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Homogeneously Catalyzed Formaldehyde Condensation to Carbohydrates

II. Instabilities and Cannizzaro Effects

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Cannizzaro reaction of formaldehyde proceeds in alkaline medium in conjunction with the "formose" condensation reaction to produce aldoses and ketoses. The ratio of the two reactions is a function of the catalyst used. In studies with $Ca(OH)_2$ catalyst at conversion levels below 4%, HCHO disappearance rate by Cannizzaro is triple that by formose condensation. Near 50% conversion, which is where the stoichiometry of the Cannizzaro reaction requires that its absolute rate pass through a maximum, HCHO disappearance by Cannizzaro is only 5% of that by formose. Reaction instabilities occur both at low and high $Ca(OH)_2$ concentration levels at fixed HCHO feed rate in a continuous stirred tank reactor (CSTR). As catalyst concentration is increased, reaction pH drops from 12 to 10.5 in the range of 0 to 100% HCHO conversion. Inordinate levels of $Ca(OH)_2$ catalyst (2 moles/mole HCHO) quench both the formose and Cannizzaro reactions—an unexpected result. The ratio of branched chain carbohydrate products, such as hydroxymethylglyceraldehyde and apiose, or straight chain species such as erythrose and arabinose, can be controlled by manipulation of operating conditions; the branched species are so subject to reduction by cross-Cannizzaro reaction with HCHO that species such as hydroxymethylglycerol are made in large quantities by HCHO condensation in the presence of NaOH.

INTRODUCTION

The Formose Reaction

The homogeneously catalyzed formose reaction is the autocatalytic condensation in the presence of alkaline catalysts of formaldehyde to a complex carbohydrate mixture, first reported by Butlerow (*1*) in 1861. The formaldehyde condensation reaction is catalyzed both by divalent metal bases such as $Ca(OH)_2$, $Ba(OH)_2$, $Sr(OH)_2$, $Mg(OH)_2$ and $Pb(OH)_2$ as well as by monovalent bases such as KOH, NaOH and TlOH (*2*). Berlin, Krylov, and Sinyak (*3*) and Krylov and others (*4*) have recently shown that tri- and tetravalent bases such as $Dy(OH)_3$, $Er(OH)_3$, $Eu(OH)_3$, $Sm(OH)_3$, $Ce(OH)_4$ and $Th(OH)_4$ catalyze the formose condensation reaction. Organic bases such as pyridine, collidine, and α-, β-picoline also are catalysts (*2*).

Glycolaldehyde (CH_2OHCHO) has been reported (*5, 6*) to be the primary reaction product. Studies by Katschmann (*7*) suggest a dual process for autocatalytic reaction in which the slow primary formation of glycolaldehyde is followed by rapid condensation and formaldehyde addition reactions. Franzen and Hauck (*8*) proposed that complexing of formaldehyde with $Ca(OH)_2$ might occur to produce a complex salt $HOCH_2OCaOH$. Weiss, LaPierre and Shapira (*9*) and Weiss and Shapira (*10*) observed complexing in a study at 60°C of the $Ca(OH)_2$ catalyzed reaction and proposed a mechanism involving decomplexing of products as the rate limiting step. The mechanism proposed is analogous to a Langmuir-Hinshelwood mechanism for a heterogeneously catalyzed reaction, in which a semantic substitution of "complexing–decomplexing" for "adsorption–desorption" was made.

The rate law developed explained in its degeneracies the observed 60°C experimental behavior of the $Ca(OH)_2$ catalyzed formose reaction:

Autocatalytic at low conversions
Zero order in organics at intermediate conversions
First order in formaldehyde at high conversions (this work)

and a suggestion was made that this type of analysis may be applicable to other autocatalytic homogeneously catalyzed reactions. It is not a requisite that the rate limiting step of a homogeneously catalyzed reaction be the reaction step itself.

The Cannizzaro Reaction

In the process of the formose reaction, the Cannizzaro reaction occurs simultaneously with the condensation of HCHO to aldoses and ketoses. The Cannizzaro reaction takes place with aldehyde molecules having no hydrogen on the α-carbon atom (that adjacent to the -CHO group) and with HCHO (*11*)

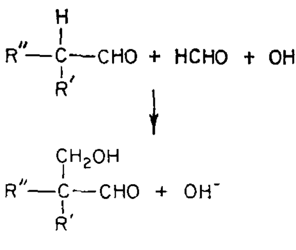
$$2RCHO + OH^- \rightarrow ROH + RCOO^-, \qquad (1)$$

$$2HCHO + OH^- \rightarrow CH_3OH + HCOO^-. \qquad (2)$$

Aldehydes with no α-hydrogen atoms can also undergo cross-Cannizzaro reactions in the presence of both HCHO and alkali.

$$RCHO + HCHO + OH^- \rightarrow RCH_2OH + HCOO^-. \qquad (3)$$

Aldehydes having α-hydrogen atoms undergo aldol condensation (HCHO addition) reactions in the presence of formaldehyde, until α-hydrogens are removed.

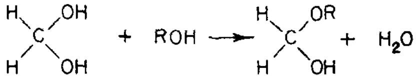


$$R''\!-\!\overset{H}{\underset{R'}{C}}\!-\!CHO + HCHO + OH^- \longrightarrow R''\!-\!\overset{CH_2OH}{\underset{R'}{C}}\!-\!CHO + OH^- \qquad (4)$$

According to Pfeil and Schroth (*12*), the extent of the Cannizzaro reaction occurring in the formose system varies with different basic catalysts in the following order

$$TlOH < Ca(OH)_2 < Ba(OH)_2 < LiOH,NaOH.$$

Cupit (*13*) has shown that alcohols influence the rate of the Cannizzaro reaction both by providing a medium of lower dielectric constant and by chemical inhibition resulting from hemiacetal formation with methylene glycol.



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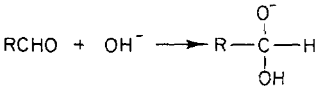
According to Cupit, the degree of chemical inhibition per mole of added alcohol is in the order

glycerol > methanol > ethanol > *n*-propanol.

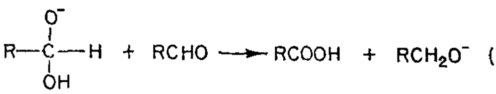
Ingold (*14*) discusses the mechanism of the Cannizzaro reaction that was suggested by Hammett (*15*). Aldehyde, by interaction with OH^-, can produce two reducing anions, the first more easily than the second.

$$R\!-\!\overset{O^-}{\underset{OH}{C}}\!-\!H \qquad R\!-\!\overset{O^-}{\underset{O^-}{C}}\!-\!H$$

Either of these can transfer a hydride ion in bimolecular fashion to a suitable acceptor, in particular to a carbonyl carbon atom of another aldehyde molecule. Geissman (*11*) published a review of Cannizzaro literature that includes the mechanisms proposed by Eitel and Lock (*16*) and March (*17*) which are in accord with a hydride ion transfer process.



$$RCHO + OH^- \longrightarrow R\!-\!\overset{O^-}{\underset{OH}{C}}\!-\!H \qquad (6)$$



$$R\!-\!\overset{O^-}{\underset{OH}{C}}\!-\!H + RCHO \longrightarrow RCOOH + RCH_2O^- \qquad (7)$$

It was predicted on the basis of these mechanisms (*9*) and shown that, at 60°C and low formaldehyde conversion rates in a continuous stirred tank reactor, the kinetics of the Cannizzaro reaction of formaldehyde with $Ca(OH)_2$ is first order with respect to both HCHO and $Ca(OH)_2$. This was also shown by Ackerlof and Mitchell (*18*) in batch studies. We also studied in our earlier paper the variation of Cannizzaro reaction with formaldehyde conversion at 60°C (*9*), and found that the Cannizzaro rate passed through a maximum at intermediate conversion levels, then decreased with increase in conversion. Near 85% conversion, it passed through a minimum and then increased sharply beyond 90% formaldehyde conversion levels. The behavior was explained and it was predicted that maximum Cannizzaro rate should occur near 50% HCHO conversion.

The overall formose reaction system is a complex interaction of condensation and Cannizzaro reactions. To help establish the reaction pathways, the present work extends the range of formose process variable reported earlier and includes studies of the NaOH catalyzed Cannizzaro reactions of pure species, such as glycolaldehyde, glyceraldehyde, and dihydroxyacetone.

EXPERIMENTAL SECTION

Formose Reactants

Formaldehyde solutions used in the reaction studies were prepared by dissolving Mallinckrodt CP paraformaldehyde. Analytical reagent grade $Ca(OH)_2$, also from Mallinckrodt, was used for all studies.

Equipment and Operating Procedures

Flow studies presented in this report were carried out in a continuous stirred tank reactor (CSTR). A detailed description of the feed system, the reactor, its operation, and analytical techniques has been published (*9*). The advantage of the CSTR for studying complex reactions is that rates can be measured directly.

pH data were obtained using a Corning Model 12 research pH meter equipped with a Sargent-Welch combination electrode. The pH in the reactor was automatically corrected to temperature.

An Ionalyzer, Model 404, Orion Research Specific Ion Meter, with a calcium activity electrode and a reference electrode was used to obtain calcium activity data. It was useful within a temperature range of 10–45°C. Calcium activity reading is not affected by pH in the range 8–12 (*19*) of this study.

RESULTS

Experimental data obtained in the CSTR are listed in order of increasing temperature (30–60°C), formaldehyde feed rate (0.0325–0.172 moles/liter/min), and increasing $Ca(OH)_2$ feed rate 0.00093–0.416 moles/liter/min. HCHO concentrations in the reactor ranged from 0.002 to 1.77 M at steady state; $Ca(OH)_2$ concentrations ranged from 0.012 to 1.33 M.

In the earlier study when formaldehyde conversion rate approached the feed rate of formaldehyde to the reactor, experimentation was terminated (since reaction rate in a CSTR cannot exceed the feed rate to the CSTR). However in the present study, experiments were pursued at higher reaction severities, i.e., past the $Ca(OH)_2$ catalyst concentration levels that were required for complete HCHO conversion. Isothermal experiments were made at constant formaldehyde feed rate while $Ca(OH)_2$ molarity in the combined feed was progressively increased.

Figure 1, which is a plot of formose rate versus $Ca(OH)_2$ concentration in the reactor (and, hence, in the product stream) shows that at 0.4 M $Ca(OH)_2$ and at temperatures of 30 and 40°C, an unexpected decrease in rate with increasing catalyst concentration was obtained. At 60°C, the decrease in reactivity was observed to a marked extent, but at very high $Ca(OH)_2$ concentration, 1.3 M. Data (Table 2) comparing formaldehyde and $Ca(OH)_2$ molarities suggest, at these high catalyst concentrations, two possible explanations: (1) formaldehyde could be isolated in complexes with $Ca(OH)_2$ so separated that there may be a low probability of one com-

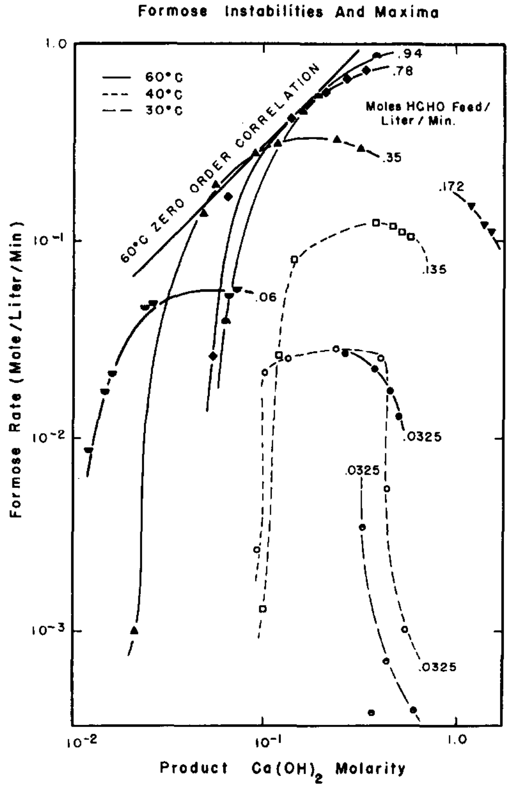


FIG. 1. Formose reaction rate (i.e., condensation reaction only) versus total $Ca(OH)_2$ present in system (parameters of HCHO feed rate and temperature noted). Note instabilities at both low and high catalyst concentrations.

plex interacting with another; (2) formaldehyde is physically adsorbed on undissolved $Ca(OH)_2$. These offer some explanation, but not a complete reason for the instability behavior.

At very low formaldehyde conversion, mainly Cannizzaro reaction occurs. Table 3 compares the formaldehyde disappearance rate by Cannizzaro reaction and by formose reaction at typical low HCHO operation.

The reaction system exhibits two concentration instabilities: for a small difference in $Ca(OH)_2$ catalyst concentration there is a large difference in formose reaction rate. Figure 1 shows that the instabilities occur both at low and at high catalyst concentration at 40°C. These instabilities are also seen on the low side at 60°C, on the high side at 30°C. *Catalyst* concentration instabilities of this nature are not known by us to have been reported before for any system, let alone for the formose system. Matsura and Kato (*20*) point out that *reactant* concentration instabilities are possible for autocatalytic CSTR reactions.

Figure 1 also shows the line approximating the zero order behavior of formose rate (in formaldehyde and product concentrations) at intermediate conversion levels. The line is taken from the earlier correlation (*9*) at 60°C. At that time data points at very low conversion levels were recognized as points scattered from the zero order correlation but not as indicators of an instability.

Cannizzaro Effect

Cannizzaro effects in the formose reaction are dependent on both the formaldehyde concentration and on the conversion level. Plots of Cannizzaro rate* versus total formaldehyde conversion rate, with parameters of HCHO feed rate and temperature, are given in Fig. 2. Note that total formaldehyde conversion rate equals formose rate plus 4 × Cannizzaro rate; and this line is shown in Fig. 2. Cannizzaro rate passes through a maximum at intermediate conversion levels, then a minimum at higher levels, and finally increases sharply above 90% conversion. This is in agreement with and extends the earlier work at 60°C (also plotted on Fig. 2) to a lower order of magnitude.

Cannizzaro reaction rate is plotted as a function of $Ca(OH)_2$ concentration in the product on Fig. 3. Parameters of constant formaldehyde feed rate and temperatures of 30, 40, and 60°C are shown. The data relationships on Fig. 3 are quite complex, but, the plots do indicate a rough similarity in form to those for the formose reaction shown on Fig. 1. For example: a rate maximum at 40°C and high and low $Ca(OH)_2$ concentration instabilities. Cannizzaro reaction rate appeared first order in both $Ca(OH)_2$ and formaldehyde at $<10\%$ HCHO conversion and 60°C (*9*), but Fig.

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* Cannizzaro rate is defined as the rate of $Ca(OH)_2$ consumption in the reaction: $Ca(OH)_2 + 4HCHO \rightarrow 2CH_3OH + Ca(OOCH)_2$.

TABLE 1

EXPERIMENTAL DATA

Temp (°C)	HCHO conversion (%)	Residence time (min)	Feed rates (moles/liter/min)		Conc in reactor (moles/liter)		pH	Ca^{2+} activity $(\times 10^4)$
			HCHO	$Ca(OH)_2$	HCHO	$Ca(OH)_2$		
30.0	16.6	22.8	0.0325	0.0145	0.595	0.321	11.54	
	6.6	12.5		0.0353	0.366	0.437	11.67	
	11.37	10.26		0.0355	0.314	0.355	11.56	
	4.8	7.1		0.0695	0.236	0.489	11.90	
40.0	10.7	18.0	0.0325	0.0052	0.524	0.090	11.90	137.0
	88.5	20.3		0.0074	0.076	0.132	11.42	38.0
	68.5	12.5		0.0077	0.129	0.096	9.25	83.0
	97.4	29.5		0.0085	0.025	0.234	10.70	32.0
	83.69	15.62		0.0266	0.083	0.408	11.93	36.0
	27.04	13.25		0.0334	0.315	0.431	10.70	170.0
	5.0	5.09		0.1060	0.157	0.539	11.46	117.0
40.0	21.8	12.33	0.135	0.0103	1.307	0.118	10.55	110.0
	2.45	9.43		0.0108	1.263	0.0968	11.21	93.0
	63.3	10.90		0.0140	0.541	0.140	10.88	54.0
	98.4	20.60		0.0193	0.044	0.366	11.40	11.0
	95.9	12.50		0.0367	0.068	0.447	11.54	11.0
	87.4	11.32		0.044	0.194	0.494	12.15	14.0
	81.9	9.80		0.0562	0.242	0.557	11.95	13.0
60.0	99.5	25.75	0.0325	0.0112	0.004	0.255	11.45	
	98.0	14.83		0.0278	0.009	0.382	11.68	
	95.5	10.27		0.0455	0.015	0.432	11.67	
	92.4	6.40		0.0795	0.016	0.483	11.63	
60.0	4.7	30.0	0.06	0.00093	1.74	0.012	9.53	
	3.2	30.0		0.00093	1.77	0.012	9.51	
	37.7	12.1		0.0017	0.771	0.016	9.73	
	42.4	21.2		0.0017	0.716	0.017	9.87	
	76.4	17.5		0.0021	0.267	0.024	10.13	
	82.8	15.2		0.0025	0.167	0.027	10.50	
	100.0	14.9		0.0053	0.002	0.068	11.20	
	99.9	14.9		0.0053	0.092	0.047		
60.0	96.5	5.68	0.172	0.248	0.031	1.17		
	93.5	3.86		0.345	0.039	1.30		
	91.2	3.27		0.416	0.049	1.33		

3 shows the limited regimes of utility of such a relationship.

pH and Calcium Activity Behavior

Figure 4 is a plot of pH of the reaction versus $Ca(OH)_2$ concentration in the reactor at 40°C. The pH decreases with increased $Ca(OH)_2$ concentration, reaches a minimum, and increases with further increase in $Ca(OH)_2$ concentration. The behavior mirrors the Cannizzaro rate and reflects the formation of acid products by Cannizzaro reaction.

TABLE 2

Reaction temp (°C)	HCHO feed rate (moles/liter/min)	$Ca(OH)_2$ conc in combined feed (moles/liter)	HCHO conc in combined feed (moles/liter)
30	0.0325	0.4916	0.248
40	0.0325	0.54	0.166

TABLE 3

Reaction temp (°C)	HCHO feed rate (moles/liter/min)	$Ca(OH)_2$ conc (moles/liter)	HCHO disappearance rate (moles/liter/min)	
			By Cannizzaro	By formose
40	0.135	0.0968	0.002	0.0013
30	0.0325	0.355	0.0012	0.0004

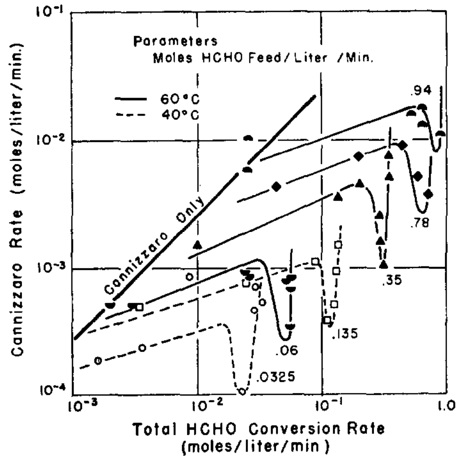


FIG. 2. The relationships between Cannizzaro rate [$Ca(OH)_2$ conversion rate] and total formaldehyde conversion rate. At low conversions, Cannizzaro reaction predominates over aldose condensation.

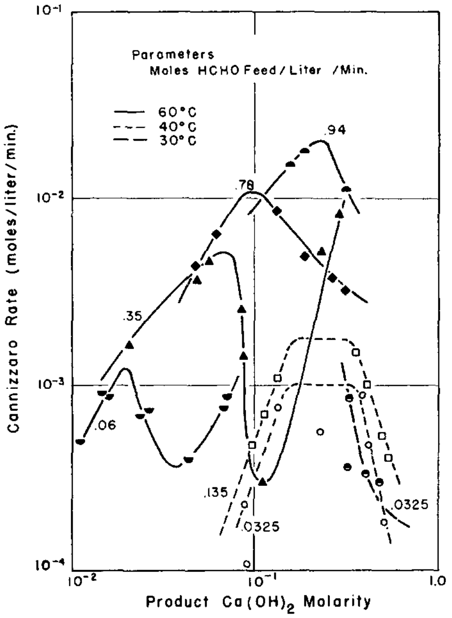


FIG. 3. Cannizzaro rates versus product $Ca(OH)_2$ molarity. Note instabilities at low and high catalyst concentrations.

Measured calcium ion activity at 40°C versus $Ca(OH)_2$ concentration in the reactor is plotted in Fig. 5. There is a correlative behavior with Cannizzaro rate. The solubility of $Ca(OH)_2$ at 40°C is indicated in Fig. 5. Calcium activity of the reaction lies well below the solubility line, reflecting the fact that the calcium is complexed. This has been reported by Rendleman (*21*).

Figure 6 is a log–log plot of formose/$Ca(OH)_2$ concentration vs HCHO concentration using the 90% conversion data at 40°C, with formaldehyde feed rate ranging from 0.0325 to 0.135 moles/liter/min. The lines drawn are force-fits showing a first order dependency of formose reaction on HCHO concentration at high conversion levels. This is in accord with the prediction made in the earlier paper (*9*) and agrees with first order in each species shown by Berl and Feazel (*22*) for studies on the self-condensation of glyceraldehyde with HCHO. Data for the first order behavior of the formose reaction are scattered at 60°C, although the data are fitted on Fig. 6 with a line having a slope of unity.

Product Distribution

Products from the CSTR experiments at 40°C and 0.0325 moles/liter/min were reduced with $NaBH_4$ and analyzed as the trimethylsilylether derivatives according to the procedure described in (*9*). Since ethylene glycol analyses are not quantitative and the amounts present were small, selectivities were calculated on the basis of 3-carbon and higher TMS polyol products. Figure 7 is a plot of the distribution by carbon number groupings of these polyol products as a function of $Ca(OH)_2$ concentration in the

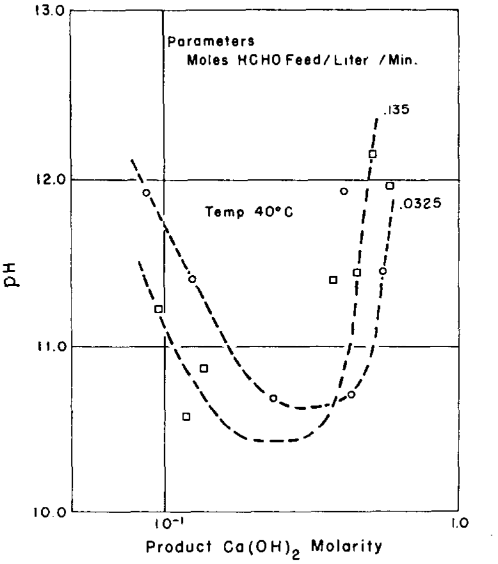


FIG. 4. pH of the reaction is plotted as a function of $Ca(OH)_2$ concentration in the reactor at 40°C. The minima correspond to rate maxima.

reactor. A HCHO conversion plot is also included on Figure 7. High selectivity for glycerol is had at low conversion levels, illustrating the consecutive nature of the formose reaction. There is no significant change in the product distribution around the rate maximum. Figure 7 shows that 5- and 6-carbon species predominate near complete conversion.

A most significant aspect of the product distribution is the presence of branched

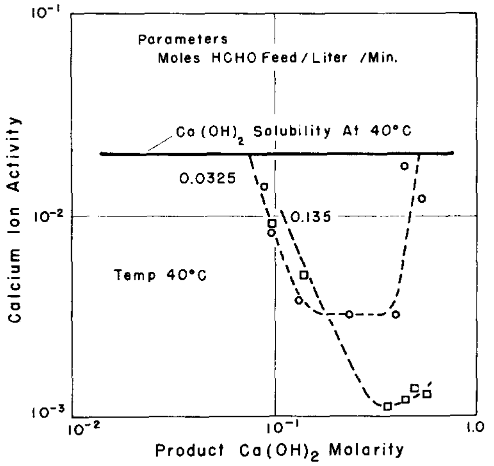


FIG. 5. Calcium ion activity of the $Ca(OH)_2$ catalyzed formose reaction at 40°C. *Minimum* Ca^{2+} activity is had at *minimum* reaction pH.

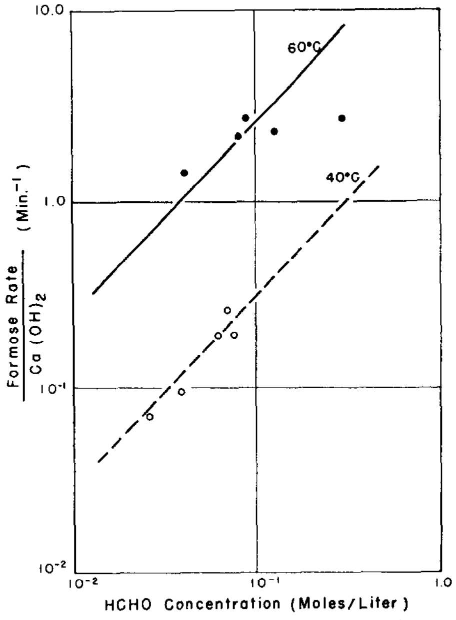
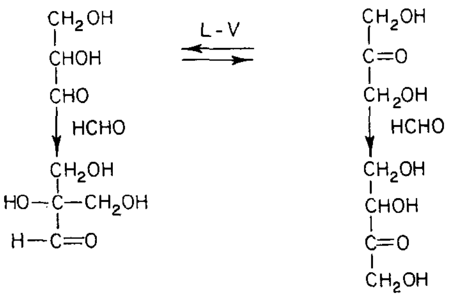


FIG. 6. Formose reaction rate is first order in both $Ca(OH)_2$ and formaldehyde at very high conversion levels.

chain compounds at high selectivity levels. Figure 8 is a plot of the fraction of branched chain species present in the 4- and 5-carbon polyols produced vs HCHO conversion. Parameters of 0.78–0.94 and 0.15–0.35 moles HCHO feed/liter/min at 60°C and 0.0325 moles HCHO feed/liter/min at 40°C are shown. Figure 8 exhibits a remarkable selectivity flip. At 50% and lower conversion levels, the C-4 and C-5 aldose and ketose products are practically pure straight chain at 40°C, practically pure branched chain at 60°C. At higher conversion level as much as 40% branched chain is present at 40°C [see also Ref. (*23*)]. Partridge, Weiss, and Todd (*24*) have presented definitive mass spectra of the branched polyols obtained by reduction of formose products, as well as identification of the 4-carbon aldose hydroxymethylglyceraldehyde.

The distribution of branched versus straight chain species may be a consequence of the base-catalyzed Lobry de Bruyn–van Eckenstein (L-V) equilibrium. Consider the addition of formaldehyde to a mixture of glyceraldehyde and dihydroxyacetone.

The relative proportion of dihydroxyacetone to glyceraldehyde will be a function



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of the rate glyceraldehyde isomerizes to dihydroxyacetone. In turn, the relative concentrations of these species as well as the relative rates of formaldehyde addition to each will define the 4-carbon branched versus straight chain distribution of aldoses and ketoses.

Cross-Cannizzaro Reaction of Formose Products

Table 4 shows the condensation scheme of formose products. The first condensation step of formaldehyde is to glycolaldehyde, which has two α-hydrogen atoms. Aldol

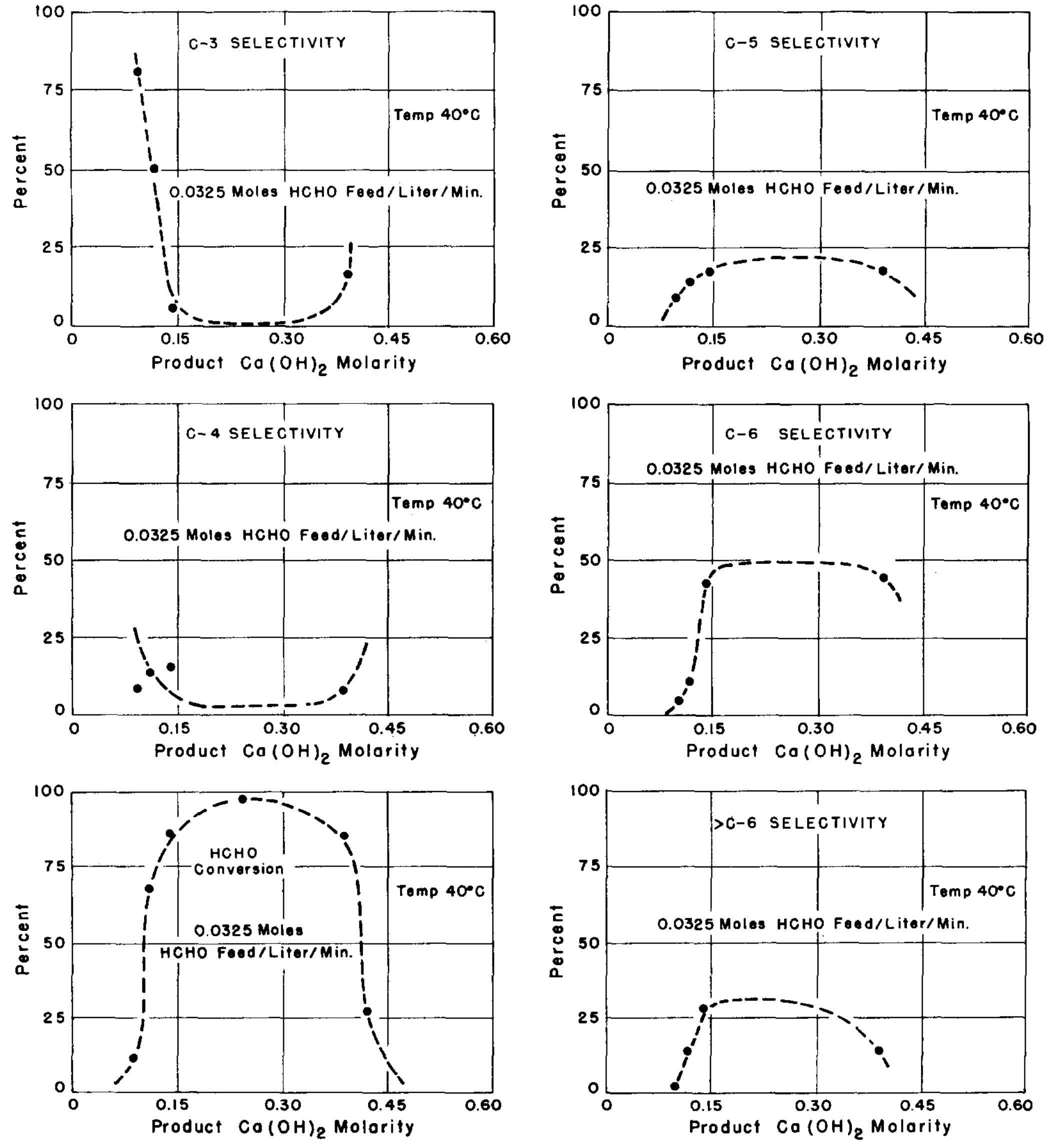


FIG. 7. Distribution by carbon number of formose polyol products at 40°C shows the consecutive nature of the reaction system.

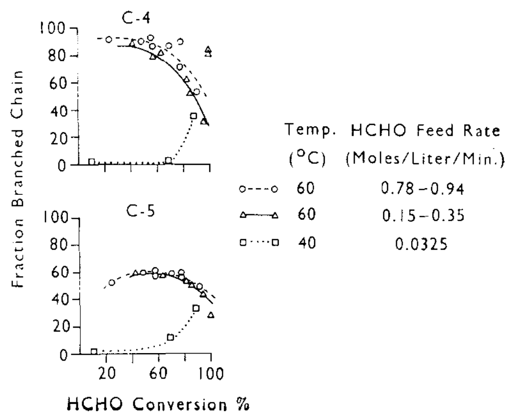
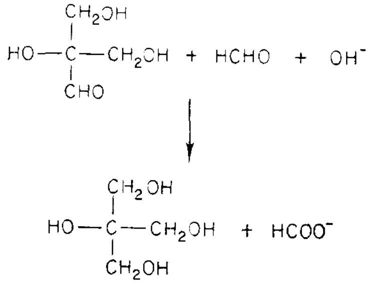


FIG. 8. Selectivity to branched chain and straight chain species can be controlled by manipulating operating conditions.

condensation must then follow to form glyceraldehyde. Glyceraldehyde can react by two pathways—either further aldol condensation to hydroxymethylglyceraldehyde or Lobry de Bruyn–van Eckenstein (L-V) rearrangement to dihydroxyacetone. Note that hydroxymethylglyceraldehyde has no α-hydrogen; and so it is a terminal product.

Dihydroxyacetone adds formaldehyde to form a 4-carbon staight chain aldose. This species can either add formaldehyde to its α-hydrogen to form hydroxymethyltetroses or isomerize by the L-V equilibrium to form the four carbon ketose, erythulose. Table 4 shows how 5-carbon straight chain aldoses and 6-carbon branched and straight chain aldoses and ketoses are formed.

As mentioned cross-Cannizzaro reactions occur mainly with aldose species with no α-hydrogen atoms—specifically, hydroxymethylglyceraldehyde, hydroxymethyltetroses, etc.



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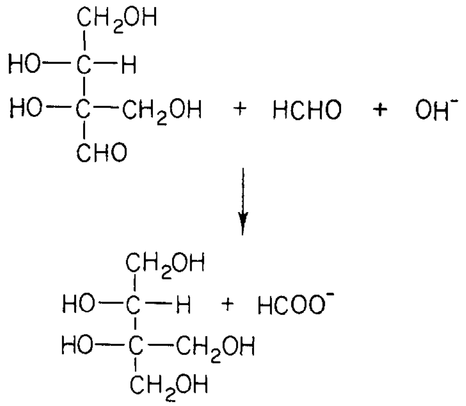

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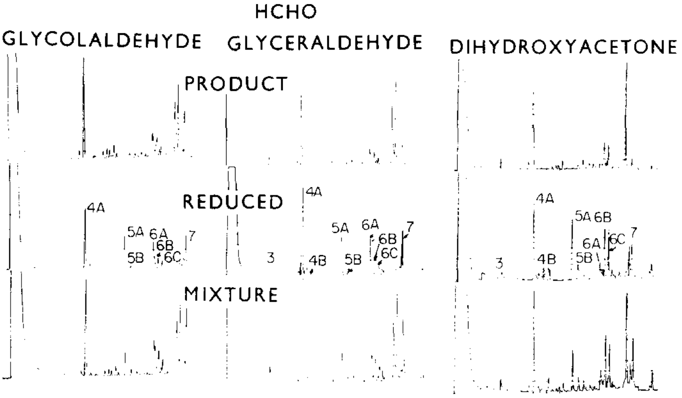
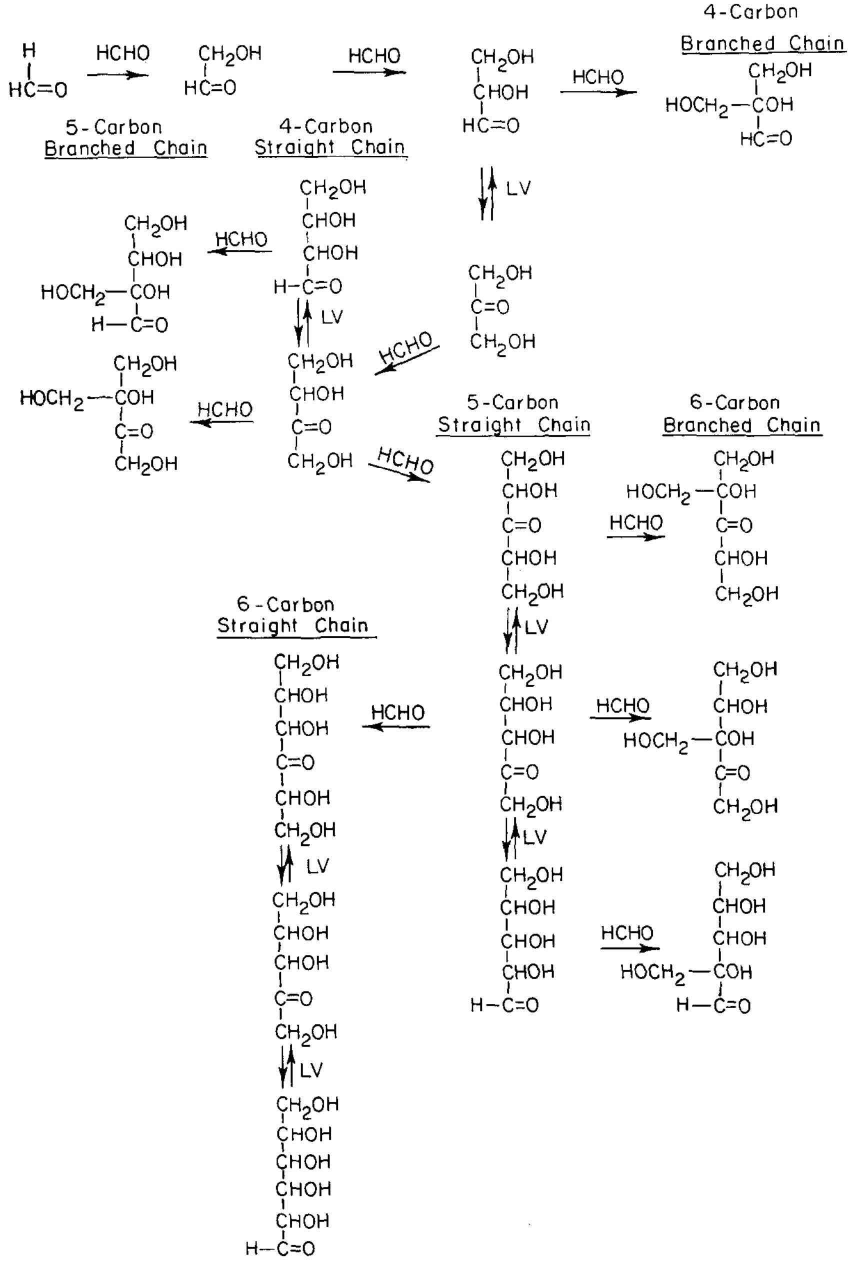


FIG. 9. Cross-Cannizzaro reaction of glycolaldehyde, glyceraldehyde, or dihydroxyacetone with HCHO in the presence of NaOH produces hydroxymethylglycerol and no significant quantities of hydroxymethylglyceraldehyde. Species identification in order of carbon number: (3) glycerol; (4A) hydroxymethylglycerol; (4B) erythritol, threitol; (5A) hydroxymethyl tetritol; (5B) adonitol, arabitol, xylitol; (6A) 2-hydroxymethylpentitol; (6B) 3-hydroxymethylpentitol; (6C) six-carbon straight chain polyols; (7) seven-carbon straight or branched chain polyols.

TABLE 4
FORMATION OF BRANCHED AND STRAIGHT CHAIN ALDOSES AND KETOSES
(ENANTIOMERS AND DIASTEREOMERS NOT SHOWN)



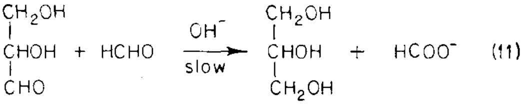
To demonstrate this type of stoichiometry sequence, three batch experiments were made with glycolaldehyde, glyceraldehyde, and dihydroxyacetone. Each of these compounds were separately mixed with HCHO (1.14 *M*) and NaOH (1.20 *M*) and allowed to react for 30 min at 29°C. Figure 9 shows chromatographic analyses of the trimethylsilylether derivatives of the products formed by these three experiments.

To distinguish between hydroxymethylglycerol and hydroxymethylglyceraldehyde in the products, samples were reduced to the corresponding polyols using $NaBH_4$.

The TMS derivatives of unreduced and reduced products can be compared in Fig. 9. A mixture of 2 μl each of the TMS derivatives of each unreduced and reduced product was then injected into the gas chromatograph. These analyses are also shown in Fig. 9. The hydroxymethylglycerol peak appears at the same retention time in all three analyses and no splitting of hydroxymethylglycerol and hydroxymethylglyceraldehyde peaks is observed in the mixed samples. The product produced in the presence of NaOH is hydroxymethylglycerol rather than hydroxymethylglyceraldehyde.

Glyceraldehyde also undergoes cross-Cannizzaro reaction directly (but to a small extent) with HCHO to yield glycerol.

Figure 9 shows small amounts of glycerol were so made. A cross-Cannizzaro network can be set up indicating major and minor pathways. This is shown on Table 5, illustrating the process through the 5-carbon level. Identification of the species noted on Fig. 9 are detailed in Partridge, Weiss and Todd (*24*). NaOH is far more effective than $Ca(OH)_2$ for the cross-Cannizzaro reaction. Formose products produced in the presence of $Ca(OH)_2$ contain hydroxymethylglyceraldehyde. Those produced in the presence of NaOH contain instead hydroxymethylglycerol.



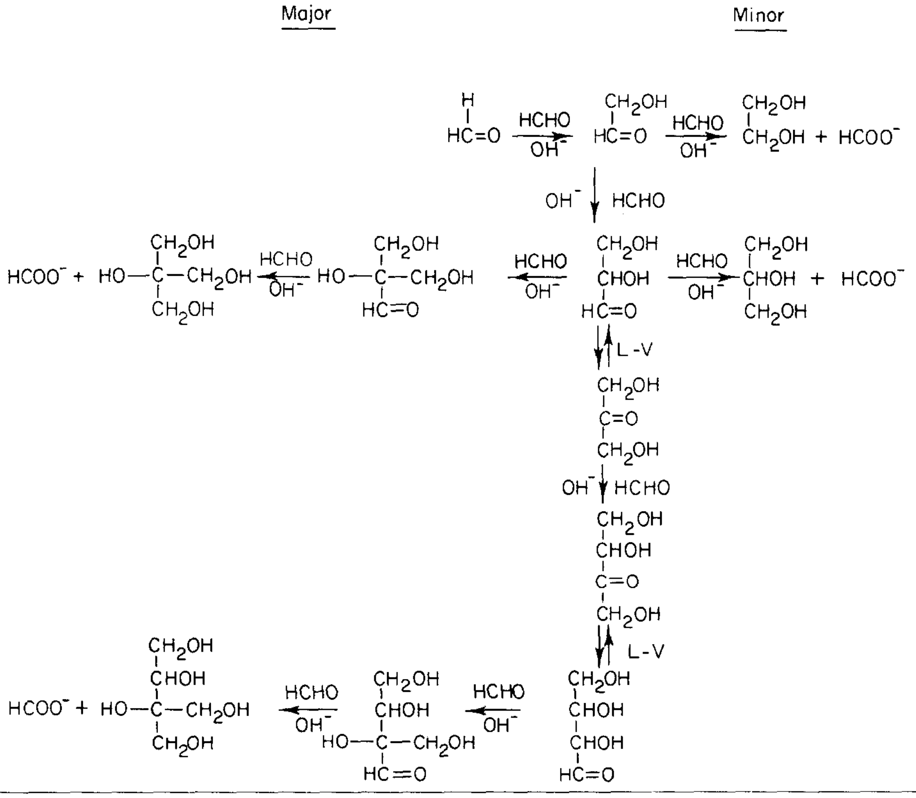
$$\begin{array}{l}CH_2OH\\ |\\ CHOH\\ |\\ CHO\end{array} + HCHO \xrightarrow[\text{slow}]{OH^-} \begin{array}{l}CH_2OH\\ |\\ CHOH\\ |\\ CH_2OH\end{array} + HCOO^- \qquad (11)$$

CONCLUSIONS

The Cannizzaro reaction of formaldehyde is far from a simple kinetic process that can be characterized by first or second order kinetics and a single reaction in which methanol and formate are produced. Rather, it proceeds in alkaline medium in conjunction with the formose reaction—the autocatalytic self-condensation of form-

TABLE 5

CROSS-CANNIZZARO REACTION NETWORK INDICATING POSSIBLE MAJOR AND MINOR PATHWAYS



aldehyde with itself—to produce glycolaldehyde which is then followed by aldol condensation to higher aldoses and ketoses. Mono-, di-, tri-, and tervalent bases, as well as nitrogen bases, have been reported to homogeneously catalyze both reactions, and the formose to Cannizzaro rate ratio will be not only a function of the catalyst but also of the formaldehyde conversion level.

In the present studies with $Ca(OH)_2$ catalyst, it was found that at HCHO conversion levels below 4%, HCHO disappearance by Cannizzaro is triple that by formose condensation. On the other hand, near 50% conversion, which is where the stoichiometry of the Cannizzaro reaction requires that its absolute rate pass through a maximum, HCHO disappearance rate by Cannizzaro is only 5% of that by formose condensation.

As catalyst concentration is increased at fixed formaldehyde initial concentration (i.e., feed rate in a continuous stirred tank reactor), the increase in absolute rate of Cannizzaro reaction neutralizes $Ca(OH)_2$ and pH of the reaction drops from approximately 12 to 10.5 in the range of 0 to 100% conversion. This autonomic behavior may be one reason for the change in reaction rate ratios; cross-Cannizzaro reaction of formaldehyde with condensation products is another reason. In any case, increasing catalyst to inordinate levels (e.g., 2 moles $Ca(OH)_2$/mole HCHO) quenches both reactions, an effect that is unexpected in a catalytic system.

In this complex reaction system, where more than one route is possible, interactive effects prevent extrapolation of rates and their ratios beyond regions of actual measurements. Selectivities were of course affected relative to the ratio of -ol to -ose products, but also the carbon number and skeletal structure of the formose condensation product itself depends on the reaction environment attained. The Lobry de Bruyn–van Eckenstein equilibrium controls the ratio of aldoses to ketoses; and, in turn, this ratio determines the ratio of branched to straight chain sugars, e.g., hydroxymethylglyceraldehyde to erythrose. The branched species is so active for cross-Cannizzaro reaction, that considerable hydroxymethylglycerol is produced when NaOH aldol condensation of formaldehyde with glycolaldehyde, glyceraldehyde, or dihydroxyacetone is attempted.

Much remains to be learned of the kinetics and the mechanisms of the multiplicity of interactive processes that proceed when organic species react. Formaldehyde in alkaline medium is ostensibly a simple situation, it has been studied for over a century, and yet the system is far from understood and modeled. Continuous stirred tank reactors, in which reaction rates can be measured directly, will be a tool of central importance, if organic chemists wish to develop understanding of even the stoichiometry of such complex reactions, let alone the kinetics and mechanism.

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