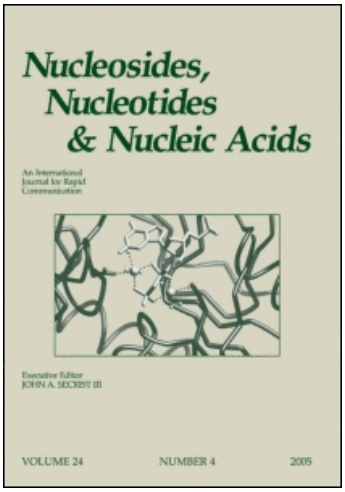

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Synthesis of 6-Substituted Purine N^7-(2-Deoxy-β-D-Ribonucleosides) via Anion Glycosylation and Anomerization During the N^7/N^9-Glycosyl Transfer

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SYNTHESIS OF 6-SUBSTITUTED PURINE N^7-(2-DEOXY-ß-D-RIBONUCLEOSIDES) VIA ANION GLYCOSYLATION AND ANOMERIZATION DURING THE N^7/N^9-GLYCOSYL TRANSFER

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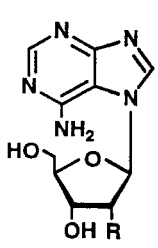
ABSTRACT: The synthesis of the 7-(2-deoxy-ß-D-*erythro*-pentofuranosyl)adenine (**1b**) as well as the corresponding hypoxanthine- and purine nucleosides **3** and **4** is described employing the stereoselective nucleobase anion glycosylation. The N^7/N^9-isomer distribution of the 6-substituted purine (2-deoxyribonucleosides) depends on 6-substituent. Glycosyl transfer of **8a** resulted in anomerization and yielded a mixture of the anomeric 6-methoxypurine N^9-(2-deoxy-D-ribonucleosides) **7a/7d**. The preferred glycosylic bond conformation of purine N^7-(2-deoxyribonucleosides) is anti.

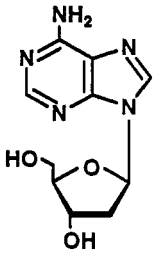
INTRODUCTION

The 7-(D-ribofuranosyl)adenine was isolated from pseudovitamin B_{12} by Friedrich and Bernhauer already in 1956[1]. Montgomery established the α-D configuration of the nucleoside and described the synthesis of the 7-(ß-D-ribofuranosyl)adenine (**1a**)[2]. Recently, our laboratory has prepared the 7-(2-deoxy-ß-D-*erythro*-pentofuranosyl)adenine (**1b**), the isomer of the DNA constituent **2**, from an imidazole precursor[3]. Compound **1b** was converted into phosphonate and phosphoramidite building blocks[4]. Oligonucleotides containing the nucleoside **1b** were synthesized. Duplex formation between the homooligomers $d[(N^7A)_{11}\text{-}A]$ and $d(T_{12})$ was observed and an oligonucleotide duplex structure in which an N^7-glycosylated adenine forms a base pair with thymine was reported for the first time[4]. The base pairing was found to be of the reverse Watson-Crick mode and the strand orientaion was antiparallel. We now report on the synthesis of 7-(2-deoxy-ß-D-*erythro*-pentofuranosyl)adenine (**1b**) as well as corresponding hypoxanthine- and purine nucleosides **3** and **4** by the glycosylation of 6-substituted purine (**5a-c**) anions

with the deoxyhalogenose **6**. Also the transfer of the 2-deoxyribofuranosyl moiety from the purine N^7 to N^9 is studied.



1a: R = OH
1b: R = H



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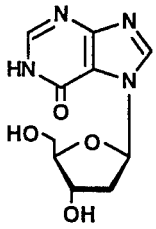

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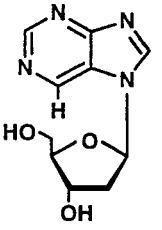

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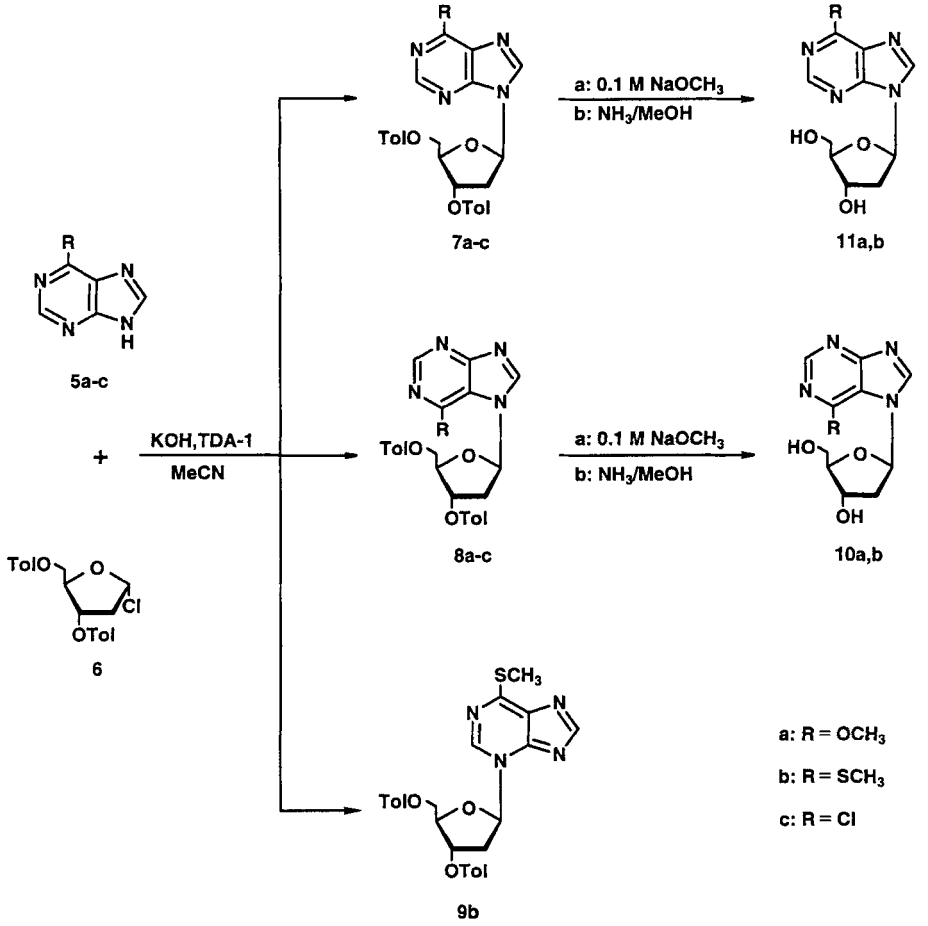
RESULTS AND DISCUSSION

Previous investigations on the nucleobase anion glycosylation[5,6] of 6-chloropurine (**5c**) with the halogenose **6**[7] furnished a mixture of N^9- and N^7-(2-deoxyribonucleosides) in a ratio of 6:1[8]. Similar observations were made in the case of pyrazolo[3,4-d]pyrimidines. Glycosylation of 4-chloropyrazolo[3,4-d]pyrimidine under liquid-liquid phase-transfer conditions only gave the N^1-(2-deoxyribofuranoside) (systematic numbering)[9]. Using NaH as base the N^2-regioisomer was formed as minor product but was not characterized[8]. The situation changed when 4-methoxypyrazolo[3,4-d]pyrimidine was used as a base. Upon its glycosylation[6] the N^2-isomer was formed in 28% yield, together with a 47% yield of the N^1-compound[10]. As a 6-methoxy group increases the yield of pyrazolo[3,4-d]pyrimidines N^2-(2-deoxy-ß-D-ribofuranoside) we have expected a similar result for the formation of purine N^7-(2-deoxy-ß-D-ribofuransides). 6-Methoxypurine (**5a**) was glycosylated with the halogenose **6** in MeCN in the presence of powdered KOH and TDA-1. 6-Chloropurine (**5c**) and 6-methylthiopurine (**5b**) were glycosylated for comparison. The reaction proceeded at room temperature within 20 min and furnished two isomers in the case of **5a** and **5c**; three glycosylation products were formed from **5b**. The reaction products were separated by flash chromatography. The total glycosylation yield was 72% for **5a**, 69% for **5b**, and 69% for **5c**. Similar total yields were obtained in the case of other bases[8,11]. The amount of the N^7-nucleoside **8a** was 28% compared to only 13% for the 6-chloropurine derivative (**8c**). The situation changed in the case of the 6-methylthiopurine (**5b**). Apart from the N^9-compound **7b** (43%) and the N^7-isomer **8b** (9%), the nucleoside **9b** was formed as the third product (16%). The UV-maximum of **9b** is strongly bathochromically shifted (316 nm) compared to those of the other isomers (**7b**: 282 nm and **8b**: 290 nm).

Detoluoylation of the 6-methoxy compounds **7a** and **8a** ($NaOCH_3$/MeOH) furnished the nucleosides **11a** and **10a**, respectively. In the case of **7b** and **8b**, methanolic NH_3 was used (room temperature) instead of $NaOCH_3$ in order to avoid the replacement of the 6-MeS group by OCH_3 which is observed on similar nucleosides[12]. The third isomer was not stable under the conditions of deprotection. The 6-methoxy compounds **10a** and **11a** as well as the 6-methylthio derivatives **10b** and **11b** were isolated crystalline. In both cases the UV-maxima of the N^7-isomer is shifted bathocromically as it was reported for other purine nucleosides[2-4].



Next, the ^{13}C NMR chemical shifts were assigned by gated-decoupled NMR -spectra (Table 1). The change of the glycosylation position from N^9 to N^7 results in a significant downfield shift of C-4 (10 ppm) and an equivalent upfield shift of C-5 which is in line with data reported for the corresponding ribonucleosides[13]. For the deprotected N^9-nucleosides as well as the N^7-compounds the C-4' signal is shifted

TABLE 1. ^{13}C-NMR Chemical Shifts of Purine (2-Deoxyribonucleosides) in (D_6)DMSO at 23°C[a].

	C-2	C-4	C-5	C-6	C-8	SCH_3	OCH_3
1b[4]	152.6	159.4	110.4	151.6	143.6	-	-
3	144.9	157.4	114.3	154.4	141.5	-	-
4	152.0[c]	157.8	124.0	142.0	147.6	-	-
7a	151.8	151.6	121.5	160.5	142.8	-	54.1
7b	151.6	147.8	131.5	160.6	143.5	11.3	-
7c	151.7	151.4	131.7	149.5	146.3	-	-
7d	151.7	151.4	121.3	160.4	141.7	-	54.1
8a	151.8	161.9	111.7	156.5	145.1	-	54.4
8b[b]	152.7	158.6	122.3	153.2	143.3	12.3	-
8c	152.1	162.1	122.0	142.5	147.6	-	-
9b	139.0	147.8	136.0	160.1	158.0	12.0	-
10a	151.6	161.5	111.8	156.6	144.6	-	54.3
10b	151.5	157.9	122.1	152.9	145.4	12.0	-
11a	151.7	151.6	121.2	160.4	142.3	-	54.3
11b	151.8	147.4	131.4	160.9	142.8	11.0	-

	C-1'	C-2'	C-3'	C-4'	C-5'
1b[4]	85.4	40.9	69.3	87.7	60.4
3	85.9	39.4	70.3	88.0	61.2
4	85.8	41.9	70.2	87.9	61.3
7a	84.3	35.6	74.9	81.9	64.0
7b	84.4	35.6	74.9	81.9	64.0
7c	84.7	35.7	74.8	82.1	63.9
7d	85.6	37.2	74.9	83.2	64.1
8a	86.4	37.6	74.6	81.8	64.2
8b[b]	87.0	41.0	74.5	83.3	61.8
8c	85.9	37.7	74.3	82.4	63.9
9b	90.7	37.1	74.6	83.2	63.9
10a	86.4	41.0	70.2	88.1	61.3
10b	86.2	41.0	69.9	88.1	60.9
11a	84.0	DMSO	70.8	88.1	61.7
11b	83.5	DMSO	70.5	87.8	61.6

a) Assignment from gated-decoupled spectra. b) Measured in $CDCl_3$. c) Tentative.

downfield compared to C-1' which is opposite to the protected compounds **7a-c** and **8a-c**. The N^3-glycosylation site was also established from the ^{13}C-NMR spectra. The upfield shift of C-2 (12 ppm) and the downfield shift of C-8 (14 ppm) together with a strongly changed C-1'-chemical shift (90.7 ppm) confirmed the structure of compound **9b**. Furthermore, the NOE data (Table 2) were in line with this observation. Upon irradiation of H-1' NOEs on H-2 and H-4' were observed establishing N^3 as glycosylation position and ß-D as anomeric configuration[14].

For the OCH_3/NH_2-conversion the 4-methoxynucleoside **8a** was treated with methanolic ammonia affording 7-(2-deoxy-ß-D-*erythro*-pentofuranosyl)adenine (**1b**). The nucleoside observed by this route was identical with an authentic sample[4] prepared earlier from an imidazole precursor. Treatment of the 6-methoxy compound **8a** with 2N NaOH furnished 7-(2-deoxy-ß-D-*erythro*-pentofuranosyl)hypoxanthine (**3**) which has been prepared earlier by the reaction of methyl-4(5)-nitroimidazole-5(4)-caboxylate with 2-deoxy-1,2,3-tri-O-acetyl-D-*erythro*-pentofuranose[15]. From compound **8c** obtained during the glycosylation of **5c** the 7-(2-deoxy-ß-D-*erythro*-pentofuranosyl)purine (**4**) was prepared by catalytic hydrogenation (Pd/C) of **8c**, followed by deprotection with methanolic ammonia.

In the case of purine ribonucleosides a regioselective synthesis of the N^7-isomers has been reported[16,17]. It was observed that the reaction of 2,6,9-tris(trimethylsilyl)-2-acetylguanine with 1,2,3,5-tetra-O-acetyl-ß-D-ribofuranose gave predominantly the N^7-ribonucleoside (95:1); the reaction was carried out in acetonitrile at ambient temperature in the presence of tin(IV)chloride. When the same reaction was performed with 1-O-acetyl-2,3,5-tri-O-benzoyl-ß-D-ribofuranose in refluxing 1,2-dichloroethane in the presence of TMS-triflate the N^9-compound dominated over the N^7-isomer by 6:1, which confirmed an earlier report of Vorbrüggen[18]. A similar result was obtained upon the reaction of 2-amino-6-chloropurine with 1,3-diisopropoxy-2-acetoxymethoxypropane at -30°. The N^7-isomer was formed as the main product[19].

Recently, Golankiewicz and Boryski[20] noted that both the N^2,2',3',5'-O-tetracetylguanosine as well as its N^7-isomer isomerize at elevated temperature yielding a N^7/N^9-mixture no matter which isomer was used as starting material. This confirmed earlier observations by Miyaki and Shimizu[21,22]. We have obtained similar results in the case of 2'-deoxy-N^2,3',5'-tri-O-(4-toluoyl)guanosine[23]. However, anomerisation of the sugar moiety was observed during the glycosyl transfer (see Figure). It is interesting to note that the formation of a N^7-compound from a N^9-nucleoside occurs only in the case of 6-oxopurines. If the carbonyl group is converted into a lactim ether either by alkylation or silylation the migration proceedes only from N^7 to N^9.

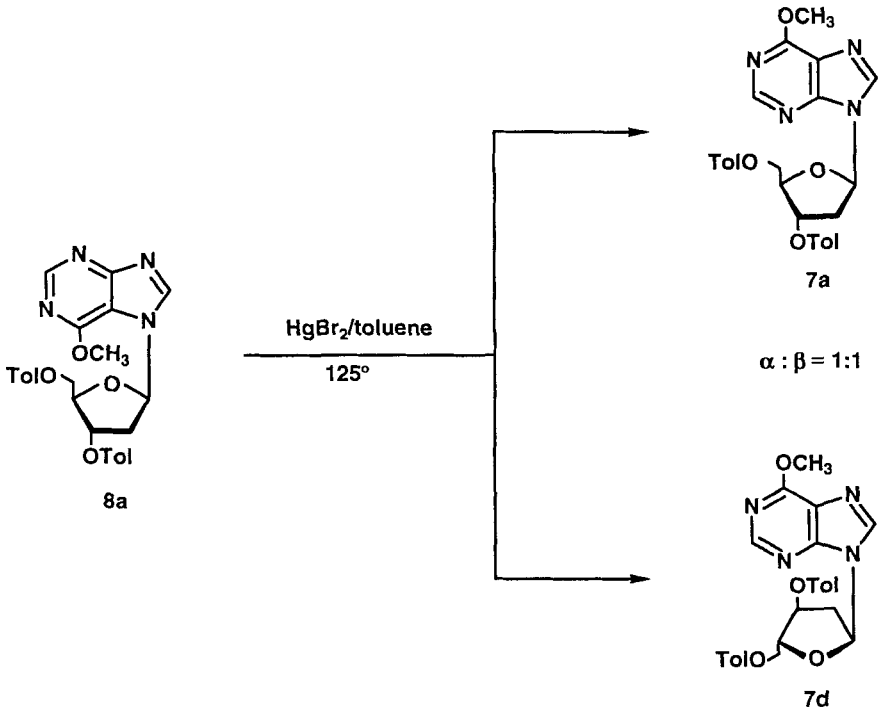
TABLE 2. ^{1}D NOE Values of Purine N^7-(2-Deoxy-ß-D-ribofuranosides) in $(D)_6$DMSO at 23°C.

	Irradiated Proton	NOE (%)
1b	H-8	H-1' (6.9), H-2' (4.6), H-3' (1.2)
4	H-8	H-1'(6.6), H-3'(1.0), H-2'(1.9), 5'-OH (0.8)
9b	H-1'	H-2' (6.2), H-4' (1.4), H-2 (9.3)
	H-2	H-1' (8.3), H-3' (1.2), H-5' (2.3)
10a	H-1'	H-8 (3.1), H-4'(2.0), H-2'(6.4), OMe (1.4)
	H-8	H-1'(2.4), H-3'(1.1), H-2'(2.7), 5'-OH (1.1)
10b	H-1'	H-8 (1.3), H-4'(1.9), H-2'(6.8), 3'-OH (0.9)
	H-8	H-1'(1.5), H-3'(1.8), H-2'(4.7), 5'-OH (1.4)

According to the regioselective formation of N^7-purine ribonucleosides at ambient temperature, a similar result under the ambient temperature conditions of nucleobase anion glycosylation (r.t., MeCN, KOH or NaH) should be expected. However, the generation of the strongly nucleophilic nucleobase anion and the increased reactivity of the 2-deoxyhalogenose **6** over the riboderivative accelerate the glycosylation rate, thereby reducing the N-selectivity. The change in isomer distribution of the 6-methoxypurine (**5a**) vs compounds **5b** and **5c** may be dependent on an altered N-nucleophilicity of the imidazolyl anion compared to the neutral species of the silylated base used during the ribonucleoside synthesis. As the total yield upon the glycosylation of **5a-c** is similar, a decomposition of the hydrolytically more labile N^7-isomers cannot accout for this finding. A migration of the sugar moiety during the alkaline glycosylation conditions can also be excluded, as an exclusive ß-D-stereoslectivity was observed which is not expected from sugar migration. The formation of the N^3-regioisomer **9b** may be explained by the glycosylation of the neutral 6-methylthiopurine. A similar observation was made during the glycosylation of 7-deaza-6-methylthiopurine[24].

Glycosyl transfer of the ß-D-ribofuranose moiety from purine N^7 to N^9 proceeds almost stereoselectively under the formation of the purine N^9-(ß-D-ribonucleosides)

which is the result of acyloxonium ion formation[21,25]. As we had synthesized purine N^7-(ß-D-2-deoxyribosides) it was of interest to elucidate the stereochemical outcome of the N^7/N^9 migration in this case. Compound **8a** was stirred with $HgBr_2$ in toluene under reflux. Similar conditions have beeen described for the isomerization of N^7-ribonucleosides[26]. The reaction was followed by TLC showing that the deoxyribofuranose moiety migrated from N^7 (slow migrating zone) to N^9 (fast migrating zone) within 4h. The inspection of the fast migrating zone showed that this zone was not homogeneous. According to its ^1H NMR spectrum two sets of signals appeared.



One set corresponds to the ß-D-nucleoside **7a**. The remaining signals showed the characteristics of an α-D-2'-deoxynucleoside with well separated H-4'-/H-5'-resonances. As the sugar signals coincide with those of other toluoylated 2'-deoxy-α-D-nucleosides[27] the structure **7d** was established. The anomeric ratio (about 1:1) determined from the ^1H NMR peak intensities indicates that the glycosyl transfer from N^7 to N^9 is not stereoselective in the case of 2'-deoxyribonucleosides (see Figure) which is the case for ribonucleosides.

Another point of interest was the orientation (syn and anti) of a heterocyclic base of the purine N^7-(2-deoxyribonucleosides) relative to the sugar moiety. The energy between these two different states is usually low (25 kJ/mol)[28,29], indicating dynamic equilibrium which might be more or less biased towards one side. Electronic effects and/or steric hindrance are responsible for preferred conformations. In the case of purine N^7-nucleosides, the 6-substituent can sterically interfere with the sugar moiety thereby influencing the syn/anti-population. For this purpose the NOE-difference spectra of compounds **1b, 4, 10a** and **10b** were measured (Table 2). The syn/anti population was determined by a graph reported recently[30]. This graph uses the NOE data of conformationally locked nucleosides. Due to the steric effects a high anti conformer population was observed for the methoxy compound **10a** (75% anti) and the methylthio derivative **10b** (89% anti) compared to the purine nucleoside **4** (58% syn). Surprisingly, a preferred syn-population was found for 7-(2-deoxy-ß-D-erythro-pentofuranosyl)adenine (**1b**) (61% syn). A similar observation has recently been made in the case of N^7-(2-deoxy-ß-D-*erythro*-pentofuranosyl)-3-deazaadenine (55% syn)[30].

EXPERIMENTAL SECTION

General[4]: Solvent systems: CH_2Cl_2/MeOH 9:1 (A), CH_2Cl_2/MeOH 4:1 (B), CH_2Cl_2/MeOH/triethylamine 83:15:2 (C), light petroleum ether /EtOAc 4:6 (D), EtOAc (E), light petroleum ether/EtOAc 3:7 (F), CH_2Cl_2/MeOH, 97:3 (G).

Glycosylation of 6-Methoxypurine (5a) with 1-Chloro-2-deoxy-3,5-di-O-(4-toluoyl)-α-D-*erythro*-pentofuranose (6).

A suspension of powdered KOH (1.20 g, 21.3 mmol) and tris[2-(2-methoxyethoxy)-ethyl]amine (TDA-1, 20 µl, 0.06 mmol) was stirred in anhyd. MeCN (110 ml, r.t.) under argon. After 30 min 6-methoxypurine (**5a**) (700 mg, 4.7 mmol) was added and stirring was continued for 15 min. The solid halogenose **6**[7] (2.3 g, 5.9 mmol) was introduced in portions. After 20 min insoluble material was filtered off and the solvent evaporated to dryness. The oily residue was chromatographed on a silica gel 60 (column 20 x 4 cm).

9-[2-Deoxy-3,5-di-O-(4-toluoyl)-ß-D-*erythro*-pentofuranosyl]-6-methoxy-9H-purine (7a).

From the fast migrating zone (eluent D), a colorless foam (1.05 g, 44%) was obtained. TLC (D): R_f 0.6. UV (MeOH): 241 nm (40200). ^{1}H-NMR ((D$_6$)DMSO):

δ 2.30, 2.40 (s, 6H, 2 Me), 2.80 and 3.35 (m, 2H, H-2'), 4.09 (s, 3H, MeO), 4.60 (m, 3H, H-4'and H-5'), 5.83 (m, 1H, H-3'), 6.61 (pt, J = 6.7 Hz, 1H, H-1'), 7.30-7.38 and 7.75-7.95 (m, aromatic H), 8.50 (s, 1H, H-2), 8.60 (s, 1H, H-8). Anal. Cald. for $C_{27}H_{26}N_4O_6$ (502.5): C, 64.53; H, 5.22; N, 11.15. Found: C, 64.64; H, 5.17; N, 11.13.

7-[2-Deoxy-3,5-di-O-(4-toluoyl)-ß-D-*erythro*-pentofuranosyl]-6-methoxy-7H-purine (8a).

The second zone (eluent E) yielded a colorless foam (670 mg, 28%). TLC (D): R_f 0.2. UV (MeOH): 240 nm (36800). ^{1}H-NMR ((D$_6$)DMSO): δ 2.35, 2.40 (s, 6H, 2 Me), 2.80 and 3.05 (m, 2H, H-2'), 4.12 (s, 3H, MeO), 4.55 (m, 3H, H-4' and H-5'), 5.70 (m, 1H, H-3'), 6.66 (pt, J = 6.5 Hz, 1H, H-1'), 7.25-7.38 and 7.75-7.95 (m, aromatic H), 8.59 (s, 1H, H-2), 8.82 (s, 1H, H-8). Anal. Cald. for $C_{27}H_{26}N_4O_6$ (502.5): C, 64.53; H 5.22; N, 11.15. Found: C 64.52; H, 5.33; N, 11.33.

Glycosylation of 6-Methylthiopurine (5b).

The reaction was performed as described for **5a**. The following amounts were used: 6-Methylthiopurine (**5b**) (1.0 g, 6.0 mmol); halogenose **6** (3.0 g, 7.7 mmol), KOH (1.8 g, 32 mmol); TDA-1 (20 μl, 0.06 mmol).

9-[2-Deoxy-3,5-di-O-(4-toluoyl)-ß-D-*erythro*-pentofuranosyl]-6-methylthio-9H-purine (7b).

From the fast migrating zone (eluent D), a colorless foam (1.33 g, 43%) was obtained. TLC (G): R_f 0.67. UV (MeOH): 240 nm (41300), 283 nm (12300). ^{1}H-NMR ((D$_6$)DMSO): δ 2.35 and 2.40 (s, 6H, 2 Me), 2.65 (s, 3H, MeS), 2.80 and 3.40 (m, 2H, H-2'), 4.60 (m, 3H, H-4' and H-5'), 5.84 (m, 1H, H-3'), 6.61 (pt, J = 6.9 Hz, 1H, H-1'), 7.25-7.38 and 7.80-7.95 (m, aromatic H), 8.67 (s, 2H, H-2 and H-8). Anal. Cald. for $C_{27}H_{26}N_4O_5S$ (518.6): C, 62.53; H, 5.05; N, 10.80. Found: C, 62.60; H, 5.29; N, 10.83.

7-[2-Deoxy-3,5-di-O-(4-toluoyl)-ß-D-*erythro*-pentofuranosyl]-6-methylthio-7H-purine (8b).

The second zone (eluent F) yielded a colorless foam (290 mg, 9%), which was crystallized from i-PrOH to yield colorless needles. M.p. 149-150°C. TLC (G): R_f 0.21. UV (MeOH): 240 nm (38500), 283 nm (14700). ^{1}H-NMR ((D$_6$)DMSO): δ 2.39 and 2.42 (s, 6H, 2 Me), 2.72 (s, 3H, MeS), 3.00 and 3.20 (m, 2H, H-2'), 4.65

(m, 3H, H-4' and H-5'), 5.75 (m, 1H, H-3'), 6.79 (pt, J = 6.9 Hz, 1H, H-1'), 7.30-7.42, 7.80-7.95 (m, aromatic H), 8.83 and 8.86 (2s, 2H, H-2 and H-8). Anal. Cald. for $C_{27}H_{26}N_4O_5S$ (518.6): C, 62.53; H, 5.05; N, 10.80. Found: C, 62.46; H, 5.04; N, 10.98.

3-[2-Deoxy-3,5-di-O-(4-toluoyl)-ß-D-*erythro*-pentofuranosyl]-6-methylthio-3H-purine (9b).

The slow migrating zone (eluent F) yielded a colorless foam (490 mg, 16%). Crystallization from i-PrOH yielded **9b** as colorless needels. M.p. 141°C. TLC (G): R_f 0.15. UV (MeOH): 239 nm (43300), 316 nm (18500). ^{1}H-NMR ((D_6)DMSO): δ 2.37 and 2.42 (s, 6H, 2 Me), 2.72 (s, 3H, MeS), 3.00 and 3.35 (m, 2H, H-2'), 4.75 (m, 3H, H-4' and H-5'), 5.90 (m, 1H, H-3'), 6.80 (pt, J = 6.9 Hz, 1H, H-1'), 7.25-7.42 and 7.75-7.95 (m, aromatic H), 8.18 (s, 1H, H-2), 8.86 (s, 1H, H-8). Anal. Cald. for $C_{27}H_{26}N_4O_5S$ (518.6): C, 62.53; H, 5.05; N, 10.80. Found: C, 62.68; H, 5.04; N, 10.71.

Glycosylation of 6-Chloropurine (5c).

A suspension of powdered KOH (1.8 g, 32 mmol) and tris[2-(2-methoxyethoxy)ethyl]amine (TDA-1, 20 μl, 0.06 mmol) was stirred in anh. MeCN (100 ml, r.t.) under argon. 6-Chloropurine (**5c**) (1.0 g, 6.47 mmol) was added, reacted with the halogenose **6** (3.0 g, 7.7 mmol) and worked up as described for **5a**.

6-Chloro-9-[2-deoxy-3,5-di-O-(4-toluoyl)-ß-D-*erythro*-pentofuranosyl]-9H-purine (7c).

From the fast migrating zone colorless crystals (1.83 g, 59%) from EtOH. M.p. 108-109°C, (Lit.[8]: 107-109°C).

6-Chloro-7-[2-deoxy-3,5-di-O-(4-toluoyl)-ß-D-*erythro*-pentofuranosyl]-7H-purine.

The slow migrating zone furnished colorless crystals (420 mg, 13%) from EtOH. M.p. 149-151°C, (Lit.[8]: 152-153°C).

Rearrangement of 8a to an Anomeric Mixture of 7a/7d.

Compound **8a** (80 mg, 0.16 mmol) in 10 ml toluene containing $HgBr_2$ (60 mg, 0.17 mmol) was stirred at 125°C for 4 h. The cold reaction mixture was extracted with 30% aq. KI (10 ml). The organic layer was washed with water, dried over Na_2SO_4 and evaporated. The oily residue was chromatographed on silica gel (column 10 x 2 cm, eluent D). From the main zone an anomeric mixture of **7a** and **7d** was obtained as colorless foam (35 mg, 44%).

9-[2-Deoxy-3,5-di-O-(4-toluoyl)-ß-D-*erythro*-pentofuranosyl]-6-methoxy-9H-purine (7a).
^{1}H-NMR ((D$_6$)DMSO): δ 2.80 and 3.35 (m, 2H, H-2'), 4.09 (s, 3H, MeO), 4.60 (m, 3H, H-4' and H-5'), 5.83 (m, 1H, H-3'), 6.61 (pt, J = 6.7 Hz, 1H, H-1'), 8.50 (s, 1H, H-2), 8.59 (s, 1H, H-8).

9-[2-Deoxy-3,5-di-O-(4-toluoyl)-α-D-*erythro*-pentofuranosyl]-6-methoxy-9H-purine (7d).
^{1}H-NMR ((D$_6$)DMSO): δ 3.06 and 3.15 (m, 2H, H-2'), 4.09 (s, 3H, MeO), 4.60 (m, 2H, H-5'), 5.00 (m, 1H, H-4'), 5.62 (m, 1H, H-3'), 6.65 (pt, J = 6.7 Hz, 1H, H-1'), 8.50 (s, 1H, H-2), 8.59 (s, 1H, H-8)[26].

7-(2-Deoxy-ß-D-*erythro*-pentofuranosyl)-6-methoxy-7H-purine (10a).
Compound **8a** (480 mg, 0.96 mmol) was stirred in 0.1 N $NaOCH_3$/MeOH (40 ml) for 2 h at r.t. The solution was adsorbed on silica gel (8 g) applied to the top of a silica gel 60 column (25 x 3 cm) and chromatographed. Elution with solvent A gave a colorless solid, which was crystallized from i-PrOH. Colorless crystals (210 mg, 82%). M.p. 152-152°C. TLC (A): R_f 0.3. UV (MeOH): 259 nm (7600). ^{1}H-NMR ((D$_6$)DMSO): δ 2.30 and 2.44 (m, 2H, H-2'), 3.55 (m, 2H, H-5'), 3.87 (m, 1H, H-4'), 4.11 (s, 3H, MeO), 4.37 (m, 1H, H-3'), 5.00 (t, J = 5.3 Hz, 1H, 5'-OH), 5.36 (d, J = 5.0 Hz, 1H, 3'-OH), 6.49 (pt, J = 6.5 Hz, 1H, H-1'), 8.56 (s, 1H, H-2), 8.82 (s, 1H, H-8). Anal. Cald. for $C_{11}H_{14}N_4O_4$ (266.3): C, 49.62; H, 5.30; N 21.04. Found: C, 49.58; H, 5.44; N, 20.98.

9-(2-Deoxy-ß-D-*erythro*-pentofuranosyl)-6-methoxy-9H-purine (11a).
Compound **7a** (1.05 g, 2.01 mmol) was stirred in 0.1 N $NaOCH_3$/MeOH (80 ml) for 2 h at r.t. The solution was adsorbed on silica gel (10 g) applied to the top of a silica gel 60 column and chromatographed (25 x 3 cm). Elution with solvent A gave a colorless solid, which was crystallized from i-PrOH. Colorless crystals (470 mg, 84%). M.p. 100°C. NMR data are identical to those reported[32].

7-(2-Deoxy-ß-D-*erythro*-pentofuranosyl)-6-methylthio-7H-purine (10b).
A solution of compound **8b** (500 mg, 0.96 mmol) in MeOH (40 ml, sat. with ammonia at 0°) was stirred for 20 h at r.t. The solvent was evaporated and the residue purified on silica gel 60 (column 25 x 3 cm). Elution with solvent A yielded a colorless solid, which crystallized from MeOH. Colorless crystals (210 mg, 77%). M.p. 102-122°C. TLC (A): R_f 0.3. UV (MeOH): 290 nm (15100). ^{1}H-NMR

((D6)DMSO): δ 2.50 and 2.70 (m, 2H, H-2'), 2.72 (s, 3H, MeS), 3.55 (m, 2H, H-5'), 3.93 (m, 1H, H-4'), 4.41 (m, 1H, H-3'), 5.05 (t, J = 4.3 Hz, 1H, 5'-OH), 5.36 (d, J = 4.0 Hz, 1H, 3'-OH), 6.64 (pt, J = 6.1 Hz, 1H, H-1'), 8.80 (s, 1H, H-2), 8.93 (s, 1H, H-8). Anal. Cald. for $C_{11}H_{14}N_4O_3S$ (282.3): C, 46.79; H, 5.00; N, 19.84. Found: C, 46.91; H, 4.97; N, 19.82.

9-(2-Deoxy-ß-D-*erythro*-pentofuranosyl)-6-methylthio-9H-purine (11b).
A solution of compound **7b** (1.0 g, 1.93 mmol) in MeOH (60 ml, saturated with ammonia at 0°C) was stirred for 20 h at r.t. The solvent was evaporated and the residue purified on silica gel 60 (column 25 x 3 cm). Elution with solvent A yielded a colorless solid, which was crystallized from i-PrOH. Colorless crystals (480 mg, 88%). M.p. 158°C, (Lit.[31]: 157-158°C).

7-(2-Deoxy-ß-D-*erythro*-pentofuranosyl)-7H-purin-6-one (3).
A solution of **10a** (300 mg, 1.13 mmol) in 2 N NaOH (20 ml) was stirred for 5 h at 55°C. The solution was neutralized with an aliquot of 2 N HCl and applied to an Amberlite XAD-4 resin (column 20 x 3 cm). Salt was removed by elution with water (1.2 l). Elution with H_2O/MeOH (4:1) yielded a colorless solid (200 mg, 70%) which gave colorless crystals from water/MeOH. M.p. 208-209°C (Lit.[15]: 210-212°). TLC (B): R_f 0.4. UV (MeOH): 255 nm (7600). ^{1}H-NMR ((D6)DMSO): δ 2.35, 2.50 (m, 2H, H-2'), 3.55 (m, 2H, H-5'), 3.88 (m, 1H, H-4'), 4.47 (m, 1H, H-3'), 6.63 (pt, J = 6.6 Hz, 1H, H-1'), 8.00 (s, 1H, H-2), 8.57 (s, 1H, H-8). Anal. Cald. for $C_{10}H_{12}N_4O_4$ (252.2): C, 47.62; H, 4.80; N, 22.21. Found: C, 47.88; H, 4.83; N, 22.04.

7-(2-Deoxy-ß-D-*erythro*-pentofuranosyl)-7H-purine (4).
To a solution of compound **8c** (400 mg, 0.78 mmol) in EtOH (100 ml) triethylamine (1 ml) and Pd/charcoal (10% Pd, 100 mg) were added. The solution was hydrogenated at regular pressure at r.t. for 2 h. Upon evaporation the residue was dissolved in MeOH (50 ml, sat. with ammonia at 0°) and stirred at r.t. for 24 h. After evaporation of the solvent the residue was purified on silica gel 60 (column 20 x 3 cm, B). From the main zone compound **4** was isolated as colorless solid (120 mg, 67%). Crystallization from water afforded colorless crystals. M.p. 163-165°C. TLC (A): R_f 0.15. UV (MeOH): 265 nm (6400). ^{1}H-NMR ((D6)DMSO): δ 2.35, 2.60 (m, 2H, H-2'), 3.60 (m, 2H, H-5'), 3.93 (m, 1H, H-4'), 4.44 (m, 1H, H-3'), 5.13 (t, J = 5.1 Hz, 1H, 5'-OH), 5.47 (d, J = 3.1 Hz, 1H, 3'-OH), 6.45 (pt, J = 6.4 Hz, 1H, H-1'), 8.93 (s, 1H, H-2), 9.00 (s, 1H, H-8), 9.36 (s, H-6). Anal. Cald. for

$C_{10}H_{12}N_4O_3$ (236.2): C, 50.84; H, 5.12; N, 23.72. Found: C, 50.67; H, 5.08; N, 23.67.

7-(2-Deoxy-ß-D-*erythro*-pentofuranosyl)-7H-adenine (1b).

From **8a**: Compound **8a** (800 mg, 1.59 mmol) in MeOH (60 ml, saturated with ammonia at 0°C) was stirred at 85°C for 6 days. The solution was evaporated to dryness and the residue purified on silica gel 60 (column 20 x 3 cm, eluent B). From the main zone a colorless solid (240 mg, 60%) was isolated yielding colorless crystals from MeOH. M.p. 187°C, (Lit.[4]: 187°C).

From **8c**: Compound **8c** (600 mg, 1.16 mmol) was dissolved in MeOH (60 ml, saturated with ammonia at 0°C) and stirred at 85 °C for 48 h. The work-up was identical as described above. (220 mg, 75%).

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