Synthesis of 8-Amino-3-deazaguanine via Imidazole Precursors. Antitumor Activity and Inhibition of Purine Nucleoside Phosphorylase

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8-Amino-3-deazaguanine (**15**), an analogue of both 3-deazaguanine (1) and 8-aminoguanine (**6**), an antitumor agent and a purine nucleoside phosphorylase (PNP) inhibitor, respectively, was synthesized from the ammonolysis of an imidazole precursor, methyl 2-(benzoylamino)-5-(cyanomethyl)-1*H*-imidazole-4-carboxylate (**13**). The requisite imidazole, methyl 2-(benzoylamino)-4-(methoxycarbonyl)-1*H*-imidazole-5-acetate (**11**), was prepared from the monoheterocyclic rearrangement of dimethyl 3-[(5-phenyl-1,2,4-oxadiazol-3-yl)amino]-2-pentenedioate (**10**) by NaH/DMF. Ammonolysis and subsequent dehydration of 11 provided the penultimate imidazole intermediate **13**. Its deprotected (NaOMe/100 °C) product, methyl 2-amino-5-(cyanomethyl)-1*H*-imidazole-4-carboxylate (**14**), was also converted to **15**. 8-Amino-3-deazaguanine, as its methanesulfonic acid (mesylate **7**), exhibited an inhibition constant (IC_{50}) of 9.9 μM against isolated mammalian PNP. It was a very weak inhibitor of T and B cell growth and did not enhance 2′-deoxyguanosine toxicity in the same cells. 8-Amino-3-deazaguanine mesylate was not significantly active in L1210 cells in vitro or L1210 leukemic mice. Thus, the amino group introduced in the 8-position of 3-deazaguanine enhances its PNP activity but diminishes its antitumor activity.

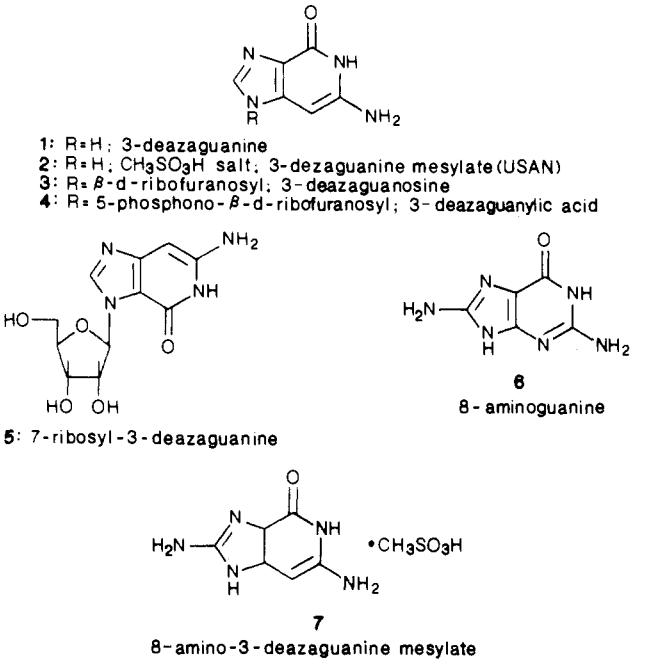
The synthesis and initial biological activity of 6-amino-1,5-dihydro-4*H*-imidazo[4,5-*c*]pyridin-4-one (3-deazaguanine, **1**, Scheme I), a potent guanine antipurine, and its metabolites, 6-amino-1,5-dihydro-1-β-D-ribofuranosyl-4*H*-imidazo[4,5-*c*]pyridin-4-one (3-deazaguanosine, **3**) and 6-amino-1,5-dihydro-1-(5-phosphono-β-D-ribofuranosyl)-4*H*-imidazo[4,5-*c*]pyridin-4-one (3-deazaguanylic acid, **4**), were first reported in 1975.[1] Following this report, 3-deazaguanine and 3-deazaguanosine have been shown by a number of laboratories to possess a variety of biological activities[2] including antitumor, antiviral, antibacterial, and antiparasitic activities. Recently, preclinical development of 3-deazaguanine as an antitumor agent was completed.[3] The treatment of cancer patients in phase 1 trials with 3-deazaguanine, formulated as its methanesulfonic acid salt (3-deazaguanine[4] mesylate, USAN, **2**), has begun.

The 7- and 9-β-D-ribofuranosyl derivatives of 3-deazaguanine possess rather diverse and interesting activities in that 3-deazaguanosine is a potent antileishmanial agent[5] and 7-β-D-ribofuranosyl-3-deazaguanine (**5**) possesses potent antibacterial activity against several Gram-negative strains in vivo without appreciable host toxicity.[6] The in vivo antibacterial activity of 7-β-D-ribofuranosyl-3-deazaguanine appears to be a result of its selective intracellular cleavage to 3-deazaguanine by an *Escherichia coli* purine nucleoside phosphorylase (PNP).[7] 3-Deazaguanosine was not a substrate for the same *E. coli* PNP.[7] On the other hand, 3-deazaguanosine has been shown to be a substrate for isolated mammalian PNP.[1a,8] 3-Deazaguanosine's activity in antitumor, antiviral, and parasitic test systems would further suggest its ready substrate activity for mammalian PNP. Thus, the requisite intermediate for biological activity of this class of antimetabolites appears to be the heterocyclic base 3-deazaguanine, which is a metabolic product from cleavage of both 7- and 9-ribosylated 3-deazaguanine by purine nucleoside phosphorylases.

The discovery of PNP inhibitors as well as nucleosides that are resistant to cleavage is of considerable current interest in immunodevelopment and purine nucleoside analogue metabolism.[9] 8-Aminoguanine (**6**) is the standard PNP inhibitor.[10]

Since 7- and 9-ribosylated 3-deazaguanines require PNP-mediated deribosylation for activity, we were interested in the 3-deaza modification of 8-aminoguanine as a potential inhibitor and/or substrate of purine nucleoside phosphorylases. Furthermore, the synthesis of the 8-amino

Scheme I



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modification of 3-deazaguanine was considered an important synthetic target in our ongoing program to develop the structure–activity relationship (SAR) of 3-deazaguanine as an antitumor agent.[11] Thus, we describe in this paper the synthesis of 8-amino-3-deazaguanine methanesulfonic acid salt (mesylate 7) and its initial antitumor screening and inhibition of PNP.

Chemistry: Synthetic Strategy/Discussion

The only known route to 3-deazaguanines and 3-deazaguanosines is the base- or acid-catalyzed cyclization of imidazole precursors such as methyl 5-(cyanomethyl)-1*H*-imidazole-4-carboxylate, -carbonitrile,[2,11] or -carboxamide as we have initially reported.[1,11] Ring,[12] peripheral,[2,11] and sugar[2,13] modifications of 3-deazaguanine and 3-deazaguanosine also have been prepared by this approach. We have continued to utilize this general approach for our synthesis of 8-amino-3-deazaguanine. Thus, the desired penultimate intermediate for the synthesis of 8-amino-3-deazaguanine would be methyl 2-amino-5-(cyanomethyl)-1*H*-imidazole-4-carboxylate (14) (Scheme II). Unfortunately, 2-aminoimidazoles are a sparsely known class of heterocycles that lack general routes for their synthesis.[14]

Our initial efforts were to effect electrophilic substitution in the 2-position of an appropriately 4,5-disubstituted imidazole to provide imidazoles with functionality in the 2-position, such as nitro, phenylazo, or bromo groups, that could be converted to the requisite 2-aminoimidazole 14 (Scheme II). However, our attempts to nitrate, diazo couple, or brominate in the 2-position of methyl 5-(cyanomethyl)-1*H*-imidazole-4-carboxylate (16) were not successful. We also were not successful in our attempts to displace the 2-chloro or 2-(benzylsulfonyl) group from methyl 2-chloro- or methyl 2-(benzylsulfonyl)-5-(cyanomethyl)-1*H*-imidazole-4-carboxylate (17) with ammonia or hydrazine at quite strenuous conditions.[11c]

Another conceivable approach that would directly provide 2-aminoimidazoles is the cyclization of α-amino or α-halo ketones with guanidine. Unfortunately, the treatment of dimethyl 2-chloro- or dimethyl 2-amino-3-oxopentanedioate (18) with guanidine did not afford the desired aminoimidazole 14. Other types of cyclization reactions may lead to 2-aminoimidazoles, but our need for a one-carbon and a two-carbon fragment in the 4- and 5-positions complicates these approaches.

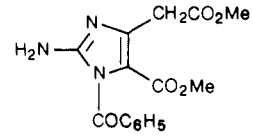
Table I. Purine Nucleoside Phosphorylase Inhibition (IC_{50}, μM)

8-amino-3-deazaguanine mesylate (7)	9.9
8-aminoguanine (6)	0.6 (0.2–1.2)[a]
3-deazaguanine (1)	77
8-aminoguanosine	1.4 (17)[a]
3-deazaguanosine (3)	>300
formycin B	102[a]
guanine	5[a]

[a] Published values in ref 9.

The approach that was successful in providing an appropriately substituted 2-aminoimidazole that could be converted to the desired penultimate imidazole was the base-catalyzed cyclization/ring-opening rearrangement sequence with the enamine adduct 10 of 5-phenyl-1,2,4-oxadiazol-3-amine (8) and dimethyl 3-oxopentanedioate (9) (Scheme II). This reaction, catalyzed by NaH/DMF, provided methyl 2-(benzoylamino)-4-(methoxycarbonyl)-1*H*-imidazole-5-acetate (11) in 65% yield. The general applicability of monoheterocyclic rearrangements to convert a heterocyclic ring into another heterocyclic ring system was reported by A. R. Katritzky's laboratory in 1967.[15] In that report, Katritzky et al. described the use of an oxygen or nitrogen nucleophile in the acyclic fragment to prepare triazoles or oxadiazoles. Subsequently, Ruccia et al. first described in 1974 the use of a carbon nucleophile in similar monoheterocyclic rearrangements;[16] 1,2,4-oxadiazole enamino ketones were converted by NaOEt/DMF to 2-(benzoylamino)-4,5-disubstituted-imidazoles. Recently, Sehgal and Agrawal reported[17] the synthesis of 2-(benzoylamino)-4,5-disubstituted-imidazoles by a similar monoheterocyclic rearrangement.

2-Amino-1-benzoyl-5-(methoxycarbonyl)-1*H*-imidazole-4-acetic acid methyl ester (20), an undesired isomer, which could conceivably arise from the carbanion attack on the 4-nitrogen atom rather than the 2-nitrogen atom of the 1,2,4-oxadiazole 10, did not form as determined by ^{1}H NMR and IR studies.



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Amination of imidazoledicarboxylate 11 with methanolic ammonia provided (carbamoylmethyl)imidazole 12 (Scheme II). This was subsequently dehydrated with $POCl_3$ to afford methyl 2-(benzoylamino)-5-(cyanomethyl)-1*H*-imidazole-4-carboxylate (13), which should serve as a penultimate intermediate to 8-amino-3-deazaguanine. The difference in the chemical shift ($\Delta\delta$ = 0.15) of the methylene group of imidazoledicarboxylate 11 on conversion to (cyanomethyl)imidazole 13 supports the cyanomethyl structure as shown rather than the undesired isomeric imidazole nitrile.[1,12d] Further data on the structure of (cyanomethyl)imidazole 13 was obtained by its deprotection with NaOMe/MeOH (160 °C) to provide methyl 2-amino-5-(cyanomethyl)-1*H*-imidazole-4-carboxylate (14) in 65% yield. The ^{1}H NMR of this compound exhibits a 2-proton resonance for the 2-amino group,

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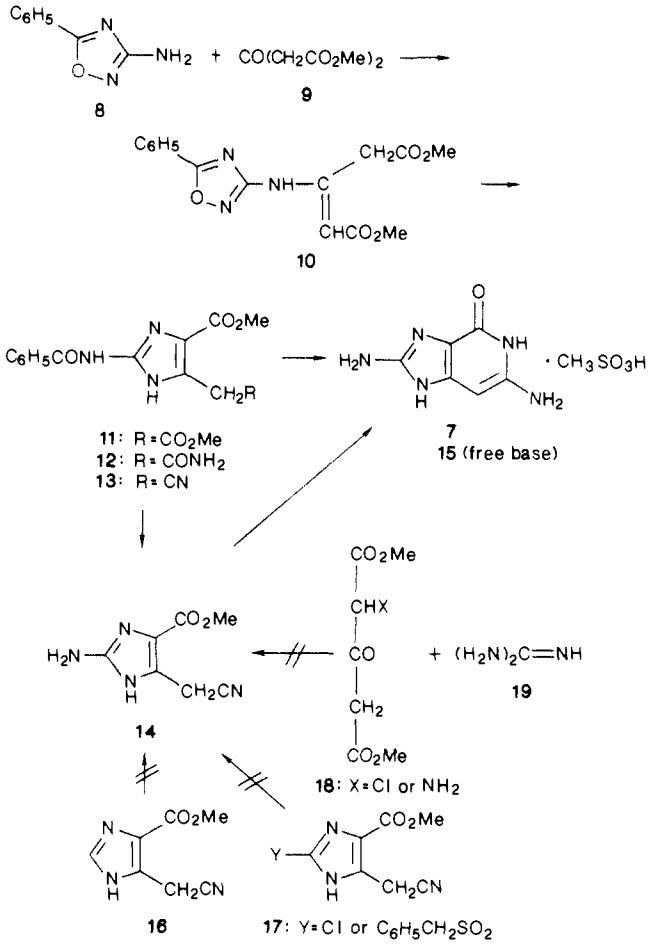
Scheme II



and there are two NH stretching bands corresponding to an aromatic amine in its IR spectrum.

(Cyanomethyl)imidazole **13** was cyclized with concomitant debenzoylation by being heated in liquid ammonia at 110 °C for 72 h to provide the desired 8-amino-3-deazaguanine (**15**) in 55% yield. The NMR spectrum of this material exhibited an aromatic amine resonance, two NH resonances, and one aromatic proton (3-position), which all were exchangeable with D_2O. The IR spectrum of 8-amino-3-deazaguanine does not exhibit an ester or nitrile group. Furthermore, a bathochromic shift from λ 280 to 310 was observed, which suggests a bicyclic structure.[1] Aminoimidazole **14** was also converted to 8-amino-3-deazaguanine by the reaction conditions described above.

8-Amino-3-deazaguanine, as its free base, has little aqueous solubility and thus was converted to the highly soluble, stable methanesulfonic acid salt (mesylate **7**).

Biological Studies

Purine Nucleoside Phosphorylase Activity. 8-Amino-3-deazaguanine mesylate (**7**, NSC-378064) was tested as an inhibitor of purine nucleoside phosphorylase. The enzyme assay was performed with use of a human erythrocyte lysate essentially as described by Fox et al.[18] Also tested in parallel for comparison purposes were 3-deazaguanine (**1**), 3-deazaguanosine (**3**), 8-aminoguanine (**6**), and 8-aminoguanosine. The enzyme-inhibition values (IC_{50}) of these compounds as well as those of formycin B and guanine are depicted in Table I. 8-Amino-3-deazaguanine mesylate is 15-fold less potent than 8-aminoguanine as an inhibitor of PNP but considerably more active than 3-deazaguanine, 3-deazaguanosine, and formycin B. Thus, the placement of an 8-amino group into 3-deazaguanine has significantly increased its PNP inhibitory activity but not enough to overcome the lack of a ring nitrogen in the 3-position of the purine ring system.

Table II. Human Lymphoblast Cytotoxicity

test substance	2′-deoxyguanosine[a]	IC_{50},[b] μM MOLT-4	MGL-8
8-amino-3-deazaguanine mesylate (**7**)	–	>100	>100
	+	>100	>100
3-deazaguanine (**1**)	–	3.7	<1
	+	5.9	<1
8-aminoguanine (**6**)	–	>500	>500
	+	1.6	>500

[a] Test substances were evaluated in the absence or presence of 10 μM 2′-deoxyguanosine. [b] IC_{50} of test substances, defined as the concentration necessary to inhibit by 50% the uptake of [^{3}H]thymidine, as compared to control cultures.

Assay of Lymphoblast Toxicity. The cytotoxicity of the PNP substrate 2′-deoxyguanosine for human T lymphoblasts can be markedly enhanced by coaddition of 8-aminoguanosine to culture.[19] Cytotoxicity is readily determined by monitoring uptake of [^{3}H]thymidine. 8-Amino-3-deazaguanine mesylate, 8-aminoguanine, and 3-deazaguanine were examined as inhibitors of T (MOLT-4) and B (MGL-8) cell growth with and without coadministration of a no-effect concentration of 2′-deoxyguanosine (10 μM). When tested alone, 8-amino-3-deazaguanine mesylate was a weak inhibitor of T and B cells (Table II) (IC_{50} > 100 μM). 8-Amino-3-deazaguanine mesylate furthermore did not enhance the cytotoxicity of coadministered 2′-deoxyguanosine. 3-Deazaguanine, tested without 2′-deoxyguanosine, significantly inhibited MOLT-4 and MGL-8 cells (IC_{50} = 3.7 and <1.0 μM, respectively) but failed to potentiate the cytotoxicity of 2′-deoxyguanosine for MOLT-4 cells. 8-Aminoguanine alone was nontoxic for T and B cells (IC_{50} > 500 μM) but exhibited considerable synergy with 2′-deoxyguanosine for MOLT-4 cells (IC_{50} = 1.6 μM) and no synergism in MGL-8 cells.

Antitumor Activity. 8-Amino-3-deazaguanine mesylate (**7**, NSC-378064) was not active in in vitro L1210 leukemia cells (ID_{50} > 1 × 10^{-4} M). In comparison, the IC_{50} values of 8-aminoguanine and 3-deazaguanine were >1 × 10^{-4} M and 1 × 10^{-6} M, respectively.[20] 8-Amino-3-deazaguanine mesylate, administered intraperitoneally (ip) in doses of 50, 100, and 200 mg/kg to L1210 leukemic mice, QD 1–5, did not provide an increase in life span of greater than 25%, the minimum value required for significant activity according to the NCI standard protocol.[21] 8-Aminoguanine has not been reported to have antitumor activity. 3-Deazaguanine exhibited a percent ILS of 63% at a dose of 80 mg/kg (QD 1–9).[22]

Conclusions

8-Amino-3-deazaguanine mesylate is a weak inhibitor of human PNP. Its PNP inhibitory activity also did not enhance coadministered 2′-deoxyguanosine toxicity in T or B cells. The IC_{50} value of 8-amino-3-deazaguanine mesylate in L1210, MOLT-4, and MGL-8 cells in vitro was

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>100 μM, and it did not increase the life span of L1210 leukemic mice. These data suggest that 8-amino-3-deazaguanine mesylate was not metabolized to a nucleotide level as is the case with 3-deazaguanine. The placement of an amino group in the 8-position of 3-deazaguanine and guanine allows greater binding to PNP than the parent heterocycle, but this substitution apparently prevents metabolism of the compound to toxic nucleotides. Thus, the introduction of an 8-amino group into 3-deazaguanine does not provide better antitumor activity than its parent heterocycle, and the removal of the ring nitrogen in the 3-position of 8-aminoguanine does not provide a more potent PNP inhibitor than its parent heterocycle.

Since the ribofuranosyl prodrug modification of 8-aminoguanine and 3-deazaguanine is a less active PNP inhibitor[9] and antitumor agent[3] than its respective bases, we have not considered, as an extension of this work, the more difficult synthesis of 8-amino-3-deazaguanosine.

Experimental Section

Melting points were determined on a Thomas-Hoover apparatus and are uncorrected. Mass spectra were determined on a Finnigan 4000 mass spectrometer with INCOS 2300 data system using direct introduction, electron impact at 70 eV and 150 °C. ^{1}H NMR spectra were obtained at 200 MHz with use of a Varian XL-200 or at 90 MHz with use of a Varian EM-390 with tetramethylsilane as an internal standard. The presence of exchangeable protons was confirmed by the addition of deuterium oxide. UV spectra were obtained on a Cary C118 UV/vis spectrophotometer. All compounds had infrared spectra (potassium bromide) consistent with their structures as determined on a Nicolet 205X FT/IR. Elemental analyses were determined by the microanalytical laboratory of this department. TLC was performed with use of E. Merck silica gel 60 F-254 precoated glass plates (0.25 mm). Flash column chromatography was effected with use of E. Merck silica gel 60, 230–400 mesh. Regular column chromatography was effected with use of E. Merck silica gel 60, 70–230 mesh.

Dimethyl 3-[(5-Phenyl-1,2,4-oxadiazol-3-yl)amino]-2-pentenedioate (10). A mixture of 5-phenyl-1,2,4-oxadiazol-3-amine[23] (**8**, 2.0 g, 12.4 mmol), dimethyl 3-oxopentanedioate (**9**, 2.16 g, 12.4 mmol), and *p*-toluenesulfonic acid (200 mg, 1.0 mmol) in toluene (25 mL) was heated at reflux for 24 h with continuous water removal via a Dean–Stark trap. The reaction mixture was cooled in an ice bath and the tan product collected. Recrystallization from ethyl acetate afforded **10** (1.25 g, 32%) as a white solid: mp 159–163 °C (after drying at 25 °C (20 torr) for 24 h); IR (KBr) 1640 (s) (C=C), 1675 (s) (CO_2Me), 1733 (s) (CO_2Me) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.7 (s, 3, CH_3), 3.75 (s, 3, CH_3), 3.79 (s, 3, CH_2), 5.0 (s, 1, C=CH), 7.5 (m, 3, Ar H), 8.0 (m, 2, Ar H), 11.0 (br s, 1, NH). Anal. ($C_{15}H_{15}N_3O_5$, 317.29) C, H, N.

Methyl 2-(Benzoylamino)-4-(methoxycarbonyl)-1*H*-imidazole-5-acetate (11). Enamine **10** (210 g, 660 mmol) was added portionwise with stirring to a mixture of sodium hydride (31.7 g, 50% mineral oil, 660 mmol) in *N*,*N*-dimethylformamide (1 L). The mixture was stirred for 1 h and then poured into a mixture of water/ice (~4 L) and acetic acid (60 mL). The aqueous layer was decanted from the amorphous product and extracted with ethyl acetate (1 L). The organic layer was added to the amorphous solid and slurried to give crude **11**. This material was triturated three times each with 1.5 L of acetonitrile. The combined filtrates were concentrated under reduced pressure to a volume of 1.5 L and cooled. Imidazole **11** was obtained as a white solid (158 g, 75%) after filtration and drying at 50 °C (20 torr) for 6 h: mp 186–190 °C; IR (KBr) 1591 (s) (amide II), 1695 (s) (amide I), 1715 (s) (CH_2CO_2Me), 1740 (m) (CO_2Me) cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 3.5 (s, 3, CH_3), 3.6 (s, 3, CH_3), 3.9 (s, 2, CH_2), 7.3–7.5 (m, 3, Ar H), 7.8–8.0 (m, 2, Ar H), 11.8 (br d, 2, NH's). Anal. ($C_{15}H_{15}N_3O_5$, 317.29) C, H, N.

Methyl 5-(2-Amino-2-oxoethyl)-2-(benzoylamino)-1*H*-imidazole-4-carboxylate (12). A solution of **11** (248 g, 780 mmol) in MeOH (3.75 L) saturated with ammonia at 0 °C was stirred at room temperature for 3 days while a stream of ammonia was passed into the solution via a fritted inlet tube. The precipitate was collected, washed sparingly with methanol, washed well with ether, and dried at 50 °C (20 torr) to yield **12** (174 g, 74%) as a white solid: mp 250–253 °C; IR (KBr) 1582 (s) (amide II), 1669 (s) (amide I), 1720 (s) (CO_2Me) cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 3.7 (s, 3, OCH_3), 3.75 (s, 2, CH_2), 7.0 (s, 1, NH), 7.3–7.6 (m, 4, Ar H, NH), 8–8.1 (m, 2, Ar H), 12.0 (br s, 2, $CONH_2$). Anal. ($C_{14}H_{14}N_4O_4$, 302.23) C, H, N.

Methyl 2-(Benzoylamino)-5-(cyanomethyl)-1*H*-imidazole-4-carboxylate (13). A mixture of **12** (44.6 g, 147 mmol) and phosphoryl chloride (350 mL) was refluxed with stirring for 2 h. The reaction solution was concentrated under reduced pressure, and the residue was dissolved in chloroform (50 mL) and poured onto ice with stirring. The mixture was neutralized with concentrated NH_4OH. The precipitated product was collected, washed well with water, and dried at 50 °C (20 torr) to give **13** (23.7 g, 57%): mp 222–225 °C; IR (KBr) 1591 (s) (amide II), 1685 (amide I), 1714 (s) (CO), 2264 (w) (CN), 3340 (m) (NH), 3377 (m) (NH) cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 3.9 (s, 3, OCH_3), 4.1 (s, 2, CH_2CN), 7.4–7.7 (m, 3, Ar H), 8.0–8.1 (m, 2, Ar H), 9–10 (br d, 2, NH's). Anal. ($C_{14}H_{12}N_4O_3$, 284.27) C, H, N.

Methyl 2-Amino-5-(cyanomethyl)-1*H*-imidazole-4-carboxylate (14). A mixture of (benzoylamino)imidazole **13** (14 g, 50 mmol), sodium methoxide (2.7 g, 50 mmol), and methanol (400 mL) was heated in a 600-mL stainless steel pressure vessel at 160 °C for 1.5 h, cooled, and vented. The reaction suspension was heated to boiling and filtered hot to remove a dark precipitate, which was discarded. The filtrate was neutralized with a small amount of acetic acid and filtered again to remove additional dark material. The filtrate was evaporated in vacuo to provide an off-white powder, which was recrystallized (charcoal) from H_2O. Aminoimidazole **14** (5.85 g, 65%) was obtained as light tan microcrystals: mp 236–240 °C dec (after drying at 50 °C (0.1 torr) overnight); IR (KBr) 3460 (m) (NH), 1653 (s) (CO), 2260 (w) (CN), 3460 (m) (NH) cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 3.35 (s, 3, OCH_3), 3.97 (s, 2, CH_2CN), 6.87 (s, 2, NH_2), 11.10 (s, 1, NH). Anal. ($C_7H_8N_4O_2$, 180.16) C, H, N.

2,6-Diamino-1,5-dihydro-4*H*-imidazo[4,5-*c*]pyridin-4-one (15). A mixture of **13** (10 g, 35 mmol) and liquid ammonia (120 mL) was heated at 100 °C for 6 days in a 200-mL stainless steel Parr pressure vessel. The pressure vessel was cooled to room temperature, and the ammonia was allowed to evaporate. Final traces of ammonia were removed by applying a 20-torr vacuum on the vessel overnight. The dark residue was triturated six times with 100-mL portions of boiling water. The combined filtrates were decolorized with charcoal and concentrated to a 100-mL volume. On cooling, a light tan solid formed, which was collected by filtration, washed with H_2O, and dried at 0.1 torr over P_2O_5 to give 8-amino-3-deazaguanine (**15**; 1.05 g, 18%): mp >300 °C; IR (KBr) 1627 (s) (amide II), 1700 (amide I) cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 5.25 (s, 1, H_7), 5.28 (s, 2, NH_2), 6.35 (s, 2, NH_2), 10.3 (d, 2, NH's); UV λ_{max} (pH 2) 216 nm (ε 33 675), 256 (11 225), 312 (9586); MS, *m*/*e* 165 (M^+). Anal. ($C_6H_7N_5O$·0.6H_2O, 175.96) C, H, N, H_2O.

2,6-Diamino-1,5-dihydro-4*H*-imidazo[4,5-*c*]pyridin-4-one Methanesulfonate (7). A mixture of **15** (1.0 g, 5.8 mmol) and methanesulfonic acid (0.4 mL, 5.8 mmol) in H_2O (10 mL) was stirred for 1 h. The solution was decolorized with charcoal and lyophilized, and the residue was recrystallized from water to provide 8-amino-3-deazaguanine mesylate (**7**; 0.47 g, 31%): mp >300 °C (after drying at 65 °C (0.1 torr); IR (KBr) 1629 (s) (amide I), 1673 (s) (amide II) cm^{-1}. Anal. ($C_7H_{11}N_5O_4S$·0.25H_2O, 265.76) C, H, N, S.

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