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Note

Identification of the products of periodate oxidation of some mono-*O*-isopropylidene derivatives of aldoses and alditols by g.l.c.–m.s.

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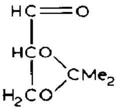
Oxidation of *O*-alkylidene derivatives of aldoses and alditols with lead tetraacetate[1,2], silver carbonate on Celite[3], and periodate[4,5] has frequently been carried out for preparative purposes. Such degradations are useful for the identification of *O*-isopropylidene derivatives[6–8] and, in this connection, a rapid procedure for identification of the oxidation products, which also could be applied to mixtures, was sought. The g.l.c.–m.s. properties of some cleavage products, formed by periodate oxidation of mono-*O*-isopropylidene derivatives of aldoses and alditols, have therefore been investigated, and the results are now reported.

The following compounds were prepared and subjected to g.l.c.–m.s.: 2,3-*O*-isopropylidene-D-glyceraldehyde[7] (**1**), 2,3-*O*-isopropylidene-D-*threo*-tetrodialdose[9] (**2**), 2,4-*O*-isopropylidene-D-erythrose[6] (**3**), 2,3-*O*-isopropylidene-L-threose (**4**),



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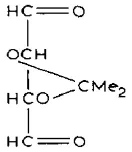

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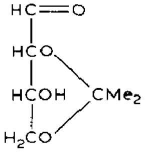

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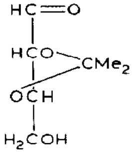

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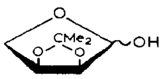

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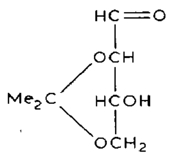

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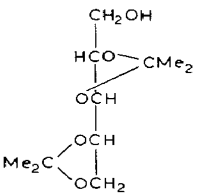

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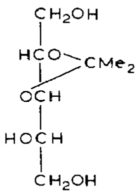

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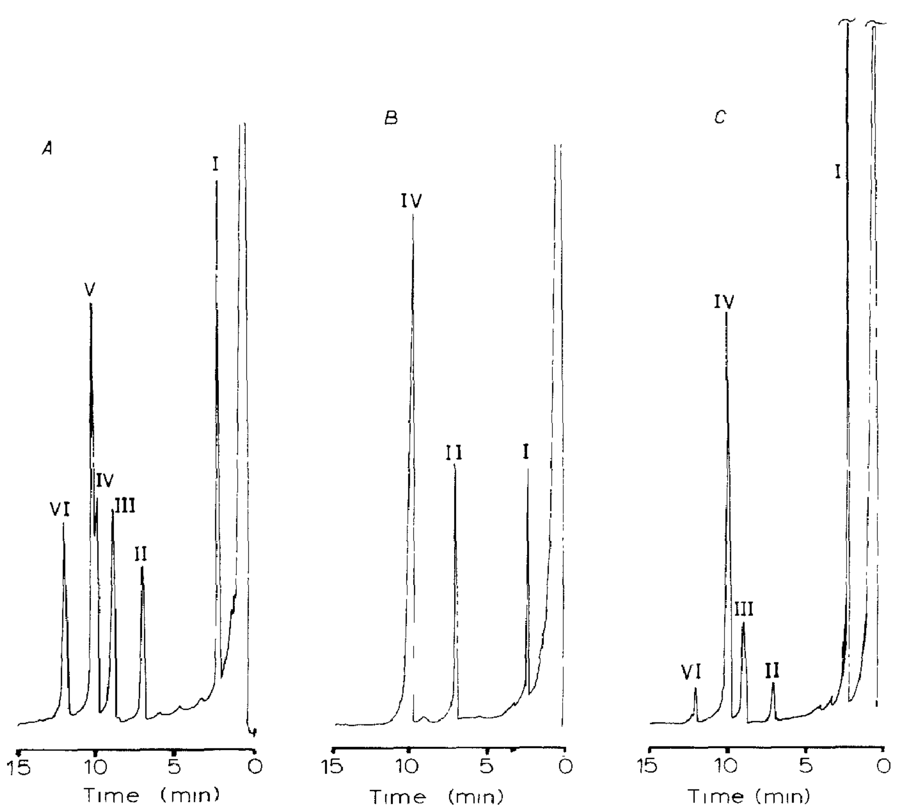

Fig. 1. Gas chromatograms of *A*, a mixture of known mono-*O*-isopropylidene derivatives; *B*, the products obtained by periodate oxidation of the mixture of mono-*O*-isopropylidene-D-glucitols prepared using acetone–Dowex 50W (H^+) resin; and *C*, as *B* but prepared using 2,2-dimethoxypropane–toluene-*p*-sulphonic acid. Key: I, 2,3-*O*-isopropylideneglyceraldehyde; II, 2,3-*O*-isopropylidene-*threo*-tetrodialdose; III, 2,4-*O*-isopropylidene-erythrose; IV, 2,3-*O*-isopropylidenethreose; V, 2,3-*O*-isopropylidene-erythrose; and VI, 2,4-*O*-isopropylidenethreose

2,3-*O*-isopropylidene-L-erythrose[3] (**5**), and 2,4-*O*-isopropylidene-D-threose[8] (**6**). The structures **3** and **6** were confirmed by mass-spectral data. Compound **4** was prepared from 2,3:4,5-di-*O*-isopropylidene-L-arabinitol (**7**) obtained, together with small proportions of the 1,2:4,5-di-*O*-isopropylidene derivative, by sulphuric acid-catalysed acetonation of L-arabinitol. Graded acid hydrolysis of these compounds gave a mixture of the easily separable L-arabinitol and its 2,3-*O*-isopropylidene derivative (**8**), and periodate oxidation of the latter gave **4**.

A gas chromatogram of the products of periodate oxidation is shown in Fig. 1*A*. The mass spectra of the compounds (Table I) are characteristic of the mode of attachment of the *O*-isopropylidene group. Thus, **1**–**4** and **6** undergo primary fragmentation of the carbon chain to give fragments of the type *A*–*D* (Fig. 2). Such fragmentation is not observed[10] for **5**, because it exists in the cyclic hemiacetal form. The spectra of the 2,4-*O*-isopropylidenetetroses (**3** and **6**) are almost identical and

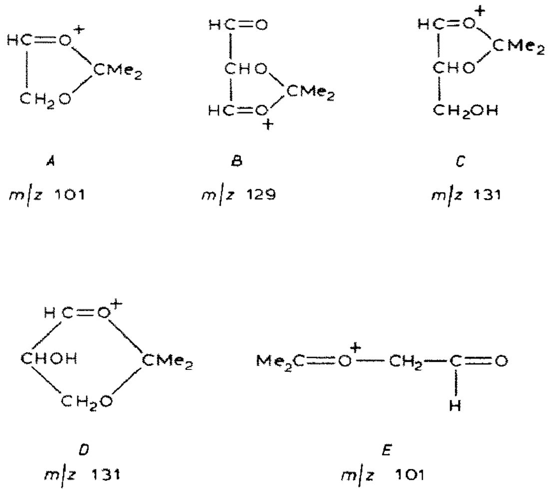

Fig. 2. Characteristic fragments obtained on mass spectrometry of **1**–**6**.

differ from that of 2,3-*O*-isopropylidene-L-threose (**4**) mainly by the lack of an *m/z* 129 peak. The possibility of a 3,4-location of the isopropylidene group is also excluded, since the peak at *m/z* 101 must be of high intensity to be indicative[11,12] of the primary fragment *A*, which would have resulted from such a structure. The peak at *m/z* 101 of low intensity in the spectra of **3** and **6** probably arises from h-rupture[13], observed for hexoses and pentoses carrying 4,6- and 3,5-*O*-isopropylidene groups, respectively[6,8,11,13], and leading to fragment *E*. The peaks at *m/z* 131 in the mass spectra of **3** and **6** correspond to fragment *D* and confirm the structures.

Two differently composed mixtures of mono-*O*-isopropylidene-D-glucitols

TABLE I

MASS-SPECTRAL DATA[a] FOR THE PERIODATE-OXIDATION PRODUCTS

2,3-*O*-Isopropylidene-D-glyceraldehyde (**1**): *m/z* 115 (45), 101 (45), 85 (20), 83 (12), 73 (6), 72 (4), 61 (15), 59 (17), and 43 (100).

2,3-*O*-Isopropylidene-D-*threo*-tetrodialdose (**2**): *m/z* 143 (8), 129 (41), 85 (16), 83 (3), 73 (9), 71 (4), 61 (10), 59 (19), 55 (33), and 43 (100).

2,4-*O*-Isopropylidene-D-erythrose (**3**): *m/z* 145 (14), 131 (27), 113 (2), 101 (6), 85 (7), 83 (2), 73 (9), 71 (5), 59 (100), and 43 (87).

2,3-*O*-Isopropylidene-L-threose (**4**): *m/z* 145 (11), 131 (35), 129 (9), 85 (20), 73 (6), 71 (3), 61 (9), 59 (80), and 43 (100).

2,3-*O*-Isopropylidene-L-erythrose (**5**): *m/z* 145 (54), 143 (4), 102 (6), 99 (10), 85 (26), 73 (8), 71 (8), 59 (97), and 43 (100).

2,4-*O*-Isopropylidene-D-threose (**6**): *m/z* 145 (24), 131 (36), 113 (4), 101 (7), 85 (10), 83 (2), 73 (6), 71 (6), 59 (100), and 43 (86).

[a] The figures in parentheses represent relative intensities (%).

were prepared by treatment of D-glucitol in *N*,*N*-dimethylformamide with acetone–Dowex 50W (H^+) resin for 24 h, and with 2,2-dimethoxypropane–toluene-*p*-sulphonic acid for 1 h, respectively. Each mixture was oxidised with periodate and the products were subjected to g.l.c.–m.s. (the gas chromatograms are shown in Fig. 1*B,C*). Periodate oxidation after resin-catalysed acetonation gave 2,3-*O*-isopropylideneglyceraldehyde, 2,3-*O*-isopropylidene-*threo*-tetrodialdose, and 2,3-*O*-isopropylidenethreose, which could only arise from 1,2- (or 5,6-), 3,4-, and 2,3-substituted glucitol, respectively. Thus, only 1,3-dioxolane rings had been formed. On the other hand, short-time acetalation with 2,2-dimethoxypropane also gave 1,3-dioxane derivatives since 2,4-*O*-isopropylidene-threose and -erythrose were present after periodate oxidation, and the high proportions of 2,3-*O*-isopropylideneglyceraldehyde also obtained showed that acetals involving the primary hydroxyl groups of the hexitol preponderated. These results accord with the previously reported tendency of the second acetalation method to give products of kinetic control[14–16], in contrast to the first method.

EXPERIMENTAL

T.l.c. was performed on Silica gel G with *A*, chloroform–methanol (5:1); and *B*, chloroform–methanol (8:1); and detection with diphenylamine–aniline–phosphoric acid[17] or charring with sulphuric acid. G.l.c. was carried out on a Perkin–Elmer F 11 instrument, equipped with a flame-ionisation detector and a glass column (6 ft. × 2 mm i.d.) filled with 3% of OV-225 on 100/120 Supelcoport. The temperature programme was 6°/min from 70→160°. For g.l.c.–m.s., a Varian Aerograph 2400 gas chromatograph in combination with a Micromass 12 F mass spectrometer was used. The ionisation energy was 70 eV, the ion-source temperature was 200°, and the accelerating voltage was 4 kV. High-resolution m.s. data were obtained with an AEI MS-902 mass spectrometer.

2,3-*O*-Isopropylidene-D-glyceraldehyde[7] (**1**), 2,3-*O*-isopropylidene-D-*threo*-tetrodialdose[9] (**2**), and 2,3-*O*-isopropylidene-L-erythrose[3] (**5**) were prepared by literature methods. Periodate oxidation[6] of 4,6-*O*-isopropylidene-D-glucose gave 2,4-*O*-isopropylidene-D-erythrose (**3**), and oxidation of 4,6-*O*-isopropylidene-D-galactose with silver carbonate on Celite in methanol[8] gave 2,4-*O*-isopropylidene-D-threose (**6**); syrupy **3** and **6** were subjected to m.s. for confirmation of the structure.

2,3-O-Isopropylidene-L-arabinitol (**8**). — A sample (400 mg) of 2,3:4,5-di-*O*-isopropylidene-L-arabinitol[18] (**7**) containing a small proportion of 1,2:4,5-di-*O*-isopropylidene-L-arabinitol was stored at room temperature in aqueous 70% acetic acid (20 mL) for 3 h. The solvents were then removed under reduced pressure below 40°, and the residue was extracted with chloroform–methanol 3:1 (10 mL). The extract was concentrated to ~5 mL, placed on top of a glass column (15 × 3 cm) of Silica gel 60 (35–70 mesh), and eluted with solvent *A* to give **8** (170 mg), $[\alpha]_D^{20}$ −17° (*c* 3, water), R_F 0.49 (solvent *A*). Mass spectrum: *m/z* 177 (14%) (M^+

− Me), 161 (2), 143 (4), 131 (25), 103 (7), 99 (5), 85 (5), 73 (11), 69 (10), 59 (100), and 43 (48).

Anal. Calc. for $C_7H_{13}O_5$ (M^+ − Me): *m/z* 177.0762. Found: *m/z* 177.0766.

*2,3-O-Isopropylidene-*L*-threose* (**4**). — To a solution of **8** (150 mg) in water (5 mL) was added sodium metaperiodate (200 mg), and the pH was adjusted to 6–7 by the addition of solid sodium hydrogencarbonate. After 45 min, 0.5M barium acetate was added until precipitation was complete, the solution was filtered and concentrated under reduced pressure, and the residue was eluted from a column (12 × 2 cm) of Silica gel 60 (35–70 mesh) with solvent *B*. The fraction eluted between 20 and 50 mL contained **4** (105 mg, 84%), $[\alpha]_D^{20}$ +14° (*c* 3, chloroform), R_F 0.52 (solvent *B*).

Anal. Calc. for $C_6H_9O_4$ (M^+ − Me): *m/z* 145.0501. Found: *m/z* 145.0504.

Treatment of **4** (45 mg) with acetone (10 mL) containing 2% of sulphuric acid for 2 h, followed by neutralisation with solid sodium hydrogencarbonate, filtration, and evaporation of the solvent, gave, after crystallisation from ethyl acetate, 1,2-*O*-isopropylidene-β-L-threofuranose (40 mg, 88%), m.p. 83–84°, $[\alpha]_D^{20}$ +12° (*c* 3, acetone), R_F 0.58 (solvent *B*); lit.[19] m.p. 84–85°, $[\alpha]_D$ +13°.

*Mono-O-isopropylidene-*D*-glucitols.* — (*a*) A solution of D-glucitol (1 g) and acetone (0.45 mL) in *N,N*-dimethylformamide (10 mL) was stirred with Dowex 50W (H^+) resin for 24 h at room temperature. Chloroform (30 mL) was then added, and the mixture was filtered, diluted with light petroleum (b.p. 40–60°, 50 mL), and kept overnight at 5–10°. The solvents were decanted from the oily product, which, after removal of residual solvents under reduced pressure, was shown by t.l.c. (solvent *A*) to contain almost exclusively components with R_F 0.25–0.30, typical of mono-*O*-isopropylidenehexitols.

(*b*) To a solution of D-glucitol (1 g) and 2,2-dimethoxypropane (0.75 mL) in *N,N*-dimethylformamide (8 mL) were added a few crystals of toluene-*p*-sulphonic acid. After 1 h at room temperature, chloroform (20 mL) was added, and the solution was neutralised with solid sodium hydrogencarbonate, filtered, and diluted with light petroleum (b.p. 60–80°, 100 mL). The oily product mixture was isolated as described above.

Periodate oxidation. — A mixture of reference *O*-isopropylidene-alditols and -aldoses and the above product mixtures (20 mg) were separately dissolved in water (3 mL), and each was treated with a solution of sodium metaperiodate (80 mg) in water (4 mL), with neutralisation using sodium hydrogencarbonate. After 1 h at room temperature, 0.5M barium acetate was added until precipitation was complete, and the solutions were filtered and concentrated under reduced pressure. The resulting thin syrup was extracted with ethyl acetate (2 × 3 mL), and the extracts were dried (Na_2SO_4) and subjected to g.l.c.–m.s.

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