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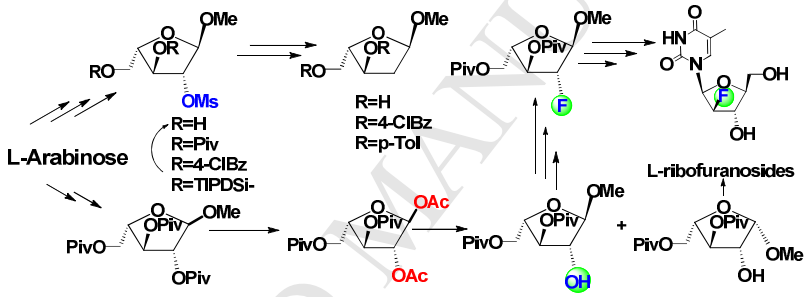

Regio- and stereoselective syntheses of L-pentose derivatives from L-arabinose

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Abstract: Novel L-arabinose, L-ribose, 2-deoxy-L-ribose and 2-fluoro-2-deoxy-L-arabinose derivatives were synthesized from readily available L-arabinose. Different synthetic routes to methyl 3,5-di-*O*-acylated-L-arabino(ribo)furanosides as valued intermediates for the preparation of C-2 functionalized L-pentoses were investigated via regioselective transformations of 1,2-di-*O*-acetyl-3,5-di-O-pivaloyl-L-arabinofuranose, and selective acylation of methyl L-arabinofuranoside with 4-chlorobenzoyl or pivaloyl chloride. Short three-five-step syntheses of methyl 2-deoxy-α-L-ribofuranoside, its 3,5-di-*O*-acyl derivatives, valuable precursors for preparation of antiviral 2′-deoxy- L-nucleosides, were accomplished via simple and efficient reduction of methyl 2-*O*-mesyl-L-arabinofuranoside with L-Selectride or tandem reaction involving a complex hydride 2-deoxygenation/ acylation of intermediate 2-deoxysugar. A new synthesis of 2′-deoxy-2′-fluoro-β- L-arabinofuranosyl thymine (L-FMAU) was performed using a mild fluorination of protected L-ribofuranoside and a novel sequence of conversions for the preparation of 2-deoxy-2-fluoro-L-arabinofuranoside derivatives.

Keywords: L-sugars / regioselective reactions / stereoselective deoxygenation / fluorination/ fluoronucleosides

1.Introduction

Carbohydrates are an interesting class of biomolecules with important biological functions and large structural variability. Modification of carbohydrates, preparation of their selectively protected derivatives provides useful precursors for the synthesis of nucleoside analogues and polysaccharides. A set of synthetic derivatives of L-carbohydrates, which are not widely abundant in nature, have been prepared in the past decades and utilized in the development of anti-HBV and -HIV-agents on the basis of L-nucleosides,[1] and the use of them in pharmaceutical application has considerably increased. The L-enantiomers of natural nucleosides have attracted great interest as useful antiviral agents, due to their potent biological activity and lower toxicity profiles in comparison with their D-counterparts.[2] Since the discovery of L-3′-thiacytidine (lamivudine, L-FTC)[3] as an anti-hepatitus B virus (HBV) drug, a series of L-nucleosides have shown antiviral activity with greatly reduced toxicity. Among these, the most active L-nucleosides with potent and selective antiviral activities include 1-(2-deoxy-β-L-ribofuranosyl)thymine (β-L-thymidine, telbivudine, **1**),[4,5] its 2′-fluorinated analogue, 1-(2-deoxy-2-fluoro-β-L-arabinofuranosyl)thymine (L-FMAU, clevudine, **2**)[6] and L-2′deoxycytidine (L-dC, **3**)[4] (Fig.1). β-L-Thymidine (**1**) is currently approved and being used for the treatment of acute and chronic hepatitis infections,[5] and clevudine (**2**) is a promising agent against HBV with excellent selectivity, few side effects and an unusual mode of action.[7] L-2′,3′-Dideoxy-2′,3′-didehydro-5-fluorocytidine (elvucitabine, **4**) was found to be active against human immunodeficiency virus (HIV).[8]

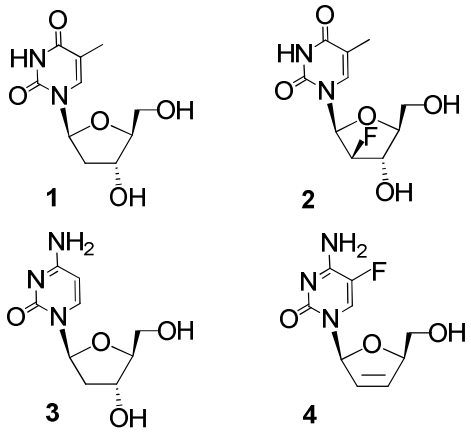


Fig. 1. Biologically active L-nucleosides with selective antiviral activities.

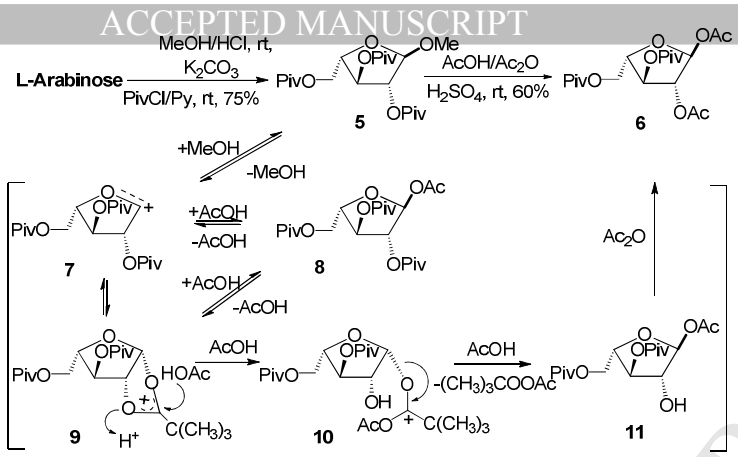
Several approaches have been reported for the synthesis of L-pentofuranonucleosides which require ready access to L-monosaccharides, especially L-ribose and L-deoxyribose derivatives. Because of the special interest in L-nucleosides modified on the sugar moiety and/or heterocyclic base, numerous synthetic methods have been published for the preparation of 2-deoxy-L-ribose, L-ribose and 2-fluoro-2-deoxy-L-arabinose derivatives.[9,10] A great deal of effort has been devoted to practical methods for the synthesis of L-deoxyribose (using predominantly radical processes on the key deoxygenation step) and L-ribose, the key intermediates for 2′-deoxy- L-ribo- and L-ribonucleosides, from readily available D-sugars,[11-16] such as D-mannitol, D-glucose, D-galactose, D-ribose, D-fructose and L-sugars, for instance, L-arabinose[17-22] as the starting materials. Therefore, elaboration of synthetic approaches for novel modified L-pentofuranose derivatives that can be used in glycosylation reactions, and designing various L-nucleosides with potent antiviral properties is of considerable interest starting from available carbohydrates.

The present paper describes new synthetic routes to L-arabinofuranose, L-ribofuranose and 2-fluoro-2-deoxy-L-arabinofuranose derivatives based on regio- and stereoselective transformations of methyl L-arabinofuranosides derived from readily available L-arabinose. It is also focused on the synthesis of methyl 2-deoxy-L-ribofuranoside and its acylated derivatives, valuable intermediates in the synthesis of antiviral 2′-deoxy-L-ribonucleosides via preparation of methyl 3,5-*O*-protected-α-L-arabinofuranosides, subsequent 2-*O*-mesylation and an efficient reduction of intermediate 2-*O*-mesyl-α-arabinofuranosides with a complex hydride on the key step. Synthesis of L-FMAU is described from L-arabinose.

2.Results and Discussion

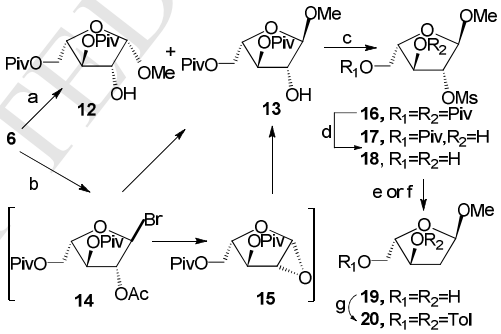
2.1. Syntheses of L-arabinofuranose and 2-deoxy-L-ribose derivatives

The synthetic strategy for L-pentoses started from the preparation of methyl L-arabinofuranosides using methanolysis of L-arabinose in methanol and HCl, then their subsequent acylation with pivaloyl chloride in pyridine. A mixture of pivaloyl derivatives of L-arabinofuranosides **5** was prepared in 75% yield after chromatography on silica gel (Scheme 1). The structures of protected methyl α- and β-arabinofuranosides were confirmed by ^{1}H and ^{13}C NMR spectroscopy and the assignments of the α- and β-anomers, the estimation of their ratio (α/β = 2.3:1) were carried out based upon analysis of the NMR data. A distinction between the two anomers was done on the basis of $^{3}J_{H1,H2}$ magnitudes. The resonances for the anomeric hydrogens of acylated α- and β-glycosides appeared as a singlet ($^{3}J_{1,2}$<1.0 Hz) and a doublet ($^{3}J_{1,2}$=4.5 Hz) at δ 4.84 and 5.08 ppm, respectively, in the ^{1}H NMR spectrum of a mixture of anomers **5**, and in the ^{13}C NMR spectrum, the C-1 signal of the α-anomer at δ 106.7 ppm resonates downfield relative to the β-anomer (δ 101.3 ppm).[23] It is noteworthy that the small value of H-1,2 coupling constant (< 1 Hz), characteristic of *trans*-relationship H1 and H2, and the C-1 chemical shift (>106 ppm) for the predominant α-anomer in the prepared mixture **5** is are consistent with the α-L-arabinofuranosyl moiety of the known protected methyl L-glycosides.[24,25] Furthermore, the assignments of α-anomer signals in the NMR spectra of **5** were supported by comparison of ^{1}H and ^{13}C NMR spectroscopic data of methyl 2,3,5-*O*-pivaloyl-α-L-arabinofuranoside prepared by acylation of individual methyl α-L-glycoside with those of the anomeric mixture. Acetolysis of protected methyl L-glycoside **5** in a mixture of acetic acid/acetic anhydride/concentrated sulphuric acid (11:1.3:1.5, v/v/v) at room temperature gave rise to peracylated L-arabinofuranose derivatives **6** as the main product of reaction in 60% yield after chromatography on silica gel. In a previous investigation into carbohydrates and nucleosides of the D-series, we reported the unconventional formation of 1,2-di-*O*-acetyl-3,5-di-*O*-pivaloyl-D-ribofuranoses along with the 1-*O*-acetyl derivative under acetolysis of pivaloylated methyl β-D-ribofuranoside in $Ac_2O/AcOH/H_2SO_4$.[26] Taking into account these findings on the acetolysis of isomeric acylated pentofuranosides under different conditions, the proposed mechanism for the formation of the 1,2-diacetate **6** during acetolysis of L-glycoside **5** in the presence of increased amount of sulphuric acid (10% vol H_2SO_4) is outlined in Scheme 1. Acetolysis of **5** under the studied conditions involves the generation of the classical oxocarbenium ion **7**, which is in equilibrium between the intermediate 1-*O*-acetyl derivative **8** and the 1,2-pivaloyloxonium ion **9** resulting from neighboring-group participation in ion **7**.



Scheme 1.

Furthermore, a relatively stable cyclic acyloxonium ion **9** can react with acetic acid in the presence of sulphuric acid on a synchronous pathway to form **10**, which in turn give rise to 1-*O*-acetyl-3,5-di-*O*-pivaloyl-L-arabinofuranose (**11**) after the release of a molecule of mixed anhydride and subsequent reaction of the intermediate oxocarbenium ion with acetic acid. The arabinofuranose derivative **11** is acetylated at the 2-hydroxyl group by acetic anhydride to result in the peracylated L-arabinofuranose **6**. The synthetic route to the diacetate **6** via intermediate ions **9** and **10** under the acid-catalyzed reaction conditions (Scheme 1) provide some fit with the mechanism proposed earlier by Wulff et. al [27,28] for the formation of *O*-acetylated α- and β-glycosides with free 2-hydroxyl groups via preparation of the intermediate 1,2-acetoxonium ion, followed by the generation of oxocarbenium ions during the study of the synthesis of sugar orthoesters from cis-glycosyl halides and alcohols. The L-arabinofuranose derivative **6** contains acyl protected groups with different reactivity under acidic and basic conditions. It should be noted that this peculiarity of **6** allows selectively protected L-arabinofuranosides **12** and **13** to be synthesize by two pathways (Scheme 2, path a and b).



Scheme 2. *Reagents and conditions*. a_1) **6**, MeOH, AcCl, rt, 20h, Py, O °C→rt, 37% to **13**, 18% to **12**; a_2) unpurified **6** prepared after acetolysis of **5**, MeOH, AcCl, rt, 16h, Py, O °C→rt, 25% to **13**, 10% to **12**; b) i) $TMSBr/CH_2Cl_2/ZnBr_2$, O °C→rt, ii) K_2CO_3, MeOH/THF, rt, 90 min, 46% to **13**, 10% to **12**; c) MsCl/Py, DMAP, O °C→rt, 16h, 90%; d) NH_3/MeOH, rt, 96h, 46% to **17**; 40% to **18**; e) $Li(i\text{-}Bu)_3BH$, THF/ 1,2-DME -78 °C→rt, 20h, 90% to **19** from **17**; f) $Li(i\text{-}Bu)_3BH$, THF, -78 °C→rt, 20h, 94% to **19** from **18**; g) p-TolCl/Py, O °C→rt, 20h, 86%.

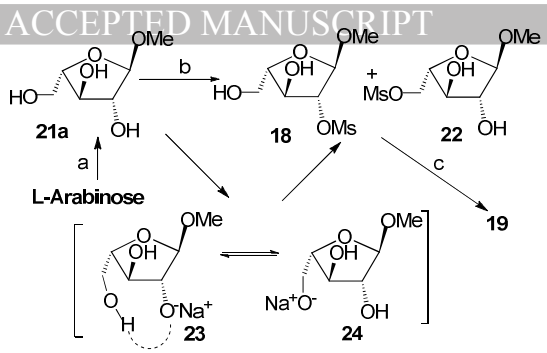
Treatment of **6** with HCl in anhydrous methanol, prepared from acetyl chloride and methanol at 0 °C, provided a mixture of 3,5-di-*O*-pivaloyl-α,β-methyl-L-arabinofuranosides which were separated by column chromatography on silica gel to give pure α- (**13**, 37%) and β-anomer (**12**, 18%) (Scheme 2, conditions a_1). The tandem reaction of **6**, including the chemoselective removal acetyl groups in **6** with 15 mol% of acetyl chloride in methanol,[29] along with methanolysis of intermediate 3,5-*O*-pivaloyl-L-arabinofuranose derivative under acidic conditions (1.2 equiv. HCl), lead to the desired methyl α- and β-L-arabinofuranosides starting from the 1,2-diacetate **6** in overall 55% yield. To optimize this method, the synthesis of isomeric protected L-arabinofuranosides was carried out by treatment of the crude product mixture prepared after acetolysis of **5**, with HCl in anhydrous methanol. The target methyl α- and β-L-arabinofuranosides were prepared in

25% and 10% yield, respectively, after chromatographic isolation on silica gel (Scheme 2, cond a_2). Another approach for the stereoselective synthesis of isomeric methyl arabinofuranosides **12** and **13** has been investigated via mild bromination of **6** with trimethylsilyl bromide (TMSBr) in the presence of a catalyst ($ZnBr_2$). This was followed by conversion of the intermediate 1-bromo derivatives **14** or 1,2-anhydro derivative **15** under treatment with potassium carbonate in a mixture of methanol/THF to give the target arabinofuranosides. Compounds **13** and **12** were prepared in 46% and 10% yield, respectively, over two steps. This method provided higher stereoselectivity than the HCl-mediated method, leading to 3,5-di-*O*-protected methyl α/β arabinofuranosides (the ratio of glycosides α/β = 5:1 compared to α/β = 2:1).

Next, a simple three-step approach for the synthesis of methyl 2-deoxy-α-L-*erythro*-ribofuranoside (**19**) from selectively protected methyl α-L-arabinofuranoside **13** was tested using a novel method of deoxygenation at the C-2 position of L-arabinofuranoside. The treatment of **13** with methanesulfonyl chloride in pyridine in the presence of 4-dimethylaminopyridine (DMAP) gave 2-*O*-mesyl derivative **16** in 90% yield. Deacylation of **16** with methanolic ammonia at room temperature afforded a mixture of mesylates **17** (46%) and **18** (40%), which were separated by column chromatography on silica gel. The key 2-deoxygenation of methyl α-L-arabinofuranoside was accomplished by nucleophilic substitution of 2-*O*-methanesulfonates in the intermediate arabinosides **17** or **18** by a hydride ion, derived from lithium tri-*sec*-butylborohydride (L-Selectride), in THF/1,2-dimethoxyethane or THF, respectively. Accordingly, methyl 2-deoxy-α-L-ribofuranoside (**19**) was prepared in 90% and 94% yield after chromatography on silica gel (Scheme 2, conditions e and f). Apparently, the presence of a α-methoxy group in compounds **17**-**18** and the application of a bulky reducing agent such as L-Selectride are two factors which prevent direct nucleophilic substitution of the 2-*O*-methanesulfonate by a hydride ion. The efficient 2-deoxygenation of L-arabinofuranosides proceeds via intermediate 2,3-epoxysugars, formed under treatment of the mesylates **17** or **18** by an excess of a complex hydride, followed by their stereoselective reductions with L-Selectride to give **19**. Toluoylation of compound **19** with *p*-toluoyl chloride in pyridine gave 3,5-di-*O*-*p*-toluloate **20** (86%), which can be used for the synthesis of β/α-L-thymidine under Vorbruggen conditions.[12] The spectroscopic data of **20** were identical to that of the 3,5-di-*O*-*p*-toluloyl derivative synthesized earlier from D-glucose.[12]

A search for more efficient synthetic routes to the 2-*O*-mesyl derivative **18** than the previous approach was undertaken from L-arabinose using Fisher glycosylation on the first step. Synthesis of methyl arabinosides has widely been investigated in methanol in the presence of hydrochloric or sulfuric acid.[23,30-35] Synthetic procedures to prepare methyl α-L-arabinofuranoside include one or three steps followed by isolation of the target furanoside by chromatography or crystallization.[26-30,32] Glycosylation of L-arabinose via a single step operation was studied in anhydrous methanol in the presence of HCl (methanolic hydrogen chloride prepared by adding acetyl chloride to methanol at 0 ^{o}C).[30] After 7 h in 0.6% or 1% methanolic solution of dry hydrogen chloride at rt and neutralization of the reaction mixture with potassium carbonate, a mixture of methyl arabinofuranosides was obtained (α/β = 2.0-2.1:1) according to ^{1}H NMR spectroscopic data. Methyl L-glycosides prepared after acidic methanolysis of L-arabinose in 0.6% HCl-MeOH solution and the treatment of the reaction mixture were subjected to column chromatography on silica gel. Methyl α-L-arabinofuranoside (**21a**) and its β-anomer **21b** were isolated in 53% and 20% yield, respectively (Scheme 3).

Mesylation of α-glycoside **21a** with mesyl chloride in THF in the presence of 80%-sodium hydride failed to give mesylated products at room temperature. Treatment of **21a** with sodium hydride in a mixture of THF/DMA(N,N-dimethylacetamide) and then mesyl chloride resulted in a mixture of *O*-mesylated arabinofuranosides, from which a mixture of mesylates **18** and **22** was isolated by colunm chromatography on silica gel in overall 48% yield (a ratio of **22**/**18** = 1.7:1, according to NMR spectroscopic data) (Scheme 3).



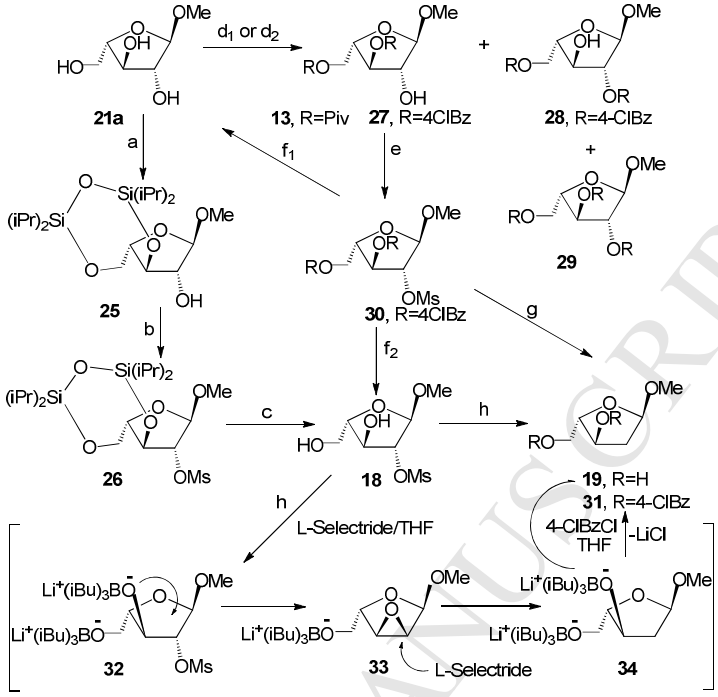
Scheme 3. *Reagents and conditions*. a) MeOH, HCl, rt, 7h, 53% to α-glycoside **21a** and 20% to β-glycoside **21b**; b) i) 1.2 eq. NaH, THF/DMA, 0 ºC→rt, 1.6 eq.MsCl, 5.5 h; ii) 0.8 eq. NaH, THF/DMA, 0 ºC→rt, 0.8 eq.MsCl,18h, 48% to **18**+**22**; (c) **18**+**22**/ $Li(i\text{-}Bu)_3BH$, THF, -78 ºC→rt, 20h, 91% to **19.**

The formation of 5-*O*-mesylate **22** and 2-*O*-mesylate **18** can be explained by the generation of intermediates **23** and **24** under treatment of **21a** with sodium hydride on the first step, followed by their mesylation with an excess of the electrophilic agent. It should be noted that the intramolecular hydrogen bond network in L-monosaccharide **21a** influencing on acidity of hydroxyl groups, stereochemistry of the carbohydrate in solution and solvating effects of the polar aprotic solvent can be considered as factors which have an impact on selectivity of the mesylation of α-glycoside in the presence of sodium hydride, as in the case of regioselective acylation and sulfonylation reactions of pyranosides.[36] From the ^{1}H NMR-spectroscopic data, the conformational analysis of methyl α-D-arabinofuranoside was earlier studied and it has been found that the N(56%)- and S(44%)-conformers are in equilibrium. The both conformers are present in approximately equimolar amounts as in the modelling of the conformational behaviour of the L-enantiomer using molecular mechanics calculations. [37,38] Based on the close values of $^3J_{H,H}$ in D_2O for L-glycoside **21a** (experimental part) and its D-counterpart,[37] conformational N/S-equilibria of isomeric arabinofuranosides are similar in solution. The intramolecular hydrogen bond between $OH_2...O_5$ in the S-conformer of **21a** in DMA seems to be the main factor for the formation of oxyanion derivatives at the first step. The intermediate oxyanion derivatives **23** and **24** are in equilibrium in solution due to hydrogen bonds between the hydroxyl groups and salt species of the sugar. In addition, the intermediate **24** is more reactive towards the mesylation than **23** because the oxyanion at C-5 compared to the one at C-2 is the less hindered and therefore more accessible to the electrophilic agent. Treatment of a mixture of isomeric mesylates **18** and **22** with an excess of a complex hydride in THF followed by chromatography afforded 2-deoxy-L-ribofuranoside **19** in 91% yield from mesylate **18**.

Furthermore, regioselective protection of the 3- and 5-hydroxy groups of L-arabinofuranoside **21a** was accomplished by the known method[24] involving selective silylation with 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane in pyridine to give **25** (98%), which was mesylated to give mesylate **26** in 85% yield on two steps (Scheme 4). The desilylation of **26** with tetra-*n*-butylammonium fluoride in THF furnished the mesylate **18** (95%) after column chromatography on silica gel.

Alternatively, direct regioselective acylation of methyl α-L-arabinofuranoside (**21a**) with 2 equiv. of 4-chlorobenzoyl chloride in a mixture of anhydrous methylene chloride and pyridine (2.8 equiv.) gave doubly acylated products, 3,5-di-*O*-benzoyl-L-arabinofuranoside **27** (40%) as the main one, along with 2,5-di-*O*-benzoylated regioisomer **28** (12%), and 2,3,5-tri-*O*-benzoyl derivative **29** (24%), which were isolated by column chromatography on silica gel. Thus, a simple two-step acylation of triol **21a** under the tested conditions using a overall twofold excess of 4-chlorobenzoyl chloride as acylating agent in the presence of pyridine provided access to novel 3,5-*O*- and 2,5-di-*O*-benzoylated L-arabinofuanosides in a ratio - 3.3:1 after chromatographic separation of regioisomeric products. Regioselectivity of the acylation reaction may be explained by the intramolecular hydrogen bond network of α-L-arabinofuranoside **21a** which influences acidity and reactivity of hydroxyl groups, as in the case of the regioselective acylations of pyranosides.[36]Acylation of **21a** with pivaloyl chloride in the similar conditions also resulted in 3,5-di-*O*-pivaloylated L-arabinofuranoside **12** as the main product which was isolated in 42% yield after column chromotography on silica gel. It should be noted that a number of

methods for the synthesis of selectively protected 3,5- or 2,5-*O*-acylated (benzylated) α-L-arabinofuanosides [13,25,39] or α-D-arabinofuranosides,[40,41] that are of considerable interest as building blocks for constructing L- or D-arabinofuranosyl-containing polysaccharides (L-arabinofuranans, arabinogalactan), have earlier been elaborated using mostly multi-step chemical processes.



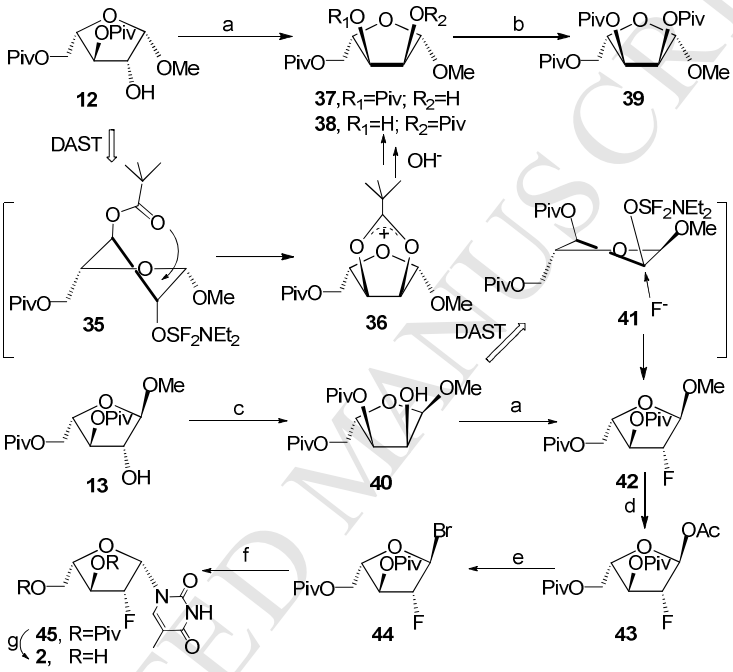
Scheme 4. *Reagents and conditions*. a) ref. 24, 98%; (b) MsCl/Py, DMAP, rt, 3h, 87%; (c) TBAF·3H$_2$O, THF, 100 min, 95%; d$_1$) i) 1 equiv. 4ClBzCl, CH_2Cl_2/Py, O $^oC\rightarrow$rt, ii) 1 equiv. 4ClBzCl, CH_2Cl_2/Py, O $^oC\rightarrow$rt, 40% to **27**; 12% to **28**; 24% to **29**; d$_2$) i) 1 equiv. PivCl, CH_2Cl_2/Py, O $^oC\rightarrow$rt, ii) 1 equiv. PivCl, CH_2Cl_2/Py, O $^oC\rightarrow$rt, 42% to **13**; e) MsCl/Py, DMAP, rt, 3h, 100%; f$_1$) NH_3/MeOH, rt, 20h, 23% to **18**; 72% to **21a**; f$_2$) NH_3/MeOH, rt, 5h, 85%, **18**; g) Li(i-Bu)$_3$BH in THF/1,2-DME, -78 $^oC\rightarrow$rt, 20h, 45% to **19** from **30**; h) (i) Li(i-Bu)$_3$BH in THF, -78 $^oC\rightarrow$rt, 22h, (ii) 4ClBzCl, THF, O $^oC\rightarrow$rt, 65%, 7h, 65% to **31** from **18**.

Subsequent mesylation of the 3,5-di-*O*-benzoyl derivative **27** followed by removal of the benzoyl groups in intermediate 2-*O*-mesyl arabinofuranoside derivative **30** in methanol saturated at 0 ^{o}C with ammonia afforded the 2-*O*-mesylate **18**. It was demonstrated that the deprotection of methyl-3,5-di-*O*-benzoyl-2-*O*-Ms-α-L-arabinofuranoside (**30**) with an excess of methanolic ammonia for 20h was accompanied by desulfonylation of the 2-*O*-methanesulfonyloxy group of glycoside with the formation of methyl α-L-arabinofuaranoside (**21a**) as the main product in 72% yield. In this case, the target mesylate was isolated only in 23% yield after chromatography. However, debenzoylation of **30** in diluted methanolic ammonia was found to give rise to the target mesylate **18** in high yield (85%).

Reduction of protected methyl-2-*O*-Ms-α-L-arabinofuranoside **30** with an excess of L-Selectride in a mixture of THF/1,2-dimethoxyethane gave methyl 2-deoxy-α-L-ribofuranoside (**19**) in moderate 45% yield after column chromatography on silica gel. A novel synthetic method to acylated 2-deoxy-α-L-ribofuranoside **31** was devised from the mesylate **18** (Scheme 4). The regioselective reduction of unprotected methyl 2-*O*-mesyl-α-L-arabinofuranoside **18** by L-Selectride in THF followed by acylation of the intermediate methyl 2-deoxy-α-L-ribofuranoside derivative with an excess of 4-chlorobenzoyl chloride in situ gave dibenzoate **31** (65%). The proposed mechanism for the formation of 2-deoxysugar **19** and its dibenzoylated derivative **31** is illustrated in Scheme 4. The 2-deoxygenation procedures under the treatment of mesylate **18** (conditions h) or mesylate **30** (conditions g) with a complex hydride include the formation of 2,3-anhydrofuranoside derivative **33** via intermediate **32**, followed by stereoselective reduction of the epoxide ring in **33** with L-Selectride at the 2-position to produce intermediate activated 2-deoxy-α-L-ribofuranoside derivative **34** in the next step. Finally, treatment of the reaction mixture or acylation of **34** with 4-chlorobenzoyl chloride in THF and chromatography on silica gel gave rise to 2-deoxy-α- L-ribofuranoside **19** or 3,5-dichlorobenzoate **31**, respectively. Thus, the most efficient synthesis of L-deoxyribose derivatives **19** and **31** was achieved via silyl derivative **26**.

2.2. Syntheses of L-ribofuranosides, 2-deoxy-2-fluoro-L-arabinofuranose derivatives and L-FMAU.

Next, preparation of 2-deoxy-2-fluoro-L-pentofuranose derivatives as the key intermediates for the synthesis of 2′-deoxy-2′-fluorinated L-nucleosides with potent antiviral activity was studied using diethylaminosulfur trifluoride (DAST) as the fluorinating agent for nucleophilic introduction of fluorine atom in methyl 3,5-di-*O*-pivaloyl-L-arabinofuranosides **12** and **13** (Scheme 5). Treatment of β-glycoside **12** with DAST in a mixture of CH_2Cl_2/Py gave a mixture of methyl 2,5-di-*O*-pivaloyl-β-L-ribofuranoside (**37**) and methyl 3,5-di-*O*-pivaloyl-β-L-ribofuranoside (**38**) (a ratio of 2,5- and 3,5-regioisomers ~ 1.2:1.0 according to ^{1}H NMR spectroscopic data) in an overall 97% yield after column chromatography on silica gel (Scheme 5). The formation of the isomeric acylated methyl β-L-ribofuranosides from β-L-arabinofuranoside **12** can be explained by the generation of activated intermediate **35** with DAST in the first step. The nucleophilic coparticipation of the 3-pivaloyloxy group in **35** (Scheme 5) leads to the formation of stable 2,3-pivaloyloxonium ion **36**, which is converted to a mixture of protected β-ribofuranosides **37** and **38** after the mildly alkaline workup of the reaction mixture.



Scheme 5. *Reagents and conditions*. a) DAST/CH_2Cl_2/Py, rt, 18h; b) PivCl, Py, rt, 18h, then 35-40 °C, 5h; c) (i) PDC/CH_2Cl_2/Ac_2O, 4A Mol.Sieves, rt, 16h; (ii) L-Selectride/THF -78 °C→rt, 5 min; d) AcOH/Ac_2O/H_2SO_4, rt 2h; e) TMSBr/CH_2Cl_2/$ZnBr_2$, O °C→rt, 16h; f) Silylated thymine, 1,2-DCE, reflux, 18h; g) MeONa/MeOH, rt, 18h.

Methyl 2,3,5-tri-*O*-pivaloyl-β-L-ribofuranoside (**39**) was prepared as the only product in 87% yield after acylation of a mixture of isomeric β-ribofuranosides **37** and **38** with pivaloyl chloride in pyridine. This fact provides support for the structures of selectively protected methyl β-L-ribofuranosides prepared after reaction of **12** with DAST.

Fluorination reaction of α-glycoside **13** with DAST under the same conditions as in the case of β-glycoside **12** also failed to yield 2-fluoro-2-deoxyribofuranoside. Furthermore, formation of 3,5-*O*-protected methyl α-L-ribofuranoside **40** or an isomeric derivative was not observed during this reaction, and after the treatment of reaction mixture unlike the reaction of **12** with DAST. The intermediate formed in the first step from **13** with DAST did not result in the formation of a stable 2,3-acyloxonium ion like **36** via nucleophilic coparticipation of the 3-pivaloyloxy group. The presence of a methoxy group in the α-anomeric configuration, and the bulky protecting group at the 3-hydroxyl group in pivaloylated α-glycoside **13** seems to be governing factors that prevent transformations of α-L-arabinofuranoside with DAST under the mild reaction conditions. However, the synthesis of selectively protected methyl α-ribofuranoside **40** was successfully accomplished from **13** prepared in two steps from L-arabinose, using an oxidation/reduction procedure for the inversion of configuration at C-2 of the arabino derivative (**13**) to produce the target ribofuranoside. Oxidation of α-glycoside **13** with pyridinium dichromate in the presence of Ac_2O in methylene chloride gave an intermediate ketone which was stereoselectively reduced by L-Selectide in THF at -78 °C to give the L-ribose derivative **40** in 71% yield after column

chromatography on silica gel. Treatment of α-L-ribofuranoside **40** with DAST in CH_2Cl_2 in the presence of pyridine at room temperature gave 2-deoxy-2-fluoro-L-arabinofuranoside derivative **42** which was isolated in 53% yield after chromatography. A mild fluorination of α-L-ribofuranoside can be accounted for the stereochemistry of the pentofuranose ring of **40** (the values of $J_{1,2}$=4.6; $J_{2,3}$=7.0, $J_{3,4}$=2.7 Hz close to those of 1,3,5-O-benzoyl-α-L-ribofuranose[7] in $CDCl_3$) and that of the activated intermediate **41** formed with DAST in the first step. Due to the bulky protecting groups at the 3,5-hydroxyl groups and the α-anomeric group, the intermediate **41** has probably a preferred C-2-exo conformation (Scheme 5) that is favorable to the nucleophilic introduction of a fluorine atom. Acetolysis of **42** in a mixture of $CH_3COOH/Ac_2O/H_2SO_4$ afforded 1-α-acetate **43** (91%) as a key intermediate for the synthesis of 2′-fluoro arabinofuranosyl L-nucleosides. Bromination of **43** with TMSBr in the presence of $ZnBr_2$, according to the known method,[42] gave 1-α-bromide **44** which was used in the next step without additional purification. The coupling of silylated thymine with bromide **44** afforded under reflux protected β-nucleoside **45** in 60% yield after chromatography. The target β-fluoronucleoside **2** was obtained by the deprotection of nucleoside **45** with MeONa-MeOH at room temperature in 80% yield. The structures of fluorosugars were supported by ^{1}H, ^{13}C and ^{19}F NMR spectroscopic data. The small coupling constants observed between the H-1 and H-2 protons ($^3J_{H\text{-}1,H\text{-}2}$ < 1.0 Hz) along with $^3J_{H\text{-}1,F\text{-}2}$ magnitudes 9.7-12.1 Hz in the ^{1}H NMR spectrum of **42-44** (doublets at δ 5.1, 6.4 and 6.52 ppm, respectively) are consistent with the α-anomeric configurations of synthesized fluorosugars. The assignments of the β-anomeric configurations of nucleosides **45** and **2** were based upon ^{1}H- and ^{13}C-NMR spectroscopic data. Long-range couplings between carbon C-6 and F-2′ were observed in the ^{13}C NMR spectra of L-nucleosides **45** and **2** ($^4J_{C\text{-}6,\ F\text{-}2'}$= 3.1 and 2.9 Hz, respectively, experimental part). A common feature of these nucleosides is the magnitudes of $^2J_{C\text{-}1,\ F\text{-}2'}$= 16.0 and 16.8 Hz that are consistent with the configurations at the anomeric centers.[43] Besides, small long-range couplings between protons H-6, H-5′ and F-2′ were first observed in the ^{1}H NMR spectrum of L-FMAU (**2**) recorded in CD_3OD ($^5J_{H\text{-}6,\ F\text{-}2'}$= 1.3 and $^5J_{H\text{-}5',\ F\text{-}2'}$= 1.1 Hz, respectively). These spectral features of **2** also confirm its β-anomeric configuration and give an indication of interesting conformational peculiarities of antiviral thymine 2′-fluoroarabinonucleoside in solution.

3.Conclusions

In summary, the synthesis of a series of L-pentose derivatives with different protecting groups was accomplished from cheap L-arabinose and commercially available chemical reagents. 3,5-Di-*O*-pivaloylated L-arabinofuranosides and –ribofuranosides were synthesized through regio- and stereoselective conversions of 1,2-di-*O*-acetyl-3,5-di-*O*-pivaloyl-L -arabinofuranose prepared in two steps from the starting material. It was first shown that classical method for pyridine-catalyzed diacylation of a free methyl α-L-arabinofuranoside with 4-chlorobenzoyl or pivaloyl chlorides under the studied conditions resulted in regioselective acylation with predominant formation of 3,5-di-*O*-acylated arabinofuranoside. Various synthetic routes to methyl 2-*O*Ms-α-L-arabinofuanoside, 2-deoxy-α-L-ribofuranoside derivatives and an efficient reductive deoxygenation of the C-2 hydroxyl group of the L-arabinofuranoside were developed. A mechanism for the stereoselective reduction of the 2-*O*-mesyl derivative of α-L-arabinofuanoside with L-Selectride was proposed. Novel and original method for preparation of 3,5-di-*O*-4-chlorobenzoylated 2-deoxy-α-L-ribofuranoside was devised starting from the 2-*O*-mesylate. A new synthesis of L-FMAU was carried out using acylated methyl 2-fluoro-2-deoxy-L-arabinofuranoside, a versatile intermediate for different 2′-fluorinated β-L-arabinofuranosyl nucleosides, prepared by a mild fluorination reaction of 3,5-*O*-protected L-ribofuranoside with DAST as the key step.

4. Experimental

4.1.General information. Column chromatography was performed on silica gel 60 H (70-230 mesh; Merck, Darmstadt, Germany), and thin-layer chromatography (TLC) on silica gel plates (Silufol, Czechoslovakia) and Merck silica gel aluminum 60 F_{254} precoated plates with visualization of the spots of L-sugars by heating. All commercially available reagents were used without further purification. The anhydrous solvents were distilled over CaH_2, P_2O_5 or magnesium prior to the use. ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded in $CDCl_3$, CD_3OD and D_2O with a Bruker Avance-500-DRX

spectrometer at 500.13, 126.76 and 470.593 MHz, respectively. ^{1}H and ^{13}C NMR chemical shifts (δ, ppm) are relative to internal chloroform peak (7.26 ppm for ^{1}H and 77.0 for ^{13}C NMR). Chemical shifts are also reported downfield from internal $SiMe_4$ (^{1}H) or external $CFCl_3$ (^{19}F). Melting points were determined on a Boetius apparatus and were uncorrected. Optical rotations were measured with ATAGO AP-300 polarimeter. IR spectra were measured on Perkin-Elmer Spectrum 100FT-IR spectrometer. High resolution mass spectra (HRMS) were recorded on an Agilent Q-TOF 6550 Instrument (USA) using ESI (electrospray ionization).

4.2. Syntheses of L-arabinofuranose and 2-deoxy-L-ribose derivatives.

*4.2.1. Methyl 2,3,5-tri-O-pivaloyl-α,β-L-arabinofuranoside (**5**).* L-Arabinose (3.0 g, 19.98 mmol) was added to a methanolic HCl solution, prepared by adding acetyl chloride (0.6 ml, 8.4 mmol) to anhydrous MeOH (60 ml) at 0 °C, then the reaction mixture was stirred for 7 h at room temperature, and neutralized with powdery K_2CO_3. After filtration through Celite, the precipitate was washed with anhydrous MeOH, and the filtrate evaporated. The residue was then coevaporated with anhydrous pyridine (2x30 ml). A mixture of methyl α/β-L-arabinofuranosides (a ratio α/β – ~2:1 according to ^{1}H NMR spectroscopic data) was dissolved in anhydrous pyridine (50 ml) and pivaloyl chloride (7.65 ml, 62.14 mmol) was added dropwise. The reaction mixture was stirred for 72 h at ambient temperature, was poured into a mixture of water and ice, and the aqueous phase extracted with CH_2Cl_2 (3x100 ml). The combined organic extracts were washed with 5%-aqueous $NaHCO_3$ (2[20 ml), water (30 ml) and dried over anhydrous Na_2SO_4, then evaporated to dryness. The residue was chromatographed on a silica gel, using a mixture of 15:1 and 8:1 petroleum ether-EtOAc to afford methyl 2,3,5-tri-*O*-pivaloyl-L-arabinofuranoside (**5**, 7.54 g, 75%) as a syrup. IR (film, $CHCl_3$): ν 2977, 2937, 1738, 1285, 1146 cm^{-1}. $[\alpha]^{25}_{D}$= -7.9 (c =1.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 5.37 (dd, 1H, *J* = 5.3 Hz, *J* = 6.3 Hz, H-3β), 5.08 (d, 1H, $J_{1,2}$ = 4.5 Hz, H-1β), 4.96-4.98 (m, 3H, H-2α, H-3α and H-2β), 4.84 (s, 2.3H, $J_{1,2}$ < 1.0 Hz, H-1α), 4.18-4.34 (m, 5H, 2H-5α, H-4α, 2H-5β), 4.05-4.08 (m, 1H, H-4β), 3.37 (s, 3H, αOCH_3), 3.33 (s, 3H, βOCH_3), 1.18-1.21 (5s, α/β COC(*C*H_3)$_3$. ^{13}C NMR ($CDCl_3$): δ 178.09, 178.05, 177.94, 177.60, 177.53, 177.26 (C=O), 106.73 (C-1α), 101.27 (C-1β), 81.37, 79.82, 75.68 (C-4α, C-2α, C-3α), 78.47, 77.09, 76.68 (C-4β, C-2β, C-3β), 65.28 (C-5β), 63.06 (C-5α), 55.4 (OCH_3β), 54.7 (OCH_3α), 38.81, 38.77, 38.59, 38.58, 38.53 [CO*C*(CH_3)$_3$], 27.1, 26.94 and 26.9 [COC(*C*H$_3$)$_3$]. HRMS (ESI$^+$): m/z calcd for $[C_{21}H_{36}O_8 + Na]^+$: 439.2308, found 439.2584.

*4.2.2. 1,2-Di-O-acetyl-3,5-di-O-pivaloyl-α,β-L-arabinofuranose (**6**).* Methyl 2,3,5-tri-*O*-pivaloyl-α,β-L-arabinofuranoside (**5**) (1.6 g, 3.84 mmol) was coevaporated with anhydrous benzene (2x20 ml), dissolved in a mixture of CH_3COOH (11.2 ml), Ac_2O (1.32 ml) and H_2SO_4 (1.46 ml), prepared previously by adding H_2SO_4 to mixture of CH_3COOH and Ac_2O and stirring the solution for 7 min. The reaction mixture was stored at ambient temperature for 8 h and then was diluted with ethyl acetate (150 ml), the prepared organic phase was washed with cooled water (4x40 ml) and then dried over anhydrous Na_2SO_4, and evaporated to dryness. The residue was chromatographed on a silica gel, using a mixture of 8:1, 6:1 and 5:1 petroleum ether-EtOAc to afford diacetate **6** (930 mg, 60%) as a syrup. IR (film, $CHCl_3$): ν 2977, 1742, 1218, 1155 cm^{-1}. $[\alpha]^{25}_{D}$ = -49.0 (c = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 6.36 (d, 0.19H, $J_{1,2}$ = 4.4 Hz, H-1β), 6.20 (s, 1H, $J_{1,2}$ <1.0 Hz, H-1α), 5.32-5.37 (dm, 2H, H-2β and H-3 β), 5.14 (br.s, 1H, H-2α), 5.04 (d, 1H, $J_{1,2}$ = 1.0 Hz, H-3α), 4.17-4.33 (m, 6H, H-4α, 2H-5α and H-4β, 2H-5β), 2.11, 2.08 and 2.06 (3s, 6H, α,βCH_3CO), 1.21, 1.20 and 1.19 (3s, 18H, α,βCOC(CH_3)$_3$]. ^{13}C NMR ($CDCl_3$): δ 177.93, 177.61, 177.34, 169.62, 169.36, 169.22, 169.09 (C=O), 99.11 (C-1 α), 93.72 (C-1 β), 82.84, 80.38, 76.50 (C-2α, C-3α, C-4α), 79.74, 75.45, 74.74 (C-2β, C-3β, C-4β), 64.17 (C-5β), 62.85 (C-5α), 38.78, 38.57 [(CO*C*(CH_3)$_3$], 27.06 and 26.85 [(COC(*C*H$_3$)$_3$], 21.03, 20.9, 20.65 and 20.35 (*C*H_3CO). HRMS (ESI$^+$): m/z calcd for $[C_{19}H_{30}O_9 + Na]^+$: 425.1788, found 425.1794.

*4.2.3. Methyl 3,5-di-O-pivaloyl-β-L-arabinofuranoside (**12**) and its α-L-anomer (**13**).*

Method A$_1$: 1,2-Diacetate **6** (930 mg, 2.31 mmol) was dissolved in 0.14 M HCl in MeOH, prepared by adding acetyl chloride (0.2 ml) in anhydrous methanol (19.2 ml) at 0 °C. The reaction mixture was stirred at room temperature for 24 h and then anhydrous pyridine (0.24 ml) was added under cooling (0 °C). The reaction mixture was stirred for 20 min at rt and then evaporated to dryness, and coevaporated with anhydrous benzene (10 ml). The residue was diluted with CH_2Cl_2

(60 ml), the organic layer was washed with water (10 ml), 5%-aqueous $NaHCO_3$ and water (15 ml), and then dried over anhydrous Na_2SO_4, evaporated to dryness. The residue was chromatographed on silica gel, using a mixture of 6:1 and 3:1 petroleum ether - EtOAc to afford methyl 3,5-di-*O*-pivaloyl-α-L-arabinofuranoside (**13**, 284 mg, 37 %) as a syrup. $[\alpha]^{25}_D$ = -72.4 (c = 0.78, $CHCl_3$). IR (film, $CHCl_3$): ν 3494, 2974, 2937, 1732, 1285, 1159 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 4.91 (br.s, 1H, H-1), 4.58 (dd, 1H, $J_{3,2}$ = 2.8 Hz, $J_{3,4}$ = 6.4 Hz, H-3), 4.33-4.36 (dm, 1H, H-4), 4.24-4.27 (dd, 2H, H-5, H-5′), 4.04 (dd, 1H, $J_{2,3}$ = 2.8 Hz, J = 1.1 Hz, H-2), 3.39 (s, 3H, OCH_3), 1.23 and 1.22 (2s, 18H, $COC(CH_3)_3$]. ^{13}C NMR ($CDCl_3$): δ 179.67, 178.11 [C=O, 2xCOC$(CH_3)_3$], 108.66 (C-1), 81.5, 81.4, 78.6 (C-4, C-3, C-2), 63.1 (C-5), 54.95 (OCH_3), 38.83, 38.65 [2xCO$C$$(CH_3)_3$], 27.14, 26.94 [2xCOC($CH_3$)$_3$]. HRMS ($ESI^+$): m/z calcd for $[C_{16}H_{28}O_7 + Na]^+$: 355.1733, found 355.1739.

Methyl 3,5-di-*O*-pivaloyl-β-L-arabinofuranoside (**12**, 140 mg, 18%) as a syrup. $[\alpha]^{25}_D$ = +57.0 (c = 0.58, $CHCl_3$). IR (film, $CHCl_3$): ν 3480, 2974, 2937, 1735, 1285, 1159 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 5.02 (t, 1H, $J_{3,4}$ = $J_{3,2}$ = 5.5 Hz, H-3), 4.91 d (1H, $J_{1,2}$ = 4.7 Hz, H-1), 4.22-4.26 (m, 3H, 2H-5, H-2), 4.09-4.11 (m, 1H, H-4), 3.46 (s, 3H, OCH_3), 2.92 (d, 1H, 2-OH), 1.22 (br.s, 18H, $COC(CH_3)_3$]. ^{13}C NMR ($CDCl_3$): δ 178.69, 178.12 [C=O, 2xCOC$(CH_3)_3$], 102.50 (C-1), 79.63, 79.41, 77.05 (C-3, C-4, C-2), 65.19 (C-5), 55.44 (OCH_3), 38.79, 38.67 [2xCO$C$$(CH_3)_3$], 27.11, 27.04 [2xCOC($CH_3$)$_3$]. HRMS ($ESI^+$): m/z calcd for $[C_{16}H_{28}O_7 + Na]^+$: 355.1733, found 355.1727.

Method A_2: Methyl 2,3,5-tri-*O*-pivaloyl-α,β-L-arabinofuranoside (**5**, 775 mg, 18.6 mmol) was coevaporated with anhydrous benzene (2x20 ml), then dissolved in a mixture of CH_3COOH (5.43 ml), Ac_2O (0.64 ml) and H_2SO_4 (0.71 ml), prepared previously by adding H_2SO_4 to mixture of CH_3COOH and Ac_2O and stirring a solution for 7 min. The reaction mixture was stored at room temperature for 8 h, and then was diluted with ethyl acetate (80 ml). The prepared organic phase was washed with cooled water (4x20 ml) and then dried over anhydrous Na_2SO_4, evaporated to dryness and used on the next step without additional chromatographic isolation. The reaction mixture was coevaporated with anhydrous benzene (2x20 ml), then dissolved in methanolic HCl solution prepared by adding acetyl chloride (0.16 ml) to anhydrous methanol (16 ml) at 0 ^{o}C. The reaction mixture was stirred at room temperature for 24 h and then anhydrous pyridine (0.2 ml) was added under cooling (0 ^{o}C). The reaction mixture was stirred at room temperature, coevaporated with anhydrous benzene (10 ml). The residue was diluted with CH_2Cl_2 (50 ml), the organic layer was washed with water (10 ml), 5%-aqueous $NaHCO_3$ (15 ml), dried over anhydrous Na_2SO_4, and then evaporated to dryness. The residue was chromatographed on silica gel, using a mixture of 6:1 and 3:1 petroleum ether-EtOAc to afford methyl 3,5-di-O-pivaloyl-α-L-arabinofuranoside (**13**, 154 mg, 25%) as a syrup and methyl 3,5-di-*O*-pivaloyl-β-L-arabinofuranoside (**12**, 62 mg, 10%) as a syrup.

Method B: TMSBr (0.28 ml, 2.16 mmol) was added to a solution of the 1,2-diacetate **6** (200 mg, 0.5 mmol) in anhydrous CH_2Cl_2 (6.0 ml) at 0 ^{o}C and the resulting mixture was stirred under argon at 0^{o}C for 10 min, then 1 h at room temperature. Anhydrous $ZnBr_2$ (56 mg, 0.27 mmol) was added to at rt. The resulting reaction mixture was stirred under argon for 90 min, then was filtered off, the precipitate was washed with anhydrous CH_2Cl_2 (16 ml), and the filtrate was evaporated. The residue was dissolved in anhydrous THF (1.4 ml) and anhydrous methanol (4.8 ml), and anhydrous potassium carbonate (120 mg, 0.92 mmol) was added to. The reaction mixture was stirred at room temperature for 90 min and then was filtered off, the precipitate was washed with anhydrous CH_2Cl_2 (40 ml) and the filtrate evaporated. The residue was chromatographed on silica gel, using a mixture of 6:1 and 3:1 petroleum ether -EtOAc to afford methyl 3,5-di-*O*-pivaloyl-α-L-arabinofuranoside (**13**) as a syrup (76 mg, 46%) and methyl 3,5-di-*O*-pivaloyl-β-L-arabinofuranoside (**12**) as a syrup (16 mg, 10%).

*4.2.4. Methyl 3,5-di-O-pivaloyl-2-O-methanesulfonyl-α-L-arabinofuranoside (**16**).* Methanesulfonyl chloride (0.11 ml, 1.41 mmol) was added dropwise to a solution of α-L-glycoside **13** (282 mg, 0.848 mmol) in anhydrous pyridine (5 ml) and 4-dimethylaminopyridine (53 mg, 0.44 mmol) under cooling. The reaction mixture was stirred for 1 h at 0 ^{o}C and for 16 h at rt and then the solution was diluted CH_2Cl_2 (30 ml), water (10 ml), the aqueous phase was extracted with CH_2Cl_2 (30 ml). The combined organic extracts were washed with 1 M HCl (3x10 ml), 5%-aqueous $NaHCO_3$, dried over anhydrous

Na_2SO_4, and evaporated to dryness. The residue was purified by chromatography on silica gel, using a mixture of 4:1 petroleum ether-EtOAc to afford compound **16** (313 mg, 90%) as a syrup. IR (film, $CHCl_3$): ν 2970, 1735, 1364, 1160, cm^{-1}. $[\alpha]^{25}_D$ = -69.8 (c = 0.64, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 5.1 (s, 1H, H-1), 5.0 (dd, 1H, $J_{3,2}$ = 1.4 Hz, $J_{3,4}$ = 4.0 Hz, H-3), 4.81 (d, 1H, H-2), 4.35-4.4 (m, 1H, H-4), 4.26 (dd, 1H, $J_{5,4}$ = 4.9 Hz, $J_{5,5'}$ = 12.1 Hz, H-5), 4.23 (dd, 1H, $J_{5',4}$ = 3.7 Hz, H-5′), 3.40 (s, 3H, OCH_3), 3.14 (s, 3H, SO_2CH_3), 1.22, 1.21 (2s, 18H, $COC(C\underline{H}_3)_3$]. ^{13}C NMR ($CDCl_3$): δ 177.99, 177.93 [C=O, 2x$COC(CH_3)_3$], 106.3 (C-1), 86.95, 79.33, 77.05 (C-3, C-4, C-2), 62.48 (C-5), 54.8 (OCH_3), 38.77, 38.58 [(2x$COC(CH_3)_3$], 38.33 (SO_2CH_3), 27.03, 26.83 [2x$COC(CH_3)_3$]. HRMS (ESI^+): m/z calcd for $[C_{17}H_{30}SO_9 + Na]^+$: 433.1508, found 433.1502.

*4.2.5. Methyl 5-O-pivaloyl-2-O-methanesulfonyl-α-L-arabinofuranoside (**17**) and methyl 2-O-methanesulfonyl-α-L-arabinofuranoside (**18**).* A solution of the mesylate **16** (218 mg, 0.53 mmol) in methanol (15 ml) saturated at 0 °C with ammonia was stored at room temperature for 96 h. The reaction mixture was evaporated to dryness. The residue was chromatographed on silica gel, using for elution chloroform, $CHCl_3$-methanol (15:1) to give as the first fraction methyl 5-*O*-pivaloyl-2-*O*-methanesulfonyl-α-L-arabinofuranoside (**17**, 79 mg, 46%) as a syrup. $[\alpha]^{25}_D$ = -59.4 (c = 0.64, $CHCl_3$). IR (film, $CHCl_3$): ν 3490, 2970, 2940, 1732, 1364, 1179 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 5.02 (br. s, 1H, H-1), 4.81 (d, 1H, H-2, $J_{2,3}$ = 2.6 Hz), 4.33 (dd, 1H, $J_{5',4}$ = 3.5 Hz, $J_{5,5'}$ = 12.2 Hz, H-5), 4.26 (dd, 1H, $J_{5',4}$ = 4.5 Hz, H-5′), 4.13-4.18 (m, 2H, H-3 и H-4), 3.40 (s, 3H, OCH_3), 3.10 (s, 3H, SO_2CH_3), 1.21 (s, 9H, $COC(CH_3)_3$]. ^{13}C NMR ($CDCl_3$): δ 178.52 [(C=O, $COC(CH_3)_3$], 105.68 (C-1), 88.37, 80.84, 76.46 (C-3, C-4, C-2), 62.70 (C-5), 55.19 (OCH_3), 38.86 [$COC(CH_3)_3$], 38.11 ($SO_2\underline{C}H_3$), 27.11 [$COC(CH_3)_3$]. HRMS (ESI^+): m/z calcd for $[C_{12}H_{22}SO_8 + Na]^+$: 349.0933, found 349.0933. The second fraction was methyl 2-O-methanesulfonyl-α-L-arabinofuranoside (**18**, 66 mg, 40%) as a syrup. $[\alpha]^{25}_D$ = -32.4 (c = 0.77, MeOH). IR (film, $CHCl_3$): ν 3454, 2931, 1357, 1179 cm^{-1}.^{1}H NMR ($CDCl_3$): δ 5.05 (br.s, 1H, H-1), 4.84 (dd, 1H, $J_{1,2}$ = 1.3 Hz, $J_{2,3}$ = 3.4 Hz, H-2), 4.31-4.39 (m, 1H, H-3), 4.05-4.8 (m, 1H, H-4), 3.91 (dd, 1H, $J_{4,5}$ = 3.3 Hz, $J_{5,5'}$ = 12.2 Hz, H-5), 3.77 (dd, 1H, $J_{4,5'}$ = 4.1 Hz, H-5′), 3.42 (s, 3H, OCH_3), 3.12 (s, 3H, $SO_2\underline{C}H_3$). ^{13}C ЯМР ($CDCl_3$): δ 105.82 (C-1), 88.86 (C-4), 82.97 (C-2), 75.30 (C-3), 61.23 (C-5), 55.23 (OCH_3), 38.15 ($SO_2\underline{C}H_3$). HRMS (ESI^+): m/z calcd for $[C_7H_{14}SO_7]^+$: 242.0460, found 242.0466.

*4.2.6. Methyl α-L-arabinofuranoside (**21a**) and methyl β-L-arabinofuranoside (**21b**).* A suspension of L-arabinose (5.5 g, 36.85 mmol) in methanolic HCl solution, prepared by adding acetyl chloride (1.1 ml, 16.8 mmol) to anhydrous methanol (110 ml) at 0 °C, was stirred at room temperature for 7 h and then was neutralized with powdery K_2CO_3. After filtration through Celite, the filtrate was evaporated. The residue was chromatographed on silica gel, using for elution chloroform and then acetone to give methyl α-L-arabinofuranoside (**21a**, 3.2 g, 53%) as a syrup. $[\alpha]^{25}_D$ = - 118.0 (c = 1.0, MeOH). IR (film): ν 3378 (brs), 2931, 2848, 1106, 1040 cm^{-1}. ^{1}H NMR (D_2O): δ 4.76 (d, 1H, $J_{1,2}$ = 1.6 Hz, H-1), 3.89 (dd, 1H, $J_{2,3}$ = 3.2 Hz, H-2), 3.87 (ddd, 1H, $J_{4,5}$ = 3.4 Hz, $J_{4,5'}$ = 5.7 Hz, H-4), 3.78 (dd, 1H, $J_{3,2}$ = 3.2 Hz, $J_{3,4}$ = 5.7 Hz, H-3), 3.65 (dd, 1H, $J_{5,4}$ = 3.2 Hz, $J_{5,5'}$ = 12.1 Hz, H-5), 3.54 (dd, 1H, $J_{5',4}$ = 5.7 Hz, H-5′), 3.25 (s, 3H, OCH_3). ^{13}C NMR (D_2O): δ 108.3 (C-1), 83.91 (C-4), 80.71 (C-2), 76.36 (C-3), 61.2 (C-5), 54.92 (OCH_3). and methyl β-L-arabinofuranoside (**21b**, 1.34 g) with admixtures of L-arabinosides. Compound **21b** was additionally purified by column chromatography on silica gel using acetone as the eluent to afford β-L-arabinofuranoside (**21b**, 1.2 g, 20%) as a syrup. $[\alpha]^{25}_D$ = + 157.5 (c = 0.7, MeOH). IR (film): ν 3388 (brs), 2934, 2853, 1132, 1033 cm^{-1}. 1H NMR (D_2O): δ 4.76 (d, 1H, $J_{1,2}$ = 4.17 Hz, H-1), 4.0 (dd, 1H, $J_{2,3}$ = 7.9 Hz, H-2), 3.87 (t, 1H, $J_{3,4}$ = 7.0 Hz, H-3), 3.74 (ddd, 1H, $J_{4,5}$ = 3.4 Hz, $J_{4,5'}$ = 7.1 Hz, H-4), 3.63 (dd, 1H, $J_{5,4}$ = 3.5 Hz, $J_{5,5'}$ = 12.2 Hz, H-5), 3.48 (dd, 1H, $J_{5',4}$ = 7.0 Hz, H-5′), 3.28 (s, 3H, OCH_3). ^{13}C NMR (D_2O): δ 102.2 (C-1), 82.05 (C-4), 76.41 (C-2), 74.59 (C-3), 63.17 (C-5), 55.18 (OCH_3). Analysis of fractions prepared after column chromatography was carried out on TLC-plates (Silufol, Czechoslovakia) using solvent systems - $CHCl_3$-petroleum ether-methanol (14:7:4) or acetone-benzene (3:2); the spots of L-sugars were detected by heating.

*4.2.7. Methyl 2-O-methanesulfonyl-α-L-arabinofuranoside (**18**) and methyl 5-O-methanesulfonyl-α-L-arabinofuranoside (**22**).* Methyl α-L-arabinoside **21a** (214 mg, 1.3 mmol) was dissolved in a mixture of anhydrous THF (4.3 ml) and anhydrous N,N-dimethylacetamide (DMA, 0.3 ml) and sodium hydride (80% in oil, 0.048 g, 1.6 mmol) was added at 0

°C. The solution was stirred at 0 °C for 10 min and, then 25 min at room temperature. The reaction mixture was cooled to 0 °C and mesyl chloride (0.16 ml, 2.06 mmol) was added dropwise. The reaction mixture was stirred for 5.5 h at room temperature. The reaction mixture was cooled to 0 °C and sodium hydride (80% in oil, 0.032 g, 1.06 mmol) was added under cooling, the solution was stirred at 0 °C for 5 min and then 15 min room temperature. Mesyl chloride (0.08 ml, 1.0 mmol) was then added to. The reaction mixture was stirred for 18 h at rt, and the prepared solution was filtered off, the precipitate was washed with anhydrous THF (15 ml). The filtrate and washings were evaporated, then the residue was coevaporated with anhydrous toluene. The residue was chromatographed on a silica gel, using for elution chloroform, $CHCl_3$-petroleum ether-methanol (15:7:2.5) to give a mixture of mesylates **18** and **22** (0.13 g, 48%; ratio of **22** (30%) and **18** (18%) - 1.7:1 according to ^{1}H NMR data, with the recovery of the starting material). ^{1}H NMR ($CDCl_3$): δ 5.05 (br.s, 1H, H-1, mesylate **18**), 4.89 (s, 1H, H-1, mesylate **22**), 4.84 (dd, 1H, $J_{1,2}$ = 1.3, $J_{2,3}$ = 3.4, H-2), 4.45 (dd, 1H, $J_{4,5}$ = 3.6, $J_{5,5'}$ = 11.4, H-5), 4.39 (dd, 1H, $J_{4,5'}$ = 5.1, H-5′), 4.29-4.31 (m, 1H, H-3), 4.17-4.20 (m, 1H, H-4), 4.10 (br.s, 1H, H-2), 4.03-4.06 (m, 1H, H-4), 3.95-3.98 (m, 1H, H-3), 3.91 (dd, 1H, $J_{4,5}$ = 3.3, $J_{5,5'}$ = 12.2, H-5), 3.77 (dd, 1H, $J_{4,5'}$ = 4.1, H-5′), 3.41 (s, 3H, OCH_3), 3.40 (s, 3H, OCH_3), 3.12 (s, 3H, $SO_2\underline{CH_3}$), 3.10 (s, 3H, $SO_2\underline{CH_3}$). ^{13}C NMR ($CDCl_3$ and CD_3OD): δ 108.86 (C-1, mesylate **22**), 105.82 (C-1, mesylate **22**), 88.49 (C-2, mesylate **18**), 82.82 (C-4, mesylate **18**), 81.57, 81.26, 77.28 (C-4, C-2, C-3, mesylate **22**), 74.99 (C-3, mesylate **18**), 69.36 (C-5, mesylate **22**), 60.99 (C-5, mesylate **18**), 55.31 (OCH_3, mesylate **22**), 55.18 (OCH_3), 38.13 ($SO_2\underline{CH_3}$, **18**), 37.51 ($SO_2\underline{CH_3}$, **22**). LRMS (ESI^+): m/z calcd for $[C_7H_{14}SO_7+Na]^+$: 265.03, found 265.0. Further elution with a mixture of $CHCl_3$-methanol (7:1) gave 0.032 г (14%, recovery of methyl α-arabinoside **21a**) as an oil.

*4.2.8. Methyl 3,5-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-2-O-methanesulfonyl-α-L-arabinofuranoside (**26**).* Methanesulfonyl chloride (0.092 ml, 1.18 mmol) was added dropwise to a solution of silylated derivative of methyl α-L-arabinofuranoside **28** (240 mg, 0.59 mmol), prepared according to the known method,[24] in anhydrous pyridine (6 ml) and 4-dimethylaminopyridine (140 mg, 1.18 mmol) at room temperature. The reaction mixture was stirred for 3 h and the solution was diluted CH_2Cl_2 (40 ml), washed with water (20 ml), and the aqueous phase was extracted with CH_2Cl_2 (60 ml). The combined organic extracts was washed with 1 M HCl (3x15 ml), 5%-aqueous $NaHCO_3$, dried over anhydrous Na_2SO_4, and evaporated to dryness. The residue was purified by chromatography on silica gel, using a mixture of 5:1 petroleum ether-EtOAc to afford **26** (248 mg, 87%) as a syrup. M.p. 49–50 °C. $[\alpha]^{25}_D$ = -87.7 (c = 0.57, $CHCl_3$). IR (KBr): ν 2951, 2871, 1364, 1186, 1000 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 4.98 (d, 1H, $J_{1,2}$ = 2.3 Hz, H-1), 4.89 (dd, 1H, $J_{2,3}$ = 5.2 Hz, H-2), 4.37 (dd, 1H, $J_{3,4}$ = 8.5 Hz, H-3), 4.00 (dd, 1H, $J_{5,4}$ = 3.1 Hz, $J_{5,5'}$ = 12.8 Hz, H-5), 3.88 (dd, 1H, $J_{5',4}$ = 3.3 Hz, H-5′), 3.91 (dt, 1H, H-4), 3.41 (s, 3H, OCH_3), 3.06 (s, 3H, $SO_2\underline{CH_3}$), 1.01-1.1 (m, 28H, 4x $(CH_3)_2CH$). ^{13}C NMR ($CDCl_3$): δ 105.1 (C-1), 88.11, 79.97, 74.76 (C-4, C-2, C-3), 60.77 (C-5), 55.46 (OCH_3), 38.03 (SO_2CH_3), 17.4, 17.2, 16.92, 16.89, 16.86 [4x$(CH_3)_2CH$], 13.4, 13.06, 12.7, 12.4 [4x$(CH_3)_2CH$]. HRMS (ESI^+): m/z calcd for $[C_{19}H_{40}O_8Si_2S + Na]^+$: 507.1875, found 507.1886.

*4.2.9. Methyl 2-O-methanesulfonyl-α-L-arabinofuranoside (**18**) from **22**.* $TBAF{\cdot}3H_2O$ (300 mg, 0.95 mmol) was added to a solution of the silyl derivative **22** (220 mg, 0.45 mmol) in anhydrous THF (4 ml) and the solution was stirred for 100 min at room temperature and then evaporated. The residue was dissolved in $CHCl_3$ (50 ml), and solution was washed with saturated aqueous $(NH_4)_2SO_4$ and evaporated to dryness. The residue was chromatographed on a silica gel, using for elution chloroform, $CHCl_3$-petroleum ether-methanol (15:7:2) to give the mesylate **18** (104 mg, 95%) as a syrup.

4.2.10. Selective acylation of methyl α-L-arabinofuranoside (21a) with acyl chlorides.

A. Acylation with 4-chlorobenzoyl chloride. 4-Chlorobenzoyl chloride (0.22 ml, 1.71 mmol) in anhydrous CH_2Cl_2 (0.4 ml) was added dropwise to a solution of methyl α-L-arabinofuranoside (**21a**, 288 mg, 1.75 mmol) in anhydrous CH_2Cl_2 (3 ml) and pyridine (0.28 ml, 3.14 mmol) at 0 °C (ice and sodium chloride). The reaction mixture was stirred for 90 min under cooling and then for 18 h at room temperature. Pyridine (0.14 ml, 1.73 mmol) and a solution of 4-chlorobenzoyl chloride (0.23 ml, 1.79 mmol) in anhydrous CH_2Cl_2 (0.4 ml) were consequently added to a prepared solution at 0 °C. After stirring for 1 h under cooling the reaction mixture was stirred for 18 h at room temperature. The solution was diluted with

CH_2Cl_2 (30 ml), water (10 ml), and the aqueous phase was extracted with CH_2Cl_2 (3x30 ml). The combined organic extracts were washed with 1 M HCl (10 ml), 5%-aqueous $NaHCO_3$, dried over anhydrous Na_2SO_4 and evaporated to dryness. The residue was chromatographed on silica gel, using a mixture of 7:1, 6:1, 4:1 and 2.5:1 hexane-EtOAc to afford as the first fraction methyl 2,3,5-tri-*O*-4-chlorobenzoyl-α-L-arabinofuranoside (**29**, 243 mg, 24%) as a syrup. M.p.43–44 °C. $[\alpha]^{25}_D$ = +42.3 (c = 1.0, $CHCl_3$). IR (KBr): ν 2940, 1729, 1597, 1269,1098 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.99, 7.93, 7.87, 7.43, 7.35 and 7.26 (6d, 12H, 3x COC_6H_4Cl), 5.50 (br.d, 1H, $J_{3,2}$ = 5.1 Hz, H-3), 5.46 (br.d, 1H, H-2), 5.17 (s, 1H, H-1), 4.85 (dd, 1H, H-5), 4.67 (dd, 1H, H-5′), 4.52-4.55 (m, 1H, H-4), 3.48 (s, 3H, OCH_3). ^{13}C NMR ($CDCl_3$): δ 165.24, 164.93 and 164.53 [(C=O, 3xCOC_6H_4Cl], 140.22, 140.16, 139.67, 131.30, 131.12, 131.07, 128.87, 128.66, 128.05, 127.39, 127.30 (3x$CO\underline{C}_6H_4Cl$), 106.68 (C-1), 82.15, 80.79, 77.99 (C-2, C-3, C-4), 63.69 (C-5), 55.04 (OCH_3). HRMS (ESI^+): m/z calcd for $[C_{27}H_{21}O_8Cl_3 + Na]^+$: 601.0200, found 601.0197. The second fraction was methyl 3,5-di-*O*-4-chlorobenzoyl-α-L-arabinofuranoside (**27**, 309 mg, 40%). M.p. 99–102 °C. $[\alpha]^{25}_D$ = -101.8 (c = 1.1, $CHCl_3$). IR (KBr): ν 3440, 2947, 1719, 1596, 1275, 1099 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.98, 7.94, 7.41 and 7.39 (4d, 8H, 2xCOC_6H_4Cl), 5.01 (br.s, 1H, H-1), 4.99 (dd, 1H, $J_{3,2}$ = 6.1 Hz, $J_{3,4}$ = 2.5 Hz, H-3), 4.70 (dd, 1H, H-5), 4.59 (dd, 1H, H-5′), 4.53-4.56 (m, 1H, H-4), 4.3 (br.d 1H, H-2), 3.43 (s, 3H, OCH_3), 3.0 (d, 2-OH). ^{13}C NMR ($CDCl_3$): δ 166.24 and 165.42 (C=O, 2xCOC_6H_4Cl], 140.25, 139.7, 131.3, 131.16, 131.08, 128.87, 128.76, 128.68, 128.02, 127.29 (2x$CO\underline{C_6H_4}Cl$),108.91 (C-1), 82.11, 81.19 (C-3, C-4), 78.83 (C-2), 64.0 (C-5), 55.11 (OCH_3). HRMS (ESI^+): m/z calcd for $C_{20}H_{19}O_7Cl_2Na[M + Na]^+$: 463.0327, found 463.0319. The third fraction was methyl 2,5-di-*O*-4-chlorobenzoyl-α-L-arabinofuranoside (**28**, 93 mg, 12%). M.p. 111–113 °C. $[\alpha]^{25}_D$ = -32.0 (c = 0.78, $CHCl_3$). IR (KBr): ν 3450, 2940, 1722, 1599, 1275, 1096 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.94, 7.92, 7.41 and 7.32 (4d, 8H, 2xCOC_6H_4Cl), 5.17 (br.s, 1H, H-1), 5.09 (dd, 1H, $J_{3,2}$ = 2.5 Hz, $J_{1,2}$ = 0.5 Hz, H-2), 4.64 (dd, 1H, H-5), 4.51 (dd, 1H, H-5′), 4.39-4.42 (m, 1H, H-4), 4.18 (dd, 1H, H-3), 3.48 (s, 3H, OCH_3). ^{13}C NMR ($CDCl_3$): δ 165.74 and 165.43 (C=O, 2xCOC_6H_4Cl], 140.37, 139.69, 131.16, 131.08, 128.98, 128.72, 127.31 (2x$CO\underline{C_6H_4}Cl$),106.34 (C-1), 85.6, 81.85 (C-3, C-4), 77.25 (C-2), 63.94 (C-5), 55.18 (OCH_3). HRMS (ESI^+): m/z calcd for $[C_{20}H_{19}O_7Cl_2 + Na]^+$: 463.0327, found 463.0320.

B. Acylation with pivaloyl chloride. To a solution of methyl α-L-arabinoside **21a** (295 mg, 1.79 mmol) in anhydrous CH_2Cl_2 (3 ml) and pyridine (0.29 ml, 2.58 mmol) at 0 °C (ice and sodium chloride) was added dropwise pivaloyl chloride (0.22 ml, 1.79 mmol) in anhydrous CH_2Cl_2 (3 ml). The reaction mixture was stirred for 1 h under cooling and then 18 h at room temperature. Pyridine (0.14 ml, 1.79 mmol) and pivaloyl chloride (0.22 ml, 1.79 mmol) in anhydrous CH_2Cl_2 (3 ml) were consequently added at 0 °C. After stirring for 2 h under cooling, the reaction mixture was stirred for 21 h at room temperature. The solution was diluted with CH_2Cl_2 (30 ml), water (10 ml), the aqueous phase was extracted with CH_2Cl_2 (3x30 ml). The combined organic extracts were washed 1 M HCl (3x10 ml), dried over anh. Na_2SO_4 and evaporated to dryness. The residue was chromatographed on silica gel (70 ml), using a mixture of a mixture of 6:1 and then 3:1 petroleum ether-EtOAc to afford 3,5-di-*O*-pivaloyl derivative **13** as a syrup (0.251 g, 42%).

*4.2.11. Methyl 3,5-di-O-4-chlorobenzoyl-2-O-methanesulfonyl-α-L-arabinofuranoside (**30**).* Methanesulfonyl chloride (0.064 ml, 0.82 mmol) was added to a solution of protected methyl α-L-arabinofuranoside **27** (180 mg, 0.41 mmol) in anhydrous pyridine (3.7 ml) and 4-dimethylaminopyridine (25 mg, 0.21 mmol) at room temperature. The reaction mixture was stirred for 3 h at rt, and then diluted with CH_2Cl_2 (30 ml), washed with water (10 ml), and the aqueous phase was extracted with CH_2Cl_2 (30 ml). The combined organic extracts were washed 1 M HCl (3x10 ml), 5%-aqueous $NaHCO_3$, dried over anhydrous Na_2SO_4, and evaporated to dryness to afford mesylate **30** (220 mg, 100%) as a syrup, which was used in the next step without additional purification. Compound **30** was purified by column chromatography on silica gel, using for elution a mixture of 3:1 and 2.5:1 hexane - EtOAc to afford an analytical sample of **30** as a syrup. $[\alpha]^{25}_D$ = -77.0 (c = 0.68, $CHCl_3$). IR (film, $CHCl_3$): ν 2931, 1725, 1371, 1271, 1099 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.98, 7.94, 7.41 and 7.39 (4d, 8H, 2 x COC_6H_4Cl), 5.38 (br.d, 1H, $J_{3,2}$ = 1.2 Hz, $J_{3,4}$ = 4.8 Hz, H-3), 5.22 (s, 1H, H-1), 5.05 (d, 1H, H-2), 4.71 (dd, 1H, $J_{5,4}$ = 3.6 Hz, $J_{5,5'}$ = 11.0 Hz, H-5), 4.61 (dd, 1H, $J_{5',4}$ = 4.2 Hz, H-5′), 4.53-4.55 (m, 1H, H-4), 3.45 (s, OCH_3), 3.13 (s, 3H, SO_2CH_3). ^{13}C NMR ($CDCl_3$): δ 165.36, 165.13 (C=O, 2xCOC_6H_4Cl), 140.47, 139.83, 131.34, 131.27, 131.21, 128.98,

128.83, 127.95, 127.05 (2xCO$\underline{C_6H_4}$Cl), 106.64 (C-1), 85.72, 79.93, 78.21 (C-2, C-3, C-4), 63.61 (C-5), 55.11 (OCH_3), 38.46 (SO_2CH_3). HRMS (ESI^+): m/z calcd for $[C_{29}H_{20}O_9SCl_2 + Na]^+$: 541.0103, found 541.0110.

*4.2.12. Methyl 2-O-methanesulfonyl-α-L-arabinofuranoside (**18**) from methyl 3,5-di-O-4-chlorobenzoyl-2-O-methanesulfonyl-α-L-arabinofuranoside (**30**).*

Methanol (40 ml) saturated at 0 °C with ammonia was added to the mesylate **30** (220 mg, 0.58 mmol). The reaction mixture was stored at room temperature for 20 h, and then was evaporated to dryness. The residue was chromatographed on a silica gel, using for elution chloroform, and a mixture of 16:1 and 5:1 $CHCl_3$-methanol to give the mesylate **18** (24 mg, 23%) as an oil and a methyl α-L-arabinofuranoside (**21a**, 50 mg, 72%) as an oil.

Methanol (5 ml) saturated at 0 °C with ammonia was added to a solution of the mesylate **30** (202 mg, 0.53 mmol) in anhydrous methanol (6 ml). The reaction mixture was stirred at room temperature for 5 h, and then was evaporated under diminished pressure at rt. The residue was chromatographed on silica gel, using for elution chloroform, and a mixture of $CHCl_3$-petroleum ether-methanol (15:7:2) to give the mesylate **18** (79 mg, 85%) as an oil.

4.2.13. Methyl 2-deoxy-α-L-erythro-pentofuranoside (19) from mesylates 17, 18, and 30.

L-Selectride (1 M in THF; 1.6 ml, 1.6 mmol) was added under argon to a solution of the mesylate **17** (79 mg, 0.219 mmol) in anhydrous 1,2-dimethoxyethane (1 ml) at -78 °C. The solution was stirred with gradually warmed to room temperature and then was stirred for 20 h. Ethanol (4 ml) was added to the prepared solution under cooling, and then evaporated to dryness. The residue was dissolved in $CHCl_3$, the precipitate was filtered off, washed with $CHCl_3$ and the filtrates were evaporated. The residue was chromatographed on silica gel, using for elution chloroform, and $CHCl_3$-methanol (12:1) to give methyl 2-deoxy-α-L-*erythro*-pentofuranoside (**19**, 32 mg, 90%) as an oil. $[\alpha]^{25}_D$ = -133.8 (c = 0.67, MeOH). IR (film, $CHCl_3$): ν 3388, 2931, 1090, 1040 cm^{-1}. ^1H NMR (CD_3OD): δ 5.02 (dd, 1H, $J_{1,2}$ = 1.6 Hz, $J_{1,2'}$ = 5.4 Hz, H-1), 4.12 (ddd, 1H, H-3), 3.89-3.92 (m, 1H, $J_{4,5}$ = 3.6 Hz, $J_{4,5'}$ = 4.9 Hz, H-4), 3.67 (dd, 1H, $J_{5,5'}$ = 11.8 Hz, H-5), 3.57 (dd, 1H, H-5`), 3.36 (s, 3H, OCH_3), 2.30 (ddd, 1H, $J_{2,3}$ = 7.7 Hz, $J_{2,2'}$ = 13.9 Hz, H-2), 1.84 (ddd, 1H, $J_{2',3}$ = 3.4 Hz, H-2′). ^{13}C NMR (CD_3OD): δ 106.33 (C-1), 86.79 (C-4), 72.35 (C-3), 63.17 (C-5), 55.19 (OCH_3), 42.34 (C-2). HRMS (ESI^+): m/z calcd for $[C_{16}H_{12}O_4 + Na]^+$: 171.0628, found 171.0725.

L-Selectride (1 M in THF; 3.0 ml, 3.0 mmol) was added under argon to a solution of the mesylate **18** (198 mg, 0.81 mmol) in anhydrous THF (0.75ml) at -78 °C. The solution was stirred with gradually warmed to room temperature and then was stirred for 20 h. Ethanol (5 ml) was added to the prepared solution under cooling, then evaporated to dryness. The residue was dissolved in $CHCl_3$, the precipitate was filtered off, washed with $CHCl_3$ and filtrates were evaporated. The residue was chromatographed on silica gel, using for elution chloroform, $CHCl_3$-methanol (12:1) to give methyl 2-deoxy-α-L-*erythro*-pentofuranoside (**19**, 120 mg, 94%) as an oil.

L-Selectride (1 M in THF; 0.82 ml, 3.0 mmol) was added to a solution of a mixture of mesylates **18** and **22** (0.052 g, 0.21 mmol, ratio - 1.8:1 according to ^1H NMR data) in anhydrous THF (0.2 ml) at -78 °C. The solution was stirred with gradually warmed to room temperature and then was stirred for 21 h. To the prepared solution was added ethanol (2 ml) under cooling, then evaporated. The residue was dissolved in $CHCl_3$, the precipitate was filtered off, and the filtrate was evaporated. The residue was chromatographed on silica gel, using for elution chloroform, and $CHCl_3$-petroleum ether-methanol (15:7:2) to give methyl 2-deoxy-α-L-erythro-pentofuranoside (**19**) (0.01 g, 91%, from mesylate **18**) as an oil.

L-Selectride (1 M in THF; 1.8 ml, 1.8 mmol) was added under argon to a solution of the mesylate **30** (132 mg, 0.25 mmol) in anhydrous 1,2-dimethoxyethane (1.6 ml) at -78 °C. The solution was stirred with gradually warmed to room temperature and then was stirred for 20 h. Ethanol (3.5 ml) was added to the prepared solution under cooling, and then evaporated to dryness. The residue was chromatographed on silica gel, using for elution chloroform, and $CHCl_3$-hexane-methanol (14:7:2) to give methyl 2-deoxy-α-L-*erythro*-pentofuranoside (**19**, 17 mg, 45%) as an oil.

*4.2.14. Methyl-2-deoxy-3,5-di-O-p-toluoyl-α-L-erythro-pentofuranoside (**20**).* Compound **19** (150 mg, 1.0 mmol) was dissolved in pyridine (2.1 ml) and cooled to 0 °C, then *p*-toluoyl chloride (0.3 ml, 2.27 mmol) was added dropwise to the prepared solution. The reaction mixture was stirred for 18 h at room temperature, diluted with cold water (10 ml), and then

extracted with CH_2Cl_2 (3x50 ml). The combined organic extracts were washed with 5%-aqueous $NaHCO_3$ (25 ml), water (30 ml), dried over anhydrous Na_2SO_4 and then evaporated to dryness. The residue was chromatographed on silica gel, using a mixture of 8:1 and 5:1 petroleum ether-EtOAc to afford compound **20** as white solid (330 mg, 86%). M.p.70–73 °C. $[\alpha]^{25}_D$ = -111.1 (c = 0.83, $CHCl_3$). IR (KBr): ν 2930, 1719, 1279, 1180, 1114 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.93 and 7.22 (m, 8H, 2x$CH_3\underline{C_6H_4}CO$), 5.42 (ddd, 1H, H-3), 5.18 (d, 1H, $J_{1,2}$ = 5.13 Hz, $J_{1,2'}$ <1.0 Hz, H-1), 4.62 (dd, 1H, $J_{5,4}$ = 4.5 Hz, $J_{5,5'}$ =12.8 Hz, H-5), 4.51-4.55 (m, 2H, $J_{5',4}$=4.2, Hz, H-4 и H-5`), 3.42 (s, 3H, OCH_3), 2.56 (ddd, 1H, $J_{2,3}$ = 8.0 Hz, $J_{2,2'}$ = 14.7 Hz, H-2), 2.41 (s, 3H, $\underline{CH_3}$-C_6H_4-C=O), 2.40 (s, 3H, $\underline{CH_3}$-C_6H_4-C=O), 2.18 (d, 1H, H-2′). ^{13} C NMR ($CDCl_3$): δ 166.49, 166.28 (CH_3-C_6H_4-$\underline{C=O}$), 143.92, 143.78, 129.82, 129.69, 129.10, 127.11, 127.03 (CH_3-$\underline{C_6H_4}$-C=O),105.06 (C-1), 80.97 (C-3), 74.61 (C-4), 64.31 (C-5), 55.09 (OCH_3), 39.27 (C-2), 21.68 and 21.69 (2x $\underline{CH_3}$-C_6H_4-C=O). HRMS (ESI^+): m/z calcd for $[C_{22}H_{24}O_6 + Na]^+$: 407.1471, found 407.1492.

*4.2.15. Methyl 2-deoxy-3,5-di-O-4-chlorobenzoyl-α-L-erythro-pentofuranoside (**31**) from mesylate **18**.* L-Selectride (1 M in THF; 1.2 ml, 1.2 mmol) was added under argon to a solution of mesylate **18** (74 mg, 0.31 mmol) in anhydrous THF (0.28 ml) at -78 °C. The solution was stirred at 0 °C for 15 min gradually warmed to room temperature and then was stirred for 22 h. Anhydrous THF (0.9 ml) was added to prepared solution, the reaction mixture was cooled to 0 °C and 4-chlorobenzoyl chloride (0.13 ml, 1.0 mmol) was added at 0 °C, and it was stirred for 7 h at room temperature. The reaction mixture was evaporated under diminished pressure, the residue was dissolved in anhydrous CH_2Cl_2 (20 ml), the prepared solution was filtered off, and the filtrate was coevaporated with silica gel. Chromatography was performed using a mixture of 9:1 to 4:1 petroleum ether-EtOAc to give compound **31** as white solid (85 mg, 65%). M.p.64–65 °C. $[\alpha]^{25}_D$ = -152.7 (c = 0.74, $CHCl_3$). IR (KBr): ν 2954, 1722, 1278, 1122, 1096 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.96 and 7.41 (2dd, 8H, 2x4-Cl-C_6H_4CO), 5.40 (ddd, 1H, $J_{3,2}$ = 8.0 Hz, $J_{3,2'}$ = 2.1 HZ, $J_{3,4}$ = 3.6Hz, H-3), 5.19 (br.d, 1H, $J_{1,2'}$ < 1.0 Hz, $J_{1,2}$ = 4.97 Hz, H-1), 4.63 (dd, 1H, $J_{5,4}$ = 3.5 Hz, $J_{5,5'}$ =11.4 Hz, H-5), 4.53 (dd 1H, $J_{5',4}$ = 4.6, H-5′), 4.5-4.53 (m, 1H, H-4), 3.42 (s, 3H, OCH_3), 2.52 (ddd, 1H, $J_{2,2'}$=14.4 Hz, H-2), 2.20 (dd, 1H, H-2′). ^{13}C NMR ($CDCl_3$): δ 165.53, 165.34 (2x4Cl-C_6H_4-*C=O*), 139.79, 139.65, 131.14, 131.02, 128.77, 128.21, 128.11 (2x4Cl-$\underline{C_6H_4}$-C=O), 104.99 (C-1), 80.76 (C-4), 74.93 (C-3), 64.56 (C-5), 55.15 (OCH_3), 39.13 (C-2). HRMS (ESI^+): m/z calcd for $[C_{20}H_{18}O_6Cl_2+Na]^+$: 447.0378, found 447.0373.

4.3. Syntheses of L-ribofuranosides, 2-deoxy-2-fluoro-L-arabinofuranose derivatives and L-FMAU.

*4.3.1. Methyl 2,3,5-tri-O-pivaloyl-β-L-ribofuranoside (**39**).* DAST (0.07 ml, 0.55 mmol) was added to a solution of β-L-glycoside **12** (60 mg, 0.18 mmol) in anhydrous CH_2Cl_2 (2.0 ml) and pyridine (0.017 ml, 1.73 mmol). The reaction mixture was stirred for 18 h at 26-27 °C under argon. The solution was diluted with CH_2Cl_2 (3 ml), poured into cooled 5%-aqueous $NaHCO_3$, and the aqueous phase was extracted with CH_2Cl_2 (3x30 ml). The combined organic extracts were washed with water (10 ml), dried over anhydrous Na_2SO_4, and then evaporated to dryness. The residue was chromatographed on silica gel, using a mixture of 10:1, 5:1 and 3:1 petroleum ether-EtOAc to afford a mixture of methyl 2,5-di-*O*-pivaloyl-β-L-ribofuranoside (**37**) and methyl 3,5-di-*O*-pivaloyl-β-L-ribofuranoside (**38**) (58 mg, 97%, a ratio of 2,5 and 3,5-regoisomers = 1.2.:1.0 according to ^{1}H NMR data) as a syrup. ^{1}H NMR ($CDCl_3$): δ 5.15 (t, 1H, H-3, comp. **38**), 5.05 (d, 1H, H-2, comp. **37**), 4.92 (s, 1H, H-1, comp. **38**), 4.88 (s, 1H, H-1, comp **37**), 4.40-4.44 (m, 1H), 4.09-4.32 (m, 7H), 3.41 (s, 3H, OCH_3, comp. **38**), 3.39 (s, 3H, OCH_3, comp. **37**), 1.24, 1.23, 1.22, 1.21 (4s, 36H, $COC(\underline{CH_3})_3$]. ^{13}C NMR ($CDCl_3$): δ 178.50, 178.22, 178.18, 177.62 (C=O, 4x*CO*C$(CH_3)_3$], 108.62 and 105.99 (2xC-1), 80.94, 78.88, 76.48, 74.34, 73.84, 71.18 (2xC-2,C-3,C-4), 64.69 and 64.24 (2xC-5), 55.33 and 55.13 (2xOCH_3), 39.09, 38.09, 38.88, 38.84 [4xCO*C*$(CH_3)_3$], 27.17 [COC(CH_3)$_3$]. HRMS (ESI^+): m/z calcd for $[C_{16}H_{28}O_7 + Na]^+$: 355.1733, found 355.1732.

Pivaloyl chloride (0.11 ml, 0.9 mmol) was added to a solution of a mixture of protected methyl β-L-arabinofuranosides **37** and **38** (30 mg, 0.09 mmol) in anhydrous pyridine (2.5 ml). The reaction mixture was stirred for 18 h at ambient temperature and then for 5 h at 35-40 °C. The solution was diluted with CH_2Cl_2 (3 ml), poured into a mixture of water and ice, and the aqueous phase was extracted with CH_2Cl_2 (3x20 ml). The combined organic extracts were washed with 5%-aqueous $NaHCO_3$ (10 ml), dried over anhydrous Na_2SO_4 and evaporated to dryness. The residue was chromatographed on silica gel, using a mixture of 15:1 and 8:1 petroleum ether-EtOAc to afford methyl 2,3,5-di-*O*-pivaloyl-β-L-ribofuranoside

(**39**, 32 mg, 85%) as a syrup. $[\alpha]^{25}_{D}$ = +17.1 (*c* = 0.3, $CHCl_3$). IR (film, $CHCl_3$): ν 2974, 2937, 1742, 1285, 1149 cm^{-1}. ^1H NMR ($CDCl_3$): δ 5.33 (dd, 1H, $J_{3,2}$ = 4.7 Hz, $J_{3,4}$ = 4.8 Hz, H-3), 5.21 (d, 1H, H-2), 4.84 (s, 1H, H-1), 4.24-4.30 (m, 2H, H-4 и H-5), 4.12 (dd, 1H, $J_{5',4}$ = 5.4 Hz, $J_{5,5'}$ = 12.2 Hz, H-5′), 3.37 (s, 3H, OCH_3), 1.23, 1.22, 1.18 (3s, 27H, $COC(CH_3)_3$]. ^{13}C NMR ($CDCl_3$): δ 178.26, 177.13, 176.99 (C=O, 3x$COC(CH_3)_3$], 106.15 (C-1), 78.65, 74.49, 71.12 (C-2, C-4, C-3), 64.06 (C-5), 55.21 (OCH_3), 38.84, 38.74 [CO*C*$(CH_3)_3$], 27.10 [COC(*C*$H_3)_3$]. HRMS (ESI^+): m/z calcd for $[C_{21}H_{36}O_8 + Na]^+$: 439.2308, found 439.2570; $[M - OCH_3]^+$: 385.2226, found 385.2409.

*4.3.2. Methyl 3,5-di-O-pivaloyl-α-L-ribofuranoside (**40**).* A solution of protected methyl α-L-arabinofuranoside **13** (396 mg, 1.2 mmol) in anhydrous CH_2Cl_2 (16 ml) was added to a mixture of pyridinium dichromate (674 mg, 1.79 mmol), Ac_2O (0.168 ml, 1.76 mmol), and pulverized 4Å molecular sieves (840 mg) in anhydrous CH_2Cl_2 (6 ml). The reaction mixture was stirred for 2 h under argon at ambient temperature and then filtered off, the powder was washed with anhydrous CH_2Cl_2 and the solution was evaporated to dryness. Ether (30 ml) was added to the oily residue, and then the prepared solution was filtered over pulverized 4Å molecular sieves, which were washed several times with ether. The filtrate and ether washings were evaporated to dryness. The residue was chromatographed on silica gel, using a mixture of 4:1 and 1:1 hexane-EtOAc to afford the intermediate ketone (288 mg, 73%) as a syrup. L-Selectride (1 M in THF; 0.92 ml, 0.92 mmol) was added under argon to a solution of keto-sugar (280 mg, 0.848 mmol) cooled to -78 °C in anhydrous THF (4 ml). The reaction mixture was stirred for 5 min, and then acetic acid (0.2 ml) was added. The prepared solution was diluted with CH_2Cl_2 (60 ml), washed with 1M HCl (15 ml), 5%-aqueous $NaHCO_3$, dried over anhydrous Na_2SO_4, and evaporated to dryness. The residue was purified by chromatography on silica gel, using a mixture of 5:1, 3:1 and 1:1 petroleum ether-EtOAc to afford methyl 3,5-di-*O*-pivaloyl-α-L-ribofuranoside (**40**, 200 mg, 71%) as a syrup. $[\alpha]^{25}_{D}$ = -98.6 (c = 0.43, $CHCl_3$). IR (film, $CHCl_3$): ν 3517, 2967, 2931, 1735, 1159 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 4.97 (dd, 1H, $J_{3,4}$ = 2.7 Hz, $J_{2,3}$ = 7.0 Hz, H-3), 4.94 (d, 1H, $J_{1,2}$ = 4.6 Hz, H-1), 4.32 (dd, 1H, $J_{5,4}$ = 3.5 Hz, $J_{5,5'}$ = 11.8 Hz, H-5), 4.24-4.27 (m, 1H, H-2), 4.21 (dd, 1H, $J_{5',4}$ = 3.85 Hz, H-5′), 4.15-4.17 (m, 1H, H-4), 3.47 (s, 3H, OCH_3), 1.23 and 1.21 (2s, 18H, $COC(CH_3)_3$]. ^{13} C NMR ($CDCl_3$): δ 177.97, 177.81 [C=O, 2x$COC(CH_3)_3$], 102.22 (C-1), 80.67, 71.49 (C-3, C-4), 77.11 (C-2), 63.78 (C-5), 55.32 (OCH_3), 38.88, 38.82 [2xCO*C*$(CH_3)_3$], 27.20, 27.07 [2x(COC$(CH_3)_3$]. HRMS (ESI^+): m/z calcd for $[C_{16}H_{28}O_7 + Na]^+$: 355.1733, found 355.2003, $[M - OCH_3]^+$: 301.1651, found 301.1808.

*4.3.3. Methyl 2-deoxy-2-fluoro-3,5-di-O-pivaloyl-α-L-arabinofuranoside (**42**).* DAST (0.2 ml, 1.56 mmol) was added dropwise to a solution of protected methyl α-L-ribofuranoside **40** (172 mg, 0.52 mmol) in anhydrous CH_2Cl_2 (5.0 ml) and pyridine (0.05 ml, 3.46 mmol). The reaction mixture was stirred for 18 h at 26-27 °C under argon. The solution was diluted with CH_2Cl_2 (7 ml), poured into cooled 5%-aqueous $NaHCO_3$, and the aqueous phase was extracted with CH_2Cl_2 (3x50 ml). The combined organic extracts were washed with water (20 ml), dried over anhydrous Na_2SO_4 and evaporated to dryness. The residue was chromatographed on silica gel, using a mixture of 10:1 and 4:1 petroleum ether-EtOAc to afford fluoride **42** (92 mg, 53%) as a syrup. $[\alpha]^{25}_{D}$ = - 46.2 (c = 0.4, $CHCl_3$). IR (film, $CHCl_3$): ν 2964, 2927, 1742, 1152, 1096, 1033 cm^{-1}. ^{1} H NMR ($CDCl_3$): δ 5.07 (dd, 1H, $J_{3,4}$ = 4.9 Hz, $J_{3,F-2}$ = 13.2 Hz, H-3), 5.07 (d, 1H, $J_{1,F-2}$ = 11.1 Hz, $J_{1,2}$ < 1.0, H-1), 4.84 (d, 1H, $J_{2,F-2}$ = 50.3 Hz, H-2), 4.40 (dd, 1H, H-5), 4.26 (dd, 1H, H-5'), 4.15-4.18 (m, 1H, H-4), 3.38 (s, 3H, OCH_3), 1.21 and 1.209 (2s, 18H, $COC(CH_3)_3$]. ^{13}C NMR ($CDCl_3$): δ 178.1, 177.6 [C=O, 2x$COC(CH_3)_3$], 105.98 (d, $J_{C-1,F}$ = 35.3 Hz, C-1), 98.26 (d, $J_{C-2,F}$ = 181.5 Hz, C-2), 80.73 (C-4), 76.72 (d,$J_{C-3,F}$ = 29.9 Hz, C-3), 62.81 (C-5), 54.65 (OCH_3), 38.86, 38.60 [2xCO*C*$(CH_3)_3$], 27.09, 26.93 [2xCOC(*C*$H_3)_3$]. ^{19} F NMR ($CDCl_3$): δ - 190.85 (ddd, F-2). HRMS (ESI^+): m/z calcd for $[C_{15}H_{24}O_5F - OCH_3]^+$: 303.1608, found 303.1750.

*4.3.4.1-O-Acetyl-2-deoxy-2-fluoro-3,5-di-O-pivaloyl-α-L-arabinofuranose (**43**).* Methyl 2-deoxy-2-fluoro-3,5-di-*O*-pivaloyl-α-L-ribofuranoside (**42**, 90 mg, 0.26 mmol) was dissolved in a mixture of CH_3COOH (0.7 ml), Ac_2O (0.17 ml) and H_2SO_4 (0.026 ml). The reaction mixture was stirred at ambient temperature for 2 h and then poured into a mixture of water and ice. The aqueous phase was extracted with $CHCl_3$ (3x50 ml). The combined organic extracts were washed with cold 5%-aqueous $NaHCO_3$, dried over anhydrous Na_2SO_4 and evaporated to dryness. Acetate **43** (89 mg, 91%) was prepared as a colorless syrup. $[\alpha]^{25}_{D}$ = - 37.1 (c = 0.35, $CHCl_3$). IR (film, $CHCl_3$): ν 2970, 1738, 1229, 1149, 1023 cm^{-1}. ^{1}H

NMR ($CDCl_3$): δ 6.36 (d, 1H, $J_{1,F-2}$ = 9.7 Hz, $J_{1,2}$ < 1.0, H-1), 5.15 (dd, 1H, $J_{3,4}$ = 3.2 Hz, $J_{3,F-2}$ = 19.9 Hz, H-3), 4.97 (d, 1H, $J_{2,F-2}$ = 48.7 Hz, H-2), 4.27-4.35 (m, 3H, H-4, H-5, H-5'), 2.09 (s, 3H, $COCH_3$), 1.23, 1.20 (2s, 18H, $COC(\underline{C}H_3)_3$]. ^{13}C NMR ($CDCl_3$): δ 177.08, 177.26 [2x$COC(CH_3)_3$], 169.02 ($COCH_3$), 98.91 (d, $J_{C-1,F}$ = 34.9 Hz, C-1), 96.96 (d, $J_{C-2,F}$ = 185.5Hz, C-2),83.58 (C-4),75.98 (d, $J_{C-3,F}$ = 30.9 Hz, C-3), 62.76 (C-5), 38.84, 38.62 [2x$CO\underline{C}(CH_3)_3$], 27.06, 26.87 [2x$COC(\underline{C}H_3)_3$], 20.85 ($\underline{CH}_3CO$). ^{19} F NMR ($CDCl_3$): δ -191.07 (ddd, F-2). HRMS (ESI^+): m/z calcd for [$C_{17}H_{27}O_7F$ + $Na]^+$: 385.1634, found 385.1640.

*4.3.5. 2-Deoxy-2-fluoro-3,5-di-O-pivaloyl-α-L-arabinofuranosyl bromide (**44**)*. To a suspension of acetate **43** (0.065 g, 0.18 mmol) and anhydrous $ZnBr_2$ (0.02 g, 0.087 mmol) in anhydrous CH_2Cl_2 (3 mL), TMSBr (0.07 mL, 0.54 mmol) was added at 0 °C. The resulting mixture was stirred under argon at 0 °C for 30 min, then 16 h at room temperature. The reaction mixture was diluted with CH_2Cl_2 (10 mL), then washed a cooled saturated solution of $NaHCO_3$. The aqueous phase was extracted with CH_2Cl_2 (2x10 mL). The combined organic extracts were washed water (2 x 5 ml), dried over anhydrous Na_2SO_4, evaporated to dryness, the residue was coevaporated with anhydrous toluene to give bromide **44** (0.07 g, 97%) as a colorless syrup which was used in the next step without the further purification. ^{1}H NMR ($CDCl_3$): δ 6.52 (d, 1H, $J_{1,F-2}$ = 12.1, $J_{1,2}$ < 1.0, H-1), 5.35 (d, 1H, $J_{2,F-2}$ = 51.1, H-2), 5.10 (dd, 1H, $J_{3,4}$ = 3.0, $J_{3,F-2}$ = 22.0, H-3), 4.45-4.49 (m, 2H, H-4, H-5), 4.36 (dd, 1H, H-5′), 1.26, 1.99 (2s, 18H, $COC(CH_3)_3$]. ^{13}C NMR ($CDCl_3$): δ 177.95, 177.58 [C=O, 2x$COC(CH_3)_3$], 100.51 (d, C-2, $J_{C-2,F}$ =191.5), 87.52 (d, C-1, $J_{C-1,F}$ = 31.9), 84.55 (C-4), 75.67 (d, C-3, $J_{C-3,F}$ = 30.92), 61.81 (C-5), 38.85, 38.61 [2x$CO\underline{C}(CH_3)_3$], 27.03, 26.89 [2x$COC(CH_3)_3$]. ^{19}F NMR ($CDCl_3$): δ -166.2 (ddd, F-2).

*4.3.6.1-(2-Deoxy-2-fluoro-3,5-di-O-pivaloyl-β-L-arabinofuranosyl)thymine (**45**)*. Thymine (0.057 g, 0.45 mmol) and HMDS (2 ml) in the presence of a catalytic amount of $(NH_2)_2SO_4$ was refluxed with stirring for 5 h and then the homogenous solution was evaporated and coevaporated with anhydrous toluene (10 ml). A solution of bromide **44** (0.07 g, 0.183 mmol) in anhydrous 1,2-dichloroethane (2.5 ml) was added to the prepared silylated thymine, and the reaction mixture was refluxed under N_2 for 18 h. After cooling the reaction mixture was poured into a mixture of water and ice, and extracted with $CHCl_3$ (3x20 ml). The combined organic extracts were washed with a cooled saturated aqueous $NaHCO_3$ (2x10 ml), water, and dried over anhydrous Na_2SO_4, evaporated to dryness. The residue (82 mg) was chromatographed on silica gel, using for elution chloroform, $CHCl_3$-petroleum ether-methanol (20:15:1) to afford β-nucleoside **45** (0.05 g, 60%). M.p. 128-131 °C (hexane). IR (KBr): ν 2974, 2940, 1735, 1285, 1152, 1040 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 8.53 (br.s, 1H, NH), 7.35 (br.s, 1H, H-6), 6.16 (dd, 1H, $J_{1',2'}$ = 2.8 Hz, $J_{1',F-2'}$ = 12.2 Hz, H-1′), 5.22 (dd, 1H, $J_{3',4'}$ = 2.8 Hz, $J_{3',2'}$ < 1.0, $J_{3',F-2'}$ = 17.3 Hz, H-3′), 5.09 (dd, 1H, $J_{2',F-2'}$ = 50.3 Hz, $J_{2',1'}$ = 2.8 Hz, $J_{2',3'}$ < 1.0, H-2′), 4.52 (dd, 1H, $J_{5',4'}$ = 5.4 Hz, $J_{5',5''}$ = 12.1 Hz, H-5'), 4.38 (dd, 1H, $J_{5'',4}$ = 3.5 Hz, H-5″), 4.13-4.16 (m, 1H, H-4′), 1.93 (d, 3H, CH_3-C5), 1.24 (s, 18H, $COC(\underline{C}H_3)_3$]. ^{13}C NMR ($CDCl_3$): δ 177.11, 177.17 [2x$COC(CH_3)_3$], 163.26 (C-4), 150.0 (C-2), 136.35 (d, $J_{C-6,F-2'}$ = 3.1 Hz, C-6), 110.47 (C-5), 92.55 (d, $J_{C-2,F}$ = 191.4Hz, C-2), 84.5 (d, $J_{C-1,F}$ = 15.95 Hz, C-1), 81.32 (C-4), 75.8 (d, $J_{C-3,F}$ = 29.9 Hz, C-3), 62.52 (C-5), 38.93, 38.74 [2x$CO\underline{C}(CH_3)_3$], 27.13, 26.98 [2x$COC(\underline{C}H_3)_3$], 12.41 (CH_3-C5). HRMS (ESI^+): m/z calcd for [$C_{20}H_{29}O_7N_2F$ + $Na]^+$: 451.1856, found 451.2048.

*4.3.7. 1-(2-Deoxy-2-fluoro-β-L-arabinofuranosyl)thymine (**2**)*. Compound **45** (0.038 g, 0.088 mmol) was stirred in 0.074M $NaOCH_3$-MeOH (2.8 ml) at room temperature for 18 h, then the reaction mixture was neutralized with acetic acid and evaporated. The residue was coevaporated with a mixture of toluene:ethanol (1:1), purified by column chromatography on silica gel using for elution chloroform, $CHCl_3$-methanol 20:1 and 15:1 to give nucleoside **2** (0.018 g, 80%) as white solid. M.p.184-185 °C. ^{1}H NMR (CD_3OD): δ 7.59 (t, 1H, $J_{H-6,\ CH3}$ = 1.3 Hz, $J_{H-6,\ F-2'}$ = 1.3 Hz, H-6), 6.17 (dd, 1H, $J_{1',2'}$ = 4.0 Hz, $J_{1',F-2'}$ = 17.0 Hz, H-1′), 5.09 (ddd, 1H, $J_{2',3'}$ = 2.6 $J_{2',F-2'}$ = 52.4 Hz, H-2′), 4.32 (ddd, 1H, $J_{3',4'}$ = 4.9 Hz $J_{3',F-2'}$ = 19.6 Hz, H-3′), 3.88-3.91 (m, 1H, H-4′), 3.84 (ddd, 1H, $J_{5',4'}$ = 3.7 Hz, $J_{5',\ F-2'}$ = 1.1 Hz, $J_{5',5''}$ = 12.6 Hz, H-5'), 3.75 (dd, 1H, $J_{5'',4}$ = 5.1 Hz, H-5″), 1.88 (d, 3H, $J_{CH3,H-6}$ = 1.3 Hz, CH_3-C5). ^{13}C NMR (CD_3OD): δ 164.92 (C-4), 150.71 (C-2), 137.3 (d, $J_{C-6,F-2'}$ = 2.9 Hz, C-6), 109.23 (C-5), 95.57 (d, $J_{C-2,F}$ = 191.0 Hz, C-2), 84.05 ($J_{C-4,F}$ = 3.2 Hz, C-4), 83.61 (d, $J_{C-1,F}$ = 16.8 Hz, C-1), 73.45 (d, $J_{C-3,F}$ = 25.1 Hz, C-3), 60.39 (C-5), 10.97 (CH_3-C5). ^{19}F NMR (CD_3OD): δ -200.76 (dt, F-2'). HRMS (ESI^+): m/z calcd for [$C_{10}H_{13}O_5N_2F$ + $Na]^+$: 283.0706, found 283.0887.

Supplementary data

Supplementary data associated with this article can be found, in the online version.

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