Synthesis of 7-Halogenated 8-Aza-7-deaza-2′-deoxyguanosines and Related Pyrazolo[3,4-*d*]pyrimidine 2′-Deoxyribonucleosides

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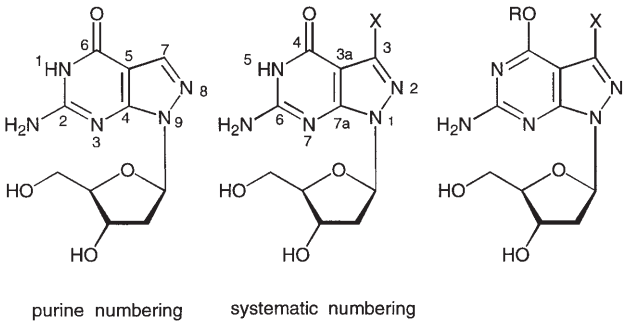
Abst**ract:** The synthesis of 7-bromo and 7-iodo derivatives of 8-aza-7-deaza-2′-deoxyguanosine (**2**, **3**) as well as the halogenated 4-alkoxy derivatives **4a–c** and **5a–c** is described. Glycosylation of the halogenated pyrazolo[3,4-*d*]pyrimidine anions of **7a–c** or **8a–c** with 2-deoxy-3,5-di-*O*-(*p*-toluoyl)-*α*-D-*erythro*-pentofuranosyl chloride (**9**) yields regioisomeric glycosylation products, the N(1)-isomers **10a–c** and **11a–c** as well as the N(2)-compounds **12a–c**. The latter isomers lose their halogen during the glycosylation in the presence of non-anhydrous KOH. Anhydrous conditions (NaH) furnished **10c**, **11c** together with the halogenated N(2)-isomers **13a**,**b**. Compounds **10a–c**, and **11a–c** were deprotected and converted to the 4-alkoxy nucleosides **4a–c** and **5a–c**. The N(1)-nucleosides **4c** and **5c** were hydrolyzed to give the 7-bromo or 7-iodo derivatives of 8-aza-7-deaza-2′-deoxyguanosines **2** and **3**. Different from regular 2′-deoxyribonucleosides the sugar moiety of pyrazolo[3,4-*d*]pyrimidine 2′-deoxyribonucleosides shows a preferred N-type pucker ($^3T_2$) in solution, a conformation which is also detected in the solid state.

Key words: pyrazolo[3,4-*d*]pyrimidines, nucleosides, halogenation, glycosylation, sugar conformation

The introduction of 7-substituents into 7-deazapurine (7-deazapurine = pyrrolo[2,3-*d*]pyrimidine) nucleosides results in duplex stabilization when such a residue is incorporated into an oligonuc]eotide instead of a purine base.[1–3] Within the series of various nucleobases related to purines the 8-aza-7-deazapurines (pyrazolo[3,4-*d*]pyrimidines) represent another heterocyclic system which can be functionalized at the same position. Pyrazolo[3,4-*d*]-pyrimidine nucleosides, such as 8-aza-7-deaza-2′-deoxyguanosine (**1**)[4] and 8-aza-7-deaza-2′-deoxyadenosine[5, 6] as well as the corresponding 2′,3′-dideoxynucleosides have already been synthesized.[7, 8] Also 8-aza-7-deazapurine ribonucleosides with 7-bromo or 7-iodo substituents have been prepared.[9–11] These compounds exhibit interesting biological activity, in particular antiparasitic effects and inhibitory activity against adenosine kinases.[9] Furthermore, pyrazolo[3,4-*d*]pyrimidine 2′-deoxyribonucleosides have already been incorporated into oligonucleotides[12, 13] and it has already been shown that the nonsubstituted 8-aza-7-deazaguanine base stabilizes the DNA-duplex compared to the parent guanine.[14,15] As we wanted to combine the stabilizing effect of the pyrazolo[3,4-*d*]pyrimidine system with the favorable properties of the 7-substituents of 7-deazapurines, halogenated nucleosides, such as the 8-aza-7-deaza-2′-deoxyguanosines **2** ($Br^7c^7z^8G_d$) and **3** ($I^7c^7z^8G_d$) as well as related alkoxypyrazolo[3,4-*d*]pyrimidine nucleosides **4a–c** and **5a–c** were synthesized.

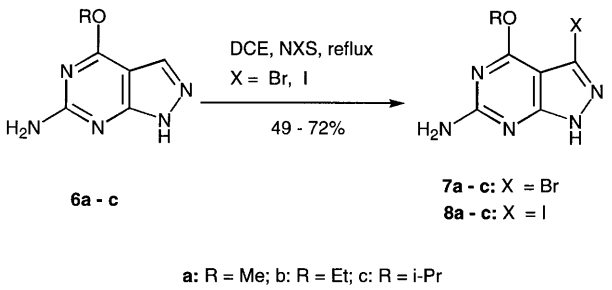
Various routes have been described for the synthesis of pyrazolo[3,4-*d*]pyrimidine nucleosides: (i) Glycosylation of pyrazole precursors which are later converted into the target nucleosides by ring annulation,[16, 17] (ii) Conversion of a glycosyl hydrazide into a pyrazolo[3,4-*d*]pyrimidine nucleoside,[18, 19] and (iii) Glycosylation of a preformed base.[4, 7] As we have already employed the stereoselective



Scheme 1

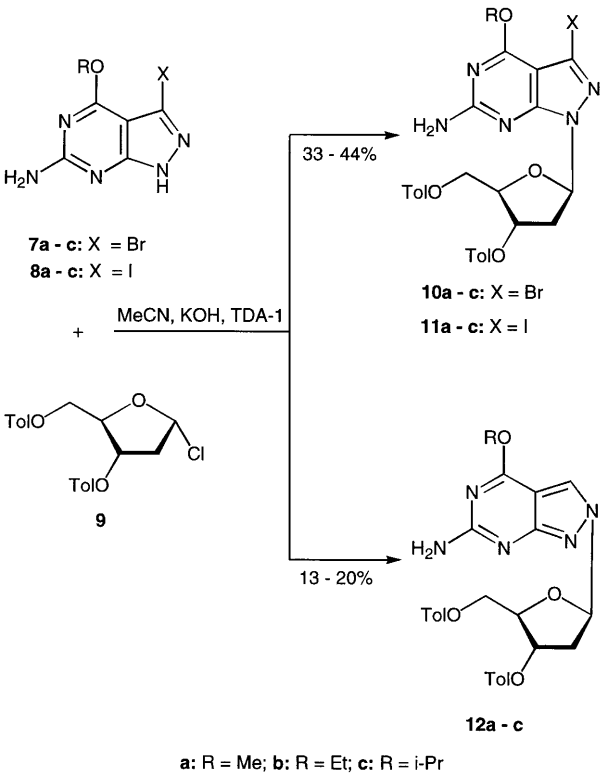
nucleobase anion glycosylation[20, 21] for the synthesis of 6-amino-4-methoxypyrazolo[3,4-*d*]pyrimidine (**6a**)[4] it was decided to also employ the halogenated compounds **7a–c** and **8a–c** for nucleoside synthesis (route iii).

Recently, the bromination of 6-amino-4-isopropoxypyrazolo[3,4-*d*]pyrimidine (**6c**) was studied and the glycosylation of the brominated derivative 7**c** was performed.[22] Originally, 6-amino-4-methoxypyrazolo[3,4-*d*]pyrimidine (**6a**) was used in the bromination reaction.[22] However, it appeared that the solubility of this base is poor in dichloroethane (DCE). Therefore, various 4-alkoxy-6-aminopyrazolo[3,4-*d*]pyrimidines were prepared in order to optimize the halogenation reactions. 6-Amino-4-chloropyrazolo[3,4-*d*]pyrimidine[4] served as the starting material which was treated with various alkali alkoxides yielding the 4-alkoxy-6-aminopyrazolo[3,4-*d*]pyrimidines **6a–c**. The 4-ethoxy and the 4-isopropoxy derivatives **6b**,**c** are described herein, while the 4-methoxy compound **6a**[4] has previously been synthesized. The alkoxy compounds **6a**,**b** were halogenated with a slight excess of *N*-bromosuccinimide or *N*-iodosuccinimide to give the halo derivatives **7a**,**b** and **8a**,**b** (Scheme 2).[23] Changing to the more lipophilic isopropoxy derivatives **7c**, **8c** increased the yield of halogenation.



Scheme 2

Next, the glycosylation reaction of the halogenated alkoxy derivatives **7a–c** and **8a–c** was performed. The reactions were carried out under standard conditions using various bases, 2-deoxy-3,5-di-*O*-(4-toluoyl)-α-D-*erythro*-pentofuranosyl chloride (**9**)[24] as sugar component, MeCN as solvent, and powdered KOH/TDA-1 to generate the nucleobase anion. Only in the case of the isopropoxy compounds **7c** and **8c** are the bases soluble in MeCN whereas the glycosylation of the methoxy and ethoxy derivatives (**7a**,**b** and **8a**,**b**) was performed in suspension. For comparison of the glycosylation yields, the reaction was also performed on 6-amino-4-isopropoxypyrazolo[3,4-*d*]pyrimidine (**6c**) with the halogenose **9** yielding compounds **10d**, **12c** (see experimental section). After workup, the glycosylation products were separated by column chromatography (CH_2Cl_2/acetone 98:2 → 95:5). The colorless amorphous N(1)-products **10a–c** and **11a–c** were isolated from the fast migrating zones. The second zones always gave the N(2)-isomers **12a–c** which did not contain halogen[22] (Scheme 3). The dehalogenation of the N(2)-nucleosides which occurred under aqueous alkaline conditions has previously been discussed.[22] For these reasons, the nucleobase-anion glycosylation was performed with NaH in anhydrous MeCN. Under these conditions the desired halogenated N(2)-isomers **13a**,**b** were isolated (Scheme 4).



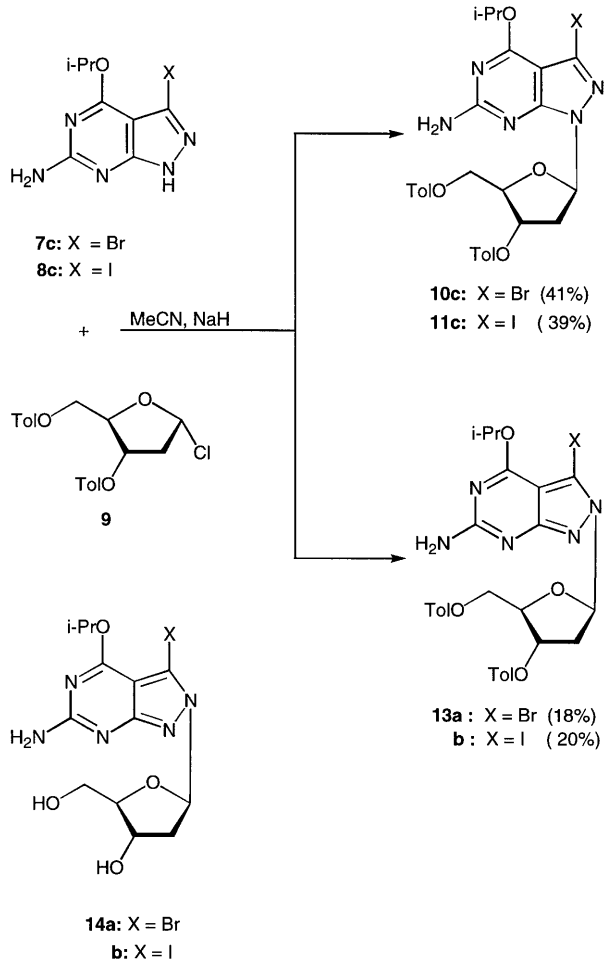
Scheme 3

The nature of the alkoxy group, as well as the presence of a halogen substituent, influences the yield of glycosylation products only marginally (Table 1). In general, the glycosylation yield is about 10% higher when the more soluble isopropoxy bases **7c** and **8c** are employed. As the N(2)-regioisomers lose their halogens the reaction yields given in Table 1 are shown for the halogenated N(1)-nucleosides as well as for the nonhalogenated N(2)-compounds. Deblocking of the N(1)-compounds **10a–c** and **11a–c** and N(2)-isomers **13a**,**b** with sodium alkoxides/alcohol furnished the alkoxy nucleosides **4a–c**, **5a–c** as well as **14a**,**b** which were purified by column chromatography. It is interesting that the dehalogenation of the N(2)-isomer did not occur under these conditions. The alkoxy nucleo-

Biographica1 Sketches

Frank Seela, born in 1939 in Dresden, studied chemistry at the University of Göttingen. There he received his Ph. D. in 1967 for synthetic work on actinomycines (H. Brockmann, sen.). He was a post-doctoral fellow at Yale University (D. M. Crothers) and received his habilitation in 1974. He spent 3 years as guest scientist at the Max-Planck-Institut für Experimentelle Medizin, Göttingen (F. Cramer). Then he joined the University of Paderborn and became Professor (C2) in 1976. He was appointed as Full Professor (C4) for Organic Chemistry at the University of Osnabrück in 1986. His research includes work on heterocycles, carbohydrates, nucleosides and oligonucleotides. The current interest is focused on the recognition of base pairs in synthetic DNA, on supramolecular assemblies, as well as oligonucleotide-hybridisation arrays. He has published more than 300 scientific papers and reviews.

Georg Becher was born in 1967 in Wissen/Sieg. He studied chemistry first at the University of Siegen and then at the University of Kassel and was awarded his Diploma in 1994 under the direction of Privatdozent I. Stahl. Since 1995 he has been working towards his Ph. D. degree under the supervision of Prof. Dr. Frank Seela at the Laboratory of Organic and Bioorganic Chemistry, University of Osnabrück.



Scheme 4

Table 1. Reaction Yields and Regioisomer Distribution of Pyrazolo[3,4-*d*]pyrimidine Nucleosides Formed by the Nucleobase Anion Glycosylation (MeCN, KOH/TDA-1)

Base	Yields (%) of Protected Nucleosides		
	N(1)	N(2)	N(1) + N(2)
6a[a]	57	13	70
7a[b]	35	14	49
8a[b]	33	18	51
7b[b]	33	13	46
8b[b]	34	16	50
6**c**	42	22	64
7c[c]	44	18	62
7c[d]	41	20	61
8c[c]	41	18	59
8c[d]	39	18	57

[a] Ref 4.
[b] Performed in suspension.
[c] Performed in solution.
[d] Performed with NaH.

sides **4c**, **5c** were then treated with 1M NaOH (60°C, 2 h) to give the target nucleosides **2** and **3**, both isolated as crystalline compounds.[25] Hydrolysis of the alkoxy functions of compounds **14a**,**b** was not successful.

Table 2. ^{13}C NMR Chemical Shifts (δ) of Pyrazolo[3,4-*d*]pyrimidines[a]

Compound [b,c]	C(3) C(7)	C(3a) C(5)	C(4)[d] C(6)	C(6)[d] C(2)	C(7a)[d] C(4	OCH_x	CH_x
6a[4]	131.6	95.4	163.5	162.0	158.9	53.1	
6b	131.7	95.6	163.3	162.7	159.0	61.6	14.5
6c	131.7	95.8	162.9	162.1	159.1	68.3	21.9
7a	118.0	95.3	163.1	162.3	159.3	53.4	
7b	118.1	95.2	162.7	162.3	159.3	61.8	14.2
7c	118.4	95.5	162.5	162.5	159.5	68.9	21.8
8a	99.2	89.1	163.1	161.9	159.0	53.3	
8b	99.0	89.2	162.8	162.0	159.0	61.6	14.2
8c	99.3	89.6	162.6	162.6	159.1	68.7	22.0

[a] Measured in DMSO-d_6.
[b] Systematic numbering.
[c] Purine numbering.
[d] Tentative.

The nucleosides described above as well as all synthetic intermediates were characterized by ^{1}H and ^{13}C NMR spectroscopy and elemental analyses (Tables 2 and 3 and experimental section). An upfield shift of the C(3) signal and a downfield shift of C(7a) is observed in the case of the N(2)-nucleosides compared to the N(1)-regioisomers. An additional upfield shift occurs on the C(3) signals in the case of the halogenated derivatives compared to the nonhalogenated counterparts. The anomeric configuration was β-D as deduced from the chemical shift differences H-C(4′) and CH_2(5′) signals from the ^{1}H NMR shift differences of the toluoylated nucleosides.[26] The UV spectra of various compounds were also measured. Generally, the UV maxima of the nonhalogenated N(2)-compounds are bathochromically shifted compared to the N(1)-isomers, a phenomenon which is also observed in the case of the related nucleosides. The halogenation results in a bathochromic shift (2–3 nm) in both series of isomers.

Next, studies on the glycosylic bond stability were performed on the nucleosides **2** and **3** and on the parent nucleoside **1** (0.5 M HCl at 25 °C) (Table 4). The reaction was followed UV spectrophotometrically by the decrease of the UV absorption. The half-life of hydrolysis of the brominated nucleoside **2** was 44 minutes (λ = 254 nm) while the iodinated compound **3** showed a half-life of 47 minutes (λ = 248 nm). These hydrolysis rates are considerably slower than for the nonhalogenated 8-aza-7-deaza-2′-deoxyguanosine (**1**; τ = 4 min, λ = 251 nm)[4, 27] and also than that of 2′-deoxyguanosine (τ = 10.6 min). Apparently, the halogen substituents exert a -I effect on the bases thereby reducing the basicity of the heterocycle. Thus the electron-withdrawing halogen substituents decrease the concentration of the protonated nucleosides and their hydrolyses are retarded. This explanation is supported by the lower pK_a values of compounds **2** and **3** (pK_a below 0) compared to **1** (pK_a = 0.5). A similar observation has been made in the case of 8-halogenated purine 2′,3′-dideoxyribonucleosides.[28]

It has been shown in the case of 7-deazapurine 2′-deoxyribonucleosides that a 7-substituent exerts stereoelectronic effects on the puckering of the sugar moiety: electron-

Table 3. ^{13}C NMR Chemical Shifts (δ) of Pyrazolo[3.4-*d*]pyrimidine 2′-Deoxyribonucleosides[a]

Compound	C(3)	C(3a) C(7)	C(4)$_b$ C(5)	C(6)$_b$ C(6)	C(7a)$_b$ C(2)	OCH^x C(4)	CH^x	C(1′)	C(2′)	C(3′)	C(4′)	C(5′)
2	122.0	98.4	158.1	156.3	156.5	–	–	83.1	37.6	70.8	87.4	62.4
3	101.9	93.7	157.5	155.1	155.8	–	–	83.2	37.7	70.9	87.5	62.4
4a	119.1	96.0	163.1	162.4	158.5	53.8	–	83.2	37.5	70.8	87.4	62.3
4b	119.2	96.0	163.1	162.3	158.5	53.8	14.2	83.2	37.5	70.8	87.4	62.4
4c	119.3	96.2	162.5	162.5	158.6	69.2	21.6	83.2	37.5	70.8	87.4	62.4
5a	100.0	90.8	163.0	162.2	158.1	53.6	–	83.3	37.5	70.9	87.4	62.4
5b	100.0	90.8	163.0	162.2	158.1	53.6	14.2	83.2	37.6	70.8	87.4	62.3
5c	100.0	90.9	162.5	162.1	158.1	69.0	21.7	83.2	37.6	70.9	87.4	62.4
10a	119.8	96.2	163.2	162.5	158.7	53.8	–	83.4	34.8	74.9	81.3	64.0
10b	119.9	96.2	163.4	162.5	158.7	62.4	14.2	83.4	34.8	74.9	81.3	64.0
10c	120.0	96.3	162.6	162.5	158.7	69.2	21.6	83.4	34.8	74.9	81.3	64.0
10d	132.5	96.6	162.8	162.1	158.1	68.6	21.6	83.4	34.9	74.9	80.9	64.0
11a	100.2	91.5	163.3	162.1	158.3	53.6	–	83.5	34.8	75.1	81.3	64.1
11b	100.2	91.5	163.3	162.1	158.3	62.2	14.3	83.5	34.8	75.1	81.3	64.1
11c	100.2	91.7	162.6	162.3	158.3	69.0	21.6	83.4	34.8	75.0	81.3	64.1
12a	124.5	97.9	165.0	161.5	163.4	53.2	–	89.9	36.7	74.3	81.9	64.1
12b	124.5	97.9	165.0	161.5	163.4	62.2	14.2	89.9	36.7	74.3	81.9	64.1
12c	124.5	98.3	164.2	161.6	163.4	68.6	21.6	89.9	36.6	74.8	81.8	64.1
13a	108.2	99.2	163.7	161.7	162.4	63.8	21.6	87.1	35.9	74.4	81.8	63.8
13b	103.8	89.2	164.0	161.3	163.5	63.9	21.6	87.1	36.3	74.5	81.7	63.9
14a	108.0	98.9	163.8	161.6	162.3	69.0	21.6	88.5	–[c]	71.0	87.1	62.4
14b	103.3	89.2	163.9	161.2	163.3	69.0	21.6	89.3	–[c]	71.2	88.5	62.4

[a] Measured in DMSO-d_6 at 298 K.
[b] Tentative.
[c] Superimposed by DMSO.

withdrawing substituents drive the N ⇔ S equilibrium towards N and the conformational equilibrium about the C(4′)–C(5′) bond is biased toward $\gamma^{(+)g}$.[29] These data were obtained in D_2O on the basis of vicinal ^3J [^{1}H, ^{1}H] coupling constants (PSEUROT 6.2).[30, 31] Applying the pseudorotational analysis to 8-aza-7-deaza-2′-deoxyguanosine (**1**) as well as to its 7-bromo derivative, 2N-conformer populations of 36% and 37% were calculated.[32] These values are about 10% higher than those of 2′-deoxyguanosine. This suggests that the N-8 has a similar influence on the sugar puckering as an electron-withdrawing 7-substituent in pyrrolo[2,3-*d*]pyrimidine 2′-deoxynucleosides.[29] The influence of the 7-halogen substituents becomes low in the case of 8-aza-7-deazanucleosides. Interestingly, the single crystal X-ray analysis of 8-aza-7-deaza-7-bromo-2′deoxyguanosine (**2**) reveals also an N ($^3T_2$)-type sugar pucker as it is preferred in solution.[32] This is different to most other 2′-deoxyribonucleosides which favor S ($^2T_3$)-conformation.

Table 4. Half-Life Values (τ) of Proton-Catalyzed Hydrolysis of the Glycosylic Bond of Halogenated Pyrazolo[3,4-*d*]pyrimidine 2′-Deoxyribonucleosides[a]

	G[d]	$c^7z^8G_d$	$Br^7c^7z^8G_d$	$I^7c^7z^8G_d$
$k \times 10^2$ (min^{-1})	6.5	13.9	1.6	1.5
τ (min)[b]	10.6	4	44	47
λ (nm)	–	251	254	248

[a] Determined UV spectrophotometrically.
[b] In 0.5 N HCl at 20 °C.

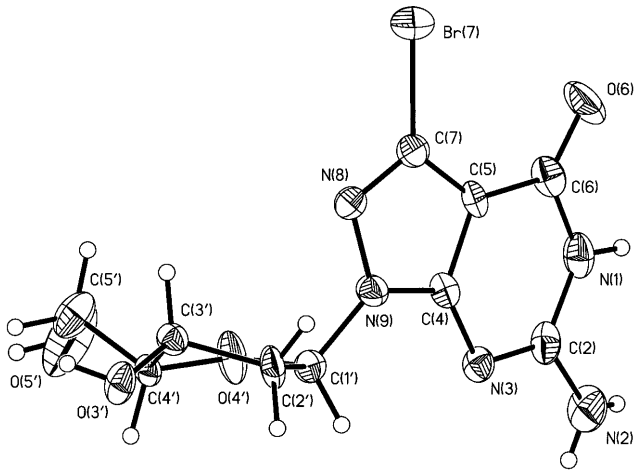


Figure. Molecular structure of 6-amino-3-bromo-1-(2′-deoxy-β-D-*erythro*-pentofuranosyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-one (**2**) taken from the X-ray analysis[33]

Another interesting feature concerns the conformation of the *N*-glycosylic bond of the base. As has been shown for 8-azapurine nucleosides, coulomb repulsion between nonbonding electron pairs of O(4′) and N-8 drives the conformation into the high-anti range ($\chi \cong -90°$).[34] The same is true for the nucleosides **2** and **3**. It will be interesting to see if the incorporation of such 2′-deoxynucleosides into oligodeoxynucleotides will result in the formation of the so-called "vertical" DNA which has been reported for oligomers containing nucleotides with a covalent link between C(8) of the base and the C-2′ position of the sugar moiety.[35]

Flash chromatography (FC): at 0.4 bar on silica gel 60 H (Merck, Darmstadt, Germany). TLC: aluminum sheets silica gel 60 F_{254} (0.2 mm, Merck, Germany). TLC Scanning: CS-930 TLC scanner (Shimadzu, Japan). Solvent systems for FC and TLC: CH_2Cl_2/MeOH 98:2 (A), CH_2Cl_2/MeOH 95:5 (B), CH_2Cl_2/MeOH 9:1 (C), CH_2Cl_2/acetone 98:2 (D), CH_2Cl_2/acetone 95:5 (E).

UV spectra were measured with a 150-20 spectrophotometer (Hitachi, Japan). NMR spectra: AC-250 and AMX-500 spectrometers (Bruker, Germany); δ values are in ppm downfield from internal TMS (^{1}H, ^{13}C). mp: Büchi-SMP-20 apparatus (Büchi, Switzerland); uncorrected. Microanalyses were performed by Mikroanalytisches Labor Beller (Göttingen, Germany).

6-Amino-4-ethoxy-1*H*-pyrazolo[3,4-*d*]pyrimidine (6b):
A solution of 6-amino-4-chloro-1*H*-pyrazolo[3,4-*d*]pyrimidine[4] (6.8 g, 0.04 mol) in 1 M NaOEt in EtOH (100 mL) was refluxed for 1 h. Upon cooling, NaCl was precipitated with Et_2O (100 mL) and was filtered off. The filtrate was neutralized with 96% AcOH and evaporated to dryness. The residue was dissolved in MeOH. The reaction product precipitated as pale yellow needles by addition of ice-cold water. Recrystallization (aq MeOH) yielded colorless needles (5.0 g, 70%); mp 213 °C; TLC (C): R_f 0.6.
UV (MeOH): λ (ε) = 244 (5400), 276 nm (7100).
^{1}H NMR (DMSO-d_6): δ = 2.33 (t, J = 5.8 Hz, CH_3); 4.41 (q, J = 7.0 Hz, CH_2); 6.55 (s, NH_2); 7.76 [s, H-C(3)]; 12.82 (s, NH).
Anal. Calcd for $C_7H_9N_5O$ (179.2): C 46.92, H 5.06, N 39.09. Found: C 46.80, H 5.18, N 39.11.

6-Amino-4-isopropoxy-1*H*-pyrazolo[3,4-*d*]pyrimidine (6c):
As described for **6b**, with 6-amino-4-chloro-1*H*-pyrazolo[3,4-*d*]pyrimidine (3.2 g, 18.9 mmol) for 1 h in 1 M i-PrONa in i-PrOH (100 mL); Recrystallization (aq MeOH) yielded colorless needles (2.8 g, 77%); mp 176 °C; TLC (C): R_f 0.6.
UV (MeOH): λ (ε) = 244 (5600), 276 nm (7400).
^{1}H NMR (DMSO-d_6): δ = 1.30 [d, J = 5.8 Hz, $(CH_3)_2$] ; 5.42–5.47 (m, OCH); 6.52 (s, NH_2); 7.73 [s, H-C(3)]; 12.78 (s, NH).
Anal. Calcd for $C_8H_{11}N_5O$ (193.2): C 49.73, H 5.74, N 36.25. Found: C 49.73, H 5.74, N 36.48.

6-Amino-3-bromo-4-methoxy-1*H*-pyrazolo[3,4-*d*]pyrimidine (7a):
To a suspension of 6a (1.0 g, 6.1 mmol) in 1,2-dichloroethane (100 mL), NBS (1.2 g, 6.7 mmol) was added. After heating under reflux for 2.5 h, the solvent was evaporated to yield an orange-colored solid which was washed with water (2 × 100 mL), filtered, and dissolved in MeOH. Decolorization with charcoal, filtration, and addition of ice-cold water gave a yellowish precipitate. Recrystallization (aq MeOH) yielded colorless needles (815 mg, 55%); mp >23 °C (d); TLC (C): R_f 0.6.
UV (MeOH): λ (ε) = 248 (5900), 277 nm (7100).
^{1}H NMR (DMSO-d_6): δ = 3.69 (s, OCH_3); 6.82 (s, NH_2); 13.1 (s, NH).
Anal. Calcd for $C_6H_6N_5BrO$ (244.1): C 29.53, H 2.48, N 28.70. Found: C 29.82, H 2.48, N 28.46.

6-Amino-3-bromo-4-ethoxy-1*H*-pyrazolo[3,4-*d*]pyrimidine (7b):
As described for 7a, with **6b** (1.0 g, 5.6 mmol) and NBS (1.1 g, 6.2 mmol, 1.5 h). Recrystallization (aq MeOH) yielded colorless needles (780 mg, 54%); mp 221 °C (d); TLC (C): R_f 0.6.
UV (MeOH): λ (ε) = 248 (5600), 277 nm (7000).
^{1}H NMR (DMSO-d_6): δ = 1.38 (t, J = 5.9 Hz, CH_3); 4.62 (q, J = 6.4 Hz, OCH_2); 6.99 (s, NH_2); 13.05 (s, NH).
Anal. Calcd for $C_7H_8N_5BrO$ (258.1): C 32.58, H 3.12, N 27.14. Found: C 32.64, H 3.15, N 27.07.

6-Amino-3-bromo-4-isopropoxy-1*H*-pyrazolo[3,4-*d*]pyrimidine (7c):
A mixture of **6c** (1.0 g, 5.2 mmol) and NBS (1.0 g, 5.6 mmol, 1.5 h) was halogenated analogously to **7a**. Recrystallization (aq MeOH) yielded colorless needles (1.1 g, 78%); mp 231°C; TLC (C): R_f 0.7.
UV (MeOH): λ (ε) = 248 (6000), 276 nm (7100).
^{1}H NMR (DMSO-d_6): δ = 1.32 [d, J = 6.4 Hz, $(CH_3)_2$]; 5.41 (m, OCH); 6.77 (s, NH_2); 13.0 (s, NH).
Anal. Calcd for $C_8H_{10}N_5BrO$ (272.1): C 35.31, H 3,70, N 25.74. Found: C 35.58, H 3.81, N 25.54.

6-Amino-3-iodo-4-methoxy-1*H*-pyrazolo[3,4-*d*]pyrimidine (8a):
Analogously to **7a**, with **6a** (1.0 g, 6.1 mmol) and NIS (2.0 g, 9.1 mmol, 9 h). Recrystallization (aq MeOH) yielded colorless needles (870 mg, 49%); mp > 230°C(d); TLC (C): R_f 0.7.
UV (MeOH): λ (ε) = 248 (5900), 276 nm (7700).
^{1}H NMR (DMSO-d_6): δ = 3.98 (s, OCH_3); 6.75 (s, NH_2); 13.11 (s, NH).
Anal. Calcd for $C_6H_6N_5IO$ (291.1): C 24.76, H 2.08, N 24.06. Found: C 24.76, H 2.16, N 24.09.

6-Amiuo-4-ethoxy-3-iodo-1*H*-pyrazolo[3,4-*d*]pyrimidine (8b):
As described for **7a**, with **6b** (1.0 g, 5.6 mmol) and NIS (1.9 g, 8.5 mmol, 9 h). Recrystallization (aq MeOH) yielded slightly yellowish needles (890 mg, 52%); mp > 230°C; TLC (C): R_f 0.6.
UV (MeOH): λ (ε) = 249 (5900), 277 nm (7500).
^{1}H NMR (DMSO-d_6): δ = 1.37 (t, J = 5.8 Hz, CH_3); 4.44 (q, J = 6.4 Hz, OCH_2); 6.7 (s, NH); 13.08 (s, NH).
Anal. Calcd for $C_7H_8N_5IO$ (305.1): C 27.56, H 2.64, N 22.96. Found: C 27.69, H 2.76, N 22.84.

6-Amino-3-iodo-4-isopropoxy-1*H*-pyrazolo[3,4-*d*]pyrimidine (8c):
A mixture of **6c** (1.0 g, 5.2 mmol) and NIS (1.3 g, 5.8 mmol, 2h) was halogenated analogously to **7a**. Recrystallization (aq MeOH) yielded slightly yellowish needles (1.16 g, 70%); mp 223 °C; TLC (C): R_f 0.7.
UV (MeOH): λ (ε) = 248 (5800), 276 nm (7500).
^{1}H NMR (DMSO-d_6): δ = 1.33 [d, J = 6.4 Hz, $(CH_3)_2$]; 5.39 (m, OCH); 6.68 (s, NH_2); 13.10 (s, NH).
Anal. Calcd for $C_8H_{10}N_5IO$ (319.1): C 30.11, H 3.16, N 21.95. Found: C 30.27, H 3.11, N 21.86.

G1ycosylation of 4-Alkoxy-6-amino-1*H*-pyrazolo[3,4-*d*]pyrimidines 7a–8c in the Presence of Powdered KOH/TDA-1; General Procedure:
Powdered KOH (1.24g, 22 mmol) and the 4-alkoxy-6-amino-1*H*-pyrazolo[3,4-*d*]pyrimidines (**7a–c** or **8a–c**) (5.5 mmol) were stirred in anhyd MeCN (100 mL). The suspension was stirred for 15 min at r.t. Then TDA-1 (tris[2-(2-methoxyethoxy)ethyl]amine; 200 µL, 0.6 mmol) was added and stirring was continued for another 15 min. 2-Deoxy-3,5-di-*O*-(*p*-toluoyl)-*α*-D-*erythro*-pentofuranosyl chloride (**9**)[24] (2.56 g, 6.6 mmol) was then added in portions. After 20 min insoluble material was filtered off and the solvent was evaporated. The resulting foam was applied to FC (silica gel; column 15 × 6 cm, solvent D followed by E) and separated in two zones in all cases. The faster migrating zone was always the N(1)-isomer, the slower migrating one contained the N(2)-compound.

6-Amino-1-[2′-deoxy-3′5 -di-O-*(*p-*toluoyl)-β*-D-erythro-*pentofuranosyl]-4-isopropoxy-1*H-*pyrazolo[3,4-*d*]*pyrimidine* (**10d**):
This compound is made in analogy with the above experiment, but starting from **6c**. Colorless foam (1.3 g, 42%); TLC (D): R_f 0.43.
UV (MeOH): λ (ε) = 241 (39000), 274 nm (11500).
^{1}H NMR (DMSO-d_6): δ = 1.33 [d, J = 6.2 Hz, $(CH_3)_2$], 2.36, 2.38 (2s, 2Ar-CH_3); 2.68 [m, H_α-(C2′)]; 3.21 [m, H_β-(C2′)]; 4.45 [m, 2H-(C5′), H-(C4′)]; 5.48 (m, OCH); 5.80 [m, H-(C3′)]; 6.60 [‘t’, J = 6.2 Hz, H-(C1′)]; 6.68 (s, NH_2); 7.28–7.92 (4d, J = 8.1 Hz, $2C_6H_4$); 7.90 [s, H-(C3)].
Anal. Calcd for $C_{29}H_31N_5O_6$ (545.6): C 63.84, H 5.73, N 12.84. Found: C 63.75, H 5.77, N 12.89.

6-Amino-2-[2′-deoxy-3′,5′-di-O-*(*p-*toluoyl)-β*-D-erythro-*pentofuranosyl]-4-isopropoxy-1*H-*pyrazolo[3,4-*d*]*pyrimidine* (**12c**):
Colorless foam (680 mg, 22%); TLC (B): R_f 0.53.
UV (MeOH): λ (ε) = 240 nm (36100), 283 (8900), 296 nm (8700).
^{1}H NMR (DMSO-d_6): δ = 1.33 [d, J = 6.2 Hz, $(CH_3)_2$], 2.36, 2.38 (2s,

2Ar-CH_3); 2.74 [m, H_α-(C2′)]; 3.10 [m, H_β-(C2′)]; 4.50 [m, 2H-(C5′), H-(C4′)]; 5.47 (m, OCH); 5.83 [m, H-(C3′)]; 6.39 [′t, *J* = 6.2 Hz, H-(C1′)]; 6.86 (s, NH_2); 7.28–7.92 (4d, *J* = 8.1 Hz, $2C_6H_4$); 7.90 [s, H-(C3)].
Anal. Calcd for $C_{29}H_{31}N_5O_6$ (545.6): C 63.84, H 5.73, N 12.84. Found: C 63.73, H 5.70, N 12.84.

6-Amino-3-bromo-1-[2′-deoxy-3′,5′-di-O-*(*p-*toluoyl)-β-*D-erythro-*pentofuranosyl]-4-methoxy-1*H-*pyrazolo[3,4-*d*]pyrimidine* (**10a**):
Amorphous solid (1.15 g, 35%); TLC (D): R_f 0.33.
UV (MeOH): λ (ε) = 242 (36300), 276 nm (10000).
^{1}H NMR (DMSO-d_6): δ = 2.39, 2.41 (2s, 2Ar-CH_3); 2.56 [m, H_α-(C2′)]; 3.17 [m, H_β-(C2′)]; 4.00 (s, OCH_3); 4.45–4.49 [m, 2H-(C5); H-(C4′)]; 5.73 [m, H-(C3)]; 6.55 [′t′, *J* = 5.7 Hz, H-(C1′)] ; 7.12 (s, NH_2); 7.34–7.93 (4d, *J* = 8.1 Hz, $2C_6H_4$).
Anal. Calcd for $C_{27}H_{26}N_5BrO_6$ (596.4): C 54.37, H 4.39, N 11.74. Found: C 54.24, H 4.38, N 11.55.
From the second zone a colorless, amorphous solid (**12a**, 460 mg, 14%) was isolated.
UV (MeOH): λ (ε) = 240 nm (34200) [Lit.[4] λ (ε) = 239 nm (33500)].

6-Amino-1-[2′-deoxy-3′,5′-di-O-*(*p-*toluoyl)-β-*D-erythro-*pentofuranosyl]-3-iodo-4-methoxy-1*H-*pyrazolo[3,4-*d*]pyrimidine* (**11a**):
Colorless, amorphous solid (1.17 g, 33%); TLC (D): R_f 0.33.
UV (MeOH): λ (ε) = 242 (36500), 276 nm (11000).
^{1}H NMR (DMSO-d_6): δ = 2.39, 2.41 (2s, 2Ar-CH_3); 2.68 [m, H_α-(C2′)] ; 3.20 [m, H_β-(C2′)]; 4.02 (s, OCH_3); 4.45–4.51 [m, H-(C5′); H-(C4′)]; 5.73 [m, H-(C3′)]; 6.55 [′t′, *J* = 6.7 Hz, H-(C1′)]; 7.01 (s, NH_2); 7.36–7.96 (4d, *J* = 8.1 Hz, $2C_6H_4$).
Anal. Calcd for $C_{27}H_{26}N_5IO_6$ (643.4): C 50.40, H 4.07, N 10.88. Found: C 50.48, H 4.22, N 10.84.
From the second main zone amorphous **12a** (640 mg, 18%) was obtained (see above).

6-Amino-3-bromo-1-[2′-deoxy-3′,5′-di-O-*(*p-toluoyl*)-β-*D-erythro-*pentofuranosyl]-4-ethoxy-1*H-*pyrazolo[3,4-*d*]pyrimidine* (**10b**):
From the fast migrating zone **10b** was isolated as a colorless, amorphous solid (1.1 g, 33%); TLC (D): R_f 0.33.
UV (MeOH): λ (ε) = 242 (35500), 277 nm (10500).
^{1}H NMR ($CDCl_3$): δ = 1.36 (t, *J* = 7.1 Hz, CH_3); 2.36, 2.38 (2s, 2Ar-CH_3); 2.66 [m, H_α-(C2′)] ; 3.17 [m, H_β-(C2′)]; 4.35–4.49 [m, OCH_2, 2H-(C5′); H-(C4′)]; 5.73 [m, H-(C3′)]; 6.53 [′t′, *J* = 6.7 Hz, H-(C1′)]; 6.80 (s, NH_2); 7.23–7.91 (4d, *J* = 8.1 Hz, $2C_6H_4$).
Anal. Calcd for $C_{28}H_{28}N_5BrO_6$ (610.5): C 55.09, H 4.62, N 11.47. Found: C 54.93, H 4.77, N 11.34.

6-Amino-2-[2′-deoxy-3′,5′-di-O-*(*p-toluoyl*)-β-*D-erythro-*pentofuranosyl]-4-ethoxy-1*H-*pyrazolo[3,4-*d*]pyrimidine* (**12b**):
From the slower migrating zone a colorless foam of **12b** (440 mg, 13%) was isolated; TLC (B): R_f 0.36.
UV (MeOH): λ (ε) = 283 (7700), 296 nm (8200).
^{1}H NMR (DMSO-d_6): δ = 1.33 (t, *J* = 7.0 Hz, CH_3); 2.34, 2.38 (2s, 2Ar-CH_3); 2.73 [m, H_α-(C2′)]; 3.09 [m, H_β-(C2′)]; 4.39–4.56 [m, OCH_2, 2H-(C5′); H-(C4′)] ; 5.82 [m, H-(C3′)]; 6.39 [′t′, *J* = 5.6 Hz, H-(C1′)]; 6.58 (s, NH_2); 7.25–7.91 (4d, *J* = 8.1 Hz, $2C_6H_4$); 8.65 [s, H-(C3)].
Anal. Calcd for $C_{28}H_{29}N_5O_6$ (531.6): C 63.27, H 5.50, N 13.17. Found: C 63.43, H 5.66, N 13.06.

6-Amino-1-[2′-deoxy-3′,5′-di-O-*(*p-*toluoyl)-β-*D-erythro-*pentofuranosyl]-4-ethoxy-3-iodo-1*H-*pyrazolo[3,4-*d*]pyrimidine* (**11b**):
Compound **11b** was isolated as a colorless amorphous solid (1.23 g, 34%); TLC (D): R_f 0.33.
UV (MeOH): λ (ε) = 241 (35500) 277 nm (9800).
^{1}H NMR ($CDCl_3$): δ = 1.43 (t, *J* = 7.2 Hz, CH_3); 2.38, 2.41 (2s, 2Ar-CH_3); 2.55 [m, H_α-(C2′)]; 3.49 [m, H_β-(C2′)]; 4.43–4.57 [m, OCH_2, 2H-(C5′); H-(C4′)]; 5.76 [m, H-(C3′)]; 6.63 [′t′, *J* = 7.2 Hz, H-(C1′)]; 6.80 (s, NH_2); 7.23–7.91 (4d, *J* = 8.1 Hz, $2C_6H_4$).
Anal. Calcd for $C_{28}H_{28}N_5IO_6$ (657.5): C 51.15, H 4.29, N 10.65. Found: C 50.99, H 4.26, N 10.51.
From the second main zone amorphous **12b** (580 mg, 16%) was isolated (see above).

6-Amino-3-bromo-1-[2′-deoxy-3′,5′-di-O-*(*p-*toluoyl)-β-*D-erythro-*pentofuranosyl]-4-isopropoxy-1*H-*pyrazolo[3,4-*d*]pyrimidine* (**10c**):
Colorless foam (1.5 g, 44%); TLC (D): R_f 0.44.
UV (MeOH): λ (ε) = 240 (39000), 277 nm (10100).
^{1}H NMR (DMSO-d_6): δ = 1.33 (d, *J* = 6.2 Hz, CH_3), 2.36, 2.38 (2s, 2Ar-CH_3); 2.65 [m, H_α-(C2′)]; 3.15 [m, H_β-(C2′)]; 4.44 [m, 2H-(C5′), H-(C4′)]; 5.43 (m, OCH); 5.74 [m, H-(C3′)]; 6.52 [′t′, *J* = 6.2 Hz, H-(C1′)]; 7.06 (s, NH_2); 7.28–7.92 (4d, *J* = 8.1 Hz, $2C_6H_4$).
Anal. Calcd for $C_{29}H_{30}N_5BrO_6$ (624.5): C 55.78, H 4.84, N 11.21, found: C 56.01, H 4.86, N 10.93.
From the second zone **12c** (630 mg, 18%) was isolated as a colorless foam (see above).

6-Amino-1-[2′-deoxy-3′,5′-di-O-*(*p-toluoyl*)-β-*D-erythro-*pentofuranosyl]-3-iodo-4-isopropoxy-1*H-*pyrazolo[3,4-*d*]pyrimidine* (**11c**):
Colorless foam (1.4 g, 41%); TLC (D): R_f 0.44.
UV (MeOH): λ (ε) = 239 (39600), 277 nm (9600).
^{1}H NMR (DMSO-d_6): δ = 1.33 [d, *J* = 6.2 Hz, $(CH_3)_2$]; 2.36, 2.38 (2s, 2Ar-CH_3); 2.67 [m, H_α-(C2′)]; 3.15 [m, H_β-(C2′)]; 4.50 [m, 2H-(C5′),H-(C4′)]; 5.43 (m, OCH); 5.73 [m, H-(C3′)]; 6.55 [′t′, *J* = 5.9 Hz, H-(C1′)]; 7.05 (s, NH_2); 7.28–7.92 (4d, *J* = 8.1 Hz, $2C_6H_4$).
Anal. Calcd for $C_{29}H_{30}N_5IO_6$ (671.5): C 51.87, H 4.50, N 10.43. Found: C 52.05, H 4.62, N 10.37.
From the second zone **12c** (650 mg, 18%) was isolated (see above).

Glycosylation of Halogenated 6-Amino-4-isopropoxy-1*H*-pyrazolo[3,4-*d*]pyrimidines (7c, 8c) in the Presence of NaH; General Procedure:
To a solution of **7c** or **8c** (5.5 mmol) in MeCN (60 mL) NaH (97%, 150 mg, 6.1 mmol) was added. After stirring at r.t. for 10 min the halogenose **9** (2.56 g, 6.6 mmol) was introduced and the stirring was continued for 20 min. The mixture was filtered and the filtrate was evaporated. The further workup was performed as described for the glycosylation using KOH/TDA-1.

6-Amino-3-bromo-2-[2′-deoxy-3′,5′-di-O-*(*p-*toluoyl)-β-*D-erythro-*pentofuranosyl]-4-isopropoxy-1*H-*pyrazolo[3,4-*d*]pyrimidine* (**13a**):
The fast migrating zone furnished compound **10c** (1.4 g, 41%). From the second zone a colorless foam of **13a** (680 mg, 17%) was isolated; TLC (B): R_f 0.5.
UV (MeOH): λ (ε) = 240 (37500), 285 (7900), 302 nm (7500).
^{1}H NMR (DMSO-d_6): δ = 1.38 [d, *J* = 5.7 Hz, $(CH_3)_2$], 2.36, 2.39 (2s, 2Ar-CH_3); 2.77 [m, H_α-(C2′)]; 3.29 [m, H_β-(C2′)]; 4.39, 4.50 [m, 2H-(C5′)]; 4.57 [m, H-(C4′)]; 5.46 (m, OCH); 5.91 [m, H-(C3′)]; 6.53 [′t′, *J* = 6.2 Hz, H-(C1′)]; 6.61 (s, NH_2); 7.28–7.92 (4d, *J* = 8.1 Hz, $2C_6H_4$).
Anal. Calcd for $C_{29}H_{30}N_5BrO_6$ (624.5): C 55.78, H 4.84, N 11.21, found: C 55.89, H 4.80, N 11.24.

6-Amino-2-[2′-deoxy-3′,5′-di-O-*(*p-*toluoyl)-β-*D-erythro-*pentofuranosyl]-3-iodo-4-isopropoxy-1*H-*pyrazolo[3,4-*d*]pyrimidine* (**13b**):
The fast migrating zone furnished compound **11c** (1.44 g, 39%); from the second zone **13b** (610 mg, 18%) was isolated both as colorless foams; TLC (B): R_f 0.5.
UV (MeOH): λ (ε) = 240 (37000), 285 (7900), 302 nm (7800).
^{1}H NMR (DMSO-d_6): δ = 1.34 [d, *J* = 6.2 Hz, $(CH_3)_2$]; 2.34, 2.38 (2s, 2Ar-CH_3); 2.75 [m, H_α-(C2′)]; 3.25 [m, H_β-(C2′)]; 4.32–4.56 [m, 2H-(C5′),H-(C4′)]; 5.41 (m, OCH); 5.92 [m, H-(C3′)]; 6.47 [′t′, *J* = 5.9 Hz, H-(C1′)]; 6.79 (s, NH_2); 7.26–7.92 (4d, *J* = 8.1 Hz, $2C_6H_4$).
Anal. Calcd for $C_{29}H_{30}N_5IO_6$ (671.5): C 51.87, H 4.50, N 10.43. Found: C 51.96, H 4.53, N 10.54.

6-Amino-3-bromo-1-[2′-deoxy-β-D-*erythro*-pentofuranosyl]-4-methoxy-1*H*-pyrazolo[3,4-*d*]pyrimidine (4a); Typical Procedure:
A solution of **10a** (500 mg, 0.84 mmol) in 0.1 M NaOMe in MeOH (50 mL) was stirred for 30 min at 40°C. Then, the solution was adsorbed on silica gel, loaded onto the top of a silica gel column (10 ×

4 cm) and chromatographed; elution with A followed by B gave a main zone which yielded a colorless solid after evaporation. Crystallization (water) gave **4a** as colorless needles (200 mg, 66%); mp 173 °C; TLC (B): R_f 0.2.
UV (MeOH): λ (ε) = 277 nm (8500).
^{1}H NMR (DMSO-d_6): δ = 2.16 [m, H_α-C(2′)]; 2.67 [m, H_β-C(2′)] ; 3.35, 3.48 [m, CH_2(5′)] ; 3.75 [m, H-C(4′)]; 3.97 (s, OCH_3); 4.34 [m, H-C(3′)]; 4.69 [t, *J* = 5.4 Hz, OH-C(5′)]; 5.22 [d, *J* = 4.1 Hz, OH-C(3′)]; 6.59 [‘t’, *J* = 6.4 Hz, H-C(1′)], 7.06 (s, NH_2).
Anal. Calcd for $C_{11}H_{14}N_5BrO_4$ (360.2): C 36.70, H 3.92, N 19.44. Found: C 36.82, H 3.90, N 19.55.

6-Amino-1-[2′-deoxy-β-D-*erythro*-pentofuranosyl]-3-iodo-4-methoxy-1*H*-pyrazolo[3,4-*d*]pyrimidine (5a):
Analogously to **4a**, with **11**a (500 mg, 0.78 mmol) in 0.1 M NaOMe in MeOH (50 mL, 30 min, 40°C). Crystallization (water) gave **5a** as colorless needles (220 mg, 69%); mp 161 °C; TLC (B): R_f 0.2.
UV (MeOH): λ (ε) = 277 nm (8400).
^{1}H NMR (DMSO-d_6): δ = 2.16 [m, H_α-C(2′)] ; 2.67 [m, H_β-C(2′)]; 3.35, 3.48 [m, CH_2(5′)] ; 3.75 [m, H-C(4′)]; 3.97 (s, OCH_3); 4.34 [m, H-C(3′)]; 4.69 [t, *J* = 5.4 Hz, OH-C(5′)]; 5.22 [d, *J* = 4.1 Hz, OH-C(3′)]; 6.59 [‘t’, *J* = 6.4 Hz, H-C(1′)], 7.06 (s, NH_2).
Anal. Calcd for $C_{11}H_{14}N_5IO_4$ (407.2): C 32.45, H 3.47, N 17.20. Found: C 32.61, H 3.55, N 17.17.

6-Amino-3-bromo-1-[2′-deoxy-β-D-*erythro*-pentofuranosyl]-4-ethoxy-1*H*-pyrazolo[3,4-*d*]pyrimidine (4b):
Compound **10b** (250 mg, 0.41 mmol) in 0.1 M NaOEt in EtOH (30 mL, 30 min, 40°C) was deprotected analogously to **4a**. A colorless solid (80 mg, 52%) was isolated; mp 171°C; TLC (B): R_f 0.2. (MeOH)
UV: λ (ε) = 276 nm (8600).
^{1}H NMR (DMSO-d_6): δ = 1.33 (t, *J* = 7.0 Hz, CH_3); 2.16 [m, H_α-(C2′)] ; 2.67 [m, H_β-(C2′)]; 3.35, 3.47 [m, CH_2(5′)] ; 3.74 [m, H-C(4′)]; 4.34 [m, H-C(3′)] ; 4.62 (q, *J* = 6.4 Hz, OCH_2); 4.69 [t, *J* = 5.6 Hz, OH-C(5′)]; 5.22 [d, *J* = 4.2 Hz, OH-C(3′)]; 6.55 [‘t’, *J* = 6.7 Hz, H-(C1′)] ; 6.80 (s, NH_2).
Anal. Calcd for $C_{12}H_{16}N_5BrO_4$ (374.2): C 38.52, H 4.31, N 18.72. Found: C 38.58, H 4.47, N 18.66.

6-Amino-1-[2′-deoxy-β-D-*erythro*-pentofuranosyl]-4-ethoxy-3-iodo-1*H*-pyrazolo[3,4*d*]pyrimidine (5b):
As described for **4a**, with **11b** (200 mg, 0.3 mmol) in 0.1 M NaOEt in EtOH (20 mL, 30 min, 40°C). A colorless solid (65 mg, 51%) was isolated; mp 164°C; TLC (B): R_f 0.2.
UV (MeOH): λ (ε) = 276 nm (8400).
^{1}H NMR (DMSO-d_6): δ = 1.33 (t, *J* = 7.0 Hz, CH_3); 2.15 [m, H_α-(C2′)]; 2.68 [m, H_β-(C2′)] ; 3.35, 346 [m, CH_2(5′)] ; 3.76 [m, H-C(4′)] ; 4.34 [m, H-C(3′)] ; 4.62 (q, *J* = 6.4 Hz, OCH_2); 4.69 [t, *J* = 5.6 Hz, OH-C(5′)]; 5.22 [d, *J* = 4.2 Hz, OH-C(3′)]; 6.57 [‘t’, *J* = 6.7 Hz, H-(C1′)] ; 6.80 (s, NH_2).
Anal. Calcd for $C_{12}H_{16}N_5IO_4$ (421.2): C 34.22, H 3.83, N 16.63. Found: C 34.30, H 3.95, N 16.64.

6-Amino-3-bromo-1-[2′-deoxy-β-D-*erythro*-pentofuranosyl]-4-isopropoxy-1*H*-pyrazolo[3,4-*d*]pyrimidine (4c):
Analogously to **4a**, with **10c** (5 g, 8 mmol) in 0.1 M i-PrONa in i-PrOH (200 mL, 3 h, 40°C). Crystallization (water) gave colorless needles (2.15 g, 69%); mp 181 °C; TLC (B): R_f 0.2.
UV (MeOH): λ (ε) = 277 nm (8700).
^{1}H NMR (DMSO-d_6): δ = 1.33 [d, *J* = 6.8 Hz, $(CH_3)^2$]; 2.18 [m, H_α-C(2′)]; 2.67 [m, H_β-C(2′)]; 3.35, 347 [m, CH_2(5′)]; 3.74 [m, H-C(4′)]; 4.34 [m, H-C(3′)]; 4.69 [t, *J* = 5.7 Hz, OH-C(5′)]; 5.22 [d, *J* = 4.3 Hz, OH-C(3′)]; 5.39 (m, OCH); 6.33 [‘t’, *J* = 6.5 Hz, H-C(1′)], 6.99 (s, NH_2).
Anal Calcd for $C_{13}H_{18}N_5BrO_4$ (388.2): C 40.22, H 4.67, N 18.04. Found: C 40. 17, H 4.63, N 18.01.

6-Amino-3-bromo-2-[2′-deoxy-β-D-*erythro*-pentofuranosyl]-4-isopropoxy-2*H*-pyrazolo[3,4-*d*]pyrimidine (14a):
As described for **4a**, with **13a** (200 mg, 0.32 mmol) in 0.1 M i-PrONa in i-PrOH (20 mL, 30 min, 40°C). A colorless solid (71 mg, 57%) was isolated; mp 171°C; TLC (C): R_f 0.44.
^{1}H NMR (DMSO-d_6): δ = 1.36 [d, *J* = 5.2 Hz, $(CH_3)_2$]; 2.29 [m, H_α-C(2′)]; 2.82 [m, H_β-C(2′)]; 3.51, 355 [m, CH_2(5′)]; 3.87 [m, H-C(4′)]; 4.48 [m, H-C(3′)]; 4.79 [t, *J* = 5.7 Hz, OH-C(5′)] ; 5.30 [d, *J* = 3.9 Hz, OH-C(3′)]; 5.45 (m, OCH); 6.34 [‘t’, *J* = 6.5 Hz, H-C(1′)], 6.53 (s, NH_2).
Anal Calcd for $C_{13}H_{18}N_5BrO_4$ (388.2): C 40.22, H 4.67, N 18.04. Found: C 40.41, H 4.81, N 17.96

6-Amino-1-[2′-deoxy-β-D-*erythro*-pentofuranosyl]-3-iodo-4-isopropoxy-1*H*-pyrazolo[3,4-*d*]pyrimidine (5c):
Compound **11c** (5 g, 7.4 mmol) in 0.1 M i-PrONa in i-PrOH (200 mL, 3 h, 40°C) was deprotected analogously to **4a**. Crystallization (water) gave **5c** as solid (2.4 g, 75%); mp 190°C; TLC (B): R_f 0.2.
UV (MeOH): λ (ε) = 277 nm (8700).
^{1}H NMR (DMSO-d_6): δ = 1.33 [d, *J* = 6.5 Hz, $(CH_3)_2$]; 2.14 [m, H_αC(2′)]; 2.69 [m, H_β-C(2′)]; 3.35, 3.44 [m, CH_2(5′)]; 3.74 [m, H-C(4′)]; 4.34 [m, H-C(3′)]; 4.7 [t, *J* = 5.7 Hz, OH-C(5′)]; 5.21 [d, *J* = 4.3 Hz, OH-C(3′)]; 5.68 (m, OCH); 6.33 [‘t’ *J* = 6.5 Hz, H-C(1′)], 7.26 (s, NH_2).
Anal. Calcd for $C_{13}H_{18}N_5IO_4$ (435.2): C 35.88, H 4.17, N 16.09. Found: C 35.69, H 4.17, N 1602.

6-Amino-2-[2′-deoxy-β-D-*erythro*-pentofuranosyl]-3-iodo-4-isopropoxy-2*H*-pyrazolo[3,4-*d*]pyrimidine (14b):
As described for **4a**, with **13b** (200 mg, 0.3 mmol) in 0.1 M i-PrONa in i-PrOH (20 mL, 30 min, 40°C). A colorless solid (79 mg, 61%) was isolated; mp 168 °C; TLC (C) R_f 0.44.
^{1}H NMR (DMSO-d_6): δ = 1.37 [d, *J* = 6.2 Hz, $(CH_3)_2$]; 2.29 [m, H_α-C(2′)]; 2.80 [m, H_β-C(2′)] ; 3.51, 355 [m, CH_2(5′)] ; 3.87 [m, H-C(4′)]; 4.48 [m, H-C(3′)]; 4.79 [t, *J* = 5.9 Hz, OH-C(5′)] ; 5.29 [d, *J* = 4.5 Hz, OH-C(3′)]; 5.45 (m, OCH); 6.33 [‘t’, *J* = 6.5 Hz, H-C(1′)], 6.45 (s, NH_2).
Anal. Calcd for $C_{13}H_{18}N_5IO_4$ (435.2): C 35.88, H 4.17, N 16.09. Found: C 35.74, H 4.07, N 15.92.

6-Amino-3-bromo-1-[2′-deoxy-β-D-*erythro*-pentofuranosyl]-1*H*-pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-one (2):
A solution of **4c** (1.8 g, 4.6 mmol) in 1 M NaOH (80 mL) was stirred for 2 h at 60°C and then neutralized with 96% AcOH under cooling. The resulting precipitate was filtered off and recrystallized (water) yielding colorless needles (1.4 g, 89%); mp 221 °C; TLC (C): R_f 0.18.
UV (MeOH): λ (ε) = 257 nm (10600).
1H NMR (DMSO-d_6): δ = 2.12 [m, H_β-C(2′)]; 2.62 [m, H_α-C(2′)]; 3.35, 3.44 [m, CH_2(5′)]; 3.73 [m, H-C(4′)]; 4.31 [m, H-C(3′)] ; 4.71 [t, *J* = 5.7 Hz, OH-C(5′)]; 5.19 (d, *J* = 4.3 Hz, OH-C(3′)] ; 6.23 [‘t’, *J* = 6.5 Hz, H-C(1′)], 7.01 (s, NH_2); 10.79 (s; NH).
Anal. Calcd for $C_{10}H_{12}N_5BrO_4$ (346.1): C 34.70, H 3.49, N 20.23. Found: C 34.50, H 3.56, N 20.12.

6-Amino-1-[2′-deoxy-β-D-*erythro*-pentofuranosyl]-3-iodo-1*H*-pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-one (3):
As described for **2**, with **5c** (1.7 g, 3.9 mmol) in 1 M NaOH (80 mL, 2 h, 60°C). The resulting precipitate was filtered off and recrystallized (water) yielding colorless needles (1.3 g, 87%); mp 221 °C; TLC (C): R_f 0.18.
UV (MeOH): λ (ε) = 258 nm (10800).
^{1}H NMR (DMSO-d_6): δ = 2.15 [m, H_α-C(2)]; 2.66 [m, H_β-C(2′)]; 3.35, 3.47 [m, CH_2(5′)] ; 3.77 [m, H-C(4′)]; 4.36 [m, H-C(3′)]; 4.7 [t, *J* = 5.7 Hz, OH-C(5′)]; 5.2 [d, *J* = 4.3 Hz, OH-C(3′)]; 6.24 [‘t’, *J* = 6.5 Hz, H-C(1′)], 6.81 (s, NH_2); 10.79 (s, NH).
Anal. Calcd for $C_{10}H_{12}N_5IO_4$ (393.1): C 30.55, H 3.10, N 17.52. Found: C 30.50, H 3.21, N 17.21

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