7-Halogenated 7-Deaza-2′-deoxyxanthine 2′-Deoxyribonucleosides

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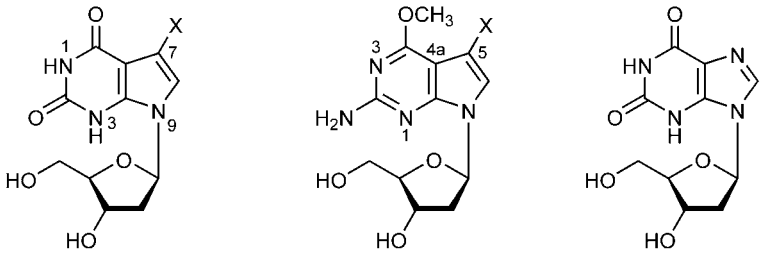
The synthesis of the 7-halogenated derivatives **1b** (7-bromo) and **1c** (7-iodo) of 7-deaza-2′-deoxyxanthosine (**1a**) is described. A partial Br → I exchange was observed when the demethylation of 6-methoxy precursor compound **4b** was performed with Me_3SiCl/NaI. This reaction is circumvented by the nucleophilic displacement of the MeO group under strong alkaline conditions. The halogenated 7-deaza-2′-deoxyxanthosine derivatives **1b**,**c** show a decreased *S*-conformer population of the sugar moiety compared to the nonhalogenated **1a**. They are expected to form stronger triplexes when they replace **1a** in the **1** · dA · dT base triplet.

Introduction. – The synthesis of 7-deaza-2′-deoxyxanthosine (**1a**) *via* the glycosylation of 2,4-dichloro-7*H*-pyrrolo[2,3-*d*]pyrimidine was already reported from our laboratory in 1985 [1]. Later the nucleoside was prepared by a deamination/demethylation route from 4-methoxy-7*H*-pyrrolo[2,3-*d*]pyrimidin-2-amine 2′-deoxyribonucleoside **2a** [2]. Compound **1a** was incorporated into oligonucleotides without base protection by solid-phase synthesis by using phosphonate chemistry [2]. Triplexes containing 7-deazaxanthine in place of thymine showed a high third-strand-binding affinity under neutral conditions [2]. Contrary to the extremely labile 2′-deoxyxanthosine (**3**), in which the glycosylic bond hydrolyzes spontaneously under physiological conditions [3–5], the glycosylic bond of the 7-deazapurine nucleoside **1a** is resistant to 'depurination' [1][2].



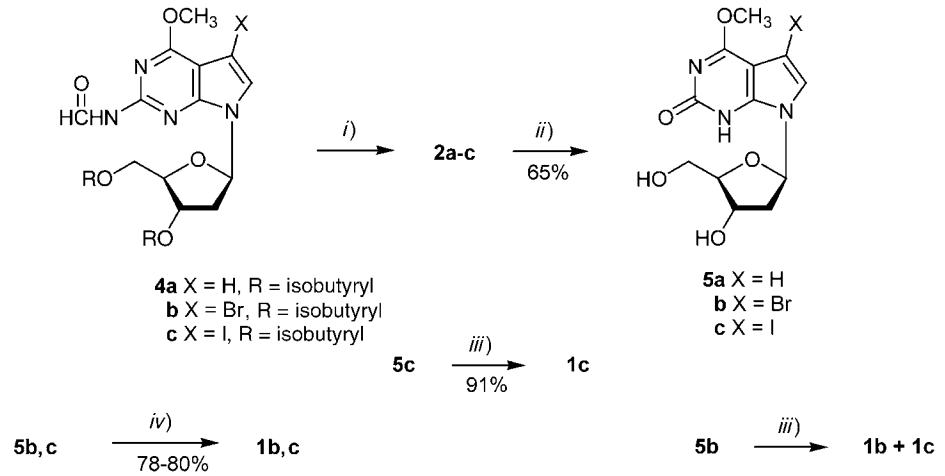
Within the series of 9-halogenated 7-deazapurine nucleosides related to dA [6][7], dG [8], dI [9], or $isoG_d$ [10], we have shown that lipophilic electron-withdrawing 7-substituents increase the duplex stability [11–13]. Due to findings reported for other

triplex-forming 9-halogenated deazapurine nucleosides [14], it is supposed that compounds **1b**,**c** can show a similar stabilizing effect when incorporated in triplexes. Also, stable duplexes are expected when compounds **1b**,**c** base pair with pyrimidine-2,4-diamine nucleosides [15].

This report describes the synthesis and the conformational properties of the 7-bromo and 7-iodo derivatives **1b**,**c** of 7-deaza-2′-deoxyxanthosine (**1a**) from compounds **2b**,**c** as key intermediates. Preliminary results of this work appeared as a short communication [16].

Results and Discussion. – 1. *Synthesis and Characterization*. Starting materials for the synthesis of **1b**,**c** were the fully protected nucleosides **4b**,**c** which were prepared by the regioselective bromination or iodination of 7-[2-deoxy-3,5-bis-*O*-(2-methylpropanoyl)-*β*-D-*erythro*-pentofuranosy]-2-(formylamino)-4-methoxy-7*H*-pyrrolo[2,3-*d*]pyrimidine with *N*-bromo- and *N*-iodosuccinimide, as described previously by our laboratory [8]. *Zemplen* deprotection of **4b**,**c** in 0.5N NaOMe/MeOH at room temperature furnished compounds **2b**,**c** in almost quantitative yield (*Scheme*). These conditions displaced neither the 4-MeO group nor the 7-halogeno substituents. Deamination of **2b**,**c** with $NaNO_2$/AcOH yielded the 2-oxo nucleosides **5b**,**c**. Next, the demethylation of **5c** was performed under conditions described for **4a** with Me_3SiCl/NaI in MeCN [2], yielding compound **1c** in 91% yield. Under the same conditions, a partial halogen exchange (Br → I) was observed for compound **5b** [17][18], yielding a nucleoside mixture **1b**/**1c**. This was confirmed by the appearance of the characteristic ^{13}C-NMR C(7) signals (purine numbering; δ(C–Br) 91.19, δ(C–I) 56.25) and by a HPLC experiment (*Fig. 1*) in which the content of the reaction products (*Fig. 1*,*b*) was compared with an artificial nucleoside mixture containing the pure nucleosides **1a**–**c**. From *Fig. 1*,*a*, it is also apparent that the 7-halogeno substituents make the parent

Scheme



i) 0.5N NaOMe/MeOH, r.t., overnight. *ii*) $NaNO_2$, 10% AcOH/H_2O, r.t., 30 min. *iii*) Me_3SiCl, NaI, MeCN, r.t., 30 min. *iv*) 2N aq. NaOH, reflux, 3 days.

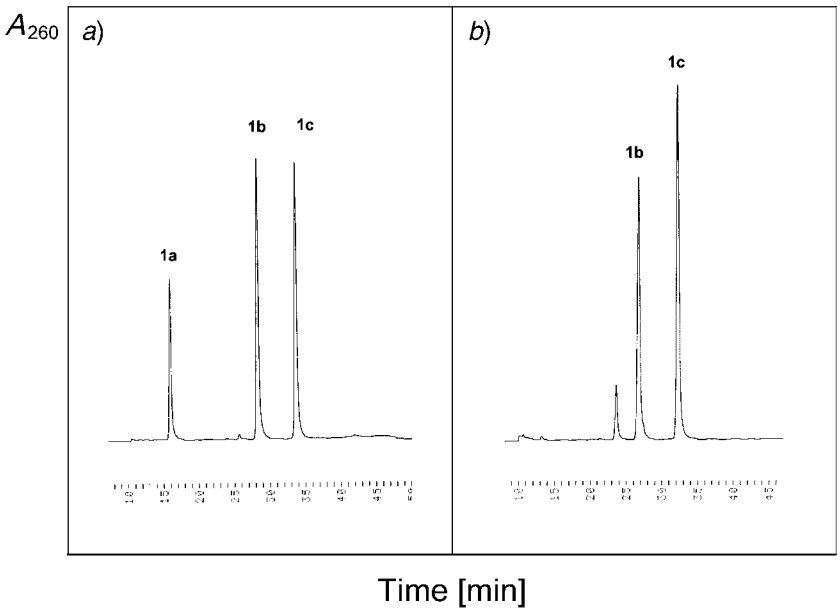


Fig. 1. *Reversed-phase HPLC profiles of* a) *an artificial mixture of the nucleosides* **1a**–**c** *and* b) *the reaction products obtained after demethylation of* **5b**. Column, *RP-18* (200 × 10 mm); gradient: 0 min 100% *B*, 10 min 3% *A*, 20 min 5% *A*, 30 min 8% *A*, 40 min 10% *A*, 50 min 13% *A* in *B*; *A* = MeCN, *B* = 0.1M (Et_3NH)OAc buffer, pH = 7.0.

nucleoside **1a** much more lipophilic, as demonstrated by the increased retention times on the reversed-phase HPLC column.

To avoid the halogen exchange during the demethylation of **5b**, the reaction was performed with NaBr instead of NaI in the presence of Me_3SiCl. Unfortunately, demethylation did not take place under these conditions. Thus, the demethylation protocol was changed. An alkaline medium (2N NaOH, reflux, 3 days) was used for the removal of the MeO group. This nucleophilic displacement reaction on compound **5b** yielded the pure nucleoside **1b**. The conditions were also applied to **5c**, thus forming **1c** (see *Scheme* and *Table 1*).

Table 1. *Demethylation of Compounds* **5b**,**c** *under Either Cleavage or Nucleophilic Displacement Conditions*

Educts	Reagents	Product	Yield [%]
5b	Me_3SiCl/NaI	**1b**/**1c** 2 : 3	
5c	Me_3SiCl/NaI	**1c**	91
5b	Me_3SiCl/NaBr	no reaction	
5b	2N aq. NaOH	**1b**	78
5c	2N aq. NaOH	**1c**	80

All compounds were characterized by ^1H- and ^{13}C-NMR spectroscopy as well as by elemental analysis (*Table 2* and *Exper. Part*). According to *Table 2*, the C(7) signals (purine numbering) of the 7-substituted 7-deaza-2′-deoxyxanthosines **1b**,**c** are shifted

Table 2. *^{13}C-NMR Chemical Shifts of 7-Deaza-2′-deoxyxanthosines*[a]) *and of Synthetic Precursors*

	C(2)[b]) C(2)[c])	C(4)[b]) C(6)[c])	C(4a)[b]) C(5)[c])	C(5)[b]) C(7)[c])	C(6)[b]) C(8)[c])	C(7a)[b]) C(4)[c])	MeO
1a [1]	150.7	159.5	99.4	103.1	117.6	138.0	
b	150.4	158.4	97.2	91.1	117.0	138.3	
c	150.3	158.8	103.1	56.2	122.2	138.7	
2b	159.7[e])	162.8[e])	96.2	87.2	118.8	153.6	53.1
c	160.2[e])	163.6[e])	99.5	49.4	124.9	155.0	52.5
4b	152.7	162.9	100.9	87.9	122.3	151.8	54.2
c	152.3	162.8	103.3	52.2	127.3	152.2	53.9
5b	160.1[e])	163.7[e])	97.8	87.2	120.3	150.9	53.6
c	159.8[e])	163.8[e])	100.2	51.9	125.5	151.7	53.5
	C(1′)	C(2′)	C(3′)	C(4′)	C(5′)		
1a [1]	85.5	[d])	70.8	87.3	61.4		
b	85.4	[d])	70.6	87.4	61.3		
c	85.4	[d])	70.6	87.4	61.3		
2b	82.1	[d])	70.9	87.1	61.9		
c	82.9	[d])	70.8	87.9	62.7		
4b	83.1	35.8	74.1	81.4	63.6		
c	82.9	37.8	74.0	81.2	63.5		
5b	83.0	[d])	70.7	87.2	61.6		
c	83.0	[d])	70.7	87.2	61.6		

[a]) Measured in (D_6)DMSO at 25°. [b]) Systematic numbering. [c]) Purine numbering. [d]) Superimposed by (D_6)DMSO. [e]) Tentative.

upfield when the C-atom is halogenated (δ(C−H) 103.11, δ(C−Br) 91.19, δ(C−I) 56.25). The UV spectra of compounds **1b**,**c** and for comparison of **1a** were measured in 0.1M sodium phosphate buffer (pH 7.0). The spectra show three distinct maxima at 215, 250, and 282 nm for **1a**, 222, 256, and 285 nm for **1b**, and 225, 259, and 285 nm for **1c**. This indicates that the 7-halogeno substituents induce a bathochromic shift. Moreover, the pK_a values were determined in the same buffer solution. Only one pK_a was found between pH 3 and 10. The pK_a value for the parent compound **1a** is 6.6, while the halogenated derivatives show lower values, *i.e.*, 6.1 for **1b** and 6.2 for **1c**. The pK_a of xanthosine is lower (5.7).

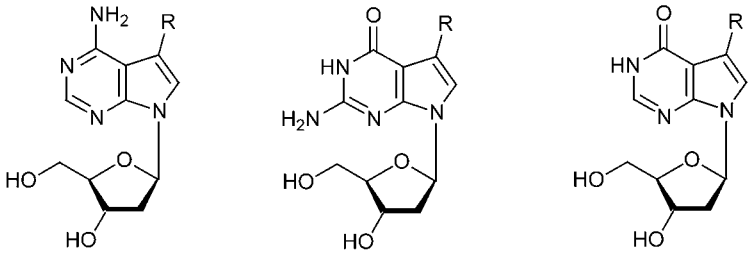
2. *Conformational Properties of the 7-Deazaxanthine Nucleosides* **1a**–**c**. From a series of 7-deazapurine 2′-deoxyribonucleosides, it was reported that substituents of the base moiety can influence the sugar puckering. Such conformational changes of 7-substituted 7-deazapurine-2′-deoxynucleosides [6][8][19][20] have been studied on the basis of vicinal ^{1}H,^{1}H-coupling constants by means of the PSEUROT 6.2 program [21][22]. Thus, calculations were performed with pseudorotational starting parameters recommended in the users manual of the program ($\Phi_{max} = 36°$ (both northern (*N*) and southern type (*S*)); $P_N = 19°$; $P_S = 156°$). The input contained the following ^{1}H,^{1}H-coupling constants: J(1′,2′), J(1′,2″), J(2′,3′), J(2″,3′), and J(3′,4′) (2″ = short form of H′−C(2′)). During the iterations, either the puckering parameters (P, Φ_{max}) of the minor conformer (*N*) or the puckering amplitudes of both conformers were constrained. In all cases, the root-mean-square (r.m.s.) values were $\leq$0.4 Hz and the

$|\Delta J_{max}| \leq 0.5$ Hz. The coupling constants $J(1',2')$, $J(1',2'')$, $J(2',3')$, $J(2'',3')$, and $J(3',4')$ are given in the *Exper. Part* and the conformer populations in *Table 3*.

Table 3. N/S-*Conformer Populations of the Sugar Moieties of Halogenated Pyrrolo[2,3-*d*]pyrimidine Nucleosides Measured in D_2O at 298 K*

	Sugar conformation			Sugar conformation	
	%*N*	%*S*		%*N*	%*S*
1a	24	76	**7a**	28	72
b	28	72	**b**	28	72
c	27	73	**c**	31	69
6a	24	76	**8a**	33	67
b	29	71	**b**	33	67
c	29	71	**c**	34	66

From the data shown in *Table 3*, some general trends can be deduced. The nonhalogenated compound **1a** shows a population of *ca.* 76% of the *S*-conformers; the conformation of the bromo and iodo derivatives **1b**,**c** are shifted towards *N* (72 and 73% *S*). These data demonstrate that the higher the electron-withdrawing effect of the 7-substituent is, the more the $N \rightleftharpoons S$ equilibrium of the sugar moiety is biased towards the *N*-conformation [23][24]. *Table 3* compares the data with a series of other 7-halogenated 7-deazapurine nucleosides **1a**–**c** related to dA, dG, and dI [6–9][25][26], *i.e.*, **6a**–**c**, **7a**–**c**, and **8a**–**c**, which show the same phenomenon. The conformation in the solid state was already reported for compound **1a** [27]. The single-crystal X-ray-analysis shows that the sugar moiety adopts the same conformation in the crystalline state.



6a R = H
b R = Br
c R = I

7a R = H
b R = Br
c R = I

8a R = H
b R = Br
c R = I

To establish the conformational parameters at the *N*-glycosylic bond, ^{1}H-NOE difference spectra of compounds **1a**–**c** were measured. As can be seen from *Table 4*, irradiation of H–C(8) resulted in an NOE at H–C(1′) of 7.3% for the nucleoside **1a**, 5% for **1b**, and 5.3% for **1c**. Application of a calibration graph for the estimation of the '*syn*'- and '*anti*'-conformer populations according to [28] gave '*anti*'-rotamer populations of 33% for **1a**, 58% for **1b**, and 55% for **1c**. These data demonstrate that the nucleosides **1b**,**c** prefer the '*anti*'-conformation at the *N*-glycosylic bond, while **1a** is

shifted toward '*syn*'. The '*syn*'-conformation of **1a** is also observed in the crystalline state [27].

Table 4. *NOE Data of 7-Deaza-2′-deoxyxanthosine Derivatives.* Purine numbering.

	Proton irradiated	NOE observed ([%])
1a	H–C(8)	H–C(1′) (7.3), H–C(2′) (2.3), H–C(3′) (0.9)
b	H–C(8)	H–C(1′) (5.0), H–C(2′) (4.5), H–C(3′) (1.0)
c	H–C(8)	H–C(1′) (5.3), H–C(2′) (4.5), H–C(3′) (1.0)

[a]) Measured in (D_6)DMSO at 45°.

It will be interesting to see whether the nucleosides **1b**,**c** can stabilize triple base pairs in triplex DNA according to the motif **I** and can base pair with the pyrimidine-2,4-diamine nucleoside (DAPy) in duplex structures as well (motif **II**). The triplexes are expected to be more stable than those incorporating **1a**, due to the presence of the lipophilic electron-withdrawing character of the 7-halogeno substituents. However, it remains to be established whether the substituents have enough space to be well accommodated in the triplex structure. Compound **1a** forms a nanotube in the solid state [27]. Thus, X-ray analyses will be performed on compounds **1b**,**c**, and the effect of the 7-substituents within the nanotube will be investigated. Moreover, the antiviral activity of the compounds will be tested as some pyrrolo[3,4-*d*]pyrimidine nucleosides show inhibitory activity against the hepatitis C virus. The synthesis of oligonucleotides containing the nucleosides **1b**,**c** as well as base-pairing studies are currently under investigation.

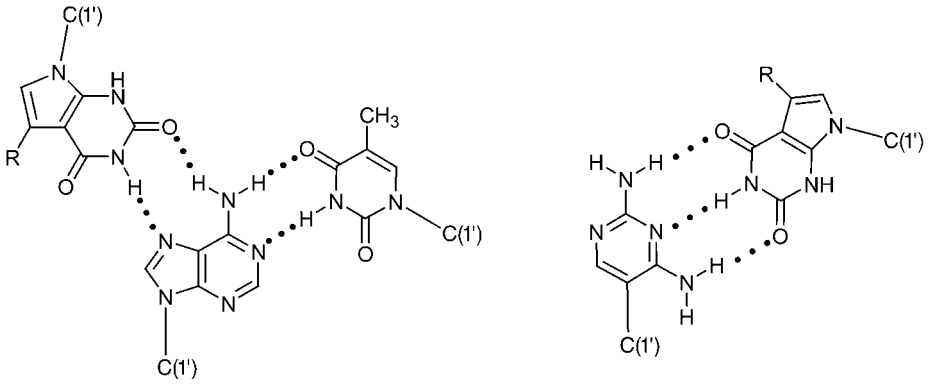


Fig. 2. *Suggested base triplet* (motif **I**) *and base duplex* (motif **II**) *of* **1a**–**c**

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Experimental Part

General. All chemicals were purchased from *Aldrich*, *Sigma*, or *Fluka* (*Sigma-Aldrich Chemie GmbH*, Deisenhofen, Germany). Solvents were of laboratory grade. TLC: aluminium sheets, silica gel *60 F_{254}*, 0.2 mm layer (*VWR*, Germany). Ion exchange: *Serdolit AD-4* resin, 0.1–0.2 mm (*Serva Electrophoresis GmbH*, Heidelberg, Germany). Column flash chromatography (FC): silica gel *60* (*Merck*, Germany) at 0.4 bar; sample collection with an *UltraRac II* fraction collector (*LKB Instruments*, Sweden). UV Spectra: *U-3200* spectrometer (*Hitachi*, Tokyo, Japan); λ_{max} (ε) in nm. NMR Spectra: *Avance-250* or *AMX-500* spectrometers (*Bruker*, Karlsruhe, Germany), at 250.13 MHz for ^{1}H and ^{13}C; δ in ppm rel. to Me_4Si as internal standard, *J* values in Hz. Elemental analyses were performed by *Mikroanalytisches Laboratorium Beller* (Göttingen, Germany).

*5-Bromo-7-(2-deoxy-β-*D-erythro-*pentofuranosyl)-4-methoxy-7*H-*pyrrolo[2,3-*d*]pyrimidin-2-amine* (**2b**). Compound **4b** (1.0 g, 1.30 mmol) [8] in 0.5M NaOMe in MeOH (50 ml) was stirred overnight at r.t. The solvent was evaporated and the residue applied to FC (silica gel, column 10 × 5 cm, CH_2Cl_2/MeOH 95:5): **2b** (512 mg, 75%). Colorless solid. M.p. 170°. TLC (silica gel, CH_2Cl_2/MeOH 9:1): R_f 0.5. UV (MeOH): 230 (28600), 265 (8300), 289 (7000). ^{1}H-NMR ((D$_6$)DMSO): 2.09 (*m*, H_α–C(2′)); 2.34 (*m*, H_β–C(2′)); 3.49 (*m*, 2 H–C(5′)); 3.76 (*m*, H–C(4′)); 3.92 (*s*, MeO); 4.28 (*d*, *J* = 2.2, H–C(3′)); 4.95 (*dd*, *J* = 5.4, 5.4, OH–C(5′)); 5.23 (*d*, *J* = 3.7, OH–C(3′)); 6.39 (*dd*, *J* = 2.6, 5.8, H–C(1′)); 6.43 (*s*, NH_2); 7.27 (*s*, H–C(6)). Anal. calc. for $C_{12}H_{15}BrN_4O_4$ (359.1): C 40.13, H 4.21, Br 22.25, N 15.60; found: C 40.20, H 4.28, Br 22.1, N 15.49.

*5-Bromo-7-(2-deoxy-β-*D-erythro-*pentofuranosyl)-1,7-dihydro-4-methoxy-2*H-*pyrrolo[2,3-*d*]pyrimidin-2-one* (**5b**). To a soln. of **2b** (407 mg, 1.13 mmol) in 10% aq. AcOH (85 ml), a soln. of $NaNO_2$ (182 mg, 2.64 mmol) in H_2O (10 ml) was added dropwise while stirring. Stirring was continued for 0.5 h, and the solvent was evaporated *in vacuo*. The residue was applied to FC (silica gel, column 10 × 2.5 cm, CH_2Cl_2/MeOH 95:5): **5b** as a colorless solid, which was crystallized from EtOH (357 mg, 87%). M.p. 169–170°. TLC (silica gel, CH_2Cl_2/MeOH 9:1): R_f 0.44. UV (MeOH): 225 (24300), 284 (6100). ^{1}H-NMR ((D$_6$)DMSO): 2.16 (*m*, H_α–C(2′)); 2.39 (*m*, H_β–C(2′)); 3.52 (*m*, 2 H–C(5′)); 3.79 (*m*, H–C(4′)); 3.97 (*s*, MeO); 4.30 (*m*, H–C(3′)); 5.04 (*s*, OH–C(5′)); 5.27 (*d*, *J* = 3.7, OH–C(3′)); 6.39 (*dd*, *J* = 6.2, 7.6, H–C(1′)); 7.45 (*s*, H–C(6)); 11.63 (br. *s*, NH). Anal. calc. for $C_{12}H_{14}BrN_3O_5$ (360.16): C 40.02, H 3.92, Br 22.19, N 11.67; found: C 40.2, H 4.06, Br 22.38, N 11.54.

*5-Bromo-7-(2-deoxy-β-*D-erythro-*pentofuranosyl)-1*H-*pyrrolo[2,3-*d*]pyrimidine-2,4(3*H,*7*H*)-dione* (**1b**). *Method A:* Compound **5b** (110 mg, 0.305 mmol) in 2N NaOH (7 ml) was stirred under reflux for 3 days. The cold soln. was neutralized with 1N aq. AcOH and evaporated and the residue dissolved in H_2O (25 ml) and subjected to ion exchange (*Serdolit AD-4*, column 12 × 1.5 cm). The salt was washed out with H_2O and the product eluted with MeOH/H_2O 1:1: **1b** (82 mg, 78%). Colorless solid that was crystallized from H_2O to give slightly colored crystals. M.p. > 210°. TLC (silica gel, CH_2Cl_2/MeOH 9:1): R_f 0.37. UV (0.1M NaH_2PO_4 buffer pH 7.0): 221 (20500), 256 (9000), 285 (5900). ^{1}H-NMR ((D$_6$)DMSO): 2.16 (*m*, H_α–C(2′)); 2.22 (*m*, H_β–C(2′)); 3.53 (*m*, 2 H–C(5′)); 3.82 (*m*, H–C(4′)); 4.29 (*m*, H–C(3′)); 5.30 (*d*, *J* = 3.2, OH–C(3′)); 6.12 (*dd*, *J* = 7, 6.5, H–C(1′)); 7.13 (*s*, H–C(6)); 10.74 (*s*, NH). ^3J(H,H) in D_2O at 298 K for pseudorotational parameters: $J(1',2') = 7.05$, $J(1',2'') = 6.60$, $J(2',3') = 6.40$, $J(2'',3') = 3.20$, $J(3',4') = 3.10$. Anal. calc. for $C_{11}H_{12}BrN_3O_5$ (346.13): C 38.17, H 3.49, Br 23.08, N 12.14; found: C 38.03, H 3.39, Br 22.68, N 11.57.

Method B: To a suspension of **5b** (550 mg, 1.52 mmol) in MeCN (20 ml) were added NaI (450 mg, 3 mmol) and Me_3SiCl (442 µl, 3.46 mmol) at r.t. while stirring. Stirring was continued for 1 h, and the mixture was filtered. The residue was washed with MeCN and crystallized from H_2O affording **1b**/**1c** (503 mg). Slightly colored crystals.

*7-(2-Deoxy-β-*D-erythro-*pentofuranosyl)-5-iodo-4-methoxy-7*H-*pyrrolo[2,3-*d*]pyrimidin-2-amine* (**2c**). A soln. of **4c** [8] (350 mg, 0.61 mmol) in 0.5N NaOMe (40 ml) was stirred overnight at r. t. The solvent was evaporated and the residue adsorbed on silica gel and subjected to FC (silica gel, column 12 × 3 cm, CH_2Cl_2/MeOH 95:5): **2c** (195 mg, 79%). Colorless solid. M.p. 159–160°. TLC (CH_2Cl_2/MeOH 9:1): R_f 0.48. UV (MeOH): 233 (31200), 266 (2800), 289 (7300). ^{1}H-NMR ((D$_6$)DMSO): 2.08 (*m*, H_α–C(2′)); 2.36 (*m*, H_β–C(2′)); 3.48 (*m*, 2 H–C(5′)); 3.75 (*m*, H–C(4′)); 3.92 (*s*, MeO); 4.27 (*d*, *J* = 2.2, H–C(3′)); 4.94 (*dd*, *J* = 5.4, 5.4, OH–C(5′)); 5.22 (*d*, *J* = 3.7, OH–C(3′)); 6.37 (*d*, *J* = 5.8, H–C(1′)); 6.39 (*s*, NH_2); 7.29 (*s*, H–C(6)). Anal. calc. for $C_{12}H_{15}IN_4O_4$ (406.1): C 35.48, H 3.72, I 31.24, N 13.79; found: C 35.62, H 3.84, I 30.72, N 13.84.

*7-(2-Deoxy-β-*D-erythro-*pentofuranosyl)-1,7-dihydro-5-iodo-4-methoxy-2*H-*pyrrolo[2,3-*d*]pyrimidin-2-one* (**5c**). To a soln. of **2c** (1.0 g, 2.46 mmol) in 10% aq. AcOH (150 ml), a soln. of $NaNO_2$ (290 mg, 4.2 mmol) in H_2O (10 ml) was added dropwise while stirring. The reaction was continued for 0.5 h. The solvent was evaporated and residue adsorbed on silica gel and applied to FC (silica gel, column 10 × 5 cm, CH_2Cl_2/MeOH

95:5): **5c** as a colorless solid, which was crystallized from EtOH to give colorless crystals (654 mg, 65%). M.p.158–160°. TLC (CH_2Cl_2/MeOH 9:1): R_f 0.4. UV (MeOH): 227 (23200), 286 (6300). ^{1}H-NMR ((D$_6$)DMSO): 2.13 (m, H$_\alpha$–C(2′)); 2.39 (m, H$_\beta$–C(2′)); 3.52 (m, 2 H–C(5′)); 3.79 (m, H–C(4′)); 3.96 (s, MeO); 4.30 (m, H–C(3′)); 5.04 (s, OH–C(3′)); 5.25 (d, J = 3.7, OH–C(5′)); 6.37 (dd, J = 6.6, 7.2, H–C(1′)); 7.46 (s, H–C(6)); 11.57 (br. s, NH). Anal. calc. for $C_{12}H_{14}IN_3O_5$ (407.1): C 35.40, H 3.47, I 31.17, N 10.32; found: C 35.48, H 3.55, I 31.20, N 10.34.

*7-(2-Deoxy-β-*D*-*erythro*-pentofuranosyl)-5-iodo-1*H*-pyrrolo[2,3-*d*]pyrimidine-2,4(3*H*,7*H*)-dione* (**1c**). *Method A:* As described for **1b**, with **5c** (50 mg, 0.12 mmol) and 2N aq. NaOH (3 ml): slightly colored **1c** (35 mg, 80%).

Method B: As described for **1b**, with **5c** (620 mg, 1.52 mmol), MeCN (20 ml), NaI (450 mg, 3 mmol), and Me_3SiCl (442 µl, 3.46 mmol): **1c** (543 mg, 91%). Slightly colored crystals. M.p. >210°. TLC (silica gel, CH_2Cl_2/MeOH 9:1): R_f 0.36. UV (0.1M aq. NaH_2PO_4 buffer, pH 7): 224 (21500), 259 (9700), 285 (6800). ^{1}H-NMR ((D$_6$)DMSO): 2.16 (m, H$_\alpha$–C(2′)); 2.27 (m, H$_\beta$–C(2′)); 3.57 (m, 2 H–C(5′)); 3.82 (m, H–C(4′)); 4.28 (m, H–C(3′)); 5.28 (d, J = 3.3, OH–C(3′)); 5.53 (s, OH–C(5′)); 6.12 (dd, J = 7, 6.5, H–C(1′)); 7.14 (s, H–C(6)); 10.70 (s, NH); 11.70 (s, NH); ^3J(H,H) coupling constants in D_2O at 298 K for pseudorotational parameters. J(1′,2′) = 6.89, J(1′,2″) = 5.90, J(2′,3′) = 5.81, J(2″,3′) = 2.75, J(3′,4′) = 3.00. Anal. calc. for $C_{11}H_{12}IN_3O_5$ (393.1): C 33.61, H 3.08, I 32.28, N 10.69; found: C 34.14, H 3.34, I 31.56, N 10.46.

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