SELECTIVE FORMOSE REACTION CATALYZED BY DIETHYLAMINOETHANOL

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Selective formose reactions were achieved by diethylaminoethanol as catalyst at 100°C in the presence and the absence of D-fructose as co-catalyst. The reaction in the presence of the co-catalyst gave 2-hydroxymethylglycerol and other three main products in high yields, whereas in its absence pentaerythritol was the sole product.

Recently the attention to the formose reaction, the condensation of formaldehyde producing a mixture of carbohydrates, has been increasing.[1]   The importance of the formose reaction mainly comes from the possibility of the production of edible sugars from a simple material. Besides this, the reaction is associated with a prebiotic synthesis of carbohydrates as the fundamental process in the generation of life.

In spite of many works on the formose reaction, mostly using inorganic bases as catalyst,[2-7] little is known on controlling the distribution of products.[8-10] For example, the reaction catalyzed by calcium hydroxide gave a mixture of about 30 products, making it so difficult to isolate each product. Thus the improvement of selectivity of the formose reaction should be the key for its practical application.

In this paper it will be reported that only one sugar alcohol was obtained by use of diethylaminoethanol (I) as a catalyst. Furthermore, in the presence of some monosaccharides, the I-catalyzed reaction gave only four main products in high yields with the suppressed rate of the Cannizzaro reaction.

Aqueous formaldehyde solution was prepared from commercial paraformaldehyde by refluxing it in water for 4 h and was purified by the subsequent filtration of the insoluble substances. The reaction was carried out at 100°C under nitrogen atmosphere, and was followed by the consumption of formaldehyde and the formation of methanol (a product of the Cannizzaro reaction) by using gas chromatography. After the reaction, the reaction mixture was neutralized with hydrochloric acid, followed by the ion exchange chromatography using IR-120B and IRA-402 resins. Then the effluent was dried at 50°C *in vacuo* into a syrup, which was subjected to gas

chromatography after trimethylsilylation by the method of the literature[11]

Figure 1 shows the gas chromatogram of the trimethylsilyl (TMS) derivative of the product of the I-catalyzed reaction at 100°C for 20 h. Here the consumption of formaldehyde and the formation of methanol were 37 and 14%, respectively. Quite interestingly, a single peak was observed. This product was identified as the TMS derivative of pentaerythritol (II) by direct comparisons of the ^{13}C-NMR spectrum and the gas chromatogram with those of the authentic compound[12] Thus a selective formose reaction was achieved under the present conditions, although the yield of II with respect to the consumption of formaldehyde was low (about 2% as estimated from the weight of the TMS derivative).
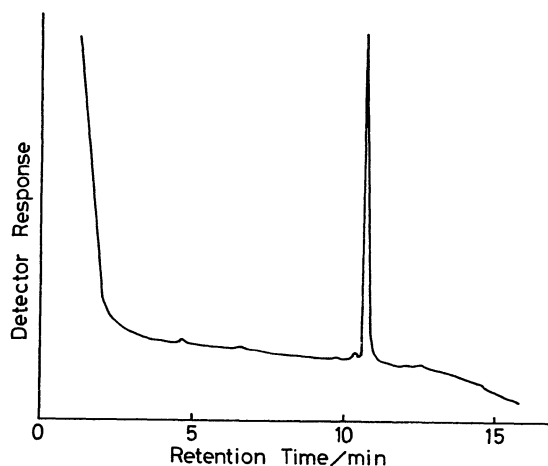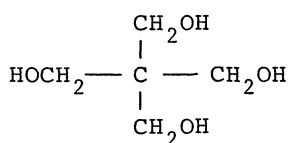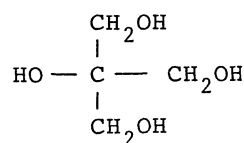

Fig. 1 The gas chromatogram of the TMS derivative of the product obtained from the formose reaction catalyzed by I in the absence of D-fructose as co-catalyst after 20 h starting from [HCHO]= 2.0 and [I]= 0.23 mol dm^{-3} at 100°C

The addition of some monosaccharides exhibited acceleration effect on the I-catalyzed formose reaction, as well as suppression effect on Cannizzaro reaction. In the presence of D-fructose (0.056 mol dm^{-3}) as co-catalyst, for example, the consumption of formaldehyde and the formation of methanol were increased to 97 and 2%, respectively, after 20 h, compared with those in the absence of D-fructose. In the I-D-fructose system, the yield of the products obtained in a syrup form with respect to the consumption of formaldehyde was 53% (w/w), which was satisfactorily high. D-Glucose, D-ribose, D-xylose and dihydroxyacetone showed similar effects. On the other hand, methyl α-D-glucoside, D-2-deoxyribose, sucrose and acetoin did not show measurable effects.

The selectivity of the I-catalyzed formose reaction was also affected by the addition of co-catalyst. Figure 2 shows the gas chromatogram of the TMS derivatives of the products of the I-catalyzed reaction in the presence of D-fructose. The number of the main peaks was only four. The sum area of these four peaks covered 80% of the total peak area,[13] showing that the reaction is more selective than the formose reaction catalyzed by calcium hydroxide[14]

Each of the products corresponding to the main four peaks 1, 4, 5 and 6 was isolated in an almost pure form by gas chromatography. The product of peak 1 was identified as the TMS derivative of 2-hydroxymethylglycerol (III) by ^{1}H-NMR, ^{13}C-NMR and mass spectroscopy measurements.[12,15] The products corresponding to peaks 4, 5 and 6 are probably carbohydrates or sugar alcohols with the carbon numbers more than six, although definite assignments have not been completed yet. These main four products were not observed in the products of the reaction between I and D-fructose in the absence of formaldehyde.
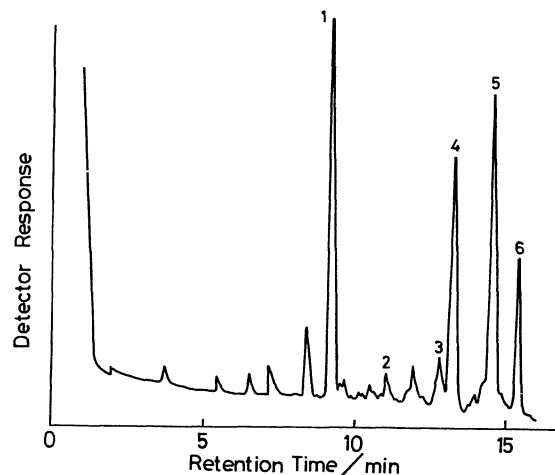

Fig. 2 The gas chromatogram of the TMS derivatives of the products obtained from the formose reaction catalyzed by I in the presence of D-fructose as co-catalyst after 20 h starting from [HCHO]= 2.0, [I]= 0.23 and [D-fructose]= 0.056 mol dm^{-3} at 100°C.

The products corresponding to peaks 2 and 3 were assigned to arabinose and mannose, respectively, by comparing the retention times of the gas chromatogram with those of the authentic compounds.

$$
\begin{array}{cc}
\text{HOCH}_2\!-\!\!\!
\begin{array}{c}
\text{CH}_2\text{OH} \\
| \\
\text{C} \\
| \\
\text{CH}_2\text{OH}
\end{array}
\!\!\!-\!\text{CH}_2\text{OH}
&
\text{HO}\!-\!\!\!
\begin{array}{c}
\text{CH}_2\text{OH} \\
| \\
\text{C} \\
| \\
\text{CH}_2\text{OH}
\end{array}
\!\!\!-\!\text{CH}_2\text{OH}
\\[2em]
(\text{ II }) & (\text{ III })
\end{array}
$$

Interestingly, the compound II, which was the sole product of the reaction in the absence of D-fructose as co-catalyst, was not produced at all in its presence.

Study on the catalyses by other amines are currently under way.

References and Notes

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12) Selective formations of II and III (ref. 10)) were reported also in the formose reaction using sodium carbonate as catalyst.

13) More than 80% of the syrup should be detected as the TMS derivatives by this gas chromatography, using the TMS derivative of erythritol as a standard compound.

14) Y. Shigemasa, A. Kamemura, E. Waki, and R. Nakashima, 40th Fall Meeting of the Chem. Soc. Jpn., Fukuoka, October, 1979, Abstr. No. 3G27.

15) The ^{1}H-NMR spectrum of the trimethylsilylate (chemical shifts given in parts per million from the trimethylsilyl signal of the product): δ 0.0(s,36H), 3.4 (s,6H). The ^{13}C-NMR spectrum of the trimethylsilylate (chemical shifts given in parts per million from the C_6D_6 signal and multiplicities based on an off-resonance spectrum): δ -128.46(q), -125.10(q), -63.94(t), -48.24(s). The mass spectrum of the trimethylsilylate: m/e 308, 218, 104, 73.