The Thermal N^9/N^7 Isomerization of N^2-Acylated 2′-Deoxyguanosine Derivatives in the Melt and in Solution

by **Bozenna Golankiewicz**[a]), **Tomasz Ostrowski**[a]), **Peter Leonard**[b]), and **Frank Seela***[b])

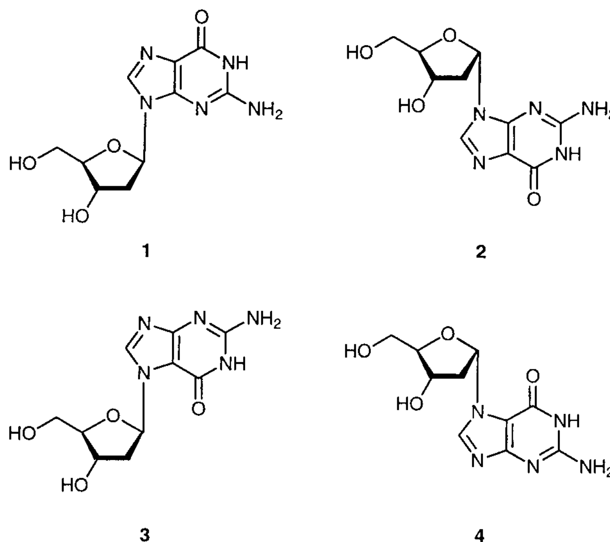
[a]) Institute of Bioorganic Chemistry, Polish Academy of Sciences, Noskowskiego 12/14, PL-61-704 Poznan
[b]) Laboratorium für Organische und Bioorganische Chemie, Universität Osnabrück, Barbarastr. 7, D-49076 Osnabrück

The protected 2′-deoxyguanosine derivatives **5a–c** undergo $N^9 \rightarrow N^7$ isomerization in the melt and in solution. The rate of isomerization is much faster than in the case of the corresponding ribonucleosides and occurs even in the absence of a catalyst. In the melt (195°, 2 min), the N^2,3′-*O*,5′-*O*-tris(4-toluoyl) derivative **5b** and the N^2-acetyl-3′,5′-bis-*O*-[(*tert*-butyl)dimethylsilyl] derivative **5c** gave anomeric mixtures of the N^7-isomers **9b/10b** (43%) and **9c/10c** (55%), respectively. In addition, the N^9-*α*-D-anomers **8b** and **8c** were obtained. Different from **5b**, the isomerization of peracetylated **5a** resulted in low yields. Compound **5b** was also prone to isomerization performed in solution (toluene, 100°, 5 min; chlorobenzene, 120°, 5 min), furnishing the N^7-regioisomers in 24–53% yield. The highest yield of the $N^9 \rightarrow N^7$ isomerization occurred in the presence of 2-deoxy-3,5-di-*O*-(4-toluoyl)-*α*-D-*erythro*-pentofuranosyl chloride.

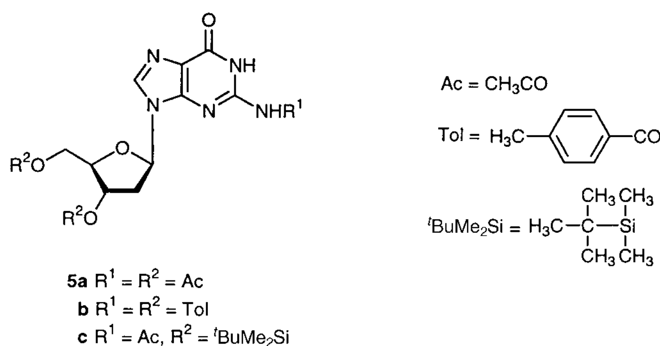
Introduction. – N^9-Glycosylated guanine is formed when silylated N^2-acetylguanine is treated with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-*β*-D-ribofuranose in the presence of trimethylsilyl trifluoromethanesulfonate (Me_3SiOTf) at reflux temperature in 1,2-dichloroethane [1]. When the glycosylation reaction is performed in MeCN with $SnCl_4$ as catalyst, the protected N^7-nucleosides are formed predominantly [2]. This indicates that the formation of regioisomeric glycosylation products depends on the catalyst, the solvent, and the temperature. The outcome of the reaction is also influenced by the structure of the base and the activated sugar [2]. The mechanism of the glycosylation reaction has been discussed by *Garner* and *Ramakanth* [3] and also recently by *Robins* and co-workers [4]. The isomerization of glycosylated intermediates is described for purine N^3-nucleosides [5]. Little attention has been paid to the fact that preformed purine N^7- or N^9-nucleosides can isomerize at elevated temperature. *Miyaki* and *Shimizu* have noted a reversible conversion of the N^2-acetyl-N^7-(2′,3′,5′-tri-*O*-benzoyl-ribosyl)guanine to the corresponding N^9-nucleoside [5]. Later, it was observed that N^9-ribosylated 6-oxopurines or corresponding acyclo derivatives, which are fully acylated undergo thermal isomerization to N^7/N^9-mixtures [6–8]. The reaction takes place even in the absence of a catalyst, when the starting material is kept in a melt for 5–10 min at a temperature exceeding 190°. While dependent on the reaction temperature and time, the ratio of regioisomers (N^7 *vs.* N^9) is also influenced by the structures of the base and the substituents, including protecting groups. Thus, elevated temperatures, applied to an isomerically pure N^9-*β*-D-ribonucleoside, can lead to the isomerization of the starting material under the formation of an N^7-regioisomer.

So far, these isomerization reactions have been performed with purine ribonucleosides and were not studied with purine 2′-deoxyribonucleosides. As the purine N^7-2′-

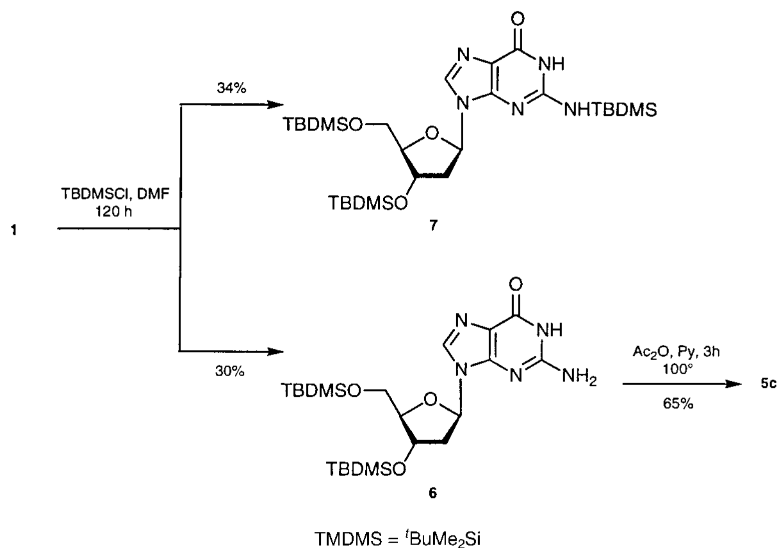
deoxyribonucleosides are not easily accessible [9–11], the thermal isomerization of a canonical DNA constituent to its N^7-isomer is of considerable interest. We now report the isomerization of protected 2′-deoxyguanosine derivatives in the melt and in solution. The absence of 2′-(acyloxy) substituents that, in case of ribonucleosides, control the stereochemistry of the reaction can lead to the formation of anomers of the isomerized 2′-deoxyribonucleosides (see **1**–**4**).



Results and Discussion. – *Starting Materials.* Three different 2′-deoxyguanosine derivatives **5a**–**c** were employed in the isomerization reactions. The acetylated 2′-deoxyguanosine **5a** was prepared as described [12]. The yield of the tris(4-toluoyl) derivative **5b** was increased from 43 to 78% [13]. The N^2-acetyl-3′,5′-bis-*O*[(*tert*-butyl)dimethylsilyl]-2′-deoxyguanosine (**5c**) has been prepared earlier [14] by acetylation of 3′,5′-bis-*O*-[(*tert*-butyl)dimethylsilyl]-2′-deoxyguanosine (**6**). In our hands, silylation of 2′-deoxyguanosine (**1**) with a tenfold excess of ^{t}BuMe$_2$SiCl at 120° furnished the 3′,5′-di-*O*-silylated derivative **6** (30%) together with N^2,3′-*O*,5′-*O*-tris [(*tert*-butyl)dimethylsilyl]-2′-deoxyguanosine (**7**) (34%) (*Scheme 1*).



Scheme 1



Isomerization of the Protected 2′-Deoxyguanosine Derivatives **5a**–**c** *in the Melt.* The thermal isomerization of 6-oxopurine ribonucleosides occurs stereoselectively with only little anomerization of the sugar moiety [15]. This is similar to what has been observed during the glycosylation by the fusion method and is in accordance with *Baker*'s *trans* rule [16]. Contrary to this, for purine 2′-deoxyribonucleosides, the situation is more complex and is expected to lead to anomerization. The thermal isomerization of peracetylated 2′-deoxyguanosine **5a** in a melt (215°, 2 min) resulted in a mixture of the N^7-β-D- and the N^7-α-D-isomers **9a** and **10a**, respectively, in only 8% yield (*Table 1*; *Scheme 2*). Chromatographic separation failed. The thermal isomerization of the N^2,3′-*O*,5′-*O*-tris(4-toluoyl)-protected 2′-deoxyguanosine derivative **5b** gave significantly higher yields, and the amount of N^7-isomers was significantly increased when compound **5b** was heated at 195° for 2 min (*Table 1*). Chromatographic separation of the resulting mixture in CH_2Cl_2/EtOH afforded sequentially a mixture of N^7-α-D- and N^7-β-D-anomers (**10b**/**9b**, 43%), the N^9-α-D anomer of the starting material (**8b**, 10%), and unchanged educt (**5b**, 13%). The mixture **9b**/**10b** was subjected to fractional crystallization from toluene followed by MeOH, which provided anomerically pure **9b** (14%) and **10b** (20%). The best separation procedure, entirely based on chromatography, was more tedious and gave lower yields (**9b**, 11%; **10b**, 17%). Deprotection of compounds **5b** and **8b**–**10b** was accomplished in 33% $MeNH_2/H_2O$, furnishing the pure 2′-deoxyguanosine (**1**) and its isomers **2**–**4** (90–95% yield), identical to those obtained by other methods [11][17].

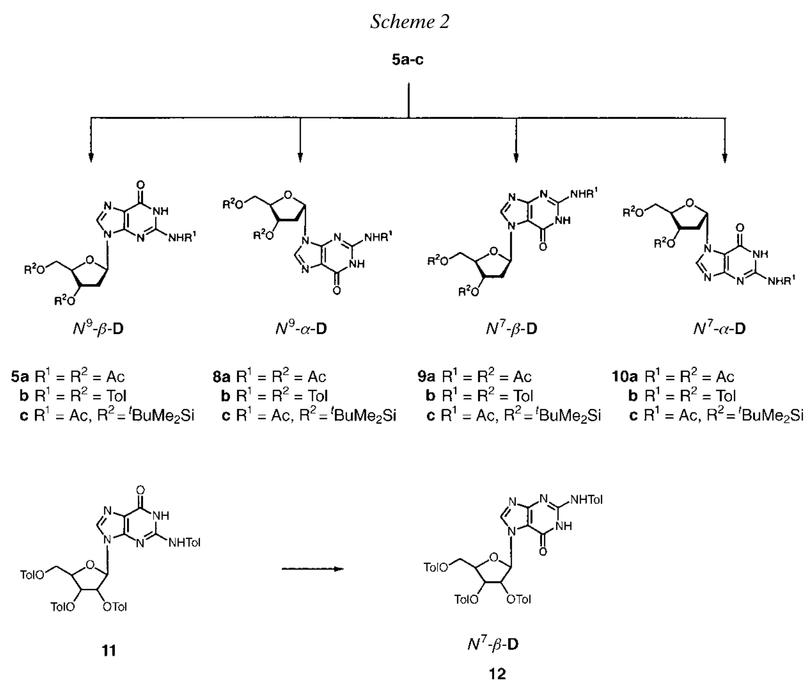
When the thermal isomerization in the melt was performed with N^2-acetyl-3′,5′-bis-*O*-[(*tert*-butyl)dimethylsilyl]-2′-deoxyguanosine (**5c**), the N^9/N^7 equilibrium moved towards the 7-isomer. The yield of the mixture **9c**/**10c** of N^7-β-D- and N^7-α-D-anomers was 55% after FC (*Table 1*). Unfortunately, the differences in the chromatographic

Table 1. *Distribution of Regioisomers* (N^7 *vs.* N^9) *and Anomers* (β *vs.* α) *Formed Upon the Thermal Isomerization of Protected 2′-Deoxyguanosine Derivatives in Dependence on Protecting Groups and Reaction Conditions*

	Protecting groups		Phase	Addition	Reaction conditions	Temp	Time	Yield [%][a])			
	R^1	R^2	(M,S)[b])		(solvent)	[°]	[min]	N^7-β	N^7-α	N^9-α	N^9-β
5a	Ac	Ac	M	none	–	215	2	3.5	4.5	14	67
5a	Ac	Ac	S	$AlCl_3$	1,2-dichloroethane	85	60	4.5	7.5	–	77
5a	Ac	Ac	S	TsOH	chlorobenzene	120	5	10	16	–	36
5b	Tol	Tol	M[c])	none	–	195	2	17	26	10	13
5b	Tol	Tol	S[c])	halogenose[d])	toluene	100	5	22	31	11	12
5b	Tol	Tol	S	TsOH	chlorobenzene	120	5	14	28	9	8
5b	Tol	Tol	S	none	chlorobenzene	120	5	14	10	–	55
5c	Ac	^{t}BuMe$_2$Si	M[c])	none	–	195	2	20	35	19	13
11				TsOH	chlorobenzene	120	5	0.4	–	–	85
						120	5	–	–	–	70

[a]) Percent of totally protected **1** subjected to isomerization determined from the ^{1}H-NMR spectra of the N^7- and N^9-isomer fractions, separated chromatographically. [b]) M = melt, S = solution. [c]) Experiments in which pure anomers were isolated. [d]) 2-Deoxy-α-D-*erythro*-3,5-di-*O*-(4-toluoyl)pentofuranosyl chloride.

Scheme 2



mobilities of **9c** ($R_f(B)$ 0.65) and **10c** ($R_f(B)$ 0.63) were too small to allow easy separation (see *Exper. Part*). Parenthetically, we noticed that the order of TLC mobility of α-D- and β-D-anomers of silylated nucleosides is reversed compared to the peracylated compounds, *i.e.*, the silylated β-D-anomers migrate faster than α-D-anomers.

Anomerically homogeneous **9c** (12%) and **10c** (23%), separated by repeated FC operations, failed to crystallize although their mixture cocrystallized (m.p. 157–159°). Compound **10c** was also partly separated from the EtOH/H_2O 2:1 mother liquors of cocrystallizing **9c/10c**. It is worth to note that although the melting point of compound **5c** is 122–123°, the thermal isomerization does not occur below 185°. Deprotection of **10c** with NH_4F in MeOH followed by FC gave the *N*-acetyl derivative of **4**, which was deblocked with 33% $MeNH_2/H_2O$ (reflux) to give **4** (44% from **10c**). The compound was identical in all respects to that obtained above *via* isomerization of the 4-toluoyl derivative. Higher deprotection yields of **9c** and **10c** (84%) were obtained when a crude desilylated material was subjected to deacetylation, followed by chromatography on silanized silica-gel column to remove F^- ions.

Isomerization in Solution. The thermal isomerization was also performed in solution in aprotic solvents. When heated at 85° for 1 h, the peracetylated 2′-deoxyguanosine **5a** isomerized in 1,2-dichloroethane solution in the presence of $AlCl_3$, providing only 12% of the N^7-isomers as an inseparable mixture of anomers. In contrast, the pertoluoylated educt **5b** gave considerably better results than obtained in the melt. When compound **5b** was heated in toluene in the presence of 2-deoxy-α-D-*erythro*-3,5-di-*O*-(4-toluoyl)pentofuranosyl chloride (1 equiv.) at 100°, within 5 min, three new faster-migrating reaction products as well as decomposed material were observed on TLC. The products were separated by FC (CH_2Cl_2/MeOH 100:0 → 98:2) to afford sequentially the N^7-α-D-anomer **10b** (31%), the N^7-β-D-anomer **9b** (22%), the N^9-α-D-anomer **8b** (11%), and unchanged substrate **5b** (12%) (*Table 1*). Compound **10b** was recrystallized from toluene and compound **9b** from MeOH, furnishing anomerically pure materials. The superiority of this approach in the presence of a sugar halide may be due to the fact that **5b** and the halogenose form a 7,9-bis(β-D-2-deoxyribofuranosyl)guanine intermediate. A similar species has been previously isolated upon the $N^9 \rightarrow N^7$ isomerization of 6-oxopurine ribonucleosides [18] and acyclonucleosides [19]. It has been postulated also in these cases that the bis-riboside is an intermediate of the $N^9 \rightarrow N^7$ isomerization [18]. The rate of $N^9 \rightarrow N^7$ transformation of the deoxynucleoside **5b** (equimolar amount of sugar halide and **5b** in toluene at 100°), is surprisingly higher than that of the protected ribonucleoside [15].

To establish which structural elements and reaction conditions are crucial for the formation of N^7-(2′-deoxyribonucleosides) *vs.* N^7-ribosides in solution, the influence of the protecting groups was studied. The reactions were performed for 5 min (like in the experiment with addition of halogenose) in chlorobenzene at 120° with TsOH as catalyst (like in [15]). The components of the obtained mixtures were separated by FC into fractions of N^7-β-D- and N^7-α-D-anomers, N^9-α-D-anomer, and unreacted substrate. The distribution of β/α-D-anomers in the N^7-isomer fraction was determined from the ^{1}H-NMR spectra. The results are summarized in *Table 1*.

It turned out that various protected 2′-deoxyguanosine derivatives generally undergo transglycosylation in solution to N^7-isomers at a much higher rate and in a better yield than their corresponding ribonucleosides. The type of protecting group is of some importance in the 2′-deoxyribo series. Peracetylated 2′-deoxy derivative **5a** isomerized into N^7-nucleosides in 26%, pertoluoylated **5b** in 42% yield. Even without catalyst, **5b** isomerized in 24% yield. As compound **5b** furnished the highest yields when the $N^9 \rightarrow N^7$ isomerization was performed in solution, the reaction was also

studied with N^2-(4-toluoyl)-9-[2′,3′,5′-tri-*O*-(4-toluoyl)-β-D-ribofuranosyl]guanine (**11**), which was subjected to the isomerization in chlorobenzene in the presence of TsOH at 120°. Unexpectedly, the formation of isomerization products, namely of the pertoluoylated N^7-β-D-guanosine **12** was rather low (traces after 5 min, 5% after 2 h). The higher stability of the *N*-glycosylic bond of the ribonucleoside may account for this finding.

The position of glycosylation (N^9 or N^7) of the compounds was assigned according to the chemical shifts of the bridgehead atoms C(4) and C(5) (*Table 2*). Coupling constants *J*(C,H) are given in *Table 3*. The anomeric configuration (β-D or α-D) was

Table 2. *^{13}C-NMR Chemical Shifts of Purine 2′-Deoxyribonucleosides*[a])[b])[c])

	C(2)	C(4)	C(5)	C(6)	C(8)	C(1′)	C(2′)	C(3′)	C(4′)	C(5′)
1	153.8[e])	151.0	117.0	156.7[e])	135.4	82.7	40.0	70.6	87.7	61.6
5b	148.4	148.6	121.0	155.1	137.9	83.5	35.8	75.3	81.9	64.2
c	147.9[e])	148.4[e])	120.2	154.8[e])	137.0	82.6	[d])	71.9	87.2	62.6
6	153.9[e])	151.1	117.0	156.8[e])	135.3	83.0	35.8	75.3	81.6	64.3
7	150.1	154.2	117.1	156.5	134.8	82.7	[d])	72.3	87.9	62.8
3	153.9[e])	160.4	107.5	155.5[e])	141.0	85.5	41.2	70.3	87.8	61.5
9b	147.6	158.1	111.0	152.4	143.5	86.0	37.6	74.8	81.9	64.2
c	146.7[e])	[f])	110.7	[f])	142.0	87.3	41.1	71.6	85.7	62.4
10b	147.3	158.0	110.7	152.6	141.8	87.6	[d])	74.7	83.7	64.0
c	146.9[e])	157.6	110.4	152.9[e])	141.9	86.9	41.1	72.4	89.0	62.7
8b	148.0[e])	148.1[d])	120.9	154.9[e])	137.4	83.3	37.4	74.8	85.0	64.0
c	147.7[e])	148.0[d])	120.8	154.8[e])	137.6	88.7	[d])	72.5	84.2	62.7

[a]) Spectra measured in (D_6)DMSO rel. to $SiMe_4$ at r.t. [b]) From ^{1}H,^{13}C gated-decoupled spectra. [c]) Purine numbering. [d]) Superimposed by DMSO. [e]) Tentative. [f]) Not detected.

Table 3. J*(C,H) Coupling Constants* [Hz] *of Purine 2′-Deoxyribonucleosides*[a])[b])

	5b	**7**	**9b**	**10b**
J(C(4), *H*–C(1′))	2.8	*s*	–	–
J(C(4), *H*–C(8))	2.7	*s*	12.0	12.8
J(C(5), *H*–C(1′))	–	–	–	*m*
J(C(5), *H*–C(8))	11.0	11.0	–	*m*
J(C(8), *H*–C(8))	215	215	212	214
J(C(8), *H*–C(1′))	4.0	3.3	3.0	3.5
J(C(1′), *H*–C(1′))	167	164	167	176
J(C(2′), *H*–C(2′))	–	–	139	–
J(C(3′), *H*–C(3′))	151	149	157	151
J(C(4′), *H*–C(4′))	154	148	152	152
J(C(5′), *H*–C(5′))	150	141	148	148

[a]) From ^{13}C-NMR spectra measured in (D_6)DMSO at 23°. [b]) Purine numbering.

determined from the chemical shift differences between H–C(4′) and 2 H–C(5′) of the protected nucleosides. For the assignment of the particular C-signals, gated-decoupled spectra were used.

Conclusions. – The pertoluoylated 2′-deoxyguanosine **5b** undergoes thermal isomerization both in the melt and in solution, furnishing the N^7-β-D-, N^7-α-D-, and

N^9-α-D-guanines besides the educt. The peracetylated compound **5a** and the N^2-acetyl-3′,5′-bis-*O*-[(*tert*-butyl)dimethylsilyl] derivative **5c** isomerize as well. Compound **5a** gives lower yields of isomeric products than **5b**, while the isomerization of **5c** furnishes the higher yields, but the separation of isomers is tedious. The isomerization approach performed on compound **5b** gives the N^7-β-D-2′-deoxyguanosine **3** in approximately the same yield as the earlier reported glycosylation of 6-isopropoxypurin-2-amine [11] but by a shorter route. From the mechanistic point of view, the formation of the N^7-nucleosides is most probably the result of a reversible transglycosylation reaction. Different from regular transglycosylation, where the reactions take place between protected nucleoside as sugar donor and a nucleobase as acceptor molecule [20], the donor and acceptor of the molecules are of identical structure. As the 9-position of the acceptor molecules **5a**–**c** is protected by the sugar moiety, a zwitterionic 7,9-bis(2-deoxyribofuranosyl)guanine intermediate can be formed. Then, the sugar moiety is released from either the N^7- or the N^9-position. As the protected 2′-deoxyribose cation can be attacked by the nucleobase from both sites, anomerization takes place.

Financial support by the *European Community* fellowship, contract 05/EGS93/547/63 (ERB 3510 PL92 0943), for *B. G.* and by the *Deutsche Forschungsgemeinschaft* for *F. S.* is gratefully acknowledged.

Experimental Part

1. *General*. Short-column chromatography (CC) and flash chromatography (FC): silica gel *60 H*, particle size 15–40 or 40–63 μm (*Merck*). TLC: precoated silica gel *60 F_{254}* glass plates (0.25 mm, *Merck*). Solvent systems: CH_2Cl_2 (*A*), CH_2Cl_2/MeOH 98:2 (*B*), CH_2Cl_2/MeOH 95:5 (*C*), CH_2Cl_2/MeOH 9:1 (*D*), CH_2Cl_2/MeOH 4:1 (*E*), BuOH/H_2O 86:14 (*F*), toluene/EtOH 95:5 (*G*), toluene/EtOH 9:1 (*H*), toluene/MeOH 6:1 (*I*), toluene/MeOH 5:1 (*J*). M.p.: *Laboratory Devices MEL-TEMP-II* capillary micromelting point apparatus; uncorrected. UV Spectra: *Perkin-Elmer Lambda-EZ201* spectrophotometer; λ_{max} (ε). ^{1}H- and ^{13}C-NMR Spectra: *Varian Unity-300* spectrometer operating at 299.95 and 75.43 MHz, resp., and *Avance-250* or *AMX-500* spectrometers (*Bruker*, Karlsruhe, Germany) at 250.13 and 500.14 MHz for ^{1}H and at 125.13 MHz for ^{13}C; δ in ppm downfield from internal $SiMe_4$. Microanalyses were performed by the *Mikroanalytisches Laboratorium Beller* (Göttingen) and by the Microanalytical Laboratories of the Institute of Organic Chemistry, Polish Academy of Sciences, Warsaw.

2. *2-(Acetylamino)-9-(3,5-di-*O*-acetyl-2-deoxy-β-*D*-*erythro*-pentofuranosyl)-1,9-dihydro-6*H*-purin-6-one* (**5a**) was prepared according to [12].

3. *Isomerization of* **5a**. *In the Melt* (*Method A*). Compound **5a** (30 mg, 0.076 mmol) was heated in an open tube at 215° for 2 min after it had melted (?). The mixture was separated by TLC (*D*) to give a faster-migrating (2.4 mg) and a slower-migrating fraction (24.3 mg). Both fractions contained mixtures of anomers: fast-migrating mixture, **9a** (3.5%) and **10a** (4.5%) and slow-migrating mixture; **5a** (67%) and **8a** (14%) (by ^{1}H-NMR).

In Solution (*Method B*). A soln. of **5a** (150 mg, 0.38 mmol) in 1,2-dichloroethane (10 ml) was heated under reflux in the presence of $AlCl_3$ (202 mg, 1.52 mmol) for 1 h. The mixture was poured into sat. $NaHCO_3$ soln. (50 ml), and the aq. phase was extracted with $CHCl_3$ (6 ×). The combined org. layer was dried (Na_2SO_4) and evaporated. The residue was submitted to CC (column 14 × 3.5 cm, *C*, 10-ml fractions): sequentially 18 mg (12%) of the N^7-isomers **10a** (7.5%) and **9a** (4.5%) (TLC (*D*): R_f 0.47) and **5a** (115 mg, 77%). Assignment was made according to the ^{1}H-NMR spectra.

In Solution (*Method C*). To a suspension of **5a** (118 mg, 0.30 mmol) in dry chlorobenzene (50 ml), TsOH · H_2O (5.7 mg, 0.03 mmol) in MeCN (300 μl) was injected. The mixture was introduced into a preheated vessel (120°, oil bath) and stirred for 5 min. The cooled soln. was evaporated. The residue was suspended in solvent *B* and subjected to CC (column 12 × 3.5 cm, *B* → *C*, 12-ml fractions): sequentially 31 mg (26%) of the N^7-isomer fraction, containing **10a** (16%) and **9a** (10%) and **5a** (42 mg, 36%).

*2-(Acetylamino)-7-[3,5-di-*O*-acetyl-2-deoxy-β-*D*-*erythro*-pentofuranosyl]-1,7-dihydro-6*H*-purin-6-one* (**9a**) *and 2-(Acetylamino)-7-[3,5-di-*O*-acetyl-2-deoxy-α-*D*-*erythro*-pentofuranosyl]-1,7-dihydro-6*H*-purin-6-one*

(**10a**). TLC (*D*): R_f 0.47. UV (MeOH): 263 (14100), 283 (sh, 11000). ^{1}H-NMR ((D_6)DMSO): 1.92, 2.02, 2.07, 2.09, 2.17 (5*s*, 6 Me); 2.56, 2.91 (2*m*, 4 H−C(2′)); 4.18 (*m*, H−C(4′), 4 H−C(5′)); 4.74 (*m*, H−C(4′)); 5.18, 5.31 (2*m*, 2 H−C(3′)); 6.53 ('*t*', H−C(1′) of **9a**); 6.59 (*dd*, H−C(1′) of **10a**); 8.35 (*s*, H−C(8) of **10a**); 8.47 (*s*, H−C(8) of **9a**); 11.61 (*s*, 2 NH); 12.15 (*s*, 2 NH).

4. *Deprotection of* **9a/10a**. The isolated mixture **9a/10a** was dissolved in 25% aq. NH_3 soln./MeOH 1:1 and kept at r.t. for 24 h. TLC (*E*) showed the change of the R_f value from 0.71 to 0.03. Evaporation gave a crude mixture **3/4** (components indistinguishable by TLC, distinguishable by ^{1}H-NMR).

5. *9-[2-Deoxy-3,5-di-*O*-(4-toluoyl)-β-*D*-*erythro*-pentofuranosyl]-1,9-dihydro-2-[(4-toluoyl)amino]-6*H*-purin-6-one* (**5b**). Anh. 2′-deoxyguanosine (**1**, 400 mg, 1.5 mmol) in anh. pyridine (20 ml) was treated with freshly distilled 4-toluoyl chloride (2.09 g, 13.5 mmol) at 50° for 4 h while stirring (TLC (*D*) monitoring). The solvent was evaporated and the residue co-evaporated with anh. toluene (twice) and applied to CC (column 15 × 3.5 cm, *A* → *B*, 15-ml fractions): **5b** (725 mg, 78%). Solid foam. Crystallization from MeOH afforded colorless crystals. M.p. 172° (soft. at 118–120°). TLC (*B* 2 ×): R_f 0.40. TLC (*D*): R_f 0.61. UV (MeOH): 243 (52400), 294 (18900). ^{1}H-NMR ((D_6)DMSO): identical to data reported in [13]. Anal. calc. for $C_{34}H_{31}N_5O_7$ (621.64): C 65.69, H 5.03, N 11.27; found: C 65.84, H 5.24, N 11.27.

6. *Isomerization of* **5b**. *In the Melt* (*Method A*). Compound **5b** (200 mg, 0.32 mmol divided into four 50-mg portions) was heated at 195° for 2 min since it had melted. TLC (*B*, 2 ×). R_f 0.75, 0.73, 0.42, and 0.40. The solvent was evaporated and the residue suspended in *A* and applied to CC (column 17 × 3.5 cm, *A* → *C*): sequentially 86 mg (43%) of N^7-α-D- and N^7-β-D-anomers **10b/9b** (26% and 17%, resp.), N^9-α-D-anomer **8b** (21 mg, 10%), and N^9-β-D-anomer **5b** (25 mg, 13%).

In Solution (*Method B*). Compound **5b** (200 mg, 0.32 mmol) was suspended in toluene (10 ml) and heated at 100° in the presence of 2-deoxy-3,5-di-*O*-(4-toluoyl)-α-D-*erythro*-pentofuranosyl chloride [21] (124 mg, 0.32 mmol) for 5 min. The solvent was evaporated and the residue applied to FC: sequentially **10b** (62 mg, 31%), **9b** (44 mg, 22%), **8b** (22 mg, 11%), and **5b** (24 mg, 12%).

In Solution (*Method C*). To a suspension of **5b** (162 mg, 0.26 mmol) in dry chlorobenzene (10 ml), TsOH · H_2O (5 mg, 0.026 mmol) in MeCN (250 μl) was added. The mixture was immersed in a thermostatted (120°) oil bath and stirred for 5 min. The soln. was evaporated at ≤35°. The residue was suspended in *A* and chromatographed (column 24 × 3.5 cm, *A* → *B*, 10-ml fractions): sequentially 68 mg (42%) of the N^7-isomers (^{1}H-NMR: **10b** (28%) and **9b** (14%) and 28 mg (17%) of the N^9-isomers **8b** (9%) and **5b** (8%)).

In Solution (*Method D*). Compound **5b** (80 mg, 0.129 mmol) was suspended in dry chlorobenzene (6 ml) and heated at 120° in an oil bath for 5 min. The resulting soln. was evaporated at ≤40°. The residue was dissolved in *A* and submitted to CC (column 14 × 3.5 cm, *A* → *B*, 6-ml fractions): sequentially 19 mg (24%) of the N^7-isomers (^{1}H-NMR: **10b** (10%) and **9b** (14%)) and 44 mg (55%) of the pure N^9-β-D-isomer **5b**.

Separation by Crystallization. The mixture **9b/10b** (86 mg, 0.14 mmol) was dissolved in toluene (64 ml, 100°) furnishing crystalline **10b** (39 mg, 20%) after cooling. Then, the mother liquor was evaporated and the residue treated with MeOH (10 ml) at r.t. inducing the crystallization of compound **9b**. The procedure was repeated (3 ×) furnishing pure **9b** (27 mg, 14%).

Separation by Chromatography. The mixture **9b/10b** (39 mg, obtained by isomerization of 100 mg of **5b**) was applied to CC (column 16 × 3 cm, *A* → *B*): sequentially **10b** (17 mg, 17%) and **9b** (11 mg, 11%).

*7-[2-Deoxy-3,5-di-*O*-(4-toluoyl)-α-*D*-*erythro*-pentofuranosyl]-1,7-dihydro-2-[(4-toluoyl)amino]-6*H*-purin-6-one* (**10b**). Colorless crystals. M.p. 255° (dec.; soft. at 139°). TLC (*B*, 2 ×): R_f 0.75. UV (MeOH): 241 (52900), 274 (21500). ^{1}H-NMR ((D_6)DMSO): 2.36, 2.40 (2*s*, 3 Me); 2.79, 3.06 (2*m*, 2 H−C(2′)); 4.53, 5.10 (2*m*, H−C(4′), 2 H−C(5′)); 5.61 (*d*, H−C(3′)); 6.72 (*dd*, H−C(1′)); 7.32, 7.62, 7.96 (3*m*, 12 arom. H); 8.50 (*s*, H−C(8)); 11.81 (*s*, NH); 12.44 (*s*, NH). Anal. calc. for $C_{34}H_{31}N_5O_7$ (621.64): C 65.69, H 5.03, N 11.27; found: C 65.54, H 5.15, N 11.35.

*7-[2-Deoxy-3,5-di-*O*-(4-toluoyl)-β-*D*-*erythro*-pentofuranosyl]-1,7-dihydro-2-[(4-toluoyl)amino]-6*H*-purin-6-one* (**9b**). Colorless crystals. M.p. 244–245° (dec.; soft. at 124°). TLC (*B*, 2 ×): R_f 0.73. UV (MeOH): 242 (53600), 275 (23800). ^{1}H-NMR ((D_6)DMSO): 2.36, 2.40, 2.41 (3*s*, 3 Me); 2.83, 3.13 (2*m*, 2 H−C(2′)); 4.59 (*m*, H−C(4′), 2 H−C(5′)); 5.71 (*d*, H−C(3′)); 6.69 ('*t*'), H−C(1′)); 7.32, 7.92 (2*m*, 12 arom. H); 8.53 (*s*, H−C(8)); 11.86 (*s*, NH); 12.50 (*s*, NH). Anal. calc. for $C_{34}H_{31}N_5O_7$ (621.64): C 65.69, H 5.03, N 11.27; found: C 65.48, H 5.25, N 11.24.

*9-[2-Deoxy-3,5-di-*O*-(4-toluoyl)-α-*D*-*erythro*-pentofuranosyl]-1,9-dihydro-2-[(4-toluoyl)amino]-6*H*-purin-6-one* (**8b**). Colorless crystals from MeOH. M.p. 212° (soft. at 165°). TLC (*B*, 2 ×): R_f 0.42. UV (MeOH): 243 (47100), 294 (17400). ^{1}H-NMR ((D_6)DMSO): 2.38, 2.40 (2*s*, 3 Me); 3.05 (*m*, 2 H−C(2′)); 4.52, 4.99 (2*m*, H−C(4′), 2 H−C(5′)); 5.66 (*d*, H−C(3′)); 6.49 (*dd*, H−C(1′)); 7.34, 7.72, 7.93 (3*m*, 12 arom. H); 8.27

(*s*, H−C(8)); 11.84 (*s*, NH); 12.36 (*s*, NH). Anal. calc. for $C_{34}H_{31}N_5O_7$ (621.64): C 65.69, H 5.03, N 11.27; found: C 65.83, H 5.16, N 11.35.

7. *General Deprotection Procedure for Compounds* **5b** *and* **8b**–**10b**. A sample of the toluoylated compound **5b** or **8b**–**10b** (10–25 mg) was heated under reflux in 33% $MeNH_2/H_2O$ (2–5 ml). After 2 h (TLC monitoring (*E*): deprotection completed), the solvent was evaporated and the residue washed with *E* (twice). The remaining insoluble material was dried and analyzed by ^{1}H-NMR. From **10b** (10 mg, 0.016 mmol); 33% $MeNH_2/H_2O$ (2 ml), 4 mg (93%) of **4**. From **9b** (15 mg, 0.024 mmol; 33% $MeNH_2/H_2O$ (3 ml)), 6 mg (94%) of **3**. From **8b** (17 mg, 0.027 mmol; 33% $MeNH_2/H_2O$ (3.5 ml)), 7 mg (96%) of **2**. From **5b** (25 mg, 0.040 mmol; 33% $MeNH_2/H_2O$ (5 ml)), 10.5 mg (98%) of **1**.

8. *2-Amino-9-{3,5-bis-*O*-[(*tert*-butyl)dimethylsilyl]-2-deoxy-β-*D*-*erythro*-pentofuranosyl-1,9-dihydro-6*H*-purin-6-one* (**6**) *and 2-[(*tert*-Butyl)dimethylsilyl)amino]-9-{3,5-bis-*O*-[(*tert*-butyl)dimethylsilyl]-2-deoxy-β-*D*-*erythro*-pentofuranosyl]-1,9-dihydro-6*H*-purin-6-one* (**7**). Anh. 2′-deoxyguanosine (**1**; 534 mg, 2 mmol) was stirred with ^{t}BuMe$_2$SiCl (1.81 g, 12 mmol) and 1*H*-imidazole (1.36 g, 20 mmol) in DMF (10 ml) at r.t. for 120 h. The mixture was poured into AcOEt/H_2O 4:1, the product that precipitated was filtered and dried to give **6** (296 mg, 30%) [14]. The org. layer was dried (Na_2SO_4) and evaporated; the residual oil was subjected to CC (filter funnel 4.5 × 6 cm, *C*, 10-ml fractions): TLC-homogeneous **7** (405 mg, 34%) after recrystallization from MeCN (265 mg, 22%). M.p. 198°. TLC (*D*): R_f 0.51. ^{1}H-NMR ((D$_6$)DMSO): 0.04, 0.10, 0.26, 0.87, 0.88, 0.94 (6*s*, 15 Me); 2.20, 2.50 (2*m*, 2 H−C(2′)); 3.68, 3.85 (2*m*, H−C(4′), 2 H−C(5′)); 4.45 (*m*, H−C(3′)); 5.83 (*s*, NH), 6.15 (‘*t*’, H−C(1′)); 7.89 (*s*, H−C(8)); 10.47 (*s*, NH).

*2-(Acetylamino)-9-{3,5-bis-*O*-[(*tert*-butyl)dimethylsilyl]-2-deoxy-β-*D*-*erythro*-pentofuranosyl}-1,9-dihydro-6*H*-purin-6-one* (**5c**). A soln. of **6** (440 mg, 0.89 mmol; TLC (*D*) R_f 0.36) in anh. pyridine (5 ml) and Ac_2O (1.02 g, 0.94 ml, 10 mmol) was stirred at 100° for 3 h. The solvent was evaporated and the residue co-evaporated with anh. EtOH (3 ×) and applied to CC (column 16 × 3 cm, *B*): solid **5c** (460 mg, 96%). Crystallization from MeOH yielded colorless crystals (310 mg, 65%). M.p. 122–123° (soft. 85°). TLC (*B*, 3 ×): R_f 0.42. TLC (*D*): R_f 0.59. UV (MeOH): 259 (23800), 276 (18700). ^{1}H-NMR ((D$_6$)DMSO): 0.04, 0.11, 0.87, 0.89, 2.18 (5*s*, 11 Me); 2.33, 2.72 (2*m*, 2 H−C(2′)); 3.68, 3.85 (2*m*, H−C(4′), 2 H−C(5′)); 4.51 (*m*, H−C(3′)); 6.19 (‘*t*’, H−C(1′)); 8.20 (*s*, H−C(8)); 11.71 (*s*, NH); 12.04 (*s*, NH). Anal. calc. for $C_{24}H_{43}N_5O_5Si_2$ (537.80): C 53.60, H 8.06, N 13.02; found: C 53.70, H 8.05, N 12.92.

9. *Isomerization of* **5c**. *In the Melt*. Open tubes containing **5c** (200 mg, 0.37 mmol, divided into 50-mg portions) were immersed in a preheated silicon-oil bath (195°) for 2 min since it had melted. The resulting oil was dissolved in CH_2Cl_2/MeOH 1:1 and analyzed by TLC (*B*, 3 ×): R_f 0.65, 0.63, 0.42, and 0.39, and some degradation products close to the start.

Separation Method A. The solvent was evaporated and the residue suspended in toluene and submitted to CC (column 16 × 3.5 cm, *G* → *H*, 12-ml fractions): Sequentially 110 mg (55%) of N^7-α-D-and N^7-β-D-anomers (^{1}H-NMR: **10c** (35%) and **9c** (20%)), unchanged N^9-β-D-anomer **5c** (26 mg, 13%) and N^9-α-D-anomer **8c** (37 mg, 19%). The mixture **9c/10c** (110 mg) was dissolved in hot EtOH/H_2O 2:1 (15 ml) and left at r.t. Pure **10c** (homogeneous on TLC (*B*, 3 ×)) remained in the mother liquor after a mixture of **9c** and **10c** had cocrystallized during several days. **9c/10c**: M.p. 157–159°. Anal. calc. for $C_{24}H_{43}N_5O_5Si_2$ (537.80): C 53.60, H 8.06, N 13.02; found: C 53.59, H 7.94, N 12.86.

After evaporation of the solvent, **10c** was obtained as a glassy solid (44 mg, 22%).

Separation Method B. The mixture after isomerization of **5c** (114 mg, 0.21 mmol) was suspended in solvent *B* and submitted to CC (column 12 × 3 cm, *B*, 7-ml fractions). *Fr. 10* contained **9c** (5 mg), *Fr. 11–12* **9c** and **10c** (37 mg), *Fr. 13–14* **10c** (12 mg), *Fr. 17–20* unchanged substrate **5c** (26 mg), *Fr. 21* **5c** and **8c** (4 mg), and *Fr. 22–26* **8c** (18 mg). The total yields of N^7- and N^9-isomers were 47 and 42%, respectively. The mixture **9c/10c** cocrystallized from EtOH/H_2O 2:1 (6 ml). Evaporation of the mother liquor gave **10c** (4 mg) as a glassy solid. The crystalline material (33 mg) was dissolved in *A* and subjected to CC (column 20 × 3 cm, *A* → *A*/*B* 1:1, 8-ml fractions). *Fr. 47–49* contained **9c** (9 mg), *Fr. 50–54* **9c** and **10c** (12 mg), and *Fr. 55–60* **10c** (10 mg). Similarly to compound **10c**, compound **9c** was a glassy solid.

*2-(Acetylamino)-7-{3,5-bis-*O*-[(*tert*-butyl)dimethylsilyl]-2-deoxy-α-*D*-*erythro*-pentofuranosyl}-1,7-dihydro-6*H*-purin-6-one* (**10c**). TLC (*B*, 3 ×): R_f 0.63. UV (MeOH): 222 (24100), 264 (16200), *ca*. 280 (sh). ^{1}H-NMR ((D$_6$)DMSO): 0.04, 0.07, 0.76, 0.89, 2.16 (5*s*, 11 Me); 2.31, 2.73 (2*m*, 2 H−C(2′)); 3.62, 4.29 (2*m*, H−C(4′), 2 H−C(5′)); 4.42 (*m*, H−C(3′)); 6.52 (*dd*, H−C(1′)); 8.30 (*s*, H−C(8)); 11.59 (*s*, NH); 12.12 (*s*, NH).

*2-(Acetylamino)-7-{3,5-bis-*O*-[(*tert*-butyl)dimethylsilyl]-2-deoxy-β-*D*-*erythro*-pentofuranosyl}-1,7-dihydro-6*H*-purin-6-one* (**9c**). TLC (*B*, 3 ×): R_f 0.65. UV (MeOH): 222 (24600), 265 (16100), *ca*. 280 (sh). ^{1}H-NMR ((D$_6$)DMSO): 0.04, 0.10, 0.87, 0.89, 2.16 (5*s*, 11 Me); 2.33, 2.70 (2*m*, 2 H−C(2′)); 3.78, 3.87 (2*m*, H−C(4′), 2 H−C(5′)); 4.50 (*m*, H−C(3′)); 6.51 (‘*t*’, H−C(1′)); 8.42 (*s*, H−C(8)); 11.59 (*s*, NH); 12.15 (*s*, NH).

*2-(Acetylamino)-9-{3,5-bis-*O*-[(*tert*-butyl)dimethylsilyl]-2-deoxy-α-*D*-*erythro*-pentofuranosyl}-1,9-dihydro-6*H*-purin-6-one* (**8c**). Recrystallized from aq. EtOH. M.p. 289–291° (dec.; soft. 163–165°). TLC (*B*, 3 ×): R_f 0.39. UV (MeOH): 259 (22400), 280 (17200). ^{1}H-NMR ((D_6)DMSO): 0.03, 0.07, 0.81, 0.89, 2.18 (5*s*, 11 Me); 2.37, 2.73 (2*m*, 2 H–C(2')); 3.60, 4.22 (2*m*, H–C(4'), 2 H–C(5')); 4.46 (*m*, H–C(3')); 6.19 (*dd*, H–C(1')); 8.12 (*s*, H–C(8)); 11.70 (*s*, NH); 12.03 (*s*, NH).

10. *Deprotection of* **9c** *and* **10c**. *Method A*. To a soln. of **10c** (44 mg, 0.082 mmol; TLC (*E*): R_f 0.89; TLC (*F*): R_f 0.78) in MeOH (5 ml), NH_4F (49 mg, 1.32 mmol) was added. After stirring for 48 h at 40°, TLC showed the presence of the N^2-acetyl derivative (R_f 0.49 (*E*), 0.71 (*F*)) and a trace of the completely deprotected compound **4** (R_f 0.03 (*E*), 0.34 (*F*)). Evaporation of the solvent gave a crude material, which was suspended in toluene and submitted to CC (column 12 × 2.5 cm, *I* → *J*, 8-ml fractions): N^2-acetyl derivative, free of F^- ions (11 mg, 44%). Heating the N^2-acetyl compound under reflux in 33% $MeNH_2/H_2O$ (2 ml) for 4 h followed by evaporation afforded **4** (9.5 mg, 44% overall yield), being homogeneous according to ^{1}H-NMR.

Method B. To the soln. of **9c**/**10c** (50 mg, 0.09 mmol) in MeOH (25 ml), NH_4F (103 mg, 2.78 mmol) was added. After stirring for 14 h under reflux (TLC (*E* and *F*): complete removal of the silyl protecting groups), the soln. was evaporated. The residue was heated under reflux in 33% $MeNH_2/H_2O$ (15 ml) for 2 h and evaporated to give fully deprotected **3** and **4**, indistinguishable from each other by TLC. This material was washed twice with CH_2Cl_2, dried *in vacuo*, and chromatographed (silanized silica-gel column (*Merck 60*, 63–200 μm, 9 × 3 cm), H_2O): 21 mg (84%) of **3**/**4**, free of F^- ions ($AgNO_3$ test). ^{1}H-NMR: presence of both anomers.

*9-(2-Deoxy-β-*D*-*erythro*-pentofuranosyl)-1,9-dihydro-6*H*-purin-6-one* (**1**). UV (H_2O): 253 (16800), 267 (sh, 12200). ^{1}H-NMR ((D_6)DMSO): 2.19, 2.50 (2*m*, 2 H–C(2')); 3.52 (*m*, 2 H–C(5')); 3.80 (*m*, H–C(4')); 4.33 (*m*, H–C(3')); 4.96 (*t*, OH–C(5')); 5.27 (*d*, OH–C(3')); 6.12 ('*t*', H–C(1')); 6.50 (*s*, NH_2); 7.91 (*s*, H–C(8)); 10.40 (*s*, NH).

*7-(2-Deoxy-β-*D*-*erythro*-pentofuranosyl)-1,7-dihydro-6*H*-purin-6-one* (**3**). UV (H_2O): 244 (sh, 5500), 287 (6400). ^{1}H-NMR ((D_6)DMSO): 2.27, 2.46 (2*m*, 2 H–C(2')); 3.56 (*m*, 2 H–C(5')); 3.82 (*q*, H–C(4')); 4.31 (*m*, H–C(3')); 4.95 (*t*, OH–C(5')); 5.27 (*d*, OH–C(3')); 6.19 (*s*, NH_2); 6.43 ('*t*', H–C(1')); 8.25 (*s*, H–C(8)); 10.80 (*s*, NH).

*7-(2-Deoxy-α-*D*-*erythro*-pentofuranosyl)-1,7-dihydro-6*H*-purin-6-one* (**4**). UV (H_2O): 243 (sh, 5900), 285 (6900). ^{1}H-NMR ((D_6)DMSO): 2.21, 2.64 (2*m*, 2 H–C(2')); 3.44 (*m*, 2 H–C(5')); 4.13 (*q*, H–C(4')); 4.25 (*q*, H–C(3')); 4.84 (*t*, OH–C(5')); 5.32 (*d*, OH–C(3')); 6.15 (*s*, NH_2); 6.46 (*dd*, H–C(1')); 8.18 (*s*, H–C(8)); 10.77 (*s*, NH).

*9-(2-Deoxy-α-*D*-*erythro*-pentofuranosyl)-1,9-dihydro-6*H*-purin-6-one* (**2**). UV (H_2O): 253 (14200), 267 (sh, 10300). ^{1}H-NMR ((D_6)DMSO): 2.20, 2.68 (2*m*, 2 H–C(2')); 3.43 (*m*, 2 H–C(5')); 4.06 (*q*, H–C(4')); 4.28 (*q*, H–C(3')); 4.83 (*t*, OH–C(5')); 5.47 (*d*, OH–C(3')); 6.10 (*dd*, H–C(1')); 6.46 (*s*, NH_2); 7.97 (*s*, H–C(8)); 10.54 (*s*, NH).

11. *1,9-Dihydro-2-[(4-toluoyl)amino]-9-[2,3,5-tri-*O*-(4-toluoyl)-β-*D*-*erythro*-pentofuranosyl]-6*H*-purin-6-one* (**11**). A suspension of anh. guanosine (460 mg, 1.62 mmol) in anh. pyridine (20 ml) was treated with 4-toluoyl chloride (2.0 g, 12.96 mmol) and stirred at 50° for 8 h. After evaporation, the residue was co-evaporated twice with toluene and purified by CC (column 16 × 5 cm, *A* → *C*): 502 mg (41%) of **11**, which was crystallized from EtOH. M.p. 235–236°. TLC (*B*): R_f 0.19. UV (MeOH): 242 (52700), 290 (13900). ^{1}H-NMR ((D_6)DMSO): 2.33, 2.36, 2.39, 2.41 (4*s*, 4 Me); 4.78 (*m*, H–C(4'), 2 H–C(5')); 6.15 (*t*, H–C(3')); 6.34 (*t*, H–C(2')); 6.46 (*d*, H–C(1')); 7.31, 7.77, 7.87 (3*m*, 16 arom. H); 8.32 (*s*, H–C(8)); 11.61 (*s*, NH); 12.32 (*s*, NH). Anal. calc. for $C_{42}H_{37}N_5O_9$ (755.77): C 66.75, H 4.93, N 9.27; found: C 66.54, H 4.76, N 9.17.

12. $N^9 \rightarrow N^7$ *Isomerization of* **11**. To a suspension of **11** (231 mg, 0.31 mmol) in dry chlorobenzene (20 ml) at r.t., a soln. of TsOH · H_2O (6 mg, 0.032 mmol) in MeCN (300 μl) was injected. The mixture was immersed in a thermostatted oil bath (120°) and stirred for 5 min. The resulting soln. was then withdrawn and evaporated at ≤35°. Chromatography (column 13 × 3.5 cm, *A* → *B*) gave, after evaporation of appropriate fractions, 1 mg (0.4%) of the N^7-isomer **12** and 197 mg (85%) of unreacted 9-isomer **12**.

The experiment carried out under identical conditions for 2 h with 190 mg (0.25 mmol) of **11**, followed by CC gave 10 mg (5%) of **12** and 133 mg (70%) of **11**.

*1,7-Dihydro-2-[(4-toluoyl)amino]-7-[2,3,5-tri-*O*-(4-toluoyl)-β-*D*-*erythro*-pentofuranosyl]-6*H*-purin-6-one* (**12**). TLC (*B*): R_f 0.27. UV (MeOH): 241 (50100), 274 (19000). ^{1}H-NMR ((D_6)DMSO): 2.34, 2.37, 2.38, 2.40 (4*s*, 4 Me); 4.72 (*m*, H–C(4'), 2 H–C(5')); 6.02 (*t*, H–C(3')); 6.21 (*t*, H–C(2')); 6.63 (*d*, H–C(1')); 7.31,7.87 (2*m*, 16 arom. H); 8.59 (*s*, H–C(8)); 11.89 (*s*, NH); 12.57 (*s*, NH).

REFERENCES

[1] H. Vorbrüggen, K. Krolikiewicz, B. Bennua, *Chem. Ber*. **1981**, *114*, 1234.
[2] H. Vorbrüggen, C. Ruh-Pohlenz, in 'Organic Reactions', Ed. L. A. Paquett, John Wiley & Sons Inc., New York-Chichester-Weinheim-Brisbane-Singapore-Toronto, 2000, Vol. 55, p. 1.
[3] P. Garner, S. Ramakanth, *J. Org. Chem*. **1988**, *53*, 1294.
[4] M. J. Robins, R. Zou, Z. Guo, S. F. Wnuk, *J. Org. Chem*. **1996**, *61*, 9207.
[5] M. Miyaki, B. Shimizu, *Chem. Pharm. Bull*. **1970**, *18*, 1446.
[6] J. Boryski, B. Golankiewicz, *Nucleic Acids Res. Symp. Ser*. **1987**, *18*, 45.
[7] J. Boryski, B. Golankiewicz, *Nucleosides Nucleotides* **1989**, *8*, 529.
[8] J. Boryski, B. Golankiewicz, Pol. Patent 1992, 157, 825; *Chem. Abstr.* **1993**, *119*, P249789r.
[9] M. J. Robins, *J. Am. Chem. Soc*. **1981**, *103*, 932.
[10] T. S. Rao, R. H. Durland, G. R. Revankar, *J. Heterocycl. Chem.* **1994**, *31*, 935.
[11] F. Seela, P. Leonard, *Helv. Chim. Acta* **1996**, *79*, 477; F. Seela, P. Leonard, *Helv. Chim. Acta* **1997**, *80*, 1301.
[12] H. Lee, E. Luna, M. Hinz, J. J. Stezowski, A. S. Kiselyov, R. G. Harvey, *J. Org. Chem*. **1995**, *60*, 5604.
[13] D. M. Brown, P. Kong Thoo Lin, *Carbohydr. Res.* **1991**, *216*, 129.
[14] K. K. Ogilvie, *Can. J. Chem*. **1973**, *51*, 3799.
[15] J. Boryski, *J. Chem. Soc., Perkin Trans. 2*, **1997**, 649.
[16] B. R. Baker, R. E. Schaub, H. M. Kissman, *J. Am. Chem. Soc*. **1955**, *77*, 5911.
[17] J. Gambino, T. F. Yang, G. E. Wright, *Tetrahedron* **1994**, *50*, 11363.
[18] L. W. Dudycz, G. E. Wright, *Nucleosides Nucleotides* **1984**, *3*, 33.
[19] J. Boryski, A. Manikowski, *Nucleosides Nucleotides* **1999**, *18*, 1057.
[20] T. Azuma, K. Isono, *Chem. Pharm. Bull*. **1977**, *25*, 3347.
[21] M. Hoffer, *Chem. Ber*. **1960**, *93*, 3041.

Received August 9, 2001