Sjöström for his interest in the work and to Mrs. Sirpa Rislakki (Food Research Laboratory, Technical Research Centre of Finland) for recording the mass spectra.

REFERENCES

1 T. VUORINEN, *Carbohydr. Res.*, 127 (1984) 319–325.
2 H. S. ISBELL, *Carbohydr. Res.*, 49 (1976) c1–c4.
3 T. HYPPANEN, E. SJÖSTRÖM, AND T. VUORINEN, *J. Chromatogr.*, 261 (1983) 320–323.
4 P. E. BETHGE AND K. LINDSTROM, *Analyst*, 99 (1974) 137–142.
5 G. PETERSSON, *Tetrahedron*, 26 (1970) 3413–3428.