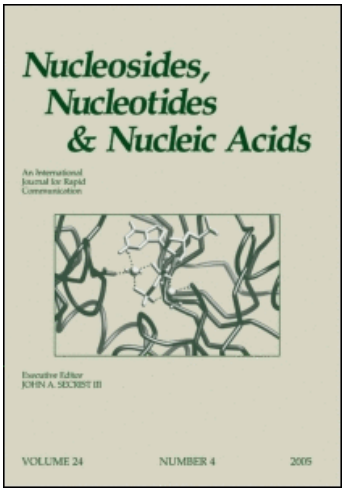

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Analogs of AICA- and *Iso*AICA Ribosides and Their Methylated Base Counterparts

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ANALOGS OF AICA- AND *ISO*AICA RIBOSIDES AND THEIR METHYLATED BASE COUNTERPARTS.

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ABSTRACT: A mild, convenient and efficient synthesis has been developed for imidazole-4-thiocarboxamide and imidazole-5-thiocarboxamide ribosides and the analogous selenocarboxamides. This methodology, *i.e.*, DMF saturated with H_2S or H_2Se, also converts the corresponding N-methylated bases to the corresponding amides. The imidazole-4(5)-selenocarboxamides were shown to be sensitive to base (pH 11) and were easily converted back to their cyano precursors. The kinetics of these reactions were determined and they indicate that the C5 amides were more reactive than their C4 analogs.

The reported chemotherapeutic activity of certain imidazole nucleosides such as Bredinin[1] (**1**) and 5-formamido-1-(2,3,5-tri-*O*-formyl-β-D-ribofuranosyl)imidazole-4-thiocarboxamide (**2**)[2] were of interest because of their structural similarity to AICAR (**3**), an imidazole nucleotide found in the purine *de novo* biosynthetic pathway. We have examined the functionalization of AICA riboside[3] in order to obtain imidazole ribosides **8**, **10**, and **12**. The corresponding isomeric nucleosides, **9**, **11**, and **13** (Figure 1) have also been synthesised to examine the effect, if any, of the position of the ribose ring on reactivity.

Two nucleosides which would be suitable for the desired conversions are those containing the cyano group at either the *C*4 or *C*5 position. 5-Amino-4-cyano-1-(β-D-ribofuranosyl)imidazole[4] (**4c**), 4-amino-5-cyano-1-(β-D-ribofuranosyl)imidazole[5b] (**5c**),

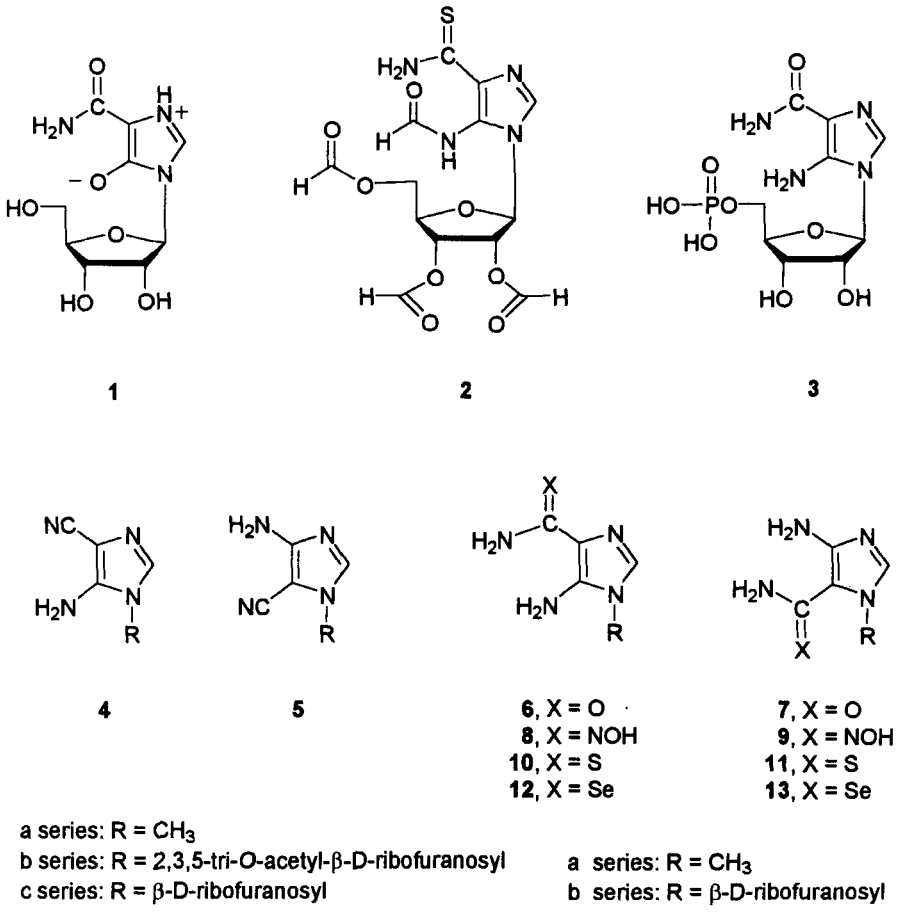

Figure 1

and their respective triacetates[5a] (**4b** and **5b**) are known and we selected these nucleosides and their methylated counterparts for starting materials. 4-Amino-5-cyano-1-methyl-imidazole (**5a**)[6] was prepared directly from 5-cyano-1-methyl-4-nitroimidazole[7] (**16**, Figure 2) using 5% Pd/C instead of Raney nickel. This change of catalyst eliminates the conversion of **5a** to its hydrochloride salt followed by neutralization to obtain the pure free base. In the case of 5-amino-4-cyano-1-methylimidazole (**4a**), a simple synthetic route did not exist. Shaw and Butler[8] have prepared this imidazole from 5-amino-1-methylimidazole-4-thiocarboxamide (**10a**).

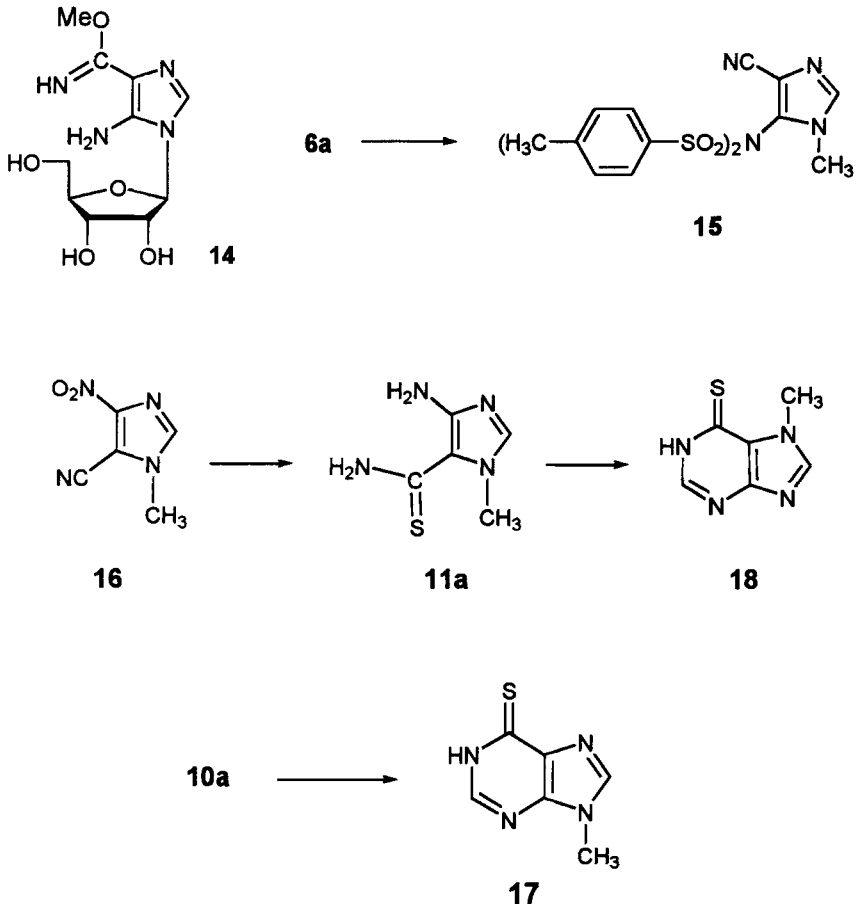

Figure 2

In order to improve the efficiency of this synthesis we attempted the dehydration of **6a** to **4a** using acid chlorides such as thionyl chloride in DMF[9] and $POCl_3$ in DMF[10] without success. Only tosyl chloride in pyridine furnished a product which possessed a cyano group (ir). ^1H NMR data and elemental analysis revealed that the product was 4-cyano-5-[di-(*p*-toluenesulfonyl)amino]-1-methylimidazole (**15**). Therefore, we abandoned this pathway and synthesized **4a** from **10a** by Shaw and Butler's original procedure. However, instead of using isopentyl formimidate hydrochloride and α-amino-α-cyanothioacetamide for the preparation **10a**, this imidazole was synthesized, in

good yield, directly from **6a** using P_2S_5 and picoline.[11] Spectroscopic (ir, UV, ^{1}H NMR) and elemental analyses as well as a subsequent conversion to **17**[12] using diethoxymethyl acetate (Figure 2), confirmed the structure of **10a**. Treatment of **10a** with mercuric chloride and methylamine afforded **4a.**[13]

Brown and coworkers[14a] have prepared the carboxamidoxime **9a** by reacting **5a** with hydroxylamine.[15] They have also prepared the nucleoside **8b** by hydrolyzing adenosine-1*N*-oxide with 1M sodium hydroxide.[14b] However, these compounds were poorly characterised. Using Brown's procedure, the carboxamidoximes **8a,b** and **9a,b** were synthesized in good yield from the respective cyano precursors.

For the synthesis of thiocarboxamides **10a,b** and **11a,b** and selenocarboxamides **12a,b** and **13a,b** the only relevant prior methodology involved reacting the appropiate cyano derivatives, with methanolic KOH saturated with H_2S, in a closed, steel reaction vessel at 100 °C.[16,17] We sought milder reaction conditions which would provide a convenient and efficient route for the preparation of the thiocarboxamide as well as the selenocarboxamide functional groups. It was found that by saturating a dry DMF and diethylamine solution containing the appropriate cyano derivative, with either H_2S or H_2Se at –10 to –20 °C, followed by heating at approximately 55 °C furnished the desired functional group. This straight forward methodology afforded **10a,b**, **11a,b**, **12a,b** and **13a,b** consistently in good yield. Notably, 5-cyano-1-methyl-4-nitroimidazole (**16**)[7] provided **11a** in one step. Thus, under these reaction conditions the nitro group is also reduced. It was found that **13a** and **13b** were extremely sensitive to a pH 11 solution. The nucleoside **13b** was converted to **5c** at 25 °C with an approximate half-life ($t_{1/2approx}$) of 36 minutes whereas the nucleoside **12b** had a $t_{1/2approx}$ at 25 °C of 571 minutes (see Figure 3) for the conversion of **4c.** This 16-fold difference in reactivity between **12b** and **13b** is an excellent example that functional groups on the C5 position of the 4-aminoimidazole ring and adjacent to a functionalized N1 position, *e.g.*, a β-**D**-ribofuranosyl moiety, are more reactive than their C4 counterparts. This corroborates an earlier report that 7-β-**D**-ribofuranosylpurines hydrolyze faster under acid conditions than the 9-β-**D**-ribofuranosypurines.[18].

The iminoether **14** was synthesized from **4b** according to the published procedure.[19] This method involved dissolving **4b** in dry methanol and then saturating this solution with HCl at 0 °C. This saturated solution was allowed to stand at 0 °C for 24 hrs. We

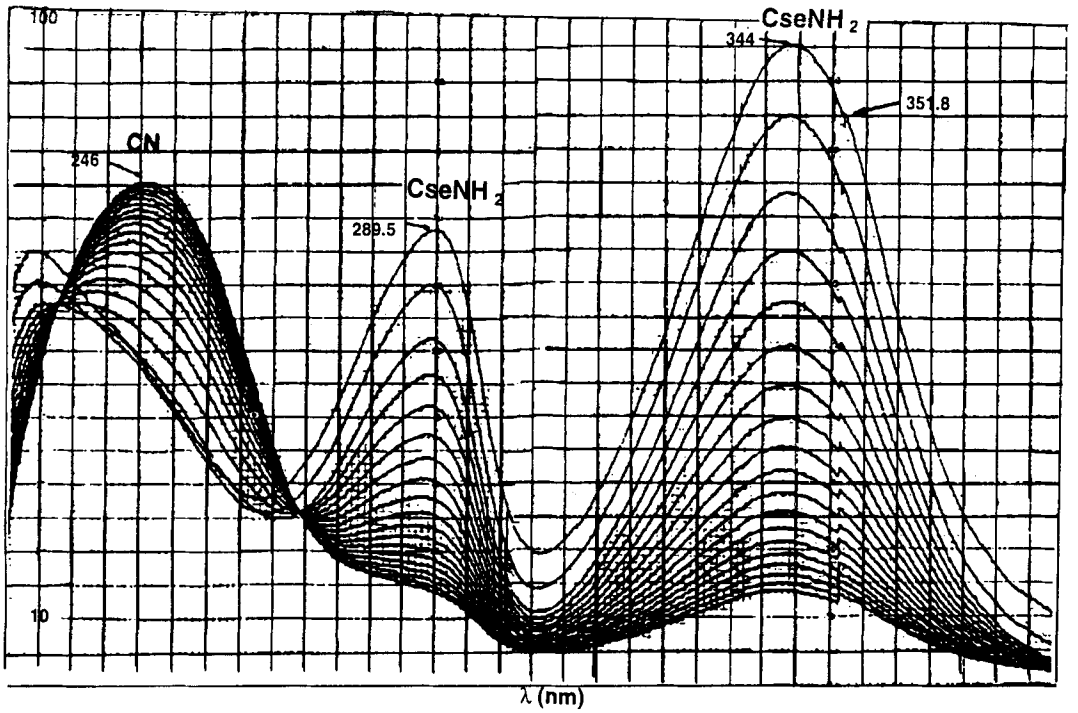

FIGURE 3. The conversion of **12b** into **4c** at 25 °C. The kinetics were run on a Beckman Acta CIII spectrophotometer at 1 h intervals. The glitch at 351.8 nm is the result of the automatic lamp change. The $t_{1/2approx}$ for this conversion is 571 min. This value takes into consideration the mixing time and placement of the pH 11 solution into the cell.

have included the preparation of this nucleoside in this paper as the reaction procedure was slightly modified and extra physicochemical data are provided (see Table 1). It is worth noting that a variety of methods[20] were tried for the conversion of either **4c** or **5c** to their respective iminoethers and all met with failure. It appears that for these imidazole nucleosides, the triacetates, *i.e.*, **4b** and possibly **5b**, facilitate the success of this reaction.

Experimental

Melting points were determined with a Thomas-Hoover apparatus and are uncorrected. ^{1}H NMR spectra were recorded on an EM-390-MHz spectrometer using DMSO-d_6 as solvent, and chemical shifts are expressed as δ values referenced to TMS. Optical rotations were measured on a Perkin-Elmer Model 141 automatic digital readout polarimeter using a thermostated cell. UV absorption spectra were recorded with a

TABLE 1. Spectral data for imidazole nucleosides and their model methyl analogs.

Compd.	λ_{max}/nm ($\varepsilon \times 10^{-3}$)			^{1}H NMR[a]					
	pH 1	MeOH	pH 11	C2*H*	C*H*$_3$	H1'($J_{1'}$-$J_{2'}$)	N*H*$_2$	N*H*$_2$	O*H*
4a[b]	253 (7.66) 233.5 (9.49)	245 (10.92)	243.5 (10.50)	7.12	3.40		6.08		
4c[c]	258sh (10.92) 238.5 (10.52)	247.5 (11.99)	246 (11.51)	7.36		5.48 (6)[d]	6.28		
5a[e]	257.5 (8.78) 238.5 (10.52)	264.5 (9.20) 227.5 (4.84)	258 (9.81)	7.43	3.57		5.76		
5c[f]	262.5 (7.47)	263 (9.20)	267 (9.03)	7.78		5.47 (5.6)[d]	5.91		
8a	278 (9.45)	258 (10.29)	255 (9.31)	6.94	3.35		5.19	5.19	8.66
8b	279.5 (9.85)	258 (10.39)	255 (9.68)	7.32		5.47 (6)[d]	5.36	5.36	5.36
9a	272 (6.66)	264 (7.37) 230 (5.69)	255 (7.70) 234.5 (7.59)	7.23	3.64		4.48	5.53	9.44
9b	273 (5.66)	269 (6.80) 230 (8.94)	260 (6.46) 235 (8.63)	7.72		5.83 (5)[d]	5.62	5.62	5.62
10a	326 (16.31) 279.5 (10.84) 251.5sh (5.87)	329 (17.78) 272.5 (10.84) 244 (5.69)	328 (16.68) 268 (10.78) 242 sh (6.19)	7.24	3.46		7.17	8.36	
10b[g]	326.5 (16.90) 278 (11.47) 255.5 sh (8.59	330 (17.09) 274 (10.09) 246.5 (6.36)	328.5 (16.70) 271 (11.08) 242 (8.43)	7.38		5.51(6.5)	7.33	8.24	
11a	324.5 (10.98) 280 (9.76)	342.5 (12.86) 283.5 (9.42)	339 (12.06) 279.5 (9.87)	7.52	3.75		6.76	8.22	
11b	325 (11.58) 282.5 (11.52)	342 (12.92) 285.5 (10.34)	339 (12.43) 281.5 (11.36)	7.88		5.66 (6.75)	7.09	8.29	
12a	349 (15.25) 296.5 (12.82)	347.5 (18.28) 292 (12.76) 244.5 sh (5.93) 222.5 (14.71)	343 (17.49) 289 (12.33) 226 (13.51)	7.15	3.42		7.38	8.70	
12b	348 (12.53) 293 (9.80)	349 (15.19) 292.5 (10.70) 249 sh (5.72) 223 (13.78)	344 (15.35) 289.5 (10.99) 229 (10.44)	7.43		5.56 (6.5)[d]	7.71	8.80	
13a	351.5 (11.33) 298.5 (10.48)	364.5 (12.59) 306.5 (10.01) 255.5 sh (4.87)	357.5 (11.13) 255 sh (6.91) 302 (8.31) 231 (9.24)	7.39	3.70		6.98	8.44	
13b	352 (10.76) 300.5 (9.12)	363 (13.33) 255 sh (2.99) 307.5 (10.89)	357 (9.15) 257 sh (7.45) 303 (6.75) 232 (8.54)	7.88		5.59 (6.75)[d]	7.44	8.69	
14	295 236	300.5 238.5	255	8.90	3.07	5.75 (4.0)	7.60[h]	7.60[h]	
15[i]	239 (28.35)	238 (29.67)	258.5sh (10.46) 229.5 (24.74)	8.11	3. 32 2.48[j]		7.53[k]	7.74[k]	

[a] In DMSO-d_6, J in Hz.. [b] IR(KBr) 2203 cm^{-1}(CN). [c] $[\alpha]_D^{25}$ −56.1° (c = 0.9, H_2O), IR(KBr) 2212 cm^{-1}(CN). [d] DMSO-$_{d6}$/D_2O. [e] IR(KBr) 2212 cm^{-1} (CN). [f] $[\alpha]_D^{25}$ −36° (c = 0.98, H_2O), IR(KBr) 2203 cm^{-1}(CN). [g] lit.[16] λ_{max} (pH 1) 327 (15.40), 282 (8.90); (pH 13) 330 (16.50), 271.5 (10.20). [h] =N*H*, N*H*$_2$. [i] IR(KBr) 2257 cm^{-1}(CN). [j] $SO_2C_6H_4$-C*H*$_3$. [k] Signals for the $AB_{quartet}$.

Beckman Acta CIII spectrophotomer. The conversions of the selenocarboxamide analogs to their respective cyano derivatives were conducted with this instrument set in the repetitive scan-mode using a thermostated cell and chamber. Infrared spectra were recorded on a Beckman IR8 spectrophotometer. Evaporations were performed under diminished pressure using a Buchi Rotary Evaporator unless noted otherwise. Thin-layer chromatography (tlc) was performed on glass plates coated (0.25 mm) with SilicAR 7GF (Mallinckrodt). Compounds of interest were detected by either short-wave ultraviolet light (254 nm) or sulfuric acid treatment followed by heating. Elemental analyses were performed by MHW Laboratories, Phoenix, AZ.

General procedure (GP1) for the synthesis of carboxamidoximes. Compounds **8a**, **8b**, **9a**, and **9b** were prepared using Brown's procedure[14a] with crystalline hydroxylamine (NH_2OH).[15] The aminocyano analogs **4a,c** and **5a,c** were suspended in abs. EtOH (30-40 mL) and to this suspension was added an equivalent amount of crystalline NH_2OH in abs. EtOH ($\approx$ 5 mL). The reaction mixture was heated at reflux for 2–4 h (**4a** and **4c**) or 10–12 h (**5a** and **5c**). The reaction was monitored by tlc ($CHCl_3$: MeOH; 8:2 V/V). A second equivalent of NH_2OH can be added, if neccessary, in order to drive the reaction to completion. To obtain compounds **8a** and **9a** the reaction mixture was cooled, taken to dryness, the crystalline residue washed (cold, abs. EtOH) and then recrystallized (aqueous EtOH). For compounds **8b** and **9b** the crude solid was taken up in hot water, the solution treated with charcoal and lyophylized to furnish the pure nucleosides. [**CAUTION: Crystalline NH_2OH is unstable and very sensitive to moisture**. If the crystalline compound melts, it is useless. The crystalline NH_2OH can be stored in a freezer, with protection from moisture, for an extended period of time].

General procedure (GP2) for the synthesis of the thiocarboxamides and seleno-carboxamides. A stirred solution of dry DMF (40-50 mL) containing diethylamine (0.5 mL) and the desired 4(5)-amino-5(4)-cyanoimidazole analog was purged with dry nitrogen gas for approximately 5-10 min. The purged solution was then saturated with either H_2S or H_2Se gas at –10 to –20 °C. A small drying tube containing Drierite was used as an indicator of saturation. When saturation of the solution is complete (*ca.* 15 min), the Drierite turns black from the excess departing gas. After the saturation period, the slow bubbling of dry nitrogen was again continued for the remainder of the reaction.

The reaction mixture was allowed to warm to room temperature, the flask fitted with a new Drierite drying tube and the reaction mixture then heated between 55 and 60 °C for 2–4 h. The H_2S reactions required longer heating times and in several cases an additional amount of H_2S was needed. The reaction mixture was then allowed to cool to room temperature and stirred for 2 hrs. At this point, the color of reaction solution should be a light-blue green. The DMF was removed *in vacuo* and the resulting solid residue was triturated (2 × 10 mL) with dry MeOH. This material was recrystallized from MeOH. [**CAUTION**: With the seleno derivatives prolonged heating in MeOH can cause precipitation of selenium metal.]

5-Amino-1-methylimidazole-4-carboxamidoxime (8a). A mixture containing **4a** (0.976 g, 8 mmol) and NH_2OH (0.3 g, 8.8 mmol) in dry abs EtOH (35 mL) was reacted according to **GP1**. The product was recrystallized from EtOH-H_2O to furnish crystalline **8a** (0.945 g, 76% yield): mp 204-206 °C. Anal. calcd for $C_5H_9N_5O$: C, 38.71; H, 5.85; N, 45.15. Found: C, 38.42; H, 6.08; N, 45.02.

5-Amino-1-(β-D-ribofuranosyl)imidazole-4-carboxamidoxime (8b). To a hot solution of **4c** (1.44 g, 6 mmol) in abs EtOH (50 mL) was added NH_2OH (0.22 g, 6.6 mmol). The preparation of **8b** from these reactants followed the **GP1** procedure. After work up, pure **8b** (1.675 g, 98.8% yield) was obtained as a fluffy light-yellow powder: mp 105 °C (sinters), 132-136 °C (dec); $[\alpha]_D^{25}$ −54.5° (*c* = .98, H_2O). Anal. calcd for $C_9H_{15}N_5O_5 \cdot 0.5\ H_2O$: C, 38.30; H, 5.75; N, 24.81. Found: C, 38.55; , 5.86; N, 24.77.

4-Amino-1-methylimidazole-5-carboxamidoxime (9a). Compound **5a** (1.342 g, 11 mmol) was suspended in abs EtOH (35 mL) and to this stirred suspension was added NH_2OH (0.4 g, 11.1 mmol). The reaction conditions and work up followed those described (**GP1**) for **8a** except that a second equivalent of NH_2OH was added after the initial 4 hr period and the heated solution was stirred for an additional 4 h. At this point, a third equivalent of NH_2OH was added and heating and stirring were continued for two more hours. The reaction reached completion (tlc) after 10 hrs. Pure **9a** (1.46 g, 85.4% yield) was isolated as buff crystals: mp 193-195 °C (dec) [lit.[14a] mp 165 °C (dec)]. Anal. calcd for $C_5H_9N_5O$: N, 45.15. Found: N, 45.32.

4-Amino-1-(β-D-ribofuranosyl)imidazole-5-carboxamidoxime (9b). Nucleoside **5c** (1.2 g, 5 mmol) was suspended in abs EtOH (40 mL) and to this suspension was added NH_2OH (0.171 g, 5.5 mmol) which was previously dissolved in abs EtOH (10

mL). The reaction was performed according to **GP1** and **9a**. Lyophylization furnished pure **9b** (1.44 g) as a yellow solid in 94.5% yield: mp 75 °C (softens), 110 °C (dec); $[\alpha]_D^{25}$ –28.9° (*c* = 0.95, H_2O). Anal. calcd for $C_9H_{15}N_5O_5.2.0\ H_2O$: C, 34.95; H, 6.19; N, 22.64. Found: C, 34.97; H 6.15; N, 22.74.

5-Amino-1-methylimidazole-4-thiocarboxamide (10a). *Method A.* To a solution of compound **6a** (3.92 g, 28.6 mmol) in hot β-picoline (70 mL) was added P_2S_5 (12.8 g, 58 mmol). This mixture was heated at reflux (vigorously) for 2 hrs. At this point, heating was stopped and, while hot ,the β-picoline was removed *in vacuo*. The resulting residue was triturated twice with xylene and each time taken to dryness *in vacuo*. The residue was taken up in hot EtOH-H_2O (500 mL) and allowed to cool. On standing, crystalline **10a** precipitated and was collected by filtration (3.04 g, 69.4%): mp 255 °C darkening, 265-267 °C (lit.[8] mp 252 °C). Anal. calcd for $C_5H_8N_4S$: N, 35.88. Found: N, 36.09. Compound **10a** was converted to **17** using diethoxymethyl acetate[5b]: λ_{max} (pH 1) 323 ($\varepsilon \times 10^{-3}$, 20.66); (MeOH) 316 (21.52); (pH 11) 309 (20.86) [lit.[12] λ_{max} (pH 1) 324 ($\varepsilon \times 10^{-3}$, 19.60); (pH 11) 310 (16.80)].

Method B. The **GP2** methodology for thiocarboxamides was employed. Compound **4a** (1.96 g, 14.6 mmol) afforded **10a** (1.81 g) in 81.2 % yield. This compound was identical in all respects to **10a** from Method A.

5-Amino-1-(β-D-ribofuranosyl)imidazole-4-thiocarboxamide (10b). This nucleoside was prepared according to **GP2** with a slight modification. To a stirred solution of dry DMF (50 mL) and diethylamine (1 mL) was added **4c** (1.92 g, 8.0 mmol). The mixture was purged with dry N_2 and slowly heated to 60 °C, then the N_2 purge was stopped and H_2S started. The solution was kept at 60 °C for 2 hrs with a steady stream of H_2S bubbling into it. Then the H_2S gas was stopped and dry N_2 started. The reaction was stirred for 1 hr at 60 °C (N_2), allowed to cool to room temperature, and then stirred at room temperature (N_2) for 1 h. The work up of **10b** followed the sequence outlined in **GP2**. Nucleoside **10b** (1.93 g) was isolated in 88% yield: mp 133-135 °C [lit.[16] 143 °C]; $[\alpha]_D^{25}$ –95.4° (*c* = 1.04, 0.1M NaOH) [lit.[16] $[\alpha]_D^{17}$ –92.5° (*c* = 2, 1M NaOH). Anal. calcd for $C_9H_{14}N_4O_4S.1.0\ H_2O$: N, 19.17. Found: N, 19.12.

4-Amino-1-methylimidazole-5-thiocarboxamide (11a). *Method A.* This imidazole was prepared by **GP2** for thiocarboxamides with a slight modification as described for **10b.** Compound **5a** was dissolved in dry DMF (50 mL) and to this solution was added

diethylamine (1.0 mL). Reaction conditions as described for **10b** were applied, followed by the usual work up for thiocarboxamides. Recrystallization from H_2O furnished **11a** (1.94 g, 75.8% yield) as cream-colored crystals: mp 184-186 °C. Anal. calcd for $C_5H_8N_4S \cdot 0.5\ H_2O$: C, 37.23; H, 5.48; N, 34.58. Found: C, 37.20; H, 5.52; N, 34.19.

Method B. Compound **5a** (0.5 g 4.1 mmol), dissolved in dry DMF (25 mL) and diethylamine (0.5 mL), was reacted according to **GP2** for thiocarboxamides. Crystallization from H_2O provided **11a** (0.48 g) in 75% yield. This material was identical in all respects to **11a** from Method A.

Method C. The reaction of compound **16**[7] (2.0 g, 13.15 mmol) dissolved in dry DMF (50 mL) and diethylamine (2.0 mL) was carried out as described for the preparation of **10b**. The crude, crystalline product was recrystallized from H_2O to furnish **11a** in 51% yield: mp 184-186 °C. The UV, IR, and ^1H NMR were identical to those obtained for **11a** from Methods A and B. Product **11a** was converted to **18** using diethoxymethyl acetate[5b]: mp 304-306 °C [lit.[6] mp 306-308 °C]; λ_{max} (pH 1) 327 (20.94); (MeOH) 321.7 (19.64); (pH 11) 315 (19.40) [lit.[6] λ_{max} (pH 1) 333 (20.30); (pH 11) 319 (21.80)].

4-Amino-1-(β-D-ribofuranosyl)imidazole-5-thiocarboxamide (11b). The synthesis of **11b** followed either the procedure for **10b** or **GP2** for thiocarboxamides; both worked equally well: mp 171-173 °C (dec); $[\alpha]_D^{25}$ –85.2° (*c* = 0.98, H_2O), $[\alpha]_D^{25}$ – 2.2° (c = 1.02, 0.1*N* NaOH). Anal. calcd for $C_9H_{14}N_4O_4S$: C, 39.41; H, 5.14; N, 20.43. Found: C, 38.99; H, 5.42; N, 20.42.

5-Amino-1-methylimidazole-4-selenocarboxamide (12a). The synthesis of **12a** from **4a** (0.991 g, 8.1 mmol) followed **GP2** (saturation at –10 °C) for selenocarboxamides. After work up and recrystallization, **12a** (1.06 g, 64.4% yield) was isolated as light-yellow crystals: mp 261.5–262.5 °C. Anal. calcd for $C_5H_8N_4Se$: C, 29.52; H, 3.97; N, 27.59. Found: C, 29.69; H, 4.10; N, 27.31.

5-Amino-1-(β-D-ribofuranosyl)imidazole-4-selenocarboxamide (12b). The synthesis of **12b** from **4c** (1.44 g, 6.0 mmol) was carried out according to **GP2** (saturation at –10 °C) for selenocarboxamides. The procedure provided **12b** (1.56 g, 81% yield) as light-yellow crystals: mp 130-132 °C (glass); $[\alpha]_D^{25}$ –100.6° (*c* = .53, MeOH). Anal. calcd for $C_9H_{14}N_4O_4Se$: C, 33.65; H, 4.39; N, 17.44. Found: C, 33.81; H, 4.09, N, 17.10.

4-Amino-1-methylimidazole-5-selenocarboxamide (13a). The preparation of **13a** from **5a** (0.61 g, 5 mmol) was conducted according to **GP2** for selenocarboxamides. After the ususal work up and recrystallization, **13a** (0.889 g) was afforded in 87% yield: mp 186-188 °C. Anal. calcd for $C_5H_8N_4Se$: C, 29.52; H, 3.97; N, 27.59. Found: C, 29.61, H, 3.96; N, 27.51.

4-Amino-1-(β-D-ribofuranosyl)imidazole-5-selenocarboxamide (13b). The synthesis of **13b** from **5c** (1.92 g, 8.0 mmol) followed the **GP2** (saturation at −10 °C) methodology for selenocarboxamides. Nucleoside **13b** (2.12 g) was obtained in 82.5% yield: mp 174 °C (darkens), 178–180 °C (dec); $[\alpha]_D^{25}$ –60.4° (*c* = .49, MeOH). Anal. calcd for $C_9H_{14}N_4O_4Se$: C, 33.65; H, 4.39; N, 17.44. Found: C, 33.81; H, 4.09; N, 17.10.

Methyl 5-Amino-1-(β-D-ribofuranosyl)imidazole-4-carboximidate hydrochloride (14). This nucleoside was prepared from **5b** (3.0 g, 3 mmol) by slightly modifying the published procedure.[19] Nucleoside **4b** (3.0 g, 8 mmol) was dissolved in dry MeOH (30 mL) and this solution was cooled to 0 °C (EtOH-dry ice bath). To this cold solution was added a cold (0 °C) saturated methanolic HCl solution (20 mL) under an inert atmosphere (N_2 glove bag) and anhydrous conditions. The sealed yellow solution was immediately placed in a 0 °C freezer for 24 hrs. The white crystalline precipitate was collected by filtration, washed well with AR acetone, and dried in a dessicator (Drierite). The iminoether **14** (2.12 g) was obtained in 85.8% yield: mp 113 °C (dec) [lit.[19] mp 113 °C (dec)].

4-Cyano-5-[di-(*p*-toluenesulfonyl)amino]-1-methylimidazole (15). To compound **6a** (0.50 g, 3.58 mmol) in dry pyridine (10 mL), *p*-toluenesulfonyl chloride (1.37 g, 7.16 mmol) was added and the mixture stirred at room temperature for 2 days. The reaction mixture became very thick and a precipitate began to form as the color changed from yellow to white and then to purple. The reaction mixture was poured onto cracked ice and a precipitate collected and dried. This material was recrystallized from EtOH to give compound **15** (0.408 g, 26.5%): mp 197-198 °C. Anal. calcd for $C_{19}H_{18}N_4O_4S_2$: C, 51.98; N, 4.54; N, 12.71. Found: C, 51.96; H, 4.36; N, 12.74.

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