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Phosphoramides: Synthesis, Spectroscopy, and X-ray Crystallography

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ABSTRACT: *A series of new phosphoramides with general formula $RP(O)X_2$, where R = amino/p-methylphenoxy and X = amine, were synthesized and characterized by ^{1}H, ^{13}C, ^{31}P nuclear magnetic resonance (NMR), and infrared (IR) spectroscopy and elemental analysis. The $^{31}P\{^{1}H\}$NMR spectra show that among compounds* **7–9** *containing 2-, 3-, and 4-aminopyridinyl moieties, respectively, the shielding order of the P atom decreases as* **7** > **9** > **8**. *Also, the structure of compound* **7** *was determined by X-ray crystallography. In this structure, repeated noncentrosymmetric dimers are formed by two strong intermolecular N(1)-H(1N)...N(2) and N(3)-H(3N)...O(1) hydrogen bonds. Taking into account weak intermolecular C(17)-H(17C)...N(4), C(17)-H(17E)...N(4), C(2)-H(2A)...O(2), and also weak aromatic C—H...C interactions, a three-dimensional polymeric chain is created in the crystalline network. The density functional theory calculations at B3LYP, B3PW91, and M06 levels using the 6–31+G** basis set were in good agreement with the X-ray crystallography data.* © 2013 Wiley Periodicals, Inc. Heteroatom Chem 00:1–9, 2013; View this article online at wileyonlinelibrary.com. DOI 10.1002/hc.21107

INTRODUCTION

In recent years, the chemistry of phosphoramides has become very attractive owing to their various important applications such as anticancer prodrug compounds [1–4]. They have been utilized as potent catalysts in aldol reactions [5, 6] and in chiral asymmetric synthesis [7–10]. The highly enantioselective vinylogous addition of 2-trimethylsilyloxyfuran to aldehydes was performed using chiral phosphoramides as Lewis bases [11]. These types of compounds are also effective inhibitors for ureas [12, 13], acetylcholinesterase [14–16], and butyrylcholinesterase [17] enzymes. The biocidal activity of phosphoramides are well known so that they are applied as pesticides and insecticides in agriculture [18, 19]. The presence of phosphoryl or carbonyl oxygen donor sites enables them to be appropriate ligands in coordination chemistry [20–23]. So far, the synthesis, spectroscopic, and structural investigations on a number of such compounds have been performed [24–28].

In this work, 10 new phosphoramides were synthesized and characterized by multinuclear (^{1}H, ^{13}C, and ^{31}P) nuclear magnetic resonance NMR, infrared IR spectroscopy, and elemental analysis. Also, the molecular structure of compound **7** was determined

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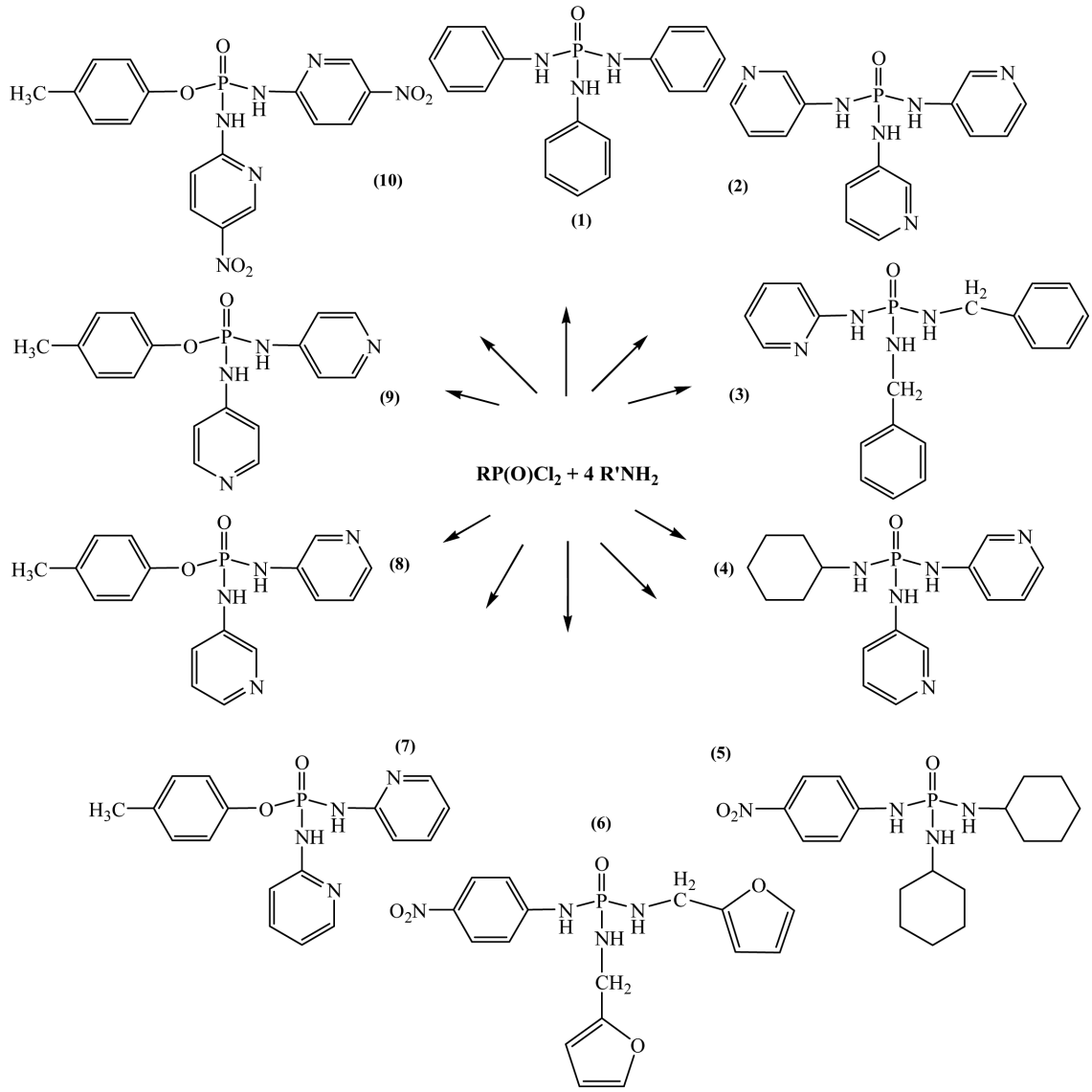

SCHEME 1 The preparation pathway of compounds 1–10.

by X-ray crystallography. The effects of various substituents on the spectroscopic results were interpreted and discussed.

RESULTS AND DISCUSSION

Spectroscopic Study

In this study, new phosphoramides **1–10** were synthesized from the reaction of $POCl_3$/$RPOCl_2$ with different amines (Scheme 1) and fully characterized by NMR and IR spectroscopy. A summary of the spectroscopic data of these compounds are given in Table 1. The comparative analysis of the spectra reveals interesting features. The $^{31}P\{^{1}H\}$NMR spectra indicate the phosphorus chemical shift, $\delta(^{31}P)$, in the range of –9.20 ppm (in **4**) to 8.94 ppm (in **6**) displaying various electron-donation powers of the substituents to the phosphorus atoms. A comparison indicates that the $\delta(^{31}P)$ values of analogues **7** and **10** as well as those of **8** and **9** are close to each other. Moreover, among compounds **7–9** containing 2-, 3- and 4-aminopyridinyl moieties, respectively, the molecule **7** has the most shielded phosphorus atom and the shielding order of the P atom decreases as **7** > **9** > **8**. Similarly, the phosphorus atom in **2** (containing three 3-aminopyridinyl groups) is more shielded than in **1** (bearing three anilinyl rings). The structures of **4** and **8** are similar to that of **2** in which one of the 3-aminopyridinyl groups is replaced with cyclohexylamine and *p*-cresol moieties, respectively. It is seen that the phosphorus atom is the most

TABLE 1 Selected Spectroscopic NMR and IR Data of Compounds **1–10**

Compound	$\delta(^{31}P)$ (ppm)	$^2J(PNH)$ (Hz)	$^2J(P,C)$ (Hz)	$^3J(P,C)$ (Hz)	$\nu(P{=}O)$ (cm^{-1})	$\nu(P{-}N)$ (cm^{-1})
1	–3.42	10.0	—	7.4	1214	928
2	–4.16	9.7	7.9	6.1	1186	955
3	2.47	7.7 (benzylamine)	—	4.5 (aminopyridine)	1196	987, 949
4	–9.20	7.2 (aminopyridine)	7.2 (aminopyridine)	5.7 (aminopyridine)	1180	1057, 929
5	5.97	10.6 (cyclohexylamine)	10.4 (nitroaniline)	6.9 (nitroaniline)	1183	1103, 907
6	8.94	11.1 (furfuryl), 8.5 (nitroaniline)	—	7.0, 7.2	1176	1104, 913
7	–8.53	—	7.7 (cresol)	9.0 (amine), 4.1 (cresol)	1217	897
8	–2.10	9.5	8.9 (aminopyridine)	7.0 (amine), 4.5 (cresol)	1212	947
9	–3.9	—	—	6.8 (amine), 4.5 (cresol)	1212	942
10	–7.42	—	6.9 (cresol)	6.0 (amine), 4.0 (cresol)	1219	908

shielded atom in **4** ($\delta(^{31}P) = -9.20$ ppm) whereas in **8**, it is the most deshielded one ($\delta(^{31}P) = -2.10$ ppm). Thus, the overall electron donation of substituents to the phosphorus atom is the highest one with the cyclohexylamine group.

The ^1H NMR spectra show geminal $^2J(PNH)$ coupling constants in the range of 11.1 Hz (in **6**) to 7.2 Hz (in **4**). The greatest $^2J(PNH)$ values are observed for compounds **5** and **6** for the coupling of NH protons of cyclohexylamine and furfuryl groups with the phosphorus atoms. As both molecules **5** and **6** include 4-nitroaniline group, it can be concluded that this electron-withdrawing moiety can cause more interaction between the phosphorus atoms and amino protons of cyclohexylamine and furfuryl groups. The comparison of the $^2J(PNH)$ indicates that the substitution of aniline rings in **1** by 3-aminopyridine groups in **2** can cause its decrease from 10.0 to 9.7 Hz. Similarly, substitution of one of 3-aminopyridine moiety in **2** by cyclohexylamine in **4** results in a decrease in $^2J(PNH)$ from 9.7 to 7.2 Hz. But, the $^2J(PNH)$ value does not change very much by the replacement of 3-aminopyridine group in **2** with *p*-cresol in **8** ($^2J(PNH) = 9.5$ Hz). The ^1H NMR spectrum of molecule **3** exhibits that the vicinal $^3J(PNCH) = 10.3$ Hz for the coupling of benzylic CH_2 protons with the phosphorus atom. Such coupling constants were also observed for previously reported phosphoramides [24–27]. The ^1H and ^{13}C NMR spectra of **10** reveal two sets of signals for the aromatic protons of the two 2-aminopyridinyl rings. This may be attributed to the different spatial orientation of the rings to each other, leading to a prochiral phosphorus atom. The ^{13}C NMR spectra exhibit $^{2,3}J(P,C_{aromatic})$ coupling constants so that in compounds **2**, **4**, **5**, **7**, **8**, and **10**, $^2J(P,C_{aromatic}) > {}^3J(P,C_{aromatic})$. Furthermore, comparing the $^{2,3}J(P,C_{aromatic})$ for analogues **2**, **4**, and **8** shows that the coupling constants values vary in the order **8** > **2** > **4**.

The analysis of the IR spectra indicate that the fundamental ν(P=O) stretching modes for compounds **1–10** appear in the range of 1176 cm^{-1} (in **6**) and 1219 cm^{-1} (in **10**), while the ν(P—N) of **6** (1104 cm^{-1}) shows the greatest value among those of **1–10**. Comparison of the ν(P=O) and ν(P–N) of the very analogous compounds **1** and **2** indicates stronger P=O but weaker P–N bonds in **1**. Interestingly, it can be seen that similar to the $\delta(^{31}P)$ values, the ν(P=O) and ν(P–N) of compounds **7** and **10** as well as those of compounds **8** and **9** are very close to each other. Moreover, among compounds **7–9** containing 2-, 3-, and 4-aminopyridinyl moieties, respectively, the molecule **7** shows the strongest P=O bond, while those of **8** and **9** are identical. A comparison of the ν(P=O) for similar molecules **2**, **4**, and **8** reveals that the P=O bond stretching frequencies change as **8** > **2** > **4**.

X-Ray Crystallography

Herein, to more investigate the structural properties of phosphoramides, the structure of compound **7** has been determined by X-ray crystallography. Single crystals of the compound were obtained from a solution of CH_3CN/*n*-hexane at room temperature. The crystallographic data and the details of the X-ray analysis are presented in Table 2, while selected bond lengths and angles are given in Table 3. Hydrogen bonding data of these structures are given in Table 4. The ORTEP view [29] and the three-dimensional polymeric chain generated by hydrogen bonds [30] are shown in Figs. 1 and 2.

In this structure, the C(10), H(10), and N(4) atoms indicate disorder. Such behavior have been observed with several crystal structures [31,32]. The P=O bond length in the molecule is 1.4696(12) Å, which is slightly longer than the normal P=O bond length (1.45 Å) [33]. The P—O bond length (between phosphorus and oxygen atom of p-cresol group)

TABLE 2 Crystallographic Data for Compound **7**

Chemical formula	$C_{17}H_{17}N_4O_2P_1$
Formula weight	340.32
Crystal system, space group	Triclinic, P –1
Temperature (K)	120(2)
a, *b*, *c* (Å)	9.6241(8), 9.8398(8), 10.6887(9)
α, β, γ (°)	73.075(2), 70.372(2), 63.275(2)
Volume (Å^3)	839.67(12)
Z	2
Density (calculated, mg/m^3)	1.346
Absorption coefficient (mm^{-1})	0.181
Crystal size (mm^3)	0.30 × 0.14 × 0.13
Theta range for data collection (°)	2.05 to 28.99
Index ranges	–13 <= h <= 13, –13 <= k <= 13, –14 <= l <= 14
Reflections collected	9327
Independent reflections	4434 [R(int) = 0.0198]
Completeness to theta = 28.99°	99.5%
Absorption correction	Semiempirical from equivalents
Maximum and minimum transmission	0.977 and 0.940
Refinement method	Full matrix least squares on F^2
Data/restraints/parameters	4434/4/218
Goodness-of-fit on F^2	0.945
Final R indices for 3613 reflections with [I > 2sigma(I)]	R1 = 0.0482, wR2 = 0.1109
R indices (all data)	R1 = 0.0599, wR2 = 0.1200
Largest differential peak and hole	0.450 and –0.356 e.Å^{-3}

TABLE 3 Selected Bond Lengths (Å) and Angles (°) for Compound **7**

P(1)—O(1)	1.4696(12)	O(1)—P(1)—O(2)	114.92(7)
P(1)—O(2)	1.5898(12)	O(1)—P(1)—N(3)	109.23(7)
P(1)—N(3)	1.6440(14)	O(2)—P(1)—N(3)	108.82(7)
P(1)—N(1)	1.6483(14)	O(1)—P(1)—N(1)	116.57(7)
O(2)—C(11)	1.4130(18)	O(2)—P(1)—N(1)	97.15(6)
N(1)—C(1)	1.394(2)	N(3)—P(1)—N(1)	109.49(7)
N(1)—H(1N)	0.8313	C(11)—O(2)—P(1)	120.25(10)
N(2)—C(1)	1.342(2)	C(1)—N(1)—P(1)	123.50(11)
N(2)—C(2)	1.345(2)	C(1)—N(1)—H(1N)	116.9
N(3)—C(6)	1.4011(19)	P(1)—N(1)—H(1N)	115.0
N(3)—H(3N)	0.8895	C(1)—N(2)—C(2)	117.57(14)
N(4)—C(6)	1.3408(10)	C(6)—N(3)—P(1)	127.02(10)
N(4)—C(7)	1.433(7)	C(6)—N(3)—H(3N)	114.1
N(4′)—C(6)	1.3426(10)	P(1)—N(3)—H(3N)	117.7
N(4′)—C(9)	1.504(4)	C(6)—N(4)—C(7)	114.0(4)
C(1)—C(5)	1.408(2)	C(6)—N(4')—C(9)	111.2(3)

TABLE 4 The Hydrogen Bonding Data of Compound **7** (Å, °)

D—*H*···*A*	*D*—*H*	*H*···*A*	*D*···*A*	∠*D*—*H*···*A*
N(1)—H(1N)...N(2)[a]	0.8300	2.1500	2.971(2)	168.00
N(3)—H(3N)...O(1)[b]	0.8900	2.0000	2.860(2)	161.00

Symmetry transformations used to generate equivalent atoms.
[a] –*x*+1,–*y*+1,–*z*.
[b] *x*+1,–*y*+1,–*z*+1.

is 1.5898(12) Å), which is smaller than the standard P—O single bond length (1.64 Å) [33]. The P atom has a slightly distorted tetrahedral configuration, that is, the surrounding angles around the P atom are in the range of 97.15(6)°–116.57(7)°. The two P—N bonds (1.6440(14) and 1.6483(14) Å) are shorter than the typical P—N single bond length (1.77 Å) [33], revealing the partial multiple bond character in them. In this compound, the angles P(1)—N(1)—C(1), P(1)—N(1)—H(1N) and C(1)—N(1)—H(1N) are 123.50(11)°, 115.0°, and 116.9°, respectively, with an average of 118.47°. The sum of surrounding angles around N(3) atom is 358.82°.

In this structure, each molecule is connected to another one by two strong intermolecular N(1)-H(1N)...N(2) and N(3))-H(3N)...O(1) hydrogen bonds, so that consecutive noncentrosymmetric dimers are formed by these H bonds. Considering weak intermolecular C(17))-H(17C)...N(4), C(17))-H(17E)...N(4), C(2))-H(2A)...O(2), and also weak aromatic C—H...C interactions, a three-dimensional polymeric chain is produced in the crystalline network (Fig. 2).

Density Functional Theory (DFT) Calculations

To further investigate the structural properties of compound **7**, its geometry was calculated using Gaussian 09 software [34] at B3LYP, B3PW91, and M06 methods with 6–31+G** standard basis set. The optimized structure has been shown in Fig. 3 [35]. The stabilization energies (kcal mole^{-1}) were calculated from the equation $\Delta E_{\text{stabilization}} = E(\text{molecule}) - \sum_i E(i)$, i = atom or ion, Table 5. It is seen that the molecule indicates the most $\Delta E_{\text{stabilization}}$ = –4619.784 kcal/mol at B3PW91/6–31+G** level. This indicates that among three computational levels, B3PW91 provides the lowest molecular energy, thus the geometrical parameters are calculated at this level to compare them with the experimental ones.

The selected bond lengths and angles calculated at B3PW91/6–31+G** level are given in Table 6 revealing a good agreement with the X-ray crystallography results. The two NH groups reveal pseudo-trans conformation relative to each other with N—H...N—H pseudo-torsion angle equal to

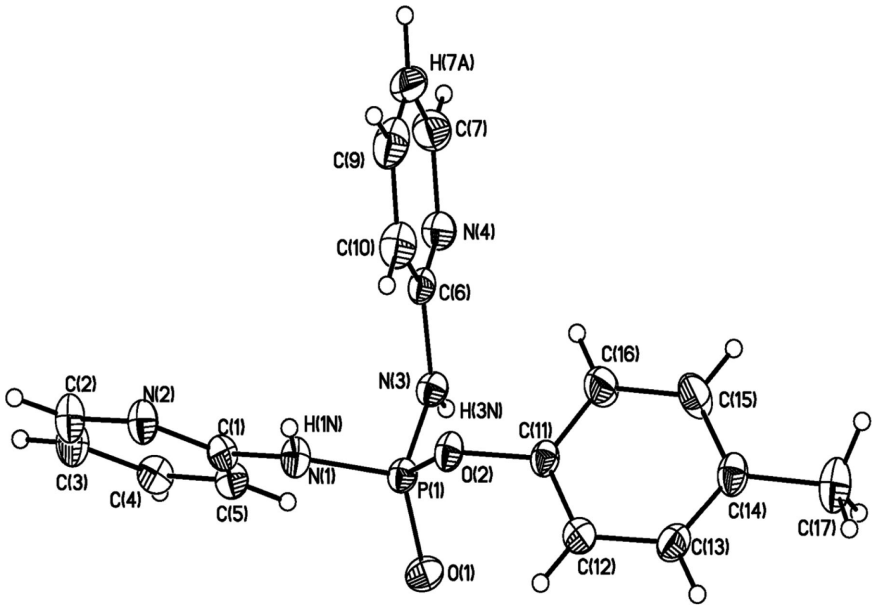

FIGURE 1 The ORTEP view of the crystal structure of compound **7**.

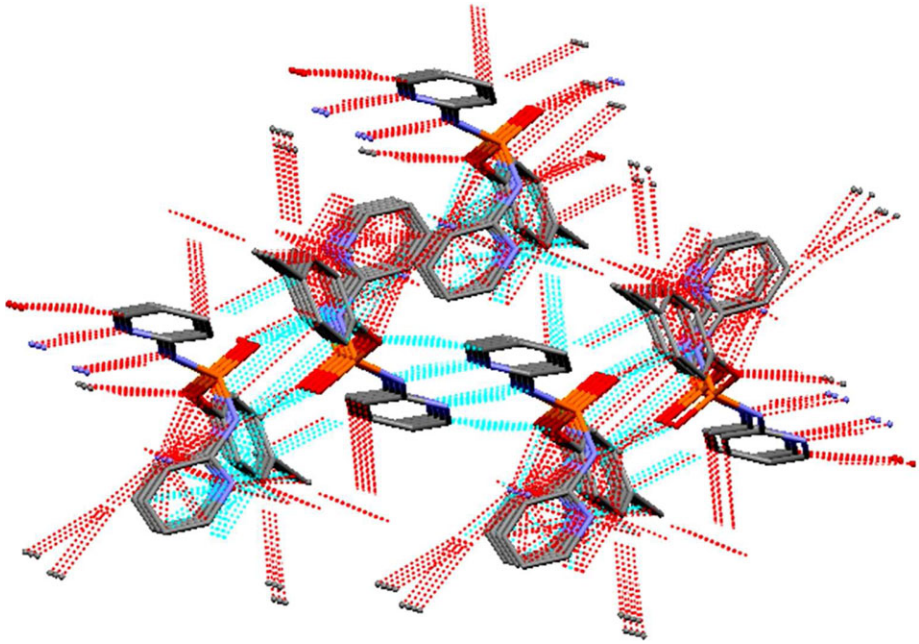

FIGURE 2 The three-dimensional polymeric chain formed by hydrogen bonds and aromatic interactions in **7**.

–24.89°. The phosphorus atom adopts a distorted tetrahedral configuration with the surrounding angles in the range of 95.48° to 118.39°.

In summary, the synthesis, spectroscopic, and structural characterization of a series of ten new phosphoramides has been performed. The structure of compound 4-CH_3-C_6H_4-OP(O)(2-NC_5H_4-$NH)_2$ (**7**) showed a three-dimensional polymeric chain in the crystalline lattice by intermolecular strong N—H . . . N, N—H . . . O and weak C—H . . . N, C—H . . . O hydrogen bonds plus aromatic C—H . . . C interactions. The ^1H and ^{13}C NMR spectra of 4-CH_3-C_6H_4-OP(O)(*p*-NO_2-2-NC_5H_3-$NH)_2$ (**10**) reveal two sets of signals for the aromatic protons of the two 2-aminopyridinyl rings that are probably due to the different spatial orientation of the rings to each other, leading to a prochiral phosphorus atom. The DFT calculations (with B3LYP, B3PW91, and M06 methods) using 6–31+G** basis set were in agreement with the X-ray crystallography results.

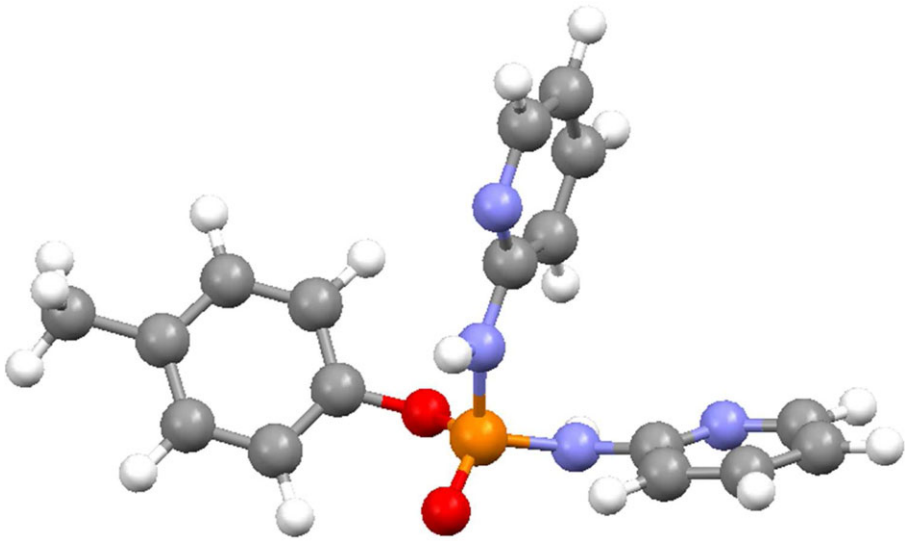

FIGURE 3 The optimized structure of compound **7** at DFT methods with 6–31+G** basis set.

TABLE 5 Stabilization Energies (kcal/mol) for Compound **7**

Method	ΔE
B3LYP/6–31+G**	–4570.490
B3PW91//6–31+G**	–4619.784
M06//6–31+G**	–4606.297

TABLE 6 Selected Bond Lengths (Å) and Angles (°) Calculated at B3PW91/6–31+G** Level for Compound **7**

P(1)—O(1)	1.4753	O(1)—P(1)—O(2)	117.87
P(1)—O(2)	1.6169	O(1)—P(1)—N(3)	108.41
P(1)—N(3)	1.6721	O(2)—P(1)—N(3)	107.36
P(1)—N(1)	1.6692	O(1)—P(1)—N(1)	118.39
O(2)—C(11)	1.3944	O(2)—P(1)—N(1)	95.48
N(1)—C(1)	1.3961	N(3)—P(1)—N(1)	108.28
N(1)—H(1N)	1.0146	C(11)—O(2)—P(1)	119.64
N(2)—C(1)	1.3321	C(1)—N(1)—P(1)	126.01
N(2)—C(2)	1.3355	C(1)—N(1)—H(1N)	113.76
N(3)—C(6)	1.3945	P(1)—N(1)—H(1N)	118.15
N(3)—H(3N)	1.0157	C(1)—N(2)—C(2)	117.57
N(4)—C(6)	1.3339	C(6)—N(3)—P(1)	132.20
N(4)—C(7)	1.3333	C(6)—N(3)—H(3N)	113.02

EXPERIMENTAL

X-ray Measurements

X-ray data of compound **7** was collected on a Bruker SMART 1000 CCD area detector [36] (Moscow, Russia) with graphite monochromated Mo Kα radiation ($\lambda = 0.71073$ Å). The structures were refined with SHELXL-97 [37] by full matrix least squares on F^2 (Moscow, Russia). 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 [38] (Moscow, Russia).

Spectroscopic Measurements

^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded on a Bruker Avance DRS 500 spectrometer. ^{1}H and ^{13}C chemical shifts were determined relative to the internal tetramethylsilane (TMS), and ^{31}P chemical shifts were determined relative to 85% H_3PO_4 as the external standard. IR spectra were recorded on a Shimadzu model IR-60 spectrometer. Elemental analysis was performed using a Heraeus CHN-O-RAPID apparatus. Melting points (mp) were obtained with an electrothermal instrument.

Synthesis

General Procedure. For the synthesis of compounds **1** and **2**, to a solution of 10 mmol phosphorylchloride in dry acetonitrile, 60 mmol of corresponding amine was dropwise added at 0°C and the mixture was stirred for 10 h. Then the solution was evaporated and the residue was washed with distilled water and dried. Compounds **3–10** were prepared in a same manner, but 40 mmol of the related amine was added to 10 mmol of corresponding R-substituted phosphoramidic dichloride ($RP(O)Cl_2$ where R = amine or *p*-cresol).

N,N′,N″-Tris(anilinyl) Phosphoric Triamide (**1**). Yield: 87%; mp = 214.9°C. Elemental analysis Calcd: C, 66.87; H, 5.57; N, 13.00. Found: C, 66.85; H, 5.59; N, 12.99. IR (KBr, cm^{-1}): 3345 (m, NH), 3025 (w), 1589 (s), 1483 (s), 1379 (s), 1280 (s), 1214

(s, P═O), 1177 (w), 1154 (w), 1024 (m), 994 (w), 928 (s, P—N), 890 (w), 784 (w), 744 (s), 690 (s), 618 (m), 505 (m), 480 (m). ^{1}H NMR (500.13 MHz, D_6-dimethylsulfoxide (DMSO), 25°C, TMS): 6.79 (t, $^3J(H,H) = 7.0$ Hz, 3H, Ar—H), 7.15 (m, 12H, Ar—H), 7.90 (d, $^2J(PNH) = 10.0$ Hz, 3H, NH). ^{13}C NMR (125.76 MHz, D_6-DMSO, 25°C, TMS): 117.42 (d, $^3J(P,C) = 7.4$ Hz), 119.91 (s), 128.58 (s), 142.08 (s). ^{31}P NMR (202.46 MHz, D_6-DMSO, 25°C, H_3PO_4 external): –3.42 (q, $^2J(PNH) = 10.0$ Hz).

*N,N′,N″-Tris(3-aminopyridinyl) Phosphoric Triamide (**2**).* Yield: 85%; mp = 243.2°C. Elemental analysis (%) Calcd: C, 57.32; H, 4.78; N, 26.75. Found: C, 57.30; H, 4.78; N, 26.76. IR (KBr, cm^{-1}): 3430 (s, NH), 3110 (s, CH), 2915 (m), 2755 (w), 1576 (s), 1494 (m), 1463 (s), 1399 (m), 1341 (w), 1262 (s), 1186 (s, P═O), 1124 (w), 1045 (m), 955 (s, P—N), 797 (m), 698 (m), 631 (w), 610 (m), 587 (w), 508 (w), 483 (w). ^{1}H NMR (500.13 MHz, D_6-DMSO, 25°C, TMS): 7.22 (t, $^3J(H,H) = 7.6$ Hz, 3H, Ar—H), 7.58 (d, $^3J(H,H) = 7.6$ Hz, 3H, Ar—H), 8.07 (d, $^3J(H,H) = 7.6$ Hz, 3H, Ar—H), 8.44 (s, 3H, Ar—H), 8.47 (d, $^2J(PNH) = 9.7$ Hz, 3H, NH). ^{13}C NMR (125.76 MHz, D_6-DMSO, 25°C, TMS): 123.63 (s), 124.18 (d, $^3J(P,C) = 6.1$ Hz), 138.35 (s), 139.55 (d, $^2J(P,C) = 7.9$ Hz, C_{ipso}), 141.64 (s). ^{31}P NMR (202.46 MHz, D_6-DMSO, 25°C, H_3PO_4 external): –4.16 (q, $^2J(PNH) = 9.7$ Hz).

*N-2-Aminopyridinyl-N′,N″-dibenzyl Phosphoric Triamide (**3**).* Yield: 86%; mp = 294.2°C. Elemental analysis (%) Calcd: C, 64.77; H, 5.97; N, 15.91. Found: C, 64.76; H, 5.99; N, 15.92. IR (KBr, cm^{-1}):ν = 3105 (s), 2915 (s), 1592 (s), 1460 (s), 1385 (m), 1301 (m), 1268 (w), 1237 (m), 1196 (s, P═O), 1145 (m), 1104 (s), 1065 (m), 987 (s, P—N), 949 (s, P—N), 890 (m), 866 (m), 821(w), 767 (m), 743 (m), 691 (m), 497 (s). ^{1}H NMR (500.13 MHz, D_6-DMSO, 25°C, TMS): δ = 4.06 (dd, $^3J(H,H) = 7.5$ Hz, $^3J(PNCH) = 10.3$ Hz, 4H, CH_2), 5.28 (d, $^2J(PNH) = 7.7$ Hz, 2H, NH), 6.78–7.55 (m, 14H, Ar—H), 8.09 (b, 1H, NH). ^{13}C NMR (125.76 MHz, D_6-DMSO, 25°C, TMS): δ = 43.75 (s, CH_2), 111.15 (d, $^3J(P,C) = 4.5$ Hz), 115.81 (s), 126.41 (s), 127.12 (s), 127.33 (s), 127.89 (s), 128.09 (s), 128.26 (s), 137.47 (s), 147.54 (s), 154.78 (s). ^{31}P NMR (202.46 MHz, D_6-DMSO, 25°C, H_3PO_4 external): δ = 2.47 (m).

*N-Cyclohexyl-N′,N″-bis(3-aminopyridinyl) Phosphoric Triamide (**4**).* Yield: 85%; mp = 204.9°C. Elemental analysis (%) Calcd: C, 58.01; H, 6.65; N, 21.15. Found: C, 58.03; H, 6.64; N, 21.17. IR (KBr, cm^{-1}): ν = 3425 (m, NH), 3160 (s, NH), 3035 (m), 2865 (s), 1578 (s, ν_{ring}), 1499 (s), 1475 (s), 1393 (m), 1333 (w), 1293 (m), 1238 (w), 1180 (s, P═O), 1125 (w), 1105 (w), 1057 (s, P—N), 929 (s, P—N), 825 (w), 794 (m), 702 (m), 616 (m), 550 (m). ^{1}H NMR (500.13 MHz, D_6-DMSO, 25°C, TMS): 0.96–1.9 (m, 10H, CH_2), 2.78 (m, 1H, CH), 4.28 (m, 1H, $NH_{cyclohexylamine}$), 6.97 (t, $^3J(H,H) = 7.8$ Hz, 2H, Ar—H), 7.18 (d, $^2J(PNH) = 7.2$ Hz, 2H, NH), 7.43 (d, $^3J(H,H) = 7.8$ Hz, 2H, Ar—H), 7.75 (d, $^3J(H,H) = 7.8$ Hz, 2H), 8.28 (s, 2H, Ar—H). ^{13}C NMR (125.76 MHz, D_6-DMSO, 25°C, TMS): 23.84 (s), 24.47 (s), 30.26 (s), 40.16 (s), 122.02 (d, $^3J(P,C) = 5.7$ Hz), 122.92 (s), 138.04 (s), 138.50 (d, $^2J(P,C) = 7.2$ Hz, C_{ipso}), 141.29 (s). ^{31}P NMR (202.46 MHz, D_6-DMSO, 25°C, H_3PO_4 external): –9.20 (m).

*N-4-Nitrophenyl-N′,N″-bis(cyclohexyl) Phosphoric Triamide (**5**).* Yield: 89%; mp = 235.7°C. Elemental analysis (%) Calcd: C, 56.84; H, 7.63; N, 14.74. Found: C, 56.82; H, 7.65; N, 14.72. IR (KBr, cm^{-1}): ν = 3380 (s, NH), 3235 (m, NH), 2905 (s), 1583 (s, NO_2), 1494 (s), 1442 (m), 1417 (w), 1321 (s, NO_2), 1299 (s), 1255 (w), 1183 (s, P═O), 1103 (s, P—N), 1047 (w), 1008 (w), 907 (s, P—N), 840 (w), 745 (w), 655 (w), 612 (w), 557 (w). ^{1}H NMR (500.13 MHz, D_6-DMSO, 25°C, TMS): δ = 0.99–1.22 (m, 10H, CH_2), 1.45–1.86 (m, 10H, CH_2), 2.85 (s, 2H, CH), 4.37 (d, $^2J(PNH) = 10.6$ Hz, 2H, $NH_{cyclohexylamine}$), 7.26 (d, $^3J(H,H) = 9.2$ Hz, 2H, Ar—H), 8.00 (m, 3H, 2Ar—H+ 1NH). ^{13}C NMR (125.76 MHz, D_6-DMSO, 25°C, TMS): δ = 23.84 (s), 24.91 (s), 35.17 (s), 35.32 (s), 49.55 (s), 116.40 (d, $^3J(P,C) = 6.9$ Hz), 124.89 (d, $^2J(P,C) = 10.4$ Hz), 138.86 (s), 150.85 (s). ^{31}P NMR (202.46 MHz, D_6-DMSO, 25°C, H_3PO_4 external): δ = 5.97 (m).

*N-4-nitrophenyl-N′,N″-bis(furfuryl) Phosphoric Triamide (**6**).* Yield: 83%; mp = 135.7°C. Elemental analysis (%) Calcd: C, 51.06; H, 4.52; N, 14.89. Found: C, 51.04; H, 4.53; N, 14.90. IR (KBr, cm^{-1}): 3360 (m, NH), 3195 (s), 2895 (w),1590 (s, NO_2), 1494 (s), 1456 (m), 1335 (s, NO_2), 1298 (s), 1250 (m), 1176 (s, P═O), 1144 (m), 1104 (m, P—N), 1083 (w), 913 (s, P—N), 839 (m), 800 (w), 731 (m), 653 (w). ^{1}H NMR (500.13 MHz, D_6-DMSO, 25°C, TMS): 3.96 (m, 4H, CH_2), 5.15 (d, $^2J(PNH) = 11.1$ Hz, $^3J(H,H) = 6.8$ Hz, 2H, NH), 6.19 (s, 2H, Ar—H), 6.31 (s, 2H, Ar—H), 7.25 (d, $^3J(H,H) = 9.2$ Hz, 2H, Ar—H), 7.48 (d, $^3J(H,H) = 9.2$ Hz, 2H, Ar—H), 8.02 (d, $^3J(H,H) = 9.2$ Hz, 2H), 8.10 (d, $^2J(PNH) = 8.5$ Hz, 1H, NH). ^{13}C NMR (125.76 MHz, D_6-DMSO, 25°C, TMS): 37.23 (s, CH_2), 106.20 (s), 110.22 (s), 116.63 (d, $^3J(P,C) = 7.0$ Hz, nitroaniline), 124.79 (s), 139.29 (s), 141.59 (s), 150.27 (s), 154.01 (d, $^3J(P,C) = 7.2$ Hz, furfuryl). ^{31}P NMR (202.46 MHz, D_6-DMSO, 25°C, H_3PO_4 external): 8.94 (m).

*N,N′-Bis(2-aminopyridinyl) Phosphoramidic Acid (4-methylphenyl) Ester (**7**).* Yield: 84%; mp = 165.5°C. Elemental analysis (%) Calcd: C, 60.00; H, 5.00; N, 16.47. Found: C, 60.01; H, 5.1; N, 16.46. IR (KBr, cm^{-1}): ν = 3405 (w, NH), 3090 (m), 3000 (m), 2920 (m), 1636 (s), 1603 (s), 1543(s), 1496 (m), 1417 (m), 1379 (w), 1276 (m), 1245 (s), 1217 (s, P═O), 1158 (w), 1071 (s, P—N), 1098 (w), 1024 (w), 995 (w), 937 (w), 897 (s, P—N), 822 (m), 798 (m), 762 (m), 720 (w), 675 (m), 618 (m), 533 (m), 520 (m), 490 (m), 468 (w). ^{1}H NMR (500.13 MHz, D_6-DMSO, 25°C, TMS): δ = 2.19 (s, 3H, CH_3), 6.93–7.05 (m, 8H, Ar—H), 7.97 (m, 2H, Ar—H), 8.12 (d, ^{3}J(H,H) = 8.1 Hz, 2H, Ar—H), 9.51 (s, 2H, NH). ^{13}C NMR (125.76 MHz, D_6-DMSO, 25°C, TMS): δ = 20.11 (s, CH_3), 113.91 (s), 114.54 (d, $^3J(P,C)_{amine}$ = 9.0 Hz), 120.32 (d, $^3J(P,C)_{cresol}$ = 4.1 Hz), 129.36 (s), 131.93 (s), 136.68 (s), 144.28 (s), 150.19 (d, $^2J(P,C)_{cresol}$ = 7.7 Hz), 152.72 (s). ^{31}P NMR (202.46 MHz, D_6-DMSO, 25°C, H_3PO_4 external): δ = –8.53 (s).

*N,N′-Bis(3-aminopyridinyl) Phosphoramidic Acid (4-methylphenyl) Ester (**8**).* Yield: 89%; mp = 217.2°C. Elemental analysis (%) Calcd: C, 60.00; H, 5.00; N, 16.47. Found: C, 60.02; H, 4.99; N, 16.48. IR (KBr, cm^{-1}): ν = 3405 (m, NH), 3130 (m), 2940 (m), 1579 (m, ν_{ring}), 1494 (s), 1467 (s), 1396 (m), 1330 (w), 1272 (m), 1212 (s, P═O), 1165 (m), 1127 (w), 1098 (w), 1016 (w), 979 (m, P—N), 947 (s, P—N), 808 (m), 748 (w), 698 (m), 609 (w), 557 (m), 492 (m). ^{1}H NMR (500.13 MHz, D_6-DMSO, 25°C, TMS): δ = 2.24 (s, 3H, CH_3), 7.08 (d, ^{3}J(H,H) = 8.0 Hz, 2H, Ar—H), 7.15 (d, ^{3}J(H,H) = 8.0 Hz, 2H, Ar—H), 7.22 (m, 4H, Ar—H), 8.08 (d, ^{3}J(H,H) = 8.2 Hz, 2H, Ar—H), 8.37 (s, 2H, Ar—H), 8.76 (d, ^{2}J(PNH) = 9.5 Hz, 2H, NH). ^{13}C NMR (125.76 MHz, D_6-DMSO, 25°C, TMS): δ = 20.22 (s, CH_3), 120.06 (d, $^3J(P,C)_{cresol}$ = 4.5 Hz), 123.76 (s), 124.00 (d, $^3J(P,C)_{amine}$ = 7.0 Hz), 130.14 (s), 134.14 (s), 137.29 (s), 139.25 (d, $^2J(P,C)_{amine}$ = 8.9 Hz), 142.09 (s), 147.70 (s). ^{31}P NMR (202.46 MHz, D_6-DMSO, 25°C, H_3PO_4 external): δ = –2.10 (t, ^{2}J(PNH) = 9.5 Hz).

*N,N′-Bis(4-aminopyridinyl) Phosphoramidic Acid (4-methylphenyl) Ester (**9**).* Yield: 92%; mp = 224.9°C. Elemental analysis (%) Calcd: C, 60.00; H, 5.00; N, 16.47. Found: C, 59.99; H, 5.01; N, 16.48. IR (KBr, cm^{-1}): ν = 3385 (w, NH), 3175 (m), 1597 (s), 1501 (s), 1459 (m), 1400 (w), 1326 (m), 1279 (m), 1240 (m), 1212 (s, P═O), 1164 (m), 1000 (s, P—N), 974 (m), 942 (s, P—N), 812 (m), 557 (w), 501 (m). ^{1}H NMR (500.13 MHz, D_6-DMSO, 25°C, TMS): δ = 2.24 (s, 3H, CH_3), 7.05–7.18 (m, 8H, Ar—H), 8.26 (m, 4H, Ar—H), 9.17 (s, 2H, NH). ^{13}C NMR (125.76 MHz, D_6-DMSO, 25°C, TMS): δ = 20.20 (s, CH_3), 112.18 (d, $^3J(P,C)_{amine}$ = 6.8 Hz), 120.03 (d, $^3J(P,C)_{cresol}$ = 4.5 Hz), 130.17 (s), 134.34 (s), 147.47 (s), 147.69 (s), 150.04 (s). ^{31}P NMR (202.46 MHz, D_6-DMSO, 25°C, H_3PO_4 external): δ = –3.9 (s).

*N,N′-Bis(2-amino-5-nitro Pyridinyl) Phosphoramidic Acid (4-methylphenyl) Ester (**10**).* Yield: 96%; mp = 164.8°C. Elemental analysis (%) Calcd: C, 47.44; H, 3.49; N, 19.53. Found: C, 47.42; H, 3.50; N, 19.51. IR (KBr, cm^{-1}): ν = 3370 (w, NH), 3225 (m, NH), 3100 (m, CH), 3000 (m), 2745 (w), 1668 (s), 1587 (m, NO_2), 1494 (s), 1346 (s, NO_2), 1283 (m), 1238 (w), 1219 (s, P═O), 1157 (w), 1113 (w), 1072 (s, P—N), 990 (w), 908 (m, P—N), 830 (m), 759 (w), 718 (w), 631 (m), 545 (m), 488 (m). ^{1}H NMR (500.13 MHz, D_6-DMSO, 25°C, TMS): δ = 2.20 (s, 3H, CH_3), 6.53 (d, ^{3}J(H,H) = 8.9 Hz, 1H), 7.04 (m, 4H, Ar—H of cresol), 7.13 (d, ^{3}J(H,H) = 8.9 Hz, 1H), 8.12 (d, ^{3}J(H,H) = 8.1 Hz, 1H), 8.38 (d, ^{3}J(H,H) = 8.1 Hz, 1H), 8.83 (s, 1H), 9.02 (s, 1H), 9.55 (s, 2H, NH). ^{13}C NMR (125.76 MHz, D_6-DMSO, 25°C, TMS): δ = 20.22 (s, CH_3), 107.76 (s), 110.74 (d, $^3J(P,C)_{amine}$ = 6.0 Hz), 120.11 (d, $^3J(P,C)_{cresol}$ = 4.0 Hz), 129.75 (s), 132.95 (s), 133.38 (s), 133.61 (s), 134.43 (s), 137.91 (s), 144.86 (s), 146.17 (s), 148.81 (d, $^2J(P,C)_{cresol}$ = 6.9 Hz), 159.11 (s), 162.64 (s). ^{31}P NMR (202.46 MHz, D_6-DMSO, 25°C, H_3PO_4 external): δ = –7.42 (s).

SUPPLEMENTARY INFORMATION

Crystallographic data for the structure **7** have been deposited with Cambridge Crystallographic Data Center as supplementary publication no. CCDC 727893 ($C_{17}H_{17}N_4O_2P_1$). Copies of the data may be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033; E-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

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