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SYNTHESIS OF C4' URIDYL ARYLOXAZOLES: A 'HETEROHOMOLOGATIVE' APPROACH

Paige J. Monsen and Frederick A. Luzzio*

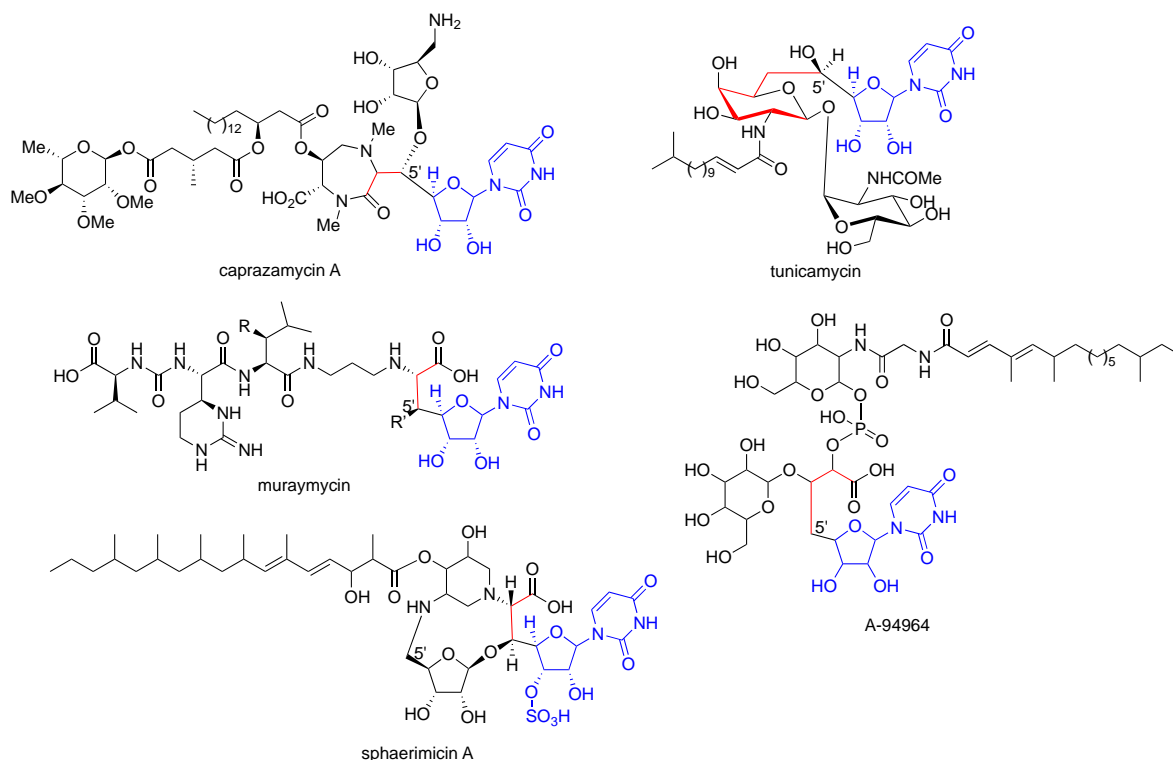
University of Louisville, Department of Chemistry, 2320 South Brook Street,
Louisville, KY 40292 USA; E-mail: faluzz01@louisville.edu

Abstract – A series of uridine-based compounds homologated at C-4' with an aryl-substituted oxazole ring were prepared. Conversion of 2',3'-*O*-cyclopentylidene uridine to the corresponding 4'-carboxylate followed by Steglich ester coupling with a series of azidoalcohols gave the corresponding azidoesters. The azidoesters were cyclized to the substituted oxazolines using Staudinger aza-Wittig conditions (PPh₃/THF). Direct treatment of the substituted oxazolines with nickel peroxide or DDQ provided the corresponding C4' uridyl aryloxazoles. Removal of the 2',3'- *O*-cyclopentylidene group was accomplished using 70% aqueous trifluoroacetic acid which afforded the target C4'-heterocyclic nucleoside analogues. The sequence could be accomplished with nitrogen or oxygen-substituted aryl azidoalcohol precursors which gave rise to the corresponding aryl-substituted C4'-oxazolyl uridine derivatives. The oxygen or nitrogen-substituted aryloxazoles underwent further derivatization to deliver ester and amide derivatives.

INTRODUCTION

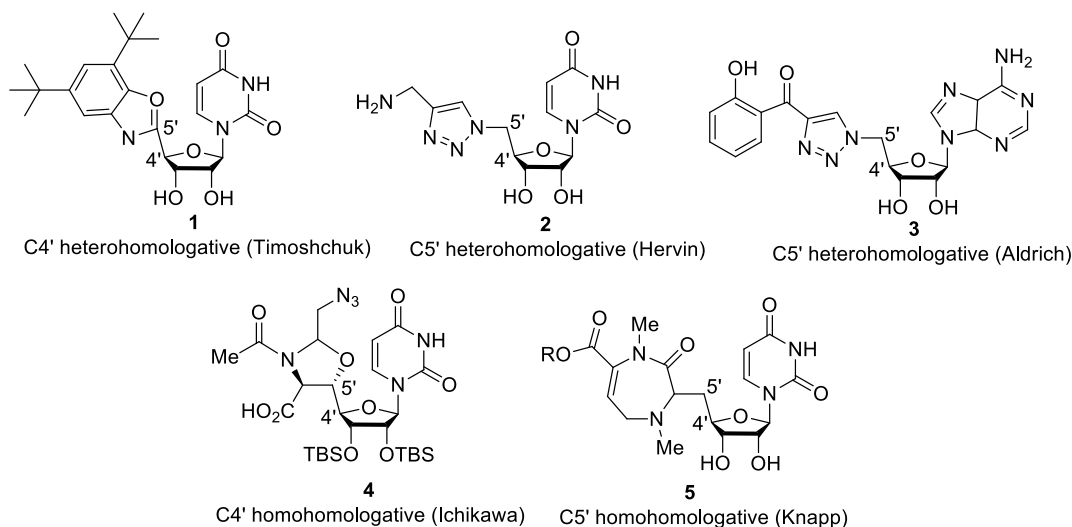
Bioactive nucleoside analogues can comprise two distinct classes of compounds and these classes include both established and experimental therapeutics in the realm of anti-infectives. Single-unit nucleoside analogues (i.e. one ribosyl/one heterocyclic base unit) have gained widespread use as antivirals¹ and have additionally seen use in the anticancer arena.² Apart from the general antiviral nucleoside analogues, there remains the class of compounds referred to as the 'nucleoside antibiotics', compounds which are naturally-occurring and many of which are based on the homologated uridine scaffold.³ The uridine class of bioactive natural products have attracted recent attention as antimicrobials whereby their activity is centered on the inhibition of bacterial cell wall construction by interfering with glycopeptide and peptidoglycan biosynthesis.⁴ Furthermore, the nucleoside classes of antibiotics have been identified as the

most promising expedients for the combat of multidrug-resistant (MDR) microorganisms.⁵ One, two and even six carbon homologs at C5' comprise the uridine-based backbone of compounds such as caprazomycin A,⁶ tunicamycin,⁷ muraymycins,⁸ A-94964,⁹ sphaerimicin A¹⁰ and other naturally-occurring antibiotics such as liposidomycin.¹¹ A goal is the design of new nucleoside antibiotic analogues with the retention of the uridine core while extending the scaffold with a series of heterocyclic structure where lipids and carbohydrates may be attached in mimicking the natural compounds.

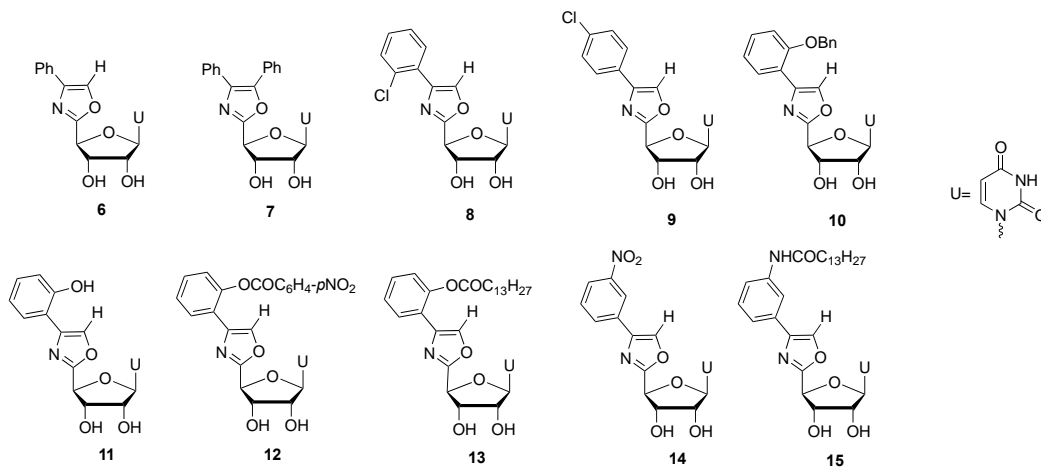


We place the core structures of C4' or C5' uridinyl heterocycles in two categories, 'heterohomologative' and 'homohomologative.' The designations depend on the position of the heteroatoms with respect to C4' or C5' and whether the carbon(s) of the heterocycle are contiguous with C5'. For example, the C4' uridinyl benzoxazole **1**, which was of interest as a nucleoside with fluorescent properties,¹² has C5' of the uridine component embedded within the heterocycle (C2 of the oxazole). The 5' carbon of **1** is flanked by a nitrogen and oxygen, terminating the carbons of the sugar and is heterohomologative. In the C5'-uridinyl triazole **2**, produced by a click reaction of the corresponding 5'-nucleosidic azide, the carbons of the nucleoside are terminated by a triazole nitrogen so that the ring carbons of the triazole are not contiguous with the ribose C5' carbon.¹³ Similarly, the click derived triazole of **3**, in which C5' is connected to a ring nitrogen, is also heterohomologative as the ribose carbons are terminated at C5'.¹⁴ The Ichikawa¹⁵ and Knapp¹⁶ intermediates (**4** and **5** respectively) contain oxazoline and diazepine heterocycles. The

connectivity of **4** and **5** are homohomologative as the C5' of the ribose ring are extended two carbons which lie within the heterocycle.

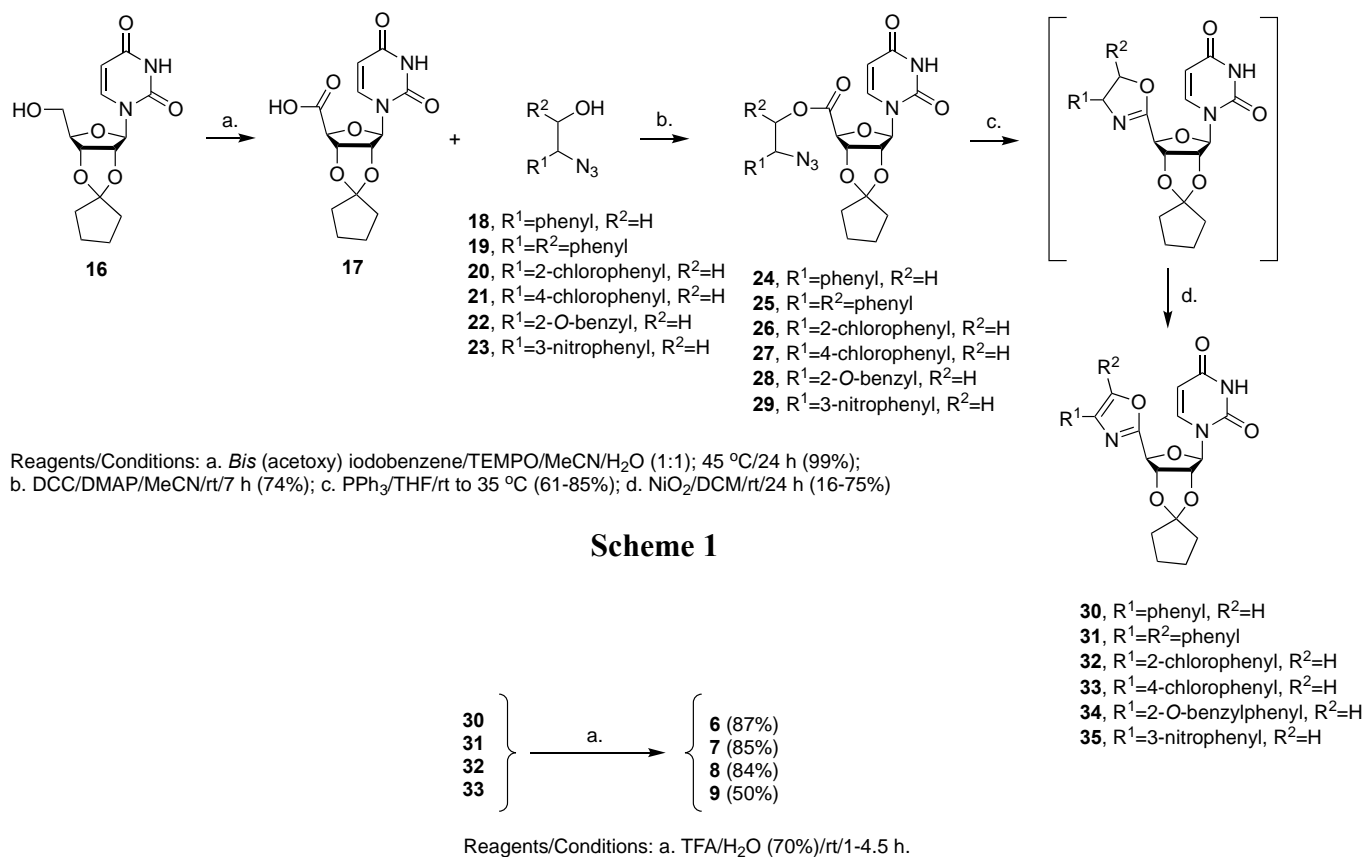


Our general strategy involves the design of uridine-based scaffolds inspired by natural product platforms which have not yet been ‘seen’ by the pathogenic microbe population. Furthermore, the elaboration of a natural product or its central “active” scaffold need not be seemingly complex, but would involve the addition or replacement of minimal structural features that would enhance or augment the activity of the central core.¹⁷ In turn such a “function-oriented” synthesis (FOS) of analogues for biological evaluation would be less complex, more rapid, and allowing for a great many targets at decreased expense. The series of targets detailed herein **6-15** comprises an oxazole ring whereby C2 of the 5-membered nitrogen-oxygen heterocycle is C5' of uridine. Since the C5' of uridine is flanked by the nitrogen and the oxygen of the oxazole we designate targets **6-15** as ‘heterohomologative.’ Further structural diversity is provided by substitution with aromatic components at positions 4 and 5 of the oxazole ring, and these components may be substituted at various positions with chlorine, nitrogen or oxygen.



RESULTS AND DISCUSSION

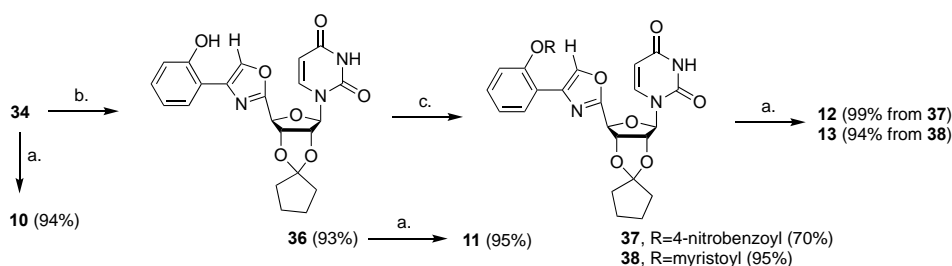
The synthesis of targets **6-15** commences with the preparation of the 2',3'-*O*-cyclopentylideneuridine-5'-carboxylic acid **17** from 2',3'-*O*-cyclopentylideneuridine **16** (Scheme 1).¹⁸ As noted in the earlier report, we find that employment of the cyclopentylidene group allows an expedient in deprotection in later steps as compared to the more conventional isopropylidene or cyclohexylidene groups. 2',3'-*O*-Cyclopentylideneuridine **16**, an intermediate that we introduced during an earlier antiviral



Scheme 2

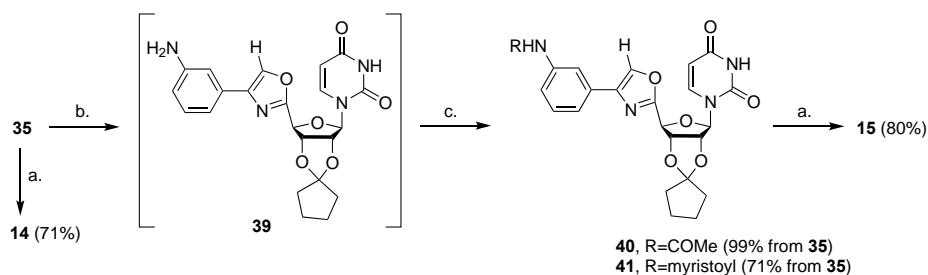
synthesis study, was oxidized to the 5'-carboxylic acid **17** (99%) using bis(acetoxyl)iodobenzene (BAIB) and (2,2,6,6-piperidiny-1-yl)oxy (TEMPO). The nucleosidic C5' carboxylic acid **17** was coupled with the 2-azido-2-phenylethanol **18-23** under Steglich conditions (DCC/DMAP/MeCN)¹⁹ to provide the intermediate uridyl carboxylic azidoesters **24-29**. The azidoalcohols **18-23** were obtained by a synthetic route involving azide-promoted ring-opening of the corresponding substituted oxiranes. After chromatographic purification, **18-23** were used as mixtures of stereoisomers in the Steglich esterification. The esterifications went smoothly and afforded the uridyl azidoesters **24-29** in yields of 61-85%. Not surprisingly the basic structure of the azidoalcohol coupling partners **18-23**, with the exception of the

(diphenyl)azidoalcohol **19**, contained a primary hydroxyl group and was an expedient toward the Steglich esterification. After nominal purification and structural confirmation, the azido esters **24-29** were directly cyclized (triphenylphosphine/THF/rt) to the intermediate oxazolines through the aza-Wittig reaction.^{20,21} The intermediate oxazolines were then nominally purified, characterized and were then directly aromatized to the corresponding oxazoles **30-35** using either 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in benzene or freshly-prepared nickel peroxide (NiO₂).^{22,23} In general, the cyclopentylidene protecting group of the C4'-uridyl oxazoles **30-33** were smoothly removed with aqueous trifluoroacetic acid (0 °C to rt, 1-4.5 h) to deliver targets **6-9** in the yield range of 85-97% (Scheme 2). In the 2-*O*-benzyl(aryl)oxazolyl series, removal of the cyclopentylidene group of **34** (70% TFA/H₂O/0 °C to rt/2.5-5.5 h) afforded the *O*-benzylated target **10** (94%) (Scheme 3). Debenzylation of **34** (Pd-C/H₂/MeOH/rt/45 min) provided the phenolic oxazole nucleoside **36** (93%) which then gave target **11** (95%) upon removal of the cyclopentylidene group (70% TFA/H₂O/0 °C to rt/1-2 h). The nitro group of **35** was reduced (Pd-C/H₂/MeOH/rt) to provide the intermediate uridyl (aminophenyl) oxazole **39** which was not isolated but characterized as the acetamide (Ac₂O/pyridine/rt/4.5 h) **40** (99%). To introduce a lipid chain present in naturally-occurring nucleoside antibiotics, acylation of amine intermediate **36** with myristoyl chloride (DMAP/CH₂Cl₂/0 °C to rt/5 h) afforded the myristamide **41** (71% from **35**). The cyclopentylidene protecting group of myristamide **41** was removed with aqueous trifluoroacetic acid (0 °C to rt/3.5 h) to give the target (amidophenyl)oxazole nucleoside **15** (80%) as a crystalline solid (Scheme 4).



Reagents/Conditions: a. 70% TFA/H₂O/0 °C to rt/1-2 h; b. H₂, Pd-C (cat)/MeOH/rt/12 h; c. 4-nitrobenzoyl chloride or myristoyl chloride/DMAP/CH₂Cl₂, 0 °C to rt/30 min.

Scheme 3



Reagents/Conditions: a. 70% TFA/H₂O/0 °C to rt/1-2 h; b. H₂, Pd-C (cat), MeOH/rt/45 min; c. Ac₂O/pyridine/rt/4.5 h; or myristoyl chloride/DMAP/CH₂Cl₂/0 °C to rt/5 h.

Scheme 4

Targets **6-15** were evaluated for antimicrobial activity and selected examples involving strains of *M. tuberculosis* (Mtb, Gram+), *S. aureus* (Gram+), *E. coli* (Gram-) and *P. aeruginosa* (Gram-) are listed herein. In the Mtb (MC2 6230) assay, all compounds exhibited an MIC of greater than 64 μM (kanamycin A, $\leq 0.5 \mu\text{M}$, positive control). In the *S. aureus* (ATCC 25923) assay, all compounds except for **15** showed an MIC of greater than 128 μM . The myristoylamide **15** inhibited *S. aureus* with an MIC of 16 μM (kanamycin A, 4 μM). Target **6** inhibited *E. coli* (MC1061) at 64 μM while the remainder of the targets (**7-15**) showed inhibition at a MIC greater than 128 μM (kanamycin A, 1 μM). Inhibition experiments involving *P. aeruginosa* (ATCC 27853) revealed that all targets exhibited an MIC of greater than 128 μM (kanamycin A, $\leq 0.5 \mu\text{M}$).

In conclusion, reported herein is a basic minimalist approach to potential new classes of nucleoside antibiotics which involved retention of the uridine scaffold. The scaffold is elaborated through a scheme we term C5' 'heterohomologation.' While many of the naturally-occurring uridine-based nucleoside antibiotics consists of homologated carbon-carbon bonds at C5', the analogues described herein incorporate C5' into the oxazole system. Hence, our heterohomologation strategy focused on the oxazole ring in which the 2-carbon is actually the 5'-carbon of the nucleoside, and aryl-substitutions of the oxazole ring at the 4-position, 5-position (or both) complete the backbone of the analogue. It was demonstrated that functionalization of the aryl rings of the oxazole backbone with oxygen or nitrogen provided anchor points for lipids. For future work the anchor points will include those for amino acid side chains and/or sugar side chains, common scaffolds found in the native natural products thereby providing the necessary diversity for lead structures. A significant drawback were the compromised yields realized in the oxidative dehydrogenation of the intermediate oxazolines to the product oxazoles, and is a step which will provide additional focus for new methods development. Given that targets **6-15** were identified as core structures, and their synthesis was the goal of this communication, the low antimicrobial activities as judged against an established antibiotic was understandable.

EXPERIMENTAL

Solvents and reagents were ACS grade and were used as commercially supplied with the exception of hexane. ACS grade hexane was purified for column chromatography according to the method described by Perrin.²⁴ All aqueous solutions, washes and extractions utilized deionized H₂O. Tetrahydrofuran (THF) was distilled under nitrogen from a mixture of sodium/benzophenone. Analytical thin-layer chromatography (TLC) utilized 0.25 mm pre-cut glass-backed plates (Merck, Silica Gel 60 F₂₅₄). Thin-layer chromatograms were visualized during chromatographic, extraction and reaction runs by rapidly dipping the plates in anisaldehyde/EtOH/sulfuric acid stain or phosphomolybdic acid/ EtOH stain and heating (hot plate). Carbohydrate intermediates and products were visualized on TLC by rapidly

dipping the plate in 10% sulfuric acid/EtOH and charring (hot plate). Flash-column chromatography utilized silica gel 60 (E. Merck 9385-9, 230-400 mesh). Melting points were taken on a Mel-Temp apparatus. Extracts and chromatographic fractions were concentrated with a Büchi rotavapor under H₂O aspirator vacuum. Disposal of metal waste was performed in accordance with the National Research Council publication *Prudent Practices in the Laboratory*.²⁵ Optical rotations were measured with a Jasco P2000 polarimeter. Nuclear magnetic resonance (¹H and ¹³C NMR) spectra were recorded with Varian VNMRS 400 (¹³C NMR-100 MHz) and Oxford AS 500 MHz (¹³C NMR-125 MHz) instruments using CDCl₃ and DMSO-*d*₆ as NMR solvents. Infrared spectra (Fourier Transform Infrared Spectroscopy, FTIR) were recorded with a Perkin-Elmer Spectrum 100 instrument or Agilent instruments. High Resolution Mass Spectra (HRMS) were measured at the Indiana University Mass Spectrometry Facility.

(3a'S,4'S,6'R,6a'R)-6'-(2,4-Dioxo-3,4-dihydropyrimidine-1(2H)-yl)tetrahydrospiro[cyclopentane-1,2'-furo[3,4-*d*][1,3]dioxole]-4'-carboxylic acid (17): To a solution of 2',3'-*O*-cyclopentylideneuridine **16** (0.55 g, 1.79 mmol) and MeCN/H₂O, 1:1 (3.0 mL) were added bis(acetoxyiodo)benzene (BAIB, 1.39 g, 4.3 mmol) and 2,2,6,6-tetramethylpiperidin-1-yl (TEMPO, 0.056 g, 0.36) mmol. The reaction mixture was stirred at 45 °C (16 h) and upon completion of the reaction as indicated by TLC, the solvents were removed under reduced pressure and the resulting residue was triturated with Et₂O. The precipitate was filtered, and dried under vacuum to yield the protected uridyl carboxylic acid **17** as a white solid (0.58 g, 98%); *R*_f = 0.19 (EtOAc/MeOH/H₂O, 85:10:5); [*α*]_D²⁰ -29.7 (*c* 0.2, MeOH); mp 167-169 °C; FT-IR (neat) 3467, 2962, 2828, 1690, 1271, 1091 cm⁻¹; ¹H NMR (MHz, DMSO) δ 12.74 (s, br, 1H), 11.34 (s, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 5.77 (s, 1H), 5.61 (dd, *J* = 8.0, 2.0 Hz, 1H), 5.17 (dd, *J* = 6.0, 2.0 Hz, 1H), 5.12 (d, *J* = 6.4 Hz, 1H), 4.58 (d, *J* = 1.6 Hz, 1H), 1.88-1.86 (m, 2H), 1.71-1.61 (m, 6H) ppm; ¹³C NMR (175 MHz, DMSO) δ 170.8, 163.5, 150.8, 145.0, 121.4, 101.3, 95.8, 86.6, 84.0, 83.6, 35.3, 23.1, 22.7 ppm. HRMS (+ESI) calcd. for C₁₄H₁₆N₂O₇ [M+Na] 347.0850; found 347.0850.

General procedure for the preparation of the azidoalcohols (18-23): To a solution of the selected epoxide (1.0 g, 6.5 mmol) in DMF (5 mL) were added NaN₃ (1.26 g, 19.4 mmol) and NH₄Cl (693 mg, 13.0 mmol) and reaction mixture was stirred at 55 °C (16 h). After completion of the reaction as indicated by TLC, the reaction mixture was diluted with H₂O (10 mL) and the resulting mixture was extracted with CH₂Cl₂ (3x10 mL). The organic layers were combined, washed with H₂O (2x10 mL), brine (2x15 mL), and dried over anhydrous MgSO₄. Removal of the drying agent by filtration and concentration of the filtrate under reduced pressure gave the azidoalcohol as a crude residue. Purification was accomplished using flash column chromatography (hexanes/EtOAc, 2:1) to provide the azidoalcohols **18-23**.

2-Azido-2-phenylethan-1-ol (18): Prepared from 2-phenyloxirane using the procedure detailed above. The spectral details were consistent with those previously reported.²⁶

2-Azido-1,2-diphenylethan-1-ol (19): Prepared from 2,3-diphenyloxirane using the procedure detailed above. The spectral details were consistent with those previously reported.²⁷

2-Azido-2-(2-chlorophenyl)ethan-1-ol (20): Prepared from 2-(2-chlorophenyl)oxirane using the procedure detailed above. The spectral details were consistent with those previously reported.²⁸

2-Azido-2-(4-chlorophenyl)ethan-1-ol (21): Prepared from 2-(4-chlorophenyl)oxirane using the procedure detailed above. The spectral details were consistent with those previously reported.²⁹

2-Azido-2-(2-(benzyloxy)phenyl)ethan-1-ol (22): Prepared from 2-(2-(benzyloxy)phenyl)oxirane²⁸ using the procedure detailed above. R_f 0.11 (hexane/EtOAc, 8:1); FT-IR (neat) 3377, 3035, 2932, 2095, 1601, 1490, 1450, 1241, 1015 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.44-7.28 (m, 7H), 7.05-6.98 (m, 2H), 5.22 (dd, $J = 7.8, 4.2$ Hz, 1H), 5.12 (s, 2H), 3.84 (ddd, $J = 11.6, 7.6, 4.0$ Hz, 1H), 3.73 (ddd, $J = 11.4, 8.0, 5.0$ Hz, 1H), 1.93 (br s, 1H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 155.9, 136.76, 129.7, 128.8, 128.3, 127.9, 127.5, 125.0, 121.4, 112.3, 70.5, 65.4, 62.2 ppm. HRMS (+ESI) calcd. for $\text{C}_{15}\text{H}_{15}\text{N}_3\text{O}_2$ [M+Na] 292.1056; found 292.1057.

2-Azido-2-(3-nitrophenyl)ethan-1-ol (23): Prepared from 2-(3-nitrophenyl)oxirane using the procedure detailed above. The spectral details were consistent with those previously reported.³⁰

1-((3a'S,4'S,6'R,6a'R)-4'-(4-Phenyloxazol-2-yl)tetrahydrospiro[cyclopentane-1,2'-furo[3,4-d][1,3]dioxol]-6'-yl)pyrimidine-2,4(1H,3H)-dione (30) through intermediate azidoester (24): To a solution of carboxylic acid **17** (93 mg, 0.287 mmol) in MeCN (3.0 mL) was added azidoalcohol **18** (56 mg, 0.344 mmol). DCC (89 mg, 0.430 mmol) and DMAP (35 mg, 0.287 mmol) were added, and the reaction mixture was stirred under nitrogen (7 h) at rt. The MeCN was evaporated under reduced pressure and cold EtOAc was added. The precipitate was removed by filtration and the filtrate was concentrated under reduced pressure to give a crude residue. The residue was passed through a short column of flash silica (toluene/EtOAc, 3:1) to give **2-azido-2-phenylethyl (3a'S,4'S,6'R,6a'R)-6'-(2,4-dioxo-3,4-dihydro-pyrimidin-1(2H)-yl)tetrahydrospiro[cyclopentane-1,2'-furo[3,4-d][1,3]dioxole]-4'-carboxylate (24)** (100 mg, 74%) as a white solid after trituration with CH_2Cl_2 /pentane; R_f 0.43 (toluene/EtOAc, 1:1). FT-IR (neat) 3208, 3071, 2965, 2877, 2102, 1743, 1690, 1454, 1378, 1270, 1093 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3 , 2 isomers) δ 8.76 (s br, 1H), 8.70 (s br, 0.65H), 7.41-7.25 (m, 9.9H), 5.72 (d, $J = 7.6$ Hz, 1.65H), 5.53 (s, 0.65H), 5.51 (s, 1H), 5.37 (dd, $J = 5.8, 1.4$ Hz, 1H), 5.31 (dd, $J = 6.9, 1.6$ Hz, 0.65H), 5.11 (d, $J = 6.4$ Hz, 1H), 5.08 (d, $J = 6.4$ Hz, 0.65H), 4.86 (dd, $J = 9.4, 3.4$ Hz, 1H), 4.80-4.76 (m, 1.65H), 4.43 (dd, $J = 11.6, 3.6$ Hz, 1H), 4.32-4.31 (m, 1.65H), 4.22 (t, $J = 6.0$ Hz, 0.65H), 4.12 (dd, $J = 11.4, 9.4$ Hz, 1H), 1.98-1.96 (m, 3.3), 1.80-1.71 (m, 9.9H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 169.4, 163.2, 150.7, 144.1, 143.9, 135.5, 131.0, 129.1, 127.3, 127.2, 123.3, 123.2, 102.9, 98.6, 98.4, 87.8, 87.6, 84.5, 84.3, 68.2, 68.0, 64.2, 64.0, 6.1, 35.9, 23.7, 23.3 ppm. To a solution of azidoester **24** (80 mg, 0.17 mmol) in dry THF (2 mL) was added triphenylphosphine (67 mg, 0.25 mmol). The reaction mixture was stirred

under nitrogen at 35 °C (16 h). The THF was removed under reduced pressure to obtain the crude oxazoline which was passed through a short column of flash silica (toluene/EtOAc, 2:1). To a solution of the intermediate oxazoline (73 mg, 0.15 mmol) in dry CH₂Cl₂ (3 mL) was added nickel peroxide (NiO₂, 50 molar excess). The reaction mixture was stirred under nitrogen (16 h) at rt. The excess NiO₂ was removed by vacuum filtration while washing with CH₂Cl₂. The resulting filtrate was concentrated under reduced pressure to obtain the crude uridyl oxazole. The crude product was submitted to flash-column chromatography (toluene/EtOAc, 2:1) to provide **30** (54 mg, 75% over two steps) as a white solid after trituration with CH₂Cl₂/pentane. Mp 105-107 °C; *R*_f 0.49 (toluene/EtOAc, 1:1); FT-IR (neat) 3056, 2928, 2856, 1692, 1452, 1380, 1269, 1109 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.09 (s br, 1H), 7.90 (s, 1H), 7.68 (d, *J* = 7.2 Hz, 2H), 7.41-7.37 (m, 4H), 5.96 (s, 1H), 5.67 (d, *J* = 8.4 Hz, 1H), 5.38-5.34 (m, 2H), 5.08 (dd, *J* = 5.6, 1.6 Hz, 1H), 2.08-2.06 (m, 2H), 1.80-1.73 (m, 6H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 162.9, 160.7, 150.1, 141.5, 134.4, 130.4, 129.0, 128.6, 125.7, 124.2, 102.8, 94.4, 84.8, 83.5, 81.7, 36.5, 36.5, 23.7, 23.3 ppm. HRMS (+ESI) calcd. for C₂₂H₂₁N₃O₆ [M+Na] 446.1323; found 446.1324.

1-((3a'S,4'S,6'R,6a'R)-4'-(4,5-Diphenyloxazol-2-yl)tetrahydrospiro[cyclopentane-1,2'-furo[3,4-d][1,3]dioxol]-6'-yl)pyrimidine-2,4(1H,3H)-dione (31) through intermediate azidoester (25)

To a solution of the uridylcarboxylic acid **17** (108 mg, 0.33 mmol) and azidoalcohol **19** (119 mg, 0.49 mmol) in MeCN (3 mL) were added DCC, 103 mg, 0.49 mmol) and DMAP (41 mg, 0.33 mmol). The reaction mixture was then stirred under nitrogen (12 h) at rt. The MeCN was removed under reduced pressure and cold EtOAc was added. The precipitate was filtered removed by filtration and the filtrate was concentrated under reduced pressure to obtain a crude residue. The residue was passed through a short flash column to provide the intermediate **2-azido-1,2-diphenylethyl (3a'S,4'S,6'R,6a'R)-6'-(2,4-dioxo-3,4-dihydropyrimidin-1-(2H)-yl)tetrahydrospiro[cyclopentane-1,2'-furo[3,4-d][1,3]dioxole]-4'-carboxylate (25)** as a white solid (111 mg, 61%) after trituration with CH₂Cl₂/pentane. *R*_f 0.36 (toluene/EtOAc, 2:1). FT-IR (neat) 3024, 2963, 2860, 2105, 1743, 1677, 1454, 1377, 1267, 1092 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, 2 isomer) δ 8.23 (s br, 1H), 7.92 (s br, 1H), 7.34-7.18 (m, 22H), 5.99 (d, *J* = 6.8 Hz, 1H), 5.95 (d, *J* = 6.4 Hz, 1H), 5.67 (d, *J* = 8.0 Hz, 1H), 5.63 (d, *J* = 8.0 Hz, 1H), 5.56 (s, 1H), 5.48 (s, 1H), 5.13 (dd, *J* = 6.2, 1.8 Hz, 1H), 5.06 (d, *J* = 6.0 Hz, 1H), 5.00 (d, *J* = 6.8 Hz, 1H), 4.94-4.92 (m, 3H), 4.62-4.60 (m, 2H), 1.97-1.95 (m, 4H), 1.73-1.62 (m, 12H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 162.7, 158.8, 150.0, 146.8, 141.3, 135.8, 131.8, 129.3, 129.0, 128.9, 128.7, 128.3, 128.0, 126.8, 124.3, 102.7, 94.0, 84.9, 83.2, 81.3, 36.5, 36.4, 23.8, 23.3 ppm. The diphenyl azidoester **25** (111 mg, 0.20 mmol) was directly dissolved in dry THF (3 mL) and triphenylphosphine (80 mg, 0.305 mmol) was added. The reaction mixture was then stirred under nitrogen (16 h) at 35 °C. After consumption of the starting material, the THF was removed under reduced pressure to obtain a crude residue containing triphenylphosphine oxide. The triphenylphosphine oxide was then removed using a

short flash silica column (toluene/EtOAc, 2:1) to provide the oxazoline (102 mg, 0.20 mmol) which was directly dissolved in benzene (2 mL). To the solution was added DDQ (92 mg, 0.40 mmol) and the mixture was stirred under nitrogen (16 h) at 80 °C. Upon completion of the reaction, the benzene was removed under reduced pressure and the residue was submitted to flash-column chromatography (hexane/EtOAc, 3:1). The uridyl oxazole **31** was obtained as a light-brown solid (22 mg, 22% over two steps) after trituration with CH₂Cl₂/pentane; *R*_f 0.35 (hexane/EtOAc, 1:1); mp 99-102 °C; FT-IR (neat) 3064, 2927, 2860, 1691, 1451, 1379, 1267, 1107 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.06 (s br, 1H), 7.61-7.53 (m, 5H), 7.38-7.37 (m, 6H), 6.04 (s, 1H), 5.67 (d, *J* = 8.4 Hz, 1H), 5.40 (s, 2H), 5.08 (d, *J* = 5.2 Hz, 1H), 2.10-2.09 (m, 2H), 1.80-1.73 (m, 6H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 162.7, 158.8, 150.0, 146.8, 141.3, 135.8, 131.8, 129.3, 129.0, 128.9, 128.7, 128.3, 128.0, 126.8, 124.3, 102.7, 94.0, 84.9, 83.2, 81.3, 36.5, 36.4, 23.8, 23.3 ppm. HRMS (+ESI) calcd. for C₂₈H₂₅N₃O₆ [M+H]⁺ 500.1816; found. 500.1813.

1-((3a'S,4'S,6'R,6a'R)-4'-(4-(2-Chlorophenyl)oxazol-2-yl)tetrahydrospiro[cyclopentane-1,2'-furo[3,4-*d*][1,3]dioxol]-6'-yl)pyrimidine-2,4(1*H*,3*H*)-dione (32) through intermediate azidoester (26):

To a solution of uridylcarboxylic acid **17** (100 mg, 0.30 mmol) in MeCN (3 mL) was added the 2-(chlorophenyl)azido alcohol **20** (74 mg, 0.37 mmol). DCC (96 mg, 0.46 mmol) and DMAP (38 mg, 0.30 mmol) were added and reaction mixture was stirred under nitrogen (16 h) at rt. The MeCN was removed under reduced pressure and cold EtOAc was added. The precipitate was removed by filtration and the filtrate was concentrated under reduced pressure to obtain a crude residue. The residue was passed through a short flash column (toluene/EtOAc, 3:1) to provide **2-azido-2-(2-chlorophenyl)ethyl (3a'S,4'S,6'R,6a'R)-6'-(2,4-dioxo-3,4-dihydropyrimidine-1(2*H*)-yl) tetrahydrospiro[cyclopentane-1,2'-furo[3,4-*d*][1,3]dioxole]-4'-carboxylate (26)** (100 mg, 65%) as a white solid after trituration with CH₂Cl₂/pentane. *R*_f 0.48 (toluene/EtOAc, 1:1); FT-IR (neat) 3233, 3068, 2958, 2875, 2101, 1746, 1678, 1452, 1377, 1269, 1092 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.05 (s, 2H), 7.44 (d, *J* = 7.6 Hz, 2H), 7.38 (d, *J* = 7.6 Hz, 2H), 7.32-7.25 (m, 6H), 5.72 (dd, *J* = 7.8, 3.8 Hz, 2H), 5.52 (d, *J* = 10.4 Hz, 2H), 5.39-5.27 (m, 4H), 5.10 (dd, *J* = 12.6, 5.8 Hz, 2H), 4.47 (dd, *J* = 11.2, 3.6 Hz, 1H), 4.35-4.24 (m, 2H), 4.07 (dd, *J* = 11.4, 9.0 Hz, 1H), 1.98-1.70 (m, 16H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 169.2, 169.2, 163.4, 163.3, 150.8, 150.7, 144.1, 144.0, 133.4, 133.2, 133.0, 130.0, 128.5, 127.6, 123.2, 123.1, 102.9, 98. To a solution of azidoester **26** (58 mg, 0.11 mmol) in dry THF (2 mL) was added triphenylphosphine (45 mg, 0.17 mmol). The reaction mixture was stirred under nitrogen (16 h) at 35 °C. The THF was removed under reduced pressure to obtain a crude residue which was passed through a short column of flash silica (toluene/EtOAc, 2:1). The resultant intermediate oxazoline (53 mg, 0.11 mmol) was dissolved in CH₂Cl₂ (3 mL), and to the solution was added NiO₂ (100 molar excess). The heterogeneous reaction mixture was stirred under nitrogen (144 h) at reflux. The excess NiO₂ was removed by vacuum filtration while rinsing

with CH₂Cl₂ and the resulting filtrate was concentrated under reduced pressure to obtain a crude residue. The residue was submitted to flash-column chromatography (toluene/EtOAc, 2:1) and provided the uridyl (2-chlorophenyl)oxazole **32** (15 mg, 28% over two steps) as a white solid after trituration with CH₂Cl₂/pentane; mp 95-98 °C; *R*_f 0.41 (toluene/EtOAc, 1:1); FT-IR (neat) 3061, 2965, 1689, 1429, 1377, 1265, 1087, 907, 730 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.65 (s br, 1H), 8.34 (s, 1H), 8.04 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.44-7.41 (m, 2H), 7.36-7.32 (m, 1H), 7.27-7.23 (m, 1H), 5.95 (d, *J* = 1.6 Hz, 1H), 5.68 (dd, *J* = 8.4, 2.0 Hz, 1H), 5.39-5.36 (m, 2H), 5.09 (dd, *J* = 5.8, 1.4 Hz, 1H), 2.10-2.07 (m, 2H), 1.82-1.70 (m, 6H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 162.9, 159.7, 150.1, 141.6, 138.1, 137.6, 131.7, 130.4, 129.8, 129.2, 127.2, 124.2, 102.8, 94.6, 84.8, 83.5, 81.7, 36.5, 36.4, 23.8, 23.3 ppm. HRMS (+ESI) calcd. for C₂₂H₂₀ClN₃O₆ [M+Na] 480.0933; found 480.0933.

1-((3a'S,4'S,6'R,6a'R)-4'-(4-(4-Chlorophenyl)oxazol-2-yl)tetrahydrospiro[cyclopentane-1,2'-furo[3,4-d][1,3]dioxol]-6'-yl)pyrimidine-2,4(1H,3H)-dione (33) through intermediate azidoester (27):

To a solution of uridylcarboxylic acid **17** (100 mg, 0.30 mmol) in MeCN (3 mL) was added the 4-(chlorophenyl)azidoalcohol **21** (74 mg, 0.37 mmol). DCC (96 mg, 0.46 mmol) and DMAP (38 mg, 0.30 mmol) were added and reaction mixture was stirred under nitrogen (16 h) at rt. The MeCN was removed under reduced pressure and cold EtOAc was added. The precipitate was removed by filtration and the filtrate was concentrated under reduced pressure to obtain a crude residue. The residue was submitted to flash column chromatography (toluene/EtOAc, 3:1) to provide **2-azido-1-(4-chlorophenyl)ethyl-(3a'S, 4'S,6'R,6a'R)-6'-(2,4-dioxo-3,4-dihydropyrimidine-1(2H)-yl) tetrahydrospiro[cyclopentane-1,2'-furo[3,4-d][1,3]dioxole]-4'-carboxylate (27)** as a white solid (100 mg, 65%) after trituration with CH₂Cl₂/pentane. *R*_f 0.31 (toluene/EtOAc, 1:1). FT-IR (neat) 3060, 3065, 2961, 2875, 2102, 1744, 1676, 1453, 1377, 1270, 1091 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.80 (s, 2H), 7.37-7.27 (m, 10H), 5.68 (t, *J* = 7.6 Hz, 2H), 5.50 (d, *J* = 5.6 Hz, 2H), 5.39 (dd, *J* = 6.0, 1.2 Hz, 1H), 5.30-5.29 (m, 1H), 5.13 (d, *J* = 6.4 Hz, 1H), 5.09 (d, *J* = 6.4 Hz, 1H), 4.87 (dd, *J* = 9.2, 3.6 Hz, 1H), 4.77-4.74 (m, 3H), 4.44 (dd, *J* = 11.6, 3.6 Hz, 1H), 4.29-4.27 (m, 2H), 4.04 (dd, *J* = 11.6, 9.6 Hz, 1H), 1.96-1.70 (m, 16H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 169.3, 169.2, 164.1, 163.9, 150.9, 150.8, 144.4, 144.2, 134.9, 134.8, 134.2, 134.2, 129.3, 128.7, 128.7, 128.6, 123.1, 123.0, 102.8, 98.8, 98.6, 87.9, 87.7, 84.5, 84.4, 84.3, 68.0, 67.6, 63.4, 63.2, 35.9, 23.7, 23.2 ppm. To a solution of azidoester **27** (100 mg, 0.19 mmol) in dry THF (3 mL) was added triphenylphosphine (78 mg, 0.29 mmol). The reaction mixture was stirred under nitrogen (16 h) at 35 °C. The THF was removed under reduced pressure to obtain a crude residue. The residue was passed through a short flash column (toluene/EtOAc, 2:1) to provide the intermediate oxazoline (91 mg, 0.19 mmol) which was used directly in the next step. To the solution of the intermediate oxazoline in dry CH₂Cl₂ (4 mL) was added NiO₂ (150 molar excess). The reaction mixture was stirred under nitrogen (144 h) at reflux. The excess NiO₂ was removed by vacuum filtration while washing with CH₂Cl₂ and the

resulting filtrate was concentrated under reduced pressure to obtain a crude residue. The residue was submitted to flash-column chromatography (toluene/EtOAc, 4:1) to provide the uridyl (4-chlorophenyl)oxazole **33** (15 mg, 16% over two steps) as a white solid after trituration with CH₂Cl₂/pentane. Mp 98-100 °C; *R*_f 0.48 (toluene/EtOAc, 1:1); FT-IR (neat) 3061, 2932, 2860, 1691, 1455, 1379, 1274, 1267, 1092 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.40 (s br, 1H), 7.90 (s, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.38 (dd, *J* = 11.2, 8.4 Hz, 3H), 5.92 (s, 1H), 5.68 (d, *J* = 8.0 Hz, 1H), 5.38 (dd, *J* = 5.8, 2.6 Hz, 1H), 5.33 (d, *J* = 2.8 Hz, 1H), 5.09 (d, *J* = 5.8 Hz, 1H), 2.09-2.04 (m, 2H), 1.82-1.73 (m, 6H) ppm; ¹³C NMR (175 MHz, CDCl₃) δ 162.9, 160.9, 150.0, 140.6, 134.5, 134.4, 134.4, 129.3, 129.1, 128.9, 127.0, 126.9, 124.3, 102.8, 94.8, 84.7, 83.5, 81.8, 36.5, 36.4, 23.8, 23.3 ppm. HRMS (+ESI) calcd. for C₂₂H₂₀ClN₃O₆ [M+H]⁺ 458.1113; found. 458.1113.

1-((3a'S,4'S,6'R,6a'R)-4'-(4-(2-Benzyloxyphenyl)oxazol-2-yl)tetrahydrospiro[cyclopentane-1,2'-furo[3,4-d][1,3]dioxol]-6'-yl)pyrimidine-2,4(1H,3H)-dione (34) through intermediate azido ester (28): To a solution of uridylcarboxylic acid **17** (300 mg, 0.92 mmol) in MeCN (5 mL) was added azidoalcohol **22** (300 mg, 1.11 mmol). DCC (286 mg, 1.39 mmol) and DMAP (113 mg, 0.92 mmol) were added and the reaction mixture was stirred under nitrogen (16 h) at rt. The MeCN was removed under reduced pressure and cold EtOAc was added. The precipitate was removed by filtration and the filtrate was concentrated under reduced pressure to obtain a crude residue. The residue was passed through a short flash column (toluene/EtOAc, 3:1) to provide **2-azido-2-(2-(benzyloxy)phenyl)ethyl-(3a'S,4'S,6'R,6a'R)-6'-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)tetrahydrospiro[cyclopentane-1,2'-furo[3,4-d][1,3]dioxole]-4'-carboxylate (28)** (388 mg, 73%) as a white solid after trituration with CH₂Cl₂/pentane; *R*_f 0.55 (toluene/EtOAc, 1:1); FT-IR (neat) 3215, 3064, 2959, 2885, 2103, 1747, 1693, 1452, 1378, 1269, 1097 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.61 (s br, 2H), 7.45-7.27 (m, 16H), 7.01-6.96 (m, 4H), 5.68 (t, *J* = 8.2 Hz, 2H), 5.54 (d, *J* = 9.6 Hz, 2H), 5.34-5.22 (m, 4H), 5.15-5.04 (m, 6H), 4.76 (dd, *J* = 4.2, 1.4 Hz, 2H), 4.47 (dd, *J* = 11.4, 3.4 Hz, 1H), 4.41-4.29 (m, 2H), 4.18 (dd, *J* = 11.2, 8.8 Hz, 1H), 2.00-1.97 (m, 4H), 1.79-1.71 (m, 12H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 169.3, 169.3, 163.2, 163.0, 150.6, 150.5, 143.8, 143.7, 136.6, 130.0, 128.9, 128.8, 128.3, 128.3, 128.1, 127.7, 127.5, 124.0, 123.9, 123.2, 123.1, 121.3, 112.2, 102.8, 98.3, 97.9, 87.5, 87.3, 84.4, 84.3, 84.2, 70.5, 70.4, 67.1, 67.0, 58.7, 58.6, 35.9, 23.7, 23.3 ppm. To a solution of azidoester **28** (350 mg, 0.60 mmol) in dry THF (5 mL) was added triphenylphosphine (287 mg, 1.09 mmol). The reaction mixture was stirred under nitrogen (16 h) at 35 °C. The THF was removed under reduced pressure which gave a crude residue. The residue was passed through a short flash column (toluene/EtOAc, 2:1) to provide the intermediate oxazoline. The intermediate oxazoline (323 mg, 0.60 mmol) was dissolved in dry CH₂Cl₂ (5 mL) and then NiO₂ (75 molar excess) was added. The heterogenous reaction mixture was stirred under nitrogen (48 h) at reflux. The excess NiO₂ was removed by vacuum filtration while washing with CH₂Cl₂ and the

resulting filtrate was concentrated under reduced pressure to obtain a crude residue. Purification was performed using flash-column chromatography (toluene/EtOAc, 4:1) which provided the pure uridyl (2-benzyloxyphenyl)oxazole **34** (175 mg, 54% over two steps) as a white solid after trituration with CH₂Cl₂/pentane; mp 99-101 °C; *R*_f 0.50 (toluene/EtOAc, 1:1); FT-IR (neat) 3068, 2932, 2875, 1693, 1490, 1379, 1269, 1107, 1059, 754 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.15 (s br, 1H), 8.07 (dd, *J* = 7.6, 1.6 Hz, 1H), 8.03 (s, 1H), 7.50 (d, *J* = 8.4 Hz, 1H), 7.47-7.38 (m, 5H), 7.32-7.27 (m, 1H), 7.09-7.03 (m, 2H), 6.01 (d, *J* = 2.4 Hz, 1H), 5.65 (dd, *J* = 8.0, 2.0 Hz, 1H), 5.35-5.31 (m, 2H), 5.18 (s, 2H), 5.05 (dd, *J* = 6.2, 2.2 Hz, 1H), 2.08-2.06 (m, 2H), 1.82-1.71 (m, 6H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 162.9, 159.2, 155.8, 150.2, 141.3, 138.3, 136.8, 136.6, 129.2, 129.1, 128.6, 128.2, 128.1, 124.3, 121.4, 119.8, 111.9, 102.8, 94.1, 85.0, 83.4, 81.5, 36.6, 36.6, 23.8, 23.4 ppm. HRMS (+ESI) calcd. for C₂₉H₂₇N₃O₇ [M+H]⁺ 530.1922; found. 530.1921.

1-((3a'S,4'S,6'R,6a'R)-4'-(4-(2-Chlorophenyl)oxazol-2-yl)tetrahydrospiro[cyclopentane-1,2'-furo[3,4-*d*][1,3]dioxol]-6'-yl)pyrimidine-2,4(1*H*,3*H*)-dione (35) through intermediate azidoester (29):

To a solution of uridylcarboxylic acid **17** (234 mg, 0.72 mmol) in MeCN (5 mL) was added azidoalcohol **23** (180 mg, 0.86 mmol). DCC (22 mg, 1.08 mmol) and DMAP (88 mg, 0.72 mmol) were added and the reaction mixture was stirred under nitrogen (16 h) at rt. The MeCN was removed under reduced pressure and cold EtOAc was added. The precipitate was removed by filtration and the filtrate was concentrated under reduced pressure. The resultant crude residue was passed through a short flash column eluting with toluene/EtOAc (4:1) to provide **2-azido-2-(3-nitrophenyl)ethyl (3a'S,4'S,6'R,6a'R)-6'-(2,4-dioxo-3,4-dihydropyrimidine-1(2*H*)-yl)tetrahydrospiro[cyclopentane-1,2'-furo[3,4-*d*][1,3]dioxole]-4'-carboxylate (29)** (314 mg, 85%) as a white solid after trituration with CH₂Cl₂/pentane; *R*_f 0.27 (toluene/EtOAc, 1:1); FT-IR (neat) 3075, 2952, 2885, 2105, 1754, 1693, 1532, 1352, 1270, 1099 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.49 (s br, 2H), 8.29-8.19 (m, 4H), 7.71 (t, *J* = 8.2 Hz, 2H), 7.61-7.56 (m, 2H), 7.27-7.24 (2H, overlay with CDCl₃), 5.71 (dd, *J* = 8.2, 2.6 Hz, 2H), 5.47 (d, *J* = 2.4 Hz, 2H), 5.39 (dd, *J* = 6.2, 1.4 Hz, 1H), 5.29 (dd, *J* = 6.4, 1.6 Hz, 1H), 5.11 (t, *J* = 6.6 Hz, 2H), 5.03 (dd, *J* = 8.8, 4.0 Hz, 1H), 4.93 (dd, *J* = 7.6, 5.2 Hz, 1H), 4.78 (d, *J* = 1.2 Hz, 1H), 4.74 (d, *J* = 1.6 Hz, 1H), 4.52 (dd, *J* = 11.6, 3.6 Hz, 1H), 4.40-4.28 (m, 2H), 4.08 (dd, *J* = 11.6, 9.2 Hz, 1H), 1.97-1.93 (m, 4H), 1.75-1.69 (m, 12H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 169.2, 169.2, 163.8, 163.8, 150.8, 150.8, 148.6, 148.6, 144.5, 144.4, 138.2, 138.1, 133.2, 130.1, 129.1, 128.7, 123.9, 123.2, 123.1, 122.8, 122.4, 112.2, 102.8, 99.0, 98.9, 88.0, 87.9, 84.5, 84.3, 79.3, 67.8, 67.4, 63.1, 62.8, 35.9, 35.8, 23.7, 23.2 ppm. To a solution of the uridyl (3-nitrophenyl)azidoester **29** (314 mg, 0.61 mmol) in dry THF (5 mL) was added triphenylphosphine (288 mg, 1.10 mmol). The reaction mixture was stirred under nitrogen (16 h) at 35 °C. The THF was removed under reduced pressure to obtain a crude residue which was passed through a flash column (hexane/EtOAc, 1:1). The intermediate oxazoline (29 mg, 0.61 mmol) was directly dissolved in dry

CH₂Cl₂ (5 mL) and NiO₂ (250 molar excess) was added. The heterogenous reaction mixture was stirred under nitrogen (96 h) at reflux. The excess NiO₂ was removed by vacuum filtration while washing with CH₂Cl₂ followed by concentrating the filtrate under reduced pressure to obtain a crude residue. The residue was submitted to flash-column chromatography (hexane/EtOAc, 2:1) to provide the uridyl (3-nitrophenyl)oxazoline **35** (60 mg, 21% over two steps) as a white solid after trituration with CH₂Cl₂/pentane. Mp 87-90 °C; *R_f* 0.33 (toluene/EtOAc, 1:1); FT-IR (neat) 3095, 2962, 2884, 1693, 1528, 1350, 1268, 1102, 810, 737 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.56 (t, *J* = 1.8 Hz, 1H), 8.37 (s br, 1H), 8.17 (dd, *J* = 8.2, 1.4 Hz, 1H), 8.05 (s, 1H), 8.03 (d, *J* = 7.6 Hz, 5H), 7.58 (t, *J* = 8.0 Hz, 1H), 7.38 (d, *J* = 7.6 Hz, 1H), 5.89 (d, *J* = 1.6 Hz, 1H), 5.72 (dd, *J* = 8.4, 2.0 Hz, 1H), 5.46 (dd, *J* = 6.4, 3.2 Hz, 1H), 5.34 (d, *J* = 2.8 Hz, 1H), 5.13 (dd, *J* = 6.0, 1.6 Hz, 1H), 2.10-2.04 (m, 2H), 1.84-1.71 (m, 6H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 162.6, 161.5, 150.0, 148.9, 142.1, 139.6, 135.5, 132.3, 131.4, 130.0, 124.3, 123.1, 120.6, 117.3, 102.9, 95.4, 84.6, 83.7, 82.2, 36.4, 23.8, 23.933 ppm. HRMS (+ESI) calcd. for C₂₂H₂₀N₄O₈ [M+Na] 491.1173; found 491.1173.

1-((3a'S,4'S,6'R,6a'R)-4'-(4-(2-Hydroxyphenyl)oxazol-2-yl)tetrahydrospiro[cyclopentane-1,2'-furo[3,4-d][1,3]dioxol]-6'-yl)pyrimidine-2,4(1H,3H)-dione (36): The uridyl (benzyloxyphenyl)oxazole **34** (125 mg, 0.23 mmol) was dissolved in MeOH (3 mL) and Pd/C (catalytic) was added. The flask containing the heterogeneous reaction mixture was fitted with a septum and H₂ (g) balloon and stirring was continued (12 h) at rt. The dark reaction suspension was filtered through Celite[®] while washing with MeOH followed by concentration under reduced pressure to obtain a crude residue. The residue was submitted to flash-column chromatography (toluene/EtOAc, 3:1) to provide the uridyl (hydroxyphenyl)oxazole **36** (97 mg, 93%) as a white solid after trituration with CH₂Cl₂/pentane; mp 205-206 °C; *R_f* 0.49 (toluene/EtOAc, 1:1); FT-IR (neat) 3244, 3147, 3075, 2971, 1712, 1669, 1450, 1395, 1286, 1102, 1082, 929, 756 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 10.15 (s, 1H), 8.63 (s br, 1H), 7.94 (s, 1H), 7.39 (d, *J* = 7.6 Hz, 1H), 7.23-7.19 (m, 2H), 6.96 (d, *J* = 8.4 Hz, 1H), 6.85 (t, *J* = 7.6 Hz, 1H), 5.71-5.69 (m, 2H), 5.45 (dd, *J* = 6.2, 2.6 Hz, 1H), 5.33 (d, *J* = 2.8 Hz, 1H), 5.18 (d, *J* = 6.0 Hz, 1H), 2.08-2.04 (m, 2H), 1.80-1.73 (m, 6H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 162.8, 160.1, 155.5, 150.0, 142.5, 140.0, 133.8, 130.3, 125.8, 124.1, 119.8, 117.9, 113.7, 103.2, 96.6, 85.5, 84.1, 82.9, 36.3, 36.3, 23.7, 23.3 ppm. HRMS (+ESI) calcd. for C₂₂H₂₁N₃O₇ [M+H]⁺ 440.1452; found 440.1453.

2-(2-((3a'R,4'R,6'S,6a'S)-4'-(2,4-Dioxo-3,4-dihydropyrimidin-1(2H)-yl)tetrahydrospirocyclopentane-1,2'-furo[3,4-d][1,3]dioxol-6'-yl)oxazol-4-yl)phenyl 4-nitrobenzoate (37): To a solution of the uridyl (hydroxyphenyl)oxazole **11** (15 mg, 0.034 mmol) in CH₂Cl₂ (0.5 mL) was added DMAP (5 mg, 0.04 mmol). The mixture was cooled to 0 °C with stirring followed by the addition of 4-nitrobenzoyl chloride (8 mg, 0.041 mmol). The reaction mixture was stirred (30 min) at rt, then quenched with H₂O (1 mL) and the resulting mixture was extracted with CH₂Cl₂ (3x2 mL). The organic layers were combined

and washed with aqueous NaHCO₃ (1x5 mL), brine (1.5 mL), dried over anhydrous Na₂SO₄ and concentrated under reduced pressure to obtain a crude residue. Submission of the residue to flash-column chromatography (hexane/EtOAc, 2:1) provided the 4-nitrobenzoic ester **37** (14 mg, 70%) as a white solid after trituration with CH₂Cl₂/pentane; mp 108-111 °C; *R*_f 0.44 (toluene/EtOAc, 1:1); FT-IR (neat) 3238, 3078, 2927, 2878, 1744, 1693, 1528, 1454, 1349, 1264, 1193, 1068 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.48 (s br, 1H), 8.44-8.38 (m, 4H), 7.97 (dd, *J* = 7.6, 2.0 Hz, 1H), 7.77 (s, 1H), 7.46-7.38 (m, 2H), 7.29-7.26 (m, 2H), 5.85 (d, *J* = 1.2 Hz, 1H), 5.66 (dd, *J* = 7.8, 2.2 Hz, 1H), 5.23-5.20 (m, 2H), 4.96 (dd, *J* = 6.0, 2.0 Hz, 1H), 2.02-2.00 (m, 2H), 1.74-1.70 (m, 6H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 163.2, 162.7, 160.5, 151.2, 150.0, 147.4, 141.7, 136.9, 136.4, 134.8, 131.5, 129.6, 129.0, 127.1, 124.2, 123.4, 123.1, 102.9, 94.9, 84.5, 83.5, 81.8, 36.4, 23.7, 23.3 ppm. HRMS (+ESI) calcd. for C₂₉H₂₄N₄O₁₀ [M+H]⁺ 589.1565; found. 589.1562.

2-(2-((3a'*R*,4'*R*,6'*S*,6a'*S*)-4'-(2,4-Dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)tetrahydrospirocyclopentane-1,2'-furo[3,4-*d*][1,3]dioxol-6'-yl)oxazol-4-yl)phenyl tetradecanoate (38): To a solution of the uridyl (hydroxyphenyl)oxazole **11** (15 mg, 0.03 mmol) in CH₂Cl₂ (0.5 mL) was added DMAP (5 mg, 0.041 mmol). The reaction mixture was cooled to 0 °C with stirring followed by the addition of myristoyl chloride (0.10 g, 0.41 mmol). The reaction mixture was stirred (30 min) at rt, quenched with H₂O (1 mL) and the resulting mixture was extracted with CH₂Cl₂ (3x2 mL). The organic layers were combined and washed with aqueous NaHCO₃ (1.5 mL), brine (1.5 mL), dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Flash-column chromatography (toluene/EtOAc, 3:1) of the residue provided the myristoyl ester **38** (21 mg, 95%) as a colorless oil; *R*_f 0.51 (toluene/EtOAc, 1:1); FT-IR (neat) 3053, 2925, 2854, 1769, 1695, 1455, 1384, 1272, 1200, 1110 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.59 (s br, 1H), 7.96 (dd, *J* = 7.4, 1.8 Hz, 1H), 7.90 (s, 1H), 7.41 (d, *J* = 8.4 Hz, 1H), 7.36-7.28 (m, 2H), 7.14 (d, *J* = 7.6 Hz, 1H), 5.94 (d, *J* = 1.2 Hz, 1H), 5.68 (dd, *J* = 7.8, 1.8 Hz, 1H), 5.34-5.33 (m, 2H), 5.08 (dd, *J* = 6.0, 1.2 Hz, 1H), 2.62 (t, *J* = 7.6 Hz, 2H), 2.10-2.05 (m, 2H), 1.81-1.770 (m, 8H), 1.41-1.26 (m, 20H), 0.88 (t, *J* = 6.8 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 171.7, 162.8, 160.2, 150.1, 147.8, 141.7, 136.7, 129.2, 128.7, 126.4, 124.2, 123.3, 123.0, 102.9, 94.6, 84.7, 83.6, 81.8, 36.5, 36.4, 34.8, 32.1, 29.8, 29.6, 29.5, 29.4, 29.3, 25.0, 23.8, 23.3, 22.8, 14.3 ppm. HRMS (+ESI) calcd. for C₃₆H₄₇N₃O₈ [M+Na] 672.3255; found 672.3256.

***N*-(3-(2-((3a'*R*,4'*R*,6'*S*,6a'*S*)-4'-(2,4-Dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)tetrahydrospiro[cyclopentane-1,2'-furo[3,4-*d*][1,3]dioxol]-6'-yl)oxazol-4-yl)phenyl)acetamide (40):** To a solution of the uridyl (nitrophenyl)oxazole **35** (15 mg, 0.03 mmol) in MeOH (1 mL) was added Pd/C (catalytic). The flask containing the dark suspension was fitted with a H₂ (g) balloon and stirring was continued (45 min) at rt. Upon disappearance of the starting material as indicated by TLC, the suspension was vacuum-filtered through Celite[®] while washing with MeOH. The filtrate was concentrated under reduced

pressure to obtain the crude amino compound **39**. The crude reduction product was then dissolved in pyridine (0.5 mL) and acetic anhydride (0.5 mL) was added followed by stirring (4.5 h) at rt. The pyridine/acetic anhydride was removed under vacuum and the residue was submitted to flash-column chromatography (hexane/EtOAc, 1:3). The acetamide **40** (15 mg, 99%) was obtained as a white solid after trituration with CH₂Cl₂/pentane; mp 114-117 °C; *R*_f 0.36 (EtOAc); FT-IR (neat) 3319, 3070, 2962, 1689, 1546, 1466, 1429, 1378, 1268, 1109 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.17 (s br, 1H), 7.90 (s br, 1H), 7.87 (s, 1H), 7.65-7.63 (m, 2H), 7.44 (m, 2H), 5.88 (s, 1H), 5.71 (d, *J* = 8.0 Hz, 1H), 5.35-5.25 (m, 3H), 2.21 (s, 3H), 2.08-2.05 (m, 2H), 1.81-1.67 (m, 6H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 169.1, 163.8, 161.2, 150.6, 142.8, 140.8, 138.9, 134.6, 131.1, 129.6, 123.8, 121.1, 120.0, 117.0, 103.1, 95.5, 84.3, 84.1, 82.7, 36.4, 36.3, 24.7, 23.8, 23.3 ppm. HRMS (+ESI) calcd. for C₂₄H₂₄N₄O₇ [M+Na] 503.1537; found 503.1536.

***N*-(3-(2-((3*a*'*R*,4'*R*,6*a*'*S*,6*a*'*S*)-4'-(2,4-Dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)tetrahydrospiro[cyclopentane-1,2'-furo[3,4-*d*][1,3]dioxol]-6'-yl)oxazol-4-yl)phenyl)tetradecanamide (**41**):** To a solution of the uridyl (nitrophenyl)oxazole **35** (5 mg, 0.01 mmol) in MeOH (1 mL) was added Pd/C (catalytic). The flask containing the dark suspension was then fitted with a H₂ (g) balloon and stirring was continued (45 min) at rt. After completion of the reaction as indicated by TLC, the suspension was filtered through Celite[®] while washing with MeOH and then concentrated under reduced pressure to give the crude intermediate uridyl (aminophenyl)oxazole **39** (5 mg, 0.01 mmol). Intermediate **39** was then directly dissolved in CH₂Cl₂ (0.5 mL) followed by the addition of DMAP (4 mg, 0.032 mmol) while stirring. The reaction mixture was cooled to 0 °C followed by the addition of myristoyl chloride (6 μL, 0.021 mmol). The reaction mixture was stirred (5 h) at rt, and then quenched with H₂O (1 mL) followed by extraction with CH₂Cl₂ (3x2 mL). The organic layers were then combined, washed with aqueous NaHCO₃ (1.5 mL) and brine (1.5 mL). The combined extracts were dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure to obtain a crude residue which was submitted to flash-column chromatography (hexane/EtOAc, 2:1). The uridyl (myristamidophenyl)oxazole **41** (5 mg, 71% from **35**) was obtained as a colorless oil; *R*_f 0.40 (toluene/EtOAc, 1:1); FT-IR (neat) 3281, 2956, 2826, 2855, 1692, 1551, 1461, 1268, 1111 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.19 (s br, 1H), 7.91 (s, 1H), 7.77 (s, 1H), 7.60-7.58 (m, 1H), 7.47-7.45 (m, 2H), 7.36-7.30 (m, 2H), 5.92 (s, 1H), 5.75 (d, *J* = 8.4 Hz, 1H), 5.35-5.30 (m, 2H), 5.23 (d, *J* = 5.6 Hz, 1H), 2.39 (t, *J* = 7.6 Hz, 2H), 2.07-2.06 (m, 2H), 1.82-1.71 (m, 8H), 1.41-1.26 (m, 20H), 0.88 (t, *J* = 6.8 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 172.0, 163.3, 161.0, 150.4, 142.6, 11.0, 138.9, 134.7, 132.2, 131.1, 129.6, 128.7, 123.9, 121.0, 119.8, 116.9, 103.1, 95.3, 84.4, 83.9, 82.5, 37.9, 36.4, 32.1, 29.8, 29.6, 29.6, 25.8, 23.8, 23.3, 22.8, 14.3 ppm. HRMS (+ESI) calcd. for C₃₆H₄₈N₄O₇ [M+Na] 671.3415; found 671.3414.

General procedure for the removal of the 2',3'-*O*-cyclopentylidene group from intermediates 30-38 and 41 to provide targets 6-15: To the uridyl oxazoles **30-38** or **41** (10 mg, 0.01-0.05 mmol) at 0 °C was added 70% aqueous trifluoroacetic acid (0.5 mL). The reaction mixture was stirred (0.5 h) at 0 °C and then allowed to warm to rt with continued stirring (4.5 h, total reaction time) while monitoring by TLC. After the reaction was complete, cold H₂O (1 mL) was added to precipitate the product. The product was collected by vacuum filtration while washing with H₂O and CH₂Cl₂ to yield the deprotected targets **6-15**.

1-((2*R*,3*R*,4*S*,5*S*)-3,4-Dihydroxy-5-(4-phenyloxazol-2-yl)tetrahydrofuran-2-yl)pyrimidine-2,4-(1*H*, 3*H*)-dione (6): Isolated as a white solid (7.0 mg, 87%); [α]_D²⁰ -28.9 (*c* 0.09, MeOH); mp 258-260 °C; *R*_f 0.29 (CHCl₃/MeOH, 9:1); FT-IR (neat) 3066, 2960, 2875, 2828, 1694, 1675, 1471, 1383, 1270, 1092 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.42 (s, 1H), 8.69 (s, 1H), 8.07 (d, *J* = 8.4 Hz, 1H), 7.80 (d, *J* = 7.2 Hz, 2H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.36 (t, *J* = 7.4 Hz, 1H), 5.99 (d, *J* = 4.8 Hz, 1H), 5.78 (dd, *J* = 8.6, 2.2 Hz, 1H), 5.79-5.73 (m, 2H), 5.01 (d, *J* = 4.0 Hz, 1H), 4.34-4.35 (m, 2H) ppm; ¹³C NMR (100 MHz, DMSO-*d*₆) δ 163.1, 161.4, 150.8, 140.6, 140.1, 136.0, 130.4, 129.0, 128.3, 125.2, 102.3, 88.9, 78.0, 73.2, 72.9 ppm. HRMS (+ESI) calcd. for C₁₇H₁₅N₃O₆ [M+Na] 380.0853; found 380.0852.

1-((2*R*,3*R*,4*S*,5*S*)-5-(4,5-Diphenyloxazol-2-yl)-3,4-dihydroxytetrahydrofuran-2-yl)pyrimidine-2,4-(1*H*, 3*H*)-dione (7): Isolated as a beige solid (11 mg, 85%); *R*_f 0.38 (CHCl₃/MeOH, 9:1); [α]_D²⁰ -12.3 (*c* 0.08, MeOH); mp 232-234 °C; FT-IR (neat) 3357, 3192, 3066, 2918, 2829, 1690, 1669, 1475, 1399, 1317, 1263, 1065 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.41 (s, 1H), 8.07 (d, *J* = 7.6 Hz, 1H), 7.61-7.57 (m, 4H), 7.51-7.40 (m, 6H), 5.99 (d, *J* = 5.6 Hz, 1H), 5.81 (m, 1H), 5.73 (d, *J* = 7.2 Hz, 1H), 5.03 (m, 1H), 4.47 (m, 1H), 4.39 (m, 1H) ppm; ¹³C NMR (175 MHz, DMSO-*d*₆) δ 163.1, 160.1, 150.8, 145.8, 140.7, 134.8, 131.5, 129.4, 129.1, 128.9, 128.6, 128.0, 127.4, 126.7, 102.2, 89.1, 78.0, 73.2, 72.9 ppm. HRMS (+ESI) calcd. for C₂₃H₁₉N₃O₆ [M+Na] 456.1166; found 456.1164.

1-((2*R*,3*R*,4*S*,5*S*)-3,4-Dihydroxy-5-(4-(2-chlorophenyl)oxazol-2-yl)tetrahydrofuran-2-yl)pyrimidine-2,4-(1*H*,3*H*)-dione (8): Isolated as a white solid (16 mg, 84%); [α]_D²⁰ -28.8 (*c* 0.13, MeOH); mp 238-240 °C; *R*_f 0.49 (CHCl₃/MeOH, 9:1); FT-IR (neat) 3326, 3188, 3068, 2938, 2851, 1691, 1668, 1472, 1318, 1268, 1181, 1108, 1067, 818 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.42 (d, *J* = 1.6 Hz, 1H), 8.76 (s, 1H), 8.04-8.01 (m, 2H), 7.59 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.52 (td, *J* = 7.6, 1.6 Hz, 1H), 7.41 (td, *J* = 7.7, 1.8 Hz, 1H), 5.99 (d, *J* = 5.6 Hz, 1H), 5.81 (s br, 2H), 5.74 (dd, *J* = 8.2, 2.0 Hz, 1H), 5.03 (d, *J* = 4.0 Hz, 1H), 4.40-4.34 (m, 2H) ppm; ¹³C NMR (175 MHz, DMSO-*d*₆) δ 163.1, 160.9, 150.8, 140.6, 138.7, 136.4, 130.6, 130.4, 129.6, 128.9, 127.7, 102.3, 89.0, 77.9, 73.3, 72.8 ppm. HRMS (+ESI) calcd. for C₁₇H₁₄ClN₃O₆ [M+H]⁺ 392.0644; found. 392.0644.

1-((2*R*,3*R*,4*S*,5*S*)-5-(4-(4-Chlorophenyl)oxazol-2-yl)-3,4-dihydroxytetrahydrofuran-2-yl)pyrimidine-2,4-(1*H*,3*H*)-dione (9): Isolated as a white solid (4 mg, 50%); mp 252-254 °C; *R*_f 0.32 (CHCl₃/MeOH, 9:1); ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.40 (s, 1H), 8.71 (s, 1H), 8.03 (d, *J* = 8.4, 1H), 7.81 (d, *J* = 8.0

Hz, 2H), 7.54 (d, $J = 8.8$ Hz, 2H), 5.97 (d, $J = 5.2$ Hz, 1H), 5.78 (d, $J = 7.6$ Hz, 1H), 5.74 (s br, 2H), 4.99 (d, $J = 8.8$ Hz, 1H), 4.37-4.34 (m, 2H) ppm. HRMS (+ESI) calcd. for $C_{17}H_{14}ClN_3O_6$ $[M+H]^+$ 392.0644; found. 392.0644.

1-((2*R*,3*R*,4*S*,5*S*)-5-(4-(2-(Benzyloxy)phenyl)oxazol-2-yl)-3,4-dihydroxytetrahydrofuran-2-yl)-pyrimidine-2,4(1*H*,3*H*)-dione (10): Isolated as a white solid (16 mg, 94%); $[\alpha]_D^{20}$ -30.6 (c 0.20, MeOH); mp 199-201 °C; R_f 0.31 (CHCl₃/MeOH, 9:1); FT-IR (neat) 3342, 3182, 3068, 2909, 2872, 1691, 1669, 1478, 1402, 1318, 1252, 1178, 1061, 744 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.40 (s, 1H), 8.26 (s, 1H), 8.05 (d, $J = 8.0$, 1H), 7.98 (d, $J = 6.8$ Hz, 1H), 7.51 (d, $J = 7.2$ Hz, 2H), 7.42 (t, $J = 7.4$ Hz, 1H), 7.37-7.30 (m, 2H), 7.21 (d, $J = 8.0$ Hz, 1H), 7.10 (t, $J = 7.4$ Hz, 1H), 5.97 (d, $J = 5.2$ Hz, 1H), 5.78 (s br, 2H), 5.74 (dd, $J = 8.2, 1.8$ Hz, 1H), 5.32 (s, 2H), 4.99 (d, $J = 4.0$ Hz, 1H), 4.37-4.33 (m, 2H) ppm; ¹³C NMR (100 MHz, DMSO-*d*₆) δ 163.2, 160.5, 155.1, 150.8, 140.6, 137.7, 136.8, 135.8, 129.1, 128.7, 128.2, 127.9, 127.2, 121.1, 119.1, 112.6, 102.3, 88.9, 78.0, 73.2, 72.9, 69.7 ppm. HRMS (+ESI) calcd. for $C_{24}H_{21}N_3O_7$ $[M+Na]$ 486.1272; found 486.1272.

1-((2*R*,3*R*,4*S*,5*S*)-3,4-Dihydroxy-5-(4-(2-hydroxyphenyl)oxazol-2-yl)tetrahydrofuran-2-yl)-pyrimidine-2,4(1*H*,3*H*)-dione (11): Isolated as a white solid (18 mg, 95%); $[\alpha]_D^{20}$ -32.9 (c 0.13, MeOH); mp 138-142 °C; R_f 0.26 (CHCl₃/MeOH, 9:1); FT-IR (neat) 3608, 3504, 3176, 3048, 2992, 1706, 1658, 1476, 1450, 1389, 1258, 1125, 1055, 819, 746 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.40 (s, 1H), 10.30 (s, 1H), 8.41 (s, 1H), 8.09 (d, $J = 8.0$, 1H), 7.87 (d, $J = 7.2$ Hz, 1H), 7.17 (t, $J = 7.2$ Hz, 1H), 6.97-6.92 (m, 2H), 5.99 (d, $J = 4.4$ Hz, 1H), 5.79-5.71 (m, 3H), 5.00 (d, $J = 3.6$ Hz, 1H), 4.39-4.32 (m, 2H) ppm; ¹³C NMR (100 MHz, DMSO-*d*₆) δ 163.0, 160.3, 154.5, 150.7, 140.5, 137.6, 136.2, 128.7, 126.9, 119.3, 117.3, 115.5, 102.2, 88.7, 78.0, 73.2, 72.9 ppm. HRMS (+ESI) calcd. for $C_{17}H_{15}N_3O_7$ $[M+H]^+$ 374.0983; found 374.0983.

2-(2-((2*S*,3*S*,4*R*,5*R*)-5-(2,4-Dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-3,4-dihydroxytetrahydrofuran-2-yl)oxazol-4-yl)phenyl 4-nitrobenzoate (12): Isolated as a white solid (11 mg, 99%); $[\alpha]_D^{20}$ -14.0 (c 0.10, MeOH); mp 240-243 °C; R_f 0.29 (CHCl₃/MeOH, 9:1); FT-IR (neat) 3361, 3207, 3071, 2914, 1750, 1694, 1669, 1532, 1521, 1478, 1319, 1266, 1183, 1108, 1070, 826, 817 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.38 (s, 1H), 8.41 (s, 4H), 8.34 (s, 1H), 7.96 (d, $J = 6.8$ Hz, 1H), 7.78 (d, $J = 8.8$ Hz, 1H), 7.51-7.46 (m, 3H), 5.89 (d, $J = 5.2$ Hz, 1H), 5.70-5.62 (m, 2H), 5.63 (d, $J = 5.6$ Hz, 1H), 4.88 (d, $J = 4.0$ Hz, 1H), 4.24-4.13 (m, 2H) ppm; ¹³C NMR (100 MHz, DMSO-*d*₆) δ 163.1, 163.0, 161.2, 150.7, 150.6, 147.1, 140.4, 137.5, 135.7, 134.2, 131.5, 129.5, 128.5, 127.0, 124.1, 123.7, 123.2, 102.3, 88.9, 77.7, 72.9, 72.7 ppm. HRMS (+ESI) calcd. for $C_{24}H_{18}N_4O_{10}$ $[M+Na]$ 545.0915; found 545.0915.

2-(2-((2*S*,3*S*,4*R*,5*R*)-5-(2,4-Dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-3,4-dihydroxytetrahydrofuran-2-yl)oxazol-4-yl)phenyl tetradecanoate (13): Isolated as a white solid (17 mg, 94%); $[\alpha]_D^{20}$ -32.9 (c 0.13, MeOH); mp 194-196 °C; R_f 0.42 (CHCl₃/MeOH, 9:1); FT-IR (neat) 3370, 3070, 2921, 2851, 1762, 1693,

1667, 1471, 1400, 1318, 1267, 1188, 1061, 819 cm^{-1} ; ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 11.40 (s, 1H), 8.42 (s, 1H), 7.98-7.93 (m, 2H), 7.41-7.40 (m, 2H), 7.23-7.21 (m, 1H), 5.97 (d, $J = 4.8$ Hz, 1H), 5.77 (d, $J = 5.6$ Hz, 1H), 5.74-5.72 (m, 2H), 5.00 (d, $J = 4.0$ Hz, 1H), 4.39-4.32 (m, 2H), 2.74 (t, $J = 7.4$ Hz, 2H), 1.63-1.61 (m, 2H), 1.24 (s br, 20H), 0.85 (t, $J = 6.2$ Hz, 3H) ppm; ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 171.7, 163.0, 161.1, 150.7, 147.3, 140.5, 137.6, 129.0, 128.0, 126.4, 123.5, 123.2, 102.3, 89.0, 77.8, 73.2, 72.9, 33.5, 31.3, 29.0, 28.9, 28.7, 28.4, 24.2, 22.1, 13.9 ppm. HRMS (+ESI) calcd. for $\text{C}_{31}\text{H}_{41}\text{N}_3\text{O}_8$ [M+Na] 606.2786; found 606.2789.

1-((2R,3R,4S,5S)-3,4-Dihydroxy-5-(4-(3-nitrophenyl)oxazol-2-yl)tetrahydrofuran-2-yl)pyrimidine-2,4(1H,3H)-dione (14): Isolated as a white solid (5 mg, 71%); $[\alpha]_D^{20}$ -19.2 (c 0.08, MeOH); mp 242-244 $^\circ\text{C}$; R_f 0.21 ($\text{CHCl}_3/\text{MeOH}$, 9:1); FT-IR (neat) 3247, 3057, 1709, 1662, 1524, 1462, 1348, 1271, 1056, 826, 763 cm^{-1} ; ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 11.41 (s, 1H), 8.95 (s, 1H), 8.61 (s, 1H), 8.23 (t, $J = 10.0$ Hz, 2H), 8.12 (d, $J = 8.0$ Hz, 1H), 7.79 (d, $J = 8.0$ Hz, 2H), 5.99 (d, $J = 4.8$ Hz, 1H), 5.78 (d, $J = 8.0$ Hz, 1H), 5.78 (s br, 2H), 5.03 (s, 1H), 4.41-4.36 (m, 2H) ppm; ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 163.0, 162.1, 150.7, 148.4, 137.7, 132.1, 131.4, 130.7, 122.8, 119.5, 102.2, 88.9, 77.9, 73.2, 72.7 ppm. HRMS (+ESI) calcd. for $\text{C}_{17}\text{H}_{14}\text{N}_4\text{O}_8$ [M+Na] 425.0704; found 425.0704.

N-(3-(2-((2S,3S,4R,5R)-5-(2,4-Dioxo-3,4-dihydropyrimidin-1(2H)-yl)-3,4-dihydroxytetrahydrofuran-2-yl)oxazol-4-yl)phenyl)tetradecanamide (15): Isolated as a white solid (5 mg, 80%); mp 145-148 $^\circ\text{C}$; R_f 0.38 ($\text{CHCl}_3/\text{MeOH}$, 9:1); FT-IR (neat) 3284, 3070, 2920, 2851, 1686, 1655, 1534, 1467, 1275, 1108, 1058 cm^{-1} ; ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 11.38 (s, 1H), 9.97 (s, 1H), 8.63 (s, 1H), 8.22 (s, 1H), 8.14 (d, $J = 8.0$ Hz, 1H), 7.45-7.35 (m, 3H), 5.99 (d, $J = 4.4$ Hz, 1H), 5.91 (d, $J = 8.8$ Hz, 1H), 5.80 (d, $J = 4.4$ Hz, 1H), 5.73 (d, $J = 5.2$ Hz, 1H), 5.00 (d, $J = 3.2$ Hz, 1H), 4.34-4.32 (m, 2H), 2.32 (t, $J = 7.2$ Hz, 2H), 1.61-1.59 (m, 2H), 1.23 (s br, 20H), 0.84 (t, $J = 6.4$ Hz, 3H) ppm; ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 171.5, 163.1, 161.7, 150.8, 140.4, 140.1, 139.9, 135.9, 130.8, 129.2, 119.9, 118.8, 115.9, 102.6, 88.6, 78.0, 73.3, 72.8, 36.4, 31.3, 29.1, 29.0, 29.0, 28.9, 28.9, 28.8, 28.7, 25.1, 22.1, 13.9 ppm. HRMS (+ESI) calcd. for $\text{C}_{31}\text{H}_{42}\text{N}_4\text{O}_7$ [M+Na] 605.2946; found 605.2957.

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