INSIGHTS INTO THE MECHANISM AND ACTIVITY OF METAL SALT-CATALYZED GLUCOSE CHEMISTRY IN AQUEOUS SOLUTION

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Abstract

Lewis acid-catalyzed glucose isomerization to fructose is an important step in biomass conversion to the platform chemical 5-hydroxymethylfurfural (HMF). While the mechanisms of glucose interconversions by heterogeneous metal-substituted zeolites have been recently elucidated, understanding the corresponding chemistry in homogeneous metal salt catalysts in aqueous solution is still limited. Here, we investigate the mechanisms of various Lewis acid metal (III) chlorides in glucose interconversions using $^{13}$C NMR and $^1$H NMR. We report glucose isomerization to fructose via 1,2 hydride transfer, stereospecific isomerization to sorbose via 1,5 hydride transfer, and epimerization to mannose via both 1,2 hydride transfer and 1,2 carbon shift, with the former being dominant. We hypothesize that the relative activity for the 1,2 carbon shift reaction correlates with the ionic radius of the catalyzing metal aqua cation. To fundamentally understand the observed wide range of activity of the metal salts, we perform an experimental and computational kinetic study coupled with DFT calculations. We expose a correlation of the binding energy of sugars on the active catalyst species with the catalytic activity for glucose conversion. These findings provide new insights into catalyst design for Lewis acid mediated sugar rearrangements in aqueous solution.

Keywords

Metal salts, glucose interconversion, hydride transfer, carbon shift, binding energies, activity, aqueous

Introduction

Synthesis of the versatile chemical HMF from biomass commonly proceeds through three consecutive reactions: cellulose hydrolysis to glucose, glucose isomerization to fructose, and fructose dehydration to HMF. However, the process is not cost-effective partly due to the high cost and equilibrium limitation of the industrial enzymatic isomerization process. Lewis acid catalysts, effective for glucose isomerization in water and compatible with Brønsted acid-catalyzed fructose dehydration, enable integration of the three aforementioned steps in one pot. A key development in this direction was the introduction of metal-substituted BEA zeolites by Davis and coworkers as active catalysts for glucose isomerization to fructose (Moliner et al., 2010), glucose epimerization to mannose (Bermejo-Deval et al., 2014), and other glucose interconversions (Gounder and Davis, 2013). The catalytic activity, selectivity, and mechanism of glucose interconversions vary with active site structures and reaction media. Sn-BEA is more active than Ti-BEA, while methanol enhances the activity compared to water. Sn-BEA and Ti-BEA catalyze glucose isomerization to fructose via an 1,2 intramolecular hydride transfer, while Na-Sn-BEA dominantly facilitates glucose epimerization to mannose via 1,2 intramolecular carbon shift. Additionally, Ti-BEA catalyzes glucose stereospecific isomerization to sorbose via 1,5 intramolecular hydride transfer. In all cases, the active sites are believed to be partially hydrolyzed, forming the so called “open site” structure.

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Another class of Lewis acids active for glucose isomerization in water entails homogeneous metal halides (Pagán-Torres et al., 2012). Mechanistic studies on CrCl$_3$ and AlCl$_3$ showed that the salts also catalyze glucose isomerization to fructose via 1,2 hydride transfer and the active sites are partially hydrolyzed cations with strikingly similar structure to the open site of Sn-BEA (Choudhary et al., 2013). The catalytic activity for glucose conversion also varies greatly with different metal salts (Wang et al., 2015). The mechanism of glucose epimerization and other interconversions, and the reason of varying metal salt activity are still not well understood. In this study, we examine for the first time the mechanism of mannose and sorbose formation from glucose in aqueous phase by metal (III) chlorides (MCl$_3$). We combine experimental and computational kinetic studies with DFT calculations to elucidate the effect of metal cation-sugar binding energy on activities for glucose conversion in aqueous solution.

**Methods and Findings**

We perform isotopic labeling experiments on glucose deuterated at C2 or labeled $^{13}$C at C1, coupling with $^{13}$C NMR and $^1$H NMR to investigate the glucose interconversion mechanism by MCl$_3$, including Cr$^{3+}$, Al$^{3+}$, Ga$^{3+}$, In$^{3+}$, La$^{3+}$, Dy$^{3+}$, and Yb$^{3+}$. The results are summarized in Scheme 1. We found that MCl$_3$ catalyze glucose isomerization to fructose via 1,2 hydride transfer (similar to Sn-BEA), and glucose stereospecific isomerization to sorbose via 1,5 hydride transfer (similar to Ti-BEA). Interestingly, MCl$_3$ catalyze glucose epimerization to mannose via two competing pathways, 1,2 hydride transfer and 1,2 carbon shift with the former being dominant. This is different from the BEA zeolites which only mediate 1,2 hydride transfer (Sn-BEA) or 1,2 carbon shift (Na-Sn-BEA). Among the MCl$_3$, the lanthanide salts can catalyze the carbon shift more easily than the Cr$^{3+}$ and Al group salts. We propose that the metal cation ionic radius and ligand coordination affect the structural flexibility of the metal-sugar complex, and eventually its ability to catalyze the 1,2 carbon shift.

![Scheme 1. Mechanism of MCl$_3$ catalyzed glucose transformation in aqueous solution](image)

In addition, we carry a comprehensive experimental and computational kinetic study on the metal salt-catalyzed glucose chemistry in combination with a speciation study in order to elucidate the effect of the metal salts’ active species concentration on the rate of glucose conversion. DFT calculations of the binding energy of sugars on the active species reveals a correlation with the rate of glucose conversion (not shown).

**Conclusions**

We reveal for the first time the mechanism of glucose interconversions to fructose, mannose and sorbose by metal salts MCl$_3$ using NMR spectroscopy. We propose the metal cation’s effective ionic radius and ligand coordination are possible traits for the difference in selectivity to 1,2 carbon shift vs. 1,2 hydride transfer. The combination of experimental and computational kinetic studies rationalizes the reactivity trends and insights into the best catalysts. These findings provide insights for further work on heterogeneous catalyst design.

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**References**


