Pergamon

SCIENCE DIRECT®

Tetrahedron 59 (2003) 4077–4083

TETRAHEDRON

Conformational analysis of cyclic phosphates derived from 5-C′ substituted 1,2-*O*-isopropylidene-α-D-xylofuranose derivatives

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Received 26 February 2003; revised 9 April 2003; accepted 9 April 2003

Abstract—Twelve 2-phenoxy-2-oxo-1,3,2-dioxaphosphorinanes fused with a 1,2-*O*-isopropylidene-α-D-xylofuranose moiety in *cis* orientation and substituted at the C′5 position were prepared in two steps from commercially available diacetone-α-D-glucose. Their conformations, and configurations were determined by ^{1}H and ^{31}P NMR and X-ray crystallographic techniques. Both, chair–twisted–chair and chair–boat equilibria were observed in solution. We observed that the strong anisotropic shielding effect of the benzene ring in the phenoxy group generates an upfield shift of the H^{1} hydrogen atom, when the cyclic phosphates adopt a boat conformation. This is due to a relative *cis*-orientation of the P-phenoxy group and the H^{1} proton of the 1,2-*O*-isopropylidene-α-D-xylofuranose moiety. Therefore, the configuration of the phosphorus center (S_P or R_P) can be determined by ^{1}H NMR spectroscopy. Interestingly, the crystal structure of one of the cyclic phosphates exhibits two independent molecules in the asymmetric unit, one with a chair and the other one with a boat conformation.

1. Introduction

During the last three decades, the conformational analysis of 2-phenoxy-2-oxo-1,3,2-dioxaphosphorinanes and similar compounds has been a field of intense research.[1] Cyclic nucleoside 3′,5′-monophosphates such as cAMP and cGMP play an important role in the cell metabolism, for which the conformational analysis of similar cyclic phosphates is relevant, since the interaction with the enzyme active site occurs probably through the pseudoaxial phosphoryl oxygen of the twist conformer.[2,3] In this regard Bentrude et al., have extensively studied the conformation of different *cis* and *trans* fused cyclic phosphates by NMR and crystallographic techniques.[1]

Herein, we report the synthesis, configurational, and conformational analyses of various novel model compounds for the above mentioned nucleoside 3′,5′-monophosphates, in which a considerable strain is imposed by the presence of a *cisoid*-like fused bicyclic structure bearing methyl, phenyl and vinyl groups attached at the C′5 position of the 1,2-*O*-isopropylidene-α-D-xylofuranose moiety.

Keywords: conformation; cyclic phosphates; anisotropic shielding effect of the benzene ring; conformational analysis.

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2. Results and discussions

The cyclic phosphates **4a–c**, **4a′–c′**, **5a–c** and **5a′–c′** were synthesized in two steps with acceptable overall yields of 40–70% (Scheme 1), whereby the 1,3-diol precursors **2a–c** and **3a–c** were obtained in yields between 42 and 73%, when applying a sequential hydrolysis–oxidation and Grignard reagent addition protocol (in one pot) to commercially available 1,2,5,6-*O*-diisopropylidene-α-D-xylofuranose (Table 1). In these reactions the lowest yield was obtained with the vinyl and the highest one with the methyl Grignard reagent (entries 1 and 3, Table 1). The diastereomeric pairs of the 1,3-diols could be separated efficiently by column chromatography.

The phosphorylation of the diols was carried out using phenyldichlorophosphate and triethylamine in CH_2Cl_2, affording, **4a–c**, **4a′–c′**, **5a–c**, **5a′–c′** with high yield (90–94%, see the Scheme 1). After the successful separation of all diastereomeric pairs by column chromatography, conformational and configurational analyses were performed using standard NMR methods together with X-ray structure determinations in the case of **4a** and **5b′**. The specific ^{1}H and ^{31}P NMR chemical shifts as well as the $^{3}J_{HH}$, $^{3}J_{HP}$ and $^{4}J_{HP}$ coupling constants of the cyclic phosphates are summarized in Tables 2 and 3.

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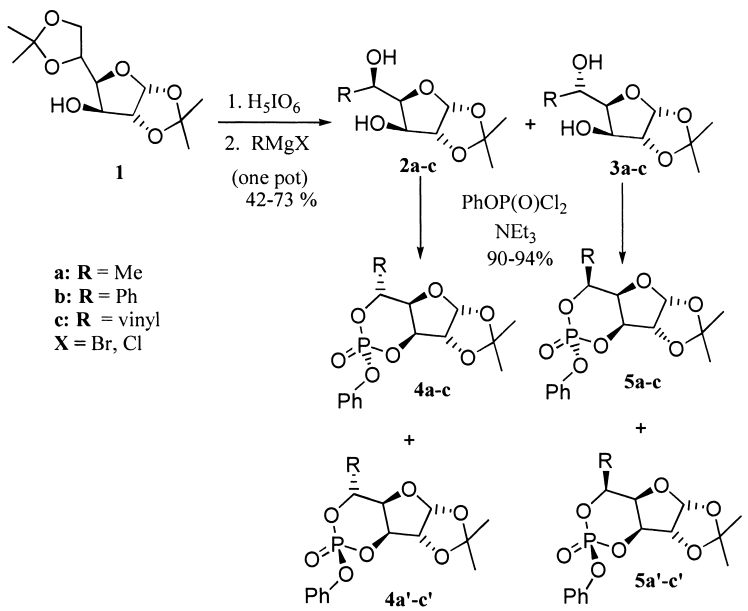
doi:10.1016/S0040-4020(03)00582-9



Scheme 1. Two step syntheses of the cyclic phosphates **4a**–**c**, **4a′**–**c′**, **5a**–**c** and **5a′**–**c′**.

Table 1. Preparation of the 1,3-diol precursors **2a**–**c** and **3a**–**c**

Entry	RMgX	Products	Yield[a]	Reference
1[b]	CH_3–	**2a** and **3a** (2:1)	73	5
2[b]	Ph–	**2b** and **3b** (1:4)	70	6
3[c]	CH_2=CH–	**2c** and **3c** (1:1)	42	7

[a] Yields correspond to the mixture of diastereomers.
[b] RMgBr.
[c] RMgCl.

Examination of the ^{31}P NMR data reveals that the signal of the cyclic phosphate **4a** is centered at higher field than the one of its diastereomer congener **4a′** (−16.2 and −15.0 ppm, respectively). This suggests that the phenoxy group of **4a** is axially oriented (S_P). The $^3J_{H5P}$ values for **4a** and **4a′** ($^3J_{H5P}$=16.0 Hz for **4a** and $^3J_{H5P}$=15.0 Hz for **4a′**, Table 3) suggest that the methyl group at C′5 is oriented pseudo-axially in the phosphorinane heterocyclic ring (indicating a non chair conformation in solution). However, a crystallographic study for **4a** showed an almost perfect chair conformation in the solid-state (see X-ray structure of **4a** in Fig. 1). Thus, a chair–twist equilibrium in solution and a permanent chair conformation in solid-state for **4a** can be proposed, as shown in Scheme 2. In contrast to the corresponding unsubstituted cyclic phosphates derived

Table 2. Chemical ^1H and ^{31}P NMR shifts of the cyclic phosphates **4a**–**c**, **4a′**–**c′**, **5a**–**c** and **5a′**–**c′**

Compound	H^1	H^2	H^3	H^4	H^5	^{31}P
4a	6.03	4.72	4.90	4.09	4.91	−16.2
4a′	5.69	4.64	4.99	4.18	4.75	−15.0
5a	6.02	4.68	4.82	4.10	4.86	−15.5
5a′[a]	5.56	4.16	4.65	3.56	4.43	−12.6
4b	6.01	4.78	4.95	4.53	5.63	−13.8
4b′	6.15	4.83	4.92	4.63	5.68	−13.0
5b	6.02	4.73	5.01	4.40	5.75	−15.2
5b′	5.60	4.61	5.12	4.42	5.84	−12.9
4c	6.08	4.75	4.92	4.25	5.25	−16.4
4c′	5.79	4.69	4.97	4.32	5.15	−15.7
5c	6.03	4.66	4.89	4.24	5.17	−15.6
5c′	5.62	4.57	5.00	4.24	5.27	−13.1

All spectra were recorded at frequencies of 400 and 161.8 MHz for proton and phosphorus, respectively. Chemical shifts (δ) are given in ppm.
[a] Recorded in C_6D_6 to get overlapping signals separated.

Table 3. $^3J_{HH}$, $^3J_{HP}$ and $^4J_{HP}$ coupling constants of the cyclic phosphates **4a**–**c**, **4a′**–**c′**, **5a**–**c** and **5a′**–**c′**

Compound	$^4J_{HP}$	$^3J_{H5aP}$	$^3J_{H5eP}$	$^3J_{H5aH4}$	$^3J_{H5eH4}$
4a			16.0		2.2
4a′			15.0		2.5
5a	2.9	[a]		2.2	
5a′[b]	2.5	[c]		[c]	
4b			10.2		3.6
4b′			11.4		4.0
5b		[a]		1.6	
5b′		[a]		2.3	
4c			18.3		2.2
4c′			15.2		2.9
5c	1.8	[a]		2.2	
5c′	1.8	[a]		2.2	

^1H spectra were recorded at 400 MHz in $CDCl_3$.
[a] Peak broadened by J_{HP} (<1.0 Hz).
[b] Recorded in C_6D_6 to get overlapping signals separated.
[c] No coupling constants observed, J_{HP} (<0.5 Hz).

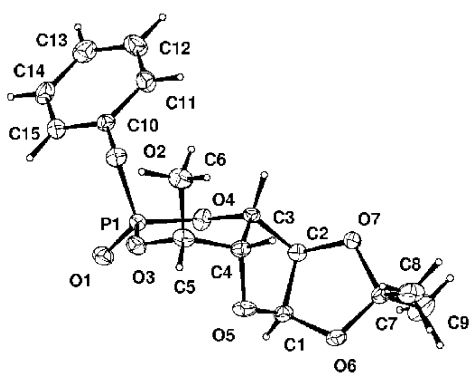
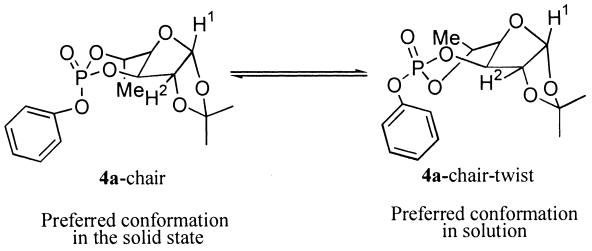


Figure 1. Perspective view of the molecular structure of **4a** in the solid-state, showing a chair conformation for the 1,3,2-dioxaphosphorinane heterocycle.



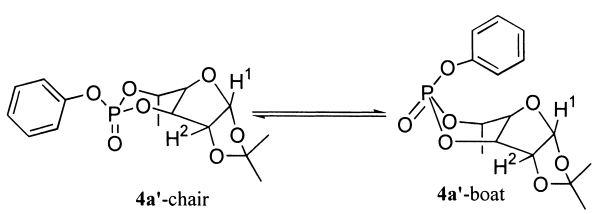
Scheme 2. Chair–twist conformational equilibrium of **4a** in solution.

from 1,2-*O*-isopropylidene-α-D-ribo and xylofuranoses (i.e. des-methyl, phenyl and vinyl **4a**–**c**) in which the vicinal coupling constants $^{3}J_{H5P}$ and crystallographic studies proved a chair form both in solution and the solid-state.[4]

It appears that the 1,3-*syn* diaxial orientation of the methyl and phenoxy groups does not affect significantly the chair conformation, at least in the solid-state. In this regard, a similar conformation has been previously reported in solution for *cis*-4-methyl-2-oxo-2-phenoxy-1,3,2-dioxaphosphorinane[8a] and *cis*-4-benzyl-2-oxo-2-phenoxy-1,3,2-dioxaphosphorinane.[8b] As already mentioned, the vicinal $^{3}J_{H5P}$ coupling constants of 15 Hz suggest a non chair conformation also for **4a′** in solution. A detailed analysis of the chemical shift displacements of the protons in the furanose ring of this compound reveals that H^1 is exposed to a shielding effect (6.03 ppm for **4a** and 5.69 ppm for **4a′**). From the inspection of Dreiding models and anomeric effect considerations,[9] it might be suggested that **4a′** adopts a boat conformation with the pseudoaxial phenoxy group in proximity to H^1 (see Scheme 3).

The above discussion can be applied also to the other pair of diastereomeric cyclic phosphates **5a** and **5a′** with the methyl group at C′5 in equatorial position. The *w*-long range coupling constants $^{4}J_{MeP}$ with values of 2.9 and 2.5 Hz for **5a** and **5a′**, respectively, and the small vicinal coupling constants, $^{3}J_{HP}$ <1 and $^{3}J_{HP}$ <0.5 for **5a** and **5a′**, respectively, do confirm the absolute stereochemistry at C′5(*S*).[5] As for **4a′**, in the case of **5a′** having the phenoxy group in equatorial or pseudoaxial orientation (R_P), a shielding effect is observed for H^1 (6.08 ppm for **5a** and 5.58 ppm for **5a′**).

At this stage, we realized that a simple ^{1}H NMR spectrum analysis might be sufficient to determine which conformational equilibrium is present in solution for these model compounds. In order to confirm our assumption, we synthesized and analysed compounds **4b**, **4b′**, **5b** and **5b′** (R=Ph). The ^{1}H NMR data of the diastereomeric pair of cyclic phosphates **4b** and **4b′**, which were derived from the minor diol **2b**, did not show any shielding effect for H^1, but



Scheme 3. Chair–boat equilibrium of **4a′** in solution.

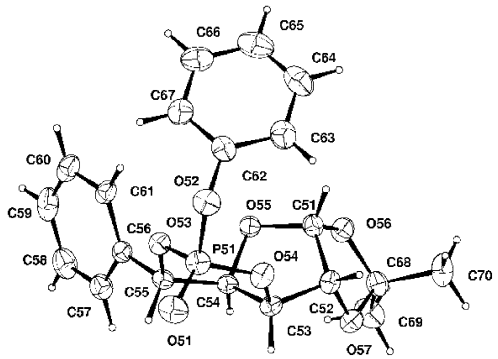


Figure 2. Perspective view of the molecular structure of **5b′** in the chair conformation.

instead, a slight downfield shift was noted for the H^1 hydrogen of **4b′** (6.15 ppm). The configuration of the phosphorus atoms was determined on the basis of the ^{31}P NMR spectra, using the criterion that signals, which are upfield shifted, can be attributed to phosphorinanes having their phenoxy group axially oriented (compare: δ=−13.8 for **4b** and −13.0 for **4b′**).[10] For the other diasteromeric phosphate pair **5b** and **5b′**, **5b′** did show again the shielding effect for H^1 (5.60 ppm and $^{3}J_{HP}$ <1 Hz for **5b′** (R_P); 6.02 ppm and $^{3}J_{HP}$ <1 Hz for **5b** (S_P)). Thus, based on the above arguments, the cyclic phosphate **5b** should present a chair–twist equilibrium and **5b′** a chair–boat equilibrium. In contrast, for both **4b** and **4b′** a chair–twist equilibrium can be deduced.

Although, in similar compounds the existence of a boat conformation has been established,[1b,11] these conformations differ from the one shown in Scheme 3.

Fortunately, a crystallographic study of **5b′** showed that our prediction for the dynamic behaviour in solution was correct. Nevertheless, this compound crystallised with two independent molecules per asymmetric unit, of which one has a chair conformation (Fig. 2) and the other one a boat conformation (Fig. 3).

It should be mentioned that this is the first case, in which the chair and boat conformations of a 2-phenoxy-2-oxo-1,3,2-dioxaphosphorinane involved in a dynamic equilibrium in solution, have been trapped simultaneously the solid-state.

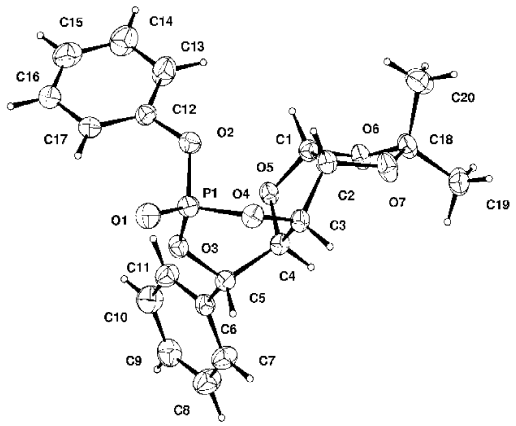


Figure 3. Perspective view of the molecular structure of **5b′** in the boat conformation.

Two further related structures with two independent molecules in the asymmetric unit have been reported: in the first case two 1,3,2-dioxaphosphorinane molecules are present in the asymmetric unit, however, both have a boat conformation.[12a] In the second case reported for a 2-thio-1,3,2-dioxaphosphorinane, one had a half-chair conformation and the other one a twisted-boat conformation.[12b]

Thus, both molecules trapped into the asymmetric unit exhibited a ready equilibrium between the chair and the boat forms in solution. This very short gap in energy between both conformations has been shown depends on the temperature, and the mole fraction of the nonchair conformer is increased upon lowering the temperature[4,11b] Therefore, we selected compound **5b′** for a variable temperature NMR experiment in the range of 213–303 K (in CD_2Cl_2). During this experiment a gradual change of the upfield shift of H^1 from 5.60 ppm at 303 K to 5.31 ppm at 203 K was observed, indicating that the population of the boat conformer is increased (H^1 and the phenoxy group spend more time closely). These results are in agreement with the VT NMR experiments of Hermans et al., even though these authors used different parameters for their conformational analysis (vicinal and geminal coupling constants, $^3J_{HP}$ and $^2J_{HH}$, respectively).[11b]

The reason for the equimolar presence of the chair and boat conformers in the solid-state of **5b′** may be attributed to intermolecular interactions in the crystal lattice. Indeed, there is an intermolecular hydrogen bonding interaction between the phosphoryl oxygen atom of the molecule in the boat conformation and the H^5 hydrogen atom of the molecule in the chair conformation (Fig. 4). The distance of the P=O–H^5 interaction is 2.32 Å, which is significantly shorter than the sum of the van-der-Waals radii between oxygen and hydrogen (2.70 Å).

It has been suggested, that for a strong enzyme-nucleoside interaction with cyclic nucleoside 3′,5′-monophosphates to occur, a pseudoaxial orientation of the phosphoryl oxygen atom of the nucleoside is required, which is only possible in a twist conformation.[2] However, according to the results presented herein, we consider that the boat conformation should be considered as a further appropriate conformation for such an intermolecular interaction.

In an effort to generalize this conformational study, we examined four additional diastereomeric cyclic phosphates,

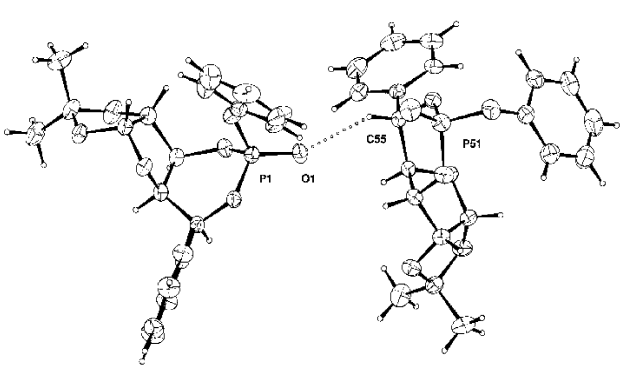


Figure 4. Intermolecular CH···O interaction between the chair and boat conformers of **5b′** in the solid-state.

which were derived from diols **2c** and **3c**. The shielding effects observed for the H^1 hydrogen atoms of **4c′** (R_P) and **5c′** (R_P) and the values of the vicinal coupling constants (5.79 ppm, $^3J_{HP}$ <1 Hz for **4c′** and 5.62 ppm, $^3J_{HP}$ <1 Hz for **5c′**) are in agreement with a chair–boat conformation. In the case of **4c** (S_P) and **5c** (S_P), their spectroscopic data are consistent with a chair–twist equilibrium, with a high population of the chair conformation for **4c** ($^3J_{HP}$=18.3 Hz), see Tables 2 and 3.

3. Conclusion

In conclusion, the conformational analysis of cyclic phosphates, which have substituents that may induce a conformational restriction, revealed the existence of very specific conformational equilibria. It could be shown that for the 2-phenoxy-2-oxo-1,3,2-dioxaphosphorinanes studied herein, the spectroscopic evidence for the dynamic equilibria in solution can be obtained not only from the well-studied vicinal coupling constant $^3J_{HP}$ and the ^{31}P NMR chemical shifts, but also from the simple chemical shift of the axially oriented hydrogen atom in the furanose ring.

4. Experimental

4.1. General

Instrumental. NMR studies were carried out on a JEOL Eclipse+400 instrument. Standards were TMS (^1H, ^{13}C) and H_3PO_4 (^{31}P). Chemical shifts are stated in parts per million. COSY, HETCOR and NOESY experiments have been carried out in order to assign the ^1H and ^{13}C spectra completely. High resolution mass spectra (FAB^+ ion mode) were obtained on a Jeol JMS-SX102A equipment (10 kV).

X-Ray crystallography. X-ray diffraction studies of single crystals were performed for **4a** and **5b′** on a Bruker Apex diffractometer ($\lambda_{Mo\ K\alpha}$=0.71069 Å, monochromator: graphite, T=293 K). Absorption corrections were applied. (SADABS); corrections were also made for Lorentz and polarization effects. Solution and refinement: direct methods (SHELXS-86)[13] for structure solution and the SHELXTL[14] and CRYSTALS[15] software package for refinement and data output. Non-hydrogen atoms were refined anisotropically, and hydrogen atoms were calculated in all cases, using a riding model during the Least-squares refinement. The most important crystallographic data have been summarised in Table 4. In the case of compound **5b′** there are two independent molecules in the asymmetric unit.

Crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC-200060-200061. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: (+44) 1223-336-033, e-mail: deposit@ccdc.cam.ac.uk, www: http://www.ccdc.cam.ac.uk).

Table 4. Crystallographic data for compounds **4a** and **5b′**

Crystal data	**4a**	**5b′**
Formula	$C_{15}H_{19}O_7P$	$C_{20}H_{21}O_7P$
Crystal size (mm^3)	0.11×0.17×0.33	0.10×0.24×0.27
MW ($g\ mol^{-1}$)	342.27	404.34
Space group	$P2_1$	$P2_12_12_1$
Cell parameters		
a (Å)	5.7607(6)	11.0021(6)
b(Å)	10.1353(11)	14.8941(9)
c (Å)	14.5184(16)	23.9451(14)
β (°)	100.919(2)	90
V ($Å^3$)	832.33(16)	3923.8(4)
Z	2	8
μ (mm^{-1})	0.197	0.180
ρ_{calcd} ($g\ cm^{-3}$)	1.366	1.369
Data collection		
θ limits (°)	$2<\theta<25$	$2<\theta<25$
hkl limits	−6, 6;, 12; −12, −17, 17	−13, 13; −17, 17; −28, 28
No. collected reflection	8035	38,246
No. ind. refl. (R_{int})	2910 (0.036)	6905 (0.057)
No. observed reflection[a]	2727	4809
Refinement		
R[b]	0.058	0.037
R_w[c]	0.122	0.087
No. of variables	212	510
GOOF	1.285	0.961
Flade parameter	−0.05	−0.08
$\Delta\rho_{min}$ ($e\ Å^{-3}$)	−0.24	−0.16
$\Delta\rho_{max}$ ($e\ Å^{-3}$)	0.26	0.14

[a] $F_o > 4\sigma(F_o)$.
[b] $R = \sum(F_o^2 - F_c^2)/\sum F_o^2$.
[c] $R_w = [\sum w(F_o^2 - F_c^2)^2/\sum w(F_o^2)^2]^{1/2}$.

4.2. General protocol for the synthesis of diols 2a–c and 3a–c

For the synthesis of **2a–c** and **3a–c** a sequential hydrolysis–oxidation–Grignard-reagent-addition reaction protocol has been carried out. A solution of **1** (0.8 mmol) and periodic acid (0.9 mmol) in 50 mL of dry ethyl acetate was stirred for 3 h, whereby a solid formed that was separated by filtration. Evaporation under reduced pressure afforded a colorless syrup, which was dissolved in 10 mL of dry diethyl ether and cooled to 0°C. Then, immediately the corresponding alkyl magnesium bromide (21 mmol) was added and the mixture was allowed to react for 4 h. After addition of a saturated solution of NH_4Cl, the product was extracted with ethyl acetate and the solution dried over Na_2SO_4. The residue obtained after evaporation under reduced pressure was purified by column chromatography.

4.2.1. (5*R*)-1,2-*O*-Isopropylidene-5-methyl-α-D-xylofuranose 2a.[5] ^{1}H NMR δ: 1.31 (s, 3H), 1.38 (d, 3H, J=6.6 Hz), 1.47 (s, 3H), 2.75 (b, 1H), 3.94 (t, 1H, J=3.6 Hz), 4.25 (b, 1H), 4.33 (m, 2H), 4.51 (d, 1H, J=3.7 Hz), 5.97 (d, 1H, J=3.7 Hz) ppm; ^{13}C NMR δ: 19.3, 26.1, 26.7, 66.5, 75.1, 82.4, 85.2, 104.8, 111.6 ppm.

4.2.2. (5*S*)-1,2-*O*-Isopropylidene-5-methyl-α-D-xylofuranose 3a.[5] ^{1}H NMR δ: 1.29 (s, 3H), 1.33 (d, 3H, J=6.6 Hz), 1.46 (s, 3H), 2.11 (b, 1H), 2.91 (b, 1H), 3.93 (t, 1H, J=3.3 Hz), 4.21 (m, 2H), 4.50 (d, 1H J=3.7 Hz), 5.94 (d, 1H, J=3.7) ppm; ^{13}C NMR δ: 20.7, 26.2, 26.8, 61.1, 76.5, 82.1, 85.6, 104.7, 111.8 ppm.

4.2.3. (5*R*)-1,2-*O*-Isopropylidene-5-phenyl-α-D-xylofuranose 2b.[6] ^{1}H NMR δ: 1.24 (s, 3H), 1.45 (s, 3H), 2.87 (d, 1H, J=5.5 Hz), 3.20 (d, 1H, J=4.7 Hz), 4.00 (m, 1H), 4.32 (m, 1H), 4.50 (d, 1H, J=3.6 Hz), 5.0 (t, 1H, J=4.7 Hz), 6.01 (d, 1H, J=6.6 Hz) ppm; ^{13}C NMR δ: 26.1, 26.7, 73.6, 75.4, 82.1, 85.1, 105.0, 111.8, 126.0, 128.3, 128.8, 139.2 ppm.

4.2.4. (5*S*)-1,2-*O*-Isopropylidene-5-phenyl-α-D-xylofuranose 3b.[6] ^{1}H NMR δ: 1.24 (s, 3H), 1.48 (s, 3H), 3.05 (b, 1H), 4.14 (b, 1H), 4.20 (m, 1H), 4.50 (d, 1H, J=3.7 Hz), 5.28 (d, 1H, J=3.0 Hz), 6.01 (d, 1H, J=3.7 Hz) ppm; ^{13}C NMR δ: 26.1, 26.8, 73.7, 75.4, 82.1, 85.2, 105.1, 111.8, 126.0, 128.3, 128.8, 138.9 ppm.

4.2.5. (5*R*)-1,2-*O*-Isopropylidene-5-vinyl-α-D-xylofuranose 2c.[7] ^{1}H NMR δ: 1.31 (s, 3H), 1.48 (s, 3H), 4.09 (t, 1H, J=3.3 Hz), 4.27 (d, 1H, J=2.6 Hz), 4.52 (m, 1H), 5.43 (d, 1H, J=10.6 Hz), 5.52 (d, 1H, J=17.2 Hz), 5.99 (m, 2H) ppm.

4.2.6. (5*S*)-1,2-*O*-Isopropylidene-5-vinyl-α-D-xylofuranose 3c.[7] ^{1}H NMR δ: 1.31 (s, 3H), 1.48 (s, 3H), 4.04 (dd, 1H, J=4.0, 2.5 Hz), 4.32 (d, 1H, J=2.5), 4.51 (d, 1H, J=3.6 Hz), 4.68 (t, 1H, J=5.2 Hz), 5.31 (dd, 1H, J=10.6, 1.1 Hz), 5.48 (dd, 1H, J=17.2, 1.1 Hz), 5.98 (m, 2H) ppm.

4.3. General protocol for the synthesis of the cyclic phosphates 4a–c, 4a′–c′, 5a–c, 5a′–c′

The synthetic protocol used for the preparation of **4a–c**, **4a′–c′**, **5a–c**, **5a′–c′** is outlined in what follows for compounds **4b** and **4b′**. To a solution of diol **2b** (580 mg,

2.17 mmol) and NEt_3 (1.52 mL, 10.89 mmol) in dry CH_2Cl_2 (20 mL) a solution of $PhOP(O)Cl_2$ in 2 mL of dry CH_2Cl_2 was added dropwise (0.390 mL, 2.6 mmol). The reaction mixture was allowed to stir for 4 h before it was quenched with H_2O. The separated organic phase was dried over Na_2SO_4. After evaporation of the solvent under reduced pressure, the products were separated by column chromatography (3:1 mixture of hexane/ethyl acetate) affording **4b** and **4b′** in global yields of 50 and 45%, respectively.

4.3.1. (5*R*, S_P)-1,2-*O*-Isopropylidene-5-methyl-3,5-*O*-phenoxyphosphoryl-α-D-xylofuranose 4a. Mp=126–127°C; ^{1}H NMR δ: 1.32 (s, 3H), 1.49 (s, 3H), 1.56 (d, 1H, J=7.3 Hz), 4.11 (dd, 1H, J=2.2, 4.4 Hz), 4.72 (d, J=3.6 Hz), 4.91 (m, 1H), 4.92 (ddd, 1H, J=16.0, 7.3, 2.2 Hz), 6.04 (d, 1H, J=3.6 Hz), 7.1–7.4 (m, 5H) ppm; ^{13}C NMR δ: 19.4, 26.1, 26.6, 73.6, 80.8, 93.9, 104.7, 112.7, 119.6, 125.4, 130.0 ppm; ^{31}P NMR δ: −16.2 ppm; FABS m/z 343.0936 $[M+H]^+$ (calcd for $C_{15}H_{19}O_7P$ 343.0947).

4.3.2. (5*R*, R_P)-1,2-*O*-Isopropylidene-5-methyl-3,5-*O*-phenoxyphosphoryl-α-D-xylofuranose 4a′. ^{1}H NMR δ: 1.28 (s, 3H), 1.46 (s, 3H), 1.62 (d, 3H, J=7.0 Hz), 4.18 (q, 1H, J=2.6 Hz), 4.64 (d, 1H, J=3.6 Hz), 4.74 (ddd, 1H, J=15.0, 7.0, 2.5 Hz), 4.99 (dd, 1H, J=5.8, 2.9 Hz), 5.69 (d, H, J=3.6 Hz), 7.1–7.3 (m, 5H) ppm; ^{13}C NMR δ: 19.7, 26.2, 28.8, 77.3, 77.9, 81.2, 84.0, 104.9, 112.7, 120.2, 125.5, 129.7 ppm; ^{31}P NMR δ: −15.0 ppm; FABS m/z 343.0936 $[M+H]^+$ (calcd for $C_{15}H_{19}O_7P$ 343.0947).

4.3.3. (5*S*, S_P)-1,2-*O*-Isopropylidene-5-methyl-3,5-*O*-phenoxyphosphoryl-α-D-xylofuranose 5a. ^{1}H NMR δ: 1.31 (s, 3H), 1.48 (s, 3H), 1.55 (dd, 3H, J=6.4, 2.9 Hz), 4.10 (m, 1H), 4.69 (d, 1H, J=3.6 Hz), 4.82 (apparent d, 1H, J=1.8 Hz), 4.86 (broad dd, 1H, J=6.6, 1.5 Hz), 6.01 (d, 1H, J=3.6 Hz), 7.1–7.4 (m, 5H) ppm; ^{13}C NMR δ: 18.4, 26.1, 26.6, 74.4, 75.6, 82.5, 83.6, 104.6, 112.6, 119.3, 125.3, 130.1, 150.2 ppm; ^{31}P NMR δ: −15.5 ppm; FABS m/z 343.0939 $[M+H]^+$ (calcd for $C_{15}H_{19}O_7P$ 343.0947).

4.3.4. (5*S*, R_P)-1,2-*O*-Isopropylidene-5-methyl-3,5-*O*-phenoxyphosphoryl-α-D-xylofuranose 5a′. ^{1}H NMR δ: 0.93 (s, 3H), 1.45 (s, 3H), 1.14 (dd, 3H, J=6.6, 2.5 Hz), 3.56 (dd, 1H, J=4.2, 2.2 Hz), 4.16 (d, 1H, J=3.6 Hz), 4.45 (q, 1H, J=6.6 Hz), 4.65 (dd, 1H, J=4.1, 2.9 Hz), 5.57 (d, 1H, J=3.6 Hz) ppm; ^{13}C NMR δ: 18.6, 26.2, 26.7, 74.3, 75.2, 82.3, 84.1, 104.6, 112.7, 120.2, 125.6, 129.7 ppm; ^{31}P NMR δ: −12.6 ppm; FABS m/z 343.0938 $[M+H]^+$ (calcd for $C_{15}H_{19}O_7P$ 343.0947).

4.3.5. (5*R*, S_P)-1,2-*O*-Isopropylidene-5-phenyl-3,5-*O*-phenoxyphosphoryl-α-D-xylofuranose 4b. Mp=108–109°C; ^{1}H NMR δ: 1.31 (s, 3H), 1.44 (s, 3H), 4.52 (dd, 1H, J=3.6, 2.9 Hz), 4.78 (d, 1H, J=3.6 Hz), 4.95 (dd, 1H, J=7.3, 2.9 Hz), 5.63 (dd, 1H, J=10.2, 3.6 Hz), 6.01 (d, 1H, J=3.6 Hz), 7.2–7.6 (m, 10H) ppm; ^{13}C NMR δ: 26.3, 26.8, 79.9, 81.9, 82.1, 84.0, 105.2, 112.9, 120.0, 125.6, 129.1, 129.8, 136.3 ppm; ^{31}P NMR δ: −13.8 ppm; FABS m/z 405.1104 $[M+H]^+$ (calcd for $C_{20}H_{21}O_7P$ 405.1103).

4.3.6. (5*R*, R_P)-1,2-*O*-Isopropylidene-5-phenyl-3,5-*O*-phenoxyphosphoryl-α-D-xylofuranose 4b′. Mp=110–112°C; ^{1}H NMR δ: 1.33 (s, 3H), 1.46 (s, 3H), 4.63 (dd, 1H, J=5.5, 3.3 Hz), 4.82 (d, 1H, J=3.6 Hz), 4.92 (apparent t, 1H, J=3.4 Hz), 5.68 (dd, 1H, J=11.2, 5.5 Hz), 6.14 (d, 1H, J=3.6 Hz), 7.0–7.5 (m, 10H) ppm; ^{13}C NMR δ: 26.3, 26.8, 79.1, 80.0, 81.9, 84.1, 105.3, 112.9, 119.8, 126.2, 129.0, 129.8, 136.1 ppm; ^{31}P NMR δ: −13.0 ppm; FABS m/z 405.1103 $[M+H]^+$ (calcd for $C_{20}H_{21}O_7P$ 405.1103).

4.3.7. (5*S*, S_P)-1,2-*O*-Isopropylidene-5-phenyl-3,5-*O*-phenoxyphosphoryl-α-D-xylofuranose 5b. Mp=191–193°C; ^{1}H NMR δ: 1.30 (s, 3H), 1.43 (s, 3H), 4.40 (m, 1H,), 4.72 (d, 1H, J=3.6 Hz), 5.0 (apparent d, J=1.8 Hz), 5.75 (broad s), 6.02 (d, 1H, J=3.6 Hz), 7.1–7.5 (m, 10H) ppm; ^{13}C NMR δ: 26.2, 26.6, 74.8, 79.6, 82.8, 83.3, 104.8, 112.7, 119.4, 125.5, 126.6, 128.6, 129.0, 134.6 ppm; ^{31}P NMR δ: −15.2 ppm; FABS m/z 405.1105 $[M+H]^+$ (calcd for $C_{20}H_{21}O_7P$ 405.1103).

4.3.8. (5*S*, R_P)-1,2-*O*-Isopropylidene-5-phenyl-3,5-*O*-phenoxyphosphoryl-α-D-xylofuranose 5b′. Mp=138–140°C; ^{1}H NMR δ: 1.24 (s, 3H), 1.30 (s, 3H), 4.42 (dd, 1H, J=3.0, 2.2 Hz), 4.60 (d, 1H, J=3.6 Hz), 5.11 (dd, 1H, J=4.5, 3.0 Hz), 5.61 (d, 1H, J=3.6 Hz), 5.84 (broad s, 1H), 7.1–7.4 (m, 10H) ppm; ^{13}C NMR δ: 26.2, 26.8, 75.6, 78.3, 82.8, 83.81, 104.8, 112.8, 120.3, 125.8, 126.6, 128.6, 129.0, 129.8, 134.5 ppm; ^{31}P NMR δ: −12.9 ppm; FABS m/z 405.1089$[M+H]^+$ (calcd for $C_{20}H_{21}O_7P$ 405.1103).

4.3.9. (5*R*, S_P)-1,2-*O*-Isopropylidene-5-vinyl-3,5-*O*-phenoxyphosphoryl-α-D-xylofuranose 4c. ^{1}H NMR δ: 1.34 (s, 3H), 1.5 (s, 3H), 4.25 (broad d, 1H, J=2.2 Hz), 4.74 (d, 1H, J=3.6 Hz), 4.92 (apparent t, 1H, J=2.5 Hz), 5.25 (dd, 1H, J=18.3, 7.3 Hz), 5.42 (broad d, 1H, J=10.6 Hz), 5.53 (d, 1H, J=17.2 Hz), 6.08 (ddd, J=17.2, 10.6, 7.3 Hz), 6.09 (d, 1H, J=3.6 Hz), 7.1–7.4 (m, 5H) ppm; ^{13}C NMR δ: 26.2, 26.6, 75.7, 80.9, 81.4, 83.8, 104.6, 112.8, 119.7, 121.4, 125.5, 129.9, 131.7 ppm; ^{31}P NMR δ: −16.4 ppm; FABS m/z 355.0932 $[M+H]^+$ (calcd for $C_{16}H_{19}O_7P$ 355.0947).

4.3.10. (5*R*, R_P)-1,2-*O*-Isopropylidene-5-vinyl-3,5-*O*-phenoxyphosphoryl-α-D-xylofuranose 4c′. ^{1}H NMR δ: 1.32 (s, 3H), 1.48 (s, 3H), 4.33 (dd, 1H, J=5.3, 2.6 Hz), 4.70 (d, 1H, J=3.6 Hz), 4.98 (dd, 1H, J=7.7, 2.9 Hz), 5.17 (d, 1H, J=15.2 Hz), 5.47 (dd, 1H, J=10.6, 1.4 Hz), 5.67 (dd, 1H, J=17.0, 1.8 Hz), 5.80 (d, 1H, J=3.6 Hz), 6.04 (ddd, 1H, J=17.0, 10.6, 6.2, 5.5 Hz), 7.1–7.4 (m, 5H) ppm; ^{13}C NMR δ: 26.2, 26.8, 75.8, 80.8, 81.6, 84.1, 105.1, 112.8, 120.2, 120.3, 125.5, 129.8, 131.5 ppm; ^{31}P NMR δ: −15.7 ppm; FABS m/z 355.0939 $[M+H]^+$ (calcd for $C_{16}H_{19}O_7P$ 355.0947).

4.3.11. (5*S*, S_P)-1,2-*O*-Isopropylidene-5-vinyl-3,5-*O*-phenoxyphosphoryl-α-D-xylofuranose 5c. ^{1}H NMR δ: 1.30 (s, 3H), 1.51 (s, 3H), 4.23 (dd, 1H, J=4.4, 2.2 Hz), 4.69 (d, 1H, J=3.6 Hz), 4.89 (apparent d, 1H, J=1.8 Hz), 5.17 (broad d, 1H, J=6.2 Hz), 5.40 (d, 1H, J=10.6 Hz), 5.50 (d, 1H, J=17.2 Hz), 6.02 (d, 1H, J=3.6 Hz), 6.04 (dddd, 1H, J=17.2, 10.6, 6.2, 1.8 Hz), 7.2–7.4 (m, 5H) ppm; ^{13}C NMR δ: 26.2, 26.6, 74.1, 79.2, 82.5, 83.6, 104.8, 112.8, 119.3, 119.5, 125.5, 130.15, 131.7 ppm; ^{31}P NMR δ: −15.6 ppm; FABS m/z 355.0958 $[M+H]^+$ (calcd for $C_{16}H_{19}O_7P$ 355.0947).

4.3.12. (5*S*, R_P)-1,2-*O*-Isopropylidene-5-vinyl-3,5-*O*-phenoxyphosphoryl-α-D-xylofuranose 5c′. ^{1}H NMR δ: 1.28 (s, 3H), 1.45 (s, 3H), 4.24 (dd, 1H, J=4.4, 2.2 Hz), 4.57 (d, 1H, J=3.6 Hz), 5.0 (dd, 1H, J=4.4, 2.5 Hz), 5.28 (broad d, 1H, J=6.2 Hz), 5.40 (d, 1H, J=10.6 Hz), 5.48 (d, 1H, J=16.1 Hz), 5.60 (d, 1H, J=3.6 Hz), 6.00 (dddd, 1H, J=16.1, 10.6, 6.2, 1.8 Hz), 7.1–7.4 (m, 5H) ppm; ^{13}C NMR δ: 26.2, 26.8, 74.9, 77.8, 82.3, 83.8, 104.8, 112.8, 119.7, 120.2, 125.7, 129.7, 131.7 ppm; ^{31}P NMR δ: −13.2 ppm; FABS m/z 355.0951 $[M+H]^+$ (calcd for $C_{16}H_{19}O_7P$ 355.0947).

Acknowledgements

We thank CONACyT for financial support, Project No. 35102 and Grants 121996, 127042 to F. S.-P. and M. S., respectively. We thank Professor Dr Jean L. Fourrey for helpful comments.

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