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FULL PAPER

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Synthesis and antimicrobial activity of novel 1,2,3-triazole-conjugates of quinazolin-4-ones

Iwona E. Głowacka[1] | Piotr Grzonkowski[1] | Paweł Lisiecki[2] | Łukasz Kalinowski[2] | Dorota G. Piotrowska[1]

[1] Bioorganic Chemistry Laboratory, Faculty of Pharmacy, Medical University of Lodz, Lodz, Poland

[2] Faculty of Pharmacy, Department of Pharmaceutical Microbiology and Microbiological Diagnostics, Medical University of Lodz, Lodz, Poland

Correspondence
Iwona E. Głowacka, Bioorganic Chemistry Laboratory, Faculty of Pharmacy, Medical University of Lodz, Muszyńskiego 1, 90-151 Lodz, Poland.
Email: iwona.glowacka@umed.lodz.pl

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Abstract

A novel series of diethyl{4-[(4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}-alkylphosphonates **9aa**–**aj** and their respective derivatives substituted at C6 of the quinazolinone moiety with a bromine atom (**9ba**–**bj**) or a nitro group (**9ca**–**cj**) were synthesized and assessed for the antibacterial activity toward selected Gram-positive and Gram-negative bacteria. Their antifungal activity was also screened. Compound **9ac** was found to be the most active against *Staphylococcus aureus* ATCC 6535 (MIC 0.625 mg/mL, MBC 1.25 mg/mL), phosphonates **9ab**–**ai** showed promising activity against *Enterococcus faecalis* ATCC 29212 (MIC = 0.625 mg/mL, MBC = 1.25 mg/mL), while compounds **9ac**–**j** appeared the most active toward *Pseudomonas aeruginosa* ATCC 27853 (MIC = 0.625 mg/mL, MBC = 1.25 mg/mL). Antifungal assays of compounds **9aa**–**aj**, **9ba**–**bj**, and **9ca**–**cj** were conducted on *Candida albicans* ATCC 10231 and *Aspergillus brasiliensis* ATCC 16404 and revealed noticeable activity of **9aa**–**aj** (MIC = 1.25 mg/mL).

KEYWORDS
1,2,3-triazoles, antibacterial, antifungal, phosphonates, quinazolin-4-ones

1 | INTRODUCTION

Quinazolines and their carbonyl derivatives, namely quinazolinones, are important structural motifs present in many natural and synthetic compounds exhibiting diverse biological activities like soporific, sedative, antidiabetic, antibacterial, antifungal, anticancer, anticonvulsant, antimalarial, antiinflamatory, antiviral, etc.[1–7] A list of already approved marketed drugs includes several compounds containing quinazoline pharmacophore, e.g., 6,7-dimethoxyquinazolin-4-amine derivatives such as prazosin, terazosin, alfuzosin, and doxazosin.[8,9] It has also been proven that even slight structural modifications in functional groups present in a quinazoline skeleton significantly change pharmacological properties of the compounds. Many substituted derivatives of quinazolin-4-one were obtained so far with intention to test their activity, among them analogues with additional substituents located at C2 and C3. On the other hand, modification or improvement of the biological potency can be also achieved by combination of two or more pharmacophores. Based on this idea various hybrids were designed and screened (Figure 1).

(1,2,4-Triazol-1-yl)-conjugate of quinazolin-4-one **1**, a fungicide known as Albaconazole (UR-9825), shows a broad-spectrum antifungal activity.[10,11] Among substituted 3-(pyrazol-3-yl)aminoquinazolin-4-one derivatives tested for their antibacterial activity, compound **2** was the most active against *Staphylococcus aureus*, *Bacillus subtilis* as well as *Escherichia coli*.[2,12] Recently, compounds **3** and **4** were synthesized based on combination of an 1,2,3-triazole moiety with a quinazolin-4-one pharmacophore and showed promising antibacterial activity against *Klebsiella pneumoniae*, *Escherichia coli*, *Staphylococcus aureus*, and *Bacillus subtilis*. Moreover, they exhibited relatively high antifungal properties against tested species.[13] (1,2,3-Triazole)-containing quinazolin-4-ones

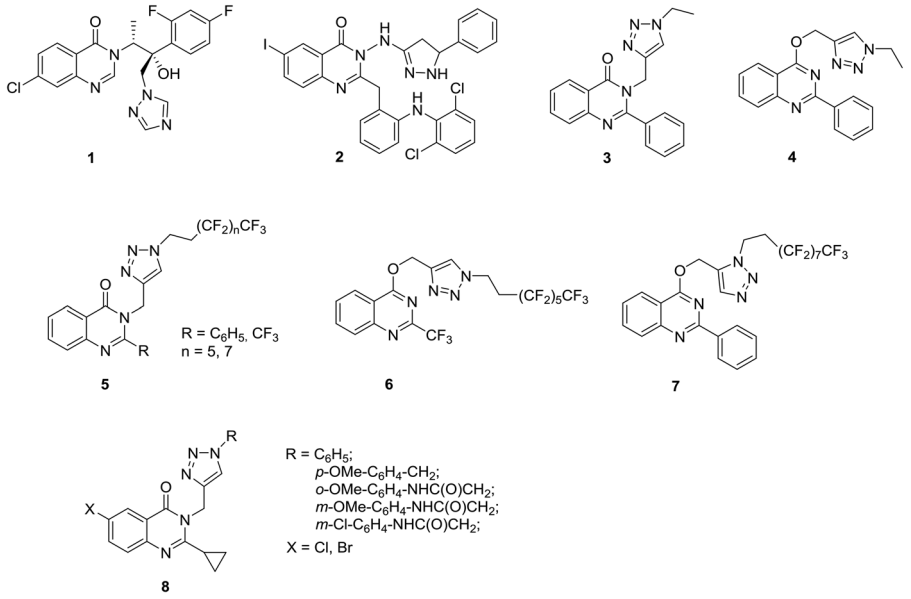


FIGURE 1 Examples of biologically active quinazoline-4-ones

having fluorinated aliphatic side chain showed significant activity against Gram-positive and Gram-negative bacteria. Among all tested analogues, compounds **5**–**7** were the most potent.[14] Rao and co-workers designed and synthesized series of new 1,2,3-triazole derivatives of quinazolin-4-ones **8** having an additional halogen atom incorporated into the quinazolin-4-one skeleton.[15] Among them several compounds exhibited a broad-spectrum activity against Gram-positive and Gram-negative bacteria comparable to ciprofloxacin used as a standard drug. Furthermore, a few of them showed also the antifungal activity toward *Candida albicans* and *Aspergillus niger* higher than fluconazole used as a reference compound.

On the other hand, a phosphonate residue is present in several molecules recognized as inhibitors of certain biosynthetic pathways and are degraded by prokaryotic microorganisms.[16] Following these observations several compounds containing C–P bond attracted a considerable interest in medicinal chemistry.[17–19] Among them substituted alkylphosphonates[20–22] as well as derivatives with various heterocyclic systems should be mentioned.[23–30]

In continuation of our search for biologically active 1,2,3-triazoles,[31–36] a new class of (1,2,3-triazol-1-yl)quinazolin-4-ones **9** was proposed. The aim of these studies was the preparation of a series of compounds having additional phosphonoalkyl group located at C4 in the 1,2,3-triazole ring (Scheme 1). We assumed that incorporation of a phosphonoalkyl residue as an additional pharmacophore may have a positive impact on the antimicrobial activity of obtained compounds.

2 | RESULTS AND DISCUSSION

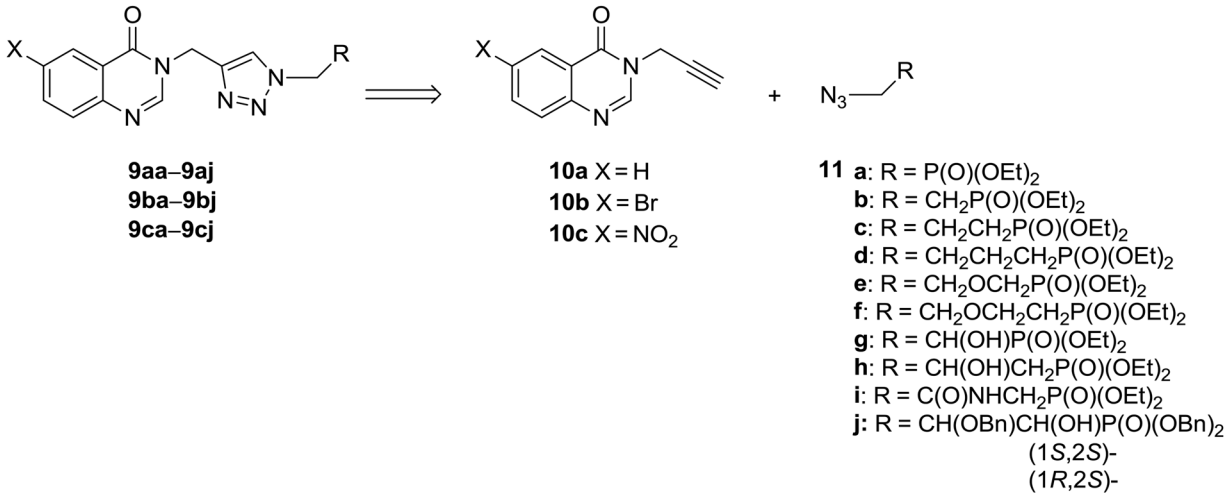
2.1 | Chemistry

Optimized preparative procedures for all ω-azidoalkylphosphonates **11a**–**j** were previously elaborated in our research groups.[31,32,34,37–39] Synthesis of N^3-propargylquinazolin-4-ones **10a** and **10b** via application of a one-pot procedure starting from anthranilic acid **12a** or its derivative **12b** and *N*,*N*-dimethylformamide dimethylacetate have been already described.[40] Furthermore, Lazrek and co-workers as well as Scriba described the synthesis of C2-substituted N^3-propargylquinazolin-4-ones in a two-step procedure, however, formation of N3- and O-substituted products was observed when potassium *tert*-butoxide/potassium carbonate was used for propargylation of the quinazolinone moiety.[41,42]

For the purpose of this paper a two-step procedure was applied (Scheme 2).[41,42] Thus, anthranilic acid **12a** or its substituted derivatives **12b**,**c** were transformed into quinazolin-4-ones **13a**–**c** which were subsequently alkylated with propargyl bromide in the presence of potassium carbonate. Selective formation of N^3-propargylquinazolin-4-ones **10a**–**c** was noticed without traces of *O*-alkylated products. Structures of compounds **10a**–**c** were confirmed based on analysis of the ^{1}H NMR data, since the respective chemical shifts for CH_2 (doublet in the range of 4.85–4.80 ppm) and ≡*CH* (triplet in the range of 2.50–2.60 ppm) protons were observed. At the same time no additional signals at δ *ca.* 5.3 and 2.1 ppm were noticed, which according to the literature data are expected for *O*-alkylated products.[41,42]

The alternative synthetic strategy for the synthesis of compounds **10a**,**b** relies on the transformation of the respective isatoic anhydrides **14a**,**b** into *N*-propargyl 2-amino-benzamides **15a**,**b** and subsequent cyclization to quinazolin-4-ones **10a**,**b** with triethyl orthoformate in the presence of acetic acid (Scheme 3).[42,43] Since installation of a propargyl residue at N3 of the quinazolin-4-one moiety in **10a**,**b** requires prior formation of the respective *N*-propargyl benzamides **15**, structures of the products **10a**,**b** were unambiguously established.

All synthesized N^3-propargylquinazolin-4-ones **10a**–**c** were then subjected to the Cu(I)-catalyzed Hüisgen dipolar cycloaddition with the selected ω-azidoalkyphosphonates **11a**–**j** to produce the respective 1,2,3-triazoles **9aa**–**aj**, **9ba**–**bj**, and **9ca**–**cj** (Scheme 1) in good to



SCHEME 1 Retrosynthesis of quinazolin-4-ones **9**

excellent yields after chromatographic purification and/or crystallization. Their structures and purity were determined by ^{1}H, ^{13}C and ^{31}P NMR and IR spectra as well as by elemental analyses.

2.2 | Antimicrobial activity

The antimicrobial activity of the 1,2,3-triazole conjugates of quinazolin-4-ones **9aa**–**aj**, **9ba**–**bj**, and **9ca**–**cj** was evaluated toward selected bacterial strains: *B. subtilis* ATCC 6633, *S. aureus* ATCC 6535, *E. faecalis* ATCC 29212, *E. coli* ATCC 8739, *P. aeruginosa* ATCC 27853 and two fungal strains: *C. albicans* ATCC 10231 and *Aspergillus brasiliensis* ATCC 16404 (Supporting Information Tables S1–S3). The antimicrobial activity of the compounds was assessed according to their minimal inhibitory concentrations (MIC) and minimal bactericidal concentrations (MBC). Gentamicin and fluconazole were used as antimicrobial standards.

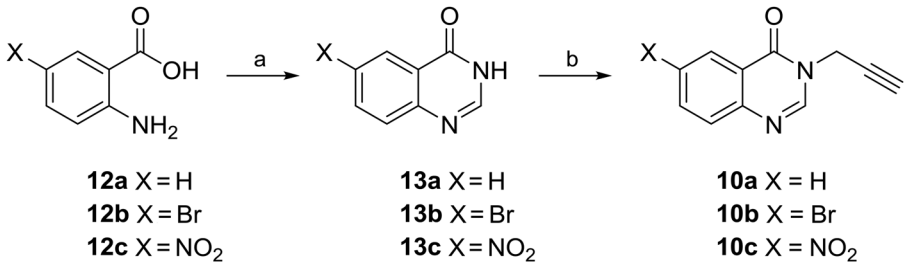
All synthesized compounds (**9aa**–**aj**, **9ba**–**bj**, and **9ca**–**cj**) showed inhibitory activity toward all tested Gram-positive (*B. subtilis* ATCC 6633, *S. aureus* ATCC 6535, *Enterococcus faecalis* ATCC 29212) and Gram-negative (*E. coli* ATCC 8739, *P. aeruginosa* ATCC 27853) bacteria. Compounds **9aa**–**aj** showed potency against all tested bacteria (MIC < 1.25 mg/mL and MBC < 2.5 mg/mL). The most active toward *E. faecalis* ATCC 29212 were compounds **9ab**–**ai** (MIC = 0.625 mg/mL, MBC = 1.25 mg/mL), while **9ac**–**aj** showed noticeable activity against *P. aeruginosa* ATCC 27853 (MIC = 0.625 mg/mL, MBC = 1.25 mg/mL). Moreover, the compound **9ac** exhibited the most promising activity against *S. aureus* ATCC 6535 (MIC 0.625 mg/mL, MBC 1.25 mg/mL).

A significant decrease in activity toward all tested Gram-positive and Gram-negative bacteria was noticed when a bromine atom (**9ba**–**bj**) or the nitro group (**9ca**–**cj**) were incorporated at C6 of the quinazolinone moiety (MIC > 5 mg/mL).

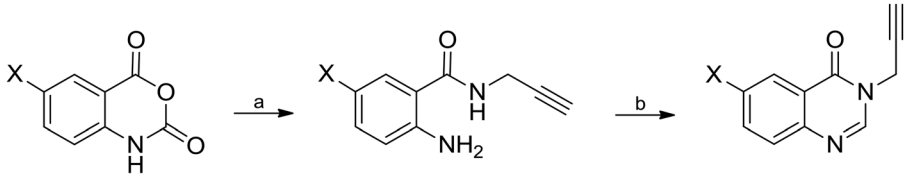
Compounds **9aa**–**aj** having an unsubstituted quinazolinone moiety showed antifungal activity against *C. albicans* ATCC 10231 (MIC = 1.25 mg/mL, MBC = 1.25 mg/mL) and *A. brasiliensis* ATCC 16404 (MIC = 1.25 mg/mL, MBC = 2.5 mg/mL), while analogous compounds substituted at C6 of the quinazolinone skeleton with a bromine atom (**9ba**–**bj**) or the nitro group (**9ca**–**cj**) appear inactive in concentrations up to 5 mg/mL.

3 | CONCLUSIONS

A novel series of diethyl {4-[(4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}alkylphosphonates **9aa**–**aj**, as well as their derivatives substituted at C6 of the quinazolin-4-one moiety with a bromine atom (**9ba**–**bj**) and the nitro group (**9ca**–**cj**) have been synthesized via Cu(I)-catalyzed dipolar cycloaddition of N^3-propargylquinazolin-4-ones **10a**–**c** with the respective ω-azidoalkylphospontates **11a**–**j** under microwave irradiation.



SCHEME 2 Synthesis of N^3-propargylquinazolin-4-ones **10a**–**c**. Reagents and conditions: (a) formamide 150°C, MW, 30 min, (b) propargyl bromide, K_2CO_3, r.t. 24 h



14a X = H
14b X = Br

15a X = H
15b X = Br

10a X = H
10b X = Br

SCHEME 3 Synthesis of N^3-propargylquinazolin-4-ones **10a**,**b**. Reagents and conditions: (a) propargyl amine, DMF, 50°C, 3 h or propargyl amine, H_2O, r.t., 3 h; (b) $(EtO)_3CH$, CH_3COOH, ethanol, 78°C, 4 h

From all synthesized compounds phosphonate **9ac** was the most active against *S. aureus* ATCC 6535 (MIC 0.625 mg/mL, MBC 1.25 mg/mL), quinazoline-4-ones **9ab**–**ai** were the most active toward *E. faecalis* ATCC 29212 (MIC = 0.625 mg/mL, MBC = 1.25 mg/mL), while **9ac**–**j** showed the highest activity against *P. aeruginosa* ATCC 27853 (MIC = 0.625 mg/mL, MBC = 1.25 mg/mL). Quinazolin-4-ones **9aa**–**aj** exhibited potency toward all tested Gram-positive and Gram-negative bacteria, whereas their derivatives having additional substituents at C6 (the nitro group or a bromine atom) in the quinazoline-4-one moiety appeared less active (**9a** vs. **9b** or **9c**).

The antifungal activity against *C. albicans* ATCC 10231 (MIC = 1.25 mg/mL, MBC = 1.25 mg/mL) and *A. brasiliensis* ATCC 16404 (MIC = 1.25 mg/mL, MBC = 2.5 mg/mL) was observed for compounds **9aa**–**aj**, while their analogous possessing a bromine atom (**9ba**–**bj**) or the nitro group (**9ca**–**cj**) at C6 of the quinazolin-4-one skeleton were inactive in concentrations up to 5 mg/mL.

4 | EXPERIMENTAL

4.1 | Chemistry

4.1.1 | General

^{1}H NMR spectra were taken in $CDCl_3$ on the following spectrometers: 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 $CDCl_3$ or DMSO-d_6 solutions on a Bruker Avance III (600 MHz) spectrometer at 151 MHz. ^{31}P NMR spectra were taken in $CDCl_3$ on Varian Mercury-200 at 81 MHz. IR spectral data were measured on a Bruker Alpha-T FT-IR spectrometer. Melting points were determined on a Boetius apparatus and were uncorrected. Elemental analyses were performed by the Microanalytical Laboratory of this faculty on a Perkin Elmer PE 2400 CHNS analyzer.

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.[44]

All microwave irradiation experiments were carried out in microwave reactors Plazmartonika RM 800 or Discover SP CEM. The reaction was carried out in a 50 mL glass vial.

5-Bromoisatoic anhydride was prepared according to the literature.[45]

Commercially available anthranilic acid (≥98%), 5-bromoanthranilic acid (97%), and 5-nitroanthranilic acid (95%) were used without further purification.

The InChI codes of the investigated compounds together with some biological activity data are provided as Supporting Information.

4.1.2 | General procedure for the synthesis of quinazolin-4(3*H*)-ones 13a–c

The mixture of anthranilic acid or 5-bromoanthranilic acid or 5-nitroanthranilic acid (1 mmol) and formamide (1 mmol) was irradiated in the microwave reactor (Discover SP CEM) at 150°C for 30 min. Then the mixture was cooled to room temperature and water (5 mL) was added. The suspension was filtered and crystallized from ethanol to give pure quinazolin-4(3*H*)-ones **13a**–**c**.

Quinazolin-4(3*H*)-one 13a[41]

From anthranilic acid **12a** (5.00 g, 36.5 mmol) and formamide (1.5 mL, 36.5 mmol) the quinazolin-4(3*H*)-one **13a** (4.553 g, 86%) was obtained as a white powder. M.p.: 218–220°C (lit.[41] m.p.: 217–219°C); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 11.52 (brs, 1H, NH), 8.34–8.30 (m, 1H, $H_{aromat.}$), 8.14 (s, 1H, $H_{aromat.}$), 7.89–7.75 (m, 2H, $H_{aromat.}$), 7.56 (ddd, *J* = 8.1 Hz, *J* = 6.2 Hz, *J* = 2.1 Hz, 1H, $H_{aromat.}$).

6-Bromoquinazolin-4(3*H*)-one 13b[46]

From 5-bromoanthranilic acid **12b** (2.00 g, 9.26 mmol) and formamide (0.368 mL, 9.26 mmol) the 6-bromoquinazolin-4-one **13b** (1.946 g, 93%) was obtained as a yellowish solid. M.p.: 271–273°C (lit.[46] m.p.: 273–275°C); ^{1}H NMR (200 MHz, DMSO-d_6): δ = 12.41 (brs, 1H, NH), 8.20–8.18 (m, 1H, $H_{aromat.}$), 8.13 (s, 1H, $H_{aromat.}$), 7.98–7.91 (m, 1H, $H_{aromat.}$), 7.62 (d, *J* = 8.7 Hz, 1H, $H_{aromat.}$).

6-Nitroquinazolin-4(3*H*)-one 13c[47]

From 5-nitroanthranilic acid **12c** (2.01 g, 11.0 mmol) and formamide (0.436 mL, 11.0 mmol) the 6-nitroquinazoline-4-one **13c** (1.809 g, 86%) was obtained as a yellow powder. M.p.: 279–281°C (lit.[47] m.p.: 283–285°C); ^{1}H NMR (200 MHz, DMSO-d_6): δ = 12.65 (brs, 1H, NH), 8.70 (dd, *J* = 2.7 Hz, *J* = 0.3 Hz, 1H, $H_{aromat.}$), 8.45 (ddd, *J* = 9.0 Hz, *J* = 2.7 Hz, *J* = 0.3 Hz, 1H, $H_{aromat.}$), 8.23 (s, 1H, $H_{aromat.}$), 7.77 (d, *J* = 9.0 Hz, 1H, $H_{aromat.}$).

4.1.3 | General procedure for the synthesis of N^3-propargylquinazolin-4(3*H*)-ones 10a–c

To a solution of quinazolin-4-one **13a–c** (1 mmol) in DMF (3 mL), K_2CO_3 (1.2 mmol) and propargyl bromide (1.2 mmol) were added. The suspension was stirred at room temperature for 24 h. Then *N*,*N*-dimethylformamide was co-evaporated with toluene (5 × 10 mL). The residue was partitioned between brine (5 mL) and ethyl acetate (10 mL). The aqueous layer was extracted with ethyl acetate (4 × 10 mL). The organic layer was dried (anhydrous $MgSO_4$), concentrated *in vacuo* and the residue was crystallized to give pure N^3-propargylquinazolin-4-ones **10a–c**.

3-(Prop-2-yn-1-yl)quinazolin-4(3*H*)-one 10a[42]

From quinazolin-4-one **13a** (1.00 g, 6.89 mmol) the 3-(prop-2-yn-1-yl) quinazolin-4-one **10a** (1.202 g, 95%) was obtained as a creamy solid after crystallization from ethyl acetate–hexane mixtures. M.p.: 118–120°C (lit.[42] m.p.: 115–116°C); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.31–8.26 (m, 2H, $H_{aromat.}$), 7.80–7.65 (m, 2H, $H_{aromat.}$), 7.49 (ddd, *J* = 8.2 Hz, *J* = 6.5 Hz, *J* = 1.9 Hz, 1H, $H_{aromat.}$), 4.80 (d, *J* = 2.6 Hz, 2H, CH_2), 2.49 (t, *J* = 2.6 Hz, 1H, CH).

6-Bromo-3-(prop-2-yn-1-yl)quinazolin-4(3*H*)-one 10b[40]

From 6-bromoquinazolin-4-one **13b** (1.00 g, 4.44 mmol) the 6-bromo-3-(prop-2-yn-1-yl)quinazolin-4-one **10b** (1.202 g, 85%) was obtained as a yellow solid after crystallization from methanol. M.p.: 132–134°C (lit.[40] m.p.: 134–136°C.); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.45–8.42 (m, 1H, $H_{aromat.}$), 8.31 (s, 1H, $H_{aromat.}$), 7.85 (ddd, *J* = 8.7 Hz, *J* = 2.3 Hz, *J* = 0.3 Hz, 1H, $H_{aromat.}$), 7.60 (d, *J* = 8.7 Hz, 1H, $H_{aromat.}$), 4.81 (d, *J* = 2.6 Hz, 2H, CH_2), 2.51 (t, *J* = 2.6 Hz, 1H, CH).

6-Nitro-3-(prop-2-yn-1-yl)quinazolin-4(3*H*)-one 10c

From 6-nitroquinazolin-4-one **13c** (0.624 g, 3.26 mmol) the 6-nitro-3-(prop-2-yn-1-yl)quinazolin-4-one **10c** (0.657 g, 88%) was obtained as a pale solid after crystallization from methanol. M.p.: 132–134°C; IR (KBr): ν = 3258, 3099, 3073, 2962, 2927, 1699, 1613, 1601, 1517, 1349, 893 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 9.19 (dd, *J* = 2.6 Hz, *J* = 0.4 Hz, 1H, $H_{aromat.}$), 8.56 (dd, *J* = 9.0 Hz, *J* = 2.6 Hz, 1H, $H_{aromat.}$), 8.46 (s, 1H, $H_{aromat.}$), 7.87 (d, *J* = 9.0 Hz, 1H, $H_{aromat.}$), 4.85 (d, *J* = 2.6 Hz, 2H, CH_2), 2.57 (t, *J* = 2.6 Hz, 1H, CH); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 159.27 (s, C═O), 151.94, 147.94, 146.24, 129.37, 128.54, 123.38, 122.00, 76.15, 75.62, 35.64. Anal. calcd. for $C_{11}H_7N_3O_3$: C, 57.65; H, 3.08; N, 18.33. Found: C, 57.48; H, 3.12; N, 18.32.

4.1.4 | Synthesis of 2-amino-*N*-(prop-2-yn-1-yl)-benzamides 15a,b from the respective isatoic anhydrides 14a,b

Synthesis of 2-amino-*N*-(prop-2-yn-1-yl)benzamides 15a,b, general procedure

Method A: To a solution of the respective isatoic anhydride **14a**,**b** (1.00 mmol) in DMF (2 mL) propargyl amine (1.00 mmol) was added and stirred at 50°C for 3 h. Then the mixture was cooled to room temperature, water (5 mL) was added and the precipitated product was filtered and dried on air to give pure 2-amino-*N*-(prop-2-yn-1-yl) benzamide **15a**,**b**.

Method B: To a solution of the respective isatoic anhydride **14a**,**b** (1.00 mmol) in water (2 mL) propargyl amine (1.00 mmol) was added and stirred to room temperature for 3 h. The solid was filtered and dried on air to give pure 2-amino-*N*-(prop-2-yn-1-yl)benzamide **15a**,**b**.

2-Amino-*N*-(prop-2-yn-1-yl)benzamide 15a

According to the general procedure (method A) from the isatoic anhydride **14a** (0.600 g, 3.68 mmol) and propargyl amine (0.256 mL, 3.60 mmol) pure 2-amino-*N*-(prop-2-yn-1-yl)benzamide **15a** (0.461 g, 72%) was obtained as a white powder. M.p.: 85–87°C (lit.[48] m.p.: 86–88°C).

According to the general procedure (method B) from the isatoic anhydride **14a** (1.066 g, 6.53 mmol) and propargyl amine (0.418 mL, 6.53 mmol) 2-amino-*N*-(prop-2-yn-1-yl)benzamide **15a** (0.953 g, 84%) was obtained as a white powder. M.p: 85–87°C (lit.[48] m.p.: 86–88°C).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.31–8.26 (m, 2H, $H_{aromat.}$), 7.80–7.65 (m, 2H, $H_{aromat.}$), 6.10 (brs, 1H, NH), 5.51 (brs, 2H, NH_2), 4.06 (dd, *J* = 5.1 Hz, *J* = 2.5 Hz, 2H, CH_2), 2.25 (t, *J* = 2.5 Hz, 1H, CH).

2-Amino-5-bromo-*N*-(prop-2-yn-1-yl)benzamide 15b

According to the general procedure (method A) from 5-bromoisatoic anhydride **14b** (0.150 g, 0.620 mmol) and propargyl amine (0.041 mL, 0.620 mmol), 2-amino-5-bromo-*N*-(prop-2-yn-1-yl)benzamide **15b** (0.101 g, 64%) was obtained as a yellow powder. M.p.: 126–127°C (lit.[49] m.p.: 125–126°C).

According to the general procedure (method B) from 5-bromoisatoic anhydride **14b** (0.100 g, 0.413 mmol) and propargyl amine (0.027 mL, 0.413 mmol), 2-amino-5-bromo-*N*-(prop-2-yn-1-yl)-benzamide **15b** (0.079 g, 75%) was isolated as a yellowish powder. M.p. = 126–127°C (lit.[49] m.p.: 125–126°C).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.43 (d, *J* = 2.1 Hz, 1H, $H_{aromat.}$), 7.31 (d, *J* = 8.7 Hz, *J* = 2.1 Hz, 1H, $H_{aromat.}$), 6.57 (d, *J* = 8.7 Hz, 1H, $H_{aromat.}$), 6.14 (brs, 1H, NH), 5.55 (brs, 2H, NH_2), 4.19 (dd, *J* = 5.2 Hz, *J* = 2.6 Hz, 2H, CH_2), 2.30 (t, *J* = 2.6 Hz, 1H, CH).

4.1.5 | Synthesis of N^3-propargylquinazolin-4-ones 10a,b from 2-amino-*N*-(prop-2-yn-1-yl)benzamides 15a,b, general procedure

To a solution of 2-amino-*N*-(prop-2-yn-1-yl)benzamides **15a**,**b** (1.00 mmol) in ethanol (5 mL) acetic acid (1.7 mmol) and triethyl orthoformate (1.1 mmol) were added and stirred at 78°C for 4 h. Then the mixture was cooled at room temperature and was extracted with dichloromethane (4 × 10 mL). The organic layer was dried (anhydrous $MgSO_4$), concentrated *in vacuo* and the residue was crystallized to give pure N^3-propargylquinazolin-4-ones **10a**,**b**.

3-(Prop-2-yn-1-yl)quinazolin-4(3*H*)-one 10a

According to the general procedure from 2-amino-*N*-(prop-2-yn-1-yl)-benzamide **15a** (0.500 g, 2.87 mmol), acetic acid (0.284 mL, 4.88 mmol, 1.7 eq.) and triethyl orthoformate (0.600 mL, 3.16 mmol, 1.1 eq.) N^3-propargylquinazolin-4-one **10a** (0.444 g, 84%) was obtained after crystallization from ethyl acetate–hexane mixtures as a creamy solid.

6-Bromo-3-(prop-2-yn-1-yl)quinazolin-4(3*H*)-one 10b

According to the general procedure from 2-amino-6-bromo-*N*-(prop-2-yn-1-yl)benzamide **15b** (0.100 g, 0.359 mmol), acetic acid (0.035 mL, 0.610 mmol, 1.7 eq.) and triethyl orthoformate (0.066 mL, 0.395 mmol, 1.1 eq.) pure 6-bromo-3-(prop-2-yn-1-yl)quinazolin-4(3*H*)-one **10b** (0.089 g, 86%) was obtained after crystallization from methanol.

4.1.6 | General procedure for the preparation of 1,2,3-triazoles 9aa–cj

To a solution of ω-azidoalkylphosphonate **11** (1.00 mmol) in EtOH (1 mL) and H_2O (1 mL), $CuSO_4 \times 5H_2O$ (0.05 mmol), sodium ascorbate (0.10 mmol) and alkynes **13** (1.00 mmol) were added. The suspension was microwave irradiated in the microwave reactor (Plazmatronika RM 800, 800 W) at 35–45°C for 2 min. After cooling the solvent was removed by vacuum evaporation. The residue was suspended in dry chloroform (5 mL) and filtered through a layer of Celite. The solution was concentrated *in vacuo* and the crude product was purified on a silica gel column with chloroform–methanol mixtures (100:1, v/v) or by crystallization to give the respective 1,2,3-triazoles **9**.

Diethyl {4-[4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}methylphosphonate 9aa

From diethyl azidomethylphosphonate **11a** (0.072 g, 0.373 mmol) and N^3-propargylquinazolin-4(3*H*)-one **13a** (0.068 g, 0.373 mmol) a phosphonate **9aa** (0.090 g, 64%) was obtained as a white powder after purification on a silica gel column with chloroform–methanol mixtures (100:1, v/v). M.p.: 131–132°C; IR (KBr): ν = 3423, 3145, 3081, 2987, 2937, 1675, 1611, 1475, 1248, 1023, 776, 756 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 8.33 (s, 1H), 8.29–8.25 (m, 1H, $H_{aromat.}$), 7.95 (s, 1H, *H*C5′), 7.80–7.65 (m, 2H, $H_{aromat.}$), 7.55–7.45 (m, 1H, $H_{aromat.}$), 5.27 (s, 2H, CH_2), 4.74 (d, *J* = 13.1 Hz, 2H, PCH_2), 4.19–4.06 (m, 4H, 2 × POCH_2CH$_3$), 1.26 (t, *J* = 7.1 Hz, 6H, 2 × POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 160.89 (s, CO), 148.18, 146.19, 142.70, 134.38, 127.68, 127.34, 126.50, 124.73, 122.01, 63.50 (d, *J* = 6.6 Hz, POC), 45.95 (d, *J* = 155.3 Hz, PC), 41.61, 16.23 (d, *J* = 5.6 Hz, POC*C*); ^{31}P NMR (81 MHz, $CDCl_3$): δ = 16.27 ppm. Anal. calcd. for $C_{16}H_{20}N_5O_4P$: C, 50.93; H, 5.34; N, 18.56. Found: C, 50.95; H, 5.22; N, 18.32.

Diethyl 2-{4-[4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}ethylphosphonate 9ab

From diethyl 2-azidoethylphosphonate **11b** (0.069 g, 0.333 mmol) and N^3-propargylquinazolin-4(3*H*)-one **13a** (0.061 g, 0.333 mmol), a phosphonate **9ab** (0.101 g, 78%) was obtained as a colorless oil after purification on a silica gel column with chloroform–methanol mixtures (100:1, v/v). IR (film): ν = 3364, 3143, 3072, 2987, 2932, 1676, 1611, 1474, 1224, 1049, 754 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 8.34 (s, 1H), 8.29–8.24 (m, 1H, $H_{aromat.}$), 7.81 (s, 1H, *H*C5′), 7.80–7.66 (m, 2H, $H_{aromat.}$), 7.54–7.45 (m, 1H, $H_{aromat.}$), 5.25 (s, 2H, CH_2), 4.64–4.50 (m, 2H, PCH_2), 4.12–3.98 (m, 4H, 2 × POCH_2CH$_3$), 2.47–2.30 (m, 2H, PCCH_2), 1.25 (t, *J* = 7.0 Hz, 6H, 2 × POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 160.97 (s, C═O), 148.19, 146.22, 142.29, 134.43, 127.68, 127.39, 126.50, 124.10, 121.98, 62.18 (d, *J* = 6.5 Hz, POC), 44.69, 41.68, 27.18 (d, *J* = 141.5 Hz, PC), 16.30 (d, *J* = 6.0 Hz, POC*C*); ^{31}P NMR (81 MHz, $CDCl_3$): δ = 26.01 ppm. Anal. calcd. for $C_{17}H_{22}N_5O_4P$: C, 52.17; H, 5.67; N, 17.89. Found: C, 51.98; H, 5.88; N, 18.12.

Diethyl 3-{4-[4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}propylphosphonate 9ac

From diethyl 3-azidopropylphosphonate **11c** (0.065 g, 0.294 mmol) and N^3-propargylquinazolin-4(3*H*)-one **13a** (0.054 g, 0.294 mmol), a phosphonate **9ac** (0.099 g, 83%) was obtained as a colorless oil after purification on a silica gel column with chloroform–methanol mixtures (100:1, v/v). IR (film): ν = 3285, 3144, 2985, 2909, 1676, 1612, 1475, 1225, 1026, 777 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 8.34 (s, 1H), 8.30–8.25 (m, 1H, $H_{aromat.}$), 7.80–7.60 (m, 3H, 2H, $H_{aromat.}$, *H*C5′), 7.54–7.50 (m, 1H, $H_{aromat.}$), 5.26 (s, 2H, CH_2), 4.42 (t, *J* = 7.0 Hz, 2H, PCCCH_2), 4.16–3.95 (m, 4H, 2 × POCH_2CH$_3$), 2.31–2.09 (m, 2H, PCCH_2), 1.79–1.61 (m, 2H, PCH_2), 1.29 (t, *J* = 7.1 Hz, 6H, 2 × POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 160.99 (s, CO), 148.20, 146.26, 142.34, 134.41, 127.68, 127.36, 126.52, 123.94, 122.01, 61.84 (d, *J* = 6.6 Hz, POC), 50.15 (d, *J* = 15.2 Hz, PCC*C*), 41.71, 23.58 (d, *J* = 4.5 Hz, PCC), 22.63 (d, *J* = 143.2 Hz, PC), 16.40 (d, *J* = 5.9 Hz, POC*C*); ^{31}P NMR (81 MHz, $CDCl_3$): δ = 30.65 ppm. Anal. calcd. for $C_{18}H_{24}N_5O_4P$: C, 53.33; H, 5.97; N, 17.28. Found: C, 53.58; H, 6.19; N, 17.52.

Diethyl 4-{4-[4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}butylphosphonate 9ad

From diethyl 4-azidobutylphosphonate **11d** (0.054 g, 0.230 mmol) and N^3-propargylquinazolin-4(3*H*)-one **13a** (0.042 g, 0.230 mmol), a phosphonate **9ad** (0.068 g, 71%) was obtained as a colorless oil after purification on a silica gel column with chloroform–methanol mixtures (100:1, v/v). IR (film): ν = 3286, 3144, 2985, 2985, 1677, 1612, 1475, 1225, 1052, 1026, 777, 754 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 8.34 (s, 1H), 8.30–8.24 (m, 1H, $H_{aromat.}$), 7.79–7.67 (m, 3H, 2H, $H_{aromat.}$, *H*C5′), 7.53–7.45 (m, 1H, $H_{aromat.}$), 5.25 (s, 2H, CH_2), 4.32 (t, *J* = 7.1 Hz, 2H, PCCCCH_2), 4.14–3.96 (m, 4H, 2 × POCH_2CH$_3$), 2.07–1.92 (m, 2H, PCCCH_2), 1.84–1.50 (m, 4H, PCH_2, PCCH_2), 1.27 (t, *J* = 7.1 Hz, 6H, 2 × POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 161.00 (s, CO), 148.22, 146.27, 142.33, 134.40, 127.70, 127.35, 126.51, 123.60, 122.02, 61.61 (d, *J* = 6.6 Hz, POC), 49.83, 41.72, 30.65 (d, *J* = 15.3 Hz, PCCC); 25.0 (d, *J* = 142.1 Hz, PC); 19.69 (d, *J* = 4.7 Hz, PCC); 16.41 (d, *J* = 5.9 Hz, POC*C*); ^{31}P NMR (81 MHz, $CDCl_3$): δ = 31.65 ppm. Anal. calcd. for $C_{19}H_{26}N_5O_4P$: C, 54.41; H, 6.25; N, 16.70. Found: C, 54.68; H, 6.02; N, 17.00.

Diethyl 2-{4-[4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}ethoxymethylphosphonate 9ae

From diethyl (2-azidoethoxy)methylphosphonate **11e** (0.080 g, 0.337 mmol) and N^3-propargylquinazolin-4(3*H*)-one **13a** (0.062 g, 0.337 mmol), a phosphonate **9ae** (0.128 g, 78%) was obtained as a colorless oil after purification on a silica gel column with chloroform–methanol mixtures (100:1, v/v). IR (film): ν = 3436, 3128, 2984, 2931, 1678, 1612, 1475, 1230, 1027, 777 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 8.36 (s, 1H), 8.30–8.25 (m, 1H, $H_{aromat.}$), 7.88 (s, 1H, *H*C5′), 7.80–7.67 (m, 2H, $H_{aromat.}$), 7.54–7.46 (m, 1H, $H_{aromat.}$), 5.27 (s, 2H, CH_2), 4.53 (t, *J* = 4.8 Hz, 2H, OCH_2CH_2N), 4.17–4.02 (m, 4H, 2 × $POCH_2CH_3$), 3.97 (t, *J* = 4.8 Hz, 2H, OCH_2CH_2N), 3.75 (d, *J* = 8.1 Hz, 2H, PCH_2O), 1.29 (t, *J* = 7.1 Hz, 6H, 2 × $POCH_2CH_3$); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 160.88 (s, CO), 148.16, 146.32, 142.30, 134.37, 127.65, 127.33, 126.54, 124.68, 122.04, 71.10 (d, *J* = 10.0 Hz, OCH_2CH_2N), 65.35 (d, *J* = 166.5 Hz, PC), 62.52 (d, *J* = 6.6 Hz, POC), 50.18 (s, OCH_2CH_2N), 41.47, 16.42 (d, *J* = 5.6 Hz, POC*C*); ^{31}P NMR (81 MHz, $CDCl_3$): δ = 21.12 ppm. Anal. calcd. for $C_{18}H_{24}N_5O_5P$: C, 51.30; H, 5.74; N, 16.62. Found: C, 51.55; H, 6.02; N, 16.39.

Diethyl 2-{4-[4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}ethoxyethylphosphonate 9af

From diethyl 2-(2-azidoethoxy)ethylphosphonate **11f** (0.063 g, 0.251 mmol) and N^3-propargylquinazolin-4(3*H*)-one **13a** (0.046 g, 0.251 mmol), a phosphonate **9af** (0.090 g, 88%) was obtained as a colorless oil after purification on a silica gel column with chloroform–methanol mixtures (100:1, v/v). IR (film): ν = 3384, 3118, 2986, 2925, 1676, 1613, 1475, 1135, 1027, 777 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 8.35 (s, 1H), 8.31–8.26 (m, 1H, $H_{aromat.}$), 7.89 (s, 1H, *H*C5′), 7.80–7.67 (m, 2H, $H_{aromat.}$), 7.53–7.45 (m, 1H, $H_{aromat.}$), 5.27 (s, 2H, CH_2), 4.50 (t, *J* = 5.0 Hz, 2H, OCH_2CH_2N), 4.13–3.98 (m, 4H, 2 × $POCH_2CH_3$), 3.79 (t, *J* = 5.0 Hz, 2H, OCH_2CH_2N), 3.67 (dt, *J* = 11.9 Hz, *J* = 7.3 Hz, 2H, PCH_2CH_2O), 2.05 (dt, *J* = 18.7 Hz, *J* = 7.3 Hz, 2H, PCH_2CH_2O), 1.29 (t, *J* = 7.1 Hz, 6H, 2 × $POCH_2CH_3$); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 160.92 (s, C═O), 148.15, 146.37, 142.15, 134.34, 127.62, 127.31, 126.55, 124.75, 122.05, 68.79 (s, OCH_2CH_2N), 65.25 (s, PCH_2CH_2O), 61.71 (d, *J* = 6.5 Hz, POC), 50.26 (s, OCH_2CH_2N), 41.55, 26.81 (d, *J* = 140.6 Hz, PC), 16.39 (d, *J* = 6.3 Hz, POC*C*); ^{31}P NMR (81 MHz, $CDCl_3$): δ = 28.64 ppm. Anal. calcd. for $C_{19}H_{26}N_5O_5P$: C, 52.41; H, 6.02; N, 16.08. Found: C, 52.14; H, 6.28; N, 15.83.

Diethyl 1-hydroxy-2-{4-[4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}ethylphosphonate 9ag

From diethyl 2-azido-1-hydroxyethylphosphonate **11g** (0.074 g, 0.332 mmol) and N^3-propargylquinazolin-4(3*H*)-one **13a** (0.061 g, 0.332 mmol), a phosphonate **9ag** (0.141 g, 81%) was obtained as a white powder after purification on a silica gel column with chloroform–methanol mixtures (100:1, v/v). M.p.: 130–132°C; IR (KBr): ν = 3267, 3159, 2910, 1676, 1613, 1476, 1217, 1048, 756 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 8.32 (s, 1H), 8.21–8.16 (m, 1H, $H_{aromat.}$), 7.97 (s, 1H, *H*C5′), 7.76–7.62 (m, 2H, $H_{aromat.}$), 7.49–7.41 (m, 1H, $H_{aromat.}$), 5.26 (AB, *J* = 14.8 Hz, 1H, CH_aH_b), 5.23 (AB, *J* = 14.8 Hz, 1H, CH_aH_b), 4.76 (ddd, *J* = 14.6 Hz, *J* = 5.1 Hz, *J* = 2.6 Hz, 1H, $PCCH_aH_b$), 4.53–4.38 (m, 1H, $PCCH_aH_b$), 4.35–4.07 (m, 5H, P*CH*(OH), 2 × $POCH_2CH_3$), 1.30 (t, *J* = 7.0 Hz, 3H, $POCH_2CH_3$), 1.29 (t, *J* = 7.0 Hz, 3H, $POCH_2CH_3$); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 160.83 (s, CO), 147.83, 146.45, 141.97, 134.42, 127.41, 127.38, 126.49, 125.48, 121.87, 67.03 (d, *J* = 164.7 Hz, PC), 63.51 (d, *J* = 7.4 Hz, POC); 63.32 (d, *J* = 7.4 Hz, POC), 51.72 (d, *J* = 9.3 Hz, PC*C*), 41.57, 16.41 (d, *J* = 5.37 Hz, POC*C*); ^{31}P NMR (81 MHz, $CDCl_3$): δ = 20.90 ppm. Anal. calcd. for $C_{17}H_{22}N_5O_5P$: C, 50.12; H, 5.44; N, 17.19. Found: C, 50.27; H, 5.48; N, 17.30.

Diethyl 2-hydroxy-3-{4-[4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}propylphosphonate 9ah

From diethyl 3-azido-2-hydroxypropylphosphonate **11h** (0.072 g, 0.304 mmol) and N^3-propargylquinazolin-4(3*H*)-one **13a** (0.055 g, 0.304 mmol), a phosphonate **9ah** (0.121 g, 96%) was obtained as a white powder after purification on a silica gel column with chloroform–methanol mixtures (100:1, v/v). M.p.: 132–133°C; IR (KBr): ν = 3267, 3159, 2910, 1676, 1613, 1476, 1217, 1048, 756 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.36 (s, 1H), 8.26 (d, *J* = 8.0 Hz, 1H, $H_{aromat.}$), 7.95 (s, 1H, *H*C5′), 7.76–7.69 (m, 2H, $H_{aromat.}$), 7.45 (t, *J* = 7.3 Hz, 1H, $H_{aromat.}$), 5.29 (AB, *J* = 15.1 Hz, 1H, CH_aH_b), 5.26 (AB, *J* = 15.1 Hz, 1H, CH_aH_b), 4.54 (dd, *J* = 17.0 Hz, *J* = 6.1 Hz, 1H, $PCCCH_aH_b$), 4.42–4.36 (m, 2H, PCC*H*(OH), $PCCCH_aH_b$), 4.15–4.07 (m, 4H, 2 × $POCH_2CH_3$), 2.00 (ddd, 1H, *J* = 18.9 Hz, *J* = 15.4 Hz, *J* = 3.5 Hz, PCH_aH_b), 1.97 (ddd, 2H, *J* = 16.7 Hz, *J* = 15.4 Hz, *J* = 8.3 Hz, PCH_aH_b), 1.32 (t, *J* = 7.1 Hz, 3H, $POCH_2CH_3$), 1.31 (t, *J* = 7.1 Hz, 3H, $POCH_2CH_3$); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 160.86 (s, C═O), 148.04, 146.35, 141.90, 134.36, 127.54, 127.33, 126.57, 125.37, 122.01, 65.49 (d, *J* = 3.5 Hz, PC*C*), 62.30 (d, *J* = 6.4 Hz, POC), 62.23 (d, *J* = 6.4 Hz, POC), 55.96 (d, *J* = 17.7 Hz, PCCC), 41.56, 30.77 (d, *J* = 140.6 Hz, PC), 16.40 (d, *J* = 5.7 Hz, POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$): δ = 28.09 ppm. Anal. calcd. for $C_{18}H_{24}N_5O_5P$: C, 51.30; H, 5.74; N, 16.62. Found: C, 51.08; H, 5.95; N, 16.33.

Diethyl {2-[4-(4-oxoquinazolin-3(4*H*)-yl)methyl)-1*H*-1,2,3-triazol-1-yl]acetamido}methylphosphonate 9ai

From diethyl (2-azidoacetamido)methylphosphonate **11i** (0.074 g, 0.296 mmol) and N^3-propargylquinazolin-4(3*H*)-one **13a** (0.054 g, 0.296 mmol), a phosphonate **9ai** (0.115 g, 90%) was obtained as a white powder after purification on a silica gel column with chloroform–methanol mixtures (100:1, v/v). M.p.: 210–211°C; IR (KBr): ν = 3289, 3070, 2993, 1680, 1612, 1475, 1218, 1051, 1027, 756 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 8.37 (s, 1H), 8.28–8.24 (m, 1H, $H_{aromat.}$), 7.98 (s, 1H, *H*C5′), 7.80–7.67 (m, 2H, $H_{aromat.}$), 7.61 (brt, *J* = 6.0 Hz, 1H, NH), 7.53–7.44 (m, 1H, $H_{aromat.}$), 5.28 (s, 2H, CH_2), 5.10 (s, 2H, CH_2), 4.15–4.00 (m, 4H, 2 × $POCH_2CH_3$), 3.70 (dd, *J* = 12.3 Hz, *J* = 5.9 Hz, 2H, PCH_2), 1.26 (t, *J* = 7.1 Hz, 6H, 2 × $POCH_2CH_3$); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 165.04 (d, *J* = 6.1 Hz, C═O), 160.97 (s, C═O), 148.21, 146.27, 142.58, 134.41, 127.69, 127.373, 126.54, 125.43, 122.02, 62.98 (d, *J* = 6.6 Hz, POC), 52.46 (s, CH_2N), 41.65, 34.92 (d, *J* = 157.6 Hz, PC), 16.30 (d, *J* = 5.6 Hz, POC*C*); ^{31}P NMR (81 MHz,

$CDCl_3$): δ = 22.30 ppm. Anal. calcd. for $C_{18}H_{23}N_6O_5P$: C, 49.77; H, 5.34; N, 19.35. Found: C, 49.91; H, 5.15; N, 19.68.

(1*S*,2*S*)-Dibenzyl 2-benzyloxy-1-hydroxy-3-{4-[4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}propylphosphonate (1*S*,2*S*)-9aj

From (1*S*,2*S*)-dibenzyl 3-azido-2-benzyloxy-1-hydroxypropylphosphonate **11j** (0.050 g, 0.109 mmol) and N^3-propargylquinazolin-4(3*H*)-one **13a** (0.020 g, 0.109 mmol), a phosphonate (1*S*,2*S*)-**9aj** (0.064 g, 92%) was obtained as a white solid after purification on a silica gel column with chloroform–methanol mixtures (100:1, v/v) and crystallization from ethyl acetate–petroleum ether. $[\alpha]_D^{20}$ = −7.7 (*c* = 1.39 in $CHCl_3$); m.p.: 96–97°C; IR (KBr): ν = 3282, 3065, 3032, 2996, 1679, 1612, 1497, 1475, 1218, 1024, 776, 752, 698 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 8.33 (s, 1H), 8.28–8.23 (m, 1H, $H_{aromat.}$), 7.80–7.68 (m, 3H, $H_{aromat.}$, *H*C5′), 7.52–7.44 (m, 1H, $H_{aromat.}$), 7.37–7.27 (m, 10H, H_{aromat}), 7.22–7.13 (m, 3H, H_{aromat}), 7.11–7.06 (m, 2H, H_{aromat}), 5.23 (AB, *J* = 14.8 Hz, 1H, C*H*$_a$H$_b$), 5.17 (AB, *J* = 14.8 Hz, 1H, CH$_a$*H*$_b$), 5.06–5.00 (m, 4H, 2 × POCH_2Ph), 4.60–4.37 (m, 3H, OC*H*$_a$H$_b$Ph, H-3a, H-3b), 4.32–4.22 (m, 1H, H-2), 4.19 (d, *J* = 10.8 Hz, 1H, OCH$_a$*H*$_b$Ph), 3.86 (brd, *J* = 8.0 Hz, 1H, H-1), 3.16 (brs, 1H, OH); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 160.85 (s, C═O), 148.11, 146.40, 142.12, 136.83, 135.95 (d, *J* = 5.6 Hz, C_{ipso}), 135.80 (d, *J* = 5.6 Hz, C_{ipso}), 134.37, 128.66, 128.64, 128.58, 128.35, 128.27, 128.18, 128.12, 128.04, 127.62, 127.32, 126.56, 125.24, 121.99, 74.08 (s, PCC), 68.58 (d, *J* = 6.8 Hz, POC), 68.37 (d, *J* = 162.0 Hz, PC), 68.28 (d, *J* = 6.8 Hz, POC), 50.78 (d, *J* = 11.7 Hz, PCCC), 41.50; ^{31}P NMR (81 MHz, $CDCl_3$): δ = 22.51 ppm. Anal. calcd. for $C_{35}H_{34}N_5O_6P$: C, 64.51; H, 5.26; N, 10.70. Found: C, 64.60; H, 5.03; N, 10.77.

(1*R*,2*S*)-Dibenzyl 2-benzyloxy-1-hydroxy-3-{4-[4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}propylphosphonate (1*R*,2*S*)-9aj

From (1*R*,2*S*)-dibenzyl 3-azido-2-benzyloxy-1-hydroxypropylphosphonate **11j** (0.050 g, 0.109 mmol) and N^3-propargylquinazolin-4(3*H*)-one **13a** (0.020 g, 0.109 mmol), a phosphonate (1*R*,2*S*)-**9aj** (0.056 g, 80%) was obtained as a white solid after purification on a silica gel column with chloroform–methanol mixtures (50:1, v/v) and crystallization from ethyl acetate–petroleum ether. $[\alpha]_D^{20}$ = +2.7 (*c* = 1.08 in $CHCl_3$); m.p.: 76–78°C; IR (KBr): ν = 3282, 3065, 3032, 2996, 1679, 1612, 1497, 1475, 1218, 1024, 776, 752, 698 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 8.34 (s, 1H), 8.30–8.23 (m, 1H, $H_{aromat.}$), 7.82–7.68 (m, 3H, $H_{aromat.}$, *H*C5′), 7.52–7.44 (m, 1H, $H_{aromat.}$), 7.36–7.24 (m, 10H, H_{aromat}), 7.21–7.13 (m, 3H, H_{aromat}), 7.11–7.03 (m, 2H, H_{aromat}), 5.23 (AB, *J* = 14.6 Hz, 1H, C*H*$_a$H$_b$), 5.18 (AB, *J* = 14.6 Hz, 1H, CH$_a$*H*$_b$), 5.06–4.99 (m, 4H, 2 × POCH_2Ph), 4.70 (dd, *J* = 14.6 Hz, *J* = 3.7 Hz, 1H, H-3a), 4.59 (dd, *J* = 14.6 Hz, *J* = 6.5 Hz, 1H, H-3b), 4.39 (AB, *J* = 11.3 Hz, 1H, OC*H*$_a$H$_b$Ph), 4.28 (d, *J* = 11.3 Hz, 1H, OCH$_a$*H*$_b$Ph), 4.19–4.07 (m, 1H, H-2), 3.97 (dd, *J* = 8.9 Hz, *J* = 5.7 Hz, 1H, H-1), 3.61 (brs, 1H, OH); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 160.85 (s, C═O), 148.12, 146.44, 141.95, 136.77, 135.92 (d, *J* = 5.5 Hz, C_{ipso}), 135.83 (d, *J* = 5.5 Hz, C_{ipso}), 134.35, 128.63, 128.60, 128.57, 128.38, 128.15, 128.12, 128.00, 127.61, 127.31, 126.56, 125.35, 122.00, 74.73 (d, *J* = 5.3 Hz, PCC), 72.80, 68.52 (d, *J* = 7.2 Hz, POC), 68.40 (d, *J* = 7.2 Hz, POC), 67.86, (d, *J* = 160.8 Hz, PC), 50.35 (d, *J* = 5.9 Hz, PCCC), 41.46; ^{31}P NMR (81 MHz, $CDCl_3$): δ = 23.59 ppm. Anal. calcd. for $C_{35}H_{34}N_5O_6P$: C, 64.51; H, 5.26; N, 10.70. Found: C, 64.77; H, 5.34; N, 10.45.

Diethyl {4-[6-bromo-4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}methylphosphonate 9ba

From diethyl azidomethylphosphonate **11a** (0.062 g, 0.321 mmol) and 6-bromo-N^3-propargylquinazolin-4(3*H*)-one **13b** (0.084 g, 0.321 mmol), a phosphonate **9ba** (0.124 g, 85%) was obtained as white needles after purification on a silica gel column with chloroform–methanol mixtures (100:1, v/v) and crystallization from diethyl ether. M.p.: 145–146°C; IR (KBr): ν = 3406, 3144, 3072, 2986, 2933, 1666, 1608, 1468, 1238, 1023, 799 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 8.39 (dd, *J* = 2.3 Hz, *J* = 0.4 Hz, 1H, $H_{aromat.}$), 8.34 (s, 1H), 7.94 (s, 1H, *H*C5′), 7.82 (dd, *J* = 8.7 Hz, *J* = 2.3 Hz, 1H, $H_{aromat.}$), 7.58 (d, *J* = 8.7 Hz, 1H, $H_{aromat.}$), 5.26 (s, 2H, CH_2), 4.73 (d, *J* = 13.1 Hz, 2H, PCH_2), 4.20–4.05 (m, 4H, 2 × POCH_2CH$_3$), 1.28 (t, *J* = 7.1 Hz, 3H, POCH$_2$C*H*$_3$), 1.27 (t, *J* = 7.1 Hz, 3H, POCH$_2$C*H*$_3$); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 159.72 (s, C═O), 147.02, 146.51, 142.37, 137.59, 129.51, 129.33, 124.77, 123.38, 121.01, 63.54 (d, *J* = 6.6 Hz, POC), 45.99 (d, *J* = 155.4 Hz, PC), 41.72, 16.26 (d, *J* = 5.6 Hz, POCC); ^{31}P NMR (81 MHz, $CDCl_3$): δ = 16.25 ppm. Anal. calcd. for $C_{16}H_{19}BrN_5O_4P$: C, 42.12; H, 4.20; N, 15.35. Found: C, 42.15; H, 4.01; N, 15.09.

Diethyl 2-{4-[6-bromo-4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}ethylphosphonate 9bb

From diethyl 2-azidoethylphosphonate **11b** (0.067 g, 0.323 mmol) and 6-bromo-N^3-propargylquinazolin-4(3*H*)-one **13b** (0.085 g, 0.323 mmol), a phosphonate **9bb** (0.102 g, 67%) was obtained as a white solid after purification on a silica gel column with chloroform–methanol mixtures (100:1, v/v) and crystallization from diethyl ether. M.p.: 103–105°C; IR (KBr): ν = 3386, 2984, 2928, 1678, 1608, 1443, 1226, 1025, 835, 785 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 8.39 (dd, *J* = 2.3 Hz, *J* = 0.3 Hz, 1H, $H_{aromat.}$), 8.34 (s, 1H), 7.82 (dd, *J* = 8.7 Hz, *J* = 2.3 Hz, 1H, $H_{aromat.}$), 7.81 (s, 1H, *H*C5′), 7.57 (d, *J* = 8.7 Hz, 1H, $H_{aromat.}$), 5.24 (s, 2H, CH_2), 4.64–4.51 (m, 2H, PCH_2), 4.13–3.99 (m, 4H, 2 × POCH_2CH$_3$), 2.47–2.30 (m, 2H, PCH_2), 1.26 (t, *J* = 7.1 Hz, 6H, 2 × POCH$_2$C*H*$_3$); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 159.79 (s, CO), 147.03, 146.54, 141.96, 137.06, 129.51, 129.12, 124.10, 123.36, 121.02, 62.18 (d, *J* = 6.4 Hz, POC), 44.73, 41.77, 27.19 (d, *J* = 141.9 Hz, PC), 16.33 (d, *J* = 5.7 Hz, POCC); ^{31}P NMR (81 MHz, $CDCl_3$): δ = 26.02 ppm. Anal. calcd. for $C_{17}H_{21}BrN_5O_4P$: C, 43.42; H, 4.50; N, 14.89. Found: C, 40.41; H, 4.22; N, 15.05.

Diethyl 3-{4-[6-bromo-4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}propylphosphonate 9bc

From diethyl 3-azidopropylphosphonate **11c** (0.063 g, 0.285 mmol) and 6-bromo-N^3-propargylquinazolin-4(3*H*)-one **13b** (0.075 g, 0.285 mmol), a phosphonate **9bc** (0.100 g, 72%) was obtained as

white needles after purification on a silica gel column with chloroform–methanol mixtures (100:1, v/v) and crystallization from diethyl ether–petroleum ether. M.p.: 92–94°C; IR (KBr): ν = 3485, 3143, 2984, 1675, 1607, 1467, 1226, 1025, 787 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 8.39 (dd, *J* = 2.3 Hz, *J* = 0.4 Hz, 1H, $H_{aromat.}$), 8.34 (s, 1H), 8.82 (dd, *J* = 8.7 Hz, *J* = 2.3 Hz, 1H, $H_{aromat.}$), 7.78 (s, 1H, *H*C5′), 7.57 (d, *J* = 8.7 Hz, 1H, $H_{aromat.}$), 5.24 (s, 2H, CH_2), 4.42 (t, *J* = 7.0 Hz, 2H, PCCCH_2), 4.16–3.98 (m, 4H, 2 × POC$H_2$$CH_3$), 2.31–2.09 (m, 2H, PCC$H_2$), 1.78–1.61 (m, 2H, PC$H_2$), 1.29 (t, *J* = 7.1 Hz, 6H, 2 × POCH_2CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): 159.82 (s, CO), 147.06, 146.56, 142.00, 137.57, 129.52, 129.14, 123.96, 123.39, 120.99, 61.83 (d, *J* = 6.6 Hz, POC), 50.17 (d, *J* = 14.9 Hz, PCC*C*), 41.81, 23.59 (d, *J* = 4.5 Hz, PC*C*), 22.65 (d, *J* = 143.7 Hz, P*C*), 16.42 (d, *J* = 6.0 Hz, POC*C*); ^{31}P NMR (81 MHz, $CDCl_3$): δ = 30.64 ppm. Anal. calcd. for $C_{18}H_{23}BrN_5O_4P$: C, 44.64; H, 4.79; N, 14.46. Found: C, 44.54; H, 5.14; N, 14.40.

Diethyl 4-{4-[6-bromo-4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}butylphosphonate 9bd

From diethyl 4-azidobutylphosphonate **11d** (0.063 g, 0.268 mmol) and 6-bromo-N^3-propargylquinazolin-4(3*H*)-one **13b** (0.070 g, 0.268 mmol), a phosphonate **9bd** (0.124 g, 93%) was obtained as a colorless oil after purification on a silica gel column with chloroform–methanol mixtures (100:1, v/v). IR (film): ν = 3346, 3128, 3076, 3059, 2989, 2955, 2872, 1680, 1606, 1467, 1247, 1209, 1057, 1028, 836, 780 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$ δ = 8.39 (d, *J* = 2.3 Hz, 1H, $H_{aromat.}$), 8.35 (s, 1H), 7.82 (dd, *J* = 8.7 Hz, *J* = 2.3 Hz, 1H, $H_{aromat.}$), 7.73 (s, 1H, *H*C5′), 7.57 (d, *J* = 8.7 Hz, 1H, $H_{aromat.}$), 5.24 (s, 2H, CH_2), 4.33 (t, *J* = 7.1 Hz, 2H, PCCCCH_2), 4.15–3.96 (m, 4H, 2 × POC$H_2$$CH_3$), 2.08–1.93 (m, 2H, PCCCH_2), 1.83–1.53 (m, 4H, PCH_2, PCCH_2), 1.28 (t, *J* = 7.1 Hz, 6H, 2 × POCH_2CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 159.83 (s, C═O), 147.06, 146.58, 141.98, 137.60, 137.56, 129.52, 129.13, 123.63, 123.39, 120.97, 61.61 (d, *J* = 6.5 Hz, POC), 49.87, 41.82, 30.65 (d, *J* = 15.3 Hz, PCC*C*); 25.00 (d, *J* = 142.5 Hz, PC); 19.71 (d, *J* = 5.0 Hz, PCC); 16.43 (d, *J* = 5.9 Hz, POC*C*); ^{31}P NMR (81 MHz, $CDCl_3$): δ = 31.66 ppm. Anal. calcd. for $C_{19}H_{25}BrN_5O_4P$: C, 45.80; H, 5.06; N, 14.05. Found: C, 45.96; H, 4.88; N, 14.22.

Diethyl 2-{4-[6-bromo-4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}ethoxymethylphosphonate 9be

From diethyl (2-azidoethoxy)methylphosphonate **11e** (0.071 g, 0.299 mmol) and 6-bromo-N^3-propargylquinazolin-4(3*H*)-one **13b** (0.076 g, 0.299 mmol), a phosphonate **9be** (0.114 g, 76%) was obtained as a colorless oil after purification on a silica gel column with chloroform–methanol mixtures (100:1, v/v). IR (film): ν = 3442, 3147, 3070, 2985, 2909, 1681, 1609, 1469, 1231, 1028, 835, 755 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 8.39 (d, *J* = 2.2 Hz, 1H, $H_{aromat.}$), 8.35 (s, 1H), 7.89 (s, 1H, *H*C5′), 7.81 (dd, *J* = 8.6 Hz, *J* = 2.2 Hz, 1H, $H_{aromat.}$), 7.57 (d, *J* = 8.6 Hz, 1H, $H_{aromat.}$), 5.25 (s, 2H, CH_2), 4.53 (t, *J* = 4.9 Hz, 2H, OCH_2CH_2N), 4.18–4.03 (m, 4H, 2 × POC$H_2$$CH_3$), 3.97 (t, *J* = 4.9 Hz, 2H, OCH_2CH_2N), 3.75 (d, *J* = 8.1 Hz, 2H, PCH_2O), 1.30 (t, *J* = 7.1 Hz, 6H, 2 × POCH_2CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 159.71 (s, C═O), 147.02, 146.64, 141.97, 137.52, 137.52, 129.48, 129.14, 124.73, 123.42, 120.92, 71.09 (d, *J* = 9.9 Hz, OCH_2CH_2N), 65.34 (d, *J* = 166.4 Hz, PC), 62.50 (d, *J* = 6.6 Hz, POC), 50.20 (s, OCH_2CH_2N), 41.57, 16.44 (d, *J* = 5.5 Hz, POC*C*); ^{31}P NMR (81 MHz, $CDCl_3$): δ = 21.13 ppm. Anal. calcd. for $C_{18}H_{23}BrN_5O_5P$: C, 43.21; H, 4.63; N, 14.00. Found: C, 42.86; H, 4.64; N, 13.70.

Diethyl 2-{4-[6-bromo-4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}ethoxyethylphosphonate 9bf

From diethyl 2-(2-azidoethoxy)ethylphosphonate **11f** (0.070 g, 0.279 mmol) and 6-bromo-N^3-propargylquinazolin-4(3*H*)-one **13b** (0.069 g, 0.279 mmol), a phosphonate **9bf** (0.112 g, 78%) was obtained as a white solid after purification on a silica gel column with chloroform–methanol mixtures (100:1, v/v) and crystallization from ethyl acetate–petroleum ether. M.p.: 102–103°C; IR (KBr): ν = 3406, 3146, 2985, 2907, 2876, 1681, 1608, 1468, 1228, 1027, 755 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 8.40 (d, *J* = 2.3 Hz, 1H, $H_{aromat.}$), 8.36 (s, 1H), 7.90 (s, 1H, *H*C5′), 7.82 (dd, *J* = 8.7 Hz, *J* = 2.3 Hz, 1H, $H_{aromat.}$), 7.57 (d, *J* = 8.7 Hz, 1H, $H_{aromat.}$), 5.26 (s, 2H, CH_2), 4.50 (t, *J* = 4.9 Hz, 2H, OCH_2CH_2N), 4.14–3.99 (m, 4H, 2 × POC$H_2$$CH_3$), 3.77 (t, *J* = 5.0 Hz, 2H, OCH_2CH_2N), 3.69 (dt, *J* = 12.2 Hz, *J* = 7.4 Hz, 2H, PCH_2CH_2O), 2.05 (dt, *J* = 14.8 Hz, *J* = 7.4 Hz, 2H, PCH_2CH_2O), 1.30 (t, *J* = 7.1 Hz, 6H, 2 × POCH_2CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 159.75 (s, C═O), 147.04, 146.67, 141.85, 137.50, 129.48, 129.15, 124.76, 123.45, 120.91, 68.77 (s, OCH_2CH_2N), 65.29 (s, PCH_2CH_2O), 61.69 (d, *J* = 6.6 Hz, POC), 50.29 (s, OCH_2CH_2N), 41.64, 26.85 (d, *J* = 140.3 Hz, PC), 16.42 (d, *J* = 6.5 Hz, POC*C*); ^{31}P NMR (81 MHz, $CDCl_3$): δ = 28.66 ppm. Anal. calcd. for $C_{19}H_{25}BrN_5O_5P$: C, 44.37; H, 4.90; N, 13.62. Found: C, 44.67; H, 4.80; N, 13.43.

Diethyl 2-{4-[6-bromo-4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}-1-hydroxyethylphosphonate 9bg

From diethyl 2-azido-1-hydroxyethylphosphonate **11g** (0.065 g, 0.291 mmol) and 6-bromo-N^3-propargylquinazolin-4(3*H*)-one **13b** (0.077 g, 0.291 mmol), a phosphonate **9bg** (0.132 g, 93%) was obtained as white needles after purification on a silica gel column with chloroform–methanol mixtures (100:1, v/v) and crystallization from ethyl acetate. M.p.: 72–73°C; IR (KBr): ν = 3261, 2985, 2931, 2910, 2868, 1681, 1609, 1469, 1224, 1048, 1023, 733 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 8.34 (d, *J* = 2.3 Hz, 1H, $H_{aromat.}$), 8.33 (s, 1H), 7.97 (s, 1H, *H*C5′), 7.80 (dd, *J* = 8.7 Hz, *J* = 2.3 Hz, 1H, $H_{aromat.}$), 7.54 (d, *J* = 8.7 Hz, 1H, $H_{aromat.}$), 5.28 (AB, *J* = 14.8 Hz, 1H, C$H_a$$H_b$), 5.22 (AB, *J* = 14.8 Hz, 1H, C$H_a$$H_b$), 4.78 (ddd, *J* = 14.1 Hz, *J* = 5.5 Hz, *J* = 2.6 Hz, 1H, PCC$H_a$$H_b$), 4.47 (ddd, *J* = 14.1 Hz, *J* = 9.9 Hz, *J* = 5.5 Hz, 1H, PCC$H_a$$H_b$), 4.33–4.08 (m, 5H, PC*H*(OH), 2 × POC$H_2$$CH_3$), 1.33 (t, *J* = 7.0 Hz, 3H, POCH_2CH_3), 1.31 (t, *J* = 7.0 Hz, 3H, POCH_2CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 159.69 (s, C═O), 146.79, 141.64, 137.54, 129.30, 129.00, 125.58, 123.21, 120.95, 66.95 (d, *J* = 164.3 Hz, PC), 63.53 (d, *J* = 6.9 Hz, POC); 63.36 (d, *J* = 6.9 Hz, POC), 51.74 (d, *J* = 9.8 Hz, PCC), 41.65, 16.43 (d, *J* = 5.8 Hz, POC*C*), 16.39 (d, *J* = 5.8 Hz, POC*C*); ^{31}P NMR (81 MHz, $CDCl_3$): δ = 20.74 ppm. Anal. calcd. for $C_{17}H_{21}BrN_5O_5P$: C, 41.99; H, 4.35; N, 14.40. Found: C, 42.07; H, 4.65; N, 14.49.

Diethyl 3-{4-[6-bromo-4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}-2-hydroxypropylphosphonate 9bh

From diethyl 3-azido-2-hydroxypropylphosphonate **11h** (0.065 g, 0.274 mmol) and 6-bromo-N^3-propargylquinazolin-4(3*H*)-one **13b** (0.072 g, 0.274 mmol), a phosphonate **9bh** (0.113 g, 82%) was obtained as a white solid after purification on a silica gel column with chloroform–methanol mixtures (50:1, v/v) and crystallization from ethyl acetate–diethyl ether. M.p.: 134–136°C; IR (KBr): ν = 3336, 3151, 3087, 2985, 2929, 2910, 2869, 1681, 1609, 1469, 1227, 1027, 732 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 8.39 (dd, *J* = 2.3 Hz, *J* = 0.3 Hz, 1H, $H_{aromat.}$), 8.35 (s, 1H), 7.93 (s, 1H, *H*C5′), 7.80 (dd, *J* = 8.7 Hz, *J* = 2.3 Hz, 1H, $H_{aromat.}$), 7.56 (d, *J* = 8.7 Hz, 1H, $H_{aromat.}$), 5.28 (AB, *J* = 14.8 Hz, 1H, C$H_a$$H_b$), 5.25 (AB, *J* = 14.8 Hz, 1H, C$H_a$$H_b$), 4.58–4.29 (m, 3H, PCCHCH_2), 4.21–4.00 (m, 4H, 2 × POC$H_2$$CH_3$), 2.08–1.67 (m, 3H, PCH_2, OH), 1.32 (t, *J* = 7.1 Hz, 3H, POCH_2CH_3), 1.31 (t, *J* = 7.1 Hz, 3H, POCH_2CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 159.69 (s, CO), 146.86, 146.75, 141.73, 137.49, 129.34, 129.06, 125.43, 123.27, 120.91, 65.42 (d, *J* = 5.0 Hz, PCC), 62.31 (d, *J* = 6.4 Hz, POC), 62.20 (d, *J* = 6.4 Hz, POC), 56.04 (d, *J* = 16.9 Hz, PCC*C*), 41.63, 30.84 (d, *J* = 140.6 Hz, PC), 16.34 (d, *J* = 5.6 Hz, POC*C*), 16.30 (d, *J* = 5.6 Hz, POC*C*); ^{31}P NMR (81 MHz, $CDCl_3$): δ = 29.06 ppm. Anal. calcd. for $C_{18}H_{23}BrN_5O_5P$: C, 43.21; H, 4.63; N, 14.00. Found: C, 43.32; H, 4.60; N, 13.93.

Diethyl {2-[4-(6-bromo-4-oxoquinazolin-3(4*H*)-yl)methyl)-1*H*-1,2,3-triazol-1-yl]acetamido}methylphosphonate 9bi

From diethyl (2-azidoacetamido)methylphosphonate **11i** (0.067 g, 0.268 mmol) and 6-bromo-N^3-propargylquinazolin-4(3*H*)-one **13b** (0.070 g, 0.268 mmol), a phosphonate **9bi** (0.101 g, 73%) was obtained as a white solid after purification on a silica gel column with chloroform–methanol mixtures (50:1, v/v) and crystallization from diethyl ether–petroleum ether. M.p.: 193–194°C; IR (KBr): ν = 3252, 3136, 3070, 2987, 2937, 1692, 1674, 1469, 1211, 1054, 1022, 879, 756 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 8.40 (d, *J* = 2.4 Hz, 1H, $H_{aromat.}$), 8.39 (s, 1H), 7.96 (s, 1H, *H*C5′), 7.82 (dd, *J* = 8.8 Hz, *J* = 2.4 Hz, 1H, $H_{aromat.}$), 7.59 (d, *J* = 8.8 Hz, 1H, $H_{aromat.}$), 7.05 (brs, 1H, NH), 5.28 (s, 2H, CH_2), 5.08 (s, 2H, CH_2), 4.17–4.02 (m, 4H, 2 × POC$H_2$$CH_3$), 3.69 (dd, *J* = 12.1 Hz, *J* = 5.9 Hz, 2H, PCH_2), 1.28 (t, *J* = 7.1 Hz, 6H, 2 × POCH_2CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 164.82 (d, *J* = 5.7 Hz, C═O), 159.80 (s, CO), 146.98, 146.56, 142.31, 137.64, 129.47, 129.18, 125.49, 123.37, 121.07, 62.95 (d, *J* = 6.6 Hz, POC), 52.57 (s, CH_2N), 41.77, 35.02 (d, *J* = 157.3 Hz, PC), 16.32 (d, *J* = 5.9 Hz, POC*C*); ^{31}P NMR (81 MHz, $CDCl_3$): δ = 22.23 ppm. Anal. calcd. for $C_{18}H_{22}BrN_6O_5P$: C, 42.12; H, 4.32; N, 16.37. Found: C, 42.17; H, 4.38; N, 16.52.

(1*S*,2*S*)-Dibenzyl 2-benzyloxy-3-{4-[6-bromo-4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}-1-hydroxypropylphosphonate (1*S*,2*S*)-9bj

From (1*S*,2*S*)-dibenzyl 3-azido-2-benzyloxy-1-hydroxypropylphosphonate (1*S*,2*S*)-**11j** (0.060 g, 0.128 mmol) and 6-bromo-N^3-propargylquinazolin-4(3*H*)-one **13b** (0.034 g, 0.128 mmol), a phosphonate (1*S*,2*S*)-**9bj** (0.078 g, 83%) was obtained as a white powder after purification on a silica gel column with chloroform–methanol mixtures (100:1, v/v). $[\alpha]_D^{20}$ = −4.2 (*c* = 1.59 in $CHCl_3$); m.p.: 105–107°C; IR (KBr): ν = 3278, 3075, 3030, 2988, 1682, 1610, 1477, 1465, 1211, 1027, 788, 752, 698 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 8.36 (d, *J* = 2.3 Hz, 1H, $H_{aromat.}$), 8.35 (s, 1H), 7.80 (dd, *J* = 8.7 Hz, *J* = 2.3 Hz, 1H, $H_{aromat.}$), 7.71 (s, 1H, *H*C5′), 7.56 (d, *J* = 8.7 Hz, 1H, $H_{aromat.}$), 7.35–7.28 (m, 10H, H_{aromat}), 7.25–7.15 (m, 3H, H_{aromat}), 7.14–7.04 (m, 2H, H_{aromat}), 5.22 (AB, *J* = 14.8 Hz, 1H, C$H_a$$H_b$), 5.18 (AB, *J* = 14.8 Hz, 1H, C$H_a$$H_b$), 5.11–4.95 (m, 4H, 2 × $POCH_2$Ph), 4.62–4.39 (m, 3H, OC$H_a$$H_b$Ph, H-3a, H-3b), 4.33–4.22 (m, 1H, H-2), 4.17 (d, *J* = 10.8 Hz, 1H, OC$H_a$$H_b$Ph), 3.88 (dd, *J* = 11.5 Hz, *J* = 3.0 Hz, 1H, H-1), 3.02 (brs, 1H, OH); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 159.66 (s, C═O), 146.95, 146.64, 141.81, 137.54, 136.75, 135.89 (d, *J* = 5.9 Hz, C_{ipso}), 135.74 (d, *J* = 5.9 Hz, C_{ipso}), 129.45, 129.17, 128.70, 128.67, 128.64, 128.39, 128.20, 128.15, 128.09, 125.23, 123.36, 125.23, 123.38, 120.97, 74.11 (s, PCC), 68.61 (d, *J* = 7.3 Hz, POC), 68.38 (d, *J* = 161.9 Hz, PC), 68.29 (d, *J* = 7.3 Hz, POC), 50.82 (d, *J* = 12.0 Hz, PCC*C*), 41.63; ^{31}P NMR (81 MHz, $CDCl_3$): δ = 22.52 ppm. Anal. calcd. for $C_{35}H_{33}BrN_5O_6P$: C, 57.54; H, 4.55; N, 9.59. Found: C, 57.82; H, 4.33; N, 9.73.

(1*R*,2*S*)-Dibenzyl 2-benzyloxy-3-{4-[6-bromo-4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}-1-hydroxypropylphosphonate (1*R*,2*S*)-9bj

From (1*R*,2*S*)-dibenzyl 3-azido-2-benzyloxy-1-hydroxypropylphosphonate (1*R*,2*S*)-**11j** (0.060 g, 0.128 mmol) and 6-bromo-N^3-propargylquinazolin-4(3*H*)-one **13b** (0.034 g, 0.128 mmol), a phosphonate (1*R*,2*S*)-**9bj** (0.082 g, 87%) was obtained as a white powder after purification on a silica gel column with chloroform–methanol mixtures (100:1, v/v). $[\alpha]_D^{20}$ = +1.6 (*c* = 1.40 in $CHCl_3$); m.p.: 116–117°C; IR (KBr): ν = 3189, 3054, 2998, 2886, 1660, 1612, 1464, 1446, 1230, 1025, 757, 699 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 8.37 (s, 1H), 8.35 (d, *J* = 2.2 Hz, 1H, $H_{aromat.}$), 7.79 (dd, *J* = 8.7 Hz, *J* = 2.2 Hz, 1H, $H_{aromat.}$), 7.71 (s, 1H, *H*C5′), 7.57 (d, *J* = 8.7 Hz, 1H, $H_{aromat.}$), 7.35–7.24 (m, 10H, H_{aromat}), 7.22–7.12 (m, 3H, H_{aromat}), 7.11–7.01 (m, 2H, H_{aromat}), 5.23 (AB, *J* = 14.8 Hz, 1H, C$H_a$$H_b$), 5.16 (AB, *J* = 14.8 Hz, 1H, C$H_a$$H_b$), 5.06–4.99 (m, 4H, 2 × $POCH_2$Ph), 4.71 (dd, *J* = 14.7 Hz, *J* = 3.5 Hz, 1H, H-3a), 4.60 (dd, *J* = 14.7 Hz, *J* = 6.4 Hz, 1H, H-3b), 4.40 (AB, *J* = 11.0 Hz, 1H, OC$H_a$$H_b$Ph), 4.26 (d, *J* = 11.0 Hz, 1H, OC$H_a$$H_b$Ph), 4.20–4.06 (m, 1H, H-2), 3.98 (dd, *J* = 9.2 Hz, *J* = 6.0 Hz, 1H, H-1), 3.01 (brs, 1H, OH); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 159.65 (s, CO), 146.91, 146.71, 141.85, 137.54, 136.72, 135.86 (d, *J* = 5.5 Hz, C_{ipso}), 135.78 (d, *J* = 5.5 Hz, C_{ipso}), 129.42, 129.18, 128.67, 128.63, 128.43, 128.18, 128.15, 128.09, 128.07, 125.42, 123.38, 120.97, 77.66 (d, *J* = 4.5 Hz, PCC), 72.86, 68.54 (d, *J* = 6.7 Hz, POC), 68.42 (d, *J* = 6.7 Hz, POC), 67.86 (d, *J* = 161.8 Hz, PC), 50.33 (d, *J* = 6.0 Hz, PCCC), 41.60; ^{31}P NMR (81 MHz, $CDCl_3$): δ = 23.69 ppm. Anal. calcd. for $C_{35}H_{33}BrN_5O_6P$: C, 57.54; H, 4.55; N, 9.59. Found: C, 57.46; H, 4.23; N, 9.80.

Diethyl {4-[6-nitro-4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}methylphosphonate 9ca

From diethyl azidomethylphosphonate **11a** (0.050 g, 0.259 mmol) and 6-nitro-N^3-propargylquinazolin-4(3*H*)-one **13c** (0.059 g, 0.259 mmol), a phosphonate **9ca** (0.096 g, 88%) was obtained as white solid after purification on a silica gel column with chloroform–methanol mixtures (100:1, v/v) and crystallization from ethyl acetate–petroleum ether. M.p.: 187–188°C; IR (KBr): ν = 3334, 3054, 2966, 2914, 1670, 1611, 1458, 1222, 1025, 844 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 9.11 (dd, *J* = 2.6 Hz, *J* = 0.4 Hz, 1H, $H_{aromat.}$), 8.51 (dd, *J* = 8.9 Hz, *J* = 2.6 Hz, 1H, $H_{aromat.}$), 8.48 (s, 1H), 7.98 (d, *J* = 0.8 Hz, 1H, *H*C5′), 7.83 (d, *J* = 8.9 Hz, 1H, $H_{aromat.}$), 5.30 (s, 2H, CH_2), 4.75 (d, *J* = 13.2 Hz, 2H, PCH_2), 4.21–4.06 (m, 4H, 2 × POCH_2CH$_3$), 1.29 (t, *J* = 7.1 Hz, 3H, POCH$_2$CH_3), 1.28 (t, *J* = 7.1 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 159.77 (s, CO), 152.16, 149.17, 146.11, 141.82, 129.73, 128.39, 124.86, 123.17, 122.24, 63.56 (d, *J* = 6.6 Hz, POC), 46.04 (d, *J* = 155.3 Hz, PC), 41.84, 16.28 (d, *J* = 5.6 Hz, POC*C*); ^{31}P NMR (81 MHz, $CDCl_3$): δ = 16.23 ppm. Anal. calcd. for $C_{16}H_{19}N_6O_6P$: C, 45.50; H, 4.53; N, 19.90. Found: C, 45.75; H, 4.22; N, 20.12.

Diethyl 2-{4-[6-nitro-4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}ethylphosphonate 9cb

From diethyl 2-azidoethylphosphonate **11b** (0.068 g, 0.328 mmol) and 6-nitro-N^3-propargylquinazolin-4(3*H*)-one **13c** (0.075 g, 0.328 mmol), a phosphonate **9cb** (0.104 g, 73%) was obtained as white solid after purification on a silica gel column with chloroform–methanol mixtures (100:1, v/v) and crystallization from ethyl acetate–petroleum ether. M.p.: 139–140°C; IR (KBr): ν = 3334, 3054, 2966, 2914, 1670, 1611, 1458, 1222, 1025, 844 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 9.12 (dd, *J* = 2.6 Hz, *J* = 0.3 Hz, 1H, $H_{aromat.}$), 8.53 (dd, *J* = 8.6 Hz, *J* = 2.6 Hz, 1H, $H_{aromat.}$), 8.49 (s, 1H), 7.84 (s, 1H, *H*C5′), 7.83 (d, *J* = 8.6 Hz, 1H, $H_{aromat.}$), 5.29 (s, 2H, CH_2), 4.66–4.53 (m, 2H, PCCH_2), 4.15–4.00 (m, 4H, 2 × POCH_2CH$_3$), 2.48–2.31 (m, 2H, PCH_2), 1.28 (t, *J* = 7.1 Hz, 6H, 2 × POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 159.83 (s, CO), 152.17, 149.22, 146.10, 141.43, 129.39, 128.38, 124.18, 123.16, 122.21, 62.19 (d, *J* = 6.5 Hz, POC), 44.79, 41.86, 27.19 (d, *J* = 141.9 Hz, PC), 16.33 (d, *J* = 6.1 Hz, POC*C*); ^{31}P NMR (81 MHz, $CDCl_3$): δ = 25.56 ppm. Anal. calcd. for $C_{17}H_{21}N_6O_6P$: C, 46.79; H, 4.85; N, 19.26. Found: C, 46.66; H, 5.02; N, 19.39.

Diethyl 3-{4-[6-nitro-4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}propylphosphonate 9cc

From diethyl 3-azidopropylphosphonate **11c** (0.108 g, 0.488 mmol) and 6-nitro-N^3-propargylquinazolin-4(3*H*)-one **13c** (0.112 g, 0.488 mmol), a phosphonate **9cc** (0.195 g, 89%) was obtained as white solid after purification on a silica gel column with chloroform–methanol mixtures (100:1, v/v) and crystallization from ethyl acetate–petroleum ether. M.p.: 91–92°C; IR (KBr): ν = 3334, 3086, 2999, 2878, 1666, 1615, 1444, 1230, 1024, 789 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 9.14 (dd, *J* = 2.6 Hz, *J* = 0.4 Hz, 1H, $H_{aromat.}$), 8.52 (dd, *J* = 8.9 Hz, *J* = 2.6 Hz, 1H, $H_{aromat.}$), 8.50 (s, 1H), 7.84 (dd, *J* = 8.9 Hz, *J* = 0.4 Hz, 1H, $H_{aromat.}$), 7.82 (s, 1H, *H*C5′), 5.29 (s, 2H, CH_2), 4.44 (t, *J* = 7.0 Hz, 2H, PCCCH_2), 4.16–4.01 (m, 4H, 2 × POCH_2CH$_3$), 2.32–2.10 (m, 2H, PCCH_2), 1.81–1.59 (m, 2H, PCH_2), 1.31 (t, *J* = 7.1 Hz, 6H, 2 × POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 159.89 (s, CO), 152.20, 149.22, 146.10, 141.45, 129.40, 128.38, 124.10, 123.21, 122.26, 61.83 (d, *J* = 6.6 Hz, POC), 50.20 (d, *J* = 15.1 Hz, PCC*C*), 41.92, 23.60 (d, *J* = 4.6 Hz, PCC), 22.64 (d, *J* = 143.4 Hz, PC), 16.42 (d, *J* = 6.1 Hz, POC*C*); ^{31}P NMR (81 MHz, $CDCl_3$): δ = 30.59 ppm. Anal. calcd. for $C_{18}H_{23}N_6O_6P$: C, 48.00; H, 5.15; N, 18.66. Found: C, 48.28; H, 5.29; N, 18.52.

Diethyl 4-{4-[6-nitro-4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}butylphosphonate 9cd

From diethyl 4-azidobutylphosphonate **11d** (0.100 g, 0.425 mmol) and 6-nitro-N^3-propargylquinazolin-4(3*H*)-one **13c** (0.097 g, 0.425 mmol), a phosphonate **9 cd** (0.166 g, 84%) was obtained as a colorless oil after purification on a silica gel column with chloroform–methanol mixtures (100:1, v/v). IR (film): ν = 3330, 3055, 2989, 2888, 1677, 1615, 1473, 1249, 1220, 1021, 840, 779 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$ δ = 9.16 (d, *J* = 2.6 Hz, 1H, $H_{aromat.}$), 8.55 (dd, *J* = 8.9 Hz, *J* = 2.6 Hz, 1H, $H_{aromat.}$), 8.53 (s, 1H), 7.86 (d, *J* = 8.9 Hz, 1H, $H_{aromat.}$), 7.79 (s, 1H, *H*C5′), 5.31 (s, 2H, CH_2), 4.38 (t, *J* = 7.1 Hz, 2H, PCCCCH_2), 4.14–4.04 (m, 4H, 2 × POCH_2CH$_3$), 2.53 (qu, *J* = 7.1 Hz, 2H, PCCCH_2), 1.80–1.74 (m, 2H, PCCH_2), 1.70–1.63 (m, 2H, PCH_2), 1.32 (t, *J* = 7.2 Hz, 6H, 2 × POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 159.90 (s, CO), 152.21, 149.22, 146.11, 141.44, 129.41, 128.38, 123.75, 123.22, 122.26, 61.63 (d, *J* = 6.6 Hz, POC), 49.94, 41.94, 30.64 (d, *J* = 15.0 Hz, PCCC); 24.99 (d, *J* = 142.2 Hz, PC); 19.70 (d, *J* = 5.2 Hz, PCC); 16.43 (d, *J* = 5.7 Hz, POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$): δ = 30.72 ppm. Anal. calcd. for $C_{19}H_{25}N_6O_6P$: C, 49.14; H, 5.43; N, 18.10. Found: C, 49.30; H, 5.18; N, 18.37.

Diethyl 2-{4-[6-nitro-4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}ethoxymethylphosphonate 9ce

From diethyl (2-azidoethoxy)methylphosphonate **11e** (0.067 g, 0.283 mmol) and 6-nitro-N^3-propargylquinazolin-4(3*H*)-one **13c** (0.065 g, 0.283 mmol), a phosphonate **9ce** (0.086 g, 65%) was obtained as a yellowish oil after purification on a silica gel column with chloroform–methanol mixtures (100:1, v/v). IR (film): ν = 3423, 3147, 3094, 2986, 1688, 1617, 1345, 1231, 1026, 665 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.14 (d, *J* = 2.6 Hz, 1H, $H_{aromat.}$), 8.54 (dd, *J* = 8.9 Hz, *J* = 2.6 Hz, 1H, $H_{aromat.}$), 8.53 (s, 1H), 7.96 (s, 1H, *H*C5′), 7.85 (d, *J* = 8.9 Hz, 1H, $H_{aromat.}$), 5.32 (s, 2H, CH_2), 4.57 (t, *J* = 4.9 Hz, 2H, OCH$_2$CH_2N), 4.17–4.12 (m, 4H, 2 × POCH_2CH$_3$), 4.00 (t, *J* = 4.9 Hz, 2H, OCH_2CH$_2$N), 3.79 (d, *J* = 8.2 Hz, 2H, PCH_2O), 1.34 (t, *J* = 7.1 Hz, 6H, 2 × POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 159.79 (s, CO), 152.19, 149.28, 146.07, 141.48, 129.36, 128.35, 124.90, 123.23, 122.29, 71.08 (d, *J* = 9.9 Hz, OCH$_2$CH$_2$N), 65.37 (d, *J* = 167.1 Hz, PC), 62.54 (d, *J* = 6.6 Hz, POC), 50.27 (s, OCH$_2$CH$_2$N), 41.72, 16.46 (d, *J* = 5.5 Hz, POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$): δ = 20.23 ppm. Anal. calcd. for $C_{18}H_{23}N_6O_7P$: C, 46.35; H, 4.97; N, 18.02. Found: C, 46.04; H, 4.84; N, 18.20.

Diethyl 2-{4-[6-nitro-4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}ethoxyethylphosphonate 9cf

From diethyl 2-(2-azidoethoxy)ethylphosphonate **11f** (0.063 g, 0.251 mmol) and 6-nitro-N^3-propargylquinazolin-4(3*H*)-one **13c** (0.058 g, 0.251 mmol), a phosphonate **9cf** (0.102 g, 85%) was obtained as a yellow oil after purification on a silica gel column with chloroform–methanol mixtures (100:1, v/v). IR (film): ν = 3385, 3055, 2988, 2866, 1671, 1620, 1433, 1224, 1020, 785 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.16 (d, *J* = 2.6 Hz, 1H, $H_{aromat.}$), 8.55 (dd, *J* = 8.9 Hz, *J* = 2.6 Hz, 1H, $H_{aromat.}$), 8.54 (s, 1H), 7.98 (s, 1H, *H*C5′), 7.86 (d, *J* = 8.9 Hz, 1H, $H_{aromat.}$), 5.33 (s, 2H, CH_2), 4.54 (t, *J* = 5.0 Hz, 2H, OCH_2CH_2N), 4.12–4.08 (m, 4H, 2 × $POCH_2CH_3$), 3.84 (t, *J* = 5.0 Hz, 2H, OCH_2CH_2N), 3.72 (dt, *J* = 12.7 Hz, *J* = 7.3 Hz, 2H, PCH_2CH_2O), 2.08 (dt, *J* = 18.7 Hz, *J* = 7.4 Hz, 2H, PCH_2CH_2O), 1.33 (t, *J* = 7.2 Hz, 6H, 2 × $POCH_2CH_3$); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 159.83 (s, C═O), 152.20, 149.34, 146.07, 141.33, 129.36, 128.34, 124.93, 123.24, 122.30, 68.77 (s, OCH_2CH_2N), 65.29 (s, PCH_2CH_2O), 61.74 (d, *J* = 6.6 Hz, POC), 50.35 (s, OCH_2CH_2N), 41.77, 26.86 (d, *J* = 140.7 Hz, PC), 16.42 (d, *J* = 6.4 Hz, POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$): δ = 27.78 ppm. Anal. calcd. for $C_{19}H_{25}N_6O_7P$: C, 47.50; H, 5.25; N, 17.49. Found: C, 47.75; H, 5.01; N, 17.11.

Diethyl 1-hydroxy-2-{4-[6-nitro-4-oxoquinazolin-3(4*H*)-yl)-methyl]-1*H*-1,2,3-triazol-1-yl}ethylphosphonate 9cg

From diethyl 2-azido-1-hydroxyethylphosphonate **11g** (0.101 g, 0.453 mmol) and 6-nitro-N^3-propargylquinazolin-4(3*H*)-one **13c** (0.104 g, 0.453 mmol), a phosphonate **9cg** (0.187 g, 91%) was obtained as white needles after purification on a silica gel column with chloroform–methanol mixtures (100:1, v/v) and crystallization from ethyl acetate. M.p.: 170–171°C; IR (KBr): ν = 3261, 2985, 2931, 2910, 2868, 1681, 1609, 1469, 1224, 1048, 1023, 733 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 9.11 (d, *J* = 2.7 Hz, 1H, $H_{aromat.}$), 8.53 (dd, *J* = 8.8 Hz, *J* = 2.7 Hz, 1H, $H_{aromat.}$), 8.51 (s, 1H), 7.99 (s, 1H, *H*C5′), 7.84 (d, *J* = 8.8 Hz, 1H, $H_{aromat.}$), 5.34 (AB, *J* = 14.8 Hz, 1H, CH_aH_b), 5.25 (AB, *J* = 14.8 Hz, 1H, CH_aH_b), 4.78 (ddd, *J* = 16.7 Hz, *J* = 5.8 Hz, *J* = 2.8 Hz, 1H, $PCCH_aH_b$), 4.55–4.40 (m, 2H, $PCCH_aH_b$, OH), 4.34–4.10 (m, 5H, PC*H*(OH), 2 × $POCH_2CH_3$), 1.35 (t, *J* = 7.1 Hz, 3H, $POCH_2CH_3$), 1.33 (t, *J* = 7.1 Hz, 3H, $POCH_2CH_3$); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 159.84 (s, C═O), 152.12, 149.34, 146.07, 141.20, 129.35, 128.39, 125.64, 123.13, 122.21, 67.07 (d, *J* = 163.6 Hz, PC), 63.65 (d, *J* = 6.9 Hz, POC); 63.45 (d, *J* = 6.9 Hz, POC), 51.66 (d, *J* = 9.1 Hz, PC*C*), 41.82, 16.45 (d, *J* = 5.6 Hz, POC*C*), 16.40 (d, *J* = 5.6 Hz, POC*C*); ^{31}P NMR (81 MHz, $CDCl_3$): δ = 20.64 ppm. Anal. calcd. for $C_{17}H_{21}N_6O_7P$: C, 45.14; H, 4.68; N, 18.58. Found: C, 44.96; H, 4.88; N, 28.39.

Diethyl 2-hydroxy-3-{4-[6-nitro-4-oxoquinazolin-3(4*H*)-yl)-methyl]-1*H*-1,2,3-triazol-1-yl}propylphosphonate 9ch

From diethyl 3-azido-2-hydroxypropylphosphonate **11h** (0.066 g, 0.278 mmol) and 6-nitro-N^3-propargylquinazolin-4(3*H*)-one **13c** (0.064 g, 0.278 mmol), a phosphonate **9ch** (0.104 g, 80%) was obtained as a white solid after purification on a silica gel column with chloroform–methanol mixtures (50:1, v/v) and crystallization from ethyl acetate. M.p.: 158–159°C; IR (KBr): ν = 3317, 2986, 2911, 1689, 1616, 1369, 1047, 1026, 752 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 9.14 (d, *J* = 2.6 Hz, 1H, $H_{aromat.}$), 8.51 (dd, *J* = 8.7 Hz, *J* = 2.6 Hz, 1H, $H_{aromat.}$), 8.50 (s, 1H), 8.01 (s, 1H, *H*C5′), 7.94 (d, *J* = 8.7 Hz, 1H, $H_{aromat.}$), 5.48 (s, 2H, CH_2), 4.60–4.25 (m, 3H, PC*CHCH*$_2$), 4.24–3.92 (m, 4H, 2 × $POCH_2CH_3$), 2.18–1.60 (m, 3H, PCH_2, OH), 1.33 (t, *J* = 7.1 Hz, 3H, $POCH_2CH_3$), 1.32 (t, *J* = 7.1 Hz, 3H, $POCH_2CH_3$); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 159.82 (s, C═O), 152.16, 149.28, 146.08, 141.31, 129.34, 128.37, 125.49, 123.26, 122.27, 65.47 (d, *J* = 4.2 Hz, PC*C*), 62.39 (d, *J* = 6.7 Hz, POC), 62.35 (d, *J* = 6.7 Hz, POC), 55.98 (d, *J* = 18.6 Hz, PCC*C*), 41.79, 30.68 (d, *J* = 140.7 Hz, PC), 16.38 (d, *J* = 6.4 Hz, POC*C*), 16.34 (d, *J* = 6.4 Hz, POC*C*); ^{31}P NMR (81 MHz, $CDCl_3$): δ = 29.03 ppm. Anal. calcd. for $C_{18}H_{23}N_6O_7P$: C, 46.35; H, 4.97; N, 18.02. Found: C, 46.06; H, 4.84; N, 17.82.

Diethyl {2-[4-(6-nitro-4-oxoquinazolin-3(4*H*)-yl)methyl)-1*H*-1,2,3-triazol-1-yl]acetamido}methylphosphonate 9ci

From diethyl (2-azidoacetamido)methylphosphonate **11i** (0.064 g, 0.256 mmol) and 6-nitro-N^3-propargylquinazolin-4(3*H*)-one **13c** (0.059 g, 0.256 mmol), a phosphonate **9ci** (0.075 g, 61%) was obtained as a white solid after purification on a silica gel column with chloroform–methanol mixtures (50:1, v/v) and crystallization from ethyl acetate. M.p.: 198–199°C; IR (KBr): ν = 3332, 3106, 2983, 2830, 1682, 1644, 1429, 1221, 1027, 756 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.16 (d, *J* = 2.8 Hz, 1H, $H_{aromat.}$), 8.55 (dd, *J* = 8.5 Hz, *J* = 2.8 Hz, 1H, $H_{aromat.}$), 8.54 (s, 1H), 8.02 (s, 1H, *H*C5′), 7.87 (d, *J* = 8.5 Hz, 1H, $H_{aromat.}$), 7.02 (brs, 1H, NH), 5.34 (s, 2H, CH_2), 5.12 (s, 2H, CH_2), 4.16–4.11 (m, 4H, 2 × $POCH_2CH_3$), 3.72 (dd, *J* = 12.4 Hz, *J* = 5.8 Hz, 2H, PCH_2), 1.32 (t, *J* = 7.0 Hz, 6H, 2 × $POCH_2CH_3$); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 164.42 (d, *J* = 5.4 Hz, C═O), 159.89 (s, C═O), 152.19, 149.18, 146.13, 141.41, 129.42, 128.45, 125.61, 123.24, 122.27, 62.96 (d, *J* = 6.5 Hz, POC), 52.67 (s, CH_2N), 41.89, 35.04 (d, *J* = 157.2 Hz, PC), 16.33 (d, *J* = 6.0 Hz, POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$): δ = 21.38 ppm. Anal. calcd. for $C_{18}H_{22}N_7O_7P$: C, 45.10; H, 4.63; N, 20.45. Found: C, 44.91; H, 4.39; N, 20.72.

(1*S*,2*S*)-Dibenzyl 2-benzyloxy-1-hydroxy-3-{4-[6-nitro-4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}-propylphosphonate (1*S*,2*S*)-9cj

From (1*S*,2*S*)-dibenzyl 3-azido-2-benzyloxy-1-hydroxypropylphosphonate (1*S*,2*S*)-**11j** (0.064 g, 0.137 mmol) and 6-nitro-N^3-propargylquinazolin-4(3*H*)-one **13c** (0.031 g, 0.137 mmol), a phosphonate (1*S*,2*S*)-**9cj** (0.065 g, 68%) was obtained as a white powder after purification on a silica gel column with chloroform–methanol mixtures (50:1, v/v). $[\alpha]_D^{20}$ = −7.3 (*c* = 1.15 in $CHCl_3$); m.p.: 194–195°C; IR (KBr): ν = 3280, 3066, 3022, 2984, 2883, 1672, 1620, 1457, 1223, 1024, 757, 699 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 9.07 (d, *J* = 2.6 Hz, 1H, $H_{aromat.}$), 8.51 (dd, *J* = 8.9 Hz, *J* = 2.6 Hz, 1H, $H_{aromat.}$), 8.47 (s, 1H), 7.82 (d, *J* = 8.9 Hz, 1H, $H_{aromat.}$), 7.72 (s, 1H, *H*C5′), 7.37–7.27 (m, 10H, H_{aromat}), 7.23–7.15 (m, 3H, H_{aromat}), 7.14–7.05 (m, 2H, H_{aromat}), 5.24 (AB, *J* = 14.6 Hz, 1H, CH_aH_b), 5.17 (AB, *J* = 14.6 Hz, 1H, CH_aH_b), 5.13–4.98 (m, 4H, 2 × $POCH_2Ph$), 4.65–4.44 (m, 3H, OCH_aH_bPh, H-3a, H-3b), 4.32–4.20 (m, 1H, H-2), 4.19 (d, *J* = 10.8 Hz, 1H, OCH_aH_bPh), 3.87 (ddd, *J* = 11.9 Hz,

J = 9.1 Hz, J = 3.0 Hz, 1H, H-1), 3.11 (dd, J = 9.1 Hz, J = 6.7 Hz, 1H, OH); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 159.75 (s, C═O), 152.14, 149.17, 146.08, 141.30, 136.67, 135.83, 135.63 (d, J = 5.5 Hz, C_{ipso}), 129.36, 128.77, 128.73, 128.70, 128.44, 128.37, 128.23, 128.18, 128.16, 125.28, 123.23, 122.21, 76.88 (d, J = 2.2 Hz), 74.14 (s, PCC), 68.67 (d, J = 7.5 Hz, POC), 68.37 (d, J = 161.1 Hz, PC), 68.33 (d, J = 7.5 Hz, POC), 50.81 (d, J = 12.1 Hz, PCCC), 41.77; ^{31}P NMR (81 MHz, $CDCl_3$): δ = 22.45 ppm. Anal. calcd. for $C_{35}H_{33}N_6O_8P$: C, 60.34; H, 4.77; N, 12.06. Found: C, 60.74; H, 4.53; N, 12.18.

(1*R*,2*S*)-Dibenzyl 2-benzyloxy-1-hydroxy-3-{4-[6-nitro-4-oxoquinazolin-3(4*H*)-yl)methyl]-1*H*-1,2,3-triazol-1-yl}-propylphosphonate (1*R*,2*S*)-9cj

From (1*R*,2*S*)-dibenzyl 3-azido-2-benzyloxy-1-hydroxypropylphosphonate (1*R*,2*S*)-**11j** (0.065 g, 0.137 mmol) and 6-nitro-N^3-propargylquinazolin-4(3*H*)-one **13c** (0.032 g, 0.137 mmol), a phosphonate (1*R*,2*S*)-**9cj** (0.067 g, 69%) was obtained as a white powder after purification on a silica gel column with chloroform–methanol mixtures (50:1, v/v). $[\alpha]_D^{20}$ = −1.9 (c = 1.34 in $CHCl_3$); m.p.: 176–177°C; IR (KBr): ν = 3179, 3120, 2988, 2855, 1667, 1642, 1424, 1244, 1027, 759, 699 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 9.06 (d, J = 2.6 Hz, 1H, $H_{aromat.}$), 8.52 (s, 1H), 8.48 (dd, J = 8.8 Hz, J = 2.6 Hz, 1H, $H_{aromat.}$), 7.80 (d, J = 8.8 Hz, 1H, $H_{aromat.}$), 7.75 (s, 1H, *HC*5′), 7.35–7.23 (m, 10H, H_{aromat}), 7.22–7.14 (m, 3H, H_{aromat}), 7.12–7.02 (m, 2H, H_{aromat}), 5.22 (s, 2H, CH_2), 5.07–4.97 (m, 4H, 2 × $POCH_2Ph$), 4.77–4.55 (m, 2H, H-3a, H-3b), 4.43 (AB, J = 11.0 Hz, 1H, OCH_aH_bPh), 4.27 (d, J = 11.0 Hz, 1H, OCH_aH_bPh), 4.20–4.05 (m, 1H, H-2), 4.03–3.30 (m, 2H, H-2, OH); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 159.75 (s, CO), 152.13, 149.31, 146.05, 141.14, 136.68, 135.80 (d, J = 5.5 Hz, C_{ipso}), 135.72 (d, J = 5.5 Hz, C_{ipso}), 129.33, 128.72, 128.69, 128.46, 128.34, 128.19, 128.16, 128.12, 128.06, 125.52, 123.21, 122.21, 77.62 (d, J = 4.4 Hz, PCC), 72.87, 68.58 (d, J = 6.6 Hz, POC), 68.45 (d, J = 6.6 Hz, POC), 67.80 (d, J = 161.4 Hz, PC), 50.31 (d, J = 6.3 Hz, PCCC), 41.73; ^{31}P NMR (81 MHz, $CDCl_3$): δ = 23.80 ppm. Anal. calcd. for $C_{35}H_{33}N_6O_8P$: C, 60.34; H, 4.77; N, 12.06. Found: C, 60.55; H, 4.83; N, 12.12.

4.2 | Antimicrobial assay

The antimicrobial tests were performed using reference microbial strains from the American Type Culture Collection (ATCC) including: *B. subtilis* ATCC 6633, *S. aureus* ATCC 6535, *E. faecalis* ATCC 29212, *E. coli* ATCC 8739, *P. aeruginosa* ATCC 27853 and two fungal strains: *C. albicans* ATCC 10231 and *A. brasiliensis* ATCC 16404. The antimicrobial activity of the compounds was assessed according to their minimal inhibitory concentrations (MIC) and minimal bactericidal concentrations (MBC). The MIC and MBC were expressed in mg/mL. Antibacterial and antifungal activities were determined using the broth micro-dilution method in liquid medium according to The European Committee on Antimicrobial Susceptibility (EUCAST) recommendations. The Mueller-Hinton liquid medium (pH ∼7.2) was used for bacteria (BioMerieux). Liquid medium RPMI-1640 (pH ∼7.2) (Sigma) was used for the fungal strains. Each tested compounds was dissolved in 10 mg/mL in sterile water. Twofold series dilutions of the different compounds in growth medium was performed in the 96-well sterile microtiter plates (Kartell Labware, Italy). Inocula were freshly prepared and standardized as microbial suspensions (McFarland scale) containing 10^8 colony forming units (cfu/mL), added at a volume of 10 µL to the wells of the microtiter plate together with the serial dilutions of the compounds in the growth medium. After 24 h of incubation at 37°C, microbial growth was evaluated spectrophotometrically at 595 nm using a Microplate Reader 680 (BioRad, France). The lowest concentration of the test compounds resulting in total growth inhibition was taken as the MIC value. To determine the MBC, 10 µL of the culture were collected from each well, where no visible growth of microorganisms was recorded and plated onto the surface of Brain Heart Infusion Agar (BioMerieux). The cultures were incubated at 37°C for 24 h, and an absence of microbial growth indicated the bactericidal activity of the tested compounds. Plates with *A. brasiliensis* were incubated at 37°C for 3 days. The tests were performed in two independent experiments. Gentamicin (Sigma) and fluconazole (Sigma) were used as antimicrobial standard.

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CONFLICT OF INTEREST

The authors have declared no conflict of interest.

ORCID

Iwona E. Głowacka http://orcid.org/0000-0001-7567-5860

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