120. 2′,3′-Dideoxy-3′-fluorotubercidin and Related Dideoxyribonucleosides: Synthesis *via* a 2′-Deoxy-3′-oxoribofuranoside Intermediate and Conformation Studies

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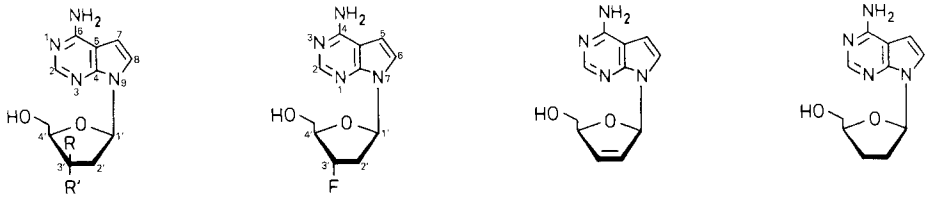
An efficient synthesis of the unknown 2′-deoxy-D-*threo*-tubercidin (**1b**) and 2′,3′-dideoxy-3′-fluorotubercidin (**2**) as well as of the related nucleosides **9a**, **b** and **10b** is described. Reaction of 4-chloro-7-(2-deoxy-β-D-*erythro*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (**5**) with (*tert*-butyl)diphenylsilyl chloride yielded **6** which gave the 3′-keto nucleoside **7** upon oxidation at C(3′). Stereoselective $NaBH_4$ reduction (→ **8**) followed by deprotection with Bu_4NF (→ **9a**) and nucleophilic displacement at C(6) afforded **1b** as well as 7-deaza-2′-deoxy-D-*threo*-inosine (**9b**). Mesylation of 4-chloro-7-{2-deoxy-5-*O*-[(*tert*-butyl)diphenylsilyl]-β-D-*threo*-pentofuranosyl}-7*H*-pyrrolo[2,3-*d*]-pyrimidine (**8**), treatment with Bu_4NF (→ **12a**) and 4-halogene displacement gave 2′,3′-didehydro-2′,3′-dideoxy-tubercidin (**3**) as well as 2′,3′-didehydro-2′,3′-dideoxy-7-deazainosine (**12c**). On the other hand, 2′,3′-dideoxy-3′-fluorotubercidin (**2**) resulted from **8** by treatment with diethylamino sulfurtrifluoride (→ **10a**), subsequent 5′-deprotection with Bu_4NF (→ **10b**), and Cl/NH_2 displacement. ^{1}H-NOE difference spectroscopy in combination with force-field calculations on the sugar-modified tubercidin derivatives **1b**, **2**, and **3** revealed a transition of the sugar puckering from the $^3T_{2'}$ conformation for **1b** *via* a planar furanose ring for **3** to the usual $^2T_{3'}$ conformation for **2**.

Introduction. – Purine and pyrimidine nucleosides without a 3′-OH group in *erythro* configuration act as chain terminators of DNA synthesis. In particular, 2′,3′-dideoxyribonucleosides, 2′,3′-didehydro-2′,3′-dideoxy, 3′-azido, and 3′-fluoro derivatives have been shown to inhibit one or more steps of the replicative cycle of HIV retroviruses [1]. Their triphosphates may also act as inhibitors of the viral reverse transcriptase but can introduce cytotoxicity within the host cell due to the inhibition of cellular DNA polymerases [2–4]. The behaviour of corresponding 7-deazapurine nucleoside triphosphates is almost unknown; however, 7-deaza-2′-deoxyguanosine triphosphate acts as a substrate of DNA polymerase [5]. As common 2′,3′-dideoxynucleosides may be deactivated by cellular-metabolyzing enzymes, interest arose in 2′,3′-dideoxynucleosides with modified nucleobases not showing such drawbacks [6].

Among the series of 7-deazaadenosine (= tubercidin; 2′-OH-**1a**) derivatives, the furanose moiety has been altered with respect to biochemical and pharmacological action [7]. Within those compounds, 7-deazaadenine β-D-xylofuranoside (= D-*xylo*-tubercidin) exhibits strong antiviral activity, in particular towards HIV [8] which is similar to adenine 3′-deoxy-3′-fluororiboside [1].

We now describe the synthesis of unknown 2′,3′-dideoxy-3′-fluorotubercidin (**2**) and 2′-deoxy-D-*threo*-tubercidin (**1b**) as well as of related nucleosides *via* a 2′-deoxy-3′-oxoribofuranoside intermediate. Moreover, an efficient 4-step synthesis (total yield 25%) of 2′,3′-didehydro-2′,3′-dideoxytubercidin (**3**) starting from the easily available 4-chloro-



1a[a]) R = H, R' = OH
b R = OH, R' = H

2[b])

3

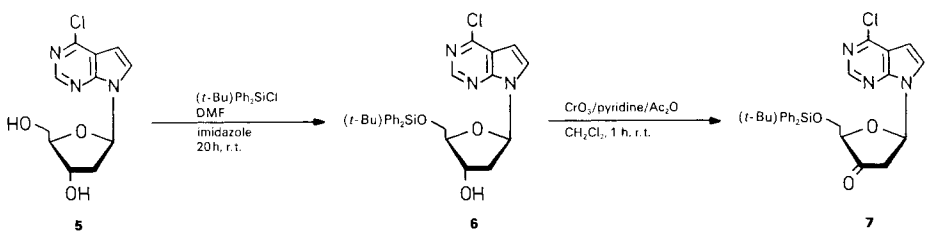
4

[a]) Purine numbering. [b]) Systematic numbering.

2'-deoxynucleoside **5** [9] is presented. An earlier synthetic approach started from the fermentation product tubercidin and afforded **3** in only 17% yield [7]. The latter can be subsequently hydrogenated almost quantitatively to give 2',3'-dideoxytubercidin (**4**) [7] [9].

Apart from synthetic investigations, conformational analysis of 2',3'-dideoxynucleosides is described, based on NMR spectroscopic studies and force-field calculations.

Results and Discussion. – *Synthesis.* For the synthesis of 3'-modified pyrrolo[2,3-*d*]-pyrimidine nucleosides with D-*erythro* configuration at C(3') and C(4'), 7-deaza-2'-deoxy-β-D-threofuranosides are suitable starting materials as their 3'-OH group (D-*threo* configuration at C(3') and C(4')) can easily be displaced by an F or N_3 group under inversion of configuration. *Hansske et al.* [10] have worked out an oxidation followed by a stereospecific reduction of purine and pyrimidine nucleosides to their corresponding 2'- or 3'-epimers. This epimerisation is now applied to pyrrolo[2,3-*d*]pyrimidine 2'-deoxyribofuranosides, in particular to 4-chloro-7-(2-deoxy-β-D-*erythro*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (**5**) which can be prepared in large scale in a convergent synthesis applying solid-liquid phase-transfer glycosylation [9] and is a versatile intermediate for subsequent transformations.



5 **6** **7**

Compound **5** was 5'-protected with (*tert*-butyl)diphenylsilyl chloride ((*t*-Bu)Ph_2SiCl) in the presence of imidazole affording **6** in 76% yield apart from 5% of a 3',5'-disilylated material. Silylation at C(5') of the main product **6** was confirmed by a downfield shift ($\Delta\delta$ = 2.4 ppm) of the ^{13}C-NMR signal of C(5') as compared to that of **5**.

Oxidation of **6** with a freshly prepared complex from CrO_3/pyridine/Ac_2O 1:2:1 [11] gave the 3'-keto nucleoside **7**. Its structure was proved by ^{1}H- and ^{13}C-NMR spectroscopy in $CDCl_3$ solution (*Table 1* and *Exper. Part*). A strong downfield shift ($\Delta\delta$ = 140.1 ppm) of the C(3') signal of **7** as compared to **6** is an unequivocal indicator for the position of oxidation. Compound **7** proved to be significantly more stable than the corresponding

Table 1. *^{13}C-NMR Chemical Shifts of 7-Deazapurine Nucleosides*[a])[b])

	C(6)	C(2)	C(4)	C(7a)	C(4)	C(5)	C(1′)	C(2′)	C(3′)	C(4′)	C(5′)
5	128.5	150.5	150.8	150.6	117.4	99.7	83.4	39.9	70.9	87.7	61.8
6	128.4	150.6	150.7	150.7	117.5	99.7	83.4	39.4	70.2	86.8	64.2
13	128.7	150.7	150.8	150.9	117.7	100.0	83.6	38.0	80.1	84.0	63.2
7	128.6	150.7	150.9	151.0	117.7	100.0	80.0	41.5	210.3	82.5	63.8
7[c])	126.0	151.0	151.3	152.4	118.2	101.4	80.3	42.9	209.6	82.9	63.5
8	129.5	150.7	150.6	150.6	117.2	99.4	82.8	41.2	69.2	85.0	63.5
9a	129.6	150.5	150.6	150.6	117.1	99.4	82.4	41.2	69.1	85.2	60.0
1b	123.2	151.4	157.6	149.1	102.9	99.3	82.5	40.9	69.4	84.3	60.0
9b	122.0	143.7	158.3	147.1	108.0	102.2	82.1	41.3	69.2	84.7	60.0
12a	128.6	150.7	150.7	150.7	117.4	99.6	88.2	125.6	134.7	87.9	63.0
3	121.3	151.9	157.6	149.9	102.8	99.9	87.7	126.3	133.8	87.2	63.6
12b	124.5	150.8	162.4	151.6	105.1	98.8	88.0	126.0	134.2	87.6	63.3
12c	120.7	144.5	158.9	147.5	108.3	102.4	87.5	126.0	134.1	88.0	63.4
10a	128.5	150.7	151.0	151.0	117.7	100.0	83.8	36.7	94.3	84.4	63.4
10b[b])	127.6	150.7	151.0	151.0	117.5	100.1	83.6	37.3	95.1	85.3	61.1
10b[c])	127.6	150.0	153.1	149.7	119.9	100.1	89.0	38.5	95.3	86.4	62.8
2	121.9	151.8	157.7	149.8	103.2	100.0	83.8	37.6	95.4	84.8	61.4

	Phenyl							$(CH_3)_3C$	$(CH_3)_3C$	CH_3O/CH_3SO_2
12b										53.6
6	135.2	135.1	133.0	132.7	130.0	127.9	127.9	26.7	18.9	
7	135.1	135.0	132.7	132.3	129.9	127.9	127.8	26.6	18.8	
7[c])	135.6	135.5	130.0	129.8	129.9	128.0	127.9	26.9	19.3	
8	135.2	135.1	133.2	133.0	129.9	129.8	127.9	26.7	18.8	
10a	135.2	135.1	132.7	132.5	130.1	128.0	127.9	26.7	18.9	
13	135.2	135.1	132.7	132.4	130.0	129.9	127.8	26.7	18.9	56.6

[a]) Systematic numbering. [b]) Measured in (D_6)DMSO. [c]) Measured in $CDCl_3$.

2′-deoxy-3′-oxoadenosine which could not be trapped due to a β-elimination of the nucleobase. However, **7** decomposed upon contact with silica gel during chromatographic workup as well as upon prolonged storage [10]. Decomposition could be monitored by ^{1}H- and ^{13}C-NMR spectroscopy in (D_6)DMSO where the resonances of a 2-(silyloxy)furan-3(2*H*)-one appear [10]. Therefore, the 3′-keto nucleoside **7** was always freshly prepared and used for further reactions without purification.

Reduction of **7** using $NaBH_4$ in EtOH (0°) resulted in the formation of the 3′-epimeric compound **8**. No traces of the corresponding D-*erythro*-configurated material **6** were detected by TLC, indicating a complete 1,1-asymmetric induction at the prochiral C(3′) of **7** according to *Cram*'s rule [12]. Desilylation of **8** was accomplished with Bu_4NF in THF and gave 4-chloro-7-(2-deoxy-β-D-*threo*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]-pyrimidine (**9a**). The structures of **8** and **9a** were proved by 1D ^{1}H- and ^{13}C-NMR spectra (*Tables 1* and *3*, *Exper. Part*) as well as 2D ^{1}H,^{1}H- and ^{1}H,^{13}C-correlation spectra. The (3′*R*)-configuration of **8** and **9a** was deduced from the reversed chemical shifts as well as the different multiplicities of the H_α–C(2′) and H_β–C(2′) signals as compared to those of compounds **5** and **6**. As only H_α–C(2′) (at lower field as H_β–C(2′)) exhibits a significant NOE value (*Table 2*) upon irradiation of H–C(1′), its assignment is unequivocal. Moreover, the NOE at H–C(4′) (*Table 2*) proves β-D-configuration at the anomeric center of **8** and **9a** [13].

Table 2. *NOE Data (%) of 7-Deazapurine Nucleosides Upon Irradiation of H–C(1′)*

	8	**9a**	**1b**	**9b**	**12a**	**12b**	**12c**	**2**
H_α–C(2′)	7.3	7.2	6.3	8.2	8.1	6.0	6.3	[a]
H_β–C(2′)	0	0	0	0				0
H–C(4′)	3.0	2.6	3.4	4.0	2.3	1.7	2.0	2.2

[a] Overlapping with solvent signal.
[b] Measured in (D_6)DMSO.

Table 3. *J(C,H) Coupling Constants of 7-Deazapurine Nucleosides*[a][c]

C	H	**9a**	**9b**	**12a**	**3**	**12b**	**12c**	**10b**	**2**
C(2)	H–C(2)	208.9	204.8	209.1	197.2	203.8	204.3	209.5	197.6
C(6)	H–C(6)	191.3	190.1	191.1	188.1	189.2	189.1	191.0	188.5
C(6)	H–C(5)	7.9	8.0	7.8	8.2	7.9	8.0	7.9	8.2
C(6)	H–C(1′)	5.1	5.1	5.0	5.0	5.0	4.9	4.4	4.4
C(4)	H–N(3)		6.5				6.6		
C(4)	NH_2				11.0				11.0
C(4)	CH_3O					3.9			
C(4a)	H–C(5)	8.7	7.8	8.1	8.0	8.2	7.8	8.0	8.1
C(4a)	H–C(6)	4.2	3.6	3.6	4.5	4.0	3.6	4.0	4.0
C(5)	H–C(5)	181.6	176.6	181.6	176.6	179.0	176.6	182.1	176.9
C(5)	H–C(6)	7.6	7.5	7.3	7.3	7.3	7.3	7.0	7.1
C(1′)	H–C(1′)	174.3	173.6	[c]	166.5	[c]	[c]	167.8	163.7
C(2′)	H–C(2′)	154.3	[b]	171.7	171.1	171.1	174.8	[b]	[b]
C(2′)	H–C(1′)			[d]	7.2	[d]	[d]	[d]	[d]
C(2′)	H–C(3′)			[d]	3.6	[d]	[d]	[d]	[d]
C(3′)	H–C(3′)	150.6	152.1	173.3	174.1	174.7	174.6	171.0	170.0
C(3′)	H–C(4′)			[d]	8.2	6.8	[d]	[d]	[d]
C(3′)	H–C(2′)			[d]	4.1	4.1	[d]	[d]	[d]
C(4′)	H–C(4′)	143.3	146.9	[c]	147.4	[c]	[c]	147.1	149.1
C(5′)	H–C(5′)	141.6	139.9	140.5	140.4	140.4	141.1	139.4	141.7
CH_3O	CH_3O					147.0			

[a] Systematic numbering.
[b] Superimposed by solvent signal.
[c] Overlapping of C(1′) and C(4′) signals.
[d] Not resolved.
[e] From spectra measured in (D_6)DMSO.

Nucleophilic displacement of the 4-Cl substituent of **9a** with either aqueous ammonia (100°, 15 h) or aqueous 2N NaOH (5 h, reflux) afforded 7-(2-deoxy-β-D-*threo*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidin-4-amine (**1b**) or the corresponding 7-deaza-2′-deoxy-D-*threo*-inosine (**9b**), respectively. 1D and 2D ^{1}H- and ^{13}C-NMR spectra as well as 1D NOE difference spectra provided the assignment shown in *Table 1* and in the *Exper. Part* and proved the structures of **9a**, **b**.

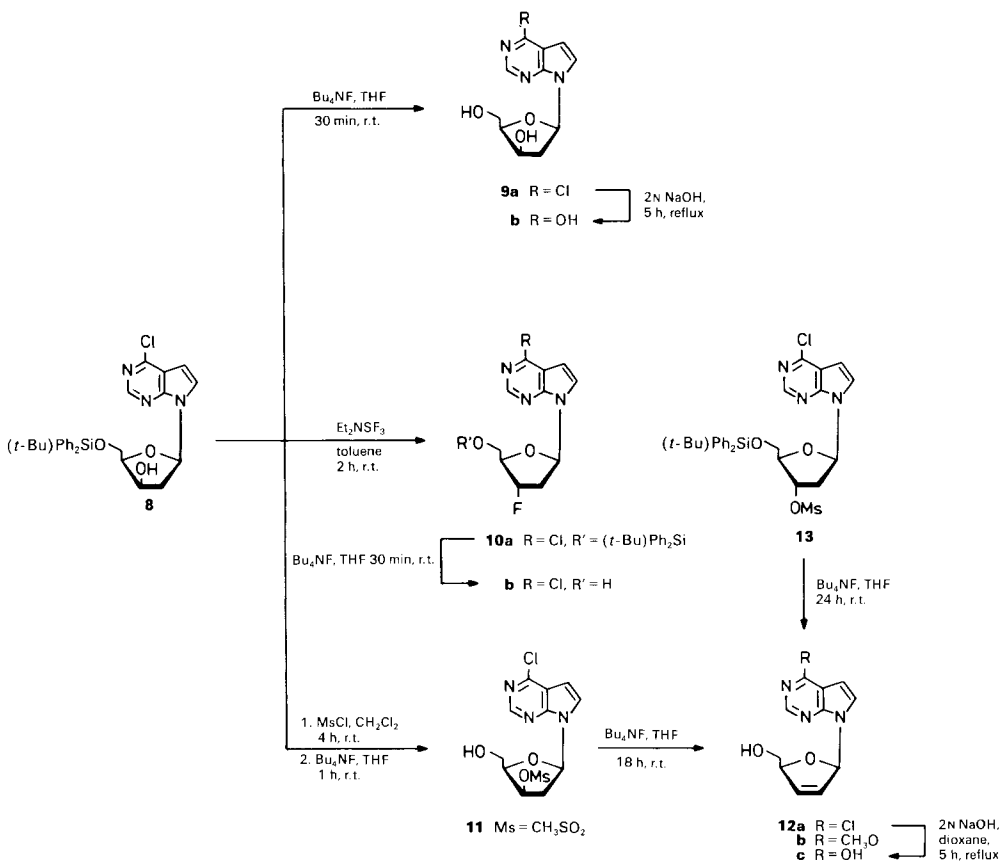
The D-*threo*-configurated 2′-deoxynucleosides **8**, **9a**, **b**, and **1b** are particularly useful for the synthesis of 3′-substituted 7-deazapurine 2′,3′-dideoxyribonucleosides with D-*erythro*-configuration at C(3′) as well as for their 2′,3′-didehydro derivatives. Thus, **8** was reacted with (diethylamino)sulfur trifluoride [14–16] to give the 3′-fluorinated compound **10a** which was characterized by ^{1}H-, ^{13}C-, and ^{19}F-NMR spectroscopy (*Tables 1* and *4*, *Exper. Part*). Desilylation was performed with Bu_4NF and gave **10b**. Subsequent dis-

Table 4. *^1H,^{19}F- and ^{13}C,^{19}F-Coupling Constants of* **10a**, **b** *and* **2**

	Solvent	H–C(3′), F–C(3′)	H–C(4′), F–C(3′)	C(3′), F	C(4′), F	C(5′), F	C(2′), F
10a	(D_6)DMSO	53.7	26.6	175.0	23.7	10.5	21.0
10b	(D_6)DMSO	54.1	26.8	174.1	22.1	11.1	20.5
10b	$CDCl_3$	53.7	28.4	175.5	23.5	11.7	20.5
2	(D_6)DMSO	53.1	27.6	173.3	22.2	11.4	20.3

placement of its 4-Cl group with aqueous ammonia resulted in the formation of 2′,3′-dideoxy-3′-fluorotubercidin (**2**). *Table 4* shows the ^1H,^{19}F- as well as the ^{19}F,^{13}C-coupling constants of **10a, b** and **2**. They are characteristic and enable the unequivocal assignment of ^1H- and ^{13}C-NMR resonances of the sugar moieties of **10a**, **b** and **2** (*Table 1* and *Exper. Part*) as well as the position of fluorination.

On a parallel reaction route, **8** was mesylated at its 3′-OH group. After desilylation with Bu_4NF (1 h, r.t.) and chromatographic workup, ^1H-NMR spectroscopy revealed the mesylat **11** which was not further purified but redissolved in 1M Bu_4NF in THF. Additional stirring at r.t. for 18 h (TLC control) and subsequent chromatographic workup gave a new product. 1D ^1H- and ^{13}C-NMR spectra as well as 2D ^1H,^1H- and ^1H,^{13}C-NMR



correlation spectra (*Tables 1* and *3* and *Exper. Part*) revealed the 2′,3′-didehydro-2′,3′-dideoxynucleoside **12a** [17], formed by β-elimination of the mesyloxy group of **11**. The same compound **12a** was also obtained from the D-*erythro*-configurated 3′-mesylate **13** upon treatment with Bu_4NF which opens a simple access to 2′,3′-didehydro-2′,3′-dideoxynucleosides. However, in the latter case, a higher excess of the reagent and a longer reaction time was necessary to drive the reaction. This may be due to the fact that *trans* elimination of the D-*threo*-configurated **11** occurs from the less-hindered α-side, while in the case of the D-*erythro*-configurated **13**, the attack of the base has to occur from the sterically hindered β-side.

The 4-Cl group of **12a** can be displaced by various nucleophiles. Thus, dissolving **12a** in saturated methanolic ammonia/aqueous ammonia 1:1 (*v/v*; for solubility reasons) and heating to 100° for 15 h in a steel bomb afforded **3** [17] in 45% yield besides small amounts of **12b**. Refluxing of **12a** in 2N aqueous NaOH/1,4-dioxane 1:1 (*v/v*) and chromatographic workup gave 2′,3′-didehydro-2′,3′-dideoxy-7-deazainosine (**12c**). All compounds were characterised by ^{1}H- and ^{13}C-NMR spectra (*Table 1* and *Exper. Part*).

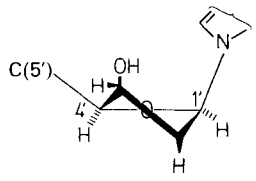
Conformational Studies on 7-Deazapurine Nucleosides. As the conformation of nucleosides (for definition of conformational modes, see [18]) influences their enzymatic phosphorylation which is a prerequisite for the inhibition of HIV reverse transcriptase and DNA polymerases in general, we applied ^{1}H-NMR NOE difference and gated-decoupled ^{13}C-NMR spectroscopy as well as force-field calculations in order to obtain informations about the preferred conformations of the sugar-modified 7-deazapurine nucleosides (*Tables 2, 3,* and *5*).

Table 5. *Computed Proton-Proton Distances* [Å] *and Torsion Angles* [°] *for* **1b**, **3**, *and* **2**

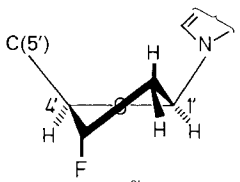
	r_{ij} of H_i–H_j		Torsion angle	
1b	*H*–C(1′), H_α–C(2′)	2.20	H–C(1′)–C(2′)–H_α	7.1
	H–C(1′), H_β–C(2′)	2.95	H–C(1′)–C(2′)–H_β	128.6
	H–C(1′), *H*–C(3′)	3.78	C(1′)–C(2′)–C(3′)–C(4′)	21.5
	H–C(1′), *H*–C(4′)	2.81	C(6)–N(7)–C(1′)–H	150.0[a])
3	*H*–C(1′), *H*–C(2′)	2.65	H–C(1′)–C(2′)–H	63.9
	H–C(1′), *H*–C(3′)	4.08	C(1′)–C(2′)–C(3′)–C(4′)	–3.2
	H–C(1′), *H*–C(4′)	3.74	C(6)–N(7)–C(1′)–H	150.0[a])
2	*H*–C(1′), H_α–C(2′)	2.32	H–C(1′)–C(2′)–H_α	28.4
	H–C(1′), H_β–C(2′)	3.02	H–C(1′)–C(2′)–H_β	150.7
	H–C(1′), *H*–C(4′)	3.78	C(1′)–C(2′)–C(3′)–C(4′)	–33.4
			C(6)–N(7)–C(1′)–H	150.0[a])

[a]) Torsion angles were calculated from ^3J(C(6),H–C(1′)) coupling constants using *Lemieux*'s relation [26].

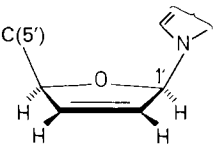
Saturation of H–C(1′) of the D-*threo*-configurated 7-deazapurine nucleosides **9a**, **b** and **1b** resulted in significant NOE's at H_α–C(2′) and H–C(4′) (*Table 2*) but none at H–C(3′) although the latter is also positioned on the α-side of the furanose ring. This can be interpreted by a pronounced population of the twist conformer **I** ($^{3'}T_{2'}$) of these nucleosides which is opposite to the situation in most D-*erythro*-configurated purine 2′-deoxyribonucleosides [19] as tubercidin and 2′-deoxytubercidin itself [20] where the $^{2'}T_{3'}$ conformation is predominant (see **II**). This finding was verified by force-field calculations on compound **1b** (*Table 5*) using the *Alchemy II* molecular modeling program (*Tripos Ass.*, Inc., 1988). After energy minimisation (see *Exper. Part*) of the model structure, a torsion angle v_2 (C(1′)–C(2′)–C(3′)–C(4′)) of +21.5° was calculated. To support these computational results, we correlated them with NOE data of **1b**: Irradiation of H–C(1′) or **1b** produced an NOE of 3.4% at



I ($^{3'}T_{2'}$)



II ($^{2'}T_{3'}$)



III

H–C(4') *(Table 2)*. Using the relation NOE(k)/NOE(u) = $[r(u)/r(k)]^6$, where $r(k)$ and $r(u)$ are the known and unknown inter-proton distance, respectively [21], and taking the distances $r(k) = r(H\text{–}C(6), H\text{–}C(5)) = 2.58$ Å as a medium-size yardstick with an NOE(k) = 5.4% [22], one calculates a distance $H\text{–}C(1'), H\text{–}C(4')$ of 2.79 Å. This value is consistent with the computed distance (2.81 Å, *Table 5*).

Force-field calculations on the 2',3'-didehydro-2',3'-dideoxynucleoside **3** *(Table 5)* imply an almost planar furanose moiety (see **III**) with a torsion angle ν_2(C(1')–C(2')–C(3')–C(4')) of –3.2°. An analogous conformation has already been reported for 2',3'-unsaturated methyl 2',3'-dideoxypentofuranosides [23]. This implies a ^3J(H–C(1'),H–C(2')) of *ca.* 1.5 Hz, a ^4J(H–C(1'),H–C(3')) of *ca.* –2 Hz [24], and a ^5J(H–C(1'),H–C(4')) of *ca.* 4 Hz which could all be found in a high-resolution ^{1}H-NMR spectrum of **3** on selective spin-decouplings (see *Exper. Part*). Moreover, a 2D ^{1}H,^{1}H-correlation spectrum of **3** exhibits cross peaks between the allylic protons H–C(1') and H–C(3') (^4J) as well as the homoallylic protons H–C(1') and H–C(4') (^5J) but none between H–C(1') and H–C(2'). As the assignment of the H–C(2') and H–C(3') resonances of 2',3'-didehydro-2',3'-dideoxynucleosides is inconsistent throughout the literature, we measured the 1D NOE difference spectra of **12a–c** with saturation of H–C(1'). Significant intensity enhancements occurred only at H–C(2') which resonates upfield from H–C(3') *(Table 2)*. This result corroborates the assignment of *Robins et al.* [25] and allows unequivocal identification of the C(2') and C(3') signals given in *Table 1*.

The averaged NOE's (6.8%) at H–C(2') of **12a–c** upon irradiation of H–C(1') correspond to an inter-proton distance of 2.60 Å which is in agreement with the computed distance ($r(H\text{–}C(1'), H\text{–}C(2')) = 2.65$ Å). This verifies the unusual sugar conformation of the 2',3'-didehydro-2',3'-dideoxynucleosides **3** and **12a–c**.

Gated-decoupled ^{13}C-NMR spectra of **3** and **12a–c** *(Table 3)* provided the ^3J coupling constants of C(6) with the anomeric proton and gave a torsion angle $\kappa = 150°$ which corresponds to glycosylic torsion angles of 30 and –90° [26]. As a result, all 2',3'-didehydro-2',3'-dideoxynucleosides exhibit *anti*-conformation of the nucleobase – a finding which also holds for compounds **9a** and **9b**. Energy minimisation on **1b**, **2**, and **3** have, therefore, been made on model structures exhibiting this fixed glycosylic torsion angle.

Force-field calculations on 2',3'-dideoxy-3'-fluorotubercidin (**2**) show a 'normal' $^{2'}T_{3'}$ conformation of the furanose moiety (see **II** and *Table 5*).

Comparison of the tubercidin derivatives **1b**, **3**, and **2** with respect to sugar puckering reveals a transition from a $^{3'}T_{2'}$ conformation (**1b**; see **I**) *via* a planar furanose ring (**3**; see **III**) to a $^{2'}T_{3'}$ conformation (**2**; see **II**; *Table 5*). This probably influences the enzymatic phosphorylation to the corresponding 5'-triphosphates. Studies on chemical as well as enzymatic 5'-phosphorylation of the modified tubercidins are in progress.

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Experimental Part

General. TLC: silica gel *SIL G-25 UV$_{254}$* plates (*Macherey-Nagel & Co.*, Düren, FRG). Column chromatography (CC): silica gel *60* (*Merck*, FRG). Flash chromatography (FC): 0.5 bar; silica gel *60 H* (*Merck*, FRG). Ion-exchange chromatography: *Amberlite XAD-4*. Connection to *Uvicord S* detector with a *MultiRac* fractions collector (*LKB Instruments*, Bromma, Sweden). Solvent systems: *A* = AcOEt/light petroleum 1:4, *B* = AcOEt/light petroleum 2:3, *C* = $CHCl_3$/MeOH 95:5, *D* = $CHCl_3$/MeOH 4:1, *E* = $CHCl_3$/MeOH 7:3, *F* = i-PrOH/H_2O 1:9. M.p.: *Büchi-SMP-20* apparatus (*Büchi*, Switzerland); not corrected. UV spectra (λ_{max} (ε) in nm): *Hitachi-150-20* spectrophotometer (*Hitachi*, Japan). NMR spectra: at 25°; *AC-250* spectrometer equipped with an *Aspect 3000*

data system, an array processor, and a variable-temperature control unit *BVT 1000* (*Bruker*, FRG); operational frequencies 250.133 (^{1}H), 62.898 (^{13}C), and 235.362 (^{19}F); δ's rel. to Me_4Si as internal standard for ^{1}H and ^{13}C and rel. to $CFCl_3$ for ^{19}F (= 0 ppm); digital resolutions: 0.275 Hz/pt (^{1}H), 0.526 Hz/pt (^{13}C), 3.815 Hz/pt (^{19}F). The assignment of the J's of the H–C(2′) and H–C(3′) signals of **3** bases on selective homodecoupling experiments. NOE measurements: degassed (D_6)DMSO solns. (*ca.* 0.1M); typical spectral conditions: number of data points 32 K; pre-irradiation delay, 1.5 s; relaxation delay, 3 s; 90° pulse angle, 9.8 μs; number of cycles, 12; for all NOE measurements, the NOEDIFF mode of the *Bruker* software package (software release 1988) was used. Homonuclear correlation spectroscopy (^{1}H,^{1}H COSY): pulse sequence D_1-90°-D_0-90°-*FID* with a relaxation period D_1 of 1 s and an initial delay D_0 of 3 μs; 2048 data points and 512 data points in the t_2 and t_1 dimensions. 2D ^{1}H,^{13}C Correlation spectra: 2048 data points and 1024 data points in the t_2 and t_1 dimensions; pulse sequence for ^{1}H, D_0-90°-D_0-δ-D_0-D_3-90°-*BB*, for ^{13}C, D_1-180°-90°-D_4-*FID*; the delays were set to $D_0 = 3$ μs, $D_1 = 2.5$ μs, $D_3 = 0.00345$ s, and $D_4 = 0.5\ D_3$; after *Gauss*ian multiplication of the domain data and *Fourier* transformation, the coutour plots with a digital resolution of 2.9 Hz/pt were obtained. Force-field calculations were performed on an *IBM-AT* using the *Alchemy II* software package, release 1988 (*Tripos Associates, Inc.*, St. Louis). Minimisation of the potential energy of a constructed molecule was performed on a force-field equation and regards the five energy terms bond stretching, angle bending, torsion deformation, *van der Waals* interactions, and out-of-plane bending. Microanalyses were performed by *Mikroanalytisches Labor Beller*, Göttingen, FRG.

*4-Chloro-7-{2-deoxy-5-*O*-[(1,1-dimethylethyl)diphenylsilyl]-β-*D*-*erythro*-pentofuranosyl}-7*H*-pyrrolo[2,3-*d*]pyrimidine* (**6**). To a soln. of **5** (1.08 g, 4 mmol) in dry DMF (30 ml), imidazole (690 mg, 10.1 mmol) and (*t*-Bu)Ph_2SiCl (1.13 ml, 1.21 g, 4.4 mmol) were added. After stirring for 20 h at r.t. and evaporation of the solvent, imidazole was precipitated by addition of AcOEt and filtered off. To the filtrate, silica gel *60* (10 g) was added and the solvent evaporated. FC (6 × 20 cm, *A*) gave, from the main zone, **6** (1.54 g, 76%) as a colorless foam. TLC (*B*): R_f 0.6. UV (MeOH): 271 (4400). ^{1}H-NMR ((D_6)DMSO): 8.62 (*s*, H–C(2)); 7.81 (*d*, J = 3.8, H–C(6)); 7.60–7.57 (*m*, 4 H, Ph); 7.48–7.30 (*m*, 6 H, Ph); 6.65 (*t*, J = 6.6, H–C(1′)); 6.62 (*d*, J = 3.8, H–C(5)); 5.44 (*d*, J = 4.5, OH–C(3′)); 4.52 (*m*, H–C(3′)); 3.96 (*m*, J = 4.1, H–C(4′)); 3.81 (*m*, J(H–C(5′),H′–C(5′)) = −11, J(H–C(5′),H–C(4′)) = 4.9, 2 H–C(5′)); 2.64 (*m*, J(H–C(1′),H_β–C(2′)) = 6.6, J(H_β–C(2′),H_α–C(2′)) = −13.3, H_β–C(2′)); 2.36 (*m*, H_α–C(2′)); 0.97(*s*, *t*-Bu). Anal. calc. for $C_{27}H_{30}ClN_3O_3Si$ (508.1): C 63.83, H 5.95, N 8.27; found: C 63.86, H 5.96, N 8.27.

*4-Chloro-7-{2-deoxy-5-*O*-[(1,1-dimethylethyl)diphenylsilyl]-3-*O*-(methylsulfonyl)-β-*D*-erythro-pentofuranosyl}-7*H*-pyrrolo[2,3-*d*]pyrimidine* (**13**). To a soln. of **6** (1.54 g, 3.03 mmol) in CH_2Cl_2 (50 ml), pyridine (11.5 ml) and methanesulfonyl chloride (4.6 ml, 6.76 g, 60 mmol) were added. The mixture was stirred for 4 h at r.t. After addition of MeOH and stirring for another 15 min, the soln. was diluted with $CHCl_3$ (150 ml) and extracted with 0.1N HCl and H_2O (150 ml, each). After drying (Na_2SO_4), the org. layer was evaporated and the residue dissolved in AcOEt and adsorbed on silica gel *60* (10 g). CC (5 × 4 cm, *A*) gave, from the main zone, **13** (1.6 g, 90%) as a colorless oil. TLC (*A*): R_f 0.9. UV (MeOH): 271 (5050). ^{1}H-NMR ((D_6)DMSO): 8.60 (*s*, H–C(2)); 7.84 (*d*, J = 3.8, H–C(6)); 7.59 (*m*, 4 H, Ph); 7.40 (*m*, 6 H, Ph); 6.65 (*m*, H–C(5), H–C(1′)); 5.54 (*m*, H–C(3′)); 4.32 (*m*, H–C(4′)); 3.87 (*m*, 2 H–C(5′)); 3.17 (*s*, CH_3SO_2); 3.09 (*m*, H_β–C(2′)); 2.77 (*m*, H_α–C(2′)); 0.98 (*s*, *t*-Bu). Anal. calc. for $C_{28}H_{32}ClN_3O_5SSi$ (586.2): C 57.37, H 5.50, N 7.17; found: C 57.53, H 5.54, N 7.03.

*4-Chloro-7-{2-deoxy-5-*O*-[(1,1-dimethylethyl)diphenylsilyl]β-*D*-glycero-pentofuranos-3-ulosyl}-7*H*-pyrrolo[2,3-*d*]pyrimidine* (**7**). A soln. of **6** (508 mg, 1 mmol) in CH_2Cl_2 (2 ml) was added to a freshly prepared complex of CrO_3/pyridine/Ac_2O 1:2:1 (300 mg/0.5 ml/0.3 ml) in CH_2Cl_2 (7 ml). The mixture was stirred at r.t. for 1 h. Then, the dark-brown soln. was poured into 50 ml of supernatant AcOEt over a *ca.* 1-cm layer of silica gel *60* contained in a 4-cm-diameter chromatography column. After filtration through the support and washing with AcOEt, the filtrate was evaporated (< 25°) to give a colorless foam (380 mg, 75%) of 7. TLC (*A*): R_f 0.2. UV (MeOH): 272 (4550). ^{1}H-NMR ((D_6)DMSO): 8.59 (*s*, H–C(2)); 7.91 (*d*, J = 3.7, H–C(6)); 7.58–7.55 (*m*, 4 H, Ph); 7.44–7.25 (*m*, 6 H, Ph); 6.95 (*t*, J = 7.1, H–C(1′)); 6.67 (*d*, J = 3.7, H–C(5)); 4.42 (*m*, H–C(4′)); *ca.* 4.0 (*m*, 2 H–C(5′)); 3.23 (*dd*, J(H–C(1′),H–C(2′)) = 7.0, J(H–C(4′),H–C(2′)) = −1.8, 2 H–C(2′)); 0.94 (*s*, *t*-Bu). ^{1}H-NMR ($CDCl_3$): 8.60 (*s*, H–C(2)); 7.65–7.58 (*m*, 4 H, Ph); 7.53 (*d*, J = 3.8, H–C(6)); 7.43–7.29 (*m*, 6 H, Ph); 6.90 (*t*, J = 7.8, H–C(1′)); 6.54 (*d*, J = 3.8, H–C(5)); 4.24 (*m*, H–C(4′)); 4.03 (*m*, 2 H–C(5′)); 3.08 (*dd*, J(H–C(2′),H–C(1′)) = 6.6, J(H–C(2′),H′–C(2′)) = −18.3, 2 H–C(2′)); 1.05 (*s*, *t*-Bu).

*4-Chloro-7-{2-deoxy-5-*O*-[(1,1-dimethylethyl)diphenylsilyl]-β-*D*-threo-pentofuranosyl}-7*H*-pyrrolo[2,3-*d*]pyrimidine* (**8**). To a soln. of **7** (1 g, 1.98 mmol) in abs. EtOH (20 ml) at 0°, $NaBH_4$ (250 mg, 6.6 mmol) was added and stirred for 2.5 h at 0°. After addition of MeOH (5 ml) and stirring for 10 min at r.t., silica gel *60* (10 g) was added. After stirring for another 15 min at r.t., the solvent was evaporated and the material applied onto the top of a silica-gel *60* column. CC (20 × 4 cm, *C*) gave, from the main zone, **8** (760 mg, 76%) as a colorless oil. TLC (*C*): R_f 0.9. UV (MeOH): 270 (4800). ^{1}H-NMR ((D_6)DMSO): 8.66 (*s*, H–C(2)); 8.00 (*d*, J = 3.7, H–C(6)); 7.66–7.59 (*m*,

4 H, Ph); 7.46–7.25 (*m*, 6 H, Ph); 6.67 (*m*, H–C(5), H–C(1′)); 5.50 (*d*, J = 3.9, OH–C(3′)); 4.40 (*m*, J = 4.1, H–C(3′)); 4.18 (*m*, J = 3.6, H–C(4′)); 4.95 (*m*, 2 H–C(5′)); 2.83 (*m*, H_α–C(2′)); 2.16 (*d*, $J(H_\alpha$–C(2′), H_β–C(2′)) = −14.7, H_β–C(2′)); 0.96 (*s*, *t*-Bu). Anal. calc. for $C_{27}H_{30}ClN_3O_3Si$ (508.1): C 63.83, H 5.95, N 8.27; found: C 63.81, H 6.07, N 8.25.

*4-Chloro-7-(2-deoxy-β-*D-threo-*pentofuranosyl)-7*H-*pyrrolo[2,3-*d*]pyrimidine* (**9a**). To a soln. of **8** (450 mg, 0.89 mmol) in THF (10 ml), Bu_4NF (1M in THF; 8.8 ml) was added. After stirring for 30 min at r.t., the solvent was evaporated. CC (20 × 4 cm, *C*) gave, from the main zone, **9a** (220 mg, 92%) as colorless crystals. M.p. 161–163° (AcOEt). TLC (*C*): R_f 0.2. UV (MeOH): 273 (4500), 228 (26500). ^{1}H-NMR ((D$_6$)DMSO): 8.64 (*s*, H–C(2)); 8.10 (*d*, J = 3.7, H–C(6)); 6.69 (*d*, J = 3.7, H–C(5)); 6.61 (*m*, J = 7.4, H–C(1′)); 5.44 (*d*, J = 3.8, OH–C(3′)); 4.68 (*t*, J = 5.5, OH–C(5′)); 4.38 (*m*, J(H–C(4′), H–C(3′)) = 4.2, H–C(3′)); 3.94 (*m*, J(H–C(4′), H–C(3′)) = 4.2, H–C(4′)); 3.68 (*m*, J(OH–C(5′), H–C(5′)) = 5.5, J(H–C(5′), H′–C(5′)) = −11.1, 2 H–C(5′)); 2.80 (*m*, H_α–C(2′)); 2.15 (*d*, $J(H_\alpha$–C(2′), H_β–C(2′)) = −13.5, H_β–C(2′)). Anal. calc. for $C_{11}H_{12}ClN_3O_3$ (269.7): C 48.99, H 4.49, N 15.58; found: C 48.98, H 4.65, N 15.59.

*7-(2-Deoxy-β-*D-threo-*pentofuranosyl)-7*H-*pyrrolo[2,3-*d*]pyrimidin-4-amine* (**1b**). A soln. of **9a** (210 mg, 0.78 mmol) in conc. aq. NH_3 soln. (30 ml) was stirred for 15 h at 100° in a steel bomb, and the solvent was evaporated. CC (10 × 4 cm, *D*) gave, from the main zone, **1b** (180 mg, 92%) as colorless foam. TLC (*E*): R_f 0.8. UV (MeOH): 271 (12500). ^{1}H-NMR ((D$_6$)DMSO): 8.05 (*s*, H–C(2)); 7.47 (*d*, J = 3.6, H–C(6)); 7.06 (*s*, NH_2); 6.56 (*d*, J = 3.6, H–C(5)); 3.31 (*dd*, J(H–C(1′), H_β–C(2′)) = 3.0, J(H–C(1′), H_α–C(2′)) = 8.9, H–C(1′)); 5.99 (*d*, J = 5.6, OH–C(3′)); 4.66 (*t*, J = 5.6, OH–C(5′)); 4.30 (*m*, J(H–C(3′), H–C(4′)) = 3.5, H–C(3′)); 3.80 (*m*, H–C(4′)); 3.64 (*m*, J(H–C(5′), H–C(4′)) = 5.8, J(H–C(5′), H′–C(5′)) = −11.2, J(H–C(5′), OH–C(5′)) = 5.8, 2 H–C(5′)); 2.74 (*m*, H_α–C(2′)); 2.12 (*dd*, $J(H_\beta$–C(2′), H–C(1′)) = 3.0, $J(H_\beta$–C(2′), H_α–C(2′)) = −14.4, H_β–C(2′)). Anal. calc. for $C_{11}H_{14}N_4O_3$ (250.3): C 52.79, H 5.64, N 22.39; found: C 52.93, H 5.72, N 22.20.

*7-(2-Deoxy-β-*D-threo-*pentofuranosyl)-7*H-*pyrrolo[2,3-*d*]*pyrimidin-4(3*H*)-one* (**9b**). For 5 h, **9a** (160 mg, 0.59 mmol) was refluxed in 2N aq. NaOH, neutralized with 80% AcOH, and desalted by ion-exchange chromatography (25 × 2 cm). After washing with H_2O (500 ml), solvent *F* eluted one main zone from which **9b** (70 mg, 47%) was obtained as colorless needles. M.p. 219–222° (MeOH). TLC (*D*): R_f 0.6. UV (MeOH): 259.5 (9550), 275 (sh, 6800). ^{1}H-NMR ((D$_6$)DMSO): 12.0 (br. *s*, NH); 7.9 (*s*, H–C(2)); 7.52 (*d*, J = 3.6, H–C(6)); 6.49 (*d*, J = 3.6, H–C(5)); 6.38 (*dd*, J(H–C(1′), H_β–C(2′)) = 2.5, J(H–C(1′), H_α–C(2′)) = 8.6, H–C(1′)); 5.40 (*d*, J = 3.7, OH–C(3′)); 4.65 (br. *m*, OH–C(5′)); 4.33 (*m*, H–C(3′)); 3.84 (*m*, H–C(4′)); 3.65 (*m*, 2 H–C(5′)); 2.75 (*m*, H_α–C(2′)); 2.08 (*dd*, $J(H_\beta$–C(2′), H–C(1′)) = 2.5, $J(H_\beta$–C(2′), H_α–C(2′)) = −14.5, H_β–C(2′)). Anal. calc. for $C_{11}H_{13}N_3O_4$ (251.3): C 52.59, H 5.22, N 16.72; found: C 52.40, H 5.28, N 16.56.

*4-Chloro-7-(2,3-dideoxy-β-*D-glycero-*pent-2-enofuranosyl)-7*H-*pyrrolo[2,3-*d*]*pyrimidine* (**12a**). *From* **8**. To a soln. of **8** (470 mg, 0.93 mmol) in CH_2Cl_2 (18 ml), pyridine (3.5 ml) and mesyl chloride (1.4 ml, 2.06 g, 18 mmol) were added. After stirring for 4 h at r.t., MeOH (5 ml) was added and stirring continued for 30 min. The mixture was diluted with $CHCl_3$ (25 ml) and extracted with 0.1N HCl and H_2O. After drying (Na_2SO_4) and evaporation the red oil crystallized after a few min. The product was suspended in THF (10 ml) and Bu_4NF (1M in THF; 6 ml) added. After stirring for 1 h at r.t., the solvent was evaporated. CC (30 × 4 cm, *C*) gave, from the main zone, **11** (270 mg, 84%) as a colorless oil. TLC (*A*): R_f 0.2. ^{1}H-NMR ($CDCl_3$): 8.54 (*s*, H–C(2)); 7.55 (*d*, J = 3.7, H–C(6)); 6.67 (*dd*, J(H–C(1′), H_α–C(2′)) = 8.2, J(H–C(1′), H_β–C(2′)) = 3.5, H–C(1′)); 6.59 (*d*, J = 3.7, H–C(5)); 3.37 (*t*, J = 3.8, OH–C(5′)); 4.23 (*m*, H–C(3′)); *ca.* 3.9 (*m*, H–C(4′), 2 H–C(5′)); 3.09 (*s*, CH_3SO_3); *ca.* 2.9 (*m*, H_β–C(2′)); 2.65 (*m*, H_α–C(2′)).

Crude **11** (after evaporation of the solvent) was dissolved in THF (6 ml), and Bu_4NF (1M in THF, 10 ml) was added. The mixture was stirred for 18 h at r.t. and the solvent evaporated. CC (20 × 4 cm, *C*) gave, from the main zone, **12a** (100 mg, 43% rel. to **8**) as a colorless oil. TLC (*C*): R_f 0.6. UV (MeOH): 275 (4650). ^{1}H-NMR ((D$_6$)DMSO): 8.67 (*s*, H–C(2)); 7.80 (*d*, J = 3.8, H–C(6)); 7.27 (*m*, H–C(1′)); 6.67 (*d*, J = 3.8, H–C(5)); 6.50 (*ddd*, J(H–C(2′), H–C(3′)) ≈ 6, J(H–C(3′), H–C(4′)) ≈ 1.5, J(H–C(3′), H–C(1′)) ≈ −2, H–C(3′)); 6.09 (*ddd*, J(H–C(3′), H–C(2′)) ≈ 6, J(H–C(2′), H–C(1′)) ≈ 1.5, J(H–C(2′), H–C(4′)) ≈ −2, H–C(2′)); 4.88 (*m*, H–C(4′)); 4.10 (br. *s*, OH); 3.58 (*d*, J = 4.0, 2 H–C(5′)). Anal. calc. for $C_{11}H_{10}ClN_3O_2$ (251.7): C 52.50, H 4.01, N 16.70; found: C 52.74, H 4.20, N 16.53.

From **13**. To a soln. of **13** (1.26 g, 2.15 mmol) in THF (20 ml), Bu_4NF (1M in THF; 60 ml) was added. After stirring for 24 h at r.t., the mixture was evaporated to a syrup. CC (20 × 4 cm, *C*) gave **12a** (445 mg, 82%) as a colorless oil upon evaporation. All anal. data are consistent with those reported above.

*7-(2,3-Dideoxy-β-*D-glycero-*pent-2-enofuranosyl)-7*H-*pyrrolo[2,3-*d*]*pyrimidin-4-amine* (**3**). A soln. of **12a** (445 mg, 1.77 mmol) in 25% aq. NH_3 soln./methanolic ammonia 1:1 (60 ml) was stirred for 15 h at 100° in a steel bomb. After evaporation, the residue was flash chromatographed (30 × 6 cm, *D*). From the fastest migrating minor zone, **12b** (60 mg, 13.6%) was obtained as colorless oil. TLC (*D*): R_f 0.6. ^{1}H-NMR ((D$_6$)DMSO): 8.46 (*s*,

H–C(2)); 7.47 (*d*, J = 3.6, H–C(6)); 7.24 (*m*, H–C(1′)); 6.55 (*d*, J = 3.6, H–C(5)); 6.47 (*td*, J(H–C(2′), H–C(3′)) = 6, H–C(2′)); 6.07 (*d*, J(H–C(3′),H–C(2′)) = 6.0, H–C(3′)); 4.97 (*t*, J = 5.3, OH–C(5′)); 4.85 (*m*, H–C(4′)); 4.05 (*s*, CH_3O); 3.56 (*m*, 2 H–C(5′)).

From the main zone, **3** (185 mg, 45%) was obtained as a colorless foam. TLC (*D*): R_f 0.5. UV (MeOH): 270 (13200). ^{1}H-NMR ((D_6)DMSO): 8.07 (*s*, H–C(2)); 7.16 (*d*, J = 3.6, H–C(6)); 7.12 (*s*, H–C(1′)); 7.04 (br. *s*, NH_2); 6.57 (*d*, J = 3.6, H–C(5)); 6.43 (*m*, J(H–C(2′),H–C(3′)) = 6, H–C(2′)); 6.03 (*m*, J(H–C(3′),H–C(2′)) = 6, H–C(3′)); 4.98 (*t*, J = 5.5, OH–C(5′)); 4.80 (*m*, H–C(4′)); 3.53 (*m*, 2 H–C(5′)). Anal. calc. for $C_{11}H_{12}N_4O_2$ (232.246): C 56.89, H 5.21, N 24.12; found: C 56.81, H 5.33, N 24.05.

*7-(2,3-Dideoxy-β-*D*-*glycero*-pent-2-enofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidin-4(3*H*)-one* (**12c**). A soln. of **12a** (200 mg, 0.79 mmol) in 1,4-dioxane/2N aq. NaOH 1:1 (50 ml) was refluxed for 5 h. After neutralization with conc. AcOH, the solvent was evaporated and the residue desalted by ion-exchange chromatography (2 × 30 cm). After washing with H_2O, solvent *F* eluted one main peak from which **12c** (115 mg, 62%) was obtained upon evaporation of the solvent and subsequent coevaporation with Et_2O. TLC (*C*): R_f 0.15. UV (MeOH): 259 (9600), 278 (sh, 6100). ^{1}H-NMR ((D_6)DMSO): 7.95 (*s*, H–C(2)); 7.14 (*d*, J = 3.5, H–C(6)); 7.09 (*m*, H–C(1′)); 6.49 (*d*, J = 3.5, H–C(5)); 6.45 (*m*, J(H–C(2′),H–C(3′)) = 6.0, H–C(2′)); 6.04 (*m*, J(H–C(3′),H–C(2′)) = 6.0, H–C(3′)); 4.81 (*m*, H–C(4′)); 3.53 (*d*, J = 4.5, 2 H–C(5′)). Anal. calc. for $C_{11}H_{11}N_3O_3$ (233.2): C 56.65, H 4.75, N 18.02; found: C 56.55, H 4.82, N 18.18.

*4-Chloro-7-(2,3-dideoxy-3-fluoro-β-*D*-*erythro*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine* (**10b**). To a soln. of **8** (790 mg, 1.55 mmol) in toluene (25 ml), (diethylamino)sulfur trifluoride (840 µl, 6.4 mmol) was added. After stirring for 2 h at r.t., the soln. was poured into 5% aq. $NaHCO_3$ soln. (50 ml) and extracted twice with AcOEt (50 ml, each). After evaporation, the residue was filtered over silica gel *60* (4 × 5 cm, *A*). The UV-active fractions were evaporated to leave **10a** as a colorless foam. TLC (*A*): R_f 0.9. UV (MeOH): 272 (4600). ^{1}H-NMR ((D_6)DMSO): 8.60 (*s*, H–C(2)); 7.82 (*d*, J = 3.8, H–C(6)); 7.62–7.27 (2 *m*, 10 H, Ph); 6.64 (*m*, H–C(1′),H–C(5)); 5.52 (*dd*, J(H–C(3′),F–C(3′)) = 53.7, J(H–C(3′),H–C(2′)) = 4.5, H–C(3′)); 4.31 (*td*, J(H–C(4′),F–C(3′)) = 26.6, J(H–C(4′),H–C(5′)) = 5.3, H–C(4′)); 3.86 (*m*, 2 H–C(5′)); 3.02–2.59 (*m*, 2 H–C(2′)); 0.99 (*s*, *t*-Bu). ^{19}F-NMR ((D_6)DMSO): −178.4.

To the oily **10a** in THF (6 ml), Bu_4NF (1M in THF; 5 ml) was added. After stirring for 30 min at r.t., the solvent was evaporated. CC (4 × 30 cm, *C*) gave, from the main zone, **10b** (320 mg, 76%) as colorless oil. TLC (*C*): R_f 0.8. UV (MeOH): 272 (4600). ^{1}H-NMR ($CDCl_3$): 8.52 (*s*, H–C(2)); *ca.* 7.3 (H–C(6), superimposed by solvent); 6.54 (*d*, J = 3.7, H–C(5)); 6.27 (*dd*, J(H–C(1′),H_α–C(2′)) = 9.9, J(H–C(1′),H_β–C(2′)) = 5.4, H–C(1′)); 5.39 (*dd*, J(H–C(3′),F–C(3′)) = 53.7, J(H–C(3′),H–C(2′)) = 4.5, H–C(3′)); 5.10 (br. *s*, OH–C(5′)); 4.38 (*d*, J(H–C(4′),F–C(4′)) = 28.4, H–C(4′)); 3.93–3.75 (*m*, J(H–C(5′),H′–C(5)) = −15.3, 2 H–C(5′)); 3.14–2.87, 2.60–2.44 (2*m*, 2 H–C(2′)). ^{19}F-NMR ((D_6)DMSO): −177.3. Anal. calc. for $C_{11}H_{11}ClFN_3O_2$ (271.7): C 48.63, H 4.08, N 15.47; found: C 48.50, H 4.14, N 15.25.

*7-(2,3-Dideoxy-3-fluoro-β-*D*-*erythro*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidin-4-amine* (**2**). To a soln. of **10b** (370 mg, 1.36 mmol) in 1,4-dioxane (10 ml), 25% aq. NH_3 soln. (50 ml) was added and stirred at 100° for 15 h in an autoclave. After evaporation, the residue was dissolved in MeOH and flash chromatographed (10 × 5 cm, *C*). Evaporation of the main zone gave **2** (260 mg, 76%) as colorless foam. TLC (*C*): R_f 0.2. UV (MeOH): 270 (16650). ^{1}H-NMR ((D_6)DMSO): 8.06 (*s*, H–C(2)); 7.38 (*d*, J = 3.7, H–C(6)); 7.11 (*s*, NH_2); 6.60 (*d*, J = 3.7, H–C(5)); 6.49 (*dd*, J(H–C(1′),H_α–C(2′)) = 9.6, J(H–C(1′),H_β–C(2′)) = 5.4, H–C(1′)); 5.48 (*t*, J = 5.8, OH–C(5′)); 5.39 (*dd*, J(H–C(3′),F–C(3′)) = 53.1, J(H–C(3′),H–C(4′)) = 4.3, H–C(3′)); 4.18 (*t*, *d*, J(H–C(4′),F–C(4′)) = 27.6, J(H–C(4′),H–C(3′)) = 4.3, H–C(4′)); 3.58 (*m*, 2 H–C(5′)); 2.95–2.65, *ca.* 2.51 (*m*, 2 H–C(2′)). ^{19}F-NMR ((D_6)DMSO): −177.05. Anal. calc. for $C_{11}H_{13}FN_4O_2$ (252.3): C 52.38, H 5.19, N 22.21; found: C 52.69, H 5.15, N 22.03.

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