Homogeneously Catalyzed Formaldehyde Condensation to Carbohydrates

IV. Alkaline Earth Hydroxide Catalysts Used with Glycolaldehyde Co-catalyst

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Ca(OH)₂, Sr(OH)₂, and Ba(OH)₂ all caused zero-order reaction behavior at intermediate conversion ranges of formaldehyde, independent of co-catalyst glycolaldehyde concentration. This is a result of the catalysis of the reaction by complexes of carbohydrate and base that are practically constant in number over the course of the reaction. At 40°C, 1.53 M HCHO, 0.187 M Ca(OH)₂, the reaction produces, at low conversion, mainly glyceraldehyde (98% of the sugars) in the presence of 0.0416 M glycolaldehyde, mainly C_4–C_7 sugars (83% of the sugars) in the absence of glycolaldehyde. That quantity of the co-catalyst almost suppresses the competing Cannizzaro reaction. The proportion of C_4 branched sugars increases with the ionic radius of the catalyst, but, because of autocondensation, the straight-to-branched C_5 and C_6 sugar ratios are independent of the catalyst. A mechanism involving ene–diol complexed species is proposed to explain the experimental behavior. The use of a CSTR near-complete conversion is recommended as the practical means of minimizing the nonautocatalytic Cannizzaro side reaction in the presence of the autocatalytic formose reaction. The product–catalyst complex is maximized, the reactant is minimized, and the co-catalyst addition is unnecessary.

INTRODUCTION

The synthesis of racemic aldose and ketose monosaccharides by the condensation of formaldehyde, discovered by Butlerow (1) more than 100 years ago, is a complex catalytic process. A variety of products are formed, mostly containing two to seven carbon atoms. Under the achiral conditions of synthesis, formaldehyde not only undergoes condensation to such carbohydrates[1] but also takes part in Cannizzaro and cross-Cannizzaro reactions leading to the formation of formic acid, methyl alcohol, and several polyols.

Weiss and co-workers (2) have shown that many of the carbohydrates formed are branched structures, which are not acceptable for human metabolism and, possibly, have toxic properties. Weiss et al. (3) obtained data on the ratio of branched-

[1] Note that the word "carbohydrate" is used in this work according to the classical definition derived from the French "hydrate de carbone" for $C_n(H_2O)_n$ and not in the modern context, which infers chirality.

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to straight-chain carbohydrates in C_4 and C_5 fractions as a function of temperature and the degree of conversion of formaldehyde. Experiments were carried out in a CSTR, using calcium hydroxide as the catalyst. Up to 50% conversion, the C_4 fraction contains practically 100% branched carbohydrates at 60°C, and only linear carbohydrates at 40°C. For conversion levels close to 100%, at both reaction temperatures, the content of branched carbohydrates approached 40–50%. Analogous results were obtained for the C_5 fraction.

To increase the selectivity of the process, it is necessary to obtain data on the dependence of branched-chain species on the nature of the catalyst, the nature and concentration of the organic co-catalyst, and other parameters. Such information so far is not available in the literature. In the present work, the dependence of the ratio of branched- to straight-chain carbohydrates on the nature of alkaline-earth hydroxide ($Ca(OH)_2$, $Sr(OH)_2$, and $Ba(OH)_2$) catalysts was investigated. The kinetics of the synthesis of carbohydrates in the presence of the above hydroxides and the dependence of the selectivity of the synthesis, catalyzed by $Ca(OH)_2$, on the concentration of glycolaldehyde used as a co-catalyst were also studied.

The catalytic activity of the alkaline-earth hydroxides for the synthesis of carbohydrates and for the Cannizzaro reaction was investigated in several works (4–7). Sinyak et al. (4) found that the catalytic activity for the synthesis of carbohydrates decreased as follows: $Ca(OH)_2 > Sr(OH)_2 > Ba(OH)_2$. Fujino et al. (5) determined the rate constants for the synthesis of carbohydrates and the Cannizzaro reaction in the presence of these catalysts. With glucose as a co-catalyst, the activity for the synthesis of carbohydrates followed the same sequence. The sequence of activity for the Cannizzaro reaction in the presence of glucose was opposite to that found for
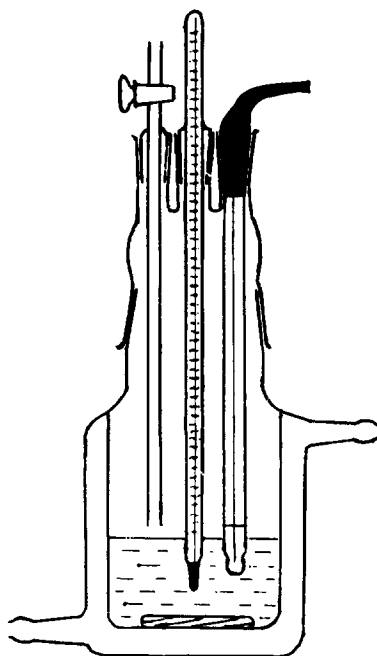

FIG. 1. Reactor.

the synthesis of carbohydrates, and the same in the absence of glucose. The ratios of the zero-order rate constants for the synthesis of carbohydrates and the Cannizzaro reaction for $Ca(OH)_2$, $Sr(OH)_2$, and $Ba(OH)_2$ in the presence of glucose were found to be 4.1, 2.1, and 0.7, respectively. The above values are in very good agreement with the ratios of the degree of conversion of formaldehyde in the presence of the same hydroxides, determined by Meier et al. (6) to be 4.0, 2.3, and 0.8, respectively.

Mizuno et al. (7) found rather small changes of the ratio of aldo to keto forms of pentoses and hexoses with various hydroxides of alkaline–earth metals in the presence of organic bases. From that it was concluded that the composition of the products is not very sensitive to the nature of the catalyst (8).

EXPERIMENTAL

The jacketed glass reactor equipped with a ground-joint cover is shown in

Fig. 1. The jacket was connected to a thermostat, allowing control of the chosen reaction temperature with an accuracy of ±0.05°C. Liquid in the reactor was mixed with a magnetic stirrer. The cover of the reactor was equipped with tapered joints for the positioning of the glass electrode, reference electrode (AgCl), argon inlet, and thermometer. The fifth joint was used for sampling. Values of pH were measured using the pH meter pH-340. The addition of a calculated amount of NaOH solution to the mixture containing formaldehyde, a salt of the alkaline-earth metal and glycolaldehyde, was taken as the beginning of reaction. The total volume of the reacting mixture was 100 ml.

Experiments were made using 1.53 M formaldehyde and 0.1875 M alkaline-earth hydroxide. Samples, taken during the course of reaction, were neutralized prior to analysis for formaldehyde, methyl alcohol, and carbohydrates. Formaldehyde was detected chromatographically on a Porapak N column at 115°C, using chromatograph LKhM-8MD (Model 5) with a thermal conductivity detector. Methyl alcohol was determined separately from formaldehyde using Porapak Q at 150°C and a flame-ionization detector.

Carbohydrates were reduced with sodium borohydride to the corresponding polyols (10 mg of NaBH$_4$ for 1 ml of the neutralized solution) before analysis in order to allow the determination of linear and branched components. After reduction (15 hr at room temperature) and neutralization, water was removed by distillation with methyl alcohol, followed by evaporation on a water bath. The last traces of alcohol and water were removed under a flow of argon. The distillation was repeated three times, initially using 10 ml, and then, in sequence, two times 2 ml of methyl alcohol. When dry, 1 ml of silylating mixture [a solution of hexamethyldisilazane and trimethylchlorosilane in pyridine (9)] was added. The formation of

volatile trimethyl silyl ether derivatives proceeded over a period of 15 hr, initially at 70°C, later at room temperature. Derivatives were extracted with chloroform by shaking with 1 ml of chloroform and 3 ml of 3 M HCl. The water layer was removed, and the chloroform phase was washed three times with water and dried with anhydrous sodium sulfate.

The chloroform solution was analyzed chromatographically, using an OV-17 S.C.O.T. column, in a Chrom-31M gas chromatograph equipped with a flame-ionization detector. The temperature was programmed (4°C/min) in the range 120–220°C. This procedure allowed for a good separation of carbohydrates containing different numbers of carbon atoms. In each group, the branched-chain carbohydrates (as polyols) appeared before the straight-chain species (2). The ratio of branched- to straight-chain carbohydrates was determined from the ratio of peak areas on the chromatogram. The area of all of the C$_3$ and higher peaks was taken as 100%.

RESULTS

Figure 2A shows for calcium hydroxide at 40°C [2] the dependence of the total conversion of formaldehyde, both to formose sugars and to Cannizzaro products, on the concentration of glycolaldehyde. In the absence of glycolaldehyde a typical autocatalytic character of the reaction was found. During the first 70–80 min, mainly Cannizzaro reaction occurred at a low, steadily increasing rate up to 20% conversion ($\alpha = 20\%$). Then formose reaction quickly accelerated to the maximum rate, which is practically constant to $\alpha = 90\%$.

[2] Note that Cannizzaro reaction conversion was not accelerated by glycolaldehyde. The Cannizzaro envelope plotted in Fig. 2A was experimentally determined by the titration of every product, and points are omitted for clarity. Figure 2A shows the autocatalytic conversion to formose sugars, the difference between total conversion, and conversion to Cannizzaro products.
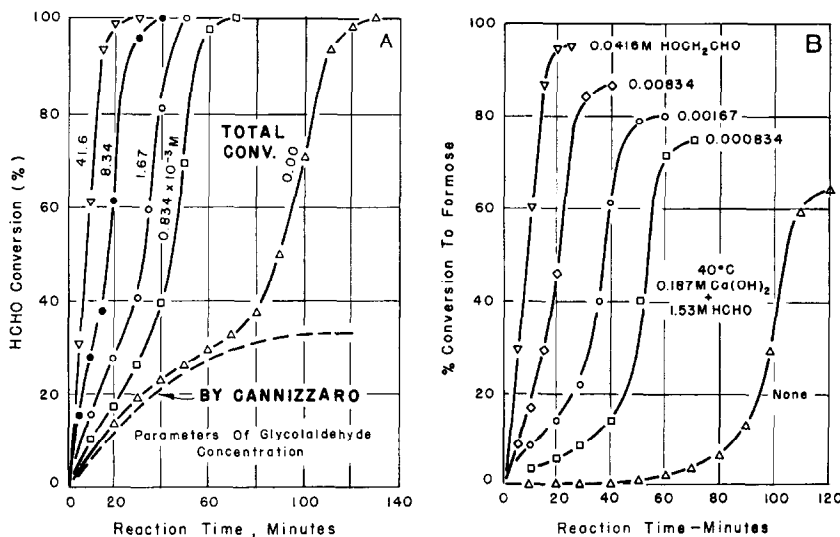
FIG. 2. (A) Total formaldehyde conversion. (B) Formaldehyde conversion to formose sugars ($[H_2CO] = 1.53\ M$; $Ca(OH)_2 = 0.1875\ M$) for different concentrations of glycolaldehyde at 40°C.

The autocatalytic character of reaction at low values of α and the zero-order dependence at intermediate values of α are in agreement with the usual kinetic description of the process (4, 10, 11).

Additions of glycolaldehyde in concentrations increasing from 0.000834 to 0.0416 M resulted in a progressive decrease of the induction period. For the highest concentration of glycolaldehyde, reaction occurs at practically constant rate (9×10^{-2} moles/min) in the range $\alpha = 0$–90%. The autocatalytic character of the reaction disappears. The Cannizzaro rate for all cases is independent of glycolaldehyde.

At intermediate conversion levels the slopes of the curves in Fig. 2B show that the formose rate increases slightly with increasing glycoaldehyde concentration. The zero-order correlation of Weiss et al. (10) showed that at intermediate conversion levels the formose rate (r_F) is zero order in organics and first order in $Ca(OH)_2$.

$$r_F = k_F[Ca(OH)_2].$$

This behavior is corroborated in Fig. 2B, where, in the regime of about 50% con-

version, conversion to formose increases in an approximately linear zero-order manner. Table 1 shows that k_F increases from 0.23 to 0.47 min^{-1} when glycolaldehyde in the reaction mixture is increased from 0 to 0.0416 M. This increase in the formose rate constant at conditions under which the Cannizzaro reaction rate is not affected is the reason for the improved formose yield shown in Fig. 2. The co-catalyst not only eliminates the induction period but also catalyzes the formose reaction more than would be expected from its contribution to the total sugar concentration (e.g., 0.0416 M HOCH$_2$CHO in 1.53 HCHO).

The slope obtained at 50°C for glycolaldehyde concentration 0.0416 M is 2.7 times greater than that at 40°C (see Fig. 3B). such an increase of the rate of reaction corresponds to an activation energy of 20 kcal/mole.

The catalytic activity of strontium hydroxide is very similar to that of calcium hydroxide. The kinetics and the values of the rate of reaction differ very little (compare Figs. 3A and 3B). The activation energy, calculated from rates of reaction in the presence of glycolaldehyde
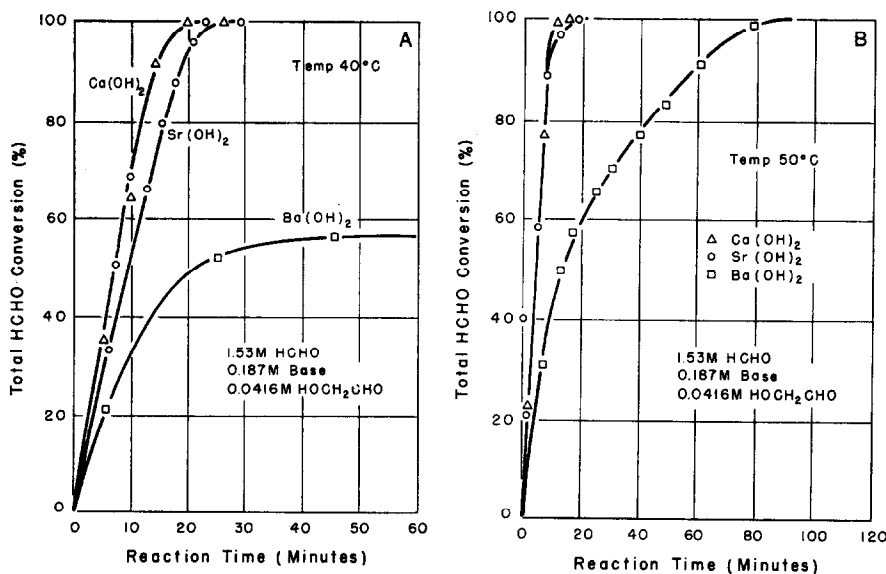
FIG. 3. Formaldehyde conversion in the presence of: (1) Ca(OH)₂, (2) Sr(OH)₂, and (3) Ba(OH)₂, (A) at 40°C; (B) at 50°C.

(0.0416 M) at 40 and 50°C, was found to be 23 kcal/mole.

The catalytic activity of barium hydroxide is much lower than the activities of hydroxides of calcium and strontium (Figs. 3 and 4). At 40°C and 0.0416 M glycolaldehyde the reaction was terminated by neutralization of Ba(OH)₂ by Cannizzaro reaction during the first 20 min, and formose and Cannizzaro rates approached zero at $\alpha = 40\%$. At 50°C the initial decrease of the rate is less noticeable, and full conversion of formaldehyde occurs in 80 min. The rate of reaction is practically constant in the range $60 < \alpha < 100\%$. At 60°C reaction takes place at a constant rate (6.2×10^{-2} moles/min) in almost the whole range of α (20–100%). The activation energy, calculated from the linear slopes at 50 and 60°C (Fig. 4), was found to be 34 kcal/mole.

The decrease of pH during the synthesis does not exceed, as a rule, one pH unit (from 11.0 to 10.0). The decrease of pH is associated with the Cannizzaro reaction, leading to the formation of formic acid and methyl alcohol from formaldehyde.

The participation of the Cannizzaro reaction in the overall conversion of formaldehyde is comparatively low in the presence of glycolaldehyde (see Table 2). Thus, for 100% total conversion, consumption of formaldehyde by the Cannizzaro reaction equals 7.2% for Ca(OH)₂, 6.0% for Sr(OH)₂ (both values at 40°C), and 18% for Ba(OH)₂ at 50°C.

Ba(OH)₂, which is the least-active catalyst for carbohydrates synthesis, was found to be the most active catalyst for the Cannizzaro reaction. Comparison of results obtained for Ca(OH)₂ in the presence and in the absence of an organic co-catalyst shows that in the latter case the proportion of Cannizzaro reaction in the overall conversion increases significantly (see Tables 2 and 3).

Hydroxides of alkaline-earth metals differ not only in their catalytic activities but also in selectivity with respect to the formation of carbohydrates containing various number of carbon atoms, and, especially, in the formation of straight-chain and branched-chain carbohydrates. Figure 5 shows the scheme of the formation

TABLE 1

Calculation of Rate Constants for the Formose Reaction in the Presence of Glycolaldehyde at 40°C.

[CHOCH₂OH] (molar)	[Ca(OH)₂] (molar)	$r_F \times 10^2$ (moles/ liter min⁻¹)	k_F (min⁻¹)
0	0.171	3.98	0.23
8.34 (10⁻⁴)	0.176	5.66	0.32
1.67 (10⁻⁴)	0.178	5.81	0.33
8.34 (10⁻³)	0.182	6.43	0.35
4.16 (10⁻²)	0.185	8.72	0.47

TABLE 2

Distribution of Carbohydrates at Complete Conversion Formed by Condensation of Formaldehyde in the Presence of Ca, Sr, and Ba Hydroxides[a]

Catalyst	Ca(OH)₂	Ca(OH)₂	Sr(OH)₂	Ba(OH)₂
HOCH₂CHO (M)	0.0416	0.000	0.0416	0.0416
Temp. (°)	40	40	40	50
Time (min)	20	135	23	50
Cann. conv. (%)	7.2	35.5	6.0	18
Carbohydrate Distribution (%)				
C₃	6.6	11.1	4.5	3.6
C₄ br	1.3	6.2	4.6	9.1
C₄ lin	5.6	9.9	2.7	2.4
ΣC₄	6.9	16.1	7.3	11.5
C₅ br	5.1	5.6	4.2	2.4
C₅ lin	15.1	21.6	9.7	5.2
ΣC₅	20.3	27.2	13.9	7.6
C₆ br	31.5	19.7	21.8	22.8
C₆ lin	16.6	15.4	16.7	10.1
ΣC₆	48.1	35.1	38.5	32.9
C₇	18.1	10.5	35.4	44.5

of carbohydrates that can be obtained via aldol condensation and Lobry de Bruyn–Alberda Van Eckenstein (L–V) transformation. Except for the initiation step of formaldehyde condensation, the system is aldol condensation at α-hydrogen locations on aldoses and ketoses. Figure 5 shows how formaldehyde adds to carbon atoms adjacent to their –C=O groups, providing that the carbon has at least one hydrogen, which is designated an α-hydrogen. Substances without α-hydrogen do not add formaldehyde but instead undergo a crossed-Cannizzaro reaction. For example, hydromethylglyceraldehyde is converted to hydromethylglycerol.

At 40°C and with maximum content of co-catalyst used (0.0416 M), calcium hydroxide at a rather low degree of conversion ($\alpha = 35\%$) yields essentially trioses (90%), small amount of tetroses (10%), and practically no higher carbohydrates (see Table 3). Under similar conditions ($\alpha = 23\%$) strontium hydroxide also gives a majority of trioses (65%) but, besides tetroses (31%), C₅ carbohydrates are also present (4). The selectivity of Sr(OH)₂ for formation of linear carbohydrates in the C₄ fraction (15%) is much lower than that found for Ca(OH)₂ (50%). The C₅ fraction contains 84% straight-chain carbohydrates. It is interesting to note that Ca(OH)₂ without a co-catalyst at a similar conversion $\alpha = 25\%$ (20% of formaldehyde was converted by the Cannizzaro reaction)

gave all fractions of carbohydrates up to C₇, and (C₆ + C₇) represented more than half of the total carbohydrates.

Table 4 shows how the ratio of branched-chain to straight-chain forms of C₄ carbohydrates changes with α and concentration of glycoaldehyde. Experiments were carried out at 40°C in the presence of Ca(OH)₂. Data in Table 4 indicate that the proportion of linear carbohydrates increases with increasing conversion, α, for all concentrations of glycolaldehyde. This is because glyceraldehyde, and not dihydroxyacetone, is the main condensation product of formaldehyde and glycolaldehyde (see Fig. 5). Only branched-chain tetroses can be formed from glyceraldehyde. Linear tetroses can arise only after L–V transformation of glyceraldehyde to dihydroxyacetone. Significantly higher rates of Lobry de
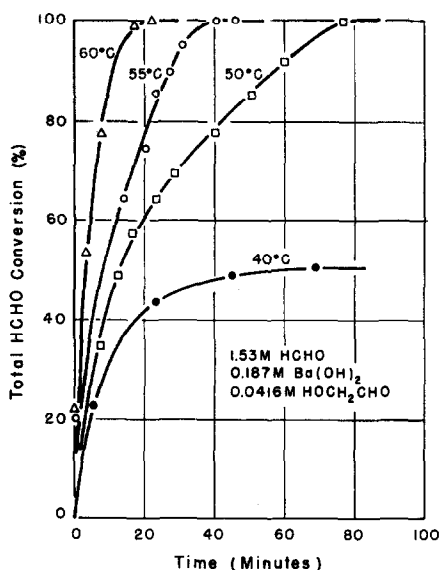
FIG. 4. Kinetic curves of formaldehyde conversion in the presence of $Ba(OH)_2$ at various temperatures.

Bruyn–Alberda Van Eckenstein transformation in the presence of $Ca(OH)_2$ (*19*) can explain observed differences in the selectivity of the investigated hydroxides with respect to the formation of linear tetroses. When the rates of L–V transformation are low, as for $Sr(OH)_2$ and $Ba(OH)_2$, and

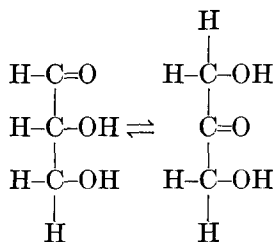### TABLE 3

Distribution of Carbohydrates at Low Conversion Formed by Condensation of Formaldehyde in the Presence of Ca and Sr Hydroxides at 40°C.

Catalyst	$Ca(OH)_2$	$Ca(OH)_2$	$Sr(OH)_2$
HOCH$_2$CHO (*M*)	0.0416	0.000	0.0416
HCHO Conv. α (%)	34.7	25.5	23.0
Cann. conv. (%)	0.1	20.6	0.4
Carbohydrate Distribution (%)			
C$_3$	89.3	16.7	65.2
C$_4$ br	5.3	6.0	25.6
C$_4$ lin	5.3	1.8	5.2
ΣC$_4$	10.6	7.8	30.8
C$_5$ br		3.0	0.7
C$_5$ lin		7.7	3.3
ΣC$_5$		10.7	4.0
C$_6$ br		22.0	
C$_6$ lin		9.5	
ΣC$_6$		31.5	
C$_7$		33.3	

when glyceraldehyde is predominantly formed, C_4 fractions should contain mainly branched-chain structures. The amount of higher carbohydrates $C_6 - C_7$ increases with increasing α, as expected. In experiments with $Ca(OH)_2$, $Sr(OH)_2$ (both at 40°C), and $Ba(OH)_2$ (50°C) at the highest concentration of the co-catalyst, the amount of $C_6 + C_7$ was 66.74, and 77%, respectively (Table 1). There was a significantly higher content of C_7 carbohydrates in the products obtained with $Sr(OH)_2$ and $Ba(OH)_2$ (35 and 45%, respectively), compared with $Ca(OH)_2$ (only 18% of C_7).

At 100% conversion of formaldehyde, the C_5 fraction contains mainly (70–75%) linear carbohydrates, the C_6 fraction mainly branched (60–70%). The most marked difference between the hydroxides in their selectivity to linear carbohydrates was found in the C_4 fraction. At 100% conversion the C_4 fraction contained $\sim 80\%$ linear carbohydrates for $Ca(OH)_2$, 35% for $Sr(OH)_2$, and only 21% for $Ba(OH)_2$.

Thus, under conditions that are far from optimum, $Ca(OH)_2$ yielded linear C_4 carbohydrates with relatively high selectivity, while $Ba(OH)_2$ gave essentially branched-chain carbohydrates C_4. The relatively small influence of the nature of catalyst on the composition of C_5 and C_6 fractions might be explained by more autocondensation of lower carbohydrates in the formation of these fractions. Reactions of autocondensation would have low specificity.

DISCUSSION OF RESULTS

The autocatalytic character of condensation of formaldehyde to carbohydrates has been discussed in several earlier works (*11–15*). From uv investigations (*15*), the catalytically active species in the synthesis of carbohydrates in the presence of calcium hydroxide are postulated to be complexes formed between the hydroxide and the enol form of carbohydrates:

glycolaldehyde or other organic species. On the basis of our results one can assume that formaldehyde has a very high affinity to the active complex. The constant concentration of the complexes obviously can explain the observed practically constant value of the rate of reaction over a wide range of α. The decrease of catalytic activity in the sequence $Ca(OH)_2 > Sr(OH)_2 > Ba(OH)_2$ may be associated with the decreasing ability of cations to form complexes. This in turn depends on the ionic radius of the cation involved.

From the present work, and other kinetic investigations (4, 5, 8, 10, 11, 17, 18), the mechanism of the formation of the first members of the carbohydrate series in the presence of glycolaldehyde could include steps such as the following, where M represents the alkali–earth cation.

$$CH_2(OH)_2 + M(OH)_2 \longrightarrow CH_2(OH)O^-.MOH^+ + H_2O \qquad (1)$$

$$CH_2(OH)O^-.MOH^+ + CH_2O \longrightarrow \left[HO\cdots M \begin{array}{c} O-\overset{\underset{\textstyle H}{|}}{C}-OH \\ \diagdown O=C \end{array} \begin{array}{c} H \\ H \\ H \end{array} \right] \qquad (2)$$

$$\left[HO\cdots M \begin{array}{c} O-\overset{\underset{\textstyle H}{|}}{C}-OH \\ \diagup O=C \end{array} \begin{array}{c} H \\ H \end{array} \right] \nearrow CH_3OH + HCOO^- + MOH^+ \qquad (3)$$
$$\searrow \begin{array}{c} CH_2-CH \\ | \quad \| \\ OH \quad O \end{array} + M(OH)_2 \qquad (4)$$

$$\begin{array}{c} CH_2-CH \\ | \quad \| \\ OH \quad O \end{array} \rightleftharpoons \begin{array}{c} CH=CH \\ | \quad | \\ OH \quad OH \end{array} \qquad (5)$$

$$\begin{array}{c} CH=CH \\ | \quad | \\ OH \quad OH \end{array} + M(OH)_2 \longrightarrow \left[\begin{array}{c} H \diagdown C^{\cdots O} \diagdown \diagup OH \\ \| \quad M \\ H \diagup C_{\cdots O} \diagdown OH \end{array} \right] \qquad (6)$$

$$\left[\begin{array}{c} H \diagdown C^{\cdots O} \diagdown \diagup OH \\ \| \quad M \\ H \diagup C_{\cdots O} \diagdown OH \end{array} \right] + CH_2O \longrightarrow \left[\begin{array}{c} H \diagdown C^{\cdots O} \diagdown \diagup OH \\ \| \quad M \\ H \diagup C_{\cdots O} \diagdown O \diagdown OH \\ \quad \overset{|}{C} \\ H \diagup \diagdown H \end{array} \right] \qquad (7)$$

$$\left[\begin{array}{c} H \diagdown C^{\cdots O} \diagdown \diagup OH \\ \| \quad M \\ H \diagup C_{\cdots O} \diagdown O \diagdown OH \\ \quad \overset{\|}{C} \\ H \diagup \diagdown H \end{array} \right] \longrightarrow \begin{array}{c} CH_2-CH-CH \\ | \quad | \quad \| \\ OH \quad OH \quad O \end{array} + M(OH)_2$$

The formation of glycolaldehyde is the rate-limiting step. After the accumulation of appreciable amounts of glycolaldehyde and other carbohydrates, further synthesis

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M^{II} = Ba, Ca, Sr
R = —$(CHOH)_n CH_2OH$

To understand the zero-order rate behavior at intermediate conversion, one must take into account the fact that reaction occurs initially in the presence of a large excess of formaldehyde. After 10–20% conversion of formaldehyde (initially mostly to lower carbohydrates), carbohydrates should form catalytically active complexes with the total amount of available hydroxide. This, most likely, explains the observed lack of dependence of the rate of reaction (in the range of constant rate) on the concentration of

TABLE 4

Ratio of Branched- to Straight-Chain C_4 Carbohydrates as a Function of Conversion and Concentration of Glycolaldehyde[a]

Conversion α (%)	Concentration of glycolaldehyde (M)			
	0.00083	0.0017	0.0083	0.0416
29		2.1		
35				1.0
40			1.3	
52			1.1	
66	1.2	1.7		0.37
83			0.7	
85		1.2		
92				0.33
100	0.6	0.4	0.5	0.23

[a] Catalyst: $Ca(OH)_2$, 40°C.

occurs via steps 5 to 8, bypassing steps 1, 2, and 4. Formaldehyde, glycolaldehyde, and glyceraldehyde can occur in basic aqueous solution not only in the form used in the above equation, but also in equilibrium with other forms:

$$H_2O + CH_2O \rightleftharpoons CH_2(OH)_2 \overset{OH^-}{\rightleftharpoons} CH_2(OH)O^- + H_2O$$

$$H_2O + CHOH = CHO^- \overset{OH^-}{\rightleftharpoons} CHOH=CHOH \overset{H_2O}{\rightleftharpoons} CH_2OH-CH(OH) \overset{OH^-}{\rightleftharpoons} CH_2OH-CH(OH)O^- + H_2O$$

$$\updownarrow$$

$$\overset{-}{C}HOH-CH(OH)_2$$

$$H_2O + CH_2OH-COH=CH\overset{-}{O} \overset{OH^-}{\rightleftharpoons} CH_2OH-COH = CHOH \overset{H_2O}{\rightleftharpoons} CH_2OHCHOHCHO \rightleftharpoons$$

$$\overset{H_2O}{\rightleftharpoons} CH_2OH-CHOH-CH(OH)_2 \overset{OH^-}{\rightleftharpoons} CH_2OHCHOHCH(OH)O^- + H_2O$$

$$\updownarrow$$

$$CH_2OH.\overset{-}{C}OH.CH(OH)_2$$

The formation of dimers and polymeric forms of formaldehyde can be neglected for the concentrations used in these investigations.

The complete mechanism of the process must include not only sequential condensation of lower molecular weight carbohydrates with formaldehyde, but also autocondensation of lower carbohydrates. This is turn should yield carbohydrates containing no more than seven atoms of carbon.

The exact composition of the complexes involved in the above mechanism is so far not completely established. Additional work is required to demonstrate unambiguously in what form carbohydrates exist in complexes used in steps 6 to 8. Is it a nonionized form (as written above), or one of the ionized forms? It is not clear what kind of complexes can be formed between formaldehyde and hydroxide. This can be either one type of complex which decomposes along two different pathways (steps 3 and 4), or two distinct kinds of complexes, resposible for the Cannizzaro reaction and the synthesis of carbohydrates, respectively. Alternatively, Weiss and John (*20*) have suggested saltlike complexes and hydride transfer to explain formose and Cannizzaro processes.

At present, all mechanisms are speculative. The one thing that can be said with certainty is that the divalency of the particular alkaline earth catalysts studied in this work is not a unique reason for their activity. Almost any base (mono-, di-, tri-, and tetravalent bases, as well as organic bases, and clays) is reported to be a catalyst for the formose reaction. Mizuno and Weiss (*7*) provide a listing of known catalysts. Even a Cannizzaro catalyst, such as NaOH, will result in a low selectivity to "brown colored material" when the reaction conditions are forced (*21*).

CONCLUSIONS

Recommendations can be made at this point for maximizing formose to the Cannizzaro selectivity ratio, if that is a goal. The alkaline-earth catalyzed reaction is best pursued with the cheapest and least-toxic catalytic material, calcium hydroxide. Formaldehyde conversions should be near 100%, but not driven to a high-severity completeness that can cause either carmelization or cross-Cannizzaro effects. Since the presence of complexed sugars competes against the Cannizzaro reaction, a batch reactor, except at the reaction completion, is always at less than the maximum possible selectivity. The practical means of minimizing the nonautocatalytic side reaction in the presence of an autocatalytic reaction will always be to use a CSTR near-complete conversion where the product–catalyst complex is maximized, the reactant is minimized, and co-catalyst or product addition is unnecessary.

ACKNOWLEDGMENTS

$$
\begin{array}{c}
\underset{\substack{|\\ H}}{HC{=}O} \xrightarrow{HCHO} \underset{\substack{|\\ CH_2OH}}{HC{=}O} \xrightarrow{HCHO} \underset{\substack{|\\ CHOH\\ |\\ CH_2OH}}{HC{=}O} \longrightarrow HOH_2C-\underset{\substack{|\\ CH_2OH}}{\overset{HC{=}O}{\underset{}{C}}OH}
\end{array}
$$

4-Carbon branched chain

aldose-ketose interconversion

$HOH_2C-\underset{\substack{|\\ CHOH\\ |\\ CH_2OH}}{\overset{HC{=}O}{\underset{}{C}}OH} \xleftarrow{HCHO} \underset{\substack{|\\ CHOH\\ |\\ CHOH\\ |\\ CH_2OH}}{HC{=}O}$

aldose-ketose interconversion

$\underset{\substack{CH_2OH\\ |\\ C{=}O\\ |\\ CH_2OH}}{}$

$\underset{\substack{CH_2OH\\ |\\ C{=}O\\ |\\ HOCH_2-COH\\ |\\ CH_2OH}}{} \xleftarrow{HCHO} \underset{\substack{CH_2OH\\ |\\ C{=}O\\ |\\ CHOH\\ |\\ CH_2OH}}{} \xleftarrow{HCHO}$

5-Carbon branched chain · · · 4-Carbon straight chain

HCHO

$\underset{\substack{CH_2OH\\ |\\ CHOH\\ |\\ C{=}O\\ |\\ CHOH\\ |\\ CHOH\\ |\\ CH_2OH}}{} \xleftarrow{HCHO} \underset{\substack{CH_2OH\\ |\\ CHOH\\ |\\ C{=}O\\ |\\ CHOH\\ |\\ CH_2OH}}{} \xrightarrow{HCHO} \underset{\substack{CH_2OH\\ |\\ CHOH\\ |\\ C{=}O\\ |\\ HOH_2C-COH\\ |\\ CH_2OH}}{}$

aldose-ketose interconversion · aldose-ketose interconversion

$\underset{\substack{CH_2OH\\ |\\ C{=}O\\ |\\ CHOH\\ |\\ CHOH\\ |\\ CHOH\\ |\\ CH_2OH}}{} \underset{\substack{CH_2OH\\ |\\ C{=}O\\ |\\ CHOH\\ |\\ CHOH\\ |\\ CH_2OH}}{} \xrightarrow{HCHO} \underset{\substack{CH_2OH\\ |\\ C{=}O\\ |\\ HOCH_2-COH\\ |\\ CHOH\\ |\\ CH_2OH}}{}$

aldose-ketose interconversion · aldose-ketose interconversion

$\underset{\substack{HC{=}O\\ |\\ CHOH\\ |\\ CHOH\\ |\\ CHOH\\ |\\ CHOH\\ |\\ CH_2OH}}{} \underset{\substack{HC{=}O\\ |\\ CHOH\\ |\\ CHOH\\ |\\ CHOH\\ |\\ CH_2OH}}{} \xrightarrow{HCHO} \underset{\substack{HC{=}O\\ |\\ HOH_2C-COH\\ |\\ CHOH\\ |\\ CHOH\\ |\\ CH_2OH}}{}$

6-Carbon straight chain · 5-Carbon straight chain · 6-Carbon branched chain

FIG. 5. Scheme for formation of linear- and branched-chain carbohydrates up to C_6.

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