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Indium-Mediated Allylation of Aldehydes: A Convenient Route to 2-Deoxy and 2,6-Dideoxy Carbohydrates

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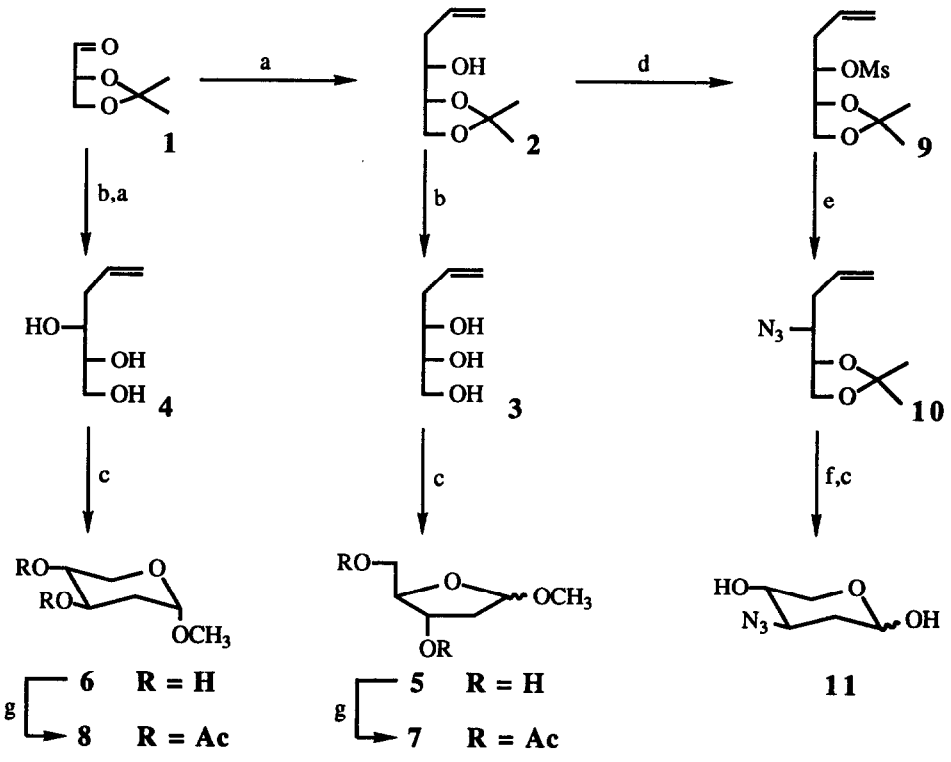
Abstract: The allylation of protected polyhydroxy aldehydes **1** and **14** has been achieved by indium metal with ultrasound promotion generating the diastereomeric pair of homoallylic polyols **3**, **4** and **16**, **17** respectively with moderate to good stereoselectivity. Pursuing this allylation strategy with the corresponding deprotected polyhydroxy aldehydes led to the same pair of homoallylic polyols but with a quite different ratio of the diastereomers generated. The polyols were further transformed to 2-deoxy (**5** and **6**) and 2,6-dideoxy (**18** and **19**) carbohydrates by ozonolysis.

Introduction

Metallic indium has been reported to enable Reformatski reactions,[1] cyclopropanations,[2] and allylations[3] of carbonyl compounds. Recently, this allylation strategy has been extended to aldimines[4] and unprotected carbohydrates.[5] We report here that indium can be used for a convenient approach leading to 2-deoxy and 2,6-dideoxy sugars. These carbohydrates are particularly interesting because they are important structural components of nucleic acids and numerous antibiotics.[6]

Results and Discussions

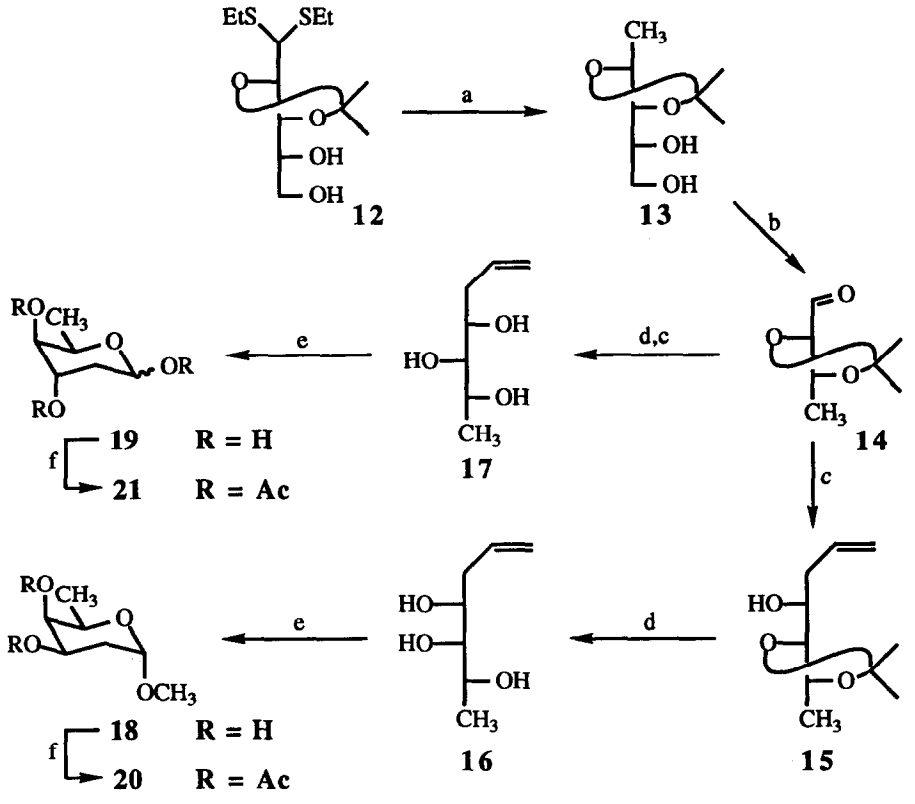
Following a route originally developed for allylzinc reagents by Fuganti *et al.*,[7] we took advantage of the fact that indium mediated allylations of aldehydes are easily performed in polar protic media. Thus, (R)-2,3-O-isopropylidene glyceraldehyde **1**[8] was treated with indium powder and allyl bromide and the suspension was sonicated in a conventional ultrasonic cleaning bath.[9] The reaction was complete within one hour. We obtained a mixture of diastereomeric alcohols[10] in a ratio of 6.5 : 1 (Scheme 1), as determined by NMR analysis. The diastereomers were not separable by conventional column chromatography. To assign the stereochemistry of the newly generated chiral center of the major diastereomer, the allyl derivative **2** was deprotected under acidic conditions and subsequently the mixture of triols was ozonised. The 2-deoxy methyl glycosides formed were easily separated by chromatography on silica gel. The major diastereomer was assigned as methyl 2-deoxy-D-ribofuranoside **5**. The physical and spectroscopical data of **5** were in full agreement with those published.[11] To



Scheme 1: (a) Allyl bromide; indium powder; ultrasound (b) Dowex 50 W; H^+ (c) O_3; -78 °C; Ph_3P (d) CH_3SO_2Cl; Et_3N (e) LiN_3; DMF (f) OsO_4; KIO_4 (g) Ac_2O; pyridine; DMAP

further establish the stereochemistry of **2** we prepared the mesyl derivative **9**. Azide introduction under inversion of configuration at C-3 yielded derivative **10**, which was further converted to 3-azido-2,3-dideoxy-D-threo-pentose **11**. Assignment of the stereocenters was easily achieved by analysis of the coupling constants in the proton NMR spectrum of **11**. As a consequence, the major diastereomer generated in the course of the allylation reaction exhibits an *erythro* relationship between the hydroxyl function formed and the stereocenter originally present at C-2 of the starting aldehyde **1**. However, performing the same allylation procedure in dioxane/water after deprotection of **1** yielded a 1 : 2 mixture of polyols **3** and **4**, thus significantly changing the stereochemical outcome of the reaction. In analogy, the major diastereomer was assigned after transformation to methyl 2-deoxy-α-D-xylopyranoside **6** and comparison with data reported.[12] To simplify the purification and NMR analysis, the 2-deoxy sugars **5** and **6** were converted to the corresponding acetyl derivatives **7** and **8**.

For additional demonstration of the applicability of this method, we synthesized aldehyde **14**. Starting from D-arabinose and following a procedure developed by Herczegh *et al.*,[13] we obtained the monoprotected mercaptal **12**. Treatment with Raney-nickel followed by lead tetraacetate cleavage afforded aldehyde **14** which was used without purification. Indium mediated allylation of **14** (Scheme 2) yielded a mixture of diastereomeric alcohols in a ratio of 20 : 1. From the major diastereomer **15**, methyl 2,6-dideoxy-D-lyxo-hexopyranoside **18**



Scheme 2: (a) Raney-Ni (b) $Pb(OAc)_4$ (c) Allyl bromide; indium powder; ultrasound (d) Dowex 50 W; H^+ (e) O_3; -78 °C; Ph_3P (f) Ac_2O; pyridine; DMAP

(D-oliose-methylglycoside) was obtained following the protocol developed for the 2-deoxy sugars. The reaction sequence was started by deprotection of aldehyde **14** yielding a mixture of diastereomeric triols **16** and **17** in a ratio of 1 : 6. Again the major diastereomer was converted to 2,6-dideoxy-D-xylo-hexopyranose **19** (D-boivinose) for structural proof.[14]

The different diastereoselectivities obtained starting either with protected or unprotected polyhydroxy aldehydes deserves some comments. With the protected aldehydes the corresponding Cram products[15] were obtained in moderate to good diastereoselectivity, which is in agreement with results reported by Mulzer *et al.*.[10a] For the unprotected aldehydes we observed the same diastereoselectivity as reported for indium[5] or tin[16] assisted allyl addition on unprotected carbohydrates thus following the chelation-Cram model.[15] However, factors due to the heterogeneous reaction conditions as well as to the presumed allyl-indium species involved[3] may play a significant role in directing the stereochemistry of the reaction.

The advantage of the syntheses presented is that starting from one aldehyde each of the two possible epimeric sugars can be obtained as the main product by simply changing the first two steps in the reaction sequence. In addition, the procedures involved easily allow upscale of the reaction to gram quantities, thus opening a convenient access to a variety of biological important carbohydrates.

Experimental Section:

General: Chemicals were purchased from Aldrich and were reagent grade. Indium powder (325 mesh) was purchased from Alfa company. Solvents were dried and distilled before use. Ultrasonication was performed in an ultrasound cleaning bath (SONOREX RK 100H). Analytical thin layer chromatography was performed on Merck plates (silica gel F_{254}, 0.25 mm thick). Compounds were visualized by spraying with a solution of 3 % $Ce(SO_4)_2$ in 2N H_2SO_4 followed by heating to 200 °C. Flash chromatography was performed using Merck Silica gel 60 (0.04 - 0.063 mm thick).
NMR spectra were recorded at 250 MHz or 400 MHz on a BRUKER AM 250 or AM 400 spectrometer, respectively. Infra red spectra were recorded on a Perkin Elmer 1600-series FTIR instrument. Mass spectra were recorded on a FINNIGAN MAT-311A spectrometer. Optical rotations were measured on a Perkin Elmer polarimeter 141. Abbreviations used are as follows: hexane (PE), ethyl acetate (EA), dichloromethane (MC), methanol (MeOH).

General method for the deprotection and allylation of the isopropylidene-proteced polyhydroxy aldehydes - Method A
To a suspension of 3.5 mmol of the isopropylidene-aldehyde in 20 mL of a mixture of water / dioxane (10:1), 3 g of DOWEX 50 W (H^+-form) were added and the mixture was stirred for one hour. The resin was removed by filtration and washed carefully with water. To the filtrate 3.5 mg-atom of In powder and 8 mmol of allyl bromide were added and the mixture was sonicated until completion of the reaction (judged by tlc.: MC / MeOH = 5 / 1). The pH of the mixture was readjusted to 7.5 by the addition of 1 N NaOH and the colorless precipitate formed was removed by centrifugation. The supernatant was decanted and the pellet washed with water. The combined aqueous phases were evaporated to dryness and the residue was purified by flash chromatography over silica gel (eluent given for the specific compounds).

General method for the allylation of isopropylidene-protected polyhydroxy aldehydes - Method B
To a solution of 5.9 mmol of isopropylidene-aldehyde in 20 mL of ethanol 5.9 mg-atom of In powder and 15 mmol of allyl bromide were added and the mixture was sonicated for one hour (tlc.: PE / EA = 3:1). The pH of the mixture was readjusted to 7.5 by the addition of 1 N NaOH and the colorless precipitate formed was removed by centrifugation. The supernatant was decanted and the pellet was washed with 20 mL of ethanol. The combined organic phases were evaporated to dryness and the residue was purified by flash chromatography over silica gel (eluent given for the specific compounds).

General method for the acetylation - Method C
To 20 mg of the dried starting material 5 mL of pyridine, 5 mL of acetic anhydride and 10 mg of 4-dimethylaminopyridine (DMAP) were added. After 18 hours the solvents were removed by codistillation with toluene at reduced pressure. The residue was purified by flash chromatography over silica gel (PE / EA = 6:1).

(2R,3S)-1,2-O-Isopropylidene-5-hexen-1,2,3-triol (2):
856 mg (6.6 mmol) of **1** were treated according to **method B** yielding 1.022 g (90%) of **2** as colorless oil. Major diastereomer: ^{1}H NMR ($CDCl_3$): δ 1.29; 1.36 (2s, 6H, 2xCH_3); 2.08-2.31 (m, 2H, H-4, H-4´); 2.35 (bs, 1H, OH); 2.69 (m, 1H, H-3); 3.82-3.98 (m, 3H, H-1, H-1´, H-2); 5.03-5.12 (m, 2H, H-6, H-6´); 5.72-5.85 (m, 1H, H-5). ^{13}C NMR ($CDCl_3$): δ 133.96; 118.03; 109.06; 78.00; 65.15; 37.53; 26.41; 25.13.

(2R,3S)-5-Hexen-1,2,3-triol (3):
To a stirred solution of 300 mg (1.74 mmol) of **2** in 18 mL of a mixture of dioxane / water (1 / 5), 2 g of Dowex 50 W (H^+-form) were added. Stirring was continued for 1 h until tlc (PE / acetone = 1 / 1) showed completion of the reaction. The resin was removed by filtration and carefully washed with water. The solvent was removed under reduced pressure (keeping the bath-temperature below 30 °C) to yield 216 mg (94%) of an unseparable mixture of **3** and **4** in a ratio of 6.5 : 1 (determined by NMR integration) as colorless oil. Major diastereomer **3**: ^{1}H NMR (D_2O; HDO set to 4.8 ppm): δ 2.20; 2.41 (2m, 2H); 3.51-3.80 (m, 4H); 5.08-5.22 (m, 2H); 5.76-5.98 (m,1H). ^{13}C NMR (D_2O, dioxane as external standard set to 67.00 ppm): δ 135.25; 118.06; 74.48; 71.46; 62.86; 36.90.

(2R,3R)-5-Hexen-1,2,3-triol (4):
550 mg (4.2 mmol) of **1** were treated according to **method A**. After flash chromatography (20 g silica gel; PE / acetone = 2 / 3), 337 mg of an unseparable mixture of **3** and **4** in a ratio of 1 : 2 were obtained. Major diastereomer **4**: ^{1}H NMR (D_2O): δ 2.12-2.35 (m,2H); 3.51-3.80 (m,4H); 5.08-5.22 (m, 2H); 5.76-5.98 (m, 1H). ^{13}C NMR (D_2O): δ 135.17; 117.97; 74.02; 71.09; 63.10; 37.39.

Methyl 2-deoxy-D-erythro-pentofuranoside (5):
A stirred solution of 154 mg (1.17 mmol) of **3** in 30 mL of a mixture of MC / MeOH (9 / 1) was cooled to -78 °C and ozone was bubbled through the reaction mixture until a blue color remained. The excess of ozone was removed by sparging with argon followed by the addition of 315 mg (1.2 mmol) of triphenylphosphine. The solution was allowed to warm up to room temperature and stirring was continued for 16 h. The solvent was removed under reduced pressure and the crude material purified by flash chromatography (20 g silica gel; MC / MeOH = 9 / 1) to yield 120 mg (70%) of a mixture of α and β anomers (the anomers were separated in their peracetylated form **7**). The spectroscopical data of **5** were in full agreement with a sample prepared from authentic 2-deoxy ribose and with data reported.[11]

Methyl 2-deoxy-α-D-threo-pentopyranoside (6):
120 mg (0.9 mmol) of **4** were ozonised analogous to the procedure for **5**. After flash chromatography 68 mg (51%) of pure α-glycoside was obtained. $[\alpha]_D^{20}$ = +118.9° (ref. 12: $[\alpha]_D^{20}$ = +125°). The spectroscopical data were identical with those reported.[12]

Methyl 3,5-di-O-acetyl-2-deoxy-D-erythro-pentofuranoside (7):
120 mg (0.81 mmol) of **5** were acetylated according to the general **method C**. After flash chromatography (20 g silica gel; PE / EA = 9 / 1), 86 mg of pure β- and 69 mg of pure α-anomer were obtained (Yield: 82%).

^{1}H NMR (α-anomer; $CDCl_3$): δ 1.95 (ddd, 1H, J = 1.6 Hz, J = 13.3 Hz, H-2); 2.04 (s, 6H, 2xCH_3); 2.33 (ddd, 1H, J = 5.0 Hz, J = 6.7 Hz, H-2´); 3.34 (s, 3H, OCH_3); 4.11 (dd, 1H, J = 5.0 Hz, J = 11.6 Hz, H-5); 4.19 (m, 1H, H-4); 4.29 (dd, 1H, J = 4.3 Hz, H-5´); 4.99 (m, 1H, H-1); 5.04 (m, 1H, H-3). ^{13}C NMR (α-anomer; $CDCl_3$): δ 170.84; 170.59; 104.90; 80.52; 73.89; 63.81; 55.07; 38.93; 20.95; 20.72. MS (70 eV): m/e 231 (M+-H; 1%); 201 (15.6); 172 (6.8); 159 (100). $[\alpha]_D^{20}$ = +54.3° ($CHCl_3$, c = 1.14) (ref 6: $[\alpha]_D^{20}$ = +56° ($CHCl_3$, c = 0.87)).
^{1}H NMR (β-anomer; $CDCl_3$): δ 1.98; 2.05 (2s, 6H, 2xCH_3); 2.13 (ddd, 1H, J = 13.3 Hz, J = 6.7 Hz, H-2); 2.32 (ddd, 1H, J = 6.7 Hz, 2.6 Hz, H-2´); 3.30 (s, 3H, OCH_3); 4.05 (dd, 1H, J = 6.7 Hz, J = 11.7 Hz, H-5); 4.18 (m, 1H, H-4); 4.26 (dd, 1H, H-5´); 5.08 (dd,1H, H-1); 5.17 (m, 1H, H-3). ^{13}C NMR (β-anomer; $CDCl_3$): δ 170.62; 170.41; 105.48; 81.70; 74.91; 64.74; 55.26; 38.88; 20.86; 20.75. Anal. for $C_{10}H_{16}O_6$ (232.23): Calcd. C, 51.72; H, 6.94; Found C, 51.86; H, 6.88.

Methyl 3,4-di-O-acetyl-2-deoxy-α-D-threo-pentopyranoside (8):
40 mg (0.27 mmol) of **6** were acetylated according to the general **method C**. After flash chromatography (8 g silica gel; PE / EA = 9 / 1), 52 mg (83%) of **8** were obtained as colorless glass. $[\alpha]_D^{20}$ = +83.2° ($CHCl_3$; c = 0.78) (ref 12.: $[\alpha]_D^{20}$ = +85.6°). ^{1}H NMR ($CDCl_3$): δ 1.76 (ddd, 1H, J = 3.2 Hz, J = 10.1 Hz, J = 13.2 Hz, H-2ax); 2.04; 2.05 (2s, 6H, 2xCH_3); 2.19 (ddd, 1H, J = 2.9 Hz); J = 4.9 Hz, H-2eq); 3.36 (s, 3H, OCH_3); 3.64 (dd, 1H, J = 9.3 Hz, J = 11.3 Hz, H-5ax); 3.79 (dd, 1H, J = 4.9 Hz, H-5eq); 4.73 (dd, 1H, H-1); 4.88 (ddd, 1H, J = 8.8 Hz, H-4); 5.25 (ddd, 1H, H-3). ^{13}C NMR ($CDCl_3$): δ 170.14; 169.97; 98.17; 69.42; 68.42; 59.72; 55.05; 34.44; 21.01; 20.85. Anal. for $C_{10}H_{16}O_6$ (232.23): Calcd. C, 51.72; H, 6.94; Found C, 51.94; H, 6.99.

(2R,3S)-1,2-O-Isopropylidene-3-O-methansulfonyl-5-hexen-1,2,3-triol (9):
To a stirred solution of 980 mg (5.73 mmol) of **2** in 40 mL of *t*-butyl methyl ether 1.25 mL (8.8 mmol) triethylamine and 0.681 mL (8.8 mmol) of methansulfonyl chloride were added. The reaction mixture was heated to 65 °C for 2 h. After cooling to room temperature, 50 mL of a 5% aqueous solution of $NaHCO_3$ were added. The organic layer was separated and the water phase extracted 3 times with 50 mL portions of $CHCl_3$. The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed in vacuum. The crude product was purified by flash chromatography (60 g silica gel; PE / acetone = 7 / 3). Yield: 1.012 g (71%) of a slightly yellowish oil (mixture of diastereomers in a ratio of 6.5 : 1). Major diastereomer: ^{1}H NMR ($CDCl_3$): δ 1.29; 1.36 (2s, 6H, 2xCH_3); 2.42-2.48 (m, 2H, H-4, H-4´); 2.98 (s, 3H, CH_3SO_2); 3.86 (dd, 1H, J = 9.2 Hz, J = 6.6 Hz, H-1); 3.99 (dd, 1H, J = 6.6 Hz, H-1´); 4.13 (dd, 1H, J = 5.9 Hz, H-2); 4.72 (ddd, 1H, H-3); 5.09-5.18 (m, 2H, H-6, H-6´); 5.71-5.83 (m, 1H, H-5). ^{13}C NMR ($CDCl_3$): δ 131.83; 119.29; 109.61; 80.41; 75.57; 65.10; 38.66; 35.95; 26.20; 25.01. MS (70 eV): m/e 235 (M^+-15, 55%); 192 (2); 179 (2); 151 (7); 139 (5).

(2R,3R)-3-Azido-1,2-O-isopropylidene-5-hexen-1,2-diol (10):
To a solution of 906 mg (3.62 mmol) of **9** in 4 mL of dry DMF, 343 mg (7 mmol) of LiN_3 were added. The reaction mixture was heated to 120 °C for 2 h. After cooling to room temperature, 100 mL of water were added and the solution was extracted 4 times with 90 mL portions of ether. The combined organic phases were subsequently washed with 50 mL of saturated NH_4Cl solution, 50 mL of 10% $NaHCO_3$ solution and 50 mL

of water. After drying over $MgSO_4$, the solvent was evaporated and the crude product purified by flash chromatography (50 g silica gel) yielding 360 mg (51%) of the pure diastereomer **10**. ^1H NMR ($CDCl_3$): δ 1.34; 1.45 (2s, 6H, 2xCH_3); 2.28-2.38 (m, 2H, H-4, H-4'); 3.22 (ddd, 1H, J = 5.9 Hz, H-3); 3.77 (dd, 1H, J = 8.0 Hz, J = 6.6 Hz, H-1); 4.00 (dd, 1H, J = 6.6 Hz, H-1'); 4.11 (ddd, 1H, H-2); 5.10-5.25 (m, 2H, H-6, H-6'); 5.71-5.89 (m, 1H, H-5). ^{13}C NMR ($CDCl_3$): δ 133.23; 118.47; 109.86; 77.70; 66.27; 62.45; 35.11; 26.24; 25.17. MS (70 eV): m/e 182 (M^+-15, 19%); 112 (2); 101 (100). IR (on Si plate): ν 2109 cm^{-1}.

3-Azido-2,3-dideoxy-D-threo-pentopyranose (11):

A solution of 70 mg (0.35 mmol) of **10** in 10 mL of a mixture of acetone / water (9 / 1) was treated with 1 mL of a solution of OsO_4 in dry THF (10 mg / mL). After addition of 80 mg of KIO_4 the reaction mixture was stirred at room temperature for 16 h. The solution was concentrated to a volume of 1 mL and then diluted with water to a final volume of 15 mL. Dowex 50 W (0.5 g; H^+-form) were added and the reaction mixture was stirred until tlc (MC / MeOH = 6 / 1) showed completion of the reaction. The resin was removed by filtration and washed 2 times with 10 mL portions of water. The combined water phases were evaporated to dryness and the crude material purified by flash chromatography (5 g silica gel). Yield: 42 mg (74%) of a colorless oil. ^1H NMR (mixture of α and β anomers; D_2O; HDO set to 4.8 ppm): δ 1.56 (ddd, 1H, J = 9.3 Hz; J = 12. 8 Hz, H-2ax, β-pyr); 1.80 (ddd, 1H, J = 3.2 Hz, J = 10.6 Hz, J = 13.7 Hz, H-2ax, α-pyr); 2.11 (ddd, 1H, J = 2.9 Hz, J = 4.4 Hz, H-2eq, α-pyr); 2.28 (ddd, 1H, J = 2.2 Hz, J = 4.0 Hz, H-2eq, β-pyr); 3.22-4.02 (m, 8H, H-3, H-4, H-5, H-5', α+β-pyr); 4.91 (dd, 1H, H-1, β-pyr); 5.27 (dd, 1H, α-pyr). ^{13}C NMR (mixture of α and β anomers; D_2O): δ 96.31; 93.23; 71.37; 71.15; 68.09; 64.56; 63.94; 61.90; 38.34; 36.35. IR (on Si plate): ν 2103 cm^{-1}. Anal. for $C_5H_9N_3O_3$ (159.14): Calcd. C, 37.74; H, 5.70; N, 26.40 Found C, 37.91; H, 5.62; N, 26.29.

3,4-O-Isopropylidene-5-deoxy-D-lyxitol (13):

To a solution of 3 g (10.1 mmol) of 2,3-O-isopropylidene-D-arabinose-diethylmercaptal **12**[13] in 100 mL of ethanol a suspension of 30 g of freshly prepared Raney-nickel in ethanol were added. The reaction mixture was heated under reflux for 80 min. The progress of the reaction was monitored by tlc (EA / PE = 1 / 2). After completion of the reaction, the suspension was filtered over a pad of Celite and washed 3 times with 30 ml portions of ethanol. The combined organic layers were evaporated under reduced pressure. A slightly yellow colored oil (1.42 g, 80%) was obtained, which was used directly for further reactions. $[\alpha]_D^{20}$ = -13.5° ($CHCl_3$; c = 0.88). ^1H NMR ($CDCl_3$): δ 1.32 (d, 3H, J = 6.0 Hz, H-5); 1.35; 1.38 (2 s, 6H, 2xCH_3); 3.0-3.4 (br s, 2H, 2xOH); 3.52 (dd, 1H, J = 5.72 Hz, J = 7.7 Hz, H-3); 3.53-3.82 (m, 3H, H-2, H-1, H-1'); 4.06 (dq, 1H, J = 6.0 Hz, J = 7.8 Hz, H-4). ^{13}C NMR ($CDCl_3$): δ 108.51; 82.47; 75.06; 72.44; 63.80; 27.27; 26.84; 18.99

2,3-O-Isopropylidene-4-deoxy-D-threose (14):

To a solution of 1.15 g (6.53 mmol) of **1** in 30 mL of ethyl acetate, 3.476 g (1.2 equiv.) of lead tetraacetate were added. The suspension was stirred for 10 min while the temperature rose to 40 °C. After completion of the reaction (as judged by tlc: PE / EA = 2 / 1), 0.5 ml of ethylene glycol were added. The suspension was filtered over a pad of Celite and washed three times with 30 mL portions of ethyl acetate. The combined organic phases were evaporated at reduced pressure (bath temperature below 30 °C, pressure of 15 torr) and

the residue was coevaporated twice with 20 mL of dry carbon tetrachloride. The oily residue which contained traces of carbon tetrachloride was used directly for further reactions. A small portion of the crude product was purified by chromatography over Florisil® for obtaining the NMR data. ^{1}H NMR ($CDCl_3$): δ 1.34 (d, 2H, J = 6.0 Hz, H-4); 1.39; 1.44 (2 s, 6H, 2xCH_3); 3.83 (dd, 1H, J = 2.5 Hz, J = 8.0 Hz, H-2); 4.04-4.12 (m, 1H, H-3); 9.67 (d, 1H, J = 2.5 Hz, H-1). ^{13}C NMR ($CDCl_3$): δ 200.81; 110.76; 85.94; 72.75; 27.03; 26.05; 18.04

(2R,3S,4R)-2,3-O-Isopropylidene-6-hepten-2,3,4-triol (15):
850 mg (5.9 mmol) of **14** were treated according to **method B**. After flash chromatography (20 g, PE / EA = 6 / 1), 660 mg (60 %) of **15** were obtained as unseparable mixture of the 4-epimers in a ratio of 20 : 1 (as judged by ^{13}C-NMR spectroscopy). Major diastereomer: ^{1}H NMR ($CDCl_3$): δ 1.28 (d, 3H, J = 6.0 Hz, H-1); 1.31; 1.34 (2s, 6H, 2xCH_3); 2.05-2.40 (m, 3H, H-5, H-5', 4-OH); 3.43 (dd, 1H, J = 5.5 Hz, J = 8.0 Hz, H-3); 3.67 (dq, 1H, J = 6.0 Hz, J = 3.85 Hz, H-2); 4.04 (dd, 1H, J = 6.0 Hz, J = 8.0 Hz, H-4); 5.05-5.14 (m, 2H, H-7, H-7'); 5.70-5.87 (m, 1H, H-6). ^{13}C NMR ($CDCl_3$): δ 134.12; 118.21; 108.02; 84.13; 73.92; 70.69; 37.77; 27.20; 26.80; 19.28

(2R,3S,4R)-6-Hepten-2,3,4-triol (16):
To a solution of 300 mg (1.61 mmol) of **15** in 10 mL of methanol, 1 g of DOWEX 50 W (H^+-form) was added. After stirring for five hours the resin was removed by filtration and washed twice with 20 mL portions of methanol. The combined organic phases were evaporated to dryness. Yield 190 mg (81 %) of **16**.
^{1}H NMR ($CDCl_3$, D_2O-exchange): δ 1.21 (d, 3H, J = 6.6 Hz, H-1); 2.3 (dq, 2H, J = 1.4, J = 8.25 Hz, H-5, H-5'); 3.28 (dd, 1H, J = 2.8, J = 4.4 Hz; H-3); 3.76 (dt, 1H, J = 4 .7, J = 8.3 Hz; H-4); 4.04 (dq, 1H, J = 3.0, J = 6.6 Hz; H-2); 5.06 - 5.17 (m, 2H, H-7, H-7'); 5.72-5.91 (m, 1H, H-6). ^{13}C NMR ($CDCl_3$): δ 134.46; 118.17; 75.97; 72.82; 66.90; 37.56; 19.49.

(2R,3S,4S)-6-Hepten-2,3,4-triol (17):
500 mg (3.47 mmol) of **14** were treated according to **method A**. After flash chromatography (20 g, $CHCl_3$ / MeOH = 6 / 1), 211 mg (41.6 %) of **17** were obtained as a colorless oil.
^{1}H NMR ($CDCl_3$, D_2O-exchange): δ 1.22 (d, 3H, J = 6.3 Hz, H-1); 2.34 (t, 2H, J = 7.15 Hz, H-5, H-5'); 3.21 (t, 1H, J = 2.7 Hz, H-3); 3.73 (dt, 1H, J = 2.5, J = 6.6 Hz, H-4); 3.9 (dq, 1H, J = 3.6, J = 6.3 Hz, H-2); 5.08 - 5.20 (m, 2H, H-7, H-7'); 5.70-5.90 (m, 1H, H-6). ^{13}C NMR ($CDCl_3$): δ 134.25; 118.00; 75.46; 72.54; 69.62; 38.48; 19.61.

Methyl 2,6-dideoxy-α-D-lyxo-hexopyranoside (18):
A solution of 190 mg (1.3 mmol) of **16** in 20 mL of a mixture of MC / MeOH = 4 / 1 was cooled to - 78 °C. Ozone was bubbled through the solution until a blue color remained. The excess of ozone was removed by sparging with argon followed by treatment with 682 mg (2 equiv.) of triphenylphosphine. The mixture was allowed to warm up to room temperature. After stirring for 10 hours the solvent was evaporated at reduced pressure and the residue was purified by flash chromatography over silica gel (10 g silica gel; $CHCl_3$ / MeOH = 12 / 1). Yield: 179 mg (85 %) of **18**. ^{1}H NMR ($CDCl_3$, D_2O-exchange): δ 1.25 (d, 3H, J = 6.6 Hz, H-6); 1.70-1.90 (m, 2H, H-2, H-2'); 3.30 (s, 3H, OCH_3); 3.60 (br s, 1H, H-4); 3.85 (q, 1H, J = 6.3 Hz, H-5);

3.90-4.00 (m, 1H, H-3); 4.74 (d, 1H, J = 3.3 Hz, H-1). ^{13}C NMR (D_2O, DMSO = 40.6 ppm as internal standard): δ 100.12; 72.01; 68.16; 66.47; 56.12; 32.52; 17.42.

2,6-Dideoxy-D-xylo-hexose (D-boivinose) (19):

Through a solution of 130 mg (0.89 mmol) of **17** in 20 mL of a mixture of MC / MeOH = 4 / 1 ozone was bubbled at - 78 °C until a blue color remained. The excess of ozone was removed by sparging with argon followed by treatment with 466 mg (2 equiv.) of triphenylphosphine. The mixture was allowed to warm up to room temperature. After 1 hour the solvent was removed at reduced pressure and the residue was purified by flash chromatography over silica gel (10 g silica gel; $CHCl_3$ / MeOH = 14 / 1) to yield 117 mg (89 %) of **19**. $[\alpha]_D^{20}$ = +2.9° (H_2O; c = 0.11) (ref. 6b: $[\alpha]_D^{20}$ = +3.9° (H_2O; c = 0.6; in equilibrium). ^1H NMR (D_2O; HDO set to 4.8 ppm, mixture of anomers, approx. 70% β): δ 1.27 (d, 3H, J = 6.6 Hz, H-6); 1.87 (m, 2H, H-2, H-2´); 3.42 (d, 1H, J = 3.0 Hz, H-3); 4.14 (dd, 1H, J = 3.0 Hz, J = 6.3 Hz, H-4); 4.45 (m, 1H, H-5); 5.10 (dd, 1H, J = 9.1 Hz, J = 3.0 Hz, H-1). ^{13}C NMR (D_2O, dioxane as external standard set to 67.00 ppm): δ 92.21; 69.75; 69.55; 68.90; 34.16; 16.17.

Methyl 3,4-di-O-acetyl-2,6-dideoxy-α-D-lyxo-hexopyranoside (20):

20 mg of **18** were reacted according to **method C**. Yield: 18 mg (59 %) of **20** as colorless oil. ^1H NMR ($CDCl_3$): δ 1.13 (d, 3H, J = 6.3 Hz, H-6); 1.82 (dd, 1H, J = 12.65 Hz, J = 12.0 Hz, J = 5.2 Hz, H-2ax); 1.95, 2.15 (2s, 6H, 2xCH_3); 2.05 (dd, 1H, J = 3.8 Hz, H-2´); 3.30 (s, 3H, OCH_3); 4.20 (q, 1H, J = 6.6 Hz, H-5); 4.84 (d, 1H, J = 3.0 Hz, H-1); 5.15 (d, 1H, J = 1.0 Hz, H-4); 5.25 (ddd, 1H, J = 3.0 Hz, J = 4.95 Hz, H-3). ^{13}C NMR ($CDCl_3$): δ 178.32; 177.53; 98.50; 69.81; 66.73; 64.47; 54.89; 29.85; 20.90; 20.74; 16.50. Anal. for $C_{11}H_{18}O_6$ (246.26): Calcd. C, 53.65; H, 7.37; Found C, 53.51; H, 7.26.

1,3,4-Tri-O-acetyl-2,6-dideoxy-β-D-xylo-hexopyranose (21):

20 mg of **19** were treated according to **method C**. Yield: 20 mg (54 %) of **21** as a colorless oil.^1H-NMR ($CDCl_3$, mixture of anomers, approx. 70 % β): δ 1.17 (d, 3H, J = 6.6 Hz, H-6); 2.08; 2.09; 2.11 (3s, 9H, 3xCH_3); 2.05-2.15 (m, 2H, H-2ax, H-2eq); 4.12 (dq, 1H, J = 7.1 Hz, J = 1.4 Hz, H-5); 4.68 (d, 1H, J = 3.3 Hz, H-4); 5.07 (m, 1H, H-3); 5.92 (dd, 1H, J = 7.0 Hz, J = 3.3 Hz, H-1). ^{13}C NMR ($CDCl_3$): δ 170.57; 169.83; 169.17; 90.57; 69.53; 68.17; 67.78; 30.31; 21.04; 20.96; 20.69; 16.26. Anal. for $C_{12}H_{18}O_7$ (274.27): Calcd. C, 52.55; H, 6.61; Found C, 52.72; H, 6.79.

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