[5-(ADENIN-9-YL)-5-DEOXY-L-PENTOFURANOSYL]PHOSPHONATES – A NOVEL TYPE OF NUCLEOTIDE ANALOGS RELATED TO HPMPA. II. SYNTHESIS OF L-*ribo* and L-*xylo* CONFIGURATED DERIVATIVES BY RECYCLIZATION OF DIETHYL (5-*RS*)-[1,2-*O*-ISOPROPYLIDENE-5-*O*-METHANESULFONYL-D-PENTOFURANOS-5-*C*-YL]PHOSPHONATES UNDER ACIDIC CONDITIONS

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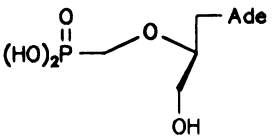
Further cyclic analogs of the antiviral (*S*)-9-(3-hydroxy-2-phosphonomethoxypropyl)adenine (*I*) were prepared: both anomers of [5-(adenin-9-yl)-5-deoxy-L-ribofuranosyl]phosphonic acid (α-*IId* and β-*IId*) and [5-(adenin-9-yl)-5-deoxy-α-L-xylofuranosyl]phosphonic acid (*IIe*). Recyclization reaction of diethyl (5*RS*)-(3-*O*-benzyl-1,2-*O*-isopropylidene-5-*O*-methanesulfonyl-D-ribofuranos-5-*C*-yl)phosphonate (*IVb*) and diethyl (5*RS*)-(3-*O*-benzyl-1,2-*O*-isopropylidene-5-*O*-methanesulfonyl-D-xylofuranos-5-*C*-yl)phosphonate (*IVd*) in trifluoroacetic acid led to cyclic aldehydes *Va* and *Vb* which were reduced to diethyl α- and β-L-ribofuranosylphosphonates *VIb* and α-L-xylofuranosylphosphonate *VIIb*. Conversion to the protected 5-*O*-tosylates *VId* and *VIId*, followed by reaction with adenine and deprotection, afforded the mentioned nucleotide analogs *IId* and *IIe*. An attempt to prepare L-pentofuranosylphosphonates *Vc* and *XIII*, suitable for the synthesis of nucleotide analogs of 3-deoxy-L-*erythro* and L-*lyxo* configuration (*IIf* and *IIg*, respectively) by the recyclization reaction of the corresponding 5-*O*-methanesulfonyl derivatives *IVf* and *XIIb* failed. In this case, anhydro derivatives *IXa*, *XVa* and *XVIa* were isolated and identified.

In our previous communication[1] we described the preparation of [5-(adenine-9-yl)-5-deoxy-L-pentofuranosyl]phosphonic acids of L-*arabino* (*IIa*), 2-deoxy-L-*erythro* (*IIb*) and 2-deoxy-L-*threo* (*IIc*) configuration from the corresponding methyl L-pentofuranosides as the basic synthons. Our further aim was the preparation of compounds of L-*ribo* (*IId*), L-*xylo* (*IIe*), 3-deoxy-L-*erythro* (*IIf*) and L-*lyxo* (*IIg*) configuration by a method that would utilize D-pentafuranoses for the synthesis of the key α- and β-L-pentofuranosylphosphonates *VIb*, *VIIb*, *Vc* and L-arabinose for the preparation of *lyxo* configurated phosphonate *XIII* as direct precursors of analogs *IId* – *IIg*. For this purpose we made use of a known recyclization reaction of several 1,2-*O*-isopropylidene-5-*O*-methanesulfonyl-D-pentofuranoses in acid medium[2]. This consists in opening of the furanose ring followed by cyclization leading to the 2,5-anhydropentose ring (attack by

the hydroxyl group in position 2 at the C(5) atom bearing the *O*-mesyl group). The cyclization proceeds with inversion of configuration at C(5) atom which thus becomes the C(1) atom of the arising compound, whereas the C(1) anomeric atom of the original D-sugar becomes the C(5) atom of the newly formed five-membered anhydro ring. Thus, the final product of this recyclization reaction is a 1,4-anhydropentose (new numbering) derivative. This principle of acid-catalyzed cyclization of mesylates has been utilized also in the synthesis of pentofuranose ring in some *C*-nucleosides[3] from a precursor containing a heterocyclic base bonded to carbon atom of acyclic chain, bearing also the *O*-mesyl group. After the reaction, the mentioned carbon atom becomes the anomeric center of the arising pentofuranoside.

On the basis of these facts we performed the addition of diethyl phosphite to the free aldehyde group of 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*ribo*-pentodialdose-(1,4) (*IIIa*, ref.[4]), 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-pentodialdose-(1,4) (*IIIb*, ref.[5]), 3-deoxy-1,2-*O*-isopropylidene-α-D-*erythro*-pentodialdose-(1,4) (*IIIc*, ref.[6]) and 3-*O*-(tetrahydropyran-2-yl)-1,2-*O*-isopropylidene-β-L-*arabino*-pentodialdose-(1,4) (*XId*), followed by mesylation of the epimeric hydroxyl group of newly formed sugar phosphonates *IVa*,



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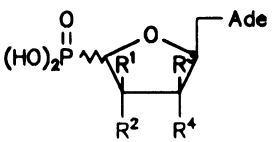
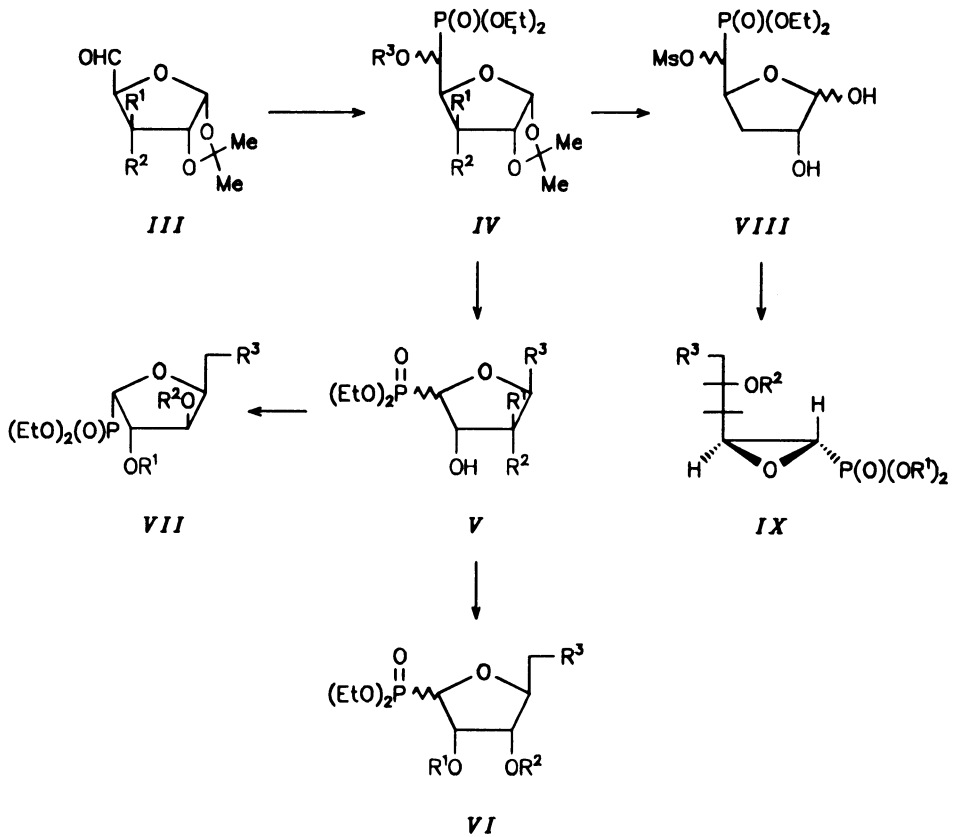


II	R^1	R^2	R^3	R^4
a	OH	H	H	OH
b	H	H	H	OH
c	H	H	OH	H
d	H	OH	H	OH
e	H	OH	OH	H
f	H	OH	H	H
g	OH	H	OH	H

IVc, *IVe* and *XIIa*. The resulting diethyl (5*RS*)-(1,2-*O*-isopropylidene-5-*O*-methanesulfonyl-D-pentofuranos-5-*C*-yl)phosphonates *IVb*, *IVd*, *IVf* and *XIIb* (ratio of epimers: 1 : 1 (*IVb*), 3 : 1 (*IVd*), 4 : 3 (*IVf*) and 5 : 3 (*XIIb*); determined by HPLC without distinguishing the *R* and *S* epimers) were subjected to the recyclization reaction in trifluoroacetic acid. In the first two cases the reaction gave probably compounds *Va* and *Vb* with free aldehyde group which was immediately reduced in an aqueous medium with sodium borohydride to the hydroxy group (Scheme 1). Whereas the recyclization of mesylates *IVf* and *XIIb* did not lead to the desired phosphonates *Vc* and *XIII*, the mesylate *IVb* afforded a mixture of anomeric diethyl (3-*O*-benzyl-L-ribofuranosyl)-phosphonates (α-*VIa* and β-*VIa*); however, their ratio was entirely different from that corresponding to the composition of the starting mesylate *IVb*. On the other hand, in the



SCHEME 1

Compound	R^1	R^2	R^3
IIIa	H	OBn	–
IIIb	OBn	H	–
IIIc	H	H	–
IVa	H	OBn	H
IVb	H	OBn	Ms
IVc	OBn	H	H
IVd	OBn	H	Ms
IVe	H	H	H
IVf	H	H	Ms
Va	H	OBn	CHO
Vb	OBn	H	CHO
Vc	H	H	CH_2OH
VIa	H	Bn	OH
VIb	H	H	OH
VIc	Me–C–Me		OH
VId	Me–C–Me		OTs
VIe	Me–C–Me		Ade
VIf	H	H	Ade
VIIa	H	Bn	OH
VIIb	H	H	OH
VIIc	H	H	OTs
VIId	THP	THP	OTs
VIIe	THP	THP	Ade
IXa	Et	H	OH
IXb	Et	H	OTs
IXc	Et	THP	OTs
IXd	Et	THP	Ade
IXe	Et	H	Ade
IXf	H	H	Ade

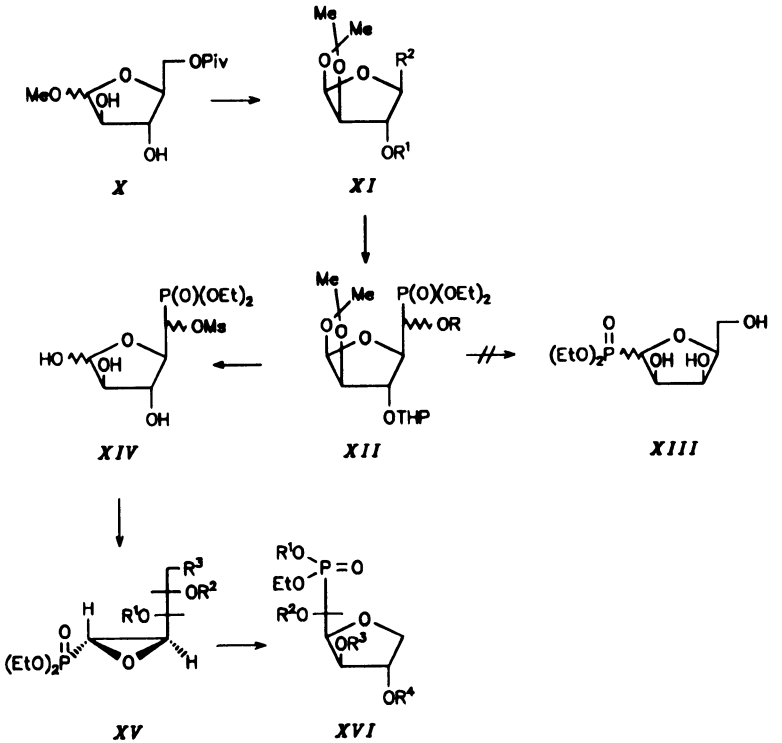
Bn, benzyl
Ms, methanesulfonyl
Ts, 4-toluenesulfonyl
Ade, adenin-9-yl
THP, tetrahydropyran-2-yl

recyclization of mesyl derivative *IVd* we isolated only diethyl (3-*O*-benzoyl-α-L-xylofuranosyl)phosphonate (*VIIa*). Interestingly, the same anomer was also isolated in 30% yield in the reaction of anomeric methyl 2,3,5-tri-*O*-(trimethylsilyl)-L-xylofuranosides (α : β = 4 : 3) with triethyl phosphite in the presence of trimethylsilyl triflate according to procedure described in ref.[1]. The isolated *O*-benzyl derivatives *VIa* and *VIIa* were hydrogenolytically debenzylated to give (L-pentofuranosyl)phosphonates *VIb* and *VIIb*. It cannot be excluded that already during the recyclization in trifluoroacetic acid the *O*-benzyl groups may be partially hydrolyzed under formation of products *VIb* and *VIIb*, but because of similarity of the R_F values we did not try to isolate these compounds from the recyclization mixture.

The recyclization reaction of mesyl derivative *IVf* under acidic conditions, followed by reduction of the product, afforded as the only identifiable product diethyl (5*S*)-[4,5-anhydro-3-deoxy-D-*erythro*-pentitol-5-*C*-yl]phosphonate (*IXa*) instead of the expected pentofuranosyl phosphonate with 3-deoxy-L-*erythro* configuration (*Vc*). Also the recyclization of mesylate *XIIb* did not lead to the expected L-*lyxo* phosphonate *XIII*. Two types of anhydro compounds were isolated: diethyl (5*R*)-[4,5-anhydro-L-arabinitol-5-*C*-yl]phosphonate (*XVa*) and diethyl (5*R*)-[1,4-anhydro-D-xylitol-5-*C*-yl]phosphonate (*XVIa*) (Scheme 2). The formation of the above-mentioned 4,5-anhydro compounds *IXa* and *XVa*, containing the oxirane ring, may be explained as follows: in the first stage, sodium borohydride reduces the aldehyde hemiacetal group in the phosphonates *VIII* and *XIV* to give open-chain structures in which then the 5-*O*-mesyl groups undergo nucleophilic substitution by the neighbouring hydroxyl under formation of the oxirane ring. The formation of 1,4-anhydro compound *XVIa* with five-membered ring can be derived only from the 4,5-anhydro derivative *XVa* in which the oxirane ring is opened by intramolecular attack by the primary hydroxyl.

On the basis of these results we may conclude that *1*) the recyclization reaction of epimeric *O*-mesyl derivatives derived from one type of sugar phosphonate proceeds via different reaction mechanism for each epimer, and *2*) 5-*O*-mesyl derivatives of different sugar phosphonates also undergo recyclization by different mechanisms, similarly as in the case of 5-*O*-tosyl derivatives of aldofuranoses[2].

The diethyl esters of (L-pentofuranosyl)phosphonates of L-*ribo* (*VIb*) and L-*xylo* (*VIIb*) configuration, and also of both *trans*-epoxyphosphonates *IXa* and *XVa*, obtained by recyclization of mesyl derivatives *IVb*, *IVd*, *IVf* and *XIIb*, were subjected to a series of reactions leading to 5-*O*-tosyl derivatives protected at the remaining secondary hydroxy groups by an isopropylidene (compounds *VId* and *XVc*) or a tetrahydropyranyl group (compounds *VIId* and *IXc*). Chemically interesting is the course of tosylation of the epimeric 1,4-anhydrophosphonates *XVIa* (the main product of recyclization of mesylates *XIIb*), that led to 2-*O*-tosyl compounds *XVIb* which were smoothly converted into the 3,5-*O*-isopropylidene derivatives *XVIc*.



Compound	R	R^1	R^2	R^3	R^4
XIa	–	H	CH_2OPiv	–	–
XIb	–	THP	CH_2OPiv	–	–
XIc	–	THP	CH_2OH	–	–
XId	–	THP	CHO	–	–
XIIa	H	–	–	–	–
XIIb	Ms	–	–	–	–
XVa	–	H	H	OH	–
XVb	–	H	H	OTs	–
XVc	–	Me–C–Me		OTs	–
XVIa	–	Et	H	H	H
XVIb	–	Et	H	H	Ts
XVIc	–	Et	Me–C–Me		Ts
XVId	–	H	Me–C–Me		Ts

Piv, pivaloyl

SCHEME 2

The thus-obtained fully protected 5-*O*-tosyl derivatives *VId*, *VIId* and *IXc* were reacted with sodium salt of adenine in dimethylformamide to give the adenine derivatives *VIe*, *VIIe* and *IXd*. On the other hand, the 2-*O*-tosyl group in compound *XVIc* is completely inert against nucleophilic substitution with adenine. In this case only one ester group in compound *XVIc* was cleaved off and the reaction mixture afforded monoester *XVId* as the only product. The final removal of the acid-labile protecting groups under acidic conditions, and of the phosphonate diethyl ester groups by treatment with bromotrimethylsilane, converted the derivatives *VIe*, *VIIe* and *IXd* into anomeric [5-(adenin-9-yl)-5-deoxy-L-ribofuranosyl]phosphonic acids (α-*IId* and β-*IId*), [5-(adenin-9-yl)-5-deoxy-α-L-xylofuranosyl]phosphonic acid (*IIe*) and (5*S*)-[1-(adenin-9-yl)-4,5-anhydro-3-deoxy-D-*ribo*-pentitol-5-*C*-yl]phosphonic acid (*IXf*).

The structure of the studied compounds was confirmed by ^{1}H and ^{13}C APT (attached proton test) NMR spectra. Tables I and II show chemical shifts and coupling constants of protons in the sugar part of the studied L-pentofuranosylphosphonates, Tables III and IV contain ^{13}C NMR data for carbon atoms of the same part of the molecule. Spectra of the other compounds are given in the Experimental. Spectra of the α- and β-L-ribofuranosylphosphonates correspond to the values published in ref.[7] and are characterized by vicinal coupling constant ^3J(H-2,P) that depends on the dihedral angle H–C(2)–C(1)–P and the magnitude of the coupling constant ^1J(C,P) (ref.[1]). As expected, for compounds of α-*xylo* configuration these values are similar to those for the α-*ribo* series. Phosphonates *IXa* – *IXf* and *XVa* – *XVc* have no furanose ring. Their proton H-5

TABLE I
^{1}H NMR chemical shifts of L-ribo- and L-xylofuranosylphosphonates

Compound	δ, ppm					
	H-1	H-2	H-3	H-4	H-5	H-5′
α-*IId*[a]	3.78	4.09	3.80	4.19	4.47	4.43
β-*IId*[a]	3.79	4.22	4.06	3.89	4.54	4.39
IIe[a]	4.26	4.39	4.25	4.56	4.50	4.41
β-*VIb*	3.38	4.12	3.77	3.71	3.50	3.37
α-*VId*	4.26	4.85	4.54	4.18	4.08	4.04
β-*VId*	4.20	4.84	4.59	4.12	4.16	4.12
α-*VIe*	4.46	5.00	4.76	4.47	4.28	4.23
β-*VIe*	4.25	4.94	4.76	4.43	4.42	4.33
VIIb	4.19	4.15	3.90	4.01	3.58	3.47
VIIc	4.17	4.12	3.94	4.19	4.18	3.97

[a] Measured in D_2O.

on the carbon atom in position α to the phosphono group is characterized by an upfield doublet of doublets (δ = 3.00 – 3.20) with coupling constants $^3J(5,4)$ = 2.4 – 3.0 Hz and $^2J(5,P)$ = 29.5 – 31.5 Hz. Also the H-4 proton does not correspond to the H-2 proton in the furanoses and is shifted upfield (δ = 3.20 – 3.35), with constants $^3J(4,5)$ = 2.4 – 3.0 Hz, $^3J(4,3)$ = 5.0 Hz and $^3J(4,P)$ = 5.0 Hz. In the proton-decoupled ^{13}C NMR spectrum, these compounds are characterized by a doublet of carbon C(5) at δ = 48 ($^1J(C,P)$ = 198 Hz)

TABLE II
^1H NMR interaction constants of L-ribo- and L-xylofuranosylphosphonates

Compound	*J*, Hz								
	1,2	2,3	3,4	4,5	4,5′	5,5′	1,P	2,P	3,P
α-*IId* [a]	2.9	3.9	8.3	3.9	5.4	14.6	7.3	0.5	–
β-*IId* [a]	2.4	5.4	8.3	2.9	8.8	14.6	6.3	7.3	–
IIe [a]	3.4	1.5	2.9	4.9	7.8	14.6	5.9	1.0	–
β-*VIb*	4.4	5.1	6.1	3.7	5.6	11.7	1.0	10.5	–
α-*VId*	3.9	6.1	1.5	6.8	4.8	13.0	9.5	1.5	–
β-*VId*	3.7	6.3	3.2	5.6	6.1	12.9	3.6	8.8	–
α-*VIe*	3.7	6.1	0.5	9.8	4.9	14.6	10.2	1.0	–
β-*VIe*	3.7	6.3	3.2	5.1	9.0	15.1	3.6	9.0	–
VIIb	3.9	1.7	2.9	5.6	6.1	11.5	3.7	1.7	2.5
VIIc	3.9	1.7	3.1	3.9	8.5	11.2	3.7	1.7	2.0

[a] Measured in D_2O.

TABLE III
^{13}C NMR chemical shifts of L-ribo- and L-xylofuranosylphosphonates

Compound	δ, ppm				
	C(1)	C(2)	C(3)	C(4)	C(5)
β-*VIb*	78.43	71.82	71.96	84.51	62.18
α-*VId*	76.99	81.71	82.06	83.37	68.81
β-*VId*	79.49	81.49	81.06	82.89	69.55
α-*VIe*	75.20	81.28	82.19	83.34	41.45
β-*VIe*	79.40	82.49	81.26	83.43	44.82
VIIc	77.11	77.02	76.17	79.01	69.80

and a singlet of carbon C(4) in the region δ = 55 – 57. In accord with refs[8,9], these values correspond to the suggested *trans*-epoxyphosphonate structure. As follows from the ^{1}H and ^{13}C APT NMR spectra and their comparison with the published[7,10] data, compounds *XVIa – XVId* have not the expected *lyxo* configuration *XIII*. In the proton-decoupled ^{13}C NMR spectrum they are characterized by a doublet of the carbon atom C(5) in position α to the phosphono group (δ = 64, ^1J(C,P) = 164 Hz), a singlet of C(4) at δ = 77 – 80, a doublet of carbon C(3) (δ = 73 – 75, ^3J(C,P) = 7 – 11 Hz), and a singlet of C(2) at δ = 84 and of C(1) at δ = 70. In the spectra of isopropylidene derivatives *XVIc* and *XVId* the quaternary carbon atom of the protecting group appears as a doublet (δ = 100, ^3J(C,P) = 11 Hz). On the basis of these data we suggested for these compounds the structures *XVI* with 1,4-anhydro ring.

None of the nucleotide analogs α-*IId*, β-*IId*, *IIe* and *IXf* showed any significant in vitro antiviral effect against a standard series of DNA viruses and retroviruses.

EXPERIMENTAL

Unless stated otherwise, the solvents were evaporated at 40 °C/2 kPa and the compounds were dried at 13 Pa over phosphorus pentoxide. In all the described procedures the reaction course was followed by TLC on Silufol UV 254 foils (Kavalier, The Czech Republic); detection in UV light, by heating or by spraying with 0.4% solution of 4-(4-nitrobenzyl)pyridine in ethanol, subsequent heating and exposure to ammonia vapours. Preparative column chromatography was carried out on spherical silica gel 20 – 40 μm (Tessek, The Czech Republic; 20 – 40 times greater amount than that of the mixture to be separated), elution at 50 kPa overpressure. Analytical and preparative thin-layer chromatography (TLC) was performed in the following solvent systems (v/v): toluene (A); toluene–ethyl acetate 49 : 1 (B), 19 : 1 (C), 9 : 1 (D), 4 : 1 (E), 1 : 1 (F); chloroform (G), chloroform–ethanol 49 : 1 (H), 19 : 1 (I), 9 : 1 (J), 17 : 3 (K), 4 : 1 (L); chloroform–methanol 4 : 1 (M); ethyl acetate–acetone–ethanol–water 4 : 1 : 1 : 1 (N), 6 : 1 : 1 : 1 (O), 12 : 2 : 2 : 1 (P); 2-propanol–conc. aqueous ammonia–water 7 : 1 : 2 (Q). HPLC analyses were carried out on a reversed phase (C18) Separon

TABLE IV
^{13}C NMR interaction constants of L-ribo- and L-xylofuranosylphosphonates

Compound	*J*, Hz			
	P,C(1)	P,C(2)	P,C(3)	P,C(4)
β-*VIb*	165.6	4.4	6.6	6.6
α-*VId*	170.0	5.1	8.8	13.9
β-*VId*	164.8	4.4	6.6	6.6
α-*VIe*	168.5	5.1	8.8	14.7
β-*VIe*	166.3	4.4	8.1	5.1
VIIc	170.7	4.4	5.9	8.1

SGX-RPS 10 μm (Laboratorní přístroje, Praha), elution with a linear gradient 10 – 40% (v/v) of methanol in 0.05 M triethylammonium acetate. The electrophoreses were performed on a Whatman 3 MM paper in 0.1 M triethylammonium hydrogen carbonate (pH 7.5) at 20 V/cm. Mass spectra were measured on a ZAB-EQ (VG Analytical) spectrometer, using the EI (electron energy 70 eV), FAB (ionization by Xe, accelerating voltage 8 kV) and SIMS (ionization by Cs^+, accelerating voltage 35 kV) techniques; matrices glycerol and thioglycerol. ^1H NMR spectra were measured on Varian Unity 200 (200 MHz) and Varian Unity 500 (500 MHz) instruments in hexadeuteriodimethyl sulfoxide with tetramethylsilane as internal standard, unless stated otherwise. Free phosphonic acids were measured in deuterium oxide containing sodium deuteroxide with sodium 3-(trimethylsilyl)-1-propanesulfonate (DSS) as internal standard. ^{13}C NMR spectra were obtained with a Varian Unity 200 (50.3 MHz) spectrometer in hexadeuteriodimethyl sulfoxide. The signals were referenced to the solvent signal and the chemical shifts were calculated using the relationship $\delta(CD_3SOCD_3) = 39.7$.

[5-(Adenin-9-yl)-5-deoxy-α-L-ribofuranosyl]phosphonic Acid (α-*IId*)

The protected phosphonate α-*VIe* (80 mg, 0.19 mmol) was first deblocked to give compound α-*VIf* (R_F 0.42 (L)) which was converted into 32 mg (52%) of phosphonate α-*IId* according to the procedures described in ref.[1]; R_F 0.55 (Q); Mas spectrum (FAB): 332 (MH^+).

[5-(Adenin-9-yl)-5-deoxy-β-L-ribofuranosyl]phosphonic Acid (β-*IId*)

Compound β-*VIe* (810 mg, 1.9 mmol) was processed in the same way as described for the phosphonate α-*IId*. Yield of the free phosphonate β-*IId* was 404 mg (64%); R_F 0.55 (Q); Mas spectrum (FAB): 332 (MH^+). For $C_{10}H_{14}N_5O_6P$ (331.2) calculated: 36.26% C, 4.26% H, 21.14% N, 9.35% P; found: 36.42% C, 4.33% H, 21.05% N, 9.24% P.

[5-(Adenin-9-yl)-5-deoxy-α-L-xylofuranosyl]phosphonic Acid (*IIe*)

Compound *VIIc* (425 mg, 1 mmol) was converted into di-*O*-tetrahydropyranyl derivative *VIId* by a series of reactions[1]. Reaction of *VIId* with sodium salt of adenine afforded product *VIIe* which on treatment with bromotrimethylsilane gave the free phosphonate *IIe* (121 mg, 37% based on *VIIc*); R_F 0.31 (Q); Mas spectrum (FAB): 332 (MH^+).

Diethyl (5*RS*)-[3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-ribofuranos-5-*C*-yl]-phosphonate (*IVa*)

A mixture of 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-ribopentodialdose-(1,4) (*IIIa*, ref.[4]; 11.7 g, 42 mmol), diethyl phosphite (5.7 ml, 44.2 mmol) and triethylamine (1.2 ml, 8.6 mmol) was heated at 80 °C for 4 h. The product was isolated on a column of silica gel in the system D; yield 15.3 g (88%) of product *IVa*; R_F 0.29 (F); Mas spectrum (FAB): 417 (MH^+). For $C_{19}H_{29}O_8P$ (416.4) calculated: 54.80% C, 7.02% H, 7.44% P; found: 55.13% C, 6.94% H, 7.56% P.

Diethyl (5*RS*)-[3-*O*-Benzyl-1,2-*O*-isopropylidene-5-*O*-methanesulfonyl-α-D-ribofuranos-5-*C*-yl]phosphonate (*IVb*)

Mesyl chloride (3.0 ml, 38.8 mmol) was added at 0 °C to a solution of phosphonate *IVa* (15.3 g, 36.7 mmol) in pyridine (40 ml). After standing at room temperature for 4 h and cooling again to 0 °C, the excess mesyl chloride was decomposed by addition of water (10 ml). The solvent was evaporated, the residue dissolved in ethyl acetate, the solution washed with saturated solution of sodium hydrogen carbonate and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave 16.6 g

(91%) of product *IVb* (ratio of epimers 1 : 1); R_F (F); Mas spectrum (FAB): 495 (MH^+). For $C_{20}H_{31}O_{10}PS$ (494.5) calculated: 48.58% C, 6.32% H, 6.26% P, 6.48% S; found: 48.77% C, 6.39% H, 6.21% P, 6.39% S.

Diethyl (5*RS*)-[3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-xylofuranos-5-*C*-yl]-phosphonate (*IVc*)

The title product was prepared from 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-pentodialdose-(1,4) (*IIIb*, ref.[5]; 11.5 g, 41.3 mmol) according to the procedure described for compound *IVa*. Yield 15 g (87%) of product *IVc*; R_F 0.29 (F); Mas spectrum (FAB): 417 (MH^+). For $C_{19}H_{29}O_8P$ (416.4) calculated: 54.80% C, 7.02% H, 7.44% P; found: 54.68% C, 7.01%H, 7.51% P.

Diethyl (5*RS*)-[3-*O*-Benzyl-1,2-*O*-isopropylidene-5-*O*-methanesulfonyl-α-D-xylofuranos-5-*C*-yl]phosphonate (*IVd*)

Compound *IVc* (15 g, 36 mmol) was mesylated according to the procedure described for compound *IVb*. Yield 16 g (90%) of product *IVd* (ratio of epimers 3 : 1); R_F 0.52 (F); Mas spectrum (FAB): 495 (MH^+). For $C_{20}H_{31}O_{10}PS$ (494.5) calculated: 48.58% C, 6.32% H, 6.26% P, 6.48% S; found: 48.41% C, 6.23% H, 6.31% P, 6.39% S.

Diethyl (5*RS*)-[3-Deoxy-1,2-*O*-isopropylidene-α-D-*erythro*-pentofuranos-5-*C*-yl]-phosphonate (*IVe*)

The product was prepared from 3-deoxy-1,2-*O*-isopropylidene-α-D-*erythro*-pentodialdose-(1,4) (*IIIc*, ref.[6]; 9.4 g, 54.6 mmol) according to the procedure described for compound *IVa*. Yield 10.5 g (62%) of product *IVe*; R_F 0.33 (F); Mas spectrum (FAB): 311 (MH^+). For $C_{12}H_{23}O_7P$ (310.3) calculated: 46.45% C, 7.47% H, 9.98% P; found: 46.55% C, 7.38% H, 10.05% P.

Diethyl (5*RS*)-[3-Deoxy-1,2-*O*-isopropylidene-5-*O*-methanesulfonyl-α-D-*erythro*-pentofuranos-5-*C*-yl]phosphonate (*IVf*)

Compound *IVe* (10.5 g, 33.8 mmol) was mesylated as described for compound *IVb*; yield 11.5 g (88%) of product *IVf* (ratio of epimers 4 : 3); R_F 0.50 (H); Mas spectrum (FAB): 389 (MH^+). For $C_{13}H_{25}O_9PS$ (388.4) calculated: 40.20% C, 6.49% H, 7.98% P, 8.26% S; found: 40.31% C, 6.56% H, 7.81% P, 8.31% S.

Diethyl α- and β-L-Ribofuranosylphosphonates (*VIb*)

A solution of compound *IVb* (16.6 g, 33.6 mmol) in a mixture of trifluoroacetic acid–dichloromethane (4 : 1, 130 ml) was set aside at room temperature for 15 h. After evaporation of the solvent and codistillation with dioxane, the residue was dissolved in water (100 ml) and cooled to 0 °C. Sodium borohydride (3.8 g, 100.5 mmol) was added in five portions during 20 min, the reaction mixture was stirred for further 30 min at room temperature, filtered and diluted with a nine-fold volume of water. The solution was successively deionized with Dowex 50 (H^+ form, 350 ml) and Dowex 1 (acetate form, 130 ml). The obtained product *VIa* (R_F 0.47 (K)) was hydrogenolytically debenzylated according to the described[1] procedure. Chromatography on silica gel in the system J afforded 2.9 g (32%) of compound *VIb* (α : β 1 : 8); R_F 0.43 (P); Mas spectrum (FAB): 271 (MH^+). For $C_9H_{19}O_7P$ (270.2) calculated: 40.00% C, 7.09% H, 11.46% P; found: 40.25% C, 7.13% H, 11.29% P.

Diethyl (2,3-*O*-Isopropylidene-5-*O*-tosyl-α- and β-L-ribofuranosyl)-phosphonates (α-*VId* and β-*VId*)

A solution of *cis*-diol *VIb* (α : β = 1 : 8; 2.6 g, 10.7 mmol) and 2,2-dimethoxypropane (2.0 ml, 16.3 mmol) in acetone (20 ml) was acidified with several drops of 1 M hydrogen chloride in dioxane (a strongly acidic reaction to moist indicator paper) and the reaction mixture was allowed to stand at room temperature for 15 h. Triethylamine (1 ml) was then added, the solvent was evaporated and the residue codistilled with toluene. The thus-obtained crude product *VIc* was dissolved in pyridine (15 ml) and tosyl chloride (2.2 g, 11.5 mmol) was added at 0 °C. After standing for 4 h at room temperature, the reaction mixture was diluted with water (5 ml) and the solvent was evaporated. The residue was dissolved in ethyl acetate, the solution was washed with saturated solution of sodium hydrogen carbonate, the organic phase was dried over anhydrous magnesium sulfate and the solvent was evaporated. Chromatography on a column of silica gel in the solvent system II afforded 301 mg (6%) of α-*VId*; R_F 0.37 (I); Mas spectrum (FAB): 465 (MH^+). For $C_{19}H_{29}O_9PS$ (464.5) calculated: 49.13% C, 6.29% H, 6.67% P, 6.90% S; found: 49.21% C, 6.24% H, 6.58% P, 6.87% S. Further elution gave 2.41 g (49%) of β-*VId*; R_F 0.44 (I); Mas spectrum (FAB): 465 (MH^+). For $C_{19}H_{29}O_9PS$ (464.5) calculated: 49.13% C, 6.29% H, 6.67% P, 6.90% S; found: 49.28% C, 6.34% H, 6.73% P.

Diethyl [5-(Adenin-9-yl)-5-deoxy-2,3-*O*-isopropylidene- α-L-ribofuranosyl]-phosphonate (α-*VIe*)

Reaction of compound α-*VId* (218 mg, 0.47 mmol) with adenine in dimethylformamide in the presence of sodium hydride (ref.[1]) afforded 94 mg (47%) of product α-*VIe*; R_F 0.37 (L); Mas spectrum (FAB): 428 (MH^+). For $C_{17}H_{26}N_5O_6P$ (427.4) calculated: 47.77% C, 6.13% H, 16.39% N, 7.25% P; found: 47.91% C, 6.23% H, 16.22% N, 7.31% P.

Diethyl [5-(Adenin-9-yl)-5-deoxy-2,3-*O*-isopropylidene- β-L-ribofuranosyl]-phosphonate (β-*VIe*)

Compound β-*VId* (1.7 g, 3.7 mmol) reacted with adenine as described in the preceding experiment to give 823 mg (53%) of product β-*VIe*; R_F 0.43 (L); Mas spectrum (FAB): 428 (MH^+). For $C_{17}H_{26}N_5O_6P$ (427.4) calculated: 47.77% C, 6.13% H, 16.39% N, 7.25% P; found: 47.93% C, 6.22% H, 16.28% N, 7.32% P.

Diethyl α-L-Xylofuranosylphosphonate (*VIIb*)

The recyclization of compound *IVd* (16 g, 32.4 mmol) and reduction were performed as described for compound *VIb*. The intermediate *VIIa* (R_F 0.49 in K) was hydrogenolytically debenzylated and subsequent column chromatography on silica gel in the solvent system J afforded 1.4 g (16%) of compound *VIIb*; R_F 0.44 (P); Mas spectrum (FAB): 271 (MH^+). For $C_9H_{19}O_7P$ (270.2) calculated: 40.00% C, 7.09% H, 11.46% P; found: 39.89% C, 7.13% H, 11.25% P.

Diethyl (5-*O*-Toluenesulfonyl-α-L-xylofuranosyl)phosphonate (*VIIc*)

Compound *VIIb* (1.4 g, 5.2 mmol) was tosylated according to the general procedure[1] to give 1.2 g (55%) of the product *VIIc*; R_F 0.39 (J); Mas spectrum (FAB): 425 (MH^+). For $C_{16}H_{25}O_9PS$ (424.4) calculated: 45.28% C, 5.94% H, 7.30% P, 7.55% S; found: 45.07% C, 6.09% H, 7.19% P, 7.62% S.

Diethyl (5*S*)-[4,5-Anhydro-3-deoxy-D-*erythro*-pentitol-5-*C*-yl]phosphonate (*IXa*)

Recyclization of mesylate *IVf* (7.5 g, 19.3 mmol) according to the procedure described for the preparation of compound *VIb* (save the catalytic hydrogenation) and subsequent isolation on a column of silica gel in the solvent system I afforded 1.6 g (33%) of product *IXa*; R_F 0.31 (K); Mas spectrum (FAB): 255 (MH^+). For $C_9H_{19}O_6P$ (254.2) calculated: 42.52% C, 7.53% H, 12.18% P; found: 42.63% C, 7.42% H, 12.04% P.

Diethyl (5*S*)-[4,5-Anhydro-3-deoxy-1-*O*-(4-toluenesulfonyl)-D-*erythro*-pentitol-5-*C*-yl]-phosphonate (*IXb*)

Compound *IXa* (1.6 g, 6.3 mmol) was tosylated according to ref.[1] to give 2.0 g (78%) of product *IXb*; R_F 0.44 (J); Mas spectrum (FAB): 409 (MH^+). For $C_{16}H_{25}O_8PS$ (408.4) calculated: 47.06% C, 6.17% H, 7.58% P. 7.85% S; found: 46.89% C, 6.22% H, 7.44% P, 7.86% S. ^{1}H NMR spectrum (500 MHz, CD_3SOCD_3): 7.80 d, 2 H, J = 8.3 (arom.); 7.50 d, 2 H, J = 8.3 (arom.); 4.02 dq, 4 H, $J(CH_2,CH_3)$ = 7.1, $^3J(CH_2,P)$ = 8.3 (2 $POCH_2$); 3.90 dd, 1 H, $J(2,1)$ = 4.1, $J(1,1')$ = 10.0 (H-1); 3.85 dd, 1 H, $J(1',2)$ = 6.1, $J(1',1)$ = 10.0 (H'-1); 3.80 m, 1 H (H-2); 3.19 dq, 1 H, $J(4,5)$ = 2.4, $J(4,3)$ = 5.4, $J(4,3')$ = 5.4, $^3J(4,P)$ = 5.6 (H-4); 2.97 dd, 1 H, $J(5,4)$ = 2.4, $^2J(5,P)$ = 31.0 (H-5); 2.40 s, 3 H (CH_3); 1.66 t, 2 H, $J(3,4)$ = 5.4, $J(3,2)$ = 5.4 (H-3); 1.21 t, 6 H, J = 7.1 (2 × CH_3).

Diethyl (5*S*)-[1-(Adenin-9-yl)-4,5-anhydro-1,3-dideoxy-D-*erythro*-pentitol-5-*C*-yl]-phosphonate (*IXe*)

Compound *IXb* (1.9 g, 4.7 mmol) was converted[1] via the tetrahydropyranyl derivative *IXc* into the fully protected adenine derivative *IXd* which was partly deprotected in an acidic medium to give phosphonate *IXe*. Final chromatography on silica gel in the solvent system J afforded 700 mg (41%) of phosphonate *IXe*; R_F 0.53 (L); Mas spectrum (FAB): 372 (MH^+). For $C_{14}H_{22}N_5O_5P$ (371.3) calculated: 45.28% C, 5.97% H, 18.86% N, 8.34% P; found: 45.13% C, 6.02% H, 18.79% N, 8.41% P. ^{1}H NMR spectrum (500 MHz, CD_3SOCD_3): 8.12 s, 1 H (H-2, adenine); 8.04 s, 1 H (H-8, adenine); 7.19 s, 2 H (NH_2); 5.35 d, 1 H, J = 5.6 (OH); 4.17 dd, 1 H, $J(1,2)$ = 3.9, $J(1,1')$ = 13.4 (H-1); 4.09 dd, 1 H, $J(1',2)$ = 7.8, $J(1',1)$ = 13.4 (H-1'); 4.06 dq, 4 H, $J(CH_2,CH_3)$ = 7.1, $^3J(CH_2,P)$ = 8.5 ($POCH_2$); 4.00 m, 1 H (H-2); 3.32 dddd, 1 H, $J(4,5)$ = 2.7, $J(4,3)$ = 4.9, $J(4,3')$ = 5.3, $^3J(4,P)$ = 5.9 (H-4); 3.12 dd, 1 H, $J(5,4)$ = 2.7, $^2J(5,P)$ = 31.0 (H-5); 1.73 ddd, 1 H, $J(3,4)$ = 4.9, $J(3,2)$ = 4.6, $J(3,3')$ = 14.4 (H-3); 1.67 dddd, 1 H, $J(3',4)$ = 5.3, $J(3',2)$ = 7.4, $J(3',3)$ = 14.4 (H-3'); 1.24 t, 6 H, J = 7.1 (2 × CH_3).

(5*S*)-[1-(Adenin-9-yl)-4,5-anhydro-1,3-dideoxy-D-*erythro*-pentitol-5-*C*-yl]phosphonic Acid (*IXf*)

Reaction of compound *IXe* (420 mg, 1.1 mmol) with bromotrimethylsilane according to the general procedure[1] afforded 214 mg (60%) of product *IXf*; R_F 0.32 (Q); Mas spectrum (FAB): 316 (MH^+). ^{1}H NMR spectrum (500 MHz, D_2O): 8.23 s, 1 H (H-2, adenine); 8.16 s, 1 H (H-8, adenine); 4.39 dd, 1 H, $J(1,2)$ = 3.0, $J(1,1')$ = 14.0 (H-1); 4.31 ddt, 1 H, $J(2,3)$ = 3.7, $J(2,3')$ = 8.0, $J(2,1)$ = 3.0, $J(2,1')$ = 8.2 (H-2); 4.25 dd, 1 H, $J(1',2)$ = 8.2, $J(1',1)$ = 14.0 (H-1'); 3.30 dddd, 1 H, $J(4,5)$ = 3.0, $J(4,3)$ = 4.6, $J(4,3')$ = 6.4, $^3J(4,P)$ = 5.2 (H-4); 2.68 dd, 1 H, $J(5,4)$ = 3.0, $^2J(5,P)$ = 31.4 (H-5); 2.00 ddd, 1 H, $J(3,4)$ = 4.6, $J(3,2)$ = 3.7, $J(3,3')$ = 14.6 (H-3); 1.74 dddd, 1 H, $J(3',4)$ = 6.4, $J(3',2)$ = 8.0, $J(3',3)$ = 14.6, $^4J(3',P)$ = 1.2 (H-3').

Methyl 5-*O*-Pivaloyl-L-arabinofuranosides (*X*)

Pivaloyl chloride (30 ml, 245 mmol) was added dropwise at 0 °C during 2 h to a solution of anomeric mixture of methyl L-arabinofuranosides[12] (α : β = 1 : 1; 40 g, 243.7 mmol) in pyridine (850 ml). After standing at 0 °C overnight, the excess acyl chloride was destroyed by addition of water (100 ml), the solution was concentrated and the residue dissolved in ethyl acetate. The solution was washed with saturated solution of sodium hydrogen carbonate and dried over anhydrous magnesium sulfate. Evaporation of the solvent afforded 50.4 g (83%) of product *X* (α : β = 1 : 1); R_F 0.43 (I). For $C_{11}H_{20}O_6$ (248.3) calculated: 53.22% C, 8.12% H; found: 53.38% C, 8.19% H.

1,2-*O*-Isopropylidene-5-*O*-pivaloyl-β-L-arabinofuranose (*XIa*)

Sulfuric acid (96%, 8 ml) and anhydrous copper sulfate (50 g) were added to a solution of pivaloyl derivative *X* (50.4 g, 203 mmol) in acetone (1 000 ml). The reaction mixture was vigorously stirred at room temperature for 48 h, filtered and the filtrate was neutralized with concentrated aqueous ammonia at 0 °C. After evaporation, the residue was dissolved in ethyl acetate, the solution washed with saturated solution of sodium hydrogen carbonate, dried over anhydrous magnesium sulfate and the solvent was evaporated. The crude product was purified on a column of silica gel in the system I to give 35.7 g (64%) of product *XIa*; R_F 0.41 (J). For $C_{13}H_{22}O_6$ (274.3) calculated: 56.92% C, 8.08% H; found: 56.77% C, 8.01% H. ^{1}H NMR spectrum (500 MHz, CD_3SOCD_3 + CD_3COOD): 5.79 d, 1 H, J(1,2) = 3.9 (H-1); 4.42 dd, 1 H, J(2,1) = 3.9, J(2,3) = 0.5 (H-2); 4.09 d, 2 H, J(5,4) = 6.3 (2 × H-5); 3.98 dd, 1 H, J(3,2) = 0.5, J(3,4) = 2.4 (H-3); 3.96 td, 1 H, J(4,3) = 2.4, J(4,5) = 6.3, J(4,5′) = 6.3 (H-4); 1.39 s, 3 H (CH_3); 1.20 s, 3 H (CH_3); 1.11 s, 9 H (3 × CH_3); before exchange 5.56 d, 1 H, J = 4.2 (OH).

1,2-*O*-Isopropylidene-5-*O*-pivaloyl-3-*O*-(tetrahydropyran-2-yl)-β-L-arabinofuranose (*XIb*)

A solution of compound *XIa* (35.7 g, 130 mmol) and 3,4-dihydro-2*H*-pyran (12.4 ml, 136.5 mmol) in dioxane (150 ml) was acidified by addition of several drops of 1 M hydrogen chloride in dioxane (strongly acid reaction to moist indicator paper) and allowed to stand for 4 h at room temperature. After neutralization with triethylamine and concentration of the mixture to about one third of the original volume, the remaining solution was taken up in ethyl acetate and washed with saturated solution of sodium hydrogen carbonate. After drying over anhydrous magnesium sulfate, the solvent was evaporated leaving 37.7 g (81%) of product *XIb*; R_F 0.52 (I).

1,2-Isopropylidene-3-*O*-(tetrahydropyran-2-yl)-β-L-arabinofuranose (*XIc*)

A solution of pivaloyl derivative *XIb* (37.7 g, 105.2 mmol) in 1 M methanolic sodium methoxide (100 ml) was set aside for 2 h at room temperature. The solvent was evaporated and the residue taken up in ethyl acetate. The extract was washed with saturated aqueous sodium hydrogen carbonate, dried over anhydrous magnesium sulfate and concentrated to give 27.5 g (96%) of compound *XIc*; R_F 0.41 (H).

Diethyl (5*RS*)-[1,2-*O*-Isopropylidene-3-*O*-(tetrahydropyran-2-yl)-β-L-arabinofuranos-5-*C*-yl]phosphonate (*XIIa*)

Dimethyl sulfoxide (8.5 ml) in dry dichloromethane (25 ml) was added at −78 °C to a stirred solution of oxalyl chloride (5 ml) in dry dichloromethane (125 ml). After stirring for 2 min, a solution of compound *XIc* (13.7 g, 50 mmol) in dichloromethane (50 ml) was added dropwise under stirring in the course of 5 min. The reaction mixture was stirred for another 15 min and then triethylamine

(35 ml) was added. The mixture was further stirred at room temperature, diluted with water (250 ml) and extracted with dichloromethane. The organic layer was dried over anhydrous magnesium sulfate, the solvent was evaporated and the remaining 1,2-*O*-isopropylidene-3-*O*-(tetrahydropyran-2-yl)-β-L-*arabino*-pentodialdose-(1,4) (*XId*) was used without purification in the next reaction step.

The aldehyde *XId* (prepared from 50 mmol of compound *XIc*) was converted into phosphonate *XIIa* as described for compound *IVa*. The product was isolated by chromatography on silica gel in the system D; yield 11.7 g (57% based on compound *XIc*); R_F 0.33 (F); Mas spectrum (FAB): 411 (MH^+). For $C_{17}H_{31}O_9P$ (410.4) calculated: 49.75% C, 7.61% H, 7.55% P; found: 49.66% C, 7.54% H, 7.47% P.

Diethyl (5*RS*)-[1,2-*O*-Isopropylidene-5-*O*-methanesulfonyl-3-*O*-(tetrahydropyran-2-yl)-β-L-arabinofuranos-5-*C*-yl]phosphonate (*XIIb*)

Compound *XIIa* (11.7 g, 28.5 mmol) was mesylated as described for compound *IVb* to give 12.3 g (88%) of product *XIIb* (epimer ratio 5 : 3); R_F 0.58 (J); Mas spectrum (FAB): 489 (MH^+). For $C_{18}H_{33}O_{11}PS$ (488.5) calculated: 44.26% C, 6.81% H, 6.34% P, 6.56% S; found: 44.33% C, 6.78% H, 6.26% P, 6.68% S.

Diethyl (5*R*)-[4,5-Anhydro-L-arabinitol-5-*C*-yl]phosphonate (*XVa*) and
Diethyl (5*R*)-[1,4-Anhydro-D-xylitol-5-*C*-yl]phosphonate (*XVIa*)

Recyclization of diethyl (5*RS*)-[1,2-*O*-isopropylidene-5-*O*-methanesulfonyl-3-*O*-(tetrahydropyran-2-yl)-β-L-arabinofuranos-5-*C*-yl]phosphonate (*XIIb*; 12.3 g, 25.2 mmol) was performed in boiling trifluoroacetic acid (125 ml) (8 h). The subsequent reduction of the reaction products was carried out as described for compound *VIa*. Chromatography on silica gel in the system J afforded phosphonate *XVa* (1.5 g, 22%) and *XVIa* (2.9 g, 43%). *XVa*: R_F 0.49 (P); Mas spectrum (FAB): 271 (MH^+). For $C_9H_{19}O_7P$ (270.2) calculated: 40.00% C, 7.09% H, 11.46% P; found: 39.89% C, 7.11% H, 11.52% P. *XVIa*: R_F 0.43 (P); Mas spectrum (FAB): 271 (MH^+). For $C_9H_{19}O_7P$ (270.2) calculated: 40.00% C, 7.09% H, 11.46% P; found: 40.14% C, 7.20% H, 11.58% P.

Diethyl (5*R*)-[4,5-Anhydro-1-*O*-(4-toluenesulfonyl)-L-arabinitol-5-*C*-yl]-phosphonate (*XVb*)

Selective tosylation[1] of compound *XVa* (1 g, 3.7 mmol) afforded 840 mg (53%) of product *XVb*; R_F 0.41 (J); Mas spectrum (FAB): 425 (MH^+). For $C_{16}H_{25}O_9PS$ (424.4) calculated: 45.28% C, 5.94% H, 7.30% P, 7.55% S; found: 45.37% C, 6.08% H, 7.22% P, 7.61% S. ^1H NMR spectrum (500 MHz, CD_3SOCD_3): 7.76 d, 2 H, J = 8.3 (arom.); 7.45 d, 2 H, J = 8.3 (arom.); 4.03 dq, 4 H, $J(CH_2,CH_3)$ = 7.0, $^3J(CH_2,P)$ = 8.8 (2 × $POCH_2$); 4.01 dd, 1 H, $J(1,2)$ = 4.2, $J(1,1')$ = 9.8 (H-1); 3.84 dd, 1 H, $J(1',2)$ = 7.6, $J(1',1)$ = 9.8 (H-1'); 3.76 ddd, 1 H, $J(2,3)$ = 3.4, $J(2,1)$ = 4.2, $J(2.1')$ = 7.6 (H-2); 3.50 m, 2 H (OH); 3.42 dd, $J(3,4)$ = 4.7, $J(3,2)$ = 3.4 (H-3); 3.23 ddd, 1 H, $J(4,5)$ = 2.4, $J(4,3)$ = 4.7, $^3J(4,P)$ = 5.1 (H-4); 3.08 dd, 1 H, $J(5,4)$ = 2.4, $^2J(5,P)$ = 31.5 (H-5); 2.39 s, 3 H (CH_3); 1.21 t, 6 H, J = 7.0 (2 × CH_3). ^{13}C NMR spectrum (50.3 MHz, CD_3SOCD_3): 145.66 s (C, tosyl); 132.89 s (C, tosyl); 130.76 s (CH, tosyl); 128.28 s (CH, tosyl); 71.72 s (C1); 69.74 s (C2 or C3); 69.14 (C2 or C3); 63.15 d, $^2J(C,P)$ = 6.6 (POC); 63.08 d, $^2J(C,P)$ = 5.9 (POC); 56.79 s (C4); 47.80 d, $^1J(C,P)$ = 198.7 (C5); 21.61 s (CH_3, tosyl); 16.75 d, $^3J(C,P)$ = 5.9 (CH_3).

Diethyl (5*R*)-[4,5-Anhydro-2,3-*O*-isopropylidene-1-*O*-(4-toluenesulfonyl)-L-arabinitol-5-*C*-yl]phosphonate (*XVc*)

Isopropenylidation of compound *XVb* (740 mg, 1.7 mmol) was performed as described for compound *VIc*. The product was isolated by chromatography on silica gel in the solvent system G. Yield 594 mg (73%) of product *XVc*; R_F 0.43 (H); Mas spectrum (FAB): 465 (MH^+). For $C_{19}H_{29}O_9PS$ (464.5) calculated: 49.13% C, 6.29% H, 6.67% P, 6.90% S; found: 49.34% C, 6.31% H, 6.76% P, 6.79% S. ^1H NMR spectrum (500 MHz, CD_3SOCD_3): 7.79 d, 2 H, J = 8.3 (arom.); 7.49 d, 2 H, J = 8.3 (arom.); 4.21 ddd, 1 H, $J(2,3)$ = 7.3, $J(2,1)$ = 2.7, $J(2,1')$ = 5.9 (H-2); 4.17 dd, 1 H, $J(1,2)$ = 2.7, $J(1,1')$ = 11.0 (H-1); 4.06 dq, 4 H, $J(CH_2,CH_3)$ = 7.1, $^3J(CH_2,P)$ = 8.5 (2 × $POCH_2$); 4.03 dd, 1 H, $J(1',2)$ = 5.9, $J(1',1)$ = 11.0 (H-1'); 3.70 dd, 1 H, $J(3,4)$ = 5.4, $J(3,2)$ = 7.3 (H-3); 3.35 ddd, 1 H, $J(4,5)$ = 2.4, $J(4,3)$ = 5.4, $^3J(4,5)$ = 5.1 (H-4); 3.20 dd, 1 H, $J(5,4)$ = 2.4, $^2J(5,P)$ = 29.5 (H-5); 2.43 s, 3 H (CH_3); 1.32 s, 3 H (CH_3); 1.26 s, 3 H (CH_3); 1.25 t, 6 H, J = 7.1 (2 × CH_3). ^{13}C NMR spectrum (50.3 MHz, CD_3SOCD_3): 145.37 s (C, tosyl); 132.16 s, (C, tosyl); 130.30 s (CH, tosyl); 127.88 s (CH, tosyl); 110.48 s (C, isopropylidene); 75.72 s (C2 or C3); 75.56 s (C2 or C3); 69.55 s, (C1); 62.88 d, $^2J(C,P)$ = 5.9 (POC); 62.73 d, $^2J(C,P)$ = 6.6 (POC); 55.47 s (C4); 47.93 d, $^1J(C,P)$ = 197.8 (C5); 26.61 s (CH_3); 26.48 s (CH_3); 21.16 s (CH_3); 16.31 d, $^3J(C,P)$ = 5.1 (CH_3).

Diethyl (5*R*)-[1,4-Anhydro-2-*O*-(4-toluenesulfonyl)-D-xylitol-5-*C*-yl]-phosphonate (*XVIb*)

Compound *XVIa* (2.5 g, 9.3 mmol) was tosylated (ref.[1]) and the obtained principal product was isolated by column chromatography on silica gel in the solvent system I. Yield 2.2 g (56%) of product *XVIb*; R_F 0.41 (J); Mas spectrum (FAB): 425 (MH^+). For $C_{16}H_{25}O_9PS$ (424.4) calculated: 45.28% C, 5.94% H, 7.30% P, 7.55% S; found: 45.39% C, 6.05% H, 7.28% P, 7.73% S. ^1H NMR spectrum (500 MHz, CD_3SOCD_3): 7.83 d, 2 H, J = 8.3 (arom.); 7.50 d, 2 H, J = 8.3 (arom.); 5.70 m, 2 H (2 × OH); 4.74 dt, 1 H, $J(2,3) \leq 1.0$, $J(2,1)$ = 3.5, $J(2,1') \leq 1.0$ (H-2); 4.11 brd, 1 H, $J(3,4)$ = 2.9, $J(3,2) \leq 1.0$ (H-3); 4.01 dd, 1 H, $J(1,2)$ = 3.5, $J(1,1')$ = 11.0 (H-1); 3.99 dq, 4 H, $J(CH_2,CH_3)$ = 7.1, $^3J(CH_2,P)$ = 7.4 (2 × $POCH_2$); 3.90 dd, 1 H, $J(5,4)$ = 9.3, $^2J(5,P)$ = 3.2 (H-5); 3.84 ddd, 1 H, $J(4,5)$ = 9.3, $J(4,3)$ = 2.9, $^3J(4,P)$ = 7.3 (H-4); 3.64 brd, 1 H, $J(1',2) \leq 1.0$, $J(1',1)$ = 11.0 (H-1'); 2.43 s, 3 H (CH_3); 1.21 t, 3 H, J = 7.1 (CH_3); 1.18 t, 3 H, J = 7.1 (CH_3). ^{13}C NMR spectrum (50.3 MHz, CD_3SOCD_3): 145.53 s (C, tosyl); 132.98 s (C, tosyl); 130.57 s (CH, tosyl); 127.76 s (CH, tosyl); 84.90 s (C2); 80.00 d, $^2J(C,P)$ = 2.9 (C4); 73.18 d, $^3J(C,P)$ = 11.0 (C3); 70.90 s (C1); 64.06 d, $^1J(C,P)$ = 164.1 (C5); 61.99 d, $^2J(C,P)$ = 7.3 (POC); 61.62 d, $^2J(C,P)$ = 6.6 (POC); 21.34 s (CH_3); 16.61 d, $^3J(C,P)$ = 5.9 (CH_3); 16.55 d, $^3J(C,P)$ = 5.9 (CH_3).

Diethyl (5*R*)-[1,4-Anhydro-3,5-*O*-isopropylidene-2-*O*-(4-toluenesulfonyl)-D-xylitol-5-*C*-yl]phosphonate (*XVIc*)

Isopropylidenylation of compound *XVIb* (2 g, 4.7 mmol) was performed as described for compound *VIc*. The product was isolated by chromatography on silica gel in the solvent system G; yield 1.7 g (78%) of compound *XVIc*; R_F = 0.43 (H); Mas spectrum (FAB): 465 (MH^+). For $C_{19}H_{29}O_9PS$ (464.5) calculated: 49.13% C, 6.29% H, 6.67% P, 6.90% S; found: 49.29% C, 6.33% H, 6.59% P, 6.87% S. ^1H NMR spectrum (500 MHz, CD_3SOCD_3): 7.86 d, 2 H, J = 8.3 (arom.); 7.51 d, 2 H, J = 8.3 (arom.); 4.83 dd, 1 H, $J(2,3) \leq 0.5$, $J(2,1)$ = 3.9, $J(2,1')$ = 1.7 (H-2); 4.30 ddd, 1 H, $J(4,5)$ = 9.0, $J(4,3)$ = 4.6, $^3J(4,P)$ = 13.9 (H-4); 4.16 brd, 1 H, $J(3,4)$ = 4.6, $J(3,2) \leq 0.5$ (H-4); 4.04 dd, 1 H, $J(1,2)$ = 3.9, $J(1,1')$ = 11.0 (H-1); 4.03 dq, 4 H, $J(CH_2,CH_3)$ = 7.1, $^3J(CH_2,P)$ = 7.8 (2 × $POCH_2$); 3.81 dd, 1 H, $J(5,4)$ = 9.0, $^2J(5,P)$ = 9.5 (H-5); 3.74 dd, 1 H, $J(1',2)$ = 1.7, $J(1',1)$ = 11.0 (H-1'); 2.43 s, 3 H (CH_3); 1.24 s (CH_3); 1.21 t, 6 H, J = 7.1 (2 × CH_3); 1.15 s, 3 H (CH_3). ^{13}C NMR

spectrum (50.3 MHz, CD_3SOCD_3): 145.70 s (C, tosyl); 132.67 s (C, tosyl); 130.54 s (CH, tosyl); 127.94 s (CH, tosyl); 100.91 d, ^3J(C,P) = 13.2 (C, isopropylidene); 83.43 s (C2); 76.67 s (C4); 74.70 d, ^3J(C,P) = 8.8 (C3); 70.50 s (C1); 64.73 d, ^1J(C,P) = 172.9 (C5); 62.62 d, ^2J(C,P) = 5.9 (POC); 62.36 d, ^2J(C,P) = 6.6 (POC); 23.96 s (CH_3); 23.25 s (CH_3); 21.27 s (CH_3); 16.42 d, J(C,P) = 5.1 (CH_3).

Ethyl (5*R*)-[1,4-Anhydro-3,5-*O*-isopropylidene-2-*O*-(4-toluenesulfonyl)-D-xylitol-5-*C*-yl]phosphonate (*XVId*)

Reaction of compound *XVIc* (500 mg, 1.1 mmol) with sodium salt of adenine in dimethylformamide was carried out as described in ref.[1] and afforded compound *XVId* (347 mg, 74%) as the sole product; R_F 0.29 (M); Mas spectrum (FAB): 459 (MH^+). For $C_{17}H_{24}NaO_9PS$ (458.4) calculated: 44.54% C, 5.28% H, 6.76% P, 6.99% S; found: 44.31% C, 5.33% H, 6.88% P, 7.11% S. ^{1}H NMR spectrum (500 MHz, CD_3SOCD_3): 7.84 d, 2 H, J = 8.3 (arom.); 7.51 d, 2 H, J = 8.3 (arom.); 4.77 brdd, 1 H, J(2,3) ≤ 0.5, J(2,1) = 3.9, J(2,1′) = 2.0 (H-2); 4.18 ddd, 1 H, J(4,5) = 8.3, J(4,3) = 3.9, ^3J(4,P) = 12.2 (H-4); 3.98 dd, 1 H, J(1,2) = 3.9, J(1,1′) = 10.7 (H-1); 3.94 brd, 1 H, J(3,4) = 3.9, J(3,2) ≤ 0.5 (H-3); 3.71 pent, 2 H, J(CH_2,CH_3) = 6.8, ^3J(CH_2,P) = 6.8 (POCH_2); 3.63 dd, 1 H, J(1′,2) = 2.0, J(1′,1) = 10.7 (H-1′); 3.45 dd, 1 H, J(5,4) = 8.3, ^2J(5,P) = 9.8 (H-5); 2.43 s, 3 H (CH_3); 1.17 s, 3 H (CH_3); 1.09 s, 3 H (CH_3); 1.05 t, 3 H, J = 6.8 (CH_3). ^{13}C NMR spectrum (50.3 MHz, CD_3SOCD_3): 146.15 s (C, tosyl): 133.25 s (C, tosyl); 130.97 s (CH, tosyl); 128.35 s (CH, tosyl); 100.63 d, ^3J(C,P) = 11.0 (C, isopropylidene); 84.12 s (C2); 78.37 s (C4); 75.02 d, ^3J(C,P) = 7.3 (C3); 70.90 s (C1); 66.33 d, ^1J(C,P) = 164.1 (C5); 61.01 d, ^2J(C,P) = 5.9 (POC); 24.18 s (CH_3); 23.92 s (CH_3); 21.62 s (CH_3); 17.22 d, ^3J(C,P) = 5.9 (CH_3).

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