101. 3′-Substituted and 2′,3′-Unsaturated 7-Deazaguanine 2′,3′-Dideoxynucleosides: Syntheses and Inhibition of HIV-1 Reverse Transcriptase

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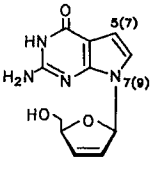
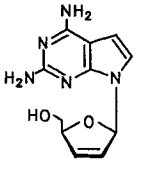
The syntheses of 2′,3′-dideoxy-2′,3′-didehydro-β-D-ribofuranoside **1** and 2′,3′-dideoxy-3′-fluoro-β-D-ribofuranoside **5** of 7-deazaguanine as well as 7-deaza-2′-deoxyxyloguanosine (**3**) are described. The corresponding 2,4-diamino compounds **2** and **4** were also prepared. Thus, silylation of 2-amino-4-chloro-7-(2-deoxy-β-D-*erythro*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (**6**) afforded **7**, which gave the oxo-nucleoside **13** after oxidation with CrO_3. $NaBH_4$ reduction yielded **14** which, upon deprotection (Bu_4NF) and nucleophilic displacement, afforded **3** and **4**. On the other hand, the N^2-formyl derivative of **7** was mesylated (→ **10**), treated with Bu_4NF, and deprotected with NH_3 yielding the 2′,3′-dideoxy-2′,3′-didehydro-nucleoside **12**. Nucleophilic displacement reactions on **12** yielded **1** and **2**. The fluoro-nucleoside **5** was obtained from **14** after methoxytritylation of the NH_2 group (→ **16**), fluorination with DAST (→ **17**), and treatment with 2M NaOH. The 5′-triphosphates of **5** and other pyrrolo[2,3-*d*]pyrimidine 2′,3′-dideoxy-3′-fluoro-nucleosides were found to be highly active inhibitors of HIV-1 reverse transcriptase, similar to those of **1** and **2**.

Purine and pyrimidine 2′,3′-dideoxyribonucleosides including those with a double bond between C(2′) and C(3′) or carrying an F-substituent at C(3′), with 3′,4′-*erythro*-configuration, show antiviral activity, in particular against retro viruses such as HIV-1 [1]. The activity is reduced, if the 3′-substituent is in *threo*-configuration [2]. On the other



1[a])



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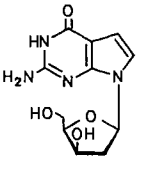

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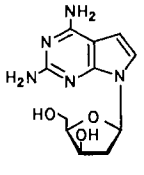

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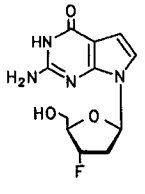

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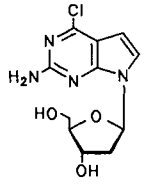

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a) Purine numbering in parentheses.

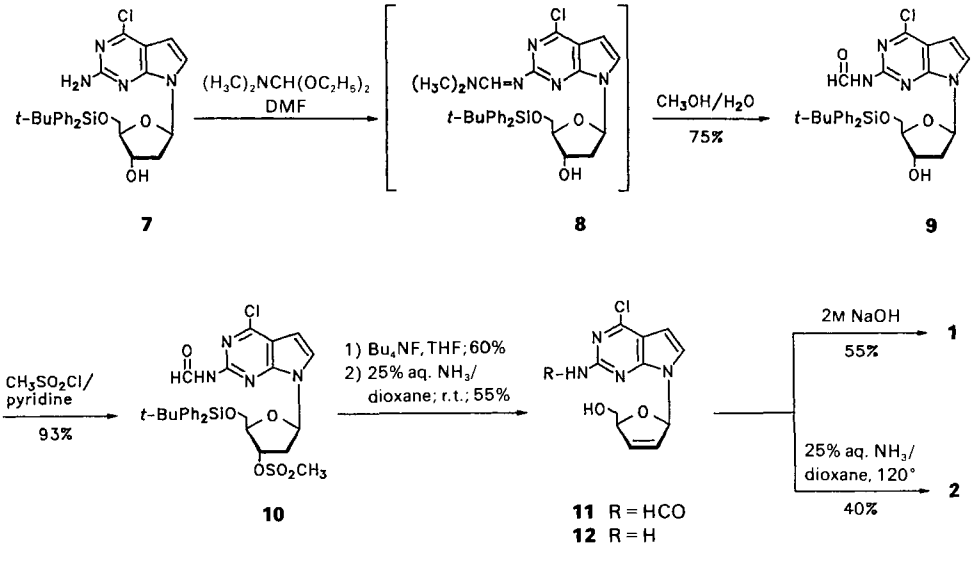
hand, 2′-deoxyxylonucleosides form unusual DNA structures, if they replace regular constituents [3].

In the following, we report on the synthesis of 7-deaza-2′,3′-dideoxy-2′,3′-didehydroguanosine (**1**) and 2-amino-7-deaza-2′,3′-dideoxy-2′,3′-didehydroadenosine (**2**) containing a pyrrolo[2,3-*d*]pyrimidine moiety instead of a purine system. Furthermore, the synthesis of the 2′-deoxyxylonucleosides **3** and **4** is described, from which the 2′,3′-dideoxy-3′-fluoro derivative **5** is prepared.

Results and Discussion. – Starting material for compounds **1–5** was 2-amino-4-chloropyrrolo[2,3-*d*]pyrimidine 2′-deoxy-β-D-ribofuranoside (**6**) [4] containing an aglycone which can be subjected to further transformations into 7-deazaguanine and 2-amino-7-deazaadenine derivatives. At first, the synthesis of the 2′,3′-dideoxy-2′,3′-didehydronucleosides **1** and **2** was carried out.

For this purpose, compound **6** [5] was protected at the 5′-position with the (*t*-Bu)Ph_2Si residue (→ **7**; *Scheme 1*). The formamidine residue was chosen for the protection of the 2-amino group. Condensation of **7** with dimethylformamide diethyl acetal gave one reaction product (TLC). However, upon chromatographic workup, an unexpected compound was formed, and according to the ^{1}H-NMR data, a mixture of amidine **8** and formyl derivative **9** was isolated (**9**: 9.4 (*d*, J = 13 Hz) and 11.1 ppm (*d*, J = 13 Hz); **8**: 3.0 and 3.1 (2 CH_3) and 8.6 ppm (*s*)). As the instability of **8** was a severe drawback for further transformations, it was subjected to hydrolysis (MeOH/H_2O) affording pure formyl compound **9** in 75% yield. Treatment of **9** with methanesulfonyl chloride gave mesylate **10**, which was purified chromatographically. Treatment of **10** with Bu_4NF afforded **11**, under removal of the silyl group and simultaneous elimination of the (methylsulfonyl)oxy group. Then, the formyl group was removed (aq. NH_3) to give compound **12**. Reaction of **12** with aq. NaOH at elevated temperature, which was

Scheme 1



allowed due to the stability of pyrrolo[2,3-*d*]pyrimidines towards strong bases as compared to purines, afforded crystalline **1**, and nucleophilic displacement with ammonia (pressure vessel) yielded **2**. Compound **2**, like the related 7-deazaadenine nucleosides, was resistant against deamination by adenosine deaminase.

Table 1. *^{13}C-NMR Chemical Shifts* ((D_6)DMSO, 23°) *of 4-Substituted 2-Aminopyrrolo[2,3-d]pyrimidine 2′,3′-Dideoxy-β-D-ribonucleosides and Related Compounds*

	C(2)	C(4)	C(4a)	C(5)	C(6)	C(7a)	CHO	CH_3O
1[a])	152.6	158.6	100.1	102.2	116.9	150.5	–	–
2[b])	160.2	158.0	96.3	100.3	117.2	152.7	–	–
3	152.4	158.6	99.8	101.8	118.3	150.2	–	–
4	159.6	157.9	96.3	99.4	119.3	151.7	–	–
5	152.8	158.7	100.2	102.7	116.8	150.9	–	–
6 [4]	159.2	151.1	108.9	99.6	122.9	153.6	–	–
7 [7]	159.4	151.1	108.8	99.8	122.6	153.7		–
9	151.9[c])	151.1[c])	113.9	100.1	126.8	151.6[c])	–	–
10	151.8[c])	151.3[c])	114.1	100.3	127.1	152.0[c])	–	–
11	151.6[c])	151.1[c])	113.8	99.9	126.9	152.0[c])	163.2	–
12	159.5	151.2	109.0	99.7	123.3	153.8	–	
14	159.4	151.1	108.9	99.4	124.4	153.6	–	–
15	159.2	151.0	108.7	99.3	124.3	153.5	–	–
16	157.3[c])	151.4[c])	109.0	98.7	124.2	150.0[c])	–	54.9
17	157.5[c])	152.0[c])	109.3	100.0	123.0	150.5[c])	–	55.0
18	159.6	151.4	108.9	100.3	122.6	154.1	–	–
19	159.5	151.1	108.9	100.2	123.0	154.1	–	–
c^7G_d [8]	152.5	158.5	100.1	102.1	116.7	150.5	–	–
c^7G [9]	152.6	158.7	100.2	102.3	117.3	151.2	–	–

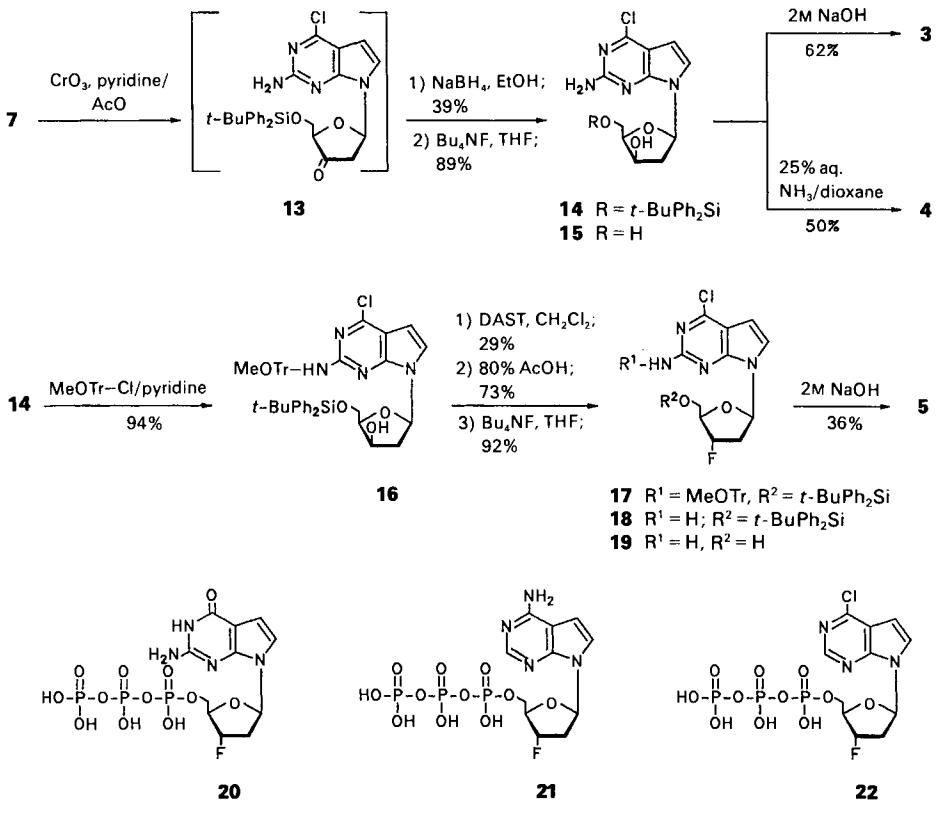
	C(1′)	C(2′)	C(3′)	C(4′)	C(5′)	$(CH_3)_3C$	$(CH_3)_3C$
1	87.4[c])	126.1	133.6	87.0[c])	63.6		–
2	87.4[c])	126.6	133.4	86.9[c])	63.9	–	–
3	81.3	[d])	69.7	84.0	59.9	–	–
4	82.0	[d])	69.3	83.7	60.0	–	–
5	82.3	37.0	95.2	84.5	61.2	–	–
6	82.4	39.2	70.8	87.1	61.8	–	–
7	82.1	39.3	70.3	86.3	64.2	26.6	18.8
9	83.0	[d])	70.1	86.6	64.2	26.6	18.8
10	83.3	[d])	80.1	83.9	63.3	26.6	18.7
11	87.9[c])	125.5	134.5	87.7[c])	62.9	–	–
12	87.6[c])	125.9	134.3	87.4[c])	63.3	–	–
14	81.9	[d])	69.2	84.4	63.5	26.7	18.9
15	81.4	[d])	69.0	84.4	59.9	–	–
16	82.4	[d])	68.9	84.6	63.3	26.6	18.7
17	83.0	40.0	94.3	84.0	63.6	26.7	18.9
18	82.4	36.6	94.4	84.0	63.6	26.7	18.9
19	82.5	36.8	95.2	84.7	61.1	–	–
c^7G_d [8]	82.2	39.5	70.84	86.9	61.9	–	–
c^7G [9]	86.1	73.7	70.6	84.6	61.8	–	–

[a]) Assigned according to the 2′,3′-dideoxynucleoside [6].
[b]) According to the 2′-deoxynucleoside [4].
[c]) Tentative assignment.
[d]) Superimposed by DMSO signals.

Table 1 summarizes the ^{13}C-NMR data of 2′,3′-dideoxy-2′,3′-didehydronucleosides and those of the precursor molecules. Assignment of the aglycone signals was established from already assigned 2′-deoxyribo- or 2′,3′-dideoxyribonucleosides [4–6]. Assignment of the sugar signals were based on already published chemical shifts for these moieties [7].

Compound **7** was also the synthetic precursor for pyrrolo[2,3-*d*]pyrimidine 2′-deoxyxylofuranosides. The epimerization at C(3′) of 2′-deoxyribofuranosides [10] [11] was considered for their preparation. It has been reported for pyrimidine 2′-deoxyribonucleosides that they can be converted into 2′,3′-dideoxy-3′-oxonucleosides [10] [11]. The latter were reduced stereoselectively into the 3′,4′-D-*threo*-compounds. However, in the case of purine 2′-deoxyribonucleosides, the 3′-oxo compounds are extremely unstable at the N-glycosylic bond. This did not allow to prepare purine 2′-deoxyxylonucleosides by this route so far. Only recently, purine 2′-deoxyribonucleosides have been converted into the D-*threo*-compounds using the *Dess-Martin 12-I-5 periodinane* reagent [12] instead of CrO_3 for oxidation. On the other hand, 2′-deoxyxylotubercidin, a purine-related nucleoside has already been prepared by a protocol using CrO_3, and the oxidation-reduction procedure yielded 90% [7]. Therefore, compound **7** was subjected to the same conditions, and *via* **13**, its D-*threo*-isomer **14** was obtained in 39% yield (*Scheme 2*). According to TLC,

Scheme 2



the D-*erythro*-compound **7** was also formed, the **14**/**7** ratio being 4.5:1. Such a non-stereoselective $NaBH_4$ reduction has already been reported in the case of pyrimidine nucleosides [11]. Apart from the nucleosides, the base of **14** was formed to a minor extent (*ca.* 10%), a process which occurred upon elimination [11]. Desilylation of **14** afforded **15**.

The D-*threo*-configuration of **15** was deduced from the order of its H–C(2') chemical shifts. Earlier assignments have shown that the H–C(2') signals change their chemical shifts upon epimerisation at C(3') [7]. In 2'-deoxy-β-D-ribonucleosides, H_β–C(2') appears downfield from H_α–C(2'), whereas in 2'-deoxy-β-D-xylonucleosides, the H_β–C(2') signal is shifted upfield compared to H_α–C(2'). As irradiation of H–C(1') resulted in an NOE (6.8%) on the low-field H–C(2') signal, it can be assigned to H_α–C(2'). Consequently, **15** must have the D-*threo*-configuration. No NOE was observed for H–C(3') indicating that the sugar moiety adopts the $^3T_2$-conformation, similarly to other 2'-deoxyxylonucleosides [7].

From compound **15**, 7-deaza-2'-deoxyxyloguanosine (**3**) as well as the corresponding diaminonucleoside **4** were obtained by nucleophilic displacement with either aq. NaOH or aq. NH_3 solution. The *Figure* shows the HPLC pattern of the 7-deaza-2'-deoxyxylonucleoside **3** and 2'-deoxyxylotubercidin (c^7xA_d) [3] in comparison to the corresponding 7-deaza-2'-deoxyribonucleosides on a reversed-phase resin; the 7-deaza-2'-deoxyxylonucleosides are well separated from the 7-deaza-2'-deoxyribo compounds, and the 7-deaza-2'-deoxyxylo compounds migrate slower than the parent 7-deaza-2'-deoxyribonucleosides. An opposite chromatographic behavior was found for xA_d compared to A_d [13]. The corresponding thymidine compounds are extremely difficult to separate [3].

The 2',3'-dideoxy-3'-fluoronucleosides exhibit antiviral activity. Therefore, the synthesis of **5** from **14** was considered. At first, the 2'-amino group was protected with a monomethoxytrityl residue (→ **16**; *Scheme 2*). Subsequently, the F-substituent was introduced with (diethylamino)sulfur trifluoride (DAST) under inversion of configuration (→ **17**) [14] [15]. AcOH/H_2O 8:2 removed the trityl residue (→ **18**), desilylation with Bu_4NF the silyl group (→ **19**) and treatment with 2M NaOH gave **5**. *Table 2* shows the

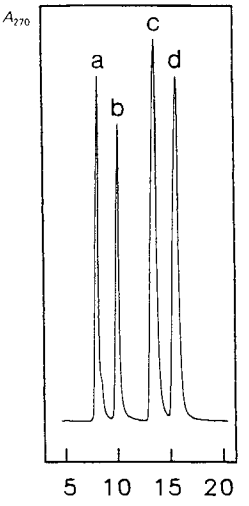


Figure. *HPLC profile of 2'-deoxynucleosides. a*) c^7G_d; *b*) c^7xG_d (**3**); *c*) c^7A_d; *d*) c^7xA_d. Absorbance at 270 nm *vs.* retention time [min]; column: 4 × 250 mm *RP-18 LiChrosorb* (*Merck*); solvents system: 0.1M $(Et_3NH)OAc$ (pH 7.0)/5% MeCN.

Table 2. *H,F- and C,F-Coupling Constants* [Hz] *for Compounds* **5** *and* **17–18**[a])

	J(F,H–C(3′))	J(F,H–C(4′))	J(F,C(2′))	J(F,C(3′))	J(F,C(4′))	J(F,C(5′))
5	53.9	27.9	20.4	173.3	22.2	11.6
17	53.9	27.0	21.0	175.7	24.4	10.9
18	54.0	27.1	21.0	174.5	23.8	11.3
19	53.8	27.4	20.3	173.3	22.3	11.1

[a]) Measured in DMSO at 23°.

H,F- as well as the F,C-coupling constants of the fluoro compounds. Assignment of the signals of the sugar moieties was made according to the literature [7].

Compared to the corresponding 2′,3′-dideoxynucleosides, the signals of C(2′), C(3′), and C(4′) of the 3′-fluoro compounds are shifted downfield, whereas those of C(1′) and C(5′) are shifted upfield. The strongest downfield shift (*ca.* 70 ppm) is observed for C(3′), with J(C,F) ≈ 175 Hz, confirming the location of the F-substituent. Small downfield shifts (C(2′): 5.5 ppm; C(4′): 3.8 ppm) are observed for the neighbouring C-atoms. On the other hand, C(1′) and C(5′) are shifted upfield by 0.7 ppm and 2.2 ppm, respectively. The 3′α-position of the F-substituent was deduced from *i*) the mechanism of the DAST reaction occurring under inversion of configuration [14], *ii*) an NOE of 3.8% H_β–C(3′) upon irradiation of CH_2(5′) in the case of the parent nucleoside triphosphate **22**, and *iii*) the ^1J(C,F) of 173.3–175.7 Hz being in the range of other 3′,4′-D-*erythro*-configurated 3′-fluoro-nucleosides [16]; D-*threo*-configurated compounds show values around 179 Hz.

In a recent study, we have shown that 7-deazapurine 2′,3′-dideoxyribonucleoside triphosphates are very effective inhibitors of HIV-1 reverse transcriptase [17]. The same was already shown for the triphosphates of **1** and **2** (*Table 3*). Therefore, it was concluded that N(7) is not required for the binding of $p_3A_{d_2^{2',3'}}$ (= ddATP) or $p_3G_{d_2^{2',3'}}$ (= ddGTP) on the active centre of the enzyme [17]. Otherwise N(1) is essential and cannot be replaced by a methine group [18]. As 3′-F substituents in the 3′,4′-D-*erythro*-configuration retain activity in case of the 3′-fluoro derivatives of A_{d_2} [16] or G_{d_2} [19], we expected the same for the corresponding pyrrolo[2,3-*d*]pyrimidine nucleotides **20** and **21**. Therefore, compound **5** was converted into its 5′-triphosphate by reaction with $POCl_3$ followed by condensation with tetrabutylammonium diphosphate according to *Ludwig* [20]. Then, the inhibitory data of fluoro-nucleoside triphosphates **20–22** as well as those of related 2′,3′-dideoxy-2′,3′-didehydronucleotides and parent purine compounds were determined. From the data summarized in *Table 3*, it can be concluded that the introduction of a 3′-F substituent retains inhibitor activity against HIV-1 reverse transcriptase in pyrrolo[2,3-*d*]-pyrimidine 2′,3′-dideoxyribonucleoside 5′-*O*-triphosphates such as **20** and **21**.

Table 3. *Inhibition of HIV-1 Reverse Transcriptase by 2′,3′-Dideoxy-*D*-ribonucleoside Triphosphates*[a])

	IC_{50} [μM]		IC_{50} [μM]
20	0.27	$p_3c^7G_{d_2^{2',3'}}en^{2'}$[b]) [17]	0.09
21	0.43	$p_3c^7A_{d_2^{2',3'}}en^{2'}$[b]) [17]	0.53
22	304.0	$p_3n^2c^7A_{d_2^{2',3'}}en^{2'}$[b]) [17]	0.39
AZTTP[b]) [17]	0.5	ddATP[b]) [17]	0.45
ddGTP[b]) [17]	0.2		

[a]) The RT inhibitory tests were performed in the Laboratories of the *Boehringer Mannheim GmbH*. A fragment of HIV-1 RNA together with an 18-meric primer and recombinant HIV-1 reverse transcriptase was used [17].

[b]) For abbreviations, see IUPAC-IUB conventions:
n = amino, az = azido, en = unsaturation, AZTTP = $p_3T_{d_2^{2',3'}az^{3'}}$, ddGTP = $p^3G_{d_2^{2',3'}}$, ddATP = $p_3A_{d_2^{2',3'}}$.

Recently, *Chu* and coworkers [21] [22] have suggested a stereochemical rational for the activity of anti-HIV nucleosides on the basis of single-crystal X-ray analysis data. It was proposed that an extreme *S*-type furanose conformation is typical for strong activity of nucleoside analogues against HIV. However, it is not clear, whether this phenomenon correlates with enzymic phosphorylation or/and inhibition of triphosphates on HIV reverse transcriptase.

In the case of a number of pyrrolo[2,3-*d*]pyrimidine 2′,3′-dideoxyribonucleosides, such as 2′,3′-dideoxy-3′-fluorotubercidin, *S*-type conformation was established from 1D NOE experiments [7]. The triphosphates of all those compounds are very strong inhibitors of HIV-1 reverse transcriptase. On the other hand, the *in vitro* activity against HIV-infected cells differs widely [13]. From these findings it is likely, if a correlation between the preferred *S*-type sugar pucker and antiviral activity exists, that it occurs on the stage of cellular 2′,3′-dideoxyribonucleoside phosphorylation.

We thank Mrs. *A. Röling* for the preparation of the triphosphates **21** and **22**, Dr. *H. Rosemeyer* for the NMR spectra, and Dr. *A. Mertens* and Dr. *B. König* from *Boehringer Mannheim GmbH* for the inhibitory tests on HIV-1 reverse transcriptase. Financial support by the *Bundesministerium für Forschung und Technologie* is greatfully acknowledged.

Experimental Part

General. See [17]. ^{19}F-NMR spectra: at 235.362 Hz; $CFCl_3$ as internal standard.

N-{*4-Chloro-7-{2-deoxy-5-O-[(1,1-dimethylethyl)diphenylsilyl]-β-*D-erythro-*pentofuranosyl}-7*H-*pyrrolo[2,3-*d*]*pyrimidin-2-yl}formamide* (**9**). To a soln. of **7** [5] (2.0 g, 3.8 mmol) in dry DMF (20 ml), *N,N*-dimethylformamide diethyl acetal (5 ml, 29 mmol) was added and the soln. stirred at 50° for 2 h. The solvent was evaporated, the residue redissolved in MeOH (100 ml) and triturated with H_2O (10 ml), the mixture heated at 60° for 48 h and then evaporated, and the residue applied to FC (column 4.5 cm × 24 cm, CH_2Cl_2/MeOH 98:2): colourless, amorphous **9** (1.6 g, 76%). TLC (silica gel, CH_2Cl_2/MeOH 95:5): R_f 0.37. UV (MeOH): 204 (36700), 244 (30700), 281 (7200), 295 (sh, 6900). ^{1}H-NMR ((D$_6$)DMSO): 0.98 (*s*, *t*-Bu); 2.32 (*m*, H$_\alpha$–C(2′)); 2.59 (*m*, H$_\beta$–C(2′)); 3.80 (*m*, CH_2(5′)); 3.93 (*m*, H–C(4′)); 4.50 (*m*, H–C(3′)); 5.42 (*d*, *J* = 4.2, OH–C(3′)); 6.53 (*m*, H–C(1′)); 6.54 (*d*, *J* = 4.0, H–C(5)); 7.39 (*m*, arom. H); 7.59 (*m*, arom. H, H–C(6)); 9.36 (*s*, NH); 11.06 (*s*, CHO). Anal. calc. for $C_{28}H_{31}ClN_4O_4Si$ (551.1): C 61.02, H 5.67, Cl 6.43, N 10.17; found: C 61.01, H 5.83, Cl 6.36, N 10.21.

N-{*4-Chloro-7-{2-deoxy-5-O-[(1,1-dimethylethyl)diphenylsilyl]-3-O-(methylsulfonyl)-β-*D-erythro-*pentofuranosyl}-7*H-*pyrrolo[2,3-*d*]*pyrimidin-2-yl}formamide* (**10**). To a soln. of **9** (2.0 g, 3.6 mmol) in pyridine (50 ml), methanesulfonyl chloride (0.8 ml, 11.0 mmol) was added dropwise at 0°. After stirring for 1 h at 0°, the soln. was stirred for additional 16 h at r.t. Then, H_2O was added (5 ml) and after 10 min CH_2Cl_2 (300 ml). The mixture was washed with 0.1M HCl and H_2O, dried (Na_2SO_4), and evaporated. The residue was purified by FC (column 4.5 cm × 30 cm, CH_2Cl_2/MeOH 97:3) yielding **10** (1.9 g, 83%) as colourless solid. TLC (silica gel, CH_2Cl_2/MeOH 95:5): R_f 0.6. UV (MeOH): 204 (37800), 244 (30800), 280 (7300), 296 (6800). ^{1}H-NMR ((D$_6$)DMSO): 0.97 (*s*, *t*-Bu); 2.74 (*m*, H$_\alpha$–C(2′)); 3.06 (*m*, H$_\beta$–C(2′)); 3.32 (*s*, $MeSO_2$); 3.79 (*dd*, *J* = 11.2; 5.3, 1 H, CH_2(5′)); 3.91 (*dd*, *J* = 11.2, 4.7, 1 H, CH_2(5′)); 4.28 (*m*, H–C(4′)); 5.50 (*m*, H–C(3′)); 6.55 (*m*, H–C(1′)); 6.58 (*d*, *J* = 3.9, H–C(5)); 7.40 (*m*, arom. H); 7.59 (*m*, arom. H, H–C(6)); 9.36 (*s*, NH); 11.07 (*s*, CHO). Anal. calc. for $C_{29}H_{33}ClN_4O_6SSi$ (629.2): C 55.36, H 5.29, Cl 5.63, N 8.90, S 5.10; found: C 55.47, H 5.21, Cl 5.72, N 8.99, S 5.12.

N-{*4-Chloro-7-(2,3-dideoxy-β-*D-glycero-*pent-2-enofuranosyl)-7*H-*pyrrolo[2,3-*d*]*pyrimidin-2-yl}formamide* (**11**). A soln. of **10** (1.9 g, 3.0 mmol) in 1M Bu_4NF in THF was heated at 60° for 24 h. The solvent was evaporated and the residue chromatographed on silica gel (column 4.5 cm × 24 cm, CH_2Cl_2/MeOH 98:2): foam which was crystallized from MeOH by the Et_2O diffusion method (0.54 g, 61%). M.p. 168°. TLC (silica gel, CH_2Cl_2/MeOH 95:5): R_f 0.34. UV (MeOH): 205 (20900), 243 (29900), 280 (7400), 296 (7000). ^{1}H-NMR ((D$_6$)DMSO): 3.58 (*t*, *J* = 4.5, CH_2(5′)); 4.87 (*s*, H–C(4′)); 4.94 (*t*, *J* = 5.3, OH–C(5′)); 6.09 (*d*, *J* = 5.6, 1 H, H–C(2′)); 6.50 (*d*, *J* = 5.6, 1 H, H–C(3′)); 6.60 (*d*, *J* = 3.8, H–C(5)); 7.17 (*m*, H–C(1′)); 7.60 (*d*, *J* = 3.8, H–C(6)); 9.42 (*d*, *J* = 9.8, NH); 11.09 (*d*, *J* = 9.8, CHO). Anal. calc. for $C_{12}H_{11}ClN_4O_3$ (294.7): C 48.91, H 3.76, Cl 12.03, N 19.01; found: C 49.03, H 3.80, Cl 12.05, N 18.99.

*2-Amino-4-chloro-7-(2,3-dideoxy-β-*D*-glycero-pent-2-enofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine* (**12**). A soln. of **11** (320 mg, 1.1 mmol) in 25% aq. NH_3/dioxane 5:3 (8 ml) was stirred at 50° for 48 h. After evaporation, the residue was chromatographed on silica gel (column 4 cm × 20 cm, CH_2Cl_2/MeOH 97:3). The material of the main zone was crystallized from MeOH: **12** (163 mg, 56%). M.p. 184°. TLC (silica gel, CH_2Cl_2/MeOH 95:5): R_f 0.42. UV (MeOH): 203 (17000), 235 (29500), 260 (5000), 317 (5900). ^{1}H-NMR ((D_6)DMSO): 3.52 (*t*, *J* = 4.8, CH_2(5′)); 4.80 (*m*, H–C(4′)); 4.90 (*t*, *J* = 5.4, OH–C(5′)); 6.03 (*d*, *J* = 5.9, H–C(2′)); 6.33 (*d*, *J* = 3.8, H–C(5)); 6.44 (*d*, *J* = 5.9, H–C(3′)); 6.72 (*s*, NH_2); 7.00 (*m*, H–C(1′)); 7.18 (*d*, *J* = 3.8, H–C(6)). Anal. calc. for $C_{11}H_{11}ClN_4O_2$ (266.7): C 49.54, H 4.16, Cl 13.29, N 21.01; found: C 49.45, H 4.15, Cl 13.38, N 21.01.

*2-Amino-7-(2,3-dideoxy-β-*D*-glycero-pent-2-enofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidin-4(3*H*)-one* (**1**). Compound **12** (110 mg, 0.41 mmol) in 2M aq. NaOH was heated at reflux for 5 h. After neutralization with AcOH and removal of insoluble material by filtration, the soln. was applied to an *Amberlite XAD-4* ion-exchange column. The column was washed with H_2O (1 l), and then compound **1** was eluted with H_2O/i-PrOH 9:1. After evaporation and crystallization from MeOH, yellowish crystals (57 mg, 56%) were obtained. M.p. 262° (dec.). TLC (silica gel, CH_2Cl_2/MeOH 9:1): R_f 0.42. UV (MeOH): 216 (24700), 259 (13900), 281 (sh, 8200). ^{1}H-NMR ((D_6)DMSO): 3.51 (*t*, *J* = 5.1, CH_2(5′)); 4.77 (*m*, H–C(4′)); 4.90 (*t*, *J* = 5.5, OH–C(5′)); 6.01 (*d*, *J* = 6.0, H–C(2′)); 6.27 (*d*, *J* = 3.6, H–C(5)); 6.28 (*s*, NH_2); 6.42 (*d*, *J* = 6.0, H–C(3′)); 6.73 (*d*, *J* = 3.6, H–C(6)); 6.90 (*m*, H–C(1′)); 10.39 (*s*, NH). Anal. calc. for $C_{11}H_{12}N_4O_3$ (248.2): C 53.22, H 4.87, N 22.57; found: C 53.20, H 4.95, N 22.54.

*2,4-Diamino-7-(2,3-dideoxy-β-*D*-glycero-pent-2-enofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine* (**2**). A soln. of **12** (270 mg, 1.0 mmol) in 25% aq. NH_3/dioxane 5:1 (60 ml) was stirred for 24 h at 120° in a steel bomb. After evaporation, the residue was redissolved in MeOH and adsorbed onto silica gel *60* (2 g). This material was placed on top of a silica-gel column (3 cm × 30 cm) and eluted with CH_2Cl_2/MeOH 9:1. Evaporation and crystallization from MeOH furnished yellowish crystals (100 mg, 40%). M.p. 193°. TLC (silica gel, CH_2Cl_2/MeOH 8:2): R_f 0.64. UV (MeOH): 222 (29500), 264 (11200), 286 (8700). ^{1}H-NMR ((D_6)DMSO): 3.50 (*t*, *J* = 5.1, CH_2(5′)); 4.74 (*m*, H–C(4′)); 4.98 (*t*, *J* = 5.4, OH–C(5′)); 5.57 (*s*, NH_2); 5.98 (*d*, *J* = 5.8, H–C(2′)); 6.36 (*d*, *J* = 3.6, H–C(5)); 6.38 (*d*, *J* = 5.8, H–C(3′)); 6.54 (*s*, NH_2); 6.71 (*d*, *J* = 3.6, H–C(6)); 6.93 (*m*, H–C(1′)). Anal. calc. for $C_{11}H_{13}N_5O_2$ (247.3): C 53.43, H 5.30, N 28.32; found: C 53.34, H 5.34, N 28.21.

*2-Amino-4-chloro-7-{2-deoxy-5-O-[(1,1-dimethylethyl)diphenylsilyl]-β-*D*-threo-pentofuranosyl}-7*H*-pyrrolo[2,3-*d*]pyrimidine* (**14**). Compound **7** [5] (520 mg, 1.0 mmol) was added to a freshly prepared complex of CrO_3/pyridin/Ac_2O 1:2:1 (300 mg/0.5 ml/0.3 ml) in anh. CH_2Cl_2 (7 ml). The mixture was stirred at r.t. for 45 min and then poured into 50 ml of supernatant AcOEt over a 1-cm layer of silica gel *60* in a 4-cm diameter chromatography column. The soln. was filtered through the support, the silica gel washed with AcOEt (100 ml), and the combined org. phase evaporated. The residue was coevaporated twice with toluene and the resulting yellowish foam (**13**) dissolved in anh. EtOH (16 ml). $NaBH_4$ (150 mg) was added and the mixture stirred at 0° for 2 h. After addition of MeOH (10 ml), stirring was continued until the end of gas evolution, the solvent was evaporated and the residue redissolved in AcOEt (100 ml). The org. layer was washed with 3M aq. NaCl containing 2% of AcOH, H_2O, and 5% aq. $NaHCO_3$ soln., dried (Na_2SO_4), and evaporated. The residue was purified by FC (column 4 cm × 27 cm, CH_2Cl_2/MeOH 98:2): **14** as colourless foam (180 mg, 35%). TLC (silica gel, CH_2Cl_2/MeOH 97:3): R_f 0.63. UV (MeOH): 203 (34300), 222 (25300), 235 (28100), 260 (4600), 317 (5600). ^{1}H-NMR ((D_6)DMSO): 0.97 (*s*, *t*-Bu); 2.05 (*d*, *J* = 15.8, H_β–C(2′)); 2.73 (*m*, H_α–C(2′)); 3.83 (*m*, 1 H, CH_2(5′)); 4.01 (*m*, 1 H, CH_2(5′)); 4.08 (*m*, H–C(4′)); 4.35 (*m*, H–C(3′)); 5.43 (*s*, OH–C(3′)); 6.32 (*d*, *J* = 3.8, H–C(5)); 6.38 (*m*, H–C(1′)); 6.70 (*s*, NH_2); 7.36 (*m*, arom. H); 7.46 (*d*, *J* = 3.8, H–C(6)); 7.63 (*m*, arom. H). Anal. calc. for $C_{27}H_{31}ClN_4O_3Si$ (523.1): C 61.99, H 5.97, N 10.71; found: C 61.87, H 6.03, N 10.62.

*2-Amino-4-chloro-7-(2-deoxy-β-*D*-threo-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine* (**15**). To a soln. of **14** (720 mg, 1.38 mmol) in THF (4 ml), 1M Bu_4NF in THF (4 ml) was added. After 30 min, the solvent was evaporated and the residue chromatographed on silica gel (column 4 cm × 23 cm, CH_2Cl_2/MeOH 95:5): **15** (350 mg, 89%) as colourless foam, which crystallized from MeOH as colourless crystals. M.p. 179° (dec.). TLC (silica gel, CH_2Cl_2/MeOH 9:1): R_f 0.67. UV (MeOH): 203 (11500), 235 (29300), 259 (4400), 317 (5900). ^{1}H-NMR ((D_6)DMSO): 2.08 (*d*, *J* = 14.6, H_β–C(2′)); 2.73 (*m*, H_α–C(2′)); 3.61 (*m*, 1 H, CH_2(5′)); 3.74 (*m*, 1 H, CH_2(5′)); 3.87 (*m*, H–C(4′)); 4.36 (*m*, H–C(3′)); 4.65 (*t*, *J* = 5.5, OH–C(5′)); 5.36 (*d*, *J* = 3.6, OH–C(3′)); 6.35 (*m*, H–C(1′)); 6.36 (*d*, *J* = 3.6, H–C(5)); 6.68 (*s*, NH_2); 7.55 (*d*, *J* = 3.6, H–C(6)). Anal. calc. for $C_{11}H_{13}ClN_4O_3$ (284.7): C 46.41, H 4.60, Cl 12.45, N 19.68; found: C 46.45, H 4.53, Cl 12.56, N 19.60.

*2-Amino-7-(2-deoxy-β-*D*-threo-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidin-4(3*H*)-one* (**3**). A soln. of **15** (120 mg, 0.42 mmol) in 2M aq. NaOH (20 ml) was heated at reflux for 5 h. The soln. was neutralized with AcOH, insoluble material removed by filtration, and the resulting clear soln. applied to an *Amberlite XAD-4* ion-exchange column. The column was washed with H_2O (0.5 l) and **3** eluted with H_2O/i-PrOH 9:1. Evaporation and crystallization from MeOH yielded colourless crystals. M.p. 231° (dec.). TLC (silica gel, CH_2Cl_2/MeOH 9:1): R_f 0.23. UV

(MeOH): 217 (21300), 259 (13200), 280 (sh, 8300). ^{1}H-NMR ((D$_6$)DMSO): 2.03 (*dd, J* = 14.3, 2.6, H$_\beta$–C(2′)); 2.67 (*ddd, J* = 14.3, 8.6, 5.8, H$_\alpha$–C(2′)); 3.58 (*m*, 1 H, CH$_2$(5′)); 3.72 (*m*, 1 H, CH$_2$(5′)); 3.79 (*m*, H–C(4′)); 4.31 (*m*, H–C(3′)); 4.61 (*t, J* = 5.5, OH–C(5′)); 5.33 (*d, J* = 4.2, OH–C(3′)); 6.16 (*m*, H–C(1′)); 6.21 (*s*, NH$_2$); 6.25 (*d, J* = 3.6, H–C(5)); 7.11 (*d, J* = 3.6, H–C(6)); 10.35 (*s*, NH). Anal. calc. for C$_{11}$H$_{14}$N$_4$O$_4$ (266.3): C 49.62, H 5.30, N 21.04; found: C 49.53, H 5.40, N 21.07.

*2,4-Diamino-7-(2-deoxy-β-*D-threo-*pentofuranosyl)-7*H-*pyrrolo[2,3-*d*]pyrimidine* (**4**). A soln. of **15** (200 mg, 0.7 mmol) in 25% aq. NH$_3$/dioxane 5:1 (60 ml) was stirred for 21 h at 110° in a steel bomb. After evaporation, the residue was redissolved in MeOH (50 ml), adsorbed on silica gel *60* (2.0 g), applied to the top of a silica-gel column (3 cm × 34 cm), and eluted with CH$_2$Cl$_2$/MeOH 8:2. Evaporation afforded pure **4** which gave colourless crystals from H$_2$O (93 mg, 50%). M.p. 256° (dec.). TLC (silica gel, CH$_2$Cl$_2$/MeOH 8:2): R_f 0.47. UV (MeOH): 221 (28000), 263 (10500), 285 (8400). ^{1}H-NMR ((D$_6$)DMSO): 2.08 (*dd, J* = 14.3, 3.1, H$_\beta$–C(2′)); 2.65 (*ddd, J* = 14.3, 8.8, 6.1, H$_\alpha$–C(2′)); 3.58 (*m*, 1 H, CH$_2$(5′)); 3.72 (*m*, 2 H, H–C(4′), CH$_2$(5′)); 4.26 (*m*, H–C(3′)); 4.60 (*m*, OH–C(5′)); 5.51 (*s*, NH$_2$); 6.01 (*m*, OH–C(3′)); 6.11 (*dd, J* = 8.8, 3.1, H–C(1′)); 6.34 (*d, J* = 3.6, H–C(5)); 6.58 (*s*, NH$_2$); 7.02 (*d, J* = 3.6, H–C(6)). Anal. calc. for C$_{11}$H$_{15}$N$_5$O$_3$ (265.3): C 49.81, H 5.70, N 26.40; found: C 49.74, H 5.80, N 26.40.

*4-Chloro-7-{2-deoxy-5-*O*-[(1,1-dimethylethyl)diphenylsilyl]-β-*D-threo-*pentofuranosyl}-2-{[(4-methoxytriphenyl)methyl]amino}-7*H-*pyrrolo[2,3-*d*]pyrimidine* (**16**). Compound **14** (1.56 g, 2.98 mmol) was dried by coevaporation with anh. pyridine and dissolved in the same solvent (10 ml). (i-Pr)$_2$EtN (2 ml, 12 mmol) and (4-methoxytriphenyl)methyl chloride (1.1 g, 3.56 mmol) were added, and the soln. was stirred for 3 h at r.t. The mixture was poured into 5% aq. NaHCO$_3$ soln. (100 ml) and extracted 3 times with CH$_2$Cl$_2$ (3 × 100 ml). The combined org. layers were dried (Na$_2$SO$_4$) and evaporated, and the residue purified by FC (column 5 cm × 30 cm, light petroleum ether/AcOEt 7:3): **16** as colourless foam (2.24 g, 94%). TLC (silica gel, light petroleum ether/AcOEt 7:3): R_f 0.71. UV (MeOH): 204 (85700), 238 (30800), 266 (sh, 11500), 317 (5800). ^{1}H-NMR ((D$_6$)DMSO): 0.99 (*s, t*-Bu); 1.64 (*d, J* = 14.7, H$_\alpha$–C(2′)); 2.34 (*m*, H$_\beta$–C(2′)); 3.68 (*s*, MeO); 3.81 (*dd, J* = 10.5, 7.1, 1 H, CH$_2$(5′)); 4.01 (*m*, 2 H, H–C(4′), CH$_2$(5′)); 4.22 (*m*, H–C(3′)); 5.18 (*d, J* = 3.1, OH–C(3′)); 5.76 (*m*, H–C(1′)); 6.24 (*d, J* = 3.8, H–C(5)); 6.81 (*m*, arom. H); 7.28 (*m*, arom. H, H–C(6)); 7.64 (*m*, arom. H); 7.85 (*s*, NH). Anal. calc. for C$_{47}$H$_{47}$ClN$_4$O$_4$Si (795.5): C 70.97, H 5.96, Cl 4.46, N 7.04; found: C 71.10, H 5.99, Cl 4.39, N 7.00.

*4-Chloro-7-{2,3-dideoxy-5-*O*-[(1,1-dimethylethyl)diphenylsilyl]-3-fluoro-β-*D-erythro-*pentofuranosyl}-2-{[(4-methoxytriphenyl)methyl]amino}-7*H-*pyrrolo[2,3-*d*]pyrimidine* (**17**). Compound **16** (800 mg, 1.0 mmol) was dried by coevaporation with pyridine and dissolved in anh. CH$_2$Cl$_2$ (10 ml). (Diethylamino)sulfur trifluoride (0.7 ml, 5.3 mmol) was added and the mixture stirred at r.t. After 15 min, 5% aq. NaHCO$_3$ soln. (50 ml) was added and the mixture extracted 3 times with CH$_2$Cl$_2$ (3 × 50 ml). The combined layers were dried (Na$_2$SO$_4$) and evaporated. The residue was applied to FC (silica gel, column 5 cm × 21 cm, light petroleum ether/AcOEt 9:1). Evaporation afforded **17** (230 mg, 29%). Colourless, amorphous foam. TLC (silica gel, light petroleum ether/AcOEt 8:2): R_f 0.83. UV (MeOH): 204 (85800), 237 (31000), 266 (sh, 11900), 318 (5500). ^{1}H-NMR ((D$_6$)DMSO): 1.01 (*s, t*-Bu); 2.17 (*m*, CH$_2$(2′)); 3.70 (*s*, MeO); 3.75 (*m*, CH$_2$(5′)); 4.16 (*dm, J* = 27.0, H–C(4′)); 5.26 (*dm, J* = 53.9, H–C(3′)); 5.84 (*m*, H–C(1′)); 6.29 (*d, J* = 3.8, H–C(5)); 6.80 (*m*, arom. H); 7.38 (*m*, arom. H, H–C(6)); 7.98 (*s*, NH). ^{19}F-NMR ((D$_6$)DMSO): −178.0. Anal. calc. for C$_{47}$H$_{46}$ClFN$_4$O$_3$Si (797.4): C 70.79, H 5.81, Cl 4.45, N 7.03; found: C 70.79, H 5.83, Cl 4.55, N 7.07.

*2-Amino-4-chloro-7-{2,3-dideoxy-5-*O*-[(1,1-dimethylethyl)diphenylsilyl]-3-fluoro-β-*D-erythro-*pentofuranosyl}-7*H-*pyrrolo[2,3-*d*]pyrimidine* (**18**). A soln. of **17** (500 mg, 0.63 mmol) in 80% aq. AcOH was stirred for 1 h at r.t. The solvent was evaporated, and traces of AcOH were removed by coevaporation with H$_2$O and toluene. The residue was applied to FC (silica gel, column 3 cm × 37 cm, CH$_2$Cl$_2$/MeOH 99:1): **18** as colourless, amorphous foam (240 mg, 73%). TLC (silica gel, CH$_2$Cl$_2$/MeOH 99:1): R_f 0.45. UV (MeOH): 203 (33300), 223 (25700), 234 (29200), 259 (5200), 317 (5600). ^{1}H-NMR ((D$_6$)DMSO): 1.01 (*s, t*-Bu); 2.61, 2.76 (2*m*, CH$_2$(2′)); 3.76 (*dd, J* = 11.4, 5.4, 1 H, CH$_2$(5′)); 3.83 (*dd, J* = 11.4, 5.6, 1 H, CH$_2$(5′)); 4.22 (*dt, J* = 27.1, 4.9, H–C(4′)); 5.47 (*dd, J* = 54.0, 3.8, H–C(3′)); 6.32 (*d, J* = 3.8, H–C(5)); 6.44 (*dd, J* = 9.0, 5.7, H–C(1′)); 6.78 (*s*, NH$_2$); 7.22 (*d, J* = 3.8, H–C(6)); 7.43 (*m*, arom. H); 7.65 (*m*, arom. H). ^{19}F-NMR ((D$_6$)DMSO): −178.0. Anal. calc. for C$_{27}$H$_{30}$ClFN$_4$O$_2$Si (525.1): C 61.76, H 5.76, Cl 6.75, N 10.67; found: C 61.92, H 5.87, Cl 6.89, N 10.70.

*2-Amino-4-chloro-7-(2,3-dideoxy-3-fluoro-β-*D-erythro-*pentofuranosyl)-7*H-*pyrrolo[2,3-*d*]pyrimidine* (**19**). A soln. of **18** (180 mg, 0.34 mmol) in THF (5 ml) was treated with 1M Bu$_4$NF in THF and stirred for 30 min at r.t. The solvent was evaporated and the residue applied to FC (silica gel, column 3 cm × 35 cm, CH$_2$Cl$_2$/MeOH 97:3). Evaporation and crystallization from H$_2$O yielded colourless crystals of **19** (90 mg, 92%). M.p. 108°. TLC (silica gel, CH$_2$Cl$_2$/MeOH 95:5): R_f 0.49. UV (MeOH): 203 (12700), 234 (28300), 259 (4400), 317 (5500). ^{1}H-NMR ((D$_6$)DMSO): 2.50, 2.77 (2*m*, CH$_2$(2′)); 3.55 (*m*, CH$_2$(5′)); 4.14 (*dt, J* = 27.4, 4.9, H–C(4′)); 5.13 (*t, J* = 5.4, OH–C(5′)); 5.37 (*dd, J* = 53.8, 4.0, H–C(3′)); 6.39 (*d, J* = 3.9, H–C(5)); 6.45 (*dd, J* = 9.4, 5.7, H–C(1′)); 6.77 (*s*,

NH_2); 7.42 (*d*, $J = 3.9$, H–C(6)). ^{19}F-NMR ((D$_6$)DMSO): −177.3. Anal. calc. for $C_{11}H_{12}ClFN_4O_2$ (286.7): C 46.08, H 4.22, N 19.54; found: C 46.26, H 4.30, N 19.45.

*2-Amino-7-(2,3-dideoxy-3-fluoro-β-*D*-*erythro*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidin-4(3*H*)-one* (**5**). A soln. of **19** (100 mg, 0.35 mmol) in 2M aq. NaOH (20 ml) was heated at reflux for 2 h. H_2O (50 ml) was added and the soln. neutralized by addition of *Dowex 50 W × 4-400* ion-exchange resin (H^+ form). The resin was removed by filtration and washed with H_2O, the filtrate evaporated, and the residue redissolved in MeOH and adsorbed to silica gel *60*. This material was applied to a silica-gel column (3 cm × 32 cm) and eluted with CH_2Cl_2/MeOH 9:1. Evaporation of the first zone and crystallization from H_2O yielded **5** (33 mg, 35%). Colourless needles. M.p. 257° (dec.). TLC (silica gel, CH_2Cl_2/MeOH 9:1): R_f 0.49. UV (MeOH): 215 (21600), 259 (13400), 279 (sh, 8100). ^{1}H-NMR ((D$_6$)DMSO): 2.50 (CH_2(2′), superimposed by DMSO), 3.53 (*m*, CH_2(5′)); 4.10 (*dt*, $J = 27.9$, 4.9, H–C(4′)); 5.12 (*t*, $J = 5.5$, OH–C(5′)); 5.34 (*dd*, $J = 53.9$, 4.4, H–C(3′)); 6.28 (*s*, NH_2); 6.29 (*d*, $J = 3.7$, H–C(5)); 6.33 (*dd*, $J = 9.6$, 5.5, H–C(1′)); 6.98 (*d*, $J = 3.7$, H–C(6)); 10.40 (*s*, NH). ^{19}F-NMR ((D$_6$)DMSO): −177.1.

From the second zone, **7** (20 mg, 23%) was isolated.

*2-Amino-7-(2,3-dideoxy-3-fluoro-β-*D*-*erythro*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidin-4(3*H*)-one Triethylammonium 5′-Triphosphate* (**20**·4 Et_3N). Phosphorylation of **5** (13 mg, 48 μmol) was carried out as described [17]. After ion-exchange column chromatography, **20**·4 Et_3N (131 A_{259} units, 10%) and the corresponding monophosphate (380 A_{259} units, 29%) were isolated. Compound **20**·4 Et_3N was purified by HPLC (*RP-18*, column 4 × 25 mm, 5% MeCN in 0.1M (Et_3NH)OAc, pH 7.0) yielding a colourless solid. ^{31}P-NMR (H_2O/D_2O 1:1, pH 8.0, 0.1M EDTA): −8.61 (*d*, $J = 19$, P(γ)); −10.65 (*d*, $J = 19$, P(α)); −21.97 (*t*, $J = 19$, P(β)).

*4-Amino-7-(2,3-dideoxy-3-fluoro-β-*D*-*erythro*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine Triethylammonium 5′-Triphosphate* (**21**·4 Et_3N). As described for **20**·4 Et_3N, 4-amino-7-(2,3-dideoxy-3-fluoro-β-D-*erythro*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine [7] (25 mg, 0.1 mmol) was phosphorylated. After chromatographical workup, **21**·4 Et_3N (244 A_{270} units, 20%) was isolated as colourless solid. ^{31}P-NMR (H_2O/D_2O 1:1, pH 8.0, 0.1M EDTA): −6.60 (*d*, $J = 19$, P(γ)); −10.66 (*d*, $J = 19$, P(α)); −21.71 (*t*, $J = 19$, P(β)).

*4-Chloro-7-(2,3-dideoxy-3-fluoro-β-*D*-*erythro*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine Triethylammonium 5′-Triphosphate* (**22**·4 Et_3N). As described for **20**·4 Et_3N, 4-chloro-7-(2,3-dideoxy-3-fluoro-β-D-*erythro*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine [7] (27 mg, 0.1 mmol) was phosphorylated. Compound **22**·4 Et_3N (216 A_{272} units, 47%) was isolated as colourless solid. ^{31}P-NMR (H_2O/D_2O 1:1, pH 8.0, 0.1M EDTA): −6.80 (*d*, $J = 19$, P(γ)); −10.52 (*d*, $J = 19$, P(α)); −21.46 (*t*, $J = 19$, P(β)).

REFERENCES

[1] M. Nasr, C. Litterst, J. McGovan, *Antiviral Res.* **1990,** *14,* 125.
[2] E. De Clercq, A. van Aerschot, D. Herdewijn, M. Baba, R. Pauwels, J. Balzarini, *Nucleos. Nucleot.* **1989,** *8,* 659.
[3] H. Rosemeyer, F. Seela, *Helv. Chim. Acta* **1991,** *74,* 748.
[4] F. Seela, H. Steker, H. Driller, U. Bindig, *Liebigs Ann. Chem.* **1987,** 15.
[5] F. Seela, H.-P. Muth, *Liebigs Ann. Chem.* **1990,** 227.
[6] F. Seela, H.-P. Muth, *Liebigs Ann. Chem.* **1988,** 215.
[7] H. Rosemeyer, F. Seela, *Helv. Chim. Acta* **1989,** *72,* 1084.
[8] H.D. Winkeler, F. Seela, *J. Org. Chem.* **1983,** *48,* 3119.
[9] F. Seela, T. Soulimane, K. Mersmann, T. Jürgens, *Helv. Chim. Acta* **1990,** *73,* 1879.
[10] F. Hansske, M.J. Robins, *Tetrahedron Lett.* **1983,** *24,* 1589.
[11] F. Hansske, D. Madej, M.J. Robins, *Tetrahedron* **1984,** *40,* 125.
[12] V. Samano, M.J. Robins, *J. Org. Chem.* **1990,** *55,* 5186.
[13] F. Seela, unpublished data.
[14] W.J. Middleton, *J. Org. Chem.* **1975,** *40,* 574.
[15] P. Herdewijn, A. Van Aerschot, L. Kerremans, *Nucleos. Nucleot.* **1989,** *8,* 65.
[16] P. Herdewijn, R. Pauwels, M. Baba, J. Balzarini, E. De Clercq, *J. Med. Chem.* **1987,** *30,* 2131.
[17] F. Seela, H.-P. Muth, A. Röling, *Helv. Chim. Acta* **1991,** *74,* 554.
[18] F. Seela, R. Gumbiowski, *Helv. Chim. Acta* **1991,** *74,* 1048.
[19] J. Balzarini, M. Baba, R. Pauwels, P. Herdewijn, S.G. Wood, M.J. Robins, E. De Clercq, *J. Mol. Pharmacol.* **1988,** *33,* 243.
[20] J. Ludwig, *Acta Biochem. Biophys. Acad. Sci. Hung.* **1981,** *16,* 131.
[21] P. Van Roey, J.M. Salerno, C.K. Chu, R.F. Schinazi, *Proc. Natl. Acad. Sci. U.S.A.* **1989,** *86,* 3929.
[22] E.W. Taylor, P. Van Roey, R.F. Schinazi, C.K. Chu, *Antiviral Chem. Chemother.* **1990,** *1,* 163.