Supplementary material for manuscript B414739A

Experimental for the synthesis of compounds **16**, **17**, **20**, **21**, **23**, **25**, **31**, **34**, **35**, **36**, **38** and **41**.

Synthesis of 5′-deoxyadenosine 16[23]

A solution of 5′-*O*-*p*-toluenesulphonyladenosine (prepared from N^6-benzoyladenosine[50] using i. TsCl/pyridine, ii. conc. NH_3 aq./MeOH[23]) (65 mg, 0.15 mmol) in 1 M lithium triethyl borohydride (Super hydride) in anhydrous THF (5 cm^3) was stirred at 30 °C for 2 h. The reaction was quenched by the addition of water (0.5 cm^3) with stirring for a further 10 min. The solution was evaporated to dryness to leave a pale yellow residue. Purification on two silica columns (50:50 and 80:20 chloroform/methanol) gave **16** (23 mg, 61%) as a colourless powder; δ_H (250 MHz; DMSO-d_6) 8.30 (1H, s, H-8), 8.11 (1H, s, H-2), 7.28 (2H, br s, N$\underline{H}_2$), 5.80 (1H, d, $J_{1',2'}$ 4.9, H-1′), 5.44 (1H, d, $J_{2',2'\text{-OH}}$ 5.7, OH-2′), 5.16 (1H, d, $J_{3',3'\text{-OH}}$ 4.6, OH-3′), 4.63 (1H, dd, $J_{1',2'} = J_{2',3'}$ 4.9, H-2′), 3.92 (2H, m, overlapping H-3′ and H-4′) and 1.26 (3H, d, $J_{4',5'}$ 5.8, H-5′ C$\underline{H}_3$); δ_C (62.9 MHz; DMSO-d_6) 156.4 (C-6), 153.0 (C-2), 149.7 (C-4), 140.2 (C-8), 119.5 (C-5), 88.1 (C-1′), 80.0 (C-4′), 74.9 (C-2′), 73.3 (C-3′) and 19.3 (C-5′); *m/z* (EI) 251 (M^+), 234 (M^+ - OH), 216 (M^+ - 2(OH) - H), 204 (M^+ - 2(OH) - CH_3 - 2H), 135 (100%, M^+ - sugar), 119 (9, 135 - NH_2); R_f (90:10 acetone/water) 0.37.

Synthesis of (*S*)-9-(2,3-dihydroxypropyl)adenine 17[24]

A stirred solution of (*S*)-9-(2,3-*O*-isopropylidene-D-glyceryl)adenine[24] (120 mg, 0.48 mmol) in 80% aqueous acetic acid (20 cm^3) was refluxed for 1 h. The reaction mixture was evaporated to give a residue which was repeatedly co-evaporated with 50% aqueous ethanol and then dried under vacuum over P_2O_5 to give **17** (100.7 mg, 100%) as colourless plates; δ_H (250 MHz; DMSO-d_6) 7.97 (1H, s, H-8), 7.88 (1H, s, H-2), 7.08 (2H, br s, N$\underline{H}_2$), 4.14 (2H,

dd, $J_{2',3'a} = J_{2',3'b}$ 3.5, $J_{3'a,3'b}$ 13.8, H-3′), 3.83 (2H, m, $J_{1'a,2'} = J_{1'b,2'}$ 8.2, $J_{1'a,1'b}$ 13.8, H-1′) and 3.66 (1H, m, H-2′); δ_C (62.9 MHz; DMSO-d_6) 156.3 (C-6), 152.6 (C-2), 150.0 (C-4), 142.0 (C-8), 118.9 (C-5), 70.0 (C-2′), 63.9 (C-3′) and 46.8 (C-1′); *m/z* (FAB) 210 (100%, M^+ + H), 192 (2, M^+ - OH), 178 (4, M^+ - CH_2OH), 148 (M^+ - $HOCH_2CHOH$); *m/z* (ES) 210.0973 (M^+ + H, $C_8H_{12}N_5O_2$ requires 210.0991, difference 8.6 ppm); R_f (90:10 chloroform/methanol) 0.05.

Synthesis of 3′-azido-2′,3′-dideoxyadenosine 20[30]

N,*O*-*bis*-Trimethylsilylacetamide (0.56 cm^3, 461 mg, 2.27 mmol) was added to a suspension of 3′-azido-3′-deoxythymidine **19** (100 mg, 0.37 mmol) and N^6-octanoyladenine[51] (178 mg, 0.68 mmol) in anhydrous acetonitrile (2.5 cm^3) and the mixture was heated at reflux for 15 min to give a translucent solution. Trimethylsilyl trifluoromethanesulphonate (82 μl, 101 mg, 0.45 mmol) was added and the mixture was refluxed under an atmosphere of nitrogen for 2 h. After allowing to cool to room temperature, the reaction mixture was evaporated to leave a yellow oil. The reaction was then repeated on the same scale. The residues from the two preparations were combined and dissolved in 1:2 ethanol/1M aqueous ammonia and the solution was applied to a column of Dowex 1 x 2-200 anion-exchange resin (100 cm^3) prepared in the OH^- form. After allowing to run into the column, the column was eluted with 1:2 ethanol/water (500 cm^3). The eluate was collected as a single fraction and evaporated to dryness to leave a yellow residue containing a colourless solid. TLC analysis (90:10 chloroform/methanol) revealed the α and β anomers of the product R_f 0.28 and 0.45. These were separated on a silica column (100 g) which was eluted with 98:2 chloroform/methanol (150 x *ca.* 10 cm^3 fractions, then 96:4 chloroform/methanol (150-215 x *ca.* 10 cm^3 fractions) and then 90:10 chloroform/methanol (216-225 x *ca.* 100 cm^3 fractions). Fractions 217-225 were combined and evaporated to leave a residue which was dried under vacuum over P_2O_5 to

give the α form (22.9 mg, 11%) as a colourless semi-crystalline oil; δ_H (250 MHz; DMSO-*d*$_6$) 8.30 (1H, s, H-8), 8.16 (1H, s, H-2), 7.34 (2H, br s, N<u>H</u>$_2$), 6.34 (1H, t, $J_{1',2'a} = J_{1',2'b}$ 5.2, H-1′), 5.11 (1H, t, $J_{5'a,5'\text{-OH}} = J_{5'b,5'\text{-OH}}$ 5.5, OH-5′), 4.39 (1H, m, H-3′), 4.29 (1H, m, H-4′), 3.55 (2H, m, *J* 4.7, H-5′a and H-5′b) and 2.96-2.69 (2H, m, $J_{1',2'a} = J_{1',2'b}$ 5.2, $J_{2'a,2'b}$ 13.8, H-2′a and H-2′b); δ_C (62.9 MHz; DMSO-*d*$_6$) 156.4 (C-6), 152.9 (C-2), 149.3 (C-4), 139.5 (C-8), 119.5 (C-5), 84.9 (C-4′), 83.8 (C-1′), 61.4 (C-5′), 60.9 (C-3′) and 36.7 (C-2′); Fractions 140-170 were combined and evaporated to leave a colourless oil which crystallised on cooling to room temperature. This was dried under vacuum over P_2O_5 to leave colourless plates (118.6 mg). NMR analysis (DMSO-*d*$_6$) revealed that the β anomer of the product had been obtained along with a relatively large amount of a carbonyl-containing impurity. This was removed on a silica column (96:4 chloroform/methanol) to give **20** (17.3 mg, 8%) as a colourless powder; δ_H (250 MHz; DMSO-*d*$_6$) 8.23 (1H, s, H-8), 8.02 (1H, s, H-2), 7.25 (2H, br s, N<u>H</u>$_2$), 6.19 (1H, t, $J_{1',2'a} = J_{1',2'b}$ 6.8, H-1′), 5.26 (1H, t, $J_{5'a,5'\text{-OH}}$ 6.0, $J_{5'b,5'\text{-OH}}$ 5.4, OH-5′), 4.52 (1H, m, H-3′), 3.82 (1H, q, $J_{3',4'} = J_{4',5'}$ 4.3, H-4′), 3.50 (2H, m, H-5′a and H-5′b), 2.85 (1H, m, $J_{1',2'a} = J_{2'a,3'}$ 6.8, $J_{2'a,2'b}$ 13.5, H-2′a) and 2.40 (1H, m, H-2′b, overlapping DMSO-*d*$_6$); δ_C (62.9 MHz; DMSO-*d*$_6$) 156.5 (C-6), 152.8 (C-2), 149.2 (C-4), 139.9 (C-8), 119.5 (C-5), 85.1 (C-4′), 83.7 (C-1′), 61.8 (C-5′), 61.5 (C-3′) and 36.5 (C-2′); *m/z* (ES) 299 (100%, M^+ + Na); *m/z* (FAB) 277 (26%, M^+ + H); *m/z* (EI) 276.107 (M^+, $C_{10}H_{12}N_8O_2$ requires 276.108, difference 3.6 ppm).

Synthesis of 9-β-D-ribofuranosylpurine (Purine riboside, Nebularine) 21[32]

A solution of 2′,3′,5′-tri-*O*-acetyladenosine[32] (500 mg, 1.27 mmol) and *n*-pentyl nitrite[52] (1.27 cm^3, 1.10 g, 9.40 mmol) in anhydrous THF (20 cm^3) was stirred at 50 °C under an atmosphere of nitrogen for *ca.* 24 h. A further addition of pentyl nitrite (1.27 cm^3, 1.10 g, 9.40 mmol) was

made each day for two more days. THF was added as appropriate to maintain the solvent level in the reaction mixture. After a total of *ca.* 3 days the reaction mixture was evaporate to leave a yellow/orange oily residue. The deaminated product was isolated from minor side products (TLC 95:5 chloroform/methanol R_f 0.42 and 0.02, 0.20, 0.25, 0.89 respectively) on a silica column (96:4 chloroform/methanol) to give 9-(2′,3′,5′-tri-*O*-acetyl-β-D-ribofuranosyl)purine (331 mg, 69%) as a colourless semi-crystalline oil; δ_H (250 MHz; $CDCl_3$) 9.12 (1H, s, H-6), 8.95 (1H, s, H-8), 8.22 (1H, s, H-2), 6.20 (1H, d, $J_{1',2'}$ 5.3, H-1′), 5.92 (1H, t, $J_{1',2'} = J_{2',3'}$ 5.3, H-2′), 5.63 (1H, t, $J_{2',3'}$ 5.3, $J_{3',4'}$ 4.7, H-3′), 4.41 (3H, m, overlapping H-4′, H-5′a and H-5′b) and 2.10, 2.06, 2.02 (9H, 3 x s, 3 x C<u>H</u>$_3$); δ_C (62.9 MHz; $CDCl_3$) 170.7, 170.0, 169.8 (3 x <u>C</u>=O), 153.3 (C-2), 151.2 (C-4), 149.5 (C-6), 144.1 (C-8), 135.0 (C-5), 86.8 (C-1′), 80.8 (C-4′), 73.4 (C-3′), 70.9 (C-2′), 63.4 (C-5′) and 21.1, 20.9, 20.8 (3 x <u>C</u>H$_3$); *m/z* (EI) 379 (53%, M^+ + H), 335 (10, M^+ - CH_3CO), 259 (72, (M^+ - 119 (purine) + H), 216 (21, 259 - CH_3CO), 121 (89, M^+ - sugar), 43 (100, CH_3CO^+).

Deprotection using sodium methoxide and recrystallisation from methanol/diethyl ether afforded **21** (78 mg, 77%) as colourless plates (Found: C, 47.75; H, 5.0; N, 22.4. $C_{10}H_{12}N_4O_4$ requires C, 47.6; H, 4.8; N, 22.2%); δ_H (250 MHz; DMSO-d_6) 9.23 (1H, s, H-6), 8.98 (1H, s, H-8), 8.89 (1H, s, H-2), 6.07 (1H, d, $J_{1',2'}$ 5.7, H-1′), 5.62 (1H, d, $J_{2',2'\text{-OH}}$ 6.0, OH-2′), 5.32 (1H, d, $J_{3',3'\text{-OH}}$ 4.9, OH-3′), 5.17 (1H, t, $J_{5'a,5'\text{-OH}} = J_{5'b,5'\text{-OH}}$ 5.5, OH-5′), 4.67 (1H, dd, $J_{1',2'}$ 5.7, $J_{2',3'}$ 5.0, H-2′), 4.22 (1H, dd, $J_{2',3'}$ 5.0, $J_{3',4'}$ 3.8, H-3′), 4.01 (1H, m, $J_{3',4'}$ 3.8, $J_{4',5'}$ 3.8, H-4′) and 3.67 (2H, m, H-5′a and H-5′b); δ_C (62.9 MHz; DMSO-d_6) 152.5 (C-2), 151.3 (C-4), 148.6 (C-6), 145.8 (C-8), 134.5 (C-5), 87.8 (C-1′), 86.1 (C-4′), 74.0 (C-3′), 70.7 (C-2′) and 61.6 (C-5′); *m/z* (EI) 252 (M^+), 235 (M^+ - OH), 222 (M^+ - CH_2OH + H), 205 (M^+ - CH_2OH - OH + H), 187 (M^+ - CH_2OH - 2(OH) + H) 133 (16%, M^+ - purine), 121 (100, M^+ - sugar); *m/z* (FAB) 253 (100%, M^+ + H), 121 (M^+ - sugar); R_f (90:10 chloroform/methanol) 0.53.

Synthesis of 1,3-dideazaadenosine 23[29]

This was prepared from 3-nitro-1,2-phenylenediamine (i. HCOOH/reflux, ii. 30% NH_4OH, 93%; iii. 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranoside/$SnCl_4$/MeCN, 37%; iv. NaOMe/ MeOH, 60%; v. 10% Pd/C /H_2/MeOH, 74%)[29] with final purification on a silica column (80:20 chloroform/methanol) to give **23** (92 mg) as a pale yellow glass; δ_H (250 MHz; DMSO-d_6) 8.24 (1H, s, H-8), 6.93 (1H, t, $J_{1,2} = J_{2,3}$ 7.7, H-2), 6.81 (1H, d, $J_{2,3}$ 7.7, H-3), 6.40 (1H, d, $J_{1,2}$ 7.7, H-1), 5.75 (1H, d, $J_{1',2'}$ 5.8, H-1′), 4.33 (1H, t, $J_{1',2'}$ 5.8, $J_{2',3'}$ 5.3, H-2′), 4.10 (1H, t, $J_{2',3'}$ 5.3, $J_{3',4'}$ 3.8, H-3′), 3.93 (1H, m, H-4′) and 3.62 (2H, m, $J_{4',5'a}$ 3.6, $J_{4',5'b}$ 3.4, $J_{5'a,5'b}$ 15.4, H-5′a and H-5′b); δ_C (62.9 MHz; $CDCl_3$) 140.7 (C-6), 139.7 (C-8), 134.0 (C-5), 132.6 (C-4), 124.1 (C-2), 105.1 (C-1), 99.1 (C-3), 89.0 (C-1′), 85.5 (C-4′), 73.9 (C-2′), 70.3 (C-3′) and 61.6 (C-5′); *m/z* (EI) 265 (17%, M^+), 133 (100, M^+ - base or M^+ - sugar + H); *m/z* (EI) 265.106 (M^+, $C_{12}H_{15}N_3O_4$ requires 265.106, difference 0.0 ppm); R_f (80:20 chloroform/methanol) 0.32.

Synthesis of 1-deoxy-1-phenyl-β-D-ribofuranoside 25

This was prepared from 1-*O*-methyl-β-D-ribofuranoside (i. BnCl/KOH/THF/reflux, 100%; ii. 0.1 M HCl/1,4-Dioxane/reflux, 84%; iii. PhMgBr/Et_2O, 59%; iv. *p*-toluenesulphonic acid monohydrate/Benzene/Reflux, 84%; v. 1 M BBr_3/CH_2Cl_2/-78 °C, 62%) with adaptations from refs. 53 and 47, the Grignard reaction was based on ref. 54. The final product was purified on a silica column with gradient elution (95:5 – 90:10 chloroform/methanol) to give **25**[31] (135 mg) as a very pale yellow semi-crystalline oil; δ_H (250 MHz; DMSO-d_6) 7.43-7.22 (5H, m, Ar-H), 4.58 (1H, d, $J_{1,2}$ 6.9, H-1), 4.02 (1H, dd, $J_{2,3}$ 5.7, $J_{3,4}$ 3.8, H-3), 3.90 (1H, dd, $J_{3,4}$ 3.8, $J_{4,5a} = J_{4,5b}$ 4.6, H-4), 3.70 (1H, dd, $J_{1,2}$ 6.9, $J_{2,3}$ 5.7, H-2) and 3.56 (2H, m, $J_{4,5a} = J_{4,5b}$ 4.6, $J_{5a,5b}$ 11.8, H-5a and H-5b); δ_C (62.9 MHz; DMSO-d_6) 141.8 (Ar-C, unprotonated), 128.3, 127.6, 127.0 (Ar-C, *o*, *m* and *p*), 85.4 (C-4), 83.4 (C-1), 78.0 (C-2), 71.8 (C-3) and 62.4 (C-5); *m/z*

(EI) 209 (48%, M^+ - H), 192 (14, M^+ - OH - H), 179 (10, M^+ - CH_2OH), 77 (24, M^+ - sugar); *m/z* (ES) 233.0791 (M^+ + Na, $C_{11}H_{14}O_4Na$ requires 233.0790, difference 0.4 ppm).

Synthesis of 6-chloropurine riboside 31

This was prepared from inosine **3** (5.0 g, 18.6 mmol) (i. Ac_2O/Pyridine, 100%; ii. $SOCl_2$/DMF/$CHCl_3$, 96%; iii. NaOMe/MeOH, 51%) to give **31**[26] (1.55 g, overall 49%) as a cream/pale yellow powder (Found: C, 41.85; H, 3.95; N, 19.8. $C_{10}H_{11}N_4O_4Cl$ requires C, 41.90; H, 3.9; N, 19.5%); δ_H (250 MHz; DMSO-d_6) 8.99 (1H, s, H-8), 8.82 (1H, s, H-2), 6.06 (1H, d, $J_{1',2'}$ 5.2, H-1′), 5.63 (1H, unresolved d, OH-2′), 5.32 (1H, unresolved d, OH-3′), 5.15 (1H, unresolved t, OH-5′), 4.60 (1H, t, $J_{1',2'}$ 5.2, $J_{2',3'}$ 4.7, H-2′), 4.21 (1H, t, $J_{2',3'}$ 4.7, $J_{3',4'}$ 4.3, H-3′), 4.01 (1H, m, $J_{4',5'a} = J_{4',5'b}$ 3.8, H-4′) and 3.66 (2H, ddd, $J_{4',5'a} = J_{4',5'b}$ 3.8, $J_{5'a,5'b}$ 12.0, H-5′a and H-5′b); δ_C (62.9 MHz; DMSO-d_6) 152.1 (C-2), 152.0 (C-4), 149.6 (C-6), 146.1 (C-8), 131.7 (C-5), 88.5 (C-1′), 86.1 (C-4′), 74.4 (C-2′), 70.4 (C-3′) and 61.3 (C-5′), *m/z* (FAB) 287 (60%, M^+ + H), 251 (6, M^+ - Cl); R_f (90:10 chloroform/methanol) 0.23.

Synthesis of N^6,N^6-dimethyladenosine 34

This was prepared from 6-chloropurine riboside **31** (200 mg, 0.80 mmol) (i. $Me_2NH.HCl$/DMF/0 ºC, ii. Et_3N/0 ºC)[27] to give **34** (99 mg, 42%) as colourless plates (Found: C, 48.8; H, 6.1; N, 23.6. ($C_{12}H_{17}N_5O_4$ requires C, 48.8; H, 5.8; N, 23.7%); δ_H (250 MHz; DMSO-d_6) 8.39 (1H, s, H-8), 8.23 (1H, s, H-2), 5.92 (1H, d, $J_{1',2'}$ 6.0, H-1′), 5.49 (1H, d, $J_{2',2'\text{-OH}}$ 6.2, OH-2′), 5.42 (1H, dd, $J_{5'a,5'\text{-OH}}$ 4.6, $J_{5'b,5'\text{-OH}}$ 6.9, OH-5′), 5.23 (1H, d, $J_{3',3'\text{-OH}}$ 4.7, OH-3′), 4.59 (1H, dd, $J_{1',2'}$ 6.0, $J_{2',3'}$ 6.0, H-2′), 4.15 (1H, dd, $J_{2',3'}$ 6.0, $J_{3',4'}$ 4.7, H-3′), 3.97 (1H, m, H-4′), 3.69 (1H, dt, $J_{4',5'a}$ 4.2, $J_{5'a,5'b}$ 11.9, H-5′a), 3.59 (1H, dt, $J_{4',5'b}$ 3.6, $J_{5'a,5'b}$ 11.9, H-5′b) and 3.38 (6H, s, 2 x C$\underline{H}_3$); δ_C (62.9 MHz; DMSO-d_6) 154.6 (C-6), 152.0 (C-2), 150.2 (C-4), 139.0

(C-8), 120.1 (C-5), 88.1 (C-1′), 86.1 (C-4′), 73.8 (C-2′), 70.9 (C-3′), 61.9 (C-5′) and *ca.* 40 (2 x $\underline{C}H_3$, overlapping DMSO-d_6); *m/z* (EI) 295 (15%, M^+), 163 (57, M^+ - sugar + H), 148 (52, 163 - CH_3), 134 (100, M^+ - base + H), 120 (20, 148 - CH_3N + H); *m/z* (ES) 296.1358 (M^+ + H, $C_{12}H_{18}N_5O_4$ requires 296.1359, difference 0.3 ppm); R_f (90:10 chloroform/methanol) 0.25.

Synthesis of N^6-*n*-butyladenosine 36[28]

A mixture of 6-chloropurine riboside **31** (200 mg, 0.80 mmol), calcium carbonate (160 mg, 1.60 mmol) and *n*-butylamine (0.238 cm^3, 176 mg, 2.40 mmol) in ethanol (20 cm^3) was stirred under reflux for *ca.* 21 h. The light brown reaction mixture was filtered to remove the calcium salts (white powder), which were washed with ethanol. The filtrate was evaporated to leave a light brown/tan coloured residue containing a pale solid. This was triturated with a little cold ethanol to give a white solid in a pale brown solution. The solid was collected under suction, washed successively with ethanol and diethyl ether, and then dried under vacuum over P_2O_5 to give **36** (39 mg, 15%) as colourless needles. The filtrate was recovered and second (24 mg) and third (17 mg) crops were collected; overall 91 mg, 35%; δ_H (250 MHz; DMSO-d_6) 8.34 (1H, s, H-8), 8.19 (1H, s, H-2), 7.93 (1H, br s, N$\underline{H}$), 5.87 (1H, d, $J_{1',2'}$ 6.1, H-1′), 5.49 (2H, m, overlapping OH-2′ and OH-5′), 5.24 (1H, d, $J_{3',3'\text{-OH}}$ 4.5, OH-3′), 4.60 (1H, dd, $J_{1',2'} = J_{2',3'}$ 6.1, H-2′), 4.13 (1H, dd, $J_{2',3'}$ 6.1, $J_{3',4'}$ 4.5, H-3′), 3.95 (1H, m, H-4′), 3.66 (1H, dt, $J_{5'a,4'}$ 4.0, $J_{5'a,5'b}$ 12.0, H-5′a), 3.54 (1H, dt, $J_{5'b,4'}$ 3.5, $J_{5'a,5'b}$ 12.0, H-5′b), 3.45 (2H, m, NHC$\underline{H}_2$, overlapping water), 1.56 (2H, quin, *J* 7.2, $NHCH_2C\underline{H}_2$), 1.32 (2H, sext, *J* 7.3, $CH_3C\underline{H}_2$) and 0.89 (3H, t, *J* 7.3, C$\underline{H}_3$); δ_C (62.9 MHz; DMSO-d_6) 155.0 (C-6), 152.7 (C-2), 151.7 (C-4), 140.0 (C-8), 120.0 (C-5), 88.3 (C-1′), 86.3 (C-4′), 73.8 (C-2′), 71.0 (C-3′), 62.0 (C-5′), 39.5 ($NH\underline{C}H_2$), 31.5 $NHCH_2\underline{C}H_2$), 19.9 ($\underline{C}H_2CH_3$) and 14.1 ($\underline{C}H_3$); *m/z* (FAB) 346 (12%, M^+ + Na), 324 (100, M^+ + H), 307 (9, M^+ - OH + H), 234 (5, M^+ - $NH(CH_2)_3CH_3$ - OH), 220 (8, 234 - CH_2), 192 (36, M^+ - sugar + H), 176 (49, 192 - CH_3); *m/z* (ES) 324.1678

(M^+ + H, $C_{14}H_{22}N_5O_4$ requires 324.1672, difference 1.9 ppm); R_f (90:10 chloroform/methanol) 0.22.

Synthesis of N^6-*n*-propyladenosine 35

This was prepared from 6-chloropurine riboside **31** (200 mg, 0.80 mmol) and *n*-propylamine (0.195 cm^3, 142 mg, 2.40 mmol) as for **36** to give **35** (30 mg, 12%) as colourless needles; δ_H (250 MHz; DMSO-d_6) 8.18 (1H, s, H-8), 8.02 (1H, s, H-2), 7.78 (1H, br s, NH), 5.70 (1H, d, $J_{1',2'}$ 6.2, H-1′), 5.32 (2H, m, overlapping OH-2′ and OH-5′), 5.09 (1H, d, $J_{3',3'\text{-OH}}$ 4.5, OH-3′), 4.43 (1H, dd, $J_{1',2'} = J_{2',3'}$ 6.2, H-2′), 3.96 (1H, dd, $J_{2',3'}$ 6.2, $J_{3',4'}$ 4.6, H-3′), 3.78 (1H, m, H-4′), 3.49 (1H, dt, $J_{4',5'a}$ 4.0, $J_{5'a,5'b}$ 12.0, H-5′a), 3.36 (1H, dt, $J_{4',5'b}$ 3.6, $J_{5'a,5'b}$ 12.0, H-5′b), 3.20 (2H, m, NHCH_2, overlapping water), 1.40 (2H, m, *J* 7.2, CH_3CH_2) and 0.71 (3H, t, *J* 7.4, CH_3); δ_C (62.9 MHz; DMSO-d_6) 155.0 (C-6), 152.7 (C-2), 148.6 (C-4), 140.0 (C-8), 119.8 (C-5), 88.2 (C-1′), 86.3 (C-4′), 73.8 (C-2′), 71.0 (C-3′), 62.0 (C-5′), 41.9 (NHCH_2), 22.7 (CH_2) and 11.7 (CH_3); *m/z* (FAB) 332 (15%, M^+ + Na), 310 (100, M^+ + H); *m/z* (ES) 332.1334 (M^+ + Na, $C_{13}H_{19}N_5O_4Na$ requires 332.1335, difference 0.3 ppm); R_f (90:10 chloroform/methanol) 0.45.

Synthesis of N^6-*n*-pentyladenosine 38

This was prepared from 6-chloropurine riboside **31** (200 mg, 0.80 mmol) and *n*-pentylamine (0.279 cm^3, 209 mg, 2.40 mmol) as for **36** to give **38** (42 mg, 15%) as colourless needles (Found: C, 52.45; H, 7.25; N, 19.35. ($C_{15}H_{23}N_5O_4$ requires C, 53.4; H, 6.9; N, 20.8%); δ_H (250 MHz; DMSO-d_6) 8.14 (1H, s, H-8), 8.00 (1H, s, H-2), 7.73 (1H, br s, NH), 5.67 (1H, d, $J_{1',2'}$ 6.2, H-1′), 5.28 (2H, m, overlapping OH-2′ and OH-5′), 5.02 (1H, d, $J_{3',3'\text{-OH}}$ 4.5, OH-3′), 4.41 (1H, dd, $J_{1',2'} = J_{2',3'}$ 6.2, H-2′), 3.93 (1H, dd, $J_{2',3'}$ 6.2, $J_{3',4'}$ 4.6, H-3′), 3.76 (1H, m, H-4′), 3.47 (1H, dt, $J_{4',5'a}$ 4.0, $J_{5'a,5'b}$ 12.1, H-5′a), 3.42 (1H, dt, $J_{4',5'b}$ 3.5, $J_{5'a,5'b}$ 12.1, H-5′b), 3.17 (2H, m, NHCH_2), 1.38 (2H, quin, *J* 6.6, $NHCH_2CH_2$), 1.10 (4H, m, $CH_3CH_2CH_2$) and 0.66 (3H, t,

J 6.6, C<u>H</u>$_3$); δ_C (62.9 MHz; DMSO-*d*$_6$) 155.0 (C-6), 152.7 (C-2), 148.5 (C-4), 140.0 (C-8), 120.0 (C-5), 88.3 (C-1′), 86.3 (C-4′), 73.8 (C-2′), 71.0 (C-3′), 62.0 (C-5′), 39.0 (NH<u>C</u>H$_2$), 29.0 NHCH$_2$<u>C</u>H$_2$), 22.3 (<u>C</u>H$_2$<u>C</u>H$_2$CH$_3$) and 14.3 (<u>C</u>H$_3$); *m/z* (FAB) 360 (7%, M^+ + Na), 338 (100, M^+ + H), 234 (8, M^+ - NH(CH$_2$)$_4$CH$_3$ - OH), 206 (47, M^+ - sugar + H), 148 (6, M^+ - sugar - (CH$_2$)$_3$CH$_3$); *m/z* (ES) 338.1832 (M^+ + Na, $C_{15}H_{26}N_5O_4$ requires 338.1828, difference 1.2 ppm); R_f (90:10 chloroform/methanol) 0.57.

Synthesis of 1,*N*^{6}-ethenoadenosine 41[33]

The pH of a solution of adenosine **1** (534 mg, 2.0 mmol) and chloroacetaldehyde (3.14 g, 40 mmol) in water (20 cm^3) was lowered to 4.2 by addition of 1 M sodium hydroxide. The solution was then stirred at 37 °C for 26 h. TLC analysis (80:20 chloroform/methanol) revealed a conversion of adenosine R_f 0.31 to a major and a minor fluorescent product R_f 0.23 and 0.05 respectively. The resultant pale yellow solution was decolourised with charcoal (200 mg) and filtered with washings of water. The filtrate was evaporated to dryness to leave a very pale yellow residue containing colourless crystals. The major product was isolated by gradient elution on a silica column (90:10 - 60:40 chloroform/methanol) to give **41** (419 mg, 72%) as a colourless powder; δ_H (250 MHz; DMSO-*d*$_6$) 9.36 (1H, s, H-8), 8.61 (1H, s, H-2), 8.13 (1H, d, *J* 1.5, Etheno-H), 7.57 (1H, d, *J* 1.5, Etheno-H), 6.05 (1H, d, $J_{1',2'}$ 5.6, H-1′), 5.71 (1H, d, $J_{2',2'\text{-OH}}$ 5.5, OH-2′), 5.42 (1H, d, $J_{3',3'\text{-OH}}$ 4.1, OH-3′), 5.23 (1H, t, $J_{5'a,5'\text{-OH}} = J_{5'b,5'\text{-OH}}$ 5.2, OH-5′), 4.60 (1H, dd, $J_{1',2'}$ 5.6, $J_{2',3'}$ 4.7, H-2′), 4.22 (1H, m, H-3′), 4.00 (1H, q, *J* 3.8, H-4′), 3.71 (1H, dt, $J_{4',5'a}$ 4.4, $J_{5'a,5'b}$ 12.0, H-5′a) and 3.59 (1H, dt, $J_{4',5'b}$ 4.8, $J_{5'a,5'b}$ 12.0, H-5′b); δ_C (75.5 MHz; DMSO-*d*$_6$) 140.8 (C-6), 140.2 (C-2), 138.7 (C-4), 137.5 (C-8), 133.1 (Etheno-C), 123.3 (C-5), 112.6 (Etheno-C), 88.1 (C-1′), 85.9 (C-4′), 74.5 (C-2′), 70.6 (C-3′) and 61.5 (C-5′); *m/z* (EI) 291 (M^+), 159 (100%, M^+ - sugar); *m/z* (ES) 292.1038 (M^+ + H, $C_{12}H_{14}N_5O_4$ requires 292.1046, difference 2.7 ppm).