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Formose Reactions. XIV. A Selective Formose Reaction in the Presence of a Slight Amount of Calcium Ions

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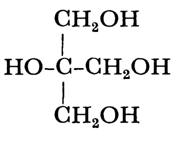
It was found that a formose reaction in the presence of small amounts of calcium and D-fructose gave rise to three products, 2-(hydroxymethyl)glycerol, 3-(hydroxymethyl)pentitol, and 2,4-bis(hydroxymethyl)pentitol, with a high selectivity. Various factors affecting the selectivity were also discussed: [Ca], pH, [D-fructose], the reaction temperature, co-catalysts, and metal hydroxides. The amount of formaldehyde relative to [Ca] is the most important factor in obtaining the selective formation of the three-branched sugar alcohols. Under these reaction conditions, the α,β-enediol structure is required in an effective co-catalyst for the formose reaction. 2-(Hydroxymethyl)glycerol, 3-(hydroxymethyl)pentitol, and 2,4-bis(hydroxymethyl)pentitol were formed with a high selectivity in the formose reactions catalyzed by KOH, $Mg(OH)_2$, $Fe(OH)_3$, and LiOH.

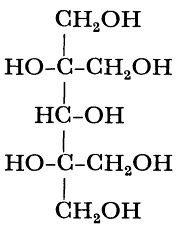
In the preceding papers,1—3) which dealt with various factors affecting formose reactions catalyzed by $Ca(OH)_2$ in a batch reactor, the continuous measurement of the oxidation-reduction potential (ORP) of the reaction mixture has proven usefull for distinct discrimination among the induction, the sugar-forming, and the sugar-decomposing periods by means of an ORP minimum and maximum appearing at the end of the induction period and at the end of the sugar-forming period respectively. The T_{min} and T_{max} symbols correspond to the times of the end of the induction and the sugar-forming periods respectively.

In the course of our recent kinetic studies of $Ca(OH)_2$-catalyzed formose reactions, we found that three kinds of branched sugar alcohols, 2-(hydroxymethyl)glycerol (2-HG), 2,4-bis(hydroxymethyl)pentitol (2,4-DHP), and most probably a diastereomeric mixture of 3-(hydroxymethyl)pentitol (3-HP), are obtained with a high selectivity when most of the dissolved calcium ions are removed as hardly soluble salts or stable chelates at the end of the induction period (T_{min}).4,5)



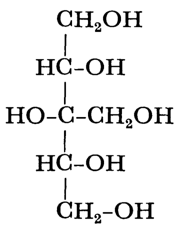
$$\begin{array}{c} CH_2OH \\ | \\ HO\text{-}C\text{-}CH_2OH \\ | \\ CH_2OH \end{array}$$

2-HG



$$\begin{array}{c} CH_2OH \\ | \\ HO\text{-}C\text{-}CH_2OH \\ | \\ HC\text{-}OH \\ | \\ HO\text{-}C\text{-}CH_2OH \\ | \\ CH_2OH \end{array}$$

2,4-DHP



$$\begin{array}{c} CH_2OH \\ | \\ HC\text{-}OH \\ | \\ HO\text{-}C\text{-}CH_2OH \\ | \\ HC\text{-}OH \\ | \\ CH_2\text{-}OH \end{array}$$

3-HP

When the formose reaction was carried out in the presence of small amounts of calcium ions and D-fructose by adjusting the pH of the reaction mixture to 12.0 with potassium hydroxide, it was found to give rise to the same products. Under these reaction conditions, furthermore, the reaction mixture is homogeneous, so the analysis of the reaction is easier than in the heterogeneous system.

The purpose of this paper is to explore the reaction conditions which give a similar selective formation of the above three kinds of branched sugar alcohols. Particular attention is placed on the following factors: the calcium-ion concentration; the formaldehyde concentration; the kind of promoters, such as D-fructose and D-glucose; the D-fructose concentration; the pH of the reaction mixture; the reaction temperature, and the kind of metal hydroxide.

Experimental

The apparatus and the experimental procedure were virtually the same as those described previously.1,2) The formaldehyde solutions were prepared from paraformaldehyde by refluxing for 4 h, followed by the filtration of the insoluble substances. The reaction was started by adding given amounts of $CaCl_2$ and D-fructose, immediately after which the pH of the reaction mixture was adjusted with concd KOH. The pH of the reaction mixture was maintained by adding concentrated aqueous KOH during the reaction.

The total saccharides were determined using the phenol-sulfuric acid method6) and were calculated as glucose from a previously prepared calibration curve. The sugar yield was calculated according to the following equation: Sugar yield $(\%) = [\text{sugars as glucose}]/([HCHO]_0 + [\text{D-fructose}]) \times 100$. The formaldehyde was determined by the method of Bricker *et al.*;7) only the optical density was measured at 579 nm, while the ORP was measured by the method described in a previous paper.1)

The products were trimethylsilylated by Sweeley's method,8) and the trimethylsilyl (TMS) derivatives were analyzed by gas chromatography, as has been described previously.9) The products were numbered according to their retention time as GP-13, GP-18, *etc.* The yield of the products (GLC%) were given by measuring the peak areas.

The calcium salts and other reagents were of an analytical grade.

Results and Discussion

Effect of the Calcium-ion Concentration. In the previous papers,4,5) it was suggested that the concentration of the dissolved calcium ions ([Ca]) at the formose-forming step was a very important factor in the selective product formation. It was found that the formose reaction in the presence of small amounts of calcium and D-fructose gave rise to similar selectivities (Table 1).

Table 1 shows the effects of [Ca] on formose reactions carried out at various pHs (9.5—12.0) of the reaction mixture. At any pH, the T_{max} value at which the consumption of formaldehyde reaches over 90% decreases, and the sugar yield increases with an increase in the amount of calcium. At [Ca] = 0.025 M, a similar relationship between T_{max} and the sugar yield with an increase in the pH of the reac-

TABLE 1. EFFECTS OF $CaCl_2$ CONCENTRATION ON THE DISTRIBUTION OF PRODUCTS[a)]

Run No.	pH	$CaCl_2$ / mM	T_{max} / min	Sugar yield / %	Products (GLC%)[e)]					
					2-HG	18	3-HP	25	2,4-DHP	T_{3p}[b)]
1	9.5	25		$(20.3)^{d)}_{270}$						
2	9.5	350	181	49.7	12.0	c)	45.4	4.9	18.7	76.1
3	9.5	500	84	59.1	8.1	5.2	36.5	20.8	6.9	51.5
4	9.5	650	59	58.7	2.6	3.4	39.1	20.0	3.1	44.8
5	9.5	900	40	63.2	c)	7.8	28.0	18.6	c)	30.0
6	10.5	25	108	43.3	15.1	c)	28.6	c)	37.2	80.9
7	10.5	50	54	55.0	9.1	5.9	24.4	12.2	12.7	46.8
8	10.5	100	27	68.3	9.3	6.2	26.4	15.3	1.8	37.5
9	10.5	250	9	69.1	1.9	9.9	9.4	19.0	c)	12.3
10	11.0	5		$(67.3)^{d)}_{180}$						
11	11.0	10	57	40.8	13.3	c)	23.4	3.0	5.14	88.1
12	11.0	25	36.5	47.1	12.0	c)	25.7	4.8	23.0	60.7
13	11.0	50	12.5	65.5	5.9	5.9	29.6	15.4	4.5	40.0
14	11.0	100	9.5	69.2	4.5	9.9	21.2	19.0	2.5	32.2
15	11.5	5	56.0	31.8	9.2	2.0	21.8	4.1	47.6	78.6
16	11.5	25	8.5	55.3	9.8	4.5	21.4	9.7	11.0	42.2
17	12.0	5	26.5	37.7	8.4	3.3	22.2	6.1	34.4	65.0
18	12.0	25	5.5	67.5	4.7	7.3	13.8	10.5	7.6	26.1

a) [HCHO] = 1.0 M; [D-fructose] = 0.01 M; the pH was adjusted by concd KOH; temp = 60 °C; total volume = 200 ml. b) Total yield of 2-HG, 3-HP, and 2,4-DHP. c) GLC was below 1%. d) The number in parentheses is the HCHO consumption(%) at the time (min) shown by the subscript. e) 2-HG: 2-(hydroxymethyl)glycerol, 3-HP: 3-(hydroxymethyl)pentitol, 2,4-DHP: 2,4-bis(hydroxymethyl)pentitol; 18 and 25: products which were shown by the peak numbers of 18 and 25 respectively in a gas chromatogram of the TMS derivatives.

tion mixture is observed (Runs 1, 6, 12, and 18): the sugar yield increases as T_{max} decreases. These phenomena are in fairly good agreement with the results reported previously.[2,3)] In this case, it could easily be considered that the sugar yield is affected by the amount of formaldehyde consumed by the Cannizzaro reaction. The sugar yield, however, is influenced by the product composition: the sugar yield decreases with an increase in the total yields of 2-HG, 3-HP, and 2,4-DHP, which are sugar alcohols. A sugar alcohol usually has little reducing power. Therefore, the sugar yield which is determined using the phenol-sulfuric acid method and calculated as glucose is useful only when the product composition is similar.

Here, the total yield (T_{3p}) of 2-HG, 3-HP, and 2,4-DHP is used as an indicator of the selectivity of the formose reaction. As is shown in Table 1, T_{3p} increases with a decrease in the pH of the reaction mixture and [Ca]. Although the yields of 2-HG and 3-HP are not affected by the pH of the reaction mixture, the yield of 2,4-DHP increases greatly with a decrease in the pH. The yield of 3-HP is not so much affected by [Ca]. The yields of 2,4-DHP and 2-HG increase with a decrease in [Ca], while the yield of GP-25, which is one of products shown by the peak number of 25 in a gas chromatogram of the TMS derivatives,[4,5)] increases with an increase in [Ca]. These results led us to conclude that the formation of 2,4-DHP and GP-25 is competitive or that GP-25 is an intermediate of 2,4-DHP.

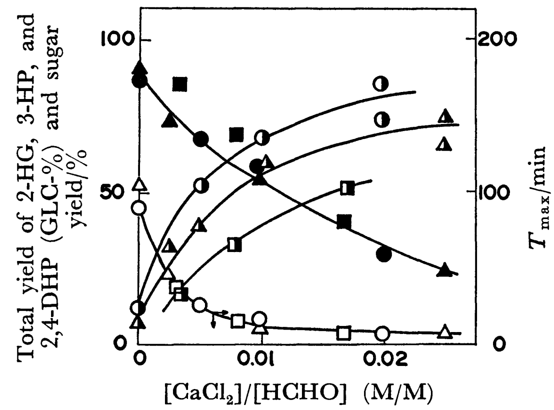


Fig. 1. Effects of $CaCl_2$ concentration on the selectivity, T_{max}, and sugar yield.
[D-Fructose] = 0.01 M; pH = 12.0 (adjusted by concd KOH); temp = 60 °C; total volume = 200 ml. T_{3p}, [HCHO](M): ●, 0.5; ▲, 1.0; ■, 3.0. T_{max}, [HCHO] (M): ○, 0.5; △, 1.0; □, 3.0. Sugar yield, [HCHO] (M): ◑, 0.5; ◭, 1.0; ◨, 3.0.

Figure 1 shows the effects of [Ca] on the sugar yield, T_{max}, and T_{3p} at given formaldehyde concentrations. The relationship between T_{max} and the sugar yield is quite similar to that shown in Table 1. Furthermore, the sugar yield increases with a decrease in the formaldehyde concentration at the same ratio of [Ca]/[HCHO]. This phenomenon is in fairly good agreement with the result reported previously.[2)]

In Fig. 1, it is clear that the selectivity (T_{3p}) increases with a decrease in [Ca], and that at any formaldehyde concentrations the same [Ca]/[HCHO] ratios give similar total yields of 2-HG, 3-HP, and 2,4-DHP (T_{3p}). On the other hand, when the formaldehyde concentration is varied at a given [Ca], the relationship between the ratio of [Ca]/[HCHO] and T_{3p} is also similar (Fig. 2) to that described above. These results suggest that these branched sugar alcohols of 2-HG, 3-HP, and 2,4-DHP are end products under these reaction conditions and that the ratio of the formaldehyde concentration to [Ca] is the most important factor in selective formation of these products. In this case, however, there is another important factor is the selective formation of the three branched sugar alcohols, namely, the role of D-fructose as a co-catalyst, for it diminishes the induction period and offers reaction conditions similar to those at T_{min}, which is the time of the beginning of the formose-forming step in the formose reaction catalyzed by calcium hydroxide.[4,5]

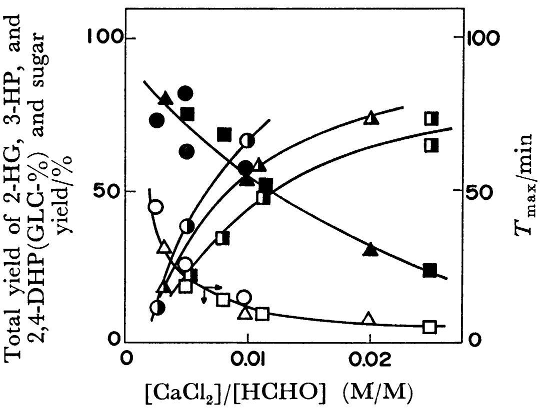


Fig. 2. Effects of HCHO concentration on T_{3p}, T_{max}, and sugar yield.
[D-Fructose]=0.01 M; pH=12.0 (adjusted by concd KOH); temp=60 °C; total volume=200 ml. T_{3p}, [CaCl$_2$] (M): ●, 0.005; ▲, 0.01; ■, 0.025. T_{max}, [CaCl$_2$] (M): ○, 0.005; △, 0.01; □, 0.025. Sugar yield, [CaCl$_2$] (M): ◑, 0.005; ◭, 0.01; ◨, 0.025.

Therefore, large amounts of 2-HG, 3-HP, and 2,4-DHP can be easily obtained at one time by starting the reaction under the usual conditions ([Ca(OH)$_2$]=0.1 M, [HCHO]=1.0 M, and temp=60 °C), followed by continuously adding a given amount of formaldehyde and adjusting the pH of the reaction mixture after T_{min}, at which the ORP curve shows a minimum. The details of these results will be presented in a subsequent paper.

Effect of the Fructose Concentration. In order to clarify the functions of D-fructose in the formose reaction, the relationship among the D-fructose concentration, [Ca], T_{max}, the sugar yield, and the product distribution was studied. The results are summarized in Table 2.

At the concentration of calcium ions ([Ca]) below 5×10^{-3} M, an increase in the D-fructose concentration led to decrease in T_{max} and to an increase in both the sugar yield and T_{3p}. At 25×10^{-3} M of [Ca], T_{3p} increases with an increase in the D-fructose concentration; however, the T_{max} and the sugar yield are little affected by the D-fructose concentration.

For a constant D-fructose concentration (10×10^{-3} or 50×10^{-3} M), an increase in [Ca] led to a decrease in both T_{max} and T_{3p} and to an increase in the sugar yield. These phenomena are the same as those described previously (Table 1). T_{3p} (2-HG, 3-HP, and 2,4-DHP) decreases, however, GP-25 increases with an increase in [Ca].

TABLE 2. EFFECTS OF FRUCTOSE CONCENTRATION[a)]

[CaCl$_2$] mM	D-Fructose mM	T_{max} min	Sugar yield %	Products (GLC%)[d)]				
				2-HG	3-HP	25	2,4-DHP	T_{3p}
2.5	0	(81.9)$^{\mathrm{b)}}_{200}$						
2.5	1	94.2	19.2	7.0	15.9	c)	43.8	66.7
2.5	5	56.2	22.5	11.0	10.4	c)	47.9	69.3
2.5	10	41.0	23.9	11.3	19.0	4.8	44.1	74.4
2.5	20	35.0	26.6	12.4	20.7	2.7	46.3	79.4
2.5	50	20.2	35.7	15.7	18.9	1.8	49.8	84.4
5.0	0	(86.6)$^{\mathrm{b)}}_{210}$						
5.0	0.5	73.2	19.7	4.9	20.8	6.0	22.3	48.0
5.0	1	56.5	23.7	5.1	23.0	4.5	27.3	55.4
5.0	5	30.5	35.6	7.5	21.8	3.1	32.5	61.8
5.0	10	26.5	37.7	8.4	22.2	6.1	34.4	65.0
5.0	20	22.5	37.5	8.5	20.7	6.2	38.2	67.4
5.0	30	21.2	34.8	8.1	22.6	2.1	40.3	71.0
5.0	50	18.0	41.3	10.6	20.2	4.9	38.4	69.2
5.0	100	12.0	41.9	7.9	13.4	8.5	33.6	54.9
25.0	0	(77.9)$^{\mathrm{b)}}_{60}$						
25.0	10	5.7	67.5	4.7	13.8	10.5	7.6	26.1
25.0	25	6.8	65.8	5.0	12.0	12.5	9.7	26.7
25.0	50	7.3	61.7	5.9	12.6	13.4	15.4	33.9
25.0	100	7.1	59.3	5.6	14.2	10.7	20.8	40.6

a) [HCHO]=1.0 M; [CaCl$_2$]=0.005 M; [metal hydroxide]=0.1 M; [D-fructose]=0.01 M; pH=12.0 (adjusted by concd KOH); temp=60 °C; total volume=200 ml. b) pH=11.5, while the other reaction conditions were the same as in a). c) GLC was below 1%. d) See Table 1.

Furthermore, the TMS derivative of D-fructose was a minor one. In another experiment, *ca.* 50% of added D-fructose was found to decompose or change to other compounds in 10 min and *ca.* 70% of D-fructose in 20 min under these reaction conditions: [D-fructose]$=10\times10^{-3}$ M, $[\text{CaCl}_2]=5\times10^{-3}$ M, pH=12.0 adjusted by concd potassium hydroxide, and temp=60 °C. These results led us to suggest that D-fructose added as a co-catalyst would react with formaldehyde or would decompose to some products, such as reductone,[10] which may then act effectively as co-catalysts.

Time Course of the Selective Formose Reaction in the Presense of a Small Amount of Calcium Ions. Figure 3 shows a typical time course of the formaldehyde consumption, the sugar yield, and ORP in the formose reaction which gives rise to 2-HG, 3-HP, and 2,4-DHP with a high selectivity when the reaction is catalyzed by potassium hydroxide and a small amount of calcium ions in the presence of D-fructose. Formaldehyde was consumed at a rather uniform rate, although the usual formose reaction catalyzed by calcium hydroxide consumed formaldehyde auto-catalytically.[1,11] This consumption curve is also different from that given by the formose reaction which is catalyzed by calcium oxide in the presence of various co-catalysts.[12]

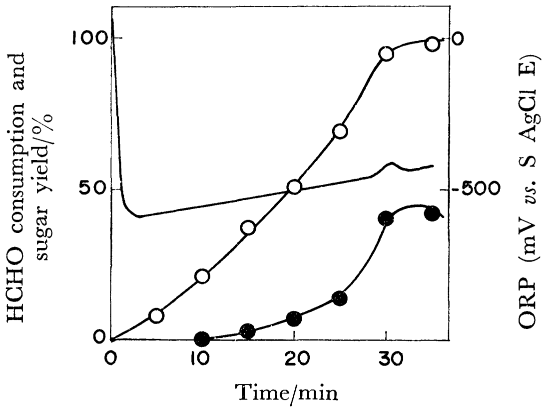


Fig. 3. Time course of HCHO consumption, sugar yield, and ORP.
[HCHO]=1.0 M; $[\text{CaCl}_2]=0.005$ M; [D-fructose]=0.01 M; pH=12.0 (adjusted by concd KOH); temp=60 °C; total volume=200 ml. ○: HCHO consumption, ●: sugar yield, —: ORP.

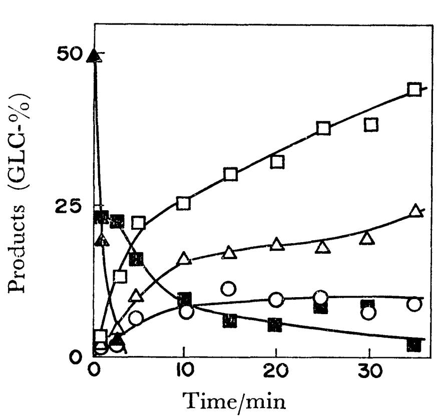


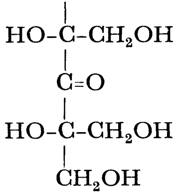
Fig. 4. Time course of selective formose reaction products.
[HCHO]=1.0 M; $[\text{CaCl}_2]=0.005$ M; [D-fructose]=0.01 M; pH=12.0 (adjusted by concd KOH); temp=60 °C; total volume=200 ml. ○, 2-HG, △, 3-HP, □, 2,4-DHP, ■, 25; ▲, fructose.

In this reaction system, the maximum ORP is found to be useful for the indicator of the end point of the reaction (T_{max}) at which the sugar yield is at its maximum. The same relationship has been observed in the usual formose reaction catalyzed by calcium hydroxide alone.[1,11]

Figure 4 shows the time course of the main products; 2-HG, 3-HP, 2,4-DHP, GP-25, and D-fructose. The added D-fructose disappears rapidly and becomes of minor importance at the end of the reaction, as has been described above. 2,4-DHP, 3-HP, and 2-HG are formed selectively even at the initial stage. Although 2-HG early reaches a constant proportion (*ca.* 10 GLC%), 2,4-DHP and 3-HP increase continuously as the reaction proceeds.

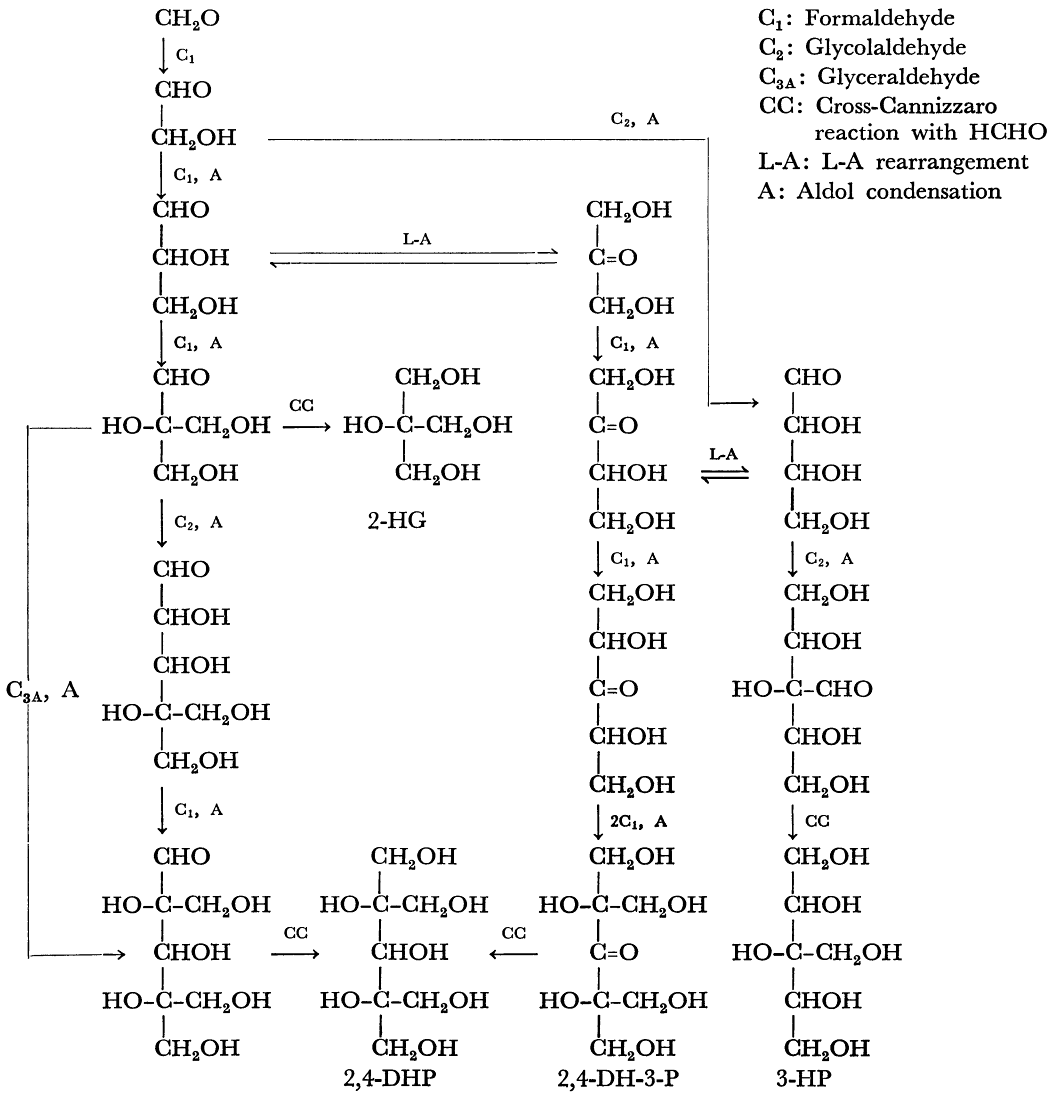
Quite importantly, GP-25 is formed with a high selectivity as one of the initial products; it then disappears with the simultaneous increase in both 2,4-DHP and 3-HP. These results suggest that GP-25 might be an intermediate of 2,4-DHP or 3-HP.

In our previous paper,[13] we have already proposed a scheme of possible pathways for the selective formation of these three branched sugar alcohols (2-HG, 3-HP, and 2,4-DHP), which may be explained by a conventional mechanism[14] involving cumulative aldol condensations, followed by the cross-Cannizzaro reaction of their aldose precursors. In addition, it has been already reported that the reduction of 2,4-bis(hydroxymethyl)-3-pentulose (2,4-DH-3-P) with sodium borohydride[15] or formaldehyde in the presence of a base[16] give 2,4-DHP. A modified scheme of possible pathways for the selective formose formation is proposed in Scheme 1. There has previously been no reasonable explanation for the occurrence of the selective formose reaction.


$$\begin{array}{c} \text{CH}_2\text{OH} \\ | \\ \text{HO-C-CH}_2\text{OH} \\ | \\ \text{C=O} \\ | \\ \text{HO-C-CH}_2\text{OH} \\ | \\ \text{CH}_2\text{OH} \end{array}$$

2,4-DH-3-P

Effect of Reaction Temperature. The formose reaction was carried out at various temperatures; the results are summarized in Table 3. T_{max} decreases with an increase in the reaction temperature, so with the decrease in T_{max} the sugar yield increases, as has been described previously.[2,3] At 80 °C, however, the sugar yield is not so high in spite of the short reaction time, because the resulting sugars easily decompose as a result of the high reaction temperature. Three branched sugar alcohols ($T_{3\text{p}}$) are formed with a high selectivity (*cf.* Table 3), although the increase in the reaction temperature leads to tendency for $T_{3\text{p}}$ to decrease.



Scheme 1. Possible pathways for the selective formose formation.

Table 3. Effects of reaction temperature[a)]

Reaction temp	$T_{\max}$	Sugar yield	Products (GLC%)[b)]				
°C	min	%	2-HG	3-HP	25	2,4-DHP	T_{3p}
50	334	33.5	16.8	27.4	16.2	31.0	75.2
60	45	42.1	13.1	18.9	5.8	45.5	77.5
70	6.3	49.3	7.7	27.7	1.0	30.4	65.8
80	1.0	45.6	11.7	18.9	1.8	22.3	52.9

a) [HCHO] = 1.0 M; [$CaCl_2$] = 0.005 M; [D-Fructose] = 0.01 M; pH = 11.5; total volume = 200 ml. b) See Table 1.

On the other hand, Tambawala *et al.*[17)] reported that, at 50% and lower conversion levels, the C_4 and C_5 aldose and ketose products are practically pure straight chains at 40 °C and practically pure branched chains at 60 °C. At higher conversion levels as much as 40% branched chains are present at 40 °C. Furthermore, as has been mentioned above, the three branched sugar alcohols are formed selectively even at the initial stage, at which the formaldehyde consumption is only 10%. It would be supposed that these differences are mainly attributable to the amount of calcium ions. At any rate, there is a remarkable effect of the reaction temperature, that is, the formation of GP-25, which might be an intermediate of 2,4-DHP or 3-HP and which increases with a decrease in the reaction temperature. Efforts are under way to separate and identify GP-25. The formation of GP-25 under various reaction conditions is also under investigation in detail.

Effect of Various Co-catalysts on the Selectivity of Products. Since Kusin[18)] and Langenbeck[12)] reported that the induction period can be eliminated or shortened by the addition to the reaction mixture of small amounts of carbohydrates, the formose reaction in the presence of carbohydrates or other compounds with an enediol form has been studied: the reaction is accelerated to a small extent, and the induction period is shortened greatly, by the addition of glycolaldehyde and glyceraldehyde; the catalytically active species is not the hydroxide of an alkaline earth metal, but its complex with a carbohydrate.[19–21]

However, there have been few reports which have discussed the effects of a formose-reaction-promoting-co-catalyst on the selectivity of products. Although we have already reported the effects of various co-catalysts on the formose reaction in the presence of a small amount of calcium ions,[22] a few other co-catalysts have been investigated in terms of how they affect the product distribution. The results are summarized in Table 4.

As has been described previously,[22] the formose reaction in the presence of acetoin or benzoin is found to give GP-13 and -14 or 1,2-diphenylglycerol respectively with a high selectivity and to give a low sugar yield as glucose. From these results, one can easily suppose that acetoin and benzoin do not act as co-catalysts, but only as substrates which are easily hydroxymethylated with formaldehyde to give a stable and unreactive compound.

On the other hand, other co-catalysts give rise to similar T_{max} values, sugar yields, and product distributions, although in the case of L-ascorbic acid the T_{max} is relatively long. In addition, phenacyl alcohol was found to form GP-16 (*ca.* 10 GLC%), which could not be detected without phenacyl alcohol. Hence, these co-catalysts would seem to function similarly to each other both as co-catalysts and substrates.

Furthermore, when DL-glyceraldehyde or dihydroxyacetone is used as a co-catalyst, the total yield of 2-HG, 3-HP, and 2,4-DHP ($T_{3\mathrm{p}}$) is very high (*ca.* 80 GLC%). This results led us to assume that DL-glyceraldehyde and dihydroxyacetone would function both as co-catalysts and as substrates which especially act as intermediates of the above three branched sugar alcohols.

On the basis of the above results, we propose that the enediol form of a co-catalyst is very important in promoting the formose reaction: the $\mathrm{R{-}\overset{HO}{\overset{|}{C}}{=}\overset{OH}{\overset{|}{C}}{-}H}$ type is effective, but the $\mathrm{R_1{-}\overset{HO}{\overset{|}{C}}{=}\overset{OH}{\overset{|}{C}}{-}R_2}$ ($\mathrm{R_1, R_2 \neq H}$) type is not effective in promoting the reaction. The same assumption has already been presented by Sakai *et al.*[23] The relatively long T_{max} with L-ascorbic acid is attributable to the time necessary to convert an enediol form of L-ascorbic acid, $\mathrm{R_1{-}\overset{HO}{\overset{|}{C}}{=}\overset{OH}{\overset{|}{C}}{-}R_2}$, to the effective type, $\mathrm{R{-}\overset{HO}{\overset{|}{C}}{=}\overset{OH}{\overset{|}{C}}{-}H}$.

Effect of Various Metal Hydroxides. In the presence of a slight amount of calcium ions, the formose reactions were carried out by various metal hydroxides in order to examine the effect of the kind of metal cation on the reaction. The results are summarized in Table 5. Judging from the results (T_{max} values, the sugar yields, and the product distributions), the catalytic activity of $\mathrm{Sr(OH)_2}$ is very similar to that of $\mathrm{Ca(OH)_2}$. The catalytic activity, furthermore, decreases in the following order: $\mathrm{Ca(OH)_2, Sr(OH)_2 > Ba(OH)_2 > Mg(OH)_2}$. These results are the same as those reported by Partridge *et al.*,[24] who supposed that the intermediate complexes must contain a carbohydrate molecule in addition to formaldehyde molecules in the coordination sphere of the catalytically active cation. In Table 5, furthermore, $\mathrm{Mg(OH)_2}$, $\mathrm{Fe(OH)_3}$, and $\mathrm{Pb_2O(OH)_2}$ have a longer T_{max} than that of the control experiment.

In the cases of $\mathrm{Cu(OH)_2}$ and LiOH, in spite of their short T_{max} values, the sugar yield is low. Pfeil *et al.*[25] reported that LiOH catalyzes the Cannizzaro reaction rather than the formose reaction. In the presence of $\mathrm{Cu(OH)_2}$, metal copper separated out from the reaction mixture, so one can easily suppose that $\mathrm{Cu(OH)_2}$ would be reduced by formaldehyde to metal copper and that formaldehyde would be oxidized to formic acid. Hence, the low sugar yield in these formose reactions is attributable to the large consumption of formaldehyde to formic acid.

2-(Hydroxymethyl)glycerol (2-HG), 3-(hydroxy-

TABLE 4. EFFECTS OF VARIOUS CO-CATALYSTS[a)]

Co-catalyst	T_{max}	Sugar yield	Products (GLC%)[e)]						
	min	%	2-HG	13	14	3-HP	1,2-DPG[b)]	2,4-DHP	$T_{3\mathrm{p}}$
D-Fructose	26.5	40.0	8.4	c)	c)	22.2	c)	34.4	65.0
D-Glucose	29.7	34.8	7.4	c)	c)	24.0	c)	35.0	66.4
D-Xylose	26.9	39.3	8.1	c)	c)	23.2	c)	31.9	63.7
Triose reductone	32.8	34.7	10.7	c)	c)	20.7	c)	33.3	64.7
DL-Glyceraldehyde	24.0	35.6	9.5	c)	c)	27.3	c)	41.4	78.2
Dihydroxyacetone dimer	28.6	30.8	10.1	c)	c)	26.4	c)	45.5	82.0
L-Ascorbic acid	50.7	29.4	10.0	c)	c)	24.9	c)	28.6	63.5
Phenacyl alcohol	25.3	39.1	8.0	c)	c)	20.7	c)	30.7	59.4
Acetoin	177.0	8.3	c)	14.4	33.4	c)	c)	c)	c)
Benzoin	94.3	11.2	c)	c)	c)	c)	89.1	c)	c)

a) $[\mathrm{HCHO}] = 1.0$ M; [co-catalyst] $= 0.01$ M; $[\mathrm{CaCl_2}] = 0.005$ M; pH $= 12.0$ (adjusted by concd KOH); temp $= 60$ °C; total volume $= 200$ ml. b) 1,2-(Diphenyl)glycerol is abbreviated as 1,2-DPG. c) GLC was below 1%. e) See Table 1.

Table 5. Effects of various metal hydroxides[a)]

Metal hydroxide	T_{max} / min	Sugar yield / %	Products (GLC%)[d)]					
			2-HG	18	3-HP	25	2,4-DHP	T_{3p}
	24.0	44.6	12.8	c)	29.0	2.3	41.9	83.7
$Mg(OH)_2$	36.8	38.5	12.0	c)	31.2	2.1	40.8	84.0
$Sr(OH)_2$	3.5	65.7	2.5	6.3	16.1	12.3	7.2	25.8
$Ba(OH)_2$	6.8	63.9	2.7	6.4	20.8	8.6	27.7	51.2
$Pb_2O(OH)_2$	76.0	26.5	1.3	10.4	22.4	5.5	1.3	25.0
$Cu(OH)_2$	8.0	7.7	8.8	4.1	18.0	4.8	18.0	44.8
$Fe(OH)_3$	70.0	14.6	19.3	c)	18.8	c)	51.8	89.9
LiOH[b)]	10.0	25.2	5.2	c)	44.0	c)	31.6	80.8
b)	45.0	38.6	13.5	c)	19.4	5.9	46.7	79.6

a) [HCHO] = 1.0 M; [$CaCl_2$] = 0.005 M; [metal hydroxide] = 0.1 M; [D-fructose] = 0.01 M; pH = 12.0 (adjusted by concd KOH); temp = 60 °C; total volume = 200 ml. b) pH = 11.5, while the other reaction conditions were the same as in a). c) GLC was below 1%. d) See Table 1.

methyl)pentitol (3-HP), and 2,4-bis(hydroxymethyl)-pentitol (2,4-DHP) are formed with a high selectivity (T_{3p}, 80 GLC%) in the formose reaction catalyzed by KOH, $Mg(OH)_2$, $Fe(OH)_3$, and LiOH in the presence of small amounts of calcium ions and D-fructose. Especially, $Fe(OH)_3$ is found to give 52 GLC% of 2,4-DHP only. $Pb_2O(OH)_2$, furthermore, give rise to an unknown product, GP-18; efforts are under way to isolate and identify this product. These results are in fair agreement with those results[5)] obtained from a modified formose reaction.

Under the same reaction conditions as in Table 5, but without calcium ions, furthermore, the formose reaction was found to give a longer T_{max} value than that in the presence of calcium ions, but the product distributions were quite similar to each other. For example, when no metal hydroxide was added, only adjusting the pH of the reaction mixture to 12.0 with concd KOH aq; the T_{max} was 182 min; at barium hydroxide, the T_{max} was 23 min.

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