Synthesis of 6-Substituted 7-Carbapurine 2′,3′-Dideoxynucleosides: Solid-Liquid Phase-Transfer Glycosylation of 4-Chloropyrrolo[2,3-*d*]pyrimidine and Deoxygenation of its 2′-Deoxyribofuranoside

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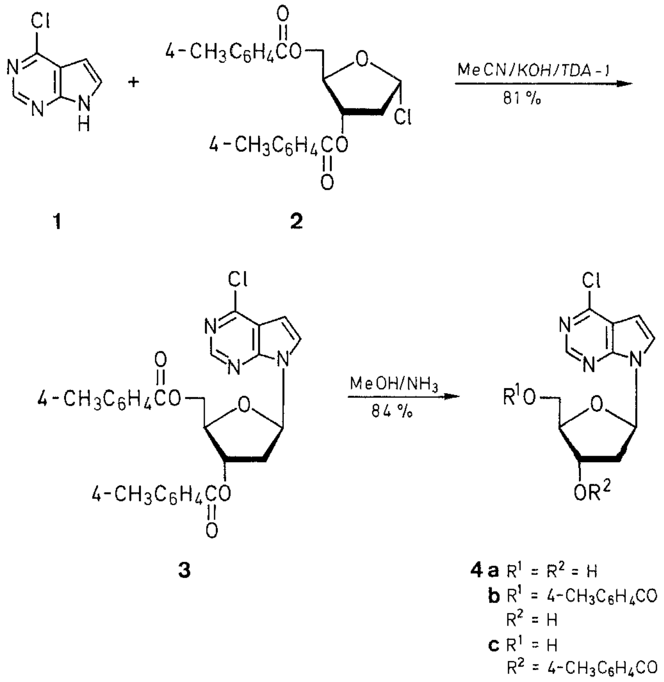
Several 4-substituted pyrrolo[2,3-*d*]pyrimidine 2′,3′-dideoxyribofuranosides including 2′,3′-dideoxytubercidin (**10**) and 2′,3′-dideoxy-7-carbainosine (**12**) are prepared from 4-chloro-7-(2,3-dideoxy-β-D-glycero-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (**8**). Compound **8** is obtained from the corresponding 4-chloro-7-(2-deoxy-β-D-erythro-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (**4a**) via Barton-deoxygenation. Its protected precursor **3** is accessible in 81 % yield by solid-liquid phase-transfer glycosylation.

2′,3′-Dideoxyribonucleoside triphosphates can act as terminators of DNA-polymerases including reverse transcriptase.[1-4] According to these properties several purine and pyrimidine 2′,3′-dideoxyribofuranosides show antiviral activity against human immunodeficiency virus (HIV).[5-6] Moreover, they are used as chain terminators during sequencing of DNA.[7-8] The severe toxicological problems associated with the common 2′,3′-dideoxynucleosides[6] have directed our interest towards the synthesis of base-modified compounds.

The 7-carba anologue of 2′,3′-dideoxyadenosine has been prepared by multistep transformation from the naturally occuring riboside tubercidin.[9-10] We have synthesized the 7-carba analogue of 2′,3′-dideoxyguanosine.[11] Both syntheses suffer from the problem that only one particular dideoxynucleoside is accessible. The need of a more general route leading to a whole group of 2′,3′-dideoxynucleosides with the same nucleobase but different substituents at a particular position required a 2′,3′-dideoxyribofuranoside with a readily displacable substituent at the nucleobase.

In the following we report on the synthesis of various 4-substituted pyrrolo[2,3-*d*]pyrimidine 2′,3′-dideoxyribofuranosides derived from the versatile intermediate **8**. Moreover, we describe its formation from the 2′-deoxynucleoside **4a**, obtained by the solid-liquid phase-transfer glycosylation.

The 4-chloro substituent of pyrrolo[2,3-*d*]pyrimidines is much more stable during chemical manipulation than that of the corresponding 6-chloro purines but can be displaced by strong nucleophiles. Compound **4a** was the molecule of choice for the synthesis of 4-substituted pyrrolo[2,3-*d*]pyrimidine 2′,3′-dideoxyribonucleosides including 2′,3′-dideoxytubercidin and 7-carba-2′,3′-dideoxyinosine, respectively.[12] Its protected precursor **3** has been already described by Robins and co-workers and was obtained in 71 % yield using the halogenose **2** and sodium hydride as condensation reagent.[13] The reaction was carried out under nitrogen, required elevated temperature and a reaction time of 2 hours. We have applied phase-transfer conditions for glycosylation of 4-chloropyrrolo[2,3-*d*]pyrimidine (**1**) with the halogenose **2** in acetonitrile with an excess of powdered potassium hydroxide and the cryptand Tris-[2-(2-methoxyethoxy) ethyl]amine (TDA-1) as catalyst.[14] This reaction is complete within 15 minutes at room temperature, does not require inert conditions and gives crystalline **3** in 81 % yield. No α-nucleoside is formed. Glycosylation under liquid-liquid conditions (50 % aqueous sodium hydroxide/dichloromethane) in the presence of tetrabutylammonium hydrogen sulfate gave only 63 % yield.[14] Solid-liquid glycosylation was also successful with powered potassium hydroxide in acetonitrile even in absence of the phase-transfer catalyst TDA-1. In that case the reaction proceeded with 70 % yield, which was lower than under TDA-1 catalysis (81 %) but the same as in case of the sodium hydride mediated reaction.[13] This result clearly indicates that complexation of the cation by the cryptand makes the nucleobase anion more nucleophilic which reduces reaction time and possible side reactions.



In the next step the protecting groups of **3** were removed. All attempts to achieve that with sodium methoxide in methanol failed, as the halogen was displaced by the methoxy group. Brief treatment with methanolic ammonia (6 h) removed the toluoyl groups only partially but without preference to the 3′- or the 5′-position. From the reaction mixture compounds **4b** and **4c** were obtained after chromatographic work-up. Structure determination of the partially deprotected molecules was made on the basis of their ^{13}C-NMR spectra (Table 1). Deprotection at the 3′-position of compound **3** shifts C-3′ upfield and C-2′ as well as C-1′ downfield (compound **4b**). Deprotection of the 5′-position results in an upfield shift of C-5′ and smaller downfield shift for the other carbons (compound **4c**).

Complete removal of the protecting groups was accomplished by prolonged treatment (48 h) of **3** with methanolic ammonia in

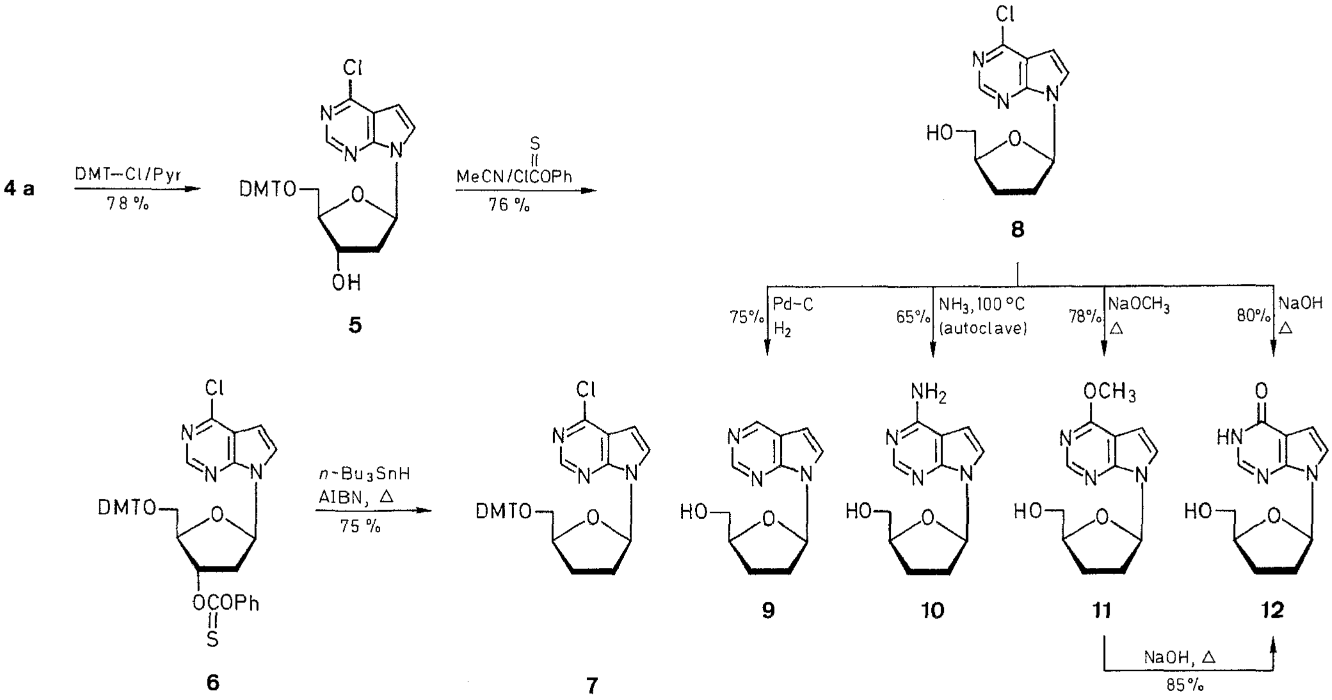


Table 1. ^{13}C-NMR Chemical Shifts of Pyrrolo[2,3-*d*]pyrimidine 2′-deoxy- and 2′,3′-dideoxyribofuranosides[a]

	C-2	C-4	C-4a	C-5	C-6	C-7a	OCH_3	C-1′	C-2′	C-3′	C-4′	C-5′	CH_3	C=S
1	150.0	150.4	116.6	98.9	128.3	151.8	–	–	–	–	–	–	–	–
3	150.7	151.0	117.7	100.2	128.7	151.1	–	81.5	36.1	75.0	84.0	64.2	21.3	–
4a	150.5	150.8	117.4	99.7	128.5	150.6	–	83.4	39.9	70.9	87.7	61.8	–	–
4b	150.7	150.8	117.5	100.0	128.6	150.9	–	83.5	39.0	70.6	84.0	64.4	21.3	–
4c	150.7	150.9	117.5	100.1	128.5	150.9	–	83.6	37.3	75.9	85.1	61.7	21.3	–
5	150.6[b]	150.9[b]	117.6	99.7	128.7	150.7[b]	–	83.7	–[c]	70.7	85.7	64.2	55.1	–
6	150.7[b]	151.1[b]	117.8	100.1	128.8	150.9[b]	–	84.2	36.0	82.8	84.7	64.0	55.1	193.7
7	150.5[b]	150.8[b]	117.4	99.3	128.4	150.5[b]	–	84.4	31.3	26.4	79.8	65.4	55.1	–
8	150.4	150.7	117.3	99.3	128.5	150.3	–	84.2	32.0	25.9	81.6	62.9	–	–
9	150.9	149.5	119.0	100.1	127.4	149.9	–	83.4	31.7	26.3	81.1	63.2	–	–
10	151.7	157.5	102.8	99.6	121.3	149.6	–	83.7	31.6	26.5	80.6	63.5	–	–
11	150.6	162.3	105.0	98.5	124.4	151.2	53.5	83.9	31.9	26.2	81.1	63.2	–	–
12	143.7	158.3	108.2	102.3	120.6	147.0	–	83.8	32.1	26.3	81.1	63.2	–	–

[a] Measured in DMSO-d_6 relative to TMS.
[b] Tentative assignment.
[c] Superimposed by DMSO signals.

a pressure bottle yielding crystalline **4a**[15] in 84% yield. The ^{13}C-NMR chemical shifts of compound **4a** were assigned on the basis of proton-coupled spectra (Table 2).

It has been shown that the phenoxythiocarbonyl group is a useful residue to be employed during Barton-deoxygenation.[11,16–18] Therefore, we have protected compound **4a** with 4,4′-dimethoxytriphenylmethyl chloride (DMT-Cl) selectively at the 5′-position and obtained **5**. Regioselective 5′-protection was confirmed on the basis of C-4′, C-5′-shifts in the ^{13}C-NMR spectrum (table 1). Compound **5** was then reacted with *O*-phenyl carbonochloridothioate to yield **6**. Treatment of the latter with tri-*n*-butylstannane in toluene at 75 °C afforded **7** in 75% yield. No side reaction affecting the 4-chloro substituent was observed. The DMT-residue was removed with acetic acid to give **8**. Compounds **5**, **6**, and **7** were obtained amorphous but ^{1}H- and ^{13}C-NMR spectra (Table 1) as well as elemental analyses confirmed their structure. The dideoxynucleoside **8** was obtained crystalline.

Several nucleophilic displacement reactions were then carried out at the 4-chloropyrrolo[2,3-*d*]pyrimidine dideoxyribofuranoside **8**. Reaction with sodium methoxide gave **11**, which could be further converted into the dideoxyinosine derivative **12** by

Table 2. *J*(C,H)-Coupling Constants (Hz) for Compounds **1**, **4a**, **8**, **9**[a]

J(C,H)		**1**	**4a**	**8**	**9**
C(2),	H–C (2)	207.6	209.1	208.9	202.9
	H–C (4)	–	–	–	10.9
C(4),	H–C (4)	–	–	–	181.6
	H–C (2)	14.7	m[b]	13.1	10.2
C(4a),	H–C (5)	7.6	7.8	8.6	m[b]
	H–C (6)	4.2	4.0	4.2	m[b]
	H–C (1′)	–	0.9	1.0	m[b]
C(5),	H–C (5)	180.1	181.5	181.5	178.3
	H–C (6)	7.7	7.1	7.2	6.8
C(6),	H–C (6)	188.5	190.9	190.7	188.9
	H–C (5)	7.5	8.0	8.0	8.4
	H–C (1′)	–	4.5	4.4	4.5
C(7a)		m[b,c]	m[b,c]	m[b,c]	m[b,c]

[a] Spectra measured in DMSO-d_6.
[b] Unresolved multiplet.
[c] Typical for 7a-carbon in pyrrolo[2,3-*d*]pyrimidines.

treatment with sodium hydroxide. Compound **12** was also obtained directly from **8** after heating with aqueous sodium hydroxide in 80 % yield. Introduction of the amino group at the 4-position was carried out by heating with ammonia in a steel bomb to give 2′,3′-dideoxytubercidin (**10**), which has been already obtained from the naturally occuring ribofuranoside by multistep conversion.[9,10] The chloro substituent of **8** was also removed by catalytic hydrogenation in the presence of 10% palladium on charcoal to yield **9**, a strongly fluorescent molecule.

As it can be seen from Table 1, the dideoxynucleoside **8–12** show very similar ^{13}C-NMR chemical shifts of the signals of their sugar moieties. As the assignment of this part of the molecule has been already accomplished on the basis of a [^1H, ^{13}C] shift correlation spectrum[11] assignment of compounds **8–12** was unequivocal. In all cases where the assignments of the aglycones were uncertain, proton-coupled spectra were measured and coupling constants were determined (Table 2), which were then used for the assignments of the compounds given in Table 1.

Compounds **8–12** are much more stable against proton-catalyzed hydrolysis at their *N*-glycosylic bond than corresponding purine 2′,3′-dideoxynucleosides. With respect to degradation by cellular enzymes it was observed that compound **10** is almost completely resistant against deamination by adenosine deaminase, which deaminates 2′,3′-dideoxyadenosine rapidly.

Elemental analyses were performed by Mikroanalytisches Laboratorium Beller (Göttingen, W. Germany). UV spectra were measured on a U-3200 spectrophotometer (Hitachi, Japan). ^1H-NMR spectra were recorded at 250 MHz and ^{13}C-NMR spectra at 62.9 MHz on a Bruker AC 250 spectrometer, chemical shifts are in δ with TMS as standard. TLC was carried out on silica gel SIL G-25 UV_{254} plates (Machery & Nagel, W. Germany), flash chromatography was carried out on silica gel 60 H (Merck, W. Germany). The columns were connected to a Uvicord S detector and an UltroRac II fraction collector (LKB Instruments, Sweden). Melting points were determined on a Linström apparatus, (Wagner & Munz, W. Germany) and are not corrected.

Pyridine and MeCN were distilled over CaH_2. TDA-1, tri-*n*-butylstannane and *O*-phenyl carbonochloridothioate are commercially available.

4-Chloro-7-(2-deoxy-3,5-di-*O*-(*p*-toluoyl)-*β*-D-erythro-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (3):

a) *By solid-liquid phase-transfer glycosylation:* To a stirred suspension of powdered KOH (1.0 g, 17.8 mmol) in dry MeCN (60 mL) is added TDA (100 μL, 0.31 mmol) at room temperature. After 5 min compound **1**[19,20] (1.23 g, 8.01 mmol) is added to the mixture and stirring is continued for another 5 min. Then the halogenose **2**[21] (3.2 g, 8.25 mmol) is added, and stirred for 15 min. The unsoluble material is removed by filtration and washed with MeCN. The filtrate is evaporated to dryness and the residue is chromatographed on a silica gel column (5 × 7 cm, $CHCl_3$). Evaporation of the eluate yields a colorless solid which crystallizes from EtOH in colorless needles; yield: 3.26 g (81 %); mp 120 °C (Lit.[13] mp 118 °C); $R_f = 0.7$ (cyclohexane/EtOAc, 3:2).

UV (MeOH): $\lambda_{max} = 226$ (log $\varepsilon = 4.61$), 240 (4.48), 270 nm (sh, 3.84).

^1H-NMR (DMSO-d_6): $\delta = 2.37, 2.40$ (s, 6 H, 2 × CH_3); 2.77 (m, 1 H, 2′-H_b); 3.18 (m, 1 H, 2′-H_a); 4.60 (m, 3 H, 4′-H + 5′-H); 5.77 (m, 1 H, 3′-H); 6.75 (d, 1 H, $J = 3.7$ Hz, 5-H); 6.78 (m, 1 H, 1′-H); 7.34, 7.91 (m, 9 H, 8 H_{arom} + 6-H); 8.65 (s, 1 H, 2-H).

b) *By solid-liquid glycosylation in the absence of a catalyst:* The reaction is carried out as described before, but omitting TDA-1. After work-up compound **3** is isolated; yield: 2.82 g (70 %).

c) *By liquid-liquid phase-transfer glycosylation:* Compound **1** (500 mg, 3.26 mmol) is dissolved in CH_2Cl_2 (20 mL) and added to 50 % aq. NaOH (9 mL). After addition of Bu_4NHSO_4 (10 mg, 0.03 mmol) the solution is stirred with a vibromixer for 1 min. Compound **2** (1.4 g, 3.61 mmol) is added and vibromixing is continued for 3 min. Subsequently, phases are separated and the water layer is extracted with CH_2Cl_2 (2 × 25 mL). The combined organic phase is dried (Na_2SO_4) and evaporated to dryness. The residue is chromatographed on a silica gel column (5 × 5 cm, $CHCl_3$). Isolation of the material of the main zone and crystallization from EtOH gives colorless needles of **3**; yield: 1.04 g (63 %); mp 180 °C (Lit.[13] mp 118 °C).

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

A solution of **3** (2.4 g, 4.7 mmol) in MeOH (100 mL, saturated with NH_3 at 0 °C) is stirred for 24 h at room temperature. The solution is evaporated to dryness, the residue adsorbed on silica gel 60 (10 g) and applied to the top of a silica gel column (4 × 10 cm, $CHCl_3$/MeOH, 95:5). From the main zone compound **4a** is isolated as a colorless solid, which is crystallized from EtOAc as colorless needles; yield: 1.07 g (84 %); mp 162 °C (Lit.[15] mp 162-163 °C); $R_f = 0.6$ ($CHCl_3$/MeOH, 9:1).

UV (MeOH): $\lambda_{max} = 224$ (log $\varepsilon = 4.42$), 273 nm (3.66).

^1H-NMR (DMSO-d_6): $\delta = 2.28$ (m, 1 H, 2′-Hb); 2.58 (m, 1 H, 2′-Ha); 3.57 (m, 2 H, 5′-H); 3.87 (m, 1 H, 4′-H); 4.40 (m, 1 H, 3′-H); 5.00 (t, 1 H, $J = 5.4$ Hz, 5′-OH); 5.35 (d, 1 H, $J = 4.2$ Hz, 3′-OH); 6.66 (m, 1 H, 1′-H); 6.72 (d, 1 H, $J = 3.8$ Hz, 5-H); 7.99 (d, 1 H, $J = 3.8$ Hz, 6-H); 8.66 (s, 1 H, 2-H).

4-Chloro(2-deoxy-5-*O*-(*p*-toluoyl)-*β*-D-*erythro*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (4b) and 4-chloro-(2-deoxy-3-*O*-(*p*-toluoyl)-*β*-D-*erythro*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]-pyrimidine (4c):

Compound **3** (2.4 g, 4.7 mmol) is treated as described for the preparation of **4a**, but the reaction is stopped after 6 h. The mixture is separated on a silica gel column (2 × 10 cm, $CHCl_3$/MeOH, 95:5). Beside the starting material **3** [fast migrating zone A; yield: 248 mg (10 %)] and fully deprotected **4a** [slow migrating zone D; yield: 331.7 mg (26 %)], the isomer **4c** (zone B) is isolated as colorless foam; yield: 437.9 mg (24 %); $R_f = 0.9$ ($CHCl_3$/MeOH, 9:1).

UV (MeOH): $\lambda_{max} = 223$ (log $\varepsilon = 4.45$), 269 nm (3.69).

^1H-NMR (DMSO-d_6): $\delta = 2.41$ (s, 3 H, CH_3); 2.65 (m, 1 H, 2′-H_b); 2.92 (m, 1 H, 2′-H_a); 2.70 (m, 2 H, 5′-H); 4.24 (m, 1 H, 4′-H); 5.25 (t, 1 H, $J = 5.5$ Hz, OH); 5.61 (m, 1 H, 3′-H); 6.77 (m, 2 H, 5-H, 1′-H); 7.37, 7.94 (m, 4 H_{arom}); 8.08 (d, 1 H, $J = 3.8$ Hz, 6-H); 8.69 (s, 1 H, 2-H).

Zone C contains the colorless amorphous isomer **4b**; yield: 418.5 mg (23 %); $R_f = 0.7$ ($CHCl_3$/MeOH).

$C_{19}H_{18}ClN_3O_4$	calc.	C 58.85	H 4.68	Cl 9.14	N 10.84
(387.8)	found	58.93	4.77	9.41	10.70

UV (MeOH): $\lambda_{max} = 225$ (log $\varepsilon = 4.46$), 270 nm (3.76).

^1H-NMR (DMSO-d_6): $\delta = 2.37$ (s, 3 H, CH_3); 2.42 (m, 1 H, 2′-H_b); 2.76 (m, 1 H, 2′-H_a); 4.14 (m, 1 H, 4′-H); 4.56 (m, 3 H, 3′-H + 5′-H); 5.60 (d, 1 H, $J = 4.4$ Hz, OH); 6.68 (m, 2 H; 5-H + 1′-H); 7.30, 7.81 (m, 4 H_{arom}); 7.90 (d, 1 H, $J = 3.8$ Hz, 6-H); 8.65 (s, 1 H, 2-H).

4-Chloro-7-(2-deoxy-*β*-D-*erythro*-pentofuranosyl-5′-*O*-(4,4′-dimethoxytrityl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (5):

Compound **4a** (1.0 g, 3.7 mmol) is dried by coevaporation with dry pyridine (10 mL). The material is dissolved in dry pyridine (20 mL), *N*,*N*-diisopropylethylamine (2 mL, 11.7 mmol) and 4,4′-dimethoxytrityl chloride (2.0 g, 5.9 mmol) are added. The solution is stirred for 3 h at room temperature. After addition of 5% aq. $NaHCO_3$ (80 mL) the resultant mixture is extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layer is dried (Na_2SO_4), filtered and the solvent evaporated. The residue is applied to a silica gel column (12 × 3 cm, CH_2Cl_2 and CH_2Cl_2/EtOAc, 9:1 as eluents). Isolation of the material of the main zone yielded yellowish amorphous **5**, which was dissolved in ether and precipitated in petroleum ether; yield: 1.66 g (78 %); $R_f = 0.3$ (CH_2Cl_2/acetone, 9:1).

$C_{32}H_{30}ClN_3O_5$	calc.	C 67.19	H 5.29	Cl 6.20	N 7.35
(572.1)	found	67.03	5.47	6.19	7.29.

UV (MeOH): $\lambda_{max} = 226$ (log $\varepsilon = 4.63$), 274 nm (3.85).

^1H-NMR (DMSO-d_6): $\delta = 2.36$ (m, 1 H, 2′-H_b); 2.70 (m, 1 H, 2′-H_a); 3.72 (s, 6 H, 2 × OCH_3); 3.18 (d, 2 H, $J = 4.5$ Hz, 5′-H); 3.99 (m, 1 H, 4′-H); 4.45 (m, 1 H, 3′-H); 5.42 (d, 1 H, $J = 4.6$ Hz, OH); 6.65 (m, 1 H, 1′-H); 6.69 (d, 1 H, $J = 3.7$ Hz, 5-H); 6.82, 7.22, 7.34 (m, 13 H_{arom}); 7.81 (d, 1 H, $J = 3.7$ Hz, 6-H), 8.64 (s, 1 H, 2-H).

4-Chloro-7-(2-deoxy-β-D-*erythro*-pentofuranosyl)-5'-*O*-(4,4'-dimethoxytrityl)-3'-*O*-phenoxythiocarbonyl-7*H*-pyrrolo[2,3-*d*]pyrimidine (6):

To a solution of **5** (1.0 g, 1.7 mmol) in dry MeCN (30 mL), 4-dimethylaminopyridine (500 mg, 4.1 mmol) and *O*-phenylcarbonochloridothioate (400 µL, 2.9 mmol) are added and the solution is stirred at room temperature for 16 h. Subsequently the mixture is evaporated to dryness and the residue applied to a silica gel column (3 × 15 cm, CH_2Cl_2). From the main zone colorless, amorphous **6** is isolated; yield: 950 mg (76 %); R_f = 0.8 (CH_2Cl_2/acetone, 95:5).

$C_{39}H_{34}ClN_3O_6S$	calc.	C 66.14	H 4.84	Cl 5.01	N 5.93	S 4.53
(708.2)	found	66.22	4.94	5.12	5.93	4.46

UV (MeOH): λ_{max} = 225 (log ε = 4.17), 274 nm (3.87).

^{1}H-NMR (DMSO-d_6): δ = 2.84 (m, 1 H, 2'-H_b); 3.21 (m, 1 H, 2'-H_a); 3.37 (m, 2 H, 5'-H); 3.72 (s, 6 H, 2 × OCH_3); 4.46 (m, 1 H, 4'-H); 5.92 (m, 1 H, 3'-H); 6.70 (m, 1 H, 1'-H); 6.76 (d, 1 H, J = 3.8 Hz, 5-H); 6.82, 7.24, 7.37, 7.49 (m, 18 H_{arom}); 7.85 (d, 1 H, J = 3.8 Hz, 6-H); 8.61 (s, 1 H, 2-H).

4-Chloro-7-(2,3-dideoxy-β-D-*glycero*-pentofuranosyl)-5'-*O*-(4,4'-dimethoxytrityl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (7):

To a stirred solution of **6** (800 mg, 1.1 mmol) and 2,2'-azobis(2-methyl)propionitrile (AIBN; 40 mg, 0.2 mmol) in dry toluene (40 mL), is added *n*-Bu_3SnH (600 µL, 2.2 mmol) under an Ar atmosphere and the reaction is continued at 75 °C for 2 h. The solvent is evaporated and the residue is chromatographed on a silica gel column (15 × 3 cm, CH_2Cl_2/EtOAc, 95:5). From the main zone colorless amorphous **7** is isolated; yield: 470 mg (75 %); R_f = 0.5 (CH_2Cl_2/acetone, 95:5).

$C_{32}H_{30}ClN_3O_4$	calc.	C 69.12	H 5.44	Cl 6.38	N 7.56
(556.1)	found	69.07	5.53	6.33	7.58

UV (MeOH): λ_{max} = 226 (log ε = 4.62), 273 nm (3.78).

^{1}H-NMR (DMSO-d_6): δ = 2.08 (m, 2 H, 3'-H); 2.10 (m, 1 H, 2'-H_b); 2.43 (m, 1 H, 2'-H_a); 3.11 (d, 2 H, J = 4.4 Hz, 5'-H); 3.71 (s, 6 H, 2 × OCH_3), 4.27 (m, 1 H, 4'-H); 6.55 (dd, 1 H, J = 3.6, 6.9 Hz, 1'-H); 6.64 (d, 1 H, J = 3.7 Hz, 5-H); 6.78, 7.18, 7.30 (m, 13 H_{arom}); 7.83 (d, 1 H, J = 3.7 Hz, 6-H); 8.67 (s, 1 H, 2-H).

4-Chloro-7-(2,3-dideoxy-β-D-*glycero*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]-pyrimidine (8):

A solution of **7** (400 mg, 0.7 mmol) in 80 % aq. AcOH (15 mL) is stirred at room temperature for 30 min. The solvent is evaporated and traces of AcOH are removed by coevaporation with H_2O. The residue is chromatographed on a silica gel column (3 × 15 cm, CH_2Cl_2 and CH_2Cl_2/MeOH, 98:2). From the main zone compound **8** is obtained after crystallization from EtOAc as colorless needles; yield: 120 mg (67 %); mp 90 °C; R_f = 0.5 (CH_2Cl_2/MeOH, 95:5).

$C_{11}H_{12}ClN_3O_2$	calc.	C 52.08	H 4.77	Cl 13.98	N 16.56
(253.7)	found	52.20	4.81	14.04	16.54

UV (MeOH): λ_{max} = 225 (log ε = 4.43), 274 nm (3.65).

^{1}H-NMR (DMSO-d_6): δ = 2.04 (m, 2 H, 3'-H); 2.28 (m, 1 H, 2'-H_b); 2.46 (m, 1 H, 2'-H_a); 3.57 (m, 2 H, 5'-H); 4.11 (m, 1 H, 4'-H); 4.95 (t, 1 H, J = 5.5 Hz, OH); 6.52 (dd, 1 H, J = 3.8, 6.9 Hz, 1'-H); 6.69 (d, 1 H, J = 3.8 Hz, 5-H); 8.01 (d, 1 H, J = 3.8 Hz, 6-H); 8.64 (s, 1 H, 2-H).

7-(2,3-Dideoxy-β-D-*glycero*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]-pyrimidine (9):

A solution of compound **8** (200 mg, 0.8 mmol) in MeOH (20 mL), containing conc. aq. NH_3 (0.5 mL, 6.6 mmol) and Pd/C (40 mg, 10 %) is stirred in an H_2 atmosphere at room temperature for 3 h. The catalyst is removed by filtration and the solvent is evaporated. The residue is dissolved in H_2O and chromatographed on an amberlite XAD-4 resin (columns 2 × 24 cm, 1. eluent H_2O; 2. eluent H_2O/MeOH (8:2). Isolation of the material of the main zone yields colorless needles upon evaporation; yield: 130 mg (75 %); mp 131 °C; R_f = 0.6 (CH_2Cl_2/MeOH, 9:1).

$C_{11}H_{13}N_3O_2$	calc.	C 60.26	H 5.98	N 19.17
(219.3)	found	60.19	5.97	19.18

UV (MeOH): λ_{max} = 222 (log ε = 4.44), 270 nm (3.56).

^{1}H-NMR (DMSO-d_6): δ = 2.06 (m, 2 H, 3'-H); 2.27 (m, 1 H, 2'-H_b); 2.42 (m, 1 H, 2'-H_a); 3.55 (m, 2 H, 5'-H); 4.09 (m, 1 H, 4'-H); 4.93 (t, 1 H, J = 5.5 Hz, OH); 6.54 (dd, 1 H, J = 4.3, 6.9 Hz, 1'-H); 6.67 (d, 1 H, J = 3.7 Hz, 5-H); 7.86 (d, 1 H, J = 3.7 Hz, 6-H); 8.79 (s, 1 H, 4-H); 9.01 (s, 1 H, 2-H).

4-Amino-7-(2,3-dideoxy-β-D-*glycero*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (2',3'-dideoxytubercidin, 10):

A suspension of **8** (200 mg, 0.8 mmol) in 25 % aq. NH_3 (60 mL) is stirred for 15 h at 100 °C under pressure in a steel bomb. Subsequently the solvent is evaporated and the residue redissolved in H_2O (200 mL) and applied to a Dowex 1 × 2 resin (column 3 × 18 cm, OH^-). The column is washed with water and compound **10** eluted with H_2O/MeOH (9:1). Evaporation of the main zone yields a colorless foam; yield: 120 mg (65 %); R_f = 0.3 (CH_2Cl_2/MeOH, 9:1).

^{1}H-NMR (DMSO-d_6): δ = 2.03 (m, 2 H, 3'-H); 2.22 (m, 1 H, 2'-H_a); 2.33 (m, 1 H, 2'-H_b); 3.53 (m, 2 H, 5'-H); 4.04 (m, 1 H, 4'-H); 4.99 (m, 1 H, OH); 6.35 (m, 1 H, 1'-H); 6.51 (d, 1 H, J = 3.6 Hz, 5-H); 7.00 (s, 2 H, NH_2); 7.34 (d, 1 H, J = 3.6 Hz, 6-H); 8.04 (s, 1 H, 2-H). (Lit.[9,10]).

7-(2,3-Dideoxy-β-D-*glycero*-pentofuranosyl)-4-methoxy-7*H*-pyrrolo[2,3-*d*]pyrimidine (11):

A solution of **8** (170 mg, 0.7 mmol) in 1 M NaOMe in MeOH (5 mL) is stirred at room temperature for 4 h. The solution is neutralized with 80 % aq. AcOH, evaporated and the residue applied to a silica gel column (3 × 20 cm, CH_2Cl_2/MeOH, 98:2). Isolation of the material of the main zone yields a colorless oil, which crystallizes on keeping in needles; yield: 130 mg (78 %); R_f = 0.8 (CH_2Cl_2/MeOH, 9:1).

$C_{12}H_{15}N_3O_3$	calc.	C 57.82	H 6.07	N 16.86
(249.3)	found	57.63	6.07	16.86

UV (MeOH): λ_{max} = 217 (log ε = 4.30), 261 nm (3.86).

^{1}H-NMR (DMSO-d_6): δ = 2.04 (m, 2 H, 3'-H); 2.24 (m, 1 H, 2'-H_b); 2.40 (m, 1 H, 2'-H_a); 3.55 (m, 2 H, 5'-H); 4.04 (s, 3 H, OCH_3); 4.07 (m, 1 H, 4'-H); 4.93 (t, 1 H, J = 5.5 Hz, OH); 6.47 (dd, 1 H, J = 4.4, 6.8 Hz, 1'-H); 6.55 (d, 1 H, J = 3.7 Hz, 5-H); 7.66 (d, 1 H, J = 3.7 Hz, 6-H); 8.42 (s, 1 H, 2-H).

7-(2,3-Dideoxy-β-D-*glycero*-pentofuranosyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one (12):

a) From **11**: A solution of **11** (120 mg, 0.48 mmol) in 2 N NaOH (6 mL) is refluxed for 3 h. The solution is neutralized with 80 % aq. AcOH and the precipitate removed by filtration. The filtrate is applied to an amberlite XAD-4 resin (column 2 × 23 cm, H_2O and H_2O/2-propanol, 9:1). Evaporation of the eluate yields a colorless foam, which is crystallized from MeOH as colorless needles; yield: 96 mg (85 %); mp 148 °C.

b) From **8**: A suspension of **8** (200 mg, 0.8 mol) in 2 N NaOH (10 mL) is refluxed for 5 h. The solution is neutralized with 80 % aq. AcOH and the insoluble material is removed by filtration. The filtrate is applied to an amberlite XAD-4 resin (column: 2 × 23 cm), the resin is washed with water (500 mL) and compound **12** eluted with H_2O/2-propanol (9:1). Evaporation of the main zone gives **12**, identical with the material obtained from **11**; yield: 160 mg (80 %); R_f = 0.5 (CH_2Cl_2/MeOH, 9:1).

$C_{11}H_{13}N_3O_3$	calc.	C 56.16	H 5.57	N 17.86
(235.3)	found	56.32	5.58	17.88

UV (MeOH): λ_{max} = 213 (log ε = 4.28), 259 nm (3.97).

^{1}H-NMR (DMSO-d_6): δ = 2.00 (m, 2 H, 3'-H); 2.16 (m, 1 H, 2'-H_b); 2.37 (m, 1 H, 2'-H_a); 3.49 (dd, 1 H, J = 4.9, 11.6 Hz, 5'-H); 3.58 (dd, 1 H, J = 4.2, 11.6 Hz, 5'-H); 4.05 (m, 1 H, 4'-H); 6.33 (dd, 1 H, J = 4.2, 6.9 Hz, 1'-H); 6.50 (d, 1 H, J = 3.5 Hz, 5-H); 7.36 (d, 1 H, J = 3.5 Hz, 6-H); 7.90 (s, 1 H, 2-H).

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