35. Synthesis of 8-Aza-1,3-dideaza-2′-deoxyadenosine and 5,6-Disubstituted Benzotriazole 2′-Deoxy-β-D-Ribofuranosides *via* Nucleobase-Anion Glycosylation

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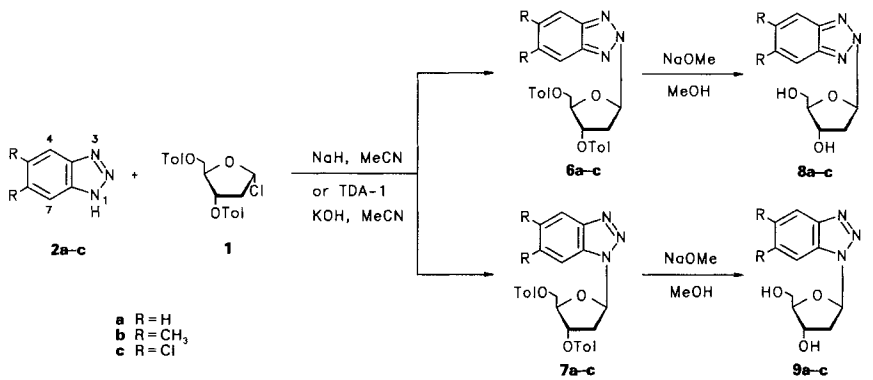
The synthesis of 8-aza-1,3-dideaza-2′-deoxyadenosine (**3a**) as well as of 4- and 5,6-substituted benzotriazole 2′-deoxy-β-D-ribonucleosides is described *(Schemes 1–3)*. Glycosylation of benzotriazole anions is stereoselective in all cases (exclusive β-D-anomer formation), but regioisomeric N^1, N^2, and N^3-(2′-deoxyribofuranosides) are formed. The distribution of the regioisomers is controlled by the nucleobase substituents. Anomeric configuration as well as the position of glycosylation are determined by UV and NMR in combination with 1D-NOE-difference spectroscopy. The unprotonated forms of 4-aminobenzotriazole 2′-deoxy-β-D-ribofuranosides **3a–c** exhibit strong fluorescence.

Introduction. – The syntheses and properties of benzotriazole ribonucleosides have been intensively investigated as their structure is related to benzimidazole nucleosides found as an integral part of vitamin B_{12} [1]. Unnatural benzotriazoles were accepted as substrates of NAD-nucleosidase [2] or show inhibitory action on bacteria or protozoae [3] [4]. Surprisingly, benzotriazole 2′-deoxyribonucleosides are unknown. We were encouraged to their syntheses as benzotriazole derivatives have found use as chemotherapeutic agents [5] [6] and interest arose to incorporate them into DNA fragments.

In 1983, our laboratory has developed a stereoselective synthesis of 2′-deoxyribonucleosides employing the nucleobase anion of a pyrrolo[2,3-*d*]pyrimidine moiety, generated under phase-transfer conditions [7]. Recently, we studied the glycosylation of benzimidazoles [8] and 1,2,3-triazolo[4,5-*d*]pyrimidines [9] with the halogenose **1** [10]. Nucleobase anions of benzotriazole (**2a**) as well as of its symmetric 5,6-dimethyl [11] and 5,6-dichloro derivatives [12] **2b** and **2c**, respectively, are now used for the synthesis of 2′-deoxyribonucleosides. Beside this, 8-aza-1,3-dideaza-2′-deoxyadenosine (**3a**) has been prepared from 4-amino- or 4-nitrobenzotriazole (**4** or **5**, resp.) [13].

Results and Discussion. – At the beginning of our studies, we have focussed on the glycosylation of benzotriazole (**2a**) and its derivatives **2b** and **2c** with halogenose **1** *(Scheme 1)*. The starting materials **2a–c** were prepared according to published procedures [11] [12] and their anions generated in MeCN either with NaH or with KOH in the presence of the cryptand tris[2-(2-methoxyethoxy)ethyl]amine (TDA-1). Both methods worked equally well. The reaction with **1** proceeded at r.t. and was complete within less than 20 min. Two types of glycosylation products, **6a–c** and **7a–c**, later assigned as N^2- and N^1-regioisomers, were formed from **2a–c**. Only **6a**/**7a** and **6b**/**7b** could be separated by column chromatography and deprotected individually (→**8a,b**, **9a,b**). The almost

Scheme 1



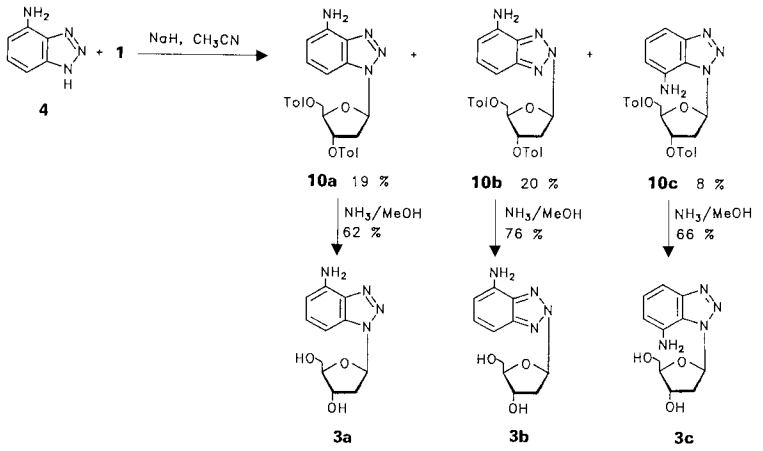
identical mobilities of the protected dichloro compounds **6c**/**7c** required purification by prep. TLC, not allowing large-scale preparation. However, the corresponding deprotected nucleosides **8c**/**9c** showed a much better chromatographic separation, permitting the isolation of **8c** and **9c** on preparative scale. The overall glycosylation yield was 85% for **6a**/**7a**, 70% for **6b**/**7b**, and 81% for **6c**/**7c**.

The anomeric configuration was established by NOE difference spectroscopy [14]. Irradiation of the anomeric proton resulted in NOEs on H–C(4′) and H_α–C(2′) *(Table 1)* establishing β-D-configuration for **8a–c** and **9a–c**. As additional NOEs on H–C(7) were observed in the case of **9a–c**, their position of glycosylation was N^1. These NOEs were not observed for the N^2-compounds **8a–c** *(Table 1)*. As the N^1- and N^2-(2′-deoxyribonucleosides) show significant changes of their UV spectra similar to those of the already reported β-D-ribonucleosides, assignment of the glycosylation position was confirmed in both series [15] [16]. As expected from the structure of the symmetrically disubstituted benzotriazoles **2a–c**, the N^1-glycosylation products should be statistically

Table 1. *NOE Data of 4-Aminobenzotriazole 2′-Deoxyribonucleosides in (D_6)DMSO at 23°*

	Irradiated proton	Observed NOE (%)
3a	H–C(1′)	H_α–C(2′) (6.8), H–C(4′) (0.8), H–C(7) (5.0)
	NH_2	H–C(5) (9.7)
	H–C(6)	H–C(5) (10.2), H–C(7) (8.2)
3b	H–C(1′)	H_α–C(2′) (5.8), H–C(4′) (1.3)
3c	H–C(1′) and H–C(6)	H_α–C(2′) (8.2), H–C(4′) (2.1), NH_2 (5.7), H–C(5) (10.4)
	NH_2	H–C(1′) and H–C(5) (5.7, 21.1), H–C(3′) (1.3)
	H–C(4′)	H–C(1′) (2.0), H–C(3′) (1.8), H–C(5′) and H′–C(5′) (1.7, 3.0)
8a	H–C(1′)	H_α–C(2′) (6.0), H–C(4′) (1.4)
8b	H–C(1′)	H_α–C(2′) (6.0), H–C(4′) (1.6)
8c	H–C(1′)	H_α–C(2′) (6.0), H–C(4′) (1.5)
9a	H–C(1′)	H_α–C(2′) (7.0), H–C(4′) (1.6), H–C(7) (6.0)
9b	H–C(1′)	H–C(4′) (1.4), H–C(7) (6.6)
9c	H–C(1′)	H–C_α(2′) (8.6), H–C(4′) (1.7), H–C(7) (10.3)
12a	H–C(1′)	H_α–C(2′) (7.7), H–C(4′) (1.6), H–C(7) (7.4)
12b	H–C(1′)	H_α–C(2′) (5.6), H–C(4′) (1.0)
12c	H–C(1′)	H_α–C(2′) (7.0), H–C(4′) (1.4)

Scheme 2



favoured. This would result in a N^1/N^2-glycosylation ratio of 2. However, lower ratios were obtained in all cases: 1.74 for **7a**/**6a** (isolated compounds), 1.8 for **7b**/**6b** (isolated compounds), and 1.5 for **7c**/**6c** (UV scanning on TLC). Thus, the N^2-isomers are kinetically preferred. The same has been already observed for corresponding ribonucleosides [15].

The 8-aza-1,3-dideaza-2′-deoxyadenosine (= 4-amino-1-(2′-deoxy-β-D-*erythro*-pentofuranosyl)-1*H*-benzotriazole; **3a**) can be considered as an analogue of the DNA constituent dA. For its preparation, the non-symmetrical 4-aminobenzotriazole (**4**) [13] was subjected to glycosylation by halogenose **1** under the same conditions as described for **2a–c**. The three expected glycosylation products **10a** (N^1), **10b** (N^2), and **10c** (N^3) were obtained in a ratio of *ca.* 5:5:2 and separated by column chromatography *(Scheme 2)*. The glycosylation position was determined more easily on the corresponding deprotected nucleosides **3a–c**.

^{1}H-NOE difference spectroscopy on **3a–c** established β-D-configuration ($(f_{4'}(1')$ *ca.* 1%) [14]. Additionally, **3a** exhibited an NOE on H–C(7) indicating N^1 as glycosylation position *(Table 1)*. Apart from that, irradiation of NH_2 gave an NOE on H–C(5) and irradiation of H–C(6) resulted in NOE effects on H–C(7) and H–C(5) confirming the assignment of aromatic protons. The structure of **3c** was also deduced from ^{1}H-NOE difference spectra *(Table 1)*. The most valuable information came from the irradiation of the NH_2 group. This resulted in NOEs on H–C(1′), H–C(5), and H–C(3′), unambiguously indicating N^3 as glycosylation position. The anomeric configuration was difficult to assign upon irradiation of H–C(1′) as the anomeric signal coincides with that of H–C(5). This problem was solved by irradiating H–C(4′) which resulted, apart from other NOEs, in an NOE on H–C(1′) (β-D-configuration). The remaining isomer **3b** gave only NOEs on H–C(4′) and H_α–C(2′) upon irradiation of H–C(1′) but not on the protons of the aglycone. Consequently, its structure is represented by formula **3b**.

The UV absorption spectra of the unprotonated species of the regioisomers **3a–c** show no significant differences *(Fig., a)*. However, in acidic medium, substantial spectral changes occur *(Fig., b)*, allowing a determination of the pK_{BH^+} values. Almost identical values were found for **3a** (1.8), **3b** (1.6), and **3c** (1.8). In the *Figure, b* and *c* show that the UV spectra of the protonated species derived from **3a** to **3c** are very similar to that of the neutral benzotriazole N^1-deoxyribofuranoside **9a**, and the UV of protonated **3b** resembles that of the N^2-compound **8a**. Therefore, protonation is considered to occur at the

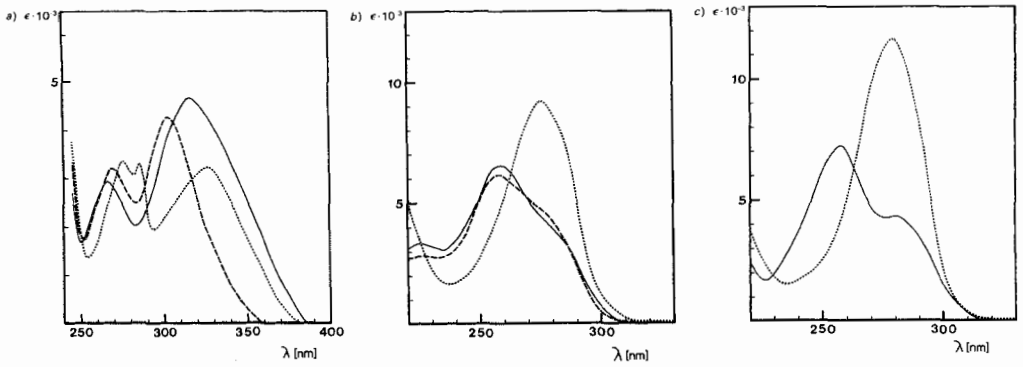


Fig. a) *UV spectra of* **3a** (——), **3b** (· · ·), *and* **3c** (– – –) *in buffer* [19] *pH 7.0;* b) *of* **3a** (——), **3b** (· · ·), *and* **3c** (– – –) in 0.5N HCl; c) *of* **8a** (· · ·) *and* **9a** (——) *in buffer pH 7.0*

amino group rather at the ring N-atoms. This is in line with earlier observations on 5-aminoindazoles [17]. The uncoupling of the lone electron pair of the NH_2 group from the aromatic system upon protonation may explain these findings.

For further studies in oligonucleotide synthesis, the moderate glycosylation yield of **10a** (19%) when starting from **4** was not satisfactory. Therefore, we were looking for an alternative. As it had been shown that anions of nucleobases carrying nitro groups can be glycosylated in excellent yields, we choose 4-nitrobenzotriazole (**5**) [13] as starting material. It was reacted with halogenose **1** as described for **2a–c** to give the three glycosylation products **11a–c** *(Scheme 3)*. Regioisomer **11a** (8% yield) was separated from **11b/11c** (56% yield) by column chromatography and deprotected by NaOMe/MeOH to the crystalline nitro nucleoside **12a**. Regioisomers **11b/11c** could not be separated. However, after detoluoylation (NaOMe/MeOH) and chromatography, **12c** was obtained in 51% yield (rel. to **11b/11c**) and **12b** in 17% yield. Nitro compounds **12a–c** were then hydrogenated to yield the amino nucleosides **3a–c**. Comparison with authentic samples confirmed their structure and also that one of the precursors **11a–c**.

Scheme 3

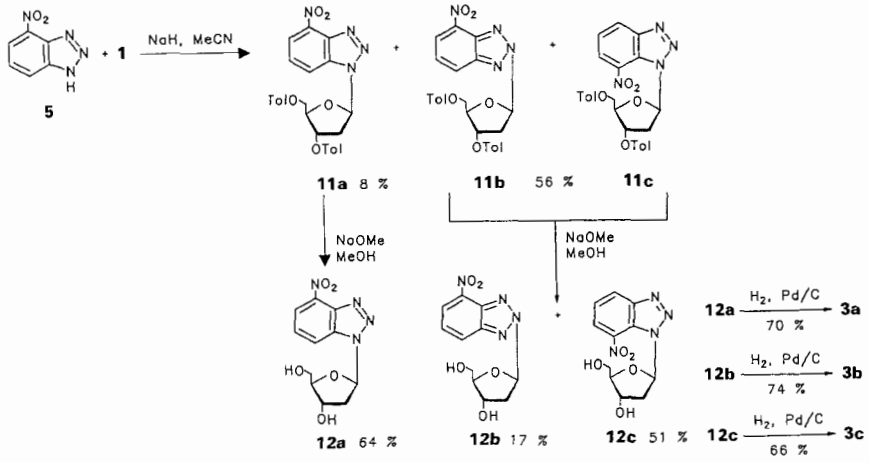


Table 2. *^{13}C-NMR Chemical Shifts of Benzotriazole Nucleosides and their Derivatives in (D_6)DMSO*

	C(4)	C(5)	C(6)	C(7)	C(3a)	C(7a)	C(1′)	C(2′)	C(3′)	C(4′)	C(5′)	CH_3	CH_3	CH_3
3a[a])	140.6	104.4	129.1	96.2	136.3	133.8	85.9	38.3	70.8	87.9	62.0			
3b[a])	145.0	104.0	128.6	103.6	139.5	136.5	92.7	DMSO	70.7	86.3	62.3			
3c[a])	147.5	110.6	125.3	106.7	124.1	134.5	87.0	38.6	70.3	88.2	61.4			
6a[d])	118.3	127.2	127.2	118.3	143.7	143.7	93.1	36.9	74.2	82.6	63.6	21.1		
6b	116.5	137.5	137.5	116.5	143.6	143.6	92.6	36.8	74.3	82.4	63.8	21.1	20.3	
6c[c])	119.7	129.8	129.8	119.7	143.1[b])	143.1[b])	93.7	37.9	74.5	83.8	63.5	21.7		
7a[d])	119.4	124.5	127.9	110.9	145.5	132.7	86.1	35.8	74.6	82.1	63.8	21.1		
7b	118.2	133.9	137.9	110.0	144.8	131.6	86.1	35.7	74.7	82.0	63.8	21.1	20.2	19.8
7c[c])	120.6	127.5[b])	129.5[b])	112.8	144.5	131.3	86.6	36.0	74.5	82.4	63.5	21.1		
8a	118.3	126.7	126.7	118.3	143.6	143.6	93.2	DMSO	70.7	88.6[e])	62.2			
8b	116.5	137.5	137.5	116.5	143.0	143.0	92.6	DMSO	70.7	88.6[e])	62.2		20.3	
8c[a])	120.1	130.1	130.1	120.1	142.5	142.5	93.7	DMSO	70.5	88.9[e])	62.0			
9a[d])	119.2	124.3	127.6	111.2	145.6	132.4	86.3	DMSO	70.7	88.2[e])	61.8			
9b	118.1	133.7	137.6	110.4	144.8	131.4	86.2	DMSO	70.7	88.1[e])	61.9		20.3	19.8
9c	120.5	127.4[b])	130.9[b])	113.2	144.6	131.6[b])	87.0	DMSO	70.4	88.3[e])	61.5			
10a	140.8	104.6	129.3[b])	95.9	136.3	134.1	85.9	35.6	74.7	81.9	63.9	21.1		
10b	145.6	104.1[b])	129.2[b])	103.6[b])	139.5	136.5	92.8	37.0	74.5	82.5	63.9	21.1		
10c	147.6	111.4	129.0[b])	107.1	124.2	134.5	87.0	35.7	74.6	82.3	63.9	21.1		
12a[a])	135.3	121.7	127.4	119.1	137.8[b])	137.9[b])	87.1	DMSO	70.4	88.6	63.1			
12b[a])	145.6	127.0	126.1	125.4	137.5[b])	136.3[b])	94.1	DMSO	70.5	89.1	62.0			
12c[a])	150.1	125.4	123.7	126.5	124.1	135.6	88.8	DMSO	70.1	88.1	61.1			

[a]) From ^{1}H,^{13}C correlation spectra and H,C-coupled spectra.
[b]) Tentative.
[c]) In $CDCl_3$.
[d]) According to [19].
[e]) From selective INAPT spectra (irradiation of H–C(1′)).

Regarding the synthesis of **3a**, the route *via* glycosylation of **4** is more efficient than the one *via* **5**. It is also worth mentioning that the ratio of N^1/N^3 *vs.* N^2-isomers in case of 4-nitrobenzotriazole derivatives is 3.3, whereas that of the 4-aminobenzotriazole compounds is 1.3. This indicates that the substituents at C(4) control the position of glycosylation.

The ^{13}C-NMR data of the benzotriazole nucleosides **3**, **10**, and **12** *(Table 2)*, which were assigned by the ^{1}H,^{13}C-coupled mode as well as from ^{1}H,^{13}C correlation spectra, show that C(1′) of N^2-glycosylated nucleosides is shifted downfield by 5–7 ppm when compared with C(1′) of $N^1(N^3)$-glycosylated isomers. The symmetrical character of N^2-compounds is also expressed by their much simpler spectra. As expected [18], the C(7a) signal of N^1-isomers **7a–c** and **9a–c** of 5,6-disubstituted benzotriazole nucleosides is shifted upfield compared to the N^2-glycosylated compounds **6a–c** and **8a–c**. These results are in agreement with those obtained earlier for compounds containing benzotriazol-1- and -2-yl moieties connected to an ethylidene bridge [19]. Also the ^{13}C-NMR spectra of the 4-aminobenzotriazole 2′-deoxyribofuranosides **3a–c** and **10a–c** exhibit strong similarities to regioisomeric 8-azaadenine 2′-deoxyribofuranosides [9].

The unprotonated 4-aminobenzotriazole 2′-deoxyribofuranosides **3a–c** are strongly fluorescent, whereas the protonated species are not. The colours of fluorescence change from white-blue (N^1-compound **3a**) over blue (N^2-isomer **3b**) to yellow (N^3-isomer **3c**). Excitation and emission data measured in H_2O are summarized in *Table 3*. As the

Table 3. *Fluorescence Data* (H_2O) *of 4-Aminobenzotriazole 2′-Deoxyribonucleosides*

	Excitation wavelength [nm]	Emission maximum [nm]
3a	317	510
3b	327	565
3c	306	525

excitatation and emission maxima are far away from the absorption maxima of common nucleosides, **3a–c** may serve as fluorescent probes within the DNA fragments.

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Experimental Part

General. See [9]. In addition: Flash chromatography = FC. The $pK_{BH\oplus}$ values of **3a–c** were determined spectrophotometrically in *Teorell-Stenhagen* buffer [20]. Fluorescence spectra: *SPF-Ratio* spectrofluorimeter (*Aminco*, USA).

*1-[2′-Deoxy-3′,5′-di-*O*-(4-toluoyl)-β-*D*-*erythro*-pentofuranosyl]-1*H*-benzotriazole* (**7a**) *and 2-[2′-Deoxy-3′,5′-di-*O*-(4-toluoyl)-β-*D*-*erythro*-pentofuranosyl]-2*H*-benzotriazole* (**6a**). *Method A*: To a soln. of benzotriazole (**2a**; 1.19 g, 10 mmol) in anh. MeCN (70 ml) was added NaH (80% in oil; 300 mg, 10 mmol). The mixture was stirred for a few min whereupon the sodium salt of **2a** precipitated. The 2-deoxy-3,5-di-*O*-(4-toluoyl)-α-*D*-*erythro*-pentofuranosyl chloride [10] (**1**; 3.9 g, 10.0 mmol) was added within 10 min portionwise, and stirring was continued for another 20 min at r.t. The mixture was filtered through *Celite* and evaporated. The oil was submitted to FC (column 5 × 20 cm; petroleum ether/AcOEt 8:2). The faster migrating product was crystallized from MeOH: **6a** as colourless needles (1.45 g, 31%). TLC (silica gel, petroleum ether/AcOEt 8:2): R_f 0.60. M.p. 131°. ^{1}H-NMR ((D$_6$)DMSO): 2.38, 2.41 (2*s*, 2 CH_3); 2.99 (*m*, H_α–C(2′)); 3.45 (*m*, H_β–C(2′))[1]; 4.53 (*m*, 2 H–C(5′)); 4.72 (*q*,

[1]) The assignment of H_α–C(2′) and H_β–C(2′) has to be reversed in the *Exper. Part* of [9].

H–C(4′)); 6.01 (*q*, *J* = 5.3, H–C(3′)); 6.89 (*dd*, *J* = 2.3, 4.5, H–C(1′)); 7.25–8.00 (*m*, arom. H). Anal. calc. for $C_{27}H_{25}N_3O_5$: C 68.78, H 5.34, N 8.91; found: C 68.63, H 5.41, N 8.90.

The slower migrating product was also crystallized from MeOH: **7a** as small colourless needles (2.56 g, 54%). TLC (silica gel, petroleum ether/AcOEt 8:2): R_f 0.30. M.p. 145–146°. ^{1}H-NMR ((D$_6$)DMSO): 2.38, 2.42 (2*s*, 2 CH_3); 2.96 (*m*, H_α–C(2′)); 3.58 (*m*, H_β–C(2′)); 4.45 (*m*, 2 H–C(5′)); 4.70 (*q*, H–C(4′)); 5.91 (*m*, H–C(3′)); 7.06 (*t*, *J* = 6.3, H–C(1′)); 7.30–8.15 (*m*, arom. H). Anal. calc. for $C_{27}H_{25}N_3O_5$: C 68.78, H 5.34, N 8.91; found: C 68.69, H 5.32, N 8.90.

Method B: A soln. of **2a** (595 mg, 5 mmol) in anh. MeCN (35 ml) containing powdered KOH (680 mg, 12.1 mmol) and the cryptand TDA-1 (100 mg, 0.3 mmol) was stirred at r.t. for 15 min. Then, **1** (1.95 g, 5 mmol) was added and stirring continued for 15 min. Unsoluble material was removed by filtration and the filtrate evaporated. The separation of **6a** (710 mg, 30%) and **7a** (1.34 g, 57%) was performed as above. ^{1}H-NMR: products identical with those described in *Method A*.

*1-[2′-Deoxy-3′,5′-di-*O*-(4-toluoyl)-β-*D*-*erythro*-pentofuranosyl]-5,6-dimethyl-1*H*-benzotriazole* (**7b**) *and 2-[2′-Deoxy-3′,5′-di-*O*-(4-toluoyl)-β-*D*-*erythro*-pentofuranosyl]-5,6-dimethyl-2*H*-benzotriazole* (**6b**). To a soln. of 5,6-dimethylbenzotriazole [11] (**2b**; 900 mg, 6.1 mmol) in anh. MeCN (30 ml), NaH (210 mg, 7 mmol; 80% in oil) was added under stirring. Stirring was continued for 10 min, whereupon a white precipitate was formed. Subsequently, **1** (2.37 g, 6.1 mmol) was added in portions and stirring continued for 20 min. The mixture was filtered through *Celite* and the filtrate evaporated. On FC (column 5 × 25 cm) petroleum ether/AcOEt 8:2, **6b** eluted first. It was crystallized from MeOH: colourless needles (0.75 g, 25%). TLC (silica gel, petroleum ether/AcOEt 8:2): R_f 0.6. M.p. 102–103°. ^{1}H-NMR ((D$_6$)DMSO): 2.36, 2.37, 2.41, 2.44 (4*s*, 4 CH_3); 2.94 (*m*, H_α–C(2′)); 3.40 (*m*, H_β–C(2′)); 4.52 (*m*, 2 H–C(5′)); 4.68 (*q*, H–C(4′)); 6.00 (*q*, *J* = 5.5, H–C(3′)); 6.80 (*dd*, *J* = 2.4, 4.4, H–C(1′)); 7.20–8.00 (*m*, arom. H). Anal. calc. for $C_{29}H_{29}N_3O_5$: C 69.72, H 5.85, N 8.41; found: C 69.89, H 5.83, N 8.40.

Compound **7b** was eluted within the second zone. It was crystallized from MeOH: colourless needles (1.38 g, 45%). TLC (silica gel, petroleum ether/AcOEt 8:2): R_f 0.40. M.p. 121°. ^{1}H-NMR ((D$_6$)DMSO): 2.31, 2.35, 2.36, 2.42 (4*s*, 4 CH_3); 2.92 (*m*, H_β–C(2′)); 3.56 (*m*, H_α–C(2′)); 4.45 (*m*, 2 H–C(5′)); 4.67 (*m*, H–C(4′)); 5.89 (*m*, H–C(3′)); 6.95 (*t*, *J* = 6.0, H–C(1′)); 7.20–8.05 (*m*, arom. H). Anal. calc. for $C_{29}H_{29}N_3O_5$: C 69.72, H 5.85, N 8.41; found: C 69.77, H 5.94, N 8.42.

*5,6-Dichloro-1-[2′-deoxy-3′,5′-di-*O*-(4-toluoyl)-β-*D*-*erythro*-pentofuranosyl]-1*H*-benzotriazole* (**7c**) *and 5,6-Dichloro-2-[2′-deoxy-3′-5′-di-*O*-(4-toluoyl)-β-*D*-erythro-pentofuranosyl]-2*H*-benzotriazole* (**6c**). To a stirred soln. of 5,6-dichlorobenzotriazole [12] (**2c**; 1.13 g, 6.0 mmol) in anh. MeCN (45 ml), NaH (210 mg, 7.0 mmol; 80% in oil) was added (→ white precipitate). Then, **1** (2.35 g, 6.04 mmol) was added and stirring continued for 20 min. Insoluble material was removed by filtration and the filtrate evaporated. The mixture was partially purified by FC (column 5 × 15 cm, petroleum ether/AcOEt 8:2): colourless amorphous **6c**/**7c** (2.28 g, 70%). A small amount was separated by prep. TLC (silica gel, petroleum ether/AcOEt 8:2): R_f 0.67 (**6c**), 0.60 (**7c**); **6c**/**7c** 2:3, by UV scanning on TLC at 260 nm. From the zone with R_f 0.67, **6c** was obtained as a white powder after crystallization from MeOH. M.p. 175–177°. ^{1}H-NMR ($CDCl_3$): 2.24, 2.46 (2*s*, 2 CH_3); 2.85 (*m*, H_β–C(2′)); 3.50 (*m*, H_α–C(2′)); 4.53 (*m*, 2 H–C(5′)); 4.77 (*m*, H–C(4′)); 6.06 (*m*, H–C(3′)); 6.75 (*dd*, *J* = 2.4, 4.4, H–C(1′)); 7.1–8.1 (*m*, arom. H). Anal. calc. for $C_{27}H_{23}Cl_2N_3O_5$: C 60.01, H 4.29, N 7.78; found: C 60.14, H 4.32, N 7.71.

The zone with R_f 0.60 afforded **7c** which crystallized from MeOH: colourless needles. M.p. 152–153°. ^{1}H-NMR ((D$_6$)DMSO): 2.38, 2.42 (2*s*, 2 CH_3); 2.97 (*m*, H_α–C(2′)); 3.58 (*m*, H_β–C(2′)); 4.45 (*m*, 2 H–C(5′)); 4.71 (*q*, H–C(4′)); 5.87 (*m*, H–C(3′)); 7.03 (*t*, *J* = 6.0, H–C(1′)); 7.2–8.5 (5*d*, arom. H). Anal. calc. for $C_{27}H_{23}Cl_2N_3O_5$: C 60.01, H 4.29, N 7.78; found: C 60.15, H 4.34, N 7.81.

*2-(2′-Deoxy-β-*D*-erythro-pentofuranosyl)-2*H*-benzotriazole* (**8a**). The suspension of **6a** (940 mg, 2.0 mmol) in MeOH (50 ml) containing 1M NaOMe/MeOH (2.5 ml) was stirred overnight at r.t. and heated under reflux for 10 min. The soln. was evaporated and the oil treated with H_2O and neutralized with AcOH. Repeated evaporation with H_2O (3 × 50 ml) removed volatile compounds. The residue crystallized from a small amount of H_2O: Colourless needles (417 mg, 89%). TLC (silica gel, $CHCl_3$/MeOH 95:5): R_f 0.45. M.p. 108–109°. UV (pH 7): 279 (11800). ^{1}H-NMR ((D$_6$)DMSO): 2.50 (*m*, H_α–C(2′)); 2.95 (*m*, H_β–C(2′)); 3.45–3.63 (*m*, 2 H–C(5′)); 3.97 (*q*, H–C(4′)); 4.61 (*m*, H–C(3′)); 4.78 (*t*, *J* = 5.5, OH–C(5′)); 5.43 (*d*, *J* = 4.4, OH–C(3′)); 6.65 (*dd*, *J* = 2.4, 4.5, H–C(1′)); 7.49 (*m*, H–C(5), H–C(6)); 7.96 (*m*, H–C(4), H–C(7)). Anal. calc. for $C_{11}H_{13}N_3O_3$: C 56.16, H 5.57, N 17.86; found: C 56.14, H 5.70, N 17.87.

*1-(2′-Deoxy-β-*D*-erythro-pentofuranosyl)-1*H*-benzotriazole* (**9a**). Procedure as described for **8a**. Colourless parallelepipeds from H_2O (361 mg, 77%). TLC (silica gel, $CHCl_3$/MeOH 95:5): R_f 0.25. M.p. 150–151°. UV (pH 7): 257 (7400), 281 (4300). ^{1}H-NMR ((D$_6$)DMSO): 2.45 (*m*, H_α–C(2′)); 3.05 (*m*, H_β–C(2′)); 3.50 (*m*, 2 H–C(5′)); 3.94 (*q*, H–C(4′)); 4.54 (*m*, H–C(3′)); 4.83 (br. *s*, OH–C(5′)); 5.45 (br. *s*, OH–C(3′)); 6.77 (*t*, *J* = 6.3, H–C(1′));

7.43, 7.57 (2 't', H–C(5), H–C(6)); 7.98, 8.07 (2*d*, H–C(4), H–C(7)). Anal. calc. for $C_{11}H_{13}N_3O_3$: C 56.16, H 5.57, N 17.86; found: C 56.00, H 5.56, N 17.85.

*2-(2'-Deoxy-β-*D-erythro-*pentofuranosyl)-5,6-dimethyl-2*H-*benzotriazole* (**8b**). Compound **6b** (500 mg, 1.0 mmol) in MeOH (40 ml) containing 1M NaOMe/MeOH (1.5 ml) was stirred for 20 h at r.t. The mixture was evaporated. FC (column 2 × 20 cm, $CHCl_3$/MeOH 9:1) yielded **8b** which was crystallized from AcOEt: colourless plates (195 mg, 74%). TLC (silica gel, $CHCl_3$/MeOH 95:5): R_f 0.50. M.p. 133°. UV (pH 7): 286 (13700), 290 (12000). ^{1}H-NMR ((D_6)DMSO): 2.37 (*s*, 2 CH_3), 2.45 (*m*, H_α–C(2')); 2.90 (*m*, H_β–C(2')); 3.40, 3.60 (2*m*, 2 H–C(5')); 3.94 (*q*, H–C(4')); 4.58 (*m*, H–C(3')); 4.76 (*t*, *J* = 5.6, OH–C(5')); 5.39 (*d*, *J* = 4.7, OH–C(3')); 6.56 (*dd*, *J* = 2.1, 4.7, H–C(1')); 7.69 (*s*, H–C(4), H–C(7)). Anal. calc. for $C_{13}H_{17}N_3O_3$: C 59.30, H 6.51, N 15.96; found: C 59.39, H 6.61, N 15.99.

*1-(2'-Deoxy-β-*D-erythro-*pentofuranosyl)-5,6-dimethyl-1*H-*benzotriazole* (**9b**). Procedure as described for **8b**. Colourless oil which crystallized after a few weeks (192 mg, 73%). TLC (silica gel, $CHCl_3$/MeOH 95:5): R_f 0.30. M.p. 54–57°. UV (pH 7): 265 (7800), 290 (4200). ^{1}H-NMR ((D_6)DMSO): 2.37, 2.40 (2*s*, 2 CH_3); 2.45 (*m*, H_α–C(2')); 3.02 (*m*, H_β–C(2')); 3.38, 3.52 (2*m*, 2 H–C(5')); 3.93 (*q*, H–C(4')); 4.52 (*m*, H–C(3')); 4.83 (*t*, *J* = 5.4, OH–C(5')); 5.42 (*d*, *J* = 4.4, OH–C(3')); 6.69 (*t*, *J* = 6.3, H–C(1')); 7.75, 7.81 (2*s*, H–C(5), H–C(7)). Anal. calc. for $C_{13}H_{17}N_3O_3$: C 59.30, H 6.51, N 15.96; found: C 59.16, H 6.61, N 15.92.

*5,6-Dichloro-2-(2'-deoxy-β-*D-erythro-*pentofuranosyl)-2*H-*benzotriazole* (**8c**) *and 5,6-Dichloro-1-(2'-deoxy-β-*D-erythro-*pentofuranosyl)-1*H-*benzotriazole* (**9c**). The mixture **6c**/**7c** (2.0 g, 3.7 mmol) was stirred with MeOH (80 ml) containing 1M NaOMe/MeOH (6 ml) for 20 h at r.t. The soln. was adsorbed on silica gel and submitted to FC (column 5 × 20 cm, $CHCl_3$/MeOH 9:1). The faster-migrating product was crystallized from aq. EtOH: **8c** as white powder (340 mg, 30%). TLC (silica gel, $CHCl_3$/MeOH 95:5): R_f 0.45. UV (H_2O): 296 (12600), 306 (10200). ^{1}H-NMR ((D_6)DMSO): 2.55 (*m*, H_α–C(2')); 2.92 (*m*, H_β–C(2')); 3.45, 3.58 (*m*, 2 H–C(5')); 3.96 (*q*, H–C(4')); 4.58 (*m*, H–C(3')); 4.76 (*t*, *J* = 5.7, OH–C(5')); 5.44 (*d*, *J* = 4.8, OH–C(3')); 6.65 (*dd*, *J* = 2.6, 4.3, H–C(1')); 8.42 (*s*, H–C(4), H–C(7)). Anal. calc. for $C_{11}H_{11}Cl_2N_3O_3$: C 43.44, H 3.65, N 13.82; found: C 43.65, H 3.75, N 13.90.

The slower-migrating product was also crystallized from aq. EtOH: **9c** as small needles (570 mg, 51%). TLC (silica gel, $CHCl_3$/MeOH 95:5): R_f 0.30. M.p. 122–123°. UV (pH 7): 266 (7200), 294 (4600). ^{1}H-NMR ((D_6)DMSO): 2.45 (*m*, H_β–C(2')); 3.00 (*m*, H_α–C(2')); 3.40, 3.56 (2 *m*, 2 H–C(5')); 3.96 (*q*, H–C(4')); 4.53 (*m*, H–C(3')); 4.86 (*t*, *J* = 5.4, OH–C(5')); 5.43 (*d*, *J* = 4.4, OH–C(3')); 6.78 (*t*, *J* = 6.1, H–C(1')); 8.50 (*s*, H–C(4), H–C(7)). Anal. calc. for $C_{11}H_{11}Cl_2N_3O_3$: C 43.44, H 3.65, N 13.82; found: C 43.52, H 3.65, N 13.75.

*4-Amino-1-[2'-deoxy-3',5'-di-*O*-(4-toluoyl)-β-*D-erythro-*pentofuranosyl]-1*H-*benzotriazole* (**10a**), *4-Amino-2-[2'-deoxy-3',5'-di-*O*-(4-toluoyl)-β-*D-erythro-*pentofuranosyl]-2*H-*benzotriazole* (**10b**), *and 4-Amino-3-[2'-deoxy-3',5'-di-*O*-(4-toluoyl)-β-*D-erythro-*pentofuranosyl]-3*H-*benzotriazole* (**10c**). A soln. of 4-aminobenzotriazole [13] (**4**; 2.68 g, 20 mmol) in anh. MeCN (150 ml) containing NaH (640 mg, 21.3 mmol; 80% in oil) was stirred for 10 min under N_2. Then, **1** (7.84 g, 20.2 mmol) was added in two portions within 5 min, and the mixture was stirred for 20 min at r.t. Insoluble material was removed by filtration through *Celite* and the filtrate evaporated to give an oil. FC (column 5 × 30 cm, petroleum ether/AcOEt 7:3) separated **10b** from **10a**/**10c**. TLC (silica gel, petroleum ether/AcOEt 7:3): R_f 0.39 (**10a**), 0.56 (**10b**), and 0.35 (**10c**). The fractions containing **10b** gave a solid foam (1.98 g, 20%). ^{1}H-NMR ((D_6)DMSO): 2.37, 2.41 (2*s*, 2 CH_3); 2.96 (*m*, H_α–C(2')); 3.46 (*m*, H_β–C(2')); 4.56 (*m*, 2 H–C(5')); 4.72 (*m*, H–C(4)); 6.00 (*q*, H–C(3')); 6.82 (*dd*, *J* = 2.1, 4.4, H–C(1')); 7.0–8.0 (*m*, arom. H). Anal. calc. for $C_{27}H_{26}N_4O_5$: C 66.66, H 5.39, N 11.52; found: C 66.55, H 5.50, N 11.39.

The mixture **10a**/**10c** was separated by FC (column 5 × 25 cm, $CHCl_3$/acetone 95:5). TLC (silica gel, $CHCl_3$/acetone 95:5): R_f 0.47 (**10a**), 0.70 (**10c**). The faster-migrating product **10c** was crystallized from MeOH giving colourless needles (750 mg, 8%). M.p. 137°. ^{1}H-NMR ((D_6)DMSO): 2.37, 2.41 (2*s*, 2 CH_3); 2.96 (*m*, H_α–C(2')); 3.80 (*m*, H_β–C(2')); 4.39 (*m*, 2 H–C(5')); 4.74 (*q*, H–C(4')); 5.87 (*m*, H–C(3')); 7.08 ('*t*', *J* = 5.9, H–C(1')); 7.1–8.1 (*m*, arom. H). Anal. calc. for $C_{27}H_{26}N_4O_5$: C 66.66, H 5.39, N 11.52; found: C 66.74, H 5.42, N 11.54.

From the slower-migrating zone, **10a** was obtained as a solid foam (1.85 g, 19%). ^{1}H-NMR ((D_6)DMSO): 2.38, 2.42 (2*s*, 2 CH_3); 2.91 (*m*, H_α–C(2')); 3.54 (*m*, H_β–C(2')); 4.47 (*m*, 2 H–C(5')); 4.65 (*q*, H–C(4')); 5.89 (*m*, H–C(3')); 6.88 ('*t*', *J* = 6.4, H–C(1')); 6.95–8.05 (*m*, arom. H). Anal. calc. for $C_{27}H_{26}N_4O_5$: C 66.66, H 5.39, N 11.52; found: C 66.80, H 5.35, N 11.57.

Glycosylation of 4-Nitrobenzotriazole (**5**) *with* **1**. A mixture of **5** [13] (0.82 g, 5 mmol) and NaH (160 mg, 5.3 mmol; 80% in oil) in MeCN (35 ml) was stirred for 15 min at r.t. The yellow sodium salt of **5** precipitated. Compound **1** (1.96 g, 5 mmol) was added in portions within 10 min under stirring, and stirring was continued for another 20 min. The suspension was filtered through *Celite* and the filtrate adsorbed on silica gel and submitted to FC (column 20 × 5 cm, petroleum ether/AcOEt 6:4). The faster-migrating zone contained **11b**/**11c** (1.45 g, 56%) and the slower one **11a**.

*1-[2'-Deoxy-3',5'-di-*O*-(4-toluoyl)-β-*D*-erythro-pentofuranosyl]-4-nitro-1*H*-benzotriazole* (**11a**). The residue of the slower-migrating zone was crystallized from MeOH yielding yellow needles (210 mg, 8%). TLC (silica gel, petroleum ether/AcOEt 8:2): R_f 0.17. M.p. 177–178°. ^{1}H-NMR ((D$_6$)DMSO): 2.35, 2.42 (2*s*, 2 CH_3); 3.03 (*m*, H_α–C(2')); 3.69 (*m*, H_β–C(2')); 4.35, 4.58 (2*m*, 2 H–C(5')); 4.75 (*m*, H–C(4')); 5.91 (*m*, H–C(3')); 7.11 (*t*, *J* = 6.2, H–C(1')); 7.1–8.25 (*m*, arom. H). Anal. calc. for $C_{27}H_{24}N_4O_7$: C 62.79, H 4.68, N 10.85; found: C 62.87, H 4.77, N 10.77.

*1-(2'-Deoxy-β-*D*-erythro-pentofuranosyl)-4-nitro-1*H*-benzotriazole* (**12a**). The soln. of **11a** (520 mg, 1 mmol) in 0.1M NaOMe/MeOH (30 ml) was stirred overnight at r.t. The mixture was adsorbed on silica gel and submitted to FC (column 18 × 2 cm; $CHCl_3$/MeOH 9:1). Crystallization of **12a** from AcOEt/MeOH gave yellow needles (180 mg, 64%). TLC (silica gel, $CHCl_3$/MeOH 9:1): R_f 0.37. M.p. 138–140°. UV (pH 7): 305 (10300). ^{1}H-NMR ((D$_6$)DMSO): 2.56 (*m*, H_α–C(2')); 3.12 (*m*, H_β–C(2')); 3.40, 3.52 (2*m*, 2 H–C(5')); 3.97 (*m*, H–C(4')); 4.58 (*m*, H–C(3')); 4.80 (*t*, *J* = 5.4, OH–C(5')); 5.48 (*d*, *J* = 4.5, OH–C(3')); 6.90 (*t*, *J* = 5.7, H–C(1')); 7.82 (*t*, *J* = 8.0, H–C(6)); 8.35 (*d*, *J* = 7.4, H–C(5)); 8.53 (*d*, *J* = 8.5, H–C(7)). Anal. calc. for $C_{11}H_{12}N_4O_5$: C 47.15, H 4.31, N 19.99; found: C 47.01, H 4.39, N 20.12.

*2-(2'-Deoxy-β-*D*-erythro-pentofuranosyl)-4-nitro-2*H*-benzotriazole* (**12b**) *and 3-(2'-Deoxy-β-*D*-erythro-pentofuranosyl)-4-nitro-3*H*-benzotriazole* (**12c**). The mixture **11b**/**11c** (1.29 g, 2.5 mmol) obtained from the glycosylation of **5** (see above) was stirred overnight in MeOH (50 ml) containing 1M NaOMe/MeOH (5 ml). The soln. was adsorbed on silica gel and submitted to FC (column 20 × 3.5 cm, $CHCl_3$/MeOH 95:5). The fractions with R_f 0.23 (TLC, silica gel) gave **12b** as yellowish oil (120 mg, 17%). UV (pH 7): 315 (8800). ^{1}H-NMR ((D$_6$)DMSO): 2.57 (*m*, H_α–C(2')); 2.95 (*m*, H_β–C(2')); 3.49, 3.63 (2*m*, 2 H–C(5')); 4.01 (*q*, H–C(4')); 4.65 (*m*, H–C(3')); 4.78 (*t*, *J* = 5.7, OH–C(5')); 5.49 (*d*, *J* = 4.8, OH–C(3')); 6.77 (*dd*, *J* = 2.9, 3.9, H–C(1')); 7.72 (*t*, *J* = 7.8, H–C(6)); 8.52 (2*d*, H–C(5), H–C(6)). Anal. calc. for $C_{11}H_{12}N_4O_5$: C 47.15, H 4.31, N 19.99; found: C 47.02 H 4.39, N 20.01.

The slower-migrating **12c** crystallized from AcOEt/MeOH: small yellow needles (360 mg, 51%). TLC (silica gel $CHCl_3$/MeOH 95:5): R_f 0.18. M.p. 158–160°. UV (pH 7): 234 (5900), 309 (5800). ^{1}H-NMR ((D$_6$)DMSO): 2.56 (*m*, H_α–C(2')); 3.09, 3.18 (2*m*, 2 H–C(5')); 3.36 (*m*, H_β–C(2')); 3.84 (*q*, H–C(4')); 4.44 (*m*, H–C(3'), OH–C(5')); 5.38 (*d*, *J* = 4.8, OH–C(3')); 6.84 (*dd*, *J* = 3.0, 3.5, H–C(1')); 7.66 (*t*, *J* = 8.0, H–C(6)); 8.37 (*d*, *J* = 7.7, H–C(5)); 8.58 (*d*, *J* = 8.2, H–C(7)). Anal. calc. for $C_{11}H_{12}N_4O_5$: C 47.15, H 4.31, N 19.99; found: C 47.01, H 4.53, N 19.97.

*4-Amino-1-(2'-deoxy-β-*D*-erythro-pentofuranosyl)-1*H*-benzotriazole* (**3a**). *Method A.* The soln. of **10a** (1.2 g, 2.45 mmol) in MeOH (35 ml) saturated with NH_3 at 0° was stirred for 24 h at r.t. and evaporated. FC (column 2 × 20 cm, $CHCl_3$/MeOH 8:2) and crystallization from EtOH gave **3a** as yellowish needles (380 mg, 62%). TLC (silica gel, $CHCl_3$/MeOH 9:1): R_f 0.44. M.p. 138–139°. UV (pH 0.3): 226 (3400), 258 (6600). UV (pH 7): 223 (20300), 265 (3000), 316.5 (4600). ^{1}H-NMR ((D$_6$)DMSO): 2.41 (*m*, H_α–C(2')); 3.02 (*m*, H_β–C(2')); 3.38, 3.52 (2*m*, 2 H–C(5')); 3.92 (*q*, H–C(4')); 4.52 (*m*, H–C(3')); 4.80 (*t*, *J* = 5.5, OH–C(5')); 5.39 (*d*, *J* = 4.5, OH–C(3')); 6.06 (*s*, NH_2); 6.44 (*d*, *J* = 7.2, H–C(5)); 6.61 ('*t*', *J* = 6.4, H–C(1')); 6.92 (*d*, *J* = 7.8, H–C(7)); 7.02 (*t*, *J* = 7.8, H–C(6)). Anal. calc. for $C_{11}H_{14}N_4O_3$: C 52.79, H 5.64, N 22.39; found: C 52.88, H 5.69, N 22.41.

Method B. The soln. of **12a** (140 mg, 0.5 mmol) in anh. EtOH containing 10% Pd/C (30 mg) was hydrogenated at regular pressure at r.t. for 3 h. The catalyst was removed by filtration and the filtrate evaporated. The residue was crystallized from a small volume of EtOH: 88 mg (70%) of **3a**. M.p. 136–139°. Spectrophotometrically and chromatographically identical with **3a** described above.

*4-Amino-2-(2'-deoxy-β-*D*-erythro-pentofuranosyl)-2*H*-benzotriazole* (**3b**). *Method A.* The soln. of **10b** (1.3 g, 2.7 mmol) in MeOH (35 ml) saturated with NH_3 at 0° was stirred for 24 h at r.t. (→yellow soln.) and evaporated. FC (column 2 × 15 cm, $CHCl_3$/MeOH 8:2) of the oil yielded **3b** as yellowish oil (510 mg, 76%). TLC (silica gel, $CHCl_3$/MeOH 9:1): R_f 0.60. UV (pH 0.3): 277 (9200). UV (pH 7): 225 (20800), 276 (3300), 286 (3300), 326 (3200). ^{1}H-NMR ((D$_6$)DMSO): 2.45 (*m*, H_α–C(2')); 2.94 (*m*, H_β–C(2')); 3.42, 3.58 (2*m*, 2 H–C(5')); 3.96 (*q*, H–C(4')); 4.61 (*m*, H–C(3')); 4.77 (*t*, *J* = 5.8, OH–C(5')); 5.39 (*d*, *J* = 4.8, OH–C(3')); 5.82 (*s*, NH_2); 6.39 (*d*, *J* = 7.2, H–C(5')); 6.56 (*dd*, *J* = 2.2, 4.6, H–C(1')); 6.99 (*d*, *J* = 8.4, H–C(7)); 7.15 (*t*, *J* = 7.3, H–C(6)). Anal. calc. for $C_{11}H_{14}N_4O_3$: C 52.79, H 5.64, N 22.39; found: C 52.83, H 5.79, N 22.26.

Method B. From **12b** as described for **3a**: 93 mg (74%) of **3b**.

*4-Amino-3-(2'-deoxy-β-*D*-erythro-pentofuranosyl)-3*H*-benzotriazole* (**3c**). *Method A.* A suspension of **10c** (530 mg, 1.1 mmol) was stirred in MeOH (20 ml) saturated with NH_3 at 0° for 20 h at r.t. Evaporation, FC (column 2 × 15 cm, CH_2Cl_2/MeOH 8:2), and crystallization from EtOH gave **3c** as colourless needles (180 mg, 66%). TLC (silica gel $CHCl_3$/MeOH 9:1): R_f 0.45. M.p. 140–141°. UV (pH 0.3): 225 (2800), 258 (6100). UV (pH 7): 222 (20700), 270 (3200), 304 (4200). ^{1}H-NMR ((D$_6$)DMSO): 2.45 (*m*, H_α–C(2')); 3.25 (*m*, H_β–C(2'), 1 H–C(5')); 3.45 (*m*, 1 H–C(5')); 3.97 (*q*, H–C(4')); 4.50 (*m*, H–C(3')); 4.83 (*t*, *J* = 5.4, OH–C(5')); 5.42 (*d*, *J* = 4.8, OH–C(3')); 5.57 (*s*, NH_2); 6.75 (*m*, H–C(1'), H–C(5)); 7.13 (*t*, *J* = 7.4, H–C(6)); 7.24 (*d*, *J* = 8.2, H–C(7)). Anal. calc. for $C_{11}H_{14}N_4O_3$: C 52.79, H 5.64, N 22.39; found: C 52.83, H 5.65, N 22.47.

Method B. From **12c** as described for **3a**: 83 mg (66%) of **3c**.

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