Steps Towards the Synthesis of L-Ribose from D-Ribose

Presented to the faculty of Lycoming College in partial fulfillment of the requirements for graduation with Departmental Honors in Chemistry

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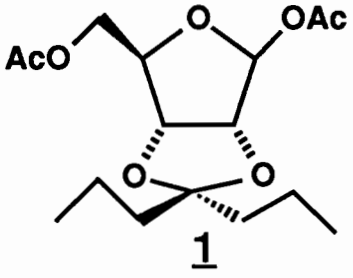
Abstract

Research has been conducted to examine the synthesis of unnatural, expensive L-ribose from natural, inexpensive D-ribose. Steps towards the synthesis of L-ribose have shown some success. We have been able to convert D-ribose to the acylated, C_2, C_3 protected version of D-ribose (1). Siloxymethylation of this molecule using dicobalt octacarbonyl[1], has produced 17% of the desired diastereomer. An important reaction, involving an H_2-activated iridium complex, was discovered during our research that enabled us to isomerize, hydrolyze, and acylate (2) in one reaction vessel. This reaction yielded 80% desired product, but only on small scale reactions (all large scale reactions failed). This was important to our research because we were then able to deprotect and re-protect in the same reaction vessel. Other methods have also been examined for the enantioconversion. One example begins with β-D-ribofuranose 1,2,3,5-tetraacetate, available in one-step from D-ribose. This route was also hindered by the siloxymethylation reaction. Results indicate a 37% yield mixture of diastereomers, however, due to incomplete chromatographic separation only 16% of the desired diastereomer was recovered.



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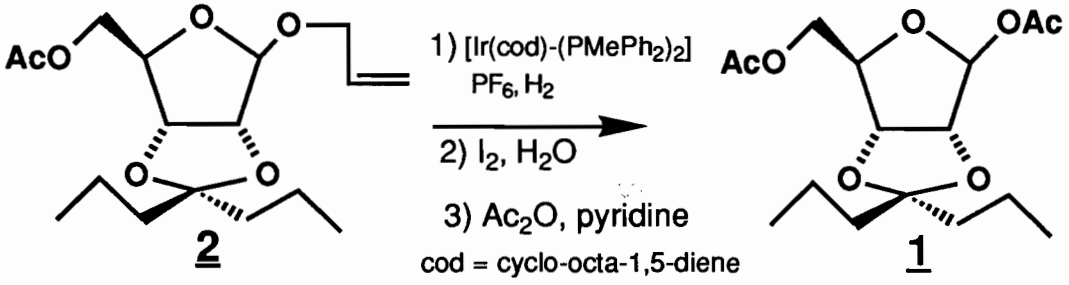


2 1

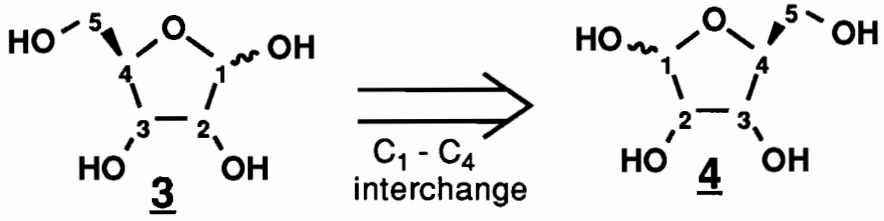
Introduction

Nature and the chemical industry have provided the organic chemist with a wide variety of readily available chiral starting materials.[2] Carbohydrates make up a large portion of these compounds. Carbohydrates have proven especially useful in the construction of oxygenated natural products in an enantiospecific manner. The following show the advantages of using carbohydrates:

1) they possess a variety of stereochemical arrangements;
2) many chain lengths are available, from one to seven chiral centers being possible for monosaccharides;
3) the tendency for five and six carbon carbohydrates to exist as hemiacetals and hemiketals allows for exclusive manipulation of both the carbonyl moiety and the hydroxyl groups contained in the sugar;
4) most carbohydrates are inexpensive.

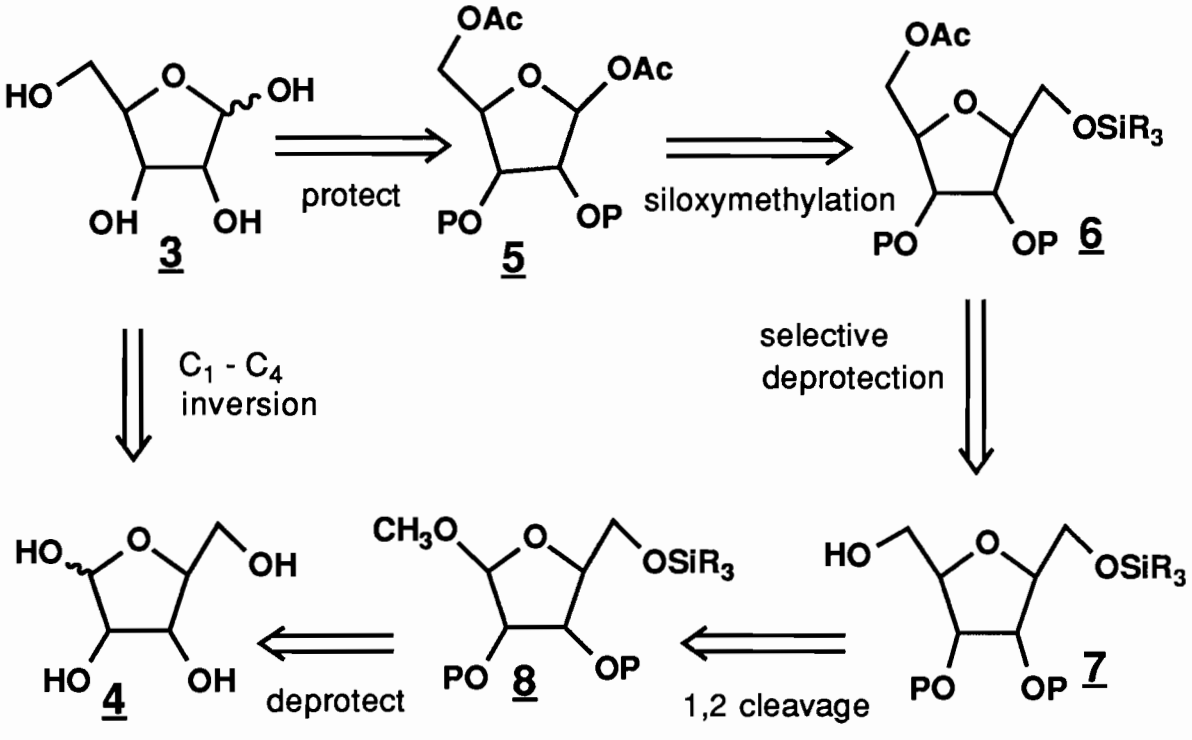
When developing highly oxygenated natural products, such as carbohydrates, problems of chemoselectivity confront the synthetic chemist. Transformations on certain functional sites must be carried out in the presence of other functionality. In some instances, specific conversions may be carried out using reagents that react with certain functionality, while ignoring other functional groups present in the molecule.[3] In other cases, protecting groups must be utilized to preserve the functionality. A protecting group must be able to withstand conditions for protection, deprotection, and reaction of other functionality present. With these constraints it is obvious that a variety of protecting groups must be available.

Mindful of the above principles, research has been undertaken toward the complete enantioconversion of natural, inexpensive D-ribose (3) to unnatural, expensive L-ribose (4). This transformation involves a C_1 to C_4 interconversion:



This transformation should be achieved via a series of protections, deprotections, an hydroxymethylation reaction, and a dehydroxymethylation reaction (Scheme 1).

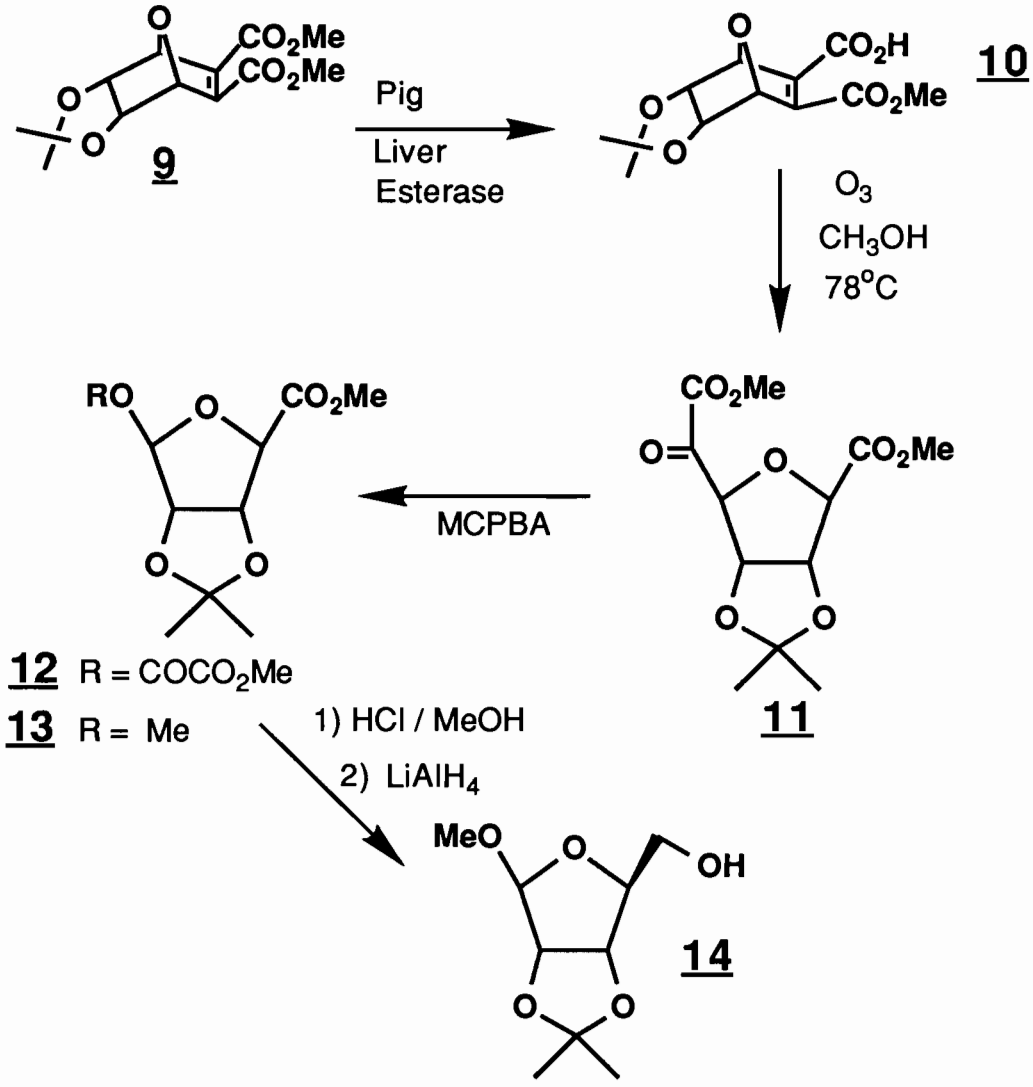
Scheme 1



Literature Review

While the complete enantioconversion from D-ribose to L-ribose has never been achieved, the synthesis of L-ribose from other compounds has been accomplished in other laboratories. Masaji Ohno describes the synthesis of methyl β-L-riboside (Scheme 2), a protected version of L-ribose.[4] His synthesis involves the use of pig liver esterase to enantioselectively hydrolyze a readily available diester (9) to form the corresponding half-ester (10). This ester is then subjected to ozonolysis in methanol at -78°C to yield an α-keto ester (11). This step is equally as important as the enzymatic step, since (11) has ideally differentiated the two functional groups at the 1- and 4- positions. The α-keto ester is then subjected to Baeyer-Villiger oxidation with *m*-chloroperbenzoic acid (MCPBA) to produce the oxalate derivative (12). This derivative is treated with dry HCl/methanol at room temperature to yield (13). The methanolysis product gets reduced with $LiAlH_4$ to afford the desired product, methyl L-riboside (14). β-D-ribofuranoside was also produced along with methyl L-riboside. An 88.5% yield of the L-ribose derivative and an 11.5% yield of methyl β-D-ribofuranoside were recovered.

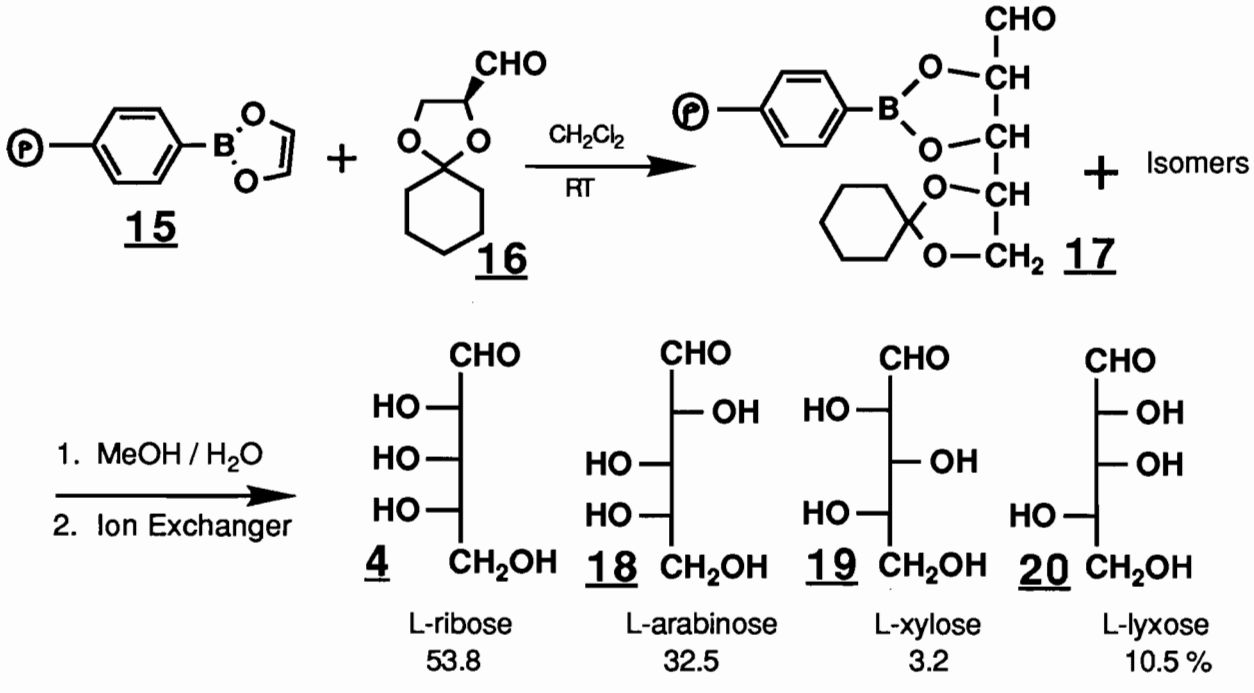
Scheme 2



Research conducted by Gunter Wulff (Scheme 3) provides a general methodology for lengthening sugar chains by two carbon atoms, thus producing a novel route for the production of rare sugars. Specifically, Wulff was able to synthesize L-ribose by reacting 2,3-O-cyclohexylidene-L-glyceraldehyde (16) with polymer bound 1,2,3-dioxaborole (15) in dichloromethane at room temperature. This reaction gave a mixture of pentoses, of which 54% enantiomerically pure L-ribose was produced. The addition products were isolated by treating the polymer with methanol/H_2O. The

eluted 4,5-isopropylidene pentoses were then deprotected by treatment with an acidic ion exchange to yield the mixture of pentoses (4), (18), (19) and (20).[5]

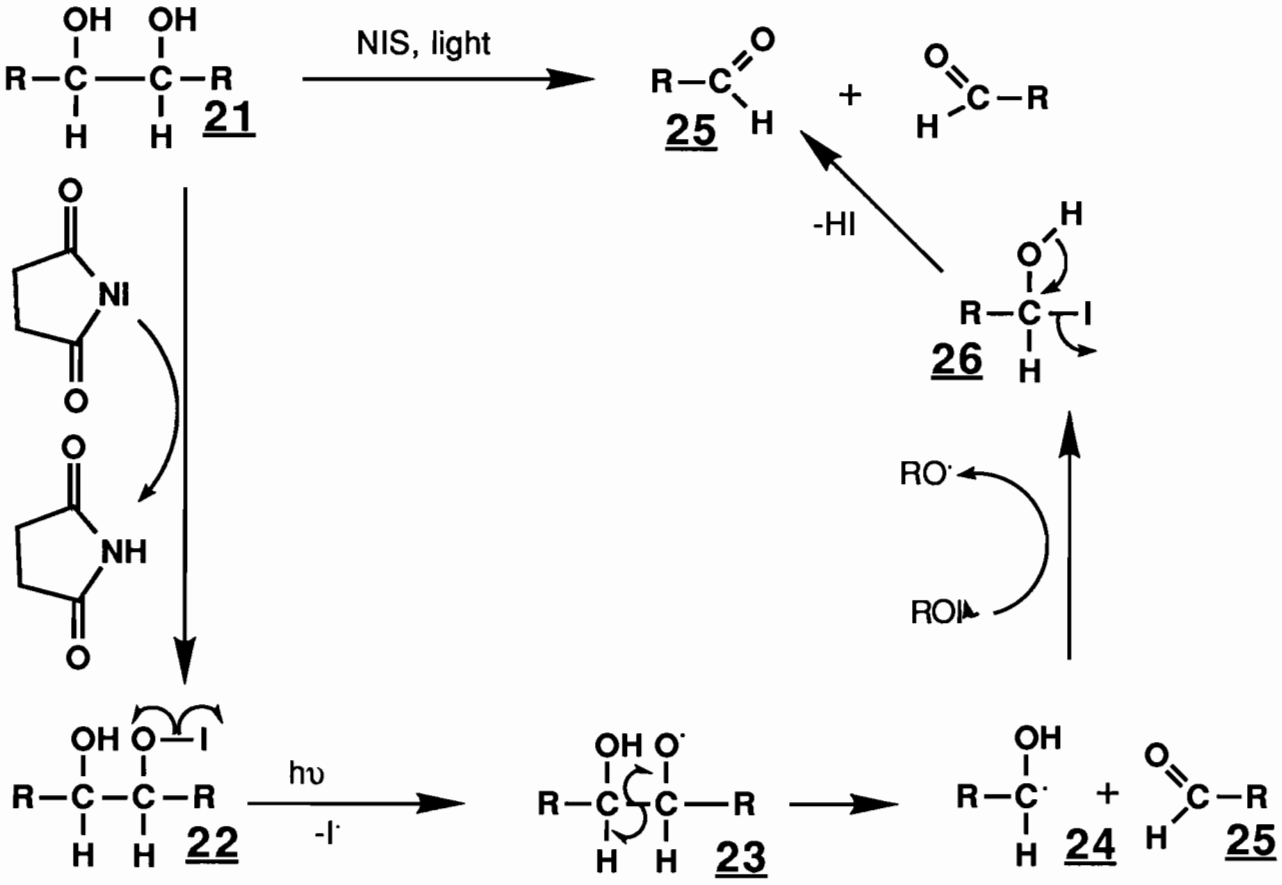
Scheme 3



In both of these cases, the L-ribose (or L-ribose derivative produced) is contaminated by other carbohydrates. This research attempts to produce L-ribose enantiospecifically from D-ribose by an interchange of the C_1 and C_4 substituents.

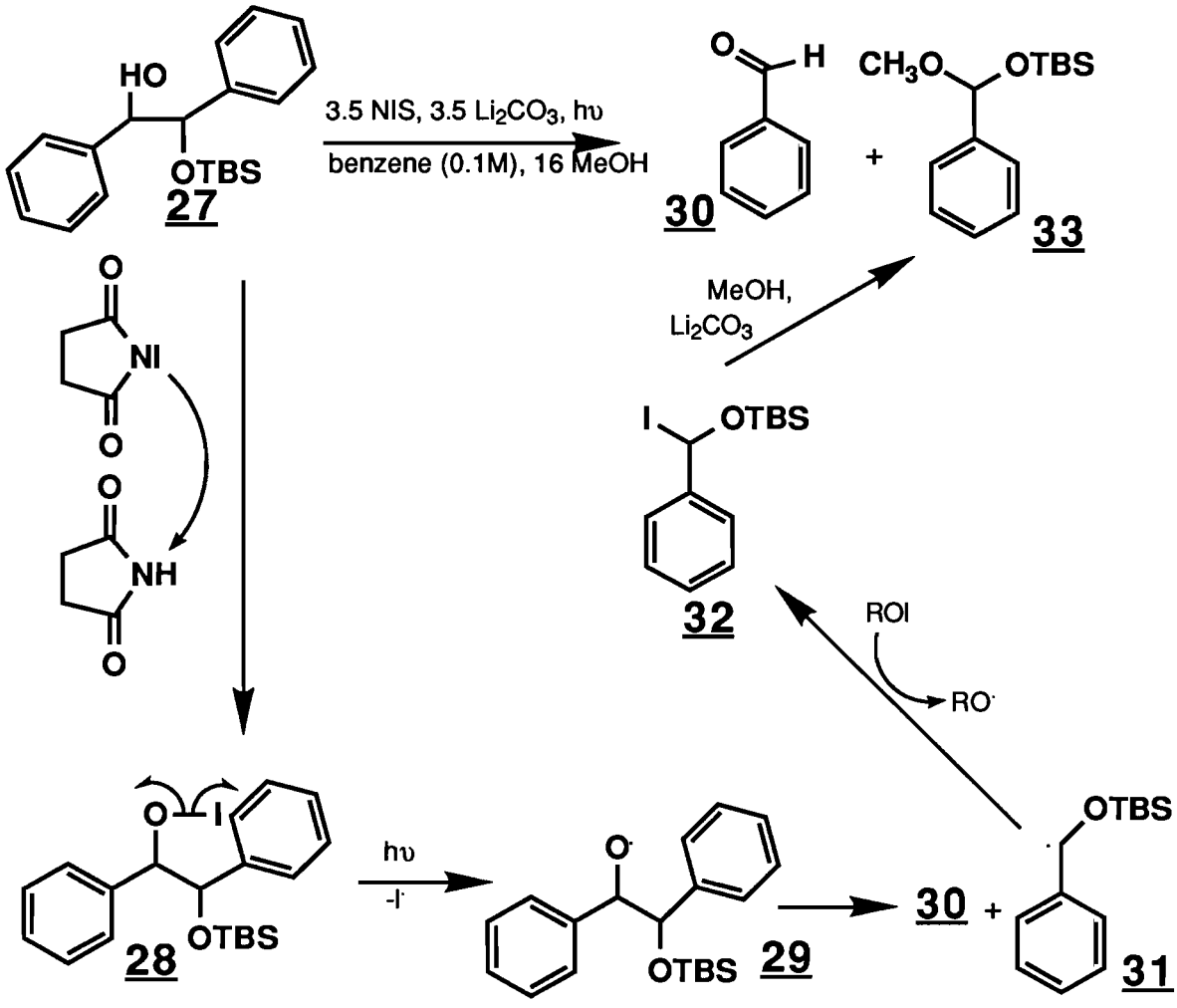
One of the key steps in the enantioconversion of D-ribose is the removal of a hydroxymethylene group. Research conducted by Dr. Thomas Beebe and Dr. Chriss McDonald has led up to this type of hydroxymethylene removal. Beebe's research involves the cleavage of 1,2-diols.[6] He proposed the following mechanism (Scheme 4), where the key step is the homolytic cleavage of the carbon-carbon bond which contains the hydroxyl groups. The corresponding aldehydes (25) were produced as a result of this cleavage.

Scheme 4

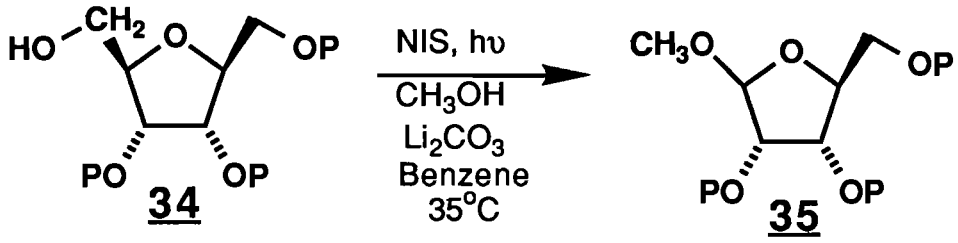


McDonald's plan (Scheme 5) was to produce an alkoxy radical (29) from the alcohol (27) which had a radical stabilizing moiety on the adjacent carbon atom (an alkoxy moiety). Hopefully, homolytic cleavage would occur to produce a single carbonyl (30) and an oxygen-stabilized carbon radical (31). Iodination of the radical by N-iodosuccinimide, I_2, or an hypoiodite would produce the corresponding, electrophilic α-iodoether (32). This α-iodoether would eventually form the mixed acetal (33) via nucleophilic displacement with methanol. Base was utilized to neutralize the strong acid produced.

Scheme 5



As can be seen, C_4 and C_5 of the tetrahydrofuran are in essence a monoprotected vicinal diol unit. The following transformation should be possible:

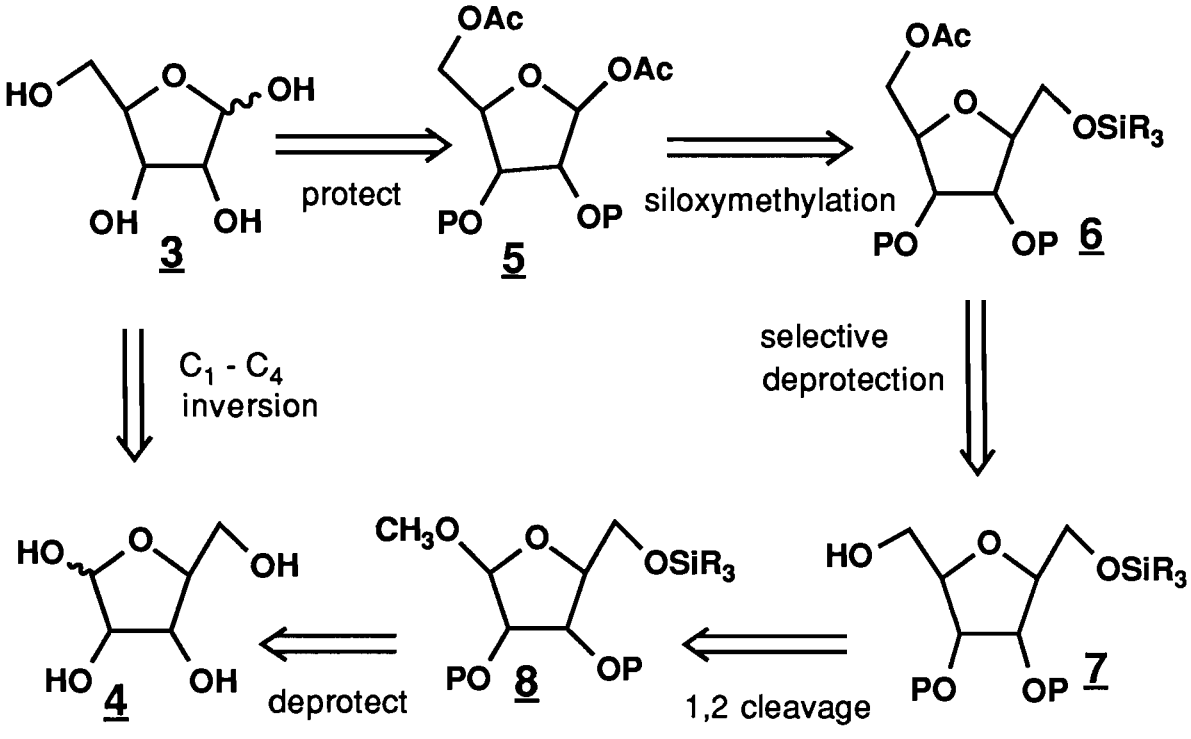


This reaction, would be a key step in the synthesis of L-ribose from D-ribose because it generates the requisite carbon framework.

Theory

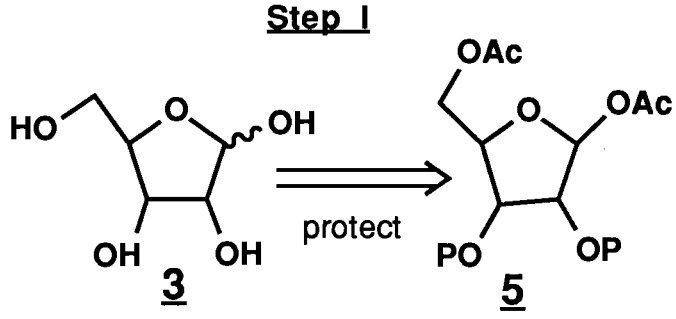
This research attempts to optimize the conversion of D-ribose to L-ribose. Optimization involves a decrease in the number of reactions from starting material to pure, enantiospecific product and an increase in the yield of product. The following reaction sequence (Scheme 1), which will be shown again for convenience, provides a general route for the synthesis:

Scheme 1

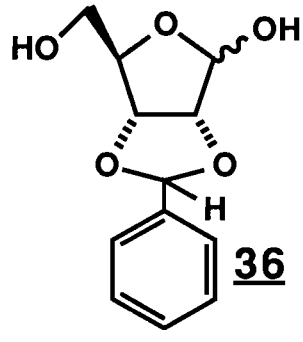


The first reaction step involves the protection of the C_2 and C_3 positions, as well as, acylation of the C_1 and C_5 positions (5). The resulting molecule is amenable to siloxymethylation, which adds the methylene group, a key step in the reaction sequence (6). Selective deprotection provides the monoprotected vicinal diol unit (7). This molecule, then, is susceptible to the NIS-mediated cleavage reaction. The resulting compound (8) can be hydrolyzed to produce (4).

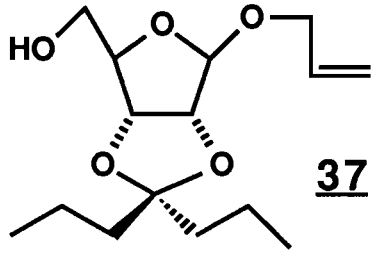
Results and Discussion



Our first experiments centered on the treatment of D-ribose with benzaldehyde under acid catalysis, to selectively protect the C_2 and C_3 positions, thus yielding 2,3-O-benzylidene β–D-ribofuranose (36).

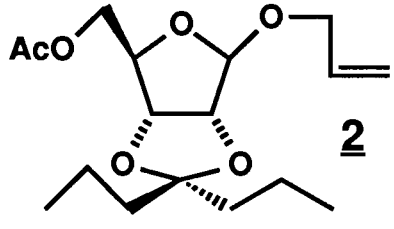


Further acylation yielded the general product noted above (5). The percent yield however, was disappointing. Only 39.4% of the 2,3-O-benzylidene β–D-ribofuranose was produced. One drawback of using a benzylidene acetal is that an uncontrolled chiral center is produced. We then decided to treat D-ribose with a symmetrically substituted ketone under acid catalysis, such as 4-heptanone, to protect the C_2 and C_3 positions. Results of this research were disappointing. Only 11.5% pure product was isolated. We then decided to selectively protect the C_1 and C_2, C_3 positions by treating D-ribose with allyl alcohol and 4-heptanone, respectively, under acid catalysis. Two equivalents of water were produced along with the protected furanose derivative (37).



37

Previous research by Dr. Chriss McDonald indicated that this type of transformation was facile.[7] We were pleased with a 56% yield, considering the the failure of the previous reactions. Further acylation (Ac_2O, pyridine, 0°C -> RT), yielded 92% of (2).

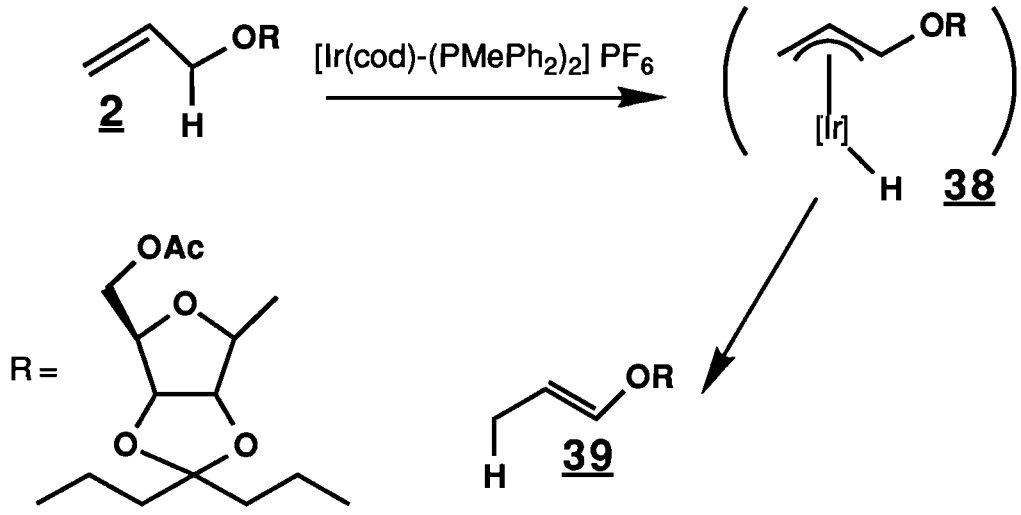


2

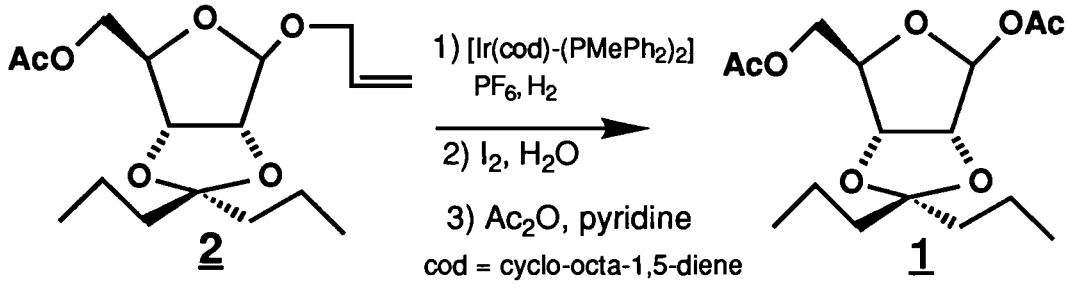
Isomerization must then be carried out to allow the C_1 position to be hydrolyzed and further acylated. Two reactions were utilized

for the isomerization step. Denise Baudry has developed a reaction, whereby, allyl alkyl ethers (2) are isomerized by H_2-activated [Ir(cyclo-octa-1,5-diene)$(PMePh_2)_2$] PF_6 in tetrahydrofuran to the corresponding trans-propenyl ethers (39).[8] The reaction (Scheme 6) is thought to proceed as follows:

Scheme 6

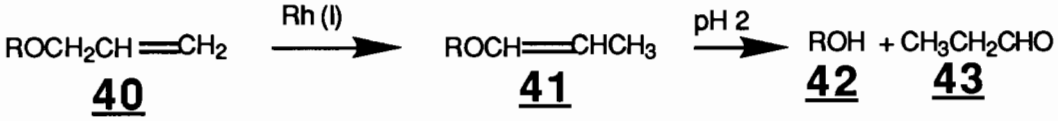


Using Baudry's reaction we were able to isomerize our molecule with success only on small scale reactions. We obtained an 80% yield of pure product. All large scale reactions failed with this technique. Interestingly, we discovered that with this reaction step we are able to isomerize, hydrolyze, and acylate our molecule in the same reaction vessel (however, only on small scale reactions - 80%).



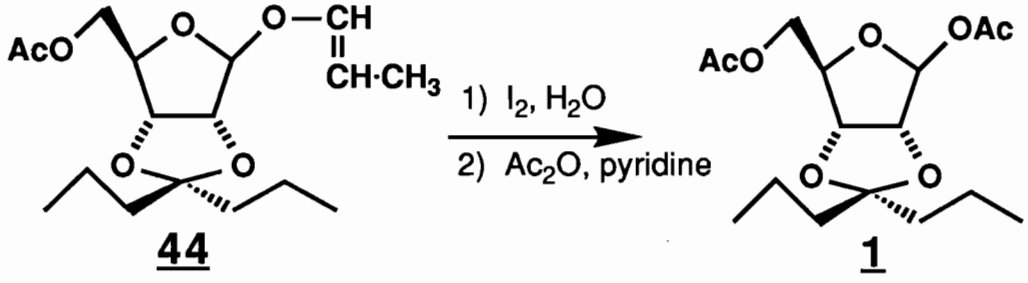
E. J. Corey has shown that rhodium (I) complexes such as $RhCl(PPh_3)_3$ catalyze the isomerization of allyl ethers (40) to 1-propenyl ethers (41) under neutral protic conditions. Hydrolysis of the enol ethers occurs rapidly at pH 2 to form the free alcohols (42) (Scheme 7).[9]

Scheme 7



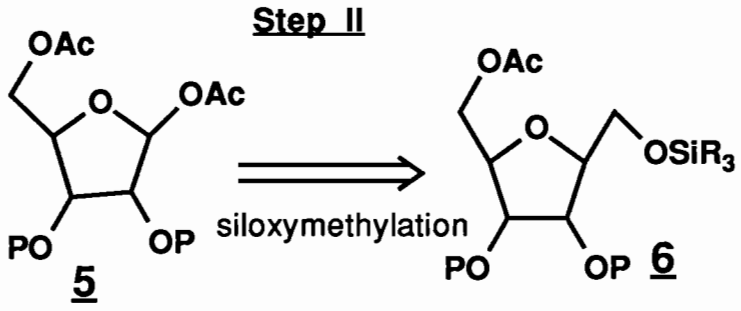
40 **41** **42** **43**

Corey's reaction proved to be very successful. We isolated 81% of the isomer (44). Further hydrolysis with I_2 and H_2O and acylation (Ac_2O, pyridine), yielded (1).



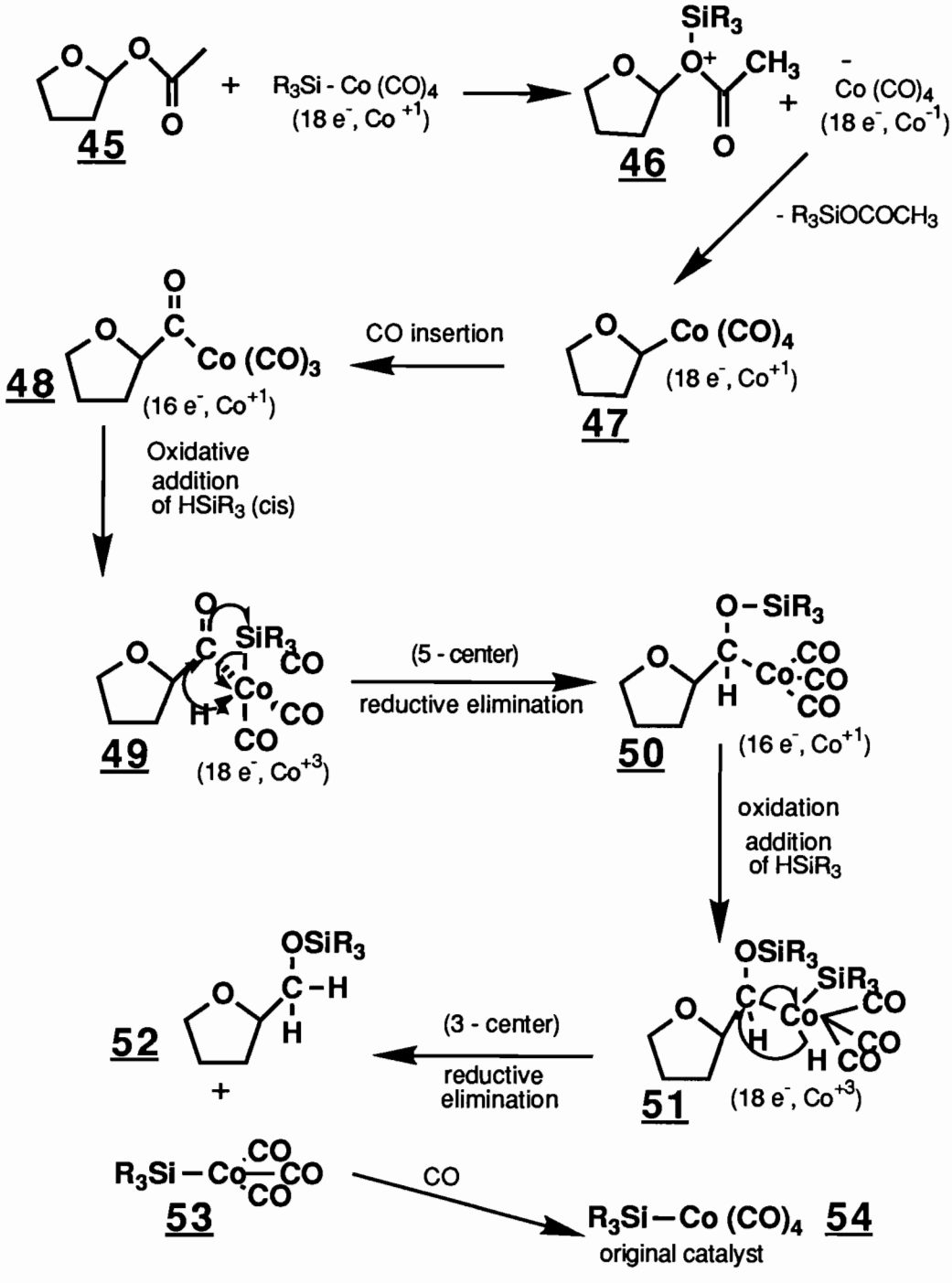
44 **1**

Future research is aimed at finding a solvent, or solvent mixture that enables the isomerization, hydrolysis, and acylation to be carried out in one reaction vessel. Using THF as solvent doesn't allow the isomerization as in the "Ir"-catalyzed reaction.
At this point, we are isolating the isomerized product and then hydrolyzing and acylating.

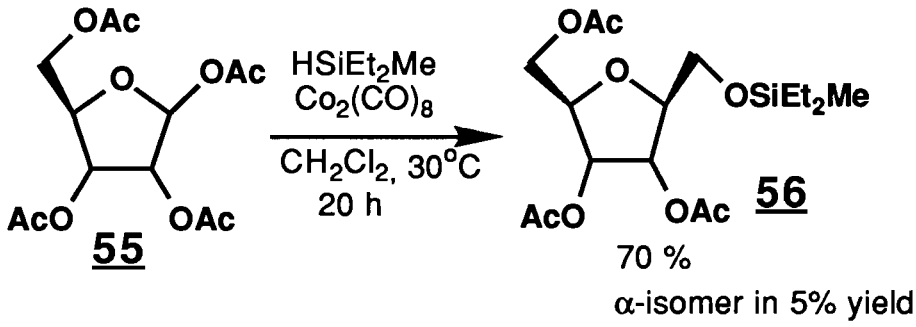


Chatani has reported a novel route for siloxymethylation of glycosides by a $HSiR_3/CO/Co_2(CO)_8$ reaction[1]; the acetoxy group at the anomeric center of glycosides can be replaced with a siloxymethyl group by the preceding reaction. The mechanism Chatani proposes is vague and not precise. Therefore, we propose the following complete mechanism (Scheme 8):

Scheme 8



Chatani reports the following transformation:



As can be seen, this molecule is very similar to ours (33). We hoped that this reaction would be facile with our molecule as well. It turns out that it wasn't. We tried a variety of reaction conditions and techniques, but none seemed to work as efficiently as Chatani noted. We isolated what we thought was pure product and recorded a yield of 17.0%. We were disappointed with our yield, so we focused on the literature reaction noted above, β–D-ribofuranose 1,2,3,5-tetraacetate to 2,5-anhydro-1-O-(diethylmethylsilyl)-D-allitol triacetate. Our best yield was 37% as a mixture of diastereomers, with only 16% being isolated as pure product, due to incomplete chromatographic separation. We were displeased with our results, especially because we weren't able to perform the literature reaction. The problem, we think, lies in the inability to monitor the amount of carbon monoxide in the reaction vessel and pressure of the reaction. Our facilities don't offer the instrumentation needed to monitor these conditions. The following is a list of reaction conditions and techniques that were used to attempt the siloxymethylation.

1) $HSiEt_2Me$, CH_2Cl_2, $Co_2(CO)_8$
   25°C, under CO atmosphere (slight depression in bubbler)
   heated to reflux after 27 hrs. --- 0.0%

2) $HSiEt_2Me$, CH_3CCl_3, $Co_2(CO)_8$
   50°C, under CO pressure (with bubbler running)
   --- 15.3%

3) $HSiEt_2Me$, CH_3CCl_3, $Co_2(CO)_8$

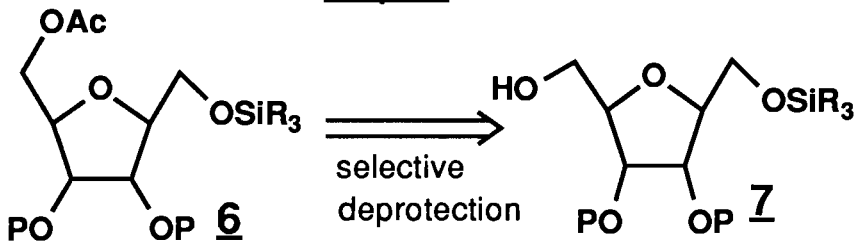
50°C, CO via gas dispersion tube
--- 6.98%

4) $HSiEt_2Me$, CH_3CCl_3, $Co_2(CO)_8$
50°C, CO only added to activate catalyst
--- 0.0%

5) $HSiEt_2Me$, CH_3CCl_3, $Co_2(CO)_8$
CO via balloon (increased pressure)
reaction heated to 50°C after 3 hrs. --- 17.0%

6) $HSiEt_2Me$, CH_3CCl_3, $Co_2(CO)_8$
CO via balloon (system was purged with CO to activate catalyst, and then CO apparatus was removed)
50°C, dark --- 37% (mixture), 16% (pure)

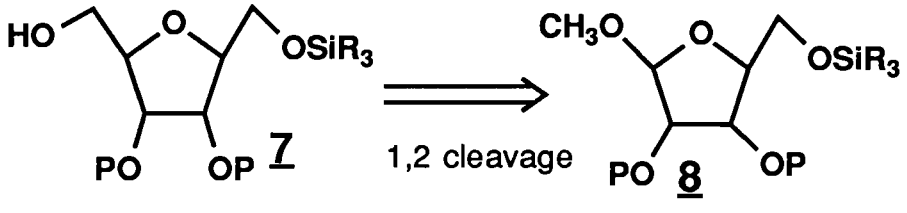
Step III



Simple, standard $LiAlH_4$ reduction should facilitate this conversion.

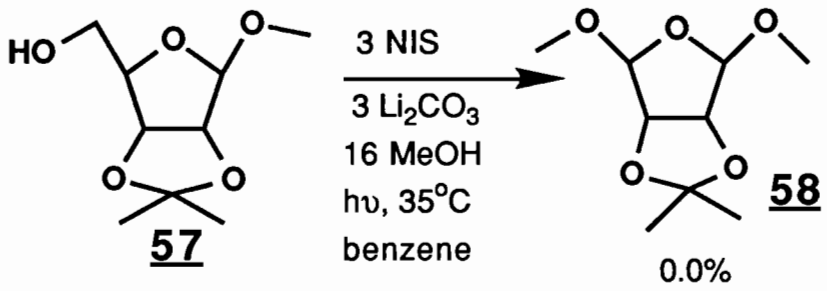
Proposed

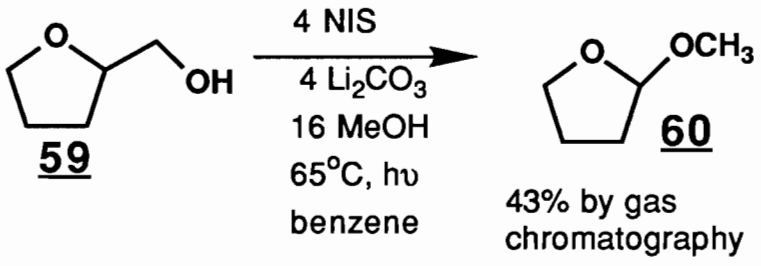
Step IV



Hopefully, this step will be amenable to our NIS-mediated 1,2-monoprotected diol cleavage reaction. Although no research has

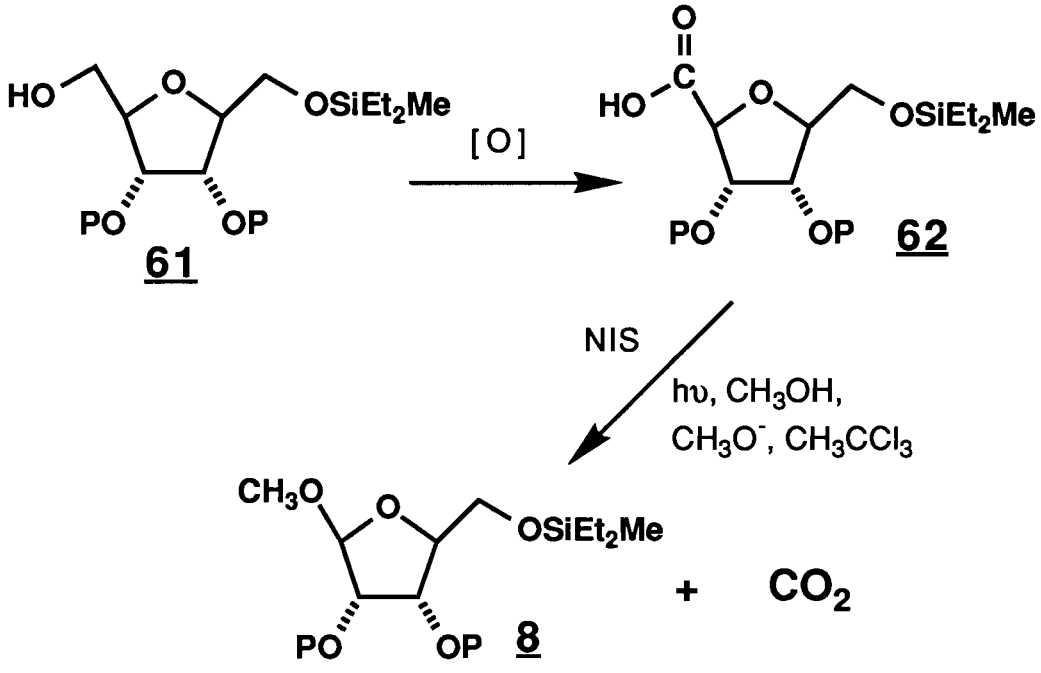
been conducted on this specific molecule, research has been conducted on similar molecules (57, 59).



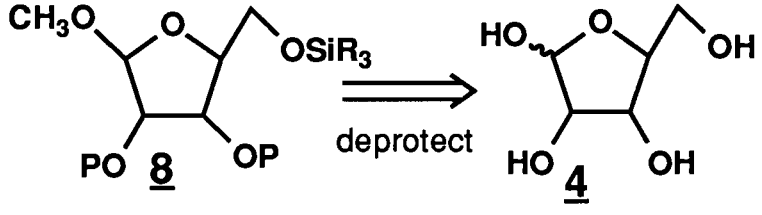


In the event that our 1,2-monoprotected diol cleavage is unsuccessful, we could oxidize the alcohol to the corresponding carboxylic acid and then conduct an N-iodosuccinimide-mediated oxidative decarboxylation (Scheme 9) to produce (8).[10]

Scheme 9



Step V

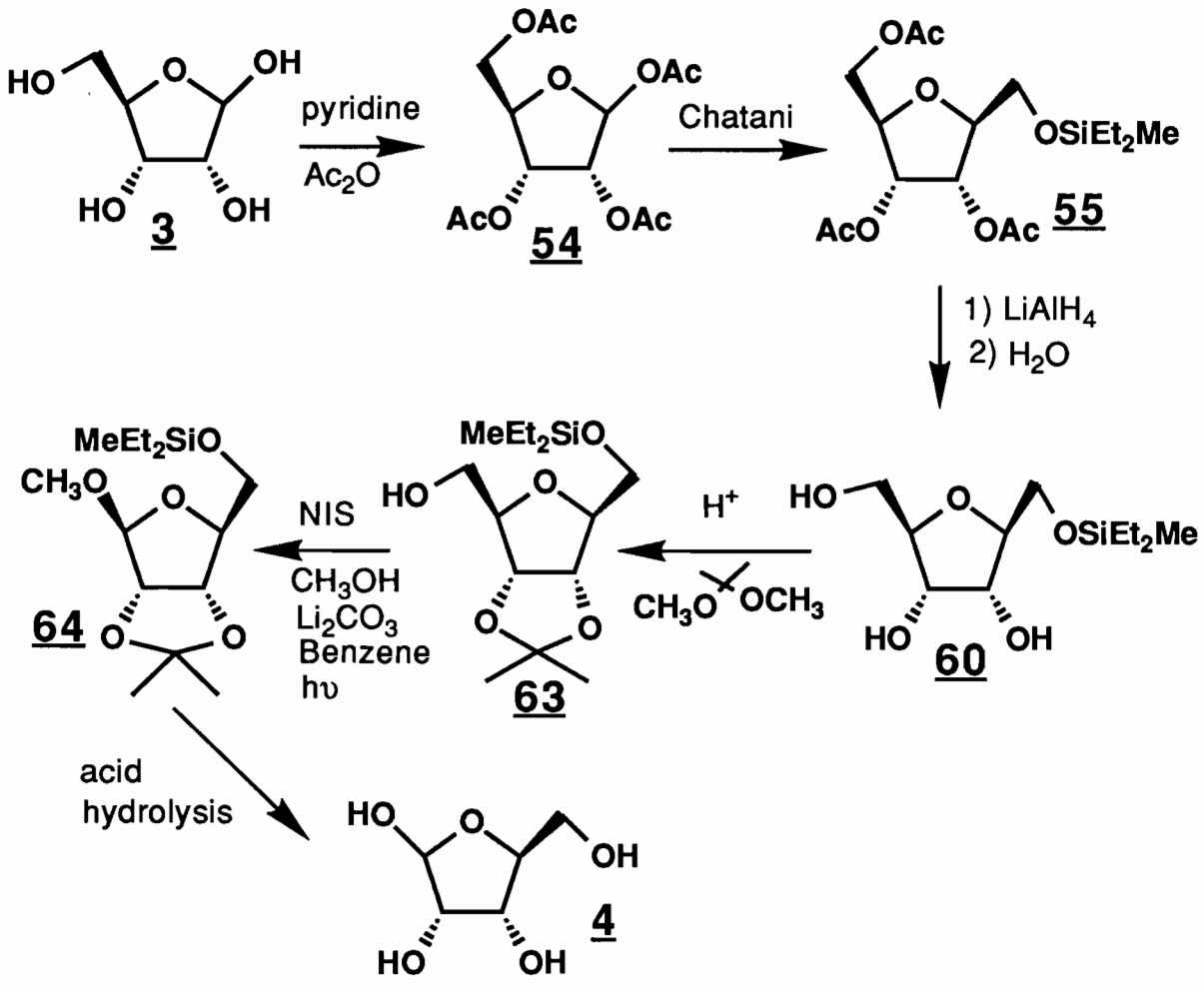


Acid hydrolysis should yield L-ribose at this point. The L-ribose could be potentially hard to isolate due to its high water solubility. If this procedure fails, we will simply leave the molecule in a protected state, as Ohno has done (see page 3).

Future research also involves alternate pathways for the enantioconversion of D-ribose to L-ribose. We are now researching a synthetic sequence that begins with β–D-ribofuranose 1,2,3,5-tetraacetate, one-step from D-ribose (acylation). Note that this

molecule is one Chatani lists in his research (see page 14). The proposed synthesis plan (Scheme 10) follows:

Scheme 10



Conclusions

Although we have not completed the total synthesis of L-ribose, we have made progress in determining a number of possible routes to its synthesis, and have made progress in these routes. We have developed a reaction step that can isomerize, hydrolyze, and acylate in one reaction vessel. This step is noteworthy because we don't have to isolate the isomerized product before continuing on

(cuts down the number of individual reactions). We hope now to find a solvent that will enable us to perform the isomerization with the rhodium-catalyzed reaction, and also the proceeding reactions.

Experimental Section

General

Thin-layer chromatography was performed using silica gel plates (purchased from Kodak and Analtech) and mixtures of ethyl acetate and hexane. Infrared spectra were taken with a Mattson Polaris, and NMR spectra were taken with a varian EM-360L spectrometer. Melting points were determined with a Thomas Hoover Capillary Melting Point Apparatus. Column chromatography was conducted using 70-270 mesh, 60A silica gel as supplied by Aldrich. Dichloromethane was distilled from calcium hydride, tetrahydrofuran was distilled from sodium benzophenone ketyl, and all other solvents were distilled under a nitrogen atmosphere and dried over 4A molecular sieves. All other reagents were used without purification as supplied by Aldrich.

2,3-O-benzylidene β-D-ribofuranose

D-ribose (5.00 g, 33.3 mmol), zinc chloride (2.50 g), glacial acetic acid (2 mL), and benzaldehyde (30 mL) were added to a round bottom flask equipped with a stir bar. The reaction was stirred vigorously in an ice bath at 0°C and let warm to room temperature. The reaction was monitored by thin layer chromatography (TLC) using 80% ethyl acetate (EtOAc)/hexane. The reaction was worked up by adding the mixture to ice water. The chloride precipitate was removed by suction filtration. The resulting mixture was extracted three times with dichloromethane. The organic layer was dried over sodium sulfate. The organic layer was then placed under reduced pressure to remove solvent. Column chromatography was set up using 50% EtOAc/hexane. Pure product was collected in fractions #16-34. These fractions were collected and placed under reduced pressure to remove solvent. The product yielded 2.93 g (13.12 mmol, 39.4%) as a white solid. 1 H-NMR delta 2.0 (2H, s), 3.8 (2H, s), 4.7 (3H, b), 5.5 (1H, s), 5.8 and 6.1 (1H, dd), 7.5 (5H, s).

2,3-O-(4)-Heptylidene-D-ribofuranose

D-ribose (0.50 g), zinc chloride (0.25 g), glacial acetic acid (0.20 mL), and 4-heptanone (3.0 mL) were added to a round bottom flask equipped with a stir bar. The reaction was stirred vigorously in an ice/salt bath at 0°C, and allowed to warm to room temperature. The reaction was monitored by TLC using 50% EtOAc/hexane as solvent. After reacting for 17.75 hrs., the reaction was worked up by filtering the reaction solution through a sintered glass funnel into a solution of saturated sodium bicarbonate and ice water with stirring (wash with dichloromethane). This filtrate was extracted five times with dichloromethane, then solvent was removed under reduced pressure. Column chromatography was set up using 33% EtOAc/hexane. Thin layer chromatography indicated fractions #15-21 contained desired product. These fractions were combined and placed under reduced pressure to remove solvent, to yield a final pure product. The product yielded 79.6 mg (0.323 mmol, 10.0%) as white crystals. 1 H-NMR delta 0.8-1.3 (6 H, s), 1.4-1.9 (8 H, b), 3.7-4.0 (2 H, b), 4.2-4.4 (2 H, b), 4.5-5.0 (3 H, b).

2,3-O-(4)-Heptylidene-D-ribofuranose

D-ribose (1.00 g, 6.66 mmol), 4-heptanone (15.2 g, 20.0 eqs.), copper sulfate (3.72 g, 3.50 eqs.), 1 drop of sulfuric acid, and tetrahydrofuran (22.2 mL, 0.3 M) were added to a round bottom flask equipped with a stir bar and condenser. The reaction was refluxed for 4 hrs. at 60°C. After this, the reaction was cooled to room temperature, suction filtered at water aspirator pressure through sand into a solution of saturated sodium bicarbonate with stirring. This solution was then transferred to a separatory funnel, water was added, extracted twice with ether, and placed under reduced pressure to remove the ether. The resulting solution was then distilled at vacuum pressure to remove 4-Heptanone. A crude NMR was taken to verify product. The NMR indicated the formation of pure product. The product yielded 189.4 mg (0.766 mmol, 11.5%) as white crystals. 1 H-NMR delta 0.6-1.2 (6 H, b), 1.3-1.8 (8 H, b), 3.2-3.8 (2 H, b), 4.1-4.8 (5 H, b), 5.3-5.4 (1 H, s).

2-Propenyl-2,3-O-(4)-heptylidene-β-D-ribofuranoside

D-ribose (1.00 g, 6.66 mmol), allyl alcohol (3.90 g, 10.0 eq.), 4-heptanone (10 mL), $CuSO_4$ (5.3 g, 5.0 eq.), THF (22.2 mL, 0.3 M), and

3 drops of H_2SO_4 were added to a round bottom flask equipped with a stir bar and condenser. The reaction was run at reflux temperature. The reaction was monitored by TLC using 15% EtOAc/hexane as solvent. After reacting for 4 hrs., the solution was worked up by filtering the reaction solution through a sintered glass funnel with sand into a solution of saturated sodium bicarbonate with stirring. This solution was then extracted three times with ether. The organic layers were combined and placed under reduced pressure to remove solvent. Column chromatography was set up using 12% EtOAc/hexane as solvent, 19/22 glassware was employed, and 20-mL fractions were collected. Thin layer chromatography indicated that fractions #10-20 contained desired product. These fractions were combined and placed under reduced pressure to remove solvent, to yield a final pure product. The product yielded 0.64 g (2.24 mmol, 33.6%) as a yellow oil. 1 H-NMR delta 0.5-1.0 (6 H, b), 1.0-1.6 (8 H, b), 2.9-3.6 (1 H, b), 3.8-4.3 (3 H, m), 4.4-4.7 (2 H, m), 4.9 (1 H, s), 5.1-5.3 (2 H, dd), 5.5-5.9 (1 H, b).

2-Propenyl-2,3-O-(4)-heptylidene-β-D-ribofuranoside

D-ribose (8.00 g, 53.3 mmol), allyl alcohol (80 mL), 4-heptanone (40 mL), $CuSO_4$ (31.9 g, 3.75 eq.), THF (80 mL), and 16 drops of H_2SO_4 were added to a sufficient round bottom flask equipped with a stir bar and condenser. The reaction was run at reflux temperature. The reaction was monitored by TLC using 15% EtOAc/hexane as solvent. After reacting for 4 hrs., the reaction was worked up as the preceding reaction. Column chromatography was set up using 12% EtOAc/hexane as solvent, 24/40 glassware was employed, and 45-mL fractions were collected. Thin layer chromatography indicated that fractions #3-15 contained desired product. These fractions were combined and placed under reduced pressure to remove solvent, to yield a final pure product. The product yielded 8.52 g (29.65 mmol, 55.6%) as a straw brown oil. 1 H-NMR delta 0.7-1.0 (6 H, b), 1.2-1.5 (8 H, b), 3.3-3.6 (1 H, b), 3.9-4.2 (3 H, m), 4.5-4.8 (2 H, dd), 5.0 (1 H, s), 5.2-5.4 (2 H, b), 5.5-6.0 (1 H, b).

1,5-O-Acetyl-2,3-O-(4)-heptylidene β-D-ribofuranose

2,3-O-(4)-Heptylidene-D-ribofuranose (1.39 g, 5.62 mmol), acetic anhydride (2.12 mL, 4.0 eqs.), and pyridine (14.05 mL, 0.4 M) were added to a round bottom flask equipped with a stir bar. Acetic

anhydride was added last to the reaction flask. The reaction was stirred vigorously in an ice/salt bath at 0°C, and allowed to warm to room temperature. The reaction was monitored by TLC using 33% EtOAc/hexane as solvent. After reacting for 19 hrs., the reaction was worked up by adding the reaction mixture to a solution of saturated sodium bicarbonate with ice water. This mixture was then transferred to a separatory funnel, and extracted four times with ether and placed under reduced pressure to remove solvent. Column chromatography was set up using 17% EtOAc/hexane as solvent. Thin layer chromatography indicated fractions #5-11 contained desired product. These fractions were combined and placed under reduced pressure to remove solvent to yield a final pure product. The product yielded 1.35 g (4.21 mmol, 74.8%) as white crystals. 1 H-NMR delta 0.5-0.8 (6 H, s), 0.9-1.4 (8 H, b), 1.7-1.9 (6 H, s), 3.7-3.9 (2 H, m), 4.1-4.6 (3 H, m), 6.0 (1 H, s).

2-Propenyl 5-O-acetyl-2,3-O-(4)-heptylidene-β-D-ribofuranoside

2-Propenyl 2,3-O-(4)-heptylidene-β-D-ribofuranoside (7.83 g, 27.24 mmol), acetic anhydride (7.73 mL, 3.0 eq.), and pyridine (45.4 mL, 0.6 M) were added to a round bottom flask equipped with a stir bar. Acetic anhydride was added last to the reaction flask. The reaction was started at 0°C, and allowed to warm to room temperature. The reaction was monitored by TLC using 20% EtOAc/hexane as solvent. After reacting for 21.5 hrs., TLC indicated the reaction had gone to completion. The solution was worked up by pouring the reaction solution into a solution of saturated sodium bicarbonate and ice water with stirring. This solution was stirred vigorously, transferred to a separatory funnel, and extracted four times with ether. The resulting organic mixture was placed under reduced pressure to remove solvent, and vacuum aspirated to remove solvent. Column chromatography was set up using 2% EtOAc/hexane as solvent, 24/40 glassware was employed, and 40-mL fractions were collected. Thin layer chromatography indicated fractions #4-19 contained desired product. These fractions were combined and placed under reduced pressure to remove solvent, to yield a final pure product. The product yielded 8.38 g (25.44 mmol, 93.4%) as a colorless oil. 1 H-NMR delta 0.7-1.1 (6 H, t), 1.4-1.6 (8 H, b), 2.0-2.1 (3 H, s), 4.0-4.3 (3 H, m), 4.7-4.9 (2 H, s), 5.1-5.2 (1 H, s), 5.2-5.5 (2 H, b), 5.6-6.0 (1 H, b).

2,3-O-(4)-Heptylidene-D-ribofuranose

2-Propenyl-2,3-O-(4)-heptylidene-β-D-ribofuranoside (186.2 mg, 0.651 mmol) was added first, to a 25 mL, two-necked round bottom flask equipped with a stir bar and a gas dispersion tube ,THF (6.51 mL, 0.1 M) was added next to the flask, [Ir(cod)-$(PMePh_2)_2$] PF_6 (1.10 mg, 0.002 eq.) was added last. After adding the catalyst, hydrogen gas was bubbled into the reaction flask until the solution changed colors from yellow to translucent (approximately 15 seconds). The reaction vessel was then purged with nitrogen for 30 seconds. The reaction had white chunks floating in the solution, so more hydrogen was added, then re-purged with nitrogen. The reaction was stirred at room temperature overnight. The reaction was monitored by TLC using 33% EtOAc/hexane as solvent. The reaction was also monitored using an I_2 chamber. After reacting for 23 hrs., 1 mL of 4 M acetic acid was added to the reaction. After reacting for another 30 minutes, the reaction solution was worked up by adding 5 mL of ether, mixing, collecting the organic layer, and removing solvent under reduced pressure. The NMR spectrum appeared similar to a spectrum run by Dr. McDonald in an analogous reaction. A percent yield was not determined

2,3-O-(4)-heptylidene-D-ribofuranose

2-Propenyl-2,3-O-(4)-heptylidene-β-D-ribofuranoside (208.5 mg, 0.726 mmol) was added first to a 25 mL round bottom flask equipped with a stir bar and a gas dispersion tube, THF (7.26 mL, 0.1 M) was added next (THF was distilled 5 min. prior to use), followed by the addition nitrogen, [Ir(cod)-$(PMePh_2)_2$] PF_6 (small chunk) was then added, and then hydrogen was added while also adding nitrogen (reaction color change from orange to translucent). The reaction was then purged with nitrogen for 15 seconds. The gas dispersion tube was then removed from the reaction flask, and the vessel was sealed up and let run overnight. After reacting for 22.5 hrs., the reaction solution was divided in two. To half of the solution was added 3.5 mL of 1 M H_2SO_4, and to the other half was added 3.5 mL of 0.5 M H_2SO_4. After reacting for 26 hrs., both reactions had formed some product, but no appreciable amount. Starting material remained in a large abundance. Both reactions were heated, the 1 M solution to 47°C, and the 0.5 M solution to 41°C. Both reaction mixtures were discarded.

1,5-O-Acetyl-2,3-O-(4)-heptylidene β-D-ribofuranoside

2-Propenyl-2,3-O-(4)-heptylidene-β-D-ribofuranoside (106.8 mg, 0.324 mmol) was added first to a 25 mL round bottom flask equipped with a stir bar and a gas dispersion tube, THF (3.24 mL, 0.1 M) was added next, followed by the addition of nitrogen, [Ir(cod)-$(PMePh_2)_2$] PF_6 (small chunk) was then added, and hydrogen was added while adding nitrogen, the flask was purged with nitrogen for 15 seconds, sealed up, and let run. The reaction was monitored by TLC using 5% EtOAc/hexane as solvent. After reacting for 3.5 hrs., 0.54 mL of pyridine and 0.184 mL of acetic anhydride (6.0 eqs.) were added to the reaction. After reacting for an additional 45 minutes, TLC indicated the desired product had been formed, and the reaction was worked up. The reaction solution was added to a solution of sodium bicarbonate and ice water with stirring, then transferred to a separatory funnel, extracted four times with ether, then placed under reduced pressure to remove solvent. Column chromatography was set up using 8% EtOAc/hexane as solvent, 14/20 glassware was employed, and 15-mL fractions were collected. Thin layer chromatography indicated that fraction #28 contained the desired product. This fraction was collected and placed under reduced pressure to remove solvent, to yield a final pure product. The product yielded 20.7 mg (0.062 mmol, 19.3%) as colorless oil. 1 H-NMR delta 0.7-1.0 (6 H, s), 1.3-1.6 (8 H, b), 2.0-2.1 (3 H, s), 3.3-3.7 (1 H, m), 4.1-4.5 (3 H, m), 4.7-4.8 (1 H, s), 5.4-5.6 (2 H, s).

trans-1-Propenyl 5-O-acetyl-2,3-(4)-heptylidene-β-D-ribofuranoside

2-Propenyl 5-O-acetyl-2,3-(4)-heptylidene-β-D-ribofuranoside (206.0 mg, 0.625 mmol), $RhCl(PPh_3)_3$ (39.87 mg), diazobicyclo [2.2.2.] octane (14.0 mg), and 10% aqueous ethanol were combined in a round bottom flask equipped with a stir bar and a condenser. The reaction was conducted at reflux temperature. The reaction was monitored by TLC using 10% EtOAc/hexane as solvent. The reaction was also monitored using an I_2 chamber. After reacting for 40 minutes, TLC and I_2 indicated that the reaction was complete. The reaction was worked up by adding water and extracting three times with hexane. The resulting organic mixture was then placed under reduced pressure to remove solvent, to yield a final pure product. An NMR was then taken, and verified the product. A percent yield was not determined. 1 H-NMR delta 0.7-1.0 (6 H, s), 1.3-1.7 (11 H,

m), 1.9-2.0 (3 H, s), 3.7-4.3 (4 H, m), 4.5-4.6 (2 H, d), 5.2 (1 H, s), 5.9-6.1 (1 H, m).

trans-1-Propenyl 5-O-acetyl-2,3-(4)-heptylidene-β-D-ribofuranoside

2-Propenyl 5-O-2,3-(4)-heptylidene-β-D-ribofuranoside (208.7 mg, 0.634 mmol), $RhCl(PPh_3)_3$ (40.44 mg), diazobicyclo [2.2.2.] octane (14.20 mg), water (0.05 mL, 4 eqs.), and THF (2.11 mL, 0.3 M) were added to a round bottom flask equipped with a stir bar and condenser. The reaction was conducted at reflux temperature. The reaction was monitored by TLC using 10% EtOAc/hexane as solvent. The reaction was also monitored using an I_2 chamber. Tetrahydrofuran was added to the reaction at different times, due to it's evaporation under reflux. During the reaction, THF dissolved part of the rubber septum, and TLC indicated that a lot of by-products had been produced. These by-products were probably due to the rubber septum. The I_2 indicated that some product had been formed, but not an appreciable amount. This reaction mixture was discarded.

trans-1-Propenyl 5-O-acetyl-2,3-(4)-heptylidene-β-D-ribofuranoside

2-Propenyl 5-O-acetyl-2,3-O-(4)-heptylidene-β-D-ribofuranoside (2.13 g, 6.45 mmol), $RhCl(PPh_3)_3$ (0.242 g), diazobicyclo [2.2.2.] octane (0.090 g), and 10% aqueous ethanol (21.5 mL, 0.3 M) were combined in a round bottom flask equipped with a stir bar and a condenser. The reaction was conducted at reflux temperature. The reaction was monitored by TLC using 10% EtOAc/hexane as solvent. The reaction was also monitored using an I_2 chamber. After reacting for 20 minutes, TLC and I_2 indicated that the reaction was complete. The reaction solution was filtered through silica gel and sand in a sintered glass funnel, and washed with hexane. This solution was worked up by adding water and extracting four times with hexane. The resulting organic mixture was then placed under reduced pressure to remove solvent, to yield a final pure product. A percent yield was not determined. 1 H-NMR delta 0.8-1.2 (6 H, s), 1.3-1.7 (11 H, m), 2.0-2.1 (3 H, s), 3.9-4.3 (4 H, m), 4.6-4.8 (2 H, d), 5.2-5.3 (1 H, s), 6.0-6.3 (1 H, b).

1,5-O-Acetyl-2,3-O-(4)-heptylidene-β-D-ribofuranoside

trans-1-Propenyl 5-O-acetyl-2,3-(4)-heptylidene-β-D-ribofuranoside (2.13 g, 6.45 mmol), I_2 (3.27 g, 2.00 eqs.), water (0.464 mL, 4.00 eqs.), and THF (21.5 mL, 0.3 M) were added to a round bottom flask equipped with a stir bar. The reaction was monitored by TLC using 10% EtOAc/hexane as solvent. After reacting for 25 minutes, TLC indicated that the corresponding alcohol was produced. At this point 10.75 mL of pyridine (0.6 M) and 3.95 mL of acetic anhydride (6.0 eqs.) were added to the reaction vessel. After reacting for 2 hrs., 1.22 mL of acetic anhydride (2.0 eqs.) was added to the reaction vessel. After reacting for another 4 hrs., TLC indicated that the reaction was complete. The reaction was worked up by dumping the reaction solution into a beaker of saturated sodium bicarbonate, ice water and sodium thiosulfate with stirring. This mixture was then transferred to a separatory funnel and extracted two times with ether. The resulting organic mixture was placed under reduced pressure to remove solvent. Column chromatography was set up using 8% EtOAc/hexane as solvent, 19/22 glassware was employed, and 20-mL fractions were collected. Thin layer chromatography indicated fractions #18-30 contained desired product. These fractions were combined and placed under reduced pressure to remove solvent, to yield a final pure product. The product yielded 1.74 g (5.22 mmol, 80.9%) as a light yellow syrup. 1 H-NMR delta 0.7-1.0 (6 H, s), 1.3-1.7 (8 H, b), 1.8-2.0 (6 H, s), 3.7-4.3 (3 H, m), 4.5-4.6 (2 H, s), 6.0 (1 H, s).

2,5-Anhydro-1-O-(diethylmethylsilyl)-3,4-O-(4-heptylidene)-6-O-acetyl-D-allitol

Dicobalt octacarbonyl (104.5 mg, 0.306 mmol) was added first to a two-necked, 25 mL round bottom flask equipped with a stir bar, the flask was flushed with carbon monoxide, diethylmethyl silane (0.500 mL, 3 eqs.) was then added and allowed to react for 5 minutes (H_2 gas evolved), a solution of 1,5-O-Acetyl-2,3-O-(4)-heptylidene-β-D-ribofuranoside (348.0 mg, 1.04 mmol) and 5 mL of 1,1,1-trichloroethane was then added, carbon monoxide was then added to the reaction flask for 10 seconds and turned off. The reaction solution appeared straw brown. The reaction was monitored by TLC using 20% EtOAc/hexane as solvent. After reacting for 1 hr., a condensor was added, and the reaction was heated to 50°C. After reacting for 10 minutes the solution turned dark purple. After reacting for a total of 6 hrs., TLC indicated that some product had

been formed. The reaction was worked up at this point. The reaction mixture was worked up by adding five drops of pyridine and bubbling air through the solution, via gas dispersion tube (a blue precipitate was formed). The resulting mixture was filtered through an hirsh funnel, and washed with 1:1 ligroine/ether. The resulting organic mixture was placed under reduced pressure to remove solvent. Column chromatography was set up using 7.5% EtOAc/hexane as solvent, 14/20 glassware was employed, and 10-mL fractions were collected. Thin layer chromatography indicated fractions #28-38 contained desired product. These fractions were combined and placed under reduced pressure to remove solvent to yield a final pure product. The product yielded 0.120 mg (0.0003 mmol, 0.028%) as colorless syrup. So little product was formed that the NMR spectrum was uninterpretable.

2,5-Anhydro-1-O-(diethylmethylsilyl)-3,4-O-(4-heptylidene)-6-O-acetyl-D-allitol

Dicobalt octacarbonyl (35.3 mg, 0.103 mmol) was first added to a 25 mL, two-necked round bottom flask, which had been cooled under a nitrogen atmosphere. The flask was then put under a carbon monoxide atmosphere and was connected to a bubbler outlet, flushing the catalyst with CO. Diethylmethyl silane (306.8 mg, 3.00 mmol) was added next under the CO atmosphere with the bubbler bubbling. This solution was stirred for five minutes. A solution of 1,5-O-Acetyl-2,3-O-(4)-heptylidene-β-D-ribofuranoside (323.6 mg, 1.01 mmol) and 5 mL of 1,1,1-trichloroethane were added last. The reaction was run at 50°C, and was monitored by TLC using 20% EtOAc/hexane as solvent. The reaction solution immediately turned brown, and then purple. After 4 hrs., TLC indicated that only starting material was present in the reaction flask, so the temperature was increased to 60°C. After reacting for a total of 20 hrs., still no product had formed, so the reaction mixture was discarded.

2,5-Anhydro-1-O-(diethylmethylsilyl)-3,4-O-(4-heptylidene)-6-O-acetyl-D-allitol

Dicobalt octacarbonyl (171.7 mg, 0.502 mmol) was added to a 25 mL round bottom flask equipped with a stir bar and a gas dispersion tube and flushed with carbon monoxide. Diethylmethyl silane (922.9 mg, 9.03 mmol) was added next, and this solution was stirred for five minutes under a CO atmosphere (using the gas

dispersion tube). 1,5-O-Acetyl-2,3-O-(4)-heptylidene-β-D-ribofuranoside (541.0 mg, 1.68 mmol) and 13 mL of 1,1,1-trichloroethane were added last. The reaction was run at 50°C and was monitored by TLC using 20% EtOAc/hexane. The gas dispersion tube was immersed in the solution and was bubbling in CO during the reaction. The reaction solution immediately turned purple. After reacting for 1 hr., 2 mL of 1,1,1-trichloroethane was added to the reaction flask because the solvent was being evaporated due to CO pressure and the heat. Another 1 mL was added after reacting another 2 hours. After reacting for 4.5 hrs., the reaction was worked up by adding water and then filtering the mixture through silica gel and sand at water aspirator pressure, washing with 2:1 ligroine/ether. The filtrate was then extracted three times with 2:1 ligroine/ether and placed under reduced pressure to remove solvent. A crude NMR was taken to verify product. Column chromatography was set up using 3% EtOAc/hexane as solvent. Thin layer chromatography and NMR indicated that fractions #31-36 contained product. These fractions were combined and placed under reduced pressure to remove solvent, to yield a final pure product. The product yielded 47.3 mg (0.117 mmol, 6.98%) as solid particles. 1 H-NMR delta 0.0 (7 H, s), 0.3-1.0 (12 H, b), 1.3-1.6 (8 H, b), 1.8-2.1 (3 H, s), 3.4-3.7 (2 H, b), 3.8-4.2 (5 H, b), 4.5-4.8 (2 H, b), 6.1 (1 H, s).

2,5-Anhydro-1-O-(diethylmethylsilyl)-3,4-O-(4-heptylidene)-6-O-acetyl-D-allitol

Dicobalt octacarbonyl (105.4 mg, 0.308 mmol) was added to a 25 mL, two-necked, round bottom flask equipped with a stir bar and condenser, followed by the addition of carbon monoxide to flush the flask. Diethylmethyl silane (0.500 mL, 3 eqs.) was added next (during the addition of the silane, the CO was turned off), followed by the addition of a solution of 1,5-O-Acetyl-2,3-O-(4)-heptylidene β-D-ribofuranoside (264.0 mg, 0.792 mmol) and 5 mL of 1,1,1-trichloroethane. The CO was turned back on just enough to cause a depression in the outlet bubbler. The reaction was run at 50°C. The reaction was monitored by TLC using 20% EtOAc/hexane as solvent. After 9.25 hrs., the reaction was worked up by adding a few drops of pyridine, followed by bubbling air through the reaction solution, via gas dispersion tube to precipitate the catalyst. The mixture was then filtered through an Hirsh funnel and washed with 1:1 ligroine/ether. The organic mixture was then placed under reduced pressure to remove solvent. Column chromatography was set up using 3%

EtOAc/hexane as solvent, 14/20 glassware was employed, and 10-mL fractions were collected. Thin layer chromatography indicated fractions #30-32 contained desired product. These fractions were combined and placed under reduced pressure to remove solvent, to yield a final pure product. The final product yielded 52.0 mg (0.129 mmol, 16.3%) as a colorless oil. Before obtaining an accurate NMR, product was destroyed when a water aspirator backed up into the reaction vessel.

2,5-Anhydro-1-O-(diethylmethylsilyl)-3,4-O-(4-heptylidene)-6-O-acetyl-D-allitol

Dicobalt octacarbonyl (69.3 mg, 0.203 mmol) was added first to a two-necked, 25 mL round bottom flask equipped with a stir bar, a balloon inflated with carbon monoxide was then put on the flask for five minutes, the balloon was removed, and diethylmethyl silane (0.235 mL, 3.0 eqs.) was added, the balloon was replaced, and allowed to react for 5-10 minutes, a solution of 1,5-O-Acetyl-2,3-O-(4)-heptylidene-β-D-ribofuranoside (180.0 mg, 0.540 mmol) and 5 mL of 1,1,1-trichloroethane was added and allowed to react under balloon pressure. After this set-up was tried, another set-up was utilized by using a 3-way selector. One end was connected to the CO tank, one connected to the balloon, and the other to the reaction vessel. This set-up was employed 30 minutes after the reaction had started. After reacting for 1 hr., a condenser was added, and the reaction was heated to 40°C. After reacting for another 1.25 hrs., the solution was further heated to 50°C. After reacting for a total of 22 hrs., the reaction was worked up by adding five drops of pyridine and bubbling air via gas dispersion tube (a blue precipitate formed). This solution was filtered through an hirsh funnel and washed with 1:1 ligroine/ether. The resulting organic solution was placed under reduced pressure to remove solvent. Column chromatography was set up using 8% EtOAc/hexane as solvent, 14/20 glassware was employed, and 10-mL fractions were collected. Thin layer chromatography indicated that no fractions contained product. Nuclear magnetic resonance spectra were taken of the molecules that did come off during chromatography, but no product was found.

2,5-Anhydro-1-O-(diethylmethylsilyl)-D-allitol triacetate

Dicobalt octacarbonyl (74.1 mg, 0.217 mmol) was added first to a 25 mL, two-necked round bottom flask equipped with a stir bar, thermometer, and condenser, and flushed with CO, then

diethylmethyl silane (766.9 mg, 7.50 mmol) was added and stirred to activate the catalyst. After stirring for 10 minutes, a solution of β–D-ribofuranose 1,2,3,5-tetraacetate (797.1 mg, 2.50 mmol) and 1,1,1-trichloroethane (5 mL) was added, and stirred at 50°C. The reaction was run under a carbon monoxide atmosphere with the bubbler outlet bubbling to release CO pressure. The reaction solution changed color, from a light brown at the start to a dark purple after 15 minutes. The reaction was monitored by TLC using 33% EtOAc/hexane as the solvent. After 2.5 hrs., the reaction was worked up. A literature method for workup was followed, but air couldn't be bubbled into the reaction flask, so only pyridine was added. This did not precipitate the catalyst as hoped. We then decided to work up the solution by adding water, and extracting three times with 2:1 ligroine/ether. The mixture was then filtered through silica gel in a sintered glass funnel. The resulting mixture was placed under reduced pressure to remove solvent. Column chromatography was set up using 18% EtOAc/hexane. The product came off in fractions #19-24. These fractions were combined and placed under reduced pressure to remove solvent, to yield a final pure product. The final product yielded 118.9 mg (0.318 mmol, 12.7%) as a colorless syrup. 1 H-NMR delta 0 (7 H, m), 0.5-1.0 (6 H, m), 2.0 (9H, s), 3.25-3.5 (2 H, d), 3.5-4.0 (4 H, m), 4.8-5.2 (2 H, b).

2,5-Anhydro-1-O-(diethylmethylsilyl)-D-allitol triacetate

Dicobalt octacarbonyl (72.0 mg, 0.211 mmol) was first added to a two-necked, 25 mL round bottom flask equipped with a gas dispersion tube and a condenser, and flushed with carbon monoxide. Diethylmethyl silane (766.8 mg, 7.50 mmol) was then added to the flask and stirred for 10 minutes. During this time, the gas dispersion tube was bubbling in CO. A stir bar was added to the flask next. Finally a solution of β-D-ribofuranose 1,2,3,5-tetraacetate (795.5 mg, 2.50 mmol) and 5 mL of 1,1,1-trichloroethane was added to the reaction flask. The reaction was run with the gas dispersion tube bubbling in CO. The reaction was run at 50°C. Twenty microliters of diethylmethyl silane were added to the reaction flask due to the gas pressure evaporating the silane. The reaction was monitored by TLC using 20% EtOAc/hexane as solvent. After reacting for 5 hrs., 2 mL of 1,1,1-trichloroethane and 20 μL of diethylmethyl silane were added to the reaction flask. After reacting for a total of 21 hrs., the reaction was worked up by adding a few drops of pyridine and bubbling in air for 15 minutes to precipitate the catalyst. The

resulting solution was then filtered through a sintered glass funnel with sand, washed with 1:1 ligroine/ether and placed under reduced pressure to remove solvent. During workup, part of the product was lost when the reaction flask was knocked onto the lab bench. Column chromatography was set up using 15% EtOAc/hexane as solvent. Thin layer chromatography indicated that fractions #11-20 contained the desired products (mixture of diastereomers). These fractions were combined and placed under reduced pressure to remove solvent, to yield a final pure product. The product yielded 49.3 mg (0.126 mmol, 5.05%) as a light yellow syrup. 1 H-NMR delta 0.0 (7 H, s), 0.3-1.0 (20 H, m), 1.7-2.0 (3 H, s), 3.4-3.5 (2 H, d), 3.8-4.2 (3 H, b), 4.9-5.2 (2 H, b), 5.9 (1 H, s).

2,5-Anhydro-1-O-(diethylmethylsilyl)-D-allitol triacetate

Dicobalt octacarbonyl (104.5 mg, 0.306 mmol) was added first to a two-necked, 25 mL round bottom flask equipped with a stir bar and condenser. The flask was then purged with carbon monoxide. Diethylmethyl silane (0.442 mL, 3.0 eqs.) was added and then put under balloon pressure with carbon monoxide, this solution was stirred for 10 minutes, the balloon was shut off and a solution of β-D-ribofuranose 1,2,3,5-tetraacetate (323.3 mg, 1.02 mmol) and 5 mL of 1,1,1-trichloroethane was added, and the balloon was re-opened. A glass stopper was used instead of a rubber septum. The reaction was conducted at 50°C. Teflon tape was used to seal up the reaction vessel and joints. The reaction solution appeared dark purple. The reaction was monitored by TLC using 33% EtOAc/hexane as solvent. After reacting for 5.25 hrs., the solution was worked in standard fashion. Column chromatography was set up using 10% EtOAc/hexane as solvent, 14/20 glassware was employed, and 10-mL fractions were collected. Thin layer chromatography indicated fractions #21-29 contained desired product. These fractions were combined and placed under reduced pressure to remove solvent, to yield a final pure product. The product yielded a mixture of diastereomers 64.8 mg (0.173 mmol, 17.0%) as a colorless syrup. 1 H-NMR delta 0.0 (7 H, s), 0.5-1.0 (6 H, m), 1.9-2.1 (9 H, s), 2.8-3.0 (1 H, s), 3.6-3.8 (1 H, s), 3.9-4.3 (4 H, m), 4.9-5.3 (2 H, b).

2,5-Anhydro-1-O-(diethylmethylsilyl)-D-allitol triacetate.

Dicobalt octacarbonyl (93.0 mg, 0.727 mmol) was added to a two-necked, 25 mL round bottom flask equipped with a stir bar and a condenser. The flask was purged with carbon monoxide. A

balloon was inflated with CO and placed on the reaction flask. Diethylmethyl silane (0.235 mL, 3.0 eqs.) was added to the vessel, and the balloon was opened to the reaction vessel (H2 gas evolution). An equivalent amount of silane was added due it's evaporation during the addition of carbon monoxide. After reacting for five minutes, the balloon was shut off. A solution of β-D-ribofuranose 1,2,3,5-tetraacetate (172.3 mg, 0.541 mmol) and 5 mL of 1,1,1-trichloroethane was added to the reaction flask, and the balloon was re-opened. After the balloon ran out of CO, the reaction flask was separated from the balloon apparatus and was sealed up, and let run. The reaction was conducted at 50°C. An outlet needle was added to the reaction flask. The reaction solution was dark brown at the start of the reaction, but soon turned pale brown as reaction proceeded. After the solution was opened to the air, the solution soon turned purple. The reaction was monitored by TLC using 33% EtOAc/hexane as solvent. After reacting for 14 hrs., the reaction was considered complete by TLC, and was worked up in the standard fashion. The precipitated catalyst looked different this time (not a blue ppt., but a brown ppt.). Column chromatography was set up using 10% EtOAc/hexane as solvent, 14/20 glassware was employed, and 10-mL fractions were collected. Thin layer chromatography indicated that fractions #26-28 contained desired product. These fractions were combined and placed under reduced pressure to remove solvent, to yield a final pure product. The product yielded 30.2 mg (0.0806 mmol, 14.9%) as a colorless syrup. The mixture of diastereomers produced a combined yield of 36.8%. 1 H-NMR delta 0.0 (7 H, s), 0.4-1.0 (6 H, m), 1.7-2.0 (9 H, s), 2.5-2.7 (1 H, s), 3.4-3.6 (1 H, s), 3.9-4.0 (4 H, m), 4.8-5.0 (1 H, b).

2,5-Anhydro-1-O-(diethylmethylsilyl)-D-allitol triacetate

Dicobalt octacarbonyl (87.5 mg, 0.256 mmol) was added first to a two-necked, 25 mL round bottom flask equipped with a stir bar and a condenser , and purged with CO. The reaction flask was cooled under a carbon monoxide atmosphere. A balloon was inflated with CO and placed on the reaction flask. Diethylmethyl silane (0.249 mL, 3.0 eqs.) was added to the reaction flask; the balloon was opened to the flask, and an equivalent amount of silane was added to the vessel due to it's evaporation under CO pressure. The balloon was closed and a solution of β–D-ribofuranose 1,2,3,5-tetraacetate (182.3 mg, 0.573 mmol) and 5 mL of 1,1,1-trichloroethane was added to the reaction vessel. The balloon apparatus was removed and the

reaction vessel was sealed up using a glass stopper and teflon tape. The reaction was conducted in the dark at 50°C. The reaction solution appeared medium brown. The reaction turned purple after heating. The reaction was monitored by TLC using 33% EtOAc/hexane as solvent. After reacting for 12 hrs., the reaction solution was worked in the standard fashion. Column chromatography was set up using 8% EtOAc/hexane as solvent, 14/20 glassware was employed, and 10-mL fractions were collected. Thin layer chromatography indicated that fractions #38-40 contained desired product. These fractions were combined and placed under reduced pressure to remove solvent, to yield a final pure product. The product yielded 19.5 mg (0.052 mmol, 9.09%) as a colorless syrup. The mixture of diastereomers produced a combined yielded 36.99%. 1 H-NMR delta 0.0 (7 H, s), 0.4-1.1 (6 H, m), 1.8-2.0 (9 H, s), 2.7-2.9 (1 H, s), 3.5-3.7 (1 H, d), 3.8-4.1 (4 H, m), 4.9-5.2 (1 H, b)

2,5-Anhydro-1-O-(diethylmethylsilyl)-3,4-O-(4-heptylidene)-D-allitol

2,5-Anhydro-1-O-(diethylmethylsilyl)-3,4-O-(4-heptylidene)-6-O-acetyl-D-allitol (47.3 mg, 0.117 mmol), lithium aluminum hydride (5 mg, 1.1 eqs.), and ether (1.17 mL, 0.1 M) were added to a round bottom flask equipped with a stir bar. The reaction was started at 0°C, and allowed to warm to room temperature. The reaction was run overnight (reaction dried up overnight). At this point, the following chemicals were added to the reaction flask, in the following sequence: 5 μL of water, 5 μL of 15% sodium hydroxide, and 15 μL of water. The reaction was monitored by TLC using 20% EtOAc/hexane as solvent. After reacting for 1 hour, the reaction was worked up by transferring the solution to a test tube and extracting three times with ether. The mixture was then placed under reduced pressure to remove solvent. Column chromatography was not utilized to purify product. An NMR was taken and yielded a very noisy spectrum which was thought to contain product. The final product yielded 4.2 mg (0.012 mmol, 6.56%). 1 H-NMR not interpretable.

2,5-Anhydro-1-O-(diethylmethylsilyl)-D-allitol

2,5-Anhydro-1-O-(diethylmethylsilyl)-D-allitol triacetate (49.3 mg, 0.126 mmol), lithium aluminum hydride (11.97 mg, 2.5 eqs.), and ether (1.26 mL, 0.1 M) were added to a round bottom flask

equipped with a stir bar. The reaction was started at 0°C in an ice/salt bath, and then removed after 15 min., and allowed to warm to room temperature. After reacting for 30 minutes, the following chemicals were added to the reaction flask in the following sequence: 12 mL water, 12 mL sodium hydroxide, and 36 mL water. This solution was then filtered at water aspirator pressure through a sintered glass funnel with sand. The resulting mixture was placed under reduced pressure to remove solvent. An NMR was taken of the resulting residue. The spectra obtained indicated that no product had been formed.

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