SYNTHESIS OF OPTICALLY ACTIVE N^6-ALKYL DERIVATIVES OF (*R*)-3-(ADENIN-9-YL)-2-HYDROXYPROPANOIC ACID AND RELATED COMPOUNDS

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Dedicated to the memory of Professor Otakar Červinka.

Reaction of ethyl (*R*)-oxiranecarboxylate (**2a**) with various nucleobases (adenine, 6-chloropurine, thymine, cytosine, N^6-benzoyladenine, 4-methoxy-5-methylpyrimidin-2(1*H*)-one and 4-methoxypyrimidin-2(1*H*)-one) afforded ethyl 3-substituted-2-hydroxypropanoates **4**–**10**. Enantioselectivity of this reaction is dependent on the type of the base: 6-chloropurine, N^6-benzoyladenine, 4-methoxy-5-methylpyrimidin-2(1*H*)-one, thymine and cytosine gave optically pure *R* enantiomers. In other cases, partial or complete racemization occurred. Optically pure ethyl (*R*)-3-(6-chloropurin-9-yl)-2-hydroxypropanoate (**5a**) was hydrolyzed to give (*R*)-3-(6-chloropurin-9-yl)-2-hydroxypropanoic acid (**11**). Reactions of **11** with various primary or secondary amines led to N^6-substituted (*R*)-3-(adenin-9-yl)-2-hydroxypropanoic acids **14**–**19**. Enantiomeric purity was determined from ^{1}H NMR spectra measured in the presence of (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol.

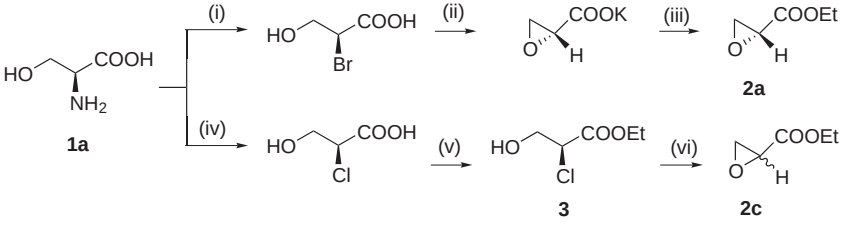
Keywords: Oxirane ring opening; Enantiomeric purity determination; Acyclic nucleoside analogues; Nucleosides; *S*-Adenosyl-L-homocysteine hydrolase inhibitors; SAH hydrolase; Adenine; Purines; Epoxides; Antivirals.

In our previous studies on acyclic adenosine analogues we have described (*RS*)-3-(adenin-9-yl)-2-hydroxypropanoic acid (AHPA) and its alkyl esters[1]. These compounds possess interesting biological characteristics: they inhibit various viruses, being non-toxic to the host cells at antivirally active concentrations[2]. Due to their irreversible inhibition of *S*-adenosyl-L-homocysteine hydrolase (SAH hydrolase, EC 3.3.1.1.) and the resulting disturbance of methylation reactions in general, AHPA and its alkyl esters exhibit a number of other biological activities[3]. However, availability of

these compounds in larger quantities was limited to their racemic form[4]. The synthesis of pure *R* and *S* enantiomers of 3-(adenin-9-yl)-2-hydroxypropanoic acid by oxidation of 5-(adenin-9-yl)-5-deoxyaldopentoses with O_2 in aqueous alkali[5] or with periodate[6] was complicated by difficult purification and low yields of the products. The aim of this work is elaboration of a simple and effective synthesis of pure *R* or *S* enantiomers of 3-(adenin-9-yl)-2-hydroxypropanoic acid and its derivatives substituted in the N^6 position of the adenine moiety, as well as their pyrimidine congeners.

For this purpose, we sought a chiral three-carbon atom synthon which should react with various nucleobases giving desired products in good yields and high optical purity. It should be easily accessible from an inexpensive optically active material. These requirements could be met by alkylation of the nucleobases with alkyl oxiranecarboxylates **2**. The synthesis of required ethyl (*R*)-oxiranecarboxylate (**2a**) was performed starting from L-serine (**1a**) using the method described for the preparation of ethyl (*R*,*R*)-2,3-epoxybutanoate from L-threonine *via* 2-bromo-3-hydroxypropanoic acid[7]. The utilization of L-serine for syntheses of (*R*)-oxiranecarboxylic acid esters was also proposed[8] (Scheme 1). Analogously to **2a**, we obtained from D-serine ethyl (*S*)-oxiranecarboxylate (**2b**). However, this preparation of **2a** and **2b** has serious drawbacks: the use of expensive crown ether and harmful diethyl sulfate.

Therefore we examined an alternative access to oxirane **2a**: transformation of L-serine to ethyl (*S*)-2-chloro-3-hydroxypropanoate (**3**) followed by the oxirane ring closure on treatment with DBU (1,8-diazabicyclo[5.4.0]-undec-7-ene) (Scheme 1). However, complete racemization occurred in this case so that the desired product, ethyl oxiranecarboxylate, was obtained as racemate **2c**. The racemic nature of the so prepared oxirane **2c** was confirmed not only by optical rotation measurement but also from the course of its nucleophilic opening with 6-chloropurine. This reaction performed

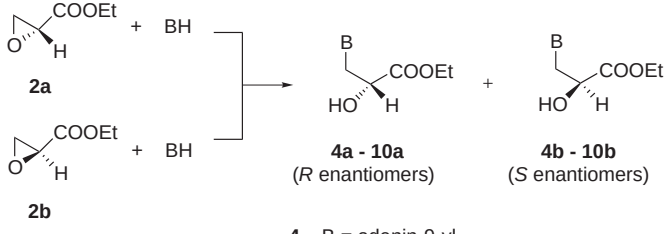


(i) HBr, $NaNO_2$, KBr; (ii) KOH, EtOH; (iii) diethyl sulfate, 18-crown-6, CH_2Cl_2; (iv) HCl, $NaNO_2$; (v) EtOH, TsOH; (vi) DBU, acetonitrile

SCHEME 1

with racemic oxirane **2c** afforded ethyl 3-(6-chloropurin-9-yl)-2-hydroxypropanoate as a racemate. Reaction details and optical purity determination of products is described below.

Nucleophilic opening of the oxirane ring in **2a** or **2b** by various nucleobases under basic conditions took place at C-3 with regiospecific formation of α-hydroxy esters (**4**–**10**, Scheme 2). This is in agreement with the data on the nucleophilic opening of 2,3-epoxy esters or 2,3-epoxy amides[9].



4, B = adenin-9-yl
5, B = 6-chloropurin-9-yl
6, B = cytosin-9-yl
7, B = 4-methoxy-5-methyl-2-oxo-1,2-dihydropyrimidin-1-yl
8, B = 4-methoxy-2-oxo-1,2-dihydropyrimidin-1-yl
9, B = thymin-1-yl
10, B = N^6-benzoyladenin-9-yl

SCHEME 2

For the determination of optical purity of esters **4**–**10**, we have used their ^{1}H NMR spectra measured after the addition of slight excess (≈2 molar equivalents) of optically pure (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol. This chiral solvating agent is known to form weak diastereomeric complexes with various compounds containing hydroxy, amino, carbonyl, sulfonyl and phosphonyl groups (for details, see review[10]). Doubling of some signals was observed when both enantiomers of the esters were present. The chemical shift nonequivalence of protons is very small (≤10 Hz at 500 HMz) but observable (usually on resolution enhanced sharp triplets of ester ethoxy protons as it is illustrated in Fig. 1) and relative intensities of signals allowed to determine their *R*:*S* ratio. The NMR spectra had to be measured in a nonpolar solvent, which itself does not associate with the optically active reagent ($CDCl_3$ was used). Therefore, the adenine derivative **4** was benzoylated with benzoyl chloride in pyridine to benzoate **20** and cytosine derivatives **6** and N^6-benzoyladenine derivative **10a** were converted to acetates **21** and **22**, while other compounds were measured directly since their solubility in $CDCl_3$ was sufficient.

Surprisingly, both ethyl oxiranecarboxylates **2a** and **2b** reacted with some nucleobases enantioselectively, while with others a partial racemisation took place. The latter finding contrasts with our previous results of analo-

gous reactions of nucleobases with optically pure glycidols: thus, base-catalyzed reactions of (*R*)-2,3-epoxypropyl butyrate with various heterocyclic bases (adenine, cytosine, 2,6-diaminopurine, 2-amino-6-chloropurine) gave optically pure (*R*)-2,3-dihydroxypropyl derivatives[11]. Also the oxirane ring opening in (*S*)-[(trityloxy)methyl]oxirane with various 8-substituted purine bases afforded (after deprotection of trityl group) optically pure *S* enantiomers of the corresponding 2,3-dihydroxypropyl derivatives[12].

The extent of racemization in the course of oxirane ring opening in the reactions of **2a** or **2b** with adenine, 6-chloropurine, 4-methoxy-5-methylpyrimidin-2-(1*H*)-one, 4-methoxypyrimidin-2-(1*H*)-one, cytosine, N^6-benzoyladenine and thymine in the presence of diverse bases (NaH, Cs_2CO_3, DBU) depends on the character of the heterocyclic base (Scheme 2, Table I). Thus, with adenine the reaction affords partially racemic ethyl 3-(adenin-9-yl)-2-hydroxypropanoate (**4**): with **2a** and sodium salt of adenine (by treatment with NaH) in dimethylformamide we obtained the *R* enantiomer of **4** in 75% optical purity only. With Cs_2CO_3, the *R*/*S* ratio of enantiomers in **4** was 65:35. The racemization was complete in the reaction of **2b** with the DBU salt of adenine in DMF [13]. Contrary to adenine, 6-chloropurine reacted with both oxiranes, **2a** or **2b**, in DMF in the presence of Cs_2CO_3 without racemisation and gave optically pure ethyl (*R*)-3-(6-chloropurin-9-yl)-

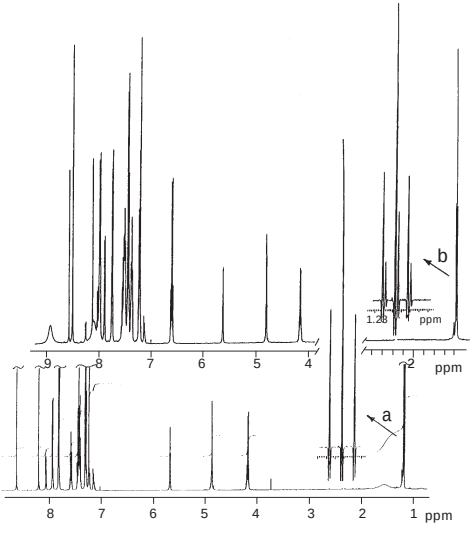


FIG. 1

^{1}H NMR spectrum of methyl protons of ethoxy group in compound **20**: a in $CDCl_3$; b after addition of (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol

2-hydroxypropanoate (**5a**) or ethyl (*S*)-3-(6-chloropurin-9-yl)-2-hydroxypropanoate (**5b**), respectively, in satisfactory yields. Under the same conditions, cytosine afforded with both enantiomers of **2** optically pure compounds **6**. Reaction of ethyl (*R*)-oxiranecarboxylate (**2a**) with 4-methoxy-5-methylpyrimidin-2(1*H*)-one and NaH in DMF afforded 95% of optically pure *R* enantiomer **7a** , while the (*S*)-oxirane **2b** gave *S* enantiomer **7b** in 85% enantiomeric purity. However, the reaction with 4-methoxypyrimidin-2(1*H*)-one gave unexpectedly nearly completely racemized compound **8** under essentially the same conditions. Direct reaction of oxiranes **2** with thymine gave a mixture of N-1 and N-3 isomers. To circumvent this problem, thymine was first converted by reaction with hexamethyldisilazane to 5-methyl-2,3-bis[(trimethylsilyl)oxy]pyrimidine and subsequently treated with oxirane **2a** in acetonitrile with $SnCl_4$ as a catalyst. This method afforded (after desilylation) ethyl (2*R*)-2-hydroxy-3-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)propanoate (**9a**) with excellent optical purity. Finally, the reaction of oxirane **2a** with N^6-benzoyladenine performed in DMF in the presence of Cs_2CO_3 gave compound **10a** without racemization, in contrast to free adenine, where all attempts to prepare an optically pure product failed (see Table I). In all cases, the exact NMR determination of the ratio of enantiomers was necessary.

TABLE I
Reaction of ethyl (*R*)-oxiranecarboxylate **2a** with various purine and pyrimidine bases

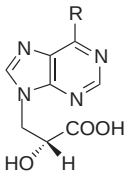
Base	Conditions	Product	Yield %	*R*:*S* ratio
Adenine	NaH, DMF, 65 °C, 2 h	**4**	40	77:23
	Cs_2CO_3, DMF, 105 °C, 2 h	**4**	31	65:35
	DBU, DMF, 110 °C, 30 min	**4**	49	44:56
6-Chloropurine	Cs_2CO_3, DMF, 105 °C, 2 h	**5**	55	100:0
Cytosine	Cs_2CO_3, DMF, 105 °C, 2 h	**6**	20–40	100:0
4-Methoxy-5-methylpyrimidin-2(1*H*)-one	NaH, DMF, 80 °C, 1.5 h	**7**	40	95:5
4-Methoxypyrimidin-2(1*H*)-one	NaH, DMF, 80 °C, 1.5 h	**8**	55	47:53
5-Methyl-2,4-bis[(trimethylsilyl)-oxy]pyrimidine	$SnCl_4$, acetonitrile, r.t.	**9**	55	100:0
N^6-Benzoyladenine	Cs_2CO_3 DMF, 105 °C, 2 h	**10**	30	100:0

Optical rotation measurement was not always very exact and useful due to extremely low values of $[\alpha]_D$ of some products, specifically 6-chloropurine and adenine derivatives.

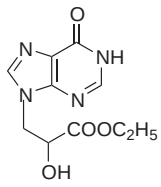
Nevertheless, consistency of signs of $[\alpha]_D$ of partially racemic adenine derivative **4** and optically pure ethyl (*R*)-3-(adenin-9-yl)-2-hydroxypropanoate described in literature[5] indicates that *R* enantiomer in compound **4** is dominant. Adenine derivative **4** obtained by methods *A*, *B* (see Experimental) was also submitted to CD spectra measurement. The course of CD curves was found identical with CD curve of authentic sample of methyl (*R*)-3-(adenin-9-yl)-2-hydroxypropanoate (obtained by oxidative degradation of 5-(adenine-9-yl)-5-deoxy-D-ribofuranose and subsequent esterification[1,6]). This is another confirmation that product **4** obtained by methods *A* and *B* is predominantly *R* enantiomer.

With respect to the known facts concerning the mechanism of the oxirane ring opening, supported by a number of our previous results, we suppose that chiral oxiranecarboxylates react with nucleobases with analogical stereochemical course as optically pure chiral glycidols[11,12]. It means that ethyl (*R*)-oxiranecarboxylate (**2a**) should react with nucleobases to *R* configurated ethyl 3-substituted-2-hydroxypropanoates, respectively *R* enantiomer should be dominant in cases with partial product racemization (see Table I). In order to verify this assumption we selected ethyl (*R*)-3-(6-chloropurin-9-yl)-2-hydroxypropanoate (**5a**), the key intermediate for further syntheses, and confirmed experimentally its absolute configuration. For this purpose compound **5a** was condensed with (+)-(*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoic acid ((*R*)-MTPA) as well as with its (–)-(*S*) enantiomer ((*S*)-MTPA) and ^{1}H NMR spectra of both so obtained diastereoisomeric esters **34** and **35** were compared. The differences of the observed chemical shifts of protons in the vicinity of chiral carbon atom are in agreement with a shielding effect of phenyl ring in the preferred conformation of corresponding MTPA-esters **34** and **35** and prove the (*R*)-configuration in starting alcohol **5a** (see Fig. 2).

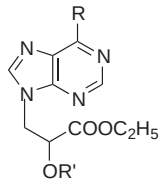
Easy availability of the optically pure 6-chloropurine derivative **5a** was exploited for the preparation of a series of N^6-substituted 3-(adenin-9-yl)-2-hydroxypropanoic acids. In order to avoid *N*-substituted carboxamide formation in aminolysis of the ester group, the ethyl esters had to be transformed first to the carboxylic acids. Attempts to remove ester groups by treatment of **5a** with bromotrimethylsilane or iodotrimethylsilane repeatedly failed. The esters were completely resistant to both reagents: heating of **5a** for several hours with a mixture of bromotrimethylsilane and potassium iodide afforded the hypoxanthine derivative **12**, while a direct reaction



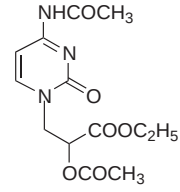
11, R = Cl



12



13, R = R' = H



21a, b

14, R = $(CH_3)_2N$-

20, R = $NHCOC_6H_5$; R' = COC_6H_5

15, R = 

22a, R = $NHCOC_6H_5$; R' = $COCH_3$

16, R = 

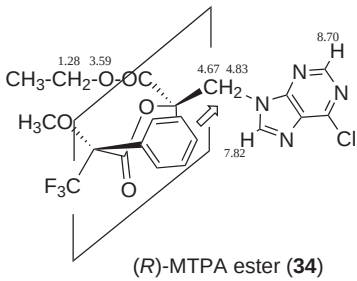
(In formulae **21**, **22**: **a** = *R* enantiomer; **b** = *S* enantiomer)

17, R = 

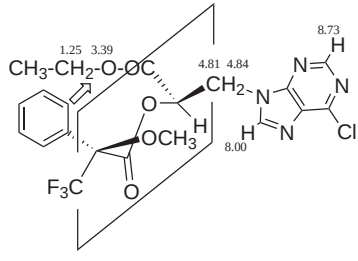
18, R = $CH_3OCH_2CH_2NH$-

19, R = $CH_2{=}CHCH_2NH$-

with iodotrimethylsilane resulted in the reductive removal of halogen and formation of purine derivative **13**; in both cases, the ester groups were preserved. Enantiomeric purity of compounds **12** and **13** was not studied. Both compounds were formed in relatively high yields. We did not find any literature precedent of such type of reaction.



(*R*)-MTPA ester (**34**)



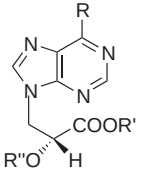
(*S*)-MTPA ester (**35**)

FIG. 2

The preferred conformation of (*R*)- and (*S*)-MTPA esters **34** and **35** of compound **5a**. Shielding effect of phenyl ring is indicated with arrows and the observed chemical shifts of involved protons confirm (*R*)-configuration of **5a**

Ester **5a** was ultimately hydrolyzed with aqueous sodium hydroxide and then acidified to give quantitatively the free acid **11**. Under the reaction conditions, there was no detectable formation of hypoxanthine derivatives.

(*R*)-3-(6-Chloropurin-9-yl)-2-hydroxypropanoic acid **11** gave on treatment with various primary and secondary amines (cyclopropylamine, pyrrolidine, morpholine, 2-methoxyethylamine, allylamine) and/or dimethylammonium dimethylcarbamate the corresponding 6-alkylaminopurine derivatives **14**–**19** as final products. For the optical purity determination of these compounds by NMR, their esterification was necessary in order to obtain compounds soluble in $CDCl_3$. This esterification had to be performed under very mild conditions to avoid product racemization. The acids **14**–**19** were transformed to their lithium salts by neutralization with LiOH and the salts were treated with excess methyl iodide or diethyl sulfate in DMF at room temperature. Under these conditions 2-methoxy or 2-ethoxy derivatives of corresponding methyl or ethyl esters **23**, **25**, **27**, **29**, **31** and **32** were obtained. The structure of these unexpected easily formed compounds was proved by their ^{1}H NMR spectra. In most cases these compounds were obtained together with esters bearing a free hydroxy group, *i.e.* compounds **24**, **26**, **28**, **30** and **33**. Both types of esters can be separated by column chromatography. The fully protected compounds **23**, **25**, **27**, **29**, **31** and **32** came out to be more suitable for ^{1}H NMR measurement with



23, R = $(CH_3)_2N$-; R' = R'' = CH_3

24, R = $(CH_3)_2N$-; R' = CH_3; R'' = H

25, R =  ; R' = R'' = CH_3

26, R = ; R' = CH_3; R'' = H

27, R =  ; R' = R'' = CH_2CH_3

28, R =  ; R' = CH_2CH_3; R'' = H

29, R =  ; R' = R'' = CH_2CH_3

30, R =  ; R' = CH_2CH_3; R'' = H

31, R = $CH_3OCH_2CH_2NH$-; R' = R'' = CH_3

32, R = CH_2=$CHCH_2NH$-; R' = R'' = CH_3

33, R = CH_2=$CHCH_2NH$-; R' = CH_3; R'' = H

(*R*)-(–)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol than esters bearing free hydroxyl group. Optical purity of the products is given in Table II. It is evident that under the conditions of aminolysis of compound **11**, no substantial racemization occurred.

In conclusion, N^6-alkyl derivatives of a biologically active compound, (*R*)-3-(adenin-9-yl)-2-hydroxypropanoic acid were prepared using of ethyl (*R*)-oxiranecarboxylate as an easily accessible three-carbon atom chiral synthon. A similar method is applicable to the synthesis of *S*-enantiomers. Biological activity tests of these compounds are under way.

EXPERIMENTAL

Unless stated otherwise, solvents were evaporated at 40 °C/2 kPa and compounds were dried at 13 Pa. Melting points were determined on a Kofler block and are uncorrected. Analytical TLC was performed on Silufol UV_{254} plates (Kavalier Votice, Czech Republic). Column chromatography was performed on silica gel 60 μm (Fluka). ^{1}H NMR spectra were recorded on a Varian UNITY 500 instrument (at 500 MHz) in DMSO-d_6 (referenced to the solvent signal at δ 2.50) or in $CDCl_3$ (with TMS as internal reference). ^{13}C NMR spectra were recorded on the same instrument (at 125.7 MHz) using APT pulse sequence in DMSO-d_6 (referenced to the solvent signal δ 39.70). Chemical shifts are given in ppm (δ-scale) and coupling constants (*J*) in Hz. (–)-(*R*)-1-(9-Anthryl)-2,2,2-trifluoroethan-1-ol (Aldrich Chem. Co.) was used as a chiral solvating agent for NMR determination of optical purity. Mass spectra were measured on ZAB-EQ (VG Analytical) spectrometer using FAB (ionization with xenon, accelerating voltage 8 kV, glycerol matrix). NMR and mass spectra of *S*-enantiomers **5b**–**7b** were identical with spectra of corresponding *R*-enantiomers. Optical rotations were measured on AUTOPOL IV polarimeter (Rudolph Research Analytical, U.S.A.) at 20 °C, $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. CD spectra were measured on a Jobin–Yvon–Spex CD6 using software CDMAX.

TABLE II
Optical purity of N^6-alkyl derivatives of (*R*)-3-(adenin-9-yl)-2-hydroxypropanoic acid **14**–**19** determined by ^{1}H NMR[a]

Compound	Ratio *R*:*S*
14	97:3
15	95:5
16	94:6
17	91:9
18	94:6
19	95:5

[a] Corresponding esters **23**, **25**, **27**, **29**, **31** and **33** were used for the determination.

Starting Materials and Solvents

All chemicals were purchased from Sigma–Aldrich (Czech Republic). N^6-Benzoyladenine was prepared according to a published procedure[14], 4-methoxypyrimidin-2(1*H*)one and 4-methoxy-5-methyl-2-pyrimidino-2(1*H*)one according to ref.[15] Dimethylformamide and acetonitrile were dried by distillation from CaH_2 (DMF *in vacuo*) and stored over molecular sieves. Silica gel was a product of Sigma (U.S.A.).

Ethyl (*S*)-2-Chloro-3-hydroxypropanoate (**3**)

A solution of sodium nitrite (19.7 g, 285.0 mmol) in water (42 ml) was added dropwise under stirring at –5 °C during 4 h to solution of L-serine (**1a**) (20.0 g, 190.0 mmol) in a mixture of water (75 ml) and 37% hydrochloric acid (40 ml). The reaction mixture was then kept at room temperature overnight and taken down *in vacuo* at 40 °C. The residue was codistilled with water (4 × 150 ml) and then absolute ethanol (150 ml) was added to precipitate NaCl. The solid material was filtered off and washed with absolute ethanol. Combined filtrates were taken down and codistilled with a mixture of benzene and absolute ethanol (5:2, 2 × 150 ml). A mixture of benzene (94 ml), absolute ethanol (40 ml) and TsOH (0.62 g, 3.2 mmol) was added to a syrupy residue. The reaction mixture was refluxed for 5 h and the volatiles distilled off under atmospheric pressure. The same volume of benzene and ethanol was added to the residue, the mixture was refluxed for additional 4 h and distilled off again. The residue was diluted with absolute ethanol (50 ml) and neutralized with Dowex 1 (HCO_3^- form). Solvents were evaporated under atmospheric pressure and the residue was then distilled in vacuum to give compound **3**. Yield 13.88 g (48%), colourless liquid, b.p. 80–85 °C (1 kPa), $[\alpha]_D^{20}$ +8.9 (*c* 1.25, ethanol). For $C_5H_9ClO_3$ (152.6) calculated: 39.36% C, 5.95% H, 23.24% Cl; found: 39.51% C, 6.10% H, 23.06% Cl. MS (EI), *m/z* (rel.%): 153 (12) [M^+]. ^{1}H NMR (DMSO-d_6): 5.45 t, 1 H, *J*(OH,3) = 6.0 (OH); 4.50 t, 1 H, *J*(2,3) = 6.0 (H-2); 4.17 q, 2 H, *J*(vic) = 7.0 (CH_2); 3.75 t, 2 H, *J*(3,2) = *J*(3,OH) = 6.0 (H-3); 1.22 t, 3 H, *J*(vic) = 7.0 (CH_3).

Ethyl (*R*)-Oxiranecarboxylate (**2a**)

The compound was prepared by a published procedure[7] from L-serine (10.5 g, 100 mmol). Yield 4.6 g (40%) of **2a** as colourless liquid. ^{1}H NMR spectrum is in agreement with ref.[16] $[\alpha]_D^{20}$ +11.9 (*c* 0.90, methanol), ref.[7] $[\alpha]_D^{20}$ +12.8.

Ethyl (*S*)-Oxiranecarboxylate (**2b**)

The compound was prepared from D-serine (5.0 g, 47.6 mmol) by the same manner as **2a**. Yield 2.5 g (45%), $[\alpha]_D^{20}$ –11.6 (*c* 0.87, methanol).

Ethyl (*RS*)-Oxiranecarboxylate (**2c**)

A solution of compound **3** (12 g, 78.6 mmol) in acetonitrile (45 ml) was heated with DBU (15.6 ml, 101.7 mmol) at 65 °C for 25 min. After cooling to room temperature, the reaction mixture was brought to pH 8 with acetic acid and taken down at 20 °C to half of its volume. This solution was applied onto a column of silica gel (300 ml) and eluted with a mixture pentane–acetone (4:1). Product-containing fractions were distilled at atmospheric pressure, the residue then distilled in vacuum (13 Pa) at 60 °C to give 3 g (33%) of **2c** as colourless liquid. ^{1}H NMR spectrum is in agreement with ref.[16] $[\alpha]_D^{20}$ +0.37 (*c* 1.32, ethanol).

Ethyl Esters **4**–**8** and **10**. General Procedure

Method A. A suspension of an appropriate nucleobase (5 mmol) and NaH dispersion in 60% paraffin oil (200 mg, 5 mmol) in DMF (15 ml) was stirred at room temperature (**7** and **8**) or at 60 °C (**4**). Oxirane **2a** or **2b** (580 mg, 5 mmol) was added and the reaction mixture was heated for 1.5–2 h (see Table I). After cooling to room temperature, the mixture was neutralized with acetic acid, taken down *in vacuo*, the residue codistilled with xylene (20 ml) and partitioned between water (50 ml) and ethyl acetate (10 × 30 ml). Combined organic extracts were dried over anhydrous sodium sulfate. The solvent was evaporated and the crude product was purified on a column of silica gel (200 ml).

Method B. A suspension of an appropriate nucleobase (5.6 mmol), oxirane **2a** or **2b** (697 mg, 6 mmol) and Cs_2CO_3 (390 mg, 1.2 mmol) in DMF (35 ml) was stirred at 105 °C for 2 h. The reaction mixture was filtered while hot through a pad of Celite, the filtrate neutralized with several drops of acetic acid and taken down *in vacuo*. The residue was codistilled with xylene (50 ml) and then partitioned between water (70 ml) and ethyl acetate (8 × 60 ml). Combined organic extracts were dried over anhydrous sodium sulfate and taken down. The crude product was purified on a column of silica gel (300 ml).

Ethyl 3-(6-Amino-9*H*-purin-9-yl)-2-hydroxypropanoate (**4**)

Methods A, B. Chromatography in the system ethyl acetate–acetone–ethanol–water (15:3:4:3) and subsequent crystallization from ethanol gave chromatographically pure partially racemic product **4**, m.p. 176–178 °C. For yields and optical purity, see Table I. Product of method *A*: $[\alpha]_D$ +7.3 (*c* 0.626, CH_3OH), ref.[5]: $[\alpha]_D$ +8.3 (*c* 0.60, CH_3OH) for pure *R* enantiomer **4**. CD spectrum: $[\Theta]_{220}$ –4000, $[\Theta]_{250}$ –200, $[\Theta]_{285}$ –1800 (*c* 4.98 × 10^{-4} mol/l, CH_3OH). CD spectrum of methyl (*R*)-3-(adenin-9-yl)-2-hydroxypropanoate[1,6]: $[\Theta]_{215}$ –2000, $[\Theta]_{250}$ +100, $[\Theta]_{285}$ –200 (*c* 1.06 × 10^{-3} mol/l, CH_3OH). Product of method *B*: $[\alpha]_D$ +1.22 (*c* 0.572, CH_3OH). CD spectrum: $[\Theta]_{220}$ –2600, $[\Theta]_{250}$ –50, $[\Theta]_{285}$ –1200 (*c* 4.98 × 10^{-4} mol/l, CH_3OH). ^{1}H NMR data (DMSO-d_6) are in agreement with ref.[5] FAB MS, *m/z* (rel.%): 252 (100) [M + H].

Method C. A suspension of adenine (1.5 mmol) and DBU (0.25 ml, 1.65 mmol) in DMF (4 ml) was heated at 110 °C untill a clear solution was obtained. Oxirane **2a** (232 mg, 2 mmol) was added and the mixture was stirred at 110 °C for 30 min. After cooling to room temperature and neutralization with acetic acid, water (1 ml) was added to the residue and the mixture taken down. The crude product was chromatographed on a column of silica gel (100 ml). For yields and optical purity, see Table I. $[\alpha]_D$ –0.5 (*c* 0.55, CH_3OH). ^{1}H NMR data (DMSO-d_6) are in agreement with ref.[5]

Ethyl (*R*)-3-(6-Chloro-9*H*-purin-9-yl)-2-hydroxypropanoate (**5a**)

From 6-chloropurine and oxirane **2a** by the method *B*. The pure product was obtained by chromatography in ethyl acetate. Yield 591 mg (39%) as an amorphous material, $[\alpha]_D$ –1.42 (*c* 0.112, CH_3OH). For $C_{10}H_{11}ClN_4O_3$ (270.7) calculated: 44.37% C, 4.10% H, 13.10% Cl, 20.70% N; found: 43.97% C, 4.18% H, 13.18% Cl, 20.42% N. FAB MS, *m/z* (rel.%): 271 (100) [M + H]. ^{1}H NMR ($CDCl_3$): 8.71 s, 1 H and 8.26 s, 1 H (H-2, H-8); 4.67 m, 2 H (H-3′a, H-3′b); 4.62 m, 1 H (H-2′); 4.23 dq, 1 H, *J*(gem) = 10.6, *J*(vic) = 7.0 and 4.18 dq, 1 H, *J*(gem) = 10.6, *J*(vic) = 7.0 (O-CH_2); 3.90 br, 1 H (OH); 1.27 t, 3 H, *J*(vic) = 7.0 (CH_3).

Ethyl (*S*)-3-(6-Chloro-9*H*-purin-9-yl)-2-hydroxypropanoate (**5b**)

From oxirane **2b** using essentially the same procedure as described for **5a**. Yield 508 mg (33%), $[\alpha]_D$ +1.1 (*c* 0.281, CH_3OH).

Ethyl (*RS*)-3-(6-Chloro-9*H*-purin-9-yl)-2-hydroxypropanoate (**5**)

From racemic oxirane **2c** in the same way as described for **5a** (method *B*). Yield 560 mg (37%). ^{1}H NMR data ($CDCl_3$) identical with **5a**. *R*:*S* 54:46 was determined by NMR.

Ethyl (*R*)-3-(4-Amino-2-oxopyrimidin-1(2*H*)-yl)-2-hydroxypropanoate (**6a**)

From cytosine and oxirane **2a** by method *B*. The crude product was chromatographed in the system ethyl acetate–acetone–ethanol–water (15:3:4:3), the product-containing fractions were combined, decolourised with active charcoal and taken down. The pure product was crystallized from methanol. Yield 255 mg (20%), m.p. 207 °C. For $C_9H_{13}N_3O_4$ (227.2) calculated: 47.57% C, 5.77% H, 18.49% N; found: 47.54% C, 5.70% H, 18.45% N. FAB MS, *m/z* (rel.%): 228 (100) [M + H]. ^{1}H NMR (DMSO-d_6): 7.44 d, 1 H, *J*(6,5) = 7.2 (H-6); 7.09 br s, 1 H and 7.02 br s, 1 H (NH_2); 5.61 d, 1 H, *J*(5,6) = 7.2 (H-5); 4.28 dd, 1 H, *J*(2′,3′a) = 4.5, *J*(2′,3′b) = 8.3 (H-2′); 4.08 q, 2 H, *J*(CH_2,CH_3) = 7.1 (O-CH_2); 4.06 dd, 1 H, *J*(3′a,2′) = 4.5, *J*(gem) = 13.4 (H-3′a); 3.57 dd, 1 H, *J*(3′b,2′) = 8.3, *J*(gem) = 13.4 (H-3′b); 1.18 t, 3 H (CH_3). ^{13}C NMR data (DMSO-d_6), see Table III.

Ethyl (*S*)-3-(4-Amino-2-oxopyrimidin-1(2*H*)-yl)-2-hydroxypropanoate (**6b**)

From oxirane **2b** by the same procedure as described for **6a**. Yield 410 mg (42%).^{1}H NMR data (DMSO-d_6) identical with **6a**.

Ethyl (*R*)-2-Hydroxy-3-(4-methoxy-5-methyl-2-oxopyrimidin-1(2*H*)-yl)propanoate (**7a**)

From oxirane **2a** and 4-methoxy-5-methylpyrimidin-2(1*H*)-one by method *A*. Chromatography in the system ethyl acetate–acetone–ethanol–water (18:3:1:1) afforded 500 mg (39%) of **7a** as colourless syrup, $[\alpha]_D$ +22.0 (*c* 0.109, CH_3OH). For $C_{11}H_{16}N_2O_5$ (256.3) calculated: 51.56% C, 6.29% H, 10.93% N; found: 51.26% C, 6.33% H, 10.99% N. FAB MS, *m/z* (rel.%): 257 (100) [M + H]. ^{1}H NMR ($CDCl_3$): 7.28 q, 1 H, *J*(6,CH_3) = 1.0 (H-6); 4.58 dd, 1 H, *J*(2′,3′a) = 3.5, *J*(2′,3′b) = 6.8 (H-2′); 4.34 dd, 1 H, *J*(3′a,3′b) = 13.8, *J*(3′a,2′) = 3.5 (H-3′a); 4.27 m, 2 H (O-CH_2); 3.97 s, 3 H (OCH_3); 3.95 dd, 1 H, *J*(3′b,3′a) = 13.8, *J*(3′b,2′) = 6.8 (H-3′b); 1.93 d, 3 H, *J*(CH_3,6) = 1.0 (5-CH_3); 1.32 t, 3 H, *J*(vic) = 7.0 (CH_3).

Ethyl (*S*)-2-Hydroxy-3-(4-methoxy-5-methyl-2-oxopyrimidin-1(2*H*)-yl)propanoate (**7b**)

From oxirane **2b** by the same procedure as described for **7a**. Yield 553 mg (43%), $[\alpha]_D$ –18.8 (*c* 0.107, CH_3OH). ^{1}H NMR data ($CDCl_3$) identical with **7a**.

Ethyl 2-Hydroxy-3-(4-methoxy-2-oxopyrimidin-1(2*H*)-yl)propanoate (**8**)

From 4-methoxypyrimidin-2(1*H*)-one and oxirane **2a** by method *A*. Chromatography in the system ethyl acetate–acetone–ethanol–water (18:3:1:1) gave 670 mg (55%) of syrupy compound **8** which crystallized on standing overnight at ambient temperature, m.p. 135–136 °C.

For $C_{10}H_{14}N_2O_5$ (242.2) calculated: 49.58% C, 5.83% H, 11.56% N; found: 49.29% C, 5.77% H, 11.78% N. FAB MS, *m/z* (rel.%): 243 (100) [M + H]. ^{1}H NMR ($CDCl_3$): 7.47 d, 1 H, *J*(6,5) = 7.2 (H-6); 5.87 d, 1 H, *J*(5,6) = 7.2 (H-5); 4.55 ddd, 1 H, *J*(2′,3′a) = 3.7, *J*(2′,3′b) = 6.6, *J*(2′,OH) = 5.3 (H-2′); 4.35 dd, 1 H, *J*(3′a,3′b) = 13.6, *J*(3′a,2′) = 3.7 (H-3′a); 4.30 dq, 1 H, *J*(gem) = 10.6, *J*(vic) = 7.2 and 4.28 dq, 1 H, *J*(gem) = 10.6, *J*(vic) = 7.2 (O-CH_2); 3.99 dd, 1 H, *J*(3′b,3′a) = 13.6, *J*(3′b,2′) = 6.6 (H-3′b); 3.96 s, 3 H (OCH_3); 3.51 d, 1 H, *J*(OH,2′) = 5.3 (OH); 1.33 t, 3 H, *J*(vic) = 7.0 (CH_3).

TABLE III
^{13}C NMR chemical shifts of compounds **6a** and **11**–**19** in DMSO-d_6

Compound	C-2	C-4	C-5	C-6	C-8	C-3′	C-2′	C-1′	Other carbons
6a	156.07	166.34	93.05	147.41	–	52.21	68.23	172.21	OCH_2: 60.64 CH_3: 14.21
11	151.71	152.29	130.85	149.09	148.33	47.01	68.37	173.01	–
12	145.68	148.62	123.86	156.79	141.15	46.46	68.84	171.58	OCH_2: 60.68 CH_3: 14.08
13	152.13	151.43	133.64	147.85	147.79	46.18	68.48	171.58	OCH_2: 60.92 CH_3: 14.03
14	151.78	150.66	119.24	154.44	140.49	47.78	70.30	174.32	NCH_3: 39.70 and 38.11
15	152.35	149.60	119.07	155.68	141.45	47.45	69.96	173.95	NCH: 24.13 CH_2: 6.64(2)
16	152.15	150.30	119.35	152.69	140.88	47.61	70.15	174.00	2×NCH_2: 48.50 and 47.11 2×CH_2: 25.88 and 23.95
17	151.73	151.04	119.08	153.37	140.94	47.63	70.09	174.53	2×OCH_2: 66.40 and 64.37 2×NCH_2: 45.00 and 43.33
18	152.28	149.30	119.01	154.63	141.41	47.74	70.60	173.92	2×OCH_2: 70.62 and 68.65 2×NCH_2: 58.23 and 58.08
19	152.32	149.00	119.05	154.44	141.43	47.52	69.98	173.78	=CH: 136.09 =CH_2: 115.09 NCH_2: 43.00

Ethyl (*R*)-3-(6-Benzamido-9*H*-purin-9-yl)-2-hydroxypropanoate (**10a**)

From N^6-benzoyladenine and **2a** by method *B*. After chromatography in ethyl acetate and crystallization from methanol, **10a** (597 mg, 30%) was isolated as white crystals, m.p. 72–77 °C, $[\alpha]_D$ +21.8 (*c* 0.313, C_2H_5OH). For $C_{17}H_{17}N_5O_4$ (355.4) calculated: 57.46% C, 4.82% H, 19.71% N; found: 57.01% C, 4.88% H, 19.21% N. FAB MS, *m/z* (rel.%): 356 (100) [M + H]. ^{1}H NMR ($CDCl_3$): 9.38 br, 1 H (NH); 8.72 s, 1 H and 8.11 s, 1 H (H-2, H-8); 8.00 m, 2 H, 7.46 m, 2 H and 7.56 m, 1 H (C_6H_5); 4.68 dd, 1 H, *J*(2′,3′a) = 3.4, *J*(2′,3′b) = 6.8 (H-2′); 4.67 dd, 1 H, *J*(3′a,3′b) = 14.4, *J*(3′a,2′) = 3.4 (H-3′a); 4.59 dd, 1 H, *J*(3′b,3′a) = 14.4, *J*(3′b,2′) = 6.8 (H-3′b); 4.13 m, 2 H (-OCH_2); 1.26 t, 3 H, *J*(vic) = 7.0 (CH_3).

Ethyl (*R*)-2-Hydroxy-3-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)propanoate (**9a**)

5-Methyl-2,4-bis[(trimethylsilyl)oxy]pyrimidine[17] (1.87 g, 6.9 mmol) and stannic chloride (0.5 ml, 2.7 mmol) were added to a stirred solution of **2a** (800 mg, 6.9 mmol) in acetonitrile (35 ml) at 0 °C under argon. The mixture was stirred at room temperature for 3 h and then set aside at 4 °C overnight. After dilution with chloroform (100 ml), the mixture was poured into a saturated solution of sodium hydrogencarbonate (100 ml) and filtered through a pad of Celite. The organic layer was separated, the aqueous phase was extracted with chloroform (8 × 40 ml). The combined extracts were dried over anhydrous magnesium sulfate and taken down. The residue gave by chromatography on a silica gel column (360 ml) in the system ethyl acetate–acetone–ethanol–water (36:6:1:1) 919 mg (55%) of **9a** as a syrup that crystallized after standing overnight, $[\alpha]_D$ +26.2 (*c* 0.137, CH_3OH). For $C_{10}H_{14}N_2O_5$ (242.2) calculated: 49.58% C, 5.83% H, 11.56% N; found: 49.57% C, 5.83% H, 11.44% N. FAB MS, *m/z* (rel.%): 243 (100) [M + H]. ^{1}H NMR ($CDCl_3$): 8.51 br, 1 H (NH); 7.11 q, 1 H, *J*(6,CH_3) = 1.1 (H-6); 4.46 dt, 1 H, *J*(2′,3′a) = 4.0, *J*(2′,3′b) = 6.4, *J*(2′,OH) = 4.0 (H-2′); 4.31 dq, 1 H, *J*(gem) = 10.7, *J*(vic) = 7.2 and 4.27 dq, 1 H, *J*(gem) = 10.7, *J*(vic) = 7.2 (O-CH_2); 4.14 dd, 1 H, *J*(3′a,3′b) = 14.2, *J*(3′a,2′) = 4.0 (H-3′a); 3.91 dd, 1 H, *J*(3′b,3′a) = 14.2, *J*(3′b,2′) = 6.4 (H-3′b); 3.39 br, 1 H (OH); 1.33 t, 3 H, *J*(vic) = 7.0 (CH_3).

(*R*)-3-(6-Chloro-9*H*-purin-9-yl)-2-hydroxypropanoic Acid (**11**)

A solution of ester **5a** (1.0 g, 3.69 mmol) in 0.5 M aqueous sodium hydroxide solution (15 ml) was stirred at room temperature for 10 min and then made weakly acidic with Dowex 50X4 (H form). The resin was filtered off, the filtrate taken down and codistilled with absolute ethanol (2 × 30 ml) to give 900 mg (100%) of free acid **11** as a solid foam, $[\alpha]_D$ +12.4 (*c* 0.611, C_2H_5OH). For $C_8H_7ClN_4O_3$ (242.6) calculated: 39.60% C, 2.91% H, 14.61% Cl, 23.09% N; found: 39.54% C, 3.16% H, 13.92% Cl, 22.44% N. FAB MS, *m/z* (rel.%): 243 (65) [M + H]. ^{1}H NMR (DMSO-d_6): 8.78 s, 1 H and 8.61 s, 1 H (H-2 and H-8); 7.00 br, 2 H (OH + COOH); 4.60 m, 1 H and 4.45 m, 2 H (H-3′ and H-2′). ^{13}C NMR data (DMSO-d_6), see Table III.

Ethyl 2-Hydroxy-3-(6-oxo-1,6-dihydro-9*H*-purin-9-yl)propanoate (**12**)

Bromotrimethylsilane (382 mg, 2.5 mmol) was added to a solution of ester **5a** (76 mg, 0.28 mmol) in DMF under argon. After stirring at room temperature overnight (no reaction took place according to TLC), potassium iodide (20 mg, 0.12 mmol) was added and the stirring was continued at room temperature for 2 days followed by heating at 75 °C for 8 h.

The reaction mixture was neutralized with 2 M triethylammonium hydrogencarbonate and taken down *in vacuo* and the residue was codistilled with water (3 × 5 ml). The crude product was purified by C_{18} reverse phase chromatography. After elution of salts with water, the product was eluted with a methanol–water gradient (0–30% methanol). Product-containing fractions were taken down and codistilled with ethanol to give 60 mg (85%) of **12** as white solid material. ^{1}H NMR (DMSO-d_6): 12.30 br s, 1 H (=NH); 8.04 s, 1 H and 7.99 s, 1 H (H-2, H-8); 6.03 d, 1 H, *J*(OH,2′) = 5.4 (2′-OH); 4.45 m, 1 H (H-2′); 4.41 dd, 1 H, *J*(3′a,2′) = 4.4, *J*(gem) = 13.8 (H-3′a); 4.30 dd, 1 H, *J*(3′b,2′) = 7.4, *J*(gem) = 13.8 (H-3′b); 4.07 m, 2 H (O-CH_2); 1.13 t, 3 H, *J*(vic) = 7.1 (CH_3). ^{13}C NMR data (DMSO-d_6), see Table III.

Ethyl 2-Hydroxy-3-(9*H*-purin-9-yl)propanoate (**13**)

Iodotrimethylsilane (0.57 ml, 4.0 mmol) was added under argon to a stirred suspension of ester **5a** (120 mg, 0.44 mmol) in acetonitrile (4 ml). The resulting solution was stirred in the dark at room temperature for 12 h, then neutralized with 2 M solution of triethylammonium hydrogencarbonate and subsequently worked up as described for compound **12**. Yield 70 mg (67%) of **13** as a white solid. ^{1}H NMR (DMSO-d_6): 9.15 s, 1 H (H-6); 8.93 s, 1 H (H-2); 8.53 s, 1 H (H-8); 6.08 d, 1 H, *J*(OH,2′) = 5.6 (OH); 4.56 m, 2 H and 4.48 m, 1 H (H-3′, H-2′); 4.06 m, 2 H (O-CH_2); 1.10 t, 3 H, *J*(vic) = 7.1 (CH_3). ^{13}C NMR data (DMSO-d_6), see Table III.

3-[6-(Alkylamino)-9*H*-purin-9-yl]-2-hydroxypropanoic Acids **14**–**19**. General Procedure

A suspension of chloro compound **11** (400 mg, 1.65 mmol) in acetonitrile (30 ml) was refluxed with excess of dimethylammonium dimethylcarbamate (6.0 mmol) or appropriate amine (cyclopropylamine, pyrrolidine, morpholine, 2-methoxyethylamine and allylamine) (8.0 mmol) for 30 min. After cooling to room temperature, the mixture was taken down, the residue was then codistilled with toluene (2 × 10 ml), ethanol (15 ml) and applied onto a Dowex 50 (H form, 100 ml). The column was eluted with water (1000 ml) and then with 2.5% aqueous ammonia. Product-containing fractions of the ammonia eluate were evaporated, the residue codistilled with ethanol (3 × 15 ml) and dried at 50 °C *in vacuo*.

(R)-3-[6-(Dimethylamino)-9H-purin-9-yl]-2-hydroxypropanoic acid (**14**). Yield 315 mg (76%) as a solid foam, $[\alpha]_D$ +41.7 (*c* 0.532, CH_3OH). HR MS (FAB): for $C_{10}H_{14}N_5O_3$ [M + H] calculated 252.1097, found 252.1076. FAB MS, *m/z* (rel.%): 252 (45) [M + H]. ^{1}H NMR (DMSO-d_6): 8.19 s, 1 H and 8.05 s, 1 H (H-2, H-8); 7.40 br, 2 H (OH + COOH); 4.50 dd, 1 H, *J*(3′a,2′) = 3.0, *J*(gem) = 13.7 (H-3′a); 4.04 dd, 1 H, *J*(3′b,2′) = 8.4, *J*(gem) = 13.7 (H-3′b); 3.97 dd, 1 H, *J*(2′,3′a) = 3.0, *J*(2′,3′b) = 8.4 (H-2′); 3.42 br s, 6 H (N(CH_3)$_2$). ^{13}C NMR data (DMSO-d_6), see Table III.

(R)-3-[6-(Cyclopropylamino)-9H-purin-9-yl]-2-hydroxypropanoic acid (**15**). Yield 139 mg (32%) as a solid foam, $[\alpha]_D$ +29.8 (*c* 0.532, CH_3OH). HR MS (FAB): for $C_{11}H_{14}N_5O_3$ [M + H] calculated 264.1097, found 264.1066. FAB MS, *m/z* (rel.%): 264 (40) [M + H]. ^{1}H NMR (DMSO-d_6): 8.23 s, 1 H and 8.04 s, 1 H (H-2, H-8); 7.83 br s, 1 H (NH); 7.30 br, 2 H (OH + COOH); 4.49 m, 1 H and 4.08 m, 2 H (H-3′, H-2′); 3.05 m, 1 H (NCH); 0.71 m, 2 H and 0.60 m, 2 H (2 × CH_2-cyclopropyl). ^{13}C NMR data (DMSO-d_6), see Table III.

(R)-2-Hydroxy-3-(6-pyrrolidin-1-yl-9H-purin-9-yl)propanoic acid (**16**). Yield 407 mg (89%) as a solid foam, $[\alpha]_D$ +29.3 (*c* 1.320, CH_3OH). HR MS (FAB): for $C_{12}H_{16}N_5O_3$ [M + H] calculated 278.1253, found 278.1183. FAB MS, *m/z* (rel.%): 278 (100) [M + H]. ^{1}H NMR (DMSO-d_6): 8.18 s, 1 H and 8.02 s, 1 H (H-2, H-8); 7.40 br, 2 H (OH + COOH); 4.49 dd, 1 H, *J*(3′a,2′) = 3.0, *J*(gem) = 13.6 (H-3′a); 4.03 dd, 1 H, *J*(3′b,2′) = 8.4, *J*(gem) = 13.6 (H-3′b); 4.02 m, 2 H

and 3.60 m, 2 H (2 × N-CH_2); 3.97 dd, 1 H, *J*(2′,3′a) = 3.0, *J*(3′b,2′) = 8.4 (H-2′); 1.92 m, 4 H (CH_2CH_2). ^{13}C NMR data (DMSO-d_6), see Table III.

(R)-2-Hydroxy-3-(6-morpholino-9H-purin-9-yl)propanoic acid (**17**). The product was isolated as morpholinium salt. Yield 400 mg (64%) as a solid foam. Recrystallization from ethanol gave compound **17**, m.p. 144–147 °C, $[\alpha]_D$ +38.5 (*c* 0.259, C_2H_5OH). HR MS (FAB): for $C_{12}H_{16}N_5O_4$ [M + H] calculated 294.1202, found 294.1185. FAB MS, *m/z* (rel.%): 294 (16) [M + H of the free acid], 88 (100), [M + H of morpholine]. ^{1}H NMR (DMSO-d_6): 8.24 s, 1 H and 8.10 s, 1 H (H-2, H-8); 6.80 br, 2 H (OH + COOH); 4.50 dd, 1 H, *J*(3′a,2′) = 3.3, *J*(gem) = 13.7 (H-3′a); 4.10 dd, 1 H, *J*(3′b,2′) = 8.3, *J*(gem) = 13.7 (H-3′b); 4.00 dd, 1 H, *J*(2′,3′a) = 3.3, *J*(2′,3′b) = 8.3 (H-2′); 4.19 m, 2 H, 3.70 t, 2 H, 3.69 t, 2 H and 2.98 t, 2 H (2 × OCH_2 and 2 × NCH_2, morpholine). ^{13}C NMR data (DMSO-d_6), see Table III.

(R)-2-Hydroxy-3-{6-[(2-methoxyethyl)amino]-9H-purin-9-yl}propanoic acid (**18**). The product was isolated as 2-methoxyethylammonium salt. Yield 418 mg (59%), amorphous material, $[\alpha]_D$ +31.5 (*c* 0.545, CH_3OH). HR MS (FAB): for $C_{11}H_{16}N_5O_4$ [M + H] calculated 282.1202, found 282.1235. FAB MS, *m/z* (rel.%): 282 (70) [M + H of the free acid], 76 (100) [M + H of 2-methoxyethylamine). ^{1}H NMR (DMSO-d_6): 8.20 s, 1 H and 8.04 s, 1 H (H-2, H-8); 7.56 br s, 1 H (NH); 7.00 br, 2 H (OH + COOH); 4.48 dd, 1 H, *J*(3′a,2′) = 2.9, *J*(gem) = 13.7 (H-3′a); 4.03 dd, 1 H, *J*(3′b,2′) = 8.4, *J*(gem) = 13.7 (H-3′b); 3.93 dd, 1 H, *J*(2′,3′a) = 2.9, *J*(2′,3′b) = 8.4 (H-2′); 3.64 m, 2 H, 3.51 t, 2 H, 3.50 t, 2 H and 2.95 t, 2 H (2 × NCH_2-CH_2O); 3.51 s, 3 H and 3.50 s, 3 H (2 × OCH_3). ^{13}C NMR data (DMSO-d_6), see Table III.

(R)-3-[6-(Allylamino)-9H-purin-9-yl]-2-hydroxypropanoic acid (**19**). Yield 308 mg (71%) as a solid foam, $[\alpha]_D$ +36.0 (*c* 0.434, CH_3OH). HR MS (FAB): for $C_{11}H_{14}N_5O_3$ [M + H] calculated 264.1097, found 264.1115. FAB MS, *m/z* (rel.%): 264 (100) [M + H]. ^{1}H NMR (DMSO-d_6): 8.19 s, 1 H and 8.05 s, 1 H (H-2, H-8); 7.85 br s, 1 H (NH); 7.20 br, 1 H (OH); 5.95 ddt, 1 H, *J*(2″,1″) = 5.1, *J*(2″,3″a) = 10.3, *J*(2″,3″b) = 17.2 (H-2″); 5.15 dq, 1 H, *J*(3″b,1″) = *J*(gem) = 1.8, *J*(3″b,2″) = 17.2 (H-3″b); 5.04 dq, 1 H, *J*(3″a,1″) = 1.6, *J*(3″a,2″) = 10.3, *J*(gem) = 1.8 (H-3″a); 4.48 dd, 1 H, *J*(3′a,2′) = 2.7, *J*(gem) = 13.2 (H-3′a); 4.15 m, 2 H (H-1″); 4.07 dd, 1 H, *J*(3′b,2′) = 8.6, *J*(gem) = 13.2 (H-3′b); 4.02 dd, 1 H, *J*(2′,3′a) = 2.7, *J*(2′,3′b) = 8.6 (H-2′). ^{13}C NMR data (DMSO-d_6), see Table III.

Ethyl 3-(6-Benzamido-9*H*-purin-9-yl)-2-(benzoyloxy)propanoate (**20**)

Benzoyl chloride (0.03 ml, 0.25 mmol) was added to a solution of compound **4** (28 mg, 0.11 mmol) in pyridine (1 ml). The mixture was set aside overnight at room temperature, ethanol (1 ml) was added and the mixture taken down. The residue was partitioned between water (10 ml) and ethyl acetate (2 × 10 ml), the organic extracts were dried over anhydrous sodium sulfate and taken down. The residue was chromatographed on a column of silica gel (20 ml) in the system toluene–ethyl acetate 3:2. Yield 35 mg (69%) as colourless oil. ^{1}H NMR ($CDCl_3$): 8.63 s, 1 H and 8.22 s, 1 H (H-2, H-8); 7.20–8.10 m, 10 H (2 × C_6H_5); 5.70 dd, 1 H, *J*(2′,3′a) = 4.5, *J*(2′,3′b) = 5.6 (H-2′); 4.91 dd, 1 H, *J*(3′a,3′b) = 14.7, *J*(3′a,2′) = 4.5 (H-3′a); 4.88 dd, 1 H, *J*(3′b,3′a) = 14.7, *J*(3′b,2′) = 5.6 (H-3′b); 4.22 dq, 1 H, *J*(gem) = 10.7, *J*(vic) = 7.2 and 4.20 dq, 1 H, *J*(gem) = 10.7, *J*(vic) = 7.2 (OCH_2); 1.22 t, 3 H, *J*(vic) = 7.2 (CH_3).

Acetylation of Compounds **6** and **10**

Acetic anhydride (51 mg, 0.5 mmol) and 4-(dimethylamino)pyridine (5 mg, 0.04 mmol) were added to a suspension of **6a**, **6b** or **10a** (0.22 mmol) in acetonitrile (3 ml). The reaction

mixture was stirred at room temperature for 2 h, then diluted with ethanol (1 ml) and taken down. The residue was chromatographed on a column of silica gel (20 ml) in system ethyl acetate–acetone–ethanol–water (18:3:1:1).

Ethyl (R)-3-(4-acetamido-2-oxopyrimidin-1(2H)-yl)-2-acetoxypropanoate (**21a**). From **6a**, yield 35 mg (51%) as a solid foam. FAB MS, *m/z* (rel.%): 312 (100) [M + H]. ^{1}H NMR ($CDCl_3$): 9.54 bs, 1 H (NH); 7.59 d, 1 H, *J*(6,5) = 7.4 (H-6); 7.42 d, 1 H, *J*(5,6) = 7.4 (H-5); 5.39 dd, 1 H, *J*(2′,3′a) = 4.1, *J*(2′,3′b) = 7.9 (H-2′); 4.52 dd, 1 H, *J*(3′a,3′b) = 13.9, *J*(3′a,2′) = 4.1 (H-3′a); 4.26 dq, 1 H, *J*(gem) = 10.7, *J*(vic) = 7.2 and 4.23 dq, 1 H, *J*(gem) = 10.7, *J*(vic) = 7.2 (O-CH_2); 4.08 dd, 1 H, *J*(3′b,3′a) = 13.9, *J*(3′b,2′) = 7.9 (H-3′b); 2.28 s, 3 H (N-CO-CH_3); 2.12 s, 3 H (O-CO-CH_3); 1.30 t, 3 H, *J*(vic) = 7.2 (CH_3).

Ethyl (S)-3-(4-acetamido-2-oxopyrimidin-1(2H)-yl)-2-acetoxypropanoate (**21b**). From **6b**, yield 41 mg (60%) as a solid foam. FAB MS, *m/z* (rel.%): 312 (100) [M + H]. ^{1}H NMR ($CDCl_3$): 9.54 bs, 1 H (NH); 7.61 d, 1 H, *J*(6,5) = 7.4 (H-6); 7.45 d, 1 H, *J*(5,6) = 7.4 (H-5); 5.39 dd, 1 H, *J*(2′,3′a) = 4.1, *J*(2′,3′b) = 8.0 (H-2′); 4.52 dd, 1 H, *J*(3′a,3′b) = 13.8, *J*(3′a,2′) = 4.1 (H-3′a); 4.25 dq, 1 H, *J*(gem) = 10.7, *J*(vic) = 7.2 and 4.22 dq, 1 H, *J*(gem) = 10.7, *J*(vic) = 7.2 (O-CH_2); 4.09 dd, 1 H, *J*(3′b,3′a) = 13.8, *J*(3′b,2′) = 8.0 (H-3′b); 2.30 s, 3 H (N-CO-CH_3); 2.12 s, 3 H (O-CO-CH_3); 1.29 t, 3 H, *J*(vic) = 7.2 (CH_3).

Ethyl (R)-2-acetoxy-3-(6-benzamido-9H-purin-9-yl)propanoate (**22a**). From **10a**, yield 63 mg (72%) as a solid foam. FAB MS, *m/z* (rel.%): 398 (47) [M + H], 105 (100) [M^+ benzoyl]. ^{1}H NMR ($CDCl_3$): 9.06 bs, 1 H (NH); 8.80 s, 1 H and 8.08 s, 1 H (H-2, H-8); 8.03 m, 2 H, 7.61 m, 1 H and 7.53 m, 2 H (C_6H_5); 5.47 dd, 1 H, *J*(2′,3′a) = 4.2, *J*(2′,3′b) = 6.3 (H-2′); 4.80 dd, 1 H, *J*(3′a,3′b) = 15.7, *J*(3′a,2′) = 4.2 (H-3′a); 4.74 dd, 1 H, *J*(3′b,3′a) = 15.7, *J*(3′b,2′) = 6.3 (H-3′b); 4.21 m, 2 H (OCH_2); 2.12 s, 3 H (O-CO-CH_3); 1.26 t, 3 H, *J*(vic) = 7.2 (CH_3).

Esterification of Compounds **14**–**19**. General Procedure

Lithium hydroxide monohydrate (8.4 mg, 0.2 mmol) was added to a solution of carboxylic acid **14**–**19** (0.2 mmol) in absolute methanol (5 ml), the solution taken down and the residue codistilled with DMF (2 × 5 ml). DMF (5 ml) and methyl iodide (0.03 ml, 0.5 mmol) or diethyl sulfate (0.06 ml, 0.5 mmol) were added and the reaction mixture stirred at room temperature for 2–12 h. The reaction course was monitored by TLC in system ethyl acetate–acetone–ethanol–water (15:3:4:3). Acetic acid (one drop) was added, the reaction mixture taken down and the residue codistilled with xylene (4 ml). The crude mixtures of dimethyl and monomethyl derivatives (**23** and **24**, **25** and **26**, **31** and **32**, **33** and **34**) and mixtures of diethyl and monoethyl derivatives (**27** and **28**, **29** and **30**) were separated on a column of silica gel (20 ml) in system ethyl acetate–acetone–ethanol–water (18:3:1:1). In all cases 2-alkoxy esters (**23**, **25**, **27**, **29**, **31** and **33**) were eluted first.

Methyl (R)-3-[6-(dimethylamino)-9H-purin-9-yl]-2-methoxypropanoate (**23**). Yield 15 mg (27%) as a colourless oil. FAB MS, *m/z* (rel.%): 280 (100) [M + H]. ^{1}H NMR ($CDCl_3$): 8.35 s, 1 H and 7.80 s, 1 H (H-2, H-8); 4.63 dd, 1 H, *J*(3′a,3′b) = 14.4, *J*(3′a,2′) = 3.7 (H-3′a); 4.34 dd, 1 H, *J*(3′b,3′a) = 14.4, *J*(3′b,2′) = 7.9 (H-3′b); 4.17 dd, 1 H, *J*(2′,3′a) = 3.7, *J*(2′,3′b) = 7.9 (H-2′); 3.77 s, 3 H ($COOCH_3$); 3.54 vb, 6 H ($N(CH_3)_2$); 3.39 s, 3 H (OCH_3).

Methyl (R)-3-[6-(dimethylamino)-9H-purin-9-yl]-2-hydroxypropanoate (**24**). Yield 26 mg (49%) as a white solid. FAB MS, *m/z* (rel.%): 266 (55) [M + H]. ^{1}H NMR ($CDCl_3$): 8.31 s, 1 H and 7.74 s, 1 H (H-2, H-8); 5.20 vb, 1 H (OH); 4.64 dd, 1 H, *J*(2′,3′a) = 3.8, *J*(2′,3′b) = 4.7 (H-2′); 4.56 m, 2 H (H-3′a, H-3′b); 3.73 s, 3 H ($COOCH_3$); 3.52 vb, 6 H ($N(CH_3)_2$).

Methyl (R)-3-[6-(cyclopropylamino)-9H-purin-9-yl]-2-methoxypropanoate (**25**). Yield 13 mg (22%) as a colourless oil. FAB MS, *m/z* (rel.%): 292 (100) [M + H]. ^{1}H NMR ($CDCl_3$): 8.49 s, 1 H and 7.73 s, 1 H (H-2, H-8); 4.62 dd, 1 H, *J*(3′a,3′b) = 14.4, *J*(3′a,2′) = 3.6 (H-3′a); 4.37 dd, 1 H, *J*(3′b,3′a) = 14.4, *J*(3′b,2′) = 7.7 (H-3′b); 4.17 dd, 1 H, *J*(2′,3′a) = 3.6, *J*(2′,3′b) = 7.7 (H-2′); 3.77 s, 3 H ($COOCH_3$); 3.40 s, 3 H (OCH_3); 3.05 b, 1 H, 0.93 m, 2 H and 0.67 m, 2 H (cyclopropyl); 2.10 vb, 1 H (NH).

Methyl (R)-3-[6-(cyclopropylamino)-9H-purin-9-yl]-2-hydroxypropanoate (**26**). Yield 26 mg (47%) as a white solid. FAB MS, *m/z* (rel.%): 278 (62) [M + H]. ^{1}H NMR ($CDCl_3$): 8.41 s, 1 H and 7.72 s, 1 H (H-2, H-8); 6.16 bs, 1 H and 5.39 b, 1 H (NH and OH); 4.64 dd, 1 H, *J*(3′a,3′b) = 15.8, *J*(3′a,2′) = 4.3 (H-3′a); 4.63 m, 1 H (H-2′); 4.50 dd, 1 H, *J*(3′b,3′a) = 15.8, *J*(3′b,2′) = 5.4 (H-3′b); 3.84 s, 3 H ($COOCH_3$); 2.96 b, 1 H, 0.89 m, 2 H, 0.70 m, 1 H and 0.67 m, 1 H (cyclopropyl).

Ethyl (R)-2-ethoxy-3-(6-pyrrolidin-1-yl-9H-purin-9-yl)propanoate (**27**). Yield 15 mg (23%) as a colourless oil. ^{1}H NMR ($CDCl_3$): 8.36 s, 1 H and 7.84 s, 1 H (H-2, H-8); 4.64 dd, 1 H, *J*(3′a,3′b) = 14.2, *J*(3′a,2′) = 3.6 (H-3′a); 4.32 dd, 1 H, *J*(3′b,3′a) = 14.2, *J*(3′b,2′) = 8.4 (H-3′b); 4.23 dd, 1 H, *J*(2′,3′a) = 3.6, *J*(2′,3′b) = 8.4 (H-2′); 4.23 q, 2 H, *J*(vic) = 7.0 ($COOC\mathbf{H}_2CH_3$); 4.20 um, 2 H, 3.75 um, 2 H and 2.04 um, 4 H (pyrrolidine); 3.71 dq, 1 H, *J*(gem) = 9.0, *J*(vic) = 7.0 and 3.34 dq, 1 H, *J*(gem) = 9.0, *J*(vic) = 7.0 ($OC\mathbf{H}_2CH_3$); 1.28 t, 3 H, *J*(vic) = 7.0 ($COOCH_2C\mathbf{H}_3$); 1.13 t, 3 H, *J*(vic) = 7.0 ($OCH_2C\mathbf{H}_3$).

Ethyl (R)-2-hydroxy-3-(6-pyrrolidin-1-yl-9H-purin-9-yl)propanoate (**28**). Yield 29 mg (47%) as a white solid material. FAB MS, *m/z* (rel.%): 306 (100) [M + H]. ^{1}H NMR ($CDCl_3$): 8.31 s, 1 H and 7.84 s, 1 H (H-2, H-8); 4.63 dd, 1 H, *J*(2′,3′a) = 3.8, *J*(2′,3′b) = 4.8 (H-2′); 4.55 m, 2 H (H-3′a, H-3′b); 4.17 m, 2 H ($O\text{-}CH_2$); 4.15 um, 2 H, 3.75 um, 2 H and 2.05 um, 4 H (pyrrolidine); 1.22 t, 3 H, *J*(vic) = 7.0 (CH_3).

Ethyl (R)-2-ethoxy-3-(6-morpholino-9H-purin-9-yl)propanoate (**29**). Yield 15 mg (21%) as a colourless oil. FAB MS, *m/z* (rel.%): 350 (100) [M + H]. ^{1}H NMR ($CDCl_3$): 8.36 s, 1 H and 7.86 s, 1 H (H-2, H-8); 4.65 dd, 1 H, *J*(3′a,3′b) = 14.2, *J*(3′a,2′) = 3.6 (H-3′a); 4.33 dd, 1 H, *J*(3′b,3′a) = 14.2, *J*(3′b,2′) = 8.2 (H-3′b); 4.30 m, 4 H and 3.84 m, 4 H (morpholine); 4.22 dd, 1 H, *J*(2′,3′a) = 3.6, *J*(2′,3′b) = 8.2 (H-2′); 4.22 q, 2 H, *J*(vic) = 7.2 ($COOC\mathbf{H}_2CH_3$); 3.71 dq, 1 H, *J*(gem) = 9.0, *J*(vic) = 7.0 and 3.35 dq, 1 H, *J*(gem) = 9.0, *J*(vic) = 7.0 ($OC\mathbf{H}_2CH_3$); 1.28 t, 3 H, *J*(vic) = 7.2 ($COOCH_2C\mathbf{H}_3$); 1.14 t, 3 H, *J*(vic) = 7.0 ($OCH_2C\mathbf{H}_3$).

Ethyl (R)-2-hydroxy-3-(6-morpholino-9H-purin-9-yl)propanoate (**30**). Yield 31 mg (48%) as a white solid. FAB MS, *m/z* (rel.%): 322 (100) [M + H]. ^{1}H NMR ($CDCl_3$): 8.32 s, 1 H and 7.78 s, 1 H (H-2, H-8); 4.61 dd, 1 H, *J*(2′,3′a) = 3.7, *J*(2′,3′b) = 5.0 (H-2′); 4.56 m, 2 H (H-3′a, H-3′b); 4.30 m, 4 H and 3.83 m, 4 H (morpholine); 4.20 dq, 1 H, *J*(gem) = 10.8, *J*(vic) = 7.1 and 4.16 dq, 1 H, *J*(gem) = 10.8, *J*(vic) = 7.1 (OCH_2); 1.24 t, 3 H, *J*(vic) = 7.1 (CH_3).

Methyl (R)-2-methoxy-3-{6-[(2-methoxyethyl)amino]-9H-purin-9-yl}propanoate (**31**). Yield 5 mg (8%) as a colourless oil. ^{1}H NMR ($CDCl_3$): 8.36 s, 1 H and 7.80 s, 1 H (H-2, H-8); 4.62 dd, 1 H, *J*(3′a,3′b) = 14.3, *J*(3′a,2′) = 3.6 (H-3′a); 4.33 dd, 1 H, *J*(3′b,3′a) = 14.3, *J*(3′b,2′) = 7.9 (H-3′b); 4.25 bs, 1 H (NH); 4.17 dd, 1 H, *J*(2′,3′a) = 3.6, *J*(2′,3′b) = 7.9 (H-2′); 3.78 s, 3 H ($COOCH_3$); 3.71 t, 2 H, *J*(vic) = 5.5 (OCH_2); 3.55 um, 2 H ($N\text{-}CH_2$); 3.39 s, 3 H ($O\text{-}CH_3$); 3.37 s, 3 H (OCH_3).

Methyl (R)-3-[6-(allylamino)-9H-purin-9-yl]-2-methoxypropanoate (**32**). Yield 17 mg (29%) as a white solid material. FAB MS, *m/z* (rel.%): 291 (52) [M^+], 276 (100) [M – CH_3]. ^{1}H NMR ($CDCl_3$): 8.41 s, 1 H and 7.84 s, 1 H (H-2, H-8); 6.10 bt, 1 H, *J*(NH,CH_2) = 5.5 (NH); 6.02 m, 1 H, 5.31 dq, 1 H and 5.19 dq, 1 H ($CH{=}CH_2$); 4.63 dd, 1 H, *J*(3′a,3′b) = 14.4, *J*(3′a,2′) = 3.6

(H-3′a); 4.37 dd, 1 H, *J*(3′b,3′a) = 14.4, *J*(3′b,2′) = 7.8 (H-3′b); 4.33 m, 1 H (NCH_2); 4.18 dd, 1 H, *J*(2′,3′a) = 3.6, *J*(2′,3′b) = 7.8 (H-2′); 3.77 s, 3 H ($COOCH_3$); 3.40 s, 3 H (OCH_3).

Methyl (R)-3-[6-(allylamino)-9H-purin-9-yl]-2-hydroxypropanoate (**33**). Yield 16 mg (29%) as a white solid material. FAB MS, *m/z* (rel.%): 277 (30) [M^+], 262 (55) [M – CH_3]. ^{1}H NMR ($CDCl_3$): 8.33 s, 1 H and 7.53 s, 1 H (H-2, H-8); 6.18 b, 1 H (NH); 5.99 m, 1 H, 5.28 dq, 1 H and 5.18 dq, 1 H (CH=CH_2); 5.45 b, 1 H (OH); 4.64 dd, 1 H, *J*(2′,3′a) = 4.7, *J*(2′,3′b) = 3.5 (H-2′); 4.61 dd, 1 H, *J*(3′a,3′b) = 14.1, *J*(3′a,2′) = 4.7 (H-3′a); 4.52 dd, 1 H, *J*(3′b,3′a) = 14.1, *J*(3′b,2′) = 3.5 (H-3′b); 4.26 b, 1 H and 4.18 b, 1 H (NCH_2); 3.80 s, 3 H ($COOCH_3$).

(*R*)-1-[(6-Chloro-9*H*-purin-9-yl)methyl]-2-ethoxy-2-oxoethyl
(*R*)-3,3,3-Trifluoro-2-methoxy-2-phenylpropanoate (**34**)

(+)-(*R*)-2-Methoxy-3,3,3-trifluoro-2-phenylpropanoic acid (8 mg, 0.034 mmol), dicyclohexylcarbodiimide (7 mg, 0.034 mmol) and 4-(dimethylamino)pyridine (0.5 mg, 0.004 mmol) were added to a solution of **5a** (9 mg, 0.034 mmol) in dichloromethane (0.1 ml). The reaction mixture was stirred at room tempetature for 2 h and then taken down. The residue was applied onto a column of silica gel (5 ml) and chromatographed in system petrolether–ethyl acetate 1:1. Yield 11 mg (66%) as a colourless oil. ^{1}H NMR ($CDCl_3$): 8.70 s, 1 H (H-2); 7.82 s, 1 H (H-8); 7.31–7.44 m, 5 H (C_6H_5); 5.66 dd, 1 H, *J*(2′,3′a) = 6.8, *J*(2′,3′b) = 3.6 (H-2′); 4.83 dd, 1 H, *J*(3′a,3′b) = 15.0, *J*(3′a,2′) = 6.8 (H-3′a); 4.67 dd, 1 H, *J*(3′b,3′a) = 15.0, *J*(3′b,2′) = 3.6 (H-3′b); 4.24 m, 2 H ($OC\mathbf{H}_2CH_3$); 3.59 q, 3 H, *J*(OCH_3,F) = 1.3 (OCH_3); 1.28 t, 3 H, *J*(vic) = 7.0 ($OCH_2C\mathbf{H}_3$).

(*R*)-1-[(6-Chloro-9*H*-purin-9-yl)methyl]-2-ethoxy-2-oxoethyl
(*S*)-3,3,3-Trifluoro-2-methoxy-2-phenylpropanoate (**35**)

This compound was prepared from **5a** (9 mg, 0.034 mmol) and (–)-(*S*)-2-methoxy-3,3,3-trifluoro-2-phenylpropanoic acid by the same manner as described for **34**. Yield 12 mg (73%) as a colourless oil. ^{1}H NMR ($CDCl_3$): 8.73 s, 1 H (H-2); 8.00 s, 1 H (H-8); 7.34–7.45 m, 5 H (C_6H_5); 5.65 dd, 1 H, *J*(2′,3′a) = 6.0, *J*(2′,3′b) = 4.7 (H-2′); 4.84 dd, 1 H, *J*(3′a,3′b) = 15.0, *J*(3′a,2′) = 6.0 (H-3′a); 4.81 dd, 1 H, *J*(3′b,3′a) = 15.0, *J*(3′b,2′) = 4.7 (H-3′b); 4.22 m, 2 H ($OC\mathbf{H}_2CH_3$); 3.39 q, 3 H, *J*(OCH_3,F) = 1.2 (OCH_3); 1.25 t, 3 H, *J*(vic) = 7.0 ($OCH_2C\mathbf{H}_3$).

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