Carbohydrate Research
Elsevier Publishing Company, Amsterdam
Printed in Belgium

GLYCOL-CLEAVAGE PRODUCTS FROM 1,2-*O*-ISOPROPYLIDENE-α-D-GLUCOFURANOSE

T. D. INCH
Chemical Defence Experimental Establishment, Porton Down, Near Salisbury, Wiltshire (Great Britain)

(Received March 10th, 1967)

INTRODUCTION

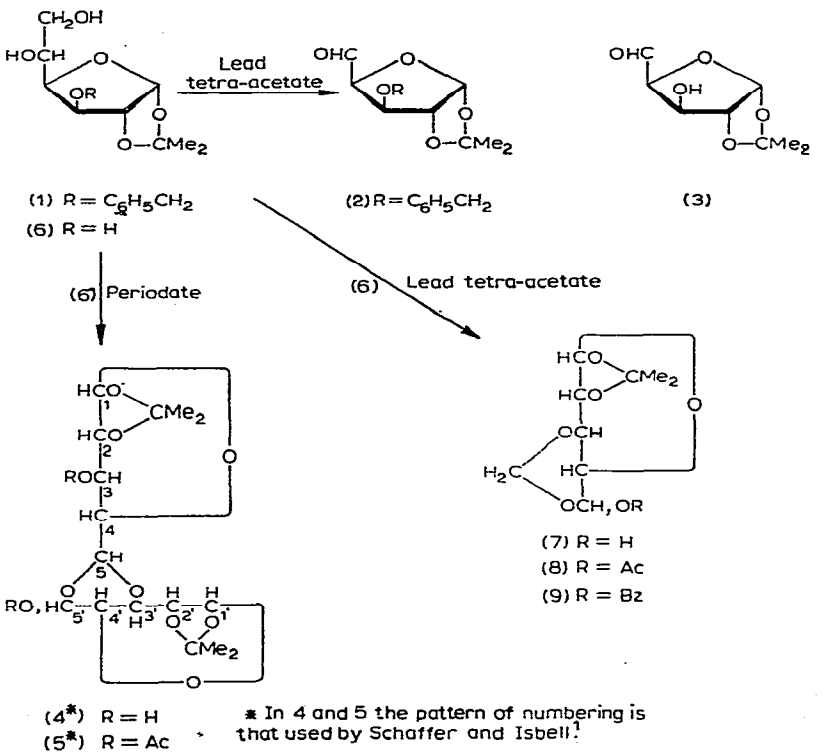
Schaffer and Isbell[1] isolated a dimeric product, and not the expected 1,2-*O*-isopropylidene-α-D-*xylo*-pentodialdo-1,4-furanose (**3**), from the reaction between sodium periodate and 1,2-*O*-isopropylidene-α-D-glucofuranose (**6**). It was suggested[2] that Grignard reagents failed to condense with **3** probably because the aldehyde group is masked in the dimeric form of **3**. However, it has been subsequently shown[3,4] that Grignard reagents do react with the product that results from the oxidation of 1,2-*O*-isopropylidene-α-D-glucofuranose (**6**) with lead tetraacetate. Since the oxidation of **6** with both sodium periodate and lead tetraacetate would be expected to yield the same product, these reactions were investigated in detail to establish the true nature of the glycol-cleavage products and to determine which of these products reacts with Grignard reagents.

DISCUSSION

In an attempt to prepare an authentic sample of 1,2-*O*-isopropylidene-α-D-*xylo*-pentodialdo-1,4-furanose (**3**), 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-pentodialdo-1,4-furanose[2] (**2**) was first prepared by oxidation of 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose[5] (**1**) with lead tetraacetate in benzene. A small sample, purified by chromatography on silica gel, had infrared and nuclear magnetic resonance spectra that were consistent with the expected structure. Catalytic hydrogenolysis of **2**, over freshly prepared palladium, gave a product whose infrared spectrum had only a weak absorption at 1725 cm^{-1} characteristic of the aldehyde group. This product was shown by thin-layer chromatography to contain a small proportion of **2** and a component of much lower mobility, which had chromatographic properties indistinguishable from those of an authentic sample of bis(5-aldo-1,2-*O*-isopropylidene-α-D-*xylo*-pentofuranose) 5,5′:3′,5-cyclic acetal (**4**)*. The slower-moving component was separated from unreacted **2** by column chromatography on silica gel, and its identity as the dimer **4** was confirmed by the usual methods.

*This name for the dimer **4** was proposed by Schaffer and Isbell[1]; **4** may also be named 1,2-*O*-isopropylidene-3,5-*O*-[4,5-*O*-isopropylidene-(L-*gluco*-tetrahydro-3,4,5-trihydroxyfurfurylidene]-(5-hydroxy-D-xylofuranose).

Since dimerisation of **3** apparently occurs so readily, it is not surprising that Schaffer and Isbell[1] obtained a good yield of **4** by oxidation of **6** with sodium periodate. This experiment was repeated by using essentially the conditions described[1], and the reaction product was examined by thin-layer chromatography. Of the two components detected, and subsequently separated by column chromatography on silica gel, the slower moving was chromatographically indistinguishable from the dimer **4**. The faster-moving component (15%, $[\alpha]_D$ +47°, chloroform) was identified as 1,2-*O*-isopropylidene-3,5-*O*-methylene-(5-hydroxy-α-D-xylofuranose) (**7**) and must result from condensation between **3** and the formaldehyde liberated during the glycol cleavage of **6**. The major component was the dimer **4** (47%). Use of chromatography gives the dimer in its anhydrous form, and not as the hydrate initially isolated by Schaffer and Isbell[1].



When 1,2-*O*-isopropylidene-α-D-glucofuranose (**6**) was oxidised with lead tetraacetate in benzene, and the reaction product chromatographed on silica gel, **7** (50%) and the dimer **4** (12%) were isolated. Again, no trace of the free aldehyde **3** was in evidence. Compound **7** was converted into an amorphous monoacetate (**8**) by acetylation with acetic anhydride in pyridine, and into a crystalline monobenzoate (**9**) by benzoylation under similar conditions. Conclusive proof of the structures of **7**, **8**, and **9**, and of the di-*O*-acetyl derivative (**5**) of **4** was obtained by analysis of their n.m.r. spectra. These results will be considered in detail later.

The supposed aldehyde **3** was characterised as its crystalline semicarbazone (m.p. 209°) by Iwadare[6] and by Wolfrom and Hanessian[2]. This semicarbazone can be obtained by treatment of either **4** or **7** with semicarbazide hydrochloride and potassium acetate. It seems probable therefore that the product previously obtained[6] from oxidation of **2** with lead tetraacetate was in fact **7** and not **3**, and also that the product obtained by Wolfrom and Hanessian[2] by hydrogenolysis of **2** was preponderantly the dimer **4**. It is interesting to contrast the reaction between formaldehyde and **3** to give **7**, which presumably occurs under weakly acidic conditions, with the reaction between formaldehyde and **4** under strongly basic conditions[7]. In sodium hydroxide solution, a mixed-aldol reaction apparently occurs, which is immediately followed by a crossed-Cannizzaro reaction, so that the product isolated is 4-*C*-(hydroxymethyl)-1,2-*O*-isopropylidene-L-*threo*-pentofuranose.

One of the main objects of this investigation was to establish which glycol-cleavage products of **6** react with Grignard reagents. From the results previously reported[4], it is obvious that **7** reacts with Grignard reagents, since **7** is the major product formed by oxidation of **6** with lead tetraacetate. It is not surprising therefore that the dimer **4** also reacts with Grignard reagents. When **4** was boiled under reflux with a freshly prepared solution of phenylmagnesium bromide in ether, two compounds were detected in the product. They were separated by column chromatography on silica gel and shown to be 1,2-*O*-isopropylidene-5-*C*-phenyl-α-D-*gluco*-pentofuranose[4] (25%) and 1,2-*O*-isopropylidene-5-*C*-phenyl-β-L-*ido*-pentofuranose[4] (66%). Although the overall yield from this reaction was much higher than when the corresponding reaction was performed[4] on the crude oxidation product of **6**, the relative proportions of the isomers were little affected. Also, it was shown chromatographically that **4** reacts with methylmagnesium iodide to give products indistinguishable from 6-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose and 6-deoxy-1,2-*O*-isopropylidene-β-L-idofuranose.

Proof of structure of oxidation products. — The n.m.r. parameters for **7**, **8**, **9**, and **5**, are listed in Table I. Compound **7** was identified as follows. The n.m.r. spectrum of **7** was integrated to reveal the presence of 6 methyl and 8 other protons. One of the latter protons was shown to be a hydroxyl proton, since it readily exchanged with deuterium oxide. It was immediately apparent that this proton count could be explained if condensation between formaldehyde and **3** had taken place. The ease of dimerisation of β-hydroxyaldehydes is well established[8], and Schaffer and Isbell[1] had already observed that the syrupy product from the oxidation of 1,2-*O*-isopropylidene-α-D-glucofuranose was difficult to free from formaldehyde, and that perhaps some unspecified reaction had occurred. The interpretation of the n.m.r. spectrum of **7** was facilitated by comparison with the spectra of authentic derivatives[9] of 1,2-*O*-isopropylidene-α-D-xylofuranose. Thus, for **7**, the doublets at 5.98 and 4.51 p.p.m., with a measured line-spacing of 3.6 Hz, may be assigned to the C-1 and C-2 ring protons, respectively. The doublets at 5.17 and 4.64 p.p.m., with a measured line-spacing of 6.5 Hz, may be assigned to the two methylene protons, since a coupling of this magnitude does not occur between ring protons in the 1,2-*O*-isopropylidene-α-D-xylofuranose system. Further, a value of 6.5 Hz for such a geminal coupling is consistent

Carbohyd. Res., 5 (1967) 53–61

TABLE I

ASSIGNMENTS IN THE N.M.R. SPECTRA OF DERIVATIVES OF 1,2-*O*-ISOPROPYLIDENE-α-D-*xylo*-PENTODIALDO-1,4-FURANOSE

Compound	*Chemical shifts*[a]							*Coupling constants*[b]				
	C-1	C-2	C-3	C-4	C-5	CH_2	CH_3	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{C<^{H}_{H}}$
7	5.98d	4.51d	3.93d	4.33d	5.32s[d]	5.17d 4.64d	1.31s 1.47s	3.6	<0.5	2.2	<0.5	6.5
8	5.98d	4.54d	3.88	4.33d	6.20s	5.0d 4.75d	1.30s 1.46s 2.12s(OAc)	3.9	<0.5	2.3	<0.5	6.8
9	6.08d	4.59d	4.06d	4.45d	6.50s	5.12d 4.80d	1.30s 1.48s	3.4	<0.5	2.0	<0.5	6.4
5[c]	5.95d (6.01d)	4.46d (4.54d)	5.27d (3.86d)	4.23q (4.30d)	5.11d (6.36s)	— —	1.30(x2) 1.48(x2) 2.06(OAc) 2.15(OAc)	3.1 (3.7)	<0.5 (<0.5)	2.8 (2.7)	5.4 (<0.1)	

[a]In p.p.m. s, singlet; d, doublet; q, quartet. [b]Coupling constants in Hz. [c]For **5**, the figures in parentheses refer to the chemical shifts and coupling constants for the C′ protons. [d]The C-5 proton appeared as a doublet until **7** was equilibrated with deuterium oxide.

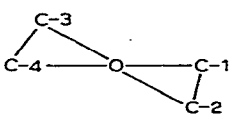
with the values listed by Cookson and co-workers[10]. The doublet at 5.32 p.p.m. collapsed to a single, sharp peak when a deuteriochloroform solution of **7** was shaken with deuterium oxide. Thus, the signal arises from the proton attached to the carbon atom also bearing the hydroxyl group. The doublets at 3.93 and 4.33 p.p.m. obviously result from the C-3 and C-4 protons, since they show the characteristic coupling of 2–3 Hz found for these protons in a 1,2-*O*-isopropylidene-α-D-xylofuranose system, in which it is unusual for there to be any measurable coupling between the protons at C-2 and C-3. From a consideration of the spectra of **7**, **8**, and **9**, it is not possible to make specific assignments for the doublets at 3.93 and 4.33 p.p.m., but, when their spectra are compared with the spectrum of **5**, it seems most likely that the doublets at 3.93 and 4.33 p.p.m. result from the protons at C-3 and C-4, respectively. Since the C-4 proton is only coupled to the C-3 proton, it is reasonable to assign the singlet at 5.32 p.p.m. to the C-5 proton. It will be noticed that acetylation of **7** causes the expected downfield-shift of the C-5 proton to 6.20 p.p.m., and that benzoylation of **7** similarly shifts the C-5 proton to 6.50 p.p.m. The chemical shifts of the other protons are little affected by esterification.

The structure assigned to the dimeric compound by Schaffer and Isbell[1] was confirmed by a consideration of the n.m.r. spectrum of the acetate **5**. The doublets at 5.95 and 6.01 p.p.m. may be assigned to the C-1 and C′-1 ring protons, and the doublets at 4.46 and 4.54 p.p.m. may be assigned to the C-2 and C′-2 ring protons. No specific assignment of these signals is possible. The doublet at 5.27 p.p.m. results from the C-3 proton, since this is the normal chemical shift for a proton attached to C-3 when C-3 also carries an acetoxy group and is in the 1,2-*O*-isopropylidene-α-D-xylofuranose system[9]. By comparison with the spectrum of **8**, it is possible to assign the single peak at 6.36 p.p.m. to the C′-5 proton. The low-field doublet at 5.11 p.p.m. must then result from the C-5 proton. The line spacing for the C-5 proton is 5.4 Hz, a spacing which is also found in the quartet at 4.23 p.p.m. The C-4 proton may therefore be placed at 4.23 p.p.m., and, in view of the close similarity between the two parts of the molecule, it seems reasonable to suggest that the doublet at 4.30 p.p.m. results from the C′-4 proton. The doublet at 3.86 must then result from the proton at C′-3. By analogy, the tentative assignments shown for the C-3 and C-4 protons in **7** are suggested. It will be recognised that the difference in chemical shift between the C-3 and C′-3 protons and between the C-5 and C′-5 protons clearly confirms their non-equivalence and is in agreement with the structure shown. A comparison of the spectra of the dimer acetate **5** and of the acetate (**8**) of the 3,5-*O*-methylene acetal shows the close relationship of the 1,3-dioxan ring formed in each case.

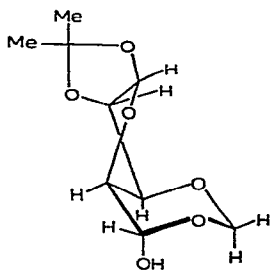
The formation of the 3,5-*O*-methylene acetal (**7**) involves the creation of one new asymmetric centre and thus could give two products, whereas formation of the dimer **4** involves the creation of two new asymmetric centres and could give four products. From the n.m.r. spectra, it is clear that one product has been isolated in each case, and, if the structures postulated are accepted, a further consideration of the n.m.r. parameters should enable a tentative assignment to be made for the configuration of the new asymmetric centres and for the conformation of the 1,3-dioxan

rings. Since the differences in chemical shift between adjacent protons in all of the reported spectra are much larger than the corresponding coupling constants, the measured line spacings can be considered to approximate closely to the true coupling constants. Various workers have attempted to substitute such constants into the Karplus equation[11] (or one of its subsequent modifications[12]), which relates coupling constants with dihedral angles, in order to determine precise molecular conformation. Although the general validity of this type of approach is well established, the dangers of attempting to make too exact a correlation between measured coupling constants and calculated dihedral angles have also been well documented[13]. Because of this, no attempt will be made here to calculate precise dihedral angles, but only the general, broad principles of the so-called Karplus curve will be invoked.

The conformation of the 1,2-*O*-isopropylidene-α-D-xylofuranose structure has been thoroughly investigated by Abraham and his co-workers[9], and the proposed skew-conformation for the puckered furanoid ring seems consistent with other evidence[14]. It was suggested that the coupling constants for the furanoid ring in this type of derivative could only arise if C-2 and C-3 are displaced below and above the other ring members (**10**). The observed coupling constants for compounds **7**, **8**, **9**, and **5** of $J_{1,2}$ 3–4 Hz, $J_{2,3}$ <0.5 Hz., and $J_{3,4}$ 2 Hz are in close agreement with the measured values from which the skew conformation for the 1,2-*O*-isopropylidene-α-D-xylofuranose ring was determined. It is therefore reasonable to assume that this conformation must have remained essentially unchanged when **3** dimerised or reacted with formaldehyde. It follows that the preferred conformation of the 1,3-dioxan ring in **7** and **4** will be that which most easily allows retention of the skew conformation postulated for the furanoid ring. A consideration of molecular models for **7** shows that one conformation for the 1,3-dioxan ring markedly favours the retention of this skew conformation. This is the conformation shown in **11**. Any other chair conformation for the dioxan ring is unfavourable for the retention of the skew conformation, and no flexible conformation for the dioxan ring appears to be sterically more favourable than the depicted chair conformation.



(10)



(11)

If this is the actual conformation, it might, at first sight, be expected that the hydroxyl substituent at C-5 would preferentially occupy the equatorial orientation. However, to explain the negligible coupling constant between the C-4 and C-5 protons,

the dihedral angle between them must be close to 90°. This only occurs when the C-5 proton is equatorially oriented. If the anomeric effect[15] operates, this will in fact be the preferred configuration, since it is well established that the anomeric effect creates preference for axial substitution at C-1 in most pyranose derivatives.

The n.m.r. parameters of **5** are consistent with a similar chair conformation of the intermediate 1,3-dioxan ring. The negligible coupling between the C′-4 and C′-5 protons again suggests that the C′-5 proton is equatorially situated. The coupling constant of 5.3 Hz between the C-5 and C-4 protons suggests that free rotation about the C-4 and C-5 bond occurs, resulting in the observed intermediate value for this vicinal coupling constant[16]. For free rotation of this type to occur, it is most likely that the 1,3-dioxan ring will be equatorially substituted at C-2. An essentially symmetrical molecule of this type is in agreement with the equivalent values observed for the methyl groups of both isopropylidene rings.

EXPERIMENTAL

Melting points are uncorrected. Thin-layer chromatography was performed on microscope slides coated with Silica Gel G, and column chromatography was performed with Silica Gel of particle size 0.05–0.22 mm (both grades of silica were manufactured by E. Merck, Darmstadt, Germany). The chromatoplates were developed with 50% sulphuric acid and/or iodine vapour. N.m.r. spectra were measured with a JEOL, JNM-4H-100 n.m.r. spectrometer at 100 MHz with deuteriochloroform as solvent and with tetramethylsilane as an internal standard. Identification of compounds was based on mixed melting points and comparison of n.m.r. and infrared spectra.

Reaction of 1,2-O-isopropylidene-α-D-glucofuranose (**6**) *with sodium metaperiodate.* — A solution of sodium metaperiodate (15 g) in water (75 ml) was added dropwise to a solution of 1,2-*O*-isopropylidene-α-D-glucofuranose (15 g) in water (100 ml) at 0°. The solution was then stored at room temperature for 30 min and concentrated by freeze drying. The residue was extracted with chloroform, and the chloroform extract was concentrated under diminished pressure at 40°. The product, shown to contain two components by t.l.c. in ether, was fractionated on silica gel with ether. The first component (2 g, 15%) had $[\alpha]_D$ +47° (*c* 10, chloroform), R_F 0.66, and was 1,2-*O*-isopropylidene-3,5-*O*-methylene-(5-hydroxy-α-D-xylofuranose) (**7**). The second component (6 g, 47%) had R_F 0.34 and $[\alpha]_D$ +21° (*c* 1.8, chloroform). This material was crystallised from ether or benzene and had m.p. 178–180° alone or 179–181° in admixture with an authentic sample of the 1,2-*O*-isopropylidene-α-D-*xylo*-pentodialdo-1,4-furanose dimer (**4**); $[\alpha]_D$ 0° (10 min)→ −26° (equil.) (*c* 1.7, water).

Acetylation of dimer **4**. — A solution of **4** (0.4 g) and acetic anhydride (0.5 ml) in pyridine (3 ml) was stored at room temperature overnight. The solution was concentrated by spin evaporation with toluene, and the residue was purified by column chromatography on silica gel with ether as solvent. The diacetate **5** (0.4 g, 80%) had $[\alpha]_D$ +43° (*c* 2.0, ethanol),

Reaction of 1,2-O-isopropylidene-α-D-glucofuranose (**6**) *with lead tetraacetate.* —

Lead tetraacetate (50 g) in benzene was added to a suspension of 1,2-*O*-isopropylidene-α-D-glucofuranose (20 g) in benzene (1 litre), and the mixture was boiled under reflux for 30 min. The cooled suspension was filtered off, the filtrate neutralised with sodium hydrogen carbonate, filtered again, and concentrated. The residue was washed with ethanol, and the ethanol extract was concentrated. The residue was washed thoroughly with ether, and the washings were filtered, concentrated, and chromatographed on silica gel with ether as eluent. The first compound isolated was the 3,5-*O*-methylene acetal (**7**) (10 g, 50%), $[\alpha]_D$ +47° (*c* 2.4, chloroform). The second compound isolated was the dimer **4** (2 g, 12%), m.p. 182°.

Esterification of 1,2-O-isopropylidene-3,5-O-methylene-(5-hydroxy-α-D-xylofuranose). — A solution of **7** in pyridine at 0° was acetylated with acetic anhydride in the usual way to give the 5-acetate **8** as a chromatographically homogeneous syrup, $[\alpha]_D$ +100° (*c* 0.6, chloroform).

A solution of **7** in pyridine at 0° was benzoylated with benzoyl chloride in the usual way to give the 5-benzoate **9**, m.p. 148–149°, $[\alpha]_D$ +113° (*c*. 1.0, chloroform) (Found: C, 59.5; H, 5.9. $C_{16}H_{18}O_7$ calc.: C, 59.6; H, 5.6%).

1,2-O-Isopropylidene-α-D-xylo-pentodialdo-1,4-furanose semicarbazone. — (*a*) A solution of **7** (0.3 g), semicarbazide hydrochloride (0.3 g), and potassium acetate (0.45 g) in water (6 ml) was stirred for 3 h at room temperature. The precipitate was filtered off and recrystallised from water to give the product (0.2 g, 52%), m.p. 209–210°.

(*b*) A solution of **4** (0.3 g), semicarbazide hydrochloride (0.3 g), and potassium acetate (0.45 g) in aqueous ethanol (10 ml) was stirred for 3 h at room temperature. The precipitate was filtered off and recrystallised from water to yield the product (0.3 g, 76%), m.p. 210–211°. Wolfrom and Hanessian[2] recorded m.p. 208–209° and Iwadare[6] recorded m.p. 208–209.5° for this product.

Reaction of phenylmagnesium bromide with the dimer **4**. — A solution of **4** (0.5 g) in ether was added to excess of phenylmagnesium bromide in ether (100 ml), and the solution was boiled for 2 h under reflux. The solution was poured into dilute, aqueous ammonium chloride, and the aqueous solution was extracted with ether. The ether solution was concentrated, and the residue was chromatographed on silica gel with carbon tetrachloride–ethanol (11:1). The first compound isolated was 1,2-*O*-isopropylidene-5-*C*-phenyl-α-D-*gluco*-pentofuranose (0.15 g, 25%), m.p. 94–95° (from di-isopropyl ether). The major product was 1,2-*O*-isopropylidene-5-*C*-phenyl-β-L-*ido*-pentofuranose (0.4 g, 66%), m.p. 159–160° [from ethanol–light petroleum (b.p. 60–80°)].

Hydrogenolysis of 3-O-benzyl-1,2-O-isopropylidene-α-D-xylo-pentodialdo-1,4-furanose (**2**). — Compound **2** (prepared from 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose (**1**) by oxidation with lead tetraacetate in benzene and purified by chromatography on silica gel with benzene–ether) had $[\alpha]_D$ −75° (10 min) (*c* 3.7, chloroform). The n.m.r. spectrum of **2** had (δ values, p.p.m.) a doublet at 9.62 (J 2.1 Hz) (aldehyde proton), a doublet at 4.07 ($J_{1,2}$ 3.9 Hz) (C-1 proton), and peaks at 1.27 and 1.40 characteristic of the isopropylidene methyl groups.

A solution of **2** (1.0 g) in methanol (20 ml) was hydrogenolysed over freshly prepared palladium. The solution was filtered, concentrated, and chromatographed on silica gel with ether as solvent. The first compound isolated was unchanged **2** (0.1 g), and the second compound isolated was the dimer **4** (0.4 g, 60%), m.p. 180–181°.

ACKNOWLEDGMENTS

The author thanks Drs. R. Schaffer and H. S. Isbell for providing a sample of bis(5-aldo-1,2-*O*-isopropylidene-α-D-*xylo*-pentofuranose) 5,5′:3′,5-cyclic acetal. The valued counsel of Professor A. B. Foster is gratefully acknowledged.

SUMMARY

Oxidation of 1,2-*O*-isopropylidene-α-D-glucofuranose with sodium periodate has been shown to yield primarily bis(5-aldo-1,2-*O*-isopropylidene-α-D-*xylo*-pentofuranose) 5,5′:3′5-cyclic acetal (**4**) with 1,2-*O*-isopropylidene-3,5-*O*-methylene-(5-hydroxy-α-D-xylofuranose) (**7**) as the minor product. When 1,2-*O*-isopropylidene-α-D-glucofuranose was oxidised with lead tetraacetate the proportions of **4** and **7** produced were reversed, and **7** became the major product of the reaction. Neither method of oxidation gave any 1,2-*O*-isopropylidene-α-D-*xylo*-pentodialdo-1,4-furanose.

A first-order analysis of the n.m.r. spectra of **7** and its derivatives and of the diacetate from **4** permits tentative assignments for their configurations and conformations.

REFERENCES

1 R. SCHAFFER AND H. S. ISBELL, *J. Am. Chem. Soc.*, 79 (1957) 3864.
2 M. L. WOLFROM AND S. HANESSIAN, *J. Org. Chem.*, 27 (1962) 1800.
3 D. HORTON, J. B. HUGHES AND, J. M. J. TRONCHET, *Chem. Commun.*, (1965) 481.
4 T. D. INCH, *Carbohyd. Res.*, 5 (1967) 45.
5 A. S. MEYER AND T. REICHSTEIN, *Helv. Chim. Acta*, 29 (1946) 152.
6 K. IWADARE, *Bull. Chem. Soc. Japan*, 16 (1941) 40.
7 R. SCHAFFER, *J. Am. Chem. Soc.*, 81 (1959) 5452.
8 A. W. JOHNSON, C. E. DOLGLEISH, W. E. HARVEY, AND C. BUCHANAN, in E. H. RODD (Ed.), *Chemistry of Carbon Compounds*, Elsevier, Amsterdam, 1951, page 703.
9 R. J. ABRAHAM, L. D. HALL, L. HOUGH, AND K. A. MCLAUCHLAN, *J. Chem. Soc.*, (1962) 3699.
10 R. C. COOKSON, T. A. CRABB, J. J. FRANKEL, AND J. HUDEC, *Tetrahedron*, Supplement No. 7, (1966) 355.
11 M. KARPLUS, *J. Chem. Phys.*, 30 (1959) 11.
12 L. D. HALL, *Advan. Carbohydrate Chem.*, 19 (1964) 51.
13 *e. g.* B. COXON, *Tetrahedron*, 21 (1965) 3481.
14 R. U. LEMIEUX, J. D. STEVENS, AND R. R. FRAZER, *Can. J. Chem.*, 40 (1962) 1955.
15 R. U. LEMIEUX, in P. DE MAYO (Ed.), *Molecular Rearrangements*, Part 2, Interscience, New York, 1963.
16 C. A. KINGSBURY AND W. B. THORNTON, *J. Org. Chem.*, 31 (1966) 1000.