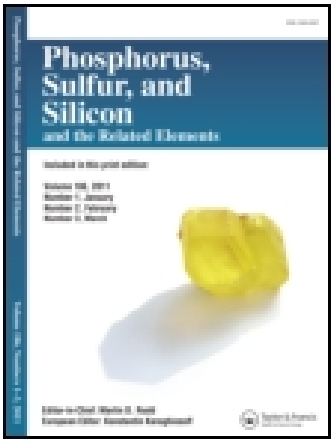

Phosphorus, Sulfur, and Silicon and the Related Elements

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Synthesis of Novel 1-Hydroxy-2-(1,2,3-triazol-1-yl)ethylphosphonates and 2-Hydroxy-3-(1,2,3-triazol-1-yl)propylphosphonates

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SYNTHESIS OF NOVEL 1-HYDROXY-2-(1,2,3-TRIAZOL-1-YL)ETHYLPHOSPHONATES AND 2-HYDROXY-3-(1,2,3-TRIAZOL-1-YL)PROPYLPHOSPHONATES

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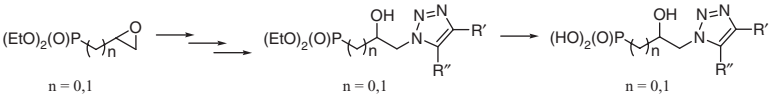
GRAPHICAL ABSTRACT



Abstract *Several new 1-hydroxy-2-(1,2,3-triazol-1-yl)ethylphosphonates and 2-hydroxy-3-(1,2,3-triazol-1-yl)propylphosphonates as well as the respective phosphonic acids were synthesized from diethyl 1,2-epoxyethylphosphonate and 2,3-epoxypropylphosphonate in the reaction sequence including the regioselective ring opening of the epoxide with azides followed by 1,3-dipolar cycloaddition of ω-azidophosphonates and selected alkynes and finally hydrolyses of the phosphonate esters.*

Supplemental materials are available for this article. Go to the publisher's online edition of Phosphorus, Sulfur, and Silicon and the Related Elements *to view the free supplemental file.*

Keywords Azidophosphonates; 1,3-dipolar cycloaddition; 1,4-disubstituted-1,2,3-triazoles; phosphonic acid

INTRODUCTION

Compoundscontaining 1,2,3-triazole moiety are known to be activate as antibacterial,[1–4] antifungal,[5–7] anticancer,[8–10] and antiviral agents.[11–13] They were also found

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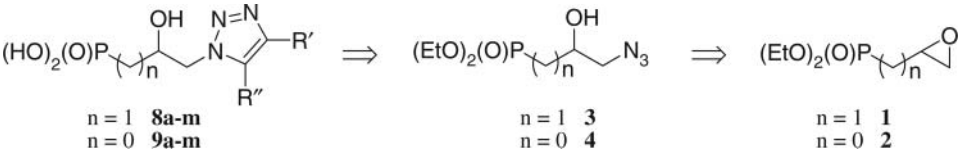
to act as $\beta 3$ adrenegic receptor agonists[14] as well as GABA $\alpha 5$ subtype inverse agonists.[15] Various molecules having 1,2,3-triazole skeleton with potential biological activity have been designed so far. The most prominent examples could be found among water-soluble calixarenes,[16] triazole-linked glycoconjugates,[17] neoglycopeptides[18] and glycopeptides,[19,20] peptides[21] and cyclic peptides,[22] enzyme inhibitors,[23,24] 1,2,3-triazole-modyfied nucleic acids,[25] vitamin D analogues,[26,27] 1,2,3-triazole dendrimers,[28,29] and nucleoside analogues.[30,31]

On the other hand, it is known that organophosphorus compounds exhibit interesting biological properties.[32] For example, introduction of a hydrophilic phosphoryl group may improve solubility and thereby drug delivery to particular targets, as has been found for steroidal alcohols, which showed better solubility in water after attaching the phosphoryl residue.[33] We reasoned that it is justified to test biological activity of phosphonylated 1,2,3-triazoles.

The conventional method for the synthesis of 1,2,3-triazoles is the Huisgen reaction. This procedure relies on the 1,3-dipolar cycloaddition of organic azides with alkynes.[34,35] While cycloaddition with terminal alkynes under thermal conditions usually gives a mixture of 1,4- and 1,5-disubstututed regioisomers,[36,37] application of copper(I) salts as catalyst leads to the formation of the 1,4-disubstituted isomers regiospecifically.[21,35]

This article describes the synthesis of substituted diethyl 2-hydroxy-3-(1,2,3-triazol-1-yl)propylphosphonates **6**, 1-hydroxy-2-(1,2,3-triazol-1-yl)ethylphosphonates **7**, and the respective acids **8** and **9** as potential cytotoxic and antiviral compounds. They are supposed to act as acyclic phosphonate analogues of natural nucleotides in which nucleobases are replaced with substituted 1,2,3-triazole framework. The retrosynthetic analysis for these compounds is outlined in Scheme 1.



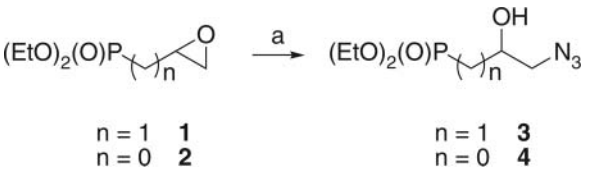
Scheme 1 Retrosynthetic analysis of phosphonylated 1,2,3-triazoles.

RESULTS AND DISCUSSION

To synthesise the 1,2,3-triazoles **6a–6j** and **7a–7j**, diethyl 2,3-epoxypropylphospho nate **1**[38,39] and 1,2-epoxyethylphosphonate **2**[40] were first subjected to azidolysis followed by 1,3-dipolar cycloaddition of the corresponding azidophosphonates with the selected alkynes.

A clean transformation of the epoxide **1** to the diethyl 3-azido-2-hydroxypropylphosphonate **3** has recently been described.[41] In a similar way, the epoxide **2** was transformed into diethyl 2-azido-1-hydroxyethylphosphonate **4** in 85% yield, and was used in the next step without further purification (Scheme 2).

Phosphonylated 1,2,3-triazoles substituted at C4 with different groups were obtained employing the 1,3-dipolar cycloaddition (Scheme 3) of azidophosphonates **3** and **4** with terminal alkynes **5a–5h** (**5a**—methyl propiolate, **5b**—propargyl benzoate, **5c**—phenylacetylene, **5d**—1-ethynyl-2-fluorobenzene, **5e**—1-ethynyl-3-fluorobenzene,

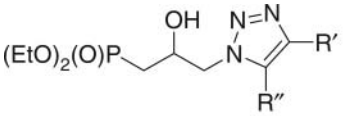


Scheme 2 Reagents and conditions: a. NaN_3, $(NH_4)_2SO_4$, MeOH, reflux, 4 h.

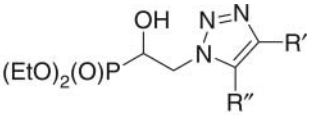
5f—1-ethynyl-2,4-difluorobenzene, **5g**—1-ethynyl-2-pyridine, **5h**—5-ethynyl-1-methyl-1*H*-imidazole). The reactions were carried out at room temperature according to a standard protocol employing Cu(I) as a catalyst, which was generated in situ from $CuSO_4$ and sodium ascorbate[23,28,42] to provide the corresponding 1,2,3-triazoles **6a–6h** and **7a–7h** in moderate to excellent yields. The products were finally purified by column chromatography on silica gel or by crystallization (Scheme 3 and Table 1).

To broaden the structural diversity of phosphonylated 1,2,3-triazole **6i** cycloaddition of diethyl 3-azidophosphonate **3** and 2-cyanoacetamide was performed in the presence of potassium carbonate and DMSO[43] to give 1,2,3-triazole **6i** in 75% yield after column chromatography and crystallization (Scheme 4).

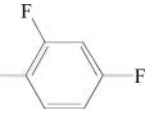
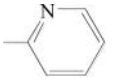
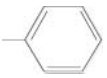
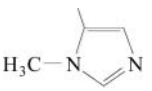
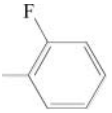
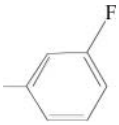
Table 1 Synthesis of substituted 1,2,3-triazoles

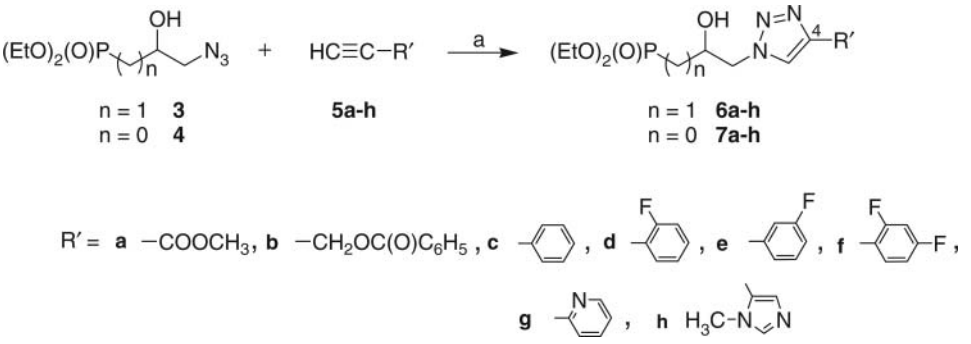


6a-j

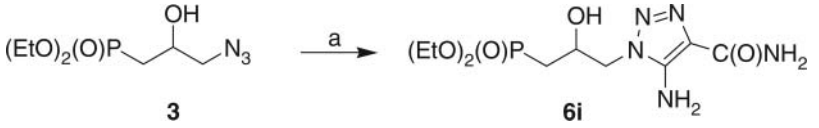


7a-j

Compounds	R′	R″	Yield (%)	Compounds	R′	R″	Yield (%)
6a	$-COOCH_3$	H	84	**6f**		H	96
7a			92	**7f**			97
6b	$-CH_2OC(O)Ph$	H	87	**6g**		H	86
7b			72	**7g**			94
6c		H	77	**6h**		H	67
7c			80	**7h**			70
6d		H	84	**6i**	$C(O)NH_2$	NH_2	84
7d			86	**7i**			—
6e		H	83	**6j**	$COOCH_3$	$COOCH_3$	75
7e			94	**7j**			91

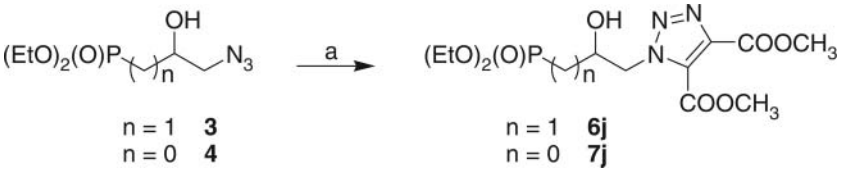


Scheme 3 Reagents and conditions: a. $CuSO_4 \times 5H_2O$ (0.05 equiv.), sodium ascorbate (0.1 equiv.), H_2O–*t*-BuOH (2:1), r.t., 12–24 h.



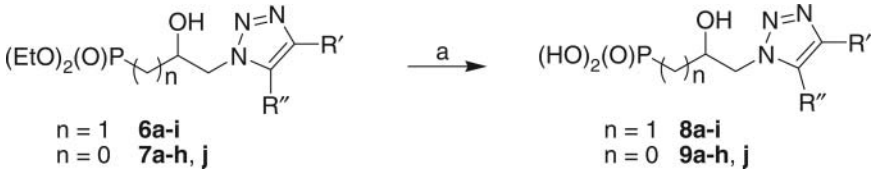
Scheme 4 Reagents and conditions: a. 2-cyanoacetamide, DMSO, K_2CO_3, 5 h, 50°C, 75%.

Futhermore, cycloaddition of azidophosphonates **3** and **4** with dimethyl acetylenedicarboxylate was carried out at 110°C according to the standard procedure[44] to give 1,2,3-triazoles **6j** and **7j** in 84% and 91% yield, respectively (Scheme 5). Studies on further functionalization of these diesters are underway in this laboratory.



Scheme 5 Reagents and conditions: a. $H_3COOCC{\equiv}CCOOCH_3$, toluene, reflux, 4 h.

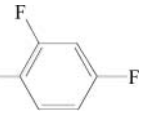
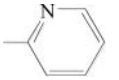
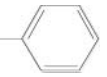
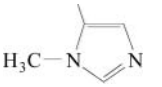
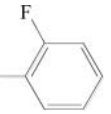
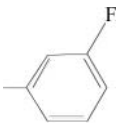
Finally, using bromotrimethylsilane diethyl phosphonates **6a–i** and **7a–h**, **j** were transformed into the respective phosphonic acids **8a–i** and **9a–h**, **j** in good yields[43] (Scheme 6 and Table 2).



Scheme 6 Reagents and conditions: a. TMSBr, CH_2Cl_2, r.t., 72 h.

Compounds **6a–j**, **8a** and **8f–g** were evaluated for their cytotoxicity toward HeLa cells. After 24 and 48 h incubation with cells, the IC_{50} values for these compounds were larger

Table 2 Synthesis of phosphonic acids **8a–i**, **9a–h**, and **9j**

Compounds	R′	R″	Yield (%)	Compounds	R′	R″	Yield (%)
8a	$-COOCH_3$	H	95	**8f**		H	95
9a			92	**9f**			97
8b	$-CH_2OC(O)Ph$	H	93	**8g**		H	85
9b			77	**9g**			94
8c		H	90	**8h**		H	67
9c			80	**9h**			70
8d		H	85	**8i**	$C(O)NH_2$	NH_2	95
9d			86	**9i**			—
8e		H	83	**8j**	$COOCH_3$	$COOCH_3$	—
9e			94	**9j**			91

than 1 mM (see the Supplemental Materials, available online). Thus, none of the compounds displayed noticeable activity toward a selected cell line.

CONCLUSIONS

An efficient method for the synthesis of diethyl 1-hydroxy-2-(1,2,3-triazol-1-yl)ethylphosphonates and 2-hydroxy-3-(1,2,3-triazol-1-yl)propylphosphonates from diethyl 1,2-epoxyethylphosphonate and 2,3-epoxypropylphosphonate has been reported. Clean transformation of the epoxides **1** and **2** to 3-azido-2-hydroxypropylphosphonate **3** and 2-azido-1-hydroxyethylphosphonate **4**, respectively, was accomplished using sodium azide in the presence of ammonium sulfate in refluxing methanol.

The 1,2,3-triazoles **6a–6h** and **7a–7h** were synthesised from azidophosphonates **3** or **4** by the copper(I)-catalyzed Huisgen 1,3-dipolar cycloaddition with selected alkynes **5a–h**. 1,2,3-Triazoles **6j** (**7j**) and **6i** were obtained by reaction azidophosphonates **3** or **4** with dimethyl acetylenedicarboxylate or 2-cyanoacetamide under thermal conditions.

The biological activity of the synthesised phosphonylated 1,2,3-triazoles will be published in due course.

EXPERIMENTAL

^1H NMR spectra were recorded with a Varian Mercury-300 spectrometer; chemical shifts δ in ppm with respect to TMS; coupling constants J in Hz. ^{13}C and ^{31}P NMR spectra were recorded on a Varian Mercury-300 machine at 75.5 and 121.5 MHz, respectively. 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.

The following absorbents 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.

Diethyl 2,3-epoxypropylphosphonate **1**[38,39] (δ^{31}P 26.71 ppm) and 1,2-epoxyethylphosphonate **2**[40] (δ^{31}P 19.84 ppm) were prepared according to the literature procedure in 61% and 60% yields, respectively.

Reaction of Epoxide 1 with Sodium Azide in the Presence of $(NH_4)_2SO_4$

A mixture of the epoxide **1** (0.826 g, 4.25 mmol), sodium azide (0.664 g, 10.21 mmol), and ammonium sulfate (1.01 g, 7.65 mmol) in methanol (5 mL) was stirred at 65°C for 4 h. After evaporation of solvents, the residue was suspended in ethyl acetate (5 mL) and filtered through a layer of Celite. The solution was concentrated in vacuo to give diethyl 3-azido-2-hydroxypropylphosphonate **3** (0.805 g, 80%) as a yellowish oil.

Diethyl 3-Azido-2-hydroxypropylphosphonate 3

IR (film) ν [cm^{-1}] 3339, 2985, 2931, 2911, 2105, 1225, 1029; ^{1}H NMR (C_6D_6, 300 MHz) δ [ppm]: 0.87 and 0.89 (2t, $J = 6.8$ Hz, 6H, 2×$POCH_2CH_3$), 1.60 (ddd, $J =$ 19.2 Hz, $J = 15.0$ Hz, $J = 3.3$ Hz, 1H, H-1b), 1.81 (ddd, $J = 16.5$ Hz, $J = 15.0$ Hz, $J =$ 9.6 Hz, 1H, H-1a), 2.02 (brs, 1H, OH), 2.82−2.87 (m, 2H, H-3a, H-3b), 3.72−3.91 (m, 4H, 2×$POCH_2CH_3$), 4.03−4.16 (m, 1H, H-2); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ [ppm]: 16.2 (d, $J = 6.3$ Hz, POC*C*), 30.7 (d, $J = 139.4$ Hz, C-1), 56.5 (d, $J = 14.3$ Hz, C-3), 61.7 and 61.9 (2d, $J = 6.6$ Hz, POC), 65.7 (d, $J = 2.9$ Hz, C-2); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ [ppm] 30.18.

Reaction of Epoxide 2 with Sodium Azide in the Presence of $(NH_4)_2SO_4$

A mixture of the epoxide **2** (2.16 g, 1.20 mmol), sodium azide (1.87 g, 2.88 mmol), and ammonium sulfate (0.244 g, 1.85 mmol) in methanol (12 mL) was stirred at 65°C for 4 h. After evaporation of solvents, the residue was suspended in ethyl acetate (5 mL) and filtered through a layer of Celite. The solution was concentrated in vacuo to give diethyl 2-azido-1-hydroxyethylphosphonate **4** (2.28 g, 85%) as a yellowish oil.

Diethyl 2-Azido-1-hydroxyethylphosphonate 4

IR (film) ν [cm^{-1}] 3310, 2988, 2921, 2135, 1220, 1029; ^{1}H NMR ($CDCl_3$, 300 MHz) δ [ppm]: 1.35 and 1.36 (2t, $J = 7.2$ Hz, 6H, 2×$POCH_2CH_3$), 3.40–3.62 (m, 2H, H-2a, H-2b), 4.05–4.26 (m, 6H, 2×CH_3CH_2OP, OH, H-1); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ [ppm] 22.18.

General Procedure for the Preparation of 1,2,3-Triazoles 6a–h and 7a–h

To a solution of the azidophosphonate (1 mmol) in *t*-BuOH (0.5 mL) and H_2O (1 mL), $CuSO_4 \times 5H_2O$ (0.05 mmol), sodium ascorbate (0.1 mmol), and alkynes **5a–h** (1 mmol)

were added. This suspension was stirred vigorously at room temperature for 12–24 h. After removal of solvents, the residue was suspended in chloroform (15 mL) and filtered through a layer of Celite. The solution was concentrated in vacuo, and the crude product was purified by column chromatography on a silica gel column with chloroform/methanol mixtures or crystallized from ethyl acetate/petroleum ether to give desired 1,2,3-triazoles **6a–h** or **7a–h**.

Diethyl 2-hydroxy-3-[4-(methoxycarbonyl)-1,2,3-triazol-1-yl]propylphosphonate 6a. The target compound was prepared from azidophosphonate **3** (0.248 g, 0.772 mmol) and methyl propiolate (0.069 mL, 0.772 mmol) using the general procedure described above. The product was purified by crystallization from ethyl acetate/petroleum ether to give compound **6a** (0.282 g, 84%) as a white short needles. Mp: 105–106°C; IR (KBr) ν [cm^{-1}] 3424, 3287, 2986, 2958, 1725, 1548, 1437, 1237, 1029, 965; ^{1}H NMR ($CDCl_3$, 300 MHz) δ [ppm] 1.32 and 1.34 (2t, $J = 7.2$ Hz, 6H, 2×POCH$_2$CH_3), 1.78 (ddd, $J = 16.8$ Hz, $J = 15.3$ Hz, $J = 3.0$ Hz, 1H, H-1b), 2.00 (ddd, $J = 19.2$ Hz, $J = 15.3$ Hz, $J = 9.3$ Hz, 1H, H-1a), 2.45 (brs, 1H, OH), 3.93 (s, 3H, COOCH_3), 4.04–4.19 (m, 4H, 2×POCH_2CH$_3$), 4.36–4.51 (m, 2H, H-3b, H-2), 4.59–4.67 (m, 1H, H-3a), 8.31 (s, 1H, $HC_{5'}$); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ [ppm] 16.5 and 16.6 (2d, $J = 6.0$ Hz, POCC), 30.8 (d, $J = 140.4$ Hz, C-1), 52.3 (s, COOCH$_3$), 56.3 (d, $J = 17.8$ Hz, C-3), 62.2 and 62.4 (2d, $J = 6.6$ Hz, 2×POC), 65.3 (d, $J = 3.8$ Hz, C-2), 129.4 (s, HC=C), 139.7 (s, HC=C), 161.1 (s, C=O); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ [ppm] 29.24; Anal. Calcd. for $C_{11}H_{20}N_3O_6P$: C, 41.12; H, 6.28; N, 13.08. Found: C, 41.18; H, 6.36; N, 12.88.

Diethyl 3-[4-(benzoyloxymethyl)-1,2,3-triazol-1-yl]-2-hydroxypropylphosphonate 6b. The target compound was prepared from azidophosphonate **3** (0.163 g, 0.417 mmol) and propargyl benzoate (0.060 mL, 0.417 mmol) using the general procedure described above. The product was chromatographed on a silica gel column with chloroform/methanol (100:1, v/v) to give compound **6b** (0.240 g, 87%) as a colorless oil; IR (film) ν [cm^{-1}] 3338, 2984, 2910, 1720, 1272, 1027, 836, 714; ^{1}H NMR ($CDCl_3$, 300 MHz) δ [ppm] 1.32 and 1.33 (2t, $J = 7.2$ Hz, 6H, 2×POCH$_2$CH_3), 1.82 (ddd, $J = 16.8$ Hz, $J = 15.3$ Hz, $J = 9.0$ Hz, 1H, H-1b), 2.01 (ddd, $J = 19.5$ Hz, $J = 15.3$ Hz, $J = 2.7$ Hz, 1H, H-1a), 2.70 (brs, 1H, OH), 4.05–4.20 (m, 4H, 2×POCH_2CH$_3$), 4.36–4.47 (m, 2H, H-3b, H-2), 4.54–4.61 (m, 1H, H-3a), 5.49 (s, 2H, CH_2OC(O)Ph), 7.40–7.45 (m, 2H, Ar−H), 7.60–7.75 (m, 1H, Ar−H), 7.92 (s, 1H, $HC_{5'}$), 8.03–8.07 (m, 2H, Ar−H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ [ppm] 16.5 and 16.6 (2d, $J = 6.0$ Hz, POCC), 30.8 (d, $J = 140.4$ Hz, C-1), 56.0 (d, $J = 17.4$ Hz, C-3), 58.1 (s, CH$_2$OC(O)Ph), 62.3 and 62.4 (2d, $J = 7.3$ Hz, 2×POC), 65.5 (d, $J = 3.8$ Hz, C-2), 123.0 (s, HC=C) 128.3, 129.6 ($C_{arom.}$), 133.1 (s, HC=C), 142.0 (C_{ipso}), 166.2 (s, C=O); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ [ppm] 28.85; Anal. Calcd. for $C_{17}H_{24}N_3O_6P$: C, 51.39; H, 6.09; N, 10.57. Found: C, 51.16; H, 6.18; N, 10.48.

Diethyl 2-hydroxy-3-(4-phenyl-1,2,3-triazol-1-yl)propylphosphonate 6c. The target compound was prepared from azidophosphonate **3** (0.182 g, 0.538 mmol) and phenylacetylene (0.059 mL, 0.538 mmol) using the general procedure described above. The product was purified by crystallization from ethyl acetate/petroleum ether to give compound **6c** (0.201 g, 77%) as a white amorphous solid. Mp: 86–87°C; IR (KBr) ν [cm^{-1}] 3327, 2984, 2908, 1227, 1029, 965; ^{1}H NMR ($CDCl_3$, 300 MHz) δ [ppm] 1.30 and 1.31 (2t, $J = 7.2$ Hz, 6H, 2×POCH$_2$CH_3), 1.85 (ddd, $J = 17.1$ Hz, $J = 15.3$ Hz, $J = 9.3$ Hz, 1H, H-1b), 2.02 (ddd, $J = 18.6$ Hz, $J = 15.3$ Hz, $J = 3.3$ Hz, 1H, H-1a), 4.02–4.17 (m, 5H, 2×POCH_2CH$_3$, OH), 4.38–4.50 (m, 2H, H-3b, H-2), 4.56–4.63 (m, 1H, H-3a), 7.29–7.34 (m, 1H, Ar−H), 7.37–7.43 (m, 2H, Ar−H), 7.79–7.83 (m, 2H, Ar−H), 7.99 (s, 1H, $HC_{5'}$); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ [ppm] 16.4 and 16.5 (2d, $J = 6.0$ Hz, POCC), 30.8 (d,

$J = 139.7$ Hz, C-1), 56.1 (d, $J = 15.9$ Hz, C-3), 62.2 and 62.3 (2d, $J = 7.3$ Hz, 2×POC), 65.5 (d, $J = 3.8$ Hz, C-2), 121.5 (s, HC=*C*), 125.5, 128.0, 128.6 ($C_{arom.}$), 130.4 (s, C_{ipso}), 147.3 (H*C*=C); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ [ppm] 28.89; Anal. Calcd. for $C_{15}H_{22}N_3O_4P$: C, 53.09; H, 6.53; N, 12.38. Found: C, 52.96; H, 6.68; N, 12.18.

Diethyl 3-[4-(2-fluorophenyl)-1,2,3-triazol-1-yl]-2-hydroxypropylphosphonate 6d. The target compound was prepared from azidophosphonate **3** (0.183 g, 0.513 mmol) and 1-ethynyl-2-fluorobenzene (0.058 mL, 0.513 mmol) using the general procedure described above. The product was purified by crystallization from ethyl acetate/petroleum ether to give compound **6d** (0.232 g, 84%) as a white solid. Mp: 79–80°C; IR (KBr) ν [cm^{-1}] 3339, 2984, 2911, 1478, 1221, 1028, 967, 818, 762; ^{1}H NMR ($CDCl_3$, 300 MHz) δ [ppm] 1.33 and 1.34 (2t, $J = 6.9$ Hz, 6H, 2×$POCH_2CH_3$), 1.83 (ddd, $J = 16.5$ Hz, $J = 15.3$ Hz, $J = 9.3$ Hz, 1H, H-1b), 1.80 (brs, 1H, OH), 2.03 (ddd, $J = 18.6$ Hz, $J = 15.3$ Hz, $J = 3.3$ Hz, 1H, H-1a), 4.06–4.21 (m, 4H, 2×CH_3CH_2OP), 4.41–4.66 (m, 3H, H-2, H-3a, H-3b), 7.14 (ddd, $J = 10.8$ Hz, $J = 7.8$ Hz, $J = 1.2$ Hz, 1H, Ar−H), 7.22–7.35 (m, 2H, Ar−H), 8.14 (d, $J = 3.6$ Hz, $HC_{5'}$), 8.28 (dt, $J = 7.8$ Hz, $J = 1.8$ Hz, 1H, Ar−H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ [ppm] 16.4 and 16.5 (2d, $J = 6.8$ Hz, POC*C*), 31.0 (d, $J = 140.3$ Hz, C-1), 56.2 (d, $J = 16.9$ Hz, C-3), 62.3 and 62.4 (2d, $J = 6.6$ Hz, POC), 65.6 (d, $J = 3.1$ Hz C-2), 115.7 (d, $J = 21.8$ Hz, C-$3_{arom.}$), 118.5 (d, $J = 12.9$ Hz, C-$1_{arom.}$), 124.6 (d, $J = 12.6$ Hz, $C_{arom.}$), 124.6 (d, $J = 3.4$ Hz, $C_{arom.}$), 127.6 (d, $J = 3.4$ Hz, H*C* = C), 129.2 (d, $J = 8.6$ Hz, C-$4_{arom.}$), 141.0 (s, *C*=CH), 159.1 (d, $J = 247.6$ Hz, C−F); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ [ppm] 28.91. Anal. Calcd. for $C_{15}H_{21}FN_3O_4P$: C, 50.42; H, 5.92; N, 11.76. Found: C, 50.44; H, 5.96; N, 11.62.

Diethyl 3-[4-(3-fluorophenyl)-1,2,3-triazol-1-yl]-2-hydroxypropylphosphonate 6e. The target compound was prepared from azidophosphonate **3** (0.175 g, 0.489 mmol) and 1-ethynyl-3-fluorobenzene (0.056 mL, 0.489 mmol) using the general procedure described above. The product was chromatographed on a silica gel column with chloroform/methanol (100:1, v/v) to give compound **6e** (0.218 g, 83%) as a colorless oil; IR (film) ν [cm^{-1}] 3326, 3141, 2985, 2911, 1466, 1229, 1030, 967, 866, 787; ^{1}H NMR ($CDCl_3$, 300 MHz) δ [ppm] 1.33 and 1.35 (2t, $J = 6.9$ Hz, 6H, 2×$POCH_2CH_3$), 1.80 (ddd, $J = 16.8$ Hz, $J = 15.3$ Hz, $J = 9.6$ Hz, 1H, H-1b), 1.85 (brs, 1H, OH), 1.97–2.09 (m, 1H, H-1a), 4.05–4.21 (m, 4H, 2×$POCH_2CH_3$), 4.39–4.51 (m, 2H, H-2, H-3b), 4.56–4.66 (m, 1H, H-3a), 6.99–7.06 (m, 1H, Ar−H), 7.35–7.42 (m, 1H, Ar−H), 7.55–7.62 (m, 2H, Ar−H), 8.01 (s, 1H, $HC_{5'}$); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ [ppm] 16.5 and 16.6 (2d, $J = 6.0$ Hz, POC*C*), 30.9 (d, $J = 140.0$ Hz, C-1), 56.2 (d, $J = 17.2$ Hz, C-3), 62.4 and 62.5 (2d, $J = 6.9$ Hz, POC), 65.6 (d, $J = 3.7$ Hz C-2), 112.7 (d, $J = 22.9$ Hz, C-$2_{arom.}$), 114.9 (d, $J = 21.2$ Hz, $C_{arom.}$), 121.3 (d, $J = 2.9$ Hz, $C_{arom.}$), 122.1 (s, H*C*=C) 130.5 (d, $J = 8.3$ Hz, $C_{arom.}$), 146.4 (s, *C*=CH), 163.1 (d, $J = 245.1$ Hz, C−F); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ [ppm] 28.93. Anal. Calcd. for $C_{15}H_{21}FN_3O_4P \times 0.25\ H_2O$: C, 49.79; H, 5.99; N, 11.61. Found: C, 49.62; H, 5.79; N, 11.64.

Diethyl 3-[4-(2,4-difluorophenyl)-1,2,3-triazol-1-yl]-2-hydroxypropylphosphonate 6f. The target compound was prepared from azidophosphonate **3** (0.118 g, 0.314 mmol) and 1-ethynyl-2,4-difluorobenzene (0.043 g, 0.314 mmol) using the general procedure described above. The product was purified by crystallization from ethyl acetate/petroleum ether to give compound **6f** (0.179 g, 96%) as a white solid. Mp: 129–130°C; IR (KBr) ν [cm^{-1}] 3286, 3136, 2988, 2907, 1628, 1600, 1561, 1493, 1196, 1072, 1036, 979, 826; ^{1}H NMR ($CDCl_3$, 300 MHz) δ [ppm] 1.33 and 1.34 (2t, $J = 6.9$ Hz, 6H, 2×$POCH_2CH_3$), 1.80 (brs, 1H, OH), 1.83 (ddd, $J = 16.8$ Hz, $J = 15.3$ Hz, $J = 9.3$ Hz,

1H, H-1b), 2.03 (ddd, $J = 19.2$ Hz, $J = 15.3$ Hz, $J = 3.0$ Hz, 1H, H-1a), 4.06–4.21 (m, 4H, 2×POCH_2CH$_3$), 4.40–4.66 (m, 3H, H-2, H-3a, H-3b), 6.87–7.03 (m, 2H, Ar—H), 7.35–7.42 (m, 1H, Ar—H), 8.09 (d, $J = 3.9$ Hz, HC$_{5'}$), 8.26 (dt, $J = 8.4$ Hz, $J = 6.3$ Hz, 1H, Ar—H); ^{13}C NMR (CDCl$_3$, 75.5 MHz) δ [ppm] 16.5 and 16.6 (2d, $J = 6.0$ Hz, POCC), 30.9 (d, $J = 140.4$ Hz, C-1), 56.2 (d, $J = 17.4$ Hz, C-3), 62.3 and 62.5 (2d, $J = 6.8$ Hz, POC), 65.6 (d, $J = 3.8$ Hz, C-2), 104.1 (t, $J = 30.2$ Hz, C-3$_{arom.}$), 112.0 (dd, $J = 21.2$ Hz, $J = 3.4$ Hz, C-1$_{arom.}$), 115.0 (dd, $J = 13.2$ Hz, $J = 3.7$ Hz, C-5$_{arom.}$), 124.1 (d, $J = 12.0$ Hz, C-6$_{arom.}$), 128.6 (dd, $J = 9.7$ Hz, $J = 5.2$ Hz, HC=C), 140.4 (s, C=C—Ph), 159.2 (dd, $J = 249.2$ Hz, $J = 12.3$ Hz, C-2$_{arom.}$), 162.4 (dd, $J = 249.2$ Hz, $J = 12.6$ Hz, C-4$_{arom.}$); ^{31}P NMR (CDCl$_3$, 121.5 MHz) δ [ppm] 29.65. Anal. Calcd. for $C_{15}H_{20}F_2N_3O_4P$: C, 48.00; H, 5.37; N, 11.20. Found: C, 48.01; H, 5.29; N, 11.09.

Diethyl 2-hydroxy-3-[4-(pyridin-2-yl)-1,2,3-triazol-1-yl]propylphosphonate 6g. The target compound was prepared from azidophosphonate **3** (0.224 g, 0.660 mmol) and 1-ethynyl-2-pyridine (0.067 mL, 0.660 mmol) using the general procedure described above. The product was chromatographed on a silica gel column with chloroform/methanol (50:1, v/v) to give compound **6g** (0.277 g, 86%) as a colorless oil; IR (film) ν [cm^{-1}] 3339, 3104, 2925, 2851, 1636, 1612, 1226, 1163, 1080, 786; ^{1}H NMR (CDCl$_3$, 300 MHz) δ [ppm] 1.34 and 1.37 (2t, $J = 7.0$ Hz, 6H, 2×POCH$_2$CH_3), 1.91–2.22 (m, 2H, H-1b, H-1a), 4.05–4.21 (m, 4H, 2× POCH_2CH$_3$), 4.21–4.59 (m, 3H, H-2, H-3b, OH), 4.61 (dd, $J = 14.2$ Hz, $J = 4.0$ Hz, 1H, H-3a), 7.22–7.26 (m, 1H, Ar—H), 7.80 (dt, $J = 7.8$ Hz, $J = 1.8$ Hz, 1H, Ar—H), 8.16 (d, $J = 7.8$ Hz, 1H, Ar—H), 8.38 (s, 1H, HC$_{5'}$), 8.37–8.60 (m 1H, Ar—H); ^{13}C NMR (CDCl$_3$, 75.5 MHz) δ [ppm] 16.6 and 16.7 (2d, $J =$ 6.0 Hz, POCC), 31.0 (d, $J = 140.4$ Hz, C-1), 56.3 (d, $J = 17.4$ Hz, C-3), 62.3 and 62.5 (2d, $J = 6.0$ Hz, POC), 65.7 (d, $J = 3.7$ Hz, C-2), 120.4 (s, C$_{arom.}$), 123.0 (s, HC=C), 124.0, 137.2 (s, C$_{arom.}$), 147.9 (s, C=CH), 149.2, 150.1 (s, C$_{arom.}$); ^{31}P NMR (CDCl$_3$, 121.5 MHz) δ [ppm] 28.85. Anal. Calcd. for $C_{14}H_{21}N_4O_4P \times H_2O$: C, 46.92; H, 6.47; N, 15.64. Found: C, 47.06; H, 6.34; N, 15.41.

Diethyl 2-hydroxy-3-[4-(1-methyl-1H-imidazol-5-yl)-1,2,3-triazol-1-yl]propylphosphonate 6h. The target compound was prepared from azidophosphonate **3** (0.186 g, 0.541 mmol) and 5-ethynyl-1-methyl-1H-imidazole (0.055 mL, 0.541 mmol) using the general procedure described above. The product was chromatographed on a silica gel column with chloroform/methanol (50:1 to 20:1 v/v) to give compound **6h** (0.180 g, 67%) as a colorless oil; IR (film) ν [cm^{-1}] 3392, 2985, 2911, 1656, 1629, 1510, 1230, 1029, 966, 833; ^{1}H NMR (CDCl$_3$, 300 MHz) δ [ppm] 1.34 and 1.35 (2t, $J = 6.9$ Hz, 6H, 2×POCH$_2$CH_3), 1.84–2.12 (m, 2H, H-1a, H-1b), 3.05 (brs, 1H, OH), 3.91 (s, 3H, CH$_3$—N), 4.07–4.21 (m, 4H, 2×POCH_2CH$_3$), 4.39–4.51 (m, 2H, H-2, H-3b), 4.60–4.68 (m, 1H, H-3a), 7.20 (brs, 1H, H$_{imid}$), 7.56 (brs, 1H, H$_{imid}$), 7.94 (s, 1H, HC$_{5'}$); ^{13}C NMR (CDCl$_3$, 75.5 MHz) δ [ppm] 16.5 and 16.6 (2d, $J = 6.0$ Hz, POCC), 31.3 (d, $J = 140.0$ Hz, C-1), 33.8 (s, CH$_3$—N), 56.4 (d, $J = 16.0$ Hz, C-3), 62.2 and 62.4 (2d, $J = 6.6$ Hz, POC), 65.4 (d, $J = 3.1$ Hz, C-2), 122.7, 123.6, 127.8 (s, HC=C), 137.9 (s, HC=C), 139.1 (s, N—CH—N); ^{31}P NMR (CDCl$_3$, 121.5 MHz) δ [ppm] 28.70. Anal. Calcd. for $C_{13}H_{22}N_5O_4P$: C, 45.48; H, 6.46; N, 20.40. Found: C, 45.44; H, 6.21; N, 20.61.

Diethyl 1-hydroxy-2-[4-(methoxycarbonyl)-1,2,3-triazol-1-yl]ethylphosphonate 7a. The target compound was prepared from azidophosphonate **4** (0.118 g, 0.383 mmol) and methyl propiolate (0.034 mL, 0.383 mmol) using the general procedure described above. The product was purified by crystallization from ethyl acetate/petroleum ether to give compound **7a** (0.149 g, 92%) as white needles. Mp: 117–119°C; IR (KBr) ν [cm^{-1}] 3262, 3106, 2986, 2987, 1723, 1549, 1245, 1224, 1024; ^{1}H NMR (CDCl$_3$,

300 MHz) δ [ppm] 1.33 and 1.34 (2t, J = 6.9 Hz, 6H, 2×POCH$_2$CH_3), 3.93 (s, 3H, COOCH_3), 4.17–4.22 (m, 5H, 2×POCH_2CH$_3$, OH), 4.29 (ddd, J = 9.9 Hz, J = 7.8 Hz, J = 2.7 Hz, 1H, H-1), 4.50 (ddd, J = 14.1 Hz, J = 9.9 Hz, J = 5.4 Hz, 1H, H-2a), 4.87 (ddd, J = 14.1 Hz, J = 5.4 Hz, J = 2.7 Hz, 1H, H-2b), 8.32 (s, 1H, HC$_{5'}$); ^{13}C NMR (CDCl$_3$, 75.5 MHz) δ [ppm] 16.6 and 16.7 (2d, J = 6.0 Hz, POCC), 52.3 (s, COOCH$_3$), 63.7 and 63.8 (2d, J = 6.8 Hz, 2×POC), 66.7 (d, J = 165.3 Hz, C-1), 129.5 (s, HC=C), 139.4 (s, HC=C), 161.0 (s, C=O); ^{31}P NMR (CDCl$_3$, 121.5 MHz) δ [ppm] 20.85; Anal. Calcd. for C$_{10}$H$_{18}$N$_3$O$_6$P: C, 39.09; H, 5.90; N, 13.68. Found: C, 39.07; H, 5.79; N, 13.78.

Diethyl 2-[4-(benzoyloxymethyl)-1,2,3-triazol-1-yl]-1-hydroxyethylphosphonate 7b. The target compound was prepared from azidophosphonate **4** (0.234 g, 0.634 mmol) and propargyl benzoate (0.092 mL, 0.634 mmol) using the general procedure described above. The crude product was chromatographed on a silica gel column with chloroform/methanol (100:1, v/v), and the appropriate fractions were crystallized from ethyl acetate/hexane to give compound **7b** (0.300 g, 72%) as a white powder. Mp: 104–105°C; IR (KBr) ν [cm^{-1}] 3328, 2982, 2890, 1722, 1268, 1025, 843, 720; ^{1}H NMR (CDCl$_3$, 300 MHz) δ [ppm] 1.32 and 1.33 (2t, J = 6.9 Hz, 6H, 2×POCH$_2$CH_3), 4.09–4.22 (m, 5H, 2×POCH_2CH$_3$, OH), 4.24–4.36 (m, 1H, H-1), 4.42–4.61 (m, 1H, H-2b), 4.78–4.84 (m, 1H, H-2a), 5.49 (s, 2H, CH_2OC(O)Ph), 7.40–7.45 (m, 2H, Ar—H), 7.48–7.60 (m, 1H, Ar—H), 7.92 (s, 1H, HC$_{5'}$), 8.03–8.10 (m, 2H, Ar—H); ^{13}C NMR (CDCl$_3$, 75.5 MHz) δ [ppm] 16.6 and 16.7 (2d, J = 5.7 Hz, POCC), 51.8 (s, C-2), 58.2 (s, CH$_2$OC(O)Ph), 63.6 and 63.8 (2d, J = 7.2 Hz, 2×POC), 67.1 (d, J = 163.5 Hz, C-1), 123.0 (s, HC=C) 128.4, 129.8 (C$_{arom.}$), 133.3 (s, HC=C), 140.2 (C$_{ipso}$), 166.4 (s, C=O); ^{31}P NMR (CDCl$_3$, 121.5 MHz) δ [ppm] 20.97; Anal. Calcd. for C$_{16}$H$_{22}$N$_3$O$_6$P: C, 50.13; H, 5.78; N, 10.96. Found: C, 49.98; H, 5.75; N, 11.04.

Diethyl 1-hydroxy-2-(4-phenyl-1,2,3-triazol-1-yl)ethylphosphonate 7c. The target compound was prepared from azidophosphonate **4** (0.123 g, 0.379 mmol) and phenylacetylene (0.042 mL, 0.379 mmol) using the general procedure described above. The product was purified by crystallization from ethyl acetate/petroleum ether to give compound **7c** (0.144 g, 80%) as a white amorphous solid. Mp: 92–94°C IR (KBr) ν [cm^{-1}] 3252, 3084, 2986, 1223, 1015, 976, 765, 692; ^{1}H NMR (CDCl$_3$, 300 MHz) δ [ppm] 1.35 and 1.36 (2t, J = 7.2 Hz, 6H, 2×POCH$_2$CH_3), 4.15–4.27 (m, 4H, 2×POCH_2CH$_3$), 4.46–4.57 (m, 3H, H-2a, H-2b, OH), 4.85 (ddd, J = 13.8 Hz, J = 7.8 Hz, J = 2.1 Hz, 1H, H-1), 7.27–7.39 (m, 3H, Ar—H), 7.69–7.72 (m, 2H, Ar—H), 7.92 (s, 1H, HC$_{5'}$); ^{13}C NMR (CDCl$_3$, 75.5 MHz) δ [ppm] 16.6 and 16.7 (2d, J = 5.3 Hz, POCC), 52.1 (d, J = 10.6 Hz, C-2), 63.4 and 63.5 (2d, J = 6.8 Hz, 2×POC), 67.0 (d, J = 165.3 Hz, C-1), 121.8, 125.5, 128.1, 128.8 (C$_{arom.}$), 130.4 (HC=C), 147.0 (HC=C); ^{31}P NMR (CDCl$_3$, 121.5 MHz) δ [ppm] 21.25; Anal. Calcd. for C$_{14}$H$_{20}$N$_3$O$_4$P: C, 51.69; H, 6.20; N, 12.92. Found: C, 51.45; H, 6.22; N, 13.00.

Diethyl 2-[4-(2-fluorophenyl)-1,2,3-triazol-1-yl]-1-hydroxyethylphosphonate 7d. The target compound was prepared from azidophosphonate **4** (0.308 g, 0.898 mmol) and 1-ethynyl-2-fluorobenzene (0.102 mL, 0.898 mmol) using the general procedure described above. The product was purified by crystallization from ethyl acetate/petroleum ether to give compound **7d** (0.408 g, 86%) as a white solid. Mp: 100–101°C; IR (KBr) ν [cm^{-1}] 3236, 2991, 2909, 1487, 1210, 1048, 760; ^{1}H NMR (CDCl$_3$, 300 MHz) δ [ppm] 1.35 and 1.37 (2t, J = 6.9 Hz, 6H, 2×POCH$_2$CH_3), 4.16–4.28 (m, 5H, 2×CH$_3$CH_2OP, OH), 4.43–4.60 (m, 2H, H-2a, H-1), 4.87 (ddd, J = 13.9 Hz, J = 5.6 Hz, J = 2.4 Hz, 1H, H-2b), 7.02–7.08 (m, 1H, Ar—H), 7.19–7.31 (m, 2H, Ar—H), 8.12 (d, J = 3.8 Hz, 1H, HC$_{5'}$), 8.15–8.21 (m, 1H, Ar—H); ^{13}C NMR (CDCl$_3$, 75.5 MHz) δ [ppm] 16.6 and

16.7 (2d, $J = 5.4$ Hz, POC*C*), 52.0 (d, $J = 10.3$ Hz, C-2), 63.5 and 63.6 (2d, $J = 7.2$ Hz, 2×POC), 67.2 (d, $J = 164.9$ Hz, C-1), 115.6 (d, $J = 21.8$ Hz, C-$3_{arom.}$), 118.2 (d, $J = 12.6$ Hz, C-$1_{arom.}$), 124.6 (d, $J = 3.4$ Hz, C-$5_{arom.}$), 124.8 (d, $J = 12.6$ Hz, $C_{arom.}$), 127.4 (d, $J = 3.4$ Hz, H*C*=C), 129.4 (d, $J = 8.6$ Hz, $C_{arom.}$), 140.6 (s, HC=*C*), 158.8 (d, $J = 247.6$ Hz, F−$C_{arom.}$); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ [ppm] 21.45. Anal. Calcd. for $C_{14}H_{19}FN_3O_4P$: C, 48.98; H, 5.58; N, 12.24. Found: C, 48.99; H, 5.38; N, 12.29.

Diethyl 2-[4-(3-fluorophenyl)-1,2,3-triazol-1-yl]-1-hydroxyethylphosphonate 7e. The target compound was prepared from azidophosphonate **4** (0.333 g, 0.971 mmol) and 1-ethynyl-3-fluorobenzene (0.112 mL, 0.971 mmol) using the general procedure described above. The product was chromatographed on a silica gel column with chloroform/methanol (100:1, v/v) to give compound **7e** (0.482 g, 94%) as a white amorphous solid. Mp: 82–83°C; IR (KBr) ν [cm^{-1}] 3316, 3101, 2991, 1476, 1225, 1022, 777; 1H NMR ($CDCl_3$, 300 MHz) δ [ppm] 1.36 and 1.37 (2t, $J = 7.2$ Hz, 6H, 2×$POCH_2CH_3$), 4.16–4.28 (m, 4H, 2×$POCH_2CH_3$), 4.40–4.57 (m, 3H, H-2, H-1b, OH), 4.83–4.90 (m, 1H, H-1a), 6.99–7.04 (m, 1H, Ar−H), 7.31–7.52 (m, 3H, Ar−H), 7.98 (s, 1H, $HC_{5'}$); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ [ppm] 16.4 and 16.5 (2d, $J = 5.3$ Hz, POC*C*), 52.1 (d, $J = 9.3$ Hz, C-2), 63.5 and 63.6 (2d, $J = 7.2$ Hz, POC), 67.0 (d, $J = 165.2$ Hz, C-1), 112.3 (d, $J = 22.6$ Hz, $C_{arom.}$), 114.9 (d, $J = 19.6$ Hz, $C_{arom.}$), 121.1 (d, $J = 2.9$ Hz, $C_{arom.}$), 122.2 (s, H*C*=C) 130.4 (d, $J = 8.6$ Hz, $C_{arom.}$), 132.3 (d, $J = 8.3$ Hz, C-$1_{arom.}$), 146.4 (s, *C*=CH), 163.1 (d, $J = 245.2$ Hz, F−$C_{arom.}$); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ [ppm] 21.19. Anal. Calcd. for $C_{14}H_{19}FN_3O_4P$: C, 48.98; H, 5.58; N, 12.24. Found: C, 49.15; H, 5.51; N, 12.18.

Diethyl 2-[4-(2,4-difluorophenyl)-1,2,3-triazol-1-yl]-1-hydroxyethylphosphonate 7f. The target compound was prepared from azidophosphonate **4** (0.239 g, 0.661 mmol) and 1-ethynyl-2,4-difluorobenzene (0.091 g, 0.661 mmol) using the general procedure described above. The product was purified by crystallization from ethyl acetate/petroleum ether to give compound **7f** (0.375 g, 97%) as a white solid; m.p.: 136–137°C; IR (KBr) ν [cm^{-1}] 3243, 2986, 2911, 1493, 1226, 1046, 979, 816; ^{1}H NMR ($CDCl_3$, 300 MHz) δ [ppm] 1.36 and 1.39 (2t, $J = 7.2$ Hz, 6H, 2×$POCH_2CH_3$), 4.16–4.31 (m, 5H, 2×$POCH_2CH_3$, OH), 4.43 (ddd, $J = 9.6$ Hz, $J = 8.4$ Hz, $J = 2.4$ Hz, 1H, H-1), 4.58 (ddd, $J = 14.1$ Hz, $J = 9.6$ Hz, $J = 5.4$ Hz, 1H, H-2b), 4.89 (ddd, $J = 14.1$ Hz, $J = 6.3$ Hz, $J = 2.4$ Hz, 1H, H-2a), 6.84–6.92 (m, 1H, Ar−H), 6.95–7.02 (m, 1H, Ar−H), 8.07 (d, $J = 3.6$ Hz, $HC_{5'}$), 8.19–8.26 (m, 1H, Ar−H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ [ppm] 16.6 and 16.7 (2d, $J = 5.3$ Hz, POC*C*), 52.0 (d, $J = 10.0$ Hz, C-2), 63.5 and 63.6 (2d, $J = 7.2$ Hz, POC), 67.2 (d, $J = 164.6$ Hz, C-1), 104.0 (t, $J = 25.8$ Hz, C-$3_{arom.}$), 112.0 (dd, $J = 21.2$ Hz, $J = 3.2$ Hz, C-$1_{arom.}$), 114.8 (dd, $J = 13.2$ Hz, $J = 3.7$ Hz, C-$5_{arom.}$), 124.4 (d, $J = 12.6$ Hz, H*C*=C), 128.4 (dd, $J = 9.4$ Hz, $J = 5.2$ Hz, C-$6_{arom.}$), 140.0 (s, HC=*C*), 159.1 (dd, $J = 254.2$ Hz, $J = 12.9$ Hz, C-$2_{arom.}$), 162.5 (dd, $J = 252.5$ Hz, $J = 12.6$ Hz, C-$4_{arom.}$); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ [ppm] 21.02. Anal. Calcd. for $C_{14}H_{18}F_2N_3O_4P$: C, 46.54; H, 5.02; N, 11.63. Found: C, 46.33; H, 4.83; N, 11.62.

Diethyl 1-hydroxy-2-[4-(pyridin-2-yl)-1,2,3-triazol-1-yl]ethylphosphonate 7g. The target compound was prepared from azidophosphonate **4** (0.307 g, 0.941 mmol) and 1-ethynyl-2-pyridine (0.095 mL, 0.941 mmol) using the general procedure described above. The product was purified by crystallization from ethyl acetate/petroleum ether to give compound **7g** (0.422 g, 94%) as a white powder. Mp: 105–106°C; IR (KBr) ν [cm^{-1}] 3254, 2985, 2931, 1606, 1222, 1023, 975, 786; ^{1}H NMR ($CDCl_3$, 300 MHz) δ [ppm] 1.36 and 1.40 (2t, $J = 7.1$ Hz, 6H, 2×$POCH_2CH_3$), 2.80 (brs, 1H, OH), 4.19–4.33 (m, 4H, 2× $POCH_2CH_3$), 4.44 (ddd, $J = 10.4$ Hz, $J = 8.3$ Hz, $J = 2.4$ Hz, 1H, H-1), 4.58 (ddd, $J = 14.1$ Hz, $J = 10.4$ Hz, $J = 5.2$ Hz, 1H, H-2b), 4.92 (ddd, $J = 14.1$ Hz, $J = 4.7$ Hz,

$J = 2.4$ Hz, 1H, H-2a), 7.10–7.18 (m, 1H, Ar—H), 7.80 (dt, $J = 8.1$ Hz, $J = 1.5$ Hz, 1H, Ar—H), 8.12 (d, $J = 8.1$ Hz, 1H, Ar—H), 8.45 (s, 1H, $HC_{5'}$), 8.50 (d, $J = 4.5$ Hz, 1H, Ar—H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ [ppm] 16.6 and 16.7 (2d, $J = 5.7$ Hz, POC*C*), 52.3 (d, $J = 10.9$ Hz, C-2), 63.3 and 63.4 (2d, $J = 8.6$ Hz, POC), 67.4 (d, $J = 166.1$ Hz, C-1), 120.5 (s, $C_{arom.}$), 122.9 (s, $C_{arom.}$), 124.2 (H*C*=C), 137.2 (s, $C_{arom.}$), 147.0 (s, *C*=CH), 148.8 (s, $C_{arom.}$), 149.6 (s, C_{ipso}); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ [ppm] 21.29. Anal. Calcd. for $C_{13}H_{19}N_4O_4P \times 1/2H_2O$: C, 46.57; H, 6.01; N, 16.71. Found: C, 46.33; H, 5.98; N, 16.62.

Diethyl 1-hydroxy-2-[4-(1-methyl-1H-imidazol-5-yl)-1,2,3-triazol-1-yl]ethyl phosphonate 7h. The target compound was prepared from azidophosphonate **4** (0.292 g, 0.888 mmol) and 5-ethynyl-1-methyl-1*H*-imidazole (0.090 mL, 0.888 mmol) using the general procedure described above. The product was chromatographed on a silica gel column with chloroform/methanol (50:1 to 20:1 v/v), and the appropriate fractions were crystallized from methanol/diethyl ether to give compound **7h** (0.302 g, 70%) as white short needles. Mp: 162–163°C; IR (KBr) ν [cm^{-1}] 3441, 3092, 2985, 2921, 2852, 1252, 1090, 1030, 976; ^{1}H NMR ($CDCl_3$, 300 MHz) δ [ppm] 1.36 and 1.37 (2t, $J = 7.2$ Hz, 6H, $2\times POCH_2CH_3$), 3.84 (s, 3H, CH_3—N), 4.19–4.29 (m, 5H, $2\times POCH_2CH_3$, OH), 4.35 (dt, $J = 10.3$ Hz, $J = 2.4$ Hz, 1H, H-1), 4.51 (ddd, $J = 13.8$ Hz, $J = 10.3$ Hz, $J = 5.1$ Hz, 1H, H-2b), 4.89 (ddd, $J = 13.8$ Hz, $J = 3.9$ Hz, $J = 2.4$ Hz, 1H, H-2a), 6.98 (brs, 1H, H_{imid}), 7.38 (brs, 1H, H_{imid}), 7.87 (s, 1H, $HC_{5'}$); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ [ppm] 16.7 and 16.8 (2d, $J = 5.4$ Hz, POC*C*), 33.9 (s, CH_3—N), 52.4 (d, $J = 10.9$ Hz, C-2), 63.2 and 63.4 (2d, $J = 7.5$ Hz, POC), 66.9 (d, $J = 166.8$ Hz C-1), 122.8, 123.6, 127.3 (s, H*C*=C), 137.4 (s, HC=*C*), 138.9 (s, N—CH—N); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ [ppm] 21.45. Anal. Calcd. for $C_{12}H_{20}N_5O_4P$: C, 43.77; H, 6.12; N, 21.27. Found: C, 43.73; H, 6.13; N, 21.37.

Preparation of Diethyl 2-Hydroxy-3-(4,5-dimethoxycarbonyl-1,2,3-triazol-1-yl)propylphosphonate 6i

A solution of the azide **3** (0.207g, 0.873 mmol) and dimethyl acetylenedicarboxylate (0.107 mL, 0.873 mmol) in toluene (2 mL) was refluxed for 4 h. The mixture was concentrated to dryness to leave a yellow solid (0.345 g), which was chromatographed on a silica gel column with chloroform/methanol (100:1, v/v) and later crystallized from ethyl acetate/petroleum ether to give phosphonate **6i** (0.277 g, 84%) as a white solid. Mp: 85–86°C; IR (KBr): ν [cm^{-1}] 3302, 2986, 2957, 2911, 1737, 1468, 1440, 1224, 1025, 963, 826, 754; ^{1}H NMR ($CDCl_3$, 300 MHz) δ [ppm] 1.33 and 1.34 (2t, $J = 6.9$ Hz, 6H, $2\times POCH_2CH_3$), 1.80 (ddd, $J = 16.5$ Hz, $J = 15.3$ Hz, $J = 9.9$ Hz, 1H, H-1a), 2.04 (ddd, $J = 18.3$ Hz, $J = 15.3$ Hz, $J = 3.0$ Hz, 1H, H-1b), 3.98 (s, 3H, $COOCH_3$), 3.99 (s, 3H, $COOCH_3$), 4.01 (d, $J = 3.0$ Hz, 1H, OH), 4.05–4.24 (m, 4H, $2\times POCH_2CH_3$), 4.31–4.50 (m, 1H, H-2), 4.70 (dd, $J = 13.8$ Hz, $J = 6.6$ Hz, 1H, H-3a), 4.82 (ddd, $J = 13.8$ Hz, $J = 3.9$ Hz, $J = 1.5$ Hz, 1H, H-3b); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ [ppm] 16.5 and 16.6 (2d, $J = 6.0$ Hz, POC*C*), 30.9 (d, $J = 140.4$ Hz, C-1), 52.8 (s, $COOCH_3$), 56.3 (s, $COOCH_3$), 55.3 (d, $J = 18.9$ Hz, C-3), 62.4 and 62.6 (2d, $J = 6.8$ Hz, $2\times$POC), 65.6 (d, $J = 3.8$ Hz, C-2), 132.1 (s, H*C*=C), 139.2 (s, HC=*C*), 159.3 (s, C=O), 160.3 (s, C=O); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ [ppm] 29.21; Anal. Calcd. for $C_{13}H_{22}N_3O_8P$: C, 41.16; H, 5.84; N, 11.08. Found: C, 41.25; H, 5.66; N, 11.08.

Preparation of Diethyl 3-(5-Amino-4-carbamoyl-1,2,3-triazol-1-yl)-2-hydroxypropylphosphonate 6j

To a solution of 2-cyanoacetamide (0.203 g, 2.42 mmol) in DMSO (1.0 mL), K_2CO_3 (0.334 g, 2.42 mmol) was added at room temperature under an argon atmosphere. The mixture was stirred at the same temperature for 30 min. After addition of diethyl 3-azido-2-hydroxypropylphosphonate **3** (0.286 g, 1.20 mmol) in DMSO (0.7 mL), the stirring was continued for 5 h at 50 °C. After evaporation of the solvent, the residue was purified by silica gel column chromatography with chloroform/methanol (20:1, 10:1 v/v), and the appropriate fractions were crystallized from ethyl acetate/petroleum ether to afford **6j** (0.341 g, 75%) as a white amorphous solid. Mp: 155–157°C; IR (KBr) ν [cm^{-1}] 3486, 3366, 3193, 2956, 2911, 1665, 1638, 1239, 1030, 949; ^{1}H NMR ($CDCl_3$, 300 MHz) δ [ppm] 1.33 and 1.35 (2t, $J = 6.9$ Hz, 6H, 2×POCH_2CH_3), 1.81 (ddd, $J = 16.2$ Hz, $J = 15.3$ Hz, $J = 10.5$ Hz, 1H, H-1b), 2.02 (ddd, $J = 19.2$ Hz, $J = 15.3$ Hz, $J = 3.0$ Hz, 1H, H-1a), 2.70 (brs, 1H, OH), 4.05–4.42 (m, 4H, 2×POCH_2CH$_3$), 4.26 (dd, $J = 14.4$ Hz, $J = 5.1$ Hz, H-3b), 4.35–4.50 (m, 2H, H-2, H-3a), 5.79 (brs, 2H, C(O)NH_2), 5.48 and 6.74 (2 × brs, 2H, NH_2); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ [ppm] 16.6 and 16.7 (2d, $J = 5.3$ Hz, POCC), 30.3 (d, $J = 139.7$ Hz, C-1), 52.6 (d, $J = 18.9$ Hz, C-3), 62.7 and 62.8 (2d, $J = 6.8$ Hz, 2×POC), 67.0 (d, $J = 3.0$ Hz, C-2), 123.0 (s, HC=C), 146.5 (s, HC=C), 164.6 (s, C=O); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ [ppm] 29.87; Anal. Calcd. for $C_{10}H_{20}N_5O_5P$: C, 37.39; H, 6.28; N, 21.80. Found: C, 37.54; H, 6.29; N, 21.68.

Preparation of Diethyl 1-Hydroxy-2-(4,5-dimethoxycarbonyl-1,2,3-triazol-1-yl)ethylphosphonate 7j

A solution of the azide **4** (0.171g, 0.766 mmol) and dimethyl acetylenedicarboxylate (0.094 mL, 0.766 mmol) in toluene (2 mL) was refluxed for 4 h. The mixture was concentrated to dryness to leave a yellow solid (0.311 g), which was chromatographed on a silica gel column with chloroform/methanol (100:1, v/v) and later crystallized from ethyl acetate/diethyl ether to give phosphonate **7j** (0.256 g, 91%) as a white solid. Mp: 97–98°C; IR (KBr): ν [cm^{-1}] 3233, 2963, 2914, 1732, 1230, 1052, 963; ^{1}H NMR ($CDCl_3$, 300 MHz) δ [ppm] 1.33 and 1.34 (2t, $J = 7.1$ Hz, 6H, 2×POCH$_2$CH_3), 3.95 (s, 3H, COOCH_3), 3.97 (s, 3H, COOCH_3), 4.10–4.21 (m, 5H, 2×POCH_2CH$_3$, OH), 4.32 (ddd, $J = 7.8$ Hz, $J = 7.0$ Hz, $J = 5.7$ Hz, 1H, H-1), 4.83–4.94 (m, 2H, H-2a, H-2b); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ [ppm] 16.5 and 16.6 (2d, $J = 6.0$ Hz, POCC), 51.1 (d, $J = 10.2$ Hz, C-2), 52.8 (s, COOCH$_3$), 53.4 (s, COOCH$_3$), 63.2 and 63.6 (2d, $J = 7.2$ Hz, 2×POC), 66.8 (d, $J = 164.4$ Hz, C-1), 131.8 (s, HC=C), 139.1 (s, HC=C), 158.9 (s, C=O), 160.2 (s, C=O); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ [ppm] 20.65; Anal. Calcd. for $C_{12}H_{20}N_3O_8P$: C, 39.46; H, 5.52; N, 11.50. Found: C, 39.37; H, 5.37; N, 11.61.

Deprotection of the Diethyl Phosphonate into 6a–i and 7a–h, j, General Procedure

Solutions of diethyl phosphonates **6a–i** (1 mmol) in CH_2Cl_2 (0.5 mL) were treated with bromotrimethylsilane (10 mmol) at room temperature under argon atmosphere. The reaction mixture was protected from light and stirred at room temperature for 24 h. After

concentration to dryness, the residue was co-evaporated with dichloromethane (5 mL) and ethanol (3 × 3 mL) to afford crude phosphonic acids **8a–i**.

2-Hydroxy-3-[4-(methoxycarbonyl)-1,2,3-triazol-1-yl]propylphosphonic acid 8a. Compound **8a** was obtained as a white powder (0.056 g, 95%), which decomposed after heating above 180°C; IR (KBr) ν [cm^{-1}] 3440, 2926, 2853, 1727, 1237, 1054; ^{1}H NMR (CD_3OD, 300 MHz) δ [ppm] 1.95–2.15 (m, 2H, H-1a, H-1b), 3.92 (s, 3H, COOC*H*$_3$), 4.22–4.34 (m, 1H, H-2), 4.46 (dd, J = 13.6 Hz, J = 7.8 Hz, 1H, H-3b), 4.76 (dd, J = 13.6 Hz, J = 2.8 Hz, 1H, H-3a), 8.51 (s, 1H, *H*C$_{5'}$); ^{13}C NMR (CD_3OD, 75.5 MHz) δ [ppm] 31.9 (d, J = 140.7 Hz, C-1), 52.3 (s, COO*C*H$_3$), 57.2 (d, J = 17.8 Hz, C-3), 65.7 (d, J = 3.6 Hz, C-2), 129.8 (s, H*C*=C), 139.5 (s, HC=*C*), 162.1 (s, C=O); ^{31}P NMR (CD_3OD, 121.5 MHz) δ [ppm] 22.55; Anal. Calcd. for $C_7H_{12}N_3O_6P\times H_2O$: C, 29.69; H, 4.98; N, 14.84. Found: C, 29.36; H, 4.88; N, 14.68.

3-[4-(Benzoyloxymethyl)-1,2,3-triazol-1-yl]-2-hydroxypropylphosphonic acid 8b. Compound **8b** was obtained as a colorless oil (0.038 g, 93%); IR (film) ν [cm^{-1}] 3444, 2936, 2858, 1727, 1237, 1059, 765, 655; ^{1}H NMR (CD_3OD, 300 MHz) δ [ppm] 1.95–2.17 (m, 2H, H-1b, H-1a), 4.32–4.46 (m, 1H, H-2), 4.54 (dd, J = 13.8 Hz, J = 8.1 Hz, 1H, H-3b), 4.82 (dd, J = 13.8 Hz, J = 3.0 Hz, 1H, H-3a), 5.52 (s, 2H, C*H*$_2$OC(O)Ph), 7.45–7.52 (m, 2H, Ar−H), 7.59–7.70 (m, 1H, Ar−H) 8.01–8.08 (m, 2H, Ar−H), 8.44 (s, 1H, *H*C$_{5'}$); ^{13}C NMR (CD_3OD, 75.5 MHz) δ [ppm] 34.0 (d, J = 136.6 Hz, C-1), 57.9 (s, *C*H$_2$OC(O)Ph), 58.3 (d, J = 11.7 Hz, C-3), 67.0 (s, C-2), 129.5, 129.7, 130.6, 134.0 (s, H*C*=C), 134.6, 167.4 (s, C=O); ^{31}P NMR (CD_3OD, 121.5 MHz) δ [ppm] 24.11; Anal. Calcd. for $C_{13}H_{16}N_3O_6P\times 2H_2O$: C, 41.38; H, 5.34; N, 11.14. Found: C, 41.52; H, 5.28; N, 11.20.

2-Hydroxy-3-(4-phenyl-1,2,3-triazol-1-yl)propylphosphonic acid 8c. Compound **8c** was obtained as a colorless oil (0.042 g, 90%); IR (film) ν [cm^{-1}] 3333, 2985, 2888, 1238, 1049, 965; ^{1}H NMR (CD_3OD, 300 MHz) δ [ppm] 2.05–2.27 (m, 2H, H-1b, H-1a), 4.43–4.56 (m, 1H, H-2), 4.65 (dd, J = 13.8 Hz, J = 8.1 Hz, 1H, H-3b), 4.92 (dd, J = 13.8 Hz, J = 3.0 Hz, 1H, H-3a), 7.49–7.60 (m, 3H, Ar−H), 7.82–7.87 (m, 2H, Ar−H), 8.88 (s, 1H, *H*C$_{5'}$); ^{13}C NMR (CD_3OD, 75.5 MHz) δ [ppm] 34.0 (d, J = 136.8 Hz, C-1), 59.3 (d, J = 11.5 Hz, C-3), 66.9 (s, C-2), 126.2, 127.2, 127.5, 130.6, 131.5, 145.8; ^{31}P NMR (CD_3OD, 121.5 MHz) δ [ppm] 25.51; Anal. Calcd. for $C_{11}H_{14}N_3O_4P\times H_2O$: C, 43.86; H, 5.35; N, 13.95. Found: C, 44.03; H, 5.59; N, 14.08.

3-[4-(2-Fluorophenyl)-1,2,3-triazol-1-yl]-2-hydroxypropylphosphonic acid 8d. Compound **8d** was obtained as a colorless oil (0.040 g, 85%); IR (film) ν [cm^{-1}] 3296, 2952, 2811, 1620, 1586, 1486, 1437, 1128, 1075, 976; ^{1}H NMR (CD_3OD, 300 MHz) δ [ppm] 2.00–2.22 (m, 2H, H-1b, H-1a), 4.40–4.51 (m, 1H, H-2), 4.59 (dd, J = 13.7 Hz, J = 8.1 Hz, 1H, H-3b), 4.85 (dd, J = 13.7 Hz, J = 3.2 Hz, 1H, H-3a), 7.25–7.33 (m, 2H, Ar−H), 7.36–7.48 (m, 1H, Ar−H), 8.00–8.08 (m, 1H, Ar−H), 8.55 (d, J = 3.2 Hz, 1H, *H*C$_{5'}$); ^{13}C NMR (CD_3OD, 75.5 MHz) δ [ppm] 34.0 (d, J = 136.8 Hz, C-1), 58.3 (d, J = 11.7 Hz, C-3), 67.0 (s, C-2), 117.3 (d, J = 22.8 Hz, C-3$_{arom.}$), 117.4 (d, J = 15.3 Hz, C-1$_{arom.}$), 126.1 (d, J = 3.4 Hz, C-6$_{arom.}$), 127.2 (d, J = 10.3 Hz), 128.9 (d, J = 2.9 Hz, HC=*C*), 132.2 (d, J = 8.3 Hz, C-4$_{arom.}$), 140.7 (s, H*C*=C), 160.6 (d, J = 249.2 Hz, C−F); ^{31}P NMR (CD_3OD, 121.5 MHz) δ [ppm] 26.81; Anal. Calcd. for $C_{11}H_{13}FN_3O_4P\times H_2O$: C, 41.39; H, 4.74; N, 13.16. Found: C, 41.69; H, 4.93; N, 13.31.

3-[4-(3-Fluorophenyl)-1,2,3-triazol-1-yl]-2-hydroxypropylphosphonic acid 8e. Compound **8e** was obtained as a colorless oil (0.052 g, 83%); IR (film) ν [cm^{-1}] 3306, 3086, 2955, 2814, 1621, 1584, 1487, 1436, 1127, 1075, 976; ^{1}H NMR (CD_3OD, 300 MHz) δ [ppm] 2.05–2.21 (m, 2H, H-1b, H-1a), 4.41–4.51 (m, 1H, H-2), 4.57 (dd, J = 13.6 Hz,

$J = 8.0$ Hz, 1H, H-3b), 4.84 (dd, $J = 13.6$ Hz, $J = 3.0$ Hz, 1H, H-3a), 7.15–7.22 (m, 1H, Ar—H), 7.49–7.60 (m, 1H, Ar—H), 7.61–7.78 (m, 2H, Ar—H), 8.68 (s, 1H, $HC_{5'}$); ^{13}C NMR (CD_3OD, 75.5 MHz) δ [ppm] 33.9 (d, $J = 137.4$ Hz, C-1), 58.8 (d, $J = 12.1$ Hz, C-3), 66.9 (d, $J = 1.5$ Hz, C-2), 114.3 (d, $J = 22.7$ Hz, C-$4_{arom.}$), 117.4 (d, $J = 22.7$ Hz, C-$2_{arom.}$), 123.1 (d, $J = 7.6$ Hz, C-$6_{arom.}$), 125.9 (s, HC=*C*), 130.7 (d, $J = 7.6$ Hz, $C_{arom.}$), 132.4 (d, $J = 15.1$ Hz, $C_{arom.}$), 145.4 (s, H*C*=C), 164.5 (d, $J = 249.2$ Hz, C—F); ^{31}P NMR (CD_3OD, 121.5 MHz) δ [ppm] 25.90; Anal. Calcd. for $C_{11}H_{13}FN_3O_4P \times H_2O$: C, 41.39; H, 4.74; N, 13.16. Found: C, 41.57; H, 4.86; N, 12.91.

3-[4-(2,4-Difluorophenyl)-1,2,3-triazol-1-yl]-2-hydroxypropylphosphonic acid 8f. Compound **8f** was obtained as a white solid (0.053 g, 95%); mp: 165—170°C; IR (KBr) ν [cm^{-1}] 3333, 3071, 2924, 2853, 1638, 1590, 1510, 1079, 946; ^{1}H NMR (CD_3OD, 300 MHz) δ [ppm] 1.98–2.19 (m, 2H, H-1b, H-1a), 4.36–4.49 (m, 1H, H-2), 4.55 (dd, $J =$ 13.8 Hz, $J = 7.8$ Hz, 1H, H-3b), 4.82 (dd, $J = 13.8$ Hz, $J = 3.3$ Hz, 1H, H-3a), 7.11–7.20 (m, 2H, Ar—H), 8.08 (dt, $J = 9.0$ Hz, $J = 6.3$ Hz, 1H, Ar—H-3), 8.48 (d, $J = 3.3$ Hz, 1H, $HC_{5'}$); ^{13}C NMR (CD_3OD, 75.5 MHz) δ [ppm] 33.8 (d, $J = 137.4$ Hz, C-1), 58.6 (d, $J = 12.3$ Hz, C-3), 66.9 (s, C-2), 105.7 (t, $J = 26.0$ Hz, C-$3_{arom.}$), 113.4 (dd, $J = 22.3$ Hz, $J = 3.4$ Hz, $C_{arom.}$), 127.2 (d, $J = 9.7$ Hz, $C_{arom.}$), 130.5 (dd, $J = 10.0$ Hz, $J = 4.6$ Hz), 139.7 (s, H*C*=C), 160.9 (dd, $J = 251.6$ Hz, $J = 12.0$ Hz C—F), 164.8 (d, $J = 250.2$ Hz, $J = 12.0$ Hz, C—F); ^{31}P NMR (CD_3OD, 121.5 MHz) δ [ppm] 24.50; Anal. Calcd. for $C_{11}H_{12}F_2N_3O_4P \times H_2O$: C, 39.18; H, 4.18; N, 12.46. Found: C, 38.89; H, 4.31; N, 12.58.

2-Hydroxy-3-[4-(pyridin-2-yl)-1,2,3-triazol-1-yl]propylphosphonic acid 8g. Compound **8g** was obtained as a colorless oil (0.044 g, 85%); IR (film) ν [cm^{-1}] 3339, 2925, 2851, 1635, 1612, 1226, 1163, 1081, 997, 936, 787; ^{1}H NMR (CD_3OD, 300 MHz) δ [ppm] 2.00–2.24 (m, 2H, H-1b, H-1a), 4.38–4.50 (m, 1H, H-2), 4.60 (dd, $J = 13.8$ Hz, $J = 7.8$ Hz, 1H, H-3b), 4.87 (dd, $J = 13.8$ Hz, $J = 3.0$ Hz, 1H, H-3a), 8.03 (dt, $J = 6.0$ Hz, $J = 0.9$ Hz, 1H, Ar—H), 8.54 (d, $J = 8.2$ Hz, 1H, Ar—H), 8.70 (dt, $J = 8.2$ Hz, J = 1.5 Hz, 1H, Ar—H), 8.82 (d, $J = 6.0$ Hz, 1H, Ar—H), 9.03 (s, 1H, $HC_{5'}$); ^{13}C NMR (CD_3OD, 75.5 MHz) δ [ppm] 34.0 (d, $J = 137.4$ Hz, C-1), 57.8 (d, $J = 11.3$ Hz, C-3), 67.1 (s, C-2), 125.5, 126.8, 128.9, 139.8, 142.6, 144.7, 148.6; ^{31}P NMR (CD_3OD, 121.5 MHz) δ [ppm] 25.82; Anal. Calcd. for $C_{10}H_{13}N_4O_4P \times H_2O$: C, 39.74; H, 5.00; N, 18.54. Found: C, 39.98; H, 4.81; N, 18.87.

2-Hydroxy-3-[4-(1-methyl-1H-imidazol-5-yl)-1,2,3-triazol-1-yl]propylphosphonic acid 8h. Compound **8h** was obtained as a colorless oil (0.035 g, 67%); IR (film) ν [cm^{-1}] 3427, 2923, 2854, 1639, 1449, 1165, 1057; ^{1}H NMR (CD_3OD, 300 MHz) δ [ppm] 2.08 (ddd, $J = 18.6$ Hz, $J = 15.3$ Hz, $J = 7.2$ Hz, 1H, H-1b), 2.20 (ddd, $J = 18.9$ Hz, $J = 15.3$ Hz, $J = 6.0$ Hz, 1H, H-1a), 4.13 (s, 3H, CH_3—N), 4.43 (ddddd, $J = 14.4$ Hz, $J = 7.8$ Hz, $J = 7.2$ Hz, $J = 6.0$ Hz, $J = 3.3$ Hz, 1H, H-2), 4.57 (dd, $J = 13.8$ Hz, $J =$ 7.8 Hz, 1H, H-3b), 4.80 (dd, $J = 13.8$ Hz, $J = 3.3$ Hz, 1H, H-3a), 7.92 (d, $J = 1.8$ Hz, 1H, H_{imid}), 8.60 (s, 1H, $HC_{5'}$), 9.11 (d, $J = 1.8$ Hz, 1H, H_{imid}); ^{13}C NMR (CD_3OD, 75.5 MHz) δ [ppm] 34.0 (d, $J = 137.4$ Hz, C-1), 36.5 (s, CH_3—N), 57.6 (d, $J = 11.7$ Hz, C-3), 67.1 (s, C-2), 119.2, 127.0, 127.6 (s, H*C*=C), 135.1 (s, HC=*C*), 137.9 (s, N—*C*H—N); ^{31}P NMR (CD_3OD, 121.5 MHz) δ [ppm] 27.65. Anal. Calcd. for $C_9H_{14}N_5O_4P \times 2H_2O$: C, 33.44; H, 5.61; N, 21.67. Found: C, 33.61; H, 5.49; N, 21.74.

3-(5-Amino-4-carbamoyl-1,2,3-triazol-1-yl)-2-hydroxypropylphosphonic acid 8i. Compound **8i** was obtained as a white powder (0.048 g, 95%), which decomposed after heating above 180°C; IR (KBr) ν [cm^{-1}] 3321, 3199, 2926, 1638, 1543, 1259, 1130, 969; ^{1}H NMR (CD_3OD, 300 MHz) δ [ppm] 1.94–2.17 (m, 2H, H-1a, H-1b), 4.24 (dd,

J = 13.6 Hz, J = 6.8 Hz, H-3b), 4.35–4.82 (m, 2H, H-2, H-3a); ^{13}C NMR (CD_3OD, 75.5 MHz) δ [ppm] 32.7 (d, J = 136.7 Hz, C-1), 52.4 (d, J = 12.4 Hz, C-3), 66.3 (s, C-2), 121.5 (s, H*C*=C), 146.5 (s, HC=*C*), 165.6 (s, C=O); ^{31}P NMR (CD_3OD, 121.5 MHz) δ [ppm] 26.31; Anal. Calcd. for $C_6H_{12}N_5O_5P\times H_2O$: C, 25.45; H, 4.98; N, 24.73. Found: C, 25.61; H, 5.13; N, 24.58.

1-Hydroxy-2-[4-(methoxycarbonyl)-1,2,3-triazol-1-yl]ethylphosphonic acid 9a. Compound **9a** was obtained as a white solid (0.049 g, 92%); mp: 134–136°C; IR (KBr) ν [cm^{-1}] 3345, 2969, 2924, 2851, 1727, 1251, 1224, 1085; ^{1}H NMR (D_2O, 300 MHz) δ [ppm] 3.88 (s, 3H, COOC*H*$_3$), 4.26 (dt, J = 10.3 Hz, J = 3.0 Hz, 1H, H-1), 4.59 (ddd, J = 14.5 Hz, J = 10.3 Hz, J = 6.0 Hz, 1H, H-2a), 4.68–4.87 (m, 1H, H-2b), 8.54 (s, 1H, *H*C$_{5'}$); ^{13}C NMR (D_2O, 75.5 MHz) δ [ppm] 52.7 (s, COO*C*H$_3$), 52.8 (s, C-2), 67.2 (d, J = 158.6 Hz, C-1), 129.9 (s, H*C*=C), 138.9 (s, HC=*C*), 162.3 (s, C=O); ^{31}P NMR (D_2O, 121.5 MHz) δ [ppm] 18.17; Anal. Calcd. for $C_6H_{10}N_3O_6P$: C, 28.70; H, 4.01; N, 16.73. Found: C, 28.57; H, 3.97; N, 16.78.

2-[4-(Benzoyloxymethyl)-1,2,3-triazol-1-yl]-1-hydroxyethylphosphonic acid 9b. Compound **9b** was obtained as a white powder (0.062 g, 77%), which decomposed after heating above 170°C; IR (KBr) ν [cm^{-1}] 3028, 2982, 2890, 1720, 1258, 1020, 847, 720; ^{1}H NMR (D_2O, 300 MHz) δ [ppm] 4.20–4.40 (m, 1H, H-1), 4.52–4.72 (m, 1H, H-2b), 4.78–4.90 (m, 1H, H-2a), 5.48 (s, 2H, C*H*$_2$OC(O)Ph), 7.47–7.58 (m, 2H, Ar−H), 7.60–7.66 (m, 1H, Ar−H), 7.90–8.01 (m, 2H, Ar−H), 8.23 (s, 1H, *H*C$_{5'}$); ^{13}C NMR (CD_3OD, 75.5 MHz) δ [ppm] 51.8 (s, C-2), 58.4 (s, *C*H$_2$OC(O)Ph), 68.3 (d, J = 160.6 Hz, C-1), 123.6 (s, HC=*C*), 128.4, 129.0, 129.8 (C$_{arom.}$), 133.3 (s, H*C*=C), 139.2 (C$_{ipso}$), 169.9 (s, C=O); ^{31}P NMR (D_2O, 121.5 MHz) δ [ppm] 18.14; Anal. Calcd. for $C_{12}H_{14}N_3O_6P\times H_2O$: C, 41.75; H, 4.67; N, 12.17. Found: C, 41.98; H, 4.75; N, 12.04.

1-Hydroxy-2-(4-phenyl-1,2,3-triazol-1-yl)ethylphosphonic acid 9c. Compound **9c** was obtained as a white powder (0.044 g, 80%); mp: 162–166°C; IR (KBr) ν [cm^{-1}] 3074, 2989, 1225, 1015, 976, 765, 692; ^{1}H NMR (D_2O, 300 MHz) δ [ppm] 4.29 (dt, J = 10.3 Hz, J = 2.0 Hz, 1H, H-1), 4.60 (ddd, J = 14.8 Hz, J = 10.3 Hz, J = 6.0 Hz, 1H, H-2a), 4.75–4.85 (m, 1H, H-2b), 7.39–7.59 (m, 3H, Ar−H), 7.62–7.80 (m, 2H, Ar−H), 8.41 (s, 1H, *H*C$_{5'}$); ^{13}C NMR (CD_3OD, 75.5 MHz) δ [ppm] 52.2 (d, J = 10.7 Hz, C-2), 67.1 (d, J = 166.3 Hz, C-1), 121.8, 125.5, 128.1, 128.8 (C$_{arom.}$), 130.4 (HC=*C*), 147.0 (H*C*=C); ^{31}P NMR (D_2O, 121.5 MHz) δ [ppm] 17.89; Anal. Calcd. for $C_{10}H_{12}N_3O_4P\times H_2O$: C, 41.82; H, 4.91; N, 14.63. Found: C, 41.45; H, 5.02; N, 14.44.

2-[4-(2-Fluorophenyl)-1,2,3-triazol-1-yl]-1-hydroxyethylphosphonic acid 9d. Compound **9d** was obtained as a white solid (0.056 g, 86%); which decomposed after heating above 180°C; IR (KBr) ν [cm^{-1}] 3231, 3012, 2989, 2909, 1487, 1210, 1048, 760; ^{1}H NMR (D_2O, 300 MHz) δ [ppm] 4.27 (dt, J = 10.7 Hz, J = 2.6 Hz, 1H, H-1), 4.53 (ddd, J = 13.9 Hz, J = 10.7 Hz, J = 5.7 Hz, 1H, H-2b), 4.75–4.87 (m, 1H H-2a), 7.11–7.21 (m, 2H, Ar−H), 7.23–7.38 (m, 1H, Ar−H), 7.79 (t, J = 7.5 Hz, 1H, Ar−H), 8.30 (d, J = 2.4 Hz, 1H, *H*C$_{5'}$); ^{13}C NMR (CD_3OD, 75.5 MHz) δ [ppm] 52.1 (d, J = 10.4 Hz, C-2), 67.4 (d, J = 165.4 Hz, C-1), 114.6 (d, J = 22.8 Hz, C-3$_{arom.}$), 117.2 (d, J = 12.4 Hz, C-1$_{arom.}$), 122.6 (d, J = 3.0 Hz, C-5$_{arom.}$), 123.8 (d, J = 12.4 Hz, C$_{arom.}$), 126.4 (d, J = 3.0 Hz, H*C*=C), 129.0 (d, J = 8.3 Hz, C$_{arom.}$), 140.2 (s, HC=*C*), 156.8 (d, J = 246.0 Hz, F−C$_{arom.}$); ^{31}P NMR (D_2O, 121.5 MHz) δ [ppm] 18.20. Anal. Calcd. for $C_{10}H_{11}FN_3O_4P\times H_2O$: C, 39.35; H, 4.29; N, 13.77. Found: C, 39.52; H, 4.28; N, 13.89.

2-[4-(3-Fluorophenyl)-1,2,3-triazol-1-yl]-1-hydroxyethylphosphonic acid 9e. Compound **9e** was obtained as a white solid (0.058 g, 94%); mp: 172–175°C; IR

(KBr) ν [cm^{-1}] 3307, 3100, 2993, 1434, 1220, 1025, 777; ^{1}H NMR (D_2O, 300 MHz) δ [ppm] 4.25 (dt, $J = 10.3$ Hz, $J = 2.4$ Hz, 1H, H-1), 4.56 (ddd, $J = 13.8$ Hz, $J = 10.3$ Hz, $J = 5.7$ Hz, 1H, H-2b), 4.66–4.80 (m, 1H H-2a), 7.09 (t, $J = 8.5$ Hz, 1H, Ar—H), 7.38–7.48 (m, 3H, Ar—H), 8.29 (s, 1H, $HC_{5'}$); ^{13}C NMR (D_2O, 75.5 MHz) δ [ppm] 52.1 (d, $J = 9.2$ Hz, C-2), 65.0 (d, $J = 155.2$ Hz, C-1), 110.3 (d, $J = 22.2$ Hz, $C_{arom.}$), 114.2 (d, $J = 19.0$ Hz, $C_{arom.}$), 117.9 (d, $J = 2.8$ Hz, $C_{arom.}$), 122.0 (s, H*C*=C) 130.4 (d, $J = 8.6$ Hz, $C_{arom.}$), 130.3 (d, $J = 8.0$ Hz, C-$1_{arom.}$), 144.4 (s, *C*=CH), 164.1 (d, $J = 245.2$ Hz, F—$C_{arom.}$); ^{31}P NMR (D_2O, 121.5 MHz) δ [ppm] 17.92. Anal. Calcd. for $C_{10}H_{11}FN_3O_4P \times H_2O$: C, 39.35; H, 4.29; N, 13.77. Found: C, 39.15; H, 4.51; N, 13.88.

2-[4-(2,4-Difluorophenyl)-1,2,3-triazol-1-yl]-1-hydroxyethylphosphonic acid 9f. Compound **9f** was obtained as a white solid (0.065 g, 97%); mp: 194–198°C; IR (KBr) ν [cm^{-1}] 3143, 2987, 2901, 1493, 1220, 1026, 979, 816; ^{1}H NMR (CD_3OD, 300 MHz) δ [ppm] 4.34 (dt, $J = 10.2$ Hz, $J = 3.0$ Hz, 1H, H-1), 4.71 (ddd, $J = 14.1$ Hz, $J = 10.2$ Hz, $J = 6.0$ Hz, 1H, H-2b), 4.95 (ddd, $J = 14.1$ Hz, $J = 4.8$ Hz, $J = 3.0$ Hz, 1H, H-2a), 7.13–7.23 (m, 2H, Ar—H), 8.06 (dt, $J = 8.1$ Hz, $J = 6.3$ Hz, 1H, Ar—H), 8.60 (d, $J = 3.0$ Hz, 1H, $HC_{5'}$); ^{13}C NMR (DMSO-d_6, 75.5 MHz) δ [ppm] 52.4 (d, $J = 10.2$ Hz, C-2), 67.2 (d, $J = 164.6$ Hz, C-1), 104.0 (t, $J = 25.8$ Hz, C-$3_{arom.}$), 112.4 (dd, $J = 21.2$ Hz, $J = 3.4$ Hz, C-$1_{arom.}$), 113.9 (dd, $J = 13.0$ Hz, $J = 3.7$ Hz, C-$5_{arom.}$), 124.4 (d, $J = 12.4$ Hz, H*C*=C), 128.4 (dd, $J = 9.4$ Hz, $J = 5.2$ Hz, C-$6_{arom.}$), 140.4 (s, HC=*C*), 159.3 (dd, $J = 254.2$ Hz, $J = 12.4$ Hz, C-$2_{arom.}$), 162.0 (dd, $J = 252.5$ Hz, $J = 12.4$ Hz, C-$4_{arom.}$); ^{31}P NMR (CD_3OD, 121.5 MHz) δ [ppm] 19.43. Anal. Calcd. for $C_{10}H_{10}F_2N_3O_4P$: C, 39.36; H, 3.30; N, 13.77. Found: C, 39.33; H, 3.53; N, 13.62.

1-Hydroxy-2-[4-(pyridin-2-yl)-1,2,3-triazol-1-yl]ethylphosphonic acid 9g. Compound **9g** was obtained as a yellow pale powder (0.422 g, 94%), which decomposed after heating above 180°C; IR (KBr) ν [cm^{-1}] 3154, 2980, 2930, 1602, 1222, 1023, 975, 786; ^{1}H NMR (D_2O, 300 MHz) δ [ppm] 4.23 (dt, $J = 10.5$ Hz, $J = 2.7$, 1H, H-1), 4.65 (ddd, $J = 14.1$ Hz, $J = 10.5$ Hz, $J = 5.7$ Hz, 1H, H-2b), 4.89 (ddd, $J = 14.1$ Hz, $J = 7.5$ Hz, $J = 2.7$ Hz, 1H, H-2a), 7.95 (t, $J = 6.6$ Hz, 1H, Ar—H), 8.36 (d, $J = 8.1$ Hz, 1H, Ar—H), 8.60 (t, $J = 8.1$ Hz, 1H, Ar—H), 8.70 (d, $J = 6.6$ Hz, 1H, Ar—H), 8.85 (s, 1H, $HC_{5'}$); ^{13}C NMR (CD_3OD, 75.5 MHz) δ [ppm] 50.4 (d, $J = 10.4$ Hz, C-2), 64.8 (d, $J = 166.8$ Hz C-1), 120.5 (s, $C_{arom.}$), 122.6 (s, $C_{arom.}$), 124.0 (H*C*=C), 137.0 (s, $C_{arom.}$), 147.0 (s, *C*=CH), 148.4 (s, $C_{arom.}$), 149.9 (s, C_{ipso}); ^{31}P NMR (D_2O, 121.5 MHz) δ [ppm] 16.61. Anal. Calcd. for $C_9H_{11}N_4O_4P \times 1/2H_2O$: C, 38.72; H, 4.33; N, 20.07. Found: C, 38.53; H, 4.48; N, 19.92.

1-Hydroxy-2-[4-(1-methyl-1H-imidazol-5-yl)-1,2,3-triazol-1-yl]ethylphosphonic acid 9h. Compound **9h** was obtained as a white solid (0.042 g, 70%), which decomposed after heating above 180°C; IR (KBr) ν [cm^{-1}] 3424, 3096, 2980, 2920, 2850, 1250, 1090, 1030, 976; ^{1}H NMR (D_2O, 300 MHz) δ [ppm] 3.91 (s, 3H, CH_3—N), 4.29 (dt, $J = 10.3$ Hz, $J = 2.0$ Hz, 1H, H-1), 4.59–4.69 (m, 1H, H-2a), 4.73–4.87 (m, 1H, H-2b), 7.70 (s, 1H, H_{imid}), 8.42 (s, 1H, $HC_{5'}$), 8.77 (s, 1H, H_{imid}); ^{13}C NMR (D_2O, 75.5 MHz) δ [ppm] 35.1 (s, CH_3—N), 52.3 (d, $J = 10.6$ Hz, C-2), 66.9 (d, $J = 160.3$ Hz C-1), 118.1, 125.1, 126.3 (s, H*C*=C), 133.7 (s, HC=*C*), 136.2 (s, N—CH—N); ^{31}P NMR (D_2O, 121.5 MHz) δ [ppm] 18.32. Anal. Calcd. for $C_8H_{12}N_5O_4P \times 1/2H_2O$: C, 34.05; H, 4.64; N, 24.82. Found: C, 34.03; H, 4.53; N, 24.67.

1-Hydroxy-2-(4,5-dimethoxycarbonyl-1,2,3-triazol-1-yl)ethylphosphonic acid 9j. Compound **9j** was obtained as a white solid (0.043 g, 91%); mp: 178–181°C; IR (KBr): ν [cm^{-1}] 3238, 2954, 2910, 1730, 1220, 1024; ^{1}H NMR (D_2O, 300 MHz) δ

[ppm] 3.94 (s, 3H, COOC*H*$_3$), 3.98 (s, 3H, COOC*H*$_3$), 4.34 (dt, $J = 10.1$ Hz, $J = 2.7$ Hz, 1H, H-1), 4.78–5.01 (m, 2H, H-2a, H-2b); ^{13}C NMR (D_2O, 75.5 MHz) δ [ppm] 51.6 (d, $J = 13.5$ Hz, C-2), 52.8 (s, COO*C*H$_3$), 53.4 (s, COO*C*H$_3$) 66.8 (d, $J = 160.0$ Hz, C-1), 131.7 (s, H*C*=C), 139.0 (s, HC=*C*), 159.9 (s, C=O), 162.2 (s, C=O); ^{31}P NMR (D_2O, 121.5 MHz) δ [ppm] 18.27; Anal. Calcd. for $C_8H_{12}N_3O_8P$: C, 31.08; H, 3.91; N, 13.59. Found: C, 31.17; H, 3.77; N, 13.61.

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