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ORIGINAL RESEARCH

Polymorphism for a novel phosphoramidate; NMR and X-ray crystallography

Khodayar Gholivand · Farzaneh Afshar · Zahra Shariatinia · Karim Zare

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Abstract New phosphoramidates with formula 3-NC_5H_4 C(O)NHP(O)XY (X=Y=Cl (**1**), X=Y=NH–$C(CH_3)_3$ (**2a**,**2b**), X=Y=$N(C_4H_9)_2$ (**3**), X=Cl, Y=$N(C_2H_5)_2$ (**4**) were synthesized and characterized by IR, ^{1}H-, ^{13}C-, ^{31}P-NMR spectroscopy and CHN elemental analysis. Surprisingly, the reaction of compound **2a** with $LaCl_3$, $7H_2O$ in 3:1 M ratio leads to a polymorph of this compound (**2b**). NMR spectra indicate that $^2J(PNH_{amide})$ in **2b** (7.0 Hz) is very much greater than in **2a** (4.1 Hz), while $\delta(^{31}P)$ values are identical for both of them. In IR spectra, υ(P=O) is weaker but υ(C=O) is stronger in **2a** than in **2b**. The structures of **2a**, **2b** were determined by X-ray crystallography. These compounds form centrosymmetric dimers via two intermolecular P=O……H–N hydrogen bonds. Strong intermolecular N–H…N, N–H…O and weak C–H…O hydrogen bonds lead to a three-dimensional polymeric cluster in the **2a** while intermolecular strong N–H……N and weak C–H……O hydrogen bonds form a two-dimensional polymeric chain in **2b**.

Keywords Phosphoramidates · NMR · X-ray crystallography · Hydrogen bonds · Polymorphism

K. Gholivand (✉)
Department of Chemistry, Tarbiat Modares University, P.O. Box 14115-175, Tehran, Iran
e-mail: gholi_kh@modares.ac.ir

F. Afshar
Department of Biology, Islamic Azad University, Garmsar branch, Garmsar, Iran

Z. Shariatinia
Department of Chemistry, Amirkabir University of Technology, P. O. Box 159163-4311, Tehran, Iran

K. Zare
Department of Chemistry, Science and Research Branch, Islamic Azad University (IAU), P.O. Box 14515-775, Tehran, Iran

K. Zare
Department of Chemistry, Shahid Beheshty University, Tehran, Iran

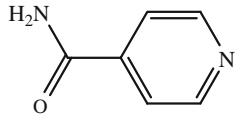
Introduction

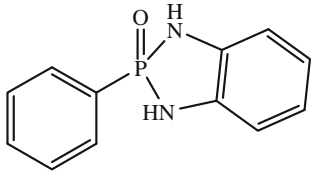
In recent years, investigation on carbacylamidophosphates is an important part of phosphoramidates chemistry. These compounds with the C(O)NHP(O) skeleton have attracted attention because of their properties as prodrugs [1–3], ureas inhibitors [4], and efficient ligands in coordination chemistry either as *O*-donor or *O*,*O*′-donor ligand [5–7]. On the other hand, isonicotinamide (Scheme 1) that is a pyridine derivative with an amidic $C(O)NH_2$ group in para position, possesses strong anti-tubecular, anti-pyretic, fibrinolytic, and anti-bacterial properties [8].

Polymorphism is an important phenomenon in different area of science especially in pharmaceutical investigations (many drugs receive regulatory approval for only a single crystal form or polymorph). In fact, the bioavailability of two polymorphs can differ appreciably, they are likely to perform differently in development and formulations processes, and are often a major problem in the delivery of pharmaceutical products. A well-known example of the effect of polymorphism causing real pharmaceutical problems is the ritonavir (an important AIDS drug), the Abbott compound [9, 10]. Norman and co-workers. reported two polymorphs of diazaphosphole compound (Scheme 2) [11].

In this work, we synthesized some new phosphoric triamides with general formula 3-NC_5H_4C(O)NHP(O)XY

Scheme 1 Isonicotinamide structure





Scheme 2 Diazaphosphole structure

(X=Y=Cl (**1**), X=Y=NH–$C(CH_3)_3$ (**2a**, **2b**), X=Y=N $(C_4H_9)_2$ (**3**), X=Cl, Y=N$(C_2H_5)_2$ (**4**) that are derived from isonicotinamide. Surprisingly, the two polymorphs of compound **2** (**2a**, **2b**) were obtained and their crystal structures were determined by X-ray crystallography. The spectroscopic and structural parameters of the polymorphs **2a** and **2b** were compared. Furthermore, the effects of substituents on ^{31}P chemical shifts and $^{2}J(PNH_{amide})$ coupling constants were discussed.

Experimental

Synthesis

*N-isonicotinyl-phosphoramidicdichloride, 3-$NC_5H_4C(O)NHP(O)Cl_2$ (**1**)*

To a suspension of phosphorous pentachloride (10 mmol, 2.08 g) in dry CCl_4, isonicotinamide (3-$NC_5H_4C(O)NH_2$) (10 mmol, 1.22 g) was added and the mixture was refluxed for 20 h. After cooling the flask, formic acid (10 mmol, 0.46 g) was added drop-wise into the solution at 0̊c and the resulting flask contents were stirred at room temperature for 6 h. The powder product was filtered, washed with CCl_4, and dried under vacuum.

Yield: 55%. Decomposed. Anal. Calc. for $C_6H_5N_2Cl_2O_2P$ (%): C 30.15, H 2.11, N 11.72. Found: C 30.14, H 2.11, N 11.73. ^{1}H-NMR (500.13 MHz, d_6-DMSO): $\delta = 7.95$ (s, 2H), 8.81 (s, 2H), 9.88 (d, ^{2}J(PNH) = 6.7 Hz), 1H, H_{amide}). ^{13}C-NMR (125.77 MHz, d_6-DMSO): $\delta = 165.10$ (s, C=O), 145.55 (s), 143.17 (s), 125.93 (s). ^{31}P-NMR (202.46 MHz, d_6-DMSO): $\delta = -4.24$ (d, ^{2}J(PNH) = 6.7 Hz). IR (KBr, cm^{-1}): $\nu_{max} = 3600$ (m, NH), 3419 (m, NH), 3068 (m, CH), 1669 (s, C=O), 1597 (s), 1520 (s), 1480 (s), 1305 (s), 1252 (s), 1225 (s, P=O), 1198 (m), 1171 (m), 1108 (s), 1053 (s), 988 (m), 940 (s), 921 (m), 885 (m), 839 (m), 799 (m), 765 (m), 749 (s), 684 (m), 671 (s), 558 (m), 542 (s), 503 (m), 482 (m), 468 (m).

*General procedure for the synthesis of compounds **2–4***

Compounds **2a** and **3** were synthesized from the reaction of 10 mmol of **1** with 20 mmol of corresponding amines and 20 mmol triethylamine in dry chloroform at −5 °C. After 6 h of stirring, the mixture was filtered and the solvent was evaporated at room temprature. The precipitate was washed with H_2O and dried. Compound **4** was prepared in the same way but 10 mmol of diethylamine plus 10 mmol of triethylamine were added to the mixture of **1**. The products were recrystallized from a mixture of choroform/n-hexan.

2a: Yield: 65%. m.p. = 267 °C. Anal. Calc. for $C_{14}H_{25}N_4O_2P$ (%): C 53.83, H 8.07, N 17.94. Found: C 53.81, H 8.08, N 17.92. ^{1}H-NMR (500.13 MHz, d_6-DMSO): $\delta = 1.21$(s, 18 H, CH_3), 4.06 (d, ^{2}J(PNH) = 7.3 Hz, 2H, H_{amine}), 7.84 (m, 2 H), 8.70 (m, 2H), 9.79 (d, ^{2}J(PNH) = 4.4 Hz, 1H, H_{amide}). ^{13}C NMR (125.77 MHz, d_6-DMSO): $\delta = 166.61$ (s, C=O), 150.07 (s), 141.12 (d, ^{3}J(P,C) = 8.2 Hz), 121.53 (s), 50.34 (s), 31.12 (d, ^{3}J(P,C) = 4.9 Hz). ^{31}P-NMR (202.46 MHz, d_6-DMSO): $\delta = 2.18$ (b). IR (KBr, cm^{-1}): $\nu_{max} = 3390$ (w, NH), 3232 (m, CH), 2967 (m), 1673 (s, C=O), 1441 (s), 1387 (s), 1361 (m), 1282 (m), 1227 (m), 1197 (s, P=O), 1119 (m), 1048 (s), 1017 (s), 887 (s), 850 (m), 820 (m), 757 (s), 695 (s), 573 (m).

3: Yield: 75%. Decomposed. Anal. Calc. for $C_{22}H_{41}N_4O_2P$ (%): C 62.24, H 9.73, N 13.20. Found: C, 62.22; H, 9.72; N, 13.21. ^{1}H-NMR (500.13 MHz, d_6-DMSO): $\delta = 0.83$ (t, ^{3}J(H,H) = 7.4 Hz, 12H), 1.21 (m, 8H), 1.45 (m, 8H), 2.96 (m, 8H), 7.77 (dd, ^{3}J(H,H) = 4.5 Hz, ^{5}J(P,H) = 1.6 Hz, 2H), 8.72 (dd, ^{3}J(H,H) = 4.5 Hz, ^{6}J(P,H) = 1.6 Hz, 2H), 9.48 (b, 1H, H_{amide}). ^{13}C NMR (125.77 MHz, d_6-DMSO): $\delta = 13.68$ (s), 19.66 (s), 30.30 (s), 45.00 (d, ^{2}J(P,C) = 3.9 Hz), 121.59 (s), 141.13 (d, ^{3}J(P,C) = 8.7 Hz), 150.10 (s), 166.83 (s, C=O). ^{31}P NMR (202.46 MHz, d_6-DMSO): $\delta = 13.11$ (m). IR (KBr, cm^{-1}): $\nu_{max} = 3072$ (m, CH), 2960 (m, CH), 2864 (m), 2735 (w), 1943 (w), 1675 (s,C=O), 1556 (m), 1457 (s), 1375 (m), 1281 (m), 1191 (s, P=O), 1040 (s), 994 (m), 932 (m), 877 (m), 840 (m), 785 (m), 755 (m), 697 (m), 555 (m), 495 (m).

4: Yield: 60%. m.p = 179 °C. Anal. Calc. for $C_{10}H_{15}N_3ClO_2P$ (%): C 43.57, H 5.48, N 15.24. Found: C 43.56, H 5.47, N 15.25. ^{1}H-NMR (500.13 MHz, d_6-DMSO): $\delta = 1.15$ (t, ^{3}J(H,H) = 7.2 Hz, 3H), 2.88 (q, ^{3}J(H,H) = 7.3 Hz, 2H), 7.78 (d, ^{3}J(H,H) = 7.6 Hz, 2H), 8.79 (d, ^{3}J(H,H) = 5.1 Hz, 2H), 9.74 (s, 1H, H_{amide}). ^{13}C-NMR (125.77 MHz, d_6-DMSO): $\delta = 165.23$ (s, C=O), 150.17 (s), 121.29 (s), 79.11 (s), 41.06 (s), 10.85 (s). ^{31}P-NMR (202.46 MHz, d_6-DMSO): $\delta = -16.39$ (s). IR

(KBr, cm^{-1}): ν_{max} = 3278 (w, NH), 3081 (w, CH), 2737 (w), 2496 (w), 1671 (s, C=O), 1655 (s), 1599 (m), 1558 (m), 1505 (s), 1455 (s), 1390 (w), 1333 (m), 1289 (m), 1239 (P=O), 1166 (w), 1105 (s), 1064 (s), 994 (m), 956 (s), 887 (m), 879 (m), 852 (m), 836 (s), 815 (s), 757 (s), 723 (m), 707 (m), 698 (m), 663 (w), 621 (w).

*N-3-isonicotinyl-N′,N″-bis(tert-butyl) phosphoric triamide, 3-$NC_5H_4C(O)NHP(O)[NH–C(CH_3)_3]_2$ (**2b**)*

To a solution of **2a** (3 mmol, 0.936 g) in absolute ethanol, $LaCl_3$, $7H_2O$ (1 mmol, 0.371 g) was added and the solution was refluxed for 4 h. The product was recrystallized from a solution of ethanol/acetonitrile.

m.p = 213 °C. Anal. Calc. for $C_{14}H_{25}N_4O_2P$ (%): C 53.83, H 8.07, N 17.94. Found: C 53.84, H 8.06, N 17.93. ^{1}H-NMR (500.13 MHz, d_6-DMSO): δ = 1.21 (s, 18 H, CH_3), 4.08 (d, ^2J(PNH) = 7.0 Hz, 2H, H_{amine}), 7.84 (m, 2H), 8.70 (m, 2H), 9.80 (d, ^2J(PNH) = 7.0 Hz, 1H, H_{amide}). ^{13}C-NMR (125.77 MHz, d_6-DMSO): δ = 166.68 (s, C=O), 150.13 (s), 141.18 (d, ^3J(P,C) = 7.8 Hz), 121.60 (s), 50.40 (s), 31.18 (d, ^3J(P,C) = 4.8 Hz). ^{31}P-NMR (202.46 MHz, d_6-DMSO): δ = 2.18 (b). IR (KBr, cm^{-1}): ν_{max} = 3379 (s, NH), 2970 (w, CH), 1663 (s, C=O), 1446 (m), 1387 (m), 1363 (m), 1289 (m), 1207 (s, P=O), 1120 (w), 1019 (s), 995 (m), 893 (m), 851 (m), 758 (m), 701 (m), 578 (s).

Spectroscopic measurements

^{1}H-, ^{13}C-, and ^{31}P-spectra were recorded on a Bruker Avance DRS 500 spectrometer. ^{1}H and ^{13}C chemical shifts were determined relative to internal Me_4Si, ^{31}P chemical shifts relative to 85% H_3PO_4 as external standards, respectively. The field strong to acquisition of ^{1}H-, ^{13}C-, and ^{31}P-NMR spectra were 500.13, 125.77, and 202.46 MHz, respectively. Infrared (IR) spectra were recorded on a Shimadzu model IR-60 spectrometer. Elemental analysis was performed using a Heraeus CHN-O-RAPID apparatus.

X-ray measurements

X-ray data of compound **2a** were collected on a Bruker SMART 1000 CCD [12] and of **2b** on a Bruker APEX II CCD area detector [13] single crystal diffractometer with graphite monochromated MoKα radiation (λ = 0.71073 Å). The structures were refined with SHELXL-97 [14] by full matrix least squares on F^2. The positions of hydrogen atoms were obtained from the difference Fourier map. Routine Lorentz and polarization corrections were applied and an absorption correction was performed using the SADABS program for these structures [15, 16].

Results and discussion

Spectroscopic study

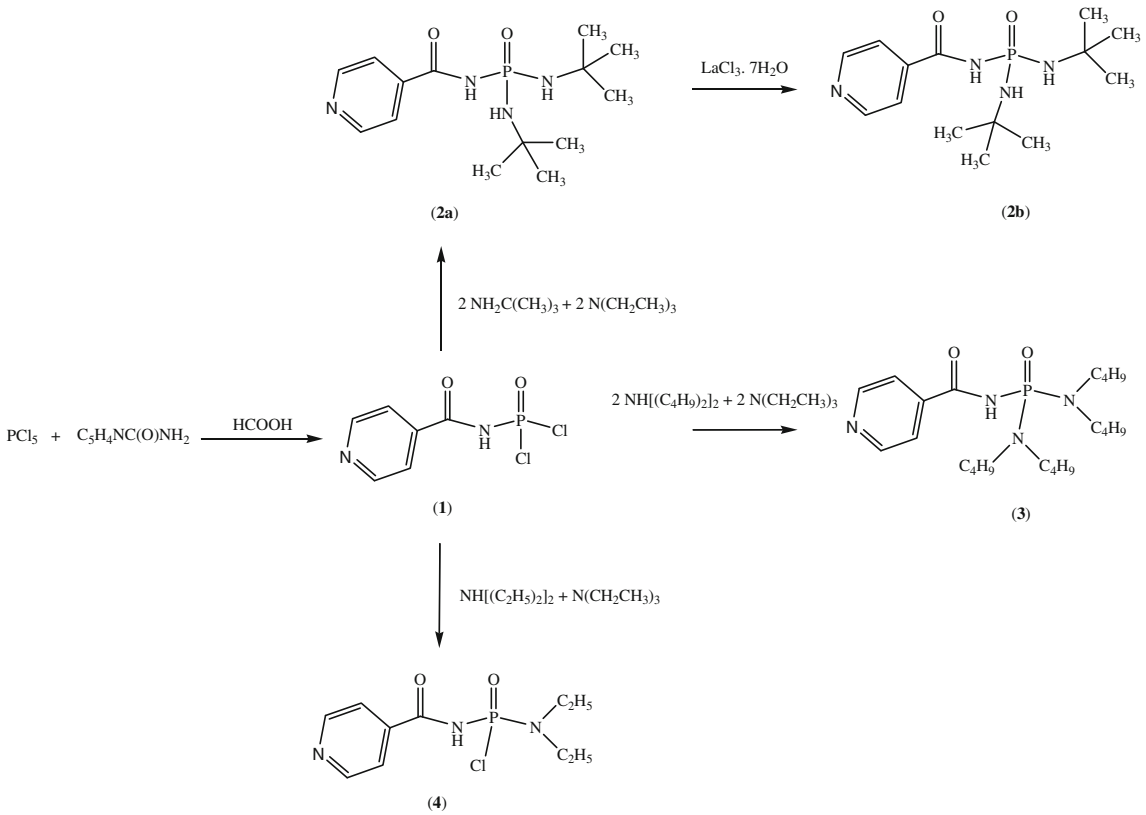
In this work, new phosphoramidates were synthesized from the reaction of PCl_5 and isonicotinamide followed by oxidation with HCOOH to yield *N*-isonicotinyl-phosphoramidicdichloride (**1**) as an intermediate. The reaction of **1** with corresponding amines in the presence of an HCl scavenger such as triethylamine gave desired phosphoramidates **2a**–**4**.

Surprisingly, the structure of **2b**, which is a polymorph of **2a**, was obtained from a solution of **2a** in presence of $LaCl_3{\cdot}7H_2O$ in 3:1 M ratio (Scheme 3). Several parameters affect the formation of a polymorph such as solvent, certain impurities or additives, concentration, temperature, the geometry of covalent bonds, and the stirring conditions [17–19]. It is noteworthy that with 2:1 M ratio of **2a**:$LaCl_3{\cdot}7H_2O$, this solution did not yield **2b** and it only gave **2a**. In this case, the presence of the metal salt in solution caused formation of this polymorph. It is probably due to the weak coordination of compound **2a** from P=O bond to La(III) center and then dissociation of O–La(III) linkage to form a new polymorph (**2b**). A possible description for the formation of **2b** with 3:1 M ratio of ligand:metal not with 2:1 ratio, maybe is the higher ligand concentration that provides more opportunities for the ligand to interact with metal ion.

It is noteable that the interaction of **2a** with other metal ions such as $CeCl_3{\cdot}7H_2O$, $ZnCl_2$, and $NiCl_2$ did not yield **2b** or a complex compound and it just left starting material. Application of $La(NO_3)_3.6H_2O$, $Ce(NO_3)_3{\cdot}7H_2O$, $Sm(NO_3)_3{\cdot}7H_2O$, $Er(NO_3)_3{\cdot}7H_2O$, $HgCl_2$, and $SnCl_2(CH_3)_2$ afforded their corresponding complexes. The metal effect on the formation of different polymorphs have been investigated [20–25]. For a related example to our work, the effect of lanthanum ions on the lipid polymorphism of phosphatidylethanolamines was reported [26].

It should be stated that this polymorphism is not owing to the effect of the water from the hydrated $LaCl_3$, because the 2:1 M ratio of **2a**:$LaCl_3{\cdot}7H_2O$ did not afford **2b**. To check the effects of H_2O solvent on the formation of polymorh **2b**, the interaction of 10 mmol of **2a** with 30 mmol of H_2O was studied, but this mixture did not give **2b**.

Since, the crystals of compound **2a** were obtained from choroform/*n*-hexan mixture and those of compound **2b** from ethanol/acetonitrile solution, thus the recrystallization of **2a** was performed again from ethanol/acetonitrile and that of **2b** from chloroform/hexane mixture, but they did not indicate any changes. Therefore, it could be concluded that these polymorphs are not formed because of solvent influence.



Scheme 3 Preparation pathway for compounds **1–4**

Some spectroscopic data of compounds **1–4** are presented in Table 1. It could be observed from the table that replacement of the two Cl atoms in **1** by electron donating amine groups in compounds **2a**, **2b**, and **3** shifts the $\delta(^{31}P)$ to down field. Also, the more electron donating dibutylamine groups have a greater effect on shifting the $\delta(^{31}P)$ to down field than *tert*-butylamine moieties. It is interesting that in **4** with one Cl atom and one amine goup the $\delta(^{31}P)$ shifts significantly to upfield. It seems that the Cl atom acts a donor group via resonance effect in **4** while comparatively it acts strongly as an electron withdrawing group in **1**. Interestingly, long-range $^{5,6}J(P,H) = 1.6$ Hz coupling constants are observed in **3** for the splitting of aromatic protons by phosphorus atom. The υ(P=O) value decreases by replacement of chlorine atoms in **1** with amine groups in **2a** and **3**. The υ(C=O) indicated an opposite trend.

Interestingly, different melting points equal to 267 °C and 213 °C are obtained for **2a** and **2b**, respectively, showing a more thermally stable structure for **2a**. Although, the $\delta(^{31}P)$ values are identical for both of them, there are several differences in the spectroscopic parameters of polymorphs **2a** and **2b**. For example, the $^{2}J(PNH_{amide})$ coupling constant in **2b** (7.0 Hz) is very much greater than in **2a** (4.4 Hz). This may be described by their

Table 1 Spectroscopic NMR and IR data of compounds **1–4**

Compound	$\delta(^{31}P)$ (ppm)	$^{2}J(PNH_{amine})$ (Hz)	$^{2}J(PNH_{amide})$ (Hz)	$^{2}J(P,C)^{*}$ (Hz)	$^{3}J(P,C)^{a}$ (Hz)	υ(P=O) (cm^{-1})	υ(C=O) (cm^{-1})
1	−4.24	–	6.7	–	–	1225	1669
2a	2.18	7.3	4.4	–	4.9 (al), 8.2 (ar)	1197	1673
2b	2.18	7.0	7.0	–	4.8 (al), 7.8 (ar)	1207	1663
3	13.11	–	–	3.9 (al)	8.7 (ar)	1191	1675
4	−16.39	–	–	–	–	1239	1671

[a] *al* Aliphatic, *ar* aromatic

Table 2 Crystal data and structure refinement for compounds **2a**, **2b**

	2a	**2b**
Empirical formula	$C_{14}H_{25}N_4O_2P$	$C_{14}H_{25}N_4O_2P$
Formula weight	312.35	312.35
Temperature (K)	120(2)	100(2)
Wavelength (Å)	0.71073	0.71073
Crystal system	Monoclinic	Triclinic
Space group	P 2_1/n	P–1
Unit cell dimensions		
a (Å)	10.7436(4)	9.2623(5)
b (Å)	9.3516(5)	9.5171(5)
c (Å)	17.3640(9)	11.0701(6)
α (°)	90	67.6917(9)
β (°)	102.083(5)	80.5703(10)
γ (°)	90	66.2391(9)
Volume (Å^3)	1705.91(15)	826.20(8)
Z	4	2
Density (calculated) (mg/m^3)	1.216	1.256
Absorption coefficient (mm^{-1})	0.171	0.177
F(000)	672	336
Crystal size (mm^3)	0.30 × 0.25 × 0.20	0.15 × 0.11 × 0.10
Theta range for data collection	2.06–29.00°	1.99–30.53°
Index ranges	$-14 \le h \le 14$	$-13 \le h \le 13$
	$-12 \le k \le 12$	$-13 \le k \le 13$
	$-23 \le l \le 23$	$-15 \le l \le 15$
Reflections collected	18372	14980
Independent reflections	4534 [R(int) = 0.0266]	5057 [R(int) = 0.0232]
Completeness to theta = 29.00°	100.00%	99.70%
Absorption correction	Semi-empirical from equivalents	Semi-empirical from equivalents
Max. and min. transmission	0.966 and 0.954	0.983 and 0.965
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data/restraints/parameters	4534/0/196	5057/0/196
Goodness-of-fit on F^2	1.006	1.01
Final R indices [for 3680 rfln with $I > 2$sigma(I)]	$R1 = 0.0452$, $wR2 = 0.1163$	$R1 = 0.0337$, $wR2 = 0.0940$
R indices (all data)	$R1 = 0.0549$, $wR2 = 0.1247$	$R1 = 0.0398$, $wR2 = 0.0983$
Largest diff. peak and hole	0.451 and −0.315 e. Å^{-3}	0.611 and −0.335 e. Å^{-3}

different spatial orientations leading to various torsion angles. The O1–P1–H1N–N1 torsion angles obtained from X-ray crystal structures are −162.5° and −154.42° for **2a** and **2b**. In the molecules the $^2J(PNH_{amine})$ and $^3J(P,C)$ coupling constants are nearly the same. The ν(P=O) in **2a** is weaker than in **2b** while ν(C=O) is stronger in **2a**. Since the P=O and C=O bond lengths in the structures of **2a** and **2b** are approximately identical (see "X-ray crystallography" section), the differences in their ν(P=O) and ν(C=O) may be interpreted by the strengths of P=O…H–N hydrogen bonds. The O1…H1N distance in **2a** and **2b** are 1.97° and 1.93°, respectively. The weaker hydrogen bonding in **2a** perhaps leads to a weaker P=O bond.

X-ray crystallography

Single crystals of compound **2a** were prepared from choroform/*n*-hexan mixture and those of compound **2b** from a solution of ethanol/acetonitrile after slow evaporation at room temperature. The crystal data and the details of the X-ray analysis are given in Table 2, selected bond lengths and angles in Table 3, and selected torsion angles in Table 4.

Table 3 Selected bond lengths (Å) and angles (°) for compounds **2a** and **2b**

2a		**2b**	
P(1)–O(1)	1.481(1)	P(1)–O(1)	1.483(1)
P(1)–N(1)	1.694(1)	P(1)–N(1)	1.697(1)
P(1)–N(2)	1.633(1)	P(1)–N(2)	1.633(1)
P(1)–N(3)	1.629(1)	P(1)–N(3)	1.629(1)
O(2)–C(1)	1.224(2)	O(2)–C(1)	1.221(1)
N(1)–C(1)	1.367(2)	N(1)–C(1)	1.370(1)
N(2)–C(7)	1.486(2)	N(2)–C(7)	1.485(1)
N(3)–C(11)	1.481(2)	N(3)–C(11)	1.485(1)
N(4)–C(4)	1.333(2)	N(4)–C(4)	1.340(1)
N(4)–C(5)	1.323(2)	N(4)–C(5)	1.339(2)
O(1)–P(1)–N(1)	106.07(6)	O(1)–P(1)–N(1)	107.69(4)
O(1)–P(1)–N(2)	119.63(6)	O(1)–P(1)–N(2)	117.97(4)
O(1)–P(1)–N(3)	111.86(6)	O(1)–P(1)–N(3)	111.79(4)
N(2)–P(1)–N(1)	101.72(6)	N(2)–P(1)–N(1)	102.77(4)
N(1)–P(1)–N(3)	112.06(6)	N(1)–P(1)–N(3)	110.15(4)
N(2)–P(1)–N(3)	105.16(6)	N(2)–P(1)–N(3)	106.01(4)
C(1)–N(1)–P(1)	125.64(9)	C(1)–N(1)–P(1)	125.49(7)
C(1)–N(1)–H(1N)	120.4	C(1)–N(1)–H(1N)	121.3
P(1)–N(1)–H(1N)	113.1	P(1)–N(1)–H(1N)	112.6

The structures of the two polymorphs **2a** and **2b** (Figs. 1, 2, respectively) display some differences in the solid state. For example, **2a** crystallizes in monoclinic system with $P2_1/n$ space group while **2b** in a triclinic system with P–1 space group. The P=O and all P–N bonds are longer in **2a** than in **2b** but the C=O bond length is

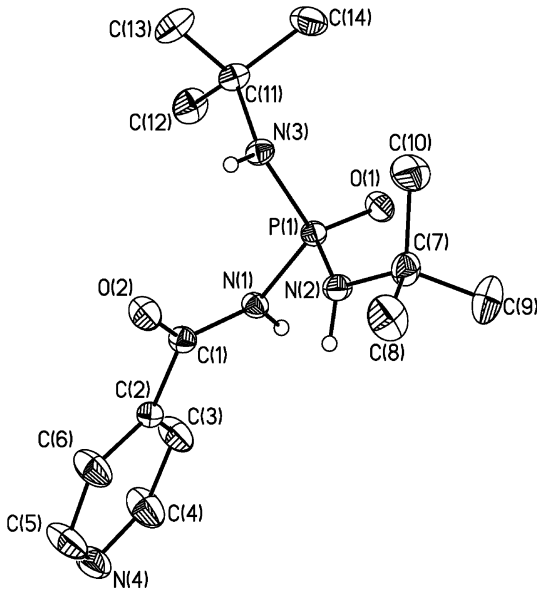


Fig. 1 Molecular structure and atom labeling scheme for compound **2a** (50% probability ellipsoids)

smaller in **2a**. The differences in the bond angles are not significant while the torsion angles differ in great extent even up to $\approx 20°$.

In these two structures, the phosphoryl and the carbonyl groups indicate anti-configurations with O(1)–P(1)–C(1)–O(1) torsion angle of −162.07° and −155.57° for **2a** and **2b**, respectively. The phosphorus atoms have distorted tetrahedral configuration, so that the bond angles around P(1) atoms in the compounds are in the range from 101.72(6)° to 119.63(6)°. The P=O bond lengths in

Table 4 Selected torsion angles (°) for compounds **2a** and **2b**

2a		**2b**	
O(1)–P(1)–N(1)–C(1)	−172.77(11)	O(1)–P(1)–N(1)–C(1)	−161.73(8)
O(1)–P(1)–N(2)–C(7)	45.15(14)	O(1)–P(1)–N(2)–C(7)	32.89(9)
O(1)–P(1)–N(3)–C(11)	39.11(13)	O(1)–P(1)–N(3)–C(11)	43.75(9)
N(1)–P(1)–N(2)–C(7)	161.46(12)	N(1)–P(1)–N(2)–C(7)	151.13(8)
N(2)–P(1)–N(1)–C(1)	61.42(12)	N(2)–P(1)–N(1)–C(1)	73.02(9)
N(3)–P(1)–N(1)–C(1)	−50.44(13)	N(3)–P(1)–N(1)–C(1)	−39.58(9)
N(1)–P(1)–N(3)–C(11)	−79.86(12)	N(1)–P(1)–N(3)–C(11)	−75.94(9)
N(2)–P(1)–N(3)–C(11)	170.46(11)	N(2)–P(1)–N(3)–C(11)	173.56(8)
N(3)–P(1)-N(2)–C(7)	−81.57(13)	N(3)–P(1)–N(2)–C(7)	−93.25(8)
P(1)–N(1)–C(1)–O(2)	10.6(2)	P(1)–N(1)–C(1)–O(2)	1.63(14)
P(1)–N(1)–C(1)–C(2)	−168.17(9)	P(1)–N(1)–C(1)–C(2)	−178.69(6)
O(2)–C(1)–C(2)–C(6)	−18.3(2)	O(2)–C(1)–C(2)–C(6)	−4.43(13)
O(2)–C(1)–C(2)–C(3)	162.90(15)	O(2)–C(1)–C(2)–C(3)	176.57(9)
P(1)–N(2)–C(7)–C(8)	162.78(12)	P(1)–N(2)–C(7)–C(8)	159.99(7)
P(1)–N(2)–C(7)–C(9)	−78.12(17)	P(1)–N(2)–C(7)–C(9)	−81.02(10)
P(1)–N(3)–C(11)–C(13)	171.50(11)	P(1)–N(3)–C(11)–C(13)	148.60(9)
P(1)–N(3)–C(11)–C(14)	−70.53(15)	P(1)–N(3)–C(11)–C(14)	−91.55(11)
P(1)–N(3)–C(11)–C(12)	52.33(16)	P(1)–N(3)–C(11)–C(12)	30.02(12)

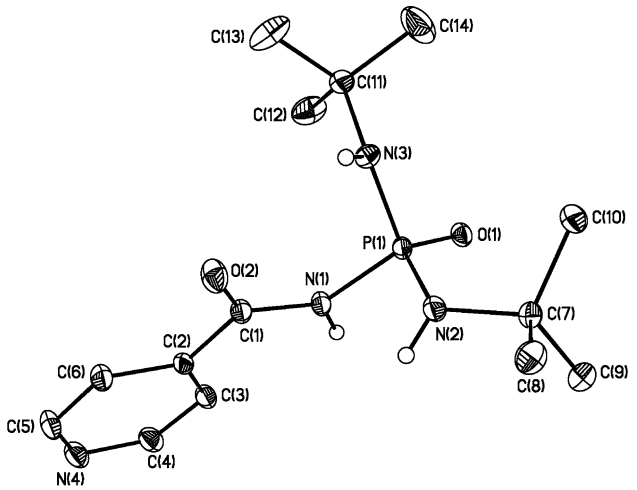


Fig. 2 Molecular structure and atom labeling scheme for compound **2b** (50% probability ellipsoids)

compounds **2a** and **2b** are 1.481(1) and 1.483(1) Å, respectively, that are larger than the normal P=O bond length (1.45 Å) [27].

The P–N_{amide} bonds (about 1.69 Å) are longer than the P–N_{amine} bonds (about 1.63 Å), because of the resonance interaction of the N_{amide} with the C=O π system that cause a partial multiple bond character in C–N_{amide} (the C–N_{amide} bond lengths are shorter than the C–N_{amine} bond lengths (Table 3). All of the P–N bonds are shorter than the typical P–N single bond (1.77 Å [27]). This is probably owing to the electrostatic effects of polar bonds that overlap with P–N sigma bond [28].

The environment of the nitrogen atoms is practically planar. In compound **2a** the angles C(1)–N(1)–P(1), C(1)–N(1)–H(1N) and P(1)–N(1)–H(1N) are 125.64(9)°, 120.4°, and 113.1°, respectively, with average 119.71°. The sum of surrounding angles around N(2), N(3), and N(4) atoms are 359.96, 354.16°, and 359.37°, respectively. Similar results were obtained for the nitrogen atoms of structure **2b** that confirm the sp^2 hybridization for the N atoms, although due to the repulsion and steric interactions, some angles are greater, and others are smaller than 120°. This observation

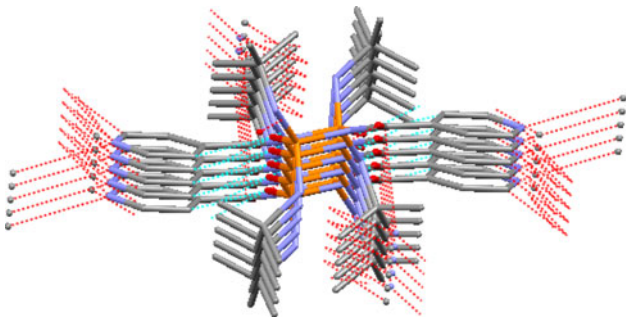


Fig. 3 A three-dimensional polymeric chain produced by strong- and weak hydrogen bonds in the crystalline lattice of compound **2a**

suggests the existence of partial multiple bond character between phosphorus and nitrogen atoms that has always been confirmed by the crystallographic data of our previously reported similar compounds [29–34].

These structures contain one amidic hydrogen atom and form centrosymetric dimers through intermolecular –P=O…H–N– hydrogen bonds (Table 5). In **2a**, there are also N(2)–H(2N)…N(4), N(3)–H(3N)…O(2) and weak C(3)–H(3A)…O(1) intermolecular H-bonds. Thus, pairs of dimers are linked into an extended three-dimensional network via these H-bonds (Fig. 3). In the network of **2b**, there are N(2)–H(2N)…N(4) and weak C(3)–H(3A)…O(1), C(13)–H(13A)…O(2) intermolecular hydrogen bonds. Moreover, there are intramolecular electrostatic interactions between O(2) of C=O group and N(3) atoms with the O…N distance of 2.980 Å in **2b**. All of the mentioned hydrogen bonds lead to a two dimensional polymeric chain (Fig. 4).

Supplementary data

Crystallographic data for the structures **2a** and **2b** have been deposited with Cambridge Crystallographic Data Center as supplementary publication nos. CCDC 740179 ($C_{14}H_{25}N_4O_2P$) and CCDC 740180 ($C_{14}H_{25}N_4O_2P$). Copies of the data may be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ,

Table 5 Hydrogen bonds for compounds **2a** and **2b** (Å, °)

Compound	D–H…A	*d*(D–H)	*d*(H…A)	*d*(D…A)	∠ DHA
2a	N(1)–H(1N)…O(1)$^{\#1}$	0.92	1.97	2.8874(16)	171
	N(2)–H(2N)…N(4)$^{\#2}$	0.89	2.27	3.1484(18)	171
2b	N(1)–H(1N)…O(1)$^{\#1}$	0.90	1.93	2.8173(11)	167
	N(2)–H(2N)…N(4)$^{\#3}$	0.90	2.23	3.1220(12)	174

Symmetry transformations used to generate equivalent atoms

$^{\#1}$ $-x + 2, -y + 1, -z$

$^{\#2}$ $-x + 3/2, y - 1/2, -z - 1/2$

$^{\#3}$ $-x + 2, -y + 2, -z$

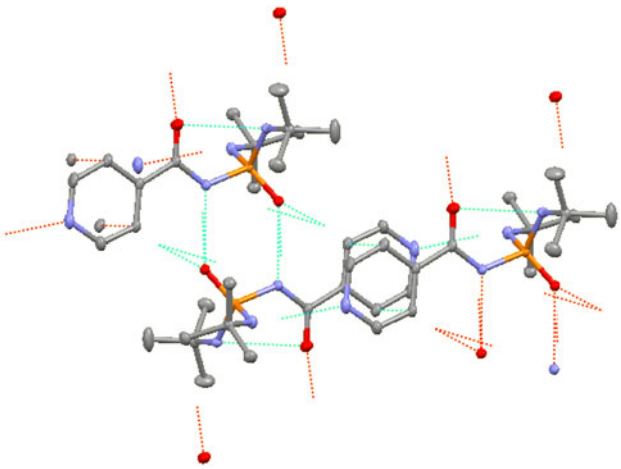


Fig. 4 A two-dimensional polymeric chain produced by strong hydrogen bonds and electrostatic interactions in the crystalline lattice of compound **2b**

UK, (fax: +441223336033; E-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

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