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<td>Kobayashi, Hirokazu; Techikawara, Kota; Fukuoka, Atsushi</td>
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<tr>
<td>Citation</td>
<td>Green chemistry, 19(14): 3350-3356</td>
</tr>
<tr>
<td>Issue Date</td>
<td>2017-07-21</td>
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<tr>
<td>Doc URL</td>
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<td>File Information</td>
<td>manuscript_20170529hk.pdf</td>
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Hydrolytic hydrogenation of chitin to amino sugar alcohol

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Abstract

Chitin is the second most abundant biomass and characteristically contains nitrogen atoms in its monomer units. These favourable features promote chitin to be a potential resource for renewable organonitrogen compounds. 2-Acetamido-2-deoxysorbitol (ADS) is an attractive target in derivatives of chitin, but the conversion of chitin to ADS has not been reported so far. In this work, we demonstrate the catalytic conversion of chitin to ADS using mechanocatalysis in the presence of H₂SO₄ and subsequent hydrolytic hydrogenation by H₂SO₄ and Ru/TiO₂ without purification process. Our study clarified that the yield of ADS is strongly influenced by the reaction temperature and pH. The hydrolysis favourably proceeds at high temperature and low pH (2.0), but hydrogenation needs low temperature and specific pH of 3–4 to achieve high selectivity. Specifically, in the hydrogenation step, acid causes various side-reactions of amide and hemiacetal groups especially in the presence of Ru catalyst, whereas even a small amount of base drastically accelerates the retro-aldol reaction to form erythritol and N-acetylenolamine. Therefore, a one-pot but two-step reaction is necessary to optimise both hydrolysis and hydrogenation steps and maximises the overall yield of ADS up to 52%.

Introduction

Chitin is the most abundant inedible biomass next to lignocellulose, and it is widely found in
both terrestrial and marine organisms.\textsuperscript{1} Lignocellulose consists of only C, H and O, but chitin also contains N atoms in its \textit{N}-acetylglucosamine (NAG) units (Scheme 1). Thus, chitin is an attractive feedstock for organonitrogen compounds, which are more valuable than the counterparts derived from cellulose.\textsuperscript{2}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{Scheme_1.png}
\caption{Reported typical derivatives of chitin.}
\end{figure}

The first step for utilisation of chitin is its depolymerisation to monomers.\textsuperscript{2a} However, recalcitrance of chitin\textsuperscript{3} has hampered efficient and selective production of its monomeric compounds. A patent discloses that NAG can be synthesized by partial hydrolysis of chitin in large excess of concentrated HCl [turnover number (TON) < 0.01], neutralisation, decolouration, deionisation, complete hydrolysis by enzymes and isolation (32\% overall yield).\textsuperscript{4} This process results in a high price of NAG up to >100 British Pounds per kilogram. Accordingly, chitin-based biorefinery has not yet been economically established regardless of the high potential.\textsuperscript{1,2}

Recent studies have been devoted to improve the efficiency of chitin depolymerisation and to increase the range of products (Scheme 1). Chitin was converted to 5-(chloromethyl)furfural in
45% yield in the presence of concentrated HCl and 1,2-dichloroethane.\textsuperscript{5} 
SnCl\textsubscript{4} catalyst converted chitin to levulinic acid in 11.5% yield in water.\textsuperscript{6} 
A combined use of AlCl\textsubscript{3} and H\textsubscript{3}BO\textsubscript{3} degraded chitin into 5-hydroxymethylfurfural (5-HMF) in 9.0% yield.\textsuperscript{7} 
Formic acid solvent transformed ball-milled chitin into 5-(formyloxymethyl)furfural (FMF) in 35% yield.\textsuperscript{8} 
These compounds are promising feedstock for producing polymers and fuels,\textsuperscript{9} but characteristic nitrogen atoms of chitin are not contained in these compounds. Instead, 
3-acetamido-5-acetylfuran (3A5AF)\textsuperscript{10} was synthesised from chitin in the presence of excess H\textsubscript{3}BO\textsubscript{3} and NaCl (7.5% yield),\textsuperscript{11} and the pretreatment of chitin increased the yield to 28.5%.\textsuperscript{12} 
A health care agent, glucosamine sulphate, was obtained as a major product in the presence of only 100 mM H\textsubscript{2}SO\textsubscript{4} by a co-solvent system, water/diethylene glycol diethyl ether, which facilitated acid-catalysed hydrolysis of both glycosidic and amide bonds.\textsuperscript{13} 
Alcoholysis of chitin provides alkyl NAGs, which are expected to be stable alternatives to NAG.\textsuperscript{14} 
Chromogen and pyrazine are also good candidates obtained from chitin to produce fine chemicals and medicines.\textsuperscript{15} 
Recently, Yan \textit{et al.} proposed a new chitin derivative, 2-acetamido-2-deoxysorbitol (ADS).\textsuperscript{16} 
The amino alcohol is a potential precursor to polyamides and polyesteramides as an analogy of valorisation of sorbitol \textit{via} isosorbide.\textsuperscript{9,17} 
Hydrogenolysis of ADS gives 3-acetylethanolamine, which is converted to an amide-containing polyether alcohol.\textsuperscript{18} 
Hydrolysis of 3-acetylethanolamine gives ethanolamine, the world annual demand of which is 1.3 million tonnes for manufacturing acid-absorbers, surfactants, emulsifiers and other various products. The presence of these potential markets shows that ADS is an attractive intermediate in chitin-based biorefinery. However, ADS was only synthesised from pure NAG, and ADS was not obtained from chitin previously.\textsuperscript{16} 

Herein, we demonstrate the first catalytic conversion of chitin to ADS (Scheme 2). 
Mechanocatalytic hydrolysis was utilised to produce oligosaccharide mixture from chitin in the first step (step 1).\textsuperscript{14b} The mixture was used for the one-pot synthesis of ADS without purification in a one-step hydrolytic hydrogenation (step 2a) and a two-step method (steps 2b, 3). Challenge in the production of ADS and its solution is discussed.
Scheme 2. Catalytic conversion of chitin to ADS. Steps 2b and 3ab were performed in one pot. Yields are based on initial amount of NAG unit.

Experimental

Determination of NAG content in chitin.

Purity of the chitin sample purchased from Wako was determined by ultra violet-visible (UV-vis) spectroscopy according to the literature, by which the content of NAG units was determined to be 88 wt% (4.3 mmol g\textsubscript{dry-chitin}{-1}).

Mechanocatalytic hydrolysis.

Chitin (5.0 g) was dispersed in 15 mL of 0.4 M H\textsubscript{2}SO\textsubscript{4} \textit{aq.} (substrate/catalyst ratio (S/C) = 3.4 [mol-NAG unit/mol-H\textsubscript{2}SO\textsubscript{4}]). After drying in \textit{vacuo}, 5.2 g of resulting powder was treated by a planetary ball-mill (Fritsch, Pulverisette 6) at 500 rpm using alumina balls (5 mm, 100 g) in a 250 mL of alumina pot. The milling time was 6 h with a 10 min interval after every 10 min of milling. The temperature was increased up to 327 K by heat of milling under the condition. The pretreated chitin sample was named \textit{Oligomer-H\textsubscript{2}SO\textsubscript{4}}, the solubility of which was measured by addition of water (100 mg/10 mL), filtration with polytetrafluoroethylene (PTFE) membrane and weighing of the dried residue. Soluble part was analysed with a high performance liquid chromatograph (HPLC; Prominence, Shimadzu) equipped with a refractive index detector (RID) and a UV detector. The column used for the analysis was Rezex RPM-Monosaccharide Pb++ (Phenomenex, ø7.8 × 300 mm). The peak of H\textsubscript{2}SO\textsubscript{4} was subtracted to determine the yield of products. Optimisation of milling conditions is shown in ESI (Tables S1–S3).
Preparation of 5 wt% Ru/TiO₂.

Ru(NO)(NO₃)₃ solution (Wako) was added to aqueous dispersion of TiO₂ (JRC-TIO-4(2), Catalysis Society of Japan). After drying at 333 K at 60 hPa with a rotary evaporator, the sample was further dried at < 1 Pa. The resulting powder was reduced under H₂ flow (30 mL min⁻¹) at 673 K for 2 h. Other supports tested in this work were ZrO₂ (JRC-ZRO-5, Catalysis Society of Japan) and carbon black (Black Pearls 2000, Cabot). The prepared catalysts were characterised by X-ray diffraction (XRD; Rigaku, Ultima IV, Cu Kα, Figs. S1 and S2), transmission electron microscopy (TEM; JEOL, JEM-2100F, 200 kV, Fig. S3) and N₂ adsorption at 77 K (Table S1). No peak for Ru was observed in the XRD patterns, which was due to high dispersion and formation of amorphous RuO₂·2H₂O in air.¹⁰ Note that the oxidised Ru species is easily reduced to metal under H₂ atmosphere.²¹

One-step hydrolytic hydrogenation.

Oligomer-H₂SO₄ (454 mg), 5 wt% Ru/TiO₂ catalyst (200 mg) and water (40 mL) were put into a SUS316 high-pressure reactor (OM-Lab Tech, MMJ-100, 100 mL). After charging 4.0 MPa of H₂, the temperature was raised from 298 to 453 K in 7 min. The rapid increase in temperature is owing to no boiling of solvent under the pressurised condition. After reaching the temperature, the reactor was quickly cooled down to room temperature by blowing air. This thermal profile is described as rapid heating-cooling condition at 453 K hereafter. Products were analysed with the HPLC system described above. Columns used for this analysis were SUGAR SH-1011 column (Shodex, ø8 × 300 mm), Rezex RPM-Monosaccharide Pb++ column (Phenomenex, ø7.8 × 300 mm) and Asahipak NH₂P-50 4E (Shodex, ø4.6 × 250 mm). A gas chromatograph with a flame ionisation detector (GC-FID; Shimadzu, GC-2025, column: DB-FFAP) and that with a mass spectrometer (GC/MS; Shimadzu, GC-2010–Parvum 2, column: HR-20M) were also utilised to determine volatile products.

Two-step hydrolytic hydrogenation.

Oligomer-H₂SO₄ (454 mg) and water (40 mL) were charged into the reactor. The hydrolysis
reaction was performed under the rapid heating-cooling condition at a designated temperature, in which heating up to the temperature took 10–14 min (e.g., 12 min to 448 K) in the absence of H₂ pressure. After finishing the hydrolysis, NaHCO₃ and Ru/TiO₂ (200 mg) were added to the reaction mixture. The reactor was pressurised with 4 MPa of H₂ prior to the hydrogenation reaction at 393 K.

**Results and discussion**

**Mechanocatalytic conversion of chitin to oligomer.**

Mechanocatalytic hydrolysis of chitin was performed in the presence of H₂SO₄ at S/C of 3.4 by a planetary mill, where physisorbed water on the sample (11 wt%) was used for the hydrolysis (Scheme 2, step 1). This reaction completely transformed chitin into water-soluble compounds. Products were NAG in 19% yield and its oligomers in 64% yield, i.e., dimer (26%), trimer (29%) and larger ones (9.0%) (Fig. 1). The amount of by-products was 17%, and HPLC analysis detected dehydrated compounds such as 5-HMF. Formation of furanics was also supported by NMR and UV-vis spectroscopy (Figs. S4, S5). The yields of NAG and oligomers in this study were higher than those in the previous report (NAG 4.7%, dimer 7.8%, trimer 11%).¹⁴b This was due to larger contents of H₂SO₄ and physisorbed water in the sample in this time (S/C = 3.4, water 11 wt%) than those in the previous case (S/C = 7.7, water 1.5 wt%). Although too much water (≥20 wt%) inhibits the mechanocatalytic hydrolysis by plasticising effect,²² a small amount of physisorbed water facilitates hydrolysis and likely avoids side-reactions by quickly trapping oxocarbenium ion intermediate. In addition, our condition did not lead to the sticking of the sample on the wall of milling pot. This is a meaningful result for upscaling, because the sticking is a considerable issue in a practical situation as reported by Rinaldi and co-workers.²³
Other liquid acids without intense oxidising or volatile properties were also tested to elucidate the effect of acid strength in the mechanocatalytic hydrolysis. HClO₄ (pKₐ = −10), H₂SO₄ (−3), MeSO₃H (−2) and perfluorobutyric acid (0.4) similarly converted chitin to NAG and oligomers in 80–85% yield, where a stronger acid tended to give smaller oligomers (Fig. 1). In contrast, H₃PO₄ (2.1) and acetic acid (4.7) provided low yields of 28% and <2%, respectively. Accordingly, acids with pKₐ less than 1 were effective for the mechanocatalytic hydrolysis of chitin. Dissociation of a glycosidic bond occurs after protonation of the oxygen atom (pKₐ ≈ −4) in the bond, which is the main cause to require a strong acid. We chose H₂SO₄ for the mechanical reaction because of the highest degree of hydrolysis as well as the lowest price. The resulting solid containing H₂SO₄ after the mechanocatalytic reaction was named Oligomer-H₂SO₄.

One-step hydrolytic hydrogenation of Oligomer-H₂SO₄

Hydrolytic hydrogenation of Oligomer-H₂SO₄ was performed under H₂ pressure of 4 MPa in water under the rapid heating-cooling condition at 453 K (Scheme 2, step 2a). The catalyst for hydrolysis was the H₂SO₄ contained in Oligomer-H₂SO₄ (S/C = 3.4), and pH of the reaction solution became 2.0 in our condition. We added water-tolerant supported Ru catalysts in this
reaction, as Ru is typically the most active metal species for the hydrogenation of sugars.\textsuperscript{25} Ru/TiO\textsubscript{2} catalyst produced ADS in 25\% yield (Table 1, entry 2), where the compound was identified as ADS with NMR (Figs. S6 and S7) and GC/MS (Fig. S8). A turnover number (TON) of surface Ru estimated by TEM (particle size 1–3 nm, dispersion 46\%, Fig. S3) was 9 for the production of ADS. TEM was only the choice for this purpose, because XRD gave no peak for Ru (Fig. S1) and CO pulse titration was less reliable due to coverage of Ru with reduced TiO\textsubscript{x} in the pre-treatment, so-called strong metal-support interaction. By-products were formed in large quantity (48\%), the GC/MS analysis of which before and after trimethylsilylation detected 2-amino-2-deoxysorbitol, acetic acid, acetamide, N-acetylgalactosamine, propylene glycol and ethylene glycol. Remaining part was unreacted NAG (4.8\% yield) and oligomers (22\%). Ru/C and Ru/ZrO\textsubscript{2} gave slightly lower yields of ADS (21\%, 19\%, entries 3, 4). Adsorption of chitin oligomers and some of by-products on Ru/C hampered handling of the catalyst. The axial face of chitin oligomers consists of lipophilic CH groups, which facilitates adsorption of the oligomers on polycyclic aromatic surface of carbon by CH–π hydrogen bonds and hydrophobic interactions.\textsuperscript{26} Basicity of ZrO\textsubscript{2}\textsuperscript{27} is unfavourable for the selective conversion of sugar molecules as described below. Accordingly, Ru/TiO\textsubscript{2} was the best catalyst for ADS production under the condition. A controlled reaction in the absence of metal catalyst gave no ADS but produced NAG in 41\% yield (entry 1). This yield is rather higher than the total yield of NAG and ADS (30\%) in the presence of Ru/TiO\textsubscript{2}, which suggests that Ru promotes not only hydrogenation of NAG to ADS but also side-reactions.
Table 1 Hydrolytic hydrogenation of Oligomer-H₂SO₄ by supported metal catalyst.$^a$

<table>
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<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Yield of product /%-NAG unit</th>
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<tr>
<td></td>
<td></td>
<td>ADS</td>
</tr>
<tr>
<td>1</td>
<td>None</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>5 wt% Ru/TiO₂</td>
<td>25</td>
</tr>
<tr>
<td>3</td>
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</tr>
<tr>
<td>4</td>
<td>5 wt% Ru/ZrO₂</td>
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</tr>
<tr>
<td>5</td>
<td>7 wt% Pt/TiO₂</td>
<td>2.9</td>
</tr>
<tr>
<td>6</td>
<td>70 wt% Ni/TiO₂</td>
<td>0.3</td>
</tr>
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$^a$Rapid heating-cooling condition at 453 K. Oligomer-H₂SO₄ 454 mg, catalyst 200 mg, water 40 mL. $p$(H₂) 4.0 MPa at 298 K. Characterisation data of catalysts are available in ESI. $^b$Adsorbed products.

We also tested Pt and Ni catalysts that showed good activity in the hydrolytic hydrogenation of cellulose.$^{27,28}$ However, Pt/TiO₂ and Ni/TiO₂ were inactive for the formation of ADS (2.9% and 0.3% yields, respectively; entries 5 and 6), regardless of the higher loading amounts of metals. Such a low activity of Pt was previously observed in the hydrolytic hydrogenation of hemicellulose in beet fibre containing proteins.$^{29}$ Pt is less active than Ru in the hydrogenation of sugars, and amine by-products probably further deactivates Pt. Ni was oxidised by proton under the acidic condition (Ni + 2H⁺ $\rightarrow$ Ni²⁺ + H₂), which suppressed both hydrolysis and hydrogenation. Thus, ADS yield was at most 25% in the catalyst screening (Ru/TiO₂, entry 2).

The low yield of ADS is contrasting to the yield of sorbitol up to 90% in the hydrolytic hydrogenation of cellulose and its oligomers despite their similar structures.$^{30}$ Presence of amide group drastically changes reactivity of the sugar molecule. Acetamide groups likely enhance the reactivity of hemiacetal and subtraction of proton at C2 position due to the electron-withdrawing effect. Moreover, the hydrolysis of acetamide produces amine, which
easily causes side-reactions with sugars known as Maillard reaction.\textsuperscript{31}

**Two-step hydrolytic hydrogenation of Oligomer-$H_2SO_4$**

The one-step hydrolytic hydrogenation caused side-reactions. To overcome this issue, we designed a one-pot but two-step reaction consisting of hydrolysis of Oligomer-$H_2SO_4$ to NAG and subsequent hydrogenation to ADS under the optimised conditions in the respective steps (Scheme 2, steps 2b and 3ab). For the hydrolysis step, as the reaction prefers short time and high temperature to maximise NAG yield,\textsuperscript{14b} we tested the rapid heating-cooling condition at different temperatures (Fig. 2). Yield of NAG increased by raising the reaction temperature and reached 61\% at 448 K. In this case, TON of $H_2SO_4$ was 2.3 for the production of NAG, showing that $H_2SO_4$ functioned as a catalyst under our condition. Further increase in temperature decreased yield of NAG due to the successive decomposition, where dark brown colour of the reaction mixture indicated the formation of humins.

![Fig. 2. Effect of reaction temperature on the hydrolysis of Oligomer-$H_2SO_4$.](image)

The reaction solution after the hydrolysis at 448 K, the temperature maximising the yield of NAG, was directly used for the subsequent hydrogenation reaction (Scheme 2, step 3a). We performed the reaction at a low temperature of 393 K, because a lower temperature generally gives higher selectivity in hydrogenation of sugars.\textsuperscript{16,32} Reduction of NAG to ADS proceeded in
a first-order manner in the presence of Ru/TiO₂ and 4 MPa of H₂ (Fig. 3a). Overall yield of ADS reached 37% at 2 h with 62% selectivity based on the consumed amount of NAG, and ADS was slowly decomposed in a longer reaction time. Thus, the two-step reaction increased the ADS yield 1.5 times higher than the one-step reaction (25%). However, side-reaction was still significant compared to the hydrogenation of pure NAG by Ru/TiO₂ in water (93% selectivity at 0.5 h; Fig. 3f).

Fig. 3. Time courses of hydrogenation of Oligomer-H₂SO₄ hydrolysate at 393 K. (a) pH 2.0 (= no neutralisation), (b) pH 3.0, (c) pH 4.0, (d) pH 5.0, (e) pH 6.8. (f) That of pure NAG in water, where the amount of NAG was the same as that in the chitin conversion (61%). Lines indicate simulation results.

The side-reactions in the hydrogenation of Oligomer-H₂SO₄ was presumably due to H₂SO₄ (pH 2.0), which motivated us to conduct the reaction after adding NaHCO₃ to adjust pH (Scheme 2, step 3b). The overall yield of ADS was increased to 52% at pH 3 and 51% at pH 4.
with improved hydrogenation selectivity of >85% (Fig. 3b, c). As expected, the selectivity approached that in the conversion of pure NAG in water. We speculate that the milder acidic condition suppresses the hydrolysis and hydrogenation of amide (Scheme S1) and the decomposition of hemiacetal by H⁺ and Ru. Owing to the higher selectivity, TON of surface Ru also increased to 19. Note that the hydrogenation reaction took a longer time (2 h) than that of pure NAG (0.5 h), which was attributed to the inhibition effect of by-products as discussed above. This was also observed in the reuse experiment of Ru/TiO₂ used at pH 3, where the catalyst showed lower activity due to further adsorption of catalyst poison in the second run (Fig. S9). However, the structure of catalyst (Fig. S10) or catalytic activity did not change during the time course in one reaction as indicated in the kinetic analysis described below. Further increase in pH to 5.0 slightly lowered the yield of ADS (46%; Fig. 3d), and the reaction at pH 6.8 drastically decreased the yield to 5% (Fig. 3e). The neutral condition produced large amounts of N-acetyleneolamine (31% [mol-product/mol-NAG unit]) and erythritol (16%) via retro-aldol reaction of NAG due to presence of HCO₃⁻ (Scheme 3). HCO₃⁻ is remaining at pH 6.8 because pKₐ of the conjugated acid (H₂CO₃; 6.3) is lower than the pH value. In addition, HCO₃⁻ spontaneously forms a stronger base by the disproportionation (2HCO₃⁻ → CO₃²⁻ + CO₂ + H₂O) at a high temperature. Indeed, the hydrogenation of pure NAG after adding H₂SO₄ and NaHCO₃ (pH 6.8) gave N-acetyleneolamine and erythritol. Neutralisation with NaHCO₃ to pH 7 is inappropriate for the synthesis of ADS, but slightly acidic condition is the best option.
Scheme 3. Formation of erythritol and N-acetylenolamine from NAG. B⁻: base.

The pseudo first-order rate constants were determined for the hydrogenation of NAG to ADS ($k_1$), NAG to by-product ($k_2$) and ADS to by-product ($k_3$) by curve-fitting of the actual experimental results (Table 2). Increase in pH from 2 to 3 had little influence on $k_1$ value, but $k_2$ decreased from 0.56 h⁻¹ to 0.08 h⁻¹ and $k_3$ reduced from 0.05 h⁻¹ to 0.03 h⁻¹. Kinetic simulation shows that $k_2$ affects ADS yield more strongly than $k_3$ (Table 3). Specifically, decrease in $k_2$ from 0.56 to 0.08 h⁻¹ increases the yield by 12–13%, whereas that in $k_3$ from 0.05 to 0.03 h⁻¹ gains 1–2%. Further increase in pH to 4–5 gave minor influence on the rate constants, but $k_2$ was dramatically elevated up to 4.6 h⁻¹ at pH 6.8 due to acceleration of the aldol reaction as described above. Hence, the minimisation of $k_2$, more accurately the ratio of $k_2/k_1$, is the major factor to maximise the yield of ADS at pH 3–4.
Table 2 Kinetic parameters determined by curve fitting of the reaction time courses.

![Diagram]

<table>
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<tr>
<th>pH</th>
<th>$k_1$ /h$^{-1}$</th>
<th>$k_2$ /h$^{-1}$</th>
<th>$k_3$ /h$^{-1}$</th>
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<tr>
<td>2.0</td>
<td>1.4</td>
<td>0.56</td>
<td>0.050</td>
</tr>
<tr>
<td>3.0</td>
<td>1.3</td>
<td>0.080</td>
<td>0.030</td>
</tr>
<tr>
<td>4.0</td>
<td>1.0</td>
<td>0.050</td>
<td>0.025</td>
</tr>
<tr>
<td>5.0</td>
<td>0.95</td>
<td>0.15</td>
<td>0.020</td>
</tr>
<tr>
<td>6.8$^a$</td>
<td>0.60</td>
<td>4.6</td>
<td>0.10</td>
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$^a$HCO$_3^-$ was present, which was different from pure water.

Table 3 Simulation of effects of kinetic parameters on ADS yield.

<table>
<thead>
<tr>
<th>$k_1$ /h$^{-1}$</th>
<th>$k_2$ /h$^{-1}$</th>
<th>$k_3$ /h$^{-1}$</th>
<th>Theoretical maximum</th>
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<tbody>
<tr>
<td>Time /h</td>
<td>ADS yield$^a$/%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.3</td>
<td>0.56</td>
<td>0.05</td>
<td>2.0</td>
</tr>
<tr>
<td>1.3</td>
<td>0.56</td>
<td>0.03</td>
<td>2.3</td>
</tr>
<tr>
<td>1.3</td>
<td>0.08</td>
<td>0.05</td>
<td>2.5</td>
</tr>
<tr>
<td>1.3</td>
<td>0.08</td>
<td>0.03</td>
<td>2.8</td>
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$^a$ Max. ADS yield = $M_{NAG} \frac{k_1}{k_1 + k_2} \frac{1}{R - 1} \left( \frac{1}{R^{1-R}} - \frac{R}{R^{1-R}} \right)$, where $M_{NAG} =$ initial amount of NAG = 61%, $R = k_3/(k_1 + k_2) \neq 1$. This formula is established by solving differential equations about kinetics. See ESI.

Conclusions

Catalytic conversion of chitin was studied to produce ADS without purifying intermediates. Planetary ball-milling of chitin gives NAG and oligomers in 83% yield by mechanocatalytic
hydrolysis in the presence of H$_2$SO$_4$. Ball-milling is known to be an energy-consuming process, but the scale-up drastically increases the efficiency.$^{23}$ The ball-milled sample (Oligomer-H$_2$SO$_4$) can be directly converted to ADS by the hydrolytic hydrogenation by Ru/TiO$_2$. However, the yield of ADS is at most 25% in this method, which is remarkably different from selective conversion of cellulose to sorbitol. An amide group in NAG drastically changes the reactivity of sugar molecule. Selectivity for ADS is improved by separating the hydrolysis and the hydrogenation steps to optimise both reactions. The hydrolysis is enhanced at high temperature (448 K) and low pH (2.0), while the hydrogenation requires low temperature (393 K) and careful control of pH. In the hydrogenation step, low pH (2.0) results in various side-reactions of amide and hemiacetal groups especially in the presence of Ru catalyst, whereas high pH (6.8) induces retro-aldol reaction to form erythritol and N-acetylethanolamine due to presence of basic species. Therefore, partial neutralisation of the solution to pH 3–4 maximises the hydrogenation selectivity and overall yield of ADS up to >85% and 52%, respectively. The produced ADS might be isolated from the reaction mixture by removing by-products with ion-exchange resin and activated carbon followed by crystallisation. The kinetic analysis has indicated that ADS is relatively stable under the reaction conditions. Hence, development of a durable hydrogenation catalyst that selectively and rapidly converts NAG to ADS even at high temperature and low pH would be promising for more efficient synthesis of ADS.

**Acknowledgments**

We utilised NMR and TEM at the Open Facility of Institute for Catalysis (ICAT), Hokkaido University, and the TEM measurement was assisted by the technical division of ICAT. This work was supported by Grant-in-Aid for Young Scientist (A) (No. 26709060) from the Japan Society for the Promotion of Science (JSPS).

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