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Synthesis of diverse 6-(1,2-disubstituted ethyl)purine bases and nucleosides via 6-(oxiran-2-yl)purines

Martin Kuchař, Radek Pohl, Blanka Klepetářová, Michal Hocek *

Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, Gilead Sciences & IOCB Research Center, Flemingovo nam. 2, CZ-16610 Prague 6, Czech Republic

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ABSTRACT

Dihydroxylation of 6-vinylpurines with *t*-BuOOH and OsO_4 gave 6-(1,2-dihydroxyethyl)purines **2**, while the epoxidation with H_2WO_4 and *t*-BuOOH afforded 6-(oxiran-2-yl)purines **3**. Oxirane ring-opening reactions of **3** with diverse nucleophiles gave a series of title 6-(1,2-disubstituted ethyl)purine bases and nucleosides, which were tested for cytostatic and antiviral activities.

1. Introduction

Purine bases and nucleosides bearing diverse *C*-substituents (aryl, alkenyl, alkynyl or alkyl groups) in position 6 are an important class of compounds possessing a broad spectrum of biological effects: e.g., cytostatic,[1] antiviral[2] and antimicrobial[3] activities or receptor modulation.[4] 6-Methylpurine and its ribonucleoside are highly cytotoxic[5] and its liberation by purine nucleoside phosphorylases from its non-toxic deoxyribonucleoside was proposed as a novel principle in the gene therapy of cancer.[6] We have been interested in the synthesis of purines bearing functionalized alkyl substituents, and reported syntheses and cytostatic effects of 6-(hydroxymethyl)-,[7] 6-(fluoromethyl)-[8] and 6-(difluoromethyl)purine,[9] 6-(2-hydroxyethyl)purine[10] bases and nucleosides and (purin-6-yl)alanines[11] and -phenylalanines.[12] Very recently, we have finished syntheses of a large series of 6-(dialkylamino)methyl-, 6-alkoxymethyl- and 6-(alkylsulfanylmethyl)purine derivatives,[13] as well as homologous 6-(dialkylamino)ethyl-, 6-(dialkylamino)vinyl-, 6-alkoxyethyl- and 6-[2-(alkylsulfanyl)ethyl]purines[14] that also exerted significant cytostatic effects and moderate non-selective anti-HCV activities.

Epoxides are among the most widely used intermediates in organic synthesis, easily leading to 1,2-disubstituted compounds via ring-opening reactions with nucleophiles. Surprisingly, so far there was only one reported example of epoxidation of an alkene in position 6 of purine by Nair and Chamberlain.[15] 6-(Prop-1-en-1-yl)-9-ethylpurine was epoxidized using *m*-chloroperbenzoic acid in dichloromethane to give the epoxide in a low yield of 16% accompanied by unwanted formation of 1-*N*-oxides. No further transformations of the oxirane were reported. Nair and Chamberlain have also reported dihydroxylation of 9-ethyl-6-vinylpurine to 6-(1,2-dihydroxypropyl)-9-ethylpurine[15] by treatment with an equimolar amount of osmium tetroxide. More examples of dihydroxylations were performed in position 2 with 2-vinylpurine, -adenine and -hypoxanthine nucleosides.[16]

As a logical extension of our previous studies on cytostatic purine nucleosides bearing functionalized *C*-substituents (Fig. 1), we have decided to prepare a series of 6-(1,2-disubstituted ethyl)purines, which can be considered as derivatives of cytostatic 6-(hydroxymethyl)purines, via 6-(oxiran-2-yl)purine intermediates.

2. Results and discussion

In order to gain access to the title purines bearing 1,2-difunctionalized ethyl groups, we have tested two approaches: (i) direct

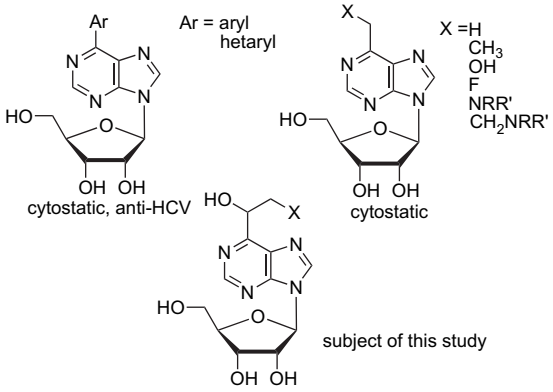

Figure 1. Biologically active 6-substituted purine nucleosides.

* Corresponding author. Tel.: +420 220183324; fax: +420 220183559.
E-mail address: hocek@uochb.cas.cz (M. Hocek).

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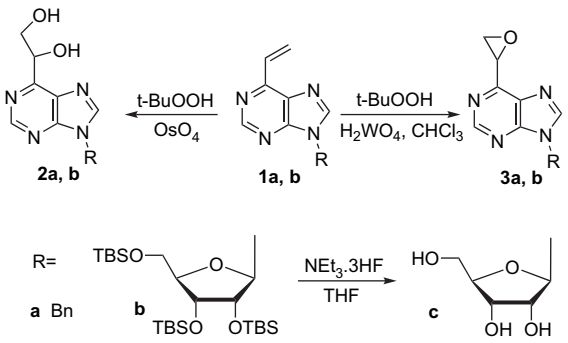
dihydroxylation of 6-vinylpurines and (ii) epoxidation of 6-vinylpurines followed by ring opening (Scheme 1).



Scheme 1. Dihydroxylation and epoxidation.

Dihydroxylation of vinylpurines was described only with an equimolar amount of osmium tetroxide in dry pyridine.[15,16] In order to avoid the use of stoichiometric amounts of this toxic reagent, we have tested several reagents and conditions (Table 1). The reactions of 9-benzyl-6-vinylpurine (**1a**) with a ruthenium catalyst[17] (entry 1) or with potassium permanganate[18] (entry 2) led to complex mixtures of degradation products. On the other hand, the reaction with catalytic amount (2 mol %) of osmium tetroxide[19] with *tert*-butylhydroperoxide as a reoxidant at rt gave the desired vicinal diol **2a** in a good yield of 67% (entry 3). This successful dihydroxylation protocol was then applied for silyl-protected 6-vinylpurine ribonucleoside **1b** giving rise to the 6-(1,2-dihydroxyethyl)purine nucleoside **2b** in 58% yield (entry 4). Epoxidation of 6-vinylpurines was also pursued using several reagents and conditions. The reaction of 6-vinylpurine **1a** with *m*-chloroperbenzoic acid in dichloromethane[15] was slow and unselective, and after 1 day formation of diol and other side products was observed by TLC and NMR spectroscopy (entry 5). Transition metal catalysts (i.e., H_2WO_4) often dramatically enhance the speed and selectivity of epoxidations.[20] The reaction of **1a** was therefore performed with 5 mol % of H_2WO_4 in chloroform with dry *tert*-butylhydroperoxide as oxidant (entry 6). Epoxidation was performed at rt for 16 h to give the oxirane **3a** in a good yield of 62%. It should be noted here that both dihydroxylation and epoxidation of nucleoside **1b** did not proceed diastereoselectively, and due to the presence of homochiral ribose moiety, the products **2b** and **3b** (as well as all other nucleoside derivatives in this paper) were isolated as 1:1 diastereomeric mixtures.

Having access to the epoxide intermediates **3a**,**b**, we have further studied the regioselectivity of ring-opening reactions of these epoxides with diverse nucleophiles (Table 2, Scheme 2). In most cases the nucleophilic reagent is expected to attack the less hindered epoxide carbon.[21] However, as purine is a strongly electron withdrawing substituent, electronic effects could also play an important role in the regioselectivity. Initially, we studied the reaction of sodium methoxide with an epoxide under various conditions (Table 2, Scheme 2).

Table 1
Dihydroxylation and epoxidation of 6-vinylpurines

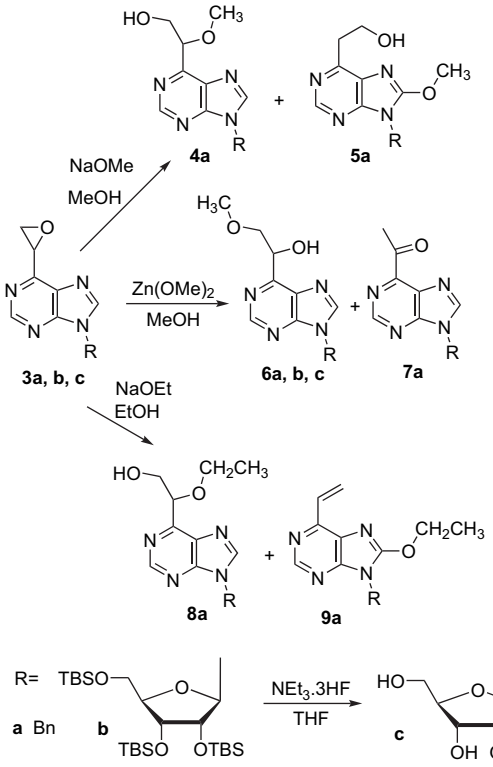
Entry	Starting compd	Reagents	Product (yield)
1	**1a**	$RuCl_3$, $NaIO_4$, H_2SO_4, H_2O, EtOAc, CH_3CN	Decomposition
2	**1a**	$KMnO_4$, acetone	Decomposition
3	**1a**	*t*-BuOOH/OsO_4	**2a** (67%)
4	**1b**	*t*-BuOOH/OsO_4	**2b** (58%)
5	**1a**	*m*-CPBA, DCM	**2a**+degradation
6	**1a**	*t*-BuOOH/H_2WO_4	**3a** (62%)
7	**1b**	*t*-BuOOH/H_2WO_4	**3b** (80%)

Table 2
Reactivity of epoxides **3** with sodium methoxide and ethoxide

Entry	Starting compd	Reagents[a]	Product (yield)
1	**3a**	MeOH, MeONa	**4a** (32%), **5a** (25%)
2	**3a**	MeOH, MeONa, $ZnCl_2$ (1)	**4a** (27%), **5a** (15%), **3a** (30%)
3	**3a**	MeOH, MeONa, $ZnCl_2$ (3)	**4a** (2%), **6a** (24%), **7a** (8%)
4	**3a**	MeOH, MeONa, $ZnCl_2$ (4)	**6a** (21%), **7a** (16%)
5	**3a**	MeOH, $ZnCl_2$	**6a** (28%), **7a** (24%)
6	**3a**	MeOH, MeONa, $ZnCl_2$ (3.6)	**6a** (43%), **7a** (7%)
7	**3b**	MeOH, MeONa, $ZnCl_2$ (3.6)	**6b** (37%)
8	**3c**	MeOH, MeONa, $ZnCl_2$ (3.6)	**6c** (15%)
9	**3a**	EtOH, EtONa	**8a** (32%), **9a** (31%)

[a] In all cases, 3 equiv of MeONa or EtONa has been used, numbers of equivalents of $ZnCl_2$ are given in parentheses.

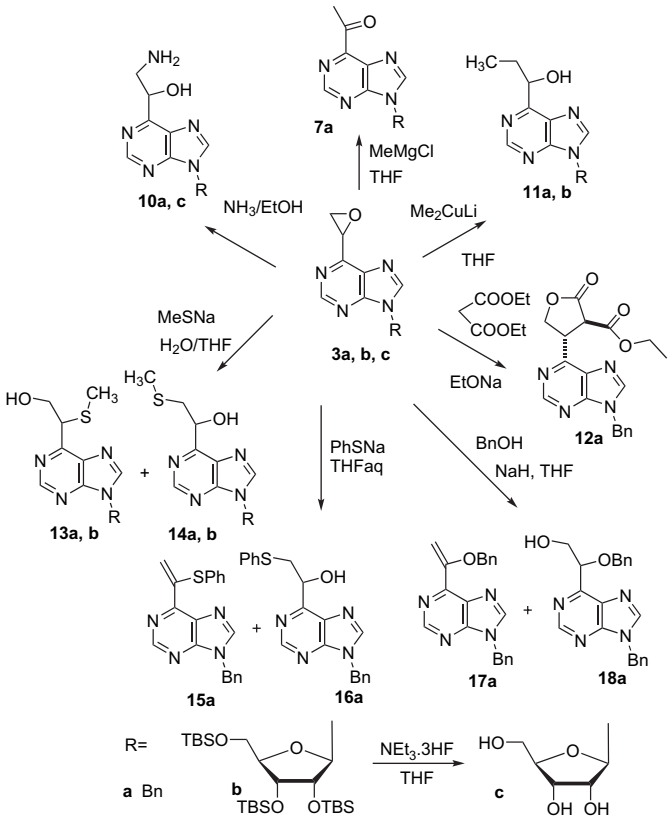
Reactions of **3a** with sodium methoxide were performed in all cases at 60 °C for 2 h. Reaction with 3 equiv of sodium methoxide without further additive led to a mixture of 9-benzyl-6-(2-hydroxy-1-methoxyethyl)purine (**4a**) and unexpected 6-(2-hydroxyethyl)-8-methoxypurine (**5a**), apparently formed as a product of an attack of the nucleophile to position 8 (entry 1). Further, we have studied the effect of additive $ZnCl_2$. When using 1 equiv of $ZnCl_2$ (entry 2), lower conversion to the same products **4a** and **5a** was observed. On the other hand, in the presence of a larger amount of $ZnCl_2$, the same reaction proceeded to form the other ring-opened isomer: 9-benzyl-6-(2-methoxy-1-hydroxyethyl)purine (**6a**), accompanied by 6-acetyl-9-benzylpurine (**7a**)[22] formed by a rearrangement of **3a** catalyzed by excessive zinc chloride (entries 4 and 5). Based on this result, we found the best conditions to be with a more diluted reaction mixture and a special ratio of sodium methoxide (3 equiv) and zinc chloride (3.6 equiv) (entry 6) leading more selectively to the formation of 9-benzyl-6-(1-hydroxy-2-methoxyethyl)purine (**6a**) in an acceptable yield of 43%. An analogous reaction was also performed on protected and free nucleosides **3b**,**c** to give the corresponding nucleosides **6b**,**c** in moderate yields. This interesting dichotomy of regioselectivity of epoxide opening by either sodium or zinc methoxide leading to 2-hydroxy-1-methoxyethyl or 1-hydroxy-2-methoxyethyl derivatives,



Scheme 2. Reactivity of epoxides **3** with sodium methoxide and ethoxide.

respectively, is unprecedented in the literature to the best of our knowledge. Furthermore, we have examined the reactivity of sodium ethoxide with epoxide. The reaction with 3 equiv of sodium ethoxide (entry 9) led to the formation of 9-benzyl-6-(2-hydroxy-1-ethoxyethyl)purine (**8a**) and 9-benzyl-8-ethoxy-6-vinylpurine (**9a**) as products of attack of ethoxide to position 8 followed by dehydration.

We have also studied the reactions of epoxides **3** with other nucleophiles (Scheme 3, Table 3). The treatment of **3a** with ethanolic ammonia proceeded slowly and after 5 days we isolated 6-(2-amino-1-hydroxyethyl)-9-benzylpurine (**10a**) in a moderate yield of 34% (entry 1). The analogous reaction of the free nucleoside **3c** led to the 2-amino derivative **10c** (entry 2). Reaction of **3a** with methylmagnesium chloride in THF gave 6-acetyl-9-benzylpurine (**7a**) formed by a rearrangement of **3a** catalyzed by magnesium chloride present in the Grignard reagent[21] (entry 3). Therefore, we tried the reaction of **3a** with the organocuprate reagent prepared from CuI and methyl lithium, which gave the desired product 9-benzyl-6-(1-hydroxypropyl)purine **11a** in good yield of 60%. The analogous reaction with nucleoside **3b** gave **11b** in a low yield of 21%. Reaction with the sodium salt of diethylmalonate generated in situ proceeded with simultaneous intramolecular lactonization leading to lactone **12a** in a low yield of 22%. The lactonization proceeded stereoselectively to give a racemic product with a trans-relative configuration. Reaction with sodium methanethiolate led to a mixture of two isomers **13a** (60%) and **14a** (13%). In the case of nucleosides **3b**, this reaction gave **13b**, as the product of nucleophilic attack at the more hindered carbon, as the main product (the other isomer was only detected on TLC in trace amounts but not isolated). Reaction with sodium thiophenolate proceeded almost quantitatively and led to a mixture of two products: dehydrated product **15a** and 1-hydroxy isomer **16a**. On the other hand, reaction with sodium benzoxide led only to one isomer **18a** accompanied by its dehydrated byproduct **17a**.



Scheme 3. Other transformations of epoxides **3**.

Table 3
Transformations of epoxides

Entry	Starting compd	Reagents	Product (yield)
1	**3a**	NH_3/EtOH, rt, 5 days	**10a** (34%)
2	**3c**	NH_3/EtOH, rt, 5 days	**10c** (42%)
3	**3a**	MeMgCl	**7a** (71%)
4	**3a**	Me_2CuLi/THF	**11a** (60%)
5	**3b**	Me_2CuLi/THF	**11b** (21%)
6	**3a**	$CH_2(COOEt)_2$, EtONa,	**12a** (22%)
7	**3a**	MeSNa/THF aq	**13a** (60%), **14a** (13%)
8	**3b**	MeSNa/THF aq	**13b** (74%)
9	**3a**	PhSNa, THF aq	**15a** (35%), **16a** (63%)
10	**3a**	*t*-BuOH, NaH, THF	No reaction
11	**3a**	PhOH, NaH, THF	No reaction
12	**3a**	BnOH, NaH, THF	**17a** (26%), **18a** (14%)

The whole series of TBS-protected nucleosides (**2b**, **3b**, **6b**, **11b** and **13b**) was deprotected by treatment with $Et_3N{\cdot}3HF$ in THF (Table 4) to give the free nucleosides **2c**, **6c**, **11c** and **13c** in good yields. In the case of silylated epoxide **3b**, the above mentioned desilylation gave the nucleoside **3c** in low yield accompanied by 6-(acetyl)-9-(β-D-ribofuranosyl)purine **7c**. However, the use of TBAF in THF gave cleanly the desired nucleoside **3c** in good yield.

All compounds were fully characterized. Crystal structures of epoxide **3a**, methylsulfanyl **14a** and 8-methoxy derivatives **5a** were determined by X-ray crystallography (Fig. 2). No significant antiviral (HCV replicon) or cytostatic effect was observed in any of the new purine bases or nucleosides reported here, with the exception of parent epoxide **3c**, which exerted a moderate cytostatic activity: IC_{50}=3.6–9 μM for CEM, HL60 and HeLa cell lines.

In conclusion, a practical synthesis of 6-(oxiran-2-yl)purine bases and nucleosides was developed based on epoxidation of 6-vinylpurines. The epoxides are reactive towards nucleophilic ring-opening reactions leading to diverse types of products. Apart from the expected addition products, in some cases (hard sodium alkoxides) we have observed rather unexpected by-products formed by attack of the nucleophile to position 8 and in some other cases products of elimination or rearrangements. Despite the moderate yields and poor selectivities of some of these reactions, the presented methodology significantly extends the portfolio of purines bearing functionalized *C*-substituents in position 6 to many novel derivatives not accessible by the established methodologies.

3. Experimental

3.1. General

Melting points were determined on a Kofler block and are uncorrected. Mass spectra were measured on a ZAB-EQ (VG Analytical) spectrometer. IR spectra were recorded on Bruker equinox 55 and FTIR spectrometer Nicolet 6700. NMR spectra were recorded on Bruker Avance 600 (^{1}H at 600 MHz, ^{13}C at 151 MHz), Bruker Avance 500 (^{1}H at 500 MHz, ^{13}C at 125.8 MHz) and Bruker Avance 400 (^{1}H at 400 MHz, ^{13}C at 100.6 MHz). ^{1}H and ^{13}C NMR spectra were referenced to the signal of TMS or to the solvent residual

Table 4
Deprotections of silylated nucleosides

Entry	Starting compd	Reagent	Product (yield)
1	**2b**	$Et_3N{\cdot}3HF$	**2c** (93%)
2	**3b**	$Et_3N{\cdot}3HF$	**3c** (39%), **7c** (20%)
3	**3b**	TBAF	**3c** (82%)
4	**6b**	$Et_3N{\cdot}3HF$	**6c** (67%)
5	**11b**	$Et_3N{\cdot}3HF$	**11c** (75%)
6	**13b**	$Et_3N{\cdot}3HF$	**13c** (92%)

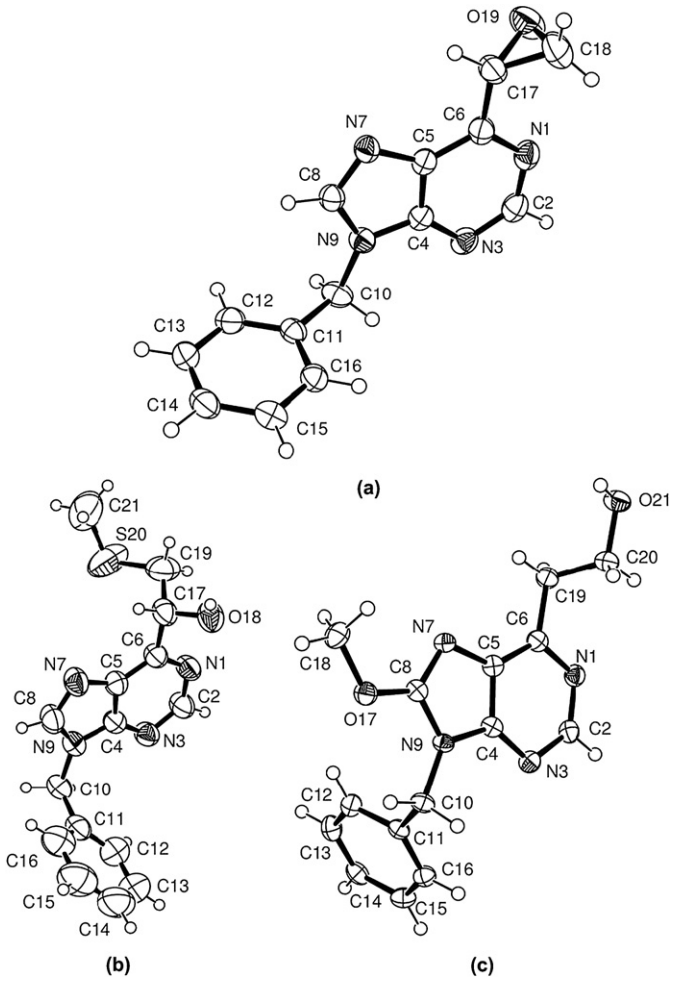


Figure 2. ORTEP drawings of crystal structures of **3a** (a), **14a** (b) and **5a** (c) with atom numbering scheme. Thermal ellipsoids are drawn at the 50% probability level.

signal [DMSO-d_6: 2.50 ppm (^{1}H), 39.70 ppm (^{13}C); CD_3OD: 3.31 ppm (^{1}H); 49.00 ppm (^{13}C)]. H,C-HSQC and H,C-HMBC experiments were performed for complete assignment of all signals. Starting compounds were prepared according to the literature procedures: **1a**[22] and **1b**.[23]

3.2. Preparation of starting *t*-BuOOH solution

Anhydrous Na_2SO_4 (50 g) was added to a mixture of *tert*-butanol (100 ml) and aqueous H_2O_2 (30% in H_2O, 200 ml) and the two phases were separated. The organic layer was dried over anhydrous $MgSO_4$ and filtered. This solution was sufficiently dry for dihydroxylations but not for epoxidations. For the use in epoxidations, chloroform (100 ml) was added to the solution, which was again dried over anhydrous $MgSO_4$ and filtered.

3.3. General method for dihydroxylation of 6-vinylpurines

A mixture of a vinylpurine **1** (1 mmol) and OsO_4 (1 ml of 2% solution in *t*-BuOH, 0.02 mmol) in a solution of *tert*-butylhydroperoxide in *tert*-butanol (50 ml) was stirred at rt for 2 days. After completion, the reaction mixture was diluted with a 10% aqueous solution of $Na_2S_2O_4$ (500 ml) and then washed with ethyl acetate (3×50 ml). The collected organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to give the product.

3.3.1. 9-Benzyl-6-(1,2-dihydroxyethyl)purine (**2a**)

Chromatography methanol/chloroform 0–3%, crystallized from chloroform/heptane, colourless crystals, yield 70%. Mp 118–120 °C. ^{1}H NMR (500 MHz, $CDCl_3$): 4.12 and 4.16 (2×dd, 2H, J_{gem}=11.5, J_{vic}=4.6, CH_2O); 4.23 and 5.22 (2×br s, 2×1H, OH); 5.35 (t, 1H, J_{vic}=4.6, CHO); 5.44 (s, 2H, CH_2Ph); 7.29–7.37 (m, 5H, H-*o*,*m*,*p*-Ph); 8.09 (s, 1H, H-8); 8.95 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 47.36 (CH_2Ph); 65.65 (CH_2O); 71.69 (CHO); 127.89 (CH-*o*-Ph); 128.62 (CH-*p*-Ph); 128.08 (CH-*m*-Ph); 130.36 (C-5); 134.64 (C-*i*-Ph); 144.32 (CH-8); 151.15 (C-4); 151.83 (CH-2); 159.37 (C-6). ESI MS: *m*/*z* (%) (65) [M^+ Na], (100) [M^+ H]. HRMS calcd for $C_{14}H_{15}N_4O_2$ [M^+ H] 271.1190, found 271.1190. Anal. Calcd for $C_{14}H_{14}N_4O_2\cdot 0.25H_2O$: C 61.19, H 5.32, N 20.39. Found: C 61.27, H 5.17, N 20.34. IR ($CHCl_3$): 3587, 3411, 3114, 3092, 3070, 1596, 1585, 1456, 1406, 1333, 1095, 1080, 1052, 1031, 998, 699, 647, 455.

3.3.2. 9-(2,3,5-Tri-O-tert-butyldimethylsilyl-β-D-ribofuranosyl)-6-[(R,S)-1,2-dihydroxyethyl]purine (**2b**)

Purified by column chromatography (silica gel, ethyl acetate/hexane 20–50%) to give yellowish foam, yield 58%, mixture of diastereoisomers 1:1. ^{1}H NMR (500 MHz, $CDCl_3$): −0.21, −0.17, −0.02, −0.01, 0.101, 0.103, 0.107, 0.112, 0.144, 0.146 and 0.154 (11×s, 36H, CH_3Si); 0.80, 0.81, 0.94, 0.961 and 0.962 (5×s, 54H, $(CH_3)_3C$); 3.58 and 3.64 (2×br t, 2×1H, J=6.5, OH); 3.81 (dd, 2H, J_{gem}=11.4, $J_{5'b,4'}$=2.6, H-5′b); 4.03 and 4.06 (2×dd, 2×1H, J_{gem}=11.4, $J_{5'a,4'}$=3.6, H-5′a); 4.11–4.19 (m, 6H, H-4′ and CH_2O); 4.31 and 4.33 (2×t, 2×1H, $J_{3',2'}$=$J_{3',4'}$=4.0, H-3′); 4.59 and 4.62 (2×dd, 2×1H, $J_{2',1'}$=4.6, $J_{2',3'}$=4.0, H-2′); 4.91 (br m, 2H, OH); 5.30 (br m, 2H, CHO); 6.14 and 6.16 (2×d, 2×1H, $J_{1',2'}$=4.6, H-1′); 8.541 and 8.543 (2×s, 2×1H, H-8); 8.93 and 8.94 (2×s, 2×1H, H-2).^{13}C NMR (125.7 MHz, $CDCl_3$): −5.40, −5.39, −5.36, −5.35, −5.04, −5.01, −4.75, −4.71, −4.69, −4.38 and −4.33 (CH_3Si); 17.83, 17.84, 18.05, 18.06 and 18.53 ($(CH_3)_3C$); 25.61, 25.62, 25.81 and 26.08 ($(CH_3)_3C$); 62.09 and 62.28 (CH_2-5′); 65.66 and 65.70 (CH_2O); 71.34, 71.60 and 71.66 (CH-3′ and CHO); 76.15 and 76.35 (CH-2′); 85.24 and 85.46 (CH-4′); 88.38 and 88.69 (CH-1′); 130.93 and 131.01 (C-5); 143.29 and 143.37 (CH-8); 150.89 and 150.98 (C-4); 151.53 and 151.61 (CH-2); 159.26 and 159.29 (C-6). ESI MS: *m*/*z* (%) (35) [M^+ H]. HRMS calcd for $C_{30}H_{59}N_4O_6Si_3$ [M^+ H] 655.3737, found 655.3723. IR ($CHCl_3$): 3589, 3413, 3120, 3074, 2956, 1597, 1584, 1497, 1472, 1464, 1408, 1391, 1334, 1257, 1083, 1071, 938, 839, 682, 648.

3.4. General method for epoxidation of 6-vinylpurines

A mixture of a vinylpurine **1** (2 mmol) and H_2WO_4 (25 mg, 0.1 mmol) in a solution of *tert*-butylhydroperoxide in *tert*-butanol and chloroform (30 ml) was stirred at rt for 16 h. After completion, the reaction mixture was filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to give the product.

3.4.1. 9-Benzyl-6-(oxiran-2-yl)purine (**3a**)

Purified by column chromatography (silica gel, ethyl acetate/hexane 30–60%), crystallized from chloroform/heptane to give colourless crystals, yield 62%. Mp 105–108 °C. ^{1}H NMR (500 MHz, $CDCl_3$): 3.34 (dd, 1H, J_{gem}=6.4, $J_{3b,2}$=4.2, H-3b-ox); 3.60 (dd, 1H, J_{gem}=6.4, $J_{3a,2}$=2.5, H-3a-ox); 4.56 (dd, 1H, $J_{2,3}$=4.2, 2.5, H-2-ox); 5.46 (s, 2H, CH_2Ph); 7.30 (m, 2H, H-*o*-Ph); 7.32–7.39 (m, 3H, H-*m*,*p*-Ph); 8.08 (s, 1H, H-8); 8.97 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 47.30 (CH_2Ph); 49.27 (CH-2-ox); 49.53 (CH_2-3-ox); 127.80 (CH-*o*-Ph); 128.65 (CH-*p*-Ph); 129.15 (CH-*m*-Ph); 132.49 (C-5); 134.87 (C-*i*-Ph); 144.80 (CH-8); 151.56 (C-4); 152.74 (CH-2); 156.01 (C-6). ESI MS: *m*/*z* (%) (100) [M^+ Na], (32) [M^+ H]. HRMS calcd for

$C_{14}H_{13}N_4O$ [M^+ H] 253.1084, found. 253.1088. Anal. Calcd for $C_{14}H_{12}N_4O$: C 66.65, H 4.79, N 22.21. Found: C 66.23, H 4.62, N 21.88. IR ($CHCl_3$): 3113, 3092, 3069, 3034, 1598, 1586, 1501, 1456, 1411, 1331, 1078, 1030, 1003, 728, 699, 644, 456.

*3.4.2. 9-(2,3,5-Tri-O-tert-butyldimethylsilyl-β-D-ribofuranosyl)-6-[(R,S)-oxiran-2-yl]purine (**3b**)*

Purified by column chromatography (silica gel, ethyl acetate/hexane 0–30%) to give white foam, yield 80%, mixture of diastereoisomers 1:1. ^{1}H NMR (600 MHz, $CDCl_3$): −0.27, −0.25, −0.04, 0.102, 0.106, 0.109, 0.144, 0.147, 0.153 and 0.158 (10×s, 36H, CH_3Si); 0.78, 0.79, 0.94, 0.96 and 0.97 (5×s, 54H, $(CH_3)_3C$); 3.336 and 3.339 (2×dd, 2×1H, J_{gem}=6.4, $J_{3b,2}$=4.2, H-3b-ox); 3.55 and 3.58 (2×dd, 2×1H, J_{gem}=6.4, $J_{3a,2}$=2.5, H-3a-ox); 3.81 (dd, 2H, J_{gem}=11.5, $J_{5'b,4'}$=2.9, H-5′b); 4.02 and 4.03 (2×dd, 2×1H, J_{gem}=11.5, $J_{5'a,4'}$=3.9, H-5′a); 4.15 and 4.16 (2×ddd, 2×1H, $J_{4',5'}$=3.9, 2.9, $J_{4',3'}$=3.8, H-4′); 4.31 and 4.33 (2×dd, 2×1H, $J_{3',2'}$=4.0, $J_{3',4'}$=3.8, H-3′); 4.58 and 4.60 (2×dd, 2×1H, $J_{2,3}$=4.2, 2.5, H-2-ox); 4.65 and 4.66 (2×dd, 2×1H, $J_{2',1'}$=5.2, $J_{2',3'}$=4.0, H-2′); 6.138 and 6.144 (2×d, 2×1H, $J_{1',2'}$=5.2, H-1′); 8.47 and 8.49 (2×s, 2×1H, H-8); 8.92 (s, 2H, H-2). ^{13}C NMR (151 MHz, $CDCl_3$): −5.38, −5.11, −5.06, −4.74, −4.68 and −4.43 (CH_3Si); 17.79, 17.81, 18.06, 18.52 and 18.53 ($(CH_3)_3C$); 25.60, 25.81 and 26.07 ($(CH_3)_3C$); 48.88 and 49.14 (CH-2-ox); 49.60 and 49.63 (CH_2-3-ox); 62.43 and 62.48 (CH_2-5′); 71.85 and 71.93 (CH-3′); 75.87 and 76.08 (CH-2′); 85.57 and 85.69 (CH-4′); 88.18 and 88.22 (CH-1′); 133.26 and 133.35 (C-5); 143.93 and 144.00 (CH-8); 151.26 (C-4); 152.53 and 152.57 (CH-2); 155.84 and 155.91 (C-6). ESI MS: *m*/*z* (%) (65) [M^+ Na], (100) [M^+ H]. HRMS calcd for $C_{30}H_{57}N_4O_5Si_3$ [M^+ H] 637.3631, found 637.3634. IR ($CHCl_3$): 3119, 3068, 2956, 1599, 1586, 1499, 1472, 1464, 1411, 1391, 1362, 1331, 1258, 1083, 1071, 938, 839, 682, 646.

3.5. Reaction of 9-benzyl-6-(oxiran-2-yl)purine (3a) with sodium methoxide

A mixture of 9-benzyl-6-(oxiran-2-yl)purine (**3a**) (252 mg, 1 mmol) and sodium methoxide (3 mmol) in methanol (20 ml) was stirred at 60 °C for 2 h. After completion, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, methanol/chloroform 0–5%) to give two isomers: 90 mg (32%) of 9-benzyl-6-(hydroxyethyl)-8-methoxypurine (**5a**) and 70 mg (25%) of 9-benzyl-6-(2-hydroxy-1-methoxyethyl)purine (**4a**). Both isomers were crystallized from chloroform/heptane to give white crystals.

*3.5.1. 9-Benzyl-6-(2-hydroxy-1-methoxyethyl)purine (**4a**)*

Mp 94–96 °C. ^{1}H NMR (500 MHz, $CDCl_3$): 3.51 (s, 3H, CH_3O); 4.10 (d, 2H, J_{vic}=5.0, CH_2O); 5.01 (t, 1H, J_{vic}=5.0, CHO); 5.46 (s, 2H, CH_2Ph); 7.33–7.41 (m, 5H, H-*o*,*m*,*p*-Ph); 8.09 (s, 1H, H-8); 9.02 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 47.37 (CH_2Ph); 58.09 (CH_3O); 64.17 (CH_2O); 81.23 (CHO); 127.99 (CH-*o*-Ph); 128.70 (CH-*p*-Ph); 129.16 (CH-*m*-Ph); 131.95 (C-5); 134.76 (C-*i*-Ph); 144.60 (CH-8); 151.65 (C-4); 152.58 (CH-2); 158.19 (C-6). ESI MS: *m*/*z* (%) (100) [M^+ Na], (45) [M^+ H]. HRMS calcd for $C_{15}H_{17}N_4O_2$ [M^+ H] 285.1346, found 285.1345. IR ($CHCl_3$): 3589, 3358, 3113, 3092, 3069, 3033, 2831, 1589, 1500, 1456, 1440, 1405, 1331, 1115, 1077, 1044, 1030, 1004, 699, 456.

*3.5.2. 9-Benzyl-6-(2-hydroxyethyl)-8-methoxypurine (**5a**)*

Mp 98–100 °C. ^{1}H NMR (500 MHz, DMSO-d_6): 3.13 (t, 2H, J_{vic}=7.0, CH_2-pur); 3.88 (td, 2H, J_{vic}=7.0, 5.6, CH_2-O); 4.17 (s, 3H, CH_3O); 4.75 (t, 1H, J_{vic}=5.6, OH); 5.22 (s, 2H, CH_2Ph); 7.26 (m, 2H, H-*o*-Ph); 7.28 (m, 1H, H-*p*-Ph); 7.33 (m, 2H, H-*m*-Ph); 8.64 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 36.26 (CH_2-pur); 44.26 (CH_2Ph); 57.90 (CH_3O); 59.54 (CH_2O); 127.55 (CH-*o*-Ph); 128.02 (CH-*p*-Ph); 128.98 (CH-*m*-Ph); 130.24 (C-5); 136.34 (C-*i*-Ph); 150.44 (CH-2); 151.17 (C-4); 154.53 (C-6); 157.82 (C-8). ESI MS: *m*/*z* (%) (90) [M^+ Na], (100) [M^+ H]. HRMS calcd for $C_{15}H_{17}N_4O_2$ [M^+ H] 285.13460, found 285.13446. Anal. Calcd for $C_{15}H_{16}N_4O_2$: C 63.37, H 5.67, N 19.71. Found: C 63.36, H 5.78, N 19.88. IR ($CHCl_3$): 3620, 3361, 3092, 3069, 3036, 1614, 1592, 1553, 1497, 1485, 1484, 1455, 1403, 1334, 1059, 1038, 1030, 699, 458.

*3.5.3. 9-Benzyl-6-(1-hydroxy-2-methoxyethyl)purine (**6a**)*

A mixture of 9-benzyl-6-(oxiran-2-yl)purine (**3a**) (126 mg, 0.5 mmol), dry $ZnCl_2$ (245 mg, 1.8 mmol) and sodium methoxide (1.5 mmol) in methanol (20 ml) was stirred at 60 °C for 2 h. After completion, the reaction mixture was diluted with water (150 ml) and then washed with ethyl acetate (3×50 ml). The collected organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, methanol/chloroform 0–5%) and crystallized from chloroform/heptane to give white crystals 61 mg (43%). Mp 115–116 °C. ^{1}H NMR (500 MHz, $CDCl_3$): 3.39 (s, 3H, CH_3O); 4.00 (dd, 2H, J_{gem}=10.1, J_{vic}=3.8, CH_aH_bO); 4.02 (dd, 2H, J_{gem}=10.1, J_{vic}=4.9, CH_aH_bO); 4.75 (br d, 1H, J=5.2, OH); 5.45 (br ddd, 1H, J=5.2, 4.9, 3.8, CHO); 5.46 (s, 2H, CH_2Ph); 7.31–7.40 (m, 5H, H-*o*,*m*,*p*-Ph); 8.05 (s, 1H, H-8); 8.99 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 47.43 (CH_2Ph); 59.50 (CH_3O); 70.61 (CHO); 75.84 (CH_2O); 127.97 (CH-*o*-Ph); 128.72 (CH-*p*-Ph); 129.19 (CH-*m*-Ph); 130.74 (C-5); 134.83 (C-*i*-Ph); 144.14 (CH-8); 151.28 (C-4); 151.94 (CH-2); 158.95 (C-6). ESI MS: *m*/*z* (%) (100) [M^+ Na], (45) [M^+ H]. HRMS calcd for $C_{15}H_{17}N_4O_2Na$ [M^+ Na] 307.1166, found 307.1162. Anal. Calcd for $C_{15}H_{16}N_4O_2$: C 63.37, H 5.67, N 19.71. Found: C 63.51, H 5.54, N 19.38. IR ($CHCl_3$): 3565, 3440, 3112, 3092, 3069, 3033, 2830, 1594, 1586, 1498, 1456, 1405, 1332, 1328, 1122, 1099, 1079, 1031, 1004, 699, 646, 456.

*3.5.4. 9-(2,3,5-Tri-O-tert-butyldimethylsilyl-β-D-ribofuranosyl)-6-[(R,S)-1-hydroxy-2-methoxyethyl]purine (**6b**)*

A mixture of 9-(2,3,5-tri-*O*-*tert*-butyldimethylsilyl-β-D-ribofuranosyl)-6-(oxiran-2-yl)purine (**3b**) (637 mg, 1 mmol), dry $ZnCl_2$ (170 mg, 1.25 mmol) and sodium methoxide (1 mmol) in methanol (15 ml) was stirred at ambient temperature for 1 day. After completion, the reaction mixture was diluted with water (150 ml) and then washed with ethyl acetate (3×50 ml). The collected organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, ethyl acetate/hexane 0–20%) to give product **6b** (250 mg, 37%), mixture of diastereoisomers 1:1. ^{1}H NMR (500 MHz, $CDCl_3$): −0.28, −0.27, −0.05, −0.04, 0.109, 0.113, 0.116, 0.139, 0.142 and 0.149 (10×s, 36H, CH_3Si); 0.77, 0.94 and 0.96 (3×s, 54H, $(CH_3)_3C$); 3.361 and 3.362 (2×s, 2×3H, CH_3O); 3.804 and 3.806 (2×dd, 2H, J_{gem}=11.4, $J_{5'b,4'}$=2.7, H-5′b); 3.99–4.01 (m, 4H, CH_2O); 4.02 and 4.04 (2×dd, 2×1H, J_{gem}=11.4, $J_{5'a,4'}$=4.0, H-5′a); 4.16 (m, 2H, H-4′); 4.33 (dd, 2H, $J_{3',2'}$=4.3, $J_{3',4'}$=3.6, H-3′); 4.65 and 4.69 (2×dd, 2×1H, $J_{2',1'}$=5.3, $J_{2',3'}$=4.3, H-2′); 4.758 and 4.761 (2×d, 2×1H, J=6.3, OH); 5.46 (m, 2H, CHO); 6.13 and 6.15 (2×d, 2×1H, $J_{1',2'}$=5.3, H-1′); 8.44 and 8.45 (2×s, 2×1H, H-8); 8.93 and 8.94 (2×s, 2×1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): −5.39, −5.21, −5.18, −4.73, −4.70, −4.69, −4.43 and −4.41 (CH_3Si); 17.80, 18.06, 18.51 and 18.52 ($(CH_3)_3C$); 25.59, 25.81 and 26.06 ($(CH_3)_3C$); 59.43 and 59.44 (CH_3O); 62.41 and 62.50 (CH_2-5′); 70.48 and 70.59 (CHO); 71.84 and 71.93 (CH-3′); 75.83 (CH_2O); 75.92 and 76.07 (CH-2′); 85.65 and 85.71 (CH-4′); 88.16 and 88.38 (CH-1′); 131.29 and 131.39 (C-5); 143.24 and 143.33 (CH-8); 150.92 and 150.97 (C-4); 151.60 and 151.65 (CH-2); 158.81 and 158.87 (C-6). ESI MS: *m*/*z* (%) (100) [M^+ Na], (80) [M^+ H]. HRMS calcd for $C_{31}H_{61}N_4O_6Si_3$ [M^+ H] 669.3893, found 669.3889. IR ($CHCl_3$): 3440, 3119, 3071, 2956, 1597, 1585, 1497, 1472, 1464, 1408, 1391, 1362, 1333, 1258, 1122, 1083, 1073, 939, 839, 682, 648.

*3.5.5. 6-[(R,S)-1-Hydroxy-2-methoxyethyl]-9-(β-D-ribofuranosyl)purine (**6c**)*

A mixture of 6-(oxiran-2-yl)-9-(β-D-ribofuranosyl)purine (**3c**) (294 mg, 1 mmol), dry $ZnCl_2$ (170 mg, 1.25 mmol) and sodium methoxide (1 mmol) in methanol (15 ml) was stirred at 60 °C for 2 h. After completion, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography (reverse phase, ethyl methanol/water 0–100%) and lyophilized from water to give **6c** (50 mg, 15%) as white foam, diastereoisomeric mixture 1:1. ^{1}H NMR (500 MHz, DMSO-d_6): 3.23 (s, 6H, CH_3O); 3.572, 3.576, 3.687 and 3.688 (4×ddd, 4×1H, J_{gem}=12.0, $J_{5',OH}$=6.0, $J_{5',4'}$=4.0, H-5′); 3.782 and 3.783 (2×dd, 2×1H, J_{gem}=9.8, J_{vic}=6.2, CH_aH_bO); 3.85 (dd, 2H, J_{gem}=9.8, J_{vic}=5.8, CH_aH_bO); 3.98 (td, 2H, $J_{4',5'}$=4.0, $J_{4',3'}$=3.5, H-4′); 4.19 (td, 2H, $J_{3',2'}$=$J_{3',OH}$=4.9, $J_{3',4'}$=3.5, H-3′); 4.65 and 4.66 (2×ddd, 2×1H, $J_{2',OH}$=6.0, $J_{2',1'}$=5.9, $J_{2',3'}$=4.9, H-2′); 5.112 and 5.113 (2×t, 2×1H, $J_{OH,5'}$=6.0, OH-5′); 5.25 (d, 2H, $J_{OH,3'}$=4.9, OH-3′); 5.32 (ddd, 2H, J_{vic}=6.2, 6.0, 5.8, CHO); 5.547 and 5.549 (2×d, 2×1H, $J_{OH,2'}$=6.0, OH-2′); 5.612 and 5.614 (2×d, 2×1H, J_{vic}=6.0, OH); 6.04 (d, 2H, $J_{1',2'}$=5.9, H-1′); 8.81 (s, 2H, H-8); 8.92 (s, 2H, H-2).^{13}C NMR (125.7 MHz, DMSO-d_6): 58.61 (CH_3O); 61.52 (CH_2-5′); 68.52 (CHO); 70.58 (CH-3′); 73.76 and 73.85 (CH-2′); 75.21 (CH_2O); 85.97 (CH-4′); 87.76 and 87.77 (CH-1′); 131.91 and 131.93 (C-5); 144.87 and 144.89 (CH-8); 151.17 (C-4); 151.95 (CH-2); 160.20 (C-6). ESI MS: *m*/*z* (%) (100) [M^+ Na], (27) [M^+ H]. HRMS calcd for $C_{13}H_{18}N_4O_6Na$ [M^+ Na] 349.1117, found 349.1112. Anal. Calcd for $C_{13}H_{18}N_4O_6\cdot 0.5H_2O$: C 46.57, H 5.77, N 16.71. Found: C 46.51, H 5.68, N 16.48. IR (KBr): 3400–2400, 2829, 1598, 1585, 1500, 1406, 1334, 1211, 1119, 1084, 1054, 1100, 811, 645. $[\alpha]_D$ −39.8 (*c* 0.26, MeOH).

3.6. Reaction of 9-benzyl-6-(oxiran-2-yl)purine (3a) with sodium ethoxide

A mixture of 9-benzyl-6-(oxiran-2-yl)purine (**3a**) (252 mg, 1 mmol) and sodium ethoxide (3 mmol) in ethanol (20 ml) was stirred at 60 °C for 2 h. Sodium ethoxide was generated from sodium hydride (3 mmol) and ethanol. After completion, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, ethyl acetate/methanol 0–10%) to give two product: 96 mg (32%) of 9-benzyl-8-ethoxy-6-vinylpurine (**9a**) and 88 mg (31%) of 9-benzyl-6-(2-hydroxy-1-ethoxyethyl)purine (**8a**).

*3.6.1. 9-Benzyl-8-ethoxy-6-vinylpurine (**9a**)*

Yellow oil. ^{1}H NMR (600 MHz, $CDCl_3$): 1.48 (t, 3H, J_{vic}=7.2, CH_3CH_2); 4.67 (q, 2H, J_{vic}=7.2, CH_3CH_2); 5.24 (s, 2H, CH_2Ph); 5.83 (dd, 1H, J_{vic}=11.0, J_{gem}=1.8, CH_aH_b); 6.88 (dd, 1H, J_{vic}=17.5, J_{gem}=1.8, =CH_aH_b); 7.16 (dd, 1H, J_{vic}=17.5, 11.0, =CH); 7.29 (m, 1H, H-*p*-Ph); 7.31 (m, 2H, H-*m*-Ph); 7.35 (m, 2H, H-*o*-Ph); 8.75 (s, 1H, H-2). ^{13}C NMR (151 MHz, $CDCl_3$): 14.47 (CH_3CH_2); 44.61 (CH_2Ph); 66.89 (CH_2CH_3); 124.27 (=CH_2); 128.00 (CH-*o*-Ph); 128.03 (CH-*p*-Ph); 128.72 (CH-*m*-Ph); 128.98 (C-5); 132.31 (=CH); 135.68 (C-*i*-Ph); 148.63 (C-6); 150.54 (CH-2); 152.62 (C-4); 157.95 (C-8). ESI MS: *m*/*z* (%) (100) [M^+ H]. HRMS calcd for $C_{16}H_{17}N_4O$ [M^+ H] 281.1398, found 281.1397. IR ($CHCl_3$): 3092, 3068, 3036, 2987, 1640, 1601, 1588, 1537, 1482, 1398, 1330, 1094, 1045, 1028, 921, 699, 455.

*3.6.2. 9-Benzyl-6-(2-hydroxy-1-ethoxyethyl)purine (**8a**)*

Yellow oil. ^{1}H NMR (600 MHz, $CDCl_3$): 1.25 (t, 3H, J_{vic}=7.0, CH_3CH_2); 3.64 and 3.66 (2×dq, 2H, J_{gem}=11.7, J_{vic}=7.0, CH_2CH_3); 4.07 (dd, 1H, J_{gem}=11.8, J_{vic}=4.6, CH_aH_bO); 4.10 (dd, 1H, J_{gem}=11.8, J_{vic}=5.9, CH_aH_bO); 5.13 (dd, 1H, J_{vic}=5.9, 4.6, CHO); 5.45 (s, 2H, CH_2Ph); 7.28–7.40 (m, 5H, H-*o*,*m*,*p*-Ph); 8.09 (s, 1H, H-8); 9.01 (s, 1H, H-2). ^{13}C NMR (151 MHz, $CDCl_3$): 15.22 (CH_3CH_2); 47.32 (CH_2Ph); 64.34 (CH_2O); 65.87 (CH_2CH_3); 79.19 (CHO); 127.98 (CH-*o*-Ph); 128.66 (CH-*p*-Ph); 129.12 (CH-*m*-Ph); 131.94 (C-5); 134.77 (C-*i*-Ph); 144.50 (CH-8); 151.57 (C-4); 152.55 (CH-2); 158.71 (C-6). ESI MS: *m*/*z* (%) (85) [M^+ Na], (50) [M^+ H]. HRMS calcd for $C_{16}H_{18}N_4O_2Na$ [M^+ Na] 321.1322, found 321.1322. IR ($CHCl_3$): 3585, 3381, 3092, 3069, 3035, 2987, 1591, 1499, 1456, 1404, 1389, 1331, 1078, 1063, 1052, 1040, 1031, 1003, 647.

*3.6.3. 9-Benzyl-6-(2-amino-1-hydroxyethyl)purine (**10a**)*

A mixture of 9-benzyl-6-(oxiran-2-yl)purine (**3a**) (252 mg, 1 mmol) and saturated ethanolic ammonia (25 ml) was stirred at ambient temperature for 5 days. After completion, the reaction mixture was concentrated under reduced pressure. The residue was purified by crystallization from chloroform/methanol/heptane to giving 90 mg (34%) of white crystals. Mp 179–182 °C. ^{1}H NMR (500 MHz, DMSO-d_6): 3.36 (m, 2H, CH_2N); 5.40 (dd, 1H, *J*=6.8, 5.7, CHO); 5.54 (s, 2H, CH_2Ph); 7.29 (m, 1H, H-*p*-Ph); 7.34 (m, 2H, H-*m*-Ph); 7.38 (m, 2H, H-*o*-Ph); 8.83 (s, 1H, H-8); 8.95 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 43.01 (CH_2N); 46.77 (CH_2Ph); 66.77 (CHO); 127.95 (CH-*o*-Ph); 128.21 (CH-*p*-Ph); 128.98 (CH-*m*-Ph); 131.04 (C-5); 136.62 (C-*i*-Ph); 146.78 (CH-8); 151.65 (C-4); 152.07 (CH-2); 157.90 (C-6). ESI MS: *m*/*z* (%) (8) [M^+ Na], (100) [M^+ H]. HRMS calcd for $C_{14}H_{16}N_5O$ [M^+ H] 270.1349, found 253.1351. IR (KBr): 3260, 3150, 3100, 3064, 3027, 1587, 1501, 1454, 1402, 1329, 1077, 1057, 1030, 727, 699, 461.

*3.6.4. 6-[(R,S)-2-Amino-1-hydroxyethyl]-9-(β-D-ribofuranosyl)purine (**10c**)*

A mixture of 6-(oxiran-2-yl)-9-(β-D-ribofuranosyl)purine (**3c**) (294 mg, 1 mmol) and saturated ethanolic ammonia (25 ml) was stirred at ambient temperature for 5 days. After completion, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography (reverse phase, water/methanol 0–100%) and lyophilized from water to give 130 mg (42%) of white foam, diastereoisomic mixture 1:1. ^{1}H NMR (600 MHz, DMSO-d_6): 3.37 (m, 4H, CH_2N); 3.57 (br ddd, 2H, J_{gem}=12.0, $J_{5'b,OH}$=5.2, $J_{5'b,4'}$=4.0, H-5′b); 3.69 (m, 2H, H-5′a); 3.986 and 3.988 (2×td, 2×1H, $J_{4',5'}$=4.0, $J_{4',3'}$=3.5, H-4′); 4.19 (br m, 2H, H-3′); 4.65 (br m, 2H, H-2′); 5.128 and 5.131 (2×br t, 2×1H, $J_{OH,5'}$=5.2, OH-5′); 5.31 (br s, 2H, OH-3′); 5.41 (dd, 2H, J_{vic}=7.3, 5.2, CHO); 5.56 (br s, 2H, OH-2′); 6.056 and 6.058 (2×d, 2×1H, $J_{1',2'}$=5.8, H-1′); 6.35 (br s, 2H, OH); 8.00 (br s, 4H, NH_2); 8.90 (s, 2H, H-8); 8.98 (s, 2H, H-2). ^{13}C NMR (151 MHz, DMSO-d_6): 42.90 (CH_2N); 61.48 (CH_2-5′); 66.57 (CHO); 70.55 (CH-3′); 73.91 and 73.95 (CH-2′); 86.03 (CH-4′); 87.76 and 87.81 (CH-1′); 131.65 and 131.67 (C-5); 145.29 and 145.34 (CH-8); 151.62 and 151.65 (C-4); 152.12 (CH-2); 158.13 and 158.14 (C-6). ESI MS: *m*/*z* (%) (100) [M^+ H]. HRMS calcd for $C_{12}H_{18}N_5O_5$ [M^+ H] 312.1303, found 312.1303. IR (KBr): 3293, 3116, 3065–2400, 1596, 1498, 1404, 1335, 1211, 1120, 1078, 1054, 811, 643. $[\alpha]_D$ −40.3 (*c* 0.22, MeOH).

*3.6.5. 6-Acetyl-9-benzylpurine (**7a**)*[22]

Methylmagnesium chloride (2 ml, 3 M in THF) was added dropwise to a mixture of 9-benzyl-6-(oxiran-2-yl)purine (**3a**) (252 mg, 1 mmol) in dry THF (5 ml) under an argon atmosphere at −30 °C. The resulting mixture was stirred for 1 day at rt. After completion, the reaction mixture was diluted with water (100 ml) and then washed with ethyl acetate (3×30 ml). The collected organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, methanol/chloroform 0–2%) and crystallized from chloroform/heptane to give **7a** as white crystals (190 mg, 71%). Mp 117–123 °C. ^{1}H NMR (500 MHz, DMSO-d_6): 2.80 (s, 3H, CH_3); 5.58 (s, 2H, CH_2Ph); 7.29 (m, 1H, H-*p*-Ph); 7.31 (m, 2H, H-*o*-Ph); 7.36 (m, 2H, H-*m*-Ph); 9.09 (s, 1H, H-8); 9.12 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 28.53 (CH_3); 47.08 (CH_2Ph); 127.97 (CH-*o*-Ph); 128.31 (CH-*p*-Ph); 129.03 (CH-*m*-Ph); 129.72 (C-5); 136.26 (C-*i*-Ph); 148.49 (C-6); 149.50 (CH-8);

151.94 (CH-2); 154.14 (C-4); 198.44 (CO). ESI MS: *m*/*z* (%) (100) [M^+ Na], (53) [M^+ H]. HRMS calcd for $C_{14}H_{13}N_4O$ [M^+ H] 253.1084, found 253.1086. IR ($CHCl_3$): 3112, 3092, 3069, 1704, 1584, 1496, 1456, 1401, 1358, 1326, 1077, 1029, 699, 646, 457.

3.7. Reaction of the epoxide with methylcuprate

THF (8 ml) was added to vacuum dried copper iodide (950 mg, 5 mmol) under an argon atmosphere. The mixture was stirred at −30 °C and a solution of methyl lithium (5 ml, 1.4 M in THF) was added dropwise. The mixture was stirred for 20 min at −30 °C and then a solution of 6-(oxiran-2-yl)purine (**3a** or **3b**, 1 mmol) in THF (7 ml) was added. The resulting mixture was stirred for 12 h at rt. After completion, the reaction mixture was diluted with water (150 ml) and then washed with ethyl acetate (3×50 ml). The collected organic layers were washed with 10% aqueous solution of EDTA (100 ml) and then with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure.

*3.7.1. 9-Benzyl-6-(1-hydroxypropyl)purine (**11a**)*

Purified by column chromatography (silica gel, methanol/chloroform 0–5%) and crystallized from chloroform/heptane to give 160 mg (60%) of white crystals. Mp 82–84 °C. ^{1}H NMR (500 MHz, $CDCl_3$): 1.02 (t, 3H, J_{vic}=7.4, C*H*$_3$CH$_2$); 1.92 (dq, 1H, J_{gem}=13.9, J_{vic}=7.4, CH$_3$CH$_a$*H*$_b$); 2.20 (dqd, 1H, J_{gem}=13.9, J_{vic}=7.4, 4.2 CH$_3$C*H*$_a$H$_b$); 4.50 (d, 1H, J_{vic}=6.5, OH); 5.27 (ddd, 1H, J_{vic}=7.4, 6.5, 4.2, CHO); 5.47 (s, 2H, CH$_2$Ph); 7.33 (m, 2H, H-*o*-Ph); 7.35–7.40 (m, 3H, H-*m*,*p*-Ph); 8.04 (s, 1H, H-8); 8.96 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 9.42 (*C*H$_3$CH$_2$); 30.53 (*C*H$_2$CH$_3$); 47.40 (CH$_2$Ph); 71.65 (CHO); 127.92 (CH-*o*-Ph); 128.71 (CH-*p*-Ph); 129.20 (CH-*m*-Ph); 130.27 (C-5); 134.90 (C-*i*-Ph); 143.90 (CH-8); 151.21 (C-4); 151.86 (CH-2); 162.03 (C-6). ESI MS: *m*/*z* (%) (100) [M^+ Na], (75) [M^+ H]. HRMS calcd for $C_{15}H_{17}N_4O$ [M^+ H] 269.1397, found 269.1401. Anal. Calcd for $C_{15}H_{16}N_4O$: C 67.15, H 6.01, N 20.88. Found: C 66.88, H 5.97, N 20.43. IR ($CHCl_3$): 3450, 3112, 3092, 3070, 3035, 1595, 1585, 1499, 1456, 1407, 1380, 1332, 1076, 1053, 1030, 699, 647, 455.

*3.7.2. 9-(2,3,5-Tri-O-tert-butyldimethylsilyl-β-D-ribofuranosyl)-6-[(R,S)-1-hydroxypropyl]purine (**11b**)*

Purified by column chromatography (silica gel, ethyl acetate/hexane 0–20%) to give 135 mg (21%) of light yellow foam, mixture of diastereoisomers 1:1. ^{1}H NMR (500 MHz, $CDCl_3$): −0.32, −0.31, −0.06, 0.113, 0.114, 0.116, 0.118, 0.137, 0.140, 0.143 and 0.147 (11×s, 36H, CH_3Si); 0.75, 0.76, 0.945, 0.946, 0.955 and 0.958 (6×s, 54H, $(CH_3)_3C$); 0.982 and 0.983 (2×t, 2×3H, J_{vic}=7.3, C*H*$_3$CH$_2$); 1.93 and 2.18 (2×m, 2×2H, C*H*$_2$CH$_3$); 3.81 (dd, 2H, J_{gem}=11.4, $J_{5'b,4'}$=2.6, H-5′b); 4.02 and 4.03 (2×dd, 2×1H, J_{gem}=11.4, $J_{5'a,4'}$=4.0, H-5′a); 4.16 (m, 2H, H-4′); 4.32 and 4.33 (2×dd, 2×1H, $J_{3',2'}$=4.4, $J_{3',4'}$=3.2, H-3′); 4.51 (d, 2H, J=6.6, OH); 4.69 and 4.70 (2×dd, 2×1H, $J_{2',1'}$=5.5, $J_{2',3'}$=4.4, H-2′); 5.28 (m, 2H, CHO); 6.13 and 6.15 (2×d, 2×1H, $J_{1',2'}$=5.5, H-1′); 8.40 and 8.41 (2×s, 2×1H, H-8); 8.909 and 8.911 (2×s, 2×1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): −5.39, −5.37, −5.28, −5.22, −4.70, −4.69, −4.67 and −4.44 (CH_3Si); 9.20 (*C*H$_3$CH$_2$); 17.80, 18.07, 18.51 and 18.52 ((CH$_3$)$_3$*C*); 25.57, 25.58, 25.82 and 26.06 ((*C*H$_3$)$_3$C); 30.46 and 30.49 (*C*H$_2$CH$_3$); 62.59 and 62.61 (CH$_2$-5′); 71.51 and 71.62 (CHO); 72.11 (CH-3′); 75.96 and 75.99 (CH-2′); 85.88 and 85.91 (CH-4′); 88.08 and 88.19 (CH-1′); 130.89 and 130.94 (C-5); 143.06 and 143.11 (CH-8); 150.94 and 150.96 (C-4); 151.58 (CH-2); 161.90 and 161.96 (C-6). ESI MS: *m*/*z* (%) (80) [M^+ Na], (100) [M^+ H]. HRMS calcd for $C_{31}H_{61}N_4O_5Si_3$ [M^+ H] 653.3944, found 653.3948. IR ($CHCl_3$): 3606, 3453, 3118, 3070, 2957, 1596, 1583, 1496, 1472, 1464, 1409, 1391, 1379, 1362, 1332, 1258, 1083, 1072, 1053, 939, 839, 683, 648.

*3.7.3. 9-Benzyl-6-[(4RS,3RS)-4-(ethoxycarbonyl)-5-oxotetrahydrofuran-3-yl]purine (**12a**)*

9-Benzyl-6-(oxiran-2-yl)purine (**3a**) (380 mg, 1.5 mmol) was added to a mixture of diethylmalonate (720 mg, 4.5 mmol) and NaH (216 mg, 4.5 mmol) in ethanol (20 ml). The resulting mixture was stirred for 2 h at rt. After completion, the reaction mixture was diluted with water (150 ml) and then washed with ethyl acetate (3×50 ml). The collected organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, ethyl acetate/hexane 0–50%) to give 120 mg (22%) of colourless oil, racemic compound of trans-relative configuration. ^{1}H NMR (500 MHz, $CDCl_3$): 1.30 (t, 3H, J_{vic}=7.2, C*H*$_3$CH$_2$O); 4.26 and 4.29 (2×dq, 2×1H, J_{gem}=10.8, J_{vic}=7.2, CH$_3$C*H*$_2$O); 4.47 (d, 1H, $J_{3,4}$=8.8, H-3-THF); 4.53 (dd, 1H, J_{gem}=8.5, $J_{5b,4}$=7.8, H-5b-THF); 4.95 (t, 1H, J_{gem}=$J_{5a,4}$=8.5, H-5a-THF); 5.01 (ddd, 1H, $J_{4,3}$=8.8, $J_{4,5}$=8.5, 7.8, H-4-THF); 5.45 (s, 2H, CH$_2$Ph); 7.31–7.40 (m, 5H, H-*o*,*m*,*p*-Ph); 8.06 (s, 1H, H-8); 8.96 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 14.01 (*C*H$_3$CH$_2$O); 42.37 (CH-4-THF); 47.47 (CH$_2$Ph); 50.11 (CH-3-THF); 62.37 (CH$_3$CH$_2$O); 70.21 (CH$_2$-5-THF); 127.96 (CH-*o*-Ph); 128.76 (CH-*p*-Ph); 129.20 (CH-*m*-Ph); 132.10 (C-5); 134.76 (C-*i*-Ph); 144.63 (CH-8); 151.50 (C-4); 152.72 (CH-2); 156.36 (C-6); 166.91 (COOEt); 171.21 (C-2-THF). ESI MS: *m*/*z* (%) (100) [M^+ Na], (65) [M^+ H]. HRMS calcd for $C_{19}H_{19}N_4O_4$ [M^+ H] 367.1401, found 367.1404. IR ($CHCl_3$): 3112, 3092, 3069, 3031, 2941, 2875, 1787, 1737, 1596, 1586, 1501, 1477, 1445, 1407, 1332, 1153, 1115, 1097, 1079, 699, 644, 619, 456.

3.8. Reaction of the epoxide with sodium methanethiolate

A mixture of 9-benzyl-6-(oxiran-2-yl)purine (**3a**) (252 mg, 1 mmol) and sodium methanethiolate (210 mg, 3 mmol) in THF (20 ml) and water (5 ml) was sonicated at rt for 3 h. After completion, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, methanol/chloroform 0–5%) to give two isomers, 20 mg (13%) of **14a** and 90 mg (60%) of **13a**. Both isomers were crystallized from chloroform/heptane to give the product.

*3.8.1. 9-Benzyl-6-[1-hydroxy-2-(methylsulfanyl)ethyl]purine (**14a**)*

White crystals, mp 99–103 °C. ^{1}H NMR (500 MHz, DMSO-d_6): 2.04 (s, 3H, CH$_3$S); 3.02 (dd, 1H, J_{gem}=13.2, J_{vic}=6.6, CH$_a$*H*$_b$S); 3.15 (dd, 1H, J_{gem}=13.2, J_{vic}=7.1, C*H*$_a$H$_b$S); 5.33 (ddd, 1H, J_{vic}=7.1, 6.6, 6.0, CHO); 5.52 (s, 2H, CH$_2$Ph); 5.76 (d, 1H, J_{vic}=6.0, OH); 7.29 (m, 1H, H-*p*-Ph); 7.35 (m, 2H, H-*m*-Ph); 7.37 (m, 2H, H-*o*-Ph); 8.73 (s, 1H, H-8); 8.92 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 15.62 (CH$_3$S); 38.68 (CH$_2$S); 46.72 (CH$_2$Ph); 68.96 (CHO); 127.92 (CH-*o*-Ph); 128.19 (CH-*p*-Ph); 129.01 (CH-*m*-Ph); 131.28 (C-5); 136.72 (C-*i*-Ph); 146.42 (CH-8); 151.34 (C-4); 152.09 (CH-2); 160.55 (C-6). ESI MS: *m*/*z* (%) (100) [M^+ Na], (35) [M^+ H]. HRMS calcd for $C_{15}H_{16}N_4OSNa$ [M^+ Na] 323.0937, found 323.0933. Anal. Calcd for $C_{15}H_{16}N_4OS$: C 59.98, H 5.37, N 18.65, S 10.67. Found: C 59.71, H 5.48, N 18.34, S 10.28. IR ($CHCl_3$): 3439, 3113, 3092, 3070, 3035, 2923, 1595, 1586, 1500, 1456, 1427, 1405, 1333, 1079, 1030, 1004, 699, 647, 455.

*3.8.2. 9-Benzyl-6-[2-hydroxy-1-(methylsulfanyl)ethyl]purine (**13a**)*

Yellowish crystals, mp 98–101 °C. ^{1}H NMR (500 MHz, $CDCl_3$): 2.17 (s, 3H, CH$_3$S); 4.30 (dd, 1H, J_{gem}=11.7, J_{vic}=5.7, CH$_a$*H*$_b$O); 4.33 (dd, 1H, J_{gem}=11.7, J_{vic}=4.4, C*H*$_a$H$_b$O); 4.41 (br s, 1H, OH); 4.51 (dd, 1H, J_{vic}=5.7, 4.4, CHS); 5.45 (s, 2H, CH$_2$Ph); 7.32–7.42 (m, 5H, H-*o*,*m*,*p*-Ph); 8.05 (s, 1H, H-8); 8.95 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 14.58 (CH$_3$S); 47.48 (CH$_2$Ph); 49.16 (CHS); 62.95 (CH$_2$S); 128.04 (CH-*o*-Ph); 128.77 (CH-*p*-Ph); 129.21 (CH-*m*-Ph); 131.11 (C-5); 134.72 (C-*i*-Ph); 144.04 (CH-8); 151.54 (C-4); 152.35 (CH-2); 160.55 (C-6). ESI MS: *m*/*z* (%) (100) [M^+ Na], (75) [M^+ H]. HRMS calcd for $C_{15}H_{16}N_4OSNa$ [M^+ Na] 323.0937, found 323.0933. IR

($CHCl_3$): 3610, 3396, 3112, 3092, 3069, 3035, 3001, 2924, 1587, 1498, 1456, 1405, 1329, 1079, 1050, 1030, 1003, 647.

*3.8.3. 9-(2,3,5-Tri-O-tert-butyldimethylsilyl-β-D-ribofuranosyl)-6-[(R,S)-2-hydroxy-1-(methylsulfanyl)ethyl]purine (**13b**)*

A mixture of **3b** (637 mg, 1 mmol) and sodium methanethiolate (210 mg, 3 mmol) in THF (20 ml) and water (5 ml) was sonicated at rt for 3 h. After completion, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, ethyl acetate/hexane 0–20%) to give 508 mg (74%) of white foam, mixture of diastereoisomers 1:1. ^{1}H NMR (500 MHz, $CDCl_3$): −0.23, −0.20, −0.025, −0.019, 0.110, 0.106, 0.113, 0.139, 0.141 and 0.146 (10×s, 36H, CH_3Si); 0.79, 0.80, 0.939, 0.940, 0.957 and 0.963 (6×s, 54H, $(CH_3)_3C$); 2.145 and 2.150 (2×s, 2×3H, CH_3S); 3.808 and 3.810 (2×dd, 2×1H, J_{gem}=11.5, $J_{5'b,4'}$=2.6, H-5′b); 4.03 and 4.04 (2×dd, 2×1H, J_{gem}=11.5, $J_{5'a,4'}$=3.8, H-5′a); 4.16 (td, 2H, $J_{4',3'}$=$J_{4',5'a}$=3.8, $J_{4',5'b}$=2.6, H-4′); 4.25–4.36 (m, 6H, H-3′ and CH_2O); 4.47–4.58 (m, 4H, CHS and OH); 4.63 and 4.64 (2×dd, 2×1H, $J_{2',1'}$=4.9, $J_{2',3'}$=4.3, H-2′); 6.13 (d, 2H, $J_{1',2'}$=4.9, H-1′); 8.48 and 8.50 (2×s, 2×1H, H-8); 8.90 (s, 2H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): −5.38, −5.36, −5.11, −5.04, −4.75, −4.74, −4.70, −4.38 and −4.37 (CH_3Si); 14.46 and 14.50 (CH_3S); 17.83, 17.84, 18.06, 18.52 and 18.53 ($(CH_3)_3C$); 25.61, 25.81 and 26.07 ($(CH_3)_3C$); 49.04 and 49.33 (CHS); 62.22 and 62.32 (CH_2-5′); 63.00 and 63.08 (CH_2O); 71.52 and 71.67 (CH-3′); 76.02 and 76.14 (CH-2′); 85.35 and 85.51 (CH-4′); 88.36 and 88.46 (CH-1′); 131.69 and 131.75 (C-5); 143.26 (CH-8); 151.20 and 151.22 (C-4); 152.11 and 152.13 (CH-2); 160.56 and 160.58 (C-6). ESI MS: *m*/*z* (%) (100) [M+Na], (95) [M+H]. HRMS calcd for $C_{31}H_{61}N_4O_5SSi_3$ [M^+ H] 685.3665, found 685.3674. IR ($CHCl_3$): 3607, 3307, 3120, 3065, 2956, 1592, 1580, 1497, 1472, 1463, 1405, 1391, 1362, 1332, 1311, 1258, 1082, 1072, 935, 839, 704, 680, 647.

3.9. Reaction of the epoxide with sodium benzenethiolate

A mixture of **3a** (127 mg, 0.5 mmol) and sodium benzenethiolate (200 mg, 1.5 mmol) in THF (10 ml) and water (2.5 ml) was sonicated at rt for 3 h. After completion, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, ethyl acetate/hexane 0–20%) to give two products **15a** (60 mg, 35%) and **16a** (115 mg, 63%).

*3.9.1. 9-Benzyl-6-[1-(phenylsulfanyl)vinyl]purine (**15a**)*

Crystallized from chloroform/heptane to give yellowish crystals. Mp 131–135 °C. ^{1}H NMR (500 MHz, $CDCl_3$): 5.474 (s, 2H, CH_2Ph); 5.475 and 7.27 (2×d, 2H, J_{gem}=0.8, =CH_2); 7.28–7.44 (m, 8H, H-*o*,*m*,*p*-Ph and H-*m*,*p*-SPh); 7.63 (m, 2H, H-*o*-SPh); 8.06 (s, 1H, H-8); 9.04 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 47.36 (CH_2Ph); 121.61 (=CH_2); 127.83 (CH-*o*-Ph); 128.66 (CH-*p*-Ph); 128.88 (CH-*p*-SPh); 129.18 (CH-*m*-Ph); 129.49 (CH-*m*-SPh); 130.14 (C-5); 131.48 (C-*i*-SPh); 134.99 (C-*i*-Ph); 135.46 (CH-*o*-SPh); 143.14 (=C); 144.49 (CH-8); 152.06 (CH-2); 152.11 (C-4); 153.26 (C-6). ESI MS: *m*/*z* (%) (25) [M+H]. HRMS calcd for $C_{20}H_{17}N_4S$ [M^+ H] 345.1168, found 345.1162. IR ($CHCl_3$): 3112, 3065, 3036, 1626, 1606, 1580, 1572, 1496, 1455, 1440, 1405, 1329, 1305, 1106, 1079, 1026, 1001, 972, 897, 883, 699, 694, 617, 476, 456, 425.

*3.9.2. 9-Benzyl-6-[1-hydroxy-2-(phenylsulfanyl)ethyl]purine (**16a**)*

Yellow oil, ^{1}H NMR (500 MHz, $CDCl_3$): 3.65 (dd, 1H, J_{gem}=13.8, J_{vic}=5.9, CH_aH_bS); 3.78 (dd, 1H, J_{gem}=13.8, J_{vic}=4.3, CH_aH_bS); 4.89 (br s, 1H, OH); 5.39 (s, 2H, CH_2Ph); 5.55 (bdd, 1H, J_{vic}=5.9, 4.3, CH-O);; 7.00 (m, 1H, H-*p*-SPh); 7.08 (m, 2H, H-*m*-SPh); 7.26 (m, 2H, H-*o*-SPh); 7.31 (m, 2H, H-*o*-Ph); 7.34–7.40 (m, 3H, H-*m*,*p*-Ph); 7.99 (s, 1H, H-8); 8.93 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 41.06 (CH_2S); 47.38 (CH_2Ph); 69.50 (CHO); 125.92 (CH-*p*-SPh); 128.02 (CH-*o*-Ph); 128.43 (CH-*m*-SPh); 128.74 (CH-*p*-Ph); 129.17 (CH-*m*-Ph); 129.68 (CH-*o*-SPh); 130.54 (C-5); 134.73 (C-*i*-Ph); 135.73 (C-*i*-SPh); 144.10 (CH-8); 151.18 (C-4); 151.73 (CH-2); 159.22 (C-6). ESI MS: *m*/*z* (%) (25) [M+Na], (100) [M+H]. HRMS calcd for $C_{20}H_{19}N_4OS$ [M^+ H] 363.1274, found 363.1273. IR ($CHCl_3$): 3438, 3112, 3068, 3035, 1594, 1587, 1499, 1456, 1405, 1333, 1288, 1180, 1156, 1079, 1026, 1000, 843, 698, 646, 617, 456.

3.10. Reaction of the epoxide with sodium benzoxide

A mixture of benzylalcohol (540 mg, 5 mmol) and NaH (72 mg, 1.5 mmol) in THF (4 ml) was stirred under an argon atmosphere. After 30 min, epoxide **3a** (127 mg, 0.5 mmol) in THF (2 ml) was added dropwise. The resulting mixture was stirred at ambient temperature for 8 h. After completion, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, ethyl acetate/hexane 0–30%) to give two products **17a** and **18a**.

*3.10.1. 9-Benzyl-6-[1-(benzyloxy)vinyl]purine (**17a**)*

Colourless oil, yield 26%. ^{1}H NMR (500 MHz, $CDCl_3$): 4.99 (dt, 1H, J_{gem}=2.7, ^5J=0.5, =CH_aH_b); 5.19 (s, 2H, OCH_2Ph); 5.45 (s, 2H, NCH_2Ph); 6.18 (d, 1H, J_{gem}=2.7, =CH_aH_b); 7.29 (m, 2H, H-*o*-NBn); 7.32–7.38 (m, 6H, H-*m*,*p*-NBn and H-*m*,*p*-OBn); 7.52 (m, 2H, H-*o*-OBn); 8.07 (s, 1H, H-8); 9.04 (s, 1H, H-2).^{13}C NMR (125.7 MHz, $CDCl_3$): 47.25 (NCH_2Ph); 70.05 (OCH_2Ph); 95.72 (=CH_2); 127.12 (CH-*o*-OBn); 127.69 (CH-*p*-OBn); 127.79 (CH-*o*-NBn); 128.47 (CH-*m*-OBn); 128.57 (CH-*p*-NBn); 129.11 (CH-*m*-NBn); 130.31 (C-5); 135.01 (C-*i*-NBn); 136.65 (C-*i*-OBn); 144.51 (CH-8); 151.81 (C-6); 152.27 (CH-2); 152.37 (C-4); 155.36 (=C). ESI MS: *m*/*z* (%) (10) [M^+ H]. HRMS calcd for $C_{21}H_{19}N_4O$ [M^+ H] 343.1553, found 343.1555. IR ($CHCl_3$): 3112, 3092, 3068, 3035, 3010, 2932, 2876, 1616, 1582, 1576, 1498, 1455, 1334, 1149, 1202, 1128, 1106, 645.

*3.10.2. 9-Benzyl-6-[1-(benzyloxy)-2-hydroxyethyl]purine (**18a**)*

Yellow oil, yield 14%. ^{1}H NMR (500 MHz, $CDCl_3$): 3.39 (br s, 1H, OH); 4.11 (br m, 2H, CH_2O); 4.60 and 4.75 (2×d, 2H, J_{gem}=11.8, OCH_2Ph); 5.19 (dd, 1H, J_{vic}=5.6, 4.5, CHO); 5.44 (s, 2H, NCH_2Ph); 7.22 (m, 1H, H-*p*-OBn); 7.25 (m, 2H, H-*m*-OBn); 7.32–7.41 (m, 7H, H-*o*-OBn and H-*o*,*m*,*p*-NBn); 8.06 (s, 1H, H-8); 9.01 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 47.38 (NCH_2Ph); 64.45 (CH_2O); 72.74 (OCH_2Ph); 78.83 (CHO); 127.77 (CH-*o*-NBn); 128.03 (CH-*p*-OBn); 128.16 (CH-*o*-OBn); 128.27 (CH-*m*-OBn); 128.73 (CH-*p*-NBn); 129.19 (CH-*m*-NBn); 132.04 (C-5); 134.81 (C-*i*-NBn); 137.58 (C-*i*-OBn); 144.50 (CH-8); 151.69 (C-4); 152.56 (CH-2); 158.42 (C-6). ESI MS: *m*/*z* (%) (100) [M^+ Na], (20) [M^+ H]. HRMS calcd for $C_{21}H_{21}N_4O_2$ [M^+ H] 361.1659, found 361.1662. IR ($CHCl_3$): 3592, 3347, 3112, 3034, 3009, 1589, 1499, 1455, 1405, 1331, 1210, 1077, 1029, 1002, 699, 646, 609, 459.

*3.10.3. 6-[(R,S)-Oxiran-2-yl]-9-(β-D-ribofuranosyl)-purine (**3c**)*

Epoxide **3b** (450 mg, 0.71 mmol) was dissolved in a solution of TBAF (674 mg, 2.17 mmol) in THF (3 ml). The mixture was stirred at ambient temperature for 2 h, evaporated and the residue was purified by column chromatography (silica gel methanol/chloroform 0–10%) to give 170 mg (82%) of light yellow foam (1:1 diastereoisomeric mixture). ^{1}H NMR (500 MHz, DMSO-d_6): 3.30 (dd, 2H, J_{gem}=6.4, $J_{3b,2}$=4.1, H-3b-ox); 3.56 and 3.57 (2×dd, 2×1H, J_{gem}=6.4, $J_{3a,2}$=2.6, H-3a-ox); 3.58 and 3.70 (2×br m, 2×2H, H-5′); 3.98 (td, 2H, $J_{4',5'}$=4.5, $J_{4',3'}$=3.4, H-4′); 4.19 (br dd, 2H, $J_{3',2'}$=5.0, $J_{3',4'}$=3.4, H-3′); 4.43 and 4.44 (2×dd, 2×1H, $J_{2,3}$=4.1, 2.6, H-2-ox); 4.61 (br dd, 2H, $J_{2',1'}$=5.5, $J_{2',3'}$=5.0, H-2′); 5.12 (br s, 2H, OH-5′); 5.28 (br s, 2H, OH-3′); 5.57 (br s, 2H, OH-2′); 6.05 (d, 2H, $J_{1',2'}$=5.5, H-1′); 8.88 (s, 2H, H-8); 8.90 (s, 2H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 48.50 (CH_2-3-ox); 48.78 and 48.84 (CH-2-ox); 61.39 (CH_2-5′); 70.44 (CH-3′); 73.96 and 73.98 (CH-2′); 85.90 (CH-4′); 87.87 and 87.89 (CH-1′); 133.08 and 133.13 (C-5); 145.60 and 145.62 (CH-8); 151.37

and 151.38 (C-4); 152.18 (CH-2); 155.20 and 155.21 (C-6). ESI MS: *m/z* (%) (50) [M^+ H]. HRMS calcd for $C_{12}H_{13}N_4O_5$ [M^+ H] 293.0881, found 293.0887. IR (KBr): 3291, 3116, 1599, 1585, 1500, 1414, 1333, 1210, 1119, 1083, 1055, 812, 644.$[\alpha]_D$ −44.5 (*c* 0.24, MeOH).

3.11. General method for the cleavage of the TBS groups

A TBS-protected nucleoside (1 mmol) was dissolved in a solution of $NEt_3 \cdot 3HF$ (1 ml, 6 mmol) in THF (3 ml). The mixture was stirred at ambient temperature for 1 day, evaporated and the residue was purified by column chromatography (silica gel methanol/chloroform 0–10% and then reverse phase methanol/water 0–100%) and lyophilized from water.

*3.11.1. 6-[(R,S)-1,2-Dihydroxyethyl]-9-(β-D-ribofuranosyl)-purine (**2c**)*

Yellowish foam, yield 93%, mixture of diastereoisomers 1:1. ^{1}H NMR (500 MHz, DMSO-d_6): 3.561, 3.562, 3.670 and 3.671 (4×dd, 4×1H, J_{gem}=11.9, $J_{5',4'}$=4.0, H-5′); 3.81 (dd, 2H, J_{gem}=10.8, J_{vic}=6.1, CH_aH_bO); 3.860 and 3.864 (2×dd, 2×1H, J_{gem}=10.8, J_{vic}=5.6, CH_aH_bO); 3.97 (td, 2H, $J_{4',5'}$=4.0, $J_{4',3'}$=3.8, H-4′); 4.18 (dd, 2H, $J_{3',2'}$=5.1, $J_{3',4'}$=3.8, H-3′); 4.587 and 4.594 (2×dd, 2×1H, $J_{2',1'}$=5.6, $J_{2',3'}$=5.1, H-2′); 4.90 (br s, 2H, OH-5′); 5.17 (dd, 2H, J_{vic}=6.1, 5.6, CHO); 5.22 (br s, 2H, OH-3′); 5.54 (br s, 2H, OH-2′); 6.03 (d, 2H, $J_{1',2'}$=5.6, H-1′); 6.26 (br s, 4H, OH); 8.81 (s, 2H, H-8); 8.90 (s, 2H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 61.55 (CH_2-5′); 64.91 and 64.93 (CH_2O); 70.46 (CH-3′); 71.24 (CHO); 74.04 and 74.12 (CH-2′); 85.99 (CH-4′); 87.94 (CH-1′); 131.99 and 132.01 (C-5); 144.63 and 144.65 (CH-8); 151.04 (C-4); 151.83 (CH-2); 160.88 and 160.89 (C-6). ESI MS: *m/z* (%) (80) [M^+ Na], (100) [M^+ H]. HRMS calcd for $C_{12}H_{16}N_4O_6Na$ [M^+ H] 335.0962, found 335.0953. Anal. Calcd for $C_{12}H_{16}N_4O_6 \cdot 1.5H_2O$: C 42.48, H 5.64, N 16.51. Found: C 42.46, H 5.29, N 16.15. IR (KBr): 3339, 1631, 1587, 1496, 1401, 1332, 1212, 1106, 1084, 1055, 808, 645. $[\alpha]_D$ −58.5 (*c* 0.08, MeOH).

*3.11.2. 6-[(R,S)-2-Hydroxy-1-(methylsulfanyl)ethyl]-9-(β-D-ribofuranosyl)purine (**13c**)*

White foam, yield 75%, diastereoisomeric mixture 1:1. ^{1}H NMR (500 MHz, DMSO-d_6): 2.08 and 2.09 (2×s, 2×3H, CH_3S); 3.57 (br dd, 2H, J_{gem}=12.1, $J_{5'b,4'}$=4.0, H-5′b); 3.69 (br dd, 2H, J_{gem}=12.1, $J_{5'a,4'}$=4.5, H-5′a); 3.97 (br dd, 2H, J_{gem}=10.3, J_{vic}=5.7, CH_aH_bO); 3.98 (ddd, 2H, $J_{4',5'}$=4.5, 4.0, $J_{4',3'}$=3.6, H-4′); 4.19 (dd, 2H, $J_{3',2'}$=4.9, $J_{3',4'}$=3.6, H-3′); 4.22 (dd, 2H, J_{gem}=10.3, J_{vic}=9.1, CH_aH_bO); 4.44 and 4.45 (2×ddd, 2×1H, J_{vic}=9.1, 5.7, CHS); 4.67 (br dd, 2H, $J_{2',1'}$=5.9, $J_{2',3'}$=4.9, H-2′); 5.03 (br s, 2H, OH); 5.12 (br s, 2H, OH-5′); 5.27 (br s, 2H, OH-3′); 5.57 (br s, 2H, OH-2′); 6.033 and 6.034 (2×d, 2×1H, $J_{1',2'}$=5.9, H-1′); 8.79 (s, 2H, H-8); 8.88 (s, 2H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 14.25 and 14.26 (CH_3S); 48.03 and 48.07 (CHS); 61.55 (CH_2-5′); 62.29 (CH_2O); 70.63 (CH-3′); 73.76 (CH-2′); 86.01 (CH-4′); 87.81 (CH-1′); 132.43 and 132.46 (C-5); 144.76 and 144.78 (CH-8); 151.05 (C-4); 152.02 (CH-2); 159.96 (C-6). ESI MS: *m/z* (%) (98) [M^+ Na], (28) [M^+ H]. HRMS calcd for $C_{13}H_{18}N_4O_5SNa$ [M^+ Na] 365.0890, found 365.0880. Anal. Calcd for $C_{13}H_{18}N_4O_5S \cdot 0.5H_2O$: C 44.44, H 5.45, N 15.94. Found: C 44.73, H 5.55, N 15.86. IR (KBr): 3413, 1594, 1499, 1475, 1468, 1433, 1400, 1333, 1212, 1123, 1080, 1057, 1038, 813, 646. $[\alpha]_D$ −31.9 (*c* 0.19, MeOH).

*3.11.3. 6-[(R,S)-1-Hydroxypropyl]-9-(β-D-ribofuranosyl)purine (**11c**)*

White foam, yield 75%, diastereoisomeric mixture 1:1. ^{1}H NMR (500 MHz, DMSO-d_6): 0.847 and 0.852 (2×t, 2×3H, J_{vic}=7.4, CH_3CH_2); 1.85–2.00 (m, 4H, CH_2CH_3); 3.570 and 3.574 (2×ddd, 2×1H, J_{gem}=12.0, $J_{5'b,OH}$=6.0, $J_{5'b,4'}$=4.2, H-5′b); 3.69 (ddd, 2H, J_{gem}=12.0, $J_{5'a,OH}$=5.2, $J_{5'a,4'}$=4.2, H-5′); 3.98 (td, 2H, $J_{4',5'}$=4.2, $J_{4',3'}$=3.5, H-4′); 4.19 (td, 2H, $J_{3',2'}$=$J_{3',OH}$=4.9, $J_{3',4'}$=3.5, H-3′); 4.646 and 4.651 (2×ddd, 2×1H, $J_{2',OH}$=6.0, $J_{2',1'}$=5.8, $J_{2',3'}$=4.9, H-2′); 5.07 (ddd, 2H, J_{vic}=7.0, 6.3, 5.9, CHO); 5.121 and 5.123 (2×dd, 2×1H, $J_{OH,5'}$=6.0, 5.2, OH-5′); 5.25 (d, 2H, $J_{OH,3'}$=4.9, OH-3′); 5.332 and 5.334 (2×d, 2×1H, J_{vic}=5.9, OH); 5.540 and 5.543 (2×d, 2×1H, $J_{OH,2'}$=6.0, OH-2′); 6.04 (d, 2H, $J_{1',2'}$=5.8, H-1′); 8.79 (s, 2H, H-8); 8.91 (s, 2H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 10.21 and 10.23 (CH_3CH_2); 29.21 (CH_2CH_3); 61.51 and 61.53 (CH_2-5′); 70.58 and 70.59 (CH-3′); 70.82 and 70.85 (CHO); 73.80 and 73.84 (CH-2′); 85.94 and 85.97 (CH-4′); 87.73 (CH-1′); 131.35 and 131.37 (C-5); 144.65 (CH-8); 151.13 (C-4); 151.96 (CH-2); 162.49 and 162.51 (C-6). ESI MS: *m/z* (%) (100) [M^+ Na]. HRMS calcd for $C_{13}H_{18}N_4O_5Na$ [M^+ Na] 333.1169, found 333.1166. IR (KBr): 3411, 1631, 1598, 1500, 1407, 1334, 1211, 1115, 1082, 1050, 811, 645. $[\alpha]_D$ −40.0 (*c* 0.11, MeOH).

3.12. Single crystal X-ray structure analysis

The diffraction data of single crystals of **3a** (colourless, 0.15×0.22×0.60 mm), **5a** (colourless, 0.04×0.15×0.76 mm) and **14a** (colourless, 0.14×0.19×0.69 mm) were collected on an Xcalibur X-ray diffractometer with Cu Kα (λ=1.54180 Å) at 150 K (**3a**, **5a**) and 298 K (**14a**). All three structures were solved by direct methods with SIR92[24] and refined by full-matrix, least-squares methods based on *F* with CRYSTALS.[25] The hydrogen atoms were located in a difference map, but those attached to carbon atoms were repositioned geometrically and then refined with riding constraints, while all other atoms were refined anisotropically in all cases.

*3.12.1. Crystal data—**3a***

$C_{14}H_{12}N_4O_1$, monoclinic, space group $P2_1/n$, a=9.8178(11) Å, b=4.7574(6) Å, c=25.341(3) Å, β=92.184(9)°, V=1182.7(2) Å^3, Z=4, M=252.28, 17,490 reflections measured, 2468 independent reflections. Final R=0.0451, wR=0.0143, GoF=1.20 for 1947 reflections with $I>2\sigma(I)$ and 173 parameters. CCDC 689513.

*3.12.2. Crystal data—**5a***

$C_{15}H_{18}N_4O_3$, monoclinic, space group $P2_1/c$, a=18.0503(9) Å, b=4.5943(3) Å, c=18.0503(9) Å, β=98.5414(2)°, V=1480.28(14) Å^3, Z=4, M=302.33, 9099 reflections measured, 3016 independent reflections. Final R=0.0644, wR=0.0748, GoF=1.15 for 2134 reflections with $I>2\sigma(I)$ and 200 parameters. CCDC 689512.

*3.12.3. Crystal data—**14a***

$C_{15}H_{16}N_4O_1S_1$, monoclinic, space group $P2_1/n$, a=10.1334(1) Å, b=8.0744(1) Å, c=18.9298(2) Å, β=98.5948(11)°, V=1531.46(3) Å^3, Z=4, M=300.39, 23,406 reflections measured, 3136 independent reflections. Final R=0.0464, wR=0.0757, GoF=1.10 for 1529 reflections with $I>2\sigma(I)$ and 190 parameters. CCDC 689514.

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