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Catalytic Deep Eutectic Solvents for Highly Efficient Conversion of Cellulose to Gluconic Acid with Gluconic Acid Self-Precipitation Separation

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chemistry.¹⁵

now used in a plethora of different application, for example, nanotechnology,¹¹ separation processes,¹² transition metal catalyzed reactions,¹³ stabilization of DNA,¹⁴ and main-group Generally, DESs have ionic liquid-like physiochemical properties and can be formed by simply heating the mixture of two cheap components while ionic liquids are generally synthesized through several steps using some expensive and toxic reagents and large amounts of organic solvents.^{16, 17} More importantly, some low-cost, nontoxic and

abundant hydrated transition metal halides are considered to be technically and economically promising components to form DESs.^{18, 19} For example, FeCl₃-choline chloride eutectic mixtures have been previously reported by Abbott et al.¹⁸ Therefore, some catalytic deep eutectic solvents (CDESs) could be achieved on the basis of the catalytic ability of these transition metal halides for various reactions. The advantage of CDESs lies in that they can change a heterogeneous reaction into homogeneous one by dissolving reactants, which can improve the reactivity significantly.²⁰ It has reported that high concentration FeCl₃ aqueous solution (60%) could catalyze the oxidation of cellulose to gluconic acid with a yield of about 50%,²¹ however, the

separation of gluconic acid and the reuse of FeCl₃ were still two problems to be solved. Moreover, a variety of DESs have been successfully applied as both catalysts and solvents in different chemical transformation.²²⁻²⁵ Herein, novel CDESs composed of FeCl₃·6H₂O and amide, polyalcohol or amino acid were designed and used as both solvent and catalyst for the direct oxidation of cellulose to gluconic acid with high efficiency. More surprisingly, the produced gluconic acid could be self-precipitated from the reaction system, which avoided the complex separating steps. Additionally, the used CDESs could be easily recycled without decreasing its activity.

The Fe-based CDESs were prepared by heating the mixture of FeCl₃·6H₂O and eight hydrogen bond donors (HBDs, Figure 1D) with different molar ratio at 40 °C, and the prepared CDESs were stable at room temperature and reaction conditions. The melting points of the obtained CDESs were much lower than

years along with the pursuit of alternatives for the gradually exhausting fossil resources.^{1, 2} In this context, great efforts have been devoted to the conversion of cellulose, which is the most abundant component in lignocellulosic biomass. For cellulose conversion, oxidation of cellulose to produce gluconic acid is one of the most promising routes because gluconic acid can be widely used as a fine chemical in pharmaceutical and food industries.³⁻⁵ Generally, cellulose can be oxidized to gluconic acid over supported noble metals (e.g., Au, Pt, Pd) under O_2 atmosphere.⁶⁻⁸ However, these developed noble metal-based catalytic systems suffered from some drawbacks, including the high cost of noble metals and the necessary use of strong base, which hinder their scalability in industries.^{9, 10} In another aspect, gluconic acid is very difficult to be separated from the reaction systems since it is usually mixed with the unreacted reactants and solvents. Therefore, development of energy-saving routes over non-noble metal catalysts with high reaction efficiency and easy separation of product is still a highly desired but challenging task for the production of gluconic acid from cellulose oxidation.

As an attractive alternative solvent to ionic liquids and conventional organic solvents, deep eutectic solvents (DESs) are

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Figure 1. FTIR spectroscopy of FeCl₃·6H₂O/ethylene glycol (a) and ethylene glycol (b) (A); viscosity and density of FeCl₃·6H₂O/ ethylene glycol as a function of temperature (B); DSC of FeCl₃·6H₂O/ethylene glycol (C); composition of all CDESs (D).

that of the individual components, indicating the formation of DESs. The interactions between FeCl₃·6H₂O and the HBDs were characterized by FT-IR spectroscopy (Figure 1A and Figure S1). As shown in Figure 1B, the C-O stretching characteristic peak appeared at 1084 cm⁻¹ for pure ethylene glycol, which shifted to the red area (1054 cm⁻¹) in the DES formed between FeCl₃·6H₂O and ethylene glycol. Meanwhile, the interactions between FeCl₃·6H₂O with other HBDs were also investigated by FT-IR spectroscopy (see ESI, Figure S1). For example, the C=O stretching characteristic peaks was 1610 cm⁻¹ for pure serine (Figure S1A), which showed a red shift to 1605 cm⁻¹ in CDESs formed between FeCl₃·6H₂O/serine. Additionally, the stretching peak of N-H at 3460 cm⁻¹ for serine appeared a red shift to 3342 cm⁻¹ in CDES FeCl₃·6H₂O/serine. These FT-IR results verified the intermolecular interaction between FeCl₃·6H₂O and the examined HBDs, which was helpful for the formation of DESs.

Generally, the fundamental physicochemical properties, especially transport properties (viscosity and conductivity) and glass-transition temperature are very important parameters for the applications of novel solvents. Herein, the viscosities, conductivities, densities, and glass-transition temperature (T_g) of the CDESs systems were investigated, and the results are showed in Table S1. The viscosities of FeCl₃·6H₂O based CDESs were usually lower than that of most commonly used ionic liquids.²⁶ For example, the viscosities of [BMIM][PF₆] and [BMIM][BF₄] were 273 mPa·s and 110 mPa·s at 298.15 K,²⁷ while the viscosities of CDESs generated between $\mbox{FeCl}_3{\cdot}\mbox{6H}_2\mbox{O}$ and ethylene glycol, glycerol or malonic acid were below 100 mPa·s at 298.15 K (Table S1). It was also found that the viscosities and densities decreased with the increasing of temperature (Figure 1C, S2, and S3). Meanwhile, the as-prepared CDESs had relatively high conductivity compared with other DESs²⁸ and ionic liquids,²⁹ which provided the potential applications of these CDESs in electrochemistry. Additionally, differential scanning calorimetry indicated that the T_g of the FeCl₃·6H₂O

based CDESs were very low (Table S1). For example, Athe Jeliof FeCl₃·6H₂O/ethylene glycol was around $^{O_1}6^{40.2}C^{39}$ (Figure $^{37}D^{3}$). These results suggested the good transport properties of the formed FeCl₃·6H₂O based CDESs, which was beneficial for the FeCl₃·6H₂O based CDESs to being used as good solvents for reaction and separation.

Considering the good transport properties of the FeCl₃·6H₂O based CDESs and the catalytic functions of FeCl₃, we attempted to apply the as-prepared FeCl₃·6H₂O based CDESs as both solvent and catalyst for the transformation of cellulose to produce gluconic acid (Figure 2). The effect of the as-prepared FeCl₃-based CDESs was initially examined for the conversion of cellulose (Table 1). In all of the examined CDESs, cellulose could be completely consumed, and FeCl₃·6H₂O/ethylene glycol provided the highest yield (52.7%) of gluconic acid (Table 1, entry 1), which was higher than that obtained from the reported catalytic system consisted by high concentration FeCl₃ aqueous solution in the similar conditions (Figure 3A). It was found that the rate for cellulose transformation was faster in FeCl₃·6H₂O/malonic acid, FeCl₃·6H₂O/serine, FeCl₃·6H₂O/alanine, and FeCl₃·6H₂O/glycine (Table 1, entries 2-5) than that in FeCl₃·6H₂O/ethylene glycol due to the relatively high acidity of these four systems (pH, see Table S2). However, higher acidity could also enhance some side-reactions, such as the decomposition of the generated gluconic acid, the dehydration of the in-situ formed glucose to 5hydroxymethylfurfural, and the formation of humins (Figure 4), which is a similar process described by König,³⁰ and thus FeCl₃·6H₂O/ethylene glycol provided the highest gluconic acid yield. Meanwhile, the higher viscosity of FeCl₃·6H₂O/glycerol (99 FeCl₃·6H₂O/xylitol (446.54 mPa·s). mPa·s) and FeCl₃·6H₂O/pentaerythritol (176.49 mPa·s) resulted in the lower conversion of the in-situ formed glucose although cellulose in these catalytic systems could be completely transformed, and thus the gluconic acid yield was lower (Table 1, entries 6-8). Control experiments using glucose as the reactant indicated that the conversion of glucose in FeCl₃·6H₂O/glycerol, FeCl₃·6H₂O/xylitol and FeCl₃·6H₂O/pentaerythritol was indeed lower than that in FeCl₃·6H₂O/ethylene glycol (Table 1, entries 9-12). These results in Table 1 indicated that FeCl₃·6H₂O/ethylene glycol was the best solvent/catalyst.



Figure 2. Schematic illustration of the reaction process.

Table 1. Conversion of cellulose in various FeCl₃·6H₂O-based CDESs.

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Entry	HBD	Temperature (°C)	Time (min)	Conversion (%)	Yield (%)
1	ethylene glycol	120	60	100	52.7
2	malonic acid	120	30	100	29.7
3	serine	120	35	100	29.3
4	alanine	120	35	100	27.8
5	glycine	120	30	100	25.7
6	glycerol	120	40	100	33.4
7	xylitol	120	60	100	24.9
8	pentaerythritol	120	60	100	28.5
9 ^a	ethylene glycol	110	50	95.1	65.2
10 ^a	glycerol	110	50	86.5	51.6
11^{a}	xylitol	110	50	66.6	24.1
12 ^a	pentaerythritol	110	50	75.3	27.0
13 ^{a,b}		110	240	83.8	52.3
14 ^c		120	120	100	50.0
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^aThe substrate was glucose. ^bThe reaction was conducted in concentrated FeCl₃ aqueous solution (40 wt%), and the data were obtained from reference ³¹. ^cThe reaction was conducted in concentrated FeCl₃ aqueous solution (60 wt% and 40 wt%), and the data were obtained from reference 21.

The effect of various reaction parameters on the oxidation of cellulose was subsequently examined in FeCl₃·6H₂O/ethylene glycol (Figure 3). Reaction temperature played the key role on the reactivity of cellulose conversion (Figure 3A). When the reaction temperature increased from 90 °C to 120 °C, the yield of gluconic acid was enhanced from 12.8% to 52.7% at the cellulose concentration of 5% (w/v) (details see Table S3). However, when the reaction temperature was further increased to 130 °C, the yield of gluconic acid decreased to 39.5%, which may be resulted from that higher reaction temperature could also increase the decomposition of gluconic acid (Figure 4). Reaction time was another parameter to affect the performance of the cellulose transformation (Figure 3B). When the reaction was conducted at the optimal reaction temperature (120 $^{\circ}$ C), the maximum yield (52.7%) appeared at 60 minutes with a cellulose concentration of 5% (w/v). However, the yield decreased with longer reaction time than 60 minutes because longer reaction time caused side reactions of gluconic acid. It suggested that 120 °C and 60 minutes were the optimal reaction temperature and time for the cellulose conversion in FeCl₃·6H₂O/ethylene glycol. In addition, the effect of cellulose concentration in FeCl₃·6H₂O/ethylene glycol on gluconic acid yield was studied at the optimal conditions. As shown in Figure 3C, lower yield of product could be detected at a low cellulose concentration, which was probable caused by the further degradation of the generated gluconic acid. The gluconic acid yield increased from 24.5% to 52.7% when the cellulose concentration increased from 2.5% to 5%. When the cellulose concentration was more than 5%, the product yield decreased sharply from 52.7% to 21.6% (Table S4), presumably because the FeCl₃·6H₂O/ethylene glycol became insufficient when cellulose loading was larger than 5%. Compared to Xie's experimental results, our catalytic system greatly reduced the reaction time and increased the yield for the oxidation of both cellulose and glucose (Table 1, entries 13 and 14). Except for the



Figure 3. The effect of reaction time (A) (\blacktriangle is from Ref. 21 and the gluconic acid yield is 50%); temperature (B); and substrate concentration (C); on product yield in the conversion of cellulose; (D) reuse of FeCl₃·6H₂O/ethylene glycol without treatment or treated with O₂ after each cycle: cellulose (500 mg), CDESs (10 mL).

good performance, another interesting finding in FeCl₃·6H₂O/ ethylene glycol was that the product gluconic acid could be selfprecipitated from the reaction system without any additional extraction solvent because the gluconic acid was insoluble in $FeCl_3 \cdot 6H_2O/ethylene$ glycol while the reactants and some byproducts were soluble. Pure gluconic acid could be obtained by recrystallization in ethyl acetate to remove small amount of FeCl₃ and by-products contamination. Additionally, in the reaction process, FeCl₃ as the oxidant would be partly reduced into FeCl₂. Therefore, the oxidative ability of FeCl₃·6H₂O/ethylene glycol suffered from some decrease with the repeated cycles (Figure 3D). However, the oxidative ability could be easily regained by treating the used FeCl₃·6H₂O/ethylene glycol in O₂ atmosphere at room temperature overnight (Figure 3D). From this point, we considered that FeCl₃·6H₂O/ethylene glycol could be easily reused with no loss of activity (Figure 3D) due to the could be self-precipitated from the reaction system.



Figure 4. The process of cellulose oxidation to gluconic acid in FeCl₃·6H₂O/ethylene glycol.

The above results demonstrated that cellulose could successfully be transformed to gluconic acid in $\mbox{FeCl}_3\mbox{-}6\mbox{H}_2\mbox{O}/$

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ethylene glycol. It is well known that FeCl₃ has strong acidity and its acidity increased with concentration.^{32, 33} So FeCl₃·6H₂O/ ethylene glycol (molar ratio 2:1) has strong acidity, which was helpful for catalyzing the hydrolysis of cellulose, an key step for cellulose oxidation. On the other hand, FeCl₃ has oxidative power (E=0.77V for Fe³⁺/Fe²⁺), and experimental results showed that glucose could be oxidized into gluconic acid by FeCl₃.³¹ On the basis of the above experimental results and discussions, the pathway for the oxidation of cellulose to gluconic acid in FeCl₃·6H₂O/ethylene glycol were described as follows. First, cellulose was dissolved rapidly in FeCl₃·6H₂O/ethylene glycol, resulting in a shift from heterogeneous reaction to homogeneous one compared with the aqueous system, and thus a high reaction efficiency could be achieved in FeCl₃·6H₂O/ ethylene glycol. Subsequently, the dissolved cellulose was hydrolyzed into glucose because of the acidity of FeCl₃·6H₂O/ ethylene glycol. Then, glucose was oxidized into gluconic acid using the oxidative power of the solvent, and FeCl₃ was partly reduced to FeCl₂, which could be re-oxidatized to FeCl₃, and thus the oxidative ability of the solvent would be regained completely. Additionally, some side-reactions could be happened in FeCl₃·6H₂O/ethylene glycol due to the catalytic function of FeCl₃.

In summary, a family of FeCl₃-based CDESs were formed, and most of the CDESs had low viscosity, high conductivity, and low melting point. These CDESs could be used as solvent and catalyst simultaneously for transformation of cellulose to gluconic acid because of the catalytic action of ferric chloride, and FeCl₃·6H₂O/ethylene glycol showed the best performance with a complete cellulose conversion and a gluconic acid yield of 52.7%. More importantly, the product gluconic acid could be self-precipitated from the reaction system, so the process of the product separation could be omitted. The present method achieved the integration of solvent and catalyst as well as reaction and separation, which is a green and sustainable process, and has great potential in industrial application.

Conflicts of interest

There are no conflicts to declare.

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