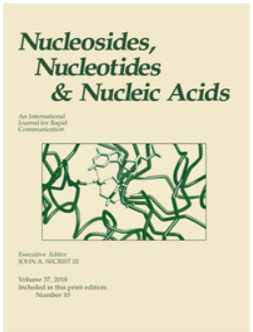

Nucleosides, Nucleotides and Nucleic Acids

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Design, synthesis and antiviral evaluation of novel acyclic phosphonate nucleotide analogs with triazolo[4,5-*b*]pyridine, imidazo[4,5-*b*]pyridine and imidazo[4,5-*b*]pyridin-2(3*H*)-one systems

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ABSTRACT

A new series of phosphonylated triazolo[4,5-*b*]pyridine (1-deaza-8-azapurine), imidazo[4,5-*b*]pyridine (1-deazapurine) and imidazo[4,5-*b*]pyridin-2(3*H*)-one (1-deazapurin-8-one) were synthesized from 2-chloro-3-nitropyridine and selected diethyl ω-aminoalkylphosphonates followed by reduction of the nitro group and cyclization. In the final step *O,O*-diethylphosphonates were transformed into the corresponding phosphonic acids. All synthesized compounds were evaluated *in vitro* for inhibitory activity against a broad variety of DNA and RNA viruses and their cytotoxic potencies were also established. Compound **12f** showed marginal activity against cytomegalovirus Davis strain ($EC_{50} = 76.47\ \mu M$) in human embryonic lung (HEL) cells while compounds **10g** ($EC_{50} = 52.53\ \mu M$) and **12l** ($EC_{50} = 61.70\ \mu M$) were minimally active against the varicella-zoster virus Oka strain in HEL cells. Compounds under investigation were not cytotoxic at the maximum concentration evaluated (100 μM).

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Aminoalkylophosphonates; acyclonucleotides; synthesis; antiviral activity

1. Introduction

Acyclic nucleoside phosphonates (ANPs) are structural analogs of nucleoside monophosphates in which aliphatic chain plays the role of a furanose ring and the isosteric and isoelectronic oxymethylphosphonate (phosphorylmethoxy) moiety [$(HO)_2P(O)–CH_2–O$] replaces the naturally occurring labile phosphate moiety [$(HO)_2P(O)–O–C(5')$].[1,2] ANPs are known since 1986 when (*S*)-9-(3-hydroxy-2-phosphonylmethoxypropyl)adenine [(*S*)-HPMPA] (Figure 1) has been synthesized and its promising antiviral activity towards DNA and RNA viruses was revealed.[3] Since then various ANPs have been obtained and several compounds have been recognized to

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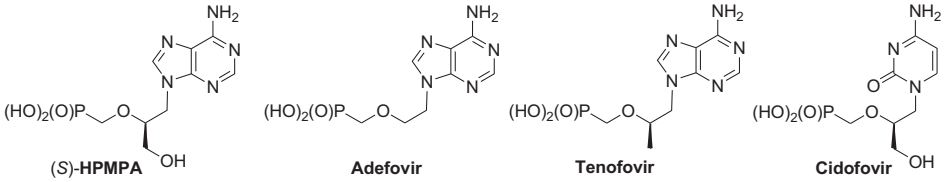


Figure 1. Acyclic nucleoside phosphonates with antiviral activity.

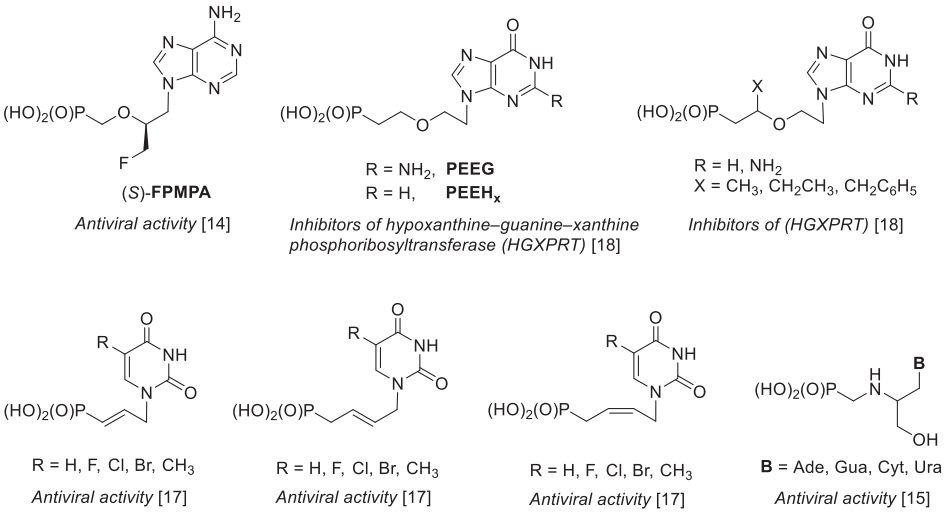


Figure 2. Acyclic nucleoside phosphonates (ANPs) with modified carbon linkers.

possess a broad spectrum of antiviral and cytostatic activities with already proved mechanism of action.[4–9] Among them, adefovir, tenofovir and cidofovir (Figure 1) as well as their prodrugs are currently applied as pharmaceuticals in the treatment of viral infections.[6–11]

However, emergence of mutant viruses after long-term treatment with antiviral drugs may result in lower sensitivity of viruses to chemotherapeutics (drug resistance) which is an important problem in the treatment of viral infections.[11–13] For this reason, a search for new antiviral compounds has been continuing for many years. Many acyclic nucleotide analogs have been synthesized and both the aliphatic chain and the nucleobase unit were altered. Modifications of the aliphatic chain are possible through carbon-chain lengthening, branching and incorporation of nitrogen, oxygen, sulfur, fluorine atoms, or the unsaturated bonds into their structures (Figure 2).[14–19]

On the other hand, modifications a purine unit were accomplished in several ways, for example, by construction of 8-azapurine analogs [1,2,3-triazolo[4,5-*d*]pyrimidines] *via* replacement of C8 with the nitrogen atom.[20–24] Various 1-, 3-, or 7-deazapurine analogs were obtained by substitution of the respective nitrogen atoms of purine moiety by the methine

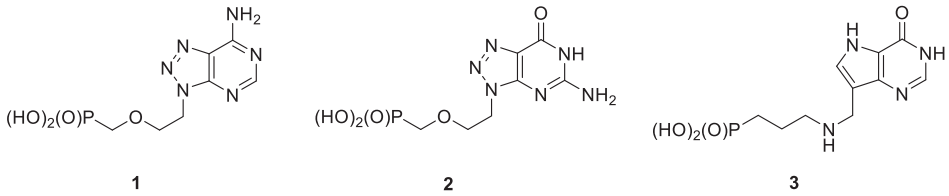


Figure 3. Examples of 8-aza and deazapurine nucleotides.

group without changes of the steric demands in the newly formed systems (Figure 3).[25–27]

For example, compound **1** exhibited inhibitory effect on the DNA viruses herpes simplex virus 1 (HSV-1), HSV-2, cytomegalovirus (CMV) ($IC_{50} = 0.4–3.5\,\mu g/mL$), varicella zoster virus (VZV) ($IC_{50} = 0.01–0.06\,\mu g/mL$), vaccinia virus ($IC_{50} = 0.7–2.0\,\mu g/mL$), and against the retroviruses Moloney murine sarcoma virus (MSV) ($IC_{50} = 0.57–0.03\,\mu g/mL$), human immunodeficiency virus type 1 (HIV-1) and HIV-2 ($IC_{50} > 0.8\,\mu g/mL$).[22] Compound **2** was active against thymidine kinase deficient (TK^-) HSV-1 and HSV-2, CMV ($IC_{50} = 2–7\,\mu g/mL$) and TK^+ and TK^- VZV ($IC_{50} = 0.04–0.4\,\mu g/mL$) as well as the retroviruses MSV ($IC_{50} = 0.32 \pm 0.1\,\mu g/mL$) and HIV-1 and HIV-2 ($IC_{50} = 2\,\mu g/mL$).[21,22] Aza-nucleotide **3** is a potent inhibitor of *Pf*HGXPRT [*Plasmodium falciparum* (*Pf*) hypoxanthine-guanine-xanthine phosphoribosyltransferase (HGXPRT)].[27]

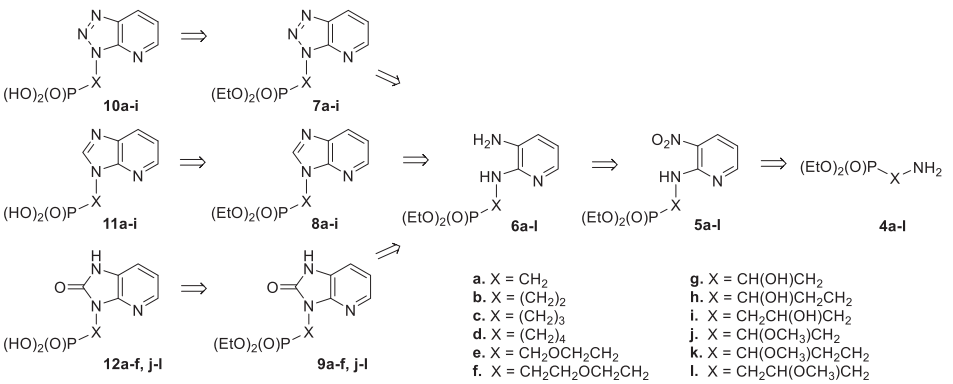
Moreover, compounds possessing 1,2,3-triazolo[4,5-*b*]pyridines, imidazo[4,5-*b*]pridines and imidazo[4,5-*b*]pyridin-2-ones units exhibited interesting pharmacological and biological activities.[28–33]

These achievements prompted us to design and synthesize new acyclic phosphonate nucleoside analogs in which the natural purine nucleobase was replaced by triazolo[4,5-*b*]pyridine (1-deaza-8-azapurine), imidazo[4,5-*b*]pyridine (1-deazapurine) and imidazo[4,5-*b*]pyridin-2(3*H*)-one (1-deazapurin-8-one) moieties with intention to evaluate their antiviral and cytotoxic properties (Scheme 1).

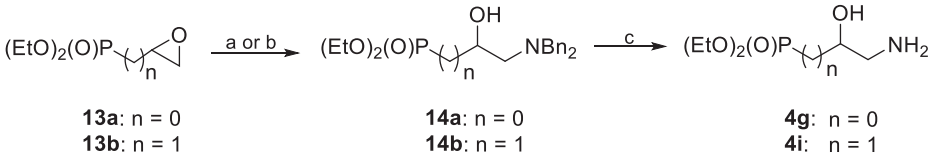
2. Results and discussion

For the purpose of this project, known diethyl ω-aminoalkylphosphonates **4a–i** (Scheme 1) were synthesized according to the procedures previously described.[16,27,34–39]

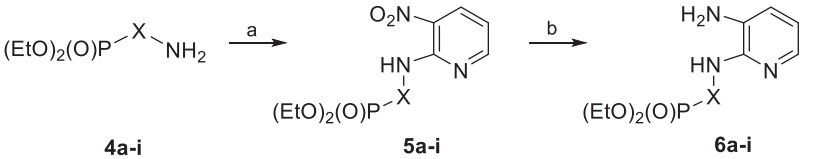
Pure racemic diethyl 2-amino-1-hydroxyethylphosphonate **4g** and diethyl 3-amino-2-hydroxypropylphosphonate **4i** were synthesized *via* slightly modified procedures which relied on the reacting the epoxyalkylphosphonate with dibenzylamine and subsequent hydrogenolytic removal of benzyl group (Scheme 2). Earlier procedure for the transformation of **13b** into 3-dibenzylamino-2-hydroxypropylphosphonate **14b** required heating of the



Scheme 1. Retrosynthesis of the designed acyclic nucleotides **7–12**.



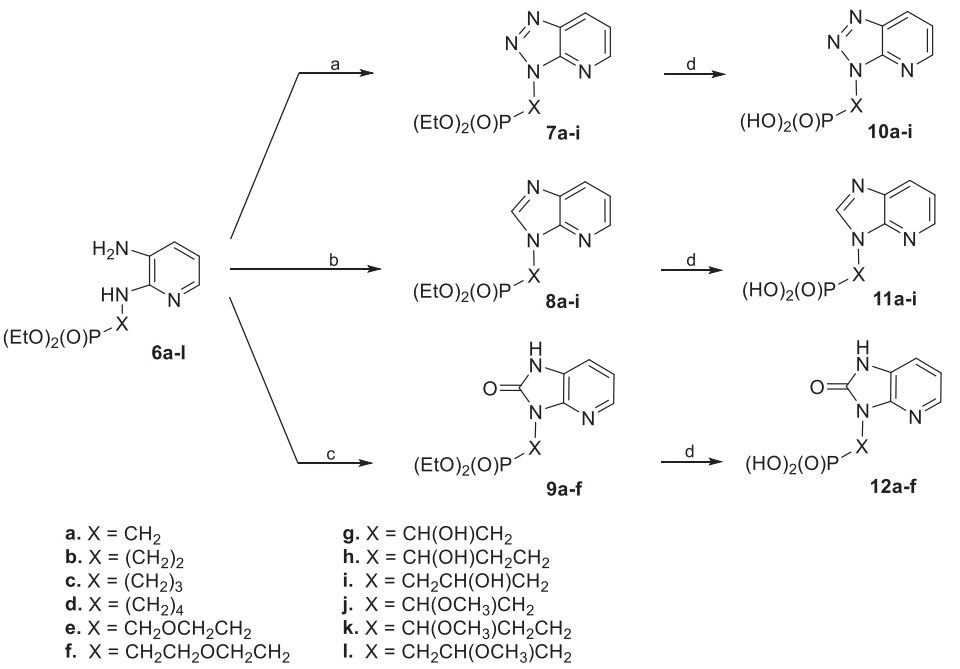
Scheme 2. Reagents and conditions: (a) $NHBn_2$, MW, 60 °C, 5 hours and (b) $NHBn_2$, 60 °C, 20 hours; H_2, 10% $Pd(OH)_2/C$, EtOH, r.t., 5 days.



Scheme 3. Reagents and conditions: (a) 2-chloro-3-nitropyridine, TEA, THF, or CH_2Cl_2, r.t., 24 hours and (b) $SnCl_2$, 36% HCl, 95% CH_3COOH, r.t., 1.5 hours.

reaction mixture at 60 °C for 20 hours.[40] However, when the reaction was carried out under microwave irradiation, a full conversion of the epoxide **13b** into 3-dibenzylamino-2-hydroxypropylphosphonate **14b** was achieved after 5 hours. After hydrogenolysis of **14b** racemic diethyl 3-amino-2-hydroxypropylphosphonate **4i** was obtained in good overall yield (77%). In the similar way, racemic diethyl 2-amino-1-hydroxyethylphosphonate **4g** was obtained from epoxyethylphosphonate **13a** (93%).

Aminoalkylphosphonates **4a–i** were then reacted with 2-chloro-3-nitropyridine (Scheme 3)[41] to give the respective diethyl [(3-nitropyridin-2-yl) amino]alkylphosphonates **5a–i** in 39%–91% yields. The reduction of the nitro group[41] in **5a-i** led to the formation of the diethyl [(3-aminopyridin-2-yl) amino]alkylphosphonates **6a–i** (Scheme 3) which were subsequently applied

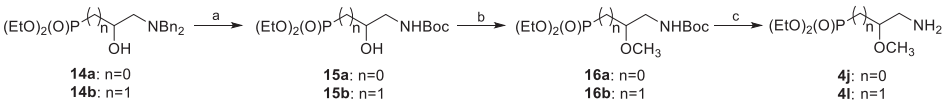


Scheme 4. Reagents and conditions: (a) $NaNO_2$, H_2SO_4, 0 °C, 1 hour; (b) $HC(OEt)_3$, *p*-TsOH, THF, r.t., 24 hours; (c) CDI, THF, r.t., 72 hours; and (d) TMSBr, CH_2Cl_2, r.t., 24 hours.

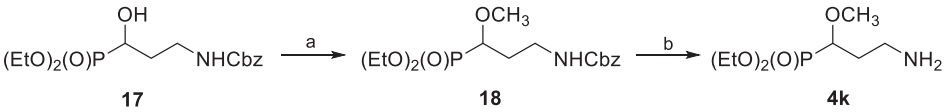
as key substrates in the synthesis of the designed nucleotide analogs (Scheme 1).

Diazotization of diethyl [(3-aminopyridin-2-yl)amino]alkylphosphonates **6a–i** followed by spontaneous intramolecular cyclization[42] led to the formation of diethyl {1,2,3-triazolo[4,5-*b*]pyridin-3-yl}alkylphosphonates **7a–i** in 47%–96% yields. 1-Deazapurine-containing analogs **8a–i** were synthesized by the reaction of **6a–i** with triethyl orthoformate in the presence of *p*-toluenesulphonic acid[43] in 32%–99% yields. In order to obtain imidazolone analogs **9a–i**, diethyl [(3-aminopyridin-2-yl)amino]alkylphosphonates **6a–i** were treated with 1,1′-carbonyldiimidazole[44] (Scheme 4). However, under these conditions only diethyl [(3-aminopyridin-2-yl)amino]alkylphosphonates **6a–f** were effectively transformed into the compounds **9a–f**. In the case of racemic phosphonates **9g–i** containing the hydroxy group in phosphonoalkyl chain reaction with 1,1′-carbonyldiimidazole led to the formation of complex mixture of products. Several attempts at separating of the crude reaction mixture on silica gel columns failed.

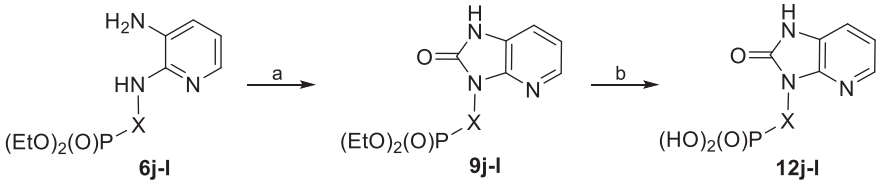
We concluded that in case of phosphonates **6g–i** transformation into the respective imidazolones required prior protection of hydroxyl groups in the phosphonoalkyl chain.[45,46] For this reason, the *O*-methyl-aminophosphonates **4j–l** were synthesized as depicted on Schemes 5 and 6. Transformation of 2-dibenzylamino-1-hydroxyethylphosphonate **14a** and



Scheme 5. Reagents and conditions: (a) H_2, 10% $Pd(OH)_2/C$, Boc_2O, EtOH, r.t., 72 hours; (b) CH_3I, Ag_2O, CH_2Cl_2, r.t., 7 days; and (c) TFA, CH_2Cl_2, r.t., 5 hours.



Scheme 6. Reagents and conditions: (a) CH_3I, Ag_2O, CH_2Cl_2, r.t., 7 days and (b) H_2, 10% $Pd(OH)_2/C$, EtOH, r.t., 72 hours.



Scheme 7. Reagents and conditions: (a) CDI, THF, r.t., 72 hours and (b) TMSBr, CH_2Cl_2, r.t., 24 hours.

3-dibenzylamino-2-hydroxypropylphosphonate **14b** into the respective *O*-methyl-aminophosphonates **4g** and **4i** was accomplished in three steps involving catalytic hydrogenation in the presence of Boc_2O,[47,48] *O*-methylation[49] and hydrolysis (Scheme 5).

On the other hand, the synthesis of diethyl 3-amino-1-methoxypropylphosphonate **4k** was achieved by reaction sequence including methylation of the hydroxy group at C(1) in **17** and catalytic hydrogenation in diethyl 3-[*N*-(benzyloxycarbonyl)amino]-1-hydroxypropylphosphonate **18** (Scheme 6).

The racemic *O*-methylated alkylphosphonates **6j–l** were applied in the reaction with 1,1′-carbonyldiimidazole to afford the respective phosphonoalkyl imidazolones **9j–l** (Scheme 7).

All diethyl phosphonates **7a–i**, **8a–i**, and **9a–f**, **j–l** were finally transformed into the respective phosphonic acids **10a–i**, **11a–i** and **12a–f**, **j–l** with trimethylsilyl bromide[50] (Schemes 4 and 7).

The structure and purity of all synthesized compounds were verified by ^1H, ^{31}P, and ^{13}C NMR and IR techniques as well as by elemental analysis.

2.1. Antiviral activity and cytotoxicity evaluation

All the synthesized diethyl phosphonates **7–9** as well as the respective phosphonic acids **10–12** were evaluated for their antiviral activities against

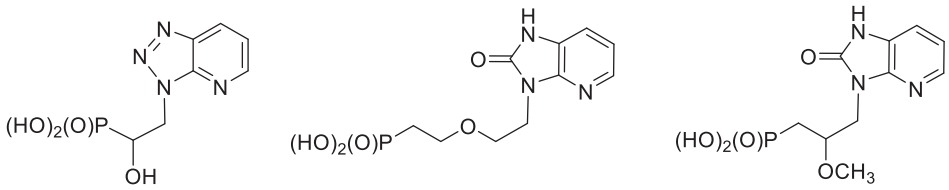


Figure 4. Structures of active compounds.

a wide variety of DNA and RNA viruses, using the following cell-based assays: (a) human embryonic lung (HEL) cells: Herpes simplex virus-1 (KOS strain), Herpes simplex virus-2 (G strain), Herpes simplex virus-1 (TK^- ACV^r KOS), Vaccinia virus, Adenovirus-2, human coronavirus, cytomegalovirus (AD-169 strain and Davis strain), varicella-zoster virus (TK^+ VZV strain OKA and TK^- VZV strain 07-1); (b) HeLa cell cultures: vesicular stomatitis virus, Coxsackie virus B4 and respiratory syncytial virus (RSV); (c): Vero cell cultures: Parainfluenza-3 virus, Reovirus-1, Sindbis virus, Coxsackie virus B4, Punta Toro virus, yellow fever virus; and (d) Madin Darby Canine Kidney (MDCK) cell cultures: influenza A virus H1N1 subtype (A/PR/8), influenza A virus H3N2 subtype (A/HK/7/87) and influenza B virus (B/HK/5/72). Ganciclovir, cidofovir, acyclovir, brivudin, zalcidabine, alovudine, *Urtica dioica* agglutinin (UDA), dextran sulfate (molecular weight 10,000, DS-10000), zanamivir, mycophenoic acid, ribavirin, amantadine, and rimantadine were used as the reference compounds. The antiviral activity was expressed as the EC_{50}: the compound concentration required to reduce virus-induced cytopathogenicity by 50% (other viruses). Among the synthesized compounds, phosphonic acid **12f** showed marginal activity only against the CMV Davis strain ($EC_{50} = 76.47\,\mu M$) but not against the AD-169 strain in HEL cells, while compounds **10g** ($EC_{50} = 52.53\,\mu M$) and **12l** ($EC_{50} = 61.70\,\mu M$) showed also very minor activity against the VZV Oka strain but not against the 07-1 strain of VZV in HEL cells (Figure 4). None of the other compounds showed any activity against the different DNA and RNA evaluated.

The cytotoxicity of the tested compounds toward the uninfected host cells was defined as the minimum cytotoxic concentration (MCC) that causes a microscopically detectable alteration of normal cell morphology. None of the compounds proved cytotoxic up to 100 μM, the highest concentration tested.

3. Conclusion

New series of phosphonylated triazolo[4,5-*b*]pyridine (1-deaza-8-azapurine), imidazo[4,5-*b*]pyridine (1-deazapurine) and imidazo[4,5-*b*]pyridin-2(3*H*)-one

(1-deazapurin-8-one) were successfully obtained from diethyl [(3-aminopyridin-2-yl)amino]alkylphosphonates **6a–l** by three different approaches: diazotization and spontaneous intramolecular cyclization (**7a–i**), cyclization with triethyl orthoformate (**8a–i**) and reaction with 1,1′-carbonyldiimidazole (**9a–i**). The corresponding diethyl [(3-aminopyridin-2-yl)amino]alkylphosphonates **6a–l** were efficiently prepared *via* reaction ω-aminoalkylphosphonates with 2-chloro-3-nitropyridine and reduction nitro group. All synthesized compounds were tested for their antiviral activity against DNA and RNA viruses and cytotoxicity properties. Antiviral activity against cytomegalovirus ($EC_{50} = 76.47\ \mu M$; $MCC > 100\ \mu M$) in human embryonic lung (HEL) cells has been observed for compound **12f**. Phosphonic acids **10 g** and **12l** indicated marginal activity against VZV ($EC_{50} = 52.53\ \mu M$ for **10g** and $EC_{50} = 61.70\ \mu M$ for **12l**; $MCC > 100\ \mu M$) in HEL cells. None of the compounds were not cytotoxic at the maximum concentration evaluated (100 μM).

4. Experimental

^{1}H NMR were taken in $CDCl_3$, D_2O, or DMSO-d_6 on the following spectrometers: Varian Mercury-300, Varian Mercury-200 and Bruker Avance III (600 MHz) with TMS as an internal standard; chemical shifts δ in ppm with respect to TMS; coupling constants *J* in Hz. ^{13}C NMR spectra were recorded for $CDCl_3$, D_2O, or DMSO-d_6 solutions on a Varian Mercury-300 and Bruker Avance III (600 MHz) spectrometer at 75.5 and 151 MHz, respectively. ^{31}P NMR spectra were taken in $CDCl_3$, D_2O, or DMSO-d_6 on Varian Mercury-300, Varian Mercury-200 and Bruker Avance III (600 MHz) at 121.5, 80.9, and 242 MHz using 85% phosphoric acid as an external standard.

IR spectral data were measured on an Infinity MI-60 FT-IR spectrometer. Melting points were determined on a Boetius apparatus and are uncorrected. Elemental analyses were performed by the Microanalytical Laboratory of this Faculty on a Perkin Elmer PE 2400 CHNS analyzer, (Perkin-Elmer Corp., Norwalk, CT, USA).

The following adsorbents were used: column chromatography, Merck silica gel 60 (70–230 mesh); analytical TLC, Merck TLC plastic sheets silica gel 60 F_{254}. TLC plates were developed in chloroform–methanol solvent systems. Visualization of spots was effected with iodine vapors. All solvents were purified by methods described in the literature.

4.1. Synthesis of diethyl 2-amino-1-methoxyethylphosphonate 4j

4.1.1. Diethyl-2-(tert-butoxycarbonylamino)-1-hydroxyethylphosphonate 15a

A solution of diethyl 2-dibenzylamino-1-hydroxyethylphosphonate **14a** (2.670 g, 7.08 mmol) and di-*tert*-butyl dicarbonate (1.545 g, 7.08 mmol) in

anhydrous ethanol (15 mL) was kept under hydrogen atmosphere over 10% $Pd(OH)_2/C$ (0.020 g, 0.01 mmol) at room temperature for 72 hours. The suspension was filtered through a pad of Celite and washed with ethanol. After evaporation of the solvent, the residue was chromatographed on a silica gel column with a chloroform–methanol (100:1, v/v) mixture to give diethyl-2-(*tert*-butoxycarbonylamino)-1-hydroxyethylphosphonate **15a** (1.490 g, 71%) as a pale yellow oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 5.22 (brs, 1 H, N*H*), 4.27–4.09 (m, 5 H, 2 × POC*H*$_2$CH$_3$, O*H*), 4.01 (ddd, $J = 7.8$ Hz, $J = 6.6$ Hz, $J = 3.6$ Hz, 1 H, PC*H*), 3.71–3.29 (m, 2 H, PCC*H*$_2$), 1.44 (s, 9 H, 3 × C*H*$_3$), 1.35 (t, $J = 7.1$ Hz, 6 H, 2 × POCH$_2$C*H*$_3$). ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]:23.17. ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 156.97, 79.67, 68.00 (d, $J = 127.2$ Hz, P*C*), 62.93 (d, $J = 6.4$ Hz, PO*C*), 62.89 (d, $J = 6.4$ Hz, PO*C*), 42.29, 28.35, 16.46 (d, $J = 5.2$ Hz, POC*C*), 16.44 (d, $J = 5.5$ Hz, POC*C*).

4.1.2. Diethyl-2-(tert-butoxycarbonylamino)-1-methoxyethylphosphonate 16a

A suspension of diethyl-2-(*tert*-butoxycarbonylamino)-1-hydroxyethylphosphonate **15a** (1.000 g, 3.36 mmol), methyl iodide (0.400 mL, 6.73 mmol) and silver(I) oxide (1.247 g, 5.38 mmol) in dichloromethane (20 mL) was stirred vigorously at room temperature for 7 days. The reaction mixture was filtered through a layer of Celite, concentrated and the crude product was chromatographed on a silica gel column with a chloroform–methanol (100:1, v/v) mixture to give a diethyl-2-(*tert*-butoxycarbonylamino)-1-methoxyethylphosphonate **16a** as a colorless oil (0.882 g, 84%). IR (film, cm^{-1}) ν_{max}: 3331, 2981, 2930, 1767, 1266, 1224, 1028, 964, 762; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 5.09 (s, 1 H, N*H*), 4.25–4.16 (m, 4 H, 2 × POC*H*$_2$CH$_3$), 3.72–3.50 (m, 2 H, PCC*H*$_2$), 3.58 (s, 3 H, PCOC*H*$_3$), 3.39–3.29 (m, 1 H, PC*H*), 1.47 (s, 9 H, 3 × C*H*$_3$), 1.38 (t, $J = 7.1$ Hz, 3 H, POCH$_2$C*H*$_3$), 1.36 (t, $J = 7.1$ Hz, 3 H, POCH$_2$C*H*$_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 155.80 (s, *C*=O), 79.46 (s, *C*CH$_3$), 76.28 (d, $J = 153.4$ Hz, P*C*), 62.61 (d, $J = 6.7$ Hz, 2 × PO*C*), 60.20 (s, PCO*C*H$_3$), 40.18 (s, PC*C*), 28.37 (s, 3×*C*H$_3$), 16.49 (d, $J = 5.5$ Hz, 2 × POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 21.06; Anal. Calcd. for $C_{12}H_{26}NO_6P$: C, 46.30; H, 8.42; N, 4.50; Found: C, 46.43; H, 8.44; N, 4.39.

4.2. Diethyl 2-amino-1-methoxyethylphosphonate 4j

To a solution of diethyl-2-(*tert*-butoxycarbonylamino)-1-methoxyethylphosphonate **16a** (0.832 g, 2.80 mmol) in dichloromethane (15 mL), trifluoroacetic acid (3.00 mL, 40.00 mmol) was added. The reaction mixture was stirred at room temperature for 5 hours. Washed with saturated sodium bicarbonate (2 × 5 mL) and organic layer was dried over anhydrous

$MgSO_4$. The crude product was purified on a silica gel column with a chloroform–methanol (100:1, v/v) mixture to give diethyl 2-amino-1-methoxyethylphosphonate **4j** (0.288 g, 51%) as a colorless oil. IR (film, cm^{-1}) ν_{max}: 3333, 2988, 2935, 1270, 1223, 1029, 964, 762; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 4.28–4.15 (m, 4 H, 2 × POCH_2CH$_3$), 3.63 (s, 3 H, OCH_3), 3.60–3.56 (m, 2 H, PCCH_2), 3.27–2.94 (m, 1 H, PC*H*), 2.54 (brs, 2 H, NH_2), 1.38 (t, J = 7.1 Hz, 3 H, POCH$_2$CH_3), 1.37 (t, J = 7.1 Hz, 3 H, POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ[ppm]: 78.48 (d, J = 161.9 Hz, P*C*), 62.59 (d, J = 6.9 Hz, PO*C*), 62.52 (d, J = 7.1 Hz, PO*C*), 60.41 (d, J = 3.9 Hz, PCO*C*), 41.57 (s, PC*C*), 16.52 (d, J = 5.5 Hz, 2 × POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 21.40; Anal. Calcd. for $C_7H_{18}NO_4P \times 0.8H_2O$: C, 37.27; H, 8.76; N, 6.21; Found: C, 37.30; H, 8.46; N, 5.98.

4.3. Synthesis of diethyl 3-amino-2-methoxypropylphosphonate 4l

4.3.1. Diethyl-3-(tert-butoxycarbonylamino)-2-hydroxypropylphosphonate 15b

A suspension of diethyl 3-dibenzylamino-2-hydroxypropylphosphonate **14 b** (1.600 g, 4.09 mmol), di-*tert*-butyl dicarbonate (0.893 g, 4.09 mmol) and 10% $Pd(OH)_2$/C (0.030 g, 0.01 mmol) in anhydrous ethanol (15 mL) was stirred under hydrogen atmosphere at room temperature for 72 hours. The catalyst was filtered off through a layer of Celite, the solution concentrated-din vacuo and the residue was chromatographed on a silica gel column with a chloroform–methanol (100:1, v/v) mixture to give diethyl-3-(*tert*-butoxycarbonylamino)-2-hydroxypropylphosphonate **15b** (1.031 g, 81%) as a pale yellow oil. IR (film, cm^{-1}) ν_{max}: 3340, 2982, 2933, 1769, 1222, 1022, 966, 766; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 5.08 (brs, 1 H, N*H*), 4.25–4.07 (m, 6 H, 2 × POCH_2CH$_3$), 3.39 (brs, 1 H, O*H*), 3.21–3.18 (m, 1 H, PCC*H*), 2.00–1.94 (m, 2 H, PCH_2), 1.47 (s, 9 H, 3 × CH_3), 1.38 (t, J = 7.1 Hz, 3 H, POCH$_2$CH_3), 1.36 (t, J = 7.1 Hz, 3 H, POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 156.60, 79.62, 66.28, 62.05 (d, J = 6.5 Hz, 2 × PO*C*), 46.71, 30.77 (d, J = 139.4 Hz, P*C*), 28.37, 16.41 (d, J = 5.6 Hz, POC*C*), 16.37 (d, J = 5.7 Hz, POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 29.71 Anal. Calcd. for $C_{12}H_{26}NO_6P \times 0.1H_2O$: C, 46.03; H, 8.43; N, 4.47; Found: C, 46.12; H, 8.53; N, 4.43.

4.3.2. Diethyl-3-(tert-butoxycarbonylamino)-2-methoxypropylphosphonate 16b

A suspension of diethyl-3-(*tert*-butoxycarbonylamino)-2-hydroxypropylphosphonate **15b** (0.915 g, 2.94 mmol), methyl iodide (0.816 g, 3.52 mmol) and silver(I) oxide (0.400 mL, 5.87 mmol) in CH_2Cl_2(10 mL) was vigorously stirred at room temperature for 7 days. The reaction mixture was filtered through a layer of Celite, concentrated and the crude product was purified on a silica gel column

with a chloroform–methanol (100:1, v/v) mixture to give a diethyl-3-(*tert*-butoxycarbonylamino)-2-methoxypropylphosphonate **16b** as a pale yellow oil (0.879 g, 92%). IR (film, cm^{-1}) ν_{max}: 3331, 2981, 2930, 1699, 1269, 1224, 1028, 964, 762; ^1H NMR (600 MHz, $CDCl_3$) δ [ppm]: 4.97 (brs, N*H*), 3.70–3.64 (m, 1 H, PCC*H*) 4.22–4.04 (m, 4 H, 2 × POCH_2CH$_3$), 3.42 (s, 3 H, PCOCH_3), 3.4–3.22 (m, 2 H, PCCCH_2), 2.17–1.89 (m, 2 H, PCH_2), 1.47 (s, 9 H, 3 × CH_3), 1.36 (t, $J = 7.0$ Hz, 6 H, 2 × POCH$_2$CH_3; ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 155.97, 79.27, 75.35, 61.79 (d, $J = 6.4$ Hz, POC), 61.63 (d, $J = 6.4$ Hz, POC), 56.99, 43.36, 29.11 (d, $J = 140.2$ Hz, PC), 28.37, 16.39 (d, $J = 5.8$ Hz, POCC), 16.37 (d, $J = 5.8$ Hz, POCC); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 28.30; Anal. Calcd. for $C_{13}H_{28}NO_6P$: C, 47.99; H, 8.67; N, 4.31; Found: C, 48.00; H, 8.32; N, 4.13.

4.4. 3-Amino-2-methoxypropylphosphonate 4l

A solution of diethyl-3-(*tert*-butoxycarbonylamino)-2-methoxypropylphosphonate **16b** (0.910 g, 2.80 mmol) and trifluoroacetic acid (3.20 mL, 0.04 mol) in dichloromethane (15 mL) was stirred at room temperature for 5 hours. After the reaction mixture was dissolved in dichloromethane and washed by saturated sodium bicarbonate solution (2 × 5 mL). Organic layer was dried over anhydrous $MgSO_4$. The crude product was purified on a silica gel column with a chloroform–methanol (100:1, v/v) mixture to give diethyl 3-amino-2-methoxypropylphosphonate **4l** (0.524 g, 87%) as a colorless oil. IR (film, cm^{-1}) ν_{max}: 3334, 2989, 2934, 1277, 1221, 1030, 964, 763; ^1H NMR (600 MHz, $CDCl_3$) δ [ppm]: 4.20–4.04 (m, 4 H, 2 × POCH_2CH$_3$), 3.59 (dddd, $J = 7.3$ Hz, $J = 5.8$ Hz, $J = 5.5$ Hz, $J = 3.7$ Hz, 1 H, PCC*H*), 3.42 (s, 3 H, CH_3), 3.04 (dd$_{ABX}$, $J = 13.5$ Hz, $J = 3.7$ Hz, 1 H, PCCCH_AH$_B$), 2.79 (dd$_{ABX}$, $J = 13.5$ Hz, $J = 5.8$ Hz, 1 H, PCCCH_BH$_A$), 2.13 (ddd, $J = 19.6$ Hz, $J = 15.4$ Hz, $J = 5.5$ Hz, 1 H, PCH_AH$_B$), 1.98 (ddd, $J = 18.1$ Hz, $J = 15.4$ Hz, $J = 7.3$ Hz, 1 H, PCH_BH$_A$), 1.36 (t, $J = 7.1$ Hz, 3 H, POCH$_2$CH_3), 1.35 (t, $J = 7.1$ Hz, POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 77.50 (s, COCH$_3$), 61.74 (d, $J = 6.5$ Hz, POC), 61.57 (d, $J = 6.5$ Hz, POC), 56.91 (s, PCC), 45.05 (d, $J = 7.4$ Hz, PCCC), 28.41 (d, $J = 139.1$ Hz, PC), 16.41 (d, $J = 6.0$ Hz, POCC), 16.39 (d, $J = 6.1$ Hz, POCC ^{31}P NMR (243 MHz, CDCl3); δ [ppm]: 28.64. Anal. Calcd. for $C_8H_{20}NO_4P$: C, 42.66; H, 8.95; N, 6.22; Found: C, 42.58; H, 8.89; N, 6.19.

4.5. Synthesis of diethyl 3-amino-1-methoxypropylphosphonate 4k

4.5.1. Diethyl 3-[N-(benzyloxycarbonyl)amino]-1-methoxypropylphosphonate 18

A suspension of diethyl 3-[*N*-(benzyloxycarbonyl)amino]-1-hydroxypropylphosphonate **17** (0.402 g, 1.64 mmol), methyl iodide (0.204 mL, 3.28 mmol) and silver(I) oxide (0.457 g, 1.97 mmol) in CH_2Cl_2 (10 mL) was vigorously stirred at room temperature for 7 days. Then the reaction mixture was filtered

through a layer of Celite, concentrated and the crude product was purified on a silica gel column with a chloroform–methanol (100:1, v/v) mixture to give a diethyl 3-[*N*-(benzyloxycarbonyl)amino]-1-methoxypropylphosphonate **18** as a colorless oil (0.366 g, 91%). IR (film, cm^{-1}) ν_{max}: 3031, 2981, 2930, 1701, 1268, 1222, 1029, 966, 762; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 7.45–7.31 (m, 5 H, Ar–*H*), 5.18 (brs, 1 H, N*H*), 5.13 (s, 2 H, CH_2Ph), 4.36–4.04 (m, 4 H, 2 × POCH_2CH$_3$), 3.55 (s, 3 H, OCH_3), 3.54–3.46 (m, 2 H, PCCH_2), 3.39–3.33 (m, 1 H, PC*H*), 2.09–1.85 (m, 2 H, PCCH_2), 1.36 (t, $J = 7.0$ Hz, 3 H, POCH_2CH$_3$), 1.35 (t, $J = 7.0$ Hz, 3 H, POCH_2CH$_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 156.41, 136.64, 128.48, 128.45, 128.06, 75.85 (d, $J = 164.9$ Hz, P*C*), 66.64, 62.51 (d, $J = 6.9$ Hz, PO*C*), 62.39 (d, $J = 7.2$ Hz, PO*C*), 60.14 (d, $J = 3.4$ Hz, PC*C*), 37.84, 30.46, 16.51 (d, $J = 5.4$ Hz, 2 × POC*C*) ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 22.83. Anal. Calcd. for $C_{16}H_{26}NO_6P$: C, 53.48; H, 7.29; N, 3.90; Found: C, 53.48; H, 7.37; N 4.00.

4.6. Diethyl 3-amino-1-methoxypropylphosphonate 4k

A solution of diethyl 3-[*N*-(benzyloxycarbonyl)amino]-1-methoxypropylphosphonate **18** (0.535 g, 1.49 mmol) in anhydrous ethanol (10 mL) was kept under hydrogen atmosphere over 10% $Pd(OH)_2$/C (0.015 g, 0.01 mmol) at room temperature for 72 hours. The suspension was filtered through a pad of Celite and washed with ethanol. After evaporation of the solvent, the residue was chromatographed on a silica gel column with a chloroform–methanol (100:1, v/v) mixture to give diethyl 3-amino-1-methoxypropylphosphonate **4k** (0.285 g, 85%) as a pale yellow oil. IR (film, cm^{-1}) ν_{max}: 3334, 2988, 2933, 1277, 1220, 1030, 966, 766; ^{1}H NMR (600 MHz, DMSO-d_6) δ [ppm]: 7.75 (brs, 2 H, NH_2), 4.14–4.03 (m, 4 H, 2 × POCH_2CH$_3$), 3.76–3.72 (m, 1 H, PC*H*), 3.45 (s, 3 H, OCH_3), 2.98–2.89 (m, 2 H, PCCCH_2), 2.03–1.83 (m, 2 H, PCH_2), 1.28 (t, $J = 7.0$ Hz, 3 H, POCH$_2$CH_3), 1.27 (d, $J = 7.0$ Hz, 3 H, POCH$_2$CH_3); ^{13}C NMR (151 MHz, DMSO-d_6) δ [ppm]: 74.13 (d, $J = 163.8$ Hz, P*C*), 62.40 (d, $J = 6.6$ Hz, PO*C*), 62.37 (d, $J = 6.6$ Hz, PO*C*), 59.75 (d, $J = 3.3$ Hz, PCO*C*), 36.11 (d, $J = 14.4$ Hz, PCC*C*), 28.24 (d, $J = 3.0$ Hz, PC*C*), 16.84 (d, $J = 5.2$ Hz, 2 × POC*C*) ^{31}P NMR (243 MHz, DMSO-d_6) δ [ppm]: 22.33; Anal. Calcd. for $C_8H_{20}NO_4P \times 0.3H_2O$: C, 41.66; H, 9.00; N, 6.07; Found: C, 41.56; H, 8.90; N, 6.20.

4.7. Synthesis of diethyl [(3-nitropyridin-2-yl)amino]alkylphosphonates 5a–l – general procedure

Solution of diethyl ω-aminoalkylphosphonate **4a–l** (1.00 mmol) in THF or dichloromethane (2 mL) was added to a mixture of 2-chloro-3-nitropyridine (1.00 mmol) and triethylamine (1.50 mmol) in appropriate solvent the THF or CH_2Cl_2 (1 mL). The reaction mixture was stirred at room

temperature for 24 hours, concentrated and the crude product was purified on a silica gel column with a chloroform–methanol (100:1, v/v) mixture to give the pure compounds **5a–l**.

4.8. Diethyl [(3-nitropyridin-2-yl)amino]methylphosphonate 5a

According to the general procedure from diethyl aminomethylphosphonate **4a** (0.281 g, 1.68 mmol) and 2-chloro-3-nitropyridine (0.266 g, 1.68 mmol) diethyl [(3-nitropyridin-2-yl)amino]methylphosphonate **5a** (0.379, 78%) was obtained as a yellow oil. IR (film, cm^{-1}) ν_{max}: 3387, 3085, 2985, 2932, 1504, 1316, 761; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 8.47–8.46 (m, 2 H, Ar–*H*), 8.35 (brs, 1 H, N*H*), 6.75 (dd, $J = 8.1$ Hz, $J = 4.6$ Hz, 1 H, Ar–*H*), 4.27–4.12 (m, 6 H, 2 × POC*H*$_2$CH$_3$, C*H*$_2$), 1.35 (t, $J = 7.0$ Hz, 6 H, 2 × POCH$_2$*CH*$_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 155.18, 151.87 (d, $J = 5.7$ Hz, Ar–*C*), 135.25, 128.87, 112.65, 62.53 (d, $J = 6.5$ Hz, 2 × POC), 36.36 (d, $J = 156.0$ Hz, PC), 16.32 (d, $J = 5.8$ Hz, 2 × POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 22.48; Anal. Calcd. for $C_{10}H_{16}N_3O_5P \times 0.25H_2O$: C, 40.89; H, 5.66; N, 14.31; Found: C, 40.85; H, 5.42; N, 14.14.

4.9. Diethyl 2-[(3-nitropyridin-2-yl)amino]ethylphosphonate 5b

According to the general procedure from diethyl 2-aminoethylphosphonate **4b** (1.000 g, 5.52 mmol) and 2-chloro-3-nitropyridine (0.875 g, 5.52 mmol) diethyl 2-[(3-nitropyridin-2-yl)amino]ethylphosphonate **5b** (1.323 g, 79%) was obtained as a yellow oil. IR (film, cm^{-1}) ν_{max}: 3392, 2984, 2932, 1572, 1391, 1247, 1035, 961, 762; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 8.49 (brs, 1 H, N*H*), 8.45–8.43 (m, 2 H, Ar–*H*), 6.69 (dd, $J = 8.0$ Hz, $J = 4.7$ Hz, 1 H, Ar–*H*), 4.33–4.06 (m, 4 H, 2 × POC*H*$_2$CH$_3$), 3.97 (ddd, $J = 17.0$ Hz, $J = 12.7$ Hz, $J = 6.9$ Hz, 2 H, PC*CH*$_2$), 2.21 (dt, $J = 17.9$ Hz, $J = 6.9$ Hz, 2 H, P*CH*$_2$), 1.37 (t, $J = 7.1$ Hz, 6 H, 2 × POCH$_2$*CH*$_3$);^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 155.48, 152.22, 135.23, 128.40, 111.95, 61.84 (d, $J = 6.5$ Hz, 2 × POC), 35.51 (d, $J = 4.4$ Hz, PC*C*), 25.96 (d, $J = 139.9$ Hz, P*C*), 16.41 (d, $J = 5.9$ Hz, 2 × POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 29.12; Anal. Calcd. for $C_{11}H_{18}N_3O_5P \times 0.3H_2O$: C, 42.80; H, 6.07; N, 13.61; Found: C, 42.78; H, 6.09; N, 13.61.

4.10. Diethyl 3-[(3-nitropyridin-2-yl)amino]propylphosphonate 5c

According to the general procedure from diethyl 3-aminopropylphosphonate **4c** (0.496 g, 2.54 mmol) and 2-chloro-3-nitropyridine (0.403 g, 2.54 mmol) diethyl 3-[(3-nitropyridin-2-yl)amino]propylphosphonate **5c** (0.629 g, 78%) was obtained as a yellow oil. IR (film, cm^{-1}) ν_{max}: 3395, 3085, 2983, 2936, 1572, 1391, 1247, 1031, 962, 762; ^{1}H NMR (600 MHz,

$CDCl_3$) δ [ppm]: 8.37 (dd, $J = 4.9$ Hz, $J = 1.8$ Hz, 1 H, Ar–*H*), 8.34 (s, 1 H, Ar–*H*), 8.25 (brs, 1 H, N*H*), 6.60 (dd, $J = 7.9$ Hz, $J = 5.0$ Hz, 1 H, Ar–*H*), 4.23–3.89 (m, 4 H, 2 × POCH_2CH$_3$), 3.68 (dd, $J = 12.8$ Hz, $J = 6.8$ Hz, 2 H, PCCCH_2), 2.08–1.54 (m, 4 H, PCH_2CH_2), 1.27 (t, $J = 7.1$ Hz, 6 H, 2 × POCH$_2$CH_3) ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 155.64, 152.67, 135.25, 128.17, 111.81, 61.61 (d, $J = 6.5$ Hz, 2 × POC), 41.28 (d, $J = 17.3$ Hz, PCCC), 23.25 (d, $J = 142.7$ Hz, PC), 22.66 (d, $J = 4.8$ Hz, PCC), 16.44 (d, $J = 5.9$ Hz, 2 × POCC); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 32.16. Anal. Calcd. for $C_{12}H_{20}N_3O_5P$: C, 45.43; H, 6.35; N, 13.24; Found: C, 45.52; H, 6.07; N, 13.30.

4.11. Diethyl 4-[(3-nitropyridin-2-yl)amino]butylphosphonate 5d

According to the general procedure from diethyl 4-aminobutylphosphonate **4d** (0.493 g, 2.36 mmol) and 2-chloro-3-nitropyridine (0.374 g, 2.36 mmol) diethyl 3-[(3-nitropyridin-2-yl)amino]propylphosphonate **5d** (0.632 g, 81%) was obtained as a yellow oil. IR (film, cm^{-1}) ν_{max}: 3395, 2982, 2938, 1573, 1391, 1245, 1027, 761; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 8.53–8.33 (m, 2 H, Ar–*H*), 8.25 (brs, 1 H, N*H*) , 6.68–6.60 (m, 1 H, Ar–*H*), 4.30–3.93 (m, 4 H, 2 × POCH_2CH$_3$), 3.65–3.20 (m, 2 H, PCCCCH_2), 1.88–1.38 (m, 6 H, PCH_2CH_2CH_2), 1.31 (t, $J = 6.9$ Hz, 6 H, 2 × POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 155.67, 152.67, 135.20, 128.00, 111.59, 61.49 (d, $J = 6.6$ Hz, 2 × POC), 40.54 (s, PCCCC), 30.21 (d, $J = 15.8$ Hz, PCCC), 25.35 (d, $J = 141.4$ Hz, PC), 20.02 (d, $J = 5.2$ Hz, PCC), 16.40 (t, $J = 5.9$ Hz, 2 × POCC)^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 32.53. Anal. Calcd. for $C_{13}H_{22}N_3O_5P \times 0.25H_2O$: C, 47.13; H, 6.69; N, 12.68; Found: C, 46.99; H, 6.59; N, 12.63.

4.12. Diethyl {2-[(3-nitropyridin-2-yl)amino]ethoxy}methylphosphonate 5e

According to the general procedure from diethyl (2-aminoethoxy)methylphosphonate **4e** (0.608 g, 2.88 mmol) and 2-chloro-3-nitropyridine (0.457 g, 2.88 mmol) diethyl 2-[(3-nitropyridin-2-yl)amino]ethoxy}methylphosphonate **5e** (0.748 g, 78%) was obtained as a yellow oil. IR (film, cm^{-1}) ν_{max}: 3397, 3085, 2984, 2933, 1573, 1391, 1246, 1027, 969; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 8.43 (dd, $J = 8.3$ Hz, $J = 1.7$ Hz, 1 H, Ar–*H*), 8.41 (dd, $J = 4.5$ Hz, $J = 1.7$ Hz, 1 H, Ar–*H*), 6.67 (dd, $J = 8.3$ Hz, $J = 4.5$ Hz, 1 H, Ar–*H*), 4.23–4.16 (m, 4 H, 2 × POCH_2CH$_3$), 3.92–3.89 (m, 2 H, PCOCH_2), 3.87 (d, $J = 8.3$ Hz, 2 H, PCH_2), 3.86–3.84 (m, 2 H, PCOCCCH_2), 1.36 (t, $J = 7.1$ Hz, 6 H, 2 × POCH$_2$CH_3) ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 155.41, 152.49, 135.28, 128.37, 111.81, 71.73 (d, $J = 10.4$ Hz, PCOC), 65.33 (d, $J = 166.2$ Hz, PC), 62.49 (d, $J = 6.5$ Hz, 2 × POC), 40.70 (s, PCOCC),

16.45 (d, $J = 5.6$ Hz, 2 × POC*C*) ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 20.74; Anal. Calcd. for $C_{12}H_{20}N_3O_6P$: C, 43.25; H, 6.05; N, 12.61; Found: C, 43.24; H, 6.07; N, 12.61.

4.13. Diethyl 2-{2-[(3-nitropyridin-2-yl)amino]ethoxy}ethylphosphonate 5f

According to the general procedure from diethyl 2-(2-aminoethoxy)ethylphosphonate **4f** (0.849 g, 3.77 mmol) and 2-chloro-3-nitropyridine (0.598 g, 3.77 mmol) diethyl 2-[(3-nitropyridin-2-yl)amino]ethoxy}methylphosphonate **5f** (1.191 g, 91%) was obtained as a yellow oil. IR (film, cm^{-1}) ν_{max}: 3396, 2984, 2932, 1572, 1390, 1245, 1027, 969, 761; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 8.58–8.29 (m, 3 H, N*H*, 2 × Ar–*H*), 6.65 (dd, $J = 8.3$ Hz, $J = 4.5$ Hz, 1 H, Ar–*H*), 4.21–4.02 (m, 4 H, 2 × POC*H*$_2$CH$_3$), 3.85 (dd, $J = 10.8$ Hz, $J = 5.4$ Hz, 2 H, PCCOC*H*$_2$), 3.77 (dt, $J = 11.5$ Hz, $J = 7.5$ Hz, 1 H, PCC*H*$_2$), 3.70 (t, $J = 5.4$ Hz, 2 H, PCCOCC*H*$_2$), 2.14 (dt, $J = 18.7$ Hz, $J = 7.5$ Hz, 2 H, PC*H*$_2$), 1.32 (t, $J = 7.1$ Hz, 6 H, 2 × POCH$_2$C*H*$_3$) ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 155.53, 152.57, 135.28, 128.30, 111.76, 69.13 (s, PCCO*C*), 65.08 (s, PC*C*), 61.68 (d, $J = 6.4$ Hz, 2 × PO*C*), 40.88 (s, PCCOC*C*), 26.99 (d, $J = 139.7$ Hz, P*C*), 16.39 (d, $J = 6.0$ Hz, 2 × POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 29.11. Anal. Calcd. for $C_{13}H_{22}N_3O_6P \times 0.4H_2O$: C, 44.04; H, 6.48; N, 11.85; Found: C, 44.10; H, 6.43; N, 11.84.

4.14. Diethyl 1-hydroxy-2-[(3-nitropyridin-2-yl)amino]ethylphosphonate 5g

According to the general procedure from diethyl 2-amino-1-hydroxyethylphosphonate **4g** (0.576 g, 2.92 mmol) and 2-chloro-3-nitropyridine (0.463 g, 2.92 mmol) diethyl 1-hydroxy-2-[(3-nitropyridin-2-yl)amino]ethylphosphonate **5g** (0.522 g, 56%) was obtained as a yellow solid. M.p. 97–98 °C; IR (KBr, cm^{-1}) ν_{max}: 3385, 3227, 3089, 2984, 1571, 1390, 1349, 1032, 977, 757; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 8.57 (brs, 1 H, N*H*), 8.46 (dd, $J = 8.3$ Hz, $J = 1.8$ Hz, 1 H, Ar–*H*), 8.37 (dd, $J = 4.6$ Hz, $J = 1.8$ Hz, 1 H, Ar–*H*), 6.73 (dd, $J = 8.3$, $J = 4.6$ Hz, 1 H, Ar–*H*), 4.31–4.13 (m, 6 H, PC*H*$_2$, 2 × POC*H*$_2$CH$_3$), 4.12–3.85 (m, 1 H, PC*H*), 1.37 (t, $J = 7.0$ Hz, 3 H, POCH$_2$C*H*$_3$), 1.30 (t, $J = 7.0$ Hz, 3 H, POCH$_2$C*H*$_3$).^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 154.88, 152.84, 135.74, 128.88, 112.37, 68.13 (d, $J = 161.9$ Hz, P*C*), 62.94 (d, $J = 6.6$ Hz, PO*C*), 62.90 (d, $J = 6.6$ Hz, PO*C*), 43.49 (d, $J = 4.6$ Hz, PCC), 16.48 (d, $J = 5.4$ Hz, POCC), 16.44 (d, $J = 5.4$ Hz, POC*C*); ^{31}P NMR (81 MHz, $CDCl_3$) δ [ppm]: 23.06; Anal. Calcd. for $C_{11}H_{18}N_3O_6P$: C, 41.38; H, 5.68; N, 13.16; Found: C, 41.64; H, 5.70; N, 13.18.

4.15. Diethyl 1-hydroxy-3-[(3-nitropyridin-2-yl)amino]propylphosphonate 5h

According to the general procedure from diethyl 3-amino-1-hydroxypropylphosphonate **4h** (0.653 g, 3.09 mmol) and 2-chloro-3-nitropyridine (0.490 g, 3.09 mmol) diethyl 1-hydroxy-3-[(3-nitropyridin-2-yl)amino]propylphosphonate **5h** (0.907 g, 88%) was obtained as a yellow oil. IR (film, cm^{-1}) ν_{max}: 3395, 3310, 3082, 2986, 1249, 1037, 967, 759; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 8.49 (s, 1 H, N*H*), 8.48 (dd, $J = 8.3$ Hz, $J = 1.7$ Hz, 1 H, Ar–*H*), 8.40 (dd, $J = 4.6$ Hz, $J = 1.7$ Hz, 1 H, Ar–*H*), 6.71 (dd, $J = 8.3$ Hz, $J = 4.6$ Hz, 1 H, Ar–*H*), 4.23–4.19 (m, 4 H, $2 \times POCH_2CH_3$), 4.11–4.05 (m, 1 H, PCCC*H*), 3.97 (ddd, $J = 11.4$ Hz, $J = 8.6$ Hz, $J = 2.9$ Hz, 1 H, PC*H*), 3.78–3.72 (m, 1 H, PCCC*H*), 1.37 (t, $J = 7.1$ Hz, 3 H, $POCH_2CH_3$), 1.35 (t, $J = 7.1$ Hz, 3 H, $POCH_2CH_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 155.05, 152.81, 135.98, 128.58, 111.88, 65.19 (d, $J = 167.7$ Hz, P*C*), 62.74 (d, $J = 7.1$ Hz, PO*C*), 62.63 (d, $J = 7.1$ Hz, PO*C*), 37.74 (d, $J = 15.8$ Hz, PCC*C*), 31.68 (s, PC*C*), 16.50 (d, $J = 5.5$ Hz, POC*C*), 16.49 (d, $J = 5.5$ Hz, POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 24.56; Anal. Calcd. for $C_{12}H_{20}N_3O_6P \times 0.3H_2O$: C, 42.56; H, 6.13; N, 12.41; Found: C, 42.40; H, 6.09; N, 12.47.

4.16. Diethyl 2-hydroxy-3-[(3-nitropyridin-2-yl)amino]propylphosphonate 5i

According to the general procedure from diethyl 3-amino-2-hydroxypropylphosphonate **4i** (0.234 g, 1.11 mmol) and 2-chloro-3-nitropyridine (0.166 g, 1.05 mmol) diethyl 2-hydroxy-3-[(3-nitropyridin-2-yl)amino]propylphosphonate **5i** (0.292 g, 79%) was obtained as a yellow oil. IR (film, cm^{-1}) ν_{max}: 3373, 3274, 2982, 2930, 1225, 1027, 964, 762; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 8.53 (s, 1 H, N*H*), 8.46 (dd, $J = 8.3$ Hz, $J = 1.6$ Hz, 1 H, Ar–*H*), 8.39 (dd, $J = 4.4$ Hz, $J = 1.4$ Hz, 1 H, Ar–*H*), 6.70 (dd, $J = 8.3$ Hz, $J = 4.5$ Hz, 1 H, Ar–*H*), 4.39 (d, $J = 3.3$ Hz, 1 H, O*H*), 4.36–4.28 (m, 1 H, PCC*H*), 4.24–4.11 (m, 4 H, $2 \times POCH_2CH_3$), 4.02–3.72 (m, 2 H, PCCCH_2), 2.07 (dd, $J = 17.9$ Hz, $J = 6.4$ Hz, 2 H, PCH_2), 1.37 (t, $J = 7.1$ Hz, 6 H, $2 \times POCH_2CH_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 155.17, 152.94, 135.57, 128.62, 112.15, 66.31 (d, $J = 3.5$ Hz, PC*C*), 62.05 (d, $J = 6.4$ Hz, PO*C*), 62.00 (d, $J = 6.6$ Hz, PO*C*), 47.35 (d, $J = 15.9$ Hz, PCC*C*), 31.39 (d, $J = 139.0$ Hz, P*C*), 16.42 (d, $J = 5.9$ Hz, POC*C*), 16.38 (d, $J = 5.9$ Hz, POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 29.04; Anal. Calcd. for $C_{12}H_{20}N_3O_6P$: C, 43.25; H, 6.05; N, 12.61; Found: C, 43.21; H, 6.07; N, 12.70.

4.17. Diethyl 1-methoxy-2-[(3-nitropyridin-2-yl)amino]ethylphosphonate 5j

According to the general procedure from diethyl 2-amino-1-methoxyethylphosphonate **4j** (0.200 g, 0.95 mmol) and 2-chloro-3-nitropyridine (0.151 g, 0.95 mmol) diethyl 1-methoxy-2-[(3-nitropyridin-2-yl)amino]ethylphosphonate

5j (0.234 g, 74%) was obtained as a yellow oil. IR (film, cm^{-1}) ν_{max}: 2294, 3085, 2984, 2934, 1573, 1392, 1251, 1024, 966, 761; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 8.55 (brs, 1 H, N*H*), 8.46 (dd, $J = 8.3$ Hz, $J = 1.6$ Hz, 1 H, Ar–*H*), 8.44 (dd, $J = 4.5$ Hz, $J = 1.6$ Hz, 1 H, Ar–*H*), 6.70 (dd, $J = 8.3$ Hz, $J = 4.5$ Hz, 1 H, Ar–*H*), 4.32–4.20 (m, 5 H, $2 \times POCH_2CH_3$, PC*H*), 3.90–3.77 (m, 2 H, PCCH_2), 3.62 (s, 3 H, CH_3), 1.40 (t, $J = 7.1$ Hz, 3 H, $POCH_2CH_3$), 1.38 (t, $J = 7.1$ Hz, 3 H, $POCH_2CH_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 155.16, 152.22, 135.46, 128.60, 111.96, 76.09 (d, $J = 164.1$ Hz, P*C*), 62.90 (d, $J = 7.1$ Hz, PO*C*), 62.59 (d, $J = 7.1$ Hz, PO*C*), 60.49 (d, $J = 5.0$ Hz, PCO*C*), 40.99 (d, $J = 5.4$ Hz, PC*C*), 16.53 (d, $J = 5.5$ Hz, POC*C*), 16.49 (d, $J = 5.6$ Hz, POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 20.82; Anal. Calcd. for $C_{12}H_{20}N_3O_6P$: C, 43.25; H, 6.05; N, 12.61; Found: C, 43.19; H, 5.83; N, 12.43.

4.18. Diethyl 1-methoxy-3-[(3-nitropyridin-2-yl)amino]propylphosphonate 5k

According to the general procedure from diethyl 3-amino-1-methoxypropylphosphonate **4k** (0.300 g, 1.33 mmol) and 2-chloro-3-nitropyridine (0.211 g, 1.33 mmol) diethyl 1-methoxy-3-[(3-nitropyridin-2-yl)amino]propylphosphonate **5k** (0.180 g, 39%) was obtained as a yellow oil. IR (film, cm^{-1}) ν_{max}: 3395, 3086, 2984, 2933, 1573, 1392, 1251, 1024, 965, 761; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 8.49 (brs, 1 H, N*H*), 8.45 (dd, $J = 4.7$ Hz, $J = 1.7$ Hz, 1 H, Ar–*H*), 8.44 (s, 1 H, Ar–*H*), 6.67 (dd, $J = 7.8$ Hz, $J = 5.0$ Hz, 1 H, Ar–*H*), 4.27–4.17 (m, 4 H, $2 \times POCH_2CH_3$), 3.97–3.77 (m, 2 H, PCCCH_2), 3.65–3.60 (m, 4 H, CH_3, PC*H*), 2.28–2.04 (m, 2 H, PCCH_2), 1.39 (t, $J = 7.2$ Hz, 3 H, $POCH_2CH_3$), 1.36 (t, $J = 7.2$ Hz, 3 H, $POCH_2CH_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 155.67, 152.63, 135.26, 128.18, 111.66, 76.33 (d, $J = 164.9$ Hz, P*C*), 62.58 (d, $J = 6.9$ Hz, PO*C*), 62.34 (d, $J = 7.2$ Hz, PO*C*), 60.31 (d, $J = 2.5$ Hz, PCO*C*), 38.46 (d, $J = 14.5$ Hz, PCC*C*), 29.89 (d, $J = 2.6$ Hz, PC*C*), 16.55 (d, $J = 5.4$ Hz, POC*C*), 16.53 (d, $J = 5.4$ Hz, POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 22.64. Anal. Calcd. for $C_{13}H_{22}N_3O_6P$: C, 44.96; H, 6.38; N, 12.10; Found: C, 44.95; H, 6.41; N, 12.03.

4.19. Diethyl 2-methoxy-3-[(3-nitropyridin-2-yl)amino]propylphosphonate 5l

According to the general procedure from diethyl 3-amino-2-methoxypropylphosphonate **4l** (0.250 g, 1.11 mmol) and 2-chloro-3-nitropyridine (0.166 g, 1.05 mmol)diethyl 2-methoxy-3-[(3-nitropyridin-2-yl)amino]propylphosphonate **5l** (0.332 g, 86%) was obtained as a yellow oil. IR (film, cm^{-1}) ν_{max}: 3395, 3085, 2984, 2933, 1572, 1392, 1249, 1024, 965, 761; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 8.47 (brs, 1 H, N*H*), 8.45 (dd, $J = 8.3$ Hz, $J = 1.8$ Hz, 1 H, Ar–*H*), 8.42 (dd, $J = 4.5$ Hz, $J = 1.7$ Hz, 1 H, Ar–*H*), 6.68

(dd, $J = 8.3$ Hz, $J = 4.5$ Hz, 1 H, Ar–*H*), 4.20–4.07 (m, 5 H, 2 × POC*H*$_2$CH$_3$, PCC*H*), 3.93–3.75 (m, 2 H, PCCC*H*$_2$), 3.49 (s, 3 H, C*H*$_3$), 2.19 (ddd, $J = 19.3$ Hz, $J = 15.4$ Hz, $J = 6.0$ Hz, 1 H, PC*H*$_b$), 2.05 (ddd, $J = 18.3$ Hz, $J = 15.4$ Hz, $J = 6.6$ Hz, 1 H, PC*H*$_a$), 1.37 (t, $J = 7.1$ Hz, 3 H, POCH$_2$C*H*$_3$), 1.35 (t, $J = 7.1$ Hz, 3 H, POCH$_2$C*H*$_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 155.54, 135.28, 128.52, 127.03, 111.89, 75.05 (s, PC*C*) 61.89 (d, $J = 6.4$ Hz, PO*C*), 61.63 (d, $J = 6.3$ Hz, PO*C*), 43.96 (d, $J = 9.1$ Hz, PCC*C*), 29.29 (d, $J = 140.0$ Hz, P*C*), 16.38 (d, $J = 6.2$ Hz, POC*C*), 16.36 (d, $J = 6.1$ Hz, POC*C*); ^{31}P NMR (243 MHz, CDCl3) δ [ppm]: 27.87; Anal. Calcd. for $C_{13}H_{22}N_3O_6P$: C, 44.96; H, 6.38; N, 12.10; Found: C, 44.62; H, 6.16; N, 12.08.

4.20. Synthesis of diethyl [(3-aminopyridin-2-ylo)amino]alkylphosphonates 6a–l – general procedure

Solution of diethyl (3-nitropyridin-2-ylo)aminoalkylphosphonate **5a–l** (1.00 mmol) in 95% acetic acid (0.240 mL) was added to mixture tin(II) chloride (3.30 mmol) in 36% hydrochloric acid (0.640 mL). The reaction mixture was stirred at room temperature for 1.5 hours. Then the reaction was neutralized with 20% NaOH and concentrated in vacuo. The residue was dissolved in chloroform, dried over anhydrous $MgSO_4$ and filtered. The solution was concentrated and the residue was chromatographed on a silica gel column with a chloroform–methanol (100:1, v/v) mixture to give diethyl [(3-aminopyridin-2-ylo)amino]alkylphosphonates **6a–l**.

4.21. Diethyl [(3-aminopyridin-2-yl)amino]methylphosphonate 6a

According to the general procedure from diethyl [(3-nitropyridin-2-yl)amino]methylphosphonate **5a** (0.784 g, 2.71 mmol) in 95% acetic acid (0.650 ml) and tin(II) chloride (1.670 g, 8.81 mmol) in 36% hydrochloric acid (1.710 ml) diethyl [(3-aminopyridin-2-yl)amino]methylphosphonate **6a** (0.485 g, 69%) was obtained as a pale red oil. IR (film, cm^{-1}) ν_{max}: 3368, 3265, 2983, 2931, 1504, 1302, 785; ^{1}H NMR (200 MHz, $CDCl_3$) δ [ppm]: 7.72 (dd, $J = 5.0$ Hz, $J = 1.5$ Hz, 1 H, Ar–*H*) , 6.86 (dd, $J = 7.4$ Hz, $J = 1.5$ Hz, 1 H, Ar–*H*), 6.57 (dd, $J = 7.4$ Hz, $J = 5.0$ Hz, 1 H, Ar–*H*), 4.48 (brs, 1 H, N*H*), 4.32–4.03 (m, 4 H, 2 × POC*H*$_2$CH$_3$), 3.93 (dd, $J = 11.8$ Hz, $J = 5.9$ Hz, 2 H, PC*H*$_2$), 3.35 (brs, 2 H, N*H*$_2$), 1.30 (t, $J = 7.1$ Hz, 6 H, 2 × POCH$_2$C*H*$_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 148.73 (d, $^3J = 8.7$ Hz, Ar–*C*), 138.20, 129.20, 121.85, 114.37, 62.43 (d, $J = 6.6$ Hz, 2 × PO*C*), 36.89 (d, $J = 156.3$ Hz, P*C*), 16.35 (d, $J = 5.9$ Hz, 2 × POC*C*); ^{31}P NMR (81 MHz, $CDCl_3$) δ [ppm]: 26.56; Anal. Calcd. for $C_{10}H_{18}N_3O_3P \times 0.25H_2O$: C, 45.54; H, 7.07; N, 15.93; Found: C, 45.74; H, 7.18; N, 15.77.

4.22. Diethyl 2-[(3-aminopyridin-2-yl)amino]ethylphosphonate 6b

According to the general procedure from diethyl 2-[(3-nitropyridin-2-yl)amino]ethylphosphonate **5b** (0.218 g, 0.72 mmol) in 95% acetic acid (0.173 ml) and tin(II) chloride (0.444 g, 2.34 mmol) in 36% hydrochloric acid (0.454 ml) diethyl 2-[(3-aminopyridin-2-yl)amino]ethylphosphonate **6b** (0.194 g, 99%) was obtained as a pale red oil. IR (film, cm^{-1}) ν_{max}: 3372, 3263, 2983, 2929, 1642, 1229, 987, 785; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 7.72 (dd, $J = 5.1$ Hz, $J = 1.5$ Hz, 1 H, Ar–*H*), 6.84 (dd, $J = 7.4$ Hz, $J = 1.5$ Hz, 1 H, Ar–*H*), 6.53 (dd, $J = 7.4$ Hz, $J = 5.1$ Hz, 1 H, Ar–*H*), 5.00 (brs, 1 H, N*H*), 4.20–4.06 (m, 4 H, 2 × POCH_2CH$_3$), 3.79 (dt, $J = 20.4$ Hz, $J = 6.5$ Hz, 2 H, PCCH_2), 3.11 (brs, 2 H, NH_2), 2.18 (dt, $J = 17.4$ Hz, $J = 6.5$ Hz, 2 H, PCH_2), 1.34 (t, $J = 7.1$ Hz, 6 H, 2 × POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 149.41, 138.31, 128.97, 121.52, 113.54, 61.75 (d, $J = 6.5$ Hz, 2 × POC), 35.71 (d, $J = 5.4$ Hz, PC*C*), 25.66 (d, $J = 139.0$ Hz, P*C*), 16.39 (d, $J = 6.0$ Hz, 2 × POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 30.95; Anal. Calcd. for $C_{11}H_{20}N_3O_3P \times 0.6H_2O$: C, 46.51; H, 7.52; N, N. 14.79; Found: C, 46.50; H, 7.52; N, 14.48.

4.23. Diethyl 3-[(3-aminopyridin-2-yl)amino]propylphosphonate 6c

According to the general procedure from diethyl 3-[(3-nitropyridin-2-yl)amino]propylphosphonate **5c** (0.393 g, 1.24 mmol) in 95% acetic acid (0.298 ml) and tin(II) chloride (0.764 g, 4.03 mmol) in 36% hydrochloric acid (0.782 ml) diethyl 3-[(3-aminopyridin-2-yl)amino]propylphosphonate **6c** (0.114 g, 32%) was obtained as a pale red oil. IR (film, cm^{-1}) ν_{max}: 3376, 3262, 3048, 2982, 2937, 1254, 1026, 965; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 7.72 (dd, $J = 5.1$ Hz, $J = 1.5$ Hz, 1 H, Ar–*H*), 6.83 (dd, $J = 7.4$ Hz, $J = 1.5$ Hz, 1 H, Ar–*H*), 6.51 (dd, $J = 7.4$ Hz, $J = 5.1$ Hz, 1 H, Ar–*H*), 4.79 (brs, 1 H, N*H*), 4.29–3.96 (m, 4 H, 2 × POCH_2CH$_3$), 3.56 (dd, $J = 10.7$ Hz, $J = 6.6$ Hz, 1 H, PCCCH_2), 3.40 (brs, 2 H, NH_2), 2.04–1.98 (m, 2 H, PCCH_2), 1.93–1.88 (m, 2 H, PCH_2), 1.33 (t, $J = 7.1$ Hz, 6 H, 2 × POCH$_2$CH_3).; ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 149.87, 138.52, 128.57, 121.23, 113.08, 61.66 (d, $J = 6.6$ Hz, 2 × POC), 41.98 (d, $J = 13.7$ Hz, PCC*C*), 23.64 (d, $J = 141.5$ Hz, P*C*), 22.43 (d, $J = 4.9$ Hz, PC*C*), 16.42 (d, $J = 6.0$ Hz, 2 × POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 32.86; Anal. Calcd. for $C_{12}H_{22}N_3O_3P \times 0.5H_2O$: C, 48.64; H, 7.82; N, 14.18; Found: C, 48.87; H, 7.82; N, 14.04.

4.24. Diethyl 4-[(3-aminopyridin-2-yl)amino]butylphosphonate 6d

According to the general procedure from diethyl 4-[(3-nitropyridin-2-yl)amino]butylphosphonate **5d** (0.666 g, 2.01 mmol) in 95% acetic acid

(0.160 ml) and tin(II) chloride (1.236 g, 6.52 mmol) in 36% hydrochloric acid (1.26 ml) diethyl 4-[(3-aminopyridin-2-yl)amino]butylphosphonate **6d** (0.279 g, 46%) was obtained as a pale red oil. IR (film, cm^{-1}) ν_{max}: 3377, 3262, 2983, 1254, 1027, 966, 784; ^1H NMR (600 MHz, $CDCl_3$) δ [ppm]: 7.73 (dd, $J = 5.1$ Hz, $J = 1.2$ Hz, 1 H, Ar–*H*), 6.83 (dd, $J = 7.3$ Hz, $J = 1.2$ Hz, 1 H, Ar–*H*), 6.50 (dd, $J = 7.3$ Hz, $J = 5.1$ Hz, 1 H, Ar–*H*), 4.40 (s, 1 H, N*H*), 4.25–3.95 (m, 4 H, 2 × POCH_2CH$_3$), 3.48–3.45 (m, 2 H, PCCCCH_2), 3.32 (brs, 2 H, NH_2), 1.87–1.72 (m, 6 H, PCH_2CH_2CH_2), 1.32 (t, $J = 7.1$ Hz, 6 H, 2 × POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 150.21, 138.74, 128.43, 121.48, 113.03, 61.51 (d, $J = 6.6$ Hz, 2 × POC), 41.12, 30.30 (d, $J = 15.0$ Hz, PCCC), 25.25 (d, $J = 140.5$ Hz, PC), 20.18 (d, $J = 5.0$ Hz, PCC), 16.42 (d, $J = 5.9$ Hz, 2 × POCC); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 33.19; Anal. Calcd. for $C_{13}H_{24}N_3O_3P \times H_2O$: C, 48.89; H, 8.21; N, 13.16; Found: C, 48.88; H, 8.36; N, 13.05.

4.25. Diethyl {2-[(3-aminopyridin-2-yl)amino]ethoxy}methylphosphonate 6e

According to the general procedure from diethyl {2-[(3-nitropyridin-2-yl)amino]ethoxy}methylphosphonate **5e** (0.380 g, 1.14 mmol) in 95% acetic acid (0.274 ml) and tin(II) chloride (0.702 g, 3.70 mmol) in 36% hydrochloric acid (0.717 ml) diethyl {2-[(3-aminopyridin-2-yl)amino]ethoxy}methylphosphonate **6e** (0.270 g, 78%) was obtained as a pale red oil. IR (film, cm^{-1}) ν_{max}: 3373, 3267, 2982, 2929, 2907, 1226, 1027, 992, 962; ^1H NMR (600 MHz, $CDCl_3$) δ [ppm]: 7.70 (dd, $J = 5.1$ Hz, $J = 1.5$ Hz, 1 H, Ar–*H*), 6.82 (dd, $J = 7.4$ Hz, $J = 1.5$ Hz, 1 H, Ar–*H*), 6.51 (dd, $J = 7.4$ Hz, $J = 5.1$ Hz, 1 H, Ar–*H*), 4.96 (brs, 1 H, N*H*), 4.27–4.10 (m, 4 H, 2 × POCH_2CH$_3$), 3.90–3.86 (m, 2 H, PCOCH_2), 3.87 (d, $J = 7.8$ Hz, 2 H, PCH_2), 3.69 (dd, $J = 10.0$ Hz, $J = 5.1$ Hz, 2 H, PCOCCH_2), 3.49 (brs, 2 H, NH_2), 1.35 (t, $J = 7.1$ Hz, 6 H, 2 × POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 149.55, 138.19, 128.93, 121.04, 113.28, 72.83 (d, $J = 9.1$ Hz, PCOC), 65.30 (d, $J = 166.6$ Hz, PC), 62.50 (d, $J = 6.6$ Hz, 2 × POC), 41.24 (s, PCOCC), 16.44 (d, $J = 5.6$ Hz, 2 × POCC); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 21.72; Anal. Calcd. for $C_{12}H_{22}N_3O_4P \times 0.2H_2O$: C, 46.96; H, 7.36; N, 13.69; Found: C, 46.95; H, 7.23; N, 13.58.

4.26. Diethyl 2-{2-[(3-aminopyridin-2-yl)amino]ethoxy}ethylphosphonate 6f

According to the general procedure from diethyl 2-{2-[(3-nitropyridin-2-yl)amino]ethoxy}ethylphosphonate **5f** (0.493 g, 1.42 mmol) in 95% acetic acid (0.341 ml) and tin(II) chloride (0.876 g, 4.62 mmol) in 36% hydrochloric acid (0.896 ml) diethyl 2-{2-[(3-aminopyridin-2-yl)amino]ethoxy}ethylphosphonate **6f** (0.428 g, 95%)was obtained as a pale red oil. IR (film,

cm^{-1}) ν_{max}: 3375, 3263, 2983, 2927, 1225, 1027, 994, 785; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 7.66 (dd, $J = 5.1$ Hz, $J = 1.5$ Hz, 1 H, Ar–*H*), 6.77 (dd, $J = 7.4$ Hz, $J = 1.5$ Hz, 1 H, Ar–*H*), 6.48 (dd, $J = 7.4$ Hz, $J = 5.1$ Hz, 1 H, Ar–*H*), 4.17–4.04 (m, 4 H, 2 × POCH_2CH$_3$), 3.80 (dt, $J = 19.5$ Hz, $J = 6.4$ Hz, 2 H, PCCH_2), 3.77–3.74 (m, 2 H, PCCOCH_2), 3.69–3.66 (m, 2 H, PCCOCCCH_2), 2.12 (dt, $J = 17.9$ Hz, $J = 6.4$ Hz, 2 H, PCH_2), 1.33 (t, $J = 7.1$ Hz, 3 H, 2 × POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 149.18, 137.34, 129.34, 120.22, 112.99, 69.64, 64.30 (d, $J = 5.6$ Hz, PC*C*), 61.78 (d, $J = 6.5$ Hz, 2 × PO*C*), 41.20, 26.75 (d, $J = 141.8$ Hz, P*C*), 16.36 (d, $J = 6.1$ Hz, 2 × POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 29.41; Anal. Calcd. for $C_{13}H_{24}N_3O_4P \times 0.8H_2O$: C, 47.07; H, 7.78; N, 12.67; Found: C, 47.05; H, 7.78; N, 12.65.

4.27. Diethyl 2-[(3-aminopyridin-2-yl)amino]-1-hydroxyethylphosphonate 6g

According to the general procedure from diethyl 1-hydroxy-2-[(3-nitropyridin-2-yl)amino]ethylphosphonate **5g** (0.488 g, 1.53 mmol) in 95% acetic acid (0.367 ml) and tin(II) chloride (0.946 g, 4.99 mmol) in 36% hydrochloric acid (0.968 ml) diethyl 2-[(3-aminopyridin-2-yl)amino]-1-hydroxyethylphosphonate **6g** (0.243 g, 55%) was obtained as a pale red oil. IR (film, cm^{-1}) ν_{max}: 3373, 3265, 3059, 2983, 2930, 1230, 1024, 970, 787; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 7.50 (d, $J = 5.4$ Hz, 1 H, Ar–*H*), 6.85 (dd, $J = 7.5$ Hz, $J = 1.4$ Hz, 1 H, Ar–*H*), 6.55 (dd, $J = 7.5$ Hz, $J = 5.4$ Hz, 1 H, Ar–*H*), 5.90 (brs, 1 H, N*H*), 4.36–4.01 (m, 6 H, PCCH_2, 2 × POCH_2CH$_3$), 3.92–3.71 (m, 3 H, PC*H*, NH_2) , 1.35 (t, $J = 7.1$ Hz, 3 H, POCH$_2$CH_3), 1.23 (t, $J = 7.1$ Hz, 3 H, POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 149.29, 135.30, 129.73, 121.71, 114.05, 70.10 (d, $J = 162.1$ Hz, P*C*), 63.07 (d, $J = 7.3$ Hz, PO*C*), 62.47 (d, $J = 7.0$ Hz, PO*C*), 45.60 (d, $J = 2.8$ Hz, PC*C*), 16.44 (d, $J = 5.8$ Hz, POC*C*), 16.32 (d, $J = 5.8$ Hz, POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 23.06; Anal. Calcd. for $C_{11}H_{20}N_3O_4P \times 0.7H_2O$: C, 43.77; H, 7.15; N, 13.92; Found: C, 43.88; H, 7.28; N, 13.65.

4.28. Diethyl 3-[(3-aminopyridin-2-yl)amino]-1-hydroxypropylphosphonate 6h

According to the general procedure from diethyl 1-hydroxy-3-[(3-nitropyridin-2-yl)amino]propylphosphonate **5h** (0.307 g, 0.92 mmol) in 95% acetic acid (0.360 ml) and tin(II) chloride (0.569 g, 3.00 mmol) in 36% hydrochloric acid (0.583 ml) diethyl 3-[(3-aminopyridin-2-yl)amino]-1-hydroxypropylphosphonate **6h** (0.103 g, 37%) was obtained as a pale red oil. IR (film, cm^{-1}) ν_{max}: 3385, 2981, 2926, 1217, 1024, 964, 763; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 7.60 (dd, $J = 5.3$ Hz, $J = 1.4$ Hz, 1 H, Ar–*H*), 6.86 (dd, $J = 7.4$ Hz, $J = 1.4$ Hz, 1 H, Ar–*H*), 6.51 (dd, $J = 7.4$ Hz, $J = 5.3$ Hz,

1 H, Ar–*H*), 5.10 (brs, 1 H, O*H*), 4.25–4.14 (m, 5 H, 2 × POC*H*$_2$CH$_3$, PC*H*), 4.01–3.88 (m, 2 H, PCCC*H*$_2$) 3.47 (brs, 1 H, N*H*), 2.10–1.90 (m, 2 H, PCC*H*$_2$), 1.36 (t, $J = 5.9$ Hz, 3 H, POCH$_2$C*H*$_3$), 1.34 (t, $J = 5.8$ Hz, 3 H, POCH$_2$C*H*$_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 150.65, 137.29, 128.48, 122.20, 113.16, 64.01 (d, $J = 170.6$ Hz, P*C*), 62.60 (d, $J = 7.1$ Hz, PO*C*), 62.51 (d, $J = 6.7$ Hz, PO*C*), 37.38 (d, $J = 16.1$ Hz, PCC*C*), 33.30, 16.51 (d, $J = 5.6$ Hz, POC*C*), 16.47 (d, $J = 5.5$ Hz, POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 26.28; Anal. Calcd. for $C_{12}H_{22}N_3O_4P \times 0.1H_2O$: C, 47.24; H, 7.33; N, 13.77; Found: C, 47.54; H, 7.43; N, 13.71.

4.29. Diethyl 3-[(3-aminopyridin-2-yl)amino]-2-hydroxypropylphosphonate 6i

According to the general procedure from diethyl 2-hydroxy-3-[(3-nitropyridin-2-yl)amino]propylphosphonate **5i** (0.106 g, 0.35 mmol) in 95% acetic acid (0.087 ml) and tin(II) chloride (0.216 g, 1.14 mmol) in 36% hydrochloric acid (0.221 ml) diethyl 3-[(3-aminopyridin-2-yl)amino]-2-hydroxypropylphosphonate **6i** (0.093 g, 96%) was obtained as a pale red oil. IR (film, cm^{-1}) ν_{max}: 3374, 3263, 2983, 1224, 1027, 966, 759; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 7.64 (dd, $J = 5.1$ Hz, $J = 1.1$ Hz, 1 H, Ar–*H*), 6.88 (dd, $J = 7.4$ Hz, $J = 1.1$ Hz, 1 H, Ar–*H*), 6.55 (dd, $J = 7.4$ Hz, $J = 5.1$ Hz, 1 H, Ar–*H*), 6.38 (brs, 1 H, N*H*), 5.01 (brs, 1 H, O*H*), 4.28–4.21 (m, 1 H, PCC*H*), 4.21–4.08 (m, 4 H, 2 × POC*H*$_2$CH$_3$), 3.83 (ddd, $J = 14.3$ Hz, $J = 5.7$ Hz, $J = 2.0$ Hz, 1 H, PCCC*H*$_a$), 3.61 (dt, $J = 14.3$ Hz, $J = 5.7$ Hz, $J = 5.7$ Hz, 1 H, PCCC*H*$_b$), 3.33 (brs, 2 H, N*H*$_2$), 2.11 (ddd, $J = 18.0$ Hz, $J = 6.7$ Hz, $J = 2.4$ Hz, 2 H, PC*H*$_2$), 1.37 (t, $J = 6.9$ Hz, 3 H, POCH$_2$C*H*$_3$), 1.36 (t, $J = 6.9$ Hz, 3 H, POCH$_2$C*H*$_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 150.02, 137.36, 128.92, 121.76, 113.66, 67.43, 61.86 (d, $J = 6.5$ Hz, PO*C*), 61.83 (d, $J = 6.4$ Hz, PO*C*), 48.58 (d, $J = 10.0$ Hz, PCC*C*), 31.34 (d, $J = 136.1$ Hz, P*C*), 16.37 (d, $J = 6.1$ Hz, 2 × POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 29.31; Anal. Calcd. for $C_{12}H_{22}N_3O_4P$: C, 47.52; H, 7.31; N, 13.85; Found: C, 47.54; H, 7.56; N, 13.74.

4.30. Diethyl 2-[(3-aminopyridin-2-yl)amino]-1-methoxyethylphosphonate 6j

According to the general procedure from diethyl 1-methoxy-2-[(3-nitropyridin-2-yl)amino]ethylphosphonate **5j** (0.197 g, 0.59 mmol) in 95% acetic acid (0.216 ml) and tin(II) chloride (0.366 g, 1.93 mmol) in 36% hydrochloric acid (0.374 ml) diethyl 2-[(3-aminopyridin-2-yl)amino]-1-methoxyethylphosphonate **6j** (0.140 g, 78%) was obtained as a pale red oil. IR (film, cm^{-1}) ν_{max}: 3382, 3263, 2983, 2933, 1233, 1024, 968; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 7.69 (d, $J = 4.7$ Hz, 1 H, Ar–*H*), 6.88 (dd, $J = 7.4$ Hz, $J = 1.3$ Hz, 1 H, Ar–*H*), 6.57 (dd, $J = 7.4$ Hz, $J = 4.7$ Hz, 1 H, Ar–*H*), 5.28

(brs, 1 H, N*H*), 4.28–4.17 (m, 4 H, 2 × POC*H*$_2$CH$_3$), 4.09–4.00 (m, 1 H, PC*H*), 3.88–3.78 (m, 2 H, PCC*H*$_2$), 1.83 (brs, 2 H, N*H*$_2$), 1.39 (t, $J = 7.1$ Hz, 3 H, POCH$_2$C*H*$_3$), 1.36 (t, $J = 7.1$ Hz, 3 H, POCH$_2$C*H*$_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 149.02, 144.42, 129.59, 121.57, 113.69, 76.10 (d, $J = 163.3$ Hz, P*C*), 62.85 (d, $J = 7.0$ Hz, PO*C*), 62.60 (d, $J = 6.9$ Hz, PO*C*), 60.07 (d, $J = 6.7$ Hz, PC*C*), 41.36, 16.50 (d, $J = 6.2$ Hz, POC*C*), 16.46 (d, $J = 6.3$ Hz, POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 22.10; Anal. Calcd. for $C_{12}H_{22}N_3O_4P \times 0.6H_2O$: C, 45.89; H, 7.44; N, 13.38; Found: C, 45.85; H, 7.45; N, 13.32.

4.31. Diethyl 3-[(3-aminopyridin-2-yl)amino]-1-methoxypropylphosphonate 6k

According to the general procedure from diethyl 1-methoxy-3-[(3-nitropyridin-2-yl)amino]propylphosphonate **5k** (0.146 g, 0.42 mmol) in 95% acetic acid (0.100 ml) and tin(II) chloride (0.258 g, 1.36 mmol) in 36% hydrochloric acid (0.264 ml) diethyl 3-[(3-aminopyridin-2-yl)amino]-1-methoxypropylphosphonate **6k** (0.084 g, 63%) was obtained as a pale red oil. IR (film, cm^{-1}) ν_{max}: 3378, 3264, 3049, 2984, 1232, 1023, 969, 786; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 7.74 (dd, $J = 5.1$ Hz, $J = 1.5$ Hz, 1 H, Ar–*H*), 6.84 (dd, $J = 7.4$ Hz, $J = 1.5$ Hz, 1 H, Ar–*H*), 6.52 (dd, $J = 7.4$ Hz, $J = 5.1$ Hz, 1 H, Ar–*H*), 4.79 (s, 1 H, N*H*), 4.24–4.16 (m, 4 H, 2 × POC*H*$_2$CH$_3$), 3.77–3.57 (m, 2 H, PCCC*H*$_2$), 3.67 (ddd, $J = 8.3$ Hz, $J = 6.7$ Hz, $J = 4.3$ Hz, 1 H, PC*H*), 3.58 (s, 3 H, C*H*$_3$), 3.32 (brs, 2 H, N*H*$_2$), 2.29–2.03 (m, 2 H, PCC*H*$_2$), 1.37 (t, $J = 7.0$ Hz, 3 H, POCH$_2$C*H*$_3$), 1.35 (t, $J = 7.0$ Hz, 3 H, POCH$_2$C*H*$_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 150.00, 138.73, 128.54, 121.35, 113.11, 76.54 (d, $J = 137.9$ Hz, P*C*), 62.55 (d, $J = 7.0$ Hz, PO*C*), 62.43 (d, $J = 7.0$ Hz, PO*C*), 60.06 (d, $J = 4.7$ Hz, PC*C*), 38.66 (d, $J = 12.3$ Hz, PCC*C*), 29.91, 16.52 (d, $J = 5.2$ Hz, POC*C*), 16.49 (d, $J = 5.1$ Hz, POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 23.63; Anal. Calcd. for $C_{13}H_{24}N_3O_4P \times 0.6H_2O$: C, 47.58; H, 7.74; N, 12.81; Found: C, 47.67; H, 7.68; N, 12.93.

4.32. Diethyl 3-[(3-aminopyridin-2-yl)amino]-2-methoxypropylphosphonate 6l

According to the general procedure from diethyl 2-methoxy-3-[(3-nitropyridin-2-yl)amino]propylphosphonate **5l** (0.263 g, 0.83 mmol) in 95% acetic acid (0.199 ml) and tin(II) chloride (0.514 g, 2.71 mmol) in 36% hydrochloric acid (0.526 ml) diethyl 3-[(3-aminopyridin-2-yl)amino]-2-methoxypropylphosphonate **6l** (0.163 g, 68%) was obtained as a pale red oil. IR (film, cm^{-1}) ν_{max}: 3373, 3274, 2982, 2930, 1225, 1027, 964, 762; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 7.71 (d, $J = 5.1$ Hz, 1 H, Ar–*H*), 6.84 (dd, $J = 7.4$ Hz, $J = 1.5$ Hz, 1 H, Ar–*H*), 6.53 (dd, $J = 7.4$ Hz, $J = 5.1$ Hz,

1 H, Ar–*H*), 4.86 (s, 1 H, N*H*), 4.20–4.07 (m, 4 H, 2 × POC*H*$_2$CH$_3$), 3.95–3.86 (m, 1 H, PCC*H*), 3.76–3.66 (m, 2 H, PCCC*H*$_2$), 3.47 (s, 3 H, C*H*$_3$), 2.24–2.10 (m, 2 H, PC*H*$_2$), 1.36 (t, $J = 7.1$ Hz, 3 H, POCH$_2$C*H*$_3$), 1.33 (t, $J = 7.1$ Hz, 3 H, POCH$_2$C*H*$_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 149.65, 138.31, 128.88, 121.28, 113.46, 75.09 (d, $J = 1.5$ Hz, PC*C*), 61.79 (d, $J = 6.4$ Hz, PO*C*), 61.76 (d, $J = 6.3$ Hz, PO*C*), 57.00, 44.52 (d, $J = 8.5$ Hz, PCC*C*), 29.95 (d, $J = 139.6$ Hz, P*C*), 16.37 (d, $J = 6.1$ Hz, PO*C*), 16.36 (d, $J = 6.1$ Hz, PO*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 29.16; Anal. Calcd. for $C_{13}H_{24}N_3O_4P \times 0.4H_2O$: C, 48.11; H, 7.70; N, 12.95; Found: C, 48.19; H, 7.68; N, 12.92.

4.33. Synthesis of diethyl (1,2,3-triazolo[4,5-b]pyridin-3-yl)alkylphosphonate 7a–i – general procedure

A solution of diethyl [(3-aminopyridin-2-yl)amino]alkylphosphonate **6a–i** (1.00 mmol) in 98% H_2SO_4 (4.40 mL) was cooled to the 0 °C and a solution of sodium nitrite (2.00 mmol) in water (7.50 mL) was added dropwise. The reaction mixture was stirred for 1 hour. Then the reaction was neutralized with 20% NaOH and concentrated in vacuo. The residue was dissolved in chloroform, dried over $MgSO_4$ and filtered. The solution was concentrated and chromatographed on a silica gel column with a chloroform–methanol (100:1, v/v) mixture to give (1,2,3-triazolo[4,5-b]pyridin-3-yl)alkylphosphonate **7a–i**.

4.34. Diethyl (1,2,3-triazolo[4,5-b]pyridin-3-yl)methylphosphonate 7a

According to the general procedure from diethyl [(3-aminopyridin-2-yl)amino]methylphosphonate **6a** (0.179 g, 0.69 mmol) in 98% H_2SO_4 (3 mL) and solution of sodium nitrite (0.095 g, 1.38 mmol) in water (5.50 mL) the phosphonate **7a** (0.127 g, 68%) was obtained as a pale orange amorphous solid. M.p. 83.5 °C–84.5 °C; IR (KBr, cm^{-1}) ν_{max}: 3066, 2989, 2961, 2920, 1591, 1241, 969, 706; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 8.73 (d, $J = 4.5$ Hz, 1 H, Ar–*H*), 8.41 (d, $J = 8.3$ Hz, 1 H, Ar–*H*), 7.40 (dd, $J = 8.3$ Hz, $J = 4.5$ Hz, 1 H, Ar–*H*), 5.18 (d, $J = 12.2$ Hz, 2 H, PC*H*$_2$), 4.23–4.04 (m, 4 H, 2 × POC*H*$_2$CH$_3$), 1.29 (t, $J = 7.1$ Hz, 6 H, 2 × POCH$_2$C*H*$_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 150.57, 145.81, 136.61, 128.71, 119.98, 63.33 (d, $J = 6.3$ Hz, 2 × PO*C*), 42.01 (d, $J = 155.8$ Hz, P*C*), 16.23 (d, $J = 6.0$ Hz, 2 × POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 15.95; Anal. Calcd. for $C_{10}H_{15}N_4O_3P \times 0.5\,H_2O$: C, 43.01; H, 5.78; N, 20.06; Found: C, 43.43; H, 5.62; N, 20.06.

4.35. Diethyl 2-(1,2,3-triazolo[4,5-b]pyridin-3-yl)ethylphosphonate 7b

According to the general procedure from diethyl 2-[(3-aminopyridin-2-yl)amino]ethylphosphonate **6b** (0.049 g, 0.18 mmol) in 98% H_2SO_4 (0.80 ml) and solution of sodium nitrite (0.025 g, 0.37 mmol) in water (1.50 mL) the phosphonate **7b** (0.049 g, 96%) was obtained as a pale yellow oil. IR (film, cm^{-1}) ν_{max}: 3474, 3062, 2985, 2930, 1739, 1257, 1054, 1025, 778; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: $\delta = 8.64$ (dd, $J = 4.5$ Hz, $J = 1.5$ Hz, 1 H, Ar–*H*), 8.33 (dd, $J = 8.3$ Hz, $J = 1.5$ Hz, 1 H, Ar–*H*), 7.32 (dd, $J = 8.3$ Hz, $J = 4.5$ Hz, 1 H, Ar–*H*), 5.06–4.85 (m, 2 H, PCCH_2), 4.10–3.98 (m, 4 H, 2 × POCH_2CH$_3$), 2.68–2.45 (m, 2 H, PCH_2), 1.24 (t, $J = 7.1$ Hz, 6 H, 2 × POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 150.24, 145.68, 137.06, 128.58, 119.85, 62.05 (d, $J = 6.5$ Hz, PO*C*), 41.40 (s, PC*C*), 26.28 (d, $J = 141.0$ Hz, P*C*), 16.32 (d, $J = 5.9$ Hz, POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 26.48; Anal. Calcd. for $C_{11}H_{17}N_4O_3P \times 0.2H_2O$: C, 45.90; H, 6.09; N, 19.46; Found: C, 45.76; H, 5.89; N, 19.21.

4.36. Diethyl 3-(1,2,3-triazolo[4,5-b]pyridin-3-yl)propylphosphonate 7c

According to the general procedure from diethyl 3-[(3-aminopyridin-2-yl)amino]propylphosphonate **6c** (0.070 g, 0.24 mmol) in 98% H_2SO_4 (1 ml) and solution of sodium nitrite (0.034 g, 0.49 mmol) in water (1.90 ml) the phosphonate **7c** (0.068 g, 93%) was obtained as a pale red oil. IR (film, cm^{-1}) ν_{max}: 3456, 3065, 2983, 1640, 1228, 964, 779; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 8.68 (dd, $J = 4.5$ Hz, $J = 1.3$ Hz, 1 H, Ar–*H*), 8.39 (dd, $J = 8.3$ Hz, $J = 1.3$ Hz, 1 H, Ar–*H*), 7.37 (dd, $J = 8.3$ Hz, $J = 4.5$ Hz, 1 H, Ar–*H*), 4.84 (t, $J = 6.9$ Hz, 2 H, PCCCH_2), 4.29–3.88 (m, 4 H, 2 × POCH_2CH$_3$), 2.60–2.29 (m, 2 H, PCCH_2), 1.97–1.73 (m, 2 H, PCH_2), 1.31 (t, $J = 7.1$ Hz, 6 H, 2 × POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 150.24, 145.85, 136.95, 128.59, 119.81, 61.72 (d, $J = 6.5$ Hz, 2 × PO*C*), 46.94 (d, $J = 18.0$ Hz, PCC*C*), 23.20 (d, $J = 143.3$ Hz, P*C*), 23.03 (d, $J = 4.6$ Hz, PC*C*), 16.39 (d, $J = 5.9$ Hz, 2 × POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 30.11; Anal. Calcd. for $C_{12}H_{19}N_4O_3P \times 0.6H_2O$: C, 46.63; H, 6.59; N, 18.13; Found: C, 46.71; H, 6.53; N, 17.98.

4.37. Diethyl 4-(1,2,3-triazolo[4,5-b]pyridin-3-yl)butylphosphonate 7d

According to the general procedure from diethyl 4-[(3-aminopyridin-2-yl)amino]butylphosphonate **6d** (0.078 g, 0.26 mmol) in 98% H_2SO_4 (1.20 ml) and solution of sodium nitrite (0.035 g, 0.51 mmol) in water (1.95 ml) the phosphonate **7d** (0.078 g, 96%) was obtained as a pale yellow oil. IR (film, cm^{-1}) ν_{max}: 3066, 2983, 2940, 1227, 1025, 964, 779; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 8.69 (dd, $J = 4.4$ Hz, $J = 1.0$ Hz, 1 H, Ar–*H*), 8.40 (dd,

$J = 8.3$ Hz, $J = 1.1$ Hz, 1 H, Ar–*H*), 7.38 (dd, $J = 8.3$ Hz, $J = 4.5$ Hz, 1 H, Ar–*H*), 4.79 (t, $J = 7.0$ Hz, 2 H, PCCCCH_2), 4.21–3.96 (m, 4 H, 2 × POCH_2CH$_3$), 2.22 (qv, 2 H, $J = 7.0$ Hz, PCCCH_2), 1.87–1.79 (m, 2 H, PCCH_2), 1.75–1.66 (m, 2 H, PCH_2), 1.31 (t, $J = 7.1$ Hz, 6 H, 2 × POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 150.12, 145.84, 136.95, 128.58, 119.73, 61.53 (d, $J = 6.5$ Hz, 2 × POC), 46.20, 30.12 (d, $J = 15.9$ Hz, PCCC), 25.03 (d, $J = 141.8$ Hz, PC), 19.79 (d, $J = 5.0$ Hz, PCC), 16.40 (d, $J = 5.9$ Hz, 2 × POCC); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 31.06; Anal. Calcd. for $C_{13}H_{21}N_4O_3P \times H_2O$: C, 47.27; H, 7.02; N, 16.96; Found: C, 47.21; H, 7.05; N, 16.87.

4.38. Diethyl {2-(1,2,3-triazolo[4,5-b]pyridin-3-yl)ethoxy}methylphosphonate 7e

According to the general procedure from diethyl {2-[(3-aminopyridin-2-yl)amino]ethoxy}methylphosphonate **6e** (0.079 g, 0.26 mmol) in 98% H_2SO_4 (1.20 ml) and solution of sodium nitrite (0.033 g, 0.51 mmol) in water (2 ml) the phosphonate **7e** (0.067 g, 82%) was obtained as a pale orange oil. IR (film, cm^{-1}) ν_{max}: 3067, 2985, 2932, 1223, 973, 779; ^{1}H NMR (200 MHz, $CDCl_3$) δ [ppm]: 8.67 (dd, $J = 4.5$ Hz, $J = 1.5$ Hz, 1 H, Ar–*H*), 8.38 (dd, $J = 8.3$ Hz, $J = 1.5$ Hz, 1 H, Ar–*H*), 7.36 (dd, $J = 8.3$ Hz, $J = 4.5$ Hz, 1 H, Ar–*H*), 4.95 (t, $J = 5.6$ Hz, 2 H, PCOCH_2), 4.22 (t, $J = 5.6$ Hz, 2 H, PCOCCH_2), 4.11–3.90 (m, 4 H, 2 × POCH_2CH$_3$), 3.79 (d, $J = 8.3$ Hz, 2 H, PCH_2), 1.21 (t, $J = 7.1$ Hz, 6 H, 2 × POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 150.21, 146.14, 136.92, 128.57, 119.78, 70.50 (d, $J = 10.6$ Hz, PCOC), 65.18 (d, $J = 165.7$ Hz, PC), 62.45 (d, $J = 6.5$ Hz, 2 × POC), 46.28, 16.33 (d, $J = 5.7$ Hz, 2 × POCC); ^{31}P NMR (81 MHz, $CDCl_3$) δ [ppm]: 20.12; Anal. Calcd. for $C_{12}H_{19}N_4O_4P \times 0.3\,H_2O$: C, 45.08; H, 6.18; N, 17.53; Found: C, 45.10; H, 6.16; N, 17.21.

4.39. Diethyl 2-{2-(1,2,3-triazolo[4,5-b]pyridin-3-yl)ethoxy}ethylphosphonate 7f

According to the general procedure from diethyl 2-{2-[(3-aminopyridin-2-yl)amino]ethoxy}ethylphosphonate **6f** (0.097 g, 0.32 mmol) in 98% H_2SO_4 (1.40 ml) and solution of sodium nitrite (0.043 g, 0.63 mmol) in water (2.40 ml) the phosphonate **7f** (0.083 g, 80%) was obtained as a pale yellow oil. IR (film, cm^{-1}) ν_{max}: 3455, 3065, 2982, 2927, 1250, 1025, 991, 778; ^{1}H NMR (200 MHz, $CDCl_3$) δ [ppm]: 8.62 (dd, $J = 4.5$ Hz, $J = 1.5$ Hz, 1 H, Ar–*H*), 8.33 (dd, $J = 8.3$ Hz, $J = 1.5$ Hz, 1 H, Ar–*H*), 7.40 (dd, $J = 8.3$ Hz, $J = 4.5$ Hz, 1 H, Ar–*H*), 4.87 (t, $J = 5.7$ Hz, 2 H, PCCOCH_2), 4.03–3.90 (m, 6 H, 2 × POCH_2CH$_3$, PCCOCCH_2), 3.64 (dt, $J = 11.2$ Hz, $J = 7.3$ Hz, 2 H, PCCH_2), 1.93 (dt, $J = 18.7$ Hz, $J = 7.3$ Hz, 2 H, PCH_2), 1.21 (t, $J = 7.1$ Hz, 6 H, 2 × POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 150.17,

146.13, 136.91, 128.54, 119.73, 68.24, 65.04, 61.59 (d, $J = 6.3$ Hz, 2 × POC), 46.48, 26.82 (d, $J = 139.6$ Hz, PC), 16.34 (d, $J = 6.0$ Hz, 2 × POCC); ^{31}P NMR (81 MHz, $CDCl_3$) δ [ppm]: 28.87; Anal. Calcd. for $C_{13}H_{21}N_4O_4P \times 0.5H_2O$: C, 46.29; H, 6.57; N, 12.61; Found: C, 46.30; H, 6.45; N, 12.65.

4.40. Diethyl 1-hydroxy-2-(1,2,3-triazolo[4,5-b]pyridin-3-yl)ethylphosphonate 7g

According to the general procedure from diethyl [(3-aminopyridin-2-yl)amino]-1-hydroxyethylphosphonate **6g** (0.052 g, 0.18 mmol) in 98% H_2SO_4 (0.8 ml) and solution of sodium nitrite (0.024 g, 0.35 mmol) in water (1.4 ml) the phosphonate **7g** (0.025 g, 47%) was obtained as a pale yellow oil. IR (film, cm^{-1}) ν_{max}: 3283, 3058, 3001, 2985, 1253, 1018, 965, 779; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 8.69 (dd, $J = 4.5$ Hz, $J = 1.4$ Hz, 1 H, Ar–*H*), 8.44 (dd, $J = 8.3$ Hz, $J = 1.4$ Hz, 1 H, Ar–*H*), 7.41 (dd, $J = 8.3$ Hz, $J = 4.5$ Hz, 1 H, Ar–*H*), 5.18 (ddd, $J = 14.6$ Hz, $J = 9.0$ Hz, $J = 2.8$ Hz, 1 H, PC*H*), 5.13–5.07 (m, 2 H, PCCH_2), 4.66 (brs, 1 H, O*H*), 4.27–4.17 (m, 4 H, 2 × POCH_2CH$_3$), 1.36 (t, $J = 7.1$ Hz, 3 H, POCH$_2$CH_3), 1.33 (t, $J = 7.1$ Hz, 3 H, POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 149.97, 146.10, 137.24, 129.19, 119.93, 67.21 (d, $J = 165.2$ Hz, P*C*), 63.26 (d, $J = 7.0$ Hz, PO*C*), 63.16 (d, $J = 7.0$ Hz, PO*C*), 50.21 (d, $J_P = 7.2$ Hz, PC*C*), 16.45 (d, $J = 5.6$ Hz, POC*C*), 16.40 (d, $J = 5.6$ Hz, POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 19.94; Anal. Calcd. for $C_{11}H_{17}N_4O_4P$: C, 44.00; H, 5.51; N, 18.66; Found: C, 44.09; H, 5.49; N, 18.45.

4.41. Diethyl 1-hydroxy-3-(1,2,3-triazolo[4,5-b]pyridin-3-yl)propylphosphonate 7h

According to the general procedure from diethyl 3-[(3-aminopyridin-2-yl) amino]-1-hydroxypropylphosphonate **6h** (0.045 g, 0.15 mmol) in 98% H_2SO_4 (0.7 ml) and solution of sodium nitrite (0.020 g, 0.15 mmol) in water (0.6 ml) the phosphonate **7h** (0.030 g, 64%) was obtained as a white powder. M.p. 65 °C–66 °C; IR (KBr, cm^{-1}) ν_{max}: 3289, 3028, 2986, 1236, 1021, 968, 782; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 8.70 (dd, $J = 4.5$ Hz, $J = 1.3$ Hz, 1 H, Ar–*H*), 8.44 (dd, $J = 8.3$ Hz, $J = 1.3$ Hz, 1 H, Ar–*H*), 7.42 (dd, $J = 8.3$ Hz, $J = 4.5$ Hz, 1 H, Ar–*H*), 5.03 (dd, $J = 9.6$ Hz, $J = 5.1$ Hz, 2 H, PCCCH_2), 4.29 (s, 1 H, O*H*), 4.24–4.16 (m, 4 H, 2 × POCH_2CH$_3$), 3.81 (ddd, $J = 11.9$ Hz, $J = 9.6$ Hz, $J = 2.9$ Hz, 1 H, PC*H*), 2.65–2.27 (m, 2 H, PCCH_2), 1.36 (t, $J = 7.1$ Hz, 3 H, POCH$_2$CH_3), 1.32 (t, $J = 7.1$ Hz, 3 H, POCH$_2$CH_3).; ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 150.19, 145.96, 137.04, 129.18, 119.95, 64.50 (d, $J = 168.7$ Hz, P*C*), 62.91 (d, $J = 6.8$ Hz, PO*C*), 62.74 (d, $J = 6.8$ Hz, POC), 43.00 (d, $J = 15.7$ Hz, PCC*C*),

31.68 (d, $J = 2.5$ Hz, PC*C*), 16.49 (d, $J = 5.3$ Hz, POC*C*), 16.46 (d, $J = 5.3$ Hz, POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 23.55; Anal. Calcd. for $C_{12}H_{19}N_4O_4P$: C, 45.86; H, 6.09; N, 17.83; Found: C, 45.76; H, 6.24; N, 17.62.

4.42. Diethyl 2-hydroxy-3-(1,2,3-triazolo[4,5-b]pyridin-3-yl)propylphosphonate 7i

According to the general procedure from diethyl 3-[(3-aminopyridin-2-yl)amino]-2-hydroxypropylphosphonate **6i** (0.148 g, 0.49 mmol) in 98% H_2SO_4 (2.1 ml) and solution of sodium nitrite (0.067 g, 0.97 mmol) in water (3.7 ml) the phosphonate **7i** (0.086 g, 56%) was obtained as a pale yellow oil. IR (film, cm^{-1}) ν_{max}: 3332, 3069, 2984, 1256, 1026, 966, 778; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 8.71 (dd, $J = 4.5$ Hz, $J = 1.4$ Hz, 1 H, Ar–*H*), 8.42 (dd, $J = 8.3$ Hz, $J = 1.4$ Hz, 1 H, Ar–*H*), 7.40 (dd, $J = 8.3$ Hz, $J = 4.5$ Hz, 1 H, Ar–*H*), 4.95 (dd_{ABX}, $J = 14.1$ Hz, $J = 4.3$ Hz, 1 H, PCCC*H*), 4.90 (dd_{ABX}, $J = 14.1$ Hz, $J = 4.3$ Hz, 1 H, PCCC*H*) 4.74–4.67 (m, 1 H, PC*H*), 4.45 (brs, 1 H, O*H*), 4.22–4.08 (m, 4 H, 2 × POCH_2CH$_3$), 2.18–2.05 (m, 2 H, PCH_2), 1.35 (t, $J = 7.1$ Hz, 3 H, POCH$_2$CH_3), 1.34 (t, $J = 7.1$ Hz, 3 H, POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 150.34, 146.23, 136.98, 128.91, 119.92, 65.86 (d, $J = 4.0$ Hz, PC*C*), 62.23 (d, $J = 6.3$ Hz, PO*C*), 62.12 (d, $J = 6.5$ Hz, PO*C*), 53.16 (d, $J = 17.5$ Hz, PCC*C*), 31.41 (d, $J = 140.7$ Hz, P*C*), 16.38 (d, $J = 6.0$ Hz, POC*C*), 16.37 (d, $J = 6.0$ Hz, POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 28.12; Anal. Calcd. for $C_{12}H_{19}N_4O_4P \times 0.3H_2O$: C, 45.08; H, 6.18; N, 17.53; Found: C, 45.16; H, 6.30; N, 17.28.

4.43. Synthesis of diethyl (imidazo[4,5-b]pyridin-3-yl)alkylophosphonate 8a–i – general procedure

A solution of diethyl [(3-aminopyridin-2-yl)amino]alkylophosphonate **6a–i** (1.00 mmol), *p*-toluenesulphonic acid (0.50 mmol) and triethyl orthoformate (10.00 mmol) in THF (12 mL) was stirred at the room temperature for 24 hours. Then the solvent was evaporated in vacuo and the residue was purified on a silica gel column with a chloroform–methanol (100:1, v/v) mixture to give diethyl (imidazo[4,5-*b*]pyridin-3-yl) alkylophosphonates **8a–i**.

4.44. Diethyl (imidazo[4,5-b]pyridin-3-yl)methylphosphonates 8a

According to the general procedure from diethyl [(3-aminopyridin-2-yl)amino]methylphosphonate **6a** (0.161 g, 0.62 mmol), *p*-toluenesulphonic acid (0.053 g, 0.31 mmol) and triethyl orthoformate (0.739 g, 6.20 mmol) the phosphonate **8a** (0.114 g, 68%) was obtained as a pale yellow powder. M.p.

68 °C–69 °C; IR (KBr, cm^{-1}) ν_{max}: 3088, 3059, 2983, 1242, 1023, 977, 776; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 8.43 (dd, $J = 4.8$ Hz, $J = 1.3$ Hz, 1 H, Ar–*H*), 8.27 (s, 1 H, NC*H*N), 8.10 (dd, $J = 8.0$ Hz, $J = 1.3$ Hz, 1 H, Ar–*H*), 7.27 (dd, $J = 8.0$ Hz, $J = 4.8$ Hz, 1 H, Ar–*H*), 4.72 (d, $J = 12.0$ Hz, 2 H, PC*H*$_2$), 4.15–4.10 (m, 4 H, 2 × POC*H*$_2$CH$_3$), 1.22 (t, $J = 7.1$ Hz, 6 H, 2 × POCH$_2$C*H*$_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 146.74 (d, $J = 2.3$ Hz, Ar–*C*), 144.47, 144.0, 134.75, 128.10, 118.54, 63.12 (d, $J = 6.6$ Hz, 2 × POC), 38.29 (d, $J = 157.7$ Hz, PC), 16.21 (d, $J = 5.8$ Hz, 2 × POCC); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 18.01; Anal. Calcd. for $C_{11}H_{16}N_3O_3P$: C, 49.07; H. 5.99; N. 15.61; Found: C. 48.97; H. 6.20; N. 15.77.

4.45. Diethyl 2-(imidazo[4,5-b]pyridin-3-yl)ethylphosphonate 8b

According to the general procedure from diethyl 2-[(3-aminopyridin-2-yl)amino]ethylphosphonate **6b** (0.044 g, 0.16 mmol), *p*-toluenesulphonic acid (0.014 g, 0.08 mmol) and triethyl orthoformate (0.192 g, 1.61 mmol) the phosphonate **8b** (0.041 g, 96%) was obtained as a pale yellow oil. IR (film, cm^{-1}) ν_{max}: 3444, 3058, 2985, 2932, 1725, 1233, 973, 777; ^{1}H NMR (200 MHz, $CDCl_3$) δ [ppm]: 8.33 (dd, $J = 4.8$ Hz, $J = 1.4$ Hz, 1 H, Ar–*H*), 8.04 (s, 1 H, NC*H*N), 8.01 (dd, $J = 8.1$ Hz, $J = 1.4$ Hz, 1 H, Ar–*H*), 7.19 (dd, $J = 8.1$ Hz, $J = 4.8$ Hz, 1 H, Ar–*H*), 4.53 (dt, $J = 14.5$ Hz, $J = 7.2$ Hz, 2 H, PCC*H*$_2$), 4.04–3.88 (m, 4 H, 2 × POC*H*$_2$CH$_3$), 2.42 (dt, $J = 18.2$ Hz, $J = 7.2$ Hz, 2 H, PC*H*$_2$), 1.16 (t, $J = 7.1$ Hz, 6 H, 2 × POCH$_2$C*H*$_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 146.72, 144.41, 144.12, 135.18, 127.89, 118.51, 61.95 (d, $J = 6.5$ Hz, 2 × POC), 38.59 (d, $J = 3.8$ Hz, PCC), 26.27 (d, $J = 140.9$ Hz, PC), 16.25 (d, $J = 6.0$ Hz, 2 × POCC).; ^{31}P NMR (81 MHz, $CDCl_3$) δ [ppm]:; Anal. Calcd. for $C_{12}H_{18}N_3O_3P \times 0.6H_2O$: C. 49.01; H. 6.58; N. 14.29; Found: C. 49.02; H. 6.60; N. 14.12.

4.46. Diethyl 3-(imidazo[4,5-b]pyridin-3-yl)propylphosphonate 8c

According to the general procedure from diethyl 3-[(3-aminopyridin-2-yl)amino]propylphosphonate **6c** (0.078 g, 0.27 mmol), *p*-toluenesulphonic acid (0.057 g, 0.33 mmol) and triethyl orthoformate (0.324 g, 2.72 mmol) the phosphonate **8c** (0.073 g, 93%) was obtained as a pale orange oil. IR (film, cm^{-1}) ν_{max}: 3425, 3088, 3058, 2984, 1600, 1228, 965, 777; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 8.40 (dd, $J = 4.8$ Hz, $J = 1.5$ Hz, 1 H, Ar–*H*), 8.12 (s, 1 H, NC*H*N), 8.08 (dd, $J = 8.0$ Hz, $J = 1.5$ Hz, 1 H, Ar–*H*), 7.25 (dd, $J = 8.0$ Hz, $J = 4.8$ Hz, 1 H, Ar–*H*), 4.44 (t, $J = 7.0$ Hz, 2 H, PCCC*H*$_2$), 4.17–4.04 (m, 4 H, 2 × POC*H*$_2$CH$_3$), 2.35–2.24 (m, 2 H, PCC*H*$_2$), 1.81–1.70 (m, 2 H, PC*H*$_2$), 1.32 (t, $J = 7.1$ Hz, 6 H, 2 × POCH$_2$C*H*$_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: $\delta = 147.00$, 144.27, 144.07, 135.52, 127.99,

118.29, 61.73 (d, $J = 6.6$ Hz, 2 × POC), 43.61 (d, $J = 15.6$ Hz, PCCC), 23.28, 22.79 (d, $J = 138.9$ Hz, PC), 16.41 (d, $J = 5.9$ Hz, 2 × POCC); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 30.25; Anal. Calcd. for $C_{13}H_{20}N_3O_3P \times 0.7H_2O$: C. 50.38; H. 6.96; N. 13.56; Found: C. 50.34; H. 7.08; N. 13.34.

4.47. Diethyl 4-(imidazo[4,5-b]pyridin-3-yl)butylphosphonate 8d

According to the general procedure from diethyl 4-[(3-aminopyridin-2-yl)amino]butylphosphonate **6d** (0.081 g, 0.27 mmol), *p*-toluenesulphonic acid (0.022 g, 0.13 mmol) and triethyl orthoformate (0.317 g, 2.66 mmol) the phosphonate **8d** (0.073 g, 96%) was obtained as a pale yellow oil. IR (film, cm^{-1}) ν_{max}: 3056, 2983, 1240, 1026, 963, 777; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 8.41 (dd, $J = 4.7$ Hz, $J = 1.4$ Hz, 1 H, Ar–*H*), 8.09 (dd, $J = 8.0$ Hz, $J = 1.4$ Hz, 1 H, Ar–*H*), 8.07 (s, 1 H, NC*H*N) 7.26 (dd, $J = 8.0$ Hz, $J = 4.7$ Hz, 1 H, Ar–*H*), 4.34 (t, $J = 7.4$ Hz, 2 H, PCCCCH_2), 4.15–4.01 (m, 4 H, 2 × POCH_2CH$_3$), 2.09 (qv, $J = 7.4$ Hz, 2 H, PCCCH_2), 1.85–1.75 (m, 2 H, PCCH_2), 1.75–1.63 (m, 2 H, PCH_2), 1.30 (t, $J = 7.1$ Hz, 6 H, 2 × POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 149.17, 137.33, 129.32, 120.21, 112.97, 69.64, 64.30 (d, $J = 5.6$ Hz, PCC), 61.78 (d, $J = 6.5$ Hz, 2 × POC), 41.20, 30.12 (d, $J = 15.8$ Hz, PCCC), 26.75 (d, $J = 141.8$ Hz, PC), 16.36 (d, $J = 6.1$ Hz, 2 × POCC); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 31.09; Anal. Calcd. for $C_{14}H_{22}N_3O_3P \times H_2O$: C. 51.06; H. 7.35; N. 12.76; Found: C. 51.21; H. 7.15; N. 12.87.

4.48. Diethyl {2-(imidazo[4,5-b]pyridin-3-yl)ethoxy}methylphosphonate 8e

According to the general procedure from diethyl {2-[(3-aminopyridin-2-yl)amino]ethoxy}methylphosphonate **6e** (0.079 g, 0.26 mmol), *p*-toluenesulphonic acid (0.024 g, 0.14 mmol) and triethyl orthoformate (0.330 g, 2.77 mmol) the phosphonate **8e** (0.067 g, 82%) was obtained as a pale orange oil, yield 82%; IR (film, cm^{-1}) ν_{max}: 3057, 2984, 2932, 1240, 1026, 972, 776; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 8.41 (dd, $J = 4.8$ Hz, $J = 1.4$ Hz, 1 H, Ar–*H*), 8.21 (s, 1 H, C*H*), 8.10 (dd, $J = 8.0$ Hz, $J = 1.4$ Hz, 1 H, Ar–*H*), 7.27 (dd, $J = 8.0$ Hz, $J = 4.8$ Hz, 1 H, Ar–*H*), 4.54 (t, $J = 5.1$ Hz, 2 H, PCOCH_2), 4.12–4.07 (m, 4 H, 2 × POCH_2CH$_3$), 4.01 (t, $J = 5.1$ Hz, 2 H, PCOCCH_2), 3.80 (d, $J = 8.3$ Hz, 2 H, PCH_2), 1.30 (t, $J = 7.1$ Hz, 6 H, 2 × POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 146.84, 144.91, 144.09, 135.32, 127.92, 118.24, 71.26 (d, $J = 10.5$ Hz, PCOC), 65.33 (d, $J = 166.5$ Hz, PC), 62.44 (d, $J = 6.5$ Hz, 2 × POC), 43.25 (s, PCOCC), 16.41 (d, $J = 5.7$ Hz, 2 × POCC); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 20.39; Anal. Calcd. for $C_{13}H_{20}N_3O_4P \times H_2O$: C. 47.13; H. 6.69; N. 12.68; Found: C. 47.12; H. 6.85; N. 12.43.

4.49. Diethyl 2-{2-(imidazo[4,5-b]pyridin-3-yl)ethoxy}ethylphosphonate 8f

According to the general procedure from diethyl 2-{2-[(3-aminopyridin-2-yl)amino]ethoxy}ethylphosphonate **6f** (0.143 g, 0.45 mmol), *p*-toluenesulphonic acid (0.039 g, 0.23 mmol) and triethyl orthoformate (0.537 g, 4.51 mmol) the phosphonate **8f** (0.118 g, 80%) was obtained as a pale yellow oil. IR (film, cm^{-1}) ν_{max}: 3168, 3071, 3033, 2983, 2933, 1223, 1026, 963, 770; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 8.38 (dd, $J = 4.7$ Hz, $J = 1.3$ Hz, 1 H, Ar–*H*), 8.20 (s, 1 H, NC*H*), 8.07 (dd, $J = 8.0$ Hz, $J = 1.3$ Hz, 1 H, Ar–*H*), 7.24 (dd, $J = 8.0$ Hz, $J = 4.7$ Hz, 1 H, Ar–*H*), 4.49 (t, $J = 5.1$ Hz, 2 H, PCCOCH_2), 4.12–4.00 (m, 4 H, 2 × POCH_2CH$_3$), 3.83 (t, $J = 5.1$ Hz, 2 H, PCCOCCH_2), 3.69 (dt, $J = 12.3$ Hz, $J = 7.4$ Hz, 2 H, PCCH_2), 2.05 (dt, $J = 18.7$ Hz, $J = 7.4$ Hz, 2 H, PCH_2), 1.29 (t, $J = 7.1$ Hz, 6 H, 2 × POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 146.86, 144.98, 144.03, 135.26, 127.84, 118.16, 68.83 (s, PCCO*C*), 65.22 (s, PCCOC*C*), 61.63 (d, $J = 6.4$ Hz, 2 × PO*C*), 43.33 (s, PC*C*), 26.94 (d, $J = 140.3$ Hz, P*C*), 16.37 (d, $J = 6.0$ Hz, 2 × POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 27.91; Anal. Calcd. for $C_{14}H_{22}N_3O_4P \times 0.8H_2O$: C. 49.21; H. 6.96; N. 12.30; Found: 49.37; H. 7.01; N. 12.33.

4.50. Diethyl 1-hydroxy-2-(imidazo[4,5-b]pyridin-3-yl)ethylphosphonate 8g

According to the general procedure from diethyl 2-[(3-aminopyridin-2-yl)amino]-1-hydroxyethylphosphonate **6g** (0.064 g, 0.22 mmol), *p*-toluenesulphonic acid (0.019 g, 0.11 mmol) and triethyl orthoformate (0.260 g, 2.18 mmol) the phosphonate **8g** (0.031 g, 47%) was obtained as a pale orange powder. M.p. 73 °C–74 °C; IR (KBr, cm^{-1}) ν_{max}: 3252, 2985, 2928, 1250, 1049, 972; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 8.35 (dd, $J = 4.8$ Hz, $J = 1.2$ Hz, 1 H, Ar–*H*), 8.15 (s, 1 H, NC*H*), 8.06 (dd, $J = 8.0$ Hz, $J = 1.2$ Hz, 1 H, Ar–*H*), 7.26 (dd, $J = 8.0$, $J = 4.8$ Hz, 1 H, Ar–*H*), 4.80 (ddd, $J = 14.8$ Hz, $J = 12.8$ Hz, $J = 2.4$ Hz, 1 H, PCCH_aH$_b$), 4.56 (ddd, $J = 14.8$ Hz, $J = 7.9$ Hz, $J = 4.0$ Hz, 1 H, PCCH$_a$$H_b$), 4.44 (ddd, $J = 10.2$ Hz, $J = 7.9$ Hz, $J = 2.4$ Hz, 1 H, PC*H*), 4.25–4.00 (m, 4 H, 2 × POCH_2CH$_3$), 1.33 (t, $J = 7.1$ Hz, 3 H, POCH$_2$CH_3), 1.21 (t, $J = 7.1$ Hz, 3 H, POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 147.02, 145.29, 143.60, 135.59, 128.44, 118.50, 67.56 (d, $J = 164.4$ Hz, P*C*), 63.16 (d, $J = 7.0$ Hz, PO*C*), 62.88 (d, $J = 7.2$ Hz, PO*C*), 47.43 (d, $J = 5.5$ Hz, PC*C*), 16.40 (d, $J = 5.6$ Hz, POC*C*), 16.24 (d, $J = 5.7$ Hz, POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 20.64; Anal. Calcd. for $C_{12}H_{18}N_3O_4P \times 0.5H_2O$: C. 46.75; H. 6.21; N. 13.63, Found: C. 46.86; H. 6.20; N. 13.36.

4.51. Diethyl 1-hydroxy-3-(imidazo[4,5-b]pyridin-3-yl)propylphosphonate 8h

According to the general procedure from diethyl 3-[(3-aminopyridin-2-yl)amino]-1-hydroxypropylphosphonate **6h** (0.049 g, 0.16 mmol), *p*-

toluenesulphonic acid (0.005 g, 0.03 mmol) and triethyl orthoformate (0.193 g, 1.62 mmol) the phosphonate **8h** (0.032 g, 64%) was obtained as a pale orange oil. IR (film, cm^{-1}) ν_{max}: 3300, 2985, 2925, 1232, 1024, 969, 776; ^1H NMR (600 MHz, $CDCl_3$) δ [ppm]: $\delta = 8.38$ (dd, $J = 4.8$ Hz, $J = 1.2$ Hz, 1 H, Ar–*H*), 8.15–8.12 (m, 2 H, Ar–*H*, C*H*), 7.29 (dd, $J = 8.4$ Hz, $J = 4.4$ Hz, 1 H, Ar–*H*), 4.69–4.43 (m, 2 H, PCCCH_2), 4.19–4.14 (m, 4 H, 2 × POCH_2CH$_3$), 3.70 (ddd, $J = 11.4$ Hz, $J = 10.3$ Hz, $J = 3.3$ Hz, 1 H, PC*H*), 2.48–2.15 (m, 2 H, PCCH_2), 1.33 (t, $J = 6.9$ Hz, 3 H, POCH$_2$CH_3), 1.31 (t, $J = 6.9$ Hz, 3 H, POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 147.22, 144.64, 144.04, 135.52, 128.66, 118.51, 63.78 (d, $J = 170.1$ Hz, PC), 62.79 (d, $J = 6.9$ Hz, POC), 62.72 (d, $J = 6.9$ Hz, POC), 39.61 (d, $J = 15.7$ Hz, PCCC), 32.20 (d, $J = 2.7$ Hz, PCC), 16.47 (d, $J = 5.5$ Hz, POCC), 16.45 (d, $J = 5.5$ Hz, POCC); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 24.16; Anal. Calcd. for $C_{13}H_{20}N_3O_4P \times 0.5H_2O$: C. 48.45; H. 6.57; N. 13.04; Found: C. 48.44; H. 6.53; N. 12.99.

4.52. Diethyl 2-hydroxy-3-(imidazo[4,5-b]pyridin-3-yl)propylphosphonate 8i

According to the general procedure from diethyl 3-[(3-aminopyridin-2-yl)amino]-2-hydroxypropylphosphonate **6i** (0.185 g, 0.61 mmol), *p*-toluenesulphonic acid (0.053 g, 0.31 mmol) and triethyl orthoformate (0.727 g, 6.10 mmol) the phosphonate **8i** (0.107 g, 56%) was obtained as a pale red oil. IR (film, cm^{-1}) ν_{max}: 3320, 3060, 2985, 2930, 1207, 1056, 965, 777; ^1H NMR (600 MHz, $CDCl_3$) δ [ppm]: 8.37 (dd, $J = 4.8$ Hz, $J = 1.2$ Hz, 1 H, Ar–*H*), 8.22 (s, 1 H, NC*H*), 8.09 (dd, $J = 8.0$ Hz, $J = 1.2$ Hz, 1 H, Ar–*H*), 7.26 (dd, $J = 8.0$ Hz, $J = 4.8$ Hz, 1 H, Ar–*H*), 4.58–4.40 (m, 3 H, PCC*H*, PCCCH_2), 4.19–4.07 (m, 4 H, POCH_2CH$_3$), 2.06–1.89 (m, 3 H, PCH_2, O*H*), 1.35 (t, $J = 7.1$ Hz, 3 H, POCH$_2$CH_3), 1.33 (t, $J = 7.1$ Hz, 3 H, POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 147.16, 145.56, 143.83, 135.42, 128.27, 118.35, 65.85 (d, $J = 2.9$ Hz, PC*C*), 62.14 (d, $J = 6.3$ Hz, POC), 62.11 (d, $J = 6.3$ Hz, POC), 50.12 (d, $J = 15.6$ Hz, PCCC), 31.00 (d, $J = 139.5$ Hz, P*C*), 16.39 (d, $J = 6.0$ Hz, POCC), 16.37 (d, $J = 6.0$ Hz, POCC); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 28.26; Anal. Calcd. for $C_{13}H_{20}N_3O_4P \times 0.6H_2O$: C. 48.18; H. 6.59; N. 12.97; Found: C. 48.36; H. 6.40; N. 12.85.

4.53. Synthesis of diethyl (2-oxo-1H-imidazo[4,5-b]pyridin-3-yl)alkylphosphonate 9a–f, j-l – general procedure

Solution of diethyl [(3-aminopyridin-2-yl)amino]alkylphosphonate **6a–f**, **j–l** (1.00 mmol) and 1,1′-carbonyldiimidazole (1.50 mmol) in THF (12 mL) was stirred at the room temperature for 72 hours. Then the solvent was evaporated in vacuo and the residue was purified on a silica gel column with a

chloroform–methanol (100:1, v/v) mixture to give diethyl (2-oxo-1H-imidazo[4,5-b]pyridin-3-yl)alkylphosphonate **9a–f**, **j–l**.

4.54. Diethyl (2-oxo-1H-imidazo[4,5-b]pyridin-3-yl)methylphosphonate 9a

According to the general procedure from diethyl [(3-aminopyridin-2-yl) amino]methylphosphonate **6a** (0.150 g, 0.58 mmol) and 1,1′-carbonyldiimidazole (0.141 g, 0.87 mmol) the phosphonate **9a** (0.137 g, 83%) was obtained as a violet oil. IR (film, cm^{-1}) ν_{max}: 3426, 3169, 2982, 2940, 2873, 1226, 964, 771; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 10.04 (s, 1 H, N*H*), 7.97 (dd, $J = 5.2$ Hz, $J = 1.4$ Hz, 1 H, Ar–*H*), 7.15 (dd, $J = 7.7$ Hz, $J = 1.4$ Hz, 1 H, Ar–*H*), 6.89 (dd, $J = 7.7$, $J = 5.2$ Hz, 1 H, Ar–*H*), 4.36 (d, $J = 10.9$ Hz, 2 H, PCH_2), 4.27–4.07 (m, 4 H, $2 \times$ POC$H_2$$CH_3$), 1.24 (t, $J = 7.0$ Hz, 6 H, $2 \times$ POCH_2CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 154.22, 143.44, 140.63, 122.75, 117.69, 115.68, 62.99 (d, $J = 6.1$ Hz, $2 \times$ POC), 35.12 (d, $J = 158.4$ Hz, PC), 16.27 (d, $J = 6.2$ Hz, $2 \times$ POCC); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 20.58; Anal. Calcd. for $C_{11}H_{16}N_3O_4P \times 0.75H_2O$: C. 44.22; H. 5.90; N. 14.07; Found: C. 44.24; H. 5.42; N. 14.07.

4.55. Diethyl 2-(2-oxo-1H-imidazo[4,5-b]pyridin-3-yl)ethylphosphonate 9b

According to the general procedure from diethyl 2-[(3-aminopyridin-2-yl) amino]ethylphosphonate **6b** (0.054 g, 0.20 mmol) and 1,1′-carbonyldiimidazole (0.049 g, 0.30 mmol) the phosphonate **9b** (0.490 g, 83%) was obtained as a pale violet powder. M.p. 85 °C–87 °C; IR (KBr, cm^{-1}) ν_{max}: 2584, 3468, 3046, 2979, 1737, 1244, 961, 769; ^{1}H NMR (200 MHz, $CDCl_3$) δ [ppm]: 9.87 (brs, 1 H, N*H*), 8.04 (dd, $J = 5.2$ Hz, $J = 1.4$ Hz, 1 H, Ar–*H*), 7.30 (dd, $J = 7.7$ Hz, $J = 1.4$ Hz, 1 H, Ar–*H*), 6.99 (dd, $J = 7.7$ Hz, $J = 5.2$ Hz, 1 H, Ar–*H*), 4.36–4.21 (m, 2 H, PCCH_2), 4.21–4.04 (m, 4 H, $2 \times$ POC$H_2$$CH_3$), 2.50–2.31 (m, 2 H, P$CH_2$), 1.32 (t, $J = 7.1$ Hz, 6 H, $2 \times$ POC$H_2$$CH_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 154.46, 143.87, 140.86, 122.39, 117.35, 115.48, 61.93 (d, $J = 6.4$ Hz, $2 \times$ POC), 34.08 (s, PC*C*), 24.65 (d, $J = 139.4$ Hz, PC), 16.36 (d, $J = 6.0$ Hz, $2 \times$ POCC); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 27.23; Anal. Calcd. for $C_{12}H_{18}N_3O_4P \times 0.3H_2O$: C. 47.31; H. 6.15; N. 13.79; Found: C. 47.66; H. 6.14; N. 13.61.

4.56. Diethyl 3-(2-oxo-1H-imidazo[4,5-b]pyridin-3-yl)propylphosphonate 9c

According to the general procedure from diethyl 3-[(3-aminopyridin-2-yl) amino]propylphosphonate **6c** (0.078 g, 0.27 mmol) and 1,1′-carbonyldiimidazole (0.066 g, 0.41 mmol) the phosphonate **9c** (0.061 g, 72%) was obtained as a pale orange powder. M.p. 75 °C–77 °C; IR (KBr, cm^{-1}) ν_{max}: 3406, 3072, 3028, 2985, 1711, 1251, 967, 888; ^{1}H NMR (600 MHz, $CDCl_3$)

δ [ppm]: 10.30 (brs, 1 H, N*H*), 8.04 (dd, $J = 5.2$ Hz, $J = 1.3$ Hz, 1 H, Ar–*H*), 7.32 (dd, $J = 7.7$ Hz, $J = 1.3$ Hz, 1 H, Ar–*H*), 7.00 (dd, $J = 7.7$ Hz, $J = 5.2$ Hz, 1 H, Ar–*H*), 4.18–4.04 (m, 4 H, $2 \times$ POC*H*$_2$CH$_3$), 2.23–2.13 (m, 2 H, PCC*H*$_2$), 1.93–1.84 (m, 2 H, PC*H*$_2$), 1.32 (t, $J = 7.1$ Hz, 6 H, $2 \times$ POCH$_2$C*H*$_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 154.98, 144.18, 140.77, 122.45, 117.29, 115.50, 61.70 (d, $J = 6.5$ Hz, $2 \times$ POC), 40.05 (d, $J = 20.7$ Hz, PCCC), 23.31 (d, $J = 142.9$ Hz, PC), 21.84 (d, $J = 4.6$ Hz, PCC), 16.42 (d, $J = 5.9$ Hz, $2 \times$ POCC); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 32.11; Anal. Calcd. for $C_{13}H_{20}N_3O_4P \times 0.3\,H_2O$: C. 48.99; H. 6.52; N. 13.19; Found: C. 48.98; H. 6.60; N. 12.96.

4.57. Diethyl 4-(2-oxo-1H-imidazo[4,5-b]pyridin-3-yl)butylphosphonate 9d

According to the general procedure from diethyl 4-[(3-aminopyridin-2-yl) amino]butylphosphonate **6d** (0.081 g, 0.27 mmol) and 1,1′-carbonyldiimidazole (0.066 g, 0.41 mmol) the phosphonate **9d** (0.068 g, 77%) was obtained as a red oil. IR (film, cm^{-1}) ν_{max}: 3449, 3085, 3056, 2982, 1240, 1026, 963, 777; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 9.77 (brs, 1 H, N*H*), 8. 06 (dd, $J = 5.2$ Hz, $J = 1.3$ Hz, 1 H, Ar–*H*), 7.32 (dd, $J = 7.7$ Hz, $J = 1.3$ Hz, 1 H, Ar–*H*), 7.01 (dd, $J = 7.7$ Hz, $J = 5.2$ Hz, 1 H, Ar–*H*), 4.15–4.06 (m, 4 H, $2 \times$ POC*H*$_2$CH$_3$), 4.04 (t, $J = 7.2$ Hz, 2 H, PCCCC*H*$_2$), 1.98 (qv, $J = 7.2$ Hz, 2 H, PCCC*H*$_2$), 1.86 (ddd, $J = 18.2$ Hz, $J = 9.6$ Hz, $J = 6.4$ Hz, 2 H, PC*H*$_2$), 1.78–1.69 (m, 2 H, PCC*H*$_2$), 1.32 (t, $J = 7.1$ Hz, 6 H, $2 \times$ POCH$_2$C*H*$_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 155.02, 144.20, 140.56, 122.53, 117.18, 115.55, 61.53 (d, $J = 6.5$ Hz, $2 \times$ POC), 39.08 (s, PCCCC), 29.16 (d, $J = 16.6$ Hz, PCCC), 25.21 (d, $J = 141.2$ Hz, PC), 19.77 (d, $J = 5.0$ Hz, PCC), 16.41 (d, $J = 6.0$ Hz, $2 \times$ POCC); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 31.69; Anal. Calcd. for $C_{14}H_{22}N_3O_4P \times H_2O$: C. 48.69; H. 7.01; N. 12.77; Found: C. 48.41; H. 7.05; N. 12.87.

4.58. Diethyl {2-(2-oxo-1H-imidazo[4,5-b]pyridin-3-yl)ethoxy}methylphosphonate 9e

According to the general procedure from diethyl {2-[(3-aminopyridin-2-yl)amino]ethoxy}methylphosphonate **6e** (0.091 g, 0.30 mmol) and 1,1′-carbonyldiimidazole (0.073 g, 0.45 mmol) the phosphonate **9e** (0.076 g, 77%) was obtained as an orange oil. IR (film, cm^{-1}) ν_{max}: 3429, 3170, 2985, 2933, 1714, 1233, 1027, 974; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 9.72 (brs, 1 H, N*H*), 8.06 (dd, $J = 5.2$ Hz, $J = 1.4$ Hz, 1 H, Ar–*H*), 7.30 (dd, $J = 7.7$ Hz, $J = 1.4$ Hz, 1 H, Ar–*H*), 7.00 (dd, $J = 7.7$ Hz, $J = 5.2$ Hz, 1 H, Ar–*H*), 4.25 (t, $J = 5.8$ Hz, 2 H, PCOC*H*$_2$), 4.13–4.07 (m, 4 H, $2 \times$ POC*H*$_2$CH$_3$), 4.04 (t, $J = 5.8$ Hz, 2 H, PCOCC*H*$_2$), 3.90 (d, $J = 8.5$ Hz, 2 H, PCH$_2$), 1.28

(t, $J = 7.1$ Hz, 6 H, $2 \times POCH_2CH_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 154.76, 144.33, 140.84, 122.31, 117.30, 115.39, 69.82 (d, $J = 11.2$ Hz, PCO*C*), 64.93 (d, $J = 165.7$ Hz, P*C*), 62.45 (d, $J = 6.5$ Hz, $2 \times$ PO*C*), 38.81 (s, PCOC*C*), 16.37 (d, $J = 5.7$ Hz, $2 \times$ POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 21.66; Anal. Calcd. for $C_{13}H_{20}N_3O_5P \times 0.3H_2O$: C. 46.65; H. 6.20; N. 12.55; Found: C. 46.76; H. 6.44; N. 12.37.

4.59. Diethyl 2-{2-(2-oxo-1H-imidazo[4,5-b]pyridin-3-yl)ethoxy}ethylphosphonate 9f

According to the general procedure from diethyl 2-{2-[(3-aminopyridin-2-yl)amino]ethoxy}ethylphosphonate **6f** (0.140 g, 0.44 mmol) and 1,1′-carbonyldiimidazole (0.107 g, 0.66 mmol) the phosphonate **9f** (0.114 g, 75%) was obtained as a violet oil. IR (film, cm^{-1}) ν_{max}: 3452, 3087, 3056, 2983, 1659, 1230, 1027, 964, 777; ^1H NMR (600 MHz, $CDCl_3$) δ [ppm]: 9.93 (brs, 1 H, N*H*), 8.06 (dd, $J = 5.2$ Hz, $J = 1.2$ Hz, 1 H, Ar–*H*), 7.32 (dd, $J = 7.7$ Hz, $J = 1.2$ Hz, 1 H, Ar–*H*), 7.01 (dd, $J = 7.7$ Hz, $J = 5.2$ Hz, 1 H, Ar–*H*), 4.23 (t, $J = 5.9$ Hz, 2 H, PCCOCH_2), 4.14–4.03 (m, 4 H, $2 \times$ POCH_2CH$_3$), 3.88 (t, $J = 5.9$ Hz, 2 H, PCCOCCH_2), 3.77 (dt, $J = 10.9$ Hz, $J = 7.6$ Hz, 2 H, PCCH_2), 2.08 (dt, $J = 18.7$ Hz, $J = 7.6$ Hz, 2 H, PCH_2), 1.31 (t, $J = 7.1$ Hz, 6 H, $2 \times POCH_2CH_3$); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 154.93, 144.33, 140.81, 122.37, 117.29, 115.47, 67.43 (s, PCCO*C*), 64.81 (s, PCCOC*C*), 61.65 (d, $J = 6.3$ Hz, $2 \times$ PO*C*), 39.17 (s, P*C*C), 26.90 (d, $J = 139.2$ Hz, P*C*), 16.38 (d, $J = 6.1$ Hz, $2 \times$ POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 28.40; Anal. Calcd. for $C_{14}H_{22}N_3O_5P \times 0.7H_2O$: C. 47.24; H. 6.63; N. 11.81; Found: C. 47.27; H. 6.81; N. 11.80.

4.60. Diethyl 1-methoxy-2-(2-oxo-1H-imidazo[4,5-b]pyridin-3-yl)ethylphosphonate 9j

According to the general procedure from diethyl 2-[(3-aminopyridin-2-yl)amino]-1-methoxyethylphosphonate **6j** (0.130 g, 0.43 mmol) and 1,1′-carbonyldiimidazole (0.104 g, 0.64 mmol) the phosphonate **9j** (0.046 g, 33%) was obtained as a red oil. IR (film, cm^{-1}) ν_{max}: 3319, 3146, 2957, 1234, 1048, 972, 786; ^1H NMR (600 MHz, $CDCl_3$) δ [ppm]: 10.28 (brs, 1 H, N*H*), 8.08 (dd, $J = 5.2$ Hz, $J = 1.0$ Hz, 1 H, Ar–*H*), 7.35 (dd, $J = 7.6$ Hz, $J = 1.0$ Hz, 1 H, Ar–*H*), 7.02 (dd, $J = 7.6$ Hz, $J = 5.2$ Hz, 1 H, Ar–*H*), 4.45 (dt, $J = 13.9$ Hz, $J = 10.0$ Hz, 1 H, PC*H*), 4.38 (ddd, $J = 10.0$ Hz, $J = 6.4$ Hz, $J = 3.9$ Hz, 1 H, PCCH_aH$_b$), 4.30–4.22 (m, 5 H, $2 \times$ POCH_2CH$_3$, PCH$_a$$H_b$), 3.45 (s, 3 H, PCOC$H_3$), 1.41 (t, $J = 7.1$ Hz, 3 H, POCH$_2$CH_3), 1.38 (t, $J = 7.1$ Hz, 2 H, POCH_2CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 155.01, 144.19, 140.78, 122.41, 117.37, 115.68, 74.28 (d, $J = 162.4$ Hz, P*C*), 62.93 (d, $J = 7.0$ Hz, PO*C*), 62.69 (d, $J = 7.0$ Hz,

POC), 60.64, 40.31, 16.52 (d, $J = 5.5$ Hz, POCC), 16.45 (d, $J = 5.5$ Hz, POCC); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 20.29; Anal. Calcd. for $C_{13}H_{20}N_3O_5P$: C. 47.42; H. 6.12; N. 12.76; Found: C. 47.37; H. 6.21; N. 12.52.

4.61. Diethyl 1-methoxy-3-(2-oxo-1H-imidazo[4,5-b]pyridin-3-yl)propylphosphonate 9k

According to the general procedure from diethyl 3-[(3-aminopyridin-2-yl) amino]-1-methoxypropylphosphonate **6k** (0.073 g, 0.23 mmol) and 1,1′-carbonyldiimidazole (0.056 g, 0.35 mmol) the phosphonate **9k** (0.035 g, 44%) was obtained as a white powder. M.p. 132 °C–133 °C; IR (KBr, cm^{-1}) ν_{max}: 3407, 3162, 3117, 2985, 1721, 1235, 1021, 986, 725; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 9.01 (s, 1 H, NH), 8.07 (d, $J = 5.2$ Hz, 1 H, Ar–H), 7.28 (d, $J = 7.4$ Hz, 1 H, Ar–H), 7.08–6.90 (m, 1 H, Ar–H), 4.38–4.02 (m, 6 H, 2 × POCH_2CH_3, PCCCH_2), 3.63 (s, 3 H, CH_3), 3.59–6.57 (m, 1 H, PCH), 2.42–2.15 (m, 2 H, PCCH_2), 1.36 (t, $J = 7.0$ Hz, 3 H, POCH$_2$CH_3), 1.32 (t, $J = 7.0$ Hz, 3 H, POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 154.43, 144.32, 140.98, 122.10, 117.23, 115.15, 75.18 (d, $J = 165.3$ Hz, PC), 62.58 (d, $J = 6.7$ Hz, POC), 62.25 (d, $J = 6.7$ Hz, POC), 60.24 (d, $J = 1.5$ Hz, PCC), 36.46 (d, $J = 16.2$ Hz, PCCC), 29.44 (s, PCOC), 16.52 (d, $J = 5.5$ Hz, POCC), 16.47 (d, $J = 5.5$ Hz, POCC); ^{31}P NMR (243 MHz, $CDCl_3$) δ [ppm]: 22.87; Anal. Calcd. for $C_{14}H_{22}N_3O_5$: C. 48.98; H. 6.46; N. 12.24; Found: C. 48.72; H. 6.29; N. 12.15.

4.62. Diethyl 2-methoxy-3-(2-oxo-1H-imidazo[4,5-b]pyridin-3-yl)propylphosphonate 9l

According to the general procedure from diethyl 3-[(3-aminopyridin-2-yl) amino]-2-methoxypropylphosphonate **6l** (0.161 g, 0.51 mmol) and 1,1′-carbonyldiimidazole (0.123 g, 0.76 mmol) the phosphonate **9l** (0.062 g, 36%) was obtained as a white powder. M.p. 63 °C–64 °C; IR (film, cm^{-1}) ν_{max}: 3398, 3071, 3032, 2984, 1721, 1219, 1027, 966, 771; ^{1}H NMR (600 MHz, $CDCl_3$) δ [ppm]: 8.05 (dd, $J = 5.1$ Hz, $J = 0.9$ Hz, 1 H, Ar–H), 7.30 (dd, $J = 7.7$ Hz, $J = 0.9$ Hz, 1 H, Ar–H), 6.99 (dd, $J = 7.7$ Hz, $J = 5.1$ Hz, 1 H, Ar–H), 4.25–4.06 (m, 8 H, 2 × POCH_2CH_3, PCCCH_2, PCCH, NH), 3.45 (s, 3 H, CH_3), 2.19 (dd, $J = 18.4$ Hz, $J = 5.6$ Hz, 2 H, PCH_2), 1.34 (t, $J = 7.0$ Hz, 3 H, POCH$_2$CH_3), 1.33 (t, $J = 7.1$ Hz, 3 H, POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ [ppm]: 155.15, 144.45, 140.79, 122.49, 117.33, 115.47, 74.29 (d, $J = 3.4$ Hz, PCC), 61.95 (d, $J = 6.3$ Hz, POC), 61.60 (d, $J = 6.3$ Hz, POC), 57.69, 43.24 (d, $J = 13.9$ Hz, PCCC), 30.11 (d, $J = 141.0$ Hz, PC), 16.38 (d, $J = 6.0$ Hz, POCC), 16.35 (d, $J = 6.0$ Hz, POCC); ^{31}P NMR (243 MHz,

$CDCl_3$) δ [ppm]: 28.50; Anal. Calcd. for $C_{14}H_{22}N_3O_5P \times 0.24H_2O$: C. 48.34; H. 6.52; N. 12.08; Found: C. 48.25; H. 6.61; N. 11.95.

4.63. Synthesis of phosphonic acids 10a–i, 11a–i, and 12a–f, j–l – general procedure

Solutions of diethyl (1,2,3-triazolo[4,5-b]pyridin-3-yl)alkylphosphonate **7a–i** (1.00 mmol), diethyl (imidazo[4,5-b]pyridin-3-yl)alkylphosphonate **8a–i** (1.00 mmol), (2-oxo-1H-imidazo[4,5-b]pyridin-3-yl)alkylphosphonate **9a–f**, **j–l** (1.00 mmol) were treated with bromotrimethylsilane (10.0 mmol) at room temperature under argon atmosphere. The reaction mixture was protected from light and stirred at room temperature for 24 hours. After water (2 mL) was added and concentration to dryness the residue was co-evaporated with ethanol (3 × 3 mL) and dichloromethane (5 mL) to afford crude phosphonic acids **10a–i**, **11a–i** and **12a–f**, **j–l** which was purified by crystallisation from a water–methanol or methanol–isopropanol mixture.

4.64. (1,2,3-Triazolo[4,5-b]pyridin-3-yl)methylphosphonic acid 10a

From **7a** (0.030 g, 0.11 mmol) the phosphonic acid **10a** (0.012 g, 49%) was obtained as a white solid. M.p. 235 °C–237 °C; IR (KBr, cm^{-1}) ν_{max}: 3426, 3260, 3086, 2987, 1609, 1597, 1129; ^{1}H NMR (600 MHz, D_2O) δ [ppm]: $\delta = 8.72$ (dd, $J = 4.6$ Hz, $J = 1.3$ Hz, 1 H, Ar–*H*), 8.49 (dd, $J = 8.4$ Hz, $J = 1.4$ Hz, 1 H, Ar–*H*), 7.54 (dd, $J = 8.4$ Hz, $J = 4.6$ Hz, 1 H, Ar–*H*), 5.02 (d, $J = 11.9$ Hz, 2 H, PCH_2); ^{13}C NMR (151 MHz, D_2O $_3$) δ [ppm]: 151.00, 144.65, 136.53, 129.49, 121.06, 44.69 (d, $J = 143.9$ Hz); ^{31}P NMR (243 MHz, D_2O) δ [ppm]: 11.60; Anal. Calcd. for $C_6H_7N_4O_3P$: C. 33.66; H. 3.30; N. 26.17; Found: C. 33.39; H. 3.34; N. 26.06.

4.65. 2-(1,2,3-Triazolo[4,5-b]pyridin-3-yl)ethylphosphonic acid 10b

From **7b** (0.048 g, 0.17 mmol) the phosphonic acid **10b** (0.031 g, 80%) was obtained as a white solid. M.p. 210 °C–215 °C; IR (KBr, cm^{-1}) ν_{max}: 3436, 3218, 3085, 3006, 2971, 1683, 15923, 1212; ^{1}H NMR (600 MHz, D_2O) δ [ppm]: 8.71 (dd, $J = 4.6$ Hz, $J = 1.2$ Hz, 1 H, Ar–*H*), 8.48 (dd, $J = 8.4$ Hz, $J = 1.2$ Hz, 1 H, Ar–*H*), 7.54 (dd, $J = 8.4$ Hz, $J = 4.6$ Hz, 1 H, Ar–*H*), 4.99 (dt, $J = 12.5$ Hz, $J = 7.7$ Hz, 2 H, PCCH_2), 2.50 (dt, $J = 17.9$ Hz, $J = 7.7$ Hz, 2 H, PCH_2); ^{13}C NMR (151 MHz, D_2O) δ [ppm]: 150.94, 144.54, 136.85, 129.44, 121.09, 42.21 (s, PC*C*), 27.28 (d, $J = 134.3$ Hz, P*C*); ^{31}P NMR (243 MHz, D_2O) δ [ppm]: 22.42; Anal. Calcd. for $C_7H_9N_4O_3P$: C. 36.85; H. 3.95; N. 24.56; Found: C. 36.67; H. 4.00; N. 24.41.

4.66. 3-(1,2,3-Triazolo[4,5-b]pyridin-3-yl)propylphosphonic acid 10c

From **7c** (0.042 g, 0.14 mmol) the phosphonic acid **10c** (0.021 g, 61%) was obtained as a white solid. M.p. 180 °C–182 °C; IR (KBr, cm^{-1}) ν_{max}: 3299, 3073, 2966, 2901, 1593, 1221; ^{1}H NMR (600 MHz, D_2O) δ [ppm]: $\delta = 8.69$ (dd, $J = 4.6$ Hz, $J = 1.4$ Hz, 1 H, Ar–*H*), 8.46 (dd, $J = 8.4$ Hz, $J = 1.4$ Hz, 1 H, Ar–*H*), 7.52 (dd, $J = 8.4$ Hz, $J = 4.6$ Hz, 1 H, Ar–*H*), 4.81 (t, $J = 6.8$ Hz, 2 H, PCCCH_2), 2.38–2.17 (m, 2 H, PCH_2), 1.84–1.64 (m, 2 H, PCCH_2); ^{13}C NMR (151 MHz, D_2O) δ [ppm]: 150.97, 144.65, 136.78, 129.43, 121.10, 47.46 (d, $J = 19.3$ Hz, PCCC), 23.94 (d, $J = 136.2$ Hz, PC), 22.86 (d, $J = 3.8$ Hz, PCC); ^{31}P NMR (243 MHz, D_2O) δ [ppm]: 28.42; Anal. Calcd. for $C_8H_{11}N_4O_3P$: C. 39.68; H. 4.58; N. 23.14; Found: 39.43; H. 4.53; N. 23.12.

4.67. 4-(1,2,3-Triazolo[4,5-b]pyridin-3-yl)butylphosphonic acid 10d

From **7d** (0.050 g, 0.16 mmol) the phosphonic acid **10d** (0.025 g, 61%) was obtained as a white powder. M.p.>260 °C; IR (KBr, cm^{-1}) ν_{max}: 3381, 3042, 3006, 2947, 1592, 1226; ^{1}H NMR (600 MHz, D_2O) δ [ppm]: $\delta = 8.70$ (d, $J = 4.1$ Hz, 1 H, Ar–*H*), 8.48 (d, $J = 8.3$ Hz, 1 H, Ar–*H*), 7.53 (dd, $J = 8.1$ Hz, $J = 4.3$ Hz, 1 H, Ar–*H*), 4.77 (t, $J = 5.6$ Hz, 2 H, PCCCCH_2), 2.13–2.06 (m, 2 H, PCCCH_2), 1.64–1.61 (m, 2 H, PCH_2), 1.54–1.51 (m, 2 H, PCCH_2); ^{13}C NMR (151 MHz, D_2O) δ [ppm]: 150.99, 144.74, 135.21, 129.41, 121.10, 46.91, 46.91, 38.89 (d, $J = 123.2$ Hz, PC), 26.40, 24.33; ^{31}P NMR (243 MHz, D_2O) δ [ppm]: 26.92; Anal. Calcd. for $C_9H_{13}N_4O_3P$: C. 42.19; H. 5.11; N. 21.87; Found: C. 42.01; H. 5.10; N. 21.80.

4.68. {2-(1,2,3-Triazolo[4,5-b]pyridin-3-yl)ethoxy}methylphosphonic acid 10e

From **7e** (0.044 g, 0.14 mmol) the phosphonic acid **10e** (0.017 g, 48%) was obtained as a white solid. M.p. 154 °C–156 °C; IR (KBr, cm^{-1}) ν_{max}: 3388, 3099, 2922, 1649, 1594, 1224; ^{1}H NMR (600 MHz, D_2O) δ [ppm]: $\delta = 8.69$ (d, $J = 4.1$ Hz, 1 H, Ar–*H*), 8.47 (d, $J = 8.7$ Hz, 1 H, Ar–*H*), 7.53 (dd, $J = 8.4$, $J = 4.2$ Hz, 1 H, Ar–*H*), 4.96 (t, $J = 5.2$ Hz, 2 H, PCOCH_2), 4.15 (t, $J = 5.2$ Hz, 2 H, PCOCCH_2), 3.70 (d, $J = 8.6$ Hz, 2 H, PCH_2); ^{13}C NMR (151 MHz, D_2O) δ [ppm]: 150.84, 144.79, 136.86, 129.66, 121.10, 70.47 (d, $J = 11.0$ Hz, PCOC), 65.76 (d, $J = 159.6$ Hz, PC), 46.85; ^{31}P NMR (243 MHz, D_2O) δ [ppm]: 18.57; Anal. Calcd. for $C_8H_{11}N_4O_4P$: C.37.22; H. 4.29; N. 21.70; Found: C. 37.03; H. 4.20; N. 21.74.

4.69. 2-{2-(1,2,3-Triazolo[4,5-b]pyridin-3-yl)ethoxy}ethylphosphonic acid 10f

From **7f** (0.033 g, 0.10 mmol) the phosphonic acid **10f** (0.012 g, 44%) was obtained as a white solid. M.p.>260 °C; IR (KBr, cm^{-1}) ν_{max}: 3388, 3035,

2955, 1643, 1595, 1225; ^{1}H NMR (600 MHz, D_2O) δ [ppm]: 8.73 (d, $J = 4.5$ Hz, 1 H, Ar–*H*), 8.52 (d, $J = 8.4$ Hz, 1 H, Ar–*H*), 7.57 (dd, $J = 8.4$ Hz, $J = 4.6$ Hz, 1 H, Ar–*H*), 4.97 (t, $J = 5.2$ Hz, 2 H, PCCOCH_2), 4.10 (t, $J = 5.2$ Hz, 2 H, PCCOCCH_2) 3.73–3.67 (m, 2 H, PCCH_2), 2.00–1.92 (m, 2 H, PCH_2); ^{13}C NMR (151 MHz, D_2O) δ [ppm]: $\delta = 150.97$, 144.90, 136.92, 129.73, 121.20, 68.00, 65.02, 46.98, 27.29 (d, $J = 133.5$ Hz, P*C*); ^{31}P NMR (243 MHz, D_2O) δ [ppm]: 26.88; Anal. Calcd. for $C_9H_{13}N_4O_4P$: C. 39.71; H. 4.81; N. 20.58; Found: C. 39.53; H. 4.70; N. 20.71.

4.70. 1-Hydroxy-2-(1,2,3-triazolo[4,5-b]pyridin-3-yl)ethylphosphonic acid 10g

From **7g** (0.030 g, 0.10 mmol) the phosphonic acid **10g** (0.014 g, 56%) was obtained as a white solid. M.p. 182 °C–184 °C; IR (KBr, cm^{-1}) ν_{max}: 3419, 3088, 2852, 1627, 1550, 1222; ^{1}H NMR (600 MHz, D_2O) δ [ppm]: 8.73 (d, $J = 4.1$ Hz, 1 H, Ar–*H*), 8.51 (d, $J = 8.4$ Hz, 1 H, Ar–*H*), 7.56 (dd, $J = 8.4$ Hz, $J = 4.1$ Hz, 1 H, Ar–*H*), 5.13–5.03 (m, 1 H, PCC*H*), 5.01–4.92 (m, 1 H, PCC*H*), 4.48–4.40 (m, 1 H, PC*H*); ^{13}C NMR (151 MHz, D_2O) δ [ppm]: 151.09, 145.18, 136.85, 129.52, 121.14, 66.42 (d, $J = 130.2$ Hz, P*C*), 49.47 (d, $J = 11.2$ Hz, PC*C*); ^{31}P NMR (243 MHz, D_2O) δ [ppm]: 16.16; Anal. Calcd. for $C_7H_9N_4O_4P$: C.34.44; H. 3.72; N. 22.95; Found: C.34.30; H. 3.70; N. 23.00.

4.71. 1-Hydroxy-3-(1,2,3-triazolo[4,5-b]pyridin-3-yl)propylphosphonic acid 10h

From **7h** (0.033 g, 0.10 mmol) the phosphonic acid **10h** (0.016 g, 59%) was obtained as a white solid. M.p. 183 °C–185 °C; IR (KBr, cm^{-1}) ν_{max}: 3443, 3090, 1643, 1505, 1223; ^{1}H NMR (600 MHz, D_2O) δ [ppm]: 8.72 (d, $J = 4.4$ Hz, 1 H, Ar–*H*), 8.49 (d, $J = 8.4$ Hz, 1 H, Ar–*H*), 7.55 (dd, $J = 8.4$ Hz, $J = 4.5$ Hz, 1 H, Ar–*H*), 5.06–4.87 (m, 2 H, PCCCH_2), 3.79–3.63 (m, 1 H, PC*H*), 2.59–2.18 (m, 2 H, PCCH_2); ^{13}C NMR (151 MHz, D_2O) δ [ppm]: $\delta = 150.98$, 144.78, 136.86, 129.45, 121.10, 65.17 (d, $J = 160.8$ Hz, P*C*), 43.97 (d, $J = 16.1$ Hz, PCC*C*), 30.90 (d, $J = 4.2$ Hz, PC*C*).; ^{31}P NMR (243 MHz, D_2O) δ [ppm]: 20.95; Anal. Calcd. for $C_8H_{11}N_4O_4P$: C. 37.22; H. 4.29; N. 21.70; Found: C. 37.20; H. 4.20; N. 21.76.

4.72. 2-Hydroxy-3-([1–3]triazolo[4,5-b]pyridin-3-yl)propylphosphonic acid 10i

From **7i** (0.036 g, 0.11 mmol) the phosphonic acid **10i** (0.018 g, 59%) was obtained as a white solid. M.p. 202 °C–205 °C; IR (KBr, cm^{-1}) ν_{max}: 3418, 2088, 2928, 1628, 1549, 1222; ^{1}H NMR (600 MHz, D_2O) δ [ppm]: 8.70 (dd, $J = 4.7$ Hz, $J = 1.4$ Hz, 1 H, Ar–*H*), 8.48 (dd, $J = 8.5$ Hz, $J = 1.6$ Hz, 1 H, Ar–*H*), 7.53 (dd, $J = 8.6$ Hz, $J = 4.6$ Hz, 1 H, Ar–*H*), 4.96–4.89 (m, H, 2 H,

PCCCH_2), 4.84–4.78 (m, 1 H, PCCH), 4.62–4.53 (m, 2 H, PCH_2); ^{13}C NMR (151 MHz, D_2O) δ [ppm]: δ = 151.11, 145.15, 136.69, 129.50, 121.12, 65.72 (d, J = 3.2 Hz, PCC), 53.05 (d, J = 15.2 Hz, PCCC), 32.43 (d, J = 134.8 Hz, PC).; ^{31}P NMR (243 MHz, D_2O) δ [ppm]: 24.24; Anal. Calcd. for $C_8H_{11}N_4O_4P$: C. 37.22; H. 4.29; N. 21.70; Found: C. 37.03; H. 4.31; N. 21.56.

4.73. (Imidazo[4,5-b]pyridin-3-yl)methylphosphonic acid 11a

From **8a** (0.030 g, 0.11 mmol) the phosphonic acid **11a** (0.015 g, 62%) was obtained as a white amorphous solid. M.p.>260 °C; IR (KBr, cm^{-1}) ν_{max}: 3424, 3050, 2990, 1624, 1602, 1414, 1233; ^{1}H NMR (600 MHz, D_2O) δ [ppm]: 9.45 (s, 1 H, NCHN), 8.71 (d, J = 4.5 Hz, 1 H, Ar–H), 8.34 (d, J = 8.3 Hz, 1 H, Ar–H), 7.72 (dd, J = 7.8 Hz, J = 4.8 Hz, 1 H, Ar–H), 4.76 (d, J = 12.0 Hz, 2 H, PCH_2).; ^{13}C NMR (151 MHz, D_2O) δ [ppm]: 148.16, 142.68, 141.91, 125.25, 123.91, 122.78, 42.49 (d, J = 140.2 Hz, PC); ^{31}P NMR (243 MHz, D_2O) δ [ppm]: 9.81; Anal. Calcd. for $C_7H_8N_3O_3P$: C. 39.45; H. 3.78; N. 19.72; Found: C. 39.22; H. 3.70; N. 19.88.

4.74. 2-(Imidazo[4,5-b]pyridin-3-yl)ethylphosphonic acid 11 b

From **8b** (0.040 g, 0.14 mmol) the phosphonic acid **11b** (0.026 g, 80%) was obtained as a white solid. M.p. 145 °C–150 °C; IR (KBr, cm^{-1}) ν_{max}: 3424, 3105, 2994, 2917, 1618, 1544, 1465, 1415, 1257; ^{1}H NMR (600 MHz, D_2O) δ [ppm]: δ = 9.49 (s, 1 H, NCHN), 8.70 (d, J = 4.0 Hz, 1 H, Ar–H), 8.33 (d, J = 8.3 Hz, 1 H, Ar–H), 7.72 (dd, J = 8.1 Hz, J = 4.9 Hz, 1 H, Ar–H), 4.84–4.76 (m, 2 H, PCCH_2), 2.47–2.40 (m, 2 H, PCH_2); ^{13}C NMR (151 MHz, D_2O) δ [ppm]: 148.09, 142.51, 142.06, 125.28, 124.23, 122.80, 41.44, 26.91 (d, J = 134.4 Hz, PC); ^{31}P NMR (243 MHz, D_2O) δ [ppm]: 20.63; Anal. Calcd. for $C_8H_{10}N_3O_3P$: C. 42.30; H. 4.44; N. 18.50; Found: C. 42.15; H. 4.40; N. 18.60.

4.75. 3-(Imidazo[4,5-b]pyridin-3-yl)propylphosphonic acid 11c

From **8c** (0.018 g, 0.06 mmol) the phosphonic acid **11c** (0.060 g, 41%) was obtained as a white solid. M.p. 141 °C–144 °C; IR (KBr, cm^{-1}) ν_{max}: 3424, 3049, 2989, 2936, 1618, 1465, 1416, 1336, 1255; ^{1}H NMR (600 MHz, D_2O) δ [ppm]: 8.39 (s, 1 H, NCHN), 8.35 (d, J = 4.7 Hz, 1 H, Ar–H), 8.12 (d, J = 7.6 Hz, 1 H, Ar–H), 7.38 (dd, J = 7.6 Hz, J = 4.7 Hz, 1 H, Ar–H), 4.39–4.34 (m, 2 H, PCCCH_2), 2.18–2.05 (m, 2 H, PCH_2), 1.64–1.50 (m, 2 H, PCCH_2); ^{13}C NMR (151 MHz, D_2O) δ [ppm]: 148.18, 145.76, 143.93, 128.21, 127.40, 118.87, 44.51 (d, J = 18.3 Hz, PCC), 25.94 (d, J = 132.3 Hz, PC), 23.93; ^{31}P

NMR (243 MHz, D_2O) δ [ppm]: 24.24; Anal. Calcd. for $C_9H_{12}N_3O_3P$: C. 44.82; H. 5.01; N. 17.42; Found: C. 44.73; H. 4.92; N. 17.55.

4.76. 4-(Imidazo[4,5-b]pyridin-3-yl)butylphosphonic acid 11d

From **8d** (0.019 g, 0.06 mmol) the phosphonic acid **11d** (0.009 g, 56%) was obtained as a white solid. M.p. 145 °C–147 °C with decomposition; IR (KBr, cm^{-1}) ν_{max}: 3418, 3063, 1938, 1621, 1548, 1462, 1288; ^1H NMR (600 MHz, D_2O) δ [ppm]: 8.82 (s, 1 H, NC*H*N), 8.53 (brs, 1 H, Ar–*H*), 8.18 (brs, 1 H, Ar–*H*), 7.48 (brs, 1 H, Ar–*H*), 4.50–4.40 (m, 2 H, PCCCCH_2), 2.12–1.95 (m, 2 H, PCH_2), 1.82–1.74 (m, 2 H, PCCCH_2), 1.69–1.57 (m, 2 H, PCCH_2); ^{13}C NMR (151 MHz, D_2O) δ [ppm]: 147.57, 142.19, 138.58, 138.12, 125.51, 122.34, 45.42, 39.43 (d, $J = 128.6$ Hz, P*C*), 29.42, 20.19; ^{31}P NMR (243 MHz, D_2O) δ [ppm]: 25.91; Anal. Calcd. for $C_{10}H_{14}N_3O_3P$: C. 47.06; H. 5.53; N. 16.46; Found: C. 46.90; H. 5.41; N. 16.52.

4.77. {2-(imidazo[4,5-b]pyridin-3-yl)ethoxy}methylphosphonic acid 11e

From **8e** (0.031 g, 0.10 mmol) the phosphonic acid **11e** (0.011 g, 43%) was obtained as a white solid. M.p. 140 °C–142 °C; IR (KBr, cm^{-1}) ν_{max}: 3418, 3060, 2923, 1622, 1548, 1415, 1168; ^1H NMR (600 MHz, D_2O) δ [ppm]: 9.50 (s, 1 H, NC*H*N), 8.67 (d, $J = 4.5$ Hz, 1 H, Ar–*H*), 8.33 (d, $J = 8.2$ Hz, 1 H, Ar–*H*), 7.70 (dd, $J = 8.2$ Hz, $J = 4.5$ Hz, 1 H, Ar–*H*), 4.75–4.65 (m, 2 H, PCOCH_2), 4.04–3.83 (m, 2 H, PCOCCH_2), 3.64–3.44 (m, 2 H, PCH_2); ^{13}C NMR (151 MHz, D_2O) δ [ppm]: 147.81, 142.67, 142.06, 125.36, 124.44, 122.60, 68.80 (d, $J = 139.4$ Hz, P*C*), 45.18, 23.74; ^{31}P NMR (243 MHz, D_2O) δ [ppm]: 15.50; Anal. Calcd. for $C_9H_{12}N_3O_4P$: C. 42.03; H. 4.70; N. 16.34; Found: C. 41.97; H. 4.65; N. 16.45.

4.78. 2-{2-(Imidazo[4,5-b]pyridin-3-yl)ethoxy}ethylphosphonic acid 11f

From **8f** (0.039 g, 0.12 mmol) the phosphonic acid **11f** (0.022 g, 67%) was obtained as a white solid. M.p. 255 °C–260 °C; IR (KBr, cm^{-1}) ν_{max}: 3423, 3090, 2923, 1618, 1534, 1416, 1117, 1061; ^1H NMR (600 MHz, D_2O) δ [ppm]: 9.47 (s, 1 H, NC*H*N), 8.70 (d, $J = 3.4$ Hz, 1 H, Ar–*H*), 8.35 (d, $J = 8.1$ Hz, 1 H, Ar–*H*), 7.72 (brs, 1 H, Ar–*H*), 4.76–4.68 (m, 2 H, PCCOCH_2), 4.01–3.89 (m, 2 H, PCCH_2), 3.74–3.60 (m, 2 H, PCCOCCH_2), 1.92–1.86 (m, 2 H, PCH_2); ^{13}C NMR (151 MHz, D_2O) δ [ppm]: 147.77, 142.83, 142.68, 125.52, 124.78, 122.54, 67.07, 65.87 (d, $J = 138.9$ Hz, P*C*), 58.55, 45.17; ^{31}P NMR (243 MHz, D_2O) δ [ppm]: 21.98; Anal. Calcd. for $C_{10}H_{14}N_3O_4P$: C. 44.29; H. 5.20; N. 15.49; Found: C. 44.15; H. 5.13; N. 15.58.

4.79. 1-Hydroxy-2-(imidazo[4,5-b]pyridin-3-yl)ethylphosphonic acid 11g

From **8g** (0.030 g, 0.10 mmol) the phosphonic acid **11g** (0.010 g, 42%) was obtained as a white powder. M.p. > 260 °C; IR (KBr, cm^{-1}) ν_{max}: 3417, 3060, 2968, 1637, 1549, 1416; ^{1}H NMR (600 MHz, D_2O) δ [ppm]: 9.44 (s, 1 H, NC*H*), 8.70 (d, $J = 3.7$ Hz, 1 H, Ar–*H*), 8.34 (d, $J = 8.0$ Hz, 1 H, Ar–*H*), 7.71 (dd, $J = 8.0$ Hz, $J = 3.7$ Hz, 1 H, Ar–*H*), 4.97–4.88 (m, 2 H, PCCH_2), 4.24–4.10 (m, 1 H, PC*H*); ^{13}C NMR (151 MHz, D_2O) δ [ppm]: 147.86, 142.86, 142.73, 125.46, 124.71, 122.55, 47.92 (d, $J = 9.7$ Hz, PC*C*), 25.57 (d, $J = 138.7$ Hz, P*C*); ^{31}P NMR (243 MHz, D_2O) δ [ppm]: 14.73; Anal. Calcd. for $C_8H_{10}N_3O_4P$: C. 39.52; H. 4.15; N. 17.28; Found: C. 39.44; H. 4.14; N. 17.31.

4.80. 1-Hydroxy-3-(imidazo[4,5-b]pyridin-3-yl)propylphosphonic acid 11h

From **8h** (0.016 g, 0.05 mmol) the phosphonic acid **11h** (0.010 g, 76%) was obtained as a white solid. M.p. 160 °C–168 °C with decomposition; IR (KBr, cm^{-1}) ν_{max}: 3415, 3058, 2959, 1620, 1528, 1477, 1413, 1161; ^{1}H NMR (600 MHz, D_2O) δ [ppm]: 8.99 (s, 1 H, NC*H*), 8.53 (brs, 1 H, Ar–*H*), 8.21 (brs, 1 H, Ar–*H*), 7.54 (brs, 1 H, Ar–*H*), 3.65–3.44 (m, 2 H, PCCCH_2), 2.40–2.23 (m, 1 H, PC*H*), 2.20–2.09 (m, 2 H, PCCH_2); ^{13}C NMR (151 MHz, D_2O) δ [ppm]: 149.11, 146.20, 140.64, 135.61, 126.61, 120.99, 42.15, 31.15, 28.01 (d, $J = 126.8$ Hz, P*C*); ^{31}P NMR (243 MHz, D_2O) δ [ppm]: 19.16; Anal. Calcd. for $C_9H_{12}N_3O_4P$: C. 42.03; H. 4.70; N. 16.34; Found: C. 41.89; H. 4.68; N. 16.51.

4.81. 2-Hydroxy-3-(imidazo[4,5-b]pyridin-3-yl)propylphosphonic acid 11i

From **8i** (0.038 g, 0.12 mmol) the phosphonic acid **11i** (0.016 g, 52%) was obtained as a white solid. M.p. 130 °C–136 °C; IR (KBr, cm^{-1}) ν_{max}: 3417, 3062, 2923, 1622, 1549, 1416; ^{1}H NMR (600 MHz, D_2O) δ [ppm]: 9.48 (s, 1 H, NC*H*N), 8.71 (d, $J = 4.8$ Hz, 1 H, Ar–*H*), 8.36 (d, $J = 8.4$ Hz, 1 H, Ar–*H*), 7.73 (dd, $J = 8.4$ Hz, $J = 4.8$ Hz, 1 H, Ar–*H*), 4.95–4.51 (m, 2 H, PCCCH_2), 4.50–4.39 (m, 1 H, PCC*H*), 2.20–1.98 (m, 2 H, PCH_2); ^{13}C NMR (151 MHz, D_2O) δ [ppm]: 148.06, 142.82, 142.59, 125.42, 124.26, 122.77, 65.19 (d, $J = 2.7$ Hz, PC*C*), 51.25 (d, $J = 14.5$ Hz, PCC*C*), 32.64 (d, $J = 133.6$ Hz, P*C*); ^{31}P NMR (243 MHz, D_2O) δ [ppm]: 22.21; Anal. Calcd. for $C_9H_{12}N_3O_4P$: C. 42.03; H. 4.70; N. 16.34; Found: C. 42.28; H. 4.61; N. 16.23.

4.82. (2-Oxo-1H-imidazo[4,5-b]pyridin-3-yl)methylphosphonic acid 12a

From **9a** (0.019 g, 0.07 mmol) the phosphonic acid **12a** (0.018 g, 88%) was obtained as a white solid. M.p.>260 °C; IR (KBr, cm^{-1}) ν_{max}: 3388, 3201, 3087, 2923, 1741, 1654, 1541, 1294; ^{1}H NMR (600 MHz, D_2O) δ [ppm]:

δ = 8.06 (dd, J = 6.0 Hz, J = 1.1 Hz, 1 H, Ar–*H*), 7.79 (dd, J = 7.9 Hz, J = 1.1 Hz, 1 H, Ar–*H*), 7.37 (dd, J = 7.9 Hz, J = 6.0 Hz, 1 H, Ar–*H*), 4.23 (d, J = 10.7 Hz, 2 H, PCH_2); ^{13}C NMR (151 MHz, D_2O) δ [ppm]: δ = 153.91, 140.59, 133.37, 125.12, 120.80, 118.27, 38.86 (d, J = 145.1 Hz, P*C*); ^{31}P NMR (243 MHz, D_2O) δ [ppm]: 12.80; Anal. Calcd. for $C_7H_8N_3O_4P$: C. 36.69; H. 3.52; N. 18.34; Found: C.36.41; H. 3.34; N. 18.51.

4.83. 2-(2-Oxo-1H-imidazo[4,5-b]pyridin-3-yl)ethylphosphonic acid 12b

From **9b** (0.027 g, 0.09 mmol) the phosphonic acid **12b** (0.011 g, 50%) was obtained as a white solid. M.p. 238 °C–240 °C; IR (KBr, cm^{-1}) ν_{max}: 3545, 3302, 3060, 2987, 1737, 1648, 1506, 1217; ^{1}H NMR (600 MHz, D_2O) δ [ppm]: 8.04 (dd, J = 5.8 Hz, J = 1.0 Hz, 1 H, Ar–*H*), 7.72 (dd, J = 7.8 Hz, J = 1.1 Hz, 1 H, Ar–*H*), 7.32 (dd, J = 7.8 Hz, J = 1.1 Hz, 1 H, Ar–*H*), 4.26–4.19 (m, 2 H, PCCH_2), 2.36–2.04 (m, 2 H, PCH_2); ^{13}C NMR (151 MHz, D_2O) δ [ppm]: 154.31, 141.04, 134.74, 124.61, 120.13, 118.24, 35.91, 26.14 (d, J = 132.0 Hz, P*C*); ^{31}P NMR (243 MHz, D_2O) δ [ppm]: 21.99; Anal. Calcd. for $C_8H_{10}N_3O_4P \times 0.7H_2O$: C. 37.57; H. 4.49; N. 16.43; Found: C. 37.35; H. 4.31; N. 16.50.

4.84. 3-(2-Oxo-1H-imidazo[4,5-b]pyridin-3-yl)propylphosphonic acid 12c

From **9c** (0.028 g, 0.09 mmol) the phosphonic acid **12c** (0.019 g, 82%) was obtained as a white solid. M.p. 238 °C–245 °C; IR (KBr, cm^{-1}) ν_{max}: 3435, 3132, 3099, 3037, 2937, 1729, 1641, 1285; ^{1}H NMR (600 MHz, D_2O) δ [ppm]: 7.81 (d, J = 5.8 Hz, 1 H, Ar–*H*), 7.47 (d, J = 7.9 Hz, 1 H, Ar–*H*), 7.08 (dd, J = 7.7 Hz, J = 6.1 Hz, 1 H, Ar–*H*), 3.86 (t, J = 6.4 Hz, 2 H, PCCCH_2), 1.86–1.77 (m, 2 H, PCH_2), 1.56–1.49 (m, 2 H, PCCH_2); ^{13}C NMR (151 MHz, D_2O) δ [ppm]: 154.86, 141.80, 135.80, 124.21, 119.64, 118.21, 40.82 (d, J = 17.5 Hz, PCC*C*), 24.16 (d, J = 134.5 Hz, P*C*), 21.98; ^{31}P NMR (243 MHz, D_2O) δ [ppm]: 26.77; Anal. Calcd. for $C_9H_{12}N_3O_4P$: C. 42.03; H. 4.70; N. 16.34; Found: C. 41.91; H. 4.78; N. 16.31.

4.85. 4-(2-Oxo-1H-imidazo[4,5-b]pyridin-3-yl)butylphosphonic acid 12d

From **9d** (0.026 g, 0.08 mmol) the phosphonic acid **12d** (0.014 g, 63%) was obtained as a white solid. M.p. 188 °C–195 °C; IR (KBr, cm^{-1}) ν_{max}: 3377, 3251, 3132, 3100, 3034, 2966, 1731, 1641, 1509, 1219; ^{1}H NMR (600 MHz, D_2O) δ [ppm]: 8.03 (d, J = 5.9 Hz, 1 H, Ar–*H*), 7.76 (d, J = 7.8 Hz, 1 H, Ar–*H*), 7.35 (dd, J = 7.9 Hz, J = 5.9 Hz, 1 H, Ar–*H*), 4.02 (t, J = 7.1 Hz, 2 H, PCCCCH_2), 1.92–1.84 (m, 2 H, PCH_2), 1.84–1.76 (m, 2 H, PCCCH_2), 1.67–1.58 (m, 2 H, PCCH_2); ^{13}C NMR (151 MHz, D_2O) δ [ppm]: 154.53, 140.82, 133.66, 124.97, 120.65, 118.18, 40.32, 28.22 (d, J = 16.1 Hz, PCC*C*),

25.95 (d, $J = 134.7$ Hz, PC), 19.50 (d, $J = 4.7$ Hz, PCC); ^{31}P NMR (243 MHz, D_2O) δ [ppm]: 30.30; Anal. Calcd. for $C_{10}H_{14}N_3O_4P$: C. 44.29; H. 5.20; N. 15.49; Found: C. 44.11; H. 5.02; N. 15.64.

4.86. {2-(2-Oxo-1H-imidazo[4,5-b]pyridin-3-yl)ethoxy}methylphosphonic acid 12e

From **9e** (0.030 g, 0.09 mmol) the phosphonic acid **12e** (0.016 g, 65%) was obtained as a white solid. M.p. 141 °C–144 °C; IR (KBr, cm^{-1}) ν_{max}: 3500, 3450, 3141, 3074, 2921, 1757, 1549, 1317; ^{1}H NMR (600 MHz, D_2O) δ [ppm]: 8.03 (d, $J = 6.2$ Hz, 1 H, Ar–H), 7.88 (d, $J = 7.9$ Hz, 1 H, Ar–H), 7.43 (dd, $J = 7.9$ Hz, $J = 6.2$ Hz, 1 H, Ar–H), 4.27 (t, $J = 4.8$ Hz, 2 H, PCOCH_2), 3.92 (t, $J = 4.8$ Hz, 2 H, PCOCCH_2), 3.70 (d, $J = 8.6$ Hz, 2 H, PCH_2); ^{13}C NMR (151 MHz, D_2O) δ [ppm]: 153.99, 140.28, 131.05, 125.95, 122.06, 118.27, 70.82 (d, $J = 11.3$ Hz, PCOC), 66.89 (d, $J = 157.3$ Hz, PC), 41.81; ^{31}P NMR (243 MHz, D_2O) δ [ppm]: 17.16; Anal. Calcd. for $C_9H_{12}N_3O_5P$: C. 39.57; H. 4.43; N. 15.38; Found: C. 39.28; H. 4.41; N. 15.47.

4.87. 2-{2-(2-Oxo-1H-imidazo[4,5-b]pyridin-3-yl)ethoxy}ethylphosphonic acid 12f

From **9f** (0.031 g, 0.09 mmol) the phosphonic acid **12f** (0.010 g, 40%) was obtained as a white solid. M.p. 170 °C–178 °C with decomposition; IR (KBr, cm^{-1}) ν_{max}: 3415, 3232, 3111, 3032, 2950, 1723, 1639, 1511, 1320; ^{1}H NMR (600 MHz, D_2O) δ [ppm]: 8.03 (d, $J = 4.9$ Hz, 1 H, Ar–H), 7.52 (d, $J = 7.5$ Hz, 1 H, Ar–H), 7.18 (dd, $J = 7.5$ Hz, $J = 4.9$ Hz, 1 H, Ar–H), 4.16 (t, $J = 5.0$ Hz, 2 H, PCCOCH_2), 3.86 (t, $J = 5.0$ Hz, 2 H, PCCOCCH_2), 3.69–3.50 (m, 2 H, PCCH_2), 1.83–1.70 (m, 2 H, PCH_2); ^{13}C NMR (151 MHz, D_2O) δ [ppm]: 151.68, 143.37, 140.23, 122.66, 118.21, 117.59, 67.06, 39.36, 30.86 (d, $J = 123.8$ Hz, PC), 15.55; ^{31}P NMR (243 MHz, D_2O) δ [ppm]: 15.93; Anal. Calcd. for $C_{10}H_{14}N_3O_5P$: C. 41.82; H. 4.91; N. 14.63; Found: C. 41.77; H. 4.90; N. 14.75.

4.88. 1-Methoxy-2-(2-oxo-1H-imidazo[4,5-b]pyridin-3-yl)ethylphosphonic acid 12j

From **9j** (0.013 g, 0.04 mmol) the phosphonic acid **12j** (0.009 g, 83%) was obtained as a white solid. M.p. 183 °C–186 °C; IR (KBr, cm^{-1}) ν_{max}: 3454, 3418, 3235, 3033, 1950, 1725, 1644, 1549, 1226; ^{1}H NMR (600 MHz, D_2O) δ [ppm]: $\delta = 8.04$ (d, $J = 5.7$ Hz, 1 H, Ar–H), 7.75 (d, $J = 8.2$ Hz, 1 H, Ar–H), 7.34 (dd, $J = 7.7$ Hz, $J = 6.1$ Hz, 1 H, Ar–H), 4.37–4.17 (m, 2 H, PCCH_2), 3.88–3.76 (m, 1 H, PCH), 3.27 (s, 3 H, OCH_3); ^{13}C NMR (151 MHz, D_2O) δ [ppm]: $\delta = 154.55$, 141.50, 134.73, 127.19, 120.41,

118.36, 76.85 (d, $J = 153.7$ Hz, PC), 59.99, 42.12; ^{31}P NMR (243 MHz, D_2O) δ [ppm]: $\delta = 14.84$; Anal. Calcd. for $C_9H_{12}N_3O_5P$: C. 39.57; H. 4.43; N. 15.38; Found: C. 39.31; H. 4.42; N. 15.23.

4.89. 1-Methoxy-3-(2-oxo-1H-imidazo[4,5-b]pyridin-3-yl)propylphosphonic acid 12k

From **9k** (0.017 g, 0.05 mmol) the phosphonic acid **12k** (0.011 g, 77%) was obtained as a white solid. M.p.>260 °C; IR (KBr, cm^{-1}) ν_{max}: 3419, 3313, 3219, 2832, 1757, 1549, 1265; ^{1}H NMR (600 MHz, D_2O) δ [ppm]: $\delta = 8.03$ (d, $J = 4.7$ Hz, 1 H, Ar–*H*), 7.52 (d, $J = 7.7$ Hz, 1 H, Ar–*H*), 7.17 (dd, $J = 7.7$ Hz, $J = 4.7$ Hz, 1 H, Ar–*H*), 4.23–4.00 (m, 2 H, PCCCH_2), 3.40 (s, 3 H, OCH_3), 3.36–3.20 (m, 1 H, PC*H*), 2.30–1.95 (m, 2 H, PCCH_2); ^{13}C NMR (151 MHz, D_2O) δ [ppm]: 152.48, 145.61, 140.15, 122.75, 118.04, 117.46, 59.55 (d, $J = 152.0$ Hz, P*C*), 55.43, 29.52, 16.44; ^{31}P NMR (243 MHz, D_2O) δ [ppm]: 12.41; Anal. Calcd. for $C_{10}H_{14}N_3O_5P$: C.41.82; H. 4.91; N. 14.63; Found: C. 41.68; H. 4.77; N. 14.68.

4.90. 2-Methoxy-3-(2-oxo-1H-imidazo[4,5-b]pyridin-3-yl)propylphosphonic acid 12l

From **9l** (0.045 g, 0.13 mmol) the phosphonic acid **12l** (0.022 g, 59%) was obtained as a white solid. M.p.>260 °C; IR (KBr, cm^{-1}) ν_{max}: 3414, 3231, 3144, 3111, 3040, 2950, 1724, 1640, 1546, 1507, 1226; ^{1}H NMR (600 MHz, D_2O) δ [ppm]: $\delta = 8.01$ (brs, 1 H, Ar–*H*), 7.59 (brs, 1 H, Ar–*H*), 7.23 (brs, 1 H, Ar–*H*), 4.35–3.83 (m, 3 H, PCC*H*, PCCCH_2), 3.27 (s, 3 H, OCH_3), 2.17–1.81 (m, 2 H, PCH_2); ^{13}C NMR (151 MHz, D_2O) δ [ppm]: $\delta = 150.42$, 142.71, 137.85, 123.43, 118.73, 118.34, 61.14, 56.90, 53.50, 34.05 (d, $J = 145.2$ Hz, P*C*); ^{31}P NMR (243 MHz, D_2O) δ [ppm]: 21.72; Anal. Calcd. for $C_{10}H_{14}N_3O_5P$: C. 41.82; H. 4.91; N. 14.63; Found: C. 41.69; H. 4.90; N. 14.68.

5. Antiviral activity assays

The compounds were evaluated against different viruses: Herpes simplex virus-1 (KOS strain), Herpes simplex virus-2 (G strain), Herpes simplex virus-1 (TK^- ACV^r KOS), Vaccinia virus, Adenovirus-2, human coronavirus, cytomegalovirus (AD-169 strain and Davis strain), VZV (TK^+ VZV strain OKA and TK^- VZV strain 07-1), vesicular stomatitis virus, Coxsackie virus B4 and RSV, Para-influenza-3 virus, Reovirus-1, Sindbis virus, Coxsackie virus B4, Punta Toro virus, yellow fever virus, influenza A virus H1N1 subtype (A/PR/8), influenza A virus H3N2 subtype (A/HK/7/87) and influenza B virus (B/HK/5/72).

Confluent cell cultures in microtiter 96-well plates were inoculated with 100 $CCID_{50}$ of virus (1 $CCID_{50}$ being the virus dose to infect 50% of the cell cultures) or with 20 plaque forming units (PFU) and the cell cultures were incubated in the presence of varying concentrations of the test compounds. Viral cytopathicity or plaque formation (VZV) was recorded as soon as it reached completion in the control virus-infected cell cultures that were not treated with the test compounds. Antiviral activity was expressed as the EC_{50} or compound concentration required to reduce virus-induced cytopathicity or viral plaque formation by 50%.

6. Cytotoxicity assays

Cytotoxicity of the test compounds was expressed as the MCC or the compound concentration that caused a microscopically detectable alteration of cell morphology.

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Disclosure statement

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