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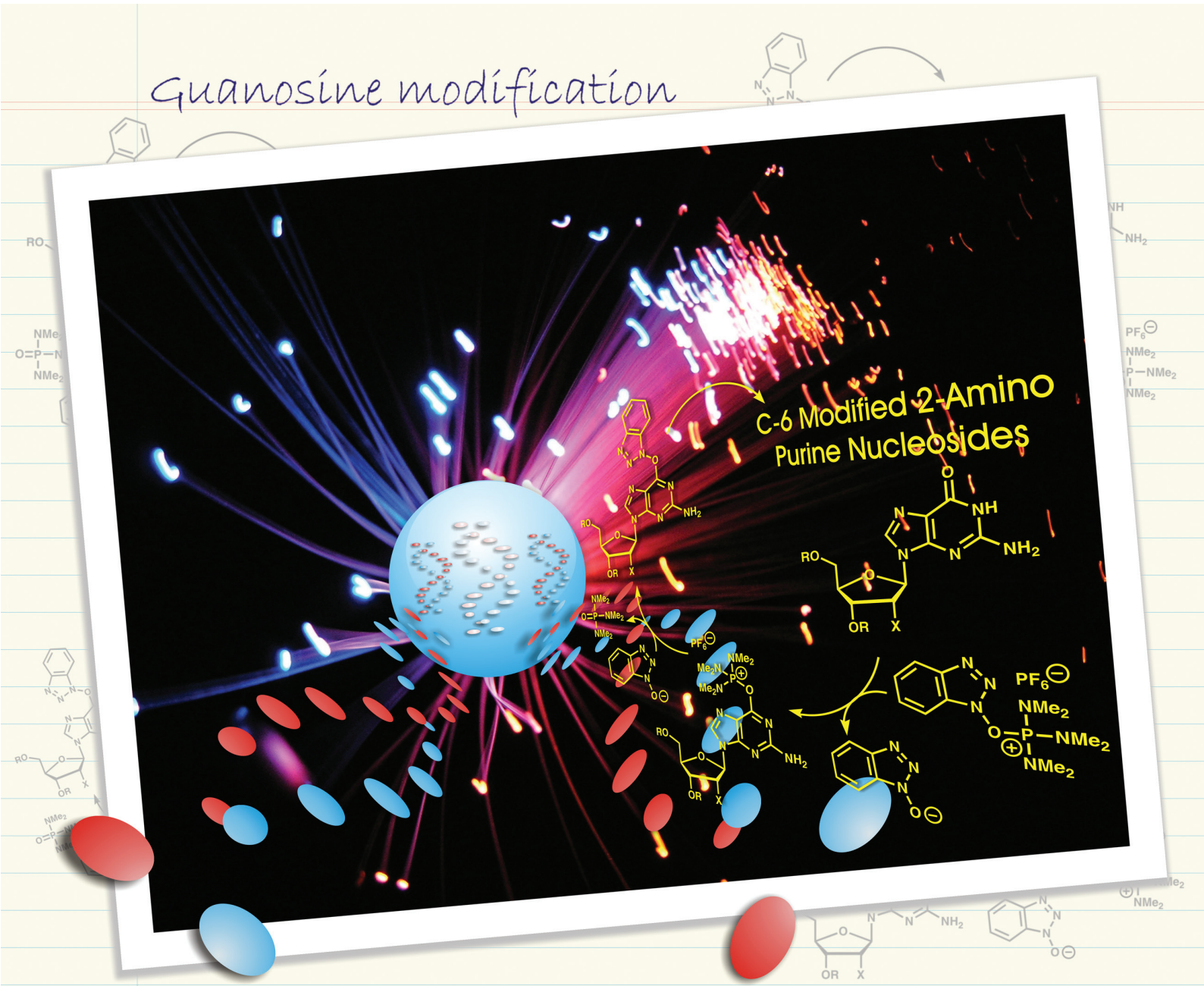

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A simple method for C-6 modification of guanine nucleosides†

Mahesh K. Lakshman* and Josh Frank

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A facile method for the introduction of various substituents at the C-6 position of guanosine and 2′-deoxyguanosine is reported. In a simple, 1-step transformation, *tert*-butyldimethylsilyl protected guanosine and 2′-deoxyguanosine were converted to the O^6-(benzotriazol-1-yl) derivatives *via* reaction with 1*H*-benzotriazol-1-yloxy-tris(dimethylamino)phosphonium hexafluorophosphate (BOP) and 1,8-diazabicyclo[5.4.0]undec-7ene (DBU). The easily isolated, stable and storable, O^6-(benzotriazol-1-yl) guanosine derivatives upon exposure to a range of nucleophiles, under appropriate conditions, led to the C-6 modified 2-amino purine nucleoside analogues in good yields.

Introduction

The development of chemical methods to modify nucleosides continues to attract attention since unnatural and unusual nucleosides play a prominent role in biochemistry, biology and medicine.[1] Typically, modification at the C-6 position of the guanine nucleus requires the introduction of a suitable leaving group at that position, followed by S_NAr displacement with nucleophiles.

Although chlorination of guanosine can be readily accomplished from its triacetate derivative,[2,3] chlorination of the 2′-deoxy analogue has been reported to be low yielding.[4] Therefore, improved methods have been reported for C-6 chlorination of 2′-deoxyguanosine 3′,5′-diacetate with careful control of reaction conditions.[5,6] In addition to C-6 chlorination of the guanine nucleosides, facile synthesis of the O^6-arylsulfonates is also known.[6–12] Thus, the 6-chloro and O^6-arylsulfonyl derivatives have served as the principal electrophilic nucleoside derivatives used in displacement reactions leading to C-6 modified 2-amino purine nucleosides.

Recently, we have developed a new class of O^6-(benzotriazol-1-yl)inosine analogues that are easily prepared *via* a reaction of either protected or unprotected inosine and 2′-deoxyinosine with 1*H*-benzotriazol-1-yloxy-tris(dimethylamino)phosphonium hexafluorophosphate (BOP).[13] The basis for this chemistry resides in the postulated formation of C-6 phosphonium salts in the reaction of the hypoxanthine moiety with PPh_3/I_2[14] or BOP.[15] We reasoned that in the absence of other nucleophiles, the hydroxybenzotriazole from BOP should react as a nucleophile on the nucleoside phosphonium salts. This was indeed the case and not only were we able to synthesize O^6-(benzotriazol-1-yl)inosine analogues, but we have been able to utilize the underlying chemistry to load inosine and 2′-deoxyinosine onto a polymer linker.[16,17] The intermediacy of nucleoside phosphonium salts has also proven important in our recently described N^2-modification of 2′-deoxyguanosine,[18] and in chemistry leading to *N*,*N*-modified adenosine analogues *via* reaction of protected inosine and 2′-deoxyinosine with hexaalkylphosphorus triamides produced *in situ* and I_2.[19] In this paper, we report our findings on the synthesis of O^6-(benzotriazol-1-yl)guanosine and 2′-deoxyguanosine, and their applications leading to C-6 modified 2-amino purine nucleoside analogues. While this work was in progress, preparation of O^6-(benzotriazol-1-yl)-3′,5′-di-*O*-(*tert*-butyldimethylsilyl)-2′-deoxyguanosine and its use for the synthesis of C-8 acetylarylamine adducts was reported.[20] However, no use of the O^6-(benzotriazol-1-yl)guanine nucleosides for other types of functionalization is currently known.

Results and discussion

In our initial work, we had shown that conversion of inosine and deoxyinosine to the O^6-(benzotriazol-1-yl) derivatives could be accomplished *via* the use of BOP and *i*-Pr_2NEt as base. Although the reactions of the hypoxanthine nucleosides proceeded to completion,[13] similar reactions of the guanine nucleosides proved to be quite slow. In fact, the literature reports reaction times of 72 h even in a solvent such as DMF.[20] Therefore, we decided to reassess this reaction at the outset.

Table 1 summarizes the results from these initial experiments. In order to avoid formation of the N^6,N^6-dimethyl-2,6-diaminopurine derivate from decomposition of DMF, we chose to conduct our first experiment in DMSO (Table 1, entry 1). In this solvent, elevated temperature and a prolonged reaction time were necessary. Upon switching to THF as solvent (entry 2), practically no reaction was observed, but when DBU was used as base a significantly fast reaction was observed (entry 3) that reached completion within 4 h. Finally, replacing THF with CH_3CN led to an improvement in reaction time and yield. In CH_3CN as solvent and with DBU as base, the reaction was complete within 2 h with a 65% isolated yield of **3** (entry 4). Under these conditions the 2′-deoxy analogue **4** could be prepared in 85% yield (the previously reported yield for **4** was 67%[20]).

Our observations on optimal solvent and base parallel those reported for the amination of 4-hydroxyquinazoline using BOP and *n*-$BuNH_2$.[21] Besides solubility considerations, one major contributor to the differences in the reactions of inosine and guanosine derivatives should be the pK_a values of the acidic

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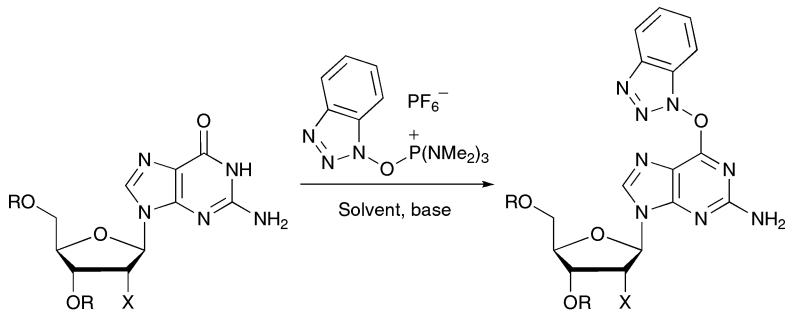
† Electronic supplementary information (ESI) available: NMR spectra of compounds **3–19** and ^1H-^1H COSY spectrum of **3**. See DOI: 10.1039/b905298d

Table 1 Initial studies at determining optimal conditions for the synthesis of O^6-(benzotriazol-1-yl)guanosine analogues **3** and **4**[a]



1: X = OTBDMS
2: X = H

3: X = OTBDMS
4: X = H

Entry	Substrate	Solvent	Base	Temperature	Time	Yield[b]
1	**1**	DMSO	*i*-Pr_2NEt	55 °C	24 h	54%
2	**1**	THF	*i*-Pr_2NEt	rt	96 h	NR[c]
3	**1**	THF	DBU	rt	4 h	45%
4	**1**	CH_3CN	DBU	rt	2 h	65%
5	**2**	CH_3CN	DBU	rt	1 h	85%

[a] Reactions were performed using 2.0 molar equiv each of BOP and DBU at ~0.1 M nucleoside concentration. [b] Where reported, yield is of isolated and purified products. [c] No reaction was observed and only **1** was present.

amide protons. Inosine is more acidic, with the amide pK_a of ~8; in guanosine it is ~9.[22,23] Nevertheless, both nucleosides can be conveniently converted to the O^6-(benzotriazol-1-yl) derivatives under the appropriate conditions.

With the synthesis of the O^6-(benzotriazol-1-yl)guanine derivatives **3** and **4** optimized, the next step was an evaluation of their use for modification at the C-6 position. For this amine, alcohol, phenol and thiol nucleophiles were selected. In addition, our prior work[13] provided a basis for this analysis and the results are shown in Table 2.

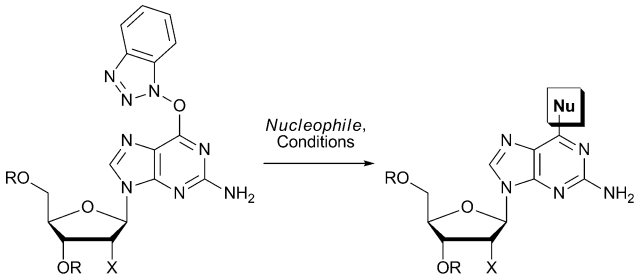
Our first examples on the S_NAr displacement involved reactions of the ribose derivative **3** and secondary amines (morpholine, diethylamine and 1-methylpiperazine) in 1,2-dimethoxyethane (DME) as solvent, without additional base. These reactions were complete at room temperature or at 55 °C, with good to high product yields (Table 2, entries 1–3). Reaction with *S*-(–)-α-methylbenzylamine also proceeded smoothly (entry 4), indicating that steric bulk proximal to the nitrogen atom does not interfere with the reaction. Displacements with alcohols (CH_3OH, CH_3CH_2OH and $CH_2{=}CHCH_2OH$) were conducted using the alcohol as solvent with Cs_2CO_3 as base, and each proceeded smoothly (entries 5–7). Reaction with benzyl mercaptan was conducted in DME with Cs_2CO_3 as base (entry 8). These results clearly demonstrated the utility of the O^6-(benzotriazol-1-yl)guanosine derivative **3** for the synthesis of C-6 modified 2-amino purine nucleosides.

With disilyl 2′-deoxyguanosine **2**, we initially explored the possibility of a 2-step, 1-pot transformation where the O^6-(benzotriazol-1-yl) derivative was generated *in situ*. Thus, **2** was exposed to BOP and DBU in CH_3CN. After disappearance of **2** (1 h), 4 molar equiv of morpholine was added. This reaction was complete within an additional 2 h and yielded the 6-morpholinyl product **13** in 91% yield. This is consistent with the reported 1-pot reaction of inosine with BOP and *i*-Pr_2NEt, followed by displacement with morpholine.[15] Similarly, we attempted a 2-step, 1-pot synthesis of the methyl ether **16** under identical conditions. However, this reaction only showed a trace of product after 52 h at room temperature. Thus it appears that the 1-pot protocol is currently only feasible with amines, although at this time we have not performed any extensive experiments on the etherification. In this context, reaction of **4** with $MeNH_2$ was performed using a 40 wt% solution in water (entry 10). The good product recovery indicates that any competing reaction with water was minimal in the presence of the amine.

Reactions with phenols (entries 14 and 15) also proceed smoothly. On the basis of these results, it becomes clear that isolation of the nucleoside O^6-(benzotriazol-1-yl) derivatives is important for fully exploiting their reactivity with a wide range of nucleophiles. The isolated compounds **3** and **4** possess excellent reactivity towards the range of nucleophiles as exemplified in Table 2.

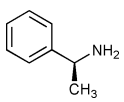
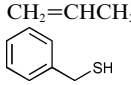
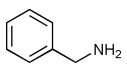
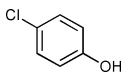
We then became interested in evaluating the mechanistic pathway involved in the formation of **3** and **4** for comparison to the reactions of inosine and 2′-deoxyinosine.[13] For this we utilized $^{31}P\{^1H\}$ NMR (Fig. 1). The resonances for BOP appear at 45.1 ppm and –143.1 ppm (PF_6^-) in CD_3CN (panel A in Fig. 1). Upon addition of **1**, no change was observed (panel B). However, two new signals at 35.7 ppm and 26.1 ppm were observed immediately upon addition of DBU (panel C). The resonance at 26.1 ppm corresponding to hexamethylphosporamide (HMPA) continued to grow (pure HMPA in CH_3CN appears at 25.6 ppm) as the one at 35.7 ppm was depleted (panel D), indicating the likely intermediacy of a nucleoside phosphonium salt (**I** in Scheme 1). Finally, this room temperature reaction appears to be complete at 120 minutes (panel E). Therefore, the plausible mechanism is one that parallels that reported previously for the hypoxanthine nucleosides,[13] involving formation of a nucleoside phosphonium salt.

Table 2 Reactions of **3** and **4** with various nucleophiles[a]



3: X = OTBDMS
4: X = H

5-12: X = OTBDMS
13-19: X = H

Entry	Substrate	Nucleophile	Conditions	Yield[b]
1	**3**		DME, 4 molar equiv morpholine, rt, 2 h	**5**: 87%
2	**3**		DME, 4 molar equiv Et_2NH, rt, 19 h	**6**: 69%
3	**3**		DME, 4 molar equiv 1-methylpiperazine, 55 °C, 3.5 h	**7**: 82%
4	**3**		DME, 4 molar equiv *S*-(−)-α-methylbenzylamine, rt, 20.5 h	**8**: 92%
5	**3**	CH_3OH	CH_3OH solvent, 2 molar equiv Cs_2CO_3, 55 °C, 2 h	**9**: 95%
6	**3**	CH_3CH_2OH	CH_3CH_2OH solvent, 2 molar equiv Cs_2CO_3, 55 °C, 2.5 h	**10**: 71%
7	**3**	$CH_2{=}CHCH_2OH$	$CH_2{=}CHCH_2OH$ solvent, 2 molar equiv Cs_2CO_3, rt, 20 h	**11**: 88%
8	**3**		DME, 2 molar equiv benzyl mercaptan, 2 molar equiv Cs_2CO_3, rt, 24 h	**12**: 89%
9	**4**		*1-Pot reaction:* CH_3CN, 2 molar equiv BOP, 2 molar equiv DBU, 4 molar equiv morpholine, rt, 3 h	**13**: 91% (94%)[d]
10	**4**		DME, 4 molar equiv Me_2NH,[c] rt, 22 h	**14**: 83% (86%)[d]
11	**4**		DME, 4 molar equiv benzyl amine, rt, 4 h	**15**: 81% (80%)[d]
12	**4**	CH_3OH	CH_3OH solvent, 2 molar equiv Cs_2CO_3, rt, 4 h	**16**: 79% (80%)[d]
13	**4**	$CH_2{=}CHCH_2OH$	$CH_2{=}CHCH_2OH$ solvent, 2 molar equiv Cs_2CO_3, rt, 7 h	**17**: 82% (71%)[d]
14	**4**		DME, 2 molar equiv phenol, 2 molar equiv Cs_2CO_3, 60 °C, 2.5 h	**18**: 89% (86%)[d]
15	**4**		DME, 2 molar equiv 4-chlorophenol, 2 molar equiv Cs_2CO_3, 60 °C, 2.5 h	**19**: 88% (90%)[d]

[a] Reaction times have not been optimized for each entry. [b] Yields of isolated and purified products. [c] A 40 wt% solution of Me_2NH in water was used. [d] Yields in parentheses are those obtained from 3′,5′-di-*O*-(*tert*-butyldimethylsilyl)-O^6-[(2,4,6-trimethylphenyl)sulfonyl]-2′-deoxyguanosine (reported in ref. 24).

It is also instructive to compare the reactions of **4** with those of 3′,5′-di-*O*-(*tert*-butyldimethylsilyl)-O^6-[(2,4,6-trimethylphenyl)-sulfonyl]-2′-deoxyguanosine (yields shown in parentheses in Table 2).[24] In this comparison **4** performs just as well as the nucleoside O^6-arylsulfonate, although synthesis and utilization of the O^6-(benzotriazol-1-yl) guanosine derivatives are generally operationally simpler.

Conclusions

In this paper we have demonstrated that silyl-protected guanosine (**1**) and 2′-deoxyguanosine (**2**) can be conveniently converted to the O^6-(benzotriazol-1-yl) derivatives **3** and **4**. Use of DBU as base in CH_3CN as solvent leads to fast conversion in good to high yield. These O^6-(benzotriazol-1-yl) derivatives are excellent reagents

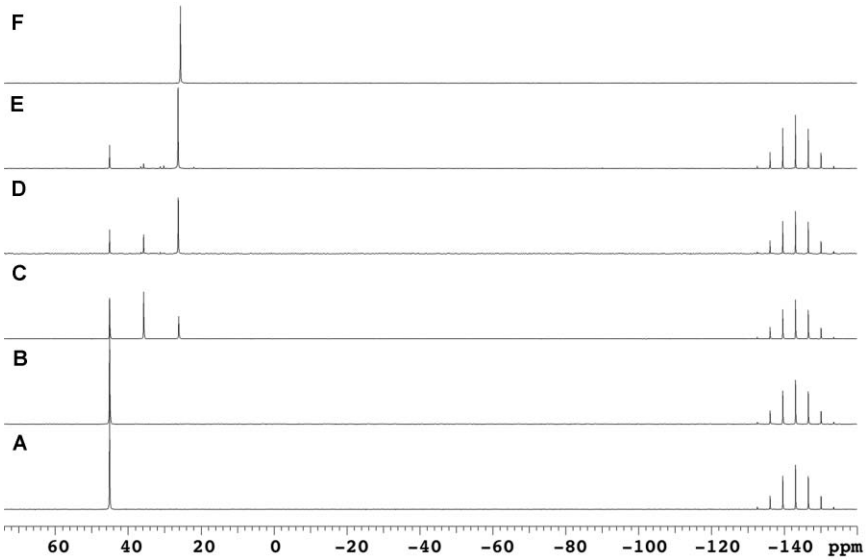
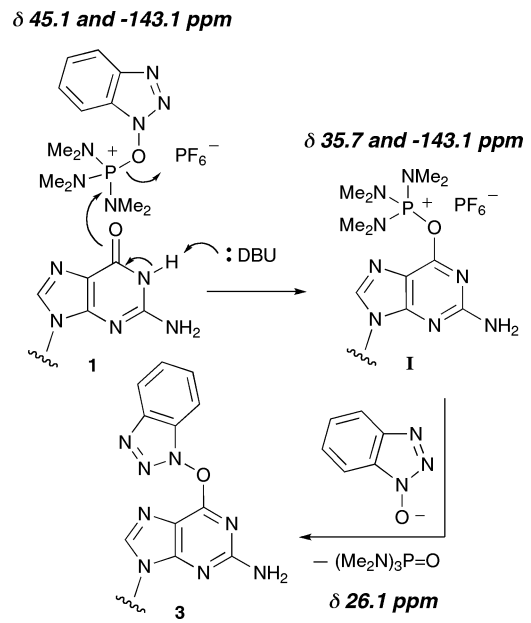


Fig. 1 Monitoring the course of the reaction between **1** and BOP at room temperature using $^{31}P\{^{1}H\}$ NMR: (A) BOP in 0.5 mL CD_3CN; (B) after addition of **1** (0.1 M in CD_3CN); (C) immediately after addition of DBU; (D) 60 minutes after addition of DBU; (E) 120 minutes after addition of DBU; (F) pure HMPA in CD_3CN.



Scheme 1 Plausible reaction pathway and chemical shifts from $^{31}P\{^{1}H\}$ NMR.

for S_NAr displacements and a variety of C-6 modified 2-amino purine nucleosides can be efficiently synthesized. It appears that amination reactions can be conducted as a 2-step, 1-pot procedure but a similar reaction with an alcohol was not successful. Extensive experimentation has not presently been conducted on a 1-pot synthesis of C-6 ethers *via* amide group activation by BOP, and work is in progress on this aspect. However, the readily isolated and stable O^6-(benzotriazol-1-yl) guanosine derivatives undergo efficient conversion to a wide variety of products using relatively simple methods.

Experimental

General experimental considerations

All reactions were carried out in oven-dried glassware. Reactions were monitored on glass-backed TLC plates coated with silica gel (250 μm), containing a fluorescent indicator. Column chromatographic purifications were performed on 200–300 mesh silica gel. CH_3CN and *i*-Pr_2NEt were distilled over CaH_2, CH_2Cl_2 was distilled over $CaCl_2$, THF was distilled over $LiAlH_4$ and then over Na. Commercially available anhydrous DMSO and DME were used without further purification. All other reagents were obtained from commercial sources and used without further purification. ^{1}H NMR spectra were recorded at 500 MHz and are referenced to residual protonated solvent. Chemical shifts are reported in parts per million (δ) and coupling constants (J) are in hertz. ^{13}C NMR spectra were obtained at 125 MHz and are referenced to the solvent resonance. The imidazolyl proton in the nucleoside is labeled H-8 and the sugar protons are numbered 1′–5′ beginning at the anomeric carbon atom and proceeding to the primary carbinol carbon atom.

General procedure for the synthesis of O^6-(benzotriazol-1-yl)-2′,3′,5′-tri-*O*-(*tert*-butyldimethylsilyl)guanosine (3) and O^6-(benzotriazol-1-yl)-3′,5′-di-*O*-(*tert*-butyldimethylsilyl)-2′-deoxyguanosine (4). In a clean, dry round-bottomed flask equipped with a stirring bar were placed the silylated nucleoside (**1** or **2**), BOP (2.0 molar equiv), and DBU (2.0 molar equiv) in dry CH_3CN (8.5 mL/mmol). The reaction mixture was flushed with nitrogen gas, stoppered and stirred at room temperature for 1 to 2 h. The reaction progress was monitored by TLC. Upon completion, the mixture was diluted with EtOAc and washed with deionized water containing a small amount of NaCl. The aqueous layer was back extracted (2×) with EtOAc. The combined organic layer was dried over Na_2SO_4, filtered and evaporated to leave a yellowish oil that

was dried under oil pump vacuum. Chromatographic purification then provided products **3** and **4**.

***O*^{6}-(Benzotriazol-1-yl)-2′,3′,5′-tri-*O*-(*tert*-butyldimethylsilyl)-guanosine (3).** Chromatography on a silica gel column using 20% EtOAc in hexanes gave a white solid (65% yield). R_f (silica, 20% EtOAc in hexanes) = 0.46; δ_H (500 MHz; $CDCl_3$) 8.23 (1H, s, H-8), 8.11 (1H, d, *J* 8.3, Ar–H), 7.54–7.48 (2H, m, Ar–H), 7.44 (1H, dt, *J* 1.5, 8.3, Ar–H), 5.95 (1H, d, *J* 4.4, H-1′), 4.75 (2H, s, NH_2), 4.47 (1H, t, *J* 4.2, H-2′), 4.30 (t, 1H, *J* 4.2, H-3′), 4.12 (1H, q, *J* 3.9, H-4′), 4.00 (1H, dd, *J* 3.4, 11.3, H-5′), 3.80 (1H, dd, *J* 3.0, 11.3, H-5′), 0.97, 0.93 and 0.84 (27H, 3 s, *tert*-Bu), 0.16, 0.15, 0.11, 0.09, 0.00 and –0.11 (18H, 6 s, $SiCH_3$); δ_C (125 MHz; $CDCl_3$) 159.6, 159.0, 156.2, 143.7, 140.2, 129.1, 128.7, 124.9, 120.6, 113.3, 109.2, 87.8, 85.9, 77.1, 72.3, 62.9, 26.4, 26.0, 25.9, 18.8, 18.3, 18.2, –4.1, –4.4, –4.6,–4.8, –5.1; HRMS (ESI) calcd for $C_{34}H_{58}N_8O_5Si_3$ $[M + H]^+$: 743.3911, found: 743.3898.

***O*^{6}-(Benzotriazol-1-yl)-3′,5′-di-*O*-(*tert*-butyldimethylsilyl)-2′-deoxyguanosine (4)[20].** Chromatography on a silica gel column using 30% EtOAc in hexanes gave a white solid (85% yield). R_f (silica, 30% EtOAc in hexanes) = 0.24; δ_H (500 MHz; $CDCl_3$) 8.12 (1H, s, H-8), 8.11 (1H, d overlapping with the singlet at 8.12, *J* 7.3, Ar–H), 7.54–7.48 (2H, m, Ar–H), 7.44 (1H, t, *J* 6.8, Ar–H), 6.35 (1H, t, *J* 6.6, H-1′), 4.76 (2H, s, NH_2), 4.60 (1H, m, H-3′), 4.00 (1H, app q, *J* 3.4, H-4′), 3.84 (1H, dd, *J* 3.9, 11.2, H-5′), 3.77 (1H, dd, *J* 2.9, 11.2, H-5′), 2.57 (1H, app quint, *J* 6.5, H-2′), 2.40 (1H, ddd, *J* 3.4, 6.3, 13.7, H-2′), 0.924 and 0.916 (18H, 2 s, *tert*-Bu), 0.108, 0.101, 0.098 (12H, 3 s, $SiCH_3$); δ_C (125 MHz; $CDCl_3$) 159.7, 158.8, 156.0, 143.6, 140.4, 129.1, 128.8, 124.9, 120.6, 113.7, 109.1, 88.1, 84.3, 72.0, 63.0, 41.4, 26.2, 26.0, 18.7, 18.3, –4.4, –4.5, –5.1, –5.2.

General procedure for the reaction of 3 with amines

In a clean, dry reaction vial equipped with a stirring bar were placed **3** (50.0 mg, 67.3 μmol), amine (4.0 molar equiv) and anhydrous DME (0.5 mL). The reaction mixture was flushed with nitrogen gas, sealed with a Teflon-lined cap and stirred either at room temperature or at 55 °C for 2–20.5 h. Progress of the reaction was monitored by TLC. Upon completion, the mixture was diluted with EtOAc and washed with deionized water containing a small amount of NaCl. The aqueous layer was back extracted (2×) with EtOAc. The combined organic layer was dried over Na_2SO_4, filtered and evaporated. Purification on a silica gel column using 20% EtOAc in hexanes then provided the C-6 amino derivatives **5–8**. Additional details and any deviations from this general procedure are noted under the individual compound headings.

2-Amino-9-[2,3,5-tri-*O*-(*tert*-butyldimethylsilyl)-β-D-ribofuranosyl]-6-(morpholin-4-yl)purine (5). Light orange solid, prepared in 87% yield using **3** (70.0 mg, 94.2 μmol) and morpholine (33 μL, 0.38 mmol) in DME (0.7 mL), in a reaction time of 2 h at room temperature. R_f (silica, 5% MeOH in CH_2Cl_2) = 0.46; δ_H (500 MHz; $CDCl_3$) 7.75 (1H, s, H-8), 5.88 (1H, d, *J* 5.4, H-1′), 4.61 (1H, t, *J* 4.7, H-2′), 4.54 (2H, s, NH_2), 4.28 (1H, t, *J* 3.9, H-3′), 4.21 (4H, br s, morpholinyl–CH_2), 4.08 (1H, app q, *J* 3.9, H-4′), 3.97 (1H, dd, *J* 4.4, 11.2, H-5′), 3.80 (4H, t, *J* 4.9, morpholinyl–CH_2), 3.76 (1H, dd, *J* 3.0, 11.2, H-5′), 0.935, 0.925 and 0.83 (27H, 3 s, *tert*-Bu), 0.11, 0.106, 0.10, 0.09, –0.03 and –0.13 (18H, 6 s, $SiCH_3$); δ_C (125 MHz; $CDCl_3$) 159.3, 154.5, 153.3, 135.3, 115.6, 88.0, 85.1, 75.6, 72.2, 67.3, 62.9, 45.7 (br), 26.4, 26.1, 26.0, 18.8, 18.4, 18.2, –4.1, –4.4, –4.5, –4.6, –5.0, –5.1; HRMS (ESI) calcd for $C_{32}H_{62}N_6O_5Si_3$ $[M + H]^+$: 695.4163, found: 695.4173.

9-[2,3,5-Tri-*O*-(*tert*-butyldimethylsilyl)-β-D-ribofuranosyl]-*N*^{6},*N*^{6}-diethyl-2,6-diaminopurine (6). Yellow solid, prepared in 69% yield using Et_2NH (28 μL, 0.27 mmol) in a reaction time of 19 h at room temperature. R_f (silica, 20% EtOAc in hexanes) = 0.47; δ_H (500 MHz; $CDCl_3$) 7.68 (1H, s, H-8), 5.85 (1H, d, *J* 5.4, H-1′), 4.68 (1H, t, *J* 4.7, H-2′), 4.48 (2H, br s, NH_2), 4.29 (1H, t, *J* 4.2, H-3′), 4.07 (1H, app q, *J* 3.9, H-4′), 3.96 (1H, dd, *J* 4.4, 11.0, H-5′), 3.90 (4H, br, NCH_2), 3.75 (1H, dd, *J* 3.4, 11.0, H-5′), 1.23 (6H, t, *J* 7.0, CH_3) 0.93, 0.92 and 0.82 (27H, 3 s, *tert*-Bu), 0.103, 0.097, 0.090, –0.03 and –0.15 (18H, 5 s, $SiCH_3$); δ_C (125 MHz; $CDCl_3$) 159.4, 154.4, 152.8, 135.2, 115.5, 88.1, 85.0, 75.0, 72.2, 62.9, 42.8 (br), 26.3, 26.1, 26.0, 18.8, 18.4, 18.2, 13.8, –4.1, –4.4, –4.5, –4.8, –5.0, –5.1; HRMS (ESI) calcd for $C_{32}H_{64}N_6O_4Si_3$ $[M + H]^+$: 681.4370, found: 681.4380.

2-Amino-9-[2,3,5-tri-*O*-(*tert*-butyldimethylsilyl)-β-D-ribofuranosyl]-6-(4-methylpiperazin-1-yl)purine (7). White solid, prepared in 82% yield using 1-methylpiperazine (30 μL, 0.27 mmol) in a reaction time of 3.5 h at 55 °C. R_f (silica, 20% EtOAc in hexanes) = 0.05; δ_H (500 MHz; $CDCl_3$) 7.74 (1H, s, H-8), 5.86 (1H, d, *J* 5.4, H-1′), 4.61 (1H, t, *J* 4.7, H-2′), 4.51 (2H, s, NH_2), 4.29 (1H, t, *J* 4.2, H-3′), 4.24 (4H, br s, piperazinyl–CH_2), 4.08 (1H, app q, *J* 3.9, H-4′), 3.99 (1H, dd, *J* 4.4, 11.2, H-5′), 3.78 (1H, dd, *J* 3.0, 11.2, H-5′), 2.51 (4H, br s, piperazinyl–CH_2), 2.34 (3H, s, CH_3), 0.93, 0.925 and 0.83 (27H, 3 s, *tert*-Bu), 0.103, 0.096, 0.087, –0.03 and –0.13 (18H, 5 s, $SiCH_3$); δ_C (125 MHz; $CDCl_3$) 159.3, 154.5, 153.3, 135.2, 115.7, 88.1, 85.1, 75.4, 72.2, 62.9, 55.4, 46.5, 45.0 (br), 26.4, 26.1, 26.0, 18.8, 18.4, 18.2, –4.1, –4.4, –4.5, –4.6, –5.0, –5.1; HRMS (ESI) calcd for $C_{33}H_{65}N_7O_4Si_3$ $[M + H]^+$: 708.4479, found: 708.4486.

9-[2,3,5-Tri-*O*-(*tert*-butyldimethylsilyl)-β-D-ribofuranosyl]-*N*^{6}-[(1*S*)-phenylethyl]-2,6-diaminopurine (8). Light yellow solid, prepared in 92% yield using (*S*)-(–)-α-methylbenzylamine (35 μL, 0.27 mmol) in a reaction time of 20.5 h at room temperature. R_f (silica, 20% EtOAc in hexanes) = 0.13; δ_H (500 MHz; $CDCl_3$) 7.85 (1H, s, H-8), 7.42 (2H, d, *J* 7.3, Ar–H), 7.31 (2H, t, *J* 7.3, Ar–H), 7.22 (1H, t, *J* 7.3, Ar–H), 6.53 (1H, br s, NH), 5.84 (1H, d, *J* 4.4, H-1′), 5.50 (1H, br s, NCH), 4.71 (2H, br s, NH_2), 4.53 (1H, t, *J* 4.4, H-2′), 4.28 (1H, t, *J* 3.9, H-3′), 4.07 (1H, app q, *J* 3.9, H-4′), 3.99 (1H, dd, *J* 4.4, 11.5, H-5′), 3.78 (1H, dd, *J* 3.0, 11.5, H-5′), 1.60 (3H, d, *J* 6.8, CH_3), 0.94, 0.92 and 0.83 (27H, 3 s, *tert*-Bu), 0.119, 0.114, 0.090, 0.00 and –0.11 (18H, 5 s, $SiCH_3$); proton assignments were made by ^1H-^1H COSY of this compound at 60 °C, where the NH sharpened to a br d (5.97 ppm, *J* 7.8), the NCH became a sharper br m (5.56 ppm) and the CH_3 d sharpened (1.61 ppm, *J* 7.3); δ_C (125 MHz; $CDCl_3$) 160.0, 154.5, 144.5, 136.4, 128.7, 127.2, 126.5, 115.0, 88.4, 84.9, 75.7, 71.8, 62.6, 26.4, 26.1, 26.0, 22.9, 18.8, 18.4, 18.2, –4.1, –4.4, –4.5, –4.6, –5.1; HRMS (ESI) calcd for $C_{36}H_{64}N_6O_4Si_3$ $[M + H]^+$: 729.4370, found: 729.4374.

General procedure for the reaction of 3 with alcohols

In a clean, dry reaction vial equipped with a stirring bar were placed **3** and Cs_2CO_3 (2.0 molar equiv) in the appropriate alcohol as solvent. The reaction mixture was flushed with nitrogen gas,

sealed with a Teflon-lined cap and stirred at 55 °C for 2–20 h. Progress of the reaction was monitored by TLC. Upon completion, the mixture was diluted with EtOAc and washed with deionized water containing a small amount of NaCl. The aqueous layer was back extracted (2×) with EtOAc. The combined organic layer was dried over Na_2SO_4, filtered and evaporated. Purification on a silica gel column using 20% EtOAc in hexanes then provided the guanosine O^6-alkyl ethers **9–11**. Additional details are listed under the specific compound headings.

2′,3′,5′-Tri-*O*-(*tert*-butyldimethylsilyl)-O^6-methylguanosine (9). Light orange solid, prepared in 95% yield using **3** (45.3 mg, 61.0 μmol) and Cs_2CO_3 (42.9 mg, 0.131 mmol) in MeOH (0.45 mL), in a reaction time of 2 h at 55 °C. R_f (silica, 20% EtOAc in hexanes) = 0.11; δ_H (500 MHz; $CDCl_3$) 7.98 (1H, s, H-8), 5.90 (1H, d, *J* 4.9, H-1′), 4.79 (2H, s, NH_2), 4.50 (1H, t, *J* 4.4, H-2′), 4.28 (1H, t, *J* 4.2, H-3′), 4.08 (1H, app q, *J* 3.0, H-4′), 4.05 (3H, s, OCH_3), 3.97 (1H, dd, *J* 3.9, 11.2, H-5′), 3.77 (1H, dd, *J* 2.4, 11.2, H-5′), 0.94, 0.92 and 0.82 (27H, 3 s, *tert*-Bu), 0.12, 0.11, 0.09, 0.08, –0.04 and –0.16 (18H, 6 s, $SiCH_3$); δ_C (125 MHz; $CDCl_3$) 161.7, 159.5, 153.8, 138.2, 116.2, 88.0, 85.4, 76.4, 72.1, 62.8, 54.0, 26.4, 26.1, 26.0, 18.8, 18.4, 18.2, 14.8, –4.1, –4.4, –4.5, –4.7, –5.1; HRMS (ESI) calcd for $C_{29}H_{57}N_5O_5Si_3$ $[M + H]^+$: 640.3741, found: 640.3745.

2′,3′,5′-Tri-*O*-(*tert*-butyldimethylsilyl)-O^6-ethylguanosine (10). White solid, prepared in 71% yield using **3** (50.0 mg, 67.3 μmol) and Cs_2CO_3 (43.8 mg, 0.134 mmol) in EtOH (0.45 mL), in a reaction time of 2.5 h at 55 °C. R_f (silica, 20% EtOAc in hexanes) = 0.20; δ_H (500 MHz; $CDCl_3$) 7.98 (1H, s, H-8), 5.91 (1H, d, *J* 4.9, H-1′), 4.76 (2H, br s, NH_2), 4.55 (2H, q, *J* 7.0, OCH_2), 4.52 (1H, t, *J* 4.4, H-2′), 4.29 (1H, t, *J* 4.3, H-3′), 4.09 (1H, app q, *J* 2.9, H-4′), 3.99 (1H, dd, *J* 3.4, 11.5, H-5′), 3.76 (1H, dd, *J* 3.0, 11.5, H-5′), 1.45 (3H, t, *J* 7.0, CH_3), 0.95, 0.93 and 0.83 (27H, 3 s, *tert*-Bu), 0.13, 0.12, 0.095, 0.09, –0.03 and –0.15 (18H, 6 s, $SiCH_3$); δ_C (125 MHz; $CDCl_3$) 161.5, 159.5, 153.9, 138.0, 116.1, 88.0, 85.4, 76.3, 72.2, 62.8, 26.4, 26.1, 26.0, 18.8, 18.4, 18.2, 14.8, –4.1, –4.4, –4.5, –4.7, –5.1; HRMS (ESI) calcd for $C_{30}H_{59}N_{65}O_5Si_3$ $[M + H]^+$: 654.3897, found: 654.3890.

O^6-Allyl-2′,3′,5′-tri-*O*-(*tert*-butyldimethylsilyl)guanosine (11). Orange solid, prepared in 88% yield using **3** (70.0 mg, 94.2 μmol) and Cs_2CO_3 (61.4 mg, 0.188 mmol) in allyl alcohol (0.7 mL), in a reaction time of 20 h at room temperature. R_f (silica, 20% EtOAc in hexanes) = 0.31; δ_H (500 MHz; $CDCl_3$) 8.00 (1H, s, H-8), 6.15 (1H, m, =CH), 5.93 (1H, d, *J* 4.6, H-1′), 5.45 (1H, dd, *J* 1.5, 18.6, $=CH_{trans}$), 5.29 (1H, dd, *J* 1.5, 11.7, $=CH_{cis}$), 5.02 (2H, d, *J* 5.9, OCH_2), 4.79 (2H, s, NH_2), 4.54 (1H, t, *J* 4.7, H-2′), 4.31 (1H, t, *J* 3.4, H-3′), 4.11 (1H, app q, *J* 3.9, H-4′), 4.01 (1H, dd, *J* 3.9, 11.2, H-5′), 3.80 (1H, dd, *J* 2.4, 11.2, H-5′), 0.97, 0.95 and 0.85 (27H, 3 s, *tert*-Bu), 0.15, 0.14, 0.12, 0.11, 0.00 and –0.13 (18H, 6 s, $SiCH_3$); δ_C (125 MHz; $CDCl_3$) 161.0, 159.4, 154.1, 138.1, 133.1, 118.4, 116.0, 87.9, 85.4, 76.4, 72.2, 67.4, 62.8, 26.4, 26.1, 26.0, 18.8, 18.4, 18.2, –4.1, –4.4, –4.5, –4.7, –5.11, –5.14; HRMS (ESI) calcd for $C_{31}H_{59}N_5O_5Si_3$ $[M + H]^+$: 666.3897, found: 666.3912.

S^6-Benzyl-2′,3′,5′-tri-*O*-(*tert*-butyldimethylsilyl)thioguanosine (12). In a clean, dry reaction vial equipped with a stirring bar were placed **3** (50.0 mg, 67.0 μmol), Cs_2CO_3 (43.8 mg, 0.134 mmol) and dry DME (0.5 mL). Benzyl mercaptan (16.0 μL, 0.134 mmol) was added, the reaction mixture was flushed with nitrogen gas, sealed with a Teflon-lined cap and allowed to stir at room temperature for 24 h. The mixture was diluted with EtOAc and washed with deionized water containing a small amount of NaCl. The aqueous layer was back extracted (2×) with EtOAc. The combined organic layer was dried over Na_2SO_4, filtered and evaporated. Purification on a silica gel column using 20% EtOAc in hexanes then provided **12** as a light yellow solid (89% yield). R_f (silica, 10% EtOAc in hexanes) = 0.47; δ_H (500 MHz; $CDCl_3$) 7.98 (1H, s, H-8), 7.43 (2H, d, *J* 7.3, Ar–H), 7.31–7.21 (3H, m, Ar–H), 5.90 (1H d, *J* 4.9, H-1′), 4.81 (s, 2H, NH_2), 4.57 (2H, AB_{quart}, *J* 13.7, SCH_2), 4.54 (1H, t, *J* 4.4, H-2′), 4.29 (t, 1H, *J* 4.2, H-3′), 4.10 (1H, app q, *J* 2.9, H-4′), 3.97 (1H, dd, *J* 3.9, 11.2, H-5′), 3.77 (1H, dd, *J* 2.9, 11.2, H-5′), 0.93, 0.927 and 0.83 (27H, 3 s, *tert*-Bu), 0.12, 0.11, 0.010, 0.09, –0.02, –0.16 (18H, 5 s, $SiCH_3$); δ_C (125 MHz; $CDCl_3$) 161.1, 159.0, 150.8, 139.0, 138.1, 129.3, 128.7, 127.4, 126.2, 88.1, 85.3, 76.1, 72.1, 62.7, 32.9, 26.4, 26.1, 26.0, 18.8, 18.4, 18.2, –4.1, –4.4, –4.5, –4.7, –5.0, –5.1; HRMS (ESI) calcd for $C_{35}H_{61}N_5O_4Si_3$ $[M + H]^+$: 732.3825, found: 732.3831.

9-[3,5-Di-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-β-D-ribofuranosyl]-6-(morpholin-4-yl)purine (13)[24].

One-pot procedure. In a clean, dry, round-bottomed flask equipped with a stirring bar were placed **2** (70.0 mg, 0.141 mmol) and BOP (0.125 g, 0.283 mmol) in anhydrous CH_3CN (1.2 mL). DBU (47.3 μL, 0.316 mmol) was added to the stirring mixture, the flask was flushed with nitrogen gas and stoppered. After being stirred at room temperature for 1 h TLC showed consumption of **2**. At this time morpholine (49.7 μl, 0.568 mmol) was added. The flask was again flushed with nitrogen gas, stoppered and the mixture was allowed to stir at room temperature for an additional 2 h at which time the reaction was complete as assessed by TLC. The mixture was diluted with EtOAc and washed with deionized water containing a small amount of NaCl. The aqueous layer was back extracted (2×) with EtOAc. The combined organic layer was dried over Na_2SO_4, filtered and evaporated to leave a yellowish oil. Purification on a silica gel column using 30% EtOAc in hexanes then provided **13** as a yellow solid (91% yield). R_f (silica, 30% EtOAc in hexanes) = 0.11; δ_H (500 MHz; $CDCl_3$) 7.72 (1H, s, H-8), 6.31 (1H, t, *J* 6.8, H-1′), 4.60 (2H, s, NH_2), 4.57 (1H, m, H-3′), 4.21 (4H, br s, morpholinyl–CH_2), 3.96 (1H, app q, *J* 4.1, H-4′), 3.79 (4H, t, *J* 4.4, morpholinyl–CH_2), 3.76 (1H, dd, *J* 4.6, 11.1, H-5′), 3.75 (1H, dd, *J* 3.6, 11.1, H-5′), 2.55 (1H, app quint, *J* 6.8, H-2′), 2.33 (1H, ddd, *J* 3.4, 6.0, 13.0, H-2′), 0.91 and 0.90 (18H, 2 s, *tert*-Bu), 0.10, 0.07 and 0.06 (12H, 3 s, $SiCH_3$); δ_C (125 MHz; $CDCl_3$) 159.4, 154.4, 153.1, 134.6, 115.4, 87.8, 83.6, 72.4, 67.3, 63.2, 45.7 (br), 40.9, 26.2, 26.0, 18.7, 18.3, –4.4, –4.5, –5.1, –5.2.

General procedure for the reaction of 4 with amines

In a clean, dry reaction vial equipped with a stirring bar were placed **4** (50.0 mg, 81.6 μmol), amine (4.0 molar equiv) and anhydrous DME (0.5 mL). The reaction mixture was flushed with nitrogen gas, sealed with a Teflon-lined cap and stirred at room temperature for 4–22 h (see details under specific compound headings). Progress of the reaction was monitored by TLC. Upon completion, the mixture was diluted with EtOAc and washed with deionized water containing a small amount of NaCl. The aqueous layer was back extracted (2×) with EtOAc. The combined organic layer was dried over Na_2SO_4, filtered and evaporated. Purification on a silica gel column using 30% EtOAc in hexanes then provided

the C-6 amino derivatives **14** and **15**. Additional details and any deviations from this general procedure are noted under the individual compound headings.

9-[3,5-Di-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-β-D-ribofuranosyl]-N^6,N^6-dimethyl-2,6-diaminopurine (14)[24]. Light yellow solid, prepared in 83% yield using a 40 wt% solution of Me_2NH in water (37.3 μL, 0.331 mmol) in a reaction time of 2 h. R_f (silica, 5% MeOH in CH_2Cl_2) = 0.43; δ_H (500 MHz; $CDCl_3$) 7.69 (1H, s, H-8), 6.30 (1H, t, *J* 6.1, H-1′), 4.67 (2H, s, NH_2), 4.56 (1H, m, H-3′), 3.95 (1H, app q, *J* 4.0, H-4′), 3.78–3.71 (2H, m, H-5′), 3.43 (6H, br s, NCH_3), 2.54 (1H, app quint, *J* 6.6, H-2′), 2.32 (1H, ddd, *J* 3.4, 6.0, 13.1, H-2′), 0.90 and 0.896 (18H, 2 s, *tert*-Bu), 0.09, 0.06 and 0.05 (12H, 3 s, $SiCH_3$); δ_C (125 MHz; $CDCl_3$) 159.4, 155.5, 152.7, 134.2, 115.7, 87.8, 83.5, 72.4, 63.2, 40.8, 38.5 (br), 26.2, 26.0, 18.7, 18.3, –4.4, –4.5, –5.1, –5.2.

N^6-Benzyl-9-[3,5-di-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-β-D-ribofuranosyl]purine (15)[24]. Light yellow solid, prepared in 81% yield using benzylamine (35.6 μL, 0.33 mmol) in a reaction time of 4 h. R_f (silica, 30% EtOAc in hexanes) = 0.08; δ_H (500 MHz; $CDCl_3$) 7.76 (1H, s, H-8), 7.37–7.27 (5H, m, Ar–H), 6.30 (1H, t, *J* 6.8, H-1′), 5.89 (1H, br s, NH), 4.79 (2H, s, NH_2), 4.71 (2H, br s, NCH_2), 4.58 (1H, m, H-3′), 3.97 (1H, app q, *J* 3.4, H-4′), 3.81 (1H, dd, *J* 4.4, 11.0, H-5′), 3.75 (1H, dd, *J* 2.9, 11.0, H-5′), 2.59 (1H, app quint, *J* 6.8, H-2′), 2.34 (1H, ddd, *J* 3.7, 6.0, 13.0, H-2′), 0.90 and 0.896 (18H, 2 s, *tert*-Bu), 0.10, 0.08 and 0.07 (12H, 3 s, $SiCH_3$); δ_C (125 MHz; $CDCl_3$) 160.0, 155.2, 139.0, 136.0, 128.8, 128.0, 127.6, 115.1, 87.9, 83.8, 72.3, 63.1, 44.7 (br), 41.0, 26.2, 26.0, 18.7, 18.3, –4.4, –4.5, –5.10, –5.2.

General procedure for the reaction of 4 with alcohols

In a clean, dry reaction vial equipped with a stirring bar were placed **4** (50.0 mg, 81.6 μmol) and Cs_2CO_3 (53.1 mg, 0.163 mmol) in the appropriate alcohol as solvent (0.5 mL). The reaction mixture was flushed with nitrogen gas, sealed with a Teflon-lined cap and stirred for 4–7 hours at room temperature. Progress of the reaction was monitored by TLC. Upon completion, the mixture was diluted with EtOAc and washed with deionized water containing a small amount of NaCl. The aqueous layer was back extracted (2×) with EtOAc. The combined organic layer was dried over Na_2SO_4, filtered and evaporated. Purification on a silica gel column using 30% EtOAc in hexanes then provided the 2′-deoxyguanosine O^6-alkyl ethers **16** and **17**. Additional details are listed under the specific compound headings.

3′,5′-Di-*O*-(*tert*-butyldimethylsilyl)-O^6-methyl-2′-deoxyguanosine (16)[24]. Light yellow solid, prepared in 79% yield using MeOH, in a reaction time of 4 h. R_f (silica, 5% MeOH in CH_2Cl_2) = 0.41; δ_H (500 MHz; $CDCl_3$) 7.91 (1H, s, H-8), 6.32 (1H, t, *J* 6.4, H-1′), 4.83 (2H, s, NH_2), 4.59 (1H, m, H-3′), 4.08 (3H, s, OCH_3), 3.97 (1H, app q, *J* 3.9, H-4′), 3.81 (1H, dd, *J* 4.4, 11.2, H-5′), 3.75 (1H, dd, *J* 3.4, 11.2, H-5′), 2.57 (1H, app quint, *J* 6.3, H-2′), 2.34 (1H, ddd, *J* 3.8, 6.1, 13.0, H-2′), 0.912 and 0.910 (18H, 2 s, *tert*-Bu), 0.10, 0.08 and 0.07 (12H, 3 s, $SiCH_3$); δ_C (125 MHz; $CDCl_3$) 161.8, 159.5, 153.7, 137.8, 116.2, 87.9, 83.9, 72.1, 63.1, 54.1, 41.2, 26.2, 26.0, 18.7, 18.3, –4.4, –4.5, –5.1, –5.2.

O^6-Allyl-3′,5′-di-*O*-(*tert*-butyldimethylsilyl)-2′-deoxyguanosine (17)[24]. Light yellow solid, prepared in 82% yield using allyl alcohol, in a reaction time of 7 h. R_f (silica, 5% MeOH in CH_2Cl_2) = 0.59; δ_H (500 MHz; $CDCl_3$) 7.90 (1H, s, H-8), 6.32 (1H, t, *J* 6.8, H-1′), 6.12 (1H, m, =CH), 5.42 (1H, dd, *J* 1.5, 18.5, $=CH_{trans}$), 5.26 (1H, dd, *J* 1.5, 11.7, $=CH_{cis}$), 5.01 (2H, d, *J* 5.4, OCH_2), 4.81 (2H, s, NH_2), 4.59 (1H, m, H-3′), 3.97 (1H, app q, *J* 3.3, H-4′), 3.81 (1H, dd, *J* 4.4, 11.1, H-5′), 3.75 (1H, dd, *J* 2.9, 11.1, H-5′), 2.57 (1H, app quint, *J* 6.0, H-2′), 2.35 (1H, ddd, *J* 3.7, 6.1, 13.1, H-2′), 0.913 and 0.910 (18H, 2 s, *tert*-Bu), 0.10, 0.08 and 0.07 (12H, 3 s, $SiCH_3$); δ_C (125 MHz; $CDCl_3$) 161.1, 159.4, 154.0, 137.8, 133.0, 118.4, 116.2, 87.9, 83.9, 72.2, 67.5, 63.1, 41.2, 26.2, 26.0, 18.7, 18.3, –4.4, –4.5, –5.1, –5.2.

General procedure for the reaction of 4 with phenols

In a clean, dry reaction vial equipped with a stirring bar were placed **4** (50.0 mg, 81.6 μmol), the appropriate phenol (2 molar equiv) and Cs_2CO_3 (53.1 mg, 0.163 mmol) in anhydrous DME (0.5 mL). The reaction mixture was flushed with nitrogen gas, sealed with a Teflon-lined cap and stirred at 60 °C for 2–2.5 hours. Progress of the reaction was monitored by TLC. Upon completion, the mixture was diluted with EtOAc and washed with deionized water containing a small amount of NaCl. The aqueous layer was back extracted (2×) with EtOAc. The combined organic layer was dried over Na_2SO_4, filtered and evaporated. Purification on a silica gel column using 30% EtOAc in hexanes then provided the 2′-deoxyguanosine O^6-aryl ethers **18** and **19**.

3′,5′-Di-*O*-(*tert*-butyldimethylsilyl)-O^6-phenyl-2′-deoxyguanosine (18)[24]. Yellowish solid, prepared in 89% yield using phenol (15.3 mg, 0.163 mmol), in a reaction time of 2.5 h. R_f (silica, 5% MeOH in CH_2Cl_2) = 0.26; δ_H (500 MHz; $CDCl_3$) 8.01 (1H, s, H-8), 7.40 (2H, t, *J* 7.8, Ar–H), 7.25–7.23 (3H, m, Ar–H), 6.34 (1H, t, *J* 6.4, H-1′), 4.82 (2H, s, NH_2), 4.60 (1H, m, H-3′), 3.99 (1H, app q, *J* 3.4, H-4′), 3.83 (1H, dd, *J* 3.9, 11.2, H-5′), 3.77 (1H, dd, *J* 2.9, 11.2, H-5′), 2.58 (1H, app quint, *J* 6.8, H-2′), 2.37 (1H, ddd, *J* 3.9, 6.4, 13.1, H-2′), 0.92 and 0.91 (18H, 2 s, *tert*-Bu), 0.10 and 0.09 (12H, 2 s, $SiCH_3$); δ_C (125 MHz; $CDCl_3$) 160.7, 159.4, 154.7, 152.8, 138.7, 129.5, 125.5, 122.2, 116.2, 88.0, 84.0, 72.1, 63.1, 41.3, 26.3, 26.0, 18.7, 18.3, –4.4, –4.5, –5.1, –5.2.

3′,5′-Di-*O*-(*tert*-butyldimethylsilyl)-O^6-(4-chlorophenyl)-2′-deoxyguanosine (19)[24]. Yellow solid, prepared in 88% yield using 4-chlorophenol (21.0 mg, 0.163 mmol), in a reaction time of 2 h. R_f (silica, 5% MeOH in CH_2Cl_2) = 0.28; δ_H (500 MHz; $CDCl_3$) 8.02 (1H, s, H-8), 7.36 (2H, *J* 8.8, Ar–H), 7.19 (2H, d, *J* 8.8, Ar–H), 6.34 (1H, t, *J* 6.4, H-1′), 4.79 (2H, s, NH_2), 4.61 (1H, m, H-3′), 3.99 (1H, app q, *J* 3.9, H-4′), 3.84 (1H, dd, *J* 4.4, 11.2, H-5′), 3.77 (1H, dd, *J* 2.9, 11.2, H-5′), 2.58 (1H, app quint, *J* 6.8, H-2′), 2.38 (1H, ddd, *J* 3.9, 5.9, 13.2, H-2′), 0.923 and 0.920 (18H, 2 s, *tert*-Bu), 0.11 and 0.10 (12H, 2 s, $SiCH_3$); δ_C (125 MHz; $CDCl_3$) 160.3, 159.3, 154.9, 151.3, 138.9, 130.8, 129.6, 123.6, 116.1, 88.0, 84.0, 72.1, 63.0, 41.3, 26.2, 26.0, 18.7, 18.3, –4.4, –4.5, –5.1, –5.2.

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