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Catalytic Production of Hexane-1,2,5,6-tetrol from Bio-renewable Levoglucosanol in Water: Effect of Metal and Acid Sites on (Stereo)-Selectivity*

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1. Abstract

We report on a new route to produce hexane-1,2,5,6-tetrol (tetrol) from cellulose-derived levoglucosanol (lgol). We investigate the reaction intermediates formed over metal and acid catalysts, and propose a reaction network for this process. Lgol is converted to tetrol in up to 90% yield over a bifunctional Pt/SiO₂-Al₂O₃ catalyst at 150°C. High tetrol yields are maintained at lgol concentrations of up to 21 wt% in water. Threo- and erythro-lgol first undergo hydrolysis to 3,4-dideoxymannose (DDM) and 3,4-dideoxyglucose (DDG), respectively. This reaction can be carried out selectively over an Amberlyst 70 acid catalyst at a temperature of 100°C. At a higher temperature of 150°C with no added catalyst, DDM and DDG undergo aldose-ketose isomerization to 3,4-dideoxyfructose (DDF). DDM is hydrogenated to cis-tetrol over a Pt/SiO₂ catalyst, while DDG is hydrogenated to trans-tetrol. Formation of DDF erases the stereocenter at the C₂ position of lgol, and hydrogenation of DDF produces a nearly 1:1 mixture of cis- and trans- tetrol. This catalytic approach to produce tetrol from cellulose-derived levoglucosanone opens the door to sustainable chemicals derived from tetrol.

2. Introduction

Conversion of lignocellulosic biomass offers opportunities to produce oxygenated molecules with unique functionalities not easily derived from petroleum. These molecules can be used to synthesize bio-based chemicals including polymers, solvents, and surfactants with different properties compared to existing chemicals.¹ For example, levoglucosanone (LGO) has recently been explored as a cellulose-derived platform molecule for the production of renewable high-value chemicals.² LGO can be produced in up to 50% yields from cellulose using a sulfuric acid catalyst in tetrahydrofuran (THF) solvent.^{2,3} In collaboration with Norske Skog, the Circa Group is currently operating a pilot plant facility (50 tons/yr) for the production of LGO from cellulosic materials using a patented sulfolane-based process.⁴

LGO can be hydrogenated to a variety of oxygenated products over metal-based catalysts. Additionally, the chiral anhydro-bridge group of LGO offers the potential for control over product stereochemistry. Hydrogenation of the C=C bond of LGO at low temperature (40°C) produces Cyrene, an environmentally benign polar aprotic solvent.^{5,6} Subsequent hydrogenation

* Electronic supplementary information (ESI) available: ¹³C NMR identification of reaction products; HPLC chromatograms of reaction products; comparison of reaction pathways to tetrol, THFDM, and THP2M5H; relevant reactions of sugars.

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of the C=O bond of Cyrene at 100°C produces levoglucosan (lgol) quantitatively, as a mixture of threo- and erythro- diastereomers.⁶ DuPont has shown that LGO can be converted to tetrahydrofuran-dimethanol (THFDM) and 1,6-hexanediol (1,6-HDO) by hydrogenolysis in 70% overall yield over Pt-based catalysts.⁷ We recently reported on the hydrogenolysis of lgol to THFDM and tetrahydropyran-2-methanol-5-hydroxyl (THP2M5H) in THF solvent over bifunctional Pt/SiO₂-Al₂O₃ (SiAl) catalysts.⁸ The THFDM cis/trans (c/t) ratio is independent of the lgol threo/erythro (t/e) ratio, indicating that the mechanism passes through an acyclic intermediate which erases the stereocenter of lgol at the C₂ alcohol position.⁶ At sufficiently high metal loadings (> 1 % Pt), the reaction rate is independent of the metal loading and the H₂ reaction order is nearly zero. In this regime, the reaction proceeds via rate-limiting, irreversible acid-catalyzed C-O cleavage and ring rearrangement followed by a fast hydrogenation step.

Hexane-1,2,5,6-tetrol (tetrol) is a partially dehydrated C₆ sugar derivative with potential applications as a polymer precursor. Corma et al. noted that >C₄ reduced polyols have applications in the production of polyesters, alkyd resins, and polyurethanes.⁹ Tetrol is a symmetric molecule with terminal, vicinal hydroxyl groups, allowing for selective reactions at these functional groups. Tetrol can also be dehydrated to the polymer precursor THFDM in up to 96% yield.^{10, 11} THFDM can further be converted into valuable polymer precursors, including 1,2,6-hexanetriol^{12,13} and 1,6-hexanediol.^{7, 14-17} Potential uses of tetrol are currently limited by the lack of an efficient, high-yield route to tetrol. Archer Daniels Midland and others have shown that tetrol can be produced in up to 50% yields from sorbitol over a copper catalyst.^{10, 18} A variety of other polyols are produced along with tetrol, thus requiring a complex separation to purify tetrol.¹⁹ Tetrol has also been reported to be formed as a side-product of 5-hydroxymethylfurfural (HMF) hydrogenation in up to 28% selectivity, in which a mixture of polyols were also produced.²⁰ The lower carbon selectivity towards tetrol and the required separation from other polyols limit the viability of these technologies to produce tetrol.¹⁰

In this paper we report a new catalytic route to produce tetrol in high yield from bio-renewable lgol in water solvent. Experiments with different metal and acid catalysts are used to determine the reaction intermediates in the conversion between lgol and tetrol. The relationship between the stereochemistry of the reactants, intermediates, and reaction products is also analyzed. We propose a reaction network for lgol conversion to tetrol, which is consistent with the experimental results obtained.

3. Experimental

Lgol was prepared via quantitative hydrogenation of Cyrene (99%, Circa Group). Cyrene in water was hydrogenated at 60°C and 51.7 bar H₂ until complete conversion was achieved.⁶ To generate lgol with a t/e ratio of 1.3, a 5% Ru/C (Strem Chemicals) catalyst was used and the Cyrene concentration in water was 20 wt%. To generate lgol with a higher t/e ratio of 3.3, a 5% Pd/Al₂O₃ synthesized by incipient wetness impregnation was used, and the Cyrene concentration in water was 3 wt%. The lgol in water samples were separated from the catalyst by filtration using a 0.22 μm polyethersulfone (PES) syringe filter. When necessary, samples were additionally centrifuged using a 10kDa centrifugal filter (Merck Millipore) operated at 5200 rpm for 0.25h, to remove small particles. THFDM (98%, Alfa Chemicals), Pt(NH₃)₄(NO₃)₂ solution

(99%, Strem Chemicals), and aluminum chloride hexahydrate (99%, Sigma Aldrich) were used as received. Grade 135 amorphous SiO₂-Al₂O₃ (SiAl) and Davisil grade SiO₂ were purchased from Sigma Aldrich. Sulfuric acid (96 wt%) was purchased from Fisher Chemical. Amberlyst 70 (possessing >2.55 mmol/g 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.

3.1. Catalyst synthesis and characterization

Pt/SiAl and Pt/SiO₂ catalysts were synthesized by incipient wetness impregnation of a Pt(NH₃)₄(NO₃)₂ solution in water. The catalysts were dried for >12h 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), then passivated at room temperature with 1% O₂/Ar. When the SiAl support was used directly in a reaction, it was calcined at 400°C in flowing air prior to use.

Pt and SiAl catalysts were characterized by CO chemisorption and NH₃-TPD to measure Pt and total acid site densities, respectively (Table 1). Except for the CO chemisorption data for the 5% Pt/SiO₂ catalyst, all catalyst characterization results were reported in our previous work, and details are provided there.⁸ Briefly, Pt site densities were measured following *in situ* reduction in H₂ of 100 mg catalyst at 400°C, either by irreversible CO uptake at 35°C after sample degassing using a Micromeritics ASAP2020, or by pulse chemisorption of 10% CO/He at 50°C using a Micromeritics Autochem 2920. These two methods yielded similar results. The 1.1% Pt/SiAl, 5.3% Pt/SiAl, and 5% Pt/SiO₂ catalysts have similar metal dispersions of 36-43%.

Acid site densities of SiAl-based catalysts were measured by NH₃-TPD using a Micromeritics Autochem 2920. The SiAl catalyst was dried under flowing He at 400°C prior to analysis, while Pt/SiAl catalysts were reduced at 260°C under flowing H₂ prior to analysis. 100 mg of catalyst was saturated with flowing 15% NH₃/He at 150°C for 0.5h, followed by flowing He for 1h. The sample was then ramped to 700°C at a rate of 10°C/min. The NH₃ signal at m/z = 17 was monitored using a quadrupole mass spectrometer (MKS Instruments), and was corrected for the presence of water using the signal at m/z = 18. A moderate decrease in acid site density is observed upon addition of 1.1% and 5.3% Pt to the SiAl support.

Table 1. Characterization of metal and acid sites on Pt and SiAl catalysts.

Catalyst	CO Uptake (μmol/g)	Pt Dispersion (%)	Acid Site Density by NH ₃ -TPD (μmol/g)
SiAl*	N/A	N/A	670
1.1% Pt/SiAl*	24	43	530
5.3% Pt/SiAl*	111	41	480
5% Pt/SiO ₂	91	36	N/A

* Reproduced from Ref. 8.

3.2. Product identification and quantification

Because tetrol, DDF, and DDM are not separated by our HPLC method, experiments were run to completion to simplify analysis of the reaction product mixture. ^{13}C NMR was used to identify reaction products. The lglol conversion was defined as the change in the lglol concentration divided by the initial lglol concentration. The yield to a given product was defined as the concentration of that product divided by the initial lglol concentration. The selectivity to a given product was defined as the yield to that product divided by the lglol conversion.

3.2.1. HPLC

A BioRad Aminex 87H column was used in a Shimadzu HPLC. 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 . Lglol, tetrol, 3,4-dideoxyglucose (DDG), 3,4-dideoxymannose (DDM), and 3,4-dideoxyfructose (DDF) were quantified by HPLC using a refractive index (RI) detector. The presence of DDF could also be monitored using a photodiode array (UV) detector at 206 nm. HPLC chromatograms of reaction products are provided in the Supplemental Information (Figure S2). Because THFDM is overlapping with lglol in the HPLC, lglol and THFDM were additionally quantified by GC when these species were both present. HPLC refractive index sensitivities for lglol, tetrol, and DDM/DDG were measured by using quantitative ^{13}C NMR with a 110mM sorbitol internal standard to measure the concentration of these samples, which were then correlated to the HPLC refractive index signal. The HPLC RI sensitivity of DDF was assumed to be equal to that of DDG/DDM. The selectivity to a minor unknown product was approximated by assuming that this compound has the same HPLC RI sensitivity as tetrol.

3.2.2 GC

Lglol, THFDM, and THP2M5H were analyzed by a Shimadzu gas chromatograph (GC) equipped with a flame ionization detector with liquid injection. A Restek RTX-VMS capillary column (length: 30 m, inner diameter: 0.25 mm, film thickness: 1.4 μm) was used. The injection port and FID were maintained at 240°C. The injection volume was 1 μL and a split ratio of 50 was used. The column temperature ramp was as follows: hold 1 min at 40°C, ramp 10°C/min to 180°C, ramp 3°C/min to 240°C, hold 5 min at 240°C. Because THFDM and THP2M5H are partially overlapped in the GC, only the total yield to these two species is reported. The GC sensitivity of THP2M5H was assumed to be equal to that of THFDM.

3.2.3. ^{13}C NMR

Quantitative ^{13}C NMR spectra were collected on a Bruker Avance 500 MHz spectrometer at room temperature, using an inverse-gated decoupling pulse sequence with a 30° pulse. 10% D_2O was added to the samples prior to analysis. The ^{13}C NMR spectra were absolute-referenced to the associated ^1H NMR spectra. 112 Scans were used, with an acquisition time of 1 sec and a relaxation delay of 30 sec. ^{13}C NMR spectra for threo-lglol, erythro-lglol, cis-tetrol, trans-tetrol, cis-THFDM, and trans-THFDM were matched to those in the literature.²¹⁻²³ DDG, DDM, and DDF were identified by ^{13}C NMR (Table S1 and Table S4). In some cases, ^{13}C NMR peaks could not be completely distinguished due to the similar chemical shifts between different carbon positions and between different tautomers. However, all chemical shifts, relative peak areas, and multiplicities of each carbon position are consistent with the assignments (details are provided in

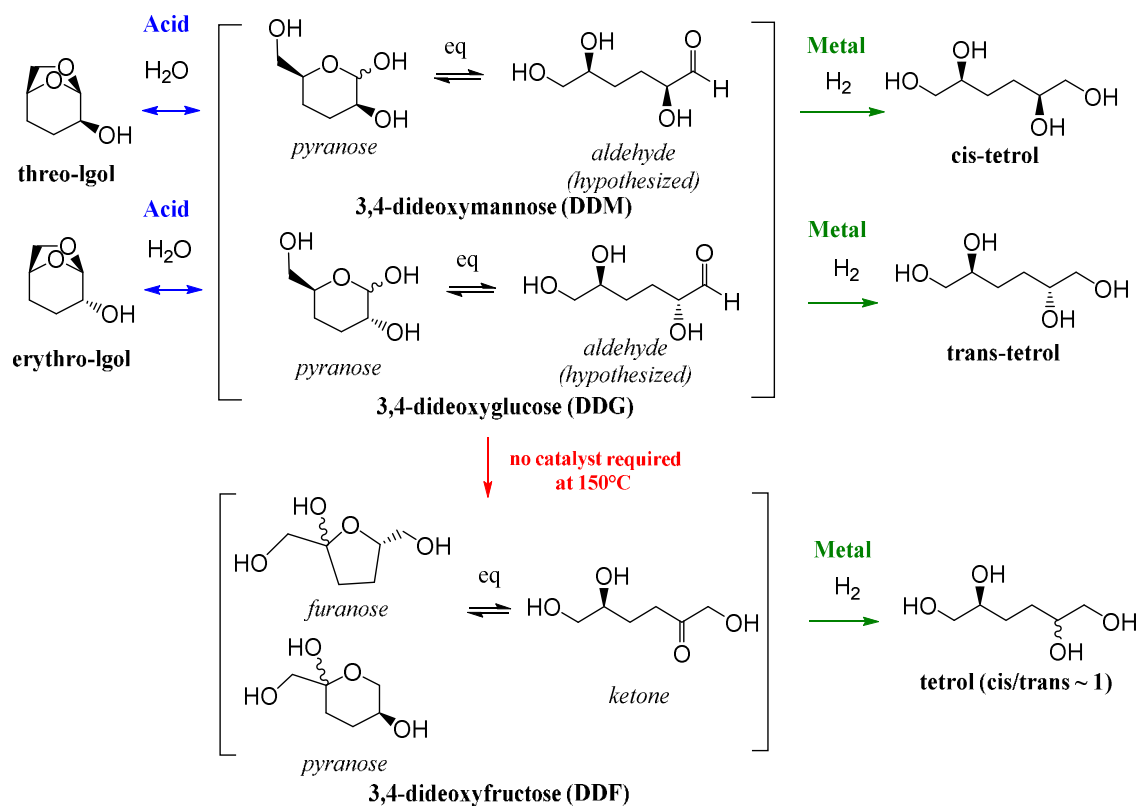
the ESI). Mestrenova (v. 12.01) was used for ^{13}C NMR prediction of reaction products. Electrospray ionization mass spectrometry (ESI-MS) was used to confirm the molecular weight of DDF (details are provided in the ESI).

3.3. Catalytic testing

Reactions of lgol with SiAl, Pt/SiAl, and Pt/SiO₂ were carried out in a 45 mL Inconel Parr reactor. 10 mL of reaction solution and a magnetic stir bar were placed in the reactor. The reactor was purged 4x with 35.5 bar gas (H₂ or Ar), pressurized to 35.5 bar, then heated to the reaction temperature. The heat-up time was in the range of 10-15 minutes. Product concentrations from Parr reactor experiments were corrected for 2.3% evaporation of water from the reaction solution, which was measured based on an apparent increase in the carbon balance in the experiment with lgol heated to 150°C in the absence of catalyst (Table 2, Entry 1). Reactions of lgol with Amberlyst 70, H₂SO₄, and AlCl₃ were carried out in 10 mL thick-walled glass reactors (sealed by a Teflon cap) submerged in an oil bath. 3 mL of reaction solution and a magnetic stir bar were placed in the glass reactor. After reaction, products were cooled to room temperature using an ice bath, filtered with a 0.22 μm PES syringe filter prior to analysis. Reaction products at higher concentration (> 5 wt%) were diluted 5-10x in water prior to analysis.

4. Results and Discussion

Lgol conversion to tetrol was studied over different metal and acid catalysts to gain insights into the reaction network for this transformation. The proposed reaction network for lgol conversion to tetrol is shown in Scheme 1. The threo- and erythro- isomers of lgol undergo acid-catalyzed hydrolysis to two diastereomers of a cyclic hemiacetal species, with threo-Lgol converted to DDM and erythro-Lgol converted to DDG. At higher temperatures (i.e., 150°C) with no added catalyst, DDM and DDG undergo aldose-ketose isomerization to a hemiketal-ketone species, DDF. Hydrogenation of DDM forms cis-tetrol; hydrogenation of DDG forms trans-tetrol; and hydrogenation of DDF forms a nearly 1:1 mixture of cis- and trans- tetrol. The following sections describe the experimental evidence for this reaction network.



Scheme 1: Proposed reaction network for lglol conversion to tetrol. “eq” indicates reactions which are assumed to be quasi-equilibrated.

4.1. Lglol conversion over Pt & SiAl catalysts

In the absence of a catalyst, the conversion of lglol at 150°C is less than 10% (Table 2, Entry 1). The conversion of lglol is also less than 10% over a 5% Pt/SiO₂ catalyst in the absence of acid sites (Table 2, Entry 2) at 150°C, indicating that the first step in this reaction is acid-catalyzed rather than metal-catalyzed. Over a bifunctional 1.1% Pt/SiAl catalyst, containing metal (Pt) and acid (SiAl) sites, lglol in water undergoes conversion to tetrol in 91% yield (Table 2, Entry 3). THFDM and THP2M5H are byproducts produced in a total yield of 5%. The product yields do not change when the reaction is run at a higher catalyst to feed ratio (Table 2, Entry 4), showing that tetrol is not reactive at these reaction conditions and that the observed THFDM is not formed via dehydration of tetrol. A physical mixture of SiAl and 5% Pt/SiO₂ shows comparable selectivity tetrol as the Pt/SiAl catalyst (Table 2, Entry 5), indicating that nanoscale proximity of metal and acid sites is not required for the selective conversion of lglol to tetrol.

We have previously reported that THFDM and THP2M5H are the main hydrogenolysis products over Pt/SiAl catalysts in THF solvent.⁸ Lglol cannot be converted to tetrol in an organic solvent, because water is a stoichiometric reactant in the formation of tetrol. The reaction mechanism to form THFDM in THF solvent is proposed to proceed via a series of carbocation intermediates. Some of the intermediates in the pathway to produce tetrol from lglol in water are the hydrated versions of these carbocation intermediates (a comparison of the proposed reaction intermediates in the production of tetrol, THFDM, and THP2M5H are shown in the ESI, Scheme S1).

When lgal is treated over SiAl in the absence of metal catalyst at 150°C (Table 2, Entry 7), the major product is a hemiketal-ketone species, DDF (Scheme 1), produced in 80% selectivity. Similar to fructose,²⁴ this species exhibits five tautomeric forms in water, which were observed by ¹³C NMR: α and β pyranose, α and β furanose, and an acyclic ketone form (Table S4). In Section 4.2, we will show that DDF is produced via aldose-ketose isomerization of DDG and DDM.

Hydrogenation of DDF (Table 2, Entry 8) over Pt/SiO₂ results in 77% selectivity to tetrol with THFDM + THP2M5H as the major side-product (15% yield). The tetrol yield is lower, at the expense of a higher THFDM + THP2M5H yield, compared to the 1.1% Pt/SiAl catalyst. A similar decrease in the tetrol yield is observed at lower H₂ pressures (Figure 1). These results suggest that when the SiAl sites are separated from the Pt metal sites, or when the rate of hydrogenation is lower (at lower H₂ pressures), reaction intermediates can be converted to THFDM precursors over SiAl acid sites prior to hydrogenation over Pt metal sites. Possible pathways to tetrol, THFDM, and THP2M5H from lgal are shown in the ESI (Scheme S1). Precursors to THFDM and THP2M5H could not be identified in the product mixture of lgal conversion over SiAl due to the low concentration of these species.

Table 2. Lgal conversion ($t/e = 1.3$) over Pt/SiAl, SiAl, and Pt/SiO₂ catalysts.

Entry	Feed	Catalyst (cat/feed ratio)	Conditions	Lgal Conversion (%)	Selectivity (%)				
					Tetrol (c/t)	DDM + DDG	DDF	THFDM + THP2M5H	Unknown
1	lgal	None	150°C, 3h, 35.5 bar H ₂	8	0	8	94	0	0
2	lgal	5% Pt/SiO ₂ (10 mg/g)	150°C, 3h, 35.5 bar H ₂	3					
3	lgal	1.1% Pt/SiAl (10 mg/g)	150°C, 6h, 35.5 bar H ₂	100	91 (1.07)	0	0	5	2
4	lgal	1.1% Pt/SiAl (20 mg/g)	150°C, 6h, 35.5 bar H ₂	100	91 (1.06)	0	0	6	2
5	lgal	SiAl + 5% Pt/SiO ₂ (10 mg/g each)	150°C, 6h, 35.5 bar H ₂	99	92 (1.06)	0	0	3	2
6	lgal	SiAl (10 mg/g)	100°C, 3h, 35.5 bar Ar	1					
7	lgal	SiAl (10 mg/g)	150°C, 6h, 35.5 bar Ar	95	0	3	80	0	2
8	Product of (7)	5% Pt/SiO ₂ (10 mg/g)	150°C, 9h, 35.5 bar H ₂	100	77 (1.00)	0	0	15	0

Conditions: 1.9 wt% lgal in water ($t/e = 1.3$), 750 rpm stir rate.

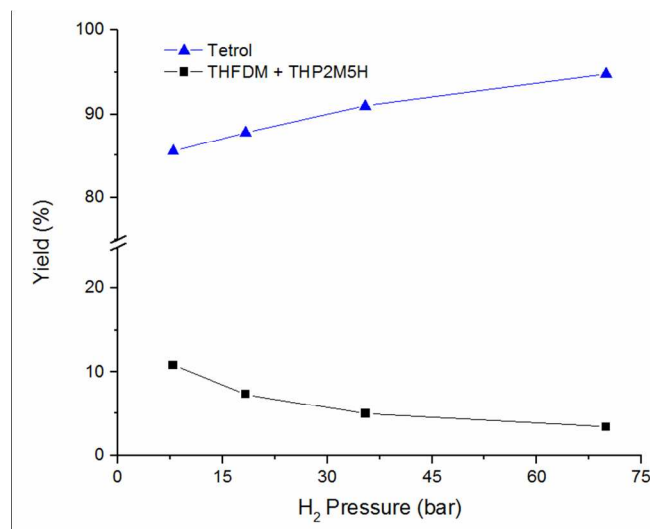


Figure 1. Effect of H₂ pressure on tetrol yield from lgol over 1.1% Pt/SiAl

Conditions: 150°C, 10mg catalyst per g feed, 1.9 wt% lgol in water ($t/e = 1.3$). Reaction time was chosen such that 100% conversion of lgol and all reaction intermediates was achieved (6h for experiments at 18.2 bar and above; 12h for the experiment at 7.9 bar). A minor unidentified product (2% selectivity) was observed in all experiments. Solid lines are visual aids.

The conversion of lgol to tetrol over Pt/SiAl catalysts was investigated at different lgol concentrations (Figure 2). Tetrol yields of up to 86% were also achieved at lgol concentrations up to 21 wt% in water over a 5.3% Pt/SiAl catalyst, demonstrating that this reaction can be carried out at more industrially relevant reactant concentrations.

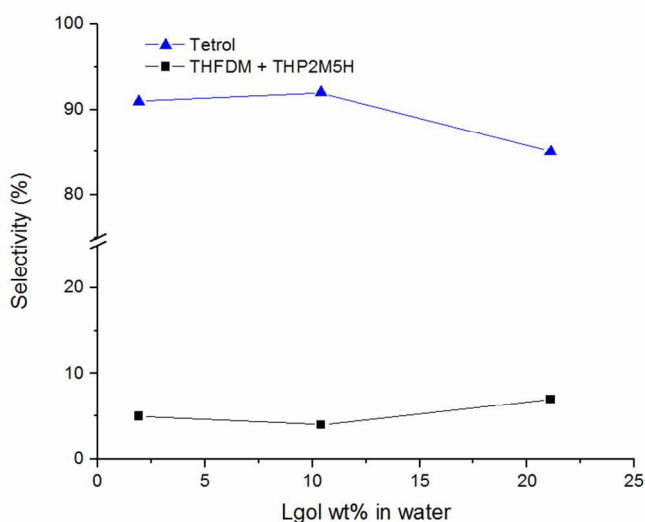
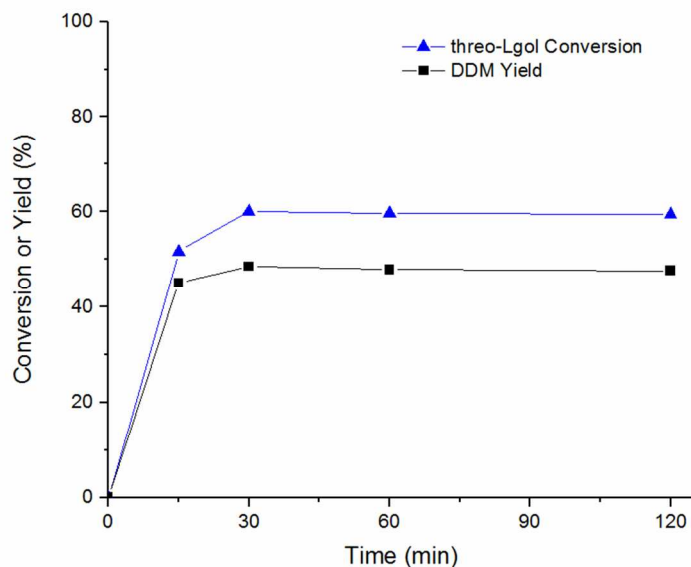


Figure 2. Effect of lgol concentration on tetrol selectivity over Pt/SiAl catalysts.

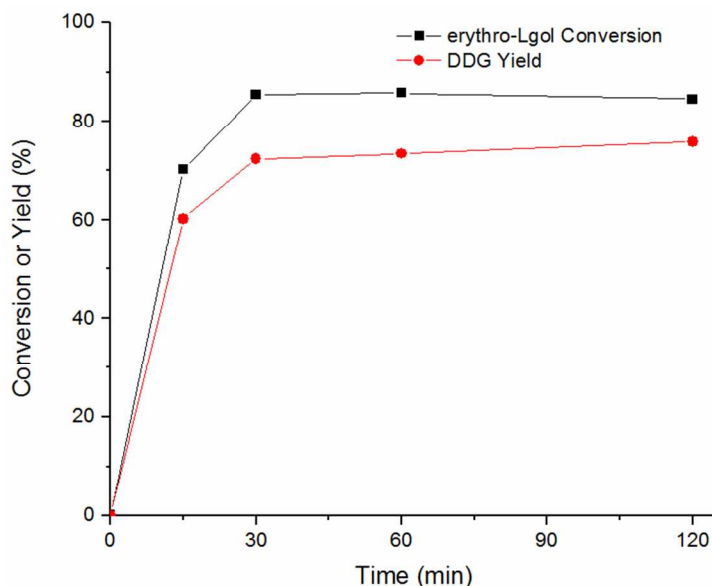
Conditions: 150°C, 35.5 bar H₂, lgol in water (*t/e* = 1.3), 10mg catalyst per g feed, 750 rpm. Catalyst metal loading and reaction time were selected to reach >95% conversion of lgol and reaction intermediates (1.1% Pt/SiAl and *t*=6h for 1.9 wt% lgol; 5.3% Pt/SiAl and *t*=6h for 10 wt% lgol; 5.3% Pt/SiAl and *t*=17h for 21 wt% lgol). The experiment at 21 wt% lgol was carried out in a 75 mL Parr reactor to maintain a stoichiometric excess of H₂. Solid lines are visual aids.

4.2. Lgol conversion over different acid catalysts

At a lower temperature of 100°C, SiAl has negligible reactivity for lgol conversion (Table 2, Entry 6). In contrast, when lgol is treated over Amberlyst 70 at 100°C, the threo- and erythro-isomers of lgol are hydrated to DDM and DDG, respectively, in 86% selectivity (Table 3, Entry 2). This reaction is similar to the hydrolysis of LGA to glucose (Scheme S2), in that water is added to the anhydro-bridge facilitated by an acid catalyst.^{25, 26} In the case of lgol hydrolysis, both C₂ epimers (i.e., the 3,4-dideoxy- versions of glucose and mannose) are produced because both the erythro- and threo- isomers of lgol are present. This reaction reaches equilibrium at 83% conversion of erythro-lgol and 58% conversion of threo-lgol, indicated by the fact that the lgol conversion and product yields do not change significantly between 30-120 min (Figure 3). Nearly identical results are achieved with H₂SO₄ catalyst (Table 3, Entry 6), verifying that the results in Figure 3 are not due to catalyst deactivation. No conversion of lgol is observed at 100°C in the absence of catalyst (Table 3, Entry 1).



3A: threo-Lgol conversion to DDM



3B: erythro-Lgol conversion to DDG

Figure 3: threo- and erythro- lgol conversion to DDM and DDG over Amberlyst 70. 16.7 mg catalyst per g feed, 1.9 wt% lgol in water ($t/e = 1.3$), $T = 100^{\circ}\text{C}$, 500 rpm. Solid lines are visual aids.

Treating DDG and DDM (formed over Amberlyst 70 or H_2SO_4) at 150°C in the absence of catalyst (Table 3, Entries 4 and 7) results in isomerization to DDF, with similar selectivity as the reaction of lgol over SiAl at the same temperature (Table 2, Entry 7). While the Brønsted acid sites of SiAl are expected to catalyze the hydrolysis of lgol to DDM and DDG, it is not clear whether the isomerization of DDM and DDG to DDF occurs on the catalyst surface or in solution. SiAl possesses both Brønsted and Lewis acid sites, whereas Amberlyst 70 contains only Brønsted acid sites.²⁷ A Lewis acid catalyst, namely AlCl_3 , was able to isomerize DDM and DDG to DDF (Table 3, Entry 5) at 100°C , under conditions at which this reaction does not proceed in the absence of a catalyst (Table 3, Entry 3). This result shows that the isomerization of DDM and DDG to DDF is promoted by Lewis acid sites, similar to glucose isomerization to fructose (Scheme S2).^{28, 29} It should be noted that there are multiple possible mechanisms of aldose-ketose isomerization which could be taking place in the transformation of DDM and DDG to DDF.

Hydrogenation of DDG + DDM over Pt/SiO_2 at 100°C forms tetrol in high selectivity (89%) (Table 3, Entry 8). The reaction was carried out at 100°C to avoid possible isomerization of DDM and DDG to DDF. We hypothesize that hydrogenation of DDM and DDG proceeds via ring-opening to the acyclic aldehyde tautomer (Scheme 1) as is the case with other cyclic hemiacetals, such as glucose (Scheme S2) and 2-hydroxytetrahydropyran.^{24, 30}

Table 3. *Lgol conversion (t/e = 1.3) over Amberlyst 70, H₂SO₄, and AlCl₃ catalysts.*

Entry	Feed	Catalyst (cat/feed ratio)	Conditions	Lgol Conversion (%) (t/e*)	Selectivity (%)			
					Tetrol (c/t)	DDM + DDG (DDM/DDG)	DDF	THFDM + THP2M5H
1	lgol	None	100°C, 2h, air	0				
2	lgol	Amberlyst 70 (16.7 mg/g)	100°C, 0.5h, air	68 (0.92)	0	87 (0.89)	0	0
3	Product of (2)	None	100°C, 2h, air	68 (0.94)	0	88 (0.87)	0	0
4**	Product of (2)	None	150°C, 3h, 35.5 bar Ar	73 (1.0)	0	3	76	0
5	Product of (2)	AlCl ₃ (50mM)	100°C, 0.5h, air	76 (0.81)	0	2	78	0
6	lgol	H ₂ SO ₄ (50mM)	100°C, 0.5h, air	66 (0.98)	0	89 (0.86)	0	0
7***	Product of (6)	None	150°C, 3h, 35.5 bar Ar	67 (0.99)	0	2	82	0
8	Product of (2)	5% Pt/SiO ₂ (10 mg/g)	100°C, 9h, 35.5 bar H ₂	73 (0.95)	89 (0.93)	0	0	1

Conditions: 1.9 wt% lgol in water (t/e = 1.3). Entries 4, 7, and 8 carried out in 45 mL Parr reactor (750 rpm stir rate). Entries 1, 2, 3, 5, and 6 carried out in 10mL thick-walled glass reactor (500 rpm stir rate).

**threo-erythro ratio of converted lgol.*

***Feedstock treated with Amberlyst 21 basic anion exchange resin (0.12 g per g solution) to remove trace anions prior to reaction.*

*** *neutralized using Amberlyst 21 basic anion exchange resin and diluted 1.4x in water prior to reaction.*

4.3. Relationship between lgol and tetrol stereochemistry

To gain further insight into the reaction network, the effect of the lgol t/e ratio on the tetrol c/t ratio was studied. The t/e ratio of lgol can be varied by hydrogenating Cyrene with different metal catalysts, as shown in our previous work.⁶ Different c/t ratios of tetrol could impact the physico-chemical properties of diastereomeric products derived from tetrol.³¹ The results of lgol conversion with a higher t/e ratio (t/e = 3.3) are summarized in Table 4.

The t/e stereochemistry of lgol is partially preserved upon conversion to tetrol over Pt/SiAl catalysts. When starting with lgol with a t/e ratio of 3.3, the tetrol c/t ratio is 1.47, corresponding to 35% preservation of the t/e stereochemistry of lgol (Table 4, Entry 1). Using a higher metal loading of 5.3% Pt/SiAl (Table 4, Entry 2) results in a tetrol c/t ratio of 2.00 (64% preservation

of the t/e stereochemistry of lgol), suggesting that using a higher Pt loading promotes the rapid hydrogenation of DDM and DDG prior to isomerization to DDF. On the other hand, when the acid (SiAl) and metal (Pt) sites are separated, DDG and DDM are isomerized to DDF prior to hydrogenation (Table 4, Entry 3). Hydrogenation of DDF at 150°C over Pt/SiO₂ presumably occurs via the acyclic ketone tautomer, and produces nearly equal amounts of cis- and trans-tetrol (Table 4, Entry 4). Similarly, hydrogenation of fructose has been reported to result in a 1:1 mixture of sorbitol and mannitol (Scheme S2) when the acyclic ketone form of fructose is hydrogenated.³² The yield of tetrol over separated SiAl and Pt/SiO₂ catalysts is lower, at the expense of a higher yield of THFDM + THP2M5H, compared to the reaction with the bifunctional 1.1% Pt/SiAl catalyst.

When lgol is hydrolyzed using Amberlyst 70 at 100°C (Table 4, Entry 5), the conversions of erythro- and threo-lgol are nearly equal to the case in which the t/e ratio is 1.3 (Table 3, Entry 2). This result is consistent with the finding that the lgol hydrolysis reaction has reached equilibrium (Figure 3). The ratio of the two diastereomers of the product, DDG and DDM, is nearly equal to the ratio of converted threo- and erythro-lgols. Hydrogenation of the mixture of DDM and DDG and lgol over 5% Pt/SiO₂ at 100°C results in nearly complete retention of the lgol t/e stereochemistry in the formation of cis and trans-tetrol (Table 4, Entry 6). Similarly, hydrogenation of glucose and mannose does not alter the C₂ stereocenter and therefore produces sorbitol and mannitol, respectively (Scheme S2).^{24, 33}

Table 4: Lgol conversion (t/e = 3.3) over metal and acid catalysts.

Entry	Feed	Catalyst (cat/feed ratio)	Conditions	Lgol Conversion (%) (t/e*)	Selectivity (%)				
					Tetrol (c/t)	DDM + DDG (DDM/DDG)	DDF	THFDM + THP2M5H	Unknown
1	lgol	1.1% Pt/SiAl (10 mg/g)	150°C, 6h, 35.5 bar H ₂	100	94 (1.47)	0	0	5	2
2	lgol	5.3% Pt/SiAl (10 mg/g)	150°C, 3h, 35.5 bar H ₂	99	89 (2.00)	0	0	3	2
3	lgol	SiAl (10 mg/g)	150°C, 6h, 35.5 bar Ar	95	0	3	74	0	2
4	Product of (3)	5% Pt/SiO ₂ (10 mg/g)	150°C, 9h, 35.5 bar H ₂	98	69 (1.08)	0	0	19	2
5	lgol	Amberlyst 70** (16.7mg/g)	100°C, 0.5h, air	63% (2.25)	0	88 (2.10)	0	0	0
6	Product of (5)	5% Pt/SiO ₂ (10 mg/g)	100°C, 9h, 35.5 bar H ₂	70% (2.48)	84 (2.30)	1	0	0	2

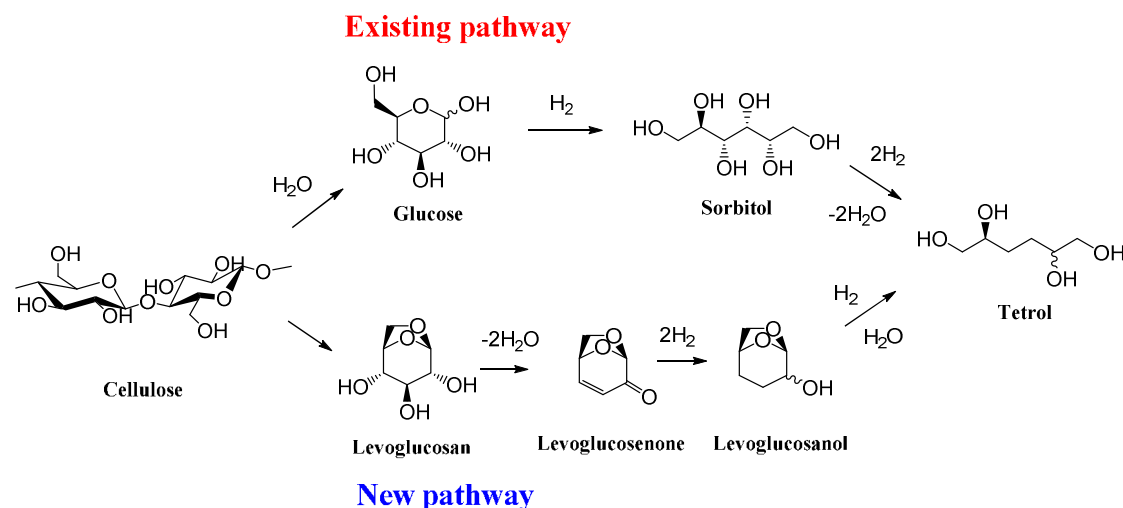
Conditions: 2 wt% lgol in water (t/e = 3.3), 750 rpm. *threo-erythro ratio of converted lgol.

**Carried out in a thick-walled glass reactor, 500 rpm

These experiments show that the c/t ratio of tetrol can be controlled by varying i) the lglol t/e ratio, ii) the type of the acid catalyst, which in turn affects the required reaction temperature, and iii) the metal-acid ratio and proximity (e.g. different metal loadings, or using separated metal and acid sites).

4.4. Comparison of catalytic pathways to produce tetrol

Scheme 2 compares the pathways to produce tetrol via sorbitol and lglol. Previous approaches to produce tetrol from hydrogenolysis of sorbitol (derived from glucose or R-glycosides) over Cu-based catalysts showed a maximum tetrol yield of < 50%, and required harsher reaction conditions ($\geq 200^\circ\text{C}$).^{10, 18} The lower tetrol yield is due to the difficulty of selectively dehydrating the C₃ and C₄ positions of sorbitol without catalyzing dehydration reactions at other carbon positions. In contrast, the route to produce tetrol from lglol is inherently more selective to tetrol because the precursor, LGO, is dehydrated at the C₃ and C₄ positions during its formation from LGA.³⁴ The pathway from LGO to tetrol involves hydrogenation of C=C and C=O bonds over a metal catalyst, C-O cleavage of an anhydro-bridge ether bond over an acid catalyst, ring-opening of a cyclic hemiacetal, and optional aldose-ketose isomerization. Because these reactions can be carried out selectively at milder conditions ($\leq 150^\circ\text{C}$), LGO can be converted to tetrol without catalyzing undesired side reactions. Furthermore, the ability to alter the lglol threo/erythro ratio, via stereoselective hydrogenation of the ketone group of Cyrene,⁶ offers control over the tetrol c/t ratio which is not available with the sorbitol conversion route.



Scheme 2: Tetrol production from cellulose via sorbitol and via levoglucosenone.

When comparing these two routes from cellulose to tetrol, it should be noted that the maximum reported yield of LGO from cellulose is about 50%, due to humin formation and other side-reactions.² One benefit of the route to tetrol via LGO is that the high selectivity to tetrol avoids the need to separate tetrol from numerous other polyols.¹⁹

5. Conclusions

We have elucidated a new route to convert bio-renewable lglol into tetrol in water solvent over metal and acid catalysts in up to 90% yield. High tetrol yields are maintained at lglol concentrations of up to 21 wt% in water. This route is significantly more selective than previously reported sorbitol hydrogenolysis routes, and offers control over the tetrol c/t ratio. The choice of acid catalyst (Amberlyst 70 or SiAl) and reaction temperature (100°C or 150°C) can be used to control which reaction intermediates (DDM and DDG, or DDF) are formed in the conversion of lglol to tetrol. The tetrol c/t ratio can be altered by varying the lglol t/e ratio, and by selecting the reaction conditions to determine whether the stereocenter at the C₂ position is preserved or erased prior to hydrogenation. This new approach to produce tetrol from cellulose-derived levoglucosenone opens the door to new, sustainable chemicals derived from tetrol.

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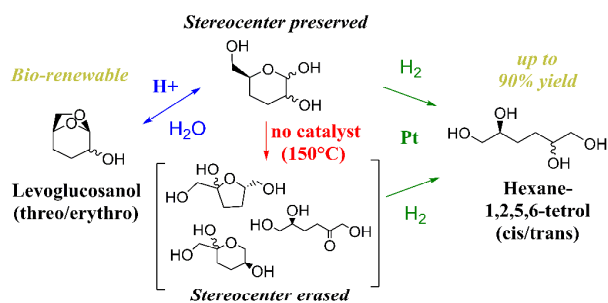
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We report on a new route to produce hexane-1,2,5,6-tetrol from cellulose-derived levoglucosan using metal and acid catalysts.