# SYNTHESIS OF NOVEL CARBOCYCLIC NUCLEOSIDE ANALOGUES DERIVED FROM 2-(HYDROXYMETHYL)BICYCLO[2.2.1]HEPTANE

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The key intermediates, [(1*R**,2*R**,4*R**,6*R**)-6- (**12a**) and [(1*R**,2*R**,4*R**,5*S**)-5-(hydroxymethyl)-bicyclo[2.2.1]heptan-2-yl]methyl benzoates (**12b**), were prepared from (1*R**,2*S**,4*R**)-bicyclo[2.2.1]hept-5-en-2-ylmethyl benzoate by hydroboration, oxidation with pyridinium dichromate and subsequent reduction of the thus obtained ketones. The Mitsunobu reaction of **12a** and **12b** with 6-chloropurine afforded 6-chloropurine derivatives, which were converted into others purine analogues. Thymine analogues were prepared from [(1*R**,2*R**,4*S**,6*S**)-6-(**25a**) and [(1*R**,2*S**,4*R**,5*S**)-5-aminobicyclo[2.2.1]heptan-2-yl]methanols (**25b**), which were prepared from alcohols **12a** and **12b** in several easy steps.

**Keywords**: Amines; Nucleosides; Carbocyclic nucleosides; Purines; Norbornanes; Bicyclic nucleosides; Antivirals; Mitsunobu reaction.

The search for new modified nucleosides as antivirals remains a promising field of research. The discovery of the antibiotic and antitumor activity of the natural carbocyclic nucleosides aristeromycin[1] and neplanocin A[2] stimulated the search for novel carbocyclic nucleoside analogues with biological activity; indeed, additional synthetic carbocyclic nucleosides with important therapeutic properties were discovered. U.S. Food and Drug Administration approved abacavir (Ziagen™; **1**)[3] for the treatment of HIV-1 infections and entecavir (Baraclude; **2**)[4] for the treatment of chronic hepatitis B virus (HBV) infections (Chart 1).

The recently described[5] bisphosphate of the 2-iodo-(6-methylamino)-purine analogue containing the oxabicyclo[2.2.1]heptane moiety displayed potent binding affinity to the human $P2Y_1$ receptor[6].

Some 6-chloro- and 2,6-dichloropurines bearing in the position 9 substituted bicyclic hydrocarbons show activity against the *Coxsackie* virus

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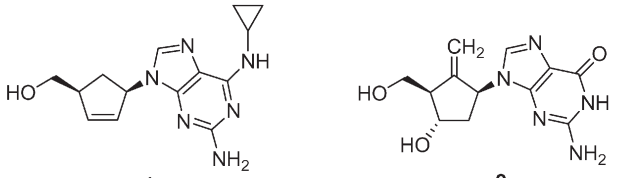



CHART 1

(CVB3)[7]. The virus is a cytolytic virus of the *Picornaviridae* family[8], an enterovirus. The enteroviruses (polioviruses, coxsackieviruses, echoviruses) are associated with several human and mammalian diseases. Enterovirus infections can be subclinical or can cause mild illness, but also aseptic meningitis, or poliomyelitis.

Recently, we reported the synthesis of novel racemic conformationally-locked carbocyclic purine nucleoside analogues derived from 4-oxatricyclo-[4.2.1.$0^{3,7}$]nonane-6-methanol[9], 4-oxatricyclo[4.2.1.$0^{3,7}$]nonane-9-methanol and their Pro-Tides[10], 5,5- and 6,6-bis(hydroxymethyl)bicyclo[2.2.1]-heptan-2-ols[11], 3-(hydroxymethyl)bicyclo[2.2.1]heptane-2,5-diol[12], and analogues[13] with a bicyclo[2.2.1]heptene or -heptane ring-substituted with nucleobase at position 7. Nucleoside analogues **3**–**8** (Chart 2) exhibit a weak activity in tests for anti-HIV-1 and anti-HIV-2 in human T-lymphocyte (CEM) cells.

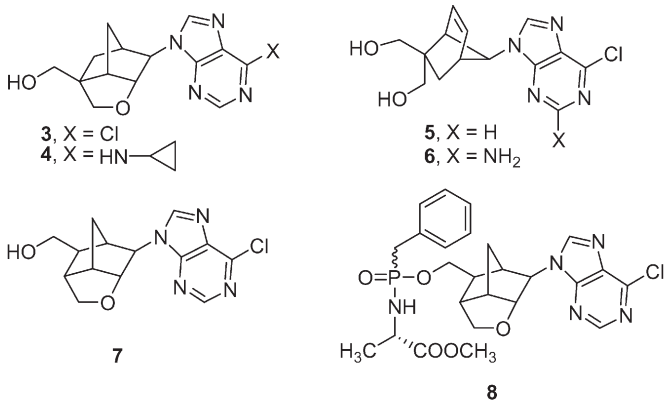



CHART 2

This study concerns synthesis of novel carbocyclic nucleosides derived from racemic 2- or 3-(hydroxymethyl)bicyclo[2.2.1]heptane. The key intermediates, 5- and 6-(hydroxymethyl)bicyclo[2.2.1]heptan-2-ols, were prepared from easily accessible bicyclo[2.2.1]hept-5-en-2-yl benzoate[14]. Chart 3 describes the target compounds.

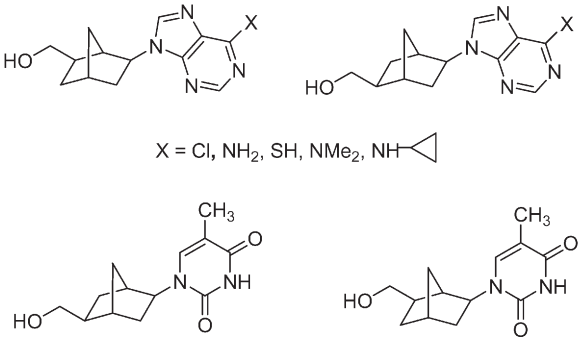
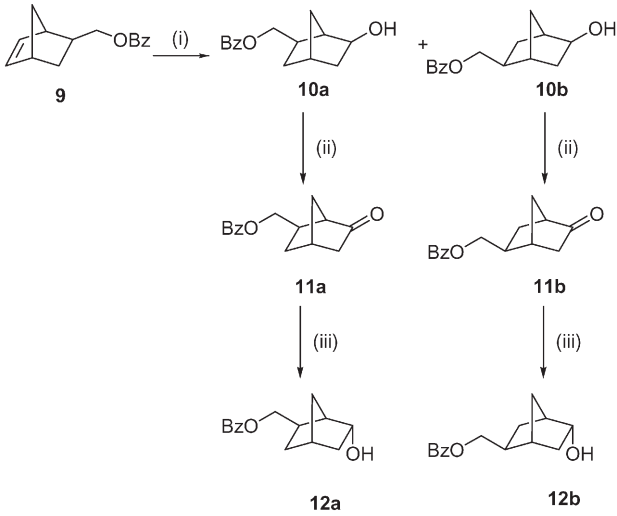



CHART 3

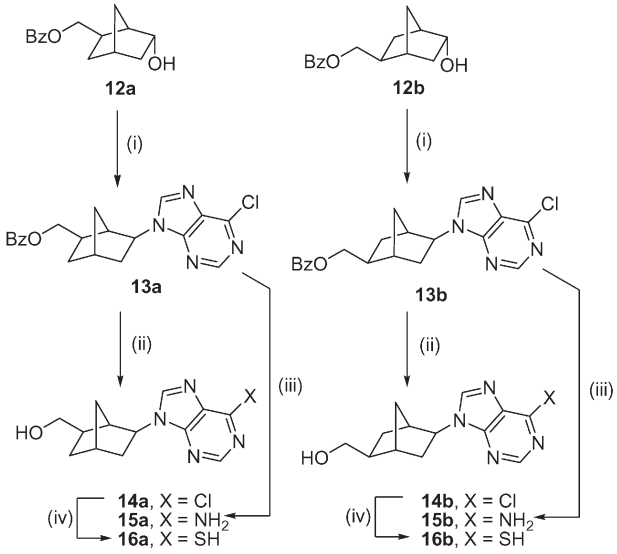
Hydroboration of the norbornene derivative **9** with the borane–tetrahydrofuran complex afforded a mixture of hydroxy derivatives **10a** and **10b** which were separated by chromatography on silica gel. The desired 2-*endo*-hydroxy derivatives **12a** and **12b** were prepared by oxidation of **10a** or **10b** with pyridinium dichromate and subsequent reduction of the thus obtained ketones **11a** or **11b** with sodium borohydride (Scheme 1).

6-Chloropurine analogues **13a** and **13b** were obtained by reaction of 6-chloropurine with hydroxy derivatives **12a** and **12b** under the Mitsunobu conditions[15]. Benzoyl derivatives **13a** and **13b** were deprotected by reductive debenzoylation with diisobutylaluminium hydride. The same reaction with lithium aluminium hydride led to low yields of deprotected compounds **14a** and **14b**, probably due to hydrolysis of the 6-chloro substituent during work-up of the reaction mixture. Chloropurine derivatives **13a** and **13b** were converted to adenine derivatives **15a** and **15b** by ammonolysis with liquid ammonia at 75 °C and subsequent methanolysis in 1 M methanolic sodium methoxide. Treatment of **13a** or **13b** with dimethylammonium dimethylcarbamate and the following debenzoylation with potassium carbonate led to 6-(dimethylamino)purine analogues **19a** and **19b**. Aminolysis of **13a** or **13b** with cyclopropylamine afforded 6-(cyclopropylamino)purine derivatives **18a** or **18b** and following debenz-




(i) 1. $BH_3$.THF, 0 °C, 2. $NaBO_3$, 47% of **10a**, 35% of **10b**; (ii) PDC/$CH_2Cl_2$, 78% of **11a**, 74% of **11b**; (iii) $NaBH_4$ / MeOH, 0 °C, 83% of **12a**, 84% of **12b**

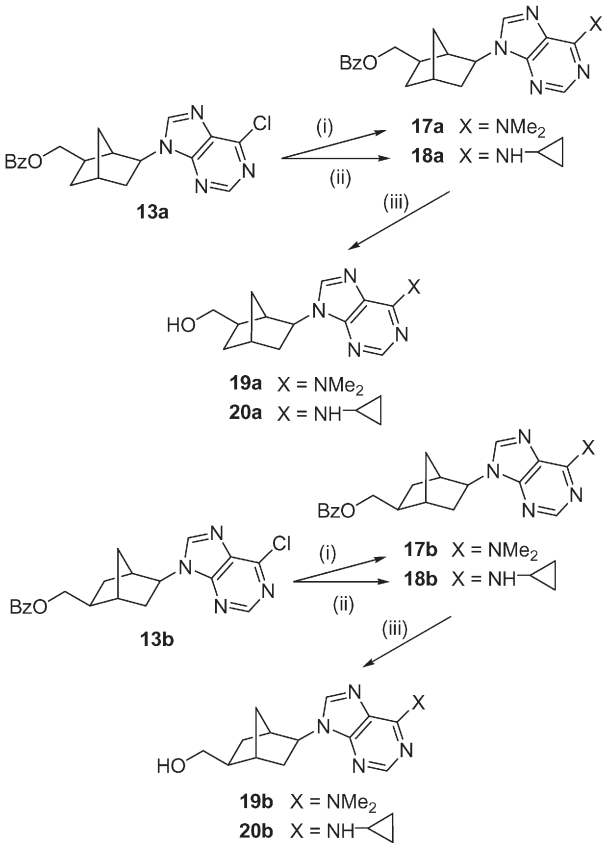
SCHEME 1




(i) 6-chloropurine, $PPh_3$, DIAD, THF, 42% of **13a**, 54% of **13b**; (ii) DIBAL-H/$CH_2Cl_2$, -78 °C, 79% of **14a**, 65% of **14b**; (iii) 1. $NH_3$, 70 °C, autoclave, 2. MeONa/MeOH, 53% of **15a**, 41% of **15b**; (iv) $CS(NH_2)_2$/EtOH, reflux, 76% of **16a**, 81% of **6b**

SCHEME 2

oylation using potassium carbonate gave **18a** or **18b**. The 6-thiopurine compounds **16a** and **16b** were prepared by reaction of **14a** and **14b** with thiourea in refluxing ethanol (Schemes 2 and 3).

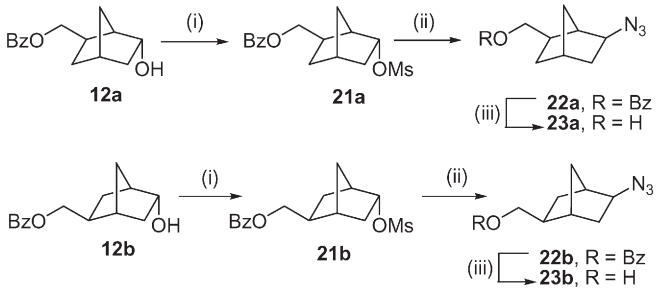



(i) $Me_2NH \cdot Me_2NCOOH$, 62% of **17a**, 73% of **17b**; (ii) cyclopropylamine, 67% of **18a**, 63% of **18b**; (iii) $K_2CO_3$, MeOH, 27% of **19a**, 70% of **19b,** 37% of **20a**, 68% of **20b**

SCHEME 3

Attempts to prepare thymine analogues from hydroxy derivatives **12a** and **12b** using the Mitsunobu reaction were unsuccessful. The reaction resulted in complex mixtures where the products were present only in traces. Thus the thymine analogues were prepared by an alternative procedure. Hydroxy derivatives **12a** and **12b** were mesylated and the thus obtained mesylates **21a** and **21b** were treated with sodium azide in dimethyl-

formamide to give azido derivatives **22a** and **22b**. Deprotection of benzoates **22a** and **22b** with methanolic sodium methoxide yielded azides **23a** and **23b** (Scheme 4). Hydrogenation of azides **22a**, **22b**, **23a**, and **23b** using palladium hydroxide on carbon as catalyst afforded amines **24a**, **24b**,

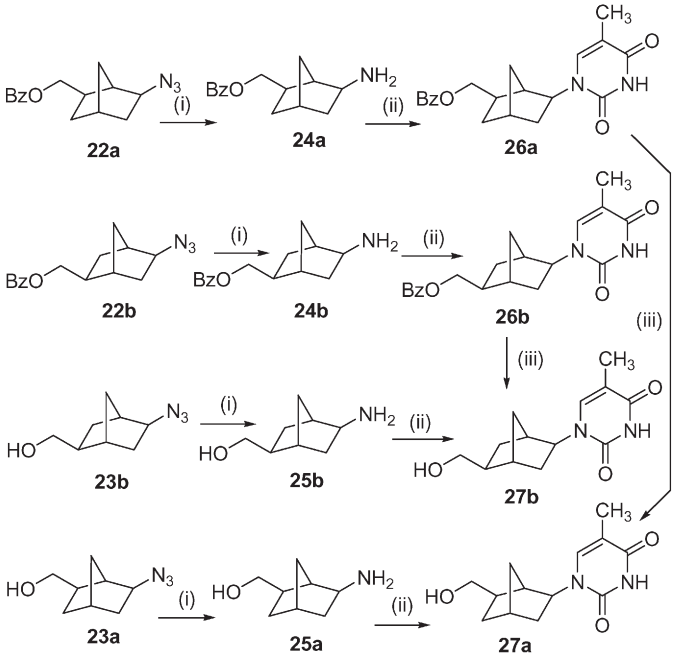



(i) MsCl/pyridine, 93% of **21a**, 84% of **21b**; (ii) $NaN_3$/ DMF, 80% of **22a**, 77% of **22b**; (iii) MeONa/MeOH, 79% of **23a**, 70% of **23b**

SCHEME 4

**25a**, and **25b**, respectively (Scheme 5). Thymine derivatives **26a** and **26b** were prepared by reacting amines **24a** and **24b** with ethyl *N*-[(2*E*)-3-ethoxy-2-methylprop-2-enoyl]carbamate in 1,4-dioxane at 100 °C and subsequent pyrimidine ring closure[16] catalyzed with dilute sulfuric acid[17]. The deprotected **27a** and **27b** were obtained by methanolysis with methanolic sodium methoxide. Compounds **27a** and **27b** were alternatively prepared from amines **25a** and **25b** using the same procedure as in preparation of benzoates **26a** and **26b**.

The structure of the prepared compounds was confirmed by NMR spectroscopy. Complete assignment of all $^1$H and $^{13}$C signals is based on combination of $^1$H, $^{13}$C APT, H,H-COSY, H,C-HSQC, H,C-HMBC and ROESY experiments. The position of the hydroxy group in compounds **12a** and **12b** was confirmed using HMBC spectra. The hydrogen adjacent to the hydroxy group exhibits a cross-peak with carbon 2 in compound **12a** and with carbon 3 in compound **12b**. Configuration on carbons 2, 3, 5, and 6 was confirmed using $^1$H NMR coupling constants – the *endo*-hydrogens do not interact with bridgehead hydrogens (their dihedral angle is close to 90°), while the *exo*-hydrogens interact with coupling constant $J$ = 4–5 Hz. Another significant interaction is between the *endo*-hydrogens in positions 2, 3, 5 and 6 and hydrogens in position 7 (W-interaction, $J$ = 1–2 Hz).




(i) $H_2$, $Pd(OH)_2$/C, 97% of **24a**, 93% of **24b**, 77% of **25a**, 88% of **25b**; (ii) 1. ethyl *N*-[(2*E*)-3-ethoxy-2-methylprop-2-enoyl]carbamate/1,4-dioxane, 100 °C, 2. 1M $H_2SO_4$, 100 °C, 41% of **26a**, 36% of **26b**, 48% of **27a**, 45% of **27b**; (iii) MeONa/MeOH, 87% of **27a**, 80% of **27b**

SCHEME 5

In conclusion, novel racemic conformationally-locked carbocyclic nucleoside analogues of thymine, 6-chloropurine, adenine, 6-(dimethylamino)purine, 6-(cyclopropylamino)purine, and 9*H*-purine-6-thiol derived from (1*R**,2*R**,4*R**,6*R**)-6- and (1*R**,2*R**,4*R**,5*S**)-5-(hydroxymethyl)bicyclo-[2.2.1]heptane-2-methanols. The target compounds were tested for the activity against *Coxsackie* virus (CVB3). The 6-chloropurine analogues **14a** and **14b** exhibits an activity (**14a**: $EC_{50}$ 15.45 μM and $CC_{50}$ 359 μM; **14b**: $EC_{50}$ 25.59 μM and $CC_{50}$ 359 μM)[18].

## EXPERIMENTAL

Melting points were determined on a Büchi B-540 apparatus and are uncorrected. NMR spectra (δ, ppm; *J*, Hz) were measured on a Bruker Avance II instrument (600.13 MHz for $^1$H and 150.92 MHz for $^{13}$C) in hexadeuterated dimethyl sulfoxide and referenced to the solvent

signal (δ 2.50 and 39.70, respectively) or in $CDCl_3$ to TMS internal standard. Mass spectra were measured on a ZAB-EQ (VG Analytical) spectrometer using the FAB ionization (ionization with Xe, accelerating voltage 8 kV, thioglycerol–glycerol 3:1 or bis(2-hydroxyethyl) disulfide matrix) and EI. Column chromatography was performed on Silica gel 60 (Fluka) and thin-layer chromatography (TLC) on Silufol Silica gel 60 F254 foils (Merck). Solvents were evaporated at 2 kPa and bath temperature 30–60 °C; the compounds were dried at 13 Pa and 50 °C.

[(1*R**,2*R**,4*R**,6*S**)-6-Hydroxybicyclo[2.2.1]heptan-2-yl]methyl Benzoate (**10a**) and
[(1*R**,2*S**,4*R**,5*S**)-5-Hydroxybicyclo[2.2.1]heptan-2-yl]methyl Benzoate (**10b**)

1 M solution of borane in THF (34 ml) was added dropwise under argon atmosphere to stirred alkene **9** (14.16 g, 62 mmol) cooled to 0 °C. The reaction mixture was stirred at 0 °C for 3 h. Excess of borane was decomposed by addition of water (1 ml) and then a solution of sodium perborate (28.7 g, 186 mmol) in water (100 ml) was added in one portion. The reaction mixture was stirred at room temperature overnight. The suspension was filtered through a Celite pad and the filter was washed with diethyl ether. The aqueous layer was separated and extracted with diethyl ether (3 × 150 ml). The combined organic layers were dried over anhydrous $Na_2SO_4$ and evaporated under reduced pressure. The resulting mixture of **10a** and **10b** was separated by chromatography on silica gel (1.3 kg) in toluene–ethyl acetate (4:1).

*[(1R*,2R*,4R*,6S*)-6-Hydroxybicyclo[2.2.1]heptan-2-yl]methyl benzoate* (**10a**): Yield 7.22 g (47%) as colorless oil. For $C_{15}H_{18}O_3$ (246.3) calculated: 73.15% C, 7.37% H; found: 73.06% C, 7.36% H. EI MS, *m/z* (%): 246 (6) [M], 124 (27), 105 (100), 80 (79). $^1$H NMR ($CDCl_3$): 1.08 dddd, 1 H, $J_{gem}$ = 12.4, *J*(3exo,2) = 5.4, *J*(3exo,4) = 4.0, *J*(3exo,5exo) = 3.0 (H-3exo); 1.28–1.37 m, 3 H (H-3endo, 5exo and 7a); 1.58 dm, 1 H, $J_{gem}$ = 10.4 (H-7b); 1.68 ddd, 1 H, $J_{gem}$ = 13.3, *J*(5endo,6) = 6.8, *J*(5endo,7a) = 2.4 (H-5endo); 1.77 m, 1 H (H-2); 2.03 bs, 1 H (OH); 2.19 m, 1 H (H-1); 2.30 m, 1 H (H-4); 3.83 dm, 1 H, *J*(6,5en) = 6.7 (H-6endo); 4.07 dd, 1 H, *J*($CH^aH$,2) = 9.1 and 4.14 dd, 1 H, *J*($CH^bH$,2) = 6.4 , $J_{gem}$ = 10.9 ($CH_2O$); 7.43 m, 2 H, 7.55 m and 8.04 m, 2 H (arom.). $^{13}$C NMR ($CDCl_3$): 31.58 (C-7); 32.54 (C-3); 35.17 (C-4); 36.38 (C-2); 41.47 (C-5); 46.55 (C-1); 67.37 ($CH_2O$); 74.38 (C-6); 128.26, 129.46, 130.15 and 132.86 (arom.); 166.60 (C=O).

*[(1R*,2S*,4R*,5S*)-5-Hydroxybicyclo[2.2.1]heptan-2-yl]methyl benzoate* (**10b**): Yield 5.32 g (35%) as colorless oil. For $C_{15}H_{18}O_3$ (246.3) calculated: 73.15% C, 7.37% H; found: 73.18% C, 7.47% H. EI MS, *m/z* (%): 246 (0.5) [M], 166 (50), 105 (100), 84 (84). $^1$H NMR ($CDCl_3$): 1.14 dt, 1 H, $J_{gem}$ = 13.1, *J*(3exo,2) = *J*(3exo,4) = 4.8 (H-3exo); 1.31–1.36 m, 2 H (H-3endo and 7a); 1.38 dm, 1 H, $J_{gem}$ = 13.2 (H-6exo); 1.58 dm, 1 H, $J_{gem}$ = 10.5 (H-7b); 1.74 ddd, 1 H, $J_{gem}$ = 13.2, *J*(6endo,5) = 6.9, *J*(6endo,7a) = 2.5 (H-6endo); 1.81 m, 1 H (H-2); 1.95 bs, 1 H (OH); 2.19 bd, 1 H, *J*(4,3exo) = 5.0 (H-4); 2.28 m, 1 H (H-1); 3.81 dm, 1 H, *J*(5,6endo) = 6.9 (H-5); 4.05 dd, 1 H, *J*($CH^aH$,2) = 9.2 and 4.10 dd, 1 H, *J*($CH^bH$,2) = 6.5, $J_{gem}$ = 10.9 ($CH_2O$); 7.44 m, 2 H, 7.56 m, 1 H and 8.04 m, 2 H (arom.). $^{13}$C NMR ($CDCl_3$): 28.72 (C-3); 31.15 (C-7); 37.61 (C-1); 39.78 (C-2); 42.18 (C-6); 44.19 (C-4); 67.84 ($CH_2O$); 74.17 (C-5); 128.28, 129.46, 130.22 and 132.85 (arom.); 166.62 (C=O).

[(1*R**,4*R**,6*R**)-6-Oxobicyclo[2.2.1]heptan-2-yl]methyl Benzoate (**11a**) and
[(1*R**,4*R**,5*S**)-5-Oxobicyclo[2.2.1]heptan-2-yl]methyl Benzoate (**11b**)

A solution of alcohol **10a** or **10b** (1.05 g, 4.3 mmol) in dichloromethane (10 ml) was added to a suspension of powdered molecular sieves (2.6 g) and pyridinium dichromate (2.5 g, 6.6 mmol) in dichloromethane (25 ml). The reaction mixure was stirred overnight. Solids were filtered off and washed with ethyl acetate. The filtrate was evaporated, diluted with ethyl acetate and filtered. Chromatography on silica gel (50 g) in toluene–ethyl acetate (24:1) afforded compounds **11a** or **11b** as colorless oils.

*[(1R*,4R*,6R*)-6-Oxobicyclo[2.2.1]heptan-2-yl]methyl benzoate* (**11a**): Yield 0.810 g (78%). For $C_{15}H_{16}O_3$ (244.3) calculated: 73.75% C, 6.60% H; found: 73.69% C, 6.82% H. EI MS, *m/z* (%): 244 (4) [M], 216 (41), 122 (48), 105 (100), 77 (60). $^1$H NMR ($CDCl_3$): 1.48 dddd, 1 H, $J_{gem}$ = 12.8, *J*(3exo,2) = 5.2, *J*(3exo,4) = 4.2, *J*(3exo,5exo) = 2.9 (H-3exo); 1.71 dm, 1 H, $J_{gem}$ = 10.9 (H-7a); 1.75 ddd, 1 H, $J_{gem}$ = 12.8, *J*(3endo,2) = 8.6, *J*(3endo,7a) = 2.3 (H-3endo); 1.80 dddd, 1 H, $J_{gem}$ = 10.9, *J*(7b,5endo) = 4.3, *J*(7b,4) = 2.0, *J*(7b,1) = 1.3 (H-7b); 1.91 dd, 1 H, $J_{gem}$ = 17.9, *J*(5endo,7b) = 4.3 (H-5endo); 2.11 dddd, 1 H, $J_{gem}$ = 17.9, *J*(5exo,4) = 4.7, *J*(5exo,3exo) = 2.9, *J*(5exo,1) = 1.0 (H-5exo); 2.32 m, 1 H (H-2); 2.67 m, 1 H (H-1); 2.73 m, 1 H (H-4); 4.17 dd, 1 H, *J*($CH^aH$,2) = 9.2 and 4.25 dd, 1 H, *J*($CH^bH$,2) = 6.1, $J_{gem}$ = 11.0 ($CH_2O$); 7.44 m, 2 H, 7.57 m, 1 H and 8.04 m, 2 H (arom.). $^{13}$C NMR ($CDCl_3$): 31.71 (C-3); 34.29 (C-7); 35.15 (C-4); 35.51 (C-2); 44.48 (C-5); 52.07 (C-1); 65.98 ($CH_2O$); 128.27, 129.47, 129.72 and 132.99 (arom.); 166.29 (C=O); 216.43 (C-6).

*[(1R*,4R*,5S*)-5-Oxobicyclo[2.2.1]heptan-2-yl]methyl benzoate* (**11b**): Yield 0.775 g (74%). For $C_{15}H_{16}O_3$ (244.3) calculated: 73.75% C, 6.60% H; found: 73.79% C, 6.85% H. EI MS, *m/z* (%): 244 (7) [M], 122 (16), 105 (100), 84 (79). $^1$H NMR ($CDCl_3$): 1.48 dt, 1 H, $J_{gem}$ = 13.3, *J*(3exo,2) = *J*(3exo,4) = 4.9 (H-3exo); 1.71 dm, 1 H, $J_{gem}$ = 10.8 (H-7a); 1.77 dddd, 1 H, $J_{gem}$ = 10.9, *J*(7b,6endo) = 4.3, *J*(7b,1) = 2.2, *J*(7b,4) = 1.2 (H-7b); 1.80 dddd, 1 H, $J_{gem}$ = 13.3, *J*(3endo,2) = 8.6, *J*(3endo,7a) = 2.3, *J*(3endo,4) = 0.7 (H-3endo); 1.90 dd, 1 H, $J_{gem}$ = 17.7, *J*(6en,7b) = 4.3 (H-6endo); 2.15 bdd, 1 H, $J_{gem}$ = 17.8, *J*(6exo,1) = 4.7 (H-6exo); 2.21 m, 1 H (H-2); 2.63 dm, 1 H, *J*(4,3exo) = 4.7 (H-4); 2.67 dm, 1 H, *J*(1,6exo) = 4.7 (H-1); 4.22 dd, 1 H, $J_{gem}$ = 10.9, *J*($CH_2$,2) = 8.7 ($OCH^aH$); 4.24 dd, 1 H, $J_{gem}$ = 10.9, *J*($CH_2$,2) = 6.6 ($OCH^bH$); 7.45 m, 2 H, 7.57 m and 8.05 m, 2 H (arom.). $^{13}$C NMR ($CDCl_3$): 27.99 (C-3); 34.43 (C-7); 37.40 (C-1); 39.21 (C-2); 45.11 (C-6); 49.56 (C-4); 67.10 ($CH_2O$); 128.27, 129.39, 129.85 and 132.94 (arom.); 166.32 (C=O); 216.89 (C-6).

[(1*R**,2*R**,4*R**,6*R**)-6-Hydroxybicyclo[2.2.1]heptan-2-yl]methyl Benzoate (**12a**) and
[(1*R**,2*R**,4*R**,5*S**)-5-Hydroxybicyclo[2.2.1]heptan-2-yl]methyl Benzoate (**12b**)

Sodium borohydride (455 mg, 12 mmol) was added stepwise to a solution of ketone **11a** or **11b** (4.9 g, 20 mmol) in methanol (150 ml) at 0 °C. Water (5 ml) was added to the mixture and, after 30 min, the solvent was evaporated and the residue solution in ethyl acetate (250 ml) was washed with brine (200 ml). The aqueous layer was separated and washed with ethyl acetate (2 × 150 ml), the combined organic layers were dried over anhydrous $Na_2SO_4$ and evaporated. The residue was co-distilled with methanol.

*[(1R*,2R*,4R*,6R*)-6-Hydroxybicyclo[2.2.1]heptan-2-yl]methyl benzoate* (**12a**): Yield 4.09 g (83%) as colorless oil. For $C_{15}H_{18}O_3$ (246.3) calculated: 73.15% C, 7.37% H; found: 73.00% C, 7.70% H. EI MS, *m/z* (%): 246 (8) [M], 124 (45), 105 (100), 80 (95). $^1$H NMR ($CDCl_3$): 0.89 dt, 1 H, $J_{gem}$ = 13.0, *J*(5endo,6) = *J*(5endo,7b) = 3.6 (H-5endo); 1.27 dddd, 1 H, $J_{gem}$ = 12.3, *J*(3exo,2) = 5.4, *J*(3exo,4) = 4.2, *J*(3exo,5exo) = 2.8 (H-3exo); 1.29 dm, 1 H, $J_{gem}$ =

10.5 (H-7a); 1.43 dm, 1 H, $J_{gem}$ = 10.5 (H-7b); 1.62 ddd, 1 H, $J_{gem}$ = 12.3, *J*(3endo,2) = 8.7, *J*(3endo,7a) = 2.4 (H-3endo); 1.98 dddd, 1 H, $J_{gem}$ = 13.0, *J*(5exo,6) = 10.2; *J*(5exo,4) = 4.9, *J*(5exo,3exo) = 2.9 (H-5exo); 2.13 bs, 1 H (OH); 2.22 m, 1 H (H-4); 2.26 m, 1 H (H-1); 2.72 m, 1 H (H-2); 4.16 m, 2 H ($CH_2O$); 4.27 dt, 1 H, *J*(6,5exo) = 10.2, *J*(6,5endo) = *J*(6,1) = 4.1 (H-6); 7.42 m, 2 H, 7.54 m, 1 H and 8.04 m, 2 H (arom.). $^{13}$C NMR ($CDCl_3$): 30.72 (C-2); 34.44 (C-3); 34.63 (C-7); 37.13 (C-4); 38.39 (C-5); 44.95 (C-1); 68.04 ($CH_2O$); 72.28 (C-6); 128.24, 129.47, 130.27 and 132.79 (arom.); 166.76 (C=O).

*[(1R*,2R*,4R*,5S*)-5-Hydroxybicyclo[2.2.1]heptan-2-yl]methyl benzoate* (**12b**): Yield 4.17 g (84%) as colorless oil. For $C_{15}H_{18}O_3$ (246.3) calculated: 73.15% C, 7.37% H; found: 72.88% C, 7.57% H. EI MS, *m/z* (%): 246 (1) [M], 123 (50), 105 (99), 84 (100). $^1$H NMR ($CDCl_3$): 0.94 dt, 1 H, $J_{gem}$ = 13.0, *J*(6endo,5) = *J*(6endo,1) = 3.4 (H-6endo); 1.05 ddt, 1 H, $J_{gem}$ = 12.8, *J*(3exo,2) = *J*(3exo,4) = 4.4, *J*(3exo,5) = 1.5 (H-3exo); 1.30 dm, 1 H, $J_{gem}$ = 10.5 (H-7a); 1.46 dm, 1 H, $J_{gem}$ = 10.6 (H-7b); 1.96 bs, 1 H (OH); 2.04 ddd, 1 H, $J_{gem}$ = 13.0, *J*(6exo,5) = 10.1, *J*(6exo,1) = 4.8 (H-6exo); 2.08 m, 1 H (H-2); 2.17 ddd, 1 H, $J_{gem}$ = 12.8, *J*(3endo,2) = 8.8, *J*(3endo,7a) = 2.4 (H-3endo); 2.19 m, 1 H (H-1); 2.31 m, 1 H (H-4); 4.10 d, 2 H, *J*($CH_2$,2) = 7.7 ($CH_2O$); 4.27 dddd, 1 H, *J*(5,6exo) = 10.0, *J*(5,6endo) = 3.2, *J*(5,4) = 4.6, *J*(5,3exo) = 1.5 (H-5); 7.44 m, 2 H, 7.55 m, 1 H and 8.05 m, 2 H (arom.). $^{13}$C NMR ($CDCl_3$): 24.64 (C-3); 34.44 (C-7); 39.10 (C-1); 39.78 (C-6); 40.88 (C-2); 42.26 (C-4); 67.96 ($CH_2O$); 72.05 (C-5); 128.27, 129.47, 130.28 and 132.81 (arom.); 166.71 (C=O).

[(1*R**,2*R**,4*S**,6*S**)-6-(6-Chloro-9*H*-purin-9-yl)bicyclo[2.2.1]heptan-2-yl]-methyl Benzoate (**13a**) and
[(1*R**,2*S**,4*R**,5*S**)-5-(6-Chloro-9*H*-purin-9-yl)bicyclo[2.2.1]heptan-2-yl]-methyl Benzoate (**13b**)

A solution of diisopropyl azodicarboxylate (2.85 ml, 14.7 mmol) in THF (20 ml) was slowly added to a solution of alcohol **12a** or **12b** (2.41 g, 9.8 mmol), triphenylphosphine (5.14 g, 19.3 mmol) and 6-chloropurine (2.27 g, 14.7 mmol) in THF (100 ml). The reaction mixture was stirred overnight and evaporated. Chromatography of the residue on silica gel (400 g) in toluene–ethyl acetate (1:1) followed by crystallization from ethanol afforded 6-chloropurine derivatives **13a** or **13b** as white crystals.

*[(1R*,2R*,4S*,6S*)-6-(6-Chloro-9H-purin-9-yl)bicyclo[2.2.1]heptan-2-yl]methyl benzoate* (**13a**): Yield 1.56 g (42%). M.p. 131–133 °C. For $C_{20}H_{19}ClN_4O_2$ (382.8) calculated: 62.74% C, 5.00% H, 9.26% Cl, 14.63% N; found: 62.77% C, 5.11% H, 9.20% Cl, 14.35% N. FAB MS, *m/z* (%): 383/385 (23/9) [M + H], 105 (100). $^1$H NMR ($CDCl_3$): 1.35 dddd, 1 H, $J_{gem}$ = 12.7, *J*(3exo,2) = 5.1, *J*(3exo,4) = 4.2, *J*(3exo,5exo) = 3.0 (H-3exo); 1.64–1.72 m, 3 H (H-7a, 7b, 3endo); 2.00 dm, 1 H, $J_{gem}$ = 13.7 (H-5exo); 2.21 ddd, 1 H, $J_{gem}$ = 13.8, *J*(5endo,6) = 8.5, *J*(5endo,7a) = 2,2 (H-5endo); 2.27 m, 1 H (H-2); 2.3 m, 1 H (H-4); 2.75 bs, 1 H (H-1); 4.16 dd, 1 H, *J*($CH^bH$,2) = 6.0 and 4.26 dd, 1 H, *J*($CH^aH$,2) = 9.4, $J_{gem}$ = 11.1 ($CH_2O$); 4.68 ddd, 1 H, *J*(6,5endo) = 8.5, *J*(6,5exo) = 4.0 (H-6); 7.44 m, 2 H, 7.57 m, 1 H and 8.04 m, 2 H (arom.); 8.24 s, 1 H (H-8′); 8.73 s, 1 H (H-2′). $^{13}$C NMR ($CDCl_3$): 32.43 (C-3); 33.45 (C-7); 36.02 (C-4); 38.20 (C-5); 39.31 (C-2); 44.36 (C-1); 58.53 (C-6); 66.63 ($CH_2O$); 128.38, 129.53, 129.91 and 133.10 (arom.); 131.95 (C-5′); 142.60 (C-8′); 150.94 (C-6′); 151.64 (C-2′); 151.82 (C-4′); 166.48 (C=O).

*[(1R*,2S*,4R*,5S*)-5-(6-Chloro-9H-purin-9-yl)bicyclo[2.2.1]heptan-2-yl]methyl benzoate* (**13b**): Yield 2.03 g (54%). M.p. 161–163 °C. For $C_{20}H_{19}ClN_4O_2$ (382.8) calculated: 62.74% C, 5.00% H, 9.26% Cl, 14.63% N; found: 62.71% C, 4.97% H, 9.28% Cl, 14.36% N. EI MS, *m/z*

(%): 382/384 (12/4) [M], 105 (52), 43 (100). $^1$H NMR ($CDCl_3$): 1.44 dt, 1 H, $J_{gem}$ = 13.2, *J*(3exo,2) = *J*(3exo,4) = 4.9 (H-3exo); 1.69 dm, 1 H, $J_{gem}$ = 11.0 (H-7a); 1.74 dm, 1 H, $J_{gem}$ = 11.1 (H-7b); 1.81 ddd, 1 H, $J_{gem}$ = 13.1, *J*(3endo,2) = 8.7, *J*(3endo,7b) = 2.4 (H-3endo); 2.00 dt, 1 H, $J_{gem}$ = 13.6, *J*(6exo,5) = *J*(6exo,1) = 4.6 (H-6exo); 2.15 m, 1 H (H-2); 2.25 ddd, 1 H, $J_{gem}$ = 13.6, *J*(6endo,5) = 8.5, *J*(6endo,7a) = 2.4 (H-6endo); 2.59 dm, 1 H, *J*(1,6exo) = 4.3 (H-1); 2.71 dm, 1 H, *J*(4,3exo) = 4.6 (H-4); 4.17 dd, 1 H, *J*($CH^bH$,2) = 9.0 and 4.22 dd, 1 H, *J*($OCH^aH$,2) = 6.3, $J_{gem}$ = 11.1 ($CH_2O$); 4.68 ddd, 1 H, *J*(5,6endo) = 8.5, *J*(5,6exo) = 4.6, *J*(5,7a) = 1.2 (H-5); 7.47 m, 2 H, 7.59 m, 1 H and 8.06 m, 2 H (arom.); 8.24 s, 1 H (H-8′); 8.76 s, 1 H (H-2′). $^{13}$C NMR ($CDCl_3$): 31.59 (C-3); 33.48 (C-7); 38.49 (C-1); 39.10 (C-6); 39.91 (C-2); 42.35 (C-4); 57.87 (C-5); 67.29 ($CH_2O$); 128.40, 129.53, 130.03 and 133.07 (arom.); 131.89 (C-5′); 142.60 (C-8′); 150.98 (C-6′); 151.69 (C-2′); 151.79 (C-4′); 166.54 (C=O).

[(1*R**,2*R**,4*S**,6*S**)-6-(6-Chloro-9*H*-purin-9-yl)bicyclo[2.2.1]heptan-2-yl]methanol (**14a**) and [(1*R**,2*S**,4*R**,5*S**)-5-(6-Chloro-9*H*-purin-9-yl)bicyclo[2.2.1]heptan-2-yl]methanol (**14b**)

*A*) A 1 M solution of lithium aluminium hydride in THF (1.3 ml) was added dropwise to a solution of compound **13a** or **13b** (0.491 g, 1.3 mmol) in THF (25 ml) at 0 °C under argon. The reaction mixture was stirred at 0 °C for 2 h and then water (5 ml) was added. The precipitate was filtered off with a Celite pad, washed with THF and the combined filtrates were evaporated. The residue was chromatographed on silica gel (50 g) in ethyl acetate–toluene–acetone–ethanol (17:4:3:1) and crystallized from diethyl ether (**14a**) or water (**14b**).

*[(1R*,2R*,4S*,6S*)-6-(6-Chloro-9H-purin-9-yl)bicyclo[2.2.1]heptan-2-yl]methanol* (**14a**): Yield 150 mg (42%). M.p. 124–125 °C. For $C_{13}H_{15}ClN_4O$ (278.7) calculated: 56.02% C, 5.42% H, 12.72% Cl, 20.10% N; found: 56.00% C, 5.38% H, 12.52% Cl, 19.71% N. FAB MS, *m/z* (%): 279/281 (78/33) [M + H], 154.9 (100). $^1$H NMR ($CDCl_3$): 1.18 dddd, 1 H, $J_{gem}$ = 12.6, *J*(3ex,2) = 5.1, *J*(3ex,4) = 4.1, *J*(3ex,5ex) = 2.9 (H-3exo); 1.54 ddd, 1 H, $J_{gem}$ = 12.6, *J*(3endo,2) = 8.6, *J*(3endo,7b) = 2.3 (H-3endo); 1.56 dm, 1 H, $J_{gem}$ = 11.0 (H-7b); 1.63 dm, 1 H, $J_{gem}$ = 11.0 (H-7a); 1.94 m, 1 H (H-5exo); 1.99 m, 1 H (H-2); 2.12 bt, 1 H, *J*($OH,CH_2$) = 5.1 (OH); 2.19 ddd, 1 H, $J_{gem}$ = 13.8, *J*(5endo,6) = 8.4, *J*(5endo,7a) = 2.3 (H-5endo); 2.56 tm, 1 H, *J*(4,3exo) = *J*(4,5exo) = 4.1 (H-4); 2.74 bs, 1 H (H-1); 3.49 ddd, 1 H, *J*($CH^bH$,2) = 9.2, *J*($CH^bH$,OH) = 5.2 and 3.57 ddd, 1 H, *J*($CH^aH$,2) = 6.0, *J*($CH^aH$,OH) = 4.1, $J_{gem}$ = 10.7 ($CH_2O$); 4.64 ddd, 1 H, *J*(6,5endo) = 8.4, *J*(6,5exo) = 4.0, *J*(6,7a) = 1.4 (H-6); 8.25 s, 1 H (H-8′); 8.75 s, 1 H (H-2′). $^{13}$C NMR ($CDCl_3$): 32.36 (C-3); 33.30 (C-7); 35.93 (C-4); 38.54 (C-5); 42.71 (C-2); 43.80 (C-1); 58.74 (C-6); 65.39 ($CH_2O$); 131.87 (C-5′); 142.77 (C-8′); 150.88 (C-6′); 151.63 (C-2′); 151.76 (C-4′).

*[(1R*,2S*,4R*,5S*)-5-(6-Chloro-9H-purin-9-yl)bicyclo[2.2.1]heptan-2-yl]methanol* (**14b**): Yield 167 mg (47%). M.p. 154–155 °C. For $C_{13}H_{15}ClN_4O$ (278.7) calculated: 56.02% C, 5.42% H, 12.72% Cl, 20.0% N; found: 55.89% C, 5.29% H, 12.44% Cl, 20.00% N. FAB MS, *m/z* (%): 279/281 (100/37) [M + H], 154.9 (89). $^1$H NMR ($CDCl_3$): 1.28 dt, 1 H, $J_{gem}$ = 13.0, *J*(3exo,2) = *J*(3exo,4) = 4.9 (H-3exo); 1.58 dm, 1 H, $J_{gem}$ = 10.9 (H-7a); 1.67 dm, 1 H, $J_{gem}$ = 10.9 (H-7b); 1.71 ddd, 1 H, $J_{gem}$ = 13.0, *J*(3endo,2) = 8.6, *J*(3endo,7b) = 2.4 (H-3endo); 1.82 t, 1 H, *J*($OH,CH_2$) = 4.8 (OH); 1.87 m, 1 H (H-2); 1,97 dt, 1 H, $J_{gem}$ = 13.5, *J*(6exo,5) = *J*(6exo,1) = 4.5 (H-6exo); 2.22 ddd, 1 H, $J_{gem}$ = 13.5, *J*(6endo,5) = 8.5, *J*(6endo,7a) = 2.5 (H-6endo); 2.56 dm, 1 H, *J*(1,6ex) = 4.3 (H-1); 2.65 dm, 1 H, *J*(4,3ex) = 4.5 (H-4); 3.50 m, 2 H ($CH_2O$); 4.65 ddd, 1 H, *J*(5,6endo) = 8.5, *J*(5,6exo) = 4.6, *J*(5,7a) = 1.4 (H-5); 8.25 s, 1 H (H-8′); 8.76 s, 1 H (H-2′). $^{13}$C NMR ($CDCl_3$): 31.45 (C-3); 33.36 (C-7); 38.04 (C-1); 39.33 (C-6); 42.29 (C-4);

43.35 (C-2); 57.98 (C-5); 65.99 ($CH_2O$); 131.84 (C-5′); 142.67 (C-8′); 150.92 (C-6′); 151.66 (C-2′); 151.78 (C-4′).

*B*) 1 M solution of DIBAL-H in dichloromethane (1.5 ml) was added dropwise to a solution of compound **13a** or **13b** (192 mg, 0.5 mmol) in dichloromethane (8 ml) at –78 °C under argon atmosphere. The reaction mixture was stirred for 45 min, excess of DIBAL-H was decomposed by addition of methanol (1 ml) and the solvent was evaporated. The residue was diluted with methanol and filtered with a Celite pad. Chromatography on silica gel (20 g) in ethyl acetate–toluene–acetone–ethanol (17:4:3:1) afforded 110 mg (79%) of **14a** and 91 mg (65%) of **14b**.

[(1*R**,2*R**,4*S**,6*S**)-6-(6-Amino-9*H*-purin-9-yl)bicyclo[2.2.1]heptan-2-yl]methanol (**15a**) and [(1*R**,2*S**,4*R**,5*S**)-5-(6-Amino-9*H*-purin-9-yl)bicyclo[2.2.1]heptan-2-yl]methanol (**15b**)

A solution of chloropurine derivative **14a** or **14b** (268 mg, 0.7 mmol) in liquid ammonia (20 ml) was heated in autoclave at 70 °C for 24 h. Ammonia was evaporated and potassium carbonate (140 mg, 1 mmol) was added to a solution of the residue in methanol (20 ml). The reaction mixture was stired overnight. Solids were filtered off and the filtrate was evaporated. The residue was crystallized from ethanol–diethyl ether.

*[(1R*,2R*,4S*,6S*)-6-(6-Amino-9H-purin-9-yl)bicyclo[2.2.1]heptan-2-yl]methanol* (**15a**): Yield 97 mg (53%). M.p. 204–205.5 °C. For $C_{13}H_{17}N_5O$ (259.3) calculated: 60.21% C, 6.61% H, 27.01% N; found: 59.89% C, 6.72% H, 26.79% N. FAB MS, *m/z* (%): 260 (100) [M + H], 135.9 (85). $^1$H NMR (DMSO-$d_6$): 1.00 dm, 1 H, $J_{gem}$ = 12.2 (H-3exo); 1.35 m, 2 H (H-7a, 3endo); 1.59 dm, 1 H, $J_{gem}$ = 10.4 (H-7b); 1.76 m, 1 H (H-2); 1.92 ddd, 1 H, $J_{gem}$ = 13.2, *J*(5endo,6) = 8.5, *J*(5endo,7a) = 1.9 (H-5endo); 2.00 dm, 1 H, $J_{gem}$ = 13.2 (H-5exo); 2.37 bt, 1 H, *J*(4,3exo) = *J*(4,5exo) = 4.2 (C-4); 2.39 bs, 1 H (H-1); 3.20 m, 2 H ($CH_2O$); 4.42 bdd, 1 H, *J*(6,5endo) = 8.3, *J*(6,5exo) = 4.1 (H-6); 4.63 bs, 1 H (OH); 7.19 bs, 2 H ($NH_2$); 8.13 s, 1 H (H-2′); 8.26 s, 1 H (H-8′). $^{13}$C NMR (DMSO-$d_6$): 32.51 (C-3); 32.60 (C-7); 35.64 (C-4); 37.51 (C-5); 42.64 (C-2); 44.42 (C-1); 57.53 (C-6); 64.40 ($CH_2O$); 119.27 (C-5′); 138.85 (C-8′); 149.76 (C-4′); 152.44 (C-2′); 156.17 (C-6′).

*[(1R*,2S*,4R*,5S*)-5-(6-Amino-9H-purin-9-yl)bicyclo[2.2.1]heptan-2-yl]methanol* (**15b**): Yield 75 mg (41%). M.p. 209–212 °C. For $C_{13}H_{17}N_5O$ (259.3) calculated: 60.21% C, 6.61% H, 27.01% N; found: 59.99% C, 6.62% H, 26.81% N. FAB MS, *m/z* (%): 260 (100) [M + H], 135.9 (64). $^1$H NMR (DMSO-$d_6$): 1.05 dt, 1 H, $J_{gem}$ = 12.7, *J*(3exo,2) = *J*(3exo,4) = 4.8 (H-3exo); 1.35 dm, 1 H, $J_{gem}$ = 10.4 (H-7a); 1.49 ddd, 1 H, $J_{gem}$ = 12.5, *J*(3endo,2) = 8.6, *J*(3endo,7b) = 2.4 (H-3endo); 1.60 dm, 1 H, $J_{gem}$ = 10.5 (H-7b); 1.65 m, 1 H (H-2); 1.92 ddd, 1 H, $J_{gem}$ = 13.0, *J*(6endo,5) = 8.5, *J*(6endo,7a) = 2.3 (H-6endo); 2.02 dt, 1 H, $J_{gem}$ = 13.1, *J*(6exo,5) = *J*(6exo,1) = 4.6 (H-6exo); 2.35 bd, 1 H, *J*(1,6exo) = 4.1 (H-1); 2.38 bd, 1 H, *J*(4,3exo) = 4.4 (H-4); 3.19 m, 2 H ($CH_2O$); 4.42 bdd, 1 H, *J*(5,6endo) = 8.5, *J*(5,6exo) = 4.7 (H-5); 4.57 t, 1 H, *J*(OH,$CH_2$) = 5.3 (OH); 7.19 bs, 2 H ($NH_2$); 8.13 s, 1 H (H-2′); 8.27 s, 1 H (H-8′). $^{13}$C NMR (DMSO-$d_6$): 31.34 (C-3); 32.52 (C-7); 37.83 (C-1); 38.07 (C-6); 42.50 (C-4); 43.49 (C-2); 56.92 (C-5); 64.81 ($CH_2O$); 119.30 (C-5′); 138.77 (C-8′); 149.76 (C-4′); 152.43 (C-2′); 156.17 (C-6′).

[(1*R**,2*R**,4*S**,6*S**)-6-(6-Sulfanyl-9*H*-purin-9-yl)bicyclo[2.2.1]heptan-2-yl]methanol (**16a**) and [(1*R**,2*S**,4*R**,5*S**)-5-(6-Sulfanyl-9*H*-purin-9-yl)bicyclo[2.2.1]heptan-2-yl]methanol (**16b**)

Thiourea (82 mg, 1.1 mmol) was added to a solution of chloropurine derivative **14a** or **14b** (245 mg, 0.9 mmol) in ethanol (10 ml) and the reaction mixture was refluxed for 2 h. The

precipitate was filtered off, washed with diethyl ether and purified by crystallization from ethanol–water (1:1).

*[(1R*,2R*,4S*,6S*)-6-(6-Sulfanyl-9H-purin-9-yl)bicyclo[2.2.1]heptan-2-yl]methanol* (**16a**): Yield 184 mg (76%). M.p. 289–292 °C. For $C_{13}H_{16}N_4OS$ (276.4) calculated: 56.50% C, 5.84% H, 20.27% N, 11.60 % S; found: 56.24% C, 5.72% H, 20.01% N, 11.57 % S. FAB MS, *m/z* (%): 277 (8) [M + H], 152.9 (100), 79 (57). $^1$H NMR (DMSO-$d_6$): 1.00 dm, 1 H, $J_{gem}$ = 12.3 (H-3exo); 1.36 m, 2 H (H-7a, 3endo); 1.54 dm, 1 H, $J_{gem}$ = 10.8 (H-7b); 1.75 m, 1 H (H-2); 1.95 m, 2 H (H-5exo, 5endo); 2.37 bt, 1 H, *J*(4,3exo) = *J*(4,5exo) = 3.9 (H-4); 2.42 bs, 1 H (H-1); 3.20 m, 2 H ($CH_2O$); 4.43 bdd, 1 H, *J*(6,5endo) = 8.2, *J*(6,5exo) = 4.3 (H-6); 4.62 bs, 1 H (OH); 8.20 d, 1 H, *J*(2′,SH) = 3.8 (H-2′); 8.43 s, 1 H (H-8′); 13.72 bs, 1 H (SH). $^{13}$C NMR (DMSO-$d_6$): 32.43 (C-3); 32.57 (C-7); 35.65 (C-4); 37.52 (C-5); 42.55 (C-2); 44.39 (C-1); 58.11 (C-6); 64.31 ($CH_2O$); 135.49 (C-5′); 141.06 (C-8′); 144.26 (C-4′); 144.87 (C-2′); 176.00 (C-6′).

*[(1R*,2S*,4R*,5S*)-5-(6-Sulfanyl-9H-purin-9-yl)bicyclo[2.2.1]heptan-2-yl]methanol* (**16b**): Yield 196 mg (81%). M.p. 330 °C (decomp.). For $C_{13}H_{16}N_4OS{\cdot}0.5H_2O$ (285.4) calculated: 54.72% C, 6.00% H, 19.63% N, 11.24% S; found: 55.01% C, 5.73% H, 19.66% N, 11.12% S. FAB MS, *m/z* (%): 277 (13) [M + H], 152.9 (100), 78.9 (64). $^1$H NMR (DMSO-$d_6$): 1.05 dt, 1 H, $J_{gem}$ = 12.7, *J*(3exo,2) = *J*(3exo,4) = 4.8 (H-3exo); 1.35 dm, 1 H, $J_{gem}$ = 10.6 (H-7a); 1.47 ddd, 1 H, $J_{gem}$ = 12.6, *J*(3endo,2) = 8.5, *J*(3endo,7b) = 2.4 (H-3endo); 1.55 dm, 1 H, $J_{gem}$ = 10.7 (H-7b); 1.64 m, 1 H (H-2); 1.93 ddd, 1 H, $J_{gem}$ = 13.1, *J*(6endo,5) = 8.4, *J*(6endo,7a) = 2.3 (H-6endo); 2.00 dt, 1 H, $J_{gem}$ = 13.2, *J*(6exo,5) = *J*(6exo,1) = 4.5 (H-6exo); 2.35 bd, 1 H, *J*(1,6exo) = 4.2 (H-1); 2.40 bd, 1 H, *J*(4,3exo) = 4.4 (H-4); 3.18 d, 2 H, *J*($CH_2$,2) = 7.5 ($CH_2O$); 4.42 dd, 1 H, *J*(5,6endo) = 8.4, *J*(5,6exo) = 4.7 (H-5); 4.59 bs, 1 H (OH); 8.19 d, 1 H, *J*(2′,SH) = 3.8 (H-2′); 8.44 s, 1 H (H-8′); 13.71 bs, 1 H (SH). $^{13}$C NMR (DMSO-$d_6$): 31.22 (C-3); 32.48 (C-7); 37.85 (C-1); 38.06 (C-6); 42.50 (C-4); 43.41 (C-2); 57.51 (C-5); 64.74 ($CH_2O$); 135.52 (C-5′); 141.00 (C-8′); 144.28 (C-4′); 144.85 (C-2′); 176.00 (C-6′).

{(1*R**,2*R**,4*S**,6*S**)-6-[6-(Dimethylamino)-9*H*-purin-9-yl]bicyclo[2.2.1]heptan-2-yl}-methyl Benzoate (**17a**) and
{(1*R**,2*S**,4*R**,5*S**)-5-[6-(Dimethylamino)-9*H*-purin-9-yl]bicyclo[2.2.1]heptan-2-yl}-methyl Benzoate (**17b**)

A solution of chloropurine derivative **13a** or **13b** (192 mg, 0.5 mmol) in dimethylammonium *N*,*N*-dimethylcarbamate (3 ml) was stirred at room temperature overnight. The reaction mixture was evaporated, the residue was dissolved in ethyl acetate and the solution was washed with water (2 × 15 ml), dried over anhydrous $Na_2SO_4$, evaporated and the residue was crystallized from diethyl ether.

*{(1R*,2R*,4S*,6S*)-6-[6-(Dimethylamino)-9H-purin-9-yl]bicyclo[2.2.1]heptan-2-yl}methyl benzoate* (**17a**): Yield 121 mg (62%). M.p. 118–119 °C. For $C_{22}H_{25}N_5O_2$ (403.5) calculated: 67.50% C, 6.44% H, 17.89% N; found: 67.21% C, 6.27% H, 17.61% N. FAB MS, *m/z* (%): 392 (100) [M + H], 164 (63), 104.9 (88). $^1$H NMR ($CDCl_3$): 1.31 dddd, 1 H, $J_{gem}$ = 12.7, *J*(3exo,2) = 5.1, *J*(3exo,4) = 4.2, *J*(3exo,5exo) = 2.9 (H-3exo); 1.61 m, 1 H (H-7a); 1.63 ddd, 1 H, $J_{gem}$ = 12.6, *J*(3endo,2) = 8.7, *J*(3endo,7b) = 2.2 (H-3endo); 1.67 dm, 1 H, $J_{gem}$ = 10.9 (H-7b); 1.89 dm, 1 H, $J_{gem}$ = 13.6 (H-5exo); 2.17 ddd, 1 H, $J_{gem}$ = 13.6, *J*(5endo,6) = 8.5, *J*(5endo,7a) = 2.3 (H-5endo); 2.26 m, 1 H (H-2); 2.57 tm, 1 H, *J*(4,3exo) = *J*(4,5exo) = 4.2 (H-4); 2.67 brs, 1 H (H-1); 3.5 brs, 6 H (N-$CH_3$); 4.14 dd, 1 H, *J*($CH^bH$,2) = 9.4 and 4.23 dd, 1 H, *J*($CH^aH$,2) = 6.2, $J_{gem}$ = 11.1 ($CH_2O$); 4.60 ddd, 1 H, *J*(6,5endo) = 8.4, *J*(6,5exo) = 4.1, *J*(6,7a) = 1.2 (H-6); 7.43 m, 2 H (H-3″); 7.55 m, 1 H, 7.83 s, 1 H and 8.04 m, 2 H (arom.); 8.36 s, 1 H (H-2′).

$^{13}$C NMR ($CDCl_3$): 32.54 (C-3); 33.40 (C-7); 36.04 (C-4); 38.54 (C-5); 39.31 (C-2); 44.27 (C-1); 57.29 (C-6); 68.86 ($CH_2O$); 120.48 (C-5′); 128.36, 129.57, 130.02, 133.00 and 135.33 (arom.); 150.57 (C-4′); 152.17 (C-2′); 154.89 (C-6′); 166.56 (C=O).

*{(1R*,2S*,4R*,5S*)-5-[6-(Dimethylamino)-9H-purin-9-yl]bicyclo[2.2.1]heptan-2-yl}methyl benzoate* (**17b**): Yield 144 mg (73%). M.p. 143–144 °C. For $C_{22}H_{25}N_5O_2$ (403.5) calculated: 67.50% C, 6.44% H, 17.89% N; found: 67.13% C, 6.47% H, 17.62% N. FAB MS, *m/z* (%): 392 (71) [M + H], 164 (90), 104.9 (100). $^1$H NMR ($CDCl_3$): 1.27 dt, 1 H, $J_{gem}$ = 13.1, *J*(3exo,2) = *J*(3exo,4) = 4.8 (H-3exo); 1.50 dm, 1 H, $J_{gem}$ = 10.7 (H-7a); 1.62–1.68 m, 2 H (H-3endo, 7b); 2.00–2.06 m, 3 H (H-2, 6endo, 6exo); 2.39 m, 1 H (H-1); 2.44 dm, 1 H, *J*(4,3exo) = 4.4 (H-4); 3.43 bs, 6 H (N-$CH_3$); 4.11 dd, 1 H, *J*($CH^bH$,2) = 8.6 and 4.13 dd, 1 H, *J*($CH^aH$,2) = 6.8, $J_{gem}$ = 11.0 ($CH_2O$); 4.49 m, 1 H (H-5); 7.54 m, 2 H, 7.67 m, 1 H and 7.98 m, 2 H (arom.); 8.21 s, 1 H (H-2′); 8.29 s, 1 H (H-8′). $^{13}$C NMR ($CDCl_3$): 31.16 (C-3); 32.70 (C-7); 37.87 (C-6); 39.28 (C-1); 39.75 (C-2); 42.42 (C-4); 56.58 (C-5); 67.56 ($CH_2O$); 119.83 (C-5′); 129.05, 129.36, 130.02 and 133.59 (arom.); 137.53 (C-8′); 150.53 (C-4′); 151.82 (C-2′); 154.46 (C-6′); 166.01 (C=O).

{(1*R**,2*R**,4*S**,6*S**)-6-[6-(Cyclopropylamino)-9*H*-purin-9-yl]bicyclo[2.2.1]heptan-2-yl}-methyl Benzoate (**18a**) and
{(1*R**,2*S**,4*R**,5*S**)-5-[6-(Cyclopropylamino)-9*H*-purin-9-yl]bicyclo[2.2.1]heptan-2-yl}-methyl Benzoate (**18b**)

A solution of chloropurine derivative **13a** or **13b** (192 mg, 0.5 mmol) in cyclopropylamine (3 ml) was left standing at room temperature overnight and then evaporated. A solution of the residue in ethyl acetate was washed with water (2 × 15 ml), dried over anhydrous $Na_2SO_4$ and evaporated. The residue was crystallized from diethyl ether.

*{(1R*,2R*,4S*,6S*)-6-[6-(Cyclopropylamino)-9H-purin-9-yl]bicyclo[2.2.1]heptan-2-yl}methyl benzoate* (**18a**): Yield 135 mg (67%). M.p. 128–129 °C. For $C_{23}H_{25}N_5O_2$ (403.5) calculated: 68.47% C, 6.25% H, 17.36% N; found: 68.57% C, 6.38% H, 17.20% N. FAB MS, *m/z* (%): 404 (70) [M + H], 176 (47), 104.9 (100). $^1$H NMR ($CDCl_3$): 0.65 m, 2 H, 0.93 m, 2 H and 3.04 brs, 1 H (cyclopropyl); 1.31 dddd, 1 H, $J_{gem}$ = 12.7, *J*(3exo,2) = 5.1, *J*(3exo,4) = 4.2, *J*(3exo,5exo) = 2.9 (H-3exo); 1.61 dm, 1 H, $J_{gem}$ = 11.0 (H-7a); 1.63 ddd, 1 H, $J_{gem}$ = 12.5, *J*(3endo,2) = 8.7, *J*(3endo,7b) = 2.2 (H-3endo); 1.69 dm, 1 H, $J_{gem}$ = 11.0 (H-7b); 1.94 dm, 1 H, $J_{gem}$ = 13.6 (H-5exo); 2.17 ddd, 1 H, $J_{gem}$ = 13.6, *J*(5endo,6) = 8.5, *J*(5endo,7a) = 2.3 (H-5endo); 2.25 m, 1 H (H-2); 2.58 tm, 1 H, *J*(4,3exo) = *J*(4,5exo) = 4.1 (H-4); 2.70 brs, 1 H (H-1); 4.15 dd, 1 H, *J*($CH^bH$,2) = 9.4 and 4.23 dd, 1 H, *J*($CH^aH$,2) = 6.1, $J_{gem}$ = 11.1 ($CH_2O$); 4.60 ddd, 1 H, *J*(6,5endo) = 8.4, *J*(6,5exo) = 4.1, *J*(6,7a) = 0.9 (H-6); 6.00 brs, 1 H (NH); 7.44 m, 2 H, 7.56 m, 1 H and 8.05 m, 2 H (arom.); 7.86 s, 1 H (H-8′); 8.50 s, 1 H (H-2′). $^{13}$C NMR ($CDCl_3$): 7.36, 2 C and 23.62 (cyclopropyl); 32.52 (C-3); 33.38 (C-7); 36.03 (C-4); 38.46 (C-5); 39.30 (C-2); 44.39 (C-1); 57.58 (C-6); 66.81 ($CH_2O$); 120.26 (C-5′); 128.36, 129.57, 130.00 and 133.02 (arom.); 137.17 (C-8′); 149.25 (C-4′); 152.98 (C-2′); 155.73 (C-6′); 166.55 (C=O).

*{(1R*,2S*,4R*,5S*)-5-[6-(Cyclopropylamino)-9H-purin-9-yl]bicyclo[2.2.1]heptan-2-yl}methyl benzoate* (**18b**): Yield 128 mg (63%). M.p. 125–126 °C. For $C_{23}H_{25}N_5O_2$ (403.5) calculated: 68.47% C, 6.25% H, 17.36% N; found: 68.54% C, 6.26% H, 17.39% N. FAB MS, *m/z* (%): 404 (86) [M + H], 176 (65), 104.9 (100). $^1$H NMR ($CDCl_3$): 0.66 m, 2 H, 0.93 m, 2 H and 3.04 brs, 1 H (cyclopropyl); 1.38 dt, 1 H (H-3exo); 1.63 dm, 1 H, $J_{gem}$ = 10.9 (H-7a); 1.72 dm, 1 H, $J_{gem}$ = 10.9 (H-7b); 1.79 ddd, 1 H, $J_{gem}$ = 13.0, *J*(3endo,2) = 8.7, *J*(3endo,7b) = 2.4 (H-3endo); 1.94 dt, 1 H, $J_{gem}$ = 13.5, *J*(6exo,5) = *J*(6exo,1) = 4.5 (H-6exo); 2.11 m, 1 H (H-2); 2.20 ddd,

1 H, $J_{gem}$ = 13.5, *J*(6endo,5) = 8.5, *J*(6endo,7a) = 2.4 (H-6endo); 2.54 dm, 1 H, *J*(1,6exo) = 4.3 (H-1); 2.65 dm, 1 H, *J*(4,3exo) = 4.4 (H-4); 4.15 dd, 1 H, *J*($CH^bH$,2) = 9.0 and 4.19 dd, 1 H, *J*($CH^aH$,2) = 6.4, $J_{gem}$ = 11.1 ($CH_2O$); 4.59 ddd, 1 H, *J*(5,6endo) = 8.5, *J*(5,6exo) = 4.6, *J*(5,7a) = 1.2 (H-5); 6.01 bd, 1 H, *J*(NH,CH) = 2.7 (NH); 7.46 m, 2 H, 7.58 m, 1 H and 8.06 m, 2 H (arom.); 7.87 s, 1 H (H-8′); 8.50 s, 1 H (H-2′). $^{13}$C NMR ($CDCl_3$): 7.37, 2 C and 23.66 (cyclopropyl); 31.63 (C-3); 33.38 (C-7); 38.48 (C-1); 39.26 (C-6); 39.98 (C-2); 42.40 (C-4); 56.89 (C-5); 67.43 ($CH_2O$); 120.19 (C-5′); 128.38, 129.54, 130.14 and 133.00 (arom.); 137.16 (C-8′); 149.19 (C-6′); 153.03 (C-2′); 155.77 (C-6′); 166.57 (C=O).

{(1*R**,2*R**,4*S**,6*S**)-6-[6-(Dimethylamino)-9*H*-purin-9-yl]bicyclo[2.2.1]heptan-2-yl}-methanol (**19a**) and
{(1*R**,2*S**,4*R**,5*S**)-5-[6-(Dimethylamino)-9*H*-purin-9-yl]bicyclo[2.2.1]heptan-2-yl}-methanol (**19b**)

*A*) Potassium carbonate (80 mg, 0.58 mmol) was added to a solution of **17a** or **17b** (135 mg, 0.47 mmol) in methanol (20 ml) and reaction mixture was stirred at room temperature overnight and then evaporated. Compound **19a** was purified by column chromatography on silica gel (20 g) in ethyl acetate–acetone–ethanol–water (36:6:5:3) and subsequent crystallization from diethyl ether and compound **19b** was crystallized from diethyl ether and then from water.

*{(1R*,2R*,4S*,6S*)-6-[6-(Dimethylamino)-9H-purin-9-yl]bicyclo[2.2.1]heptan-2-yl}methanol* (**19a**): Yield 33 mg (27%). M.p. 113–114 °C. For $C_{15}H_{21}N_5O$ (287.4) calculated: 62.69% C, 7.37% H, 24.37% N; found: 62.59% C, 7.25% H, 24.20% N. FAB MS, *m/z* (%): 288.1 (100) [M + H], 164 (45). $^1$H NMR (DMSO-$d_6$): 1.01 m, 1 H (H-3exo); 1.34 dm, 1 H, $J_{gem}$ = 10.7 (H-7a); 1.37 ddd, 1 H, $J_{gem}$ = 12.2, *J*(3endo,2) = 8.6, *J*(3endo,7b) = 2.2 (H-3endo); 1.56 dm, 1 H, $J_{gem}$ = 10.7 (H-7b); 1.76 m, 1 H (H-2); 1.94 m, 2 H (H-5exo, 5endo); 2.37 m, 1 H (H-4); 2.39 m, 1 H (H-1); 3.20 m, 2 H ($CH_2O$); 3.40 m, 6 H (N-$CH_3$); 4.44 m, 1 H (H-6); 8.21 s, 1 H (H-2′); 8.27 s, 1 H (H-8′). $^{13}$C NMR (DMSO-$d_6$): 32.49 (C-3); 32.59 (C-7); 35.64 (C-4); 37.62 (C-5); 42.65 (C-2); 44.26 (C-1); 57.41 (C-6); 64.37 ($CH_2O$); 119.77 (C-5′); 137.58 (C-8′); 150.52 (C-4′); 151.79 (C-2′); 155.43 (C-6′).

*{(1R*,2S*,4R*,5S*)-5-[6-(Dimethylamino)-9H-purin-9-yl]bicyclo[2.2.1]heptan-2-yl}methanol* (**19b**): Yield 84 mg (70%). M.p. 161.5–163 °C. For $C_{15}H_{21}N_5O{\cdot}0.5H_2O$ (296.4) calculated: 60.79% C, 7.48% H, 23.63% N; found: 60.82% C, 7.35% H, 23.24% N. FAB MS, *m/z* (%): 288.1 (100) [M + H], 164 (32). $^1$H NMR (DMSO-$d_6$): 1.05 dt, 1 H, $J_{gem}$ = 12.7, *J*(3exo,2) = *J*(3exo,4) = 5.0 (H-3exo); 1.34 dm, 1 H, $J_{gem}$ = 10.4 (H-7a); 1.49 ddd, 1 H, $J_{gem}$ = 12.5, *J*(3endo,2) = 8.5, *J*(3endo,7b) = 2.4 (H-3endo); 1.56 dm, 1 H, $J_{gem}$ = 10.5 (H-7b); 1.65 m, 1 H (H-2); 1.93 ddd, 1 H, $J_{gem}$ = 13.0, *J*(6endo,5) = 8.4, *J*(6endo,7a) = 2.3 (H-6endo); 1.98 dt, 1 H, $J_{gem}$ = 13.2, *J*(6exo,5) = *J*(6exo,1) = 4.8 (H-6exo); 2.35 m, 2 H (H-4, 1); 3.18 m, 2 H ($CH_2O$); 3.40 bs, 6 H (N-$CH_3$); 4.44 ddd, 1 H, *J*(5,6endo) = 8.4, *J*(5,6exo) = 4.9, *J*(5,7a) = 1.1 (H-5); 4.60 bs, 1 H (OH); 8.20 s, 1 H (H-2′); 8.28 s, 1 H (H-8′). $^{13}$C NMR (DMSO-$d_6$): 31.33 (C-3); 32.48 (C-7); 37.83 (C-1); 38.07 (C-6); 42.44 (C-4); 43.47 (C-2); 56.80 (C-5); 64.80 ($CH_2O$); 119.81 (C-5′); 137.53 (C-8′); 150.53 (C-4′); 151.79 (C-2′); 154.43 (C-6′).

*B*) A solution of chloropurine derivative **14a** (140 mg, 0.5 mmol) in dimethylammonium dimethylcarbamate (3 ml) was stirred at room temperature overnight and then evaporated. The residue was dissolved in ethyl acetate and the solution was washed with water (2 × 15 ml), dried over anhydrous $Na_2SO_4$ and evaporated. Chromatography on silica gel (20 g) in ethyl

acetate–acetone–ethanol–water (36:6:5:3) and subsequent crystallization from diethyl ether furnished 122 mg (85%) of product **19a**.

{(1*R**,2*R**,4*S**,6*S**)-6-[6-(Cyclopropylamino)-9*H*-purin-9-yl]bicyclo[2.2.1]heptan-2-yl}-methanol (**20a**) and
{(1*R**,2*S**,4*R**,5*S**)-5-[6-(Cyclopropylamino)-9*H*-purin-9-yl]bicyclo[2.2.1]heptan-2-yl}-methanol (**20b**)

*A*) Potassium carbonate (90 mg, 0.65 mmol) was added to a solution of **18a** or **18b** (166 mg, 0.41 mmol) in methanol (20 ml) and the reaction mixture was stirred at room temperature overnight and then evaporated. Compound **20a** was purified by chromatography on silica gel (20 g) in ethyl acetate–acetone–ethanol–water (36:6:5:3) and subsequent crystallization from diethyl ether and compound **20b** was crystallized from diethyl ether and then from water.

*{(1R*,2R*,4S*,6S*)-6-[6-(Cyclopropylamino)-9H-purin-9-yl]bicyclo[2.2.1]heptan-2-yl}methanol* (**20a**): Yield 45 mg (37%). M.p. 101.5–103 °C. For $C_{16}H_{21}N_5O$ (299.4) calculated: 64.19% C, 7.07% H, 23.39% N; found: 63.99% C, 7.38% H, 23.01% N. FAB MS, *m/z* (%): 300.1 (86) [M + H], 176 (100), 79 (50). $^1$H NMR (DMSO-$d_6$): 0.60 m, 2 H, 0.71 m, 2 H and 3.04 brs, 1 H (cyclopropyl); 1.01 m, 1 H (H-3exo); 1.36 m, 2 H (H-3endo, 7a); 1.59 dm, 1 H, $J_{gem}$ = 10.5 (H-7b); 1.77 m, 1 H (H-2); 1.93 ddd, 1 H, $J_{gem}$ = 13.2, *J*(5endo,6) = 8.4, *J*(5endo,7a) = 1.8 (H-5endo); 2.00 m, 1 H (H-5exo); 2.37 m, 1 H (H-4); 2.40 bs, 1 H (H-1); 3.20 m, 2 H ($CH_2O$); 4.43 bdd, 1 H, *J*(6,5endo) = 8.3, *J*(6,5exo) = 4.3 (H-6); 4.60 t, 1 H, *J*(OH,$CH_2$) = 5.4, 7.83 bs, 1 H (NH); 8.23 bs, 1 H (H-2′); 8.26 s, 1 H (H-8′). $^{13}$C NMR (DMSO-$d_6$): 6.62 ($CH_2$-cyclopropyl); 32.52 (C-3); 32.60 (C-7); 35.65 (C-4); 37.53 (C-5); 42.65 (C-2); 44.41 (C-1); 57.52 (C-6); 64.41 ($CH_2O$); 119.65 (C-5′); 138.70 (C-8′); 152.36 (C-2′); 155.72 (C-6′).

*{(1R*,2S*,4R*,5S*)-5-[6-(Cyclopropylamino)-9H-purin-9-yl]bicyclo[2.2.1]heptan-2-yl}methanol* (**20b**): Yield 84 mg (68%). M.p. 151–152 °C. For $C_{16}H_{21}N_5O{\cdot}0.5H_2O$ (308.4) calculated: 62.38% C, 7.25% H, 11.19% N; found: 62.35% C, 7.37% H, 11.01% N. FAB MS, *m/z* (%): 300 (69) [M + H], 176 (100), 79 (43). $^1$H NMR (DMSO-$d_6$): 0.60 m, 2 H, 0.70 m, 2 H and 2.99 brs, 1 H (cyclopropyl); 1.05 dt, 1 H, $J_{gem}$ = 12.6, *J*(3exo,2) = *J*(3exo,4) = 4.8 (H-3exo); 1.34 dm, 1 H, $J_{gem}$ = 10.5 (H-7a); 1.49 ddd, 1 H, $J_{gem}$ = 12.5, *J*(3endo,2) = 8.6, *J*(3endo,7b) = 2.4 (H-3endo); 1.59 dm, 1 H, $J_{gem}$ = 10.5 (H-7b); 1.65 m, 1 H (H-2); 1.92 ddd, 1 H, $J_{gem}$ = 13.0, *J*(6endo,5) = 8.5, *J*(6endo,7a) = 2.3 (H-6endo); 2.01 dt, 1 H, $J_{gem}$ = 13.1, *J*(6exo,5) = *J*(6exo,1) = 4.6 (H-6exo); 2.35 bd, 1 H, *J*(1,6exo) = 4.4 (H-1); 2.37 bd, 1 H, *J*(4,3exo) = 4.5 (H-4); 3.19 m, 2 H ($CH_2O$); 4.43 ddd, 1 H, *J*(5,6endo) = 8.5, *J*(5,6exo) = 4.8, *J*(5,7a) = 0.9 (H-5); 4.60 bs, 1 H (OH); 7.86 bs, 1 H (NH); 8.23 bs, 1 H (H-2′); 8.27 s, 1 H (H-8′). $^{13}$C NMR (DMSO-$d_6$): 6.57 ($CH_2$-cyclopropyl); 31.33 (C-3); 32.51 (C-7); 37.83 (C-1); 38.08 (C-6); 42.50 (C-4); 43.49 (C-2); 56.90 (C-5); 64.81 ($CH_2O$); 119.67 (C-5′); 138.60 (C-8′); 149.12 (C-4′); 152.33 (C-2′); 155.72 (C-6′).

B) A solution of chloropurine derivative **14a** (140 mg, 0.5 mmol) in cyclopropylamine (3 ml) was left overnight at room temperature. The reaction mixture was evaporated, the residue was dissolved in ethyl acetate and washed with water (2 × 15 ml), dried over anhydrous $Na_2SO_4$ and evaporated. Chromatography on silica gel (20 g) in ethyl acetate–acetone–ethanol–water (36:6:5:3) and the following crystallization from diethyl ether furnished 129 mg (86%) of product **20a** as white crystals.

[(1*R**,2*R**,4*R**,6*R**)-6-(Mesyloxy)bicyclo[2.2.1]heptan-2-yl]methyl Benzoate (**21a**) and [(1*R**,2*S**,4*R**,5*R**)-5-(Mesyloxy)bicyclo[2.2.1]heptan-2-yl]methyl Benzoate (**21b**)

Mesyl chloride (2.1 ml, 27 mmol) was added to a solution of **12a** or **12b** (3.33 g, 13.5 mmol) in pyridine (120 ml) at 0 °C. The reaction mixture was stirred for 1 h and excess of mesyl chloride was decomposed by addition of water (10 ml). The solvents were evaporated, the residue was dissolved in ethyl acetate (150 ml) and the solution was washed with 5% hydrochloric acid (100 ml), water (50 ml), 10% aqueous $NaHCO_3$ (100 ml), and water (50 ml). The organic layer was dried over anhydrous $Na_2SO_4$ and evaporated. The analytical sample was obtained by chromatography on silica gel in toluene–ethyl acetate (4:1).

*[(1R*,2R*,4R*,6R*)-6-(Mesyloxy)bicyclo[2.2.1]heptan-2-yl]methyl benzoate* (**21a**): Yield 4.09 g (93%) as colorless oil. For $C_{16}H_{20}O_5S$ (324.4) calculated: 59.24% C, 6.21% H, 9.88% S; found: 59.11% C, 6.03% H, 9.88% S. EI MS, *m/z* (%): 324 (0.04) [M], 202 (14), 105 (89), 84 (100). $^1$H NMR ($CDCl_3$): 1.28 dt, 1 H, $J_{gem}$ = 13.7, *J*(5endo,6) = *J*(5endo,7a) = 3.7 (H-5endo); 1.32 dddd, 1 H, $J_{gem}$ = 12.5, *J*(3exo,2) = 5.4, *J*(3exo,4) = 4.2, *J*(3exo,5exo) = 2.9 (H-3exo); 1.36 dm, 1 H, $J_{gem}$ = 11.0 (H-7b); 1.56 dm, 1 H, $J_{gem}$ = 11.0 (H-7a); 1.68 ddd, 1 H, $J_{gem}$ = 12.5, *J*(3endo,2) = 8.8, *J*(3endo,7b) = 2.4 (H-3endo); 2.14 dddd, 1 H, $J_{gem}$ = 13.7, *J*(5exo,6) = 10.5, *J*(5exo,4) = 4.8, *J*(5exo,3exo) = 3.0 (H-5exo); 2.34 tm, 1 H, *J*(4,3exo) = *J*(4,6exo) = 4.7 (H-4); 2.64 dm, 1 H, *J*(1,6exo) = 4.4 (H-1); 2.67 m, 1 H (H-2); 3.00 s, 3 H (Ms); 4.13 dd, 1 H, *J*($CH^bH$,2) = 9.1 and 4.20 dd, 1 H, *J*($CH^aH$,2) = 6.3, $J_{gem}$ = 10.8 ($CH_2O$); 5.03 ddd, 1 H, *J*(6,5exo) = 10.4, *J*(6,5endo) = 3.8, *J*(6,1) = 4.4 (H-6); 7.45 m, 2 H, 7.56 m, 1 H and 8.04 m, 2 H (arom.). $^{13}$C NMR ($CDCl_3$): 31.52 (C-2); 33.79 (C-7); 34.11 (C-3); 35.96 (C-5); 36.23 (C-4); 38.34 (Ms); 43.62 (C-1); 67.11 ($CH_2O$); 81.43 (C-6); 128.38, 129.52, 130.10 and 132.97 (arom.); 166.63 (C=O).

*[(1R*,2S*,4R*,5R*)-5- (Mesyloxy)bicyclo[2.2.1]heptan-2-yl]methyl benzoate* (**21b**): Yield 3.69 g (84%) as colorless oil. For $C_{16}H_{20}O_5S$ (324.4) calculated: 59.24% C, 6.21% H, 9.88% S; found: 59.32% C, 6.21% H, 9.62% S. EI MS, *m/z* (%): 324 (0.06) [M], 106 (20), 84 (100), 47 (44). $^1$H NMR ($CDCl_3$): 1.18 m, 1 H (H-3exo); 1.32 dd, 1 H, $J_{gem}$ = 13.7, *J*(6endo,5) = 3.2 (H-3exo); 1.36 dm, 1 H, $J_{gem}$ = 11.0 (H-7b); 1.57 dm, 1 H, $J_{gem}$ = 11.0 (H-7a); 2.14 m, 2 H (H-2, 3endo); 2.16 ddd, 1 H, $J_{gem}$ = 13.7, *J*(6exo,5) = 10.3, *J*(6exo,1) = 4.7 (H-6exo); 2.29 dm, 1 H, *J*(1,6exo) = 4.7 (H-1); 2.64 m, 1 H (H-4); 3.02 s, 3 H (Ms); 4.12 m, 2 H ($CH_2O$); 5.03 dddd, 1 H, *J*(5,6exo) = 10.5, *J*(5,4) = 4.5, *J*(5,6endo) = 3.0, *J*(5,3exo) = 1.6 (H-5); 7.45 m, 2 H, 7.57 m, 1 H and 8.04 m, 2 H (arom.). $^{13}$C NMR ($CDCl_3$): 25.51 (C-3); 34.15 (C-7); 37.29 (C-6); 38.23 (Ms); 38.31 (C-1); 40.45 (C-2); 41.29 (C-4); 67.54 ($CH_2O$); 81.52 (C-5); 128.36, 129.52, 130.16 and 132.97 (arom.); 166.61 (C=O).

[(1*R**,2*R**,4*S**,6*S**)-6-Azidobicyclo[2.2.1]heptan-2-yl]methyl Benzoate (**22a**) and [(1*R**,2*S**,4*R**,5*S**)-5-Azidobicyclo[2.2.1]heptan-2-yl]methyl Benzoate (**22b**)

Sodium azide (4.5 g) was added to a solution of **21a** or **21b** (3.98 g, 12.3 mmol) in DMF (50 ml) and the reaction mixture was stirred at room temperature under argon overnight. The solvent was evaporated and a solution of the residue in ethyl acetate was washed with water. The organic layer was dried over anhydrous $Na_2SO_4$ and evaporated. The product was purified by chromatography on silica gel (1.4 kg) in toluene.

*[(1R*,2R*,4S*,6S*)-6-Azidobicyclo[2.2.1]heptan-2-yl]methyl benzoate* (**22a**): Yield 2.65 g (80%) as colorless oil. For $C_{15}H_{17}N_3O_2$ (271.3) calculated: 66.40% C, 6.32% H, 15.49% N; found: 66.76% C, 6.38% H, 15.30% N. EI MS, *m/z* (%): 272 (0.06) [M + H], 216 (22), 105 (100), 77 (65). $^1$H NMR ($CDCl_3$): 1.16 dddd, 1 H, $J_{gem}$ = 12.5, *J*(3exo,2) = 5.4, *J*(3exo,4) = 4.0,

*J*(3exo,5exo) = 2.9 (H-3exo); 1.38 dm, 1 H, $J_{gem}$ = 10.6 (H-7a); 1.43 ddd, 1 H, $J_{gem}$ = 12.6, *J*(3endo,2) = 8.6, *J*(3endo,7b) = 2.5 (H-3endo); 1.49 dm, 1 H, $J_{gem}$ = 10.6 (H-7b); 1.53 m, 1 H (H-5exo); 1.67 ddd, 1 H, $J_{gem}$ = 13.4, *J*(5endo,6) = 7.5, *J*(5endo,7a) = 2.3 (H-5exo); 1.88 m, 1 H (H-2); 2.34 m, 1 H (H-1); 2.37 tm, 1 H, *J*(4,3exo) = *J*(4,5exo) = 4.1 (H-4); 3.56 dm, 1 H, *J*(6,5endo) = 7.5 (H-6); 4.08 dd, 1 H, *J*($CH^bH$,2) = 9.1 and 4.17 dd, 1 H, *J*($CH^aH$,2) = 6.3, $J_{gem}$ = 11.0 ($CH_2O$); 7.45 m, 2 H, 7.57 m, 1 H and 8.04 m, 2 H (arom.). $^{13}$C NMR ($CDCl_3$): 32.50 (C-7); 32.92 (C-3); 35.54 (C-4); 37.48 (C-5); 37.86 (C-2); 44.24 (C-1); 63.98 (C-6); 67.14 ($CH_2O$); 128.37, 129.54, 130.14 and 132.98 (arom.); 166.56 (C=O).

*[(1R*,2S*,4R*,5S*)-5-Azidobicyclo[2.2.1]heptan-2-yl]methyl benzoate* (**22b**): Yield 2.57 g (77%) as colorless oil. For $C_{15}H_{17}N_3O_2$ (271.3) calculated: 66.40% C, 6.32% H, 15.49% N; found: 66.40% C, 6.18% H, 15.24% N. EI MS, *m/z* (%): 271 (0.6) [M], 149 (3.4), 105 (100), 77 (60). $^1$H NMR ($CDCl_3$): 1.24 dt, 1 H, $J_{gem}$ = 13.2, *J*(3exo,4) = *J*(3exo,2) = 4.8 (H-3exo); 1.40 dm, 1 H, $J_{gem}$ = 10.6 (H-7a); 1.43 ddd, 1 H, $J_{gem}$ = 13.2, *J*(3endo,2) = 8.6, *J*(3endo,7a) = 2.3 (H-3endo); 1.48 dm, 1 H, $J_{gem}$ = 10.6 (H-7b); 1.56 dm, 1 H, $J_{gem}$ = 13.3 (H-6exo); 1.71 ddd, 1 H, $J_{gem}$ = 13.3, *J*(6endo,5) = 7.6, *J*(6endo,7a) = 2.5 (H-6endo); 1.89 m, 1 H (H-2); 2.33 dm, 1 H, *J*(1,6exo) = 4.6 (H-1); 2.36 dm, 1 H, *J*(4,3exo) = 4.8 (H-4); 3.53 ddd, 1 H, *J*(5,6endo) = 7.7, *J*(5,6exo) = 3.5, *J*(5,7a) = 1.6 (H-5); 4.06 dd, 1 H, *J*($CH^bH$,2) = 9.1 and 4.11 dd, 1 H, *J*($CH^aH$,2) = 6.4, $J_{gem}$ = 11.0 ($CH_2O$); 7.45 m, 2 H, 7.57 m, 1 H and 8.04 m, 2 H (arom.). $^{13}$C NMR ($CDCl_3$): 30.18 (C-3); 32.15 (C-7); 37.96 (C-1); 38.27 (C-6); 40.11 (C-2); 41.80 (C-4); 63.68 (C-5); 67.54 ($CH_2O$); 128.34, 129.51, 130.19 and 132.94 (arom.); 166.56 (C=O).

[(1*R**,2*R**,4*S**,6*S**)-6-Azidobicyclo[2.2.1]heptan-2-yl]methanol (**23a**) and
[(1*R**,2*S**,4*R**,5*S**)-5-Azidobicyclo[2.2.1]heptan-2-yl]methanol (**23b**)

A solution of compound **22a** or **22b** (1.044 g, 3.9 mmol) in 1 M methanolic sodium methoxide (30 ml) was stirred at room temperature overnight. The reaction mixture was neutralized with Dowex 50 ($H^+$). Dowex was filtered off, washed with methanol and the combined filtrates were evaporated. Chromatography of the residue on silica gel (150 g) in toluene–ethyl acetate (1:1) afforded compounds **23a** and **23b** as colorless oils.

*[(1R*,2R*,4S*,6S*)-6-Azidobicyclo[2.2.1]heptan-2-yl]methanol* (**23a**): Yield 506 mg (79%). For $C_8H_{13}N_3O$ (167.2) calculated: 57.40% C, 7.84% H, 25.13% N; found: 57.51% C, 7.94% H, 24.90% N. FAB MS, *m/z* (%): 168 (10) [M + H], 140 (67), 55 (44). $^1$H NMR ($CDCl_3$): 1.00 dddd, 1 H, $J_{gem}$ = 12.4, *J*(3exo,2) = 5.3, *J*(3exo,4) = 3.8, *J*(3exo,5exo) = 3.1 (H-3exo); 1.26 dm, 1 H, $J_{gem}$ = 10.5 (H-7a); 1.32 ddd, 1 H, $J_{gem}$ = 12.4, *J*(3endo,2) = 8.5, *J*(3endo,7b) = 2.4 (H-3endo); 1.43 dm, 1 H, $J_{gem}$ = 10.5 (H-7b); 1.48 m, 1 H (H-5exo); 1.59 m, 1 H (H-2); 1.63 ddd, 1 H, $J_{gem}$ = 13.4, *J*(5endo,6) = 7.6, *J*(5endo,7a) = 2.4 (H-5endo); 2.31 m, 1 H (H-1); 2.32 m, 1 H (H-4); 3.42 m, 2 H ($CH_2O$); 3.53 dm, 1 H, *J*(6,5endo) = 7.6 (H-6). $^{13}$C NMR ($CDCl_3$): 32.36 (C-7); 32.77 (C-3); 35.43 (C-4); 37.58 (C-5); 41.32 (C-2); 43.74 (C-1); 64.20 (C-6); 65.83 ($CH_2O$).

*[(1R*,2S*,4R*,5S*)-5-Azidobicyclo[2.2.1]heptan-2-yl]methanol* (**23b**): Yield 451 mg (70%). For $C_8H_{13}N_3O$ (167.2) calculated: 57.40% C, 7.84% H, 25.13% N; found: 57.46% C, 7.98% H, 25.10% N. FAB MS, *m/z* (%): 168 (8) [M + H], 140 (76), 55 (100). $^1$H NMR ($CDCl_3$): 1.08 dt, 1 H, $J_{gem}$ = 13.1, *J*(3exo,4) = *J*(3exo,2) = 4.8 (H-3exo); 1.29 dm, 1 H, $J_{gem}$ = 10.5 (H-7a); 1.33 ddd, 1 H, $J_{gem}$ = 13.1, *J*(3endo,2) = 8.6, *J*(3endo,7a) = 2.4 (H-3endo); 1.42 dm, 1 H, $J_{gem}$ = 10.5 (H-7b); 1.51 dm, 1 H, $J_{gem}$ = 13.2 (H-6exo); 1.60 m, 1 H (H-2); 1.68 ddd, 1 H, $J_{gem}$ = 13.2, *J*(6endo,5) = 7.5, *J*(6endo,7a) = 2.5 (H-6endo); 1.79 bs, 1 H (OH); 2.28 dm, 1 H, *J*(1,6exo) = 4.6 (H-1); 2.31 bd, 1 H, *J*(4,3exo) = 4.9 (H-4); 3.38 m, 2 H ($CH_2O$); 3.50 ddd, 1 H,

*J*(5,6endo) = 7.7, *J*(5,6exo) = 3.4, *J*(5,7a) = 1.7 (H-5). $^{13}$C NMR ($CDCl_3$): 30.07 (C-3); 32.02 (C-7); 37.46 (C-1); 38.35 (C-6); 41.71 (C-4); 43.65 (C-2); 63.80 (C-5); 66.15 ($CH_2O$).

[(1*R**,2*R**,4*S**,6*S**)-6-Aminobicyclo[2.2.1]heptan-2-yl]methyl Benzoate (**24a**) and
[(1*R**,2*S**,4*R**,5*S**)-5-Aminobicyclo[2.2.1]heptan-2-yl]methyl Benzoate (**24b**)

$Pd(OH)_2$/C (20%, 0.14 g) was added to a solution of **22a** or **22b** (2.55 g, 9.4 mmol) in methanol (100 ml) and hydrogen was bubbled through the reaction mixture for 6 h. The catalyst was filtered off and the filtrate was evaporated. Pure samples for analytical purposes were obtained by chromatography on silica gel in toluene–ethyl acetate (4:1).

*[(1R*,2R*,4S*,6S*)-6-Aminobicyclo[2.2.1]heptan-2-yl]methyl benzoate* (**24a**): Yield 2.24 g (97%) as colorless oil. For $C_{15}H_{19}NO_2$ (245.3) calculated: 73.44% C, 7.81% H, 5.71% N; found: 73.25% C, 7.73% H, 5.94% N. FAB MS, *m/z* (%): 246 (31) [M + H], 104.9 (100). $^1$H NMR ($CDCl_3$): 1.10 m, 2 H (H-3exo, 5exo); 1.29 dm, 1 H, $J_{gem}$ = 10.5 (H-7a); 1.36 ddd, 1 H, $J_{gem}$ = 12.3, *J*(3en,2) = 8.7, *J*(3endo,7b) = 2.4 (H-3endo); 1.45 dm, 1 H, $J_{gem}$ = 10.5 (H-7b); 1.68 ddd, 1 H, $J_{gem}$ = 12.5, *J*(5endo,6) = 7.6, *J*(5endo,7a) = 2.3 (H-5endo); 1.86 m, 1 H (H-2); 1.99 bs, 1 H (H-1); 2.28 m, 1 H (H-4); 2.89 bdd, 1 H, *J*(6,5endo) = 7.7, *J*(6,5exo) = 2.7 (H-6); 4.08 dd, 1 H, *J*($CH^bH$,2) = 9.1 and 4.12 dd, 1 H, *J*($CH^aH$,2) = 6.5, $J_{gem}$ = 10.9 ($CH_2O$); 7.44 m, 2 H, 7.56 m, 1 H and 8.05 m, 2 H (arom.). $^{13}$C NMR ($CDCl_3$): 31.34 (C-7); 32.51 (C-3); 35.64 (C-4); 38.47 (C-2); 41.24 (C-5); 47.33 (C-1); 54.69 (C-6); 67.56 ($CH_2O$); 128.20, 129.42, 130.21 and 132.76 (arom.); 166.54 (C=O).

*[(1R*,2S*,4R*,5S*)-5-Aminobicyclo[2.2.1]heptan-2-yl]methyl benzoate* (**24b**): Yield 2.14 g (93%) as colorless oil. For $C_{15}H_{19}NO_2$ (245.3) calculated: 73.44% C, 7.81% H, 5.71% N; found: 73.48% C, 7.82% H, 5.42% N. FAB MS, *m/z* (%): 246 (7) [M + H], 104.9 (100). $^1$H NMR ($CDCl_3$): 1.13 m, 2 H (H-6exo, 3exo); 1.32 dm, 1 H, $J_{gem}$ = 10.5 (H-7a); 1.40 ddd, 1 H, $J_{gem}$ = 12.8, *J*(3endo,2) = 8.6, *J*(3endo,7b) = 2.4 (H-3endo); 1.47 dm, 1 H, $J_{gem}$ = 10.5 (H-7b); 1.72 ddd, 1 H, $J_{gem}$ = 12.7, *J*(6endo,5) = 7.7, *J*(6endo,7a) = 2.5 (H-6endo); 1.85 m, 1 H (H-2); 2.00 dm, 1 H, *J*(4,3exo) = 4.4 (H-4); 2.25 dm, 1 H, *J*(1,6exo) = 4.3 (H-1); 2.88 ddd, 1 H, *J*(5,6endo) = 7.7, *J*(5,6exo) = 3.7, *J*(5,7a) = 1.0 (H-5); 4.05 dd, 1 H, *J*($CH^bH$,2) = 9.2 and 4.10 dd, 1 H, *J*($CH^aH$,2) = 6.4, $J_{gem}$ = 10.8 ($CH_2O$); 7.44 m, 2 H, 7.55 m, 1 H and 8.04 m, 2 H (arom.). $^{13}$C NMR ($CDCl_3$): 30.92 (C-3); 31.10 (C-7); 38.16 (C-1); 39.78 (C-2); 41.81 (C-6); 44.97 (C-4); 54.18 (C-5); 67.89 ($CH_2O$); 128.22, 129.43, 130.25 and 132.76 (arom.); 166.54 (C=O).

[(1*R**,2*R**,4*S**,6*S**)-6-Aminobicyclo[2.2.1]heptan-2-yl]methanol (**25a**) and
[(1*R**,2*S**,4*R**,5*S**)-5-Aminobicyclo[2.2.1]heptan-2-yl]methanol (**25b**)

$Pd(OH)_2$/C (20%, 30 mg) was added to a solution of **23a** or **23b** (430 mg, 2.6 mmol) in methanol (40 ml) and hydrogen was bubbled through the reaction mixture for 6 h. The catalyst was filtered off and the filtrate was evaporated. Residue was purified by chromatography on Dowex 50 ($H^+$, 10 ml).

*[(1R*,2R*,4S*,6S*)-6-Aminobicyclo[2.2.1]heptan-2-yl]methanol* (**25a**): Yield 281 mg (77%) as colorless oil. For $C_8H_{15}NO$ (141.2) calculated: 68.04% C, 10.71% H, 9.92% N; found: 67.92% C, 10.98% H, 9.71% N. FAB MS, *m/z* (%): 142 (100) [M + H], 78.9 (34). $^1$H NMR (DMSO-$d_6$): 0.82 m, 1 H (H-3exo); 0.92 m, 1 H (H-5exo); 1.01 dm, 1 H, $J_{gem}$ = 10.1 (H-7a); 1.10 ddd, 1 H, $J_{gem}$ = 12.1, *J*(3endo,2) = 8.5, *J*(3endo,7b) = 2.4 (H-3endo); 1.37 m, 2 H (H-2,7b); 1.45 ddd, 1 H, $J_{gem}$ = 12.4, *J*(5endo,6) = 7.6, *J*(5endo,7a) = 2.3 (H-5endo); 1.80 m, 1 H (H-1); 2.07 m,

1 H (H-4); 2.66 dd, 1 H, *J*(6,5endo) = 7.6, *J*(6,5exo) = 3.2 (H-6); 3.12 m, 2 H ($CH_2O$). $^{13}C$ NMR (DMSO-$d_6$): 30.95 (C-7); 32.88 (C-3); 35.37 (C-4); 41.30 (C-5); 42.10 (C-2); 47.02 (C-1); 54.94 (C-6); 64.84 ($CH_2O$).

*[(1R*,2S*,4R*,5S*)-5-Aminobicyclo[2.2.1]heptan-2-yl]methanol* (**25b**): Yield 320 mg (88%) as colorless oil. For $C_8H_{15}NO$ (141.2) calculated: 68.04% C, 10.71% H, 9.92% N; found: 67.77% C, 10.97% H, 9.56% N. FAB MS, *m/z* (%): 142 (79) [M + H], 79 (45). $^1H$ NMR (DMSO-$d_6$): 0.83 dt, 1 H, $J_{gem}$ = 12.5, *J*(3exo,4) = *J*(3exo,2) = 4.6 (H-3exo); 0.95 m, 1 H (H-6exo); 1.05 dm, 1 H, $J_{gem}$ = 10.0 (H-7a); 1.13 ddd, 1 H, $J_{gem}$ = 12.4, *J*(3endo,2) = 8.5, *J*(3endo,7a) = 2.3 (H-3endo); 1.36 m, 2 H (H-2,7b); 1.46 ddd, 1 H, $J_{gem}$ = 12.2, *J*(6endo,5) = 7.6, *J*(6endo,7a) = 2.4 (H-6endo); 1.78 bd, 1 H, *J*(4,3exo) = 4.4 (H-4); 2.05 bd, 1 H, *J*(1,6exo) = 5.1 (H-4); 2.66 ddd, 1 H, *J*(5,6endo) = 7.7, *J*(5,6exo) = 3.7, *J*(5,7a) = 0.8 (H-5); 3.09 m, 2 H ($CH_2O$). $^{13}C$ NMR (DMSO-$d_6$): 30.60 (C-7); 30.92 (C-3); 37.55 (C-1); 41.87 (C-6); 43.78 (C-2); 44.81 (C-4); 54.39 (C-5); 65.10 ($CH_2O$).

[(1*R**,2*R**,4*S**,6*S**)-6-(5-Methyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-1-yl)-bicyclo[2.2.1]heptan-2-yl]methyl Benzoate (**26a**) and
[(1*R**,2*S**,4*R**,5*S**)-5-(5-Methyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-1-yl)-bicyclo[2.2.1]heptan-2-yl]methyl Benzoate (**26b**)

A solution of **24a** or **24b** (2.03 g, 8.3 mmol) and ethyl [(2*E*)-3-ethoxy-2-methylprop-2-enoyl]carbamate (1.67 g, 8.3 mmol) in 1,4-dioxane (75 ml) was stirred at 100 °C for 2.5 h. 1 M sulfuric acid (25 ml) was then added and the mixture was stirred at 100 °C for another 6 h. 1,4-Dioxane was evaporated and the residue was extracted with ethyl acetate (3 × 50 ml). The organic layer was dried over anhydrous $Na_2SO_4$ and evaporated. Crystallization from ethanol gave the product as white crystals.

*[(1R*,2R*,4S*,6S*)-6-(5-Methyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-1-yl)bicyclo[2.2.1]heptan-2-yl]methyl benzoate* (**26a**): Yield 1.19 g (41%). M.p. 180–181 °C. For $C_{20}H_{22}N_2O_4$ (354.4) calculated: 67.78% C, 6.26% H, 7.90% N; found: 67.53% C, 6.32% H, 7.67% N. FAB MS, *m/z* (%): 355 (23) [M + H], 127 (25), 104.9 (100), 79 (25), 79 (25). $^1H$ NMR (DMSO-$d_6$): 1.16 m, 1 H (H-3exo); 1.44–1.49 m, 3 H (H-3endo, 7a, 7b); 1.58 dm, 1 H, $J_{gem}$ = 13.4 (H-5exo); 1.78 d, 3 H, *J*($CH_3$,6′) = 1.2 (5′-$CH_3$); 1.85 ddd, 1 H, $J_{gem}$ = 13.3, *J*(5endo,6) = 8.6, *J*(5endo,7) = 1.0 (H-5endo); 2.02 m, 1 H (H-2); 2.33 bt, 1 H, *J*(4,3exo) = *J*(4,5exo) = 4.0 (H-4); 2.40 bs, 1 H (H-1); 4.10 m, 2 H ($CH_2O$); 4.17 dd, 1 H, *J*(6,5endo) = 8.3, *J*(6,5exo) = 4.5 (H-6); 7.52 m, 2 H, 7.65 m, 1 H and 7.97 m, 2 H (arom.); 7.56 q, 1 H, *J*(6′,$CH_3$) = 1.2 (H-6′); 11.20 bs, 1 H (NH). $^{13}C$ NMR (DMSO-$d_6$): 12.37 (5′-$CH_3$); 32.26 (C-3); 33.14 (C-7); 35.57 (C-4); 37.99 (C-5); 39.56 (C-2); 42.64 (C-1); 58.94 (C-6); 67.02 ($CH_2O$); 108.27 (C-5′); 128.99, 129.38, 129.96 and 133.55 (arom.); 137.44 (C-6′); 151.40 (C-2′); 163.98 (C-4′); 165.97 (C=O).

*[(1R*,2S*,4R*,5S*)-5-(5-Methyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-1-yl)bicyclo[2.2.1]heptan-2-yl]methyl benzoate* (**26b**): Yield 1.07 g (36%). M.p. 204–205.5 °C. For $C_{20}H_{22}N_2O_4 \cdot H_2O$ (372.4) calculated: 64.50% C, 6.50% H, 7.52% N; found: 64.89% C, 6.23% H, 7.29% N. FAB MS, *m/z* (%): 355 (20) [M + H], 127 (33), 104.9 (100), 79 (36). $^1H$ NMR (DMSO-$d_6$): 1.23 dt, 1 H, $J_{gem}$ = 13.0, *J*(3exo,2) = *J*(3exo,4) = 4.9 (H-3exo); 1.47 dm, 1 H, $J_{gem}$ = 10.5 (H-7a); 1.50–1.55 m, 2 H (H-3endo, 7b); 1.58 dt, 1 H, $J_{gem}$ = 13.2, *J*(6exo,5) = *J*(6exo,1) = 4.8 (H-6exo); 1.79 d, 3 H, *J*($CH_3$,6′) = 1.2 (5′-$CH_3$); 1.88 ddd, 1 H, $J_{gem}$ = 13.1, *J*(6endo,5) = 8.4, *J*(6endo,7a) = 2.3 (H-6endo); 1.96 m, 1 H (H-2); 2.28 bd, 1 H, *J*(1,6exo) = 4.4 (H-1); 2.38 bd, 1 H, *J*(4,3exo) = 4.3 (H-4); 4.09 m, 2 H ($CH_2O$); 4.18 bdd, 1 H, *J*(5,6endo) = 8.4, *J*(5,6exo) = 5.1 (H-5); 7.54 m, 3 H, 7.66 m, 1 H and 7.97 m, 2 H (H-6′, arom.); 11.22 bs, 1 H (NH).

$^{13}$C NMR (DMSO-$d_6$): 12.40 (5′-$CH_3$); 32.04 (C-3); 33.15 (C-7); 38.15 (C-1); 38.62 (C-6); 39.64 (C-2); 40.55 (C-4); 58.00 (C-5); 67.56 ($CH_2O$); 108.48 (C-5′); 129.03, 129.34, 130.00 and 133.57 (arom.); 137.31 (C-6′); 151.43 (C-2′); 164.00 (C-4′); 165.97 (C=O).

1-[(1*R**,2*S**,4*S**,6*R**)-6-(Hydroxymethyl)bicyclo[2.2.1]heptan-2-yl]-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (**27a**) and 1-[(1*R**,2*S**,4*R**,5*S**)-5-(Hydroxymethyl)bicyclo[2.2.1]heptan-2-yl]-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (**27b**)

*A*) A solution of compound **26a** or **26b** (692 mg, 1.95 mmol) in 1 M methanolic sodium methoxide (25 ml) was stirred at room temperature for 3 days. The reaction mixture was neutralized with Dowex 50 ($H^+$). Dowex was filtered off, washed with methanol and the combined filtrates were evaporated. The residue was crystallized from diethyl ether.

*1-[(1R*,2S*,4S*,6R*)-6-(Hydroxymethyl)bicyclo[2.2.1]heptan-2-yl]-5-methylpyrimidine-2,4(1H,3H)-dione* (**27a**): Yield 424 mg (87%). M.p. 178–179 °C. For $C_{13}H_{18}N_2O_3$ (250.3) calculated: 62.38% C, 7.25% H, 11.19% N; found: 62.35% C, 7.37% H, 11.01% N. FAB MS, *m/z* (%): 251 (48) [M + H], 127 (100), 79 (31). $^1$H NMR (DMSO-$d_6$): 0.95 dm, 1 H, $J_{gem}$ = 12.4 (H-3exo); 1.31 m, 2 H (H-3endo, 7a); 1.38 dm, 1 H, $J_{gem}$ = 10.9 (H-7b); 1.52 dm, 1 H, $J_{gem}$ = 13.4 (H-5exo); 1.63 m, 1 H (H-2); 1.78 d, 3 H, $J$($CH_3$,6′) = 1.2 (5′-$CH_3$); 1.81 ddd, 1 H, $J_{gem}$ = 13.4, $J$(5endo,6) = 8.5, $J$(5endo,7a) = 2.3 (H-5endo); 2.26 tm, 1 H, $J$(4,3exo) = $J$(4,5exo) = 4.1 (H-4); 2.33 bs, 1 H (H-1); 3.18 m, 2 H ($CH_2O$); 4.08 ddd, 1 H, $J$(6,5endo) = 8.3, $J$(6,5exo) = 4.5, $J$(6,7a) = 0.8 (H-6); 4.59 t, 1 H, $J$(OH,$CH_2$) = 5.3 (OH); 7.526 q, 1 H, $J$(6′,$CH_3$) = 1.2 (H-6′); 11.20 bs, 1 H (NH). $^{13}$C NMR (DMSO-$d_6$): 12.37 (5′-$CH_3$); 32.36 (C-3); 32.96 (C-7); 35.49 (C-4); 38.48 (C-5); 42.23 (C-1); 43.45 (C-2); 59.19 (C-6); 64.25 ($CH_2O$); 108.25 (C-5′); 137.40 (C-6′); 151.39 (C-2′); 164.00 (C-4′).

*1-[(1R*,2S*,4R*,5S*)-5-(Hydroxymethyl)bicyclo[2.2.1]heptan-2-yl]-5-methylpyrimidine-2,4(1H,3H)-dione* (**27b**): Yield 389 mg (80%). M.p. 186–187 °C. For $C_{13}H_{18}N_2O_3$ (250.3) calculated: 62.38% C, 7.25% H, 11.19% N; found: 62.21% C, 7.31% H, 10.88% N. FAB MS, *m/z* (%): 251 (100) [M + H], 127 (69), 79 (18). $^1$H NMR (DMSO-$d_6$): 0.99 dt, 1 H, $J_{gem}$ = 12.6, $J$(3exo,2) = $J$(3exo,4) = 4.9 (H-3exo); 1.30 dm, 1 H, $J_{gem}$ = 10.5 (H-7a); 1.36 ddd, 1 H, $J_{gem}$ = 12.4, $J$(3endo,2) = 8.5, $J$(3endo,7b) = 2.4 (H-3endo); 1.42 dm, 1 H, $J_{gem}$ = 10.5 (H-7b); 1.54 dt, 1 H, $J_{gem}$ = 13.1, $J$(6exo,5) = $J$(6exo,1) = 4.8 (H-6exo); 1.58 m, 1 H (H-2); 1.78 ddd, 1 H, $J_{gem}$ = 13.0, $J$(6endo,5) = 8.3, $J$(6endo,7a) = 2.3 (H-6endo); 1.78 d, 3 H, $J$($CH_3$,6′) = 1.2 (5′-$CH_3$); 2.24 dm, 1 H, $J$(1,6exo) = 4.2 (H-1); 2.28 bd, 1 H, $J$(4,3exo) = 4.5 (H-4); 3.15 m, 2 H ($CH_2O$); 4.14 bdd, 1 H, $J$(5,6endo) = 8.4, $J$(5,6exo) = 5.2 (H-5); 4.55 bt, 1 H, $J$(OH,$CH_2$) = 4.8 (OH); 7.52 q, 1 H, $J$(6′,$CH_3$) = 1.2 (H-6′); 11.20 bs, 1 H (NH). $^{13}$C NMR (DMSO-$d_6$): 12.39 (5′-$CH_3$); 32.20 (C-3); 32.93 (C-7); 37.74 (C-1); 38.78 (C-6); 40.60 (C-4); 43.40 (C-2); 58.19 (C-5); 64.76 ($CH_2O$); 108.44 (C-5′); 137.35 (C-6′); 151.43 (C-2′); 166.96 (C-4′).

*B*) A solution of **25a** or **25b** (230 mg, 1.6 mmol) and ethyl [(2*E*)-3-ethoxy-2-methylprop-2-enoyl]carbamate (328 mg, 1.6 mmol) in dioxane (10 ml) was stirred at 100 °C for 3 h. 1 M sulfuric acid (15 ml) was then added and the mixture was stirred at 100 °C for another 10 h. The mixture was neutralized with $NaHCO_3$, and chromatographed on silica gel (20 g) in ethyl acetate–acetone–ethanol–water (36:6:5:3). 196 mg (48%) of compound **27a** or 183 mg (45%) of compound **27b** was obtained.

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