Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron
ELSEVIER
Tetrahedron 60 (2004) 10927–10941

Conformational analysis of six-membered ring dioxaphosphinanes. Part 1: Anancomeric thiophosphates

Javier Hernández,[†] Rafael Ramos,[‡] Noé Sastre, Rocío Meza,[§] Herbert Hommer,[¶] Magali Salas and Barbara Gordillo*

Departamento de Química, Centro de Investigación y de Estudios Avanzados del Instituto Politécnico Nacional, Apartado Postal 14-740, Mexico, D F., Mexico

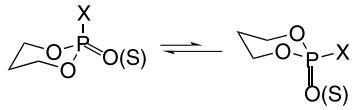
Received 27 March 2004; revised 2 September 2004; accepted 9 September 2004

Available online 1 October 2004

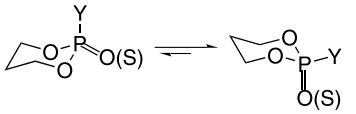
Abstract—A study of the conformation of a series of anancomeric axial and equatorial 2-aryloxy-2-thio-1,3,2λ^5-dioxaphosphinanes **2**–**12** in solution and solid state is reported. In accord to the stereoelectronic theory, aryl thiophosphates substituted with electron-withdrawing (EW) groups will tend to occupy axial positions in chair ring conformations due to the stabilizing *endo*-anomeric (n_πO–σ^*_{P-X}) hyperconjugative interaction. The antiperiplanar orientation of the orbitals involved in the stereoelectronic interaction is a requirement that is fulfiled in the axial series of compounds when the ring adopts a chair conformation. Therefore, in the equatorial series of thiophosphates, the axial seeking characteristics of aryloxy-EW groups might render the molecule with distortion of the chair conformation. An opposite trend is anticipated for the less axial seeking aryl thiophosphates substituted with electron releasing (ER) groups. A detailed analysis of the $^3J_{HH}$, $^3J_{PH}$ and $^3J_{CP}$ coupling constants allowed us to conclude that there is no contribution of high energy twist-boat conformations in the equatorial thiophosphates substituted with aryl-EW groups in solution. In consequence, single chair conformations were found in solid state for aryl thiophosphates in both configurations. X-ray geometrical analysis of bond distances and bond angles supports clearly the participation of hyperconjugative *endo*-anomeric (n_πO–σ^*_{P-OAr}) effect in the stabilization of axial series of compounds and the participation of *endo*-anomeric (n_πO–$\sigma^*_{P=S}$) effect in the stabilization of the equatorial thiophosphates in chair conformations.

1. Introduction

Six-membered ring thiophosphates are interesting systems from the conformational point of view since there are several electronic effects, as the *endo*- and *exo*-anomeric effects, that can play an important role in the conformational preferences of the substituents on phosphorus.[1–3] Steric effects in thiophosphates are not very important as in the monosubstituted cyclohexanes[4] or as in the closest heterocyclic system, the 2-substituted-1,3-dioxanes.[5] The decreased 1,3-*syn* axial steric hindrance of the substituent with the 4,6-hydrogens of the 1,3,2-dioxaphosphinane ring is due to the longer P–O (1.58 Å) *endo*-cyclic bond distances as compared to C–O in 1,3-dioxanes (1.42 Å) or C–C in cyclohexane (1.54 Å),[6] as well as the propensity of the *endo*-cyclic oxygens to adopt sp^2 hybridization instead of sp^3 that renders the ring with more flexibility than the corresponding 1,3-dioxane or cyclohexane.[7] As observed in the pentacoordinative chemistry of phosphorus compounds,[8] electronegative substituents in phosphates and thiophosphates will tend to adopt axial orientations, and electron-donating substituents, equatorial ones (Scheme 1).[9]



X = electronegative atom or group



Y = electron releasing atom or group

Scheme 1.

Keywords: Dioxaphosphinanes; Thiophosphates; Conformation; NMR; LFER correlations; X-ray crystal structures.

* Corresponding author. Tel.: +525 5061 3729; fax: +525 5747 7113; e-mail: ggordill@cinvestav.mx

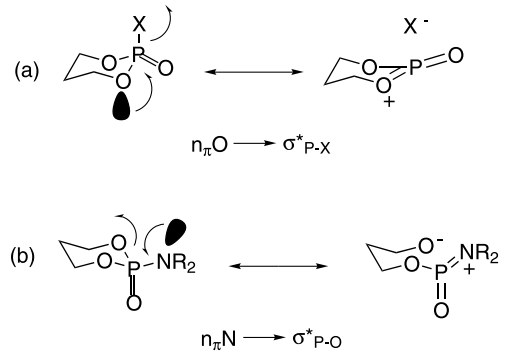
† Present address: Centro de Investigación en Alimentación y Desarrollo A. C. Hermosillo Sonora, Mexico.

‡ Present address: Unidad de Servicios de Apoyo en Resolución Analítica Universidad Veracruzana, Xalapa Veracruz, Mexico.

§ Present address: Departamento Ciencias Básicas Ingeniería y Tecnología Universidad Autónoma de Tlaxcala, Tlaxcala, Mexico.

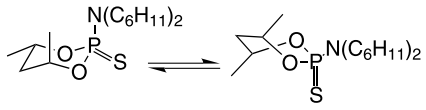
¶ Present address: Degussa Construction Polymers GmbH, D-83308 Trostberg, Germany.

0040–4020/$ - see front matter © 2004 Published by Elsevier Ltd.
doi:10.1016/j.tet.2004.09.025



Scheme 2.

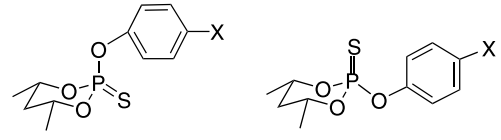
These preferences rely on stereoelectronic grounds, the *endo*-anomeric ($n_\pi O–\sigma^*_{P–X}$) effect favoring the axial conformer when the X-substituent is electronegative (such as halogen, OR, etc.), because the acceptor σ^* antibonding orbital of an electronegative substituent is lower-lying than the antibonding orbital of an electron-releasing substituent, therefore giving rise to a more stabilizing 2 electrons/2 orbitals interaction (Scheme 2a).[3,10] On the contrary, the *exo*-anomeric ($n_\pi Y–\sigma^*_{P–O\ endo\text{-cyclic}}$) hyperconjugative interaction will promote that an electron releasing substituent, such as an amine, tend to occupy the equatorial position in a dioxaphosphinane ring (Scheme 2b).[7] The equatorial isomer might also be favored by the $n_\pi O–\sigma^*_{P=S}$ *endo*-hyperconjugative intraction.[11]



Scheme 3.

From experimental point of view, van Nuffel et al.[12] have proved the participation of stereoelectronic interactions in the axial conformational preference of several phosphates and their thio derivatives, through the shortening of the *endo*-cyclic P–O bond and the lengthening of the P–X bond that is based on the resonance hybrids shown in Scheme 2. It is worth of mention that since the interconversion barrier of chair-to-twist or chair-to-boat conformations in 1,3,2-dioxaphosphinanes is very low (0.5–3.5 kcal/mol),[1] the stabilizing *endo*- or *exo*-anomeric interactions and/or the steric hindrance when the substituents are bulky, can force the molecule to adopt a twist-boat conformation in preference to the chair (Scheme 3).[7]

Reported in this work is the conformational analysis in solution and solid state of a series of axial and equatorial anancomeric aryl thiophosphates substituted with electron-withdrawing (EW) and electron-releasing (ER) groups (**2**–**12**), (Scheme 4). Spectroscopic data, as ^1H, ^{13}C and ^{31}P NMR are correlated with Hammett constants (σ_p),[13] within the context of LFER theory.[14] We analyzed thoroughly the X-ray geometrical parameters of two axial and two equatorial compounds substituted with EW or ER groups to account for the participation of the *endo*-anomeric ($n_\pi O–\sigma^*_{P–OAr}$) and ($n_\pi O–\sigma^*_{P=S}$) stabilizing interactions.



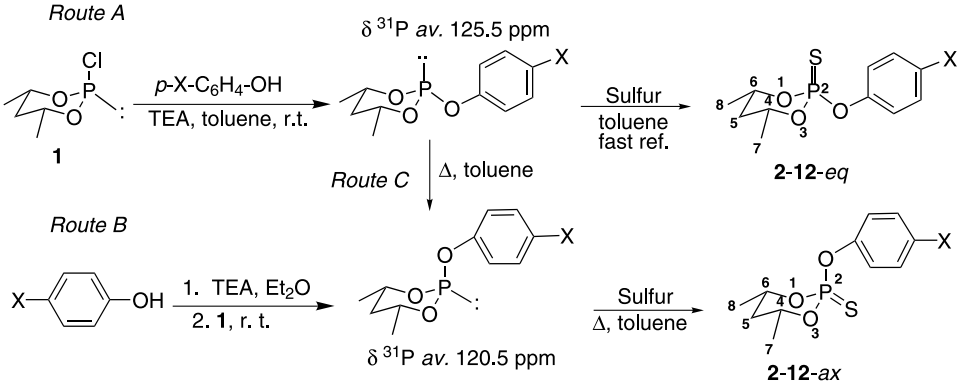
axial (ax) *equatorial (eq)*

2, X= NO_2
3, X= CN
4, X= CHO
5, X= Br
6, X= Cl
7, X= $NHCOCH_3$
8, X= H
9, X= C_6H_5
10, X= CH_3
11, X= OCH_3
12, X= NH_2

Scheme 4.

2. Results

The synthesis of both series of aryl thiophosphates **2**–**12**-*ax* and **2**–**12**-*eq* was accomplished through the stereoselective formation of the phosphite intermediates from the phosphochloridite and aryl alcohols as shown in Scheme 5. Due to the epimerization of the equatorial phosphite intermediate in the presence of an excess of phenol,[15] in route A, the *p*-X-substituted phenol was slowly added to the phosphorochloridite (**1**). On the contrary, in route B the thermodynamically more stable axial phosphite was obtained by addition of **1** to the corresponding *p*-X-substituted phenol.



Scheme 5.

Table 1. Selected ^{1}H and ^{31}P NMR chemical shifts (in ppm) for axial aryl thiophosphates **2–12** in $CDCl_3$

Chemical shifts (δ)	^{1}H				^{31}P
Compound	$H_{4,6a}$	H_{5a}	H_{5e}	$H_{7,8}$	
2-*ax* (X=NO_2)	4.76	1.86	1.90	1.42	54.3
3-*ax* (X=CN)	4.73	1.85	1.87	1.43	54.5
4-*ax* (X=CHO)	4.75	1.83	1.85	1.42	55.1
5-*ax* (X=Br)	4.75	1.82	1.87	1.42	55.5
6-*ax* (X=Cl)	4.75	1.83	1.90	1.45	55.6
7-*ax* (X=$NHCOCH_3$)	4.77	1.86	1.88	1.44	55.9
8-*ax* (X=H)	4.79	1.82	1.88	1.43	55.8
9-*ax* (X=C_6H_5)	4.81	1.83	1.88	1.44	55.8
10-*ax* (X=CH_3)	4.77	1.82	1.84	1.41	56.2
11-*ax* (X=OCH_3)	4.77	1.81	1.86	1.42	56.7
12-*ax* (X=NH_2)	[a]	[a]	[a]	[a]	56.8

[a] Undetermined (mixed with the equatorial epimer).

Table 2. Selected ^{1}H and ^{31}P NMR chemical shifts (in ppm) for equatorial aryl thiophosphates **2–12** in $CDCl_3$

Chemical shifts (δ)	^{1}H				^{31}P
Compound	$H_{4,6a}$	H_{5a}	H_{5e}	$H_{7,8}$	
2-*eq* (X=NO_2)	4.85	1.77	1.90	1.41	59.2
3-*eq* (X=CN)	4.84	1.79	1.87	1.41	59.3
4-*eq* (X=CHO)	4.79	1.54	1.69	1.34	59.5
5-*eq* (X=Br)	4.76	1.64	1.77	1.32	60.0
6-*eq* (X=Cl)	4.83	1.71	1.87	1.39	60.1
7-*eq* (X=$NHCOCH_3$)	4.80	1.75	1.85	1.38	60.4
8-*eq* (X=H)	4.83	1.70	1.89	1.39	60.4
9-*eq* (X=C_6H_5)	4.78	1.67	1.77	1.34	60.4
10-*eq* (X=CH_3)	4.80	1.59	1.72	1.34	60.9
11-*eq* (X=OCH_3)	4.73	1.63	1.75	1.31	61.0
12-*eq* (X=NH_2)	4.52	1.68	1.82	1.38	61.3

Table 3. ^{1}H NMR backbone coupling constants (in Hz) for axial aryl thiophosphates **2–12**. First-order analysis in $CDCl_3$ at 27 °C

Compound/coupling constant	$^{3}J_{H4,6aH5a}$	$^{3}J_{H4,6aH5e}$	$^{3}J_{H4,6aH7,8}$	$^{2}J_{H5aH5e}$	$^{3}J_{H4,6aP}$	$^{4}J_{H5aP}$	$^{4}J_{H5eP}$	$^{4}J_{H7,8P}$
2-*ax* (X=NO_2)	11.3	3.0	6.2	14.6	2.6	1.0	2.6	2.3
3-*ax* (X=CN)	10.5	2.5	6.4	14.8	1.2	1.5	1.3	2.5
4-*ax* (X=CHO)	8.0	2.7	6.2	13.0	1.2	[a]	1.5	2.2
5-*ax* (X=Br)	10.8	2.8	6.2	14.8	1.2	1.0	2.7	2.2
6-*ax* (X=Cl)	11.1	3.0	6.6	14.1	1.1	1.1	1.3	2.1
7-*ax* (X=$NHCOCH_3$)	12.9	2.9	6.2	13.0	1.3	1.0	1.8	2.3
8-*ax* (X=H)	10.8	2.8	6.6	14.4	1.3	1.1	2.6	2.6
9-*ax* (X=C_6H_5)	9.9	2.9	6.2	13.8	1.2	1.0	2.9	2.2
10-*ax* (X=CH_3)	10.7	3.0	6.2	14.5	1.2	1.1	2.7	2.2
11-*ax* (X=OCH_3)	10.8	3.3	6.2	14.5	1.2	1.0	3.0	2.2
12-*ax* (X=NH_2)	[b]	[b]	[b]	[b]	[b]	[b]	[b]	[b]

[a] The signal was not observed.
[b] Undetermined (mixed with its equatorial epimer).

The thermal equilibration of equatorial phosphites to the axial epimers was achieved by heating them in toluene (route C). The equatorial phosphite intermediates substituted with EW groups tend to epimerize to the axial ones in shorter heating times than those substituted with ER groups. The equatorial or axial phosphites were reacted stereospecifically with sulfur to produce the thiophosphates **2–12**-*eq* or **2–12**-*ax* under the conditions shown in Scheme 5. We observed that equatorial aryl thiophosphates were obtained in a cleaner manner, without their configurational isomers, if the reaction was maintained under vigorously toluene reflux, particularly in the case of aryl-EW thiophosphates.

The conformational analysis of the axial and equatorial series of thiophosphates (**2–12**) was assessed by analysis of their spectral NMR characteristics. The chemical shifts (δ) of ^{1}H are reported in Tables 1 and 2. The correct assignment of the signals and the backbone coupling constants in the ^{1}H NMR (Tables 3 and 4) were obtained through the first-order analysis of the spectra, along with homo and heteronuclear decoupling experiments. The complete assignment of ^{13}C signals (Tables 5 and 6), was achieved by means of ^{1}H, ^{13}C correlated 2D NMR spectra, as well as inverse ^{1}H-detected HMQC and HMBC experiments. Two-dimensional techniques were particularly useful for the assignment of ^{13}C NMR signals of the configurational *p*-phenyl thiophosphates (**9**-*ax* and **9**-*eq*). The participation of the stereoelectronic interactions was analyzed in the solid state through

Table 4. ^{1}H NMR backbone coupling constants (in Hz) for equatorial aryl thiophosphates **2–12**. First-order analysis in $CDCl_3$ at 27 °C

Compound/coupling constant	$^{3}J_{H4,6aH5a}$	$^{3}J_{H4,6aH5e}$	$^{3}J_{H4,6aH7,8}$	$^{2}J_{H5aH5e}$	$^{3}J_{H4,6aP}$	$^{4}J_{H5aP}$	$^{4}J_{H5eP}$	$^{4}J_{H7,8P}$
2-*eq* (X=NO_2)	10.5	2.6	6.3	14.6	1.2	1.0	2.8	2.2
3-*eq* (X=CN)	11.2	2.7	6.6	14.5	3.3	[a]	3.6	2.0
4-*eq* (X=CHO)	10.4	2.7	6.3	14.5	2.8	1.8	2.3	2.3
5-*eq* (X=Br)	10.6	2.8	5.9	14.5	2.6	[a]	2.3	2.0
6-*eq* (X=Cl)	11.2	3.0	6.6	14.0	2.5	[a]	2.3	2.0
7-*eq* (X=$NHCOCH_3$)	10.8	2.3	6.2	14.1	2.6	[a]	2.3	2.4
8-*eq* (X=H)	10.9	2.6	6.3	14.5	2.3	[a]	2.3	2.3
9-*eq* (X=C_6H_5)	9.9	2.9	6.2	14.2	3.0	[a]	2.3	2.0
10-*eq* (X=CH_3)	11.2	2.6	6.6	14.5	2.6	2.3	2.6	2.6
11-*eq* (X=OCH_3)	10.9	2.6	6.3	14.5	2.6	[a]	2.6	2.0
12-*eq* (X=NH_2)	11.2	2.6	6.6	14.5	3.3	[a]	2.6	2.0

[a] The signal was not observed.

Table 5. Selected ^{13}C NMR signal assignments in axial aryl thiophosphates **2–12**[a]

Compound	$C_{4,6}$	C_5	$C_{7,8}$	C_i	C_o
2-*ax* (X=NO_2)	77.7 (9.1)	40.6 (4.9)	22.4 (9.6)	156.2 (6.1)	121.3 (5.4)
3-*ax* (X=CN)	77.1 (9.3)	40.3 (5.2)	22.3 (9.9)	154.3 (6.2)	121.3 (5.2)
4-*ax* (X=CHO)	76.7 (8.9)	40.2 (5.6)	22.1 (10.0)	155.4 (5.5)	120.7 (5.5)
5-*ax* (X=Br)	77.2 (8.9)	40.8 (4.8)	22.4 (9.6)	150.6 (6.4)	122.6 (4.9)
6-*ax* (X=Cl)	76.7 (10.4)	40.6 (4.9)	22.6 (9.5)	149.5 (6.3)	121.7 (5.2)
7-*ax* (X=$NHCOCH_3$)	76.8 (9.5)	42.7 (5.0)	22.5 (9.8)	147.5 (6.2)	121.9 (5.0)
8-*ax* (X=H)	76.2 (8.8)	39.9 (4.4)	21.9 (9.9)	150.5 (7.0)	119.8 (5.5)
9-*ax* (X=C_6H_5)	77.1 (8.9)	40.7 (4.7)	22.5 (9.6)	150.8 (6.5)	121.0 (5.0)
10-*ax* (X=CH_3)	76.9 (8.9)	40.7 (4.6)	22.4 (9.9)	148.8 (6.2)	120.4 (4.8)
11-*ax* (X=OCH_3)	76.9 (8.9)	40.7 (4.8)	22.4 (9.5)	144.9 (7.2)	121.7 (4.8)
12-*ax* (X=NH_2)	76.2 (9.3)	40.5 (4.7)	22.3 (9.8)	143.8 (7.8)	121.1 (5.2)

[a] Chemical shifts (δ) in ppm from TMS in $CDCl_3$. In parentheses J_{CP} in Hz.

Table 6. Selected ^{13}C NMR signal assignments in equatorial aryl thiophosphates **2–12**[a]

Compound	$C_{4,6}$	C_5	$C_{7,8}$	C_i	C_o
2-*eq* (X=NO_2)	76.1 (5.5)	40.8 (5.5)	22.1 (8.9)	155.0 (7.7)	122.1 (4.4)
3-*eq* (X=CN)	76.0 (5.5)	40.9 (6.6)	22.1 (8.9)	152.6 (6.6)	122.4 (4.4)
4-*eq* (X=CHO)	75.9 (5.4)	40.8 (5.8)	22.1 (10.0)	155.0 (6.0)	122.0 (4.4)
5-*eq* (X=Br)	75.6 (5.5)	40.9 (5.5)	22.0 (10.0)	149.5 (8.9)	123.1 (4.5)
6-*eq* (X=Cl)	76.1 (5.7)	41.3 (5.1)	22.5 (9.5)	149.4 (8.0)	123.1 (5.0)
7-*eq* (X=$NHCOCH_3$)	75.8 (5.5)	41.1 (5.5)	22.4 (9.5)	149.6 (8.1)	121.7 (4.6)
8-*eq* (X=H)	75.4 (5.5)	41.0 (4.4)	22.1 (10.0)	150.3 (7.7)	121.1 (4.4)
9-*eq* (X=C_6H_5)	75.5 (5.5)	41.0 (5.5)	22.1 (10.0)	149.9 (7.7)	121.5 (5.5)
10-*eq* (X=CH_3)	75.3 (5.5)	41.0 (5.5)	22.1 (10.0)	148.3 (7.7)	121.0 (5.5)
11-*eq* (X=OCH_3)	75.6 (5.5)	40.9 (5.6)	22.0 (10.0)	144.0 (7.7)	122.0 (4.4)
12-*eq* (X=NH_2)	75.8 (5.5)	40.8 (5.5)	21.9 (9.9)	142.6 (8.8)	121.8 (4.4)

[a] Chemical shifts (δ) in ppm from TMS in $CDCl_3$. In parentheses J_{CP} in Hz.

the X-ray diffraction analysis of four thiophosphates, two of the axial series [**2**-*ax* (X=NO_2), and **10**-*ax* (X=CH_3)] and two of the equatorial [**2**-*eq* (X=NO_2) and **11**-*eq* (X=OCH_3)]. These molecules are examples of aryl thiophosphates with EW or ER groups in both configurations.

3. Discussion

3.1. NMR analysis

As observed in Tables 1 and 2, in the axial series of thiophosphates (**2–12**), the proton H_{5a} is slightly upfield shifted (ca. 0.05 ppm) than the H_{5e}, this trend is also observed for the equatorial epimers (**2–12**). The chemical shift of protons $H_{4,6a}$ for the axial thiophosphates is at around 4.75 ppm meanwhile the same protons in the equatorial series appear at around 4.85 ppm. ^{13}C NMR chemical shifts of carbons in the heterocycle are scarcely sensitive to configuration, however a slight downfield shift (1.3 ppm in average) is observed for $C_{4,6}$ for the axial compounds, thus not giving evidence of a γ-*gauche* effect (see discussion below). The coupling constants $^{2}J_{CP}$ of $C_{4,6}$ for the axial thiophosphates are 3–5 Hz larger than the equatorial ones (Tables 5 and 6). The conformational analysis of the complete series of thiophosphates was performed with the coupling constants $^{3}J_{HH}$, $^{3}J_{HP}$ and $^{3}J_{CP}$ (Tables 3–6). Heteronuclear $^{1}H\{^{31}P\}$decoupling experiments led to simplification of the signals, therefore vicinal $^{3}J_{HP}$ were easily obtained by direct comparison with the ^{1}H NMR signals of the undecoupled spectra. For compounds (**2–11**)-*ax* the irradiation at 1.41–1.45 ppm (CH_3's at C_4, C_6) led to decoupling of the methine ($H_{4,6a}$) multiplet to an apparent doublet of double doublet (ddd) with

$^3J_{HH}$=9.9–11.3 Hz (*anti*), $^3J_{HH}$=2.5–3.3 Hz (*gauche*) and $^3J_{HP}$=1.2–2.6 Hz, these coupling constants are consistent with a chair conformation.[2,16] A similar experiment was performed for the compounds (**2**–**12**)-*eq*, irradiation at 1.31–1.41 ppm led to a double of triplets (dt) for the methine (H_{4a}) with $^3J_{HH}$=9.9–11.2 Hz (*anti*), $^3J_{HH}$=2.6–3.0 Hz (*gauche*) and $^3J_{HP}$=2.3–3.6 Hz, here also values of coupling constants suggest that in solution the series of equatorial thiophosphates are in chair conformation. On the other hand, the $^3J_{C5P}$ and $^3J_{C7,8P}$ coupling constants obtained from the ^{13}C NMR spectra of compounds (**2**–**12**) are in the range of 4.4–5.7 and 8.9–10.0 Hz, respectively, for both, axial and equatorial, series of thiophosphates (Tables 5 and 6) suggesting also a chair conformation for the six-membered ring in solution.[2,17] The fact that the $^3J_{CP}$ is not showing dependence on configuration, support the argument given by Quin[18] and Nifantiev[19] on the uses of $^3J_{CP}$ as the most useful C–P coupling constant to analyze the conformation of dioxaphosphinanes (note that in an ideal chair conformation the dioxaphosphinane dihedral angles $\omega_{C5-C4-O3-P}$ and $\omega_{C5-C6-O1-P}$ are 60° meanwhile $\omega_{C8-C6-O1-P}$ and $\omega_{C7-C4-O3-P}$ are 180°).

3.2. Electronic effects

In phosphorus compounds with aromatic rings, it has been demonstrated that EW or ER groups in the *para* position of the ring, causes polarization of charge density inducing changes in chemical shifts and coupling constants on the phosphorus and linked atoms.[20] Depending upon the aromatic organophosphorus compound, the so-called substituent-induced chemical shifts (SCS) exhibits in ^{31}P NMR one of the two possible tendencies, one that correlates ^{31}P chemical shifts directly with Hammett (σ_p) constants and the other that correlates them reversibly.[21] The factors that determine the tendency are the electronegativity of the α-atoms directly linked to phosphorus and the phosphorus hybridization,[22] and it has been observed frequently that these two factors cannot be separated for to understand the behavior.[23] Thus as expected, an EW group in aryl phosphazanes[24] provoke dishielding of the phosphorus nucleus resulting in a downfield shift of ^{31}P NMR signal. Nevertheless, the opposite behavior is observed for cinnamyl phosphonates[25] and aryl phosphates.[9a] The fundamental difference between these three types of organophosphorus compounds is that in phosphonates or phosphates the aromatic ring is in a group linked to phosphorus through a single bond; however, in aryl phosphazenes the aromatic ring is in a group linked to phosphorus through a double bond. From this observation it is evident that the transfer of charge density from the aromatic ring to phosphorus or vice versa follows a different mechanism when the transmission is through a σ or through a π bond.[26] In this work we found that the ^{31}P NMR signals of arylthiophosphates are reversibly correlated with σ_p being the correlation factor R=0.979 for the axial series of thiophosphates and R=0.982 for the equatorial. From the slope of the lines m=−1.871 for the axial series and m=−1.631 for the equatorial it can be deduced that the phosphorus of the axial isomers is more sensitive to charge polarization of the aromatic ring than the phosphorus of the equatorial ones. The reversible correlation may be explained by a change in bond distances and bond angles involving α-bonded atoms to phosphorus and the changes in torsion angles with β-atoms as proposed by Gorenstein for phosphates.[27] We will discuss this point in the structural analysis below. On the other hand, neither the ^{1}H nor the ^{13}C chemical shifts of the dioxaphosphinane ring correlate well with the Hammett (σ_p) constants. However, a good normal correlation of ^{13}C chemical shifts of the C_{ipso} with σ_p was found (R=0.926 for the axial and R=0.911 for the equatorial), C_{ipso} of NO_2 substituted arylthiophosphate being downfield shifted from C_{ipso} of OCH_3 aryl thiophosphate, as shown in Tables 5 and 6.

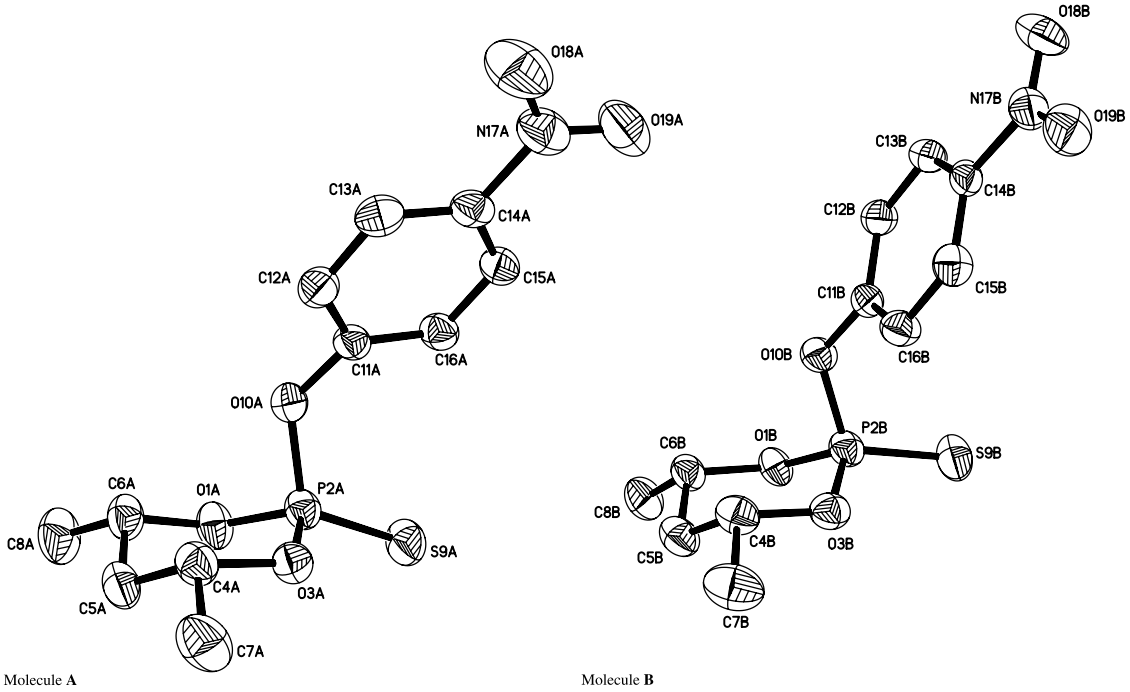


Figure 1. ORTEP drawing of *ax*-2-*p*-nitrophenoxy-2-thio-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphinane (**2**-*ax*), molecule **A** and **B**.

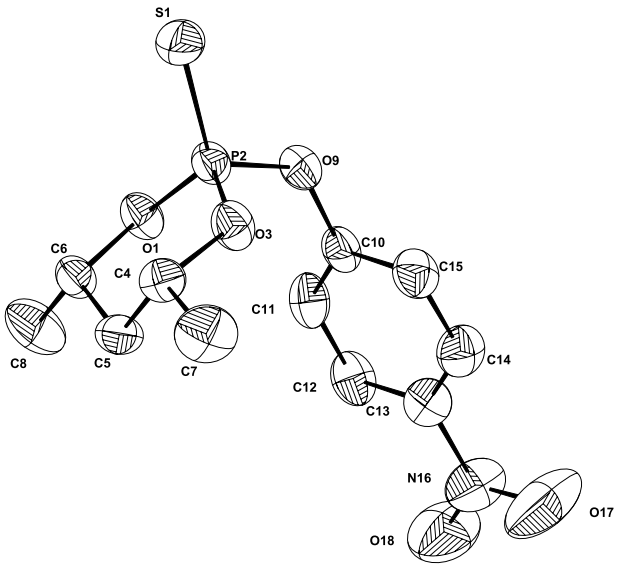


Figure 2. ORTEP drawing of *eq*-2-*p*-nitrophenoxy-2-thio-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphinane (**2**-*eq*).

Based on the grounds of the stereoelectronic theory, EW groups will show more propensity to occupy axial orientations than ER groups (Scheme 2), therefore a detailed comparison of the structural parameters of the two axial **2**-*ax* (X=NO_2), and **10**-*ax* (X=CH_3) and the two equatorial **2**-*eq* (X=NO_2) and **11**-*eq* (X=OCH_3) thiophosphates not only led us to account for the participation of stereoelectronic interactions in the conformation adopted for the molecules but also for the reversible correlation found in the chemical shift of the signals of ^{31}P NMR with σ_p. We also analyzed the steric compression of the aryloxy group in the axial thiophosphates and the flexibility of the 1,3,2-dioxaphosphinane ring for to relieve the intramolecular van der Waals repulsive compression of the nonbonded substituents through compromise between the intraannular torsional strain and the Baeyer strain, as proposed for highly hindered thiophosphoramidates.[7]

3.3. Structural analysis

The ORTEP drawings obtained from the X-ray analysis of **2**-*ax*, **2**-*eq*, **10**-*ax* and **11**-*eq* are shown in Figures 1–4. Data collection and refinement parameters, bond distances, bond angles, and torsion angles are provided in Tables 7–10.

Thiophosphates **2**-*ax*, **2**-*eq* and **11**-*eq* crystallized in the monoclinic space group $P2_1/n$, $P2_1/c$ and $P2_1/a$ correspondingly, whereas **10**-*ax* crystallized in the orthorhombic *P* space group $P2_1$ *n b*. In the case of compound **2**-*ax*, two molecules were found in the asymmetric unit. Molecules A and B are not in equivalent positions, and it is interesting to note that the change of torsion angle P2–O10–C11–C12 by 74° brings with it a change in bond angle C4–O3–P2 (from 120° in molecule A to 117° in molecule B) that speaks about the high flexibility of the dioxaphosphinane ring in the OPO region ascribed to the propensity of the *endo*-cyclic oxygens to change from sp^3 to sp^2 hybridization.[7]

3.4. Torsion and bond angles

The geometry at the phosphorus center is tetrahedral for all the compounds; the sum of the four angles at the phosphorus goes from 436.04 to 439.71° (see Table 11). However, it is notable that equatorial thiophosphates are closer than the axial to the expected ideal tetrahedral angle (436°). The dioxaphosphinane ring lacks of perpendicular symmetry, the oxygens are almost flat edges [the internal COP angles are of around 119° for **2**-*ax*, **2**-*eq* and **10**-*ax* and around 116° for **11**-*eq*] and the phosphorus is a puckery end [the OPO angles are of around 106° for **2**-*ax*, **2**-*eq* and **10**-*ax* and 104° for **11**-*eq*]. There is ring flattening in the OPO region for both the axial and equatorial thiophosphates [torsion angles:

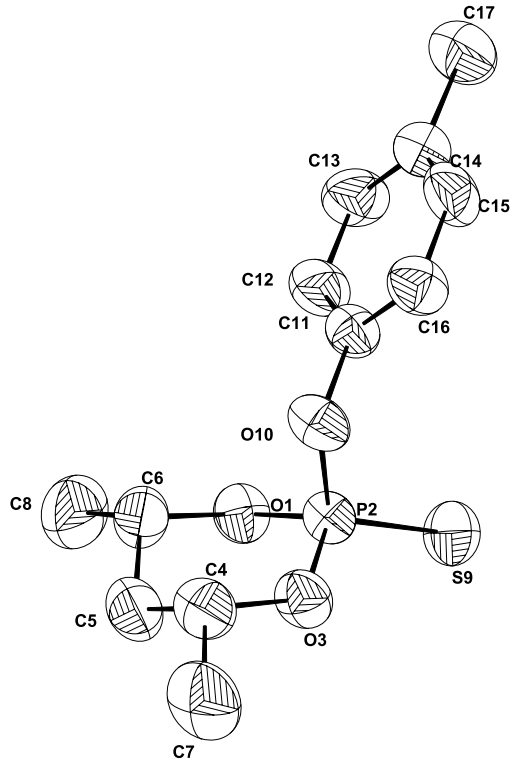


Figure 3. ORTEP drawing of *ax*-2-*p*-methylphenoxy-2-thio-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphinane (**10**-*ax*).

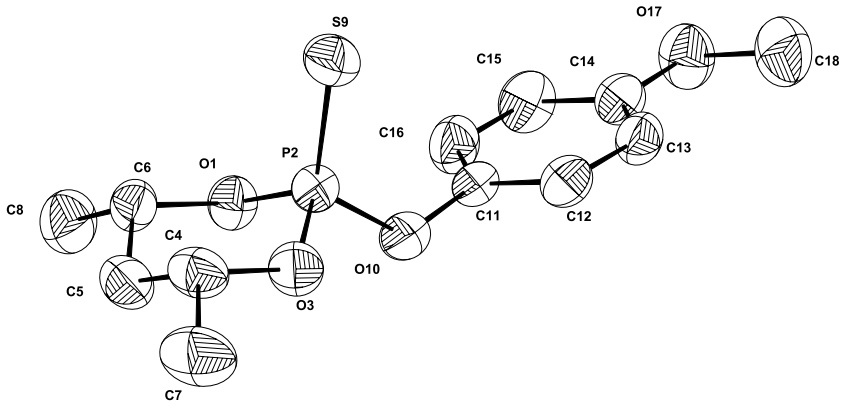


Figure 4. ORTEP drawing of *eq*-2-*p*-methoxyphenoxy-2-thio-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphinane (**11**-*eq*).

(ω_{POCC5}) are in the range of 44.6–55.8°; and the internal (ω_{OPOC}) are in the range of 33.1–52.7°] being the flattening less severe for **11**-*eq* than all others. The OPO ring flattening has also been found in analog phosphates.[9a]

The Baeyer and Pitzer strain[4,29] are summarized in Table 11 for compounds **2**-*ax*, **2**-*eq*, **10**-*ax* and **11**-*eq* [calculated as the average of the internal bond angles (θ), and torsion angles (ω) of the dioxaphosphinane ring, respectively]. Taking into consideration that the bond angle in a molecule free of Baeyer strain (propane) is 112.4°, the molecule with the highest Baeyer strain is **2**-*eq* (113.1°). Contrary to what is expected, the intraannular torsion angles also decrease for **2**-*eq* more than for any other compound (51.7–54.3° vs 47.5°) leading to considerable Pitzer strain. As a consequence, there is not a very good agreement between the values of $\cos\omega$ and $-\cos\theta/(1+\cos\theta)$ for this molecule (0.68 vs 0.65) as for the others, indicating that the compromise between bond angles and torsion angles imposed by the constraint of the dioxaphosphinane ring which leads to the minimum strain in **2**-*eq*, is not perfect. We have observed that for thiophosphoramidates in conformations other than chair, the compromise between $\cos\omega$ and $-\cos\theta/(1+\cos\theta)$ is not fulfilled either.[7] Our interpretation of this result is that due to the axial seeking characteristics of the *p*-NO_2-phenoxy substituent, the molecule will tend to deform out of an ideal chair that otherwise in the case of **2**-*eq* obligates the aryloxy group to

Table 7. X-ray crystal data for compounds **2**, **10**-*ax* and **11**-*eq*[a]

	2-*ax*	**2**-*eq*	**10**-*ax*	**11**-*eq*
Formula	$C_{11}H_{14}NO_5PS$	$C_{11}H_{14}NO_5PS$	$C_{12}H_{17}O_3PS$	$C_{12}H_{17}O_4PS$
Fw	303.26	303.28	272.29	288.30
Crystal system	Monoclinic	Monoclinic	Orthorombic *P*	Monoclinic
Crystal size (mm)	0.12×0.18×0.24	0.54×0.45×0.39	0.50×0.50×0.30	0.33×0.30×0.18
Space group	$P2_1/n$	$P2_1/c$	$P2_1\ n\ b$	$P2_1/a$
Radiation	Mo Kα	Mo Kα	Mo Kα	Mo Kα
Wavelength (Å)	0.71073	0.71073	0.71073	0.71073
a (Å)	8.04550(10)	6.856(1)	9.7597(10)	7.9454(10)
b (Å)	26.9886(4)	22.911(1)	11.257(2)	20.1215(10)
c (Å)	13.06750(10)	9.128(1)	12.9736(10)	9.4777(10)
α (deg)	90.00	90.00	90.00	90.00
β (deg)	95.805(6)	91.3(11)	90.00	104.407(10)
γ (deg)	90.00	90.00	90.00	90.00
V (Å^3)	2822.88(6)	1433.3(10)	1425.4(4)	1467.6(7)
Z	8	4	4	4
$2\theta_{max}$ (deg)	4.36–49.94	11–12	4.80–53.94	11–12
ρ_{calc} (mg m^{-3})	1.427	1.41	1.269	1.30
Absorption coefficient (mm^{-1})	0.357	0.351	0.333	0.333
No. of reflections collected	5315	3475	1645	2101
No. of independent reflections	4947	3122	1645	1792
No. of observed reflections	2142	2348	1298	1285
R_1 [$F>4\sigma(F)$]	0.0380	0.037	0.0338	0.0327
wR_2	0.1002	0.047	0.0961	0.0395
R_1 (all data)	0.1587	0.057	0.0500	0.0549
wR_2	0.1377	0.048	0.1060	0.0423
GOF on F^2	0.963	1.028	1.034	1.111
Max. shift for final cycle of least-squares	0.000	0.0004	0.000	0.0002
Δ/σ	0.000	0.000	0.001	0.000
Max. peak in final difference syntheses (e/Å^3)	0.223	0.33	0.344	0.17

[a] Standard deviations are in parentheses.

Table 8. Selected bond lengths (Å) for **2**, **10**-*ax* and **11**-*eq*[a]

	2-*ax* molecule A	**2**-*ax* molecule B	**2**-*eq*	**10**-*ax*	**11**-*eq*
O1–P2	1.559(3)	1.560(2)	1.5732(12)	1.565(3)	1.572(2)
O3–P2	1.562(3)	1.574(3)	1.5691(13)	1.568(2)	1.567(2)
O10–P2	1.605(3)	1.604(3)	1.5889(14)	1.601(3)	1.578(2)
S9–P2	1.8952(15)	1.8946(16)	1.9093(7)	1.9009(13)	1.9091(10)
O1–C6	1.476(6)	1.478(4)	1.466(2)	1.500(5)	1.472(3)
O3–C4	1.481(4)	1.470(5)	1.469(2)	1.508(6)	1.470(4)
C4–C5	1.515(5)	1.515(5)	1.504(3)	1.493(7)	1.494(4)
C5–C6	1.509(6)	1.512(5)	1.497(3)	1.519(7)	1.504(4)
C6–C8	1.505(5)	1.505(5)	1.502(3)	1.487(7)	1.498(4)
C4–C7	1.506(6)	1.513(5)	1.498(3)	1.511(7)	1.509(5)
C11–O10	1.403(4)	1.395(4)	1.403(2)	1.407(4)	1.406(3)

[a] Standard deviations in parentheses.

Table 9. Selected bond angles (θ) in deg for **2**, **10**-*ax* and **11**-*eq*[a]

	2-*ax* molecule A	**2**-*ax* molecule B	**2**-*eq*	**10**-*ax*	**11**-*eq*
O1–P2–O3	106.49(14)	105.92(14)	105.72(7)	105.78(14)	104.06(11)
O1–P2–O10	98.72(15)	99.94(14)	103.39(7)	105.33(15)	102.53(11)
O1–C6–C5	107.5(3)	108.6(3)	109.71(14)	106.9(3)	109.0(2)
O3–C4–C5	109.7(3)	109.0(3)	108.20(14)	110.0(3)	109.2(2)
O3–P2–O10	105.24(14)	104.81(14)	102.39(7)	100.33(15)	98.50(11)
O1–P2–S9	114.64(12)	114.83(11)	116.24(6)	113.65(11)	115.76(8)
O3–P2–S9	112.68(12)	113.82(12)	116.23(6)	114.77(12)	116.90(9)
C4–O3–P2	120.2(2)	117.0(2)	120.33(11)	120.6(3)	116.48(18)
C6–O1–P2	118.2(2)	119.3(2)	122.57(11)	118.0(3)	116.49(16)
C6–C5–C4	112.7(3)	113.5(3)	112.27(14)	111.8(4)	114.7(2)
P2–O10–C11	126.5(2)	124.2(2)	121.4(1)	122.2(2)	124.34(17)
O10–C11–C12	116.9(3)	115.9(3)	120.10(16)	121.8(3)	118.3(3)
O10–C11–C16	121.3(4)	121.9(3)	117.67(16)	117.0(3)	120.2(3)
S9–P2–O10	117.58(11)	116.01(11)	111.24(5)	115.58(11)	116.61(9)

[a] Standard deviations in parentheses.

Table 10. Selected torsion angles (ω) in deg. for **2**, **10**-*ax* and **11**-*eq*[a,b]

	2-*ax* molecule A	**2**-*ax* molecule B	**2**-*eq*	**10**-*ax*	**11**-*eq*
S9–P2–O3–C4	−165.36	−174.17	93.03	−165.97	76.35
O10–P2–O3–C4	65.30	58.07	−145.52	69.46	−157.93
O1–P2–O3–C4	−38.85	−47.07	−37.58	−39.85	−52.66
O1–C6–C5–C4	61.66	56.05	57.24	61.99	54.84
S9–P2–O1–C6	169.23	172.06	−97.54	170.43	−77.19
O10–P2–O1–C6	−64.92	−63.10	140.29	−62.08	154.73
O3–P2–O1–C6	43.90	45.56	33.06	43.62	52.50
P2–O3–C4–C5	47.03	55.30	50.56	49.23	55.77
P2–O3–C4–C7	170.86	179.08	177.98	171.63	179.03
P2–O1–C6–C8	−179.80	−173.55	−169.53	179.79	−178.82
P2–O1–C6–C5	−56.48	−51.43	−44.60	−56.37	−55.20
C11–O10–P2–O1	−179.36	−176.28	−61.19	−82.74	98.19
C11–O10–P2–O3	70.80	74.18	48.53	167.59	−155.26
C11–O10–P2–S9	−55.59	−52.24	173.35	43.57	−29.35
C12–C11–O10–P2	−124.54	132.16	80.42	59.32	112.70
C16–C11–O10–P2	58.92	−50.53	−102.95	−123.37	−72.75
O3–C4–C5–C6	−57.14	−58.85	−61.68	−58.90	−55.09
O10–P2–O3–C4	65.30	58.07	−145.52	69.46	−157.93
O1–P2–O3–C4	−38.85	−47.07	−37.58	−39.85	−52.66
P2–O1–C6–C5	−56.48	−51.43	−44.60	−56.37	−55.20

[a] Standard deviations in parentheses.
[b] Right-hand rule.[28]

be in the equatorial position. This argument might be supported by the fact that the aryloxy group in **2**-*eq* has torsion angles [$\omega_{O10PO1C6}=140.3°$ and $\omega_{O10PO3C4}=145.5°$] that are almost 40° away from the 180° (expected for the group in equatorial orientation) and pointing towards a pseudo-axial position.

3.5. Stereoelectronic interactions

Several years ago, Gorenstein[30] coined the term '*gauche* NMR effect' to support the observation that in molecules with *gauche* segments all the atoms that conform the segment tend to be shielded, therefore upfield shifted. In

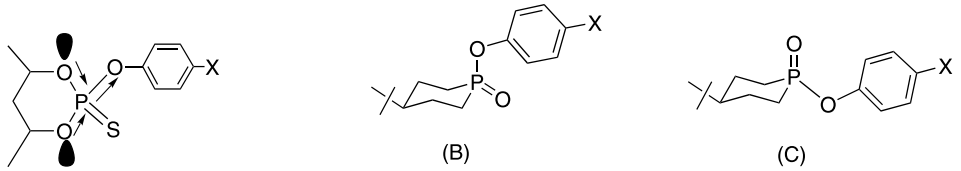
Table 11. Structural properties of **2**, **10**-*ax* and **11**-*eq*

	11-*eq*	**2**-*eq*	**10**-*ax*	**2**-*ax*	
				Molecule **A**	Molecule **B**
Geometry at phosphorus[a]	437.56	436.04	438.40	439.71	438.63
Baeyer strain[b]	111.66	113.13	112.18	112.47	112.22
Pitzer strain[c]	54.34	47.46	51.66	50.84	52.38
$\cos\omega$	0.58	0.68	0.62	0.63	0.61
$-\cos\theta/(1+\cos\theta)$	0.58	0.65	0.61	0.62	0.61

[a] Calculated as the sum of the bond angles (O1P2O3), [OP2O10(mean)], [OP2S9(mean)] and (S9P2O10) in deg.
[b] Calculated as the average value of the bond angles (O1P2O3), (O1C6C5), (O3C4C5), (C4O3P2), (C6C5C4), and (C6O1P2) in deg.
[c] Calculated as the average absolute value of the torsion angles (O1P2O3C4), (O1C6C5C4), (O3P2O1C6), (O3C4C5C6), (P2O3C4C5), and (P2O1C6C5) in deg.

cyclic six-membered ring dioxaphosphinanes the ^{31}P NMR signal of axial substituted compounds is normally upfield shifted from the equatorial,[2] thus demonstrating the participation of a *gauche* NMR effect. The ground, in which this *gauche* NMR effect relies is the decrease in the intraannular OPO bond of the dioxaphosphinanes, and it was nicely demonstrated by Gorenstein[27] that at least in phosphates there is a correlation between the OPO bond angle and the ^{31}P NMR chemical shift. We thought of the possibility to explain the observed reversibility of ^{31}P NMR shifts with σ_p or substituent-induced chemical shifts (SCS) with the changes in OPO bond angles, however unfortunately we found the opposite, that means that the compounds of the same series of thiophosphates, axial or equatorial, with smaller intraannular OPO bond are downfield shifted than those with larger OPO bond angles. For example, the OPO angle for **2**-*ax* is 106.2° and for **10**-*ax* is 105.78° and their ^{31}P NMR are shifted to 54.3 and 56.2 ppm, respectively; by the same taken, the OPO bond angle for **2**-*eq* is 105.72° and for **11**-*eq* is 104.06° and their ^{31}P NMR signals are shifted to 59.2 and 61.0 ppm, respectively. The other factor that can be disregarded from our data is that the shielding of the ^{31}P NMR signal is due to a dπ–pπ interaction involving the aryloxy group[31,32] because in such case, we would expect that an ER group as *p*-OCH_3 would enhance the orbital overlap causing an upfield shift of the signal and an EW group as *p*-NO_2 a downfield shift. Alternatively the reversibility found in SCS may be explained by an effect of a compensation of charge density to the ^{31}P nucleus given by the assistance of the free electron pairs of the *endo*-cyclic oxygens of the dioxaphosphinane ring, when an EW group is substituted in the *para* position of the phenyl ring of the aromatic thiophosphate, as shown in Scheme 6 (structure A). This hypothesis is supported by the fact that analog phosphinanes[33] where compensation of charge density on phosphorus by *endo*-cyclic α-atoms is not possible, show a normal SCS trend (Scheme 6, structures B and C).

It is worthwhile to note that the transfer of charge density by *endo*-cyclic oxygens to phosphorus give rise to the known attractive *endo*-anomeric $n_\pi O–\sigma^*_{P–OAr}$ hyperconjugative interaction for axial thiophosphates that stabilize the chair conformation with the aryl-EW group more than with the aryl-ER. On the other hand, the attractive *endo*-anomeric $n_\pi O–\sigma^*_{P=S}$ hyperconjugative interaction for equatorial thiophosphates stabilizes the P=S group in the axial position of a chair conformation more than P=O in analog equatorial phosphates.[34] Indeed, by doing an individual examination of the bond lengths (Table 8), we observed that the data indicate clearly that both *endo*-hyperconjugative interactions do participate in the stabilization of these anancomeric thiophosphates (see Scheme 2). In particular, for **2**-*ax* we found that *endo*-cyclic O1–P2 or O3–P2 bonds are shorter [1.560 Å (mean between molecule A and B) and 1.568 Å (mean between molecule A and B), respectively] than the *exo*-cyclic O10–P [1.605 Å (mean between molecule A and B)]. For **10**-*ax* we also found evidence of the $n_\pi O–\sigma^*_{P–OAr}$ *endo*-hyperconjugative interaction since the O1–P2 or O3–P2 bonds (1.565 and 1.568 Å, respectively) are shorter than O10–P2 (1.601 Å). The fact that the shortening of the *endo*-cyclic O–P bonds in **2**-*ax* (X=NO_2) is more pronounced than in **10**-*ax* (X=Me) [1.564 Å (mean) for **2**-*ax* vs 1.567 Å (mean) for **10**-*ax*] and the lengthening of the O10–P2 bond is also more important for **2**-*ax* than for **10**-*ax* [1.605 Å for **2**-*ax* vs 1.601 Å for **10**-*ax*] is in agreement with the increase in the axial seeking characteristics of aryloxy substituted with EW as compared with ER groups. On the other hand, for the equatorial thiophosphates **2**-*eq* (X=NO_2) and **11**-*eq* (X=OCH_3) the anomeric $n_\pi O–\sigma^*_{P=S}$ *endo*-hyperconjugative interaction is supported by the shortening of the *endo*-cyclic O1–P2 or



Scheme 6.

O3–P2 bonds [1.572 Å (mean) for **2**-*eq* and 1.570 Å (mean) for **11**-*eq*], although somewhat less than in the axial isomers, and slight lengthening of the P=S bonds (1.909 Å for **2**-*eq* or **11**-*eq* vs 1.895 and 1.901 Å for **2**-*ax* and **10**-*ax*, respectively). It is clear that this stereoelectronic mechanism of stabilization of the equatorial thiophosphates is less important than the axial one, because in the equilibria of mobile aryl thiophosphates the axial conformer always predominates over the equatorial.[1,2] This might be a result of the bonding electron repulsion caused by the lone pairs on sulfur when it is in the axial position.[11]

4. Conclusions

The conformational analysis of a series of axial and equatorial anancomeric *p*-X-aryloxy thiophosphates is analyzed in terms of the electronic characteristics of the *p*-substituent. The coupling constants $^{3}J_{HH}$, $^{3}J_{HP}$ and $^{3}J_{CP}$ and X-ray structures suggest that in solution and solid state, the 1,3,2-dioxaphosphinane ring is in a chair conformation regardless of configuration. We observed that there is a reverse substituent-induced chemical shifts on the ^{31}P NMR signals being the effect more pronounced for axial than for equatorial thiophosphates. These results could be explained by the compensation of charge density on phosphorus by the lone pairs on *endo*-cyclic oxygens of the dioxaphosphinane ring for thiophosphates substituted with aryl EW groups.

The structural analysis performed by X-ray on four thiophosphates, two axial and two equatorial, led to the conclusion that in all cases, the dioxaphosphinane ring is flatten in the OPO region and is lacking of perpendicular symmetry being the *endo*-cyclic oxygens flat regions of the ring and the phosphorus atom a puckery end. A thoroughful analysis of bond distances allowed to support the participation of the anomeric $n_{\pi}O–\sigma^{*}_{P–OAr}$ *endo*-hyperconjugative interaction for to stabilization of axial thiophosphates and the anomeric $n_{\pi}O–\sigma^{*}_{P=S}$ *endo*-hyperconjugative interaction for to stabilization equatorial thiophosphates, both in chair conformations.

5. Experimental

Melting points are uncorrected. Nuclear magnetic resonance spectra were recorded on Jeol Eclipse 270 and Bruker Avance 300 spectrometers in $CDCl_3$ (δ 7.26, ^{1}H; δ 77.0, ^{13}C), ^{1}H at 270.2 and 300.1 MHz, ^{13}C at 67.8 and 75.5 MHz, and ^{31}P at 109.3 and 121.5 MHz, respectively. Phosphorus NMR spectra are reported in ppm downfield (+) from 85% H_3PO_4 used as external standard. Mass spectra (EI) were measured on a Hewlett Packard 5989A spectrometer using electron impact (EI) at 70 eV. The reactions were performed under an atmosphere of nitrogen in oven-dried glassware. Solvents and solutions were transferred by syringe-septum and cannula techniques. Toluene was of reagent grade and was dried and distilled immediately before use from sodium/benzophenone. Triethylamine was dried and distilled from $LiAlH_4$. Products were purified by flash column chromatography on silica gel 230–400 mesh. Yields are given for isolated products. Galbraith Laboratories, Inc., Knoxville, TN performed microanalyses of configurational isomers **3**–**9**. Microanalyses of configurational isomers **2**, **10**, **11** and **12**-*eq* were recorded in Thermo Finnigan Flash 1112 analyzer.

n-Hexane was used for recrystallization of all samples, affording crystals suitable for X-ray diffraction analysis. Crystallographic work was performed in an Enraf-Nonius CAD-4 diffractometer. Data collection: CAD-4 Software.[35] Cell refinement: CAD-4 Software. Data reduction for the axial structures **2**-*ax* and **10**-*ax*: WINGX,[36] solved by direct methods SHELXS97[37] and refined with SHELXL97.[38] Data reduction for the equatorial structures **2**-*eq* and **11**-*eq*: CRYSTALS,[39] solved and refined with CRYSTALS.[39] Molecular graphics: CAMERON[40] and dihedral angles: PLATON.[41] Crystallographic data for structures have been deposited at Cambridge Crystallographic Data Center and the deposition numbers are: CCDC 234720 for **2**-*ax*, CCDC 234719 for **10**-*ax*, CCDC 235613 for **2**-*eq*, and CCDC 235614 for **11**-*eq*.

5.1. General procedure for the preparation of intermediates arylphosphites

Route A. In a three-necked 250 mL flask, fitted with a stirbar, and rubber septa, were placed 3.64 mmol of *p*-X-phenol, and 45 mL of dry toluene. The solution was stirred at room temperature until the *p*-X-phenol was solubilized (in the case of some *p*-X-phenols as *p*-acetamido, and *p*-amino, 10 mL of acetonitrile was added in order to solubilize them), then 3.64 mmol of the phosphorochloridite **1**, followed by 3.64 mmol of triethylamine were added at once, via syringe, resulting in precipitation of triethylammonium chloride. The suspension was stirred for 5 min and the solid was filtered off through a filter tipped cannula. The solid was washed two times with 15 mL of dry toluene collecting the filtrate in a round-bottomed flask. The solvent was then removed under vacuum without heating to avoid epimerization of the equatorial phosphites to the axial ones. In all cases, products were yellowish oils.

Route B. In a three-necked 250 mL flask, fitted with dropping funnel, a stirbar, and rubber septa, were placed 3.64 mmol of *p*-X-phenol, 3.64 mmol of triethylamine, and 45 mL of dry ethyl ether. The mixture was stirred at room temperature for 30 min and 3.64 mmol of the phosphorochloridite **1** was added dropwise via syringe maintaining the stirring for additional 30 min. The solid in the resulting suspension was filtered off through a filter tipped cannula and the filtrate added to a lateral outlet round-bottomed flask equipped with a stirbar, rubber septa and reflux condenser. The solution was heated under reflux for 2 h and after cooling, the solvent was removed in a rotary evaporator. In all cases, products were yellowish oils.

Route C. In a round-bottomed 250 mL flask, fitted with reflux condenser, a stirbar, and rubber septa, were placed 3.64 mmol of the equatorial phosphites (obtained from route A) and 45 mL of dry toluene. The solution was stirred under reflux for 12–48 h until the epimerization to the axial isomers was complete. The epimerization process was followed by ^{31}P NMR (equatorial phosphites are downfield shifted than axial phosphites by around 5 ppm, see

Scheme 5). Phosphites substituted with electron releasing groups (ERG) took longer for to epimerize than those substituted with electron-withdrawing groups (EWG). After cooling, the solvent was removed under vacuum in a rotary evaporator.

5.2. General procedure for the preparation of aryl thiophosphates 2–12

In a round-bottomed 100 mL flask, fitted with a reflux condenser, a stirbar, and rubber septa, were placed 2.21 mmol of elemental sulfur. A solution of 2.21 mmol of equatorial phosphite (obtained from route A) or axial phosphite (obtained from route B or C) in 60 mL of dry toluene was added to the flask and the resulting suspension was stirred under reflux for 24 h. After cooling, the suspension was concentrated under vacuum and the residue washed with an aqueous solution of 10% sodium bicarbonate. The product was extracted with methylene chloride and the organic layer dried over sodium sulfate. The solvent was removed in a rotary evaporator and the crude product was purified by flash chromatography using hexane/ethyl acetate as eluent.

5.2.1. *ax*-2-Chloro-*cis*-4,6-dimethyl-1,3,2-λ^3-dioxaphosphinane (1). This compound was obtained from a mixture of *meso*- and *rac*-pentanediols and phosphorus trichloride by the stereoselective approach reported by us.[42]

5.2.2. *ax*-2-*p*-Nitrophenoxy-2-thio-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphinane (2-*ax*). According to the general procedure described above, 1.0 g (3.69 mmol) of axial *p*-nitrophenyl phosphite (route B), was treated with elemental sulfur. Flash chromatography (hexanes/ethyl acetate 75:25) gave 1.0 g of yellow crystals (90% yield) of mp 111–112 °C. ^{1}H NMR δ 1.42 (d, J=2.3 Hz, 6H), 1.86 (m, J=14.6, 11.3, 1.0 Hz, 1H), 1.90 (m, J=14.6, 3.0, 2.6 Hz, 1H), 4.76 (m, J=11.3, 6.2, 3.0, 2.6 Hz, 2H), 7.36 (dd, ^3J=8.9 Hz, $^4J_{HP}$=1.2 Hz, 2H), 8.24 (d, ^3J=8.9 Hz, 2H); ^{13}C NMR δ 22.4 (d), 40.6 (d), 77.7 (d), 121.3 (d, C_o), 126.0 (s, C_m), 145.1 (s, C_p), 156.2 (d, C_i); ^{31}P NMR δ 54.3. Mass spectrum (*m*/*z*) 303 (M^+), 262 (M^+-41), 236 (M^+-67), 218 (M^+-85), 171 (M^+-132), 149 (M^+-154), 123 (M^+-180), 97 (M^+-206), 69 (M^+-234), 41 (M^+-262). Anal. Calcd for $C_{11}H_{14}O_5PNS$: C, 43.57; H, 4.65. Found: C, 43.67; H, 4.85.

5.2.3. *eq*-2-*p*-Nitrophenoxy-2-thio-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphinane (2-*eq*). According to the general procedure described above, 1.5 g (5.54 mmol) of equatorial *p*-nitrophenyl phosphite (route A), was treated with elemental sulfur. Flash chromatography (hexanes/ethyl acetate 75:25) gave 1.52 g of pale yellow crystals (91% yield) of mp 90–91 °C. ^{1}H NMR δ 1.41(d, J=2.2 Hz, 6H), 1.77 (m, J=14.6, 10.5, 1.0 Hz, 1H), 1.90 (m, J=14.6, 2.6, 2.8 Hz, 1H), 4.85 (m, J=10.5, 6.3, 2.6, 1.2 Hz, 2H), 7.35 (dd, ^3J=9.2 Hz, $^4J_{HP}$=1.6 Hz, 2H), 8.23 (d, ^3J=8.9 Hz, 2H); ^{13}C NMR δ 22.1 (d), 40.8 (d), 76.1 (d), 122.1 (d, C_o), 125.4 (s, C_m), 145.1 (s, C_p), 155.0 (d, C_i); ^{31}P NMR δ 59.2. Mass spectrum (*m*/*z*) 303 (M^+), 262 (M^+-41), 236 (M^+-67), 218 (M^+-85), 205 (M^+-98), 171 (M^+-132), 149 (M^+-154), 123 (M^+-180), 97 (M^+-206), 69 (M^+-234), 41 (M^+-262). Anal. Calcd for $C_{11}H_{14}O_5PNS$: C, 43.57; H, 4.65. Found: C, 43.80; H, 4.51.

5.2.4. *ax*-2-*p*-Cyanophenoxy-2-thio-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphinane (3-*ax*). According to the general procedure described above, 1.0 g (3.98 mmol) of axial *p*-cyanophenyl phosphite (route B), was treated with elemental sulfur. Flash chromatography (hexanes/ethyl acetate 85:15) gave 1.04 g of the product as pale yellow crystals (93% yield) of mp 110–111 °C. ^{1}H NMR δ 1.43 (d, J=2.5 Hz, 6H), 1.85 (m, J=14.8, 10.5, 1.5 Hz, 1H), 1.87 (m, J=14.8, 2.5, 1.3 Hz, 1H), 4.73 (m, J=10.5, 6.4, 2.5, 1.2 Hz, 2H), 7.30 (dd, ^3J=9.1 Hz, $^4J_{HP}$=1.3 Hz, 2H), 7.65 (d, ^3J=9.1 Hz, 2H); ^{13}C NMR δ 22.3 (d), 40.3 (d), 77.1 (d), 108.8 (s, CN), 118.3 (s, C_p), 121.3 (d, C_o), 134.1 (s, C_m), 154.3 (d, C_i); ^{31}P NMR δ 54.5. Mass spectrum (*m*/*z*) 283 (M^+), 242 (M^+-41), 216 (M^+-67), 197 (M^+-86), 165 (M^+-118), 149 (M^+-134), 119 (M^+-164), 90 (M^+-193), 69 (M^+-234), 41 (M^+-242). Anal. Calcd for $C_{12}H_{14}O_3PNS$: C, 50.88; H, 4.98. Found: C, 50.91; H, 5.16.

5.2.5. *eq*-2-*p*-Cyanophenoxy-2-thio-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphinane (3-*eq*). According to the general procedure described above, 1.5 g (5.97 mmol) of equatorial *p*-cyanophenyl phosphite (route A), was treated with elemental sulfur. Flash chromatography (hexanes/ethyl acetate 80:20) gave 1.52 g of the product as pale yellow crystals (90% yield) of mp 106–107 °C. ^{1}H NMR δ 1.41 (d, J=2.0 Hz, 6H), 1.79 (m, J=14.5, 11.2 Hz, 1H), 1.87 (m, J=14.5, 2.7, 3.6 Hz, 1H), 4.84 (m, J=11.2, 6.6, 2.7, 3.3 Hz, 2H), 8.26 (d, ^3J=8.6 Hz, 2H), 8.57 (d, ^3J=8.9 Hz, 2H); ^{13}C NMR δ 22.1 (d), 40.9 (d), 76.0 (d), 109.4 (s, CN), 118.1 (s, C_p), 122.4 (s, C_o), 133.8 (s, C_m), 152.6 (d, C_i); ^{31}P NMR δ 59.3. Mass spectrum (*m*/*z*) 283 (M^+), 242 (M^+-41), 216 (M^+-67), 197 (M^+-86), 165 (M^+-118), 149 (M^+-134), 119 (M^+-164), 90 (M^+-193), 69 (M^+-234), 41 (M^+-242). Anal. Calcd for $C_{12}H_{14}O_3PNS$: C, 50.88; H, 4.98. Found: C, 51.02; H, 5.21.

5.2.6. *ax*-2-*p*-Formylphenoxy-2-thio-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphinane (4-*ax*). According to the general procedure described above, 1.0 g (3.94 mmol) of axial *p*-formylphenyl phosphite (route B), was treated with elemental sulfur. Flash chromatography (hexanes/ethyl acetate 60:40) gave 1.01 g of the product as oil (90% yield). ^{1}H NMR δ 1.42 (d, J=2.2 Hz, 6H), 1.83 (m, J=13.0, 8.0 Hz, 1H), 1.85 (m, J=13.0, 2.7, 1.5 Hz, 1H), 4.75 (m, J=8.0, 6.2, 2.7, 1.2 Hz, 2H), 7.35 (dd, ^3J=8.6 Hz, $^4J_{HP}$=1.5 Hz, 2H), 7.87 (d, ^3J=8.6 Hz, 2H), 9.94 (s, CHO); ^{13}C NMR δ 22.1 (d), 40.2 (d), 76.7 (d), 120.7 (d, C_o), 131.7 (d, C_m), 133.3 (s, C_p), 155.4 (d, C_i), 190.8 (s, CHO); ^{31}P NMR δ 55.1. Mass spectrum (*m*/*z*) 286 (M^+), 245 (M^+-41), 219 (M^+-67), 199 (M^+-87), 167 (M^+-119), 149 (M^+-137), 138 (M^+-148), 121 (M^+-165), 97 (M^+-189), 69 (M^+-217), 41 (M^+-245). Anal. Calcd for $C_{12}H_{15}O_4PS$: C, 50.35; H, 5.28. Found: C, 50.46; H, 5.40.

5.2.7. *eq*-2-*p*-Formylphenoxy-2-thio-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphinane (4-*eq*). According to the general procedure described above, 1.0 g (3.94 mmol) of equatorial *p*-formylphenyl phosphite (route A), was treated with elemental sulfur. Flash chromatography (hexanes/ethyl acetate 60:40) gave 1.02 g of brown crystals (91% yield)

of mp 55–57 °C. ^{1}H NMR δ 1.34 (d, J=2.3 Hz, 6H), 1.54 (m, J=14.5, 10.4, 1.8 Hz, 1H), 1.69 (m, J=14.5, 2.7, 2.3 Hz, 1H), 4.79 (m, J=10.4, 6.3, 2.7, 2.8 Hz, 2H), 7.30 (m, 2H), 7.80 (m, 2H), 9.91 (s, CHO); ^{13}C NMR δ 22.1 (d), 40.8 (d), 75.9 (d), 122.0 (d, C_o), 131.4 (d, C_m), 133.6 (s, C_p), 155.0 (d, C_i), 190.8 (s, CHO); ^{31}P NMR δ 59.5. Mass spectrum (*m/z*) 286 (M^+), 219 (M^+-67), 199 (M^+-87), 169 (M^+-117), 149 (M^+-137), 138 (M^+-148), 122 (M^+-164), 85 (M^+-201), 69 (M^+-217), 41 (M^+-245). Anal. Calcd for $C_{12}H_{15}O_4PS$: C, 50.35; H, 5.28. Found: C, 50.35; H, 5.41.

5.2.8. *ax*-2-*p*-Bromophenoxy-2-thio-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphinane (5-*ax*). According to the general procedure described above, 1.0 g (3.27 mmol) of axial *p*-bromophenyl phosphite (route B), was treated with elemental sulfur. Flash chromatography (hexanes/ethyl acetate 85:15) gave 1.03 g of white crystals (93% yield) of mp 132–133 °C. ^{1}H NMR δ 1.42 (d, J=2.2 Hz, 6H), 1.82 (m, J=14.8, 10.8, 1.0 Hz, 1H), 1.87 (m, J=14.8, 2.8, 2.7 Hz, 1H), 4.75 (m, J=10.8, 6.2, 2.8, 1.2 Hz, 2H), 7.19 (dd, ^3J=8.9 Hz, $^4J_{HP}$=1.4 Hz, 2H), 7.49 (d, ^3J=8.9 Hz, 2H); ^{13}C NMR δ 22.4 (d), 40.8 (d), 77.2 (d), 118.3 (s, C_p), 122.6 (d, C_o), 133.1 (s, C_m), 150.6 (d, C_i); ^{31}P NMR δ 55.5 (56.0). Mass spectrum (*m/z*) 338 (M^++1), 296 (M^+-41), 270 (M^+-67), 188 (M^+-149), 172 (M^+-165), 149 (M^+-188), 69 (M^+-268), 41 (M^+-296). Anal. Calcd for $C_{11}H_{14}O_3PSBr$: C, 39.19; H, 4.19. Found: C, 39.17; H, 4.16.

5.2.9. *eq*-2-*p*-Bromophenoxy-2-thio-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphinane (5-*eq*). According to the general procedure described above, 1.5 g (4.91 mmol) of equatorial *p*-bromophenyl phosphite (route A), was treated with elemental sulfur. Flash chromatography (hexanes/ethyl acetate 80:20) gave 1.54 g of white crystals (90% yield) of mp 64–65 °C. ^{1}H NMR δ 1.32 (d, J=2.0 Hz, 6H), 1.64 (m, J=14.5, 10.6 Hz, 1H), 1.77 (m, J=14.5, 2.8, 2.3 Hz, 1H), 4.76 (m, J=10.9, 6.3, 2.6, 2.3 Hz, 2H), 7.01 (dd, ^3J=8.6 Hz, $^4J_{HP}$=1.3 Hz, 2H), 7.38 (d, ^3J=8.6 Hz, 2H); ^{13}C NMR δ 22.0 (d), 40.9 (d), 75.6 (d), 118.6 (s, C_p), 123.1 (d, C_o), 132.5 (s, C_m), 149.5 (d, C_i); ^{31}P NMR δ 60.0. Mass spectrum (*m/z*) 338 (M^++1), 305 (M^+-32), 252 (M^+-85), 190 (M^+-147), 172 (M^+-165), 149 (M^+-188), 101 (M^+-236), 69 (M^+-268), 41 (M^+-296). Anal. Calcd for $C_{11}H_{14}O_3PSBr$: C, 39.19; H, 4.19. Found: C, 39.21; H, 4.28.

5.2.10. *ax*-2-*p*-Chlorophenoxy-2-thio-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphinane (6-*ax*). According to the general procedure described above, 2.8 g (10.73 mmol) of axial *p*-chlorophenyl phosphite (route A-to-C), was treated with elemental sulfur. Flash chromatography (hexanes/ethyl acetate 85:15) gave 0.72 g of white crystals (23% yield) of mp 126–128 °C. ^{1}H NMR δ 1.45 (d, J=2.1 Hz, 6H), 1.83 (m, J=14.1, 11.1, 1.1 Hz, 1H), 1.90 (m, J=14.1, 3.0, 1.3 Hz, 1H), 4.75 (m, J=11.1, 6.6, 3.0, 1.1 Hz, 2H), 7.12 (d, ^3J=8.8 Hz, 2H), 7.30 (d, ^3J=8.8 Hz, 2H); ^{13}C NMR δ 22.6 (d), 40.6 (d), 76.7 (d), 121.7 (d, C_o), 129.8 (s, C_p), 130.5 (s, C_m), 149.5 (d, C_i); ^{31}P NMR δ 55.6. Mass spectrum (*m/z*) 292 (M^+), 224 (M^+-68), 149 (M^+-143), 128 (M^+-164), 99 (M^+-193), 69 (M^+-154), 41 (M^+-251). Anal. Calcd for $C_{11}H_{14}O_3PSCl$: C, 45.14; H, 4.82. Found: C, 45.27; H, 5.04.

5.2.11. *eq*-2-*p*-Chlorophenoxy-2-thio-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphinane (6-*eq*). According to the general procedure described above, 2.8 g (10.73 mmol) of equatorial *p*-chlorophenyl phosphite (route A), was treated with elemental sulfur. Flash chromatography (hexanes/ethyl acetate 90:10) gave 1.54 g of white crystals (50% yield) of mp 59–60 °C. ^{1}H NMR δ 1.39 (d, J=2.0 Hz, 6H), 1.71 (m, J=14.0, 11.2 Hz, 1H), 1.87 (m, J=14.0, 3.0, 2.3 Hz, 1H), 4.83 (m, J=11.2, 6.6, 3.0, 2.5 Hz, 2H), 7.16 (d, ^3J=8.6 Hz, 2H), 7.38 (d, ^3J=8.6 Hz, 2H); ^{13}C NMR δ 22.5 (d), 41.3 (d), 76.1 (d), 122.9 (d, C_p), 123.1 (d, C_o), 130.1 (d, C_m), 149.4 (d, C_i); ^{31}P NMR δ 60.1. Mass spectrum (*m/z*) 292 (M^+), 224 (M^+-68), 149 (M^+-143), 128 (M^+-164), 99 (M^+-193), 69 (M^+-154), 41 (M^+-251). Anal. Calcd for $C_{11}H_{14}O_3PSCl$: C, 45.14; H, 4.82. Found: C, 45.17; H, 4.98.

5.2.12. *ax*-2-*p*-Acetamidophenoxy-2-thio-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphinane (7-*ax*). According to the general procedure described above, 3.0 g (10.73 mmol) of axial *p*-acetamidophenyl phosphite (route A-to-C), was treated with elemental sulfur. Flash chromatography (hexanes/ethyl acetate 85:15) gave 0.75 g of white crystals (22% yield) of mp 188–190 °C. ^{1}H NMR δ 1.44 (d, J=2.3 Hz, 6H), 1.86 (m, J=13.0, 12.9, 1.0 Hz, 1H), 1.88 (m, J=13.0, 2.9, 1.8 Hz, 1H), 2.79 (s, 3H), 4.77 (m, J=12.9, 6.2, 2.9, 1.3 Hz, 2H), 7.12 (d, ^3J=8.9 Hz, 2H), 7.49 (d, ^3J=8.9 Hz, 2H), 8.56 (s, 1H); ^{13}C NMR δ 22.5 (d), 24.7 (s), 42.7 (d), 76.8 (d), 121.9 (d, C_o), 122.6 (s, C_p), 135.1 (s, C_m), 147.5 (d, C_i), 168.4 (s); ^{31}P NMR δ 55.9. Mass spectrum (*m/z*) 315 (M^+), 273 (M^+-42), 205 (M^+-110), 187 (M^+-128), 125 (M^+-190), 108 (M^+-207), 69 (M^+-246), 43 (M^+-272). Anal. Calcd for $C_{13}H_{18}O_4PNS$: C, 49.52; H, 5.75. Found: C, 49.64; H, 5.79.

5.2.13. *eq*-2-*p*-Acetamidophenoxy-2-thio-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphinane (7-*eq*). According to the general procedure described above, 3.0 g (10.73 mmol) of equatorial *p*-acetamidophenyl phosphite (route A), was treated with elemental sulfur. Flash chromatography (hexanes/ethyl acetate 70:30) gave 1.54 g of pale yellow crystals (90% yield) of mp 102–104 °C. ^{1}H NMR δ 1.38 (d, J=2.4 Hz, 6H), 1.75 (m, J=14.1, 10.8 Hz, 1H), 1.85 (m, J=14.1, 2.3, 2.3 Hz, 1H), 2.14 (s, 3H), 4.80 (m, J=10.8, 6.2, 2.3, 2.6 Hz, 2H), 7.10 (dd, ^3J=8.6 Hz, $^4J_{HP}$=1.3 Hz, 2H), 7.46 (d, ^3J=8.6 Hz, 2H), 7.64 (s, 1H); ^{13}C NMR δ 22.4 (d), 24.7 (s), 41.1 (d), 75.8 (d), 121.0 (s, C_p), 121.7 (d, C_o), 135.5 (s, C_m), 149.6 (d, C_i), 168.6 (s); ^{31}P NMR δ 60.4. Mass spectrum (*m/z*) 315 (M^+), 273 (M^+-42), 229 (M^+-86), 205 (M^+-110), 187 (M^+-128), 125 (M^+-190), 108 (M^+-207), 69 (M^+-246), 43 (M^+-272). Anal. Calcd for $C_{13}H_{18}O_4PNS$: C, 49.52; H, 5.75. Found: C, 49.64; H, 5.92.

5.2.14. *ax*-2-Phenoxy-2-thio-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphinane (8-*ax*).[15] According to the general procedure described above, 1.0 g (4.42 mmol) of axial phenyl phosphite (route B), was treated with elemental sulfur. Flash chromatography (hexanes/ethyl acetate 95:5) gave 1.05 g of white crystals (92% yield) of mp 120–122 °C. ^{1}H NMR δ 1.43 (d, J=2.6 Hz, 6H), 1.82 (m, J=13.8, 9.9,

1.0 Hz, 1H), 1.88 (m, J=14.4, 2.8, 2.6 Hz, 1H), 4.79 (m, J=10.8, 6.6, 2.8, 1.3 Hz, 2H), 7.19 (m, 3H), 7.35 (m, ^3J=8.9 Hz, 2H); ^{13}C NMR δ 21.9 (d), 39.9 (d), 76.2 (d), 119.8 (d, C_o), 125.5 (s, C_p), 129.5 (s, C_m), 150.5 (d, C_i); ^{31}P NMR δ 55.8.

5.2.15. *eq*-2-Phenoxy-2-thio-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphinane (8-*eq*).[15] According to the general procedure described above, 3.0 g (13.27 mmol) of equatorial phenyl phosphite (route A), was treated with elemental sulfur. Flash chromatography (hexanes/ethyl acetate 98:2) gave 3.18 g of white crystals (93% yield) of mp 55–56 °C. ^{1}H NMR δ 1.39 (d, J=2.3 Hz, 6H), 1.70 (m, J=14.5, 10.9 Hz, 1H), 1.89 (m, J=14.5, 2.6, 2.3 Hz, 1H), 4.83 (m, J=10.9, 6.3, 2.6, 2.3 Hz, 2H), 7.20 (m, 3H), 7.35 (m, 2H); ^{13}C NMR δ 22.1 (d), 41.0 (d), 75.4 (d), 121.1 (d, C_o), 125.5 (s, C_p), 129.5 (s, C_m), 150.3 (d, C_i); ^{31}P NMR δ 60.4.

5.2.16. *ax*-2-*p*-Phenylphenoxy-2-thio-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphinane (9-*ax*). According to the general procedure described above, 3.5 g (11.59 mmol) of axial *p*-phenylphenyl phosphite (route B, or the sequence A-to-C), was treated with elemental sulfur. Flash chromatography (hexanes/ethyl acetate 98:2) gave 3.48 g of white powder (90% yield) of mp 145–146 °C. ^{1}H NMR δ 1.44 (d, J=2.2 Hz, 6H), 1.83 (m, J=13.8, 9.9, 1.0 Hz, 1H), 1.88 (m, J=13.8, 2.9, 2.9 Hz, 1H), 4.81 (m, J=9.9, 6.2, 2.9, 1.2 Hz, 2H), 7.27 (m, 2H), 7.35 (m, 1H), 7.44 (m, 2H), 7.59 (m, 4H); ^{13}C NMR δ 22.5 (d), 40.7 (d), 77.1 (d), 121.0 (d, C_o), 127.4 (s, C_m), 127.8 (s, $C_{p'}$), 128.7 (s, $C_{o'}$), 129.2 (s, $C_{m'}$), 138.5 (s, C_p), 140.5 (s, $C_{i'}$), 150.8 (d, C_i); ^{31}P NMR δ 55.8. Mass spectrum (*m*/*z*) 334 (M^+), 266 (M^+-68), 186 (M^+-148), 170 (M^+-164), 141 (M^+-193), 91 (M^+-243), 69 (M^+-265), 28 (M^+-306). Anal. Calcd for $C_{17}H_{19}O_3PS$: C, 61.07; H, 5.73. Found: C, 61.05; H, 5.44.

5.2.17. *eq*-2-*p*-Phenylphenoxy-2-thio-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphinane (9-*eq*). According to the general procedure described above, 2.5 g (8.27 mmol) of equatorial *p*-phenylphenyl phosphite (route A), was treated with elemental sulfur. Flash chromatography (hexanes/ethyl acetate 98:2) gave 2.51 g of white powder (91% yield) of mp 165–166 °C. ^{1}H NMR δ 1.34 (d, J=2.0 Hz, 6H), 1.67 (m, J=14.2, 9.9 Hz, 1H), 1.77 (m, J=14.2, 2.9, 2.3 Hz, 1H), 4.78 (m, J=9.9, 6.2, 2.9, 3.0 Hz, 2H), 7.19 (m, 2H), 7.28 (m, 1H), 7.36 (m, 2H), 7.48 (m, 4H); ^{13}C NMR δ 22.1 (d), 41.0 (d), 75.5 (d), 121.5 (d, C_o), 127.0 (s, $C_{m'}$), 127.3 (s, $C_{p'}$), 128.2 (s, $C_{o'}$), 128.8 (s, C_m), 138.6 (d, C_p), 140.2 (s, $C_{i'}$), 149.9 (d, C_i); ^{31}P NMR δ 60.4. Mass spectrum (*m*/*z*) 334 (M^+), 266 (M^+-68), 186 (M^+-148), 170 (M^+-164), 141 (M^+-193), 115 (M^+-219), 85 (M^+-249), 69 (M^+-265), 41 (M^+-293). Anal. Calcd for $C_{17}H_{19}O_3PS$: C, 61.07; H, 5.73. Found: C, 61.28; H, 6.00.

5.2.18. *ax*-2-*p*-Methylphenoxy-2-thio-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphinane (10-*ax*). According to the general procedure described above, 1.5 g (6.25 mmol) of axial *p*-methylphenyl phosphite (route B, or the sequence A-to-C), was treated with elemental sulfur. Flash chromatography (hexanes/ethyl acetate 80:20) gave 1.03 g of white crystals (89% yield) of mp 138–139 °C. ^{1}H NMR δ 1.41 (d, J=2.2 Hz, 6H), 1.82 (m, J=14.5, 10.7, 1.1 Hz, 1H), 1.84 (m, J=14.5, 3.0, 2.7 Hz, 1H), 2.32 (s, CH_3), 4.77 (m, J=10.7, 6.2, 3.0, 1.2 Hz, 2H), 7.06 (dd, ^3J=8.5 Hz, $^4J_{HP}$=1.5 Hz, 2H), 7.17 (d, ^3J=8.5 Hz, 2H); ^{13}C NMR δ 20.9 (s, CH_3), 22.4 (d), 40.7 (d), 76.9 (d), 120.4 (s, C_p), 130.6 (d, C_o), 135.3 (s, C_m), 148.8 (d, C_i); ^{31}P NMR δ 56.2. Mass spectrum (*m*/*z*) 272 (M^+), 204 (M^+-68), 186 (M^+-86), 149 (M^+-123), 124 (M^+-148), 108 (M^+-164), 91 (M^+-181), 69 (M^+-203), 43 (M^+-229), 41 (M^+-231). Anal. Calcd for $C_{12}H_{17}O_3PS$: C, 52.93; H, 6.29. Found: C, 53.03; H, 6.40.

5.2.19. *eq*-2-*p*-Methylphenoxy-2-thio-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphinane (10-*eq*). According to the general procedure described above, 3.5 g (14.58 mmol) of equatorial *p*-methylphenyl phosphite (route A), was treated with elemental sulfur. Flash chromatography (hexanes/ethyl acetate 80:20) gave 3.6 g of white crystals (91% yield) of mp 82–83 °C. ^{1}H NMR δ 1.34 (d, J=2.6 Hz, 6H), 1.59 (m, J=14.5, 11.2, 2.3 Hz, 1H), 1.72 (m, J=14.5, 2.6, 2.6 Hz, 1H), 2.27 (s, CH_3), 4.80 (m, J=10.9, 6.3, 2.6, 2.6 Hz, 2H), 7.03 (dd, ^3J=8.6 Hz, $^4J_{HP}$=2.0 Hz, 2H), 7.08 (d, ^3J=8.6 Hz, 2H); ^{13}C NMR δ 20.8 (s, CH_3), 22.1 (d), 41.0 (d), 75.3 (d), 121.0 (d, C_o), 129.9 (d, C_o), 135.1 (s, C_m), 148.3 (d, C_i); ^{31}P NMR δ 60.9. Mass spectrum (*m*/*z*) 272 (M^+), 204 (M^+-68), 186 (M^+-86), 149 (M^+-123), 124 (M^+-148), 108 (M^+-164), 91 (M^+-181), 69 (M^+-203), 43 (M^+-229), 41 (M^+-231). Anal. Calcd for $C_{12}H_{17}O_3PS$: C, 52.93; H, 6.29. Found: C, 52.73; H, 6.41.

5.2.20. *ax*-2-*p*-Methoxyphenoxy-2-thio-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphinane (11-*ax*). According to the general procedure described above, 3.0 g (11.71 mmol) of axial *p*-methoxyphenyl phosphite (route B, or the sequence A-to-C), was treated with elemental sulfur. Flash chromatography (hexanes/ethyl acetate 85:15) gave 2.93 g of white powder (92% yield) of mp 94–96 °C. ^{1}H NMR δ 1.42 (d, J=2.2 Hz, 6H), 1.81 (m, J=14.5, 10.8, 1.0 Hz, 1H), 1.86 (m, J=14.5, 3.3, 3.0 Hz, 1H), 3.78 (s, OCH_3), 4.77 (m, J=10.8, 6.2, 3.3, 1.2 Hz, 2H), 6.78 (dd, ^3J=8.8 Hz, $^4J_{HP}$=1.5 Hz, 2H), 6.87 (d, ^3J=8.8 Hz, 2H); ^{13}C NMR δ 22.4 (d), 40.7 (d), 56.0 (s, OCH_3), 76.9 (d), 115.0 (s, C_m), 121.7 (d, C_o), 144.9 (d, C_i), 157.29 (d, C_p); ^{31}P NMR δ 56.7. Mass spectrum (*m*/*z*) 288 (M^+), 220 (M^+-68), 202 (M^+-86), 140 (M^+-148), 124 (M^+-164), 95 (M^+-193), 69 (M^+-219), 41 (M^+-247). Anal. Calcd for $C_{12}H_{17}O_4PS$: C, 49.99; H, 5.94. Found: C, 50.06; H, 6.11.

5.2.21. *eq*-2-*p*-Methoxyphenoxy-2-thio-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphinane (11-*eq*). According to the general procedure described above, 2.5 g (9.76 mmol) of equatorial *p*-methoxyphenyl phosphite (route A), was treated with elemental sulfur. Flash chromatography (hexanes/ethyl acetate 80:20) gave 1.54 g of white crystals (90% yield) of mp 93–94 °C. ^{1}H NMR δ 1.31 (d, J=2.0 Hz, 6H), 1.63 (m, J=14.5, 10.9 Hz, 1H), 1.75 (m, J=14.5, 2.6, 2.6 Hz, 1H), 3.71 (s, OCH_3), 4.73 (m, J=10.9, 6.3, 2.6, 2.6 Hz, 2H), 6.77 (dd, ^3J=8.9 Hz, $^4J_{HP}$=1.6 Hz, 2H), 7.04 (d, ^3J=8.9 Hz, 2H); ^{13}C NMR δ 22.0 (d), 40.9 (d), 55.6 (s, OCH_3), 75.6 (d), 114.3 (s, C_m), 122.0 (d, C_o), 144.0 (d, C_i), 156.9 (d, C_p); ^{31}P NMR δ 61.0. Mass spectrum (*m*/*z*) 288 (M^+), 220 (M^+-68), 202 (M^+-86), 170 (M^+-118), 140 (M^+-148), 124 (M^+-164), 119 (M^+-169), 95 (M^+-193), 69 (M^+-219), 41 (M^+-247). Anal. Calcd

for $C_{12}H_{17}O_4PS$: C, 49.99; H, 5.94. Found: C, 49.81; H, 6.29.

5.2.22. *ax*-2-*p*-Aminophenoxy-2-thio-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphinane (12-*ax*). A mixture of 1.3 g (11.86 mmol) of *p*-aminophenyl phosphites (*ax*/*eq* 7:93) was obtained through route B. The mixture was maintained at room temperature because heating led to decomposition of the intermediate phosphites. The mixture of phosphites was treated with elemental sulfur according to the general procedure described above. Flash chromatography (hexanes/ethyl acetate 35:65) was unsuccessful to purify the axial isomer, therefore it was analyzed as a mixture. ^{13}C NMR δ 22.3 (d), 40.5 (d), 76.2 (d), 116.5 (s, C_m), 121.1 (d, C_o), 144.8 (d, C_i), 143.8 (s, C_p); ^{31}P NMR δ 56.8.

5.2.23. *eq*-2-*p*-Aminophenoxy-2-thio-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphinane (12-*eq*). According to the general procedure described above, 4.0 g (23.73 mmol) of equatorial *p*-aminophenyl phosphite (route A), was treated with elemental sulfur. Flash chromatography (hexanes/ethyl acetate 35:65) gave 1.5 g of brown crystals (23% yield) of mp 93–94 °C. ^{1}H NMR δ 1.38 (d, J=2.0 Hz, 6H), 1.68 (m, J=14.5, 11.2 Hz, 1H), 1.82 (m, J=14.5, 2.6, 2.6 Hz, 1H), 3.25 (br, NH_2), 4.52 (m, J=11.2, 6.6, 2.6, 3.3 Hz, 2H), 6.64 (m, 2H), 6.98 (m, 2H); ^{13}C NMR δ 21.9 (d), 40.8 (d), 75.8 (d), 115.4 (s, C_m), 121.8 (d, C_o), 142.6 (d, C_i), 142.6 (s, C_p); ^{31}P NMR δ 61.3. Mass spectrum (*m*/*z*) 274 ($M^+ + 1$), 205 ($M^+ - 68$), 187 ($M^+ - 86$), 125 ($M^+ - 148$), 109 ($M^+ - 164$), 94 ($M^+ - 179$), 69 ($M^+ - 204$), 41 ($M^+ - 232$). Anal. Calcd for $C_{11}H_{16}O_3PNS$: C, 48.35; H, 5.90. Found: C, 48.52; H, 6.04.

Acknowledgements

We thank CONACyT (México) for financial support (Grant 32221-E). We are grateful to Geiser Cuellar for the elemental analysis of some of the compounds.

References and notes

1. Bentrude, W. G. Steric and Stereoelectronic Effects in 1,3,2-Dioxaphosphorinanes. In *Conformational Behavior of Six Membered Rings. Analysis, Dynamics and Stereoelectronic Effects*; Juaristi, E., Ed.; VCH: New York, 1995; pp 245–293.
2. Maryanoff, B. E.; Hutchins, R. O.; Maryanoff, C. A. *Top. Stereochem.* **1979**, *11*, 187.
3. Gorenstein, D. G. *Chem. Rev.* **1987**, *87*, 1049.
4. (a) Eliel, E. L.; Wilen, S. H.; Mander, L. N. *Stereochemistry of Organic Compounds*; Wiley: New York, 1994; Chapter 11. (b) Kellie, G. M.; Ridell, F. G. *Top. Stereochem.* **1974**, 8, 225.
5. (a) Eliel, E. L.; Knoeber, M. C. *J. Am. Chem. Soc.* **1968**, *90*, 3444. (b) Riddell, F. G.; Robinson, J. T. *Tetrahedron* **1967**, *23*, 3417. (c) Pihlaja, K. *Acta Chem. Scand.* **1948**, *22*, 716.
6. Dean, J. A. *Handbook of Organic Chemistry*; McGraw-Hill: New York, 1987; Chapter 3.
7. Domínguez, Z. J.; Cortez, M. T.; Gordillo, B. *Tetrahedron* **2001**, *57*, 9799.
8. Holmes, R. R.; Day, R. O.; Dieters, J. A.; Kumara Swamy, K. C.; Holmes, J. M.; Hans, J.; Burton, S. D.; Prakasha, T. K. In *Phosphorus Chemistry Developments in American Science*; Walsh, E. N., Griffith, E. J., Parry, R. W., Quin, L. D., Eds.; ACS Symposium Series, 486; American Chemical Society: Washington, DC, 1992; Chapter 11.
9. (a) Eliel, E. L.; Gordillo, B.; White, P. S.; Harris, D. L. *Heteroat. Chem.* **1997**, *8*, 509. (b) McEwen, W. E. *Top. Phosphorus Chem.* **1965**, *2*, 1.
10. Tatcher, G. R. J.; Kluger, R. In *Advances in Physical Organic Chemistry*; Bethell, D., Ed.; Academic: New York, 1989; Vol. 25, p 99.
11. Verkade, J. G. *Phosphorus Sulfur* **1976**, *2*, 251.
12. Van Nuffel, P.; Van Alsenoy, C.; Lenstra, A. T. H.; Geise, H. J. *J. Mol. Struct.* **1984**, *125*, 1.
13. Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165.
14. Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry. Part A: Structure and Mechanisms*, 3rd ed.; Plenum: New York, 1990; Chapter 4.
15. Gordillo, B.; Garduño, C.; Guadarrama, G.; Hernández, J. *J. Org. Chem.* **1995**, *60*, 5180.
16. The value of $^3J_{HaHa}$=8 Hz for compounds **4**-*ax* (X=CHO) is somewhat small, however values of $^3J_{HaHe}$=2.8 Hz and $^3J_{HP}$=1.2 Hz discard population of a twist conformer.
17. Quin, L. D. *The Heterocyclic Chemistry of Phosphorus*; Wiley: New York, 1981; Chapter 6.
18. Quin, L. D. Stereospecificity in ^{31}P-Element Couplings: Phosphorus–Carbon Coupling. In *Phosphorus-31 NMR Spectroscopy in Stereochemical Analysis: Organic Compounds and Metal Complexes*; Quin, L. D., Verkade, J. G., Eds.; VCH: Deerfield Beach, FL, 1987; p 391.
19. Nifantiev, E. E.; Sorokina, S. F.; Borisenko, A. A. *J. Gen. Chem.* **1984**, *55*, 1481.
20. Pomerantz, M.; Chou, W.-N.; Witczak, M. K.; Smith, C. G. *J. Org. Chem.* **1987**, *52*, 159.
21. Gorenstein, D. G. In *Phosphorus-31 NMR; Principles and Applications*; Gorenstein, D. G., Ed.; Academic: New York, 1984; Chapter 1.
22. Cremlyn, R. J.; Woods, M. *J. Chem. Eng. Data* **1981**, *26*, 231.
23. (a) Letcher, J. H.; Van Wazer, J. R. *J. Chem. Phys.* **1966**, *44*, 815. (b) Letcher, J. H.; Van Wazer, J. R. *Top. Phosphorus Chem.* **1967**, 5.
24. Pomerantz, M.; Marynick, D. S.; Rajeshwar, K.; Chou, W.-N.; Throckmorton, L.; Tsai, E. W.; Chen, P. C. Y.; Cain, T. *J. Org. Chem.* **1986**, *51*, 1223.
25. Robinson, C. N.; Slater, C. D. *J. Org. Chem.* **1987**, *52*, 2011.
26. Chesnut, D. B.; Rusiloski, B. E. Chemical Shift Theory. In *Phosphorus-31 NMR Spectral Properties in Compound Characterization and Structural Analysis*; Quin, L. D., Verkade, J. G., Eds.; VCH: New York, 1994; Chapter 1.
27. Gorenstein, D. G. *J. Am. Chem. Soc.* **1975**, *97*, 898.
28. Klyne, W.; Prelog, V. *Experientia* **1972**, *16*, 521.
29. Romers, C.; Altona, C.; Havinga, E. *Top. Stereochem.* **1969**, *4*, 39.
30. Gorenstein, D. G. *J. Am. Chem. Soc.* **1977**, *99*, 2254.
31. Kumamoto, J. R.; Cox, J. R. Jr.; Westheimer, F. H. *J. Am. Chem. Soc.* **1956**, *78*, 4858.
32. Blackburn, G. M.; Cohen, J. S.; Todd, L. *Tetrahedron Lett.* **1964**, 2873.
33. Tasz, M. K.; Gamliel, A.; Rodríguez, O. P.; Lane, T. M.; Cremer, S. E. *J. Org. Chem.* **1995**, *60*, 6281.
34. Bentrude, W. G. Steric and Stereoelectronic Effects in 1,3,2-Dioxaphosphorinanes. In *Conformational Behavior of Six Membered Rings. Analysis, Dynamics and Stereoelectronic Effects*; Juaristi, E., Ed.; VCH: New York, 1995; p 264.

35. Enraf-Nonius. *CAD-4 Software*. *Version 5.0*; Enraf-Nonius, Delft: The Netherlands, 1989.
36. Ferrugia, L. J. *J. Appl. Crystallogr.* **1999**, *32*, 837.
37. Sheldrick, G. M. *SHELEXS97*: *Program for the Solution of Crystal Structures*; University of Göttingen: Germany, 1997.
38. Sheldrick, G. M. *SHELXL97*: *Program for the Refinement of Crystal Structures*; University of Göttingen: Germany, 1997.
39. Betterridge, P. W.; Carruthers, J. R.; Coopers, R. I.; Prout, K.; Watkin, D. J. *J. Appl. Crystallogr.* **2003**, *36*, 1847.
40. Watkin, D. J.; Prout, C. K.; Pearce, L. J. *Cameron*; Chemical Crystallography Laboratory, University of Oxford: Oxford, 1996.
41. Spek, A. L. *Platon, A Multipurpose Crystallographic Tool*; Utrecht University: Utrecht, The Netherlands, 1998.
42. Gordillo, B.; Hernández, J. *Org. Prep. Proc. Int.* **1997**, *29*, 195.