TRANSFORMATION OF 8-[(2-HYDROXYALKYL)SULFANYL]ADENINES TO 6-AMINO-7*H*-PURIN-8(9*H*)-ONE DERIVATIVES

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Alkylation of 6-amino-7*H*-purin-8(9*H*)-thione (8-sulfanyladenine, **1**) with one equivalent of (*R*)-[(trityloxy)methyl]oxirane gave its *S*-alkyl derivative **2**, which was converted to the 6-amino-7*H*-purin-8(9*H*)-one (**3**), while alkylation of **1** with two equivalents of (*S*)-[(trityloxy)methyl]oxirane afforded a mixture of N^3,*S*-dialkylated product **4a**, N^9-monoalkyl and N^7,N^9-dialkyl derivatives of 6-amino-7*H*-purin-8(9*H*)-one, **5a** and **6a**, respectively. This approach can be used for rapid and easy transformation of 8-[(2-hydroxyalkyl)sulfanyl]adenines to the derivatives of 6-amino-7*H*-purin-8(9*H*)-one (8-hydroxyadenine) using NaH or Cs_2CO_3 in DMF. The course of the S→O transformation strictly depends on the character of the starting compounds and on the reaction conditions. N^9-Alkyl-8-[(2-hydroxyalkyl)sulfanyl]adenines **10**, **12**, **14** and **17** were rapidly converted to the corresponding 6-amino-7*H*-purin-8(9*H*)-one derivatives **11**, **13**, **11** and **18**, respectively. N^9-Unsubstituted **2** reacts slowly, and N^3-alkyl derivative **4a** is stable under the same reaction conditions. The described transformation does not occur when the hydroxy group in 8-[(2-hydroxyalkyl)sulfanyl]adenine derivative **15** is protected. The reaction using NaH proceeds more rapidly than that using Cs_2CO_3.

Keywords: Purines; Acyclic nucleoside and nucleotide analogs; Alkylation; Thiols; Thiones; Hydrolysis.

The removal of sulfur atom attached to the purine moiety in position 6 and subsequent exchange for oxygen atom are old and well-known procedures in the nucleoside chemistry[1–3]. Sulfur can be easily exchanged for oxygen *via* the (2-hydroxyethyl)sulfanyl procedure employed for the conversion of 1,7(9)-dihydro-6*H*-purin-6-thione to 1,7(9)-dihydro-6*H*-purin-6-one (hypoxanthine)[1] and of 2-amino-9-(2′-deoxy-β-D-ribofuranosyl)purin-6-thione to 2′-deoxyguanosine[2]. 6-[(2-Hydroxyethyl)sulfanyl]purines are hydrolyzed readily in either alkaline or acidic solutions, and the hydrolysis proceeds even at pH 7, though more slowly[1]. A mechanism of this hydrolysis was proposed in an earlier published paper[1].

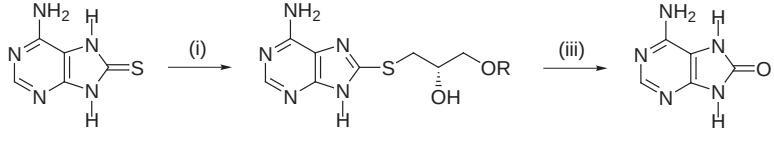
The oxidative desulfurization using alkaline hydrogen peroxide is superior to the above mentioned method[3]. Also photolysis of the 1,7(9)-dihydro-6*H*-purin-6-thione derivatives in the presence of oxygen affords hypoxanthines and purines depending on the solvent used[4,5].

Herein, we report on an easy transformation of 8-[(2-hydroxyalkyl)-sulfanyl]adenine derivatives using NaH or Cs_2CO_3 under aprotic conditions which is strictly dependent on the nature of alkylpurine regioisomers.

RESULTS AND DISCUSSION

In the course of the SAR study of purine acyclic nucleoside and nucleotide analogs[6–8], two principal approaches were used for the preparation of 8-substituted purine derivatives: (i) modification of the corresponding acyclic nucleoside or nucleotide derivative in position 8 of the purine moiety or, (ii) preparation of the 8-substituted purine base and its subsequent alkylation. In the recent studies we have shown that the alkylation of 6-amino-7*H*-purin-8(9*H*)-thione (**1**) preferentially occurs at the sulfur atom and the alkylation of 8-(methylsulfanyl)adenine gives rise to a mixture of N^3-alkylated and N^9-alkylated regioisomers[7], while the alkylation of 6-amino-7*H*-purin-8(9*H*)-one (**3**) leads to a mixture of N^9-monoalkylated and N^7,N^9-dialkylated products[8].

Alkylation of 6-amino-7*H*-purin-8(9*H*)-thione (**1**) with 1 equivalent of (*R*)-[(trityloxy)methyl]oxirane in the presence of Cs_2CO_3 gave only the product of alkylation at the sulfur atom (**2a**, Scheme 1). The detritylation of



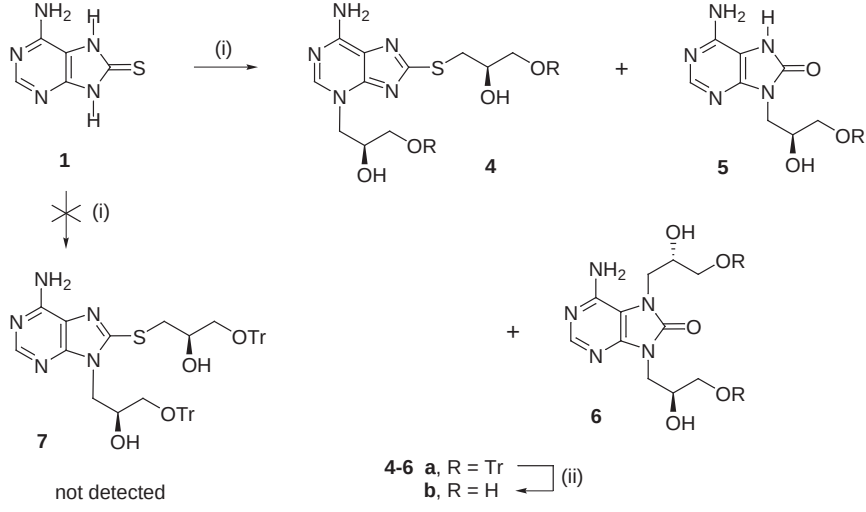
(i) (*R*)-[(trityloxy)methyl]oxirane, Cs_2CO_3, DMF, 100 °C; (ii) 80% AcOH, 80 °C; (iii) 0.1 M aq. HCl or 0.1 M aq. NaOH, reflux

SCHEME 1

the trityl derivative **2a** afforded compound **2b**. Compound **2b** resisted the action of both 0.1 M NaOH and 0.1 M HCl at room temperature for 2 days as well as prolonged treatment with 1 equivalent of NaH in DMF at room temperature, or at 100 °C. Only in refluxing 0.1 M NaOH or 0.1 M HCl,

compound **2b** slowly and partially hydrolysed to 6-amino-7*H*-purin-8(9*H*)-one (**3**) (according to TLC and MS spectra[8]), while its reflux in 1 M HCl led to destruction of the purine moiety.

In order to investigate the directive effect of sulfur substituents in position 8 of the purine moiety[7,9], successive alkylation of compound **1** with excess (2.2 equivalents) (*S*)-[(trityloxy)methyl]oxirane was also performed (Scheme 2). The alkylation at elevated temperature resulted in a mixture of N^3,*S*-dialkylated products (yields are given in parentheses) **4a** (30%), N^9-monoalkylated 6-amino-7*H*-purin-8(9*H*)-one **5a** (20%) and N^7,N^9-dialkylated derivative **6a** (15%). Acid treatment of compounds **4a**, **5a** and **6a** afforded compounds **4b**, **5b** and **6b** in high yields. Both compound **5a** and compound **6a** (together with their detritylated derivatives **5b** and **6b**) are identical with authentic compounds prepared earlier by alkylation of 6-amino-7*H*-purin-8(9*H*)-one (**3**) with (*S*)-[(trityloxy)methyl]oxirane[8].



(i) (*S*)-[(trityloxy)methyl]oxirane, Cs_2CO_3, DMF, 110 °C, 7 h; (ii) 80% AcOH, 80 °C, 0.5 h;

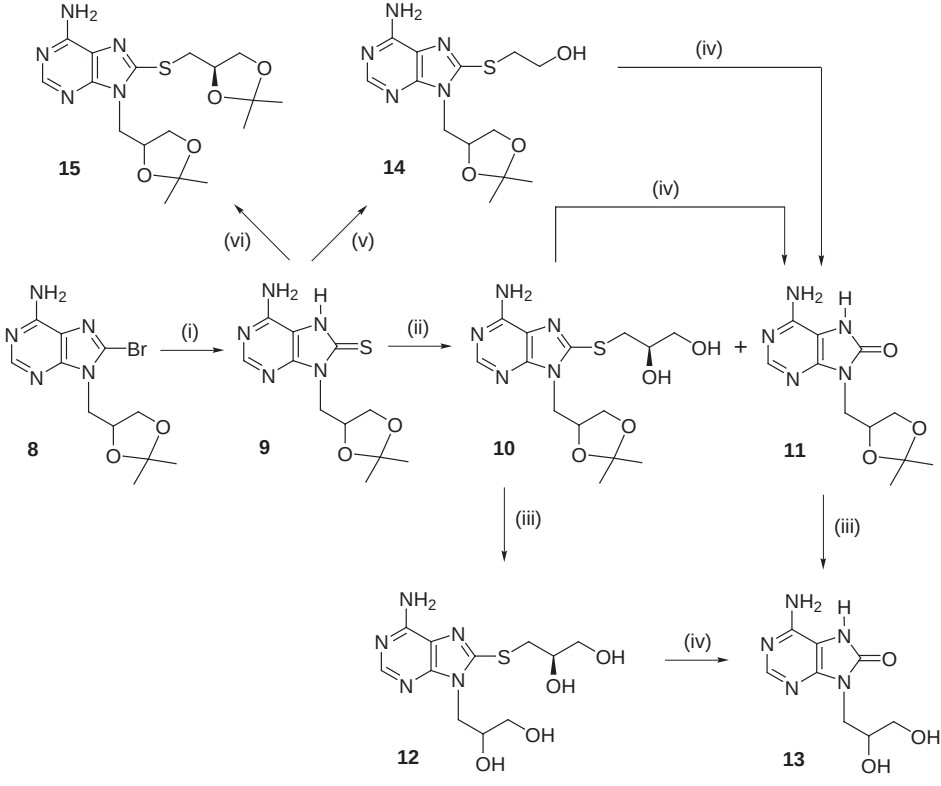
SCHEME 2

Evidently, *S*-alkylated intermediate analogous to compound **2a**, which is formed in the first step of the above alkylation, is further alkylated similarly to 8-(methylsulfanyl)adenine under the formation of a mixture of N^3-substituted and N^9-substituted derivatives[7]. The expected N^9,*S*-dialkylated intermediate **7** (Scheme 2) was not detected in the reaction mixture. Under the reaction conditions, such intermediate **7** would be simultaneously transformed to the N^9-monosubstituted derivative **5a**,

which is further alkylated in position 7 of the purine moiety[8] to form compound **6a**.

On the other hand, the N^3,*S*-dialkyl derivative **4a** seems to be stable under the same conditions and no product of its transformation at C-8 is formed. There is a fundamental difference in electron distribution in the purine moiety in both types of the intermediates **4a** and **7**, which is reflected by their different reactivity.

In order to eliminate the influence of the hydroxy group present in the alkyl moiety attached to nitrogen N^9 on the course of the sulfur exchange reaction, the protected derivative **9** was prepared by the reaction of bromo derivative **8** (ref.[10]) with thiourea (Scheme 3). When compound **9** was



(i) thiourea, EtOH, reflux, 6 h; (iia) (*S*)-[(trityloxy)methyl]oxirane, Cs_2CO_3, DMF, 110 °C, 3 h (giving a mixture of **10** and **11**); (iib) (*S*)-[(trityloxy)methyl]oxirane, NaH, DMF, 100 °C, 2.5 h (giving **11** only); (iii) 80% AcOH, 80 °C, 1 h; (iv) NaH, DMF, 25 °C, 0.5 h; (v) $ClCH_2CH_2OH$, NaH, DMF, 100 °C, 0.5 h; (vi) D-2,3-*O*-isopropylideneglycerol tosylate, NaH, DMF, 110 °C, 1 h

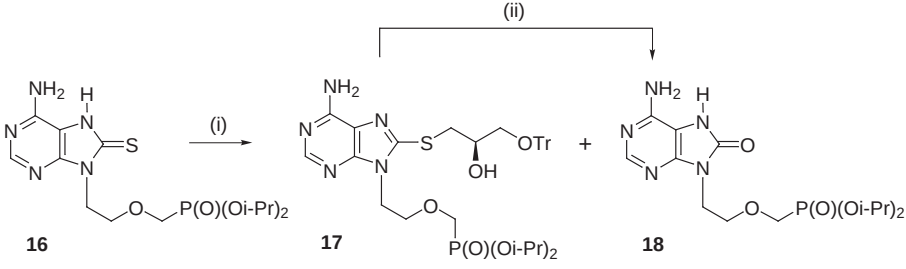
SCHEME 3

heated with (*S*)-[(trityloxy)methyl]oxirane in DMF in the presence of Cs_2CO_3 for 3 h, a mixture of N^9,*S*-disubstituted sulfanyladenine **10** and N^9-substituted 6-amino-7*H*-purin-8(9*H*)-one **11** in the ratio 1 : 1 was obtained, while heating of compound **9** with (*S*)-[(trityloxy)methyl]oxirane in the presence of NaH (1 equivalent) in DMF gave compound **11** in 64% yield as the only product. The above 8-[(2-hydroxyalkyl)sulfanyl]adenine derivative **10**, the analog of hypothetical compound **7** (Scheme 2), was rapidly and completely converted to compound **11** by treatment with 1 equivalent of NaH in DMF at room temperature. Finally, acid deprotection of both compounds **10** and **11** afforded compounds **12** and **13**, respectively. Compound **12** was readily transformed to compound **13** with NaH in DMF within 0.5 h.

Compared to N^9,*S*-disubstituted derivative **10**, N^3,*S*-dialkylated derivative **4b** resisted the treatment of 1 equivalent of NaH in DMF at room temperature or at 100 °C, as well as the prolonged action of 0.1 M NaOH or 0.1 M HCl at room temperature or at reflux temperature.

8-[(2-Hydroxyethyl)sulfanyl]adenines can be considered to be the simplest model compounds for such transformation in position 8 of the purine moiety. Thus, (2-hydroxyethyl)sulfanyl derivative **14** was prepared by the reaction of compound **9** with 2-chloroethan-1-ol in DMF in the presence of NaH at 100 °C (Scheme 3). In analogy to compound **10**, compound **14** was transformed by the treatment with NaH in DMF at room temperature to the derivative **11** during 0.5 h.

Similarly to compound **9**, the treatment of 9-[2-(phosphonomethoxy)-ethyl] (PME) derivative **16** (ref.[7]) with (*S*)-[(trityloxy)methyl]oxirane in DMF in the presence of Cs_2CO_3 afforded a mixture of *S*-substituted derivative **17** and 8-oxoadenine derivative **18** in the ratio 2 : 1 (Scheme 4). The facile transformation of compound **17** to compound **18** was again achieved by treatment with NaH in DMF at room temperature.

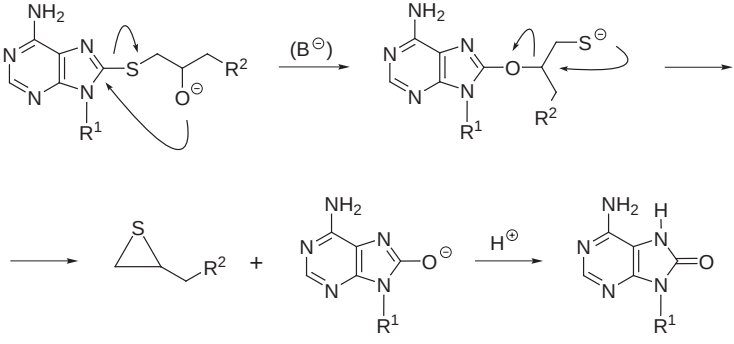


(i) (*S*)-[(trityloxy)methyl]oxirane, Cs_2CO_3, DMF, 100 °C, 2 h; (ii) NaH, DMF, 25 °C, 0.5 h

SCHEME 4

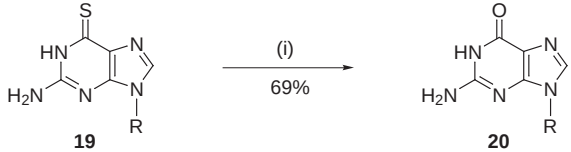
On the other hand, compound **15** prepared by the reaction of **9** with (*R*)-2,2-dimethyl-4-[(tosyloxy)methyl]-1,3-dioxolane (D-2,3-*O*-isopropylideneglycerol tosylate) and NaH in DMF resisted the treatment with 1 equivalent NaH in DMF at room temperature overnight (Scheme 3).

Free β-hydroxy group at the aliphatic chain attached to the sulfur atom in position 8 plays the crucial role in the transformations in the presence of base (NaH or Cs_2CO_3) in DMF. A tentative reaction mechanism of the described transformations is shown in Scheme 5.



SCHEME 5

We also examined the possibility to perform the described S→O transformation at the position 6 of the purine ring. The reaction of compound **19** with 1 equivalent of both (*RS*)-[(trityloxy)methyl]oxirane and NaH in DMF afforded smoothly the guanine derivative **20** (ref.[11]) in 69% yield (Scheme 6).



R = $CH_2CH_2OCH_2P(O)(Oi\text{-}Pr)_2$

(i) (*RS*)-[(trityloxy)methyl]oxirane, NaH, DMF, 100 °C, 3.5 h

SCHEME 6

All new compounds were fully characterized by ^{1}H NMR (and ^{13}C NMR), MS and HRMS or microanalysis. The structures of the compounds prepared by alkylation of the modified adenine bases were determined by proton-coupled ^{13}C NMR spectra: N^9,*S*-Disubstituted derivatives are characterised by doublets of C-6-carbons (δ ≈ 154.3, *J*(C-6,H-2) = 11.7) and C-2-carbons (δ ≈

151.9, *J*(C-2,H-2) = 198.2), by doublet of triplets of C-4-carbon (δ ≈ 151.5, *J*(C-4,H-2) = 11.7, *J*(C-4,H-1′) = 3.9), by pentet of C-8-carbon (δ ≈ 149.0, *J*(C-8,H-1′) = *J*(C-8,H″) = 3.9) and by triplet of C-5-carbon atom (δ ≈ 118.9, *J*(C-5,NH_2) = 3.9); after addition of D_2O these interactions disappear. In N^3,*S*-disubstituted derivatives we have observed characteristic effects of alkylations and multiplicity changes at the carbons C-2 (doublet of triplets, upifeld shift approximately –8 ppm, *J*(C-2,H-2) = 208.0, *J*(C-2, H-1′) = 3.9) and C-8 (triplet, lowfield shift approximately 12 ppm, *J*(C-8, H-1″) = 3.9, in agreement with the authentic material[7,8].

In diastereoisomeric mixtures of compounds **10**, **12** and **15**, doubling of some NMR signals was observed (in ^{1}H NMR spectrum of compound **10** and in ^{1}H NMR and ^{13}C NMR spectra of compounds **12** and **15**).

In conclusion, the S→O transformations take place *via* 8-[(2-hydroxyalkyl)sulfanyl]adenine derivatives. This transformation proceeds less readily than analogous hydrolysis in position 6 of the purine moiety[1] and is more dependent on substitution of the purine base. The base- or acid-catalyzed hydrolysis of 6-[(2-hydroxyethyl)sulfanyl]purines proceeds easily either with unsubstituted purine[1] or with N^9-alkylated base[2]. A similar transformation using NaH in DMF takes place also in the position 6 as documented by the reaction of 2-amino-6-sulfanylpurine derivative **19** (Scheme 6). In the case of the 8-[(2-hydroxyethyl)sulfanyl]adenine derivatives, the situation is different: N^9-alkylated compounds can be readily converted to the corresponding 6-amino-7*H*-purin-8(9*H*)-one derivatives while the conversion of unsubstituted 8-[(2-hydroxyalkyl)sulfanyl]adenine **2** is slow. N^3-Substituted derivative **4b** is stable at elevated temperature. The free hydroxy group in 8-[(2-hydroxyalkyl)sulfanyl]adenine derivatives is essential for the described transformation.

EXPERIMENTAL

Unless otherwise stated, solvents were evaporated at 40 °C/2 kPa and compounds were dried at 2 kPa over P_2O_5. Melting points were determined on a Büchi melting point B-545 apparatus. Analytical TLC were performed on Silufol UV 254 plates (Kavalier Votice, Czech Republic) in the systems chloroform–methanol (9 : 1) (S1), chloroform–methanol (85 : 15) (S2), chloroform–methanol (8 : 2) (S3), water–ethanol–acetone–ethyl acetate (1 : 1 : 1 : 4) (S4). Preparative TLC were carried out on 40 × 17 × 0.4 cm loose-layer plates of silica gel containing a UV indicator (made in the Service Laboratory of the Institute). NMR spectra were measured on a Varian Unity 500 spectrometer (500 MHz for ^{1}H and 125.7 MHz for ^{13}C NMR) in hexadeuteriodimethyl sulfoxide (DMSO-d_6) referenced to the solvent signals (2.5 ppm for ^{1}H and 39.7 ppm for ^{13}C NMR), or in deuterium oxide containing sodium deuteroxide with sodium 3-(trimethylsilyl)propane-1-sulfonate as an internal standard for ^{1}H NMR and dioxane as an external standard for ^{13}C NMR (δ 66.86 ppm). Chemical shifts are given in ppm

(δ-scale), coupling constants (*J*) in Hz. Mass spectra were measured on a ZAB-EQ (VG Analytical) spectrometer using FAB (ionization by Xe, accelerating voltage 8 kV, glycerol matrix). UV absorption spectra were measured on a UV mini-1240 Shimadzu spectrometr, CD spectra on a Jobin Yvon Mark V instrument.

Starting Materials and Reagents

NaH and Cs_2CO_3 were purchased from Aldrich. Dimethylformamide was distilled from P_2O_5 and stored over molecular sieves (4 Å).

Alkylation of 6-Amino-7*H*-purin-8(9*H*)-thione (**1**) with (*R*)- or (*S*)-[(Trityloxy)methyl]oxirane. General Procedure

A. With 1 Equivalent of (*R*)-[(Trityloxy)methyl]oxirane

A mixture of compound **1** (1 g, 6 mmol), DMF (20 ml), (*R*)-tritylglycidol (1.9 g, 6 mmol) and caesium carbonate (0.4 g, 1.2 mmol)) was stirred at 100 °C for 4 h. The hot suspension was filtered over Celite and evaporated. The residue afforded, by column chromatography on silica gel (chloroform–methanol), 1.78 g (62%) of compound **2a**.

8-{[(S)-2-Hydroxy-3-(trityloxy)propyl]sulfanyl}adenine (**2a**). White powder, m.p. 177 °C, R_F 0.65 (S1). FAB MS, *m/z* (rel.%): 484 (10) [M + H]; 243 (100) [Tr]. ^{1}H NMR (DMSO-d_6): 3.00 (dd, 1 H, *J*(3′b,2′) = 5.5, *J*(gem) = 9.3, H-3′b); 3.08 (dd, 1 H, *J*(3′a,2′) = 5.5, *J*(gem) = 9.3, H-3′a); 3.40 (dd, 1 H, *J*(1′b,2′) = 6.7, *J*(gem) = 13.2, H-1′b); 3.55 (dd, 1 H, *J*(1′a,2′) = 4.6, *J*(gem) = 13.2, H-1′a); 3.98 (m, 1 H, H-2′); 5.50 (br, 1 H, OH); 6.91 (brs, 2 H, NH_2); 7.23 (t, 3 H, arom. H); 7.30 (t, 6 H, arom. H); 7.40 (d, 6 H, arom. H); 8.07 (s, 1 H, H-2); 12.90 (br, 1 H, NH). Exact mass (FAB HRMS) found: 484.1808; calculated for $C_{27}H_{26}N_5O_2S$ [M + H]: 484.1807.

B. With 2.2 Equivalents of (*S*)-[(Trityloxy)methyl]oxirane

A mixture of compound **1** (1 g, 6 mmol), DMF (40 ml), (*S*)-[(trityloxy)methyl]oxirane (4.2 g, 13 mmol) and caesium carbonate (0.4 g, 1.2 mmol)) was stirred at 110 °C for 7 h. The same workup as in A afforded compounds **4a** (1.45 g, 30%), **5a** (0.56 g, 20%) and **6a** (0.7 g, 15%).

3-[(S)-2-Hydroxy-3-(trityloxy)propyl]-8-{[(R)-2-hydroxy-3-(trityloxy)propyl]sulfanyl}adenine (**4a**). White powder, m.p. 130 °C, R_F 0.62 (S2). FAB MS, *m/z* (rel.%): 800 (5) [M + H]; 243 (100) [Tr]. ^{1}H NMR (DMSO-d_6): 2.94 (dd, 1 H, *J*(3′b,2′) = 5.6, *J*(gem) = 9.5, H-3′b); 3.00 (dd, 1 H, *J*(3″b,2″) = 5.5, *J*(gem) = 9.3, H-3″b); 3.005 (dd, 1 H, *J*(3′a,2′) = 4.9, *J*(gem) = 9.5 (H-3′a); 3.07 (dd, 1 H, *J*(3″a,2″) = 5.5, *J*(gem) = 9.3, H-3″a); 3.34 (dd, 1 H, *J*(1″b,2″) = 6.5, *J*(gem) = 13.4, H-1″b); 3.46 (dd, 1 H, *J*(1″a,2″) = 5.1, *J*(gem) = 13.4, H-1″a); 3.98 (m, 1 H, H-2″); 4.10 (dd, 1 H, *J*(1′b,2′) = 8.8, *J*(gem) = 13.3, H-1′b); 4.19 (m, 1 H, H-2′); 4.46 (dd, 1 H, *J*(1′a,2′) = 3.3, *J*(gem) = 13.3, H-1′a); 5.47 (d, 1 H, *J*(OH,2′) = 5.7, OH); 5.68 (brs, 1 H, OH); 7.21 (t, 3 H, arom. H); 7.23 (t, 3 H, arom. H); 7.28 (t, 6 H, arom. H); 7.32 (t, 6 H, arom. H); 7.40 (d, 6 H, arom. H); 7.41 (d, 6 H, arom. H); 7.66 (brs, 2 H, NH_2); 8.12 (s, 1 H, H-2). ^{13}C NMR (DMSO-d_6): 36.10 (C-1″); 53.39 (C-1′); 66.30 (C-3′); 67.09 (C-3″); 67.30 (C-2″); 70.12 (C-2′); 86.45 (C-Ph); 86.61 (C-Ph); 120.67 (C-5); 127.43 (3 C, C-arom.); 127.53 (3 C, C-arom.); 128.29 (6 C, C-arom.); 128.39 (6 C, C-arom.); 128.83 (6 C, C-arom.); 128.86 (6 C, C-arom.); 143.80 (C-2); 144. 23 (3 C, C-arom.); 144.46 (3 C, C-arom.); 150.91 (C-4); 152.52 (C-6); 161.20 (C-8).

6-Amino-9-[(S)-2-hydroxy-3-(trityloxy)propyl]-7H-purin-8(9H)-one (**5a**) *and 6-amino-7,9-bis-[(2S)-2-hydroxy-3-(trityloxy)propyl]-7H-purin-8(9H)-one* (**6a**). Compounds **5a** and **6a** were identi-

fied by comparison (^{1}H NMR and ^{13}C NMR spectra) with authentic materials[8] prepared by alkylation of 6-amino-7*H*-purin-8(9*H*)-one (**3**).

Deprotection of the Trityl Derivatives **2a**, **4a**, **5a** and **6a**. General Procedure

The trityl derivative (1 mmol) in aqueous acetic acid (80%, 20 ml) was refluxed for 30–45 min, the solvent was evaporated *in vacuo* and the residue codistilled with water (3 × 15 ml). Water (50 ml) was added and the mixture extracted with ether (3 × 20 ml). The aqueous phase was evaporated *in vacuo* and the residue crystallized from water.

8-[((S)-2,3-Dihydroxypropyl)sulfanyl]adenine (**2b**). White crystals, slow decomposition >200 °C, yield 80%, R_F 0.27 (S1). FAB MS, *m/z* (rel.%): 242 (60) [M + H]. ^{1}H NMR (DMSO-d_6): 3.24 (dd, 1 H, *J*(1′b,2′) = 7.3, *J*(gem) = 13.2, H-1′b); 3.38 (dd, 1 H, *J*(3′b,2′) = 5.9, *J*(gem) = 11.0, H-3′b); 3.44 (dd, 1 H, *J*(3′a,2′) = 5.3, *J*(gem) = 11.0, H-3′a); 3.47 (dd, 1 H, *J*(1′a,2′) = 4.5, *J*(gem) = 13.2, H-1′a); 3.74 (m, 1 H, H-2′); 4.75 (br, 1 H, OH); 5.15 (br, 1 H, OH); 6.94 (brs, 2 H, NH_2); 8.03 (s, 1 H, H-2); 12.90 (br, 1 H, NH). ^{13}C NMR (DMSO-d_6): 35.71 (C-1′); 64.59 (C-3′); 70.59 (C-2′); 119.36 (C-5); 147.96 (C-8); 151.71 (C-2); 152.39 (C-4); 153.91 (C-6). For $C_8H_{11}N_5O_2S$ (241.3) calculated: 39.83% C, 4.60% H, 29.03% N, 13.29% S; found: 39.74% C, 4.62% H, 28.78% N, 13.04% S. UV, λ_{max} (ε_{max}): (pH 2) 287 (19 600); (pH 7) 284 (19 300); (pH 12) 285 (18 900).

3-((S)-2,3-Dihydroxypropyl)-8-[((R)-2,3-dihydroxypropyl)sulfanyl]adenine (**4b**). Yellowish crystals, m.p. 100–102 °C, yield 68%, R_F 0.31 (S1). FAB MS, *m/z* (rel.%): 316 (100) [M + H]. ^{1}H NMR (500 MHz, DMSO-d_6):): 3.24 (dd, 1 H, *J*(1″b,2″) = 6.3, *J*(gem) = 13.6, H-1″b); 3.33 (dd, 1 H, *J*(3″b,2″) = 6.0, *J*(gem) = 11.2, H-3″b); 3.37 (dd, 1 H, *J*(1″a,2″) = 5.0, *J*(gem) = 13.6, H-1″a); 3.37–3.46 (m, 3 H, H-3′a, H-3′b, H-3″a); 3.75 (qd, 1 H, *J*(2″,1″a) = 5.0, *J*(2″,1″b) = *J*(2″,3″) = 6.3, H-2″); 3.93 (dtd, 1 H, *J*(2′,1′a) = 3.3, *J*(2′,3′) = 5.5, *J*(2′,1′b) = 8.4, H-2′); 4.04 (dd, 1 H, *J*(1′b,2′) = 8.4, *J*(gem) = 13.6, H-1′b); 4.41 (dd, 1 H, *J*(1′a,2′) = 3.3, *J*(gem) = 13.6, H-1′a); 5.20 (br, 4 H, OH); 7.65 (brs, 2 H, NH_2); 8.10 (s, 1 H, H-2). ^{13}C NMR (DMSO-d_6): 35.17 (C-1″); 52.71 (C-1′); 63.65 (C-3″); 64.45 (C-3′); 68.65 (C-2″); 71.44 (C-2′); 121.38 (C-5); 143.44 (C-2); 151.20 (C-4); 152.26 (C-6); 161.38 (C-8). For $C_{11}H_{17}N_5O_4S$ (315.3) calculated: 41.90% C, 5.43% H, 22.21% N, 10.17% S; found: 41.47% C, 5.57% H, 21.95% N, 9.86% S. UV, λ_{max} (ε_{max}): (pH 2) 296 (33 200), 235 (12 800); (pH 7) 307 (16 800), 235 (12 900); (pH 12) 307 (16 500), 235 (12 800). CD, λ (Δε) (MeOH): 303 (–0.92), 277 (–0.90), 250 (–0.44), 198 (–5.02).

6-Amino-9-((S)-2,3-dihydroxypropyl)-7H-purin-8(9H)-one (**5b**). Yellowish crystals, m.p. 168–170 °C, yield 86%, R_F 0.37 (S1). FAB MS and ^{13}C NMR spectra are identical with the authentic material[8]. ^{1}H NMR (DMSO): 3.30 (m, 2 H, H-3′); 3.72 (d, 2 H, *J*(1′,2′) = 6.7, H-1′); 3.90 (m, 1 H, H-2′); 4.66 (t, 1 H, *J*(OH,3′) = 5.5, OH); 4.89 (d, 1 H, *J*(OH,2′) = 5.2, OH); 6.47 (brs, 2 H, NH_2); 8.00 (s, 1 H, H-2); 10.30 (br, 1 H, NH). ^{1}H NMR (DMSO + AcOD): 3.31 (dd, 1 H, *J*(3′b,2′) = 5.4, *J*(gem) = 11.4, H-3′b); 3.35 (dd, 1 H, *J*(3′a,2′) = 5.6, *J*(gem) = 11.4, H-3′a); 3.72 (d, 2 H, *J*(1′,2′) = 6.7, H-1′); 3.89 (brpent, 1 H, H-2′); 8.00 (s, 1 H, H-2). ^{13}C NMR (DMSO): 43.23 (C-1′); 64.08 (C-3′); 68.99 (C-2′); 103.50 (C-5); 146.72 (C-6); 148.17 (C-4); 151.02 (C-2); 153.20 (C-8).

6-Amino-7,9-bis((S)-2,3-dihydroxypropyl)-7H-purin-8(9H)-one (**6b**). White crystals, m.p. 129 °C, yield 81%. All spectra are identical with the authentic material[8].

6-Amino-9-[(*RS*)-(2,2-dimethyl-1,3-dioxolan-4-yl)methyl]-7*H*-purin-8(9*H*)-thione (**9**)

A mixture of the 8-bromo derivative[10] **8** (2.5 g, 7.6 mmol) and thiourea (4.6 g, 60 mmol), in ethanol (60 ml) was refluxed for 6 h, and evaporated *in vacuo*. The residue was suspended in hot chloroform (100 ml), thiourea was filtered off and washed with hot chloroform (250 ml). The chloroform solution was taken down *in vacuo*. Chromatography of the residue in chloroform on a column of silica gel (60 g) with chloroform–methanol gradient, followed by crystallization from ethyl acetate afforded 0.55 g (26%) of compound **9**. White crystals, m.p. 216 °C, R_F 0.38 (S2). FAB MS, *m/z* (rel.%): 282 (100) [M + H]. ^{1}H NMR (DMSO-d_6): 1.21 (s, 3 H, CH_3); 1.40 (s, 3 H, CH_3); 3.95 (d, 2 H, *J*(3′,2′) = 5.3, H-3′); 4.14 (dd, 1 H, *J*(1′b,2′) = 6.6, *J*(gem) = 13.5, H-1′b); 4.26 (dd, 1 H, *J*(1′a,2′) = 6.5, *J*(gem) = 13.5, H-1′a); 4.63 (tt, 1 H, J = 5.3 and 6.5, H-2′); 6.86 (brs, 2 H, NH_2); 8.15 (s, 1 H, H-2); 12.38 (brs, 1 H, NH). ^{13}C NMR (DMSO-d_6): 25.39 (CH_3); 27.02 (CH_3); 45.38 (C-1′); 66.78 (C-3′); 72.25 (C-2′); 107.02 (C-5); 109.04 (C-*ipso*); 147.81 (C-6); 149.56 (C-4); 152.71 (C-2); 166.97 (C-8). For $C_{11}H_{15}N_5O_2S$ (281.3) calculated: 46.96% C, 5.37% H, 24.89% N, 11.40% S; found: 46.90% C, 5.47% H, 24.63% N, 11.25% S. UV, λ_{max} (ε_{max}): (MeOH) 307 (24 700), 233 (14 900).

Reaction of Compound **9** with (*S*)-[(Trityloxy)methyl]oxirane

Method A: A mixture of compound **9** (0.5 g, 1.8 mmol), DMF (15 ml), (*S*)-[(trityloxy)methyl]oxirane (0.6 g, 1.9 mmol) and caesium carbonate (0.12 g, 0.4 mmol) was stirred at 110 °C for 3 h. The same workup as described for alkylation of compound **1** afforded 0.42 g (40%) of compound **10** and 0.2 g (42%) of compound **11**.

Method B: A mixture of compound **9** (0.5 g, 1.8 mmol), DMF (20 ml) and NaH (72 mg of 60% dispersion, 1.8 mmol) was stirred at 100 °C for 0.5 h. (*S*)-[(Trityloxy)methyl]oxirane (0.6 g, 1.9 mmol) was added and the mixture was stirred at 100 °C for another 2.5 h. The same workup as in method *A* afforded 0.3 g (64%) of compound **11**.

9-[((RS)-2,2-Dimethyl-1,3-dioxolan-4-yl)methyl]-8-{[(R)-2-hydroxy-3-(trityloxy)propyl]sulfanyl}-adenine (**10**). White crystals, m.p. 94–95 °C, R_F 0.42 (S1). FAB MS, *m/z* (rel.%): 598 (25) [M + H]; 243 (100) [Tr]. ^{1}H NMR (DMSO-d_6): 1.19 (s, 3 H, CH_3); 1.26 and 1.265 (2 × s, 3 H, CH_3); 2.935 and 2.94 (2 × dd, 1 H, *J*(3″b,2″) = 5.4, *J*(gem) = 9.3, H-3″b); 3.02 (brdd, 1 H, *J*(3″a,2″) = 5.5, *J*(gem) = 9.3, H-3″a); 3.425 and 3.44 (2 × dd, 1 H, *J*(1″b,2″) = 5.5, *J*(gem) = 13.2, H-1″b); 3.51 and 3.52 (2 × dd, 1 H, *J*(1″a,2″) = 5.2, *J*(gem) = 13.2, H-1″a); 3.815 and 3.82 (2 × dd, 1 H, *J*(3′b,2′) = 5.0, *J*(gem) = 8.7, H-3′b); 3.95 (brsext, 1 H, *J* = 5.5, H-2″); 3.987 and 3.99 (2 × dd, 1 H, *J*(3′a,2′) = 6.6, *J*(gem) = 8.7, H-3′a); 4.02 (dd, 0.5 H, *J*(1′b,2′) = 6.5, *J*(gem) = 14.5, H-1′b); 4.05 (d, 1 H, *J*(1′,2′) = 5.7, H-1′); 4.08 (dd, 0.5 H, *J*(1′a,2′) = 5.1, *J*(gem) = 14.5, H-1′a); 4.42 (pent, 1 H, *J* = 5.7, H-2′); 5.38 (d, 1 H, *J*(OH,2″) = 5.4, OH-2″); 7.06 (brs, 2 H, NH_2); 7.23 (t, 3 H, arom. H); 7.29 (t, 6 H, arom. H); 7.36 (d, 6 H, arom. H); 8.09 (s, 1 H, H-2). ^{13}C NMR (DMSO-d_6): 25.19 (CH_3); 26.65 (CH_3); 37.24 (C-1″); 45.67 (C-1′); 66.360 and 66.365 (C-3′ and C-3″); 68.63 (C-2″); 73.35 (C-2′); 86.05 (C-Ph); 109.18 (C-i-Pr); 118.90 (C-5); 127.12 (3 C, C-arom.); 127.97 (6 C, C-arom.); 128.44 (6 C, C-arom.); 143.89 (3 C, C-arom.); 149.06 (C-8); 151.54 (C-4); 151.90 (C-2); 154.28 (C-6).

6-Amino-9-[(RS)-(2,2-dimethyl-1,3-dioxolan-4-yl)methyl]-7H-purin-8(9H)-one (**11**). White crystals, m.p. 229 °C, R_F 0.18 (S1). FAB MS, *m/z* (rel.%): 266 (100) [M + H]. ^{1}H NMR (DMSO-d_6): 1.21 (s, 3 H, CH_3); 1.32 (s, 3 H, CH_3); 3.75 (dd, 1 H, *J*(1′b,2′) = 6.3, *J*(gem) = 13.9, H-1′b); 3.84 (dd, 1 H, *J*(3′b,2′) = 4.8, *J*(gem) = 8.7, H-3′b); 3.85 (dd, 1 H, *J*(1′a,2′) = 6.3, *J*(gem) = 13.9, H-1′a); 3.97 (dd, 1 H, *J*(3′a,2′) = 6.2, *J*(gem) = 8.7, H-3′a); 4.42 (qd, 1 H, *J*(2′,3′b) = 4.8, *J*(2′,3′a) = *J*(2′,1′) = 6.3, H-2′); 6.43 (brs, 2 H, NH_2); 8.02 (s, 1 H, H-2); 10.18 (brs, 1 H, NH).

^{13}C NMR (DMSO-d_6): 25.40 (CH_3); 26.99 (CH_3); 42.46 (C-1′); 66.85 (C-3′); 72.79 (C-2′); 103.38 (C-5); 108.91 (C-i-Pr); 146.80 (C-6); 147.77 (C-4); 151.12 (C-2); 152.29 (C-8). For $C_{11}H_{15}N_5O_3$ (265.3) calculated: 49.81% C, 5.70% H, 26.40% N; found: 49.68% C, 5.70% H, 26.22% N. UV, λ_{max} (ε_{max}): (MeOH) 270 (10 200).

Deprotection of Compounds **10** and **11**. General Procedure

Compound **10** or **11** (0.5 mmol) in aqueous acetic acid (80%, 20 ml) was refluxed for 1 h, the solvent was evaporated *in vacuo* and the residue codistilled with water (3 × 15 ml). Water (40 ml) was added and the mixture extracted with ether (3 × 20 ml). The aqueous phase was evaporated and the residue was crystallized from ethanol to give compounds **12** and **13**, respectively.

9-((RS)-2,3-Dihydroxypropyl)-8-[((R)-2,3-dihydroxypropyl)sulfanyl]adenine (**12**). White crystals, m.p. 115–117 °C, yield 60%, R_F 0.22 (S3). FAB MS, *m/z* (rel.%): 316 (100) [M + H]. ^{1}H NMR (DMSO-d_6): 3.27 and 3.29 (2 × dd, 1 H, *J*(1″b,2″) = 5.2, *J*(gem) = 12.9, H-1″b); 3.33 (dt, 1 H, *J*(3′b,2′) = *J*(3′b,OH) = 5.6, *J*(gem) = 11.2, H-3′b); 3.37 and 3.43 (2 × m, 2 H, H-3″); 3.39 (dt, 1 H, *J*(3′a,2′) = *J*(3′a,OH) = 5.5, *J*(gem) = 11.2, H-3′a); 3.51 (dd, *J*(1″a,2″) = 4.3, *J*(gem) = 12.9, H-1″a); 3.75 (m, 1 H, H-2″); 3.92 (m, 1 H, H-2′); 4.00 (dd, 1 H, *J*(1′b,2′) = 8.3, *J*(gem) = 13.9, H-1′b); 4.14 (dd, 1 H, *J*(1′a,2′) = 4.1, *J*(gem) = 13.9, H-1′a); 4.72 (t, 1 H, *J*(OH,3″) = 5.7, OH-3″); 4.83 (t, 1 H, *J*(OH,3′) = 5.7, OH-3′); 5.02 (d, 1 H, *J*(OH,2′) = 5.4, OH-2′); 5.12 (2 × d, 1 H, *J*(OH,2″) = 5.2, OH-2″); 7.055 (s, 2 H, NH_2); 8.06 (s, 1 H, H-2). ^{1}H NMR (DMSO-d_6 + DAc): 3.27 and 3.29 (2 × dd, 1 H, *J*(1″b,2″) = 5.2, *J*(gem) = 12.9, H-1″b); 3.33 (dd, 1 H, *J*(3′b,2′) = 5.6, *J*(gem) = 11.2, H-3′b); 3.370 and 3.373 (2 × dd, 1 H, *J*(3″b,2″) = 5.6, *J*(gem) = 11.0, H-3″b); 3.39 (dd, 1 H, *J*(3′a,2′) = 5.4, *J*(gem) = 11.2, H-3′a); 3.440 and 3.435 (2 × dd, 1 H, *J*(3″a,2″) = 5.4, *J*(gem) = 11.0, H-3″a); 3.51 (dd, 1 H, *J*(1″a,2″) = 4.4, *J*(gem) = 12.9, H-1″a); 3.749 and 3.753 (2 × m, 1 H, H-2″); 3.91 (dtd, 1 H, H-2′); 4.00 (dd, 1 H, *J*(1′b,2′) = 8.3, *J*(gem) = 14.0, H-1′b); 4.13 (dd, *J*(1′a,2′) = 4.1, *J*(gem) = 14.0, H-1′a). ^{13}C NMR (DMSO-d_6): 36.87 and 36.93 (C-1″); 46.76 (C-1′); 63.98 (C-3′); 64.79 and 64.82 (C-3″); 69.73 (C-2′); 70.545 (C-2″); 119.005 (C-5); 150.075 and 150.11 (C-8); 151.66 (C-2); 151.97 (C-4); 154.16 and 154.22 (C-6). Exact mass (FAB HRMS) found: 316.1042; calculated for $C_{11}H_{18}N_5O_4S$ [M + H]: 316.1079. UV, λ_{max} (ε_{max}): (pH 2) 284 (17 000); (pH 7) 281 (16 500), 221 (17 600); (pH 12) 281 (15 900). CD, λ ($\Delta\varepsilon$) (H_2O): 315 (0.04), 280 (–1.21), 234 (1.18), 206 (–0.98).

6-Amino-9-((RS)-2,3-dihydroxypropyl)-7H-purin-8(9H)-one (**13**). White crystals, m.p. 171 °C, yield 94%, R_F 0.15 (S1). FAB MS, *m/z* (rel.%): 226 (100) [M + H]. ^{1}H NMR spectrum is identical with the authentic material[8]. For $C_8H_{11}N_5O_3$ (225.2) calculated: 42.67% C, 4.92% H, 31.10% N; found: 42.59% C, 5.08% H, 30.88% N. UV, λ_{max} (ε_{max}): (pH 2) 280 (10 000); (pH 12) 280 (10 200).

Reaction of Compound **9** with 2-Chloroethan-1-ol

A mixture of compound **9** (0.48 g, 1.7 mmol), DMF (15 ml) and NaH (72 mg of 60% dispersion, 1.8 mmol) was stirred at 100 °C for 0.5 h. 2-Chloroethan-1-ol (0.28 g, 1.9 mmol) was added and the mixture was stirred at 100 °C for another 0.5 h. The same workup as for the reaction of compound **9** with (*S*)-[(trityloxy)methyl]oxirane afforded 0.43 g (78%) of compound **14**.

9-[((RS)-2,2-Dimethyl-1,3-dioxolan-4-yl)methyl]-8-[(2-hydroxyethyl)sulfanyl]adenine (**14**). White crystals, m.p. 148 °C (ethyl acetate), R_F 0.23 (S1). FAB MS, *m/z* (rel.%): 326 (100) [M +

H]. ^{1}H NMR (DMSO-d_6): 1.21 (s, 3 H, CH_3); 1.30 (s, 3 H, CH_3); 3.37 (t, 2 H, J(1″,2″) = 6.5, H-1″); 3.68 (brq, 2 H, J(2″,OH) = 5.4, J(2″,1″) = 6.5, H-2″); 3.86 (dd, 1 H, J(3′b,2′) = 5.0, J(gem) = 8.8, H-3′b); 4.02 (dd, 1 H, J(3′a,2′) = 6.5, J(gem) = 8.8, H-3′a); 4.14 (dd, 1 H, J(1′b,2′) = 6.5, J(gem) = 14.4, H-1′b); 4.19 (dd, 1 H, J(1′a,2′) = 5.1, J(gem) = 14.4, H-1′a); 4.49 (m, 1 H, H-2′); 5.02 (t, 1 H, J(OH,2″) = 5.4, OH); 7.12 (brs, 2 H, NH_2); 8.09 (s, 1 H, H-2). ^{13}C NMR (DMSO-d_6): 25.23 (CH_3); 26.69 (CH_3); 35.42 (C-1″); 45.77 (C-1′); 60.09 (C-2″); 66.42 (C-3′); 73.35 (C-2′); 109.21 (C-i-Pr); 118.91 (C-5); 148.75 (C-8); 151.64 (C-4); 151.90 (C-2); 154.29 (C-6). For $C_{13}H_{19}N_5O_3S$ (325.4) calculated: 47.99% C, 5.89% H, 21.52% N, 9.85% S; found: 47.84% C, 6.05% H, 21.29% N, 10.08% S. UV, λ_{max} (ε_{max}): (MeOH) 279 (15 500), 222 (17 500).

Reaction of Compound **9** with (*R*)-2,2-Dimethyl-4-[(tosyloxy)methyl]-1,3-dioxolane (D-2,3-*O*-Isopropylideneglycerol Tosylate)

A mixture of compound **9** (0.20 g, 0.7 mmol), DMF (15 ml) and NaH (31 mg of 60% dispersion, 0.77 mmol) was stirred at 100 °C for 0.5 h. D-2,3-*O*-Isopropylideneglycerol tosylate (0.30 g, 1.1 mmol) was added and the mixture was stirred at 110 °C for 1 h. The same workup as for the reaction of compound **9** with (*S*)-[(trityloxy)methyl]oxirane afforded 0.22 g (79%) of compound **15**.

9-[((RS)-2,2-Dimethyl-1,3-dioxolan-4-yl)methyl]-8-{[((R)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl]-sulfanyl}adenine (**15**). Oil, R_F 0.32 (S1). FAB MS, *m/z* (rel.%): 396 (100) [M + H]. ^{1}H NMR (DMSO-d_6): 1.205 (s, 3 H, CH_3); 1.25 (s, 3 H, CH_3); 1.285 and 1.29 (2 × s, 3 H, CH_3); 1.33 (s, 3 H, CH_3); 3.445 and 3.45 (2 × dd, 1 H, J(1″b,2″) = 6.0, J(gem) = 13.4, H-1′b); 3.50 (brdd, 1 H, J(1″a,2″) = 5.9, J(gem) = 13.4 (H-1″a); 3.705 and 3.71 (2 × dd, 1 H, J(3″b, 2″) = 6.0, J(gem) = 8.6, H-3″b); 3.85 and 3.855 (2 × dd, 1 H, J(3″a,2″) = 5.1, J(gem) = 8.6, H-3″a); 4.025 and 4.03 (2 × dd, 1 H, J(3′b,2′) = 6.5, J(gem) = 8.6, H-3′b); 4.05 and 4.055 (2 × dd, 1 H, J(3′a,2′) = 6.2, J(gem) = 8.6, H-3′a); 4.13 and 4.135 (2 × dd, 1 H, J(1′b,2′) = 6.5, J(gem) = 14.4, H-1′b); 4.19 and 4.195 (2 × dd, 1 H, J(1′a,2′) = 4.9, J(gem) = 14.4, H-1′a); 4.36 and 4.37 (2 × qd, 1 H, H-2″); 4.48 and 4.485 (2 × qd, 1 H, H-2′); 7.14 (brs, 2 H, NH_2); 8.09 (s, 1 H, H-2). ^{13}C NMR (DMSO-d_6): 29.19 (CH_3); 25.55 (CH_3); 26.61 (CH_3); 26.83 (CH_3); 35.57 (C-1″); 45.74 (C-1′); 66.37 (C-3′); 67.87 (C-3″); 73.37 (C-2′); 74.20 (C-2″); 109.02 (C-i-Pr); 109.20 (C-i-Pr); 118.88 (C-5); 148.26 and 148.29 (C-8); 151.69 (C-4); 151.98 (C-2); 154.34 (C-6). Exact mass (FAB HRMS) found: 395.4732; calculated for $C_{17}H_{26}N_5O_4S$ [M + H]: 395.4726.

Reaction of Compound **16** with (*S*)-[(Trityloxy)methyl]oxirane

A mixture of compound **16** (1.24 g, 3.2 mmol), DMF (25 ml), (*S*)-[(trityloxy)methyl]oxirane (1.05 g, 3.3 mmol) and caesium carbonate (0.2 g, 0.6 mmol) was stirred at 100 °C for 2 h. The same workup as described for alkylation of compound **9** afforded 1.33 g (59%) of compound **17** and 0.4 g (33%) of compound **18**.

9-{2-[(Diisopropoxyphosphoryl)methoxy]ethyl}-8-{[(R)-2-hydroxy-3-(trityloxy)propyl]sulfanyl}adenine (**17**). White crystals, m.p. 64–66 °C (ethyl acetate), R_F 0.86 (S1). FAB MS, *m/z* (rel.%): 706 (15) [M + H]; 243 (100) [Tr]. ^{1}H NMR (DMSO-d_6): 1.08 (d, 3 H, J(CH_3,CH) = 6.2, CH_3); 1.09 (d, 3 H, J(CH_3,CH) = 6.2, CH_3); 1.125 (d, 3 H, J(CH_3,CH) = 6.2, CH_3); 1.13 (d, 3 H, J(CH_3,CH) = 6.2, CH_3); 2.96 (dd, 1 H, J(3″b,2″) = 5.5, J(gem) = 9.3, H-3″b); 3.05 (dd, 1 H, J(3″a,2″) = 5.5, J(gem) = 9.3, H-3″a); 3.43 (dd, 1 H, J(1″b,2″) = 6.6, J(gem) = 13.1, H-1″b); 3.55 (dd, 1 H, J(1″a,2″) = 5.0, J(gem) = 13.1, H-1″a); 3.73 (d, 2 H, J(P,CH) = 8.1, PCH_2); 3.84 (t, 2 H, J(2′,1′) = 5.2 (H-2′); 3.96 (m, 1 H, H-2″); 4.16 and 4.17 (2 × t, 1 H, J(1′,2′) = 5.2,

H-1′); 4.45 (m, 2 H, POCH); 5.40 (d, 1 H, *J*(OH,2″) = 5.4, OH); 7.02 (brs, 2 H, NH_2); 7.24 (t, 3 H, arom. H); 7.30 (t, 6 H, arom. H); 7.38 (d, 6 H, arom. H); 8.08 (s, 1 H, H-2). ^{13}C NMR (DMSO-d_6): 23.68 (d, *J*(P,C) = 4.9, CH_3); 23.69 (d, *J*(P,C) = 4.9, CH_3); 23.86 (d, 2 C, *J*(P,C) = 3.9, CH_3); 37.01 (C-1″); 42.23 (C-1′); 64.85 (d, *J*(P,C) = 163.6, PC); 66.39 (C-3″); 68.61 (C-2″); 69.75 (d, *J*(P,C) = 11.2, C-2′); 70.33 (d, 2 C, *J*(P,C) = 6.4, POC); 86.05 (C-Ph); 119.00 (C-5); 127.13 (3 C, C-arom.); 127.99 (6 C, C-arom.); 128.45 (6 C, C-arom.); 143.90 (3 C, C-arom.); 148.53 (C-8); 151.57 (C-4); 151.81 (C-2); 154.22 (C-6).

6-Amino-9-{2-[(diisopropoxyphosphoryl)methoxy]ethyl}-7H-purin-8(9H)-one (**18**). White crystals, m.p. 168 °C (ethanol), R_F 0.44 (S1). According to ^{1}H and ^{13}C NMR spectra, compound **18** is identical with the authentic material[8].

Treatment of Compounds **10**, **12**, **14** and **17** with NaH in DMF. General Procedure

A mixture of **10**, **12**, **14** or **17** (0.10 mmol), DMF (5 ml) and NaH (0.11 mmol, 4.5 mg of 60% dispersion) was stirred at room temperature for 0.5 h. According to the TLC and MS, UV and ^{1}H NMR spectra, the hydrolysis was complete, affording products **11**, **13**, **11** and **18**, respectively.

9-[2-[(Diisopropoxyphosphoryl)methoxy]ethyl]guanine[11] (**20**)

A mixture of compound **19** (0.5 g, 1.3 mmol), DMF (15 ml) and sodium hydride (54 mg, 1.35 mmol)) was stirred at 100 °C for 15 min, then (*RS*)-[(trityloxy)methyl]oxirane (0.45 g, 1.4 mmol) was added and the mixture was stirred at 100 °C for another 3.5 h. The standard workup described for alkylation products followed by crystallization from water afforded 0.33 g (69%) of compound **20**. White crystals, m.p. 225 °C, R_F 0.26 (S3). FAB MS, *m/z* (rel.%): 374 (100) [M + H]. ^{1}H NMR spectrum is identical with that of the authentic compound[11]. For $C_{14}H_{24}N_5O_5P$ (373.4) calculated: 45.04% C, 6.48% H, 18.76% N, 8.30% P; found: 45.12% C, 6.67% H, 18.60% N, 8.14% P.

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