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Note

Analysis, by g.l.c.–m.s. after isopropylidenation, of the product mixtures obtained by aldol condensation of glycolaldehyde and 1,3-dihydroxy-2-propanone

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The replacement of alkali or alkaline-earth hydroxides with strongly basic anion-exchange resins as catalysts in triose aldol-condensation enhances the relative amount of fructose in the product mixture[1,2]. This observation suggested an investigation of the effect of anion-exchange resins on the stereoselectivity of the aldol condensation of glycolaldehyde and 1,3-dihydroxy-2-propanone. Alkaline-earth hydroxides[3–6] and carbonates[7] have previously been used as catalysts; although aldopentoses were the products after 14 days of reaction[3], shorter reaction times gave 2-pentuloses as main products[4–7]. A mixture containing mainly *threo*-2-pentulose was formed after 30 min with calcium hydroxide as catalyst[6], whereas, with calcium carbonate as the catalyst, *erythro*-2-pentulose was the main product[7]. In addition to pentoses, the product mixtures from this aldol condensation are expected to contain tetroses from the competing reaction between two molecules of glycolaldehyde, whereas self-condensation of 1,3-dihydroxy-2-propanone would give the branched ketohexose dendroketose[8].

G.l.c.–m.s. of the isopropylidene derivatives has been applied to most of the expected products of this aldol condensation[2,9], the exceptions being the tetroses. Threose affords only the 1,2-*O*-isopropylidene derivative, and only the 2,3-isopropylidene acetal is formed from erythrose with acetone–sulphuric acid[10]. Isopropylidenation usually gives mixtures of products less complex than those obtained on trimethylsilylation, and the isopropylidene derivatives have more characteristic mass spectra[2,9,11].

1,2-*O*-Isopropylidenethreose, 2,3-*O*-isopropylidene-erythrose, and the derivative obtained from *glycero*-tetrulose were easily separated from each other and from the derivatives of the other aldol condensation products by g.l.c. on OV-225 (Fig. 1). Their e.i.-mass spectra were clearly different (see Experimental), and that of the threose derivative showed a relatively prominent peak at *m/z* 127, attributed[12] to ($M^+ - Me - H_2O$). This peak was not observed in the spectrum of the

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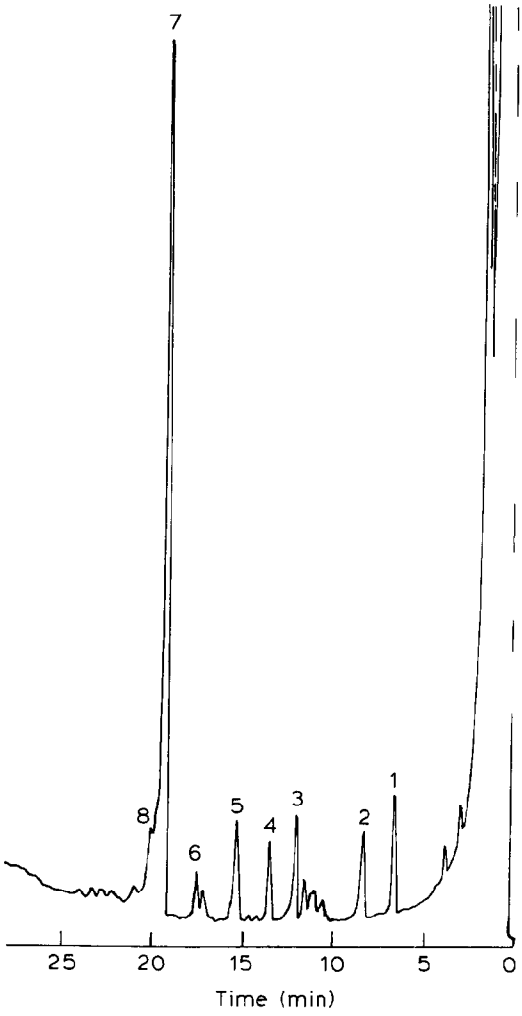

Fig. 1. Gas chromatogram on OV-225 of *O*-isopropylidene derivatives of the products formed by the aldol condensation of glycolaldehyde and 1,3-dihydroxy-2-propanone catalysed by Amberlite IRA-400 (HO^-); 1, DL-*erythro*-2-pentulose; 2, DL-erythrose; 3, DL-threose; 4, DL-xylose; 5 + 6, DL-dendroketose; 7, DL-*threo*-2-pentulose; and 8, DL-*lyxo*-3-hexulose.

erythrose derivative, which, on the other hand, showed a small peak at *m/z* 143, due to the loss of HO-1 from M^+ and usually seen in spectra of derivatives having the anomeric hydroxyl group unsubstituted[9,11,13]. The mass spectrum of the isopropylidenation product of *glycero*-tetrulose indicated it to be the 3,4-*O*-isopropylidene derivative; the base peak appeared at *m/z* 101, corresponding to the C-3,4 part of the molecule after primary fragmentation[11] between C-2 and C-3.

The peak areas from the isopropylidene derivatives in the gas chromatograms are proportional to the molar concentration of the parent sugar (Table I),

TABLE I

CHROMATOGRAPHIC DATA FOR THE *O*-ISOPROPYLIDENE DERIVATIVES

Sugar	*O-Isopropylidene derivative*	T *value*[a]	*Molar response*[b]
erythro-2-Pentulose	1,2:3,4	0.30	0.73
glycero-Tetrulose	3,4	0.34	—
Erythrose	2,3	0.37	0.54
Threose	1,2	0.53	0.52
Xylose	1,2:3,5	0.60	1.01
Dendroketose	1,2:3,4	0.68	0.44
	2,3:4,4′	0.78	0.27
threo-2-Pentulose	2,3	0.86	0.55
lyxo-3-Hexulose	1,2:3,4	0.89	—

[a]Retention time relative to that of 2,3:5,6-di-*O*-isopropylidene-D-mannose. [b]Peak areas obtained from a mixture of the parent sugar in equimolar amounts, relative to that from mannose.

TABLE II

PRODUCTS OF ALDOL CONDENSATION OF GLYCOLALDEHYDE AND 1,3-DIHYDROXY-2-PROPANONE AT ROOM TEMPERATURE

Catalyst	*Reaction time (min)*	*Products (mg)*[a]					
		erythro-2-*Pentulose*	*Erythrose*	*Threose*	*Xylose*	*Dendro-ketose*	threo-2-*Pentulose*
$Ca(OH)_2$ (0.01M)	60	1.6	0.4	0.6	1.6	0.6	5.0
$Ba(OH)_2$ (0.01M)	60	1.4	0.3	0.8	0.2	0.8	5.8
NaOH (0.02M)	60	1.5	0.4	1.4	0.2	0.9	6.6
Dowex 1 (HO^-) resin	15	0.9	0.4	0.5	0.4	1.0	7.0
Amberlite IRA-400 (HO^-) resin	15	0.7	0.6	0.8	0.3	1.0	8.0

[a]Obtained from 8 mg of glycolaldehyde and 12 mg of 1,3-dihydroxy-2-propanone, determined from peak areas of gas chromatograms.

thereby allowing determination of the relative proportions of the products in the aldol condensations (Table II). The yield of *threo*-2-pentulose was higher after 15 min with resin catalysis than after 60 min with the other catalysts. In particular, Amberlite IRA-400 (HO^-) resin gave a high yield of *threo*-2-pentulose, and the *threo*/*erythro* ratio was 11:1, whereas, with the metal hydroxides, the ratio was 3–4:1. This resin also effected the highest stereoselectivity in the triose aldol-condensation[2]. All of the catalysts caused the formation of small proportions of erythrose, threose, dendroketose, and xylose in addition to the pentuloses. The xylose was

formed by isomerisation of *threo*-2-pentulose. Also formed were small proportions of a hexose, the di-*O*-isopropylidene derivative of which was identified by g.l.c.–m.s. as 1,2:3,4-di-*O*-isopropylidene-β-DL-*lyxo*-3-hexulofuranose by comparison with the authentic D-enantiomer[14]. Presumably, the 3-hexulose was formed by isomerisation of aldotetroses to *glycero*-tetrulose and subsequent reaction with glycolaldehyde[6]. The tetrulose was not observed in the reaction mixtures after 15 min with the resins or after 60 min with the other catalysts, but it was present in small proportions after shorter reaction times with the metal hydroxides.

EXPERIMENTAL

General methods. — T.l.c. was performed on Silica gel G with 5:1 chloroform–methanol, and detection with diphenylamine –aniline–phosphoric acid[15]. G.l.c. was performed with a Perkin–Elmer F 11 gas chromatograph, 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 4°/min from 90→200°. For g.l.c.–m.s., a Varian Aerograph 2400 gas chromatograph was used in combination with a Micromass 12 F mass spectrometer; the ionisation energy was 70 eV, the ion-source temperature 200°, and the accelerating voltage 4 kV.

Materials. — DL-Dendroketose[8], L-*erythro*-2-pentulose[16], D-*threo*-2-pentulose[17], D-threose[10], L-erythrose[10], D-*lyxo*-3-hexulose[14], and D-*glycero*-tetrulose[18] were prepared by literature methods.

Aldol condensations. — A solution of 1,3-dihydroxy-2-propanone (12 mg) and glycolaldehyde (8 mg) in water (4 mL) containing the catalyst (Table II) was stored at room temperature until t.l.c. showed that all or most of the starting material had reacted. The solutions containing metal hydroxides were then neutralised with Dowex 50W (H^+) resin, filtered, and concentrated under reduced pressure. After the resin-catalysed condensations, the solution was filtered, the resin was washed with aqueous 50% acetic acid (20 mL), and the combined filtrate and washings were concentrated.

For quantification of the products, D-mannose (4 mg) was added as an internal standard after neutralisation of the reaction mixture.

Preparation of O-isopropylidene derivatives. — The products of the above reactions, or from the concentration of aqueous solutions of reference sugars, were stirred with acetone containing 2% (v/v) of conc. sulphuric acid (3 mL) for 90 min at room temperature. After neutralisation with solid sodium hydrogencarbonate, the solutions were used immediately for g.l.c. or g.l.c.–m.s.

Mass spectra: 2,3-*O*-isopropylidene-L-erythrose, *m/z* 145 (54%), 143 (4), 102 (6), 99 (10), 85 (26), 73 (8), 71 (8), 59 (97), 58 (15), 57 (15), 56 (14), 55 (8), and 43 (100); 1,2-*O*-isopropylidene-β-D-threofuranose, *m/z* 145 (37%), 127 (11), 102 (4), 85 (46), 71 (6), 59 (100), 55 (7), and 43 (56); 3,4-*O*-isopropylidene-D-*glycero*-tetrulose, *m/z* 145 (17%), 143 (5), 101 (100), 59 (26), and 43 (93).

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