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Synthesis of Phosphoramidates Based on Aminopyridines

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Abstract—Reaction of diethyl chlorophosphate with aminopyridines furnished a series of new diethyl phosphoramidates. The effect on the reactivity of substituents in the pyridine ring was studied. Structure of the obtained compound was characterized by ^{1}H, ^{13}C, ^{31}P, 2D HMBC ^{1}H–^{15}N NMR spectroscopy, mass-spectrometry, and single crystal X-ray diffraction analysis.

Keywords: diethyl chlorophosphate, phosphoramidates, aminopyridines, phosphorylation

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Phosphorus-containing compounds are an important field of applied chemistry due to their use in medicine and agriculture as fertilizers, pesticides, and plant growth regulators [1, 2].

Recently, the interest of researchers in amidophosphates has noticeably increased due to their high lyophilicity. In medicinal chemistry, they are used as prodrugs to significantly improve the therapeutic potential of the parent drugs [3, 4]. Thus, more than ten nucleoside amidophosphate prodrugs have been tested *in vitro* as potential drugs for the treatment of viral infections of herpes, varicella, and cytomegalovirus [5]. Amidophosphates can be used as peptide-nucleotide antibiotics with various biological activities [6]. In addition, the possibility of their use as flame retardants [7, 8] and abscisic acid agonists [9] has been found.

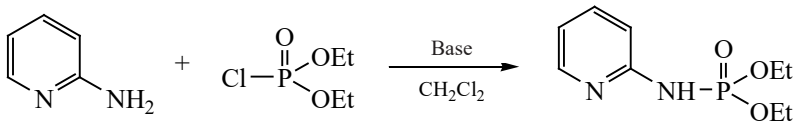
The targeted synthesis of biologically active amidophosphates with desired properties has been reported [10–12]. As part of these studies, several series of heterocyclic phosphoramidates (including pyridinones) were obtained, which exhibited inhibitory activity against the α-amylase enzyme.

It has been shown that the identification of low-molecular-weight metabolites using MALDI-TOF mass spectrometry can be facilitated by their derivatization by *N*-phosphorylation, which improves the efficiency of ionization, as well as suppresses matrix-related ion effects due to the high proton affinity in the gas phase of the phosphoryl group [13].

The possibility of using amidophosphates as precursors in the synthesis of azetidines has been shown [14, 15]. In addition, amidophosphates are important scaffolds in many biologically active molecules [16] and in some industrially significant reactions of alkene hydroamination [17]. In recent years, amidophosphates have been used as ligands for catalytic reactions that limit the rate of the initial nucleoside phosphorylation step. Chinese researchers [18] used chiral amidophosphates as organocatalysts for some reactions, such as the addition of oxindoles to nitrostyrenes or the Michael reaction of fluorinated silyl enol ethers [19]. It was recently found that chiral pyridinium phosphoramidates are effective catalysts in the Diels–Alder reaction [20]. It is worth noting the tendency of amidophosphates to spontaneous enzymatic hydrolysis and the ability of molecules with a P–N bond to integrate into the natural nucleotides structure [21].

However, despite the wide practical use of amidophosphates, methods for their preparation are limited. Historically, the first method is the aminolysis of chlorophosphates [22], which was subsequently modified by *in situ* generation of chlorophosphate (Todd–Atherton reaction) [23]. Amidophosphates can also be obtained by the reaction of trialkyl phosphites with organic azides

Table 1. Effect of the reaction conditions on conversion[a] of aminopyridine **1a**



1a **2** **3a**

Entry	Base	Temperature, °C	Time, h	Conversion, %
1	K_2CO_3	40	7	100
2	K_2CO_3	25	20	100
3	Et_3N	40	12	100
4	MgO	40	24	0
5	Py	40	24	20

[a] The preparative yield is somewhat lower.

generated *in situ* from a halogen derivative and sodium azide [24]. Amidophosphates can be obtained in good yield by the reaction of arenes with phosphorylated azides [25]. Recently, a direct route was proposed for the preparation of amidophosphates by the photoactivated reaction of amines with trialkyl phosphite in the presence of organic dyes [26]. A number of reports have shown the possibility of using iodine as a catalyst for the phosphorylation of amines with dialkyl [27, 28] and trialkyl phosphites [29].

In our studies, diethyl chlorophosphate was used as a phosphorylating agent due to its availability and high reactivity. Diethyl chlorophosphate is a versatile reagent that can be used as a mild phosphorylating [30, 31] and crosslinking agent [32–34]. Its ability to form mixed anhydrides with carboxylic acids is often used for the synthesis of esters and amides [35–37].

Aminopyridines, which are widely used in the design of synthetic biologically active compounds, were chosen as the substrates [38–40]. Some representatives of pyridin-2-ylphosphoramidates have been obtained by the Todd–Atherton reaction, and their antibacterial activity has been shown [41]. However, the effect of substituents in the pyridine ring on the yield of target amidophosphates has not been studied.

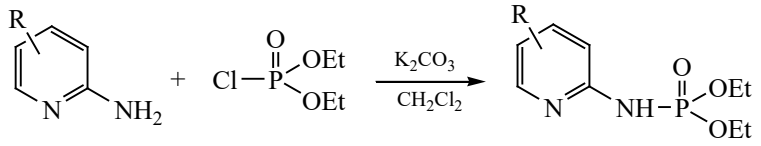
Herein, we reported a study of a new reaction of diethyl chlorophosphate with aminopyridines, the pharmacophoric properties of which suggest, in combination with a phosphorus group, a wide biological activity of the final amidophosphates.

The reaction took place at room temperature with vigorous stirring of the reagents in anhydrous solvent (methylene chloride, benzene) in the presence of a base (triethylamine, pyridine, potassium carbonate). It is well known that acylation [42, 43] of 2-aminopyridines with carboxylic acid chlorides leads to the formation of acylaminopyridines exclusively. This suggests that phosphorylation may proceed in the same direction.

It should be noted that the reaction is very sensitive to the presence of even trace amounts of moisture both in the solvent and in the air. The bases catalyze the rapid hydrolysis of the starting diethyl chlorophosphate to diethyl phosphate, which leads through its reaction with diethyl chlorophosphate to the formation of tetraethyl pyrophosphate. Therefore, carrying out the reaction is difficult and requires great care in its implementation. The reaction progress was monitored by ^{31}P NMR spectroscopy. The results obtained are presented in Table 1.

The optimal conditions for the reaction of 2-aminopyridines **1a**–**1h** with diethyl chlorophosphate **2** are the use of methylene chloride as a solvent and K_2CO_3 as a base (Scheme 1). The undoubted advantage of using K_2CO_3, in comparison with triethylamine, is the facilitation of the isolation of the final product. The yield of target diethyl (pyridin-2-yl)phosphoramidates **3a**–**3h** was 73–95%. The substituent nature in the aminopyridine ring is expected to influence the reaction time. Aminopyridines with donor substituents in the pyridine ring are more reactive in reactions with diethyl chlorophosphate than their analogues with acceptor groups. Thus, complete

Scheme 1.



R = H (**a**), 5-Cl (**b**), 5-Br (**c**), 3-Me (**d**), 4-Me (**e**), 6-Me (**f**), 5-CF_3 (**g**), 6-NH_2 (**h**), 3-NH_2 (**i**), 4-NH_2 (**j**).

conversion of aminopyridines with donor substituents is achieved by boiling for 7 h. A similar reaction with 2-amino-5-trifluoromethylpyridine **1g** reaches complete conversion in 24 h. Due to low conversion, the product could not be isolated. When carrying out the reaction with 2-amino-6-bromopyridine, no products were detected in the ^{31}P NMR spectrum of the reaction mixture. This suggests the reaction path through the primary attack on the pyridine nitrogen atom with further migration of the phosphoryl residue to the exocyclic nitrogen.

The reaction with 3- and 4-aminopyridines proceeds similarly, leading to the formation of pyridin-3(4)-ylamidophosphates **3i** and **3j**, respectively. It should be noted that amidophosphate **3i** has been reported earlier [44, 45], but no spectral data were presented.

It was expected that the reaction of 2,6-diaminopyridine **1h** with diethyl chlorophosphate could proceed with the participation of both NH_2 groups. However, the use of a 2-fold excess of phosphorylating agent **2** resulted in the formation of a monophosphorylation product. The formation of only one P–N covalent bond was determined using single crystal X-ray diffraction analysis data. Amidophosphate **3h** was isolated as a diethylphosphoric acid salt, which was confirmed by ^{31}P NMR data. The chemical shift of phosphorus at the exocyclic nitrogen atom is –1.69 ppm, while the diethyl phosphate residue of the counterion resonates at 0.00 ppm, which was confirmed by ^{1}H–^{31}P HMBC data. The assignment of chemical shifts in the ^{1}H NMR spectrum was done using the ^{1}H–^{15}N HMBC technique. Thus, the presence of a cross peak of the H^5 proton (6.32 ppm) with the NH_2 group indicates its position in a stronger field relative to the H^3 proton (6.50 ppm).

The resulting amidophosphates generally have a crystalline structure and good solubility in water. Their structure was proved by the ^{1}H, ^{13}C, ^{31}P, ^{15}N NMR spectroscopy methods. For example, in the ^{1}H NMR spectrum of amidophosphate **3a**, in addition to the characteristic signals of ethoxyl groups in the phosphoryl fragment, there are doublet signals of H^3 (7.13 ppm, $^{3}J_{HH}$ 8.3 Hz) and H^6 (8.38 ppm, $^{3}J_{HH}$ 4.7 Hz) protons and more complex spectral pattern for the H^4 (7.60 ppm, $^{3}J_{HH}$ 8.3, $^{3}J_{HH}$ 8.5 Hz) and H^5 protons (6.89 ppm, $^{3}J_{HH}$ 4.2, $^{3}J_{HH}$ 8.5 Hz). The ^{13}C NMR spectrum of amidophosphate **3a** showed doublet signals of C^6 (147.99 ppm, $^{4}J_{CP}$ 2.7 Hz) and C^2 atoms (153.61 ppm, $^{2}J_{CP}$ 6.4 Hz). Structure of amidophosphates **3b**, **3d**, and **3h** was unambiguously confirmed by single crystal X-ray diffraction analysis data (Fig. 1).

In conclusion, a possibility of obtaining pyridinyl amidophosphates by the chemoselective reaction of diethyl chlorophosphate with aminopyridines was shown.

EXPERIMENTAL

^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded on a Bruker Avance III HD 400 NanoBay spectrometer operating at 400.17, 100.63, and 162.01 MHz, respectively. $CDCl_3$ was used as a solvent. Chemical shifts of the phosphorus were given relative to the external 85% phosphoric acid. Signals in the ^{1}H and ^{13}C NMR spectra were assigned using the methods of two-dimensional heteronuclear spectroscopy (HMBC). High-resolution mass spectra (ESI) were recorded on a Bruker MicrOTOF mass spectrometer (ionization chamber temperature was 180°C; ionization voltage was 70 and 100 eV). Melting points were measured on a Kofler table (VEB Wägetechnik Rapido, PHMK 81/2969). Single crystal X-ray diffraction analysis was performed on a Rigaku Oxford Diffraction XtaLAB Synergy-S HyPix-6000HE diffractometer at 100 K. The data were integrated using the CrysAlisPro software package [46]. The structures were solved using the double space algorithm and refined

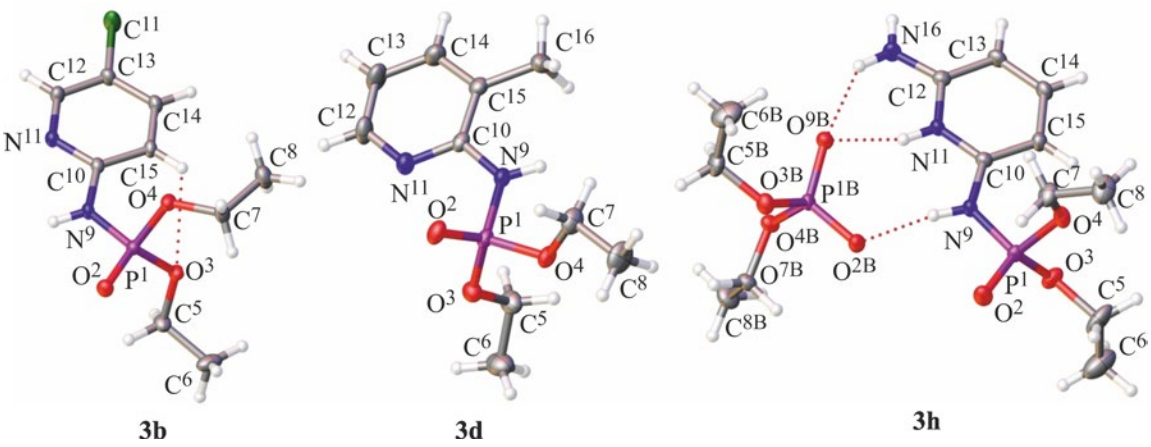


Fig. 1. ORTEP representations of molecular structure of compounds **3b**, **3d** and **3h** with 50% probability thermal ellipsoids. The dotted lines show hydrogen bonding.

using the SHELX programs [47, 48] built into the OLEX2 complex [49]. The positions of hydrogen atoms were calculated using the algorithms implemented into the SHELX software package, where $U_{iso}(H) = 1.5U_{eq}(C)$ and C–H 0.98 Å for CH_3 groups, $U_{iso}(H) = 1.2U_{eq}(C)$ and C–H 0.99 Å for CH_2 groups, $U_{iso}(H) = 1.2U_{eq}(C)$ and C–H 0.95 Å for CH groups of cyclic fragments, $U_{iso}(H) = 1.2U_{eq}(N)$ and N–H 0.88 Å for NH groups and $U_{iso}(H) = 1.2U_{eq}(N)$ and N–H 0.86 Å for NH_2 groups. Crystallographic data were deposited at the Cambridge Crystallographic Data Center [CCDC 2182498 (**3b**), 2182499 (**3d**), 2182911 (**3h**)].

General procedure for the synthesis of amidophosphates. To a solution of 1 mmol of aminopyridine **1a**–**1j** in 5 mL of anhydrous methylene chloride was added 1.1 mmol of freshly calcined anhydrous K_2CO_3 or triethylamine and 1.2 mmol of diethyl chlorophosphate. The reaction mixture was vigorously stirred at reflux until the reaction was complete (^{31}P NMR control). The reaction product was extracted with water, which was removed in vacuum. The residue was recrystallized from ethyl acetate or an ethyl acetate–isooctane mixture, 2 : 1.

Diethyl (pyridin-2-yl)phosphoramidate (3a). Yield 92%, mp 92–93°C, white crystals. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.23 t (6H, C$\underline{H}_3$CH$_2$O, $^3J_{HH}$ 7.1 Hz), 4.11 m (4H, CH$_3$C$\underline{H}_2$O), 6.80 d. d (1H, ^{5}H, $^3J_{HH}$ 4.2, $^3J_{HH}$ 8.5 Hz), 7.07 d (1H, ^{3}H, $^3J_{HH}$ 8.3 Hz), 7.51 m (1H, ^{4}H), 8.35 d (1H, ^{6}H, $^3J_{HH}$ 4.2 Hz), 9.36 br. s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 16.12 d (C$\underline{H}_3$CH$_2$O, $^3J_{CP}$ 7.1 Hz), 62.80 d (CH$_3$C$\underline{H}_2$O, $^2J_{CP}$ 5.1 Hz), 110.98 (^{5}C), 116.76 (^{3}C), 138.36 (^{4}C), 147.98 d (^{6}C, $^4J_{CP}$ 2.7 Hz), 153.88 d (^{2}C, $^2J_{CP}$ 6.4 Hz). ^{31}P NMR spectrum: δ_P 0.87 ppm. Mass spectrum (HRMS-ESI), *m*/*z*: 231.0897 $[M + H]^+$ (calculated for $C_9H_{16}N_2O_3P^+$: 231.0893). Spectral characteristics are similar to those described earlier [29].

Diethyl (5-chloropyridin-2-yl)phosphoramidate (3b). Yield 95%, white crystals, mp 103–104°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.35 t (6H, C$\underline{H}_3$CH$_2$O, $^3J_{HH}$ 7.0 Hz), 4.18 m (4H, CH$_3$C$\underline{H}_2$O), 7.09 d (1H, ^{3}H, $^3J_{HH}$ 8.9 Hz), 7.56 d. d (1H, ^{4}H, $^3J_{HH}$ 8.9, $^4J_{HH}$ 2.6 Hz), 7.78 br. s (1H, NH), 8.29 d (1H, ^{6}H, $^4J_{HH}$ 2.6 Hz). ^{13}C NMR spectrum, δ_C, ppm: 16.08 d (C$\underline{H}_3$CH$_2$O, $^3J_{CP}$ 7.1 Hz), 63.29 d (CH$_3$C$\underline{H}_2$O, $^2J_{CP}$ 5.0 Hz), 111.68 (^{3}C), 124.48 (^{5}C), 138.06 (^{4}C), 146.79 d (^{6}C, $^4J_{CP}$ 2.4 Hz), 151.93 d (^{2}C, $^2J_{CP}$ 3.2 Hz). ^{31}P NMR spectrum: δ_P 0.31 ppm. Mass spectrum (HRMS-ESI), *m*/*z*: 265.0508 $[M + H]^+$ (calculated for $C_9H_{15}N_2O_3PCl^+$: 265.0503). X-ray diffraction data: $C_9H_{14}ClN_2O_3P$, space group $P2_1/n$, *a* 9.3134(2), *b* 24.7216(6), *c* 16.3383(4) Å; β 101.390(2)°, *V* 3687.68(15) Å^3, *Z* 12, d_{calc} 1.430 g/cm^3, μ(MoK_α) 0.435 mm^{-1}, R_1 0.0381 and wR_2 0.1012 (for 8926 $|F_o| \geq 4\sigma F$).

Diethyl (5-bromopyridin-2-yl)phosphoramidate (3c). Yield 91%, white crystals, mp 40–41°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.36 d (6H, C$\underline{H}_3$CH$_2$O, $^3J_{HH}$ 7.1 Hz), 4.22 m (4H, CH$_3$C$\underline{H}_2$O), 6.68 br. s (1H, NH), 7.05 d (1H, ^{3}H, $^3J_{HH}$ 8.8 Hz), 7.70 d. d (1H, ^{4}H, $^3J_{HH}$ 8.8, $^4J_{HH}$ 2.5 Hz), 8.32 d (1H, ^{6}H, $^4J_{HH}$ 2.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 16.15 d (C$\underline{H}_3$CH$_2$O, $^3J_{CP}$ 7.0 Hz), 63.37 d (CH$_3$C$\underline{H}_2$O, $^2J_{CP}$ 5.2 Hz), 112.08 (^{3}C), 112.33

(^{5}C), 140.65 (^{4}C), 149.13 d (^{6}C, $^4J_{CP}$ 2.4 Hz), 151.91 d (^{2}C, $^2J_{CP}$ 6.4 Hz). ^{31}P NMR spectrum: δ_P –0.22 ppm.

Diethyl (3-methylpyridin-2-yl)phosphoramidate (3d). Yield 86%, white crystals, mp 79–80°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.34 t (6H, C$\underline{H}_3$CH$_2$O, $^3J_{HH}$ 7.2 Hz), 2.22 s (3H, CH$_3$), 4.23 m (4H, CH$_3$C$\underline{H}_2$O), 5.50 br. s (1H, NH), 6.80 d. d (1H, ^{5}H, $^3J_{HH}$ 7.0, $^3J_{HH}$ 4.3 Hz), 7.38 d. d (1H, ^{4}H, $^3J_{HH}$ 7.0, $^4J_{HH}$ 1.0 Hz), 8.13 d (1H, ^{6}H, $^3J_{HH}$4.3 Hz). ^{13}C NMR spectrum, δ_C, ppm: 16.16 d (C$\underline{H}_3$CH$_2$O, $^3J_{CP}$ 7.2 Hz), 17.29 (CH$_3$), 63.26 d (CH$_3$C$\underline{H}_2$O, $^2J_{CP}$ 5.6 Hz), 117.10 (^{5}C), 118.80 (^{3}C), 138.32 (^{4}C), 145.85 (^{6}C), 152.00 d (^{2}C). ^{31}P NMR spectrum: δ_P 0.92 ppm. Mass spectrum (HRMS-ESI), *m/z*: 245.1055 $[M + H]^+$ (calculated for $C_{10}H_{18}N_2O_3P^+$: 245.1050). X-ray diffraction data: $C_{10}H_{17}N_2O_3P$, space group *Cc*, *a* 10.7812(3), *b* 14.3252(3), *c* 17.1110(4) Å, β 108.293(3)°, *V* 2509.13(12) Å^3, *Z* 8, d_{calc} 1.293 g/cm^3, μ(MoK_α) 0.214 mm^{-1}, R_1 0.0290 and wR_2 0.0750 (for 6364 $|F_o| \geq 4\sigma F$).

Diethyl(4-methylpyridin-2-yl)phosphoramidate (3e). Yield 88%, white crystals, mp 73–74°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.33 t (6H, C$\underline{H}_3$CH$_2$O, $^3J_{HH}$ 7.1 Hz), 2.31 s (3H, CH$_3$), 4.17 m (4H, CH$_3$C$\underline{H}_2$O), 6.72 d (1H, ^{5}H, $^3J_{HH}$ 5.2 Hz), 6.96 s (1H, ^{3}H), 8.22 d (1H, ^{6}H, $^3J_{HH}$ 5.2 Hz), 8.55 br. s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 16.13 d (C$\underline{H}_3$CH$_2$O, $^3J_{CP}$ 6.9 Hz), 21.32 (CH$_3$), 62.91 d (CH$_3$C$\underline{H}_2$O, $^2J_{CP}$ 4.9 Hz), 111.19 (^{5}C), 118.36 (^{3}C), 147.80 d (^{6}C, $^4J_{CP}$ 2.6 Hz), 149.65 (^{4}C), 153.70 d (^{2}C, $^2J_{CP}$ 6.6 Hz). ^{31}P NMR spectrum: δ_P 0.18 ppm. Mass spectrum (HRMS-ESI), *m/z*: 245.1054 $[M + H]^+$ (calculated for $C_{10}H_{18}N_2O_3P^+$: 245.1050).

Diethyl (6-methylpyridin-2-yl)phosphoramidate (3f). Yield 93%, yellowish oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.38 t (6H, C$\underline{H}_3$CH$_2$O, $^3J_{HH}$ 7.1 Hz,), 2.64 s (3H, CH$_3$), 4.24 m (6H, CH$_3$C$\underline{H}_2$O, $^3J_{HH}$ 7.2, $^3J_{HP}$ 10.1 Hz), 6.91 d (1H, ^{5}H, $^3J_{HH}$ 7.0 Hz), 7.57 d (1H, ^{3}H, $^3J_{HH}$ 8.7 Hz), 7.83 m (1H, ^{4}H, $^3J_{HH}$ 8.7, $^3J_{HH}$ 7.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 16.14 d (C$\underline{H}_3$CH$_2$O, $^3J_{CP}$ 7.1 Hz), 19.20 (CH$_3$), 63.30 (CH$_3$C$\underline{H}_2$O, $^2J_{CP}$ 5.6 Hz), 110.64 (^{5}C), 116.67 (^{3}C), 139.07 (^{4}C), 152.21 d (^{2}C, $^2J_{CP}$ 6.9 Hz), 155.32 (^{6}C). ^{31}P NMR spectrum: δ_P 0.83 ppm.

Diethyl (5-trifluoromethylpyridin-2-yl)phosphoramidate (3g). Yield 82%, yellowish oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.35 t (6H, C$\underline{H}_3$CH$_2$O, $^3J_{HH}$ 7.1 Hz), 4.11–4.29 m (4H, CH$_3$C$\underline{H}_2$O), 7.22 d (1H, ^{3}H, $^3J_{HH}$ 8.8 Hz), 7.80 d. d (1H, ^{4}H, $^3J_{HH}$ 8.8, $^4J_{HH}$ 2.5 Hz), 8.60 s (1H, ^{6}H). ^{13}C NMR spectrum, δ_C, ppm: 15.84 d (C$\underline{H}_3$CH$_2$O, $^3J_{CP}$ 7.2 Hz), 63.32 d (CH$_3$C$\underline{H}_2$O, $^2J_{CP}$ 5.1 Hz), 63.00 d (CH$_3$C$\underline{H}_2$O, $^2J_{CP}$ 5.2 Hz), 110.70 d (^{3}C, $^3J_{CP}$ 3.2 Hz), 119.62 q (^{5}C, $^2J_{CF}$ 33.1 Hz), 123.78 q (CF$_3$, $^1J_{CF}$ 270.9 Hz), 135.32 q (^{4}C, $^3J_{CF}$ 3.5 Hz), 145.62 q (^{6}C, $^3J_{CF}$ 2.7 Hz), 156.65 d (^{2}C, $^2J_{CP}$ 5.8 Hz). ^{31}P NMR spectrum: δ_P –0.12 ppm.

2-Amino-6-[(diethoxyphosphoryl)amino]-pyridinium diethyl phosphate (3h). Yield 73%, white crystals, mp 143–144°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.27 t (6H, C$\underline{H}_3$CH$_2$O, $^3J_{HH}$ 7.1 Hz), 1.32 t (6H, C$\underline{H}_3$CH$_2$O, $^3J_{HH}$ 7.1 Hz), 3.97 d. t (4H, CH$_3$C$\underline{H}_2$O, $^3J_{HH}$ 7.1, $^3J_{HP}$ 7.1 Hz), 4.12–4.20 m (4H, CH$_3$C$\underline{H}_2$O, $^3J_{HH}$ 7.1, $^3J_{HP}$ 10.1 Hz), 6.32 d (1H, ^{5}H, $^3J_{HH}$ 8.50 Hz), 6.50 d (1H, ^{3}H, $^3J_{HH}$ 8.1Hz), 7.46 t (1H, ^{4}H, 8.3 Hz). ^{13}C NMR spectrum, δ_C, ppm: 16.04 d (C$\underline{H}_3$CH$_2$O, $^3J_{CP}$ 7.0 Hz), 16.39 d (C$\underline{H}_3$CH$_2$O, $^3J_{CP}$ 7.3 Hz), 61.62 (CH$_3$C$\underline{H}_2$O, $^2J_{CP}$ 5.7 Hz), 63.88 (CH$_3$C$\underline{H}_2$O, $^2J_{CP}$ 5.7 Hz), 97.85 (^{3}C), 102.30 (^{5}C), 144.11 (^{4}C), 147.11 d (^{2}C, $^2J_{CP}$ 9.6 Hz), 154.10 (^{6}C). ^{31}P NMR spectrum, δ_P, ppm: –1.69, 0.00. X-ray diffraction data: $(C_9H_{17}N_3O_3P)\cdot(C_4H_{10}O_4P)$, space group $P2_1/n$, *a* 9.7315(2), *b* 12.8348(3), *c* 31.4508(8) Å, β 98.804(2)°, *V* 3881.98(17) Å^3, *Z* 8, d_{calc} 1.366 g/cm^3, μ(MoK_α) 0.262 мм$^{-1}$, R_1 0.0438 and wR_2 0.1082 (for 7160 $|F_o| \geq 4\sigma F$).

Diethyl (pyridin-3-yl)phosphoramidate (3i). Yield 94%, white crystals, mp 105–107°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.36 t (6H, C$\underline{H}_3$CH$_2$O, $^3J_{HH}$ 7.1 Hz), 4.18–4.27 m (4H, CH$_3$C$\underline{H}_2$O), 7.79 d. d (1H, ^{5}H, $^3J_{HH}$ 8.7, $^3J_{HH}$ 5.5 Hz), 8.31 d (1H, ^{4}H, $^3J_{HH}$ 5.5 Hz), 8.51 d (1H, ^{6}H, $^3J_{HH}$ 8.7 Hz), 9.12 s (1H, ^{2}H), 9.38 d (1H, NH, $^2J_{HP}$ 7.9 Hz). ^{13}C NMR spectrum, δ_C, ppm: 16.13 d (C$\underline{H}_3$CH$_2$O, $^3J_{CP}$ 6.9 Hz), 64.12 d (CH$_3$C$\underline{H}_2$O, $^2J_{CP}$ 5.7 Hz), 127.07 (^{5}C), 130.48 d (^{4}C, $^3J_{CP}$ 12.4 Hz), 131.71 (^{6}C), 132.75 d (^{2}C, $^3J_{CP}$ 4.3 Hz), 142.94 d (^{3}C, $^2J_{CP}$ 3.4 Hz). ^{31}P NMR spectrum: δ_P –0.87 ppm.

Diethyl(pyridin-4-yl)phosphoramidate (3k). Yield 90%, white crystals, mp 143–144°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.37 t (6H, C$\underline{H}_3$CH$_2$O, $^3J_{HH}$ 7.1 Hz), 4.22–4.28 m (4H, CH$_3$C$\underline{H}_2$O), 7.87 d (2H, ^{3,5}H, $^3J_{HH}$ 6.5 Hz), 8.42 d (2H, ^{2,6}H, $^3J_{HH}$ 6.5 Hz), 10.45 d (1H, NH, $^2J_{HP}$ 8.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 16.13 d (C$\underline{H}_3$CH$_2$O, $^3J_{CP}$ 6.9 Hz), 64.43 d (CH$_3$C$\underline{H}_2$O, $^2J_{CP}$ 5.5 Hz), 113.84 d (^{3,5}C, $^3J_{CP}$ 8.1 Hz), 140.31 (^{2,6}C), 157.66 d (^{4}C, $^2J_{CP}$ 1.9 Hz). ^{31}P NMR spectrum: δ_P –2.34 ppm.

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CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

SUPPLEMENTARY INFORMATION

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