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ARTICLE TYPE

Intramolecular Dehydration of Mannitol in High-Temperature Liquid Water without Acid Catalysts

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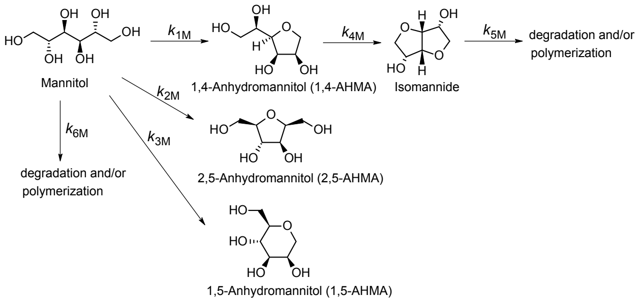
Intramolecular dehydration of mannitol in high-temperature liquid water without adding any hazardous acid catalysts and their kinetic analyses were carried out. The dehydration behavior of mannitol was compared with that of sorbitol. 2,5-Anhydromannitol and 1,4-anhydromannitol were major products from the mannitol monomolecular dehydration in contrast with the only major product, 1,4-anhydrosorbitol, from the sorbitol monomolecular dehydration.

Production of chemicals and fuels from renewable biomass has attracted much attention for a sustainable society.[1] Sugar alcohols such as sorbitol and mannitol are promising biomass-derived materials from cellulose and hemicellulose for providing the chemicals.[2] Recently, Fukuoka and Dhepe succeeded to produce sorbitol by one-step cracking of cellulose using a platinum catalyst and hydrogen in water[3] and we reported that cellulose and hemicellulose in the wood chips were directly converted to sugar alcohols such as sorbitol, mannitol, and xylitol.[4] From these results, the chemistry for intramolecular dehydration of the sugar alcohols in high-temperature liquid water into valuable chemicals is important to utilize biomass resources.

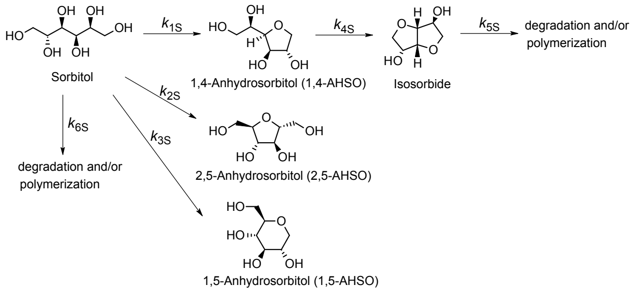
The intramolecular dehydration of mannitol can provide valuable chemicals, anhydromannitol, and isomannide, by intramolecular dehydration. Anhydromannitol is a key material to produce naturally-derived surfactant and non-toxic food additives. Isomannide has commanded attention as a raw material for drugs[5] and an additive for polymers.[6] 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,[7] 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%.[7a, 8] 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.[9] We reported that isosorbide could be produced from sorbitol dehydration in high-temperature liquid water without adding any acid catalysts,[10] 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-anhydrosorbitol, from the sorbitol



Scheme 1 The reaction pathway of mannitol dehydration



Scheme 2 The reaction pathway of sorbitol dehydration

monomolecular dehydration. The yield of isomannide, 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 arabitol 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%,[7a] 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,[10] 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-AHSO 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-AHSO 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-AHSO 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-AHSO 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_{5S} 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_{5M} 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_{6M}) 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_{2M} (mannitol to 2,5-AHMA) was the largest, compared with the other rate constants (k_{1M}, k_{3M}, k_{4M}, and k_{6M}), 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

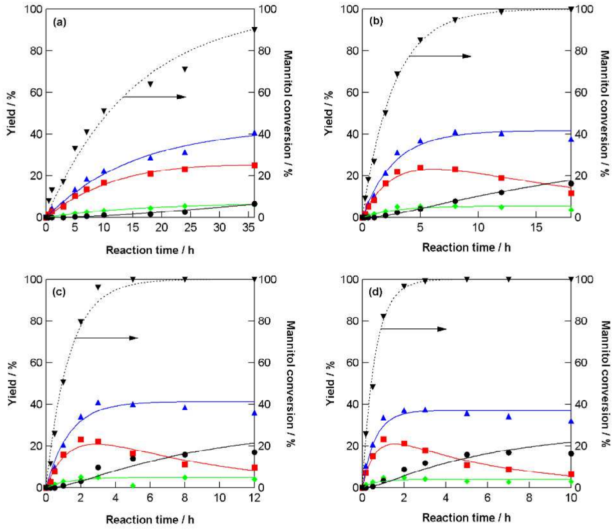


Fig. 1 Yields of 1,4-AHMA (■), 2,5-AHMA (▲), 1,5-AHMA (◆) and isomannide (●), and mannitol conversion (▼), as a function of elapsed time for mannitol dehydration reactions at (a) 523, (b) 548, (c) 560 and (d) 573 K in water (initial mannitol concentration: 0.5 mol dm^{-3}) The lines show the best fit for the obtained data to the equations in the Electronic Supplemental Information with the kinetic parameters in Table 1.

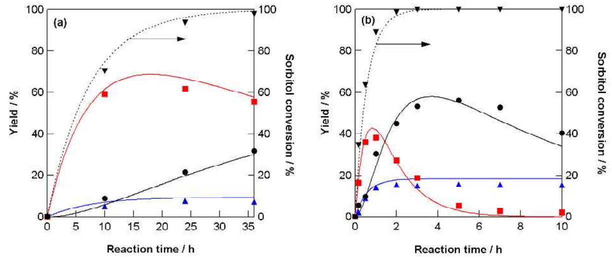


Fig. 2 Yields of 1,4-AHSO (■), 2,5-AHSO (▲) and isosorbide (●), and sorbitol conversion (▼), as a function of elapsed time for sorbitol dehydration reactions at (a) 523 and (b) 573 K in water (initial sorbitol concentration: 0.5 mol dm^{-3}) The lines show the best fit for the obtained data of sorbitol dehydration (1.0 mol dm^{-3})[10] to the equations in the Electronic Supplemental Information with the kinetic parameters in Table S1.

Table 1 Kinetic parameters for dehydration reactions of mannitol (initial mannitol concentration: 0.5 mol dm^{-3})

T^a (K)	523	548	560	573	Ea^b (kJ mol^{-1})
k_{1M} (mol h^{-1})	0.023	0.12	0.22	0.44	148
k_{2M} (mol h^{-1})	0.028	0.15	0.31	0.60	153
k_{3M} (mol h^{-1})	0.0044	0.020	0.038	0.065	135
k_{4M} (mol h^{-1})	0.0093	0.053	0.12	0.17	151
k_{6M} (mol h^{-1})	0.0097	0.077	0.18	0.51	196

^{a} Reaction temperature, ^{b} Activation energy

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_{3M} / (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.[10] In the case of sorbitol dehydration, the yield of 2,5-AHSO was less than 20% (Fig. 2), which was also consistent with the calculated 2,5-AHSO yield (k_{2S} / (k_{1S} + k_{2S} + k_{3S} + k_{6S})) (Table S1). The rate constant of k_{1S} (sorbitol to 1,4-AHSO) was the largest; thus, high-yield isosorbide (yield ca. 60%) could be obtained by a stepwise dehydration of 1,4-AHSO. On the other hand, the dehydration pathway from mannitol to 1,4-AHMA was not dominant; thus, the yield of isomannide (ca. 20%) was not so high as that of isosorbide.

Fig. S1 shows the Arrhenius plots of the rate constants during the mannitol dehydration in high-temperature liquid water. The activation energies for rate constants (k_{1M}, k_{2M}, k_{3M}, k_{4M}, and k_{6M}) were shown in Table 1. The activation energies of k_{1M} and k_{2M} (mannitol to 1,4-AHMA and 2,5-AHMA, respectively) were 148 and 153 kJ mol^{-1}, which were almost the same to each other. On the other hand, the activation energy of k_{1S} (sorbitol to 1,4-AHSO) was 127 kJ mol^{-1}, which was much lower than that of k_{2S} (166 kJ mol^{-1}) (sorbitol to 2,5-AHSO) (Table S2).

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 major products of monomolecular dehydration from sorbitol and mannitol were different from each other. The following reason can be given as a probable dehydration mechanism. The hydroxyl groups at the C-2 and C-3 positions in sorbitol are *trans*-form during the process of intramolecular dehydration from sorbitol to 1,4-AHSO and the major product of monomolecular dehydration was 1,4-AHSO, indicating that 1,4-AHSO are the favorable product without a structural hindrance of hydroxyl groups at the C-2 and C-3 positions. On the other hand, the hydroxyl groups at the C-2 and C-3 positions in mannitol are *cis*-form during the process from mannitol to 1,4-AHMA; thus, the structural hindrance causes a difficulty in reaction pathway to 1,4-AHMA and the 2,5-AHMA can be obtained as a major product. To confirm this dehydration mechanism, the arabitol dehydration (Scheme S1) in high-temperature liquid water was carried out. The intramolecular dehydration of arabitol provides 1,4-anhydroarabitol, 2,5-anhydroarabitol, and 1,5-anhydroarabitol (less than 5%). The yield of 1,4-anhydroarabitol was always more than twice larger than that of 2,5-anhydroarabitol (Fig. S2). The difference between 1,4-anhydroarabitol and 2,5-anhydroarabitol is only the conformation of *cis*- and *trans*-form in the hydroxyl groups of cyclic ethers. The favorable product of 1,4-anhydroarabitol from the arabitol dehydration has *trans*-form, indicating that the hydroxyl groups at the C-2 and C-3 positions in sugar alcohols dehydration are important and *trans*-form provide a favorable product. The *cis*-form of hydroxyl groups at the C-2 and C-3 positions in mannitol to 1,4-AHMA causes a difficulty in reaction pathway to 1,4-AHMA during the mannitol dehydration.

In summary, we have succeeded in the intramolecular dehydration of mannitol in high-temperature liquid water without adding any hazardous acid catalysts and compared mannitol dehydration behavior with that of sorbitol. 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-anhydrosorbitol, from the sorbitol monomolecular dehydration and that the yield of isomannide was lower than that of isosorbide.

Notes and references

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† Electronic Supplementary Information (ESI) available: [Experimental section, rate equations and kinetic parameters for dehydration reactions, and Arrhenius plot of mannitol dehydration]. See DOI: 10.1039/b000000x/

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