CYTOSTATIC 6-ARYLPURINE NUCLEOSIDES II.[+]
SYNTHESIS OF SUGAR-MODIFIED DERIVATIVES: 9-(2-DEOXY-β-D-*erythro*-PENTOFURANOSYL)-, 9-(5-DEOXY-β-D-RIBOFURANOSYL)- AND 9-(2,3-DIHYDROXYPROPYL)-6-PHENYLPURINES

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9-(2-Deoxy-β-D-*erythro*-pentofuranosyl)-6-(4-substituted phenyl)purines, 9-(5-deoxy-β-D-ribofuranosyl)-6-(4-substituted phenyl)purines and 9-(2,3-dihydroxypropyl)-6-(4-substituted phenyl)purines were prepared by the Suzuki–Miyaura cross-coupling reactions of the corresponding protected 9-substituted 6-chloropurines with substituted phenylboronic acids followed by MeONa mediated deprotection. In contrast to the highly active 6-phenylpurine ribonucleosides, the title compounds did not show any considerable cytostatic activity.
Key words: Purines; Nucleosides; Cross-coupling reactions; Boronic acids; Acyclic nucleoside analogues; 5′-Deoxyribonucleosides; 2′-Deoxyribonucleosides; Cytostatic activity; Antitumor agents.

Purines bearing a carbon substituent in the position 6 display diverse types of biological activity. The parent compound of this group, 6-methylpurine[1], is known for its cytotoxicity; its liberation from the 2′-deoxyribonucleoside by purine nucleoside phosphorylases is used for detection of mycoplasma in cell cultures[2]. It is highly potent and toxic to non-proliferating and proliferating tumor cells. Recently, the use of cytotoxic bases, *i.e.* 6-methylpurine, liberated by purine nucleoside phosphorylases was proposed as a novel principle in the gene therapy of cancer[3]. Very little has been known about biological activity of other 6-C-substituted purines until recent new findings of cytokinin activity of 6-(arylalkynyl)-, 6-(arylalkenyl)- and


+ Part I of this Series, see ref.[8]

6-(arylalkyl)purines[4], cytostatic activity of 6-(trifluoromethyl)purine riboside[5], corticotropin-releasing hormone antagonist activity of some 2,8,9-trisubstituted 6-arylpurines[6] and antimycobacterial activity of 6-aryl-9-benzylpurines[7].

Recently we have discovered a new class of cytostatic compounds – substituted 6-phenylpurine derivatives[8]. The structure–activity relationship (SAR) studies revealed a crucial influence of the presence of the β-D-ribofuranosyl moiety and substitution effect on the biological activity. The 6-(substituted phenyl)purine ribonucleosides displayed significant *in vitro* cytostatic activity (inhibition of the cell growth of L1210, HeLa S3 and CCRF-CEM cell cultures, IC_{50} = 0.25–10 μmol/l); their corresponding 2′,3′,5′-tri-*O*-acetates showed lower activity (IC_{50} > 4 μmol/l), while the 6-phenylpurine bases and 2-amino-6-phenylpurine ribonucleosides were entirely inactive in these assays. Analogous 6-(het)arylpurine acyclic nucleotide analogues were also devoid of any cytostatic activity[9].

There are several possible metabolic pathways of purine ribonucleosides: (i) cleavage (*e.g.* by purine nucleoside phosphorylase) to the purine bases, which can be further catabolized or transformed to their 2′-deoxyribonucleosides or (ii) phosphorylation by nucleoside and nucleotide kinases to their 5′-phosphates, 5′-diphosphates and eventually 5′-triphosphates which then participate in or interfere with the nucleic acids synthesis *de novo* or are transformed to the corresponding 2′-deoxyribonucleotides with similar potential activity. Many enzymes take part in these processes and thus might be potential targets for the action of biologically active modified nucleosides. Moreover, purine nucleosides can directly interfere with multiple regulation processes. In order to extend the SAR study and to gain a first insight into the understanding of the mechanism of action of the cytostatic 6-phenylpurine ribonucleosides, we wish to report here on the synthesis and activity of selected sugar-modified derivatives of the parent compounds. The first group of the modified nucleosides under study were the 2′-deoxyribosides since many enzymes specifically recognize them as substrates or inhibitors. The 5′-deoxyribofuranosides lacking the nucleoside kinase phosphorylation site were the second class of compounds selected for their potential generation of purine bases by PNPase[10]. The third group of target compounds examined in this study were racemic 9-(2,3-dihydroxypropyl)-6-phenylpurines. These acyclic nucleoside analogues are known to mimic the parent ribonucleosides and due to the absence of the labile nucleosidic bond they do not undergo cleavage by phosphorylases. Since in the series of the parent 6-(4-X-substituted phenyl)purine ribonucleosides the most active compounds were 6-phenyl-, 6-(4-fluorophenyl)- and

6-(4-methoxyphenyl)purine derivatives, in this study we have also focussed on these three types of 6-(4-substituted phenyl)purines in each series of sugar modified nucleosides.

Encouraged by our recent experience[5] with facile regio- and stereo-selective glycosidations and alkylations of 6-(trifluoromethyl)purine, the first approach chosen for the preparation of the target 9-glycosyl-6-phenyl-purines was the glycosidation of 6-phenylpurine bases. Thus 6-phenyl-purine **2a** and 6-(4-methoxyphenyl)purine **2c** (easily prepared as shown in Scheme 1) were glycosylated with 3,5-bis-*O*-(4-toluoyl)-2-deoxy-α-D-*erythro*-pentofuranosyl chloride (**3**) in the presence of NaH under standard conditions. Unfortunately, these reactions were not stereoselective and insepara-ble anomeric mixtures of N-9 glycosyl derivatives **4** and **5** were obtained (Scheme 1).


1,2,4,5	X
a	H
c	OCH₃
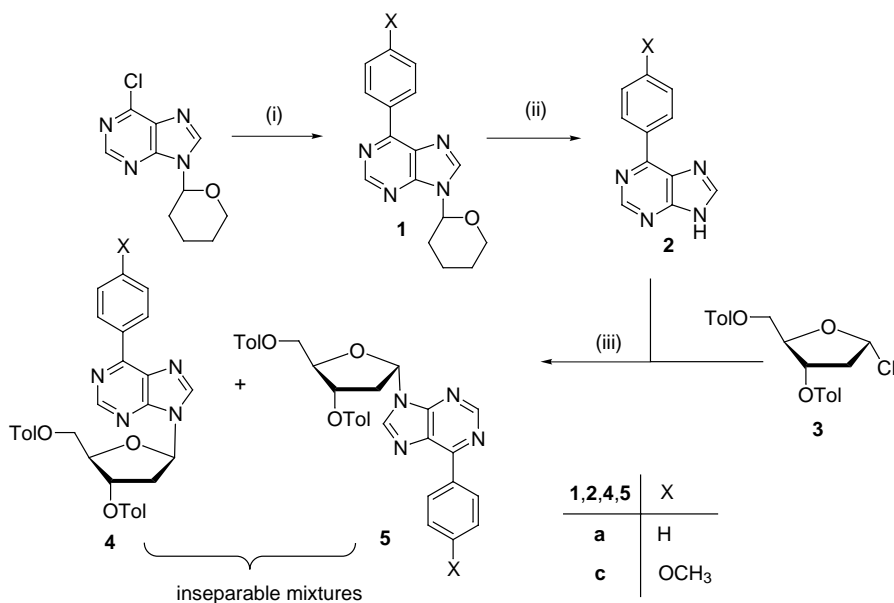
(i) 4-X-PhB(OH)₂, Pd(PPh₃)₄, K₂CO₃, toluene; (ii) Dowex 50X8 (H⁺), MeOH, H₂O; (iii) NaH, acetonitrile

Tol = 4-CH₃C₆H₄CO-

SCHEME 1

Therefore we have chosen the second approach consisting in preparation of suitably protected 9-glycosyl- or 9-(2,3-dihydroxypropyl)-6-chloro-purines followed by the Suzuki–Miyaura cross-coupling reactions[11] with substituted phenylboronic acids and deprotection. Due to the known
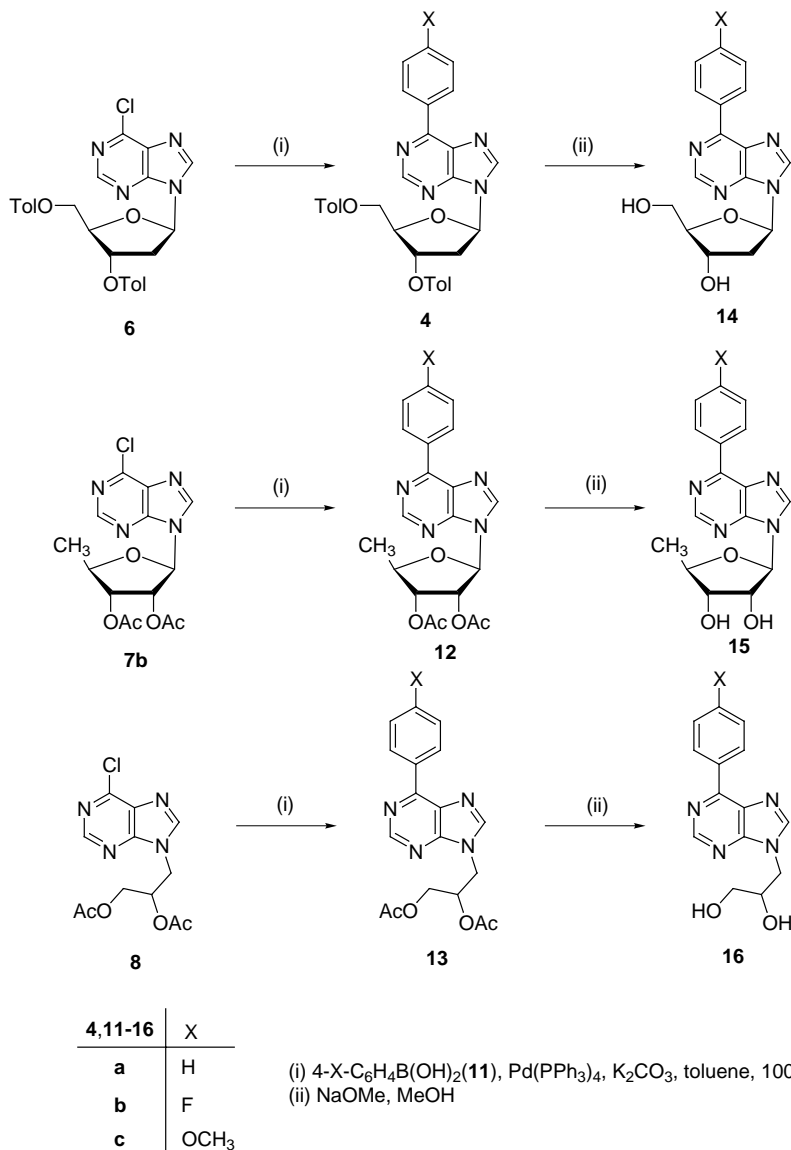
lability of 6-C-substituted nucleosides under acidic conditions[12] we have selected acyl protective groups cleavable by base-catalyzed transesterification under anhydrous conditions. Both 9-(3,5-bis-O-(4-toluoyl)-2-deoxy-β-D-*erythro*-pentofuranosyl)-[13] (**6**) and 9-(2,3-diacetoxypropyl)-6-chloropurine[14] (**8**) were prepared by known methods. 1,2,3-Tri-O-acetyl-5-deoxy-D-ribose (**9**, *ca* 1 : 1 anomeric mixture) was prepared in four steps from D-ribose by a procedure recently published for its L-enantiomer[15]. Attempted glycosidation reaction of its corresponding halogenose with sodium salt of 6-chloropurine gave a complex mixture with only trace amounts of the desired product. Therefore we used a direct approach making use of $SnCl_4$-mediated reaction[16] of 6-chloropurine (**10**) with the 5-deoxyribosyl acetate **9**. In contrast to analogous selective glycosidations[15,17] of other heterocyclic bases with compound **9** and to relatively selective ribosylation[18] of silylated 6-chloropurine with 1,2,3,5-tetra-O-acetylribose that give β-nucleosides in *ca* 50%, this reaction was neither regio- nor stereoselective and a complex mixture containing four isomers (7-/9- and α-/β-) was obtained. The desired 9-β-isomer **7b** was isolated in 30% yield (*ca* 90% purity) from this mixture by column chromatography, followed by the 9-α-isomer **7a** (13%) and 7-α-isomer **7c** (4%) (Scheme 2). The lack of selectivity in this glycosidation is quite surprising and indicates that in this particular case the reactions does not proceed exclusively *via* a neighbouring group participation mechanism (leading selectively to β-anomers) as usual[19] for 2-O-acylated pentofuranosyl donors of *ribo*-configuration.
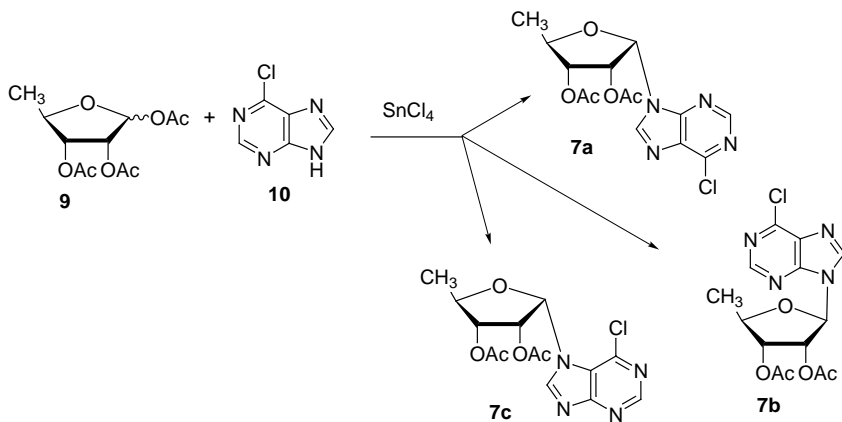
SCHEME 2

The appropriate 9-substituted 6-chloropurine intermediates **6**, **7b** and **8** were used for the $Pd(PPh_3)_4$ catalyzed cross-coupling reactions with substi-

tuted phenylboronic acids **11a–11c** under standard conditions in toluene at 100 °C in the presence of K_2CO_3 (Scheme 3). All these reactions proceeded smoothly to give the corresponding 6-phenylpurine derivatives **4a–4c**, **12a–12c** and **13a–13c** in good yields. The standard deprotection protocol[8]

4,11-16	X
a	H
b	F
c	OCH₃

(i) 4-X-C₆H₄B(OH)₂(**11**), Pd(PPh₃)₄, K₂CO₃, toluene, 100 °C
(ii) NaOMe, MeOH

SCHEME 3

making use of the reaction of acyl-protected ribonucleosides with NaOMe in methanol followed by neutralization with Dowex 50X8 (H$^+$) could not have been used due to extreme lability of the free deoxyribosides towards acids; in compound **14a** we have observed a complete cleavage of the nucleosidic bond during treatment with Dowex 50X8 (H$^+$) within 5 min giving quantitatively 6-phenylpurine (**2a**). Therefore the deprotection has been performed using strictly catalytic (5 mole %) amount of MeONa with prolonged reaction times (48 h) and the products were isolated without neutralization by column chromatography followed by crystallization giving the target nucleosides **14a–14c** and **15a–15c** in good yields. In contrast to the nucleosides, the 2,3-dihydroxypropyl derivatives **16a–16c** were perfectly stable and were isolated by the standard method using neutralization.

The structure assignment was based on NMR experiments. All compounds were fully characterized by ^{1}H and ^{13}C NMR spectra. As some of the glycosidation reactions leading to key intermediates were neither regio- nor stereoselective, complete NMR assignment (^{1}H-NOE, COSY, ^{1}H-^{13}C HMQC, HMBC experiments) of selected intermediates was essential.

To analyse the inseparable mixtures of compounds **4** and **5** (Scheme 1) with respect to the regioselectivity of glycosidation reaction ^{1}H-^{13}C HMBC experiments, providing three-bond correlations, were used. In both cases **4** and **5**, the crosspeaks in HMBC spectra indicate connectivities between protons H-1′ and carbon atoms C-8 and C-4, which is characteristic for N-9 regioisomers. The determination of anomeric configurations of compounds **4** and **5** was based on NOE (DPFGSE NOE) experiments, providing correlation between nuclei which are close in space (less than 0.5 nm). While for the major compounds **4a** and **4c** we observed NOE connectivities between protons H-1′ and H-2′a and between H-3′ and H-2′b, in minor compounds **5a** and **5c** NOE between H-1′ and H-2′b and between H-3′ and H-2′ were found. These results indicate β-anomeric configuration of the prevailing deoxyribosides **4a** and **4c**, while the configuration of minor compounds **5a** and **5c** is α. Comparison of ^{1}H NMR spectra of pure β-anomers **4a** and **4c** prepared in an alternative way (Scheme 3) with the spectra of prevailing isomers in the mixtures of **4** and **5** confirmed that the expected deoxyribosides **4** are N-9-β-isomers.

Complete NMR analysis was also used to examine a complex mixture of all four possible isomers after the reaction of 6-chloropurine (**10**) with acetate **9**. The crosspeaks in HMBC spectra of compounds **7a** and **7b** indicating connectivities between protons H-1′ and carbons C-8 and C-4 confirm the expected N-9 substitution, while in the compound **7c** the connectivities between proton H-1′ and carbon C-8 and C-5 establish the N-7 substitution.

For the determination of anomeric configuration of isolated isomers NOE experiments were used. In 5′-deoxyriboside **7b** NOE interaction was observed between protons H-1′ and H-4′ but not between H-1′ and CH$_3$-5′ that characterizes β-anomer. On the other hand, NOE connectivities between protons H-1′ and CH$_3$-5′ and the absence of NOE between protons H-1′ and H-4′ confirm α-anomeric configuration of compounds **7a** and **7c**. The clearly assigned 9-β-configuration of the intermediate **7b** and similar complete NMR analysis establishing 9-β-configuration of 5′-deoxyriboside **15a** was sufficient for the determination of the configuration and constitution in the series of **12** and **15**.

In conclusion, 2-deoxy- and 5-deoxyribonucleosides **14** and **15** as well as acyclic nucleoside analogues **16** derived from substituted 6-phenylpurines were prepared by the Suzuki–Miyaura cross-coupling reactions of the corresponding 9-substituted 6-chloropurines **6**, **7b**, **8** with phenylboronic acids **11a**–**11c** followed by MeONa mediated deprotection in good yields. The deoxyribosides **14** and **15** appeared to be extremely acidolabile. The title nucleoside analogues **14a**–**14c**, **15a**–**15c** and **16a**–**16c** were tested for their cytostatic activity (inhibition of cell growth of the following cell cultures: mouse leukemia L1210 cells (ATCC CCL 219), murine L929 cells (ATCC CCL 1), human cervix carcinoma HeLaS3 cells (ATCC CCL 2.2) and human T lymphoblastoid CCRF-CEM cell line (ATCC CCL 119)). In contrast to the significant *in vitro* activity of the corresponding ribonucleosides in these cell lines, none of the deoxyribosides **14** and **15** or acyclonucleosides **16** exerted any considerable activity in any of these assays. Since the absence of activity could be caused either by specific interactions with target cell systems or by insufficient transport into the cell, at this stage no conclusion about mechanism of action of the parent group of compounds could be made.

EXPERIMENTAL

Unless otherwise stated, solvents were evaporated at 40 °C/2 kPa and compounds were dried at 60 °C/2 kPa over P$_2$O$_5$. Melting points were determined on a Kofler block and are uncorrected. Optical rotations were measured at 25 °C on a Perkin–Elmer 141 MC polarimeter, [α]$_D$ values are given in 10^{-1} deg cm^2 g^{-1}. NMR spectra were measured on Bruker AMX-3 400 (400 MHz for ^{1}H, 100.6 MHz for ^{13}C and 376.5 MHz for ^{19}F nuclei), Bruker DRX 500 (500 MHz for ^{1}H, 125.7 MHz for ^{13}C and 470.59 MHz for ^{19}F) and Varian Gemini 300HC (300.075 MHz for ^{1}H and 75.462 MHz for ^{13}C). TMS was used as internal standard for the ^{1}H and ^{13}C NMR spectra; CFCl$_3$ was an internal standard for ^{19}F spectra. Chemical shifts are given in ppm (δ-scale), coupling constants (*J*) in Hz. Mass spectra were measured on a ZAB-EQ (VG Analytical) spectrometer using FAB (ionization by Xe, accelerating voltage 8 kV, glycerol matrix) or EI (electron energy 70 eV) techniques. Toluene was degassed *in vacuo* and

stored over molecular sieves under argon. Substituted phenylboronic acids **11a**–**11c** were supplied by Aldrich.

1,2,3-Tri-*O*-acetyl-5-deoxy-D-ribose (**9**)

This compound was prepared in four steps from D-ribose in the same way as described[15] for its L-enantiomer. The anomeric ratio of the product was *ca* 1 : 1 (NMR). Its spectral data were identical with the reported values[17].

6-(4-Methoxyphenyl)-9-(tetrahydropyran-2-yl)purine (**1c**)

Toluene (30 ml) was added to an argon purged flask containing 6-chloro-9-(tetrahydropyran-2-yl)purine (1.19 g, 5.0 mmol), K_2CO_3 (1.0 g, 7.5 mmol), 4-methoxyphenylboronic acid (1.0 g, 6.6 mmol) and $Pd(PPh_3)_4$ (236 mg, 0.2 mmol) and the mixture was stirred under argon at 100 °C for 8 h. After cooling down to ambient temperature the mixture was evaporated *in vacuo* and the residue was chromatographed on a silica gel column (50 g, ethyl acetate–light petroleum 1 : 2 to 9 : 1). Evaporation and drying of the product-containing fractions afforded compound **1c** as an amorphous solid. Yield 1.3 g (84%), m.p. 152–154 °C (CH_2Cl_2–heptane). FAB MS, *m/z* (rel.%): 311 (20) [M + H], 227 (100). ^{1}H NMR (400 MHz, $CDCl_3$): 1.64–2.20 (m, 6 H, CH_2); 3.77–3.84 (m, 1 H, CH_2O); 3.90 (s, 3 H, CH_3O); 4.16–4.21 (m, 1 H, CH_2O); 5.84 (dd, 1 H, *J* = 2.7 and 10.4, NCHO); 7.07 (d, 2 H, *J* = 8.9, H-arom.); 8.30 (s, 1 H, H-8); 8.81 (d, 2 H, *J* = 8.9, H-arom.); 8.96 (s, 1 H, H-2). For $C_{17}H_{18}N_4O_2$ (310.4) calculated: 65.79% C, 5.85% H, 18.05% N; found: 65.87% C, 5.90% H, 17.96% N.

6-(4-Methoxyphenyl)purine (**2c**)

A mixture of a THP-protected base **1c** (1.1 g, 3.54 mmol), Dowex 50X8 (H$^+$) (*ca* 300 mg), methanol (20 ml) and water (1 ml) was refluxed for 1 h, then filtered while hot and the resin was washed with saturated methanolic ammonia (5 ml) followed by methanol (20 ml). The combined filtrates were evaporated and the residue codistilled with toluene. Crystallization of the residue from methanol–toluene with addition of heptane afforded the product as colourless crystals (710 mg, 89%), m.p. 271–274 °C. FAB MS, *m/z* (rel.%): 227 (100) [M + H]. ^{1}H NMR (400 MHz, $CDCl_3$): 3.87 (s, 3 H, CH_3O); 7.14 (d, 2 H, *J* = 9.0, H-arom.); 8.58 (s, 1 H, H-8); 8.84–8.89 (m, 3 H, H-arom. and H-2); 13.50 (vbr, 1 H, NH). For $C_{12}H_{10}N_4O$ (226.2) calculated: 63.71% C, 4.46% H, 24.76% N; found: 63.37% C, 4.57% H, 24.39% N.

Glycosidations of 6-Phenylpurines **2a** and **2c** with Halogenose **3**

A mixture of 6-phenylpurine **2a** or **2c** (1.5 mmol), NaH (61 mg, 1.6 mmol, 60% dispersion in mineral oil) and acetonitrile (10 ml) was sonicated for 10 min and then stirred at 70 °C for 30 min. After cooling to room temperature, halogenose **3** (1.2 g, 3.1 mmol) was added and the mixture was stirred at ambient temperature overnight. The solvent was evaporated and the residue chromatographed on silica gel (ethyl acetate–light petroleum). Inseparable anomeric mixtures **4a**/**5a** [7 : 3 (NMR), 430 mg, 52%] or **4c**/**5c** [9 : 1 (NMR), 585 mg, 67%] were obtained, respectively.

Mixture **4a**/**5a**. FAB MS, *m/z* (rel.%): 549 (35) [M + H], 197 (100). ^{1}H NMR (500 MHz, $CDCl_3$): **4a**: 2.37 (s, 3 H, CH_3); 2.45 (s, 3 H, CH_3); 2.91 (ddd, 1 H, *J*(2′a,2′b) = 13.3, *J*(2′a,1′) = 5.8, *J*(2′a,3′) = 2.2, H-2′a); 3.22 (ddd, 1 H, overlapped, H-2′b); 4.67 (m, 2 H, H-4′ and 5′a);

4.79 (dd, 1 H, $J(5'a,5'b) = 13.2$, $J(2'b,4') = 5.1$, H-5'b); 5.86 (m, 1 H, H-3'); 6.65 (dd, 1 H, $J(1',2'a) = 5.8$, $J(1',2'b) = 8.1$, H-1'); 7.19 (d, 2 H, $J = 8.1$, H-arom.); 7.29 (d, 2 H, $J = 8.1$, H-arom.); 7.55 (m, 3 H, H-arom.); 7.88 (d, 2 H, $J = 8.2$, H-arom.); 7.98 (d, 2 H, $J = 8.2$, H-arom.); 8.31 (s, 1 H, H-8); 8.74 (dd, 2 H, $J = 1.8$ and 8.2, H-arom.); 8.98 (s, 1 H, H-2). **5a**: 2.31 (s, 3 H, CH$_3$); 2.43 (s, 3 H, CH$_3$); 3.08 (m, 1 H, H-2'b); 3.22 (m, 1 H, overlapped, H-2'a); 4.67 (m, 2 H, H-5'a and 5'b); 4.95 (m, 1 H, H-4'); 5.71 (m, 1 H, H-3'); 6.72 (dd, 1 H, $J(1',2'a) = 1.4$, $J(1',2'b) = 6.9$, H-1'); 7.10 (d, 2 H, $J = 8.1$, H-arom.); 7.29 (2 H, overlapped, H-arom.); 7.55 (m, 3 H, H-arom.); 7.88 (2 H, overlapped, H-arom.); 7.98 (2 H, overlapped, H-arom.); 8.47 (s, 1 H, H-8); 8.74 (2 H, overlapped, H-arom.); 8.98 (s, 1 H, H-2).

Mixture **4c/5c**. FAB MS, m/z (rel.%): 579 (38) [M + H], 227 (100). ^{1}H NMR (500 MHz, CDCl$_3$): **4c**: 2.36 (s, 3 H, CH$_3$); 2.44 (s, 3 H, CH$_3$); 2.90 (ddd, 1 H, $J(2'a,2'b) = 14.2$, $J(2'a,1') = 5.9$, $J(2'a,3') = 2.0$, H-2'a); 3.20 (ddd, 1 H, $J(2'a,2'b) = 14.2$, $J(2'b,1') = 8.1$, $J(2'b,3') = 6.5$, H-2'b); 3.90 (s, 3 H, OCH$_3$); 4.68 (m, 2 H, H-4' and 5'a); 4.78 (dd, 1 H, $J(5'a,5'b) = 13.3$, $J(2'b,4') = 5.2$, H-5'b); 5.86 (m, 1 H, H-3'); 6.64 (dd, 1 H, $J(1',2'a) = 5.9$, $J(1',2'b) = 8.1$, H-1'); 7.06 (d, 2 H, $J = 8.9$, H-arom.); 7.19 (d, 2 H, $J = 8.0$, H-arom.); 7.28 (d, 2 H, $J = 8.0$, H-arom.); 7.89 (d, 2 H, $J = 8.1$, H-arom.); 7.98 (d, 2 H, $J = 8.1$, H-arom.); 8.28 (s, 1 H, H-8); 8.78 (d, 2 H, $J = 8.9$, H-arom.); 8.93 (s, 1 H, H-2). **5c**: 2.31 (s, 3 H, CH$_3$); 2.42 (s, 3 H, CH$_3$); 3.08 (m, 1 H, H-2'b); 3.20 (m, 1 H, overlapped, H-2'a); 3.91 (s, 3 H, OCH$_3$); 4.60–5.0 (3 H, overlapped, H-4', 5'a and 5'b); 5.71 (m, 1 H, H-3'); 6.72 (dd, 1 H, $J(1',2'a) = 1.8$, $J(1',2'b) = 6.9$, H-1'); 7.10 (2 H, overlapped, H-arom.); 7.29 (2 H, overlapped, H-arom.); 7.55 (2 H, overlapped, H-arom.); 7.88 (2 H, overlapped, H-arom.); 7.98 (2 H, overlapped, H-arom.); 8.44 (s, 1 H, H-8); 8.74 (2 H, overlapped, H-arom.); 8.93 (s, 1 H, H-2).

Glycosidation of 6-Chloropurine (**10**) with 1,2,3-Tri-*O*-acetyl-5-deoxyribofuranose (**9**)

Tin(IV) chloride (5 ml, 42.8 mmol) was added to a stirred suspension of 6-chloropurine (3.4 g, 22 mmol) and 1,2,3-tri-*O*-acetyl-5-deoxyribofuranose (*ca* 1 : 1 anomeric mixture, 4.5 g, 17.3 mmol) in dry acetonitrile (120 ml) and the mixture was stirred at ambient temperature overnight. Then the mixture was added dropwise into 10% aqueous NaHCO$_3$ (500 ml) and extracted with ethyl acetate (3 × 250 ml). The collected organic layers were washed with 10% aqueous NaHCO$_3$ (300 ml) and water (200 ml), dried over anhydrous MgSO$_4$ and evaporated. The residue was chromatographed on a silica gel column (500 g, heptane–ethyl acetate – gradient 8 : 1 to 1 : 1). The first fraction afforded the 9-α-isomer **7a** (810 mg, 13%); the second fraction gave the 9-β-isomer **7b** (1.84 g, 30%) and, after the third fraction containing 500 mg of an inseparable complex mixture, the final fraction gave the 7-α-isomer **7c** (220 mg, 4%).

9-(2,3-Di-O-acetyl-5-deoxy-α-D-ribopentofuranosyl)-6-chloropurine (**7a**). Yellowish oil; purity *ca* 90% (NMR, contaminated by minor amounts of the other isomers). FAB MS, m/z (rel.%): 355 (35) [M + H], 201 (100). ^{1}H NMR (500 MHz, CDCl$_3$): 1.51 (d, 3 H, $J = 6.5$, 3 × H-5'); 2.08 and 2.19 (2 × s, 2 × 3 H, 2 × CH$_3$CO); 4.67 (dq, 1 H, $J = 4.5$ and 6.5, H-4'); 5.15 (m, 1 H, H-3'); 5.89 (brm, 1 H, H-2'); 6.31 (d, 1 H, $J = 2.0$, H-1'); 8.31 (s, 1 H, H-8); 8.80 (s, 1 H, H-2). ^{13}C NMR (125.8 MHz, CDCl$_3$): 18.68 (CH$_3$-5'); 20.61 and 20.68 (2 × **C**H$_3$CO); 80.10 (CH-2' and CH-3'); 81.86 (CH-4'); 88.56 (CH-1'); 132.03 (C-5); 143.40 (CH-8); 151.16 and 151.35 (C-4 and C-6); 152.24 (CH-2); 169.44 and 169.62 (2 × CO). FAB HRMS, calculated for C$_{14}$H$_{16}$ClN$_4$O$_5$ [M + H]: 355.0809; found: 355.0782.

9-(2,3-Di-O-acetyl-5-deoxy-β-D-ribopentofuranosyl)-6-chloropurine (**7b**). Yellowish oil; purity *ca* 90% (NMR, contaminated by minor amounts of the other isomers). FAB MS, m/z (rel.%): 355

(42) [M + H], 201 (100). ^{1}H NMR (500 MHz, CDCl$_3$): 1.53 (d, 3 H, J = 6.4, 3 × H-5′); 2.09 and 2.16 (2 × s, 2 × 3 H, 2 × CH$_3$CO); 4.37 (dq, 1 H, J = 5.5 and 6.4, H-4′); 5.41 (dd, 1 H, J = 5.0 and 5.5, H-3′); 5.98 (dd, 1 H, J = 5.0 and 4.8, H-2′); 6.13 (d, 1 H, J = 4.8, H-1′); 8.23 (s, 1 H, H-8); 8.79 (s, 1 H, H-2). ^{13}C NMR (125.8 MHz, CDCl$_3$): 18.67 (CH$_3$-5′); 20.37 and 20.54 (2 × **C**H$_3$CO); 73.17 (CH-2′); 74.39 (CH-3′); 79.00 (CH-4′); 87.21 (CH-1′); 132.47 (C-5); 143.74 (CH-8); 151.20 and 151.54 (C-4 and C-6); 152.24 (CH-2); 169.42 and 169.68 (2 × CO). FAB HRMS, calculated for C$_{14}$H$_{16}$ClN$_4$O$_5$ [M + H]: 355.0809; found: 355.0773.

7-(2,3-Di-O-acetyl-5-deoxy-α-D-ribopentofuranosyl)-6-chloropurine (**7c**). Yellowish oil; purity *ca* 90% (NMR, contaminated by minor amounts of the other isomers). FAB MS, *m/z* (rel.%): 355 (32) [M + H], 201 (100). ^{1}H NMR (500 MHz, CDCl$_3$): 1.50 (d, 3 H, J = 6.6, 3 × H-5′); 1.80 and 2.03 (2 × s, 2 × 3 H, 2 × CH$_3$CO); 4.72 (dq, 1 H, J = 3.6 and 6.6, H-4′); 5.27 (dd, 1 H, J = 3.6 and 5.5, H-3′); 5.89 (dd, 1 H, J = 5.5 and 5.7, H-2′); 6.92 (d, 1 H, J = 5.7, H-1′); 8.60 (s, 1 H, H-8); 8.91 (s, 1 H, H-2). ^{13}C NMR (125.8 MHz, CDCl$_3$): 19.32 (CH$_3$-5′); 19.95 and 20.46 (2 × **C**H$_3$CO); 70.82 (CH-2′); 74.44 (CH-3′); 80.48 (CH-4′); 84.86 (CH-1′); 122.19 (C-5); 142.66 (C-6); 147.42 (CH-8); 152.48 (CH-2); 162.15 (C-4); 168.51 and 169.36 (2 × CO). FAB HRMS, calculated for C$_{14}$H$_{16}$ClN$_4$O$_5$ [M + H]: 355.0809; found: 355.0792.

Cross-Coupling Reactions of 6-Chloropurines **6**, **7b** or **8** with Phenylboronic Acids **11a**–**11c**. General Procedure

Toluene (10 ml) was added to an argon purged flask containing a 6-chloropurine derivative (1.0 mmol), K$_2$CO$_3$ (200 mg, 1.5 mmol), a phenylboronic acid **11** (1.5 mmol) and Pd(PPh$_3$)$_4$ (59 mg, 0.05 mmol) and the mixture was stirred under argon at 100 °C for 8 h. After cooling down to ambient temperature, the mixture was evaporated *in vacuo* and the residue was chromatographed on a silica gel column (50 g, ethyl acetate–light petroleum 1 : 2 to 9 : 1). Evaporation and drying of the product containing fractions afforded the 6-phenylpurines **4a**–**4c**, **12a**–**12c** and **13a**–**13c** as foams or amorphous solids.

9-[3,5-Bis-O-(4-toluoyl)-2-deoxy-β-D-erythropentofuranosyl]-6-phenylpurine (**4a**). Yield 94%, colourless foam. FAB MS, *m/z* (rel.%): 549 (35) [M + H], 197 (100). ^{1}H NMR (400 MHz, CDCl$_3$): 2.36 (s, 3 H, CH$_3$); 2.45 (s, 3 H, CH$_3$); 2.91 (ddd, 1 H, J(2′a,2′b) = 14.1, J(2′a,1′) = 5.8, J(2′a,3′) = 2.2, H-2′a); 3.23 (ddd, 1 H, J(2′b,2′a) = 14.1, J(2′b,1′) = 8.1, J(2′b,3′) = 6.4, H-2′b); 4.64–4.71 (m, 2 H, H-4′ and 5′); 4.77–4.82 (m, 1 H, H-5′); 5.86 (ddd, 1 H, J(3′,2′b) = 6.4, J(3′,4′) = 4.1, J(3′,2′a) = 2.2, H-3′); 6.65 (dd, 1 H, J = 5.8 and 8.1, H-1′); 7.20 (d, 2 H, J = 8.1, H-arom.); 7.30 (d, 2 H, J = 8.1, H-arom.); 7.53–7.59 (m, 2 H, H-arom.); 7.89 (d, 2 H, J = 8.2, H-arom.); 8.00 (d, 2 H, J = 8.2, H-arom.); 8.30 (s, 1 H, H-8); 8.74 (dd, 2 H, J = 2.8 and 8.2, H-arom.); 8.98 (s, 1 H, H-2). FAB HRMS, calculated for C$_{32}$H$_{29}$N$_4$O$_5$ [M + H]: 549.2137; found: 549.2138.

9-[3,5-Bis-O-(4-toluoyl)-2-deoxy-β-D-erythropentofuranosyl]-6-(4-fluorophenyl)purine (**4b**). Yield 95%, yellowish foam. FAB MS, *m/z* (rel.%): 567 (31) [M + H], 215 (100). ^{1}H NMR (400 MHz, CDCl$_3$): 2.37 (s, 3 H, CH$_3$); 2.45 (s, 3 H, CH$_3$); 2.91 (ddd, 1 H, J(2′a,2′b) = 14.2, J(2′a,1′) = 5.9, J(2′a,3′) = 2.1, H-2′a); 3.22 (ddd, 1 H, J(2′b,2′a) = 14.2, J(2′b,1′) = 8.0, J(2′b,3′) = 6.5, H-2′b); 4.65–4.70 (m, 2 H, H-4′ and 5′); 4.76–4.82 (m, 1 H, H-5′); 5.85 (m, 1 H, H-3′); 6.64 (dd, 1 H, J = 5.9 and 8.0, H-1′); 7.16–7.30 (m, 6 H, H-arom.); 7.88 (d, 2 H, J = 8.2, H-arom.); 7.99 (d, 2 H, J = 8.2, H-arom.); 8.29 (s, 1 H, H-8); 8.82 (dd, 2 H, J = 3.3 and 8.9, H-arom.); 8.95 (s, 1 H, H-2). ^{13}C NMR (100 MHz, CDCl$_3$): 21.65 and 21.75 (2 × CH$_3$); 37.95 (CH$_2$-2′); 63.98 (CH$_2$-5′); 75.14 (CH-3′); 83.22 (CH-4′); 85.07 (CH-1′); 115.73 (d, J(F,C) = 21.5, CH-arom.); 126.44 and 126.65 (2 × C-arom.); 129.27, 129.33, 129.63 and 129.85 (4 ×

CH-arom.); 131.44 (C-5); 131.74 (d, J(F,C) = 3.0, C-i-arom); 132.06 (d, J(F,C) = 8.7, CH-arom.); 142.42 (CH-8); 144.18 and 144.59 (2 × CH-arom.); 151.96 (C-4); 152.41 (CH-2); 153.98 (C-6); 164.82 (d, J(F,C) = 268, C-F); 165.99 (2 × CO). FAB HRMS, calculated for $C_{32}H_{28}FN_4O_5$ [M + H]: 567.2044; found: 567.2061.

9-[3,5-Bis-O-(4-toluoyl)-2-deoxy-β-D-erythropentofuranosyl]-6-(4-methoxyphenyl)purine (**4c**). Yield 97%, yellowish foam. FAB MS, *m/z* (rel.%): 579 (29) [M + H], 227 (100). ^{1}H NMR (400 MHz, CDCl$_3$): 2.37 (s, 3 H, CH$_3$); 2.45 (s, 3 H, CH$_3$); 2.90 (ddd, 1 H, J(2′a,2′b) = 14.2, J(2′a,1′) = 5.9, J(2′a,3′) = 2.0, H-2′a); 3.21 (ddd, 1 H, J(2′b,2′a) = 14.2, J(2′b,1′) = 8.1, J(2′b,3′) = 6.5, H-2′b); 3.90 (s, 3 H, OCH$_3$); 4.66–4.71 (m, 2 H, H-4′ and 5′); 4.76–4.81 (m, 1 H, H-5′); 5.85 (m, 1 H, H-3′); 6.64 (dd, 1 H, J = 5.9 and 8.1, H-1′); 7.07 (d, 2 H, J = 8.9, H-arom.); 7.20 (d, 2 H, J = 8.0, H-arom.); 7.29 (d, 2 H, J = 8.0, H-arom.); 7.89 (d, 2 H, J = 8.2, H-arom.); 7.99 (d, 2 H, J = 8.1, H-arom.); 8.27 (s, 1 H, H-8); 8.78 (d, 2 H, J = 8.9, H-arom.); 8.92 (s, 1 H, H-2). FAB HRMS, calculated for $C_{33}H_{31}N_4O_6$ [M + H]: 579.2244; found: 579.2214.

9-(2,3-Di-O-acetyl-5-deoxy-β-D-ribopentofuranosyl)-6-phenylpurine (**12a**). Yield 96%, colourless oil. FAB MS, *m/z* (rel.%): 397 (100) [M + H], 197 (94). ^{1}H NMR (400 MHz, CDCl$_3$): 1.54 (d, 3 H, J = 6.4, 3 × H-5′); 2.08 and 2.15 (2 × s, 2 × 3 H, 2 × CH$_3$CO); 4.37 (dq, 1 H, J = 5.2 and 6.4, H-4′); 5.45 (dd, 1 H, J = 5.2 and 5.5, H-3′); 6.04 (dd, 1 H, J = 5.1 and 5.5, H-2′); 6.20 (d, 1 H, J = 5.1, H-1′); 7.52–7.58 (m, 3 H, H-arom.); 8.22 (s, 1 H, H-8); 8.73–8.76 (m, 2 H, H-arom.); 9.04 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, CDCl$_3$): 18.71 (CH$_3$-5′); 20.41 and 20.58 (2 × **CH$_3$**CO); 73.23 (CH-2′); 74.56 (CH-3′); 78.82 (CH-4′); 86.75 (CH-1′); 128.67, 129.84 and 131.10 (CH-arom.); 131.82 and 135.48 (C-i-arom. and C-5); 142.81 (CH-8); 152.04 and 155.42 (C-4 and C-6); 152.68 (CH-2); 169.45 and 169.72 (2 × CO). FAB HRMS, calculated for $C_{20}H_{21}N_4O_5$ [M + H]: 397.1512; found: 397.1569.

9-(2,3-Di-O-acetyl-5-deoxy-β-D-ribopentofuranosyl)-6-(4-fluorophenyl)purine (**12b**). Yield 89%, colourless oil. FAB MS, *m/z* (rel.%): 415 (91) [M + H], 215 (100). ^{1}H NMR (400 MHz, CDCl$_3$): 1.54 (d, 3 H, J = 6.5, 3 × H-5′); 2.09 and 2.16 (2 × s, 2 × 3 H, 2 × CH$_3$CO); 4.37 (dq, 1 H, J = 5.4 and 6.5, H-4′); 5.45 (dd, 1 H, J_1 = J_2 = 5.4, H-3′); 6.04 (dd, 1 H, J = 5.0 and 5.4, H-2′); 6.20 (d, 1 H, J = 5.0, H-1′); 7.21–7.26 (m, 2 H, H-arom.); 8.22 (s, 1 H, H-8); 8.81–8.86 (m, 2 H, H-arom.); 9.01 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, CDCl$_3$): 18.74 (CH$_3$-5′); 20.39 and 20.56 (2 × **CH$_3$**CO); 73.22 (CH-2′); 74.53 (CH-3′); 78.80 (CH-4′); 86.78 (CH-1′); 115.72 (d, J = 21.5, CH-arom.); 131.40 and 131.67 (C-i-arom. and C-5); 132.06 (d, J = 8.1, CH-arom.); 142.80 (CH-8); 152.02 and 154.15 (C-4 and C-6); 152.61 (CH-2); 164.74 (d, J = 252.0, C-F); 169.44 and 169.71 (2 × CO). ^{19}F NMR (376.5 MHz, CDCl$_3$): –109.30 (s, FPh). FAB HRMS, calculated for $C_{20}H_{20}FN_4O_5$ [M + H]: 415.1417; found: 415.1456.

9-(2,3-Di-O-acetyl-5-deoxy-β-D-ribopentofuranosyl)-6-(4-methoxyphenyl)purine (**12c**). Yield 96%, yellowish oil. FAB MS, *m/z* (rel.%): 427 (92) [M + H], 227 (100). ^{1}H NMR (400 MHz, CDCl$_3$): 1.54 (d, 3 H, J = 6.4, 3 × H-5′); 2.08 and 2.15 (2 × s, 2 × 3 H, 2 × CH$_3$CO); 3.90 (s, 3 H, OCH$_3$); 4.36 (dq, 1 H, J = 5.2 and 6.4, H-4′); 5.44 (dd, 1 H, J_1 = J_2 = 5.2, H-3′); 6.03 (dd, 1 H, J = 5.0 and 5.2, H-2′); 6.20 (d, 1 H, J = 5.0, H-1′); 7.07 (d, 2 H, J = 8.7, H-arom.); 8.19 (s, 1 H, H-8); 8.79 (d, 2 H, J = 8.7, H-arom.); 8.97 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, CDCl$_3$): 18.78 (CH$_3$-5′); 20.41 and 20.58 (2 × **CH$_3$**CO); 55.38 (OCH$_3$); 73.22 (CH-2′); 74.56 (CH-3′); 78.78 (CH-4′); 86.62 (CH-1′); 114.11 (CH-arom.); 128.17 and 131.22 (C-i-arom. and C-5); 131.61 (CH-arom.); 142.25 (CH-8); 151.83 and 155.02 (C-4 and C-6); 152.63 (CH-2); 162.16 (C-OCH$_3$); 169.43 and 169.72 (2 × CO). FAB HRMS, calculated for $C_{21}H_{23}N_4O_6$ [M + H]: 427.1618; found: 427.1594.

9-(2,3-Diacetoxypropyl)-6-phenylpurine (**13a**). Yield 82%, colourless amorphous solid. FAB MS, *m/z* (rel.%): 355 (100) [M + H]. ^{1}H NMR (400 MHz, CDCl$_3$): 2.04 and 2.09 (2 × s, 2 ×

3 H, 2 × CH$_3$CO); 4.15 (dd, 1 H, J = 12.2 and 4.9, H-3′a); 4.38 (dd, 1 H, J = 12.2 and 4.5, H-3′b); 4.52 (dd, 1 H, J = 14.7 and 7.0, H-1′a); 4.62 (dd, 1 H, J = 14.7 and 3.9, H-1′b); 5.43–5.49 (m, 1 H, H-2′); 7.51-7.59 (m, 3 H, H-arom.); 8.13 (s, 1 H, H-8); 8.79 (d, 2 H, J = 6.8, H-arom.); 9.02 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, CDCl$_3$): 20.60 and 20.71 (CH$_3$); 43.66 (CH$_2$-1′); 62.36 (CH$_2$-3′); 69.38 (CH-2′); 128.65, 129.78 and 131.08 (CH-arom.); 130.00 and 135.50 (C-i-arom. and C-5); 144.32 (CH-8); 152.65 (CH-2 and C-4); 155.10 (C-6); 169.66 and 170.23 (CO). FAB HRMS, calculated for C$_{18}$H$_{19}$N$_4$O$_4$ [M + H]: 355.1406; found: 355.1380.

9-(2,3-Diacetoxypropyl)-6-(4-fluorophenyl)purine (**13b**). Yield 81%, colourless amorphous solid. FAB MS, *m/z* (rel.%): 373 (100) [M + H]. ^{1}H NMR (400 MHz, CDCl$_3$): 2.05 and 2.10 (2 × s, 2 × 3 H, 2 × CH$_3$CO); 4.15 (dd, 1 H, J = 12.2 and 5.0, H-3′a); 4.38 (dd, 1 H, J = 12.2 and 4.5, H-3′b); 4.53 (dd, 1 H, J = 14.7 and 7.0, H-1′a); 4.64 (dd, 1 H, J = 14.7 and 4.0, H-1′b); 5.43–5.49 (m, 1 H, H-2′); 7.23–7.28 (m, 2 H, H-arom.); 8.13 (s, 1 H, H-8); 8.84–8.89 (m, 2 H, H-arom.); 9.00 (s, 1 H, H-2). ^{19}F NMR (376.5 MHz, CDCl$_3$): –109.33 (s, FPh). FAB HRMS, calculated for C$_{18}$H$_{18}$FN$_4$O$_4$ [M + H]: 373.1312; found: 373.1398.

9-(2,3-Diacetoxypropyl)-6-(4-methoxyphenyl)purine (**13c**). Yield 85%, yellowish amorphous solid. FAB MS, *m/z* (rel.%): 385 (100) [M + H]. ^{1}H NMR (400 MHz, CDCl$_3$): 2.04 and 2.10 (2 × s, 2 × 3 H, 2 × CH$_3$CO); 3.91 (s, 3 H, OCH$_3$); 4.15 (dd, 1 H, J = 12.0 and 4.6, H-3′a); 4.38 (dd, 1 H, J = 12.0 and 4.0, H-3′b); 4.51 (dd, 1 H, J = 14.3 and 6.8, H-1′a); 4.63 (dd, 1 H, J = 14.3 and 3.2, H-1′b); 5.45 (brm, 1 H, H-2′); 7.08 (d, 2 H, J = 8.5, H-arom.); 8.10 (s, 1 H, H-8); 8.82 (d, 2 H, J = 8.5, H-arom.); 8.97 (s, 1 H, H-2). FAB HRMS, calculated for C$_{19}$H$_{21}$N$_4$O$_5$ [M + H]: 385.1512; found: 385.1489.

Deacylation of the Protected Nucleosides. General Procedure

Method A: A 1 M solution of MeONa (50 µl, 0.05 mmol) was added to a solution of the protected nucleoside (0.5–0.8 mmol) in MeOH (20 ml) and the mixture was stirred at ambient temperature for 48–72 h (monitored by TLC, until completion of the reaction). Then the solvent was evaporated and the residue was chromatographed on a column of silica gel (50 g, EtOAc–MeOH, 10 : 0 to 7 : 3). Evaporation of the appropriate product-containing fractions, crystallization and/or drying afforded a free nucleosides as crystals or amorphous solids.

Method B: A 1 M solution of MeONa (200 µl, 0.2 mmol) was added to the solution of the protected nucleoside (0.5–0.8 mmol) in MeOH (20 ml) and the mixture was stirred at ambient temperature overnight. The crystals (when formed) were filtered off. Then the solution was neutralized by an addition of Dowex 50X8 (H$^+$) (*ca* 100 mg) and filtered. The ion-exchanger was washed with saturated methanolic ammonia (5 ml) followed by methanol (20 ml) and the combined filtrates were evaporated to dryness. The collected crystals and residue were recrystallized from EtOH–toluene to give the free nucleosides.

9-(2-Deoxy-β-D-erythropentofuranosyl)-6-phenylpurine (**14a**). Yield 88% (method *A*), colourless crystals, m.p. 122–124 °C (MeOH–toluene–heptane), [α]$_D$ –17.6 (*c* 0.2, DMF). FAB MS, *m/z* (rel.%): 313 (45) [M + H], 197 (100). ^{1}H NMR (400 MHz, DMSO-d_6): 2.40 (ddd, 1H, J(2′b,2′a) = 13.2, J(2′b,1′) = 6.7, J(2′b,3′) = 3.6, H-2′b); 2.82 (ddd, 1 H, J(2′a,2′b) = 13.2, J(2′a,1′) = 6.7, J(2′a,3′) = 6.4, H-2′a); 3.58 (ddd, 1 H, J(5′a,5′b) = 10.4, J(5′b,4) = J(5′b,OH) = 5.4, H-5′b); 3.65 (ddd, 1 H, J(5′a,5′b) = 10.4, J(5′a,4)= J(5′a,OH) = 5.4, H-5′a); 3.93 (m, 1 H, H-4′); 4.48 (m, 1 H, H-3′); 5.00 (t, 1 H, J = 5.4, 5′-OH); 5.36 (d, 1 H, J = 4.1, 3′-OH); 6.54 (t, 1 H, J(1′,2′a) = J(1′,2′b) = 6.7, H-1′); 7.59 (m, 3 H, H-arom.); 8.85–8.79 (m, 2 H, H-arom.);

8.88 (s, 1 H, H-8); 9.00 (s, 1 H, H-2). ^{13}C NMR (100 MHz, DMSO-d_6): ≈39 (overlapped by DMSO, C-2′); 61.49 (C-5′); 70.57 (C-3′); 83.72 (C-1′); 87.99 (C-4′); 128.62, 129.33 and 131.05 (3 × CH-arom.); 130.84 and 135.26 (C-5 and C-i-arom.); 144.77 (CH-8); 151.77 (CH-2); 151.90 and 152.84 (C-6 and C-4). For $C_{16}H_{16}N_4O_3$ (312.3) calculated: 61.53% C, 5.16% H, 17.94% N; found: 61.14% C, 5.21% H, 17.61% N.

9-(2-Deoxy-β-D-erythropentofuranosyl)-6-(4-fluorophenyl)purine (**14b**). Yield 85% (method *A*), colourless crystals, m.p. 122–124 °C (MeOH–toluene–heptane), [α]$_D$ –18.3 (*c* 0.2, DMF). FAB MS, *m/z* (rel.%): 331 (65) [M + H], 215 (100). ^{1}H NMR (400 MHz, DMSO-d_6): 2.40 (ddd, 1 H, *J*(2′b,2′a) = 13.1, *J*(2′b,1′) = 6.7, *J*(2′b,3′) = 3.7 H-2′b); 2.81 (ddd, 1 H, *J*(2′a,2′b) = 13.1, *J*(2′a,1′) = 6.7, *J*(2′a,3′) = 6.4, H-2′a); 3.58 (ddd, 1 H, *J*(5′a,5′b) = 10.3, *J*(5′b,4) = *J*(5′b,OH) = 5.4, H-5′b); 3.66 (ddd, 1 H, *J*(5′a,5′b) = 10.3, *J*(5′a,4)= *J*(5′a,OH) = 5.4, H-5′a); 3.92 (m, 1 H, H-4′); 4.48 (m, 1 H, H-3′); 5.00 (t, 1 H, *J* = 5.4, 5′-OH); 5.36 (d, 1 H, *J* = 4.1, 3′-OH); 6.53 (t, 1 H, *J*(1′,2′a) = *J*(1′,2′b) = 6.7, H-1′); 7.43 (t, 2 H, *J* = 8.8, H-arom); 8.88 (s, 1 H, H-8); 8.90 (m, 2 H arom. overlapped); 8.98 (s, 1 H, H-2). ^{13}C NMR (100 MHz, DMSO-d_6): ≈39 (overlapped by DMSO, C-2′); 61.45 (C-5′); 70.53 (C-3′); 83.71 (C-1′); 87.97 (C-4′); 115.66 (d, *J*(C,F)= 21.5, CH-arom); 130.54 (C-i-arom. and C-5); 131.74 (d, *J*(C,F)= 8.7, CH-arom.); 144.87 (CH-8); 151.62 and 151.88 (C-4 and C-6); 151.76 (CH-2); 163.84 (d, *J*(C,F)= 248.1, CF). ^{19}F NMR (376.5 MHz, DMSO-d_6): –108.74 (s, FPh). For $C_{16}H_{15}FN_4O_3$ (330.3) calculated: 58.18% C, 4.58% H, 16.96% N; found: 57.87% C, 4.56% H, 16.59% N.

9-(2-Deoxy-β-D-erythropentofuranosyl)-6-(4-methoxyphenyl)purine (**14c**). Yield 89% (method *A*), colourless crystals, m.p. 138–141 °C (MeOH-toluene–heptane) , [α]$_D$ –19.9 (*c* 0.2, DMF). FAB MS, *m/z* (rel.%): 343 (65) [M + H], 227 (100). ^{1}H NMR (500 MHz, DMSO-d_6): 2.39 (ddd, 1 H, *J*(2′a,2′b) = 13.3, *J*(2′a,1′) = 6.7, *J*(2′a,3′) = 3.6, H-2′a); 2.81 (ddd, 1 H, *J*(2′b,2′a) = 13.3, *J*(2′b,1′) = 6.7, *J*(2′b,3′) = 6.7, H-2′b); 3.53–3.58 and 3.62–3.68 (2 × m, 2 × 1 H, H-5′); 3.87 (s, 3 H, OCH$_3$); 3.93 (brm, 1 H, H-4′); 4.47 (brs, 1 H, H-3′); 5.04 (t, 1 H, *J*(OH,5′) = 5.5, OH-5′); 5.38 (d, 1 H, *J*(OH,3′) = 4.1, OH-3′); 6.53 (dd, 1 H, *J*(1′,2′a) = *J*(1′,2′b) = 6.7, H-1′); 7.16 (d, 2 H, *J* = 8.9, H-arom.); 8.84 (s, 1 H, H-8); 8.85 (d, *J* = 8.9, H-arom.); 8.93 (s, 1 H, H-2). ^{13}C NMR (125 MHz, DMSO-d_6): 39.35 (CH$_2$-2′); 55.53 (OCH$_3$); 61.72 (CH$_2$-5′); 70.79 (CH-3′); 83.86 (CH-1′); 88.15 (C-4′); 114.30 (CH-arom.); 127.91 (C-i-arom.); 130.35 (C-5); 131.30 (CH-arom.); 144.45 (CH-8); 151.79 (C-4); 151.93 (CH-2); 152.84 (C-6); 161.86 (C-OMe). For $C_{17}H_{18}N_4O_4$ (342.4) calculated: 59.64% C, 5.30% H, 16.37% N; found: 59.88% C, 5.58% H, 16.01% N.

9-(5-Deoxy-β-D-ribopentofuranosyl)-6-phenylpurine (**15a**). Yield 72% (method *A*), colourless crystals, m.p. 163–165 °C (96% aqueous EtOH), [α]$_D$ –60.6 (*c* 0.2, DMF). FAB MS, *m/z* (rel.%): 313 (75) [M + H], 197 (100). ^{1}H NMR (500 MHz, DMSO-d_6): 1.36 (d, 3 H, *J* = 5.9, 3 × H-5′); 4.03–4.06 (m, 2 H, H-3′ and H-4′); 4.77 (m, 1 H, CH-2′); 5.24 (d, 1 H, *J* = 4.8, 3′-OH); 5.53 (d, 1 H, *J* = 5.6, 2′-OH); 6.05 (d, 1 H, *J* = 4.8, H-1′); 7.57–7.62 (m, 3 H, H-arom.); 8.81–8.83 (m, 2 H, H-arom.); 8.87 (s, 1 H, H-8); 9.02 (s, 1 H, H-2). ^{13}C NMR (125.8 MHz, DMSO-d_6): 18.93 (CH$_3$-5′); 73.10 (CH-2′); 74.58 and 80.11 (CH-3′ and CH-4′); 88.05 (CH-1′); 128.67, 129.38 and 131.12 (CH-arom.); 130.89 (C-5); 135.24 (C-i-arom.); 145.29 (CH-8); 151.98 (CH-2); 152.21 (C-4); 152.99 (C-6). For $C_{16}H_{16}N_4O_3$·1/2H_2O (321.3) calculated: 59.80% C, 5.33% H, 17.44% N; found: 60.15% C, 5.14% H, 17.29% N.

9-(5-Deoxy-β-D-ribopentofuranosyl)-6-(4-fluorophenyl)purine (**15b**). Yield 76% (method *A*), colourless crystals, m.p. 172–175 °C (96% aqueous EtOH), [α]$_D$ –50.0 (*c* 0.2, DMF). FAB MS, *m/z* (rel.%): 331 (53) [M + H], 215 (100). ^{1}H NMR (500 MHz, DMSO-d_6): 1.36 (d, 3 H, *J* = 5.8, 3 × H-5′); 4.01–4.06 (m, 2 H, H-3′ and H-4′); 4.76 (m, 1 H, H-2′); 5.21 (d, 1 H, *J* = 4.7, 3′-OH); 5.51 (d, 1 H, *J* = 5.6, 2′-OH); 6.05 (d, 1 H, *J* = 4.8, H-1′); 7.42–7.46 (m, 2 H, H-arom.);

8.87 (s, 1 H, H-8); 8.89–8.92 (m, 2 H, H-arom.); 9.01 (s, 1 H, H-2). ^{13}C NMR (125.8 MHz, DMSO-d_6): 18.91 (CH$_3$-5′); 73.11 (CH-2′); 74.58 and 80.12 (CH-3′ and CH-4′); 88.09 (CH-1′); 115.76 (d, J(C,F) = 21.9, CH-arom.); 130.63 (C-5 and C-i-arom.); 131.81 (d, J(C,F) = 8.3, CH-arom.); 145.37 (CH-8); 151.97 (CH-2); 151.83 and 152.21 (C-4 and C-6); 163.91 (d, J(C,F) = 250.3, C-F). ^{19}F NMR (376.5 MHz, CDCl$_3$): –108.70 (s, FPh). For C$_{16}$H$_{15}$FN$_4$O$_3$·1/2H$_2$O (339.3) calculated: 56.63% C, 4.75% H, 16.51% N; found: 56.78% C, 4.49% H, 16.48% N.

9-(5-Deoxy-β-D-ribopentofuranosyl)-6-(4-methoxyphenyl)purine (**15c**). Yield 76% (method *A*), colourless crystals, m.p. 118–121 °C (96% aqueous EtOH), [α]$_D$ –68.4 (*c* 0.2, DMF). FAB MS, *m/z* (rel.%): 343 (51) [M + H], 227 (100). ^{1}H NMR (500 MHz, DMSO-d_6): 1.35 (d, 3 H, J = 5.7, 3 × H-5′); 3.87 (s, 3 H, OCH$_3$); 4.03–4.07 (m, 2 H, H-3′ and H-4′); 4.75 (m, 1 H, H-2′); 5.21 (d, 1 H, J = 4.7, 3′-OH); 5.51 (d, 1 H, J = 5.6, 2′-OH); 6.03 (d, 1 H, J = 4.8, H-1′); 7.16 (d, 2 H, J = 8.8, H-arom.); 8.81 (s, 1 H, H-8); 8.84 (d, 2 H, J = 8.8, H-arom.); 8.94 (s, 1 H, H-2). ^{13}C NMR (125.8 MHz, DMSO-d_6): 18.90 (CH$_3$-5′); 55.35 (OCH$_3$); 73.10 (CH-2′); 74.58 and 80.04 (CH-3′ and CH-4′); 88.00 (CH-1′); 114.13 (CH-arom.); 127.70 (C-i-arom.); 130.21 (C-5); 131.14 (CH-arom.); 144.70 (CH-8); 151.91 (CH-2); 152.80 (C-4 and C-6); 161.71 (C-OMe). For C$_{17}$H$_{18}$N$_4$O$_4$·1/2H$_2$O (351.4) calculated: 58.11% C, 5.45% H, 15.95% N; found: 58.05% C, 5.57% H, 16.04% N.

9-(2,3-Dihydroxypropyl)-6-phenylpurine (**16a**). Yield 75% (method *B*), colourless crystals, m.p. 159–162 °C (EtOH-toluene–heptane). EI MS, *m/z* (rel.%): 270 (13) [M], 252 (38), 239 (42), 209 (100), 196 (95). ^{1}H NMR (400 MHz, DMSO-d_6): 3.36–3.52 (m, 2 H, 2 × H-3′, in part overlapped with H$_2$O); 3.91–3.99 (m, 1 H, H-2′); 4.20 (dd, 1 H, J = 13.9 and 8.6, H-1′a); 4.50 (dd, 1 H, J = 13.9 and 3.4, H-1′b); 4.87 (t, 1 H, J = 5.6, 3′-OH); 5.16 (d, 1 H, J = 5.5, 2′-OH); 7.56–7.63 (m, 3 H, H-arom.); 8.60 (s, 1 H, H-8); 8.86 (dd, 2 H, J = 1.8 and 8.0, H-arom.); 8.99 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, DMSO-d_6): 46.79 (CH$_2$-1′); 63.61 (CH$_2$-3′); 69.46 (CH-2′); 128.61, 129.31 and 130.91 (CH-arom.); 130.30 and 135.51 (C-i-arom. and C-5); 147.30 (CH-8); 151.57 (CH-2); 152.35 and 152.68 (C-4 and C-6). EI HRMS, calculated for C$_{14}$H$_{14}$N$_4$O$_2$ [M]: 270.1117; found: 270.1125. For C$_{14}$H$_{14}$N$_4$O$_2$ (270.3) calculated: 62.21% C, 5.22% H, 20.73% N; found: 61.87% C, 5.14% H, 20.37% N.

9-(2,3-Dihydroxypropyl)-6-(4-fluorophenyl)purine (**16b**). Yield 70% (method *B*), colourless crystals, m.p. 158–161 °C (EtOH-toluene–heptane). EI MS, *m/z* (rel.%): 288 (21) [M], 270 (23), 257 (29), 227 (57), 214 (63), 43 (100). ^{1}H NMR (400 MHz, DMSO-d_6): 3.34–3.50 (m, 2 H, 2 × H-3′, in part overlapped with H$_2$O); 3.94 (brm, 1 H, H-2′); 4.20 (dd, 1 H, J = 13.9 and 8.6, H-1′a); 4.50 (dd, 1 H, J = 13.9 and 2.7, H-1′b); 4.87 (t, 1 H, J = 5.3, 3′-OH); 5.15 (d, 1 H, J = 5.3, 2′-OH); 7.44 (dd, 2 H, J = 8.7, H-arom.); 8.60 (s, 1 H, H-8); 8.85–8.88 (m, 2 H, H-arom.); 8.99 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, DMSO-d_6): 46.81 (CH$_2$-1′); 63.61 (CH$_2$-3′); 69.45 (CH-2′); 115.66 (d, J(C,F) = 21.2, CH-arom.); 130.03 and 135.25 (C-i-arom. and C-5); 131.75 (CH-arom.); 147.39 (CH-8); 151.56 (CH-2); 151.17 and 152.68 (C-4 and C-6); 163.80 (d, J(C,F) = 249.3, C-F). ^{19}F NMR (376.5 MHz, CDCl$_3$): –109.12 (s, FPh). EI HRMS, calculated for C$_{14}$H$_{13}$FN$_4$O$_2$ [M]: 288.1035; found: 288.1023. For C$_{14}$H$_{13}$FN$_4$O$_2$ (288.3) calculated: 58.33% C, 4.55% H, 19.44% N; found: 57.99% C, 4.68% H, 19.08% N.

9-(2,3-Dihydroxypropyl)-6-(4-methoxyphenyl)purine (**16c**). Yield 73% (method *B*), colourless crystals, m.p. 164–166 °C (EtOH-toluene–heptane). EI MS, *m/z* (rel.%): 300 (52) [M], 283 (19), 269 (36), 239 (56), 226 (100). ^{1}H NMR (400 MHz, DMSO-d_6): 3.36–3.51 (m, 2 H, 2 × H-3′); 3.88 (s, 3 H, OCH$_3$); 3.89–3.97 (m, 1 H, H-2′); 4.18 (dd, 1 H, J = 13.9 and 8.5, H-1′a); 4.48 (dd, 1 H, J = 13.9 and 3.4, H-1′b); 4.85 (t, 1 H, J = 5.6, 3′-OH); 5.14 (d, 1 H, J = 5.5, 2′-OH); 7.16 (d, 2 H, J = 8.9, H-arom.); 8.54 (s, 1 H, H-8); 8.88 (d, 2 H, J = 8.9, H-arom.);

8.92 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, DMSO-d_6): 46.73 (CH$_2$-1′); 55.35 (OCH$_3$); 63.63 (CH$_2$-3′); 69.48 (CH-2′); 114.09 (CH-arom.); 128.00 and 129.65 (C-i-arom. and C-5); 131.07 (CH-arom.); 146.75 (CH-8); 151.54 (CH-2); 152.20 and 152.38 (C-4 and C-6); 161.56 (C-OMe). EI HRMS, calculated for C$_{15}$H$_{16}$N$_4$O$_3$ [M]: 300.1222; found: 300.1258. For C$_{15}$H$_{16}$N$_4$O$_3$ (330.3) calculated: 59.99% C, 5.37% H, 18.66% N; found: 59.61% C, 5.23% H, 18.40% N.

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