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Synthesis and Biological Properties of C-2 Triazolylinosine Derivatives

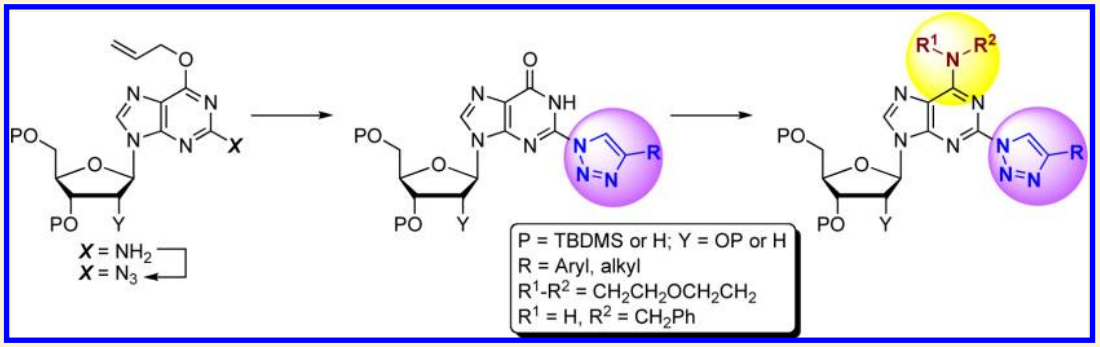
Mahesh K. Lakshman,*[,†] Amit Kumar,[†] Raghavan Balachandran,[‡] Billy W. Day,[‡,§] Graciela Andrei,[∥] Robert Snoeck,[∥] and Jan Balzarini[∥]

[†]Department of Chemistry, The City College and The City University of New York, 160 Convent Avenue, New York, New York 10031, United States

[‡]Department of Pharmaceutical Sciences, and [§]Department of Chemistry, University of Pittsburgh, Pennsylvania 15213, United States

[∥]Laboratory of Virology and Chemotherapy, Rega Institute for Medical Research, Minderbroedersstraat 10, B 3000 Leuven, Belgium

Supporting Information



ABSTRACT: O^6-(Benzotriazol-1*H*-yl)guanosine and its 2′-deoxy analogue are readily converted to the O^6-allyl derivatives that upon diazotization with *t*-BuONO and TMS-N_3 yield the C-2 azido derivatives. We have previously analyzed the solvent-dependent azide·tetrazole equilibrium of C-6 azidopurine nucleosides, and in contrast to these, the O^6-allyl C-2 azido nucleosides appear to exist predominantly in the azido form, relatively independent of solvent polarity. In the presently described cases, the tetrazole appears to be very minor. Consistent with the presence of the azido functionality, each neat C-2 azide displayed a prominent IR band at 2126−2130 cm^{-1}. A screen of conditions for the ligation of the azido nucleosides with alkynes showed that CuCl in *t*-BuOH/H_2O is optimal, yielding C-2 1,2,3-triazolyl nucleosides in 70−82% yields. Removal of the silyl groups with $Et_3N{\cdot}3HF$ followed by deallylation with $PhSO_2Na/Pd(PPh_3)_4$ gave the C-2 triazolylinosine nucleosides. In a continued demonstration of the versatility of O^6-(benzotriazol-1*H*-yl)purine nucleosides, one C-2 triazolylinosine derivative was converted to two adenosine analogues via these intermediates, under mild conditions. Products were desilylated for biological assays. The two C-2 triazolyl adenosine analogues demonstrated pronounced antiproliferative activity in human ovarian and colorectal carcinoma cell cultures. When evaluated for antiviral activity against a broad spectrum of DNA and RNA viruses, some of the C-2 triazolylinosine derivatives showed modest inhibitory activity against cytomegalovirus.

INTRODUCTION

The Cu-catalyzed version[1,2] of the classic Huisgen azide−alkyne cycloaddition[3−9] is a highly atom-economical reaction, often requiring mild conditions. Both factors render Cu-catalyzed azide−alkyne cycloaddition (CuAAC) highly attractive for the modification of complex and sensitive molecules such as nucleosides. We have recently reported a facile and general synthesis of C-6 azidopurine nucleosides and their use in CuAAC reactions, where some of these new compounds showed low cytostatic activity against ovarian carcinoma cell lines.[10] In general, azide−alkyne cycloaddition reactions have been a highly important transformation in the chemistry of nucleosides and DNA.[11−13]

To our knowledge, our previous report on the CuAAC reactions of 6-azidopurine nucleosides was the first to describe such reactions at the C-6 position of purine nucleosides.[10] On the other hand, CuAAC chemistry involving C-2 azidopurine nucleosides has been reported in the context of adenosine A_3 receptor research[14] as well as in the development of antituberculosis agents,[15] and both describe reactions of 2-azidoadenosine analogues. In general, there are three methods for the synthesis of 2-azidoadenosine derivatives. The first involves treatment of 6-amino-2-hydrazino ribofuranosylpurine with nitrous acid,[16] the second is a Cu-catalyzed azidation of tri-*O*-silyl 6-amino-2-iodo ribofuranosylpurine,[17] and the third involves diazotization/azidation of tri-*O*-acetyl 2-amino-6-chlororibofuranosylpurine with isoamylONO/azidotrimethylsilane (TMS-N_3), followed by replacement of the chloride with an amino group.[18]

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Scheme 1. Synthesis of Protected O^6-Allyl-2-azidoinosine and O^6-Allyl-2-azido-2′-deoxyinosine

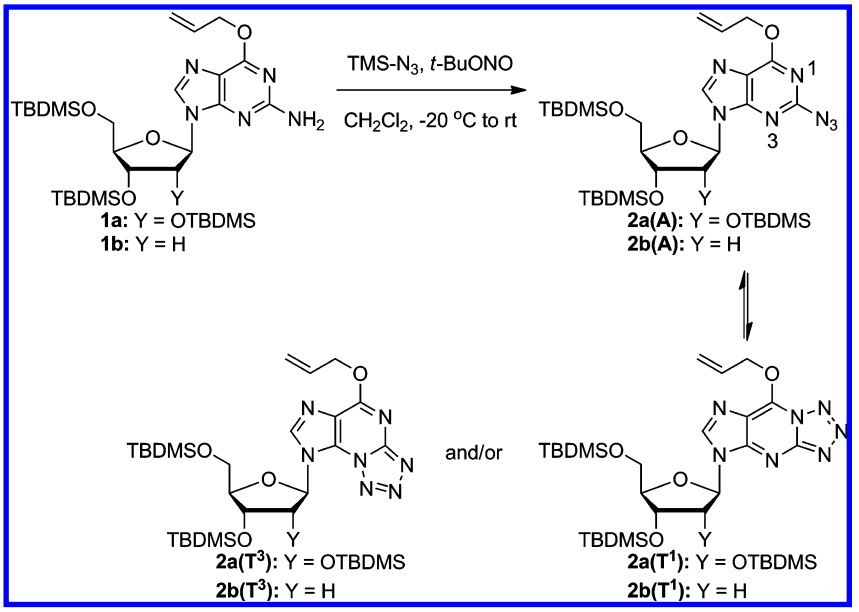
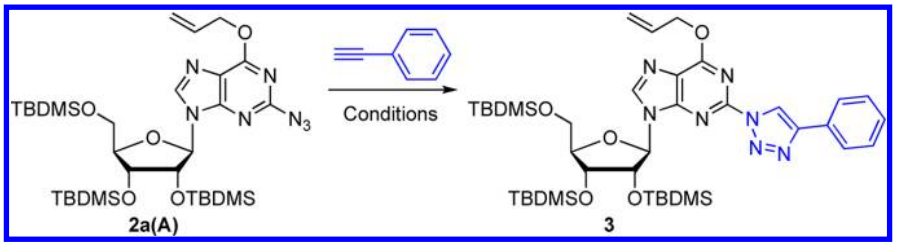


Table 1. Optimization of Azide−alkyne Ligation Conditions Using Trisilyl O^6-Allyl-2-azidoinosine 2a and Phenylacetylene[a]



entry	catalytic system	solvent (1:1)	time (h)	% yield of 3[b]
1	20 mol % $CuSO_4$/40 mol % Na ascorbate	CH_2Cl_2/H_2O	24	30 (60% of **2a** recovered)
2	20 mol % $CuSO_4$/40 mol % Na ascorbate	*t*-BuOH/H_2O	36	54
3	20 mol % Cu(I) thiophene-2-carboxylate	*t*-BuOH/H_2O	48	68
4	20 mol % CuCl	*t*-BuOH/H_2O	36	82

[a]Conditions: 0.1 M **2a** in the solvents indicated, room temperature (reactions were monitored for completion by TLC analysis). [b]Yield of isolated and purified product.

For the current study, we were interested in the CuAAC reactions of 2-azidoinosine and its 2′-deoxy analogue. Syntheses of 2-azidoinosine derivatives are less well developed in comparison to the adenosine analogues. Reaction of 2-chloroinosinic acid with NaN_3 has been shown to yield 2-azidoinosine-5′-monophosphate, which was subsequently converted to 2-azidoinosine by reaction with acid phosphatase.[19] Similarly, 2-fluoro-2′-deoxyinosine, which requires relatively nontrivial synthesis,[20] has been converted to the 2-azido derivative within the context of a DNA oligomer.[21] For our purposes, we needed a simple, general access to 2-azidoinosine and 2-azido-2′-deoxyinosine. In this paper we report the synthesis of suitable O^6-protected 2-azidoinosine derivatives and their applicability toward CuAAC reactions. We have evaluated the anticancer and antiviral properties of C-2 (1,2,3-triazol-1*H*-yl)inosine and 2′-deoxyinosine analogues after appropriate deprotection protocols. We also report methodology for conversion of C-2 triazolylinosine derivatives to adenosine analogues via their O^6-(benzotriazol-1*H*-yl) derivatives, as well as the development of doubly reactive 2-azido-O^6-(benzotriazol-1*H*-yl)purine ribonucleoside.

RESULTS AND DISCUSSION

Synthesis of C-2 Triazolylinosine and 2′-Deoxyinosine Derivatives. We have recently reported that O^6-(benzotriazol-1*H*-yl)inosine and -guanosine derivatives, as well as the corresponding 2′-deoxy analogues, are exceptionally effective reagents for the introduction of substituents at the C-6 position of these purine nucleosides.[22−26] On the basis of these results, we reasoned that O^6-allylguanosine and 2′-deoxyguanosine would be excellent precursors for the present work.[25] We have previously developed the synthesis of 2-chloro-3′,5′-di-*O*-(*tert*-butyldimethylsilyl)-2′-deoxyinosine from an O^6-allyl-2′-deoxyguanosine precursor,[27] and as reported for 2-chloroinosinic acid,[19] this can potentially be used to generate the 2-azidoinosine derivative. Despite this, as shown in Scheme 1, it is more expeditious to directly install the azido group at the C-2 position by diazotization of the amino group in the presence of TMS-N_3.[18]

Silyl-protected O^6-allyl-2-azidoinosine **2a**(**A**) and the 2′-deoxyinosine analogue **2b**(**A**) could be synthesized via this procedure in ca. 60% yield. C-2 azido derivatives of purines[28,29] and purine nucleosides[16,30−33] can exist in equilibrium with two possible tetrazolyl isomers. Similarly, **2a**,**b** can exist as two

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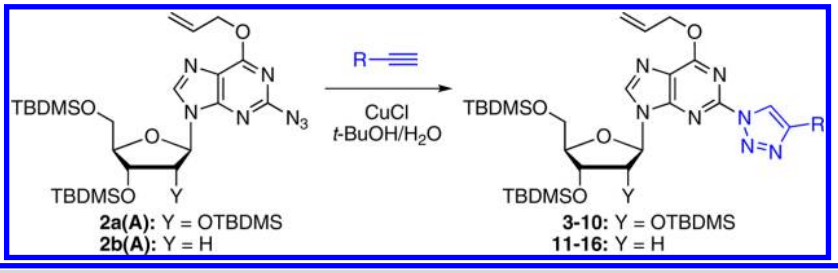
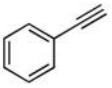
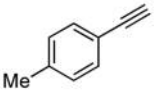
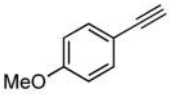
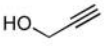
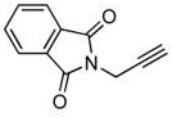
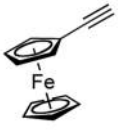
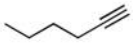
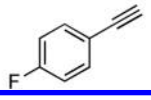
Table 2. Azide−alkyne Ligation Reactions of Nucleosides 2a and 2b[a]



entry	substrate	alkyne	reaction time (h)	product: % yield[b]
1	**2a**		36	**3:** 82
2	**2b**		34	**11:** 74
3	**2a**		48	**4:** 79
4	**2a**		48	**5:** 78
5	**2b**		24	**12:** 78
6	**2a**		28	**6:** 79
7	**2b**		24	**13:** 70
8	**2a**		48	**7:** 82
9	**2b**		36	**14:** 73
10	**2a**		48	**8:** 78
11	**2b**		24	**15:** 72
12	**2a**		44	**9:** 75
13	**2b**		24	**16:** 71
14	**2a**		48	**10:** 71

[a]Conditions: 0.5 M **2a** or **2b** in 1:1 *t*-BuOH/H_2O, 20 mol % of CuCl, room temperature (reactions were monitored for completion by TLC analysis). [b]Yields are of isolated and purified products.

tautomers termed **2a,b**($\mathbf{T^1}$) and **2a,b**($\mathbf{T^3}$), depending upon the nitrogen atom of the purine that is involved. Among the two azide derivatives, synthesis of **2b** from the C-2 triflate has been reported in 26% yield, and this compound was reported not to display any tetrazole tautomer.[34] In our case, assessment by ^{1}H NMR indicated that both **2a** and **2b** exist predominantly as the azide **2a**(**A**) and **2b**(**A**) (≥90% in $CDCl_3$, acetone-d_6, and DMSO-d_6). Consistent with this, IR spectra of **2a** and **2b** showed absorptions at 2126 and 2130 cm^{-1}, respectively. By comparison, 2-azidoadenosine derivatives demonstrated 17−55% of the tetrazolyl isomer.[14,15,30,31,33] Apart from factors such as temperature and solvent polarity,[31,33] the electronic nature of substituents also influences the azide/tetrazole ratio of purinyl derivatives.[33] Whereas electron-donating substituents favor the ring-closed tetrazolyl form, the azide form is preferred with electron-withdrawing groups.[33] The significantly greater proportion of the azido rather than the tetrazolyl forms of 2-azidoinosine derivatives **2a,b** as compared to the 2-azidoadenosines is possibly linked to this substituent effect. Between the two tetrazolyl forms, the $\mathbf{T^1}$ form is generally invoked for nucleosides.[14,15,32,33]

With the synthesis of the C-2 azido derivatives **2a,b** completed, conditions for effectuating their ligation reactions with alkynes were evaluated (Table 1). In previous work with 6-azidopurine nucleosides, we had observed that reduction of the azide to the amine was a competing process and that biphasic conditions were essential in order to obtain satisfactory azide−alkyne ligation.[10] Interestingly, application of those conditions here resulted in an unsatisfactory outcome (entry 1). Switching the solvent to 1:1 *t*-BuOH/H_2O gave an improved result (entry 2). Cu(I) thiophene-2-carboxylate as the catalyst gave a modest improvement (entry 3), whereas CuCl proved to be the best under the conditions tested, affording a product yield of 82% (entry 4). Therefore, the generality of azide−alkyne ligation

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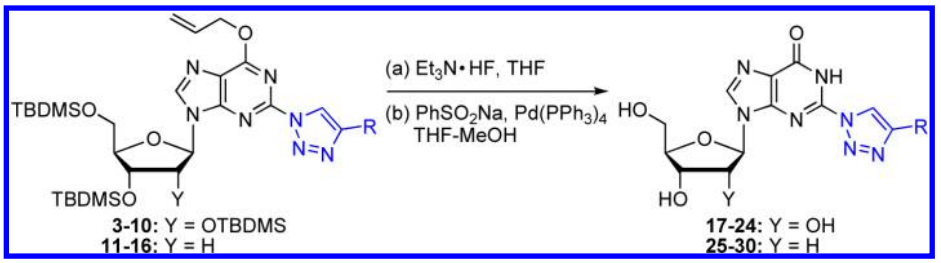
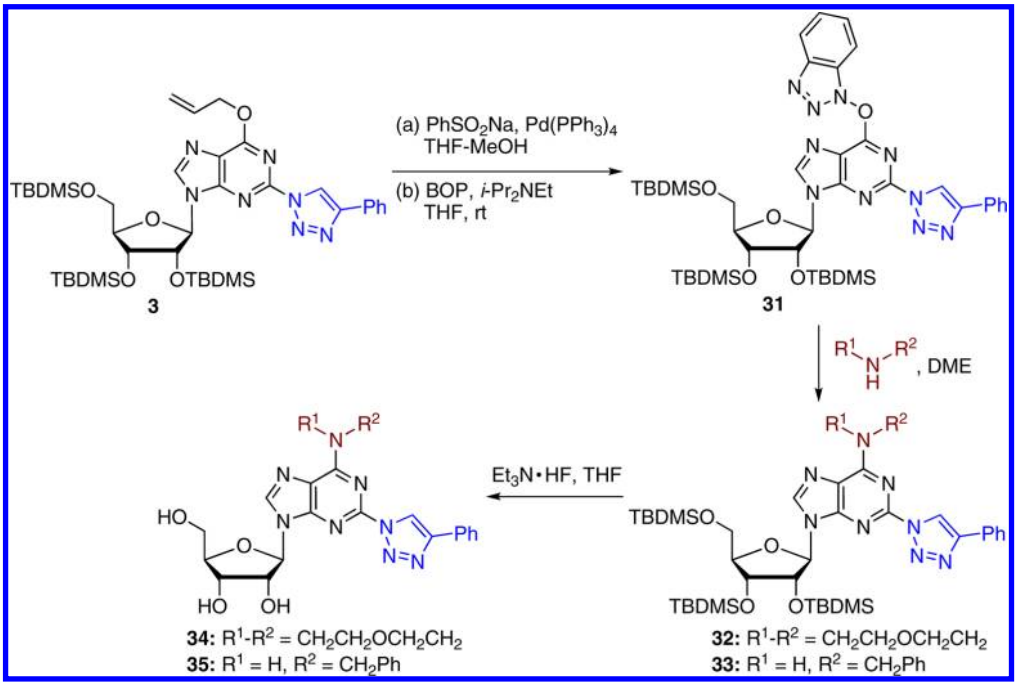
Scheme 2. Deprotection of O^6-Allyl C-2 Triazolylinosine and 2′-Deoxyinosine Analogues



Scheme 3. Synthesis of C-2 Triazolyladenosine Analogues via O^6-Benzotriazolyl Derivatives



chemistry was next investigated using both the ribose derivative **2a** as well as the 2′-deoxy analogue **2b**. Results from these experiments are summarized in Table 2.

With a series of O^6-protected C-2 triazolylinosine and 2′-deoxyinosine derivatives available, deprotection of the products became the focus. Two possible sequences could be envisioned; either deprotection of the O^6-allyl group followed by desilylation or vice versa. Desilylation by $Et_3N{\cdot}HF$ followed by deallylation was the preferred order. This is because we have noted that nucleoside desilylations with amine·HF complexes can leave a fluoride contaminant in some instances, which can be difficult to eliminate. Hence, our chosen deprotection sequence offers the possibility to chromatographically purify the products of desilylation prior to deallylation. We also generally recommend checking products of desilylation by ^{19}F NMR. Several conditions were tested for this purpose: $Pd_2(dba)_3$/(±)-BINAP with morpholine in THF, $Pd_2(dba)_3$/(±)-BINAP with $Et_2NH_2^+HCO_3^-$, in CH_2Cl_2, and $Pd(PPh_3)_4$ with sodium benzenesulfinate ($PhSO_2Na$) in THF. The first two sets of conditions were not very successful, but use of $Pd(PPh_3)_4$/$PhSO_2Na$ proved optimal. Scheme 2 shows the products prepared by deprotection.

Synthesis of C-2 Triazolyladenosine Derivatives. Having synthesized a series of C-2 triazolylinosine and 2′-deoxyinosine analogues, which can also be considered as modified guanine nucleosides by virtue of the C-2 nitrogen atom, we considered methodology for facile synthesis of C-2 triazolyladenosine analogues (derivatives of 2,6-diaminopurine nucleosides). For this purpose, our previously described methodology for activation of the amide linkage, via the O^6-(benzotriazol-1*H*-yl) derivative, appeared to be a reasonable approach.[22,25,26]

As shown in Scheme 3, deallylation of **3** followed by exposure of the resulting silyl-protected C-2 triazolylinosine derivative to 1*H*-benzotriazol-1-yloxytris(dimethylamino)-phosphonium hexafluorophosphate (BOP) and *i*-Pr_2NEt in THF at room temperature led to the formation of the corresponding O^6-(benzotriazolyl) derivative **31** in 55% yield. Reactions of **31** with morpholine and benzyl amine were conducted in 1,2-dimethoxyethane (DME) to yield the adenosine derivatives **32** and **33** in 77% and 90% yields, respectively. The products were then desilylated to yield the C-2 triazolyl adenosine analogues **34** and **35**.

Synthesis of a Doubly Reactive Purine Nucleoside Derivative. The foregoing experiments clearly showed that azide−alkyne ligation could be effectively utilized to synthesize C-2 triazolyl nucleoside analogues. This in combination with chemistry leading to O^6-(benzotriazol-1*H*-yl)purine nucleosides produces a powerful new approach to difunctionalization at C-2 and C-6 of the purine scaffold. At this point, we considered whether an appropriately functionalized, doubly reactive purine nucleoside derivative could be obtained.

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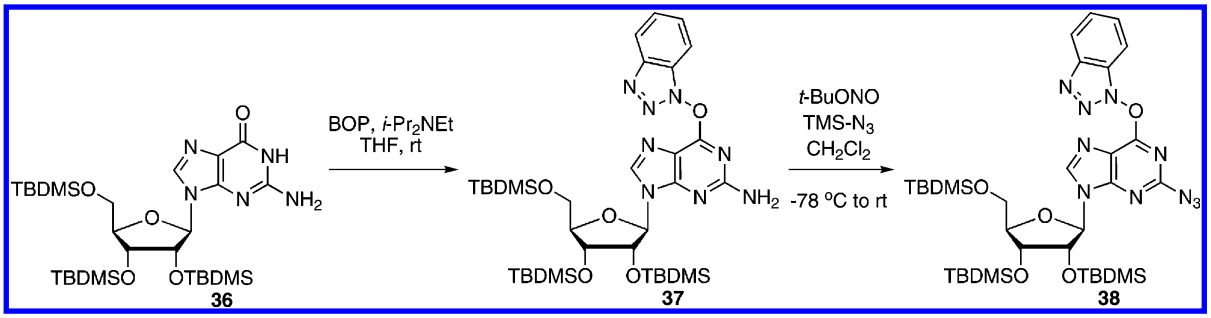
Scheme 4. Synthesis of Difunctionalizable Purine Nucleoside Derivative



Therefore, the synthesis of a 2-azido-O^6-(benzotriazol-1*H*-yl)purine nucleoside derivative was investigated. This would not only allow us to evaluate the stability of the benzotriazolyl moiety to the diazotization/azidation conditions but also provide a route to novel reactive nucleosides that can be difunctionalized at the C-2 and the C-6 positions of the purine. In this context, hydroxyl-protected O^6-(benzotriazolyl)-guanosine derivatives have been converted to the C-2 halo (F, Cl, and I) purine nucleosides.[35] We chose to diazotize O^6-(benzotriazol-1*H*-yl)-2′,3,5′-tri-*O*-(*tert*-butyldimethylsilyl)-guanosine (**37**)[25] with *t*-BuONO/TMS-N_3 (Scheme 4), along the lines of previously published methods.[18,31] This reaction gave a 49% unoptimized yield of **38** indicating the general stability of the O^6-(benzotriazol-1*H*-yl) group to the reaction conditions.

The ^{1}H and ^{13}C NMR spectra of **38** in $CDCl_3$ showed the presence of three isomers, presumably the azide and the two tetrazolyl forms (**T**[1] and **T**[3]). For example, three singlets are observed in the ^{1}H NMR spectrum (δ 8.63, 8.58, and 8.55 ppm) corresponding to the purinyl resonances. Although only two resonances are observed for H-1′ (δ 6.16 and 6.05 ppm), the HMQC spectrum clearly shows three C-1′ resonances (δ 89.61, 89.06, 88.99 ppm). The three H-2′ resonances at δ 4.58 (22%), 4.54 (42%), and 4.47 ppm (36%) ppm were used to determine the isomer ratio. At this time, no attempts have been made to assign structures to these isomers. The IR spectrum of **38** showed an absorption at 2128 cm^{-1}. Doubly reactive compounds, such as **38**, with two preinstalled reactive entities can potentially be functionalized at the C-2 and the C-6 by CuAAC and S_NAr chemistry, respectively. Further work along these lines is forthcoming.

Biological Activities of the New Compounds. The compounds were evaluated for their antiviral activity against a broad variety of DNA and RNA viruses. Several compounds (i.e., **18**, **22**, and **25**, see Table 3) showed marginal activity against cytomegalovirus (CMV), whereas the anti-CMV activity of **23** was somewhat more pronounced. Indeed, the inosine derivative **23** showed activity against CMV in human embryonic lung (HEL) cells at an EC_{50} of 39−73 μM. None of the compounds showed antiviral activity against other viruses at subtoxic concentrations except the inosine derivative **17** that was endowed with moderate antivesicular stomatitis virus (VSV) activity (27 ± 2.4 μM) in human cervix carcinoma HeLa cell cultures. This activity could not be confirmed in human embryonic lung (HEL) fibroblast cell cultures against the same virus, making the moderate activity rather cell-type specific. Yet, in the HeLa and HEL cell cultures toxicity of **17** was observed at 100−240 μM. This may also mean that the anti-VSV activity noticed for **17** in the VSV/HeLa cell assay can be due to underlying toxicity to the host cells, rather than to a specific antiviral activity of the compound. From the antiviral assay systems performed, compound **34** had the highest impact on mammalian cell morphology, but this highly depended on the nature of the cell line used as the virus host [minimum detectable morphology-altering (cytotoxic) concentration (MCC): 8.3 μM against canine kidney MDCK, 42 μM against HeLa, 83 μM against feline kidney CRFK, 210 μM against green monkey kidney Vero, and ≥40 μM against HeLa cells].

The inosine derivatives **17**−**24** and 2′-deoxyinosine derivatives **25**−**30** were also evaluated for their cytostatic activity against murine leukemia L1210, human lymphocyte CEM, and HeLa cells. Modest cytostatic activity was noticed for several compounds. In particular, the HeLa cells were usually somewhat more sensitive to the inhibitory potential of these compounds than the other cell lines. Also, the ribose derivatives were consistently more cytostatic than their corresponding 2′-deoxyribose derivatives. Among all compounds tested, **17** proved most cytostatic, irrespective the nature of the tumor cell line (IC_{50}: 34−124 μM). Both adenosine derivatives **34** and **35** were poorly cytostatic (IC_{50} for **34** 98−185 μM, for **35** 90−120 μM).

Table 3. Anti-CMV Activity of the Test Compounds in HEL Cell Cultures

	anti-CMV activity EC_{50}[a] (μM)		HEL cell effects (μM)	
compd	AD-169 strain	Davis strain	cell morphology (MDC)[b]	cell growth (IC_{50})[c]
17	>50	>50	240	nd[d]
18	118	151	>240	≥240
19	≥230	≥230	>230	>230
20	>270	>270	>270	nd[d]
21	≥200	>200	>200	>200
22	120	123	≥190	123
23	73	39	≥260	>250
24	>230	>230	>230	nd[d]
25	≥250	158	>250	188
26	>240	>240	>240	nd[d]
27	>290	>290	>290	nd[d]
28	>210	>210	>210	nd[d]
29	≥200	≥200	>200	>200
30	>270	>270	>270	nd[d]
34	>40	>40	≥40	nd[d]
35	>40	>40	200	nd[d]

[a]Effective concentration required to reduce virus plaque formation by 50%. Virus input was 100 plaque-forming units (PFU). [b]Minimum cytotoxic concentration that caused a microscopically detectable alteration of cell morphology. [c]Concentration required to reduce cell growth by 50%. [d]Not determined.

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All of the newly synthesized C-2 triazolyl nucleoside analogues were also tested for their antiproliferative activity using human ovarian cancer 1A9 cells and their paclitaxel-resistant clones, 1A9-PTX10 and 1A9-PTX22, and colorectal carcinoma HCT116 cells and their clones (Table 4). Several compounds were modestly active against 1A9 and 1A9-PTX22, but all were inactive against 1A9-PTX10. Adenosine derivatives **34** and **35** showed the best activity against 1A9, and among the two, **34** bearing a morpholinyl group at C-6 was most active (0.18 μM). Inosine derivative **21** with a phthalimido triazolyl substituent also showed activity at <10 μM. Against HCT116, only **34** showed notable activity (3.7 μM), and this compound was also active against HCT116 p53 knockout cells, albeit at a higher concentration (10.4 μM). In the series, adenosine derivative **34** emerged as the most interesting cytostatic candidate showing activity against 1A9, 1A9-PTX22, HCT116, and HCT116 p53 knockout cells.

Table 4. GI_{50} (μM) of the Test Compounds against Ovarian (1A9), Two Paclitaxel-Resistant (PTX10 and PTX22) Ovarian, Colorectal (HCT116), and p53KO HCT116 Cancer Cell Lines

compd	1A9	PTX10	PTX22	HCT116	p53KO
17	22.8	>50	4.76	>50	>50
18	38.0	>50	13.4	>50	>50
19	29.5	>50	8.56	>50	>50
20	20.4	>50	3.53	>50	42.6
21	6.32	>50	14.1	>50	>50
22	29.7	>50	12.9	>50	>50
23	37.0	>50	28.1	>50	>50
24	34.0	>50	31.0	>50	>50
25	31.0	>50	14.8	>50	>50
26	37.2	>50	15.7	>50	>50
27	49.4	>50	32.9	>50	>50
28	49.6	>50	32.2	>50	>50
29	41.6	>50	18.0	>50	>50
30	46.1	>50	26.9	>50	>50
34	0.18	11.73	0.95	3.7	10.4
35	5.0	>50	24.5	43.61	>50
paclitaxel (nM)	1.51	79	68	6.85	8.58

CONCLUSIONS

In this paper, we describe syntheses of O^6-allyl-2-azidoinosine and 2′-deoxyinosine derivatives and their use in CuAAC reactions. In contrast to the C-6 azidopurine nucleosides, these C-2 azides do not exhibit significant azide·tetrazole equilibrium, and the azido form appears to predominate. In comparison, C-2 azidoadenosine analogues show a greater proportion of the tetrazolyl form. This is possibly linked to the greater electron-withdrawing allyloxy group at the C-6 position in the present cases. The products from the CuAAC reactions were desilylated and evaluated for their potential antiviral activity. Unfortunately, none of the compounds proved antivirally active at subtoxic concentrations with the exception of compound **17** that was endowed with a moderate inhibitory activity against vesicular stomatitis virus and compound **23**, which showed activity against cytomegalovirus. It is, however, currently unclear whether the anti-VSV activity is a specific antiviral effect or due to underlying compound toxicity.

The C-2 triazolylinosine nucleosides, which can be considered as modified guanine analogues, were also converted to the O^6-(benzotriazol-1*H*-yl) derivatives. S_NAr substitution of the benzotriazolyloxy group with amines then furnished C-2 triazolyl adenosine analogues. In addition, we have converted silyl-protected O^6-(benzotriazol-1*H*-yl)guanosine to a doubly reactive 2-azido-O^6-(benzotriazol-1*H*-yl)purine nucleoside derivative. Interestingly, based upon the NMR results, this compound appears to exist as the azide and two tetrazolyl isomers. This nucleoside derivative, which can react at the C-2 via CuAAC and at the C-6 via S_NAr, should find broad utility in greatly diversifying the purine nucleoside scaffold via generally simple operational procedures.

EXPERIMENTAL SECTION

General Experimental Considerations. Thin-layer chromatography was performed on 250 μm silica plates, and column chromatographic purifications were performed on 200−300 mesh silica gel. CH_2Cl_2 was distilled over $CaCl_2$, and THF and 1,2-DME were distilled over $LiAlH_4$ and then over Na prior to use. All other reagents were obtained from commercial sources and were used as received. ^{1}H NMR spectra were recorded at 500 MHz, in the solvents indicated, and are referenced to residual protonated solvent resonance. ^{13}C NMR data were recorded at 125 MHz in the solvents indicated and are referenced to the solvent resonance. In all cases, for HRMS analyses ESI ionization and a TOF analyzer were used. Although **1a** and **1b** are reported in the literature,[25] larger scale syntheses are described below.

***O*^{6}-Allyl-2′,3′,5′-tri-*O*-(*tert*-butyldimethylsilyl)guanosine (1a).**[25] In a clean, dry 100 mL round-bottomed flask equipped with a stirring bar were placed O^6-(benzotriazol-1*H*-yl)-2′,3′,5′-tri-*O*-(*tert*-butyldimethylsilyl)guanosine[25] (5.0 g, 6.7 mmol), allyl alcohol (50 mL), and Cs_2CO_3 (4.74 g, 14.1 mmol). The reaction mixture was flushed with nitrogen gas and stirred at room temperature for 2 h after which the mixture was evaporated to dryness. Chromatographic purification of the crude material on a silica gel column using 20% EtOAc in hexanes afforded 3.60 g (81% yield) of **1a** as a white foam. R_f (SiO_2/20% EtOAc in hexanes) = 0.52. ^{1}H NMR ($CDCl_3$): δ 7.96 (s, 1H, Ar-H), 6.16−6.08 (m, 1H, =CH), 5.92 (d, 1H, H-1′, J = 5.3 Hz), 5.41 (dd, 1H, $=CH_{trans}$, J = 1.4, 17.2 Hz), 5.25 (dd, 1H, $=CH_{cis}$, J = 1.4, 10.2 Hz), 5.05 (s, 1H, NH_2), 4.98 (d, 2H, OCH_2, J = 5.7 Hz), 4.48 (t, 1H, H-2′, J = 4.6 Hz), 4.27 (t, 1H, H-3′, J = 3.4 Hz), 4.09 (app q, 1H, H-4′, $J_{app} \approx$ 3.2 Hz), 3.96 (dd, 1H, H-5′, J = 3.6, 11.4 Hz), 3.77 (dd, 1H, H-5′, J = 2.5, 11.4 Hz), 0.96, 0.95, and 0.82 (3s, 27H, *t*-Bu), 0.15, 0.14, 0.13, 0.12, −0.02, and −0.16 (6s, 18H, $SiCH_3$). ^{13}C NMR ($CDCl_3$): δ 160.7, 159.1, 153.8, 137.7, 132.7, 118.0, 115.6, 87.5, 85.2, 76.2, 72.0, 67.2, 62.6, 26.0, 25.8, 25.6, 18.5, 18.0, 17.9, −4.3, −4.7, −5.0, −5.4. HRMS: calcd for $C_{31}H_{60}N_5O_5Si_3$ $[M + H]^+$ 666.3897, found 666.3909.

***O*^{6}-Allyl-3′,5′-di-*O*-(*tert*-butyldimethylsilyl)-2′-deoxyguanosine (1b).**[25] As described for the synthesis of **1a**, this compound was prepared by a reaction of O^6-(benzotriazol-1*H*-yl)-3′,5′-di-*O*-(*tert*-butyldimethylsilyl)-2′-deoxyguanosine[25] (5.0 g, 8.16 mmol), allyl alcohol (50 mL), and Cs_2CO_3 (5.64 g, 17.1 mmol). Chromatographic purification of the crude material on a silica gel column using 30% EtOAc in hexanes) afforded 3.71 g (87% yield) of **1b** as a white foam. R_f (SiO_2/40% EtOAc in hexanes) = 0.60. ^{1}H NMR ($CDCl_3$): δ 7.93 (s, 1H, Ar-H), 6.34 (t, 1H, H-1′, J = 6.5 Hz), 6.17−6.09 (m, 1H, =CH), 5.43 (dd, 1H, $=CH_{trans}$, J = 1.4, 17.2 Hz), 5.27 (dd, 1H, $=CH_{cis}$, J = 1.4, 10.4 Hz), 5.01 (d, 2H, OCH_2, J = 5.7 Hz), 4.94 (s, 1H, NH_2), 4.66−4.58 (m, 1H, H-3′), 3.99 (app q, 1H, H-4′, $J_{app} \approx$ 3.5 Hz), 3.83 (dd, 1H, H-5′, J = 4.4, 11.2 Hz), 3.77 (dd, 1H, H-5′, J = 3.4, 11.2 Hz), 2.57 (app quint, 1H, H-2′, $J_{app} \approx$ 6.5 Hz), 2.37 (ddd, 1H, H-2′, J = 4.0, 6.0, 13.0 Hz), 0.92 (s, 18H, *t*-Bu), 0.11 and 0.09 (2s, 12H, $SiCH_3$). ^{13}C NMR ($CDCl_3$): δ 160.0, 159.2, 153.5, 137.8, 132.8, 118.4, 116.0, 87.8, 88.8, 72.1, 67.5, 63.0, 41.1, 26.1, 25.9, 18.6, 18.1, −4.4, −4.6, −5.2, −5.3. HRMS: calcd for $C_{25}H_{46}N_5O_4Si_2$ $[M + H]^+$ 536.3083, found 536.3093.

***O*^{6}-Allyl-2-azido-2′,3′,5′-tri-*O*-(*tert*-butyldimethylsilyl)-inosine (2a).** To a solution of **1a** (3.0 g, 4.5 mmol) in dry CH_2Cl_2 (40

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mL) at −20 °C was added TMS-N_3 (5.92 mL, 45.1 mmol) dropwise, followed by the addition of *t*-BuONO (5.67 mL, 45.1 mmol). The reaction mixture was stirred at −20 °C for 1 h and then brought to room temperature and allowed to stir for 24 h. The reaction mixture was diluted with MeOH/H_2O (1:1), allowed to stir for 1 h, and then extracted with CH_2Cl_2 (3 × 25 mL). The organic layer was washed with water and brine. Evaporation of the solvent followed by chromatographic purification on a silica gel column using 15% acetone in hexanes afforded 1.83 g (59% yield) of **2a** as a thick, pale-yellow oil. R_f (SiO_2/20% EtOAc in hexanes) = 0.60. IR (neat): 2958, 2927, 2857, 2929, 2856, 2126, 1597 cm^{-1}. ^1H NMR ($CDCl_3$): δ 8.26 (s, 1H, Ar-H), 6.23−6.12 (m, 1H, =CH), 6.03 (d, 1H, H-1′, J = 4.8 Hz), 5.49 (dd, 1H, $=CH_{trans}$, J = 1.2, 17.1 Hz), 5.34 (dd, 1H, $=CH_{cis}$, J = 1.2, 10.3 Hz), 5.11 (d, 2H, OCH_2, J = 5.9 Hz), 4.51 (t, 1H, H-2′, J = 4.4 Hz), 4.32 (t, 1H, H-3′, J = 4.4 Hz), 4.13 (app q, 1H, H-4′, $J_{app} \approx$ 4.0 Hz), 4.03 (dd, 1H, H-5′, J = 3.9, 11.7 Hz), 3.77 (dd, 1H, H-5′, J = 2.5, 11.7 Hz), 0.95, 0.94, and 0.84 (3s, 27H, *t*-Bu), 0.17, 0.16, 0.12, 0.11, −0.02, and −0.14 (6s, 18H, $SiCH_3$). Resonances of the tetrazolyl form (<10%): δ 8.29 (s, 1H, Ar-H), 4.60 (t, 1H, H-2′, J = 4.4 Hz), 4.34 (t, 1H, H-3′ J = 4.4 Hz), 4.06 (d, 1H, H-5′, J = 4.2 Hz). ^{13}C NMR ($CDCl_3$): δ 160.9, 155.8, 153.0, 140.8, 131.9, 119.1, 119.0, 88.3, 85.1, 76.0, 71.5, 68.1, 62.2, 26.1, 25.8, 25.6, 18.5, 18.0, 17.8, −4.4, −4.6, −4.8, −5.3. ^1H NMR (DMSO-d_6): δ 8.53 (s, 1H, Ar-H), 6.17−6. 09 (m, 1H, =CH), 5.92 (d, 1H, H-1′, J = 5.8 Hz), 5.46 (d, 1H, $=CH_{trans}$, J = 17.2 Hz), 5.33 (d, 1H, $=CH_{cis}$, J = 10.7 Hz), 5.06 (d, 2H, OCH_2, J = 5.4 Hz), 4.82 (t, 1H, H-2′, J = 4.9 Hz), 4.32 (t, 1H, H-3′, J = 3.0 Hz), 4.00−3.98 (m, 1H, H-4′), 3.95 (dd, 1H, H-5′, J = 4.6, 11.2 Hz), 3.74 (dd, 1H, H-5′, J = 3.7, 11.2 Hz), 0.91, 0.90, and 0.74 (3s, 27H, *t*-Bu), 0.13, 0.11, 0.10, 0.08, −0.07, and −0.30 (6s, 18H, $SiCH_3$). Resonances of the tetrazolyl form (<10%): δ 8.63 (s, 1H, Ar-H), 4.89 (t, 1H, H-2′ J = 5.0 Hz), 4.38 (q, 1H, H-3′ J = 3.0 Hz). HRMS: calcd for $C_{31}H_{58}N_7O_5Si_3$ $[M + H]^+$ 692.3802, found 692.3808.

***O*^{6}-Allyl-2-azido-3′,5′-di-*O*-(*tert*-butyldimethylsilyl)-2′-deoxyinosine (2b).**[34] As described for the synthesis of **2a**, this compound was prepared by a reaction **1b** (3.0 g, 5.6 mmol) with TMS-N_3 (10 molar equiv) and *t*-BuONO (10 molar equiv). Chromatographic purification of the crude material on a silica gel column using 20% EtOAc in hexanes afforded 1.98 g (63% yield) of **2b** as a viscous, yellow oil. R_f (SiO_2/30% EtOAc in hexanes) = 0.63. IR (neat): 2956, 2930, 2857, 2130, 1600 cm^{-1}. ^1H NMR ($CDCl_3$): δ 8.18 (s, 1H, Ar-H), 6.42 (t, 1H, H-1′, J = 6.4 Hz), 6.18−6.11 (m, 1H, =CH), 5.49 (dd, 1H, $=CH_{trans}$, J = 1.4, 17.2 Hz), 5.33 (dd, 1H, $=CH_{cis}$, J = 1.4, 10.2 Hz), 5.11 (d, 2H, OCH_2, J = 5.8 Hz), 4.61−4.59 (m, 1H, H-3′), 4.01 (app q, 1H, H-4′, $J_{app} \approx$ 3.4 Hz), 3.88 (dd, 1H, H-5′, J = 4.0, 10.2 Hz), 3.79 (dd, 1H, H-5′, J = 3.0, 10.2 Hz), 2.56 (app quint, 1H, H-2′, $J_{app} \approx$ 6.5 Hz), 2.43 (ddd, 1H, H-2′, J = 3.9, 5.9, 10.3 Hz), 0.93 and 0.92 (2s, 18H, *t*-Bu), 0.11 (s, 12H, $SiCH_3$). Resonances of the tetrazolyl form (<5%): δ 8.25 (s, 1H, Ar-H), 4.64−4.63 (m, 1H, H-3′), 2.64−2.62 (m, 1H, H-2′). ^{13}C NMR ($CDCl_3$): δ 161.0, 155.8, 153.0, 140.6, 132.1, 119.3, 88.1, 84.5, 71.9, 68.6, 68.2, 62.9, 41.6, 26.1, 25.9, 18.5, 18.1, −4.4, −4.6, −5.3. ^1H NMR (DMSO-d_6): δ 8.47 (s, 1H, Ar-H), 6.32 (t, 1H, H-1′, J = 6.4 Hz), 6.16−6.09 (m, 1H, =CH), 5.46 (d, 1H, $=CH_{trans}$, J = 18.0 Hz), 5.33 (d, 1H, $=CH_{cis}$, J = 10.7 Hz), 5.07 (d, 2H, OCH_2, J = 5.4 Hz), 4.62 (m, 1H, H-3′), 3.58 (d, 1H, H-4′, J = 4.0 Hz), 3.78 (dd, 1H, H-5′, J = 5.9, 11.2 Hz), 3.67 (dd, 1H, H-5′, J = 4.4, 11.2 Hz), 2.90 (app quint, 1H, H-2′, $J_{app} \approx$ 6.5 Hz), 2.34 (dd, 1H, H-2′, J = 5.2, 11.2 Hz), 0.93 and 0.83 (2s, 18H, *t*-Bu), 0.12, 0.01, and −0.0.1 (3s, 12H, $SiCH_3$). Resonances of the tetrazolyl form (<10%): δ 8.57 (s, 1H, Ar-H), 4.70 (m, 1H, H-3′), 0.81 (s, 18H, *t*-Bu), 0.13, 0.04, and −0.03 (3s, 12H, $SiCH_3$). HRMS: calcd for $C_{25}H_{43}N_7O_4Si_2Na$ $[M + Na]^+$ 584.2807 found: 584.2818.

Typical Procedure for the Ligation Reactions of 2a. *O*^{6}-Allyl-2-(4-phenyl-1,2,3-triazol-1*H*-yl)-2′,3′,5′-tri-*O*-(*tert*-butyldimethylsilyl)inosine (3). Azide **2a** (492.0 mg, 0.711 mmol) and CuCl (14.0 mg. 0.2 mol %) were suspended in 8 mL of *t*-BuOH/H_2O (1:1), and the reaction mixture was flushed with nitrogen gas. Phenylacetylene (155 μL, 1.42 mmol) was added, and the heterogeneous mixture was stirred at room temperature until TLC revealed no starting material (see Table 2 for reaction times). The reaction mixture was diluted with CH_2Cl_2 and washed with water followed by brine. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. Chromatographic purification on a silica gel column using 20% EtOAc in hexanes afforded 461.0 mg (82% yield) of **3** as an off-white foam. R_f (SiO_2/20% EtOAc in hexanes) = 0.57. ^1H NMR ($CDCl_3$): δ 8.74 (s, 1H, Ar-H), 8.50 (s, 1H, Ar-H), 7.96 (d, 2H, Ar-H, J = 7.8 Hz), 7.48 (t, 2H, Ar-H, J = 7.3 Hz), 7.39 (t, 1H, Ar-H, J = 7.3 Hz), 6.23−6.19 (m, 1H, =CH), 6.17 (d, 1H, H-1′, J = 4.4 Hz), 5.57 (dd, 1H, $=CH_{trans}$, J = 1.0, 17.2 Hz), 5.37 (d, 1H, $=CH_{cis}$, J = 10.3 Hz), 5.26 (d, 2H, OCH_2, J = 6.3 Hz), 4.55 (t, 1H, H-2′, J = 4.4 Hz), 4.35 (t, 1H, H-3′, J = 4.2 Hz), 4.18 (br s, 1H, H-4′), 4.10 (dd, 1H, H-5′, J = 3.4, 11.7 Hz), 3.84 (dd, 1H, H-5′, J = 2.0, 11.7 Hz), 0.97, 0.94, and 0.83 (3s, 27H, *t*-Bu), 0.18, 0.16, 0.11, 0.10, −0.02, and −0.07 (6s, 18H, $SiCH_3$). ^{13}C NMR ($CDCl_3$): δ 160.4, 151.8, 147.8, 147.0, 141.5, 131.1, 129.6, 128.2, 127.8, 125.3, 120.6, 119.6, 117.8, 88.1, 84.6, 75.8, 70.8, 68.2, 61.6, 25.5, 25.2, 25.0, 17.9, 17.5, 17.2, −4.9, −5.2, −5.3, −5.9. HRMS: calcd for $C_{39}H_{64}N_7O_5Si_3$ $[M + H]^+$ 794.4271, found 794.4281.

***O*^{6}-Allyl-2-[4-(4-methylphenyl)-1,2,3-triazol-1*H*-yl]-2′,3′,5′-tri-*O*-(*tert*-butyldimethylsilyl)inosine (4).** Synthesized from **2a** (413.0 mg, 0.597 mmol) and 4-ethynyltoluene (138 μL, 1.19 mmol). Chromatography of the crude reaction mixture on a silica gel column using 15% EtOAc in hexanes yielded 380.1 mg (79% yield) of **4** as a white, foamy solid. R_f (SiO_2/20% EtOAc in hexanes) = 0.60. ^1H NMR ($CDCl_3$): δ 8.70 (s, 1H, Ar-H), 8.50 (s, 1H, Ar-H), 7.85 (d, 2H, Ar-H, J = 7.8 Hz), 7.30 (d, 2H, Ar-H, J = 7.8 Hz), 6.25−6.17 (m, 1H, =CH), 6.16 (d, 1H, H-1′, J = 4.4 Hz), 5.56 (dd, 1H, $=CH_{trans}$, J = 1.0, 17.1 Hz), 5.37 (dd, 1H, $=CH_{cis}$, J = 1.0, 10.1 Hz), 5.26 (d, 2H, OCH_2, J = 6.3 Hz), 4.52 (t, 1H, H-2′, J = 4.4 Hz), 4.35 (t, 1H, H-3′, J = 4.2 Hz), 4.18 (q, 1H, H-4′, J = 3.0 Hz), 4.10 (dd, 1H, H-5′, J = 3.4, 11.2 Hz), 3.84 (dd, 1H, H-5′, J = 2.4, 11.2 Hz), 2.41 (s, 3H, CH_3), 0.97, 0.94, and 0.83, (3s, 27H, *t*-Bu), 0.18, 0.16, 0.11, 0.09, −0.02, and −0.06 (6s, 18H, $SiCH_3$). ^{13}C NMR ($CDCl_3$): δ 161.0, 152.5, 148.6, 147.8, 142.2, 138.5, 131.9, 129.7, 129.1, 126.0, 121.2, 119.8, 118.2, 88.8, 85.3, 76.6, 71.5, 68.9, 62.3, 26.3, 26.0, 25.8, 21.4, 18.7, 18.2, 18.0, −4.1, −4.5, −4.6, −5.1. HRMS: calcd for $C_{40}H_{66}N_7O_5Si_3$ $[M + H]^+$ 808.4428, found 808.4435.

***O*^{6}-Allyl-2-[4-(4-methoxyphenyl)-1,2,3-triazol-1*H*-yl]-2′,3′,5′-tri-*O*-(*tert*-butyldimethylsilyl)inosine (5).** Synthesized from **2a** (403.0 mg, 0.582 mmol) and 4-ethynylanisole (154 μL, 1.16 mmol). Chromatography of the crude reaction mixture on a silica gel column using 20% EtOAc in hexanes yielded 373.3 mg (78% yield) of **5** as a white, foamy solid. R_f (SiO_2/20% EtOAc in hexanes) = 0.46. ^1H NMR ($CDCl_3$): δ 8.66 (s, 1H, Ar-H), 8.55 (s, 1H, Ar-H), 7.88 (d, 2H, Ar-H, J = 8.3 Hz), 7.00 (d, 2H, Ar-H, J = 8.3 Hz), 6.22 (m, 1H, =CH), 6.16 (d, 1H, H-1′, J = 3.9 Hz), 5.56 (d, 1H, $=CH_{trans}$, J = 17.1 Hz), 5.36 (d, 1H, $=CH_{cis}$, J = 10.3 Hz), 5.25 (d, 2H, OCH_2, J = 5.7 Hz), 4.47 (br t, 1H, H-2′, J = 3.9 Hz), 4.33 (t, 1H, H-3′, J = 3.9 Hz), 4.18 (br s, 1H, H-4′), 4.10 (dd, 1H, H-5′, J = 2.9, 11.7 Hz), 3.86 (s, 3H, OCH_3), 3.83 (br d, 1H, H-5′, J = 11.7 Hz), 0.96, 0.91, and 0.82 (3s, 27H, *t*-Bu), 0.18, 0.15, 0.09, 0.079, −0.00, and −0.07 (6s, 18H, $SiCH_3$). ^{13}C NMR ($CDCl_3$): δ 161.2, 160.0, 152.6, 148.6, 147.6, 142.2, 131.9, 127.4, 123.01, 121.3, 119.8, 117.7, 114.5, 88.7, 85.3, 76.6, 71.6, 68.9, 62.3, 55.5, 26.3, 26.0, 25.8, 18.7, 18.2, 18.0, −4.1, −4.9, −4.5, −4.6, −5.1, −5.2. HRMS: calcd for $C_{40}H_{66}N_7O_6Si_3$ $[M + H]^+$ 824.4377, found 824.4380.

***O*^{6}-Allyl-2-[4-(hydroxymethyl)-1,2,3-triazol-1*H*-yl]-2′,3′,5′-tri-*O*-(*tert*-butyldimethylsilyl)inosine (6).** Synthesized from **2a** (368.0 mg, 0.532 mmol) and propargyl alcohol (61 μL, 1.06 mmol). Chromatography of the crude reaction mixture on a silica gel column using 40% EtOAc in hexanes yielded 311.3 mg (79% yield) of **6** as a white, foamy solid. R_f (SiO_2/40% EtOAc in hexanes) = 0.48. ^1H NMR ($CDCl_3$): δ 8.54 (s, 1H, Ar-H), 8.49 (s, 1H, Ar-H), 6.25−6.18 (m, 1H, =CH), 6.16 (d, 1H, H-1′, J = 4.3 Hz), 5.56 (dd, 1H, $=CH_{trans}$, J = 1.5, 17.2 Hz), 5.38 (dd, 1H, $=CH_{cis}$, J = 1.5, 10.3 Hz), 5.24 (d, 2H, OCH_2, J = 5.6 Hz), 4.97 (s, 2H, CH_2), 4.58 (t, 1H, H-2′ J = 4.2 Hz), 4.35 (t, 1H, H-3′, J = 4.2 Hz), 4.19 (q, 1H, H-4′, J = 3.6 Hz), 4.09 (dd, 1H, H-5′, J = 3.6, 11.6 Hz), 3.85 (dd, 1H, H-5′, J = 2.0, 11.6 Hz), 0.99, 0.96, and 0.83 (3s, 27H, *t*-Bu), 0.20, 0.18, 0.13, 0.12, 0.02, and −0.11 (6s, 18H, $SiCH_3$). ^{13}C NMR ($CDCl_3$): δ 161.1, 152.5, 148.5, 147.9, 142.4, 131.8, 121.9, 121.1, 119.7, 88.8, 85.5, 76.5, 71.7, 68.9, 62.4, 56.6,

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26.2, 25.9, 25.7, 18.6, 18.2, 17.9, −4.1, −4.5, −4.6, −4.7, −5.2. HRMS: calcd for $C_{34}H_{62}N_7O_6Si_3$ $[M + H]^+$ 748.4064, found 748.4064.

O^6-Allyl-2-[4-(*N*-phthalimidomethyl)-1,2,3-triazol-1*H*-yl]-2′,3′,5′-tri-*O*-(*tert*-butyldimethylsilyl)inosine (7). Synthesized from **2a** (418 mg, 0.604 mmol) and *N*-propargylphthalimide (223.0 mg, 1.20 mmol). Chromatography of the crude reaction mixture on a silica gel column using 20% EtOAc in hexanes yielded 435.3 mg (82% yield) of **7** as an off-white, foamy solid. R_f (SiO_2/20% EtOAc in hexanes) = 0.44. ^{1}H NMR ($CDCl_3$): δ 8.53 (s, 1H, Ar-H), 8.49 (s, 1H, Ar-8), 7.89 (dd, 2H, Ar-H, J = 3.2, 5.4 Hz), 7.74 (dd, 2H, Ar-H, J = 3.2, 5.4 Hz), 6.22−6.14 (m, 1H, =CH), 6.10 (d, 1H, H-1′, J = 4.1 Hz), 5.56 (dd, 1H, $=CH_{trans}$, J = 1.2, 17.2 Hz), 5.35 (br d, 1H, $=CH_{cis}$, J = 10.4 Hz), 5.22 (d, 2H, OCH_2, J = 5.9 Hz), 5.12 (s, 2H, NCH_2), 4.51 (t, 1H, H-2′, J = 4.0 Hz), 4.34 (t, 1H, H-3′, J = 4.0 Hz), 4.17 (app q, 1H, H-4′, $J_{app} \approx$ 4.0 Hz), 4.10 (dd, 1H, H-5′, J = 3.5, 11.6 Hz), 3.82 (dd, 1H, H−5′, J = 2.6, 11.6 Hz), 0.96, 0.93, and 0.81 (3s, 27H, *t*-Bu), 0.17, 0.15, 0.11, 0.08, 0.00, and −0.10 (6s, 18H, $SiCH_3$). ^{13}C NMR ($CDCl_3$): δ 167.6, 161.1, 152.4, 148.4, 143.0, 142.3, 142.3, 134.2, 132.2, 123.6, 122.1, 121.2, 119.8, 88.9, 85.2, 76.5, 71.4, 68.9, 62.2, 33.2, 26.2, 25.9, 25.7, 18.6, 18.2, 17.9, −4.1, −4.6, −5.1, −5.2. HRMS: calcd for $C_{42}H_{65}N_8O_7Si_3$ $[M + H]^+$ 877.4279, found 877.4293.

O^6-Allyl-2-(4-ferrocenyl-1,2,3-triazol-1*H*-yl)-2′,3′,5′-tri-*O*-(*tert*-butyldimethylsilyl)inosine (8). Synthesized from **2a** (482.0 mg, 0.697 mmol) and ethynylferrocene (292.0 mg, 1.39 mmol). Chromatography of the crude reaction mixture on a silica gel column using 10% EtOAc in hexanes yielded 492.8 mg (78% yield) of **8** as a brown, foamy solid. R_f (SiO_2/20% EtOAc in hexanes) = 0.62. ^{1}H NMR ($CDCl_3$): δ 8.53 (s, 1H, Ar-H), 8.43 (s, 1H, Ar-H), 6.26−6.19 (m, 1H, =CH), 6.18 (d, 1H, H-1′, J = 3.9 Hz), 5.58 (br d, 1H, $=CH_{trans}$, J = 17.1 Hz), 5.38 (br d, 1H, $=CH_{cis}$, J = 10.4 Hz), 5.27 (d, 2H, OCH_2, J = 5.8 Hz), 4.84 (app q, 1H, ferrocenyl-H, $J_{app} \approx$ 1.9 Hz), 4.82 (app q, 1H, ferrocenyl-H, $J_{app} \approx$ 1.9 Hz), 4.52 (t, 1H, H-2′ J = 4.3 Hz), 4.35 (d, 2H, ferrocenyl-H, J = 1.9 Hz), 4.34 (t, 1H, H-3′, J = 3.9 Hz), 4.18 (br s, 1H, H-4′), 4.12 (s, 5H, ferrocenyl-H), 4.09 (dd, 1H, H-5′, J = 3.5, 11.5 Hz), 3.84 (dd, 1H, H-5′, J = 2.3, 11.5 Hz), 1.00, 0.96, and 0.87 (3s, 27H, *t*-Bu), 0.21, 0.19, 0.14, 0.12, 0.05, and −0.03 (6s, 18H, $SiCH_3$). ^{13}C NMR ($CDCl_3$): δ 161.0, 152.4, 148.3, 146.9, 141.8, 131.8, 120.9, 119.7, 117.2, 88.5, 85.1, 76.6, 74.7, 71.3, 69.5, 68.8, 68.7, 66.8, 62.1, 26.1, 25.8, 25.6, 18.5, 18.0, 17.8, −4.3, −4.6, −4.7, −4.8, −5.3, −5.4. HRMS: calcd for $C_{43}H_{68}FeN_7O_5Si_3$ $[M + H]^+$ 902.3934, found 902.3936.

O^6-Allyl-2-(4-*n*-butyl-1,2,3-triazol-1*H*-yl)-2′,3′,5′-tri-*O*-(*tert*-butyldimethylsilyl)inosine (9). Synthesized from **2a** (595.0 mg, 0.860 mmol) and propargyl alcohol (197 μL, 1.72 mmol). Chromatography of the crude reaction mixture on a silica gel column using 15% EtOAc in hexanes yielded 501.3 mg (75% yield) of **9** as a white, foamy solid. R_f (SiO_2/20% EtOAc in hexanes) = 0.48. ^{1}H NMR ($CDCl_3$): δ 8.48 (s, 1H, Ar-H), 8.26 (s, 1H, Ar-H), 6.25−6.17 (m, 1H, =CH), 6.16 (d, 1H, H-1′, J = 4.3 Hz), 5.56 (dd, 1H, $=CH_{trans}$, J = 1.4, 17.2 Hz), 5.38 (dd, 1H, $=CH_{cis}$, J = 1.4, 10.5 Hz), 5.25 (d, 2H, OCH_2, J = 5.9 Hz), 4.54 (t, 1H, H-2′, J = 4.2 Hz), 4.35 (t, 1H, H-3′, J = 4.3 Hz), 4.18 (app q, 1H, H-4′, $J_{app} \approx$ 3.5 Hz), 4.09 (dd, 1H, H-5′, J = 3.5, 11.5 Hz), 3.84 (dd, 1H, H-5′, J = 2.2, 11.5 Hz), 2.84 (t, 2H, butyl-CH_2, J = 7.6 Hz), 1.75 (quint, 2H, butyl-CH_2, J = 7.6 Hz), 1.46 (sextet, 2H, butyl-CH_2, J = 7.5 Hz), 0.99 (t, 3H, butyl-CH_3, J = 7.5 Hz), 0.98, 0.95, and 0.83 (3s, 27H, *t*-Bu), 0.19, 0.17, 0.12, 0.11, −0.02, and −0.09 (6s, 18H, $SiCH_3$). ^{13}C NMR ($CDCl_3$): δ 161.3, 152.6, 148.8, 148.6, 142.2, 132.0, 121.2, 120.1, 119.8, 88.9, 85.4, 76.7, 71.7, 69.0, 62.5, 31.6, 26.4, 26.1, 25.9, 25.5, 22.5, 18.8, 18.3, 18.1, 14.0, −4.1, −4.4, −4.5, −4.6, −5.1. HRMS: calcd for $C_{37}H_{68}N_7O_5Si_3$ $[M + H]^+$ 774.4584, found 774.4582.

O^6-Allyl-2-[4-(4-fluorophenyl)-1,2,3-triazol-1*H*-yl]-2′,3′,5′-tri-*O*-(*tert*-butyldimethylsilyl)inosine (10). Synthesized from **2a** (600.0 mg, 0.867 mmol) and 4-ethynylfluorobenzene (200 μL, 1.73 mmol). Chromatography of the crude reaction mixture on a silica gel column using 15% EtOAc in hexanes yielded 500.1 mg (71% yield) of **10** as an off-white, foamy solid. R_f (SiO_2/20% EtOAc in hexanes) = 0.61. ^{1}H NMR ($CDCl_3$): δ 8.70 (s, 1H, Ar-H), 8.52 (s, 1H, Ar-H), 7.95 (dd, 2H, Ar-H, J = 5.3, 8.6 Hz), 7.19 (t, 2H, Ar-H, J = 8.6 Hz), 6.27−6.19 (m, 1H, =CH), 6.08 (d, 1H, H-1′, J = 4.3 Hz), 5.57 (dd, 1H, $=CH_{trans}$, J = 1.0, 17.2 Hz), 5.39 (dd, 1H, $=CH_{cis}$, J = 1.0, 10.4 Hz), 5.29 (d, 2H, OCH_2, J = 5.9 Hz), 4.57 (t, 1H, H-2′, J = 4.2 Hz), 4.37 (t, 1H, H-3′, J = 4.2 Hz), 4.20 (br s, 1H, H-4′), 4.11 (dd, 1H, H-5′, J = 3.6, 11.6 Hz), 3.82 (dd, 1H, H-5′, J = 2.1, 11.6 Hz), 0.99, 0.96, and 0.85 (3s, 27H, *t*-Bu), 0.20, 0.18, 0.13, 0.12, 0.04, and −0.06 (6s, 18H, $SiCH_3$). ^{13}C NMR ($CDCl_3$): δ 164.1 and 162.1 (d, ^1J = 246.8 Hz), 161.2, 152.6, 148.5, 146.9, 142.4, 131.9, 128.0 and 127.9 (d, ^3J = 8.2 Hz), 126.6, 121.4, 119.8, 118.2, 116.2 and 116.0 (d, ^2J = 21.8 Hz), 88.8, 85.5, 76.7, 71.6, 69.0, 62.4, 26.3, 26.0, 25.8, 18.7, 18.3, 18.0, −4.1, −4.4, −4.5, −4.6, −5.1. HRMS: calcd for $C_{39}H_{62}FN_7O_5Si_3Na$ $[M + Na]^+$ 834.3996, found 834.3993.

O^6-Allyl-2-(4-phenyl-1,2,3-triazol-1*H*-yl)-3′,5′-di-*O*-(*tert*-butyldimethylsilyl)-2′-deoxyinosine (11). Synthesized from **2b** (320.0 mg, 0.569 mmol) and phenylacetylene (125 μL, 1.13 mmol). Chromatography of the crude reaction mixture on a silica gel column using 30% EtOAc in hexanes yielded 281.2 mg (74% yield) of **11** as an off-white, foamy solid. R_f (SiO_2/20% EtOAc in hexanes) = 0.50. ^{1}H NMR ($CDCl_3$): δ 8.76 (s, 1H, Ar-H), 8.41 (s, 1H, Ar-H), 7.99 (d, 2H, Ar-H, J = 8.0 Hz), 7.49 (t, 2H, Ar-H, J = 7.5 Hz), 7.40 (t, 1H, Ar-H, J = 7.5 Hz), 6.64 (t, 1H, H-1′, J = 6.2 Hz), 6.26−6.19 (m, 1H, =CH), 5.58 (d, 1H, $=CH_{trans}$, J = 17.2 Hz), 5.39 (d, 1H, $=CH_{cis}$, J = 10.4 Hz), 5.27 (d, 2H, OCH_2, J = 5.3 Hz), 4.68 (br s, 1H, H-3′), 4.07 (m, 1H, H-4′), 3.95 (br d, 1H, H-5′, J = 11.3 Hz), 3.79 (br d, 1H, H-5′, J = 11.3 Hz), 2.62 (app quint, 1H, H-2′, $J_{app} \approx$ 6.5 Hz), 2.58−2.54 (m, 1H, H-2′), 0.95 (s, 18H, *t*-Bu), 0.14 (s, 12H, $SiCH_3$). ^{13}C NMR ($CDCl_3$): δ 161.1, 152.5, 148.5, 147.9, 142.0, 131.9, 130.3, 129.0, 128.7, 126.2, 121.1, 119.8, 118.8, 88.3, 84.7, 71.9, 69.0, 62.9, 42.2, 26.2, 25.9, 18.6, 18.2, −4.3, −4.5, −5.1, −5.2. HRMS: calcd for $C_{33}H_{49}N_7O_4Si_2Na$ $[M + Na]^+$ 686.3277, found 686.3285.

O^6-Allyl-2-[4-(4-methoxyphenyl)-1,2,3-triazol-1*H*-yl]-3′,5′-di-*O*-(*tert*-butyldimethylsilyl)-2′-deoxyinosine (12). Synthesized from **2b** (352.0 mg, 0.626 mmol) and 4-ethynylanisole (165 μL, 1.25 mmol). Chromatography of the crude reaction mixture on a silica gel column using 40% EtOAc in hexanes yielded 302.3 mg (78% yield) of **12** as an off-white, foamy solid. R_f (SiO_2/30% EtOAc in hexanes) = 0.54. ^{1}H NMR ($CDCl_3$): δ 8.67 (s, 1H, Ar-H), 8.42 (s, 1H, Ar-H), 7.91 (d, 2H, Ar-H, J = 8.0 Hz), 7.02 (d, 2H, Ar-H, J = 8.0 Hz), 6.64 (br s, 1H, H-1′), 6.17 (br m, 1H, =CH), 5.58 (d, 1H, $=CH_{trans}$, J = 17.0 Hz), 5.38 (d, 1H, $=CH_{cis}$, J = 10.3 Hz), 5.26 (br d, 2H, OCH_2, J = 4.6 Hz), 4.68 (br s, 1H, H-3′), 4.06 (br s, 1H, H-4′), 3.94 (br d, 1H, H-5′, J = 11.2 Hz), 3.88 (s, 3H, OCH_3), 3.83 (br d, 1H, H-5′, J = 11.2 Hz), 2.64−2.54 (br m, 2H, H-2′), 0.94 (s, 18H, *t*-Bu), 0.14 (s, 12H, $SiCH_3$). ^{13}C NMR ($CDCl_3$): 161.1, 160.0, 152.5, 148.6, 147.7, 142.1, 132.0, 127.5, 123.0, 121.2, 119.7, 117.9, 114.5, 88.3, 84.7, 71.9, 68.9, 62.9, 55.5, 42.1, 26.1, 25.9, 18.6, 18.2, −4.3, −4.5, −4.9, −5.3. HRMS: calcd for $C_{34}H_{51}N_7O_5Si_2Na$ $[M + Na]^+$ 716.3382, found 716.3395.

O^6-Allyl-2-[4-(hydroxymethyl)-1,2,3-triazol-1*H*-yl]-3′,5′-di-*O*-(*tert*-butyldimethylsilyl)-2′-deoxyinosine (13). Synthesized from **2b** (350.0 mg, 0.622 mmol) and propargyl alcohol (272 μL, 1.24 mmol). Chromatography of the crude reaction mixture on a silica gel column using 50% EtOAc in hexanes yielded 272.1 mg (70% yield) of **13** as a white, foamy solid. R_f (SiO_2/40% EtOAc in hexanes) = 0.21. ^{1}H NMR ($CDCl_3$): δ 8.55 (s, 1H, Ar-H), 8.40 (s, 1H, Ar-H), 6.59 (t, 1H, H−1′, J = 6.3 Hz), 6.20−6.15 (m, 1H, =CH), 5.52 (d, 1H, $=CH_{trans}$, J = 17.2 Hz), 5.34 (d, 1H, $=CH_{cis}$, J = 10.4 Hz), 5.20 (d, 2H, OCH_2, J = 5.9 Hz), 4.93 (d, 2H, CH_2, J = 5.9 Hz), 4.65 (app q, 1H, H-3′, $J_{app} \approx$ 4.5 Hz), 4.02 (br d, 1H, H-4′ J = 3.2 Hz), 3.91 (dd, 1H, H-5′, J = 3.5, 11.5 Hz), 3.80 (dd, 1H, H−5′, J = 2.7, 11.3 Hz), 3.01 (t, 1H, OH, J = 5.9 Hz), 2.60 (app quint, 1H, H-2′, $J_{app} \approx$ 6.5 Hz), 2.56−2.52 (ddd, 1H, H-2′ J = 4.5, 6.0, 10.6 Hz), 0.92 (s, 18H, *t*-Bu), 0.11 (s, 12H, $SiCH_3$). ^{13}C NMR ($CDCl_3$): δ 161.1, 152.4, 148.4, 148.0, 142.2, 131.9, 121.4, 121.2, 119.7, 88.3, 84.7, 71.8, 68.9, 62.9, 56.8, 42.1, 26.1, 25.9, 18.6, 18.2, −4.4, −4.5, −5.1, −5.2. HRMS: calcd for $C_{28}H_{47}N_7O_5Si_2Na$ $[M + Na]^+$ 640.3069, found 640.3077.

O^6-Allyl-2-[4-(*N*-phthalimidomethyl)-1,2,3-triazol-1*H*-yl]-3′,5′-di-*O*-(*tert*-butyldimethylsilyl)-2′-deoxyinosine (14). Synthesized from **2b** (365.0 mg, 0.649 mmol) and *N*-propargylphthalimide (240 μL, 1.29 mmol). Chromatography of the crude reaction mixture on a silica gel column using 35% EtOAc in hexanes yielded 351.8 mg (73% yield) of **14** as a white, foamy solid. R_f (SiO_2/20%

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EtOAc in hexanes) = 0.28. ^{1}H NMR ($CDCl_3$): δ 8.56 (s, 1H, Ar-H), 8.39 (s, 1H, Ar-H), 7.88 (dd, 2H, Ar-H, J = 3.0, 5.5 Hz), 7.74 (dd, 2H, Ar-H, J = 3.0, 5.5 Hz), 6.57 (t, 1H, H-1′, J = 6.3 Hz), 6.21−6.13 (m, 1H, =CH), 5.53 (dd, 1H, =CH_{trans}, J = 1.4, 17.2 Hz), 5.34 (dd, 1H, =CH_{cis}, J = 1.4, 10.4 Hz), 5.20 (d, 2H, OCH_2, J = 5.9 Hz), 5.12 (s, 2H, NCH_2), 4.64 (app q, 1H, H-3′, $J_{app} \approx$ 4.0), 4.02 (app q, 1H, H-4′, $J_{app} \approx$ 3.3 Hz), 3.92 (dd, 1H, H-5′, J = 3.5, 11.3 Hz), 3.80 (dd, 1H, H-5′, J = 2.9, 11.3 Hz), 2.57 (app quint, 1H, H-2′, $J_{app} \approx$ 6.5 Hz), 2.50 (ddd, 1H, H-2′, J = 4.5, 6.3, 10.6 Hz), 0.92 and 0.90 (2s, 18H, t-Bu), 0.12 and 0.10 (2s, 12H, $SiCH_3$). ^{13}C NMR ($CDCl_3$): δ 167.5, 160.9, 152.1, 148.1, 142.8, 141.8, 134.1, 132.0, 131.7, 123.4, 122.2, 119.5, 88.1, 84.5, 71.6, 68.7, 62.6, 58.1, 41.9, 33.0, 25.9, 25.7, 18.4, 18.0, −4.6, −4.8, −5.3, −5.5. HRMS: calcd for $C_{36}H_{50}N_8O_6Si_2Na$ [M + Na]$^+$ 769.3284, found 769.3290.

O^6-Allyl-2-(4-ferrocenyl-1,2,3-triazol-1*H*-yl)-3′,5′-di-*O*-(*tert*-butyldimethylsilyl)-2′-deoxyinosine (15). Synthesized from **2b** (595.0 mg, 1.05 mmol) and ethynylferrocene (444 μL, 2.11 mmol). Chromatography of the crude reaction mixture on a silica gel column using 20% EtOAc in hexanes yielded 620.2 mg (72% yield) of **15** as a reddish-brown, foamy solid. R_f (SiO_2/30% EtOAc in hexanes) = 0.30. ^{1}H NMR ($CDCl_3$): δ 8.40 (s, 1H, Ar-H), 8.35 (s, 1H, Ar-H), 6.64 (br s, 1H, H-1′), 6.23 (br m, 1H, =CH), 5.57 (d, 1H, =CH_{trans}, J = 17.0 Hz), 5.40 (d, 1H, =CH_{cis}, J = 10.0 Hz), 5.26 (br s, 2H, OCH_2), 5.04 (br s, 2H, ferrocenyl-H), 4.66 (br s, 1H, H-3′), 4.54(br s, 2H, ferrocenyl-H), 4.28 (br s, 5H, ferrocenyl-H), 4.06 (br s, 1H, H-4′), 3.93 (dd, 1H, H-5′, J = 3.0, 11.2 Hz), 3.82 (dd, 1H, H-5′, J = 2.0, 11.2 Hz), 2.59−2.57 (br m, 2H, H-2′), 0.95 and 0.94 (2s, 18H, t-Bu), 0.14 and 0.13 (2s, 12H, $SiCH_3$). ^{13}C NMR ($CDCl_3$) δ 161.2, 152.6, 148.7, 147.3, 142.0, 132.1, 121.1, 119.8, 117.7, 88.4, 84.6, 72.0, 69.8, 69.1, 69.0, 67.2, 67.1, 63.0, 42.3, 26.2, 26.0, 18.7, 18.3, −4.4, −4.6, −5.1, −5.3. HRMS: calcd for $C_{37}H_{54}FeN_7O_4Si_2$ [M + H]$^+$ 772.3120, found 772.3126.

O^6-Allyl-2-(4-*n*-butyl-1,2,3-triazol-1*H*-yl)-3′,5′-di-*O*-(*tert*-butyldimethylsilyl)-2′-deoxyinosine (16). Synthesized from **2b** (393.0 mg, 0.699 mmol) and 1-hexyne (160 μL, 1.39 mmol). Chromatography of the crude reaction mixture on a silica gel column using 20% EtOAc in hexanes yielded 320.1 mg (71% yield) of **16** as a white, foamy solid. R_f (SiO_2/20% EtOAc in hexanes) = 0.40. ^{1}H NMR ($CDCl_3$): δ 8.41 (s, 1H, Ar-H), 8.28 (s, 1H, Ar-H), 6.62 (t, 1H, H-1′, J = 6.3 Hz), 6.23−6.15 (m, 1H, =CH), 5.53 (dd, 1H, =CH_{trans}, J = 1.4, 17.2 Hz), 5.36 (dd, 1H, =CH_{cis}, J = 1.4, 10.4 Hz), 5.22 (d, 2H, OCH_2, J = 5.9 Hz), 4.64 (m, 1H, H-3′), 4.02 (app q, 1H, H-4′, $J_{app} \approx$ 3.5 Hz), 3.92 (dd, 1H, H-5′, J = 3.4, 11.3 Hz), 3.81 (dd, 1H, H-5′, J = 2.7, 11.3 Hz), 2.83 (t, 2H, butyl-CH_2, J = 7.7 Hz), 2.57 (app quint, 1H, H-2′, $J_{app} \approx$ 6.5 Hz), 2.52 (ddd, 1H, H-2′, J = 4.3, 6.3, 11.0 Hz), 1.74 (quint, 2H, butyl-CH_2, J = 7.5 Hz), 1.44 (sextet, 2H, butyl-CH_2, J = 7.5 Hz), 0.96 (t, 3H, butyl-CH_3, J = 7.5 Hz), 0.93 and 0.92 (2s, 18H, t-Bu), 0.12 and 0.11 (2s, 12H, $SiCH_3$). ^{13}C NMR ($CDCl_3$): δ 160.9, 152.3, 148.6, 148.5, 141.9, 131.8, 120.9, 120.0, 119.5, 88.1, 84.5, 71.7, 68.7, 62.8, 41.9, 31.5, 26.0, 25.8, 25.3, 22.3, 18.5, 18.0, 13.8, −4.5, −4.7, −5.3, −5.4. HRMS: calcd for $C_{31}H_{54}N_7O_4Si_2$ [M + H]$^+$ 644.3770, found 644.3777.

Typical Procedure for Disilylation and Deallylation Reactions of the Triazolyl Nucleosides. 2-(4-Phenyl-1,2,3-triazol-1*H*-yl)inosine (17). *Step 1: Desilylation.* $Et_3N{\cdot}3HF$ (389 μL, 2.39 mmol) was added to a solution of **3** (380.0 mg, 0.47 mmol) in dry THF (5.0 mL), and the reaction mixture was stirred at room temperature for 24 h. The mixture was evaporated under a stream of nitrogen gas using a polypropylene pipet. The crude product was purified by chromatography on silica gel column using 10% MeOH in EtOAc to give 171.2 mg (80% yield) of the O^6-allyl-protected nucleoside as colorless, amorphous solid. R_f (SiO_2/10% MeOH in EtOAc) = 0.31. ^{1}H NMR (DMSO-d_6): δ 9.42 (s, 1H, Ar-H), 8.74 (s, 1H, Ar-H), 8.00 (d, 2H, Ar-H, J = 8.3 Hz), 7.52 (t, 2H, Ar-H, J = 7.5 Hz), 7.43 (t, 1H, Ar-H, J = 7.5 Hz), 6.26−6.15 (m, 1H, =CH), 6.08 (d, 1H, H-1′, J = 5.8 Hz), 5.64 (br s, 1H, OH), 5.56 (dd, 1H, =CH_{trans}, J = 1.6, 17.2 Hz), 5.39 (br d, 1H, =CH_{cis}, J = 17.2 Hz), 5.37 (br s, 1H, OH), 5.28 (d, 2H, OCH_2, J = 5.8 Hz), 5.11 (t, 1H, OH, J = 5.3 Hz), 4.66 (br s, 1H, H-2′), 4.23 (br s, 1H, H-3′), 4.01 (app q, 1H, H-4′, $J_{app} \approx$ 3.6 Hz), 3.71 (ddd, 1H, H-5′, J = 2.8, 7.2, 11.2 Hz), 3.63 (ddd, 1H, H-5′, J = 5.0, 7.2, 11.2 Hz).

Step 2: Deallylation. A solution of $PhSO_2Na$ (14.5 mg, 0.088 mmol) in MeOH (1.0 mL) was added to a suspension of the desilylated product obtained in step 1 (40.0 mg, 0.088 mmol) and $Pd(PPh_3)_4$ (5.1 mg, 5 mol %) in dry THF (2.0 mL), at room temperature. The reaction mixture was stirred at room temperature for 2 h, at which time TLC revealed no starting material. The reaction mixture was concentrated under reduced pressure and triturated with EtOAc to give 26.4 mg (72% yield) of **17** as a white solid. R_f (SiO_2/MeOH) = 0.54. ^{1}H NMR (DMSO-d_6): δ 9.07 (s, 1H, Ar-H), 8.01 (s, 1H, Ar-H), 7.98 (d, 2H, Ar-H, J = 7.8 Hz), 7.48 (t, 2H, Ar-H, J = 7.3 Hz), 7.36 (t, 1H, Ar-H, J = 7.3 Hz), 5.86 (d, 1H, H-1′, J = 6.3 Hz), 5.46 (d, 1H, OH, J = 6.3 Hz), 5.20 (d, 1H, OH, J = 4.6 Hz), 5.08 (t, 1H, OH, J = 6.0 Hz), 4.66 (app q, 1H, H-2′, $J_{app} \approx$ 5.9 Hz), 4.19 (app q, 1H, H-3′, $J_{app} \approx$ 4.0 Hz), 3.95 (q, 1H, H-4′, J = 3.4 Hz), 3.71−3.66 (m, 1H, H-5′), 3.59−3.54 (m, 1H, H-5′). ^{13}C NMR (DMSO-d_6): δ 167.8, 151.5, 150.6, 147.4, 137.8, 131.9, 129.6, 128.8, 126.0, 125.5, 120.6, 87.9, 86.2, 73.9, 71.4, 62.5. HRMS: calcd for $C_{18}H_{17}N_7O_5Na$ [M + Na]$^+$ 434.1183, found 434.1200.

2-[4-(4-Methylphenyl)-1,2,3-triazol-1*H*-yl]inosine (18). *Step 1: Desilylation.* Using the procedure described for **17**, this compound was synthesized from **4** (300.0 mg, 0.371 mmol) and $Et_3N{\cdot}3HF$ (300 μL, 1.85 mmol). Chromatography of the crude reaction mixture on a silica gel column using 10% MeOH in EtOAc yielded 130.8 mg (76% yield) of the O^6-allyl-protected nucleoside as a white, foamy solid. R_f (SiO_2/10% MeOH in EtOAc) = 0.27. ^{1}H NMR (DMSO-d_6): δ 9.37 (s, 1H, Ar-H), 8.74 (s, 1H, Ar-H), 7.95 (d, 2H, Ar-H, J = 7.9 Hz), 7.32 (d, 2H, Ar-H, J = 7.9 Hz), 6.26−6.18 (m, 1H, =CH), 6.08 (d, 1H, H-1′, J = 5.8 Hz), 5.57 (d, 1H, OH, J = 5.4 Hz), 5.56 (br s, 1H, =CH_{trans}), 5.38 (d, 1H, =CH_{cis}, J = 10.5 Hz), 5.31 (d, 1H, OH, J = 5.6 Hz), 5.28 (d, 2H, OCH_2, J = 5.7 Hz), 5.04 (t, 1H, OH, J = 5.5 Hz), 4.66 (app q, 1H, H-2′, $J_{app} \approx$ 5.5 Hz), 4.22 (app q, 1H, H-3′, $J_{app} \approx$ 4.0 Hz), 4.00 (br d, 1H, H-4′, J = 3.5 Hz), 3.74−3.69 (m, 1H, H-5′), 3.63−3.59 (m, 1H, H-5′), 2.36 (s, 3H, CH_3).

Step 2: Deallylation. The desilylated product (80.0 mg, 0.172 mmol) obtained in step 1 was deallylated as described for **17** using $Pd(PPh_3)_4$ (5.1 mg, 5 mol %) and $PhSO_2Na$ (26.9 mg, 0.172 mmol) to yield 52.2 mg (71% yield) of **18** as a pale yellow solid. R_f (SiO_2/MeOH) = 0.64. ^{1}H NMR (DMSO-d_6): δ 8.95 (s, 1H, Ar-H), 7.95 (s, 1H, Ar-H), 7.87 (d, 2H, Ar-H, J = 8.0 Hz), 7.28 (d, 2H, Ar-H, J = 8.0), 5.82 (d, 1H, H-1′, J = 6.3 Hz), 5.41 (d, 1H, OH, J = 6.3 Hz), 5.12 (d, 1H, OH, J = 4.6 Hz), 5.04 (t, 1H, OH, J = 5.6 Hz), 4.65 (app q, 1H, H-2′, $J_{app} \approx$ 6.0 Hz), 4.15 (app q, 1H, H-3′, $J_{app} \approx$ 4.5 Hz), 4.00 (app q, 1H, H-4′, $J_{app} \approx$ 3.7 Hz), 3.69−3.64 (m, 1H, H-5′), 3.57−3.52 (m, 1H, H-5′), 2.34 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6): δ 167.4, 150.9, 150.1, 146.2, 137.6, 137.4, 129.8, 128.2, 125.7, 123.9, 119.5, 87.6, 85.9, 73.6, 71.1, 61.2, 21.3. HRMS: calcd for $C_{19}H_{19}N_7O_5Na$ [M + Na]$^+$ 448.1340, found 448.1342.

2-[4-(4-Methoxyphenyl)-1,2,3-triazol-1*H*-yl]inosine (19). *Step 1: Desilylation.* Using the procedure described for **17**, this compound was synthesized from **5** (290.0 mg, 0.351 mmol) and $Et_3N{\cdot}3HF$ (285 μL, 1.75 mmol). Chromatography of the crude reaction mixture on a silica gel column using 10% MeOH in EtOAc yielded 135.0 mg (80% yield) of the O^6-allyl-protected nucleoside as a white, foamy solid. R_f (SiO_2/5% MeOH in EtOAc) = 0.19. ^{1}H NMR (DMSO-d_6): δ 9.32 (s, 1H, Ar-H), 8.75 (s, 1H, Ar-H), 7.95 (d, 2H, Ar-H, J = 8.6 Hz), 7.00 (d, 2H, Ar-H, J = 8.6 Hz), 6.26−6.18 (m, 1H, =CH), 6.07 (d, 1H, H-1′, J = 5.7 Hz), 5.56 (dd, 1H, =CH_{trans}, J = 1.1, 17.2 Hz), 5.37 (dd, 1H, =CH_{cis}, J = 1.1, 10.4 Hz), 5.28 (d, 2H, OCH_2, J = 5.5 Hz), 4.63 (t, 1H, H-2′, J = 5.2 Hz), 4.23 (app t, 1H, H-3′, $J_{app} \approx$ 4.2 Hz), 4.17 (app q, 1H, H-4′, $J_{app} \approx$ 3.8), 3.82 (s, 3H, OCH_3), 3.70 (dd, 1H, H-5′, J = 4.2, 12.0 Hz), 3.60 (dd, 1H, H-5′, J = 4.0, 12.0 Hz).

Step 2: Deallylation. The desilylated product (94.0 mg, 0.195 mmol) obtained in step 1 was deallylated as described for **17** using $Pd(PPh_3)_4$ (11.2 mg, 5 mol %) and $PhSO_2Na$ (31.9 mg, 0.195 mmol) to yield 72.1 mg (84% yield) of **19** as a white solid. R_f (SiO_2/MeOH) = 0.73. ^{1}H NMR (DMSO-d_6): δ 8.94 (s, 1H, Ar-H), 8.01 (s, 1H, Ar-H), 7.99 (d, 2H, Ar-H, J = 8.7 Hz), 7.04 (d, 2H, Ar-H, J = 8.7 Hz), 5.85 (d, 1H, H-1′, J = 6.3 Hz), 5.46 (d, 1H, OH, J = 6.3 Hz), 5.19 (d,

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1H, OH, J = 4.6 Hz), 5.11 (t, 1H, OH, J = 6.3 Hz), 4.64 (app q, 1H, H-2′, J_{app} ≈ 5.8 Hz), 4.17 (app q, 1H, H-3′, J_{app} ≈ 4.1 Hz), 3.94 (app q, 1H, H-4′, J_{app} ≈ 3.5 Hz), 3.80 (s, 3H, OCH_3), 3.71−3.65 (m, 1H, H-5′), 3.59−3.53 (m, 1H, H-5′). ^{13}C NMR (DMSO-d_6): δ 167.1, 159.7, 150.4, 146.2, 137.4, 127.4, 124.9, 124.0, 119.3, 115.0, 94.7, 87.9, 86.2, 73.9, 71.4, 62.5, 55.8. HRMS: calcd for $C_{19}H_{19}N_7O_6Na$ $[M + Na]^+$ 464.1289, found 464.1299.

2-[4-(Hydroxymethyl)-1,2,3-triazol-1*H*-yl]inosine (20). *Step 1: Desilylation.* Using the procedure described for **17**, this compound was synthesized from **6** (210.0 mg, 0.280 mmol) and $Et_3N{\cdot}3HF$ (228 μL, 1.40 mmol). Chromatography of the crude reaction mixture on a silica gel column using 10% MeOH in EtOAc yielded 95.0 mg (83% yield) of the O^6-allyl-protected nucleoside as a white, foamy solid. R_f (SiO_2/10% MeOH in EtOAc) = 0.46. ^{1}H NMR (DMSO-d_6): δ 8.77 (s, 1H, Ar-H), 8.74 (s, 1H, Ar-H), 6.24−6.16 (m, 1H, ═CH), 6.05 (d, 1H, H-1′, J = 5.7 Hz), 5.58 (d, 1H, OH, J = 5.9 Hz), 5.53 (br d, 1H, ═CH_{trans}, J = 17.2 Hz), 5.39 (d, 1H, OH, J = 6.2 Hz), 5.36 (br d, 1H, ═CH_{cis}, J = 10.3 Hz), 5.30 (d, 1H, OH, J = 4.9 Hz), 5.24 (d, 2H, OCH_2, J = 5.9 Hz), 5.04 (t, 1H, OH, J = 5.3 Hz), 4.66−4.63 (m, 3H, CH_2 and H-2′), 4.22 (app q, 1H, H-3′, J_{app} ≈ 4.5 Hz), 3.99 (app q, 1H, H-4′, J_{app} ≈ 4.0 Hz), 3.73−3.68 (m, 1H, H-5′), 3.62−3.58 (m, 1H, H-5′).

Step 2: Deallylation. The desilylated product (35.2 mg, 0.085 mmol) obtained in step 1 was deallylated as described for **17** using $Pd(PPh_3)_4$ (4.9 mg, 5 mol %) and $PhSO_2Na$ (14.0 mg, 0. 085 mmol) to yield 20.4 mg (64% yield) of **20** as a white solid. R_f (SiO_2/MeOH) = 0.54. ^{1}H NMR (DMSO-d_6): δ 8.43 (s, 1H, Ar-H), 7.97 (s, 1H, Ar-H), 5.83 (d, 1H, H-1′, J = 5.8 Hz), 5.42 (d, 1H, OH, J = 6.2 Hz), 5.23 (t, 1H, OH, J = 5.8 Hz), 5.15 (d, 1H, OH, J = 4.8 Hz), 5.06 (t, 1H, OH, J = 5.8 Hz), 4.63 (q, 1H, H-2′, J = 5.9 Hz), 4.58 (d, 2H, CH_2, J = 5.4 Hz), 4.15 (m, 1H, H-3′), 3.92 (m, 1H, H-4′), 3.67−3.62 (dt, 1H, H-5′, J = 4.4, 11.7 Hz), 3.56−3.51 (ddd, 1H, H-5′, J = 4.4, 6.3, 11.2 Hz). ^{13}C NMR (DMSO-d_6): δ 166.9, 150.9, 150.1, 147.8, 137.0, 124.5, 121.4, 87.6, 85.8, 73.6, 71.1, 62.2, 55.4. HRMS: calcd for $C_{13}H_{15}N_7O_6Na$ $[M + Na]^+$ 388.0976, found 388.0982.

2-[4-(*N*-Phthalimidomethyl)-1,2,3-triazol-1*H*-yl]inosine (21). *Step 1: Desilylation.* Using the procedure described for **17**, this compound was synthesized from **7** (350.0 mg, 0.428 mmol) and $Et_3N{\cdot}3HF$ (348 μL, 2.14 mmol). Chromatography of the crude reaction mixture on a silica gel column using 10% MeOH in EtOAc yielded 165.0 mg (72% yield) of the O^6-allyl-protected nucleoside as a white, foamy solid. R_f (SiO_2/EtOAc) = 0.23. ^{1}H NMR (DMSO-d_6): δ 8.90 (s, 1H, Ar-H), 8.73 (s, 1H, Ar-H), 7.93 (dd, 2H, Ar-H, J = 3.2, 5.4 Hz), 7.74 (dd, 2H, Ar-H, J = 3.2, 5.4 Hz), 6.22−6.14 (m, 1H, ═CH), 6.03 (d, 1H, H-1′, J = 5.8 Hz), 5.56 (d, 1H, OH, J = 6.2 Hz), 5.53 (br d, 1H, ═CH_{trans}, J = 17.5 Hz), 5.35 (d, 1H, ═CH_{cis}, J = 10.5 Hz), 5.28 (d, 1H, OH, J = 5.0 Hz), 5.22 (d, 2H, OCH_2, J = 5.6 Hz), 5.02 (t, 1H, OH, J = 5.4 Hz), 4.97 (s, 2H, NCH_2), 4.62 (app q, 1H, H-2′ J_{app} ≈ 5.5 Hz), 4.20 (app q, 1H, H-3′, J_{app} ≈ 4.5 Hz), 3.98 (app q, 1H, H-4′, J_{app} ≈ 4.1 Hz), 3.71−3.66 (m, 1H, H-5′), 3.60−3.56 (m, 1H, H-5′).

Step 2: Deallylation. The desilylated product (150.0 mg, 0.280 mmol) obtained in step 1 was deallylated as described for **17** using $Pd(PPh_3)_4$ (16.2 mg, 5 mol %) and $PhSO_2Na$ (45.9 mg, 0.128 mmol) to yield 110.0 mg (79% yield) of **21** as a white solid. R_f (SiO_2/MeOH) = 0.70. ^{1}H NMR (DMSO-d_6): δ 8.53 (s, 1H, Ar-H), 7.97 (s, 1H, Ar-H), 7.92 (dd, 2H, Ar-H, J = 3.2, 5.4 Hz), 7.864 (dd, 2H, Ar-H, J = 3.2, 5.4 Hz), 5.80 (d, 1H, H-1′, J = 6.3 Hz), 5.40 (d, 1H, OH, J = 6.3 Hz), 5.13 (d, 1H, OH, J = 4.6 Hz), 5.03 (t, 1H, OH, J = 5.9 Hz), 4.91 (s, 2H, NCH_2), 4.60 (app q, 1H, H-2′, J_{app} ≈ 5.6 Hz), 4.13 (app q, 1H, H-3′, J_{app} ≈ 4.7 Hz), 3.90 (app q, 1H, H-4′, J_{app} ≈ 3.4 Hz), 3.65−3.10 (m, 1H, H-5′), 3.53−3.48 (m, 1H, H-5′). ^{13}C NMR (DMSO-d_6): δ 167.8, 166.3, 150.4, 150.0, 142.2, 137.2, 134.9, 132.1, 124.5, 123.6, 122.1, 87.6, 85.9, 73.7, 71.1, 62.2, 33.3. HRMS: calcd for $C_{21}H_{19}N_8O_7$ $[M + H]^+$ 495.1371, found 495.1379.

2-(4-Ferrocenyl-1,2,3-triazol-1*H*-yl)inosine (22). *Step 1: Desilylation.* Using the procedure described for **17**, this compound was synthesized from **8** (400.0 mg, 0.442 mmol) and $Et_3N{\cdot}3HF$ (359 μL, 2.21 mmol). Chromatography of the crude reaction mixture on a silica gel column using 10% MeOH in EtOAc yielded 175.0 mg (65% yield) of the O^6-allyl-protected nucleoside as a brown, foamy solid. R_f (SiO_2/5% MeOH in EtOAc) = 0.20. ^{1}H NMR (DMSO-d_6): δ 8.94 (s, 1H, Ar-H), 8.69 (s, 1H, Ar-H), 6.21−6.13 (m, 1H, ═CH), 6.02 (d, 1H, H-1′, J = 5.7 Hz), 5.53 (br s, 1H, OH), 5.52 (br d, 1H, ═CH_{trans}, J = 17.0 Hz), 5.33 (d, 1H, ═CH_{cis}, J = 10.3 Hz), 5.27 (s, 1H, OH), 5.23 (d, 2H, OCH_2, J = 5.6 Hz), 5.00 (t, 1H, OH, J = 4.3 Hz), 4.88 (s, 2H, ferrocenyl-H), 4.60 (br t, 1H, H-2′, J = 4.5 Hz), 4.33 (s, 2H, ferrocenyl-H), 4.10 (br s, 1H, H-3′), 4.04 (s, 5H, ferrocenyl-H), 3.95 (br s, 1H, H-4′), 3.67−3.65 (m, 1H, H-5′), 3.57−3.55 (m, 1H, H-5′).

Step 2: Deallylation. The desilylated product (95.0 mg, 0.156 mmol) obtained in step 1 was deallylated as described for **17** using $Pd(PPh_3)_4$ (9.0 mg, 5 mol %) and $PhSO_2Na$ (25.6 mg, 0.156 mmol) to yield 70.1 mg (86% yield) of **22** as a brown red solid. R_f (SiO_2/MeOH) = 0.71. ^{1}H NMR (DMSO-d_6): δ 8.66 (s, 1H, Ar-H), 7.99 (s, 1H, Ar-H), 5.84 (d, 1H, H-1′, J = 6.3 Hz), 5.46 (br s, 1H, OH), 5.20 (br s, 1H, OH), 5.09 (t, 1H, OH, J = 5.3 Hz), 4.86 (s, 2H, ferrocenyl-H), 4.63 (br s, 1H, H-2′), 4.33 (s, 2H, ferrocenyl-H), 4.17 (br s, 1H, H-3′), 4.07 (s, 5H, ferrocenyl-H), 3.94 (br s, 1H, H-4′), 3.69−3.66 (m, 1H, H-5′), 3.57−3.54 (m, 1H, H-5′). ^{13}C NMR (DMSO-d_6): δ 166.9, 150.8, 150.2, 145.2, 137.1, 124.5, 118.9, 87.5, 85.9, 79.6, 76.2, 73.7, 71.2, 69.7, 68.7, 66.8, 62.2. HRMS: calcd for $C_{22}H_{22}FeN_7O_5$ $[M + H]^+$ 520.1026, found 520.1006.

2-(4-*n*-Butyl-1,2,3-triazol-1*H*-yl)inosine (23). *Step 1: Desilylation.* Using the procedure described for **17**, this compound was synthesized from **9** (172.0 mg, 0.222 mmol) and $Et_3N{\cdot}3HF$ (180 μL, 1.10 mmol). Chromatography of the crude reaction mixture on a silica gel column using 10% MeOH in EtOAc yielded 70.1 mg (73% yield) of the O^6-allyl-protected nucleoside as a white, foamy solid. R_f (SiO_2/10% MeOH in EtOAc) = 0.57. ^{1}H NMR (DMSO-d_6): δ 8.73 (s, 1H, Ar-H), 8.69 (s, 1H, Ar-H), 6.23−6.16 (m, 1H, ═CH), 6.05 (d, 1H, H-1′, J = 5.7 Hz), 5.65 (s, 1H, OH), 5.53 (dd, 1H, ═CH_{trans}, J = 1.2, 17.2 Hz), 5.36 (dd, 1H, ═CH_{cis}, J = 1.2, 10.2 Hz), 5.24 (d, 2H, OCH_2, J = 5.7 Hz), 5.07 (s, 1H, OH), 4.64 (t, 1H, H-2′, J = 5.0 Hz), 4.23 (t, 1H, H-3′, J = 3.8 Hz), 4.00 (app q, 1H, H-4′, J_{app} ≈ 4.0 Hz), 3.70 (br d, 1H, H-5′, J = 10.2 Hz), 3.60 (br d, 1H, H-5′, J = 10.2 Hz), 2.74 (t, 2H, butyl-CH_2, J = 7.6 Hz), 1.68 (quint, 2H, butyl-CH_2, J = 7.6 Hz), 1.37 (sextet, 2H, butyl-CH_2, J = 7.3 Hz), 0.93 (t, 3H, butyl-CH_3, J = 7.3 Hz). ^{13}C NMR (DMSO-d_6): δ 160.7, 153.2, 148.1, 143.7, 132.8, 121.3, 120.6, 119.5, 87.9, 86.2, 74.2, 70.7, 68.4, 61.6, 31.3, 24.3, 24.8, 22.0, 14.0.

Step 2: Deallylation. The desilylated product (30.0 mg, 0.069 mmol) obtained in step 1 was deallylated as described for **17** using $Pd(PPh_3)_4$ (4.0 mg, 5 mol %) and $PhSO_2Na$ (11.4 mg, 0. 069 mmol) to yield 19.4 mg (70% yield) of **23** as a white solid. R_f (SiO_2/MeOH) = 0.51. ^{1}H NMR (DMSO-d_6): δ 8.32 (s, 1H, Ar-H), 7.96 (s, 1H, Ar-H), 5.82 (d, 1H, H-1′, J = 6.3 Hz), 5.43 (d, 1H, OH, J = 6.2 Hz), 5.16 (d, 1H, OH, J = 3.9 Hz), 5.07 (t, 1H, OH, J = 5.8 Hz), 4.63 (app q, 1H, H-2′, J_{app} ≈ 5.9 Hz), 4.15 (app q, 1H, H-3′, J_{app} ≈ 4.3 Hz), 3.92 (app q, 1H, H-4′, J_{app} ≈ 3.4 Hz), 3.67−3.63 (m, 1H, H-5′), 3.56−3.51 (m, 1H, H-5′), 2.69 (t, 2H, butyl-CH_2, J = 7.6 Hz), 1.64 (quint, 2H, butyl-CH_2, J = 7.5 Hz), 1.36 (sextet, 2H, butyl-CH_2, J = 7.5 Hz), 0.92 (t, 3H, butyl-CH_3, J = 7.3 Hz). ^{13}C NMR (DMSO-d_6): δ 166.9, 150.9, 150.2, 146.8, 137.1, 124.4, 120.6, 87.6, 85.9, 73.7, 71.1, 62.2, 31.4, 25.0, 22.0, 14.1. HRMS: calcd for $C_{16}H_{21}N_7O_5Na$ $[M + Na]^+$ 414.1496, found 414.1499.

2-[4-(4-Fluorophenyl)-1,2,3-triazol-1*H*-yl]inosine (24). *Step 1: Desilylation.* Using the procedure described for **17**, this compound was synthesized from **10** (310.0 mg, 0.381 mmol) and $Et_3N{\cdot}3HF$ (310 μL, 1.90 mmol). Chromatography of the crude reaction mixture on a silica gel column using 10% MeOH in EtOAc yielded 143.8 mg (80% yield) of the O^6-allyl-protected nucleoside as a white, foamy solid. R_f (SiO_2/10% MeOH in EtOAc) = 0.48. ^{1}H NMR (DMSO-d_6): δ 9.45 (s, 1H, Ar-H), 8.77 (s, 1H, Ar-H), 8.11 (dd, 2H, Ar-H, J = 5.3, 8.6 Hz), 7.36 (t, 2H, Ar-H, J = 8.6 Hz), 6.26−6.20 (m, 1H, ═CH), 6.18 (d, 1H, H-1′, J = 5.8 Hz), 5.66 (br s, 1H, OH), 5.57 (dd, 1H, ═CH_{trans}, J = 1.5, 17.2 Hz), 5.43 (br s, 1H, OH), 5.39 (dd, 1H, ═CH_{cis}, J = 1.2, 10.4 Hz), 5.29 (d, 2H, OCH_2, J = 5.9 Hz), 5.08 (t, 1H, OH, J = 4.0 Hz), 4.68 (t, 1H, H-2′, J = 5.2 Hz), 4.24 (t, 1H, H-3′, J = 3.9 Hz), 4.01 (app q, 1H, H-4′, J_{app} ≈ 4.0 Hz), 3.74 (dd, 1H, H-5′, J = 4.2, 11.8 Hz), 3.62 (dd, 1H, H-5′, J = 3.4, 11.8 Hz).

Step 2: Deallylation. The desilylated product (24.0 mg, 0.048 mmol) obtained in step 1 was deallylated as described for **17** using

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$Pd(PPh_3)_4$ (2.8 mg, 5 mol %) and $PhSO_2Na$ (8.0 mg, 0. 048 mmol) to yield 15.0 mg (72% yield) of **24** as a white solid. R_f (SiO_2/MeOH) = 0.42. ^1H NMR (DMSO-d_6): δ 9.12 (s, 1H, Ar-H), 8.05 (s, 1H, Ar-H), 8.03 (br t, 2H, Ar-H, $J_{app} \approx$ 6.8 Hz), 7.31 (t, 2H, Ar-H, J = 8.5 Hz), 5.87 (d, 1H, H-1′, J = 6.2 Hz), 5.54 (br d, 1H, OH, J = 4.6 Hz), 5.28 (br s, 1H, OH), 5.10 (t, 1H, OH, J = 5.5 Hz), 4.66 (br d, 1H, H-2′, J = 4.5 Hz), 4.18 (br s, 1H, H-3′), 3.94 (br s, 1H, H-4′), 3.69−3.66 (m, 1H, H-5′), 3.57−3.54 (m, 1H, H-5′). ^{13}C NMR (DMSO-d_6): δ 167.1, 163.2 and 161.3 (d, ^1J = 244.6 Hz), 150.8, 150.2, 145.2, 137.4, 127.9 and 127.8 (d, ^3J = 8.2 Hz), 127.6, 124.5, 120.0, 116.3 and 116.1 (d, ^2J = 21.5 Hz), 87.6, 86.0, 73.7, 71.1, 62.2. HRMS: calcd for $C_{18}H_{16}FN_7O_5Na$ $[M + Na]^+$ 452.1089, found 452.1090.

2-(4-Phenyl-1,2,3-triazol-1*H*-yl)-2′-deoxyinosine (25). *Step 1: Desilylation.* Using the procedure described for **17**, this compound was synthesized from **11** (230.0 mg, 0.346 mmol) and $Et_3N{\cdot}3HF$ (187 μL, 1.15 mmol). Chromatography of the crude reaction mixture on a silica gel column using 8% MeOH in EtOAc yielded 120.1 mg (76% yield) of the O^6-allyl-protected nucleoside as a white, foamy solid. R_f (SiO_2/10% MeOH in EtOAc) = 0.50. ^1H NMR (DMSO-d_6): δ 9.44 (s, 1H, Ar-H), 8.72 (s, 1H, Ar-H), 8.07 (d, 2H, Ar-H, J = 7.8 Hz), 7.51 (t, 2H, Ar-H, J = 7.5 Hz), 7.41 (t, 1H, Ar-H, J = 7.5 Hz), 6.51 (t, 1H, H-1′, J = 6.4 Hz), 6.26−6.18 (m, 1H, =CH), 5.56 (br d, 1H, =CH_{trans}, J = 17.2 Hz), 5.38 (br d, 1H, =CH_{cis}, J = 10.4 Hz), 5.28 (d, 2H, OCH_2, J = 5.9 Hz), 4.49 (br s, 1H, H-3′), 3.91 (br d, 1H, H-4′, J = 2.5 Hz), 3.67 (dd, 1H, H-5′, J = 4.5, 11.8 Hz), 3.57 (dd, 1H, H-5′, J = 4.3, 11.8 Hz), 2.79 (app quint, 1H, H-2′, $J_{app} \approx$ 6.5 Hz), 2.39 (ddd, 1H, H-2′, J = 2.5, 6.0, 9.5 Hz). ^{13}C NMR (DMSO-d_6): 160.7, 152.9, 147.9, 147.2, 143.8, 132.9, 130.3, 129.4, 128.9, 126.0, 120.8, 120.7, 119.7, 88.6, 84.2, 71.1, 68.6, 61.9, 40.2.

Step 2: Deallylation. The desilylated product (95.0 mg, 0.218 mmol) obtained in step 1 was deallylated as described for **17** using $Pd(PPh_3)_4$ (12.6 mg, 5 mol %) and $PhSO_2Na$ (35.7 mg, 0. 218 mmol) to yield 64.3 mg (75% yield) of **25** as a white solid. R_f (SiO_2/MeOH) = 0.54. ^1H NMR (DMSO-d_6): δ 9.06 (s, 1H, Ar-H), 8.00 (s, 1H, Ar-H), 7.98 (d, 2H, Ar-H, J = 7.6 Hz), 7.46 (t, 2H, Ar-H, J = 7.5 Hz), 7.36 (t, 1H, Ar-H, J = 7.1 Hz), 6.31 (t, 1H, H-1′, J = 6.7 Hz), 5.30 (br s, 1H, OH), 4.97 (br s, 1H, OH), 4.42 (br s, 1H, H-3′), 3.85 (br s, 1H, H-4′), 3.63−3.60 (m, 1H, H-5′), 3.55−3.50 (m, 1H, H-5′), 2.72 (app quint, 1H, H-2′, $J_{app} \approx$ 6.6 Hz), 2.24 (br dd, 1H, H-2′, J = 3.0, 11.3 Hz). ^{13}C NMR (DMSO-d_6): δ 166.8, 150.8, 149.9, 146.0, 136.7, 131.1, 129.3, 128.3, 125.8, 121.5, 120.0, 88.1, 83.6, 71.5, 62.4, 40.1. HRMS: calcd for $C_{18}H_{17}N_7O_4Na$ $[M + Na]^+$ 418.1234, found 418.1240.

2-[4-(4-Methoxyphenyl)-1,2,3-triazol-1*H*-yl]-2′-deoxyinosine (26). *Step 1: Desilylation.* Using the procedure described for **17**, this compound was synthesized from **12** (171.0 mg, 0.24 mmol) and $Et_3N{\cdot}3HF$ (133 μL, 0.821 mmol). Chromatography of the crude reaction mixture on a silica gel column using 10% MeOH in EtOAc yielded 104.1 mg (93% yield) of the O^6-allyl-protected nucleoside as a white, foamy solid. R_f (SiO_2/10% MeOH in EtOAc) = 0.38. ^1H NMR (DMSO-d_6): δ 9.33 (s, 1H, Ar-H) 8.72 (s, 1H, Ar-H), 7.99 (d, 2H, Ar-H, J = 8.6 Hz), 7.07 (d, 2H, Ar-H, J = 8.6 Hz), 6.48 (t, 1H, H-1′, J = 6.7 Hz), 6.26−6.18 (m, 1H, =CH), 5.56 (d, 1H, =CH_{trans}, J = 17.4 Hz), 5.42 (d, 1H, OH, J = 4.0 Hz), 5.38 (d, 1H, =CH_{cis}, J = 10.5 Hz), 5.28 (d, 2H, OCH_2, J = 5.6 Hz), 4.96 (t, 1H, OH, J = 5.4 Hz), 4.49 (br s, 1H, H-3′), 3.92 (br d, 1H, H-4′, J = 2.9 Hz), 3.82 (s, 3H, OCH_3), 3.68−3.64 (m, 1H, H-5′), 3.60−3.55 (m, 1H, H-5′), 2.80 (app quint, 1H, H-2′, $J_{app} \approx$ 7.0 Hz), 2.40 (ddd, 1H, H-2′, J = 3.0, 6.5, 10.5 Hz).

Step 2: Deallylation. The desilylated product (100.0 mg, 0.214 mmol) obtained in step 1 was deallylated as described for **17** using $Pd(PPh_3)_4$ (12.4 mg, 5 mol %) and $PhSO_2Na$ (35.1 mg, 0. 048 mmol) to yield 78.1 mg (80% yield) of **26** as a pale yellow solid. R_f (SiO_2/MeOH) = 0.46. ^1H NMR (DMSO-d_6): δ 8.97 (s, 1H, Ar-H), 8.02 (s, 1H, Ar-H), 7.91 (d, 2H, Ar-H, J = 8.1 Hz), 7.03 (d, 2H, Ar-H, J = 8.1 Hz), 6.32 (t, 1H, H-1′, J = 6.6 Hz), 5.30 (br s, 1H, OH), 4.99 (br s, 1H, OH), 4.43 (br s, 1H, H-3′), 3.86 (br s, 1H, H-4′), 3.80 (s, 3H, OCH_3), 3.63−3.61 (m, 1H, H-5′), 3.54−3.52 (m, 1H, H-5′), 2.73 (app quint, 1H, H-2′, $J_{app} \approx$ 6.6 Hz), 2.25 (br dd, 1H, H-2′, J = 5.5, 11.5 Hz). ^{13}C NMR (DMSO-d_6): δ 166.9, 159.4, 150.9, 149.9, 145.9, 139.6, 127.1, 124.4, 123.7, 119.0, 114.7, 88.1, 83.5, 71.5, 62.4, 55.6, 40.1. HRMS: calcd for $C_{19}H_{19}N_7O_5Na$ $[M + Na]^+$ 448.1340, found 448.1346.

2-[4-(Hydroxymethyl)-1,2,3-triazol-1*H*-yl]-2′-deoxyinosine (27). *Step 1: Desilylation.* Using the procedure described for **17**, this compound was synthesized from **13** (211.0 mg, 0.341 mmol) and $Et_3N{\cdot}3HF$ (183 μL, 1.13 mmol). Chromatography of the crude reaction mixture on a silica gel column using 15% MeOH in EtOAc yielded 103.5 mg (78% yield) of the O^6-allyl-protected nucleoside as a white, foamy solid. R_f (SiO_2/10% MeOH in EtOAc) = 0.33. ^1H NMR (DMSO-d_6): δ 8.77 (s, 1H, Ar-H), 8.70 (s, 1H, Ar-H), 6.48 (t, 1H, H-1′, J = 6.8 Hz), 6.23−6.15 (m, 1H, =CH), 5.53 (br d, 1H, =CH_{trans}, J = 17.3 Hz), 5.38 (d, 1H, OH, J = 4.2 Hz), 5.35 (br d, 1H, =CH_{cis}, J = 10.6 Hz), 5.36 (t, 1H, OH, J = 5.6 Hz), 5.22 (d, 2H, OCH_2, J = 5.9 Hz), 4.92 (t, 1H, OH, J = 5.6 Hz), 4.64 (d, 2H, CH_2, J = 5.6 Hz), 4.46 (m, 1H, H-3′), 3.91 (app q, 1H, H-4′, $J_{app} \approx$ 3.2 Hz), 3.65−3.61 (m, 1H, H-5′), 3.57−3.52 (m, 1H, H-5′), 2.78 (app sextet, 1H, H-2′, $J_{app} \approx$ 6.5 Hz), 2.40 (ddd, 1H, H-2′, J = 3.7, 6.3, 10.0 Hz).

Step 2: Deallylation. The desilylated product (82.0 mg, 0.210 mmol) obtained in step 1 was deallylated as described for **17** using $Pd(PPh_3)_4$ (12.1 mg, 5 mol %) and $PhSO_2Na$ (34.4 mg, 0. 210 mmol) to yield 65.0 mg (88% yield) of **27** as a pale yellow solid. R_f (SiO_2/MeOH) = 0.50. ^1H NMR (DMSO-d_6): δ 8.44 (s, 1H, Ar-H), 7.98 (s, 1H, Ar-H), 6.28 (t, 1H, H-1′, J = 6.4 Hz), 5.30 (d, 1H, OH, J = 3.4 Hz), 5.24 (t, 1H, OH, J = 5.7 Hz), 4.96 (t, 1H, OH, J = 5.4 Hz), 4.58 (d, 2H, CH_2, J = 5.0 Hz), 4.40 (br s, 1H, H-3′), 3.84 (br s, 1H, H-4′), 3.61−3.58 (m, 1H, H-5′), 3.52−3.50 (m, 1H, H-5′), 2.70 (app quint, 1H, H-2′, $J_{app} \approx$ 5.5 Hz), 2.22 (br dd, 1H, H-2′, J = 3.0, 12.7 Hz). ^{13}C NMR (DMSO-d_6): δ 166.5, 150.6, 149.9, 147.8, 136.8, 124.3, 121.5, 88.1, 83.5, 71.4, 62.4, 55.4, 40.1. HRMS: calcd for $C_{13}H_{15}N_7O_5Na$ $[M + Na]^+$ 372.1027, found 372.1029.

2-[4-(*N*-Phthalimidomethyl)-1,2,3-triazol-1*H*-yl]-2′-deoxyinosine (28). *Step 1: Desilylation.* Using the procedure described for **17**, this compound was synthesized from **14** (289.0 mg, 0.387 mmol) and $Et_3N{\cdot}3HF$ (201 μL, 1.29 mmol). Chromatography of the crude reaction mixture on a silica gel column using 10% MeOH in EtOAc yielded 159.3 mg (79% yield) of the O^6-allyl-protected nucleoside as a yellow, foamy solid. R_f (SiO_2/10% MeOH in EtOAc) = 0.56. ^1H NMR (DMSO-d_6): δ 8.91 (s, 1H, Ar-H), 8.70 (s, 1H, Ar-H), 7.93 (br d, 2H, Ar-H, J = 3.6 Hz), 7.88 (br d, 2H, Ar-H, J = 3.6 Hz), 6.46 (t, 1H, H-1′, J = 6.7 Hz), 6.21−6.13 (m, 1H, =CH), 5.52 (d, 1H, =CH_{trans}, J = 16.5 Hz), 5.38 (d, 1H, OH, J = 4.0 Hz), 5.34 (d, 1H, =CH_{cis}, J = 10.6 Hz), 5.20 (d, 2H, OCH_2, J = 5.6 Hz), 4.97 (s, 2H, NCH_2), 4.92 (t, 1H, OH, J = 5.4 Hz), 4.45 (br s, 1H, H-3′), 3.89 (br d, 1H, H-4′, J = 2.8 Hz), 3.64−3.60 (m, 1H, H-5′), 3.56−3.52 (m, 1H, H-5′), 2.80 (app quint, 1H, H-2′, $J_{app} \approx$ 6.5 Hz), 2.36 (ddd, 1H, H-2′, J = 3.4, 6.0, 9.6 Hz).

Step 2: Deallylation. The desilylated product (144.0 mg, 0.277 mmol) obtained in step 1 was deallylated as described for **17** using $Pd(PPh_3)_4$ (16.0 mg, 5 mol %) and $PhSO_2Na$ (45.4 mg, 0. 277 mmol) to yield 98.9 mg (75% yield) of **28** as a pale yellow solid. R_f (SiO_2/MeOH) = 0.49. ^1H NMR (DMSO-d_6): δ 8.54 (s, 1H, Ar-H), 7.97 (s, 1H, Ar-H), 7.92 (dd, 2H, Ar-H, J = 3.0, 5.4 Hz), 7.86 (dd, 2H, Ar-H, J = 3.0, 5.4 Hz), 6.26 (t, 1H, H-1′, J = 6.2 Hz), 5.32 (d, 1H, OH, J = 4.0 Hz), 4.94 (t, 1H, OH, J = 5.7 Hz), 4.81 (s, 2H, NCH_2), 4.38 (br s, 1H, H-3′), 3.85 (app q, 1H, H-4′, $J_{app} \approx$ 4.5 Hz), 3.60−3.57 (m, 1H, H-5′), 3.56−3.48 (m, 1H, H-5′), 2.70 (app quint, 1H, H-2′, $J_{app} \approx$ 5.5 Hz), 2.38 (ddd, 1H, H-2′, J = 2.5, 5.2, 11.0 Hz). ^{13}C NMR (DMSO-d_6): δ 167.8, 166.6, 150.6, 149.8, 142.2, 136.7, 134.9, 132.1, 124.4, 123.6, 122.1, 88.1, 83.5, 71.4, 62.4, 40.2, 33.3. HRMS: calcd for $C_{21}H_{18}N_8O_6Na$ $[M + Na]^+$ 501.1242, found 501.1241.

2-(4-Ferrocenyl-1,2,3-triazol-1*H*-yl)-2′-deoxyinosine (29). *Step 1: Desilylation.* Using the procedure described for **17**, this compound was synthesized from **15** (394.0 mg, 0.480 mmol) and $Et_3N{\cdot}3HF$ (257 μL, 1.60 mmol). Chromatography of the crude reaction mixture on a silica gel column using 10% MeOH in EtOAc yielded 240.8 mg (84% yield) of the O^6-allyl-protected nucleoside as a brown, foamy solid. R_f (SiO_2/10% MeOH in EtOAc) = 0.58. ^1H NMR (DMSO-d_6): δ 9.00 (s, 1H, A-H) 8.71 (s, 1H, Ar-H), 6.51 (t, 1H, H-1′, J = 6.7 Hz), 6.26−6.18 (m, 1H, =CH), 5.57 (dd, 1H, =CH_{trans}, J = 1.5, 17.2 Hz), 5.42 (d, 1H, OH, J = 4.0 Hz), 5.34 (br d, 1H, =CH_{cis}, J

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= 11.2 Hz), 5.28 (d, 2H, OCH_2, J = 5.6 Hz), 4.96 (t, 1H, OH, J = 5.5 Hz), 4.94 (s, 2H, ferrocenyl-H), 4.49 (br s, 1H, H-3′), 4.39 (s, 2H, ferrocenyl-H), 4.10 (s, 5H, ferrocenyl-H), 3.92 (br d, 1H, H-4′, J = 3.0 Hz), 3.68−3.64 (m, 1H, H-5′), 3.60−3.56 (m, 1H, H-5′), 2.78 (app quint, 1H, H-2′, $J_{app} \approx$ 6.5 Hz), 2.40 (ddd, 1H, H-2′, J = 3.5, 6.5, 9.5 Hz).

Step 2: Deallylation. The desilylated product (189.0 mg, 0.319 mmol) obtained in step 1 was deallylated as described for **17** using $Pd(PPh_3)_4$ (18.4 mg, 5 mol %) and $PhSO_2Na$ (52.3 mg, 0. 319 mmol) to yield 135.1 mg (84% yield) of **29** as a brownish red solid. R_f (SiO_2/MeOH) = 0.53. ^{1}H NMR (DMSO-d_6): δ 8.65 (s, 1H, Ar-H), 7.98 (s, 1H, Ar-H), 6.51 (t, 1H, H-1′, J = 6.2 Hz), 5.32 (d, 1H, OH, J = 3.9 Hz), 4.98 (t, 1H, OH, J = 5.7 Hz), 4.86 (s, 2H, ferrocenyl-H), 4.42 (br s, 1H, H-3′), 4.34 (s, 2H, ferrocenyl-H), 4.07 (s, 5H, ferrocenyl-H), 3.86 (br d, 1H, H-4′, J = 2.3 Hz), 3.64−3.60 (m, 1H, H-5′), 3.56−3.51 (m, 1H, H-5′), 2.71 (app quint, 1H, H-2′, $J_{app} \approx$ 6.6 Hz), 2.24 (ddd, 1H, H-2′, J = 2.0, 6.0. 10.9 Hz). ^{13}C NMR (DMSO-d_6): δ 166.6, 150.7, 149.9, 145.2, 136.5, 131.9, 129.1, 118.9, 88.1, 83.5, 76.2, 71.5, 69.6, 68.7, 66.8, 62.4, 40.2. HRMS: calcd for $C_{22}H_{21}FeN_7O_4Na$ $[M + Na]^+$ 526.0897, found 526.0890.

2-(4-*n*-Butyl-1,2,3-triazol-1*H*-yl)-2′-deoxyinosine (30). *Step 1: Desilylation.* Using the procedure described for **17**, this compound was synthesized from **16** (275.1 mg, 0.427 mmol) and $Et_3N{\cdot}3HF$ (231 μL, 1.42 mmol). Chromatography of the crude reaction mixture on a silica gel column using 8% MeOH in EtOAc yielded 152.3 mg (86% yield) of the O^6-allyl-protected nucleoside as a brown, foamy solid. R_f (SiO_2/10% MeOH in EtOAc) = 0.50. ^{1}H NMR (DMSO-d_6): δ 8.70 (s, 2H, Ar-H), 6.48 (t, 1H, H-1′, J = 6.6 Hz), 6.24−6.16 (m, 1H, =CH), 5.54 (d, 1H, $=CH_{trans}$, J = 17.2 Hz), 5.39 (br s, 1H, OH), 5.36 (d, 1H, $=CH_{cis}$, J = 10.6 Hz), 5.22 (d, 2H, OCH_2, J = 5.4 Hz), 4.93 (br s, 1H, OH), 4.48 (br s, 1H, H-3′), 3.91 (br d, 1H, H-4′, J = 2.7 Hz), 3.65 (br d, 1H, H-5′, J = 10.5 Hz), 3.57 (br d, 1H, H-5′, J = 10.5 Hz), 2.80−2.73 (m, 3H, butyl-CH_2, and H-2′) 2.38 (br dd, 1H, H-2′, J = 3.4, 7.5 Hz), 1.69 (quint, 2H, butyl-CH_2, J = 7.5 Hz), 1.39 (sextet, 2H, butyl-CH_2, J = 7.5 Hz), 0.94 (t, 3H, butyl-CH_3, J = 7.3 Hz).

Step 2: Deallylation. The desilylated product (144.0 mg, 0.346 mmol) obtained in step 1 was deallylated as described for **17** using $Pd(PPh_3)_4$ (20.0 mg, 5 mol %) and $PhSO_2Na$ (56.7 mg, 0. 346 mmol) to yield 89.3 mg (69% yield) of **30** as a white solid. R_f (SiO_2/MeOH) = 0.55. ^{1}H NMR (DMSO-d_6): δ 8.35 (s, 1H, Ar-H), 8.00 (s, 1H, Ar-H), 6.28 (t, 1H, H-1′, J = 6.3 Hz), 5.32 (br s, 1H, OH), 4.98 (br s, 1H, OH), 4.41 (br s, 1H, H-3′), 3.85 (br s, 1H, H-4′), 3.61−3.59 (m, 1H, H-5′), 3.52−3.50 (m, 1H, H-5′), 2.73−2.65 (m, 3H, butyl-CH_2, and H-2′), 2.38 (ddd, 1H, H-2′, J = 3.5, 8.5, 11.0 Hz), 1.63 (quint, 2H, butyl-CH_2, J = 7.4 Hz), 1.35 (sextet, 2H, butyl-CH_2, J = 7.4 Hz), 0.91 (t, 3H, butyl-CH_3, J = 7.3 Hz). ^{13}C NMR (DMSO-d_6): δ 166.9, 150.8, 149.9, 146.8, 136.7, 124.2, 120.6, 88.1, 83.5, 71.5, 62.4, 40.1, 31.4, 25.0, 22.1, 14.1. HRMS: calcd for $C_{16}H_{21}N_7O_4Na$ $[M + Na]^+$ 398.1547, found 398.1553.

O^6-(1-Benzotriazol-1*H*-yl)-2-(4-phenyl-1,2,3-triazol-1*H*-yl)-2′,3′,5′-tri-*O*-(*tert*-butyldimethylsilyl)inosine (31). *Step 1: Deallylation.* Following the procedure described for the preparation of **17**, compound **3** (170 mg, 0.214 mmol) was deallylated using $Pd(PPh_3)_4$ (12.3 mg, 5 mol %) and $PhSO_2Na$ (35.1 mg, 0.214 mmol). Chromatographic purification of the crude material on a silica gel column using 10% MeOH in EtOAc afforded 146.3 mg (91% yield) of the deallylated compound as a clear gum. R_f (SiO_2/10% MeOH in EtOAc) = 0.46. ^{1}H NMR (DMSO-d_6): δ 8.96 (s, 1H, Ar-H), 8.05 (s, 1H, Ar-H), 7.95 (d, 2H, Ar-H, J = 7.6 Hz), 7.47 (t, 2H, Ar-H, J = 7.2 Hz), 7.36 (t, 1H, Ar-H, J = 7.2 Hz), 5.85 (d, 1H, H-1′, J = 6.4 Hz), 5.12 (t, 1H, H-2′, J = 5.0 Hz), 4.30 (br s, 1H, H-3′), 4.08 (dd, 1H, H-5′, J = 6.9, 10.8 Hz), 3.97 (br s, 1H, H-4′), 3.72 (dd, 1H, H-5′, J = 3.5, 10.8 Hz), 0.92, 0.86, and 0.72 (3s, 27H, *t*-Bu), 0.14, 0.12, 0.07, 0.05, −0.10, and −0.31 (6s, 18H, $SiCH_3$).

Step 2: Introduction of the O^6-Benzotriazolyl Group. In a clean, dry round-bottomed flask equipped with a stirring bar were placed the 2-(4-phenyl-1,2,3-triazol-1*H*-yl)-2′,3′-5′-tri-*O*-(*tert*-butyldimethylsilyl)-inosine derivative **3** (160.0 mg, 0.212 mmol), BOP (187.7 mg, 0.424 mmol), and *i*-Pr_2NEt (45 μL, 0.318 mmol) in dry THF (4.0 mL). The reaction mixture was flushed with nitrogen gas, and stirred at room temperature for 24 h, at which time TLC indicated complete reaction. The mixture was diluted with EtOAc and washed with water containing a small amount of NaCl, and the aqueous layer was separated and reextracted with EtOAc. The combined organic layer was dried over Na_2SO_4 and evaporated to dryness. Chromatographic purification of the crude material on a silica gel column using 20% EtOAc in hexanes provided 101.4 mg (55% yield) of **31** as a white foam. R_f (SiO_2/20% EtOAc in hexanes) = 0.57. ^{1}H NMR ($CDCl_3$): δ 8.75 (s, 1H, Ar-H), 8.21 (d, 1H, Ar-H, J = 8.4 Hz), 7.87 (s, 1H, Ar-H), 7.74 (d, 2H, Ar-H, J = 7.3 Hz), 7.59−7.49 (m, 3H, Ar-H), 7.40 (t, 2H, Ar-H, J = 7.4 Hz), 7.33 (t, 1H, Ar-H, J = 7.4 Hz), 6.21 (d, 1H, H-1′, J = 3.7 Hz), 4.61 (t, 1H, H-2′, J = 3.9 Hz), 4.37 (t, 1H, H-3′, J = 4.6 Hz), 4.22 (app q, 1H, H-4′, $J_{app} \approx$ 3.6 Hz), 4.14 (dd, 1H, H-5′, J = 3.6, 11.6 Hz), 3.85 (dd, 1H, H-5′, J = 2.5, 11.6 Hz), 0.98, 0.93, and 0.85 (3s, 27H, *t*-Bu), 0.19, 0.17, 0.12, 0.09, 0.06, and 0.02 (6s, 18H, $SiCH_3$). ^{13}C NMR ($CDCl_3$): δ 159.7, 155.1, 147.9, 147.8, 145.4, 143.6, 129.8, 129.4, 129.2, 129.0, 128.8, 126.1, 125.3, 120.9, 119.4, 118.5, 108.8, 89.7, 85.4, 76.6, 71.2, 62.1, 26.3, 26.0, 25.9, 18.8, 18.3, 18.1, −4.1, −4.6, −5.1, −5.2. HRMS: calcd for $C_{42}H_{63}N_{10}O_5Si_3$ $[M + H]^+$ 871.4285, found 871.4298.

6-(Morpholin-4-yl)-2-(4-phenyl-1,2,3-triazol-1*H*-yl)-9-[2′,3′,5′-tri-*O*-(*tert*-butyldimethylsilyl)-β-D-ribofuranosyl]-purine (32). In a clean, dry reaction vial equipped with a stirring bar was placed **31** (50.0 mg, 0.057 mmol) in dry DME (2 mL). Morpholine (20.0 μL, 0.229 mmol) was added, the reaction mixture was flushed with nitrogen gas and allowed to stir at room temperature for 1 h. The reaction mixture was evaporated, the residue was dissolved in EtOAc and washed with water containing a small amount of NaCl. The aqueous layer was separated and reextracted with EtOAc. The combined organic layer was dried over Na_2SO_4 and evaporated to dryness. Chromatographic purification of the crude material on a silica gel column using 20% EtOAc in hexanes afforded 36.1 mg (77% yield) of **32** as a white foam. R_f (SiO_2/30% EtOAc in hexanes) = 0.70. ^{1}H NMR ($CDCl_3$): δ 8.69 (s, 1H, Ar-H), 8.20 (s, 1H, Ar-H), 7.95 (d, 2H, Ar-H, J = 7.2 Hz), 7.46 (t, 2H, Ar-H, J = 7.5 Hz), 7.36 (t, 1H, Ar-H, J = 7.5 Hz), 6.11 (d, 1H, H-1′, J = 4.5 Hz), 4.60 (t, 1H, H-2′, J = 4.5 Hz), 4.48−4.35 (br m, 4H, $2CH_2$), 4.34 (t, 1H, H-3′, J = 4.3 Hz), 4.15 (app q, 1H, H-4′, $J_{app} \approx$ 3.6 Hz), 4.08 (dd, 1H, H-5′, J = 3.7, 11.4 Hz), 3.88 (t, 4H, $2CH_2$, J = 4.8 Hz), 3.82 (dd, 1H, H-5′, J = 2.8, 11.4 Hz), 0.96, 0.94, and 0.88 (3s, 27H, *t*-Bu), 0.16, 0.14, 0.12, 0.10, 0.01, and −0.06 (6s, 18H, $SiCH_3$). ^{13}C NMR ($CDCl_3$): δ 153.8, 151.3, 149.0, 147.2, 138.3, 130.4, 128.8, 128.2, 125.9, 119.5, 118.4, 88.3, 85.0, 75.9, 71.5, 66.9, 62.3, 45.8 (br s), 26.1, 25.8, 25.6, 18.5, 18.0, 17.8, −4.3, −4.7, −5.3. HRMS: calcd for $C_{40}H_{67}N_8O_5Si_3$ $[M + H]^+$ 823.4537, found 823.4550.

6-*N*-Benzyl-2-(4-phenyl-1,2,3-triazol-1*H*-yl)-2′,3′,5′-tri-*O*-(*tert*-butyldimethylsilyl)adenosine (33). As described for the synthesis of **32**, this compound was prepared by a reaction between **31** (50.0 mg, 0.057 mmol) and benzylamine (25.0 μL, 0.228 mmol) in dry DME (2.0 mL) at room temperature over 10 h. Workup as described for **32** and chromatographic purification of the crude material on a silica gel column using 20% EtOAc in hexanes afforded 43.1 mg (90% yield) of **33** as a white foam. R_f (30% EtOAc in hexanes) = 0.55. ^{1}H NMR ($CDCl_3$): δ 8.68 (s, 1H, Ar-H), 8.41 (br s, 1H, Ar-H), 7.95 (d, 2H, Ar-H, J = 7.8 Hz), 7.48−7.45 (m, 4H, Ar-H Hz), 7.38−7.34 (m, 3H, Ar-H), 7.28 (app t, 1H, Ar-H, J = 7.3 Hz), 6.90 (br s, 1H, NH), 6.10 (d, 1H, H-1′, J = 3.8 Hz), 4.93 (br s, 2H, CH_2), 4.58 (t, 1H, H-2′, J = 3.9 Hz), 4.34 (t, 1H, H-3′, J = 4.6 Hz), 4.17 (br s, 1H, H-4′), 4.12 (br d, 1H, H-5′, J = 11.0 Hz), 3.83 (dd, 1H, H-5′, J = 2.0, 11.0 Hz), 0.97, 0.92, and 0.86 (3s, 27H, *t*-Bu), 0.17, 0.15, 0.11, 0.09, 0.05, and 0.02 (6s, 18H, $SiCH_3$). ^{13}C NMR ($CDCl_3$): δ 154.3, 150.3, 148.8, 147.4, 138.5, 137.7, 130.4, 128.9, 128.8, 128.4, 128.1, 127.8, 126.0, 118.7, 89.3, 84.3, 76.2, 70.6, 61.8, 60.4, 45.2, 26.2, 25.9, 25.8, 18.6, 18.1, 18.0, −4.1, −4.4, −4.7, −5.1, −5.3. HRMS: calcd for $C_{43}H_{67}N_8O_4Si_3$ $[M + H]^+$ 843.4588, found 843.4596.

6-(Morpholin-4-yl)-2-(4-phenyl-1,2,3-triazol-1*H*-yl)-9-(β-D-ribofuranosyl)purine (34). Using the procedure described for **17**, this compound was synthesized from **32** (30.0 mg, 0.036 mmol) and $Et_3N{\cdot}3HF$ (29.0 μL, 0.18 mmol). Chromatography of the crude reaction mixture on a silica gel column using 10% MeOH in EtOAc

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yielded 13.9 mg (80% yield) of **34** as a white, foamy solid. R_f (SiO_2/30% MeOH in EtOAc) = 0.57. ^{1}H NMR (DMSO-d_6): δ 9.34 (s, 1H, Ar-H), 8.55 (s, 1H, Ar-H), 8.05 (d, 2H, Ar-H, J = 7.8 Hz), 7.50 (t, 2H, Ar-H, J = 7.5 Hz), 7.39 (t, 1H, Ar-H, J = 7.5 Hz), 6.03 (d, 1H, H-1′, J = 5.8 Hz), 5.53 (d, 1H, OH, J = 6.0 Hz), 5.27 (d, 1H, OH, J = 4.9 Hz), 5.01 (t, 1H, OH, J = 5.6 Hz), 4.64 (app quint, 1H, H-2′, $J_{app} \approx$ 5.8 Hz), 4.48−4.35 (br m, 4H, $2CH_2$), 4.22 (app q, 1H, H-3′, $J_{app} \approx$ 4.8 Hz), 3.98 (app q, 1H, H-4′, J = 3.8 Hz), 3.80 (t, 4H, $2CH_2$, J = 4.8 Hz), 3.79−3.70 (m, 1H, H-5′), 3.62−3.58 (m, 1H, H-5′). ^{13}C NMR (DMSO-d_6): δ 153.7, 151.8, 148.8, 146.9, 140.2, 130.5, 129.3, 128.3, 126.0, 120.5, 119.2, 87.7, 86.2, 74.2, 70.8, 66.6, 61.8, 46.0 (br s). HRMS: calcd for $C_{22}H_{24}N_8O_5Na$ $[M + Na]^+$ 503.1762, found 503.1765.

6-*N*-Benzyl-2-(4-phenyl-1,2,3-triazol-1*H*-yl)adenosine (35). Using the procedure described for **17**, this compound was synthesized from **33** (35.0 mg, 0.041 mmol) and $Et_3N{\cdot}3HF$ (34.0 μL, 0.207 mmol). Chromatography of the crude reaction mixture on a silica gel column using 10% MeOH in EtOAc yielded 16.8 mg (82% yield) of **35** as a white, foamy solid. R_f (SiO_2/30% MeOH in EtOAc) = 0.44. ^{1}H NMR (DMSO-d_6): δ 9.22 (s, 1H, Ar-H), 9.04 (br s, 1H, NH), 8.51 (s, 1H, Ar-H), 8.02 (d, 2H, Ar-H, J = 7.6 Hz), 7.50 (m, 4H, Ar-H), 7.39 (t, 1H, Ar-H, J = 7.3 Hz), 7.33 (t, 2H, Ar-H, J = 7.5 Hz), 7.23 (t, 1H, Ar-H, J = 7.3 Hz), 6.00 (d, 1H, H-1′, J = 6.0 Hz), 5.51 (d, 1H, OH, J = 5.6 Hz), 5.25 (d, 1H, OH, J = 3.9 Hz), 5.00 (t, 1H, OH, J = 5.8 Hz), 4.81−4.90 (m, 2H, CH_2), 4.69−4.62 (m, 1H, H-2′), 4.28−4.24 (m, 1H, H-3′), 4.17 (m, 1H, H-4′), 3.72−3.70 (m, 1H, H-5′), 3.62−3.58 (m, 1H, H-5′). ^{13}C NMR (DMSO-d_6): δ 155.1, 151.3, 149.8, 149.3, 146.8, 141.1, 140.0, 130.5, 129.3, 128.7, 128.1, 127.3, 126.0, 120.3, 119.4, 87.6, 86.2, 74.1, 70.9, 61.9, 43.8. HRMS: calcd for $C_{25}H_{24}N_8O_4Na$ $[M + Na]^+$ 523.1813, found 523.1822.

2-Azido-O^6-(benzotriazol-1*H*-yl)-2′,3′,5′-tri-*O*-(*tert*-butyldimethylsilyl)inosine (38). A solution of **37**[25] (50.0 mg, 0.067 mmol) in CH_2Cl_2 (3 mL) was cooled to −78 °C. To this stirred solution TMS-N_3 (0.088 mL, 0.67 mmol) was added followed by dropwise addition of *t*-BuONO (0.08 mL, 0.67 mmol). The reaction mixture was allowed to warm to rt and stirred for 9 h. To the reaction mixture were added 1:1 H_2O/MeOH (1 mL), and the stirring was continued for 1 h. The mixture was then extracted with CH_2Cl_2. After layer separation, the organic layer was removed, washed with water, dried over Na_2SO_4, and evaporated to dryness. The crude product was purified on silica gel column using 10% EtOAc/hexanes to afford 25.5 mg (49% yield) of **38** as white, foamy solid. R_f (SiO_2/30% EtOAc in hexanes) = 0.66. IR (neat): 2955, 2930, 2857, 2128, 1618, 1570 cm^{-1}. The following ^{1}H and ^{13}C NMR data list all discernible signals of the isomer mixture. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.63, 8.58, and 8.55 (3s, 1H, Ar-H), 8.13 (m, 1H, Ar-H), 7.57−7.43 (m, 3H, Ar-H), 6.16 and 6.05 (2d, 1H, H-1′, J = 4.9, 3.9 Hz, respectively), 4.58, 4.54, and 4.47 (3t, 1H, H-2′, J = 4.4, 4.2, 4.2 Hz, respectively), 4.35−4.31 (m, 1H, H-3′), 4.19−4.15 (m, 1H, H-4′), 4.08−4.02 (m, 1H, H-5′), 3.83−3.79 (m, 1H, H-5′), 0.972, 0.969, 0.96, 0.93, 0.925, 0.85, 0.84, and 0.81 (8s, 27H, *t*-Bu), 0.17, 0.16, 0.15, 0.10, 0.09, 0.02, 0.01, −0.008, −0.12, and −0.17 (10s, 18H, $SiCH_3$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.81, 159.22, 155.97, 155.60, 155.10, 154.06, 152.81, 151.63, 144.62, 144.09, 143.72, 143.64, 143.57, 129.21, 129.12, 129.03, 128.94, 128.91, 125.14, 125.06, 125.03, 120.84, 120.10, 119.22, 117.19, 108.86, 108.77, 108.72, 89.61, 89.06, 88.99, 85.70, 85.56, 85.39, 76.66, 76.61, 76.46, 71.76, 71.47, 71.42, 62.45, 62.28, 62.19, 26.33, 26.31, 26.02, 25.86, 18.78, 18.75, 18.27, 18.09, 18.07, −4.09, −4.12, −4.15, −4.45, −4.49, −4.53, −4.57, −4.59, −4.72, −5.11, −5.19, −5.23. HRMS: calcd for $C_{34}H_{57}N_{10}O_5Si_3$ $[M + H]^+$ 769.3816, found 769.3839.

Biological Assays. The cytostatic effects of the test compounds on murine leukemia cells (L1210), human T-lymphocyte cells (CEM), and human cervix carcinoma cells (HeLa) were evaluated as follows: an appropriate number of cells suspended in growth medium were allowed to proliferate in 200 μL wells of 96-well microtiter plates in the presence of variable amounts of test compounds at 37 °C in a humidified CO_2-controlled atmosphere. After 48 h (L1210), 72 h (CEM), or 96 h (HeLa), the number of cells was counted in a Coulter counter. The IC_{50} value is defined as the concentration required to inhibit cell proliferation by 50%.

The antiviral assays (except antihuman immunodeficiency virus (HIV) assays) were based on inhibition of virus-induced cytopathicity in HEL [herpes simplex virus type 1 (HSV-1), HSV-2 (G), vaccinia virus, and vesicular stomatitis virus, cytomegalovirus, and varicella-zoster virus], Vero (parainfluenza-3, reovirus-1, Coxsackie B4, and Punta Toro virus), HeLa (vesicular stomatitis virus, Coxsackie virus B4, and respiratory syncytial virus), MDCK (influenza A (H1N1; H3N2) and B virus) and CrFK (feline corona virus (FIPV) and feline herpes virus) cell cultures. Confluent cell cultures in microtiter 96-well plates were inoculated with 100 cell culture inhibitory dose-50 ($CCID_{50}$) of virus (1 $CCID_{50}$ being the virus dose to infect 50% of the cell cultures) in the presence of varying concentrations (100, 20, 4, 0.8 μg/mL) of the test compounds. Viral cytopathicity was recorded as soon as it reached completion in the control virus-infected cell cultures that were not treated with the test compounds.

The methodology of the anti-HIV assays was as follows: human CEM (~3 × 10^5 cells/mL) cells were infected with 100 $CCID_{50}$ of $HIV(III_B)$ or HIV-2(ROD)/mL and seeded in 200 μL wells of a microtiter plate containing appropriate dilutions of the test compounds. After 4 days of incubation at 37 °C, HIV-induced CEM giant cell formation was examined microscopically. The 50% effective concentration (EC_{50}) was defined as the compound concentration required to inhibit syncytia formation by 50%. The 50% cytostatic concentration (CC_{50}) was defined as the compound concentration required to inhibit CEM cell proliferation by 50% in comparison to mock-infected cell cultures.

Determination of GI_{50}s using ovarian cancer and colon carcinoma cell lines were essentially as described.[10,36−38] A 10 mM stock solution of paclitaxel (PTX), obtained from the Drug Synthesis Branch of the National Cancer Institute, was prepared in DMSO. Control samples contained 1% (v/v) DMSO vehicle, a level equivalent to that in the drug-treated cultures. Ovarian cancer cells were cultured in RPMI 1640 medium without phenol red containing 10% fetal bovine serum at 37 °C in a humidified 5% carbon dioxide incubator. 1A9/PTX10 and 1A9/PTX22 cells were maintained in the presence of 15 ng/mL of PTX and 5 μg/mL of verapamil. This medium was replaced with regular medium 2−3 days before plating the cells in 96-well plates. HCT116 and $p53KO^{-/-}$ cell lines were maintained in McCoy medium with 10% fetal bovine serum.

Cells were plated in 96-well tissue culture plates for 48 h and the compounds (prepared in 100% DMSO as a stock solution) were added in quadruplicate. At least five different concentrations were tested for each compound. In each experiment, one plate consisted entirely of cells and medium used for time zero cell number determination, at the time/day of addition of compounds. After four days, 20 μL of Promega Cell Titer reagent was added into each well and plates were incubated in the tissue culture incubator. Approximately 2 h later, the plates were read using a plate reader at 490 nm minus 630 nm absorbance wavelengths. The data was then analyzed using an Excel Spreadsheet grid. Resulting average values ranging from <50 or >50 cell culture expansion for two or more concentrations were used to calculate the GI_{50}.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra of **1a,b**, **2a,b**, and **3**−**35**, IR spectra of **2a**, **2b**, and **38**, ^{1}H NMR spectra of O^6-allyl intermediates obtained by desilylation of **3**−**16** and the deallylation product of **3**, ^{13}C NMR spectra of O^6-allyl intermediates obtained by desilylation **9** and **11**, ^{1}H NMR spectrum of product obtained by the deallylation of **3**, ^{1}H−^{1}H COSY spectra of **1b**, **3**, **11**, **19**, **29**, and **38**, and HMQC spectra of **10** and **38**. This material is available free of charge via the Internet at http://pubs.acs.org

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AUTHOR INFORMATION

Corresponding Author

*Tel: (212) 650-7835. Fax: (212) 650-6107. E-mail: lakshman@sci.ccny.cuny.edu.

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