

Homogeneously Catalyzed Condensation of Formaldehyde to Carbohydrates

VII. An Overall Formose Reaction Model

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Carbohydrates may be naturally present in ppm quantities in paraformaldehyde and these are believed to be the cause of autocatalysis in the Ca(OH)₂-catalyzed formose reaction of paraformaldehyde solutions. Sublimed paraformaldehyde was not transformed at 40°C, 1.75 M HCHO, 0.197 M Ca(OH)₂ to sugars by formose reaction, only to methanol and formate by Cannizzaro reaction. A minute trace of added glycolaldehyde—3 ppm—was sufficient to initiate autocatalysis. The autocatalytic process does not require that formaldehyde react with itself for initiation. The overall formose system was described by five reactions: (1) aldol condensation of formaldehyde with sugars; (2) aldol condensation; (3) dealdolization of sugars; (4) Cannizzaro reaction; and (5) saccharinic acid formation. Crossed Cannizzaro reaction was neglected. Simple power law kinetics resulted in a formose reaction model that described the autocatalytic progress of formaldehyde conversion to sugars in time. The relative rates for the reactions at 40°C, 3 ppm glycolaldehyde, vary with conversion because of the different processes. At 49% conversion, the relative rates are (1) 59, (2) 1.0, (3) 7.3, (4) 2.5, (5) 0.28.

INTRODUCTION

The formose reaction is the base-catalyzed autocatalytic condensation of formaldehyde to form a mixture of carbohydrates.³ The reaction was discovered by Butlerow (1) in 1861. A review of research done on formose sugar properties and prep-

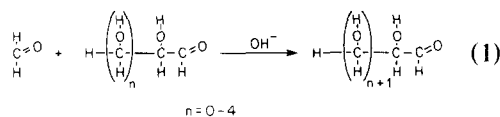
aration to 1973 was published by Mizuno and Weiss (2). A series of articles in this journal reports studies by Weiss *et al.* (3-8) on identification of products, catalysis, kinetics, and mechanism.

Base-catalyzed condensation of formaldehyde with aldoses or ketoses having α -hydrogens (i.e., hydrogen α or adjacent to the carbonyl group) is well known and is designated as aldol condensation. Formose sugars of carbon number greater than 7 are only found in small quantities. Representing aldoses and ketoses generically as formaldehyde oligomers, one can write:

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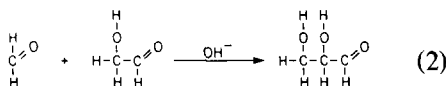
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³ Note that the word "carbohydrate" is used in this work according to the classical definition derived from the French "hydrate de carbone" for C_n(H₂O)_n and not in the modern context, which infers chirality and the ability to exist in a cyclic form.

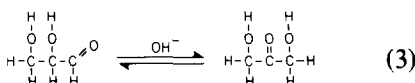


The reaction is unidirectional at usual formose conditions.

A typical reaction such as that of (1) might be the addition of formaldehyde to glycolaldehyde (the lowest-molecular-weight sugar) to form glyceraldehyde:

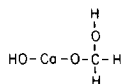


The glyceraldehyde isomerizes to its ketose analog, dihydroxyacetone, in the alkaline medium via the Lobry de Bruyn-Alberda van Ekenstein reaction:



Analogous pathways have been developed to explain the formation of the higher-carbon-number aldoses and ketoses, and these are given in the cited references.

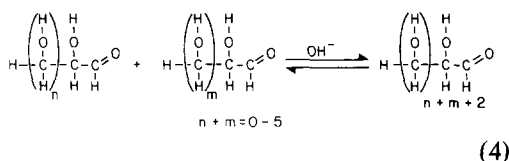
The actual condensation of formaldehyde with itself to form glycolaldehyde cannot proceed by aldol condensation, since formaldehyde has no α -hydrogen atoms. Much of the cited work reported on formose has been addressed to elucidating the mechanism of such a first step, particularly in terms of the complex that is formed between the formose base catalyst and formaldehyde. In the case of $\text{Ca}(\text{OH})_2$, the catalyst used in this work, the formaldehyde complex is considered to be (8)



In fact, a mechanism was developed in which observed reaction kinetics were explained by product decomplexing (3). In any event, the mechanism to explain the reaction of formaldehyde with itself as the initiation reaction of the formose sequence has not yet evolved. In this present work, data are presented which show that the reaction of formaldehyde condensation to glycolaldehyde can be completely neglected. These data suggest that formalde-

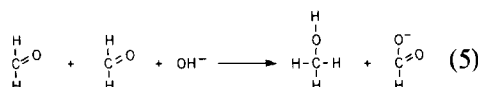
hyde can, for all practical purposes, only react by aldol condensation with sugars already present in the system, but not with itself.

Aldol condensation between two carbohydrates is a reversible reaction. The back reaction is termed dealdolization.

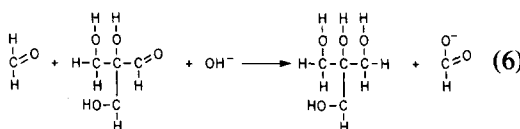


Khomenko *et al.* (9) used radioactive ^{14}C labeling to show that at typical formose conditions of 60°C , 30% of a 0.055 *M* glucose solution in 0.027 *M* $\text{Ca}(\text{OH})_2$ was converted by dealdolization. It has been recognized previously (10, 11) that the increased number of sugar molecules in a system that results from dealdolization may be the reason for the autocatalytic nature of the formose reaction.

Side reactions that do not form aldoses or ketoses are part of the formose system. The most important is the Cannizzaro reaction of Formaldehyde to form methanol and formate ion:



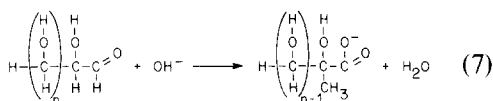
Crossed Cannizzaro reaction between formaldehyde and an aldose that does not have an α -hydrogen also takes place to a minor extent. As an example, hydroxymethylglyceraldehyde (one of the uncommon branched species formed in the formose system (12)) reacts with formaldehyde to form hydroxymethyl glycerol plus formate:



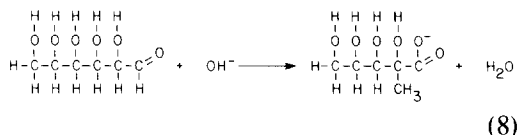
Except at high starting concentrations of carbohydrates, crossed Cannizzaro reaction is not important in the reaction model

to be presented subsequently since, at advanced conversion where it would proceed, HCHO is only present in small amounts.

Saccharinic acids also form from the sugars in the formose system. The formation of these species can be considered to be the mechanistic equivalent of an intramolecular crossed Cannizzaro reaction (13):



For example, glucose yields glucosaccharinic acid.



Although the formation of sugars is not affected by the presence of saccharinic acids, at high formaldehyde conversion reaction (7) becomes important since it represents degradation of desired sugar products.

The aldol condensations involving formaldehyde addition either to a sugar of carbon number i or j , or between two sugars C_i or C_j (where $i + j \leq 7$) can be written as a simple network. This is shown on Fig. 1, where formaldehyde addition pathways are indicated by the heavy lines. The reaction scheme of Fig. 1 allows nei-

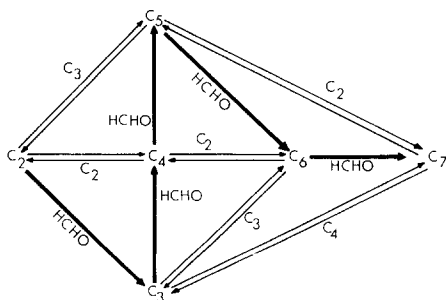
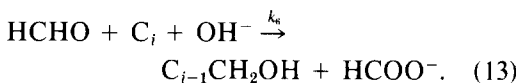
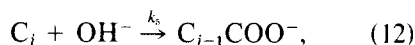
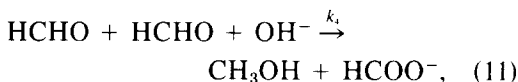
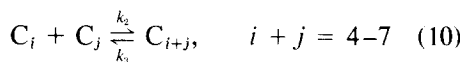


FIG. 1. Aldol condensations and dealdolization reactions in the formose system. Formaldehyde addition reactions are shown by the heavy arrows. Note that formaldehyde does not react with itself.

ther formaldehyde addition to itself nor dealdolization to form formaldehyde, nor does it allow for the structural differences between isomeric or enantiomeric sugars of the same carbon number.

Assuming that the rate constants for a given reaction are equal, no matter what the carbon numbers of the reacting species are, it is possible to effect an even greater simplification by lumping carbon numbers. The overall formose system can be described by five equations: aldol condensation of HCHO with sugars, aldol condensation-dealdolization of sugars, Cannizzaro reaction, saccharinic acid formation, and crossed Cannizzaro reaction:



This scheme will be used for subsequent kinetic analyses, with the assumption that the rate of crossed Cannizzaro reaction approximates zero.

EXPERIMENTAL PROCEDURE

Experiments were made in a batch reactor consisting of a 300-ml Berzelius beaker with a Teflon cover, a motor-driven stirrer, a thermometer for temperature sensing and control ($\pm 0.1^\circ\text{C}$, using a Matheson Lab-Stat temperature controller), an immersion heater, pH electrodes, and inert gas and sampling ports.

In order to prevent contamination by trace amounts of carbohydrates, the reactor and related equipment were cleaned with chromic acid cleaning solution prior to each run.

Reactions were carried by bringing an aqueous solution of paraformaldehyde (and/or other organic species such as gly-

colaldehyde or glucose, when used) to reaction temperature and then adding base in the form of $\text{Ca}(\text{OH})_2$ powder to start the reaction.

All materials used were reagent grade except paraformaldehyde, which was prepared by purifying technical-grade paraformaldehyde powder. The purification, which removed nonvolatile carbohydrates, involved subliming solid paraformaldehyde and dissolving the resultant HCHO vapor in distilled water.

Product samples were removed from the reactor with a pipet and were acidified immediately with 0.3–1.0 *M* hydrochloric acid to stop the reactions.

The formaldehyde concentration of reaction samples was determined by gas chromatography. A Perkin–Elmer Model 154-B vapor fractometer equipped with a thermal conductivity detector and a 4.6-m \times 6.35-mm-o.d. (15 ft \times $\frac{1}{4}$ in.) column of 15 wt% sucrose octaacetate on Columnpak T, 40/60 mesh (Fisher Scientific Co.) was used. The separation of formaldehyde, methanol, and water on this column is discussed by Mann and Hahn (14). The column and detector were isothermal at $93 \pm 1^\circ\text{C}$ and the injector was maintained at $200 \pm 3^\circ\text{C}$. Helium carrier gas flow rate was 30 ml/min.

RESULTS

Figure 2 is a plot of total formaldehyde conversion rate vs time comparing the behavior of absolutely carbohydrate-free sublimed formaldehyde to that with 3 ppm glycolaldehyde added to the system. Figure 2 shows that if two molecules of formaldehyde do actually condense to form glycolaldehyde, the rate of this reaction must be very much slower than those of the other reactions in the formose system. The curve represented by the triangles in Fig. 2 shows the formaldehyde conversion for formaldehyde purified by sublimation. This conversion was due entirely to Cannizzaro reaction and no condensation to sugars was observed within the 350 min that the reac-

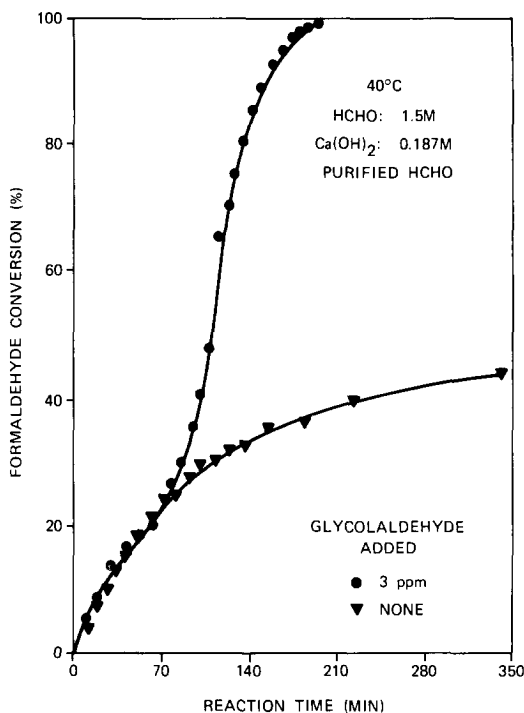


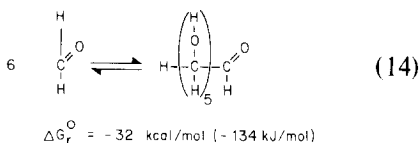
FIG. 2. Formose reaction to sugars does not proceed at all when highly purified HCHO is used. Only Cannizzaro reaction occurs. Contamination by a trace of carbohydrate is sufficient to initiate the formose reaction.

tion was studied. The curve represented by the circles shows the conversion when $5.05 \times 10^{-5} M$ (3 ppm by weight) glycolaldehyde was added to an identical reaction mixture. In this case, Cannizzaro reaction still occurred since reaction conditions did not differ, but it was accompanied by sugar formation initiating at 70 min and complete HCHO conversion within 200 min. If the formation of glycolaldehyde from two molecules of formaldehyde did occur even at a trace rate (for example, a rate which would produce $5.05 \times 10^{-5} M$ glycolaldehyde within 70 min) the purified formaldehyde would be expected to behave in a manner similar to that of the reaction mixture containing the added glycolaldehyde at the start.

It appears that in order to prove that two molecules of formaldehyde condense to form the first molecule of glycolaldehyde,

which starts the autocatalytic cycle of the formose reaction, one must prove that the initial reaction mixture contains absolutely *no* glycolaldehyde. It is necessary to prove that there are no carbohydrates of any kind in the initial reaction mixture because by dealdolization, other carbohydrates can form glycolaldehyde.

However, it is not possible to envision that paraformaldehyde of commerce has no carbohydrates at all. The thermodynamics of carbohydrate formation in paraformaldehyde are quite favorable (of course, the kinetics are not, except at formose conditions). For example, free energy data from (15) show that at equilibrium, in principle, 99.9% formaldehyde is converted to glucose at 25°C:



The rate constant for the $\text{Ca}(\text{OH})_2$ -catalyzed Cannizzaro reaction, k_4 , was determined by testing several simple rate laws for this reaction. The rate law was found to be first order in $\text{Ca}(\text{OH})_2$ and second order in formaldehyde concentrations. This is in agreement with the work of Pajunen (16), Martin (17) and Cupit (18), all of whom found the same third-order relationship when they studied the Cannizzaro reaction of formaldehyde in sodium hydroxide.

Figure 3 shows the results obtained when experimental data at four temperatures were plotted as the integrated form of the

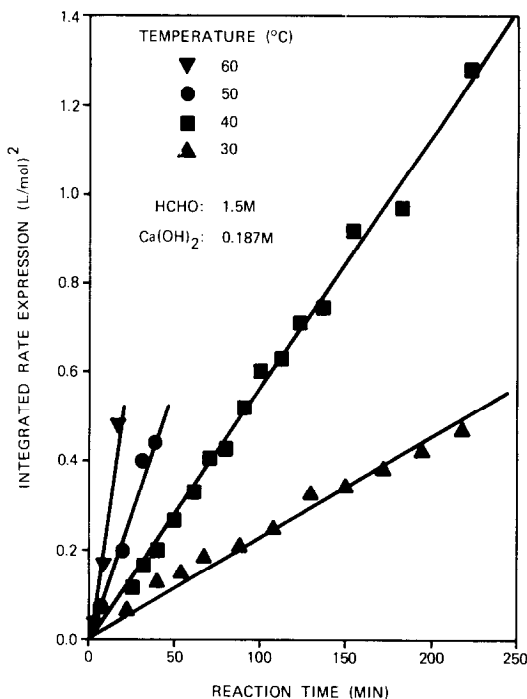


FIG. 3. Calcium hydroxide-catalyzed Cannizzaro reaction of formaldehyde is first order in base, second order in HCHO.

rate expression. The rate constants determined from the slopes of the straight lines are listed in Table 1 along with their 95% confidence limits. The activation energy for the $\text{Ca}(\text{OH})_2$ -catalyzed Cannizzaro reaction of formaldehyde is 68.6 kJ/mol (16.4 kcal/mol).

A similar analysis was employed to determine the rate constant for saccharinic acid formation. Glucose was used as a model carbohydrate for this purpose. Saccharinic acid formation follows a second-

TABLE I

Third-Order Cannizzaro Reaction Rate Constants

Temperature (K)	Slope, b ($\text{l}^2 \cdot \text{mol}^{-2} \cdot \text{min}^{-1} \times 10^9$)	95% Confidence limits, cl ($\text{l}^2 \cdot \text{mol}^{-2} \cdot \text{min}^{-1} \times 10^9$)	cl/b (%)
303	2.27	± 0.104	± 4.59
313	5.62	± 0.099	± 1.76
323	11.7	± 1.13	± 9.62
333	26.9	± 4.21	± 15.6

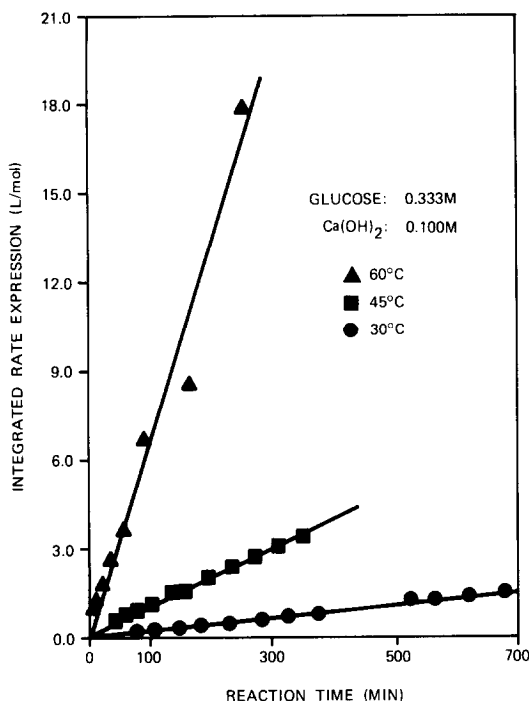


FIG. 4. Calcium hydroxide-catalyzed conversion of glucose to saccharinic acids is first order in glucose, first order in base.

order rate law, first order each in $\text{Ca}(\text{OH})_2$ and in glucose. The integrated form of the second-order rate law is plotted on Fig. 4 at 30, 45, and 60°C. The rate constants obtained from the slopes of these lines are listed in Table 2. The activation energy calculated for saccharinic acid formation from glucose based on these three constants is 93.4 kJ/mol (22.3 kcal/mol).

DISCUSSION OF RESULTS

Using reactions (9), (10), (11), and (12) as a basis, rate expressions for the rate of

production of each carbohydrate C_2 through C_7 and for the rate of consumption of HCHO and of OH^- can be written. Table 3 lists the set of differential equations describing the formose system. It is assumed that the aldol condensation reaction is first order in each reactant and first order in base, which is generally the case (19). The set of differential equations was numerically integrated using the Runge-Kutta method.

The rate constants k_1 , k_2 , and k_3 were determined by fitting the resulting formaldehyde conversion curve to experimental data using the Rosenbrock gradientless optimization technique.

An example of the fit obtained is shown in Fig. 5, where the data from the experiment shown in Fig. 2 at 40°C (313 K) using 1.5 M HCHO , 0.187 M $\text{Ca}(\text{OH})_2$, and 5.05×10^{-5} M glycolaldehyde are plotted as circles. The best fit is represented by the heavy line. The criterion for best fit was the minimization of the sum of the squares of the difference between experiment and model.

The values obtained for k_1 , k_2 , and k_3 in this way are:

$$k_1 = 2.98 \text{ liters}^2 \cdot \text{mol}^{-2} \cdot \text{min}^{-1},$$

$$k_2 = 6.64 \text{ liters}^2 \cdot \text{mol}^{-2} \cdot \text{min}^{-1},$$

$$k_3 = 0.203 \text{ liter} \cdot \text{mol}^{-1} \cdot \text{min}^{-1}.$$

The experimentally measured values of k_4 and k_5 from Tables 1 and 2, respectively, were used. These are:

$$k_4 = 5.62 \times 10^{-3} \text{ liter}^2 \cdot \text{mol}^{-2} \cdot \text{min}^{-1},$$

$$k_5 = 6.95 \times 10^{-3} \text{ liter} \cdot \text{mol}^{-1} \cdot \text{min}^{-1}.$$

TABLE 2

Second-Order Rate Constants for Saccharinic Acid Formation from Glucose

Temperature (K)	Slope, b ($\text{l} \cdot \text{mol}^{-1} \cdot \text{min}^{-1} \times 10^3$)	95% confidence limits, cl ($\text{l} \cdot \text{mol}^{-1} \cdot \text{min}^{-1} \times 10^3$)	cl/b (%)
303	2.29	± 0.067	± 2.94
318	10.1	± 0.260	± 2.57
333	66.0	± 7.56	± 11.5

TABLE 3
Formose Reaction Model

$$\begin{aligned}
 -d[\text{HCHO}]/dt &= [\text{OH}^-] \left\{ k_1[\text{HCHO}] \sum_{i=2}^6 [\text{C}_i] + 2k_4 [\text{HCHO}]^2 \right\} \\
 d[\text{C}_2]/dt &= [\text{OH}^-] \left\{ -k_1[\text{HCHO}][\text{C}_2] - k_2[\text{C}_2] \left([\text{C}_2] + \sum_{i=2}^5 [\text{C}_i] \right) + k_3 \left([\text{C}_4] + \sum_{i=4}^7 [\text{C}_i] \right) \right\} \\
 d[\text{C}_3]/dt &= [\text{OH}^-] \left\{ k_1[\text{HCHO}][\text{C}_2] - [\text{C}_3] - k_2[\text{C}_3] \left([\text{C}_3] + \sum_{i=2}^4 [\text{C}_i] \right) + k_3 \left([\text{C}_6] + \sum_{i=5}^7 [\text{C}_i] \right) - k_5[\text{C}_3] \right\} \\
 d[\text{C}_4]/dt &= [\text{OH}^-] \left\{ k_1[\text{HCHO}][\text{C}_3] - [\text{C}_4] + k_2 \left([\text{C}_2]^2 - [\text{C}_4] \sum_{i=2}^3 [\text{C}_i] \right) + k_3 \left(\sum_{i=6}^7 [\text{C}_i] - [\text{C}_4] \right) - k_5[\text{C}_4] \right\} \\
 d[\text{C}_5]/dt &= [\text{OH}^-] \left\{ k_1[\text{HCHO}][\text{C}_4] - [\text{C}_5] + k_2[\text{C}_2][\text{C}_3] - [\text{C}_5] + k_3([\text{C}_7] - [\text{C}_5]) - k_5[\text{C}_5] \right\} \\
 d[\text{C}_6]/dt &= [\text{OH}^-] \left\{ k_1[\text{HCHO}][\text{C}_5] - [\text{C}_6] + k_2([\text{C}_3]^2 + [\text{C}_2][\text{C}_4]) - 2k_5[\text{C}_6] - k_5[\text{C}_6] \right\} \\
 d[\text{C}_7]/dt &= [\text{OH}^-] \left\{ k_1[\text{HCHO}][\text{C}_6] + k_2[\text{C}_3][\text{C}_4] + [\text{C}_2][\text{C}_5] - 2k_5[\text{C}_7] - k_5[\text{C}_7] \right\} \\
 -d[\text{OH}^-]/dt &= [\text{OH}^-] \left\{ k_4[\text{HCHO}]^2 + k_5 \sum_{i=3}^7 [\text{C}_i] \right\}
 \end{aligned}$$

The value for k_5 at 40°C was obtained from the Arrhenius plot of the constants determined at 30, 45, and 60°C.

The quantity k_2/k_3 can be considered a "lumped" equilibrium constant for the

aldolization/dealdolization reactions. Its value is 32.7 liters/mol at 40°C, the condition shown in Fig. 5. This agrees with the experimental results of others. For example, Berl and Feazel (20) also found that the equilibrium favors the higher-carbon-number species.

Also shown in Fig. 5 is the sensitivity of the calculated curve to changes in the three constants, k_1 , k_2 , and k_3 . The lighter curves on Fig. 5 show the effect of alternately increasing and decreasing each of the three constants by 25%, while keeping the other constants at their original values.

As expected, the model is most sensitive to the value of k_3 , the rate constant for dealdolization. This is the rate-limiting (and, therefore, the most important) reaction over most of the conversion range. The model is also quite sensitive to the value of k_1 , which is the rate constant for the aldol condensation reactions of formaldehyde with sugars. These reactions become rate limiting at high conversion levels. The model is least sensitive to changes in k_2 , the rate constant for the condensation reactions between carbohydrates, since these reactions neither directly involve formaldehyde nor act as rate-limiting steps at any

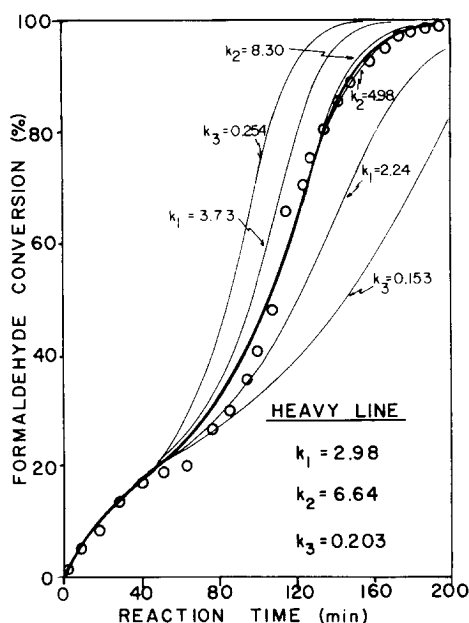


FIG. 5. Fitting experimental data using the formose reaction model. The heavy line is the best fit. The light lines show the sensitivity of the model to 25% changes in k_1 , k_2 , and k_3 .

time during the course of reaction. Therefore, they are not as important as the other two constants, k_1 and k_3 , in determining the kinetics of formaldehyde conversion. They will be important, however, in determining carbohydrate carbon-number distribution.

As can also be seen from Fig. 5, none of the three rate constants have a significant effect on the early part of the reaction, where only Cannizzaro reaction (whose rate is determined by the value of k_4) is dominant.

In Table 4 the carbohydrate distribution predicted by the model is compared to measurements made by Khomenko *et al.* (6) at 25 and 100% formaldehyde conversion. The initial concentrations of HCHO, $\text{Ca}(\text{OH})_2$, and glycolaldehyde used for the model calculations were 1.5, 0.187, and $5.05 \times 10^{-5} M$, respectively, at 40°C. Khomenko's data were obtained using the same starting conditions except that no glycolaldehyde was intentionally added. Autocatalytic behavior was observed, however, due most likely to trace amounts of carbohydrates present in the HCHO solution. Because the model assumes that reactivity of the carbohydrates is independent of carbon number, it fails to reflect the relative stability observed for the C_6 species and the very high reactivity of glycolaldehyde. The model could probably be improved by including these two factors in its formulation, but a large amount of data would be necessary to do this accurately.

Although the model does not accurately predict carbohydrate distribution, it may nevertheless be useful for qualitative predictions.

TABLE 4

Carbohydrate Distribution—Predicted and Observed

	HCHO conversion = 25%		HCHO conversion = 100%	
	Predicted	Observed ^a	Predicted	Observed ^a
	C_2	5.2	0.0	15.0
C_3	9.4	16.7	15.6	11.1
C_4	11.3	7.8	16.1	16.1
C_5	12.5	10.7	17.4	27.2
C_6	10.4	31.5	16.4	35.1
C_7	51.3	33.3	19.5	10.5

^a Data of Khomenko *et al.* (6).

The model can be used to show the relative importance of reactions (9) through (12) as a function of HCHO conversion. The rates of these reactions (relative to the rate of carbohydrate/carbohydrate aldol condensation at 49% HCHO conversion) are listed in Table 5 for formaldehyde conversions of 25, 49, and 91%. Table 5 shows that initially the reactions involving formaldehyde are much faster than those involving only carbohydrates. However, as formaldehyde is depleted, the carbohydrate reactions become more important.

Figure 6 shows the experimental results obtained using conditions similar to those shown in Fig. 5, but with very low glycolaldehyde concentrations of 4.93×10^{-6} and $1.69 \times 10^{-6} M$. The constants found above (using $5.05 \times 10^{-5} M$ glycolaldehyde) were again used in the equations, and the formaldehyde conversion predicted is shown by the solid lines in Fig. 6. The model predicts that the Cannizzaro period (the induction

TABLE 5

Calculated Relative Reaction Rates in the Formose System at 40°C

HCHO conversion (%)	Aldol condensation HCHO/carb.	Aldol condensation carb./carb.	Dealdolization	Cannizzaro	Saccharinic acid formation
25	13	0.017	1.3	6.6	0.051
49	58	1.0	7.3	2.5	0.28
91	40	19	19	0.076	0.78

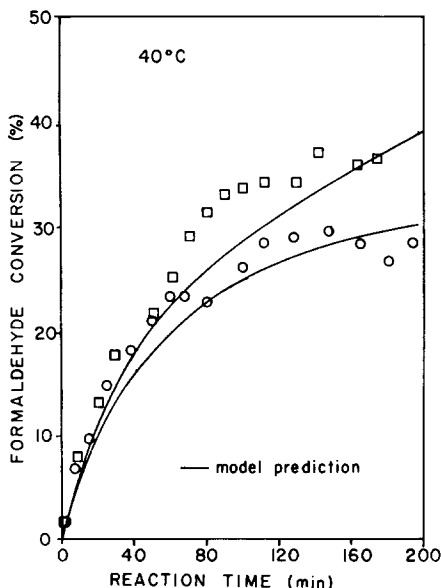


FIG. 6. Predictive capability of the model at low glycolaldehyde concentrations. Formose reaction at 40°C, 1.75 M HCHO, 0.187 M Ca(OH)₂. Initial glycolaldehyde molarity: □, 4.93×10^{-6} ; ○, 1.69×10^{-6} .

period) will extend beyond 200 min at these conditions and, indeed, this is observed.

Using the constants listed earlier, the model was used to predict behavior at much higher initial glycolaldehyde concentrations. Figure 7 shows that, qualitatively, the model behaves quite similarly to the experimental system. As the glycolaldehyde concentration is progressively increased, the model predicts a shortening of the induction period until the autocatalytic nature of the reaction disappears. This is exactly what is found experimentally. The quantitative amount that the induction period is shortened by a particular amount of glycolaldehyde over the range 5.05×10^{-3} to 4.16×10^{-2} is not predicted in Fig. 7 with great accuracy, however. This is most likely due to the fact that the constants k_1 , k_2 , and k_3 are averaged or lumped constants, and that the average changes when the glycolaldehyde concentration is varied over several orders of magnitude.

To check this point, the model was also fitted to a set of data obtained at high glycolaldehyde concentration by Kho-

menko *et al.*, who used 1.5 M HCHO, 0.187 M Ca(OH)₂, and 1.67×10^{-3} M glycolaldehyde at 313 K (40°C). The constants which gave the best fit were:

$$k_1 = 10.4 \text{ liters}^2 \cdot \text{mol}^{-2} \cdot \text{min}^{-1},$$

$$k_2 = 11.3 \text{ liters}^2 \cdot \text{mol}^{-2} \cdot \text{min}^{-1},$$

$$k_3 = 0.223 \text{ liter} \cdot \text{mol}^{-1} \cdot \text{min}^{-1}.$$

In this case, the average difference between experiment and model was 3.7% conversion.

Figure 8 shows the fit obtained and also the predictions based on this fit for the other experimental conditions used by Khomenko *et al.* In this figure, the heavy solid line is that obtained by fitting the model to the data represented by the circles. The other curves are the predictions based on this fit for the other experiments they made. The prediction is quite good for these experiments. The constants giving the best fit increased with increasing glycolaldehyde concentration. The two sets of

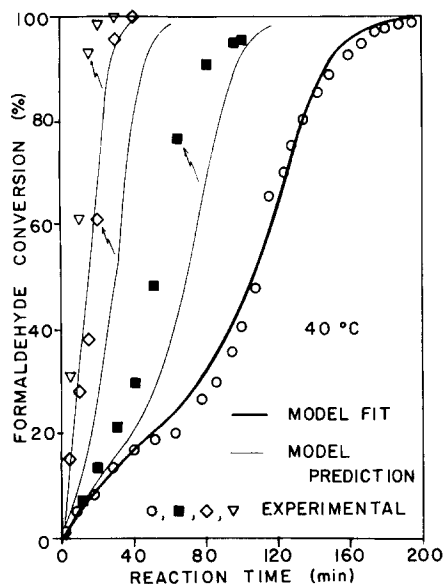


FIG. 7. Predictive capability of the model at high glycolaldehyde concentrations. Formose reaction at 40°C, 1.5 M HCHO, 0.187 M Ca(OH)₂. Initial glycolaldehyde molarity: ○, 5.05×10^{-3} ; ■, 3.63×10^{-3} ; ◇, 8.34×10^{-3} ; ▽, 4.16×10^{-2} (◇, ▽ are data of Khomenko *et al.* (6)).

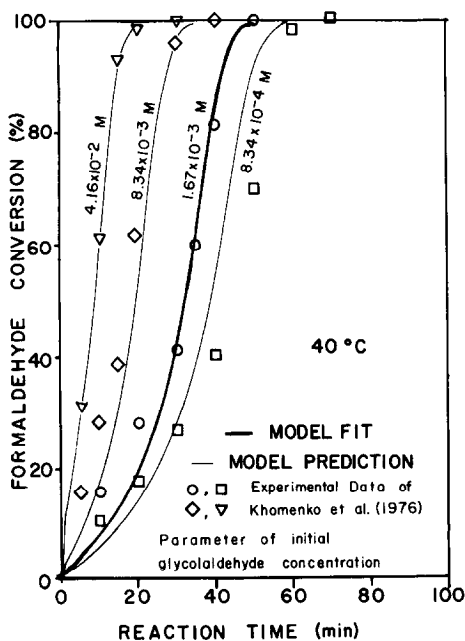


Fig. 8. Fitting the model at higher initial glycolaldehyde concentration required larger rate constants.

constants obtained at the two conditions are compared in Table 6.

The model appears to predict formaldehyde conversion more accurately at higher glycolaldehyde concentrations, perhaps because the effects of impurity levels of carbohydrates become much less important under these conditions.

The omission of the crossed Cannizzaro reaction from the reaction model may have been justified at very low initial glycolaldehyde concentrations. However, at the higher initial concentrations of glycolaldehyde shown on Figs. 7 and 8, it may have proceeded at the start of the reaction at an important rate. This was just the condition of both high formaldehyde and high carbohydrate concentrations that would favor crossed Cannizzaro and, if its rate is indeed significant, it would drain glycolaldehyde quickly from the system. Some of the fitting problems near the start of the reactions of Fig. 8 may be a consequence of this. Certainly, future work on the reaction model will need to include a term for crossed Cannizzaro reaction for formose reactions

that are initiated with a large amount of added carbohydrate. In future work, it may also be useful to try other more sensitive parameter estimation techniques such as that due to Marquardt. (21).

CONCLUSIONS

An important conceptual step has been made in understanding the calcium hydroxide-catalyzed formose reaction, the condensation of formaldehyde to sugars. This has been to accept the fact that for all practical purposes formaldehyde does not react with itself. The experimental proof has been to use sublimed paraformaldehyde, rather than solutions of paraformaldehyde which may contain trace carbohydrate impurities. Even so, as little as 3 ppm carbohydrate added as glycolaldehyde was effective in initiating the formose reaction using purified sublimed formaldehyde. Otherwise, for all practical purposes, the reaction did not proceed. The usual experimental observation is that the autocatalytic formose reaction is self-initiating without addition of glycolaldehyde when unpurified paraformaldehyde dissolved in water is used as the reactant. Of course, the inference that it is "carbohydrates" that are the responsible trace impurities in paraformaldehyde of commerce is not proven here experimentally. This is probably not feasible at the ppm level.

The simplicity of the reaction model is disarming. A set of power law rate expressions is used, and wherever aldoses or ketoses appear, their quantities are lumped for the spectrum of carbon numbers in the system. That a single rate constant de-

TABLE 6

The Effect of Initial Glycolaldehyde Concentration on Rate Constants at 40°C, 1.5 M HCHO, 0.187 M Ca(OH)₂

$5.05 \times 10^{-3} M$ HOCH ₂ CHO	$1.67 \times 10^{-3} M$ HOCH ₂ CHO
$k_1 = 2.98$	$k_1 = 10.4$
$k_2 = 6.64$	$k_2 = 11.3$
$k_3 = 0.203$	$k_3 = 0.223$

scribes, e.g., formaldehyde addition to sugars of varying structure and carbon number suggests that the addition reaction mechanism is the same for all of the species. The same holds true for the aldol condensation of sugars and their dealdolization.

The rate constant for Cannizzaro reaction is straightforward and on firm ground experimentally. That for saccharinic acid formation needs to be tested with other sugars and over a wider spectrum of experimental conditions. The rates of crossed Cannizzaro reactions need to be quantitatively established and incorporated into the reaction model.

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