# CYTOSTATIC 6-ARYLPURINE NUCLEOSIDES III.+ SYNTHESIS AND STRUCTURE–ACTIVITY RELATIONSHIP STUDY IN CYTOSTATIC ACTIVITY OF 6-ARYL-, 6-HETARYL- AND 6-BENZYLPURINE RIBONUCLEOSIDES

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A series of fifteen 6-aryl-, 6-hetaryl- and 6-benzylpurine ribonucleosides has been prepared by Pd-catalyzed cross-coupling reactions of 6-chloro-9-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-purine with arylboronic acids, hetarylzinc halides, hetarylstannanes or benzylzinc halides followed by deprotection. Structure–activity relationship study revealed that besides 6-(4-substituted phenyl)purine nucleosides, also some 6-hetaryl- and 6-benzylpurine ribonucleosides possess considerable cytostatic activity.

**Keywords**: Purines; Nucleosides; Cross-coupling reactions; Antineoplastic agents; Antitumor activity; Arylboronic acids; Stannanes; Organozinc reagents; Suzuki reaction.

Purines bearing a carbon substituent in 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 formation of cytotoxic bases liberated by purine nucleoside phosphorylases such as 6-methylpurine 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 a cytokinin activity of 6-(arylalkynyl)-, 6-(arylalkenyl)- and 6-(arylalkyl)purines[4], a cytostatic activity of 6-(trifluoromethyl)purine

+ Part II of this Series, see ref.[10]


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riboside[5,6], a corticotropin-releasing hormone antagonist activity of some 2,8,9-trisubstituted 6-arylpurines[7] and an antimycobacterial activity of 6-aryl-9-benzylpurines[8].

Recently we have discovered a new class of cytostatic compounds – substituted 6-phenylpurine derivatives[9]. The SAR studies revealed a crucial influence of the presence of the β-D-ribofuranosyl moiety in the position N-9 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 $l^{-1}$), while the 6-phenylpurine bases and 2-amino-6-phenylpurine ribonucleosides were entirely inactive in these assays. Sugar-modified 6-arylpurine nucleosides[10] (2′- or 5′-deoxyribosides and acyclonucleosides) as well as 6-(het)arylpurine acyclic nucleotide analogues[11,12] were also devoid of any cytostatic activity. As an extension of the SAR study of this class of compounds, we report here on the synthesis and cytostatic activity of purine ribonucleosides bearing selected aryl, hetaryl or benzyl substituents in position 6.

## RESULTS AND DISCUSSION

### *Chemistry*

Since in the initial series the most active compounds were 6-(4-X-substituted phenyl)purine ribosides (where X = H, halogen or alkoxy substituent), the first group of compounds under study were analogous purine nucleosides bearing phenyl ring substituted with some other types of substituents in position 4 (X = $SCH_3$, $N(CH_3)_2$, $CF_3$ and OH) as well as 3,4-dimethoxyphenyl and 3,4-(methylenedioxy)phenyl moieties occurring in many cytostatic natural products such as alkaloids. To study steric limitations of the aryl moiety, purine nucleosides bearing 1- or 2-naphthyl substituents in position 6 were devised. Replacement of the phenyl ring by a six- or five-membered heterocyclic moiety was another structural modification studied. Finally, 6-benzylpurine derivatives were selected in order to test whether a conjugation of the aryl and purine moieties is necessary for the cytostatic activity.

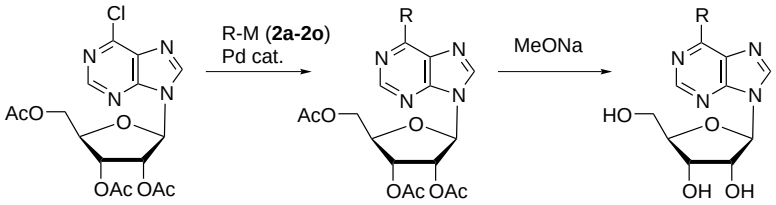
The Suzuki reaction of 6-halopurines with boronic acids was reported[13] to be a facile and efficient method for the preparation of diverse purines bearing a carbon substituent in position 6. A major advantage of this method for the preparation of compounds for biological activity screening in comparison with cross-coupling reactions with other types of organometallics

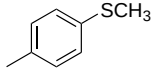
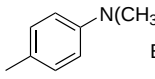
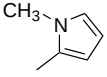
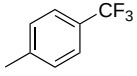
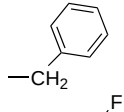
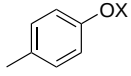
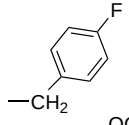
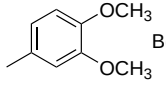
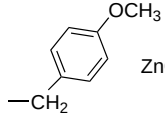
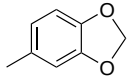
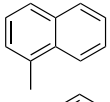
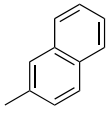
(*e.g.* stannanes, organozinc reagents, cuprates) consists in the fact that no toxic metal-containing by-products are formed. Since the use of this reaction under anhydrous conditions in toluene was found[9,13] to be superior for the introduction of phenyl groups bearing electron-rich, electroneutral or weakly electron-withdrawing substituents, it was the method of choice for the introduction of substituted phenyl and naphthyl substituents. Thus the reaction of 6-chloro-9-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)purine (**1**) with a series of commercially available phenyl- or naphthylboronic acids **2a**–**2h** in toluene under $Pd(PPh_3)_4$ catalysis afforded the protected 6-arylpurine ribonucleosides **3a**–**3h** in good yields (Scheme 1). In contrast to the lack of reactivity[9,13] of other electron-deficient phenylboronic acids (nitro-, cyano-, formyl-, acetyl- and pentafluorophenyl) under anhydrous conditions, 4-(trifluoromethyl)phenylboronic acid (**2c**) reacted under these conditions relatively smoothly. The THP-protected boronic acid **2d** was used as a 4-hydroxyphenyl precursor and the THP group in compound **3d** was quantitatively cleaved under very mild conditions (catalytic amount of HCl in methanol at ambient temperature) prior to deacetylation (*vide infra*).

The Negishi cross-coupling reactions of organozinc reagents with 6-halopurines are the most versatile methods for the introduction of diverse types of carbon substituents[11,12,14,15] (alkyl, alkenyl, aryl and hetaryl). The drawback of this approach is its lower tolerance to the presence of some unprotected functional groups and difficult removal of the residual zinc compounds which often make strong complexes with purines. In our study, this approach was successfully used for the introduction of nitrogen-hetaryl (2-pyridyl and 1-methylpyrrol-2-yl) and substituted benzyl substituents. Thus the protected 6-chloropurine nucleoside **1** reacted smoothly with the hetaryl- or benzylzinc halides **2i**–**2m** in THF in the presence of $Pd(PPh_3)_4$ to afford the protected 6-hetaryl- or 6-benzylpurine nucleosides **3i**–**3m**. The zinc residues were removed by extraction with EDTA. While the use of commercially available benzylzinc chlorides (Rieke® organozinc reagents) **2k**–**2m** well tolerated the presence of the acetyl-protected ribofuranose to give the protected nucleosides **3k**–**3m** in good yields, the reactions of hetarylzinc chlorides **2i** (commercial Rieke® organozinc reagent) and **2j** [generated from 1-methylpyrrole by the use of BuLi in the presence of *N*,*N*,*N*′,*N*′-tetramethylethane-1,2-diamine (TMEDA) followed by transmetallation with $ZnCl_2$] was accompanied by partial deacetylation during the work-up giving the triacetyl nucleosides **3i** and **3j** in low yields only.

Another approach widely used for the introduction[11,12,14,16–18] of alkyl, alkenyl, aryl and hetaryl substituents is the Stille coupling of organo-

Scheme 1:




| Entry | R | M | Yield of **3** | Yield of **4** | Entry | R | M | Yield of **3** | Yield of **4** |
|---|---|---|---|---|---|---|---|---|---|
| **a** |  | $B(OH)_2$ | 68% | 65% | **i** |  | ZnCl | 27% | 65% |
| **b** |  | $B(OH)_2$ | 82% | 63% | **j** |  | ZnCl | 22% | 86% |
| **c** |  | $B(OH)_2$ | 55% | 79% | **k** |  | ZnCl | 62% | 66% |
| **d**[a] |  | $B(OH)_2$ | 83% | 60% | **l** |  | ZnCl | 76% | 67% |
| **e** |  | $B(OH)_2$ | 74% | 67% | **m** |  | ZnCl | 60% | 88% |
| **f** |  | $B(OH)_2$ | 72% | 71% | **n** |  | $SnBu_3$ | 89% | 66% |
| **g** |  | $B(OH)_2$ | 76% | 70% | **o** |  | $SnBu_3$ | 85% | 59% |
| **h** |  | $B(OH)_2$ | 72% | 78% | | | | | |

[a] **3d**, X = THP $\xrightarrow{\text{1. HCl, 2. MeONa}}$ **4d**, X = H

stannanes with 6-halopurines. As in the previous case, the major drawback of this method is a difficult removal of highly toxic organotin reagents and side-products. In this study, commercially available 2-thienyl- and 2-furylstannanes **2n** and **2o** reacted smoothly with the 6-chloropurine **1** in DMF in the presence of $PdCl_2(PPh_3)_2$ to give the protected 6-hetarylpurine nucleosides **3n** and **3o** in good yields. Standard[14] treatment of the crude products with methanolic KF to destroy the stannanes led simultaneously to deacetylation. Therefore the organostannanes were removed by repeated column chromatography.

All the triacetyl nucleosides **3a**–**3o** were quantitatively deprotected by the use of catalytic amount of MeONa in methanol and the free nucleosides **4a**–**4o** were isolated in good yields (59–88%) after crystallization.

All compounds were characterized by spectral and analytical methods. Assignment of the $^1H$ and $^{13}C$ NMR spectra was based on a combination of COSY, HMBC and HMQC experiments in selected typical compounds. UV spectra of the series of compounds **4a**–**4o** revealed a significant effect of the substituent in position 6 displaying the maxima between 263–265 nm for the 6-benzylpurine derivatives **4k**–**4m**, and between 290–375 nm for the 6-aryl- and 6-hetarylpurines **4a**–**4j** and **4n** and **4o**.

*Cytostatic Activity Evaluation*

The title 6-substituted purine ribonucleosides **4a**–**4o** were tested on their *in vitro* inhibition of the cell growth in the following cell cultures: (i) mouse leukemia L1210 cells (ATCC CCL 219); murine L929 cells (ATCC CCL 1); human cervix carcinoma HeLa S3 cells (ATCC CCL 2.2); and human T-lymphoblastoid CCRF-CEM cell line (ATCC CCL 119). The results (Table I) show that, analogously to the results[9] of the parent group of 6-phenylpurine ribonucleosides, most of the nucleosides **4** possessed powerful cytostatic potency against T-lymphoblastoids (CCRF-CEM: $IC_{50}$ values from 0.5 to 15 μmol $l^{-1}$), while L1210 and HeLa S3 cells were much less sensitive and only marginal effects have been found toward L929 cell line (data not shown).

These results make an extension of the structure–activity relationship study of this group of compounds. In addition to the previously reported[9] high antiproliferative activity of 6-phenyl-, 6-(4-halophenyl)- and 6-(4-alkoxyphenyl)purine ribonucleosides, comparably high submicromolar activity was found in 6-[4-(methylsulfanyl)phenyl]purine derivative **4a**. Compound **4d** bearing an acidic phenol moiety was about one order of magnitude less effective than the 4-alkoxyphenyl derivatives, while basic

4-(dimethylamino)phenyl derivative **4b** was much less active. The 4-(trifluoromethyl)phenyl derivative **4c** was entirely inactive. Introduction of a second alkoxy group into the phenyl moiety caused a dramatic decrease of cytostatic potency (compounds **4e** and **4f**). Also attachment of a bulky naphthyl moiety to the purine ring led to less active or inactive compunds (**4g** and **4h**). The best results were obtained with purine nucleosides bearing a six- or five-membered heteroaromatic moiety in position 6: the

TABLE I
Cytostatic activity of 6-R-substituted purine ribonucleosides **4**

| Compound | R | $IC_{50}$[a], μmol $l^{-1}$ | | |
|---|---|---|---|---|
| | | CCRF-CEM | L1210 | HeLa S3 |
| **4a** | 4-$(CH_3S)C_6H_4$ | 0.8 | NA | NA |
| **4b** | 4-$[(CH_3)_2N]C_6H_4$ | 20.0 | NA | NA |
| **4c** | 4-$CF_3C_6H_4$ | NA | NA | NA |
| **4d** | 4-$HOC_6H_4$ | 1.25 | 5.0 | 32.5 |
| **4e** | 3,4-di$(CH_3O)C_6H_3$ | NA | NA | NA |
| **4f** | 3,4-$(OCH_2O)C_6H_3$ | 5.0 | NA | NA |
| **4g** | 1-naphthyl | NA | NA | NA |
| **4h** | 2-naphthyl | 20.0 | NA | NA |
| **4i** | 2-pyridyl | 0.9 | 4.3 | 9.7 |
| **4j** | 1-methylpyrrol-2-yl | 2.0 | NA | NA |
| **4k** | benzyl | 8.8 | NA | NA |
| **4l** | 4-fluorobenzyl | 7.0 | NA | NA |
| **4m** | 4-methoxybenzyl | NA | NA | NA |
| **4n** | 2-thienyl | 0.6 | 0.4 | 25.0 |
| **4o** | 2-furyl | 0.6 | 2.0 | 25.0 |
| | phenyl[b] | 0.7 | 9.0 | 2.7 |
| | 4-fluorophenyl[b] | 0.75 | 4.5 | 2.5 |
| | 4-methoxyphenyl[b] | 0.25 | 1.5 | 4.3 |

[a] NA = not active (inhibition of cell growth at $c$ = 10 μmol $l^{-1}$ was lower than 20%). [b] Taken from ref.[9]

6-(2-pyridyl)- (**4i**), 6-(2-thienyl)- (**4n**) and 6-(2-furyl)purine (**4o**) derivatives displayed submicromolar activity towards CCRF-CEM and micromolar activity towards L1210 and HeLa cells. The 1-methylpyrrol-2-yl derivative **4j** was less active, analogously to the previously described[9] inactive *ortho*-substituted phenylpurine nucleosides. Surprisingly, a lower but still considerable inhibition of the cell growth was found in 6-benzylpurines **4k** and **4l**, showing that conjugation of the aryl and purine rings is not crucial for the cytostatic activity.

## CONCLUSIONS

Cross-coupling reactions of 6-chloro-9-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-purine (**1**) with arylboronic acids, hetaryl- or benzylzinc chlorides and hetarylstannanes afforded effectively a series of 6-aryl-, 6-hetaryl- and 6-benzylpurine ribonucleosides. The cytostatic activity was strongly dependent on the nature and steric demands of substituent in position 6. Besides some 6-(4-substituted phenyl)purine derivatives, also 6-hetaryl nucleosides showed a significant cytostatic activity. Compounds bearing more bulky substituents were less active or inactive. Considerable cytostatic activity was also found in 6-benzylpurine ribonucleosides. These and previous[9,10] findings enable us to formulate the following structural features of the pharmacophore for the cytostatic activity of this group of compounds: a purine nucleoside bearing a β-D-ribofuranosyl residue in position 9 and an aryl group in position 6 which might consist in (i) phenyl moiety bearing a halogeno, alkoxy or methylsulfanyl substituents in *para*-position or in (ii) six- or five-membered heterocycle. Further studies will be necessary to investigate the mechanism of action of this group of compounds.

## EXPERIMENTAL

Unless otherwise stated, solvents were evaporated at 40 °C/2kPa and compounds were dried at 60 °C/2kPa over $P_2O_5$. 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, $[\alpha]_D$ values are given in $10^{-1}$ deg cm$^2$ g$^{-1}$. NMR spectra were measured on a Bruker AMX-3 400 (400 MHz for $^1$H, 100.6 MHz for $^{13}$C and 376.5 MHz for $^{19}$F nuclei), a Bruker DRX 500 (500 MHz for $^1$H, 125.7 MHz for $^{13}$C and 470.59 MHz for $^{19}$F). 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). UV absorption spectra ($\lambda_{max}$, nm; ε, l mol$^{-1}$ cm$^{-1}$) were measured on a Shimadzu UVmini 1240 spectrometer in methanolic solutions. Toluene was degassed *in vacuo* and stored over molecular sieves under argon. DMF was distilled from

$P_2O_5$, degassed *in vacuo* and stored over molecular sieves under argon. THF was refluxed with Na and benzophenone under argon and freshly distilled prior to use. Substituted phenylboronic acids **2a–2f** were purchased from Frontier Scientific (U.K.), naphthylboronic acids **2g** and **2h**, Rieke® organozinc reagents **2i** and **2k–2m**, as well as stannanes **2n** and **2o** were supplied by Aldrich. Cytostatic activity tests were performed as described in ref.[9].

Cross-Coupling Reactions of 6-Chloropurine Nucleoside **1** with Arylboronic Acids. General Procedure

Toluene (10 ml) was added to an argon-purged flask containing the protected 6-chloropurine nucleoside[19] **1** (413 mg, 1 mmol), $K_2CO_3$ (200 mg, 1.5 mmol), arylboronic acid **2a–2h** (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 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 6-arylpurines **3a–3h** as foams or amorphous solids.

*6-[4-(Methylsulfanyl)phenyl]-9-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)purine* (**3a**). Yellowish amorphous solid, yield 68%. FAB MS, *m/z* (rel.%): 501 (44) [M + H], 243 (100). $^1$H NMR (400 MHz, $CDCl_3$): 2.09, 2.14 and 2.17 (3 × s, 3 × 3 H, 3 × $CH_3CO$); 2.56 (s, 3 H, $SCH_3$); 4.36–4.48 (m, 3 H, H-4′ and 2 × H-5′); 5.71 (dd, 1 H, *J* = 4.5 and 5.4, H-3′); 6.01 (t, 1 H, *J* = 5.4, H-2′); 6.30 (d, 1 H, *J* = 5.4, H-1′); 7.40 (d, 2 H, *J* = 8.6, H-arom.); 8.26 (s, 1 H, H-8); 8.73 (d, 2 H, *J* = 8.6, H-arom.); 8.99 (s, 1 H, H-2). $^{13}$C NMR (100 MHz, $CDCl_3$): 15.12 ($SCH_3$); 20.41, 20.55 and 20.78 (3 × $CH_3$); 63.11 ($CH_2$-5′); 70.73 (CH-3′); 73.14 (CH-2′); 80.45 (CH-4′); 86.42 (CH-1′); 125.74 (CH-arom.); 130.12 (CH-arom.); 131.39 and 131.88 (C-5 and C-*i*-arom.); 142.24 (H-8); 143.23 (C-SMe); 152.01 (C-4); 152.71 (C-2); 154.90 (C-6); 169.38, 169.59 and 170.32 (3 × CO). HR MS (FAB), calculated for $C_{23}H_{25}N_4O_7S$ [M + H]: 501.1444; found: 501.1455.

*6-[4-(Dimethylamino)phenyl]-9-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)purine* (**3b**). Yellow amorphous solid, yield 82%. FAB MS, *m/z* (rel.%): 498 (45) [M + H], 240 (42), 93 (100). $^1$H NMR (400 MHz, $CDCl_3$): 2.08, 2.13 and 2.15 (3 × s, 3 × 3 H, 3 × $CH_3CO$); 3.08 (s, 6 H, $N(CH_3)_2$); 4.36–4.47 (m, 3 H, H-4′ and 2 × H-5′); 5.71 (dd, 1 H, *J* = 4.2 and 5.4, H-3′); 6.00 (t, 1 H, *J* = 5.4, H-2′); 6.29 (d, 1 H, *J* = 5.4, H-1′); 6.83 (d, 2 H, *J* = 8.9, H-arom.); 8.19 (s, 1 H, H-8); 8.76 (d, 2 H, *J* = 8.9, H-arom.); 8.90 (s, 1 H, H-2). $^{13}$C NMR (100.6 MHz, $CDCl_3$): 20.41, 20.57 and 20.79 (3 × $CH_3$); 40.13 ($(CH_3)_2N$); 63.17 ($CH_2$-5′); 70.79 (CH-3′); 73.13 (CH-2′); 80.38 (CH-4′); 86.15 (CH-1′); 111.63 (CH-arom.); 122.95 and 130.55 (C-5 and C-*i*-arom.); 131.37 (CH-arom.); 141.15 (H-8); 151.58 (C-$NMe_2$); 152.46 and 155.68 (C-4 and C-6); 152.71 (C-2); 169.38, 169.61 and 170.36 (3 × CO). HR MS (FAB), calculated for $C_{24}H_{28}N_5O_7$ [M + H]: 498.1989; found: 498.1954.

*9-(2,3,5-Tri-O-acetyl-β-D-ribofuranosyl)-6-[4-(trifluoromethyl)phenyl]purine* (**3c**). Yellowish amorphous solid, yield 55%. FAB MS, *m/z* (rel.%): 523 (44) [M + H], 264 (100). $^1$H NMR (400 MHz, $CDCl_3$): 2.11, 2.14 and 2.18 (3 × s, 3 × 3 H, 3 × $CH_3CO$); 4.40–4.51 (m, 3 H, H-4′ and 2 × H-5′); 5.72 (dd, 1 H, *J* = 4.6 and 5.4, H-3′); 6.02 (t, 1 H, *J* = 5.4, H-2′); 6.31 (d, 1 H, *J* = 5.2, H-1′); 7.82 (d, 2 H, *J* = 8.3, H-arom.); 8.32 (s, 1 H, H-8); 8.91 (d, 2 H, *J* = 8.2, H-arom.); 9.07 (s, 1 H, H-2). $^{19}$F NMR (376.5 MHz, $CDCl_3$): –63.42 (s, $CF_3$). HR MS (FAB), calculated for $C_{23}H_{22}F_3N_4O_7$ [M + H]: 523.1441; found: 523.1430.

*6-{4-[(Tetrahydropyran-2-yl)oxy]phenyl}-9-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)purine* (**3d**). Colourless amorphous solid, yield 83%. FAB MS, *m/z* (rel.%): 555 (48) [M + H], 471 (12)

[M + H – THP], 213 (100). $^1$H NMR (400 MHz, $CDCl_3$): 1.62–1.74 and 1.88–1.93 (2 × m, 6 H, $CH_2$, THP); 2.09, 2.14 and 2.16 (3 × s, 3 × 3 H, 3 × $CH_3CO$); 3.61–3.67 and 3.87–3.95 (2 × m, 2 × 1 H, $OCH_2$, THP); 4.36–4.47 (m, 3 H, H-4′ and 2 × H-5′); 5.56 (brm, 1 H, NCHO, THP); 5.71 (dd, 1 H, *J* = 4.1 and 5.3, H-3′); 6.01 (t, 1 H, *J* = 5.3, H-2′); 6.29 (d, 1 H, *J* = 5.3, H-1′); 7.22 (d, 2 H, *J* = 8.4, H-arom.); 8.24 (s, 1 H, H-8); 8.77 (d, 2 H, *J* = 8.4, H-arom.); 8.97 (s, 1 H, H-2). $^{13}$C NMR (100.6 MHz, $CDCl_3$): 18.66 ($CH_2$, THP); 20.41, 20.57 and 20.79 (3 × $CH_3$); 25.18 and 30.26 ($CH_2$, THP); 62.06 and 63.12 ($CH_2O$, THP and $CH_2$-5′); 70.75 (CH-3′); 73.14 (CH-2′); 80.44 (CH-4′); 86.34 (CH-1′); 96.18 (NCHO, THP); 116.49 (CH-arom.); 128.77 and 131.16 (C-5 and C-*i*-arom.); 131.53 (CH-arom.); 142.01 (H-8); 151.91 and 155.20 (C-4 and C-6); 152.70 (C-2); 159.77 (C-OTHP); 169.37, 169.59 and 170.33 (3 × CO). HR MS (FAB), calculated for $C_{27}H_{31}N_4O_9$ [M + H]: 555.2091; found: 555.2085.

*6-(3,4-Dimethoxyphenyl)-9-(2,3,5-tri-O-acetyl-*β*-D-ribofuranosyl)purine* (**3e**). Yellowish amorphous solid, yield 74%. FAB MS, *m/z* (rel.%): 515 (30) [M + H], 257 (100). $^1$H NMR (400 MHz, $CDCl_3$): 2.09, 2.14 and 2.17 (3 × s, 3 × 3 H, 3 × $CH_3CO$); 3.98 and 4.04 (2 × s, 2 × 3 H, 2 × $OCH_3$); 4.38–4.50 (m, 3 H, H-4′ and 2 × H-5′); 5.71 (ddt, 1 H, *J* = 4.4, 5.4, H-3′); 6.01 (t, 1 H, *J* = 5.4, H-2′); 6.30 (d, 1 H, *J* = 5.3, H-1′); 7.05 (d, 1 H, *J* = 8.6, H-arom.); 8.25 (s, 1 H, H-8); 8.41 (d, 1 H, *J* = 1.6, H-arom.); 8.58 (dd, 1 H, *J* = 1.6 and 8.6, H-arom.); 8.97 (s, 1 H, H-2). HR MS (FAB), calculated for $C_{24}H_{27}N_4O_9$ [M + H]: 515.1778; found: 515.1761.

*6-[3,4-(Methylenedioxy)phenyl]-9-(2,3,5-tri-O-acetyl-*β*-D-ribofuranosyl)purine* (**3f**). Yellowish amorphous solid, yield 72%. FAB MS, *m/z* (rel.%): 499 (27) [M + H], 241 (100). $^1$H NMR (400 MHz, $CDCl_3$): 2.09, 2.14 and 2.17 (3 × s, 3 × 3 H, 3 × $CH_3CO$); 4.38–4.50 (m, 3 H, H-4′ and 2 × H-5′); 5.71 (dd, 1 H, *J* = 4.6, 5.4, H-3′); 6.01 (t, 1 H, *J* = 5.4, H-2′); 6.07 (s, 2 H, $OCH_2O$); 6.29 (d, 1 H, *J* = 5.4, H-1′); 7.00 (d, 1 H, *J* = 8.3, H-arom.); 8.25 (s, 1 H, H-8); 8.33 (d, 1 H, *J* = 1.7, H-arom.); 8.51 (dd, 1 H, *J* = 1.7 and 8.3, H-arom.); 8.96 (s, 1 H, H-2). HR MS (FAB), calculated for $C_{23}H_{23}N_4O_9$ [M + H]: 499.1465; found: 499.1508.

*6-(1-Naphthyl)-9-(2,3,5-tri-O-acetyl-*β*-D-ribofuranosyl)purine* (**3g**). Yellowish amorphous solid, yield 76%. FAB MS, *m/z* (rel.%): 505 (19) [M + H], 247 (100). $^1$H NMR (400 MHz, $CDCl_3$): 2.13, 2.14 and 2.18 (3 × s, 3 × 3 H, 3 × $CH_3CO$); 4.40–4.52 (m, 3 H, H-4′ and 2 × H-5′); 5.76 (dd, 1 H, *J* = 5.5 and 4.4, H-3′); 6.09 (dd, 1 H, *J* = 5.1 and 5.5, H-2′); 6.33 (d, 1 H, *J* = 5.1, H-1′); 7.49–7.56 (m, 2 H, H-arom.); 7.65 (t, 1 H, *J* = 7.7, H-arom.); 7.92–7.95 (m, 1 H, H-arom.); 8.03 (d, 2 H, *J* = 7.6, H-arom.); 8.26 (s, 1 H, H-8); 8.26–8.29 (m, 1 H, H-arom.); 9.17 (s, 1 H, H-2). HR MS (FAB), calculated for $C_{26}H_{25}N_4O_7$ [M + H]: 505.1723; found: 505.1720.

*6-(2-Naphthyl)-9-(2,3,5-tri-O-acetyl-*β*-D-ribofuranosyl)purine* (**3h**). Yellowish amorphous solid, yield 72%. FAB MS, *m/z* (rel.%): 505 (48) [M + H], 360 (100). $^1$H NMR (400 MHz, $CDCl_3$): 2.11, 2.16 and 2.18 (3 × s, 3 × 3 H, 3 × $CH_3CO$); 4.40–4.51 (m, 3 H, H-4′ and 2 × H-5′); 5.74 (dd, 1 H, *J* = 5.4 and 4.4, H-3′); 6.05 (t, 1 H, *J* = 5.4, H-2′); 6.34 (d, 1 H, *J* = 5.4, H-1′); 7.52–7.59 (m, 2 H, H-arom.); 7.91 (d, 1 H, *J* = 7.5, H-arom.); 8.02 (d, 1 H, *J* = 8.7, H-arom.); 8.08 (d, 1 H, *J* = 7.4, H-arom.); 8.34 (s, 1 H, H-8); 8.87 (dd, 1 H, *J* = 8.7 and 1.2, H-arom.); 9.09 (s, 1 H, H-2); 9.41 (s, 1 H, H-arom.). HR MS (FAB), calculated for $C_{26}H_{25}N_4O_7$ [M + H]: 505.1723; found: 505.1763.

### Cross-Coupling Reactions of 6-Chloropurine Nucleoside **1** with Organozinc Halides. General Procedure

THF (10 ml) was added to an argon-purged flask containing the 6-chloropurine **1** (413 mg, 1 mmol) and $Pd(PPh_3)_4$ (59 mg, 0.05 mmol). The mixture was stirred at ambient tempera-

ture for 10 min and, after dissolution of the solids, a solution of organozinc halide **2i**–**2m** (**2i** and **2k**–**2m**: Rieke® organozinc reagents, 0.5 M solution in THF, 3 ml, 1.5 mmol; **2j** (2 mmol) was generated according to published procedure) was added dropwise (within 10 min) at ambient temperature. The stirring at ambient temperature was continued for 15 min followed by stirring at 60 °C for 8 h. Then the reaction mixture was allowed to stand overnight at ambient temperature and poured into saturated aqueous $NH_4Cl$ (10 ml). To this mixture, saturated aqueous $Na_2EDTA$ (10 ml) was added and the mixture was stirred for 10 min. Then the reaction mixture was extracted with ethyl acetate (3 × 20 ml) and the collected organic layers were washed with saturated aqueous $Na_2EDTA$ (20 ml) and brine (20 ml), dried with anhydrous $MgSO_4$ and evaporated *in vacuo*. Column chromatography of the residue on silica gel (50 g, ethyl acetate–light petroleum 1 : 2 to 9 : 1) afforded, after evaporation and drying, the 6-hetaryl- or 6-benzylpurines **3i**–**3m** as amorphous solids.

*6-(2-Pyridyl)-9-(2,3,5-tri-O-acetyl-*β*-D-ribofuranosyl)purine* (**3i**). Yellowish amorphous solid, yield 27%. FAB MS, *m/z* (rel.%): 456 (35) [M + H], 198 (100). $^1$H NMR (400 MHz, $CDCl_3$): 2.09, 2.14 and 2.18 (3 × s, 3 × 3 H, 3 × $CH_3CO$); 4.39–4.50 (m, 3 H, H-4′ and 2 × H-5′); 5.71 (dd, 1 H, *J* = 5.4 and 4.3, H-3′); 6.02 (t, 1 H, *J* = 5.4, H-2′); 6.34 (d, 1 H, *J* = 5.4, H-1′); 7.46 (dd, 1 H, *J* = 6.6 and 4.8, H-arom.); 7.94 (dt, 1 H, *J* = 1.7 and 7.8, H-arom.); 8.38 (s, 1 H, H-8); 8.80 (d, 1 H, *J* = 7.9, H-arom.); 8.97 (d, 1 H, *J* = 4.0, H-arom.); 9.15 (s, 1 H, H-2). HR MS (FAB), calculated for $C_{21}H_{22}N_5O_7$ [M + H]: 456.1519; found: 456.1536.

*6-(1-Methylpyrrol-2-yl)-9-(2,3,5-tri-O-acetyl-*β*-D-ribofuranosyl)purine* (**3j**). Yellowish amorphous solid, yield 22%. FAB MS, *m/z* (rel.%): 458 (70) [M + H], 200 (100). $^1$H NMR (400 MHz, $CDCl_3$): 2.08, 2.14 and 2.16 (3 × s, 3 × 3 H, 3 × $CH_3CO$); 4.20 (s, 3 H, $CH_3N$); 4.36–4.49 (m, 3 H, H-4′ and 2 × H-5′); 5.70 (dd, 1 H, *J* = 5.4 and 4.4, H-3′); 6.00 (t, 1 H, *J* = 5.4, H-2′); 6.26 (d, 1 H, *J* = 5.4, H-1′); 6.31 (dd, 1 H, *J* = 2.5 and 3.9, H-arom.); 6.88 (brs, 1 H, H-arom.); 7.83 (dd, 1 H, *J* = 1.6 and 3.9, H-arom.); 8.16 (s, 1 H, H-8); 8.83 (s, 1 H, H-2). $^{13}$C NMR (100 MHz, $CDCl_3$): 20.38, 20.53 and 20.76 (3 × $CH_3CO$); 38.30 ($CH_3N$); 63.11 ($CH_2$-5′); 70.68 (CH-3′); 73.02 (CH-2′); 80.29 (CH-4′); 86.12 (CH-1′); 109.11, 119.88 and 129.73 (CH-arom.); 126.91 and 129.50 (C-5 and C-*i*-arom.); 141.10 (CH-8); 150.24 and 150.74 (C-4 and C-6); 152.05 (CH-2); 169.33, 169.57 and 170.34 (3 × CO). HR MS (FAB), calculated for $C_{21}H_{24}N_5O_7$ [M + H]: 458.1676; found: 458.1691.

*6-Benzyl-9-(2,3,5-tri-O-acetyl-*β*-D-ribofuranosyl)purine* (**3k**). Colourless amorphous solid, yield 62%. FAB MS, *m/z* (rel.%): 469 (14) [M + H], 211 (100). $^1$H NMR (400 MHz, $CDCl_3$): 2.07, 2.10 and 2.15 (3 × s, 3 × 3 H, 3 × $CH_3CO$); 4.35–4.47 (m, 3 H, H-4′ and 2 × H-5′); 4.52 (s, 2 H, $CH_2Ph$); 5.68 (dd, 1 H, *J* = 4.3 and 5.5, H-3′); 5.98 (dd, 1 H, *J* = 5.3, 5.5, H-2′); 6.23 (d, 1 H, *J* = 5.3, H-1′); 7.17–7.49 (m, 5 H, H-arom.); 8.20 (s, 1 H, H-8); 8.90 (s, 1 H, H-2). $^{13}$C NMR (100 MHz, $CDCl_3$): 20.40, 20.54 and 20.74 (3 × $CH_3$); 39.57 ($CH_2Ph$); 63.08 ($CH_2$-5′); 70.69 (CH-3′); 73.07 (CH-2′); 80.45 (CH-4′); 86.43 (CH-1′); 126.75, 128.62 and 129.39 (CH-arom.); 133.17 and 137.62 (C-5 and C-*i*-Ph); 142.52 (H-8); 150.80 (C-4); 152.92 (C-2); 161.34 (C-6); 169.36, 169.57 and 170.31 (3 × CO). HR MS (FAB), calculated for $C_{23}H_{25}N_4O_7$ [M + H]: 469.1723; found: 469.1694.

*6-(4-Fluorobenzyl)-9-(2,3,5-tri-O-acetyl-*β*-D-ribofuranosyl)purine* (**3l**). Colourless amorphous solid, yield 76%. FAB MS, *m/z* (rel.%): 487 (56) [M + H], 229 (100). $^1$H NMR (400 MHz, $CDCl_3$): 2.08, 2.11 and 2.15 (3 × s, 3 × 3 H, 3 × $CH_3CO$); 4.35–4.50 (m, 3 H, H-4′ and 2 × H-5′); 4.49 (s, 2 H, $CH_2PhF$); 5.68 (dd, 1 H, *J* = 4.7 and 5.3, H-3′); 5.97 (t, 1 H, *J* = 5.3, H-2′); 6.23 (d, 1 H, *J* = 5.3, H-1′); 6.94–6.98 and 7.40–7.45 (2 × m, 2 × 2 H, H-arom.); 8.21 (s, 1 H, H-8); 8.90 (s, 1 H, H-2). $^{13}$C NMR (100 MHz, $CDCl_3$): 20.33, 20.46 and 20.68 (3 × $CH_3$); 38.60 ($CH_2PhF$); 62.98 ($CH_2$-5′); 70.57 (CH-3′); 73.03 (CH-2′); 80.35 (CH-4′); 86.48 (CH-1′);

115.36 (d, $^2J_{C,F}$= 21.3, CH-arom.); 130.79 (d, $^3J_{C,F}$ = 7.9, CH-arom.); 133.85 (C-5); 133.99 (d, $^4J_{C,F}$= 2.1, CH-arom.); 142.53 (H-8); 150.73 (C-4); 152.86 (C-2); 160.55 (C-6); 161.98 (d, $^1J_{C,F}$= 201.5, C-F); 169.30, 169.50 and 170.23 (3 × CO). $^{19}$F NMR (376.5 MHz, $CDCl_3$): –116.85 (s, FPh). HR MS (FAB), calculated for $C_{23}H_{24}FN_4O_7$ [M + H]: 487.1629; found: 487.1655.

*6-(4-Methoxybenzyl)-9-(2,3,5-tri-O-acetyl-*β*-D-ribofuranosyl)purine* (**3m**). Colourless amorphous solid, yield 60%. FAB MS, *m/z* (rel.%): 499 (27) [M + H], 241 (100). $^1$H NMR (400 MHz, $CDCl_3$): 2.08, 2.11 and 2.15 (3 × s, 3 × 3 H, 3 × $CH_3CO$); 3.76 (s, 3 H, $OCH_3$); 4.35–4.47 (m, 3 H, H-4′ and 2 × H-5′); 4.46 (s, 2 H, $CH_2$PhOMe); 5.68 (brm, 1 H, H-3′); 5.98 (t, 1 H, *J* = 5.2, H-2′); 6.23 (d, 1 H, *J* = 5.2, H-1′); 6.83 (d, 2 H, *J* = 8.3, H-arom.); 7.39 (d, 2 H, *J* = 8.3, H-arom.); 8.20 (s, 1 H, H-8); 8.90 (s, 1 H, H-2). $^{13}$C NMR (100 MHz, $CDCl_3$): 20.34, 20.47 and 20.68 (3 × $CH_3$); 38.64 ($CH_2$Ph); 55.18 ($OCH_3$); 63.02 ($CH_2$-5′); 70.64 (CH-3′); 73.01 (CH-2′); 80.38 (CH-4′); 86.35 (CH-1′); 114.04 and 130.31 (CH-arom.); 129.64 and 132.99 (C-5 and C-*i*-Ph); 142.37 (CH-8); 152.88 (CH-2); 150.71, 158.43 and 161.65 (C-4, C-6 and C-OMe); 169.30, 169.51 and 170.25 (3 × CO). HR MS (FAB), calculated for $C_{24}H_{27}N_4O_8$ [M + H]: 499.1829; found: 499.1797.

Cross-Coupling Reactions of 6-Chloropurine Nucleoside **1** with Stannanes. General Procedure

DMF (5 ml) was added to an argon-purged flask containing the 6-chloropurine **1** (413 mg, 1 mmol), a hetaryl(tributyl)tin **2n** or **2o** (1.5 mmol) and $PdCl_2(PPh_3)_2$ (35 mg, 0.05 mmol). The mixture was stirred at 100 °C for 12 h and the solvent was evaporated *in vacuo*. The residue was twice chromatographed on a silica gel column (50 g, ethyl acetate–light petroleum 1 : 3 to 9 : 1) to give the 6-hetarylpurine nucleosides **3n** and **3o** as amorphous solids.

*6-(2-Thienyl)-9-(2,3,5-tri-O-acetyl-*β*-D-ribofuranosyl)purine* (**3n**). Colourless amorphous solid, yield 89%. FAB MS, *m/z* (rel.%): 461 (100) [M + H]. $^1$H NMR (400 MHz, $CDCl_3$): 2.09, 2.14 and 2.16 (3 × s, 3 × 3 H, 3 × $CH_3CO$); 4.37–4.50 (m, 3 H, H-4′ and 2 × H-5′); 5.70 (dd, 1 H, *J* = 5.4 and 4.4, H-3′); 6.00 (t, 1 H, *J* = 5.4, H-2′); 6.28 (d, 1 H, *J* = 5.4, H-1′); 7.27 (m, 1 H, H-arom. overlapped with $CHCl_3$); 7.63 (dd, 1 H, *J* = 4.9 and 0.9, H-arom.); 8.26 (s, 1 H, H-8); 8.66 (dd, 1 H, *J* = 3.7 and 0.9, H-arom.); 8.90 (s, 1 H, H-2). $^{13}$C NMR (100 MHz, $CDCl_3$): 20.37, 20.49 and 20.74 (3 × $CH_3$); 63.04 ($CH_2$-5′); 70.67 (CH-3′); 73.11 (CH-2′); 80.42 (CH-4′); 86.33 (CH-1′); 128.82 (CH-arom.); 129.44 (C-5); 131.11 and 132.95 (CH-arom.); 139.70 (C-*i*-arom.); 142.47 (CH-8); 150.64 and 151.58 (C-4 and C-6); 152.75 (CH-2); 169.32, 169.54 and 170.27 (3 × CO). HR MS (FAB), calculated for $C_{20}H_{21}N_4O_7S$ [M + H]: 461.1131; found: 461.1137.

*6-(2-Furyl)-9-(2,3,5-tri-O-acetyl-*β*-D-ribofuranosyl)purine* (**3o**). Colourless amorphous solid, yield 85%. FAB MS, *m/z* (rel.%): 445 (34) [M + H], 187 (100). $^1$H NMR (400 MHz, $CDCl_3$): 2.09, 2.13 and 2.16 (3 × s, 3 × 3 H, $CH_3CO$); 4.37–4.48 (m, 3 H, H-4′ and 2 × H-5′); 5.70 (dd, 1 H, *J* = 5.5 and 4.4, H-3′); 6.00 (dd, 1 H, *J* = 5.3 and 5.5, H-2′); 6.28 (d, 1 H, *J* = 5.3, H-1′); 6.68 (m, 1 H, H-arom.); 7.78 (m, 1 H, H-arom.); 7.87 (d, 1 H, *J* = 3.5, H-arom.); 8.27 (s, 1 H, H-8); 8.96 (s, 1 H, H-2). $^{13}$C NMR (100 MHz, $CDCl_3$): 20.32, 20.41 and 20.69 (3 × $CH_3$); 62.96 ($CH_2$-5′); 70.57 (CH-3′); 73.06 (CH-2′); 80.36 (CH-4′); 86.33 (CH-1′); 112.63 and 117.74 (CH-arom.); 128.83 (C-5); 142.72 (CH-8); 146.05 (CH-arom.); 146.36 (C-6); 149.41 (C-*i*-arom.); 151.53 (C-4); 152.83 (CH-2); 169.26, 169.48 and 170.21 (3 × CO). HR MS (FAB), calculated for $C_{20}H_{21}N_4O_8$ [M + H]: 445.1359; found: 445.1334.

Deprotection of Nucleosides **3**. General Procedure

*Method A*: A 1 M methanolic MeONa (200 μl, 0.2 mmol) was added to a solution of a protected nucleoside **3a**–**3c** and **3e**–**3o** (0.5–0.8 mmol) in MeOH (20 ml) and the mixture was stirred at ambient temperature overnight. The crystals (if formed) were filtered off. Then the solution was neutralized by 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 the residue were recrystallized from EtOH–toluene to give free nucleosides **4a**–**4c** and **4e**–**4o**.

*Method B*: A 1 M methanolic HCl (100 μl, 0.1 mmol) was added to a solution of THP-protected nucleoside **3d** (443 mg, 0.8 mmol) in methanol (20 ml) and the mixture was stirred at ambient temperature overnight (complete cleavage of the THP group; TLC). Then a 1 M methanolic MeONa (300 μl, 0.3 mmol) was added and the solution was stirred at room temperature for 8 h. The work-up was done in the same manner as in method *A* to afford the free nucleoside **4d**.

*6-[4-(Methylsulfanyl)phenyl]-9-(*β-*D-ribofuranosyl)purine* (**4a**). Yellowish crystals, yield 65%, m.p. 186–188 °C, $[\alpha]_D$ –61.4 (*c* 0.2, DMF). FAB MS, *m/z* (rel.%): 375 (62) [M + H], 243 (100). $^1$H NMR (400 MHz, DMSO-$d_6$): 2.57 (s, 3 H, $SCH_3$); 3.55–3.65 and 3.68–3.78 (2 × m, 2 H, 2 × H-5′); 4.01 (m, 1 H, H-4′); 4.22 (m, 1 H, H-3′); 4.65 (ddd, 1 H, *J* = 5.0, 5.5 and 5.9, H-2′); 5.12 (t, 1 H, *J* = 5.5, 5′-OH); 5.23 (d, 1 H, *J* = 5.0, 3′-OH); 5.54 (d, 1 H, *J* = 5.9, 2′-OH); 6.09 (d, 1 H, *J* = 5.5, H-1′); 7.47 (d, 1 H, *J* = 8.5, H-arom.); 8.80 (d, 1 H, *J* = 8.5, H-arom.); 8.90 (s, 1 H, H-8); 9.00 (s, 1 H, H-2). $^{13}$C NMR (100 MHz, DMSO-$d_6$): 14.07 ($SCH_3$); 61.18 ($CH_2$-5′); 70.22 (CH-3′); 73.71 (CH-2′); 85.63 (CH-4′); 87.64 (CH-1′); 125.29 (CH-arom.); 129.63 (CH-arom.); 130.48 and 131.41 (C-5 and C-*i*-arom.); 142.73 (C-SMe); 144.62 (C-8); 151.84 (C-2); 152.05 and 152.46 (C-4 and C-6). UV (MeOH), $\lambda_{max}$ ($\varepsilon_{max}$): 332 (1 700). For $C_{17}H_{18}N_4O_4S$ (374.4) calculated: 54.53% C, 4.85% H, 14.96% N, 8.56% S; found: 54.32% C, 4.87% H, 14.57% N, 8.50% S.

*6-[4-(Dimethylamino)phenyl]-9-(*β-*D-ribofuranosyl)purine* (**4b**). Yellow crystals, yield 63%, m.p. 206–208 °C, $[\alpha]_D$ –72.6 (*c* 0.2, DMF). FAB MS, *m/z* (rel.%): 372 (42) [M + H], 240 (35) [M + H – Rf], 93 (100). $^1$H NMR (400 MHz, DMSO-$d_6$): 2.50 (s, 6 H, $N(CH_3)_2$); 3.56–3.62 and 3.68–3.74 (2 × m, 2 × 1 H, 2 × H-5′); 4.00 (m, 1 H, H-4′); 4.21 (m, 1 H, H-3′); 4.65 (ddd, 1 H, *J* = 4.9, 5.7 and 5.0, H-2′); 5.16 (t, 1 H, *J* = 5.8, 5′-OH); 5.21 (d, 1 H, *J* = 4.9, 3′-OH); 5.51 (d, 1 H, *J* = 6.0, 2′-OH); 6.05 (d, 1 H, *J* = 5.7, H-1′); 6.87 (d, 2 H, *J* = 9.0, H-arom.); 8.76, 8.78 and 8.82 (3 × s, 4 H, H-2, H-8 and 2 × H-arom.). $^{13}$C NMR (100 MHz, DMSO-$d_6$): ≈39 ($N(CH_3)_2$ overlapped by DMSO); 61.25 ($CH_2$-5′); 70.27 (CH-3′); 73.59 (CH-2′); 85.59 (CH-4′); 87.54 (CH-1′); 111.34 (CH-arom.); 122.16 and 129.52 (C-5 and C-*i*-arom.); 130.74 (CH-arom.); 143.44 (C-8); 151.68 (C-2); 151.41, 152.10 and 153.50 (C-$NMe_2$, C-4 and C-6). UV (MeOH), $\lambda_{max}$ ($\varepsilon_{max}$): 375 (27 300), 243 (12 300). For $C_{18}H_{21}N_5O_4$ (371.4) calculated: 58.21% C, 5.70% H, 18.86% N; found: 57.90% C, 5.85% H, 18.63% N.

*9-(*β-*D-Ribofuranosyl)-6-[4-(trifluoromethyl)phenyl]purine* (**4c**). Colourless crystals, yield 79%, m.p. 179–181 °C, $[\alpha]_D$ –42.9 (*c* 0.2, DMF). FAB MS, *m/z* (rel.%): 397 (19) [M + H], 265 (100). $^1$H NMR (400 MHz, DMSO-$d_6$): 3.58–3.64 and 3.70–3.76 (2 × m, 2 H, 2 × H-5′); 4.02 (m, 1 H, H-4′); 4.24 (m, 1 H, H-3′); 4.67 (m, 1 H, H-2′); 5.11 (t, 1 H, *J* = 5.3, 5′-OH); 5.24 (d, 1 H, *J* = 5.0, 3′-OH); 5.55 (d, 1 H, *J* = 5.8, 2′-OH); 6.12 (d, 1 H, *J* = 5.4, H-1′); 7.99 (d, 1 H, *J* = 8.3, H-arom.); 9.00 (s, 1 H, H-8); 9.02 (d, 1 H, *J* = 8.2, H-arom.); 9.08 (s, 1 H, H-2). $^{13}$C NMR (100 MHz, DMSO-$d_6$): 61.11 ($CH_2$-5′); 70.15 (CH-3′); 73.77 (CH-2′); 85.65 (CH-4′); 87.75

(CH-1′); 124.04 (q, $^1J_{C,F}$ = 272.0, $CF_3$); 125.59 (d, $^3J_{C,F}$ = 3.6, CH-arom.); 129.95 (CH-arom.); 130.73 (d, $^2J_{C,F}$ = 31.7, **C**$CF_3$); 131.22 (C-5); 138.99 (C-*i*-arom.); 145.57 (C-8); 151.07 (C-4); 151.94 (H-2); 152.50 (C-6). $^{19}$F NMR (376.5 MHz, DMSO-$d_6$): –60.90 (s, $CF_3$). UV (MeOH), $\lambda_{max}$ ($\varepsilon_{max}$): 290 (14 400), 245 (7 000). For $C_{17}H_{15}F_3N_4O_4$ (396.3) calculated: 51.52% C, 3.81% H, 14.38% F, 14.14% N; found: 51.25% C, 3.73% H, 14.25% F, 13.83% N.

*6-(4-Hydroxyphenyl)-9-(*β-D-*ribofuranosyl)purine* (**4d**). Method *B*; white hygroscopic crystals, yield 60%, m.p. 172–175 °C, $[\alpha]_D$ –51.31 (*c* 0.2, DMF). FAB MS, *m/z* (rel.%): 345 (14) [M + H], 93 (100). $^1$H NMR (400 MHz, DMSO-$d_6$): 3.60 (dd, 1 H, *J* = 3.7 and 11.9, H-5′a); 3.72 (dd, 1 H, *J* = 3.6 and 11.9, H-5′b); 4.00 (ddd, 1 H, *J* = 3.6, 3.6 and 3.7, H-4′); 4.22 (dd, 1 H, *J* = 3.6 and 4.6, H-3′); 4.65 (dd, 1 H, *J* = 4.6, 5.6, H-2′); 5.16 (br, 1 H, 5′-OH); 5.22 (br, 1 H, 3′-OH); 5.54 (br, 1 H, 2′-OH); 6.06 (d, 1 H, *J* = 5.6, H-1′); 6.97 (d, 2 H, *J* = 8.6, H-arom.); 8.75 (d, 2 H, *J* = 8.6, H-arom.); 8.84 and 8.90 (2 × s, 2 × 1 H, H-2 and H-8); 10.20 (brs, 1 H, OH). $^{13}$C NMR (100 MHz, DMSO-$d_6$): 61.24 ($CH_2$-5′); 70.27 (CH-3′); 73.69 (CH-2′); 85.64 (CH-4′); 87.61 (CH-1′); 115.52 (CH-arom.); 126.14 and 129.95 (C-5 and C-*i*-arom.); 131.32 (CH-arom.); 144.07 (C-8); 151.74 (C-2); 153.18 and 160.47 (C-4 and C-6). UV (MeOH), $\lambda_{max}$ ($\varepsilon_{max}$): 317 (17 000). For $C_{16}H_{16}N_4O_5 \cdot 4/3H_2O$ (368.3) calculated: 52.17% C, 5.11% H, 15.21% N; found: 52.27% C, 5.24% H, 14.91% N.

*6-(3,4-Dimethoxyphenyl)-9-(*β-D-*ribofuranosyl)purine* (**4e**). Yellowish crystals, yield 67%, m.p. 137–139 °C (90% aqueous EtOH), $[\alpha]_D$ –56.7 (*c* 0.2, DMF). FAB MS, *m/z* (rel.%): 389 (46) [M + H], 360 (100). $^1$H NMR (400 MHz, DMSO-$d_6$): 3.61 (dd, 1 H, *J* = 3.8 and 12.0; H-5′a); 3.73 (dd, 1 H, *J* = 3.8 and 12.0; H-5′b); 3.88 and 3.89 (2 × s, 2 × 3 H, 2 × $OCH_3$); 4.01 (m, 1 H, H-4′); 4.23 (m, 1 H, H-3′); 4.65 (brt, 1 H, J= 5.2, H-2′); OH signals were exchanged; 6.09 (d, 1 H, *J* = 5.5, H-1′); 7.19 (d, 1 H, *J* = 8.6, H-arom.); 8.47 (d, 1 H, *J* = 1.6, H-arom.); 8.60 (dd, 1 H, *J* = 1.6 and 8.6, H-arom.); 8.88 and 8.94 (2 × s, 2 × 1 H, H-8 and H-2). $^{13}$C NMR (100.6 MHz, DMSO-$d_6$): 55.43 and 55.54 ($OCH_3$); 61.17 ($CH_2$-5′); 70.20 (CH-3′); 73.71 (CH-2′); 85.59 (CH-4′); 87.61 (CH-1′); 111.50, 111.82 and 123.47 (CH-arom.); 127.68 and 130.23 (C-*i*-arom. and C-5); 144.35 (CH-8); 151.69 (CH-2); 148.60, 151.45, 151.88 and 152.69 (C-4, C-6 and 2 × CO). UV (MeOH), $\lambda_{max}$ ($\varepsilon_{max}$): 329 (17 100). For $C_{18}H_{20}N_4O_6 \cdot H_2O$ (406.4) calculated: 53.20% C, 5.46% H, 13.79% N; found: 53.53% C, 5.25% H, 13.40% N.

*6-[3,4-(Methylenedioxy)phenyl]-9-(*β-D-*ribofuranosyl)purine* (**4f**). Yellowish crystals, yield 71%, m.p. 130–135 °C (96% aqueous EtOH–toluene), $[\alpha]_D$ –53.5 (*c* 0.2, DMF). FAB MS, *m/z* (rel.%): 373 (65) [M + H], 360 (100). $^1$H NMR (400 MHz, DMSO-$d_6$): 3.57–3.64 and 3.70–3.75 (2 × m, 2 H, 2 × H-5′); 4.00 (m, 1 H, H-4′); 4.22 (m, 1 H, H-3′); 4.65 (ddd, 1 H, *J* = 4.8, 5.5 and 5.9, H-2′); 5.11 (t, 1 H, *J* = 5.5, 5′-OH); 5.20 (d, 1 H, *J* = 5.0, 3′-OH); 5.51 (d, 1 H, *J* = 5.9, 2′-OH); 6.08 (d, 1 H, *J* = 5.5, H-1′); 6.15 (s, 2 H, $OCH_2O$); 7.15 (d, 1 H, *J* = 8.3, H-arom.); 8.36 (d, 1 H, *J* = 1.5, H-arom.); 8.55 (dd, 1 H, *J* = 1.5 and 8.3, H-arom.); 8.88 and 8.93 (2 × s, 2 × 1 H, H-8 and H-2). $^{13}$C NMR (100.6 MHz, DMSO-$d_6$): 61.18 ($CH_2$-5′); 70.21 (CH-3′); 73.70 (CH-2′); 85.62 (CH-4′); 87.65 (CH-1′); 101.62 ($OCH_2O$); 108.48, 108.64 and 124.82 (CH-arom.); 129.29 and 130.19 (C-*i*-arom. and C-5); 144.46 (CH-8); 151.69 (CH-2); 147.67, 149.83, 151.97 and 152.35 (C-4, C-6 and 2 × CO). UV (MeOH), $\lambda_{max}$ ($\varepsilon_{max}$): 331 (13 000), 231 (8 700). For $C_{17}H_{16}N_4O_6 \cdot 1/2H_2O$ (372.3) calculated: 53.54% C, 4.49% H, 14.69% N; found: 53.40% C, 4.49% H, 14.35% N.

*6-(1-Naphthyl)-9-(*β-D-*ribofuranosyl)purine* (**4g**). Yellowish crystals, yield 70%, m.p. 133–139 °C (slow dec., 96% aqueous EtOH–toluene), $[\alpha]_D$ –52.9 (*c* 0.2, DMF). FAB MS, *m/z* (rel.%): 379 (25) [M + H], 247 (100). $^1$H NMR (400 MHz, DMSO-$d_6$): 3.61 (dd, 1 H, *J* = 3.6 and 11.9, H-5′a); 3.73 (dd, 1 H, *J* = 3.7 and 11.9, H-5′b); 4.03 (m, 1 H, H-4′); 4.24 (m, 1 H, H-3′); 4.70 (dd, 1 H, *J* = 4.8 and 5.6, H-2′); 5.15, 5.55 and 5.82 (3 × vbrs, 3 × OH); 6.14 (d,

1 H, *J* = 5.6, H-1′); 7.49–7.72 (m, 3 H, H-arom.); 7.96–8.17 (m, 4 H, H-arom.); 8.86 (s, 1 H, H-8); 9.12 (s, 1 H, H-2). $^{13}$C NMR (100.62 MHz, DMSO-$d_6$): 61.27 ($CH_2$-5′); 70.33 (CH-3′); 73.72 (CH-2′); 85.76 (CH-4′); 87.72 (CH-1′); 125.13, 125.76, 126.14, 126.60, 128.28, 129.66 and 130.19 (7 × CH-arom.); 130.51, 132.42, 132.72 and 133.41 (3 × C-arom. and C-5); 145.10 (CH-8); 151.74 (CH-2); 156.68 (C-4 and C-6). UV (MeOH), $\lambda_{max}$ ($\varepsilon_{max}$): 311 (6 900), 260 sh (7 200), 249 (8 000). For $C_{20}H_{18}N_4O_4 \cdot 1/2H_2O$ (387.4) calculated: 62.01% C, 4.94% H, 14.46% N; found: 62.12% C, 4.82% H, 14.11% N.

*6-(2-Naphthyl)-9-(*β-D-*ribofuranosyl)purine* (**4h**). Yellowish crystals, yield 78%, m.p. 193–195 °C (96% aqueous EtOH), $[\alpha]_D$ –63.8 (*c* 0.2, DMF). FAB MS, *m/z* (rel.%): 379 (40) [M + H], 247 (100). $^1$H NMR (400 MHz, DMSO-$d_6$): 3.62–3.68 and 3.74–3.80 (2 × m, 2 × 1 H, 2 × H-5′); 4.05 (m, 1 H, H-4′); 4.27 (m, 1 H, H-3′); 4.71 (m, 1 H, H-2′); 5.17 (t, 1 H, *J* = 5.1, 5′-OH); 5.27 (d, 1 H, *J* = 4.0, 3′-OH); 5.60 (d, 1 H, *J* = 3.7, 2′-OH); 6.16 (d, 1 H, *J* = 5.3, H-1′); 7.60–7.68 (m, 2 H, H-arom.); 8.02 (d, 1 H, *J* = 7.4, H-arom.); 8.14–8.17 (m, 2 H, H-arom.); 8.92 (d, 1 H, *J* = 8.6, H-arom.); 9.00 and 9.08 (2 × s, 2 × 1 H, H-8 and H-2); 9.51 (s, 1 H, H-arom.). $^{13}$C NMR (100.62 MHz, DMSO-$d_6$): 61.21 ($CH_2$-5′); 70.25 (CH-3′); 73.83 (CH-2′); 85.68 (CH-4′); 87.83 (CH-1′); 125.63, 126.71, 127.66, 127.79, 128.15, 129.18 and 130.26 (7 × CH-arom.); 131.12, 132.67, 132.77 and 134.15 (3 × C-arom. and C-5); 145.02 (CH-8); 151.93 (CH-2); 152.27 and 152.86 (C-4 and C-6). UV (MeOH), $\lambda_{max}$ ($\varepsilon_{max}$): 314 (22 200), 267 (23 100). For $C_{20}H_{18}N_4O_4 \cdot 1/2H_2O$ (387.4) calculated: 62.01% C, 4.94% H, 14.46% N; found: 62.21% C, 4.76% H, 14.30% N.

*6-(2-Pyridyl)-9-(*β-D-*ribofuranosyl)purine* (**4i**). Yellowish crystals, yield 65%, m.p. 136–139 °C (96% aqueous EtOH–toluene), $[\alpha]_D$ –51.5 (*c* 0.2, DMF). FAB MS, *m/z* (rel.%): 330 (38) [M + H], 198 (100). $^1$H NMR (500 MHz, DMSO-$d_6$): 3.58–3.62 and 3.69–3.75 (2 × m, 2 H, 2 × H-5′); 4.01 (m, 1 H, H-4′); 4.22 (m, 1 H, H-3′); 4.67 (ddd, 1 H, *J* = 5.9, 5.5 and 4.8, H-2′); 5.14 (t, 1 H, *J* = 5.5, 5′-OH); 5.27 (d, 1 H, *J* = 5.0, 3′-OH); 5.58 (d, 1 H, *J* = 5.9, 2′-OH); 6.12 (d, 1 H, *J* = 5.5, H-1′); 7.57 (dd, 1 H, *J* = 6.5 and 4.8, H-4-Py); 8.05 (dt, 1 H, *J* = 1.7 and 7.8, H-5-Py); 8.61 (d, 1 H, *J* = 7.9, H-6-Py); 8.84 (d, 1 H, *J* = 4.0, H-arom.); 8.93 (s, 1 H, H-8); 9.07 (s, 1 H, H-2). $^{13}$C NMR (100.6 MHz, DMSO-$d_6$): 61.14 ($CH_2$-5′); 70.19 (CH-3′); 73.72 (CH-2′); 85.61 (CH-4′); 87.64 (CH-1′); 124.97 (CH-4-Py); 125.34 (CH-6-Py); 131.41 (C-5); 136.83 (CH-5-Py); 145.50 (C-8); 149.81 (CH-3-Py); 151.78 (C-2); 152.62, 153.08 and 153.26 (C-4, C-6 and C-1-Py). HR MS (FAB), calculated for $C_{15}H_{16}N_5O_4$ [M + H]: 330.1202; found: 330.1187. UV (MeOH), $\lambda_{max}$ ($\varepsilon_{max}$): 295 (13 000). For $C_{15}H_{15}N_5O_4 \cdot H_2O$ (347.3) calculated: 51.87% C, 4.93% H, 20.16% N; found: 51.82% C, 4.73% H, 20.02% N.

*6-(1-Methylpyrrol-2-yl)-9-(*β-D-*ribofuranosyl)purine* (**4j**). Yellowish crystals, yield 86%, m.p. 176–178 °C (EtOH–toluene), $[\alpha]_D$ –62.9 (*c* 0.2, DMF). FAB MS, *m/z* (rel.%): 332 (38) [M + H], 200 (100). $^1$H NMR (500 MHz, DMSO-$d_6$): 3.56–3.61 and 3.68–3.73 (2 × m, 2 H, 2 × H-5′); 3.99 (m, 1 H, H-4′); 4.15 (s, 3 H, $CH_3$); 4.21 (m, 1 H, H-3′); 4.64 (ddd, 1 H, *J* = 4.9, 5.7 and 6.0, H-2′); 5.15 (t, 1 H, *J* = 5.7, 5′-OH); 5.23 (d, 1 H, *J* = 5.0, 3′-OH); 5.53 (d, 1 H, *J* = 6.0, 2′-OH); 6.04 (d, 1 H, *J* = 5.7, H-1′); 6.25 (dd, 1 H, *J* = 2.5 and 3.9, H-arom.); 7.14 (brt, 1 H, *J* = 1.9, H-arom.); 7.80 (dd, 1 H, *J* = 1.9 and 3.9, H-arom.); 8.75 (s, 1 H, H-8); 8.81 (s, 1 H, H-2). $^{13}$C NMR (125.77 MHz, DMSO-$d_6$): 38.05 ($CH_3$); 61.32 ($CH_2$-5′); 70.35 (CH-3′); 73.71 (CH-2′); 85.67 (CH-4′); 87.54 (CH-1′); 108.63, 119.35 and 130.10 (CH-arom.); 126.32 and 128.62 (C-5 and C-*i*-arom.); 143.45 (CH-8); 148.91 and 150.75 (C-6 and C-4); 151.33 (CH-2). UV (MeOH), $\lambda_{max}$ ($\varepsilon_{max}$): 343 (25 500), 240 (8 600). For $C_{15}H_{17}N_5O_4$ (331.3) calculated: 54.38% C, 5.17% H, 21.14% N; found: 54.41% C, 5.27% H, 20.78% N.

*6-Benzyl-9-(*β-D-*ribofuranosyl)purine* (**4k**). Colourless crystals, yield 66%, m.p. 97–100 °C (EtOH–toluene–heptane), $[\alpha]_D$ –47.7 (*c* 0.2, DMF). FAB MS, *m/z* (rel.%): 343 (16) [M + H], 52

(32), 185 (45), 93 (100). $^1$H NMR (500 MHz, DMSO-$d_6$): 3.55–3.60 and 3.66–3.71 (2 × m, 2 H, 2 × H-5′); 3.98 (m, 1 H, H-4′); 4.19 (m, 1 H, H-3′); 4.42 (s, 2 H, $CH_2$Ph); 4.65 (m, 1 H, H-2′); 5.09 (t, 1 H, *J* = 5.5, 5′-OH); 5.22 (d, 1 H, *J* = 4.8, 3′-OH); 5.51 (d, 1 H, *J* = 5.9, 2′-OH); 6.02 (d, 1 H, *J* = 5.7, H-1′); 7.15–7.39 (m, 5 H, H-arom.); 8.81 and 8.83 (2 × s, 2 × 1 H, H-8 and H-2). $^{13}$C NMR (100 MHz, DMSO-$d_6$): 38.57 ($CH_2$Ph); 61.23 ($CH_2$-5′); 70.29 (CH-3′); 73.52 (CH-2′); 85.67 (CH-4′); 87.58 (CH-1′); 126.32, 128.34 and 129.02 (CH-arom.); 132.36 and 137.92 (C-5 and C-*i*-arom.); 144.52 (C-8); 151.88 (C-2); 150.67 and 159.75 (C-4 and C-6). UV (MeOH), $\lambda_{max}$ ($\varepsilon_{max}$): 263 (5 600). For $C_{17}H_{18}N_4O_4$ (342.3) calculated: 59.64% C; 5.30% H, 16.37% N; found: 59.25% C, 5.31% H, 15.99% N.

*6-(4-Fluorobenzyl)-9-(*β-D-*ribofuranosyl)purine* (**4l**). Colourless crystals, yield 67%, m.p. 89–91 °C (EtOH–toluene–heptane), $[\alpha]_D$ –45.6 (*c* 0.2, DMF). FAB MS, *m/z* (rel.%): 361 (8) [M + H], 279 (82), 93 (100). $^1$H NMR (500 MHz, DMSO-$d_6$): 3.56–3.60 and 3.66–3.71 (2 × m, 2 H, 2 × H-5′); 3.98 (m, 1 H, H-4′); 4.19 (m, 1 H, H-3′); 4.42 (s, 2 H, $CH_2$PhF); 4.64 (m, 1 H, H-2′); 5.09 (t, 1 H, *J* = 5.2, 5′-OH); 5.22 (d, 1 H, *J* = 4.5, 3′-OH); 5.51 (d, 1 H, *J* = 5.7, 2′-OH); 6.02 (d, 1 H, *J* = 5.6, H-1′); 7.07–7.11 and 7.38–7.42 (2 × m, 2 × 2 H, H-arom.); 8.81 and 8.83 (2 × s, 2 × 1 H, H-8 and H-2). $^{13}$C NMR (100 MHz, DMSO-$d_6$): 37.65 ($CH_2$Ph); 61.23 ($CH_2$-5′); 70.29 (CH-3′); 73.54 (CH-2′); 85.68 (CH-4′); 87.59 (CH-1′); 115.05 (d, $J_{F,C}$ = 20.9, CH-arom.); 130.88 (CH-arom.); 132.29 and 134.00 (C-5 and C-*i*-arom.); 144.56 (C-8); 151.90 (C-2); 150.69 and 159.55 (C-4 and C-6), 160.83 (d, $J_{F,C}$ = 256.0, C-F). $^{19}$F NMR (376.5 MHz, DMSO-$d_6$): –116.19 (s, FPh). UV (MeOH), $\lambda_{max}$ ($\varepsilon_{max}$): 264 (7 700). For $C_{17}H_{17}FN_4O_4$ (360.3) calculated: 56.66% C, 4.76% H, 15.55% N; found: 56.37% C, 4.67% H, 15.29% N.

*6-(4-Methoxybenzyl)-9-(*β-D-*ribofuranosyl)purine* (**4m**). Colourless crystals, yield 88%, m.p. 120–123 °C (EtOH–toluene–heptane), $[\alpha]_D$ –47.4 (*c* 0.2, DMF). FAB MS, *m/z* (rel.%): 373 (8) [M + H], 279 (100). $^1$H NMR (400 MHz, DMSO-$d_6$): 3.55–3.61 and 3.66–3.72 (2 × m, 2 H, 2 × H-5′); 3.70 (s, 3 H, $OCH_3$); 3.99 (m, 1 H, H-4′); 4.21 (m, 1 H, H-3′); 4.37 (s, 2 H, $CH_2$Ph); 4.66 (ddd, 1 H, *J* = 4.6, 5.7 and 5.9, H-2′); 5.10 (t, 1 H, *J* = 5.5, 5′-OH); 5.23 (d, 1 H, *J* = 4.8, 3′-OH); 5.52 (d, 1 H, *J* = 5.9, 2′-OH); 6.04 (d, 1 H, *J* = 5.7, H-1′); 6.84 (d, 2 H, *J* = 8.4, H-arom.); 7.30 (d, 2 H, *J* = 8.4, H-arom.); 8.81 and 8.83 (2 × s, 2 × 1 H, H-8 and H-2). $^{13}$C NMR (100.6 MHz, DMSO-$d_6$): 37.79 ($CH_2$Ph); 54.98 ($OCH_3$); 61.31 ($CH_2$-5′); 70.37 (CH-3′); 73.59 (CH-2′); 85.73 (CH-4′); 87.64 (CH-1′); 113.86 and 130.07 (CH-arom.); 129.86 and 132.28 (C-*i*-arom. and C-5); 144.48 (CH-8); 151.93 (CH-2); 150.71, 157.90 and 160.23 (C-4, C-6 and C-OMe). UV (MeOH), $\lambda_{max}$ ($\varepsilon_{max}$): 265 (6 900). HR MS (FAB), calculated for $C_{18}H_{21}N_4O_5$ [M + H]: 373.1512; found: 373.1479. For $C_{18}H_{20}N_4O_5$ (372.4) calculated: 58.06% C, 5.41% H, 15.05% N; found: 57.92% C, 5.59% H, 14.59% N.

*6-(2-Thienyl)-9-(*β-D-*ribofuranosyl)purine* (**4n**). Colourless crystals, yield 66%, m.p. 126–129 °C (96% aqueous EtOH–toluene), $[\alpha]_D$ –55.3 (*c* 0.2, DMF). FAB MS, *m/z* (rel.%): 335 (19) [M + H], 93 (100). $^1$H NMR (400 MHz, DMSO-$d_6$): 3.58–3.64 and 3.70–3.75 (2 × m, 2 H, 2 × H-5′); 4.01 (m, 1 H, H-4′); 4.22 (m, 1 H, H-3′); 4.65 (ddd, 1 H, *J* = 4.7, 5.4 and 5.9, H-2′); 5.13 (t, 1 H, *J* = 5.5, 5′-OH); 5.24 (d, 1 H, *J* = 5.0, 3′-OH); 5.55 (d, 1 H, *J* = 5.9, 2′-OH); 6.07 (d, 1 H, *J* = 5.4, H-1′); 7.35 (dd, 1 H, *J* = 3.2 and 4.9, H-arom.); 7.94 (d, 1 H, *J* = 4.9, H-arom.); 8.65 (d, 1 H, *J* = 3.2, H-arom.); 8.87 and 8.90 (2 × s, 2 × 1 H, H-8 and H-2). $^{13}$C NMR (100.6 MHz, DMSO-$d_6$): 61.23 ($CH_2$-5′); 70.27 (CH-3′); 73.80 (CH-2′); 85.71 (CH-4′); 87.76 (CH-1′); 128.63 (C-5); 129.13, 131.87 and 132.54 (CH-arom.); 139.59 (C-*i*-arom.); 145.06 (CH-8); 148.76 (C-6); 151.67 (C-4); 152.02 (CH-2). UV (MeOH), $\lambda_{max}$ ($\varepsilon_{max}$): 323 (23 300), 270 (6 400), 228 (8 900). For $C_{14}H_{16}N_4O_5S \cdot H_2O$ (352.4) calculated: 47.72% C, 4.58% H, 15.90% N; found: 47.81% C, 4.60% H, 15.67% N.

*6-(2-Furyl)-9-(β-D-ribofuranosyl)purine* (**4o**). Colourless crystals, yield 59%, m.p. 165–168 °C (96% aqueous EtOH–toluene), $[\alpha]_D$ –54.1 (*c* 0.2, DMF). FAB MS, *m/z* (rel.%): 319 (15) [M + H], 93 (100). $^1$H NMR (400 MHz, DMSO-$d_6$): 3.57–3.63 and 3.69–3.74 (2 × m, 2 H, 2 × H-5′); 3.99 (m, 1 H, H-4′); 4.21 (m, 1 H, H-3′); 4.64 (m, 1 H, H-2′); 5.13 (t, 1 H, *J* = 5.5, 5′-OH); 5.24 (d, 1 H, *J* = 4.6, 3′-OH); 5.55 (d, 1 H, *J* = 5.7, 2′-OH); 6.06 (d, 1 H, *J* = 5.4, H-1′); 6.82 (brs, 1 H, H-arom.); 7.85 (d, 1 H, *J* = 3.0, H-arom.); 8.08 (brs, 1 H, H-arom.); 8.87 and 8.90 (2 × s, 2 × 1 H, H-8 and H-2). $^{13}$C NMR (100.6 MHz, DMSO-$d_6$): 61.22 ($CH_2$-5′); 70.26 (CH-3′); 73.76 (CH-2′); 85.70 (CH-4′); 87.69 (CH-1′); 112.95 and 117.56 (CH-arom.); 128.25 (C-5); 144.84 (C-6); 145.00 (CH-8); 146.61 (CH-arom.); 148.95 (C-*i*-arom.); 151.56 (C-4); 152.05 (CH-2). UV (MeOH), $\lambda_{max}$ ($\varepsilon_{max}$): 325 (17 200), 315 (18 500), 227 (8 800). For $C_{14}H_{16}N_4O_6 \cdot 1/2H_2O$ (327.3) calculated: 51.38% C, 4.62% H, 17.12% N; found: 51.58% C, 4.56% H, 16.88% N.

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