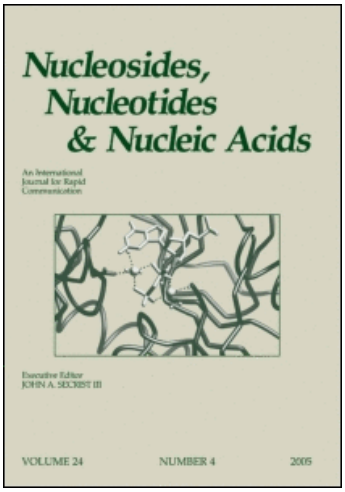

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Novel 2.6-Disubstituted Adenosine Analogues: Potential Agonists for Adenosine Receptors

Vasu Nair[a]; Allen J. Fasbender[a]
[a] Department of Chemistry, The University of lowa, lowa City, lowa

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NOVEL 2,6-DISUBSTITUTED ADENOSINE ANALOGUES: POTENTIAL AGONISTS FOR ADENOSINE RECEPTORS

Vasu Nair* and Allen J. Fasbender
Department of Chemistry, The University of Iowa
Iowa City, Iowa 52242

Abstract. Synthesis of novel 2-iodo- and 2-oxo- N^6-cyclosubstituted adenosine analogues with potential adenosine A_1 or A_2 agonist activity is described. The procedure for the 2-oxo compounds represents a new and general synthetic approach to isoguanosine analogues.

INTRODUCTION

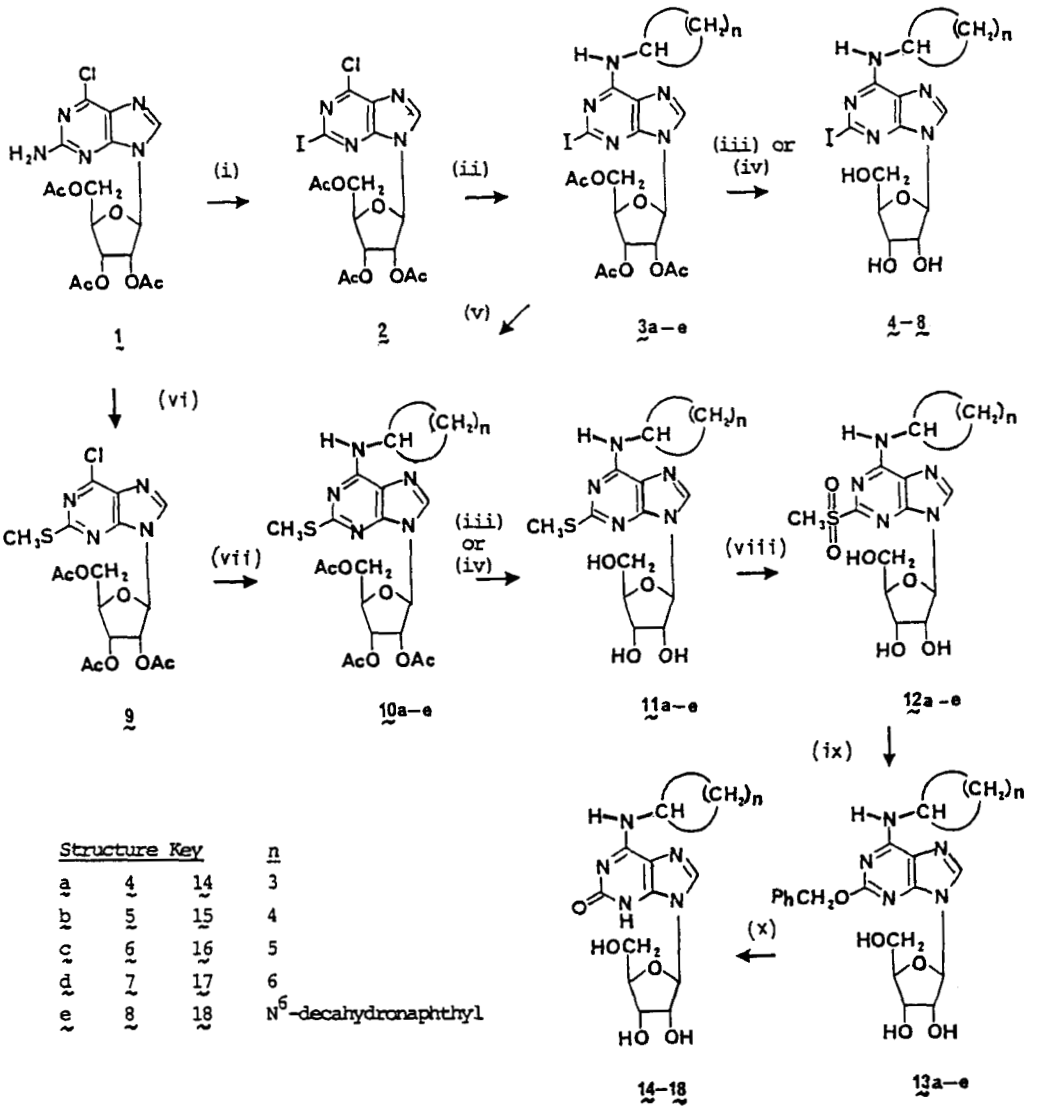
Although the cardiovascular effects of adenosine were first described by Drury and Szent-Gyorgyi in 1929,[1] it was not until much later and particularly in the last decade that the biochemical basis for the physiological effects of adenosine began to be understood.[2-6] Adenosine exerts its effects *via* the extracellular receptors, A_1 and A_2, distributed throughout a wide variety of tissues in the mammalian body. The chemistry and biology of the adenosinergic system and the physiological effects mediated by adenosine have been reviewed.[2,3,5,7,8] Adenosine appears to act as a local hormone, produced on demand in response to a pathological stimulus such as ischemia or in response to increases in cellular electrical activity.[7] Adenosine has recently been approved clinically for the treatment of acute supraventricular tachycardia and, while effective, suffers from a half-life in the bloodstream of much less than ten seconds.[9] Thus, there has been considerable interest in developing adenosine analogues that mimic the pharmacological properties of adenosine but with

high A_1 or A_2 receptor specificity and with resistance to rapid metabolic degradation.[3] Several recent reports of highly selective and potent analogues for both the A_1 and A_2 receptors,[10-20] have focused attention on 2- and/or N^6-modified adenosines. The natural minor nucleoside, isoguanosine (2-hydroxyadenosine) has been reported to have vasodepressor activity greatly exceeding that of adenosine.[19,21] However, very few examples of isoguanosine analogues of related interest are known.[22,23] This paper reports on the synthesis of novel 2-iodo- and 2-oxo-N^6-cyclosubstituted adenosines with potential A_1 or A_2 agonist activity and cellular stability.

RESULTS AND DISCUSSION

Synthesis of 2-iodo-N^6-cyclosubstituted adenosines were achieved by taking advantage of the known nucleophilic lability of the 6-chloro group in 2-iodo-6-chloro purine nucleoside.[24] This precursor, in its protected form (i.e. **2**), can be prepared by the deamination-iodination of 2-amino-6-chloropurine riboside **1**.[24] Treatment of **2** with the primary amine to be substituted at the 6-position in chloroform at 60 °C gave **3a-e** in excellent yields. Deprotections of compounds **3** were carried out with sodium methoxide in methanol or with ethanolic ammonia to give the target compounds **4 - 8**. Compound **8** was produced as a diastereoisomeric mixture. Overall yields from guanosine were of the order of 40%. The structures of these compounds were confirmed by ^{1}H NMR and UV data and elemental analyses.

The strategy for the synthesis of the novel isoguanosine analogues was more complicated. Although a number of approaches are available for the synthesis of isoguanosine, these methodologies were not easily applicable to the synthesis of the 2-oxo-N^6-cycloalkylated adenosines. These include the selective deamination of 2,6-diaminopurine nucleoside with nitrous acid,[25,26] cyclization of a 4,5-dicyanoimidazole nucleoside precursor,[27]



Structure Key			n
a	4	14	3
b	5	15	4
c	6	16	5
d	7	17	6
e	8	18	N^6-decahydronaphthyl

(i) CH_2I_2, n-$C_5H_{11}ONO$, CH_3CN, Δ; (ii) RNH_2, TEA, $CHCl_3$, Δ; (iii) $NaOCH_3$, MeOH; (iv) NH_3, EtOH; (v) CH_3SSCH_3, CH_3CN, hv; (vi) CH_3SSCH_3, $C_5H_{11}ONO$, CH_3CN, Δ; (vii) RNH_2, TEA, DMF, Δ; (viii) oxone, acetate buffer; (ix) sodium benzyloxide, DMF, Δ; (x) H_2, 10% Pd/C, EtOH.

photolysis of adenosine N^1-oxide,[28] or synthesis from AICA-riboside.[29] In 1985, Nair and Young reported a photochemical synthesis of isoguanosine.[24] However, this procedure, while easily applicable for the photohydration of 2-iodoadenosine to natural isoguanosine, was unsuccessful for the photohydration reaction of the 2-iodo-N^6-cyclosubstituted compounds **4-8.**

We now report a new approach to the preparation of isoguanosine and related N^6-substituted analogues of isoguanosine. The precursor for this synthesis was the 2-amino-6-chloro compound **1** which was converted to **9** through a thermal radical deamination-thioalkylation with n-pentyl nitrite and dimethyl disulfide in acetonitrile.[30,31] The thioalkylated compound **9** was converted to compounds **10** by displacement of the 6-chloro group with the cyclic primary amines. These intermediates (i.e. **10a-e**) were also prepared from compounds **3** by photochemical thioalkylation.[30] Formation of the thiomethyl group at the 2-position was to convert it eventually to a good leaving group for introduction of the oxo group. Thus, compounds **10** were converted to the sulfones **12** by deprotection followed by oxidation with oxone in acetate buffer. Treatment of the sulfones **12** with the sodium salt of benzyl alcohol followed by hydrogenolysis of the resulting 2-benzyloxy compounds **13** with 10% Pd/C and 30 p.s.i. of H_2, gave the target compounds **14-18.** Overall yields starting from guanosine *via* the photochemical thioalkylation pathway were of the order of 9% whereas the yields were slightly higher (~12 %) for the pathway involving thermal thioalkylation. In theory, compounds **14-18** could be prepared more directly from **12** by treatment with aqueous sodium hydroxide. However, this reaction gave only low yields of product. The structures of the target novel isoguanosine analogues were confirmed by ^1H NMR, FTIR and UV data and by elemental analyses.

In summary, N^6-cycloalkylated analogues of 2-iodo and 2-oxo adenosines have been synthesized by highly efficient methods. The procedure for the

2-oxo compounds represents a new and general approach to isoguanosine analogues. The target compounds described are of potential interest as A_1 or A_2 agonists with respect to these adenosine receptors. They are not substrates for mammalian adenosine deaminase.

EXPERIMENTAL

The reported melting points are uncorrected and were determined on a Thomas-Hoover melting point apparatus fitted with a microscope. Nuclear magnetic resonance spectra were recorded on JEOL Model FX90Q and Bruker MSL 300 pulse Fourier transform spectrometers. Ultraviolet spectra were recorded on a Varian Cary Model 219 or a Gilford Response spectrophotometer. Infrared spectra were recorded on a Mattson Cygnus 25 Fourier transform instrument. Elemental analyses were carried out by Galbraith Laboratories Inc., Knoxville, TN. Preparative layer chromatography plates were prepared by coating six 20cm x 20cm plates with a slurry made from 150g of E. Merck PF_{254} silica gel in 400 mL of water. The silica gel plates were allowed to dry slowly and were then activated for 3 h at 150 °C. Flash chromatography was carried out in glass columns packed with 230-400 mesh silica gel.

General Synthetic Procedures (A - F). Procedure A: Preparation of N^6-substituted-2-iodo-9-(2',3',5'-tri-O-acetyl-β-D-ribofuranosyl)purines. A solution containing 6-chloro-2-iodo-9-(2',3',5'-tri-O-acetyl-β-D-ribofuranosyl)purine (6.6 mmol) 2,[32] triethylamine (7.9 mmol), and the amine to be substituted in the 6-position (7.9 mmol) was stirred in chloroform (30 mL) and heated at 60 °C for 2 h. The solvent was evaporated and the residue was purified by flash chromatography eluting with 1% methanol/ chloroform. Alternatively, the N^6-substituted-2-iodo compound could be prepared by doubling the equivalents of the amine to be substituted and omitting the triethylamine.

Procedures B-1 and B-2: Deprotection of triacetylated purine ribofuranosides. Procedure B-1: To a solution of triacetylated nucleoside (7.4 mmol) in methanol (50 mL) was added sodium methoxide (25.7 mmol). The solution was stirred for 1 h at 25 °C at which time NH_4Cl (31.7 mmol) was added. Stirring was continued for 1 h. The solvent was removed and the residue triturated with 9:1 chloroform/methanol and filtered. The filtrate was concentrated and the residue was purified on silica gel plates with 10% methanol/chloroform in the case of the 2-iodo analogues or by flash chromatography eluting with 2% methanol/chloroform in the case of the 2-methylthio analogues.

Deprotection of triacetylated purine ribofuranosides. Procedure B-2: Alternatively, the triacetylated nucleoside was dissolved in absolute ethanol (200 mL) and the solution was saturated with anhydrous ammonia at 0 °C. The solution was allowed to stand at room temperature for 24 h. The solvent was then removed and the residue triturated with o-xylene and the acetamide/o-xylene azeotrope and excess o-xylene were distilled off and the residue was purified as described in B-1.

Procedure C: Photochemical preparation of 2-methylthio-N^6-substituted-9-(2',3',5'-tri-O-acetyl-β-D-ribofuranosyl)purines. A nitrogen-purged solution of **3b** or **3c** (1.8 mmol) containing dimethyl disulfide (25 mmol) in acetonitrile (100 mL) was irradiated under N_2 for 40 h with ultraviolet light of principle wavelength 254 nm using a Rayonet Photochemical Reactor.[30] The solvent was then removed and the residue was incorporated into a silica gel plug and purified by flash chromatography eluting with ethyl acetate/hexanes.

Procedure D: Preparation of 2-methylsulfonyl-N^6-substituted-9-(β-D-ribofuranosyl)purines (12a-12e). Compounds **11a-11e** (6.4 mmol) were dissolved in each case in methanol (20 mL) and cooled to 0 °C in an ice

bath. Oxone (10.2 mmol) was dissolved in acetate buffer at pH 4.2 and added slowly to the nucleoside. The reaction mixture was allowed to attain room temperature and was stirred for 4 h and then neutralized with NaOH. The solvent was removed and the residue was triturated with 9:1 chloroform/methanol and filtered. The filtrate was incorporated into a silica gel plug and purified by flash chromatography eluting with 2% methanol/chloroform.

Procedure E: Preparation of 2-benzyloxy-N^6-substituted-9-(β-D-ribofuranosyl)purines (13a-13e). To a solution of the 2-methylsulfonyl-N^6-substituted ribonucleoside (2.9 mmol) in DMF (30 mL) was added sodium benzyloxide (0.389 g Na in excess benzyl alcohol, 5 mL). The solution was heated to 60 °C for 2 h with stirring at which time the reaction mixture was cooled to room temp and NH_4Cl (19.2 mmol) was added. Stirring was continued for an additional 1 h. The DMF was removed under reduced pressure (50 °C) and the resulting syrup incorporated into a silica gel plug and purified by flash chromatography eluting initially with chloroform to remove benzyl alcohol and then with 6% methanol/chloroform to elute the product.

Procedure F: Catalytic reduction of 2-benzyloxy-N^6-substituted-9-(β-D-ribofuranosyl)purines. A solution of each of the compounds **13a-13e** (0.4 mmol) in absolute ethanol (150 mL) was purged with N_2 and to it was added one fourth the mass of 10% Pd/C. The suspension was then hydrogenated at 30 p.s.i. of H_2 for 18 h on a Parr Hydrogenation Apparatus. The suspension was then suction filtered through a fritted glass filter and the solvent was removed. The residue was purified on silica gel plates with 10% methanol/chloroform. The product was subsequently crystallized from isopropanol/diethyl ether.

N^6-Cyclobutyl-2-iodo-9-(β-D-ribofuranosyl)purine (4). Compound **3a** was prepared from **2**[32] using Procedure A (88% yield) and deprotected to give **4**

using Procedure B-1 (92% yield). The product obtained by preparative layer chromatography was crystallized from ethanol/diethyl ether/hexanes to give **4** as white crystals: m.p. 109-112 °C dec.; ^{1}H NMR (Me_2SO-d_6) δ 1.65-2.20 (m, 7H), 3.61 (m, 2H), 3.96 (m, 1H), 4.09 (m, 1H), 4.52 (m, 1H), 5.00 (t, 1H), 5.17 (m, 1H), 5.44 (d, 1H), 5.83 (d, 1H), 8.33 (s, 1H), 8.47 (d, 1H); UV (Ethanol) λ_{max} 274 nm (ε 15,080).

Anal. Calcd. for $C_{14}H_{18}IN_5O_4$: C, 37.60; H, 4.06; N, 15.66. Found: C, 36.91; H, 4.53; N, 14.75

N^6-Cyclopentyl-2-iodo-9-(β-D-ribofuranosyl)purine (5) was prepared from **2** using in sequence Procedure A (93% yield) and Procedure B-2 (88%) to give **5** which crystallized from ethanol/diethyl ether/hexanes as white crystals: m.p. 173-175 °C; ^{1}H NMR (Me_2SO-d_6) δ 1.61 (m, 9H), 3.63 (m, 2H), 3.93 (m, 1H), 4.13 (m, 1H), 4.52 (m, 1H), 5.01 (m, 1H), 5.21 (m, 1H), 5.43 (m, 1H), 5.79 (d, 1H), 8.15 (d, 1H), 8.28 (s, 1H); UV (Ethanol) λ_{max} 274.5 nm (ε 14,980).

Anal. Calcd. for $C_{15}H_{20}IN_5O_4$: C, 39.06; H, 4.37; N, 15.18. Found: C, 39.12; H, 4.42; N, 14.60

N^6-Cyclohexyl-2-iodo-9-(β-D-ribofuranosyl)purine (6) was prepared from **2** by using Procedure A (80% yield) followed by Procedure B-2 (73% yield). Compound **6** crystallized from ethanol/diethyl ether/hexanes to provide white crystals: m.p. 110-115 °C dec.; ^{1}H NMR (Me_2SO-d_6) δ 1.23-1.75 (m, 11H), 3.64 (m, 2H), 3.95 (m, 1H), 4.13 (m, 1H), 4.50 (m, 1H), 5.02 (m, 1H), 5.19 (m, 1H), 5.46 (m, 1H), 5.80 (d, 1H), 8.03 (d, 1H), 8.28 (s, 1H); UV (Ethanol) λ_{max} 273.5 nm (ε 14,480).

Anal. Calcd. for $C_{16}H_{22}IN_5O_4$: C, 40.43; H, 4.66; N, 14.73. Found: C, 40.69; H, 4.87; N, 14.64.

N^6-Cycloheptyl-2-iodo-9-(β-D-ribofuranosyl)purine (7) was prepared from **2** using in sequence Procedure A (90% yield) and Procedure B-1

(91% yield). Compound **7** crystallized from ethanol/ diethyl ether/hexanes as white crystals: m.p. 115-118 °C; ^{1}H NMR (Me_2SO-d_6) δ 1.55 (m, 13H), 3.61 (m, 2H), 3.95 (m, 1H), 4.15 (m, 1H), 4.53 (m, 1H), 5.00 (m, 1H), 5.17 (m, 1H), 5.41 (m, 1H), 5.83 (d, 1H), 8.07 (d, 1H), 8.32 (s, 1H); UV (Ethanol) λ_{max} 273.5 nm (ε 16,070).

Anal. Calcd. for $C_{17}H_{24}IN_5O_4$: C, 41.73; H, 4.94; N, 14.31. Found: C, 42.32; H, 5.21; N, 13.90.

N^6-(2-Decahydronaphthyl)-2-iodo-9-(β -D-ribofuranosyl)purine (8) was prepared from **2** by Procedure A (60% yield) using DMF as the solvent at 90 °C for 5 h to give **3e** which was deprotected using Procedure B-1 (90% yield) to give **8**. Compound **8** crystallized from ethanol/ diethyl ether/ hexanes as white crystals: m.p. 132-134 °C; ^{1}H NMR (Me_2SO-d_6) δ 1.56 (m, 17H), 3.60 (m, 2H), 3.95 (m, 1H), 4.09 (m, 1H), 4.52 (m, 1H), 5.02 (m, 1H), 5.21 (m, 1H), 5.44 (m, 1H), 5.83 (d, 1H), 8.04 (m, 1H), 8.32 (s, 1H); UV (Ethanol) λ_{max} 273.5 nm (ε 17,600).

Anal. Calcd. for $C_{20}H_{28}IN_5O_4$: C, 45.38; H, 5.33; N, 13.23. Found: C, 45.15; H, 6.00; N, 12.94.

6-Chloro-2-methylthio-9-(2',3',5'-tri-O-acetyl-β -D-ribofuranosyl) purine (9).[30,31] To a solution of **1** (14.7 mmol) in acetonitrile (60 mL) at 0 °C was added dimethyl disulfide (147.0 mmol), and n-pentyl nitrite (88.0 mmol). The solution was purged with N_2 for 30 min, and was heated at 60 °C under N_2 for 16 h. The solvent was removed under reduced pressure and the residue incorporated into a silica gel plug and purified by flash chromatography eluting with 1% methanol/ chloroform. The product was isolated as a yellow oil in 85% yield. ^{1}H NMR (Me_2SO-d_6) δ 1.97 (s, 3H), 2.08 (s, 3H), 2.12 (s, 3H), 2.64 (s, 3H), 4.40 (m, 3H), 5.71 (m, 1H), 6.06 (m, 1H), 6.32 (d, 1H), 8.71 (s, 1H); UV (Ethanol) λ_{max} 264, 304.5 nm.

N^6-Cyclobutyl-2-oxo-9-(β-D-ribofuranosyl)purine (14). Compound **10a** was prepared from **9** by Procedure A except in DMF at 90 °C for 5 h (80% yield).

It was then converted to **11a** using Procedure B-1 (81% yield). **11a:** m.p. 96-100 °C dec.; ^{1}H NMR (Me_2SO-d_6) δ 1.77-2.24 (m, 7H), 2.59 (s, 3H), 3.67 (m, 2H), 4.01 (m, 1H), 4.24 (m, 1H), 4.62 (m, 1H), 5.08-5.38 (m, 3H), 5.89 (d, 1H), 7.90 (d, 1H), 8.17 (s, 1H); UV (Ethanol) λ_{max} 244, 283 nm. Compound **11a** was then converted to **12a** by procedure D (75% yield). The sulfone methyl singlet appears at 3.34 ppm and the UV_{max} shifts to 269 nm. The IR shows absorbance due to the sulfone group at 1306 and 1130 cm^{-1}. The sulfone **12a** was converted to **13a** by Procedure E (60% yield) to provide **13a:** m.p. 94-98 °C dec.; ^{1}H NMR (Me_2SO-d_6) δ 1.65-2.2 (m, 7H), 3.61 (m, 2H), 3.93 (m, 1H), 4.17(m, 1H), 4.55 (m, 1H), 4.85-5.45 (m, 3H), 5.35 (s, 2H), 5.83 (d, 1H), 7.44 (m, 5H), 8.02 (d, 1H), 8.19 (s, 1H); UV (Ethanol) λ_{max} 274 nm. The 2-oxo compound **14** was prepared from **13a** by Procedure F (58% yield) and was crystallized from isopropanol/diethyl ether to provide white crystals: m.p. 167-170 °C; ^{1}H NMR (Me_2SO-d_6) δ 1.72-2.17 (m, 7H), 3.59 (m, 2H), 3.93 (m, 1H), 4.08 (m, 1H), 4.48 (m, 1H), 4.74 (m, 1H), 5.08 (m, 1H), 5.32 (m, 1H), 5.70 (d, 1H), 7.98 (s, 1H), 8.15 (m, 1H); UV (Ethanol) λ_{max} 249 (ε 9,110), 284.5 (8,260), 302.5 nm (6,890); IR (carbonyl) 1652 cm^{-1}.

Anal. Calcd. for $C_{14}H_{19}N_5O_5$: C, 49.85; H, 5.68; N, 20.76. Found: C, 49.22; H, 5.70; N, 20.06.

N^6-Cyclopentyl-2-oxo-9-(β-D-ribofuranosyl)purine (15). Compound **10b** was prepared from **3b** using procedure C (62% yield) and was deprotected using procedure B-1 (82% yield) to provide **11b:** m.p. 108-110 °C; ^{1}H NMR (Me_2SO-d_6) δ 1.61 (m, 9H), 2.56 (s, 3H), 3.58 (m, 1H), 3.92 (m, 1H), 4.11 (m, 1H), 4.56 (m, 1H), 5.00-5.41 (m, 3H), 5.83 (d, 1H), 7.77 (d, 1H), 8.20 (s, 1H); UV (Ethanol) λ_{max} 244, 280 nm. Compound **11b** was converted to **13b** using in sequence Procedure D (70% yield) and Procedure E (50% yield). **13b:** m.p. 96-100 °C; ^{1}H NMR (Me_2SO-d_6) δ 1.60 (m, 9H), 3.62 (m, 2H), 3.91 (m, 1H), 4.12 (m, 1H), 4.62 (m, 1H), 5.13 (m, 3H), 5.33 (s,2H), 5.80 (d, 1H), 7.38 (m, 5H), 7.67 (d, 1H), 8.14 (s, 1H); UV (Ethanol) λ_{max} 274.5 nm.

Compound **13b** was then hydrogenated using Procedure F (76% yield) to obtain the 2-oxo compound **15**, which was crystallized from isopropanol/diethyl ether to give white crystals: m.p. 186-188 °C; ^{1}H NMR (Me_2SO-d_6) δ 1.59-1.81 (m, 9H), 3.58 (m, 2H), 3.94 (m, 1H), 4.09 (m, 1H), 4.49 (m, 1H), 5.09-5.53 (m, 3H), 5.67 (d, 1H), 7.71 (m, 1H), 7.97 (s, 1H); UV (Ethanol) λ_{max} 248.5 (ε 9,410), 284 (8,210), 302.5 nm (7,860); IR (carbonyl) 1639 cm^{-1}.

Anal. Calcd. for $C_{15}H_{21}N_5O_5.H_2O$: C, 48.78; H, 5.73; N, 18.96. Found: C, 48.44; H, 6.17; N, 18.56.

N^6-Cyclohexyl-2-oxo-9-(β-D-ribofuranosyl)purine (16). Compound **11c** was prepared from **3c** by using in sequence Procedure C (70% yield) and Procedure B-1 (76% yield). **11c:** m.p. 107-109 °C; ^{1}H NMR (Me_2SO-d_6) δ 1.32-1.74 (m, 11H), 2.52 (s, 3H), 3.59 (m, 2H), 3.94 (m, 1H), 4.21 (m, 1H), 4.29 (m, 1H), 5.07-5.37 (m, 3H), 5.86 (d, 1H), 7.60 (d, 1H), 8.20 (s, 1H); UV (Ethanol) λ_{max} 244, 280 nm. Compound **11c** was then converted to **13c** using in sequence Procedure D (65% yield) and Procedure E (62% yield): m.p. 98-102 °C dec.; ^{1}H NMR (Me_2SO-d_6) δ 1.23-1.76 (m, 9H), 3.60 (m, 2H), 3.97 (m, 1H), 4.18 (m, 1H), 4.62 (m, 1H), 4.70-5.60 (m, 3H), 5.34 (s, 2H), 5.82 (d, 1H), 7.41 (m, 5H), 7.72 (d, 1H), 8.17 (s, 1H); UV (Ethanol) λ_{max} 275 nm. Compound **13c** was then hydrogenated to provide the 2-oxo compound **16**, using Procedure F (70% yield). Crystallization from isopropanol/diethyl ether gave **16** as white crystals: m.p. 170-172 °C; ^{1}H NMR (Me_2SO-d_6) δ 1.32-1.88 (m, 11H), 3.60 (m, 2H), 3.95 (m, 1H), 4.10 (m, 1H), 4.49 (m, 1H), 5.12-5.38 (m, 3H), 5.69 (d, 1H), 7.64 (m, 1H), 7.97 (m, 1H); UV (Ethanol) λ_{max} 248.5 (ε 9,290), 284.5 (7,770), 302.5 nm (7,990); IR (carbonyl) 1643 cm^{-1}.

Anal. Calcd. for $C_{16}H_{23}N_5O_5.H_2O$: C, 50.12; H, 6.05; N, 18.27. Found: C, 49.72; H, 6.89; N, 17.37.

N^6-Cycloheptyl-2-oxo-9-(β -D-ribofuranosyl)purine (17). Compound **11d** was prepared from **9** using in sequence Procedure A, except in DMF at 90 °C for 2 h (71% yield) and Procedure B-1 (64% yield): m.p. 95-98 °C; ^{1}H NMR

(Me_2SO-d_6) δ 1.57-1.80 (m, 13H), 2.54 (s, 3H), 3.62 (m, 2H), 3.89 (m, 1H), 4.16 (m, 1H), 4.60 (m, 1H), 5.05-5.38 (m, 3H), 5.85 (d, 1H), 7.6 (d, 1H), 8.23 (s, 1H); UV (Ethanol) λ_{max} 244, 283 nm. Compound **11d** was then converted to **12d** by Procedure D (75% yield) and subsequently the methylsulfonyl group was displaced by the benzyloxy anion using Procedure E (68% yield) to provide **13d:** ^1H NMR (Me_2SO-d_6) δ 1.55-1.76 (m, 13H), 3.62 (m, 2H), 3.94 (m, 1H), 4.21 (m, 1H), 4.55 (m, 1H), 5.01-5.49 (m, 3H), 5.35 (s, 2H), 5.82 (m, 1H), 7.41 (m, 5H), 7.67 (d, 1H), 8.17 (s, 1H); UV (Ethanol) λ_{max} 274 nm. Compound **13d** was then hydrogenated to the 2-oxo compound **17** using Procedure F (72% yield). The product crystallized from isopropanol/diethyl ether as light tan crystals: m.p. 155-157 °C; ^1H NMR (Me_2SO-d_6) δ 1.56 (m, 13H), 3.61 (m, 2H), 3.96 (m, 1H), 4.11 (m, 1H), 4.49 (m, 1H), 5.05-5.39 (m, 3H), 5.70 (d, 1H), 7.71 (m, 1H), 7.99 (s, 1H); UV (Ethanol) λ_{max} 248.5 (ε 10,000), 284 (8,830), 302 nm (8,170); IR (carbonyl) 1636 cm^{-1}.

Anal. Calcd. for $C_{17}H_{25}N_5O_5.H_2O$: C, 51.38; H, 6.34; N, 17.62. Found: C, 51.60; H, 6.92; N, 17.34.

N^6-(2-Decahydronaphthyl)-2-oxo-9-(β-D-ribofuranosyl)purine (18). Compound **11e** was prepared from **9** using in sequence Procedure A, except in DMF at 90 °C for 18 h (58% yield) and Procedure B-2 (60% yield): m.p. 110-114 °C dec.; ^1H NMR (Me_2SO-d_6) δ 1.56-1.76 (m, 17H), 2.53 (s, 3H), 3.64 (m, 2H), 3.95 (m, 1H), 4.15 (m, 1H), 4.60 (m, 1H), 5.04 (m, 1H), 5.19 (m, 1H), 5.44 (m, 1H), 5.85 (d, 1H), 7.64 (d, 1H), 8.24 (s, 1H); UV (Ethanol) λ_{max} 244, 283 nm. Compound **11e** was converted to **13e** using in sequence Procedure D (64% yield) and Procedure E (48% yield): m.p. 111-114 °C; ^1H NMR (Me_2SO-d_6) δ 1.54 (m, 17H), 3.61 (m, 2H), 3.93 (m, 1H), 4.18 (m, 1H), 4.58 (m, 1H), 5.34 (s, 2H), 4.90-5.58 (m, 3H), 5.83 (d, 1H), 7.42 (m, 5H), 7.61 (m, 1H), 8.17 (s, 1H); UV (Ethanol) λ_{max} 274.5 nm. Compound **13e** was then converted to the 2-oxo compound **18** using Procedure F (71% yield). The

product crystallized from isopropanol/diethyl ether as white crystals: m.p. 175-180 °C dec.; ^{1}H NMR (Me_2SO-d_6) δ 1.54 (m, 17H), 3.59 (m, 2H), 3.96 (m, 1H), 4.11 (m, 1H), 4.50 (m, 1H), 5.07-5.35 (m, 3H), 5.69 (d, 1H), 7.64 (m, 1H), 7.97 (s, 1H); UV (Ethanol) λ_{max} 249 (ε 9,490), 283.5 (8,920), 302 nm (7,250); IR (carbonyl) 1636 cm^{-1}

Anal. Calcd. for $C_{20}H_{29}N_5O_5$: C, 57.27; H, 6.97; N, 16.69. Found: C, 57.79; H, 7.12; N, 16.39.

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