

62. Facile Synthesis of 2'-Deoxyribofuranosides of Allopurinol and 4-Amino-1*H*-pyrazolo[3,4-*d*]pyrimidine via Phase-Transfer Glycosylation

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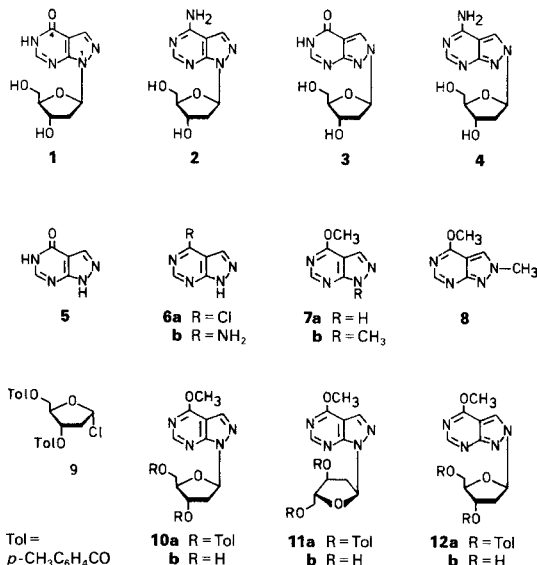
Phase-transfer glycosylation of 4-methoxy-1*H*-pyrazolo[3,4-*d*]pyrimidine with the 2-deoxyribofuranosyl chloride **9** formed the N(1)- β -nucleoside **10a** as main product (39%). As by-products the α -*D*-anomer **11a** (7%) and the N(2)-isomer **12a** (18%) were isolated. Assignment of these isomers was made on the basis of their ¹H- and ¹³C-NMR spectra. Removal of the sugar-protecting groups yielded the 4-methoxy-nucleosides **10b**, **11b**, and **12b**, respectively. Nucleophilic displacement of the 4-MeO-group gave the 2-deoxyribofuranosides **1–4** of allopurinol and 4-amino-1*H*-pyrazolo[3,4-*d*]pyrimidine.

Modern strategies of oligonucleotide synthesis, in particular the use of phosphoramidites [1] and the application of polymeric matrices [2] allow the rapid preparation of oligonucleotides of defined sequences. This new methodology has recently been applied to rare or modified nucleosides [3] which, after incorporation into a DNA sequence, can alter biochemical or biophysical properties of the oligonucleotide. As an immediate consequence, efficient methods for the synthesis of modified 2'-deoxynucleosides have to be developed.

For the last few years, we have been dealing with the synthesis of pyrrolo[2,3-*d*]pyrimidine nucleosides [4] which have then been enzymatically polymerized and which we are now incorporating into DNA sequences [5]. We now are extending our work to pyrazolo[3,4-*d*]pyrimidine nucleosides, in particular to the 2-deoxyribofuranosyl derivatives of allopurinol (**5**) and 4-amino-1*H*-pyrazolo[3,4-*d*]pyrimidine (**6b**). The allopurinol β -*D*-ribonucleoside is active against *Leishmania donovani* [6]. Enzymatic amination of allopurinol nucleoside leads to the β -*D*-ribofuranosyl derivative of **6b** [7] [8].

Previous to our work, the (2'-deoxyribofuranosyl) allopurinol **1** was unknown. The corresponding aminonucleoside **2** which is an isostere of 2'-deoxyadenosine is only available by enzymatic reactions using 2'-deoxyribosyltransferase from *Lactobacillus Leishmania* [9].

The glycosylation of allopurinol presents difficulties, due to nonregioselective reactions [10–12]. Recently, a regioselective synthesis of allopurinol ribonucleoside has been described starting with 4,6-dichloro-1*H*-pyrazolo[3,4-*d*]pyrimidine and employing trifluoromethanesulfonate as catalyst [13]. One disadvantage of this method as it was applied to ribonucleosides is that it is very long because of the transformation of the aglycon. We now report a facile synthesis of the 2'-deoxyribofuranosyl derivatives **1–4** using commercially available allopurinol (**5**) [14–16] as starting material.



Treatment of **5** with phosphorus trichloride oxide resulted in the formation of compound **6a** which is highly reactive at the 4-position. Even under conditions of ¹³C-NMR experiments in Me₂SO solution (see below, *Table 1*) it was hydrolyzed to the starting material due to traces of H₂O. Nucleophilic displacement of the 4-halogen atom in **6a** by Na-methoxide furnished the 4-MeO derivative **7a**. According to other pyrazolo[3,4-*d*]-pyrimidines such as compound **6b**, it can be expected that also in **7a** a rapid proton transfer can occur between N(1) and N(2), whereby the system with the proton at N(1) should be the favoured tautomer [17].

Glycosylation of pyrrolo[2,3-*d*]pyrimidines with the 2-deoxyribofuranosyl chloride **9** has shown that electrophilic attack at N(7) of pyrrolo[2,3-*d*]pyrimidines is favoured if the nucleobase anion is generated and phase-transfer conditions are employed. Therefore, it was concluded that regioselective alkylation [18] and glycosylation of compound **7a** could be achieved in a similar way. Phase-transfer glycosylation was carried out in a biphasic mixture of CH₂Cl₂ and 50% aq. NaOH solution. The organic layer contained the chromophore **7a**, the chloride **9**, and Bu₄NHSO₄ as catalyst. The glycosylation took place by thorough mixing with a vibromixer and was complete within a few minutes at room temperature. Preparative separation of the main and the two side products was accomplished by silica-gel column chromatography. The 3 compounds **10a**, **11a**, and **12a** were isolated in 39, 7, and 18% yield. Two of them, **10a** and **11a**, exhibited identical UV spectra with a main absorption maximum at 241 nm. The UV spectrum of **12a** was slightly different. All 3 compounds gave identical elemental analyses which agreed with the structure of a protected glycosylation product of **7a**.

Since the toluoyl groups masked the UV absorbance of the heterocyclic base in **10a**, **11a**, and **12a**, they were split off by the action of NaOMe. After chromatographic purification, 3 crystalline products **10b**, **11b**, and **12b**, respectively, were obtained that again gave identical elemental analyses. The UV spectrum of **12b** was different from the one of **10b** and **11b**, but similar to that of the methylated chromophore **8** [18]; therefore it

Table 1. ¹³C-NMR Chemical Shifts of Pyrazolo[3,4-d]pyrimidines and their 2'-Deoxyribofuranosyl Derivatives, in [D₆]Me₂SO^a)

Com- pound	C(3)	C(3a)	C(4)	C(6)	C(7a)	CHO ₃	C(1')	C(2')	C(3')	C(4')	C(5')	2 C(1'')-C=O	2 C(1'')	2 C(2'')	2 C(3'')	2 C(4'')	2 CH ₃ -C(4'')	2 C(5'')	2 C(6'')
11a (α-D)	132.0	102.4	163.2	155.2	154.9	54.0	84.8	35.5	73.9	80.8	63.8	165.3	143.5	129.0	126.5	20.9			
11b (α-D)	131.7	102.3	163.3	155.1	154.5	53.9	83.6	38.0	70.2	86.5	61.1								
10a (β-D)	132.3	102.4	163.3	155.3	154.9	54.0	84.3	35.2	74.6	81.3	63.7	165.1	143.5	129.0	126.4	20.9			
10b (β-D)	131.9	102.4	163.3	155.2	154.5	54.0	84.2	38.0	70.9	87.6	62.2								
1 (β-D)	134.9	106.2	156.8	148.1	152.3		84.0	38.1	70.9	87.7	62.3								
2 (β-D)	132.8	100.4	157.3	155.7	153.6		84.1	38.0	71.0	87.5	62.3								
12a (β-D)	124.3	102.2	b)	155.2	160.8	53.7	90.6	37.0	74.4	82.3	63.7	165.1	143.5	129.0	126.3	20.8			
12b (β-D)	123.1	102.0	164.9	154.9	160.6	53.9	90.9	40.5	69.9	88.4	61.3								
3 (β-D)	127.5	106.8	158.3	146.8	158.6		90.3	40.5	70.1	88.2	61.5								
4 (β-D)	123.6	101.3	159.4	156.6	159.5		90.5	40.3	70.6	88.3	62.0								
5	134.1	105.6	157.4	147.5	154.4														
6a	132.5	112.5	154.5	154.5	153.5														
6b	132.3	99.5	157.9	155.6	154.8														
7a	131.1	101.2	163.2	154.6	156.1	53.6													

^a) δ Values given in ppm relative to Me₄Si as internal standard.

b) Masked by C(1'')-C=O.

was concluded that its structure is represented by *Formula 12b*. The glycosylation site in **12b** was confirmed by the regular and the $^{13}\text{C}/^1\text{H}$ -coupled ^{13}C -NMR spectra (*Tables 1* and *2*) and its anomeric configuration determined by the ^1H -NMR data of **12a**.

Compared to the chromophore **7a**, **12b** exhibits a strong upfield shift in the ^{13}C -NMR for the C(3) signal, which is located at a position close to that of the methyl compound **8** [18]. Unambiguous information about the glycosylation position came from the $J_{\text{C,H}}$ of **12b** (*Table 2*). Besides the coupling with H–C(3) ($^1J = 198.6$ Hz), the C(3) signal exhibits an additional coupling ($^3J = 2.1$ Hz) with the anomeric proton which is not observed with the other glycosylation products. It has been already observed by *Nuhn et al.* [19] for regular 2'-deoxynucleosides and found by us for pyrrolo[2,3-*d*]pyrimidine 2'-deoxynucleosides that the ^1H -NMR signals of H–C(4') and 2H–C(5') are well separated in the series of the α -D-anomers but coincide for the β -D-compounds. As *Table 3* shows, H–C(4') and 2H–C(5') of **12a** appear at almost the same chemical shift indicating β -D-configuration.

Table 2. $J_{\text{C,H}}$ Values [Hz] of (2-Deoxyribofuranosyl)pyrazolo[3,4-*d*]pyrimidines^{a)}

$J_{\text{C,H}}$	11b	10b	1	2	12b	3	4
C(3),H–C(3)	196.7	196.5	192.2	193.0	198.6	195.2	195.1
C(3),H–C(1')					2.1	2.1	1.8
C(3a),H–C(3)	10.4	10.5	9.9	10.4	7.8	7.6	7.4
C(4),H–C(6)	b)	11.0	6.9	11.1	b)	6.7	10.6
C(4),CH ₃ O		4.2					
C(6),H–C(6)	205.8	205.6	205.8	196.5	203.5	204.5	195.6
C(7a),H–C(1')	b)	b)	1.8	1.7			
C(7a),H–C(3)			4.6	3.4	7.9	7.3	12.2
C(7a),H–C(6)			13.2	11.3	12.6	14.1	12.2
C(1'),H–C(1')	165.3	165.4	162.9	164.8	168.5	168.5	169.1
C(3'),H–C(3')	147.3	148.8	151.0	150.4	151.5	148.9	149.0
C(4'),H–C(4')	148.3	147.1	147.0	146.9	147.3	147.3	147.9
C(5'),H–C(5')	139.2	139.6	139.6	139.1	138.1	139.9	141.0

a) Data taken from ^{13}C -NMR spectra measured in $[\text{D}_6]\text{Me}_2\text{SO}$.

b) Not resolved.

From the identical UV data (λ_{max} 247 nm) of **10b** and **11b** it was concluded that these compounds are anomers. This is underlined by the ^{13}C -NMR data for their chromophore moieties which are almost identical and also very similar to those of compound **7a** (*Table 1*). The assignment of the anomeric configuration of **10b** and **11b** cannot be made on the basis of the ^{13}C -NMR chemical shifts of the sugar moieties (see [20]); it was given by the ^1H -NMR data of **10a** and **11a**, respectively, indicating β -D-configuration for the major (39%) glycosylation product **10a** and hence for **10b** (see *Table 3* and discussion of the ^1H -NMR data of **12a** above).

It can be concluded that the phase-transfer glycosylation is an efficient method to obtain the β -D-nucleoside **10a** in good yield from easily accessible starting materials. The α -D-anomer **11a**, which is formed in about equal amounts by other glycosylation procedures using the 2'-deoxyribofuranosyl chloride **9**, is a minor product (7%) of the phase-transfer glycosylation. Unfortunately, the N(2)-glycosylation product **12a** is also formed to some extent, but other glycosylation products were not detected. The conversion of the 4-methoxynucleosides **10b** and **12b** into the allopurinol nucleosides **1** and **3**, respectively, without cleaving the N-glycosylic bond was difficult. Cleavage of the MeO-group with acid resulted in hydrolysis of the N-glycosylic bond. However, earlier findings on the methylated chromophores **7b** or **8** [18] have shown that the 4-MeO-group can be con-

Table 3. ¹H-NMR Chemical Shifts of (2-Deoxyxythofuranosyl)pyrazolo[3,4-d]pyrimidine in [D₆] Me₂SO^d

Compound	H-C(3)	H-C(6)	CH ₃ O- or NH ₂ -C(4)/H-N(5)	H-C(1')	H _a -C(2')	H _b -C(2')	H-C(3')	OH-C(3')	H-C(4)	OH-C(5')	2 H-C(5)	2 C ₆ H ₄	2 CH ₃
11a (α-D)	8.34 (s)	8.61 (s)	4.10 (s, 3H)	6.84 (dd, J = 4.4, 7.4)	3.22 (q, J = 7.7)	2.99 (dt', J = 4.6, 14.2)	5.58 (ddd ^b)	-	4.74 (dt, J = 4.5, 4.7)	4.51 (dAB ^b)	7.30, 7.87 (4d, J = 8.1, 8.2)	2.36 (2s)	
11b (α-D)	8.37 (s)	8.65 (s)	4.12 (s, 3H)	6.60 (t', J = 6.5)	2.78 ('quint.', J = 6.9)	2.67 ('quint.', J = 6.9)	4.16 ('quint.', J = 6.8)	5.47 (d, J = 6.7)	3.96 (dt ^b)	3.41, 3.57 (dAB ^b)	4.74 (t, J = 5.7)		
10a (β-D)	8.37 (s)	8.64 (s)	4.11 (s, 3H)	6.87 (t', J = 6.0)	3.30 (ddd ^b)	2.81 (ddd ^b)	5.87 (ddd ^b)	-	4.48 (dt ^b) + 4.48 (dAB ^b)		7.33, 7.89 (4d, J = 8.0)	2.39 (2s)	
10b (β-D)	8.32 (s)	8.63 (s)	4.11 (s, 3H)	6.67 (t', J = 6.4)	2.84 ('quint.', J = 6.4)	2.31 (ddd, J = 4.4, 6.8, 13.1)	4.46 (ddd ^b)	5.31 (d, J = 4.6)	3.83 (dt, J = 3.6, 5.8)	3.36, 3.52 (dAB ^b)	4.72 (t, J = 5.7)		
1 (β-D)	8.14 (s) / 8.17 (s)	12.22 (s, 1H)	6.52 (t', J = 6.6)	2.76 ('quint.', J = 6.3)	2.26 (ddd, J = 4.5, 6.8, 13.1)	4.43 (ddd ^b)	5.30 (d')	3.81 (dt, J = 3.6, 5.8)	3.30, 3.50 (dAB ^b)	4.74 (t ^b)			
2 (β-D)	8.14 (s) / 8.18 (s)	7.72 (s, 2H)	6.54 (t', J = 6.5)	2.80 ('quint.', J = 6.4)	2.23 (ddd, J = 4.0, 6.6, 13.2)	4.43 (ddd ^b)	5.24 (d, J = 4.5)	3.81 (dt, J = 3.3, 5.5)	3.37, 3.52 (dAB ^b)	4.80 (t, J = 5.7)			
12a (β-D)	8.59 (s) / 8.83 (s)	4.05 (s, 3H)	6.64 (t', J = 5.6)	3.20 ('quint.', J = 5.4)	2.90 ('quint.', J = 5.1)	5.85 (ddd ^b)	-	4.57 (dt ^b) + 4.57 (dAB ^b)		7.38, 7.86 (4d, J = 8.1)	2.36 (2s)		
12b (β-D)	8.56 (s) / 8.87 (s)	4.08 (s, 3H)	6.36 (t', J = 5.8)	2.62 ('quint.', J = 6.3)	2.41 ('quint.', J = 6.3)	4.40 (ddd ^b)	5.34 (d, J = 4.4)	3.92 (dt ^b)	3.51, 3.63 (dAB ^b)	4.96 (t, J = 5.3)			
3 (β-D)	8.00 (s)	8.74 (s)	11.75 (s, 1H)	6.22 (t', J = 5.9)	2.59 ('quint.', J = 6.0)	2.33 ('quint.', J = 6.1)	4.38 (ddd ^b)	5.31 (d, J = 4.3)	3.87 (dt, J = 4.2, 4.5)	3.53 (dAB ^b)	4.93 (t, J = 5.9)		
4 (β-D)	8.14 (s) / 8.50 (s)	7.67 (s, 2H)	6.31 (t', J = 5.9)	2.62 ('quint.', J = 6.1)	2.36 ('quint.', J = 6.2)	4.37 (ddd ^b)	5.33 (d, J = 4.3)	3.91 (dt, J = 4.0, 5.0)	3.53 (dAB ^b)	4.90 (t, J = 5.5)			

^a) δ Values given in ppm relative to Me₂Si as internal standard. Coupling constants *J* in Hz. Splitting pattern: s, singlet; d, doublet; t, triplet; t', pseudo-triplet; AB, AB 'quadruplet'; quint., pseudoquintuplet.

^b) Splitting pattern not resolved.

verted into an OH-group by storing these compounds in dilute NaOH solution. Applying these conditions of nucleophilic displacement to **10b** and **12b** converted them within 2 h, into the crystalline allopurinol nucleosides **1** and **3**, respectively, without formation of any side product. This was confirmed by the ¹H- and ¹³C-NMR spectra of **1** and **3** (Tables 1–3).

TLC monitoring showed the reaction to be more rapid in the case of **12b** than in the case of **10b**. In order to quantify the nucleophilic displacement, it was followed spectrophotometrically in 1N NaOH/MeOH 1:1. From the change of the UV absorption (**10b** at 270 nm; **12b** at 260 nm) the half-life at 25°C was calculated and found to be 123 min for **10b** and 37 min for **12b**. An increase of the NaOH concentration (2N NaOH/MeOH 1:1) did not affect the kinetics of the N(2)-nucleoside **12b**, whereas the half-life of the N(1)-isomer was now 69 min.

Replacing the aq. NaOH solution by conc. aq. ammonia compounds **10b** and **12b** were converted into the crystalline amino nucleosides **2** and **4**, respectively, within 3 days at room temperature. Only traces of the corresponding allopurinol nucleosides **1** and **3** could be detected under these conditions. The ¹H- and ¹³C-NMR data of **1–4** (Tables 1–3) were in agreement with their structures. Moreover, the synthetic nucleoside **2** was identical in its spectroscopic and chromatographic properties to an authentic sample of **2** obtained by enzymatic preparation [12].

In the ¹³C-NMR spectra of nucleosides, the ¹J_{C,H} coupling constants allow a rapid identification of the anomeric C-atom among all other sugar signals due to the fact that ¹J_{C(1'),H-C(1')} exhibits values around 165 Hz, whereas the other ¹J_{C,H} of the sugar moiety are definitely smaller (140–150 Hz) [21]. Applying these findings to the analysis of the spectra of the N(1)-nucleosides **1**, **2**, **10b**, or **11b**, the sequence of the chemical shifts of the sugar C-atoms is found to be the same (C(4'), C(1'), C(3'), C(5'), C(2')) as for purine or pyrrolo[2,3-*d*]pyrimidine 2'-deoxynucleosides. In contrast, the sequence of the sugar signals of the N(2)-nucleosides **3**, **4**, and **12b** is different. As can be seen from the coupling pattern (Table 2) the low-field signal of the sugar moieties shows the largest coupling constant (ca. 170 Hz). Therefore the sequence of the sugar signals is C(1'), C(4'), C(3'), C(5'), C(2'). Hence, only the chemical shifts of C(1') and C(2') differ between N(1)- and N(2)-nucleosides, whereas the δ's of C(3'), C(4'), and C(5') are almost unaffected.

The facile synthesis of the nucleosides **1** and **2** implies that phase-transfer glycosylation could also be applicable to other pyrazolo[3,4-*d*]pyrimidine nucleosides of biological interest. Investigations towards the synthesis of such nucleosides are in progress.

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Note Added in Proof. – Compound **2** has recently been described by Z. Kazimierzuk, H. B. Cottam, G. R. Revankar, R. K. Robins, *J. Am. Chem. Soc.* **1984**, *106*, 6379.

Experimental Part

General. M.p.s were determined on a Linstrom apparatus (Wagner & Munz, W.-Germany) and are not corrected. UV spectra (λ_{max}(ε) in nm) were measured on a Uvikon 810 spectrometer (Kontron, Switzerland); NMR spectra were recorded on a Bruker WM 250 spectrometer, δ's are relative to Me₄Si as internal standard for ¹H and ¹³C. Elemental analyses were performed by Mikroanalytisches Labor Beller (Göttingen, W.-Germany). TLC was carried out on silica gel SIL G-25 UV₂₅₄ plates (Macherey-Nagel & Co., Düren, W.-Germany). Silica gel 60 (230–400 mesh ASTM; Merck, Darmstadt, W.-Germany), Amberlite-XAD-4 resin (Serva, Heidelberg, W.-Germany), and Dowex 1 × 2 ion-exchange resin (OH⁻ form, Serva, Heidelberg, W.-Germany) were used for column chromatography. The columns were connected to an Uvicord-S detector and an UltroRac fraction collector (LKB Instruments, Bromma, Sweden). Chromatography was performed with solvent systems CH₂Cl₂ (A), CH₂Cl₂/AcOEt 95:5 (B), CH₂Cl₂/AcOEt 9:1 (C), cyclohexane/AcOEt 4:1 (D), CHCl₃/MeOH 95:5 (E), CHCl₃/MeOH 9:1 (F), and CHCl₃/MeOH 4:1 (G). Allopurinol (**5**) was purchased from Sigma Chemical Co. (St. Louis, USA).

Phase-Transfer Glycosylation of 4-Methoxy-1H-pyrazolo[3,4-d]pyrimidine (7a) with 2-Deoxy-3,5-di-O-(p-toluoyl)- α -D-erythro-pentofuranosyl Chloride (9). A suspension of **7a** [6] [14] (514 mg, 3.4 mmol) and Bu₄NHSO₄ (122 mg, 0.36 mmol) in CH₂Cl₂ (20 ml) and an equal volume of 50% aq. NaOH soln. was stirred with a vibromixer at r.t. The chloride **9** [22] (1.47 g, 3.8 mmol) in CH₂Cl₂ (17 ml) was dropped into the emulsion within 2 min and mixing was continued for 1 min. Thereupon the org. layer was separated and the aq. layer extracted 3× with CH₂Cl₂ (50 ml). The org. layers were combined, dried over Na₂SO₄, filtered, and evaporated to dryness. The oily residue was dissolved in CH₂Cl₂ and chromatographed on a silica-gel column (20 × 4 cm). From the fast migrating main zone (eluant A), colorless 1-[2-deoxy-3,5-di-O-(p-toluoyl)- β -D-erythro-pentofuranosyl]-4-methoxy-1H-pyrazolo[3,4-d]pyrimidine (**10a**) was isolated (673 mg, 39%). Crystallization from i-PrOH yielded colorless needles, m.p. 95–98° (sintering at 70°). TLC(D): R_f 0.6 UV (MeOH): 241 (36400). Anal. calc. for C₂₇H₂₆N₄O₆: C 64.53, H 5.22, N 11.15; found: C 64.67, H 5.40, N 11.18.

From the second zone (eluted partially with A then with B) colorless amorphous 1-[2-deoxy-3,5-di-O-(p-toluoyl)- α -D-erythro-pentofuranosyl]-4-methoxy-1H-pyrazolo[3,4-d]pyrimidine (**11a**; 120 mg, 7.0%) was obtained. TLC(D): R_f 0.55. UV (MeOH): 241 (38700). Anal. calc. for C₂₇H₂₆N₄O₆: C 64.53, H 5.22, N 11.15; found: C 64.44, H 5.34, N 11.01.

The slow migrating zone (eluted with C) yielded colorless foamy 2-[2-deoxy-3,5-di-O-(p-toluoyl)- β -D-erythro-pentofuranosyl]-4-methoxy-2H-pyrazolo[3,4-d]pyrimidine (**12a**; 304 mg, 17.7%) upon evaporation. Crystallization from i-PrOH led to colorless crystals of m.p. 162–164°. TLC(D): R_f 0.2. UV (MeOH): 242 (36000). Anal. calc. for C₂₇H₂₆N₄O₆: C 64.53, H 5.22, N 11.15; found: C 64.70, H 5.36, N 11.16.

1-(2-Deoxy- β -D-erythro-pentofuranosyl)-4-methoxy-1H-pyrazolo[3,4-d]pyrimidine (**10b**). A soln. of **10a** (1.31 g, 2.61 mmol) in 0.1M NaOMe/MeOH (70 ml) was stirred for 4 h at r.t. Then the soln. was adsorbed onto silica gel (13 g) and chromatographed on a silica-gel column (10 × 5 cm). Elution with E resulted in a main zone which yielded a colorless solid. Crystallization from H₂O gave **10b** as colorless needles (555 mg, 80%) with m.p. 176°. TLC(F): R_f 0.6. UV (MeOH): 247 (7700), 263 (sh, 4700). Anal. calc. for C₁₁H₁₄N₄O₄: C 49.62, H 5.30, N 21.04; found: C 49.76, H 5.34, N 21.14.

1-(2-Deoxy- α -D-erythro-pentofuranosyl)-4-methoxy-1H-pyrazolo[3,4-d]pyrimidine (**11b**). A soln. of **11a** (240 mg, 0.48 mmol) in 0.1M NaOMe/MeOH (15 ml) was treated as **10a** above. After chromatography, colorless amorphous **11b** was isolated which crystallized from H₂O as colorless plates (88 mg, 69%) with m.p. 150–152°. TLC(F): R_f 0.63. UV (MeOH): 247 (7900), 263 (sh, 4700). Anal. calc. for C₁₁H₁₄N₄O₄: C 49.62, H 5.30, N 21.04; found: C 49.45, H 5.39, N 21.10.

2-(2-Deoxy- β -D-erythro-pentofuranosyl)-4-methoxy-2H-pyrazolo[3,4-d]pyrimidine (**12b**). Treatment of **12a** (1.06 g, 2.11 mmol) in 0.1 M NaOMe/MeOH (60 ml) as described for **10b** gave colorless foamy **12b** after chromatography (F). Crystallization from H₂O yielded colorless needles (427 mg, 76%) with m.p. 180–181°. TLC(G): R_f 0.46. UV (MeOH): 260 (9600). Anal. calc. for C₁₁H₁₄N₄O₄: C 49.62, H 5.30, N 21.04; found: C 49.76, 5.38, N 21.08.

1-(2-Deoxy- β -D-erythro-pentofuranosyl)-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one (= 2'-Deoxyribofuranosyl)allopurinol, **1**). A soln. of **10b** (505 mg, 1.9 mmol) in 2N aq. NaOH (50 ml) was stirred for 2 h at r.t. The soln. was neutralized with an aliquot of 2N HCl and then applied to an Amberlite-XAD-4 column (20 × 2 cm). Inorg. salt was removed by washing with H₂O, **1** was eluted with H₂O/i-PrOH 9:1 (v/v). Crystallization from i-PrOH yielded **1** as colorless needles (406 mg, 85%) with m.p. 202–203° [23]. TLC(F): R_f 0.2. UV (MeOH): 251 (7500). Anal. calc. for C₁₀H₁₂N₄O₄: C 47.62, H 4.80, N 22.21; found: C 47.76, H 4.91, N 22.18.

2-(2-Deoxy- β -D-erythro-pentofuranosyl)-2H-pyrazolo[3,4-d]pyrimidin-4(5H)-one (**3**). A soln. of **12b** (261 mg, 0.98 mmol) in 2M aq. NaOH (25 ml) was treated as described for **10b**. After chromatographic separation on an Amberlite-XAD-4 column (20 × 2 cm), the residue of the main zone was crystallized from H₂O to yield colorless crystals of **3** as a hydrate. This became amorphous by drying at 120° *in vacuo* (196 mg, 79%). TLC(G): R_f 0.42. UV (MeOH): 261 (9100), 264 (9100). Anal. calc. for C₁₀H₁₂N₄O₄: C 47.62, H 4.80, N 22.21; found: C 47.70, H 4.84, N 22.41.

4-Amino-1-(2-deoxy- β -D-erythro-pentofuranosyl)-1H-pyrazolo[3,4-d]pyrimidine (**2**). A soln. of **10b** (333 mg, 1.25 mmol) in conc. aq. NH₃ (200 ml) was stored at r.t. for 3 days. The solv. was evaporated and the residue crystallized from i-PrOH yielding **2** as colorless crystals (268 mg, 85%) with m.p. 245–246° [12]. TLC(G): R_f 0.42. UV (MeOH): 260 (9500), 275 (10900). Anal. calc. for C₁₀H₁₃N₅O₃: C 47.81, H 5.22, N 27.88; found: C 47.62, H 5.34, N 27.98.

4-Amino-2-(2-deoxy- β -D-erythro-pentofuranosyl)-2H-pyrazolo[3,4-d]pyrimidine (**4**). A soln. of **12b** (354 mg, 1.33 mmol) in conc. NH₃ (100 ml) was stirred at r.t. for 3 days, then the solv. evaporated, the residue dissolved in H₂O (50 ml), and the soln. adsorbed onto a Dowex I × 2 ion-exchange column (15 × 2 cm, OH⁻ form). Elution with MeOH/H₂O 3:2 to H₂O (600 ml, each; linear gradient) afforded a main zone from which **4** was obtained.

Recrystallization from EtOH/pentane yielded colorless crystals (228 mg, 68%) with m.p. 197–200°. TLC(G): R_f 0.17. UV (MeOH): 231 (7400), 260 (6800), 268 (7700), 292 (10200). Anal. calc. for $C_{10}H_{13}N_3O_3$: C 47.81, H 5.22, N 27.88; found: C 47.97, H 5.18, N 27.83.

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