Development of sustainable esterification reactions and the transformation of carbohydrates into applicable building blocks
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Deoxydehydration (DODH) is a direct method to convert polyols into alkenes, a process that is of particular interest in biomass conversion. In ring systems such as glycosides, only cis-diols are selectively eliminated providing an example of site-selective functionalization. In literature, heterogeneous ReO$_x$-Au/CeO$_2$ and ReO$_x$-Pd/CeO$_2$ catalysts have been utilized to convert glycosides into cis-diol-eliminated products. The alkene was further reduced to the alkane when a ReO$_x$-Pd/CeO$_2$ catalyst was used. Since the reaction is selective for cis-diol elimination, naturally abundant glycosides including glucopyranosides and fructofuranosides are not suitable substrates. To directly utilize an abundant sugar such as fructose, we have synthesized several fructopyranosides because these contain a cis-diol moiety and can be used in a rhenium-catalyzed DODH reaction. Next to the application of this reaction on novel substrates, the DODH reaction of glycosides has been performed with a flow reactor to analyze the reactivity of the catalyst over time. The DODH reaction with ReO$_x$-Au/CeO$_2$ eliminated the cis-diol of methyl mannopyranoside resulting in 89% conversion to a mixture of alkene and alkane (72:28). Due to the incomplete conversion and moderate chemical selectivity of the reaction, we switched our focus on utilizing ReO$_x$-Pd/CeO$_2$ catalyst. ReO$_x$-Pd/CeO$_2$ catalyzed DODH reactions converted a number of alkyl glycosides to alkane with full conversion. However, due to high catalyst loading and short active time of the catalyst, performing big-scale DODH reaction of alkyl glycosides with this method is not practical.


3.1 Introduction

The transformation of biomass-derived feedstocks such as polysaccharides, sugars, and their derived polyols provides in principle a sustainable route for the production of solvents and fine chemicals. Due to their molecular complexity, conversion into various polymer building blocks, fine chemicals, and pharmaceuticals is in principle possible.\cite{1,2} Nevertheless, this high degree of functionality, in the case of carbohydrates the number of hydroxy groups, makes biomass difficult for direct utilization. Biological, chemical, or thermochemical treatment is required to remove excess hydroxy groups and convert the biomass into simpler building blocks for further exploitation.\cite{1} For example, 6-hydroxymethylfurfural (HMF), a versatile component for the production of levulinic acid, 2,5-dimethylfuran, and 2,5-furandicarboxylic acid, is produced by multiple dehydration of carbohydrates such as cellulose and inulin.\cite{3} In the case of HMF, all chiral centers in the starting material are removed. For fine chemical production this is not always desired, and to retain part of the chirality in the dehydration process, more selective methods to remove hydroxy groups are desired.

Deoxydehydration (DODH), carried out either in a stoichiometric or a catalytic fashion, converts vicinal diols into alkenes and alkanes and is, therefore, a potential method for controlled “dehydration”.\cite{4} The resulting alkenes are useful building blocks for further functionalization.\cite{5} In particular, rhenium-based catalysts are intensively explored for DODH reactions under reductive conditions. Other metal catalysts such as vanadium and molybdenum are also applied in this reaction, but usually require a higher temperature compared to the rhenium-catalyzed DODH reaction.\cite{6–12} The process requires a stoichiometric reductant, and triphenylphosphine,\cite{8,11} sacrificial alcohols,\cite{10,13} and hydrogen\cite{12} have been studied and used in this respect. The commonly proposed catalytic cycle of the rhenium-catalyzed DODH reaction is depicted in scheme 1.\cite{6} In pathway A, trioxorhenium species I is condensed with a diol, the starting material in the reaction, leading to the formation of II. In the presence of a reductant, II is converted into reduced species III. Subsequent “extrusion” of the alkene leads to...
the regeneration of species I that enters the next catalytic cycle. In pathway B, the trioxorhenium species I is first reduced to IV, and subsequent chelation of the diol leads to the formation of III. The catalytic species I is regenerated after “extrusion” of the alkene.[6] The sequence of condensation and reduction as well as the identification of the rate-limiting step are the main points of dispute about the mechanism of DODH reaction.[14] The Cp*ReO₃-catalyzed DODH reaction developed by Cook and Andrews was suggested to follow pathway B with PPh₃ as the reductant. Furthermore, alkene extrusion was the rate-limiting step.[15] The MeReO₃-catalyzed DODH reaction under hydrogen pressure developed by Abu-Omar et al. was proposed to follow pathway B as well,[16] while a subsequent DFT study of this developed method indicated pathway A as energetically more favorable.[17] The MeReO₃-catalyzed DODH reaction mediated by 3-pentanol was postulated to proceed via pathway B by Shiramizu and Toste; whether the rate-limiting step was the reduction of MeReO₃ or alkene extrusion could not be concluded.[10] The reason leading to those disputes of the mechanism, in essence, depends on the nature of the reductant and reaction conditions.

Scheme 1: Proposed general mechanism of the rhenium catalyzed DODH reaction
In parallel, also heterogeneous catalysts for DODH have been developed. Jentoft et al. developed a carbon-supported perrhenate catalyst to perform the reaction with glycols leading to good conversion to alkenes, although leaching of catalytic species was observed and the soluble rhenium species also partly catalyzed the reaction.\cite{18} Palkovits et al. developed a ReO$_x$/TiO$_2$ catalyst to convert 1,2-hexanediol to 1-hexene in good yield. The catalyst was very stable and catalyzed DODH reactions without loss of activity after seven consecutive runs.\cite{19} Unsupported rhenium nanoparticles produced by Abu-Omar et al. converted glycerol and 1,2-hexane diol into the corresponding alkenes with good conversion. The unsupported catalyst was found to be stable without significant loss of activity after recycled seven times.\cite{20} ReO$_x$/ZrO$_2$-catalyzed DODH reaction was carried out by Wang et al. to obtain a precursor of adipic acid from D-glucaric acid-1,4-lactone; in which subsequent hydrogenation catalyzed by Pd/C led to 82% of the precursor.\cite{21} Tomishige et al. developed ceria-supported rhenium catalysts with additional metals as promoters.\cite{22,23} With palladium, ReO$_x$-Pd/CeO$_2$ catalyzed reactions did not only stop at the alkene stage but further hydrogenation to the alkane took place, transforming glycerol into 1-propanol in 87% yield.\cite{23} On the other hand, with gold as a promoter, ReO$_x$-Au/CeO$_2$ underwent a DODH reaction converting glycerol into allyl alcohol in 91% yield.\cite{22}

In cyclic molecules, the ReO$_x$-Pd/CeO$_2$ and ReO$_x$-Au/CeO$_2$ catalysts in principle selectively eliminate cis-diols, while the conversion of trans-diols is negligible since the Re-diolate species cannot be formed.\cite{24,25} Although some trans-configured simple cyclic diols such as 1,2-hexanediol and tetrahydro-3,4-furandiol could also be deoxydehydrated, the trans-cyclic diols were isomerized into the cis-configuration in the presence of heterogeneous catalysts before diol-elimination.\cite{24,25} Regarding more complicated cyclic systems, several commercially available methyl glycosides were exploited as substrates in DODH reactions catalyzed by ReO$_x$-Pd/CeO$_2$ and ReO$_x$-Au/CeO$_2$ in hydrogen to yield saturated and unsaturated diol-eliminated pyranosides, respectively.\cite{26,27} With this heterogeneous catalyst, as expected only cis-diols in the glycosides were selectively removed and the stereochemistry of other hydroxy groups remained unchanged. \cite{26,27}
In general, one can state that the development of rhenium-catalyzed DODH of biomass-derived polyols is progressing, though slowly, but the turnover numbers inhibit commercialization. Furthermore, several glycosides have been successfully converted into corresponding diol-eliminated products.\textsuperscript{[26]} Nevertheless, the work also demonstrates an important limitation of (rhenium-catalyzed) DODH using glycosides and other cyclic molecules as substrates. Trans-configured diols in principle do not react, the vicinal hydroxy groups have to be \textit{cis}-configured.\textsuperscript{[26]} This limitation is significant, as the most abundant monosaccharides; gluco- and glucosamine pyranosides, and fructofuranosides, are all-trans configured. Thus, whereas DODH of methyl mannos (2,3-\textit{cis}), methyl galactoside (3,4-\textit{cis}), and several other monosaccharides has successfully been demonstrated,\textsuperscript{[26,27]} these starting materials are far less abundant and therefore more costly than the “big three” (glucose, glucosamine, and fructose).

Herein we demonstrate two strategies to approach the all-trans problem in the most readily available monosaccharides. Epimerization (inversion) of a hydroxy group in glucose and \textit{N}-acetyl glucosamine leads to the corresponding allo-configured compounds that do contain a \textit{cis}-configured diol. For fructose holds that its (uncommon) pyranose form possesses a \textit{cis}-configured diol as well. As the heterogeneous ReO\textsubscript{x}-Au/CeO\textsubscript{2} and ReO\textsubscript{x}-Pd/CeO\textsubscript{2} catalysts of Tomishige \textit{et al.} currently rank among the best catalysts for DODH reactions of glycosides, this system was selected to determine whether the newly developed substrates would produce the desired diol-eliminated products. Furthermore, in connection with the research on esterification, DODH of alkyl glycosides leads to novel carbohydrate-based diols, which is another added value to study this reaction on those particular substrates. Last but not least, some benchmark reactions were also carried out in a flow system to understand the catalytic activity over time.
3.2 Results and Discussions

We initially prepared the ReO₆-Au/CeO₂ catalyst according to the deposition-precipitation method developed by Tomishige and coworkers. The prepared catalyst was subsequently tested by converting Me-mannopyranoside 1 as a benchmark reaction. In our hands, we only found limited conversion of Me-mannopyranoside 1 when the conditions of the reaction were the same as reported in the literature. The difference in conversion may result from differences in the reaction setup compared to that of Tomishige, or the quality of the catalyst may vary from batch to batch. To maximize the conversion, we screened the reaction conditions for our system and determined that using 750 mg of the catalyst and 23 bar of hydrogen at 175 °C gave the highest conversion with decent selectivity (Table S1).

Although the optimized conditions were determined, the conversion and selectivity were not always reproducible. We found out that the reproducibility could be improved by adding more solvent to our system (Table S2) although the conversion was somewhat reduced. In addition, our prepared ReO₆-Au/CeO₂ catalyst gave a mixture of alkane and alkene instead of the reported high selectivity toward the formation of alkene. Since in our case the ReO₆-Au/CeO₂ only gave a mixture of products without full conversion, we switched our focus to the ReO₆-Pd/CeO₂ catalyzed reaction to achieve high selectivity toward alkane formation.

The substrate scope of the ReO₆-Pd/CeO₂ catalyzed DODH reaction is shown in table 1. The ReO₆-Pd/CeO₂ catalyzed reaction was initially tested with Me-mannopyranoside 1 at 175 °C and 76 bar of hydrogen, and full conversion was
achieved in 45 h to give 50% yield of the targeted product 3. Other over-hydrogenated moieties were also observed, implying the possible formation of volatile species. This led, despite the full conversion, to a low yield of the product after purification. To develop the substrate scope of the reaction, several different types of monosaccharides were studied. iPr-mannopyranoside 4 was successfully transformed into 5 in 56% conversion in 24 h. Me-galactopyranoside 6 was fully converted in 45 h but only 63% yield of 7 was isolated. To this end, we found that full conversion could be achieved by a longer time of reaction, i.e. 45 h, but that also poses the risk of excessive hydrogenation of the product to give volatile species. Aminoglycosides were also tested for this type of reaction. To obtain a cis-diol containing aminoglycoside, we performed a two-step site-selective epimerization on the C3-hydroxy group of Me-N-acetyl-glucosamine 17 to give Me-N-acetyl-allosamine 8 (Supporting Information). However, the allosamine species did not give any conversion even though the time of reaction was extended to 45 h. On the other hand, Me-N-acetyl-galactosamine 10 showed 52% conversion in 45 h. These two aminoglycosides in principle give the same final product 9, but the stereochemistry leads to different reactivity. The amide adjacent to the cis-diol of the allosamine 8 possibly interferes with the reaction by coordination to the rhenium or provides steric hindrance. As for the galactosamine 10, with the amide trans to the adjacent diol, the steric interference was avoided. However, the existing amide group from galactosamine 10 can still coordinate to the catalytic center leading to a low conversion. Several fructose species were tested in their pyranose form. The reaction of isopropylidene-fructose 11 reached full conversion in 24 h and 75% yield of the targeted product 12 was observed. The methyl-fructose 13 was fully converted but only 52% of the targeted product 14 was observed by NMR. The low carbon yield of DODH of 13 probably also resulted from excessive hydrogenation. As for the reaction with fructose 15, the allyl group was also hydrogenated leading to a mixture of deoxydehydrated product 16 and propyl-fructose 17 in moderate yield. Although DODH of the tested alkyl glycosides generally led to full consumption of the starting materials, the yields of obtained diols were just moderate. Since the catalyst loading of this reaction producing the carbohydrate-based diols was high, to obtain those diols by performing the developed heterogeneous DODH on alkyl glycosides is not practical.
<table>
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<th>Starting material</th>
<th>Product</th>
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<tr>
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<td>45 h</td>
<td>0%</td>
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<tr>
<td><img src="image8.png" alt="Chemical Structure 8" /></td>
<td>45 h</td>
<td>&gt; 99%</td>
<td><img src="image9.png" alt="Chemical Structure 9" /></td>
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<tr>
<td><img src="image15.png" alt="Chemical Structure 15" /></td>
<td>24 h</td>
<td>0%</td>
<td><img src="image16.png" alt="Chemical Structure 16" /></td>
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</tbody>
</table>

Conditions: Substrates (1.72 mmol), ReO$_x$-Pd/CeO$_2$ (1 g), dioxane (40 mL), H$_2$ (76 bar), 175 ºC, stirring speed (350 rpm), in a 300 mL autoclave

*Yield determined by NMR with trimethoxybenzene as the internal standard
*Isolated yields are shown in brackets

Table 1. The substrate scope of ReO$_x$-Pd/CeO$_2$ catalyzed reaction
To study the reactivity of the catalyst over time, the ReOₓ-Pd/CeO₂ catalyzed reaction was also performed in a flow system. A stock solution of Me-mannopyranoside (1 mg/mL) was introduced to the system at a flow rate of 0.1 mL/min (Figure 1), and the reactor was filled with 1 g of the ReOₓ-Pd/CeO₂ catalyst. The system reached 39% conversion in 6 h and the conversion started to gradually reduce afterward. The conversion dropped below 10% in 24 h. Due to the low concentration of the stock solution, most of the reagents were adsorbed on the catalyst at the beginning leading to a low combined yield of the starting material and the product in the first 6 h. The system started to reach to steady-state after 8 h. To shorten the time to reach steady-state, we decided to increase the concentration of the reagent ten times to “saturate” the catalyst faster. To this end, we introduced iPr-mannopyranoside 4 as the substrate since it has a higher solubility in dioxane than Me-mannopyranoside 1 in the same solvent. The flow rate of the stock solution was kept at 0.1 ml/min to be introduced to the reactor filled with the same amount of the catalyst. By increasing the concentration of the stock solution, the time of reaching steady-state was reduced to 1-2 h though we still could see a minor reduction of the observed yield of the reaction species due to the adsorption to the catalyst (Figure 2). The catalyst showed its highest reactivity at 2 h and the reactivity started to gradually decrease afterward. After 8 h, the observed yield of the alkane turned below 10%. Based on our flow study, the batch reactor showed its highest turnover frequency in first 2 h but its reactivity started to gradually reduced afterward. The reactivity of the catalyst usually became negligible after 24 h. Compared with the results from the batch reactor, the batch reactor is a better system to synthesize a substantial amount of the deoxydehydrated product. As the catalyst only showed its highest turnover frequency in the first few hours, the limitation of using the dilute stock solution and low flow speed on the flow system leads to the low amount of the product.
Figure 1. The ReO$_x$-Pd/CeO$_2$-catalyzed DODH reaction in flow (Me-mannopyranoside 1), the lines connecting the points are just to guide the eye.

Figure 2. ReO$_x$-Pd/CeO$_2$-catalyzed DODH reaction in flow (iPr-mannopyranoside 5)
3.3 Conclusion

In our research, we have produced the ReO\textsubscript{x}-Au/CeO\textsubscript{2} and ReO\textsubscript{x}-Pd/CeO\textsubscript{2} catalysts according to the literature\cite{26,27}. In our hands, though the deoxydehydration reaction was observed, the ReO\textsubscript{x}-Au/CeO\textsubscript{2} catalyst led to a mixture of alkene and alkane instead of the reported high selectivity toward the alkene. Additionally, this catalyst did not result in a full conversion of the substrate. To this end, we switched our focus to the ReO\textsubscript{x}-Pd/CeO\textsubscript{2} catalyst as it showed high selectivity toward alkane formation, and full conversion was achieved. With this catalyst, we successfully converted common glycosides into the corresponding bis-dehydroxy compounds. Furthermore, fructopyranosides also showed compatibility with the ReO\textsubscript{x}-Pd/CeO\textsubscript{2} catalyst and yielded the corresponding deoxydehyrated products. Aminoglycosides were more difficult substrates for this methodology as full conversion was not achieved with those substrates. According to our DODH studies on a series of alkyl glycosides, performing DODH on those glycosides is not yet a practical and efficient method to obtain novel carbohydrate-based diols.

The reactivity of the ReO\textsubscript{x}-Pd/CeO\textsubscript{2} catalyst over time was also studied by performing reactions in a flow system. The catalyst showed its highest activity at first few hours of the reaction and then started to lose activity afterward. The ReO\textsubscript{x}-Pd/CeO\textsubscript{2} catalyst had become almost inactive after 24 h. The reaction in batch is still preferred to synthesize a substantial amount of deoxydehyrated product since the turnover number of the DODH reaction in flow also depends on the flow speed and the concentration of the stock solution. The short active time of the catalyst also makes the synthesis in flow less applicable.

3.4 Acknowledgement

Dr. Q. Yuan (Qingqing) and Prof. Dr. P. Deuss (ENTEG, UG) are acknowledged for the expertise and collaboration in the synthesis of the heterogeneous Re-based catalysts and the development of the continuous system for the DODH reaction.
3.5 Experimental

Solvents and Reagents

All carbohydrates used for synthesis were commercially available, and used without further purification: Methyl α-D-mannopyranoside (TCI), D(-)-fructose (TCI), D(+)-Mannose (Sigma-Aldrich), Methyl α-D-galactopyranoside (Carbosynth), N-acetyl-D-glucosamine (Sigma-Aldrich), N-acetyl-D-galactosamine (Carbosynth), Amberlyst® 15 hydrogen form (Sigma-Aldrich). All materials used for the preparation of the heterogeneous catalysts for the DODH reaction were commercially available and utilized without further treatment: CeO$_2$ (nanopowder, < 50 nm particle size (BET), 99.95% trace rare earth metals basis, Sigma-Aldrich), HAuCl$_4$·xH$_2$O (49% Au, Strem), Pd(NO$_3$)$_2$·2H$_2$O (Sigma-Aldrich), NH$_4$ReO$_4$ (> 99%, Sigma-Aldrich). All solvents used were commercially available and used without further treatment: 1,4-dioxane (anhydrous, 99.8%, Sigma-Aldrich).

Analysis

$^1$H-, $^{13}$C- and HMBC-NMR were recorded on a Varian AMX400 spectrometer (400, 100 MHz, respectively) using CD$_3$OD as solvent. Chemical shift values are reported in ppm with the solvent resonance as the internal standard (CD$_3$OD: δ 3.31 for $^1$H, δ 49.15 for $^{13}$C). Data are reported as follows: chemical shifts (δ), multiplicity (s = singlet, d = doublet, dd = double doublet, ddd = double double doublet, t = triplet, appt = apparent triplet, q = quartet, m = multiplet), coupling constants J (Hz), and integration. High-Resolution Mass spectrometry measurements were performed using a ThermoScientific LTQ OrbitrapXL spectrometer. GC analysis was performed by treating an aliquot of the reaction mixture with N,O-bis(trimethylsilyl)trifluoroacetamide$^{[29]}$ (>99%, Sigma-Aldrich) followed by injection on GC (Agilent 6890N) equipped with a DB-5ht column (30.0 m × 250 μm × 0.10 μm) and FID detection.

Instrumentation of GC analysis

An Agilent GC-FID instrument equipped with a Hewlett Packard GC carousel 18596C autosampler, a 6890 series gas chromatographer with a split/splitless injector, and a 6890 FID detector, was used for the analysis of conversion and selectivity of DODH reactions. The gas chromatographer was equipped with a J&W DB-5ht 5975T column (30.0 m × 250 μm × 0.10 μm). The injector temperature was kept at 350 °C. The helium carrier gas flow rate was kept at 1.7 mL/min. The temperature of the oven started from 40 °C and increased to 200 °C at a rate of 5 °C/min. The temperature was further increased to 350 °C at a rate of 50 °C/min. The temperature of FID was kept at 300 °C with a combination of H$_2$ (40 mL/min) and air flow (300 mL/min); in which N$_2$ was used as a makeup flow (25 mL/min).
General procedures

Synthesis of fructopyranosides

The synthesis of fructopyranose derivatives was carried out according to a literature procedure with some modifications.[30,31] Acetyl chloride (5 mL, 70 mmol) was added at rt to the corresponding alcohol (200 mL) followed by stirring for 30 min. D-(−)-fructose (25 g, 138 mmol) or inulin (25 g) was added to the mixture followed by stirring at rt. Depending on the solvent and the starting material, a white precipitate formed in a period between 20 min to 30 h. The precipitate was collected by filtration followed by washing with ethanol and diethyl ether. Subsequently, vacuo was applied to remove traces of the solvents. The product was analyzed by \(^1\text{H}\), \(^{13}\text{C}\)-NMR and the molecular composition was determined by HRMS.

Preparation of the deoxydehydration catalysts

Preparation of ReO\(_x\)-Au/CeO\(_2\) catalyst\([26]\)

For the preparation of ReO\(_x\)-Au/CeO\(_2\) catalyst (1 wt% Re, Au/Re = 0.3 mass ratio), CeO\(_2\) (4 g, pre-calcined in air at 700 °C for 1 h), and 0.3 mM HAuCl\(_4\)·xH\(_2\)O (200 mL) was mixed in a 250 mL round-bottom flask, which was placed in a sand bath at 50 °C and stirred at 600 rpm. After the temperature was increased to 70 °C, the pH was adjusted to 9 by adding 0.1 M ammonia dropwise. The resulted mixture was kept stirring at 70 °C for 4 h. The suspension was filtered and washed with Milli-Q water (1.5 L). The obtained solids were dried in an oven at 110 °C overnight. The products were ground and then calcined in air at 400 °C for 4 h using a temperature ramp of 10 °C/min. Afterward, 0.7 mL of a 0.3 M aqueous NH\(_4\)ReO\(_4\) solution was slowly dropped in the obtained Au/CeO\(_2\) catalyst while being stirred continuously until all the solid support was evenly wetted. The mixture was dried in an oven first at 80 °C for 2 h then heated up to 110 °C overnight. The resulted solid was ground and then calcined in air at 400 °C for 4 h using a temperature ramp of 10 °C/min. The obtained solids were ReO\(_x\)-Au/CeO\(_2\) catalysts (1 wt% Re, Au/Re = 0.3 mass ratio).

Preparation of ReO\(_x\)-Pd/CeO\(_2\) catalyst\([27]\)

For the preparation of ReO\(_x\)-Pd/CeO\(_2\) catalyst (2 wt% Re, Pd/Re = 0.25, molar ratio), 1.4 mL of 0.3 M aqueous NH\(_4\)ReO\(_4\) solution was slowly dropped in CeO\(_2\) powder (4 g, pre-calcined in air at 600 °C for 3 h) while being stirred continuously until all the solid support was evenly wetted. The mixture was dried in an oven first at 80 °C for 2 h then heated up to 110 °C overnight. The resulted solid was ground and then calcined in air at 500 °C for 3 h using a temperature ramp of 10 °C/min. Subsequently, 0.35 mL of 0.3 M aqueous Pd(NO\(_3\))\(_2\) solution was added to the collected Re/CeO\(_2\) catalyst while stirring until all the powder was evenly wetted. The mixture was dried in an oven first at 80 °C for 2 h then heated up to 110 °C overnight. The resulted solid was ground and then calcined in air at 500 °C for 3 h using a temperature ramp of 10 °C/min. The obtained solids were ReO\(_x\)-Pd/CeO\(_2\) catalyst (2 wt%, Re, Pd/Re = 0.25 molar ratio).
Deoxydehydration reaction, general procedure\textsuperscript{[26,27]}

The \textit{ReO\textsubscript{x}-Au/CeO\textsubscript{2}} catalyzed reaction

The substrate (1.29 mmol, 1 eq.), \textit{ReO\textsubscript{x}-Au/CeO\textsubscript{2}} catalyst (750 mg), and 1,4-dioxane (10 mL) were added to an autoclave (300 mL) equipped with a stirring bar. The autoclave was closed and the system flushed with nitrogen three times. The system was subsequently flushed with hydrogen three times and then pressurized to 12 bar of hydrogen at rt. The autoclave was placed in a heating mantle equipped with a thermocouple to indicate the external temperature. The stirring speed was adjusted to 350 rpm and the external temperature was set to 175 °C. The starting point of the DODH reaction was defined as the time the external temperature reached 175 °C. After the corresponding reaction time, the autoclave was cooled down to rt, followed by pressure release. The reaction mixture was collected and the autoclave was washed with methanol. After removal of the solid catalyst by centrifugation, the crude mixture was concentrated \textit{in vacuo} and analyzed with \textit{\textsuperscript{1}H-}, \textit{\textsuperscript{13}C-NMR}, and GC-FID.

The \textit{ReO\textsubscript{x}-Pd/CeO\textsubscript{2}} catalyzed reaction

The substrate (1.72 mmol, 1 eq.), \textit{ReO\textsubscript{x}-Pd/CeO\textsubscript{2}} catalyst (1 g), and 1,4-dioxane (40 mL) were added to an autoclave (300 mL) equipped with a stirring bar. The autoclave was closed and the system flushed with nitrogen three times. The system was subsequently flushed with hydrogen three times and then pressurized to 48 bar of hydrogen at rt. The autoclave was placed in a heating mantle equipped with a thermocouple to indicate the external temperature. The stirring speed was adjusted to 350 rpm and the external temperature was set to 175 °C. The starting point of the DODH reaction was defined as the time the external temperature reached 175 °C. After the corresponding reaction time, the autoclave was cooled down to rt, followed by pressure release. The reaction mixture was collected and the autoclave was washed with methanol. After removal of the solid catalyst by centrifugation, the crude mixture was concentrated \textit{in vacuo} and analyzed with \textit{\textsuperscript{1}H-}, \textit{\textsuperscript{13}C-NMR}, and GC-FID.

Sample preparation for GC analysis of deoxydehydration

The crude mixture of the deoxydehydration reaction was derivatized using a literature procedure for GC analysis.\textsuperscript{[29]} The crude mixture was dissolved in DMF with a concentration of 1 mg/mL, which was followed by the addition of 0.2 mL of \textit{N,O-Bis(trimethylsilyl)trifluoroacetamide}. The combined mixture was stirred at 80 °C for 30 min and then injected into GC. The conversion of the deoxydehydration reaction was calculated based on calibration curves and the selectivity was determined by the ratio of peak area of representative peaks from the alkene and alkane.

General procedure of performing the DODH reaction in a flow system

1 g of the catalyst was filled in a reactor (a column with diameter = 0.5 cm, length = 6.5 cm) equipped with homemade metallic filters. The reactor was closed and installed on the flow system, then pressurized to 20 bar with hydrogen at a flow speed of 25 mL/min. After reaching the targeted
Deoxydehydration of Monosaccharides in Batch and Continuous Systems

pressure, the stock solution was introduced to the system at a flow speed of 0.1 mL/min. As soon as seeing the first droplet coming out from the system, the reactor was heated with an oven to 175 ºC and the outgoing mixture was started to be collected. The collection flask was replaced with a new one after a period of time, and the conversion was analyzed with NMR and GC-FID.

Figure S1. Schematic representation of the flow system
Chapter 3

Optimization of DODH reaction

![Chemical structure diagram]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Cat. Loading (mg)</th>
<th>$P_{H_2}$ (bar)</th>
<th>Temp. ($^\circ$C)</th>
<th>Conversion (2:3)</th>
<th>Yield 2+3 (%)</th>
<th>Recovered SM (%)</th>
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<tr>
<td>1</td>
<td>500</td>
<td>20</td>
<td>140</td>
<td>32% (83:17)</td>
<td>28</td>
<td>59</td>
</tr>
<tr>
<td>2</td>
<td>500</td>
<td>80</td>
<td>140</td>
<td>44% (48:52)</td>
<td>53</td>
<td>48</td>
</tr>
<tr>
<td>3</td>
<td>500</td>
<td>20</td>
<td>155</td>
<td>53% (76:24)</td>
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<td>37</td>
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<tr>
<td>4</td>
<td>500</td>
<td>23</td>
<td>175</td>
<td>73% (79:21)</td>
<td>63</td>
<td>16</td>
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<tr>
<td>5</td>
<td>750</td>
<td>23</td>
<td>175</td>
<td>89% (72:28)</td>
<td>79</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

Catalysts include 1 wt% Re, Au/Re = 0.3
External temperature was indicated
Conversion and selectivity were determined by NMR
10 mL of 1,4-dioxane in a 300 mL autoclave

Table S1: Optimization of DODH of glycosides 1

Reproducibility test of different batches of catalyst

The reproducibility test was tested with a different batch of catalyst

![Chemical structure diagram]

<table>
<thead>
<tr>
<th>Batch</th>
<th>Conversion</th>
<th>Selectivity (alkane%)</th>
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<tbody>
<tr>
<td>A</td>
<td>56%</td>
<td>92%</td>
</tr>
<tr>
<td>B</td>
<td>66%</td>
<td>70%</td>
</tr>
<tr>
<td>C</td>
<td>63%</td>
<td>75%</td>
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<tr>
<td>D</td>
<td>61%</td>
<td>85%</td>
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</table>

Conversion and selectivity were determined by NMR

Table S2: Reproducibility test with different batches of catalyst
Preparation of the starting materials

**Synthesis of isopropyl α-mannopyranose (4)**

D-(+)-mannose (20 g, 111 mmol) and Amberlyst® 15 hydrogen form (24 g) were added to isopropanol (740 mL, 0.15 M). The mixture was brought to reflux and stirred for 21 h. After completion of the reaction indicated by TLC, the resin was removed by filtration. The filtrate was concentrated under reduced pressure and the crude product was washed with DCM and diethyl ether resulting in a white solid 4 (18.6 g, 84 mmol, 75% yield). $^1$H NMR (400 MHz, D$_2$O) $\delta$ 4.99 (s, 1H), 4.04 (p, $J = 6.2$ Hz, 1H), 3.93-3.85 (m, 2H), 3.84-3.73 (m, 2H), 3.73-3.62 (m, 2H), 1.24 (d, $J = 6.3$ Hz, 3H), 1.20 (d, $J = 6.1$ Hz, 3H) $^{13}$C NMR (101 MHz, D$_2$O) $\delta$ 97.5, 72.7, 70.5, 70.4, 69.8, 66.8, 60.9, 20.1 The NMR data matched with those in the literature.[32]

**Synthesis of methyl N-acetyl α-allosamine (8)**[33]

Methyl α-N-acetyl-D-glucosamine (18)

N-acetyl-D-glucosamine (5 g, 23 mmol) and Amberlyst® 15 hydrogen form (6 g) were added to methanol (150 mL, 0.15 M). The mixture was brought to reflux and stirred for 24 h. After completion of the reaction indicated by TLC, the resin was removed by filtration. The filtrate was concentrated under reduced pressure and the product was purified by column chromatography resulting in a white solid 18 (3.5 g, 14.7 mmol, 64% yield). $^1$H NMR (400 MHz, CD$_3$OD) $\delta$ 4.66 (d, $J = 3.6$ Hz, 1H), 3.99 (dd, $J = 10.8$, 3.6 Hz, 1H), 3.86-3.79 (m, 1H), 3.72-3.66 (m, 1H), 3.66-3.60 (m, 1H), 3.57-3.51 (m, 1H), 3.37 (s, 3H), 3.35 (s, 1H), 1.98 (s, 3H). The NMR data matched with those in the literature.[33]

Methyl 3-keto-α-N-acetyl-D-glucosamine (19)

Methyl α-N-acetyl-D-glucosamine 18 (1.9 g, 1 eq., 7.9 mmol) and benzoquinone (0.9 g, 1.05 eq., 8.3 mmol) were added to methanol (32 mL, 0.25 M). The mixture was stirred at rt for 15 min followed by the addition of [neocuproine]PdOAc$_2$OTf$_2$ (167 mg, 0.02 eq., 0.16 mmol). The reaction was monitored by TLC until completion (about 1 h). After completion of the reaction, celite was added and the mixture was concentrated under reduced pressure. The residue was purified by column chromatography resulting in a grayish solid 19 (1.9 g, quantitative yield). $^1$H NMR (400 MHz, CD$_3$OD) $\delta$ 5.08 (d, $J = 4.0$ Hz, 1H), 4.87 (s, 1H), 4.29 (d, $J = 9.6$ Hz, 1H), 3.91-3.85 (m, 1H), 3.85-3.79 (m, 1H), 3.73-3.66 (m, 1H), 3.38 (s, 3H), 2.03 (s, 3H). The NMR data matched with those in the literature.[33]
Methyl α-N-acetylgalactosamine (8)

The ketosugar 19 (1.9 g, 1 eq., 8.1 mmol) was dissolved in methanol (65 mL, 0.125 M), and the stirred solution was cooled to 0 °C. Sodium borohydride (0.9 g, 3 eq., 24.3 mmol) was gradually added to the solution, and the mixture was stirred at 0 °C for 1 h. After completion of the reaction indicated by TLC, Amberlyst® 15 hydrogen form was added until pH~7 was reached. The solids were removed by filtration and the filtrate was concentrated under reduced pressure. The crude mixture was purified with column chromatography resulting in slightly brownish solid product 8 (1.7 g, 96% yield).

1H NMR (400 MHz, CD3OD) δ 4.66 (d, J = 4.0 Hz, 1H), 4.04 (t, J = 3.6 Hz, 1H), 3.92-3.89 (m, 1H), 3.87-3.83 (m, 1H), 3.78-3.68 (m, 2H), 3.52 (dd, J = 9.8, 3.1 Hz, 1H), 3.39 (s, 3H), 2.00 (s, 3H). The NMR data matched with those in the literature.[33]

Synthesis of Methyl α-N-acetylgalactosamine (10)

N-acetyl-D-galactosamine (1 g, 4.5 mmol) and Amberlyst® 15 hydrogen form (1.2 g) were added to methanol (30 mL, 0.15 M). The mixture was heated to reflux and stirred for 24 h. After completion of the reaction, the resin was removed by filtration. The filtrate was concentrated under reduced pressure and the mixture was purified with column chromatography resulting in white solid product 10 (666 mg, 2.8 mmol, 63% yield). The similar synthetic method reported in literature reported 65% yield.[34] 1H NMR (400 MHz, CD3OD) δ 4.68 (d, J = 3.7 Hz, 1H), 4.27 (dd, J = 11.0, 3.6 Hz, 1H), 3.89-3.86 (m, 1H), 3.79-3.69 (m, 4H), 3.37 (s, 3H), 1.99 (s, 3H). 13C NMR (101 MHz, CD3OD) δ 174.0, 100.0, 72.3, 70.4, 69.9, 62.8, 55.6, 51.5, 22.6. HRMS (ESI) calculated for C9H17NO6 ([M+Na]+): 258.0948, found: 258.0945. The NMR data matched with those in the literature.[34]

Synthesis of 1,2-isopropylidene-fructopyranose (11)[35,36]

1,2,4,5-diisopropylidene-fructopyranose (20)

The synthesis of 20 was based on a slightly modified literature procedure.[35] To 180 mL acetone, sulfuric acid (0.9 mL, 0.3 eq., 17 mmol) was added, followed by stirring at rt for 10 min. D-(−)-fructose (9.6 g, 1 eq., 53 mmol) was subsequently added. The reaction was monitored by TLC until completion (about 2 h). Subsequently, 1 M NaOH was added dropwise to the mixture at 0 °C till neutral as indicated by pH strips. The precipitate was removed by filtration, and the filtrate was concentrated under reduced pressure. The crude mixture was extracted with dichloromethane and water. The organic layer was washed with brine and further dried with MgSO4. The resulted organic layer was concentrated under reduced pressure and purified by recrystallization from heptane resulting in 20 as a colorless solid (5.4 g, 39% yield). The reported yield in literature is 88%. 1H NMR (400 MHz,
CDCl\textsubscript{3} δ 4.22-4.19 (m, 1H), 4.17 (d, J = 8.8 Hz, 1H), 4.14-4.08 (m, 2H), 4.02-3.95 (m, 2H), 3.65 (dd, J = 8.3, 6.9 Hz, 1H), 2.04 (d, J = 8.3 Hz, 1H), 1.52 (s, 3H), 1.50 (s, 3H), 1.43 (s, 3H), 1.36 (s, 3H). The NMR data matched with those in the literature.\textsuperscript{[37]}

1,2-β-isopropylidene-fructopyranose (11)

The synthesis of 11 was based on a slightly modified literature procedure.\textsuperscript{[36]} Fructopyranoside 20 (2.2 g, 1 eq., 8.5 mmol) was added to 75% acetic acid in water (32 mL, 0.27 M final concentration). The reaction was stirred at 55 °C for 4 h, and monitored by TLC. After completion of the reaction, the solution was concentrated under reduced pressure to give a syrup. The syrup was further purified with column chromatography resulting in white solid product 11 (1.1 g, 61% yield). The reported yield in literature is 98%.\textsuperscript{[36]}

\textbf{Synthesis of Methyl β-fructopyranose (13)}\textsuperscript{[30,31]}

Chloroethyl β-fructopyranoside (21)

According to the general procedure,\textsuperscript{[30,31]} 50 g of D(-)-fructose reacted 3 h with 400 mL 2-chloroethanol pretreated with 10 mL acetyl chloride leading to 21 as a white solid (64 g, 95% yield). The yield reported in literature is 90%.\textsuperscript{[10]} \textbf{1H NMR} (400 MHz, DMSO-d\textsubscript{6}) δ 4.57 (t, J = 6.0 Hz, 1H), 4.49 (d, J = 6.0 Hz, 1H), 4.45 (d, J = 3.2, 1H), 4.37 (d, J = 6.0 Hz, 1H), 3.78-3.69 (m, 5H), 3.68-3.66 (m, 1H), 3.66-3.60 (m, 2H), 3.56-3.47 (m, 3H) \textbf{13C NMR} (101 MHz, DMSO-d\textsubscript{6}) δ 100.4, 69.1, 69.04, 68.96, 64.0, 62.4, 61.0, 44.3 [α] = -160.4° \textbf{HRMS} (ESI) calculated for C\textsubscript{8}H\textsubscript{15}ClO\textsubscript{6} ([M+Na]+): 265.0449 and 267.0420, found: 265.0446 and 267.0416.

Methyl β-fructopyranoside (13)

To a suspension of 21 (8 g, 33 mmol) in methanol (120 mL, 0.28 M) was added acetyl chloride (1.2 mL, 17 mmol). The mixture was stirred at rt for 6 h during which the reaction became homogeneous. The mixture was neutralized with Amberlyst® A21 free base. Solids were removed by filtration and the filtrate was concentrated under reduced pressure. The concentrated mixture was recrystallized in methanol leading to 13 as colorless crystals (4.5 g, 71%). The yield reported in literature is 50%.\textsuperscript{[31]} \textbf{1H NMR} (400 MHz, CD\textsubscript{3}OD) δ 3.90 (d, J = 9.8 Hz, 1H), 3.85-3.82 (m, 1H), 3.77-3.69 (m, 4H), 3.69-3.64 (m, 1H), 3.28 (s, 3H) \textbf{13C NMR} (101 MHz, CD\textsubscript{3}OD) δ 101.5, 71.5, 71.0, 70.6, 65.1, 63.0, 49.0 [α] = -174.0° \textbf{HRMS} (ESI) calculated for C\textsubscript{7}H\textsubscript{14}O\textsubscript{6} ([M+Na]+): 217.0683, found: 217.0682.
\(^1\text{H NMR}\) (400 MHz, D\(_2\)O) \(\delta\) 4.02-3.98 (m, 1H), 3.94 (d, \(J = 10.0\) Hz, 1H), 3.87 (dd, \(J = 10.0, 3.4\) Hz, 1H), 3.84-3.78 (m, 3H), 3.77-3.72 (m, 1H), 3.30 (s, 3H) \(^1\text{C NMR}\) (101 MHz, D\(_2\)O) \(\delta\) 100.3, 69.5, 69.0, 68.3, 63.7, 60.8, 48.4. The NMR data are the same as reported in literature.\[^{[39]}\]

**Synthesis of Allyl 6-fructopyranose (15)\[^{[30,31]}\]**

The preparation was according to the synthesis of fructopyranoses described in the general procedure.\[^{[30,31]}\] 25 g of D-(−)-fructose reacted over 30 h with 100 mL allyl alcohol pretreated with 2.5 mL acetyl chloride leading to white solid product 15 (11.3 g, 34% yield). The similar synthetic procedure reported in literature led to 49% yield.\[^{[40]}\]

\(^1\text{H NMR}\) (400 MHz, CD\(_3\)OD) \(\delta\) 5.94 (ddt, \(J = 17.3, 10.4, 5.2\) Hz, 1H), 5.31 (dq, \(J = 17.2, 1.8\) Hz, 1H), 5.12 (dq, \(J = 10.5, 1.6\) Hz, 1H), 4.18-4.00 (m, 2H), 3.93 (d, \(J = 9.8\) Hz, 1H), 3.86-3.83 (m, 1H), 3.81 (dd, \(J = 9.8, 3.4\) Hz, 1H), 3.79-3.73 (m, 2H), 3.72-3.63 (m, 2H) \(^1\text{C NMR}\) (101 MHz, CD\(_3\)OD) \(\delta\) 136.4, 116.1, 102.0, 71.5, 71.0, 70.5, 65.3, 63.5, 62.9 [\(\alpha\) = -119.8°] HRMS (ESI) calculated for C\(_9\)H\(_{16}\)O\(_6\) ([M+Na]\(^+\)): 243.0839, found: 243.0839.

**Rhenium-catalyzed deoxydehydration**

**Deoxyhydrated product from methyl α-D-mannopyranoside (2)**

The product was obtained using the general procedure for the deoxydehydration reaction.\[^{[26,27]}\] 1.29 mmol of methyl α-D-mannopyranoside 1 and 750 mg of ReO\(_x\)-Au/CeO\(_2\) catalyst (1 wt% Re, Au/Re = 0.3) were mixed in 10 mL 1,4-dioxane for 8 h using the described conditions which resulted in 89% conversion (alkene : alkane = 72:28) according to NMR. \(^1\text{H NMR}\) (400 MHz, CDCl\(_3\)) \(\delta\) 5.96 (dt, \(J = 10.2, 2.4\) Hz, 1H), 4.88-4.86 (m, 1H), 4.25-4.16 (m, 1H), 3.91-3.82 (m, 2H), 3.72-3.65 (m, 1H), 3.44 (s, 3H), 2.62-2.56 (m, 1H), 2.39-2.31 (m, 1H) \(^1\text{C NMR}\) (101 MHz, CDCl\(_3\)) \(\delta\) 133.7, 126.2, 95.5, 71.6, 64.4, 62.9, 56.0. The NMR data matched with those in the literature.\[^{[26]}\]

**Deoxyhydrated product from methyl α-D-mannopyranoside (3)**

Synthesized from ReO\(_x\)-Au/CeO\(_2\) catalyzed reaction:

The product was obtained using the general procedure for the deoxydehydration reaction.\[^{[26,27]}\] 1.29 mmol of methyl α-D-mannopyranoside 1 and 750 mg of ReO\(_x\)-Au/CeO\(_2\) catalyst (1 wt% Re, Au/Re = 0.3) were mixed in 10 mL 1,4-dioxane for 8 h at described conditions resulting in 89% conversion (alkene : alkane = 72:28) according to NMR.
Synthesized from ReOₓ-Pd/CeO₂ catalyzed reaction:

The product was obtained using the general procedure for the deoxydehydration reaction.[26,27] 1.72 mmol of methyl α-D-mannopyranoside 1 and 1 g of ReOₓ-Pd/CeO₂ catalyst (2 wt% Re, Pd/Re = 0.25) were mixed in 40 mL 1,4-dioxane. 48 bar of hydrogen pressure was charged in the system at rt, and then the reaction was carried out at 175 °C for 45 h leading to full conversion according to NMR. The mixture was purified by column chromatography to afford 3 as colorless oil in 50% yield. ¹H NMR (400 MHz, CDCl₃) δ 4.66 (d, J = 2.8 Hz, 1H), 3.8 (d, J = 4.0 Hz, 2H), 3.65-3.55 (m, 1H), 3.55-3.49 (m, 1H), 3.34 (s, 3H), 2.75 (bs, 1H), 2.59 (bs, 1H), 1.89-1.69 (m, 6H) ¹³C NMR (101 MHz, CDCl₃) δ 97.5, 72.9, 67.1, 63.2, 54.7, 29.3, 27.3 [α] = +158.3° HRMS (ESI) calculated for C₇H₁₄O₄ ([M+Na]⁺): 185.0784, found: 185.0784.

¹H NMR (400 MHz, D₂O) δ 4.78 (s, 1H), 3.84 (dd, J = 11.8, 1.8 Hz, 1H), 3.71 (dd, J = 12.0, 4.3 Hz, 1H), 3.60-3.49 (m, 2H), 3.37 (s, 3H), 1.97-1.86 (m, 1H), 1.86-1.71 (m, 2H), 1.71-1.58 (m, 1H) ¹³C NMR (101 MHz, D₂O) δ 97.3, 73.4, 65.1, 60.9, 54.1, 28.1, 26.0. The NMR data matched with those in literature.[27]

Deoxydehydrated product from isopropyl α-D-mannopyranoside (5)

The product was obtained using the general procedure for the deoxydehydration reaction.[26,27] 1.72 mmol of isopropyl α-D-mannopyranoside 4 and 1 g of ReOₓ-Pd/CeO₂ catalyst (2 wt% Re, Pd/Re = 0.25) were mixed in 40 mL 1,4-dioxane. 48 bar of hydrogen pressure was charged in the system at rt, and then the reaction was carried out at 175 °C for 24 h leading to 56% conversion according to NMR. The mixture was purified by column chromatography to afford 5 as colorless oil in 44% yield. ¹H NMR (400 MHz, CD₃OD) δ 4.91-4.89 (m, 1H), 4.01-3.90 (m, 1H), 3.77 (dd, J = 11.6, 2.6 Hz, 1H), 3.65 (dd, J = 11.6, 5.6 Hz, 1H), 3.60-3.53 (m, 1H), 3.48-3.40 (m, 1H), 1.83-1.76 (m, 2H), 1.75-1.69 (m, 2H), 1.21 (d, J = 6.3 Hz, 3H), 1.13 (d, J = 6.1 Hz, 3H) ¹³C NMR (101 MHz, CD₃OD) δ 94.9, 75.8, 68.9, 67.2, 63.1, 30.8, 28.1, 23.8, 21.6 [α] = +147.6° HRMS (ESI) calculated for C₉H₁₈O₄ ([M+Na]⁺): 213.1097, found: 213.1098.

Deoxydehydrated product methyl α-D-galactopyranoside (7)

The product was obtained using the general procedure for the deoxydehydration reaction.[26,27] 1.72 mmol of methyl α-D-galactopyranoside 6 and 1 g of ReOₓ-Pd/CeO₂ catalyst (2 wt% Re, Pd/Re = 0.25) were mixed in 40 mL 1,4-dioxane. 48 bar of hydrogen pressure was charged in the system at rt, and then the reaction was carried out at 175 °C for 45 h leading to full conversion according to NMR. The mixture was purified by column chromatography to afford 7 as colorless oil in 60% yield. ¹H NMR (400 MHz, CD₃OD) δ 4.60 (d, J = 3.5 Hz, 1H), 3.75-3.64 (m, 1H), 3.62-3.54 (m, 1H), 3.48 (d, J = 5.3 Hz, 2H), 3.42 (s, 3H), 1.90-1.72 (m, 2H), 1.71-1.64 (m, 1H), 1.52-1.33 (m, 1H) ¹³C NMR (101 MHz, CD₃OD) δ 101.0, 70.0, 69.5, 65.9, 55.2, 27.7, 27.3 [α] = +143.7° HRMS (ESI) calculated for C₇H₁₄O₄ ([M+Na]⁺): 185.0784, found: 185.0785.
Deoxydehydrated product from methyl \( \alpha-N \)-galactosamine (9)

The product was obtained using the general procedure for the deoxydehydration reaction.\[26,27\] 1.72 mmol of methyl \( \alpha-N \)-galactosamine 10 and 1 g of ReO\(_x\)-Pd/CeO\(_2\) catalyst (2 wt% Re, Pd/Re = 0.25) were mixed in 40 mL 1,4-dioxane. 48 bar of hydrogen pressure was charged in the system at rt, and then the reaction was carried out at 175 °C for 45 h leading to 52% conversion according to NMR. The mixture was purified by column chromatography to afford 9 as colorless oil in 30% yield.

**\( ^1H \) NMR** (400 MHz, CD\(_3\)OD) \( \delta \) 4.61 (d, \( J = 3.4 \) Hz, 1H), 4.00-3.82 (m, 1H), 3.77-3.69 (m, 1H), 3.50 (d, \( J = 5.2 \) Hz, 2H), 3.40 (s, 3H), 1.93 (s, 3H), 1.87-1.74 (m, 1H), 1.73-1.65 (m, 2H), 1.53-1.40 (m, 1H) 13\( ^C \) NMR (101 MHz, CD\(_3\)OD) \( \delta \) 172.9, 99.3, 70.1, 66.0, 55.2, 49.8, 27.8, 24.9, 22.5 [\( \alpha \) = +136.9° HRMS (ESI) calculated for C\(_9\)H\(_{17}\)NO\(_4\) ([M+Na\(^+\)]: 226.1050, found: 226.1051.

Deoxydehydrated product from isopropylidene \( \beta \)-fructopyranose (12)

The product was obtained using the general procedure for the deoxydehydration reaction.\[26,27\] 1.72 mmol of isopropylidene \( \beta \)-fructopyranose 11 and 1 g of ReO\(_x\)-Pd/CeO\(_2\) catalyst (2 wt% Re, Pd/Re = 0.25) were mixed in 40 mL 1,4-dioxane. 48 bar of hydrogen pressure was charged in the system at rt, and then the reaction was carried out at 175 °C for 24 h leading to full conversion according to NMR. The mixture was purified by column chromatography to afford 12 as colorless oil in 63% yield.

**\( ^1H \) NMR** (400 MHz, CD\(_3\)OD) \( \delta \) 4.13 (d, \( J = 8.6 \) Hz, 1H), 3.83-3.75 (m, 2H), 3.59-3.53 (m, 1H), 3.47-3.41 (m, 1H), 1.93-1.85 (m, 1H), 1.80-1.61 (m, 3H), 1.48 (s, 3H), 1.41 (s, 3H) 13\( ^C \) NMR (101 MHz, CD\(_3\)OD) \( \delta \) 112.6, 106.8, 72.9, 68.4, 62.1, 29.7, 27.4, 26.6, 26.4 [\( \alpha \) = -85.3°

Deoxydehydrated product from Methyl \( \beta \)-fructopyranose (14)

The product was obtained using the general procedure for the deoxydehydration reaction.\[26,27\] 1.72 mmol of methyl \( \beta \)-fructopyranose 13 and 1 g of ReO\(_x\)-Pd/CeO\(_2\) catalyst (2 wt% Re, Pd/Re = 0.25) were mixed in 40 mL 1,4-dioxane. 48 bar of hydrogen pressure was charged in the system at rt, and then the reaction was carried out at 175 °C for 24 h leading to full conversion according to NMR. The mixture was purified by column chromatography to afford 14 as colorless oil in 34% yield. 1\( ^H \) NMR (400 MHz, CD\(_3\)OD) \( \delta \) 3.78-3.73 (m, 1H), 3.73-3.69 (m, 1H), 3.63-3.58 (m, 1H), 3.58-3.52 (m, 2H), 3.29 (s, 3H), 1.81-1.72 (m, 2H), 1.72-1.58 (m, 2H) 13\( ^C \) NMR (101 MHz, CD\(_3\)OD) \( \delta \) 99.6, 70.3, 63.2, 61.5, 48.5, 28.2, 26.2 [\( \alpha \) = -102.7° HRMS (ESI) calculated for C\(_7\)H\(_{14}\)O\(_4\) ([M+Na\(^+\)]: 185.0784, found: 185.0785.

Deoxydehydrated product from Allyl \( \beta \)-fructopyranose (16)

The product was obtained using the general procedure for the deoxydehydration reaction.\[26,27\] 1.72 mmol of allyl \( \beta \)-fructopyranose 15 and 1 g of ReO\(_x\)-Pd/CeO\(_2\) catalyst (2 wt% Re, Pd/Re = 0.25) were mixed in 40 mL 1,4-dioxane. 48 bar of hydrogen pressure was charged in the system at rt, and then the reaction was carried out at 175 °C for 24 h leading to full conversion according to NMR. The mixture was purified by column
chromatography to afford 16 as colorless oil in 34% yield. $^1$H NMR (400 MHz, CD$_3$OD) δ 3.81-3.67 (m, 2H), 3.66-3.52 (m, 3H), 3.52-3.41 (m, 2H), 1.90-1.78 (m, 1H), 1.78-1.66 (m, 2H), 1.66-1.58 (m, 3H), 0.98 (t, J = 7.4 Hz, 3H) $^{13}$C NMR (101 MHz, CD$_3$OD) δ 99.6, 70.3, 63.7, 62.9, 61.4, 28.2, 26.3, 24.4, 11.2 $^{[\alpha]}$ = -86.0$^o$ HRMS (ESI) calculated for C$_9$H$_{18}$O$_4$ ([M+Na]$^+$): 213.1097, found: 213.1095.

Side product from deoxydehydration of allyl β-fructopyranose (17)

The product was obtained using the general procedure for the deoxydehydration reaction.$^{[26,27]}$ 1.72 mmol of allyl β-fructopyranose 15 and 1 g of ReO$_x$-Pd/CeO$_2$ catalyst (2 wt% Re, Pd/Re = 0.25) were mixed in 40 mL 1,4-dioxane. 48 bar of hydrogen pressure was charged in the system at rt, and then the reaction was carried out at 175 $^o$C for 24 h leading to full conversion according to NMR. The mixture was purified by column chromatography to afford 17 as a white solid in 11% yield. $^1$H NMR (400 MHz, CD$_3$OD) δ 3.91 (d, J = 9.9 Hz, 1H), 3.86-3.83 (m, 1H), 3.83-3.76 (m, 2H), 3.73 (d, J = 8.7 Hz, 2H), 3.70-3.64 (m, 2H), 3.64-3.52 (m, 1H), 3.47 (td, J = 6.8, 1.3 Hz, 2H), 1.60 (q, J = 7.2 Hz, 2H), 0.95 (t, J = 7.4 Hz, 3H). $^{13}$C NMR (101 MHz, CD$_3$OD) δ 101.6, 71.6, 71.1, 70.6, 65.2, 63.48, 63.46, 24.3, 11.1 $^{[\alpha]}$ = -96.2$^o$ HRMS (ESI) calculated for C$_9$H$_{18}$O$_6$ ([M+Na]$^+$): 245.0996, found: 245.0995.

3.6 References

Chapter 3


