This is an Accepted Manuscript, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. This Accepted Manuscript will be replaced by the edited, formatted and paginated article as soon as this is available.

You can find more information about Accepted Manuscripts in the Information for Authors.

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal’s standard Terms & Conditions and the Ethical guidelines still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this Accepted Manuscript or any consequences arising from the use of any information it contains.
Intramolecular dehydration of mannitol in high-temperature liquid water without adding any hazardous acid catalysts and their kinetic analyses were carried out. The dehydration behavior of mannitol was compared with that of sorbitol, 2,5-anhydromannitol and 1,4-anhydromannitol were major products from the mannitol monomolecular dehydration in contrast with the only major product, 1,4-anhydroinositol, from the sorbitol monomolecular dehydration.

Production of chemicals and fuels from renewable biomass has attracted much attention for a sustainable society. Sugar alcohols such as sorbitol and mannitol are promising biomass-derived materials from cellulose and hemicellulose for use in the production of valuable chemicals, anhydromannitol, and isomannide, by intramolecular dehydration of the sugar alcohols in high-temperature liquid water into valuable chemicals is important to utilize biomass resources.

The intramolecular dehydration of mannitol can provide valuable chemicals, anhydromannitol, and isomannide, by intramolecular dehydration. Anhydromannitol is a key material to produce naturally-derived surfactant and non-toxic food additives. Isomannide has commanded attention as a raw material for drugs and an additive for polymers. The isomannide and isosorbide, biomass-based diols with rigid structures, can dramatically improve the thermal stability of the polymers, opening possible applications as alternatives of petroleum-based monomers; however, syntheses of isosorbide and isomannide from sorbitol and mannitol are generally done with strong acids, which cause a serious corrosion and require neutralization processes. It is notable that isomannide yield (35%) from the mannitol dehydration was lower than isosorbide yield (64%) by sulfuric acid at 377 K and that 2,5-anhydromannitol was obtained with the yield of 40%. The dehydration behavior of mannitol has not been reported in detail to our knowledge and we report here for the first time the kinetics for the reaction network of mannitol dehydration in high-temperature liquid water.

High-temperature liquid water is a promising reaction media for acid-catalyzed reactions. We reported that isosorbide could be produced from sorbitol dehydration in high-temperature liquid water without adding any acid catalysts, which can enhance the prospect for a biomass-based monomer. To produce anhydromannitol and isomannide with a green method, the mannitol dehydration without any acid catalysts is important, which has been never reported. Also, the chemistry of intramolecular dehydration of sugar alcohols provides a key technology for developing an efficient conversion process of biomass derivatives to useful materials; however, sorbitol and mannitol have six hydroxyl groups in a molecule and their intramolecular dehydration mechanisms are complicated. The stereoisomers of sorbitol and mannitol are epimers, where their differences are only in the stereochemistry of hydroxyl group and hydrogen at the C-2 position; however, the dehydration behaviors are completely different.

In this manuscript, we report the intramolecular dehydration of mannitol in high-temperature liquid water without adding any hazardous acid catalysts (Scheme 1) and compare it with the sorbitol dehydration (Scheme 2). We found that 2,5-anhydromannitol and 1,4-anhydromannitol were major products from the mannitol monomolecular dehydration in contrast with the only major product, 1,4-anhydroinositol, from the sorbitol dehydration.

Scheme 1 The reaction pathway of mannitol dehydration

Scheme 2 The reaction pathway of sorbitol dehydration
monomolecular dehydration. The yield of isomaltooltriose, 1,4-3,6-dianhydromannitol, was lower than that of isosorbide. The difference in selectivity between mannitol and sorbitol dehydration is discussed along with the results of arabinose dehydration. We also report the rate constants and activation energies of mannitol dehydration reactions and compare them with those of sorbitol dehydration to understand the dehydration chemistry of C6 sugar alcohols.

Dehydration of mannitol (0.5 mol dm$^{-3}$) proceeded in high-temperature liquid water at 523 K without any acid catalysts and 1,4-AHMA, 2,5-AHMA, 1,5-AHMA, and isomannide were obtained (Scheme 1, Fig. 1 (a)). The material balance, which is defined as sum of the unreacted mannitol and the dehydrated products (1,4-AHMA, 2,5-AHMA, 1,5-AHMA, and isomannide), was more than 90% at 523 K even for 36 h of reaction. The conversion of mannitol increased with reaction time and reached 51% at 10 h and 90% at 36 h and the major products of monomolecular dehydration obtained were 2,5-AHMA and 1,4-AHMA with the yield of 41% and 25% at 523 K for 36 h, respectively. On the other hand, 1,5-AHMA was obtained with the yield of only 6% at 523 K for 36 h. The 2,5-AHMA yield from mannitol dehydration by 3 mol dm$^{-3}$ sulfuric acid at 377 K was reported to be 40%, which was the same as dehydration in high-temperature liquid water, as revealed in this report.

In the case of sorbitol (0.5 mol dm$^{-3}$) dehydration (Scheme 2) at 523 K, the conversion of sorbitol was faster than that of mannitol and it reached 70% at 10 h and almost 100% at 36 h (Fig. 2 (a)). The dehydration behavior from different initial sorbitol concentrations (3.0, 2.0, 1.0, and 0.5 (Fig. 2) mol dm$^{-3}$) were quite similar to each other at 523 and 573 K, indicating that the dehydration of sorbitol follows a first-order dependence on sorbitol concentration. The major product of monomolecular dehydration obtained was only 1,4-AHHSO with the highest yield of 62% at 523 K for 24 h and the yield of isosorbide from bimolecular dehydration of sorbitol increased with reaction time.

On the other hand, 2,5-AHHSO was obtained with the yield of 8% at 523 K for 24 h and it did not change with the reaction time after 24 h. The yield of 1,5-AHHSO was always less than 1% at 523 K. The dehydration behaviors of sorbitol and mannitol were quite different from each other. The major monomolecular dehydration products were 1,4-AHHSO from sorbitol, and 2,5-AHMA and 1,4-AHMA from mannitol. We will compare the dehydration kinetics in the following section.

The dehydration of mannitol was also carried out at 548, 560, and 573 K in high-temperature liquid water (Fig. 1 (b), (c) and (d)). At all the temperatures (523-573 K), 2,5-AHMA and 1,4-AHMA were produced at the beginning of reaction. The initial formation rates of 2,5-AHMA and 1,4-AHMA increased with an increase of reaction temperature and the 2,5-AHMA yield was higher than the 1,4-AHMA yield during the mannitol dehydration. The 1,4-AHMA yield had maximum and decreased with reaction time; on the other hand, the 2,5-AHMA yield was almost constant or started to decrease slightly at 573 K. Isomannide was produced later than the formation of 1,4-AHMA because isomannide “1,4-3,6-dianhydromannitol” was formed by the stepwise dehydration of 1,4-AHMA (Scheme 1). We have succeeded in mannitol dehydration in high-temperature liquid water without adding any acid catalysts, producing 2,5-AHMA, 1,4-AHMA and isomannide.

Dehydration reactions of mannitol and sorbitol in high-temperature liquid water proceeded via the sequence of steps in Schemes 1 and 2. The reverse reaction did not proceed as confirmed by the reaction behavior of 1,4-AHSO, isosorbide, and isomannide in high-temperature liquid water. The amount of the formed isosorbide decreased in high-temperature liquid water ($k_{SS}$ step in Scheme 2), as shown in Fig. 2 (b); on the other hand, the amount of the formed isomannide did not decrease largely ($k_{SM}$ was treated as zero in Scheme 1). The concentrations of the reactant and products in mannitol dehydration were represented as Eqs. (6)-(10) (Electronic Supplemental Information) using the rate constants ($k_{1M}$, $k_{2M}$, $k_{3M}$, $k_{4M}$, $k_{5M}$ and $k_{6M}$ in Scheme 1). The rate constants ($k_{1M}$, $k_{2M}$, $k_{3M}$, $k_{4M}$, and $k_{5M}$) were estimated (Table 1) using linear regression analyses with minimization of residuals for the data of mannitol, 2,5-AHMA, 1,4-AHMA, 1,5-AHMA, and isomannide yields. The rate constant of $k_{SM}$ (mannitol to 2,5-AHMA) was the largest, compared with the other rate constants ($k_{1M}$, $k_{2M}$, $k_{3M}$, and $k_{5M}$), indicating that the first dehydration step of mannitol to 2,5-AHMA proceeded faster than the other dehydration steps. The final yields of 2,5-AHMA could be
predicted from the constant of \((k_{2M} / (k_{1M} + k_{2M} + k_{3M} + k_{6M}))\) in Table S1. The obtained yields of 2,5-AHMA (Fig. 1) could be reproduced by the calculated prediction (37-44%) at each temperature and that of 1,5-AHMA was also reproduced by the calculation (4.0-6.8%) of \((k_{1M} / (k_{1M} + k_{2M} + k_{3M} + k_{6M}))\) (Table S1). We reported the kinetic parameter of sorbitol dehydration in high-temperature liquid water in Scheme 2 and Table S2. In the case of sorbitol dehydration, the yield of 2,5-AHHSO was less than 20% (Fig. 2), which was also consistent with the calculated 2,5-AHHSO yield \((k_2S / k_1S + k_2S + k_3S + k_4S)\) (Table S1). The rate constant of \(k_1S\) (sorbitol to 1,4-AHHSO) was the largest; thus, high-

<table>
<thead>
<tr>
<th>Temperature (K)</th>
<th>523</th>
<th>548</th>
<th>560</th>
<th>573</th>
<th>Activation energy (kJ mol(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>(k_{1M}) (mol h(^{-1}))</td>
<td>0.023</td>
<td>0.12</td>
<td>0.22</td>
<td>0.44</td>
<td>148</td>
</tr>
<tr>
<td>(k_{2M}) (mol h(^{-2}))</td>
<td>0.028</td>
<td>0.15</td>
<td>0.31</td>
<td>0.60</td>
<td>153</td>
</tr>
<tr>
<td>(k_{3M}) (mol h(^{-1}))</td>
<td>0.0044</td>
<td>0.020</td>
<td>0.038</td>
<td>0.065</td>
<td>135</td>
</tr>
<tr>
<td>(k_{4M}) (mol h(^{-1}))</td>
<td>0.0093</td>
<td>0.053</td>
<td>0.12</td>
<td>0.17</td>
<td>151</td>
</tr>
<tr>
<td>(k_{6M}) (mol h(^{-2}))</td>
<td>0.0097</td>
<td>0.077</td>
<td>0.18</td>
<td>0.51</td>
<td>196</td>
</tr>
</tbody>
</table>

\(^{a}\) Reaction temperature, \(^{b}\) Activation energy