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Sugar-modified derivatives of cytostatic 7-(het)aryl-7-deazaadenosines: 2′-*C*-methylribonucleosides, 2′-deoxy-2′-fluoroarabinonucleosides, arabinonucleosides and 2′-deoxyribonucleosides

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ABSTRACT

A series of novel sugar-modified derivatives of cytostatic 7-hetaryl-7-deazaadenosines (2′-*C*-methylribonucleosides, 2′-deoxy-2′-fluoroarabinonucleosides, arabinonucleosides and 2′-deoxyribonucleosides) was prepared and screened for biological activity. The synthesis consisted of preparation of the corresponding sugar-modified 7-iodo-7-deazaadenine nucleosides and their aqueous-phase Suzuki-Miyaura cross-coupling reactions with (het)arylboronic acids or Stille couplings with hetarylstannanes in DMF. The synthesis of 7-iodo-7-deazaadenine nucleosides was based on a glycosidation of 6-chloro-7-iodo-7-deazapurine with a suitable sugar synthon or on an interconversion of 2′-OH stereocenter (for arabinonucleosides). Several examples of 2′-*C*-Me-ribonucleosides showed moderate anti-HCV activities in a replicon assay accompanied by cytotoxicity. Several 7-hetaryl-7-deazaadenine fluoroarabino- and arabinonucleosides exerted moderate micromolar cytostatic effects. The most active was 7-ethynyl-7-deazaadenine fluoroarabinonucleoside which showed submicromolar antiproliferative activity. However, all the sugar-modified derivatives were less active than the parent ribonucleosides.

1. Introduction

Nucleoside cytostatic or cytotoxic agents[1] are one of the most important classes of drugs clinically used for treatment of solid or hematological malignancies. Within our long-term program[2] on new biologically active base-modified nucleosides, we have recently discovered two novel types of nucleoside cytostatic: 6-hetaryl-7-deazapurine ribonucleosides[3] **1** and 7-hetaryl-7-deazaadenosines[4] **2**. Both types of compounds displayed nanomolar cytostatic activities towards a wide panel of leukemia and cancer cell-lines. Our on-going study on mechanism of action is still under way but in parallel we systematically study the SAR. In both series, the most active compounds were derivatives bearing furyl or thienyl groups at the position 6 or 7 of the 7-deazapurine. In the 6-hetaryl-7-deazapurine ribonucleoside series we were able to prepare their *cyclo*Sal-phosphate and phosphoramidate prodrugs[5] to find that they are less active due to increased efflux from the cells and a series of sugar modified derivatives:[6] 2′-*C*-methylribonucleosides, arabinonucleosides and 2′-fluoroarabinonucleosides that were all entirely inactive indicating that ribo-configuration of the sugar might be crucial for the activity in this particular class of compounds. Here we report the synthesis and biological activity profiling of analogous sugar-modified derivatives derived from 7-hetaryl-7-deazaadenine (Chart 1).

7-Deazaadenosine (tubercidin) is a natural cytostatic antibiotic[7] and extensive studies have focused[8] on its diverse derivatives. Some 7-substituted derivatives of tubercidin bearing halogens, carboxamides or alkynes were reported[9] to exert cytotoxic, antiparasitic, and/or antiviral activities mostly through inhibition of adenosine kinase. An important class of derivatives are 7-substituted 2′-*C*-methylribonucleosides that are selective inhibitors of HCV replication.[10] Therefore, our present study also complements the SAR of the base- and sugar-modified derivatives of tubercidin[11].

2. Results and discussion

2.1. Chemistry

The synthesis of 7-substituted 7-deaza-2′-*C*-methyladenosines **7** began with the Vorbrüggen-type condensation of 6-chloro-7-iodo-7-deazapurine **3** with 1,2,3,5-tetra-*O*-benzoyl-2-*C*-methyl-β-

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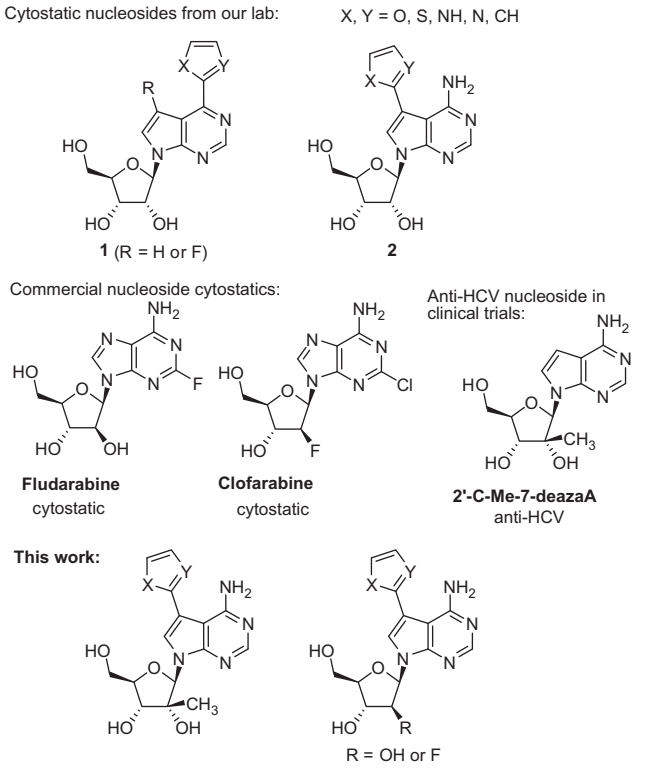
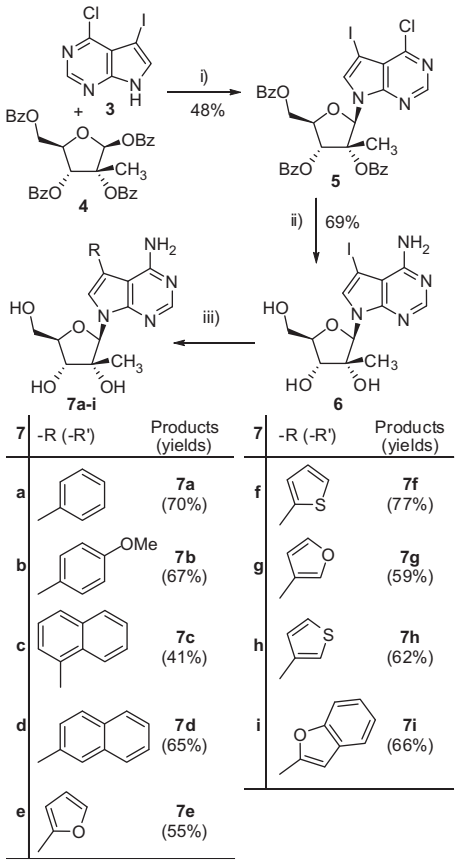


Chart 1.



Scheme 1. Reagents and conditions: (i) TMSOTf, DBU, MeCN, 70 °C; (ii) aq NH_3 (26% w/w), dioxane, 120 °C; (iii) R-$B(OH)_2$, Na_2CO_3, $Pd(OAc)_2$, TPPTS, H_2O/MeCN (2:1), 100 °C.

D-ribofuranose **4** (Scheme 1). Among the conditions screened, the one-pot DBU/TMSOTf procedure[12] was found to be the best, affording protected 2′-*C*-methyl-β-D-ribofuranoside **5** in 48% yield. Amination/deprotection of compound **5** by heating with aqueous ammonia in dioxane provided 7-deaza-7-iodo-2′-*C*-methyladenosines **6** in 69% yield. Finally, aqueous Suzuki–Miyaura reactions[13] of **6** with a series of boronic acids gave desired 7-(het)aryl substituted 7-deaza-2′-*C*-methyladenosines **7a–i** in good yields.

The route towards 7-substituted 7-deazaadenine 2′-deoxy-2′-fluoroarabinonucleosides commenced with nucleobase-anion glycosylation[14] of 6-chloro-7-iodo-7-deazapurine **3** with 2-deoxy-2-fluoroarabinosyl bromide **9** (Scheme 2). The bromide **9**[15] was obtained by treatment of 2-deoxy-2-fluoro-1,3,5-tri-*O*-benzoyl-α-D-arabinofuranose **8** with 30% HBr in acetic acid. The reaction of deazapurine **3** with bromose **9** in the presence of KOH, TDA-1 {TDA-1 = tris[2-(2-methoxyethoxy)ethyl]amine)} in acetonitrile provided protected 6-chloro-7-iodo-7-deazapurine 2′-deoxy-2′-fluoro-β-D-arabinofuranoside **10** in excellent 85% yield. Nucleoside **10** was converted to unprotected 7-iodo-7-deazaadenine 2′-deoxy-2′-fluoroarabinoside **11** by treatment with aqueous ammonia in dioxane in steel bomb in 84% yield. Palladium-catalyzed cross-coupling reactions of iodide **11** with (het)arylboronic acids under aqueous-phase conditions or with stannanes in DMF afforded the corresponding 7-(het)aryl substituted 7-deazaadenine 2′-deoxy-2′-fluoroarabinonucleosides **12a**,**e**–**h**,**j** in good yields. The 4-pyrazolyl derivative **12j** was synthesized by the Stille reaction of **11** with 1-dimethylsulfamoyl-4-tributylstannylpyrazole[16] followed by acid catalyzed deprotection (1 M aq HCl) of dimethylsulfamoyl group (80% yield in two steps).

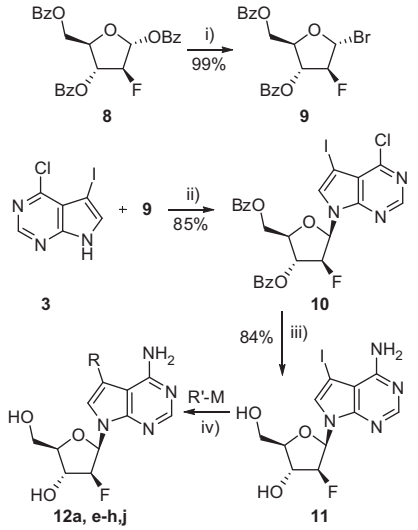
The Sonogashira reaction of **11** with (trimethylsilyl)acetylene and subsequent base promoted protodesilylation of intermediate **13** afforded ethynyl derivative **12k** in high yield (Scheme 3). 7-Triazolyl derivative **12l** was prepared by copper mediated [3+2] cycloadition[17] of ethynyl compound **12k** with trimethylsilylazide in moderate yield of 27%.

A synthetic path to 7-hetaryl-7-deazaadenine arabinonucleosides was developed starting from the corresponding ribonucleoside **14**[18] (Scheme 4). At first, the 3′- and 5′-hydroxy groups of 7-iodotubercidin **14** were protected using the Markiewicz reagent. As the starting material **14** is poorly soluble in pyridine, it was necessary to co-evaporate it several times with pyridine prior to silylation to obtain the silylated derivative **15** in good yield (89%). Oxidation by Dess-Martin periodinane that provided high yields with a similar substrate in our previous study of 7-deazapurine nucleosides[6] did not proceed with **15**. Therefore, the 2′-hydroxyl group was oxidized with CrO_3 in presence of acetic anhydride and pyridine to give ketone **16** (59%). The crude ketone **16** was subsequently selectively reduced by sodium borohydride to arabinoside **17** (85%). The key intermediate, free arabinoside **18**, was prepared by deprotection of compound **17** by $Et_3N{\cdot}3HF$ in high yield (93%).

Arabinoside **18** was used as a starting material for a series of Suzuki cross-coupling reactions with hetarylboronic acids in presence of sodium carbonate, TPPTS and palladium acetate in acetonitrile:water (1:2) at 100 °C. A set of five 6-amino-7-hetaryl-7-deazapurine arabinonucleosides **19a**,**e**–**h** was obtained in good yields (64–92%) (Scheme 5).

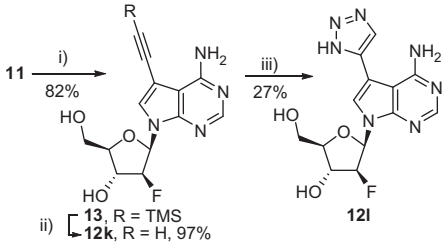
An ethynyl group was introduced to the position 7 of 7-deazaadenine arabinoside **18** by the Sonogashira reaction of **18** with (trimethylsilyl)acetylene in presence of copper(I) iodide, Et_3N and $PdCl_2(PPh_3)_2$ in DMF to obtain TMS-ethynyl derivative **20** (51% yield) which was deprotected using potassium carbonate in methanol. 7-Ethynyl-7-deazaadenine arabinoside **19k** was obtained in 77% yield (Scheme 6).

A series of 7-hetaryl-7-deazaadenine 2-deoxyribonucleosides was synthesized from 2′-deoxy-7-iodo–tubercidin **21**[19]

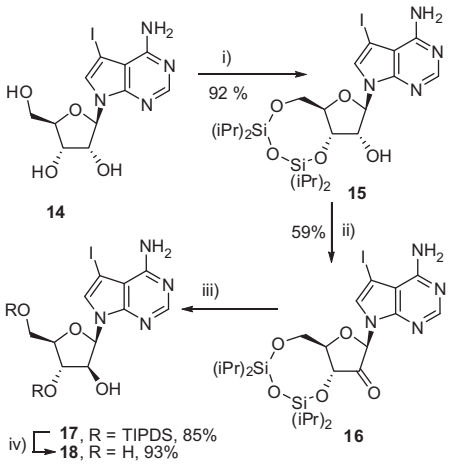


12	R (R')	M	Products (yields)
a		$B(OH)_2$	**12a** (86%)
e		$SnBu_3$	**12e** (75%)
f		$SnBu_3$	**12f** (82%)
g		$B(OH)_2$	**12g** (89%)
h		$B(OH)_2$	**12h** (90%)
j		$SnBu_3$	**12j** (80%)

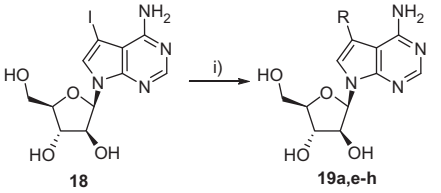
Scheme 2. Reagents and conditions: (i) HBr, AcOH; (ii) KOH, TDA-1, MeCN; (iii) aq NH_3 (26% w/w), dioxane, 120 °C; (iv) For M = $B(OH)_2$: R-$B(OH)_2$, Na_2CO_3, $Pd(OAc)_2$, TPPTS, H_2O/MeCN (2:1), 100 °C; For M = $SnBu_3$: R(R′)-$SnBu_3$, $PdCl_2(PPh_3)_2$, DMF, 100 °C.



Scheme 3. Reagents and conditions: (i) Trimethylsilylacetylene, $PdCl_2(PPh_3)_2$, CuI, NEt_3, DMF, rt; (ii) K_2CO_3, MeOH; (iii) $TMSN_3$, CuI, DMF/MeOH.



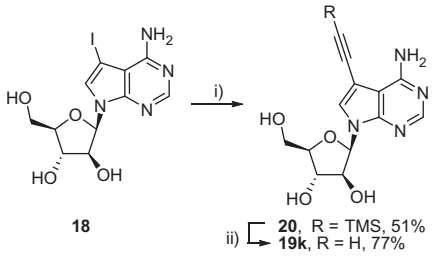
Scheme 4. Reagents and conditions: (i) $TIPDSCl_2$/py; (ii) CrO_3, Ac_2O, py/CH_2Cl_2, 0 °C; (iii) $NaBH_4$/EtOH, 0 °C; (iv) $Et_3N{\cdot}3HF$/THF, rt.



19	R	Product (yield)
a		**19a** (73%)
e		**19e** (64%)
f		**19f** (77%)

19	R	Product (yield)
g		**19g** (73%)
h		**19h** (92%)

Scheme 5. Reagents and conditions: (i) R-$B(OH)_2$, Na_2CO_3, TPPTS, $Pd(OAc)_2$, CH_3CN/H_2O (1:2), 100 °C.

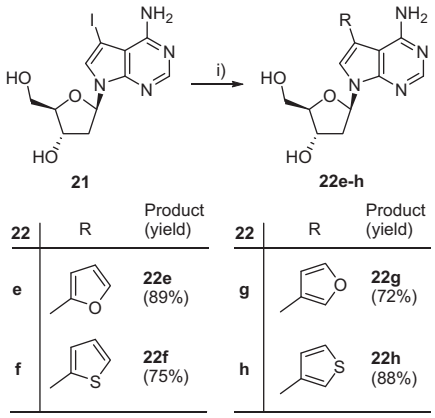


Scheme 6. Reagents and conditions: (i) (Trimethylsilyl)acetylene, $PdCl_2(PPh_3)_2$, CuI, Et_3N, DMF, rt; (ii) K_2CO_3, MeOH, rt.

(Scheme 7). The Suzuki cross-coupling reactions with hetarylboronic acids were performed in the presence of sodium carbonate, TPPTS and palladium acetate in acetonitrile:water (1:2) at 100 °C. Target 7-hetaryl-7-deazaadenine 2′-deoxyribonucleosides **22e–h** were prepared in good yields (72–89%).

2.2. Biological activity profiling

All the title nucleosides were subjected to biological activity screening. The cytotoxic activity in vitro was studied on the following cell cultures: (i) human promyelocytic leukemia HL60 cells (ATCC CCL 240); (ii) human cervix carcinoma HeLa S3 cells (ATCC CCL 2.2); (iii) human T lymphoblastoid CCRF-CEM cell line (ATCC CCL 119), and (iv) hepatocellular carcinoma cells HepG2 (ATCC HB 8065). Cell viability was determined following a 3-day incubation using metabolic 2,3-bis-(2-methoxy-4-nitro-5-sulfophenyl)-2*H*-tetrazolium-5-carboxanilide (XTT) based method.[20] Table 1 shows the activities of selected most potent compounds. Several examples of 7-hetaryl-7-deazaadenine 2′-*C*-methyl-ribo-



Scheme 7. Reagents and conditions: (i) R-B(OH)$_2$, Na_2CO_3, TPPTS, $Pd(OAc)_2$, CH_3CN/H_2O (1:2), 100 °C.

nucleosides **7**, and 2′-fluoro-2′-deoxyribonucleosides **12** and arabinonucleosides **19** exerted μM cytostatic effects. The most active was the 7-ethynyl-7-deazaadenine 2′-fluoro-2′-deoxyribonucleoside **12k** which showed submicromolar effects. The 2′-deoxyribonucleosides **22** were entirely inactive.

Cytostatic activity of selected nucleosides was also evaluated against further four cell-lines derived from various human solid tumors including lung (NCI-H23), prostate (Du145), colon (HCT 116), and breast (Hs 578) carcinomas. Concentrations inhibiting the cell growth by 50% (GIC_{50}) were determined using a quantitative cellular staining with sulforhodamine B (SRB)[21] following a 5-day treatment. The SRB method allowed for a quantitative measurement of a net effect on cell growth by subtracting the background signal generated by the cell culture inoculum at the beginning of treatment. Again, several compounds exerted micromolar effects (Table 2). The 7-ethynyl fluoroarabinonucleoside **12k** displayed nanomolar activity against Du145.

The title modified nucleosides were also tested up to 100 μM for antiviral activities in HCV genotype 1A and 1B replicons[22] (Table 3). They generally displayed micromolar antiviral activities in the HCV replicon. Unfortunately, in most cases the compounds lacked selectivity and the antiviral effect was accompanied by cytotoxicity. With the exception of 7-iododeazaadenine 2′-*C*-Me-ribonucleoside **6** (which showed ca 65-fold selectivity), in most compounds the selectivities were <10-fold. These results suggest that, similarly to the previously reported ribonucleosides, these sugar-modified deazapurine ribonucleosides interfere with critical cell growth processes and most of the activity toward HCV viral replication is non-specific. Shortly before submission of this work, a paper by Di Francesco et al.[23] appeared reporting micromolar anti-HCV activities of related (but different derivatives) 7-hetaryl-7-deazaadenine 2′-*C*-Me-ribonucleosides but no cytotoxicity data were reported.

Table 1
Cytotoxic activities of title nucleosides (XTT)

Compound	IC_{50} (μM)[a]			
	HL60	HeLa S3	CCRF-CEM	HepG2
6	>10	7.50	4.38	nd[b]
7d	>10	>10	3.95	nd
7i	>10	>10	7.81	nd
12f	>10	5.60	7.50	>10
12j	>10	>10	9.07	nd
12k	0.20	0.22	0.18	nd
12l	>10	6.66	3.45	nd
18	6.44	3.19	7.02	6.12
19e	>10	7.62	6.64	6.62
19f	13.51	5.38	4.25	12.23
19g	>10	8.36	4.67	6.10
19h	12.99	7.03	3.10	>15
19k	>10	3.77	>10	9.86

[a] Cytostatic activity was determined by XTT assay following a 3-day incubation with tested compounds. Values represent 2–4 independent experiments.
[b] nd, not determined.

Table 2
Further cytostatic activities of selected nucleosides (SRB)

Compound	GIC_{50} (μM)[a]			
	HCT 116	NCI-H23	Hs 578	Du 145
6	6.65	0.79	4.39	3.38
7e	>10	6.08	9.05	8.89
12e	>10	>10	8.49	8.52
12k	0.108	0.048	0.065	0.002
12l	7.64	5.36	1.82	9.41

[a] Cytostatic activity was determined by SRB (GIC_{50}) following a 3-day incubation with tested compounds. Values represent 2–4 independent experiments.

Table 3
Anti-HCV activities of title nucleosides

Compound	HCV replicon 1A		HCV replicon 1B	
	EC_{50} (μM)	CC_{50} (μM)	EC_{50} (μM)	CC_{50} (μM)
6	0.37	19.75	0.38	26.27
7a	35.43	>44	27.07	>44
7b	11.99	>44	9.44	>44
7c	24.67	>44	24.13	>44
7d	4.91	20.13	5.31	29.59
7e	nd	nd	8.96	49.63
7f	nd	nd	14.19	48.09
7g	18.33	>44	12.28	>44
7h	36.31	>44	15.54	>44
7i	6.15	29.42	6.13	38.77
12a	26.36	>44	43.47	>44
12e	15.70	>44	12.05	>44
12f	2.80	>44	4.07	42.85
12g	36.98	>44	16.994	>44
12h	10.94	33.65	10.81	24.35
12j	22.36	>44	8.45	>44
12k	0.36	12.11	0.36	2.68
12l	1.83	21.66	0.92	10.91
18	1.39	13.72	1.39	9.97
19a	>44	>44	>44	>44
19e	3.41	>44	3.02	>44
19f	35.32	>44	20.64	>44
19g	25.16	>44	22.47	>44
19h	37.75	>44	33.98	>44
19k	1.54	23.05	1.75	17.43
22e	11.08	>44	4.16	>44
22f	7.58	>44	5.16	>44
22g	24.03	>44	5.26	>44
22h	11.39	>44	5.91	>44

nd, not determined.

2.3. Conclusions

We have prepared a large series of new sugar-modified derivatives of previously reported[4] nanomolar cytostatic agents, 7-hetaryl-7-deazaadenine ribonucleosides. In all cases, the synthesis was based on preparation of key 7-iodo-7-deazaadenine nucleoside followed by cross-coupling reactions. All compounds were tested on cytostatic and anti-HCV effects. Many examples of 7-hetaryl-7-deazaadenine 2′-*C*-methyl-ribonucleosides **7**, and 2′-fluoro-2′-deoxyribonucleosides **12** and arabinonucleosides **19** exerted μM cytostatic effects, whereas the 2′-deoxyribonucleosides **22** were entirely inactive. In all cases, the level of activities is significantly lower than the activities of the ribonucleosides.[4] However, these

results are interesting because these compounds are the first examples of biologically active hetaryl-7-deazapurine nucleosides (please note that the corresponding 6-hetaryl-7-deazapurine sugar-modified nucleosides were all inactive[6]). They also clearly indicate that the mechanism of action of 7-hetaryl-7-deazaadenosines[4] is different from the second class of related nanomolar cytostatics, 6-hetaryl-7-deazapurine ribonucleosides reported[3] earlier. Our deeper studies on the mechanisms are under way.

3. Experimental part

Melting points were determined on a Kofler block and are uncorrected. Optical rotations were measured at 25 °C, $[\alpha]_D^{20}$ values are given in 10^{-1} deg cm^2 g^{-1}. NMR spectra were measured at 400.1 MHz for ^{1}H and 100.6 MHz for ^{13}C nuclei, or at 499.8 MHz for ^{1}H and 125.7 MHz for ^{13}C, or at 600.1 MHz for ^{1}H and 150.9 MHz for ^{13}C in $CDCl_3$ (TMS was used as internal standard), DMSO-d_6 (referenced to the residual solvent signal). ^{19}F spectra were recorded at 470.3 MHz. Chemical shifts are given in ppm (δ-scale), coupling constants (*J*) in Hz. Complete assignment of all NMR signals was performed using a combination of H,H-COSY, H,H-ROESY, H,C-HSQC and H,C-HMBC experiments. High resolution mass spectra were measured using electrospray ionization. Reverse phase high performance flash chromatography (HPFC) purifications were performed with Biotage SP1 apparatus on KP-C18-HS columns. 2-Deoxy-2-fluoro-1,3,5-tri-*O*-benzoyl-α-D-arabinofuranose **8** and 1,2,3,5-tetra-*O*-benzoyl-2-*C*-methyl-β-D-ribofuranose **4** were purchased from Nucleo Chemisty Co. (Shenzhen, China).

3.1. 4-Chloro-5-iodo-7-(2-*C*-methyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-7*H*-pyrrolo [2,3-*d*]pyrimidine (5)

To a mixture of 4-chloro-5-iodo-7*H*-pyrrolo[2,3-*d*]pyrimidine **3** (903 mg, 3.23 mmol), 2-*C*-methyl-1,2,3,5-tetra-*O*-benzoyl-β-D-ribofuranose **4** (1.7 g, 2.93 mmol) and DBU (1.3 ml, 8.69 mmol) in MeCN (20 ml), TMSOTf (2.1 ml, 11.62 mmol) was added dropwise at 0 °C and the mixture was then stirred at 70 °C for 24 h. After cooling, the mixture was diluted with AcOEt (100 ml), washed with aq $NaHCO_3$ (sat., 25 ml), H_2O (25 ml) and brine (25 ml). The organic layer was dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica (hexanes/toluene, 1:1; then hexanes/toluene/MeCN, 49:49:2→3:3:4) affording title compound **5** as a white foam (1.04 g, 48%). Product was recrystallized from EtOH. Mp 95–97 °C. $[\alpha]_D^{20}$ −69.3 (*c* 0.280, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): 1.59 (s, 3H, CH_3); 4.72 (td, 1H, $J_{4',3'} = J_{4',5'b} = 5.8$, $J_{4',5'a} = 3.4$, H-4′); 4.85 (dd, 1H, $J_{gem} = 12.2$, $J_{5'b,4'} = 5.8$, H-5′b); 4.95 (dd, 1H, $J_{gem} = 12.2$, $J_{5'a,4'} = 3.4$, H-5′a); 6.03 (d, 1H, $J_{3',4'} = 5.8$, H-3′); 6.95 (s, 1H, H-1′); 7.34, 7.46 and 7.47 (3 × m, 3 × 2H, H-*m*-Bz); 7.54, 7.59 and 7.61 (3 × m, 3 × 1H, H-*p*-Bz); 7.69 (s, 1H, H-6); 7.96, 8.10 and 8.11 (3 × m, 3 × 2H, H-*o*-Bz); 8.75 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 17.92 (CH_3); 52.68 (C-5); 63.33 (CH_2-5′); 75.55 (CH-3′); 80.04 (CH-4′); 84.93 (C-2′); 88.95 (CH-1′); 117.71 (C-4a); 128.49, 128.54 and 128.63 (CH-*m*-Bz); 128.65, 129.50 and 129.61 (C-*i*-Bz); 129.78, 129.83 and 129.92 (CH-*o*-Bz); 132.66 (CH-6); 133.38, 133.66, 133.72 (CH-*p*-Bz); 150.68 (C-7a); 151.17 (CH-2); 153.15 (C-4); 165.09, 165.33 and 166.32 (CO). MS (FAB): *m*/*z* 738 [M+H]. HRMS (FAB) for $C_{33}H_{26}ClIN_3O_7$ [M+H] Calcd: 738.0504. Found: 738.0491. Anal. Calcd for $C_{33}H_{25}ClIN_3O_7$: C, 53.71; H, 3.41; N, 5.69. Found: C 53.91; H 3.29; N 5.38.

3.2. 4-Amino-5-iodo-7-(2-*C*-methyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (6)

A mixture of compound **5** (200 mg, 0.27 mmol) and aq ammonia (25% w/w, 3 ml) in dioxane (3 ml) was stirred in a sealed tube at 120 °C for 10 h. After cooling, the volatiles were evaporated and the crude product was purified by chromatography on silica ($CHCl_3$→$CHCl_3$/MeOH, 8:2) and then re-purified by reverse phase chromatography (0→100% MeOH in H_2O) to afford title compound **6** as white solid (76 mg, 69%). Product was recrystallized from MeOH/MeCN. Mp 207–208 °C. $[\alpha]_D^{20}$ −39.0 (*c* 0.274, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6): 0.67 (s, 3H, CH_3); 3.65 (ddd, 1H, $J_{gem} = 12.1$, $J_{5'b,OH} = 4.8$, $J_{5'b,4'} = 2.7$, H-5′b); 3.81 (ddd, 1H, $J_{gem} = 12.1$, $J_{5'a,OH} = 4.8$, $J_{5'a,4'} = 2.0$, H-5′a); 3.79 (ddd, 1H, $J_{4',3'} = 9.1$, $J_{4',5'} = 2.7$, 2.0, H-4′); 3.93 (bd, 1H, $J_{3',4'} = 9.1$, H-3′); 5.14 (s, 1H, OH-2′); 5.16 (bs, 1H, OH-3′); 5.22 (t, 1H, $J_{OH,5'} = 4.8$, OH-5′); 6.10 (s, 1H, H-1′); 6.67 (bs, 2H, NH_2); 7.82 (s, 1H, H-6); 8.10 (s, 1H, H-2). ^{13}C NMR (151 MHz, DMSO-d_6): 19.89 (CH_3); 51.68 (C-5); 59.46 (CH_2-5′); 71.76 (CH-3′); 78.87 (C-2′); 82.39 (CH-4′); 90.71 (CH-1′); 103.11 (C-4a); 126.81 (CH-6); 149.88 (C-7a); 152.23 (CH-2); 157.43 (C-4). MS (FAB): *m*/*z* 407 [M+H]. HRMS (FAB) for $C_{12}H_{16}IN_4O_4$ [M+H] Calcd: 407.0216. Found: 407.0225. Anal. Calcd for $C_{12}H_{15}IN_4O_4$: C, 35.48; H, 3.72; N, 13.79. Found: C, 35.37; H 3.72; N 13.39.

3.3. 4-Amino-7-(2-*C*-methyl-β-D-ribofuranosyl)-5-phenyl-7*H*-pyrrolo[2,3-*d*]pyrimidine (7a)

An argon purged mixture of compound **6** (49 mg, 0.12 mmol), phenylboronic acid (23 mg, 0.18 mmol), Na_2CO_3 (144 mg, 1.36 mmol), TPPTS (9 mg, 0.016 mmol) and $Pd(OAc)_2$ (1.4 mg, 6.2 μmol) in H_2O/MeCN (2:1, 1.8 ml) was stirred at 80 °C for 1 h. After cooling, volatiles were removed by evaporation and the residue was purified by reverse phase chromatography (0→100% MeOH in H_2O) affording title compound **7a** as white solid (30 mg, 70%). Mp >129 °C (slow melting due to dehydration). $[\alpha]_D^{20}$ −55.7 (*c* 0.226, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6): 0.75 (s, 3H, CH_3); 3.65 (bdd, 1H, $J_{gem} = 12.2$, $J_{5'b,4'} = 2.9$, H-5′b); 3.82 (bdd, 1H, $J_{gem} = 12.2$, $J_{5'a,4'} = 2.1$, H-5′a); 3.86 (ddd, 1H, $J_{4',3'} = 9.1$, $J_{4',5'} = 2.9$, 2.1, H-4′); 4.02 (d, 1H, $J_{3',4'} = 9.1$, H-3′); 5.15 (bs, 3H, OH-2′,3′,5′); 6.10 (bs, 2H, NH_2); 6.23 (s, 1H, H-1′);7.36 (m, 1H, H-*p*-Ph); 7.44–7.50 (m, 4H, H-*o*,*m*-Ph); 7.70 (s, 1H, H-6); 8.16 (s, 1H, H-2). ^{13}C NMR (151 MHz, DMSO-d_6): 20.00 (CH_3); 59.60 (CH_2-5′); 72.01 (CH-3′); 78.88 (C-2′); 82.39 (CH-4′); 90.51 (CH-1′); 100.09 (C-4a); 116.41 (C-5); 120.75 (CH-6); 127.05 (CH-*p*-Ph); 128.64 (CH-*o*-Ph); 129.23 (CH-*m*-Ph); 134.89 (C-*i*-Ph); 150.67 (C-7a); 151.94 (CH-2); 157.49 (C-4). MS (FAB) *m*/*z* 357 [M+H]. HRMS (FAB) for $C_{18}H_{21}N_4O_4$: [M+H] Calcd: 357.1563. Found: 357.1557. Anal. Calcd for $C_{18}H_{20}N_4O_4 \cdot 1.6H_2O$: C, 56.13; H, 6.07; N, 14.54. Found: C, 56.52; H, 5.74; N, 14.14.

3.4. 4-Amino-5-(4-methoxyphenyl)-7-(2-*C*-methyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (7b)

Compound **7b** was prepared as described for **7a** by the reaction of compound **6** (73 mg, 0.18 mmol) and 4-methoxyphenylboronic acid. Yield 47 mg (67%). White solid, mp 127–129 °C. $[\alpha]_D^{20}$ −48.4 (*c* 0.225, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6): 0.74 (s, 3H, CH_3); 3.64 (bdd, 1H, $J_{gem} = 12.21$, $J_{5'b,4'} = 2.9$, H-5′b); 3.80 (s, 3H, CH_3O); 3.81 (bdd, 1H, $J_{gem} = 12.1$, $J_{5'a,4'} = 2.1$, H-5′a); 3.85 (ddd, 1H, $J_{4',3'} = 9.1$, $J_{4',5'} = 2.9$, 2.1, H-4′); 4.01 (d, 1H, $J_{3',4'} = 9.1$, H-3′); 5.13 (bs, 3H, OH-2′,3′,5′); 6.08 (bs, 2H, NH_2); 6.22 (s, 1H, H-1′); 7.04 (m, 2H, H-*m*-C_6H_4OMe); 7.36 (m, 2H, H-*o*-C_6H_4OMe); 7.60 (s, 1H, H-6); 8.14 (s, 1H, H-2). ^{13}C NMR (151 MHz, DMSO-d_6): 19.99 (CH_3); 55.39 (CH_3O); 59.61 (CH_2-5′); 72.03 (CH-3′); 78.87 (C-2′); 82.34 (CH-4′); 90.47 (CH-1′); 100.31 (C-4a); 114.65 (CH-*m*-C_6H_4OMe); 116.06 (C-5); 120.14 (CH-6); 127.04 (C-*i*-C_6H_4OMe); 129.91 (CH-*o*-C_6H_4OMe); 150.45 (C-7a); 151.85 (CH-2); 157.51 (C-4); 158.58 (C-*p*-C_6H_4OMe). MS (FAB) *m*/*z* 387 [M+H]. HRMS (FAB) for $C_{19}H_{23}N_4O_5$ [M+H] Calcd: 387.1668. Found: 387.1665. Anal. Calcd for $C_{19}H_{22}N_4O_5 \cdot 1.6H_2O$: C, 54.96; H, 6.12; N, 13.49. Found: C, 55.30; H, 5.91; N, 13.18.

3.5. 4-Amino-7-(2-*C*-methyl-β-D-ribofuranosyl)-5-(naphthalen-1-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (7c)

Compound **7c** was prepared as described for **7a** by the reaction of compound **6** (92 mg, 0.23 mmol) and naphthalene-1-boronic acid. Yield 38 mg (41%). Crude product was prepurified by chromatography on silica (0→20% MeOH in $CHCl_3$), before final reverse phase chromatography. Tan solid, mp 142–144 °C. $[\alpha]_D^{20}$ −58.6 (*c* 0.239, MeOH). ^{1}H NMR (500 MHz, DMSO-d_6, T = 353 K): 0.90 (s, 3H, CH_3); 3.67 (dd, 1H, J_{gem} = 12.2, $J_{5'b,4'}$ = 3.5, H-5′b); 3.83 (dd, 1H, J_{gem} = 12.2, $J_{5'a,4'}$ = 2.3, H-5′a); 3.91 (ddd, 1H, $J_{4',3'}$ = 8.9, $J_{4',5'}$ = 3.5, 2.3, H-4′); 4.04 (d, 1H, $J_{3',4'}$ = 8.9, H-3′); 4.89 (bs, 3H, OH-2′,3′,5′); 5.39 (bs, 2H, NH_2); 6.34 (s, 1H, H-1′); 7.500 (ddd, 1H, $J_{7,8}$ = 8.3, $J_{7,6}$ = 6.9, $J_{7,5}$ = 1.3, H-7-naphth); 7.502 (dd, 1H, $J_{2,3}$ = 6.9, $J_{2,4}$ = 1.3, H-2-naphth); 7.56 (ddd, 1H, $J_{6,5}$ = 8.1, $J_{6,7}$ = 6.9, $J_{6,8}$ = 1.3, H-6-naphth); 7.60 (dd, 1H, $J_{3,4}$ = 8.3, $J_{3,2}$ = 6.9, H-3-naphth); 7.63 (s, 1H, H-6); 7.75 (dddd, 1H, $J_{8,7}$ = 8.3, $J_{8,6}$ = 1.3, $J_{8,4}$ = 1.0, $J_{8,5}$ = 0.8, H-8-naphth); 7.98 (ddd, 1H, $J_{4,3}$ = 8.3, $J_{4,2}$ = 1.3, $J_{4,8}$ = 1.0, H-4-naphth); 8.01 (ddd, 1H, $J_{5,6}$ = 8.1, $J_{5,7}$ = 1.3, $J_{5,8}$ = 0.8, H-5-naphth); 8.19 (s, 1H, H-2). ^{13}C NMR (151 MHz, DMSO-d_6, *T* = 353 K): 19.73 (CH_3); 59.70 (CH_2-5′); 72.30 (CH-3′); 78.69 (C-2′); 82.28 (CH-4′); 90.64 (CH-1′); 102.10 (C-4a); 113.02 (C-5); 121.50 (CH-6); 125.27 (CH-8-naphth); 125.38 (CH-3-naphth); 125.98 (CH-6-naphth); 126.42 (CH-7-naphth); 127.82 (CH-4-naphth); 128.12 (CH-2,5-naphth); 131.63 (C-1-naphth); 132.13 (C-8a-naphth); 133.39 (C-4a-naphth); 150.05 (C-7a); 151.61 (CH-2); 156.96 (C-4). MS (ESI) *m*/*z* 407 [M+H], 429 [M+Na]. HRMS (ESI) for $C_{22}H_{23}N_4O_4$ [M+H] Calcd: 407.1714. Found: 407.1704. Anal. Calcd for $C_{22}H_{22}N_4O_4{\cdot}1.5H_2O$: C, 60.96; H, 5.81; N, 12.93. Found: C, 61.30; H, 5.72; N, 13.28.

3.6. 4-Amino-7-(2-*C*-methyl-β-D-ribofuranosyl)-5-(naphthalen-2-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (7d)

Compound **7d** was prepared as described for **7a** by the reaction of compound **6** (91 mg, 0.22 mmol) and naphthalene-2-boronic acid. Yield 58 mg (65%). Crude product was prepurified by chromatography on silica (0→20% MeOH in $CHCl_3$), before final reverse phase chromatography. Cream solid, mp 143–145 °C. $[\alpha]_D^{20}$ −64.3 (*c* 0.253, MeOH). ^{1}H NMR (500 MHz, DMSO-d_6): 0.79 (s, 3H, CH_3); 3.66 (ddd, 1H, J_{gem} = 12.6, $J_{5'b,OH}$ = 5.0, $J_{5'b,4'}$ = 2.9, H-5′b); 3.84 (ddd, 1H, J_{gem} = 12.6, $J_{5'a,OH}$ = 5.0, $J_{5'a,4'}$ = 2.1, H-5′a); 3.88 (ddd, 1H, $J_{4',3'}$ = 9.1, $J_{4',5'}$ = 2.9, 2.1, H-4′); 4.06 (bdd, 1H, $J_{3',4'}$ = 9.1, $J_{3',OH}$ = 4.6, H-3′); 5.11–5.17 (bm, 3H, OH-2′,3′,5′); 6.19 (bs, 2H, NH_2); 6.27 (s, 1H, H-1′); 7.52 (m, 1H, H-6-naphth); 7.55 (m, 1H, H-7-naphth); 7.62 (dd, 1H, $J_{3,4}$ = 8.5, $J_{3,1}$ = 1.8, H-3-naphth); 7.81 (s, 1H, H-6); 7.94–7.97 (m, 3H, H-1,5,8-naphth); 8.01 (d, 1H, $J_{4,3}$ = 8.5, H-4-naphth); 8.18 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 20.03 (CH_3); 59.66 (CH_2-5′); 72.08 (CH-3′); 78.90 (C-2′); 82.41 (CH-4′); 90.57 (CH-1′); 100.24 (C-4a); 116.45 (C-5); 121.14 (CH-6); 126.10 (CH-6-naphth); 126.76 (CH-7-naphth); 126.82 (CH-1-naphth); 127.23 (CH-3-naphth); 127.87 and 128.02 (CH-5,8-naphth); 128.70 (CH-4-naphth); 132.00 (C-4a-naphth); 132.35 (C-1-naphth); 133.46 (C-8a-naphth); 150.82 (C-7a); 152.02 (CH-2); 157.61 (C-4). MS (ESI) *m*/*z* 407 [M+H], 429 [M+Na]. HRMS (ESI) for $C_{22}H_{23}N_4O_4$ [M+H] Calcd: 407.1714. Found: 407.1715. Anal. Calcd for $C_{22}H_{22}N_4O_4{\cdot}1.3H_2O$: C, 61.47; H, 5.77; N, 13.03. Found: C, 61.83; H, 5.51; N, 12.65.

3.7. 4-Amino-5-(furan-2-yl)-7-(2-*C*-methyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (7e)

Compound **7e** was prepared as described for **7a** by the reaction of compound **6** (97 mg, 0.24 mmol) and furan-2-boronic acid. Yield 46 mg (55%). White solid, mp 130–132 °C. $[\alpha]_D^{20}$ −53.3 (*c* 0.250, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6): 0.72 (s, 3H, CH_3); 3.68 and 3.85 (2 × bd, 2H, J_{gem} = 12.0, H-5′); 3.87 (ddd, 1H, $J_{4',3'}$ = 9.1, $J_{4',5'}$ = 2.9, 2.0, H-4′); 4.00 (bd, 1H, $J_{3',4'}$ = 9.1, H-3′); 5.16 (bs, 2H, OH-2′,3′); 5.25 (bs, 1H, OH-5′); 6.19 (s, 1H, H-1′); 6.58 (dd, 1H, $J_{3,4}$ = 3.3, $J_{3,5}$ = 0.8, H-3-furyl); 6.60 (dd, 1H, $J_{4,3}$ = 3.3, $J_{4,5}$ = 1.9, H-4-furyl); 6.90 (bs, 2H, NH_2); 7.78 (dd, 1H, $J_{5,4}$ = 1.9, $J_{5,3}$ = 0.8, H-5-furyl); 8.01 (s, 1H, H-6); 8.14 (s, 1H, H-2). ^{13}C NMR (151 MHz, DMSO-d_6): 19.91 (CH_3); 59.66 (CH_2-5′); 71.92 (CH-3′); 78.85 (C-2′); 82.48 (CH-4′); 90.60 (CH-1′); 99.03 (C-4a); 105.22 (CH-3-furyl); 106.10 (C-5); 112.13 (CH-4-furyl); 120.07 (CH-6); 142.17 (CH-5-furyl); 148.98 (C-2-furyl); 150.60 (C-7a); 152.35 (CH-2); 157.46 (C-4). MS (ESI) *m*/*z* 347 [M+H], 369 [M+Na]. HRMS (ESI) for $C_{16}H_{19}N_4O_5$ [M+H] Calcd: 347.1355. Found: 347.1347. Anal. Calcd for $C_{16}H_{18}N_4O_5{\cdot}0.7H_2O$: C, 53.54; H, 5.45; N, 15.61. Found: C, 53.86; H, 5.48; N, 15.22.

3.8. 4-Amino-7-(2-*C*-methyl-β-D-ribofuranosyl)-5-(thiophen-2-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (7f)

Compound **7f** was prepared as described for **7a** by the reaction of compound **6** (100 mg, 0.25 mmol) and thiophene-2-boronic acid. Yield 69 mg (77%). White solid. Mp 130–132 °C. $[\alpha]_D^{20}$ −51.4 (*c* 0.255, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6): 0.73 (s, 3H, CH_3); 3.65 (dd, 1H, J_{gem} = 12.3, $J_{5'b,4'}$ = 2.9, H-5′b); 3.83 (dd, 1H, J_{gem} = 12.3, $J_{5'a,4'}$ = 2.1, H-5′a); 3.86 (ddd, 1H, $J_{4',3'}$ = 9.1, $J_{4',5'}$ = 2.9, 2.1, H-4′); 4.00 (bd, 1H, $J_{3',4'}$ = 9.1, H-3′); 5.20 (bs, 3H, OH-2′,3′,5′); 6.19 (s, 1H, H-1′); 6.30 (bs, 2H, NH_2); 7.13 (dd, 1H, $J_{3,4}$ = 3.5, $J_{3,5}$ = 1.2, H-3-thienyl); 7.16 (dd, 1H, $J_{4,5}$ = 5.2, $J_{4,3}$ = 3.5, H-4-thienyl); 7.55 (dd, 1H, $J_{5,4}$ = 5.2, $J_{5,3}$ = 1.1, H-2-thienyl); 7.82 (s, 1H, H-6); 8.16 (s, 1H, H-2). ^{13}C NMR (151 MHz, DMSO-d_6): 19.96 (CH_3); 59.37 (CH_2-5′); 71.76 (CH-3′); 78.88 (C-2′); 82.38 (CH-4′); 90.53 (CH-1′); 100.27 (C-4a); 108.51 (C-5); 121.64 (CH-6); 125.93 (CH-5-thienyl); 126.42 (CH-3-thienyl); 128.53 (CH-4-thienyl); 136.04 (C-2-thienyl); 150.40 (C-7a); 152.26 (CH-2); 157.47 (C-4). MS (ESI) *m*/*z* 363 [M+H], 385 [M+Na]. HRMS (ESI) for $C_{16}H_{19}N_4O_4S$ [M+H] Calcd: 363.1127. Found: 363.1121. Anal. Calcd for $C_{16}H_{18}N_4O_4S{\cdot}0.95H_2O$: C, 50.64; H, 5.28; N, 14.76. Found: C, 51.03; H, 5.06; N, 14.40.

3.9. 4-Amino-5-(furan-3-yl)-7-(2-*C*-methyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (7g)

Compound **7g** was prepared as described for **7a** by the reaction of compound **6** (50 mg, 0.12 mmol) and furan-3-boronic acid. Reaction time 2.5 h. Yield 25 mg (59%) of white solid. Mp >123 °C (slow melting due to dehydration). $[\alpha]_D^{20}$ −54.5 (*c* 0.217, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6): 0.72 (s, 3H, CH_3); 3.65 (dd, 1H, J_{gem} = 12.2, $J_{5'b,4'}$ = 3.0, H-5′b); 3.82 (dd, 1H, J_{gem} = 12.2, $J_{5'a,4'}$ = 2.1, H-5′a); 3.85 (ddd, 1H, $J_{4',3'}$ = 9.1, $J_{4',5'}$ = 3.0, 2.1, H-4′); 3.99 (d, 1H, $J_{3',4'}$ = 9.1, H-3′); 5.16 (bs, 3H, OH-2′,3′,5′); 6.19 (s, 1H, H-1′); 6.25 (bs, 2H, NH_2); 6.66 (dd, 1H, $J_{4,5}$ = 1.7, $J_{4,2}$ = 0.8, H-4-furyl); 7.65 (s, 1H, H-6); 7.79 (t, 1H, $J_{5,2}$ = $J_{5,4}$ = 1.7, H-5-furyl); 7.80 (dd, 1H, $J_{2,5}$ = 1.7, $J_{2,4}$ = 0.8, H-2-furyl); 8.13 (s, 1H, H-2). ^{13}C NMR (151 MHz, DMSO-d_6): 19.99 (CH_3); 59.74 (CH_2-5′); 72.08 (CH-3′); 78.87 (C-2′); 82.41 (CH-4′); 90.56 (CH-1′); 100.67 (C-4a); 106.27 (C-5); 111.78 (CH-4-furyl); 119.00 (C-3-furyl); 120.61 (CH-6); 139.79 (CH-2-furyl); 144.43 (CH-5-furyl); 150.52 (C-7a); 152.03 (CH-2); 157.68 (C-4). MS (ESI) *m*/*z* 347 [M+H]. HRMS (ESI) for $C_{16}H_{19}N_4O_5$ [M+H] Calcd: 347.1350. Found: 347.1349. Anal. Calcd for $C_{16}H_{18}N_4O_5{\cdot}1.7H_2O$: C, 50.98; H, 5.72; N, 14.86. Found: C, 51.30; H, 5.33; N, 14.46.

3.10. 4-Amino-7-(2-*C*-methyl-β-D-ribofuranosyl)-5-(thiophen-3-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (7h)

Compound **7h** was prepared as described for **7a** by the reaction of compound **6** (101 mg, 0.25 mmol) and thiophene-3-boronic

acid. Yield 56 mg (62%) of white solid. Mp 128–130 °C. $[\alpha]_D^{20}$ −60.3 (*c* 0.222, MeOH). ^{1}H NMR (600 MHz, DMSO-d_6): 0.74 (s, 3H, CH_3); 3.65 (ddd, 1H, J_{gem} = 12.1, $J_{5'b,OH}$ = 4.8, $J_{5'b,4'}$ = 2.9, H-5′b); 3.82 (ddd, 1H, J_{gem} = 12.1, $J_{5'a,OH}$ = 4.8, $J_{5'a,4'}$ = 2.1, H-5′a); 3.85 (ddd, 1H, $J_{4',3'}$ = 9.0, $J_{4',5'}$ = 2.9, 2.1, H-4′); 4.00 (dd, 1H, $J_{3',4'}$ = 9.0, $J_{3',OH}$ = 7.1, H-3′); 5.12 (d, 1H, $J_{OH,3'}$ = 7.1, OH-3′); 5.13 (s, 1H, OH-2′); 5.16 (t, 1H, $J_{OH,5'}$ = 4.8, OH-5′); 6.20 (s, 1H, H-1′); 6.20 (bs, 2H, NH_2); 7.24 (dd, 1H, $J_{4,5}$ = 4.9, $J_{4,2}$ = 1.4, H-4-thienyl); 7.49 (dd, 1H, $J_{2,5}$ = 2.9, $J_{2,4}$ = 1.4, H-2-thienyl); 7.698 (dd, 1H, $J_{5,4}$ = 4.9, $J_{5,2}$ = 2.9, H-5-thienyl); 7.70 (s, 1H, H-6); 8.14 (s, 1H, H-2). ^{13}C NMR (151 MHz, DMSO-d_6): 20.01 (CH_3); 59.67 (CH_2-5′); 72.04 (CH-3′); 78.89 (C-2′); 82.41 (CH-4′); 90.55 (CH-1′); 100.44 (C-4a); 111.08 (C-5); 120.73 (CH-6); 122.11 (CH-2-thienyl); 127.66 (CH-5-thienyl); 128.72 (CH-4-thienyl); 135.16 (C-3-thienyl); 150.38 (C-7a); 151.96 (CH-2); 157.57 (C-4). IR (KBr): 3475, 3351, 3240, 3200, 3120, 3107, 1621, 1594, 1575, 1549, 1510, 1465, 1409, 1378, 1346, 1297, 1139, 1123, 1072, 1045, 861, 788. MS (ESI) *m*/*z* 363 [M+H], 385 [M+Na]. HRMS (ESI) for $C_{16}H_{19}N_4O_4S$ [M+H] Calcd: 363.1122. Found: 363.1122. Anal. Calcd for $C_{16}H_{18}N_4O_4S{\cdot}1.1H_2O$: C, 50.28; H, 5.33; N, 14.66. Found: C, 50.42; H, 5.20; N, 14.45.

3.11. 4-Amino-5-(benzofuran-2-yl)-7-(2-*C*-methyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (7i)

Compound **7i** was prepared as described for **7a** by the reaction of compound **6** (100 mg, 0.25 mmol) and benzofuran-2-boronic acid. Yield 64 mg (66%). White solid. Mp 248 °C (dec). $[\alpha]_D^{20}$ −55.0 (*c* 0.220, MeOH). ^{1}H NMR (500 MHz, DMSO-d_6): 0.76 (s, 3H, CH_3); 3.72 (ddd, 1H, J_{gem} = 12.5, $J_{5'b,OH}$ = 5.0, $J_{5'b,4'}$ = 2.9, H-5′b); 3.88 (ddd, 1H, J_{gem} = 12.5, $J_{5'a,OH}$ = 5.0, $J_{5'a,4'}$ = 2.0, H-5′a); 3.90 (ddd, 1H, $J_{4',3'}$ = 9.2, $J_{4',5'}$ = 2.9, 2.0, H-4′); 4.04 (dd, 1H, $J_{3',4'}$ = 9.2, $J_{3',OH}$ = 7.0, H-3′); 5.17 (d, 1H, $J_{OH,3'}$ = 7.0, OH-3′); 5.19 (s, 1H, OH-2′); 5.28 (t, 1H, $J_{OH,5'}$ = 5.0, OH-5′); 6.23 (s, 1H, H-1′); 6.98 (bs, 2H, NH_2); 7.04 (d, 1H, $J_{3,7}$ = 1.0, H-3-benzofuryl); 7.27 (td, 1H, $J_{5,4}$ = $J_{5,6}$ = 7.3, $J_{5,7}$ = 1.4, H-5-benzofuryl); 7.29 (td, 1H, $J_{6,5}$ = $J_{6,7}$ = 7.3, $J_{6,4}$ = 1.7, H-6-benzofuryl); 7.61–7.67 (m, 2H, H-4,7-benzofuryl); 8.19 (s, 1H, H-2); 8.26 (s, 1H, H-6). ^{13}C NMR (125.7 MHz, DMSO-d_6): 19.96 (CH_3); 59.72 (CH_2-5′); 71.97 (CH-3′); 78.91 (C-2′); 82.59 (CH-4′); 90.74 (CH-1′); 99.19 (C-4a); 101.58 (CH-3-benzofuryl); 105.47 (C-5); 111.30 (CH-7-benzofuryl); 120.81 (CH-4-benzofuryl); 122.32 (CH-6); 123.73 (CH-5-benzofuryl); 124.08 (CH-6-benzofuryl); 129.01 (C-3a-benzofuryl); 150.94 (C-7a); 151.45 (C-2-benzofuryl); 152.58 (CH-2); 154.00 (C-7a-benzofuryl); 157.50 (C-4). MS (ESI, negative mode) *m*/*z* 395 (M-H). HRMS (ESI, negative mode) for $C_{20}H_{19}N_4O_5$: [M-H] Calcd: 395.1350. Found: 395.1358. Anal. Calcd for $C_{20}H_{20}N_4O_5{\cdot}{}^1/_3H_2O$: C, 59.70; H, 5.18; N, 13.92. Found: C, 59.98; H, 5.13; N, 13.46.

3.12. 4-Chloro-5-iodo-7-(2-deoxy-2-fluoro-3,5-di-*O*-benzoyl-β-D-arabinofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (10)

A mixture of powdered KOH (875 mg, 85%, 13.28 mmol), TDA-1 (0.13 ml, 0.4 mmol) in dry MeCN (50 ml) was stirred at rt for 10 min before 6-chloro-7-iodo-7-deazapurine **3** (1.75 g, 6.26 mmol) was added. Stirring was continued for 15 min and then 2-deoxy-2-fluoro-3,5-di-*O*-benzoyl-β-D-arabinofuranosyl bromide **9**[15] (3.17 g, 7.5 mmol, prepared from **8**) in MeCN (50 ml) was added at once. The mixture was vigorously stirred at rt for 45 min (during that time highly insoluble product precipitated out). The mixture was quenched with aq NH_4Cl (sat, 200 ml) and extracted with dichloromethane (200 ml, then 2 × 50 ml). Combined organics were dried over $MgSO_4$ and volatiles removed in vacuo. Resulting solid was crystallized from chloroform/2-propanol affording nucleoside **10** as beige powder (3.32 g, 85%). Alternatively the crude product can be purified by column chromatography on silica (hexanes/AcOEt, 6:1). Product **10** crystallizes from hexanes/AcOEt as colorless needles. Mp 202–204 °C. ^{1}H NMR (499.8 MHz, DMSO-d_6): 4.67 (dddd, 1H, $J_{4',5'}$ = 5.5, 3.7, $J_{4',3'}$ = 4.9, $J_{H,F}$ = 0.4, H-4′); 3.72 (dd, 1H, J_{gem} = 12.0, $J_{5'b,4'}$ = 5.5, H-5′b); 4.79 (dd, 1H, J_{gem} = 12.0, $J_{5'a,4'}$ = 3.7, H-5′a); 5.74 (ddd, 1H, $J_{H,F}$ = 50.8, $J_{2',1'}$ = 4.2, $J_{2',3'}$ = 2.5, H-2'); 5.89 (ddd, 1H, $J_{H,F}$ = 19.3, $J_{3',4'}$ = 4.9, $J_{3',2'}$ = 2.5, H-3′); 6.90 (dd, 1H, $J_{H,F}$ = 17.7, $J_{1',2'}$ = 4.2, H-1'); 7.53 (m, 2H, H-*m*-Bz-5′); 7.59 (m, 2H, H-*m*-Bz-3′); 7.67 (m, 1H, H-*p*-Bz-5′); 7.73 (m, 1H, H-*p*-Bz-3′); 8.00 (bs, 1H, H-6); 8.01 (m, 2H, H-*o*-Bz-5′); 8.09 (m, 2H, H-*o*-Bz-3′); 8.72 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 54.59 (C-5); 63.82 (CH_2-5′); 76.43 (d, $J_{C,F}$ = 28.6, CH-3′); 78.34 (d, $J_{C,F}$ = 3.4, CH-4′); 82.39 (d, $J_{C,F}$ = 16.6, CH-1′); 93.44 (d, $J_{C,F}$ = 192.1, CH-2′); 116.61 (C-4a); 128.84 (C-*i*-Bz-3′); 129.03, 129.04 (CH-*m*-Bz-3′,5′); 129.42 (CH-*o*-Bz-5′); 129.44 (C-*i*-Bz-5′); 129.87 (CH-*o*-Bz-3′); 133.80 (CH-*p*-Bz-5′); 134.19 (CH-*p*-Bz-3′); 134.64 (d, $J_{C,F}$ = 4.6, CH-6); 150.75 (C-7a); 151.29 (CH-2); 151.65 (C-4); 165.01 (CO-Bz-3′); 165.70 (CO-Bz-5′). ^{19}F NMR (470.3 MHz, DMSO-d_6):-193.91. MS (ESI) *m*/*z* 622 [M+H], 644 [M+Na]. HRMS (ESI) for $C_{25}H_{19}N_3ClFIO_5$ [M+H] Calcd: 622.0036. Found: 622.00365.

3.13. 4-Amino-5-iodo-7-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (11)

A suspension of nucleoside **10** (3.31 g, 5.32 mmol) in aq ammonia (25% w/w, 15 ml) and dioxane (15 ml) was stirred in a steel bomb at 120 °C for 16 h. After cooling the volatiles were evaporated and the residue was co-evaporated with silica and chromatographed on the column of silica (4% MeOH in $CHCl_3$) affording 7-iodo-7-deazaadenine nucleoside **11** as white crystalline solid (1.77 g, 84%). Compound was recrystallized from H_2O. Mp 214–216 °C. $[\alpha]_D$ +28 (c 0.429, DMSO). ^{1}H NMR (499.8 MHz, DMSO-d_6): 3.60 (dddd, 1H, J_{gem} = 11.9, $J_{5'b,OH}$ = 5.7, $J_{5'b,4'}$ = 5.1, $J_{H,F}$ = 0.9, H-5′b); 3.66 (dddd, 1H, J_{gem} = 11.9, $J_{5'a,OH}$ = 5.7, $J_{5'a,4'}$ = 4.1, $J_{H,F}$ = 1.5, H-5′a); 3.79 (tdd, 1H, $J_{4',5'}$ = 5.1, 4.1, $J_{4',3'}$ = 5.1, $J_{H,F}$ = 0.8, H-4′); 4.35 (dtd, 1H, $J_{H,F}$ = 19.0, $J_{3',4'}$ = $J_{3',OH}$ = 5.1, $J_{3',2'}$ = 3.8, H-3′); 5.08 (t, 1H, $J_{OH,5'}$ = 5.7, OH-5′); 5.10 (ddd, 1H, $J_{H,F}$ = 52.7, $J_{2',1'}$ = 4.5, $J_{2',3'}$ = 3.8, H-2′); 5.90 (d, 1H, $J_{OH,3'}$ = 5.1, OH-3′); 6.53 (dd, 1H, $J_{H,F}$ = 14.9, $J_{1',2'}$ = 4.5, H-1′); 6.71 (bs, 2H, NH_2); 7.53 (d, 1H, $J_{H,F}$ = 2.1, H-6); 8.12 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 52.24 (C-5); 60.48 (CH_2-5′); 72.78 (d, $J_{C,F}$ = 23.3, CH-3′); 81.25 (d, $J_{C,F}$ = 16.9, CH-1′); 83.19 (d, $J_{C,F}$ = 5.4, CH-4′); 95.89 (d, $J_{C,F}$ = 191.7, CH-2′); 102.91 (C-4a); 127.88 (d, $J_{C,F}$ = 3.5, CH-6); 149.96 (C-7a); 152.36 (CH-2); 157.38 (C-4). ^{19}F NMR (470.3 MHz, DMSO-d_6): −194.45. MS (ESI) *m*/*z* 395 [M+H], 417 [M+Na]. HRMS (ESI) for $C_{11}H_{13}N_4FIO_3$ [M+H] Calcd: 395.0011. Found: 395.0010. Calcd for $C_{11}H_{12}N_4FIO_3{\cdot}H_2O$: C, 32.06; H, 3.42; N, 13.59. Found: C, 32.40; H, 3.23; N, 13.21.

3.14. 4-Amino-7-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-5-phenyl-7*H*-pyrrolo[2,3-*d*]pyrimidine (12a)

An argon purged mixture of compound **11** (276 mg, 0.70 mmol), phenylboronic acid (127 mg, 1.04 mmol), Na_2CO_3 (221 mg, 2.08 mmol), TPPTS (49 mg, 0.086 mmol) and $Pd(OAc)_2$ (8 mg, 0.035 mmol) in H_2O/MeCN (2:1, 5 ml) was stirred at 80 °C for 3 h. After cooling, the mixture was co-evaporated with silica and column chromatography on silica (3% MeOH in $CHCl_3$) afforded product **12a** as colorless foam (207 mg, 86%). Crystallization from H_2O (little MeOH) gave long colorless needles. Mp 118–120 °C. $[\alpha]_D$ +26.8 (c 0.574, DMSO). ^{1}H NMR (499.8 MHz, DMSO-d_6): 3.62 (ddd, 1H, J_{gem} = 11.8, $J_{5'b,OH}$ = 5.8, $J_{5'b,4'}$ = 5.4, H-5′b); 3.67 (dddd, 1H, J_{gem} = 11.8, $J_{5'a,OH}$ = 5.8, $J_{5'a,4'}$ = 4.4, $J_{H,F}$ = 1.4, H-5′a); 3.79 (m, 1H, $J_{4',5'}$ = 5.4, 4.4, $J_{4',3'}$ = 5.0, $J_{H,F}$ = 0.8, H-4′); 4.40 (dtd, 1H, $J_{H,F}$ = 19.0, $J_{3',4'}$ = $J_{3',OH}$ = 5.0, $J_{3',2'}$ = 3.7, H-3′); 5.06 (t, 1H, $J_{OH,5'}$ = 5.8, OH-5'); 5.16 (ddd, 1H, $J_{H,F}$ = 52.8, $J_{2',1'}$ = 4.5, $J_{2',3'}$ = 3.7, H-2′); 5.90 (t, 1H, $J_{OH,3'}$ = 5.0, OH-3′); 6.16 (bs, 2H, NH_2); 6.64 (dd, 1H, $J_{H,F}$ = 15.4,

$J_{1',2'}$ = 4.5, H-1′); 7.38 (m, 1H, H-*p*-Ph); 7.42 (d, 1H, $J_{H,F}$ = 2.2, H-6); 7.48 (m, 4H, H-*o*,*m*-Ph); 8.18 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 60.60 (CH_2-5′); 72.97 (d, $J_{C,F}$ = 23.3, CH-3′); 81.15 (d, $J_{C,F}$ = 16.8, CH-1′); 83.17 (d, $J_{C,F}$ = 5.2, CH-4′); 96.02 (d, $J_{C,F}$ = 191.7, CH-2′); 100.06 (C-4a); 116.60 (C-5); 121.81 (d, $J_{C,F}$ = 3.4, CH-6); 127.16 (CH-*p*-Ph); 128.59 (CH-*o*-Ph); 129.21 (CH-*m*-Ph); 134.49 (C-*i*-Ph); 150.82 (C-7a); 152.12 (CH-2); 157.46 (C-4). ^{19}F NMR (470.3 MHz, DMSO-d_6): -197.87. MS (ESI) *m*/*z* 345 [M+H], 367 [M+Na]. HRMS (ESI) for $C_{17}H_{18}N_4FO_3$ [M+H] Calcd: 345.1357. Found: 345.1357. Calcd for $C_{17}H_{17}N_4FO_3{\cdot}H_2O$: C, 56.35; H, 5.29; N, 15.46. Found: C, 56.05; H, 5.14; N, 15.22.

3.15. 4-Amino-7-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-5-(furan-2-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (12e)

An argon purged mixture of iodide **11** (197 mg, 0.5 mmol), 2-(tributylstannyl)furan (232 mg, 0.65 mmol) and $PdCl_2(PPh_3)_2$ (18 mg, 0.025 mmol) in DMF (2 ml) was stirred at 100 °C for 2 h. After cooling volatiles were removed in vacuo and the residue was several times co-evaporated with toluene and finally with silica. Column chromatography on silica (0→4% MeOH in $CHCl_3$) afforded product **12e** as a solid foam (125 mg, 75%). Compound crystallized from MeOH/H_2O as beige microcrystalline needles. Mp 209–211 °C. $[\alpha]_D$ +39.1 (c 0.417, DMSO). ^{1}H NMR (499.8 MHz, DMSO-d_6): 3.65 (dddd, 1H, J_{gem} = 11.9, $J_{5'b,OH}$ = 5.8, $J_{5'b,4'}$ = 5.3, $J_{H,F}$ = 0.7, H-5′b); 3.70 (dddd, 1H, J_{gem} = 11.9, $J_{5'a,OH}$ = 5.8, $J_{5'a,4'}$ = 4.3, $J_{H,F}$ = 1.5, H-5′a); 3.83 (dddd, 1H, $J_{4',5'}$ = 5.3, 4.3, $J_{4',3'}$ = 5.0, $J_{H,F}$ = 0.8, H-4′); 4.39 (dtd, 1H, $J_{H,F}$ = 19.1, $J_{3',OH}$ = $J_{3',4'}$ = 5.0, $J_{3',2'}$ = 3.7, H-3′); 5.11 (t, 1H, $J_{OH,5'}$ = 5.8, OH-5′); 5.15 (ddd, 1H, $J_{H,F}$ = 52.8, $J_{2',1'}$ = 4.5, $J_{2',3'}$ = 3.7, H-2′); 5.92 (d, 1H, $J_{OH,3'}$ = 5.0, OH-3′); 6.61 (dd, 1H, $J_{H,F}$ = 15.3, $J_{1',2'}$ = 4.5, H-1′); 6.61 (dd, 1H, $J_{4,3}$ = 3.3, $J_{4,5}$ = 1.8, H-4-furyl); 6.70 (dd, 1H, $J_{3,4}$ = 3.3, $J_{3,5}$ = 0.8, H-3-furyl); 6.93 (bs, 2H, NH_2); 7.71 (d, 1H, $J_{H,F}$ = 2.1, H-6); 7.78 (dd, 1H, $J_{5,4}$ = 1.8, $J_{5,3}$ = 0.8, H-5-furyl); 8.16 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 60.68 (CH_2-5′); 73.03 (d, $J_{C,F}$ = 23.4, CH-3′); 81.34 (d, $J_{C,F}$ = 16.9, CH-1′); 83.32 (d, $J_{C,F}$ = 5.0, CH-4′); 95.96 (d, $J_{C,F}$ = 191.8, CH-2′); 98.96 (C-4a); 105.58 (CH-3-furyl); 106.52 (C-5); 112.14 (CH-4-furyl); 121.15 (d, $J_{C,F}$ = 3.2, CH-6); 142.27 (CH-5-furyl); 148.62 (C-2-furyl); 150.77 (C-7a); 152.54 (CH-2); 157.46 (C-4). ^{19}F NMR (470.3 MHz, DMSO-d_6): -194.40. MS (ESI) *m*/*z* 335 [M+H], 357 [M+Na]. HRMS (ESI) for $C_{15}H_{16}N_4FO_4$ [M+H] Calcd: 335.1150. Found: 335.1150. Calcd for $C_{15}H_{15}N_4FO_4{\cdot}0.1H_2O$: C, 53.6; H, 4.56; N, 16.67. Found: C, 53.44; H, 4.40; N, 16.52.

3.16. 4-Amino-7-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-5-(thiophen-2-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (12f)

An argon purged mixture of iodide **11** (197 mg, 0.5 mmol), 2-(tributylstannyl)thiophene (242 mg, 0.65 mmol) and $PdCl_2(PPh_3)_2$ (18 mg, 0.025 mmol) in DMF (2 ml) was stirred at 100 °C for 2 h. After cooling volatiles were removed in vacuo and the residue was several times co-evaporated with toluene and finally with silica. Column chromatography on silica (0→4% MeOH in $CHCl_3$) afforded product **12f** as beige solid (144 mg, 82%). Mp 99–101 °C. $[\alpha]_D$ +35.4 (c 0.475, DMSO). ^{1}H NMR (499.8 MHz, DMSO-d_6): 3.61 (dddd, 1H, J_{gem} = 12.1, $J_{5'b,OH}$ = 5.7, $J_{5'b,4'}$ = 5.0, $J_{H,F}$ = 0.6, H-5′b); 3.67 (dddd, 1H, J_{gem} = 12.1, $J_{5'a,OH}$ = 5.7, $J_{5'a,4'}$ = 4.0, $J_{H,F}$ = 1.3, H-5′a); 3.81 (m, 1H, $J_{4',3'}$ = 5.4, $J_{4',5'}$ = 5.0, 4.0, $J_{H,F}$ = 0.9, H-4′); 4.39 (dddd, 1H, $J_{H,F}$ = 19.2, $J_{3',4'}$ = 5.4, $J_{3',OH}$ = 5.0, $J_{3',2'}$ = 3.8, H-3′); 5.12 (t, 1H, $J_{OH,5'}$ = 5.7, OH-5′); 5.17 (ddd, 1H, $J_{H,F}$ = 52.8, $J_{2',1'}$ = 4.6, $J_{2',3'}$ = 3.8, H-2′); 5.93 (d, 1H, $J_{OH,3'}$ = 5.0, OH-3′); 6.39 (bs, 2H, NH_2); 6.61 (dd, 1H, $J_{H,F}$ = 14.9, $J_{1',2'}$ = 4.6, H-1′); 7.16 (dd, 1H, $J_{3,4}$ = 3.4, $J_{3,5}$ = 1.2, H-3-thienyl); 7.18 (dd, 1H, $J_{4,5}$ = 5.1, $J_{4,3}$ = 3.4, H-4-thienyl); 7.49 (d, 1H, $J_{H,F}$ = 2.1, H-6); 7.57 (dd, 1H, $J_{5,4}$ = 5.1, $J_{5,3}$ = 1.2, H-5-thienyl); 8.18 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 60.46 (CH_2-5′); 72.80 (d, $J_{C,F}$ = 23.3, CH-3′); 81.17 (d, $J_{C,F}$ = 16.7, CH-1′); 83.17 (d, $J_{C,F}$ = 5.4, CH-4′); 96.02 (d, $J_{C,F}$ = 191.8, CH-2′); 100.22 (C-4a); 108.84 (C-5); 122.65 (d, $J_{C,F}$ = 3.4, CH-6); 126.09 (CH-5-thienyl); 126.64 (CH-3-thienyl); 128.57 (CH-4-thienyl); 135.54 (C-2-thienyl); 150.57 (C-7a); 152.49 (CH-2); 157.47 (C-4). ^{19}F NMR (470.3 MHz, DMSO-d_6): -194.41. MS (ESI) *m*/*z* 351 [M+H], 373 [M+Na]. HRMS (ESI) for $C_{15}H_{16}N_4FO_3S$ [M+H] Calcd: 351.0922. Found: 351.0922. Calcd for $C_{15}H_{15}N_4FO_3S{\cdot}0.5H_2O{\cdot}0.15CH_4O$: C, 49.97; H, 4.59; N, 15.38. Found: C, 50.08; H, 4.38; N, 15.16.

3.17. 4-Amino-7-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-5-(furan-3-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (12g)

Compound **12g** was prepared as described for **12a** from compound **11** (197 mg, 0.5 mmol) and furan-3-boronic acid. Yield 149 mg (89%). Compound crystallized from H_2O/MeOH as beige needles of trihydrate. Mp >102 °C (slow melting due to dehydration). $[\alpha]_D$ +27.1 (c 0.591, DMSO). ^{1}H NMR (500.0 MHz, DMSO-d_6): 3.61 (ddd, 1H, J_{gem} = 11.9, $J_{5'b,OH}$ = 5.8, $J_{5'b,4'}$ = 5.0, H-5′b); 3.67 (dddd, 1H, J_{gem} = 11.9, $J_{5'a,OH}$ = 5.8, $J_{5'a,4'}$ = 4.4, $J_{H,F}$ = 1.5, H-5′a); 3.80 (ddd, 1H, $J_{4',3'}$ = 5.2, $J_{4',5'}$ = 5.0, 4.4, H-4′); 4.38 (dddd, 1H, $J_{H,F}$ = 19.0, $J_{3',4'}$ = 5.2, $J_{3',OH}$ = 5.0, $J_{3',2'}$ = 3.6, H-3′); 5.09 (t, 1H, $J_{OH,5'}$ = 5.8, OH-5′); 5.13 (ddd, 1H, $J_{H,F}$ = 52.8, $J_{2',1'}$ = 4.5, $J_{2',3'}$ = 3.6, H-2′); 5.93 (d, 1H, $J_{OH,3'}$ = 5.0, OH-3′); 6.32 (bs, 2H, NH_2); 6.60 (dd, 1H, $J_{H,F}$ = 15.6, $J_{1',2'}$ = 4.5, H-1′); 6.70 (dd, 1H, $J_{4,5}$ = 1.8, $J_{4,2}$ = 1.0, H-4-furyl); 7.38 (d, 1H, $J_{H,F}$ = 2.2, H-6); 7.81 (dd, 1H, $J_{5,4}$ = 1.8, $J_{5,2}$ = 1.5, H-5-furyl); 7.84 (dd, 1H, $J_{2,5}$ = 1.5, $J_{2,4}$ = 1.0, H-2-furyl); 8.15 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 60.70 (CH_2-5′); 73.07 (d, $J_{C,F}$ = 23.3, CH-3′); 81.17 (d, $J_{C,F}$ = 16.8, CH-1′); 83.20 (d, $J_{C,F}$ = 5.1, CH-4′); 96.05 (d, $J_{C,F}$ = 191.6, CH-2′); 100.63 (C-4a); 106.64 (C-5); 111.72 (d, $J_{C,F}$ = 6, CH-4-furyl); 118.63 (C-3-furyl); 121.67 (d, $J_{C,F}$ = 3.5, CH-6); 139.97 (CH-2-furyl); 144.47 (CH-5-furyl); 150.72 (C-7a); 152.25 (CH-2); 157.67 (C-4). ^{19}F NMR (470.3 MHz, DMSO-d_6): -194.23. MS (ESI) *m*/*z* 335 [M+H], 357 [M+Na]. HRMS (ESI) for $C_{15}H_{16}N_4FO_4$ [M+H] Calcd: 335.1150. Found: 335.1150. Calcd for $C_{15}H_{15}N_4FO_4{\cdot}3H_2O$: C, 46.39; H, 5.45; N, 14.43. Found: C, 46.66; H, 5.43; N, 14.22.

3.18. 4-Amino-7-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-5-(thiophen-3-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (12h)

Compound **12h** was prepared as described for **12a** from compound **11** (276 mg, 0.7 mmol) and thiophene-3-boronic acid. Yield 222 mg (90%). Compound crystallized from H_2O/MeOH as off-white needles. Mp 105–107 °C. $[\alpha]_D$ +16.6 (c 0.525, DMSO). ^{1}H NMR (499.8 MHz, DMSO-d_6): 3.62 (dt, 1H, J_{gem} = 12.1, $J_{5'b,OH}$ = $J_{5'b,4'}$ = 5.7, H-5′b); 3.68 (dddd, 1H, J_{gem} = 12.1, $J_{5'a,OH}$ = 5.7, $J_{5'a,4'}$ = 4.3, $J_{H,F}$ = 1.4, H-5′a); 3.82 (m, 1H, $J_{4',5'}$ = 5.7, 4.3, $J_{4',3'}$ = 5.2, $J_{H,F}$ = 0.5, H-4′); 4.40 (dddd, 1H, $J_{H,F}$ = 19.0, $J_{3',4'}$ = 5.2, $J_{3',OH}$ = 5.0, $J_{3',2'}$ = 3.8, H-3′); 5.09 (t, 1H, $J_{OH,5'}$ = 5.7, OH-5′); 5.15 (ddd, 1H, $J_{H,F}$ = 52.8, $J_{2',1'}$ = 4.5, $J_{2',3'}$ = 3.8, H-2′); 5.93 (d, 1H, $J_{OH,3'}$ = 5.0, OH-3′); 6.25 (bs, 2H, NH_2); 6.63 (dd, 1H, $J_{H,F}$ = 15.4, $J_{1',2'}$ = 4.5, H-1′); 7.27 (dd, 1H, $J_{4,5}$ = 4.9, $J_{4,2}$ = 1.3, H-4-thienyl); 7.43 (d, 1H, $J_{H,F}$ = 2.2, H-6); 7.53 (dd, 1H, $J_{2,5}$ = 2.9, $J_{2,4}$ = 1.3, H-2-thienyl); 7.71 (dd, 1H, $J_{5,4}$ = 4.9, $J_{5,2}$ = 2.9, H-5-thienyl); 8.17 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 60.67 (CH_2-5′); 73.03 (d, $J_{C,F}$ = 23.3, CH-3′); 81.19 (d, $J_{C,F}$ = 16.7, CH-1′); 83.20 (d, $J_{C,F}$ = 5.2, CH-4′); 96.06 (d, $J_{C,F}$ = 191.6, CH-2′); 100.44 (C-4a); 111.35 (C-5); 121.78 (d, $J_{C,F}$ = 3.5, CH-6); 122.37 (CH-2-thienyl); 127.69 (CH-5-thienyl); 128.65 (CH-4-thienyl); 134.76 (C-3-thienyl); 150.59 (C-7a); 152.23 (CH-2); 157.60 (C-4). ^{19}F NMR (470.3 MHz, DMSO-d_6): -194.25. MS (ESI) *m*/*z* 351 [M+H], 373 [M+Na]. HRMS (ESI) for $C_{15}H_{16}N_4FO_3S$ [M+H] Calcd: 351.0922. Found: 351.0922. Calcd for $C_{15}H_{15}N_4FO_3S{\cdot}3.35H_2O{\cdot}0.1CH_4O$: C, 43.82; H, 5.38; N, 13.54. Found: C, 44.14; H, 5.03; N, 13.21.

3.19. 4-Amino-7-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-5-(1H-pyrazol-4-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (12j)

An argon purged mixture of iodide **11** (276 mg, 0.7 mmol), 1-dimethylsulfamoyl-4-tributylstannylpyrazole[16] (488 mg, 1.05 mmol), $PdCl_2(PPh_3)_2$ (25 mg, 0.035 mmol) in DMF (3 ml) was stirred at 100 °C for 3 h. Volatiles were removed under reduced pressure, the residue was several times co-evaporated with toluene/MeOH and finally with silica. Column chromatography on silica (0→8% MeOH in $CHCl_3$) afforded product protected on pyrazole nitrogen by dimethylsulfamoyl group. This material was directly deprotected by the addition of aq HCl (1 M, 17 ml) and stirring at 100 °C for 6 h. Volatiles were removed in vacuo, and the residue was co-evaporated with H_2O/MeOH (5×), once with aq ammonia (25% w/w), then with H_2O (3×) and finally with silica. Column chromatography on silica (10% MeOH, 2% aq ammonia in $CHCl_3$) afforded product **12j** as solid foam (187 mg, 80%). Compound crystallized from H_2O/MeOH as white needles. Mp 157–159 °C. $[\alpha]_D$ +31.8 (c 0.535, DMSO). ^{1}H NMR (499.8 MHz, DMSO-d_6): 3.61 (dddd, 1H, J_{gem} = 11.8, $J_{5'b,OH}$ = 5.8, $J_{5'b,4'}$ = 5.3, $J_{H,F}$ = 0.9, H-5′b); 3.66 (dddd, 1H, J_{gem} = 11.8, $J_{5'a,OH}$ = 5.8, $J_{5'a,4'}$ = 4.3, $J_{H,F}$ = 1.5, H-5′a); 3.79 (td, 1H, $J_{4',5'}$ = 5.3, 4.3, $J_{4',3'}$ = 5.3, H-4′); 4.37 (dddd, 1H, $J_{H,F}$ = 19.0, $J_{3',4'}$ = 5.3, $J_{3',OH}$ = 5.0, $J_{3',2'}$ = 3.6, H-3′); 5.05 (t, 1H, $J_{OH,5'}$ = 5.8, OH-5′); 5.12 (ddd, 1H, $J_{H,F}$ = 52.8, $J_{2',1'}$ = 4.5, $J_{2',3'}$ = 3.6, H-2′); 5.89 (d, 1H, $J'_{OH,3}$ = 5.0, OH-3′); 6.18 (bs, 2H, NH_2); 6.60 (dd, 1H, $J_{H,F}$ = 16.0, $J_{1',2'}$ = 4.5, H-1′); 7.28 (d, 1H, $J_{H,F}$ = 2.4, H-6); 7.62 and 7.90 (2 × bs, 2 × 1H, H-3,5-pyrazole); 8.13 (s, 1H, H-2); 13.04 (bs, 1H, NH-pyrazole). ^{13}C NMR (125.7 MHz, DMSO-d_6): 60.74 (CH_2-5′); 73.13 (d, $J_{C,F}$ = 23.3, CH-3′); 81.11 (d, $J_{C,F}$ = 16.8, CH-1′); 83.17 (d, $J_{C,F}$ = 5.1, CH-4′); 96.07 (d, $J_{C,F}$ = 191.5, CH-2′); 100.91 (C-4a); 107.16 (C-5); 113.40 (C-4-pyrazole); 121.24 (d, $J_{C,F}$ = 3.6, CH-6); 127.31 and 138.42 (CH-3,5-pyrazole); 150.47 (C-7a); 152.05 (CH-2); 157.73 (C-4). ^{19}F NMR (470.3 MHz, DMSO-d_6): -194.17. MS (ESI) *m*/*z* 335 [M+H], 357 [M+Na]. HRMS (ESI) for $C_{14}H_{16}N_6FO_3$ [M+H] Calcd: 335.12624. Found: 335.12625. Calcd for $C_{14}H_{15}N_6FO_3{\cdot}1.2H_2O$: C, 47.24; H, 4.93; N, 23.61. Found: C, 47.43; H, 4.71; N, 23.36.

3.20. 4-Amino-7-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-5-[(trimethylsilyl)ethynyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine (13)

An argon purged mixture of iodide **11** (394 mg, 1 mmol), $PdCl_2(PPh_3)_2$ (35 mg, 0.05 mmol), CuI (19 mg, 0.1 mmol), trimethylsilylacetylene (1.4 ml, 10 mmol) and triethylamine (1 ml) was stirred in DMF (4 ml) at rt for 16 h. Volatiles were removed in vacuo and the rest was twice co-evaporated with EtOH and loaded on silica by co-evaporation from EtOH. Column chromatography on silica (0→3% MeOH in $CHCl_3$) afforded white solid, which after recrystallization from chloroform gave product **13** (297 mg, 82%). Mp 211–213 °C. ^{1}H NMR (400.1 MHz, DMSO-d_6): 0.24 (s, 9H, CH_3-TMS); 3.57–3.72 (m, 2H, H-5′b & H-5′a); 3.80 (tdd, 1H, $J_{4',5'}$ = 5.1, 4.1, $J_{4',3'}$ = 5.0, $J_{H,F}$ = 0.8, H-4′); 4.37 (dtd, 1H, $J_{H,F}$ = 19.0, $J_{3',4'}$ = $J_{3',OH}$ = 5.0, $J_{3',2'}$ = 4.8, H-3′); 5.10 (t, 1H, $J_{OH,5'}$ = 5.7, OH-5′); 5.13 (ddd, 1H, $J_{H,F}$ = 52.7, $J_{2',1'}$ = 4.7, $J_{2',3'}$ = 4.8, H-2′); 5.92 (d, 1H, $J_{OH,3'}$ = 5.0, OH-3′); 6.53 (dd, 1H, $J_{H,F}$ = 13.8, $J_{1',2'}$ = 4.7, H-1′); 6.71 (bs, 2H, NH_2); 7.71 (d, 1H, $J_{H,F}$ = 1.8, H-6); 8.15 (s, 1H, H-2). MS (ESI) *m*/*z* 365 [M+H], 387 [M+Na]. HRMS (ESI) for $C_{16}H_{22}N_4FO_3Si$ [M+H] Calcd: 365.1440. Found: 365.1440.

3.21. 4-Amino-7-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-5-ethynyl-7*H*-pyrrolo[2,3-*d*]pyrimidine (12k)

A mixture of the TMS compound **13** (282 mg, 0.77 mmol) and K_2CO_3 (107 mg, 0.77 mmol) in MeOH (10 ml) was stirred at rt for 1 h, followed by the co-evaporation with silica. Column chromatography on silica (4% MeOH in $CHCl_3$) provided title compound **12k** as white crystalline solid (219 mg, 97%). Compound was recrystallized from MeOH. Mp 220–222 °C. $[\alpha]_D$ +41.6 (c 0.370, DMSO). ^{1}H NMR (499.8 MHz, DMSO-d_6): 3.62 (dddd, 1H, J_{gem} = 12.1, $J_{5'b,OH}$ = 5.6, $J_{5'b,4'}$ = 5.2, $J_{H,F}$ = 0.7, H-5′b); 3.68 (dddd, 1H, J_{gem} = 12.1, $J_{5'a,OH}$ = 5.6, $J_{5'a,4'}$ = 4.0, $J_{H,F}$ = 1.6, H-5′a); 3.81 (dddd, 1H, $J_{4',3'}$ = 5.4, $J_{4',5'}$ = 5.2, 4.0, $J_{H,F}$ = 0.7, H-4′); 4.28 (s, 1H, HC≡C); 4.37 (dddd, 1H, $J_{H,F}$ = 19.0, $J_{3',4'}$ = 5.4, $J_{3',OH}$ = 5.0, $J_{3',2'}$ = 4.0, H-3′); 5.11 (t, 1H, $J_{OH,5'}$ = 5.6, OH-5′); 5.14 (ddd, 1H, $J_{H,F}$ = 52.8, $J_{2',1'}$ = 4.7, $J_{2',3'}$ = 4.0, H-2′); 5.91 (d, 1H, $J'_{OH,3}$ = 5.0, OH-3′); 6.54 (dd, 1H, $J_{H,F}$ = 14.0, $J_{1',2'}$ = 4.7, H-1′); 6.71 (bs, 2H, NH_2); 7.69 (d, 1H, $J_{H,F}$ = 1.9, H-6); 8.15 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 60.42 (CH_2-5′); 72.65 (d, $J_{C,F}$ = 23.2, CH-3′); 77.30 (C≡CH); 81.34 (d, $J_{C,F}$ = 16.8, CH-1′); 83.23 (d, $J_{C,F}$ = 5.4, CH-4′); 83.36 (HC≡C); 94.34 (C-5); 95.81 (d, $J_{C,F}$ = 192.2, CH-2′); 101.99 (C-4a); 128.11 (d, $J_{C,F}$ = 2.9, CH-6); 149.44 (C-7a); 153.23 (CH-2); 157.69 (C-4). ^{19}F NMR (470.3 MHz, DMSO-d_6):-194.82. MS (ESI) *m*/*z* 293 [M+H], 315 [M+Na]. HRMS (ESI) for $C_{13}H_{14}N_4FO_3$ [M+H] Calcd: 293.10445. Found: 293.10458. Calcd for $C_{13}H_{13}N_4FO_3$: C, 53.42; H, 4.48; N, 19.17. Found: C, 53.16; H, 4.42; N, 18.83.

3.22. 4-Amino-7-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-5-(1*H*-1,2,3-triazol-4-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (12l)

An argon purged mixture of ethynyl compound **12k** (178 mg, 0.609 mmol), CuI (6 mg, 0.031 mmol) and $TMSN_3$ (240 μl, 1.83 mmol) in MeOH (130 μl)/DMF (1 ml) was stirred at 100 °C for 24 h. Volatiles were evaporated under reduced pressure, the residue was twice co-evaporated with MeOH, suspended in MeOH and filtered through celite. Filtrate was co-evaporated with silica and column chromatography on silica (10% MeOH in $CHCl_3$) afforded triazolyl derivative **12l** as yellowish solid (56 mg, 27%). Compound was recrystallized from MeOH as white solid. Mp 288–290 °C. $[\alpha]_D$ +42.5 (c 0.386, DMSO). ^{1}H NMR (499.8 MHz, DMSO-d_6+DCl): 3.67 (ddd, 1H, J_{gem} = 12.1, $J_{5'b,4'}$ = 5.5, $J_{H,F}$ = 1.0, H-5′b); 3.71 (ddd, 1H, J_{gem} = 12.1, $J_{5'a,4'}$ = 4.4, $J_{H,F}$ = 1.4, H-5′a); 3.90 (dddd, 1H, $J_{4',5'}$ = 5.5, 4.4, $J_{4',3'}$ = 5.3, $J_{H,F}$ = 0.8, H-4′); 4.40 (ddd, 1H, $J_{H,F}$ = 18.7, $J_{3',4'}$ = 5.3, $J_{3',2'}$ = 3.8, H-3′); 5.22 (ddd, 1H, $J_{H,F}$ = 52.5, $J_{2',1'}$ = 4.5, $J_{2',3'}$ = 3.8, H-2′); 6.62 (dd, 1H, $J_{H,F}$ = 14.4, $J_{1',2'}$ = 4.5, H-1′); 8.26 (d, 1H, $J_{H,F}$ = 1.8, H-6); 8.50 (s, 1H, H-2); 8.65 (s, 1H, H-triazole). ^{13}C NMR (125.7 MHz, DMSO-d_6+DCl): 60.80 (CH_2-5′); 73.00 (d, $J_{C,F}$ = 23.2, CH-3′); 82.26 (d, $J_{C,F}$ = 16.9, CH-1′); 84.10 (d, $J_{C,F}$ = 5.0, CH-4′); 95.78 (d, $J_{C,F}$ = 192.8, CH-2′); 99.24 (C-4a); 108.96 (C-5); 124.05 (CH-6); 124.80 (CH-triazole); 139.76 (C-triazole); 143.80 (CH-2); 147.57 (C-7a); 151.84 (C-4). MS (ESI) *m*/*z* 336 [M+H], 358 [M+Na]. HRMS (ESI) for $C_{13}H_{15}N_7FO_3$ [M+H] Calcd: 336.12149. Found: 336.12145. Calcd for $C_{13}H_{14}N_7FO_3{\cdot}0.4H_2O$: C, 45.59; H, 4.36; N, 28.63. Found: C, 45.92; H, 4.10; N, 28.36.

3.23. 4-Amino-5-iodo-7-[3,5-*O*-(tetraisopropyldisiloxan-1,3-diyl)-β-D-ribofuranosyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine (15)

7-Iodotubercidin (**14**) (4.00 g, 10.2 mmol) was co-evaporated twice with anhydrous pyridine (20 ml) and dissolved in anhydrous pyridine (80 ml). $TIPDSCl_2$ (10.2 mmol, 3.26 ml) was added to the solution and the reaction mixture was stirred for 4 h at rt Then, volatiles were removed in vacuo, the residue was dissolved in EtOAc (100 ml) and extracted with water (60 ml). The organic phase was dried over $MgSO_4$ and evaporated under reduced pressure. The crude product was purified by column chromatography on silica (hexane-EtOAc 1:1) to afford silylated product **15** (5.98 g, 92%). ^{1}H NMR (500 MHz, $CDCl_3$): 0.97–1.18 (m, 28H, $((CH_3)_2CH)$; 4.03 (dd, 1H, J_{gem} = 12.4 Hz, $J_{5'a,4'}$ = 3.0 Hz, H-5′a); 4.09 (bddd, 1H, $J_{4',3'}$ = 8.0 Hz, $J_{4',5'b}$ = 3.8 Hz, $J_{4',5'a}$ = 3.0 Hz, H-4′); 4.14 (dd, 1H, J_{gem} = 12.4 Hz, $J_{5'b,4'}$ = 3.8 Hz, H-5′b); 4.37 (dd, 1H, $J_{2',3'}$ = 5.4 Hz, $J_{2',1'}$ = 1.6 Hz, H-2′); 4.80 (dd, 1H, $J_{3',4'}$ = 7.9 Hz, $J_{3',2'}$ = 5.4 Hz, H-3′); 5.78 (bs, 2H, NH_2); 6.09 (d, 1H, $J_{1',2'}$ = 1.6 Hz,

H-1′); 7.31 (s, 1H, H-6); 8.24 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 12.59, 12.80, 13.04 and 13.35 ((CH_3)$_2$**C**H); 16.89, 16.95, 17.00, 17.08, 17.29, 17.43, 17.45 and 17.53 ((**C**H$_3$)$_2$CH); 50.25 (C-5); 61.41 (CH_2-5′); 70.23 (CH-3′); 75.34 (CH-2′); 81.81 (CH-4′); 89.63 (CH-1′); 104.74 (C-4a); 126.97 (CH-6); 149.48 (C-7a); 152.00 (CH-2); 156.74 (C-4). MS (ESI) *m*/*z* (%): 635 (100) [M+H], 657 (85) [M+Na]; HRMS (ESI) Calcd for $C_{23}H_{40}O_5N_4ISi_2$ [M+H]: 635.15764. Found: 635.15753.

3.24. 4-Amino-5-iodo-7-[3,5-*O*-(tetraisopropyldisiloxan-1,3-diyl)-β-D-erythro-pentofuran-2-ulosyl] -7*H*-pyrrolo[2,3-*d*]pyrimidine (16)

Mixture of chromium (VI) oxide (2.36 g, 23.6 mmol), pyridine (3.79 ml, 47.1 mmol) and acetic anhydride (2.22 ml, 23.6 mmol) in anhydrous dichloromethane (60 ml) was cooled to 0 °C and stirred for 30 min until chromium oxide was completely dissolved. Then solution of compound **15** (5.98 g, 9.42 mmol) in dichloromethane (60 ml) was slowly added. The reaction mixture was stirred at 0 °C for 1.5 h. Then ice-cold EtOAc (235 ml) was added. The precipitate was filtered off through a pad of silica (46 g). The filtrate was evaporated under reduced pressure. The residue was purified by column chromatography on silica (hexane-EtOAc 3:2). Ketone **16** (3.51 g, 59%) was obtained as yellow foam. ^{1}H NMR (400.0 MHz, $CDCl_3$): 1.06–1.17 (m, 28H, (CH_3)$_2$CHSi); 3.99 (dt, 1H, $J_{4',3'}$ = 9.6, $J_{4',5'}$ = 3.2, H-4′); 4.12, 4.19 (2 × dd, 2 × 1H, J_{gem} = 12.8, $J_{5',4'}$ = 3.2, H-5′); 5.44 (d, 1H, $J_{3',4'}$ = 9.6, H-3′); 5.65 (s, 1H, H-1′); 6.10 (bs, 2H, NH_2); 7.11 (s, 1H, H-6); 8.07 (s, 1H, H-2). MS (ESI) *m*/*z* (%): 633 (62) [M+H], 655 (100) [M+Na]; HRMS (ESI) Calcd for $C_{23}H_{38}O_5N_4ISi_2$ [M+H]: 633.14199. Found: 633.14215.

3.25. 4-Amino-5-iodo-7-[3,5-*O*-(tetraisopropyldisiloxan-1,3-diyl)-β-D-arabinofuranosyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine (17)

Ketone **16** (2.85 g, 4.50 mmol) was dissolved in ethanol (99%, 170 ml) and the solution was cooled to 0 °C. Sodium borohydrate (340 mg, 9.00 mmol) was added. The reaction mixture was stirred at 0 °C for 1.5 h. The reacion was quenched with aq NH_4Cl (sat., 50 ml) and extracted with EtOAc (150 ml). The organic phase was dried over $MgSO_4$ and evaporated under reduced pressure. The crude product was purified by column chromatography on silica (hexane-EtOAc 1:1) to give arabinoside **17** (2.43 g, 85%) as a yellowish foam. ^{1}H NMR (500 MHz, $CDCl_3$): 0.95–1.29 (m, 28H, ((CH_3)$_2$CH); 3.83 (dt, 1H, $J_{4',3'}$ = 8.6 Hz, $J_{4',5'a}$ = $J_{4',5'b}$ = 2.7 Hz, H-4′); 4.03 (dd, 1H, J_{gem} = 13.2 Hz, $J_{5'a,4'}$ = 3.0 Hz, H-5′a); 4.10 (dd, 1H, J_{gem} = 13.2 Hz, $J_{5'b,4'}$ = 2.5 Hz, H-5′b); 4.45 (t, 1H, $J_{3',4'}$ = $J_{3',2'}$ = 8.4 Hz, H-3′); 4.65 (dd, 1H, $J_{2',3'}$ = 8.1 Hz, $J_{2',1'}$ = 6.3 Hz, H-2′); 6.34 (d, 1H, $J_{1',2'}$ = 6.2 Hz, H-1′); 6.83 (bs, 2H, NH_2); 7.60 (s, 1H, H-6); 8.13 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 12.40, 12.92, 13.00 and 13.54 ((CH_3)$_2$**C**H); 16.89, 16.92, 16.95, 17.06, 17.33, 17.42, 17.53 and 17.74 ((**C**H$_3$)$_2$CH); 50.89 (C-5); 60.67 (CH_2-5′); 72.90 (CH-3′); 76.39 (CH-2′); 80.96 (CH-4′); 83.97 (CH-1′); 103.63 (C-4a); 129.13 (CH-6); 147.03 (CH-2); 148.65 (C-7a); 154.74 (C-4). MS (ESI) *m*/*z* (%): 635 (100) [M+H], 657 (30) [M+Na]; HRMS (ESI) Calcd for $C_{23}H_{40}O_5N_4ISi_2$ [M+H]: 635.15764. Found: 635.15782.

3.26. 4-Amino-5-iodo-7-(β-D-arabinofuranosyl)-7*H*-pyrrolo[*2,3-d*]pyrimidine (18)

Arabinoside **17** (670 mg, 1.06 mmol) was dissolved in anhydrous THF (12 ml) and $Et_3N{\cdot}3HF$ (344 μl, 2.11 mmol) was added. The reaction mixture was stirred overnight at rt The precipitate of compound **18** was filtered off and washed with methanol. Arabinoside **18** (385 mg, 93%) was obtained as white crystalline solid. Mp 218–220 °C. ^{1}H NMR (500 MHz, DMSO-d_6): 3.60 (dm, 1H, J_{gem} = 11.7 Hz, H-5′a); 3.66 (dm, 1H, J_{gem} = 11.7 Hz, H-5′b); 3.72 (btd, 1H, $J_{4',5'a}$ = $J_{4',3'}$ = 4.8 Hz, $J_{4',5'b}$ = 4.1 Hz, H-4′); 4.02–4.09 (m, 2H, H-2′,3′); 5.07 (m, 1H, OH-5′); 5.45 (bd, 1H, $J_{OH,3'}$ = 3.6 Hz, OH-3′); 5.47 (d, 1H, $J_{OH,2'}$ = 5.3 Hz, OH-2′); 6.40 (d, 1H, $J_{1',2'}$ = 4.5 Hz, H-1′); 6.61 (bs, 2H, NH_2); 7.51 (s, 1H, H-6); 8.09 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 50.63 (C-5); 61.05 (CH_2-5′); 75.26 (CH-3′); 76.04 (CH-2′); 83.46 (CH-1′); 83.88 (CH-4′); 102.87 (C-4a); 128.98 (CH-6); 150.04 (C-7a); 151.92 (CH-2); 157.20 (C-4). MS (ESI) *m*/*z* (%): 393 (90) [M+H], 415 (100) [M+Na]; HRMS (ESI) Calcd for $C_{11}H_{14}O_4N_4I$ [M+H]: 393.00542. Found: 393.00547.

3.27. 4-Amino-5-phenyl-7-(β-D-arabinofuranosyl)-7*H*-pyrrolo[2,3-d]pyrimidine (19a)

An argon purged mixture of compound **18** (150 mg, 0.38 mmol), phenylboronic acid (58 mg, 0.48 mmol), Na_2CO_3 (122 mg, 1.14 mmol), $Pd(OAc)_2$ (4.3 mg, 19 μmol) and TPPTS (33 mg, 0.057 mmol) in water–MeCN (2:1, 2.5 ml) was stirred at 100 °C for 3 h. After cooling, the mixture was neutralized by the addition of aq HCl (1 M), volatiles were removed in vacuo. The residue was purified twice by reverse phase HPFC on C-18 column (0→100% MeOH in water). Compound **19a** (96 mg, 73%) was obtained as a white crystalline solid after recrystallization (MeOH-water 1:4). Mp 140–142 °C. $[\alpha]_D^{20}$ −18.8 (c 0.202, DMSO). IR (ATR): 3337, 1623, 1591, 1458, 1084, 1005 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6): 3.61 (bdm, 1H, J_{gem} = 11.8 Hz, H-5′a); 3.68 (bdm, 1H, J_{gem} = 11.8 Hz, H-5′b); 3.75 (btd, 1H, $J_{4',5'a}$ = $J_{4',3'}$ = 4.7 Hz, $J_{4',5'b}$ = 4.1 Hz, H-4′); 4.11 (q, 1H, $J_{3',4'}$ = $J_{3',2'}$ = $J_{3',OH}$ = 4.5 Hz, H-3′); 4.13 (m, 1H, H-2′); 5.07 (bt, 1H, $J_{OH,5'a}$ = $J_{OH,5'b}$ = 4.8 Hz, OH-5′); 5.47 (d, 1H, $J_{OH,3'}$ = 4.5 Hz, OH-3′); 5.50 (d, 1H, $J_{OH,2'}$ = 5.6 Hz, OH-2′); 6.07 (bs, 2H, NH_2); 6.51 (d, 1H, $J_{1',2'}$ = 4.8 Hz, H-1′); 7.36 (m, 1H, H-*p*-Ph); 7.44 (s, 1H, H-6); 7.44–7.51 (m, 2 × 2H, H-*o*,*m*-Ph); 8.15 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 61.18 (CH_2-5′); 75.48 (CH-3′); 76.21 (CH-2′); 83.26 (CH-1′); 83.82 (CH-4′); 100.06 (C-4a); 115.40 (C-5); 123.10 (CH-6); 126.94 (CH-*p*-Ph); 128.53 (CH-*o*-Ph); 129.22 (CH-*m*-Ph); 134.97 (C-*i*-Ph); 150.91 (C-7a); 151.66 (CH-2); 157.29 (C-4). MS (ESI) *m*/*z* (%): 343 (100) [M+H], 365 (8) [M+Na]; HRMS (ESI) Calcd for $C_{17}H_{19}O_4N_4$ [M+H]: 343.14008. Found: 343.14007. For $C_{17}H_{18}O_4N_4$ Calcd: 59.64% C, 5.30% H, 16.37% N. Found: 59.50% C, 5.65% H, 16.45% N.

3.28. 4-Amino-5-(furan-2-yl)-7-(β-D-arabinofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (19e)

Compound **19e** was prepared as described for compound **19a** from compound **18** (150 mg, 0.38 mmol) and furan-2-boronic acid. The crude product was purified by reverse phase HPFC on C-18 column (water-MeOH 0→100%). Arabinoside **19e** (81 mg, 64%) was obtained as a yellowish lyophilizate (*t*-BuOH). Mp 117–119 °C. $[\alpha]_D^{20}$ −41.0 (c 0.056, DMSO). IR (ATR): 3462, 1626, 1558, 1472, 1310, 1221, 1068, 1013 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6): 3.64 (dm, 1H, J_{gem} = 11.8 Hz, H-5′a); 3.70 (dm, 1H, J_{gem} = 11.8 Hz, H-5′b); 3.76 (btd, 1H, $J_{4',5'a}$ = $J_{4',3'}$ = 4.8 Hz, $J_{4',5'b}$ = 3.9 Hz, H-4′); 4.09 (q, 1H, $J_{3',4'}$ = $J_{3',2'}$ = $J_{3',OH}$ = 4.5 Hz, H-3′); 4.11 (m, 1H, H-2′); 5.09 (m, 1H, OH-5′); 5.47 (d, 1H, $J_{OH,3'}$ = 4.6 Hz, OH-3′); 5.48 (d, 1H, $J_{OH,2'}$ = 5.6 Hz, OH-2′); 6.47 (d, 1H, $J_{1',2'}$ = 4.7 Hz, H-1′); 6.60 (dd, 1H, $J_{4,3}$ = 3.3 Hz, $J_{4,5}$ = 1.8 Hz, H-4-furyl); 6.62 (dd, 1H, $J_{3,4}$ = 3.3 Hz, $J_{3,5}$ = 0.9 Hz, H-3-furyl); 6.83 (bs, 2H, NH_2); 7.70 (s, 1H, H-6); 7.77 (dd, 1H, $J_{5,4}$ = 1.8 Hz, $J_{5,3}$ = 0.9 Hz, H-5-furyl); 8.13 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 61.19 (CH_2-5′); 75.41 (CH-3′); 76.09 (CH-2′); 83.45 (CH-1′); 83.92 (CH-4′); 98.99 (C-4a); 105.06 (CH-3-furyl); 105.28 (C-5); 112.07 (CH-4-furyl); 122.43 (CH-6); 142.00 (CH-5-furyl); 149.10 (C-2-furyl); 150.77 (C-7a); 152.02 (CH-2); 157.25 (C-4). MS (ESI) *m*/*z* (%): 333 (100) [M+H], 355 (10) [M+Na]; HRMS (ESI) Calcd for $C_{15}H_{17}O_5N_4$ [M+H]: 333.11935. Found: 333.11934. For $C_{15}H_{16}O_5N_4$ Calcd: 54.21% C, 4.85% H, 16.86% N. Found: 54.08% C, 4.70% H, 16.63% N.

3.29. 4-Amino-5-(thiophen-2-yl)-7-(β-D-arabinofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (19f)

Compound **19f** was prepared as described for compound **19a** from compound **18** (150 mg, 0.38 mmol) and thiophene-2-boronic acid. The crude product was purified twice by reverse phase HPFC on C-18 column (0→100% MeOH in water). Compound **19f** (103 mg, 77%) was obtained as an off-white crystalline solid after recrystallization (MeOH-water 1:4). Mp 150–154 °C. $[\alpha]_D^{20}$ −26.8 (c 0.205, DMSO). IR (ATR): 3441, 1616, 1596, 1552, 1456, 1351, 1305, 1181, 1068, 1049, 1015 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6): 3.61 (dt, 1H, J_{gem} = 11.7 Hz, $J_{5'a,4'} = J_{5'a,OH}$ = 5.1 Hz, H-5′a); 3.68 (ddd, 1H, J_{gem} = 11.7 Hz, $J_{5'b,OH}$ = 5.5 Hz, $J_{5'b,4'}$ = 4.1 Hz, H-5′b); 3.75 (btd, 1H, $J_{4',5'a} = J_{4',3'}$ = 4.7 Hz, $J_{4',5'b}$ = 4.2 Hz, H-4′); 4.09 (q, 1H, $J_{3',4'} = J_{3',2'} = J_{3',OH}$ = 4.6 Hz, H-3′); 4.12 (bdt, 1H, $J_{2',OH}$ = 5.6 Hz, $J_{2',3'} = J_{2',1'}$ = 4.7 Hz, H-2′); 5.08 (t, 1H, $J_{OH,5'a} = J_{OH,5'b}$ = 5.4 Hz, OH-5′); 5.47 (d, 1H, $J_{OH,3'}$ = 4.5 Hz, OH-3′); 5.52 (d, 1H, $J_{OH,2'}$ = 5.6 Hz, OH-2′); 6.27 (s, 2H, NH_2); 6.48 (d, 1H, $J_{1',2'}$ = 4.8 Hz, H-1′); 7.12 (dd, 1H, $J_{3,4}$ = 3.5 Hz, $J_{3,5}$ = 1.2 Hz, H-3-thienyl); 7.17 (dd, 1H, $J_{4,5}$ = 5.2 Hz, $J_{4,3}$ = 3.5 Hz, H-4-thienyl); 7.50 (s, 1H, H-6); 7.55 (dd, 1H, $J_{5,4}$ = 5.2 Hz, $J_{5,3}$ = 1.2 Hz, H-5-thienyl); 8.15 (s, 1H, H-2). ^{13}C NMR (150.9 MHz, DMSO-d_6): 61.04 (CH_2-5′); 75.32 (CH-3′); 76.11 (CH-2′); 83.28 (CH-1′); 83.83 (CH-4′); 100.19 (C-4a); 107.55 (C-5); 123.87 (CH-6); 125.72 (CH-5-thienyl); 126.20 (CH-3-thienyl); 128.45 (CH-4-thienyl); 136.16 (C-2-thienyl); 150.63 (C-7a); 152.01 (CH-2); 157.28 (C-4). MS (ESI) *m*/*z* (%): 349 (100) [M+H], 371 (18) [M+Na]; HRMS (ESI) Calcd for $C_{15}H_{17}O_4N_4S$ [M+H]: 349.09650. Found: 349.09647. For $C_{15}H_{16}O_4N_4{\cdot}0.75H_2O$ Calcd: 49.78% C, 4.87% H, 15.48% N. Found: 50.05% C, 4.66% H, 15.12% N.

3.30. 4-Amino-5-(furan-3-yl)-7-(β-D-arabinofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (19g)

Compound **19f** was prepared as described for compound **19a** from compound **18** (150 mg, 0.38 mmol) and furan-3-boronic acid. The crude product was purified by reverse phase HPFC on C-18 column (0→100% MeOH in water). Compound **19g** (93 mg, 73%) was obtained as a yellow crystalline solid after recrystallization (MeOH-water 1:4). Mp 148–152 °C. $[\alpha]_D^{20}$ −21.0 (c 0.205, DMSO). IR (ATR): 3433, 1626, 1592, 1559, 1446, 1068, 1003 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): 3.61 (dd, 1H, J_{gem} = 11.7 Hz, $J_{5'a,4'}$ = 5.1 Hz, H-5′a); 3.68 (dd, 1H, J_{gem} = 11.7 Hz, $J_{5'b,4'}$ = 4.1 Hz, H-5′b); 3.74 (btd, 1H, $J_{4',5'a} = J_{4',3'}$ = 4.9 Hz, $J_{4',5'b}$ = 4.1 Hz, H-4′); 4.08 (bq, 1H, $J_{3',4'} = J_{3',2'} = J_{3',OH}$ = 4.4 Hz, H-3′); 4.10 (m, 1H, H-2′); 5.06 (bs, 1H, OH-5′); 5.46 (d, 1H, $J_{OH,3'}$ = 4.3 Hz, OH-3′); 5.48 (d, 1H, $J_{OH,2'}$ = 5.5 Hz, OH-2′); 6.21 (bs, 2H, NH_2); 6.47 (d, 1H, $J_{1',2'}$ = 4.6 Hz, H-1′); 6.67 (dd, 1H, $J_{4,5}$ = 1.8 Hz, $J_{4,2}$ = 1.0 Hz, H-4-furyl); 7.41 (s, 1H, H-6); 7.80 (bt, 1H, $J_{5,4} = J_{5,2}$ = 1.6 Hz, H-5-furyl); 7.81 (bdd, 1H, $J_{2,5}$ = 1.6 Hz, $J_{2,4}$ = 1.0 Hz, H-2-furyl); 8.12 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 61.25 (CH_2-5′); 75.52 (CH-3′); 76.16 (CH-2′); 83.23 (CH-1′); 83.80 (CH-4′); 100.58 (C-4a); 105.27 (C-5); 111.70 (CH-4-furyl); 119.00 (C-3-furyl); 122.85 (CH-6); 139.63 (CH-2-furyl); 144.34 (CH-5-furyl); 150.71 (C-7a); 151.64 (CH-2); 157.38 (C-4). MS (ESI) *m*/*z* (%): 333 (100) [M+H]; HRMS (ESI) Calcd for $C_{15}H_{17}O_5N_4$ [M+H]: 333.11935. Found: 333.11934. For $C_{15}H_{16}O_5N_4{\cdot}0.25CH_3OH{\cdot}0.5H_2O$ Calcd: 52.43% C, 5.19% H, 16.04% N. Found: 52.22% C, 4.95% H, 15.75% N.

3.31. 4-Amino-5-(thiophen-3-yl)-7-(β-D-arabinofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (19h)

Compound **19h** was prepared as described for compound **19a** from compound **18** (150 mg, 0.38 mmol) and thiophene-3-boronic acid. The crude product was purified by reverse phase HPFC on C-18 column (0→100% MeOH in water). Compound **19h** (123 mg, 92%) was obtained as a white crystalline solid after recrystallization (MeOH-water 1:4). Mp 214–217 °C. $[\alpha]_D^{20}$ −37.2 (c 0.207, DMSO). IR (ATR): 3442, 1619, 1599, 1554, 1083, 1038, 1001 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): 3.61 (dd, 1H, J_{gem} = 11.7 Hz, $J_{5'a,4'}$ = 5.0 Hz, H-5′a); 3.68 (dd, 1H, J_{gem} = 11.7 Hz, $J_{5'b,4'}$ = 4.0 Hz, H-5′b); 3.74 (btd, 1H, $J_{4',5'a} = J_{4',3'}$ = 4.8 Hz, $J_{4',5'b}$ = 4.1 Hz, H-4′); 4.07–4.14 (m, 2H, H-2′,3′); 5.08 (bs, 1H, OH-5′); 5.47 (bd, 1H, $J_{OH,3'}$ = 4.3 Hz, OH-3′); 5.50 (bd, 1H, $J_{OH,2'}$ = 5.4 Hz, OH-2′); 6.24 (bs, 2H, NH_2); 6.49 (d, 1H, $J_{1',2'}$ = 4.8 Hz, H-1′); 7.29 (dd, 1H, $J_{4,5}$ = 4.9 Hz, $J_{4,2}$ = 1.3 Hz, H-4-thienyl); 7.46 (s, 1H, H-6); 7.49 (dd, 1H, $J_{2,5}$ = 2.9 Hz, $J_{2,4}$ = 1.3 Hz, H-2-thienyl); 7.71 (dd, 1H, $J_{5,4}$ = 4.9 Hz, $J_{5,2}$ = 2.9 Hz, H-5-thienyl); 8.15 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 61.15 (CH_2-5′); 75.36 (CH-3′); 76.18 (CH-2′); 83.26 (CH-1′); 83.80 (CH-4′); 100.30 (C-4a); 110.22 (C-5); 121.94 (CH-2-thienyl); 123.09 (CH-6); 127.62 (CH-5-thienyl); 128.61 (CH-4-thienyl); 135.13 (C-3-thienyl); 150.46 (C-7a); 151.31 (CH-2); 157.10 (C-4). MS (ESI) *m*/*z* (%): 349 (100) [M+H], 371 (10) [M+Na]; HRMS (ESI) Calcd for $C_{15}H_{17}O_4N_4S$ [M+H]: 349.09650. Found: 349.09648. For $C_{15}H_{16}O_4N_4{\cdot}1H_2O$ Calcd: 49.17% C, 4.95% H, 15.29% N. Found: 49.05% C, 4.64% H, 15.09% N.

3.32. 4-Amino-5-[(trimethylsilyl)ethynyl]-7-(β-D-arabinofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (20)

An argon purged mixture of compound **18** (150 mg, 0.38 mmol), CuI (7.3 mg, 0.038 mmol), $PdCl_2(PPh_3)_2$ (13 mg, 0.019 mmol), trimethylsilylacetylene (545 µl, 3.83 mmol) and triethylamine (150 µl, 1.07 mmol) in anhydrous DMF (600 µl) was stirred overnight at rt Volatiles were removed in vacuo and the residue was twice co-evaporated with EtOH. The crude product was purified by silicagel column chromatography (3.5% MeOH in $CHCl_3$) to obtain compound **20** (70 mg, 51%) as a colorless foam. ^1H NMR (400 MHz, DMSO-d_6): 0.24 (s, 9H, CH_3Si); 3.59–3.69 (2H, H-5′a, H-5′b); 3.73 (bq, 1H, $J_{4',5'a} = J_{4',3'} = J_{4',5'b}$ = 4.4 Hz, H-4′); 4.03–4.11 (m, 2H, H-3′, H-2′); 5.09 (t, 1H, $J_{OH,5'a} = J_{OH,5'b}$ = 5.6 Hz, OH-5′); 5.45–5.47 (m, 2H, OH-3′, OH-2′); 6.38 (d, 2H, $J_{1',2'}$ = 4.8 Hz, H-1′); 7.64 (s, 1H, H-6); 8.11 (s, 1H, H-2). MS (ESI) *m*/*z* (%): 363 (100) [M+H], 385 (15) [M+Na]; HRMS (ESI) Calcd for $C_{16}H_{23}O_4N_4Si$ [M+H]: 363.14831. Found: 363.14828.

3.33. 4-Amino-5-ethynyl-7-(β-D-arabinofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (19k)

A solution of compound **20** (70 mg, 0.19 mmol) and K_2CO_3 (13.3 mg, 0.97 mmol) in methanol (5 ml) was stirred for 1 h at rt Then the reaction mixture was co-evaporated with silica under reduced pressure and chromatographed on silicagel column (5% MeOH in $CHCl_3$). Product **19k** (43 mg, 77%) was obtained as white crystalline solid after recrystallization (MeOH:$CHCl_3$:hexane). Mp 198–201 °C. $[\alpha]_D^{20}$ −21.8 (c 0.072, DMSO). IR (ATR): 3472, 1635, 1592, 1570, 1482, 1455, 1314, 1303, 1035 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): 3.62 (bdt, 1H, J_{gem} = 11.7 Hz, $J_{5'a,4'} = J_{5'a,OH}$ = 5.2 Hz, H-5′a); 3.67 (bddd, 1H, J_{gem} = 11.7 Hz, $J_{5'b,OH}$ = 5.5 Hz, $J_{5'b,4'}$ = 4.0 Hz, H-5′b); 3.74 (bq, 1H, $J_{4',5'a} = J_{4',5'b} = J_{4',3'}$ = 4.4 Hz, H-4′); 4.06 (m, 1H, H-3′); 4.09 (m, 1H, H-2′); 4.23 (s, 1H, CH≡C); 5.09 (t, 1H, $J_{OH,5'a} = J_{OH,5'b}$ = 5.4 Hz, OH-5′); 5.47 (d, 1H, $J_{OH,3'}$ = 4.4 Hz, OH-3′); 5.48 (d, 1H, $J_{OH,2'}$ = 5.4 Hz, OH-2′); 6.40 (d, 1H, $J_{1',2'}$ = 4.8 Hz, H-1′); 6.60 (bs, 2H, NH_2); 7.65 (s, 1H, H-6); 8.11 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 60.95 (CH_2-5′); 75.10 (CH-3′); 76.02 (CH-2′); 77.86 (CH≡*C*); 82.82 (*C*H≡C); 83.57 (CH-1′); 83.94 (CH-4′); 93.02 (C-5); 102.06 (C-4a); 129.25 (CH-6); 149.49 (C-7a); 152.79 (CH-2); 157.56 (C-4). MS (ESI) *m*/*z* (%): 291 (100) [M+H], 313 (20) [M+Na]; HRMS (ESI) Calcd for $C_{13}H_{15}O_4N_4$ [M+H]: 291.10878. Found: 291.10882. For $C_{13}H_{14}O_4N_4$ Calcd: 53.79% C, 4.86% H, 19.30% N. Found: 53.66% C, 4.99% H, 18.98% N.

3.34. 4-Amino-5-(furan-2-yl)-7-(2-deoxy-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (22e)

Compound **22e** was prepared as described for compound **19a** from compound **21** (150 mg, 0.40 mmol) and furan-2-boronic acid. The crude product was purified by reverse phase HPFC on C-18 column (0→100% MeOH in water). Compound **22e** (108 mg, 89%) was obtained as a beige crystalline solid after recrystallization (MeOH-water 1:4). Mp 205–208 °C. $[\alpha]_D^{20}$ −24.9 (c 0.181, DMSO). IR (ATR): 3381, 1629, 1557, 1496, 1458, 1219, 1161, 1072, 1054, 1017 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): 2.21 (ddd, 1H, J_{gem} = 13.1 Hz, $J_{2'a,1'}$ = 6.0 Hz, $J_{2'a,3'}$ = 2.8 Hz, H-2′a); 2.52 (ddd, 1H, J_{gem} = 13.1 Hz, $J_{2'b,1'}$ = 8.1 Hz, $J_{2'b,3'}$ = 5.8 Hz, H-2′b); 3.53 (ddd, 1H, J_{gem} = 11.7 Hz, $J_{5'a,OH}$ = 5.9 Hz, $J_{5'a,4'}$ = 4.5 Hz, H-5′a); 3.60 (dt, 1H, J_{gem} = 11.7 Hz, $J_{5'b,OH}$ = $J_{5'b,4'}$ = 5.0 Hz, H-5′b); 3.84 (td, 1H, $J_{4',5'a}$ = $J_{4',5'b}$ = 4.5 Hz, $J_{4',3'}$ = 2.6 Hz, H-4′); 4.37 (m, 1H, H-3′); 5.05 (t, 1H, $J_{OH,5'a}$ = $J_{OH,5'b}$ = 5.6 Hz, OH-5′); 5.27 (d, 1H, $J_{OH,3'}$ = 4.1 Hz, OH-3′); 6.56 (dd, 1H, $J_{1',2'b}$ = 8.1 Hz, $J_{1',2'a}$ = 6.0 Hz, H-1′); 6.61 (dd, 1H, $J_{4,3}$ = 3.3 Hz, $J_{4,5}$ = 1.9 Hz, H-4-furyl); 6.68 (dd, 1H, $J_{3,4}$ = 3.3 Hz, $J_{3,5}$ = 0.9 Hz, H-3-furyl); 6.89 (bs, 2H, NH_2); 7.78 (dd, 1H, $J_{5,4}$ = 1.9 Hz, $J_{5,3}$ = 0.9 Hz, H-5-furyl); 7.82 (s, 1H, H-6); 8.13 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 39.87 (CH_2-2′); 62.11 (CH_2-5′); 71.11 (CH-3′); 83.11 (CH-1′); 87.58 (CH-4′); 99.38 (C-4a); 105.47 (CH-3-furyl); 106.38 (C-5); 112.06 (CH-4-furyl); 120.18 (CH-6); 142.12 (CH-5-furyl); 148.80 (C-2-furyl); 150.63 (C-7a); 152.28 (CH-2); 157.42 (C-4). MS (ESI) *m*/*z* (%): 317 (100) [M+H], 339 (62) [M+Na]; HRMS (ESI) Calcd for $C_{15}H_{17}O_4N_4$ [M+H]: 317.12443. Found: 317.12442. For $C_{15}H_{16}O_4N_4$ Calcd: 59.96% C, 5.10% H, 17.71% N. Found: 59.66% C, 4.94% H, 17.47% N.

3.35. 4-Amino-5-(thiophen-2-yl)-7-(2-deoxy-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (22f)

Compound **22f** was prepared as described for compound **19a** from compound **21** (150 mg, 0.40 mmol) and thiophene-2-boronic acid. The crude product was purified by reverse phase HPFC on C-18 column (0→100% MeOH in water). Compound **22f** (99 mg, 75%) was obtained as a white lyophilizate (*t*-BuOH). Mp 88–92 °C. $[\alpha]_D^{20}$ −17.5 (c 0.223, DMSO). IR (ATR): 3461, 1623, 1589, 1576, 1548, 1463, 1191, 1092, 1051 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6): 2.20 (ddd, 1H, J_{gem} = 13.1 Hz, $J_{2'a,1'}$ = 6.0 Hz, $J_{2'a,3'}$ = 2.7 Hz, H-2′a); 2.54 (ddd, 1H, J_{gem} = 13.1 Hz, $J_{2'b,1'}$ = 8.3 Hz, $J_{2'b,3'}$ = 5.8 Hz, H-2′b); 3.52 (ddd, 1H, J_{gem} = 11.7 Hz, $J_{5'a,OH}$ = 5.8 Hz, $J_{5'a,4'}$ = 4.2 Hz, H-5′a); 3.58 (bdt, 1H, J_{gem} = 11.7 Hz, $J_{5'b,OH}$ = $J_{5'b,4'}$ = 4.8 Hz, H-5′b); 3.84 (td, 1H, $J_{4',5'a}$ = $J_{4',5'b}$ = 4.4 Hz, $J_{4',3'}$ = 2.5 Hz, H-4′); 4.36 (m, 1H, H-3′); 5.06 (t, 1H, $J_{OH,5'a}$ = $J_{OH,5'b}$ = 5.6 Hz, OH-5′); 5.26 (d, 1H, $J_{OH,3'}$ = 4.1 Hz, OH-3′); 6.31 (s, 2H, NH_2); 6.57 (dd, 1H, $J_{1',2'b}$ = 8.2 Hz$J_{1',2'a}$ = 5.9 Hz, H-1′); 7.15 (dd, 1H, $J_{3,4}$ = 3.5 Hz, $J_{3,5}$ = 1.3 Hz, H-3-thienyl); 7.18 (dd, 1H, $J_{4,5}$ = 5.1 Hz, $J_{4,3}$ = 3.5 Hz, H-4-thienyl); 7.57 (dd, 1H, $J_{5,4}$ = 5.1 Hz, $J_{5,3}$ = 1.2 Hz, H-5-thienyl); 7.59 (s, 1H, H-6); 8.15 (s, 1H, H-2). ^{13}C NMR (150.9 MHz, DMSO-d_6): 39.97 (CH_2-2′); 62.09 (CH_2-5′); 71.18 (CH-3′); 83.21 (CH-1′); 87.61 (CH-4′); 100.70 (C-4a); 108.67 (C-5); 121.79 (CH-6); 126.00 (CH-5-thienyl); 126.56 (CH-3-thienyl); 128.41 (CH-4-thienyl); 135.72 (C-2-thienyl); 150.36 (C-7a); 152.19 (CH-2); 157.42 (C-4). MS (ESI) *m*/*z* (%): 333 (100) [M+H], 355 (23) [M+Na]; HRMS (ESI) Calcd for $C_{15}H_{17}O_3N_4S$ [M+H]: 333.10159. Found: 333.10160. For $C_{15}H_{16}O_3N_4S$ Calcd: 54.20% C, 4.85% H, 16.86% N. Found: 54.28% C, 5.12% H, 16.58% N.

3.36. 4-Amino-5-(furan-3-yl)-7-(2-deoxy-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (22g)

Compound **22g** was prepared as described for compound **19a** from compound **21** (150 mg, 0.40 mmol) and furan-3-boronic acid. The crude product was purified by column chromatography on silica (2% MeOH in $CHCl_3$). Compound **22g** (94 mg, 72%) was obtained as a yellowish crystalline solid after recrystallization (MeOH-water 1:4). Mp 184–190 °C. $[\alpha]_D^{20}$ −20.2 (c 0.218, DMSO). IR (ATR): 3233, 1616, 1581, 1554, 1456, 1049, 1021 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): 2.18 (ddd, 1H, J_{gem} = 13.1 Hz, $J_{2'a,1'}$ = 6.0 Hz, $J_{2'a,3'}$ = 2.7 Hz, H-2′a); 2.52 (ddd, 1H, J_{gem} = 13.1 Hz, $J_{2'b,1'}$ = 8.3 Hz, $J_{2'b,3'}$ = 5.8 Hz, H-2′b); 3.51 (ddd, 1H, J_{gem} = 11.7 Hz, $J_{5'a,OH}$ = 5.9 Hz, $J_{5'a,4'}$ = 4.4 Hz, H-5′a); 3.57 (ddd, 1H, J_{gem} = 11.7 Hz, $J_{5'b,OH}$ = 5.3 Hz, $J_{5'b,4'}$ = 4.8 Hz, H-5′b); 3.83 (td, 1H, $J_{4',5'a}$ = $J_{4',5'b}$ = 4.5 Hz, $J_{4',3'}$ = 2.5 Hz, H-4′); 4.35 (m, 1H, H-3′); 5.05 (bt, 1H, $J_{OH,5'a}$ = $J_{OH,5'b}$ = 5.6 Hz, OH-5′); 5.25 (d, 1H, $J_{OH,3'}$ = 4.1 Hz, OH-3′); 6.24 (bs, 2H, NH_2); 6.55 (dd, 1H, $J_{1',2'b}$ = 8.3 Hz, $J_{1',2'a}$ = 5.9 Hz, H-1′); 6.70 (dd, 1H, $J_{4,5}$ = 1.8 Hz, $J_{4,2}$ = 0.9 Hz, H-4-furyl); 7.48 (s, 1H, H-6); 7.80 (t, 1H, $J_{5,4}$ = $J_{5,2}$ = 1.7 Hz, H-5-furyl); 7.83 (dd, 1H, $J_{2,5}$ = 1.6 Hz, $J_{2,4}$ = 0.9 Hz, H-2-furyl); 8.12 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 39.84 (CH_2-2′); 62.19 (CH_2-5′); 71.22 (CH-3′); 83.06 (CH-1′); 87.50 (CH-4′); 101.06 (C-4a); 106.47 (C-5); 111.73 (CH-4-furyl); 118.76 (C-3-furyl); 120.64 (CH-6); 139.82 (CH-2-furyl); 144.31 (CH-5-furyl); 150.49 (C-7a); 151.94 (CH-2); 157.62 (C-4). MS (ESI) *m*/*z* (%): 317 (17) [M+H], 339 (100) [M+Na]; HRMS (ESI) Calcd for $C_{15}H_{17}O_4N_4$ [M+H]: 317.12443. Found: 317.12445. For $C_{15}H_{16}O_4N_4$ Calcd: 59.96% C, 5.10% H, 17.71% N. Found: 57.72% C, 5.26% H, 17.63% N.

3.37. 4-Amino-5-(thiophen-3-yl)-7-(2-deoxy-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (22h)

Compound **22h** was prepared as described for compound **19a** from compound **21** (150 mg, 0.40 mmol) and thiophene-3-boronic acid. The crude product was purified by reverse phase HPFC on C-18 column (0→100% MeOH in water). Compound **22h** (112 mg, 88%) was obtained as a white crystalline solid after recrystallization (MeOH-water 1:4). Mp 105–108 °C. $[\alpha]_D^{20}$ −14.3 (c 0.231, DMSO). IR (ATR): 3441, 1616, 1596, 1552, 1456, 1351, 1305, 1181, 1068, 1048, 1015 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6): 2.19 (ddd, 1H, J_{gem} = 13.1 Hz, $J_{2'a,1'}$ = 6.0 Hz, $J_{2'a,3'}$ = 2.7 Hz, H-2′a); 2.54 (ddd, 1H, J_{gem} = 13.1 Hz, $J_{2'b,1'}$ = 8.3 Hz, $J_{2'b,3'}$ = 5.9 Hz, H-2′b); 3.51 (btd, 1H, J_{gem} = 11.8 Hz, $J_{5'a,OH}$ = $J_{5'a,4'}$ = 5.0 Hz, H-5′a); 3.58 (bdt, 1H, J_{gem} = 11.8 Hz, $J_{5'b,OH}$ = $J_{5'b,4'}$ = 4.9 Hz, H-5′b); 3.83 (td, 1H, $J_{4',5'a}$ = $J_{4',5'b}$ = 4.5 Hz, $J_{4',3'}$ = 2.5 Hz, H-4′); 4.36 (m, 1H, H-3′); 5.05 (bt, 1H, $J_{OH,5'a}$ = $J_{OH,5'b}$ = 5.4 Hz, OH-5′); 5.26 (bd, 1H, $J_{OH,3'}$ = 3.0 Hz, OH-3′); 6.19 (s, 2H, NH_2); 6.57 (dd, 1H, $J_{1',2'b}$ = 8.3 Hz, $J_{1',2'a}$ = 6.0 Hz, H-1′); 7.27 (dd, 1H, $J_{4,5}$ = 4.9 Hz, $J_{4,2}$ = 1.3 Hz, H-4-thienyl); 7.51 (dd, 1H, $J_{2,5}$ = 2.9 Hz, $J_{2,4}$ = 1.3 Hz, H-2-thienyl); 7.53 (s, 1H, H-6); 7.70 (dd, 1H, $J_{5,4}$ = 4.9 Hz, $J_{5,2}$ = 2.9 Hz, H-5-thienyl); 8.14 (s, 1H, H-2). ^{13}C NMR (150.9 MHz, DMSO-d_6): 39.87 (CH_2-2′); 62.18 (CH_2-5′); 71.23 (CH-3′); 83.09 (CH-1′); 87.53 (CH-4′); 100.85 (C-4a); 111.21 (C-5); 120.77 (CH-6); 122.18 (CH-2-thienyl); 127.49 (CH-5-thienyl); 128.70 (CH-4-thienyl); 134.93 (C-3-thienyl); 150.35 (C-7a); 151.92 (CH-2); 157.54 (C-4). MS (ESI) *m*/*z* (%): 333 (100) [M+H], 355 (56) [M+Na]; HRMS (ESI) Calcd for $C_{15}H_{17}O_3N_4S$ [M+H]: 333.10159. Found: 333.10162. For $C_{15}H_{16}O_3N_4S{\cdot}H_2O$ Calcd: 51.42% C, 5.18% H, 15.99% N. Found: 51.45% C, 5.07% H, 15.73% N.

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