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Precipitation of chitosan from ionic liquid solutions by compressed CO_2 anti-solvent method†

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The utilization of compressed CO_2 as anti-solvent to precipitate chitosan from acetate-based ionic liquid (IL) solutions is presented. Volume expansion and solvatochromic behavior of IL are investigated to explain the precipitation
10 **mechanism. The regenerated chitosan is characterized and utilized as a catalyst in the formation of imines efficiently.**

Chitosan is a kind of abundant and bio-renewable polysaccharide. The excellent biocompatible and biodegradable properties of chitosan make it useful for fertilizer, industrial separation
15 membranes, ion-exchange resins, pharmaceutics, cosmeticology and so on.[1] Unfortunately, chitosan is insoluble in many conventional organic solvents, which restricts their applications. Recently, ionic liquids (ILs), which have outstanding solvation potential,[2] have been regarded as an efficient substitute of
20 conventional solvents for chitosan dissolution.[1b, 3] The utilization of ILs can overcome some drawbacks of traditional systems, such as volatile, corrosive or toxic. However, the separation of ILs and chitosan are difficult since both the ILs and chitosan have negligible vapour pressure.[4] Up to date, molecular solvents such
25 as water or ethanol have been used as anti-solvent to regenerate chitosan from ILs;[3g, 5] but it is worth noting that these commonly used methods may give rise to another problem – the separation of the ILs and the anti-solvent, which is not so applicable in industry. So, the investigation on chitosan separation from ILs is
30 of great importance.

Compressed or supercritical CO_2 is abundant, nontoxic, nonflammable, and can be recycled easily.[6] Dissolution of CO_2 can change the properties of the liquid solvents considerably.[7] The properties of the liquid solvents can be tuned continuously by
35 controlling the pressure or temperature of CO_2. Compressed CO_2 is quite soluble in various organic solvents and causes them to expand greatly.[8] However, many solutes are soluble in organic solvents but not in CO_2. To some extent, the CO_2 in organic solvents can act as a gas anti-solvent, including recovery of the
40 nanoparticles and extraction of organic compounds.[9] In addition, utilization of CO_2 is environmentally benign, because it can be easily removed by depressurization, which makes the post-processing easier in comparison with the conventional additives that usually cause contamination or modification of the products.
45 In the present work, considering that CO_2 can dissolve in ILs, but IL does not dissolve in CO_2, we attempt to explore the recovery of chitosan after dissolution in IL by compressed CO_2. By control of the pressure and reaction time, chitosan micro-

particles could be precipitated and recovered. The effects of CO_2
50 and the operating conditions on the properties of IL by this method were also investigated, including the volume expansion and solvatochromic behavior of IL. Finally, the regenerated chitosan was characterized to examine its structure and thermal stability and used to catalyze the synthesis of imines efficiently.
55 The IL, 1-butyl-3-methylimidazolium acetate ([Bmim]OAc), which is one of the most efficient ILs for the dissolution of biomass,[1b, 5b, 10] was utilized to solubilize chitosan. It is worth noting that previous researches on the solubility of biomass in ILs were paid little attention on the effect of atmosphere. For the
60 purpose of practical production, we investigated the chitosan dissolution in [Bmim]OAc under the dry air atmosphere. As shown in Fig. 1, the solubility of chitosan under the dry air is increased with the temperature. The solubility in [Bmim]OAc at 130 °C (13.1) is nearly 3 times that at 80 °C (4.4), which implies
65 that some of hydrogen bonds in chitosan have been disrupted by the increase of temperature.
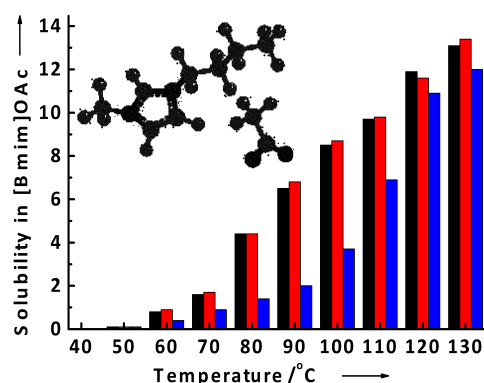
Fig. 1 Solubilities (gram per 100 g of the IL) of chitosan in [Bmim]OAc at different temperatures under air (black bar), N_2 (red bar) and CO_2 (blue bar) atmosphere. The
70 inset shows the stucture of [Bmim]OAc.

For comparison, the chitosan dissolution in [Bmim]OAc under the N_2 atmosphere was investigated. The results show that the chitosan solubilities in [Bmim]OAc under the two atmospheres are nearly identical. It can be explained by the fact that the
75 solubilities of N_2 and O_2 in ILs are both very low,[11] and the content of other components in air such as CO_2 is at a low level,

which cannot affect the solvation ability of IL. Thinking about the possible interaction between CO_2 and [Bmim]OAc, we also use CO_2 as flowing gas in this part. From Fig. 1, it can also be concluded the dissolution process became harder below 110 °C if CO_2 is used. CO_2 can be absorbed by [Bmim]OAc at low temperature, and the content of CO_2 decreases with the increasing temperature. In addition, at each temperature the sample is swept by N_2 and the ability of dissolving chitosan can be recovered. This suggests that CO_2 molecule occupies the bulk volume of IL and hinders the cleavage and formation of hydrogen bonds between IL and chitosan, which acts as a gas anti-solvent and plays a more negative role in the dissolution of chitosan, while the influence of the atmosphere became unimportant over 120 °C. Furthermore, CO_2 could be easily separated from the system, so the dissolution of chitosan can be switched by the selection of N_2/CO_2.

As is known, the solubility of chitosan in the acetate-based ILs increases with increasing of temperature. But acetate-based ILs have a lower thermal stability than other commonly used ILs. The thermal stability of the ILs is also studied since the dissolution of chitosan in ILs usually employs at a relatively high temperature. Attenuated Total Reflection Fourier Transform Infra Red (ATR-FTIR) spectroscopy in Fig. S1 showed that a small amount of acetic acid existed in [Bmim]OAc at 140 °C. The absorption band between 1747 and 1669 cm^{-1} in the acetic acid spectrum is associated mainly to the C=O bond stretching vibration,[12] while the IL [Bmim]OAc does not show any absorbance in this frequency interval. It can be concluded that acetate acid may be generated at 140 °C (Scheme S1), because the imidazolium cation may react with acetate anion to generate a carbene.[3c, 13] So, when the ILs was used circularly in the process of chitosan dissolution, the operated temperature may not higher than 130 °C.

As is described above, how to separate the chitosan from IL is a significant issue. In this part, the regenerated chitosan were isolated from the 9.0 wt% chitosan/[Bmim]OAc solution by compressed CO_2. Table 1 shows that the regenerated chitosan can be formed until the pressure reached 6.60 MPa at 25 °C. With further increases in pressure, the yield of regenerated chitosan cannot increase (Table 1, Entry 1-6). The yield increased with the increasing reaction time at 6.63 MPa in 5 h. After that, the yield keeps constant, even at 10 MPa (Table 1, Entry 7-10). So, the best condition for regenerated chitosan from 9.0 wt% solution by compressed CO_2 is under 6.60 MPa at 25 °C for 5 h. The effect of initial concentration of chitosan in [Bmim]OAc show that the minimum concentration of the system for regenerated chitosan is between 3.0-4.0 wt% (Fig. S2 and Table 1, Entry 11-14). In addition, the intrinsic viscosity of the regenerated chitosan in HAc/NaAc solution was measured by using an Ubbelodhe viscometer in order to obtain the average molecular weight of the regenerated chitosan by different anti-solvent, and then the degree of polymerization (DP) of the regenerated chitosan was calculated and shown in Fig. 2. Generally, the regenerated chitosan by compressed CO_2 has a higher molecular weight than other regenerated ones. Combined with the chitosan 5, we can conclude that some long chain molecule may be recovered prior by using compressed CO_2, which made the average molecular weight of the regenerated chitosan more centralized. It was also

shown that lower pressure (5.39 MPa) was suitable at a lower temperature of 15 °C (Table 1, Entry 15).

Table 1 The effect of initial concentration (IC), temperature (T), pressure (P) and reaction time (RT) on regenerated chitosan using compressed CO_2

Entry	IC / wt% [a]	T / °C	P / MPa	RT / h	Yield / % [b]
1	9.0	25	6.63	5	60.6
2	9.0	25	8.00	5	60.8
3	9.0	25	10.01	5	61.7
4	9.0	25	12.03	5	61.3
5	9.0	25	6.07	5	--
6	9.0	25	6.02	10	--
7	9.0	25	10.00	10	61.0
8	9.0	25	6.67	1	22.4
9	9.0	25	6.63	3	47.7
10	9.0	25	6.69	10	60.9
11	6.0	25	6.63	5	43.5
12	6.0	25	8.04	5	42.6
13	6.0	25	10.00	5	43.9
14	3.0	25	6.65	5	--
15	9.0	15	5.39	5	62.2

[a] The chitosan/[Bmim]OAc systems with different concentrations.

[b] Isolated yields.
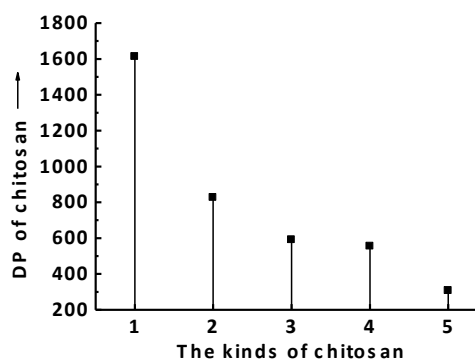
Fig. 2 Degree of polymerization of the regenerated and native chitosan. The kinds of chitosan: 1 was the native one; 2, 3 and 4 were the regenerated chitosan by compressed CO_2, ethanol and deionized water respectively; 5 was regenerated the remnant chitosan by ethanol after the step of anti-solvent process by compressed CO_2.

At the pressure of 6.60 MPa, compressed CO_2 can be dissolved greatly into the chitosan/IL solution. CO_2 is non-polar, while it has a relatively high quadrupole,[14] so it can be strongly interacted with the cations and anions of IL. Considering the fact that chitosan as a solute may affect the property of IL, a comparison between volume expansion with and without chitosan has been carried out, which showed that the addition of chitosan has a neglectable effect on it. It can be easily seen that the solution can expand after dissolution of CO_2 in it (Fig. S3). The volume expansion of IL caused by compressed CO_2 at the high

pressure may disrupt hydrogen bonding between chitosan and IL due to the longer distance between them. The compressed CO_2, whose attractive intermolecular force might drive the chitosan molecule to a more favorable region, has more free volume and distribute abundantly around the chitosan to form some molecular cluster, which can promote the separation between chitosan and IL.

It is known that in a gas anti-solvent process, the liquid solvent properties can be tuned by pressure adjustment, because the solubility of the gas in the solvent is a function of pressure. The mixture of a pure gas and a solution system can be defined as gas expanded liquids (GXLs). Since the solvent power of GXLs can be tuned by varying the liquid phase concentration as a function of pressure, some of the physical or chemical properties of the liquid or solvent may be modified at the same time, making it less viscous and thereby changing its mass transport properties. In order to analyze the role of CO_2, we measured the Kamlet-Taft parameter, including π^*, α and β, for the mixture of [Bmim]OAc and CO_2 as functions of pressure based on the solvatochromic behavior of the indicator *N,N*-diethyl-4-nitro-aniline (DENA), 4-nitroaniline (NA) and Reichardt's dye 33.[7d, 15]
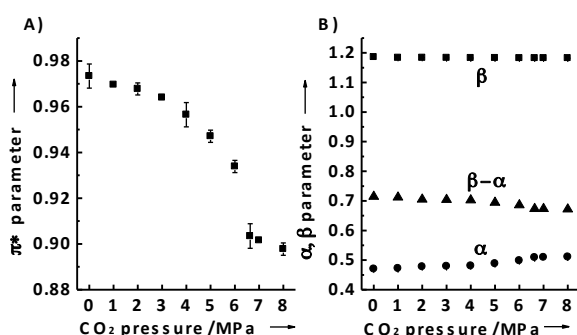

Fig. 3 Kamlet-Taft parameters for [Bmim]OAc/CO_2 mixtures at 25 °C under different pressure, including the π^*, α, β and (β-α) parameters.

We assume that the amount of probe molecules partitioning into the CO_2 fluid phase is negligible. A plot of the Kamlet-Taft parameters against CO_2 pressure at 25 °C is shown for [Bmim]OAc in Fig. 3. It can be observed that a relatively dramatically decrease in π^* value with adding of CO_2 under the pressure of 6.6 MPa, while it decreased slight above 6.6 MPa. It indicated that the polarity of the system and some non-specific interactions between the cations and anions such as dipole-dipole interaction and dipole-induced dipole interactions have changed, especially after increasing the CO_2 pressure to 6.60 MPa. As a small molecule, CO_2 can occupy the volume between the cations and anions, which can be also explained that it might interact with the dye directly or interact with cations and anions in such a way as to disrupt their interactions with the dye. On the other hand, CO_2 under different pressures had little effect on α and β parameters, and it can be shown a decreasing trend for the "net basicity of hydrogen bonds"[16] of [Bmim]OAc, which are well in agreement with the experimental results of other ILs in the previous references.[7c, 15a] It revealed that the synergistic action between the dissolution of CO_2 in IL and cations or anions has a possible influence on the process of the chitosan separation from the IL.

Furthermore, the regenerated chitosan was used as catalyst in the dehydration reaction between carbonyl compounds and amines to form Schiff's base imines,[17] intermediates of the Strecker reaction. The reaction of aniline and 2-hydroxybenzaldehyde was chosen the model reaction and carried out under mild conditions. The reaction mixture liquefies completely in a minimum amount of ethanol and then the chitosan were added in. The yields of imines catalysed by different kinds of chitosan as the increasing of time are shown in Fig. 4, and more detailed results of the reaction are summarized in Table S1. The blank experiment showed that no desired products were formed in the absence of chitosan even after 24 h at room temperature (Table S1, Entry 1). The desired imines could be detected in 6 h with 6 mg native chitosan as catalyst (Table S1, Entry 2), which can be attributed to the forming of intermediate via hydrogen bond between the reactants and the hydroxyl and amine groups of chitosan. As the catalyst, the regenerated chitosan by compressed CO_2 can make the reaction reach the equilibrium in 3 h (Fig. 4). It exhibited higher yield in a shorter reaction time than the chitosan regenerated by ethanol and the native powder (Table S1, Entry 2-6). It may be ascribed that some of inter- and intra- hydrogen bonds of chitosan have been broken[16, 18] and more chitosan micro-particles were formed in the dissolution and regeneration process, as evidenced by FT-IR spectra, X-ray diffraction (XRD), thermogravimetric analysis (TGA) and transmission electron microscop (TEM) (Fig. S4-S7), which could perform lower steric hindrance effect and more active in the catalytic reaction. Moreover, the regenerated chitosan, including alcogels and aerogels, exhibited a high surface area, so more –NH_2 group can play a catalytic role in the reaction and they may be more suitable and effective in the synthesis of imines. The same optimized conditions were applied to other amines and aldehydes for the synthesis of other imines (Table S1, Entry 7-16), it is obvious that using renewable chitosan with ILs pretreatment and anti-solvent recovery in the synthesis of imines is a simple and efficient method.
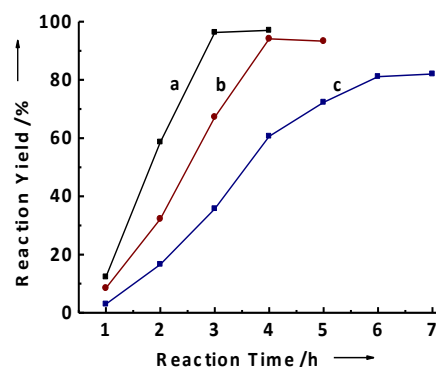

Fig. 4 The yields of imines via the reaction between aniline and 2-hydroxybenzaldehyde catalysed by the regenerated chitosan by compressed CO_2 (a), the regenerated chitosan by ethanol (b), and the native chitosan (c) in ethanol under room temperature.

Conclusion

In summary, the precipitation of chitosan from IL by using compressed CO_2 has been investigated. It is a sustainable route for chitosan separation and IL recycling. CO_2 can expand IL and change the solvatochromic behavior of IL, which affect the dissolution of chitosan in IL. Besides, the renewable chitosan with ILs pre-treatment and anti-solvent recovery is a kind of eminent heterogeneous catalyst in the Schiff's base reaction for synthesis of imines. It is worthwhile to promote and expand this method into other fields of biomass treatment and application in the future.

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Notes and references

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Table of contents

Chitosan can be efficiently regenerated from ionic liquid by using compressed carbon dioxide.