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Synthesis of Hexane-Tetrols and -Triols with Fixed Hydroxyl Group Positions and Stereochemistry from Methyl Glycosides over Supported Metal Catalysts

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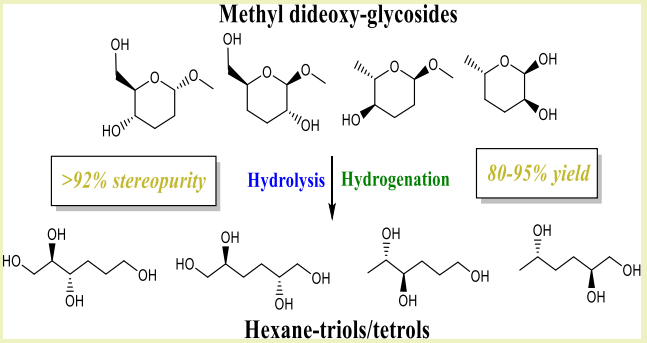
Supporting Information

ABSTRACT: Carbohydrates are a renewable feedstock for the production of partially reduced polyols, but typical hydrogenolysis processes are unselective toward C−O bond cleavage at different positions and erase the stereocenters present in the feedstock. In this study, we demonstrate the synthesis of new types of acyclic polyols from methyl glycosides with fixed hydroxyl group positions and stereochemistry. Products include (2*R*,3*S*)-1,2,3,6-hexanetetrol, (2*R*,5*S*)-1,2,5,6-hexanetetrol, (2*S*,5*S*)-1,2,5-hexanetriol, and (4*R*,5*S*)-1,4,5-hexanetriol. Methyl glycosides are first selectively deoxydehydrated and hydrogenated to methyl dideoxy-glycosides as reported in previous work. These methyl dideoxy-glycosides are then converted to hexane-triols and -tetrols over Pt-based catalysts in water in 80−95% yield via methoxy bond hydrolysis and hydrogenation. This route largely preserves the stereocenters of the remaining hydroxyl groups (>92% stereopurity). The nature of the intermediates formed depends on the structure of the glycoside feedstock. 3,4-Dideoxy-glycosides can undergo inversion of the C_2−OH stereocenter because of an aldose-ketose isomerization reaction, which can be mitigated by using a bifunctional metal−acid catalyst to facilitate the reaction at lower temperature. By demonstrating a new route to produce renewable polyols with fixed hydroxyl group positions and stereochemistry, this report lays the groundwork for further research into the applications of these molecules in the chemical industry.



KEYWORDS: *glycosides, polyols, catalysis, renewable, stereochemistry, hexanetriol, hexanetetrol*

INTRODUCTION

Carbohydrates are valuable bio-renewable feedstocks for the production of oxygenated chemicals.[1] They are also useful precursors for chiral product synthesis because of their well-defined stereochemistry.[2] The feedstocks in this work include the methyl glycosides of D-galactose, derived from milk sugar;[3] D-mannose, derived from plant sources or produced from glucose epimerization;[4] L-rhamnose, a 6-deoxy sugar predominantly found in plant pectin;[5] and L-fucose, a 6-deoxy-sugar predominantly found in algae.[6] Sugars as well as lignocellulosic biomass can be hydrodeoxygenated to partially reduced polyols over heterogeneous metal-acid catalysts.[1,7,8] However, these processes are typically not regio-selective because of the indiscriminate cleavage of hydroxyl groups, which results in a complex mixture of polyols.[9−11] These catalytic steps typically also erase the stereocenters present in the original sugar feedstock. It would be highly desirable to selectively produce polyols from sugars with fixed hydroxyl group positions and stereochemistry.

Tomishige and co-workers recently reported on a route to selectively remove cis-vicinal OH groups from a variety of methyl glycoside feedstocks in 82−92% yield using a ReO_x−Pd/CeO_2 catalyst by deoxydehydration and successive hydrogenation, resulting in stereopure methyl dideoxy-glycosides.[12−14] Methyl glycosides can be produced from sugars in nearly quantitative yields in methanol over an acid catalyst.[15]

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Scheme 1. Reaction Network for Conversion of Methyl 2,3-Dideoxy-glycosides

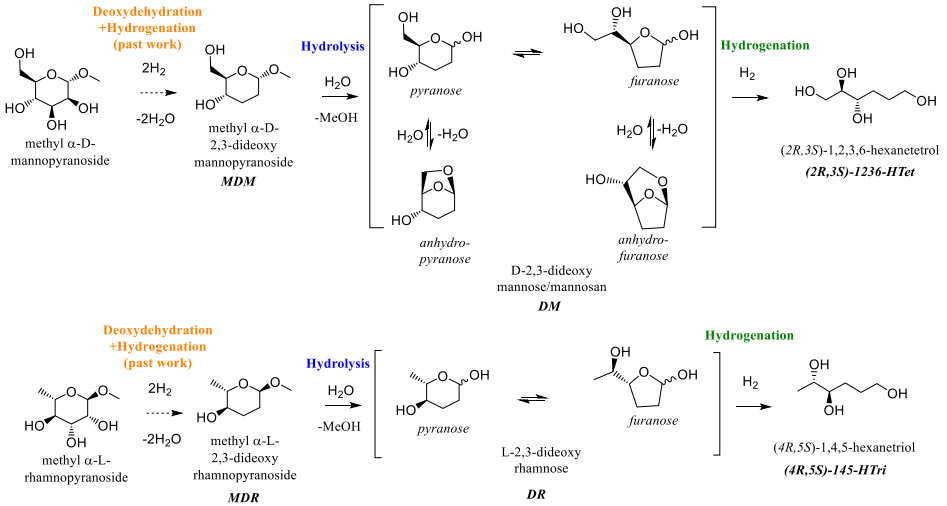

Table 1. Conversion of Methyl 2,3-Dideoxy-glycosides to Hexane-Triols and Hexanetetrols[a]

entry	feed	catalyst	conversion (%)	major product	HPLC selectivity (%)	diastereomer selectivity
1	MDM	5% Pt/SiO_2	100	1236-HTet	95	>99% (2*R*,3*S*)
2A	MDM	none	100	DM		
2B	product of 2A	5% Pt/SiO_2	100	1236-HTet	96	>99% (2*R*,3*S*)
3	MDR	5% Pt/SiO_2	100	145-HTri	92	>99% (4*R*,5*S*)
4A	MDR	none	100	DR		
4B	product of 4A	5% Pt/SiO_2	96	145-HTri	76	>99% (4*R*,5*S*)

[a]Conditions: 2 wt % feed in water (10−15 g), 120 °C, 21 h, 10 mg cat/g solution, 1000 psi H_2. Additional details are provided in Table S5 of the Supporting Information.

In one example, a 3,4-dideoxy-arabinoside feedstock was further converted to (2*R*)-1,2,5-pentanetriol using methoxy bond hydrolysis followed by hydrogenation.[12] Product stereochemistry can be critical for applications such as pharmaceuticals, fine chemicals, and polymer synthesis.[2,16]

Use of bio-derived monomers in the chemical industry offers numerous benefits including a lower carbon footprint than petroleum-derived materials and the potential for new materials with unique properties and performance.[17,18] Partially reduced polyols are valuable intermediates, with applications as polymer precursors (e.g., in alkyd resins), surfactants, and nontoxic solvents.[1] For example, 1,2,6-hexanetriol can be produced from petroleum via acrolein dimerization[19] or from biomass via 5-hydroxymethylfurfural.[20,21] 1,2,6-Hexanetriol has applications as a surfactant, nontoxic solvent, and cross-linker in alkyd resins.[22,23] Derivatives of 1,2,6-hexanetriol are used in hydraulic fluids, corrosion inhibitors,[24] and plasticizers.[23] 1,2,5,6-hexanetetrol (1256-HTet), a partially reduced, symmetric C_6 polyol, has attracted industrial interest as an intermediate to polyesters, alkyd resins, and polyurethanes.[10,25] A recent Archer Daniels Midland patent reported the production of 1256-HTet in up to 50% yield from hydrogenolysis of sugars over a Cu catalyst, along with a complex mixture of other polyols.[10] We recently reported on a new route to produce 1256-HTet from biomass-derived levoglucosanol in up to 90% yield.[26] Hydrolysis of levoglucosanol forms 3,4-dideoxy sugar intermediates that are then hydrogenated to a mixture of (2*R*,5*S*)-1256-HTet and (2*S*,5*S*)-1256-HTet. De bruyn and co-workers synthesized chiral mesoporous polyboronates from 1256-HTet, showing that the stereochemistry of 1256-HTet influences the porosity properties of these materials.[27]

Polyol-based nonionic surfactants, comprised of a hydrophilic polyol head group and hydrophobic tail, have gained attention for cosmetics and pharmaceuticals applications because of their biodegradability and nontoxicity. Key properties, such as hydrophilicity and phase behavior, are a strong function of the number, positions, and stereochemistry of hydroxyl groups.[28] Further work is needed to synthesize materials from novel biomass-derived polyols to understand the relationship between the monomer structure and product properties.[17]

In this work, we show that the methyl dideoxy-glycosides can be converted into hexanetriols and hexanetetrols with fixed hydroxyl group positions and stereochemistry over a supported metal catalyst (Pt was selected as a model hydrogenation catalyst). We propose a reaction mechanism involving methoxy bond hydrolysis and hydrogenation based on the experimental results. Our results demonstrate a selective catalytic approach to produce hexanetetrols and hexanetriols as valuable monomers for the chemical industry.

RESULTS AND DISCUSSION

Conversion of Methyl 2,3-Dideoxy-glycosides. The reaction networks for the conversion of methyl 2,3-dideoxy-mannopyranoside (MDM) and methyl 2,3-dideoxy-rhamnopyranoside (MDR) are shown in Scheme 1. Using a 5% Pt/SiO_2 catalyst at 120 °C in water, MDM is converted to (2*R*,3*S*)-1,2,3,6-hexanetetrol (1236-HTet) in 95% yield and >99% stereopurity [Table 1, entry 1; NMR and high-performance liquid chromatography (HPLC) provided in

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Scheme 2. Reaction Network for Conversion of Methyl 3,4-Dideoxy-glycosides

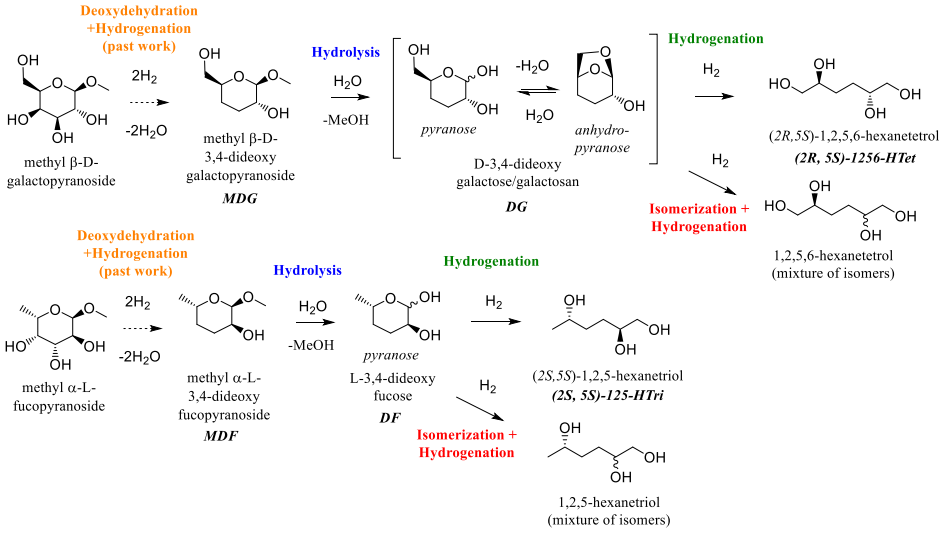

Table 2. Conversion of Methyl 3,4-Dideoxy-glycosides to Hexane-Triols and Hexanetetrols[a]

entry	feed	catalyst	conditions	conversion (%)	major product	HPLC selectivity (%)	diastereomer selectivity
1	MDG	5% Pt/SiO_2	150 °C, 15 h[b]	94	1256-HTet	83	95% (2*R*,5*S*), 5% (2*S*,5*S*)
2A	MDG	Amberlyst 70	100 °C, 2 h	100	DG		
2B	product of 2A	5% Pt/SiO_2	100 °C, 32 h	100	1256-HTet	77[c]	94% (2*R*,5*S*), 6% (2*S*,5*S*)
3	MDG	5.3% Pt/SiAl	100 °C, 62 h	94	1256-HTet	87	98% (2*R*,5*S*), 2% (2*S*,5*S*)
4	MDF	5% Pt/SiO_2	150 °C, 15 h[b]	100	125-HTri	90	82% (2*S*,5*S*), 18% (2*R*,5*S*)
5A	MDF	Amberlyst 70	100 °C, 2 h	100	DF		
5B	product of 5A	5% Pt/SiO_2	100 °C, 32 h	100	125-HTri	79	93% (2*S*,5*S*), 7% (2*R*,5*S*)
6	MDF	5.3% Pt/SiAl	100 °C, 62 h	100	125-HTri	84	92% (2*S*,5*S*), 8% (2*R*,5*S*)

[a]Conditions: 2 wt % feed in water (10−15 g), experiments with Pt catalysts conducted with 10 mg cat/g solution and 1000 psi H_2. Experiments with Amberlyst 70 catalysts conducted with 8.33 mg cat/g solution and 500 psi Ar. Additional details are provided in Table S5 of the Supporting Information. [b]Reaction at 120 °C for 21 h resulted in ∼10% conversion. [c]16% yield of anhydro-DG. Anhydro-DG would only be converted to 1256-HTet in the presence of a metal−acid catalyst.

Supporting Information, pages S5−S7]. Incorporating the 96% yield of MDM from methyl mannopyranoside,[12] the overall yield of 1236-HTet from methyl mannopyranoside is 91%. At the same reaction conditions, MDR is converted to (4*R*,5*S*)-1,4,5-hexanetriol (145-HTri), in 92% yield and >99% stereopurity (Table 1, entry 3; NMR, HPLC, and relative stereochemistry assignment by derivatization provided in the Supporting Information, pages S8−S13). Incorporating the 92% yield of MDR from methyl rhamnopyranoside,[12] the overall yield of 145-HTri from methyl rhamnopyranoside is 85%.

Carrying out the reaction without any catalyst demonstrates that the first step is hydrolysis of the methoxy group. For MDM conversion, 36 ^{13}C NMR peaks are observed at complete reactant conversion (Table 1, entry 2A). These intermediates are identified as the α and β pyranose, α and β furanose, anhydro-furanose, and anhydro-pyranose forms of 3,4-dideoxy-mannose/mannosan (DM), based on ^{13}C NMR chemical shifts, multiplicities, and electrospray ionization mass spectrometry (ESI-MS) data (Supporting Information, pages S19−S21). Some of these intermediates may exist in equilibrium in water at room temperature. Hydrogenation of this mixture (Table 1, entry 2B) produces 1236-HTet in high yield, showing that DM is an intermediate to 1236-HTet. Cyclic hemiacetals exist in equilibrium with an aldehyde form.[29] While the aldehyde forms are not observed by ^{13}C NMR at room temperature, likely because of their expected low concentration, the aldehyde is expected to be the reactive intermediate toward hydrogenation.

For the MDR case, 24 ^{13}C NMR peaks are observed at 100% reactant conversion (Table 1, entry 4A). These intermediates are identified as four C_6 species, namely the α and β pyranose and α and β furanose of 2,3-dideoxy-rhamnose (DR), based on ^{13}C NMR chemical shifts, multiplicities, and ESI-MS data (Supporting Information, pages S21−S22). Some of these intermediates may exist in equilibrium in water at room temperature. DR cannot convert into an anhydrosugar because of the lack of a C_6−OH group. Over Pt/SiO_2, these intermediates are hydrogenated to 145-HTri in 76% selectivity (Table 1, entry 4B). The decrease in selectivity from the one-step case (entry 3) to the two-step case (entries 4A−B) could be because of side reactions that occur when the metal is not present to rapidly hydrogenate intermediates. Small unknown peaks are observed in the HPLC, whose yield sums to 9% (assuming they have the same RI sensitivity as 145-HTri).

Conversion of Methyl 3,4-Dideoxy-glycosides. The reaction networks for conversion of methyl 3,4-dideoxy-glycosides are shown in Scheme 2. Hydrogenation of these feedstocks at 120 °C for 21 h over 5% Pt/SiO_2 results in low (∼10%) conversion, under conditions where the two methyl 2,3-dideoxy-glycosides achieve 100% conversion. A higher temperature of 150 °C was therefore used for the conversion of methyl 3,4-dideoxy-glycosides. The lower reactivity of methyl

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3,4-dideoxy-glycoside (MDG, MDF) compared to methyl 2,3-dideoxy-glycosides (MDM, MDR) is consistent with the fact that the hydrolysis rate of methyl 2-deoxy-glucopyranoside has been reported to be three orders of magnitude greater than that of methyl glucopyranoside.[15] This effect is likely because of the electron-withdrawing nature of the C_2−OH group, which destabilizes the carbocation transition state.

Over 5% Pt/SiO_2 at 150 °C, methyl 3,4-dideoxy-galactopyranoside (MDG) is converted to (2*R*,5*S*)-1256-HTet with 83% selectivity and 95% (2*R*,5*S*) stereopurity (Table 2, entry 1). Incorporating the 88% yield of MDG from methyl galactopyranoside,[12] the overall selectivity of 1256-HTet from methyl galactopyranoside is 71%. At the same reaction conditions, methyl-3,4-dideoxy-fucopyranoside is converted to (2*S*,5*S*)-1,2,5-hexanetriol (125-HTri) in 90% selectivity and 82% (2*S*,5*S*) stereopurity (Table 2, entry 4). Incorporating the 82% yield of MDF from methyl fucopyranoside,[12] the overall selectivity of 125-HTri from methyl fucopyranoside is 74%.

While 2,3-dideoxy feedstocks can be converted to hexanetetrols/triols with >99% stereopurity, 3,4-dideoxy feedstocks display some selectivity toward C_2−OH stereo-inversion products (Table 2). In our past work, we reported that DG can undergo aldose-ketose isomerization to form a hemiketal-ketone species, 3,4-dideoxy-fructose.[26] This reaction occurs in the absence of catalyst at 150 °C but is largely suppressed at a lower temperature of 100 °C. Formation of the ketone group at the C_2 position erases the original C_2 stereocenter and hydrogenation results in a 1:1 mixture of diastereomers of 1256-HTet.[26] Therefore, we expect that the decrease in preservation of the C_2−OH stereocenter in MDG and MDF conversion is because of aldose-ketose isomerization of DG and DF prior to hydrogenation (Scheme 2). The isomerization is only possible for sugars containing a C_2−OH group and is not possible for MDM or MDR.

To investigate the reaction network for MDG and MDF conversion, we treated these feedstocks with an Amberlyst 70 acid catalyst at 100 °C to hydrolyze the methoxy group while avoiding aldose-ketose isomerization (Table 2, entries 2A and 5A). MDG is hydrolyzed to form a mixture of 3,4-dideoxy-galactopyranose (DG-pyranose) and 3,4-dideoxy-galactosan (anhydro-DG) intermediates (Table 2, entry 2A). In our previous work, we reported that anhydro-DG is hydrolyzed to DG-pyranose with an equilibrium conversion of 83% at 100 °C over an acid catalyst in water.[26] The same equilibrium distribution between anhydro-DG and DG-pyranose is observed here (Supporting Information, page S23). Unlike DM and DR, DG cannot form a furanose tautomer because of the lack of a C_4−OH group. Hydrogenation of DG results in the formation of (2*R*,5*S*)-1256-HTet with high selectivity (77%) and stereopurity (95%) (Table 2, entry 2B), confirming that these are key intermediates between MDG and 1256-HTet. The 16% residual anhydro-DG is not converted in this second step over Pt/SiO_2, as hydrolysis of this intermediate requires an acid catalyst. It is noteworthy that a fraction of the dideoxy sugars DG and DM can be dehydrated to anhydro-species in water at 100 °C, whereas for regular sugars such as glucose, the equilibrium greatly favors glucose over levoglucosan in water.[30] This suggests that the removal of hydroxyl groups from sugar molecules changes the relative stabilities of sugar and anhydro-sugar in water.

At the same reaction conditions, MDF is hydrolyzed to intermediates that are identified as the α and β pyranose forms of 3,4-dideoxy-fucose (DF), based on ^{13}C NMR chemical shifts and multiplicities and ESI-MS data (Table 2, entry 5A) (Supporting Information, page S24). Some of these intermediates may exist in equilibrium in water at room temperature. A furanose tautomer cannot be formed because of the lack of a C_4−OH group, and an anhydro-species cannot be formed because of the lack of a C_6−OH group. Hydrogenation of DF produces (2*S*,5*S*)-125-HTri in high yield and stereopurity (Table 2, entry 5B), confirming that DF is a key intermediate between MDF and 125-HTri.

To further increase the preservation of stereochemistry for MDG and MDF conversion relative to the experiments with 5% Pt/SiO_2 at 150 °C, we used a bifunctional metal−acid catalyst, 5% Pt/SiAl, at 100 °C. The acid sites facilitate methoxy bond hydrolysis at lower temperature where the aldose-ketose isomerization is suppressed, while the metal sites rapidly hydrogenate the DG/DF intermediates. Using this approach, the stereopurity of 1256-HTet increases from 95% (2*R*,5*S*) to 98% (Table 2, entry 3) with 87% total selectivity to 1256-HTet (NMR and HPLC provided in the Supporting Information, pages S13−S16). Incorporating the 88% yield of MDG from methyl galactopyranoside,[12] the overall selectivity of 1256-HTet from methyl galactopyranoside is 77%. The stereopurity of 125-HTri increases from 82% (2*S*,5*S*) to 92% (Table 2, entry 6) with 84% overall selectivity to 125-HTri (NMR and HPLC provided in the Supporting Information, pages S16−S19). Incorporating the 82% yield of MDF from methyl fucopyranoside,[12] the overall selectivity of 125-HTri from methyl fucopyranoside is 69%.

METHODS

Chemicals and Materials. $Pt(NH_3)_4(NO_3)_2$ solution (99%, Strem Chemicals) was used as received. Grade 135 amorphous SiO_2−Al_2O_3 (SiAl) and Davisil grade SiO_2 were purchased from Sigma-Aldrich. Amberlyst 70 (possessing >2.55 mmol/g acid sites as reported by the vendor) was purchased from Dow Chemical, and was washed, crushed, and dried prior to use. Milli-Q water was used for all reactions and catalyst syntheses. The synthesis of methyl dideoxy-glycosides from methyl glycosides was reported in our previous work[12] and is described in the Supporting Information (pages S2−S4).

Catalyst Synthesis and Characterization. Pt/SiAl and Pt/SiO_2 catalysts were synthesized by incipient wetness impregnation of a $Pt(NH_3)_4(NO_3)_2$ solution in water. The catalysts were dried at 110 °C in air, calcined at 400 °C in flowing air (1 °C/min ramp, 3 h hold), reduced at 260 °C in flowing hydrogen (1 °C/min ramp, 4 h hold), and then passivated at room temperature with 1% O_2/Ar. When the SiAl support was used directly in a reaction, it was calcined at 400 °C in flowing air prior to use. Pt site densities measured by CO chemisorption and the acid site density of the 5.3% Pt/SiAl catalyst measured by NH_3-temperature programmed desorption are reported in our previous work.[26,31] The 5% Pt/SiO_2 catalyst possesses 91 μmol/g surface Pt sites based on irreversible CO titration, corresponding to a Pt dispersion of 36%. The 5.3% Pt/SiAl catalyst possesses 111 μmol/g surface Pt sites based on irreversible CO titration, corresponding to a Pt dispersion of 41%, and 480 μmol/g acid sites based on NH_3-TPD after adsorption at 150 °C. Safe use of hazardous gases (CO, NH_3, H_2) was ensured by leak checking all gas lines prior to use and venting effluent gases into a fume hood.

Product Identification and Quantification. "Conversion" was defined as the change in reactant concentration divided by initial reactant concentration (measured by HPLC or ^{13}C NMR). "Yield" was defined as the product concentration (measured by HPLC) divided by the initial reactant concentration (accounting for feedstock purity as measured by GC, see Supporting Information pages S2−S4). "Selectivity" was defined as the yield divided by the conversion.

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"Diastereoselectivity" was defined as the concentration of the major diastereomer divided by the sum of concentrations of both diastereomers, measured by ^{13}C NMR. If only a single diastereomer was observed, the diastereoselectivity was reported as >99% based on the detection limit of the measurement.

Product concentrations were quantified using Shimadzu HPLC equipped with a BioRad Aminex 87H column. The mobile phase was 5 mM H_2SO_4 (HPLC grade, Ricca Chemical) operated at a flow rate of 0.6 mL/min with a column temperature of 30 °C and an injection volume of 3 μL. Reaction products were quantified by HPLC using a refractive index (RI) detector. Chemical standards of the reaction products in this work are not commercially available. 1256-HTet was prepared from dihydrolevoglucosenone, according to our previous work.[26] The RI sensitivity of 1236-HTet was assumed to be equal to that of 1256-HTet. For quantification of 145-HTri and 125-HTri, the RI sensitivity of these species was assumed to be equal to that of 1,2,6-hexanetriol.

^{13}C NMR spectra were collected on a Bruker AVANCE 500 MHz spectrometer at room temperature, using a Bruker DCH CryoProbe for increased sensitivity. 10% D_2O was added to the samples prior to analysis. The ^{13}C NMR spectra were absolute-referenced to the associated ^{1}H NMR spectra. ^{13}C spectra were collected using 1H-decoupling using a 30° pulse, 128 scans, an acquisition time of 1 s, and a relaxation delay of 2 s. Quantitative ^{13}C NMR spectra were collected using inverse-gated decoupling, using a 30° pulse, 112 scans, an acquisition time of 1 s and a relaxation delay of 30 s. Diastereoselectivities were measured by integrating the ^{13}C NMR peaks for the two diastereomers. ^{1}H spectra were collected using "presaturation" water suppression, with a 30° pulse, 8 scans, an acquisition time of 3 s, and a relaxation delay of 15 s. Distortionless enhancement by polarization transfer spectra were used to assign the multiplicities of ^{13}C peaks. NMR and HPLC analyses of the reaction products are provided in the Supporting Information.

ESI-MS analysis of reaction intermediates was done on a Bruker maXis ultra-high resolution, time-of-flight mass spectrometer using infusion in positive-ion mode. Samples were diluted 50,000–100,000× in 80% methanol/20% water (v/v) prior to analysis. Samples were infused at 3 μL/min with a source voltage of 3500 V. The source temperature was set to 180 °C, while the nebulizer pressure was 0.4 bar, and the drying gas flow was 4 L/min. The mass range measured was 75–1550 m/z.

Optical rotation measurements were performed on a PerkinElmer 241 Polarimeter using a 589.3 nm Na lamp and compared to literature values when possible. Reaction product samples were dried using a vacuum oven and diluted with methanol prior to analysis.

For (4*R*,5*S*)-145-HTri, relative stereochemistry was independently verified by derivatization with phenylboronic acid to produce the cyclic boronate ester, 3-(5-methyl-2-phenyl-1,3,2-dioxaborolan-4-yl)-propan-1-ol (MPDPO). (4*R*,5*S*)-145-HTri was dissolved in $CHCl_3$, and an equimolar amount of phenylboronic acid was added. The mixture was stirred for 1 h at room temperature. A small amount of anhydrous $MgSO_4$ was then added to remove the formed water. After filtration of the $MgSO_4$, the target compound was obtained by evaporation of $CHCl_3$. The relative stereochemistry of MPDPO was confirmed by nuclear Overhauser effect NMR measurements as discussed in the Supporting Information.

Reaction Testing. Reactions were carried out in a 45 mL Inconel Parr reactor using a Parr Series 5000 multiple high-pressure reactor system equipped with magnetic stirring, 250 W resistive heating wells, and high-pressure gas manifold. Premixed (10–15 g) feedstock solution and a magnetic stir bar were placed in the reactor, followed by addition of the catalyst. The reactor was purged 4× with 35.5 bar gas (H_2 or Ar) and then pressurized to the desired pressure using a gas manifold. The stir rate was gradually increased to a value of 750 rpm. Next, the reactor was heated to the desired temperature with a heat-up time of 10–15 min and controlled at the set point temperature using a PID controller. After reaction, products were cooled to room temperature using an ice bath and filtered with a 0.22 μm polyethersulfone syringe filter prior to analysis. Typically, a ~0.5 g aliquot was sampled from the reactor. If necessary, the reaction was run for a longer time in order to reach high conversion of reactant and intermediates. We note that because reactions were run to nearly 100% conversion in this work, reaction times should not be interpreted as reflecting intrinsic reaction rates. Product concentrations were corrected for 2.3% evaporation of water during the reaction, as measured in our previous work.[26] Safe operation of Parr reactors was ensured by purging the reactor headspace prior to reaction, pressurizing and de-pressurizing the reactor in a fume hood, and equipping the reactor with a pressure rupture disk to prevent over-pressurization.

CONCLUSIONS

We have demonstrated a new route to produce hexane-tetrols and -triols with fixed hydroxyl group positions and stereochemistry from methyl glycoside feedstocks. Methyl glycosides are first subjected to deoxydehydration and hydrogenation of cis-vicinal OH groups over a ReO_x–Pd/CeO_2 catalyst in 82–92% yield. Next, the resulting dideoxy-glycoside feedstocks are converted over Pt-based catalysts with selectivities of 80–95% while largely preserving feedstock stereochemistry (>92%). MDM is converted into (2*R*,3*S*)-1236-HTet; MDR is converted into (4*R*,5*S*)-145-HTri; MDG is converted into (2*R*,5*S*)-1256-HTet; and MDF is converted into (2*S*,5*S*)-125-HTri. Each of the four dideoxy-glycoside feedstocks is hydrolyzed to a set of intermediates consistent with the structure of the feedstocks, followed by hydrogenation to hexane-triols and -tetrols. 2,3-Dideoxy feedstocks (MDM and MDR) are more reactive than 3,4-dideoxy feedstocks (MDG and MDF). Furthermore, 3,4-dideoxy feedstocks can undergo aldose-ketose isomerization at the C_2–OH position, which decreases the stereopurity. Inversion of the C_2–OH stereocenter can be suppressed by introduction of a bifunctional metal–acid catalyst. This work provides insights into controlling reactivity in the hydrogenation of carbohydrates over supported metal catalysts. By demonstrating a new route to produce targeted polyols derived from glycosides with fixed hydroxyl group positions and stereochemistry, this report lays the groundwork for further research into the applications of these molecules in the polymers and fine chemical industries.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acssuschemeng.9b04634.

Synthesis of dideoxy-glycoside feedstocks; Experimental details for hexane-tetrol and -triol synthesis experiments; NMR, HPLC, and polarimetry analysis of hexane-tetrols and -triols; and NMR and ESI-MS analysis of reaction intermediates (PDF)

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Notes

The authors declare no competing financial interest.

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