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Condition screening and process investigation of aldose transformation in borate-containing acidic phosphate buffer system under microwave irradiation†

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The highly selective isomerization and dehydration of various carbohydrates (glucose, xylose, cellobiose and cellulose) are one-pot conversions conducted in a simple borate-containing phosphate buffer solution (PBS) under microwave irradiation. It is demonstrated that the key to glucose converting into 5-hydromethylfurfural (5-HMF) with a high selectivity is matching the isomerization and dehydration processes of glucose at the appropriate boron/glucose mole ratio (B/G) and pH of PBS with the aid of microwave irradiation. Moreover, the interaction between borate and glucose in the isomerization process has been demonstrated by both Raman spectra and theoretical calculations. Furthermore, the reusability of such a PBS system with borate has been accomplished by the successive addition of glucose and by the continual removal of 5-HMF in a biphasic system. These results not only deepen the understanding of the isomerization and dehydration behavior of glucose, but also provide the possibility for practical applications, owing to the appealing green, inexpensive and sustainable characteristics of such a catalytic system.

1. Introduction

Interest in searching for green, renewable and sustainable resources of energy and chemicals has increased significantly in recent years, due to limited fossil resources, exhausted gas emissions and growing energy demands.[1] Biomass resources containing rich carbohydrates are one of the most promising alternative carbon sources for the construction of chemicals and materials for human survival in the future. More importantly, biomass is well-sourced, environmental friendly and low cost.[2] Therefore, study on the comprehensive utilization of biomass resources is attracting ever more attention. Among the possibilities, 5-hydromethylfurfural (5-HMF), firstly reported at the end of 19th century by heating inulin with oxalic acid solution,[3] is one of the most significant biomass-derived platform compounds. As an important intermediate, 5-HMF can be converted into various useful compounds, such as dimethylfuran, furandicarboxylic acid, levulinic acid (LA), and γ-valerolactone.[4–6] Consequently, 5-HMF provides the possibility to synthesize chemicals and biofuels from carbohydrates, and so alleviates the demand pressure of fossil resources.

Generally, 5-HMF is mainly obtained from the dehydration of hexoses, such as fructose and glucose, or disaccharides, like sucrose and cellobiose.[6,7] To date, most preparations of 5-HMF have been derived from fructose as the raw material, due to its higher selectivity and yield of 5-HMF compared to other hexoses. However, the relatively high cost of fructose greatly restricts its prospect in industrial applications. Unlike fructose, glucose has more sources in the natural world, since it can be obtained from the hydrolysis of cellulose.[8] However, unfortunately, glucose suffers from a poor dehydration performance in the preparation of 5-HMF, due to its much more stable aldose structure than fructose.[9] Nevertheless, its much lower cost indicates that the direct conversion of glucose into 5-HMF is still the focus of scientific attention. In addition to glucose, cellobiose and cellulose are the two most desired raw materials to be converted directly into 5-HMF, also due to their much lower cost and higher availability compared with the other carbohydrates in nature.[10] However, in fact, the conversion of cellulose is much more difficult than glucose and disaccharides, because its special β-1,4-glycosidic bonds lead to poor solubility and difficult conversion in aqueous solution.[6] Thus, some extreme strategies,

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† Electronic supplementary information (ESI) available: The data of the conversion of glucose into 5-HMF in the PBS system without borate addition, the conversions of glucose in the pure water under microwave irradiation and conventional heating, the influence of B/F ratio on the conversion of fructose into 5-HMF, and two kinds of Gibbs free-energy profiles and structures of the intermediates and transition states of the isomerization of glucose to fructose. See DOI: 10.1039/c4ra02612h

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such as high acid concentration and reaction temperature or expensive ionic liquids, have to be used to swell and convert cellulose.[11] Therefore, the one-pot conversion of cellulose into 5-HMF is an encouraging route but is still far from practical.

In addition, it is worth mentioning that the main reason for the unsatisfying results of aldose conversion into 5-HMF, based on plenty of research results, is believed to be because a pretreatment process is needed before the dehydration. Taking glucose as an example, it has to first isomerize into fructose, which then dehydrates into 5-HMF.[7] During the whole reaction, the conversion rate of glucose mainly depends on its isomerization rate.[8,12,13] Moreover, the formation of 5-HMF in aqueous solution is largely affected by some undesirable by-products obtained from the rehydration of 5-HMF, such as LA and formic acid (FA), as well as the insoluble/soluble polymeric compounds, such as humins. To date, the conversion of glucose into 5-HMF has not been achieved in a large-scale industrial production yet, due to its low conversion rate and 5-HMF selectivity, which is believed to be the greatest challenge remaining.

Recently, an acidic phosphate buffer solution (PBS) using sodium borate as a promoter was developed to highly selectively catalyze glucose dehydration into 5-HMF under microwave irradiation by our group.[14] Herein, the evolution process of the glucose conversion is highlighted in borate-assistant PBS medium and the key factors, such as the effect of pH, the buffer system, and the boron/glucose mole ratio (B/G), on the conversion of glucose and the selectivity of 5-HMF, as well as the effect of microwave irradiation, are studied systematically. The highly selective conversion of various carbohydrates (glucose, xylose, cellobiose and α-cellulose) into 5-HMF/furfural is thereby accomplished in such a system. Moreover, the interaction between borate and glucose, as well as its effect on the glucose isomerization, are proved by Raman spectra and theoretical calculation. Finally, a biphasic system is employed to further improve the selectivity of 5-HMF and to achieve the sustainability of the homogenous catalytic system.

2. Experimental

2.1 Chemicals

D-(+)-Glucose (≥99.5%) was purchased from Sigma-Aldrich. D-(+)-Xylose (≥99%), D-(+)-cellobiose (98.0%) and α-cellulose (25 μm) were purchased from Aladdin. $Na_2B_4O_7\cdot10H_2O$ (≥99.5%), methyl-isobutylketone (MIBK) (≥99.0%) and 2-butanol (≥98.0%) were purchased from Sinopharm Chemical Reagent Co., Ltd. H_3PO_4 (85.0%) was purchased from Shanghai Feida Chemical Co., Ltd. $NaH_2PO_4\cdot2H_2O$ (≥99.0%) and HCl (36.0–38.0%) were purchased from Jiangsu Chemical Co., Ltd. NaOH (96.0%) was purchased from Shanghai Fourth Reactant Factory. All the chemicals were used without further purification. Deionized water produced from a laboratory water purification system (RO DI Digital plus) was used to prepare all the aqueous solutions.

2.2 Dehydration of carbohydrates

All the PBSs with different components, as well as the acidic solution, were prepared according to their stoichiometric ratios in 50 mL flasks. The catalytic reactions in the PBS containing borate were performed in a 30 mL reactor under microwave irradiation provided by Nova-2S from Preekem Scientific Instruments Co., Ltd. In a typical procedure, glucose (1.2 g) and borax (0.3 g) were dissolved by the ultrasonic bath in the above PBS system, and the total volume of the reaction solution was kept at 12 mL. Then, the mixture was put in the microwave-assisted reactor at 160 °C. For xylose and cellobiose conversion, the glucose was replaced by 1.2 g of xylose and cellobiose in the above process. For cellulose conversion, α-cellulose (2.4 g) and NaCl (3.0 g) were dissolved by the ultrasonic bath in 1.5 M H_3PO_4 (10.0 g) and the mixture was placed in the microwave-assisted reactor for 15 min at 160 °C. After the reaction, the solution was filtered, and NaH_2PO_4 and borax were added to maintain the $H_3PO_4 : NaH_2PO_4$ ratio $= 1:1$ and B/G $= 0.5$. Finally, the mixture solution was put in the microwave-assisted reactor for 30 min at 160 °C. For the conventional heating experiments, the above glucose reaction system was heated in the oven at the same temperature. For the biphasic system, all the procedures were the same as the above PBS system, but the organic solvent consisting of MIBK and 2-butanol (volume ratio $= 7:3$) was added before the microwave irradiation.

2.3 Computational details

First-principles density functional theory (DFT) calculations were performed with the M06-2x/6-31+G(d) method.[15,16] M06-2X is by far one of the most accurate DFT functional methods in predicting energy barriers.[15] To account for the solvation effect, the calculations were performed with the IEFPCM solvation model[17] with radii and non-electrostatic terms in Truhlar and coworkers' SMD solvation model.[18] All the geometry optimizations and vibrational frequency analyses were performed with the solvation effect considered. The default geometry convergence criterion of Gaussian 09 (ref. 19) was used. The integral grid used for all the DFT calculation is a pruned (99 590) grid (the "ultrafine" grid as defined by Gaussian 09). To consider the effect of pH while reducing the computational efforts to a manageable degree, a solvated proton was simplified as H_3O^+ during the calculations. Since the computed harmonic vibrational frequencies were systematically higher than the experimental vibrational frequencies,[20] the calculated vibrational frequencies were scaled by a factor of 0.97 in order to directly compare to experimental spectra. All these calculations were performed using the Gaussian 09 quantum software package.[19]

2.4 Products analysis

Samples were taken at setting time and analyzed *via* an external standard method by high performance liquid chromatography (HPLC) equipped with a refractive index detector and a shodex SH1011 sugar column purchased from Shimadzu Corporation.

The HPLC was detected at 40 °C with 0.5 mM H_2SO_4 mobile phase in a flow rate of 1.0 mL min^{-1}. Before being injected into

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the HPLC, the samples needed to be filtered through a microsyringe filter (VWR, 0.22 μm PTFE for the organic samples and PES for the aqueous samples). The retention times (HPLC) of all the reactants and products were determined with the standard samples, and are as follows: glucose (7.0 min), fructose (7.4 min), xylose (7.5 min), erythrose (8.4 min), glycolal (8.8 min), FA (9.4 min), AA (10.6 min), LA (11.7 min), 5-HMF (23.3 min) and furfural (35.7 min), respectively. Raman spectra data were obtained by taking 400 μL of each sample interrogated in 8 mm glass vials and detected by the Inspector785 (200–2000 cm^{-1}) purchased from SciAps Inc.

To avoid operating errors, the concentrations of products were corrected by an internal standard. The yields (%) and selectivities (%) of the products were based on the initial concentration of carbohydrates and were calculated as follows:

$$\text{Yield}(\%) = \frac{\text{Product concentration}}{\text{Theoretical product concentration}} \times 100\%$$

$$\text{Conversion}(\%) = \left(1 - \frac{\text{Carbohydrate concentration}}{\text{Initial carbohydrate concentration}}\right) \times 100\%$$

$$\text{Selectivity}(\%) = \frac{\text{Yield}}{\text{Conversion}} \times 100\%$$

3. Results and discussion

3.1 Dehydration of glucose, xylose, cellobiose and α-cellulose

The dehydration condition of various carbohydrates in aqueous solution is optimized by a series of experiments, including pH of the PBS system and the borate content, which will be explained in detail later. Table 1 shows the results of glucose, xylose, cellobiose and α-cellulose conversion into 5-HMF/furfural in the optimum borate-assistant PBS system under microwave irradiation. With the assistance of microwave irradiation and borate, 62.0% of glucose is converted into 34.6% of 5-HMF with a selectivity of 55.8% in 90 min at 160 °C (Entry 1). However, the selectivity of 5-HMF displays a decrease with a prolonged reaction time, due to the formation of by-products such as LA, FA and humins. For example, with the prolonging of the reaction time from 90 to 150 min, the conversion of glucose increases from 62.0% to 79.4%, while the selectivity of 5-HMF decreases from 55.8% to 45.1%. Moreover, xylose displays the same trend as the glucose in conversion and selectivity (Entry 2). Therefore, the timely removal of product has to be taken into consideration.

Cellobiose and cellulose, which are composed of multi-glucose molecules, are considered promising for application in the preparation of 5-HMF, due to their low cost and adequate sources. Herein, under the same condition as glucose, the conversion of cellobiose reaches 60.5% and produces as much as 5-HMF of 33.2% in 120 min, which is quite good performance for cellobiose in aqueous solution (Entry 3). For cellulose, it is inspiring that a fast hydrolysis of α-cellulose is observed in a NaCl-assisted H_3PO_4 system and that a 25.9% yield of glucose (5.2 wt%) is obtained from 20 wt% α-cellulose solution without any pretreatment in 15 min under microwave irradiation (Entry 4). Furthermore, a 48.8% selectivity of 5-HMF based on the as-prepared glucose can be achieved from the above hydrolytic solution of α-cellulose in such a PBS system (Entry 5). These impressive results are believed to be attributed to the solution acidity, the buffer system, and the effect of borate, which lead to perfect matching of the isomerization and dehydration rates during the glucose/xylose conversion.

3.2 Effect of PBS system

Different mineral acidic solutions at different pH values containing a fixed amount of borate have been employed to study the isomerization and dehydration of glucose. As shown in Table 2, glucose in the PBS system at different pH values can be transformed to various products. In the stronger acid system (pH = 1.1), 5-HMF, LA, and FA are formed, indicating the instability of 5-HMF at such a pH value. When the pH reaches 4.7, glucose

Table 1 The dehydration results of glucose, cellobiose and α-cellulose in the PBS system under microwave irradiation[a]

Entry	Aldose	Time (min)	Conv. (%)	Y^b (%)	S^b (%)
1	Glucose	90	62.0	34.6	55.8
		120	71.3	37.1	52.0
		150	79.4	35.8	45.1
2	Xylose[c]	30	56.8	27.6	48.6
		60	86.1	37.1	43.1
3	Cellobiose	90	51.7	30.5	59.0
		120	60.5	33.2	54.9
4	α-Cellulose[d]	15	—	25.9	—
5	As-prepared glucose[e] (5.2 wt%)	30	43.0	21.0	48.8

[a] Reaction conditions: 10 wt% glucose, cellobiose in 0.5 M H_3PO_4/0.5 M NaH_2PO_4 PBS system, borax = 0.3 g, and reaction temperature = 160 °C. [b] Yield and selectivity of 5-HMF for Entries 1, 3 and 5; yield and selectivity of furfural for Entry 2; yield of glucose for Entry 4. [c] 10 wt% xylose in 0.5 M H_3PO_4/0.5 M NaH_2PO_4 PBS system with B/X = 0.25. [d] Reaction condition: 20 wt% α-cellulose in 1.5 M H_3PO_4 solution with 3 g NaCl in 15.4 g reaction solution. [e] Filtered solution from Entry 3 reacted in 1.5 M H_3PO_4/1.5 M NaH_2PO_4 PBS system with B/G = 0.5. Conv.: conversion, *Y*: yield, *S*: selectivity.

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Table 2 The conversion of glucose (10 wt%) and the corresponding product distributions in PBS at different pH values under microwave irradiation[a]

Solution	pH	Conv. (%)	$Y_{5\text{-HMF}}$ (%)	$Y_{\text{Fru.}}$ (%)	Y_{LA} (%)	Y_{FA} (%)	Y_{AA} (%)	$Y_{\text{Ery.}}$ (%)
1.0 M H_3PO_4	1.1	37.0	9.7	0.0	3.1	16.0	0.0	0.0
0.5 M H_3PO_4/0.5 M NaH_2PO_4	2.1	62.0	34.6	3.8	0.7	11.1	0.0	0.0
1.0 M NaH_2PO_4	4.7	93.1	6.6	0.0	0.0	11.3	3.9	8.3
0.5 M NaH_2PO_4/0.5 M Na_2HPO_4	6.8	94.8	0.0	0.0	0.0	14.1	4.2	36.9

[a] Reaction conditions: reaction time = 90 min, B/G = 0.5, and reaction temperature = 160 °C. 5-HMF: 5-hydromethylfurfural; Fru.: fructose; LA: levulinic acid; FA: formic acid; AA: acetic acid; Ery.: erythrose; Conv.: conversion; *Y*: yield.

seems to prefer other conversion routes rather than the dehydration way, such as retro-aldol condensation, and hence erythrose is detected in the reaction system. Furthermore, the formation of erythrose becomes predominant at a pH of 6.8, and no 5-HMF could then be observed. Only at a pH of 2.1 does the reaction display the best result. Furthermore, it is found that the conversion of glucose decreases with the increasing acidity of the system, *i.e.*, the lowest conversion is obtained at a pH of 1.1. This is contrary to the results of fructose conversion in the solution at different pH values.[14] Moreover, it is surprising that other reaction systems, such as the diluted strong acid system at different pH values (Table 3) and PBS systems without borate addition (Fig. S1, ESI†), also display the same trend, not only for the selectivity of 5-HMF but also for the conversion of glucose, *i.e.* the best performance of the reaction is at a pH of 2.1 and the lowest conversion of glucose is at a pH of 1.1. These results clearly show the importance of acidity in the glucose dehydration. On the one hand, when the pH value is lower than 2.1, the ring-structure of glucose is more stable and is not easy to isomerize into fructose, even with the existence of borate. It is believed that $B(OH)_4^-$ can form stable chelate complexes with carbohydrates and can catalyze the isomerization of aldoses to ketoses.[21–24] However, in the strong acidic system, the concentration of $B(OH)_4^-$ is quite low due to the limitation of the borate hydrolysis equilibrium, as shown by eqn (1).

$$H_3BO_3 + H_2O \rightleftharpoons B(OH)_4^- + H^+ \tag{1}$$

The higher H^+ concentration suppresses the shift of equilibrium from left to right at lower pH values, and thereby influences the glucose isomerization rate. Furthermore, in the strong acid solution, the 5-HMF formed is inclined to rehydrate into LA and FA, which leads to a poor selectivity of 5-HMF. On the other hand, when the pH value is higher than 2.1, such as at 4.7 or 6.8, the increase in the glucose isomerization rate and other side-reaction rates causes a higher conversion of glucose and a lower selectivity of 5-HMF. This can also be demonstrated by the conversion of xylose into furfural. As shown in Fig. 1A, the highest selectivity of furfural is achieved at a pH of 2.1, and high acidity (pH 1.1) leads to a low conversion of xylose in the borate-containing PBS system.

Since the pH value of the reaction system has a dramatic effect on the conversion of glucose, the use of a buffer system is critical for its ability to maintain the pH value during the reaction. A series of experiments were conducted to study the effect of the buffer system during glucose dehydration in the H_2SO_4 solution with different pH values, similar to those in the PBS systems. As shown in Table 3, after being irradiated for 90 min, glucose converts only 16.0% and the yield of 5-HMF is merely 8.2%, which is far less than the results obtained in the buffer system at the same pH value (2.1). It is obvious that the solution with the appropriate pH value only at the beginning is not enough for a good catalytic performance during the whole reaction. The generation of FA during the reaction at all pH values ranging from 1.1 to 6.8 will have an impact on the acidity of the reaction system. Therefore, it is difficult for the diluted acid solution consisting of H_2SO_4 to maintain its pH value during the whole reaction and so its acidity becomes stronger alongside the generation of the organic acid. This can be demonstrated by its product distributions at different pH

Table 3 The conversion of glucose (10 wt%) and the corresponding product distributions in H_2SO_4 solution at different pH values under microwave irradiation[a]

pH	Conv. (%)	$Y_{5\text{-HMF}}$ (%)	Y_{FA} (%)	$Y_{\text{Ery.}}$ (%)	$Y_{\text{Gly.}}$ (%)
1.1	13.9	3.6	10.0	0.0	0.0
2.1	16.0	8.2	3.2	0.0	0.0
4.7	26.3	10.6	1.1	4.8	0.0
6.8	71.8	0.0	6.2	14.1	16.1

[a] Reaction conditions: reaction time = 90 min, B/G = 0.5, and reaction temperature = 160 °C. 5-HMF: 5-hydromethylfurfural; FA: formic acid; Ery.: erythrose; Gly.: glycolal; Conv.: conversion; *Y*: yield.

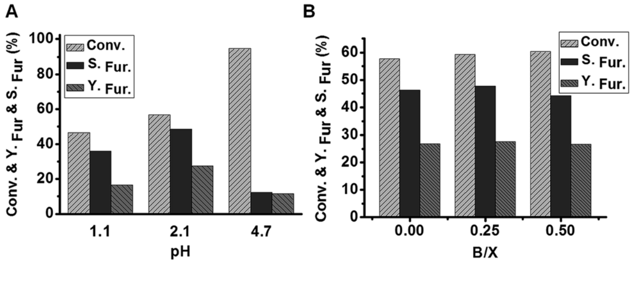

Fig. 1 Effects of pH value (A) and B/X ratio (B) on the conversion of xylose (10 wt%) into furfural under microwave irradiation. For all, the reaction time is 30 min and the reaction temperature is 160 °C. Fur.: furfural; Conv.: conversion; *Y*: yield; *S*: selectivity.

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values, which regularly move to more acidic ones compared to those of PBS systems (Table 2). Moreover, the shift of pH values toward the stronger acidic system will also suppress the conversion of glucose, as indicated above. On the contrary, the PBS system is able to provide a self-regulation reaction environment, and so the acidity of the solution is not infected notably by the generated organic acids. As a consequence, the use of the PBS system is one of the key indispensables for a high selectivity of 5-HMF and a fast conversion of glucose.

3.3 Effect of borate

Table 4 displays the effect of B/G ratios on the conversion of glucose into 5-HMF. Obviously, an increasing B/G ratio leads to an accelerating conversion rate of glucose, but very diverse yields and selectivities of 5-HMF within the same reaction time when the pH value of the reaction system is fixed at 2.1. According to Table 4, without the addition of borate, the conversion of glucose is only 43.0% in 90 min. On the contrary, the glucose converts faster with the addition of borate, and the conversion of glucose can then reach 86.0% at a 1.5 B/G ratio in 30 min. This result is consistent with those of Table 2 and Fig. S1 (ESI†). It is clear that borate can accelerate the conversion rate of glucose. Moreover, in the borate-containing reaction system, fructose is detected during the reaction, which indicates that borate has a positive effect on the isomerization of glucose into fructose. Furthermore, this can be further supported by theoretical calculations (see below). During the reaction, glucose first isomerizes into fructose, which then dehydrates into 5-HMF continuously with the assistance of mineral acid and borate in the PBS system.

However, the selectivity of 5-HMF displays a quite different trends with the increasing B/G ratio; *i.e.*, the highest selectivity of 5-HMF is obtained at B/G = 0.5 with a relatively high conversion of glucose. When the B/G ratio is lower, the accelerating effect of borate for the isomerization of glucose is not enough, although there is an acceptable selectivity of 5-HMF. When the B/G ratio becomes higher, such as a B/G of 1.5, the reaction shows the fastest conversion of glucose and the lowest selectivity of 5-HMF. Moreover, the yields of the by-products LA and FA derived from the rehydration of 5-HMF also show the same trend as that of 5-HMF, indicating that the decrease of 5-HMF selectivity at the high B/G ratio could be assigned to the occurrence of other side-reactions before the dehydration of fructose. Although $B(OH)_4^-$, which is formed by the hydrolysis of boric acid, can facilitate the isomerization of aldoses into ketoses by forming stable chelate complexes with aldoses/ketoses, the strong complexation between $B(OH)_4^-$ and glucose/fructose also blocks the elimination of water in the first step of the fructose conversion into 5-HMF and will induce other side-reactions.[24] Therefore, an excessive amount of borate will upset the dehydration of fructose, although it can also accelerate the conversion of glucose into fructose, which can be proved by the results of fructose dehydration with borate-containing PBS system (Table S1, ESI†). As shown in Table S1,† a high boron/fructose mole ratio (B/F) also results in a low selectivity of 5-HMF. Moreover, the content of glucose is stable with increasing B/F ratios during the reaction, which implies that the high B/F ratio has a great influence on the conversion of fructose rather than on its isomerization toward glucose. Furthermore, the similar conversion of fructose and the low yield of 5-HMF further indicate the occurrence of other side-reactions during the dehydration of fructose with the increase of B/F ratio. In addition, the same trend is also observed in the dehydration of xylose into furfural in Fig. 1B. With increasing B/X ratios, the conversion of xylose into furfural is accelerated, but the best result can be obtained at B/X = 0.25. Consequently, it can be concluded that a suitable B/G ratio is the key to the isomerization of glucose and the dehydration of fructose, and that a good yield of 5-HMF is only achieved with good matching between them.

To further study the effect of borate, a series of Raman spectra are measured, as shown in Fig. 2A–C. Moreover, the theoretical spectra are given in Fig. 2D to verify these Raman analyses. For the pure borate solution (Fig. 2Aa), only the characteristic peaks of $B(OH)_4^-$ and H_3BO_3 appear at 743 cm^{-1} and 877 cm^{-1}, respectively.[25] In the pure glucose solution

Table 4 Influence of B/G ratio on the conversion of glucose into 5-HMF under microwave irradiation[a]

B/G	Time (min)	Conv. (%)	$Y_{5\text{-HMF}}$ (%)	$S_{5\text{-HMF}}$ (%)	$Y_{\text{Fru.}}$ (%)	Y_{LA} (%)	Y_{FA} (%)
0	90	43.0	22.0	51.1	0.0	1.1	7.0
0.25	90	48.2	24.8	51.5	0.3	0.7	5.6
0.5	90	62.0	34.6	55.8	3.8	0.7	11.1
	120	71.3	37.1	52.0	4.0	1.8	17.7
0.75	90	71.9	36.6	50.9	5.5	1.3	17.5
1	60	69.3	33.7	48.6	7.4	0.3	0.0
	90	83.2	39.5	47.5	3.9	0.7	0.0
1.25	60	82.7	34.9	42.2	5.1	0.0	0.6
	90	91.7	37.1	40.5	3.9	0.5	1.8
1.5	30	86.0	21.6	25.1	4.0	0.0	0.0
	60	93.9	23.0	24.5	2.1	0.0	0.8
	90	98.6	16.3	16.5	0.0	0.0	1.8

[a] Reaction conditions: 10 wt% glucose in 0.5 M H_3PO_4/0.5 M NaH_2PO_4 PBS system, B/G = 0–1.5, and reaction temperature = 160 °C. 5-HMF: 5-hydromethylfurfural; Fru.: fructose; LA: levulinic acid; FA: formic acid; Conv.: conversion; *Y*: yield; *S*: selectivity.

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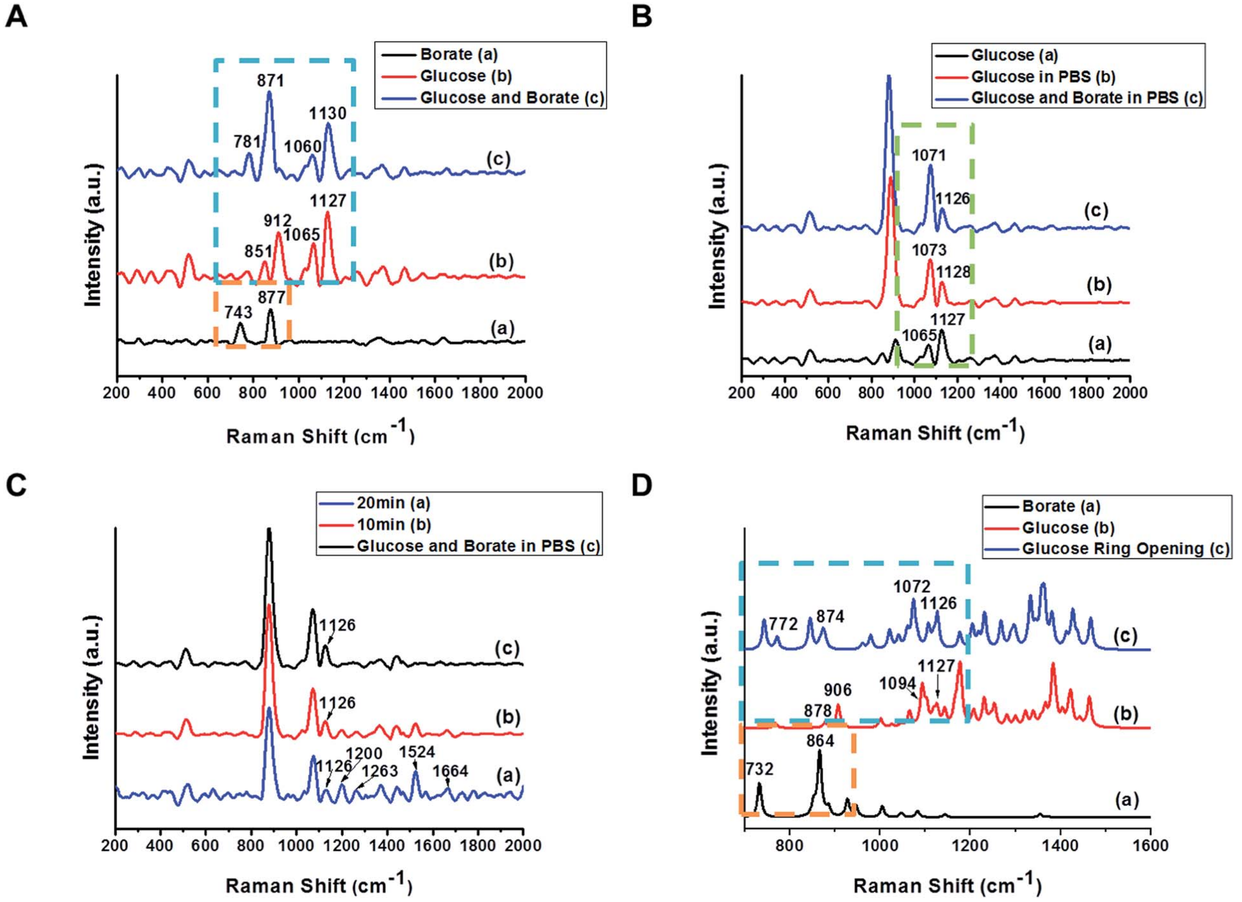

Fig. 2 Raman spectra of the reaction system. (A) Raman spectra of borate solution (a), 10 wt% glucose solution (b) and 10 wt% glucose solution containing borate (c); (B) Raman spectra of 10 wt% glucose solution (a), 10 wt% glucose in PBS (b) and 10 wt% glucose in PBS containing borate (c); (C) Raman spectra of the system reacted for 20 min (a) and 10 min (b), and the original reaction system (c); (D) theoretical Raman spectra of borate solution (a), glucose solution (b), and the ring-opening form of the $B(OH)_4^-$–glucose chelate complex (c).

(Fig. 2Ab), the peaks emerging at 912 cm^{-1} and 851 cm^{-1} are assigned to the in-plane stretching vibration of C–C=O, and the signals at 1127 cm^{-1}, 1065 cm^{-1} are the peaks of the out-of-plane stretching vibration of C–C=O.[26] However, in the solution of borate and glucose mixture (Fig. 2Ac), the in-plane stretching vibration of C–C=O in the glucose molecule displays a great change compared to that of pure glucose solution, and moves to lower wavenumber (781 cm^{-1} and 871 cm^{-1}), which indicates the formation of $B(OH)_4^-$–glucose chelate complexes. Moreover, this interaction could also be proved by the theoretical calculations as well; *i.e.*, borate does have an effect on the ring opening process of glucose during the reaction, as shown in Fig. 2Dc. In addition, the out-of-plane stretching vibration of its C–C=O also shows a clear change, although the change is slight. However, when glucose is dissolved in PBS medium consisting of 0.5 M H_3PO_4 and 0.5 M NaH_2PO_4, the in-plane stretching vibration of C–C=O in glucose is totally covered by the strong peaks caused by the mineral acid and salt (Fig. 2Bb). Only the small change on the out-of-plane stretching vibration of C–C=O could still be observed (Fig. 2Bc).

To get a better understanding of the conversion process of glucose, the reaction was determined by Raman spectra every 10 min under microwave irradiation. It is clear that, during the reaction, some new peaks arise at 1664 cm^{-1}, 1524 cm^{-1}, 1263 cm^{-1}, and 1200 cm^{-1}, respectively in Fig. 2C, which can be assigned to the generation of 5-HMF.[27] In addition, the increasing intensity of the 5-HMF characteristic peaks and the decreasing glucose peak at 1126 cm^{-1} also imply the conversion of glucose into 5-HMF (Fig. 2C).

Moreover, these experimental Raman spectra agree well with the calculation results, especially in the spectra of the borate and glucose ring-opening process. The experimental results of $B(OH)_4^-$ and H_3BO_3 at 743 cm^{-1} and 877 cm^{-1} in Fig. 2Aa are consistent with the theoretical ones at 732 cm^{-1} and 864 cm^{-1} in Fig. 2Da. As shown in Fig. 2Ac, the characteristic peaks at 781 cm^{-1}, 871 cm^{-1}, 1060 cm^{-1}, and 1130 cm^{-1} of the glucose solution containing borate correspond with the calculated ones of the ring-opening form of the $B(OH)_4^-$–glucose chelate complex (Fig. 2Dc). Accordingly, it is believed that tetrahydroxyborate $[B(OH)_4^-]$ plays an important role in the isomerization of glucose.

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3.4 Effect of microwave irradiation

The effect of microwave heating on the conversion of glucose was also studied, and the results are shown in Fig. 3. Obviously, microwave irradiation leads to a faster conversion of glucose and a higher selectivity of 5-HMF compared with the results under oven heating. For example, the reaction system under microwave heating can achieve a glucose conversion of 62.0% with a 5-HMF selectivity of 55.8% within 90 min at 160 °C, but under oven heating this just reaches a glucose conversion of 63.1% with a 5-HMF selectivity of 50.9% within 120 min at the same temperature. The observed rate enhancement can be contributed to the nature of the microwave direct, volumetric heating model and the reaction system with a high ion concentration.[28] This acidic PBS solution containing borate contains an abundance of ions such as $H_2PO_4^-$, HPO_4^{2-}, PO_4^{3-}, $B(OH)_4^-$, H_3O^+, Na^+, which leads to a rapid temperature rise under microwave irradiation, since ionic conduction is one of the two main microwave heating models.[29] Such instantaneous heating process results in not only a fast conversion of glucose but also a high selectivity of 5-HMF, because an extended reaction time could cause the formation of by-products and a decrease of selectivity.[29] These results can also explain the reason for the similar results of glucose conversion in the pure water heated by conventional means and by microwave irradiation (Fig. S2, ESI†). The ion concentration in the water is very low, and so the instantaneous heating effect of the microwave field becomes insignificant. Therefore, the difference in glucose conversion in the pure water between conventional heating and microwave heating cannot be clearly observed. Therefore, microwave irradiation is also another influence factor on the highly selective conversion of glucose into 5-HMF in such a PBS system.

3.5 Computational study

Theoretical calculations were performed to understand the isomerization mechanism of glucose to fructose in acidic solution with or without borate. The calculations indicate that the isomerization begins with the opening of the 6-member ring-close form of glucose (glucopyranose) by breaking its C–O bond in the ring with the help of a proton. The resulting opening form of glucose (acyclic-glucose) undergoes an intramolecular hydrogen transfer to the opening form of fructose (acyclic-fructose). Acyclic-fructose then undergoes a ring closing process to form the ring-close form of fructose. The Gibbs free-energy profiles and the structures of the intermediates and transition states of the isomerization process without borate are presented in Fig. 4. Fig. 4 shows that the overall free-energy barrier for the isomerization of glucose into fructose is 29.3 kcal mol^{-1} when borate is absent.

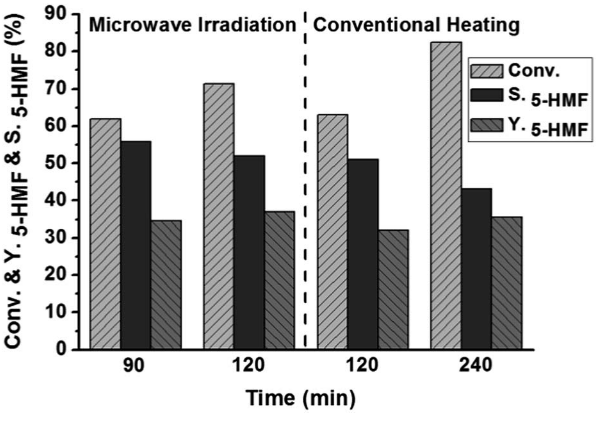

Fig. 3 The conversions of 10 wt% glucose in the borate-containing PBS system under microwave irradiation and with conventional heating at 160 °C. 5-HMF: 5-hydromethylfurfural; Conv.: conversion; *Y*: yield; *S*: selectivity.

In the reaction system containing borate, $B(OH)_4^-$ can form the stable chelate complex, boroglucopyronose, with glucose, by anchoring with two hydroxyl groups of glucose through the removal of two water molecules. Similar to the results of Anders Riisager *et al.*,[24] we find that 4,6-boroglucopyronose and 3,4-boroglucopyronose are the two most stable complexes between $B(OH)_4^-$ and glucose, and the former is slightly more stable than the latter by 3.2 kcal mol^{-1} at 298.15 K in Gibbs free energy. Under the reaction conditions, these two complexes can be viewed as if in equilibrium with each other. Starting from either 4,6-boroglucopyronose or 3,4-boroglucopyronose, a similar isomerization pathway as that one without borate as presented in Fig. 4 can be determined in Fig. 5 and S3 (ESI†). However, it is found that the pathway starting with 4,6-boroglucopyronose has a higher energy barrier (with an overall free-energy barrier of 25.5 kcal mol^{-1}, Fig. S3, ESI†) than that starting with 3,4-boroglucopyronose (Fig. 5). The latter one has an overall free-energy barrier of just 17.9 kcal mol^{-1}. As can be seen from Fig. 4 and 5, the addition of borate can greatly lower the energy barrier of the isomerization. Binding with $B(OH)_4^-$ increases the tension of the 6-membered ring of glucose, which lowers its Gibbs free-energy barrier for the opening from the closed-form to the open-form through the transition state TS1 from 22.8 kcal mol^{-1} to just 17.9 kcal mol^{-1}. The second step, the hydrogen migration from $-C^{(2)}HOH-$ to the terminal $-C^{(1)}H{=}O$ of acyclic-glucose to form acyclic-fructose, is also greatly enhanced, with the free-energy-barrier lowering from 19.9 kcal mol^{-1} to 13.5 kcal mol^{-1}.

In the calculation, $B(OH)_4^-$ is also replaced by H_3PO_4, in order to study if H_3PO_4 can accelerate the isomerization of glucose as well. A similar pathway as presented in Fig. 5 is computed (Fig. S4, ESI†). The overall Gibbs free-energy barrier in the reaction system containing H_3PO_4 is 25.1 kcal mol^{-1}, which is higher than that with the help of $B(OH)_4^-$ (17.9 kcal mol^{-1}, Fig. 5), but is lower than that with only protons but without other additives (29.3 kcal mol^{-1}, Fig. 4). This means that H_3PO_4 can also facilitate the isomerization of glucose, but its effect is weaker than that of borate. The results are consistent with experimental data and prove the key role of borate in accelerating the isomerization of glucose. In addition, it is worth mentioning that the pathway of anchoring two glucose molecules with one $B(OH)_4^-$ is considered to mimic the effect of borate concentration and changed the B/G ratio from 1 to 0.5. When the borate content is decreased, the overall Gibbs free-energy barrier of the glucose isomerization process increased to 20.9 kcal mol^{-1}. This implies that the isomerization is faster with a B/G ratio of 1 than that of 0.5, which is also consistent

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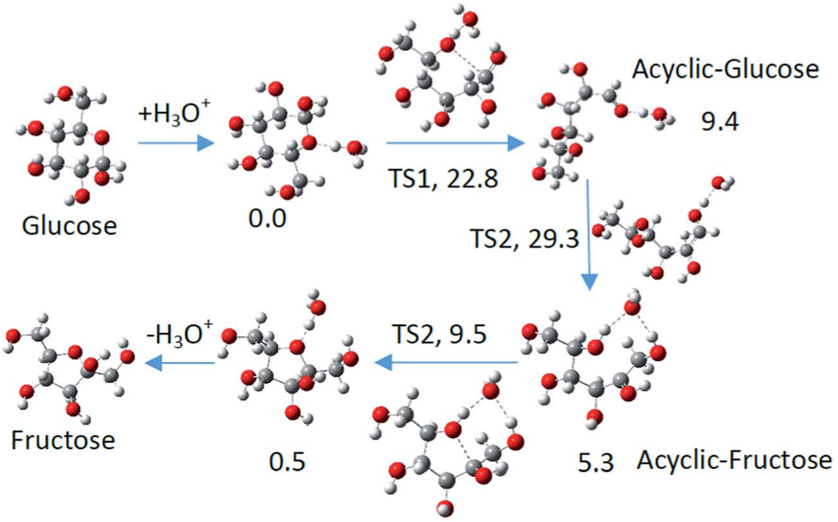

Fig. 4 Gibbs free energy profiles at 298.15 K and structures of the intermediates and transition states of the isomerization of glucose to fructose with the help of proton. The numbers are relative free energies (in kcal mol^{-1}) to the complex between glucose and H_3O^+.

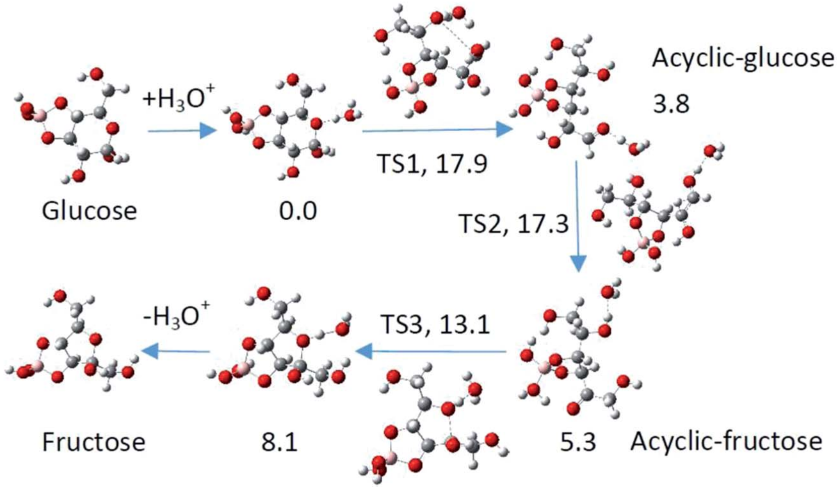

Fig. 5 Gibbs free energy profiles at 298.15 K and structures of the intermediates and transition states of the isomerization of glucose to fructose *via* 3,4-boroglucopyronose with the help of protons. The numbers are relative free energies (in kcal mol^{-1}) of the complexes between D-glucose and H_3O^+.

with the experimental results (Table 4). Besides, our calculations also indicate that the ring opening form of 3,4-boroglucopyronose is a stable intermediate during the isomerization process: its relative free energy to 3,4-boroglucopyronose is just 3.8 kcal mol^{-1} (Fig. 5). Its conversion back to 3,4-boroglucopyronose has a free-energy barrier of 14.1 kcal mol^{-1} (transition state TS1), while its isomerization to acyclic-fructose through hydrogen-migration is 13.5 kcal mol^{-1} (transition state TS2). Therefore, it is possible to observe this intermediate during the isomerization process. In fact, the Raman spectrum of this intermediate agrees well with the experimental Raman spectrum of glucose in the PBS solution containing borate (Fig. 2). This agreement is also strong evidence for the reliability of our theoretical calculations and the proposed isomerization mechanism.

3.6 Sustainability of PBS system with borate

Compared with the solid acid catalyst, one of the biggest disadvantages of liquid acids is their poor reusability. Solid acid catalysts can be easily recycled and reused after a series of processes, while liquid acid catalysts normally cannot be recycled and used again after the reaction. Moreover, the general mineral acids (HCl and H_2SO_4) are highly corrosive for the reaction vessel. Compared to them, this PBS system consisting of phosphoric acid/acid phosphate and borate is safer and less corrosive. Furthermore, as indicated by Dumesic,[30] such a PBS system can also allow the possibility of recycling by a biphasic

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Table 5 The sustainability of the PBS system with borate[a]

	Glucose (wt%)	Time (min)	Conv. (%)	$Y_{5\text{-HMF}}$ (%)	$S_{5\text{-HMF}}$ (%)
Run 1	10	90	57.8	34.6	60.0
Run 2	5	90	51.3	30.5	59.5
Run 3	5	90	43.9	26.0	59.2
Total	20	270	74.0	44.7	60.4
Original	20	90	74.9	39.6	52.9

[a] Reaction conditions: reaction temperature = 160 °C and B/G = 0.5 in a biphasic system. An organic phase (MIBK : 2-butanol = 7 : 3) with the same volume as the aqueous phase is added into the above PBS system before reaction. 5-HMF: 5-hydromethylfurfural; Conv.: conversion; *Y*: yield; *S*: selectivity.

system, that is, by continuously removing 5-HMF by organic solvents and the continual feed of glucose. Herein, three stepwise additions of glucose and organic phase were used to investigate the possibility of the reusability of this system. As shown in Table 5, the selectivity of 5-HMF could be maintained after three additions of glucose, and reaches 60% even when the total glucose concentration is up to 20 wt%. Moreover, the results of separately adding one is higher than not only that of 10 wt% glucose in pure PBS phase (Entry 1, Table 1) but also from 20 wt% glucose in the biphasic system (Table 5), although the conversion of glucose is almost at the same level. In addition, the PBS catalysts can also be recovered by neutralizing them into their salts such as Na_3PO_4. Generally, the solubility of Na_3PO_4 in water is poorer and more sensitive to temperature compared to its acidic form, and can be easily recrystallized. For example, if the PBS solution is neutralized to Na_3PO_4 by the addition of NaOH, 31 wt%, 53 wt%, and 74 wt% of Na_3PO_4 could be recovered in theory at 20 °C, 10 °C, and 0 °C, respectively.[31] According to our experiments, more than 90% of the theoretical amount of Na_3PO_4 could be obtained. These results suggest a possible reusability of the PBS system for future practical applications.

4. Conclusions

In summary, PBS system containing borate with an appropriate pH has been shown to be able to convert glucose, cellobiose and α-cellulose into 5-HMF/furfural directly with a high selectivity. It is found that the key factor for the highly selective conversion of glucose to 5-HMF is the matching of the isomerization and dehydration processes of glucose, *i.e.* matching among appropriate pHs (2.1), B/G ratios (0.5) and the PBS system under microwave irradiation. Only under that unique condition, can glucose isomerize into fructose and then dehydrate into 5-HMF continuously at the matched speed. Both the Raman spectra and theoretical calculations prove the interaction between borate and glucose, as well as the borate-assistant isomerization process of glucose. Moreover, the PBS system with borate is expected to achieve reusability and stable catalytic performance in the biphasic system. These results not only deepen the understanding of the one-pot conversion process of glucose to 5-HMF involved in the matching of isomerization and dehydration processes, but also present the possibility of achieving a sustainable green process for carbohydrates conversion.

Acknowledgements

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