49. Total Syntheses of Two Self-polymerizable Carbocyclic Analogues of 2′-Deoxyribonucleosides

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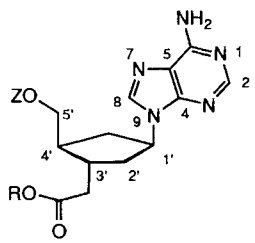
A short regio- and stereoselective synthesis of two carbocyclic 3′-deoxynucleoside analogues is described, the key step of which consists in the photosensitized addition of MeOH to a cyclopent-2-enone derivative. As in both cases functional groups capable to react with each other are present in the same molecule, the synthetic compounds can form polymers similar to oligonucleotides.

In the recent past, interest on synthetic nucleic-acid analogues has rapidly grown as an approach of increasing cell permeation and nuclease stability of chemotherapeutics designed to inhibit gene expression *in vivo* [1]. Thus, besides a quite large number of oligonucleotide analogues with modified ligands on the P-atom (*e.g.* methylphosphonates, phosphorothionates, phosphoramidates, *etc.*) [2], different types of compounds have been synthesized in which the phosphodiester backbone was replaced by other repetitive functional groups like carbonate [3], glycolate [4], α-oxyacetamidate [5], carbamate [6], siloxane [7], formacetal [8], thioether [9], and acetamidate [10] as connecting links between nucleoside units. In two cases ([9] [10]), even the 3′-OH group of the 2′-deoxyribofuranose ring was replaced by an aliphatic residue of appropriate length.

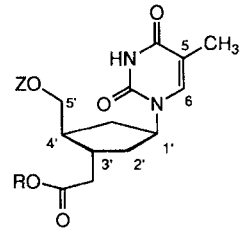
The target of the present work is the synthesis of *carbocyclic* 2′-deoxynucleoside analogues (*i.e.* **1b** and **2b**) containing two functional groups in the same molecule capable to react together just in presence of a catalyst, thus yielding polymers. To assure an intramolecular separation between the monomer units in these polymers similar to that present in nucleic acids, an acetic-acid chain was introduced on C(3′) of the cyclopentane ring of **1b** and **2b**. Comparison of the known geometrical parameters of methyl acetate [11] with those of dipentosyl phosphates [12] shows indeed that the maximum distance between the C(3′) and C(5′) atoms of two adjacent cyclopentane rings in polymers of **1b** and **2b** should be close to the corresponding distance in a nucleic-acid chain (*ca.* 4.84 *vs.* 5.18 Å). Accordingly, it was recently reported that dimers of a thymidine analogue connected by acetamide groups hybridize to RNA as strongly as does normal DNA [10].

Carbocyclic Adenylic-Acid Analogues 1. – Our concept for the synthesis of nucleotide isosters of the types **1b** and **2b** is outlined in the *Scheme*. Indeed, the preparation of oligomers of **1b** and **2b** consisting of only one diastereoisomer requires the use of

[1]) Part of the Ph. D. thesis of *J. W.*, Universität Freiburg i. Ue., 1993. Abstracts of this work were presented at the XIIth International Symposium on Medicinal Chemistry in Basle, September 13–17, 1992, and at the autumn meeting of the Swiss Chemical Society in Bern, October 16, 1992.



1a Z = *t*-Bu, R = Bu[2])
b Z = H, R = Bu[2])



2a Z = (*t*-Bu)Me_2Si, R = $PhCH_2$[2])
b Z = H, R = $PhCH_2$[2])

enantiomerically pure monomers of both nucleotide analogues. However, the recent report on the synthesis of some cyclopentanol derivatives (namely *rac*-**8c**, *rac*-**9c** [13], **8d**, and **9d** [14]) as well as of the carbocyclic adenosine analogue (**10b**) [13] which are very similar to our key intermediates *rac*-**8a**,**b**,-**9a**,**b**, and -**10a**, respectively (see below), prompt us to report here our own synthetic approach to the racemic derivatives **1b** and **2b**. Stereospecific syntheses of both compounds are at present in progress.

The key intermediates *rac*-**7a** and -**7b** can be synthesized in four steps with an overall yield of 43% using bicyclo[2.2.1]hept-5-en-2-one (= norbornenone; *rac*-**3**) [15] as starting material. The latter was transformed into *cis*-4-hydroxycyclopent-2-ene-1-acetic acid (*rac*-**4**) by *Baeyer-Villiger* oxidation followed by alkaline hydrolysis according to the procedure described in [16] [17]. As norbornenone can be easily resolved in its enantiomers [18], the absolute configuration of which was established [19], the synthetic approach outlined here can be used also for the synthesis of enantiomerically pure **4** of known absolute configuration. Alternatively, the (*S*,*S*)-enantiomer of the latter was prepared (as the corresponding methyl ester) by *Montforts et al.* [20] from optically active (+)-(1*R*,4*S*)-4-hydroxycyclopent-2-enyl acetate, which was previously obtained by enzymatic partial hydrolysis of racemic *cis*-cyclopent-2-en-1,4-diyl diacetate.

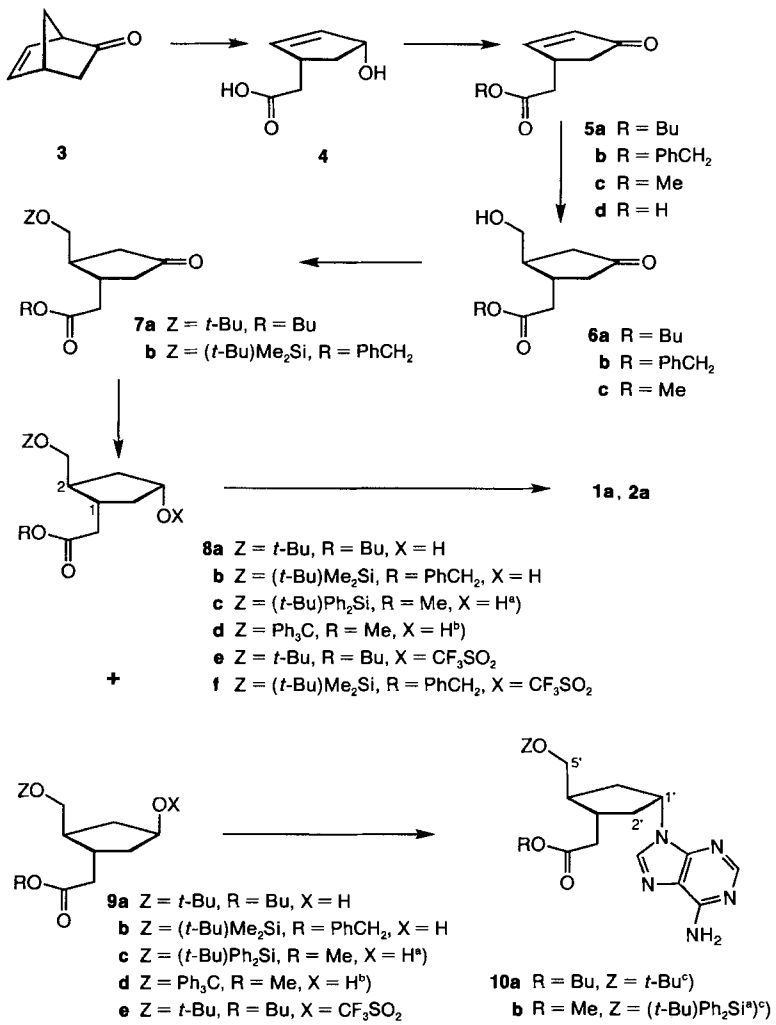
Oxidation of *rac*-**4** with *Jones* reagent yields the corresponding 4-oxocyclopent-2-ene-1-acetic acid (*rac*-**5d**) [16] [17]. Alternative syntheses of the (*S*)-enantiomer [21] and its methyl ester [22] were recently reported in the literature. For our purpose, it was advantageous to transform acid *rac*-**5d** into the corresponding butyl and benzyl ester *rac*-**5a** and -**5b**, respectively.

The crucial step in the present synthesis of *rac*-**7a**,**b** is the introduction of the hydroxymethyl group present at C(2) of their precursors *rac*-**6a**,**b**. Among the different possibilities which can be envisaged to achieve this reaction, the conjugate addition of [(*tert*-butoxy)methyl]lithium, as a 'hydroxymethyl-anion equivalent' [23], at the C=C bond of *rac*-**5a** and -**5b** appeared to be the more straightforward approach. In our hands, however, this reagent failed to yield the desired product on reaction with both substrates.

Less wide-spread than the conjugate addition of organometallics to electron-deficient C=C bonds is the photosensitized addition of primary alcohols to enones [24]. In the present case, this reaction proved to be an efficient tool to introduce the desired functional group into *rac*-**5a** and -**5b**. The corresponding adducts *rac*-**6a** and -**6b** were obtained in 73 and 67% yield, respectively. Unfortunately, however, the assignment of

[2]) Numbering as in [13] [14].

Scheme



[a]) From [13]. [b]) From [14]. [c]) Numbering as in [13] [14].

the relative configuration of both products was not feasible on the basis of their ^{1}H-NMR spectra, because the overlap of the relevant signals at 2.82–2.00 ppm. Therefore, the methyl ester *rac*-**6c** was synthesized, under the same conditions, for the sake of comparison with the *cis*-isomer which was prepared by *Baeyer-Villiger* oxidation of *cis*-bicyclo[3.3.0]octane-3,7-dione and subsequent hydrolysis of the resulting lactone according to [25]. As both compounds proved to be different, the relative configuration of *rac*-**6c** as well as that of *rac*-**6a** and **-6b**, which were obtained by the same procedure, must be *trans*. This assignment is supported by ^{1}H{^{1}H}NOE difference experiments which were carried out after transformation of *rac*-**6a** into the corresponding *tert*-butyl ether *rac*-**7a**

(see *Exper. Part*). Moreover, reduction of *rac*-**7a** with $NaBH_4$ afforded an epimer mixture *rac*-**8a/9a** 1:1, the ^{1}H-NMR data of which agree very well with those of related cyclopentanol derivatives recently reported [13] [14] (*cf. Tables 1* and *2*). As compounds *rac*-**8c**, **8d**, *rac*-**9c**, and **9d** were synthesized by a stereospecific route which ensures a *trans*-arrangement of the substituents on C(1) and C(2), the correspondence of their spectroscopic data with those of *rac*-**8a** and *rac*-**9a** confirms the assignment made above. Thus, like in some other cases [24], the photoinduced addition of MeOH to the cyclopentenones **5a–c**, occurs from the less-hindered side of the molecule and is highly regio- and stereoselective.

Table 1. *^{1}H-NMR Data* (200 MHz, $CDCl_3$) *of Compounds* **8a** *and* **8b** *Compared with Literature Data of Related Derivatives.* δ in ppm rel. to Me_4Si, J in Hz.

	rac-**8a**[a])	*rac*-**8b**[b])	*rac*-**8c**[c])	**8d**[d])
H–C(1), H–C(2),	1.30–1.47 (*m*, 3 H[e]))	1.34–1.44 (*m*, 1 H)	1.36–1.43 (*m*, 1 H)	1.38 (*dddd*, 1 H)
CH_2(3), CH_2(5)	1.52–1.68 (*m*, 3 H[f]))	1.53–1.65 (*m*, 1 H)	1.70 (*dd*, 1 H)	1.59 (*ddd*, 1 H)
(6 H in total)	1.74–1.88 (*m*, 1 H)	1.70–1.82 (*m*, 1 H)	1.75–1.84 (*m*, 1 H)	1.83–1.90 (*m*, 2 H[g]))
	1.97–2.14 (*m*, 2 H[g]))	1.96–2.28 (*m*, 3 H[g]))	2.07–2.30 (*m*, 1 H)	2.01–2.11 (*m*, 1 H)
	2.18–2.35 (*m*, 2 H)	2.35–2.48 (*m*, 1 H)	2.37 (*dd*, 1 H)	2.15–2.26 (*m*, 2 H)
CH_a–C(1)	2.38 (*dd*[h]), 1 H)	2.44 (*dd*[i]), 1 H)	?	2.38 (*dd*[j]), 1 H)
CH_b–C(1)	2.67 (*dd*[k]), 1 H)	2.69 (*dd*[l]), 1 H)	?	2.60 (*dd*[m]), 1 H)
CH_2–C(2)	3.29 (*d*[n]), 2 H)	3.53 (*d*[o]), 2 H)	2.60 (*dd*[p]), 2 H)	3.02–3.09 (*m*, 2 H)
H–C(4)	4.23–4.32 (*m*, 1 H)	4.21–4.30 (*m*, 1 H)	4.27–4.33 (*m*, 1 H)	4.26–4.30 (*m*, 1 H)

[a]) Other signals: 0.93 (*t*, J = 7.2, *Me*$(CH_2)_3$); 1.16 (*s*, *t*-Bu); 4.06 (*t*, J = 6.6, $MeCH_2CH_2CH_2$). [b]) Other signals: 0.02 (*s*, Me_2Si); 0.88 (*s*, *t*-BuSi); 5.10 (*s*, $PhCH_2$); 7.33 (*s*, Ph). [c]) See [13]. [d]) See [14]. [e]) Incl. $MeCH_2CH_2CH_2$. [f]) Incl. $MeCH_2CH_2CH_2$. [g]) Incl. OH. [h]) J = 15.4, 8.3. [i]) J = 15.4, 8.2. [j]) J = 15.6, 8.8. [k]) J = 15.4, 4.6. [l]) J = 15.4, 4.4. [m]) J = 15.6, 4.8. [n]) J = 5.7. [o]) J = 5.2. [p]) J = 5.2, 1.0.

Table 2. *^{1}H-NMR Data* (200 MHz, $CDCl_3$) *of Compounds* **9a** *and* **9b** *Compared with Literature Data of Related Derivatives.* δ in ppm rel. to Me_4Si, J in Hz.

	rac-**9a**[a])	*rac*-**9b**[b])	*rac*-**9c**[c])	**9d**[d])
H–C(1), H–C(2),	1.29–1.48 (*m*, 3 H[e]))	1.20–1.47 (*m*, 1 H)	1.41–1.50 (*m*, 1 H)	1.39–1.51 (*m*, 1 H)
CH_2(3), CH_2(5),	1.52–1.69 (*m*, 3 H[f]))	1.47–1.60 (*m*, 1 H)	1.55–1.63 (*m*, 1 H)	1.82–1.97 (*m*, 3 H[g]))
CH_2–C(1)	1.82–2.18 (*m*, 3 H)	1.85–2.19 (*m*, 3 H)	1.84–1.94 (*m*, 1 H)	2.12–2.19 (*m*, 1 H)
(8 H in total)			1.94–2.06 (*m*, 1 H)	2.22 (*dd*, 1 H)
			2.09–2.30 (*m*, 3 H)	2.39–2.47 (*m*, 1 H)
	2.32–2.55 (*m*, 3 H)	2.36–2.53 (*m*, 3 H)	2.43–2.57 (*m*, 2 H)	2.51 (*dd*, 1 H)
CH_a–C(2)	3.34 (*dd*[h]), 1 H)	3.56 (*dd*[i]), 1 H)	3.62 (*dd*[j]), 2 H)	3.14 (*dd*[k]), 1 H)
CH_b–C(2)	3.42 (*dd*[l]), 1 H)	3.63 (*dd*[m]), 1 H)		3.18 (*dd*[n]), 1 H)
H–C(4)	4.06–4.19 (*m*, 1 H)	4.10–4.22 (*m*, 1 H)	4.23–4.27 (*m*, 1 H)	4.22–4.27 (*m*, 1 H)

[a]) Other signals: 0.94 (*t*, J = 7.2, *Me*$(CH_2)_3$); 1.22 (*s*, *t*-Bu); 4.06 (*t*, J = 6.8, $MeCH_2CH_2CH_2$). [b]) Other signals: 0.55 (*s*, Me_2Si); 0.88 (*s*, *t*-BuSi); 3.35 (*d*, J = 8.2, OH); 5.08 (*dd*, J = 19.9, 12.3, $PhCH_2$); 7.32 (*s*, Ph). [c]) See [13]. [d]) See [14]. [e]) Incl. $MeCH_2CH_2CH_2$. [f]) Incl. $MeCH_2CH_2CH_2$. [g]) Incl. OH. [h]) J = 8.5, 2.9. [i]) J = 9.7, 3.5. [j]) J = 4.5, 2.5. [k]) J = 9.1, 5.2. [l]) J = 8.5, 2.6. [m]) J = 9.7, 3.2. [n]) J = 9.1, 5.4.

Examination of the spectroscopic data summarized in *Tables 1* and *2* gives also a first hint concerning the relative configurations of *rac*-**8a** and -**9a** at C(4), which can be fairly well correlated with those of their counterparts, established in [13] [14] by stereospecific synthesis. Particularly, the ^{1}H-NMR signals of $COCH_2$–C(1) become clearly discernible

in the 4α-epimer, in which the acetic-ester chain and OH–C(4) are *cis* to each other. The confirmation of these assignments was postponed, therefore, to the final stage of the synthesis of the corresponding nucleotide analogues.

Thus, *rac*-**8a** and -**9a** were transformed into the trifluoromethanesulfonates *rac*-**8e** and -**9e**, respectively, which, on reaction with unprotected adenine in the presence of NaH and [18]crown-6 as phase-transfer catalyst (*cf.* [26]), yielded the substitution products *rac*-**1a** and -**10a**, respectively. Their UV spectra indicate that both compounds are N^9-substituted adenine epimers, since N^7-alkyl-substituted adenine derivatives have, in general, bathochromically shifted UV maxima relative to the N^9-regioisomers [27] (*cf. Table 3*). Moreover, the ^{13}C-NMR chemical-shift values of the purine C-atoms of both *rac*-**1a** and -**10a** agree better with those of 9-methyladenine than of the 7-isomer [28], except for C(2), for which the differences in the resonance frequencies are too small to be significant (see *Table 3*). Indeed, an unequivocal proof of the relative configuration at C(1′)[2]) was obtained by ^{1}H{^{1}H}NOE difference experiments.

Thus, irradiation of H–C(1′) of *rac*-**1a** (*m* at δ 5.03) results in the enhancement of the 2*dd* at δ 2.66 and 2.31 assigned to the diastereotopic protons $COCH_2$–C(3′). No NOE is observed at the OCH_2–C(4′) group (2*dd* at δ 3.47 and 3.44 ppm). Correspondingly, irradiation of H–C(1′) of *rac*-**10a** (*m* at δ 4.91) results in the enhancement of the *dd* at δ 3.34 (one of the diastereotopic protons OCH_2–C(4′) (*cf. Tables 1* and *2*). No NOE is observed at $COCH_2$–C(3′) (2*dd* at δ 2.74 and 2.41 ppm).

The above assignments corroborate that nucleophilic displacement of the triflate group by the adenide anion occurred under inversion of the configuration at C(4) of both *rac*-**8a** and -**9a**. Reaction of *rac*-**1a** with conc. hydrochloric acid in BuOH afforded the hydroxyester *rac*-**1b** in 89% yield.

Table 3. *UV Absorption* (MeOH) *and* ^{13}*C-NMR Chemical Shifts of the Purine Moiety of Compounds* rac-**1a** *and* rac-**10a** *and of 9- and 7-Methyladenine* (see text)

	UV		δ (^{13}C) [ppm]				
	λ_{max} [nm]	log ε	C(2)	C(4)	C(5)	C(6)	C(8)
rac-**1a**	262	4.16	153.1	150.6	120.4	156.1	139.4
rac-**10a**	262	4.16	152.7	150.3	120.2	155.5	139.4
9-Methyladenine	262	4.08	152.5	149.9	118.7	155.9	141.1
7-Methyladenine	270	4.02	152.3	159.8	111.7	151.9	145.9

Carbocyclic Thymidylic-Acid Analogues 2. – Analogously to *rac*-**6a**, the CH_2OH group of benzyl ester *rac*-**6b** was protected – this time by reaction with (*tert*-butyl)dimethylsilyl chloride – and the corresponding silyl ether *rac*-**7b** was reduced with $NaBH_4$. As before, the relative configurations of the obtained epimeric alcohols *rac*-**8b** and -**9b** (1:1) were assigned on the basis of the ^{1}H-NMR data (*Tables 1* and *2*). Reaction of the 4-α-isomer *rac*-**8b** with trifluoromethanesulfonyl chloride afforded the corresponding triflate *rac*-**8f** which was reacted with thymine in presence of K_2CO_3 and [18]crown-6 to yield *rac*-**2a**. The regioselective formation of the desired thymidin-1-yl derivative as the main product of the reaction becomes evident from the mutual NOE between H–C(6) and H–C(1′) (numbering as in [13] [14]; *cf. Exper. Part*). H–C(1′) also shows an NOE with both diastereotopic protons $COCH_2$–C(3′). Thus, the pyrimidine

ring and the acetic-ester substituent on C(3′) must be *trans* to each other. Reaction of *rac*-**2a** with Bu_4NF in THF afforded hydroxyester *rac*-**2b** in 73% yield.

Under transesterification conditions, both enantiomerically pure **1b** and **2b** should lead to polymer analogues of polyadenylic and polythymidylic acid, respectively. The investigation of this reaction is in progress in our laboratory, at present.

Financial support of this work from the *Swiss National Science Foundation* is gratefully acknowledged. NMR spectra on the *Bruker-AM-360* instrument and mass spectra were recorded by *F. Fehr* and *F. Nydegger*, respectively. Elemental analyses were carried out by *Ciba Geigy AG*, Forschungszentrum, CH–1723 Marly.

Experimental Part

General. All air- and water-sensitive reactions were carried out under Ar. *N,N′*-Dicyclohexylcarbodiimide (DCC), 4-(dimethylamino)pyridine, and other reagents were purchased from *Fluka Chemie AG*. Solvents were generally dried and distilled prior to use. Reactions were monitored by thin-layer chromatography (TLC). TLC: *E. Merck* silica gel *60* F_{254} (0.2 mm) precoated aluminium foils, developed with a 1% aq. $KMnO_4$ and 2% aq. NaOH soln. or in I_2 vapour. Column chromatography (CC): *E. Merck* silica gel *60* (230–400 mesh). M.p.'s: *Kofler* hot-stage apparatus (*Thermovar, C. Reichert AG*, Vienna); uncorrected. UV: *Hewlett-Packard 8452A* diode array spectrophotometer; MeOH solns.; λ_{max} ($\log\varepsilon$) in nm. IR: *Perkin-Elmer-IR-599*; in cm^{-1}. NMR: *Varian XL 200* (^1H: 200 MHz; ^{13}C: 50.30 MHz) or *Bruker-AM-360* (^1H) equipped with a data system *Aspekt 3000*; $CDCl_3$ solns.; chemical shifts δ in ppm rel. to Me_4Si as internal standard, J values in Hz; assignments based on homonuclear COSY, $^1H\{^1H\}$NOE difference correlations, attached proton test (APT) and/or chemical shifts; NOE: δ of enhanced signal, in parentheses: % enhancement and irradiation frequency; MS: *Vacuum Generators Micromass 7070 E* equipped with a data system *DS 11-250*. EI-MS (electron ionization): acceleration voltage 70 eV. FAB-MS (fast-atom bombardement): at 6 kV in 2-nitrobenzyl alcohol with Ar at 8 kV; rel. intensities (%) in parentheses.

*Butyl (±)-*t*-4-(6-Amino-9*H*-purin-9-yl)-*t*-2-[(*tert*-butoxy)methyl]cyclopentane-*r*-1-acetate* (*rac*-**1a**). To a suspension of adenine (0.8 g, 5.9 mmol) in anh. DMF (40 ml) were added NaH (0.2 g, 4.8 mmol; 55–60% dispersion in mineral oil) and [18]crown-6 (1.6 g). The mixture was heated for 4 h at 70°. Then, the white suspension was cooled to 0°, *rac*-**8e** (2.0 g, 4.8 mmol) in anh. DMF (10 ml) added at once, the mixture stirred at 0° for 10 h, at r.t. for 12 h, and then at 40° for 8 h, and the solid residue filtered off. The filtrate was diluted with CH_2Cl_2 (800 ml), washed with sat. aq. KCl (4 × 300 ml) and H_2O (2 × 200 ml), dried (Na_2SO_4) and evaporated. After CC (CH_2Cl_2/MeOH 10:1 (*v/v*)), the solid residue was crystallized from AcOEt: *rac*-**1a** (0.7 g, 36%). White solid. M.p. 91–92.5°. UV: 212 (4.24), 262 (4.16). IR (KBr): 3350*m* (br.), 3150*m* (br.), 2985*s*, 2940*m*, 2880*m*, 1730*s*, 1650*s*, 1600*s*, 1575*m*, 1480*m*, 1360*m*, 1310*m*, 1180*m*, 1075*m*, 650*m*. ^1H-NMR (360.13 MHz)[2]): 8.35 (*s*, H–C(2)); 8.12 (*s*, H–C(8)); 5.70 (*s*, NH_2); 5.07–4.99 (*m*, H–C(1′)); 4.06 (*t*, J = 6.8, $MeCH_2CH_2CH_2$); 3.47 (*dd*, J = 9.1, 4.5, 1 H–C(5′)); 3.44 (*dd*, J = 9.0, 4.6, 1 H–C(5′)); 2.66 (*dd*, J = 15.2, 4.6, $COCH_a$–C(3′)); 2.61–2.49 (*m*, 2 H); 2.36–2.27 (*m*, 1 H); 2.31 (*dd*, J = 15.2, 9.1, $COCH_b$–C(3′)); 2.08–1.92 (*m*, 3 H); 1.63–1.55 (*m*, $MeCH_2CH_2CH_2$); 1.43–1.30 (*m*, $MeCH_2CH_2CH_2$); 1.21 (*s*, *t*-Bu); 0.91 (*t*, J = 7.2, $MeCH_2CH_2CH_2$). NOE: 8.35 (0.4, 5.03); 8.12 (2.6, 5.03); 2.66 (1, 5.03); 2.31 (1, 5.03); 2.61–2.49 (5.8, 5.02); 2.08–1.92 (19.5, 5.03); 5.07–4.99 (2.7, 8.12); 2.61–2.49 (2.4, 8.12); 2.36–2.27 (24, 8.12); 2.08–1.92 (14.4, 8.12). ^{13}C-NMR: 173.08 (*s*, CO); 156.11 (*s*, C(6)); 153.13 (*d*, C(2)); 150.56 (*s*, C(4)); 139.40 (*d*, C(8)); 120.37 (*s*, C(5)); 73.27 (*s*, Me_3C); 64.76 (*t*); 63.47 (*t*); 54.20 (*d*); 45.10 (*d*); 39.72 (*t*, 2 C); 37.39 (*d*); 36.70 (*t*); 31.12 (*t*); 27.96 (*q*, Me_3C); 19.59 (*t*); 13.69 (*q*, $Me(CH_2)_3$). EI-MS: 403 (0.5, M^+), 346 (100), 316 (15.4), 274 (12.5), 202 (4.1), 162 (6.9), 136 (77.9), 108 (11.5). Anal. calc. for $C_{21}H_{33}N_5O_3$ (403.45): C 62.52, H 8.24, N 17.36; found: C 62.52, H 8.46, N 17.37.

*Butyl (±)-*t*-4-(6-Amino-9*H*-purin-9-yl)-*t*-2-(hydroxymethyl)cyclopentane-*r*-1-acetate* (*rac*-**1b**). A soln. of *rac*-**1a** (210 mg, 0.52 mmol) and 32% aq. HCl soln. (1.5 ml) in BuOH (15 ml) was stirred at 100° for 12 h. After cooling to r.t., solid Na_2CO_3 (2 g) was added, the mixture filtered, and the filtrate evaporated. The residue was purified by CC (EtOH/CH_2Cl_2 1:3) and crystallized from AcOEt: 161 mg (89%) of *rac*-**1b**. White solid. M.p. 118–120°. IR (KBr): 3600 (br., OH), 3220*s* (NH), 2960*m*, 2935*m*, 2850*m*, 1735*s*, 1680*s*, 1620*s*, 1575*m*, 1475*m*, 1340*m*, 1250*m*, 1200*m*, 1175*m*, 1155*m*, 1120*m*, 1070*m*, 1015*m*, 800*m*, 680*m*. ^1H-NMR (200 MHz)[2]): 8.27 (*s*, H–C(2)); 8.00 (*s*, H–C(8)); 6.47 (*s*, NH_2); 4.98–4.93 (*m*, H–C(1′)); 4.32 (*s*, OH); 4.03 (*t*, J = 6.6, $MeCH_2CH_2CH_2$); 3.73 (*d*, J = 3.6, CH_2OH); 2.68–2.46 (*m*, 3 H); 2.42–2.25 (*m*, 2 H); 2.17–1.89 (*m*, 3 H); 1.62–1.48

(*m*, $MeCH_2CH_2CH_2$); 1.38–1.22 (*m*, $MeCH_2CH_2CH_2$); 0.89 (*t*, *J* = 7.2, $MeCH_2CH_2CH_2$). ^{13}C-NMR: 173.36 (*s*, CO); 156.18 (*s*); 153.08 (*d*); 150.25 (*s*); 139.40 (*d*); 120.29 (*s*); 65.00 (*t*); 64.17 (*t*); 54.62 (*d*); 46.98 (*d*); 39.68 (*t*); 39.43 (*t*); 36.54 (*d*); 36.13 (*t*); 31.05 (*t*); 19.54 (*t*); 13.69 (*q*, $Me(CH_2)_3$). EI-MS: 346 (5.8, $[M - H]^+$), 316 (27.4), 274 (11.3), 246 (10.2), 232 (4.2), 202 (8.0), 162 (23.8), 136 (100), 108 (21.7), 79 (8.9), 56 (61.0).

*Benzyl (±)-*t*-2-{[(*tert*-butyl)dimethylsilyloxy]methyl}-*t*-4-(1,2,3,4-tetrahydro-5-methyl-2,4-dioxopyrimidin-1-yl)cyclopentane-*r*-1-acetate* (*rac*-**2a**). A mixture of *rac*-**8f** (7.0 g, 14 mmol) and thymine (4 g, 32 mmol) in dry DMF (150 ml) containing [18]crown-6 (5 g) and K_2CO_3 (4.0 g) was stirred at 40° for 14 h and then at 50° for 5 h. After dilution with AcOEt (1 l), the mixture was washed with H_2O (4 × 400 ml), the org. layer dried (Na_2SO_4) and evaporated, and the residue submitted to CC (AcOEt/$CHCl_3$/EtOH 20:20:1): 2.5 g (38%) of *rac*-**2a**. ^{1}H-NMR (360.13 MHz)[2]): 8.53 (*s*, NH); 7.36 (*s*, Ph); 7.04 (*d*, *J* = 1.2, H–C(6)); 5.11 (*dd*, *J* = 16.7, 12.3, $PhCH_2$); 5.05–4.98 (*m*, H–C(1′)); 3.62 (*d*, *J* = 4.4, CH_2OSi); 2.66 (*dd*, *J* = 15.4, 4.7, $COCH_a$–C(3′)); 2.48–2.38 (*m*, 1 H); 2.29 (*dd*, *J* = 15.4, 9.4, $COCH_b$–C(3′)); 2.23–2.12 (*m*, 1 H); 2.05–1.97 (*m*, 1 H); 1.92 (*d*, *J* = 1.2, Me–C(5)); 1.90–1.92 (*m*, 2 H); 1.64–1.57 (*m*, 1 H); 0.89 (*s*, *t*-Bu); 0.04 (*d*, *J* = 2.3, Me_2Si). NOE: 1.92 (7, 7.04); 5.05–4.98 (2, 7.04); 7.04 (2, 5.02); 2.66 (1, 5.02); 2.29 (1, 5.02). ^{13}C-NMR: 172.30 (*s*, CO); 163.53 (*s*); 151.01 (*s*); 136.45 (*d*); 136.45 (*s*); 128.62 (*d*); 128.33 (*d*); 128.25 (*d*); 111.19 (*s*); 66.34 (*t*); 64.09 (*t*); 53.91 (*d*); 45.95 (*d*); 39.38 (*t*); 37.19 (*t*); 36.47 (*d*); 34.83 (*t*); 25.91 (*q*, Me_3C); 18.28 (*s*, Me_3C); 12.59 (*q*, Me); –5.43 (*q*, Me_2Si). FAB-MS: 509 (32, $[M + Na]^+$), 487 (24, $[M + H]^+$), 429 (12), 361 (16), 217 (13), 183 (30), 169 (17), 127 (100), 115 (18).

*Benzyl (±)-*t*-2-(Hydroxymethyl)-*t*-4-(1,2,3,4-tetrahydro-5-methyl-2,4-dioxopyrimidin-1-yl)-cyclopentane-*r*-1-acetate* (*rac*-**2b**). A soln. of *rac*-**2a** (0.5 g, 1.0 mmol) in THF (20 ml) containing $Bu_4NF \cdot 3\,H_2O$ (0.4 g) was stirred at r.t. for 3.5 h. The solvent was evaporated and the residue purified by prep. TLC (alumina *507C, Fluka*, AcOEt/CH_2Cl_2/EtOH 5:5:1: *rac*-**2b** (280 mg, 73%). Colourless oil. ^{1}H-NMR (200 MHz)[2]): 7.34 (*s*, Ph); 7.13 (*d*, *J* = 1.1, H–C(6)); 5.12 (*s*, $PhCH_2$); 5.09–4.89 (*m*, H–C(1′)); 3.64 (*d*, *J* = 4.6, CH_2OH); 2.66–2.33 (*m*, 3 H); 2.28–2.15 (*m*, 2 H); 2.08–1.58 (*m*, 3 H); 1.92 (*s*, Me). ^{13}C-NMR: 173.21 (*s*, CO); 163.89 (*s*); 151.40 (*s*); 137.17 (*d*); 136.16 (*s*); 129.06 (*d*); 128.77 (*d*, 2 C); 115.55 (*s*); 67.07 (*t*); 64.07 (*t*); 54.69 (*d*); 46.73 (*d*); 39.65 (*t*); 37.60 (*t*); 36.33 (*d*); 35.19 (*t*); 12.95 (*q*, Me). EI-MS: 372 (1.9, M^+), 354 (0.6), 309 (0.2), 293 (0.4), 281 (3.8), 263 (4.6) 221 (11.2), 91 (6.0), 127 (34.3), 107 (8.9), 91 (100). Anal. calc. for $C_{20}H_{24}N_2O_5$ (372.43): C 64.50, H 6.50, N 7.52; found: C 64.52, H 6.58, N 7.49.

Butyl (±)-4-Oxocyclopent-2-eneacetate (*rac*-**5a**). A soln. of *rac*-**5d** [16] [17] (4.5 g, 32 mmol), DCC (8.0 g), BuOH (3.0 g, 40 mmol), and 4-(dimethylamino)pyridine (0.1 g) in CH_2Cl_2 (120 ml) was stirred at r.t. for 2 h. The precipitated *N,N′*-dicyclohexylurea was filtered off and the solvent evaporated. The residue was purified by CC (AcOEt/hexane 1:3): *rac*-**5a** (5.2 g, 83%). Colourless oil. IR (neat): 2960*s*, 2925*s*, 2875*m*, 1705*s*, 1605*m*, 1582*m*, 1460*m*, 1405*m*, 1342*m*, 1270*m*, 1175*s*, 1065*m*, 785*m*. ^{1}H-NMR (200 MHz): 7.66 (*dd*, *J* = 5.6, 2.4, H–C(2)); 6.20 (*dd*, *J* = 5.6, 2.1, H–C(3)); 4.12 (*t*, *J* = 6.7, $MeCH_2CH_2CH_2$); 3.37 (*m*, H–C(1)); 2.67–2.43 (*m*, 3 H); 2.07 (*dd*, *J* = 18.9, 2.3, 1 H); 1.66–1.58 (*m*, $MeCH_2CH_2CH_2$); 1.41–1.35 (*m*, $MeCH_2CH_2CH_2$); 0.93 (*t*, *J* = 7.2, Me). ^{13}C-NMR: 208.27 (*s*, CO); 171.17 (*s*, ester CO); 166.04 (*d*, C(2)); 134.45 (*d*, C(3)); 64.59 (*t*, $MeCH_2CH_2CH_2$); 40.63 (*t*); 38.77 (*t*); 37.58 (*d*); 30.58 (*t*); 19.06 (*t*, $MeCH_2CH_2CH_2$); 13.54 (*q*, Me). EI-MS: 196 (39, M^+), 140 (82), 122 (71), 95 (100), 81 (36), 67 (39).

Benzyl (±)-4-Oxocyclopent-2-eneacetate (*rac*-**5b**) was obtained as described for *rac*-**5a** in 91% yield by esterification of *rac*-**5d** with benzyl alcohol. IR (neat): 2930*m*, 2850*m*, 1730*s*, 1710*s*, 1585*m*, 1500*m*, 1450*m*, 1410*m*, 1380*m*, 1350*m*, 1270*m*, 1180*s*, 1000*m*, 790*m*, 750*m*, 700*m*. ^{1}H-NMR (200 MHz): 7.61 (*dd*, *J* = 5.6, 2.4, H–C(2)); 7.34 (*s*, Ph); 6.16 (*dd*, *J* = 5.6, 2.0, H–C(3)); 5.14 (*s*, $PhCH_2$); 3.36 (*m*, H–C(1)); 2.67–2.50 (*m*, 3 H); 2.04 (*dd*, *J* = 18.8, 2.6, 1 H). ^{13}C-NMR: 208.88 (*s*, CO); 171.54 (*s*, ester CO); 166.59 (*d*, C(2)); 136.08 (*s*); 135.03 (*d*, C(3)); 129.09 (*d*); 128.88 (*d*); 128.77 (*d*); 67.04 (*t*, $PhCH_2$); 41.09 (*t*); 39.16 (*t*); 38.03 (*d*, C(1)). EI-MS: 230 (10.8, M^+), 202 (4.7), 107 (2.7), 91 (100), 77 (6.0), 65 (10.2).

*Butyl (±)-*trans*-2-(Hydroxymethyl)-4-oxocyclopentaneacetate* (*rac*-**6a**). A soln. of *rac*-**5a** (4.2 g, 21 mmol) in MeOH (1.4 l) containing 0.7 g (3.8 mmol) of benzophenone was poured in a *Pyrex* tube equipped with a cold finger through which cold H_2O was circulated. The tube was introduced into a *Rayonet* reactor (model *RPR-100*) and the soln. flushed with N_2 (glass capillary) for 1 h to remove O_2. Then the lamps (λ_{max} 360 nm) were switched on, the N_2 gas flow being maintained. After 8 h, the solvent was evaporated and the residue purified by CC (AcOEt/hexane 1:1): *rac*-**6a** (3.5 g, 73%). Colourless oil. IR (neat): 2960*s*, 2880*s*, 1720*s*, 1460*m*, 1400*m*, 1380*m*, 1185*s*, 1060*m*, 1040*m*, 980*m*, 950*m*, 910*m*. ^{1}H-NMR (200 MHz): 4.09 (*t*, *J* = 6.6, $MeCH_2CH_2CH_2$); 3.70 (*d*, *J* = 4.5, CH_2OH); 2.77 (br. *s*, OH); 2.70–1.90 (*m*, 8 H); 1.69–1.57 (*m*, $MeCH_2CH_2CH_2$); 1.48–1.30 (*m*, $MeCH_2CH_2CH_2$); 0.93 (*t*, *J* = 7.2, Me). ^{13}C-NMR: 216.95 (*s*, CO); 172.52 (*s*, ester CO); 64.48 (*t*, $MeCH_2CH_2CH$); 62.96 (*t*, CH_2OH); 44.71 (*t*); 44.03 (*d*); 41.32 (*t*); 38.44 (*t*); 34.48 (*d*); 30.44 (*t*); 18.94 (*t*, $MeCH_2CH_2CH_2$); 13.47 (*q*, Me). EI-MS: 229 (0.4, $[M + H]^+$), 210 (79), 154 (3.0), 141 (9.3), 137 (6.6), 126 (5.8), 113 (13.1), 109 (70.3), 95 (17.2), 85 (15.6), 41 (100).

Benzyl (±)-trans-*2-(Hydroxymethyl)-4-oxocyclopentaneacetate* (*rac*-**6b**) was obtained as a colourless oil in 67% yield from *rac*-**5b** as described for *rac*-**6a**. IR (neat): 3475*s* (br., OH), 3300*m*, 2910*s*, 1725*s*, 1450*m*, 1400*m*, 1390*m*, 1330*m*, 1170*m*, 1080*m*, 1040*m*, 910*m*, 750*m*, 700*m*. ^{1}H-NMR (200 MHz): 7.34 (*s*, Ph); 5.11 (*s*, PhCH_2); 3.65 (*d*, J = 4.2, CH_2OH); 2.76–1.90 (*m*, 9 H, incl. OH). ^{13}C-NMR: 216.74 (*s*, CO); 172.42 (*s*, ester CO); 135.60 (*s*); 128.63 (*d*); 128.44 (*d*); 128.34 (*d*); 66.61 (*t*, PhCH_2); 63.16 (*t*, CH_2OH); 44.86 (*t*); 44.22 (*d*); 41.46 (*t*); 38.58 (*t*); 34.60 (*d*). EI-MS: 262 (0.3, M^+), 244 (1.4), 234 (2.4), 183 (2.4), 168 (3.0), 153 (2.9), 112 (6.4), 108 (17), 91 (100), 81 (6.4).

Methyl (±)-trans-*2-(Hydroxymethyl)-4-oxocyclopentaneacetate* (*rac*-**6c**) was obtained as a colourless oil in 80% yield from *rac*-**5c** [16] as described for *rac*-**6a**. IR (neat): 3450*s* (br. OH), 2950*s*, 2910*s*, 1740*s*, 1720*s*, 1440*m*, 1400*m*, 1370*m*, 1330*m*, 1175*s*, 1075*m*, 1045*m*, 700*m*. ^{1}H-NMR (200 MHz): 3.71 (*d*, J = 4.8, CH_2OH); 3.70 (*s*, Me); 2.75–2.65 (*m*, 1 H); 2.65–2.50 (*m*, 2 H); 2.47–2.35 (*m*, 2 H); 2.27–2.20 (*m*, 1 H); 2.15–1.95 (*m*, 2 H). ^{13}C-NMR: 216.78 (*s*, CO); 173.13 (*s*, ester CO); 63.25 (*t*, CH$_2$OH); 51.85 (*q*, Me); 44.94 (*t*); 44.26 (*d*); 41.53 (*t*); 38.33 (*t*); 34.63 (*d*). EI-MS: 187 (0.6, $[M + H]^+$), 168 (31.5), 155 (19.6), 137 (12.9), 127 (12.3), 113 (19.7), 109 (100), 99 (24), 95 (53), 85 (38).

Butyl (±)-trans-*2-[(*tert-*Butoxy)methyl]-4-oxocyclopentaneacetate* (*rac*-**7a**). At 0°, 2-methylprop-1-ene was bubbled into a stirred soln. of *rac*-**6a** (2.7 g, 12 mmol) in CH_2Cl_2 (80 ml) for *ca.* 20 min, before 96% H_2SO_4 (0.5 ml) was added slowly. The bubbling of 2-methylprop-1-ene was continued for 2 h, then the flask was stoppered and stirred at r.t. for 5 h. The soln. was neutralized with 10% aq. $NaHCO_3$ soln. (2 × 50 ml), washed with H_2O (50 ml), dried (Na_2SO_4), and evaporated. The residue was purified by CC (AcOEt/hexane 1:10): *rac*-**7a** (1.7 g, 51%). Colourless oil. IR (neat): 2985*s*, 2930*m*, 2870*m*, 1730*s*, 1415*m*, 1395*m*, 1365*m*, 1180*s*, 1090*m*, 1020*m*, 880*m*. ^{1}H-NMR (360.13 MHz): 4.15 (*t*, J = 6.6, MeCH_2CH_2CH_2); 3.41 (*d*, J = 4.6, *t*-BuOCH_2); 2.76 (*dd*, J = 15.4, 4.6, COCH$_a$–C(1)); 2.66–2.57 (*m*, 1 H); 2.54–2.48 (*m*, H–C(1)); 2.46–2.35 (*m*, 1 H); 2.31 (*dd*, J = 15.4, 9.0, COCH$_b$–C(1)); 2.16–2.08 (*m*, 2 H); 2.04–1.89 (*m*, 1 H); 1.65–1.57 (*m*, MeCH$_2$CH_2CH$_2$); 1.47–1.30 (*m*, MeCH_2CH$_2$CH$_2$); 1.17 (*s*, *t*-Bu); 0.94 (*t*, J = 7.2, Me). NOE: 2.76 (1.4, 3.41); 2.54–2.48 (3.2, 3.41); 2.16–2.08 (7.1, 3.41); 1.17 (5.9, 3.41); 2.76 (25.5, 2.31); 2.04–1.89 (3.5, 2.31); 2.46–2.35 (27, 2.76); 3.41 (2.4, 2.76). ^{13}C-NMR: 217.35 (*s*, CO); 172.37 (*s*, ester CO); 72.80 (*s*, Me$_3$*C*); 64.42 (*t*); 63.26 (*t*); 44.96 (*t*); 42.18 (*d*); 41.85 (*t*); 39.20 (*t*); 35.89 (*d*); 30.72 (*t*); 27,46 (*q*, *Me*$_3$C); 19.19 (*t*, MeCH$_2$CH$_2$CH$_2$); 13.70 (*q*, Me). EI-MS: 285 (12, $[M + H]^+$), 229 (82), 211 (32), 173 (15), 155 (100), 137 (42), 109 (33). Anal. calc. for $C_{16}H_{28}O_4$ (284.40): C 67.57, H 9.92; found: C 67.6, H 9.73.

Benzyl (±)-trans-*2-{[(*tert-*Butyl)dimethylsilyloxy]methyl}-4-oxocyclopentaneacetate* (*rac*-**7b**). A soln. of *rac*-**6b** (38 g, 0.14 mol) and *t*-BuMe$_2$SiCl (26 g, 0.17 mol) in dry DMF (150 ml) containing 24 g of 1*H*-imidazole was stirred at r.t. for 4 h. Then, the mixture was diluted with AcOEt (800 ml) and washed with H_2O (4 × 400 ml). The org. layer was dried (Na_2SO_4) and evaporated and the residue purified by CC (AcOEt/hexane 1:5): *rac*-**7b** (51 g, 93%). Colourless oil. IR (neat): 2950*s*, 2930*s*, 2880*m*, 2860*s*, 1735*s*, 1495*m*, 1470*m*, 1460*m*, 1405*m*, 1390*m*, 1360*m*, 1330*m*, 1250*s*, 1170*s*, 1100*s*, 1000*m*, 835*s*, 780*m*, 750*m*, 700*m*, 680*m*. ^{1}H-NMR (200 MHz): 7.33 (*s*, Ph); 5.11 (*s*, PhCH_2); 3.68 (*dd*, J = 8.0, 1.3, 1 H); 3.64 (*dd*, J = 8.0, 1.2, 1 H); 2.76 (*dd*, J = 14.9, 4.1, 2 H); 2.65–1.90 (*m*, 6 H); 0.87 (*s*, *t*-Bu); 0.03 (*s*, Me$_2$Si). ^{13}C-NMR: 216.97 (*s*, CO); 171.91 (*s*, ester CO); 135.78 (*s*); 128.59 (*d*); 128.33 (*d*); 128.32 (*d*); 68.38 (*t*); 64.09 (*t*); 44.81 (*t*); 43.66 (*d*); 41.20 (*t*); 38.88 (*t*); 35.16 (*d*); 25.84 (*q*, *Me*$_3$C); 18.20 (*s*, Me$_3$*C*); −5.53 (*q*, Me$_2$Si). FAB-MS: 399 (12, $[M + Na]^+$), 377 (26, $[M + H]^+$), 319 (31), 269 (25), 245 (11), 181 (12), 147 (21), 91 (100).

Butyl (±)-t-*2-[(*tert-*Butoxy)methyl]*-c-*4-hydroxycyclopentane*-r-*1-acetate* (*rac*-**8a**). $NaBH_4$ (1.0 g, 2.6 mmol) was added in portions to a stirred soln. of *rac*-**7a** (6 g, 21 mmol) in MeOH (100 ml) at 0°. Stirring was continued for 2 h at the same temp. before most of the MeOH was evaporated. Then, H_2O (100 ml) was added, the mixture extracted with AcOEt (3 × 150 ml), and the combined extract dried (Na_2SO_4) and evaporated. The residue was fractionated by CC (AcOEt/CH_2Cl_2 1:3). From the second of the two main fractions, *rac*-**8a** (2.9 g, 48%) was isolated as a colourless oil. IR (neat): 3430*s* (br., OH), 2970*s*, 2930*s*, 2870*s*, 1730*s*, 1460*m*, 1430*m*, 1390*m*, 1360*s*, 1230*m*, 1200*s*, 1150*m*, 1070*s*, 1020*m*, 880*m*. ^{1}H-NMR (200 MHz): *Table 1*. ^{13}C-NMR: 173.61 (*s*, CO); 72.71 (*d*, C(4)); 72.42 (*s*, Me$_3$*C*); 64.92 (*t*); 64.13 (*t*); 43.43 (*d*); 41.96 (*t*); 40.29 (*t*); 39.65 (*d*); 37.77 (*t*); 30.74 (*t*); 27.52 (*q*, *Me*$_3$C); 19.18 (*t*, MeCH$_2$CH$_2$CH$_2$); 13.69 (*q*, Me). EI-MS: 287 (0.5, $[M + H]^+$), 269 (23.4), 213 (26.3), 211 (20.0), 157 (49.4), 155 (29.62), 139 (45.2), 137 (100), 121 (16.7), 109 (10.7), 97 (21.4), 93 (35.4). Anal. calc. for $C_{16}H_{30}O_4$ (286.42): C 67.10, H 10.56; found: C 66.87, H 10.56.

Benzyl (±)-t-*2-{[(*tert-*Butyl)dimethylsilyloxy]methyl}*-c-*4-hydroxycyclopentane*-r-*1-acetate* (*rac*-**8b**). $NaBH_4$ (0.5 g, 13 mmol) was added in portions into a stirred soln. of *rac*-**7b** (14 g, 37 mmol) in MeOH (100 ml) at 0°. After the addition was complete, the soln. was stirred at 0° for 1 h and then allowed to stand at r.t. for 30 min. Then, the soln. was diluted with AcOEt (1 l) and the mixture washed with H_2O (2 × 500 ml). The org. layer was

dried (Na_2SO_4), the solvent evaporated, and the residue fractionated by CC (CH_2Cl_2/MeOH (1–5%)). From the second of the 2 main fractions, *rac*-**8b** (6.1 g, 44%) was isolated as a colourless oil. IR (neat): 4310 (br., OH), 2960*s*, 2930*s*, 2860*s*, 1740*s*, 1500*m*, 1475*m*, 1465*m*, 1390*m*, 1360*m*, 1255*s*, 1150*m*, 1100*m*, 1000*m*, 845*s*, 785*s*, 750*m*, 700*m*. ^{1}H-NMR (200 MHz): *Table 1*. ^{13}C-NMR: 173.17 (*s*, CO); 136.08 (*s*); 128.51 (*d*); 128.12 (*d*, 2 overlapping signals); 72.68 (*d*); 66.06 (*t*); 65.73 (*t*); 45.20 (*d*); 41.89 (*t*); 40.25 (*t*); 38.87 (*t*); 36.95 (*d*); 25.91 (*q*, Me_3C); 18.23 (*s*, Me_3C); −5.45 (*q*, Me_2Si). FAB-MS: 401 (5, $[M + Na]^+$), 379 (18, $[M + H]^+$), 361 (11), 321 (17), 271 (14), 169 (16), 139 (18), 115 (24), 91 (100). Anal. calc. for $C_{21}H_{36}O_4Si$ (380.60): C 66.27, H 9.53; found: C 65.99, H 9.18.

*Butyl (±)-*t*-2-[(*tert*-Butoxy)methyl]-*c*-4-[(trifluoromethyl)sulfonyloxy]cyclopentane-*r*-1-acetate* (*rac*-**8e**). A soln. of 4-(dimethylamino)pyridine (50 mg) and Et_3N (0.9 g) in CH_2Cl_2 (30 ml) was added dropwise, under stirring, into a chilled (5–10°) soln. of *rac*-**8a** (2.5 g, 8.7 mmol) in CH_2Cl_2 (120 ml) containing trifluoromethanesulfonyl chloride (1.5 g, 8.9 mmol). Then, the mixture was stirred for 2 h before H_2O (10 ml) was added. The org. layer was separated, washed with H_2O (2 × 30 ml), dried (Na_2SO_4), and evaporated. The residue was purified by CC (AcOEt/hexane 1:10): *rac*-**8e** (3.3 g, 90%). Colourless oil. IR (neat): 2970*s*, 2940*s*, 2880*s*, 1730*s*, 1465*m*, 1435*m*, 1400*m*, 1365*m*, 1190*s*, 1130*s*, 1070*m*, 875*s*. ^{1}H-NMR (200 MHz): 5.11–4.98 (*m*, H–C(4)); 4.07 (*t*, J = 6.4, $MeCH_2CH_2CH_2$); 3.31 (*m*, *t*-BuOCH_2); 2.73–2.60 (2*m*, 1 H); 2.51–2.0 (*m*, 5 H); 1.90–1.78 (*m*, 1 H); 1.72–1.52 (*m*, 3 H, incl. $MeCH_2CH_2CH_2$); 1.48–1.25 (*m*, $MeCH_2CH_2CH_2$); 1.17 (*s*, *t*-Bu); 0.94 (*t*, J = 7.2, Me).

*Benzyl (±)-*t*-2-{[(*tert*-Butyl)dimethylsilyloxy]methyl}-*c*-4-[(trifluoromethylsulfonyl)oxy]cyclopentane-*r*-1-acetate* (*rac*-**8f**). As described for *rac*-**8e**, from *rac*-**8b** (2.3 g, 6 mmol). CC (AcOEt/hexane 1:5) gave *rac*-**8f** (2.4 g, 78%). IR (neat): 2960*s*, 2935*s*, 2860*s*, 1740*s*, 1500*m*, 1475*m*, 1465*m*, 1390*m*, 1255*m*, 1200*s*, 1130*s*, 1000*m*, 840*s*, 780*m*, 750*m*, 700*m*. ^{1}H-NMR ($CDCl_3$, 200 MHz): 7.35 (*s*, Ph); 5.12 (*s*, PhCH_2); 5.05 (*m*, H–C(4)); 3.57 (*d*, J = 4.2, $SiOCH_2$–C(2)); 2.76–2.63 (*m*, 1 H); 2.47–1.68 (3*m*, 7 H); 0.87 (*s*, *t*-Bu); 0.03 (*s*, Me_2Si).

*Butyl (±)-*t*-2-[(*tert*-Butoxy)methyl]-*t*-4-hydroxycyclopentane-*r*-1-acetate* (*rac*-**9a**) was isolated as a colourless oil (2.8 g, 47%) from the fraction eluted first by CC of the reaction mixture containing *rac*-**8a**. IR (neat): 3430*s* (br., OH), 2970*s*, 2930*s*, 2870*s*, 1730*s*, 1460*m*, 1430*m*, 1390*m*, 1360*m*, 1200*s*, 1175*s*, 1150*m*, 1080*s*, 1035*m*, 1020*m*, 880*m*. ^{1}H-NMR (200 MHz): *Table 2*. ^{13}C-NMR: 173.46 (*s*, CO); 73.91 (*s*, Me_3C); 73.08 (*d*, C(4)); 64.56 (*t*); 63.87 (*t*); 44.26 (*t*); 43.82 (*t*); 40.78 (*d*); 39.29 (*t*); 36.18 (*d*); 31.14 (*t*); 27.77 (*q*, Me_3C); 19.58 (*t*, $MeCH_2CH_2CH_2$); 14.84 (*q*, Me). EI-MS: 287 (7.4, $[M + H]^+$), 269 (0.4), 231 (19.6), 213 (40.6), 211 (31.1), 157 (20.9), 139 (36.2), 137 (48.8), 97 (21.4), 93 (33.9), 79 (24.3), 57 (100).

*Benzyl (±)-*t*-2-[(*tert*-Butoxy)methyl]-*t*-4-hydroxycyclopentane-*r*-1-acetate* (*rac*-**9b**) was isolated as a colourless oil (6.4 g, 46%) from the fraction eluted first by CC of the reaction mixture containing *rac*-**9a**. IR (neat): 3650 (br., OH), 2960*s*, 2930*s*, 2860*s*, 1740*s*, 1500*m*, 1462*m*, 1425*m*, 1390*m*, 1235*m*, 1255*s*, 1145*m*, 1100*m*, 1035*m*, 1000*m*, 840*s*, 735*s*, 745*m*, 700*m*. ^{1}H-NMR (360.13 MHz): *Table 2*. ^{13}C-NMR: 172.63 (*s*, CO); 136.05 (*s*); 128.55 (*d*); 128.22 (*d*, 2 overlapping signals); 72.54 (*d*); 66.13 (*t*); 65.98 (*t*); 45.20 (*d*); 43.47 (*t*); 40.07 (*t*); 38.75 (*t*); 38.75 (*d*); 35.62 (*q*, Me_3C); 18.38 (*s*, Me_3C); −5.53 (*q*, Me_2Si). FAB-MS: 401 (3, $[M + Na]^+$), 379 (18, $[M + H]^+$), 361 (6), 321 (14), 281 (11), 207 (20), 169 (10), 147 (80), 91 (100).

*Butyl (±)-*t*-2-[(*tert*-Butoxy)methyl]-*t*-4-[(trifluoromethyl)sulfonyloxy]cyclopentane-*r*-1-acetate* (*rac*-**9e**) was obtained as a colourless oil (3.4 g, 94%) from 2.5 g (8.7 mmol) of *rac*-**9a** as described for *rac*-**8e**. IR (neat): 2970*s*, 2940*s*, 2880*s*, 1730*s*, 1465*m*, 1465*m*, 1435*m*, 1400*m*, 1365*m*, 1195*s*, 1130*s*, 1080*m*, 865*s*. ^{1}H-NMR (200 MHz): 5.07 (*m*, H–C(4)); 4.09 (*t*, J = 6.4, $MeCH_2CH_2CH_2$); 3.32 (*m*, *t*-BuOCH_2–C(2)); 2.72–2.62 (*m*, 1 H); 2.44–2.18 (*m*, 5 H); 1.93–1.60 (*m*, 2 H); 1.70–1.54 (*m*, $MeCH_2CH_2CH_2$); 1.49–1.22 (*m*, $MeCH_2CH_2CH_2$); 1.17 (*s*, *t*-Bu); 0.90 (*t*, J = 7.2, Me).

*Butyl (±)-*c*-4-(6-Amino-9*H*-purin-9-yl)-*t*-2-[(*tert*-butoxy)methyl]cyclopentane-*r*-1-acetate* (*rac*-**10a**) was obtained as a white solid (0.82 g, 42%) from 2.0 g (4.8 mmol) of *rac*-**9e** as described for *rac*-**1a**. M.p. 119–121° (from AcOEt). UV: 212 (4.24); 262 (4.16). IR (KBr): 3350*m* (br., NH), 3150*m* (br., NH), 2960*s*, 2930*m*, 2870*m*, 1720*s*, 1650*s*, 1600*s*, 1575*m*, 1485*m*, 1410*m*, 1360 *m*, 1310*m*, 1240*m*, 1200*m*, 1155*m*, 1085*m*, 735*m*. ^{1}H-NMR (360.13 MHz)[2]): 8.35 (*s*, H–C(2)); 7.87 (*s*, H–C(8)); 5.64 (*s*, NH_2); 4.95–4.86 (*m*, H–C(1′)); 4.07 (*t*, J = 6.7, $MeCH_2CH_2CH_2$); 3.39 (*dd*, J = 8.7, 5.2, H_a–C(5′)); 3.34 (*dd*, J = 8.7, 5.4, H_b–C(5′)); 2.74 (*dd*, J = 15.2, 4.8, $COCH_a$–C(3′)); 2.64–2.57 (*m*, 1 H); 2.41 (*dd*, J = 15.2, 8.7, $COCH_b$–C(3′)); 2.32–2.15 (*m*, 4 H); 1.95–1.85 (*m*, 1 H); 1.65–1.57 (*m*, $MeCH_2CH_2CH_2$); 1.42–1.32 (*m*, $MeCH_2CH_2CH_2$); 1.19 (*s*, *t*-Bu); 0.93 (*t*, J = 7.2 Me). NOE: 7.87 (3, 4.91); 3.34 (1, 4.91). ^{13}C-NMR: 172.72 (*s*, CO); 155.45 (*s*, C(6)); 152.73 (*d*, C(2)); 150.26 (*s*, C(4)); 120.19 (*s*, C(5)); 72.69 (*s*, Me_3CO); 64.35 (*t*, 2 C); 54.34 (*d*); 43.34 (*t*); 39.76 (*d*); 39.41 (*t*); 38.06 (*t*); 35.54 (*t*); 30.72 (*t*); 27.54 (*q*, Me_3C); 19.17 (*t*); 13.69 (*q*, Me). EI-MS: 403 (0.5, M^+), 346 (1.3), 330 (14.8), 288 (8.9), 274 (8.5), 232 (6.6), 136 (100), 108 (9.5), 57 (35.5).

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