Synthesis and Biological Evaluation of 6-(Alkyn-1-yl)furo[2,3-*d*]pyrimidin-2(3*H*)-one Base and Nucleoside Derivatives[1]

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Derivatives of the 2′-deoxynucleoside of furo[2,3-*d*]pyrimidin-2(3*H*)-one with long-chain alkyl (or 4-alkylphenyl) substituents at C6 exhibit remarkable anti-VZV (varicella-zoster virus) potency and selectivity, and analogous 2′,3′-dideoxynucleoside derivatives show anti-HCMV (human cytomegalovirus) activity. We now report a synthetic approach that enables the preparation of long-chain 6-(alkyn-1-yl)furo[2,3-*d*]pyrimidin-2(3*H*)-ones in which the rodlike acetylene spacer replaces the 4-substituted-phenyl ring at C6. Analogues with methyl, β-D-ribofuranosyl, β-D-arabinofuranosyl, and 2-deoxy-β-D-*erythro*-pentofuranosyl substituents at N3 have been prepared. Long-chain derivatives at C6 in the 2′-deoxynucleoside series showed virus-encoded nucleoside kinase-sensitive anti-VZV activity. Surprisingly, 3-methyl-6-(octyn-1-yl)furo[2,3-*d*]-pyrimidin-2(3*H*)-one (prepared as a negative anti-VZV test control) exhibited anti-HCMV activity, which supports the possibility of development of non-nucleoside anti-HCMV agents originating from uncomplicated derivatives of such bicyclic ring systems.

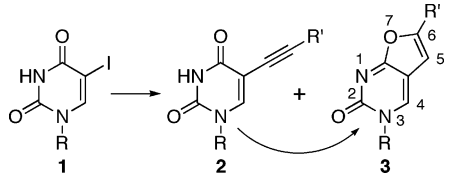
Introduction

Furo[2,3-*d*]pyrimidin-2(3*H*)-one 2′-deoxynucleosides were reported in 1981.[2a] Base and nucleoside derivatives of **3** (Scheme 1) were initially isolated as byproducts from Sonogashira cross-coupling reactions of 5-iodouracil derivatives with terminal alkynes. It also was demonstrated that efficient 5-endo-dig cyclizations of the cross-coupled 5-(alkyn-1-yl)uracil compounds were catalyzed by CuI.[2] Anticancer and antiviral activities were observed with certain of the 5-(alkyn-1-yl)uracil 2′-deoxynucleosides,[3a] but no antiviral activity was exhibited by the cyclized 6-butylfuro[2,3-*d*]pyrimidin-2(3*H*)-one 2′-deoxynucleoside.[3b]

Two decades later, the remarkably potent and selective activity of longer chain homologues against varicella-zoster virus (VZV) was discovered by McGuigan et al.[4] The preparation[4,5] and biological evaluation of numerous analogues of **3** have been reported.[6] The basic synthetic approach for all of these analogues employed our original strategy.[2] Although this approach is efficient, its scope is limited to the availability of substituted terminal alkynes and is not amenable to generation of compound libraries with a broad diversity of substituents at C6.

Furo[2,3-*d*]pyrimidin-2(3*H*)-one 2′-deoxynucleosides with a 4-alkylphenyl substituent at C6 have shown extremely potent anti-VZV activity.[4b] We reasoned that replacement of the phenyl ring at C6 by a rigid alkyne spacer might produce compounds with analogous structural features and biological profiles. We now report effective syntheses of key 6-bromofuro[2,3-*d*]-pyrimidin-2(3*H*)-one intermediates **6a**−**d** and their conversion to novel 6-(alkyn-1-yl)furo[2,3-*d*]pyrimidin-2(3*H*)-one derivatives **7** and **8** (Scheme 2), compounds[7] that were not accessible by our original cross-coupling/cyclization approach.[2−4,6]

Scheme 1. Synthesis of Furo[2,3-*d*]pyrimidin-2(3*H*)-ones **3**[2]



The 6-bromofuro[2,3-*d*]pyrimidin-2(3*H*)-one moiety[7] also enables elaboration into a diverse series of compounds (e.g., via Sonogashira, Heck, Suzuki, Stille, and carbonyl-insertion couplings and by aryl bromide chemistries involving lithium−halogen exchange and reactions of the lithio species with electrophiles).

Results and Discussion

Chemistry. The furopyrimidine starting materials **5a**−**d** (Scheme 2) were prepared by minor modifications of our Cu(I)-promoted cyclization methodology.[2] Because the selective anti-VZV activity of the bicyclic 2′-deoxynucleoside analogues is consistent with activation by a virus-expressed nucleoside kinase,[4,6] we also prepared derivatives of 1-methylfuro[2,3,-*d*]-pyrimidin-2(3*H*)-one[2] (**5a**) to serve as negative controls for the biological evaluations.

Treatment of **5a** with bromine in DMF gave 6-bromo-1-methylfuro[2,3-*d*]pyrimidin-2(3*H*)-one (**6a**) in 60% isolated yield. However, the acetylated nucleosides **5b**−**d** underwent decomposition under these conditions, and decomposition of **5c** also occurred with pyridinium tribromide in CH_2Cl_2. The latter reagent in acetonitrile converted **5c** into **6c** in 56% yield, but the reaction progress was sluggish at ambient temperature (24 h was required for completion). Bromination conditions reported for the preparation of 2,3-dibromobenzo[*b*]furan[8] worked well, and such treatment (Br_2/KOAc/$CHCl_3$) of **5b** and **5d** for 1−2 h at ambient temperature gave the 6-bromo analogues **6b** and **6d** in 80−87% yields without detected formation of regioisomers.

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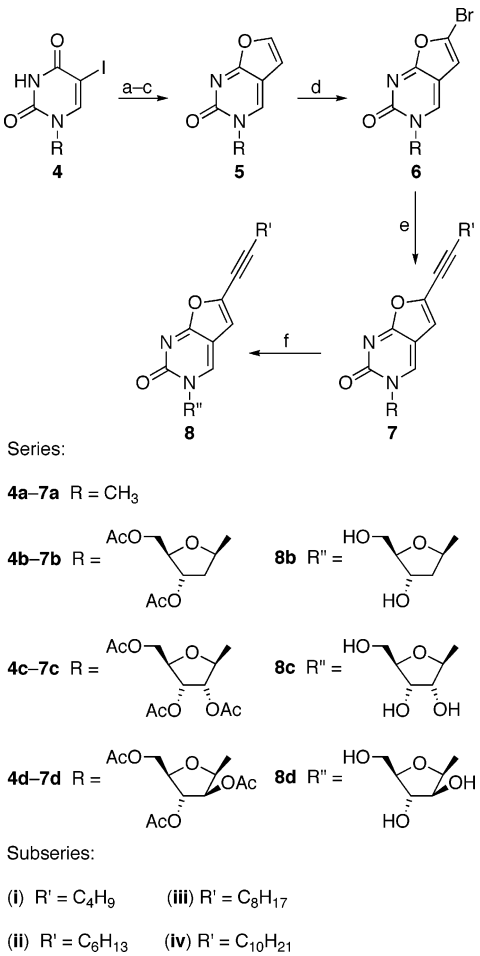
Scheme 2. Synthesis of the Test Compounds[a]



[a] Reagents: (a) TMS−acetylene/$(Ph_3P)_4Pd$/CuI/Et_3N/DMF; (b) NH_4F/MeOH; (c) CuI/Et_3N/DMF; (d) Br_2/KOAc/$CHCl_3$ (or Br_2/DMF) (or pyridinium tribromide/MeCN); (e) 1-alkyne/$(Ph_3P)_4Pd$/CuI/Et_3N/DMF; (f) NH_3/MeOH.

Sonogashira coupling of selected 1-alkynes with the 6-bromo derivatives **6a**−**d** proceeded smoothly to give the 6-(alkyn-1-yl) analogues **7a**−**d**(**i**−**iv**) in 53−98% yields. Ammonolysis of the acetyl groups from **7b**−**d**(**i**−**iv**) proceeded without difficulty to provide the unprotected nucleosides **8b**−**d**(**i**−**iv**).

Biological Testing. Compounds **7a**(**i**−**iv**) and **8b**−**d**(**i**−**iv**) were evaluated for activity against VZV in human embryonic lung (HEL) cells (Table 1). The 3-methyl series **7a** (negative controls) showed no activity against all three strains. As expected, the 2′-deoxy series **8b** exhibited the most potent anti-VZV activity, which peaked for the 6-(octyn-1-yl) **8b**(**ii**) and 6-(decyn-1-yl) **8b**(**iii**) derivatives [with lower potencies for the 6-(hexyn-1-yl) **8b**(**i**) and 6-(dodecyn-1-yl) **8b**(**iv**) compounds]. The EC_{50} values for **8b**(**ii**) (1.5 μM with a TK^+ strain and ∼25 μM with two TK^- strains] are in harmony with activation by a virus-encoded nucleoside kinase as the most significant pathway for inhibition by these 6-(alkyn-1-yl)furo[2,3-*d*]pyrimidin-2(3*H*)-one analogues. The anti-VZV activity of **8b**(**ii**) was comparable with that of acyclovir, but BVDU and 6-alkylfuro[2,3-*d*]-pyrimdin-2(3*H*)-ones prepared by the McGuigan group[4] are several orders of magnitude more potent in cell culture. No anti-VZV selectivity for TK^+ versus TK^- strains was apparent with the β-D-ribofuranosyl **8c** and β-D-arabinofuranosyl **8d** series of compounds, but weak selectivity for the TK^- strains relative to cytotoxicity was observed with these two series of analogues.

Compounds **7a**(**i**−**iv**) and **8b**−**d**(**i**−**iv**) were also evaluated against human cytomegalovirus (HCMV) in HEL cells. The

Table 1. Antiviral and Cytotoxic Activity of the Test Compounds in Human Embryonic Lung Cell Cultures

	EC_{50}[a] (μM)					cytotoxicity (μM)	
	VZV			HCMV			
compd	YS[b]	07/1[c]	YS/R[c]	AD-169	Davis	MCC[d]	CC_{50}[e]
7a(i)	217	>87	>87	>217	139	≥217	>217
7a(ii)	≥89	>77	23	31	37	194	>194
7a(iii)	>175	>70	>175	>175	>175	>175	>175
7a(iv)	>150	>150	>150	>150	>150	>150	>150
8b(i)	87	≥135	90	>150	>150	>150	>150
8b(ii)	1.5	25	22	21	19	≥97	138
8b(iii)	2.7	>13	6.5	7.4	7.6	52	77
8b(iv)	≥5.7	≥6.0	2.5	>4.8	>4.8	30	36
8c(i)	≥113	144	52	>144	>144	>144	>144
8c(ii)	≥39	39	19	>133	>53	≥133	>133
8c(iii)	>12	≥12	6.2	7.3	≥9.3	49	62
8c(iv)	>4.6	4.6	3.5	>4.6	>4.6	12	44
8d(i)	>144	>144	63	>144	>144	>144	>144
8d(ii)	≥43	34	21	>53	>53	133	>53
8d(iii)	≥11	11	3.7	> 12	12	49	124
8d(iv)	≥16	>12	5.7	>12	>12	46	116
ACV	1.4	36	24	ND	ND	>222	>889
BVDU	0.01	≥99	≥126	ND	ND	>150	>150
GCV	ND	ND	ND	5.1	8.7	>197	>197
f	0.0001	>20	>5	ND	ND	≥20	>200

[a] Inhibitory concentration required to reduce virus plaque formation by 50%. Virus input was 100 plaque forming units (pfu). [b] TK^+. [c] TK^-. [d] Minimum cytotoxic concentration that caused a microscopically visible alteration of cell morphology. [e] Cytotoxic concentration required to reduce cell growth by 50%. [f] 3-(2-Deoxy-β-D-*erythro*-pentofuranosyl)-6-(4-pentylphenyl)furo[2,3-*d*]pyrimidin-2(3*H*)-one (data from ref 4b).

6-(decyn-1-yl) 2′-deoxy analogue **8b**(**iii**) had EC_{50} values comparable to those of ganciclovir (GCV), and the 6-(octyn-1-yl) homologue **8b**(**ii**) also showed activity. Surprisingly, 3-methyl-6-(octyn-1-yl)furo[2,3-*d*]pyrimidin-2(3*H*)-one [**7a**(**ii**)] showed weak activity (EC_{50} = 31−37 μM), whereas other homologues in the "negative control" series were inactive. Only **8c**(**iii**) in the β-D-ribofuranosyl series and **8d**(**iii**) in the β-D-arabinofuranosyl series showed some indication of activity.

The unexpected activity exhibited by the 3-methyl-6-(octyn-1-yl) derivative **7a**(**ii**), as well as the weak effects of the ribonucleoside **8c**(**iii**) and arabino analogue **8d**(**iii**), suggested the possibility of development of novel anti-HCMV agents without deoxysugar-derived substituents. Mechanisms distinct from phosphorylation by nucleoside kinases and direct interference with nucleic acid synthesis were implied.[7] Subsequently, it was reported that 2′,3′-dideoxynucleoside analogues had anti-HCMV activity that was attributed to interference with viral entry into cells.[9] Derivatives of furo[2,3-*d*]pyrimidin-2(3*H*)-one with alkyl and other uncomplicated substituents are more readily accessible and cheaper to produce than the 2′-deoxy and 2′,3′-dideoxy nucleoside derivatives that have been shown to exhibit potent and selective anti-VZV and anti-HCMV activities.

Summary and Conclusions

We have developed effective syntheses of the 6-bromofuro-[2,3-*d*]pyrimidin-2(3*H*)-ones **6a**−**d** and employed them for Sonogashira cross-couplings to give 6-(alkyn-1-yl)furo[2,3-*d*]-pyrimidin-2(3*H*)-ones that were inaccessible by our prior methodology.[2−4,6] The anti-VZV and anti-HCMV activities for these novel 6-(alkyn-1-yl) analogues were affected primarily by the N3 substituent and the length of the alkynyl side chain at C6. The most active compounds had 8 or 10 carbon atoms in the 6-(alkyn-1-yl) side chains. The rodlike alkyne linker joining C6 and a C_{6-8} alkyl group did not support the enhancement of anti-VZV activity comparably to that observed with compounds linked by a 4-substituted phenyl ring. A 3-methyl-

6-(octyn-1-yl) derivative showed weak anti-HCMV activity, which was not expected for such a non-nucleoside analogue. A variety of 3-alkyl and 6-substituted furo[2,3-*d*]pyrimidin-2(3*H*)-one analogues are accessible via elaboration of the 6-bromo intermediates, and studies targeting such compounds are in progress.

Experimental Section

Reactions were performed under an inert atmosphere (N_2 or Ar) at ambient temperature unless otherwise indicated. EtOAc, MeOH, MeCN, CH_2Cl_2, $CHCl_3$, and Et_3N were dried by refluxing with and distillation from calcium hydride. DMF and 1-hexyne were dried over 4-Å molecular sieves. 1-Octyne, 1-decyne, 1-dodecyne, Br_2, and other starting materials were used as received from commercial suppliers. CuI (98%) purchased from Aldrich was used for coupling/cyclization reactions unless otherwise indicated.

UV spectra were determined with solutions in MeOH. ^{1}H NMR spectra (300 or 500 MHz) were measured with internal references at δ 7.27 ($CDCl_3$), 2.50 (DMSO-d_6), and 3.31 (CD_3OD) and ^{13}C NMR spectra (75 or 125 MHz) at δ 77.3 ($CDCl_3$), 39.5 (DMSO-d_6), and 49.2 (CD_3OD). NMR spectra were determined in $CDCl_3$ unless otherwise indicated. High-resolution mass spectra were obtained in the FAB mode unless otherwise indicated. Developed TLC plates were visualized under 254-nm UV light, with ninhydrin spray, with a H_2SO_4/EtOH (5:95) spray and charring, with a phosphomolybdic acid dip, or with an iodine chamber. Flash chromatography was performed with silica gel (230−400 mesh) and reagent grade solvents.

The 1-methyl-5-(trimethylsilylethynyl)uracil,[10] 1-(3,5-di-*O*-acetyl-2-deoxy-β-D-*erythro*-pentofuranosyl)-5-(trimethylsilylethynyl)-uracil,[2] 1-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-5-(trimethylsilylethynyl)uracil,[11] and 1-(2,3,5-tri-*O*-acetyl-β-D-arabinofuranosyl)-5-(trimethylsilylethynyl)uracil)[12] starting materials were prepared by our standard methodology.[2,13]

General Procedure A: Desilylation of the TMS−Acetylene Group. A solution of the 5-(trimethylsilylethynyl)uracil derivative and NH_4F (98%, 5 equiv.) in MeOH was heated at reflux until desilylation was completed (TLC, 1−3 h). Volatiles were flash evaporated, and the residue was purified by flash chromatography.

General Procedure B: CuI-Promoted 5-Endo-Dig Cyclization. A solution of the 5-ethynyluracil derivative and CuI (1.0 equiv) in freshly distilled and deoxygenated solvents was heated (70−100 °C) until the starting material was converted completely into the fluorescent furo[2,3-*d*]pyrimidin-2(3*H*)-one product (TLC). Volatiles were flash evaporated and the product was isolated by flash chromatography.

General Procedure C: Cross-Coupling of 6-Bromofuro[2,3-*d*]pyrimidin-2(3*H*)-ones and 1-Alkynes. A solution of the 6-bromofuro[2,3-*d*]pyrimidin-2(3*H*)-one derivative, $(Ph_3P)_4Pd$ (0.1 equiv), CuI (0.2 equiv), and a 1-alkyne (5 equiv) in deoxygenated DMF/Et_3N was stirred under an inert atmosphere until the starting material was completely consumed (TLC, 1−2 h). Volatiles were evaporated, and the residue was purified by flash chromatography.

General Procedure D: Ammonolysis of Acetyl Protecting Groups. A solution of the acetylated nucleoside derivative in saturated NH_3/MeOH was stirred at 0 °C until the starting material was completely deprotected (TLC, ∼3 h). Volatiles were evaporated, and the residue was purified by flash chromatagraphy.

3-Methylfuro[2,3-*d*]pyrimidin-2(3*H*)-one (5a). Treatment of 1-methyl-5-(trimethylsilylethynyl)uracil[10] (1.0 g, 4.5 mmol) by general procedure A [NH_4F (850 mg, 22.5 mmol), MeOH (50 mL)] resulted in separation of a light yellow precipitate. Heating was continued for ∼3 h (TLC), and the mixture was stored in a refrigerator overnight. The solid was filtered, washed with a minimum volume of ice-cold MeOH, and dried over P_2O_5 to give 5-ethynyl-1-methyluracil (545 mg, 81%): mp ∼240 °C (dec); UV λ_{max} 291, 228 nm (ϵ 14 600, 12 300), λ_{min} 251 nm (ϵ 3350); ^{1}H NMR (DMSO-d_6) δ 11.56 (br s, 1H), 8.10 (s, 1H), 4.07 (s, 1H), 3.24 (s, 3H); ^{13}C NMR (DMSO-d_6) δ 162.3, 150.5, 150.2, 96.1, 83.3, 76.3, 35.5; MS (EI) *m*/*z* 150.0413 (M^+ [$C_7H_6N_2O_2$] = 150.0430).

Treatment of a mixture of this material (25 mg, 0.16 mmol) and CuI (99.9%, 32 mg, 0.16 mmol) in DMF (1.5 mL) and Et_3N (0.5 mL) by general procedure B (100 °C, 8 h; chromatography (CH_2Cl_2/MeOH, 20:1)] gave **5a** (20 mg, 80%) as a yellow solid: mp ∼287 °C (dec); UV λ_{max} 327, 241 nm (ϵ 5540, 9460), λ_{min} 264, 236 nm (ϵ 666, 9230); ^{1}H NMR (DMSO-d_6) δ 8.65 (s, 1H), 7.71 (d, J = 2.7 Hz, 1H), 6.80 (d, J = 2.7 Hz, 1H), 3.51 (s, 3H); ^{13}C NMR (DMSO-d_6) δ 171.2, 144.1, 143.9, 104.7, 104.4, 104.1, 38.4; MS (CI) *m*/*z* 151.0512 (MH^+ [$C_7H_7N_2O_2$] = 151.0507).

6-Bromo-3-methylfuro[2,3-*d*]pyrimidin-2(3*H*)-one (6a). A suspension of **5a** (201 mg, 1.34 mmol) in dried DMF (12 mL) was cooled at 0 °C for 15 min. Br_2 (86 μL, 268 mg, 1.67 mmol) was added dropwise with stirring, and stirring was continued at 0 °C for 1 h. The flask was removed from the ice bath, and the mixture was allowed to warm to ambient temperature. Stirring was continued until all **5a** was converted to **6a** (TLC, ∼1 h). Dried Et_3N was added until the solution was basic. Volatiles were evaporated, and the residue was flash chromatographed (CH_2Cl_2/MeOH, 20:1) to give **6a** as a brown solid (180 mg, 60%): mp ∼200 °C (dec); UV λ_{max} 331, 248 nm (ϵ 3600, 7120), λ_{min} 275, 230 nm (ϵ 217, 5210); ^{1}H NMR (DMSO-d_6) δ 8.63 (s, 1H), 7.03 (s, 1H), 3.50 (s, 3H); ^{13}C NMR (DMSO-d_6) δ 171.1, 154.5, 143.8, 126.2, 106.8, 105.8, 39.0; MS (EI) *m*/*z* 227.9545 (M^+ [$C_7H_7\ ^{79}BrN_2O_2$] = 227.9534).

6-(Hexyn-1-yl)-3-methylfuro[2,3-*d*]pyrimidin-2(3*H*)-one [7a(i)]. Treatment of **6a** (25 mg, 0.11 mmol), $(Ph_3P)_4Pd$ (13 mg, 0.01 mmol), CuI (5 mg, 0.02 mmol), Et_3N (1.0 mL), DMF (2.0 mL), and 1-hexyne (52 μL, 36 mg, 0.44 mmol) by general procedure C [65 °C, 2 h; chromatography (CH_2Cl_2/MeOH, 20:1)] gave a material that was flash chromatographed (EtOAc/MeOH, 20:1) to give **7a(i)** (19 mg, 74%) as a pale-yellow solid: mp ∼152 °C (dec); UV λ_{max} 343, 278, 266 nm (ϵ 9310, 13 160, 17 900), λ_{min} 290, 275, 238 nm (ϵ 1930, 12 300, 6990); ^{1}H NMR δ 7.90 (s, 1H), 6.49 (s, 1H), 3.66 (s, 3H), 2.47 (t, J = 6.9 Hz, 2H), 1.66−1.56 (m, 2H), 1.53−1.41 (m, 2H), 0.95 (t, J = 7.2 Hz, 3H); ^{13}C NMR δ 175.5, 156.1, 140.7, 139.4, 107.0, 106.5, 100.4, 70.2, 40.2, 30.2, 22.2, 19.6, 13.8; MS (EI) *m*/*z* 230.1051 (M^+ [$C_{13}H_{14}N_2O_2$] = 230.1055). Anal. ($C_{13}H_{14}N_2O_2$) C, H, N.

3-Methyl-6-(octyn-1-yl)furo[2,3-*d*]pyrimidin-2(3*H*)-one [7a(ii)]. Treatment of **6a** (50 mg, 0.22 mmol), $(Ph_3P)_4Pd$ (25 mg, 0.02 mmol), CuI (9 mg, 0.05 mmol), Et_3N (2.0 mL), DMF (5.0 mL), and 1-octyne (200 μL, 121 mg, 1.10 mmol) by general procedure C [65 °C, 2 h; chromatography (EtOAc/MeOH, 20:1)] gave **7a(ii)** (30 mg, 53%) as a pale-yellow solid: mp ∼158 °C (dec); UV λ_{max} 343, 278, 266, 217 nm (ϵ 10 500, 14 400, 20 000, 17 500), λ_{min} 289, 275, 238 nm (ϵ 1340, 13 300, 7250); ^{1}H NMR δ 7.89 (s, 1H), 6.49 (s, 1H), 3.67 (s, 3H), 2.47 (t, J = 7.0 Hz, 2H), 1.67−1.57 (m, 3H), 1.42−1.41 (m, 2H), 1.32−1.25 (m, 3H), 0.90 (t, J = 6.75 Hz, 3H); ^{13}C NMR δ 171.4, 156.1, 140.9, 139.4, 107.0, 106.6, 100.4, 70.2, 40.2, 31.5, 28.8, 28.2, 22.7, 19.9, 14.3; MS (EI) *m*/*z* 258.1367 (M^+ [$C_{15}H_{18}N_2O_2$] = 258.1368). Anal. ($C_{15}H_{18}N_2O_2$) C, H, N.

6-(Decyn-1-yl)-3-methylfuro[2,3-*d*]pyrimidin-2(3*H*)-one [7a(iii)]. Treatment of **6a** (50 mg, 0.22 mmol), $(Ph_3P)_4Pd$ (25 mg, 0.02 mmol), CuI (9 mg, 0.05 mmol), Et_3N (2.0 mL), DMF (5.0 mL), and 1-decyne (202 μL, 152 mg, 1.10 mmol) by general procedure C [65 °C, 2 h; chromatography (EtOAc/MeOH, 20:1)] gave **7a(iii)** (35 mg, 56%) as a pale-yellow solid: mp ∼165 °C (dec); UV λ_{max} 343, 278, 266, 217 nm (ϵ 13 300, 18 300, 25 600, 21 600), λ_{min} 289, 275, 238 nm (ϵ 1320, 16 900, 8630, 14 900); ^{1}H NMR δ 7.90 (s, 1H), 6.49 (s, 1H), 3.67 (s, 3H), 2.46 (t, J = 7.0 Hz, 2H), 1.67−1.57 (m, 2H), 1.46−1.40 (m, 2H), 1.29 (br s, 8H), 0.88 (t, J = 6.45 Hz, 3H); ^{13}C NMR δ 171.5, 156.1, 141.0, 139.4, 107.0, 106.6, 100.4, 70.2, 40.1, 32.0, 29.3, 29.2, 29.1, 28.2, 22.9, 19.9, 14.3; MS (EI) *m*/*z* 286.1681 (M^+ [$C_{17}H_{22}N_2O_2$] = 286.1681). Anal. ($C_{17}H_{22}N_2O_2$) C, H, N.

6-(Dodecyn-1-yl)-3-methylfuro[2,3-*d*]pyrimidin-2(3*H*)-one [7a(iv)]. Treatment of **6a** (80 mg, 0.35 mmol), $(Ph_3)_4Pd$ (41 mg, 0.035 mmol), CuI (14 mg, 0.07 mmol), Et_3N (2.0 mL), DMF (5.0 mL), and 1-dodecyne (380 μL, 290 mg, 1.75 mmol) by general

procedure C [65 °C, 2 h; chromatography (EtOAc/MeOH, 20:1)] gave **7a(iv)** (47 mg, 68%) as a pale-yellow solid: mp ~174 °C (dec); UV λ_{max} 344, 278, 266 nm (ϵ 11 800, 16 300, 22 800), λ_{min} 289, 276, 239 nm (ϵ 1210, 14 900, 8100); ^{1}H NMR δ 7.88 (s, 1H), 6.49 (s, 1H), 3.66 (s, 3H), 2.46 (t, J = 7.0 Hz, 2H), 1.64−1.59 (m, 3H), 1.46−1.38 (m, 3H), 1.27 (br s, 10H), 0.88 (t, J = 6.6 Hz, 3H); ^{13}C NMR δ 171.2, 155.8, 140.4, 139.2, 106.3, 100.2, 77.2, 69.9, 40.0, 31.9, 29.6, 29.5, 29.3, 29.1, 28.9, 28.0, 22.7, 19.6, 14.1; MS (EI) *m*/*z* 314.2008 (M^+ [$C_{19}H_{26}N_2O_2$] = 314.1994). Anal. ($C_{19}H_{26}N_2O_2$) C, H, N.

3-(3,5-Di-*O*-acetyl-2-deoxy-β-D-*erythro*-pentofuranosyl)furo-[2,3-*d*]pyrimidin-2(3*H*)-one (5b). A solution of 1-(3,5-di-*O*-acetyl-2-deoxy-β-D-*erythro*-pentofuranosyl)-5-(trimethylsilylethynyl)-uracil[2] (50 mg, 0.12 mmol) and NH_4F (23 mg, 0.61 mmol) in MeOH (1 mL) was treated by general procedure A [ambient temperature, 1 h; chromatography (60% EtOAc/hexanes → 80% EtOAc/hexanes)] to give 1-(3,5-di-*O*-acetyl-2-deoxy-β-D-*erythro*-pentofuranosyl)-5-ethynyluracil (35 mg, 86%) as a white solid foam: UV λ_{max} 287, 227 nm (ϵ 12 600, 11 800), λ_{min} 249 nm (ϵ 2600); ^{1}H NMR δ 8.70 (s, 1H), 7.91 (s, 1H), 6.30 (dd, J = 7.5, 6.0 Hz, 1H), 5.26−5.24 (m, 1H), 4.42−4.30 (m, 3H), 3.21 (s, 1H), 2.57 (ddd, J = 14.5, 5.5, 2.5 Hz, 1H), 2.24−2.19 (m, 1H), 2.18 (s, 3H), 2.12 (s, 3H); ^{13}C NMR δ 170.6, 170.4, 161.0, 149.2, 143.0, 100.0, 85.9, 83.0, 82.5, 74.7, 74.1, 64.0, 38.6, 21.11, 21.09; MS (EI) *m*/*z* 336.0963 (M^+ [$C_{15}H_{16}N_2O_7$] = 336.0957).

This material (100 mg, 0.29 mmol), CuI (58 mg, 0.29 mmol), Et_3N (3 mL), and EtOAc (6 mL) were treated by general procedure B [70 °C; chromatography (EtOAc → 5% MeOH/EtOAc)] to give **5b** as a white solid foam (92 mg, 94%): UV λ_{max} 328, 241 nm (ϵ 5300, 7500), λ_{min} 263 nm (ϵ 490); ^{1}H NMR δ 8.39 (s, 1H), 7.38 (d, J = 2.7 Hz, 1H), 6.56 (d, J = 2.7 Hz, 1H), 6.32 (dd, J = 7.5, 5.5 Hz, 1H), 5.24 (d, J = 6.3 Hz, 1H), 4.43 (s, 3H), 3.0 (ddd, J = 14.4, 5.4, 2.1 Hz, 1H), 2.13 (s, 4H), 2.07 (s, 3H); ^{13}C NMR δ 172.2, 170.6, 170.5, 154.6, 145.2, 136.4, 106.2, 104.6, 88.9, 83.6, 74.2, 63.9, 39.6, 21.1, 21.0; MS (EI) *m*/*z* 336.0972 (M^+ [$C_{15}H_{16}N_2O_7$] = 336.0957).

3-(3,5-Di-*O*-acetyl-2-deoxy-β-D-*erythro*-pentofuranosyl)-6-bromofuro[2,3-*d*]pyrimidin-2(3*H*)-one (6b). A mixture of **5b** (25 mg, 74 μmol), KOAc (3 mg, 30 μmol), Br_2 (19 μL, 59 mg, 0.37 mmol), and dried $CHCl_3$ (3 mL) was stirred at ambient temperature for 2 h in a flame-dried flask. The mixture was cooled to 0 °C and dried Et_3N was added (until the solution was basic). Volatiles were evaporated, and the residue was flash chromatographed (80% EtOAc/hexanes) to give **6b** (27 mg, 87%) as a yellow solid foam: UV λ_{max} 334, 248 nm (ϵ 8000, 14 300), λ_{min} 276, 231 nm (ϵ 870, 10 800); ^{1}H NMR δ 8.33 (s, 1H), 6.55 (s, 1H), 6.28 (dd, J = 7.5, 6.5 Hz, 1H), 5.22 (d, J = 6.0 Hz, 1H), 4.41 (s, 3H), 2.98 (ddd, J = 14.0, 5.0, 2.0 Hz, 1H), 2.12 (s, 3H), 2.10−2.07 (m, 1H), 2.06 (s, 3H); ^{13}C NMR δ 171.9, 170.6, 170.5, 154.1, 134.9, 129.1, 107.8, 106.1, 88.9, 83.7, 74.2, 63.8, 39.5, 21.1, 21.0; MS (EI) *m*/*z* 414.0247 (M^+ [$C_{15}H_{15}{}^{79}BrN_2O_7$] = 414.0262).

3-(3,5-Di-*O*-acetyl-2-deoxy-β-D-*erythro*-pentofuranosyl)-6-(hexyn-1-yl)furo[2,3-*d*]pyrimidin-2(3*H*)-one [7b(i)]. Treatment of **6b** (150 mg, 0.36 mmol), $(Ph_3P)_4Pd$ (46 mg, 0.04 mmol), CuI (14 mg, 0.07 mmol), Et_3N (3.0 mL), DMF (1.5 mL), and 1-hexyne (220 μL, 148 mg, 1.81 mmol) by general procedure C [ambient temperature, 2 h; chromatography (EtOAc/hexanes, 6:4)] gave **7b(i)** (137 mg, 91%) as a yellow glass: UV λ_{max} 344, 278, 266 nm (ϵ 11 100, 13 900, 19 100), λ_{min} 289, 275, 240 nm (ϵ 1400, 12 600, 8310); ^{1}H NMR δ 8.29 (s, 1H), 6.52 (s, 1H), 6.29 (dd, J = 7.5, 6.0 Hz, 1H), 5.22 (d, J = 6.3 Hz, 1H), 4.41 (s, 3H), 2.97 (ddd, J = 14.4, 5.4, 2.1 Hz, 1H), 2.48 (t, J = 7.05 Hz, 2H), 2.12 (s, 3H), 2.12−2.05 (m, 1H), 2.05 (s, 3H), 1.66−1.57 (m, 2H), 1.53−1.41 (m, 2H), 0.95 (t, J = 7.2 Hz, 3H); ^{13}C NMR δ 171.3, 170.7, 170.5, 154.7, 139.7, 135.3, 107.1, 106.9, 100.6, 88.9, 83.6, 74.3, 70.1, 63.9, 39.6, 30.2, 22.2, 21.14, 21.06, 19.6, 13.8; MS (EI) *m*/*z* 416.1586 (M^+ [$C_{21}H_{24}N_2O_7$] = 416.1583).

3-(2-Deoxy-β-D-*erythro*-pentofuranosyl)-6-(hexyn-1-yl)furo-[2,3-*d*]pyrimidin-2(3*H*)-one [8b(i)]. Treatment of **7b(i)** (100 mg, 0.24 mmol) by general procedure D [NH_3/MeOH (30 mL); chromatography (EtOAc → 5% MeOH/EtOAc)] gave **8b(i)** as a white solid (65 mg, 81%): mp = 138−140 °C; UV λ_{max} 343, 278, 266 (ϵ 12 000, 15 800, 21 300), λ_{min} 289, 275, 240 (ϵ 1400, 14 300, 9420); ^{1}H NMR (CD_3OD) δ 8.96 (s, 1H), 6.78 (s, 1H), 6.27 (t, J = 6.25 Hz, 1H), 4.38 (q, J = 5.0 Hz, 1H), 4.06 (q, J = 2.8 Hz, 1H), 3.88 (dd, J = 12.0, 3.0 Hz, 1H), 3.78 (dd, J = 12.0, 4.0 Hz, 1H), 2.61 (ddd, J = 14.0, 6.0, 4.5 Hz, 1H), 2.52 (t, J = 7.0 Hz, 2H), 2.21 (dt, J = 13.5, 6.0 Hz, 1H), 1.64−1.58 (m, 2H), 1.53−1.46 (m, 2H), 0.97 (t, J = 7.5 Hz, 3H); ^{13}C NMR (CD_3OD) δ 172.3, 156.9, 140.3, 140.2, 109.0, 108.3, 100.8, 90.2, 89.9, 71.4, 70.8, 62.4, 43.0, 31.4, 23.1, 19.9, 14.0; MS (EI) *m*/*z* 332.1364 (M^+ [$C_{17}H_{20}N_2O_5$] = 332.1372). Anal. ($C_{17}H_{20}N_2O_5$) C, H, N.

3-(3,5-Di-*O*-acetyl-2-deoxy-β-D-*erythro*-pentofuranosyl)-6-(octyn-1-yl)furo[2,3-*d*]pyrimidin-2(3*H*)-one [7b(ii)]. Treatment of **6b** (200 mg, 0.483 mmol), $(Ph_3P)_4Pd$ (56 mg, 0.05 mmol), CuI (19 mg, 0.10 mmol), Et_3N (4.0 mL), DMF (2.0 mL), and 1-octyne (355 μL, 266 mg, 2.41 mmol) by general procedure C [ambient temperature, 2 h; chromatography (EtOAc/hexanes, 6:4)] gave **7b(ii)** (175 mg, 82%) as a yellow glass: UV λ_{max} 344, 278, 266 nm (ϵ 9980, 12 600, 17 300), λ_{min} 289, 275, 240 nm (ϵ 1230, 11 400, 7500); ^{1}H NMR δ 8.29 (s, 1H), 6.52 (s, 1H), 6.30 (dd, J = 7.2, 5.7 Hz, 1H), 5.23 (d, J = 6.3 Hz, 1H), 4.41 (s, 3H), 2.47 (t, J = 7.05 Hz, 2H), 2.22 (ddd, J = 14.7, 5.7, 2.1 Hz, 1H), 2.12 (s, 3H), 2.12−2.06 (m, 1H), 2.06 (s, 3H), 1.67−1.58 (m, 2H), 1.49−1.39 (m, 2H), 1.34−1.25 (m, 4H), 0.90 (t, J = 6.75 Hz, 3H); ^{13}C NMR δ 171.4, 170.7, 170.5, 154.7, 139.8, 135.3, 107.1, 106.9, 100.6, 88.9, 83.6, 74.3, 70.1, 63.9, 39.6, 31.5, 28.8, 28.2, 22.7, 21.2, 21.1, 19.9, 14.3; MS (EI) *m*/*z* 444.1909 (M^+ [$C_{23}H_{28}N_2O_7$] = 444.1896).

3-(2-Deoxy-β-D-*erythro*-pentofuranosyl)-6-(octyn-1-yl)furo-[2,3-*d*]pyrimidin-2(3*H*)-one [8b(ii)]. Treatment of **7b(ii)** (100 mg, 0.25 mmol) by general procedure D [NH_3/MeOH (30 mL); chromatography (EtOAc → 5% MeOH/EtOAc)] gave **8b(ii)** as a white solid (48 mg, 59%): mp = 142−144 °C; UV λ_{max} 343, 278, 266 (ϵ 10 100, 13 500, 17 700), λ_{min} 289, 275, 240 (ϵ 1070, 11 900, 7740); ^{1}H NMR (CD_3OD) δ 8.95 (s, 1H), 6.77 (s, 1H), 6.26 (t, J = 6.25 Hz, 1H), 4.38 (q, J = 4.8 Hz, 1H), 4.06 (q, J = 3.5 Hz, 1H), 3.88 (dd, J = 12.0, 3.5 Hz, 1H), 3.78 (dd, J = 12.5, 3.5 Hz, 1H), 2.61 (ddd, J = 13.5, 6.0, 5.0 Hz, 1H), 2.51 (t, J = 7.25 Hz, 2H), 2.21 (dt, J = 13.5, 6.0 Hz, 1H), 1.65−1.59 (m, 2H), 1.50−1.44 (m, 2H), 1.38−1.34 (m, 4H), 0.92 (t, J = 6.75 Hz, 3H); ^{13}C NMR (CD_3OD) δ 172.3, 156.9, 140.3, 140.2, 109.1, 108.3, 100.8, 90.2, 89.9, 71.4, 70.9, 62.4, 43.0, 32.6, 29.8, 29.3, 23.7, 20.2, 14.5; MS (EI) *m*/*z* 360.1673 (M^+ [$C_{19}H_{24}N_2O_5$] = 360.1685). Anal. ($C_{19}H_{24}N_2O_5$) C, H, N.

3-(3,5-Di-*O*-acetyl-2-deoxy-β-D-*erythro*-pentofuranosyl)-6-(decyn-1-yl)furo[2,3-*d*]pyrimidin-2(3*H*)-one [7b(iii)]. Treatment of **6b** (150 mg, 0.362 mmol), $(Ph_3P)_4Pd$ (46 mg, 0.04 mmol), CuI (14 mg, 0.07 mmol), Et_3N (3.0 mL), DMF (1.5 mL), and 1-decyne (330 μL, 250 mg, 1.81 mmol) by general procedure C [ambient temperature, 2 h; chromatography (EtOAc/hexanes, 6:4)] gave **7b(iii)** (151 mg, 88%) as a yellow glass: UV λ_{max} 344, 278, 266 nm (ϵ 11 900, 15 000, 20 600), λ_{min} 289, 275, 240 nm (ϵ 1460, 13 600, 8940); ^{1}H NMR δ 8.29 (s, 1H), 6.52 (s, 1H), 6.29 (t, J = 6.5 Hz, 1H), 5.22 (d, J = 6.5 Hz, 1H), 4.41 (s, 3H), 2.97 (ddd, J = 14.5, 6.0, 2.5 Hz, 1H), 2.46 (t, J = 7.25 Hz, 2H), 2.12−2.10 (m, 1H), 2.11 (s, 3H), 2.05 (s, 3H), 1.65−1.59 (m, 2H), 1.44−1.41 (m, 2H), 1.30−1.27 (m, 8H), 0.89 (t, J = 6.75 Hz, 3H); ^{13}C NMR δ 171.3, 170.6, 170.5, 154.7, 139.7, 135.3, 107.0, 106.9, 100.6, 88.9, 83.6, 74.3, 70.1, 63.9, 39.5, 32.0, 29.3, 29.2, 29.1, 28.2, 22.9, 21.1, 21.0, 19.9, 14.3; MS (EI) *m*/*z* 472.2200 (M^+ [$C_{25}H_{32}N_2O_7$] = 472.2209).

3-(2-Deoxy-β-D-*erythro*-pentofuranosyl)-6-(decyn-1-yl)furo-[2,3-*d*]pyrimidin-2(3*H*)-one [8b(iii)]. Treatment of **7b(iii)** (80 mg, 0.17 mmol) by general procedure D [NH_3/MeOH (30 mL); chromatography (EtOAc → 5% MeOH/EtOAc)] gave **8b(iii)** as a white solid (45 mg, 68%): mp = 152−154 °C; UV λ_{max} 343, 278, 266 (ϵ 10 800, 14 100, 19 000), λ_{min} 289, 275, 240 (ϵ 1290, 12 800, 8410); ^{1}H NMR (CD_3OD) δ 8.95 (s, 1H), 6.77 (s, 1H), 6.27 (t, J = 5.75 Hz, 1H), 4.38 (q, J = 7.5 Hz, 1H), 4.06 (q, J = 5.0 Hz, 1H), 3.88 (dd, J = 12.5, 3.0 Hz, 1H), 3.78 (dd, J = 12.0, 4.0 Hz, 1H), 2.61 (ddd, J = 14.0, 6.0, 4.5 Hz, 1H), 2.51 (t, J = 7.0 Hz, 2H), 2.21 (dt, J = 13.5, 6.0 Hz, 1H), 1.65−1.59 (m, 2H), 1.47−

1.43 (m, 2H), 1.33−1.28 (m, 8H), 0.90 (t, J = 6.75 Hz, 3H); ^{13}C NMR (CD_3OD) δ 172.3, 156.9, 140.3, 140.2, 109.1, 108.3, 100.8, 90.2, 89.9, 71.4, 70.9, 62.4, 43.0, 33.1, 30.5, 30.3, 30.1, 29.3, 23.7, 20.2, 14.6; MS (EI) m/z 388.1999 (M^+ [$C_{21}H_{28}N_2O_5$] = 388.1998). Anal. ($C_{21}H_{28}N_2O_5$) C, H, N.

3-(3,5-Di-*O*-acetyl-2-deoxy-*β*-D-*erythro*-pentofuranosyl)-6-(dodecyn-1-yl)furo[2,3-*d*]pyrimidin-2(3*H*)-one [7b(iv)]. Treatment of **6b** (125 mg, 0.302 mmol), $(Ph_3P)_4Pd$ (35 mg, 0.03 mmol), CuI (12 mg, 0.06 mmol), Et_3N (3.0 mL), DMF (1.5 mL), and 1-dodecyne (322 μL, 250 mg, 1.50 mmol) by general procedure C [ambient temperature, 2 h; chromatography (EtOAc/hexanes, 6:4)] gave **7b(iv)** (125 mg, 82%) as a yellow glass: UV λ_{max} 343, 278, 266 nm (ϵ 10 500, 13 300, 18 300), λ_{min} 289, 275, 240 nm (ϵ 1340, 12 100, 7990); ^{1}H NMR δ 8.29 (s, 1H), 6.52 (s, 1H), 6.29 (dd, J = 7.5, 6.0 Hz, 1H), 5.22 (d, J = 6.0 Hz, 1H), 4.41 (s, 3H), 2.97 (ddd, J = 15.0, 5.5, 2.0 Hz, 1H), 2.46 (t, J = 7.25 Hz, 2H), 2.12 (s, 3H), 2.11−2.07 (m, 1H), 2.05 (s, 3H), 1.65−1.59 (m, 2H), 1.44−1.40 (m, 2H), 1.29−1.27 (m, 12H), 0.88 (t, J = 7.0 Hz, 3H); ^{13}C NMR δ 171.3, 170.6, 170.5, 154.7, 139.7, 135.3, 107.1, 106.9, 100.6, 88.9, 83.6, 74.3, 70.1, 63.9, 39.6, 32.1, 29.8, 29.7, 29.5, 29.3, 29.1, 28.2, 22.9, 21.1, 21.0, 19.9, 14.3; MS (EI) m/z 500.2532 (M^+ [$C_{27}H_{36}N_2O_7$] = 500.2522).

3-(2-Deoxy-*β*-D-*erythro*-pentofuranosyl)-6-(dodecyn-1-yl)furo-[2,3-*d*]pyrimidin-2(3*H*)-one [8b(iv)]. Treatment of **7b(iv)** (100 mg, 0.20 mmol) by general procedure D [NH_3/MeOH (30 mL); chromatography (EtOAc → 5% MeOH/EtOAc)] gave **8b(iv)** as a white solid (55 mg, 66%): mp = 157−159 °C; UV λ_{max} 343, 278, 266 (ϵ 10 400, 13 600, 18 300), λ_{min} 289, 275, 240 (ϵ 1090, 12 300, 8030); ^{1}H NMR (CD_3OD) δ 8.95 (s, 1H), 6.77 (s, 1H), 6.27 (t, J = 6.25 Hz, 1H), 4.37 (q, J = 7.5 Hz, 1H), 4.06 (q, J = 3.5 Hz, 1H), 3.88 (dd, J = 12.0, 3.0 Hz, 1H), 3.77 (dd, J = 12.0, 3.0 Hz, 1H), 2.60 (ddd, J = 13.5, 5.5, 5.0 Hz, 1H), 2.51 (t, J = 7.0 Hz, 2H), 2.20 (dt, J = 13.5, 6.0 Hz, 1H), 1.65−1.59 (m, 2H), 1.49−1.43 (m, 2H), 1.33−1.29 (m, 12H), 0.89 (t, J = 6.75 Hz, 3H); ^{13}C NMR (CD_3OD) δ 172.2, 156.8, 140.3, 140.1, 108.9, 108.3, 100.7, 90.1, 89.8, 71.3, 70.8, 62.3, 43.0, 33.1, 30.73, 30.68, 30.5, 30.2, 30.0, 29.2, 23.8, 20.1, 14.5; MS m/z 439.2216 (MNa^+ [$C_{23}H_{32}N_2O_5Na$] = 439.2209). Anal. ($C_{23}H_{32}N_2O_5$) C, H, N.

3-(2,3,5-Tri-*O*-acetyl-*β*-D-ribofuranosyl)furo[2,3-*d*]pyrimidin-2(3*H*)-one (5c). Treatment of 2′,3′,5′-tri-*O*-acetyl-5-(trimethylsilylethynyl)uridine[11] (25 mg, 54 μmol) by general procedure A [NH_4F (10 mg, 0.27 mmol), MeOH (1 mL), reflux, 1 h; chromatography (EtOAc/hexanes, 6:4)] gave 2′,3′,5′-tri-*O*-acetyl-5-ethynyluridine (16 mg, 75%) as a pale-yellow solid foam: UV λ_{max} 285, 223 nm (ϵ 14 900, 13 500), λ_{min} 248 nm (ϵ 3160); ^{1}H NMR δ 8.37 (s, 1H), 7.86 (s, 1H), 6.09 (d, J = 4.5 Hz, 1H), 5.34 (d, J = 4.2 Hz, 2H), 4.41−4.39 (m, 3H), 3.23 (s, 1H), 2.22 (s, 3H), 2.14 (s, 3H), 2.13 (s, 3H); ^{13}C NMR δ 170.3, 169.9, 169.8, 160.9, 149.3, 142.9, 100.4, 87.7, 82.7, 80.5, 74.6, 73.5, 73.3, 63.1, 21.1, 20.7, 20.6; MS (FAB) m/z 395.1100 (MH^+ [$C_{17}H_{19}N_2O_9$] = 395.1090).

Treatment of this material (500 mg, 1.27 mmol), CuI (246 mg, 1.27 mmol), Et_3N (20 mL), and MeCN (40 mL) by general procedure B [reflux, 8 h; chromatography (80% EtOAc/hexanes → EtOAc)] gave **5c** (307 mg, 61%) as a white solid foam: UV λ_{max} 330, 244 nm (ϵ 6280, 8300), λ_{min} 265 nm (ϵ 552); ^{1}H NMR δ 8.31 (s, 1H), 7.38 (d, J = 3.0 Hz, 1H), 6.52 (d, J = 3.0 Hz, 1H), 6.26 (d, J = 3.5 Hz, 1H), 5.44 (dd, J = 5.5, 4.0 Hz, 1H), 5.31 (t, J = 5.75 Hz, 1H), 4.49−4.41 (m, 3H), 2.17 (s, 3H), 2.14 (s, 3H), 2.10 (s, 3H); ^{13}C NMR δ 172.4, 170.3, 169.7, 169.6, 154.6, 145.6, 136.8, 106.8, 104.6, 90.4, 79.9, 74.3, 69.4, 62.7, 21.0, 20.7, 20.6; MS (FAB) m/z 417.0910 (MNa^+ [$C_{17}H_{18}N_2O_9Na$] = 417.0910).

3-(2,3,5-Tri-*O*-acetyl-*β*-D-ribofuranosyl)-6-bromofuro[2,3-*d*]-pyrimidin-2(3*H*)-one (6c). A mixture of **5c** (30 mg, 76 μmol), pyridinium tribromide (90%, 27 mg, 76 μmol), and MeCN (3 mL) was stirred at ambient temperature for 24 h, and dried Et_3N was added. Volatiles were evaporated, and the residue was flash chromatographed (80% EtOAc/hexanes) to give **6c** (20 mg, 56%) as a yellow solid foam: UV λ_{max} 334, 248 nm (ϵ 6270, 11 600), λ_{min} 275, 232 nm (ϵ 437, 8840); ^{1}H NMR δ 8.26 (s, 1H), 6.52 (s, 1H), 6.22 (d, J = 3.9 Hz, 1H), 5.43 (dd, J = 5.4, 3.6 Hz, 1H), 5.29 (t, J = 5.85 Hz, 1H), 4.49−4.39 (m, 3H), 2.16 (s, 3H), 2.14 (s, 3H), 2.10 (s, 3H); ^{13}C NMR δ 172.1, 170.3, 169.8, 169.7, 154.1, 135.1, 129.8, 108.5, 105.9, 90.3, 80.1, 74.3, 69.5, 62.8, 21.1, 20.74, 20.71; MS (FAB) m/z 495.0020 (MNa^+ [$C_{17}H_{18}{}^{79}BrN_2O_9Na$] = 495.0021).

3-(2,3,5-Tri-*O*-acetyl-*β*-D-ribofuranosyl)-6-(hexyn-1-yl)furo-[2,3-*d*]pyrimidin-2(3*H*)-one [7c(i)]. Treatment of **6c** (50 mg, 0.11 mmol), $(Ph_3P)_4Pd$ (12 mg, 0.01 mmol), CuI (4 mg, 0.02 mmol), Et_3N (0.5 mL), DMF (1.0 mL), and 1-hexyne (61 μL, 43 mg, 0.53 mmol) by general procedure C [ambient temperature, 1 h; chromatography (EtOAc/hexanes, 1:1)] gave **7c(i)** (35 mg, 70%) as a pale-yellow glass: UV λ_{max} 344, 278, 266 nm (ϵ 13 200, 17 300, 24 600), λ_{min} 289, 275, 240 nm (ϵ 1980, 15 800, 11 600); ^{1}H NMR δ 8.22 (s, 1H), 6.49 (s, 1H), 6.25 (d, J = 3.6 Hz, 1H), 5.43 (t, J = 4.5 Hz, 1H), 5.31 (t, J = 5.7 Hz, 1H), 4.49−4.43 (m, 3H), 2.49 (t, J = 7.0 Hz, 2H), 2.17 (s, 3H), 2.14 (s, 3H), 2.10 (s, 3H), 1.67−1.58 (m, 2H), 1.54−1.44 (m, 2H), 0.96 (t, J = 7.2 Hz, 3H); ^{13}C NMR δ 171.5, 170.3, 169.7, 169.6, 154.7, 140.1, 135.6, 107.7, 106.7, 100.8, 90.3, 80.0, 74.3, 70.0, 69.4, 62.7, 30.1, 22.2, 21.0, 20.7, 20.6; MS (EI) m/z 474.1640 (M^+ [$C_{23}H_{26}N_2O_9$] = 474.1638).

6-(Hexyn-1-yl)-3-(*β*-D-ribofuranosyl)furo[2,3-*d*]pyrimidin-2(3*H*)-one [8c(i)]. Treatment of **7c(i)** (60 mg, 0.13 mmol) by general procedure D [NH_3/MeOH (30 mL); chromatography (EtOAc → 5% MeOH/EtOAc)] gave **8c(i)** as a white solid (35 mg, 80%): mp = 158−160 °C; UV λ_{max} 344, 278, 266 (ϵ 10 800, 14 100, 18 900), λ_{min} 289, 275, 241 (ϵ 1500, 12 800, 9280); ^{1}H NMR (CD_3OD) δ 9.09 (s, 1H), 6.77 (s, 1H), 5.95 (s, 1H), 4.16 (br s, 3H), 4.02 (dd, J = 12.6, 2.7 Hz, 1H), 3.83 (dd, J = 12.6, 1.8 Hz, 1H), 2.52 (t, J = 7.05 Hz, 2H), 1.66−1.55 (m, 2H), 1.54−1.43 (m, 2H), 0.97 (t, J = 7.35 Hz, 3H); ^{13}C NMR (CD_3OD) δ 172.4, 157.1, 140.5, 140.4, 109.0, 108.5, 100.8, 94.4, 85.9, 76.9, 70.8, 69.5, 61.0, 31.4, 23.1, 19.9, 14.0; MS m/z 371.1230 (MNa^+ [$C_{17}H_{20}N_2O_6Na$] = 371.1219).

3-(2,3,5-Tri-*O*-acetyl-*β*-D-ribofuranosyl)-6-(octyn-1-yl)furo-[2,3-*d*]pyrimidin-2(3*H*)-one [7c(ii)]. Treatment of **6c** (80 mg, 0.17 mmol), $(Ph_3P)_4Pd$ (20 mg, 0.02 mmol), CuI (7 mg, 0.04 mmol), Et_3N (1.0 mL), DMF (2.0 mL), and 1-octyne (130 μL, 93 mg, 0.85 mmol) by general procedure C [ambient temperature, 1 h; chromatography (EtOAc/hexanes, 1:1)] gave **7c(ii)** (68 mg, 80%) as a pale-yellow glass: UV λ_{max} 344, 278, 266 nm (ϵ 12 400, 16 400, 23 200), λ_{min} 289, 275, 240 nm (ϵ 1850, 14 900, 10 900); ^{1}H NMR δ 8.22 (s, 1H), 6.50 (s, 1H), 6.24 (d, J = 3.6 Hz, 1H), 5.43 (t, J = 4.5 Hz, 1H), 5.30 (t, J = 5.7 Hz, 1H), 4.84−4.24 (m, 3H), 2.48 (t, J = 7.0 Hz, 2H), 2.16 (s, 3H), 2.14 (s, 3H), 2.10 (s, 3H), 1.68−1.58 (m, 2H), 1.46−1.41 (m, 2H), 1.34−1.26 (m, 4H), 0.91 (t, J = 6.75 Hz, 3H); ^{13}C NMR δ 171.6, 170.3, 169.8, 169.7, 154.7, 140.2, 135.5, 107.8, 106.6, 101.0, 90.2, 80.0, 74.4, 70.1, 69.5, 62.8, 31.5, 28.8, 28.1, 22.7, 21.1, 20.8, 20.7, 19.9, 14.3; MS (EI) m/z 502.1953 (M^+ [$C_{25}H_{30}N_2O_9$] = 502.1951).

6-(Octyn-1-yl)-3-(*β*-D-ribofuranosyl)furo[2,3-*d*]pyrimidin-2(3*H*)-one [8c(ii)]. Treatment of **7c(ii)** (60 mg, 0.12 mmol) by general procedure D [NH_3/MeOH (30 mL); chromatography (EtOAc → 5% MeOH/EtOAc)] gave **8c(ii)** as a white solid (25 mg, 56%): mp = 164−166 °C; UV λ_{max} 343, 278, 266 (ϵ 9900, 12 900, 17 400), λ_{min} 289, 275, 241 (ϵ 1260, 11 700, 8490); ^{1}H NMR (CD_3OD) δ 9.09 (s, 1H), 6.76 (s, 1H), 5.95 (s, 1H), 4.17−4.12 (m, 3H), 4.02 (dd, J = 12.5, 2.0 Hz, 1H), 3.84 (dd, J = 12.0, 2.0 Hz, 1H), 2.51 (t, J = 7.25 Hz, 2H), 1.65−1.59 (m, 2H), 1.50−1.44 (m, 2H), 1.38−1.31 (m, 4H), 0.93 (t, J = 7.0 Hz, 3H); ^{13}C NMR (CD_3OD) δ 172.4, 157.1, 140.5, 140.4, 109.0, 108.5, 100.9, 94.4, 85.9, 76.9, 70.8, 69.5, 61.0, 32.6, 29.8, 29.3, 23.7, 20.2, 14.5; MS m/z 399.1527 (MNa^+ [$C_{19}H_{24}N_2O_6Na$] = 399.1532). Anal. ($C_{19}H_{24}N_2O_6$) C, H, N.

3-(2,3,5-Tri-*O*-acetyl-*β*-D-ribofuranosyl)-6-(decyn-1-yl)furo-[2,3-*d*]pyrimidin-2(3*H*)-one [7c(iii)]. Treatment of **6c** (100 mg, 0.212 mmol), $(Ph_3)_4Pd$ (24 mg, 0.02 mmol), CuI (8 mg, 0.04 mmol), Et_3N (1.0 mL), DMF (2.0 mL), and 1-decyne (190 μL, 146 mg, 1.06 mmol) by general procedure C [ambient temperature, 1 h; chromatography (EtOAc/hexanes, 1:1)] gave **7c(iii)** (94 mg, 84%) as a pale-yellow glass: UV λ_{max} 345, 278, 266, 218 nm (ϵ 12 000, 16 000, 22 700, 21 200), λ_{min} 289, 275, 240 nm (ϵ 1640, 14 500, 10 600); ^{1}H NMR δ 8.22 (s, 1H), 6.49 (s, 1H), 6.24 (d, J = 3.6

Hz, 1H), 5.43 (t, J = 4.5 Hz, 1H), 5.30 (t, J = 5.7 Hz, 1H), 4.48−4.42 (m, 3H), 2.47 (t, J = 7.0 Hz, 2H), 2.16 (s, 3H), 2.14 (s, 3H), 2.10 (s, 3H), 1.66−1.58 (m, 2H), 1.43 (br s, 2H), 1.29−1.25 (m, 8H), 0.89 (t, J = 6.3 Hz, 3H); ^{13}C NMR δ 171.6, 170.3, 169.8, 169.7, 154.7, 140.2, 135.4, 107.8, 106.6, 101.0, 90.2, 80.0, 74.4, 70.1, 69.5, 62.8, 32.1, 29.4, 29.3, 29.1, 28.2, 22.9, 21.1, 20.8, 20.7, 19.9, 14.4; MS m/z 553.2177 (MNa^+ [$C_{27}H_{34}N_2O_9Na$] = 553.2162).

6-(Decyn-1-yl)-3-(β-D-ribofuranosyl)furo[2,3-*d*]pyrimidin-2(3*H*)-one [8c(iii)]. Treatment of **7c(iii)** (40 mg, 75 μmol) by general procedure D [NH_3/MeOH (30 mL); chromatography (EtOAc → 5% MeOH/EtOAc)] gave **8c(iii)** as a white solid (20 mg, 67%): mp = 166−168 °C; UV λ_{max} 343, 278, 266 (ϵ 11 200, 14 700, 19 700), λ_{min} 289, 275, 241 (ϵ 1340, 13 300, 9630); ^{1}H NMR (CD_3OD) δ 9.09 (s, 1H), 6.76 (s, 1H), 5.95 (s, 1H), 4.18−4.12 (m, 3H), 4.02 (dd, J = 12.0, 1.5 Hz, 1H), 3.84 (dd, J = 13.0, 2.5 Hz, 1H), 2.51 (t, J = 6.75 Hz, 2H), 1.65−1.59 (m, 2H), 1.48−1.44 (m, 2H), 1.34−1.29 (m, 8H), 0.90 (t, J = 6.75 Hz, 3H); ^{13}C NMR (CD_3OD) δ 172.4, 157.1, 140.5, 140.4, 109.0, 108.5, 100.9, 94.4, 85.9, 76.9, 70.9, 69.5, 61.0, 33.1, 30.5, 30.3, 30.1, 29.3, 23.9, 20.2, 14.6; MS m/z 427.1849 (MNa^+ [$C_{21}H_{28}N_2O_6Na$] = 427.1845). Anal. ($C_{21}H_{28}N_2O_6$•CH_3OH) C, H (calcd: 7.39, found: 6.86), N.

3-(2,3,5-Tri-*O*-acetyl-β-D-ribofuranosyl)-6-(dodecyn-1-yl)furo-[2,3-*d*]pyrimidin-2(3*H*)-one [7c(iv)]. Treatment of **6c** (100 mg, 0.212 mmol), $(Ph_3P)_4Pd$ (24 mg, 0.02 mmol), CuI (8 mg, 0.04 mmol), Et_3N (1.0 mL), DMF (2.0 mL), and 1-dodecyne (230 μL, 176 mg, 1.06 mmol) by general procedure C [ambient temperature, 1h; chromatography (EtOAc/hexanes, 1:1)] gave **7c(iv)** (93 mg, 79%) as a pale-yellow glass: UV λ_{max} 345, 278, 266, 220 nm (ϵ 13 400, 17 500, 24 800, 21 500), λ_{min} 289, 275, 240 nm (ϵ 1620, 15 800, 11 200); ^{1}H NMR δ 8.22 (s, 1H), 6.49 (s, 1H), 6.23 (d, J = 3.6 Hz, 1H), 5.43 (t, J = 4.5 Hz, 1H), 5.30 (t, J = 5.7 Hz, 1H), 4.48−4.39 (m, 3H), 2.47 (t, J = 7.0 Hz, 2H), 2.16 (s, 3H), 2.13 (s, 3H), 2.09 (s, 3H), 1.67−1.58 (m, 2H), 1.27 (br s, 14H), 0.88 (t, J = 6.5 Hz, 3H); ^{13}C NMR δ 171.6, 170.3, 169.8, 169.7, 154.7, 140.2, 135.4, 107.8, 106.6, 101.0, 90.2, 80.0, 74.4, 70.0, 69.5, 62.8, 32.1, 29.8, 29.7, 29.5, 29.3, 29.1, 28.2, 22.9, 21.1, 20.74, 20.70, 19.9, 14.4; MS m/z 581.2480 (MNa^+ [$C_{29}H_{38}N_2O_9Na$] = 581.2475).

6-(Dodecyn-1-yl)-3-(β-D-ribofuranosyl)furo[2,3-*d*]pyrimidin-2(3*H*)-one [8c(iv)]. Treatment of **7c(iv)** (90 mg, 0.16 mmol) by general procedure D [NH_3/MeOH (25 mL); chromatography (EtOAc → 5% MeOH/EtOAc)] gave **8c(iv)** as a white solid (53 mg, 76%): mp = 172−174 °C; UV λ_{max} 343, 278, 266 (ϵ 11 300, 14 900, 19 900), λ_{min} 289, 275, 241 (ϵ 1340, 13 400, 9740); ^{1}H NMR (CD_3OD/DMSO-d_6 9:1) δ 9.06 (s, 1H), 6.82 (s, 1H), 5.93 (d, J = 1.5 Hz, 1H), 4.13−4.08 (m, 3H), 3.97 (dd, J = 12.5, 2.5 Hz, 1H), 3.79 (dd, J = 12.5, 2.5 Hz, 1H), 2.52 (t, J = 7.0 Hz, 2H), 1.64−1.58 (m, 2H), 1.46−1.42 (m, 2H), 1.35−1.27 (m, 12H), 0.88 (t, J = 7.2 Hz, 3H); ^{13}C NMR (CD_3OD/DMSO-d_6 9:1) δ 172.3, 156.7, 140.6, 139.8, 109.4, 108.0, 101.0, 94.0, 85.9, 76.8, 71.1, 69.6, 61.0, 33.1, 30.8, 30.7, 30.5, 30.3, 30.0, 29.3, 23.8, 20.2, 14.8; MS m/z 455.2164 (MNa^+ [$C_{23}H_{32}N_2O_6Na$] = 455.2158). Anal. ($C_{23}H_{32}N_2O_6$) C, H, N.

3-(2,3,5-Tri-*O*-acetyl-β-D-arabinofuranosyl)furo[2,3-*d*]pyrimidin-2(3*H*)-one (5d). Treatment of 1-(2,3,5-tri-*O*-acetyl-β-D-arabinofuranosyl)-5-(trimethylsilylethynyl)uracil[12] (25 mg, 54 μmol) by general procedure A [NH_4F (10 mg, 0.27 mmol), MeOH (2 mL), reflux, 1 h; chromatography (60% EtOAc/hexanes)] gave 1-(2,3,5-tri-*O*-acetyl-β-D-arabinofuranosyl)-5-ethynyluracil (16 mg, 76%) as a white solid foam: UV λ_{max} 284, 224 nm (ϵ 11 200, 9930), λ_{min} 248 nm (ϵ 2100); ^{1}H NMR δ 8.81 (s, 1H), 7.84 (s, 1H), 6.30 (d, J = 3.9 Hz, 1H), 5.45 (dd, J = 4.0, 2.0 Hz, 1H), 5.15 (dd, J = 3.6, 1.8 Hz, 1H), 4.43 (d, J = 4.8 Hz, 2H), 4.23 (q, J = 4.4 Hz, 1H), 3.21 (s, 1H), 2.18 (s, 3H), 2.15 (s, 3H), 2.07 (s, 3H); ^{13}C NMR δ 170.7, 169.8, 168.8, 160.7, 148.7, 144.1, 98.9, 84.6, 82.4, 80.9, 76.2, 74.6, 74.4, 62.7, 21.1, 20.9, 20.7; MS m/z 417.0928 (MNa^+ [$C_{17}H_{18}N_2O_9Na$] = 417.0910).

Treatment of this material (1.88 g, 4.77 mmol), CuI (0.925 g, 4.77 mmol), MeCN (160 mL), and Et_3N (80 mL) by general procedure B [80 °C, 6 h; chromatography (80% EtOAc/hexanes)] gave **5d** (1.31 g, 70%): UV λ_{max} 330, 242 nm (ϵ 5200, 7040), λ_{min} 263 nm (ϵ 340); ^{1}H NMR δ 8.34 (s, 1H), 7.39 (d, J = 2.7 Hz, 1H), 6.60 (d, J = 2.7 Hz, 1H), 6.44 (d, J = 3.6 Hz, 1H), 5.66 (t, J = 1.8 Hz, 1H), 5.09 (br s, 1H), 4.51−4.31 (m, 3H), 2.17 (s, 3H), 2.15 (s, 3H), 1.91 (s, 3H); ^{13}C NMR δ 172.2, 170.8, 169.8, 168.2, 154.2, 145.2, 138.1, 105.9, 104.7, 87.1, 81.8, 76.5, 74.0, 63.0, 21.0, 20.9, 20.6; MS m/z 395.1101 (MH^+ [$C_{17}H_{19}N_2O_9$] = 395.1091.

3-(2,3,5-Tri-*O*-acetyl-β-D-arabinofuranosyl)-6-bromofuro[2,3-*d*]pyrimidin-2(3*H*)-one (6d). A mixture of **5d** (50 mg, 0.12 mmol), KOAc (5 mg, 51 μmol), Br_2 (33 μL, 102 mg, 0.63 mmol), and dried $CHCl_3$ (3 mL) was stirred at ambient temperature for 1 h in a flame-dried flask and then cooled to 0 °C. Dried Et_3N was added until the solution was basic, and volatiles were evaporated. The residue was flash chromatographed (80% EtOAc/hexanes) to give **6d** (50 mg, 83%) as a yellow solid foam: UV λ_{max} 335, 248 nm (ϵ 2800, 5700), λ_{min} 288, 233 nm (ϵ 670, 4600); ^{1}H NMR δ 8.28 (s, 1H), 6.58 (s, 1H), 6.41 (d, J = 3.3 Hz, 1H), 5.64 (d, J = 3.6 Hz, 1H), 5.07 (br s, 1H), 4.56−4.29 (m, 3H), 2.17 (s, 3H), 2.14 (s, 3H), 1.92 (s, 3H); ^{13}C NMR δ 171.7, 170.9, 169.9, 168.3, 153.6, 137.1, 129.6, 107.9, 106.3, 87.4, 82.2, 76.5, 74.0, 63.0, 21.1, 20.9, 20.7; MS (EI) m/z 474.0083 (M^+ [$C_{17}H_{17}{}^{81}BrN_2O_9$] = 474.0097).

3-(2,3,5-Tri-*O*-acetyl-β-D-arabinofuranosyl)-6-(hexyn-1-yl)furo-[2,3-*d*]pyrimidin-2(3*H*)-one [7d(i)]. Treatment of **6d** (100 mg, 0.212 mmol), $(Ph_3P)_4Pd$ (24 mg, 0.02 mmol), CuI (8 mg, 0.04 mmol), Et_3N (1.0 mL), DMF (2.0 mL), and 1-hexyne (122 μL, 87 mg, 1.06 mmol) by general procedure C [50 °C, 2 h; chromatography (EtOAc/hexanes, 1:1)] gave **7d(i)** (197 mg, 98%) as a pale-yellow glass: UV λ_{max} 345, 277, 265 nm (ϵ 10 700, 14 300, 19 900), λ_{min} 289, 275, 241 nm (ϵ 1640, 13 100, 10 200); ^{1}H NMR δ 8.23 (s, 1H), 6.56 (s, 1H), 6.43 (d, J = 3.9 Hz, 1H), 5.64 (d, J = 2.4 Hz, 1H), 5.08 (br s, 1H), 4.54−4.29 (m, 3H), 2.49 (t, J = 7.0 Hz, 2H), 2.17 (s, 3H), 2.15 (s, 3H), 1.91 (s, 3H), 1.65−1.57 (m, 2H), 1.54−1.44 (m, 2H), 0.96 (t, J = 7.2 Hz, 3H); ^{13}C NMR δ 171.5, 170.9, 169.9, 168.3, 154.3, 139.9, 137.0, 106.9, 106.8, 100.7, 87.2, 81.9, 76.6, 74.1, 70.1, 63.1, 30.2, 22.2, 21.1, 21.0, 20.7, 19.6, 13.8; MS m/z 497.1533 (MNa^+ [$C_{23}H_{26}N_2O_9Na$] = 497.1536).

3-(β-D-Arabinofuranosyl)-6-(hexyn-1-yl)furo[2,3-*d*]pyrimidin-2(3*H*)-one [8d(i)]. Treatment of **7d(i)** (100 mg, 0.21 mmol) by general procedure D [NH_3/MeOH (25 mL); chromatography (EtOAc → 5% MeOH/EtOAc)] gave **8d(i)** as a white solid (60 mg, 81%): mp = 167−169 °C; UV λ_{max} 344, 278, 266 (ϵ 12 800, 21 900, 16 800), λ_{min} 289, 275, 240 (ϵ 1370, 15 100, 11 100); ^{1}H NMR (CD_3OD) δ 8.69 (s, 1H), 6.80 (s, 1H), 6.31 (d, J = 3.6 Hz, 1H), 4.34−4.32 (m, 1H), 4.11−4.06 (m, 2H), 3.86−3.84 (m, 2H), 2.52 (t, J = 6.9 Hz, 2H), 1.66−1.57 (m, 2H), 1.56−1.46 (m, 2H), 0.97 (t, J = 7.2 Hz, 3H); ^{13}C NMR (CD_3OD) δ 172.3, 156.9, 141.8, 140.2, 109.0, 107.8, 100.7, 90.9, 88.0, 78.2, 76.4, 70.9, 62.9, 31.4, 23.1, 19.9, 14.0; MS (EI) m/z 348.1318 (M^+ [$C_{17}H_{20}N_2O_6$] = 348.1321). Anal. ($C_{17}H_{20}N_2O_6$) C, H, N.

3-(2,3,5-Tri-*O*-acetyl-β-D-arabinofuranosyl)-6-(octyn-1-yl)furo-[2,3-*d*]pyrimidin-2(3*H*)-one [7d(ii)]. Treatment of **6d** (50 mg, 0.11 mmol), $(Ph_3P)_4Pd$ (12 mg, 0.01 mmol), CuI (4 mg, 0.02 mmol), Et_3N (0.5 mL), DMF (1.0 mL), and 1-octyne (81 μL, 58 mg, 0.53 mmol) by general procedure C [50 °C, 2 h; chromatography (EtOAc/hexanes, 1:1)] gave **7d(ii)** (44 mg, 82%) as a pale yellow glass: UV λ_{max} 345, 277, 241 nm (ϵ 11 800, 15 600, 21 800), λ_{min} 289, 275, 241 nm (ϵ 1880, 14 400, 11 200); ^{1}H NMR δ 8.26 (s, 1H), 6.59 (s, 1H), 6.45 (d, J = 3.3 Hz, 1H), 5.67 (t, J = 3.3 Hz, 1H), 5.11 (br s, 1H), 4.57−4.50 (m, 1H), 4.46−4.41 (m, 1H), 4.35−4.31 (m, 1H), 2.51 (t, J = 7.0 Hz, 2H), 2.19 (s, 3H), 2.18 (s, 3H), 1.94 (s, 3H), 1.68−1.61 (m, 2H), 1.48−1.45 (m, 2H), 1.36−1.29 (m, 4H), 0.94 (t, J = 6.75 Hz, 3H); ^{13}C NMR δ 171.5, 170.9, 169.9, 168.3, 154.3, 139.9, 137.0, 106.9, 106.8, 100.8, 87.2, 81.9, 76.6, 74.1, 70.1, 63.1, 31.5, 28.8, 28.2, 22.7, 21.1, 21.0, 20.7, 19.9, 14.3; MS m/z 525.1838 (MNa^+ [$C_{25}H_{30}N_2O_9Na$] = 525.1849).

3-(β-D-Arabinofuranosyl)-6-(octyn-1-yl)furo[2,3-*d*]pyrimidin-2(3*H*)-one [8d(ii)]. Treatment of **7d(ii)** (100 mg, 0.20 mmol) by general procedure D [NH_3/MeOH (30 mL); chromatography (EtOAc → 5% MeOH/EtOAc)] gave **8d(ii)** as a white solid (56 mg, 75%): mp = 168−170 °C; UV λ_{max} 344, 278, 266 (ϵ 11 000, 14 500, 18 800), λ_{min} 289, 275, 240 (ϵ 1200, 12 900, 9620); ^{1}H NMR (CD_3OD) δ 8.69 (s, 1H), 6.79 (s, 1H), 6.30 (d, J = 3.6 Hz, 1H), 4.34−4.32 (m, 1H), 4.11−4.06 (m, 2H), 3.86−3.84 (m, 2H),

2.51 (t, J = 6.9 Hz, 2H), 1.67−1.58 (m, 2H), 1.52−1.42 (m, 2H), 1.37−1.29 (m, 4H), 0.93 (t, J = 6.9 Hz, 3H); ^{13}C NMR (CD_3OD) δ 172.3, 156.9, 141.8, 140.2, 109.1, 107.8, 100.7, 90.9, 88.0, 78.2, 76.4, 70.9, 62.9, 32.6, 29.8, 29.3, 23.7, 20.2, 14.5; MS (EI) m/z 376.1638 (M^+ [$C_{19}H_{24}N_2O_6$] = 376.1634). Anal. ($C_{19}H_{24}N_2O_6$) C, H, N.

3-(2,3,5-Tri-*O*-acetyl-β-D-arabinofuranosyl)-6-(decyn-1-yl)furo-[2,3-*d*]pyrimidin-2(3*H*)-one [7d(iii)]. Treatment of **6d** (200 mg, 0.424 mmol), $(Ph_3P)_4Pd$ (49 mg, 0.04 mmol), CuI (16 mg, 0.08 mmol), Et_3N (2.0 mL), DMF (4.0 mL), and 1-decyne (390 μL, 290 mg, 2.10 mmol) by general procedure C [50 °C, 2 h; chromatography (EtOAc/hexanes, 1:1)] gave **7d(iii)** (177 mg, 79%) as a pale yellow glass: UV λ_{max} 345, 277, 265 nm (ϵ 12 400, 16 200, 22 700), λ_{min} 289, 275, 241 nm (ϵ 1250, 14 700, 11 200); ^{1}H NMR δ 8.23 (s, 1H), 6.56 (s, 1H), 6.42 (d, J = 3.9 Hz, 1H), 5.64 (d, J = 2.4 Hz, 1H), 5.08 (br s, 1H), 4.54−4.47 (m, 1H), 4.43−4.38 (m, 1H), 4.32−4.27 (m, 1H), 2.48 (t, J = 7.0 Hz, 2H), 2.16 (s, 3H), 2.14 (s, 3H), 1.91 (s, 3H), 1.66−1.58 (m, 2H), 1.43 (br s, 2H), 1.29 (m, 8H), 0.89 (t, J = 6.45 Hz, 3H); ^{13}C NMR δ 171.5, 170.9, 169.9, 168.3, 154.3, 139.9, 137.0, 106.9, 106.8, 100.7, 87.2, 81.9, 76.6, 74.1, 70.1, 63.1, 32.0, 29.4, 29.3, 29.1, 28.2, 22.9, 21.1, 21.0, 20.7, 19.9, 14.3; MS m/z 553.2160 (MNa^+ [$C_{27}H_{34}N_2O_9Na$] = 553.2162).

3-(β-D-Arabinofuranosyl)-6-(decyn-1-yl)furo[2,3-*d*]pyrimidin-2(3*H*)-one [8d(iii)]. Treatment of **7d(iii)** (125 mg, 0.23 mmol) by general procedure D [NH_3/MeOH (35 mL); chromatography (EtOAc → 5% MeOH/EtOAc)] gave **8d(iii)** as a white solid (35 mg, 80%): mp = 171−173 °C; UV λ_{max} 344, 278, 266 (ϵ 13 500, 20 500, 26 400), λ_{min} 291, 275, 243 (ϵ 3390, 18 700, 16 200); ^{1}H NMR (CD_3OD) δ 8.69 (s, 1H), 6.79 (s, 1H), 6.30 (d, J = 3.3 Hz, 1H), 4.34−4.32 (m, 1H), 4.11−4.06 (m, 2H), 3.86−3.84 (m, 2H), 2.51 (t, J = 6.45 Hz, 2H), 1.68−1.58 (m, 2H), 1.47 (br s, 2H), 1.33 (br s, 8H), 0.91 (t, J = 6.75 Hz, 3H); ^{13}C NMR (CD_3OD) δ 172.3, 156.9, 141.8, 140.2, 109.0, 107.8, 100.7, 90.9, 88.0, 78.2, 76.4, 70.9, 62.9, 33.1, 30.5, 30.3, 30.1, 29.3, 23.9, 20.2, 14.6; MS (EI) m/z 404.1964 (M^+ [$C_{21}H_{28}N_2O_6$] = 404.1967). Anal. ($C_{21}H_{28}N_2O_6$) C, H, N.

3-(2,3,5-Tri-*O*-acetyl-β-D-arabinofuranosyl)-6-(dodecyn-1-yl)furo[2,3-*d*]pyrimidin-2(3*H*)-one [7d(iv)]. Treatment of **6d** (100 mg, 0.212 mmol), $(Ph_3P)_4Pd$ (24 mg, 0.02 mmol), CuI (8 mg, 0.04 mmol), Et_3N (1.0 mL), DMF (2.0 mL), and 1-dodecyne (230 μL, 176 mg, 1.06 mmol) by general procedure C [50 °C, 2 h; chromatography (EtOAc/hexanes, 1:1)] gave **7d(iv)** (94 mg, 80%) as a pale yellow glass: UV λ_{max} 344, 277, 265 nm (ϵ 12 000, 15 200, 21 000), λ_{min} 289, 275, 241 nm (ϵ 2140, 13 900, 12 600); ^{1}H NMR δ 8.23 (s, 1H), 6.56 (s, 1H), 6.43 (d, J = 3.6 Hz, 1H), 5.64 (d, J = 3.6 Hz, 1H), 5.08 (br s, 1H), 4.54−4.48 (m, 1H), 4.44−4.38 (m, 1H), 4.32−4.29 (m, 1H), 2.48 (t, J = 7.05 Hz, 2H), 2.17 (s, 3H), 2.15 (s, 3H), 1.91 (s, 3H), 1.66−1.59 (m, 2H), 1.44 (br s, 2H), 1.28 (br s, 12H), 0.88 (t, J = 6.45 Hz, 3H); ^{13}C NMR δ 171.5, 170.9, 169.9, 168.3, 154.3, 139.8, 137.0, 106.9, 106.8, 100.7, 87.14. 81.9, 76.6, 74.1, 70.0, 63.0, 32.1, 29.8, 29.7, 29.5, 29.3, 29.1, 28.2, 22.9, 21.1, 20.9, 20.7, 19.8, 14.3; MS m/z 581.2477 (MNa^+ [$C_{29}H_{38}N_2O_9Na$] = 581.2475).

3-(β-D-Arabinofuranosyl)-6-(dodecyn-1-yl)furo[2,3-*d*]pyrimidin-2(3*H*)-one [8d(iv)]. Treatment of **7d(iv)** (93 mg, 0.16 mmol) by general procedure D [NH_3/MeOH (25 mL); chromatography (EtOAc → 5% MeOH/EtOAc)] gave **8d(iv)** as a white solid (61 mg, 65%): mp = 178−180 °C; UV λ_{max} 344, 278, 266 (ϵ 11 900, 18 100, 23 200), λ_{min} 291, 275, 243 (ϵ 3100, 16 600, 14 400); ^{1}H NMR (CD_3OD) δ 8.69 (s, 1H), 6.80 (s, 1H), 6.31 (d, J = 3.6 Hz, 1H), 4.34−4.32 (m, 1H), 4.11−4.06 (m, 2H), 3.86−3.84 (m, 2H), 2.51 (t, J = 7.05 Hz, 2H), 1.68−1.58 (m, 2H), 1.47 (br s, 2H), 1.30 (br s, 12 H), 0.90 (t, J = 6.9 Hz, 3H); ^{13}C NMR (CD_3OD) δ 172.3, 156.9, 141.8, 140.2, 109.0, 107.8, 100.7, 90.9, 88.0, 78.2, 76.4, 70.9, 62.9, 33.2, 30.83, 30.78, 30.6, 30.3, 30.1, 29.3, 23.9, 20.2, 14.6; MS m/z 455.2164 (MNa^+ [$C_{23}H_{32}N_2O_6Na$] = 455.2158). Anal. ($C_{23}H_{32}N_2O_6$) C, H, N.

Antiviral Assays. The antiviral assays were based on inhibition of virus-induced cytopathicity or plaque formation in human embryonic lung (HEL) fibroblasts. The varicella-zoster virus (VZV) wild-type strain YS, the thymidine-kinase deficient (TK^-) VZV strains YS/R and 07/1, and the human cytomegalovirus (HCMV) strains Davis and AD-169 were used. Confluent HEL cells were grown in 96-well microtiter plates and infected at 20 (VZV) or 100 (HCMV) pfu per well. After a 2-h incubation period, residual virus was removed and the infected cells were further incubated with the medium containing different concentrations of the test compounds (in duplicate). After incubation for 5 days (VZV) or 7 days (HCMV) at 37 °C, virus-induced cytopathogenicity (HCMV) or plaque formation (VZV) was monitored microscopically after ethanol fixation and staining with Giemsa. Antiviral activity was expressed as the EC_{50} or concentration required to reduce virus-induced cytopathogenicity (HCMV) or viral plaque formation (VZV) by 50%. EC_{50} values were calculated from graphic plots of the percentage of cytopathogenicity or viral plaque formation as a function of concentration of the test compounds.

Cytotoxicity Assays. Cytotoxicity measurements were based on the inhibition of HEL cell growth. HEL cells were seeded into 96-well microtiter plates (5×10^3 cells/well) and allowed to proliferate for 24 h. Then, medium containing different concentrations of the test compounds was added. After 3 days of incubation at 37 °C, the cell number was determined with a Coulter counter. The cytostatic concentration was calculated as the CC_{50}, or the compound concentration required to reduce cell growth by 50% relative to the number of cells in the untreated controls. CC_{50} values were estimated from graphic plots of the number of cells (percentage of control) as a function of the concentration of the test compounds. Cytotoxicity was expressed as the minimum cytotoxic concentration (MCC) or the compound concentration that causes a microscopically visible alteration of cell morphology.

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Supporting Information Available: Elemental analyses and ^{1}H and ^{13}C NMR spectra of **8c(i)**. This material is available free of charge via the Internet at http://pubs.acs.org.

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