Selective Formation of Triose from Formaldehyde catalysed by Ethylbenzothiazolium Bromide

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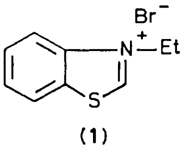
Dihydroxyacetone was obtained selectively by condensation of formaldehyde using 3-ethylbenzothiazolium bromide as a catalyst in the presence of base.

Increased interest has recently been shown in the formose reaction (the condensation of formaldehyde to produce a mixture of carbohydrates and their analogues in the presence of base) in view of its possible importance in the manufacture of edible carbohydrates from a simple material, and in the prebiotic synthesis of carbohydrates.[1—5] The product of the formose reaction is usually a complex mixture, and a selective reaction is highly desirable. However, the examples reported so far are very limited, and the selective products isolated are branched compounds.[6,7]

In this communication we report that triose was obtained with high selectivity by the use of 3-ethylbenzothiazolium bromide (**1**) as a catalyst in the presence of base.

A typical reaction was carried out as follows: commercial paraformaldehyde (1.8 g, 60 mmol as HCHO), (**1**)† (3 mmol), triethylamine (3 mmol), and ethanol (10 ml) were placed in a 50 ml flask fitted with a three-way tap and a reflux condenser; the reaction mixture was refluxed at 65 °C for 6 h under a nitrogen atmosphere with magnetic stirring. An aliquot of the reaction mixture (1 ml) was poured into water, and the aqueous solution was evaporated to dryness at 35 °C under reduced pressure in order to remove unchanged formaldehyde, giving a syrupy product, formose. Figure 1 shows the g.l.c. pattern of the trimethylsilylated (TMS) oxime of formose, prepared by the reaction of formose with hydroxylamine hydrochloride in pyridine, followed by trimethylsilylation.[8] The retention time of peak 2 corresponds to that of the TMS oxime of dihydroxyacetone synthesized separately, and peaks 1 and 3 correspond to those of glyceraldehyde. It should be noted that the peak corresponding to glycerol is not observed in Figure 1. On chromatography of formose on cellulose powder with butanol saturated with water as eluent, a white solid (0.036 g) was isolated, which was identified as dihydroxyacetone by a direct comparison of its ^{1}H and ^{13}C n.m.r. spectra with those of an authentic sample.[9]



(**1**)

A further aliquot of the formose reaction mixture (1 ml) was poured into water and reduced with sodium borohydride at room temperature. After neutralization with 1 M hydrochloric acid, the water was removed under reduced pressure by distillation with methanol to leave a white solid, which was subjected to trimethylsilylation. The TMS derivative was extracted with chloroform which was evaporated to leave 0.22 g of the TMS derivative of reduced formose, an almost colourless liquid, which corresponds to about 40 mol % of the starting formaldehyde. As shown in Figure 2, the g.l.c. pattern of the TMS derivative of reduced formose obtained from the reaction catalysed by (**1**) is dramatically simple. The main product in reduced formose, corresponding after trimethylsilylation to peak 1 in Figure 2, was isolated by ion exchange chromatography with Amberlite IR-120B and Amberlite IRA-47, using

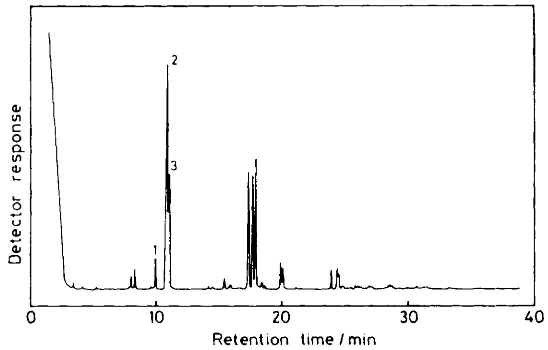


Figure 1. G.l.c. of the trimethylsilylated oxime of formose obtained from the formose reaction catalysed by 3-ethylbenzothiazolium bromide (**1**).

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† Compound (**1**) was prepared by heating benzothiazole with ethyl bromide: m.p. 211—212 °C; ^{1}H n.m.r. (CD_3OD) δ 1.70 (t, 3H, $-CH_3$), 4.94 (q, 2H, $-CH_2-$), 7.62—8.52 (m, 4H, aromatic). Satisfactory analytical data were obtained for compound (**1**).

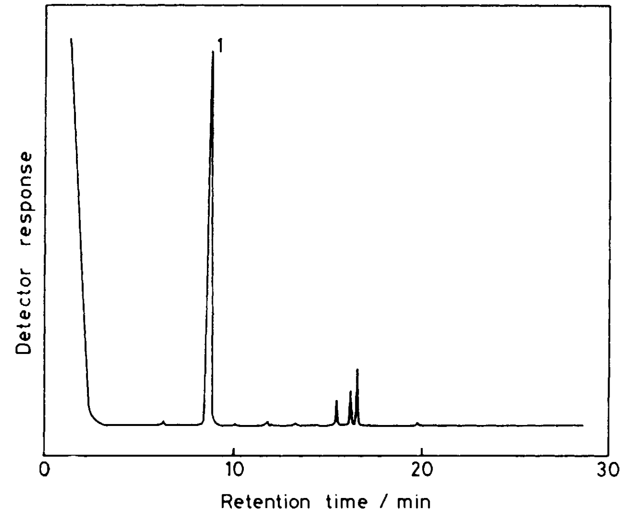

Figure 2. G.l.c. of the trimethylsilyl derivative of reduced formose obtained from the formose reaction catalysed by 3-ethylbenzothiazolium bromide (**1**).

water as eluent, to give a syrupy substance. The TMS derivative of this isolated product was identified as that of glycerol by direct comparison of the i.r. and the ^{1}H n.m.r. spectra and the retention time in the g.l.c. with those of an authentic compound. From the area of peak 1 in Figure 2, the amount of the TMS derivative of glycerol was estimated to correspond to 82 weight % of the total TMS derivative of reduced formose, or 35 mol % of the starting formaldehyde.

The very simple g.l.c. pattern of the TMS derivative of reduced formose was also observed in reactions using other bases *e.g.* sodium hydroxide, diethylaminoethanol, trioctylamine, and imidazole, although the activity of formose formation is strongly dependent on the basicity. The reaction in methanol and butanol gave similar results. Thus, the formation of glycerol as an almost exclusive product from reduced formose indicates that triose is formed selectively from formaldehyde in the condensation reaction catalysed by 3-ethylbenzothiazolium bromide.

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