Reaction Kinetics and Mechanism of the Molybdate-Catalyzed Epimerization of Glucose in Aqueous Solutions Using A Microstructured Reactor

Berta Spasova[a],*, Christof Kuesters[b], Bruno Stengel[b], Juergen J. Brandner[a]

[a] Karlsruhe Institute Of Technology, Institute for Micro Process Engineering, Campus North,
Hermann-Von-Helmholtz-Platz 1, D-76344 Eggenstein-Leopoldshafen, Germany
[b] Cargill R&D Centre Europe, Havenstraat 84, B-1800 Vilvoorde, Belgium

Abstract: In this research work the reaction kinetics of the molybdate-catalyzed epimerization of glucose in aqueous solutions has been mathematical modeled and investigated. Experiments were performed in a microstructured reactor in continuous flow regime. The results show high yield of mannose in the range between 21-27.1%, which exceeds the actual literature data with a ratio 3:1.

The kinetic model is presented here as a four component systems, which describes the reaction mechanism of the molybdate-catalyzed epimerization of glucose in aqueous solutions using a microstructured reactor. Using this four component systems it is entirely possible to explain all the existing pathways of the reaction system. Furthermore, applying this kinetic model all reaction rate constants for every existing component in the examined system can be calculated.

The kinetic data obtained previously, where the reaction was handled as four component systems with individual nine specific rate constants, indicated that the conversion of glucose to fructose or mannose is a reverse reaction, and the epimerization of glucose to mannose is a reaction of first-order. The kinetics of this reaction in microstructured reactors can be helpful for future reactor design and construction (for example scale-up).

Keywords: reaction kinetics, modeling, reaction mechanism, molybdate-catalyzed, epimerization, glucose, mannose, microreactor.

I. INTRODUCTION

In general, modern carbohydrate chemistry explains the carbohydrate transformation by using the Lobry de Bruyn-Alberda van Ekenstein reaction scheme, which has usually been considered to embrace both epimerization of aldoses and ketoses and aldose-ketose isomerization. Actually, Lobry de Bruyn and Alberda van Ekenstein observed all three reactions, thus, an experimental basis for defining the transformation has existed almost the time of its first recognition. The transformation of an aldose may proceed with significant epimerization at C2, considerably more isomerization to the corresponding 2-keto sugar, and slight C3-epimerization of this ketose [1]. It is a classical synthesis method for the production of mannose with bases, usually sodium hydroxide, and can be accomplished from glucose or fructose across an ene-diol transition state [1, 2]. After the reaction, results are mixtures of glucose, fructose and mannose with higher yield of the ketose (fructose) [3]. The catalytic reaction with Ni and Ca ions as active species can be used as alternative process for the epimerization of mono- and oligosaccharides [4-8]. Kusin [9] found that by treating glucose with 1 equivalent of calcium hydroxide in aqueous solution at ambient temperature, mannose was formed, but not fructose. In contrast to this, the treatment with sodium hydroxide under the same conditions gave a high content of fructose and only small amounts of mannose [8].

Bilik [10, 11] epimerized with catalytic amounts of molybdate acid at C2 to a thermodynamic equilibrium mixture of the two epimers. The first example was observed in 1972; the reaction requires 4h at 90 °C [8, 12].

In the work of Hayes et al. [13] it was postulated, that a molybdate complex involving four oxygen atoms acts as intermediate in the Bilik reaction. The molybdate ion is binuclear and much larger than the calcium cation. Most likely, both metal atoms are involved in the formation of a complex. There is no hindrance to complex formation regardless of configuration at C4 [8]. Sodium molybdate (Na_2MoO_4), ammonium heptamolybdate ($(NH_4)_6Mo_7O_{24}$), MoO_3, and further Mo sources were used as precursors for homogeneous catalysts over the years. Generally, a binuclear molybdate species forms a complex with the hydroxyl groups at C1, C2, C3 and C4 carbon atom of the aldose in a first step. After that the C2-C3 bond is simultaneously cleaved with the following formation of new bond between C1-C3 [3]. Extensive studies based on the epimerization of monosaccharides catalyzed by molybdate components in aqueous media can be found in

[10, 12-23].

The Mo(VI)-catalyzed saccharide transformations were also studied by the application of microwave irradiation, to examine the effect of microwave activation on the Bilik reaction in which Mo(VI) complexes play a critical role in isomerization of reducing sugars [24]. The experiments were realized in a domestic microwave oven (0-800 W), where a series of monosaccharides (such as arabinose, ribose, xylose and glucose) were isomerized in aqueous media with catalytic amounts of molybdic acid. The reaction was performed in Pyrex glass vessels and the reaction volume was not more than 1/5th of the vessel, allowing head space for pressure build-up during the microwave treatment. The tube was exposed to irradiation for different time to prevent the decomposition. The microwave irradiation heating produced epialdoses i.e. aldoses at equilibrium after 2-3 min. Fast complex formation, subsequent intramolecular rearrangements and release of the epialdoses from molybdate complexes resulted in good yield. The most studied case, D-Glucose/D-Mannose and D-Mannose/D-Glucose epimerization, was 60 times faster than the conventional approach [14, 15] and the yield slightly improved in favour of D-Mannose (1:2.5 compared to 1:3). The same is valid for the D-Galactose/D-Talose system with reverse epimerization compared to 1:4. However, the true thermodynamic equilibrium was not reached in several cases, because the prolonged microwave irradiation (more than 10 min) led to the decomposition of saccharides. The presented approach by Hricoviniova [24] is applicable to semi-preparative scale.

For example stereospecific intramolecular rearrangement was used for the isomerization of 5-, 6-, and 7-deoxysugars in a microwave field with Mo(VI) as a catalyst to form a highly reactive catalytic active dimolybdate complexes. The microwave-enhanced Mo(VI)-catalyzed transformation of deoxyaldoses occurred with full stereospecificity resulting in the formation of the corresponding epi-deoxyaldoses with very good yields. The transformation gives a thermodynamic equilibrium mixture after five minutes. All the deoxyaldoses examined reacted similarly, producing equilibrium mixtures of two C2-epimers [25]. The results with Mo(VI) catalysis evaluated towards a thermodynamic equilibrium within 3-5 min with microwave irradiation with a power of 600 W. For example 6-deoxy-L-glucose to 6-deoxy-L-mannose achieved a ratio of deoxyaldoses/epi-deoxyaldose of 2.3 to 1 and the yield was 64:29 % after isomerization. Different final concentrations of 2-epimers were obtained under different reaction conditions [25] and this is in agreement with epimerizations of aldoses where final product concentrations also vary [24]. Examination of the data suggested that final concentrations depended upon the stereochemistry of starting compounds, namely cis- or trans-configurations of C3 and C4 carbons. It appears, that the C3 and C4 carbons are an important factor that influences the final equilibria of the products obtained under microwave conditions [25]. The primary reaction produces the 2-epimers. However, in case of longer conventional heating, secondary products are also formed in addition to the 2-epimers [10, 22, 25]. Such a secondary reaction produces a certain amount of 3-epimer of the starting deoxyaldoses, which immediately equilibrates with its 2-epimer [25].

When long reaction times or other forcing conditions are used, secondary products are formed [13]. Bilik proposed that secondary products formed by the simultaneous inversion of trans-hydroxyl groups in pyranosyl sugars caused by the simultaneous exchange of hydrogen atoms at C2 and C3 in an aldopyranose-molybdate complex [26].

The kinetic of the epimerization have been mostly analyzed in terms of first order reactions with respect to the monosaccharide [13, 17, 21, 22]. However, the first order coefficients were found to be dependent on conversion [21]. In the work of Sankovic et al. [27] the kinetic data and the steady-state kinetic and thermodynamic activation constants of heptamolybdate ion-catalyzed glucose/mannose epimerization was interpreted in terms of Michaelis-Menten type kinetics. Moreover, neither the influence of pH nor of catalyst concentration on the rate of the epimerization has been accounted up to date [28]. The epimerization reaction of glucose with heptamolybdate ion catalyzed C2 carbon atom itself was reported by many researchers [29-31]. This reaction obeys Michaelis-Menten, metalloenzyme-like kinetics, and the activation parameters confirm the high-energy process as being rate limiting [32].

In the present paper the molybdate-catalyzed epimerization of glucose in aqueous solutions was studied using continuous flow in a microstructured reactor. It was tried to demonstrate the performance of this reaction in miniaturized equipment to obtain the reaction kinetics and mechanism for the used reaction. The aim of the current work is an extensive investigation of all specific rate constants and explanation of all existing reaction to support future reactor design.

1. Experimental procedure

As already mentioned, the epimerization reaction was investigated using a microstructured reactor [33, 34]. The molybdate-catalyzed reaction of glucose in aqueous solutions with ammonium heptamolybdate tetrahydrate $(NH_4)_6 \cdot Mo_7O_{24} \cdot 4H_2O$ (Merck KGaA) was operated in continuous flow conditions. The experimental setup used in this work is schematic represented in Figure 1. The conversion of glucose by epimerization using the molybdate catalyst $((NH_4)_6 \cdot Mo_7O_{24} \cdot 4H_2O)$ was performed at a reaction temperature of

200 °C without H_2SO_4 with catalyst concentration of 0.05 wt.% using different reaction times in the range of 18 to 180 s. The kinetic data have been investigated for the same range. The product compositions after the catalytic conversion of glucose epimerization reaction were analysed by the application of a HPLC method. More details can be founded in [35].
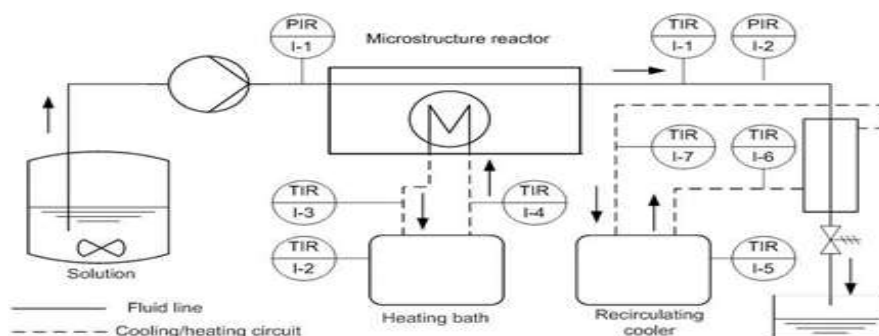

Fig. 1: Schematic sketch of the experimental setup ($T_{Reaction}$ = 200 °C and 0.05 wt.% catalyst).

II.   RESULTS AND DISCUSSION

a.   Kinetic model

Taking the sequence of all composite reactions in the microstructured reactor into account a kinetic model for the epimerization of glucose to mannose using molybdate catalyst was developed. The product composition obtained from HPLC-analysis shows after $T_{Reaction}$ = 200 °C with 0.05 wt.% catalyst (reaction time = 72 s) a main part of unreacted glucose with about 63.6 %, a relatively high yield of mannose of about 27.1 %, some fructose (0.8 %) and a sum of by-products (for example the degree of polymerization (dp1+), allose/tagatose/unknown component (UC) and sum of different unknown component (UC*)) in the range of 8.5 %. No hydroxymethylfurfural (HMF) was formed during the reaction. The ratio between glucose (G) and mannose (M) reaches 2.3, which exceeds the previously known yield with a ratio 63.6:27.1 % found in actual literature data [14]. From this it seems that the operation of the epimerization is running in a regime where the reaction equilibrium is more favourable [36]. The product composition of reaction is summarized in Table 1, here for different reaction times in the range from 18 to 180 s. In this study, the use of a microstructured reactor in continuous flow regime demonstrated that the thermodynamic equilibrium is reached much faster than in other studies. In this case the reaction is shifted to mannose. The conversion of glucose is ultimately higher in the experiments described here in comparison to other literature data [14, 21, 36, 37, 38]. An amount of 25 % of mannose was observed after 0.6 min, whereas an amounts of 27.1 % was found after 1.2 min with a ratio of glucose:mannose of 63.6:27.1 % at thermodynamic equilibrium (see Table 1). The effect of mannose production is higher as in conventional process with a ratio of glucose:mannose of 75:25 % after 180 min (90 °C) [14]. The glucose conversion rate is 36.5 % after 1.2 min, which is higher than with microwave irradiation, where the glucose conversion rate is about 31 %, with a ratio of glucose:mannose of 69:27 % after 3 min [24]. The final equilibrium of products depends on the configuration of C3 and C4 carbons, where after the interconversion between glucose/mannose and mannose/glucose leads to trans-configuration of hydroxyl groups. The reasons for this effect are not fully understood, however according to Hricoviniova [24], it might originate with lower stability of cis-configurated aldoses due to steric effects at C3 and C4 carbons leading to easier decomposition under microwave irradiation. In fact, when attempting to reach the expected equilibria in cis-configurated saccharides using longer irradiation times (15 min), partial decomposition was observed. The effectivity of the method was demonstrated in the semi-preparative scale [24].

Thermal effects resulted from dipolar polarization as a consequence of dipole-dipole interactions between polar molecules and the electromagnetic field [25]. The different concentrations of the product are based on the formation of secondary products in addition to the 2-epimer, so that the secondary product produce a certain amount of 3-epimer in insignificant quantities of up to 3 %, which immediately equilibrates with its 2-epimer. In the case of Mo(VI)-catalyzed isomerizations of 6-deoxy-L-glucose to 6-deoxy-L-mannose under microwave, the amount of secondary products is 7 % in this case with a ratio of deoxyaldoses/epi-deoxyaldose of 2.3:1 [25]. This yield was obtained with a microwave irradiation power of 600 W. However, in the presented work the required energy was significantly lower in the range from 10 to 100 W (Δ T = 180 °C).

The process using microstructure equipment shows a higher productivity than the conventional process techniques, such as reaction vessel [21], use of microwave irradiation [24] or glass reactor [36]. The biggest advantage is that the conventional process can be replaced by a continuous flow process by using microreactors designed with micro channels. Additional advantage of the microstructured reactor is that it increases

significantly the heat transfer and the mass transfer, which can be employed for the conversion of glucose. The amount of converted material is small and ultimately the diffusion path/flux per unit volume or unit area is faster. The short diffusional distance and the time for a reactant molecule to diffuse through the interface to react with other molecule species is reduced in time. Therefore the conversion rate is significantly enhanced and the chemical reaction process appears to be more efficient [38].

Table 1: Product composition determined from HPLC-analysis at $T_{Reaction}$ = 200 °C (without H_2SO_4 and 0.05 wt.% catalyst).

$T_{Reaction}$	Reaction time	Glucose (G)	Mannose (M)	Fructose (F)	dp1+	Allose/Tagatose/UC	Sum UC*	By-products (By-P*)	C-balance	X(Glucose)
[°C]	[s]	[%]	[%]	[%]	[%]	[%]	[%]	[%]	[%]	[%]
	18	75.3	21	0.4	1.5	0.6	1.2	3.3	100	24.7
	24	75.1	21.4	0.3	1.5	0.6	1.1	3.2	100	24.9
200	36	69.3	24.9	0.5	2.5	1.1	1.7	5.3	100	30.7
	72	63.6	27.1	0.8	4.5	1.6	2.4	8.5	100	36.4
	180	50.6	26.3	1.7	12.0	3.4	6.0	21.4	100	49.4
Standard deviation (SD)	-	9.2	2.5	0.5	3.95	1.04	1.82	6.8	0.0	9.2

By-P = dp1+, allose/tagatose/unknown component (UC) and sum of different unknown component (UC)

The reaction system has been illustrated as a four component system which consists of glucose (G), mannose (M), fructose (F) and by-products (By-P), which are the sum of the other products such as: dp1+, allose/tagatose/unknown component (UC) and sum of different unknown component (UC*). The kinetics model is represented schematically in Fig. 2.
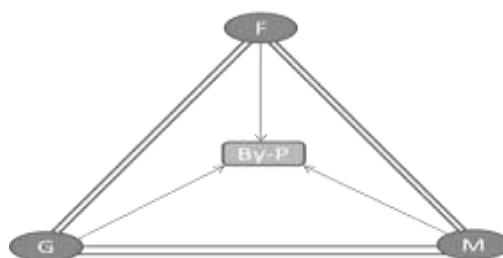

Fig. 2: Schematic representation of the kinetic model for the epimerization of glucose to mannose in a microstructured reactor as a four component systems.

The possible reaction pathways were (glucose to mannose (G→M), mannose to fructose (M→F) and fructose to glucose (F→G) as shown in Figure 2. The individual reaction system is presented as a triangle respectively, so that employs equilibrium for each major product between two components. There is also still a connection between each of the nine specific rate constants for each reaction pathways (k_1 to k_9) according to Figure 3.
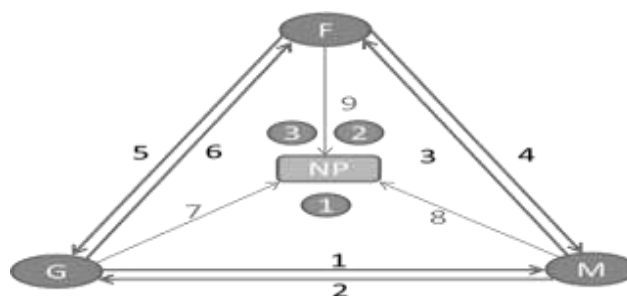

Fig. 3: Modification of the four component systems with representation of three subsystems in combination with nine specific rate constants (k_1 to k_9).

To simplify the kinetic model of the four component system it has been divided into three subsystems (1 to 3). The relationships between the equilibrium constant and the rate constant can easily be determined then. In each case, two status conditions have been created for the complete system. It means that subsystem (1) represents the relationship between three components G-M-By-P with the equilibrium constant (K_{G-M}^{eq}) and the

rate constants k_7 and k_8. The next subsystem (2) illustrates the path way in the system M-F-By-P with the equilibrium constant (K^{eq}_{M-F}) and the rate constants k_9 and k_8 (see Fig. 3). The last subsystem (3) presents the correlation between the three components F-G-By-P correspondent to the equilibrium constant (K^{eq}_{F-G}) and the rate constants k_9 and k_7. In this way all existing connections can be determined and the four component system (G-M-F and By-P) is simplified. Finally, the estimated kinetics data could be validated using the two main requirement conditions, given above. In general, the determined constants can be calculated from the thermodynamic equilibrium. The values of the equilibrium constants for each reaction pathways were calculated from the specific rate constants for the forward and reverse reactions (for example $K^{eq}_{G-M} = \dfrac{k_1}{k_2}$, $K^{eq}_{M-F} = \dfrac{k_3}{k_4}$,

$$K^{eq}_{F-G} = \dfrac{k_5}{k_6} \text{).}$$

Table 2: Summary of specific rate constants for the individual reaction pathways by the epimerization of glucose.

Reaction pathways	Rate constants
1: G → M	$k_1 = k_{G-M}$
2: M → G	$k_2 = k_{M-G}$
3: M → F	$k_3 = k_{M-F}$
4: F → M	$k_4 = k_{F-M}$
5: F → G	$k_5 = k_{F-G}$
6: G → F	$k_6 = k_{G-F}$
7: G → By-P	$k_7 = k_{G-By-P}$
8: M → By-P	$k_8 = k_{M-By-P}$
9: F → By-P	$k_9 = k_{F-By-P}$

b. Thermodynamic equilibrium

To illustrate the kinetic model it was applied for the epimerization of glucose with a reaction temperature of $T_{Reaction} = 200$ °C, with 0.05 wt.% of catalyst and without H_2SO_4 at different reaction times in the range from 18 to 180 s. The results after HPLC-analysis are shown in section 3.1 (Kinetic model). The equilibrium constants (K_i) were calculated for the system glucose-mannose-fructose as a function of reaction temperature in the range $T_{Reaction} = 0$-210 °C (273 K- 483 K). Results are presented in Figure 4. The values of equilibrium constants at the reaction temperature ($T_{Reaction} = 200$ °C) are in this case: (i) $K^{eq}_{G-M} = 0.44$, (ii) $K^{eq}_{M-F} = 3.00$, (iii) $K^{eq}_{F-G} = 0.76$ and (iv) $K^{eq}_{G-F} = 1.32$.

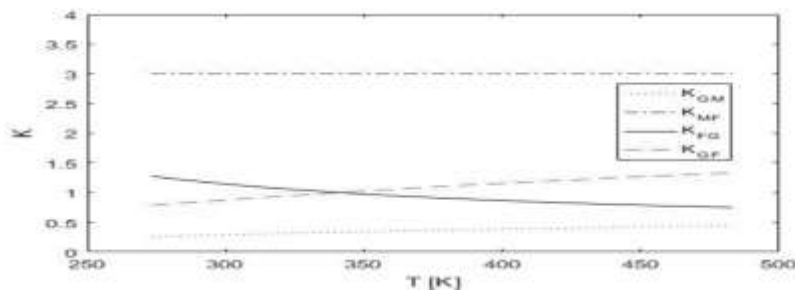**Fig. 4:** Equilibrium constants K for the system glucose-mannose-fructose as a function of the reaction temperature ($T_{Reaction} = 0$-210 °C (273 K- 483 K).

After the precise HPLC analysis the product composition was quantified for each case and for each reaction product relating to the conversion of glucose during the epimerization in a microstructured reactor as function of reaction time. The results show that with the increase in reaction time, the concentration of glucose

decreases. The yield of mannose, fructose and by-products increase at the same time (see Fig. 5). The reaction of the epimerization most likely needs a shorter reaction time in the range from 72 to 180 s. The changes in concentration of glucose, mannose, fructose and by-products are shown in Figure 5. For the investigated reaction conditions sloping curves together with the coefficient of determination have been presented in the diagrams.
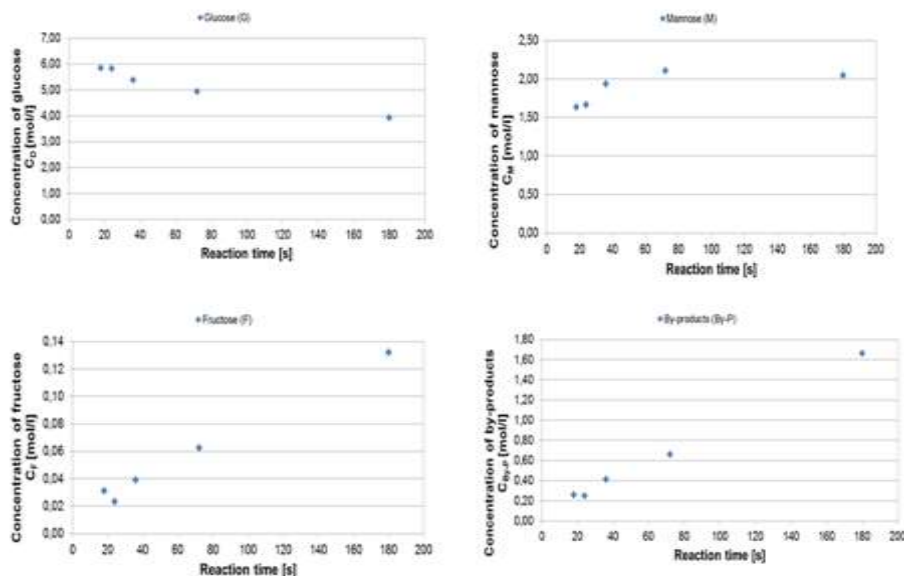

Fig. 5: Concentration changes for each reaction part as a function of reaction time ($T_{Reaction}$ = 200 °C and 0.05 wt.% catalyst).

c. Rate constants of epimerization

For the performed operating conditions of 0.05 wt.% molybdate catalyst at $T_{Reaction}$ = 200 °C without H_2SO_4, the reaction rate so-called "apparent k-values" are implemented as a function of reaction time. This has been done for the formation of a product "p" such as mannose, fructose and by-products. The starting sugar "s" was chosen, or the disappearance of the starting sugar at time "t". The expression for the disappearance of glucose can be defined in [39], which corresponds to equation (1) in the presented form used in this work. This equation was used by the calculation of the expression for the disappearance (such as k_{-G} presented in Table 3). The calculated data for glucose-mannose (k_1), glucose-fructose (k_6) and glucose-by-products (k_7) are presented in Table 4.

$$k = \frac{2.303}{t} \log \frac{100}{s} \text{ or } k = \frac{2.303}{t} \log \frac{100}{100 - p} \tag{1}$$

Table 3: Apparent k-values for the disappearance of glucose, mannose and fructose.

Reaction time [s]	Apparent k-values k_{-G} [s^{-1}]	Expression for the disappearance
18	1.58E-02	$k_{-G} \rightarrow G = M+F+By-P \rightarrow (k_1+k_6+k_7)$
24	1.19E-02	
36	1.02E-02	$k_{-M} \rightarrow M = G+F+By-P \rightarrow (k_2+k_3+k_8)$
72	6.29E-03	
180	3.79E-03	$k_{-F} \rightarrow F = G+M+By-P \rightarrow (k_4+k_5+k_9)$
Standard deviation (SD)	4.12E-03	-

Table 4: Summary of specific rate constants for the epimerization of glucose with 0.05 wt.% molybdate catalyst at $T_{Reaction}$ = 200 °C (without H_2SO_4).

Reaction time [s]	Apparent k-values k_1 [s^{-1}]	Apparent k-values k_2 [s^{-1}]	Apparent k-values k_3 [s^{-1}]	Apparent k-values k_4 [s^{-1}]	Apparent k-values k_5 [s^{-1}]	Apparent k-values k_6 [s^{-1}]	Apparent k-values k_7 [s^{-1}]	Apparent k-values k_8 [s^{-1}]	Apparent k-values k_9 [s^{-1}]
18	1.31E-02	2.99E-02	6.66E-06	2.22E-07	1.70E-04	2.20E-04	1.86E-03	5.60E-01	2.373E-01
24	1.00E-02	2.29E-02	2.87E-06	9.60E-07	1.00E-04	1.30E-04	1.36E-03	5.60E-01	2.379E-01
36	7.96E-03	1.82E-02	2.53E-06	8.40E-07	1.10E-04	1.40E-04	1.51E-03	5.60E-01	2.377E-01
72	4.39E-03	1.00E-02	1.12E-06	3.70E-07	8.00E-05	1.10E-04	1.23E-03	5.61E-01	2.380E-01
180	1.70E-03	3.87E-03	3.70E-07	1.20E-07	7.00E-05	1.00E-04	1.34E-03	5.60E-01	2.379E-01
Standard deviation (SD)	4.03E-03	9.21E-03	2.18E-06	3.36E-7	3.50E-05	4.24E-05	2.19E-04	4.00E-04	2.50E-04

From the thermodynamic equilibrium for the system glucose-mannose (K_{G-M}^{eq}) and for the system fructose-glucose (K_{F-G}^{eq}) two other apparent are k-values k_5 and k_2 are expected (see Table 4). This is to fulfill the condition according to the principle of microscopic reversibility, which is $k_1*k_3*k_5 = k_2*k_4*k_6$ and $K_{G-M}^{eq} * K_{M-F}^{eq} * K_{F-G}^{eq} = 1$ (see section 3.1: Kinetic model). For at equilibrium state the forward and backward reaction rates must be equal and the same set of reactions can be obtained to the backward reaction consistent with the thermodynamic equilibrium, the following expression: $K_{F-M}^{eq} = \dfrac{k_4}{k_3}$ can be explained. This results in the fact that the three subsystems from the modified four component systems can be connected to the other missing apparent k-values, such as k_8, k_9, k_3 and k_4 (see Table 4).

Apparent k-values for the disappearance of glucose (G), mannose (M) and fructose (F) are shown in Table 5. Values for k_{-G}, k_{-M} and k_{-F} were calculated from the expression between the specific rate constants in the reactions of glucose, mannose and fructose, respectively (see Table 5). The particular k-values are in the range $k_{-M} > k_{-F} > k_{-G}$.

Table 5: Summary of the apparent k-values for the disappearance of glucose (G), mannose (M) and fructose (F).

Reaction time [s]	Apparent k-values $k_{-G} = (k_1+k_6+k_7)$ [s^{-1}]	Apparent k-values $k_{-M} = (k_2+k_3+k_8)$ [s^{-1}]	Apparent k-values $k_{-F} = (k_4+k_5+k_9)$ [s^{-1}]
18	1.52E-02	5.90E-01	2.375E-01
24	1.15E-02	5.83E-01	2.379E-01
36	9.61E-03	5.78E-01	2.378E-01
72	5.74E-03	5.71E-01	2.381E-01
180	3.13E-03	5.64E-01	2.379E-01
Standard deviation (SD)	4.25E-03	9.06E-03	1.96E-04

In addition, the rate constants of the separate system of glucose-mannose-fructose were calculated using the relation from Table 5. These calculations show how much shares of each substance react from other material. They were presented as a sum of the relevant rate constants determined by calculation (see Table 5). At the end of the kinetic modeling and calculating all the rate constants of the epimerization of glucose with molybdate-catalyst were inspected with the overall kinetic mechanism by using the two basic requirements given above, the following equations were applied:

condition 1: $\left(\dfrac{k_1}{k_2} * \dfrac{k_3}{k_4} * \dfrac{k_5}{k_6} \right) = 1$ (2)

and

condition 2: $(k_1 * k_3 * k_5) = (k_2 * k_4 * k_6)$ (3)

The results are summarized in Table 6 after verification of the presented kinetic mechanism for the system of glucose-mannose-fructose.

Table 6: Two basic requirements for the verification of the investigated specific rate constants.

Reaction time [s]	Requirement 1 $(k_1/k_2)*(k_3/k_4)*(k_5/k_6) = 1$	Requirement 2 $(k_1*k_3*k_5) = (k_2*k_4*k_6)$ Forward reaction $(k_1*k_3*k_5)$	Backward reaction $(k_2*k_4*k_6)$
18	1.00E+00	1.48E-11	1.48E-11
24	1.00E+00	2.74E-12	2.74E-12
36	1.00E+00	2.13E-12	2.13E-12
72	1.00E+00	4.17E-13	4.17E-13
180	1.00E+00	4.53E-14	4.53E-14
Standard deviation (SD)	0.00E+00	5.48E-12	5.48E-12

d. Initial- and reactions rate of epimerization

The initial reaction rate of epimerization was obtained from the conversion (X) and the initial concentration of glucose ($C_{0,G}$). The reaction rate was calculated by the equation (4).

$$r_0 = \frac{X(Glu\cos e)}{t} * (C_{0,G}), where \ X(Glu\cos e)[\%]/100, \ C_{0,G} = 7.771[mol/l] \tag{4}$$

As basis for the calculation of the reaction rate for each of the sugars glucose (G), mannose (M), fructose (F) and for the by-products (By-P), expressed by the pseudo-first-order rate reactions for the kinetic model (see Fig. 2), the following equations were applied:

$$r_1 = \frac{d[G]}{dt} = -(k_1 + k_6 + k_7)*[G] + k_2*[M] + k_5*[F] \tag{5}$$

$$r_2 = \frac{d[M]}{dt} = k_1*[G] - (k_2 + k_3 + k_8)*[M] + k_4*[F] \tag{6}$$

$$r_3 = \frac{d[F]}{dt} = k_6*[G] + k_3*[M] - (k_4 + k_5 + k_9)*[F] \tag{7}$$

$$r_4 = \frac{d[By-P]}{dt} = k_7*[G] + k_8*[M] + k_9*[F] \tag{8}$$

The values of the initial rate of epimerization and the rates for each of the sugars glucose, mannose and fructose were determined. The results are summarized in Table 7.

Table 7: Initial- and reactions rate of epimerization.

Reaction time [s]	Initial rate of epimerization r_0 [mol/l*s]	r_1 [mol/l*s]	r_2 [mol/l*s]	r_3 [mol/l*s]	r_4 [mol/l*s]
18	1.07E-01	-4.01E-02	-8.86E-01	-6.05E-03	9.32E-01
24	8.06E-02	-2.91E-02	-9.12E-01	-4.74E-03	9.45E-01
36	6.63E-02	-1.66E-02	-1.08E+00	-8.52E-03	1.10E+00
72	3.93E-02	-7.24E-03	-1.18E+00	-1.42E-02	1.20E+00
180	2.13E-02	-4.38E-03	-1.15E+00	-3.10E-02	1.18E+00
Standard deviation (SD)	3.02E-02	1.34E-02	1.21E-01	9.61E-03	1.14E-01

III.   CONCLUSIONS

The reaction kinetics of the molybdate-catalyzed epimerization of glucose in aqueous solutions by application of a microstructured reactor can be described using a four component system with nine specific rate

constants. The used kinetic mechanism indicated that the conversion of glucose to mannose or fructose is a reverse reaction and the epimerization of glucose to mannose is a reaction first-order.

The complete reaction system has been successfully developed and decrypted with all pathways. Finally all the rate constants, thermodynamic equilibrium and reaction rates were calculated accordingly for each substance. The kinetics of the reaction in a microstructured reactor can be helpful for a future reactor design and construction (for example scale-up).

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