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Preliminary communication

The favored formation of D,L-arabinitol in the formose reaction*

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Prior studies[1—7] have shown that formose reactions in water or methanol lead to 2-*C*-(hydroxymethyl)glycerol, 3-*C*-(hydroxymethyl)pentitol, 2,4-bis(hydroxymethyl)pentitol, pentaerythritol, 2,4-bis(hydroxymethyl)-3-pentulose, 3-*C*-(hydroxymethyl)pentofuranose, and 3-deoxy-3,3-bis(hydroxymethyl)-tetrono-1,4-lactone, which have been isolated in a pure form. Glucose[8], 2-*C*-(hydroxymethyl)glycerol[9], pentaerythritol[9], 1,2-ethanediol[10], glycolaldehyde[11], 3-ketopentulose[12], and glyceraldehyde[13] were reported to be formed selectively in the formose reaction in water or methanol as a solvent. However, these compounds, except 2-*C*-(hydroxymethyl)glycerol[9] and pentaerythritol[9], were not isolated in a pure form. Recently, dihydroxyacetone was also found in the formose reaction[1,14] and was separated from the mixture. The present study shows that the formation of D,L-arabinitol is favored when the formose reaction is carried out in the presence of boric acid.

In a typical experiment, the reaction was performed with M aqueous formaldehyde (200 mL) in the presence of 0.3M calcium chloride, 20mM D-fructose, and 0.1M boric acid at 60° under nitrogen, with adjustment of the pH of the mixture to 11.0 with saturated potassium hydroxide during the reaction. At various time-intervals, aliquots (5 mL) were transferred into a 10-mL flask and the reaction was quenched immediately by acidification with 9M hydrochloric acid. These aliquots were analyzed for formaldehyde by the method of Bricker and Johnson[15], except that the optical density was measured at 579 nm. The product distribution as per(trimethylsilyl)ated products was determined by g.l.c., the pattern of which (Fig. 1b) clearly indicated the favored formation of a product corresponding to peak number 13 (GP-13) (yield, 33% by g.l.c.).

The product was isolated by treating the formose mixture with Diaion WA-30 (OH^-) anion-exchange resin, and the nonionic product was acetylated with acetic anhy-

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*Formose reactions. Part 22. For Part 21, see ref. 1.

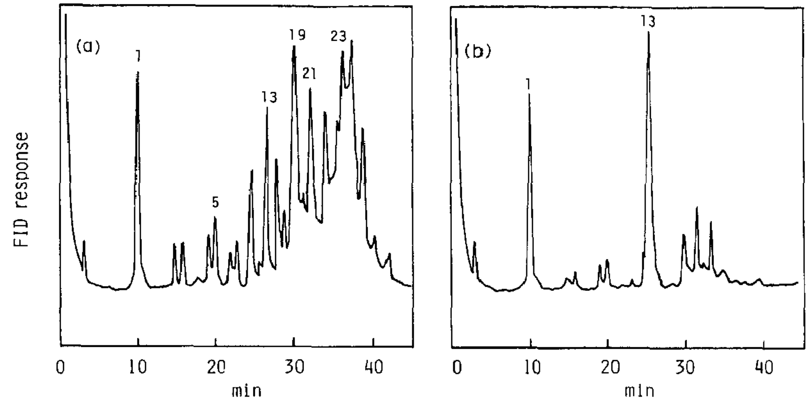

Fig. 1. G.l.c. patterns of per(trimethylsilyl)ated products obtained from: (a) Conventional formose reaction in water starting from M formaldehyde, 0.3M $CaCl_2$, and 30mM D-fructose at 60°, and by adjusting the pH of the reaction mixture to 11.0 with sat. KOH from start to finish. (b) Selective formose reaction in the presence of 0.1 M boric acid.

dride–pyridine, followed by chromatography on silica gel with 1:4 (v/v) diethyl ether–chloroform as eluent, to give white slender crystals, m.p. 93–94° (uncorr.), $[\alpha]_D^{20}$ 0° (*c* 1.42, chloroform); ^{1}H-n.m.r. ($CDCl_3$; int. standard, Me_4Si); δ 2.0–2.2 (m, 15 H, 5 CH_3), 4.0–4.4 (m, 4 H, 2 CH_2OH), and 5.2–5.6 (m, 3 H, 3 *CH*OH); ^{13}C-n.m.r. ($CDCl_3$; int. standard, Me_4Si); δ 20.7 (q), 61.7 (t), 62.0 (t), 68.0 (d), 68.3 (d), and 169.6–170.6 (s), corresponding to 5 CH_3, 2 CH_2, and 3 CH groups, and 5 carbonyl C atoms; c.i.–m.s. (isobutane, NH_3, and ND_3 as a reagent gas[16]): quasi-molecular ion at *m/z* 363 (MH^+), 380 ($M{\cdot}NH_4^+$), and 384 ($M{\cdot}ND_4^+$), respectively, which indicated a mol. wt. of 362 and no active H in the molecule; ν_{max} (acetate) 1740 cm^{-1} (strong, CO); (deacetylated compound) 3300–3400 cm^{-1} (OH) and no carbonyl group. After deacetylation and trimethylsilyation, the product had the same retention time in g.l.c. as GP-13. 1,2,3,4,5-Penta-*O*-acetyl-D-arabinitol, 1,2,3,4,5,-penta-*O*-acetyl-L-arabinitol, and the racemate[17] showed m.p. 76.0, 76.0, and 95.0°; and $[\alpha]_D^{19}$ +37.2, −37.0, and 0° (chloroform), respectively. These results indicate that the product corresponding to GP-13 is D,L-arabinitol.

The product corresponding to GP-1 was identified as glycerol by the retention times of the per(trimethylsilyl) and acetyl derivatives, and the m.s. of the acetyl derivative.

At the present time, the mechanism for the formation of D,L-arabinitol is not clear. This compound did not derive from D-fructose, because the optical activity of D-fructose was not maintained in the product, and D,L-arabinitol was also found to be formed in the formose reactions using glycolaldehyde, dihydroxyacetone, D-xylose, L-sorbose, D-galactose, D-mannose, and D-glucose instead of D-fructose.

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