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Conformational and configurational analysis of 2-phenoxy-2-oxo-1,3,2-dioxaphosphorinanes. Conformational and configurational dependence upon conformation of the diol precursor

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Abstract—Diastereomeric 5-*tert*-butyl-4-methyl-2-phenoxy-2-oxo-1,3,2-dioxaphosphorinanes were synthesized, and studied by NMR and computational methods in order to determine their predominant conformations as well as their relative configurations. The study was performed assuming a novel criteria, in which, the conformation and configuration of the diastereomeric 5-*tert*-butyl-4-methyl-2-phenoxy-2-oxo-1,3,2-dioxaphosphorinanes depend upon the conformation of the corresponding diol precursors. In other words, the orientation or pseudo orientation of the groups into the ring framework of the heterocyclic is initially acquired by the direct phosphorylation reaction with the diol precursor in the most stable conformation, and then, once the heterocyclic is formed, the final conformation is dictated by stereoelectronic and steric effects.

1. Introduction

The conformational and configurational study of the well-known 1,3,2-dioxaphosphorinanes is one of the most exciting in the field of the physic-organic chemistry.[1] These studies have found more popularity since the report from the Bentrude's group, which suggests that the twist conformation of the cAMP and cGMP is the predominant in the cell metabolism.[2] Apparently, the ΔG^0 for the chair-twist equilibria is provided by binding forces within an enzyme active sites.[2] Thus, attention turned to the conformational study of 2-phenoxy-2-oxo-1,3,2-dioxaphosphorinanes fused in *transoid* fashion, in which, a small molecular distortion is observed and two twist forms and only one boat form can be assumed as accessible.[1] Similar behavior is observed for those analogous fused in *cisoid* fashion.[1,3,4]

In this regard, we recently reported the trapping of two different molecules into a crystal asymmetric unit, one molecule in chair conformation and another one in boat conformation.[4] Thus, the ready dynamic equilibrium between the chair and the boat conformation in solution was absolutely corroborated in solid state. This finding, put forward that the boat conformation should be considered as a further appropriate conformation for intermolecular interaction between the cAMP and cGMP and the enzyme active site that regulate the role in the cell metabolism.[5]

For less strained 2-phenoxy-2-oxo-1,3,2-dioxaphosphorinanes, the chair–non-chair and the chair–chair equilibria are spontaneous operations. So, their configurational and conformational analyses turn very complicated due to the existence of more conformational forms than those 2-phenoxy-2-oxo-1,3,2-dioxaphosphorinanes fused in *trans* or *cisoid* fashion.[1]

Apparently, one of the best ways for monitoring the specific conformational equilibria is by means of analysis of the well-known stereospecificity between the vicinal coupling constant and its dihedral angle.[1] Additionally, assignments of the preferred configuration and conformation of 2-oxo-2-phenoxy-1,3,2-dioxaphosphorinanes and related compounds could be performed by the analysis of the vicinal $^1H-^1H$ scalar coupling constants, and the well-established $^3J_{H,P}$ coupling constant relationship. Herein, the equatorial H–P coupling constant is typically $\geq$20 Hz, while the corresponding axial H–P coupling is usually $\leq$5 Hz.[1] A further key factor in these assignments is the preference of the P–OR bond to be axially oriented, which is clearly observed in the phosphorus chemical shift value, i.e. signals which are up-field shifted can be attributed to phosphorinanes having their phenoxy group at the axial position.[1,6]

Previously, we reported that the chair–boat equilibria for 2-oxo-2-phenoxy-1,3,2-dioxaphosphorinanes derived from

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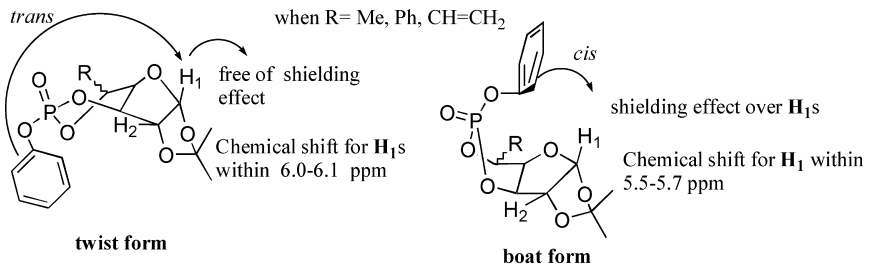
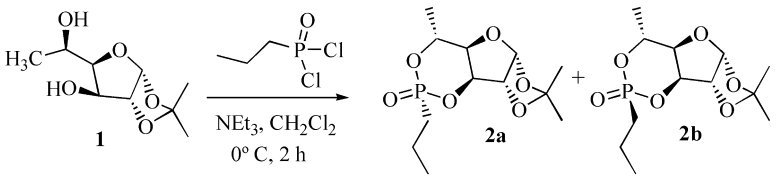
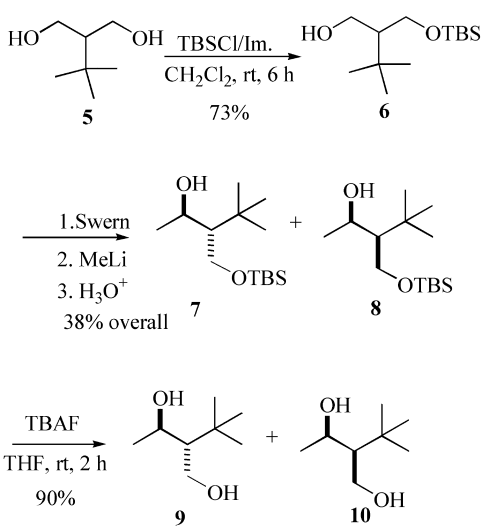


Figure 1. Aromatic ring current effect in the chemical shift of the anomeric furanose protons.



Scheme 1. Synthesis of cyclic phosphonates.



Scheme 2. Synthesis of diols **9** and **10**.

1,2-*O*-isopropylidene-α-D-xylofuranose can be observed by the analysis of the chemical shift of anomeric protons, which are oriented *cis* to the P-phenoxy group (Fig. 1).[4]

In fact, the driving force that aid to get the above non-chair conformations is the strain 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 (see Figure 1) and the strong pseudo-axial seeking force caused by phenoxy group. In this sense, herein, we report further information that allows, in a way, to observe and predict specific conformational equilibria and relative configurational assignment of non-fused 2-oxo-2-phenoxy-1,3,2-dioxaphosphorinanes disubstituted at C5 and C3.

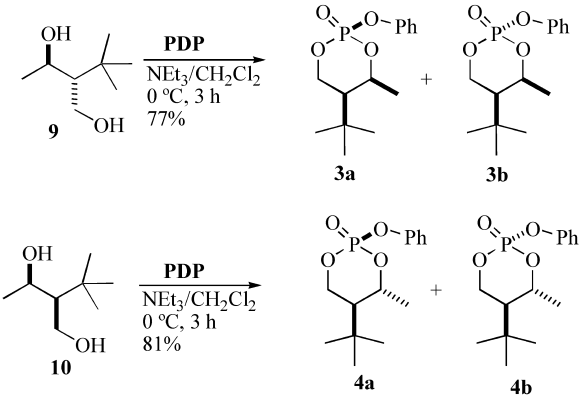
2. Results and discussion

As just mentioned, the strong anisotropic shielding effect of the aromatic ring of the phenoxy group, generates an up-field shift in the H_1 furanose anomeric hydrogen atoms when are oriented *cis* to the P-phenoxy group. Therefore, the replacement of the phenoxy group with an alkyl group should not generate any up-field shift in the H_1 furanose anomeric hydrogen atoms. Thus, cyclic phosphonates **2a** and **2b** were synthesized from diol **1** and propylphosphonic dichloride in the presence of triethylamine, in 80% yield, on a 2:1 ratio, respectively, Scheme 1.

As expected, due to the absence of the benzene ring current effect, there was not observed any shielding effect over the anomeric hydrogen (5.96 ppm for **2a** and 6.09 ppm for **2b**). Furthermore, on the basis of the vicinal H,P H,H coupling constants, and 2D-NOESY interactions, and due also to the absence of the stronger anomeric effect that phenoxy group incorporates into the dynamic motion, the chair-twist equilibrium for both phosphonates is proposed.[7]

Then, we proceed to synthesize four diasteromeric 2-phenoxy-2-oxo-1,3,2-dioxaphosphorinanes incorporating the methyl group at C4 and *tert*-butyl group at C5 (**3a**, **3b**, **4a** and **4b**). First, the monosilylation of diol **5** is performed. Then, a sequential Swern[8] oxidation, followed by methyl addition affords the *anti* and *syn* monosilylated alcohols **7** and **8** in a 1:1 ratio. Finally, desilylation of **7** and **8** yielded to the *anti* and *syn* diols **9** and **10** (Scheme 2).

Diols **9** and **10** are converted in a mixture of two pairs of



Scheme 3. Synthesis of phosphorinanes **3a**, **3b**, **4a** and **4b**.

Table 1. Coupling constants (Hz) for dioxaphosphorinanes **3a**, **3b**, **4a**, and **4b**[a]

	$^3J_{H4,P}$	$^3J_{H6,P}$	$^3J_{H6',P}$	$^3J_{H4,H5}$	$^3J_{H5,H6'}$	$^3J_{H5,H6}$	$^3J_{H4,H6}$	$^3J_{H6,H6'}$
3a	21.0	22.1	2.4	3.8	11.0	3.5	1.3	11.4
3b	15.4	11.1	11.0	4.0	10.3	4.4	0	11.2
4a	14.0	17.1	8.9	6.6	9.0	5.3	0	11.5
4b	19.8[b]	20.0[b]	7.3[b]	2.8[b]	4.0[b]	3.3[b]	0.8[b]	12.3[b]

[a] $CDCl_3$ solution unless otherwise noted.
[b] Spectrum recorded on C_6D_6 (insufficient resolution in $CDCl_3$).

Table 2. ^1H and ^{31}P chemical shift for dioxaphosphorinanes **3a**, **3b**, **4a**, and **4b**[a]

	δ_{H4}	δ_{H5}	δ_{H6}	$\delta_{H6'}$	$\delta_{t\text{-Bu}}$	δ_{Me}	δ_P
3a	4.87	2.45	4.54	4.38	0.98	1.57	−12.7
3b	4.85	2.16	4.58	4.40	1.00	1.62	−12.3
4a	4.61	1.82	4.43	4.22	0.97	1.60	−9.00
4b	4.48[b]	0.70[b]	4.12[b]	4.04[b]	0.80[b]	1.22[b]	−11.0[b]

[a] $CDCl_3$ solution unless other wise noted.
[b] Spectrum recorded on C_6D_6 (insufficient resolution in $CDCl_3$).

Doing a preliminary evaluation for all the diasteromeric dioxaphosphorinanes, it can be said that each pair of dioxaphosphorinanes has one conformer with a permanent chair and another one with a non-chair conformation (Fig. 2).

Nevertheless, the correct assignment of the non-chair conformation without crystallographic studies, continues being a difficult task; the vicinal H,P coupling constants from 8 to 16 Hz may describe either twist, boat or twist-boat conformations.

The primary interest of this conformational and configurational study of 2-oxo-2-phenoxy-1,3,2-dioxaphosphorinanes bearing the methyl and *tert*-butyl groups at C4 and C5, respectively, concerns in the introduction of a novel way of rationalize and predict the preferred conformations of these heterocyclic compounds by virtue of the specific conformation of the diol precursors.

Till now, it is considered that the chair–chair and

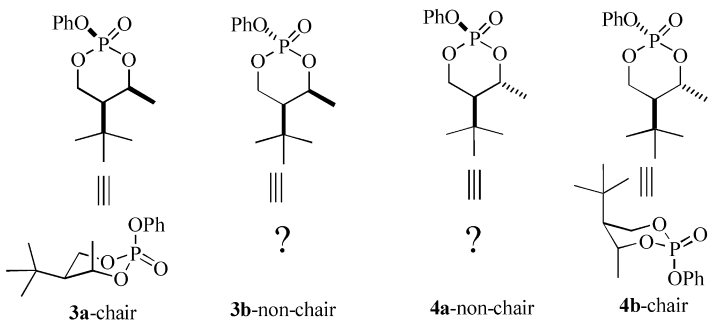


Figure 2. Predominant chair conformation for **3a** and **4b** and known non-chair for **4a** and **4b**.

cyclic phosphates **3a** and **3b**, **4a** and **4b** by treatment with phenyl dichlorophosphate (**PDP**), and triethylamine in dichloromethane. Both pairs of diasteromeric phosphorinanes are separated by column chromatography on silica gel giving **3a**, **3b** and **4a**, **4b** in good yields (77 and 81%, respectively). The diastereomeric ratio was 1:1 in both cases (Scheme 3).

Table 1 shows the $^3J_{H,P}$, $^3J_{H,H}$ and ^4J_w values. It is clear for compounds **3a** and **4b** that they are predominantly in a chair conformation. The H4 and H6 are quite comfortable in equatorial position leading to the methyl group in axial position ($^3J_{H4,P}$=20.1 Hz, $^3J_{H6,P}$=22.1 Hz for **3a** and $^3J_{H4,P}$=19.4 Hz, $^3J_{H6,P}$=20.0 Hz for **4b**). The analysis of the H4,H5 coupling constants for **3a** are in agreement with the equatorial position for *tert*-butyl group ($^3J_{H4,H5}$=3.8 Hz). Additionally, if the *tert*-butyl is equatorially and the methyl axially oriented, the stereochemistry for diol **9** should be *anti*, and obviously **10** have to be *syn*. NMR data for the another two phosphorinanes **3b** and **4a** revealed that both are away from the chair conformation ($^3J_{H4,P}$=15.4 Hz, $^3J_{H6,P}$=11.1 Hz for **3b** and $^3J_{H4,P}$=14.0 Hz, $^3J_{H6,P}$=17.1 Hz for **4a**). The configuration of the phosphorus atom was determined on the bias of the ^{31}P chemical shift: phosphorinanes that appear at upper field than their diastereomer congener suggest that phenoxy group is oriented in axial position (see Table 2).[6]

chair–non-chair equilibria of 1,3,2-dioxaphosphorinanes (and similar others) is dictated after phosphorylation reaction is achieved. To our best knowledge, any work has considered that the predominant conformation of these heterocycles may depend on the most stable conformation of 1,3-diols precursors; especially those disubstituted.

The above idea was originated from the absence of the expected chair conformations for **3bc′** and **4ac′**. In the case of **3bc′**, the anomeric effect caused by the phenoxy group, and the lack of 1,3-diaxial interactions between the

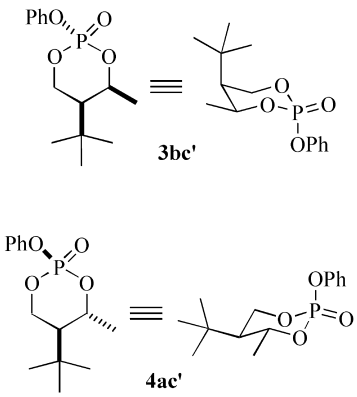


Figure 3. Expectable conformations for **3b** and **4a**.

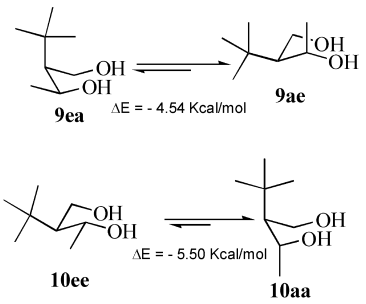


Figure 4. Preferred conformation of diols **9** and **10**.

tert-butyl and methyl groups should afford a very comfortable chair conformation (see Figure 3). Similar criteria should be applied for **4ac′**, although in this case the gauche interaction between the *tert*-butyl and methyl groups might appear as a lightly unfavorable situation for the chair conformation (see Figure 3).

In this sense, it was found by computational calculations (using the PC GAMESS program, with the 6-31G** basis set[9]) that conformers **9ae** and **10aa** are more stable by 4.54 and 5.50 kcal/mol, respectively (see Figure 4).

Thus, direct phosphorylation reaction of diol **9** in the preferred conformation **9ae** should afford **3ac** and **3bc**. Phosphorinane **3ac** is locked in a comfortable chair conformation (as previously was described). On the other hand, **3bc** escapes from the chair conformation to the boat conformation **3bb** due to the strong pseudo-axial seeking force caused by phenoxy group (see Figure 5). Chemical shift of H5 revealed for phosphorinane **3bb** to be exposed to a shielding effect caused by phenoxy group (δ: 2.45 ppm for **3ac** and 1.95 ppm for **3bb**) indicating that the boat conformation **3bb** with H5 and phenoxy group in proximity is predominant (Fig. 5).[4] Computational calculations (geometry optimization with semi-empirical PM3 level and ab initio calculations at HF/6-31G** level[9]) and NMR data support the boat conformation.

On the other hand, direct phosphorylation of diol **10** in the preferred conformation **10aa** affords phosphorinanes **4ac** and **4bc**. Now, phosphorinane **4bc** is locked in a comfortable chair conformation (Fig. 6). Apparently, **4bc** should be more stable in the chair conformation than **3ac** because in this case, the *tert*-butyl and methyl groups are oriented *anti*-diaxial minimizing most of the steric destabilizing contributions (Fig. 6). Nevertheless, larger values of $^{3}J_{H4,P}$ and $^{3}J_{H6,P}$ for **3ac** suggest that **3ac** is more predominant in chair conformation than **4bc**. Computational calculations are in agreement with this assessment: it was found that **3ac** is more stable than **4bc** by 2.7 kcal/mol. It is important to mention that in both cases, the methyl and phenoxy groups are oriented *syn*-1,3-diaxial, and steric repulsions may destabilize the chair conformation. Reports

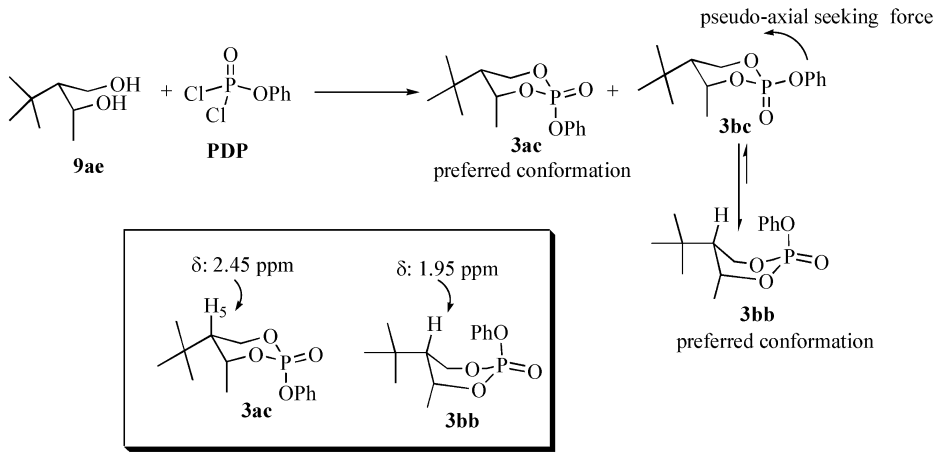


Figure 5. Direct phosphotylation reaction of diol **9** in the preferred **9ae** conformation.

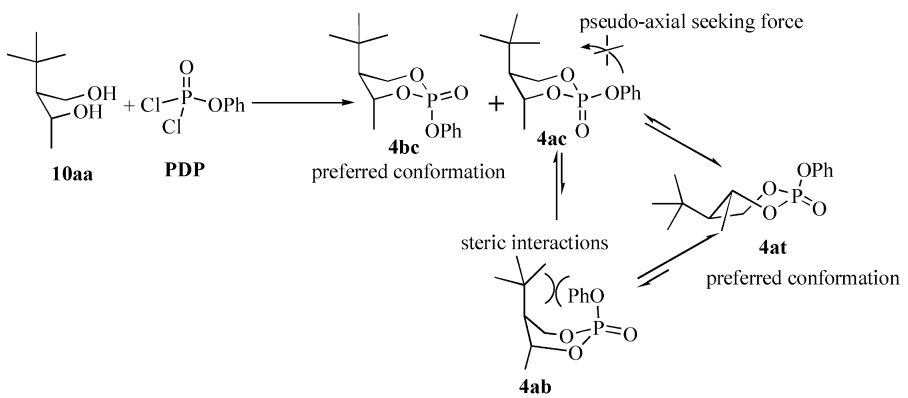


Figure 6. Direct phosphorylation reaction of diol **10** in the preferred **10aa** conformation.

from Majoral[10] and us[11] have showed that *syn*-1,3 diaxial interactions between methyl or benzyl and phenoxy groups appear do not considerably affect the chair conformation.

On the other hand, **4ac** places the phenoxy group in unstable equatorial position, very similar to **3bc**. However, in this case, the non-chair conformation in the boat fashion **4ab** cannot be assumed. The pseudo-axial seeking force caused by phenoxy group is now considerably diminished by the strong steric interaction that the phenoxy and *tert*-butyl groups encounter when the boat conformation is operating. Now, the non-chair conformation is accommodated in a classical twist conformation **4at**. Thus, applying the same computational treatment, phosphorinane **4a** found the lowest relative energy in the twist conformation **4at** (Fig. 6).

By use of the H,P dihedral angle values of the phosphorinanes **3a**, **3b**, **4a** and **4b** in the conformation given by the computational calculations and applying them to the Lee and Sarma correlation[12] ($^3J_{POCH}$=18.1 $\cos^2\theta$−4.8 $\cos\theta$), we found close agreement values with the experimental ones, especially for phosphorinanes **3a**, **3b** and **4b**, where the difference between the calculated and observed are less than 2 Hz. In the case of **4a** some values are slightly higher; this means that the degree of twisting of phosphorinane ring is affected by the presence (in very small contribution) of further boat conformation (see Fig. 6).

It is important to consider the direct phosphorylation reaction of the diols **9** and **10** in the unfavorable **9ea** and **10ee** conformations. Phosphorinanes **3ac′** and **4ac′** should be expected as the major conformers along with their corresponding non-chair conformers. Unfortunately, small values of $^3J_{H4,P}$ and $^wJ_{Me,P}$ for those diastereomeric phosphorinanes were not observed (Fig. 7).[10,11]

Although the conformation and configuration study developed herein is well applied for 1,3-diols-1,2-disubstituted with methyl and *tert*-butyl groups, it is necessary to take some cautions with 1,3-diols-1,2-disubstituted

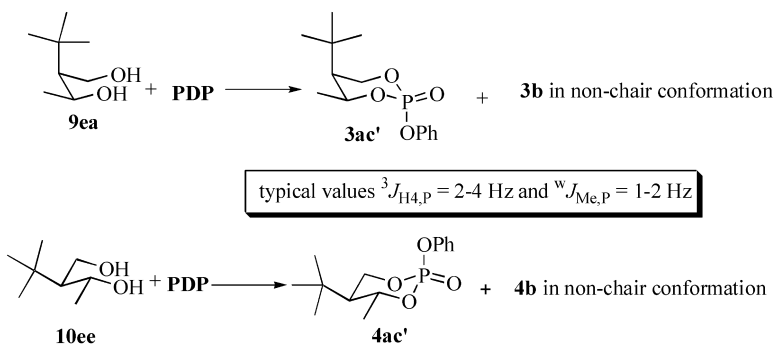
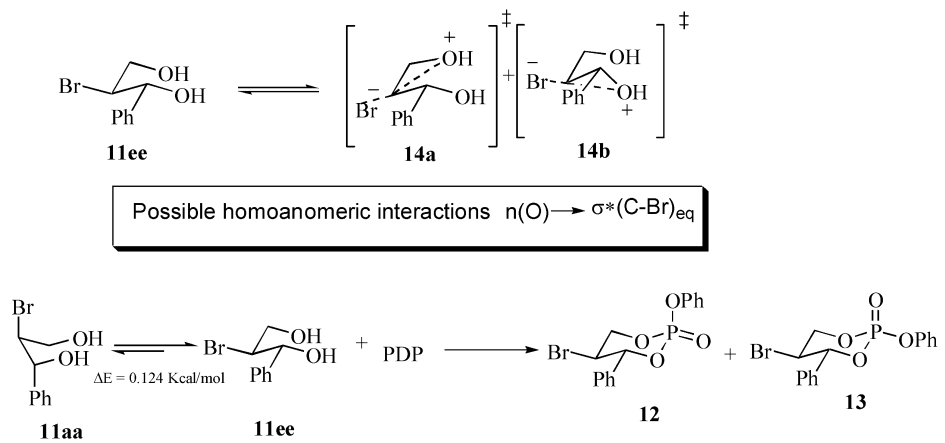


Figure 7. Hypothetic direct phosphorylation reactions of diols **9** and **10** in the unfavorable **9ea** and **10ee** conformations.



	δ_P [a]	$^3J_{H4,P}$ [b]	$^3J_{H4,H5}$ [b]	$^3J_{H6,P}$ [b]	$^3J_{H6',P}$ [b]
12	-13.5	0.8	10.4	26.1	1.0
13	-9.1	2.2	10.1	25.9	3.5

a: ppm, b: Hz

Figure 8. Homoanomeric interactions controlling diol and phosphorinanes conformation.

bearing electronegative groups like halides. In that case, stereoelectronic effects[13] turn more important than steric ones, and reversal behaviors may appear.

In this regard, we reviewed the phosphorylation reaction of the diol **11**.[14] Applying the same computational treatment, it was found that conformer **11ee** is more stable for 0.124 kcal/mol than **11aa**. Direct phosphorylation reaction of the diol **11** in the preferred conformation **11ee** affords phosphorinanes **12** and **13** in very comfortable chair conformation. In both cases, the bromine atom in placed in equatorial position (Fig. 8).

It is very well-known that the classic anomeric interactions[15] are stronger than any homoanomeric ones,[16] but the latter turns more important when the ability of σ^* orbitals increases as a result of bond stretching and/or polarization.[15] So, homoanomeric interactions involving W-and/or Plough effects[16,17] (n(O)→σ^*(C–Br)eq) are present when diol **11** is found in the **11ee** conformation. Besides, the above interactions may be also interpreted as a typical homoconjugation between n(O)→σ^*(C–Br)eq orbitals leading to a type of close shell solvolysis **14a** and **14b** intermediates (Fig. 7).

3. Conclusion

To the best of our knowledge, herein it has been introduced a novel way to predict and rationalize the conformational equilibria and relative configurational assignment of 5,4-disustituted-2-phenoxy-2-oxo-1,3,2-dioxaphosphorinanes. Although this study only involved two different types of 1,3-diols 1,2-disubstituted with different chemical properties, we anticipate very similar behavior for those with few variants into the framework, and will function analogously albeit on different time scales. Besides, due to few reports about the homoanomeric interactions in non-cyclic system (even in cyclic systems), further efforts in design and study new model molecules with specific structural featuring are currently underway and will be reported soon.

4. Experimental

4.1. Calculation methods

All geometries were fully optimized, and the nature of the resulting stationary point was characterized by vibrational frequencies at HF/6-31G(d,p) and PM3 levels for diols and phosphorinanes, respectively. The PC GAMESS[9a] program resided on a PIV computer and all optimized structures were visualized by using the MOLEKEL 4.3 program.[9b,c] The application of more accurate basis sets such as HF/6-31G(d,p) for phosphorinanes would exert enormous demand on our available computers.

4.1.1. (5*R*,S_P)-1,2-Isopropyliden-5-methyl-3,5-*O*-propylphosphoryl-α-D-xylofuranose (2a) and (5*R*,R_P)-1,2-Isopropyliden-5-methyl-3,5-*O*-propylphosphoryl-α-D-xylofuranose (2b). A solution of diol (**1**) (120 mg, 0.59 mmol) and triethylamine (0.2 mL, 0.88 mmol) in 15 mL of CH_2Cl_2 at 0 °C was added dropwise propyldichlorophosphonate (0.12 mL, 0.88 mmol) dissolved in 5 mL of CH_2Cl_2. The reaction mixture was allowed to stir for 2 h before quenched with H_2O (20 mL). Extracted with CH_2Cl_2, dried over Na_2SO_4 and evaporated under pressure reduced. The residue was purified by column chromatography (2:1, mixture of hexane/ethyl acetate) affording **2a** and **2b** in 80% yield with a ratio of 2:1 respectively.

Compound **2a**. $[\alpha]_D$=22.4 (c=1, $CHCl_3$); ^{1}H NMR δ: 1.01 (td, 3H,. J=7.5, 2.0 Hz), 1.34 (s, 3H), 1.5 (s, 3H), 1.64 (d, 6H, J=7.2 Hz), 1.75–1.85 (m, 4H), 4.21 (dd, 1H, J=2.4, 2.0 Hz), 4.58 (ddd, 1H, J=14.1, 7.2, 2.0 Hz), 4.65 (d, 1H, J=3.6 Hz), 4.95 (apparent t, 1H, J=2.0 Hz), 5.96 (d, 1H, J=3.6 Hz); ^{13}C NMR δ: 15.0, 15.8, 20.3, 26.0, 26.5, 27.5, 74.0, 76.2, 77.7, 83.9, 104.6, 112.5; ^{31}P NMR δ: 27.9; FABS m/z: 293.1159 $[M+H]^+$ (calcd for $C_{12}H_{22}O_6P$ 293.1154).

Compound **2b**. Mp 130–132 °C; $[\alpha]_D$=78.1 (c=1, $CHCl_3$); ^{1}H NMR δ: 1.04 (td, 3H, J=7.6, 1.5 Hz), 1.3 (s, 3H), 1.50 (s, 3H), 1.51 (d, 3H, J=6.3 Hz), 1.6–1.9 (m, 4H), 4.27 (apparent t, 1H, J=3.6 Hz), 4.57 (dd, 1H, J=5.2, 3.6 Hz), 4.62 (ddd, 1H, J=13.4, 6.3, 1.8 Hz), 4.75 (d, 1H, J=3.6 Hz), 6.01 (d, 1H, J=3.6 Hz); ^{13}C NMR δ: 15.2, 15.9, 19.8, 26.3, 26.9, 27.4, 72.9, 79.8, 81.0, 84.1, 105.6, 112.5; FABS m/z: 293. 1159 $[M+H]^+$ (calcd for $C_{12}H_{22}O_6P$ 293.1156).

4.1.2. 2-*tert*-Butyl-3-(*tert*-butyldimethylsiloxy)-1-propanol (6). To solution of **5** (1.2 g, 9 mmol) and imidazole (0.71 g, 9.8 mmol) in dry CH_2Cl_2 (40 mL) was added dropwise *tert*-butyldimethylsilyl chloride (1.4 g, 10.8 mmol) in CH_2Cl_2 (15 mL). The mixture was allowed to stir for 12 h, then, reaction was quenched with water and organic phase extracted with CH_2Cl_2, dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography on silica gel (eluent hexane/ethyl acetate: 8:1) gave **3** (1.55 g, 71%). ^{1}H NMR ($CDCl_3$) δ: 0.08 (s, 6H), 0.9 (s, 18H), 1.59 (m, 1H), 3.3 (d, 1H, J=6 Hz), 3.73 (t, 1H, J=9.4 Hz), 3.81 (t broad, 1H, J=9 Hz), 3.9 (dd, 1H, J=8.0, 5.0 Hz); ^{13}C NMR ($CDCl_3$) δ: −5.3, 18.1, 23.3, 29.0, 33.1, 51.2, 64.9, 65.7; EIHRMS: m/z: 189.1327 (M+·−t-Bu), calcd for $C_9H_{21}O_2Si$: m/z: 189.1311.

4.1.3. *anti* and *syn*-2-*tert*-Butyl-1-(*tert*-butyldimethylsiloxy)-3-butanol (8 and 9). To a solution of oxalyl chloride (1 mL) in CH_2Cl_2 (30 mL) at −70 °C was added dropwise dry DMSO (5 mL) and, after stirring for 15 min, a solution of **6** (1 g, 4 mmol) in CH_2Cl_2 (5 mL) followed by triethylamine (3.5 mL). The reaction mixture was then allowed to warm to room temperature then quenched with water. The aqueous phase was extracted with CH_2Cl_2 and the combined organic layers dried ($MgSO_4$) and evaporated in vacuo. The crude reaction mixture was dissolved in dry THF (10 mL) and cooled to 0 °C and MeLi (6 mL, of 1.4 M in ether) was added. After 2 h the reaction was quenched with aqueous NH_4Cl (10 mL) and the organic phase was extracted with CH_2Cl_2, dried ($MgSO_4$) and evaporated in vacuo. Purification by flash chromatography on silica gel (eluent hexane/ethyl acetate: 4/1) gave of *anti*-**7** (0.21 g, 18%) and *syn*-**8** (0.19 g, 15%).

anti-2-tert-Butyl-1-(tert-butyldimethylsiloxy)-2-butanol (**7**). ^{1}H NMR ($CDCl_3$) δ: 0.09 (s, 6H), 0.9 (s, 9H), 1.0 (s, 9H), 1.1 (m, 1H), 1.28 (d, 3H, J=6.6 Hz), 3.43 (d, 1H, J=8.7 Hz),

3.81 (dd, 1H, J=11.0, 4.2 Hz), 4.02 (dd, 1H, J=11.0, 4.0 Hz), 4.14 (qd, 1H, J=6.6, 0.8 Hz); ^{13}C NMR ($CDCl_3$) δ: −5.5, 17.1, 25.4, 25.9, 29.1, 33.2, 53.7, 61.6, 68.4; EIHRMS: m/z: 245.1942 (M+·−Me), calcd for $C_{13}H_{29}O_2Si$: m/z: 245.1937.

syn-2-tert-Butyl-1-(tert-butyldimethylsiloxy)-2-butanol (**8**). ^{1}H NMR ($CDCl_3$) δ: 0.09 (s, 6H), 0.87 (s, 9H), 0.95 (s, 9H), 1.35 (d, 3H, J=6.5 Hz), 1.85 (m, 1H), 3.73 (d, 1H, J=10 Hz), 3.9 (d, 1H, J=9.5 Hz), 4.05 (m, 1H); ^{13}C NMR ($CDCl_3$) δ: −4.5, 19.2, 25.8, 27.1, 29.0, 31.0, 53.9, 61.4, 68.8; EIHRMS: m/z: 245.1930 (M+·−Me), calcd for $C_{13}H_{29}O_2Si$: m/z: 245.1937.

4.1.4. *anti*-2-*tert*-Butyl-1,3-butandiol (9). To solution of **8** (100 mg, 0.4 mmol) in THF (3 mL) was added Bu_4NF (0.8 mL, 1.0 M in THF, 0.8 mmol) at 0 °C. The reaction mixture was then warmed to room temperature and allowed to stir for 3 h before it was diluted with water and extracted with CH_2Cl_2, dried ($MgSO_4$) and evaporated in vacuo. Flash chromatography on silica gel (eluent: hexane/ethyl acetate: 2/1) gave **9** (50 mg, 90%). ^{1}H NMR ($CDCl_3$) δ: 1.0 (s, 9H), 1.12 (m, 1H), 1.32 (d, 3H, J=6.5 Hz), 2.5 (broad, 1H), 2.7 (broad, 1H), 4.0 (m, 2H), 4.25 (qd, 1H, J=6.5, 1.0 Hz). ^{13}C NMR ($CDCl_3$) δ: 25.8, 28.9, 33.1, 54.3, 61.2, 68.6. EIHRMS: m/z: 147.1377 (M+·+H), calcd for $C_8H_{19}O_2$: m/z: 147.1385.

4.1.5. *syn*-2-*tert*-Butyl-1,3-butandiol (10). Was obtained analogously to **9**, also in 90% yield. ^{1}H NMR ($CDCl_3$) δ: 0.92 (s, 9H), 1.32 (d, 3H, J=6.5 Hz), 1.86 (m, 1H), 2.8 (broad, 1H), 3.9 (m, 2H), 4.23 (qd, 1H, J=6.5, 1.1 Hz); ^{13}C NMR ($CDCl_3$) δ: 19.5, 29.1, 31.5, 54.6, 61.3, 69.7. EIHRMS: m/z: 147.1383 (M+·+H), calcd for $C_8H_{19}O_2$: m/z: 147.1385.

4.1.6. 2*S,4*S**,5*R**-5-*tert*-Butyl-4-methyl-2-phenoxy-2-oxo-1,3,2-dioxaphosphorinane (3a) and 2*R**,3*S**,5*R**-5-*tert*-butyl-4-methyl-2-phenoxy-2-oxo-1,3,2-dioxaphosphorinane (3b).** $PhOPOCl_2$ (0.04 mL, 0.28 mmol) was added dropwise to solution of **9** (40 mg, 0.276 mmol) and triethylamine (0.08 mL, 0.56 mmol) in CH_2Cl_2 (8 mL). The mixture stirred for 6 h before the reaction was quenched with water and the aqueous phase extracted with ethyl acetate and the combined organic layers dried ($MgSO_4$) and evaporated in vacuo. Chromatography over column chromatography (eluent: hexane/ethyl acetate: 5/1) gave **3a** (15 mg, 38%) and **3b** (16 mg, 39%). **3a**, a white solid, mp 90 °C; ^{13}C NMR ($CDCl_3$) δ 17.2, 28.1, 31.5, 48.1, 66.1, 80.2, 119.5, 124.7, 129.7, 152.8. Anal. Calcd for $C_{14}H_{21}O_4P$: C, 59.15; H, 7.45. Found: H, 59.02; C, 7.41. Compound **2**, a white solid mp 82 °C; ^{13}C NMR ($CDCl_3$) δ: 18.9, 28.9, 31.6, 47.3, 67.9, 80.4, 120.2, 125.2, 129.8, 152.2. EIHRMS: m/z: 284.1188 (M+·), calcd for $C_{14}H_{21}O_4P$: m/z: 284.1178.

4.1.7. 2*S,4*R**,5*R**-5-*tert*-Butyl-4-methyl-2-phenoxy-2-oxo-1,3,2-dioxaphosphorinane (4a) and 2*R**,3*R**,5*R**-5-*tert*-butyl-4-methyl-2-phenoxy-2-oxo-1,3,2-dioxaphosphorinane (4b).** Were obtained analogously to **3a** and **3b**, in 40% for **4a** and 41% for **4b**.

Compound **4a**, a white solid, mp 70 °C; ^{13}C NMR ($CDCl_3$) δ: 23.0, 28.5, 32.6, 49.8, 66.4, 78.1, 119.2, 124.0, 129.7, 150.2; EIHRMS: m/z: 284.1181 (M+·), calcd for $C_{14}H_{21}O_4P$: m/z: 284.1175.

Compound **4b**. ^{13}C NMR ($CDCl_3$) δ: 25.1, 28.1, 32.0, 51.2, 68.4, 78.8, 120.1, 125.2, 129.8, 153.0; EIHRMS: m/z: 284.1179 (M+·), calcd for $C_{14}H_{21}O_4P$: m/z: 284.1178.

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