Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

European Journal of Medicinal Chemistry 70 (2013) 703–722

Contents lists available at ScienceDirect

European Journal of Medicinal Chemistry

journal homepage: http://www.elsevier.com/locate/ejmech

Original article

The synthesis, antiviral, cytostatic and cytotoxic evaluation of a new series of acyclonucleotide analogues with a 1,2,3-triazole linker

Iwona E. Głowacka [a,*], Jan Balzarini [b], Andrzej E. Wróblewski [a]

[a] Bioorganic Chemistry Laboratory, Faculty of Pharmacy, Medical University of Łódź, Muszyńskiego 1, 90-151 Łódź, Poland
[b] Rega Institute for Medical Research, KU Leuven, Minderbroedersstraat 10, B-3000 Leuven, Belgium

ARTICLE INFO

Article history:
Received 5 July 2013
Received in revised form
16 October 2013
Accepted 23 October 2013
Available online 30 October 2013

Keywords:
Aziodophosphonates
Acyclonucleotides
1,2,3-Triazoles
Synthesis
Antiviral
Cytostatic

ABSTRACT

The efficient synthesis of a new series of acyclonucleotide analogues with a 1,2,3-triazole linker is described starting from diethyl azidomethyl-, 2-azidoethyl-, 3-azidopropyl-, 4-azidobutyl-, 2-azido-1-hydroxyethyl-, 3-azido-2-hydroxypropyl- and 3-azido-1-hydroxypropylphosphonates and selected alkynes under microwave irradiation. Several *O,O*-diethylphosphonate acyclonucleotides were transformed into the respective phosphonic acids. All compounds were evaluated in vitro for activity against a broad variety of DNA and RNA viruses and cytostatic activity against murine leukaemia L1210, human T-lymphocyte CEM and human cervix carcinoma HeLa cells. Acyclonucleotide **22e** exhibited activity against both herpes simplex viruses (HSV-1, HSV-2) in HEL cell cultures (EC_{50} = 17 μM) and feline herpes virus (EC_{50} = 24 μM) in CRFK cell cultures, while compounds **20k**, **21k**, **22k** and **23k** preferentially inhibited proliferation of human T-lymphocyte CEM cells at IC_{50} in the 2.8–12 μM range.

1. Introduction

Several acyclic nucleosides and nucleotides exhibit antiviral or anticancer activities. However, in most cases, the clinical use of antiviral nucleosides is hampered by the drug resistance and/or toxicity problems. Under these circumstances intensive search for new drugs effective in the chemotherapy of viruses such as HIV, herpes virus, hepatitis viruses and cytomegalovirus has been conducted by many laboratories. A large number of modifications has been introduced to both the nucleobase and the sugar moieties of natural nucleosides. Consequently, several analogues like adefovir [1,2], tenofovir [3] and cidofovir [4] (Fig. 1) were synthesised in which the furanose ring and the readily hydrolysable phosphate ester linkage present in natural nucleotides have been replaced by an acyclic chain and phosphonate moiety, respectively.

In drug discovery replacement of canonical nucleobases [5] by substituted five-membered heterocyclic rings such as imidazole or triazole has been particularly successful. Ribavirin [6–12], AICA [13,14], Bredinin [15,16] and TSAO analogues [17,18] are the best known examples among these analogues (Fig. 2).

Further efforts in this field led to the synthesis of several analogues containing both modified nucleobases and 1,2,3-triazole moieties [19–37]. Among them compounds **1**–**11** [27–37] in which nucleobases or their mimetics and substituted triazoles are linked by the methylene group are of special interest (Fig. 3).

Moreover, several compounds possessing the 1,2,3-triazole ring show cytostatic [38–45], antiviral [46–49], antibacterial [50–56] or antifungal activities [57–60]. The conventional synthesis of 1,2,3-triazoles relies on the Hüisgen [3 + 2] cycloaddition between alkynes and organic azides and usually provides a mixture of 1,4- and 1,5-disubstitued regioisomers [61,62]. Recent discovery of copper(I) as an efficient and regiospecific catalyst for this transformation [63,64] provides a general and mild approach for the preparation of 1,4-disubstituted 1,2,3-triazole derivatives.

In continuation of our studies on nucleotide analogues [65–70] a new series of modified phosphonylated 1,2,3-triazoloa cyclonucleosides bearing selected nucleobases or their mimetics at C-4 of the 1,2,3-triazole moiety (Scheme 1) has been synthesised and subjected to biological evaluation.

2. Results and discussion

2.1. Chemistry

Compounds **20**–**26** **a**–**l** were obtained by the 1,3-dipolar cycloaddition of azidoalkylphosphonates **12**–**18** with propargylated nucleobases **19a**–**l**: N^9-propargyladenine **19a** [27], N^1-

* Corresponding author. Tel.: +48 42 677 92 37; fax: +48 42 678 83 98.
E-mail address: iwona.glowacka@umed.lodz.pl (I.E. Głowacka).

0223-5234/$ – see front matter © 2013 Elsevier Masson SAS. All rights reserved.
http://dx.doi.org/10.1016/j.ejmech.2013.10.057

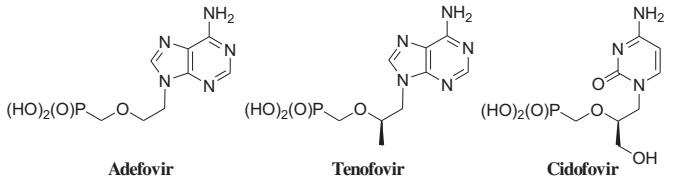


Fig. 1. Acyclic nucleoside phosphonates used in the treatment of viral infections.

propargylthymine **19b** [27], N^1-propargyluracil **19c** [71] and N^4-acetyl-N^1-propargylcytosine **19d** [71] and mimetics of nucleobases: N^3-benzoyl-N^1-propargylquinazoline-2,4-dione **19e**, N^1-propargyl-6-azauracil **19f** [30], 8-chloro-N^7-propargyltheophylline **19g** [72], N^1-propargyltheobromine **19h** [73,74], N^7-propargyltheophylline **19i** [75], 5,6-dimethyl-N^1-propargylbenzimidazole **19j** [76], 3-acetyl-*N*-propargylindole **19k** [77], *N*-propargyl-2-pyridon **19l** [76]. The required azidoalkylphosphonates **12**–**18** were synthesised according to the procedures described previously [65,66,69,78,79].

Except for N^3-benzoyl-N^1-propargylquinazoline-2,4-dione **19e** all alkynes used in this paper have already been described in the literature. N^3-Benzoyl-N^1-propargylquinazoline-2,4-dione **19e** was synthesised in 19% overall yield in three steps from quinazoline-2,4-dione **27** beginning with bis-N^1,N^3-benzoylation to **28** followed by the selective N^1-debenzoylation to **29** and propargylation (Scheme 2). The N^3-benzoylquinazoline-2,4-dione **29** was previously obtained from 2-benzoylaminobenzoxazinone in less than 5% yield [80].

The structure of N^3-benzoyl-N^1-propargylquinazoline-2,4-dione **19e** was confirmed on the basis of ^{1}H, ^{13}C NMR and IR spectral data and finally proved by 2D COSY and NOESY experiments (Fig. 4).

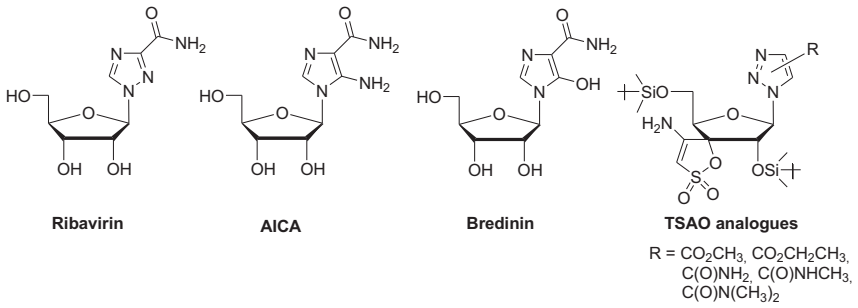


Fig. 2. Ribavirin, AICA, Bredinin and TSAO analogues.

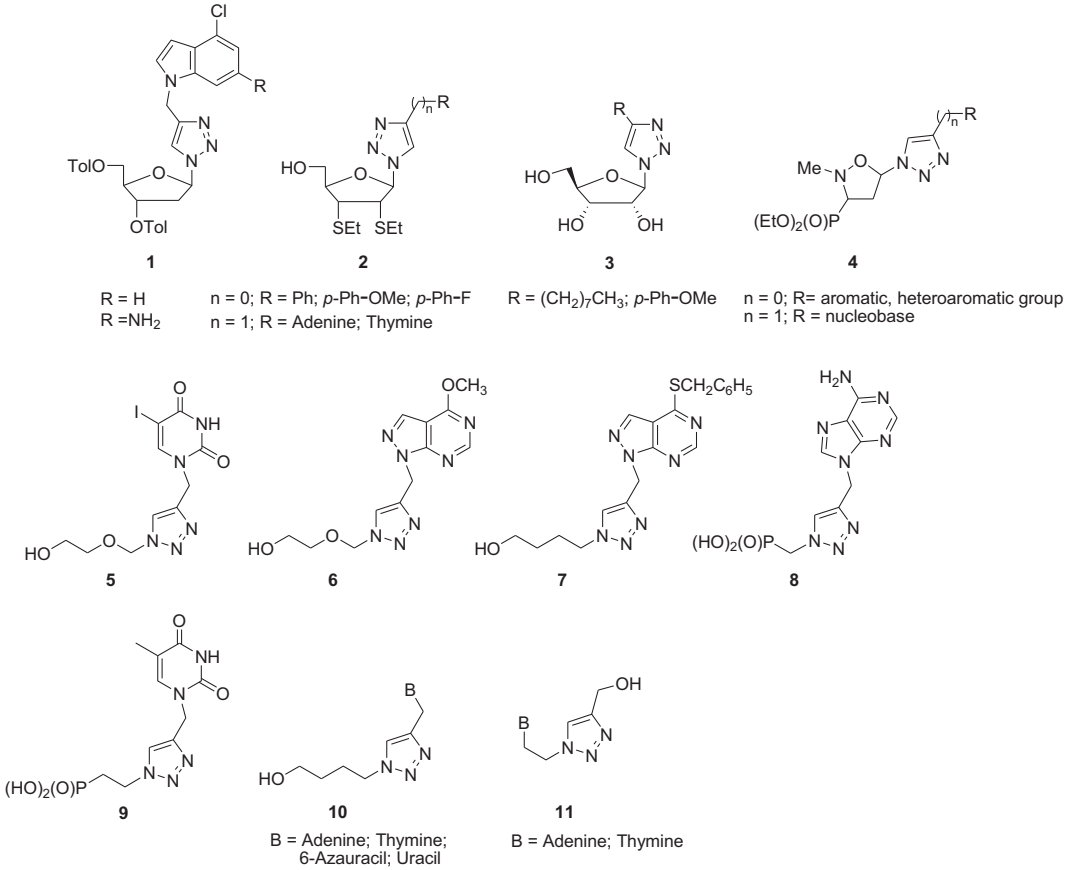
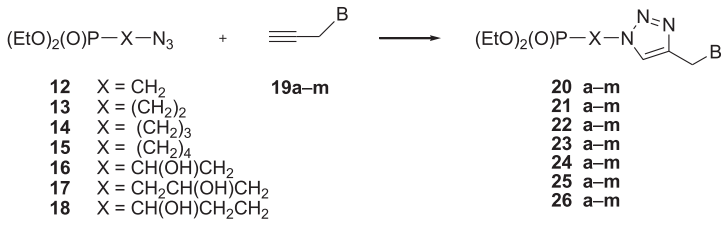


Fig. 3. Nucleoside analogues having natural nucleobases connected to the 1,2,3-triazole ring by a methylene linker.



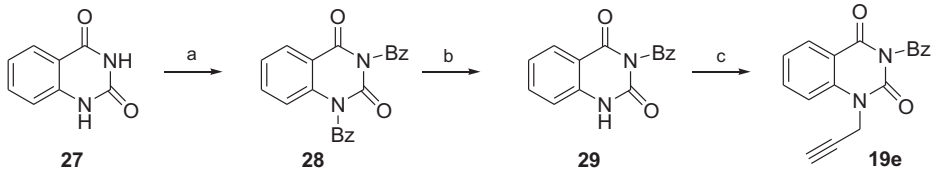
12 X = CH_2
13 X = $(CH_2)_2$
14 X = $(CH_2)_3$
15 X = $(CH_2)_4$
16 X = $CH(OH)CH_2$
17 X = $CH_2CH(OH)CH_2$
18 X = $CH(OH)CH_2CH_2$

19a–m

20 a–m
21 a–m
22 a–m
23 a–m
24 a–m
25 a–m
26 a–m

B = a. Adenine; **b.** Thymine; **c.** Uracil; **d.** N^4-Acetylcytosine; **e.** N^3-Benzoylquinazoline-2,4-dione; **f.** 6-Azauracil; **g.** 8-Chlorotheophylline; **h.** Theobromine; **i.** Theophylline; **j.** 5,6-dimethylbenzimidazole; **k.** 3-Acetyloindole; **l.** 2-Pyridon; **m.** N^3-benzoyluracil

Scheme 1. Synthesis of phosphonylated 1,2,3-triazoloacyclonucleosides **20**–**26 a**–**m**.



27 **28** **29** **19e**

Scheme 2. Reagents and conditions: a. benzoyl chloride (2.2 equiv.), pyridine, CH_3CN, r.t, 12 h, 87%; b. 1 N K_2CO_3 aq., dioxane, r.t., 24 h, 23%; c. propargyl bromide (1.2 equiv.), K_2CO_3 (1.1 equiv.), DMF, r.t., 24 h, 97%.

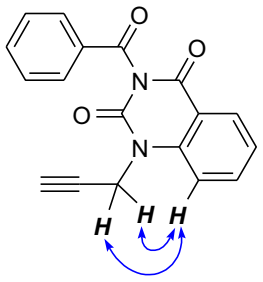


Fig. 4. NOESY correlations in **19e**.

All 1,2,3-triazoles **20**–**26** were obtained in good yields in 1,3-dipolar cycloadditions which were carried out in a microwave oven at 40–45 °C. This approach caused significant improvements in purity of the final products and allows to shorten the reaction time from 48 h at room temperature to 10 min of irradiation. Since syntheses of phosphonylated 1,2,3-triazoles **20a**–**d**, **21a**–**d**, **22a**–**d**, **24a**–**d** and **25a**–**d** have already been described and their biological activity evaluated [32,69], N^9-propargyladenine **19a**, N^1-propargylthymine **19b**, N^1-propargyluracil **19c** and N^4-acetyl-N^1-propargylcytosine **19d** were reacted with two azidophosphonates **15** and **18**, only. However, mimetics of nucleobases **19e**–**l** were applied in cycloadditions with all seven azidophosphonates **12**–**18** (Schemes 3 and 4).

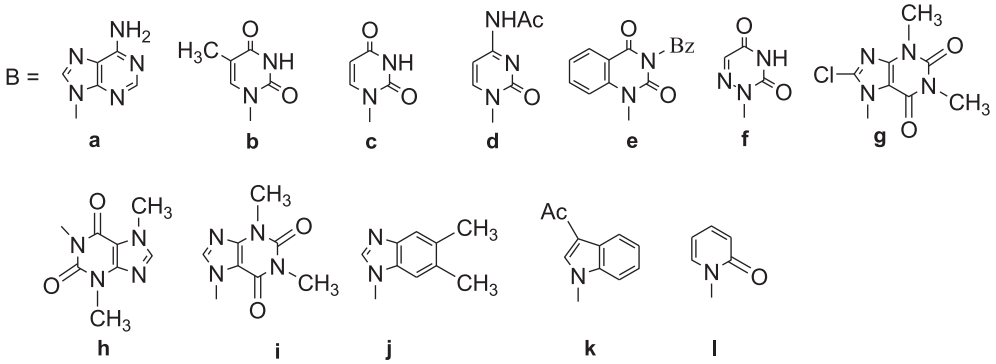
Since the preliminary experiments have demonstrated antiviral activity of compound **22e** against herpes simplex viruses (HSV-1, HSV-2) in HEL cell cultures (EC_{50} = 17 μM) and feline herpes virus (EC_{50} = 24 μM) in CRFK cell cultures, phosphonate **22m** was synthesised in order to establish the influence of the fused phenyl ring in **22e** on the observed activity (Scheme 5).

Our synthesis of N^3-benzoyl-N^1-propargyluracil **19m** by propargylation of N^3-benzoyluracil with propargyl bromide (Scheme 6) appeared more efficient (95%) in comparison to the previously

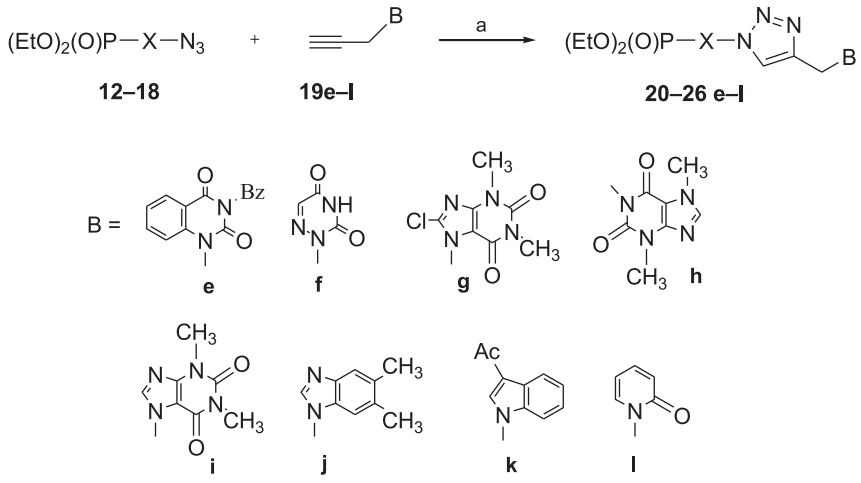
15 X = $(CH_2)_4$
18 X = $CH(OH)CH_2CH_2$

19a–19l

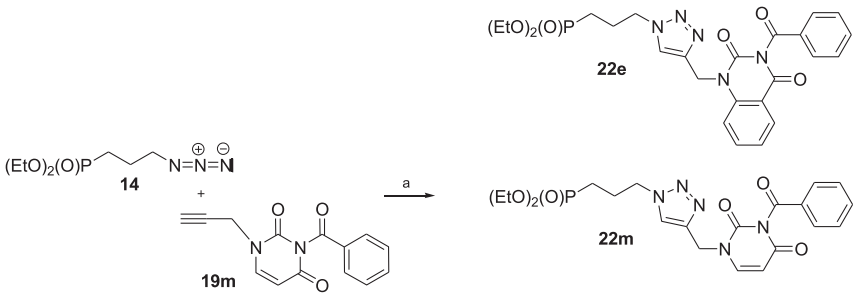
23a–l
26a–l



Scheme 3. Reagents and conditions: a. $CuSO_4 \times 5H_2O$ (0.05 equiv.), sodium ascorbate (0.1 equiv.), H_2O–EtOH (1:1), MW, 40–45 °C, 10 min.



Scheme 4. Reagents and conditions: a. $CuSO_4 \times 5H_2O$ (0.05 equiv.), sodium ascorbate (0.1 equiv.), H_2O–EtOH (1:1), MW, 40–45 °C, 10 min.



Scheme 5. Reagents and conditions: a. $CuSO_4 \times 5H_2O$ (0.05 equiv.), sodium ascorbate (0.1 equiv.), H_2O–EtOH (1:1), MW, 40–45 °C, 10 min.

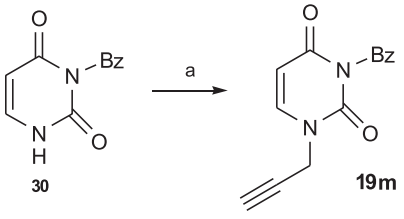
described approach from N^3-benzoyluracil and propargyl alcohol via the Mitsunobu reaction (76% yield) [81].

Finally, using bromotrimethylsilane [82] selected diethyl phosphonates **22e**, **22g**, **22j**, **22m**, **23a**–**c** and **24i** were transformed into the respective phosphonic acids in good yields (Scheme 7).

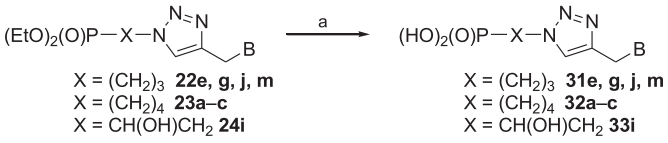
2.2. Conformational analysis

Conformational preferences of phosphonates described in this paper were ascertained by analyses of ^1H, $^1H\{^{31}P\}$ and ^{13}C NMR spectra. Since all vicinal proton–proton couplings within the H_2C–CH_2 fragment in phosphonates **21e**–**l** were observed around 7 Hz, it was concluded that the rotation around the PCH_2–CH_2N bond is fully unrestricted. On the other hand, based on the values of $^3J_{H1-H2a} = 10.0$ Hz, $^3J_{H1-H2b} = 2.9$ Hz [83] and small values of $^3J_{P-H2a}$ and $^3J_{P-H2b}$ (ca. 5.5 Hz) [84,85] one may deduce that phosphonates **24e**–**l** exist in the antiperiplanar conformation **34** which is probably stabilised by the intramolecular hydrogen bond (Fig. 5). Conformational behaviour of the three-carbon linkers between the diethoxyphosphoryl and substituted 1,2,3-triazole groups in phosphonates **22e**–**l**, **25e**–**l** and **26e**–**l** is primarily governed by the presence of the hydroxy groups. Thus, values of vicinal proton–proton couplings within PCH_2–CH_2 and CH_2–CH_2N subunits in **22e**–**l** (ca. 7 Hz) can only be observed when free rotation around these bonds is allowed. 2-Hydroxyphosphonates **25e**–**l** adopt the H-bond stabilised antiperiplanar conformation **35** along the PCH_2–CH bond [$^3J_{H1a-H2} = 3.9$ Hz, $^3J_{H1b-H2} = 8.6$ Hz, $^3J_{P-H2} = 12.0$ and $^3J_{P-C3} = 14$–18 Hz [85–87], while the rotation around the CH–CH_2N bond is unrestricted [$^3J_{H2-H3a} = 3.0$ Hz, $^3J_{H2-H3b} = 7.0$ Hz]. To establish a conformational behaviour of 1-hydroxyphosphonates **26a**–**l** the extensive NMR studies on 1-hydroxyphosphonate **26i** were conducted at 600 MHz. From the values of $^3J_{H1-H2a} = 3.3$ Hz, $^3J_{H1-H2b} = 10.9$ Hz as well as $^3J_{P-H2a} = 6.1$ and $^3J_{P-H2b} = 6.4$, $^3J_{P-C3} = 15$–18 Hz, it is evident that along the PCH–CH_2 bond, this phosphonate exists in the antiperiplanar conformation **36**, while based on the values of $^3J_{H2a-H3a} = {}^3J_{H2a-H3b} = 8.0$ Hz, $^3J_{H2b-H3a} = 5.9$ Hz and $^3J_{H2b-H3b} = 5.9$ Hz one may suggest that along the CH_2–CH_2N bond in **26i** the rotation is almost free.

The anticipated full conformational freedom along the tetramethylene linker in the butylphosphonates **23a**–**l** is confirmed by the values of $^3J_{H-H} = 7.1$ Hz between all methylene groups (Fig. 5).



Scheme 6. Reagents and conditions: a. propargyl bromide (1.2 equiv.), K_2CO_3 (1.1 equiv.), DMF, r.t., 24 h, (95%).



Scheme 7. Reagents and conditions: a. TMSBr, CH_2Cl_2, r.t., 24 h.

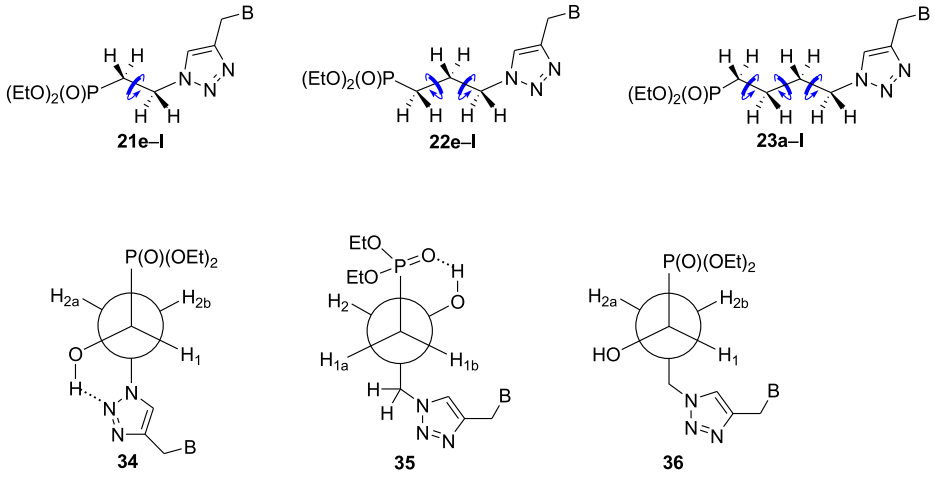


Fig. 5. Preferred conformations of phosphonates investigated in this paper.

2.3. Antiviral activity and cytotoxicity evaluation

All the synthesised compounds **20**–**26 a**–**m**, **31e**, **31g**, **31j**, **31m**, **32a**–**c** and **33i** were evaluated for their antiviral activities against a wide variety of DNA and RNA viruses, using the following cell-based assays: (a) human embryonic lung (HEL) cells: herpes simplex virus-1 (KOS), herpes simplex virus-2 (G), herpes simplex virus-1 (TK^- ACV^r KOS), vaccinia virus and vesicular stomatitis virus; (b) CEM cell cultures: human immunodeficiency virus-1 [HIV-1] and HIV-2; (c): Vero cell cultures: para-influenza-3 virus, reovirus-1, Sindbis virus, Coxsackie virus B4, Punta Toro virus; (d): HeLa cell cultures: vesicular stomatitis virus, Coxsackie virus B4 and respiratory syncytial virus; (e): Crandell-Rees Feline Kidney (CRFK) cell cultures: feline corona virus (FIPV) and feline herpes virus (FHV); (f): Madin Darby Canine Kidney (MDCK) cell cultures: influenza A virus H1N1 subtype (A/PR/8), influenza A virus H3N2 subtype (A/HK/7/87) and influenza B virus (B/HK/5/72). Ganciclovir, cidofovir, acyclovir, brivudin, (*S*)-9-(2,3-dihydroxypropyl)adenine [(*S*)-DHPA], *Hippeastrum* hybrid agglutinin (HHA), *Urtica dioica* agglutinin (UDA), dextran sulphate (molecular weight 5000, DS-5000), ribavirin, oseltamivir carboxylate, amantadine and rimantadine were used as the reference compounds. The antiviral activity was expressed as the EC_{50}: the compound concentration required to reduce virus plaque formation (VZV) by 50% or to reduce virus-induced cytopathogenicity by 50% (other viruses).

The cytotoxicity of the tested compounds toward the uninfected host cells was defined as the minimum cytotoxic concentration (MCC) that causes a microscopically detectable alteration of normal cell morphology. The 50% cytotoxic concentration (CC_{50}), causing a 50% decrease in cell viability was determined using a colorimetric 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2*H*-tetrazolium (MTS) assay system.

Among all the 1,2,3-triazole derivatives tested, compound **22e** having a three carbon fragment between the phosphorus atom and the 1,2,3-triazole ring substituted at C4′ with N^3-benzoyl-N^1-methylquinazoline-2,4-dione showed a moderate activity against both herpes simplex viruses (HSV-1, HSV-2) ($EC_{50} = 17$ μM) in HEL cell cultures, and feline herpes virus ($EC_{50} = 24$ μM) in CRFK cell cultures.

2.4. Evaluation of cytostatic activity

The cytostatic activity of the tested compounds was defined as the 50% cytostatic inhibitory concentration (IC_{50}), causing a 50% decrease in cell proliferation was determined against murine leukaemia L1210, human lymphocyte CEM and human cervix carcinoma HeLa cells. Most compounds were not cytostatic at 200 μM.

Several compounds showed very moderate inhibitory against the proliferation of tumour cell lines (Table 1), although in a few cases, the compounds seemed to be preferentially cytostatic against human tumour cell lines (esp. lymphocyte CEM cells) than murine (L1210) cells. In particular, compound **20k**, **21k**, **22k** and **23k** were antiproliferative at IC_{50} values ranging between 2.8 and 12 μM.

2.5. Structure–activity relationship

Structure–activity relationship studies on a series of 1,2,3-triazoloacyclonucleotides **20**–**26 a**–**m** and **30e**, **g**, **j**, **m**, **31a**–**c** and **32i** revealed cytostatic activity of compounds substituted at C4′ of the 1,2,3-triazole ring with 3-acetylindole, N^3-benzoylquinazoline-2,4-dione and 5,6-dimethylbenzimidazole. Regardless of the length of the linker (1–4 carbon atoms) all derivatives of the 1,2,3-triazoles with 3-acetylindole were the most active towards CEM cell lines (e.g. $IC_{50} = 2.78 \pm 1.4$ μM for **20k**) and also some of them against HeLa cells. Furthermore, compounds **21j**, **22e**, **23k**, **24k**, **25e** and **26e** selectively inhibited the proliferation of human T-lymphocyte (CEM).

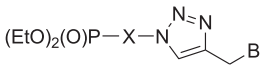
As could be expected the phosphonic acids were found inactive in all biological tests including these acids for which the corresponding diethyl esters displayed significant activity (**22e** vs. **31e** and **22j** vs. **31j**). This is in full agreement with observation that lipophilic phosphonate esters better penetrate through membranes in comparison with phosphonic acids and thus the sufficient concentration of the ester is achieved in cells to undergo further reactions.

For compound **22e** containing a three methylene linker between the phosphorus atom and the 1,2,3-triazole ring substituted at C4′ with N^3-benzoyl-N^1-methylquinazoline-2,4-dione activity against both herpes simplex viruses (HSV-1, HSV-2) ($EC_{50} = 17$ μM) in HEL cell cultures, and feline herpes virus ($EC_{50} = 24$ μM) in CRFK cell cultures was established. The presence of the quinazoline ring appeared necessary for **22e** to display antiviral activity, since its structural analogue lacking the condensed phenyl ring (compound **22m**) was found inactive $EC_{50} > 200$ μM.

3. Conclusion

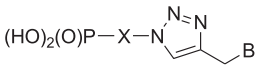
A new series of 1,2,3-triazoloacyclonucleotides **20**–**26 a**–**m** has been efficiently obtained from diethyl azidomethyl-, 2-azidoethyl-, 3-azidopropyl-, 4-azidobutyl-, 2-azido-1-hydroxyethyl-, 3-azido-2-

Table 1
Inhibitory effect of tested compounds against the proliferation of murine leukaemia (L1210), human T-lymphocyte (CEM) and human cervix carcinoma cells (HeLa).



20–26 a–l

20 X = CH_2
21 X = $(CH_2)_2$
22 X = $(CH_2)_3$
23 X = $(CH_2)_4$
24 X = $CH(OH)CH_2$
25 X = $CH_2CH(OH)CH_2$
26 X = $CH(OH)CH_2CH_2$



X = $(CH_2)_3$ **31e, g, j, m**
X = $(CH_2)_4$ **32a–c**
X = $CH(OH)CH_2$ **33i**

Compound	B	IC_{50}[a] (μM)		
		CEM	L1210	HeLa
20e	N^3-Benzoylquinazoline-2,4-dione	≥72	>200	≥89
20f	6-Azauracil	>200	>200	>200
20g	8-Chlorotheophylline	>200	>200	>200
20h	Theobromine	>200	>200	≥149
20i	Theophylline	>200	>200	>200
20j	5,6-Dimethylbenzimidazole	97 ± 35	>200	42 ± 16
20k	3-Acetylindole	2.78 ± 1.4	72 ± 19	11 ± 7.6
20l	2-Pyridon	>200	>200	>200
21f	6-Azauracil	>200	>200	>200
21g	8-Chlorotheophylline	>200	>200	200
21h	Theobromine	>200	>200	159 ± 59
21i	Theophylline	>200	>200	>200
21j	5,6-Dimethylbenzimidazole	23.4 ± 7.9	≥200	>200
21k	3-Acetylindole	11.4 ± 2.2	197 ± 4.2	18 ± 3.5
21l	2-Pyridon	>200	>200	>200
22e	N^3-Benzoylquinazoline-2,4-dione	44 ± 42	>200	129 ± 78
22f	6-Azauracil	>200	>200	>200
22g	8-Chlorotheophylline	>200	>200	>200
22h	Theobromine	>200	>200	>200
22i	Theophylline	>200	>200	>200
22j	5,6-Dimethylbenzimidazole	14 ± 8.3	189 ± 16	101 ± 23
22k	3-Acetylindole	4.54 ± 1.24	164 ± 52	19 ± 13
22l	2-Pyridon	>200	>200	>200
22m	N^3-Benzoyluracil	>200	>200	>200
23a	Adenine	>200	>200	>200
23b	Thymine	>200	>200	>200
23c	Uracil	>200	>200	>200
23d	N^4-Acetylcytosine	>200	>200	>200
23f	6-Azauracil	>200	>200	>200
23g	8-Chlorotheophylline	>200	>200	>200
23h	Theobromine	>200	>200	>200
23i	Theophylline	>200	>200	>200
23j	5,6-Dimethylbenzimidazole	24.7 ± 8.1	>200	172 ± 40
23k	3-Acetylindole	12 ± 3.5	200	>200
23l	2-Pyridon	>200	>200	>200
24e	N^3-Benzoylquinazoline-2,4-dione	≥77	>200	>200
24f	6-Azauracil	>200	>200	>200
24g	8-Chlorotheophylline	>200	>200	>200
24h	Theobromine	>200	>200	>200
24i	Theophylline	>200	>200	>200
24j	5,6-Dimethylbenzimidazole	>200	>200	>200
24k	3-Acetylindole	21 ± 0.14	>200	>200
24l	2-Pyridon	>200	>200	>200
25e	N^3-Benzoylquinazoline-2,4-dione	72 ± 45	>200	>200
25f	6-Azauracil	>200	>200	>200
25g	8-Chlorotheophylline	>200	>200	>200
25h	Theobromine	>200	>200	>200
25i	Theophylline	>200	>200	>200
25j	5,6-Dimethylbenzimidazole	78 ± 26	>200	≥150
25k	3-Acetylindole	43 ± 3.5	>200	97 ± 80
25l	2-Pyridon	>200	>200	>200
26b	Thymine	>200	>200	>200
26c	Uracil	>200	>200	>200
26d	N^4-Acetylcytosine	>200	>200	>200
26e	N^3-Benzoylquinazoline-2,4-dione	70 ± 18	>200	>200
26f	6-Azauracil	>200	>200	>200
26g	8-Chlorotheophylline	>200	>200	>200
26h	Theobromine	>200	>200	>200
26i	Theophylline	>200	>200	>200
26j	5,6-Dimethylbenzimidazole	163 ± 53	>200	>200
26k	3-Acetylindole	100 ± 2.8	124 ± 62	>200
26l	2-Pyridon	>200	>200	>200
31e	N^3-Benzoylquinazoline-2,4-dione	>200	>200	>200
31g	8-Chlorotheophylline	>200	>200	>200

Table 1 (*continued*)

Compound	B	IC_{50}[a] (μM)		
		CEM	L1210	HeLa
31j	5,6-Dimethylbenzimidazole	>200	>200	>200
31m	N^3-Benzoyluracil	>200	>200	>200
32a	Adenine	>200	>200	>200
32b	Thymine	>200	>200	>200
32c	Uracil	>200	>200	>200
33i	Theophylline	>200	>200	>200

[a] 50% Inhibitory concentration or compound concentration required to inhibit tumour cell proliferation by 50%.

hydroxypropyl- and 3-azido-1-hydroxypropylphosphonates and selected *N*-propargyl alkynes including *N*-propargyl nucleobases (N^9-propargyladenine **19a**, N^1-propargylthymine **19b**, N^1-propargyluracil **19c** and N^4-acetyl-N^1-propargylcytosine **19d**) and several mimetics (N^3-benzoyl-N^1-propargylquinazoline-2,4-dione **19e**, N^1-propargyl-6-azauracil **19f**, 8-chloro-N^7-propargyltheophylline **19g**, N^1-propargyltheobromine **19h**, N^7-propargyltheophylline **19i**, 5,6-dimethyl-N^1-propargylbenzimidazole **19j**, 3-acetyl-*N*-propargylindole **19k**, *N*-propargyl-2-pyridon **19l** and N^3-benzoyl-N^1-propargyluracil **19m**) via 1,3-dipolar cycloadditions carried out under microwave irradiation.

The N^3-benzoyl-N^1-propargylquinazoline-2,4-dione **19e** was synthesised from quinazoline-2,4-dione **27** in the sequence of reactions including bis-N^1,N^3-benzoylation followed by the selective N^1-debenzoylation and propargylation.

Under standard conditions (TMSBr, ethanol) several *O*,*O*-diethyl phosphonates **22e**, **g**, **j**, **m**, **23a**–**c** and **24i** were transformed into their respective phosphonic acid.

All synthesised compounds were evaluated against a variety of DNA and RNA viruses. Compound **22e** containing a three carbon linker between the phosphorus atom and the 1,2,3-triazole ring substituted at C4′ with N^3-benzoyl-N^1-methylquinazoline-2,4-dione showed a moderate activity (EC_{50} = 17 μM) against both herpes simplex viruses (HSV-1, HSV-2) in HEL cell cultures and feline herpes virus (EC_{50} = 24 μM) in CRFK cell cultures.

All synthesised compounds were also evaluated for their antiproliferative activity against three tumour cell lines (L1210, CEM and HeLa) and several compounds, i.e. **20k**, **21j**–**k**, **22j**–**k**, **23j**–**k** and **24k** were found to be the most active (and preferentially inhibitory) towards T-lymphocyte CEM cell proliferation.

4. Experimental

4.1. Chemistry

^{1}H NMR were taken in $CDCl_3$, CD_3OD or D_2O on the following spectrometers: Varian Mercury-300 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 $CDCl_3$, CD_3OD, DMSO-d_6 or D_2O solutions on a Varian Mercury-300 and Bruker Avance III (600 MHz) spectrometer at 75.5 and 150.5 MHz, respectively. ^{31}P NMR spectra were taken in $CDCl_3$, CD_3OD or D_2O on Varian Mercury-300 at 121.5 MHz.

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 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. Visualisation of spots was effected with iodine vapours. All solvents were purified by methods described in the literature.

All microwave irradiation experiments were carried out in microwave reactor Plazmartonika RM 800. The reaction carried out in 50 mL glass vial.

4.1.1. Synthesis of 1,3-dibenzoylquinazoline-2,4-dione **28**

The benzoyl chloride (6.48 mL, 0.056 mol) was added to a stirred suspension of quinazoline-2,4-dione (4.00 g, 0.025 mol) in dry acetonitrile (25 mL) containing dry pyridine (10 mL) at room temperature. After 24 h the products were concentrated under reduced pressure. The residue was partitioned between dichloromethane (100 mL) and water (100 mL). The organic layer was dried ($MgSO_4$), concentrated *in vacuo* and the residue was crystallised from ethanol to give 1,3-dibenzoylquinazoline-2,4-dione **28** (7.985 g, 87%) as a white powder; m.p.: 159–160 °C; IR (KBr): ν = 3040, 1753, 1723; 1674, 1605, 1472, 974; 866; 753, 688 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.28 (dd, *J* = 7.9 Hz, *J* = 1.5 Hz, 1H, H5); 8.02–7.98 (m, 4H, 4× *o*-CH); 7.73–7.63 (m, 3H, 2× *p*-CH, H7); 7.56–7.48 (m, 4H, 4× *m*-CH); 7.36 (dt, *J* = 7.9 Hz, *J* = 0.7 Hz, 1H, H6); 7.10 (d, *J* = 8.4 Hz, 1H, H8); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 169.2; 167.8; 160.9; 147.9; 138.6; 136.1; 135.7; 135.3; 131.8; 131.4; 130.6; 130.5; 129.5; 129.3; 129.1; 124.8; 115.2; 114.9; Anal. Calcd. for $C_{22}H_{14}N_2O_4$: C, 71.35; H, 3.81; N, 7.56. Found: C, 71.49; H, 3.76; N, 7.44.

4.1.2. Synthesis of N^3-benzoylquinazoline-2,4-dione **29**

A mixture of 1,3-dibenzoylquinazoline-2,4-dione **28** (1.73 g, 4.67 mmol), dioxane (50 mL) and 1 N K_2CO_3 aq. (25 mL) was stirred at room temperature. After 24 h glacial acetic acid was added to pH 5. The products were concentrated under reduced pressure and the residue was stirred with saturated aqueous sodium bicarbonate (200 mL) at room temperature for 2 h. The solid was filtered off, washed with cold water and dried on air. The crude product was chromatographed on a silica gel column with chloroform–methanol (200:1, 100:1, v/v) and crystallised from ethyl acetate–petroleum ether to give the compound **29** (0.255 g, 23%) as white needles; m.p.: 209–211 °C; IR (KBr): ν = 3436, 3063, 2937, 1753, 1707, 1668, 1400, 760, 687 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.34 (brs, 1H, NH); 8.13 (dd, *J* = 7.9 Hz, *J* = 1.5 Hz, 1H); 8.03–7.99 (m, 2H, 2× *o*-CH); 7.71–7.62 (m, 2H); 7.55–7.49 (m, 2H); 7.29 (dd, *J* = 7.9 Hz, *J* = 0.9 Hz, 1H); 7.31 (ddd, *J* = 8.2 Hz, *J* = 0.9 Hz, *J* = 0.5 Hz, 1H); ^{13}C NMR (151 MHz, DMSO-d_6): δ = 170.3; 162.3; 149.3; 140.9; 136.4; 135.9; 132.0; 130.9; 129.9; 127.7; 123.6; 116.4; 114.3; Anal. Calcd. for $C_{15}H_{10}N_2O_3$: C, 67.67; H, 3.79; N, 10.52. Found: C, 67.48; H, 3.91; N, 10.45.

4.1.3. Synthesis of N^3-benzoyl-N^1-propargylquinazoline-2,4-dione **19e**

A suspension of N^3-benzoylquinazoline-2,4-dione **29** (0.239 g, 0.898 mmol), potassium carbonate (0.135 g, 0.978 mmol) and propargyl bromide (0.081 mL, 1.08 mmol) in DMF (3 mL) was stirred at room temperature for 24 h. The mixture was co-evaporated with toluene (5 × 10 mL). The residue was dissolved in chloroform

(10 mL) and washed with brine (2 × 5 mL). The organic phase was dried over $MgSO_4$, concentrated *in vacuo* and the residue was crystallised from methanol–diethyl ether to give compound **19e** (0.265 g, 97%) as a white powder; m.p.: 180–182 °C; IR (KBr): ν = 3256, 3002, 2925, 1751, 1697, 1659, 1482, 756, 684 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.26 (dd, J = 7.9 Hz, J = 1.3 Hz, 1H, H5); 8.12–7.99 (m, 2H, 2× *o*-CH); 7.83 (dt, J = 7.3 Hz, J = 1.4 Hz, 1H, H7); 7.69–7.67 (m, 1H, *p*-CH); 7.54–7.50 (m, 3H, 2× *m*-CH, H8); 7.31 (brt, J = 7.6 Hz, 1H); 4.96 (d, J = 2.5 Hz, 2H, CH≡CCH_2); 3.74 (t, J = 2.5 Hz, 1H, CH≡CCH_2); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 168.4 (s, C=O); 160.9 (s, C=O); 148.8 (s, C=O); 139.6; 136.1; 135.1; 131.7; 130.5; 129.2; 129.2; 123.9; 115.8; 114.7; 73.8; 32.8; Anal. Calcd. for $C_{18}H_{12}N_2O_3$: C, 71.05; H, 3.97; N, 9.21. Found: C, 70.92; H, 4.05; N, 9.14.

4.1.4. N^3-Benzoyl-N^1-propargyluracil ***19m***

A suspension of N^3-benzoyluracil **30** (0.506 g, 0.234 mmol), potassium carbonate (0.356 g, 0.257 mmol) and propargyl bromide (0.211 mL, 0.281 mmol) in DMF (4 mL) was stirred at room temperature for 24 h. The mixture was co-evaporated with toluene (5 × 10 mL). The residue was dissolved in chloroform (10 mL) and washed with brine (2 × 5 mL). The organic phase was dried over $MgSO_4$, concentrated *in vacuo* and crystallised from methanol–diethyl ether to give compound **19m** (0.562 g, 95%) as a white solid; m.p.: 139–140 °C; ^1H NMR (600 MHz, $CDCl_3$): 7.95–7.92 (m, 2H, 2× *o*-CH); 7.69–7.63 (m, 1H, *p*-CH); 7.58 (d, J = 8.1 Hz, 1H, *H*C=CH); 7.55–7.48 (m, 2H, *m*-CH); 5.89 (d, J = 8.1 Hz, 1H, *H*C=CH); 4.59 (d, J = 2.6 Hz, 2H, CH≡CCH_2); 2.55 (t, J = 2.6 Hz, 1H, CH≡CCH_2).

4.1.5. General procedure for the preparation of 1,2,3-triazoles

To a solution of azidoalkylphosphonate (1.00 mmol) in EtOH (1 mL) and H_2O (1 mL) were added $CuSO_4 \times 5H_2O$ (0.05 mmol), sodium ascorbate (0.10 mmol) and alkynes (1.00 mmol). The suspension was microwave irradiated in the microwave reactor (Plazmatronika RM 800, 800 W) at 40–45 °C for 10 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 (50:1, 20:1 or 10:1, v/v) to give the appropriate 1,2,3-triazoles.

4.1.5.1. Diethyl {4-[(3-benzoyl-2,4-dioxoquinazolin-1-yl)methyl]-1H-1,2,3-triazol-1-yl}methylphosphonate ***20e***. From azide **12** (0.095 g, 0.492 mmol) and N^3-benzoyl-N^1-propargylquinazoline-2,4-dione **19e** (0.150 g, 0.492 mmol) the phosphonate **20e** (0.199 g, 81%) was obtained as a colourless oil after purification on a silica gel column with chloroform–methanol (50:1, v/v). IR (film): ν = 3030, 2982, 1750, 1700, 1662, 1021, 757, 671 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.20 (dd, J = 7.9 Hz, J = 1.6 Hz, 1H, H5); 7.99–7.95 (m, 2H, 2× *o*-CH); 7.88 (brd, J = 8.5 Hz, 1H, H8); 7.86 (s, 1H, *H*C5′); 7.76 (ddd, J = 8.5 Hz, J = 7.9 Hz, J = 1.6 Hz, 1H, H7); 7.68–7.64 (m, 1H, *p*-CH); 7.52–7.49 (m, 2H, 2× *m*-CH); 7.31 (dt, J = 7.9 Hz, J = 0.6 Hz, 1H, H6); 5.42 (s, 2H, CH_2); 4.73 (d, J = 13.1 Hz, 2H, PCH_2); 4.17–4.06 (m, 4H, 2× POCH_2CH$_3$); 1.25 (t, J = 7.2 Hz, 3H, POCH$_2$CH_3); 1.24 (t, J = 7.2 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 168.6 (s, C=O); 161.1 (s, C=O); 149.5 (s, C=O); 142.8 (s, H*C*=C); 140.2; 136.2; 135.2; 131.6; 130.6; 129.4; 129.0; 124.8 (s, HC=*C*); 123.9; 116.0; 115.3; 63.7 (d, J = 6.5 Hz, POC); 46.1 (d, J = 154.9 Hz, PC); 38.9; 16.5 (d, J = 5.7 Hz, POC*C*); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 16.49 ppm. Anal. Calcd. for $C_{23}H_{24}N_5O_6P$: C, 55.53; H, 4.86; N, 14.08. Found: C, 55.24; H, 4.73; N, 13.86.

4.1.5.2. Diethyl {4-[(3,5-dioxo-1,2,4-triazin-2-yl)methyl]-1H-1,2,3-triazol-1-yl}methylphosphonate ***20f***. From azide **12** (0.132 g, 0.683 mmol) and N^1-propargyl-6-azauracil **19f** (0.103 g, 0.683 mmol) the phosphonate **20f** (0.184 g, 78%) was obtained as a white solid after purification on silica gel with chloroform–methanol (50:1, v/v); m.p.: 139–140 °C; IR (KBr): ν = 3344, 2988, 1697, 1668, 1235, 1025 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 10.6 (s, 1H, NH); 7.94 (s, 1H); 7.40 (s, 1H); 5.22 (s, 2H, CH_2); 4.76 (d, J = 13.3 Hz, 2H, PCH_2); 4.18–4.07 (m, 4H, 2× POCH_2CH$_3$); 1.30 (t, J = 6.9 Hz, 3H, POCH$_2$CH_3); 1.29 (t, J = 6.9 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 155.9 (s, C=O); 149.1 (C=O); 142.2 (s, H*C*=C); 134.8 (s, HC=N); 125.1 (s, HC=*C*); 66.9 (d, J = 6.6 Hz, POC); 46.0 (d, J = 155.5 Hz, PC); 34.7; 16.5 (d, J = 5.8 Hz, POCC); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 16.83 ppm. Anal. Calcd. for $C_{11}H_{17}N_6O_5P$: C, 38.38; H, 4.98; N, 24.41. Found: C, 38.50; H, 4.80; N, 24.55.

4.1.5.3. Diethyl {4-[(8-chloro-1,3-dimethyl-2,6-dioxopurin-7-yl) methyl]-1H-1,2,3-triazol-1-yl}methylphosphonate ***20g***. From azide **12** (0.100 g, 0.518 mmol) and 8-chloro-N^7-propargyltheophylline **19g** (0.131 g, 0.518 mmol) the phosphonate **20g** (0.210 g, 91%) was obtained as a white solid after purification on silica gel with chloroform–methanol (50:1, v/v); m.p.: 156–157 °C; IR (KBr): ν = 2996, 2955, 1707, 1667, 1251, 1025, 757 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.98 (s, 1H, *H*C5′); 5.65 (s, 2H, CH_2); 4.74 (d, J = 13.1 Hz, 2H, PCH_2); 4.18–4.07 (m, 4H, 2× POCH_2CH$_3$); 3.54 (s, 3H, CH_3); 3.40 (s, 3H, CH_3); 1.30 (t, J = 7.2 Hz, 3H, POCH$_2$CH_3); 1.28 (t, J = 7.2 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 154.3 (s, C=O); 151.1 (s, C=O); 147.3; 142.0; 138.9; 124.5; 107.5; 63.7 (d, J = 6.5 Hz, POC); 46.0 (d, J = 154.9 Hz, PC); 41.0; 30.0; 28.1; 16.4 (d, J = 5.7 Hz, POCC); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 16.48 ppm. Anal. Calcd. for $C_{15}H_{21}ClN_7O_5P$: C, 40.41; H, 4.75; N, 21.99. Found: C, 40.53; H, 4.60; N, 21.80.

4.1.5.4. Diethyl {4-[(3,7-dimethyl-2,6-dioxopurin-1-yl)methyl]-1H-1,2,3-triazol-1-yl}methylphosphonate ***20h***. From azide **12** (0.116 g, 0.601 mmol) and N^1-propargyltheobromine **19h** (0.131 g, 0.601 mmol) the phosphonate **20h** (0.194 g, 79%) was obtained as a white solid after purification on silica gel with chloroform–methanol (50:1, v/v); m.p.: 139–140 °C; IR (KBr): ν = 2984, 2944, 2830, 1706, 1663, 1237, 1028 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.83 (s, 1H); 7.52 (s, 1H); 5.33 (s, 2H, CH_2); 4.73 (d, J = 13.1 Hz, 2H, PCH_2); 4.17–4.06 (m, 4H, 2× POCH_2CH$_3$); 3.99 (s, 3H, CH_3); 3.56 (s, 3H, CH_3); 1.29 (t, J = 7.0 Hz, 3H, POCH$_2$CH_3); 1.28 (t, J = 7.0 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 154.7 (s, C=O); 151.2 (s, C=O); 148.9; 144.0; 141.7; 124.3; 107.7; 63.6 (d, J = 6.6 Hz, POC); 45.9 (d, J = 154.9 Hz, PC); 36.1; 33.8; 29.9; 16.5 (d, J = 5.7 Hz, POCC); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 16.84 ppm. Anal. Calcd. for $C_{15}H_{22}N_7O_5P$: C, 43.80; H, 5.39; N, 23.84. Found: C, 43.69; H, 5.21; N, 23.66.

4.1.5.5. Diethyl {4-[(1,3-dimethyl-2,6-dioxopurin-7-yl)methyl]-1H-1,2,3-triazol-1-yl}methylphosphonate ***20i***. From azide **12** (0.136 g, 0.704 mmol) and N^7-propargyltheophylline **19i** (0.154 g, 0.704 mmol) the phosphonate **20i** (0.254 g, 88%) was obtained as a white solid after purification on a silica gel column with chloroform–methanol (50:1, v/v); m.p.: 105–108 °C; IR (KBr): ν = 2994, 2945, 1705, 1660, 1244, 1026 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.02 (s, 1H); 7.80 (s, 1H); 5.60 (s, 2H, CH_2); 4.74 (d, J = 13.1 Hz, 2H, PCH_2); 4.18–4.08 (m, 4H, 2× POCH_2CH$_3$); 3.57 (s, 3H, CH_3); 3.40 (s, 3H, CH_3); 1.29 (t, J = 6.9 Hz, 3H, POCH$_2$CH_3); 1.28 (t, J = 6.9 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 155.3 (s, C=O); 151.6 (s, C=O); 149.0; 142.6; 141.3; 124.7; 106.5; 63.7 (d, J = 6.6 Hz, POC); 46.2 (d, J = 154.9 Hz, PC); 41.7; 30.0; 28.2; 16.5 (d, J = 5.7 Hz, POC*C*); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 16.50 ppm. Anal. Calcd. for $C_{15}H_{22}N_7O_5P$: C, 43.80; H, 5.39; N, 23.84. Found: C, 43.88; H, 5.45; N, 23.69.

*4.1.5.6. Diethyl {4-[(5,6-dimethylbenzimidazol-1-yl)methyl]-1H-1,2,3-triazol-1-yl}methylphosphonate **20j**.* From azide **12** (0.091 g, 0.471 mmol) and 5,6-dimethyl-N^1-propargylbenzimidazole **19j** (0.087 g, 0.471 mmol) the phosphonate **20j** (0.121 g, 68%) was obtained as a white powder after purification on silica gel with chloroform–methanol (50:1, v/v); m.p.: 100–102 °C; IR (KBr): ν = 3004, 2960, 2945, 1025, 846, 757 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.93 (s, 1H); 7.52 (s, 1H); 7.56 (s, 1H); 7.18 (s, 1H); 5.46 (s, 2H, CH_2); 4.69 (d, J = 13.3 Hz, 2H, PCH_2); 4.11–4.01 (m, 4H, 2× POCH_2CH$_3$); 3.36 (s, 6H, 2× CH_3); 1.22 (t, J = 7.2 Hz, 6H, 2× POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 143.5; 142.1; 141.9; 132.4; 131.8; 131.3; 123.3; 120.1; 110.0; 63.6 (d, J = 6.6 Hz, POC); 46.0 (d, J = 154.9 Hz, PC); 40.5; 20.6; 20.3; 16.3 (d, J = 5.8 Hz, POCC); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 16.52 ppm. Anal. Calcd. for $C_{17}H_{24}N_5O_3P$: C, 54.11; H, 6.41; N, 18.56. Found: C, 53.97; H, 6.38; N, 18.44.

*4.1.5.7. Diethyl {4-[(3-acetylindol-1-yl)methyl]-1H-1,2,3-triazol-1-yl}methylphosphonate **20k**.* From azide **12** (0.109 g, 0.564 mmol) and 3-acetyl-*N*-propargylindole **19k** (0.111 g, 0.564 mmol) the phosphonate **20k** (0.164 g, 75%) was obtained as a white solid after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); m.p.: 128–129 °C; IR (KBr): ν = 3004, 2960, 2945, 1025, 846, 757 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.42–8.34 (m, 1H); 7.86 (s, 1H, *H*C5′); 7.62 (s, 1H); 7.45–7.36 (m, 1H); 7.33–7.24 (m, 2H); 5.48 (s, 2H, CH_2); 4.70 (d, J = 13.3 Hz, 2H, PCH_2); 4.10–4.00 (m, 4H, 2× POCH_2CH$_3$); 2.25 (s, 3H, CH_3); 1.21 (t, J = 6.9 Hz, 6H, 2× POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 192.9 (s, C═O); 143.6; 136.6; 134.6; 126.6; 123.7; 123.3; 123.0; 122.9; 117.9; 109.9; 63.8 (d, J = 6.5 Hz, POC); 46.3 (d, J = 155.4 Hz, PC); 42.7; 27.9 (s, CH_3); 16.5 (d, J = 5.7 Hz, POCC); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 16.51 ppm. Anal. Calcd. for $C_{18}H_{23}N_4O_4P$: C, 55.38; H, 5.94; N, 14.35. Found: C, 55.35; H, 6.03; N, 14.21.

*4.1.5.8. Diethyl {4-[(2-oxopyridin-1-yl)methyl]-1H-1,2,3-triazol-1-yl} methylphosphonate **20l**.* From azide **12** (0.120 g, 0.621 mmol) and *N*-propargyl-2-pyridon **19l** (0.083 g, 0.621 mmol) the phosphonate **20l** (0.178 g, 88%) was obtained as a brown solid after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); m.p.: 82–85 °C; IR (KBr): ν = 3080, 2985, 2935, 1660, 1025, 978 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.93 (s, 1H); 7.56 (dd, J = 6.7 Hz, J = 1.9 Hz, 1H); 7.31 (ddd, J = 9.2 Hz, J = 6.7 Hz, J = 1.9 Hz, 1H); 6.59 (d, J = 9.2 Hz, 1H); 6.17 (dt, J = 6.7 Hz, J = 1.2 Hz, 1H); 5.20 (s, 2H, CH_2); 4.73 (d, J = 13.1 Hz, 2H, PCH_2); 4.18–4.07 (m, 4H, 2× POCH_2CH$_3$); 1.29 (t, J = 6.9 Hz, 3H, POCH$_2$CH_3); 1.28 (t, J = 6.9 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 162.1 (s, C═O); 142.9 (s, H*C*═C); 139.9; 137.6; 124.9 (s, HC═*C*); 106.4; 63.5 (d, J = 6.7 Hz, POC); 45.8 (d, J = 154.5 Hz, PC); 44.4; 16.3 (d, J = 5.7 Hz, POCC); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 16.62 ppm. Anal. Calcd. for $C_{13}H_{19}N_4O_4P$: C, 47.85; H, 5.87; N, 17.17. Found: C, 48.01; H, 6.00; N, 17.25.

*4.1.5.9. Diethyl 2-{4-[(3,5-dioxo-1,2,4-triazin-2-yl)methyl]-1H-1,2,3-triazol-1-yl}ethylphosphonate **21f**.* From azide **13** (0.147 g, 0.710 mmol) and N^1-propargyl-6-azauracil **19f** (0.107 g, 0.710 mmol) the phosphonate **21f** (0.227 g, 89%) was obtained as a white solid after purification on silica gel with chloroform–methanol (50:1, v/v); m.p.: 119–121 °C; IR (KBr): ν = 3301, 2999, 2985, 1688, 1220, 1045 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 11.80 (s, 1H, NH); 7.90 (s, 1H); 7.41 (s, 1H); 5.22 (s, 2H, CH_2); 4.68–4.50 (m, 2H, PCH_2); 4.16–4.04 (m, 4H, 2× POCH_2CH$_3$); 2.78–2.62 (m, 2H, PCCH_2); 1.31 (t, J = 7.1 Hz, 6H, 2× POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 155.9 (s, C═O); 149.1 (C═O); 141.6 (s, H*C*═C); 134.7 (s, HC═N); 124.4 (s, HC═*C*); 62.5 (d, J = 6.6 Hz, POC); 44.5; 34.6; 27.2 (d, J = 140.9 Hz, PC); 16.4 (d, J = 6.0 Hz, POCC); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 27.15 ppm. Anal. Calcd. for $C_{12}H_{19}N_6O_5P$: C, 40.23; H, 5.35; N, 23.46. Found: C, 40.28; H, 5.29; N, 23.52.

*4.1.5.10. Diethyl 2-{4-[(8-chloro-1,3-dimethyl-2,6-dioxopurin-7-yl) methyl]-1H-1,2,3-triazol-1-yl}ethylphosphonate **21g**.* From azide **13** (0.130 g, 0.628 mmol) and 8-chloro-N^7-propargylthephylline **19g** (0.159 g, 0.628 mmol) the phosphonate **21g** (0.254 g, 88%) was obtained as a white solid after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); m.p.: 101–103 °C; IR (KBr): ν = 3426, 3139, 2953, 2903, 1703, 1661, 1250, 1043 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.85 (s, 1H, *H*C5′); 5.65 (s, 2H, CH_2); 4.63–4.56 (m, 2H, PCH_2); 4.13–4.05 (m, 4H, 2× POCH_2CH$_3$); 3.56 (s, 3H, CH_3); 3.43 (s, 3H, CH_3); 2.45–2.39 (m, 2H, PCCH_2); 1.32 (t, J = 7.0 Hz, 6H, 2× POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 155.4 (s, C═O); 151.2 (s, C═O); 147.4; 141.8; 139.0; 123.9; 107.3; 62.2 (d, J = 6.0 Hz, POC); 44.7; 40.9; 29.8; 28.0; 27.2 (d, J = 141.9 Hz, PC); 16.3 (d, J = 5.7 Hz, POCC); ^{31}P NMR (243 MHz, $CDCl_3$): δ = 25.20 ppm. Anal. Calcd. for $C_{16}H_{23}ClN_7O_5P$: C, 41.79; H, 5.04; N, 21.32. Found: C, 41.85; H, 4.94; N, 21.43.

*4.1.5.11. Diethyl 2-{4-[(3,7-dimethyl-2,6-dioxopurin-1-yl)methyl]-1H-1,2,3-triazol-1-yl}ethylphosphonate **21h**.* From azide **13** (0.130 g, 0.628 mmol) and N^1-propargyltheobromine **19h** (0.137 g, 0.628 mmol) the phosphonate **21h** (0.219 g, 82%) was obtained as a white solid after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); m.p.: 100–102 °C; IR (KBr): ν = 3133, 3087, 2989, 2830, 1701, 1665, 1233, 1023 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.67 (s, 1H); 7.52 (d, J = 0.6 Hz, 1H, *H*C5′); 5.32 (s, 2H, CH_2); 4.62–4.52 (m, 2H, PCH_2); 4.14–4.00 (m, 4H, 2× POCH_2CH$_3$); 3.99 (d, J = 0.6 Hz, 3H, CH_3); 3.57 (s, 3H, CH_3); 2.46–2.34 (m, 2H, PCCH_2); 1.29 (t, J = 7.0 Hz, 6H, 2× POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 154.7 (s, C═O); 151.2 (s, C═O); 148.9; 143.6; 141.7; 123.5; 107.6; 62.2 (d, J = 6.3 Hz, POC); 52.4; 44.6; 36.1; 31.9 (d, J = 293.7 Hz, PC); 28.3; 26.5; 16.5 (d, J = 6.0 Hz, POCC); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 26.59 ppm. Anal. Calcd. for $C_{16}H_{24}N_7O_5P$: C, 45.18; H, 5.69; N, 23.05. Found: C, 45.00; H, 5.56; N, 22.96.

*4.1.5.12. Diethyl 2-{4-[(1,3-dimethyl-2,6-dioxopurin-7-yl)methyl]-1H-1,2,3-triazol-1-yl}ethylphosphonate **21i**.* From azide **13** (0.130 g, 0.628 mmol) and N^7-propargylthephylline **19i** (0.137 g, 0.628 mmol) the phosphonate **21i** (0.219 g, 82%) was obtained as a colourless oil after purification on silica gel with chloroform–methanol (50:1, v/v); IR (film): ν = 3033, 2987, 2889, 2830, 1703, 1666, 1230, 1023 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.89 (s, 1H); 7.82 (s, 1H, *H*C5′); 5.60 (s, 2H, CH_2); 4.63–4.55 (m, 2H, PCH_2); 4.13–4.08 (m, 4H, 2× POCH_2CH$_3$); 3.59 (s, 3H, CH_3); 3.43 (s, 3H, CH_3); 2.45–2.39 (m, 2H, PCCH_2); 1.31 (t, J = 7.0 Hz, 6H, 2× POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 155.4 (s, C═O); 151.6 (s, C═O); 149.0; 142.2; 141.4; 123.9; 106.5; 62.2 (d, J = 5.8 Hz, POC); 44.7; 41.4; 29.7; 28.0; 27.2 (d, J = 141.9 Hz, PC); 16.3 (d, J = 6.0 Hz, POCC); ^{31}P NMR (243 MHz, $CDCl_3$): δ = 25.15 ppm. Anal. Calcd. for $C_{16}H_{24}N_7O_5P$: C, 45.18; H, 5.69; N, 23.05. Found: C, 45.30; H, 5.77; N, 23.17.

*4.1.5.13. Diethyl 2-{4-[(5,6-dimethylbenzimidazol-1-yl)methyl]-1H-1,2,3-triazol-1-yl}ethylphosphonate **21j**.* From azide **13** (0.139 g, 0.671 mmol) and 5,6-dimethyl-*N*-propargylbenzimidazole **19j** (0.124 g, 0.671 mmol) the phosphonate **21j** (0.196 g, 75%) was obtained as a colourless oil after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); IR (film): ν = 3014, 2950, 2895, 1045, 856, 759 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.93 (s, 1H); 7.58 (s, 1H); 7.43 (s, 1H); 7.23 (s, 1H); 5.45 (s, 2H, CH_2); 4.54 (dt, J = 12.7 Hz, J = 7.7 Hz, 2H, PCH_2); 4.06–4.00 (m, 4H, 2× POCH_2CH$_3$); 2.38 (dt, J = 18.5 Hz, J = 7.7 Hz, 2H, PCCH_2); 2.39 (s, 3H, CH_3); 2.38 (s, 3H, CH_3); 1.26 (t, J = 7.0 Hz, 6H, 2× POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 143.3; 142.4; 142.0; 132.5; 132.0;

131.4; 122.5; 120.3; 109.9; 62.2 (d, J = 6.5 Hz, POC); 44.7 (d, J = 1.7 Hz, PCC); 40.4; 27.0 (d, J = 142.0 Hz, PC); 20.5; 20.2; 16.2 (d, J = 6.4 Hz, POCC); ^{31}P NMR (243 MHz, $CDCl_3$): δ = 25.27 ppm. Anal. Calcd. for $C_{18}H_{26}N_5O_3P$: C, 55.24; H, 6.70; N, 17.89. Found: C, 55.08; H, 6.84; N, 17.72.

4.1.5.14. Diethyl 2-{4-[(3-acetylindol-1-yl)methyl]-1H-1,2,3-triazol-1-yl}ethylphosphonate ***21k***. From azide **13** (0.100 g, 0.483 mmol) and 3-acetyl-*N*-propargylindole **19k** (0.095 g, 0.483 mmol) the phosphonate **21k** (0.144 g, 74%) was obtained as a white solid after purification on silica gel with chloroform–methanol (50:1, v/v); m.p.: 83–84 °C; IR (KBr): ν = 3430, 3110, 2989, 1642, 1528, 1390, 1026, 753 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.44–8.32 (m, 1H); 7.87 (s, 1H, *H*C5′); 7.47 (s, 1H); 7.45–7.42 (m, 1H); 7.32–7.29 (m, 2H); 5.47 (s, 2H, CH_2); 4.61–4.52 (m, 2H, PCH_2); 4.05–3.94 (m, 4H, 2× POCH_2CH$_3$); 2.55 (s, 3H, CH_3); 2.42–2.31 (m, 2H, PCCH_2); 1.22 (t, J = 6.8 Hz, 6H, 2× POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 192.9 (s, C=O); 142.8; 136.4; 134.8; 126.3; 123.5; 122.7; 122.7; 122.6; 117.4; 109.8; 62.2 (d, J = 6.6 Hz, POC); 44.7 (d, J = 2.0 Hz, PCC); 42.3; 27.7 (s, CH_3); 27.1 (d, J = 141.4 Hz, PC); 16.4 (d, J = 5.7 Hz, POCC); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 26.39 ppm. Anal. Calcd. for $C_{19}H_{25}N_4O_4P$: C, 56.43; H, 6.23; N, 13.85. Found: C, 56.54; H, 6.14; N, 13.72.

4.1.5.15. Diethyl 2-{4-[(2-oxopyridin-1-yl)methyl]-1H-1,2,3-triazol-1-yl}ethylphosphonate ***21l***. From azide **13** (0.147 g, 0.710 mmol) and *N*-propargyl-2-pyridon **19l** (0.095 g, 0.710 mmol) the phosphonate **21l** (0.214 g, 89%) was obtained as a brown oil after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); IR (film): ν = 3110, 2976, 2875, 1668, 1035, 988 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.84 (s, 1H); 7.59 (dd, J = 6.8 Hz, J = 1.6 Hz, 1H); 7.33 (ddd, J = 9.2 Hz, J = 6.8 Hz, J = 2.0 Hz, 1H); 6.55 (dd, J = 9.2 Hz, J = 0.5 Hz, 1H); 6.19 (dt, J = 6.8 Hz, J = 1.6 Hz, 1H); 5.18 (s, 2H, CH_2); 4.62–4.52 (m, 2H, PCH_2); 4.13–4.03 (m, 4H, 2× POCH_2CH$_3$); 2.46–2.35 (m, 2H, PCCH_2); 1.29 (t, J = 7.0 Hz, 3H, POCH$_2$CH_3); 1.28 (t, J = 6.9 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 162.2 (s, C=O); 142.5 (s, HC=C); 140.0; 137.7; 124.3 (s, HC=*C*); 120.6; 106.5; 62.2 (d, J = 6.3 Hz, POC); 44.6 (d, J = 2.8 Hz, PCC); 27.1 (d, J = 141.2 Hz, PC); 16.4 (d, J = 6.0 Hz, POCC); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 26.37 ppm. Anal. Calcd. for $C_{14}H_{21}N_4O_4P$: C, 49.41; H, 6.22; N, 16.46. Found: C, 49.24; H, 6.09; N, 16.28.

4.1.5.16. Diethyl 3-{4-[(3-benzoyl-2,4-dioxoquinazolin-1-yl)methyl]-1H-1,2,3-triazol-1-yl}propylphosphonate ***22e***. From azide **14** (0.100 g, 0.452 mmol) and N^3-benzoyl-N^1-propargylquinazoline-2,4-dione **19e** (0.138 g, 0.452 mmol) the phosphonate **22e** (0.198 g, 83%) was obtained as a colourless oil after purification on silica gel with chloroform–methanol (50:1, v/v); IR (film): ν = 3141, 3064, 2939, 1799, 1606, 1481; 1220, 1025 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.20 (dd, J = 7.9 Hz, J = 1.6 Hz, 1H); 8.00–7.95 (m, 2H, 2× *o*-CH); 7.91 (d, J = 8.5 Hz, 1H); 7.78 (ddd, J = 8.5 Hz, J = 7.9 Hz, J = 1.6 Hz, 1H); 7.71 (s, 1H, *H*C5′); 7.70–7.62 (m, 1H, *p*-CH); 7.54–7.48 (m, 2H, 2× *m*-CH); 7.32 (dt, J = 7.9 Hz, J = 0.8 Hz, 1H); 5.40 (s, 2H, CH_2); 4.41 (t, J = 7.0 Hz, 2H, PCCCH_2); 4.16–3.99 (m, 4H, 2× POCH_2CH$_3$); 2.20 (dqu, J = 14.5 Hz, J = 7.0 Hz, 2H, PCCH_2); 1.71 (dt, J = 18.7 Hz, J = 7.0 Hz, 2H, PCH_2); 1.30 (t, J = 7.1 Hz, 6H, 2× POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 168.6 (s, C=O); 161.0 (s, C=O); 149.5 (s, C=O); 142.4 (s, HC=C); 140.2; 136.2; 135.2; 131.5; 130.5; 129.2; 128.9; 123.9 (s, HC=*C*); 123.8; 115.5; 115.3; 61.8 (d, J = 6.7 Hz, POC); 50.3 (d, J = 15.7 Hz, PCC*C*); 38.9; 23.7 (d, J = 4.9 Hz, PCC); 22.8 (d, J = 142.9 Hz, PC); 16.6 (d, J = 6.0 Hz, POC*C*); ^{31}P NMR (121 MHz, $CDCl_3$): δ = 30.82 ppm. Anal. Calcd. for $C_{25}H_{28}N_5O_6P$: C, 57.14; H, 5.37; N, 13.33. Found: C, 57.27; H, 5.49; N, 13.40.

4.1.5.17. Diethyl 3-{4-[(3,5-dioxo-1,2,4-triazin-2-yl)methyl]-1H-1,2,3-triazol-1-yl}propylphosphonate ***22f***. From azide **14** (0.154 g, 0.697 mmol) and N^1-propargyl-6-azauracil **19f** (0.105 g, 0.697 mmol) the phosphonate **22f** (0.215 g, 83%) was obtained as a white solid after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); m.p.: 96–97 °C; IR (KBr): ν = 3384, 3232, 3138, 2984, 2908, 1730, 1677, 1217, 1025 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 11.51 (s, 1H, NH); 7.77 (s, 1H, *H*C5′); 7.40 (s, 1H); 5.22 (s, 2H, CH_2); 4.44 (t, J = 7.0 Hz, 2H, PCCCH_2); 4.16–4.03 (m, 4H, 2× POCH_2CH$_3$); 2.21 (dqu, J = 14.9 Hz, J = 7.0 Hz, 2H, PCCH_2); 1.75 (dt, J = 19.0 Hz, J = 7.0 Hz, 2H, PCH_2); 1.32 (t, J = 7.0 Hz, 6H, 2× POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 155.8 (s, C=O); 148.9 (C=O); 141.3 (s, HC=C); 134.5 (s, HC=N); 124.2 (s, HC=*C*); 62.0 (d, J = 6.4 Hz, POC); 50.0 (d, J = 15.1 Hz, PCCC); 34.5; 23.4 (d, J = 4.3 Hz, PCC); 22.2 (d, J = 143.0 Hz, PC); 16.4 (d, J = 6.0 Hz, POCC); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 31.41 ppm. Anal. Calcd. for $C_{13}H_{21}N_6O_5P$: C, 41.94; H, 5.69; N, 22.57. Found: C, 41.92; H, 5.52; N, 22.41.

4.1.5.18. Diethyl 3-{4-[(8-chloro-1,3-dimethyl-2,6-dioxopurin-7-yl)methyl]-1H-1,2,3-triazol-1-yl}propylphosphonate ***22g***. From azide **14** (0.160 g, 0.723 mmol) and 8-chloro-N^7-propargyltheophylline **19g** (0.183 g, 0.723 mmol) the phosphonate **22g** (0.298 g, 84%) was obtained as a white solid after purification on silica gel with chloroform–methanol (50:1, v/v); m.p.: 127–128 °C; IR (KBr): ν = 3362, 3101, 2981, 2935, 1707, 1679, 1224, 1020, 956 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.83 (s, 1H, *H*C5′); 5.66 (s, 2H, CH_2); 4.46 (t, J = 7.0 Hz, 2H, PCCCH_2); 4.15–4.05 (m, 4H, 2× POCH_2CH$_3$); 3.57 (s, 3H, CH_3); 3.44 (s, 3H, CH_3); 2.23 (dqu, J = 14.7 Hz, J = 7.0 Hz, 2H, PCCH_2); 1.74 (dt, J = 18.7 Hz, J = 7.0 Hz, 2H, PCH_2); 1.34 (t, J = 7.1 Hz, 6H, 2× POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 154.5 (s, C=O); 151.2 (s, C=O); 147.4; 141.8; 139.0; 123.7; 107.4; 61.8 (d, J = 6.4 Hz, POC); 50.1 (d, J = 15.2 Hz, PCC*C*); 41.0; 29.8; 27.9; 23.6 (d, J = 4.8 Hz, PCC); 22.6 (d, J = 142.3 Hz, PC); 16.4 (d, J = 6.1 Hz, POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$): δ = 29.80 ppm. Anal. Calcd. for $C_{17}H_{25}ClN_7O_5P$: C, 43.09; H, 5.32; N, 20.69. Found: C, 42.88; H, 5.44; N, 20.71.

4.1.5.19. Diethyl 3-{4-[(3,7-dimethyl-2,6-dioxopurin-1-yl)methyl]-1H-1,2,3-triazol-1-yl}propylphosphonate ***22h***. From azide **14** (0.160 g, 0.723 mmol) and N^1-propargyltheobromine **19h** (0.158 g, 0.723 mmol) the phosphonate **22h** (0.270 g, 85%) was obtained as a white powder after crystallisation from diethyl ether; m.p.: 175–176 °C; IR (KBr): ν = 3444, 3001, 2984, 1704, 1668, 1221, 1020 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.76 (s, 1H); 7.53 (s, 1H, *H*C5′); 5.35 (s, 2H, CH_2); 4.42 (t, J = 7.0 Hz, 2H, PCCCH_2); 4.15–4.05 (m, 4H, 2× POCH_2CH$_3$); 4.02 (s, 3H, CH_3); 3.60 (s, 3H, CH_3); 2.22 (dqu, J = 14.2 Hz, J = 7.0 Hz, 2H, PCCH_2); 1.74 (dt, J = 18.7 Hz, J = 7.0 Hz, 2H, PCH_2); 1.34 (t, J = 7.0 Hz, 6H, 2× POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 154.8 (s, C=O); 151.4 (s, C=O); 148.9; 143.7; 141.6; 123.4; 107.7; 61.7 (d, J = 6.5 Hz, POC); 50.0 (d, J = 16.1 Hz, PCCC); 36.0; 33.6; 29.7; 23.6 (d, J = 4.5 Hz, PCC); 22.7 (d, J = 143.1 Hz, PC); 16.4 (d, J = 5.8 Hz, POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$): δ = 30.03 ppm. Anal. Calcd. for $C_{17}H_{26}N_7O_5P$: C, 46.47; H, 5.96; N, 22.31. Found: C, 46.36; H, 5.90; N, 22.06.

4.1.5.20. Diethyl 3-{4-[(1,3-dimethyl-2,6-dioxopurin-7-yl)methyl]-1H-1,2,3-triazol-1-yl}propylphosphonate ***22i***. From azide **14** (0.091 g, 0.412 mmol) and N^7-propargyltheophylline **19i** (0.090 g, 0.412 mmol) the phosphonate **22i** (0.181 g, 74%) was obtained as a white solid after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); m.p.: 187–190 °C; IR (KBr): ν = 3440, 2996, 2984, 1704, 1668, 1225, 1018 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.87 (s, 1H); 7.83 (s, 1H, *H*C5′); 5.61 (s, 2H, CH_2); 4.46 (t, J = 7.0 Hz, 2H, PCCCH_2); 4.16–4.05 (m, 4H, 2× POCH_2CH$_3$); 3.60 (s, 3H, CH_3); 3.44 (s, 3H, CH_3); 2.24 (dqu,

J = 14.6 Hz, J = 7.0 Hz, 2H, PCCH_2); 1.74 (dt, J = 18.7 Hz, J = 7.0 Hz, 2H, PCH_2); 1.34 (t, J = 7.0 Hz, 6H, 2× POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 155.4 (s, C═O); 151.5 (s, C═O); 149.0; 142.2; 141.4; 123.8; 106.4; 61.8 (d, J = 6.5 Hz, POC); 50.1 (d, J = 15.3 Hz, PCCC); 41.4; 29.7; 27.9; 23.6 (d, J = 4.8 Hz, PCC); 22.6 (d, J = 142.4 Hz, PC); 16.4 (d, J = 5.8 Hz, POCC); ^{31}P NMR (243 MHz, $CDCl_3$): δ = 29.75 ppm. Anal. Calcd. for $C_{17}H_{26}N_7O_5P$: C, 46.47; H, 5.96; N, 22.31. Found: C, 46.59; H, 6.11; N, 22.45.

4.1.5.21. Diethyl 3-{4-[(5,6-dimethylbenzimidazol-1-yl)methyl]-1H-1,2,3-triazol-1-yl}propylphosphonate ***22j***. From azide **14** (0.160 g, 0.723 mmol) and 5,6-dimethyl-N^1-propargylbenzimidazole **19j** (0.133 g, 0.723 mmol) the phosphonate **22j** (0.221 g, 76%) as a colourless oil after purification on silica gel with chloroform–methanol (50:1, v/v); IR (film): ν = 3446, 2990, 2938, 1498, 1444, 1224, 1050, 965 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.33 (s, 1H); 7.61 (s, 1H); 7.54 (s, 1H); 7.32 (s, 1H); 5.55 (s, 2H, CH_2); 4.43 (t, J = 7.0 Hz, 2H, PCCCH_2); 4.15–4.05 (m, 4H, 2× POCH_2CH$_3$); 2.41 (s, 3H, CH_3); 2.40 (s, 3H, CH_3); 2.21 (dqu, J = 14.6 Hz, J = 7.0 Hz, 2H, PCCH_2); 1.70 (dt, J = 19.2 Hz, J = 7.0 Hz, 2H, PCH_2); 1.34 (t, J = 7.1 Hz, 6H, 2× POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 143.4; 142.3; 142.0; 132.4; 131.4; 122.4; 120.3; 109.9; 61.8 (d, J = 6.5 Hz, POC); 50.0 (d, J = 14.5 Hz, PCCC); 40.5; 23.5 (d, J = 4.5 Hz, PCC); 22.4 (d, J = 142.3 Hz, PC); 20.5; 20.1; 16.4 (d, J = 5.8 Hz, POCC); ^{31}P NMR (243 MHz, $CDCl_3$): δ = 29.68 ppm. Anal. Calcd. for $C_{19}H_{28}N_5O_3P$: C, 56.29; H, 6.96; N, 17.27. Found: C, 56.07; H, 7.14; N, 17.10.

4.1.5.22. Diethyl 3-{4-[(3-acetylindol-1-yl)methyl]-1H-1,2,3-triazol-1-yl}propylphosphonate ***22k***. From azide **14** (0.110 g, 0.497 mmol) and 3-acetyl-*N*-propargylindole **19k** (0.098 g, 0.497 mmol) the phosphonate **22k** (0.202 g, 97%) was obtained as a colourless oil after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); IR (film): ν = 3394, 3110, 2941, 2825, 1648, 1229, 1029 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.43–8.38 (m, 1H); 7.88 (s, 1H, *H*C5′); 7.43–7.38 (m, 2H); 7.36–7.27 (m, 2H); 5.48 (s, 2H, CH_2); 4.44 (t, J = 7.0 Hz, 2H, PCCCH_2); 4.10–4.01 (m, 4H, 2× POCH_2CH$_3$); 2.53 (s. 3H, CH_3); 2.20 (dqu, J = 14.7 Hz, J = 7.0 Hz, 2H, PCCH_2); 1.65 (dt, J = 18.4 Hz, J = 7.0 Hz, 2H, PCH_2); 1.29 (t, J = 7.1 Hz, 6H, 2× POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 192.9 (s, C═O); 142.9; 136.4; 134.7; 126.3; 123.5; 122.7; 122.6; 122.5; 117.5; 109.9; 61.9 (d, J = 6.3 Hz, POC); 50.0 (d, J = 14.9 Hz, PCCC); 42.4; 27.8; 23.6 (d, J = 4.9 Hz, PCC); 22.1 (d, J = 142.8 Hz, PC); 16.4 (d, J = 6.1 Hz, POCC); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 30.85 ppm. Anal. Calcd. for $C_{20}H_{27}N_4O_4P$: C, 57.41; H, 6.50; N, 13.39. Found: C, 57.60; H, 6.73; N, 13.50.

4.1.5.23. Diethyl 3-{4-[(2-oxopyridin-1-yl)methyl]-1H-1,2,3-triazol-1-yl}propylphosphonate ***22l***. From azide **14** (0.154 g, 0.696 mmol) and *N*-propargyl-2-pyridon **19l** (0.093 g, 0.696 mmol) the phosphonate **22l** (0.206 g, 83%) was obtained as a brown oil after purification on silica gel with chloroform–methanol (50:1, v/v); IR (film): ν = 3426, 3144, 2986, 1657, 1226; 1026, 968 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.81 (s, 1H, *H*C5′); 7.60 (ddd, J = 6.8 Hz, J = 2.1 Hz, J = 0.7 Hz, 1H); 7.32 (ddd, J = 9.2 Hz, J = 6.6 Hz, J = 2.1 Hz, 1H); 6.56 (ddd, J = 9.2 Hz, J = 1.3 Hz, J = 0.7 Hz, 1H); 6.20 (dt, J = 6.8 Hz, J = 1.3 Hz, 1H); 5.19 (s, 2H, CH_2); 4.41 (t, J = 7.1 Hz, 2H, PCCCH_2); 4.15–4.03 (m, 4H, 2× POCH_2CH$_3$); 2.22 (dqu, J = 14.9 Hz, J = 7.1 Hz, 2H, PCCH_2); 1.66 (dt, J = 18.2 Hz, J = 7.1 Hz, 2H, PCH_2); 1.34 (t, J = 6.9 Hz, 3H, POCH$_2$CH_3); 1.33 (t, J = 6.9 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 162.1 (s, C═O); 142.5 (s, HC═C); 139.9; 137.6; 124.0 (s, HC═*C*); 120.4; 106.4; 61.8 (d, J = 6.4 Hz, POC); 50.0 (d, J = 16.1 Hz, PCCC); 44.5; 23.5 (d, J = 4.4 Hz, PCC); 22.1 (d, J = 147.1 Hz, PC); 16.4 (d, J = 6.0 Hz, POCC); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 31.05 ppm. Anal. Calcd. for $C_{15}H_{23}N_4O_4P$: C, 50.84; H, 6.54; N, 15.81. Found: C, 50.61; H, 6.39; N, 15.64.

4.1.5.24. Diethyl 3-(4-{[3-benzoyl-2,4-dioxopyrimidin-1-yl]methyl}-1H-1,2,3-triazol-1-yl)propylphosphonate ***22m***. From azide **14** (0.201 g, 0.909 mmol) and N^3-benzoyl-N^1-propargylquinazoline-2,4-dione **19m** (0.230 g, 0.909 mmol) the phosphonate **22m** (0.399 g, 93%) was obtained as a colourless oil after chromatography on a silica gel column with chloroform–methanol (100:1; 50:1, 20:1 v/v); IR (film): ν = 3020, 3005, 2963, 2899, 1669, 1664, 1220, 1020, 772, 689 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.94–7.90 (m, 2H, 2× *o*-CH); 7.71 (s, 1H, *H*C5′); 7.69–7.63 (m, 1H, *p*-CH); 7.64 (d, J = 8.0 Hz, 1H, *H*C═CH); 7.53–7.47 (m, 2H, 2× *m*-CH); 5.84 (d, J = 8.0 Hz, 1H, HC═C*H*); 5.02 (s, 2H, CH_2); 4.46 (t, J = 7.3 Hz, 2H, PCCCH_2); 4.18–4.01 (m, 4H, 2× POCH_2CH$_3$); 2.23 (dqu, J = 14.7 Hz, J = 7.3 Hz, 2H, PCCH_2); 1.73 (dt, J = 18.7 Hz, J = 7.3 Hz, 2H, PCH_2); 1.31 (t, J = 7.1 Hz, 6H, 2× POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 168.7 (s, C═O); 162.2 (s, C═O); 144.2 (s, C═O); 141.3 (s, HC═C); 135.2; 131.3; 130.4; 129.2; 124.1 (s, HC═*C*); 102.5; 61.9 (d, J = 6.6 Hz, POC); 50.2 (d, J = 15.4 Hz, PCCC); 43.5; 23.7 (d, J = 4.7 Hz, PCC); 22.7 (d, J = 143.0 Hz, PC); 16.6 (d, J = 6.0 Hz, POCC); ^{31}P NMR (121 MHz, $CDCl_3$): δ = 30.12 ppm. Anal. Calcd. for $C_{21}H_{26}N_5O_6P$: C, 53.05; H, 5.51; N, 14.73. Found: C, 52.89; H, 5.33; N, 14.58.

4.1.5.25. Diethyl 4-(4-{[6-aminopurin-9-yl]methyl}-1H-1,2,3-triazol-1-yl)butylphosphonate ***23a***. From azide **15** (0.061 g, 0.259 mmol) and N^9-propargyladenine **19a** (0.045 g, 0.259 mmol) the phosphonate **23a** (0.097 g, 92%) was obtained as a white powder after chromatography on a silica gel column with chloroform–methanol (10:1, v/v); m.p.: 119–120 °C; IR (KBr): ν = 3462, 3306, 3140, 2984, 2912, 2870, 1662, 1597, 1244, 1033 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.41 (s, 1H); 8.02 (s, 1H); 7.68 (s, 1H); 5.59 (brs, 2H, NH_2); 5.51 (s, 2H, CH_2); 4.36 (t, J = 7.1 Hz, 2H, PCCCCH_2); 4.14–4.04 (m, 4H, 2× POCH_2CH$_3$); 2.03 (qu, J = 7.1 Hz, 2H, PCCCH_2); 1.80–1.73 (m, 2H, PCH_2); 1.65 (dqu, J = 14.1 Hz, J = 7.1 Hz, 2H, PCCH_2); 1.32 (t, J = 7.0 Hz, 6H, 2× POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 155.6; 153.1; 149.8; 142.4; 140.4; 122.8; 119.5; 61.6 (d, J = 6.6 Hz, POC); 49.9; 38.6; 30.6 (d, J = 15.1 Hz, PCCC); 24.9 (d, J = 142.1 Hz, PC); 19.6 (d, J = 5.0 Hz, PCC); 16.4 (d, J = 6.2 Hz, POCC); ^{31}P NMR (243 MHz, $CDCl_3$): δ = 30.73 ppm. Anal. Calcd. for $C_{16}H_{25}N_8O_3P$: C, 47.06; H, 6.17; N, 27.44. Found: C, 46.88; H, 6.02; N, 27.29.

4.1.5.26. Diethyl 4-(4-{[5-methyl-2,4-dioxopyrimidin-1-yl]methyl}-1H-1,2,3-triazol-1-yl)butylphosphonate ***23b***. From azide **15** (0.100 g, 0.425 mmol) and N^1-propargylthymine **19b** (0.070 g, 0.425 mmol) the phosphonate **23b** (0.165 g, 97%) was obtained as a white powder after crystallisation from ethyl acetate–petroleum ether mixtures; m.p.: 63–65 °C; IR (KBr): ν = 3425, 3132, 2986, 2912, 2827, 1688, 1219, 1027 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.69 (brs, 1H, NH); 7.72 (s, 1H, *H*C5′); 7.36 (d, J = 1.0 Hz, 1H, *H*C═CCH$_3$); 4.97 (s, 2H, CH_2); 4.38 (t, J = 7.1 Hz, 2H, PCCCCH_2); 4.16–4.06 (m, 4H, 2× POCH_2CH$_3$); 2.06 (qu, J = 7.1 Hz, 2H, PCCCH_2); 1.93 (d, J = 1.0 Hz, 3H, HC═CCH_3); 1.78 (dt, J = 15.7 Hz, J = 7.1 Hz, 2H, PCH_2); 1.69–1.64 (m, 2H, PCCH_2); 1.33 (t, J = 7.0 Hz, 6H, 2× POCH$_2$CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 164.2 (s, C═O); 151.2 (s, C═O); 142.1; 140.2; 123.7; 111.3; 61.6 (d, J = 6.6 Hz, POC); 49.9; 43.0; 30.6 (d, J = 15.2 Hz, PCCC); 24.9 (d, J = 142.0 Hz, PC); 19.7 (d, J = 5.2 Hz, PCC); 16.4 (d, J = 6.2 Hz, POCC); 12.2 (s, CH_3); ^{31}P NMR (243 MHz, $CDCl_3$): δ = 30.84 ppm. Anal. Calcd. for $C_{16}H_{26}N_5O_5P$: C, 48.12; H, 6.56; N, 17.54. Found: C, 47.90; H, 6.33; N, 17.41.

4.1.5.27. Diethyl 4-(4-{[2,4-dioxopyrimidin-1-yl]methyl}-1H-1,2,3-triazol-1-yl)butylphosphonate ***23c***. From azide **15** (0.100 g, 0.425 mmol) and N^1-propargyluracil **19c** (0.064 g, 0.425 mmol) the phosphonate **23c** (0.133 g, 81%) was obtained as a white powder after crystallisation from ethyl acetate–petroleum ether mixtures; m.p.: 124–125 °C; IR (KBr): ν = 3435, 3142, 2994, 2952, 2867, 1648,

1229, 1023 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.80 (brs, 1H, NH); 7.72 (s, 1H, *HC*5′); 7.53 (d, *J* = 8.0 Hz, 1H, *HC*=CH); 5.73 (d, *J* = 8.0 Hz, 1H, HC=C*H*); 5.00 (s, 2H, CH_2); 4.39 (t, *J* = 7.1 Hz, 2H, PCCCCH_2); 4.16–4.06 (m, 4H, 2× POC$H_2$$CH_3$); 2.06 (qu, *J* = 7.1 Hz, 2H, PCCCH_2); 1.82–1.76 (m, 2H, PCCH_2); 1.71–1.64 (dqu, *J* = 14.3 Hz, *J* = 7.1 Hz, 2H, PCH_2); 1.34 (t, *J* = 7.0 Hz, 6H, 2× POCH_2CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 163.7 (s, C=O); 151.1 (s, C=O); 144.3; 141.9; 123.7; 102.7; 61.6 (d, *J* = 6.6 Hz, POC); 49.9; 43.2; 30.6 (d, *J* = 15.2 Hz, PCC*C*); 25.0 (d, *J* = 142.0 Hz, PC); 19.7 (d, *J* = 5.3 Hz, PC*C*); 16.5 (d, *J* = 6.0 Hz, POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$): δ = 30.77 ppm. Anal. Calcd. for $C_{15}H_{24}N_5O_5P$: C, 46.75; H, 6.28; N, 18.17. Found: C, 46.84; H, 6.36; N, 18.00.

4.1.5.28. Diethyl 4-(4-{[N^4-acetylamino-2-oxopyrimidin-1-yl] methyl}-1H-1,2,3-triazol-1-yl)butylphosphonate ***23d***. From azide **15** (0.060 g, 0.259 mmol) and N^4-acetyl-N^1-propargylcytosine **19d** (0.050 g, 0.259 mmol) the phosphonate **23d** (0.078 g, 72%) was obtained as a white powder after purification on silica gel with chloroform–methanol (20:1, v/v); m.p.: 159–161 °C; IR (KBr): ν = 3217, 3133, 3084, 2982, 1707, 1650, 1217, 1025 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.83 (brs, 1H, NH); 7.96 (d, *J* = 7.3 Hz, 1H, *HC*=CH); 7.84 (s, 1H, *HC*5′); 7.40 (d, *J* = 7.3 Hz, 1H, HC=C*H*); 5.16 (s, 2H, CH_2); 4.37 (t, *J* = 7.1 Hz, 2H, PCCCCH_2); 4.16–4.04 (m, 4H, 2× POC$H_2$$CH_3$); 2.25 (s, 3H, CH_3); 2.05 (qv, *J* = 7.1 Hz, 2H, PCCCH_2); 1.79 (dt, *J* = 15.5 Hz, *J* = 7.1 Hz, 2H, PCH_2); 1.71–1.63 (m, 2H, PCCH_2); 1.33 (t, *J* = 7.0 Hz, 6H, 2× POCH_2CH_3); ^{13}C NMR (151 MHz, CD_3OD): δ = 163.1 (s, C=O); 157.0 (s, C=O); 149.4; 142.1; 124.1; 96.9; 61.8 (d, *J* = 6.6 Hz, POC); 49.3; 44.9; 30.2 (d, *J* = 16.2 Hz, PCCC); 23.7 (d, *J* = 140.4 Hz, PC); 23.2; 19.1 (d, *J* = 5.2 Hz, POC*C*); 15.4; ^{31}P NMR (243 MHz, $CDCl_3$): δ = 30.90 ppm. Anal. Calcd. for $C_{17}H_{27}N_6O_5P$: C, 47.88; H, 6.38; N, 19.71. Found: C, 47.63; H, 6.41; N, 19.52.

4.1.5.29. Diethyl 4-{4-[(3,5-dioxo-1,2,4-triazin-2-yl)methyl]-1H-1,2,3-triazol-1-yl}butylphosphonate ***23f***. From azide **15** (0.151 g, 0.642 mmol) and N^1-propargyl-6-azauracil **19f** (0.097 g, 0.642 mmol) the phosphonate **23f** (0.240 g, 97%) was obtained as a colourless oil after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); IR (film): ν = 3439, 3231, 3141, 3012, 2909, 1730, 1676, 1216, 1027, 754 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 11.58 (brs, 1H, NH); 7.70 (s, 1H, *HC*5′); 7.39 (s, 1H, *HC*=N); 5.20 (s, 2H, CH_2); 4.33 (t, *J* = 7.2 Hz, 2H, PCCCCH_2); 4.15–4.03 (m, 4H, 2× POC$H_2$$CH_3$); 2.01 (qu, *J* = 7.1 Hz, 2H, PCCCH_2); 1.83–1.56 (m, 4H, PCH_2CH_2); 1.31 (t, *J* = 7.0 Hz, 6H, 2× POCH_2CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 155.9 (s, C=O); 148.9 (s, C=O); 141.5; 134.6; 123.8; 61.8 (d, *J* = 6.6 Hz, POC); 49.7; 34.5; 30.6 (d, *J* = 15.5 Hz, PCC*C*); 24.7 (d, *J* = 141.4 Hz, PC); 19.5 (d, *J* = 4.9 Hz, PC*C*); 16.4 (d, *J* = 6.1 Hz, POC*C*); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 32.44 ppm. Anal. Calcd. for $C_{14}H_{23}N_6O_5P$: C, 43.52; H, 6.00; N, 21.75. Found: C, 43.65; H, 5.87; N, 21.69.

4.1.5.30. Diethyl 4-{4-[(8-chloro-1,3-dimethyl-2,6-dioxopurin-7-yl) methyl]-1H-1,2,3-triazol-1-yl}butylphosphonate ***23g***. From azide **15** (0.129 g, 0.473 mmol) and 8-chloro-N^7-propargyltheophylline **19g** (0.119 g, 0.473 mmol) the phosphonate **23g** (0.242 g, 98%) was obtained as a white solid after chromatography on a silica gel column with chloroform–methanol (20:1, v/v); m.p.: 69–70 °C; IR (KBr): ν = 3013, 2988, 2962, 1707, 1668, 1225, 1015 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 7.79 (s, 1H, *HC*5′); 5.62 (s, 2H, CH_2); 4.35 (t, *J* = 7.3 Hz, 2H, PCCCCH_2); 4.14–4.04 (m, 4H, 2× POC$H_2$$CH_3$); 3.55 (s, 3H, CH_3); 3.42 (s, 3H, CH_3); 2.04 (qu, *J* = 7.3 Hz, 2H, PCCCH_2); 1.77 (dt, *J* = 14.8 Hz, *J* = 7.3 Hz, 2H, PCH_2); 1.69–1.61 (m, 2H, PCCH_2); 1.32 (t, *J* = 7.0 Hz, 6H, 2× POCH_2CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 154.5 (s, C=O); 151.2 (s, C=O); 147.4; 141.7; 139.1; 123.5; 107.3; 61.6 (d, *J* = 6.5 Hz, POC); 49.8; 41.0; 30.6 (d, *J* = 15.1 Hz, PCC*C*); 29.8; 28.0; 24.9 (d, *J* = 142.1 Hz, PC); 19.6 (d, *J* = 4.8 Hz, PC*C*); 16.4 (d, *J* = 5.9 Hz, POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$): δ = 30.49 ppm. Anal. Calcd. for $C_{18}H_{27}ClN_7O_5P$: C, 44.31; H, 5.58; N, 20.10. Found: C, 44.56; H, 5.44; N, 20.35.

4.1.5.31. Diethyl 4-{4-[(3,7-dimethyl-2,6-dioxopurin-1-yl)methyl]-1H-1,2,3-triazol-1-yl}butylphosphonate ***23h***. From azide **15** (0.135 g, 0.573 mmol) and N^1-propargyltheobromine **19h** (0.125 g, 0.573 mmol) the phosphonate **23h** (0.224 g, 88%) was obtained as a white solid after purification on silica gel with chloroform–methanol (20:1, v/v); m.p.: 59–61 °C; IR (KBr): ν = 3432, 3115, 2983, 2952, 1708, 1662, 1235, 1025 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 7.62 (s, 1H); 7.51 (s, 1H); 5.33 (s, 2H, CH_2); 4.33 (t, *J* = 7.3 Hz, 2H, PCCCCH_2); 4.13–4.05 (m, 4H, 2× POC$H_2$$CH_3$); 4.01 (s, 3H, CH_3); 3.59 (s, 3H, CH_3); 2.02 (qu, *J* = 7.3 Hz, 2H, PCCCH_2); 1.73 (dt, *J* = 18.0 Hz, *J* = 7.3 Hz, 2H, PCH_2); 1.63 (dqu, *J* = 14.0 Hz, *J* = 7.3 Hz, 2H, PCCH_2); 1.32 (t, *J* = 7.0 Hz, 6H, 2× POCH_2CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 154.8 (s, C=O); 151.3 (s, C=O); 148.9; 143.6; 141.7; 123.1; 107.6; 61.6 (d, *J* = 6.5 Hz, POC); 49.6; 36.0; 33.5; 30.7 (d, *J* = 15.3 Hz, PCCC); 29.7; 25.0 (d, *J* = 144.9 Hz, PC); 19.6 (d, *J* = 4.7 Hz, PCC); 16.4 (d, *J* = 6.1 Hz, POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$): δ = 30.91 ppm. Anal. Calcd. for $C_{18}H_{28}N_7O_5P$: C, 47.68; H, 6.22; N, 21.62. Found: C, 47.74; H, 6.03; N, 21.71.

4.1.5.32. Diethyl 4-{4-[(1,3-dimethyl-2,6-dioxopurin-7-yl)methyl]-1H-1,2,3-triazol-1-yl}butylphosphonate ***23i***. From azide **15** (0.146 g, 0.535 mmol) and N^7-propargyltheophylline **19i** (0.117 g, 0.535 mmol) the phosphonate **23i** (0.189 g, 72%) was obtained as a white solid after chromatography on a silica gel column with chloroform–methanol (20:1, v/v); m.p.: 58–59 °C; IR (KBr): ν = 3432, 3115, 2983, 2952, 1708, 1662, 1235, 1025 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 7.84 (s, 1H); 7.83 (s, 1H); 5.60 (s, 2H, CH_2); 4.37 (t, *J* = 7.1 Hz, 2H, PCCCCH_2); 4.15–4.05 (m, 4H, 2× POC$H_2$$CH_3$); 3.60 (s, 3H, CH_3); 3.44 (s, 3H, CH_3); 2.06 (qu, *J* = 7.1 Hz, 2H, PCCCH_2); 1.80–1.74 (m, 2H, PCH_2); 1.69–1.62 (m, 2H, PCCH_2); 1.33 (t, *J* = 7.4 Hz, 6H, 2× POCH_2CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 155.4 (s, C=O); 151.6 (s, C=O); 149.0; 142.2; 141.4; 123.5; 106.5; 61.6 (d, *J* = 6.4 Hz, POC); 49.9; 41.5; 30.6 (d, *J* = 14.7 Hz, PCC*C*); 29.8; 25.0 (d, *J* = 142.2 Hz, PC); 19.6 (d, *J* = 4.5 Hz, PCC); 16.4 (d, *J* = 6.4 Hz, POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$): δ = 30.79 ppm. Anal. Calcd. for $C_{18}H_{28}N_7O_5P$: C, 47.68; H, 6.22; N, 21.62. Found: C, 47.80; H, 6.00; N, 21.74.

4.1.5.33. Diethyl 4-{4-[(5,6-dimethylbenzimidazol-1-yl)methyl]-1H-1,2,3-triazol-1-yl}butylphosphonate ***23j***. From azide **15** (0.150 g, 0.549 mmol) and 5,6-dimethyl-N^1-propargylbenzimidazole **19j** (0.100 g, 0.549 mmol) the phosphonate **23j** (0.122 g, 74%) was obtained as a yellow oil after purification on silica gel with chloroform–methanol (50:1, v/v); IR (film): ν = 3303, 3102, 2982, 1219, 1027 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.30 (s, 1H); 7.60 (s, 1H); 7.30 (s, 1H); 7.32 (s, 1H); 5.48 (s, 2H, CH_2); 4.38 (t, *J* = 7.4 Hz, 2H, PCCCCH_2); 4.16–4.04 (m, 4H, 2× POC$H_2$$CH_3$); 2.40 (s, 3H, CH_3); 2.39 (s, 3H, CH_3); 1.99 (qu, *J* = 7.4 Hz, 2H, PCCCH_2); 1.75 (dt, *J* = 18.2 Hz, *J* = 7.4 Hz, 2H, PCH_2); 1.63 (dq, *J* = 15.4 Hz, *J* = 7.4 Hz, 2H, PCCH_2); 1.31 (t, *J* = 7.1 Hz, 6H, 2× POCH_2CH_3); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 143.0; 132.7; 130.8; 122.1; 120.3; 61.6 (d, *J* = 6.6 Hz, POC); 49.8; 30.5 (d, *J* = 15.1 Hz, PCC*C*); 24.9 (d, *J* = 142.1 Hz, PC); 20.4; 20.2; 19.5 (d, *J* = 4.7 Hz, PCC); 16.4 (d, *J* = 5.8 Hz, POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$): δ = 30.84 ppm. Anal. Calcd. for $C_{20}H_{30}N_5O_3P$: C, 57.27; H, 7.21; N, 16.70. Found: C, 57.10; H, 7.08; N, 16.79.

4.1.5.34. Diethyl 4-{4-[(3-acetylindol-1-yl)methyl]-1H-1,2,3-triazol-1-yl}butylphosphonate ***23k***. From azide **15** (0.114 g, 0.485 mmol) and 3-acetyl-*N*-propargylindole **19k** (0.096 g, 0.485 mmol) the phosphonate **23k** (0.187 g, 89%) was obtained as a colourless oil after chromatography on a silica gel column with chloroform–

methanol (20:1, v/v); IR (film): ν = 3283, 3110, 2983, 2872, 1797, 1231, 1045, 750 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.45–8.38 (m, 1H); 7.76 (s, 1H, *H*C5′); 7.43–7.39 (m, 1H); 7.36–7.27 (m, 3H); 5.42 (s, 2H, CH_2); 4.37 (t, J = 7.0 Hz, 2H, PCCCC*H*$_2$); 4.10–4.00 (m, 4H, 2× POC*H*$_2$CH$_3$); 2.53 (s, 3H, CH_3); 1.98 (qu, J = 7.0 Hz, 2H, PCCC*H*$_2$); 1.85–1.50 (m, 4H, PC*H*$_2$C*H*$_2$); 1.28 (t, J = 7.0 Hz, 6H, 2× POCH$_2$C*H*$_3$); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 193.0 (s, C=O); 143.0; 136.5; 134.8; 123.5; 122.7; 122.7; 122.1; 117.5; 109.9; 61.7 (d, J = 6.4 Hz, POC); 50.0; 42.5; 30.8 (d, J = 15.2 Hz, PCC*C*); 27.8; 24.9 (d, J = 141.7 Hz, P*C*); 19.7 (d, J = 4.9 Hz, PC*C*); 16.6 (d, J = 6.0 Hz, POC*C*); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 31.92 ppm. Anal. Calcd. for $C_{21}H_{29}N_4O_4P$: C, 58.32; H, 6.76; N, 12.96. Found: C, 58.48; H, 6.81; N, 13.10.

4.1.5.35. Diethyl 4-{4-[(2-oxopyridin-1-yl)methyl]-1H-1,2,3-triazol-1-yl}butylphosphonate ***23l***. From azide **15** (0.123 g, 0.523 mmol) and *N*-propargyl-2-pyridon **19l** (0.070 g, 0.523 mmol) the phosphonate **23l** (0.182 g, 94%) was obtained as a brown oil after purification on silica gel with chloroform–methanol (20:1, v/v); IR (film): ν = 3134, 2996, 2935, 1659, 1222; 1020, 968 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.78 (s, 1H, *H*C5′); 7.60 (dd, J = 6.7 Hz, J = 2.2 Hz, 1H); 7.38 (ddd, J = 9.1 Hz, J = 6.7 Hz, J = 2.2 Hz, 1H); 6.54 (d, J = 9.1 Hz, 1H); 6.19 (dt, J = 6.7 Hz, J = 1.5 Hz, 1H); 5.18 (s, 2H, CH_2); 4.33 (t, J = 7.2 Hz, 2H, PCCCC*H*$_2$); 4.17–4.00 (m, 4H, 2× POC*H*$_2$CH$_3$); 2.22–1.96 (m, 2H, PCCC*H*$_2$); 1.82–1.60 (m, 4H, PC*H*$_2$C*H*$_2$); 1.31 (t, J = 6.9 Hz, 6H, 2× POCH$_2$C*H*$_3$); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 162.3 (s, C=O); 142.7 (s, HC=C); 140.0; 137.8; 123.9 (s, HC=*C*); 120.8; 106.6; 61.7 (d, J = 6.5 Hz, POC); 49.9; 44.7; 30.8 (d, J = 15.5 Hz, PCC*C*); 25.1 (d, J = 141.7 Hz, P*C*); 19.8 (d, J = 5.2 Hz, PC*C*); 16.6 (d, J = 6.0 Hz, POC*C*); 12.2 (s, CH_3); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 32.08 ppm. Anal. Calcd. for $C_{16}H_{25}N_4O_4P$: C, 52.17; H, 6.84; N, 15.21. Found: C, 51.90; H, 6.78; N, 15.11.

4.1.5.36. Diethyl 2-(4-{[3-benzoyl-2,4-dioxopyrimidin-1-yl]methyl}-1H-1,2,3-triazol-1-yl)-1-hydroxyethylphosphonate ***24e***. From azide **16** (0.146 g, 0.654 mmol) and N^3-benzoyl-N^1-propargylquinazoline-2,4-dione **19e** (0.199 g, 0.654 mmol) the phosphonate **24e** (0.340 g, 98%) was obtained as a colourless oil after purification on silica gel with chloroform–methanol (50:1, v/v); IR (film): ν = 3356, 2982, 2831, 1750, 1702, 1668, 1234, 1027, 785, 688 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.16 (dd, J = 7.9 Hz, J = 1.4 Hz, 1H); 7.97–7.94 (m, 2H, 2× *o*-CH); 7.92 (s, 1H, *H*C5′); 7.88 (brd, J = 8.3 Hz, 1H); 7.75 (ddd, J = 8.3 Hz, J = 7.9 Hz, J = 1.4 Hz, 1H); 7.68–7.62 (m, 1H, *p*-CH); 7.52–7.46 (m, 2H, 2× *m*-CH); 7.31 (dt, J = 7.9 Hz, J = 0.6 Hz, 1H); 5.44 (AB, J = 15.8 Hz, 1H, C*H*$_a$H$_b$); 5.42 (AB, J = 15.8 Hz, 1H, CH$_a$*H*$_b$); 4.77 (ddd, J = 14.3 Hz, J = 5.3 Hz, J = 2.8 Hz, 1H, PCC*H*$_a$H$_b$); 4.48 (ddd, J = 14.3 Hz, J = 10.0 Hz, J = 5.8 Hz, 1H, PCCH$_a$*H*$_b$); 4.23 (ddd, J = 10.3 Hz, J = 7.9 Hz, J = 2.8 Hz, 1H, P*C*H(OH)); 4.16–4.04 (m, 4H, 2× POC*H*$_2$CH$_3$); 1.27 (t, J = 7.0 Hz, 3H, POCH$_2$C*H*$_3$); 1.26 (t, J = 7.0 Hz, 3H, POCH$_2$C*H*$_3$); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 168.6 (s, C=O); 161.0 (s, C=O); 149.4 (s, C=O); 142.0 (s, H*C*=C); 140.2; 136.2; 135.2; 131.6; 130.5; 129.3; 128.8; 125.6 (s, HC=*C*); 123.8; 115.5; 115.4; 67.0 (d, J = 163.2 Hz, PC); 63.8 (d, J = 7.5 Hz, POC); 63.6 (d, J = 7.5 Hz, POC); 51.6 (d, J = 10.0 Hz, PC*C*); 39.0; 16.6 (d, J = 5.3 Hz, POC*C*); 16.5 (d, J = 5.3 Hz, POC*C*); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 21.21 ppm. Anal. Calcd. for $C_{24}H_{26}N_5O_7P$: C, 54.65; H, 4.97; N, 13.28. Found: C, 54.47; H, 5.11; N, 13.12.

4.1.5.37. Diethyl 2-{4-[(3,5-dioxo-1,2,4-triazin-2-yl)methyl]-1H-1,2,3-triazol-1-yl}-1-hydroxyethylphosphonate ***24f***. From azide **16** (0.138 g, 0.618 mmol) and N^1-propargylazauracil **19f** (0.093 g, 0.618 mmol) the phosphonate **24f** (0.161 g, 70%) was obtained as a white solid after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); m.p.: 145–147 °C; IR (KBr): ν = 3300, 2913, 2837, 1729, 1674, 1023 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 12.07 (s, 1H, NH); 7.92 (s, 1H); 7.41 (s, 1H); 5.30 (brs, 1H, OH); 5.15 (s, 2H, CH_2); 4.82 (ddd, J = 14.0 Hz, J = 4.6 Hz, J = 2.2 Hz, 1H, PCC*H*$_a$H$_b$); 4.52–4.34 (m, 2H, P*C*H(OH), PCCH$_a$*H*$_b$); 4.15–4.02 (m, 4H, 2× POC*H*$_2$CH$_3$); 1.36 (t, J = 6.9 Hz, 3H, POCH$_2$C*H*$_3$); 1.34 (t, J = 6.9 Hz, 3H, POCH$_2$C*H*$_3$); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 155.9 (s, C=O); 149.5 (C=O); 141.2 (s, H*C*=C); 135.1 (s, HC=N); 125.7 (s, HC=*C*); 66.8 (d, J = 144.0 Hz, PC); 63.8 (d, J = 6.6 Hz, POC); 63.7 (d, J = 6.6 Hz, POC); 51.7 (d, J = 10.6 Hz); 34.7; 16.6 (d, J = 5.5 Hz, POC*C*); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 21.60 ppm. Anal. Calcd. for $C_{12}H_{19}N_6O_6P$: C, 38.51; H, 5.12; N, 22.45. Found: C, 38.27; H, 5.02; N, 22.55.

4.1.5.38. Diethyl 2-{4-[(8-chloro-1,3-dimethyl-2,6-dioxopurin-7-yl)methyl]-1H-1,2,3-triazol-1-yl}-1-hydroxyethylphosphonate ***24g***. From azide **16** (0.100 g, 0.448 mmol) and 8-chloro-N^7-propargyltheophylline **19g** (0.113 g, 0.448 mmol) the phosphonate **24g** (0.185 g, 87%) was obtained as a white solid after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); m.p.: 183–184 °C; IR (KBr): ν = 3281, 3057, 2986, 1707, 1665, 1216, 1047 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.95 (s, 1H, *H*C5′); 5.61 (s, 2H, CH_2); 5.08 (t, J = 5.7 Hz, 1H, OH); 4.75 (ddd, J = 14.2 Hz, J = 5.1 Hz, J = 2.6 Hz, 1H, PCC*H*$_a$H$_b$); 4.44 (ddd, J = 14.2 Hz, J = 10.0 Hz, J = 5.6 Hz, 1H, PCCH$_a$*H*$_b$); 4.28 (dddd, J = 10.0 Hz, J = 8.0 Hz, J = 5.7 Hz, J = 5.1 Hz, 1H, P*C*H(OH)); 4.21–4.10 (m, 4H, 2× POC*H*$_2$CH$_3$); 3.51 (s, 3H, CH_3); 3.37 (s, 3H, CH_3); 1.33 (t, J = 7.0 Hz, 3H, POCH$_2$C*H*$_3$); 1.32 (t, J = 7.0 Hz, 3H, POCH$_2$C*H*$_3$); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 154.4 (s, C=O); 151.1 (s, C=O); 147.3; 139.0; 125.2; 107.4; 67.0 (d, J = 163.8 Hz, PC); 63.7 (d, J = 7.2 Hz, POC); 63.5 (d, J = 7.2 Hz, POC); 51.7 (d, J = 9.7 Hz, PCC); 41.1; 30.0; 28.2; 16.6 (d, J = 5.5 Hz, POC*C*); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 20.42 ppm. Anal. Calcd. for $C_{16}H_{23}ClN_7O_6P$: C, 40.39; H, 4.87; N, 20.61. Found: C, 40.55; H, 4.87; N, 20.47.

4.1.5.39. Diethyl 2-{4-[(3,7-dimethyl-2,6-dioxopurin-1-yl)methyl]-1H-1,2,3-triazol-1-yl}-1-hydroxyethylphosphonate ***24h***. From azide **16** (0.100 g, 0.448 mmol) and N^1-propargyltheobromine **19h** (0.098 g, 0.448 mmol) the phosphonate **24h** (0.190 g, 96%) was obtained as a white powder after purification on silica gel with chloroform–methanol (50:1, v/v); m.p.: 166–168 °C; IR (KBr): ν = 3237, 2989, 1708, 1663, 1235, 1023 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.80 (s, 1H); 7.53 (s, 1H, *H*C5′); 5.35 (AB, J = 14.6 Hz, 1H, C*H*$_a$H$_b$); 5.30 (AB, J = 14.6 Hz, 1H, CH$_a$*H*$_b$); 4.79 (ddd, J = 14.2 Hz, J = 6.0 Hz, J = 2.5 Hz, 1H, PCC*H*$_a$H$_b$); 4.47 (ddd, J = 14.2 Hz, J = 9.7 Hz, J = 5.2 Hz, 1H, PCCH$_a$*H*$_b$); 4.40–4.34 (m, 1H, P*C*H(OH)); 4.27–4.15 (m, 4H, 2× POC*H*$_2$CH$_3$); 4.06 (dd, J = 9.4 Hz, J = 5.8 Hz, 1H); 4.01 (s, 3H, CH_3); 3.60 (s, 3H, CH_3); 1.38 (t, J = 7.0 Hz, 3H, POCH$_2$C*H*$_3$); 1.36 (t, J = 7.0 Hz, 3H, POCH$_2$C*H*$_3$); ^{13}C NMR (151.5 MHz, $CDCl_3$): δ = 154.7 (s, C=O); 151.2 (s, C=O); 148.8; 143.2; 141.9; 124.9; 107.6; 67.0 (d, J = 165.1 Hz, PC); 64.4 (d, J = 6.9 Hz, POC); 63.2 (d, J = 6.9 Hz, POC); 51.7 (d, J = 9.6 Hz, PC*C*); 36.0; 33.6; 29.7; 16.4 (d, J = 5.3 Hz, POC*C*); ^{31}P NMR (243 MHz, $CDCl_3$): δ = 19.86 ppm. Anal. Calcd. for $C_{16}H_{24}N_7O_6P$: C, 43.54; H, 5.48; N, 22.21. Found: C, 43.67; H, 5.28; N, 22.30.

4.1.5.40. Diethyl 2-{4-[(1,3-dimethyl-2,6-dioxopurin-7-yl)methyl]-1H-1,2,3-triazol-1-yl}-1-hydroxyethylphosphonate ***24i***. From azide **16** (0.100 g, 0.448 mmol) and N^7-propargyltheophylline **19i** (0.098 g, 0.448 mmol) the phosphonate **24i** (0.145 g, 73%) was obtained as a white powder after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); m.p.: 164–165 °C; IR (KBr): ν = 3264, 3152, 2990, 1705, 1660, 1224, 1025 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.00 (s, 1H); 7.84 (s, 1H, *H*C5′); 5.62 (AB, J = 15.0 Hz, 1H, C*H*$_a$H$_b$); 5.58 (AB, J = 15.0 Hz, 1H, CH$_a$*H*$_b$); 4.80 (ddd, J = 14.3 Hz, J = 5.2 Hz, J = 2.7 Hz, 1H, PCC*H*$_a$H$_b$); 4.78 (dd, J = 13.3 Hz, J = 5.9 Hz, 1H); 4.49 (ddd, J = 14.3 Hz, J = 10.0 Hz, J = 5.6 Hz, 1H, PCCH$_a$*H*$_b$); 4.36–4.28 (m, 1H, P*C*H(OH)); 4.27–4.16

(m, 4H, 2× POCH_2CH$_3$); 3.57 (s, 3H, CH$_3$); 3.41 (s, 3H, CH$_3$); 1.37 (t, J = 7.1 Hz, 3H, POCH$_2$CH_3); 1.36 (t, J = 7.1 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (151 MHz, CDCl$_3$): δ = 155.4 (s, C═O); 151.6 (s, C═O); 148.9; 141.8; 141.5; 125.4; 106.5; 67.0 (d, J = 164.6 Hz, PC); 63.6 (d, J = 7.4 Hz, POC); 63.4 (d, J = 7.4 Hz, POC); 51.7 (d, J = 9.6 Hz, PC*C*); 41.4; 29.8; 27.9; 16.4 (d, J = 5.9 Hz, POC*C*); ^{31}P NMR (243 MHz, CDCl$_3$): δ = 19.90 ppm. Anal. Calcd. for $C_{16}H_{24}N_7O_6P$: C, 43.54; H, 5.48; N, 22.21. Found: C, 43.38; H, 5.55; N, 22.30.

4.1.5.41. Diethyl 2-{4-[(5,6-dimethylbenzoimidazol-1-yl)methyl]-1H-1,2,3-triazol-1-yl}-1-hydroxyethylphosphonate ***24j***. From azide **16** (0.100 g, 0.448 mmol) and 5,6-dimethyl-*N*-propargylbenzimidazole **19j** (0.083 g, 0.448 mmol) the phosphonate **24j** (0.118 g, 65%) was obtained as a yellow oil after purification on silica gel with chloroform–methanol (50:1, v/v); IR (film): ν = 3131, 2990, 2945, 1217, 1048, 757 cm^{-1}; ^{1}H NMR (600 MHz, CDCl$_3$): δ = 7.91 (s, 1H); 7.76 (s, 1H); 7.43 (s, 1H); 7.23 (s, 1H); 5.38 (AB, J = 15.7 Hz, 1H, CH_aH$_b$); 5.34 (AB, J = 15.7 Hz, 1H, CH$_a$$H_b$); 4.82 (ddd, J = 14.2 Hz, J = 4.9 Hz, J = 2.5 Hz, 1H, PCCH_aH$_b$); 4.46 (ddd, J = 14.2 Hz, J = 9.9 Hz, J = 5.3 Hz, 1H, PCCH$_a$$H_b$); 4.31 (dt, J = 9.9 Hz, J = 5.2 Hz, 1H, PC*H*(OH)); 4.12–4.06 (m, 4H, 2× POCH_2CH$_3$); 2.34 (s, 3H, CH$_3$); 2.33 (s, 3H, CH$_3$); 1.32 (t, J = 7.0 Hz, 3H, POCH$_2$CH_3); 1.30 (t, J = 7.0 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (151 MHz, CDCl$_3$): δ = 142.1; 141.5; 141.2; 132.7; 131.7; 131.6; 124.5; 119.6; 110.1; 66.6 (d, J = 166.1 Hz, PC); 63.4 (d, J = 7.1 Hz, POC); 63.2 (d, J = 7.1 Hz, POC); 51.7 (d, J = 9.6 Hz, PC*C*); 40.2; 20.7; 20.4; 16.7 (d, J = 5.4 Hz, POC*C*); ^{31}P NMR (243 MHz, CDCl$_3$): δ = 21.28 ppm. Anal. Calcd. for $C_{18}H_{26}N_5O_4P$: C, 53.07; H, 6.43; N, 17.19. Found: C, 52.88; H, 6.17; N, 17.05.

4.1.5.42. Diethyl 2-{4-[(3-acetylindol-1-yl)methyl]-1H-1,2,3-triazol-1-yl}-1-hydroxyethylphosphonate ***24k***. From azide **16** (0.142 g, 0.636 mmol) and 3-acetyl-*N*-propargylindole **19k** (0.125 g, 0.636 mmol) the phosphonate **24k** (0.196 g, 73%) was obtained as a colourless oil after purification on silica gel with chloroform–methanol (50:1, v/v); IR (film): ν = 3266, 2959, 2911, 1642, 1528, 1390, 1217, 1024, 754 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ = 8.36–8.26 (m, 1H); 7.84 (s, 1H, *H*C5′); 7.62 (s, 1H); 7.43–7.35 (m, 1H); 7.30–7.23 (m, 2H); 5.46 (AB, J = 15.4 Hz, 1H, CH_aH$_b$); 5.44 (AB, J = 15.4 Hz, 1H, CH$_a$$H_b$); 4.77 (ddd, J = 14.3 Hz, J = 6.0 Hz, J = 2.6 Hz, 1H, PCCH_aH$_b$); 4.44 (ddd, J = 14.3 Hz, J = 10.0 Hz, J = 5.6 Hz, 1H, PCCH$_a$$H_b$); 4.21 (ddd, J = 10.0 Hz, J = 7.9 Hz, J = 2.6 Hz, 1H, PC*H*(OH)); 4.14–4.06 (m, 4H, 2× POCH_2CH$_3$); 3.85 (brs, 1H, OH); 2.51 (s, 3H, CH$_3$); 1.29 (t, J = 6.8 Hz, 6H, 2× POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, CDCl$_3$): δ = 194.0 (s, C═O); 142.6; 136.6; 135.0; 126.4; 124.2; 123.6; 122.8; 122.7; 117.5; 110.0; 66.2 (d, J = 159.3 Hz, PC); 63.4 (d, J = 7.0 Hz, POC); 63.3 (d, J = 7.0 Hz, POC); 51.9 (d, J = 9.7 Hz, PC*C*); 42.4; 27.7 (s, CH$_3$); 16.6 (d, J = 5.4 Hz, POC*C*); ^{31}P NMR (121.5 MHz, CDCl$_3$): δ = 21.03 ppm. Anal. Calcd. for $C_{19}H_{25}N_4O_5P$: C, 54.28; H, 5.99; N, 13.33. Found: C, 54.10; H, 6.12; N, 13.20.

4.1.5.43. Diethyl 1-hydroxy-2-{4-[(2-oxopyridin-1-yl)methyl]-1H-1,2,3-triazol-1-yl}ethylphosphonate ***24l***. From azide **16** (0.134 g, 0.600 mmol) and *N*-propargy-2-pyridon **19l** (0.080 g, 0.600 mmol) the phosphonate **24l** (0.172 g, 80%) was obtained as a brown oil after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); IR (film): ν = 3274, 2984, 2831, 1673, 1027 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ = 8.03 (s, 1H); 7.64 (ddd, J = 6.7 Hz, J = 2.0 Hz, J = 0.6 Hz, 1H); 7.36 (ddd, J = 9.2 Hz, J = 6.7 Hz, J = 2.0 Hz, 1H); 6.52 (dd, J = 9.2 Hz, J = 0.6 Hz, 1H); 6.22 (dt, J = 6.7 Hz, J = 1.3 Hz, 1H); 5.20 (AB, J = 14.3 Hz, 1H, CH_aH$_b$); 5.12 (AB, J = 14.3 Hz, 1H, CH$_a$$H_b$); 4.79 (ddd, J = 14.2 Hz, J = 5.0 Hz, J = 2.6 Hz, 1H, PCCH_aH$_b$); 4.51 (ddd, J = 14.2 Hz, J = 10.0 Hz, J = 5.0 Hz, 1H, PCCH$_a$$H_b$); 4.36 (ddd, J = 10.0 Hz, J = 8.9 Hz, J = 2.6 Hz, 1H, PC*H*(OH)); 4.26–4.14 (m, 4H, 2× POCH_2CH$_3$); 2.56 (brs, 1H, OH); 1.35 (t, J = 7.0 Hz, 3H, POCH$_2$CH_3); 1.33 (t, J = 6.9 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, CDCl$_3$): δ = 162.3 (s, C═O); 141.9 (s, H*C*═C); 140.2; 137.8; 125.6 (s, HC═*C*); 120.2; 106.9; 66.7 (d, J = 164.9 Hz, PC); 63.3 (d, J = 7.1 Hz, POC); 63.2 (d, J = 7.1 Hz, POC); 51.8 (d, J = 10.4 Hz, PC*C*); 44.5; 16.5 (d, J = 5.2 Hz, POC*C*); ^{31}P NMR (121.5 MHz, CDCl$_3$): δ = 21.29 ppm. Anal. Calcd. for $C_{14}H_{21}N_4O_5P$: C, 47.19; H, 5.94; N, 15.72. Found: C, 47.01; H, 6.10; N, 15.80.

4.1.5.44. Diethyl 3-(4-{[3-benzoyl-2,4-dioxopyrimidin-1-yl]methyl}-1H-1,2,3-triazol-1-yl)-2-hydroxyethylphosphonate ***25e***. From azide **17** (0.115 g, 0.485 mmol) and N^3-benzoyl-N^1-propargylquinazoline-2,4-dione **19e** (0.148 g, 0.485 mmol) the phosphonate **25e** (0.235 g, 89%) was obtained as a white solid after purification on silica gel with chloroform–methanol (50:1, v/v); m.p.: 75–77 °C; IR (KBr): ν = 3386, 3054, 2988, 2851, 1754, 1709, 1658, 1224, 1025, 795, 694 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ = 8.17 (dd, J = 7.9 Hz, J = 1.5 Hz, 1H); 7.97–7.93 (m, 2H, 2× *o*-CH); 7.87 (brd, J = 8.4 Hz, 1H); 7.85 (s, 1H, *H*C5′); 7.75 (ddd, J = 8.4 Hz, J = 7.9 Hz, J = 1.5 Hz, 1H); 7.67–7.61 (m, 1H, *p*-CH); 7.51–7.45 (m, 2H, 2× *m*-CH); 7.29 (dt, J = 7.9 Hz, J = 0.5 Hz, 1H); 5.44 (AB, J = 14.2 Hz, 1H, CH_aH$_b$); 5.36 (AB, J = 14.2 Hz, 1H, CH$_a$$H_b$); 4.45 (dd, J = 15.4 Hz, J = 6.5 Hz, 1H, PCCCH_aH$_b$); 4.44–4.32 (m, 2H, PCC*H*CH$_a$$H_b$); 4.14–4.01 (m, 4H, 2× POCH_2CH$_3$); 3.40 (brs, 1H, OH); 1.96 (ddd, J = 19.2 Hz, J = 15.1 Hz, J = 3.3 Hz, 1H, PCH_aH$_b$); 1.73 (ddd, J = 16.4 Hz, J = 15.1 Hz, J = 9.1 Hz, 1H, PCH$_a$$H_b$); 1.30 (t, J = 7.0 Hz, 3H, POCH$_2$CH_3); 1.27 (t, J = 7.0 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, CDCl$_3$): δ = 168.6 (s, C═O); 161.0 (s, C═O); 149.5 (s, C═O); 142.3 (s, H*C*═C); 140.3; 136.3; 135.2; 131.6; 130.6; 129.3; 128.9; 125.4 (s, HC═*C*); 123.8; 115.6; 115.4; 65.5 (d, J = 4.0 Hz, PC*C*); 62.5 (d, J = 5.8 Hz, POC); 62.4 (d, J = 5.8 Hz, POC); 52.4 (d, J = 14.1 Hz, PCC*C*); 39.0; 30.0 (d, J = 140.4 Hz, PC); 16.6 (d, J = 5.2 Hz, POC*C*); ^{31}P NMR (121.5 MHz, CDCl$_3$): δ = 29.27 ppm. Anal. Calcd. for $C_{25}H_{28}N_5O_7P$: C, 55.45; H, 5.21; N, 12.93. Found: C, 55.28; H, 5.15; N, 13.11.

4.1.5.45. Diethyl 3-{4-[(3,5-dioxo-1,2,4-triazin-2-yl)methyl]-1H-1,2,3-triazol-1-yl}-2-hydroxypropylphosphonate ***25f***. From azide **17** (0.151 g, 0.637 mmol) and *N*-propargyl-6-azauracil **19f** (0.096 g, 0.637 mmol) the phosphonate **25f** (0.188 g, 76%) was obtained as a colourless oil after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); IR (film): ν = 3302, 2986, 2913, 2833, 1730, 1673, 1028, 970 cm^{-1}; ^{1}H NMR (600 MHz, CDCl$_3$): δ = 11.80 (s, 1H, NH); 7.89 (s, 1H); 7.46 (s, 1H); 5.25 (AB, J = 15.6 Hz, 1H, CH_aH$_b$); 5.19 (AB, J = 15.6 Hz, 1H, CH$_a$$H_b$); 4.55 (dd, J = 13.7 Hz, J = 3.0 Hz, 1H, PCCCH_aH$_b$); 4.43 (ddddd, J = 8.6 Hz, J = 7.0 Hz, J = 3.9 Hz, J = 3.0 Hz, 1H, PCC*H*(OH)); 4.38 (dd, J = 13.7 Hz, J = 7.0 Hz, 1H, PCCCH$_a$$H_b$); 4.19–4.02 (m, 4H, 2× POCH_2CH$_3$); 2.05 (ddd, 2H, J = 19.2 Hz, J = 15.2 Hz, J = 3.9 Hz, PCH_aH$_b$); 1.97 (ddd, 2H, J = 17.6 Hz, J = 15.2 Hz, J = 8.6 Hz, PCH$_a$$H_b$); 1.31 (t, J = 7.2 Hz, 3H, POCH$_2$CH_3); 1.30 (t, J = 7.2 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, CDCl$_3$): δ = 156.0 (s, C═O); 149.4 (C═O); 141.4 (s, H*C*═C); 135.1 (s, HC═N); 125.7 (s, HC═*C*); 65.6 (s, PC*C*); 62.7 (d, J = 6.3 Hz, POC); 62.4 (d, J = 6.3 Hz, POC); 56.2 (d, J = 16.6 Hz, PCC*C*); 34.8; 31.0 (d, J = 140.9 Hz, PC); 16.6 (d, J = 6.0 Hz, POC*C*); ^{31}P NMR (243 MHz, CDCl$_3$): δ = 29.38 ppm. Anal. Calcd. for $C_{13}H_{21}N_6O_6P$: C, 40.21; H, 5.45; N, 21.64. Found: C, 40.08; H, 5.59; N, 21.72.

4.1.5.46. Diethyl 3-{4-[(8-chloro-1,3-dimethyl-2,6-dioxopurin-7-yl) methyl]-1H-1,2,3-triazol-1-yl}-2-hydroxypropylphosphonate ***25g***. From azide **17** (0.125 g, 0.527 mmol) and 8-chloro-N^7-propargyltheophylline **19g** (0.133 g, 0.527 mmol) the phosphonate **25g** (0.211 g, 82%) was obtained as a white solid after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); m.p.: 137–139 °C; IR (KBr): ν = 3354, 3151, 2983, 2928, 1702, 1675, 1221, 1027 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.93 (s, 1H, *H*C5′); 5.63 (s, 2H, CH$_2$); 4.53–4.33 (m, 3H, PCC*H*CH$_2$); 4.17–4.03 (m, 4H, 2× POCH_2CH$_3$); 3.52 (s, 3H, CH$_3$); 3.38 (s, 3H, CH$_3$); 1.98 (ddd,

J = 19.0 Hz, J = 15.3 Hz, J = 3.1 Hz, 1H, PCH_aH$_b$); 1.77 (ddd, J = 16.8 Hz, J = 15.3 Hz, J = 9.2 Hz, 1H, PCH$_a$$H_b$); 1.32 (t, J = 7.0 Hz, 3H, POCH$_2$CH_3); 1.31 (t, J = 7.0 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, CDCl$_3$): δ = 154.3 (s, C=O); 151.1 (s, C=O); 147.2; 141.4; 138.9; 125.2; 107.4; 65.4 (d, J = 3.7 Hz, PCC); 62.4 (d, J = 6.5 Hz, POC); 62.3 (d, J = 6.5 Hz, POC); 56.0 (d, J = 18.4 Hz, PCCC); 41.1; 30.8 (d, J = 135.9 Hz, PC); 30.0; 28.2; 16.6 (d, J = 5.7 Hz, POCC); 16.5 (d, J = 5.7 Hz, POCC); ^{31}P NMR (121.5 MHz, CDCl$_3$): δ = 28.72 ppm. Anal. Calcd. for $C_{17}H_{25}ClN_7O_6P$: C, 41.68; H, 5.14; N, 20.02. Found: C, 41.70; H, 4.97; N, 19.90.

4.1.5.47. Diethyl 3-{4-[(3,7-dimethyl-2,6-dioxopurin-1-yl)methyl]-1H-1,2,3-triazol-1-yl}-2-hydroxypropylphosphonate ***25h***. From azide **17** (0.108 g, 0.455 mmol) and N^1-propargyltheobromine **19h** (0.099 g, 0.455 mmol) the phosphonate **25h** (0.192 g, 93%) was obtained as a white powder after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); m.p.: 148–150 °C; IR (KBr): ν = 3445, 2984, 2924, 1707, 1664, 1231, 1025 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.78 (s, 1H); 7.51 (d, J = 0.6 Hz, 1H, *H*C5′); 5.30 (s, 2H, CH$_2$); 4.52–4.32 (m, 3H, PCC*H*C*H*$_2$); 4.17–4.03 (m, 4H, 2× POC*H*$_2$CH$_3$); 3.98 (d, J = 0.6 Hz, 3H, CH$_3$); 3.55 (s, 3H, CH$_3$); 3.02 (brs, 1H, OH); 2.46–2.34 (m, 2H, PC*H*$_2$); 1.30 (t, J = 7.0 Hz, 3H, POCH$_2$CH_3); 1.28 (t, J = 7.0 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, CDCl$_3$): δ = 154.8 (s, C=O); 151.3 (s, C=O); 148.9; 143.5; 141.7; 124.9; 107.7; 65.6 (d, J = 3.8 Hz, PCC); 62.5 (d, J = 6.4 Hz, POC); 62.4 (d, J = 6.4 Hz, POC); 55.8 (d, J = 15.3 Hz, PCCC); 36.2; 33.9; 32.0 (d, J = 292.9 Hz, PC); 31.7; 30.0; 16.6 (d, J = 5.6 Hz, POCC); 16.5 (d, J = 5.6 Hz, POCC); ^{31}P NMR (121.5 MHz, CDCl$_3$): δ = 29.53 ppm. Anal. Calcd. for $C_{17}H_{26}N_7O_6P$: C, 44.84; H, 5.75; N, 21.53. Found: C, 44.70; H, 5.59; N, 21.60.

4.1.5.48. Diethyl 3-{4-[(1,3-dimethyl-2,6-dioxopurin-7-yl)methyl]-1H-1,2,3-triazol-1-yl}-2-hydroxypropylphosphonate ***25i***. From azide **17** (0.105 g, 0.443 mmol) and N^7-propargyltheophylline **19i** (0.097 g, 0.443 mmol) the phosphonate **25i** (0.182 g, 90%) was obtained as a white solid after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); m.p.: 132–133 °C; IR (KBr): ν = 2994, 2989, 2930, 1701, 1663, 1245, 1033 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.97 (s, 1H); 7.81 (s, 1H, *H*C5′); 5.58 (s, 2H, CH$_2$); 4.55–4.39 (m, 3H, PCC*H*C*H*$_2$); 4.18–4.04 (m, 4H, 2× POC*H*$_2$CH$_3$); 3.55 (s, 3H, CH$_3$); 3.38 (s, 3H, CH$_3$); 2.46–2.34 (m, 2H, PC*H*$_2$); 1.31 (t, J = 7.0 Hz, 3H, POCH$_2$CH_3); 1.28 (t, J = 7.0 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, CDCl$_3$): δ = 155.2 (s, C=O); 151.5 (s, C=O); 148.8; 141.9; 141.4; 125.3; 106.5; 65.5 (d, J = 3.8 Hz); 62.4 (d, J = 6.6 Hz, POC); 62.2 (d, J = 6.6 Hz, POC); 56.1 (d, J = 17.2 Hz, PCCC); 41.6; 31.8; 29.0 (d, J = 136.6 Hz, PC); 16.6 (d, J = 6.0 Hz, POCC); 16.5 (d, J = 6.0 Hz, POCC); ^{31}P NMR (121.5 MHz, CDCl$_3$): δ = 29.34 ppm. Anal. Calcd. for $C_{17}H_{26}N_7O_6P$: C, 44.84; H, 5.75; N, 21.53. Found: C, 44.77; H, 5.67; N, 21.32.

4.1.5.49. Diethyl 3-{4-[(5,6-dimethylbenzoimidazol-1-yl)methyl]-1H-1,2,3-triazol-1-yl}-2-hydroxypropylphosphonate ***25j***. From azide **17** (0.101 g, 0.427 mmol) and 5,6-dimethyl-*N*-propargylbenzimidazole **19j** (0.078 g, 0.427 mmol) the phosphonate **25j** (0.146 g, 82%) was obtained as a yellow oil after purification on silica gel with chloroform–methanol (50:1, v/v); IR (film): ν = 3339, 3140, 2982, 2935, 1222, 1048, 965, 838 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.83 (s, 1H); 7.61 (s, 1H); 7.49 (s, 1H); 7.20 (s, 1H); 5.36 (s, 2H, CH$_2$); 4.53–4.47 (m, 1H, PCCCH_aH$_b$); 4.42–4.28 (m, 2H, PCC*H*CH$_a$$H_b$); 4.15–4.05 (m, 4H, 2× POC*H*$_2$CH$_3$); 3.63 (brs, 1H, OH); 2.34 (s, 3H, CH$_3$); 2.33 (s, 3H, CH$_3$); 2.04–1.75 (m, 2H, PC*H*$_2$); 1.30 (t, J = 7.0 Hz, 3H, POCH$_2$CH_3); 1.28 (t, J = 7.0 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, CDCl$_3$): δ = 142.5; 141.9; 141.5; 132.7; 131.9; 131.6; 124.3; 119.8; 110.2; 65.3 (d, J = 3.4 Hz, PCC); 62.4 (d, J = 6.3 Hz, POC); 62.3 (d, J = 6.3 Hz, POC); 56.3 (d, J = 16.0 Hz, PCCC); 40.5; 31.1 (d, J = 139.8 Hz, PC); 20.7; 20.4; 16.6 (d, J = 6.3 Hz, POCC); 16.5 (d, J = 6.3 Hz, POCC); ^{31}P NMR (121.5 MHz, CDCl$_3$): δ = 28.53 ppm. Anal. Calcd. for $C_{19}H_{28}N_5O_4P$: C, 54.15; H, 6.70; N, 16.62. Found: C, 53.98; H, 6.64; N, 16.56.

4.1.5.50. Diethyl 3-{4-[(3-acetylindol-1-yl)methyl]-1H-1,2,3-triazol-1-yl}-2-hydroxypropylphosphonate ***25k***. From azide **17** (0.105 g, 0.443 mmol) and 3-acetyl-*N*-propargylindole **19k** (0.087 g, 0.443 mmol) the phosphonate **25k** (0.186 g, 97%) was obtained as a colourless oil after purification on silica gel with chloroform–methanol (50:1, v/v); IR (film): ν = 3352, 2984, 2924, 1799, 1528, 1391, 1025 cm^{-1}; ^{1}H NMR (600 MHz, CDCl$_3$): δ = 8.40–8.34 (m, 1H); 7.88 (s, 1H, *H*C5′); 7.65 (s, 1H); 7.47–7.41 (m, 1H); 7.33–7.28 (m, 2H); 5.46 (s, 2H, CH$_2$); 4.54–4.47 (m, 1H, PCCCH_aH$_b$); 4.40–4.32 (m, 2H, PCC*H*CH$_a$$H_b$); 4.17–4.01 (m, 4H, 2× POCH_2CH$_3$); 2.49 (s, 3H, CH$_3$); 1.97 (ddd, J = 19.3 Hz, J = 15.2 Hz, J = 3.2 Hz, 1H, PCH_aH$_b$); 1.77 (ddd, J = 16.6 Hz, J = 15.2 Hz, J = 9.0 Hz, 1H, PCH$_a$$H_b$); 1.32 (t, J = 6.9 Hz, 3H, POCH$_2$CH_3); 1.30 (t, J = 6.9 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, CDCl$_3$): δ = 193.2 (s, C=O); 142.6; 136.5; 135.0; 126.3; 124.1; 123.5; 122.7; 122.6; 117.4; 109.9; 65.4 (d, J = 3.7 Hz, PCC); 62.4 (d, J = 6.4 Hz, POC); 62.3 (d, J = 6.4 Hz, POC); 56.1 (d, J = 17.2 Hz, PCCC); 42.4; 30.8 (d, J = 140.0 Hz, PC); 27.7 (s, CH$_3$); 16.6 (d, J = 6.0 Hz, POCC); 16.5 (d, J = 6.0 Hz, POCC); ^{31}P NMR (243 MHz, CDCl$_3$): δ = 28.12 ppm. Anal. Calcd. for $C_{20}H_{27}N_4O_5P$: C, 55.29; H, 6.26; N, 12.90. Found: C, 55.04; H, 6.14; N, 13.06.

4.1.5.51. Diethyl 2-hydroxy-3-{4-[(2-oxopyridin-1-yl)methyl]-1H-1,2,3-triazol-1-yl}propylphosphonate ***25l***. From azide **17** (0.151 g, 0.637 mmol) and *N*-propargyl-2-pyridon **19l** (0.085 g, 0.637 mmol) the phosphonate **25l** (0.218 g, 92%) was obtained as a brown oil after purification on silica gel with chloroform–methanol (50:1, v/v); IR (film): ν = 3307, 2988, 2909, 1658, 1226; 1048, 776 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.95 (s, 1H); 7.60 (dd, J = 6.6 Hz, J = 3.0 Hz, 1H); 7.33 (ddd, J = 9.3 Hz, J = 6.3 Hz, J = 1.8 Hz, 1H); 6.53 (d, J = 9.0 Hz, 1H); 6.20 (dt, J = 6.6 Hz, J = 0.9 Hz, 1H); 5.18 (AB, J = 14.4 Hz, 1H, CH_aH$_b$); 5.16 (AB, J = 14.4 Hz, 1H, CH$_a$$H_b$); 4.53 (dd, J = 15.6 Hz, J = 6.6 Hz, 1H, PCCCH_aH$_b$); 4.56–4.34 (m, 2H, PCC*H*CH$_a$$H_b$); 4.18–4.03 (m, 4H, 2× POCH_2CH$_3$); 2.95 (brs, 1H, OH); 2.07–1.80 (m, 2H, PCH$_2$); 1.33 (t, J = 6.9 Hz, 3H, POCH$_2$CH_3); 1.32 (t, J = 6.9 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, CDCl$_3$): δ = 162.2 (s, C=O); 141.8 (s, H*C*=C); 140.1; 137.8; 125.4 (s, HC=*C*); 120.2; 106.7; 65.2 (d, J = 2.6 Hz, PCC); 62.2 (d, J = 6.6 Hz, POC); 61.9 (d, J = 6.6 Hz, POC); 55.9 (d, J = 14.9 Hz, PCCC); 44.4; 31.0 (d, J = 139.7 Hz, PC); 16.3 (d, J = 6.0 Hz, POCC); ^{31}P NMR (121.5 MHz, CDCl$_3$): δ = 29.28 ppm. Anal. Calcd. for $C_{15}H_{23}N_4O_5P$: C, 48.65; H, 6.26; N, 15.13. Found: C, 48.88; H, 6.34; N, 15.00.

4.1.5.52. Diethyl 1-hydroxy-3-(4-{[5-methyl-2,4-dioxopyrimidin-1(2H)-yl]methyl}-1H-1,2,3-triazol-1-yl)propylphosphonate ***26b***. From azide **18** (0.105 g, 0.443 mmol) and N^1-propargylthymine **19b** (0.073 g, 0.443 mmol) the phosphonate **26b** (0.150 g, 84%) was obtained as a white powder after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); m.p.: 169–171 °C; IR (KBr): ν = 3410, 2989, 2938, 1682, 1225, 1022 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ = 9.89 (brs, 1H, NH); 7.87 (s, 1H, *H*C5′); 7.37 (d, J = 1.0 Hz, 1H, *H*C=CH); 4.95 (AB, J = 14.9 Hz, 1H, CH_aH$_b$); 4.92 (AB, J = 14.9 Hz, 1H, CH$_a$$H_b$); 4.63–4.55 (m, 2H, PCCCH_2); 4.23–4.09 (m, 4H, 2× POCH_2CH$_3$); 3.80 (ddd, J = 10.7 Hz, J = 6.3 Hz, J = 3.3 Hz, 1H, PC*H*(OH)); 2.40–2.17 (m, 3H, PCCH_2, OH); 1.91 (d, J = 1.0 Hz, 3H, CH$_3$); 1.33 (t, J = 6.9 Hz, 3H, POCH$_2$CH_3); 1.30 (t, J = 6.9 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, CD$_3$OD): δ = 166.7 (s, C=O); 152.6 (s, C=O); 142.6; 125.5; 111.6; 65.1 (d, J = 167.8 Hz, PC); 64.4 (d, J = 7.5 Hz, POC); 64.2 (d, J = 7.5 Hz, POC); 47.7 (d, J = 16.1 Hz, PCCC); 43.9; 33.2 (d, J = 4.0 Hz, PCC); 17.0 (d, J = 4.9 Hz, POCC); 16.9 (d, J = 4.9 Hz, POCC); 12.5; ^{31}P NMR (121.5 MHz, CDCl$_3$): δ = 24.76 ppm.

Anal. Calcd. for $C_{15}H_{24}N_5O_6P$: C, 44.89; H, 6.03; N, 17.45. Found: C, 44.90; H, 6.16; N, 17.50.

4.1.5.53. Diethyl 3-(4-{[2,4-dioxopyrimidin-1-yl]methyl}-1H-1,2,3-triazol-1-yl)-1-hydroxypropylphosphonate ***26c***. From azide **18** (0.108 g, 0.455 mmol) and N^1-propargyluracil **19c** (0.068 g, 0.455 mmol) the phosphonate **26c** (0.143 g, 81%) was obtained as a white solid after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); m.p.: 136–138 °C; IR (KBr): ν = 3405, 2984, 2932, 1680, 1227, 1025 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 10.49 (brs, 1H, NH); 7.90 (s, 1H, *H*C5′); 7.59 (d, J = 7.9 Hz, 1H, *H*C═CH); 5.72 (d, J = 7.9 Hz, 1H, HC═C*H*); 5.01 (AB, J = 15.5 Hz, 1H, CH_aH_b); 4.97 (AB, J = 15.5 Hz, 1H, CH_aH_b); 4.61 (brt, J = 6.4 Hz, 2H, PCCCH_2); 4.23–4.10 (m, 4H, 2× POCH_2CH$_3$); 3.86–3.74 (m, 1H, PC*H*(OH)); 2.44–2.17 (m, 2H, PCCH_2); 1.32 (t, J = 7.0 Hz, 3H, POCH$_2$CH_3); 1.30 (t, J = 7.0 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 164.5 (s, C═O); 151.4 (s, C═O); 144.9; 141.7; 124.9; 102.6; 64.0 (d, J = 166.0 Hz, PC); 63.3 (d, J = 7.0 Hz, POC); 63.1 (d, J = 7.0 Hz, POC); 46.7 (d, J = 17.2 Hz, PCC*C*); 43.3; 31.9; 16.6 (d, J = 5.4 Hz, POCC); 16.5 (d, J = 5.4 Hz, POCC); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 24.84 ppm. Anal. Calcd. for $C_{14}H_{22}N_5O_6P$: C, 43.41; H, 5.73; N, 18.08. Found: C, 43.57; H, 5.61; N, 17.89.

4.1.5.54. Diethyl 3-(4-{[N^4-acetylamino-2-oxopyrimidin-1-yl]methyl}-1H-1,2,3-triazol-1-yl)-1-hydroxypropylphosphonate ***26d***. From azide **18** (0.130 g, 0.548 mmol) and N^4-acetyl-N^1-propargylcytosine **19d** (0.105 g, 0.548 mmol) the phosphonate **26d** (0.186 g, 79%) was obtained as a white powder after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); m.p.: 175–177 °C; IR (KBr): ν = 3406, 3124, 2930, 2873, 1706, 1654, 1221, 1021 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 10.96 (brs, 1H, NH); 8.71 (s, 1H, *H*C5′); 7.93 (d, J = 7.4 Hz, 1H, *H*C═CH); 7.44 (d, J = 7.4 Hz, 1H, *H*C═CH); 5.32 (d, J = 14.6 Hz, 1H, CH_aH_b); 5.05 (d, J = 14.6 Hz, 1H, CH_aH_b); 4.91–4.83 (m, 1H, PCCCH_aH_b); 4.75–4.65 (m, 1H, PCCCH$_a$H$_b$); 4.25–4.14 (m, 2H, POCH_2CH$_3$); 4.13–4.03 (m, 2H, POCH_2CH$_3$); 3.87–3.81 (m, 1H, PC*H*(OH)); 2.32–2.24 (m, 3H, PCCH_2, OH); 2.24 (s, 3H, CH$_3$); 1.35 (t, J = 7.1 Hz, 3H, POCH$_2$CH_3); 1.27 (t, J = 7.1 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, CD_3OD): δ = 172.8; 164.4; 158.2; 150.7; 143.2; 125.9; 98.4; 65.0 (d, J = 168.0 Hz, PC); 64.4 (d, J = 7.5 Hz Hz, POC); 64.1 (d, J = 7.5 Hz, POC); 47.7 (d, J = 16.3 Hz, PCC*C*); 46.4; 33.2 (s, PC*C*); 24.7; 16.9 (d, J = 4.9 Hz, POCC); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 25.96 ppm. Anal. Calcd. for $C_{16}H_{25}N_6O_6P$: C, 44.86; H, 5.88; N, 19.62. Found: C, 45.10; H, 6.00; N, 19.74.

4.1.5.55. Diethyl 3-(4-{[3-benzoyl-2,4-dioxopyrimidin-1-yl]methyl}-1H-1,2,3-triazol-1-yl)-1-hydroxyethylphosphonate ***26e***. From azide **18** (0.102 g, 0.430 mmol) and N^3-benzoyl-N^1-propargylquinazoline-2,4-dione **19e** (0.131 g, 0.430 mmol) the phosphonate **26e** (0.213 g, 91%) was obtained as a white powder after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); m.p.: 82–84 °C; IR (KBr): ν = 3299, 2988, 1746, 1702, 1664, 1233, 1027, 757, 674 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.20 (dd, J = 7.9 Hz, J = 1.6 Hz, 1H); 7.99–7.95 (m, 2H, 2× *o*-CH); 7.93 (brd, J = 8.5 Hz, 1H); 7.78 (ddd, J = 8.5 Hz, J = 7.9 Hz, J = 1.6 Hz, 1H); 7.74 (s, 1H, *H*C5′); 7.70–7.64 (m, 1H, *p*-CH); 7.54–7.46 (m, 2H, 2× *m*-CH); 7.29 (dt, J = 7.9 Hz, J = 0.8 Hz, 1H); 5.42 (AB, J = 15.7 Hz, 1H, CH_aH_b); 5.36 (AB, J = 15.7 Hz, 1H, CH_aH_b); 4.66–4.54 (m, 2H, PCCCH_2); 4.18–4.04 (m, 4H, 2× POCH_2CH$_3$); 3.78 (ddd, J = 10.7 Hz, J = 6.2 Hz, J = 3.4 Hz, 1H, PC*H*(OH)); 2.38–2.10 (m, 2H, PCCH_2); 1.30 (t, J = 7.0 Hz, 3H, POCH$_2$CH_3); 1.28 (t, J = 7.0 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 168.7 (s, C═O); 161.1 (s, C═O); 149.6 (s, C═O); 142.3 (s, HC═C); 140.3; 136.3; 135.2; 131.6; 130.7; 129.3; 128.9; 124.4 (s, HC═*C*); 123.9; 115.6; 115.4; 64.4 (d, J = 166.4 Hz, PC); 63.3 (d, J = 6.8 Hz, POC); 63.0 (d, J = 6.8 Hz, POC); 48.6 (d, J = 16.1 Hz, PCC*C*); 39.0; 31.9, 16.7 (d, J = 5.2 Hz, POC*C*); 16.6 (d, J = 5.2 Hz, POC*C*); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 24.57 ppm. Anal. Calcd. for $C_{25}H_{28}N_5O_7P$: C, 55.45; H, 5.21; N, 12.93. Found: C, 55.60; H, 5.34; N, 13.09.

4.1.5.56. Diethyl 1-hydroxy-3-{4-[(3,5-dioxo-1,2,4-triazin-2-yl)methyl]-1H-1,2,3-triazol-1-yl}-1-hydroxypropylphosphonate ***26f***. From azide **18** (0.131 g, 0.552 mmol) and N^1-propargyl-6-azauracil **19f** (0.083 g, 0.552 mmol) the phosphonate **26f** (0.193 g, 90%) was obtained as a yellow solid after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); m.p.: 116–118 °C; IR (KBr): ν = 3284, 3152, 2988, 2912, 1731, 1658, 1050 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 12.1 (s, 1H, NH); 7.85 (s, 1H); 7.40 (s, 1H); 5.17 (s, 1H, CH_2); 4.60–4.51 (m, 2H, PCCCH_2); 4.21–4.09 (m, 4H, 2× POCH_2CH$_3$); 3.87 (ddd, J = 10.1 Hz, J = 6.1 Hz, J = 2.9 Hz, 1H, PC*H*(OH)); 2.41–2.16 (m, 3H, PCCH_2, OH); 1.31 (t, J = 7.0 Hz, 3H, POCH$_2$CH_3); 1.29 (t, J = 7.0 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 155.9 (s, C═O); 149.4 (C═O); 141.4 (s, HC═C); 135.0 (s, HC═N); 124.8 (s, HC═*C*); 64.1 (d, J = 166.3 Hz, PC); 63.3 (d, J = 7.2 Hz, POC); 63.2 (d, J = 7.2 Hz, POC); 46.6 (d, J = 17.2 Hz, PCCC); 34.7; 31.9; 16.6 (d, J = 5.6 Hz, POCC); 16.5 (d, J = 5.6 Hz, POCC); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 25.12 ppm. Anal. Calcd. for $C_{13}H_{21}N_6O_6P$: C, 40.21; H, 5.45; N, 21.64. Found: C, 40.05; H, 5.61; N, 21.77.

4.1.5.57. Diethyl 3-{4-[(8-chloro-1,3-dimethyl-2,6-dioxopurin-7-yl)methyl]-1H-1,2,3-triazol-1-yl}-1-hydroxypropylphosphonate ***26g***. From azide **18** (0.109 g, 0.460 mmol) and 8-chloro-N^7-propargyltheophylline **19g** (0.116 g, 0.460 mmol) the phosphonate **26g** (0.187 g, 83%) was obtained as a white powder after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); m.p.: 164–165 °C; IR (KBr): ν = 3300, 2993, 1706, 1663, 1217, 1027 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.84 (s, 1H); 5.64 (AB, J = 14.8 Hz, 1H, CH_aH_b); 5.61 (AB, J = 14.8 Hz, 1H, CH_aH_b); 4.60–4.50 (m, 2H, PCCCH_2); 4.21–4.09 (m, 4H, 2× POCH_2CH$_3$); 3.80 (ddd, J = 10.7 Hz, J = 6.3 Hz, J = 3.4 Hz, 1H, PC*H*(OH)); 3.54 (s, 3H, CH$_3$); 3.40 (s, 3H, CH$_3$); 3.25 (brs, 1H, OH); 2.37–2.20 (m, 2H, PCCH$_2$); 1.33 (t, J = 6.9 Hz, 3H, POCH$_2$CH_3); 1.31 (t, J = 6.9 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 154.3 (s, C═O); 151.0 (s, C═O); 147.2; 141.4; 138.9; 124.1; 107.3; 64.1 (d, J = 165.7 Hz, PC); 63.1 (d, J = 7.1 Hz, POC); 62.9 (d, J = 7.1 Hz, POC); 46.6 (d, J = 15.8 Hz, PCCC); 41.0; 31.9 (d, J = 2.6 Hz, PC*C*); 29.9; 28.1; 16.6 (d, J = 5.2 Hz, POCC); 16.5 (d, J = 5.2 Hz, POC*C*); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 24.61 ppm. Anal. Calcd. for $C_{17}H_{25}ClN_7O_6P$: C, 41.68; H, 5.14; N, 20.02. Found: C, 41.79; H, 5.08; N, 20.10.

4.1.5.58. Diethyl 3-{4-[(3,7-dimethyl-2,6-dioxopurin-1-yl)methyl]-1H-1,2,3-triazol-1-yl}-1-hydroxypropylphosphonate ***26h***. From azide **18** (0.110 g, 0.464 mmol) and N^1-propargyltheobromine **19h** (0.101 g, 0.464 mmol) the phosphonate **26h** (0.167 g, 79%) was obtained as a white powder after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); m.p.: 129–130 °C; IR (KBr): ν = 3288, 2984, 1707, 1661, 1233, 1049 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.69 (s, 1H); 7.54 (s, 1H); 5.33 (AB, J = 14.5 Hz, 1H, CH_aH_b); 5.28 (AB, J = 14.5 Hz, 1H, CH_aH_b); 4.65–4.45 (m, 2H, PCCCH_2); 4.21–4.09 (m, 4H, 2× POCH_2CH$_3$); 4.00 (s, 3H, CH$_3$); 3.85–3.76 (m, 1H, PC*H*(OH)); 3.57 (s, 3H, CH$_3$); 2.33–2.16 (m, 3H, PCH$_2$, OH); 1.32 (t, J = 6.4 Hz, 3H, POCH$_2$CH_3); 1.31 (t, J = 6.4 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 154.5 (s, C═O); 151.0 (s, C═O); 148.6; 143.2; 141.8; 123.7; 107.4; 64.4 (d, J = 166.3 Hz, PC); 62.8 (d, J = 7.2 Hz, POC); 62.7 (d, J = 7.2 Hz, POC); 46.3 (d, J = 16.0 Hz, PCCC); 35.9; 33.6; 31.9; 29.7; 16.4 (d, J = 5.5 Hz, POCC); 16.2 (d, J = 5.5 Hz, POC*C*); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 24.85 ppm. Anal. Calcd. for $C_{17}H_{26}N_7O_6P$: C, 44.84; H, 5.75; N, 21.53. Found: C, 44.62; H, 5.66; N, 21.46.

*4.1.5.59. Diethyl 3-{4-[(1,3-dimethyl-2,6-dioxopurin-7-yl)methyl]-1H-1,2,3-triazol-1-yl}-1-hydroxypropylphosphonate **26i**.* From azide **18** (0.111 g, 0.468 mmol) and N^7-propargyltheophylline **19i** (0.102 g, 0.468 mmol) the phosphonate **26i** (0.183 g, 86%) was obtained as a white powder after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); m.p.: 123–125 °C; IR (KBr): ν = 3365, 2991, 1704, 1658, 1222, 1050 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.89 (s, 1H); 7.87 (s, 1H); 5.62 (AB, J = 14.9 Hz, 1H, CH_aH_b); 5.59 (AB, J = 14.9 Hz, 1H, CH_aH_b); 4.63–4.55 (m, 2H, PCCCH_2); 4.22–4.09 (m, 4H, 2× POCH_2CH$_3$); 3.80 (ddd, J = 10.9 Hz, J = 6.2 Hz, J = 3.3 Hz, 1H, PCH(OH)); 3.59 (s, 3H, CH_3); 3.43 (s, 3H, CH_3); 2.37 (ddddd, J = 14.4 Hz, J = 8.0 Hz, J = 8.0 Hz, J = 6.1 Hz, J = 3.3 Hz, 1H, PCCH_aH_b); 2.26 (ddddd, J = 14.4 Hz, J = 10.9 Hz, J = 6.4 Hz, J = 5.6 Hz, J = 5.6 Hz, 1H, PCCH_aH_b); 1.35 (t, J = 6.9 Hz, 3H, POCH$_2$CH_3); 1.33 (t, J = 6.9 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 155.2 (s, C=O); 151.4 (s, C=O); 148.7; 141.9; 141.6; 124.3; 106.3; 64.0 (d, J = 166.1 Hz, PC); 63.1 (d, J = 7.1 Hz, POC); 62.9 (d, J = 7.1 Hz, POC); 46.6 (d, J = 15.8 Hz, PCCC); 41.3; 31.9 (d, J = 2.8 Hz, PCC); 29.9; 28.1; 16.6 (d, J = 5.4 Hz, POCC); 16.5 (d, J = 5.4 Hz, POCC); ^{31}P NMR (243 MHz, $CDCl_3$): δ = 23.44 ppm. Anal. Calcd. for $C_{17}H_{26}N_7O_6P$: C, 44.84; H, 5.75; N, 21.53. Found: C, 45.00; H, 5.90; N, 21.40.

*4.1.5.60. Diethyl 3-{4-[(5,6-dimethylbenzoimidazol-1-yl)methyl]-1H-1,2,3-triazol-1-yl}-1-hydroxypropylphosphonate **26j**.* From azide **18** (0.103 g, 0.434 mmol) and 5,6-dimethyl-N^1-propargylbenzimidazole **19j** (0.080 g, 0.434 mmol) the phosphonate **26j** (0.146 g, 80%) was obtained as a yellow oil after purification on silica gel with chloroform–methanol (50:1, v/v); IR (film): ν = 3339, 3140, 2982, 2935, 1222, 1048, 965, 838 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.08 (s, 1H); 7.56 (s, 1H); 7.53 (s, 1H); 7.25 (s, 1H); 5.45 (s, 2H, CH_2); 4.64–4.54 (m, 2H, PCCCH_2); 4.18–4.05 (m, 4H, 2× POCH_2CH$_3$); 3.75 (ddd, J = 10.5 Hz, J = 6.5 Hz, J = 3.2 Hz, 1H, PCH(OH)); 3.40 (brs, 1H, OH); 2.37 (s, 3H, CH_3); 2.35 (s, 3H, CH_3); 2.34–2.14 (m, 2H, PCCH_2); 1.29 (t, J = 7.0 Hz, 3H, POCH$_2$CH_3); 1.26 (t, J = 7.0 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 142.7; 142.0; 141.4; 132.6; 131.8; 131.6; 123.1; 119.7; 110.2; 64.0 (d, J = 151.2 Hz, PC); 62.8 (d, J = 7.1 Hz, POC); 62.8 (d, J = 7.1 Hz, POC); 46.7 (d, J = 15.7 Hz, PCCC); 40.5; 32.0; 20.7; 20.4; 16.6 (d, J = 6.3 Hz, POCC); 16.6 (d, J = 6.3 Hz, POCC); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 24.71 ppm. Anal. Calcd. for $C_{19}H_{28}N_5O_4P$: C, 54.15; H, 6.20; N, 16.62. Found: C, 54.00; H, 6.89; N, 16.70.

*4.1.5.61. Diethyl 3-{4-[(3-acetylindol-1-yl)methyl]-1H-1,2,3-triazol-1-yl}-1-hydroxypropylphosphonate **26k**.* From azide **18** (0.107 g, 0.451 mmol) and 3-acetyl-*N*-propargylindole **19k** (0.089 g, 0.451 mmol) the phosphonate **26k** (0.182 g, 93%) was obtained as a colourless oil after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); IR (film): ν = 3330, 3140, 2984, 1799, 1527, 1389, 1223, 1022 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.38–8.33 (m, 1H); 7.86 (s, 1H, *H*C5′); 7.47 (s, 1H); 7.43–7.38 (m, 1H); 7.31–7.25 (m, 2H); 5.41 (s, 2H, CH_2); 4.60–4.45 (m, 2H, PCCCH_2); 4.16–4.03 (m, 4H, 2× POCH_2CH$_3$); 3.72 (ddd, J = 10.8 Hz, J = 6.4 Hz, J = 3.5 Hz, 1H, PCH(OH)); 2.49 (s, 3H, CH_3); 2.36–2.11 (m, 2H, PCCH_2); 1.29 (t, J = 7.0 Hz, 3H, POCH$_2$CH_3); 1.26 (t, J = 7.0 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 193.3 (s, C=O); 142.8; 136.5; 135.0; 126.4; 123.6; 123.0; 122.8; 122.7; 117.5; 109.9; 64.2 (d, J = 165.9 Hz, PC); 63.2 (d, J = 6.3 Hz, POC); 62.9 (d, J = 6.3 Hz, POC); 46.7 (d, J = 15.6 Hz, PCCC); 42.4; 31.9 (d, J = 2.9 Hz, PCC); 27.8 (s, CH_3); 16.7 (d, J = 6.0 Hz, POCC); 16.6 (d, J = 6.0 Hz, POCC); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 24.60 ppm. Anal. Calcd. for $C_{20}H_{27}N_4O_5P$: C, 55.29; H, 6.26; N, 12.90. Found: C, 55.40; H, 6.10; N, 13.03.

*4.1.5.62. Diethyl 1-hydroxy-3-{4-[(2-oxopyridin-1-yl)methyl]-1H-1,2,3-triazol-1-yl}propylphosphonate **26l**.* From azide **18** (0.131 g, 0.552 mmol) and *N*-propargyl-2-pyridon **19l** (0.074 g, 0.552 mmol) the phosphonate **26l** (0.168 g, 82%) was obtained as a brown oil after chromatography on a silica gel column with chloroform–methanol (50:1, v/v); IR (film): ν = 3401, 2986, 2912, 1656, 1224; 1025 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.90 (s, 1H, *H*C5′); 7.63 (ddd, J = 6.8 Hz, J = 2.0 Hz, J = 0.6 Hz, 1H); 7.34 (ddd, J = 9.1 Hz, J = 6.8 Hz, J = 2.0 Hz, 1H); 6.55 (ddd, J = 9.1 Hz, J = 1.3 Hz, J = 0.6 Hz, 1H); 6.21 (dt, J = 6.8 Hz, J = 1.3 Hz, 1H); 5.22 (AB, J = 14.3 Hz, 1H, CH_aH_b); 5.16 (AB, J = 14.3 Hz, 1H, CH_aH_b); 4.86 (s, brs, 1H, OH); 4.60–4.45 (m, 2H, PCCCH_2); 4.22–4.09 (m, 4H, 2× POCH_2CH$_3$); 3.79 (ddd, J = 10.8 Hz, J = 6.2 Hz, J = 3.2 Hz, 1H, PCH(OH)); 2.41–2.16 (m, 2H, PCCH_2); 1.33 (t, J = 6.9 Hz, 3H, POCH$_2$CH_3); 1.30 (t, J = 6.9 Hz, 3H, POCH$_2$CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 162.4 (s, C=O); 142.3 (s, *H*C=C); 140.3; 137.9; 124.9 (s, HC=*C*); 120.6; 106.9; 64.0 (d, J = 165.8 Hz, PC); 63.1 (d, J = 7.1 Hz, POC); 62.9 (d, J = 7.1 Hz, POC); 46.6 (d, J = 16.0 Hz, PCCC); 44.8; 31.9 (d, J = 3.1 Hz, PCC); 16.7 (d, J = 5.2 Hz, POCC); 16.6 (d, J = 5.2 Hz, POCC); ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 24.85 ppm. Anal. Calcd. for $C_{15}H_{23}N_4O_5P$: C, 48.65; H, 6.26; N, 15.13. Found: C, 48.76; H, 6.12; N, 15.03.

4.1.6. General procedure for the synthesis of phosphonic acids

Solutions of diethyl phosphonates **22e**, **22g**, **22j**, **22m**, **23a–c** or **24i** (1.00 mmol) in CH_2Cl_2 (3 mL) were treated with bromotrimethylsilane (10.0 mmol) at room temperature under argon atmosphere. The reaction mixture was protected from light and stirred at room temperature for 24 h. After concentration to dryness the residue was co-evaporated with dichloromethane (5 mL) and ethanol (3 × 3 mL) to afford crude phosphonic acids **31e**, **31g**, **31j**, **31m**, **32a–c** or **33i** which was purified by crystallisation from methanol–diethyl ether mixtures.

*4.1.6.1. 3-(4-{[3-Benzoyl-2,4-dioxopyrimidin-1-yl]methyl}-1H-1,2,3-triazol-1-yl)propylphosphonic acid **31e**.* From **22e** (0.165 g, 0.314 mmol) phosphonic acid **31e** (0.118 g, 80%) was obtained as a white powder; m.p.: 130–133 °C; IR (KBr): ν = 3341, 3014, 2939, 1746, 1699, 1662; 1478; 1240, 987; 756; 674 cm^{-1}; ^{1}H NMR (300 MHz, CD_3OD): δ = 8.16 (dd, J = 7.9 Hz, J = 1.6 Hz, 1H); 8.07 (s, 1H, *H*C5′); 8.06–8.03 (m, 2H, 2× *o*-CH); 7.82 (ddd, J = 8.6 Hz, J = 7.9 Hz, J = 1.6 Hz, 1H); 7.77–7.68 (m, 2H, *p*-CH, H8); 7.60–7.54 (m, 2H, 2× *m*-CH); 7.32 (dt, J = 7.9 Hz, J = 0.9 Hz, 1H); 5.49 (s, 2H, CH_2); 4.49 (t, J = 7.0 Hz, 2H, PCCCH_2); 2.29–2.10 (m, 2H, PCCH_2); 1.73–1.67 (m, 2H, PCH_2); ^{13}C NMR (151 MHz, CD_3OD): δ = 168.6 (s, C=O); 161.4 (s, C=O); 149.6 (s, C=O); 141.2 (s, HC=C); 140.2; 136.2; 135.1; 131.6; 130.3; 129.1; 128.2; 125.3 (s, HC=*C*); 123.7; 115.5; 114.9; 51.2 (d, J = 17.8 Hz, PCCC); 37.7; 23.4 (d, J = 3.7 Hz, PCC); 23.4 (d, J = 140.7 Hz, PC); ^{31}P NMR (121 MHz, CD_3OD): δ = 29.05 ppm. Anal. Calcd. for $C_{21}H_{20}N_5O_6P \times H_2O$: C, 51.75; H, 4.55; N, 14.37. Found: C, 51.55; H, 4.32; N, 14.83.

*4.1.6.2. 3-{4-[(8-Chloro-1,3-dimethyl-2,6-dioxopurin-7-yl)methyl]-1H-1,2,3-triazol-1-yl}propylphosphonic acid **31g**.* From **22g** (0.088 g, 0.180 mmol) phosphonic acid **31g** (0.061 g, 79%) was obtained as a white powder; m.p.: 216–220 °C; solubility of **31g** in methanol or water was insufficient to measure the ^{13}C NMR spectrum; IR (KBr): ν = 3124, 2998, 2978, 1608, 1463, 1220, 1028, 968 cm^{-1}; ^{1}H NMR (600 MHz, CD_3OD): δ = 8.09 (s, 1H); 5.70 (s, 2H, CH_2); 4.51 (t, J = 7.0 Hz, 2H, PCCCH_2); 3.37 (s, 3H, CH_3); 3.34 (s, 3H, CH_3); 2.17 (dqv, J = 14.0 Hz, J = 7.0 Hz, 2H, PCCH_2); 1.70 (dt, J = 19.2 Hz, J = 7.0 Hz, 2H, PCH_2); ^{31}P NMR (243 MHz, CD_3OD): δ = 27.81 ppm. Anal. Calcd. for $C_{13}H_{17}ClN_5O_5P \times H_2O$: C, 35.83; H, 4.39; N, 22.50. Found: C, 35.60; H, 4.32; N, 22.33.

*4.1.6.3. 3-{4-[(5,6-Dimethyl-benzimidazol-1-yl)methyl]-1H-1,2,3-triazol-1-yl}propylphosphonic acid **31j**.* From **22j** (0.065 g, 0.160 mmol) phosphonic acid **31j** (0.046 g, 83%) was obtained as a

white powder; m.p.: 148–151 °C; IR (KBr): ν = 3100, 2999, 2948, 2889, 1244, 1040, 965 cm^{-1}; ^1H NMR (600 MHz, CD_3OD): δ = 9.44 (s, 1H); 8.31 (s, 1H); 7.78 (s, 1H); 7.63 (s, 1H); 5.86 (s, 2H, CH_2); 4.55 (t, J = 7.0 Hz, 2H, PCCCH_2); 2.50 (s, 3H, CH_3); 2.47 (s, 3H, CH_3); 2.22 (dqv, J = 14.3 Hz, J = 7.0 Hz, 2H, PCCH_2); 1.70 (dt, J = 18.7 Hz, J = 7.0 Hz, 2H, PCH_2); ^{13}C NMR (151 MHz, CD_3OD): δ = 140.1; 139.6; 137.4; 137.1; 129.5; 129.4; 125.1; 114.0; 112.7; 50.4 (d, J = 18.1 Hz, PCC*C*); 41.6; 23.6 (d, J = 4.0 Hz, PC*C*); 23.5 (d, J = 139.2 Hz, P*C*); 19.3; 19.1; ^{31}P NMR (243 MHz, CD_3OD): δ = 28.08 ppm. Anal. Calcd. for $C_{15}H_{20}N_5O_3P$: C, 51.57; H, 5.77; N, 20.05. Found: C, 51.80; H, 5.52; N, 19.92.

4.1.6.4. 3-(4-{[3-Benzoyl-2,4-dioxopyrimidin-1-yl]methyl}-1H-1,2,3-triazol-1-yl)propylphosphonic acid ***31m****.* From **22m** (0.130 g, 0.274 mmol) phosphonic acid **31m** (0.093 g, 81%) was obtained as a colourless oil; IR (film): ν = 3396, 3010, 2983, 2967, 1665, 1654, 1436; 1237, 978, 782, 701 cm^{-1}; ^1H NMR (300 MHz, CD_3OD): δ = 8.30 (s, 1H, *H*C5′); 7.98–7.94 (m, 2H, H_{aromat}); 7.91 (d, J = 8.0 Hz, 1H, *H*C═CH); 7.75–7.69 (m, 1H, H_{aromat}); 7.58–7.52 (m, 2H, H_{aromat}); 5.86 (d, J = 8.0 Hz, 1H, HC═C*H*); 5.15 (s, 2H, CH_2); 4.60 (t, J = 7.1 Hz, 2H, PCCCH_2); 2.29–2.18 (m, 2H, PCCH_2); 1.83–1.71 (m, 2H, PCH_2); ^{13}C NMR (75.5 MHz, CD_3OD): δ = 168.9 (s, C═O); 163.1 (s, C═O); 150.0 (s, C═O); 145.8; 140.4; 135.2; 131.4; 130.2; 129.2; 129.1; 128.3; 126.3; 101.6; 101.6; 51.5 (d, J = 17.9 Hz, PCC*C*); 42.4; 23.3 (s, J = 1.4 Hz, PC*C*); 23.4 (d, J = 146.8 Hz, P*C*); ^{31}P NMR (121 MHz, CD_3OD): δ = 29.63 ppm. Anal. Calcd. for $C_{15}H_{18}N_5O_6P \times H_2O$: C, 46.69; H, 4.61; N, 16.01. Found: C, 46.74; H, 4.70; N, 15.94.

4.1.6.5. 4-(4-{[6-Aminopurin-9-yl]methyl}-1H-1,2,3-triazol-1-yl) butylphosphonic acid ***32a****.* From **23a** (0.063 g, 0.154 mmol) phosphonic acid **32a** (0.050 g, 93%) was obtained as a white powder; m.p: 217–220 °C; solubility of **32a** in methanol or water was insufficient to measure the ^{13}C NMR spectrum; IR (KBr): ν = 3460, 3300, 3100, 2981, 2910, 2880, 1660, 1647, 1240, 1023 cm^{-1}; ^1H NMR (600 MHz, CD_3OD): δ = 8.45 (s, 1H); 8.42 (s, 1H); 8.15 (s, 1H); 5.65 (s, 2H, CH_2); 4.46 (t, J = 7.0 Hz, 2H, PCCCCH_2); 2.03 (qv, J = 7.0 Hz, 2H, PCCCH_2); 1.77–1.72 (m, 2H, PCH_2); 1.64–1.57 (m, 2H, PCCH_2); ^{31}P NMR (243 MHz, CD_3OD): δ = 29.02 ppm. Anal. Calcd. for $C_{12}H_{17}N_8O_3P \times H_2O$: C, 38.92; H, 5.17; N, 30.26. Found: C, 39.09; H, 4.99; N, 30.49.

4.1.6.6. 4-(4-{[6-Aminopurin-9-yl]methyl}-1H-1,2,3-triazol-1-yl) butylphosphonic acid ***32b****.* From **23b** (0.060 g, 0.150 mmol) phosphonic acid **32b** (0.042 g, 80%) was obtained as an amorphous solid; m.p.: 224–226 °C; solubility of **32b** in methanol or water was insufficient to measure the ^{13}C NMR spectrum; IR (KBr): ν = 3445, 3102, 2980, 2910, 1668, 1223, 1025 cm^{-1}; ^1H NMR (600 MHz, CD_3OD): δ = 8.30 (s, 1H, *H*C5′); 7.60 (d, J = 1.0 Hz, 1H, *H*C═CCH$_3$); 5.08 (s, 2H, CH_2); 4.55 (t, J = 7.1 Hz, 2H, PCCCCH_2); 2.09 (qv, J = 7.0 Hz, 2H, PCCCH_2); 1.90 (d, J = 1.0 Hz, 3H, HC═CCH_3); 1.84–1.79 (m, 2H, PCH_2); 1.70–1.63 (m, 2H, PCCH_2); ^{31}P NMR (243 MHz, CD_3OD): δ = 29.86 ppm. Anal. Calcd. for $C_{12}H_{18}N_5O_5P \times H_2O$: C, 39.89; H, 5.58; N, 19.38. Found: C, 40.10; H, 5.43; N, 19.24.

4.1.6.7. 4-(4-{[2,4-Dioxopyrimidin-1-yl]methyl}-1H-1,2,3-triazol-1-yl)butylphosphonic acid ***32c****.* From **23c** (0.072 g, 0.187 mmol) phosphonic acid **32c** (0.052 g, 84%) was obtained as an amorphous solid; m.p.: 204–206 °C; IR (KBr): ν = 3440, 3112, 2980, 2942, 1667, 1219, 1020 cm^{-1}; ^1H NMR (600 MHz, CD_3OD): δ = 8.27 (s, 1H, *H*C5′); 7.74 (d, J = 7.9 Hz, 1H, *H*C═CH); 5.71 (d, J = 7.9 Hz, 1H, HC═C*H*); 5.01 (s, 2H, CH_2); 4.39 (t, J = 7.0 Hz, 2H, PCCCCH_2); 2.06 (qv, J = 7.3 Hz, 2H, PCCCH_2); 1.84–1.78 (m, 2H, PCCH_2); 1.70–1.62 (m, 2H, PCH_2); ^{13}C NMR (151 MHz, CD_3OD): δ = 166.5 (s, C═O); 151.9 (s, C═O); 146.6; 141.5; 125.5; 102.1; 50.5; 43.0; 30.6 (d, J = 16.7 Hz, PCCC); 25.5 (d, J = 135.3 Hz, PC); 19.0 (d, J = 4.5 Hz, PCC); ^{31}P NMR (243 MHz, CD_3OD): δ = 29.81 ppm. Anal. Calcd. for $C_{11}H_{16}N_5O_5P \times H_2O$: C, 38.05; H, 5.22; N, 20.17. Found: C, 38.17; H, 5.48; N, 20.02.

4.1.6.8. 3-{4-[(1,3-Dimethyl-2,6-dioxopurin-7-yl)methyl]-1H-1,2,3-triazol-1-yl}-1-hydroxyethyphosphonic acid ***33i****.* From **24i** (0.116 g, 0.263 mmol) phosphonic acid **33i** (0.071 g, 70%) was obtained as a white powder; m.p.: <244 °C; solubility of **33i** in methanol or water was insufficient to measure the ^{13}C NMR spectrum; IR (KBr): ν = 3344, 3102, 2986, 1699, 1672, 1220, 1015 cm^{-1}; ^1H NMR (300 MHz, CD_3OD): δ = 8.19 (s, 1H); 8.17 (s, 1H); 5.69 (s, 2H, CH_2); 4.80 (ddd, J = 14.2 Hz, J = 4.0 Hz, J = 2.7 Hz, 1H, PCCH_aH$_b$); 4.51 (ddd, J = 14.2 Hz, J = 10.3 Hz, J = 5.8 Hz, 1H, PCCH$_a$$H_b$); 4.17 (dt, J = 10.3 Hz, J = 2.7 Hz, 1H, P*C*H(OH)); 3.53 (s, 3H, CH_3); 3.35 (s, 3H, CH_3); ^{31}P NMR (121 MHz, CD_3OD): δ = 19.61 ppm. Anal. Calcd. for $C_{12}H_{16}N_7O_6P$: C, 37.41; H, 4.19; N, 25.45. Found: C, 37.56; H, 4.28; N, 25.30.

4.2. Antiviral activity assays

The antiviral assays were based on inhibition of virus-induced cytopathicity in HEL [herpes simplex virus type 1 (HSV-1), HSV-2 (G), vaccinia virus and vesicular stomatitis virus], Vero (parainfluenza-3, reovirus-1, Sindbis, Coxsackie B4, and Punta Toro virus), HeLa (vesicular stomatitis virus, Coxsackie virus B4, and respiratory syncytial virus), MDCK (influenza A (H1N1 and H3N1) and influenza B virus) or CRFK (feline herpes virus; feline corona virus (FIPV)) cell cultures. Confluent cell cultures in microtiter 96-well plates were inoculated with 100 cell culture inhibitory dose-50 ($CCID_{50}$) of virus (1 $CCID_{50}$ being the virus dose to infect 50% of the cell cultures) in the presence of varying concentrations (100, 20, 4, … μM) of the test compounds. Viral cytopathicity was recorded as soon as it reached completion in the control virus-infected cell cultures that were not treated with the test compounds. The antiviral concentration was expressed as the EC_{50} or 50%-effective compound concentration required to inhibit virus-induced cytopathicity by 50%.

4.3. Cytotoxicity and cytostatic assays

The cytotoxicity of the test compounds was monitored as a microscopically visible alteration of cell morphology, and expressed as the minimal cytotoxic concentration (MCC) or compound concentration required to afford a microscopically detectable alteration of cell culture morphology.

The cytostatic activity of the test compounds was determined as the 50% cytostatic concentration (IC_{50}) or compound concentration required to inhibit cell proliferation by 50%. For this purpose, cells were seeded in 200 μl-wells of 96-well microtiter plates and allowed to proliferate for 2 (murine leukaemia L1210) to 3 (human T-lymphocyte CEM, human cervix carcinoma HeLa) days in the absence or presence of different serial concentrations of the test compounds. At the end of the exponential proliferation phase, the cells were counted by an automated Coulter ZI particle counter (Analis, Ghent, Belgium).

Acknowledgements

The authors wish to express their gratitude to Mrs. Małgorzata Pluskota, Mrs. Leentje Persoons, Mrs. Frieda De Meyer and Mrs. Lizette van Berckelaer for excellent technical assistance. This work was supported by the National Science Centre under Decision UMO-2011/01/D/NZ4/01276. The virological part of this work was supported by the K.U. Leuven (GOA no. 10/014).

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.ejmech.2013.10.057.

References

[1] L. Naesens, R. Snoeck, G. Andrei, J. Balzarini, J. Neyts, E. De Clercq, HPMPC (cidofovir), PMEA (adefovir) and related acyclic nucleoside phosphonate analogues: a review of their pharmacology and clinical potential in the treatment of viral infections, Antivir. Chem. Chemother. 8 (1997) 1–23.

[2] J.E. Starrett Jr., D.R. Tortolani, M.J. Hitchcock, J.C. Martin, M.M. Mansuri, Synthesis and in vitro evaluation of a phosphonate prodrug: bis(pivaloyloxymethyl) 9-(2-phosphonylmethoxyethyl)adenine, Antivir. Res. 19 (1992) 267–273.

[3] R.V. Srinivas, A. Fridland, Antiviral activities of 9-*R*-2-phosphono methoxypropyl adenine (PMPA) and bis(isopropyloxymethylcarbonyl)PMPA against various drug-resistant human immunodeficiency virus strains, Antimicrob. Agents Chemother. 42 (1998) 1484–1487.

[4] E. De Clercq, Towards an effective chemotherapy of virus infections: therapeutic potential of cidofovir [(*S*)-1-[3-hydroxy-2-(phosphonomethoxy)propyl]cytosine, HPMPC] for the treatment of DNA virus infections, Collect. Czech. Chem. Commun. 63 (1998) 480–506.

[5] T. Carell, C. Brandmayr, A. Hienzsch, M. Müller, D. Pearson, V. Reiter, I. Thoma, P. Thumbs, M. Wagner, Structure and function of noncanonical nucleobases, Angew. Chem. Int. Ed. 51 (2012) 7110–7131.

[6] R.G. Gish, Treating HCV with ribavirin analogues and ribavirin-like molecules, J. Antimicrob. Chemother. 57 (2006) 8–13.

[7] J.D. Graci, C.E. Cameron, Mechanism of action of ribavirin against distinct viruses, Rev. Med. Virol. 16 (2006) 37–48.

[8] K. Moriyama, T. Suzuki, K. Negishi, J.D. Graci, C.N. Thompson, C.E. Cameron, M. Watanabe, Effect of introduction of hydrophobic group on ribavirin base on mutation induction and Anti-RNA viral activity, J. Med. Chem. 51 (2008) 159–166.

[9] E. Brochot, S. Castelain, G. Duverlie, D. Carpon, E. Nguyen-Khac, C. François, Ribavirin monitoring in chronic hepatitis C therapy: anemia versus efficacy, Antivir. Ther. 15 (2010) 687–695.

[10] B.W. Parker, Metabolism and antiviral activity of ribavirin, Virus Res. 101 (2005) 165–171.

[11] J.T. Witkowski, R.K. Robins, G.P. Khare, R.W. Sidwell, Synthesis and antiviral activity of 1,2,4-triazole-3-thiocarboxamide and 1,2,4-triazole-3-carboxamidine ribonucleosides, J. Med. Chem. 16 (1973) 935–937.

[12] L.B. Allen, K.H. Boswell, T.A. Khwaja, R.B. Meyer Jr., R.W. Sidwell, J.T. Witkowski, L.F. Christensen, R.K. Robins, Synthesis and antiviral activity of some phosphate of the broad-spectrum antiviral nucleoside, 1-β-D-ribofuranosyl-1,2,4-triazole-3-carboxamide (ribavirin), J. Med. Chem. 21 (1978) 742–746.

[13] B. Guigas, K. Sakamoto, N. Taleux, S.M. Reyna, N. Musi, B. Viollet, L. Hue, Beyond AICA riboside: in search of new specific AMP-activated protein kinase activators, IUBMB Life 61 (2009) 18–26.

[14] Acadesine AICA riboside, ARA 100, arasine, GP 1–110, Drugs R & D 9 (2008) 169–175.

[15] S.M. Firestine, W. Wu, H. Youn, V.J. Davisson, Interrogating the mechanism of a tight binding inhibitor of AIR carboxylase, Bioorg. Med. Chem. 17 (2009) 794–803.

[16] J.P. Ferris, B. Devadas, Ch.-H. Huang, W.-Y. Ren, Nucleosides from carbohydrate adducts of diaminomaleonitrile. A novel synthesis of 5-amino-1-(β-D-ribopyranosyl)imidazole-4-carboxamide, J. Org. Chem. 50 (1985) 747–754.

[17] R. Alvarez, S. Velázquez, A. San-Félix, S. Aquaro, E. De Clercq, C.-F. Perno, A. Karlsson, J. Balzarini, M.J. Camarasa, 1,2,3-Triazole-[2,5-bis-*O*-(tert-butyldimethylsilyl)-beta-D-ribofuranosyl]-3′-spiro-5′-(4′-amino-1′,2′-oxathiole 2′,2′-dioxide) (TSAO) analogs: synthesis and anti-HIV-1 activity, J. Med. Chem. 37 (1994) 4185–4194.

[18] A. San-Félix, R. Alvarez, S. Velázquez, E. De Clercq, J. Balzarini, M.J. Camarasa, Synthesis and anti-HIV-1 activity of 4- and 5-substituted 1,2,3-triazole-TSAO derivatives, Nucleosides & Nucleotides 14 (1995) 595–598.

[19] S.G. Agalave, S.R. Maujan, V.S. Pore, Click chemistry: 1,2,3-triazoles as pharmacophores, Chem. Asian J. 6 (2011) 2696–2718.

[20] M. Koszytkowska-Stawińska, E. Mironiuk-Puchalska, T. Rowicki, Synthesis of 1,2,3-triazolo-nucleosides via the post-triazole N-alkylation, Tetrahedron 68 (2012) 214–225.

[21] O. Kaczmarek, H.A. Scheidt, A. Bunge, D. Föse, S. Karsten, A. Arbuzova, D. Huster, J. Liebscher, 2′-Linking of lipids and other functions to uridine trough 1,2,3-triazoles and membrane anchoring of the amphiphilic products, Eur. J. Org. Chem. (2010) 1579–1586.

[22] M. Ganesan, K.M. Muraleedharan, Synthesis of β-hydroxyphosphonate and 1,2,-dihydroxyacyclic nucleoside analogs via 1,3-dipolar cycloaddition strategy, Nucleosides, Nucleotides and Nucleic Acids 29 (2010) 91–96.

[23] S.M. Park, H. Yang, S.-K. Park, H.M. Kim, B.H. Kim, Design, synthesis, and anticancer activities of novel perfluoroalkyltriazole-appended 2′-deoxyuridines, Bioorg. Med. Chem. Lett. 20 (2010) 5831–5834.

[24] P.M. Chaudhary, S.R. Chavan, F. Shirazi, M. Razdan, P. Nimkar, S.P. Maybhate, A.P. Likhite, R. Gonnade, B.G. Hazara, M.V. Deshpande, S.R. Deshpande, Exploration of click reaction for the synthesis of modified nucleosides as chitin synthase inhibitors, Bioorg. Med. Chem. 17 (2009) 2433–2440.

[25] T. Fujino, N. Yamazaki, H. Isobe, Convergent synthesis of oligomers of triazole-linked DNA analogue (^{TL}DNA) in solution phase, Tetrahedron Lett. 50 (2009) 4101–4103.

[26] Y.-S. Lee, S.M. Park, H.M. Kim, S.-K. Park, K. Lee, Ch. W. Lee, B.H. Kim, C5-Modified nucleosides exhibiting anticancer activity, Bioorg. Med. Chem. Lett. 19 (2009) 4688–4691.

[27] H.B. Lazrek, M. Taourirte, T. Oulih, J.L. Barascut, J.L. Imbach, C. Pannecouque, M. Witvrouw, E. De Clercq, Synthesis and anti-HIV activity of new modified 1,2,3-triazole acyclonucleosides, Nucleosides, Nucleotides and Nucleic Acids 20 (2001) 1949–1960.

[28] O. Moukha-Chafiq, M.L. Taha, H.B. Lazrek, C. Pannecouque, M. Witvrouw, E. De Clercq, Synthesis and biological evaluation of some 4-substituted 1-[1-(4-hydroxybutyl)-1,2,3-triazol-(4 & 5)-ylmethyl]-1*H*-pyrazolo[3,4-*d*]pyrimidines, Nucleosides, Nucleotides and Nucleic Acids 20 (2001) 1811–1821.

[29] O. Moukha-Chafiq, M.L. Taha, H.B. Lazrek, J.J. Vasseur, C. Pannecouque, M. Witvrouw, E. De Clercq, J.L. Barascut, J.L. Imbach, Synthesis and biological activity of 4-substituted 1-[1-(2-hydroxyethoxy)-methyl-1,2,3-triazol-(4 & 5)-ylmethyl]-1*H*-pyrazolo[3,4-*d*]pyrimidines, Nucleosides, Nucleotides and Nucleic Acids 20 (2001) 1797–1810.

[30] J. Krim, M. Taourirte, J.W. Engels, Synthesis of 1,4-disubstituted mono and bis-triazolocarboacyclonucleoside analogues of 9-(4-hydroxybutyl)guanine by Cu(I)-catalyzed click azide–alkyne cycloaddition, Molecules 17 (2012) 179–190.

[31] S. Trakossas, E. Coutouli-Argyopoulou, D. Hadjipavlou-Litina, Synthesis of modified triazole nucleosides possessing one or two base moieties via a click chemistry approach, Tetrahedron Lett. 14 (2011) 1673–1676.

[32] H. Elayadi, M. Smietana, Ch. Pannecouque, P. Leyssen, J. Neyts, J.-J. Vasseur, H.B. Lazrek, Straightforward synthesis of triazoloacyclonucleotide phosphonates as potential HCV inhibitors, Bioorg. Med. Chem. Lett. 20 (2010) 7365–7368.

[33] H.B. Lazrek, M. Taourirte, T. Oulih, Y. Kabbaj, J.L. Barascut, J.L. Imbach, N.A. Almasoudi, W. Pfleiderer, Nucleosides & Nucleotides 16 (1997) 1073–1077.

[34] P. Chittepu, V.R. Sirivolu, F. Seela, Nucleosides and oligonucleotides containing 1,2,3-triazole residues with nucleobase tethers: synthesis via the azide–alkyne "click" reaction, Bioorg. Med. Chem. 16 (2008) 8427–8439.

[35] J.-L. Yu, Q.-P. Wu, Q.-S. Zhang, Y.-H. Liu, Y.-Z. Li, Z.-M. Zhou, Synthesis and antitumor activity of novel 2′,3′-dideoxy-2′,3′-diethanethionucleosides bearing 1,2,3-triazole residue, Bioorg. Med. Chem. Lett. 20 (2010) 240–243.

[36] D.G. Piotrowska, J. Balzarini, I.E. Głowacka, Design, synthesis, antiviral and cytostatic evaluation of novel isoxazolidine nucleotide analogues with 1,2,3-triazole linker, Eur. J. Med. Chem. 47 (2012) 501–509.

[37] J.-L. Yu, Q.-P. Wu, Q.-S. Zhang, Y.-H. Liu, Y.-Z. Li, Z.-M. Zhou, Synthesis and antitumor activity of novel 2′,3′-dideoxy-2′,3′-diethane thionucleosides bearing 1,2,3-triazole residues, Bioorg. Med. Chem. Lett. 20 (2010) 240–243.

[38] A. Kamal, N. Shankaraiah, V. Devaiah, K.L. Reddy, A. Juvekar, S. Sen, N. Kurian, S. Zingde, Synthesis of 1,2,3-triazole-linked pyrrolobenzodiazepine conjugates employing 'click' chemistry: DNA-binding affinity and anticancer activity, Bioorg. Med. Chem. Lett. 18 (2008) 1468–1473.

[39] Y. Chen, M. Lopez-Sanchez, D.N. Savoy, D.D. Billadeau, G.S. Dow, A.P. Kozikowski, A series of potent and selective, triazolylphenyl-based histone deacetylases inhibitors with activity against pancreatic cancer cells and *Plasmodium falciparum*, J. Med. Chem. 51 (2008) 3437–3448.

[40] J. Vantikommu, S. Palle, P.S. Reddy, V. Ramanatham, M. Khagga, V.R. Pallapothula, Synthesis and cytotoxicity evaluation of novel 1,4-disubstituted 1,2,3-triazoles via CuI catalysed 1,3-dipolar cycloaddition, Eur. J. Med. Chem. 45 (2010) 5044–5050.

[41] K.E. Akri, K. Bougrin, J. Balzarini, A. Faraj, R. Benhida, Efficient synthesis and in vitro cytostatic activity of 4-substituted triazoyl-nucleosides, Bioorg. Med. Chem. Lett. 16 (2007) 6656–6659.

[42] S.-J. Yan, Y.-J. Liu, Y.-L. Chen, L. Liu, J. Lin, An efficient one pot synthesis of heterocycle-fused 1,2,3-triazole derivatives as anti-cancer agents, Bioorg. Med. Chem. Lett. 20 (2010) 5225–5228.

[43] A.R. Elanki, A. Islam, V.S. Rama, R.P. Pulipati, D. Rambadu, G.R. Krishna, C.M. Reddy, K. Mukkanti, G.R. Vanaja, A.M. Kalle, K.S. Kumar, M. Pal, Solvent effect on copper-catalyzed azide–alkyne cycloaddition (CuAAC): synthesis of novel triazolyl substituted quinazolines as potential anticancer agents, Bioorg. Med. Chem. Lett. 22 (2012) 3455–3459.

[44] P. Singh, R. Raj, V. Kumar, M.P. Mahajan, P.M.S. Bedi, T. Kaur, A.K. Saxena, 1,2,3-Triazole tethered β-lactam-chalkone bifunctional hybrids: synthesis and anticancer evaluation, Eur. J. Med. Chem. 47 (2012) 594–600.

[45] L. Zhou, A. Amer, M. Korn, R. Burda, J. Balzarini, E. De Clercq, E.R. Kern, P.F. Torrence, Synthesis and antiviral activities of 1,2,3-triazole functionalized thymidines: 1,3-dipolar cycloaddition for efficient regioselective diversity generation, Antivir. Chem. Chemother. 16 (2005) 375–383.

[46] S. Mohan, S. McAtamney, T. Haselhorst, M. von Itzstein, B.M. Pinto, Carbocycles related to oseltamivir as influenza virus group-1-specific neuraminidase inhibitors. Binding to N1 enzymes in the context of virus-like particles, J. Med. Chem. 53 (2010) 7377–7391.

[47] H. Miyakoshi, S. Miyahara, T. Yokogawa, K. Endoh, T. Muto, W. Yano, T. Wakas, H. Ueno, K.T. Chong, J. Tagichi, M. Nomura, Y. Tako, A. Fujioka, A. Hashimoto, K. Itou, K. Yamamura, S. Shoto, H. Nagasawa, M. Fukuoka, 1,2,3-Triazole-containing uracil derivatives with excellent pharmacokinetics as novel class of potent human deoxyuridine triphosphate inhibitors, J. Med. Chem. 55 (2012) 6427–6437.

[48] H. Cheng, J. Wan, M.-I. Lin, X. Lu, J. Liu, Y. Xu, J. Chen, Z. Tu, Y.-S.E. Cheng, K. Ding, Design, synthesis, and in vitro biological evaluation of 1*H*-1,2,3-triazole-4-carboxyamide derivatives as new anti-influenza A agents, J. Med. Chem. 55 (2012) 2144–2153.
[49] M. Aufort, J. Herscovici, P. Bouhours, N. Moreau, C. Girard, Synthesis and antibiotic activity of a small molecules library of 1,2,3-triazole derivatives, Bioorg. Med. Chem. Lett. 18 (2008) 1195–1198.
[50] J.A. Demaray, J.E. Thuener, M.N. Dawson, S.J. Sucheck, Synthesis of triazole-oxazolidinones via a one-pot reaction and evaluation of their antimicrobial activity, Bioorg. Med. Chem. Lett. 18 (2008) 4868–4871.
[51] X.-L. Wang, K. Wan, Ch.-H. Zhou, Synthesis of novel sulfanilamide-derived 1,2,3-triazoles and their evaluation for antibacterial and antifungal activities, Eur. J. Med. Chem. 45 (2010) 4631–4639.
[52] I.E. Valverde, F. Lecaille, G. Lalmonach, V. Aucagne, A.F. Delmas, Synthesis of a biologically active triazole-containing analogue of cystatin A through successive peptidomimetic alkyne-azide ligations, Angew. Chem. Int. Ed. 51 (2012) 718–722.
[53] V.L. Lampo, R. Sesti-Costa, Z.A. Carneiro, J.S. Silva, S. Schenkman, I. Carvalho, Design, synthesis and the effect of 1,2,3-triazole sialylmimetic neoglycoconiugates on *Trypanosoma cruzi* and its cell surface *trans*-sialidase, Bioorg. Med. Chem. 20 (2012) 145–156.
[54] Ø.W. Akselsen, K. Odlo, J.-J. Cheng, G. Maccari, M. Botta, T.V. Hansen, Synthesis, biological evaluation and molecular modeling of 1,2,3-triazole analogs of combretastatin A-1, Bioorg. Med. Chem. 20 (2012) 234–242.
[55] O. Singh, P. Singh, M. Kumar, J. Gut, P.J. Rosenthal, K. Kumar, V. Kumar, M.P. Mahajan, K. Bisetty, Synthesis, docking and in vitro antimalarian evaluation of bifunctional hybrids derived from β-lactams and 7-chloroquinoline using click chemistry, Bioorg. Med. Chem. Lett. 22 (2012) 57–61.
[56] D.C.M. Chan, C.A. Laughton, S.F. Queener, M.F.G. Stevens, Structural studies on bioactive compounds. part 36: design, synthesis and biological evaluation of pyrimethamine-based antifolates against *Pneumocystis carinii*, Bioorg. Med. Chem. 10 (2002) 3001–3010.
[57] D.B. Jordan, G.S. Basarab, D.-I. Liao, W.M.P. Johnson, K.N. Winzenberg, D.A. Winkler, Structure-based design of inhibitors of the rice blast fungal enzyme trihydroxynaphtalene reductase, J. Mol. Graph. Modell. 19 (2001) 434–447.
[58] L.V.R. Reddy, P.V. Reddy, N.N. Mishra, P.K. Shukla, G. Yadav, R. Srivastava, A.K. Shaw, Synthesis and biological evaluation of glycal-derived novel tetrahydrofuran 1,2,3-triazoles by 'click' chemistry, Carbohydr. Res. 345 (2010) 1515–1521.
[59] J. McNulty, J.J. Nair, N. Vurgun, B.R. DiFrancesco, C.E. Brown, B. Tsoi, D.J. Crankshaw, A.C. Holloway, Discovery of novel class of aldol-derived 1,2,3-triazoles: potent and selective inhibitors of human cytochrome P450 !9A1 (aromatase), Bioorg. Med. Chem. Lett. 22 (2012) 718–722.
[60] Y. Zou, Q. Zhao, J. Liao, H. Hu, S. Yu, X. Chai, M. Xu, New triazole derivatives as antifungal agents: synthesis via click reaction, in vitro evaluation and molecular docking studies, Bioorg. Med. Chem. Lett. 22 (2012) 2959–2962.
[61] P. Norris, D. Horton, B.R. Levine, Cycloaddition of acetylenes with 5-azido-5-deoxy-D-aldopentose derivatives: synthesis of triazole reversed nucleoside analogs, Heterocycles 43 (1996) 2643–2655.
[62] R.R. Talekar, R.H. Wightman, Synthesis of same pyrrolo[2,3-*d*]pyrimidine and 1,2,3-triazole isonucleosides, Tetrahedron 53 (1997) 3831–3842.
[63] C.W. Tornøe, C. Christensen, M. Meldal, Peptidotriazoles on solid phase: [1,2,3]-triazoles by regiospecific copper(I)-catalyzed 1,3-dioplar cycloadditions of terminal alkynes to azides, J. Org. Chem. 67 (2002) 3057–3064.
[64] V.V. Rostovtsev, L.G. Green, V.V. Fokin, K.B. Sharpless, A stepwise Huisgen cycloaddition process: copper(I)-catalyzed regioselective "ligation" of azides and terminal alkynes, Angew. Chem. Int. Ed. 41 (2002) 2596–2599.
[65] I.E. Głowacka, Synthesis of enantiomerically pure diethyl (*R*)- and (*S*)-2-hydroxy-3-(1,2,3-triazol-1-yl)propylphosphonates, Tetrahedron: Asymmetry 20 (2009) 2270–2278.
[66] I.E. Głowacka, M. Cieślak, D.G. Piotrowska, Synthesis of novel 1-hydroxy-2-(1,2,3-triazol-1-yl)ethylphosphonates and 2-hydroxy-3-(1,2,3-triazol-1-yl) propylphosphonates, Phosphorus, Sulfur and Silicon 186 (2011) 431–449.
[67] A.E. Wróblewski, I.E. Głowacka, Synthesis of (1*R*,2*S*)- and (1*S*,2*S*)-3-(4-carbamoyl-1,2,3-triazol-1-yl)-1,2-dihydroxypropylphosphonates, Tetrahedron: Asymmetry 15 (2004) 1457–1464.
[68] A.E. Wróblewski, I.E. Głowacka, Synthesis of four enantiomerically pure 4-(4-carbamoyl-1,2,3-triazol-1-yl)-2,3-dihydroxy-1-methoxybutylphosphonic acids, Tetrahedron: Asymmetry 16 (2005) 4056–4064.
[69] I.E. Głowacka, J. Balzarini, A.E. Wróblewski, Design, synthesis, antiviral, and cytotoxic evaluation of novel phosphonylated 1,2,3-triazoles as acyclic nucleotide analogues, Nucleosides, Nucleotides and Nucleic Acids 31 (2012) 293–318.
[70] I.E. Głowacka, J. Balzarini, A.E. Wróblewski, Synthesis and biological evaluation of novel 1,2,3-triazolonucleotides, Arch. Pharm. Chem. Life Sci. 346 (2013) 278–291.
[71] W.E. Lindsell, Ch. Murray, P.N. Preston, T.A.J. Woodman, Synthesis of 1,3-diynes in the purine, pyrimidine, 1,3,5-triazine and acridine series, Tetrahedron 56 (2000) 1233–1245.
[72] F. Himmelsbacg, M. Mark, M. Eckhardt, E. Langkopf, R. Maier, Xanthine derivatives, the preparation thereof and use as pharmaceutical compositions, US2002/198205, 2002 (A1).
[73] M.J.A. Waer, P.A.M.M. Herdewijn, W.E. Pfleiderer, Immunosupressive effects of 8-substituted xanthine derivatives, US7,253,176 B1, 2007.
[74] A. Casaschi, R. Grigg, J.M. Sansano, Palladium catalysed tandem cyclization-anion capture. Part 6:[1] synthesis of sugar. Nucleoside, purine, benzodiazepinone and β-lactam analogues via capture of in situ generated vinylstannanes, Tetrahedron 56 (2000) 7553–7560.
[75] J.W. Daly, W.L. Padgett, M.T. Shamim, Analogues of caffeine and theophylline: effect of structural alterations on affinity at adenosine receptors, J. Med. Chem. 29 (1986) 1305–1308.
[76] A. Casaschi, R. Grigg, J.M. Sansano, Palladium catalysed tandem cyclization-anion capture. Part 7:[1] synthesis of α-amino esters, nitrogen heterocycles and β-aryl/hetroaryl ethylamines via in situgenerated vinylstannanes, Tetrahedron 57 (2001) 607–615.
[77] L. Pérez-Serrano, L. Casarrubios, G. Dominguez, P. González-Pérez, J. Pérez-Castells, Synthesis of enynoindoles via vinyl and ethynyl indoles, Synthesis 13 (2002) 1810–1812.
[78] E. Bankowska, J. Balzarini, I.E. Głowacka, A.E. Wróblewski, Design, synthesis and antiviral and cytotoxic evaluation of novel acyclic phosphonate nucleotide analogues with a 5,6-dihydro-1*H*-[1,2,3]triazolo[4,5-*d*]pyridazine-4,7-dione system, Monatsh. Chem. (2013) under review.
[79] I.E. Głowacka, J. Balzarini, A.E. Wróblewski, Synthesis of a new series of phosphonylated 1,2,3-triazoles as acyclic analogues of ribavirin, Arch. Pharm. Chem. Life Sci. 346 (2013) 677–687.
[80] U. Neumann, M. Gütschow, 3,1-Benzothiazin-4-ones and 3,1-benzoxazin-4-ones: highly different activities in chymotrypsin inactivation, Bioorg. Chem. 32 (1995) 72–88.
[81] Y.-S. Lee, B.H. Kim, Heterocyclic nucleoside analogues: design and synthesis of antiviral, modified nucleosides containing isoxazole heterocycles, Bioorg. Med. Chem. Lett. 12 (2002) 1395–1397.
[82] Y. Saito, V. Escuret, D. Durantel, F. Zoulim, R.F. Schinazi, L.A. Agrofoglio, Synthesis of 1,2,3-triazolo-carbonucleoside analogues of ribavirin targeting an HCV in replication, Bioorg. Med. Chem. 11 (2003) 3633–3639.
[83] M. Karplus, Vicinal proton coupling in nuclear magnetic resonance, J. Am. Chem. Soc. 85 (1963) 2870–2871.
[84] C. Benezra, The variation of vicinal $^{31}P-C-C-^{1}H$ couplings with dihedral angle in phosphonates, J. Am. Chem. Soc. 95 (1973) 6890–6894.
[85] J.-R. Neeser, J.M.J. Tronchet, E.J. Charollais, Structural analysis of 3-*C*-phosphonates, -phosphinates, and -phosphine oxides of branched-chain sugars, Can. J. Chem. 61 (1983) 2112–2120.
[86] G. Adiwidjaja, B. Meyer, J. Thiem, Synthesis and crystal structure of endo-2-dimethylphosphono-exo-2-hydroxy-(−)-camphane for the determination of ^{3}J(CCCP) vicinal coupling constants, Z. Naturforsch. 34b (1979) 1547–1551.
[87] G.W. Buchanan, K. Bourque, A. Seeley, ^{13}C and ^{31}P NMR spectra of 1-diethylphosphono-1-hydroxycycloalkanes, Magn. Res. Chem. 24 (1986) 360–367.