Synthesis of 7-alkynylated 8-aza-7-deaza-2′-deoxyadenosines *via* the Pd-catalysed cross-coupling reaction

Frank Seela * and Matthias Zulauf

Laboratorium für Organische und Bioorganische Chemie, Institut für Chemie, Universität Osnabrück, Barbarastr. 7, D-49069 Osnabrück, Germany

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The synthesis of 7-alkynylated 8-aza-7-deazaadenine (pyrazolo[3,4-*d*]pyrimidine) 2′-deoxyribonucleosides is described. Nucleobase anion-glycosylation of 8-aza-7-deaza-7-iodo-6-methoxypurine (**15**) with 2-deoxy-3,5-di-*O*-(*p*-toluoyl)-α-D-*erythro*-pentofuranosyl chloride (**16**) furnishes the 8-aza-7-deaza-7-iodo-6-methoxypurine N^1-β-D-2′-deoxyribonucleoside **17a** as the main product (38% yield). After detoluoylation of products **17a** and **17b**[27] (⟶ **19a,b**) and amination the 7-bromo and the 7-iodo derivatives of 8-aza-7-deaza-2′-deoxyadenosine (compounds **2b,c**) were obtained. Compound **2b** served as the starting material for a series of 7-alkynyl- or 7-alkenyl-8-aza-7-deazaadenine 2′-deoxynucleosides **3**–**13** by employing the Pd^0/Cu^I-catalysed cross-coupling reaction. The 7-halogenated or 7-alkynylated nucleosides show a more stable glycosylic bond than does 8-aza-7-deaza-2′-deoxyadenosine (**2a**).

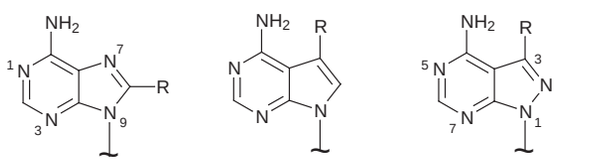
Introduction

The stability of DNA-duplexes or DNA–RNA hybrids is of decisive importance for antisense oligonucleotides, of primer DNA-hybrids carrying reporter groups or otherwise modified DNA molecules.[1] The incorporation of lipophilic residues can confer increased duplex stability[2,3] and a more efficient take-up of oligonucleotides into cells.[4] Several positions of the nucleobase, the sugar and the phosphate residues were subject to such structural modifications.[5]

It has been shown that introduction of lipophilic substituents at the 5-position of pyrimidine bases has the expected favourable properties, *e.g.* form stable DNA-duplex structures and allow an efficient incorporation of the corresponding triphosphates into DNA by DNA-polymerases.[6,7] Recently, the incorporation of 5-alkynylated 2′-deoxyuridines into oligonucleotides has been described, leading to duplexes with an increased stability.[8] Steric constraints induced by the substituents at the pyrimidine position 6 or the purine positions 2 or 8 (**A**) (purine numbering is used throughout the general part) destabilize the duplex structure significantly.[8–11]

It has been reported that substituents at the 7-position of a 7-deazapurine (pyrrolo[2,3-*d*]pyrimidine) base (**B**) is sterically well accommodated in a DNA-duplex,[12–14] and is therefore an ideal attachment site for reporter groups. Within the series of related bases the 8-aza-7-deazapurines (pyrazolo[3,4-*d*]-pyrimidines) (**C**) represent the only other class of purine analogues which can be derivatized at the 7-position of the modified purine base and are capable of forming regular Watson–Crick base pairs.[15] As the DNA-duplex-stabilizing effect of 8-aza-7-deaza-2′-deoxyadenosine (**2a**) itself has already been reported,[16] it was of interest to combine the properties of this heterocycle with the favourable properties of halogeno or alkyne 7-substituents.[17–19]

The synthesis of various 7-substituted 8-aza-7-deazapurine ribonucleosides including compounds **1b,c** has been reported.[20–23] Also 2'-deoxyribonucleosides carrying a 7-aminoalkyl group have been prepared.[24,25] However, these syntheses lack general applicability. As the side-chains are introduced during the annelation of the pyrimidine ring on a glycosylated pyrazole precursor, those methods are too laborious when the side-chains have to be altered. This manuscript reports on a general route for the synthesis of 8-aza-7-deaza-2′-deoxyadenosines carrying 7-alkynyl or 7-alkenyl residues (**3**–**13**). They were prepared from the 7-bromo or 7-iodo compounds **2b,c** as central intermediates *via* the Pd-catalysed cross-coupling reaction. Furthermore, the conformation of the nucleoside **2c** will be investigated in solution, and the influence of lipophilic 7-substituents on the glycosylic-bond stability will be studied.



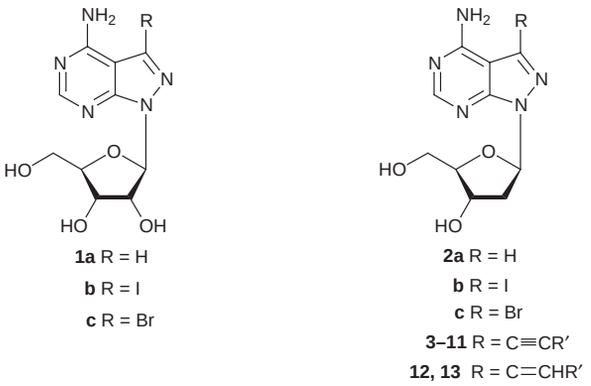
Structure of purine analogues.

Results and discussion

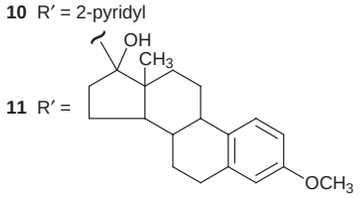
Synthesis

Earlier, the halogenation of several 8-aza-7-deazapurine bases was reported,[26] and the regioselective bromination of 8-aza-7-deaza-6-methoxypurine **14** has also been described.[27] It was found that compound **14** can also serve as starting material for the iodination which was performed with *N*-iodosuccinimide (NIS) in 1,2-dichloroethane to give the iodo compound **15** in 70% yield (Scheme 1). According to the synthesis of compound **2a**,[28] the methoxy group of compound **15** is sufficiently reactive to be displaced later by an amino substituent but will be stable during the glycosylation.[28]

Compound **15** was treated with 2-deoxy-3,5-di-*O*-(*p*-toluoyl)-α-D-*erythro*-pentofuranosyl chloride[29] (**16**) under the conditions of stereoselective nucleobase-anion glycosylation [MeCN, powdered KOH (containing 15% water) and TDA-1 {tris-[2-(2-methoxyethoxy)ethyl]amine as catalyst}].[30] The three formed nucleosides were separated by flash chromatography. The first zone furnished the iodinated N^1-isomer **17a** (38% yield), the second zone gave the iodinated N^2-isomer **18a** (11%) whereas

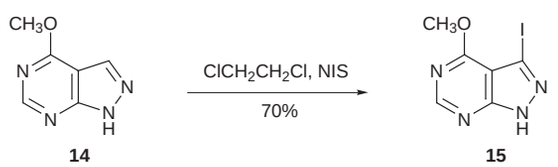


3 R′ = CH_3
4 R′ = $(CH_2)_2CH_3$
5 R′ = $(CH_2)_4CH_3$
6 R′ = cyclohexyl
7 R′ = Ph
8 R′ = $C_6H_4CH_3$-*p*-
9 R′ = C_6H_4(C≡CH)-*m*
10 R′ = 2-pyridyl

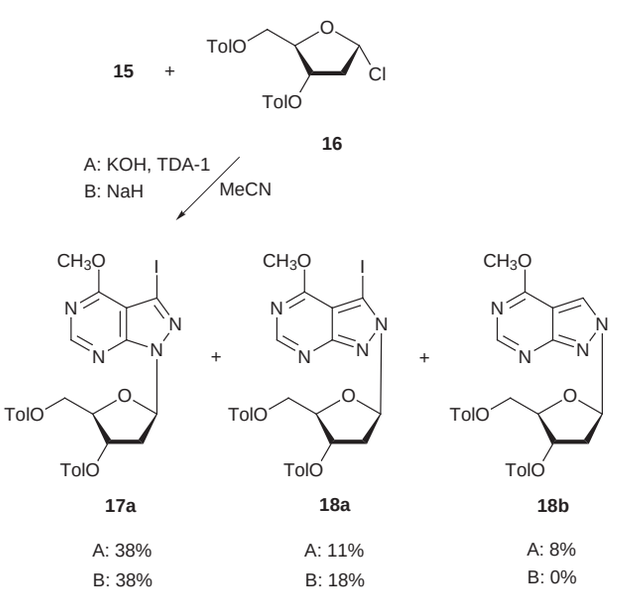


12 R′ = H
13 R′ = CO_2CH_3

7-Substituted 8-aza-7-deazaadenine 2′-deoxyribofuranosides.



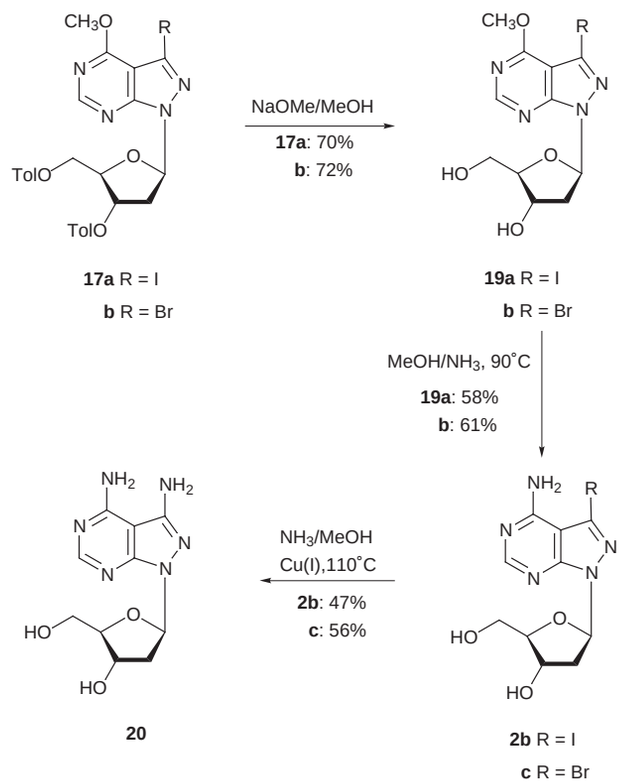
Scheme 1 Iodination of 8-aza-7-deaza-6-methoxypurine. NIS = *N*-iodosuccinimide.



Scheme 2 Glycosylation of the nucleobase **15**.

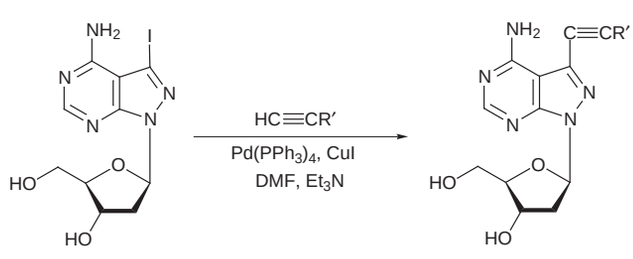
the third zone yielded the deiodinated N^2-nucleoside **18b**[28] (8%) (Scheme 2). An analogous formation of the dehalogenated nucleoside has already been observed during the glycosylation of 8-aza-7-bromo-7-deaza-6-methoxypurine performed under the same conditions.[27] Dehalogenation of the N-2 isomer **18a** occurs upon treatment of this compound with KOH (containing 15% water) in MeCN and furnishes compound **18b**. The dehalogenation is not observed when anhydrous NaH is employed. In this case, the desired 3-iodo N^1-isomer **17a** (38% yield) is formed together with the iodinated N^2-isomer **18a** (18%). According to these findings the 7-iodo- and 7-bromo-8-aza-7-deazapurine N^1-nucleosides **17a,b** are stable for further reactions while the instability of the N-2 compounds towards base restricts their application, *e.g.* as components in oligonucleotide synthesis.

The protected N^1-nucleosides **17a** and **17b**[27] were deblocked (NaOMe) to yield the nucleosides **19a,b**. Subsequently, the 4-methoxy substituent of compounds **19a,b** was displaced with methanolic ammonia in an autoclave (90 °C) to furnish compounds **2b** and **2c**. The 7-halogeno substituents are stable against nucleophilic displacement under regular conditions. However, when the 7-bromo or 7-iodo nucleoside **2b,c** was treated with ammonia–MeOH in the presence of CuCl or CuBr the 7-amino derivative **20** was formed (Scheme 3). A similar reaction takes place with the 7-bromoribonucleoside **1c**.[21]



Scheme 3 Synthetic pathway to the 7-halogeno- or 7-amino-modified 8-aza-7-deaza-2′-deoxyadenosines.

Next, the iodo compound **2b** served as starting material for the synthesis of a series of 7-substituted 8-aza-7-deaza-2′-deoxyadenosines **3**–**11** (Scheme 4). They are carrying alkynyl, alkynylaryl and alkynylheteroaryl groups as well as the bulky 17α-ethynylestradiol 3-*O*-methyl ether and were prepared to



Scheme 4 Synthetic pathway to the acetylenically modified 8-aza-7-deaza-2′-deoxyadenosines.

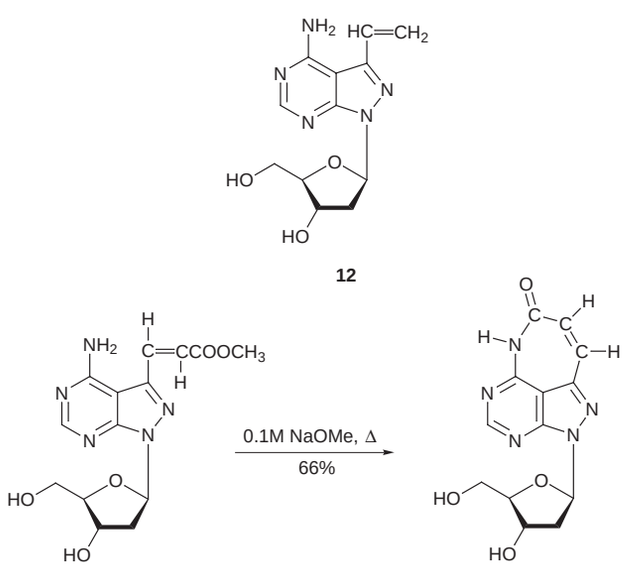
Table 1 ^{13}C NMR chemical shifts (δ_C) of 8-aza-7-deazaadenine 2′-deoxyribofuranosides, measured in $(CD_3)_2SO$

[a] / [b]	C(3) / C(7)	C(3a) / C(5)	C(4) / C(6)	C(6) / C(2)	C(7a) / C(4)	OMe	C(1′)	C(2′)	C(3′)	C(4′)	C(5′)
2a	133.9	101.3	158.9	156.9	154.5		84.9	38.8	72.0	88.4	63.3
2b	91.0	103.5	157.6	156.2	154.0		84.0	37.9	70.9	87.7	62.3
2c	118.9	99.8	157.3	156.9	154.5		84.0	37.8	70.8	87.7	62.3
14	131.1	101.2	163.2	154.5	154.1	53.6					
15	89.4	105.4	163.2	155.5	156.3	54.4					
17a	90.1	106.5	163.1	155.5	155.1	54.0	84.4	35.1	74.4	81.4	63.5
18a	82.2	108.3	[c]	155.6	160.9	54.3	90.1	35.9	74.2	82.2	63.5
19a	90.4	106.4	163.2	155.8	155.0	54.5	84.3	37.9	70.8	87.8	62.2
19b	118.8	102.5	163.2	156.4	155.3	54.6	84.3	37.9	70.7	87.8	62.1

[a] Systematic numbering. [b] Purine numbering. [c] Superimposed by C=O.

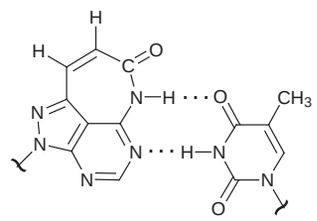
study the effect of those side-chains with regard to DNA duplex stability and as oligonucleotide components to enhance DNA cell delivery. The cross-coupling reactions were performed under palladium-catalysed conditions.[31,32] Although it is possible to use the bromo derivative **2c** instead of the iodo compound **2b** the reaction requires higher temperature [see formation of compound **7** from iodide **2b** at rt (49% yield) or from bromide **2c** at 70 °C (45% yield)].

Apart from the alkynes, the cross-coupling reaction can also be performed with alkenes which are useful as side-chains for DNA-labelling. By using iodide **2b** and tributylvinylstannane as coupling reagents the ethenyl nucleoside **12** was obtained. The coupling reaction on iodide **2b** was also performed with methyl acrylate. This furnished compound **13**. Similarly to earlier observations[32,33] only one geometrical stereoisomer (*E*) was formed. Treatment of acrylate **13** with NaOMe–MeOH led to an intramolecular cyclization resulting in the formation of the tricyclic compound **21**, which is derivative of a new heterocyclic ring system (Scheme 5). A similar ring-closure and configurational change has already been observed with 5-[(2-ethoxycarbonyl)ethenyl] pyrimidines[34] and the corresponding 7-deazaadenine 2′-deoxyribonucleosides.[35]



Scheme 5 Structure and synthetic pathway for alkenylated 8-aza-7-deaza-2′-deoxyadenosines.

When compound **21** is elaborated to become a constituent of oligonucleotides it is expected that base pairing with dT will be strengthened (base pair **I**). This results from the better proton-donor properties of the acylated amino group and had already been observed for tricyclic 2′-deoxycytidine analogues[36] and other acylated nucleosides.[37] Furthermore, one can expect that the new donor–acceptor motif (C=O, NH, =N) is able to form a



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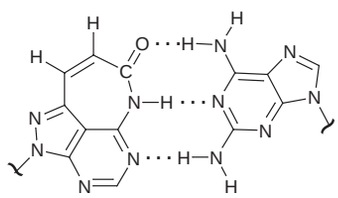

II

Two possible base pairs of compound **21** with pyrimidine and purine bases.

tridentate purine–purine base pair with 2,6-diaminopurine (base pair **II**).

All new compounds were characterized by microanalyses and/or FAB-mass spectra, ^1H NMR and ^{13}C NMR (Tables 1,2) spectra. For the assignment of ^{13}C NMR signals gated-decoupled as well as heteronuclear correlation spectra were used. The assignment of the ^{13}C NMR signals was supported by the literature.[28,38] Upon iodination of compound **14** a strong upfield shift of carbon-3 is observed which is due to a positive mesomeric effect of the iodo atom of the product (compound **15**). The position of glycosylation was derived from the ^{13}C NMR spectra. According to Table 1 an upfield shift of carbon-3 is observed for the N-2 nucleoside **18a** in comparison with the N^1-isomer **17a** which shows similar chemical shifts to the free nucleobase **15**. The β-D configuration was confirmed by the ^1H NMR spectra using the shift differences of 4′-H and 5′-H_2 of the toluoylated compounds.[39] The *E*-stereochemistry of compound **13** was deduced from the coupling constants [^3J(H,H) = 15.7 Hz] of the olefinic protons. In the case of the ring-closure product **21** the olefinic protons have to be 'cis' (*Z*) [^3J(H,H) = 12 Hz]. Similar coupling constants have already been observed for 5-[(2-ethoxycarbonyl)ethenyl] pyrimidines[34] and the corresponding 7-deazaadenine 2′-deoxyribonucleosides.[35]

The 6-amino group of the halogeno nucleosides **2b,c** as well as of the alkynyl derivatives **3**–**11** shows two separate signals (*syn* and *anti* near δ 7 and 8) in the ^1H NMR spectra (see Experimental section). In contrast, the unsubstituted 8-aza-7-deaza-2′-deoxyadenosine **2a** and the alkenyl compounds **12** and **13** as well as the diamino derivative **20** do not show this behaviour (*e.g.*, **2a**; one signal at δ 7.75). Several factors could be responsible for this phenomenon: (i) rotation around the C–NH_2 bond is hindered sterically by the 7-substituent; (ii)

Table 2 ^{13}C NMR chemical shifts (δ_C) of 7-alkynylated and other 8-aza-7-deazaadenine 2′-deoxyribofuranosides, measured in $(CD_3)_2SO$

[a] / [b]	C(3) C(7)	C(3a) C(5)	C(4) C(6)	C(6) C(2)	C(7a) C(4)	C≡C	C(1′)	C(2′)	C(3′)	C(4′)	C(5′)
3	127.5	100.8	157.8	156.7	153.7	93.0, 71.3	84.0	38.0	71.1	87.8	62.5
4	127.2	[c]	157.7	156.5	153.6	96.5, 72.2	84.0	37.9	70.9	87.7	62.3
5	127.3	100.8	157.7	156.5	153.6	96.7, 72.1	84.0	37.9	70.9	87.7	62.3
6	127.2	100.0	157.8	156.6	153.6	*c*, 72.2	84.0	37.8	70.9	87.6	62.3
7	126.6	100.8	157.7	156.7	153.8	93.5, 80.7	84.2	37.9	70.9	87.7	62.3
8	126.7	100.8	157.7	156.6	153.8	93.8, 80.2	84.1	37.9	70.9	87.8	62.3
9	126.3	100.8	157.7	156.7	153.8	92.2, 82.4, 81.7, 81.4	84.2	37.9	70.9	87.8	62.3
10	124.2	101.2	157.7	156.8	153.8	93.1, 79.5	84.2	38.0	70.9	87.8	62.3
11	126.7	101.1	157.7	156.6	153.6	99.9, 76.3	84.3	37.9	70.8	87.7	62.2
12	141.8	98.2	158.2	155.9	154.8	[d] 127.5, 118.4	84.1	38.2	71.3	87.9	62.6
13	139.0	99.0	158.0	156.0	155.0	[d] 134.2, 121.1	84.1	38.2	71.0	87.9	62.3
20	148.0	90.6	157.9	156.2	154.6		82.8	37.5	71.3	87.1	62.8
21	141.4	103.9	157.9	155.0	153.6	[d] 131.2, 129.3	84.5	37.9	70.8	87.8	62.1

[a] Systematic numbering. [b] Purine numbering. [c] No signal. [d] Olefinic carbons.

Table 3 HPLC retention time (t_R) and half-life value (τ) of proton-catalysed glycosylic bond hydrolysis of 8-aza-7-deazaadenine 2′-deoxyribonucleosides

Compd[a]	t_R/min [b]	τ/h [b,c]
dA	10.0	[d]
$z^8c^7A_d$ **2a**	10.6	24
$z^8c^7I^7A_d$ **2b**	18.5	132
$z^8c^7Br^7A_d$ **2c**	17.0	250
$z^8c^7pry^7A_d$ **3**	20.2	65
$z^8c^7phy^7A_d$ **7**	34.8	110
$z^8c^7NH_2{}^7A_d$ **20**	8.1	4

[a] pry = prop-1-ynyl, phy = phenylethynyl. [b] Determined with an RP-18 HPLC column [gradient *I* (see Experimental section)] at 260 nm. [c] In 0.5 M HCl at 20 °C. [d] Not determined.

hydrogen bonding might occur between one proton of the 6-amino group and the electron-rich 7-substituent; (iii) the electron-withdrawing effect of the 7-alkynyl or 7-halogeno substituents might reduce the bond length between carbon-6 and the amino group. As the bond length between C(6) and the nitrogen of the 6-amino group is similar for compounds **2a** (132.6 pm [40]), **2b** (132.4 pm [40]) and **2c** (132.9 pm [40]) an electronic effect is excluded. Either steric factors or hydrogen bonding between the exocyclic amino proton and the electron pairs of a 7-halogeno substituent or a 7-alkynyl group could be responsible for the separation of the amino protons into a '*syn*' and an '*anti*' signal. Indeed, a deviation of the 6-amino group as well as of the 7-halogen substituent from the plane of the heterocycle is observed, indicating steric repulsion. Also, the distance between one amino-group proton and the 7-bromo substituent (284.5 pm [40]) is in the range of a hydrogen bond.

Properties of nucleosides

As it was hoped to incorporate the 7-substituted nucleosides into oligonucleotides the stability of the glycosylic bond is of importance because an acidic step is necessary for the removal of protecting 4,4′-dimethoxytrityl (DMT) groups. Hydrolysis of the nucleosides **2b,c,3,7** and **20** was performed in 0.5 M HCl (Table 3 and Experimental section) and was followed by reversed phase HPLC. According to Table 3 the halogeno derivatives **2b,c** or alkynyl nucleosides **3,7** show increased retention times due to their higher lipophilicity compared with the parent 8-aza-7-deaza-2′-deoxyadenosine (**2a**).

The hydrolysis rates of the halogenated (**2b,c**) or alkynylated (**3,7**) nucleosides are considerably lower than for the unsubstituted compound **2a** (Table 3). Here, the bromo nucleoside is the most stable compound. The diamino compound **20** is the most labile derivative. From the hydrolysis data it can be concluded that the ease of protonation of the base moieties controls the hydrolysis. Electron-withdrawing substituents stabilize the molecule as protonation becomes more difficult.

Table 4 ^3J (H,H) Coupling constants and conformer populations of the sugar moieties for calculation of pseudorotational parameters [a,b]

	^3J(H,H)/Hz					Conformation[c]	
Compd	1′,2′$_\beta$	1′,2′$_\alpha$	2′$_\alpha$,3′	2′$_\beta$,3′	3′,4′	%*N*	%*S*
$z^8c^7A_d$ **2a** [44]	6.55	6.70	4.00	6.45	3.70	37	63
$z^8c^7Br^7A_d$ **2c**	6.40	6.40	4.50	6.60	3.30	39	61
$z^8c^7pry^7A_d$ **3**	6.60	6.65	4.05	6.20	3.65	37	63

[a] Measured at 303 K in D_2O. [b] r.m.s. ≤ 0.4 Hz, $|\Delta J_{max}| \leq 0.5$ Hz. [c] For definition of *N* and *S*, see refs. 41 and 42.

Recently, it was shown that 7-substituents of 7-deazapurine nucleosides reveal stereoelectronic effects on the conformation of the sugar moiety: electron-withdrawing substituents drive the N⟺S equilibrium towards the N-conformer.[41] On the basis of vicinal ^3J (H,H) coupling constants (Table 4 and 'PSEUROT 6.2' [42,43]) the N-conformer population of 8-aza-7-deaza-2′-deoxyadenosine (**2a**) was measured to be 37%.[44] Compared with 7-deaza-2′-deoxyadenosines (24–29% N-type) [44] the 8-aza-7-deaza-2′-deoxyadenosines exhibit a higher N-conformer population which is due to an electron deficiency caused by the electron-withdrawing effect of the nitrogen-8. The additional 7-bromo or the 7-propynyl substituents of 8-aza-7-deazaadenine nucleosides have almost no influence on the sugar conformation (**2c** = 39% N; **3** = 37% N), which is different to the situation for the corresponding 7-deazapurine nucleosides.[44] The X-ray structures of compounds **2a–c** and the incorporation of these nucleosides as well as of the alkynyl derivatives into oligonucleotides will be described elsewhere.

Experimental

General

Solvents were of laboratory grade, except those used for HPLC which were of HPLC grade. CHN analyses were performed by Mikroanalytisches Labor Beller (Göttingen, Germany). Propyne gas was purchased from ABCR (Germany). All other chemicals were supplied by Aldrich, Sigma or Fluka. NMR Spectra were measured on AC 250 or AMX 500 spectrometers (Bruker, Germany) operating at proton resonance frequencies of 250.13 MHz and 500.14 MHz (125.13 MHz for ^{13}C) respectively. Chemical shifts are in ppm relative to TMS as internal standard. *J*-Values are given in Hz. Mps were measured with a Büchi SMP-20 apparatus (Büchi, Switzerland) and are uncorrected. Positive ion Fast Atom Bombardment (FAB) mass spectra were performed by Universität Heidelberg (Germany) with 3-nitrobenzyl alcohol as matrix. UV Spectra were recorded on a U 3200 spectrometer (Hitachi, Japan). TLC was performed on aluminium sheets, silica gel 60 F_{254}, 0.2 mm layer (Merck, Germany), and column chromatography (FC) on silica

gel 60 (Merck, Germany) at 0.4 bar (4×10^4 Pa) using the following solvent systems: (A) petroleum spirit–ethyl acetate (1:1, v/v); (B) CH_2Cl_2–MeOH (95:5, v/v); (C) CH_2Cl_2–MeOH (9:1, v/v). RP-18 HPLC: 250 × 4 mm RP-18 column; Merck-Hitachi HPLC; gradient of 0.1 M $(Et_3NH)OAc$ (pH 7.0)–MeCN 95:5 (*A*) and MeCN (*B*); gradient *I*: 50 min 0–50% *B* in *A*, flow rate 1 cm^3 min^{-1}. Petroleum spirit refers to the fraction with distillation range 40–65 °C.

Determination of glycosylic bond stability. The nucleosides (0.01 mmol) were dissolved in MeOH (100 mm^3). To this solution was added 0.5 M HCl (2 cm^3) under stirring. After intervals of time, aliquots were taken and injected onto an RP-18 HPLC column (gradient *I*, UV detection at 260 nm). The half-life-times τ were determined from the decrease of the peaks of the nucleosides.

Chemical synthesis

3-Iodo-4-methoxy-1*H*-pyrazolo[3,4-*d*]pyrimidine 15. To a suspension of compound **14**[28] (1.0 g, 6.6 mmol) in 1,2-dichloroethane (50 cm^3) was added NIS (2.25 g, 10 mmol) at rt. After heating of the mixture under reflux for 30 min, the solvent was evaporated off, and the residue was subjected to FC (column 10 × 4 cm). Elution with dichloromethane–methanol (0% ⟶ 5% methanol, v/v) furnished a main zone from which crystals of the *title compound* were obtained (1.3 g, 70%), mp 201–204 °C [from CH_2Cl_2–MeOH (1:1), decomp.] (Found: C, 26.2; H, 1.9; N, 20.3. $C_6H_5IN_4O$ requires C, 26.11; H, 1.83; N, 20.30%); R_f (B) 0.4; λ_{max}(MeOH)/nm 248 (ε/dm^3 mol^{-1} cm^{-1} 6900) and 272 (5500); δ_H[250 MHz; $(CD_3)_2SO$] 4.09 (3 H, s, OCH_3), 8.50 (1 H, s, 6-H) and 14.26 (1 H, s, NH).

Nucleobase anion-glycosylation of compound 15 with the halogenose 16[29] in the presence of KOH–TDA-1 (Method A). To a suspension of compound **15** (1.5 g, 5.4 mmol) in MeCN (60 cm^3) were added KOH (85%; 500 mg, 7.6 mmol) and TDA-1 (50 mm^3) 50 at rt. After stirring the mixture for 10 min compound **16**[29] (2.5 g, 6.4 mmol) was introduced, and stirring was continued for another 30 min. Insoluble material was filtered off, and after evaporation the residue was subjected to FC (column 20 × 4 cm). Elution was performed with ethyl acetate–petroleum spirit (25–66% ethyl acetate, v/v).

*1-[2-Deoxy-3,5-di-O-(p-toluoyl)-β-D-erythro-pentofuranosyl]-3-iodo-4-methoxy-1H-pyrazolo[3,4-d]pyrimidine **17a**.* From the fast migrating main zone *compound* **17a** was isolated as needles (1.29 g, 38%), mp 149–151°C [from (A), decomp.] (Found: C, 51.6; H, 4.1; N, 9.0. $C_{27}H_{25}IN_4O_6$ requires C, 51.61; H, 4.01; N, 8.92%); R_f (A) 0.7; λ_{max}(MeOH)/nm 238 (ε/dm^3 mol^{-1} cm^{-1} 43 500) and 273 (10 000); δ_H[250 MHz; $(CD_3)_2SO$] 2.37 and 2.38 (6 H, 2 s, 2 × CH_3), 2.76 (1 H, m, 2′-H_α), 3.26 (1 H, m, 2′-H_β), 4.11 (3 H, s, OCH_3), 4.47 (2 H, m, 5′- and 5″-H), 4.55 (1 H, m, 4′-H), 5.77 (1 H, m, 3′-H), 6.79 (1 H, 't', *J* 6.3, 1′-H), 7.34, 7.91 (8 H, 2 d, *J* 7.9, 2 × C_6H_4) and 8.62 (1 H, s, 6-H).

*2-[2-Deoxy-3,5-di-O-(p-toluoyl)-β-D-erythro-pentofuranosyl]-3-iodo-4-methoxy-2H-pyrazolo[3,4-d]pyrimidine **18a**.* From the second zone was obtained title compound **18a** as a foam (376 mg, 11%) (Found: C, 51.6; H, 4.1; N, 9.1%); R_f (A) 0.5; λ_{max}(MeOH)/nm 241 (ε/dm^3 mol^{-1} cm^{-1} 30 400), 282 (6000) and 296 (6000); δ_H[250 MHz; $(CD_3)_2SO$] 2.33 and 2.38 (6 H, 2 s, 2 × CH_3), 2.84 (1 H, m, 2′-H_α), 3.27 (1 H, m, 2′-H_β), 4.08 (3 H, s, OCH_3), 4.35 (1 H, m, 5′-H), 4.48 (1 H, m, 5′-H), 4.61 (1 H, m, 4′-H), 5.93 (1 H, m, 3′-H), 6.68 (1 H, 't', *J* 6, 1′-H), 7.28 and 7.87 (8 H, 2 d, *J* 7.9, 2 × C_6H_4) and 8.58 (1 H, s, 6-H).

2-[2-Deoxy-3,5-di-O-(p-toluoyl)-β-D-erythro-pentofuranosyl]-4-methoxy-2H-pyrazolo[3,4-d]pyrimidine[28] ***18b**.* Evaporation of the slow migrating zone yielded compound **18b**[28] as a foam (220 mg, 8%), λ_{max}(MeOH)/nm 240 (ε/dm^3 mol^{-1} cm^{-1} 34 100) [lit.,[28] 242 (36 000)].

Nucleobase anion-glycosylation of compound 15 with the halogenose 16[29] in the presence of NaH (Method B). To a suspension of compound **15** (1.5 g, 5.4 mmol) in MeCN (100 cm^3) was added NaH (97%; 150 mg, 6.1 mmol). After stirring of the mixture for 10 min at rt compound **16**[29] (2.6 g, 6.6 mmol) was introduced, and stirring was continued for 30 min. The mixture was filtered and the filtrate was evaporated. Further work-up was identical with method A. The fast migrating zone furnished compound **17a** (1.28 g, 38%). From the second zone compound **18a** was isolated (610 mg, 18%).

1-(2-Deoxy-β-D-*erythro*-pentofuranosyl)-3-iodo-4-methoxy-1*H*-pyrazolo[3,4-*d*]pyrimidine 19a. Compound **17a** (1.0 g, 1.6 mmol) was stirred for 4 h with 0.4 M $NaOCH_3$ in MeOH (100 cm^3). The solution was evaporated to dryness, and the residue was subjected to FC [column 10 × 4 cm, solvent (B)]. Crystallization from MeOH yielded crystals of the *title compound* **19a** (440 mg, 70%), mp 150–151 °C (from MeOH; decomp.) (Found: C, 33.7; H, 3.5; N, 14.3. $C_{11}H_{13}IN_4O_4$ requires C, 33.69; H, 3.34; N, 14.28%); R_f (C) 0.6; λ_{max}(MeOH)/nm 277 (ε/dm^3 mol^{-1} cm^{-1} 5800); δ_H[250 MHz; $(CD_3)_2SO$] 2.31 (1 H, m, 2′-H_α), 2.79 (1 H, m, 2′-H_β), 3.50 (2 H, m, 5′- and 5″-H), 3.81 (1 H, m, 4′-H), 4.11 (3 H, s, OCH_3), 4.43 (1 H, m, 3′-H), 4.72 (1 H, t, *J* 5.6, 5′-OH), 5.31 (1 H, d, *J* 4.5, 3′-OH), 6.58 (1 H, 't', *J* 6.3, 1′-H) and 8.61 (1 H, s, 6-H).

3-Bromo-1-(2-deoxy-β-D-*erythro*-pentofuranosyl)-4-methoxy-1*H*-pyrazolo[3,4-*d*]pyrimidine 19b. Compound **17b**[27] (1.0 g, 1.7 mmol) was treated as described for the iodide **19a**. Crystallization from MeOH afforded crystals of *title bromide* **19b** (420 mg, 72%), mp 148–149 °C (from MeOH, decomp.) (Found: C, 38.8; H, 4.0; N, 16.4. $C_{11}H_{13}BrN_4O_4$ requires C, 38.28; H, 3.80; N, 16.23%); R_f (C) 0.6; λ_{max}(MeOH)/nm 247 (ε/dm^3 mol^{-1} cm^{-1} 7200) and 272 (6600); δ_H[500 MHz; $(CD_3)_2SO$] 2.32 (1 H, m, 2′-H_α), 2.80 (1 H, m, 2′-H_β), 3.52 (2 H, m, 5′- and 5″-H), 3.84 (1 H, m, 4′-H), 4.14 (3 H, s, OCH_3), 4.45 (1 H, m, 3′-H), 4.70 (1 H, t, *J* 5.0, 5′-OH), 5.30 (1 H, d, *J* 4.1, 3′-OH), 6.63 (1 H, 't', *J* 5.8, 1′-H) and 8.66 (1 H, s, 6-H).

4-Amino-1-(2-deoxy-β-D-*erythro*-pentofuranosyl)-3-iodo-1*H*-pyrazolo[3,4-*d*]pyrimidine 2b. Compound **19a** (300 mg, 0.77 mmol) was stirred at 90 °C for 3 h with a saturated (0 °C) NH_3–MeOH solution (200 cm^3) in an autoclave. The solution was evaporated to dryness and the residue was subjected to FC [column 10 × 3 cm, solvent (C)]. Crystallization from MeCN afforded the title iodide **2b** as crystals (167 mg, 58%), mp 216 °C (from MeCN, decomp.) (Found: C, 32.1; H, 3.2; N, 18.7. $C_{10}H_{12}IN_5O_3$ requires C, 31.85; H, 3.21; N, 18.57%); R_f (C) 0.4; λ_{max}(MeOH)/nm 241 (ε/dm^3 mol^{-1} cm^{-1} 7900), 262 (7300) and 284 (8900); δ_H[250 MHz; $(CD_3)_2SO$] 2.23 (1 H, m, 2′-H_α), 2.74 (1 H, m, 2′-H_β), 3.45 (2 H, m, 5′- and 5″-H), 3.80 (1 H, m, 4′-H), 4.40 (1 H, m, 3′-H), 4.76 (1 H, t, *J* 5.3, 5′-OH), 5.27 (1 H, d, *J* 4.0, 3′-OH), 6.49 (1 H, 't', *J* 6.1, 1′-H), 6.80 and 7.80 (2 H, 2 br s, NH_2) and 8.21 (1 H, s, 6-H).

4-Amino-3-bromo-1-(2-deoxy-β-D-*erythro*-pentofuranosyl)-1*H*-pyrazolo[3,4-*d*]pyrimidine 2c. Compound **19b** (300 mg, 0.87 mmol) was stirred at 90 °C for 4 h with a saturated (0 °C) NH_3–MeOH solution (200 cm^3) in an autoclave. The solution was evaporated to dryness and the residue was subjected to FC [column 10 × 3 cm, solvent (C)]. Crystallization from MeCN afforded the title bromide **2c** as crystals (175 mg, 61%), mp 214 °C (from MeCN, decomp.) (Found: C, 36.2; H, 3.7; N, 21.1. $C_{10}H_{12}BrN_5O_3$ requires C, 36.38; H, 3.66; N, 21.21%); R_f (C) 0.4; λ_{max}(MeOH)/nm 231 (ε/dm^3 mol^{-1} cm^{-1} 4700), 264 (4600) and 281 (6100); δ_H[250 MHz; $(CD_3)_2SO$] 2.24 (1 H, m, 2′-H_α), 2.74 (1 H, m, 2′-H_β), 3.45 (2 H, m, 5′- and 5″-H), 3.79 (1 H, m, 4′-H), 4.39 (1 H, m, 3′-H), 4.74 (1 H, t, *J* 5.6, 5′-OH), 5.26 (1 H, d, *J* 4.5, 3′-OH), 6.51 (1 H, 't', *J* 6.1, 1′-H), 7.0 and 7.95 (2 H, 2 br s, NH_2) and 8.23 (1 H, s, 6-H).

Pd-Catalysed cross-coupling; general procedure. *Method 1.* A suspension of 4-amino-1-(2-deoxy-β-D-*erythro*-pentofuranosyl)-3-iodo-1*H*-pyrazolo[3,4-*d*]pyrimidine **2b** (200 mg, 0.53 mmol) and CuI (20.2 mg, 0.106 mmol) in anhydrous DMF (3 cm^3) was treated with an alkyne (10 equiv.) [or alkene (10 equiv.)], anhydrous Et_3N (108 mg, 1.06 mmol), and $Pd(PPh_3)_4$ (62 mg, 0.054 mmol). The mixture was stirred under Ar at rt.

After the reaction was complete (TLC), the mixture was diluted with MeOH–CH_2Cl_2 (5 cm^3; 1:1) and Dowex 1X8 (100–200 mesh; 500 mg, HCO_3^- form) was added. After being stirred for 45 min the mixture was filtered, and the resin was washed twice with MeOH–CH_2Cl_2 (20 cm^3; 1:1). The combined filtrates were evaporated and the residue was subjected to FC (column 10 × 4 cm) using CH_2Cl_2 with an increasing amount of MeOH (2–10%) as eluent. The main zone afforded the nucleoside derivative upon evaporation.

Method 2. A suspension of bromide **2c** (200 mg, 0.61 mmol) and CuI (20.2 mg, 0.106 mmol) in anhydrous DMF (3 cm^3) was treated with an alkyne (10 equiv.), anhydrous Et_3N (108 mg, 1.06 mmol), and $Pd(PPh_3)_4$ (62 mg, 0.054 mmol) as described above except that the reaction was carried out at 70 °C.

4-Amino-1-(2-deoxy-β-D-erythro-pentofuranosyl)-3-(prop-1-ynyl)-1H-pyrazolo[3,4-d]pyrimidine ***3***. Method 1 with propyne (propyne gas was introduced into the ice-cold DMF solution until saturation; 30 min); the reaction time was 6 h; *title product* **3** was a foam (80 mg, 52%) (Found: C, 54.0; H, 5.3; N, 24.3. $C_{13}H_{15}N_5O_3$ requires C, 53.97; H, 5.23; N, 24.21%); R_f (C) 0.4; λ_{max}(MeOH)/nm 248 (ε/dm^3 mol^{-1} cm^{-1} 9700) and 286 (9700); δ_H[500 MHz; $(CD_3)_2SO$] 2.17 (3 H, s, CH_3), 2.24 (1 H, m, 2′-H_α), 2.76 (1 H, m, 2′-H_β), 3.45 (2 H, m, 5′- and 5″-H), 3.82 (1 H, m, 4′-H), 4.43 (1 H, m, 3′-H), 4.74 (1 H, t, *J* 5.7, 5′-OH), 5.25 (1 H, d, *J* 4.5, 3′-OH), 6.53 (1 H, 't', *J* 6.3, 1′-H), 6.68 and 7.95 (2 H, 2 br s, NH_2) and 8.23 (1 H, s, 6-H).

4-Amino-1-(2-deoxy-β-D-erythro-pentofuranosyl)-3-(pent-1-ynyl)-1H-pyrazolo[3,4-d]pyrimidine ***4***. Method 1 with pent-1-yne; the reaction time was 7 h; *title product* **4** was a foam (96 mg, 57%) (Found: C, 56.9; H, 6.1; N, 22.0. $C_{15}H_{19}N_5O_3$ requires C, 56.77; H, 6.03; N, 22.07%); R_f (C) 0.5; λ_{max}(MeOH)/nm 248 (ε/dm^3 mol^{-1} cm^{-1} 9700) and 286 (9500); δ_H[500 MHz; $(CD_3)_2SO$] 1.00 (3 H, t, *J* 7.3, CH_3), 1.63 (2 H, sextet, *J* 7.3, CH_2CH_3), 2.20 (1 H, m, 2′-H_α), 2.53 (2 H, t, *J* 7.2, CH_2), 2.73 (1 H, m, 2′-H_β), 3.48 (2 H, m, 5′- and 5″-H), 3.80 (1 H, m, 4′-H), 4.41 (1 H, m, 3′-H), 4.75 (1 H, t, *J* 5.7, 5′-OH), 5.24 (1 H, d, *J* 4.5, 3′-OH), 6.49 (1 H, 't', *J* 6.4, 1′-H), 6.68 and 7.95 (2 H, 2 br s, NH_2) and 8.22 (1 H, s, 6-H).

4-Amino-1-(2-deoxy-β-D-erythro-pentofuranosyl)-3-(hept-1-ynyl)-1H-pyrazolo[3,4-d]pyrimidine ***5***. Method 1 with hept-1-yne; the reaction time was 6 h; title product **5** was a foam (77 mg, 42%) [Found: (FAB) $(M + H)^+$, 346.3. $C_{17}H_{23}N_5O_3$ requires *M*, 345.4]; R_f (C) 0.5; λ_{max}(MeOH)/nm 249 (ε/dm^3 mol^{-1} cm^{-1} 9300) and 287 (9700); δ_H[500 MHz; $(CD_3)_2SO$] 0.89 (3 H, t, *J* 7.2, CH_3), 1.35 (4 H, m, $CH_2CH_2CH_3$), 1.60 (2 H, quintet, *J* 7.1, $CH_2CH_2C{\equiv}C$), 2.24 (1 H, m, 2′-H_α), 2.52 (2 H, m, $CH_2C{\equiv}C$, superimposed by DMSO), 2.77 (1 H, m, 2′-H_β), 3.44 (2 H, m, 5′- and 5″-H), 3.81 (1 H, m, 4′-H), 4.42 (1 H, m, 3′-H), 4.74 (1 H, t, *J* 5.6, 5′-OH), 5.24 (1 H, d, *J* 4.5, 3′-OH), 6.53 (1 H, 't', *J* 6.4, 1′-H), 6.60 and 8.00 (2 H, 2 br s, NH_2) and 8.23 (1 H, s, 6-H).

4-Amino-3-[2-(cyclohexyl)ethynyl]-1-(2-deoxy-β-D-erythro-pentofuranosyl)-1H-pyrazolo[3,4-d]pyrimidine ***6***. Method 1 with cyclohexylacetylene; the reaction time was 4 h; title product **6** was a foam (91 mg, 48%) [Found: H, 6.3; N, 19.3; *m*/*z* (FAB) $(M + H)^+$, 358.3. $C_{18}H_{23}N_5O_3$ requires H, 6.49; N, 19.60%; *M*, 357.4]; R_f (C) 0.5; λ_{max}(MeOH)/nm 252 (ε/dm^3 mol^{-1} cm^{-1} 11 200) and 287 (11 100); δ_H[500 MHz; $(CD_3)_2SO$] 1.29–1.92 (10 H, several m, 10 × H-cyclohexyl), 2.24 (1 H, m, 2′-H_α), 2.78 (2 H, m, 2′-H and CH-cyclohexyl), 3.45 (2 H, m, 5′- and 5″-H), 3.81 (1 H, m, 4′-H), 4.42 (1 H, m, 3′-H), 4.75 (1 H, t, *J* 5.5, 5′-OH), 5.25 (1 H, d, *J* 4.2, 3′-OH), 6.45 and 8.00 (2 H, 2 br s, NH_2), 6.53 (1 H, 't', *J* 6.3, 1′-H) and 8.24 (1 H, s, 6-H).

4-Amino-1-(2-deoxy-β-D-erythro-pentofuranosyl)-3-(2-phenylethynyl)-1H-pyrazolo[3,4-d]pyrimidine ***7***. Method 1 with phenylacetylene; the reaction time was 7 h; compound **7** was a foam (92 mg, 49%).

Method 2: the reaction time was 6 h at 70 °C; *title compound* **7** was a foam (84 mg, 45%) (Found: C, 61.7; H, 4.8; N, 20.0. $C_{18}H_{17}N_5O_3$ requires C, 61.53; H, 4.88; N, 19.93%); R_f (C) 0.5; λ_{max}(MeOH)/nm 272 (ε/dm^3 mol^{-1} cm^{-1} 17 200) and 294 (19 100); δ_H[500 MHz; $(CD_3)_2SO$] 2.26 (1 H, m, 2′-H_α), 2.81 (1 H, m, 2′-H_β), 3.46 (2 H, m, 5′- and 5″-H), 3.83 (1 H, m, 4′-H), 4.44 (1 H, m, 3′-H), 4.78 (1 H, t, *J* 5.7, 5′-OH), 5.27 (1 H, d, *J* 4.5, 3′-OH), 6.58 (1 H, 't', *J* 6.4, 1′-H), 7.00 and 7.75 (2 H, 2 br s, NH_2), 7.47 and 7.74 (5 H, 2 m, Ph) and 8.27 (1 H, s, 6-H).

4-Amino-1-(2-deoxy-β-D-erythro-pentofuranosyl)-3-[2-(p-tolyl)ethynyl]-1H-pyrazolo[3,4-d]pyrimidine ***8***. Method 1 with compound **2b** (100 mg, 0.27 mmol) and *p*-tolylacetylene; the reaction time was 4 h; title product **8** was a solid (52 mg, 53%), mp 200–203 °C (decomp.) (Found: C, 61.7; H, 4.9; N, 18.5; *m*/*z* (FAB) $(M + H)^+$, 366.1. $C_{19}H_{19}N_5O_3$ requires C, 62.46; H, 5.24; N, 19.17%; *M*, 365.4); R_f (C) 0.5; λ_{max}(MeOH)/nm 245 (ε/dm^3 mol^{-1} cm^{-1} 11 700), 275 (18 400) and 297 (20 200); δ_H[500 MHz; $(CD_3)_2SO$] 2.28 (1 H, m, 2′-H_α), 2.35 (3 H, s, CH_3), 2.82 (1 H, m, 2′-H_β), 3.45 (2 H, m, 5′- and 5″-H), 3.82 (1 H, m, 4′-H), 4.44 (1 H, m, 3′-H), 4.77 (1 H, t, *J* 5.6, 5′-OH), 5.28 (1 H, d, *J* 4.4, 3′-OH), 6.57 (1 H, 't', *J* 6.3, 1′-H), 6.98 and 7.90 (2 H, 2 br s, NH_2), 7.27 (2 H, d, *J* 7.9, 2 × ArH), 7.62 (2 H, d, *J* 7.9, 2 × ArH) and 8.26 (1 H, s, 6-H).

4-Amino-1-(2-deoxy-β-D-erythro-pentofuranosyl)-3-{2-[(m-ethynyl)phenyl]ethynyl}-1H-pyrazolo[3,4-d]pyrimidine ***9***. Method 1 with *m*-diethynylbenzene; the reaction time was 3 h; *title product* **9** was a foam (88 mg, 44%) (Found: C, 64.5; H, 4.8; N, 18.5. $C_{20}H_{17}N_5O_3$ requires C, 63.99; H, 4.56; N, 18.66%); R_f (C) 0.5; λ_{max}(MeOH)/nm 248 (ε/dm^3 mol^{-1} cm^{-1} 21 900) and 295 (22 500); δ_H[500 MHz; $(CD_3)_2SO$] 2.29 (1 H, m, 2′-H_α), 2.83 (1 H, m, 2′-H_β), 3.48 (2 H, m, 5′- and 5″-H), 3.85 (1 H, m, 4′-H), 4.31 (1 H, s, C≡CH), 4.46 (1 H, m, 3′-H), 4.77 (1 H, t, *J* 5.7, 5′-OH), 5.28 (1 H, d, *J* 4.5, 3′-OH), 6.60 (1 H, 't', *J* 6.4, 1′-H), 6.98 and 7.85 (2 H, 2 br s, NH_2), 7.48–7.92 (3 H, 2 d, t, 3 × ArH), 7.92 (1 H, s, ArH) and 8.28 (1 H, s, 6-H).

4-Amino-1-(2-deoxy-β-D-erythro-pentofuranosyl)-3-[2-(2-pyridyl)ethynyl]-1H-pyrazolo[3,4-d]pyrimidine ***10***. Method 1 with (2-pyridyl)acetylene; the reaction time was 4 h; *title product* **10** was a solid (97 mg, 52%), mp 245–248 °C (decomp.) (Found: C, 57.8; H, 4.7; N, 23.7. $C_{17}H_{16}N_6O_3$ requires C, 57.95; H, 4.58; N, 23.85%); R_f (C) 0.4; λ_{max}(MeOH)/nm 298 (ε/dm^3 mol^{-1} cm^{-1} 24 200); δ_H[500 MHz; $(CD_3)_2SO$] 2.29 (1 H, m, 2′-H_α), 2.81 (1 H, m, 2′-H_β), 3.45 (2 H, m, 5′- and 5″-H), 3.82 (1 H, m, 4′-H), 4.44 (1 H, m, 3′-H), 4.75 (1 H, br, 5′-OH), 5.29 (1 H, br, 3′-OH), 6.59 (1 H, 't', *J* 6.3, 1′-H), 6.64 and 7.92 (2 H, 2 br s, NH_2), 7.48 (1 H, m, ArH), 7.91 (2 H, m, 2 × ArH), 8.29 (1 H, s, 6-H) and 8.65 (1 H, m, ArH).

4-Amino-1-(2-deoxy-β-D-erythro-pentofuranosyl)-3-[2-(17-hydroxy-3-methoxy-1,3,5[10]-estratriene-17α-yl)ethynyl]-1H-pyrazolo[3,4-d]pyrimidine ***11***. Method 1 with 17α-ethynyl-3-*O*-methylestradiol; the reaction time was 6 h; *title compound* **11** was obtained as crystals (181 mg, 61%), mp 210–212 °C (from MeOH, decomp.) (Found: C, 66.8; H, 6.7; N, 12.6. $C_{31}H_{37}N_5O_5$ requires C, 66.53; H, 6.66; N, 12.51%); R_f (C) 0.5; λ_{max}(MeOH)/nm 251 (ε/dm^3 mol^{-1} cm^{-1} 12 800), 280 (13 500) and 287 (13 700); δ_H[500 MHz; $(CD_3)_2SO$] 0.86 (3 H, s, CH_3), 1.35–2.81 [11 H, several m, 2′-H_α, 2′-H_β, and steroidal (6-, 7-, 8-, 9-, 11-, 12-, 14-, 15-, 16-H)], 3.46 (2 H, m, 5′- and 5″-H), 3.69 (3 H, s, OCH_3), 3.82 (1 H, m, 4′-H), 4.42 (1 H, m, 3′-H), 4.74 (1 H, br, 5′-OH), 5.25 (1 H, br, 3′-OH), 5.93 (1 H, s, steroidal 17-OH), 6.40 and 8.12 (2 H, 2 br s, NH_2), 6.55 (1 H, 't', *J* 6.4, 1′-H), 6.61 (1 H, s, steroidal 4-H), 6.67 (1 H, d, *J* 7.6, steroidal 2-H), 7.16 (1 H, d, *J* 8.6, steroidal 1-H) and 8.27 (1 H, s, 6-H).

4-Amino-1-(2-deoxy-β-D-erythro-pentofuranosyl)-3-ethenyl-1H-pyrazolo[3,4-d]pyrimidine ***12***. Method 1 with tri-*n*-butylvinylstannane (20 equiv.); the reaction time was 12 h at 40 °C; *title product* **12** was a foam (82 mg, 56%) (Found: C, 52.2; H, 5.3; *m*/*z* (FAB) $(M + H)^+$, 278.2. $C_{12}H_{15}N_5O_3$ requires C, 51.98; H, 5.45%; *M*, 277.3); R_f (C) 0.3; λ_{max}(MeOH)/nm 249 (ε/dm^3 mol^{-1} cm^{-1} 9300) and 284 (8300); δ_H[500 MHz; $(CD_3)_2SO$] 2.24 (1 H, m, 2′-H_α), 2.79 (1 H, m, 2′-H_β), 3.48 (2 H, m, 5′- and 5″-H), 3.83 (1 H, m, 4′-H), 4.46 (1 H, m, 3′-H), 4.82 (1 H, t,

J 5.8, 5′-OH), 5.24 (1 H, d, *J* 4.5, 3′-OH), 5.44 (1 H, d, *J* 12.3, CH_2), 6.03 (1 H, d, *J* 17.1, CH_2), 6.56 (1 H, 't', *J* 6.4, 1′-H), 7.26 (1 H, dd, *J* 11.0 and 5.8, CH=C), 7.44 (2 H, br s, NH_2) and 8.17 (1 H, s, 6-H).

4-Amino-1-(2-deoxy-β-D-erythro-pentofuranosyl)-3-[2-(methoxycarbonyl)ethenyl]-1H-pyrazolo[3,4-d]pyrimidine ***13***. Method 1 with methyl acrylate (20.0 g); the reaction time was 24 h at 70 °C; *title ester* **13** was obtained as crystals (94 mg, 53%), mp 231–233 °C (from MeOH–Pr^iOH 1:1, decomp.) (Found: C, 50.3; H, 5.1; N, 20.4. $C_{14}H_{17}N_5O_5$ requires C, 50.15; H, 5.11; N, 20.89%); R_f (C) 0.4; λ_{max}(MeOH)/nm 268 (ε/dm^3 mol^{-1} cm^{-1} 17 100) and 289 (14 900); δ_H[500 MHz; $(CD_3)_2SO$] 2.30 (1 H, m, 2′-H_β), 2.82 (1 H, m, 2′-H_α), 3.48 (2 H, m, 5′- and 5″-H), 3.77 (3 H, s, OCH_3), 3.85 (1 H, m, 4′-H), 4.50 (1 H, m, 3′-H), 4.76 (1 H, t, *J* 5.7, 5′-OH), 5.27 (1 H, d, *J* 4.5, 3′-OH), 6.61 (1 H, 't', *J* 6.3, 1′-H), 6.74 (1 H, d, *J* 15.7, CH), 7.66 (2 H, br s, NH_2), 8.10 (1 H, d, *J* 15.7, CH) and 8.24 (1 H, s, 6-H).

2-(2-Deoxy-β-D-*erythro*-pentofuranosyl)-2,6-dihydroazepine-[4,3,2-*gh*](8-aza-7-deazapurin)-7-one 21. Compound **13** (50 mg, 150 mmol) in 0.1 M NaOMe (20 cm^3) was heated under reflux for 3 h. Evaporation and FC [column 10 × 3 cm, solvent (C)] afforded the *title lactam* **21** as a solid (30 mg, 66%), mp 227–229 °C (Found: C, 50.9; H, 4.6; N, 22.7. $C_{13}H_{13}N_5O_4$ requires C, 51.48; H, 4.32; N, 23.10%); R_f (C) 0.5; λ_{max}(MeOH)/nm 240 (ε/dm^3 mol^{-1} cm^{-1} 15 000) and 285 (8600); δ_H[500 MHz; $(CD_3)_2SO$] 2.33 (1 H, m, 2′-H_β), 2.84 (1 H, m, 2′-H_α), 3.46 (2 H, m, 5′- and 5″-H), 3.85 (1 H, m, 4′-H), 4.47 (1 H, m, 3′-H), 4.73 (1 H, t, *J* 5.6, 5′-OH), 5.32 (1 H, d, *J* 4.5, 3′-OH), 6.32 (1 H, d, *J* 12.0, CH), 6.58 (1 H, 't', *J* 6.4, 1′-H), 7.36 (1 H, d, *J* 12.0, CH), 8.58 (1 H, s, 4-H) and 11.57 (1 H, s, NH).

3,4-Diamino-1-(2-deoxy-β-D-*erythro*-pentofuranosyl)-1*H*-pyrazolo[3,4-*d*]pyrimidine 20. To compound **2c** (23 mg, 0.07 mmol) were added saturated ammonia–MeOH (20 cm^3) and CuCl or CuBr (either 3 mg). The mixture was heated in a steel bomb for 12 h at 110 °C. After filtration and evaporation, the residue was purified by FC [column 10 × 2 cm, CH_2Cl_2–MeOH (4:1, v/v)]. Title compound **20** was obtained as a foam (10 mg, 56%).

Method B. As described above but using iodide **2b** (50 mg, 0.13 mmol) as precursor, CuCl (5 mg) and saturated ammonia–MeOH (20 cm^3). Reaction time 12 h at 110 °C. Compound **20** was obtained as a foam (16 mg, 47%) [Found: *m*/*z* (FAB) $(M + H)^+$, 267.1. $C_{10}H_{14}N_6O_3$ requires *M*, 266.2]; R_f (C) 0.1; λ_{max}(MeOH)/nm 289 (ε/dm^3 mol^{-1} cm^{-1} 3400); δ_H[500 MHz; $(CD_3)_2SO$] 2.09 (1 H, m, 2′-H_α), 2.67 (1 H, m, 2′-H_β), 3.43 (2 H, m, 5′- and 5″-H), 3.75 (1 H, m, 4′-H), 4.34 (1 H, m, 3′-H), 4.84 (1 H, t, *J* 5.8, 5′-OH), 5.19 (1 H, d, *J* 4.3, 3′-OH), 5.87 (1 H, s, NH_2), 6.40 (1 H, 't', *J* 6.6, 1′-H), 7.32 (2 H, br s, NH_2) and 8.03 (1 H, s, 6-H).

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