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Catalytic Condensation of Glycolaldehyde and Glyceraldehyde with Formaldehyde in Neutral and Weakly Alkaline Aqueous Media: Kinetics and Mechanism

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Abstract—The kinetics of glycolaldehyde and glyceraldehyde condensation with formaldehyde in a neutral aqueous medium in the presence of homogeneous phosphates and in a weakly alkaline medium in the presence of MgO was studied. The temperature dependences of the observed kinetic constants and the apparent activation energies of the reactions were determined. A reaction scheme for the interaction of lower monosaccharides with formaldehyde was derived from analyses of the reaction products.

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INTRODUCTION

Monosaccharides are traditionally obtained by the hydrolysis of biopolymers. However, no available natural sources have been found for many monosaccharides that could be of interest as substrates for fine organic synthesis or could be used in the pharmaceutical and fragrance industries. Some rare monosaccharides can be synthesized by the rearrangement of other carbohydrates via the Lobry de Bruyn–Alberda van Ekenstein reactions [1], the epimerization of aldoses catalyzed by Ca^{2+} [1] or Ni^{2+} [2] cations and the Bilik reaction [3]. All these processes are reversible, and, therefore, the complete conversion of one monosaccharide into another is impossible. The rearrangement yields a mixture of at least two substances, which has to be separated. Sometimes the yield of the desired monosaccharide after its isolation from the mixture is as low as 10%. This fact explains the very high cost of the rare carbohydrates.

The formose reaction was considered for a long time as a possible method for the synthesis of monosaccharides. This reaction, discovered more than 100 years ago, is formaldehyde condensation into monosaccharides in an alkali medium. However, extensive studies of this reaction in the middle of the 20th century showed no way of controlling its selectivity. Our studies [4, 5] showed that the classical formose reaction in a strongly alkaline medium in the presence of calcium ions can be classified as a chain reaction with degenerate chain branching. In the mechanism proposed by us, the degenerate branching step is the calcium-catalyzed retro-aldol cleavage of the resulting monosaccharides. That is why the search for conditions of the selective synthesis of individual monosaccharides in a strongly alkaline medium and in the presence of calcium ions seems unpromising.

Earlier [6], we described the reaction between dihydroxyacetone (DHA) and formaldehyde proceeding via aldol condensation and preferentially yielding two rare monosaccharides, namely erythrulose and 3-pentulose, which are of great interest to the fragrance industry [7, 8]. Examples of the selective synthesis of erythrulose, 3-pentulose and 2-hydroxymethyl-3-pentulose from formaldehyde in nonaqueous solvents, such as DMF and DMSO, in the presence of the organic catalysts 2-dimethylaminoethanol and thiaminehydrochloride were described earlier [9–12]. Our method for the synthesis of erythrulose and 3-pentulose has a clear advantage, because it requires no organic catalysts or environmentally hazardous solvents. In addition, we found that glycolaldehyde (GA) and glyceraldehyde (GCA) can be obtained from formaldehyde by UV irradiation [13]. Thus, the direct synthesis of rare carbohydrates from formaldehyde is possible by combining the photoinduced synthesis of GA and GCA with their subsequent catalytic condensation with formaldehyde.

In this work formaldehyde, GA, and GCA were chosen as the substrates for the synthesis of higher monosaccharides. The reactions were carried out in a neutral medium in the presence of a phosphate buffer [6] or in a weakly alkaline medium in the presence of MgO as the catalyst. The purpose of this work included a study of the dependence of the product composition on the synthesis conditions and search for the optimum conditions maximizing the selectivity of the reaction.

Table 1. Products of the condensation of glycolaldehyde and glyceraldehyde with formaldehyde in the presence of MgO at different temperatures

Entry	Starting monosaccharide	T, °C	Time, h	Lower monosaccharides, mmol/l			Reaction products, mmol/l						
				GA	GCA	DHA	**I**	**II**	**III**	**IV**	**V**	**VI**	**VII**
1	GA	30	1	3.34	0.11	0.89	0.02	0.02	0.02	0.21	0.01	0.00	0.01
2			2	2.50	0.09	1.28	0.07	0.03	0.05	0.34	0.04	0.04	0.07
3			4	1.50	0.09	1.29	0.16	0.05	0.10	0.53	0.09	0.14	0.33
4		50	0.5	2.28	0.09	1.33	0.11	0.04	0.08	0.63	0.08	0.06	0.07
5			1	1.04	0.14	1.08	0.25	0.07	0.20	1.01	0.18	0.26	0.48
6		70	0.16	1.63	0.17	1.28	0.06	0.01	0.05	0.22	0.05	0.05	0.05
7			0.42	0.36	0.15	0.41	0.34	0.02	0.13	0.14	0.22	0.34	0.76
8			0.58	0.28	0.12	0.26	0.26	0.08	0.11	0.17	0.25	0.46	0.79
9	GCA	30	1	0.00	3.51	0.13	0.22	0.01	0.16	0.31	0.13	0.10	0.25
10			2	0.00	2.37	0.15	0.30	0.02	0.21	0.38	0.16	0.21	0.56
11			4	0.00	1.07	0.10	0.33	0.03	0.17	0.37	0.17	0.43	1.08
12		50	0.33	0.00	2.06	0.26	0.26	0.01	0.21	0.45	0.17	0.16	0.17
13			0.75	0.06	0.75	0.17	0.27	0.01	0.20	0.47	0.16	0.33	0.61
14			1	0.07	0.39	0.13	0.23	0.03	0.17	0.50	0.17	0.43	0.80
15		70	0.08	0.00	2.57	0.35	0.26	0.01	0.21	0.52	0.20	0.14	0.14
16			0.16	0.08	0.68	0.27	0.27	0.04	0.35	1.00	0.31	0.37	0.70
17			0.33	0.22	0.19	0.19	0.09	0.05	0.16	0.75	0.20	0.59	1.05

Note: Reaction conditions: $[GA]_0 = [GCA]_0 = 5$ mmol/l, $[CH_2O]_0 = 0.1$ mol/l, $[MgO] = 0.027$ mol/l, pH 10.4.

EXPERIMENTAL

Solutions and Chemicals

The following chemicals were used as received: H_2SO_4 (special-purity grade, EKROS), Na_2HPO_4 (analytical grade), KH_2PO_4 (analytical grade), MgO (analytical grade), glycolaldehyde (>99%, Aldrich), glyceraldehyde (>99%, Aldrich), acetonitrile (special purity grade, sort 0, Kriokhrom), paraform (high-purity grade), and ethanol (96%).

A formaldehyde solution was prepared by the dissolution of paraform in water in a boiling-water bath. 2,4-Dinitrophenylhydrazine (high-purity grade) was recrystallized from ethanol. Water purified using a Milli-Q system (Millipore, United States) was used in all experiments.

Experimental Procedure

Experiments were carried out in a deaerated glass reactor, whose temperature was maintained with a KRIO-VT-01 thermostat (Russia). The initial concentration of the starting monosaccharide (GA, GCA) was 5×10^{-3} mol/l, and that of formaldehyde was 0.1 mol/l. The pH of the reaction mixture was measured by an Anion-4101 pH-meter/ionometer (Infaspak-Analit, Russia). Samples for analysis were taken from the reactor during the reaction. They were acidified with sulfuric acid and were then analyzed for the formaldehyde and carbohydrate contents.

In the experiments in the presence of MgO, a weighed sample of GA (30 mg) or GCA (45 mg) and the necessary quantity of a concentrated formaldehyde solution were added to a suspension of MgO (108 mg) in water (100 ml). The concentration of MgO was 0.027 mol/l, and the pH of the solution was 10.4. The reactions were carried out at 30, 40, 50, 60, and 70°C (Table 1).

The experiments in the presence of homogeneous phosphates were carried out by dissolving formaldehyde and GA or GCA in a 0.2 M solution (100 ml) of phosphates (Na_2HPO_4 + KH_2PO_4) with pH 7.3. The experiments were carried out at 60, 70, and 80°C (Table 2).

Analytical Methods

Reaction products, GA, and GCA were analyzed by HPLC (after derivatization with 2,4-dinitrophenylhy-

Table 2. Products of the condensation of glycolaldehyde and glyceraldehyde with formaldehyde in a phosphate buffer solution at different temperatures

Entry	Starting monosaccharide	T, °C	Time, h	Lower monosaccharides, mmol/l			Higher monosaccharides, mmol/l						
				GA	GCA	DHA	**I**	**II**	**III**	**IV**	**V**	**VI**	**VII**
18	GA	60	2	3.16	0.59	0.40	0.29	0.03	0.11	0.51	0.05	0.04	0.03
19			3	2.63	0.62	0.73	0.39	0.02	0.11	0.32	0.05	0.03	0.03
20			4	2.02	0.50	0.88	0.61	0.01	0.00	0.50	0.08	0.06	0.10
22		70	0.75	2.76	0.68	0.48	0.28	0.01	0.06	0.24	0.03	0.00	0.00
23			1	2.34	0.64	0.66	0.45	0.02	0.08	0.37	0.05	0.03	0.00
24			1.5	1.62	0.49	0.74	0.79	0.05	0.22	0.42	0.15	0.09	0.20
25		80	0.5	1.67	0.50	0.72	0.66	0.05	0.15	0.56	0.23	0.09	0.05
26			0.75	0.94	0.31	0.70	1.09	0.06	0.19	0.86	0.35	0.12	0.10
27			1	0.60	0.14	0.61	1.25	0.08	0.20	1.01	0.39	0.19	0.17
28	GCA	60	2	0.00	0.72	1.59	0.92	0.04	0.04	0.29	0.08	0.03	0.05
29			3	0.00	0.29	1.55	1.22	0.05	0.15	0.58	0.11	0.07	0.07
30			4	0.00	0.13	1.14	1.33	0.11	0.21	0.83	0.17	0.12	0.12
31		70	0.75	0.00	0.70	1.56	1.48	0.05	0.11	0.48	0.14	0.08	0.07
32			1	0.00	0.35	1.49	1.65	0.08	0.15	0.75	0.19	0.11	0.08
33			1.5	0.00	0.13	1.05	2.04	0.12	0.18	1.20	0.20	0.13	0.10
34		80	0.5	0.00	0.14	1.17	1.79	0.11	0.22	0.91	0.16	0.05	0.08
35			0.75	0.00	0.04	0.64	2.02	0.11	0.09	1.33	0.28	0.28	0.21
36			1	0.00	0.02	0.34	2.07	0.16	0.14	1.69	0.25	0.36	0.28

Note: Reaction conditions: $[GA]_0 = [GCA]_0 = 5$ mmol/l, $[CH_2O]_0 = 0.1$ mol/l, $[Na_2HPO_4 + KH_2PO_4] = 0.2$ mol/l, pH 7.3.

drazine [14, 15]) on a Milichrom A-02 chromatograph (Econova, Russia) equipped with a UV detector and a column 75 mm long and 2 mm in diameter packed with ProntoSIL-120-5-C18 AQ. Chromatographic peaks were identified by comparing the retention times of the analyzed and standard substances. To identify substances whose standards were lacking, we carried out a detailed analytical study according to the procedure described in [6] using semipreparative HPLC, NMR methods, and chromatography coupled with mass spectrometry. The formaldehyde concentration in solutions was determined spectrophotometrically using the chromotropic acid method [16].

RESULTS AND DISCUSSION

Kinetics of Glycoladehyde and Glyceraldehyde Condensation with Formaldehyde in the Presence of MgO

Formaldehyde is known to condense into monosaccharides in aqueous solutions in the presence of magnesium oxide and an initiator [17, 18]. However, in the studies cited above, the reactions were carried out at high temperatures (120°C under a pressure of 2 atm [17] and 75–100°C [18]). In our experiments, 0.1 M solutions of formaldehyde were incubated in the presence of the most active initiators of the formose reaction (GA or GCA) and MgO (~100 g/l) at 70°C and lower temperatures (Table 1). We observed no S-like time dependence of formaldehyde conversion characteristic of autocatalytic and branched chain reactions. Analyses demonstrated that the concentration of the starting lower monosaccharides (GA and GCA) decreased and the higher monosaccharides erythrulose and 3-pentulose appeared in the reaction solutions. In other words, under the chosen conditions, the lower carbohydrates react stoichiometrically with formaldehyde, and the selectivity of this reaction is substantially higher than the selectivity of the synthesis of the monosaccharides from formaldehyde via the formose reaction. In the optimization of reaction conditions for the selective condensation of the lower monosaccha-

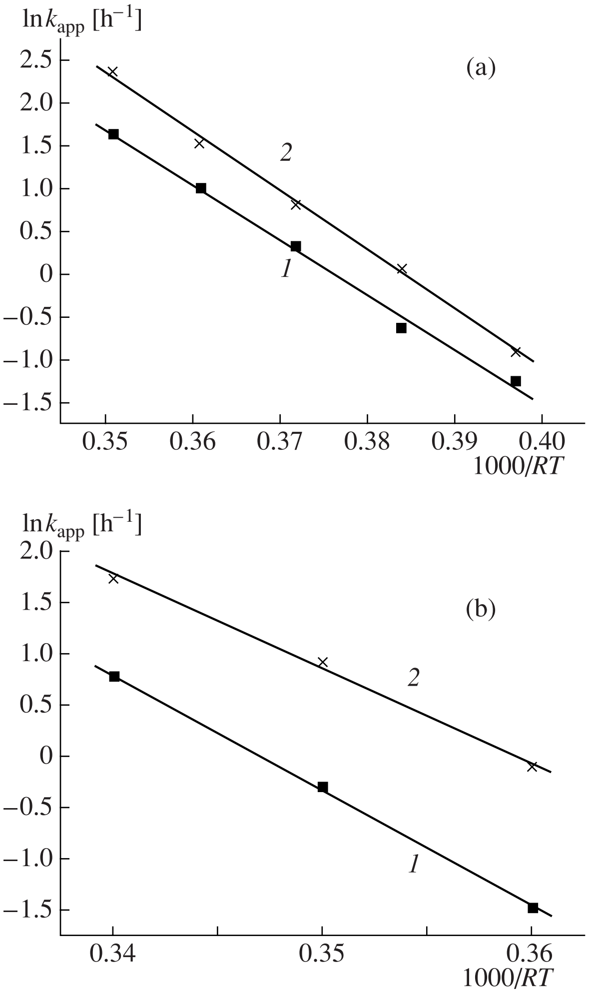


Fig. 1. Arrhenius plots of the apparent rate constants of the condensation of (*1*) GA and (*2*) GCA with formaldehyde in the presence of (a) MgO ($[CH_2O]_0$ = 0.1 mol/l; $[GA]_0$ = 5 mmol/l; $[GCA]_0$ = 5 mmol/l; $[MgO]_0$ = 0.027 mol/l; pH 10.4; T = 30, 40, 50, 60, and 70°C) and (b) the homogeneous phosphates ($[CH_2O]_0$ = 0.1 mol/l; $[GA]_0$ = 5 mmol/l; $[GCA]_0$ = 5 mmol/l; $[Na_2HPO_4 + KH_2PO_4]_0$ = 0.2 mol/l; pH 7.3; T = 60, 70, and 80°C).

rides with formaldehyde, we chose MgO as the catalyst. This compound creates an alkaline medium in the reaction mixture, thus favoring an increase in the rate of the aldol condensation reactions.

For a deeper understanding of lower monosaccharide condensation with formaldehyde in neutral and alkaline media, we studied the kinetics of this reaction in detail. Since the ratio of the initial concentrations of formaldehyde and GA (or GCA) was 20 : 1 in our experiments, the formaldehyde concentration decreased insignificantly during the reactions. The pH value of the reaction mixture was 10.4 and remained constant during the conversion. The time dependence of the concentration of the starting lower monosaccharide is described well by a descending exponential curve; i.e., the apparent order of the rate equations of the processes with respect to this reactant is unity. The Arrhenius plots of the rate constants of lower monosaccharide condensation with formaldehyde are shown in Fig. 1. The numerical values of the apparent rate constants at different temperatures were determined from kinetic curves in semilogarithmic coordinates. Using the temperature dependences of the apparent rate constants (Fig. 1), we calculated the apparent activation energies of the reactions. The rate constants of GA and GCA condensation with formaldehyde (k_{GA}, k_{GCA}) in the presence of MgO are described by the equations

$$k_{GA} = 3.7 \times 10^{10}\exp(-7800/T)\ h^{-1}, \tag{1}$$

$$k_{GCA} = 4.2 \times 10^{11}\exp(-8300/T)\ h^{-1}. \tag{2}$$

The apparent activation energies of reactions (1) and (2) are 64 ± 3 and 69 ± 4 kJ/mol, respectively.

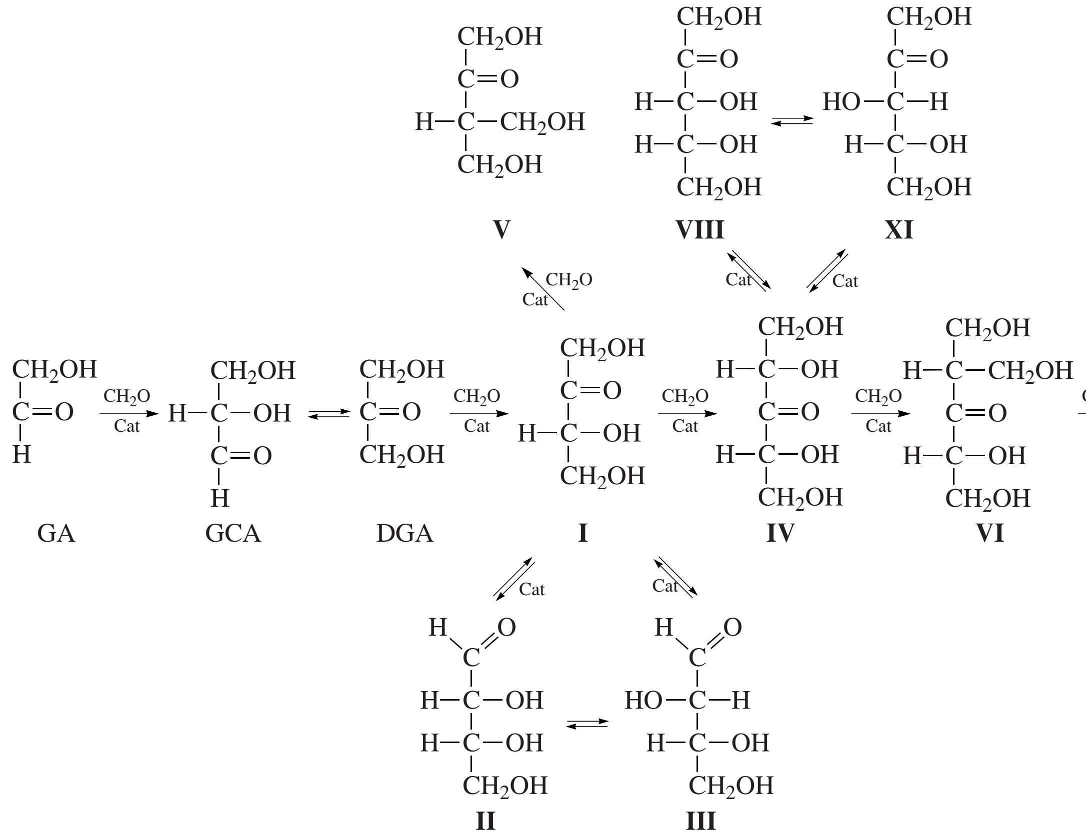
Kinetics of the Condensation of Glycolaldehyde and Glyceraldehyde with Formaldehyde in the Presence of Homogeneous Phosphates

We found earlier that the condensation of the lower monosaccharide dihydroxyacetone with formaldehyde in the presence of homogeneous and heterogeneous phosphates in a neutral medium yields erythrulose and 3-pentulose with a high selectivity [6]. Tests of various phosphate-based catalytic systems show that the best catalyst for the process is the homogeneous phosphate mixture $Na_2HPO_4 + KH_2PO_4$. This mixture maintains pH 7.3 in the reaction medium [6]. For achieving a sufficiently high reaction rate and the highest yield of the desired monosaccharides, the optimum concentration of the homogeneous phosphates is 0.2 mol/l [6].

In this work, we studied the kinetics of the condensation of glycoladehyde and glyceraldehyde with formaldehyde in the presence of the homogeneous phosphates at their total concentration of 0.2 mol/l and pH 7.3. In this case, as in the presence of MgO and as was found earlier [6], the formaldehyde concentration and pH change insignificantly during the reaction and the changes in the GA and GCA concentrations are described by descending exponential curves. The apparent reaction rate constants were determined from the semilogarithmic plots of the concentration of the starting lower monosaccharides versus reaction time. The apparent activation energies of GA and GCA condensation with formaldehyde in the presence of the homogeneous phosphates are 109 ± 8 and 90 ± 4 kJ/mol, respectively, as determined from the Arrhenius plots of the apparent rate constants (Fig. 1b). The apparent rate constants of GA and GCA condensation with formaldehyde in the presence of the homogeneous phosphates are described by the equations

$$k_{GA} = 6.4 \times 10^{16}\exp(-13400/T)\ h^{-1}, \tag{3}$$

$$k_{GCA} = 2.3 \times 10^{14}\exp(-11100/T)\ h^{-1}. \tag{4}$$



I is erythrulose, **II** is erythrose, **III** is threose, **IV** is 3-pentulose, **V** is 3C-hydroxymethylerythrulose,
VI is 2C-hydroxymethyl-3-pentulose, **VII** is 2,4Cdihydroxymethyl-3-pentulose, **VIII** is ribulose, and **IX** is xylulose

Scheme. Condensation of glycolaldehyde and formaldehyde in the presence of basic catalysts.

Products of Glycolaldehyde and Glyceraldehyde Condensation with Formaldehyde and the Reaction Mechanism

The glycoladehyde–formaldehyde condensation scheme derived from product analysis data (Tables 1, 2) is presented below. When GA and formaldehyde are the starting substrates, they condense in the first step to form GCA and then the latter is rearranged into DHA. In the experiments with GCA, DHA forms first in the reaction mixture and then a formaldehyde molecule joins DHA to form erythrulose (**I**). The further growth of the carbon backbone of the monosaccharides is due to the subsequent addition of formaldehyde molecules yielding 3-pentulose (**IV**) and the branched monosaccharides 3C-hydroxymethylerythrulose (**V**), 2C-hydroxymethyl-3-pentulose (**VI**), and 2,4C-dihydroxymethyl-3-pentulose (**VII**). In addition, erythrose (**II**) and threose (**III**) form via erythrulose isomerization already at low conversions of the starting lower monosaccharides. Trace amounts of ribulose (**VIII**) and xylulose (**IX**), which are the products of 3-pentulose isomerization, were found in the reaction mixture at high conversions. In addition, one more peak appears in the chromatograms at high conversions, which has not been identified as yet.

We believe that the reaction between GA and formaldehyde and the further growth of the monosaccharide chain take place via base-catalyzed aldol condensation. It is well known that the first step of this mechanism is deprotonation by the base from the α-carbon atom of the starting monosaccharide, yielding a carbanion [19]. Then formaldehyde joins the deprotonated molecule of the substrate. The rearrangement of GCA into DHA proceeds via the Lobry de Bruyn–Alberda van Ekenstein reaction, which includes the intermediate formation of enediols [20]. This reaction, as well as aldol condensation, is catalyzed by bases, and its first step is the deprotonation of the α-carbon atom of the starting monosaccharide. In the reactions examined here, when the phosphates are present in the neutral medium, the role of the basic catalyst is likely played by the hydrophosphate ion. When MgO is used, both the hydroxide ion, which exists in the solution at pH 10.4, and the hydroxy groups on the oxide surface can serve as the catalyst. Taking into account the above considerations, we suggest the following mechanism of glycoladehyde and glyceraldehyde consumption in the systems examined:

glycolaldehyde:

$$\mathrm{H_2C(OH)CHO + B^-} \xrightleftharpoons[k_{-1}]{k_1} \mathrm{HC^-(OH)CHO + HB}, \qquad \text{(I)}$$

$$\mathrm{HC^-(OH)CHO + H_2CO} \xrightarrow{k_2} \mathrm{H_2C(OH)HC(OH)CHO}; \qquad \text{(II)}$$

glyceraldehyde:

$$\mathrm{H_2C(OH)HC(OH)CHO + B^-} \xrightleftharpoons[k_{-3}]{k_3} \mathrm{H_2C(OH)C^-(OH)CHO + HB}, \qquad \text{(III)}$$

$$\mathrm{H_2C(OH)C^-(OH)CHO} \xrightarrow{k_4} \mathrm{H_2C(OH)C(OH)CHO^-} \xrightarrow{k_5} \mathrm{H_2C(OH)C(O)C^-HOH}. \qquad \text{(IV)}$$

Here, B^- is the basic catalyst and HB is its protonated form. The pH of the solution remains unchanged during the reaction, and the concentration ratio of the basic catalyst to its protonated form (C_{B^-} and C_{HB}, respectively) is primarily determined by the pH value rather than the progress of the processes. Therefore, these concentrations can be included in the rate constants; i.e., $k'_1 = k_1 C_{B^-}$, $k'_3 = k_3 C_{B^-}$, $k'_{-1} = k_{-1} C_{HB}$, and $k'_{-3} = k_{-3} C_{HB}$. Accepting that the concentrations of the $HC^-(OH)CHO$ and $H_2C(OH)C^-(OH)CHO$ active carbanions are quasi-steady-state and taking into account that the formaldehyde (FA) concentration is constant, one can obtain kinetic equations describing the changes in the concentrations of the starting glycolaldehyde and glyceraldehyde during their condensation with formaldehyde:

glycolaldehyde

$$\frac{\mathrm{d}C_{GA}}{\mathrm{d}t} = -\frac{k'_1 k_2 C_{FA}}{k'_{-1} + k_2 C_{FA}} C_{GA}; \qquad (5)$$

glyceraldehyde

$$\frac{\mathrm{d}C_{GCA}}{\mathrm{d}t} = -\frac{k'_3 k_4}{k'_{-3} + k_4} C_{GCA}. \qquad (6)$$

Integrating these equations, we obtain the following exponential time dependences of the glycolaldehyde and glyceraldehyde concentrations:

$$C_{GA} = C^0_{GA} \exp(-k_{\mathrm{app,\,GA}} t),$$

where (7)

$$k_{\mathrm{app,\,GA}} = \frac{k'_1 k_2 C_{FA}}{k'_{-1} + k_2 C_{FA}};$$

$$C_{GA} = C^0_{GCA} \exp(-k_{\mathrm{app,\,GCA}} t),$$

where (8)

$$k_{\mathrm{app,\,GCA}} = \frac{k'_3 k_4}{k'_{-3} + k_4}.$$

The approximations of the quasi-steady-state concentrations of the $HC^-(OH)CHO$ and $H_2C(OH)C^-(OH)CHO$ carbanions imply that the following conditions are satisfied: $[GA] \gg [HC^-(OH)CHO]$ and $[GCA] \gg [H_2C(OH)C^-(OH)CHO]$. These conditions will be satisfied if steps (I) and (III) of the above mechanism are rate determining. Earlier, when studying the reaction of DHA with formaldehyde in the presence of the homogeneous phosphates, we observed a linear dependence between the reaction rate and phosphate concentration [6]. Similar dependences indicating that the catalytic deprotonation of the substrate (steps (I) and (III)) is indeed the rate-determining step should also be expected for the condensation of GA and GCA with formaldehyde. Therefore, the carbanions are consumed mainly in steps (II) and (IV), and the $k_2 C_{FA} \gg k'_{-1}$ and $k_4 \gg k'_{-3}$ equations are valid; i.e., the apparent rate constants are $k_{\mathrm{app,\,GA}} = k'_1$ and $k_{\mathrm{app,\,GCA}} = k'_3$.

Equations (7) and (8) describe the observed exponential character of the kinetic curves. The first-order rate constants referring to the consumption of GA (Eqs. (1) and (3)) and GCA (Eqs. (2) and (4)) are equal to the rate constants of the catalytic deprotonation of GA (k'_1) and GCA (k'_3). Since the compounds considered are chemically very similar, the apparent rate constants are also similar. We will not discuss the difference between the preexponential factors for different catalysts, because these factors include the concentrations of the catalyst and its protonated form, whose determination seems impossible. The fact that the apparent activation energies for GA and GCA condensation in the presence of MgO are lower than those in the presence of the phosphates can be explained as follows. Hydroxide ions (both free and those on the MgO surface) are strong bases, and, therefore, the deprotonation of the α-carbon atom in this occurs more readily than the same process in the reaction catalyzed by the hydrophosphate ion.

Our kinetic studies were aimed, first of all, at finding reaction conditions for the efficient and selective synthesis of erythrulose and 3-pentulose from formaldehyde and glycol- and glyceraldehydes. In the presence of MgO, the reactions occur selectively to yield 3-pentulose only at substrate conversions lower than 40% (Table 1, entry 1). An increase in the conversion is accompanied by a sharp decrease in the selectivity and by the formation of considerable amounts of branched monosaccharides (Table 1, entries 2–17). The carbohydrates undergo partial cleavage to lower monosaccharides at high temperatures (60–70°C) and high conversions in the presence of MgO (Table 1, entries 8, 17).

In the presence of the homogeneous phosphates as the catalyst, the major reaction products are again erythrulose and 3-pentulose even at high temperatures and high substrate conversions and no isomerization of the resulting monosaccharides occurs (Table 2, entries 18–36). Therefore, in order to synthesize valuable monosaccharides (erythrulose and 3-pentulose), it is appropriate to carry out the condensation of the lower monosaccharides GA and GCA with formaldehyde in the presence of a mixture of the homogeneous phosphates ($Na_2HPO_4 + KH_2PO_4$). The optimum synthesis conditions ensuring a high rate and selectivity of the reactions and a fairly high yield of the desired products are as follows: 80°C, reaction time of 45 min, and GA conversion of 80% or GCA conversion of 99% (Table 2, entries 26, 35). Under these conditions, the erythrulose yield is 40% and the 3-pentulose yield is ~35%.

Thus, we have investigated the reaction kinetics and product composition for the condensation of glycolaldehyde and glyceraldehyde with formaldehyde in a weakly alkaline medium in the presence of the heterogeneous catalyst MgO and in a neutral medium in the presence of the homogeneous phosphates ($Na_2HPO_4 + KH_2PO_4$). Under the chosen conditions, the observed reaction order with respect to the starting lower monosaccharides is unity. The temperature dependences of the apparent rate constants of the condensation reactions and the apparent activation energies were determined. In the presence of the homogeneous phosphates, the condensation of the lower monosaccharides with formaldehyde proceeds selectively to yield erythrulose and 3-pentulose. In the presence of MgO, 3-pentulose and erythrulose form selectively only at substrate conversions lower than 40%. Branched monosaccharides become the major products at high conversions. The kinetic scheme suggested for the early reaction steps provides a satisfactory description for experimental data, for the molecular mechanism of the processes, and for the formation of all of the products. The optimum synthesis conditions ensuring a suitable process rate and good erythrulose and 3-pentulose yields (40 and 35%, respectively) are as follows: reaction temperature of 80°C, pH 7.3, and a $KH_2PO_4 + Na_2HPO_4$ mixture at a total concentration of 0.2 mol/l as the catalyst.

The results of this study make it possible to optimize the conditions and duration of the catalytic step for the combined photoinduced synthesis of GA and GCA from formaldehyde followed by their catalytic condensation with formaldehyde. A feasibility analysis of this process will be presented in a forthcoming publication.

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