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Conformational Analysis of 2-OAryl-2-oxo-4,6-dimethyl- and -4-methyl-1,3,2λ^5-dioxaphosphorinanes. Spectroscopic, X-Ray, and Solid-State ^{13}C and ^{31}P Studies

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ABSTRACT

*Results of IR and ^1H, ^{13}C, and ^{31}P NMR studies of the anancomeric title compounds (***2–5***) and compound* **1** *(Scheme 1) are analyzed to search for the existence of high-energy boat or twist-boat conformations in the equatorial epimers. While the difference in frequencies $(\Delta\nu)_{P=O}$ between the axial and equatorial compounds and ^{13}C NMR J_{POCC} and anti J_{POCCH3} values suggest the participation of twist-boat conformations for the equatorial isomers, coupling constants in ^1H NMR J_{H4H5a} or J_{H6H5a} and J_{H4H5e} or J_{H6H5e} of the equatorial isomers* **2e–4e** *along with the lack of a large $^3J_{PH}$ in ^{31}P NMR are consistent with predominant chair conformations. In addition, an X-ray structure of the equatorial 2-p-nitrophenoxy-2-oxo-cis-4,6-dimethyl-1,3,2-dioxaphosphorinane (***4e***) showed that the molecule adopts a chair conformation with no severe ring flattening in the OPO region in the solid state. X-ray structures of trans-***4*** and trans-***5*** displayed chair conformations with mild ring flattening especially in the axial methyl region, presumably as a result of the steric methyl-oxygen interaction. CPMAS ^{13}C and ^{31}P NMR spectra of* **4a** *and* **4e** *provide evidence against the presence of a significant contribution of a twist-boat conformation in solid equatorial* **4e***. The NMR spectral analysis of* **1e,** *on the other hand, suggests a substantial contribution of a twist conformation as well as, possibly, some contribution of the inverted chair.*
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INTRODUCTION

In connection with our studies of the basic hydrolysis of cyclic phosphates [1] where a lack of stereochemical control was observed, we have analyzed the conformation of the title compounds (**1–5**) (Scheme 1) to obtain insight into the possible presence of high-energy conformers [2] that might complicate stereochemical interpretations.

The ring conformations of analogous OAr phosphates have been postulated to be chairs for the axial isomers **A** but twist **B** or boat **C** conformations [3] for the equatorial ones. This has been ascribed to the preference of the OAr group to occupy the axial position as a consequence of the anomeric effect [4] (Scheme 2).

In some compounds of biological interest

Dedicated to Prof. William E. McEwen on the occasion of his seventy-fifth birthday.

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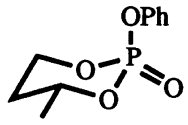
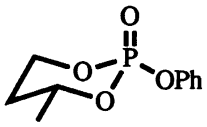
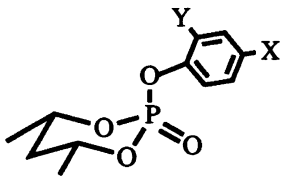
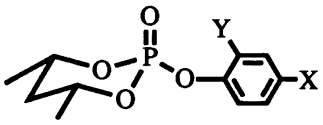


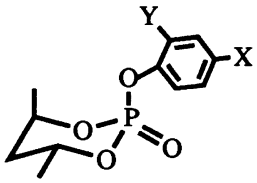
1a



1e

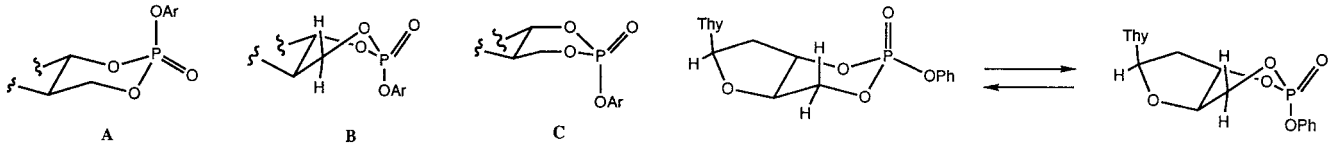






X = Y = H	**2a**	**2e**	X = Y = H *trans*-**2**
X = OMe, Y = H	**3a**	**3e**	
X = NO_2, Y = H	**4a**	**4e**	X = NO_2, Y = H *trans*-**4**
X = Y = NO_2	**5a**	*	X = Y = NO_2 *trans*-**5**

SCHEME 1



SCHEME 2

Thy = thymine

SCHEME 3

(Scheme 3), the phosphate ring adopts twist rather than chair conformations [5] even for phosphates substituted with moderately electronegative groups such as OPh [6]. This situation may, in part, be due to the inherent difficulty of *trans*-fusing a five-membered ring (normal torsion angle <40°) diequatorially to a six-membered chair (normal torsion angle ~65°).

EXPERIMENTAL SECTION

Spectral Analyses. ^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded at 250 MHz, 62.9 MHz, and 101.26 MHz, respectively. ^{31}P shifts are reported in δ ppm upfield (−) from external 85% H_3PO_4. Solid-state ^{13}C spectra were recorded in a Bruker MSL 360 wide-bore spectrometer operating at 90.53 MHz. Spectra were recorded with spinning of the sample at the magic angle and ^{1}H–^{13}C cross-polarization. Solid-state ^{31}P spectra were recorded on a Bruker A-200 spectrometer using a Doty MAS probe operating at 80.96 MHz. Referencing of the ^{31}P shifts was achieved by using an external standard sample of NaH_2PO_4 (δ = 0).

*2-Aryloxy-2-oxo-4,6-dimethyl-1,3,2λ^5-dioxaphosphorinanes (***1–5***).* These compounds were obtained following literature procedures [1b] except in the case of **5.**

*2,4-Dinitrophenoxy-2-oxo-4,6-dimethyl-1,3,2λ^5-dioxaphosphorinane (***5***).* Dry THF (10 mL) was placed in a N_2-flushed 25 mL round-bottomed flask that contained 2,4-dinitrophenol (1.01 g, 5.5 mmol), and the flask was cooled to 0°C. A solution of *n*-BuLi (4.0 mL, 5.5 mmol) 1.39 M in hexanes was added dropwise via syringe. The yellow solution turned

deep red upon *n*-BuLi addition. The mixture was stirred for 1 hour. The red oxyanion solution was transferred via cannula dropwise into another N_2-flushed round-bottomed flask that contained 2-chloro-2-oxo-2,4-dimethyl-1,3,2λ^5-dioxaphosphorinane [1b] (1.0 g, 5.4 mmol; mixture of stereoisomers) and 15 mL of dry THF. After the addition was completed, the resulting red solution was stirred at 0–3°C for an additional 3 hours. Then 100 mL of ammonium chloride and 100 mL of ether were added to the reaction mixture that was transferred to a separatory funnel. The combined organic layers were washed with 100 mL of brine and 200 mL of sodium carbonate solution and dried over Mg_2SO_4. After filtration, the solvent was removed under reduced pressure to yield a black oil that, after treatment with norit-A, gave 0.58 g (32%) of a yellow oil. Flash column chromatography (elution with 50/50 *n*-hexanes/ethyl acetate) resulted in 0.14 g (7.8%) of a pale yellow solid, axial **5a** [7], and 0.2 g (11.1%) of another yellow pale solid, *trans*-**5,** which, after recrystallization from petroleum ether, gave crystals mp 99.5–100.5°C. *trans*-**5** ^{1}H NMR ($CDCl_3$): δ 1.51 (dd, J_{HCCH} = 6.3 Hz, J_{HCCOP} = 2.5 Hz, 3H, CH_3 eq. at C_4 or C_6), 1.56 (d, J_{HCCH} = 7.58 Hz, 3H, CH_3 ax. at C_4 or C_6), 1.99 (dm, J_{gem} = 14.1 Hz, 1H, H_5 eq.), 2.19 (m, 1H, H_5 ax.), 5.02 (m, 2H, $H_{4,6}$), 8.05 (dd, J = 9.2 Hz, J = 0.7 Hz, 1H, $H_{arom.}$), 8.44 (dd, J = 9.3 Hz, J = 2.8 Hz, 1H, $H_{arom.}$), 8.79 (dd, J = 2.8 Hz, J = 1.2 Hz, 1H, $H_{arom.}$).

RESULTS AND DISCUSSION

IR Spectroscopy. Infrared analysis is based on the widely accepted observation that the stretching frequency (P=O) of an axial phosphoryl bond is 20–30 cm^{-1} lower than the equatorial (P=O) stretching frequency [8]. Infrared frequencies for the epimeric phosphates (**1–5**) are summarized in Table 1.

TABLE 1 Stretching Frequencies (P=O) for Phosphates (**1–5**)

Cmpd[a]	*OAr-axial* (**a**)	*OAr-equatorial* (**e**)	$\Delta\nu$ (cm^{-1})
1	1302	1296	6
2	1296	1290, 1278[b]	6–18
trans-**2**	1290	—	—
3	1308, 1290[b]	1278	12–30
4	1308	1284	24
trans-**4**	1308, 1284[b]	—	—
5	1308	—	—
trans-**5**	1308	—	—

[a]Values in either KBr or neat depending on whether the compound is solid or liquid. Values for **4a** and **4e** in $CDCl_3$.
[b]Two peaks observed in this region.

The stretching frequencies for the esters **3a–5a,** as well as *trans*-**4** and *trans*-**5** (1308 cm^{-1}, see Table 1) are of the order expected. These signals are moderately sharp, except for **3a** and *trans*-**4** [9], which points to a single chair conformation with axial OAr that is also favored by the anomeric effect [4]. In contrast, the equatorial isomers **1e–4e** present broader peaks possibly due to the presence of two or more phosphate ring conformations [10,11]; however, as in previous work [9,10], the results are not clear-cut and therefore not conclusive.

NMR Analyses. Analysis of ^{13}C NMR spectra data of phosphates (**1–5**) are summarized in Table 2.

Coupling constants, $^3J_{POCC}$ for C_5 and anti $^3J_{POCCH_3}$ (methyl groups in C_4, C_6) for the equatorial isomers (**1e–4e**), are in the range of conformationally heterogeneous systems [12,13]: The $^3J_{P-C_5}$ = 6.2–7.8 Hz values are too large to represent the $^3J_{PC}$ expected for a pure chair conformation with a 60° torsion angle $\chi_{C_5\text{-}C_4\text{-}O\text{-}P}$ (J = 3.7–5.6 Hz for **1a–5a**). Also, $^3J_{P-CH_3}$ ($C_{4,6\alpha}$) = 5.7–8.3 Hz is small compared to the expected $^3J_{PC}$ at torsion angle $\chi_{CH_3\text{-}C_4\text{-}O\text{-}P}$ or $\chi_{CH_3\text{-}C_6\text{-}O\text{-}P}$ of 180° (J = 8.5–10 Hz [13]; observed 9.5–9.9 Hz for **1a–5a**). All this evidence points to contributions of twist-boat conformations to **1e–4e.** The slightly more upfield resonance of Me_4 (21.53 ppm) in **1e** compared to **1a–5a** (21.85–22.05 ppm) may indicate a contribution of the inverted chair conformer to **1e.**

By contrast, coupling constants in ^{1}H NMR, $J_{H_{4a}H_{5a}}$ or $J_{H_{6a}H_{5a}}$ (11.4–11.6 Hz) and $J_{H_{4a}H_{5e}}$ or $J_{H_{6a}H_{5e}}$ (2.5–2.7 Hz) for the equatorial isomers (Table 3) are consistent with a chair or boat phosphate ring conformation according to the Karplus relationship) [14]. Moreover, the lack of large $^3J_{POCH}$ coupling constants (chair: synclinal P–$H_{4,6}$ relationship, boat: antiperiplanar P–$H_{4,6}$ relationship) in ^{31}P–H undecoupled NMR spectra for the equatorial **2e–4e** speaks against a substantial population of boat or twist-boat conformers. The situation is different for **1e** whose $^3J_{PH}$ coupling constant (Table 3) is much smaller than that for **1a** and falls in the range [8a] expected for a twist-boat conformation. The intermediate $^3J_{PH}$ in the *trans* isomers suggests some contribution of twist conformations to these compounds also [8a]. In addition, long-range coupling constants $^4J_{POCCH3}$ = 2.3–2.8 for the methyl group in C_4 and/or C_6 for both the axial and equatorial **1–5** are also within the values observed for chair conformations, with the methyl group being equatorial. ^{31}P signals are shifted upfield for axial **1a–4a** and shifted downfield for equatorial **1e–4e** as expected [3a].

The solvent dependence of the ^{31}P chemical shift difference between epimers was tested in the most "axial-seeking" compound studied, the *p*-nitrophenyl derivative. No significant change in $\Delta\delta$ ^{31}P chemical

TABLE 2 Room-Temperature ^{13}C NMR Signal Assignments in Phosphates (**1–5**)[a,b]

Cmpd	*C-4*	*C-5*	*C-6*	*C-4α*	*C-6α*	*C1′*	*C2′,6′*	*C3′,5′*	*C4′*	*QMe*
1a	77.65	32.78	68.28	21.90	—	150.23	119.26	129.41	124.74	—
	(7.4)	(5.6)	(7.2)	(9.5)		(6.5)	(5.4)	(2.6)		
1e	77.00	32.06	66.28	21.53	—	150.67	120.07	129.69	125.14	—
		(7.8)	(6.4)	(5.7)		(7.4)	(5.0)			
2a	76.60	40.36	76.60	21.99	21.99	150.57	119.42	129.77	124.79	—
		(4.5)		(9.9)	(9.9)	(7.8)	(5.3)			
2e	75.93	39.99	75.93	22.01	22.01	150.58	120.78	129.44	125.01	—
	(5.7)	(6.2)	(5.7)	(8.3)	(8.3)	(7.2)	(5.2)			
trans-**2**	73.19	37.21	75.51	20.43[c]	21.76[c]	150.62	119.52	129.55	124.65	—
	(6.8)	(7.5)	(7.2)	(1.5)	(8.2)	(6.7)				
3a	76.48	40.43	76.48	22.00	22.00	144.23	120.36	114.78	156.60	55.59
	(7.3)	(3.7)	(7.3)	(9.7)	(9.7)	(6.6)	(5.4)			
3e	75.80	40.30	75.80	22.18	22.18	144.41	121.23	114.54	156.63	55.62
	(5.7)	(6.3)	(5.7)	(8.0)	(8.0)	(7.1)	(5.2)			
4a	77.33	40.34	77.33	22.05	22.05	155.36	120.08	125.76	—	—
	(7.1)	(3.8)	(7.1)	9.5	(9.5)	(5.8)	(5.7)			
4e	76.80	40.10	76.80	22.20	22.20	155.51	120.85	125.58	145.00	—
	(6.0)	(7.5)	(6.0)	(7.7)	(7.7)		(5.7)			
trans-**4**	73.97	37.40	76.16	20.59[d]	22.02[d]	—	120.26	125.72	—	—
	(7.7)	(7.9)	(7.5)		(7.7)		(5.6)	(5.6)		
5a	78.18	40.25	78.18	21.85	21.85	148.13	140.05[d]	129.0[c,d]	143.26[d]	—
	(7.5)	(3.7)	(7.5)	(9.4)	(9.4)	(5.9)	121.52[d]	122.9[d]		
trans-**5**	74.90	37.12	77.72	20.37[d]	21.80[d]	—	—	128.79[d]	143.25[d]	—
	(7.7)	(7.6)	(7.7)		(8.6)	—	121.34[d]	123.20[d]		

[a]Shift in ppm from TMS in $CDCL_3$, J_{PC} in Hz in parentheses.
[b]Aromatic signals were assigned according to Ref. [29].
[c]These assignments could be interchanged; however, the axial methyl should have the smaller $^3J_{CP}$.
[d]These assignments could be interchanged.

TABLE 3 ^1H NMR Backbone Coupling Constants (in Hz)[a] and ^{31}P Shifts (in ppm) and Selected Coupling Constants, $^3J_{POCHe}$ (in Hz) in $CDCl_3$

Cmpd	$^3J_{h4,6aH5a}$	$^3J_{H4,6aH5e}$	$^2J_{H5a5e}$	$\delta^{31}P$	$^3J_{POCHe}$
1a	[b]	[b]	−14.7	−14.9	25.9
1e	[b]	[b]	[b]	−13.2	9.0[c]
2a	14.6	3.1	−14.6	−14.9	
2e	14.7	2.6	−14.7	−12.2	
trans-**2**	[b]	[b]	−15.6	−14.8	16.6
3a	[b]	2.8	[b]	−14.3	
3e	11.4	2.5	−14.6	−11.6	
4a	11.1	2.6	−14.5	−15.9	
4e	11.6	2.7	−14.7	−13.1	
trans-**4**	[b]	[b]	−14.5	−15.9	17.1
5a	10.9	2.6	−14.8	−16.8	
trans-**5**	[b]	[b]	−14.1	−16.6	19.5

[a]First-order analysis.
[b]Undetermined.
[c]The signal was almost a quintet; this finding and the fact that this value is much smaller than expected suggest a twist conformation for **1e** [15,16].

TABLE 4 $\Delta\delta$ ^{31}P NMR Chemical Shift for *cis*-2-Nitrophenyl-2-oxo-4,6-dimethyl-1,3,2λ^5-dioxaphosphorinanes (**4a**–**4e**)

Solvent	**4a**	**4e**	$\Delta\delta$ ^{31}P
Chloroform-*d*	−15.87	−13.06	−2.81
Acetone-d_6	−14.34	−11.77	−2.57
Methanol-d_4	−12.68	−11.00	−1.68

TABLE 5 ^{13}C and ^{31}P CPMAS Spectra of **4a** and **4e** Compared to ^{13}C and ^{31}P Chemical Shift of **4a** and **4e** in $CDCl_3$[a]

Entry	*Cmpd*	*C4,6*	*C-5*	*C4α,6α*	δ ^{31}P
1	**4a** ($CDCl_3$)	77.33	40.34	22.05	−15.9
		(7.1)	(3.8)	(9.5)	
2	**4a** (solid)	77.36	37.51	21.01	−17.0
$\Delta\delta$ (1–2)		−0.03	2.83	1.04	1.1
3	**4e** ($CDCl_3$)	76.80	40.10	22.20	−13.1
		(6.0)	(7.5)	(7.7)	
4	**4e** (solid)	73.31	37.32	19.47	−10.0
$\Delta\delta$ (3–4)		3.49	2.78	2.73	−3.1

[a]J_{CP} in Hz in parentheses.

TABLE 6 Selected Torsion Angles (ω) (deg), Bond Lengths (Å), and Bond Angles (deg) in Equatorial 2-*p*-Nitrophenoxy-2-oxo-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphorinane **4e**

Torsion Angles (deg)	*Bond Lengths (Å)*	*Bond Angles (deg)*
7-2-3-4 = 81.1(2)	1-2 = 1.567(3)	1-2-3 = 105.4(2)
7-2-1-6 = −78.1(2)	1-6 = 1.482(4)	1-6-5 = 107.8(3)
4α-4-3-2 = 172.9(3)	2-3 = 1.566(3)	1-2-8 = 104.2(2)
1-2-3-4 = −47.6(2)	2-7 = 1.451(3)	1-6-6α = 106.6(3)
3-2-1-6 = 51.9(2)	2-8 = 1.573(3)	2-3-4 = 118.9(2)
8-2-3-4 = −155.2(2)	3-4 = 1.476(4)	3-2-8 = 99.6(2)
8-2-1-6 = 155.7(2)	4-5 = 1.527(6)	3-4-5 = 109.4(3)
6α-6-1-2 = 177.7(3)	4-4α = 1.512(6)	3-4-4α = 105.3(3)
5-4-3-2 = 50.3(2)	5-6 = 1.524(5)	4-5-6 = 113.4(3)
5-6-1-2 = −59.3(2)	6-6α = 1.500(5)	5-4-4α = 113.8(4)
	8-1′ = 1.401(4)	5-6-6α = 114.2(3)
	1′-2′ = 1.392(4)	7-2-1 = 114.7(2)
	1′-6′ = 1.380(4)	7-2-3 = 116.9(2)
	2′-3′ = 1.377(5)	7-2-8 = 114.7(2)
	3′-4′ = 1.373(5)	8-1′-2′ = 120.9(3)
	4′-5′ = 1.377(5)	8-1′-6′ = 117.4(3)
	5′-6′ = 1.388(6)	
	4′-N = 1.478(5)	

TABLE 7 Selected Torsion Angles (ω) (deg), Bond Lengths (Å), and Bond Angles (deg) in Axial 2-*p*-Nitrophenoxy-2-oxo-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphorinane **4a**

Torsion Angles (deg)	*Bond Lengths (Å)*	*Bond Angles (deg)*
7-2-3-4 = 171.1(3)	1-2 = 1.554(2)	1-2-3 = 107.2(1)
7-2-1-6 = −169.1(3)	1-6 = 1.475(3)	1-6-5 = 109.3(2)
4α-4-3-2 = −173.3(3)	2-3 = 1.550(2)	1-2-8 = 100.2(1)
1-2-3-4 = 43.4(2)	2-7 = 1.448(2)	1-6-6α = 105.7(2)
3-2-1-6 = −42.4(2)	2-8 = 1.606(2)	2-3-4 = 119.0(2)
8-2-3-4 = −62.9(2)	3-4 = 1.484(3)	3-2-8 = 105.7(1)
8-2-1-6 = 67.7(2)	4-5 = 1.513(4)	3-4-5 = 108.6(2)
6α-6-1-2 = 171.5(4)	4-4α = 1.502(4)	3-4-4α = 105.8(2)
5-4-3-2 = −50.9(2)	5-6 = 1.504(4)	4-5-6 = 115.0(2)
5-6-1-2 = 49.0(2)	6-6α = 1.505(4)	5-4-4α = 113.7(3)
	8-1′ = 1.376(3)	5-6-6α = 113.4(3)
	1′-2 = 1.395(4)	7-2-1 = 114.9(1)
	1′-6′ = 1.389(4)	7-2-3 = 113.2(2)
	2′-3′ = 1.380(4)	7-2-8 = 114.5(1)
	3′-4′ = 1.381(4)	8-1′-2′ = 123.0(3)
	4′-5′ = 1.384(4)	8-1′-6′ = 115.7(3)
	5′-6′ = 1.373(4)	
	4′-N = 1.469(4)	

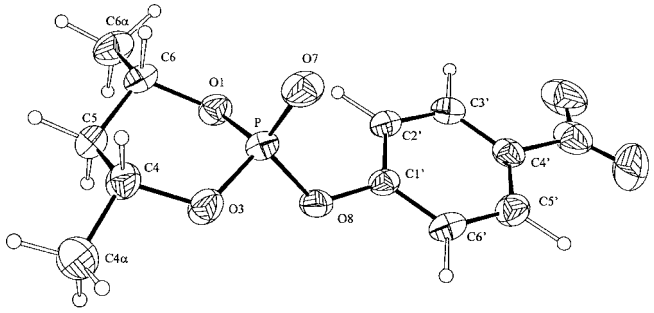


FIGURE 1 ORTEP representation of compound **4e.**

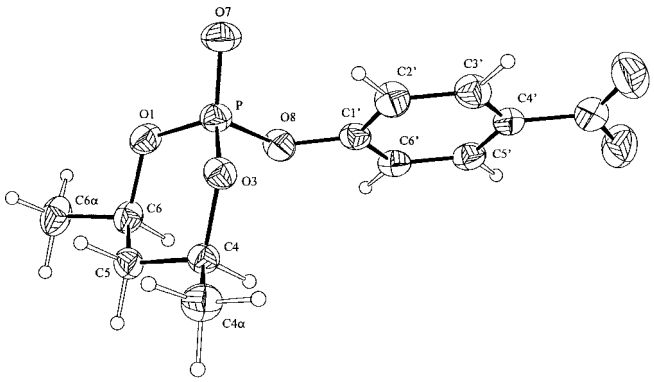


FIGURE 2 ORTEP representation of compound **4a.**

TABLE 8 Selected Torsion Angles (ω) (deg), Bond Lengths (Å), and Bond Angles (deg) in axial 2-*p*-Nitrophenoxy-2-oxo-*trans*-4,6-dimethyl-1,3,2λ^5-dioxaphosphorinane *trans*-**4**

Torsion Angles (deg)	*Bond Lengths (Å)*	*Bond Angles (deg)*
7-2-3-4 = −165.5(2)	1-2 = 1.550(2)	1-2-3 = 107.9(1)
7-2-1-6 = 156.2(2)	1-6 = 1.474(4)	1-6-5 = 109.8(3)
4α-4-3-2 = 177.0(3)	2-3 = 1.554(3)	1-2-8 = 101.0(1)
1-2-3-4 = −37.9(1)	2-7 = 1.445(2)	1-6-6α = 109.5(3)
3-2-1-6 = 29.9(1)	2-8 = 1.599(2)	2-3-4 = 119.1(2)
8-2-3-4 = 69.2(1)	3-4 = 1.480(3)	3-2-8 = 105.0(2)
8-2-1-6 = −80.1(1)	4-5 = 1.502(5)	3-4-5 = 107.8(3)
6α-6-1-2 = 89.7(2)	4-4α = 1.501(5)	3-4-4α = 106.8(3)
5-4-3-2 = 54.5(2)	5-6 = 1.518(5)	4-5-6 = 113.9(3)
5-6-1-2 = −38.0(1)	6-6α = 1.500(4)	5-4-4α = 113.7(3)
	8-1′ = 1.395(3)	5-6-6α = 115.6(3)
	1′-2′ = 1.380(4)	7-2-1 = 114.8(2)
	1′-6′ = 1.374(4)	7-2-3 = 112.5(2)
	2′-3′ = 1.385(4)	7-2-8 = 114.6(1)
	3′-4′ = 1.375(3)	8-1′-2′ = 122.8(2)
	4′-N = 1.463(3)	8-1′-6′ = 115.5(2)
	4′-5′ = 1.386(4)	
	5′-6′ = 1.382(4)	

shift difference for **4a–4e,** upon change of solvent from chloroform to acetone, was found, but a ca. 1.0 ppm difference was found upon switching to the more polar methanol, which may mean a change in conformational population for **4e** in this solvent [17] (Table 4).

CPMAS ^{13}C and ^{31}P NMR spectra were recorded for the *p*-nitro epimers **4a** and **4e** to study the con-

TABLE 9 Selected Torsion Angles (ω) (deg), Bond Lengths (Å), and Bond Angles (deg) in 2,4-Dinitrophenoxy-2-oxo-*trans*-4,6-dimethyl-1,3,2λ^5-dioxaphospharinane *trans*-**5**

Torsion Angles (deg)	*Bond Lengths (Å)*	*Bond Angles (deg)*
7-2-3-4 = 165.0(4)	1-2 = 1.541(5)	1-2-3 = 108.4(3)
7-2-1-6 = −150.5(5)	1-6 = 1.480(9)	1-6-5 = 110.7(1)
4α-4-3-2 = −176.6(11)	2-3 = 1.541(4)	1-2-8 = 101.7(3)
1-2-3-4 = 35.3(3)	2-7 = 1.435(5)	1-6-6α = 107.6(7)
3-2-1-6 = −23.1(3)	2-8 = 1.600(4)	2-3-4 = 120.6(4)
8-2-3-4 = −73.1(3)	3-4 = 1.454(8)	3-2-8 = 105.7(3)
8-2-1-6 = 88.1(4)	4-5 = 1.487(12)	3-4-5 = 105.9(6)
6α-6-1-2 = −95.3(6)	4-4α = 1.468(11)	3-4-4α = 108.4(6)
5-4-3-2 = −54.9(4)	5-6 = 1.481(14)	4-5-6 = 114.5(6)
5-6-1-2 = 32.9(4)	6-6α = 1.478(15)	5-4-4α = 113.1(7)
	8-1′ = 1.385(7)	5-6-6α = 116.4(8)
	1′-2′ = 1.394(8)	7-2-1 = 116.2(3)
	1′-6′ = 1.350(10)	7-2-3 = 112.2(3)
	2′-3′ = 1.362(9)	7-2-8 = 111.6(3)
	3′-4′ = 1.363(12)	8-1′-2′ = 120.9(6)
	4′-5′ = 1.379(11)	8-1′-6′ = 118.9(5)
	5′-6′ = 1.394(9)	
	4′-N = 1.475(9)	

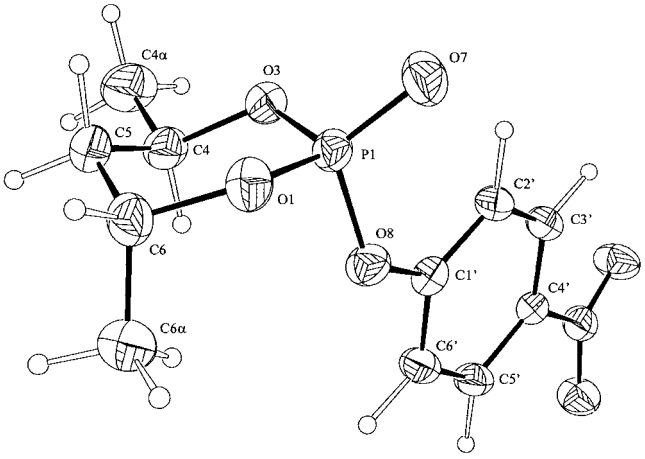


FIGURE 3 ORTEP representation of compound *trans*-**4.**

formational equilibrium chair ⇄ twist-boat under static conditions [18,19]. The results are summarized in Table 5.

Although the differences in chemical shifts $\Delta\delta^{20}$ between solution and solid spectra for the equatorial **4e** isomer are larger than for the axial **4a,** especially for $C_{4,6}$ (3.49 vs. −0.03 ppm) and for the ^{31}P signals (−3.1 vs. 1.1 ppm), the potential participation of a twist-boat conformation in the equatorial epimer **4e** could not be established due to the absence (<5%) of a second set of signals. This result speaks against a contribution of the twist-boat conformation in the equatorial *p*-nitrophenyl phosphate **4e** in the solid

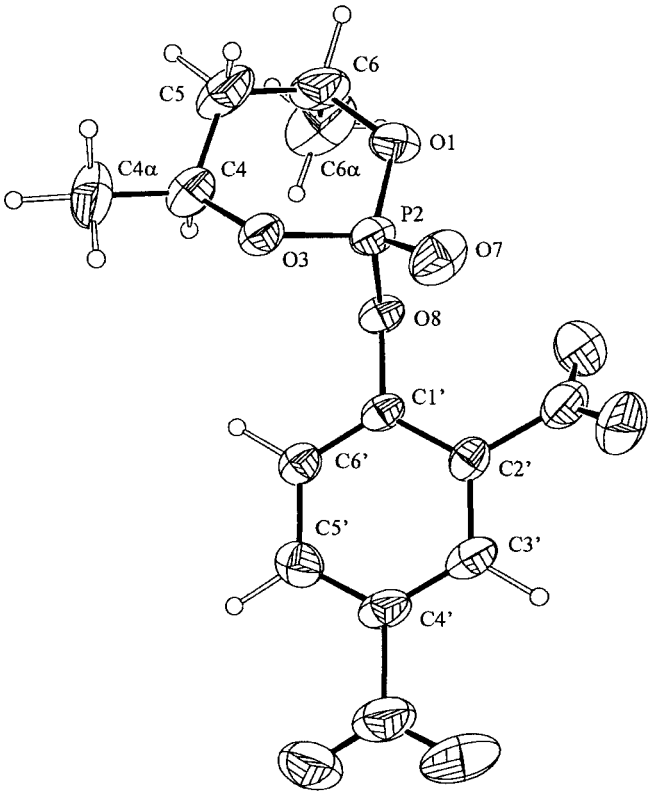


FIGURE 4 ORTEP representation of compound *trans*-**5.**

state; however, the increased ($\Delta\delta$) for **4e** may be due to the appearance of a contributing nonchair conformation in solution affecting the (averaged) spectrum.

X-RAY ANALYSES [22–25]

In order to establish irrefutable structural evidence for select compounds, at least in the solid state, an X-ray structure determination for the equatorial 2-*p*-nitrophenoxy-2-oxo-*cis*-4,6-dimethyl-1,3,2λ^5-dioxaphosphorinane (**4e**) was carried out. Selected torsion angles, bond distances, and bond angles are shown in Table 6; an ORTEP drawing of the molecule is shown in Figure 1. The molecule adopts a chair conformation with no severe ring flattening in the OPO region (torsion angles $\omega_{O_1PO_3C_4} = -47.6°$ and $\omega_{O_3PO_1C_6} = 51.9°$) as compared to the axial isomer **4a** ($\omega_{O_1PO_3C_4} = 43.4°$; $\omega_{O_3PO_1C_6} = -42.4°$). The slightly greater pucker in **4e** can also be judged from the decrease of the bond angles C_4-O_3-P and C_6-O_1-P from 119.3° (mean) for **4a** to 117.4° (mean) in **4e** [26]. The X-ray structure of **4a** is presented in Figure 2, and selected data are presented in Table 7. The unequal P–OAr exocyclic and P–O endocyclic bond lengths for **4a** are 1.61 and 1.55 Å (mean), respectively,

which, in comparison with the corresponding identical bond lengths in **4e,** 1.57 and 1.57 Å (mean), presumably supports the presence of the anomeric effect ($n_{\Pi}O \rightarrow \sigma^*$ (P–OAr) [4a] in the axial isomer **4a.** X-ray analyses were also performed for the *trans*-**4** and *trans*-**5** compounds. In these phosphate esters, the steric interaction methyl(4)- or methyl(6)-axial-OAr may introduce an additional factor promoting distortion of the phosphate ring. However, as in the other cases, these phosphates present chair conformations with increased ring flattening on the methyl-axial side of the ring ($\omega_{O_3PO_1C_6} = -29.9$ vs. $\omega_{O_1PO_3C_4} = 37.9$ for *trans*-**4** and $\omega_{O_3PO_1C_6} = -23.1$ vs. $\omega_{O_1PO_3C_4} = 35.3$ for *trans*-**5**). Selected torsion angles, bond lengths, bond angles for *trans*-**4** and *trans*-**5** are shown in Tables 8 and 9, respectively, with ORTEP drawings in Figure 3 and 4. The sum of PO distances in **4a, 4e,** *trans*-**4,** and *trans*-**5** are 6.16, 6.16, 6.15, and 6.12 Å, respectively, in accord with Cruickshank's predictions [25,26].

CONCLUSION

The X-ray analysis of **4e** shows that the conformation in the crystal is a chair with an equatorial OC_6H_4-*p*-NO_2 group; compounds **4a,** *trans*-**4,** and *trans*-**5** are also in chair conformations with axial OAr substituents in the solid state. Ring flattening in the OPO region, notably observed in *trans*-**4** and *trans*-**5,** is no doubt a consequence of the Me_4–OAr syn-axial interaction in the *trans* isomers.

The participation of boat or twist-boat conformations in equatorial *cis* compounds **2e–4e** is hinted at by ^{1}H, ^{31}P, and ^{13}C NMR data and seems to be more pronounced in the singly conformationally anchored **1e.** There may be a small contribution of the inverted chair in **1e** also. However, twist-boat conformations in **2e–4e** are not as highly populated as in decalin phosphates [8a] or in pentose phosphates with biological activity [6,27]. The influence of a second ring attached to a cyclic phosphate seems to be essential for stabilization of twist-boat conformations. The anomeric effect [4] in **4e** and steric interactions in *trans*-**4** and *trans*-**5** are, in any case, insufficient to force these molecules into a twist-boat conformation in the solid state.

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Supplementary Material Available. A complete description of the X-ray crystallographic structure determinations have been deposited with the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, UK.

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