Direct Conversion of Chitin into a *N*-containing Furan Derivative

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Abstract

This paper describes the direct conversion of chitin into a nitrogen-containing (*N*-containing) furan derivative for the first time. Under optimized conditions, the yield of 3A5AF reaches 7.5% with ca. 50% chitin conversion by using boric acid as the catalyst, alkaline chlorides as additives, and NMP as solvent. A variety of other compounds, including levoglucosenone, 4-(acetylamino)-1,3-benzenediol, acetic acid and chitin-humins, have been identified as side products, based on which a plausible reaction network involved in the reaction is proposed. Mechanism investigation by NMR studies and poison tests confirm the formation of a boron complex intermediate during the reaction, shedding light on the promotional effects of boric acid. Kinetic study shows that the depolymerization of the chitin crystalline region is rate-determining, and therefore disruption of the hydrogen bonding in the crystalline region of chitin, either before or during the reaction, is the key to further improve the reaction yields.

1. Introduction

The imperative to reduce society's dependence on crude oil has led to significant research efforts on the conversion of biomass[1, 2]. So far, remarkable progress has been made for the conversion of lignocellulosic biomass into bioethanol[3] and value-added platform chemicals[4-9]. On the other hand, much less attention has been directed to the utilization of chitin, which is a major component of the exoskeletons of insects and crustaceans[10], and the second most abundant biopolymer on earth. The chemical structure of chitin is highly similar with cellulose, consisting of *N*-acetyl-D-glucosamine (NAG) monosaccharide units as the building blocks linked together by β-glycosidic bonds (see Figure 1). Chitin has an underestimated but remarkable potential for the production of renewable, value-added chemicals, especially *N*-containing compounds, as it comprises 7 wt% of biologically-fixed nitrogen. Nowadays, the manufacture of *N*-containing chemicals is typically laborious and energy intensive starting from high temperature, high pressure ammonia synthesis. Chitin is an attractive, sustainable and cheap organic nitrogen resource that holds the potential to revolutionize the production of certain *N*-containing chemicals.

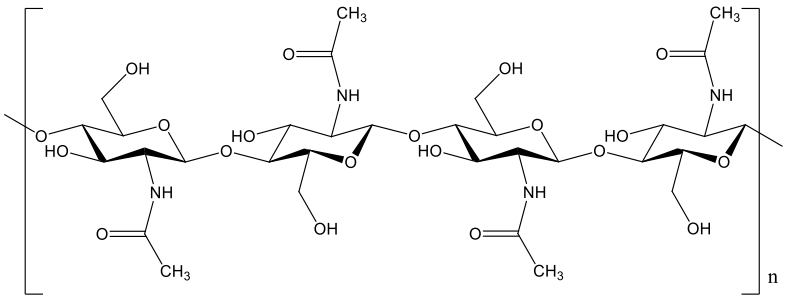

Figure 1 The chain structure of chitin polymer.

Current utilization of chitin remains very limited. Chemical derivatizations have been frequently conducted to modify the properties of chitin[11-13]. However, these are based on stoichiometric chemical reactions on the substitution groups on chitin polymer chains, and therefore are unable to produce non-polymeric chemicals. Pyrolysis or radiolysis of chitin/chitosan to produce volatile aromatic heterocyclic compounds such as pyrazines, pyridines, pyrroles and furans has been reported[14-16]. Nevertheless, these methods cannot achieve a selective degradation resulting in trace amount of products (< 2 %). Hydrolysis of chitin by enzymes or concentrated acids affords NAG and oligomers, but this route suffers from low efficiency, environmental issues and limited product diversity[17, 18]. Starting from chitin, the production of 5-(chloromethyl)furfural,[19] levulinic acid (LA),[20] and 5-hydroxymethylfurfural (5-HMF)[21] with yields ranging from 9-11% were reported very recently. Unfortunately, the precious, biologically fixed nitrogen was lost during the transformation. To the best of our knowledge, direct catalytic conversion of chitin into value-added nitrogen-containing chemicals with appreciable yields has not yet been realized.

In 2012, the transformation of NAG into 3-acetamido-5-acetylfuran (3A5AF) was reported by dehydration reactions, demonstrating the feasibility of obtaining *N*-containing furan derivatives from chitin monomers[22, 23]. Encouraged by this advancement, we for the first time tested the possibility of producing 3A5AF directly from chitin, which, in principle, could be obtained by combining chitin hydrolysis and NAG dehydration. In this paper, 6 solvents, 26 catalysts and their combinations were evaluated for the reaction. For the optimized catalytic system, detailed studies concerning the reaction kinetics, reaction pathway, effects of water as an additive, and mechanistic investigation using NMR and poison tests were conducted.

2. Experimental

Materials

Chitin was purchased from Wako Pure Chemical Industry. Boric acid was purchased from Amresco. Sodium chloride (NaCl) was purchased from Schedelco. Lithium chloride (LiCl), dimethylacetamide (DMA) were purchased from Alfa Aesar. *N*-acetyl-D-glucosamine (NAG), iron (II), tin(II), barium and cesium chloride salts ($FeCl_2$, $SnCl_2$, $BaCl_2$ and CsCl, respectively), *N*-methyl-2-pyrrolidone (NMP) and dimethyl sulfoxide (DMSO) were purchased from Sigma Aldrich. Dimethylformamide (DMF) and glycerine (Gly) were from Fisher Scientific. Ethylene glycol (EG) was purchased from Fluka. DMSO-d_6 was purchased from VWR Singapore. Other chemicals, such as copper chloride ($CuCl_2$), tungsten oxide (WO_3), cobalt chloride ($CoCl_2$), nickel chloride ($NiCl_2$) and calcium chloride ($CaCl_2$), were obtained from Sinopharm Chemical Reagent (SCR). All chemicals were used as received.

General procedure

Under optimized conditions, chitin (100 mg, 0.5 mmol based on NAG monomer) was placed in a thick-wall glass tube (35 mL). Following that a magnetic stir bar, boric acid (122 mg, 2.0 mmol), NaCl (58 mg, 1.0 mmol) and anhydrous NMP (3 mL) were added. The tube was sealed by a Teflon stopper and placed into a pre-heated oil bath at 215 ºC for 1 h under a stirring speed of 400 rpm. After the reaction, the reaction mixture was cooled down to room temperature. Methanol (15 mL) was added. After thorough mixing, a portion of the liquid sample (1 mL) was filtered by a PTFE syringe filter with 0.2 μm pore size before analyzing by high-performance liquid chromatography (HPLC).

Noteworthy, all the reactions were carried out in a similar manner whilst varying the following parameters: catalyst (or catalyst amount), solvent, reaction time and temperature.

HPLC analysis was performed on an Agilent 1200 Series (Agilent Technologies, Germany) LC system by using an Agilent ZORBAX Eclipse carbon-18 column. The mobile phase was 83% water and 17% acetonitrile. The flow rate was kept at 0.5 ml/min with run time 20 min. A UV-vis detector setting at 230 nm was used to analyze the product. 3A5AF standard was prepared following a literature method[22] and the purity verified by nuclear magnetic resonance (NMR) spectroscopy. A calibration curve (Figure S1) was generated with a series of 3A5AF standard solutions and used for quantification of the product.

To obtain the conversion of chitin, the reaction mixture was centrifuged after the reaction. The remaining solid was washed with water three times and dried in an oven over 24 h at 70 ºC and weighed. The conversion of chitin is calculated as:

$$Conversion = \frac{Starting\ chitin\ (mg) - Residual\ solid(mg)}{Starting\ chitin\ (mg)} * 100\%$$

Identification of other products

After the reactions, the liquid samples from six parallel experiments were combined. Then, reduced pressure distillation was applied for the removal of NMP solvent. Edwards Rotary Vane Pump (Model RV3) with ultimate pressure 0.002 mbar was used. The liquids were put into a round bottle flask and heated at about 90˚C under vacuum. After the majority of solvent was removed, column chromatography was employed for separation using silica gel with particle size ranging from 40 to 63 μm as the stationary phase and 5% methanol and 95% dichloromethane as the mobile phase. Afterwards the collected fractions were concentrated by the evaporator and analyzed on Gas chromatography-mass spectrometry (GC-MS).

Characterization

X-ray powder diffraction (XRD) was performed on a Bruker D8 Advanced Diffractometer with Cu Kα radiation at 40 kV. Gel permeation chromatography (GPC) analysis was carried out with a system equipped with a Waters 2410 refractive index detector, a Waters 515 HPLC pump and two Waters styragel columns (HT 3 and HT 4) using DMF as eluent at a flow rate of 1 ml/min at 25 ˚C. The raw data were processed using narrow polydispersity polystyrene standards and calibration using the software Breeze. Fourier transform infrared spectroscopy (FTIR) was conducted on a Bio-Rad FTS-3500 ARX instrument. Gas chromatography-mass spectrometry (GC-MS) was performed on an Agilent 7890A GC system with 7693 Autosampler and 5975C inert MSD with triple-axis detector. Elemental analysis (EA) was conducted using an Elementar Vario Micro Cube. Proton, boron and carbon NMR (^{1}H, ^{11}B and ^{13}C NMR) were performed on a Bruker ultrashield 400 plus spectrometer.

3. Results and discussion

Solvent screening

Similar with cellulose[24-26], one of the major challenges for chitin conversion is its robust crystal structure with extensive inter- and intra- hydrogen bonds among the polymer chains. Solvent or solvent systems that are able to dissolve chitin should prove advantageous in its transformation. Previously, dipolar aprotic solvents combined with metal salts, such as 5-7% LiCl/NMP and LiCl/DMA systems, have been reported to dissolve chitin[27]. We started by screening 6 solvents including DMA, DMF, DMSO, NMP, EG and Gly. The first four solvents are commonly used for sugar dehydration[28-32] whereas EG and Gly are selected because their hydroxyl groups may disrupt the hydrogen bonding network in chitin. When chitin was dispersed in these 6 solvents under 195 or 225˚C for 1 h, no 3A5AF was detected. LiCl (5 wt%, based on solvent) was added into these solvents as a solubility enhancer agent, but the yield of 3A5AF remained 0% in all cases. These two series of experiments indicate chitin dehydration is a catalytic process and 3A5AF could not be obtained by thermal decomposition under the temperatures investigated, irrespective of the solvent used.

To differentiate the solvent effect in converting chitin into 3A5AF, different catalysts that are active in sugar dehydration, such as HCl[33-35], boric acid[36-38], and their combination with LiCl, were added into the solvents. The results are shown in Figure S2. By adding HCl, 3A5AF was obtained in DMA, DMF

and NMP (2.3, 1.1 and 3.0% respectively). By adding boric acid, 3A5AF was obtained in DMA, DMF, DMSO and NMP. No 3A5AF was detected in EG and Gly under these conditions. The best performance was achieved in the presence of boric acid and LiCl in NMP, reaching a 3A5AF yield of 5%. From above DMA, DMF, DMSO and NMP are all suitable solvents for chitin conversion but NMP appears to be most effective. Previously, DMF and DMA were identified to be the best solvents for chitin monomer dehydration, and NMP was slightly less effective. The different performances may be ascribed to the structure difference of chitin and NAG. DMA and DMF are smaller in their molecular size, which may favor the solute-solvent interaction in sugar monomer conversion. On the other hand, a major challenge in chitin conversion is its low solubility, and therefore NMP is more effective considering LiCl/NMP represents a classic solvent system for chitin dissolution. After that, the system was further optimized by conducting the reaction at different temperatures and with different solvent to chitin ratio (Figure S3 & S4). The optimal temperature was identified to be 215 ºC and the optimal solvent to chitin ratio to be 3 mL to 100 mg.

Catalyst/additives screening

We systematically evaluated the performance of a wide range of catalysts for chitin conversion into 3A5AF in NMP under selected conditions. These catalysts included 13 metal chlorides, 6 organic/simple inorganic acids, 5 bases and 3 heteropolyacids (Figure 2A). Heteropolyacids, which have been reported to be excellent catalysts for glucose/cellulose dehydration[39-41], did not produce any 3A5AF. Bases were not effective either. $Ba(OH)_2$ is the only basic catalyst that produced 3A5AF, but the yield was very low (0.4%). Metal chlorides are widely used as the catalysts for glucose dehydration to 5-HMF[42-46], and in our experiments $CrCl_3$ effectively promoted 3A5AF formation (2.5%). Organic acids such as phenylboronic acid and acetic acid are not able to catalyze the reaction. Among the inorganic acids, HCl is the only one effective for chitin conversion into 3A5AF with a yield of 2.2%, indicating the promotional effect of chloride ion in the reaction. This is consistent with previous finding in NAG, glucose and cellulose conversion where chloride played an important role[22, 47, 48]. It is very likely that chloride acts as a promoter to disrupt the hydrogen bonding in the substrate rather than as a catalyst, considering the majority of metal chlorides are inactive in 3A5AF formation. Boric acid is the most effective catalyst for the reaction with a 3A5AF yield of 3.6%. Presumably, boric acid promotes both the hydrolysis of chitin and the dehydration due to its acidity and this gives rise to its catalytic ability. In previous studies it was proposed that boric acid coordinated with the hydroxyl groups of glucose and this catalyzes its dehydration to generate 5-HMF[38].

In an attempt to obtain higher yields, combinations of catalysts were investigated. Since boric acid is the most effective single component catalyst, the combinations are based on boric acid and another catalyst (see Figure 2B). Interestingly, the combination of boric acid with some metal chlorides, such as $MnCl_2$, $SnCl_4$, CuCl and $ZnCl_2$, and heteropolyacids did not afford any 3A5AF from chitin. Boric

acid with $CuCl_2$, WO_3, $CoCl_2$ and $NiCl_2$ led to 3A5AF formation but the yield was lower than using boric acid alone as the catalyst. On the other hand, the combinational use of boric acid with $CrCl_3$, LiCl, NaCl and $CaCl_2$ resulted in enhanced yields. Since the highest yields were obtained by using the combination of boric acid and alkali/alkaline earth metal chlorides, more detailed optimizations were conducted on a series of alkali/alkaline earth metal chlorides, or HCl, combined with boric acid. Different amounts of catalysts were investigated, and the results are compiled in Figure S5. This led to the discovery of a few catalyst systems that are able to produce 6-7 % 3A5AF directly from chitin within one hour. These include: 1) the combination of 400 mol% boric acid and 200 mol% NaCl; 2) the combination of 200 mol% boric acid and 100 mol% LiCl; 3) the tri-component combination of 400 mol% boric acid, 200 mol% LiCl and 100 mol% HCl. The last combination is slightly better than the other two, reaching a 3A5AF yield of 6.2%. The addition of HCl is assumed to facilitate the hydrolysis of chitin.

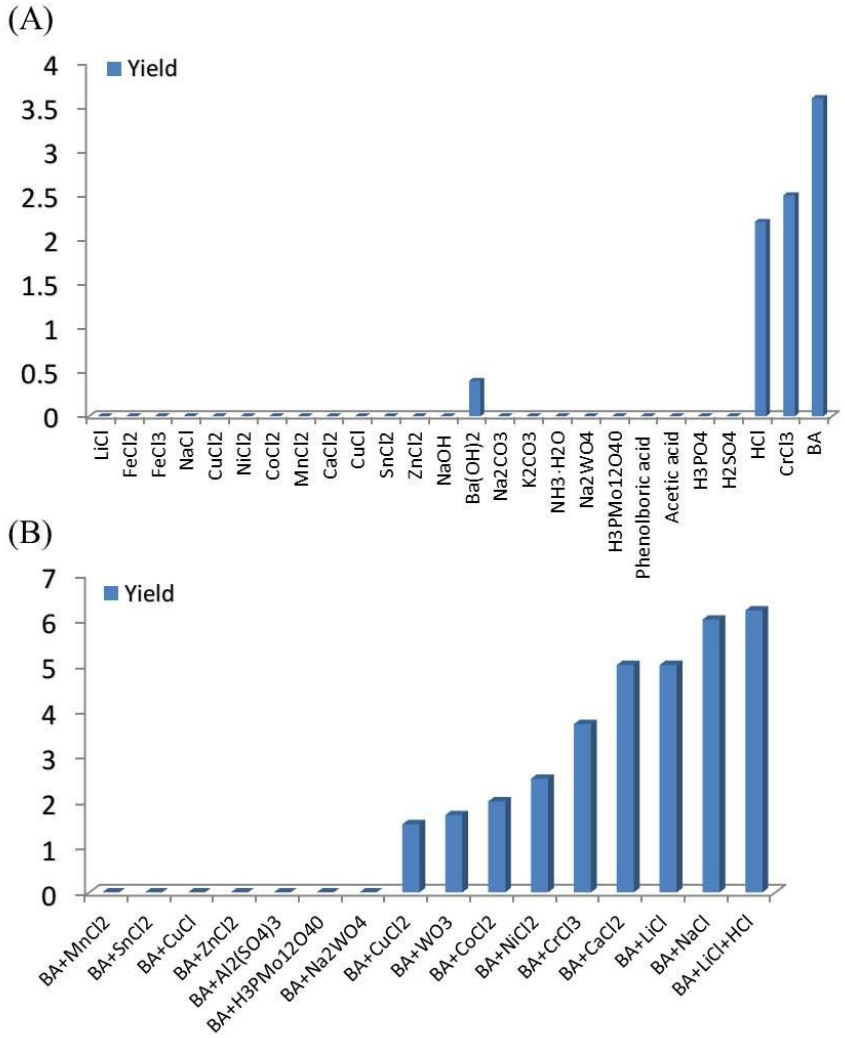

Figure 2 Catalyst screening for chitin conversion into 3A5AF. Reaction conditions: 215˚C, 1 h, NMP (3 mL), chitin (100 mg), 200 mol% catalyst based on chitin monomer (400 mol% for boric acid). (A) single component screening; (B) combinations of catalysts. (BA is short for boric acid).

Catalytic kinetics

The combination of boric acid and NaCl was chosen to study the chitin conversion and the 3A5AF yield as a function of reaction time (see Figure 3). Note that the chitin conversion is calculated based on the recovered solids after reaction, the value will be underestimated if insoluble char or humins forms during the reaction. In the first few minutes, the product was not yet formed despite a chitin conversion of 24%. Normally, chitin has an amorphous and a crystalline part[10, 49, 50], and amorphous chitin is more easily converted. The crystalline index for chitin ranges from 70-80%. Therefore the initial conversion can be ascribed to the conversion of amorphous chitin, which depolymerized and generated soluble, low-molecular weight oligomers. As the reaction proceeded from 5 min to 2 hours, the conversion and yield increase simultaneously. It is not unreasonable to speculate that the chitin crystalline region began to depolymerize at a later stage, because the conversion rate slows down significantly compared to the initial conversion speed. After 2 hours, a maximum 3A5AF yield of 7.5% was achieved with a chitin conversion of 58%. As the reaction further progressed, the yield dropped sharply probably due to 3A5AF decomposition. Interestingly, the chitin conversion decreased slightly after 2 hours, which is indicative of the formation of insoluble solids such as char or humins. During the entire reaction, NAG is not observed, suggesting NAG dehydration is not rate-determining. Since the depolymerization of crystalline chitin is slow and that the products are not stable, the 3A5AF yield cannot be further improved simply by prolonging the reaction time.

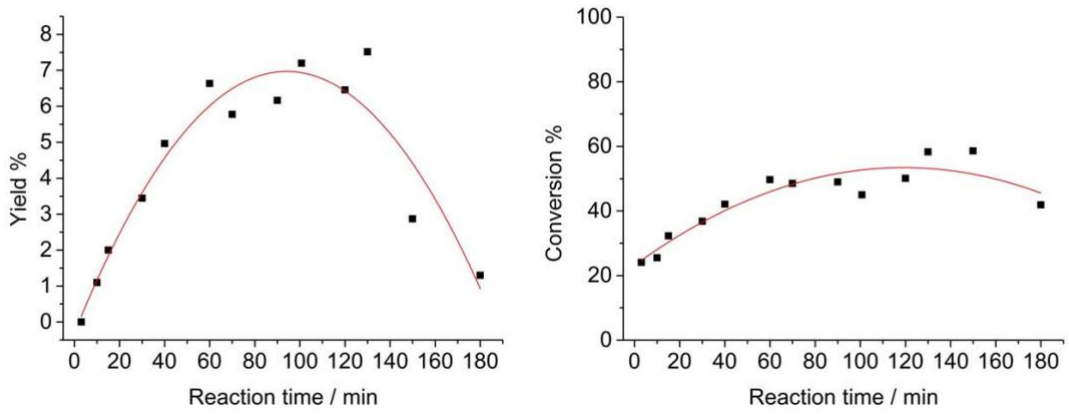

Figure 3 (A) 3A5AF yield as a function reaction time; (B) chitin conversion as a function reaction time. Reaction conditions: 215˚C, NMP (3 mL), chitin (100 mg), boric acid (400 mol%), NaCl (200 mol%).

Chitin and the recovered solids after the reaction (1 h reaction time) have been characterized by FTIR, XRD and EA. As shown in the FTIR spectrum of chitin (see Figure 4, dash line), the bands at 3452 and 3266 cm^{-1} are attributed to the OH and NH stretching, respectively. The shape and intensity of these

peaks will change if the hydrogen bonding network in chitin is altered. The bands ranging from 2886 to 2961 cm^{-1} represent CH, CH_3 symmetric stretching and CH_2 asymmetric stretching. And the CH bending, symmetric CH_3 deformation and CH_2 wagging bands appear at 1380 and 1312 cm^{-1}. The peaks at 1629 and 1662 cm^{-1} are assigned to Amide I band (two types of hydrogen bonds in a C=O group with the NH group of the adjacent chain and the OH group of the inter-chain). Amide II band (in-plane N-H bending and C-N stretching mode) and Amide III band (in-plane mode of CONH group) are observed at 1558 and 1312 cm^{-1}, respectively. The bands ranging from 1027 to 1163 cm^{-1} are attributed to the asymmetric bridge oxygen and C-O stretching[51, 52]. In the FTIR spectrum of recovered solid after the reaction, the shape, position and relative intensity of all characteristic peaks in chitin remain unchanged, indicating no appreciable modifications on the chemical structure or hydrogen bonding network in chitin. In XRD analysis (see Figure 5), the peak at $2\theta = 19^{\circ}$ represents the (110) plane of crystalline chitin[53]. The XRD pattern of the recovered solid highly resembles that of the chitin standard, suggesting there is negligible change in the crystalline region. The EA data further corroborate with FTIR and XRD analysis, as C, H, and N content remains at similar level in the recovered solid and chitin (see Table S1). From above, we can conclude that the unreacted solids maintain the chemical backbone, the hydrogen bonding network, and the crystalline structure of chitin. Chitin polymer undergoes depolymerization prior to any other transformations towards 3A5AF and side products.

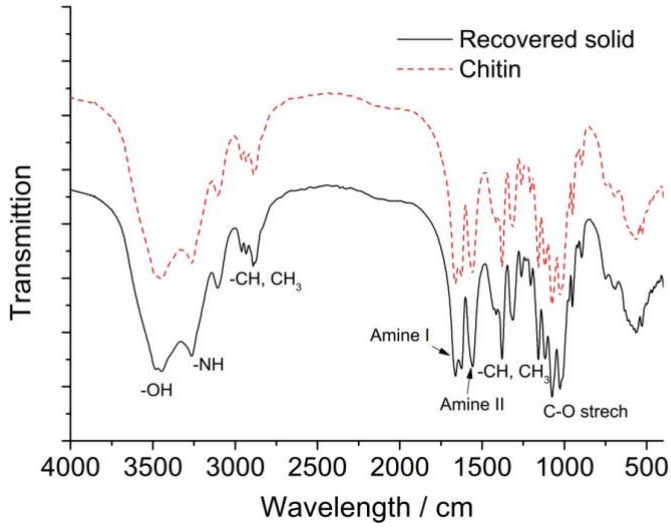

Figure 4 FTIR spectra of chitin and recovered solid after the reaction.

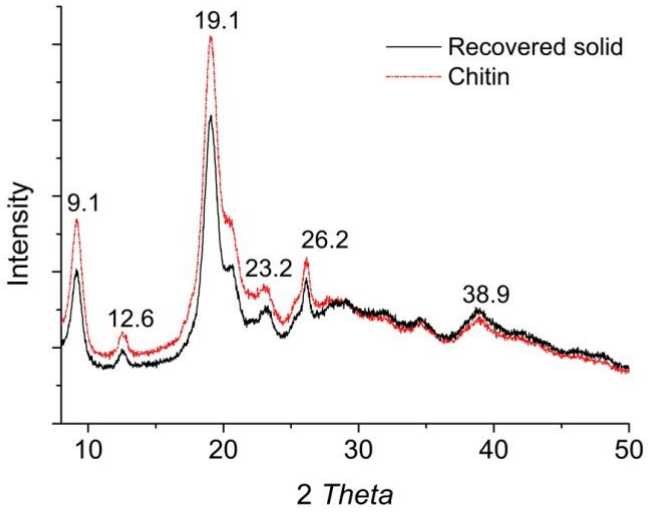

Figure 5 XRD of chitin and recovered solid after the reaction.

Reaction pathway elucidation

Under optimized conditions, 3A5AF was obtained with ca. 7.5 % yield despite a much higher chitin conversion (50%). In the following work, significant effort was spent on the identification of other products generated from chitin, by combining column chromatography, GC-MS, HPLC, EA, GPC, NMR and FTIR analysis. The major product, 3A5AF, was further confirmed by NMR technique after column chromatography separation (see Figure S6). From GC-MS a variety of other products have been identified, including levoglucosenone, acetic acid and 4-(acetylamino)-1,3-benzenediol. Besides, a black solid fraction was obtained after separation and characterized by GPC, FTIR and EA. It shares some similarities with humins reported in glucose/cellulose conversion,[54] as both are polymeric black solid and have a higher C/H ratio (see Table S1). On the other hand, the structure of the black solid from chitin is not identical with previously reported humin materials. Humins generated from glucose/cellulose conversion are assumed to form by aldol condensation between sugars and furanics, and the furanic and C=C conjugating bands can be observed in the FTIR spectra[55]. These bands are absent in the FTIR spectrum of the black solid from chitin. Furthermore, humins from glucose/cellulose contains no nitrogen, whereas the nitrogen content in the black solid (8%) is even higher than that in chitin. We tentatively term this black solid fraction as chitin-humins. GPC analysis indicates the average molecular weight of the chitin-humins is at around 1 kDa (Figure S7). Interestingly, GPC analysis of the raw reaction mixture revealed another fraction of products with MW of 3-4 kDa, in addition to small molecules and chitin-humins (Figure S8). This fraction may be the partially depolymerized and solubilized part of chitin generated in the reaction.

Based on these we propose a plausible reaction pathway for the formation of 3A5AF and other products (see Figure 6). Hydrolysis of chitin is the first step in the reaction, leading to the partially depolymerized chitin, NAG oligomers and eventually NAG. NAG generated in-situ undergoes three parallel reaction pathways. In the first pathway, 3A5AF is generated via a five-membered ring formed from the open ring aldose. The subsequent enolization and dehydration afford the *N*-containing furan derivative, similar to that proposed in an earlier study[22]. Alternatively, NAG dehydrates to hexatriene, after which keto-enol tautomerism, electrolytic rearrangement and dehydration take place to form six-membered ring product. The formation of aromatic compound is not unusual in biomass conversion. For example, 1,2,4-benzenetriol is widely reported in glucose conversion via 5-HMF as an intermediate[56-58]. The difference is that 1,2,4-benzenetriol forms via a five-membered furan ring whereas 4-(acetylamino)-1,3-benzenediol forms via a six-member ring intermediate. Finally, hydrolysis of acetyl amide in NAG affords acetic acid and amino-sugar. With further deamination and dehydration, levoglucosenone can be generated. The formation pathway of chitin-humin is not fully understood but it should involve the condensation reactions between NAG and amino-sugar considering its high nitrogen content.

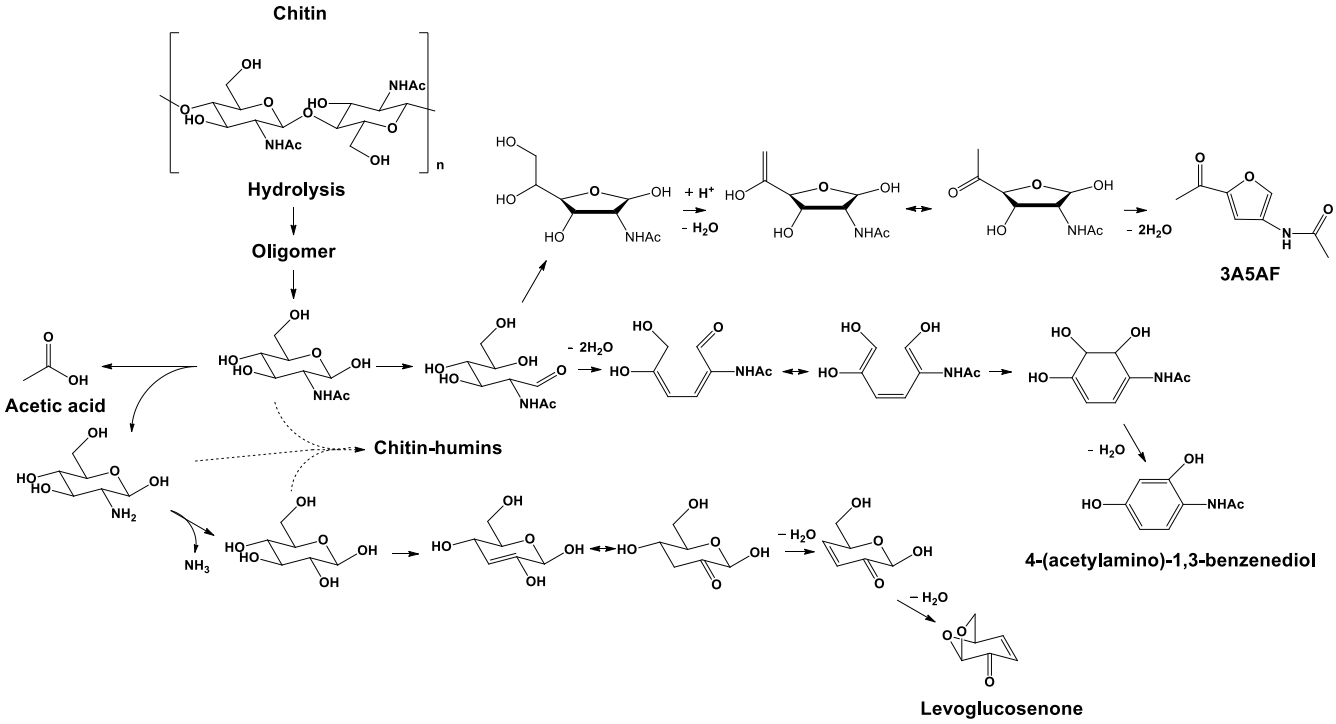

Figure 6 Proposed reaction pathway of the formation of other identified products.

Mechanism investigation

Influence of water

The reaction pathway from chitin to 3A5AF is a combination of hydrolysis and dehydration reactions. Water is required for the hydrolysis step but should have negative effects on the dehydration steps.

Furthermore, the solubility of chitin in the solvent is inversely related to water content. The influence of water was examined (Figure S9) by adding 1%, 2%, 4%, 6% and 8% water into the solvent before reaction. The addition of water clearly shows a significant inhibitory effect on chitin conversion to 3A5AF in all cases. For example, the 3A5AF yield and chitin conversion decrease by 50% in the presence of 2% water, whereas the 3A5AF yield drops to 0.5% when 8% water is added. These experiments unambiguously demonstrated the detrimental effect of water. We conclude that the trace amount of water present in chitin and the solvent is sufficient to initiate chitin hydrolysis, and the water produced during subsequent dehydration is sufficient to sustain chitin hydrolysis. The water content should be kept below 1% to enable efficient chitin conversion.

Poison test

It is known that boric acid can coordinate with the hydroxyl groups of the substrates. During the interaction, complexes with an acyclic structure or five/six-membered-ring chelate structures could be formed[44]. The specific coordination configuration could be differentiated by a simple poison test. If an acyclic complex is formed during the reaction, the conversion will be inhibited by the addition of a simple alcohol such as ethanol. If five- or six-membered-ring structure is formed, the addition of ethylene glycol (EG) and 1,3-propanediol (1,3-PG) will inhibit the reaction. In the poison tests, ethanol, EG and 1,3-PG (ratio 2:1 to the substrate) were added. For chitin conversion (see Figure 7), ethanol did not affect the product yield. However, upon the addition of EG or 1,3-PG, the 3A5AF yield decreased from 4% to 1% and 0.2%, respectively. 1,3-PG seems to be a stronger poison compared with EG. The poison experiments were conducted using NAG as the starting material (see Figure S10), and exactly the same trend was observed. Afterward, isopropanol (IPA), 1,2-PG, glycerol (Gly), 1,3-butanediol and 2,3-butanediol were added. IPA had no observable effect on the reaction whereas 1,2-PG, Gly, 1,3- and 2,3-butanediol all inhibited the reaction significantly (data not shown). As such, the 3A5AF formation is achieved via five- and six-membered ring boron complexes, and it is likely that the six-membered ring complex is dominant.

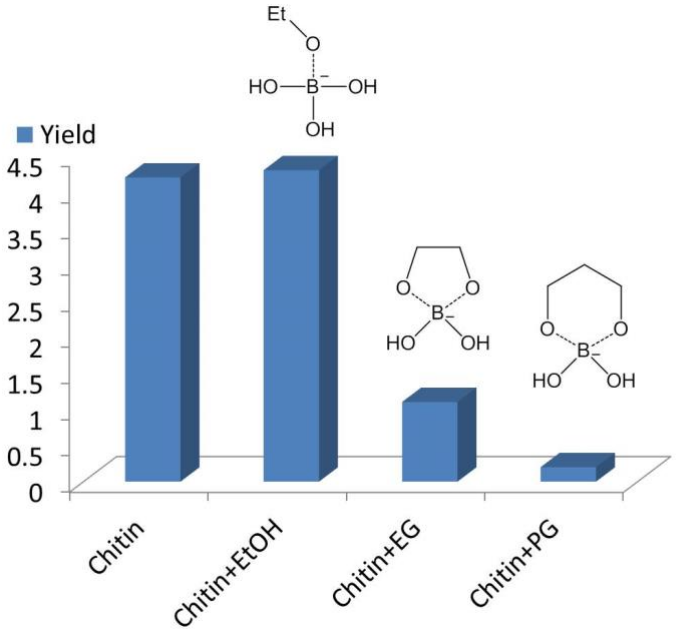

Figure 7 The inhibition effect of different alcohols as additives. Reaction condition: 215˚C, NMP (3 mL), chitin (100 mg), boric acid (200 mol%), NaCl (200 mol%).

NMR studies

In order to get some further understanding on boric acid catalyzed chitin transformation into 3A5AF, ^{1}H, ^{13}C and ^{11}B NMR techniques have been utilized. Since the solubility of NAG is much higher than chitin, and that the NMR signal of NAG is much easier to be identified and followed, the measurements were conducted by using NAG as a model substrate in the presence of 100 mol% boric acid in DMSO-d_6 (see Figure 8 for ^{13}C and Figure S10 for ^{1}H NMR). When NAG is freshly dissolved in DMSO-d_6, the ^{13}C NMR and ^{1}H spectra were predominantly by peaks from its α-anomer. By adding boric acid at room temperature, significant changes were observed in both ^{1}H and ^{13}C NMR spectra. Interestingly, two peaks belonging to the proton on OH groups disappear in the ^{1}H NMR spectrum and a group of new peaks arise (see Figure S11). A series of new peaks are also observed in the ^{13}C NMR spectrum (see Figure 8b). In accordance with these changes, a new broad peak appears on ^{11}B NMR compared with pure boric acid (Figure 9A). These observations strongly suggest each boric acid interacts with two hydroxyl group and forms boron containing complex. ^{1}H NMR of NAG in DMA-d_9 has been investigated previously[59]. By comparison, it appears that the two peaks disappeared in the ^{1}H NMR spectrum could be assigned to the hydroxyl groups on C_3/C_4 and C_6, respectively. DFT calculation suggests that boron coordinated with OH groups at the C_4 and C_6 was most stable for glucose conversion in the presence of boric acid[36]. It is not unreasonable to speculate that boric acid interacts with OH groups on C_4 and C_6 and forms a six-membered-ring boron complex, in perfect agreement with poison tests.

After heating at 50, 80 and 110˚C, the peaks assigned to boron complex keep decreasing and new peaks intensify concurrently, indicating the boron complex is intermediate for further conversion. The new peaks can be categorized into two groups. By referring to the standard ^{13}C NMR spectra, one group of the rising peaks can be unambiguously assigned to the β-anomer of NAG. Meanwhile, another group is likely to be assigned to the dimer of NAG. The formation of β-anomer suggests that boric acid facilitates the ring-opening reaction of the α-anomer, since the linear form of NAG is required for β-anomer formation. At the same time, this provides a plausible explanation for the promotional effect of boric acid, as formation of 3A5AF starts with the ring opening of NAG. After heating at 160˚C, the color of the sample became dark black and a variety of peaks appear in the ^{13}C NMR spectrum (see Figure 9B). The peaks belonging to 3A5AF, 4-(acetylamino)-1,3-benzenediol and acetic acid have been assigned. Levoglucosenone is not found possibly due to its low concentration. There are many other peaks in the carbon-carbon double bond (100-150 ppm) and unsaturated alcoholic alkane range (50-80 ppm), which might be assigned to precursors for chitin-humin and other side products.

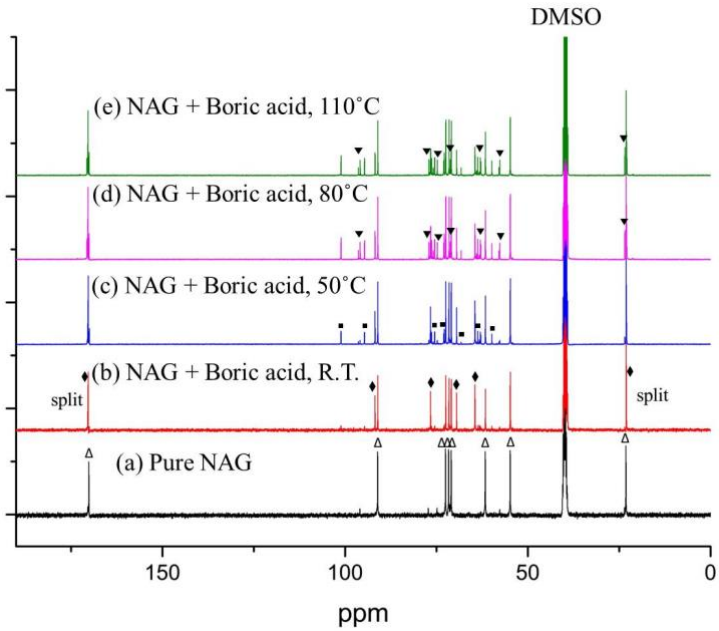

Figure 8 ^{13}C NMR of pure NAG and with boric acid at different temperatures. The sample was maintained at each temperature for 1 hour before NMR analysis. ▼ denotes the peaks of β-anomer; ♦ denotes the peaks assigned to boron complex; ■ denotes the peaks assigned to dimer; Δ denotes the peaks for α-anomer. The peaks at about 23 and 170 ppm are split upon the addition of boric acid, which may not be obviously seen in the figure.

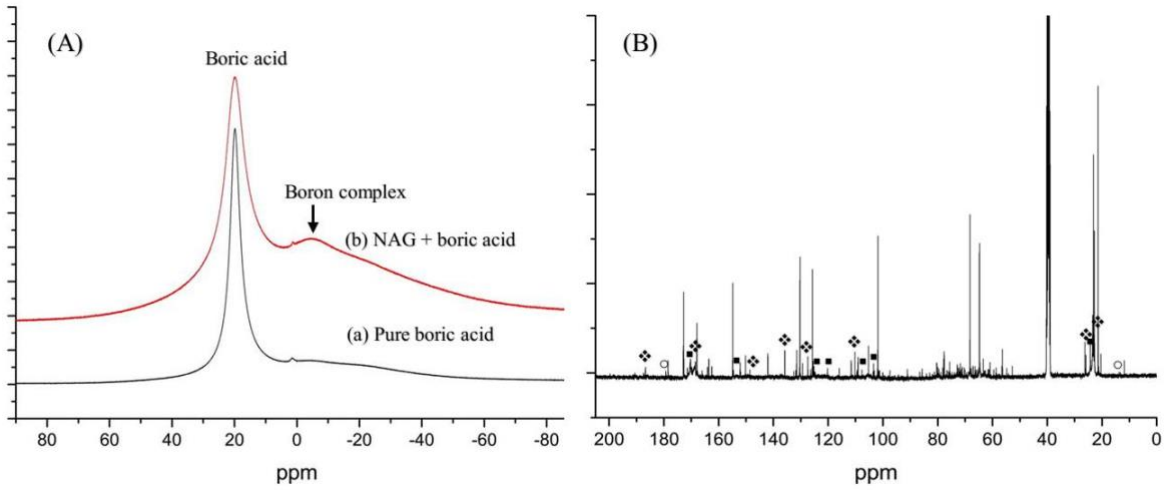

Figure 9 (A) ^{11}B NMR of boric acid (a) and boric acid with NAG (b); (B) ^{13}C NMR of the sample in DMSO-d_6 after heating at 160˚C for 1h. ❖ denotes the peaks for the major product 3A5AF; ▪ possibly denotes 4-(acetylamino)-1,3-benzenediol; ○ denotes the peaks for acetic acid.

4. Conclusion

For the first time, direct conversion of chitin into a nitrogen containing furan derivative (3A5AF) was systematically investigated. Boric acid is identified as the best catalyst and NMP as the best solvent. Under optimized conditions, 3A5AF reaches an unprecedented yield of 7.5% from chitin in one hour. NMR studies and poison tests provided mechanistic insights by confirming the formation of a six-membered ring boron complex intermediate. Water is detrimental to the reaction and its content should be kept below 1%. The entire reaction network from chitin to 3A5AF and side products has been established by a combination of instrumentation techniques. A kinetics study suggests hydrolysis of the crystalline region of chitin is likely to be rate-determining, and the product is not stable at high temperatures or for elongated reaction times.

Two strategies to further increase the one-pot conversion of chitin into nitrogen containing chemicals such as 3A5AF can be envisaged. Chitin pretreatment may be essential for chitin depolymerization as it can break down the robust structure and hydrogen bonding network effectively. Solvents that exhibit better solubility towards chitin dissolution, such as ionic liquids, could also be attempted. Investigations along these directions are currently underway in the lab.

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