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Catalytic consequences of borate complexation and pH on the epimerization of L-arabinose to L-ribose in water catalyzed by Sn-Beta zeolite with borate salts

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ABSTRACT

Sn-Beta zeolite with sodium tetraborate cooperatively catalyzes the epimerization of aldoses via an intramolecular 1,2 carbon-shift mechanism. L-Arabinose is one of the seven common sugars and its epimer, L-ribose, is a valuable rare sugar with applications in antiviral and anticancer agents. Here, a full factorial experimental design is performed to demonstrate the catalytic consequences of varying key reaction parameters such as pH, borate to sugar ratio, and reaction time. Reactivity data revealed that isomerization is favored under acidic pH conditions ($pH < 7.0$); that epimerization dominates under neutral conditions (pH ranging from 7.0 to 7.8); and that drastic inhibition of both epimerization and isomerization rates occur under basic conditions ($pH > 7.8$). Using a 5 wt% arabinose feed and 100:1 sugar–metal ratios at 343 K, conversions ranging from 20% to 30% were obtained with selectivities of 75%, 84%, and 91% for boron–sugar ratios of 0.2:1, 0.5:1, and 1:1, respectively. The predominance of epimerization over isomerization products with substoichiometric borate suggests that one borate can influence the reactivity of several sugar molecules and may influence the Sn active site directly. Reaction data obtained under differential conditions revealed that the epimerization reaction follows first order kinetics over a wide temperature range with an apparent activation energy of 98 kJ/mol and pre-exponential factor of $1.9 \times 10^{14}\,\mathrm{L\,mol\,Sn^{-1}\,s^{-1}}$.

1. Introduction

Carbohydrates are involved in important biological processes and also serve as valuable building blocks in many commercial applications. For instance, the common pentose D-ribose is a major component in ribonucleic acid (RNA), adenosine triphosphate (ATP), and nicotinamide adenine dinucleotide (NADH) in metabolism. The industrial production of riboflavin also involves the use of D-ribose [1]. The rare pentose, L-ribose, has found applications in anti-viral and anti-cancer drugs because its reverse stereochemistry alters the interaction with enzymes, inhibiting the nucleoside synthesis-replication process [2]. Additionally, L-RNA binds tightly to natural RNA and is resistant to degradation by nucleases, allowing it to silence gene expression. Consequently, L-ribose is part of several pharmaceuticals presently on the market or undergoing clinical trials [3]. To meet the demand for such rare sugars, costly and complex biochemical [4] and synthetic organic processes are currently used to produce them from common carbohydrates [5]. Therefore, the development of simpler and more effective catalytic pathways to produce rare sugars is of great relevance.

The selective epimerization of aldoses is an attractive pathway for the production of rare sugars. L-Arabinose is a common sugar found in the hemicellulose fraction of biomass. As depicted in Fig. 1, arabinose is interconverted into an equilibrium mixture consisting of ca. 66% arabinose, 11% ribulose and 23% ribose in the presence of isomerase enzymes or inorganic base catalysts at 333 K [6]. Ribulose is the ketose isomer, while ribose is the aldose epimer, typically formed by way of a double isomerization process. The direct epimerization of arabinose into ribose may be accomplished using epimerase enzymes to generate a distribution of 74% arabinose and 26% ribose at 333 K. However, most epimerases only function on substrates modified with phosphate or nucleotide groups. Direct epimerization yields a product distribution that does not contain ribulose, and is therefore more amenable for purification. Epimerization of arabinose to ribose is slightly endothermic, and consequently, high temperatures lead to higher equilibrium ribose yields (see Fig. S1). In this respect, inorganic catalysts may be attractive epimerization candidates given that they are not limited by temperature or substrate functionalization in the same manner as biological catalysts [6].

Hydrophobic zeolites with metal atoms substituted in the crystalline microporous framework have recently emerged as a new

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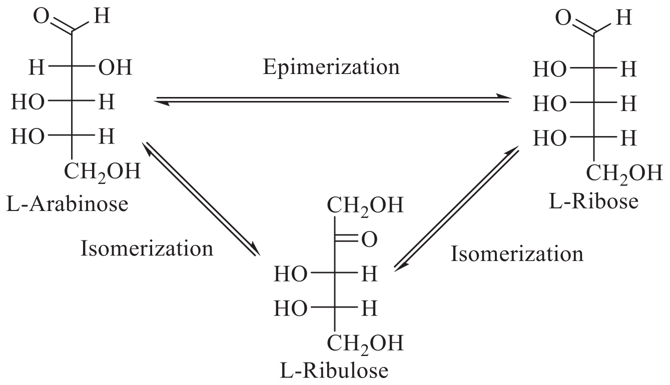

Fig. 1. Schematic representation of the isomerization and epimerization of L-arabinose. The D form is the mirror image of the L form.

class of Lewis acid catalysts capable of activating carbonyl functional groups in the presence of water. The highly dispersed tetrahedrally-coordinated metal centers can accept electron pairs through empty d orbitals and expand their coordination shells from 4 to 5 or 6 sites due to their large covalent radii. Tin-containing zeolites are active in the Meerwein–Ponndorf–Verley reduction [7,8], Baeyer–Villiger oxidation [9–11], and carbonyl-ene reaction [12]. In the context of carbohydrate chemistry, the incorporation of Sn, Ti, and Zr in the framework of Beta zeolite has found applications in the conversion of hexoses [13,14], pentoses [15–18], and trioses [19–22] via intramolecular hydride shifts, as well as in the production of gamma-valerolactone from xylose [23] and alpha-hydroxyacids [24,25] from C-2 and C-4 oxygenates. Recent work shows that Sn-Beta catalyzes the chiral Baeyer–Villiger oxidation of sugar derivatives [26].

Our recent work has shown that Sn-Beta with sodium tetraborate cooperatively catalyzes the selective epimerization of aldoses in aqueous media under mild conditions [27]. The reaction mechanism, investigated using ^{13}C-labeled sugars and nuclear magnetic resonance (NMR), proceeds by way of a 1,2 carbon-shift mechanism whereby C1 forms a new C—C bond with C3, while C2 moves to the C1 position. In the absence of the borate promoter, no carbon backbone rearrangement occurs and Sn-Beta catalyzes a regular aldose–ketose isomerization via an intramolecular hydride shift as reported in previous studies [14]. The epimerization mechanism is analogous to the Bilik reaction using molybdenum-based catalysts that form rigid complexes by interacting with the hydroxyl groups of C1–C4 in the sugar [28,29].

Isomorphic substitution of tin for silicon tetrahedrally-coordinated in the crystalline zeolite framework generates a closed site. Hydration with two water molecules produces a Sn site with octahedral coordination, while hydrolysis of one of the Sn–O–Si bridges generates an open site. For the isomerization of glucose to fructose, Davis and co-workers showed that the open-site in Sn-Beta promotes the ring opening and the hydride transfer steps more favorably than the closed site [30]. In the presence of borate, the 1,2 hydride-shift isomerization pathway is drastically inhibited in favor of a 1,2 carbon-shift epimerization pathway. Interestingly, a similar 1,2 carbon-shift product has been recently reported using Sn-Beta in methanol, although epimerization rates are lower when compared to the Sn-Beta/borate system in water [31]. Borates can interact with the hydroxyl groups found in carbohydrates and with the silanol groups found near the Sn open site, both with a strong dependence on pH [32]. We hypothesize that the borate additive interacts with the sugar and/or the active site to change the reaction from a hydride-shift isomerization to a carbon-shift epimerization pathway. Here, we present a full factorial experimental design to investigate the impact of pH, sugar to borate ratio, and reaction time on the epimerization of L-arabinose to L-ribose. The conversion of arabinose to ribose provided a high value added case to investigate the role of sugar–borate complexation. Understanding which species and reactions are dominant under controlled reaction conditions provides insight into the role of additives in directing the sugar conversion pathway. Thus, we show a comparison of isomerization activity with the fraction of free sugar under low borate loadings and use ^{11}B NMR and Raman spectroscopy characterization to identify sugar borate dimers and polyborates in solution. A temperature study is performed to extract kinetic parameters and optical rotation measurements are used to assess stereospecificity.

2. Experimental

2.1. Catalyst synthesis

Sn-Beta was synthesized as follows: 26.735 g of aqueous tetraethylammonium hydroxide (Sigma–Aldrich, 35% (w/w)) and 24.069 g of tetraethylorthosilicate (Sigma–Aldrich, 99% (w/w)) were added to a Teflon® (Polytetrafluoroethylene, [PTFE]) dish, which was magnetically stirred at room temperature for 90 min and then cooled in an ice bath. Then, 0.261 g of tin (II) chloride dihydrate (Sigma–Aldrich, 98% (w/w)) dissolved in 15 g of cold deionized water (DI H_2O) was added dropwise. Sn(II) which oxidizes to Sn(IV) in water was used in place of $SnCl_4 \cdot 5H_2O$ and has resulted in Sn-Beta consistently free of extraframework SnO_2. The solution was left uncovered on a stir plate for 10 h to reach a total mass of 35 g. Next, 2.600 g of aqueous hydrofluoric acid (Sigma–Aldrich, 48% (w/w)) was added dropwise and the mixture was homogenized using a PTFE spatula, resulting in a thick gel. Then, 0.358 g of previously-made Sn-Beta was seeded into the mixture, which was allowed to evaporate to 33.776 g, which corresponds to a final molar composition of SiO_2/0.01 $SnCl_2$/0.55 TEAOH/0.54 HF/7.52 H_2O. The thick paste was transferred to a 45 ml PTFE-lined stainless steel autoclave and heated to 413 K for 40 days under static conditions. The solids were recovered by filtration, washed with DI H_2O, dried at 373 K and calcined at 853 K for 10 h with a 1 K min^{-1} ramp and 1 h stops at 423 and 623 K, leading to an overall inorganic oxide yield of 80–90%.

Powder X-ray diffraction (PXRD) patterns were collected using a Bruker D8 diffractometer with Cu Kα radiation, which confirmed that the solid material has the Beta topology (see Supplementary Fig. S2). Ultraviolet–visible (UV–vis) measurements were recorded using a Varian Cary 5000 UV-vis-NIR spectrometer with a diffuse reflectance cell after calcination without subsequent drying. The ultraviolet–visible diffuse reflectance spectrum of the calcined sample shows the presence of a unique band at ~200 nm, which has been associated with Sn tetrahedrally coordinated into the zeolite framework (see Supplementary Fig. S3); as additional confirmation of framework incorporation, ^{119}Sn NMR of an analogous sample is included in Fig. S4. Sn content was measured using a Horiba Jobin Yvon ACTIVA-S ICP-AES. Catalyst samples were dissolved in a few drops of 48% HF and diluted in 2% nitric acid after evaporation of the HF.

2.2. Solutions

Within this study, the sugar content was held constant and the borate content was varied to obtain the desired ratios. The sodium to borate ratio was adjusted by mixing boric acid, sodium tetraborate, sodium metaborate and sodium hydroxide on a mass basis on a 50 ml solution scale (see Table S1). The pH was measured with a Mettler Toledo FiveEasy FE20 probe, calibrated with pH 6, 7 and 10 buffers prior to use at 298 K. For the control experiments, the pH-adjusted solutions without borate were very sensitive and were