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Isomerization of Glucose into Fructose and Mannose in Presence of Anion-Exchanged Resins

LINGJUAN LV[1,2], XIANGHAI GUO[1,2], PENG BAI[1,2,*] and SHUO ZHAO[1,2]

[1]School of Chemical Engineering and Technology, Tianjin University, Tianjin, P.R. China
[2]Key Laboratory of System Bioengineering, Ministry of Education, Tianjin University, Tianjin, P.R. China

*Corresponding author: Tel: +86 22 27406186; E-mail: chemeng114_tju@163.com

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Much attention has been paid to the conversion of bio-regenerable glucose into valuable chemicals and liquid fuels, like fructose, 5-hydroxymethyl furfural (5-HMF), mannose and levulinic acid. The isomerization of glucose into fructose and mannose simultaneously was studied in the presence of commercial anion-exchanged resins. An OA16 (4^5) orthogonal experiment was designed investigating the following four variables *i.e.*, resin types (factor A), reaction temperature (factor B), pH value (factor C) and D-glucose to resin ratio (factor D). Reaction temperature was identified as a prominent factor of this transformation. Ideal conversions and selectivities were obtained even in the case of high glucose concentration. In contrast to other catalysts reported like Tin-beta, anion-exchanged resins highlight by reasonable catalytic activity and selectivity under mild conditions, easy regeneration and separation and low cost. Further efforts were worthwhile in this area.

Keywords: Glucose, Isomerization, Anion-exchanged resins.

INTRODUCTION

Due to the dwindling of fossil energy, much attention has been paid on the conversion of renewable biomass into valuable chemicals and liquid fuels. It is of international concerns to find novel regenerated energy and reduce the dependence on fossil fuels[1,2].

Among the renewable biomass, 75 % of them are carbohydrates[3]. Glucose may be the most abundant monosaccharide, which can easily be produced from the hydrolysis of cellulose[4,5], a renewable material from biomass. Isomerization of glucose is crucial for producing rare monosaccharide[6], for example, high-fructose corn syrup, fructose and mannose. Mannose is the only sugar used for nutrients in clinic currently, which is widely distributed in body fluids and tissues, especially in the nerves, skin, retina, liver and gut. Mannose can be used as food additive[7]. It can be synthesized into glycoprotein directly, participating in immune regulation[8-10]. Fructose is generally chosen as sweetening agent, which is better and 30 % sweeter than glucose in taste[11]. Still, fructose can be converted to 5-hydroxymethyl furfural (5-HMF), an important platform material to the production of high value polymers. Conversion of fructose to 5-hydroxymethyl furfural have received considerable efforts and can be realized at high yields[12-14]. Catalytic system that converts glucose to fructose in water has been studied for hundreds of years though, an efficient, environmental friendly, energy saving system remains to be discovered.

According to the researches during the past several decades, mannose are generally obtained from the hydrolysis of mannan[15,16] or epimerization of glucose and fructose[17,18], while fructose can be obtained from the isomerization of glucose over various catalysts, such as enzymes[19], borate ion[20,21], zeolites[22] and basic resins[23-25]. As traditional conversion system, enzyme catalysis pathway possess apparent advantages of high efficiency and satisfying selectivity. Nevertheless, its large scale application is limited by tendency of being poisoned by certain metal ions, harsh reaction conditions, upper limit of 42 % conversion ratio and exorbitant costs[26,27]. Various catalysts emerged in this area, but with regard to the purpose of conversion ratio and selectivity, they seldom make both ends satisfying. Lecomte *et al.*[28] isomerized glucose into fructose in the presence of anion-modified hydrotalcite. They achieved selectivity more than 90 % on the condition of unsatisfying glucose conversion (15 %). Manuel *et.al* reported that Tin-beta zeolite was able to isomerize glucose into fructose, 10 % glucose solution produced yields of 46 % glucose, 31 % fructose and 9 % mannose[11].

It was reported years ago that resin-catalyst could be used in the catalytic isomerization of glucose[23-25], generating fructose and mannose. Resin, as catalyst, had the advantages of stable, unfeasible to deactivation, renewable and easier separation with the reaction solution. However, due to various reasons, large-scale use of resin for preparation of rare monosaccharides was still impossible. This paper chose four resins to heterogeneously catalyze glucose into fructose and mannose and compare their conversion rate, selectivity and yield. Orthogonal experiments also took into consideration the operating temperature, pH value and D-glucose to resin ratio. This work may lay foundation for the large-scale application of resin-catalysts.

EXPERIMENTAL

D-glucose (99 %), D-fructose (99 %), D-mannose (98 %) were obtained from Sangon Biotech Co, Ltd (Shanghai, China); Anion-exchanged resins used in this assay (201 × 7, D261, D290 and D296R) were purchased from Tianjin Nankai HECHENG Technology Co, Ltd (Tianjin, China). These resins are strongly basic anion exchanger resins and have similar physical and chemical properties, but differ in pore size. They are pretreated with 4 % HCl and 2 % NaOH successively for three circles and finally washed by distilled water to pH of the water.

Different countries and companies do give resins diverse names, Table-1 shows the properties of the resins and the corresponding product names and types mainly used abroad.

Table-1 suggested that the four resins have similar physical and chemical properties, especially maximum operating temperature and pH range. OA_{16} (4^5 matrix) orthogonal experiments (Table-2) were carried out in consideration with resin types (201 × 7, D261, D290 and D296 R), reaction temperature (303, 313, 323 and 333 K), pH (6, 8, 10 and 12) and D-glucose to resin ratio (1:1, 1:2, 1:5 and 1:10 g/mL).

Each experiment was performed three times in parallel in shaking bath for 12 h, the feedstock were 10 mL resin and 50 mL D-glucose aqueous solution of certain concentration. With regard to the ratio of sugar to resin (g/mL), the sediment volume of wet resin was 10 mL, the concentration of D-glucose vary from 4-20 % (w/w). For example, the sugar to resin ratio 1:5 means 50 mL 4 % D-glucose reacted with 10 mL anion-exchanged resin.

Analysis: The results of orthogonal experiment were detected by high performance liquid chromatography (HPLC), using Agilent (USA) 1260 infinity HPLC with G1311X pump, G1362A RID detector, autosampler and a Bio-Rad (USA) HPX-87C (Ca^{2+}) aminex resin-based column (300 × 7.8 mm) fixed in Agilent automatically controlled HPLC thermostat. The pump, autosampler, RID detector and thermostat were controlled by a PC with software (Open LAB Control Panel). The mobile phase was degassed deionized water at a flow rate of 0.6 mL/min. The column was thermostated at 353 K in the course of measurements and the amount of sample was 10 μL. Under the operating parameters mentioned above, the retention times were as follows: D-glucose-10.1 min, D-mannose-11.7 min, D-fructose-13.3 min. The concentration of each monosaccharide was analyzed by external standard method in view of peak area.

The conversion ratio (α) of D-glucose is the ratio of the amount of D-glucose consumed to the amount of D-glucose added. The selectivity (S) in fructose or mannose was defined as the ratio of D-fructose or D-mannose formed to D-glucose consumed, taking into account the initial adsorption of D-glucose on the catalyst. Product yield (Y) means the sum of D-mannose and D-fructose formed.

$$\alpha = \frac{m_{\text{D-glucose consumed}}}{m_{\text{D-glucose added to the system}}} \times 100\ \%$$

$$S_1 = \frac{m_{\text{D-mannose formed}}}{m_{\text{D-glucose consumed}}} \times 100\ \%$$

$$S_2 = \frac{m_{\text{D-fructose formed}}}{m_{\text{D-glucose consumed}}} \times 100\ \%$$

$$S = S_1 + S_2$$

$$Y = \alpha(S_1 + S_2) \times 100\ \%$$

RESULTS AND DISCUSSION

Typical HPLC chromatogram: Under the operating parameters mentioned above, the retention times were as follows: D-glucose-10.1 min, D-mannose-11.7 min, D-fructose-13.3 min. Fig. 1 was a sample of HPLC chromatogram.

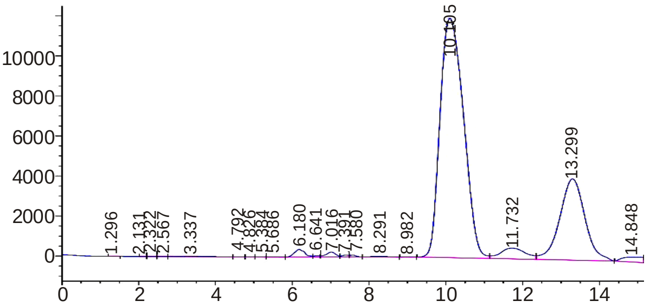

Fig. 1. A sample of HPLC chromatogram for isomerized D-glucose solution

Results of OA_{16} matrix: Four kinds of anion exchanged resins: 201 × 7, D261, D290 and D296R, were chosen to catalyze the reaction. The results of the orthogonal experiments are given in Table-2, including the conversion ratio of D-glucose,

TABLE-1
PROPERTIES OF RESINS USED AND THEIR ANALOGUES

Resins	Functional group	Total exchange capacity (mmol/mL)	Pearl size (0.3-1.25 mm) (%)	Maximum operating temperature (K)	pH Range	Analogues
201 × 7	$-N^+(CH_3)_3$	≥ 1.4	≥ 95	333 (OH type) 348 (Cl type)	1-14	Amberlite IRA-400, AB-17, Diaion SA-10A
D261		≥ 1.1				Amberlite IRA-900, Duolite A-161
D290		≥ 1.0				Amberlite IRA-900, Duolite A-161
D296R		≥ 1.0				Amberlite IRA-400

the selectivity for D-mannose and D-fructose and their practical yield. The extra column remaining in the column assignment is experimental error, which can be used to indicate the reliability of the whole experiments.

It wasn't difficult to discover that the best results for α, S_1, S_2, S and Y were attained in the trial No. 4, 11, 14, 16, 7, respectively. Data analysis of various goals (Tables 3 and 4) was carried out through the range analysis (R_{JI}) and analysis of variance (ANOVA) to reflect the optimal reaction conditions and their magnitudes. The effects of different resins and operating conditions on response value were obtained after the orthogonal experiments and subsequent data analysis. The results are shown in Fig. 2, the vertical coordinate value of each figure were obtained from $\overline{K_{JI}}$. ANOVA, R_{JI} and $\overline{K_{JI}}$ were computed in the same way as reported by Wu *et al.*[29]. It should be noted that J represents factor A, B, C and D, I means level 1, 2, 3 and 4).

It can be seen from Table-3 that the order of significant factors for conversion ratio of D-glucose is B > D > C > A, for the selectivity in D-mannose B > C > A > D, for the selectivity in D-fructose A > C > D > B, for total selectivity A > C > B > D and for the product yield B > A > D > C. To sum up, reaction temperature and the type of resin used in the reaction effect the response value most. Generally speaking, D261, D290 and D296R were better than 201 × 7. The results of operating temperature 313 K, 323 K surpassed that of 303 and 333 K.

TABLE-2
RESULTS OF THE ORTHOGONAL EXPERIMENTS

Trial no.	Factors				Results				
	Resin types	Reaction temperature (K)	pH value	D-glucose to resin ratio (g/mL)	α	S_1	S_2	S	Y
1	201 × 7	303	6	1:1	10.6	5.8	40.2	46.1	4.9
2	201 × 7	313	8	1:2	32.7	12.2	55.4	67.7	22.2
3	201 × 7	323	10	1:5	60.5	13.1	38.7	51.8	31.3
4	201 × 7	333	12	1:10	73.0	11.3	26.0	37.2	27.2
5	D261	303	8	1:5	25.0	8.3	53.4	61.7	15.4
6	D261	313	6	1:10	40.0	12.1	50.1	62.2	24.9
7	D261	323	12	1:1	52.6	13.4	50.5	63.9	33.6
8	D261	333	10	1:2	51.3	10.4	48.9	59.3	30.4
9	D290	303	10	1:10	48.6	6.6	40.0	46.5	22.6
10	D290	313	12	1:5	56.6	11.3	42.7	54.0	30.6
11	D290	323	6	1:2	42.7	13.8	59.7	73.5	31.4
12	D290	333	8	1:1	43.7	11.8	57.6	69.5	30.4
13	D296R	303	12	1:2	23.3	5.4	47.6	53.0	12.4
14	D296R	313	10	1:1	29.3	8.6	63.5	72.1	21.1
15	D296R	323	8	1:10	51.7	12.8	52.9	65.7	34.0
16	D296R	333	6	1:5	37.7	11.6	63.4	75.1	28.3

TABLE-3
RANGE ANALYSIS (R_{JI})

Response	Item	A	B	C	D	Response	Item	A	B	C	D
α	$\overline{K_{j1}}$	44.2	26.9	32.8	34.1	S_1	$\overline{K_{j1}}$	10.6	6.5	10.8	9.9
	$\overline{K_{j2}}$	42.2	39.7	38.3	37.5		$\overline{K_{j2}}$	11.1	11.1	11.3	10.5
	$\overline{K_{j3}}$	47.9	51.9	47.4	45.0		$\overline{K_{j3}}$	10.9	13.3	9.7	11.1
	$\overline{K_{j4}}$	35.5	51.4	51.4	53.3		$\overline{K_{j4}}$	9.6	11.3	10.4	10.7
	R_1	12.4	25	18.6	19.2		R_2	1.5	6.8	1.6	1.2
S_2	$\overline{K_{j1}}$	40.1	45.3	53.4	53.0	S	$\overline{K_{j1}}$	50.7	51.8	64.2	62.9
	$\overline{K_{j2}}$	50.7	52.9	54.8	52.9		$\overline{K_{j2}}$	61.8	64	66.1	63.4
	$\overline{K_{j3}}$	50	50.5	47.8	49.6		$\overline{K_{j3}}$	60.9	63.7	57.4	60.7
	$\overline{K_{j4}}$	56.9	49.0	41.7	42.3		$\overline{K_{j4}}$	66.5	60.3	52.0	52.9
	R_3	16.8	7.6	13.1	10.7		R_4	15.8	12.2	14.1	10.5
Y	$\overline{K_{j1}}$	21.4	13.8	22.4	22.5						
	$\overline{K_{j2}}$	26.1	24.7	25.5	24.1						
	$\overline{K_{j3}}$	28.7	32.6	26.4	26.4						
	$\overline{K_{j4}}$	23.9	29.1	25.9	27.2						
	R_5	7.3	18.7	4.0	4.7						

Since factor A, B, C, D and experimental error had 4 levels, their degree of freedom (df) were 3. As for F-test ($\alpha = 0.05$), the critical value can be obtained from the distraction table of F-value: $F_{0.05}(3,3) = 9.28$. Aiming at α (conversion ratio), it is clear that all the four factors affect α significantly. With regard to S_2 and S, none of these factors showed markedly effects on them. It can be seen from Table-4 that F ratio of factor B (operating temperature) is higher than the critical F-value in three cases of five, indicating that operating temperature is the prominent factors affecting the results.

The trends of α, S_1, S_2, S, Y developed with different levels of each factor, shown in Fig. 2a-d, were given by mean value ($\overline{K_{JI}}$) of each level as horizontal axis, the results as vertical axis. These figures were used to exhibit the trends of each factor, not for forecasting the values of non-performed experiments. It can be observed in Fig. 2a that 201 × 7 as catalyst was a little inferior for almost all the responses, while both D261 and D290 contributed to better α, S and Y. On contrast to the resins mentioned above, D296R results to the highest selectivity for D-fructose (56.9 %) and mean selectivity for D-mannose, but it brought about the worst conversion ratio (α) (35.5 %). Hence, D261 and D290 were ideal candidates for catalyzing D-glucose to rare monosaccharaides. As reaction temperature getting higher, the responses in Fig. 2b increased steadily to a maximum and then decreased a bit. S_2 and S reached to the maximum of 52.9 and 64 %, respectively at 313 K, while the best results for α, S_1 and Y were reached at 323 K, the values being 51.9, 13.3 and 32.6 %. Considering α and Y as the prominent responses, the optimal operating temperature should be 323 K. As mentioned in Table-1, the maximum reaction temperature of the resins was 333 K, results in Fig. 1b indicated that increasing temperature promoted isomerization of glucose, but temperature as high as 333 K might hinder the reaction or aggravate side-reaction. In addition, the colour of sugar solution and resin became brown during the experiments, which is more evident when pH value is alkaline, HPLC results of corresponding samples revealed more side-products, indicating augment of side-reaction. The pH value seems to have tremendous impact (Fig. 2c) on conversion

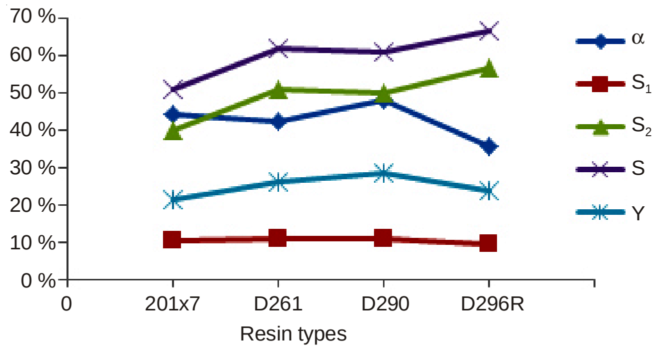

Fig. 2a. Effect of different resins on results

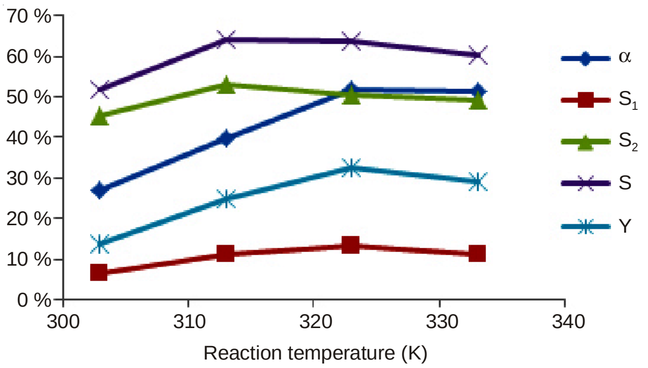

Fig. 2b. Effect of reaction temperature on results

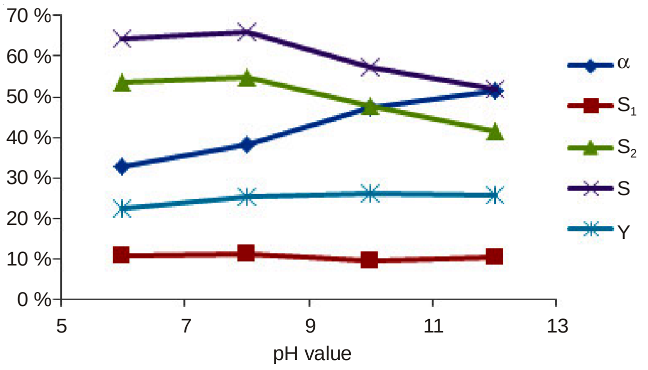

Fig. 2c. Effect of pH value on results

TABLE-4
ANALYSIS OF VARIANCE (ANOVA) IN OA_{16} MATRIX

Response	Factors	SS	df	V	F	$F_{0.05}$ (3, 3)	Significance	Response	Factors	SS	df	V	F	$F_{0.05}$ (3, 3)	Significance
α	A	324.5	3	108.2	148.7	9.28	*	S_1	A	5.0	3	1.7	3.2	9.28	
	B	1679.2	3	559.7	769.6	9.28	*		B	97.6	3	32.5	62.7	9.28	*
	C	863.7	3	287.9	395.8	9.28	*		C	5.6	3	1.9	3.6	9.28	
	D	878.3	3	292.8	402.5	9.28	*		D	2.9	3	1.0	1.9	9.28	
	Error	2.18	3	0.7					Error	1.56	3	0.5			
S_2	A	578.3	3	192.8	6.8	9.28		S	A	529.3	3	176.4	4.9	9.28	
	B	122.1	3	40.7	1.4	9.28			B	387.1	3	129	3.6	9.28	
	C	427.9	3	142.6	5.0	9.28			C	503.6	3	167.9	4.7	9.28	
	D	304.0	3	101.3	3.6	9.28			D	282.5	3	94.2	2.6	9.28	
	Error	85.3	3	28.4					Error	107.2	3	35.7			
Y	A	117.0	3	39	6.7	9.28									
	B	795.2	3	265.1	45.7	9.28	*								
	C	39.6	3	13.2	2.3	9.28									
	D	55.5	3	18.5	3.2	9.28									
	Error	17.4	3	5.8											

SS: Sum of square deviation; df: Degree of freedom; V: Variance; F: the F ratio

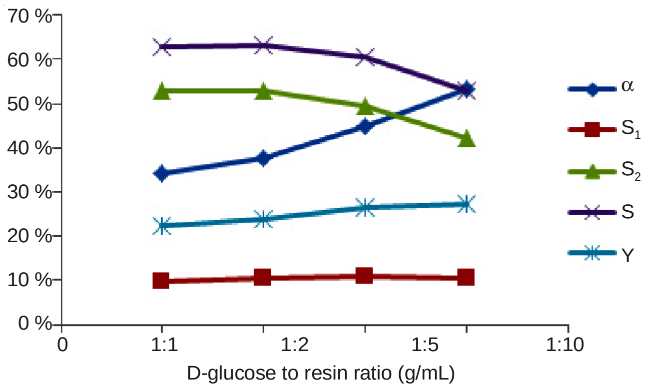

Fig. 2d. Effect of D-glucose to resin ratio on results

ratio (α), with a change from 32.8 to 51.4 % when pH increased from 6 to 12. However, selectivity for D-fructose and D-mannose decreased from 64.2 to 52 % and yield exhibited no significant changes. The phenomenon mentioned above may be interpreted as excess hydrolyzation of D-glucose but less isomerization. Considering α and Y, the appropriate pH value should be 8. On the other hand, ratio of sugar to resin clearly influenced the isomerization reaction (Fig. 2d): lower D-glucose concentration bought about better α, decreasing S and slightly increasing Y. High efficiency production can be achieved at the ratio of 1:1. It can be observed from Fig. 2(a-d) that selectivity for D-mannose (S_1) were all around 10 %, hence S had similar trends with S_2, since S was the sum of S_1 and S_2.

Conclusion

This work chose four kinds of anion-exchanged resin and compared their influence on the isomerization of D-glucose through OA_{16} matrix orthogonal experiments and statistical analysis. The reaction temperature, pH value of D-glucose solution and ratio of sugar to resin were also considered in the OA_{16} matrix, a blank column was added to the matrix as experimental error. According to the range analysis, the type of resin and operating temperature were significant factors for the responses since they were always at the front of the ranking. $\overline{K_{JI}}$ (J represents factor A, B, C and D; I means level 1, 2, 3 and 4) was the mean value of each level in the four factor. Analysis of $\overline{K_{JI}}$ showed that the maximum level for A, B, C and D were D290 anion resin, temperature of 323 K, pH 8 and sugar to resin ratio of 1:1. Analysis of variance (ANOVA) once again manifested operating temperature as the most important factor affecting the results.

Though resin has advantages mentioned above and possesses favorable conversion ratio and selectivity, its yield could be further improved. A lot of work still needs to be done in this area. There is a long way to go for the large-scale application of resin catalysts.

There exist many opportunities and challenges and some of them are as follows:

- Optimizing the catalysis condition of existing routes may bring better results. More importantly, special attention should be paid to developing new routes or even seeking for novel strategies to produce new potential products.
- Modify the structure of the resins or synthesize new resins are areas worth working on, striving to enhance the conversion and selectivity. For example, sodium borate can catalyze glucose into fructose and mannose[21], but when dissolving in water, sodium borate is difficult to separate from solution, if we can load it on the resin, there is huge possibility to form new effective resin.
- Since D-glucose, D-fructose and D-mannose can transform to each other in aqueous solutions, separation of these monosaccharides is thus of great importance. Simulated moving bed technology has been successfully used to separate D-glucose and D-fructose. We can improve the operation condition or integrate more than one set of equipment, realizing separation of three substances through one route.

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