Pergamon

Tetrahedron 54 (1998) 6605–6626

TETRAHEDRON

Syntheses of Novel Hydroxylamine Carbanucleosides

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Received 5 March 1998; accepted 15 April 1998

Abstract: Enantiomerically pure 4'-hydroxylamino-adenine-derived carbanucleosides have been synthesized as isosteric 4'-hydroxymethyl analogs to carbovir, ddA, and aristeromycin. The key steps in the syntheses involved an enzymatic desymmetrization, two subsequent Mitsunobu reactions, and a highly diastereoselective ruthenium tetroxide-mediated dihydroxylation, overcoming the *syn*-directing effect seen in osmium tetroxide-mediated dihydroxylations. Hydroxylamino-propane analogs were also synthesized through similar methodology to afford adenine and cyclopropylamino purine analogs to acyclovir.

Carbanucleosides have become an important class of compounds due to their ability to serve as more metabolically stable structural analogs of natural, as well as unnatural, antiviral, antifungal, and antibacterial nucleosides.[1,2] Nucleosides are a diverse class of biologically important compounds including such examples as nikkomycin Z (**1**), carbovir (**2**), 2',3'-dideoxyadenosine (ddA) (**3**), acyclovir (**4**), aristeromycin (**5**), and noraristeromycin (**6**) (Figure 1).[3-8] Within this broad class, variation of the 4'-substituent markedly affects biological activity. For instance, nikkomycin Z (**1**), an antifungal agent, contains a peptide side chain and serves as an inhibitor of chitin synthesis in fungal cell walls.[9] Nucleosides such as carbovir (**2**), ddA (**3**), and acyclovir (**4**) contain a hydroxymethyl side chain and serve as antiviral agents, acting as inhibitors of viral reverse transcriptase.[10] Aristeromycin (**5**) is a naturally occurring carbocyclic nucleoside possessing antiviral activity, but clinical use is prohibited due to its cytotoxicity. Noraristeromycin (**6**), a structural analog of aristeromycin, contains a 4'-hydroxyl instead of a 4'-hydroxymethyl substituent and shows improved antiviral activity with less cytotoxicity than aristeromycin.[11,12]

Most effective antiviral agents act as prodrug phosphorylated metabolites. The 5'-hydroxyl is recognized and phosphorylated by viral phosphorylases, thereby, transforming the nucleoside into its respective nucleotide. The nucleotide can then be incorporated into the growing viral nucleic acid strand, and therefore, disrupt the reverse transcription process.[13] Consequently, in the search for more effective nucleoside analogs, modification of the 5'-hydroxyl moiety usually has been avoided and instead, the furanose ring, purine or pyrimidine bases, and/or the 2' and 3'-positions have been the most common sites of modification.[1,2]

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0040-4020/98/$19.00
PII: S0040-4020(98)00359-7

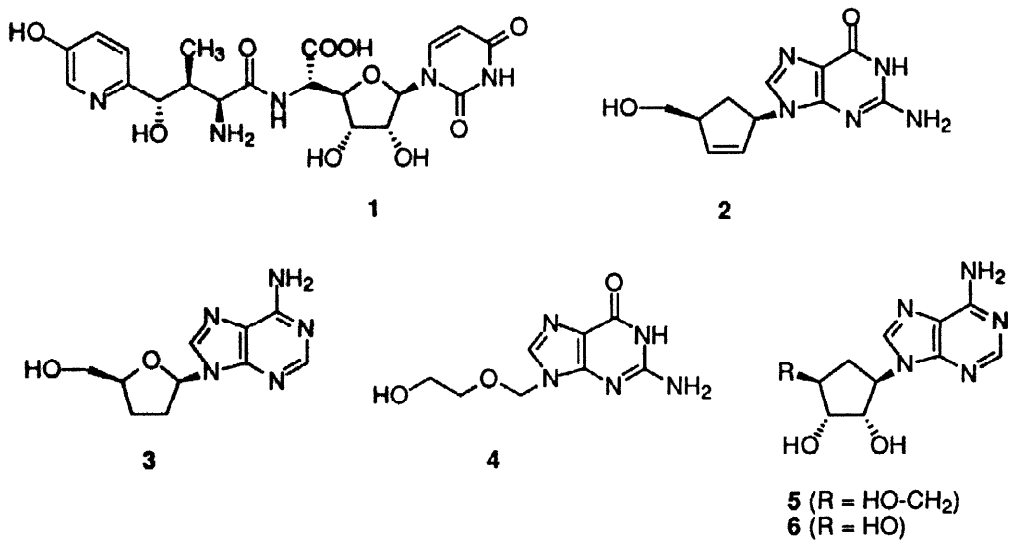


Figure 1: Natural and unnatural nucleoside analogs

Recognizing the need for a better understanding of the structure-activity relationships amongst nucleosides, we postulated that a hydroxylamine (HO-NH-) moiety at the 4'-position could serve as an isostere to hydroxymethyl (HO-CH_2-). Substitution of a hydroxylamine moiety for the natural hydroxymethyl group could be of interest for several reasons: 1) the N-O bond in hydroxylamine is weaker than the hydroxymethyl C-O bond and may, therefore, allow for subsequent chemistry after phosphorylation; 2) unlike other nucleoside analogs which contain charged species at the 4'-position (in some cases limiting cell membrane permeability), the hydroxylamine carbanucleosides would be essentially neutral at physiological pH (*N*-methylhydroxylammonium has pKa = 5.96);[14] and 3) structurally, the hydroxylamine-based nucleosides contain a 5-hydroxyl which is the appropriate functionality needed for recognition by viral kinases. We hereby disclose the synthesis of eight novel enantiomerically pure hydroxylamine carbanucleosides **7**, **9-14** serving as adenine and cyclopropylamino purine analogs to carbovir (**2**), ddA (**3**), acyclovir (**4**), and aristeromycin (**5**) (Figure 2). Also, novel acetylated hydroxamic acid analog **8** was synthesized in order to provide an analog with iron (III) chelating functionality, which might facilitate microbial uptake.[15,16] The hydroxamic acid functionality would also provide a slightly lower hydroxyl pKa (pKa = 9.5), as well as a non-nucleophilic nitrogen at the 4'-position.[17]

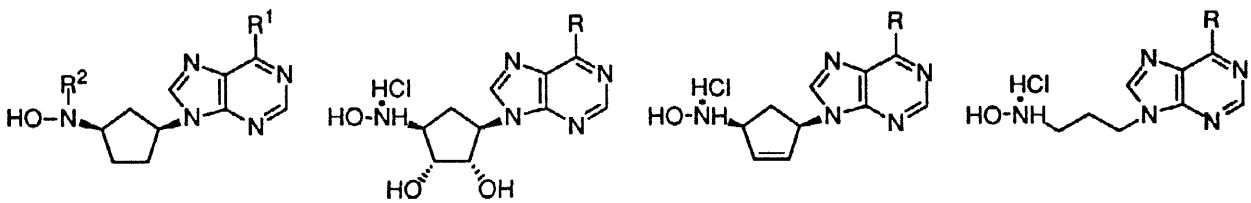
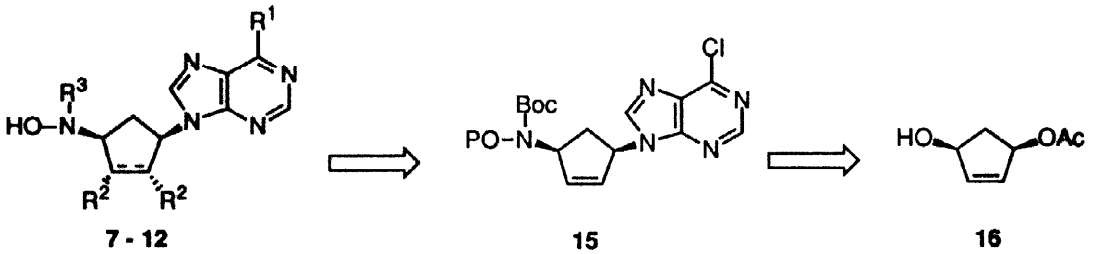


Figure 2: Novel hydroxylamine carbocyclic nucleoside analogs.

Retrosynthetically, target molecules **7-12** could be generated from one common advanced intermediate **15** (Scheme 1). Protected analog **15** was envisioned to be derived from subsequent Pd(0) or Mitsunobu additions of adenine and a suitably protected hydroxylamine to (+)-*cis*-4-hydroxy-2-cyclopentenylacetate **16**.[18-20]



Scheme 1

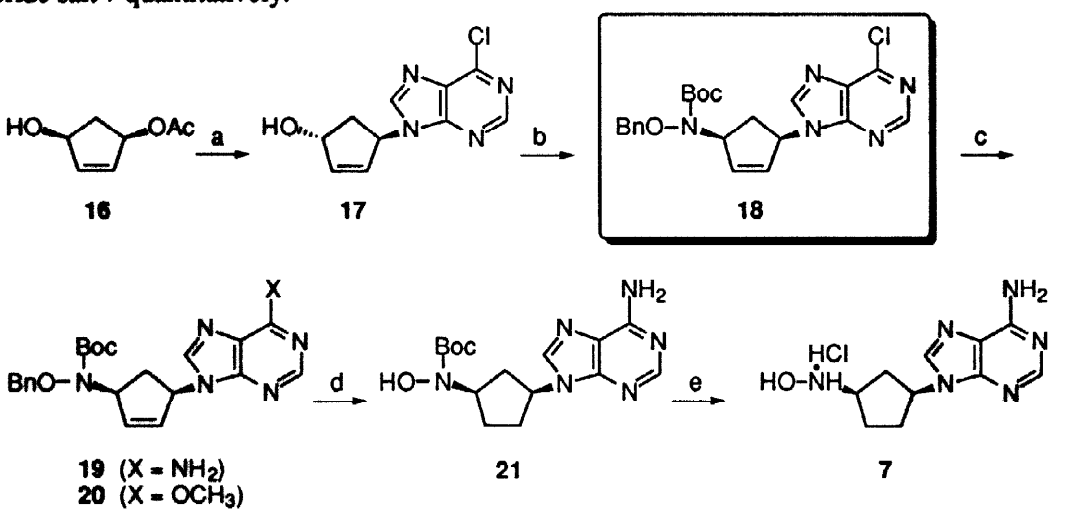
Pd(0)-catalyzed alkylations have been widely used in the construction of carbocyclic nucleosides.[21-24] Therefore, we initially focused on the use of this methodology for the incorporation of an adenine moiety as well as an appropriately protected hydroxylamine into monoacetate **16**.[25] However, low yields and complex mixtures of unidentified products generated from the Pd(0) route diverted the synthesis to a more applicable route.[26]

Mitsunobu chemistry also has been extensively utilized in the construction of carbocyclic nucleosides.[27-29] In order for successful Mitsunobu coupling of a hydroxylamine, appropriate protecting groups for this coupling partner needed to be chosen. Of the many *N*, *O*-protected hydroxylamines,[25] *N*-(*tert*-butoxycarbonyl)-*O*-benzylhydroxylamine (BocNHOBn) was determined to be ideal, since in the synthesis of hydroxylamine adducts **7** and **8**, both the olefin and the benzyl group could be removed simultaneously.

RESULTS AND DISCUSSION

Inititally, target molecules **7**, **8**, and **9** were envisioned to be derived from one advanced intermediate, **18** (Scheme 2). The synthesis of enantiomerically pure **18** began with allylic alcohol **16**, readily prepared from cyclopentadiene in two steps.[30] Allylic alcohol **16** and 6-chloropurine were subjected to standard Mitsunobu conditions (diisopropylazodicarboxylate [DIAD], Ph_3P, and THF) followed by direct solvolysis (KCN, MeOH) to afford *trans*-allylic 6-chloropurine analog **17** in 65% overall yield.[18-20] Attempts to utilize other deacetylation techniques led to diminished yields. Potassium carbonate in methanol led to substitution of chlorine by methoxy at the 6-position in the purine ring. Reductive conditions such as DIBAL or $LiAlH_4$ led to decomposition of product. Saponification under aqueous conditions, 1N NaOH in THF, afforded alcohol **17**, but in low yield (45%). Catalytic potassium cyanide in methanol proved to be the ideal reagent for removal of the acetate.[20] Treatment of **17** with BocNHOBn under Mitsunobu conditions afforded protected hydroxylamine carbocyclic nucleoside **18** in 80% yield. Attempts to convert 6-chloropurine to adenine by literature procedures[31] which included ammonium hydroxide in acetonitrile at rt, required 120 h and afforded a 50% yield of adduct **19**. Amination of 6-chloropurine with ammonia in methanol according to several literature procedures[11,29,32-34] required harsh reaction conditions including heating to 150 °C for 5 days in a sealed tube and afforded only modest yields. Amination of 6-chloropurine adduct **18** with ammonia in methanol afforded

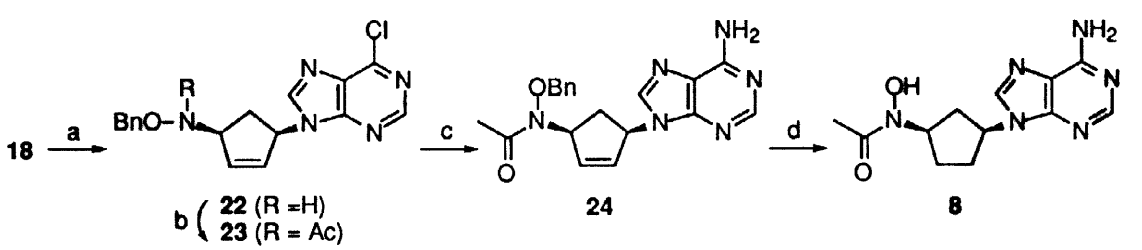
a 50/50 mixture of aminated product **19** and the corresponding 6-methoxyadduct **20**. In order to avoid methoxy addition, treatment of **18** with ammonia in THF in a sealed tube for 24 h at rt yielded adenine adduct **19** quantitatively.[27] Adduct **19**, upon hydrogenolytic removal of the benzyl group with $Pd(OH)_2/C$, afforded hydroxamic acid **21** in 80% yield. Attempts to remove the benzyl group of **19** with Pd/C proved to be quite sluggish. Typical reaction times were in excess of 48 h, presumably due to poisoning of the catalyst by the purine ring.[35] Attempts to deprotect the Boc group under aqueous acidic conditions led to decomposition. In order to avoid aqueous media, yet retain a polar solvent system, methanolic HCl was prepared from acetylchloride and methanol[36] and reacted with *N*-hydroxycarbamate **21** to yield deprotected hydroxylamine hydrochloride salt **7** quantitatively.



(a) i. DIAD, PPh_3, 6-chloropurine, THF, 16 h, 50 °C; ii. KCN, MeOH, 1 h, 65% overall for 2 steps; (b) DBAD, PPh_3, THF, Boc-NH-OBn, 16 h, rt, 80%; (c) NH_3, THF, 24 h, rt, 100%; (d) **19**, H_2, $Pd(OH)_2/C$, MeOH, 60 h, rt, 80%; (e) 20% AcCl, MeOH, 1 h, 0 °C to rt, 100%.

Scheme 2

Similar methodology was utilized for the synthesis of carbocyclic hydroxamic acid nucleoside **8** (Scheme 3). Thus, key intermediate **18** was treated with TFA to afford amine **22** in 75% yield. Acetylation of the resulting amine afforded intermediate **23**, which upon treatment with ammonia afforded adenine adduct **24** quantitatively in the two steps. Protected hydroxylamine **24** was hydrogenolyzed to saturated hydroxamic acid carbocyclic nucleoside **8** in 80% yield.



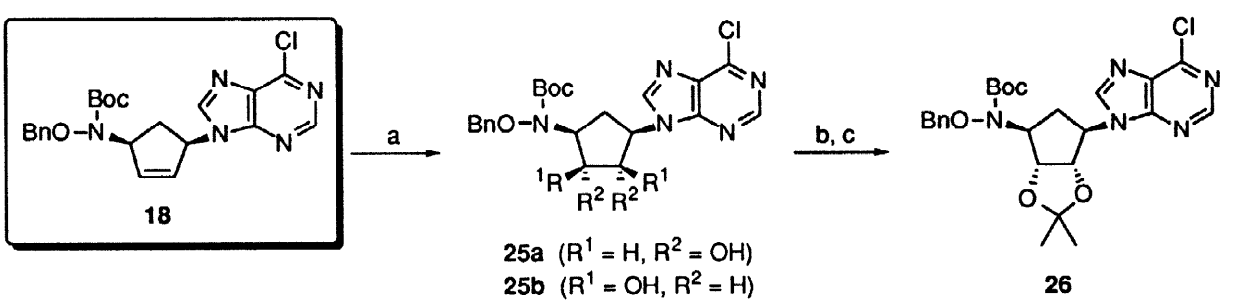
(a) 33% TFA, CH_2Cl_2, 45 min, rt, 75%; (b) Ac_2O, pyridine, DMAP, CH_2Cl_2, 12 h, rt, 100%; (c) NH_3, THF, rt, 24 h, 100%; (d) H_2, $Pd(OH)_2/C$, MeOH, 60 h, rt, 80%.

Scheme 3

Upon completion of the synthesis of hydroxylamine carbocyclic nucleoside analogs **7** and **8**, attention was turned to the preparation of hydroxylamine aristeromycin analog **9**. The dihydroxylation step was crucial in this synthesis. In our previous syntheses of carbocyclic nucleosides, osmium-mediated dihydroxylations proceeded with virtually no facial selectivity.[37] Osmium-mediated dihydroxylation of *Z*-olefins are known to proceed with limited stereocontrol.[38] In many instances, coordination effects govern the stereochemical outcome of such diol formation. For instance, a remarkable *syn*-directing effect was observed by Ganem and co-workers during their synthesis of mannostatin A.[39] The same effect was observed by Trost and coworkers in the synthesis of (±)-aristeromycin.[21] Highly polarizable groups such as amides and nitrosulfonylmethyl substituents reportedly serve to chelate osmium and direct the dihydroxylation to the β-face.[40]

Initial studies of the dihydroxylation of **18** with osmium tetroxide reproducibly afforded a 2:1 ratio of diastereomeric diols. In an enantioselective synthesis of *cis*-4-*tert*-butoxycarbamoyl-1-methoxylcarbonyl-2-cyclopentene, Trost and co-workers reported the role of solvent effects on the diastereoselectivity of osmium-mediated dihydroxylations.[41] In our case, application of different solvents, including methylene chloride and tetrahydrofuran failed to increase the diastereoselectivity. The addition of pyridine, which has been shown to enhance facial selectivity with approach of osmium tetroxide from the less hindered face, also failed to improve the diastereoselectivity to greater than 2:1 of **25a**:**25b**.[40,42,43] Sharpless asymmetric dihydroxylation also was attempted but resulted in decomposition of starting material presumably due to the basic nature of the AD mixture.[44,45] Thus, an alternative dihydroxylating agent was sought.

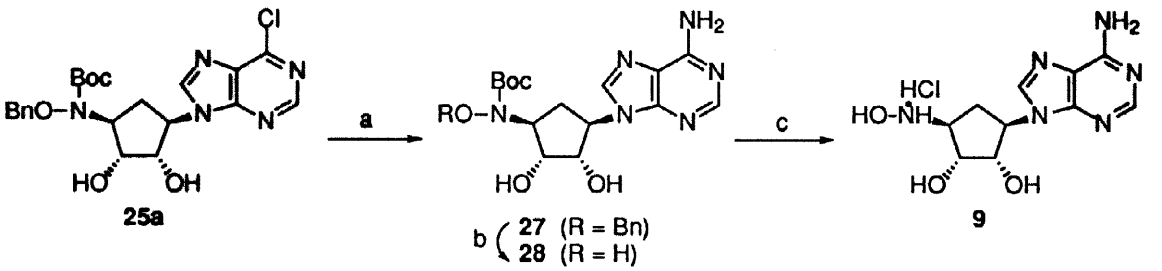
Ruthenium tetroxide is a very powerful oxidizing agent that can be generated *in situ* from $RuCl_3 \cdot 3H_2O$ and $NaIO_4$. While normally used to oxidatively cleave alkenes, ruthenium tetroxide has been shown to behave as a dihydroxylating agent at low temperatures for short reaction times, and in some cases has afforded exceptional diastereoselectivity.[46] Whether reaction of **18** with ruthenium tetroxide would provide better selectivity than osmium tetroxide and if over-oxidation could be avoided to furnish a sufficient yield of the desired diol was questionable. To our delight, reaction of compound **18** with $RuCl_3 \cdot 3H_2O$ and $NaIO_4$ in ethyl acetate, acetonitrile, and water, for 2 min at 0 °C afforded a 78% yield of a 15:1 mixture of diastereomeric diols **25a,b** (Scheme 4). The stereochemistry of major isomer **25a** was proven by X-ray crystallographic analysis of the corresponding acetonide **26**.[47] *Thus, in this case, ruthenium oxidation is significantly superior to osmium oxidation presumably due to the ability of ruthenium tetroxide to be directed by steric and not electronic effects.*



(a) $RuCl_3 \cdot (H_2O)_3$, $NaIO_4$, 3:3:1 EtOAc, CH_3CN, H_2O, 0 °C, 2.5 min, 78%,15:1 ratio of **25a**:**b**; (b) chromatographic separation; (c) **25a**, 2,2-dimethoxypropane, acetone, *p*-TsOH, rt, 12 h, 95%.

Scheme 4

With the dihydroxylation dilemma solved, diol **25a** was treated with ammonia to provide adenine-derived diol **27** quantitatively (Scheme 5). Diol **27** was then hydrogenolyzed to afford hydroxamic acid **28** in 75% yield. Subsequent Boc deprotection with 1:2:2 acetylchloride-MeOH-THF afforded desired hydroxylamine hydrochloride salt **9** in quantitative yield.

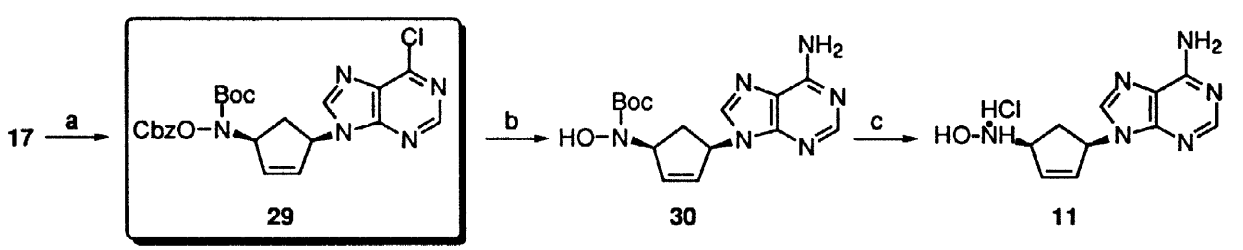


(a) NH_3/THF, rt, 24 h, 100%; (b) H_2, $Pd(OH)_2$/C, MeOH, 60 h, rt, 75%; (c) AcCl, MeOH, THF (1:2:2), 0 °C, 1 h, 100%.

Scheme 5

Upon demonstration that novel hydroxylamine analogs **7**, **8** and **9** were stable isolable compounds in deprotected form, the project was pushed towards the syntheses of other unique, but related, hydroxylamine carbanucleosides **10**, **11**, and **12** by also utilizing a common advanced intermediate. The synthesis of carbanucleosides **11** and **12** required a suitable protecting group for the oxygen on the *N*-Boc-hydroxylamine moiety which could be selectively removed in the presence of an alkene. While Cbz groups are usually removed under hydrogenolytic conditions not compatible with alkenes, we anticipated that removal of a Cbz group under amination conditions would also be possible.[25] The *O*-Cbz hydroxylamine carbonate would provide a versatile protecting group which would allow for subsequent deprotection of the hydroxylamine as well as functional group interconversion of the 6-chloropurine moiety in one step. Also, a protecting group such as the Cbz group would hopefully provide enough steric interference[48] to assist in directing the ruthenium dihydroxylation *anti* to the substituents on the cyclopentene ring in the synthesis of hydroxylamine carbocyclic nucleoside **10**. *O*-Cbz-hydroxylamino carbocyclic nucleoside **29** was prepared in 85% yield from the coupling of *N*-Boc-*O*-Cbz-hydroxylamine to intermediate **17** under Mitsunobu conditions (Scheme 6).[25] Intermediate **29** proved to be a versatile precursor for the syntheses of hydroxylamine carbocyclic nucleosides **10**, **11**, and **12**.

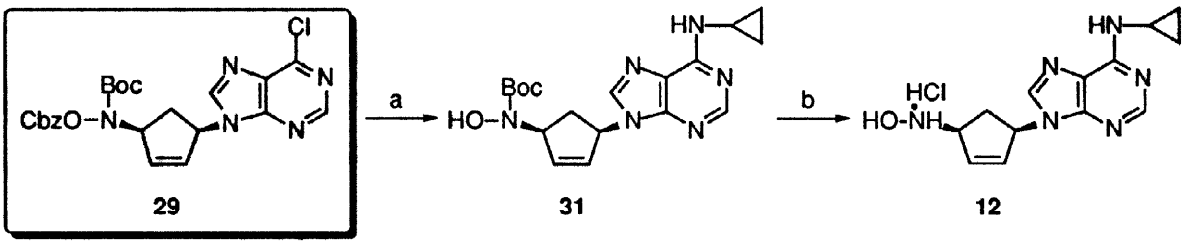
Thus, the synthesis of analog **11** only required two additional steps. Treatment of **29** with ammonia converted 6-chloropurine to adenine and removed the Cbz group to afford hydroxamic acid **30**. Acidic removal of the Boc group afforded hydroxylamine carbocyclic nucleoside **11** quantitatively in the two steps.



(a) Boc-NH-OCbz, DBAD, PPh_3, THF, 10 h, rt, 85%; (b) NH_3/THF, rt, 24 h, 100%; (c) 20% AcCl, MeOH, rt, 30 min, 100%.

Scheme 6

Recently reported modification of the guanine base of carbovir to a cyclopropylamino guanine analog has provided analogs with enhanced antiviral activity.[49] We anticipated that simple substitution of cyclopropylamine for ammonia used in the preparation of **11** from **29** would afford **12**. Indeed, treatment of **29** with cyclopropylamine afforded hydroxamic acid **31** in 90% yield (Scheme 7). Removal of the Boc carbamate from **31** in acidic methanol produced hydroxylamine carbocyclic nucleoside **12** quantitatively.

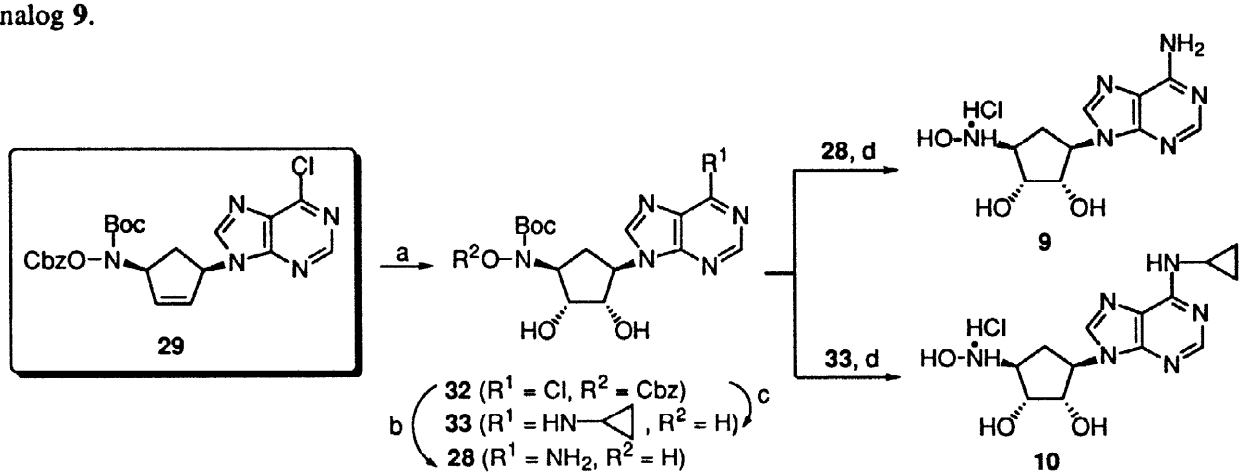


(a) cyclopropylamine, THF, rt, 24 h, 90%; (b) 20% AcCl, MeOH, rt, 30 min, 100%.

Scheme 7

Bis-hydroxyl-analog **10** was prepared by treatment of **29** with $RuCl_3 \cdot 3H_2O$ and $NaIO_4$ in ethyl acetate, acetonitrile, and water to afford diol **32** as a single desired diastereomer in 71% yield (Scheme 8). This result confirmed our belief that ruthenium tetroxide was directed by steric and not electronic effects. Diol **32** was then reacted with cyclopropylamine in THF for 24 h, to afford hydroxamic acid **33** quantitatively. Compound **33** was deprotected in the usual manner to give cyclopropylaminopurine carbocyclic nucleoside **10** in quantitative yield.

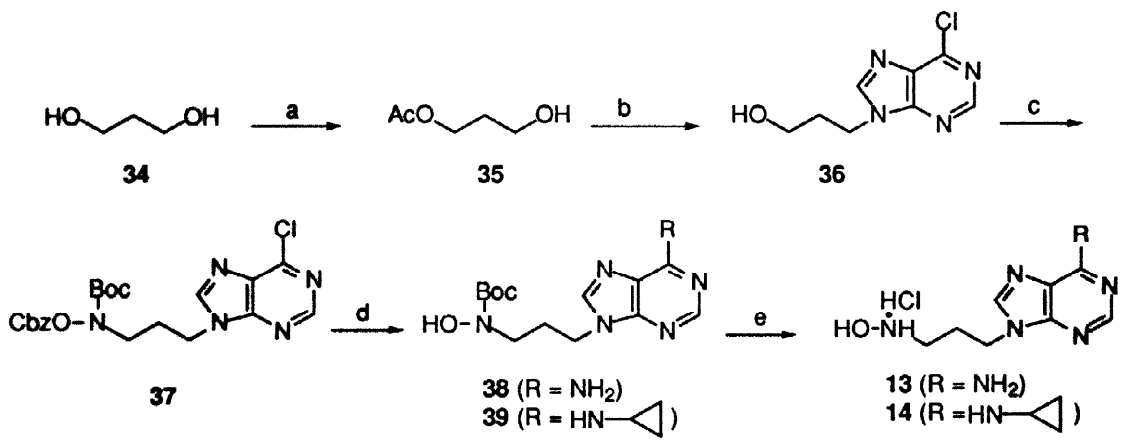
With the ease of *O*-Cbz hydroxylamine deprotection under amination conditions used to convert 6-chloropurine to adenine, it was decided to utilize intermediate **29** in the synthesis of hydroxylamine aristeromycin analog **9** (Scheme 6). The improved synthesis began with the amination of intermediate **29** to afford hydroxamic acid derivative **28**, therefore eliminating the slow hydrogenation step previously used in the synthesis. Hydroxamic acid **28** was then subjected to methanolic HCl to afford hydroxylamine aristeromycin analog **9**.



(a) $RuCl_3 \cdot [H_2O]_3$, $NaIO_4$, 3:3:1 EtOAc, CH_3CN, H_2O, 0 °C, 2 min, 71%; (b) NH_3/THF, rt, 24 h,100%; (c) cyclopropylamine, THF, rt, 24 h, 90%; (d) 20% AcCl, MeOH, rt, 30 min, 100%.

Scheme 8

Acyclic hydroxylamine carbanucleosides **13** and **14** were synthesized as adenine-derived hydroxylamine analogs to acyclovir (**4**). The preparation of these compounds began with careful acetylation of 1,3 propanediol (**34**) to give monoacetate **35** in 95% yield. Monoacetate **35** was coupled with 6-chloropurine under Mitsunobu conditions followed by direct saponification (1N NaOH, THF) of the acetate to afford alcohol **36** in 36% overall yield. The low yield was due to degradation of the product resulting from elimination of 6-chloropurine under the basic conditions. To avoid this problem, KCN in methanol[20] was used to remove the acetyl group and afforded alcohol **36** cleanly in a 70% two step yield. Alcohol **36** was subjected to di-*tert*-butyl azodicarboxylate (DBAD), triphenylphosphine, and *N*-Boc-*O*-Cbz-hydroxylamine in THF to afford alkylated hydroxylamine **37** in 92% yield. Protected hydroxylamine **37** was then separately subjected to ammonia and cyclopropylamine in THF followed by Boc-deprotection to afford acyclic hydroxylamine hydrochloride carbanucleosides **13** and **14**, respectively, in two quantitative steps (Scheme 9).



(a) Ac_2O, pyridine DMAP, CH_2Cl_2, 95%; (b) (i) 6-chloropurine, Ph_3P, DIAD, THF, rt, 16 h; (ii) KCN, MeOH, 70% overall for 2 steps; (c) Boc-NH-OCbz, DBAD, PPh_3, THF, rt, 92%; (d) **38** (R = NH_2), NH_3,THF, rt, 24 h, 100%/**39** (R = cyclopropylamine), cyclopropylamine, THF, rt, 24 h, 100%; (e) 20% AcCl, MeOH, rt, 30 min, 100%.

Scheme 9

CONCLUSIONS

We have demonstrated efficient and enantioselective syntheses of hydroxylamine-based carbanucleosides **7-12** through two common advanced Mitsunobu-derived protected hydroxylamine intermediates, **18** and **29**. Acyclic hydroxylamine carbanucleosides **13** and **14** were also synthesized by similar methodology. Diastereoselective ruthenium tetroxide-mediated dihydroxylation of advanced intermediates **18** and **29** led to superior facial selectivity than that observed with osmium tetroxide. Preliminary biological studies of the synthesized hydroxylamine nucleosides using the brine shrimp assay[50] suggest that some of these new analogs are biologically active. Detailed biological studies are in progress and will be reported in due course.

EXPERIMENTAL

General Methods. Instruments and general methods used have been described previously.[51]

***trans*-4(*R*)-(6-Chloro-9*H*-purin-9-yl)-1(*R*)-2-cyclopentenol (17)** A solution of 6-chloropurine (2.62 g, 16.92 mmol) in THF (80 mL) was treated with triphenylphosphine (4.44 g, 16.92 mmol), allylic alcohol **16** (2.0 g, 14.1 mmol), and diisopropylazodicarboxylate (DIAD) (4.44 g, 16.92 mmol). The reaction was stirred under argon at 50 °C for 16 h. The solvent was removed *in vacuo*, and the crude product was purified by column chromatography (silica gel; eluted with 0-50% EtOAc/CH_2Cl_2) to afford the *trans*-allylic acetate plus triphenylphosphine oxide. The crude mixture was dissolved in 100 mL of MeOH to which 290 mg (4.4 mmol) of KCN was added. The reaction was stirred under an argon atmosphere for 1.5 h. Methanol was removed *in vacuo*, and the product purified by column chromatography (silica gel; eluted with a gradient ranging from 33% EtOAc/CH_2Cl_2 to 4:1 EtOAc/CH_2Cl_2 to 3% MeOH/EtOAc) to afford 2.60 g (65% overall yield) of *trans*-allylic alcohol **17** as a white solid (recrystallized from EtOAc/hexanes): R_f 0.20 (EtOAc); mp 123-125 °C; IR (KBr) 3374, 2964, 1589, 1554, 1400, 1333, 1205, 1180, 1051, 949, 795 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.01 (bs, 1H), 2.42 (ddd, J= 4.2, 6.9, 14.7 Hz, 1H), 2.54 (ddd, 3.6, 8.0, 14.7 Hz, 1H), 5.32 (bs, 1H), 5.99 (m, 1H), 6.13 (ddd, J = 1.2, 2.4, 14.7, 1H), 6.42 (dt, J = 2.1, 5.7 Hz, 1H), 8.04 (s, 1H), 8.76 (s, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 47.8, 60.0, 75.8, 131.1, 131.9, 141.0, 143.1, 151.0, 151.4, 151.8; HRMS (FAB) calcd for $C_{10}H_{10}N_4OCl$ (MH^+) 237.0543, found 237.0543.

***cis*-4(*R*)-(6-Chloro-9*H*-purin-9-yl)-1(*S*)-*N*-[*N*-*tert*-butyloxycarbonyl(benzyloxy)amino]cyclopent-2-ene (18).** A THF solution (20 mL) of alcohol **17** (3.4 g, 14.4 mmol) was charged with triphenylphosphine (5.7 g, 21.6 mmol), *N*-Boc-*O*-benzylhydroxylamine (4.8 g, 21.6 mmol), and di-*tert*-butyl azodicarboxylate (5.0 g, 21.6 mmol). The reaction was stirred under argon for 16 h at rt. The solvent was removed *in vacuo*, and the crude product was purified by column chromatography (silica gel; eluted with 20-33% EtOAc/hexanes) to afford 5.09 g (80%) of **18** as a white solid (recrystallized from EtOAc/hexanes): R_f 0.60 (EtOAc); mp 104-106 °C; IR (KBr) 3030, 2975, 2940, 1698, 1588, 1559, 1481, 1458, 1427, 1368, 1349, 1332, 1310, 1256, 1197, 1162, 949, 856, 790, 751, 700, 639 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.54 (s, 9H), 1.93 (ddd, J = 5.1, 5.3, 14.7 Hz, 1H), 3.01 (ddd, J = 8.9, 9.0, 14.4 Hz, 1H), 4.48 (d, J = 9.9 Hz, 1H), 4.91 (d, J = 9.9 Hz, 1H), 5.27 (m, 1H), 5.72 (m, 1H), 5.72 (m, 1H), 5.98 (dt, J = 2.1, 5.7 Hz, 1H), 6.12 (dt, J = 2.1, 5.7 Hz, 1H), 7.34 (m, 5H0, 8.04 (s, 1H), 8.72 (s, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) 28.2, 34.6, 57.7, 64.3, 78.8, 82.4, 128.6, 129.0, 129.7, 131.2, 131.5, 134.8, 136.5, 143.9, 150.8, 151.3, 151.7, 156.8; HRMS (FAB) calcd for $C_{22}H_{25}N_5O_3Cl$ (MH^+) 442.1646, found 442.1642.

***cis*-4(*R*)-(6-Chloro-9*H*-purin-9-yl)-1(*S*)-*N*-[(benzyloxy)amino]cyclopent-2-ene (22).** A solution of **18** (700 mg, 1.6 mmol) in 33% TFA/CH_2Cl_2 (10 mL) was stirred at 0 °C under argon and allowed to warm to rt. After 45 min, the reaction was complete. CH_2Cl_2 was added and the organic layer was washed with saturated $NaHCO_3$. The saturated $NaHCO_3$ solution was back-extracted with EtOAc. The organic layers were combined, washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo* to a yellow oil.

The oil was chromatographed (silica gel; eluted with EtOAc) to afford 400 mg (75%) of hydroxylamine **22** as a tan oil. R_f 0.25 (EtOAc); IR (neat) 3220, 3060, 3025, 2995, 1590, 1560, 1540, 1485, 1450, 1435, 1420, 1400, 1330, 1260, 1205, 1145, 950, 910, 855, 770, 740, 700, 630 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.94 (dt, J = 3.6, 15.0 Hz, 1H), 2.87 (ddd, J = 8.1, 9.0, 15.0 Hz, 1H), 4.29 (m, 1H), 4.69 (s, 2H), 5.71 (m, 1H), 5.88 (bs, 1H), 5.98 (dt, J = 1.8, 5.4 Hz, 1H), 6.24 (dt, J= 1.8, 5.7 Hz, 1H), 7.32 (m, 5H), 8.32 (s, 1H), 8.69 (s, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 35.7, 58.6, 65.4, 76.6, 128.0, 128.4, 128.5, 131.3, 131.8, 137.3, 137.5, 144.6, 150.8, 151.2, 151.6; HRMS (FAB) calcd for $C_{17}H_{17}N_5OCl$ (MH^+) 342.1122, found 342.1119.

***cis*-4(*R*)-(6-Chloro-9*H*-purin-9-yl)-1(*S*)-*N*-[*N*-acetyl(benzyloxy)amino]cyclopent-2-ene (23).** A solution of **22** (190 mg, 0.56 mmol) in CH_2Cl_2 (2.5 mL) was charged with acetic anhydride (0.16 mL, 1.70 mmol), pyridine (0.14 mL, 1.70 mmol), and dimethylaminopyridine (5mg, 0.035 mmol) and stirred under argon for 12 h. The organic layer was washed with 1N HCl, saturated $NaHCO_3$, distilled water, brine, dried over Na_2SO_4, and filtered. The solution was concentrated *in vacuo* to a yellow oil, and column chromatographed (silica gel; eluted with 4:1 EtOAc/hexanes) to afford 215 mg (quantitative) of acetamide **23** as a white solid (recrystallized from EtOAc/hexanes): R_f 0.20 (EtOAc); mp 46-47 °C; IR (KBr) 3072, 1659, 1590, 1563, 1489, 1435, 1390, 1336, 1304, 1209, 1140, 973, 956, 915, 856, 793, 752, 703 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.11 (dt, J = 6.0, 14.1 Hz, 1H), 2.20 (s, 3H), 3.10 (dt, J = 8.7, 14.1 Hz, 1H), 4.94 (d, J = 9.9 Hz, 1H), 4.95 (d, J = 9.9 Hz, 1H), 5.63 (m, 1H), 5.76 (m, 1H), 6.10 (dt, J = 2.4, 5.4 Hz, 1H), 6.30 (dt, J = 2.1, 5.4 Hz, 1H), 7.39 (m, 5H), 8.08 (s, 1H), 8.70 (s, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 21.2, 35.2, 57.9, 62.2, 79.5, 128.9, 129.0, 129.4, 131.5, 131.73, 133.8, 136.0, 143.7, 150.9, 151.4, 151.8, 174.2; HRMS (FAB) calcd for $C_{19}H_{19}N_5O_2Cl$ (MH^+) 384.1227, found 384.1223.

5(*R*)-(6-Chloro-9*H*-purin-9-yl)-1(*S*),2(*R*)-dihydroxy-3(*S*)-*N*-[*N*-*tert*-butyloxycarbonyl(benzyloxy)amino]cyclopentane (25a, 25b). A solution of **18** in EtOAc (9 mL) and acetonitrile (9 mL) was cooled to 0 °C. In a separate flask, $RuCl_6 \cdot 3H_2O$ (23 mg, 0.112 mmol) and $NaIO_4$ (513 mg, 2.4 mmol) were dissolved in 3.5 mL of distilled water. The ruthenium tetroxide solution was then transferred to the EtOAc/acetonitrile solution containing **18**, and the heterogeneous black mixture was allowed to stir at 0 °C for 2.5 min. The reaction was quenched with 30 mL of saturated $Na_2S_2O_5$ solution and allowed to stir for 30 min at rt. The aqueous layer was extracted with EtOAc. The organic layers were combined, washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo* to an oil. The diols were separated by column chromatography (silica gel; eluted with 33-80% EtOAc/CH_2Cl_2) to afford a 71% yield of diols **25a** and **25b** in a 15:1 ratio. The diastereomeric mixture was recrystallized from EtOAc/hexanes to afford pure diol **25a**: R_f 0.45 (EtOAc); mp 161-162 °C; IR (KBr) 3412, 3305, 2976, 1714, 1595, 1565, 1496, 1442, 1394, 1369, 1340, 1311, 1256, 1204, 1151, 1040, 944, 753, 701, 633 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.57 (s, 9H), 2.41 (m, 1H), 2.61 (ddd, J = 8.0, 8.0, 12.6 Hz, 1H), 4.44 (m, 3H), 4.71 (m, 1H), 4.93 (s, 2H), 7.36 (s, 5H), 8.04 (s, 1H), 8.68 (s, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 28.2, 60.4, 63.7, 72.5, 74.4, 78.6, 82.8, 128.5, 128.9, 129.3, 131.8, 134.9, 144.7, 151.0, 151.4, 151.6, 157.4; HRMS (FAB) calcd for $C_{22}H_{27}N_5O_5Cl$ (MH^+) 476.1701, found 476.1897.

5(*R*)-(6-Chloro-9*H*-purin-9-yl)-3(*S*)-*N*-[*N*-*tert*-butyloxycarbonyl(benzyloxy)amino]-1(*S*),2(*R*)-(isopropylidenedioxy)cyclopentane (26). Diol **25a** (300 mg, 0.63 mmol) and *p*-TsOH•H_2O (5 mg, 0.026 mmol) was dissolved in 1.5 mL of acetone and 2,2-dimethoxypropane (1.5 mL, 12.6 mmol) and placed under argon and allowed to stir overnight. The reaction was concentrated *in vacuo*, dissolved in CH_2Cl_2, and washed with a saturated $NaHCO_3$, brine, dried over Na_2SO_4, and filtered. Acetonide **26** was column chromatographed (silica gel; eluted with 3:1 hexanes:EtOAc) and recrystallized from EtOAc/hexanes to obtain 308 mg (95%) of acetonide **26** as a white solid: R_f 0.70 (EtOAc); mp 146-148 °C; IR (KBr) 3066, 2985, 2933, 2882, 1723, 1595, 1564, 1405, 1369, 1318, 1246, 1195, 1164, 1103, 1072, 933, 856, 749, 692, 641 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.27 (s, 3H), 1.56 (s, 9H), 1.58 (s, 3H), 2.57 (ddd, J = 11.7, 11.7, 11.7 Hz, 1H); 2.88 (ddd, J = 5.7, 7.2, 12.9, 1H), 4.56 (ddd, J = 4.5, 6.9, 11.1 Hz, 1H), 4.78 (ddd, J = 6.0, 6.0, 12.0 Hz, 1H), 4.85 (m, 1H), 4.94 (m, 3H), 7.37-7.47 (m, 5H), 8.13 (s, 1H), 8.70 (s, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 25.1, 27.5, 28.3, 32.6, 60.6, 63.3, 78.7, 80.5, 82.5, 82.7, 114.0, 128.6, 128.9, 129.5, 132.2, 135.0, 144.2, 151.3, 151.6, 151.8, 156.8; HRMS (FAB) calcd for $C_{25}H_{31}N_5O_5Cl$ (MH^+) 516.2114, found 516.2035.

***cis*-4(*R*)-(6-Chloro-9*H*-purin-9-yl)-1(*S*)-*N*-[(*N*-*tert*-butyloxycarbonyl-*O*-carbobenzyloxy)amino]cyclopent-2-ene (29).** A THF solution (50 mL) of alcohol **17** (1.6 g, 6.8 mmol) was charged with triphenylphosphine (3.6 g, 13.6 mmol), *N*-Boc-*O*-Cbz-hydroxylamine (7.28 g, 27.2 mmol), and di-*tert*-butyl azodicarboxylate (3.13 g, 13.6 mmol). The reaction was stirred under argon for 10 h at rt. The solvent was removed *in vacuo*, and the crude product was purified by column chromatography (silica gel; eluted with 20-33% EtOAc/hexanes) to afford 5.09 g (85%) of **29** as a clear oil: R_f 0.25 (1:1 EtOAc:hexanes); IR (neat) 2860, 1785, 1580, 1555, 1490, 1470, 1360, 1210, 1145, 1090, 900, 720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.41 (s, 9H), 1.95 (ddd, J = 4.8, 4.8, 15.0 Hz, 1H), 3.16 (ddd, J = 9.0, 9.0, 15.0 Hz, 1H), 5.28 (bs, 2H), 5.44 (bs, 1H), 5.75 (m, 1H), 5.99 (bs, 1H), 6.21 (bs, 1H), 7.37 (m, 5H), 8.18 (s, 1H), 8.74 (s, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 27.9, 35.0, 57.6, 64.2, 71.4, 83.8, 128.7, 128.7, 129.0, 131.6, 132.4, 134.2, 135.4, 143.6, 151.0, 151.3, 151.9, 154.1, 154.4; HRMS (FAB) calcd for $C_{23}H_{25}N_5O_5Cl$ (MH^+) 486.1544, found 486.1563.

1-Acetoxy-3-propanol (35). A solution of 1,3-propanediol **34** (60.0 g, 632 mmol), acetic anhydride (15.0 mL, 158 mmol), pyridine (14.0 mL, 174 mmol), and dimethylaminopyridine (catalytic) in CH_2Cl_2 (1.0 L) was stirred for 12 h. The organic layer was washed with 15% HCl, adding enough to ensure that the aqueous layer was acidic. The aqueous layers were combined and saturated with sodium chloride and washed with CH_2Cl_2. The organic layers were combined, washed with brine, dried over Na_2SO_4, and filtered. The organic solution was concentrated *in vacuo*, affording a clear oil. The product was column chromatographed (silica gel; eluted with 2:1 hexanes:EtOAc) to afford 18.6 g (95%) of monoacetate **35** as a clear oil: R_f 0.30 (EtOAc); IR (neat) 3450, 3020, 2990, 2900, 1730, 1370, 1250, 1150, 760 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.88 (t, J = 6.0 Hz, 2H), 2.07 (s, 3H), 2.53 (bs, 1H), 3.70 (t, J = 6.0 Hz, 2H), 4.22, (t, J = 6.0 Hz, 2H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 20.8, 31.5, 58.9, 61.4, 171.5; HRMS (FAB) calcd for $C_6H_{11}O_3$ (MH^+) 119.0708 found 119.0686.

3-(6-Chloro-9*H*-purin-9-yl)-1-propanol (36). A solution of 6-chloropurine (1.50 g, 6.5 mmol) in THF (65 mL) was treated with triphenylphosphine (2.72 g, 10.4 mmol), alcohol **35** (0.77 g, 6.5 mmol), and diisopropylazodicarboxylate (2.04 g, 10.4 mmol). The reaction mixture was stirred under argon at 40 °C for 16 h. The solvent was removed *in vacuo*, and the crude product was purified by column chromatography (silica gel; eluted with 33-80% EtOAc:hexanes) to give the 6-chloropurine adduct plus triphenylphosphine oxide. The crude mixture was dissolved in 18 mL of MeOH and charged with 180 mg (2.75 mmol) of KCN at rt under argon for approximately 1.5 h, at which time the MeOH was removed *in vacuo*. The product was column chromatographed (silica gel; eluted with 50-100% EtOAc/CH_2Cl_2 to 5% MeOH/CH_2Cl_2/EtOAc) to afford 0.97 mg (70% overall yield) of alcohol **36** as a white solid (recrystallized from EtOAc/hexanes): R_f 0.15 (EtOAc); mp 120-121 °C; IR (KBr) 3287, 3103, 3076, 1590, 1561, 1449, 1332, 1217, 1062, 956, 645 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, CD_3OD) δ 2.14 (t, J = 6.3 Hz, 2H), 2.42 (bs, 1H), 3.60 (t, J = 5.7 Hz, 2H), 4.51 (t, J = 6.6 Hz, 2H), 8.25 (s, 1H), 8.76 (s, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 31.9, 41.0, 57.8, 131.4, 145.9, 151.0, 151.7, 151.8; HRMS (FAB) calcd for $C_8H_{10}N_4OCl$ (MH^+) 213.0543 found 213.0558. Anal. Calcd for $C_8H_9N_4OCl$: C, 45.19; H, 4.27; N, 26.35. Found: C, 45.05; H, 4.24; N, 26.13.

3-(6-Chloro-9*H*-purin-9-yl)-1-*N*-[(*N*-*tert*-butyloxycarbonyl-*O*-carbobenzyloxy)amino]propane(37). A THF solution (10 mL) of alcohol **36** (240 mg, 1.13 mmol) was charged with triphenylphosphine (532 mg, 2.03 mmol), *N*-Boc-*O*-Cbz-hydroxylamine (1.20 g, 4.52 mmol), and then diisopropylazodicarboxylate (0.41 mL, 2.03 mmol). The reaction was stirred under argon at rt for 12 h. The solvent was removed *in vacuo*, and the crude product was purified by column chromatography (silica gel; eluted with 25-33% hexanes/EtOAc) to give 420 mg (92%) of **37** as a clear oil: R_f 0.5 (EtOAc); IR (neat) 2950, 1785, 1720, 1590, 1500, 1440, 1400, 1370, 1340, 1255, 1220, 1150, 1100, 910, 740 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.42 (s, 9H), 2.21 (pentet, J = 6.3 Hz, 2H), 3.65 (t, J = 6.0 Hz, 2H), 4.44 (t, J = 6.9 Hz, 2H), 5.28 (s, 2H), 7.39 (m, 5H), 8.18 (s, 1H), 8.72 (s, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 26.9, 27.8, 41.6, 47.0, 71.2, 83.4, 128.4, 128.6, 128.9, 131.6, 134.0, 145.7, 150.8, 151.6, 151.7, 154.4, 154.6; HRMS (FAB) calcd for $C_{21}H_{25}N_5O_5Cl$ (MH^+) 462.1544, found 462.1551.

5(*R*)-(6-Chloro-9*H*-purin-9-yl)-1(*S*),2(*R*)-dihydroxy-3(*S*)-*N*-[(*N*-*tert*-butyloxycarbonyl-*O*-carbobenzyloxy)amino]cyclopentane (32). A solution of **29** (900 mg, 1.85 mmol) in 11 mL of EtOAc and 11 mL of CH_3CN was cooled to 0 °C. In a separate flask, 26 mg (0.25 mmol) of $RuCl_3 \cdot 3H_2O$ and 594 mg (2.78 mmol) of $NaIO_4$ were dissolved in 3.7 mL of distilled water. The ruthenium tetroxide solution was then transferred to the above solution of **29**, and the heterogeneous black mixture was allowed to stir for 2.5 min at 0 °C. The reaction was quenched with a 25 mL saturated solution of $Na_2S_2O_5$ and allowed to stir for 30 min at rt. The aqueous layer was extracted with EtOAc. The organic layers were combined, washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo* to an oil. The diol was purified by column chromatography (silica gel; eluted with 3-5% MeOH/CH_2Cl_2) to afford 681 mg (71%) of diol **32** as a white solid (recrystallized from EtOAc/hexanes): R_f 0.35 (EtOAc); mp 118-120 °C; IR (KBr) 3420, 2980, 1795, 1715, 1595, 1560, 1390, 1340, 1220, 1155 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, 60 °C) δ 1.45 (s, 9H), 2.45 (ddd, J = 10.2, 10.2, 13.5 Hz, 1H), 2.72 (ddd, J = 8.1, 8.1, 13.5 Hz, 1H), 3.57 (bs, 1H), 4.04 (bs, 1H), 4.50 (m, 2H), 4.61 (ddd, J = 4.5, 8.4, 9.8 Hz, 1H), 4.77 (ddd, J = 6.0, 8.4, 9.8 Hz, 1H), 5.28 (s, 2H),

7.36 (m, 5H), 8.16 (s, 1H), 8.63 (s, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 27.3, 27.5, 59.7, 62.8, 70.6, 71.4, 73.0, 82.7, 128.3, 128.5, 128.7, 131.6, 134.8, 147.4, 149.1, 151.0, 151.9, 153.9, broadening and overlapping of peaks due to rotational isomers; HRMS (FAB) calcd for $C_{23}H_{27}N_5O_7Cl$ (MH^+) 520.1599, found 520.1594. Anal. Calcd for $C_{23}H_{26}N_5O_7Cl$: C, 53.13; H, 5.04; N, 13.47. Found: C, 53.33; H, 5.22; N, 13.41.

General Procedure for 6-Cyclopropylaminopurine/6-Aminopurine Preparation from 6-Chloropurine Adduct *via* Amination. Protected hydroxylamine 6-chloropurine adduct was dissolved in a minimal amount of THF in a sealed tube and cooled to -78 °C. The solution was charged with ammonia or cyclopropylamine (500%) and sealed with a teflon cap and allowed to warm to rt and stir until the reaction was complete by TLC analysis (24 h). The reaction mixture was cooled to -78 °C and the contents transferred to an Erlenmeyer flask. The tube was washed with MeOH to completely transfer the reaction mixture. The solvent and ammonia (or cyclopropylamine) were concentrated *in vacuo*. Without workup (due to the high water solubility of the product), the mixture was dry loaded and chromatographed on silica gel. The yields ranged from 90-100%.

***cis*-4(*R*)-(6-Amino-9*H*-purin-9-yl)-1(*S*)-*N*-[*N*-*tert*-butyloxycarbonyl(benzyloxy)amino]cyclopent-2-ene (19).** Following the general procedure, 700 mg (1.6 mmol) of **18** was treated with ammonia to afford 707 mg (quantitative) of amine **19** as a white solid (recrystallized from hot EtOAc): R_f 0.40 (5% MeOH/EtOAc); mp 69-71 °C; IR (KBr) 3456, 3313, 3159, 2776, 1702, 1646, 1595, 1574, 1471, 1369, 1302, 1246, 1164, 1082, 1010, 749, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.54 (s, 9H), 1.93 (ddd J = 5.4, 5.4, 14.4 Hz, 1H), 3.00 (ddd, J = 8.7, 8.7, 14.4 Hz, 1H), 4.80 (d, J = 9.9 Hz, 1H), 4.93 (d, J = 9.9 Hz, 1H), 5.27 (m, 1H), 5.65 (m, 1H), 5.92 (bs, 2H), 5.98 (dt, J = 2.1, 5.7 Hz, 1H), 6.09 (dt, J = 2.1, 5.7 Hz, 1H), 7.36 (m, 5H), 7.70 (s, 1H), 8.34 (s, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 28.3, 34.8, 57.0, 64.3, 78.8, 82.3, 119.3, 128.6, 129.0, 129.7, 132.2, 134.9, 135.4, 139.0, 149.6, 152.8, 155.4, 156.8; HRMS (FAB) calcd for $C_{22}H_{27}N_6O_3$ (MH^+) 423.2145, found 423.2148.

***cis*-4(*R*)-(6-Amino-9*H*-purin-9-yl)-1(*S*)-*N*-[acetyl(benzyloxy)amino]cyclopent-2-ene (24).** Following the general procedure, 6-chloropurine adduct **23** (100 mg, 0.26 mmol) was treated with ammonia. The product was isolated by column chromatography (silica gel; eluted with 5% MeOH/CH_2Cl_2) affording 94 mg (quantitative) of amine **24** as a white solid (recrystallized from EtOAc/Hexanes): R_f 0.125 (9% MeOH/CH_2Cl_2); mp 58-61 °C; IR (KBr) 3355, 3180, 2880, 1670, 1655, 1640, 1595, 1520, 1470, 1410, 1370, 1295, 1195, 960 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.10 (dt, J = 6.0, 14.1 Hz, 1H), 2.20 (s, 3H), 3.08 (dt, J = 8.7, 14.1 Hz, 1H), 4.94 (s, 1H), 4.95 (s, 1H), 5.68 (m, 2H), 6.10 (m, 1H), 6.25 (m, 1H), 6.35 (s, 2H), 7.39 (m, 5H), 7.76 (s, 1H), 8.33 (s, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 21.2, 35.3, 57.1, 62.0, 79.4, 119.4, 128.8, 129.0, 129.2, 132.7, 133.9, 135.0, 138.7, 149.6, 152.8, 155.7, 174.0; HRMS (FAB) calcd for $C_{19}H_{21}N_6O_2$ (MH^+) 365.1726, found 365.1722.

5(*R*)-(6-Amino-9*H*-purin-9-yl)-1(*S*),2(*R*)-dihydroxy-3(*S*)-*N*-[*N*-*tert*-butyloxycarbonyl(benzyloxy)amino]cyclopentane (27). Following the general procedure, 85 mg

(0.178 mmol) of **25a** was treated with ammonia. The mixture was column chromatographed (silica gel; eluted with 5% MeOH/EtOAc) affording 76 mg (95%) of compound **27** as a white solid (recrystallized from hot EtOAc): R_f 0.14 (5% MeOH/EtOAc); mp 177-178 °C; IR (KBr) 3333, 3190, 2974, 2933, 1707, 1641, 1600, 1477, 1369, 1328, 1302, 1251, 1159, 743, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.56 (s, 9H), 1.71 (bs, 2H), 2.62 (ddd, J = 7.8, 7.8, 12.6 Hz, 1H), 2.30 (m, 1H), 4.35 (m, 2H), 4.55 (m, 2H), 4.90 (d, J = 9.9 Hz, 1H), 4.98 (d, J = 9.9 Hz, 1H), 5.73 (s, 2H), 7.34 (s, 5H), 7.64 (s, 1H), 8.28 (s, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 28.0, 28.4, 59.0, 63.6, 72.0, 74.6, 78.5, 82.6, 119.1, 128.4, 128.7, 129.3, 134.8, 139.1, 149.5, 152.1, 155.4, 157.2; HRMS (FAB) calcd for $C_{22}H_{29}N_6O_5$ (MH^+) 457.2199, found 457.2216.

***cis*-4(*R*)-(6-Amino-9*H*-purin-9-yl)-1(*S*)-*N*-[*N*-*tert*-butyloxycarbonylhydroxamino]-cyclopent-2-ene (30).** Following the general procedure, 500 mg (1.03 mmol) of **29** was treated with ammonia. The mixture was chromatographed (silica gel; eluted with 0-8% MeOH/CH_2Cl_2) and afforded 340 mg (quantitative) of **30** as a white solid (recrystallized from MeOH:THF): R_f 0.3 (10% MeOH:CH_2Cl_2); mp 190 °C (decomposition); IR (KBr) 3788, 3199, 2960, 1707, 1642, 1604, 1550, 1480, 1412, 1369, 1164, 1094; ^1H NMR (300 MHz, $CDCl_3$) δ 1.52 (s, 9H), 2.09 (dt, J = 3.9, 15.0 Hz, 1H), 3.03 (ddd, J = 9.0, 9.0, 15.0 Hz, 1H), 5.35 (m, 1H), 5.67 (m, 1H), 6.00 (dt, J = 2.1, 5.7 Hz, 1H), 6.19 (dt, J = 1.8, 5.7 Hz, 1H), 6.28 (bs, 2H), 8.08 (s, 1H), 8.29 (s, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 28.3, 34.9, 57.4, 63.6, 82.2, 118.5, 131.9, 136.1, 139.5, 149.2, 152.8, 155.5, 156.6; HRMS (FAB) calcd for $C_{15}H_{21}N_6O_3$ (MH^+) 333.1675, found 333.1671. Anal. Calcd for $C_{15}H_{20}N_6O_3$: C, 54.21; H, 6.07; N, 25.29. Found: C, 54.06; H, 6.00; N, 25.17.

***cis*-4(*R*)-(6-Cyclopropylamino-9*H*-purin-9-yl)-1(*S*)-*N*-[*N*-*tert*-butyloxycarbonylhydroxamino]cyclopent-2-ene (31).** Following the general procedure, 300 mg (0.62 mmol) of **29** was aminated with cyclopropylamine. The mixture was column chromatographed (silica gel; eluted with 4% MeOH:CH_2Cl_2) and recrystallized from MeOH:THF to afford 230 mg (quantitative) of **31** as a white solid: R_f 0.3 (4% MeOH:CH_2Cl_2); mp 194 °C (decomposition); IR (KBr) 3322, 2982, 2286, 1683, 1621, 1531, 1477, 1393, 1369, 1328, 1305, 1246, 1168, 1099, 752 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.69 (m, 2H), 0.91 (m, 2H), 1.51 (s, 9H), 2.03 (ddd, J = 4.2, 4.2, 14.7 Hz, 1H), 3.02 (m, 2H), 5.33 (m, 1H), 5.63 (m, 1H), 6.00 (dt, J = 1.8, 5.7 Hz, 1H), 6.16 (dt, J = 1.8, 5.7 Hz, 1H), 7.13 (bs, 1H), 7.96 (s, 1H), 8.42 (s, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 6.9, 23.4, 28.2, 34.7, 57.5, 63.5, 81.9, 118.9, 131.6, 136.1, 138.8, 147.9, 152.9, 155.5, 156.4; HRMS (FAB) calcd for $C_{18}H_{25}N_6O_3$ (MH^+) 373.1988, found 373.1996.

1(*R*)-(6-Cyclopropylamino-9*H*-purin-9-yl)-2(*S*),3(*R*)-dihydroxy-4(*S*)-*N*-[*N*-*tert*-butyloxycarbonylhydroxamino]cyclopentane (33). Following the general procedure, 200 mg (0.38 mmol) of 6-chloropurine adduct **32** was aminated with cyclopropylamine. The mixture was column chromatographed (silica gel; eluted with 5-8% MeOH:CH_2Cl_2) and recrystallized from MeOH:THF to afford 139 mg (90%) of **33** as a white solid: R_f 0.2 (8% MeOH:CH_2Cl_2); mp 109 °C (decomposition); IR (KBr) 3321, 1693, 1624, 1480, 1370, 1354, 1252, 1161, 1099, 756 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$ + 2 drops CD_3OD) δ 0.67 (m, 2H), 0.94 (m, 2H), 1.51 (s, 9H), 2.33 (ddd, J = 7.5, 9.0, 13.8 Hz, 1H), 2.74 (ddd, J =

9.0, 9.0, 13.8 Hz), 2.98 (bs, 1H), 3.86 (s, 2H), 4.29 (dd, J = 3.9, 5.4 Hz), 4.43 (dd, J = 5.7, 7.2 Hz, 1H), 4.60 (ddd, J = 3.6, 7.5, 8.8 Hz, 1H), 4.76 (overlapping dd, J = 9.0 Hz, 1H), 8.01 (s, 1H), 8.37 (s, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$ + 2 drops CD_3OD) δ 6.9, 23.3, 28.0, 28.7, 59.2, 62.4, 72.8, 75.5, 81.9, 119.6, 138.8, 148.3, 152.3, 155.6, 156.8; HRMS (FAB) calcd for $C_{18}H_{26}N_6O_5$ (MH^+) 407.2043, found 407.2049.

3-(6-Cyclopropylamino-9*H*-purin-9-yl)-1-*N*-[*N*-*tert*-butyloxycarbonylhydroxamino]propane (39). Following the general procedure, 210 mg (0.456 mmol) of protected hydroxyamine **37** was aminated with cyclopropylamine. The mixture was column chromatographed (silica gel; eluted with 4% MeOH:CH_2Cl_2) to afford 157 mg (quantitative) of **39** as a white solid (recrystallized from CH_2Cl_2/hexanes): R_f 0.2 (4% MeOH:CH_2Cl_2); mp 54-56 °C; IR (KBr) 3309, 1699, 1621, 1480, 1368, 1236, 1161, 1111, 756, 646 cm^{-1}; ^{1}H NMR (300MHz, $CDCl_3$ + 2 drops CD_3OD) δ 0.71 (m, 2H), 0.94 (m, 2H), 1.49 (s, 9H), 2.19 (m, 2H), 3.31 (bs, 1H), 3.59 (t, J = 6.0 Hz, 2H), 4.29 (t, J = 7.5 Hz, 2H), 7.01 (bs, 1H), 7.84 (s, 1H), 8.43 (s, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$ + 2 drops CD_3OD) δ 7.0, 23.5, 27.8, 28.2, 41.5, 47.1, 81.4, 119.4, 140.1, 152.8, 155.7, 155.8, 157.0; HRMS (FAB) calcd for $C_{16}H_{25}N_6O_3$ (MH^+) 349.1988, found 349.2003. Anal. Calcd for $C_{16}H_{24}N_6O_3$: C, 55.16; H, 6.94; N, 24.12. Found: C, 55.08; H, 6.94; N, 23.92.

3-(6-Amino-9*H*-purin-9-yl)-1-*N*-[*N*-*tert*-butyloxycarbonylhydroxamino]propane (38). Following the general procedure, 180 mg (0.390 mmol) of protected hydroxyamine **37** was aminated with cyclopropylamine. The mixture was column chromatographed (silica gel; eluted with 4% MeOH:CH_2Cl_2) to afford 120 mg (quantitative) of **38** as a white solid (recrystallized from CH_2Cl_2/hexanes): R_f 0.2 (8% MeOH:CH_2Cl_2); mp 168-169 °C; IR (KBr) 3401, 3134, 2973, 1710, 1669, 1613, 1572, 1480, 1368, 1331, 1313, 1252, 1120, 1055, 716, 654 cm^{-1}; ^{1}H NMR (300 MHz, CD_3OD) δ 1.42 (s, 9H), 2.19 (dt, J = 6.6, 7.2 Hz, 2H), 3.49 (t, J = 6.6 Hz, 2H), 4.30 (t, J = 7.2 Hz, 2H), 4.88(s, 2H), 8.12 (s, 1H), 8.22 (s, 1H); ^{13}C NMR (75.4 MHz, CD_3OD) δ 28.4, 28.5, 42.4, 48.6, 82.3, 120.1, 142.8, 150.5, 153.6, 157.3, 158.4; HRMS (FAB) calcd for $C_{13}H_{21}N_6O_3$ (MH^+) 309.1675, found 309.1676. Anal. Calcd for $C_{13}H_{20}N_6O_3$: C, 50.64; H, 6.54 N, 27.26. Found: C, 50.46; H, 6.44; N, 27.25.

General Procedure for Hydroxamic Acid Preparation. A methanolic solution of *O*-protected hydroxylamine adduct was charged with 15% $Pd(OH)_2$/C and 15% Pd/C and placed under hydrogen atmosphere at rt and 1 atm for 8-72 h, until reaction was complete as indicated by TLC analysis. The Pd/C species were filtered off and washed with MeOH. Due to the polar nature of the product, the hydroxamic acid was dry loaded onto a silica gel column and chromatographed. The yields were typically 75-80%.

***cis*-3(*S*)-(6-Amino-9*H*-purin-9-yl)-1(*R*)-*N*-[*N*-*tert*-butyloxycarbonylhydroxamino]cyclopentane (21).** Following the general procedure, amine **19** (300 mg, 0.71 mmol) was subjected to hydrogenation for 60 h. The hydroxamic acid was purified by column chromatography (silica gel; eluted with 7% MeOH/EtOAc) to afford 191 mg (80%) of hydroxamic acid **21** as an off white solid (recrystallized from MeOH/THF): R_f 0.25 (10% MeOH/EtOAc); mp 199-200 °C; IR (KBr) 3385, 3345, 3150, 2990, 2890, 1690, 1670, 1605, 1580, 1415, 1370, 1335, 1315, 1260, 1250, 1170, 1110, 1010, 805, 755 cm^{-1}; ^{1}H NMR (300 MHz, CD_3OD) δ 1.48 (s, 9H), 1.94-2.35 (m, 5H), 2.54 (ddd, J = 7.8,

7.8, 12.9 Hz, 1H), 4.73 (m, 1H), 4.89 (m, 1H), 8.19 (s, 1H), 8.27 (s, 1H); ^{13}C NMR (75.4 MHz, CD_3OD) δ 27.8, 28.6, 32.2, 35.5, 55.7, 59.1, 82.4, 120.3, 140.7, 150.7, 153.5, 157.3, 158.4, HRMS (FAB) calcd for $C_{15}H_{23}N_6O_3$ (MH^+) 335.1832, found 335.1834. Anal. Calcd for $C_{15}H_{22}N_6O_3$: C, 53.88; H, 6.63; N, 25.13. Found: C, 53.87; H, 6.54; N, 25.39.

***cis*-3(*S*)-(6-Amino-9*H*-purin-9-yl)-1(*R*)-*N*-[*N*-acetylhydroxamino]cyclopentane (8).** Following the general procedure, protected hydroxylamine **24** (70 mg, 0.20 mmol) was hydrogenated for 8 h. The hydroxamic acid was chromatographed (silica gel; eluted with 1:8 $MeOH/CH_2Cl_2$) to afford 44 mg (80%) of hydroxamic acid **8** as an off white solid (recrystallized from MeOH/THF): R_f 0.15 (1:8 $MeOH/CH_2Cl_2$); mp 165 °C (decomposition); IR (KBr) 3549, 3116, 2960, 1677, 1637, 1607, 1574, 1475, 1444, 1414, 1317, 683 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 1 drop DMSO-d_6) 1.98 (m, 1H), 2.14 (s, 3H), 2.25 (m, 4H), 2.57 (dt, J = 8.1, 13.8 Hz, 1H), 4.92 (m, 1H), 5.14 (m, 1H), 6.76 (s, 2H), 8.08 (s, 1H), 8.25 (s, 1H), 9.92 (bs, 1H); ^{13}C NMR (75.4 MHz $CDCl_3$, 1 drop DMSO-d_6) δ 19.9, 26.1, 30.7, 33.7, 52.9, 53.2, 118.8, 137.9, 148.3, 151.2, 155.1, 170.1; HRMS (FAB) calcd for $C_{12}H_{17}N_6O_2$ (MH^+) 277.1413, found 277.1399. Anal. Calcd for $C_{12}H_{18}N_6O_3$: C, 48.97; H, 6.16; N, 28.55. Found: C, 48.84; H, 6.16; N, 28.52.

5(*R*)-(6-Amino-9*H*-purin-9-yl)-1(*S*),2(*R*)-dihydroxy-3(*S*)-*N*-[*N*-*tert*-butyloxycarbonylhydroxamino]cyclopentane (28). Method A: Following the general hydrogenation procedure, diol **27** (250 mg, 0.55 mmol) was subjected to hydrogenation for 60 h. The hydroxamic acid was purified by column chromatography (silica gel; eluted with 12% $MeOH/CH_2Cl_2$) to afford 149 mg (75%) of hydroxamic acid **28** as an off white solid.

Method B: Hydroxamic acid **28** was also prepared from diol **32** following the general amination conditions, in which 450 mg (0.865 mmol) of **32** was treated with ammonia to afford 315 mg (quantitative) of hydroxamic acid **28** as a white solid (recrystallized from MeOH/THF): R_f 0.15 (12% MeOH/EtOAc); mp 170 °C (decomposition); IR (KBr) 3344, 3210, 3025, 2974, 1656, 1641, 1600, 1482, 1410, 1369, 1333, 1251, 1164, 1128, 1102 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6,) δ 1.41 (s, 9H), 2.23 (m, 2H), 4.04 (bs, 1H), 4.30 (m, 2H), 4.61 (m, 1H), 4.94 (m, 1H), 5.13 (m, 1H), 5.45 (bs, 1H), 7.20 (s, 2H), 8.11 (s, 1H), 8.15 (s, 1H), 9.36 (s, 1H); ^{13}C NMR (75.4 MHz, DMSO-d_6) δ 28.0, 28.5, 58.2, 62.3, 71.5, 73.7, 79.8, 119.2, 139.6, 149.7, 152.2, 155.9, 156.0; HRMS (FAB) calcd for $C_{15}H_{23}N_6O_5$ (MH^+) 367.1730, found 367.1768.

General Procedure for Boc-Deprotection. A solution of acetylchloride and MeOH (2:3) were premixed at 0 °C and stirred for 45 min. The solution was allowed to warm to rt and stir for an additional 30 min. From this solution, an aliquot was taken and added to Boc-hydroxamic acid at 0 °C. The solution became homogenous over time. After 10 min of stirring, the solution was allowed to warm to rt, and stirred for an additional 20 min (or until complete by TLC analysis). If the product had not precipitated at this point, THF was added until the hydroxylamine HCl salt precipitated from the solution. The solvent was removed *in vacuo* to afford white solids which were washed with either a 1:1 MeOH:Et_2O solution or Et_2O and decanted off. The yields were typically quantitative.

***cis*-3(*S*)-(6-Amino-9*H*-purin-9-yl)-1(*R*)-*N*-[hydroxamino]cyclopentane hydrochloride (7).**

Following the general procedure, 100 mg (0.31 mmol) of compound **21** was subjected to methanolic HCl at 0 °C. The reaction proceeded for 30 min, when **7** began to precipitate out of the solution. The reaction was terminated, and MeOH was decanted off. The product was triturated with Et_2O, affording 71 mg of **7** as a white solid (quantitative): mp 100 °C (decomposition); IR (KBr) 3060, 2890, 2800-2400, 1690, 1605, 1595, 1500, 1435, 1395, 1290, 900, 780, 720, 640 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 2.00-2.66 (m, 5H), 2.85 (ddd, 8.1, 8.1, 13.8 Hz, 1H), 4.04 (bs, 1H), 5.14 (m, 1H), 8.55 (s, 1H), 8.87 (s, 1H), 9.00 (bs, 1H), 9.70 (bs, 1H), 11.91 (bs, 1H), 11.99 (bs, 1H); ^{13}C NMR (75.4 MHz, DMSO-d_6) δ 25.1, 30.4, 33.7, 54.1, 59.2, 118.0, 142.4, 144.5, 148.4, 150.2; HRMS (FAB) calcd for $C_{10}H_{15}N_6O$ (MH^+) 235.1307, found 235.1327.

5(*R*)-(6-Amino-9*H*-purin-9-yl)-1(*S*),2(*R*)-dihydroxy-3(*S*)-*N*-[hydroxamino]cyclopentane hydrochloride (9). Following the general procedure, 100 mg (0.272) of compound **28** was subjected to a mixture of acetyl chloride:MeOH:THF (1:2:2) at 0 °C. The reaction proceeded for 30 min, when **9** began to precipitate out of the solution. The reaction was terminated and worked up as usual affording 72 mg of HCl salt **9** as a white solid (quantitative): mp 140 °C (decomposition); IR (KBr) 3506, 3338, 3077, 1689, 1602, 1420, 1235, 1120, 687 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 2.23 (ddd, J = 7.5, 10.5, 14.1 Hz, 1H), 2.63 (overlapping ddd, J = 8.4, 8.4, 14.1 Hz, 1H), 3.60 (m, 1H), 4.20 (d, J = 5.4 Hz, 1H), 4.69 (dd, J = 5.4 Hz, 1H), 4.85 (m, 1H), 8.48 (s, 1H), 8.75 (s, 1H); ^{13}C NMR (75.4 MHz, DMSO-d_6) δ 27.9, 57.7, 63.2, 69.1, 74.1, 118.2, 142.5, 144.8, 148.9, 150.2; HRMS (FAB) calcd for $C_{10}H_{15}N_6O_3$ (MH^+) 267.1206, found 267.1206.

5(*R*)-(6-Cyclopropylamino-9*H*-purin-9-yl)-1(*S*),2(*R*)-dihydroxy-1(*S*)-*N*-[hydroxamino]cyclopentane hydrochloride (10). Following the general procedure, 150 mg (0.38 mmol) of compound **33** was subjected to methanolic HCl at 0 °C then allowed to warm to rt. The reaction proceeded for 30 min, when **10** began to precipitate out of the solution. The reaction was terminated and worked up as usual affording 116 mg of HCl salt **10** as a white solid (quantitative): mp 140 °C (decomposition); IR (KBr) 3346, 2294, 1676, 1593, 1526, 1408, 1335, 1230, 1134, 1085, 778, 643 cm^{-1}; ^1H NMR (300 MHz, CD_3OD) δ 0.98 (m, 2H), 1.12 (m, 2H), 2.55 (ddd, J = 8.7, 10.8, 13.5 Hz, 1H), 2.79 (ddd, J = 8.1, 8.1, 13.5 Hz, 1H), 2.90 (m, 1H), 3.85 (ddd, J = 3.3, 8.5, 8.5 Hz, 1H), 4.45 (dd, J = 3.1, 5.7 Hz, 1H), 4.67 (dd, J = 5.7, 8.5 Hz, 1H), 4.96 (m, 1H), 8.47 (s, 1H), 8.49 (s, 1H); ^{13}C NMR (75.4 MHz, DMSO-d_6) δ 7.2, 24.0, 28.2, 57.7, 63.2, 69.2, 74.3, 118.4, 142.3, 144.8, 147.9, 149.9; HRMS (FAB) calcd for $C_{13}H_{18}N_6O_3$ (MH^+) 307.1519, found 307.1515.

***cis*-4(*R*)-(6-Amino-9*H*-purin-9-yl)-1(*S*)-*N*-[hydroxamino]cyclopent-2-ene hydrochloride (11).** Following the general procedure, 200 mg (0.615 mmol) of Boc-protected hydroxylamine analog **30** was subjected to methanolic HCl at 0 °C. The reaction was allowed to warm to rt and proceeded for 20 min when HCl salt **11** began to precipitate out of the solution. The reaction was worked up as usual affording 143 mg (quantitative) of **11** as a white solid: mp 160 °C (decomposition); IR (KBr) 3115, 1725, 1686, 1597, 1499, 1413, 1366, 1220, 1172, 1080, 714 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 2.19 (ddd, J = 5.0, 5.0, 14.7 Hz, 1H), 3.06 (m, 1H), 4.55 (s, 1H), 5.75 (m, 1H), 6.29 (d, J = 5.4 Hz, 1H), 6.37 (d, J = 5.4 Hz,

1H), 8.58 (s, 1H), 8.61 (s, 1H), 9.00 (bs, 1H), 9.66 (bs, 1H), 12.01 (bs, 2H); ^{13}C NMR (300 MHz, DMSO-d_6) + 2 drops CD_3OD) δ 32.6, 58.1, 64.7, 118.0, 130.7, 135.9, 142.4, 145.1, 148.0, 150.4; HRMS (FAB) calcd for $C_{10}H_{13}N_6O$ (MH^+) 233.1151, found 233.1158.

***cis*-4(*R*)-(6-Cyclopropylamino-9*H*-purin-9-yl)-1(*S*)-*N*-[hydroxamino]cyclopent-2-ene hydrochloride (12).** Following the general procedure, 200 mg (0.55 mmol) of Boc-protected hydroxylamine analog **31** was subjected to a 2:3 ratio of acetylchloride:MeOH at 0 °C then allowed to warm to rt. The reaction proceeded for an additional 20 min upon which HCl salt **12** began to precipitate out of the solution. The reaction was worked up as usual affording 148 mg (quantitative) of **12** as a white solid: mp 172 °C (decomposition); IR (KBr) 3406, 3042, 2285, 1678, 1601, 1425, 769, 612 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.83 (m, 2H), 0.99 (d, J = 5.1 Hz, 2H), 2.21 (ddd, J = 5.1, 5.1, 14.7 Hz, 1H), 2.94 (bs, 1H), 3.08 (ddd, J = 9.0, 9.0, 14.7 Hz, 1H), 4.58 (bs, 1H), 5.78 (bs, 1H), 6.30 (m, 1H), 6.38 (m, 1H), 8.62 (s, 1H), 8.65 (s, 1H); ^{13}C NMR (75.4 MHz, DMSO-d_6) δ 7.1, 23.8, 32.6, 58.3, 64.7, 118.3, 130.8, 135.8, 142.4, 145.1, 146.9, 149.9; HRMS (FAB) calcd for $C_{13}H_{17}N_6O$ (MH^+) 273.1464, found 273.1461.

3-(6-Amino-9*H*-purin-9-yl)-*N*-[hydroxamino]propane hydrochloride (13). Following the general procedure, 100 mg (0.325 mmol) of compound **37** was subjected to methanolic HCl at 0 °C. The reaction was allowed to warm to rt and proceeded for 30 min, when **7** began to precipitate out of the solution. The reaction was terminated, and MeOH was decanted off. The product was triturated with Et_2O, affording 67 mg (quantitative) of **13** as a white solid: mp 135 °C (decomposition); IR (KBr) 3450, 3058, 1692, 1607, 1498, 1422, 1276, 1222, cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.23 (m, 2H), 3.11 (m, 2H), 4.40 (t, J = 6.9 Hz, 2H), 8.56 (s, 1H), 8.62 (s, 1H), 8.97 (bs, 1H), 9.67 (bs, 1H), 11.73 (bs, 2H); ^{13}C NMR (75.4 MHz, DMSO-d_6) δ 23.8, 41.3, 47.1, 118.0, 144.0, 144.6, 148.5, 150.1; HRMS (FAB) calcd for $C_8H_{13}N_6O$ (MH^+) 209.1151, found 209.1158.

3-(6-Cyclopropylamino-9*H*-purin-9-yl)-*N*-[hydroxamino]propane hydrochloride (14). Following the general procedure, 100 mg (0.287 mmol) of compound **38** was subjected to methanolic HCl at 0 °C. The reaction was allowed to warm to rt and proceeded for 30 min, when **14** began to precipitate out of the solution. The reaction was terminated, and MeOH was decanted off. The product was triturated with Et_2O, affording 71 mg of **14** as a white solid (quantitative): mp 189 °C (decomposition); IR (KBr) 3450, 3042, 1686, 1603, 1434, 1268, 772 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6 +3 drops CD_3OD) δ 0.83 (bs, 2H), 0.99 (m, 2H), 2.27 (m, 2H), 2.93 (bs, 1H), 3.14 (t, J = 6.6 Hz, 2H), 4.45 (t, J = 6.6 Hz, 2H), 8.58 (s, 1H), 8.67 (s, 1H); ^{13}C NMR (75.4 MHz, DMSO-d_6) δ 7.1, 23.8, 24.1, 41.4, 47.1, 118.1, 143.7, 145.0, 147.4, 149.9; HRMS (FAB) calcd for $C_{11}H_{17}N_6O$ (MH^+) 249.1464, found 249.1461.

ACKNOWLEDGMENTS

We gratefully acknowledge the NIH (AI 30988) for partial support of this research, and the Lizzadro Magnetic Resonance Research Center at Notre Dame for NMR facilities, as well as Dr. B. Boggess and N. Sevova for Mass Spectrometry facilities. M. J. Mulvihill also appreciated support from the University of Notre

Dame in the form of Nieuwland and Lubrizol fellowships. The authors would like to thank Joseph F. Miller for performing the brine-shrimp assays, Prof. Richard Taylor for many helpful conversations, Dr. M. Shang for the X-ray structure determination of compound **26**, and Maureen Wickham for assistance with the manuscript.

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