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A convenient synthesis of L-ribose from D-fructose

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ABSTRACT

An efficient method for the stereoselective synthesis of L-ribose was accomplished starting from commercially inexpensive D-fructose. The intermediates in the process can serve as versatile precursors for the preparation of L-nucleoside analogues.

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1. Introduction

Nucleoside analogues based on modifications of heterocyclic bases and/or modifications on the sugar moiety of natural nucleosides are found to be prominent drugs in the management of several viral infections.[1] In the beginning of 90s replacement of D-ribose in natural nucleosides with the corresponding sugar enantiomer, L-ribose, leading to the formation of L-nucleosides, has opened a new era in development of novel antiviral agents. Since then, a large number of L-nucleoside analogues have been synthesized and their antiviral activities were evaluated.[2] As a result, clevudine (**1**, L-FMAU, 2′-fluoro-5-methyl-β-L-arabinofuranosyluridine, Chart 1),[3] is in the market and elvucitabine (**2**, L-Fd4C, L-2′,3′-Dideoxy-2′,3′-didehydro-5-fluorocytidine)[4] in under phase II clinical trials[4c] for the treatment of HBV infection due to their potent inhibitory activity against chronic hepatitis B virus (HBV) DNA polymerase. Two other L-nucleoside analogues, valtorcitabine (**3**, Val-L-dC, 3-*O*-valinyl-L-2′-deoxycytidine)[5] and telbivudine (**4**, L-dT, L-thymidine)[6] were proven to be extremely specific and selective anti-HBV agents with exceptional safety profile. R1518 **6**,[7] a valine ester prodrug of levovirin (**5**, 1-(β-L-ribofuranosyl)-1,2,4-triazole-3-carboxamide)[8] was found to exhibit anti-HCV activity is currently undergoing clinical trials. An L-ribofuranosyl benzimidazole namely maribavir (**7**, 1*H*-β-L-ribofuranoside-2-isopropylamino-5,6-dichlorobenzimidazole)[9] was found to be a potent and selective oral antiviral drug to inhibit cytomegalovirus (CMV) infection (Chart 1). Recently, NOX-E36, a 40-meric L-RNA oligonucleotide was developed to target the chemokine MCP-1 for treating inflammatory diseases like lupus nephritis.[10] Apparently the advantages of L-nucleoside analogues are their less cytotoxicity and higher metabolic stability over D-nucleosides while maintaining comparable and sometimes greater antiviral activity. One of the essential starting materials for the synthesis of all these L-nucleoside based antiviral agents is a conveniently protected L-ribose.

Several good synthetic methods were reported for L-ribose[11] starting from chiral pool L-sugars, such as L-arabinose,[12] L-xylose,[13]

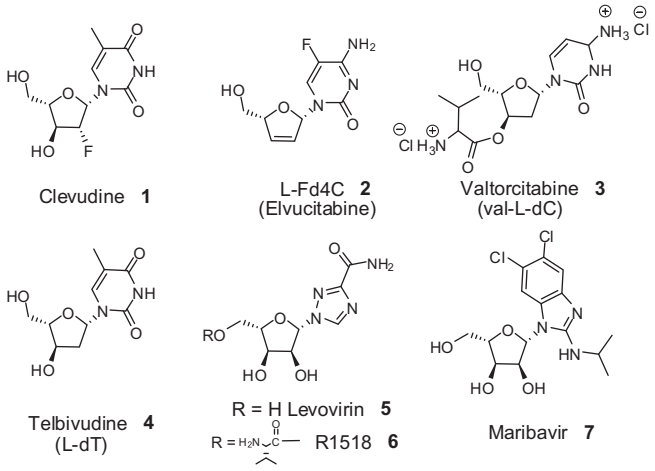

Chart 1. L-Ribose derived pharmaceuticals either in the market or under clinical trials.

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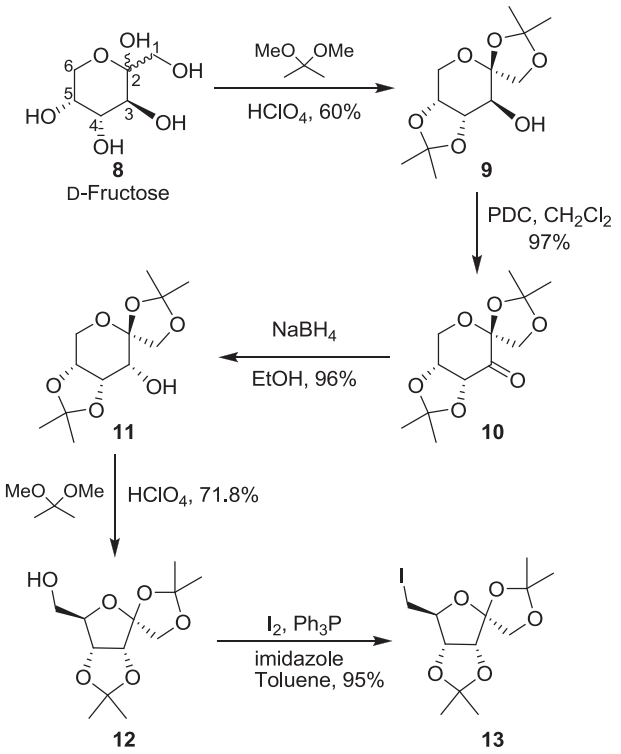
and D-sugars, for instance D-ribose,[14] D-glucose,[15] D-galactose,[16] and D-mannose.[17] However, the high prices of L-ribose indicate the requirement of an alternative synthetic method, which is simple, efficient, and inexpensive. Even though, molybdenum catalyzed epimerization of L-arabinose[18] (Bílik reaction) is one of the efficient method to produce L-ribose, its separation equipment using an ion-exchange resin and a recovery step for the starting material makes the preparation cumbersome. Owing to the importance of L-ribose in drug development, herein we wish to report an efficient method for the stereoselective synthesis of L-ribose and its derivatives from commercially inexpensive raw material, D-fructose. Furthermore, the present synthesis involves easy workup and purification techniques, which can be adaptable for large scale production of L-ribose.

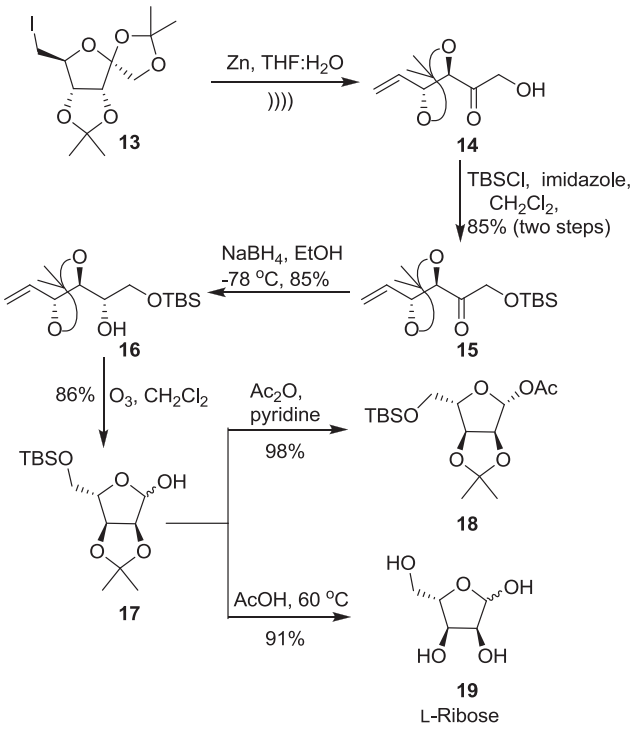
2. Results and discussion

As shown in Scheme 1, D-fructose **8** was converted to 1,2:4,5-di-*O*-isopropylidene-D-fructose **9**[19] by the conventional method. Pyridinium dichromate mediated oxidation of **9** to give 1,2:4,5-di-*O*-isopropylidene-D-*erythro*-2,3-hexodiulo-2,6-pyranose **10**[19] followed by stereoselective reduction afforded 1,2:4,5-di-*O*-isopropylidene-D-psicopyranose **11**[19] in excellent yield. Isomerization of pyranose **11** to its furanose isomer 1,2:3,4-di-*O*-isopropylidene-D-psicofuranose **12**[19,20] was accomplished using catalytic $HClO_4$ in acetone and 2,2-dimethoxy propane.[21] Substitution of the primary hydroxyl group in **12** with iodine using I_2/Ph_3P/imidazole under reflux in toluene provided 6-deoxy-6-iodo-1,2:3,4-di-*O*-isopropylidene-D-psicofuranose **13**[19,20] in 95% yield.



Scheme 1. Synthesis of 6-deoxy-6-iodo-1,2:3,4-di-*O*-isopropylidene-D-psicofuranose **13**.

Zinc mediated fragmentation of **13** in THF/H_2O (9:1) under sonication gave α-hydroxy ketone **14**. However, substantial decomposition of compound **14** was observed during column chromatography. Due to this a one-pot metal mediated fragmentation followed by protection of the free hydroxyl group with *tert*-butyldimethylsilyl (TBDMS) was carried out to produce compound **15**[22] in good yield (85% over two steps). Compound **15** upon reaction with $NaBH_4$ at −78 °C in ethanol[23] underwent a stereoselective reduction producing the 2,3-*anti* alcohol **16**[24] as a single diastereomer. Ozonolysis of the olefin in **16** gave 2,3-*O*-isopropylidene-5-*O*-(*tert*-butyldimethylsilyl)-L-ribose **17**[24,25] as an anomeric mixture in 86% yield. Acetylation of the anomeric alcohol using acetic anhydride resulted 1-*O*-acetyl-2,3-*O*-isopropylidene-5-*O*-(*tert*-butyldimethylsilyl)-β-L-ribofuranose **18** as single diastereomer.[26] On the other hand a one-pot deprotection of acetonide and TBDMS using acetic acid at 60 °C provided pure L-ribose **19**[27] in 91% yield (Scheme 2).



Scheme 2. Synthesis of L-ribose.

3. Conclusion

In conclusion, an efficient synthetic method for the production of L-ribose in an overall yield of 21.5% from D-fructose was developed. Further, the preparation of L-nucleoside analogues is in progress.

4. Experimental section

4.1. General

All the reactions were carried out under inert atmosphere with dry solvents under anhydrous conditions unless otherwise mentioned. Acetone was distilled from potassium permanganate, CH_2Cl_2 was distilled from calcium hydride, ethanol was distilled from sodium ethoxide followed magnesium, pyridine was distilled from KOH and toluene was distilled from sodium. TLC was run on Silica Gel 60 F_{254} (Merck) and the spots were detected by staining with H_2SO_4 in methanol (5%, v/v) or phosphomolybdic acid in ethanol (5%, w/v) and heat. Silica gel (100–200 mesh) was used as a stationary phase for column chromatography. NMR spectra were recorded at 25 °C on a Bruker AvanceIII 400 (400 MHz for ^1H and 100 MHz for ^{13}C) or 500 (500 MHz for ^1H and 125 MHz for ^{13}C) instrument with $CDCl_3$ or D_2O as solvent and residual $CHCl_3$ (δ_H 7.26 ppm) or D_2O (δ_H 4.79 ppm) as internal standard for ^1H and

$CDCl_3$ (δ_C 77.0 ppm) as internal standard for ^{13}C. Chemical shifts are given in δ (ppm) and coupling constants (J) in hertz. IR spectra were recorded on JASCO FT/IR-5300. Elemental analyses were recorded on a Thermo Finnigan Flash EA 1112 analyzer. Mass spectra were recorded on Shimadzu-LCMS-2010A mass spectrometer.

*4.1.1. 1,2:4,5-Di-O-isopropylidene-D-fructopyranose (**9**)*[19]. To a stirred suspension of D-fructose **8** (150 g, 0.83 mol) in a mixture of acetone (3 L) and 2,2-dimethoxy propane (60.26 mL, 0.49 mol) at 0 °C was added 70% perchloric acid (35 mL, 0.40 mol) dropwise. The reaction mixture was stirred for 6 h while slowly allowing it to 25 °C. After completion of the reaction (by TLC) the mixture was quenched with concd ammonium hydroxide (39.2 mL) and the solvents were evaporated to give a crystalline residue, which was dissolved in CH_2Cl_2 (1.6 L). The solution was washed with brine (2×150 mL), dried over anhydrous Na_2SO_4, and evaporated. The crude product was recrystallized from CH_2Cl_2/hexane to give **9** (130 g, 60%) as white needles. δ_H (500 MHz, $CDCl_3$): 4.21 (dd, 1H, J=2, 6 Hz), 4.18 (d, 1H, J=9 Hz), 4.13 (dd, 1H, J=5.6, 7.5 Hz), 4.10 (d, 1H, J=2.5 Hz), 4.01 (d, 1H, J=13.5 Hz), 3.97 (d, 1H, J=9 Hz), 3.66 (dd, 1H, J=7, 8 Hz), 2.00 (d, 1H, J=8.5 Hz), 1.53 (s, 3H), 1.51 (s, 3H), 1.43 (s, 3H), 1.36 (s, 3H). δ_C (125 MHz, $CDCl_3$): 111.7, 109.1, 104.4, 77.1, 73.2, 72.0, 70.1, 60.5, 27.8, 26.2, 26.2, 25.8.

*4.1.2. 1,2:4,5-Di-O-isopropylidene-D-erythro-2,3-hexodiulo-2,6-pyranose (**10**)*[19]. A solution of 1,2:4,5-di-*O*-isopropylidene-D-fructose **9** (40 g, 0.15 mol) in dry CH_2Cl_2 (320 mL) was added to a mixture of pyridinium dichromate (42 g, 0.11 mol) and acetic anhydride (48.5 mL, 0.51 mol) in dry CH_2Cl_2 (500 mL) under nitrogen atmosphere. The resulting mixture was stirred under reflux until the complete conversion (~6 h), then cooled to 25 °C and solvent was removed in vacuo. Et_2O was added (1 L) to the solid residue and the mixture was filtered over Celite. The Celite bed was washed several times with Et_2O. Removal of Et_2O under vacuum provided the crude compound, which was purified by column chromatography using EtOAc/hexane (4:1) to give pure **10** (38.5 g, 97%) as a white solid. R_f (20% EtOAc/hexane) 0.63; δ_H (400 MHz, $CDCl_3$): 4.72 (d, 1H, J=5.6 Hz), 4.61 (d, 1H, J=5.6 Hz), 4.54 (dd, 1H, J=1.6, 5.6 Hz), 4.38 (dd, 1H, J=2, 13.2 Hz), 4.12 (d, 1H, J=13.2 Hz), 3.98 (d, 1H, J=9.6 Hz), 1.54 (s, 3H), 1.45 (s, 3H), 1.39 (s, 6H). δ_C (100 MHz, $CDCl_3$): 196.9, 113.8, 110.6, 104.1, 77.9, 75.8, 70.0, 60.0, 27.1, 26.5, 26.1, 26.0.

*4.1.3. 1,2:4,5-Di-O-isopropylidene-D-psicopyranose (**11**)*[19]. To a stirred solution of **10** (22 g, 85.2 mmol) in ethanol (220 mL) was added $NaBH_4$ (1.6 g, 42.3 mmol) at 15 °C. After stirring at this temperature for 1 h the solvent was evaporated under reduced pressure. Et_2O (132 mL) and saturated NH_4Cl solution (80 mL) were added to the residue. The mixture was again stirred for 4 h at 25 °C. Et_2O layer was recovered and the aqueous layer was extracted with Et_2O (3×50 mL). The combined Et_2O layers were dried over anhydrous Na_2SO_4 and evaporated. The crude product was recrystallized in hexane to give compound **11** (21.3 g, 96%) as a white solid. R_f (20% EtOAc/hexane) 0.33; δ_H (400 MHz, $CDCl_3$): 4.42 (dd, 1H, J=4, 6.4 Hz), 4.22 (m, 2H), 3.93–4.02 (m, 3H), 3.73 (dd, 1H, J=4, 6.4 Hz), 2.43 (d, 1H, J=6.4 Hz), 1.53 (s, 3H), 1.47 (s, 3H), 1.38 (s, 3H), 1.35 (s, 3H). δ_C (100 MHz, $CDCl_3$): 111.0, 109.4, 104.8, 72.9, 72.1, 71.8, 68.6, 61.1, 26.4, 26.1, 25.9, 25.0.

*4.1.4. 1,2:3,4-Di-O-isopropylidene-D-psicofuranose (**12**)*[21]. To a stirred solution of compound **11** (22 g, 84.61 mmol) in a mixture of acetone (230 mL) and 2,2-dimethoxy propane (5.48 mL, 44.98 mmol) at 0 °C was added 70% perchloric acid (1.32 mL, 14.38 mmol) dropwise. The reaction mixture was stirred for 3 h while slowly allowing it to 25 °C. After completion of the reaction (by TLC) the mixture was quenched with concd, ammonium hydroxide (2.53 mL) and the solvents were evaporated. The residue was partitioned between Et_2O (100 mL) and water (50 mL) and the water layer was extracted with Et_2O (3×50 mL). The combined Et_2O layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and evaporated. The crude product was purified by flash column chromatography on silica gel to give compound **12** (15.8 g, 71.8%) as a white solid. R_f (20% EtOAc/hexane) 0.75; δ_H (400 MHz, $CDCl_3$): 4.92 (d, 1H, J=5.6 Hz), 4.66 (d, 1H, J=6 Hz), 4.30–4.36 (m, 2H), 4.08 (d, 1H, J=10.6 Hz), 3.76 (br d, 1H, J=12.4 Hz), 3.65 (td, 1H, J=3.2, 10.4 Hz), 3.20 (dd, 1H, J=2.8, 10.4 Hz), 1.52 (s, 3H), 1.45 (s, 3H), 1.41 (s, 3H), 1.33 (s, 3H). δ_C (100 MHz, $CDCl_3$): 113.4, 112.3, 111.7, 86.8, 85.8, 81.6, 69.9, 63.9, 26.5, 26.3, 26.1, 24.8.

*4.1.5. 6-Deoxy-6-iodo-1,2:3,4-di-O-isopropylidene-D-psicofuranose (**13**)*[19]. To a mixture of 1,2:3,4-di-*O*-isopropylidene-D-psicofuranose **12** (13 g, 49.98 mmol), triphenylphosphine (39.33 g, 149.94 mmol), and imidazole (9.74 g, 149.94 mmol) in toluene (1 L) at 80 °C was added iodine (25.39 g, 99.96 mmol) portion wise for a period of 1 h. Once the addition was completed the reaction mixture was refluxed for 7 h. Upon completion of the reaction, it was brought to 25 °C and aqueous saturated Na_2CO_3 solution (800 mL) was added. After the solution become clear iodine was added slowly until the organic layer became colored. Stirred for 10 min, sodium thiosulfate was added until decolorization occurs. The mixture was transferred to a separating funnel and the organic layer was diluted with toluene. The organic layer was washed with water dried over anhydrous $MgSO_4$, and concentrated. Et_2O and hexane were added to precipitate out the triphenylphosphine oxide. Filtration and concentration followed by column chromatography afforded compound **13** (17.5 g, 95%) as a pale yellow color liquid that was solidified after 7 days at 0 °C. R_f (10% EtOAc/hexane) 0.69; δ_H (400 MHz, $CDCl_3$): 4.78 (d, 1H, J=5.6 Hz), 4.60 (d, 1H, J=5.6 Hz), 4.34 (dd, 1H, J=6, 10 Hz), 4.24 (d, 1H, J=10 Hz), 4.00 (d, 1H, J=10 Hz), 3.25 (dd, 1H, J=6, 10 Hz), 3.20 (t, 1H, J=10 Hz), 1.45 (s, 3H), 1.41 (s, 3H), 1.35 (s, 3H), 1.30 (s, 3H). δ_C (100 MHz, $CDCl_3$): 113.7, 112.7, 111.7, 86.1, 85.4, 83.4, 69.6, 26.4, 26.3, 26.3, 25.0, 6.8. Low-resolution MS (EI): m/z: 371 (M^++1). Anal. Calcd for $C_{12}H_{19}IO_5$: C, 38.93; H, 5.17. Found: C, 38.85; H, 5.23.

*4.1.6. (4R,5R)-1-(2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl)-2-(tert-butyldimethylsilyloxy)ethan-1-one (**15**)*[22]. To a solution of 6-deoxy-6-iodo-1,2:3,4-di-*O*-isopropylidene-D-psicofuranose **13** (6.0 g, 16.21 mmol) in THF/water (9:1 v/v, 420 mL), zinc dust (10.6 g, 162.1 mmol) was added. The resulting suspension was sonicated at 40 °C until TLC showed complete consumption of starting material (~2 h). The reaction mixture was cooled to 25 °C and treated with Et_2O (500 mL) and water (100 mL) and filtered through a plug of Celite to separate the Et_2O and water layers. The aqueous layer was extracted with Et_2O (3×200 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated to give crude α-hydroxy ketone **14** as a yellow oil (3.0 g). R_f (30% EtOAc/hexane) 0.27; δ_H (400 MHz, $CDCl_3$): 5.57–5.64 (m, 1H), 5.43 (dd, 1H, J=16.8 Hz), 5.26 (d, 1H, J=10.4 Hz), 4.87 (m, 1H), 4.71 (d, 1H, J=8.4 Hz), 4.52 (dd, 1H, J=4.8, 20.4 Hz), 4.22 (d, 1H, J=4.8, 20.4 Hz), 2.88 (t, 1H, J=4.8Hz), 1.60 (s, 3H), 1.39 (s, 3H). δ_C (100 MHz, $CDCl_3$): 209.2, 131.2, 119.1, 110.9, 81.7, 78.4, 67.9, 26.5, 24.4. The oily residue (3 g) was redissolved in CH_2Cl_2 (50 mL), imidazole (4.41 g, 54.86 mmol) and *tert*-butyldimethylsilyl chloride (4.48 g, 32.38 mmol) were added sequentially. The reaction mixture was stirred overnight at 25 °C and quenched with saturated NH_4Cl solution (50 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3×20 mL). Combined organic layers were washed with brine then dried over anhydrous Na_2SO_4 and filtered. The crude product was purified by flash column chromatography using EtOAc/hexane (1:24) to afford pure ketone **15** (4.15 g, 85% from **13**) as a colorless liquid. R_f (10% EtOAc/hexane) 0.62; IR (neat): 3088, 2932, 2895, 1738, 1645, 1572, 1464, 1381 cm^{-1}.

δ_H (400 MHz, $CDCl_3$): 5.64–5.72 (m, 1H), 5.40 (d, 1H, J=16.8 Hz), 5.23 (d, 1H, J=10.4 Hz), 4.87 (m, 2H), 4.45 (d, 1H, J=18.8 Hz), 4.20 (d, 1H, J=18.8 Hz), 1.59 (s, 3H), 1.38 (s, 3H), 0.91 (s, 9H), 0.06 (br s, 6H). δ_C (100 MHz, $CDCl_3$): 206.4, 132.6, 118.8, 110.2, 81.8, 78.1, 68.5, 26.9, 25.8, 24.8, 18.3, −5.4, −5.5. Low-resolution MS (EI): m/z: 301 (M^++1). Anal. Calcd for $C_{15}H_{28}O_4Si$: C, 59.96; H, 9.39. Found: C, 59.78; H, 9.45.

*4.1.7. (4S,5R)-1-(2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl)-2-(tert-butyldimethylsilyloxy)-1(S)-ethan-1-ol (**16**)*[24]. A solution of ketone **15** (4 g, 13.33 mmol) in ethanol (40 mL) was added to $NaBH_4$ (1 g, 26.66 mmol) dissolved in ethanol (80 mL) at −78 °C. After 2 h the reaction was quenched with saturated NH_4Cl solution (10 mL) and allowed it to 25 °C. The reaction mixture was concentrated under reduced pressure to give a thick semi solid. EtOAc (150 mL) and water (50 mL) were added and the organic layer was separated and the aqueous layer was extracted with EtOAc (3×50 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and the solvent was concentrated under reduced pressure. The crude product was purified by flash column chromatography using EtOAc/hexane (3:97) to give alcohol **16** (3.42 g, 85%) as a colorless liquid. R_f (10% EtOAc/hexane) 0.58; IR (neat): 3562, 2986, 2934, 2858, 1645, 1464, 1371 cm^{-1}. δ_H (400 MHz, $CDCl_3$): 6.01–6.09 (m, 1H), 5.41 (dt, 1H, J=1.6, 17.2 Hz), 5.28 (d, 1H, J=10.4 Hz), 4.68 (t, 1H, J=6.4 Hz), 4.05 (dd, 1H, J=6.4, 8.8 Hz), 3.80 (dd, 1H, J=2.8, 9.6 Hz), 3.61–3.70 (m, 2H), 2.51 (d, 1H, J=5.2 Hz), 1.46 (s, 3H), 1.35 (s, 3H), 0.91 (s, 9H), 0.08 (br s, 6H). δ_C (100 MHz, $CDCl_3$): 134.1, 117.5, 108.7, 78.7, 77.4, 69.5, 64.3, 27.8, 25.8, 25.4, 18.3, −5.4, −5.5. Low-resolution MS (EI): m/z: 303 (M^++1). Anal. Calcd for $C_{15}H_{30}O_4Si$: C, 59.56; H, 10.00. Found: C, 59.38, 10.12.

*4.1.8. 2,3-O-Isopropylidene-5-O-(tert-butyldimethylsilyl)-L-ribose (**17**)*[24,25]. A stirred solution of alcohol **16** (3.2 g, 10.59 mmol) in dry CH_2Cl_2 (90 mL) was cooled to −78 °C and ozone was passed until persistence of the blue color. At the same temperature dimethyl sulfide (5 mL) was added and the temperature was slowly allowed to 25 °C. Removal of CH_2Cl_2 followed by flash column chromatography afforded acetal **17** (2.78 g, 86%) as a colorless liquid. R_f (10% EtOAc/hexane) 0.36; major isomer: δ_H (400 MHz, $CDCl_3$): 5.27 (d, 1H, J=10.2 Hz), 4.78 (d, 1H, J=10.2 Hz), 4.69 (d, 1H, J=6 Hz), 4.50 (d, 1H, J=6 Hz), 4.34 (br s, 1H), 3.75 (m, 2H), 1.47 (s, 3H), 1.31 (s, 3H), 0.92 (s, 9H), 0.14 (s, 3H), 0.13 (s, 3H). δ_C (100 MHz, $CDCl_3$): 112.0, 103.4, 87.5, 86.9, 81.7, 64.7, 26.4, 25.8, 24.8, 18.2, −5.6, −5.7. Low-resolution MS (EI): m/z: 305 (M^++1). Anal. Calcd for $C_{14}H_{28}O_5Si$: C, 55.23; H, 9.27. Found: C, 55.14, 9.32.

*4.1.9. 1-O-Acetyl-2,3-O-isopropylidene-5-O-(tert-butyldimethylsilyl)-β-L-ribofuranose (**18**)*[26]. To a stirred solution of acetal **17** (0.5 g, 1.64 mmol) in dry pyridine (20 mL) at 0 °C was added acetic anhydride (0.62 mL, 6.57 mmol). The reaction mixture was stirred overnight and concentrated under reduced pressure. EtOAc (100 mL) and water (30 mL) were added. The organic layer was separated and the aqueous layer was extracted with EtOAc (3×25 mL). The combined organic layers were washed with saturated $CuSO_4$ solution, brine, and dried over anhydrous Na_2SO_4. The solution was filtered and concentrated to give compound **18** (0.55 g, 98%) as a colorless oil. R_f (10% EtOAc/hexane) 0.55; δ_H (400 MHz, $CDCl_3$): 6.14 (s, 1H), 4.76 (d, 1H, J=6.4 Hz), 4.66 (d, 1H, J=6.4 Hz), 4.28 (dd, 1H, J=5.2, 7.6 Hz,), 3.66 (dd, 1H, J=4.8, 10.4 Hz), 3.52 (dd, 1H, J=8, 10.8 Hz), 2.07 (s, 3H), 1.47 (s, 3H), 1.32 (s, 3H), 0.88 (s, 9H), 0.05 (s, 6H). δ_C (100 MHz, $CDCl_3$): 169.5, 112.7, 102.6, 88.1, 85.1, 81.6, 63.5, 26.5, 25.8, 25.1, 21.2, 18.2, −5.4. Low-resolution MS (EI): m/z: 347 (M^++1). Anal. Calcd for $C_{16}H_{30}O_6Si$: C, 55.46; H, 8.73. Found: C, 55.61, 8.64.

*4.1.10. L-Ribose (**19**)*[27]. A solution of acetal **17** (1 g, 3.28 mmol) in 80% aqueous acetic acid (25 mL) was stirred at 60 °C overnight. After complete disappearance of starting material the reaction mixture was concentrated and traces of acetic acid was removed by co-evaporation with toluene. The compound was dissolved in water (25 mL) and washed with CH_2Cl_2 (2×15 mL). Concentration of the water layer provided pure L-ribose **19** (0.45 g, 91%) as a white solid. Major isomer δ_C (100 MHz, D_2O): 93.7, 70.9, 68.8, 67.1, 62.9.

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Supplementary data

Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2011.04.012.

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