

**CYTOSTATIC AND ANTIVIRAL 6-ARYLPURINE RIBONUCLEOSIDES IX.⁺
SYNTHESIS AND EVALUATION OF 6-SUBSTITUTED 3-DEAZAPURINE
RIBONUCLEOSIDES**Petr NAUŠ, Martin KUČAŘ and Michal HOCEK^{1,*}

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Dedicated to the memory of Professor Otto Exner.

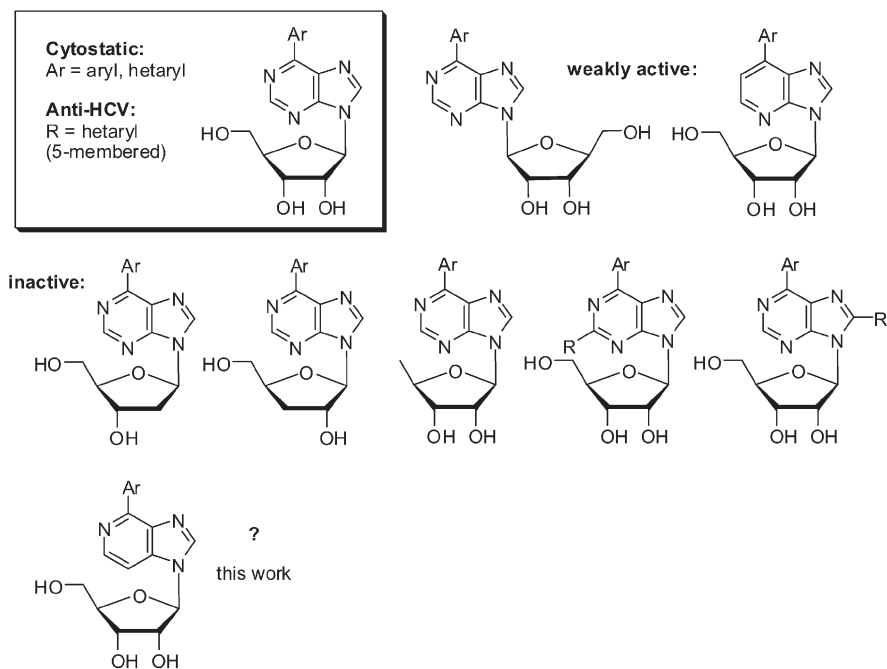
A series of 3-deazapurine ribonucleosides **5a–5l** bearing diverse *C*-substituents (alkyl, aryl and heteroaryl) in the position 6 were prepared by Pd-catalyzed cross-coupling reactions of either free 6-chloro-3-deazapurine ribonucleoside **4** or its acetyl protected congener **3** followed by deprotection. An improved synthesis of the starting 4-chloro-1-(2,3,5-tri-*O*-acetyl- β -D-ribofuranosyl)-1*H*-imidazo[4,5-*c*]pyridine (**3**) was developed by the application of Vorbrüggen glycosylation of silylated nucleobase with 1,2,3,5-tetra-*O*-acetyl- β -D-ribofuranose (**2**). None of compounds **5a–5l** showed any considerable cytostatic or antiviral activity.

Keywords: Purines; Imidazo[4,5-*c*]pyridines; 3-Deazapurines; Nucleosides; Glycosidations; Cross-coupling reactions; Cytostatic activity.

Purine nucleosides bearing aryl or hetaryl substituents in position 6 are cytostatic¹. Moreover, some 6-hetarylpurine ribonucleosides also exert strong anti-HCV activities². However, the cytotoxic or cytostatic side effect prevents clinical applications as anti-HCV drugs. Therefore, in order to achieve selective inhibition of HCV RNA polymerase, some additional modifications were pursued. From the previous studies on sugar-modified derivatives it is known 2'- and 5'-deoxyribonucleosides³, 3'-deoxyribonucleosides⁴, as well as 2'-*C*-methylribonucleosides⁵ of the 6-aryl- or 6-hetarylpurine series are all inactive, while some carbocyclic homonucleosides

+ For Part VIII, see ref.⁴

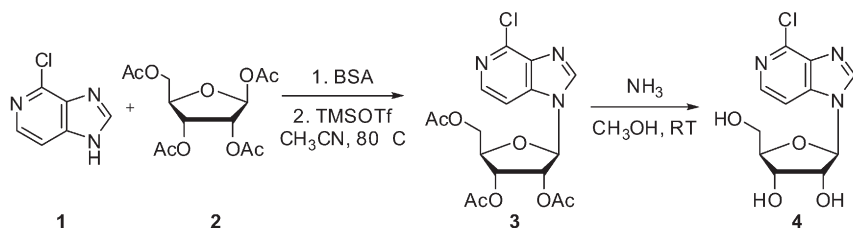
were reported⁶ to still exert some cytostatic effects. Very recently, some L-ribonucleosides were found⁷ to exert weak anti-HCV effect in replicon assay but their triphosphates did not inhibit HCV RNA polymerase. Also modifications of purine ring have been pursued to show that most 2-substituted⁸ and 8-substituted⁹ 6-arylpurine ribonucleosides were inactive, while some 6-aryl-1-deazapurine nucleosides¹⁰ still exerted some activities. This shows that the N-1 nitrogen is not crucial for the interaction of these compounds with the target biological system (presumably RNA polymerase and the complementary nucleobase). Therefore the next logical step was to look into the role of N-3 nitrogen which does not make H-bonds with the complementary pyrimidine nucleobase during biosynthesis of RNA but is responsible for crucial minor groove interactions in the active site of the polymerase. In this paper we report on the synthesis and evaluation of cytostatic and anti-HCV activity of novel 6-aryl-3-deazapurine ribonucleosides. Taking into account also known cytostatic activities of 6-methylpurine¹¹ and recently reported 6-cyclopropylpurine ribonucleosides¹², the series of 6-aryl and hetaryl derivatives was also complemented by examples of 6-alkyl-3-deazapurine nucleosides.



3-Deazaadenosine (c^3A , 4-aminoimidazo[4,5-*c*]pyridine) and its analogues are substrates and potent inhibitors of *S*-adenosyl-*L*-homocysteine hydro-lase¹³ and subsequent perturbation of transmethylations reactions is at least partly responsible for their diverse biological effects. These compounds exert antiviral¹⁴, cytotoxic¹⁵, tuberculostatic¹⁶ immunosuppressive and antiinflammatory properties¹⁷. No 3-deazapurine bearing a *C*-substituent in position 6 was reported to the best of our knowledge.

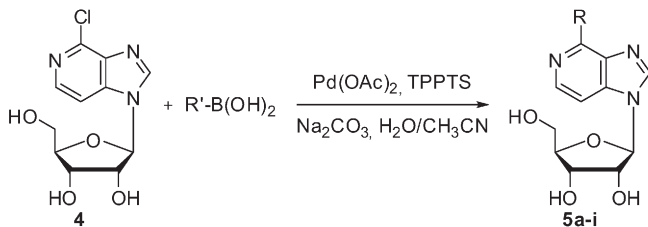
RESULTS AND DISCUSSION

At first we had to prepare either protected or free 6-chloro-3-deazapurine riboside intermediates as starting compounds for Pd-catalyzed cross-coupling reactions with aryl(hetaryl)organometallics and boronic acids. To our surprise all the known syntheses of these nucleosides based on glycosylation of 6-chloro-3-deazapurine **1** rely either on mercury salt method¹⁸ or fusion method¹⁹ both suffering from low overall yield, need for excess of glycosyl component, complicated separation from by-products and possible contamination by mercury salts. Therefore we were attracted by the application of the Hilbert–Johnson reaction performed under Vorbrüggen conditions²⁰ as this approach was recently successfully employed for 3,6-difluoro-3-deazapurine²¹. Thus 4-chloroimidazo[4,5-*c*]pyridine²² (**1**) was silylated by treatment with BSA in acetonitrile and then reacted with 1,2,3,5-tetra-*O*-acetyl- β -D-ribofuranose (**2**) in presence of TMSOTf at 80 °C for 1 h to afford the desired crystalline acetylated nucleoside **3** in 89% yield (Scheme 1). Deprotection of **3** by treatment with methanolic ammonia at room temperature for 24 h afforded desired free nucleoside **4** in 86% yield after crystallization.



SCHEME 1

TABLE I
Suzuki–Miyaura reaction of chloride **4** with boronic acids under Shaughnessy conditions

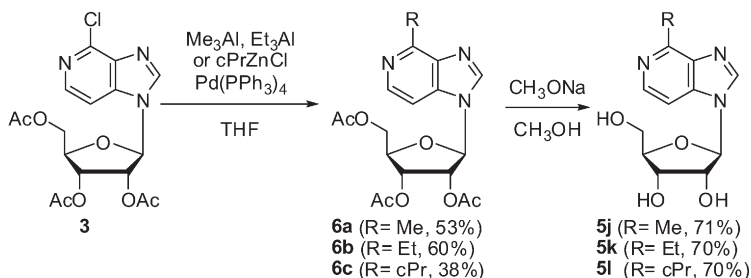


Entry	$R'-B(OH)_2$	R	Reaction time, h	Cross-Coupling Product (yield)
1			3	5a (92%)
2			3	5b (88%)
3			3	5c (90%)
4			2	5d (72%)
5			2	5e (78%)
6			24	5f (50%)
7			15	5g (61%)
8 ^a			24	5h (10%) ^a
9			20	5i (96%)

^a 82% of starting material **4** recovered.

With starting compounds in hands we have performed cross-coupling reactions leading to our desired 6-substituted derivatives. At first, we attempted aqueous Suzuki–Miyaura reactions of free ribonucleoside **4** under the Shaughnessy conditions^{23,24}. The treatment of 6-chloro-3-deazapurine riboside **4** with diverse aryl- or hetarylboronic acids in the presence of Pd(OAc)₂, TPPTS, and Na₂CO₃ in H₂O–CH₃CN (2:1) at 100 °C provided desired 6-aryl(hetaryl)-3-deazapurine ribosides **5a–5i** (Table I). The reactions proceeded smoothly and cleanly for phenyl-, 3-pyridyl- and for 2- and 3-furyl- and thienylboronic acids, providing the desired products in high yields (entries 1–5, 9). For 2-pyrrolyl and 3-pyrrolyl the isolated yields of products **5f** and **5g** were only moderate (entries 6, 7), but all starting chloride **4** was always fully consumed indicating possible partial decomposition of products **5f** and **5g** under reaction conditions. It should be also noted, that *N*-protecting groups in both starting pyrrolylboronic acids were simultaneously removed under the conditions of coupling (BOC for 2-pyrrolyl and triisopropylsilyl for 3-pyrrolyl). The reaction of **4** with 1*H*-pyrazole-5-boronic acid was very sluggish giving product **5h** (entry 8) in only 10% yield after crystallization and 82% of starting chloride **4** was recovered.

While the attempts to introduce similarly methyl and ethyl substituents by Suzuki reaction of **4** with corresponding alkylboronic acids under above mentioned conditions failed (in the case of methyl only trace of the product was obtained and for ethyl no reaction was observed) we turned to reactions with trialkylaluminums known²⁵ to be suitable for introduction of alkyl substituents to purines. Thus acetylated 6-chloro-3-deazapurine riboside **3** was reacted with trimethyl- and triethylaluminums in the presence of Pd(PPh₃)₄ in refluxing THF affording 6-alkylpurine nucleosides **6a** and **6b** in 53 and 60% yields, respectively (Scheme 2). These acetylated products **6a** and **6b** were deprotected with catalytic sodium methoxide in methanol giving the desired nucleosides **5j** and **5k** in 71 and 70% yields, re-



SCHEME 2

spectively, after recrystallization. For the preparation cyclopropyl derivative Negishi reaction between chloride **3** and cyclopropylzinc chloride in the presence of Pd(PPh₃)₄ was conducted to furnish protected cyclopropyl derivative **6c** in moderate 38% yield and subsequent deprotection gave free nucleoside **5l** (70%).

It should be noted, that some of the attempted cross-couplings (successful in 6-chloropurines) failed here with 6-chloro-3-deazapurines **3** or **4**. The Stille reaction of acetylated nucleoside **3** with 2-(tributylstannyl)thiazole or 2-(tributylstannyl)pyridine and the Negishi reaction with benzoyloxymethylzinc iodide²⁶ can serve as example. Markedly decreased reactivity of 3-deazapurine derivatives compared to corresponding purines in nucleophilic substitutions of 6-chloro group is known¹⁹.

All the title 6-substituted 3-deazapurine ribonucleosides **5a–5l** were subjected to biological activity screening. The cytostatic activity in vitro (inhibition of cell growth) was studied on the following cell cultures: mouse leukemia L1210 cells (ATCC CCL 219), human promyelocytic leukemia HL60 cells (ATCC CCL 240), human cervix carcinoma HeLaS3 cells (ATCC CCL 2.2) and human T lymphoblastoid CCRF-CEM cell line (ATCC CCL 119). Antiviral activity of nucleosides **5a–5l** was evaluated in a HCV subgenomic replicon assay²⁷. None of the compounds showed any considerable cytostatic or antiviral activity in these assays up to 10 μM concentration. Apparently, removal of the N-3 nitrogen leads to inactive compounds indicating that some specific interactions of this nitrogen with the target biological system (most probably minor groove H-bond interaction in the active site of the RNA polymerase) are crucial for the biological activity of this class of compounds.

EXPERIMENTAL

NMR spectra were recorded on Bruker Avance 400 MHz (¹H at 400 MHz, ¹³C at 100.6 MHz) and Bruker Avance 500 MHz (500 MHz for ¹H and 125.7 MHz for ¹³C) spectrometers. Chemical shifts (in ppm, δ-scale) were referenced to TMS as internal standard. Coupling constants (*J*) are given in Hz. The assignment of carbons was based on C,H-HSQC and C,H-HMBC experiments. IR spectra (wavenumbers in cm⁻¹) were recorded on a Bruker IFS 88 spectrometer. Melting points were determined on a Kofler block and are uncorrected. Optical rotations were measured at 25 °C on an Autopol IV (Rudolph Research Analytical) polarimeter, [α]_D values are given in 10⁻¹ deg cm² g⁻¹. High resolution mass spectra (HR MS) were measured on a LTQ Orbitrap XL (Thermo Fisher Scientific) spectrometer using electrospray ionization. High performance flash chromatography (HPFC) purifications were performed using SP1™ Flash Purification System (Biotage) on C-18 columns using water-methanol gradient. THF was dried and freshly distilled from sodium/benzophenone.

4-Chloro-1-(2,3,5-tri-*O*-acetyl- β -D-ribofuranosyl)-1*H*-imidazo[4,5-*c*]pyridine (**3**)

To a slurry of 4-chloro-1*H*-imidazo[4,5-*c*]pyridine²² (**1**; 1.69 g, 11 mmol) in dry CH₃CN (50 ml), BSA (2.72 ml, 11 mmol) was added and the mixture was stirred at RT for 20 min (clear solution), followed by addition of tetracetyl ribose **2** (3.85 g, 12.1 mmol). TMSOTf (1.99 ml, 11 mmol) was then added dropwise at 0 °C and the mixture was heated at 80 °C for 3 h. After cooling and dilution with CHCl₃ (100 ml) the mixture was washed with saturated aqueous NaHCO₃ (50 ml). Aqueous phase was re-extracted with CHCl₃ (2 × 10 ml), collected organics were dried over MgSO₄ and final column chromatography on silica (hexanes-AcOEt, 1:1) provided nucleoside **3** (4.05 g, 89%) as a colorless crystalline solid, m.p. 160–161 °C (hexane–AcOEt); ref.¹⁹ 158.5–159 °C. ¹H NMR (400 MHz, CDCl₃): 2.10, 2.15, 2.16 (3 × s, 3 × 3 H, CH₃CO); 4.39 (dd, 1 H, $J_{\text{gem}} = 12.6$, $J_{5'b,4'} = 2.7$, H-5'b); 4.46 (dd, 1 H, $J_{\text{gem}} = 12.6$, $J_{5'a,4'} = 2.9$, H-5'a); 4.51 (ddd, 1 H, $J_{4',3'} = 5.1$, $J_{4',5'} = 2.9$, 2.7, H-4'); 5.38 (dd, 1 H, $J_{3',2'} = 5.3$, $J_{3',4'} = 5.1$, H-3'); 5.51 (t, 1 H, $J_{2',1'} = 5.3$, $J_{2',3'} = 5.3$, H-2'); 6.07 (d, 1 H, $J_{1',2'} = 5.3$, H-1'); 7.53 (d, 1 H, $J_{7,6} = 5.6$, H-7); 8.23 (d, 1 H, $J_{6,7} = 5.6$, H-6); 8.27 (s, 1 H, H-2). ¹³C NMR (100.6 MHz, CDCl₃): 20.32, 20.45 and 20.73 (3 × CH₃CO); 62.46 (CH₂-5'); 69.81 (CH-3'); 73.53 (CH-2'); 80.54 (CH-4'); 87.44 (CH-1'); 105.94 (CH-7); 138.25 (C-7a); 138.63 (C-3a); 141.78 (CH-2); 142.08 (CH-6); 143.34 (C-4); 169.27, 169.46 and 170.00 (3 × CO). IR (CCl₄): 2959, 2927, 2855, 1759, 1234, 1219, 1211, 967. HR MS (ESI): calculated for C₁₇H₁₈ClN₃NaO₇ [M + Na] 434.0731, found 434.0727. For C₁₇H₁₈ClN₃O₇ calculated: 49.58% C, 4.41% H, 10.20% N; found: 49.41% C, 4.38% H, 10.04% N.

4-Chloro-1-(β -D-ribofuranosyl)-1*H*-imidazo[4,5-*c*]pyridine (**4**)

Acetylated nucleoside **3** (3.29 g, 7.99 mmol) was treated with methanolic ammonia (24%, 70 ml) at RT for 24 h. After removal of volatiles under reduced pressure, the product was crystallized from 96% ethanol affording chloro riboside **4** (1.96 g, 86%) as colorless prisms, m.p. 192–193 °C; ref.¹⁹ 192.5–193.5 °C. [α]_D –39.1 (c 0.13, DMSO); ref.¹⁸ [α]_D –39.1 (c 1.02, MeOH); ref.¹⁹ [α]_D –41.6 (c 1.25, MeOH). ¹H NMR (400 MHz, DMSO-*d*₆): 3.64 (ddd, 1 H, $J_{\text{gem}} = 12.0$, $J_{5'b,OH} = 5.1$, $J_{5'b,4'} = 3.5$, H-5'b); 3.69 (ddd, 1 H, $J_{\text{gem}} = 12.0$, $J_{5'a,OH} = 5.3$, $J_{5'a,4'} = 3.5$, H-5'a); 4.01 (td, 1 H, $J_{4',5'} = 3.5$, $J_{4',3'} = 3.0$, H-4'); 4.12 (ddd, 1 H, $J_{3',2'} = 5.1$, $J_{3',OH} = 4.6$, $J_{3',4'} = 3.0$, H-3'); 4.34 (ddd, 1 H, $J_{2',OH} = 6.3$, $J_{2',1'} = 6.3$, $J_{2',3'} = 5.1$, H-2'); 5.20 (dd, 1 H, $J_{OH,5'a} = 5.3$, $J_{OH,5'b} = 5.1$, OH-5'); 5.27 (d, 1 H, $J_{OH,3'} = 4.6$, OH-3'); 5.54 (d, 1 H, $J_{OH,2'} = 6.3$, OH-2'); 5.93 (d, 1 H, $J_{1',2'} = 6.3$, H-1'); 7.91 (d, 1 H, $J_{7,6} = 5.5$, H-7); 8.17 (d, 1 H, $J_{6,7} = 5.6$, H-6); 8.70 (s, 1 H, H-2). ¹³C NMR (100.6 MHz, DMSO-*d*₆): 61.59 (CH₂-5'); 70.63 (CH-3'); 74.69 (CH-2'); 86.62 (CH-4'); 89.73 (CH-1'); 108.25 (CH-7); 138.00 (C-3a); 139.71 (C-7a); 141.55 (C-4); 141.59 (CH-6); 145.07 (CH-2). IR (KBr): 1604, 1570, 1489, 1445, 1309, 1216, 1202, 1114, 1082, 1043. HR MS (ESI): calculated for C₁₁H₁₂ClN₃NaO₄ [M + Na] 308.0414, found 308.0408. For C₁₁H₁₂ClN₃O₄ calculated: 46.25% C, 4.23% H, 14.71% N; found: 46.11% C, 4.26% H, 14.31% N.

Preparation of 6-Aryl(hetaryl)-3-deazapurine Ribosides **5a–5i**. General Procedure

To an argon purged flask containing 6-chloro-3-deazapurine riboside **4** (214 mg, 0.75 mmol), boronic acid (0.94 mmol) and Na₂CO₃ (236 mg, 2.25 mmol), a pre-prepared solution of Pd(OAc)₂ (8 mg, 0.037 mmol) and TPPTS (53 mg, 0.093 mmol) in water-CH₃CN (2:1, 4 ml) was added. The reaction mixture was stirred at 100 °C for 2–24 h. After cooling the mixture

was neutralized by the addition of aqueous HCl (3 M solution) and after concentration in vacuo final purification by reverse phase chromatography afforded products **5a–5i**.

4-Phenyl-1-(β-D-ribofuranosyl)-1H-imidazo[4,5-c]pyridine (5a). Yield 92%. Reaction time 3 h. White solid after lyophilization, m.p. 99–104 °C. $[\alpha]_D$ –59.5 (c 1.6, DMSO). $^1\text{H NMR}$ (400 MHz, DMSO- d_6): 3.66 (ddd, 1 H, $J_{\text{gem}} = 12.0$, $J_{5'b,\text{OH}} = 5.1$, $J_{5'b,4'} = 3.5$, H-5'b); 3.71 (ddd, 1 H, $J_{\text{gem}} = 12.0$, $J_{5'a,\text{OH}} = 5.3$, $J_{5'a,4'} = 3.5$, H-5'a); 4.03 (td, 1 H, $J_{4',5'} = 3.5$, $J_{4',3'} = 3.1$, H-4'); 4.16 (ddd, 1 H, $J_{3',2'} = 5.1$, $J_{3',\text{OH}} = 4.7$, $J_{3',4'} = 3.1$, H-3'); 4.42 (ddd, 1 H, $J_{2',\text{OH}} = 6.4$, $J_{2',1'} = 6.3$, $J_{2',3'} = 5.1$, H-2'); 5.21 (dd, 1 H, $J_{\text{OH},5'a} = 5.3$, $J_{\text{OH},5'b} = 5.1$, OH-5'); 5.30 (d, 1 H, $J_{\text{OH},3'} = 4.7$, OH-3'); 5.57 (d, 1 H, $J_{\text{OH},2'} = 6.4$, OH-2'); 5.97 (d, 1 H, $J_{1',2'} = 6.3$, H-1'); 7.42–7.56 (m, 3 H, H-*m,p*-Ph); 7.82 (d, 1 H, $J_{7,6} = 5.5$, H-7); 8.46 (d, 1 H, $J_{6,7} = 5.5$, H-6); 8.68–8.72 (m, 3 H, H-2 and H-*o*-Ph). $^{13}\text{C NMR}$ (100.6 MHz, DMSO- d_6): 61.17 (CH₂-5'); 70.15 (CH-3'); 73.97 (CH-2'); 85.89 (CH-4'); 88.87 (CH-1'); 106.50 (CH-7); 128.19 (CH-*m*-Ph); 128.91 (CH-*o*-Ph); 128.97 (CH-*p*-Ph); 137.62 (C-*i*-Ph); 138.26 (C-3a); 138.95 (C-7a); 141.43 (CH-6); 143.64 (CH-2); 147.72 (C-4). IR (KBr): 1602, 1585, 1574, 1301, 1221, 1100, 1060. HR MS (ESI): calculated for C₁₇H₁₈N₃O₄ [M + H] 328.1297, found 328.1295. For C₁₇H₁₇N₃O₄·0.7H₂O calculated: 60.06% C, 5.46% H, 12.36% N; found: 60.38% C, 5.23% H, 12.05% N.

4-(Furan-2-yl)-1-(β-D-ribofuranosyl)-1H-imidazo[4,5-c]pyridine (5b). Yield 88%. Reaction time 3 h. Colorless crystals from water, m.p. 119–122 °C. $[\alpha]_D$ –57.2 (c 3.5, DMSO). $^1\text{H NMR}$ (400 MHz, DMSO- d_6): 3.65 (ddd, 1 H, $J_{\text{gem}} = 12.0$, $J_{5'b,\text{OH}} = 5.1$, $J_{5'b,4'} = 3.5$, H-5'b); 3.71 (ddd, 1 H, $J_{\text{gem}} = 12.0$, $J_{5'a,\text{OH}} = 5.3$, $J_{5'a,4'} = 3.5$, H-5'a); 4.02 (td, 1 H, $J_{4',5'} = 3.5$, $J_{4',3'} = 3.1$, H-4'); 4.15 (ddd, 1 H, $J_{3',2'} = 5.1$, $J_{3',\text{OH}} = 4.7$, $J_{3',4'} = 3.1$, H-3'); 4.40 (ddd, 1 H, $J_{2',\text{OH}} = 6.4$, $J_{2',1'} = 6.3$, $J_{2',3'} = 5.1$, H-2'); 5.21 (dd, 1 H, $J_{\text{OH},5'a} = 5.3$, $J_{\text{OH},5'b} = 5.1$, OH-5'); 5.29 (d, 1 H, $J_{\text{OH},3'} = 4.7$, OH-3'); 5.57 (d, 1 H, $J_{\text{OH},2'} = 6.4$, OH-2'); 5.95 (d, 1 H, $J_{1',2'} = 6.3$, H-1'); 6.72 (dd, 1 H, $J_{4,3} = 3.4$, $J_{4,5} = 1.8$, H-4-furyl); 7.72 (dd, 1 H, $J_{3,4} = 3.4$, $J_{3,5} = 0.9$, H-3-furyl); 7.76 (d, 1 H, $J_{7,6} = 5.6$, H-7); 7.90 (dd, 1 H, $J_{5,4} = 1.8$, $J_{5,3} = 0.9$, H-5-furyl); 8.36 (d, 1 H, $J_{6,7} = 5.6$, H-6); 8.68 (s, 1 H, H-2). $^{13}\text{C NMR}$ (100.6 MHz, DMSO- d_6): 61.19 (CH₂-5'); 70.18 (CH-3'); 74.05 (CH-2'); 85.94 (CH-4'); 88.92 (CH-1'); 106.24 (CH-7); 112.15 (CH-4-furyl); 113.44 (CH-3-furyl); 136.25 (C-3a); 138.35 (C-7a); 140.24 (C-4); 141.39 (CH-6); 143.93 and 144.14 (CH-2 and CH-5-furyl); 150.81 (C-2-furyl). IR (KBr): 1596, 1499, 1480, 1407, 1311, 1216, 1121, 1107, 1084, 1013. HR MS (ESI): calculated for C₁₅H₁₅N₃NaO₅ [M + Na] 340.0909, found 340.0905. For C₁₅H₁₅N₃O₅·1.5H₂O calculated: 52.32% C, 5.27% H, 12.20% N; found: 52.71% C, 5.00% H, 12.03% N.

1-(β-D-Ribofuranosyl)-4-(thiophen-2-yl)-1H-imidazo[4,5-c]pyridine (5c). Yield 90%. Reaction time 3 h. Cotton-like colorless crystals from 99% EtOH, m.p. 192–193 °C. $[\alpha]_D$ –41.3 (c 0.1, DMSO). $^1\text{H NMR}$ (400 MHz, DMSO- d_6): 3.65 (ddd, 1 H, $J_{\text{gem}} = 12.0$, $J_{5'b,\text{OH}} = 5.1$, $J_{5'b,4'} = 3.5$, H-5'b); 3.71 (ddd, 1 H, $J_{\text{gem}} = 12.0$, $J_{5'a,\text{OH}} = 5.3$, $J_{5'a,4'} = 3.5$, H-5'a); 4.03 (td, 1 H, $J_{4',5'} = 3.5$, $J_{4',3'} = 3.1$, H-4'); 4.15 (ddd, 1 H, $J_{3',2'} = 5.1$, $J_{3',\text{OH}} = 4.7$, $J_{3',4'} = 3.1$, H-3'); 4.40 (ddd, 1 H, $J_{2',\text{OH}} = 6.4$, $J_{2',1'} = 6.3$, $J_{2',3'} = 5.1$, H-2'); 5.20 (dd, 1 H, $J_{\text{OH},5'a} = 5.3$, $J_{\text{OH},5'b} = 5.1$, OH-5'); 5.29 (d, 1 H, $J_{\text{OH},3'} = 4.7$, OH-3'); 5.57 (d, 1 H, $J_{\text{OH},2'} = 6.4$, OH-2'); 5.95 (d, 1 H, $J_{1',2'} = 6.3$, H-1'); 7.25 (dd, 1 H, $J_{4,5} = 5.1$, $J_{4,3} = 3.7$, H-4-thienyl); 7.69 (dd, 1 H, $J_{5,4} = 5.1$, $J_{5,3} = 1.2$, H-5-thienyl); 7.75 (d, 1 H, $J_{7,6} = 5.6$, H-7); 8.31 (d, 1 H, $J_{6,7} = 5.6$, H-6); 8.58 (dd, 1 H, $J_{3,4} = 3.7$, $J_{3,5} = 1.2$, H-3-thienyl); 8.71 (s, 1 H, H-2). $^{13}\text{C NMR}$ (100.6 MHz, DMSO- d_6): 61.16 (CH₂-5'); 70.15 (CH-3'); 74.04 (CH-2'); 85.93 (CH-4'); 88.93 (CH-1'); 106.19 (CH-7); 128.37 (CH-4-thienyl); 128.46 (CH-5-thienyl); 129.06 (CH-3-thienyl); 136.32 (C-3a); 138.53 (C-7a); 141.34 (CH-6); 142.53 (C-2-thienyl); 143.66 (C-4); 144.00 (CH-2). IR (KBr): 1592, 1578, 1465, 1278, 1213, 1131, 1085, 1075, 1065, 1046, 992. HR MS (ESI): calculated for

C₁₅H₁₆N₃O₄S [M + H] 334.0862, found 334.0859. For C₁₅H₁₅N₃O₄S calculated: 54.04% C, 4.54% H, 12.60% N, 9.62% S; found: 53.74% C, 4.48% H, 12.45% N, 9.46% S.

4-(Furan-3-yl)-1-(β-D-ribofuranosyl)-1H-imidazo[4,5-c]pyridine (5d). Yield 72%. Reaction time 2 h. Cotton-like white crystals from water, m.p. 181–186 °C. [α]_D –59.3 (c 1.8, DMSO). ¹H NMR (400 MHz, DMSO-*d*₆): 3.65 (ddd, 1 H, *J*_{gem} = 12.0, *J*_{5'a,OH} = 5.3, *J*_{5'a,4'} = 3.5, H-5'a); 3.70 (ddd, 1 H, *J*_{gem} = 12.0, *J*_{5'a,OH} = 5.3, *J*_{5'a,4'} = 3.5, H-5'a); 4.04 (td, 1 H, *J*_{4',5'} = 3.5, *J*_{4',3'} = 3.1, H-4'); 4.15 (ddd, 1 H, *J*_{3',2'} = 5.1, *J*_{3',OH} = 4.7, *J*_{3',4'} = 3.1, H-3'); 4.39 (ddd, 1 H, *J*_{2',OH} = 6.4, *J*_{2',1'} = 6.3, *J*_{2',3'} = 5.1, H-2'); 5.19 (dd, 1 H, *J*_{OH,5'a} = 5.3, *J*_{OH,5'b} = 5.1, OH-5'); 5.28 (d, 1 H, *J*_{OH,3'} = 4.7, OH-3'); 5.55 (d, 1 H, *J*_{OH,2'} = 6.4, OH-2'); 5.94 (d, 1 H, *J*_{1',2'} = 6.3, H-1'); 7.33 (dd, 1 H, *J*_{4,5} = 1.8, *J*_{4,2} = 0.8, H-4-furyl); 7.73 (d, 1 H, *J*_{7,6} = 5.5, H-7); 7.82 (dd, 1 H, *J*_{5,4} = 1.8, *J*_{5,2} = 1.6, H-5-furyl); 8.35 (d, 1 H, *J*_{6,7} = 5.6, H-6); 8.66 (s, 1 H, H-2); 8.75 (dd, 1 H, *J*_{2,5} = 1.6, *J*_{2,4} = 0.8, H-2-furyl). ¹³C NMR (100.6 MHz, DMSO-*d*₆): 61.17 (CH₂-5'); 70.16 (CH-3'); 74.00 (CH-2'); 85.89 (CH-4'); 88.89 (CH-1'); 105.85 (CH-7); 109.40 (CH-4-furyl); 124.62 (C-3-furyl); 137.43 (C-3a); 138.01 (C-7a); 141.47 (CH-6); 143.08 (C-4); 143.60 (2 C, CH-2 and CH-5-furyl); 143.82 (CH-2-furyl). IR (KBr): 1592, 1304, 1222, 1111, 1096, 1066, 873. HR MS (ESI): calculated for C₁₅H₁₆N₃O₅ [M + H] 318.1090, found 318.1088. For C₁₅H₁₅N₃O₅·H₂O calculated: 53.73% C, 5.11% H, 12.53% N; found: 53.74% C, 4.96% H, 12.50% N.

1-(β-D-Ribofuranosyl)-4-(thiophen-3-yl)-1H-imidazo[4,5-c]pyridine (5e). Yield 78%. Reaction time 2 h. Yellowish crystals from water, m.p. 105–109 °C. [α]_D –66.5 (c 2.6, DMSO). ¹H NMR (400 MHz, DMSO-*d*₆): 3.65 (ddd, 1 H, *J*_{gem} = 12.0, *J*_{5'b,OH} = 5.1, *J*_{5'b,4'} = 3.5, H-5'b); 3.71 (ddd, 1 H, *J*_{gem} = 12.0, *J*_{5'a,OH} = 5.4, *J*_{5'a,4'} = 3.5, H-5'a); 4.03 (td, 1 H, *J*_{4',5'} = 3.5, *J*_{4',3'} = 3.1, H-4'); 4.16 (ddd, 1 H, *J*_{3',2'} = 5.1, *J*_{3',OH} = 4.7, *J*_{3',4'} = 3.1, H-3'); 4.41 (ddd, 1 H, *J*_{2',OH} = 6.4, *J*_{2',1'} = 6.3, *J*_{2',3'} = 5.1, H-2'); 5.20 (dd, 1 H, *J*_{OH,5'a} = 5.4, *J*_{OH,5'b} = 5.1, OH-5'); 5.29 (d, 1 H, *J*_{OH,3'} = 4.7, OH-3'); 5.56 (d, 1 H, *J*_{OH,2'} = 6.4, OH-2'); 5.95 (d, 1 H, *J*_{1',2'} = 6.3, H-1'); 7.65 (dd, 1 H, *J*_{5,4} = 5.1, *J*_{5,2} = 3.0, H-5-thienyl); 7.76 (d, 1 H, *J*_{7,6} = 5.6, H-7); 8.21 (dd, 1 H, *J*_{4,5} = 5.1, *J*_{4,2} = 1.1, H-4-thienyl); 8.38 (d, 1 H, *J*_{6,7} = 5.6, H-6); 8.70 (s, 1 H, H-2); 8.83 (dd, 1 H, *J*_{2,5} = 3.0, *J*_{2,4} = 1.1, H-2-thienyl). ¹³C NMR (100.6 MHz, DMSO-*d*₆): 61.18 (CH₂-5'); 70.16 (CH-3'); 74.00 (CH-2'); 85.89 (CH-4'); 88.89 (CH-1'); 106.07 (CH-7); 125.80 (CH-5-thienyl); 126.89 (CH-2-thienyl); 127.63 (CH-4-thienyl); 137.44 (C-3a); 138.58 (C-7a); 140.01 (C-3-thienyl); 141.39 (CH-6); 143.71 (CH-2); 144.50 (C-4). IR (KBr): 1596, 1580, 1463, 1221, 1106, 1061, 1037. HR MS (ESI): calculated for C₁₅H₁₆N₃O₄S [M + H] 334.0862, found 334.0857. For C₁₅H₁₅N₃O₄S·H₂O calculated: 51.27% C, 4.88% H, 11.96% N; found: 51.13% C, 4.81% H, 11.75% N.

4-(Pyrrol-2-yl)-1-(β-D-ribofuranosyl)-1H-imidazo[4,5-c]pyridine (5f). Yield 50%. Reaction time 24 h. White crystals from MeOH, m.p. 205–206 °C. [α]_D –53.4 (c 1.9, DMSO). ¹H NMR (400 MHz, DMSO-*d*₆): 3.64 (ddd, 1 H, *J*_{gem} = 12.0, *J*_{5'b,OH} = 5.1, *J*_{5'b,4'} = 3.5, H-5'b); 3.70 (ddd, 1 H, *J*_{gem} = 12.0, *J*_{5'a,OH} = 5.3, *J*_{5'a,4'} = 3.5, H-5'a); 4.01 (td, 1 H, *J*_{4',5'} = 3.5, *J*_{4',3'} = 3.0, H-4'); 4.14 (ddd, 1 H, *J*_{3',2'} = 5.1, *J*_{3',OH} = 4.6, *J*_{3',4'} = 3.0, H-3'); 4.39 (ddd, 1 H, *J*_{2',OH} = 6.1, *J*_{2',1'} = 6.3, *J*_{2',3'} = 5.1, H-2'); 5.18 (dd, 1 H, *J*_{OH,5'a} = 5.3, *J*_{OH,5'b} = 5.1, OH-5'); 5.28 (d, 1 H, *J*_{OH,3'} = 4.6, OH-3'); 5.56 (d, 1 H, *J*_{OH,2'} = 6.1, OH-2'); 5.91 (d, 1 H, *J*_{1',2'} = 6.3, H-1'); 6.21 (dt, 1 H, *J*_{4,3} = 3.7, *J*_{4,5} = *J*_{4,NH} = 2.4, H-4-pyrr); 6.95 (ddd, 1 H, *J*_{5,NH} = 2.7, *J*_{5,4} = 2.4, *J*_{5,3} = 1.6, H-5-pyrr); 7.38 (ddd, 1 H, *J*_{3,4} = 3.7, *J*_{3,NH} = 2.3, *J*_{3,5} = 1.6, H-3-pyrr); 7.58 (d, 1 H, *J*_{7,6} = 5.6, H-7); 8.26 (d, 1 H, *J*_{6,7} = 5.6, H-6); 8.63 (s, 1 H, H-2); 11.54 (br s, 1 H, NH-pyrr). ¹³C NMR (100.6 MHz, DMSO-*d*₆): 61.18 (CH₂-5'); 70.14 (CH-3'); 73.97 (CH-2'); 85.81 (CH-4'); 88.80 (CH-1'); 104.27 (CH-7); 109.28 (CH-4-pyrr); 111.56 (CH-3-pyrr); 120.89 (CH-5-pyrr); 129.58 (C-2-pyrr); 135.53 (C-3a); 138.17 (C-7a); 141.17 (CH-6); 142.71 (C-4); 143.08 (CH-2). IR (KBr): 3352, 1601, 1588, 1470, 1220, 1135, 1084, 1063, 1045. HR MS (ESI): calculated for

$C_{15}H_{17}N_4O_4$ [M + H] 317.1250, found 317.1248. For $C_{15}H_{16}N_4O_4 \cdot 0.5H_2O$ calculated: 55.38% C, 5.27% H, 17.22% N; found: 55.49% C, 4.92% H, 16.95% N.

4-(Pyrrol-3-yl)-1-(β -D-ribofuranosyl)-1H-imidazo[4,5-c]pyridine (5g). Yield 61%. Reaction time 15 h. Greenish solid from water, m.p. 119–126 °C. $[\alpha]_D -48.8$ (c 1.7, DMSO). 1H NMR (400 MHz, DMSO- d_6): 3.64 (ddd, 1 H, $J_{gem} = 11.9$, $J_{5'b,OH} = 5.1$, $J_{5'b,4'} = 3.65$, H-5'b); 3.70 (ddd, 1 H, $J_{gem} = 11.9$, $J_{5'a,OH} = 5.3$, $J_{5'a,4'} = 3.6$, H-5'a); 4.00 (td, 1 H, $J_{4',5'} = 3.6$, $J_{4',3'} = 3.2$, H-4); 4.14 (ddd, 1 H, $J_{3',2'} = 5.1$, $J_{3',OH} = 4.7$, $J_{3',4'} = 3.2$, H-3') 4.39 (ddd, 1 H, $J_{2',OH} = 6.5$, $J_{2',1'} = 6.3$, $J_{2',3'} = 5.1$, H-2'); 5.17 (dd, 1 H, $J_{OH,5'a} = 5.3$, $J_{OH,5'b} = 5.1$, OH-5'); 5.26 (d, 1 H, $J_{OH,3'} = 4.7$, OH-3'); 5.54 (d, 1 H, $J_{OH,2'} = 6.5$, OH-2'); 5.89 (d, 1 H, $J_{1',2'} = 6.3$, H-1'); 6.84 (td, 1 H, $J_{5,4} = J_{5,NH} = 2.6$, $J_{5,2} = 2.0$, H-5-pyrr); 7.03 (td, 1 H, $J_{4,5} = J_{4,NH} = 2.6$, $J_{4,2} = 1.5$, H-4-pyrr); 7.51 (d, 1 H, $J_{7,6} = 5.6$, H-7); 8.03 (ddd, 1 H, $J_{2,NH} = 2.8$, $J_{2,5} = 2.0$, $J_{2,4} = 1.5$, H-2-pyrr); 8.23 (d, 1 H, $J_{6,7} = 5.6$, H-6); 8.55 (s, 1 H, H-2); 11.10 (br s, 1 H, NH-pyrr). ^{13}C NMR (100.6 MHz, DMSO- d_6): 61.23 (CH₂-5'); 70.16 (CH-3'); 73.90 (CH-2'); 85.72 (CH-4'); 88.72 (CH-1'); 103.68 (CH-7); 107.69 (CH-4-pyrr); 118.23 (CH-5-pyrr); 120.58 (CH-2-pyrr); 122.08 (C-3-pyrr); 136.47 (C-3a); 137.94 (C-7a); 141.26 (CH-6); 142.47 (CH-2); 146.96 (C-4). IR (KBr): 3388, 1588, 1552, 1480, 1460, 1217, 1111, 1063, 1041. HR MS (ESI): calculated for $C_{15}H_{17}N_4O_4$ [M + H] 317.1250, found 317.1245. For $C_{15}H_{16}N_4O_4 \cdot 1.5H_2O$ calculated: 52.47% C, 5.58% H, 16.32% N; found: 52.76% C, 5.45% H, 16.04% N.

4-(1H-Pyrazol-5-yl)-1-(β -D-ribofuranosyl)-1H-imidazo[4,5-c]pyridine (5h). Yield 10% after crystallization, 82% of starting compound 4 recovered. Reaction time 24 h. Colorless crystals from water, m.p. 139–143 °C. $[\alpha]_D -59.0$ (c 1.7, DMSO). 1H NMR (500 MHz, DMSO- d_6 + DCI): 3.66, 3.71 (2 × dd, 2 × 1 H, $J_{gem} = 12.2$, $J_{5',4'} = 3.2$, H-5'b); 4.08 (dt, 1 H, $J_{4',3'} = 3.6$, $J_{4',5'} = 3.2$, H-4'); 4.17 (dd, 1 H, $J_{3',2'} = 5.1$, $J_{3',4'} = 3.6$, H-3'); 4.37 (dd, 1 H, $J_{2',1'} = 5.7$, $J_{2',3'} = 5.1$, H-2'); 6.14 (d, 1 H, $J_{1',2'} = 5.7$, H-1'); 7.64 (d, 1 H, $J_{4,5} = 2.4$, H-4-pyrazoly); 8.13 (d, 1 H, $J_{5,4} = 2.4$, H-5-pyrazoly); 8.38 (d, 1 H, $J_{7,6} = 6.7$, H-7); 8.48 (d, 1 H, $J_{6,7} = 6.7$, H-6); 9.17 (s, 1 H, H-2). ^{13}C NMR (125.7 MHz, DMSO- d_6 + DCI): 60.97 (CH₂-5'); 70.25 (CH-3'); 75.19 (CH-2'); 86.85 (CH-4'); 90.20 (CH-1'); 108.95 (CH-7); 109.25 (CH-4-pyrazoly); 132.09 (CH-5-pyrazoly); 134.12 (CH-6); 137.18 (C-3a); 138.05 (C-4); 140.54 (C-3-pyrazoly); 143.30 (C-7a); 148.84 (CH-2). IR (KBr): 3429, 1633, 1605, 1592, 1482, 1402, 1304, 1221, 1137, 1112, 1084. HR MS (ESI): calculated for $C_{14}H_{15}N_5NaO_4$ [M + Na] 340.1022, found 340.1018. For $C_{14}H_{15}N_5O_4 \cdot 1.35H_2O$ calculated: 49.22% C, 5.22% H, 20.50% N; found: 49.47% C, 5.09% H, 20.22% N.

4-(Pyridin-3-yl)-1-(β -D-ribofuranosyl)-1H-imidazo[4,5-c]pyridine (5i). Yield 96%. Reaction time 20 h. White crystalline solid from water, m.p. 111–115 °C. $[\alpha]_D -55.3$ (c 1.7, DMSO). 1H NMR (400 MHz, DMSO- d_6): 3.66 (ddd, 1 H, $J_{gem} = 12.0$, $J_{5'b,OH} = 5.1$, $J_{5'b,4'} = 3.5$, H-5'b); 3.72 (ddd, 1 H, $J_{gem} = 12.0$, $J_{5'a,OH} = 5.3$, $J_{5'a,4'} = 3.5$, H-5'a); 4.04 (td, 1 H, $J_{4',5'} = 3.5$, $J_{4',3'} = 3.1$, H-4); 4.16 (ddd, 1 H, $J_{3',2'} = 5.1$, $J_{3',OH} = 4.7$, $J_{3',4'} = 3.1$, H-3'); 4.42 (ddd, 1 H, $J_{2',OH} = 6.3$, $J_{2',1'} = 6.3$, $J_{2',3'} = 5.1$, H-2'); 5.22 (dd, 1 H, $J_{OH,5'a} = 5.3$, $J_{OH,5'b} = 5.1$, OH-5'); 5.31 (d, 1 H, $J_{OH,3'} = 4.7$, OH-3'); 5.59 (d, 1 H, $J_{OH,2'} = 6.3$, OH-2'); 5.99 (d, 1 H, $J_{1',2'} = 6.3$, H-1'); 7.57 (ddd, 1 H, $J_{5,4} = 8.0$, $J_{5,6} = 4.8$, $J_{5,2} = 1.0$, H-5-py); 7.90 (d, 1 H, $J_{7,6} = 5.5$, H-7); 8.50 (d, 1 H, $J_{6,7} = 5.5$, H-6); 8.65 (dd, 1 H, $J_{6,5} = 4.7$, $J_{6,4} = 1.7$, H-6-py); 8.75 (s, 1 H, H-2); 8.97 (ddd, 1 H, $J_{4,5} = 8.0$, $J_{4,2} = 2.2$, $J_{4,6} = 1.7$, H-4-py); 9.81 (dd, 1 H, $J_{2,4} = 2.2$, $J_{2,5} = 1.0$, H-2-py). ^{13}C NMR (100.6 MHz, DMSO- d_6): 61.17 (CH₂-5'); 70.18 (CH-3'); 74.06 (CH-2'); 85.99 (CH-4'); 88.97 (CH-1'); 107.20 (CH-7); 123.53 (CH-5-py); 133.14 (C-3-py); 135.89 (CH-4-py); 138.51 (C-3a); 138.97 (C-7a); 141.74 (CH-6); 144.21 (CH-2); 145.37 (C-4); 149.69 and 149.78 (CH-2,6-py). IR (KBr): 1606, 1592, 1583, 1502, 1460, 1101, 1050, 984, 940. HR MS (ESI): calculated for $C_{16}H_{17}N_4O_4$

[M + H] 329.1250, found 329.1247. For $C_{16}H_{16}N_4O_4 \cdot 1.8H_2O$ calculated: 53.27% C, 5.48% H, 15.53% N; found: 53.42% C, 5.37% H, 15.34% N.

4-Methyl-1-(2,3,5-tri-*O*-acetyl- β -D-ribofuranosyl)-1*H*-imidazo[4,5-*c*]pyridine (**6a**)

An argon purged flask containing a mixture of acetylated 6-chloro-3-deazapurine riboside **3** (300 mg, 0.73 mmol), trimethylaluminum (2 M solution in toluene; 0.73 ml, 1.46 mmol) and Pd(PPh₃)₄ (42 mg, 0.036 mmol) in THF (4 ml) was stirred at 100 °C for 3 h. The mixture was diluted with CHCl₃ (20 ml) and treated with saturated aqueous NH₄Cl (20 ml). The slurry was filtered through cellite and after phase separation, aqueous phase was re-extracted with CHCl₃ (2 × 10 ml). Collected organic extracts were dried over MgSO₄, volatiles were removed in vacuo and the residue was chromatographed on silica gel (AcOEt) affording product **6a** as colorless oil (151 mg, 53%). ¹H NMR (400 MHz, CDCl₃): 2.09, 2.17 and 2.19 (3 × s, 3 × 3 H, 3 × CH₃CO); 2.90 (s, 3 H, CH₃); 4.41 (dd, 1 H, $J_{gem} = 12.6$, $J_{5'b,4'} = 2.8$, H-5'b); 4.46 (dd, 1 H, $J_{gem} = 12.6$, $J_{5'a,4'} = 3.0$, H-5'a); 4.50 (ddd, 1 H, $J_{4',3'} = 4.4$, $J_{4',5'} = 3.0$, 2.8, H-4'); 5.43 (dd, 1 H, $J_{3'2'} = 5.6$, $J_{3'4'} = 4.4$, H-3'); 5.56 (t, 1 H, $J_{2',1'} = J_{2',3'} = 5.6$, H-2'); 6.08 (d, 1 H, $J_{1',2'} = 5.6$, H-1'); 7.39 (d, 1 H, $J_{7,6} = 5.7$, H-7); 8.17 (s, 1 H, H-2); 8.35 (d, 1 H, $J_{6,7} = 5.7$, H-6). ¹³C NMR (100.6 MHz, CDCl₃): 19.85 (CH₃); 20.31, 20.50 and 20.75 (3 × CH₃CO); 62.73 (CH₂-5'); 70.10 (CH-3'); 73.29 (CH-2'); 80.40 (CH-4'); 87.05 (CH-1'); 104.05 (CH-7); 136.92 (C-7a); 139.82 (C-3a); 140.39 (CH-2); 142.20 (CH-6); 152.68 (C-4); 169.20, 169.49 and 170.09 (3 × CO). IR (CCl₄): 1758, 1602, 1590, 1371, 1219, 1100, 1063, 1048. HR MS (ESI): calculated for C₁₈H₂₂N₃O₇ [M + H] 392.1458, found 392.1453.

4-Ethyl-1-(2,3,5-tri-*O*-acetyl- β -D-ribofuranosyl)-1*H*-imidazo[4,5-*c*]pyridine (**6b**)

An argon purged flask containing a mixture of acetylated 6-chloro-3-deazapurine riboside **3** (288 mg, 0.70 mmol), triethylaluminum (1 M solution in hexane; 1.4 ml, 1.4 mmol) and Pd(PPh₃)₄ (40 mg, 0.035 mmol) in THF (4 ml) was stirred at 100 °C for 3 h. The mixture was diluted with CHCl₃ (20 ml) and treated with saturated aqueous NH₄Cl (20 ml). The slurry was filtered through cellite and after phase separation, aqueous phase was re-extracted with CHCl₃ (2 × 10 ml). Collected organic extracts were dried over MgSO₄, volatiles were removed in vacuo and the residue was chromatographed on silica gel (AcOEt) affording product **6b** as colorless oil (169 mg, 60%). ¹H NMR (400 MHz, CDCl₃): 1.44 (t, 3 H, $J_{vic} = 7.6$, CH₂CH₃); 2.10, 2.17, 2.18 (3 × s, 3 × 3 H, 3 × CH₃CO); 3.28 (q, 2 H, $J_{vic} = 7.6$, CH₂CH₃); 4.41 (dd, 1 H, $J_{gem} = 12.5$, $J_{5'b,4'} = 2.8$, H-5'b); 4.46 (dd, 1 H, $J_{gem} = 12.5$, $J_{5'a,4'} = 3.0$, H-5'a); 4.50 (ddd, 1 H, $J_{4',3'} = 4.3$, $J_{4',5'} = 3.0$, 2.8, H-4'); 5.43 (dd, 1 H, $J_{3'2'} = 5.6$, $J_{3'4'} = 4.3$, H-3'); 5.56 (t, 1 H, $J_{2',1'} = J_{2',3'} = 5.6$, H-2'); 6.09 (d, 1 H, $J_{1',2'} = 5.6$, H-1'); 7.39 (d, 1 H, $J_{7,6} = 5.7$, H-7); 8.16 (s, 1 H, H-2); 8.39 (d, 1 H, $J_{6,7} = 5.7$, H-6). ¹³C NMR (100.6 MHz, CDCl₃): 13.22 (CH₃CH₂); 20.33, 20.50 and 20.76 (3 × CH₃CO); 26.85 (CH₂CH₃); 62.73 (CH₂-5'); 70.11 (CH-3'); 73.30 (CH-2'); 80.37 (CH-4'); 87.04 (CH-1'); 104.01 (CH-7); 137.09 (C-7a); 139.20 (C-3a); 140.33 (CH-2); 142.32 (CH-6); 157.55 (C-4); 169.22, 169.50 and 170.10 (3 × CO). IR (CCl₄): 1757, 1600, 1588, 1371, 1220, 1103, 1063, 1048. HR MS (ESI): calculated for C₁₉H₂₄N₃O₇ [M + H] 406.1614, found 406.1609.

4-Cyclopropyl-1-(2,3,5-tri-*O*-acetyl- β -D-ribofuranosyl)-1*H*-imidazo[4,5-*c*]pyridine (**6c**)

Tetrahydrofuran (4 ml) was added to flame-vacuum dried zinc chloride (340 mg, 2.5 mmol) under argon. The mixture was stirred at -10 °C and a solution of cyclopropylmagnesium

bromide (1 M solution in THF; 2.5 ml) was added dropwise. The mixture was stirred for 40 min and then a solution of a 6-chloro-3-deazapurine riboside **3** (205 mg, 0.5 mmol) and Pd(PPh₃)₄ (40 mg, 0.035 mmol) in THF (5 ml) was added. The resulting mixture was stirred at 70 °C for 8 h. Then the reaction mixture was diluted with water (50 ml) and washed with ethyl acetate (3 × 50 ml). The collected organic layers were washed with brine, dried over MgSO₄ and the residue was purified by column chromatography on silica gel (AcOEt-hexane 0–30%) providing compound **6c** as a white foam (80 mg, 38%). ¹H NMR (500 MHz, CDCl₃): 1.13 and 1.31 (2 × m, 2 × 2 H, H-2,3-cycloprop); 2.09, 2.17 and 2.18 (3 × s, 3 × 3 H, CH₃CO); 2.87 (tt, 1 H, *J*_{vic} = 8.3, 4.7, H-1-cycloprop); 4.41 (dd, 1 H, *J*_{gem} = 12.5, *J*_{5'b,4'} = 2.9, H-5'b); 4.45 (dd, 1 H, *J*_{gem} = 12.5, *J*_{5'a,4'} = 3.0, H-5'a); 4.49 (ddd, 1 H, *J*_{4',3'} = 4.3, *J*_{4',5'} = 3.0, 2.9, H-4'); 5.43 (dd, 1 H, *J*_{3',2'} = 5.6, *J*_{3',4'} = 4.3, H-3'); 5.55 (dd, 1 H, *J*_{2',1'} = 5.9, *J*_{2',3'} = 5.6, H-2'); 6.07 (d, 1 H, *J*_{1',2'} = 5.9, H-1'); 6.07 (d, 1 H, *J*_{7,6} = 5.9, H-7); 8.16 (s, 1 H, H-2); 8.28 (d, 1 H, *J*_{6,7} = 5.9, H-6). ¹³C NMR (125.7 MHz, CDCl₃): 10.01 and 10.04 (CH₂-2,3-cycloprop); 12.67 (CH-1-cycloprop); 20.30, 20.50 and 20.75 (CH₃CO); 62.77 (CH₂-5'); 70.13 (CH-3'); 73.26 (CH-2'); 80.38 (CH-4'); 86.97 (CH-1'); 102.90 (CH-7); 136.63 (C-7a); 139.52 (C-3a); 140.31 (CH-2); 142.42 (CH-6); 157.06 (C-4); 169.21, 169.52 and 170.14 (CO). IR (CHCl₃): 1591, 1372, 1232, 1199, 1096, 1067. HR MS (ESI): calculated for C₂₀H₂₄N₃O₇ [M + H] 418.1609, found 418.1602.

4-Methyl-1-(β-D-ribofuranosyl)-1H-imidazo[4,5-c]pyridine (**5j**)

Compound **6a** (129 mg, 0.33 mmol) was treated with 1 M NaOMe/MeOH (100 μl, 0.1 mmol) in MeOH (2 ml) at RT for 1 h and, after removal of volatiles, the crude product was desalted by reverse phase chromatography and crystallized from water affording nucleoside **5j** as colorless crystals (62 mg, 71%), m.p. 245–249 °C. [α]_D –68.3 (c 2.2, DMSO). ¹H NMR (400 MHz, DMSO-*d*₆): 2.70 (s, 3 H, CH₃); 3.62 (ddd, 1 H, *J*_{gem} = 11.9, *J*_{5'b,OH} = 5.1, *J*_{5'b,4'} = 3.5, H-5'b); 3.67 (ddd, 1 H, *J*_{gem} = 11.9, *J*_{5'a,OH} = 5.3, *J*_{5'a,4'} = 3.5, H-5'a); 3.99 (td, 1 H, *J*_{4',5'} = 3.5, *J*_{4',3'} = 3.0, H-4'); 4.12 (ddd, 1 H, *J*_{3',2'} = 5.1, *J*_{3',OH} = 4.6, *J*_{3',4'} = 3.0, H-3'); 4.36 (ddd, 1 H, *J*_{2',OH} = 6.4, *J*_{2',1'} = 6.4, *J*_{2',3'} = 5.1, H-2'); 5.16 (dd, 1 H, *J*_{OH,5'a} = 5.3, *J*_{OH,5'b} = 5.0, OH-5'); 5.26 (d, 1 H, *J*_{OH,3'} = 4.6, OH-3'); 5.51 (d, 1 H, *J*_{OH,2'} = 6.5, OH-2'); 5.88 (d, 1 H, *J*_{1',2'} = 6.4, H-1'); 7.64 (d, 1 H, *J*_{7,6} = 5.7, H-7); 8.19 (d, 1 H, *J*_{6,7} = 5.7, H-6); 8.53 (s, 1 H, H-2). ¹³C NMR (100.6 MHz, DMSO-*d*₆): 19.53 (CH₃); 61.20 (CH₂-5'); 70.15 (CH-3'); 73.86 (CH-2'); 85.78 (CH-4); 88.77 (CH-1'); 105.29 (CH-7); 137.02 (C-7a); 139.35 (C-3a); 140.96 (CH-6); 142.80 (CH-2); 150.65 (C-4). IR (KBr): 3366, 3254, 1603, 1592, 1493, 1466, 1419, 1314, 1305, 1121, 1092, 1081, 1081, 1045. HR MS (ESI): calculated for C₁₂H₁₆N₃O₄ [M + H] 266.1141, found 266.1133. For C₁₂H₁₅N₃O₄ calculated: 54.33% C, 5.70% H, 15.84% N; found: 53.98% C, 5.79% H, 15.51% N.

4-Ethyl-1-(β-D-ribofuranosyl)-1H-imidazo[4,5-c]pyridine (**5k**)

Compound **6b** (149 mg, 0.37 mmol) was treated with 1 M NaOMe/MeOH (110 μl, 0.11 mmol) in MeOH (2 ml) at RT for 1 h and, after removal of volatiles, the crude product was desalted by reverse phase chromatography and crystallized from water affording nucleoside **5k** as colorless crystals (72 mg, 70%), m.p. 94 °C. [α]_D –41.0 (c 1.4, DMSO). ¹H NMR (400 MHz, DMSO-*d*₆): 1.31 (t, 3 H, *J*_{vic} = 7.6, CH₃CH₂); 3.10 (q, 2 H, *J*_{vic} = 7.6, CH₂CH₃); 3.62 (ddd, 1 H, *J*_{gem} = 11.9, *J*_{5'b,OH} = 5.1, *J*_{5'b,4'} = 3.5, H-5'b); 3.67 (ddd, 1 H, *J*_{gem} = 11.9, *J*_{5'a,OH} = 5.3, *J*_{5'a,4'} = 3.5, H-5'a); 3.99 (td, 1 H, *J*_{4',5'} = 3.5, *J*_{4',3'} = 3.0, H-4'); 4.12 (ddd, 1 H, *J*_{3',2'} = 5.1, *J*_{3',OH} = 4.6, *J*_{3',4'} = 3.0, H-3'); 4.37 (ddd, 1 H, *J*_{2',OH} = 6.4, *J*_{2',1'} = 6.3, *J*_{2',3'} = 5.1, H-2'); 5.16 (dd, 1 H,

$J_{\text{OH},5'a} = 5.3$, $J_{\text{OH},5'b} = 5.0$, OH-5'); 5.26 (d, 1 H, $J_{\text{OH},3'}$ = 4.6, OH-3'); 5.51 (d, 1 H, $J_{\text{OH},2'}$ = 6.5, OH-2'); 5.88 (d, 1 H, $J_{1',2'}$ = 6.3, H-1'); 7.64 (d, 1 H, $J_{7,6}$ = 5.7, H-7); 8.22 (d, 1 H, $J_{6,7}$ = 5.7, H-6); 8.52 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, DMSO- d_6): 13.13 (CH_3CH_2); 26.11 (CH_2CH_3); 61.23 (CH_2 -5'); 70.19 (CH-3'); 73.84 (CH-2'); 85.81 (CH-4'); 88.75 (CH-1'); 105.32 (CH-7); 137.21 (C-7a); 138.73 (C-3a); 141.03 (CH-6); 142.81 (CH-2); 155.40 (C-4). IR (KBr): 3280, 1605, 1593, 1493, 1477, 1415, 1312, 1217, 1119, 1087, 998. HR MS (ESI): calculated for $\text{C}_{13}\text{H}_{18}\text{N}_3\text{O}_4$ [M + H] 280.1297, found 280.1291. For $\text{C}_{13}\text{H}_{17}\text{N}_3\text{O}_4 \cdot \text{H}_2\text{O}$ calculated: 52.52% C, 6.44% H, 14.13% N; found: 52.57% C, 6.46% H, 14.09% N.

4-Cyclopropyl-1-(β -D-ribofuranosyl)-1H-imidazo[4,5-c]pyridine (51)

Compound **6c** (72 mg, 0.17 mmol) was treated with 1 M NaOMe/MeOH (52 μl , 0.52 mmol) in MeOH (2 ml) at RT for 1 h and, after removal of volatiles, the crude product was desalted by reverse phase chromatography and crystallized from water–MeOH affording nucleoside **51** as colorless crystals (35 mg, 70%), m.p. 107–113 $^{\circ}\text{C}$. $[\alpha]_{\text{D}} -43.0$ (c 0.23, MeOH). ^1H NMR (500 MHz, DMSO- d_6): 1.13 and 1.22 (2 \times m, 2 \times 2 H, H-2,3-cycloprop); 2.86 (tt, 1 H, $J_{\text{vic}} = 8.1$, 4.8, H-1-cycloprop); 3.72 and 3.77 (2 \times dd, 2 H, $J_{\text{gem}} = 12.0$, $J_{5',4'}$ = 3.6, H-5'); 4.08 (td, 1 H, $J_{4',5'}$ = 3.6, $J_{4',3'}$ = 3.1, H-4'); 4.21 (dd, 1 H, $J_{3',2'}$ = 5.2, $J_{3',4'}$ = 3.1, H-3'); 4.44 (dd, 1 H, $J_{2',1'}$ = 6.4, $J_{2',3'}$ = 5.2, H-2'); 5.96 (d, 1 H, $J_{1',2'}$ = 6.4, H-1'); 7.63 (d, 1 H, $J_{7,6}$ = 5.6, H-7); 8.24 (d, 1 H, $J_{6,7}$ = 5.6, H-6); 8.62 (s, 1 H, H-2). ^{13}C NMR (125.7 MHz, DMSO- d_6): 9.84 and 9.86 (CH_2 -2,3-cycloprop); 12.68 (CH-1-cycloprop); 61.44 (CH_2 -5'); 70.37 (CH-3'); 74.14 (CH-2'); 86.01 (CH-4'); 89.02 (CH-1'); 104.51 (CH-7); 137.07 (C-7a); 139.23 (C-3a); 141.47 (CH-6); 143.08 (CH-2); 155.14 (C-4). IR (KBr): 3480, 3403, 1601, 1593, 1473, 1455, 1388, 1366, 1221, 1102, 1063, 989, 976. HR MS (ESI) calculated for $\text{C}_{14}\text{H}_{18}\text{N}_3\text{O}_4$ [M + H] 292.1292, found 292.1291. For $\text{C}_{14}\text{H}_{17}\text{N}_3\text{O}_4 \cdot 1.15\text{H}_2\text{O}$ calculated: 53.89% C, 6.23% H, 13.47% N; found: 53.83% C, 6.22% H, 13.43% N.

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