PYRROLO[2,3-*d*]PYRIMIDINE β-L-NUCLEOSIDES CONTAINING 7-DEAZAADENINE, 2-AMINO-7-DEAZAADENINE, 7-DEAZAGUANINE, 7-DEAZAISOGUANINE, AND 7-DEAZAXANTHINE

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Received March 15, 2006
Accepted April 26, 2006

This article is dedicated to Professor Antonín Holý, a good friend and a great scientist, on the occasion of his 70th birthday.

The synthesis and properties of 7-deazapurine β-L-nucleosides are described. The stereoselective glycosylation of the anions of 2-amino-6-chloro-7-deazapurines **9a**, **9b** or 6-chloro-7-deazapurines **13a**, **13d** with 3,5-di-*O*-(4-methylbenzoyl)-2-deoxy-α-L-*erythro*-pentofuranosyl chloride (**8**) furnished the β-L-2′-deoxyribonucleosides **1**–**4**. The synthesis of β-L-ribonucleosides **5**–**7** used the Silyl–Hilbert–Johnson reaction (TMSOTf/BSA/MeCN) performed under Vorbrüggen conditions for the glycosylation of 7-halogenated 6-chloro-2-pivalamido-7-deazapurines **17b**–**17d** with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-L-ribofuranose (**16**). Single-crystal X-ray analyses were performed and CD spectra were measured to assign the configuration. The antiviral activity against selected DNA and RNA viruses is reported.

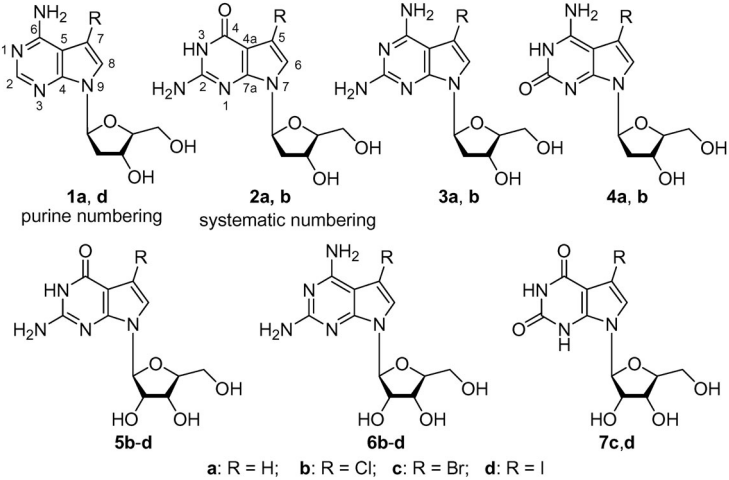
Keywords: Nucleosides; Purines; 7-Deazapurines; Pyrrolo[2,3-*d*]pyrimidines; β-L-2′-Deoxyribonucleosides; β-L-Ribonucleosides; Nucleobase anion glycosylation; NMR spectroscopy; CD spectroscopy; Antiviral activity.

The first L-nucleoside (β-L-dT) was synthesized by Šmejkal and Šorm in 1964 [1a]; in the same year Acton, Ryan, and Goodman described β-L-adenosine[1b]. Related β-L-ribonucleosides were reported by Shimizu in 1967 [2a] and by Holý and Šorm in 1969 [2b]. It was believed that D-nucleosides are always more active than the L-enantiomers and little attention has been given to the L-nucleosides. The discovery of the antiviral activity of 3TC, which is more active and less toxic than its D-counterpart, attracted the interest in the pharmacological activity of L-nucleosides[3–8]. Their antiviral activity is sometimes comparable or even higher than that of their D-enantiomers[3,7,8].

doi:10.1135/cccc20060956

It was found that cellular kinases are able to phosphorylate L-nucleosides to their triphosphates. A better toxicological profile and a greater metabolic stability are observed in several cases[3]. L-Nucleosides and their analogues have become effective drugs for the treatment of viral diseases. A number of them, such as lamivudine (3TC) and FTC [3,6,7] are commercialized; others like L-dT and L-FMAU are expected to get approval by the FDA [3,7a].

A number of 7-deazapurine (pyrrolo[2,3-*d*]pyrimidine) β-D-nucleosides, such as tubercidin, toyocamycin, sangivamycin, 5′-deoxy-7-iodotubercidin, and queuosine, exhibit a broad spectrum of biological activity[9–12] (purine numbering is used throughout the general section and systematic numbering in Experimental). Recently, a new class of 7-deazapurine β-D-ribonucleosides with a methyl group 'up' in the 2′-position was discovered showing strong inhibition of the hepatitis C virus growth[13]. Therefore, we became interested in combining the favorable properties of the 7-deazapurine system with a β-L-sugar moiety thereby generating new molecules with a low toxicity profile. Up to now only very few reports have appeared on the synthesis and properties of 7-deazapurine β-L-nucleosides[14,15]. This prompted us to undertake studies on a series of L-enantiomers containing the pyrrolo[2,3-*d*]pyrimidine system. Herein, we report on the synthesis of the 7-deazapurine β-L-2′-deoxyribonucleosides **1**–**4** and β-L-ribonucleosides such as **5**–**7** (Scheme 1). Their physical properties are discussed and data on their antiviral activity are reported.



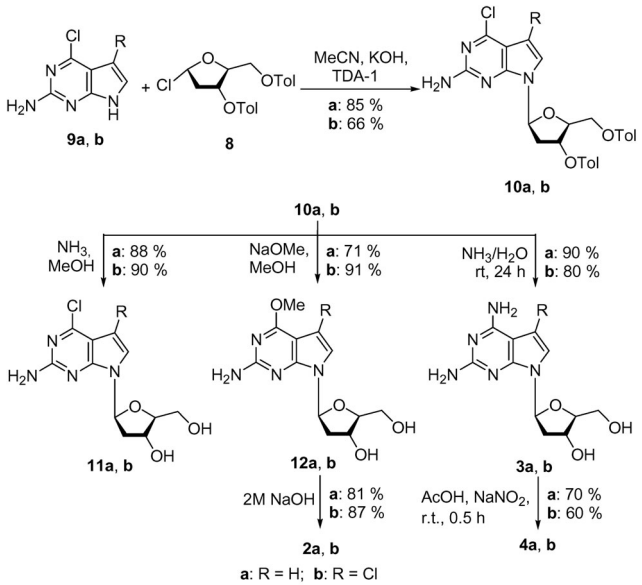
SCHEME 1

RESULTS AND DISCUSSION

Considering identical chemical properties of L- and D-nucleosides and their precursors in a nonchiral environment, the protocols developed for the chemical synthesis of 7-deazapurine D-nucleoside can be employed for the preparation of the L-enantiomers[16]. Instead of the 3,5-di-*O*-(4-methylbenzoyl)-2-deoxy-α-D-*erythro*-pentofuranosyl chloride and 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-D-ribofuranose, the corresponding L-enantiomers are used as sugar components. The 3,5-di-*O*-(4-methylbenzoyl)-2-deoxy-α-L-*erythro*-pentofuranosyl chloride (**8**), which was already described in 1964 [1a], was prepared according to the procedure for the corresponding D-halogenose[17a] and was employed in the synthesis of the 7-deazapurine β-L-2′-deoxyribonucleosides. The 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-L-ribofuranose (**16**)[1b,17b] was used for β-L-ribonucleoside synthesis.

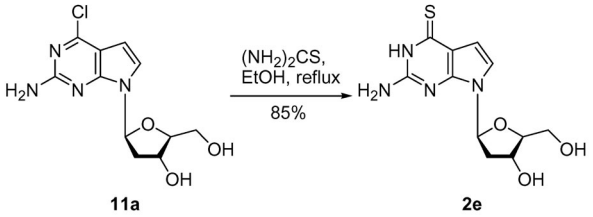
Synthesis of 7-Deazapurine β-L-*2′-Deoxyribonucleosides via the Stereoselective Nucleobase Anion Glycosylation*

The glycosylation of the 2-amino-4-chloro-7-deazapurines **9a**,**9b** [18,19] with the α-L-2-deoxyribofuranosyl halide **8** was performed in MeCN in the presence of powdered KOH using TDA-1 (tris[2-(2-methoxyethoxy)ethyl]amine) as phase-transfer catalyst (nucleobase-anion glycosylation conditions[20]) (Scheme 2). This reaction furnished the β-L-2′-deoxyribonucleosides **10a**



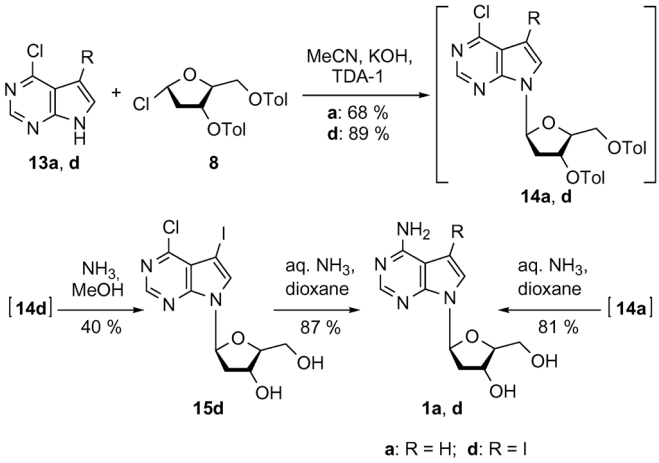
SCHEME 2

(85%) or **10b** (66%), exclusively. Compounds **10a**, **10b** were deprotected in saturated methanolic ammonia at room temperature affording the β-L-nucleosides **11a**, **11b**. The protected nucleosides **10a**, **10b** were also employed in various nucleophilic displacement reactions. The nucleosides were treated with 0.5 M NaOMe/MeOH under reflux to give the 4-methoxy derivatives **12a**, **12b**, which were converted to the 2′-deoxyguanosine analogs **2a**, **2b** (2 M NaOH). Removal of the toluoyl groups and subsequent displacement of the 6-chloro substituents of **10a**,**10b** were performed using 25% aq. NH_3 in a sealed steel vessel, furnishing the 2,6-diamino nucleosides **3a**, **3b**. Selective deamination of **3a**, **3b** with sodium nitrite in $AcOH/H_2O$ yielded the 7-deazaisoguanine nucleosides **4a**, **4b** in 60–70% yield. The 6-thio compound **2e** was obtained from **11a** reacting with thiourea in ethanol under reflux (Scheme 3).



SCHEME 3

Similarly, the glycosylation of **13a**, **13d** with halogenose **8** (MeCN/KOH/TDA-1) afforded the toluoyl-protected β-L-2′-deoxyribonucleosides **14a**, **14d** which were not purified (Scheme 4). The β-L-2′-deoxytubercidin (**1a**) was obtained from **14a** by nucleophilic displacement of the chloro substituent

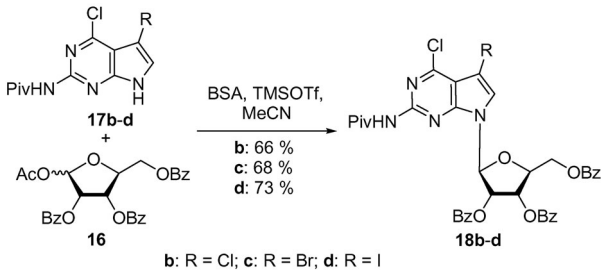


SCHEME 4

(aq. NH_3/dioxane, 80 °C). Compound **14d** was treated with methanolic ammonia to yield **15d**, which was converted to β-L-2′-deoxy-7-iodotubercidin (**1d**) in aq. NH_3/dioxane (120 °C).

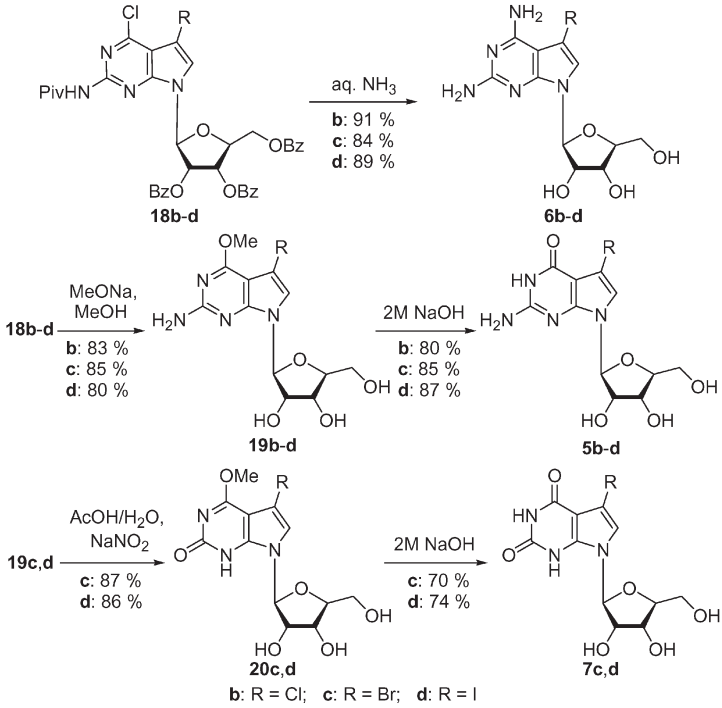
Synthesis of 7-Deazapurine β-L-*Ribonucleosides by the One-Pot Silyl–Hilbert–Johnson Reaction under Vorbrüggen Conditions*

Recently, we have reported on an efficient method for the synthesis of 7-substituted 7-deazapurine ribonucleosides using commercially available 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-D-ribofuranose as a sugar moiety[18]. Considering the similarity of the L-ribonucleosides and D-ribonucleosides, we now applied this protocol for the preparation of 7-substituted 7-deazapurine β-L-ribonucleosides. In this method, the glycosylation reaction is performed in MeCN using *N,O*-bis(trimethylsilyl)acetamide (BSA) as a silylating reagent and trimethylsilyl trifluoromethanesulfonate (TMSOTf) as catalyst. The glycosylation of the 2-pivalamido 7-deazapurine derivatives **17b**–**17d** [21] with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-L-ribofuranose (**16**) (BSA/TMSOTf/MeCN) afforded the β-L-ribonucleosides **18b**–**18d** in 66–73% yield (Scheme 5).



SCHEME 5

The nucleosides **18b**–**18d** were converted to the 2,6-diamino nucleosides **6b**–**6d** in aq. NH_3 at 120 °C in an autoclave (Scheme 6). The 4-methoxy compounds **19b**–**19d** were obtained by treatment of **18b**–**18d** with 0.5 M NaOMe under reflux conditions and the 7-deazaguanosine derivatives **5b**–**5d** were prepared from **19b**–**19d** by methyl ether cleavage (2 M NaOH). Deamination of compounds **19c**, **19d** with $NaNO_2$/AcOH yielded the 2-oxo nucleosides **20c**, **20d**; the methoxy group was displaced by a hydroxy function upon treatment with 2 M NaOH under reflux conditions for 36 h yielding the 7-substituted 7-deazaxanthosines **7c**, **7d**.



SCHEME 6

Physical Properties and Characterization

All compounds were characterized by ^{1}H NMR (Experimental) and ^{13}C NMR spectra (Table I) as well as by elemental analyses (Experimental). The assignments of the ^{13}C NMR chemical shifts are made according to the corresponding D-nucleosides[18,21–23]. The structure of 2′-deoxy-7-iodotubercidin (**1d**) was confirmed by single-crystal X-ray analysis (Fig. 1) (data will be published elsewhere).

The β-L-configuration was deduced from the CD spectra measured for both the 7-deazapurine L-nucleosides and the corresponding D-enantiomers. Selected spectra are shown in Fig. 2. By comparing the CD spectra of the β-L- and β-D-nucleosides (Fig. 2a–2d), mirror images of the ellipticities confirmed the enantiomeric character. The β-L-nucleosides show a positive lobe while a negative lobe is formed by the β-D-enantiomers. All 7-deazapurine nucleosides show rather low ellipticity values compared to the parent purine nucleosides, which explains the moderate quality of the spectra.

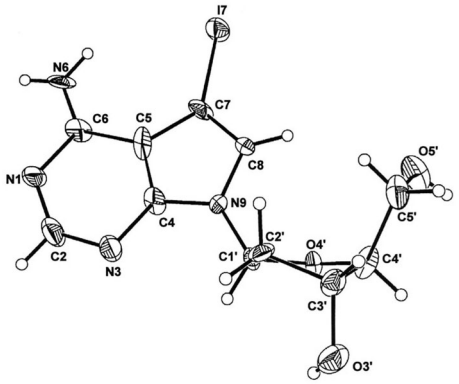


FIG. 1

Perspective views of compound **1d**. Displacement ellipsoids are shown at the 50% probability level and H atoms are shown as spheres of arbitrary size

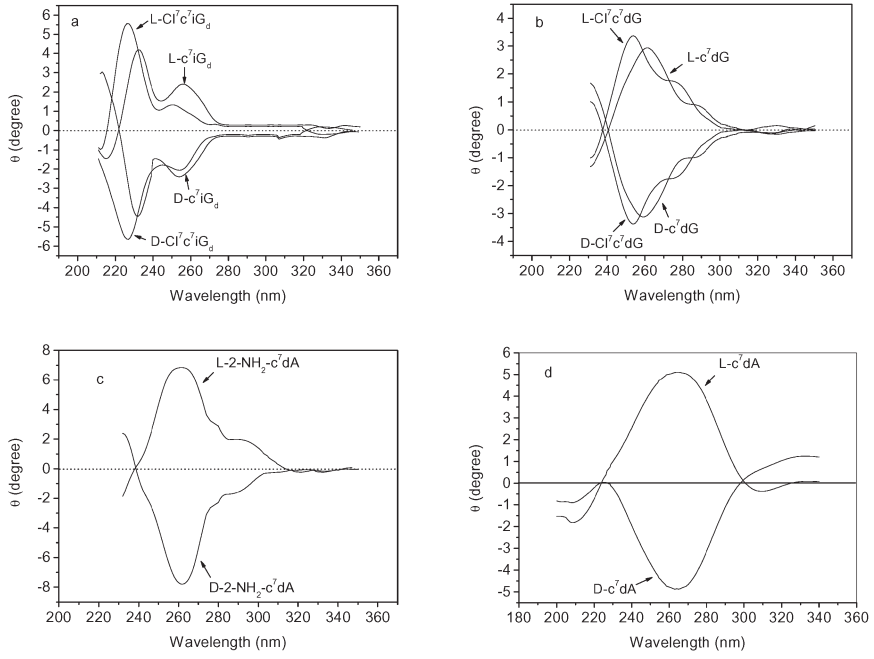


FIG. 2

The CD spectra measured in MeOH at concentrations (in mol/l): 4.5×10^{-5} (a), 4.1×10^{-5} (b), 9.8×10^{-5} (c), 9.5×10^{-5} (d)

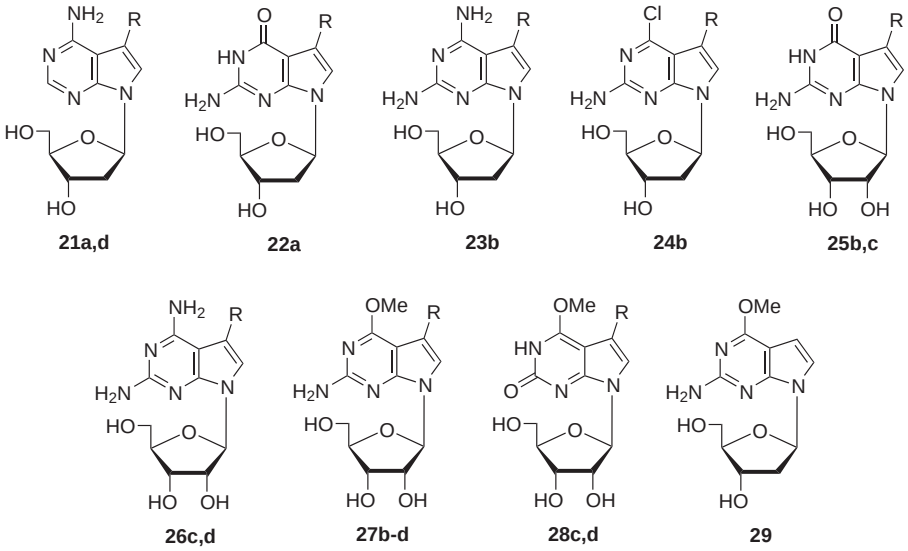
TABLE I
^{13}C NMR chemical shifts (δ) of 7-deazapurine L-nucleosides[a]

Compd[b,c]	C(2)[d] C(2)	C(4)[d] C(6)	C(4a) C(5)	C(5) C(7)	C(6) C(8)	C(7a)[d] C(4)	C(1′)	C(2′)	C(3′)	C(4′)	C(5′)
					β-L-2′-Deoxyribonucleosides						
1a	151.9	157.8	103.2	100.0	122.0	150.0	83.6	[e]	71.5	87.6	62.5
1d	151.7	157.0	103.1	52.1	126.9	149.6	83.0	[e]	70.9	87.4	61.9
2a	158.6	152.6	99.9	102.2	116.7	150.5	82.1	[e]	70.9	86.9	62.0
2b	157.5	153.1	97.0	106.3	114.0	149.8	82.1	[e]	70.9	87.1	61.9
2e	152.2	175.7	104.3	113.1	120.1	147.0	82.2	[e]	70.9	87.1	61.9
3a	153.1	156.1	92.4	100.7	119.0	[f]	83.3	[e]	71.1	87.1	62.1
3b	152.5	156.3	90.2	103.7	116.3	[f]	82.6	[e]	70.9	87.2	61.9
4a	159.9	157.9	96.3	100.0	117.4	152.5	82.6	[e]	71.2	86.9	62.3
4b	161.2	158.0	94.2	104.1	115.4	152.7	82.8	[e]	71.8	87.8	62.8
10a	158.6	153.6	11.3	101.3	122.5	152.8	84.1	37.3	75.2	82.0	64.2
10b	158.9	152.9	108.0	106.4	119.9	152.8	84.1	37.8	75.3	82.5	64.2
11a	159.3	153.7	99.8	108.8	123.0	151.1	82.3	[e]	70.9	87.1	61.9
11b	159.6	152.8	104.9	103.0	120.2	150.5	82.2	[e]	70.8	87.3	61.7
12a	162.8	159.4	97.1	99.0	119.4	154.2	82.2	[e]	71.0	86.9	62.0
12b	162.8	159.9	95.0	103.2	116.4	153.2	82.1	[e]	71.0	87.1	61.9
15d	150.7	151.0	116.5	53.4	133.4	150.4	83.4	[e]	70.7	87.7	61.5
					β-L-Ribonucleosides						
5b	153.0	157.5	97.1	106.3	114.3	150.4	85.7	73.6	70.5	84.8	61.5
5c	152.9	157.7	98.1	90.4	116.8	150.8	85.7	73.6	70.5	84.8	61.5
5d	152.5	158.1	99.9	54.5	121.9	151.0	85.9	73.8	70.4	84.6	61.5
6b	160.3	157.2	93.5	103.3	115.1	152.4	85.8	73.4	70.6	84.7	61.7
6c	160.2	157.3	94.5	87.5	117.5	152.7	85.7	73.4	70.6	84.7	61.7
6d	159.7	157.5	96.5	52.3	123.0	153.2	85.8	73.3	70.6	84.7	61.7
7c	151.1	158.7	97.3	91.1	117.5	140.1	85.7	74.0	70.6	89.1	61.3
7d	150.3	158.9	99.1	56.3	122.9	139.0	85.7	74.1	70.6	89.1	61.3
18b	152.4	150.7	110.1	103.5	126.0	150.6	87.7	71.3	74.0	79.3	63.7
18c	152.4	151.5	111.5	88.2	129.6	151.7	88.8	71.6	74.2	79.6	63.9
18d	151.8	151.6	113.3	54.1	128.4	151.3	87.6	71.2	73.9	79.1	63.7
19b	159.8	162.7	95.0	103.2	116.6	153.7	85.6	73.5	70.5	84.8	61.6
19c	159.7	162.8	96.3	87.2	119.1	154.2	85.7	73.5	70.5	84.8	61.6
19d	159.4	162.8	98.8	51.8	124.5	154.8	85.6	73.5	70.5	84.8	61.6
20c	160.6	163.9	98.4	87.3	120.9	[f]	86.4	73.8	70.5	85.2	61.4
20d	160.3	163.9	100.5	52.0	126.8	[f]	86.4	73.8	70.5	85.1	61.4

[a] Measured in DMSO-d_6. [b] First line – systematic numbering. [c] Second line – purine numbering. [d] Tentative. [e] Superimposed by DMSO. [f] Not detected.

Inhibitory Activity

The 7-deazapurine β-L-nucleosides described above as well as their β-D-isomers were evaluated in cell culture experiments to test the inhibition of the replication of RNA viruses including human immunodeficiency virus-1 (HIV-1), bovine viral diarrhea virus (BVDV), yellow fever virus (YFV), dengue virus (DENV-2), and West Nile virus (WNV). A retrovirus, namely human immunodeficiency virus-1 (HIV-1) and a DNA virus (Hepatitis B virus, HBV) were used as well. The data are summarized in Tables II and III; schemes of compounds **21**–**29**, see Chart 1. The results show that most of these compounds do not show significant antiviral activity. Only in the case of β-D-2′-deoxytubercidin (**21a**), selective activity against HBV was observed (EC_{50} = 0.5 μM), while this is not the case of the corresponding L-isomer **1a**. Its 7-iodo derivative **1d** is cytotoxic against HIV-1 and HBV as well as the 2,6-diamino-7-deazapurine D-ribonucleosides **26c**, **26d** and 2-amino-6-methoxy-7-deazapurine analogs **27b**–**27d** (Table II). Compounds **26c**, **26d** are also toxic against YFV (Table III).



a: R = H; **b**: R = Cl; **c**: R = Br; **d**: R = I

CHART 1

TABLE II
Antiviral activities of 7-deazapurine β-L-nucleosides and the corresponding β-D-nucleosides against HIV-1 and HBV viruses[a]

	HIV-1		HBV RI	HBV Tox		HIV-1		HBV RI	HBV Tox
	EC_{50}[b]	CC_{50}[c]	EC_{50}[d]	CC_{50}[e]		EC_{50}[b]	CC_{50}[c]	EC_{50}[d]	CC_{50}[e]
L-**1a**	>100	>100	>10	>100	D-**26c**[18]	>3	3	n.d.	n.d.
D-**21a**[22]	>100	>100	0.5	>100	D-**26d**[18]	>1.3	1.3	n.d.	n.d.
L-**1d**	16/18	16/18	>4	4	D-**24b**[21]	>77	77	>10	>50
D-**21d**[23]	n.d.	3.7	n.d.	n.d.	L-**12a**	>100	>100	>10	>100
L-**2a**	>100	>100	n.d.	n.d.	D-**27b**[18]	>4	4	n.d.	n.d.
D-**22a**[20]	>100	>100	10	>100	D-**27c**[18]	>1.4	1.4	n.d.	n.d.
L-**3a**	>100	>100	n.d.	n.d.	D-**27d**[18]	>0.7	0.7	>10	12
D-**23b**[21]	>48	48	>10	>50	D-**28c**[18]	>100	>100	n.d.	n.d.
L-**4a**	>100	>100	n.d.	n.d.	D-**28d**[18]	>100	>100	n.d.	n.d.
D-**25b**[18]	>100	>100	n.d.	n.d.	L-**15d**	>5.3	5.3	>10	10
D-**25c**[18]	>100	>100	n.d.	n.d.					

[a] n.d., not yet determined. [b] Compound concentration (μM) required to achieve 50% protection of $CD4^+$ human T-cells containing an integrated HTLV-1 genome (MT-4 cells) from the HIV-1-induced cytopathogenicity, as determined by the MTT method. [c] Compound concentration (μM) required to reduce the viability of mock-infected MT-4 cells by 50%, as determined by the MTT method. [d] Compound concentration (μM) required to reduce the intracellular HBV DNA (HBV RI). [e] Compound concentration (μM) required to reduce the viability of hepatocellular carcinoma (HepG2) cells by 50%, as determined by the MTT method.

Conclusion

The stereoselective synthesis of a number of 7-deazapurine β-L-2′-deoxyribonucleosides and β-L-ribonucleosides was accomplished using nucleobase anion glycosylation or Silyl–Hilbert–Johnson reaction performed under Vorbrüggen conditions (TMSOTf/BSA/MeCN). The 3,5-di-*O*-(4-methylbenzoyl)-2-deoxy-α-L-*erythro*-pentofuranosyl chloride (**8**) and 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-L-ribofuranose (**16**) were employed for the glycosylation reaction. The mirror images of the CD spectra of the β-L- and β-D-nucleosides confirmed the enantiomeric character. Most of the 7-deazapurine β-L-nucleosides do not show significant antiviral activity; some of them are cytotoxic.

TABLE III
Antiviral activities of 7-deazapurine β-L-nucleosides and the corresponding β-D-nucleosides against RNA viruses[a]

	BVDV		YFV		DENV-2		WNV	
	EC_{50}[b]	CC_{50}[c]	EC_{50}[d]	CC_{50}[e]	EC_{50}[d]	CC_{50}[e]	EC_{50}[d]	CC_{50}[e]
L-**1a**	>100	>100	>100	>100	>100	>100	>100	>100
D-**21a**	>100	>100	>100	>100	>100	>100	>100	>100
L-**1d**	36/46	36/46	12/14	12/14	>20/12	20/12	>20/12	20/12
L-**2a**	>100	>100	>100	>100	n.d.	n.d.	n.d.	n.d.
D-**22a**	>100	>100	>100	>100	>100	>100	>100	>100
L-**2b**	>100	>100	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
L-**3a**	>100	>100	>100	>100	n.d.	n.d.	n.d.	n.d.
D-**23a**	>73	73	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
L-**3b**	>73	73	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
D-**23b**	>79	79	>100	>100	>100	>100	>100	>100
L-**4a**	>250[f]	>250	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
L-**4b**	>100	>100	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
L-**5b**	>100	>100	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
D-**25b**	>100	>100	>100	>100	n.d.	n.d.	n.d.	n.d.
L-**5c**	>100	>100	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
D-**25c**	>100	>100	>100	>100	n.d.	n.d.	n.d.	n.d.
L-**5d**	>100	>100	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
L-**6c**	>100	>100	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
D-**26c**	>80	>80	>1.7	1.7	n.d.	n.d.	n.d.	n.d.
L-**6d**	>100	>100	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
D-**26d**	>22	22	>3	3	n.d.	n.d.	n.d.	n.d.
L-**11b**	>50	50	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
D-**24b**	>100	>100	>100	>100	>100	>100	>100	>100
L-**12a**	>100	>100	>100	>100	n.d.	n.d.	n.d.	n.d.
D-**29**[20a]	>100	>100	>100	>100	>100	>100	>100	>100
L-**19b**	>100	>100	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
D-**27b**	>26	26	>100	≥100	n.d.	n.d.	n.d.	n.d.
L-**19c**	>100	>100	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
D-**27c**	>10	10	>71	71	n.d.	n.d.	n.d.	n.d.
L-**19d**	>100	>100	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
D-**27d**	>11	>11	>16	16	>29	29	>29	29
L-**20c**	>100	>100	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
D-**28c**	>250[f]	>250	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
L-**20d**	>100	>100	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
D-**28d**	>175[f]	>175	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
L-**15d**	>51	51	>45	45	>78	78	>78	78

[a] n.d., not yet determined. [b] Compound concentration (μM) required to achieve 50% protection of pre-infected Madin Darby Bovin Kidney (MDBK) cells from the BVDV-induced cytopathogenicity, as determined by the MTT method. [c] Compound concentration (μM) required to reduce the viability of mock-infected MDBK cells by 50%, as determined by the MTT method. [d] Compound concentration (μM) required to achieve 50% protection of Baby Hamster Kidney (BHK-21) cells from the YFV, DENV-2 and WNV-induced cytopathogenicity, as determined by the MTT method. [e] Compound concentration (μM) required to reduce the viability of mock-infected BHK cells by 50%, as determined by the MTT method. [f] Compound concentration (μM) required to protect 50% of non-pre-infected MDBK cells from the BVDV-induced cytopathogenicity, as determined by the MTT method.

EXPERIMENTAL

General

All chemicals were purchased from Sigma–Aldrich (Sigma–Aldrich Chemie GmbH, Taufkirchen, Germany). 3,5-Di-*O*-(4-methylbenzoyl)-2-deoxy-α-L-*erythro*-pentofuranosyl chloride (**8**)[1a] and 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-L-ribofuranose (**16**)[1b] were prepared as described for the corresponding D-isomers[17a,17b]. Solvents were of laboratory grade. Thin-layer chromatography (TLC): aluminum sheets, silica gel 60 F_{254}, 0.2 mm layer (VWR International, Darmstadt, Germany). Column flash chromatography (FC): silica gel 60 (VWR International, Darmstadt, Germany) at 0.4 bar. Sample collection with a MultiRac fractions collector (LKB Instruments Sweden). UV spectra were recorded on a U-3200 spectrophotometer (Hitachi, Japan), λ_{max} in nm, ε in $dm^3\ mol^{-1}\ cm^{-1}$. The CD spectra were measured with a Jasco J-600A spectropolarimeter (Jasco, Japan) at room temperature using a 1.0 ml water-jacketed cylindrical cells of 1-cm path length. The spectra were recorded between 200 nm and 350 nm in intervals of 0.5 nm. NMR spectra were measured on an Avance DPX 250 or an AMX-500 spectrometer (Bruker, Rheinstetten, Germany); chemical shifts (δ) are in ppm downfield from internal TMS (^{1}H, ^{13}C). The *J* values are given in Hz. Melting points were determined with a Linström apparatus and are not corrected. Elemental analyses were performed by the Mikroanalytisches Laboratorium Beller, Göttingen, Germany.

4-Chloro-7-[2-deoxy-3,5-di-*O*-(4-methylbenzoyl)-β-L-*erythro*-pentofuranosyl]-7*H*-pyrrolo[2,3-*d*]pyrimidin-2-amine (**10**a)

To a suspension of powdered KOH (85%, 1.15 g, 17.42 mmol) and TDA-1 (0.2 ml, 0.63 mmol) in MeCN (60 ml), 2-amino-4-chloro-7*H*-pyrrolo[2,3-*d*]pyrimidine (**9a** [19]; 842 mg, 4.99 mmol) was added at room temperature. After the mixture was stirred for 5 min, 3,5-di-*O*-benzoyl-2-deoxy-α-L-*erythro*-pentofuranosyl chloride (**8** [1a,17a]; 2.53 g, 6.51 mmol) was introduced within 15 min, and the stirring was continued for 30 min. The insoluble material was filtered off, the precipitate was washed with MeCN, and the filtrate was evaporated to dryness. The residue was dissolved in CH_2Cl_2, applied onto flash chromatography (FC) (silica gel, column 6 × 12 cm), and the compound was eluted with CH_2Cl_2. The product-containing fractions were combined and evaporated to give a colorless foam (2.21 g, 85%). TLC (silica gel, CH_2Cl_2/MeOH, 99:1): R_F 0.25. For $C_{27}H_{25}ClN_4O_5$ (521.0) calculated: 62.25% C, 4.84% H, 10.75% N; found: 62.20% C, 4.91% H, 10.80% N. ^{1}H NMR (250 MHz, $CDCl_3$): 2.42 s, 3 H (CH_3); 2.44 s, 3 H (CH_3); 2.64–2.69 m, 1 H (H-2′); 2.85–2.91 m, 1 H (H-2′); 4.57–4.64 m, 2 H (H-5′); 4.71–4.77 m, 1 H (H-4′); 5.06 s, 2 H (NH_2); 5.73–5.76 m, 1 H (H-3′); 6.38 d, 1 H, *J*(5,6) = 3.8 (H-5); 6.58 dd, 1 H, *J*(1′,2′) = 5.8, 8.4 (H-1′); 7.01 d, 1 H, *J*(5,6) = 3.8 (H-6); 7.24–7.97 m, 8 H (C_6H_4).

4,5-Dichloro-7-[2-deoxy-3,5-di-*O*-(4-methylbenzoyl)-β-L-*erythro*-pentofuranosyl]-7*H*-pyrrolo[2,3-*d*]pyrimidin-2-amine (**10b**)

As described for **10a**, with 2-amino-4,5-dichloro-7*H*-pyrrolo[2,3-*d*]pyrimidine (**9b**[18]; 1.02 g, 5.02 mmol), halogenose **8** (2.53 g, 6.51 mmol), MeCN (60 ml), KOH (85%, 1.15 g, 17.42 mmol), and TDA-1 (0.2 ml, 0.63 mmol). FC (silica gel, column 6 × 12 cm, CH_2Cl_2) afforded a colorless foam (1.83 g, 66%). TLC (silica gel, CH_2Cl_2/MeOH, 99:1): R_F 0.28. For $C_{27}H_{24}Cl_2N_4O_5$ (555.4) calculated: 58.39% C, 4.36% H, 10.09% N; found: 58.61% C, 4.35% H, 9.95% N.

^{1}H NMR (250 MHz, $CDCl_3$): 2.66 s, 3 H (CH_3); 2.67 s, 3 H (CH_3); 2.88–2.90 m, 1 H (H-2′); 2.99–3.02 m, 1 H (H-2′); 4.77–4.87 m, 2 H (H-5′); 4.88–4.96 m, 1 H (H-4′); 5.33 s, 2 H (NH_2); 5.93–5.95 m, 1 H (H-3′); 6.79 t, 1 H, *J*(1′,2′) = 6.4 (H-1′); 7.48–7.52 m, 5 H (H-6, arom H); 8.14–8.21 m, 4 H (arom H).

4-Chloro-7-(2-deoxy-β-L-*erythro*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidin-2-amine (**11a**)

A solution of compound **10a** (782 mg, 1.50 mmol) in NH_3/MeOH (saturated at 0 °C, 50 ml) was stirred at room temperature overnight. The clear solution was evaporated, and the residue was applied onto FC (silica gel, column 4 × 16 cm, CH_2Cl_2/MeOH, 95:5). After evaporation, the main zone yielded a colorless solid (350 mg, 82%). TLC (silica gel, CH_2Cl_2/MeOH, 9:1): R_F 0.39. For $C_{11}H_{13}ClN_4O_3$ (284.7) calculated: 46.41% C, 4.60% H, 19.68% N; found: 46.30% C, 4.53% H, 19.50% N. UV (MeOH): 234 (28700), 258 (4300), 316 (sh 5700). ^{1}H NMR (250 MHz, DMSO-d_6): 2.10–2.17 m, 1 H (H-2′); 2.35–2.46 m, 1 H (H-2′); 3.46–3.56 m, 2 H (H-5′); 3.74–3.79 m, 1 H (H-4′); 4.30–4.33 m, 1 H (H-3′); 4.90 t, 1 H, *J* = 5.1 (OH-5′); 5.25 d, 1 H, *J* = 3.5 (OH-3′); 6.35 d, 1 H, *J*(5,6) = 3.6 (H-5); 6.42 t, 1 H, *J*(1′,2′) = 6.9 (H-1′); 6.69 br s, 2 H (NH_2); 7.37 d, 1 H, *J*(5,6) = 3.6 (H-6).

4,5-Dichloro-7-(2-deoxy-β-L-*erythro*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidin-2-amine (**11b**)

As described for **11a**, with compound **10b** (1.11 g, 2.00 mmol) and NH_3/MeOH (saturated at 0 °C, 60 ml). FC resulted in a colorless solid (574 mg, 90%). TLC (silica gel, CH_2Cl_2/MeOH, 9:1): R_F 0.39. For $C_{11}H_{12}Cl_2N_4O_3$ (319.1) calculated: 41.40% C, 3.79% H, 17.56% N; found: 41.49% C, 3.74% H, 17.40% N. UV (MeOH): 241 (29700), 264 (4000), 324 (5400). ^{1}H NMR (250 MHz, DMSO-d_6): 2.12–2.16 m, 1 H (H-2′); 2.36–2.39 m, 1 H (H-2′); 3.49–3.54 m, 2 H (H-5′); 3.78–3.81 m, 1 H (H-4′); 4.31–4.33 m, 1 H (H-3′); 4.96 t, 1 H, *J* = 5.6 (OH-5′); 5.28 d, 1 H, *J* = 3.6 (OH-3′); 6.31 dd, 1 H, *J*(1′,2′) = 6.0, 8.1 (H-1′); 6.94 br s, 2 H (NH_2); 7.55 s, 1 H (H-6).

7-(2-Deoxy-β-L-*erythro*-pentofuranosyl)-4-methoxy-7*H*-pyrrolo[2,3-*d*]pyrimidin-2-amine (**12a**)

A solution of **10a** (1.04 g, 2.00 mmol) in 0.5 M NaOMe/MeOH (60 ml) was stirred under reflux for 3 h. The mixture was neutralized with AcOH and evaporated. The residue was applied onto FC (silica gel, CH_2Cl_2/MeOH, 95:5→9:1). After evaporation, the main zone gave a colorless solid (400 mg, 71%). TLC (silica gel, CH_2Cl_2/MeOH, 9:1): R_F 0.43. For $C_{12}H_{16}N_4O_4$ (280.3) calculated: 51.42% C, 5.75% H, 19.99% N; found: 51.20% C, 5.99% H, 19.96% N. UV (MeOH): 224 (23600), 261 (9300), 287 (7300). ^{1}H NMR (250 MHz, DMSO-d_6): 2.06–2.10 m, 1 H (H-2′); 2.34–2.40 m, 1 H (H-2′); 3.45–3.50 m, 1 H (H-5′); 3.73–3.76 m, 1 H (H-4′); 3.91 s, 3 H (OMe); 4.28–4.32 m, 1 H (H-3′); 4.94 br s, 1 H (OH-5′); 5.22 br s, 1 H (OH-3′); 6.22–6.26 m, 3 H (NH_2, H-1′); 6.41 d, 1 H, *J*(5,6) = 3.8 (H-5); 7.10 d, 1 H, *J*(5,6) = 3.8 (H-6).

5-Chloro-7-(2-deoxy-β-L-*erythro*-pentofuranosyl)-4-methoxy-7*H*-pyrrolo[2,3-*d*]pyrimidin-2-amine (**12b**)

As described for **12a**, with compound **10b** (833 mg, 1.50 mmol) and 0.5 M NaOMe/MeOH (40 ml). FC resulted in a colorless solid (430 mg, 91%). TLC (silica gel, CH_2Cl_2/MeOH, 9:1): R_F 0.45. For $C_{12}H_{15}ClN_4O_4$ (314.7) calculated: 45.80% C, 4.80% H, 17.80% N; found: 45.92% C,

4.87% H, 18.00% N. UV (MeOH): 230 (27200), 265 (8300), 289 (6700). ^{1}H NMR (250 MHz, DMSO-d_6): 2.06–2.11 m, 1 H (H-2′); 2.29–2.40 m, 1 H (H-2′); 3.46–3.50 m, 1 H (H-5′); 3.74–3.76 m, 1 H (H-4′); 3.92 s, 3 H (OMe); 4.27–4.31 m, 1 H (H-3′); 4.95 t, 1 H, *J* = 5.2 (OH-5′); 5.25 d, 1 H, *J* = 2.7 (OH-3′); 6.36–6.45 m, 3 H (NH_2, H-1′); 7.23 s, 1 H (H-6).

2-Amino-7-(2-deoxy-β-L-*erythro*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidin-4(3*H*)-one (**2a**)

A solution of compound **12a** (140 mg, 0.50 mmol) in 2 M NaOH (40 ml) was heated under reflux for 3 h. After cooling and neutralization with 2 M HCl, the crude product of **2a** was chromatographed on a Serdolit AD-4 column (3 × 12 cm, resin 0.1–0.2 mm; Serva, Germany). The column was washed with H_2O (150 ml), and the product was eluted with H_2O/i-PrOH (9:1, 200 ml). The product containing fractions were collected and the solvent was removed to ca. 30 ml. Compound **2a** crystallized from H_2O. Colorless crystals (108 mg, 81%), m.p. 247–248 °C (dec. H_2O). TLC (silica gel, CH_2Cl_2/MeOH, 9:1): R_F 0.22. For $C_{11}H_{14}N_4O_4$ (266.3) calculated: 49.62% C, 5.30% H, 21.04% N; found: 49.52% C, 5.46% H, 20.82% N. UV (MeOH): 218 (20500), 260 (12400), 285 (6500). ^{1}H NMR (250 MHz, DMSO-d_6): 2.05–2.10 m, 1 H (H-2′); 2.30–2.36 m, 1 H (H-2′); 3.45–3.50 m, 1 H (H-5′); 3.73–3.76 m, 1 H (H-4′); 4.26–4.30 m, 1 H (H-3′); 4.90 br s, 1 H (OH-5′); 5.21 br s, 1 H (OH-3′); 6.27–6.30 m, 4 H (H-5, NH_2, H-1′); 6.91 d, 1 H, *J*(5,6) = 3.8 (H-6); 10.44 s, 1 H (NH).

2-Amino-5-chloro-7-(2-deoxy-β-L-*erythro*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidin-4(3*H*)-one (**2b**)

Compound **2b** was prepared from **12b** (315 mg, 1.00 mmol) and 2 M NaOH (60 ml) as described for **2a**. Colorless needles (262 mg, 87%), m.p. 206–207 °C (dec. H_2O). TLC (silica gel, CH_2Cl_2/MeOH, 9:1): R_F 0.24. For $C_{11}H_{13}ClN_4O_4$ (300.7) calculated: 43.94% C, 4.36% H, 18.63% N; found: 43.80% C, 4.40% H, 18.52% N. UV (MeOH): 222 (20600), 265 (12100), 287 (7100). ^{1}H NMR (250 MHz, DMSO-d_6): 2.05–2.09 m, 1 H (H-2′); 2.27–2.32 m, 1 H (H-2′); 3.45–3.52 m, 1 H (H-5′); 3.73–3.75 m, 1 H (H-4′); 4.26–4.29 m, 1 H (H-3′); 4.94 t, 1 H, *J* = 5.0 (OH-5′), 5.21 d, 1 H, *J* = 3.3 (OH-3′); 6.29 dd, 1 H, *J*(1′,2′) = 6.1, 7.7 (H-1′); 6.41 s, 2 H (NH_2); 7.06 s, 1 H (H-6), 10.54 s, 1 H (NH).

2-Amino-7-(2-deoxy-β-L-*erythro*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine-4(3*H*)-thione (**2e**)

A solution of **11a** (200 mg, 0.70 mmol) and thiourea (160 mg, 2.10 mmol) in ethanol (10.0 ml) was stirred under reflux for 30 min. The solvent was evaporated and the residue was applied onto FC (silica gel, CH_2Cl_2/MeOH, 95:5→9:1). Evaporation of the main zone gave crude **2e** as a colorless solid (168 mg, 85%). TLC (silica gel, CH_2Cl_2/MeOH, 5:1): R_F 0.5. For $C_{11}H_{14}N_4O_3S$ (282.3) calculated: 46.80% C, 5.00% H, 19.85% N, 11.36% S; found: 46.67% C, 4.69% H, 19.68% N, 11.30% S. UV (MeOH): 236 (20500), 269 (10600), 338 (13700). ^{1}H NMR (250 MHz, DMSO-d_6): 2.10–2.13 m, 1 H (H-2′); 2.31–2.36 m, 1 H (H-2′); 3.47–3.55 m, 1 H (H-5′); 3.77–3.78 m, 1 H (H-4′); 4.30–4.31 m, 1 H (H-3′); 4.88 t, 1 H, *J* = 5.4 (OH-5′); 5.22 d, 1 H, *J* = 3.7 (OH-3′); 6.30 dd, 1 H, *J*(1′,2′) = 6.1, 7.9 (H-1′); 6.41 d, 1 H, *J*(5,6) = 3.6 (H-5); 6.61 br s, 2 H (NH_2); 7.14 d, 1 H, *J*(5,6) = 3.6 (H-6); 10.44 s, 1 H (NH).

7-(2-Deoxy-β-L-*erythro*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine-2,4-diamine (**3a**)

A suspension of compound **10a** (782 mg, 1.50 mmol) in dioxane (20 ml) and 25% concentrated aq. NH_3 (60 ml) was introduced in an autoclave and stirred at 120 °C for 24 h. The clear solution was evaporated, and the residue was applied onto FC (silica gel, column 4 × 12 cm, CH_2Cl_2/MeOH, 95:5→9:1). After evaporation, the main zone was evaporated yielding crude **3a**, which was crystallized from MeOH, giving colorless crystals (358 mg, 90%), m.p. 213–215 °C (dec.). TLC (silica gel, CH_2Cl_2/MeOH, 9:1): R_F 0.31. For $C_{11}H_{15}N_5O_3$ (265.3) calculated: 49.81% C, 5.70% H, 26.40% N; found: 49.62% C, 5.62% H, 26.12% N. UV (MeOH): 223 (27500), 265 (10500), 287 (8400). ^{1}H NMR (250 MHz, DMSO-d_6): 2.01–2.08 m, 1 H (H-2′); 2.34–2.43 m, 1 H (H-2′); 3.47–3.52 m, 2 H (H-5′); 3.74–3.79 m, 1 H (H-4′); 4.28–4.30 m, 1 H (H-3′); 5.14–5.18 m, 2 H (OH-5′, OH-3′); 5.51 br s, 2 H (NH_2); 6.29–6.39 m, 2 H (H-1′, H-5); 5.54 br s, 2 H (NH_2); 6.89 d, 1 H, *J*(5,6) = 3.7 (H-6).

5-Chloro-7-(2-deoxy-β-D-*erythro*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine-2,4-diamine (**3b**)

As described for **3a**, compound **3b** was prepared from **10b** (833 mg, 1.50 mmol), 25% concentrated aq. NH_3 (60 ml), and dioxane (20 ml). Colorless needles (360 mg, 80%), m.p. 203–204 °C (dec. H_2O). TLC (silica gel, CH_2Cl_2/MeOH, 9:1): R_F 0.33. For $C_{11}H_{14}ClN_5O_3$ (299.7) calculated: 44.08% C, 4.71% H, 23.37% N; found: 44.15% C, 4.81% H, 23.31% N. UV (MeOH): 229 (28100), 269 (9600), 288 (7400). ^{1}H NMR (DMSO-d_6): 2.00–2.07 m, 1 H (H-2′); 2.27–2.38 m, 1 H (H-2′); 3.47–3.49 m, 2 H (H-5′); 3.74–3.78 m, 1 H (H-4′); 4.26–4.28 m, 1 H (H-3′); 5.01 t, 1 H, *J* = 5.1 (OH-5′), 5.22 d, 1 H, *J* = 3.5 (OH-3′); 5.84 br s, 2 H (NH_2); 6.31–6.37 m, 3 H (H-1′, NH_2); 7.09 s, 1 H (H-6).

4-Amino-7-(2-deoxy-β-L-*erythro*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidin-2(3*H*)-one (**4a**)

To a solution of compound **3a** (265 mg, 1.00 mmol) in AcOH/H_2O (1:5 v/v; 40.0 ml), a solution of $NaNO_2$ (250 mg, 3.62 mmol) in H_2O (8.0 ml) was added dropwise at room temperature under stirring. The stirring was continued for 30 min, and the pH of the dark solution was adjusted to pH 6.0 (25% aq. NH_3). The solution was applied onto a Serdolit AD-4 column (4 × 20 cm, resin 0.1–0.2 mm; Serva, Germany). The column was washed with H_2O (200 ml), and the product was eluted with H_2O/i-PrOH (95:5, 500 ml). Compound **4a** crystallized from H_2O as yellowish needles (186 mg, 70%), m.p. 231–233 °C (dec.). TLC (silica gel, CH_2Cl_2/MeOH, 5:1): R_F 0.28. For $C_{11}H_{14}N_4O_4$ (266.3) calculated: 49.62% C, 5.30% H, 21.04% N; found: 49.75% C, 5.23% H, 21.09% N. UV (MeOH): 227 (28700), 257 (7600), 305 (7400). ^{1}H NMR (250 MHz, DMSO-d_6): 2.02–2.09 m, 1 H (H-2′); 2.30–2.41 m, 1 H (H-2′); 3.48–3.53 m, 2 H (H-5′); 3.75–3.79 m, 1 H (H-4′); 4.26–4.29 m, 1 H (H-3′); 5.20–5.22 m, 2 H (OH-5′, OH-3′); 6.21 dd, 1 H, *J*(1′,2′) = 6.5, 7.5 (H-1′); 6.41 d, 1 H, *J*(5,6) = 3.5 (H-5); 6.90 d, 1 H, *J*(5,6) = 3.5 (H-6); 7.61 br s, 2 H (NH_2); 10.97 br s, 1 H (NH).

4-Amino-5-chloro-7-(2-deoxy-β-L-*erythro*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidin-2(3*H*)-one (**4b**)

As described for **4a**, with **3b** (300 mg, 1.00 mmol), AcOH/H_2O (1:5 v/v; 40 ml), and a solution of $NaNO_2$ (250 mg, 3.62 mmol) in H_2O (8.0 ml). Colorless needles from H_2O (180 mg, 60%), m.p. 223–234 °C (dec.). TLC (silica gel, CH_2Cl_2/MeOH, 5:1): R_F 0.29. For $C_{11}H_{13}ClN_4O_4$ (300.7) calculated: 43.94% C, 4.36% H, 18.63% N; found: 43.75% C, 4.23% H,

18.39% N. UV (MeOH): 231 (27600); 265 (6100); 311 (5600). ^{1}H NMR (250 MHz, DMSO-d_6): 2.06–2.08 m, 1 H (H-2′); 2.28–2.33 m, 1 H (H-2′); 3.48–3.55 m, 2 H (H-5′); 3.77–3.78 m, 1 H (H-4′); 4.26–4.27 m, 1 H (H-3′); 5.10 br s, 1 H (OH-5′); 5.25 d, 1 H, *J* = 3.0 (OH-3′); 6.26 t, 1 H, *J*(1′,2′) = 5.9 (H-1′); 7.15 br s, 3 H (H-6, NH_2); 10.80 br s, 1 H (NH).

7-(2-Deoxy-β-L-*erythro*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidin-4-amine (**1a**)

To a solution of 4-chloro-7*H*-pyrrolo[2.3-*d*]pyrimidine (**13a** [25]; 671 mg, 4.37 mmol) in MeCN (60 ml), powdered KOH (85%, 0.5 g, 7.57 mmol) and TDA-1 (0.075 ml, 0.24 mmol) were added at room temperature. After stirring for 10 min, halogenose **8** (1.7 g, 4.37 mmol) was added and the stirring was continued for another 10 min. Insoluble material was filtered off and washed several times with hot acetone. The combined filtrates were evaporated to dryness. The residue was applied onto FC (silica gel, column 5 × 15 cm, elution with petroleum ether/EtOAc, 4:1). The fractions containing product were evaporated to give 4-chloro-7-[2-deoxy-3,5-di-*O*-(4-methylbenzoyl)-β-L-*erythro*-pentofuranosyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine (**14a**) as a colorless solid (1.5 g, 68%). A suspension of compound **14a** (1.4 g, 2.77 mmol) in a mixture of 25% aq. NH_3/dioxane (1:1, 160 ml) was stirred at 85 °C for 72 h in an autoclave. The clear solution was evaporated and the residue was applied onto FC (silica gel, column 5 × 20 cm, CH_2Cl_2/MeOH, 9:1). Compound **1a** was obtained as colorless solid (560 mg, 81%). TLC (silica gel, CH_2Cl_2/MeOH, 9:1): R_F 0.16. For $C_{11}H_{14}N_4O_3$ (250.3) calculated: 52.79% C, 5.64% H, 22.39% N; found: 52.61% C, 5.62% H, 22.24% N. UV (MeOH): 271 (11500). ^{1}H NMR (250 MHz, DMSO-d_6): 2.09–2.18 m, 1 H (H-2'); 2.45–2.54 m, 1 H (H-2'); 3.49–3.56 m, 2 H (H-5'); 3.81–3.82 m, 1 H (H-4'); 4.30–4.33 m, 1 H (H-3'); 5.17 t, 1 H, *J* = 5.5 (OH-5'); 5.25 d, 1 H, *J* = 3.9 (OH-3'); 6.48 dd, 2 H, *J*(1',2') = 5.9, 8.2 (H-1'); 6.57 d, 1 H, *J*(5,6) = 3.6 (H-5); 7.04 br s, 2 H (NH_2); 7.34 d, 1 H, *J*(5,6) = 3.6 (H-6); 8.04 s, 1 H (H-2).

4-Chloro-7-(2-deoxy-β-L-*erythro*-pentofuranosyl)-5-iodo-7*H*-pyrrolo-[2,3-*d*]pyrimidine (**15d**)

To a solution of 4-chloro-5-iodo-7*H*-pyrrolo[2.3-*d*]pyrimidine (**13d** [24]; 1.0 g, 3.58 mmol) in MeCN (60 ml), powdered KOH (85%, 0.5 g, 7.57 mmol) and TDA-1 (0.075 ml, 0.24 mmol) were added at room temperature. After stirring for 10 min, halogenose **8** (1.7 g, 4.37 mmol) was introduced and the stirring was continued for another 10 min. Insoluble material was filtered off and washed several times with hot acetone. The combined filtrates were evaporated to dryness. The residue was applied onto FC (silica gel, column 5 × 15 cm, elution with petroleum ether/EtOAc, 4:1). The combined fractions containing the product were evaporated to yield 4-chloro-7-[2-deoxy-3,5-di-*O*-(4-methylbenzoyl)-β-L-*erythro*-pentofuranosyl]-5-iodo-7*H*-pyrrolo[2,3-*d*]pyrimidine (**14d**) as a colorless solid (2.02 g, 89%). A solution of compound **14d** (1.8 g, 2.85 mmol) in NH_3/MeOH (saturated at 0 °C, 145 ml) was stirred at room temperature for 24 h and the solvent was evaporated. FC (silica gel, column 4 × 16 cm, CH_2Cl_2/MeOH, 9:1) yielded compound **15d** as colorless solid (0.45 g, 40%). TLC (silica gel, CH_2Cl_2/MeOH, 9:1): R_F 0.45. For $C_{11}H_{11}ClIN_3O_3$ (395.6) calculated: 33.40% C, 2.80% H, 10.62% N; found: 33.41% C, 2.72% H, 10.52% N. UV (MeOH): 234 (27100), 269 (3600), 305 (3400). ^{1}H NMR (250 MHz, DMSO-d_6): 2.23–2.29 m, 1 H (H-2′); 2.49–2.57 m, 1 H (H-2′); 3.50–3.62 m, 2 H (H-5′); 3.84–3.85 m, 1 H (H-4′); 4.36–4.37 m, 1 H (H-3′); 5.00 t, 1 H, *J* = 4.9 (OH-5′); 5.32 d, 1 H, *J* = 3.5 (OH-3′); 6.62 t, 1 H, *J*(1′,2′) = 6.8 (H-1′); 8.20 s, 1 H (H-6); 8.65 s, 1 H (H-2).

7-(2-Deoxy-β-L-*erythro*-pentofuranosyl)-5-iodo-7*H*-pyrrolo[2,3-*d*]pyrimidin-4-amine (**1d**)

A suspension of compound **15d** (580 mg, 1.47 mmol) in a mixture of 25% aq. NH_3/dioxane (1:1, 120 ml) was stirred at 110 °C for 17 h in an autoclave. The clear solution was evaporated, the residue was applied onto FC (silica gel, column 4 × 12 cm, CH_2Cl_2/MeOH, 9:1). Compound **1d** was obtained as colorless solid (480 mg, 87%). TLC (silica gel, CH_2Cl_2/MeOH, 9:1): R_F 0.32. For $C_{11}H_{13}IN_4O_3$ (376.2) calculated: 35.12% C, 3.48% H, 14.89% N; found: 34.82% C, 3.35% H, 14.72% N. UV (MeOH): 283 (8500). ^{1}H NMR (250 MHz, DMSO-d_6): 2.11–2.18 m, 1 H (H-2′); 2.39–2.50 m, 1 H (H-2′); 3.50–3.59 m, 2 H (H-5′); 3.80–3.829 m, 1 H (H-4′); 4.31–4.33 m, 1 H (H-3′); 5.07 br s, 1 H (OH-5′), 5.30 br s, 1 H (OH-3′); 6.47 t, 1 H, J(1′,2′) = 6.9 (H-1′); 6.72 br s, 2 H (NH_2); 7.66 s, 1 H (H-6); 8.10 s, 1 H (H-2).

4,5-Dichloro-2-pivalamido-7-(2,3,5-tri-*O*-benzoyl-β-L-ribofuranosyl)-7*H*-pyrrolo-[2,3-*d*]pyrimidine (**18b**). General Procedure for the Preparation of **18b**–**18d**

To a stirred suspension of 4,5-dichloro-2-pivalamido-7*H*-pyrrolo[2,3-*d*] pyrimidine (**17b** [21]; 574 mg, 2.00 mmol) in anhydrous MeCN (14 ml), *N*,*O*-bis(trimethylsilyl)acetamide (BSA, 97%, 0.6 ml, 2.41 mmol) was added at room temperature under stirring. After 5 min, trimethylsilyl trifluoromethanesulfonate (TMSOTf: 0.50 ml, 2.59 mmol) was added and the temperature was raised to 50 °C (oil bath). Then 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-L-ribofuranose (**16** [1b,17b]; 2.02 g, 4.00 mmol) was introduced in three portions within 24 h (one every 8 h). The reaction was cooled to room temperature and diluted with CH_2Cl_2 (50 ml). The organic phase was washed with saturated aq. $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, evaporated under reduced pressure to give a syrup, which was applied onto FC (silica gel, column 4 × 12 cm, CH_2Cl_2). The main zone afforded compound **18b** as a yellowish foam (0.97 g, 66%). TLC (silica gel, CH_2Cl_2/MeOH, 99:1): R_F 0.30. For $C_{37}H_{32}Cl_2N_4O_8$ (731.6) calculated: 60.74% C, 4.41% H, 7.66% N; found: 60.72% C, 4.30% H, 7.65% N. ^{1}H NMR (250 MHz, DMSO-d_6): 1.19 s, 9 H (3 Me); 4.61–4.86 m, 3 H (H-4′, H-5′); 6.35–6.38, 6.41–6.44 2 m, 2 H (H-3′, H-2′); 6.52 d, 1 H, J(1′,2′) = 3.7 (H-1′); 7.42–7.49 m, 6 H (arom H); 7.63–7.65 m, 3 H (arom H); 7.88–7.96 m, 6 H (arom H); 8.03 s, 1 H (H-6); 10.39 s, 1 H (NH).

*5-Bromo-4-chloro-2-pivalamido-7-(2,3,5-tri-O-benzoyl-*β*-L-ribofuranosyl)-7H-pyrrolo[2,3-d]pyrimidine* (**18c**). As described for **18b**, compound **18c** was prepared from 5-bromo-4-chloro-2-pivalamido-7*H*-pyrrolo[2,3-*d*]pyrimidine (**17c** [21]; 663 mg, 2.00 mmol), the sugar **16** (2.02 g, 4.00 mmol), MeCN (14 ml), BSA (97%, 0.6 ml, 2.41 mmol), and TMSOTf (0.50 ml, 2.59 mmol). FC resulted in a yellowish foam (1.06 g, 68%). TLC (silica gel, CH_2Cl_2/MeOH, 99:1): R_F 0.30. For $C_{37}H_{32}ClBrN_4O_8$ (776.0) calculated: 57.27% C, 4.16% H, 7.22% N; found: 57.57% C, 4.01% H, 7.08% N. ^{1}H NMR (250 MHz, DMSO-d_6): 1.16 s, 9 H (3 Me); 4.60–4.84 m, 3 H (H-4′, H-5′); 6.34–6.37, 6.42–6.47 2m, 2 H (H-3′, H-2′); 6.50 d, 1 H, J(1′,2′) = 3.6 (H-1′); 7.40–7.49 m, 6 H (arom H); 7.62–7.65 m, 3 H (arom H); 7.86–7.93 m, 6 H (arom H); 8.01 s, 1 H (H-6); 10.38 s, 1 H (NH).

*4-Chloro-5-iodo-2-pivalamido-7-(2,3,5-tri-O-benzoyl-*β*-L-ribofuranosyl)-7H-pyrrolo[2,3-d]pyrimidine* (**18d**). As described for **18b**, compound **18d** was prepared from 4-chloro-5-iodo-2-pivalamido-7*H*-pyrrolo[2,3-*d*]pyrimidine (**17d** [21]; 757 mg, 2.00 mmol), ribose 16 (2.02 g, 4.00 mmol), MeCN (14 ml), BSA (97%, 0.6 ml, 2.41 mmol), and TMSOTf (0.50 ml, 2.58 mmol). Compound **18d** was obtained as a yellowish foam (1.2 g, 73%). TLC (silica gel, CH_2Cl_2/MeOH, 99:1): R_f 0.30. For $C_{37}H_{32}ClIN_4O_8$ (823.0) calculated: 54.00% C, 3.92% H, 6.81% N; found: 54.14% C, 4.30% H, 6.63% N. ^{1}H NMR (250 MHz, DMSO-d_6): 1.18 s, 9 H (3 Me); 4.62–4.85 m, 3 H (H-4′, H-5′); 6.33–6.37 m, 1 H (H-3′); 6.42–6.47 m, 1 H (H-2′);

6.51 d, 1 H, *J*(1′,2′) = 3.7 (H-1′); 7.42–7.49 m, 6 H (arom H); 7.63–7.65 m, 3 H (arom H), 7.89–7.94 m, 6 H (arom H); 8.06 s, 1 H (H-6); 10.34 s, 1 H (NH).

5-Chloro-4-methoxy-7-(β-L-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidin-2-amine (**19b**). General Procedure for the Preparation of **19b**–**19d**

A solution of **18b** (1.1 g, 1.50 mmol) in 0.5 M MeONa/MeOH (20.0 ml) was heated under reflux for 3 h. The reaction mixture was neutralized with 2 M AcOH, the solvent was removed, and the residue was applied onto FC (silica gel, column 3 × 8 cm, elution with CH_2Cl_2/MeOH, 95:5). The fractions, containing the desired material, were collected and evaporated to dryness to give compound **19b** as a colorless solid (412 mg, 83%). TLC (silica gel, CH_2Cl_2/MeOH, 9:1): R_F 0.43. For $C_{12}H_{15}ClN_4O_5$ (330.7) calculated: 43.58% C, 4.57% H, 16.94% N; found: 43.58% C, 4.47% H, 16.95% N. UV (MeOH): 229 (27000), 264 (8500), 289 (6800). ^{1}H NMR (250 MHz, DMSO-d_6): 3.50–3.57 m, 2 H (H-5′); 3.79–3.82 m, 1 H (H-4′); 3.93 s, 3 H (OMe); 4.02–4.05 m, 1 H (H-3′); 4.24–4.26 m, 1 H (H-2′); 4.99 t, 1 H, *J* = 5.4 (OH-5′); 5.06 d, 1 H, *J* = 4.2 (OH-3′); 5.26 d, 1 H, *J* = 6.2 (OH-2′); 5.96 d, 1 H, *J*(1′,2′) = 6.4 (H-1′); 6.44 s, 2 H (NH_2); 7.25 s, 1 H (H-6).

5-Bromo-4-methoxy-7-(β-L-ribofuranosyl)-7H-pyrrolo[2,3-d]pyrimidin-2-amine (**19c**). Compound **19c** was prepared from nucleoside **18c** (1.17 g, 1.51 mmol) as described for **19b**. FC resulted in a colorless solid (478 mg, 84%). TLC (silica gel, CH_2Cl_2/MeOH, 9:1): R_F 0.45. For $C_{12}H_{15}BrN_4O_5$ (375.2): 38.42% C, 4.03% H, 14.93% N; found: 38.75% C, 4.20% H, 15.05% N. UV (MeOH): 230 (29300), 264 (8700), 289 (7300). ^{1}H NMR (250 MHz, DMSO-d_6): 3.50–3.59 2 m, 2 H (H-5′); 3.82–3.84 m, 1 H (H-4′); 3.94 s, 3 H (OMe); 4.02–4.04 m, 1 H (H-3′); 4.27–4.28 m, 1 H (H-2′); 5.02 t, 1 H, *J* = 4.8 (OH-5′); 5.08 d, 1 H, *J* = 4.2 (OH-3′); 5.28 d, 1 H, *J* = 6.2 (OH-2′); 5.98 d, 1 H, *J*(1′,2′) = 6.4 (H-1′); 6.43 s, 2 H (NH_2); 7.30 s, 1 H (H-6).

5-Iodo-4-methoxy-7-(β-L-ribofuranosyl)-7H-pyrrolo[2,3-d]pyrimidin-2-amine (**19d**). Compound **19d** was prepared from compound **18d** (1.23 g, 1.49 mmol) as described for **19b**. Colorless solid (507 mg, 81%). TLC (silica gel, CH_2Cl_2/MeOH, 9:1): R_F 0.46. For $C_{12}H_{15}IN_4O_5$ (422.2) calculated: 34.14% C, 3.58% H, 13.27% N; found: 34.55% C, 3.57% H, 13.29% C. UV (MeOH): 227 nm (24500), 265 (8000), 288 (7200). ^{1}H NMR (250 MHz, DMSO-d_6): 3.47–3.61 m, 2 H (H-5′); 3.80–3.82 m, 1 H (H-4′); 3.93 s, 3 H (OMe); 4.01–4.03 m, 1 H (H-3′); 4.23–4.30 m, 1 H (H-2′); 5.01 t, 1 H, *J* = 5.3 (OH-5′); 5.05 d, 1 H, *J* = 4.3 (OH-3′); 5.25 d, 1 H, *J* = 6.2 (OH-2′); 5.94 d, 1 H, *J*(1′,2′) = 6.4 (H-1′); 6.38 s, 2 H (NH_2); 7.31 s, 1 H (H-6).

2-Amino-5-chloro-7-(β-L-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidin-4(3*H*)-one (**5b**). General Procedure for the Preparation of **5b**–**5d**

Compound **19b** (149 mg, 0.45 mmol) was dissolved in 2 M NaOH (40 ml) and 1,4-dioxane (6 ml). The mixture was stirred under reflux for 3 h. After neutralization with 2 M HCl followed by the evaporation of 1,4-dioxane, the crude product was chromatographed on a Serdolit AD-4 column (3 × 12 cm, resin 0.1–0.2 mm; Serva, Germany). The inorganic salt was eluted with H_2O (150 ml), and the product was eluted with H_2O/i-PrOH (95:5, 500 ml). The product containing fractions were collected and the solution was reduced to ca. 15 ml. Compound **5b** was crystallized from H_2O as colorless crystals (114 mg, 80%), m.p. > 290 °C (dec.). TLC (silica gel, CH_2Cl_2/MeOH, 5:1): R_F 0.22. For $C_{11}H_{13}ClN_4O_5$ (316.7) calculated: 41.72% C, 4.14% H, 17.69% N; found: 41.92% C, 4.46% H, 17.52% N. UV (MeOH): 221 (20900), 264 (11500), 290 (6000). ^{1}H NMR (250 MHz, DMSO-d_6): 3.44–3.56 m, 2 H (H-5′); 3.79–3.81 m, 1 H (H-4′); 4.00–4.02 m, 1 H (H-3′); 4.17–4.23 m, 1 H (H-2′); 4.97 t, 1 H, *J* =

5.1 (OH-5′); 5.04 d, 1 H, *J* = 4.1 (OH-3′); 5.26 d, 1 H, *J* = 6.1 (OH-2′); 5.86 d, 1 H, *J*(1′,2′) = 6.2 (H-1′); 6.39 s, 2 H (NH_2); 7.06 s, 1 H (H-6); 10.52 s, 1 H (NH).

2-Amino-5-bromo-7-(β-L-ribofuranosyl)-7H-pyrrolo[2,3-d]pyrimidin-4(3H)-one (**5c**). The preparation of **5c** followed the protocol described for **5b** employing **19c** (199 mg, 0.53 mmol), 2 M NaOH (40 ml), and 1,4-dioxane (6 ml). Colorless crystals (163 mg, 85%), m.p. > 290 °C (dec. H_2O). TLC (silica gel, CH_2Cl_2/MeOH, 5:1): R_F 0.23. For $C_{11}H_{13}BrN_4O_5$ (361.2) calculated: 36.58% C, 3.63% H, 15.51% N; found: 37.02% C, 3.82% H, 15.11% N. UV (MeOH): 222 (22000), 262 (11300), 289 (7200). ^{1}H NMR (250 MHz, DMSO-d_6): 3.49–3.58 m, 2 H (H-5′); 3.81–3.82 m, 1 H (H-4′); 4.01–4.03 m, 1 H (H-3′); 4.20-4.23 m, 1 H (H-2′); 4.99 t, 1 H, *J* = 5.3 (OH-5′); 5.05 d, 1 H, *J* = 4.3 (OH-3′); 5.27 d, 1 H, *J* = 5.2 (OH-2′); 5.87 d, 1 H, *J*(1′,2′) = 6.4 (H-1′); 6.37 s, 2 H (NH_2); 7.12 s, 1 H (H-6); 10.51 s, 1 H (NH).

2-Amino-5-iodo-7-(β-L-ribofuranosyl)-7H-pyrrolo[2,3-d]pyrimidin-4(3H)-one (**5d**). The preparation of **5d** followed the protocol described for **5b** employing **19d** (422 mg, 1.0 mmol), 2 M NaOH (60 ml), and 1,4-dioxane (10 ml). FC resulted in colorless crystals from H_2O (355 mg, 87%), m.p. > 239 °C (dec.). TLC (silica gel, CH_2Cl_2/MeOH, 5:1): R_F 0.28. For $C_{11}H_{13}IN_4O_5$ (408.2) calculated: 32.37% C, 3.21% H, 13.73% N; found: 32.58% C, 3.19% H, 13.67% N. UV (MeOH): 266 (11400), 289 (7200). ^{1}H NMR (250 MHz, DMSO-d_6): 3.52–3.59 m, 2 H (H-5′); 3.83–3.85 m, 1 H (H-4′); 4.05–4.06 m, 1 H (H-3′); 4.21–4.24 m, 1 H (H-2′); 4.97–4.98 m, 2 H (OH-5′, OH-3′); 5.21 d, 1 H, *J* = 6.1 (OH-2′); 5.87 d, 1 H, *J*(1′,2′) = 6.3 (H-1′); 6.29 s, 2 H (NH_2); 7.16 s, 1 H (H-6); 10.47 s, 1 H (NH).

5-Chloro-7-(β-L-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine-2,4-diamine (**6b**).

General Procedure for the Preparation of **6b**–**6d**

A suspension of **18b** (732 mg, 1.0 mmol) in dioxane (30 ml) and 25% NH_3/H_2O (70 ml) was stirred in an autoclave at 120 °C for 24 h. The clear solution was reduced to 10 ml and stored in the refrigerator for 24 h, then compound **6b** was crystallized from H_2O affording colorless needles (287 mg, 91%), m.p. 238 °C (dec.). TLC (silica gel, CH_2Cl_2/MeOH, 9:1): R_F 0.20. For $C_{11}H_{14}ClN_5O_4$ (315.7) calculated: 41.85% C, 4.47% H, 22.18% N; found: 41.45% C, 4.35% H, 21.99% N. UV (MeOH): 228 (33000), 268 (10600), 289 (9000). ^{1}H NMR (250 MHz, DMSO-d_6): 3.47–3.61 m, 2 H (H-5′); 3.80–3.82 m, 1 H (H-4′); 4.01–4.03 m, 1 H (H-3′); 4.22–4.27 m, 1 H (H-2′); 5.03 d, 1 H, *J* = 3.8 (OH-3′); 5.09 t, 1 H, *J* = 4.8 (OH-5′); 5.23 d, 1 H, *J* = 4.9 (OH-2′); 5.83 s, 2 H (NH_2); 5.90 d, 1 H, *J*(1′,2′) = 6.4 (H-1′); 6.34 s, 2 H (NH_2); 7.10 s, 1 H (H-6).

5-Bromo-7-(β-L-ribofuranosyl)-7H-pyrrolo[2,3-d]pyrimidine-2,4-diamine (**6c**). The procedure described for **6b** was applied to **6**c employing **18c** (512 mg, 0.66 mmol), dioxane (20 ml), and 25% NH_3/H_2O (50 ml). Colorless crystals from H_2O (200 mg, 85%), m.p. 238 °C (dec.). TLC (silica gel, CH_2Cl_2/MeOH, 9:1): R_F 0.20. For $C_{11}H_{14}BrN_5O_4$ (360.2) calculated: 36.68% C, 3.92% H, 19.44% N; found: 36.87% C, 3.78% H, 19.34% N. UV (MeOH): 229 (33100), 268 (10100), 288 (8800). ^{1}H NMR (250 MHz, DMSO-d_6): 3.46–3.59 2 m, 2 H (H-5′); 3.80–3.81 m, 1 H (H-4′); 4.01–4.02 m, 1 H (H-3′); 4.22–4.29 m, 1 H (H-2′); 5.04 d, 1 H, *J* = 4.3 (OH-3′); 5.09 t, 1 H, *J* = 5.3 (OH-5′); 5.24 d, 1 H, *J* = 6.2 (OH-2′); 5.85 s, 2 H (NH_2); 5.90 d, 1 H, *J*(1′,2′) = 6.4 (H-1′); 6.29 br s, 2 H (NH_2); 7.17 s, 1 H (H-6).

5-Iodo-7-(β-L-ribofuranosyl)-7H-pyrrolo[2,3-d]pyrimidine-2,4-diamine (**6d**). The procedure described for **6b** was applied to **6d** employing **18d** (1.14 g, 1.38 mmol), dioxane (40 ml), and 25% NH_3/H_2O (90 ml). Colorless crystals from H_2O (500 mg, 89%), m.p. 236 °C (dec.). TLC (silica gel, CH_2Cl_2/MeOH, 9:1): R_F 0.20. For $C_{11}H_{14}IN_5O_4$ (407.2) calculated: 32.45% C,

3.47% H, 17.20% N; found: 32.59% C, 3.51% H, 17.36% N. UV (MeOH): 231 (33000), 269 (10200), 289 (8900). ^{1}H NMR (250 MHz, DMSO-d_6): 3.47–3.57 m, 2 H (H-5′); 3.80–3.82 m, 1 H (H-4′); 4.00–4.02 m, 1 H (H-3′); 4.26–4.28 m, 1 H (H-2′); 5.04 d, 1 H, *J* = 5.1 (OH-3′); 5.11 t, 1 H, *J* = 5.3 (OH-5′); 5.22 d, 1 H, *J* = 5.3 (OH-2′); 5.80 s, 2 H (NH_2); 5.88 d, 1 H, *J*(1′,2′) = 6.3 (H-1′); 6.19 s, 2 H (NH_2); 7.20 s, 1 H (H-6).

5-Bromo-4-methoxy-7-(β-L-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidin-2(1*H*)-one (**20c**)

To a solution of **19c** (375 mg, 1.0 mmol) in AcOH/H_2O (v/v 1:7, 60 ml), a solution of $NaNO_2$ (170 mg, 2.46 mmol) in H_2O (2.0 ml) was added dropwise while stirring at room temperature. The stirring was continued for 30 min, and pH of the yellow solution was adjusted to 7.0 with 25% aq. NH_3. The solution was applied to a Serdolit AD-4 column (4 × 20 cm, resin 0.1–0.2 mm; Serva, Germany). Inorganic salt was eluted with H_2O (200 ml), and the product with MeOH/H_2O (1:1 v/v, 300 ml). The product-containing fractions were reduced to 20% of its original volume and compound **20c** was crystallized from H_2O to yield colorless needles (327 mg, 87%), m.p. 220 °C (dec. H_2O). TLC (silica gel, CH_2Cl_2/MeOH, 5:1): R_F 0.57. UV (MeOH): 226 (23500), 287 (6400). For $C_{12}H_{14}BrN_3O_6$ (376.2) calculated: 38.32% C, 3.75% H, 11.17% N; found: 38.43% C, 3.86% H, 11.23% N. ^{1}H NMR (250 MHz, DMSO-d_6): 3.53–3.62 m, 2 H (H-5′); 3.87–3.88 m, 1 H (H-4′); 3.99 s, 3 H (OMe); 4.04–4.07 m, 1 H (H-3′); 4.28–4.30 m, 1 H (H-2′); 5.10–5.15 m, 2 H (OH-5′, OH-3′); 5.36 d, 1 H, *J* = 6.1 (OH-2′); 5.97 d, 1 H, *J*(1′,2′) = 5.2 (H-1′); 7.49 s, 1 H (H-6); 11.63 s, 1 H (NH).

5-Iodo-4-methoxy-7-(β-L-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidin-2(1*H*)-one (**20d**)

Compound **20d** was prepared from **19d** (422 mg, 1.00 mmol) as described for **20c**. Colorless needles from H_2O (364 mg, 86%), m.p. 220 °C (dec.). TLC (silica gel, CH_2Cl_2/MeOH, 5:1): R_F 0.57. For $C_{12}H_{14}IN_3O_6$ (423.2) calculated: 34.06% C, 3.33% H, 9.93% N; found: 33.98% C, 3.40% H, 9.87% N. UV (MeOH): 229 (23400), 287 (6100). ^{1}H NMR (250 MHz, DMSO-d_6): 3.50–3.57 m, 2 H (H-5′); 3.86–3.87 m, 1 H (H-4′); 3.97 s, 3 H (MeO); 4.03–4.05 m, 1 H (H-3′); 4.27–4.29 m, 1 H (H-2′); 5.12–5.13 br s, 2 H (OH-5′, OH-3′); 5.33 d, 1 H, *J* = 5.9 (OH-2′); 5.93 d, 1 H, *J*(1′,2′) = 5.0 (H-1′); 7.48 s, 1 H (H-6); 11.55 s, 1 H (NH).

5-Bromo-7-(β-L-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (**7c**)

A solution of compound **20c** (188 mg, 0.50 mmol) in a mixture of 2 M NaOH (40 ml) and 1,4-dioxane (6 ml) was heated under reflux for 40 h while stirring. After neutralization with 2 M HCl and evaporation of 1,4-dioxane, the crude product was chromatographed on a Serdolit AD-4 column (3 × 12 cm, resin 0.1–0.2 mm; Serva, Germany). The column was washed with H_2O (150 ml), and the product was eluted with MeOH/H_2O (1:1 v/v, 200 ml). The volume of the product-containing fractions was reduced to 20% of their original volume. Compound **7c** was crystallized from H_2O as colorless crystals (127 mg, 70%), m.p. 220 °C (dec.). TLC (silica gel, CH_2Cl_2/MeOH, 5:1): R_F 0.40. For $C_{11}H_{12}BrN_3O_6$ (362.1) calculated: 36.48% C, 3.34% H, 11.60% N; found: 36.54% C, 3.46% H, 11.54% N. UV (0.1 M NaH_2PO_4 in H_2O): 222 (23900), 256 (10100), 285 (6500). ^{1}H NMR (250 MHz, DMSO-d_6): 3.60–3.62 m, 2 H (H-5′); 3.92–3.94 m, 1 H (H-4′); 4.00–4.02 m, 1 H (H-3′); 4.15–4.19 m, 1 H (H-2′); 5.17–5.55 m, 3 H (OH-2′, OH-3′, OH-5′); 5.67 d, 1 H, *J*(1′,2′) = 6.4 (H-1′); 7.07 s, 1 H (H-6); 10.59, 11.63 2 s, 2 H (2 NH).

5-Iodo-7-(β-L-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (**7d**)

Compound **7d** was prepared from **20d** (351 mg, 0.83 mmol) as described for **7c** using 2 M NaOH (60 ml) and 1,4-dioxane (10 ml). Colorless crystals from H_2O (251 mg, 74%), m.p. 230 °C (dec.). TLC (silica gel, CH_2Cl_2/MeOH, 5:1): R_F 0.40. For $C_{11}H_{12}IN_3O_6$ (409.1) calculated: 32.29% C, 2.96% H, 31.02% I, 10.27% N; found: 32.41% C, 3.12% H, 30.74% I, 10.20% N. UV (0.1 M NaH_2PO_4 in H_2O): 224 (21700), 258 (9600), 285 (6800). ^{1}H NMR (250 MHz, DMSO-d_6): 3.60–3.62 m, 2 H (H-5′); 3.93–3.94 m, 1 H (H-4′); 3.99–4.00 m, 1 H (H-3′); 4.11–4.15 m, 1 H (H-2′); 5.18 d, 1 H, *J* = 3.8 (OH-3′); 5.35 d, 1 H, *J* = 6.2 (OH-2′); 5.68 m, 2 H (OH-5′, H-1′); 7.11 s, 1 H (H-6); 10.72 s, 1 H (NH); 11.61 br s, 1 H (NH).

We appreciate technical assistance of Ms E.-M. Albertmann and thank Ms S. Budow and Ms K. Xu for the measurement of NMR spectra. We thank Prof. P. La Colla (Cagliary, Italy) and Idenix Pharmaceuticals (Cambridge, U.S.A.) for the antiviral tests and Dr R. Storer, Dr G. Gosselin, and Prof. J.-L. Imbach for helpful discussions. Part of the work was supported by European Community (Project: Flavitherapeutics, QLK3-CT-2001-00506).

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