JOC*Note*

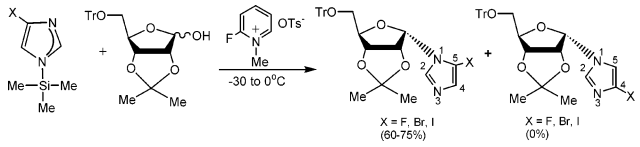
Regio- and Stereoselective Glycosylation: Synthesis of 5-Haloimidazole α-Ribonucleosides

Tilak Chandra,[†] Xiang Zou,[†] Edward J. Valente,[‡] and Kenneth L. Brown*,[†]

Department of Chemistry and Biochemistry, Ohio University, Athens, Ohio 45701, and Department of Chemistry, Mississippi College, Clinton, Mississippi 39085

brownk3@ohiou.edu

Received January 16, 2006



We describe the synthesis of novel 5-haloimidazole ribonucleosides as precursors of modified cobalamins. A regio- and stereoselective glycosylation of protected ribose with silylated 4(5)-haloimidazoles produces 5-haloimidazole ribonucleosides predominantly in the α-configuration (60−75%) without any 4-substituted imidazole ribonucleoside. The structure of the 5-fluoroimidazole ribonucleoside was confirmed by X-ray crystallography and 2D NMR spectroscopy.

Vitamin B_{12} derivatives with altered lower axial ligands are of interest as probes for the mechanism of action of coenzyme B_{12} (5′-deoxyadenosylcobalamin, AdoCbl; Figure 1).[1−6] To delineate the role of the lower axial ligand in the enzymatic activation of coenzyme B_{12}, it is necessary to synthesize vitamin B_{12} derivatives with altered axial nucleosides. Semisynthesis of such cobalamin derivatives is best achieved by coupling a cobyric acid mixed anhydride[7] with a nucleoside 3′-phosphodiester having an (*R*)-(−)-1-amino-2-propanol residue. For the synthesis of the latter nucleotide, the critical step is the synthesis of the nucleoside, which has the unusual α-*N*-glycosidic bond configuration.[8−13]

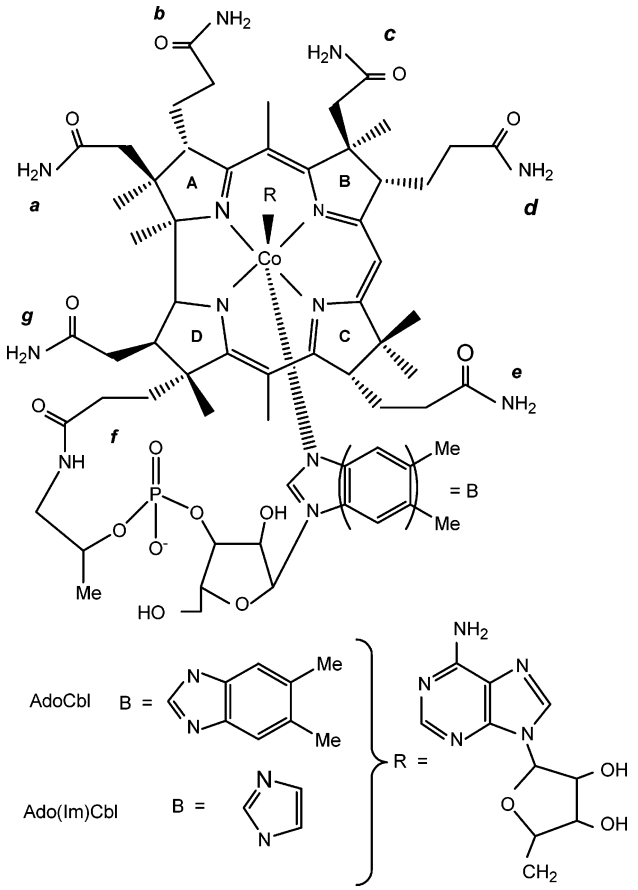


FIGURE 1. Structural formula of coenzyme B_{12} and Coβ-5′-deoxyadenosylimidazolyl-cobamide, a coenzyme B_{12} analogue with an imidazole axial nucleoside.

The effect of the steric bulk of the axial nucleoside base on the enzymatic activation of coenzyme B_{12} has been investigated using the coenzyme analogue in which imidazole replaces the bulky 5,6-dimethylbenzimidazole ligand (Ado(Im)Cbl, Figure 1).[3] The effect of the basicity of the axial nucleoside may be similarly probed using 5-substituted imidazole nucleosides. To this end, we now report a simple and robust method for the preparation of 5-halosubstituted imidazole ribonucleosides in the α-configuration.

The reaction of TMS-protected 4(5)-fluoro-, bromo-, and iodoimidazole with 2,3-*O*-(1-isopropylidene)-5-*O*-(triphenylmethyl)-α/β-D-ribofuranose produces 5-haloimidazole ribonucleosides predominantly in the α-configuration in 60−75% yield without any 4-substituted imidazole ribonucleoside (Scheme 1, Table 1). The 5-halo regioisomer was formed exclusively, and the α-anomer was predominated by 3:1 to 5:1.

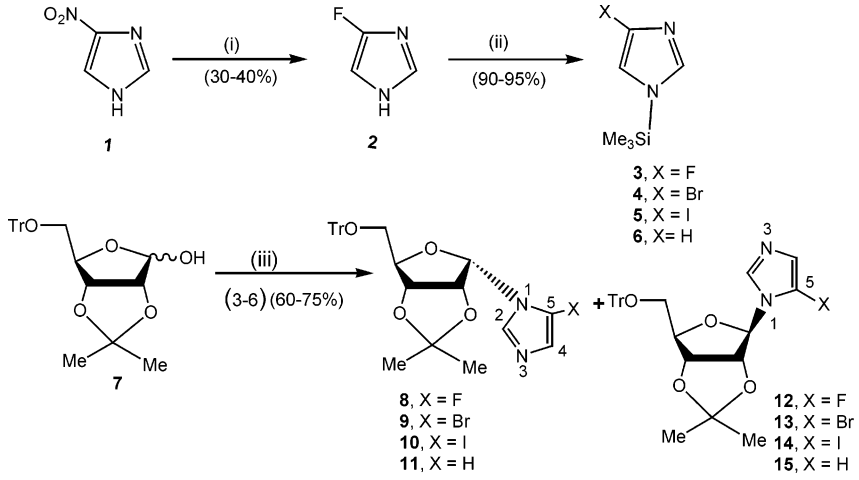
The observation of absolute regiospecificity is unique. It is known that trimethylsilyltriflate-catalyzed glycosylation of 4(5)-

* To whom correspondence should be addressed. Fax: 740-594-0148. Tel: 740-593-1737.
[†] Ohio University.
[‡] Mississippi College.

(1) Brown, K. L. Chemistry and Enzymology of Vitamin B_{12}. *Chem. Rev.* **2005**, *105*, 2075.
(2) Hamza, M. S. A.; Zou, X.; Banka, R.; Brown, K. L.; van Eldik, R. *Dalton Trans.* **2005**, 782.
(3) Brown, K. L.; Zou, X.; Banka, R. R.; Perry, C. B.; Marques, H. M. *Inorg. Chem.* **2004**, *43*, 8130.
(4) Brown, K. L.; Zou, X.; Li, J.; Chen, G. *Inorg. Chem.* **2001**, *40*, 5942.
(5) Brown, K. L.; Li, J. *J. Am. Chem. Soc.* **1998**, *120*, 9466.
(6) Brown, K. L.; Cheng, S.; Zou, X.; Li, J.; Chen, G.; Valente, E. J.; Zubkowski, J. D.; Marques, H. M. *Biochemistry* **1998**, *37*, 9704.
(7) (a) Renz, P. *Methods Enzymol*. **1971**, *18C*, 82−92. (b) Bonnett, R.; Godfrey, J. M.; Redman, D. G. *J. Chem. Soc. C* **1969**, 1163.
(8) Chandra, T.; Zou, X.; Brown, K. L. *Tetrahedron Lett.* **2004**, *45*, 7783.
(9) Chandra, T.; Brown, K. L. *Tetrahedron Lett.* **2005**, *46*, 2071.
(10) Brown, K. L.; Chandra, T.; Zou, S.; Valente, E. J. *Nucleosides, Nucleotides & Nucleic Acids* **2005**, *24*, 1147.
(11) Kumar, P.; Chandra, T.; Zou, S.; Brown, K. L. *J. Phys. Chem.* **2006**, *110* (1), 5.
(12) Chandra, T.; Brown, K. L. *Tetrahedron Lett*. **2005**, *46*, 8617.
(13) Mukaiyama, T.; Hashimoto, Y.; Hayashi, Y.; Shoda, S. I. *Chem. Lett*. **1984**, 557.

10.1021/jo060087s CCC: $33.50
Published on Web 05/19/2006

SCHEME 1. Synthesis of 5-Haloimidazole α-Ribonucleosides



Reagents and conditions:

(i), $NaNO_2$, Zn dust, HBF_4, photolysis, (ii) 4 - bromo, 4 - iodoimidazole and imidazole, HMDS, reflux

(iii) 2-fluoromethyl pyridinium tosylate, DIEA, methylene chloride, -30 °C to 0 °C,

TABLE 1. Isolated Yields and Crude Ratios of α/β-5-Haloimidazole Ribonucleosides

α/β-ribonucleoside	crude ratio α/β (%)[a]	isolated yields (%) α	isolated yields (%) β	total yields (%) α + β
5-fluoroimidazole	80:20	75	15	90
5-bromoimidazole	70:30	65	15	80
5-iodoimidazole	80:20	65	20	85
imidazole	70:30	60	18	78

[a] Determined by NMR.

substituted imidazole with protected ribose produces both 4- and 5-substituted α-imidazole ribosides with the 4-regioisomers predominating.[14,15] From steric considerations only, the 4-isomer would be expected to be favored.[16] However, in this work, crude reaction mixtures showed only two products, the α- (major) and β-anomer (minor) of the 5-haloimidazole ribonucleoside, as established using ^{1}H nOe.

For spectroscopic comparison, the α- and β-ribonucleosides of imidazole were also prepared using the same methodology (Scheme 1). The absence of an nOe between the C(5) imidazole proton and the anomeric proton, readily observable in the imidazole nucleoside, confirms the structure of the 5-haloimidazole ribonucleosides. A possible mechanism to explain the regiospecificity is shown in Scheme 2, in which the unprotected imidazole nitrogen directly attacks the ribose catalyst adduct.

For the synthesis of the 5-fluoroimidazole α-ribonucleoside, the 4(5)-fluoroimidazole base[17,18] was prepared from 4(5)-nitroimidazole in moderate yield by conversion to the diazonium salt followed by irradiation in aqueous tetrafluoroboric acid. After purification, the free base was converted to the TMS-fluoroimidazole by refluxing in HMDS for 10 h. For coupling of the TMS protected base to the protected ribose, a mixture of 2-fluoro-1-methylpyridinium tosylate[10,13] and 2,3-*O*-(1-isopropylidene)-5-*O*-(triphenylmethyl)-α/β-D-ribofuranose was stirred in methylene chloride at −30 to −10 °C in basic medium for 3 h and the TMS protected base was added at 10 °C. The crude reaction mixture showed only the 5-halosubstituted α-ribonucleoside along with a minor amount of β-anomer by NMR. After flash chromatography, the crude mixture afforded 75% α-anomer and 15−20% β-anomer (Table 1). The other 5-haloimidazole ribonucleosides were obtained from the 4(5)-haloimidazoles similarly.

The anomeric configuration of **8** was confirmed by X-ray crystallography. Crystals suitable for X-ray diffraction were grown by slow crystallization at room temperature in ether/hexane (1:1). The molecule is chiral; the glycosidic bond length is 1.446 Å, and the glycosidic torsion angle, C(4)−N(1)−C(1)−O(1), is −52.55°, slightly outside the narrow range of indoline α-ribonucleosides.[10]

The anomeric proton and the fluorine atom are separated by 2.386 Å in space. A similar distance is expected between the anomeric proton and the C-5 proton of imidazole in its α-ribonucleoside, so it shows a strong nOe between those protons. In the NMR, a doublet was observed at 6.54 ppm for the imidazole H-4 ($^3J_{HF}$ = 6.9 Hz). In the ^{19}F NMR, a doublet was observed at −154.6 with a *J* value of 7.5 Hz, whereas 4(5)-fluoroimidazole itself had a ^{19}F NMR doublet at −136.6 ppm with a *J* value of 8.0 Hz. For the 5-haloimidazole α-ribonucleosides, the anomeric protons appeared at 6.2−6.5 ppm and the 1′-2′ coupling constant was 4.0 Hz. All protected α-ribonucleosides have an nOe between the isopropylidene methyl protons and the imidazole C-2 proton, but the β-anomer does not have an nOe between these protons. Imbach's rule[19−22] suggests that the difference in the ^{1}H chemical shifts between the two methyl signals of the isopropylidene group, Δδ, can be used to

(14) Seley, K. L.; Salim, S.; Zhang, L. *Org. Lett.* **2005**, *7*, 63.
(15) Seley, K. L.; Salim, S.; Zhang, L.; O'Daniel, P. I. *J. Org. Chem.* **2005**, *70*, 1612.
(16) Matthews, H. R.; Rapoport, H. *J. Am. Chem. Soc*. **1973**, *95*, 2297.
(17) Kirk, K. L.; Nagai, W.; Cohen, L. A. *J. Am. Chem. Soc*. **1973**, *95*, 8389.
(18) Kirk, K. L.; Cohen, L. A. *J. Org. Chem*. **1973**, *38*, 3647.
(19) Imbach, J. L. *Ann. N.Y. Acad. Sci*. **1975**, *255*, 177.
(20) Rayner, B.; Tapiero, C.; Imbach, J. L. *Carbohydr. Res.* **1976**, *47*, 195.
(21) Imbach, J. L.; Barascut, J. L.; Kam, B. L.; Rayner, B.; Tamby, C.; Tapiero, C. *J. Heterocycl. Chem.* **1973**, *10*, 1069.
(22) Imbach, J. L.; Barascut, J. L.; Kam, B. L.; Tapiero, C. *Tetrahedron Lett*. **1974**, *2*, 129.

SCHEME 2. Possible Mechanism for the Formation of 5-Haloimidazole α-Ribonucleosides

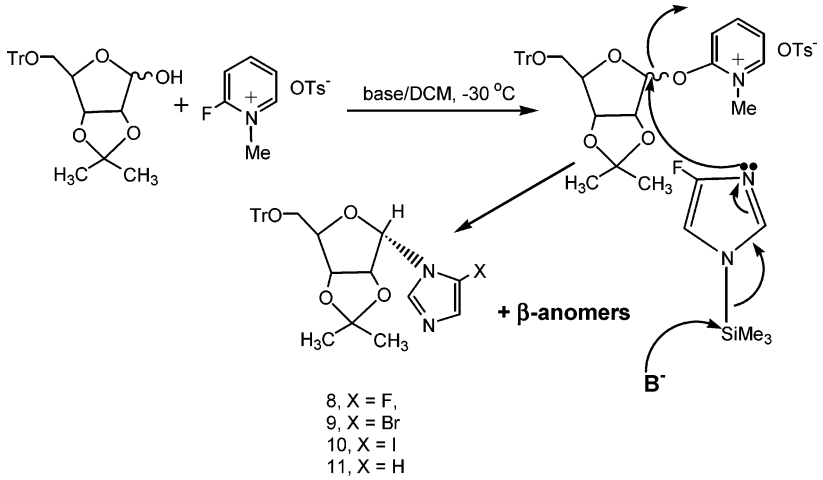


TABLE 2. Methyl Proton Separation in (Δ ppm) for α/*β*-Imidazole Ribonucleosides

compd no.	compd	Me_1 (δ ppm)	Me_2 (δ ppm)	Δ ppm	solvent
8	α-5-fluoroimidazole	1.318	1.406	0.088	$CDCl_3$
9	α-5-bromoimidazole	1.301	1.394	0.093	$CDCl_3$
10	α-5-iodoimidazole	1.29	1.39	0.10	$CDCl_3$
8	α-5-fluoroimidazole	1.296	1.307	0.011	CD_3OD
9	α-5-bromoimidazole	1.390	1.658	0.026	CD_3OD
10	α-5-iodoimidazole	1.280	1.356	0.076	CD_3OD
8	α-5-fluoroimidazole	1.277	1.310	0.033	DMSO-d_6
9	α-5-bromoimidazole	1.246	1.340	0.094	DMSO-d_6
10	α-5-iodoimidazole	1.297	1.250	0.047	DMSO-d_6
12	*β*-5-fluoroimidazole	1.359	1.586	0.22	$CDCl_3$
13	*β*-5-bromoimidazole	1.370	1.617	0.24	$CDCl_3$
12	*β*-5-fluoroimidazole	1.345	1.546	0.20	CD_3OD
13	*β*-5-bromoimidazole	1.339	1.556	0.21	CD_3OD

distinguish between the α- and *β*-anomers such that $0.18 < \Delta\delta < 0.23$ for the *β*-anomers and $0 < \Delta\delta < 0.10$ for the α-anomers. ^{1}H examination of these ribonucleosides by high-resolution ^{1}H NMR (Table 2) shows that the 5-haloimidazole ribonucleosides obey Imbach's rule in $CDCl_3$ and in CD_3OD. A strong nOe was observed between the H-5 imidazole proton and the anomeric proton in imidazole α-ribonucleoside, whereas the 5-haloimidazole ribonucleosides do not have an nOe between these protons, which strongly supports the structure of the bromoimidazole and iodoimidazole α-ribonucleosides.

Efficient regio- and stereoselective syntheses of a variety of 5-halosubstituted imidazole α-ribonucleosides have been achieved using 2-fluoro-1-methylpyridinium tosylate. This method does not produce any 4-substituted haloimidazole α-ribonucleosides. The structures of all prepared ribonucleosides were confirmed by ^{1}H NMR, 2D NMR, and X-ray crystallography (5-fluoroimidazole ribonucleoside). These glycosylation reactions produce α-ribonucleosides in good yields without the need for complicated purification. Further use and subsequent reactions of these nucleosides for the semisynthesis of cobalamin derivatives are currently under study.

Experimental Section

4-Fluoroimidazole[17,18] (2): White crystalline solid; $R_f = 0.6$; ^{1}H NMR ($CDCl_3$) δ 6.3 (dd, J = Hz, 1H), 7.07 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 93.9 (d, $J = 37.8$ Hz), 128.5 (d, $J = 15.87$ Hz), 155.6 (d, $J = 233.5$ Hz); ^{19}F NMR ($CDCl_3$) −136.61 (d, $J = 8$ Hz).

1-(Trimethylsilanyl)-4-fluoroimidazole (3): White solid; ^{1}H NMR ($CDCl_3$) δ 0.57 (s, 9H), 6.39 (dd, $J = 2.5$, 6 Hz, 1H, Im), 7.13 (s, 1H, Im); ^{13}C NMR ($CDCl_3$) δ −0.7 ($SiMe_3$), 97.7 (d, $J = 36.77$ Hz), 133.7 (d, $J = 17.22$ Hz), 155.6 (d, $J = 230$ Hz); HRMS *m*/*z* 159.067 (calcd for $C_6H_{12}FSiN_2$, 159.0753) (M + H).

1-(Trimethylsilanyl)-4-iodoimidazole (5): White solid; ^{1}H NMR ($CDCl_3$) δ 0.57 (s, 9H), 6.97 (s, 1H), 7.40 (s, 1H); ^{13}C NMR ($CDCl_3$) δ −0.70 ($SiMe_3$), 83.6 (Cquat), 125.6 (CH), 141.3 (CH).

1-(2′,3′-*O*-Isopropylidene-5′-*O*-triphenylmethyl-α-D-ribofuranosyl)-5-fluoroimidazole (8): To a precooled mixture of 2-fluoro-1-methylpyridinium tosylate (1.0 g, 3.5 mmol) in dry, degassed methylene chloride (5 mL) at −30 to −40 °C was slowly added a mixture of 2,3-*O*-(1-isopropylidene)-5-*O*-(triphenylmethyl)-α/*β*-D-ribofuranose[23] (1.0 g, 2.3 mmol) in methylene chloride (5 mL) and *N*,*N*-diisopropylethylamine (0.5 mL) under nitrogen, and this mixture was stirred for 3 h at −30 °C. The temperature was raised to −10 °C, and the cooling bath was removed from the reaction mixture and replaced with an ice bath. A solution of 1-(trimethylsilyl)-1-*H*-4-fluoroimidazole (1.2 g, 7.5 mmol) was prepared in degassed dry methylene chloride and slowly added to the above mixture at −10 °C. The resulting solution was stirred for 3 h at −10 °C and then further stirred for 6 h at room temperature. After completion, the reaction mixture was poured into water (50 mL), the organic layer was separated and dried over anhydrous sodium sulfate, and the methylene chloride was removed under reduced pressure. The crude mixture was dissolved in methylene chloride (50 mL), and silica gel (10 g) was added to the flask. Following removal of the solvent under reduced pressure, the resulting powder was loaded onto a silica gel column. The column was eluted with an ether/benzene gradient (20−50% ether/ benzene): yield 60−70%; white crystalline solid; mp 160−65 °C; $R_f = 0.6$; ^{1}H NMR ($CDCl_3$) δ 1.31 (s, 3H, CH_3), 1.40 (s, 3H, CH_3), 3.18 (dd, $J = 2.38$, 7.69 Hz, 1H, 5′), 3.65 (dd, $J = 2.83$, 7.29 Hz, 1H, 5″), 4.42 (bt, 1H, 4′), 4.70 (d, $J = 5.67$ Hz, 1H, 3′), 4.96 (t, $J = 4.45$ Hz, 1H, 2′), 6.21 (d, $J = 4$ Hz, 1H, 1′), 6.54 (d, $J = 6.88$ Hz, 1H, H-4 imidazole), 7.26 (t, 3H, Ar−trityl), 7.34 (t, 6H, Ar−trityl), 7.40 (d, 6H, Ar−trityl), 7.47 (s, 1H, imidazole); ^{1}H NMR (CD_3OD) δ 1.29 (s, 3H, CH_3), 1.30 (s, 3H, CH_3), 3.25 (dd, $J = 2.43$, 8 Hz, 1H, 5′), 3.49 (dd, $J = 2.43$, 8 Hz, 1H, 5″), 4.42 (bt, 1H, 4′), 4.70 (d, $J = 6$ Hz, 1H, 3′), 5.007 (t, $J = 4.45$ Hz, 1H, 2′), 6.18 (d, $J = 4.5$ Hz, 1H), 6.52 (d, $J = 7$ Hz, H-4 imidazole), 7.28 (t, 3H, Ar−trityl), 7.33−7.37 (m, 6H, Ar−trityl), 7.43 (d, 6H, Ar−trityl), 7.49 (s, 1H, imidazole); ^{13}C NMR ($CDCl_3$) δ 24.5 (CH_3), 25.6 (CH_3), 65.3 (CH_2, 5′), 80.2 (2′), 82.2 (4′), 82.5 (3′), 85.9 (1′), 87.8 (Cquat), 105.0 (d, $J = 8$ Hz, imidazole), 113.8 (Cquat), 127.4 (CH), 128.0 (CH), 128.5 (CH), 129.8 (d, $J = 6.12$ Hz), 143.2 (Cquat), 146.4

(23) Cousineau, T. J.; Secrist, J. A., III. *J. Org. Chem.* **1979**, *44*, 4351.

(d, $J = 270$ Hz); ^{19}F NMR ($CDCl_3$) −154.6 (d, $J = 7.5$ Hz); HRMS *m*/*z* 501.2173 (calcd for $C_{30}H_{30}FN_2O_4$, 501.217) (M + H); MS (FAB) *m*/*z* 501, 243.

1-(2′,3′-*O*-Isopropylidene-5′-*O*-triphenylmethyl-α-D-ribofuranosyl)-5-bromoimidazole (9): (1.0 g, 2.3 mmol, yield 65%); white fluffy solid; $R_f = 0.6$ (ether/benzene, 20:80); mp 70−75 °C (decomposes); ^{1}H NMR ($CDCl_3$) δ 1.30 (s, 3H, CH_3), 1.39 (s, 3H, CH_3), 3.18 (dd, $J = 2.43$, 8 Hz, 1H, 5′), 3.65 (dd, $J = 2.43$, 8 Hz, 1H, 5″), 4.42 (bt, 1H, 4′), 4.70 (d, $J = 6$ Hz, 1H, 3′), 5.0 (t, $J = 4.45$ Hz, 1H, 2′), 6.49 (d, $J = 4$ Hz, 1H, 1′), 7.07 (s, 1H, imidazole), 7.28 (t, 3H, Ar−trityl), 7.33−7.37 (m, 6H, Ar−trityl), 7.43 (d, 6H, Ar−trityl), 7.91 (s, 1H, imidazole); ^{13}C NMR ($CDCl_3$) δ 24.3 (CH_3), 25.6 (CH_3), 65.6 (CH_2, 5′), 79.9 (2′), 82.06 (4′), 82.6 (3′), 87.9 (Cquat), 88.5 (1′), 100.6 (Cquat), 113.4 (Cquat), 127.3 (CH), 128.0 (CH), 128.5 (CH), 128.9 (CH), 138.0 (CH), 143.1 (Cquat); HRMS *m*/*z* 561.1387 (calcd for $C_{30}H_{29}BrN_2O_4$, 561.1385) (M + H); MS (FAB) *m*/*z* 565.1463, 564.1405, 561.1387, 517, 447, 338, 244, 245.

1-(2′,3′-*O*-Isopropylidene-5′-*O*-triphenylmethyl-α-D-ribofuranosyl)-5-iodoimidazole (10): (1.0 g, 2.3 mmol, yield 65%); white fluffy solid; $R_f = 0.6$ (ether/benzene, 20:80); ^{1}H NMR ($CDCl_3$) δ 1.29 (s, 3H, CH_3), 1.39 (s, 3H, CH_3), 3.16 (dd, $J = 2.8$, 8.5 Hz, 1H, 5′), 3.64 (dd, $J = 2.5$, 8 Hz, 1H, 5″), 4.42 (bt, 1H, 4′), 4.72 (d, $J = 5.5$ Hz, 1H, 3′), 5.01 (t, $J = 5.5$ Hz, 1H, 2′), 6.46 (d, $J = 4.5$ Hz, 1H, 1′), 7.16 (s, 1H, imidazole), 7.26 (t, 3H, Ar−trityl), 7.34 (m, 6H, Ar−trityl), 7.45 (d, 6H, Ar−trityl), 7.95 (s, 1H, imidazole); ^{13}C NMR ($CDCl_3$) δ 24.3 (CH_3), 25.6 (CH_3), 65.7 (CH_2, 5′), 66.5 (Cquat), 79.8 (2′), 81.9 (4′), 82.6 (3′), 87.8 (Cquat), 90.5 (1′), 113.3 (Cquat), 127.3 (CH), 128.0 (CH), 128.5 (CH), 136.0 (CH), 140.0 (Cquat), 143.1 (Cquat); HRMS *m*/*z* 609.1246 (calcd for $C_{30}H_{30}IN_2O_4$, 609.1209) (M + H); MS (FAB) *m*/*z* 609, 610, 611, 613, 615, 617, 243.

1-(2′,3′-*O*-Isopropylidene-5′-*O*-triphenylmethyl-α-D-ribofuranosyl)-imidazole (11): (1.0 g, 2.3 mmol, yield 65%); white fluffy solid; $R_f = 0.6$; mp 60−65°C (decomposes); ^{1}H NMR ($CDCl_3$) δ 1.312 (s, 3H, CH_3), 1.447 (s, 3H, CH_3), 3.21 (dd, $J = 3.2$, 7.29 Hz, 1H, 5′), 3.53 (dd, $J = 3.2$, 7.29 Hz, 1H, 5″), 4.39 (bt, $J = 2.4$ Hz, 1H, 4′), 4.77 (d, $J = 6$ Hz, 1H, 3′), 4.92 (t, $J = 4$ Hz, 1H, 2′), 6.20 (d, $J = 4.03$ Hz, 1H, 1′), 7.08 (s, 1H, imidazole), 7.13 (s, 1H, imidazole), 7.27 (d, 3H, Ar−trityl), 7.33 (t, $J = 7.2$ Hz, 6H, Ar−trityl), 7.39 (d, $J = 7.7$ Hz, 6H, Ar−trityl), 7.72 (s, 1H, imidazole); ^{13}C NMR ($CDCl_3$) δ 24.4 (CH_3), 25.7 (CH_3), 65.3 (CH_2, 5′), 80.5 (2′), 82.1 (4′), 82.4 (3′), 87.6 (Cquat), 88.5 (1′), 113.7 (Cquat), 118.3 (CH), 127.3 (CH), 128.0 (CH), 128.4 (CH), 128.6 (CH), 136.6 (CH), 143.2 (Cquat); HRMS *m*/*z* 483.2456 (calcd for $C_{30}H_{30}N_2O_4$, 483.2456) (M + H); MS (FAB) *m*/*z* 484, 287, 246.

1-(2′,3′-*O*-Isopropylidene-5′-*O*-triphenylmethyl-*β*-D-ribofuranosyl)-5-bromoimidazole (13): (1.0 g, 2.3 mmol, yield 15%); viscous oil; $R_f = 0.5$ (ether/benzene); ^{1}H NMR ($CDCl_3$) δ 1.37 (s, 3H, CH_3), 1.61 (s, 3H, CH_3), 3.38 (d, $J = 4.5$ Hz, 1H, 5′ & 5″), 4.37 (q, 1H, 4′), 4.74−4.75 (m, 1H, 3′), 4.86−4.88 (m, 1H, 2′), 5.87 (d, $J = 2.8$ Hz, 1H, 1′), 7.05 (s, 1H, imidazole), 7.26 (t, 3H, Ar−trityl), 7.32 (t, 6H, Ar−trityl), 7.42 (d, 6H, Ar−trityl), 7.69 (s, 1H, imidazole); ^{13}C NMR ($CDCl_3$) δ 25.4 (CH_3), 27.2 (CH_3), 63.5 (CH_2, 5′), 80.8 (3′), 84.6 (4′), 85.1 (2′), 87.1 (Cquat), 91.2 (1′), 100.6 (Cquat), 114.7 (Cquat), 127.2 (CH), 127.9 (CH), 128.6 (CH), 130.5 (CH), 136.2 (CH), 143.3 (Cquat); HRMS *m*/*z* 561.1355 (calcd for $C_{30}H_{29}BrN_2O_4$, 561.1385) (M + H); MS (FAB) *m*/*z* 565.1463, 564.1405, 561.1387, 517, 447, 338, 244, 245.

Acknowledgment. This research was supported by the National Institute of General Medical Sciences, Grant GM 48858 (to K.L.B.).

Supporting Information Available: General methods, synthesis of compounds, 1D and 2D NMR (^{19}F, COSY, NOESY, and HMQC for compounds **8**−**11** and **13**), ORTEP diagram of compound **8**, and CIF file. This material is available free of charge via the Internet at http://pubs.acs.org.

JO060087S