**N-Oxides of Adenosine-Type Nucleosides Undergo Pyrimidine Ring
Opening and Closure To Give 5-Amino-4-(1,2,4-oxadiazol-3-yl)imidazole
Derivatives**

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Supporting Information (1)

Pages S2–S8: General experimental details, procedures, and characterization data.

Experimental Section

General: Uncorrected melting points were determined with a Hoover capillary apparatus. UV spectra were determined with solutions in MeOH. ^1H (500 MHz) and ^{13}C (125 MHz) NMR spectra were recorded with solutions in CDCl_3 unless noted. EI mass spectra were obtained at 70 eV, and FAB-MS were determined with a glycerol or thioglycerol matrix. Acid anhydrides were purchased or synthesized by known procedures.¹ Reagent quality chemicals and solvents were used.

Treatment of Adenosine 1-Oxide with Acetic Anhydride in Pyridine: A mixture of adenosine 1-oxide (**5**) (3.18 g, 11.2 mmol), Ac_2O (20 mL) and pyridine (30 mL) was stirred overnight at ambient temperature. Volatiles were evaporated, and the residue was chromatographed (EtOAc/hexanes, 1:3 $\rightarrow$ EtOAc) to give a mixture of two compounds (3.0 g, 4:5) as a yellow oil. This material was subjected to (a) methanolysis and (b) ammonolysis as follows:

(a) 5-Acetamido-1-(2,3,5-tri-*O*-acetyl- β -D-ribofuranosyl)-4-(5-methyl-1,2,4-oxadiazol-3-yl)imidazole (6a**).** A solution of the mixture (0.17 g) in MeOH was heated at 105 °C for 1.5 h. Volatiles were evaporated, and the residue was chromatographed (EtOAc $\rightarrow$ EtOAc/MeOH, 10:1) to give **6a** (0.15 g): ^1H NMR δ 2.08, 2.12, 2.13, 2.23, 2.60 (5 $\times$ s, 5 $\times$ 3H), 4.29–4.44 (m, 3H), 5.28 (t, J = 5.9 Hz, 1H), 5.61 (br s, 1H), 5.94 (br s, 1H), 7.86, 8.04 (2 $\times$ br s, 2 $\times$ 1H); ^{13}C NMR δ 11.7, 19.9, 20.0, 20.2, 22.7, 61.8, 68.8, 73.7, 78.9, 86.9, 122.3, 126.3, 133.4, 162.9, 168.8, 169.1, 170.0, 170.6, 175.7; FAB-MS m/z 466 (60%, $\text{M}^+ + 1$), 259 (100%); HRMS Calcd for $\text{C}_{19}\text{H}_{24}\text{N}_5\text{O}_9$: 466.1573, Found: 466.1555.

(b) 5-Acetamido-1-(β -D-ribofuranosyl)-4-(5-methyl-1,2,4-oxadiazol-3-yl)imidazole (6b**).** A solution of the mixture (0.20 g) in NH_3/MeOH (~14%) was stirred overnight at ambient temperature. Volatiles were evaporated, and acetamide was removed by sublimation under vacuum. The residue was chromatographed (EtOAc $\rightarrow$ EtOAc/MeOH, 10:1 $\rightarrow$ 3:1) to give **6b** (0.15 g): ^1H NMR (CD_3OD) δ 2.05, 2.62 (2 $\times$ s, 2 $\times$ 3H), 3.74, 3.86 (2 $\times$ dd, J = 2.9, 12.2 Hz, 2 $\times$ 1H), 4.03–4.05 (m, 1H), 4.27 (t, J = 5.1 Hz, 1H), 4.32 (t, J = 4.6 Hz, 1H), 5.60 (d, J = 3.9 Hz, 1H), 8.19 (s, 1H); ^{13}C NMR (CD_3OD) δ 12.1, 22.9, 62.2, 71.3, 77.1, 86.4, 90.6, 124.8, 128.0, 136.6, 164.7, 174.4, 178.3; FAB-MS m/z 362 (65%, $\text{M}^+ + \text{Na}$), 237 (100%); HRMS Calcd for $\text{C}_{13}\text{H}_{17}\text{N}_5\text{O}_6\text{Na}$: 362.1076, Found: 362.1086.

Procedure A: Synthesis of 2',3',5'-Tri-*O*-acetyladenosine 1-Oxide² (7**).** H_2O_2 (30%, 8 mL) was added to a stirred solution of 2',3',5'-tri-*O*-acetyladenosine³ (10.0 g, 27.7 mmol) in AcOH (100 mL), and stirring was continued for 12 h at 50 °C (oil bath). Volatiles were evaporated (at 45 °C). The residue can

¹ (a) Wallace, J. M.; Copenhaver, J. E. *J. Am. Chem. Soc.* **1941**, 63, 699–700. (b) Braude E. A.; Timmons, C. J. *J. Chem. Soc.* **1955**, 3766–3772.

² Prepared by a modification of the procedure of Kikugawa, K.; Suehiro, H.; Yanase, R.; Aoki, A. *Chem. Pharm. Bull.* **1977**, 25, 1959–1969.

³ Nowak, I.; Conda-Sheridan, M.; Robins, M. J. *J. Org. Chem.* **2005**, 70, 7455–7458.

be used directly in the next step. Column chromatography (EtOAc $\rightarrow$ EtOAc/MeOH, 10:1 $\rightarrow$ 3:1) gave **7** (8.1 g, 78%) as a pink oil: UV max 262 nm (ϵ 10 100), min 254 nm (ϵ 9300); ^1H NMR δ 2.09, 2.12, 2.16 (3 $\times$ s, 3 $\times$ 3H), 4.35–4.47 (m, 3H), 5.60 (t, J = 4.9 Hz, 1H), 5.88 (t, J = 5.4 Hz, 1H), 6.14 (d, J = 5.4 Hz, 1H), 7.58 (br s, 2H), 8.07, 8.72 (2 $\times$ s, 2 $\times$ 1H); ^{13}C NMR δ 20.2, 20.3, 20.5, 62.8, 70.3, 72.8, 79.9, 86.2, 119.4, 141.6, 142.1, 144.3, 148.6, 169.3, 169.4, 170.3; FAB-MS m/z 432 (100%, M^+ + Na); HRMS Calcd for $\text{C}_{16}\text{H}_{19}\text{N}_5\text{O}_8\text{Na}$: 432.1131, Found: 432.1132.

2',3',5'-Tri-*O*-(4-methylbenzoyl)adenosine 1-Oxide⁴ (8**).** Treatment of 2',3',5'-tri-*O*-(4-methylbenzoyl)adenosine³ by procedure A gave **8** (93%): ^1H NMR δ 2.25, 2.36, 2.40 (3 $\times$ s, 3 $\times$ 3H), 4.64 (dd, J = 3.9, 12.2 Hz, 1H), 4.76–4.79 (m, 1H), 4.87 (dd, J = 2.9, 12.2 Hz, 1H), 6.13 (t, J = 5.1 Hz, 1H), 6.30 (t, J = 5.4 Hz, 1H), 6.37 (d, J = 5.5 Hz, 1H), 7.12, 7.18, 7.20 (3 $\times$ d, J = 7.8 Hz, 3 $\times$ 2H), 7.77 (br s, 2H), 7.79, 7.88, 7.95 (3 $\times$ d, J = 7.8 Hz, 3 $\times$ 2H), 8.08, 8.57 (2 $\times$ s, 2 $\times$ 1H); ^{13}C NMR δ 21.39, 21.42, 21.5, 63.2, 71.1, 73.5, 80.5, 87.0, 119.5, 125.4, 125.8, 126.3, 128.9–129.6 (ovlp), 141.9, 142.1, 143.9, 144.2, 144.3, 148.6, 165.0, 165.1, 165.9; FAB-MS m/z 660 (100%, M^+ + Na); HRMS Calcd for $\text{C}_{34}\text{H}_{31}\text{N}_5\text{O}_8\text{Na}$: 660.2070, Found: 660.2059.

Procedure B: Treatment of 2',3',5'-Tri-*O*-acetyladenosine 1-Oxide with Thiophenol in Acetic Anhydride. Typically, 2',3',5'-tri-*O*-acetyladenosine 1-oxide (**7**) (2.0 g, 4.9 mmol), acetic anhydride [3.67 mL, 3.96 g, 14.7 mmol (3 equiv)] and thiophenol (1.61 g, 14.7 mmol) were heated for 0.5 h at 80 $^\circ\text{C}$.^{5,6} Volatiles were evaporated, and the residue was deposited on silica gel and chromatographed (EtOAc/hexanes, 1:3 $\rightarrow$ 3:1) to give **9a** (*E/Z*, ~8:1).

1-(2,3,5-Tri-*O*-acetyl- β -D-ribofuranosyl)-4-(5-methyl-1,2,4-oxadiazol-3-yl)-5-[(phenylsulfanylmethylene)amino]imidazole (9a**).** Yellow oil: UV max 247, 322 nm (ϵ 12 500, 7900), min 234, 286 nm (ϵ 11 200, 4700); ^1H NMR δ 2.11, 2.14, 2.15, 2.60 (4 $\times$ s, 4 $\times$ 3H), 4.26–4.40 (m, 3H), 5.42 (t, J = 5.4 Hz, 1H), 5.61 (t, J = 5.1 Hz, 1H), 5.95 (d, J = 4.4 Hz, 1H), 7.42–7.46 (m, 3H), 7.64–7.66 (m, 2H), 7.71 (s, 1H), 9.78 (s, 1H); ^{13}C NMR δ 11.9, 20.1, 20.2, 20.4, 62.6, 69.8, 73.3, 79.4, 86.3, 115.5, 128.9, 129.1, 129.4, 132.7, 133.2, 139.0, 164.1, 168.8, 169.2, 170.0, 171.4, 175.7; FAB-MS m/z 566 (100%, M^+ + Na); HRMS Calcd for $\text{C}_{24}\text{H}_{25}\text{N}_5\text{O}_8\text{SNa}$: 566.1321, Found: 566.1328.

1-[2,3,5-Tri-*O*-(4-methylbenzoyl)- β -D-ribofuranosyl]-4-(5-methyl-1,2,4-oxadiazol-3-yl)-5-[(phenylsulfanylmethylene)amino]-imidazole (10a**).** Treatment of **8** by procedure B gave **10a** (58%) as a yellow oil: ^1H NMR δ 2.89 (s, 6H), 2.41, 2.58 (2 $\times$ s, 2 $\times$ 3H), 4.62 (dd, J = 4.4, 12.2 Hz, 1H),

⁴ Prepared by the modified procedure of Kikugawa, K.; Suehiro, H.; Yanase, R.; Aoki, A. *Chem. Pharm. Bull.* **1977**, 25, 1959–1969.

⁵ The molar equivalents and reaction time were doubled with benzoic anhydride.

⁶ Solutions of the higher (C_6 – C_{10}) aliphatic anhydrides and benzoic anhydride in 1,2-dichloroethane were used for reactions with **7**.

4.70–4.72 (m, 1H), 4.79 (dd, $J = 2.9, 12.2$ Hz, 1H), 5.87 (dd, $J = 4.9, 5.9$ Hz, 1H), 5.95 (t, $J = 5.4$ Hz, 1H), 6.21 (d, $J = 5.4$ Hz, 1H), 7.17–8.00 (m, 18H), 9.73 (s, 1H); ^{13}C NMR δ 12.0, 21.5 (3C), 63.6, 71.1, 74.3, 80.3, 86.3, 115.5, 125.6, 125.8, 126.3, 128.8–129.7 (ovlp), 132.4, 133.3, 139.3, 144.0, 144.27, 144.30, 164.2, 164.7, 165.1, 166.0, 171.2, 175.6; FAB-MS m/z 794 (100%, $\text{M}^+ + \text{Na}$), 487 (100%); HMRS Calcd for $\text{C}_{42}\text{H}_{37}\text{N}_5\text{O}_8\text{SNa}$: 794.2260, Found: 794.2263.

Procedure C: Conversion of 9, 10, 14, and 17 into 11 and 16. I_2 (0.5 molar equiv) was added to a stirred solution of the starting material in MeOH (30 mL) at 65 °C. Within 0.5 h the color of the reaction mixture turned from brown to pale yellow. Volatiles were evaporated, and the residue was dissolved in CH_2Cl_2 (20 mL). Et_3N (3 equiv) was added, the solution was concentrated, and the material was deposited on silica gel. Column chromatography (EtOAc/hexanes, 1:1 $\rightarrow$ EtOAc $\rightarrow$ EtOAc/MeOH, 10:1) gave the purified product.

5-Amino-1-(2,3,5-tri-*O*-acetyl- β -D-ribofuranosyl)-4-(5-methyl-1,2,4-oxadiazol-3-yl)imidazole (11a). Recrystallized (MeOH): mp 161–163 °C; ^1H NMR δ 2.13, 2.15, 2.16, 2.61 (4 $\times$ s, 4 $\times$ 3H), 4.35–4.49 (m, 3H), 5.03 (br s, 2H), 5.36 (t, $J = 5.4$ Hz, 4H), 5.56 (t, $J = 5.4$ Hz, 4H), 5.74 (d, $J = 5.4$ Hz, 4H), 7.38 (s, 1H); ^{13}C NMR δ 11.8, 20.03, 20.08, 20.3, 61.9, 69.2, 72.0, 79.6, 86.4, 109.9, 129.9, 139.0, 164.2, 169.2, 169.5, 169.8, 175.0; FAB-MS m/z 446 (100%, $\text{M}^+ + \text{Na}$); HRMS Calcd for $\text{C}_{17}\text{H}_{21}\text{N}_5\text{O}_8\text{Na}$: 446.1288, Found: 446.1283.

5-Amino-1-[2,3,5-tri-*O*-(4-methylbenzoyl)- β -D-ribofuranosyl]-4-(5-methyl-1,2,4-oxadiazol-3-yl)imidazole (11b). Recrystallized (MeOH): mp 219–221 °C; ^1H NMR δ 2.40 (s, 6H), 2.42, 2.58 (2 $\times$ s, 2 $\times$ 3H), 4.73–4.84 (m, 3H), 5.08 (br s, 2H), 5.82 (t, $J = 4.9$ Hz, 1H), 5.97 (t, $J = 5.4$ Hz, 1H), 6.00 (d, $J = 4.9$ Hz, 1H), 7.20 (d, $J = 8.3$ Hz, 4H), 7.28 (d, $J = 7.8$ Hz, 2H), 7.44 (s, 1H), 7.85, 7.86 (2 $\times$ d, $J = 8.3$ Hz, 2 $\times$ 2H), 7.98 (d, $J = 7.8$ Hz, 2H); ^{13}C NMR δ 12.2, 21.7 (3C), 62.9, 70.2, 73.0, 80.5, 87.1, 110.6, 125.5, 125.7, 126.2, 129.25, 129.29, 129.4, 129.7, 129.8, 129.9, 130.1, 139.3, 144.4, 144.7, 144.9, 164.6, 165.3, 165.5, 166.3, 175.2; FAB-MS m/z 674 (100%, $\text{M}^+ + \text{Na}$); HRMS Calcd for $\text{C}_{35}\text{H}_{33}\text{N}_5\text{O}_8\text{Na}$: 674.2227, Found: 674.2226.

Procedure D: Ammonolysis of 9. Compounds **9a–9h** were dissolved in NH_3/MeOH (~14%, 5 mL) and stirred overnight at 50 °C (oil bath). Volatiles were evaporated, and the residues were deposited on silica gel and chromatographed (EtOAc $\rightarrow$ EtOAc/MeOH, 10:1) to give **12a–12h**. These compounds were purified by recrystallization from MeOH unless indicated, except compounds **12f–12h** were repurified by chromatography (EtOAc $\rightarrow$ EtOAc/MeOH, 20:1).

5-Amino-1-(β -D-ribofuranosyl)-4-(5-methyl-1,2,4-oxadiazol-3-yl)imidazole (12a). mp 185–187 °C; UV max 241, 280 nm (ϵ 8100, 9000), min 217, 260 nm (ϵ 5400, 6900); ^1H NMR (CD_3OD) δ 2.59 (s, 3H), 3.76 (dd, $J = 2.9, 12.2$ Hz, 1H), 3.81 (dd, $J = 3.0, 11.8$ Hz, 1H), 4.06–4.08 (m, 1H), 4.24

(dd, $J = 2.9, 5.4$ Hz, 1H), 4.51 (dd, $J = 5.9, 6.3$ Hz, 1H), 5.60 (d, $J = 6.8$ Hz, 1H), 7.49 (s, 1H); ^{13}C NMR (DMSO- d_6) δ 12.0, 61.2, 70.4, 73.1, 85.5, 87.7, 106.6, 131.3, 141.2, 164.4, 175.4; FAB-MS m/z 297 (2%, M^+), 149 (100%); HRMS Calcd for $\text{C}_{11}\text{H}_{15}\text{N}_5\text{O}_5$: 297.1073, Found: 297.1077.

5-Amino-1-(β -D-ribofuranosyl)-4-(5-ethyl-1,2,4-oxadiazol-3-yl)imidazole (12b). mp 140–142 °C; UV max 242, 280 nm (ϵ 8000, 8600), min 218, 260 nm (ϵ 5400, 6700); ^1H NMR (DMSO- d_6) δ 1.31 (t, $J = 7.5$ Hz, 3H), 2.93 (q, $J = 7.5$ Hz, 2H), 3.56–3.64 (m, 2H), 3.90–3.92 (m, 1H), 4.04–4.07 (m, 1H), 4.30–4.33 (m, 1H), 5.20 (d, $J = 4.4$ Hz, 1H), 5.27 (t, $J = 5.1$ Hz, 1H), 5.40 (d, $J = 6.8$ Hz, 1H), 5.53 (d, $J = 6.3$ Hz, 1H), 5.78 (s, 2H), 7.49 (s, 1H); ^{13}C NMR ($\text{Me}_2\text{CO}-d_6$) δ 11.1, 20.6, 62.5, 72.4, 73.6, 86.9, 90.7, 108.4, 132.6, 142.0, 165.4, 180.2; FAB-MS m/z 312 (100%, M^+); HRMS Calcd for $\text{C}_{12}\text{H}_{18}\text{N}_5\text{O}_5$: 312.1308, Found: 312.1295.

5-Amino-1-(β -D-ribofuranosyl)-4-(5-propyl-1,2,4-oxadiazol-3-yl)imidazole (12c). Recrystallized (THF): mp 160–162 °C; UV max 241, 281 nm (ϵ 8400, 9100), min 217, 261 nm (ϵ 5600, 6800); ^1H NMR (DMSO- d_6) δ 0.96 (t, $J = 7.3$ Hz, 3H), 1.75–1.82 (m, 2H), 2.90 (t, $J = 7.3$ Hz, 2H), 3.56–3.64 (m, 2H), 3.91–3.93 (m, 1H), 4.04–4.07 (m, 1H), 4.30–4.33 (m, 1H), 5.20 (d, $J = 4.4$ Hz, 1H), 5.29 (t, $J = 5.1$ Hz, 1H), 5.41 (d, $J = 6.8$ Hz, 1H), 5.53 (d, $J = 6.8$ Hz, 1H), 5.79 (s, 2H), 7.50 (s, 1H); ^{13}C NMR (DMSO- d_6) δ 13.4, 19.6, 27.5, 61.1, 70.3, 73.0, 85.4, 87.7, 106.6, 131.2, 141.1, 164.3, 178.1; FAB-MS m/z 348 (100%, $\text{M}^+ + \text{Na}$); HRMS Calcd for $\text{C}_{13}\text{H}_{19}\text{N}_5\text{O}_5\text{Na}$: 348.1284, Found: 348.1286.

5-Amino-1-(β -D-ribofuranosyl)-4-[5-(1-methylethyl)-1,2,4-oxadiazol-3-yl]imidazole (12d). mp 183–186 °C; UV max 241, 281 nm (ϵ 8500, 9200), min 217, 261 nm (ϵ 5700, 6900); ^1H NMR (DMSO- d_6) δ 1.35 (d, $J = 7.3$ Hz, 6H), 3.23–3.31 (m, 1H), 3.56–3.66 (m, 2H), 3.91–3.95 (m, 1H), 4.06–4.09 (m, 1H), 4.30–4.35 (m, 1H), 5.21 (d, $J = 4.4$ Hz, 1H), 5.29 (t, $J = 4.9$ Hz, 1H), 5.41 (d, $J = 6.8$ Hz, 1H), 5.54 (d, $J = 6.3$ Hz, 1H), 5.79 (s, 2H), 7.50 (s, 1H); ^{13}C NMR (DMSO- d_6) δ 19.9, 26.7, 61.1, 70.3, 73.0, 85.4, 87.7, 106.7, 131.2, 141.1, 164.2, 182.0; FAB-MS m/z 348 (100%, $\text{M}^+ + \text{Na}$); HRMS Calcd for $\text{C}_{13}\text{H}_{19}\text{N}_5\text{O}_5\text{Na}$: 348.1284, Found: 348.1284.

5-Amino-1-(β -D-ribofuranosyl)-4-[5-(1,1-dimethylethyl)-1,2,4-oxadiazol-3-yl]imidazole (12e). mp 209–212 °C; UV max 240, 281 nm (ϵ 8100, 9000), min 217, 260 nm (ϵ 5700, 6700); ^1H NMR (DMSO- d_6) δ 1.41 (s, 9H), 3.56–3.65 (m, 2H), 3.92–3.94 (m, 1H), 4.06–4.09 (m, 1H), 4.31–4.34 (m, 1H), 5.21 (d, $J = 4.4$ Hz, 1H), 5.30 (t, $J = 4.9$ Hz, 1H), 5.41, 5.54 (2 $\times$ d, $J = 6.8$ Hz, 2 $\times$ 1H), 5.79 (s, 2H), 7.50 (s, 1H); ^{13}C NMR (DMSO- d_6) δ 28.0, 33.1, 61.1, 70.3, 73.0, 85.4, 87.7, 106.7, 131.2, 141.1, 164.2, 184.2; FAB-MS m/z 362 (100%, $\text{M}^+ + \text{Na}$); HRMS Calcd for $\text{C}_{14}\text{H}_{21}\text{N}_5\text{O}_5\text{Na}$: 362.1440, Found: 362.1440.

5-Amino-1-(β -D-ribofuranosyl)-4-(5-pentyl-1,2,4-oxadiazol-3-yl)imidazole (12f). UV max 240, 280 nm (ϵ 8600, 8900), min 217, 261 nm (ϵ 6200, 7000); ^1H NMR (DMSO- d_6) δ 0.86–0.89 (m,

3H), 1.30–1.36 (m, 4H), 1.72–1.79 (m, 2H), 2.91 (t, $J = 7.3$ Hz, 2H), 3.56–3.64 (m, 2H), 3.91–3.93 (m, 1H), 4.05–4.08 (m, 1H), 4.30–4.33 (m, 1H), 5.20 (d, $J = 4.4$ Hz, 1H), 5.28 (t, $J = 4.9$ Hz, 1H), 5.41 (d, $J = 6.8$ Hz, 1H), 5.53 (d, $J = 6.4$ Hz, 1H), 5.78 (s, 2H), 7.50 (s, 1H); ^{13}C NMR ($\text{Me}_2\text{CO}-d_6$) δ 14.2, 22.9, 26.8, 27.0, 31.9, 62.5, 72.0, 73.7, 87.0, 90.8, 108.0, 132.7, 142.0, 165.2, 179.5; FAB-MS m/z 376 (100%, $\text{M}^+ + \text{Na}$); HRMS Calcd for $\text{C}_{15}\text{H}_{23}\text{N}_5\text{O}_5\text{Na}$: 376.1597, Found: 376.1605.

5-Amino-1-(β -D-ribofuranosyl)-4-(5-heptyl-1,2,4-oxadiazol-3-yl)imidazole (12g). UV max 240, 280 nm (ϵ 8300, 8800), min 218, 261 nm (ϵ 6100, 6800); ^1H NMR ($\text{DMSO}-d_6$) δ 0.86 (m, $J = 7.8$ Hz, 3H), 1.22–1.38 (m, 8H), 1.72–1.79 (m, 2H), 2.91 (t, $J = 7.3$ Hz, 2H), 3.56–3.64 (m, 2H), 3.90–3.93 (m, 1H), 4.05–4.08 (m, 1H), 4.30–4.34 (m, 1H), 5.20 (d, $J = 4.4$ Hz, 1H), 5.28 (t, $J = 4.9$ Hz, 1H), 5.41, 5.53 (2 $\times$ d, $J = 6.8$ Hz, 2 $\times$ 1H), 5.78 (s, 2H), 7.50 (s, 1H); ^{13}C NMR ($\text{DMSO}-d_6$) δ 13.9, 22.0, 25.6, 26.0, 28.2, 28.3, 31.1, 61.1, 70.3, 73.0, 85.4, 87.6, 106.6, 131.1, 141.1, 164.2, 178.3; FAB-MS m/z 404 (100%, $\text{M}^+ + \text{Na}$); HRMS Calcd for $\text{C}_{17}\text{H}_{27}\text{N}_5\text{O}_5\text{Na}$: 404.1910, Found: 404.1903.

5-Amino-1-(β -D-ribofuranosyl)-4-(5-phenyl-1,2,4-oxadiazol-3-yl)imidazole (12h).

Recrystallized (pyridine/MeOH): mp. 218–219 °C dec.; UV max 266 nm (ϵ 30 800), min 219 nm (ϵ 8500); ^1H NMR ($\text{DMSO}-d_6$) δ 3.58–3.66 (m, 2H), 3.92–3.95 (m, 1H), 4.07–4.10 (m, 1H), 4.32–4.37 (m, 1H), 5.21 (d, $J = 4.4$ Hz, 1H), 5.31 (t, $J = 5.1$ Hz, 1H), 5.44 (d, $J = 6.8$ Hz, 1H), 5.58 (d, $J = 6.4$ Hz, 1H), 5.95 (s, 2H), 7.54 (s, 1H), 7.63–7.73 (m, 3H), 8.22 (d, $J = 7.4$ Hz, 2H); ^{13}C NMR ($\text{DMSO}-d_6$) δ 61.2, 70.4, 73.0, 85.6, 87.8, 106.4, 123.7, 128.0, 129.5, 131.4, 133.1, 141.6, 165.0, 173.6.

3',5'-Di-*O*-acetyl-2'-adenosine 1-Oxide² (13). H_2O_2 (30%, 2.0 mL) was added to a stirred solution of 3',5'-di-*O*-acetyl-2'-deoxyadenosine³ (2.0 g, 6.0 mmol) in AcOH (20 mL), and stirring was continued for 24 h at 45 °C.⁷ Volatiles were evaporated in vacuo (at 45 °C), and the residue was chromatographed (EtOAc $\rightarrow$ EtOAc/MeOH, 10:1 $\rightarrow$ 3:1) to give **13** (1.91 g, 91%) as a pale-yellow oil that crystallized. Recrystallization (EtOH) gave **13**: mp 175–177 °C; UV max 263 nm (ϵ 10 300), min 254 nm (ϵ 9500); ^1H NMR δ 2.09, 2.15 (2 $\times$ s, 2 $\times$ 3H), 2.66 (ddd, $J = 2.9, 5.8, 14.2$ Hz, 1H), 2.94 (ddd, $J = 6.3, 7.8, 14.2$ Hz, 1H), 4.33–4.43 (m, 3H), 5.41–5.53 (m, 1H), 6.39 (dd, $J = 6.3, 7.8$ Hz, 1H), 7.52 (br s, 2H), 8.09, 8.72 (2 $\times$ s, 2 $\times$ 1H); ^{13}C NMR δ 20.5, 20.7, 36.9, 63.4, 74.2, 82.3, 84.5, 119.4, 141.2, 142.0, 144.0, 148.6, 170.1, 170.3; FAB-MS m/z 374 (100%, $\text{M}^+ + \text{Na}$); HRMS Calcd for $\text{C}_{14}\text{H}_{17}\text{N}_5\text{O}_6\text{Na}$: 374.1076, Found: 374.1067.

1-(3,5-Di-*O*-acetyl- β -D-erythro-pentofuranosyl)-4-(5-methyl-1,2,4-oxadiazol-3-yl)-5-[(phenylsulfanylmethylene)amino]imidazole (14a). ^1H NMR δ 2.10, 2.15 (2 $\times$ s, 2 $\times$ 3H), 2.43 (ddd, $J = 2.9, 5.9, 14.2$ Hz, 1H), 2.50 (dt, $J = 14.2, 6.8$ Hz, 1H), 2.61 (s, 3H), 4.25–4.38 (m, 3H), 5.25–5.28 (m,

⁷ Higher reaction temperatures caused significant glycosyl cleavage.

1H), 6.10 (dd, 7.4, 6.3 Hz, 1H), 7.40–7.65 (m, 5H), 7.71 (s, 1H), 9.79 (s, 1H); FAB-MS m/z 508 (100%, M^+); HRMS Calcd for $C_{22}H_{23}N_5O_6SNa$: 508.1267, Found: 508.1268.

1-(3,5-Di-*O*-acetyl- β -D-erythro-pentofuranosyl)-4-(5-pentyl-1,2,4-oxadiazol-3-yl)-5-[(phenylsulfanylmethylene)amino]imidazole (14b). 1H NMR δ 0.88–0.92 (m, 3H), 1.33–1.38 (m, 4H), 1.79–1.88 (m, 2H), 2.10, 2.15 ($2 \times s$, $2 \times 3H$), 2.42 (ddd, $J = 2.9, 5.9, 14.2$ Hz, 1H), 2.50 (ddd, $J = 14.2, 6.8, 7.8$ Hz, 1H), 2.89 (t, $J = 7.8$ Hz, 2H), 3.56–3.64 (m, 2H), 4.25–4.38 (m, 3H), 5.25–5.27 (m, 1H), 6.10 (dd, $J = 5.9, 7.3$ Hz, 1H), 7.40–7.66 (m, 5H), 7.71, 9.80 ($2 \times s$, $2 \times 1H$); FAB-MS m/z 542 (100%, $M^+ + 1$); HRMS Calcd for $C_{26}H_{32}N_5O_6S$: 542.2073, Found: 542.2076.

5-Amino-1-(2-deoxy- β -D-erythro-pentofuranosyl)-4-(5-methyl-1,2,4-oxadiazol-3-yl)imidazole (15a). Recrystallized (MeOH): mp 192–195 °C dec.; UV max 240, 279 nm (ϵ 8400, 9100), min 217, 260 nm (ϵ 5900, 7200); 1H NMR (DMSO- d_6) δ 2.17 (ddd, $J = 2.9, 5.9, 13.2$ Hz, 1H), 2.42–2.47 (m, 1H), 2.58 (s, 3H), 3.51–3.58 (m, 2H), 3.80–3.84 (m, 1H), 4.32–4.34 (m, 1H), 5.13 (t, $J = 5.1$ Hz, 1H), 5.30 (d, $J = 3.9$ Hz, 1H), 5.77 (s, 2H), 5.98 (dd, $J = 5.9, 7.8$ Hz, 1H), 7.52 (s, 1H); ^{13}C NMR (DMSO- d_6) δ 11.9, 39.3, 61.4, 70.7, 83.7, 87.5, 106.6, 130.7, 141.0, 164.4, 175.3; FAB-MS m/z 282 (100%, $M^+ + 1$); HRMS Calcd for $C_{11}H_{16}N_5O_4$: 282.1202, Found: 282.1203.

5-Amino-1-(2-deoxy- β -D-erythro-pentofuranosyl)-4-(5-pentyl-1,2,4-oxadiazol-3-yl)imidazole (15b). Recrystallized (MeOH) mp 193–195 °C dec.; UV max 241, 280 nm (ϵ 8700, 9200), min 216, 261 nm (ϵ 5600, 7000); 1H NMR (DMSO- d_6) δ 0.86–0.89 (m, 3H), 1.30–1.36 (m, 4H), 1.72–1.79 (m, 2H), 2.17 (ddd, $J = 2.4, 5.9, 12.7$ Hz, 1H), 2.42–2.47 (m, 1H), 2.49–2.52 (m, 2H), 2.91 (t, $J = 7.2$ Hz, 2H), 3.52–3.58 (m, 2H), 3.80–3.84 (m, 1H), 4.32–4.34 (m, 1H), 5.14 (t, $J = 4.9$ Hz, 1H), 5.30 (d, $J = 3.9$ Hz, 1H), 5.77 (s, 2H), 5.98 (dd, $J = 5.9, 7.8$ Hz, 1H), 7.52 (s, 1H); ^{13}C NMR (DMSO- d_6) δ 13.8, 21.7, 25.6, 15.7, 30.6, 39.3, 61.4, 70.7, 83.8, 87.5, 106.7, 130.7, 141.0, 164.3, 175.3; FAB-MS m/z 338 (100%, $M^+ + 1$); HRMS Calcd for $C_{15}H_{24}N_5O_4$: 338.1828, Found: 338.1825.

5-Amino-1-(3,5-di-*O*-acetyl- β -D-erythro-pentofuranosyl)-4-(5-methyl-1,2,4-oxadiazol-3-yl)imidazole (16). UV max 241, 276 nm (ϵ 8100, 8700), min 215, 259 nm (ϵ 5800, 7500); 1H NMR δ 2.08, 2.13 ($2 \times s$, $2 \times 3H$), 2.42 (ddd, $J = 2.4, 5.4, 14.2$ Hz, 1H), 2.61 (s, 3H), 2.91 (ddd, $J = 6.8, 8.8, 14.2$ Hz, 1H), 4.26–4.41 (m, 3H), 4.95 (br s, 2H), 5.30–5.32 (m, 1H), 5.92 (dd, $J = 5.4, 8.3$ Hz, 1H), 7.27 (s, 1H); ^{13}C NMR δ 12.0, 20.4, 20.6, 35.6, 63.2, 73.7, 82.1, 84.7, 109.9, 129.9, 139.8, 164.3, 170.1 (2C), 175.1; FAB-MS m/z 388 (100%, $M^+ + Na$); HRMS Calcd for $C_{15}H_{19}N_5O_6Na$: 388.1239, Found: 388.1244.

1-(2,3,5-Tri-*O*-acetyl- β -D-ribofuranosyl)-3-(5-methyl-1,2,4-oxadiazol-3-yl)-2-[(phenylsulfanylmethylene)amino]pyrrole (19). A solution of 2',3',5'-tri-*O*-acetyltubercidin (1.35 g, 3.3 mmol) and MCPBA (77%; 1.5 g, 6.7 mmol) in CH_2Cl_2 (20 mL) was stirred for 2 h at ambient

temperature. Volatiles were evaporated, Ac₂O (1.0 g, 9.9 mmol) and PhSH (1.1 g, 9.9 mmol) were added, and stirring was continued for 1 h. Volatiles were evaporated, and the dark-red residue was chromatographed (EtOAc/hexanes, 1:6 → 1:1) to give **19** (*E/Z*, ~8:1) (0.43 g, 24%) as a yellow oil: UV max 251, 341 nm (ϵ 17 000, 9800), min 237, 295 nm (ϵ 4500, 14 600); ¹H NMR δ 2.09 (s, 3H), 2.14 (s, 6H), 2.57 (s, 3H), 5.41 (t, *J* = 5.4 Hz, 1H), 5.52 (t, *J* = 5.6 Hz, 1H), 6.11 (d, *J* = 5.3 Hz, 1H), 6.68, 6.78 (2 × d, *J* = 3.4 Hz, 2 × 1H), 7.38–7.50 (m, 3H), 7.63–7.66 (m, 2H), 9.58 (s, 1H); ¹³C NMR δ 11.7, 20.0, 20.1, 20.3, 62.9, 70.0, 73.2, 78.7, 85.9, 97.9, 109.8, 115.3, 128.4, 128.9, 129.3, 132.5, 138.8, 164.5, 167.7, 168.8, 169.1, 169.9, 174.8; FAB-MS *m/z* 565 (100%, M⁺ + Na); HMRS Calcd for C₂₅H₂₆N₄O₈SNa: 565.1369, Found: 565.1368.

Treatment of 2',3',5'-Tri-*O*-acetylformycin 6-Oxide with Thiophenol in Hexanoic Anhydride.

A mixture of 2',3',5'-tri-*O*-acetylformycin 6-oxide² (1.5 g, 3.6 mmol), PhSH (1.2 g, 11.0 mmol) and hexanoic anhydride (2.36 g, 11.0 mmol) was stirred at 50 °C for 1 h. Volatiles were evaporated, and chromatography (EtOAc → EtOAc/MeOH, 10:1) revealed a complex mixture.

Procedure E: Acetylation of 11a. A solution of **11a** (0.65 g, 1.54 mmol) in Ac₂O (2 mL) and pyridine (2 mL) was stirred at 100 °C for 1 h. Volatiles were evaporated, and the residue was chromatographed (EtOAc/hexanes, 1:2 → EtOAc) to give 5-(*N,N*-diacetylamino)-1-(2,3,5-tri-*O*-acetyl- β -D-ribofuranosyl)-4-(5-methyl-1,2,4-oxadiazol-3-yl)imidazole (**20a**) (0.75 g, 96%): ¹H NMR δ 2.08, 2.15, 2.17, 2.24, 2.46, 2.62 (6 × s, 6 × 3H), 4.30–4.43 (m, 3H), 5.41 (dd, *J* = 3.4, 5.4 Hz, 1H), 5.57 (d, *J* = 6.3 Hz, 1H), 5.60 (dd, *J* = 5.4, 5.9 Hz, 4H), 7.99 (s, 1H); ¹³C NMR δ 12.2, 20.2, 20.5, 20.7, 25.4, 26.1, 62.8, 70.3, 73.2, 80.7, 85.4, 126.2, 127.9, 135.2, 162.8, 169.1, 169.5, 170.0, 172.4, 172.7, 176.7; FAB-MS *m/z* 530 (82%, M⁺ + Na), 488 (100%); HMRS Calcd for C₂₁H₂₅N₅O₁₀Na: 530.1499, Found: 530.1483.

Acetylation of 16. Treatment of **16** by procedure E gave 5-(*N,N*-diacetylamino)-1-(3,5-di-*O*-acetyl- β -D-erythro-pentofuranosyl)-4-(5-methyl-1,2,4-oxadiazol-3-yl)imidazole (**20b**) (89%): ¹H NMR δ 2.10, 2.12, 2.13 (3 × s, 3 × 3H), 2.58 (ddd, *J* = 2.0, 5.4, 14.2 Hz, 1H), 2.60, 2.62 (2 × s, 2 × 3H), 2.73 (ddd, *J* = 6.8, 8.3, 14.2 Hz, 1H), 4.24–4.32 (m, 3H), 5.33–5.35 (m, 1H), 5.74 (dd, *J* = 5.9, 8.3 Hz, 1H), 7.97 (s, 1H); ¹³C NMR δ 12.1, 20.5, 20.7, 24.8, 26.5, 37.6, 63.4, 73.9, 82.7, 83.9, 125.7, 127.8, 134.7, 162.7, 170.0 (2C), 172.0, 173.3, 176.6; FAB-MS *m/z* 450 (30%, M⁺ + 1), 250 (100%); HRMS Calcd for C₁₉H₂₄N₅O₈: 450.1624, Found: 450.1624.