Synthesis and Anti-HIV Activity of Triazolo-Fused, Medium-Sized Cyclic Nucleoside Analogs Prepared by an Intramolecular *Huisgen* 1,3-Dipolar Cycloaddition

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Medium-sized cyclic nucleosides containing a fused triazole ring were synthesized *via* intramolecular *Huisgen* 1,3-dipolar cycloadditon reaction. 2′,3′-*seco*-Uridine was employed as the key intermediate for the introduction of azido and alkynyl moieties in the defined positions of the reaction precursors. The cycloaddition reactions were achieved in high yields by heating the precursor in refluxing toluene. The uracil base in these target compounds was successfully transformed to the corresponding cytosine. The synthesized compounds were evaluated in a MAGI assay for their anti-HIV activities, and in a H9 T lymphocytes assay for their cell toxicities.

Introduction. – Modified nucleosides constitute a cornerstone in antiviral therapies with broad spectra [1]. The modifications have been conducted on the nucleobase, the sugar, or both moieties in nucleosides. In particular, for structural manipulations of the sugar moiety, a variety of strategies have been employed, which include: *1*) introduction of functionalities in different positions of the intact natural pentose ring [1b][2]; *2*) change of the configuration at C(1′) to form L-nucleosides [3]; *3*) replacement of O(4′) with other atoms, such as with a C-atom to form carbocyclic nucleosides [4]; *4*) changing the pentose ring to a chain structure to form acyclic nucleosides [5]; *5*) conjunction of the pentose ring with a new ring system to form conformationally constrained nucleosides [6]; and *6*) changing the pentose ring to other ring size by ring contraction [7] and expansion [8].

In a 'normal' nucleoside, the pentose ring is not planar, instead it exists in equilibrium of *North* (C(3′) up) and *South* (C(3′) down) conformations, and the molecule has limited flexibility [9]. In an acyclic nucleoside, in which the pentose ring is replaced with a chain structure, the molecule can freely rotate and has large flexibility [5][10]. Contrarily, in a ring-conjunctional nucleoside, the molecule is locked in rigid conformation and has low flexibility. Ideally, a nucleoside inhibitor can be converted, by a series of enzymes, to its corresponding active triphosphate form and is utilized in gene-material synthesis of the targeted virus, but it is not or to a much lower extend involved in that of the host cell [11]. Thus, a candidate nucleoside should have a certain structural flexibility to fit the enzymes involved in its activating course and inhibiting the virus, and, on the other hand, the nucleoside should have a certain rigidity to

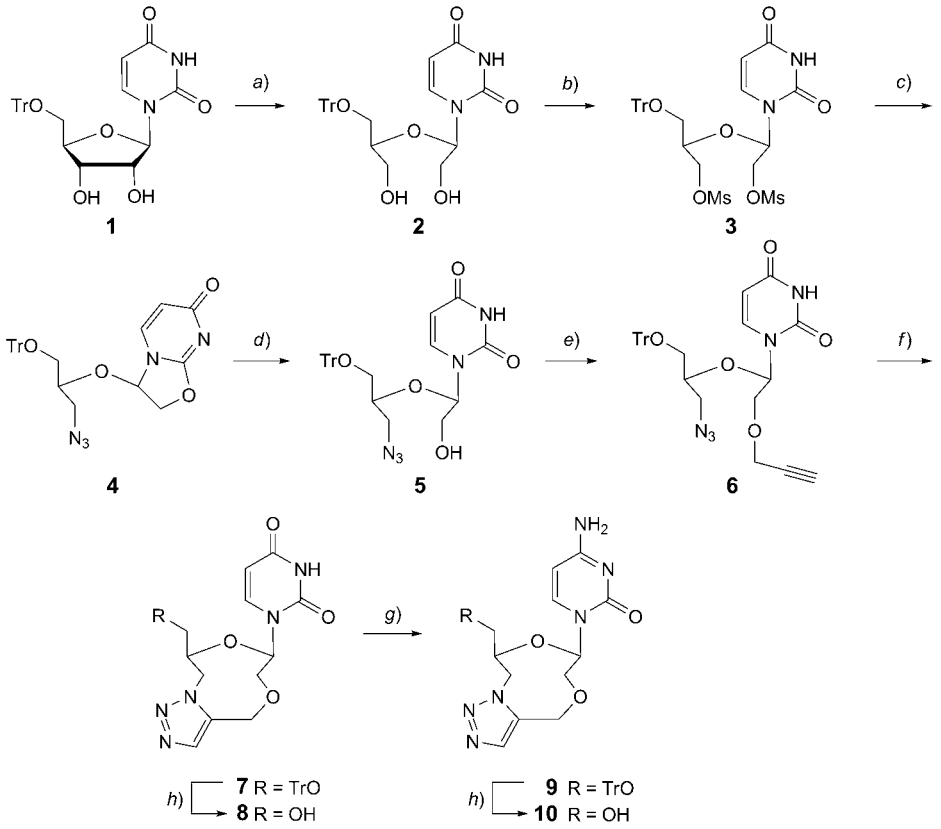
differentiate it from the natural substrate for the enzymes of the host. The medium-sized cyclic nucleosides, which have been rarely explored, possess the dual feature of structural flexibility and rigidity [8a].

Recently, we have developed a methodology for the synthesis of triazolo-fused cyclic nucleosides by employing intramolecular *Huisgen* 1,3-dipolar cycloadditions between azido and alkynyl moieties within the reaction precursor [12]. Our research interests rely on the combination of a conformational restriction concept with a triazole structural feature in the drug design. Several members of the 1,2,3-triazole family have been already shown to possess interesting biological properties, and the triazole with its novel structural features and physiochemical properties is regarded as a privileged structure in drug design and discovery [13]. Herein, we report the construction of triazolo-fused, medium-sized cyclic nucleosides *via* an intramolecular 1,3-dipolar cycloaddition between an N_3 and an alkynyl moiety. The subsequent transformation of the uracil to the corresponding cytosine in the cyclic nucleosides and the anti-HIV activities of some of the synthesized compounds are also included.

Results and Discussions. – We started our synthesis of 2′,3′-fused medium-sized cyclic uridine **8** from 5′-trityluridine (**1**) (Tr = triphenylmethyl), which was treated with $NaIO_4$ to lead to oxidative diol cleavage of the C(2′)–C(3′) bond, followed by reduction with $NaBH_4$ to give 2′,3′-*seco*-uridine **2** [14] (*Scheme 1*). Mesylation of 2′- and 3′-OH groups in **2** gave compound **3**. Treatment of the bis(methanesulfonate) **3** with 1 equiv. of LiN_3 at room temperature for 3 h afforded 2,2′-*O*-anhydro-3′-azido compound **4**. Obviously, the product formed in this reaction resulted from selective replacement of the MsO group at C(3′) by an N_3 group, while the MsO at C(2′) was attacked by O(2) [15]. Hydrolysis of **4** with aq. NaOH afforded 2′-OH intermediate **5**. Propargylation of the 2′-OH group was carried out by treatment of **5** with NaH under ultrasonic irradiation, followed by addition of 3-bromoprop-1-yne to give the cycloaddition precursor **6** [16]. Heating **6** under reflux in toluene led to the intramolecular 1,3-dipolar cycloaddition between N_3 and the propargyl group to reconstitute a bicyclic nucleoside **7** with a triazolo-fused nine-membered ring system. Its structure was elucidated based on the ^{1}H- and ^{13}C-NMR data, in which a resonance at 7.67 ppm for a H-atom, and two resonances at 143.2 and 139.1 ppm for two C-atoms characterized the triazole structure. A standard condition of 80% AcOH was employed for the deprotection of the 5′-*O*-Tr group to give 5′-OH uridine **8**. The nucleobase uracil in compound **7** was successfully transformed to cytosine by a two-step procedure to give compound **9** [17], which was treated with acid for deprotection to give the corresponding cyclic cytidine **10** (*Scheme 1*).

We then continued our synthesis for the second target compound **17**, an isomer of **8** in which the triazole moiety is directly linked to C(2′). The synthesis started with compound **3**, which was treated with base to form the 2,2′-anhydro-2′,3′-*seco*-uridine **11**. Nucleophilic replacement of the MsO group at C(3′) with benzoyl anion furnished compound **12**, and subsequent opening of the 2,2′-anhydro ring with N_3 anion gave 2′-azido-2′,3′-*seco*-uridine **13**. Hydrolysis of the BzO group at C(3′) and selective propargylation of the 3′-OH group of compound **14** the afforded cycloaddition precursor **15**, which was then treated under the same conditions as for **7** to give compound **16**. Similarly, the uracil in **16** was converted to the corresponding cytosine to

Scheme 1

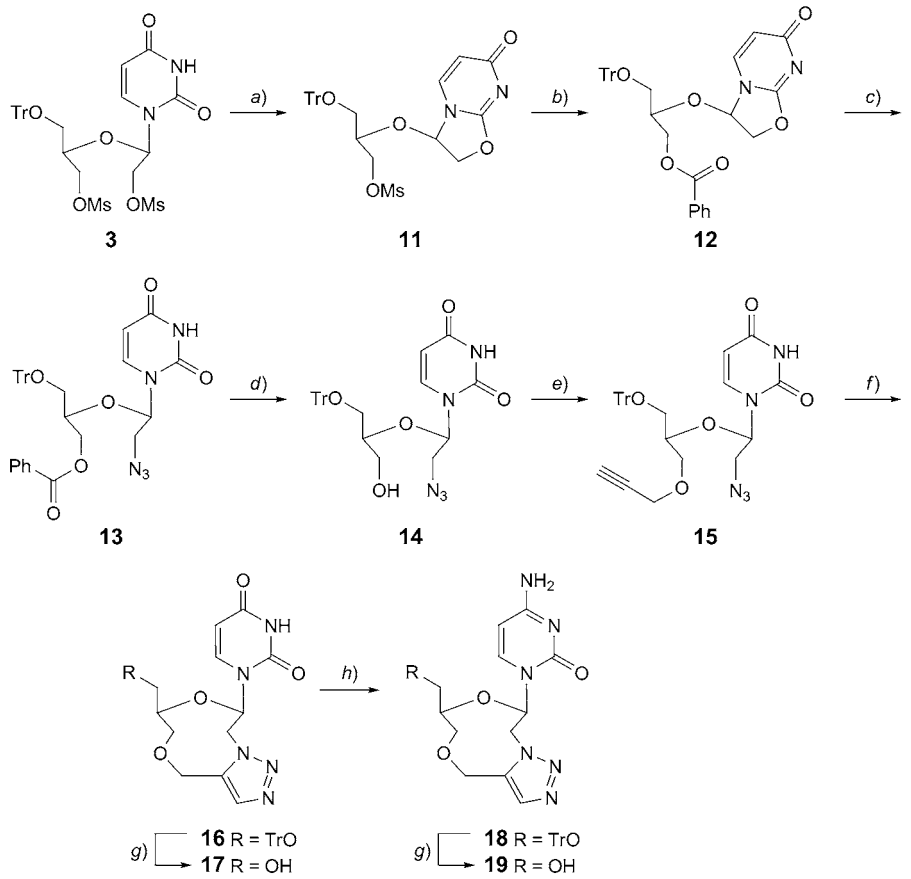


a) $NaIO_4$, $NaBH_4$, Et_3N, dioxane; 87%. *b*) MsCl, Py, 0°. *c*) LiN_3, DMF; 64% (2 steps). *d*) 1N NaOH aq., THF; 86%. *e*) NaH, THF, propargyl bromide, ultrasonic irradiation; 88%. *f*) Toluene, reflux; 80%. *g*) 1. $POCl_3$, 1*H*-1,2,4-triazole, MeCN, Et_3N; 2. dioxane, $NH_3 \cdot H_2O$; 54% (2 steps). *h*) AcOH, 45°; 80% (for **8**), 82% (for **10**).

give **18** by the same procedure for nucleobase transformation as described for compound **9**. Removal of the Tr group of compound **16** and **18** afforded 5′-OH free compound **17** and **19**, respectively (*Scheme 2*).

Next, we carried out the synthesis of 3′,5′-fused medium-sized cyclic uridine **27**, which, by retrosynthetic analysis, was derived from the precursor **26**, in which the N_3 moiety as dipole is directly linked to C(3′), and the propargyl group as dipole acceptor is located at C(5′). Propargyl group was introduced at the early stage of the synthesis by the treatment of propargyl bromide (3-bromoprop-1-yne) with isopropylene uridine **20** under the same conditions as described for **6** to give compound **21**. This transformation fulfilled two purposes: allocating the dipole donor in the required place and protecting the 5′-OH group in one manipulation. Removal of the isopropylene group gave diol **22**, which was converted to 2′,3′-*seco*-uridine **23** under the same condition as for **2**. Similarly, mesylation of 2′- and 3′-OH groups in **23** afforded bis(methanesulfonate) **24**,

Scheme 2

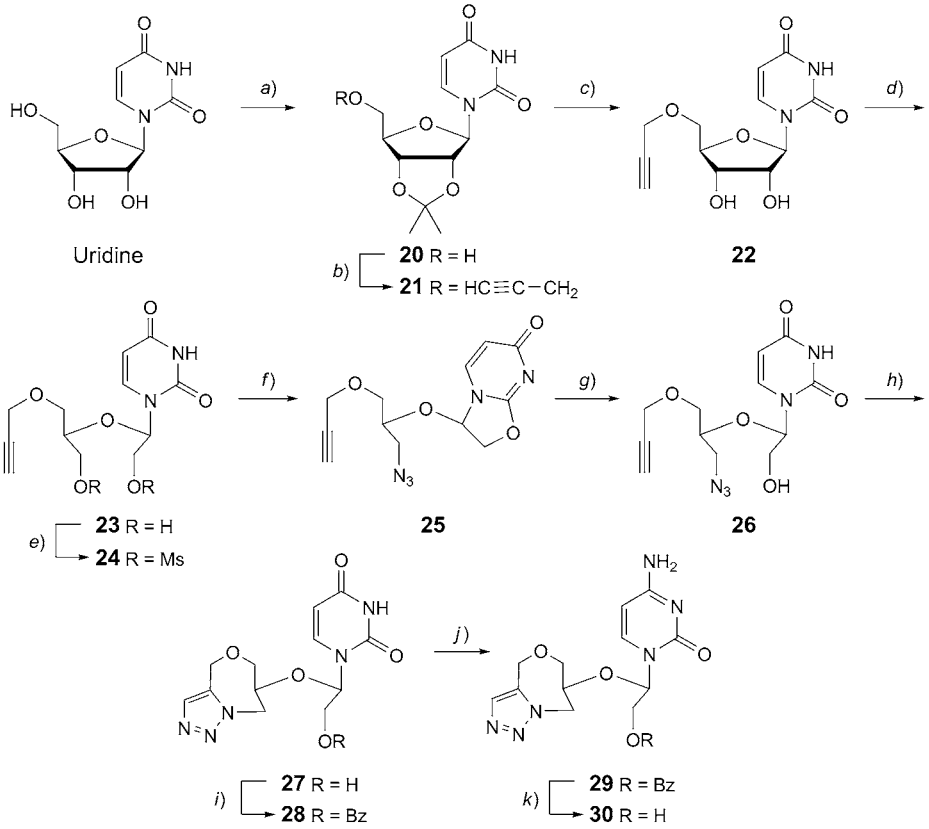


a) 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU), THF. *b*) PhCOOK, 80°, DMF; 74% (2 steps). *c*) NaN_3, DMF, 70°; 75%. *d*) MeONe, THF; 87%. *e*) NaH, THF, propargyl bromide (= bromoprop-1-yne), ultrasonic irradiation; 86%. *f*) Toluene, reflux; 75%. *g*) AcOH, 45°, for compound **17**: 73%, for compound **19**: 83%. *h*) 1. $POCl_3$, 1*H*-1,2,4-triazole, MeCN, Et_3N; 2. dioxane, $NH_3 \cdot H_2O$; 58% (2 steps).

nucleophilic replacement of the MsO group at C(3′) with N_3 provided 3′-azido-2,2′-anhydro compound **25**. The cycloaddition between the 5′-propargyl and the 3′-N_3 groups took place in refluxing toluene to give the triazolo-fused, seven-membered nucleoside **27**. After protection of the 2′-OH by a BzO group to give compound **28**, the uracil was transformed to cytosine under the standard condition to give cytidine nucleoside **29**. The Bz group was removed with MeONa in MeOH to afford the corresponding cytidine **30** with a free OH group (*Scheme 3*).

Finally, we selected the synthesized compounds **10** and **19** for the preliminary evaluation of their anti-HIV activities. In the biological tests, MAGI-CCR5 cells infected by HIV-1 NL4-3 particle, were treated with 50 μM of each compound. The cell toxicities of these compounds were evaluated with H9 T lymphocytes. 3′-Azidothymi-

Scheme 3



a) Acetone, $CuSO_4$, conc. H_2SO_4; 80%. *b*) NaH, THF, propargyl bromide, ultrasonic irradiation; 87%. *c*) 1N HCl, MeOH, 45°; 87%. *d*) $NaIO_4$, $NaBH_4$, Et_3N, dioxane; 83%. *e*) MsCl, Et_3N, THF, 0°. *f*) 1. DBU, THF; 2. LiN_3, DMF, 70°; 73% (3 steps). *g*) 1N NaOH, THF; 75%. *h*) Toluene, reflux, 24 h; 69%. *i*) BzCl (Bz, benzoyl), pyridine, 0°; 96%. *j*) 1. $POCl_3$, 1*H*-1,2,4-triazole, MeCN, Et_3N; 2. dioxane, $NH_3 \cdot H_2O$; 56% (2 steps). *k*) 1N NaOMe, MeOH, r.t.; 54%.

dine (AZT) was selected as the reference compound in the tests (viral infectivity, 1; and cell toxicity, 100). The results showed that the two compounds had no toxicity, but were inferior to AZT in inhibition of infection.

Conclusions. – We have successfully extended the methodology of intramolecular 'click chemistry' involving N_3 and alkynyl groups to the synthesis of triazolo-fused cyclic nucleosides containing a medium-sized ring, which is of synthetic challenge and biological interest. The triazole moiety of these analogs has been shown to be tolerated in a standard procedure for transforming the 4-CO to the 4-NH_2 group in a nucleobase. Though the anti-HIV activities of these compounds are inferior to that of AZT, the unique structural features of the molecules remain interesting to be tested for antiviral activities to other viruses.

Experimental Part

General. All reactions were carried out under N_2. CH_2Cl_2 was dried (anh. $CaCl_2$). All other commercial reagents were used as received without additional purification. Anal. TLC: 2.5 × 5-cm plates coated with a 0.25-mm thickness of silica gel *GF 254*. Column chromatography (CC): silica gel *G* (SiO_2; 200–300 mesh; *Qingdao Haiyang Chemical Company*, P. R. China). ^{1}H- and ^{13}C-NMR spectra: at 300 (^{1}H) and 75 MHz (^{13}C), resp.; in $CDCl_3$ or (D_6)DMSO; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. HR-MS: *Bruker micrOTOF-Q-II* mass spectrometer equipped with an electrospray-ionization (ESI) source; in *m*/*z*. MS: *Applied-Biosystems-ABI-Q-Trap* mass spectrometer equipped with an atmospheric-pressure chemical-ionization (APCI) source; in *m*/*z*.

*1-(2-Hydroxy-1-{[1-hydroxy-3-(triphenylmethoxy)propan-2-yl]oxy}ethyl)pyrimidine-2,4(1*H,*3*H*)-dione* (**2**). To a soln. of **1** (7.59 g, 15.4 mmol) in a mixture of 1,4-dioxane (150 ml) and H_2O (50 ml) was added a soln. of $NaIO_4$ (4.94 g, 23.1 mmol) in 1,4-dioxane (80 ml), and the mixture was stirred at r.t. in the dark for 2 h, until the reactant was consumed (checked by TLC). The mixture was diluted with 1,4-dioxane (100 ml), filtered to remove salts, and the solid was washed with 50 ml of 1,4-dioxane. The combined filtrate was treated with $NaBH_4$ (0.65 g, 17.1 mmol) for 30 min at r.t. The reaction was quenched with AcOH/pyridine 1 : 1 (*v*/*v*; 5 ml), and concentrated to 100 ml. The residue was then diluted with CH_2Cl_2 (100 ml) and washed with sat. aq. Na_2CO_3 (100 ml). The combined org. layers were dried (Na_2SO_4), filtered, and evaporated to give pure **2** (6.6 g, 87%). White foam. ^{1}H-NMR ($CDCl_3$): 9.70 (*s*, 1 H); 7.20–7.43 (*m*, 16 H); 5.93 (*d*, *J* = 6.3, 1 H); 5.55 (*d*, *J* = 7.8, 1 H); 4.08–4.16 (*m*, 1 H); 3.64–3.73 (*m*, 4 H); 3.16–3.22 (*m*, 2 H); 2.04 (*s*, 2 H).

*3-{[1-Azido-3-(triphenylmethoxy)propan-2-yl]oxy}-2,3-dihydro-7*H*-[1,3]oxazolo[3,2-*a*]pyrimidin-7-one* (**4**). To a soln. of **2** (5.86 g, 12 mmol) in anh. CH_2Cl_2 (100 ml), Et_3N (3.8 ml, 26.4 mmol) was added at 0°, followed by dropwise addition of MsCl. Then, H_2O (50 ml) was added after consumption of reactant (checked by TLC), and the mixture was stirred violently. The org. layer was separated and dried (Na_2SO_4), filtered, and evaporated to give a product as a pure white powder. The solid was dissolved in DMF (25 ml), and the soln. was heated to 55°. Then, LiN_3 (0.59g, 12 mmol) was added, and the mixture was stirred for 3 h, poured into 200 ml of ice-water, and extracted with AcOEt (3 × 50 ml). The combined extract was dried (Na_2SO_4) and concentrated, and the crude product was purified by CC (SiO_2; CH_2Cl_2/MeOH 30 : 1): **4** (3.83 g, 64%). ^{1}H-NMR ($CDCl_3$): 7.25–7.39 (*m*, 16 H); 5.87 (*d*, *J* = 6.5, 1 H); 5.80 (*d*, *J* = 8.0, 1 H); 4.75 (*dd*, *J* = 9.6, 10.8, 1 H); 4.56 (*dd*, *J* = 9.0, 8.7, 1 H); 3.74–3.86 (*m*, 1 H); 3.35–3.45 (*m*, 2 H); 3.24–3.38 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$): 172.1; 160.3; 143.0; 135.4; 128.4; 128.0; 127.4; 109.6; 87.5; 79.1; 73.3; 64.1; 52.8. HR-ESI-MS: 496.1984 ([*M* + H]$^+$, $C_{28}H_{26}N_5O_4^+$; calc. 496.1979).

*1-(1-{[1-Azido-3-(triphenylmethoxy)propan-2-yl]oxy}-2-hydroxyethyl)pyrimidine-2,4(1*H,*3*H*)-dione* (**5**). To a soln. of **4** (1.8 g 3.6 mmol) in THF (30 ml), was added 1N NaOH aq. (8 ml). The mixture was stirred at r.t. for 2 h. Then, the mixture was consentrated to dryness, and the crude product was purified by CC (SiO_2; CH_2Cl_2/MeOH 30 : 1): **5** (1.5 g, 86%). ^{1}H-NMR ($CDCl_3$): 9.58 (*s*, 1 H); 7.23–7.36 (*m*, 16 H); 5.92 (*d*, *J* = 12.3, 1 H); 5.55 (*d*, *J* = 6.5, 1 H); 3.76–3.86 (*m*, 1 H); 3.70–3.80 (*m*, 1 H); 3.46–3.54 (*m*, 2 H); 3.38–3.43 (*m*, 1 H); 3.15–3.25 (*m*, 2 H); 1.76 (*s*, 1 H). ^{13}C-NMR ($CDCl_3$): 163.3; 151.2; 143.2; 140.0; 128.4; 127.9; 127.3; 102.8; 87.3; 83.6; 77.9; 63.4; 63.1; 51.6. HR-ESI-MS: 514.2091 ([*M* + H]$^+$, $C_{28}H_{28}N_5O_5^+$; calc. 514.2085).

*1-[1-{[1-Azido-3-(triphenylmethoxy)propan-2-yl]oxy}-2-(prop-2-yn-1-yloxy)ethyl]pyrimidine-2,4(1*H,*3*H*)-dione* (**6**) To a soln. of **5** (1.4 g, 2.9 mmol) in dry THF (25 ml) was added NaH (60%, 350 mg, 5.8 mmol), and the mixture was stirred in an ice bath for 30 min. Then, 3-bromoprop-1-yne (0.26 ml, 3.0 mmol) was added, and the mixture was activated by ultrasonic irradiation (50 min) at r.t. After the reactants were consumed, 3 ml of MeOH and 15 ml H_2O were added. Then, the mixture was extracted with AcOEt (3 × 10 ml). The combined extract was dried (Na_2SO_4) and concentrated, and the crude product was purified by CC (SiO_2; CH_2Cl_2/MeOH 80 : 1): **6** (1.3 g, 88%). ^{1}H-NMR ($CDCl_3$): 8.86 (*s*, 1 H); 7.26–7.33 (*m*, 16 H); 6.01 (*t*, *J* = 6.0, 1 H); 5.59 (*d*, *J* = 6.4, 1 H); 4.17 (*s*, 2 H); 3.70–3.76 (*m*, 2 H); 3.55–3.63 (*m*, 2 H); 3.50–5.54 (*m*, 1 H); 3.43 (*s*, 1 H); 3.15–3.24 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$): 162.7; 143.3; 128.5; 127.9; 127.3; 102.7; 82.0; 69.2; 63.4; 58.8; 51.7. HR-ESI-MS: 552.2246 ([*M* + H]$^+$, $C_{31}H_{30}N_5O_5^+$; calc. 552.2241).

*6,7,9,10-Tetrahydro-1-{9-[(triphenylmethoxy)methyl]-4*H*-[1,2,3]triazolo[5,1-*f*][1,4,7]dioxazonin-7-yl}pyrimidine-2,4(1*H*,3*H*)-dione* (**7**) A soln. of **6** (0.52 g, 1 mmol) in 10 ml of toluene was heated to reflux for 18 h and then cooled to r.t. The mixture was concentrated *in vacuo* to yield a crude product that was purified by a short CC (SiO_2; CH_2Cl_2/MeOH 40 : 1): **7** (0.41 g, 80%). ^{1}H-NMR ($CDCl_3$): 8.65 (*s*, 1 H); 7.67 (*s*, 1 H); 7.30–7.39 (*m*, 16 H); 5.65 (*d*, *J* = 5.0, 1 H); 5.50 (*dd*, *J* = 6.3, 1 H); 5.05 (*d*, *J* = 8.0, 1 H); 4.86 (*s*, 2 H); 4.49 (*d*, *J* = 8.7, 1 H); 3.75–3.81 (*m*, 2 H); 3.34–3.42 (*m*, 1 H); 3.29–3.33 (*m*, 1 H). ^{13}C-NMR ($CDCl_3$): 162.9; 149.7; 143.2; 139.1; 134.9; 128.4; 127.9; 127.3; 102.8; 87.3; 85.8; 81.4; 71.0; 64.5; 63.9; 62.6; 51.4. HR-ESI-MS: 552.2237 ($[M+H]^+$, $C_{31}H_{30}N_5O_5^+$; calc. 552.2241).

*6,7,9,10-Tetrahydro-1-[9-(hydroxymethyl)-4*H*-[1,2,3]triazolo[5,1-*f*][1,4,7]dioxazonin-7-yl]pyrimidine-2,4(1*H*,3*H*)-dione* (**8**). A soln. of **7** (0.3 g, 0.57 mmol) in 80% AcOH aq. (9 ml) was heated to 45° for 5 h. Then, the mixture was concentrated to dryness under reduced pressure and was purified by CC (SiO_2; CH_2Cl_2/MeOH 20 : 1): **8** (0.12 g, 80%). ^{1}H-NMR ($CDCl_3$): 11.34 (*s*, 1 H); 7.78 (*s*, 1 H); 7.68 (*s*, 1 H); 5.58 (*d*, *J* = 6.6, 1 H); 5.44 (*t*, *J* = 8.4, 1 H); 4.98–4.04 (*m*, 1 H); 4.84–4.94 (*m*, 2 H); 4.51–4.61 (*m*, 1 H); 3.87 (*d*, *J* = 3.7, 1 H); 3.74 (*d*, *J* = 3.5, 1 H); 3.42–3.48 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$): 163.3; 150.3; 140.8; 136.0; 134.8; 127.8; 127.6; 126.7; 101.7; 85.4; 81.8; 70.5; 61.3; 61.2; 50.5. HR-ESI-MS: 332.0962 ($[M+Na]^+$, $C_{12}H_{15}N_5NaO_5^+$; calc. 332.0965).

*4-Amino-6,7,9,10-tetrahydro-1-{9-[(triphenylmethoxy)methyl]-4*H*-[1,2,3]triazolo[5,1-*f*][1,4,7]dioxazonin-7-yl}pyrimidin-2(1*H*)-one* (**9**). To a soln. of **7** (0.7 g, 1.32 mmol) in MeCN (20 ml), were added 1*H*-1,2,4-triazole (1.46 g, 21 mmol) and Et_3N (3.6 ml, 26 mmol), and the resulting mixture was stirred at 0° for 0.5 h under N_2. $POCl_3$ (0.43 ml, 4.8 mmol) was then added, the mixture was filtered, and the solid was washed with a soln. of Et_3N/MeCN 1 : 4 (100 ml). The filtrate was evaporated to dryness, and the residue was dissolved in dioxane (10 ml) and treated with sat. $NH_3 \cdot H_2O$ (3 ml). After stirring for 2 h, the mixture was concentrated, and the crude product was purified by CC (SiO_2; CH_2Cl_2/MeOH 50 : 1): **9** (0.4 g, 54%). ^{1}H-NMR ($CDCl_3$): 7.62 (*s*, 1 H); 7.45 (*s*, 1 H); 7.43 (*s*, 1 H); 7.22–7.30 (*m*, 15 H); 5.65–5.71 (*m*, 1 H); 5.60–5.64 (*d*, *J* = 6.6, 1 H); 5.0 (*d*, *J* = 8.0, 1 H); 4.83 (*s*, 2 H); 4.46–5.54 (*m*, 1 H); 3.87–3.95 (*m*, 1 H); 3.26–3.38 (*m*, 4 H). ^{13}C-NMR ($CDCl_3$): 165.6; 155.1; 143.2; 139.9; 135.2; 134.5; 128.3; 127.8; 127.2; 95.6; 87.0; 85.7; 80.6; 71.5; 63.7; 62.5; 51.4. HR-ESI-MS: 551.2399 ($[M+H]^+$, $C_{31}H_{31}N_6O_4^+$; calc. 551.2401).

*4-Amino-1-{9-(hydroxymethyl)-6,7,9,10-tetrahydro-4*H*-[1,2,3]triazolo[5,1-*f*][1,4,7]dioxazonin-7-yl}-pyrimidin-2(1*H*)-one* (**10**) Prepared as described for **8**. ^{1}H-NMR ($CDCl_3$): 7.75 (*s*, 1 H); 7.52 (*s*, 1 H); 7.24 (*s*, 1 H); 7.14 (*s*, 1 H); 5.68 (*d*, *J* = 6.7, 1 H); 5.48–5.64 (*m*, 1 H); 4.89–4.93 (*m*, 3 H); 4.47–4.55 (*m*, 1 H); 3.75–3.85 (*m*, 1 H); 3.56–3.68 (*m*, 4 H); 1.54 (*s*, 1 H). ^{13}C-NMR ($CDCl_3$): 165.8; 154.9; 141.0; 136.1; 134.7; 94.3; 85.8; 81.5; 70.9; 61.4; 61.3; 50.6. HR-ESI-MS: 309.1300 ($[M+H]^+$, $C_{12}H_{17}N_6O_4^+$; calc. 309.1306).

*2-[(2,3-Dihydro-7-oxo-7*H*-[1,3]oxazolo[3,2-*a*]pyrimidin-3-yl)oxy]-3-(triphenylmethoxy)propyl Benzoate* (**12**). To a soln. of **3** (6.75 g, 10.5 mmol) in THF (100 ml) was added DBU (4.6 ml, 30mmol). The mixture was stirred at r.t. for 2 h. Then, H_2O (500 ml) was added, after stirring for 10 min. CH_2Cl_2 (100 ml) was added, and org. layer was separated, washed with H_2O (3 × 50 ml), dried (Na_2SO_4), and concentrated to give white foam. The solid was dissolved in dry DMF (100 ml), PhCOOK (1.85 g, 11.6 mmol) was added, and the mixture was heated to 100° for 4 h. Then, 500 ml of H_2O were added, and the mixture was extracted with AcOEt (3 × 200 ml). The combined extract was dried (Na_2SO_4) and concentrated, and the crude product was purified by CC (SiO_2; CH_2Cl_2/MeOH 70 : 1): **12** (4.48 g, 74%; 2 steps). ^{1}H-NMR ($CDCl_3$): 7.90–7.96 (*m*, 2 H); 7.54–7.60 (*m*, 1 H); 7.43–4.47 (*m*, 2 H); 7.28–7.39 (*m*, 16 H); 5.95 (*d*, *J* = 5.8, 1 H); 5.78 (*d*, *J* = 6.3, 1 H); 4.64 (*dd*, *J* = 8.3, 10.3, 1 H); 4.42–4.54 (*m*, 2 H); 4.28–4.42 (*m*, 1 H); 4.10–4.18 (*m*, 1 H); 3.42–3.50 (*m*, 1 H); 3.33–3.39 (*m*, 1 H). ^{13}C-NMR ($CDCl_3$): 171.8; 166.2; 143.2; 135.2; 133.7; 129.7; 128.8; 128.7; 128.2; 127.6; 110.1; 87.7; 78.8; 73.2; 64.6; 63.9. HR-ESI-MS: 575.2183 ($[M+H]^+$, $C_{35}H_{31}N_2O_6^+$; calc. 575.2177).

*2-[2-Azido-1-(3,4-dihydro-2,4-dioxopyrimidin-1(2*H*)-yl)ethoxy]-3-(triphenylmethoxy)propyl Benzoate* (**13**). To a soln. of **12** (4.7 g, 8.2 mmol) in dry DMF (80 ml), was added NaN_3 (0.63 g, 9.8 mmol). The mixture was heated to 70° and stirred for 5 h. The mixture was poured into ice-water (800 ml), and the precipitate was collected. The crude product was purified by CC (SiO_2; CH_2Cl_2/MeOH 50 : 1): **13** (3.8 g, 75%). ^{1}H-NMR ($CDCl_3$): 8.45 (*s*, 1 H); 7.97–8.03 (*m*, 3 H); 7.57–7.63 (*m*, 1 H); 7.30–7.49 (*m*, 17 H); 6.11 (*t*, *J* = 6.1, 1 H); 5.57 (*d*, *J* = 6.7, 1 H); 4.60–4.66 (*m*, 1 H); 4.38–3.42 (*m*, 1 H); 3.81–3.89 (*m*,

1 H); 3.35–3.44 (*m*, 4 H). ^{13}C-NMR ($CDCl_3$): 166.1; 162.7; 150.4; 143.2; 139.3; 133.4; 129.8; 129.0; 128.4; 128.0; 127.4; 103.0; 90.4; 87.5; 82.5; 63.4; 62.9; 53.3. HR-ESI-MS: 618.2342 ($[M+H]^+$, $C_{35}H_{32}N_5O_6^+$; calc. 618.2347).

*1-(2-Azido-1-{[1-hydroxy-3-(triphenylmethoxy)propan-2-yl]oxy}ethyl)pyrimidine-2,4(1*H*,3*H*)-dione* (**14**). To a soln. of **13** (1 g, 1.6 mmol) in MeOH (15 ml) was added 1N MeONa (1.7 ml). The mixture was stirred for 30 min at r.t., and the solvent was evaporated under reduced pressure. The residue was purified by CC (SiO_2; CH_2Cl_2/MeOH 30:1): **14** (0.7 g, 87%). ^{1}H-NMR ($CDCl_3$): 7.47 (*s*, 1 H); 7.30–7.44 (*m*, 15 H); 6.04 (*t*, *J* = 6.0, 1 H); 5.57 (*d*, *J* = 6.6, 1 H); 3.70–3.74 (*m*, 2 H); 3.54–3.68 (*m*, 1 H); 3.48 (*t*, *J* = 3.3, 1 H); 3.20–3.32 (*m*, 2 H); 1.23 (*t*, *J* = 1.2, 2 H). ^{13}C-NMR ($CDCl_3$): 163.2; 150.7; 143.3; 139.5; 128.5; 128.5; 127.8; 127.2; 102.9; 87.2; 79.7; 63.6; 62.3; 53.3. HR-ESI-MS: 514.1910 ($[M+Na]^+$, $C_{28}H_{28}N_5NaO_5^+$; calc. 536.1904).

*1-(2-Azido-1-{[1-(prop-2-yn-1-yloxy)-3-(triphenylmethoxy)propan-2-yl]oxy}ethyl)pyrimidine-2,4(1*H*,3*H*)-dione* (**15**). Prepared as described for **6**. ^{1}H-NMR ($CDCl_3$): 8.67 (*s*, 1 H); 7.49 (*s*, 1 H); 6.02 (*t*, *J* = 6.1, 1 H); 5.56 (*d*, *J* = 6.5, 1 H); 4.16 (*d*, *J* = 8.2, 2 H); 3.62–3.74 (*m*, 4 H); 3.43–3.49 (*m*, 2 H); 3.21–3.29 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$): 163.3; 150.5; 143.3; 139.7; 128.5; 127.8; 127.2; 102.6; 87.2; 82.8; 69.5; 63.45; 58.5; 53.2. HR-ESI-MS: 552.2242 ($[M+H]^+$, $C_{31}H_{30}N_5O_5^+$; calc. 552.2241).

*1-{6,7,9,10-Tetrahydro-7-[(triphenylmethoxy)methyl]-4*H*-[1,2,3]triazolo[5,1-*f*][1,4,7]dioxazonin-9-yl}pyrimidine-2,4(1*H*,3*H*)-dione* (**16**). Prepared as described for **7**. ^{1}H-NMR ($CDCl_3$): 8.85 (*s*, 1 H); 7.65 (*s*, 1 H); 7.26–7.28 (*m*, 16 H); 6.03 (*t*, *J* = 6.0, 1 H); 5.68 (*d*, *J* = 6.2, 1 H); 5.10 (*d*, *J* = 8.2, 1 H); 4.96 (*d*, *J* = 8.5, 1 H); 4.76 (*d*, *J* = 8.7, 2 H); 3.70–3.86 (*m*, 2 H); 3.30–3.40 (*m*, 1 H); 3.02–3.14 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$): 163.0; 150.2; 143.2; 139.8; 134.4; 128.4; 127.9; 127.3; 102.5; 86.9; 84.3; 83.8; 70.3; 64.4; 62.9; 62.8; 52.6. HR-ESI-MS: 552.2243 ($[M+H]^+$, $C_{31}H_{30}N_5O_5^+$; calc. 552.2241).

*1-[6,7,9,10-Tetrahydro-7-(hydroxymethyl)-4*H*-[1,2,3]triazolo[5,1-*f*][1,4,7]dioxazonin-9-yl]pyrimidine-2,4(1*H*,3*H*)-dione* (**17**). Prepared as described for **8**. ^{1}H-NMR ((D_6)DMSO): 11.43 (*s*, 1 H); 7.79 (*s*, 1 H); 7.50–7.64 (*m*, 1 H); 5.77–5.85 (*m*, 1 H); 5.62 (*d*, *J* = 6.6, 1 H); 5.06–5.10 (*m*, 1 H); 4.90 (*t*, *J* = 8.8, 1 H); 4.72–4.84 (*m*, 2 H); 3.60–3.66 (*m*, 2 H); 3.41–3.45 (*m*, 2 H). ^{13}C-NMR ((D_6)DMSO): 163.3; 150.3; 140.6; 135.6; 135.0; 101.4; 84.3; 84.2; 68.8; 61.3; 60.6; 52.7. HR-ESI-MS: 310.1149 ($[M+H]^+$, $C_{12}H_{16}N_5O_5^+$; calc.310.1146).

*4-Amino-1-{6,7,9,10-tetrahydro-7-[(triphenylmethoxy)methyl]-4*H*-[1,2,3]triazolo[5,1-*f*][1,4,7]dioxazonin-9-yl}pyrimidin-2(1*H*)-one* (**18**). Prepared as described for **9**. ^{1}H-NMR ($CDCl_3$): 7.61 (*s*, 2 H); 7.26–7.28 (*m*, 17 H); 6.11 (*m*, 1 H); 5.59–5.67 (*m*, 1 H); 5.08–5.14 (*m*, 1 H); 4.90–5.00 (*m*, 1 H); 4.70–4.86 (*m*, 2 H); 3.75–3.87 (*m*, 2 H); 3.28–3.88 (*m*, 1 H); 3.01–3.11 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$): 165.8; 154.7; 143.4; 140.7; 135.2; 134.5; 128.1; 127.9; 127.0; 94.1; 85.9; 84.4; 81.4; 68.7; 63.2; 61.8; 52.5. HR-ESI-MS: 551.2398 ($[M+H]^+$, $C_{31}H_{31}N_6O_4^+$; calc. 551.2401).

*4-Amino-1-[6,7,9,10-tetrahydro-7-(hydroxymethyl)-4*H*-[1,2,3]triazolo[5,1-*f*][1,4,7]dioxazonin-9-yl]-pyrimidin-2(1*H*)-one* (**19**). Prepared as described for **8**. ^{1}H-NMR ($CDCl_3$): 7.76 (*s*, 1 H); 7.53 (*s*, 1 H); 7.45 (*s*, 1 H); 7.24 (*s*, 1 H); 5.80 (*d*, *J* = 6.5, 1 H); 4.92–4.96 (*m*, 1 H); 4.88–4.92 (*m*, 2 H); 4.71–4.79 (*m*, 2 H); 3.60–4.70 (*m*, 2 H); 3.63 (*d*, *J* = 3.3, 1 H); 3.15 (*s*, 2 H); 1.89 (*s*, 1 H). ^{13}C-NMR ($CDCl_3$): 165.7; 154.7; 141.0; 135.5; 134.8; 93.9; 84.6; 83.6; 68.9; 61.5; 60.7; 52.7. HR-ESI-MS: 309.1308 ($[M+H]^+$, $C_{12}H_{17}N_6O_4^+$; calc. 309.1306).

2′,3′-O-*(1-Methylethylidene)uridine* (**20**). To a soln. of uridine (24.40 g, 0.1 mol) in dry acetone (500 ml) was added anh. $CuSO_4$ (32.00 g, 0.2 mol) and conc. H_2SO_4 (0.7 ml). The mixture was stirred at 40° for 48 h and filtered. The filtrate was then neutralized with $NaHCO_3$ and filtered. The precipitate was washed with actone several times and the filtrate was concentrated. The residue was dissolved in AcOEt (500 ml) and washed with H_2O (3 × 100 ml). The org. layer was dried (Na_2SO_4) and concentrated, and the crude product was purified by CC (SiO_2; CH_2Cl_2/MeOH 30:1): **20** (22.5 g, 80%). ^{1}H-NMR (300 MHz, $CDCl_3$) 8.86 (*s*, 1 H); 7.37 (*d*, *J* = 8.1, 1 H); 5.74 (*d*, *J* = 8.2, 1 H); 5.57 (*d*, *J* = 3.0, 1 H); 5.05 (*dd*, *J* = 6.4, 3.0, 1 H); 4.97 (*dd*, *J* = 6.5, 3.4, 1 H); 4.33–4.26 (*m*, 1 H); 3.93 (*d*, *J* = 12.3, 1 H); 3.86–3.77 (*m*, 1 H); 1.58 (*s*, 3 H); 1.37 (*s*, 3 H).

2′,3′-O-*(1-Methylethylidene)-5′*-O-*(prop-2-yn-1-yl)uridine* (**21**). Prepared as described for **6**. ^{1}H-NMR (300 MHz, $CDCl_3$) 9.07 (*s*, 1 H); 7.55 (*d*, *J* = 8.1, 1 H); 5.88 (*d*, *J* = 1.9, 1 H); 5.71 (*d*, *J* = 8.1, 1 H); 4.80 (*t*, *J* = 1.9, 2 H); 4.40 (*dd*, *J* = 6.2, 2.6, 1 H); 4.18 (*t*, *J* = 2.5, 2 H); 3.81 (*dd*, *J* = 10.3, 2.8, 1 H); 3.72 (*dd*, *J* = 10.4, 4.0, 1 H); 2.48 (*t*, *J* = 2.3, 1 H); 1.57 (*s*, 3 H); 1.34 (*s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$)

163.6; 150.2; 141.3; 114.1; 102.1; 93.1; 85.4; 84.9; 81.0; 78.6; 75.4; 69.7; 58.6; 27.1; 25.2. HR-ESI-MS: 323.1234 ($[M+H]^+$, $C_{15}H_{19}N_2O_6^+$; calc. 323.1238), 645.2393 ($[2M+H]^+$, $C_{30}H_{37}N_4O_{12}^+$; calc. 645.2402).

5′-O-(Prop-2-yn-1-yl)uridine (**22**). To a soln. of **21** (3.00 g, 9.32 mmol) in MeOH (10 ml) was added 1N HCl (100 ml). The mixture was stirred at 45° for 30 min. The solvent was concentrated to one-fifth of the original volume and extracted with AcOEt (5 × 20 ml). The org. layer was dried ($MgSO_4$), and the solvents were evaporated to give white solid: **22** (2.30 g, 87%). ^{1}H-NMR (300 MHz, $CDCl_3$) 9.64 (*s*, 1 H); 7.91 (*d*, *J* = 8.1, 1 H); 5.89 (*s*, 1 H); 5.74 (*d*, *J* = 6.8, 1 H); 4.28 (*s*, 3 H); 3.91 (*d*, *J* = 10.4, 1 H); 3.73 (*d*, *J* = 10.4, 2 H); 2.50 (*t*, *J* = 2.4, 1 H). ^{13}C-NMR (75 MHz, (D_6)DMSO): 163.1; 150.7; 140.6; 101.8; 88.1; 82.7; 80.0; 77.5; 73.2; 70.2; 69.3; 57.9. HR-ESI-MS: 283.0930 ($[M+H]^+$, $C_{12}H_{15}N_2O_6^+$; calc. 283.0925), 565.1769 ($[2M+H]^+$, $C_{24}H_{29}N_4O_{12}^+$; calc. 565.1776).

*1-(2-Hydroxy-1-{[1-hydroxy-3-(prop-2-yn-1-yloxy)propan-2-yl]oxy}ethyl)pyrimidine-2,4(1*H,*3*H*)-dione* (**23**). To a soln. **22** (1.80 g, 6.4 mmol) in a mixture of dioxane (100 ml) and H_2O (20 ml) was added a soln. of $NaIO_4$ (1.50 g, 7.02 mmol) in H_2O (30 ml). The resulting mixture was stirred for 1 h at r.t., and a white precipitate was formed. Additional dioxane (50 ml) was added, and the suspension was stirred for additional 15 min. The suspension was filtered, and the precipitate was washed with dioxane (2 × 25 ml). To the combined filtrate was added $NaBH_4$ (797 mg, 21.1 mmol), and the resulting mixture was stirred for 30 min. The mixture was neutralized by the addition of buffer (pyridine/AcOH 1:1 (*v*/*v*); 10 ml). The solvent was concentrated to one-third of the original volume. The mixture was washed with sat. $NaHCO_3$ (30 ml) and extracted with AcOEt (4 × 20 ml). The org. layer was dried ($MgSO_4$), concentrated, and the crude product was purified by CC (SiO_2; CH_2Cl_2/MeOH 50:1): **23** (1.50 g, 83%). ^{1}H-NMR (300 MHz, (D_6) DMSO) 7.40 (*d*, *J* = 7.5, 4 H); 5.77 (*t*, *J* = 5.5, 1 H); 5.44 (*d*, *J* = 7.8, 1 H); 3.49–3.34 (*m*, 10 H). ^{13}C-NMR (75 MHz, (D_6)DMSO): 168.5; 156.5; 146.4; 106.3; 88.9; 85.1; 83.7; 82.3; 74.4; 66.5; 65.4; 62.9. HR-ESI-MS: 285.1073 ($[M+H]^+$, $C_{12}H_{17}N_2O_6^+$; calc. 285.1081), 569.2076 ($[2M+H]^+$, $C_{24}H_{33}N_4O_{12}^+$; calc. 569.2089).

*3-{[1-Azido-3-(prop-2-yn-1-yloxy)propan-2-yl]oxy}-2,3-dihydro-7*H*-[1,3]oxazolo[3,2-*a*]pyrimidin-7-one* (**25**). To a soln. of **23** (176 mg, 0.63 mmol) in THF (10 ml) at 0° were added Et_3N (152 mg, 1.38 mmol) and MsCl (0.1 ml, 1.29 mmol) dropwise. The resulting mixture was stirred for 5–10 min. Then, H_2O (20 ml) was added, and the mixture was extracted with AcOEt (2 × 20 ml). The combined org. phases was dried ($MgSO_4$) and concentrated to give white solid. To a soln. of the white solid in CH_2Cl_2 (70 ml) was added DBU (0.95 mg, 0.63 mmol), and the mixture was then stirred at r.t. for 2 h. The mixture was concentrated, and the residue was purified by CC (SiO_2; CH_2Cl_2/MeOH 50:1) to give white solid. The solid was dissolved in DMF (10 ml), and LiN_3 (32 mg, 0.63 mmol) was added. The resulting mixture was stirred at 60° for 3 h. Then, the mixture was concentrated, and crude product was purified by CC (SiO_2; CH_2Cl_2/MeOH 80:1): **25** (133 mg, 73%; 3 steps). ^{1}H-NMR (300 MHz, $CDCl_3$) 7.64 (*d*, *J* = 7.5, 1 H); 6.07 (*dd*, *J* = 6.0, 2.2, 1 H); 6.02 (*d*, *J* = 7.4, 1 H); 4.81 (*dd*, *J* = 10.6, 6.0, 1 H); 4.62 (*dd*, *J* = 10.6, 2.3, 1 H); 4.40–4.31 (*m*, 2 H); 4.27–4.22 (*m*, 1 H); 4.21 (*dd*, *J* = 2.3, 1.1, 2 H); 3.70–3.63 (*m*, 2 H); 3.09 (*s*, 3 H); 2.54 (*t*, *J* = 2.4, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$) 172.5; 160.7; 36.1; 110.0; 88.0; 78.8; 77.9; 76.0; 73.7; 69.3; 69.2; 59.0; 37.9. HR-ESI-MS: 292.1046 ($[M+H]^+$, $C_{12}H_{14}N_5O_4^+$; calc. 292.1040).

*1-[(1*R*)-1-{[(2*S*)-1-Azido-3-(prop-2-yn-1-yloxy)propan-2-yl]oxy}-2-hydroxyethyl]pyrimidine-2,4(1*H,*3*H*)-dione* (**26**). To a soln. of **25** (291 mg, 1.0 mmol) in THF (10 ml) was added 1N NaOH (2.2 ml), and the mixture was then stirred at r.t. for 3 h. The mixture was concentrated, and the residue was purified by CC (SiO_2; CH_2Cl_2/MeOH 50:1): 26 (233 mg, 75%). ^{1}H-NMR (300 MHz, $CDCl_3$): 7.51 (*d*, *J* = 8.1, 1 H); 5.98 (*t*, *J* = 5.4, 1 H); 5.76 (*d*, *J* = 8.1, 1 H); 4.10 (*d*, *J* = 2.3, 1 H); 4.08 (*d*, *J* = 2.3, 1 H); 3.87 (*dd*, *J* = 12.1, 5.1, 2 H); 3.77 (*dd*, *J* = 12.2, 5.6, 1 H); 3.60–3.54 (*m*, 1 H); 3.52 (*d*, *J* = 2.2, 1 H); 3.51 (*s*, 1 H); 3.43 (*dd*, *J* = 13.2, 6.2, 1 H); 2.47 (*t*, *J* = 2.2, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$) 163.3, 151.5, 140.5, 136.5, 132.1, 102.0, 81.3, 74.5, 70.2, 62.7, 60.8, 60.6, 49.8. HR-ESI-MS: 310.1149 ($[M+H]^+$, $C_{12}H_{16}N_5O_5^+$; calc. 310.1146).

*1-{1-[(7*S*)-7,8-Dihydro-4*H*,6*H*-[1,2,3]triazolo[5,1-*c*][1,4]oxazepin-7-yloxy]-2-hydroxyethyl}pyrimidine-2,4(1*H,*3*H*)-dione* (**27**). Prepared as described for **7**. ^{1}H-NMR (300 MHz, (D_6)DMSO): 11.30 (*s*, 1 H); 7.63 (*s*, 1 H); 7.46 (*d*, *J* = 8.1, 1 H); 5.87–5.74 (*m*, 1 H); 5.59 (*d*, *J* = 8.0, 1 H); 5.11 (*s*, 1 H); 5.06–4.99(*m*, 1 H); 4.80 (*dd*, *J* = 18.6, 14.7, 2 H); 4.64 (*s*, 1 H); 4.52 (*d*, *J* = 38.5, 2 H); 3.88 (*d*, *J* = 18.1, 3 H); 2.50 (*d*, *J* = 1.3, 5 H). ^{13}C-NMR (75 MHz, (D_6)DMSO): 163.4; 151.7; 140.6; 136.7; 132.2; 102.1; 81.4; 74.6;

70.4; 62.8; 61.0; 60.7; 50.0. HR-ESI-MS: 310.1136 ($[M+H]^+$, $C_{12}H_{16}N_5O_5^+$; calc. 310.1136), 619.2213 ($[2M+H]^+$, $C_{24}H_{31}N_{10}O_{10}^+$; calc. 619.2219).

*2-[(7*S*)-7,8-Dihydro-4*H*,6*H*-[1,2,3]triazolo[5,1-*c*][1,4]oxazepin-7-yloxy]-2-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)ethyl Benzoate* (**28**). To a soln. of **27** (260 mg, 0.84 mmol) in dry pyridine (10 ml) was added BzCl (0.1 ml, 0.88 mmol) dropwise at 0°. Then, H_2O (20 ml) and sat. $NaHCO_3$ aq. (10 ml) were added, the mixture was extracted with AcOEt (2 × 20 ml), the org. layer was dried (Na_2SO_4) and concentrated, and the residue was purified by CC (SiO_2; CH_2Cl_2/MeOH 50:1): **28** (333 mg, 96%). ^{1}H-NMR (300 MHz, $CDCl_3$): 9.21 (*s*, 1 H); 7.92 (*d*, *J* = 7.2, 2 H); 7.56 (*d*, *J* = 6.2, 2 H); 7.43 (*t*, *J* = 7.6, 2 H); 7.23 (*d*, *J* = 11.1, 1 H); 6.35 (*t*, *J* = 6.0, 1 H); 5.76 (*d*, *J* = 8.0, 1 H); 5.24 (*d*, *J* = 9.7, 1 H); 4.89 (*d*, *J* = 14.8, 1 H); 4.60 (*dd*, *J* = 21.3, 15.0, 2 H); 4.36 (*t*, *J* = 5.5, 2 H); 4.17 (*d*, *J* = 13.3, 1 H); 4.04 (*s*, 1 H); 3.94 (*d*, *J* = 13.8, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 165.5; 162.3; 150.7; 138.7; 135.7; 133.5; 132.6; 129.7; 128.78; 128.5; 103.6; 79.8; 74.8; 72.4; 62.9; 62.5; 51.1. HR-ESI-MS: 414.1408 ($[M+H]^+$, $C_{19}H_{20}N_5O_6^+$; calc. 414.1408), 827.2731 ($[2M+H]^+$, $C_{38}H_{39}N_{10}O_{12}^+$; calc. 827.2743).

*2-(4-Amino-2-oxopyrimidin-1(2*H*)-yl)-2-{[(7*S*)-7,8-dihydro-4*H*,6*H*-[1,2,3]triazolo[5,1-*c*][1,4]oxazepin-7-yl]oxy}ethyl Benzoate* (**29**). Prepared as described for **9**. ^{1}H-NMR (300 MHz, (D_6)DMSO): 7.84 (*d*, *J* = 8.3, 2 H); 7.74–7.47 (*m*, 5 H); 7.27 (*d*, *J* = 12.3, 2 H); 6.32 (*t*, *J* = 5.9, 1 H); 5.75 (*d*, *J* = 7.4, 1 H); 5.08 (*d*, *J* = 5.3, 1 H); 4.82 (*dd*, *J* = 19.0, 14.8, 2 H); 4.63 (*d*, *J* = 14.6, 1 H); 4.28 (*dd*, *J* = 11.4, 5.9, 2 H); 3.94 (*s*, 2 H); 3.86 (*s*, 1 H). ^{13}C-NMR (75 MHz, (D_6)DMSO): 165.6; 165.0; 155.6; 140.6; 136.6; 133.6; 132.1; 129.3; 128.9; 128.7; 95.1; 79.3; 74.6; 70.6; 63.5; 61.0; 50.0. HR-ESI-MS: 413.1565 ($[M+H]^+$, $C_{19}H_{21}N_6O_5^+$; calc. 413.1568), 825.3037 ($[2M+H]^+$, $C_{38}H_{41}N_{12}O_{10}^+$; calc. 825.3063).

*4-Amino-1-(1-{[(7*S*)-7,8-dihydro-4*H*,6*H*-[1,2,3]triazolo[5,1-*c*][1,4]oxazepin-7-yl]oxy}-2-hydroxyethyl)pyrimidin-2(1*H*)-one* (**30**). To a soln. of **29** (113 mg, 0.28 mmol) in MeOH (10 ml) was added 1N NaOMe (0.3 ml) in MeOH, and the mixture was stirred at r.t. for 2.5 h. The mixture was concentrated, and the residue was purified by CC (SiO_2; CH_2Cl_2/MeOH 10:1): **31** (44 mg, 54%). ^{1}H-NMR (300 MHz, (D_6)DMSO): 7.62 (*s*, 1 H); 7.48–7.39 (*d*, 1 H); 7.17 (*d*, *J* = 18.9, 2 H); 5.93 (*t*, *J* = 5.7, 1 H); 5.70 (*d*, *J* = 7.4, 1 H); 5.12–4.95 (*m*, 1 H); 4.78 (*t*, *J* = 15.4, 2 H); 4.61 (*d*, *J* = 14.6, 1 H); 3.87 (*d*, *J* = 2.0, 2 H); 3.72 (*s*, 1 H); 3.63 (*s*, 1 H). ^{13}C-NMR (75 MHz, (D_6)DMSO): 165.5; 156.3; 141.2; 136.6; 132.1; 94.5; 81.6; 74.8; 70.3; 61.0; 60.9; 50.0. HR-ESI-MS: 309.1308 ($[M+H]^+$, $C_{12}H_{17}N_6O_4^+$; calc. 309.1306), 617.2539 ($[2M+H]^+$, $C_{24}H_{33}N_{12}O_8^+$; calc. 617.2539).

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