Stereoselective Synthesis of 4′-α-Alkylcarbovir Derivatives Based on an Asymmetric Synthesis or Chemoenzymatic Procedure

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Stereoselective synthesis of 4′-α-alkylcarbovir derivatives 4 was described based on asymmetric synthesis or a chemoenzymatic procedure. The asymmetric alkylation of chiral acetal 7 gave the alkylated enol ethers 9a—c possessing a chiral quaternary carbon. The key carbocyclic intermediates 14a—c were synthesized from 9a—c *via* eleven-steps. Coupling of 14a—c with 2-amino-6-chloropurine followed by desilylation and subsequent hydrolysis afforded the target compounds 4a—c in moderate yield. The optically active cyclopentene intermediates 5a—c and 6a—c were also prepared by enzymatic resolution of (±)-5a—c and (±)-6a—c, respectively.

Key words carbocyclic nucleoside; 4′-α-alkylcarbovir; enantioselective acetylation; lipase

Carbocyclic nucleosides, where the ribose ring oxygen has been replaced by a methylene group, appear to be promising antiviral and antitumor agents. Carbovir **1** and other cyclopentenyl nucleosides have been extensively investigated for their potential as anti-human immunodeficiency virus (HIV) agents.[1)] Numerous syntheses of carbovir and other carbocyclic nucleosides have been reported.[2)] The most common approach to carbocyclic nucleosides is a convergent synthesis achieved by condenzation of a purine or pyrimidine base with a cyclopentene moiety. The base part is easy to modify[3)] but the cyclopentene moiety generally has few functions. Recently, Maag[4)] and Meguro[5)] reported the anti-HIV activity of various 4′-α-substituted nucleosides **2**, and the synthesis and biological evaluation of 4′-α-substituted carbocyclic nucleosides have also been reported.[6)] For example, 4′-α-hydroxyl and 4′-α-fluoro derivatives **3** have been synthesised starting from aristeromycin, and these show potent anti-herpetic activity.[6a)] The most common synthesis of the optically active 4′-α-substituted carbocyclic nucleosides is transformation from a natural product such as aristeromycin, and therefore, the functionalization of the cyclopentene moiety is restricted. We wish to report here the chemo- and enzymatic synthesis of optically active intermediates for 4′-α-alkylcarbovir derivatives **4**.[7)]

Firstly we tried the asymmetric synthesis of **4**. Our synthetic plan is as shown (Chart 1). (1) The target compounds **4** could be obtained from **5** by the Mitsunobu reaction. (2) The key carbocyclic intermediate **5** may be prepared from **6** *via* stereospecific Pd-catalyzed allylic rearrangement. (3) The construction of the stereogenic quaternary carbon can be achieved by asymmetric alkylation of the chiral acetal **7**.

Asymmetric alkylation of chiral acetal **7** derived from methyl 2-oxocyclopentane-carboxylate **8** and (*R*,*R*)-cycloheptane-1,2-diol,[8)] was reported to give the alkylated enol ethers **9**.[9)] Iodoacetalization of the enol ethers **9** using iodine (2 eq) in the presence of triethylamine (1 eq) in tetrahydrofuran (THF) at −40 °C for 12 h gave the iodoacetals **10** as a single diastereomer. The stereochemistry of **10** was determined by nuclear Overhauser effect (NOE) experiments and the observed NOE enhancements of each proton signal upon irradiation of H_a and Me protons in **10a** are listed in Fig. 2. On irradiation of H_a, H_b and H_d were enhanced. Furthermore, H_e was enhanced on irradiation of the methyl proton. The NOE enhancement patterns of **10b** were very similar to those of **10a**.[10)]

Thus, the *S*-configuration for the C_3 of **10a** was deter-

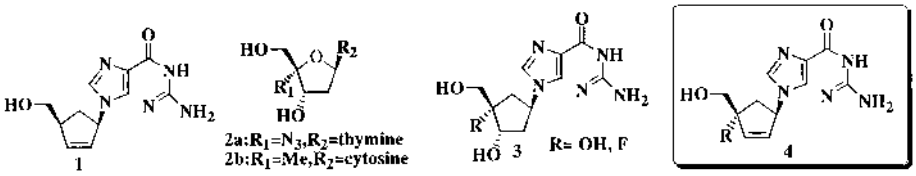

Fig. 1

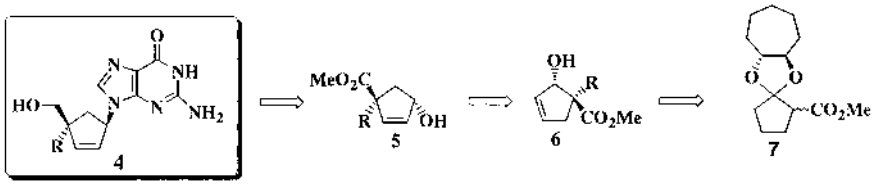

Chart 1

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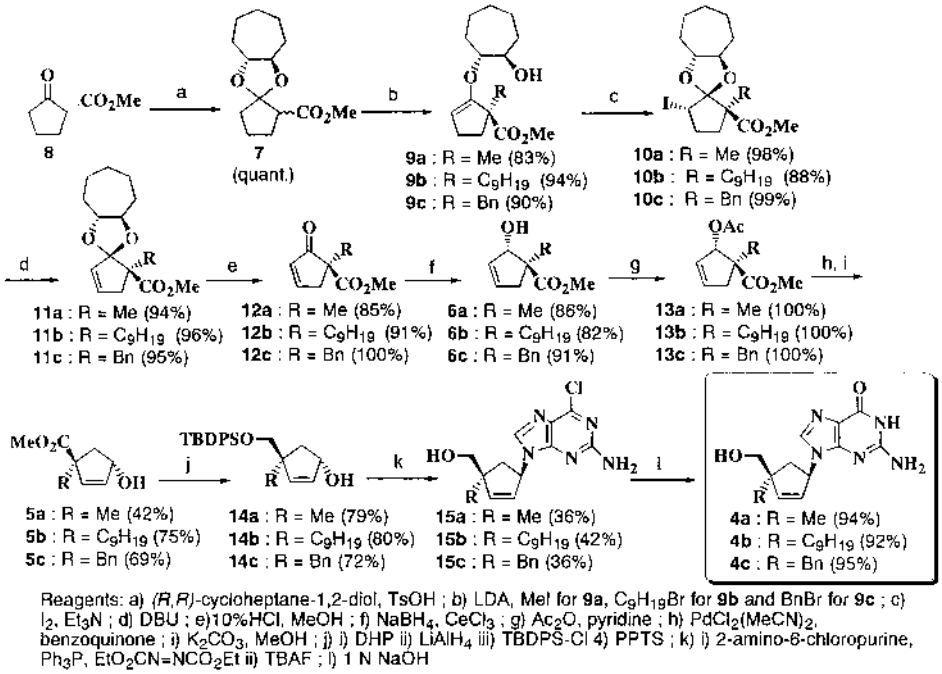
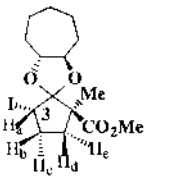


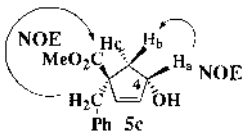
Chart 2



observed NOE (%)

irr.	H_a	H_b	H_c	H_d	H_e
H_a	-	5.2	0	2.7	0
Me	0	0	0	0	3.0

Fig. 2



observed NOE (%)

irr.	H_a	H_b	H_c
H_a	-	4.9	0
CH_2Ph	0	0	2.6

Fig. 3

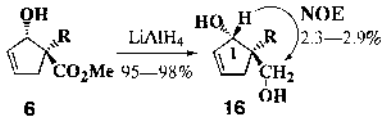
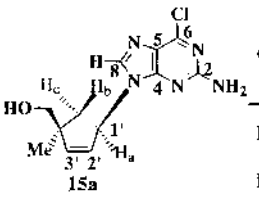


Chart 3

mined as shown in Fig. 2. Treatment of the iodoacetals **10a**—**c** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) at 95—100 °C for 1 h afforded the cyclopentene derivatives **11a**—**c**. Acid hydrolysis of **11a**—**c** gave the chiral enone esters **12a**—**c**, accompanied by (*R*,*R*)-cycloheptane-1,2-diol. Luche reduction[11] of **12a**—**c** using $NaBH_4/CeCl_3$ in MeOH gave the hydroxy esters **6a**—**c** in a highly regio- and diastereoselective manner. The stereochemistry of **6a**—**c** was confirmed by NOE experiments after conversion to diol **16a**—**c** (Chart 3). On irradiation of C_1-H, the methylene protons of the hydroxymethyl group were enhanced (**16a**: 2.2%, **16b**: 2.9%, **16c**: 2.3%) but the methylene protons of the R substituent were not. Thus,the *S*-configuration for the C_1 of **6** was determined. Acetylation of **6** followed by treatment with Pd-catalyst in the presence of benzoquinone in THF gave the desired rearranged products,[12] which were subjected to methanolysis to afford **5c** as a single diastereomer. The stereochemistry of **5c** was determined by NOE experiments and the observed NOE enhancements of each proton signal, upon irradiation of H_a and the methylene protons at the benzyl group in **5c** are listed in Fig. 3. On irradiation of H_a, H_b was enhanced but H_c was not. Furthermore, H_c was enhanced on irradiation of the methylene protons of the benzyl group but H_b was not. The NOE enhancement patterns of **5a** and **5b** were very similar to those of **5c**. Thus, the *S*-configuration for the C_4 of **5** was determined as shown in Fig. 3.

The hydroxy esters **5a**—**c** were converted to the intermediates **14a**—**c** by the following four-step sequence. Protection of the secondary alcohol group in **5a**—**c** with dihydropyranyl (DHP) gave the tetrahydro-pyranyl (THP) ethers which were reduced with $LiAlH_4$ to give a primary alcohol. Protection of the generated primary alcohol group with *tert*-butyldiphenylsilyl chloride (TBDPS-Cl) afforded the corresponding TBDPS-ethers which were treated with pyridinium *p*-toluenesulfonate (PPTS) to provide the desired compounds **14a**—**c**. The Mitsunobu reaction[13] of **14a**—**c** with 2-amino-6-chloropurine followed by desilylation afforded the 6-chloropurine derivatives **15a**—**c**, which were hydrolyzed



observed NOE (%)

irr.	H_a	H_b	H_c	C_8-H	CH_2OH	Me
H_b	0	-	18.3	3.9	1.5	0
H_c	12.7	18.9	-	0	0	11.0

Fig. 4

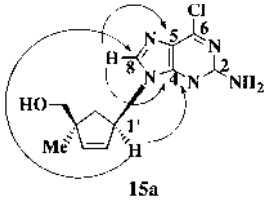


Fig. 5. 2D HMBC Correlation of **15a**

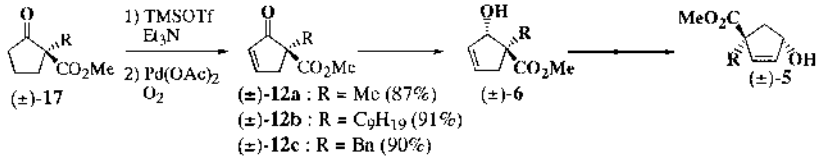
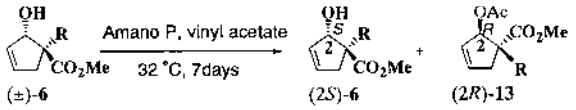


Chart 4

Table 1. Enantioselective Acetylation of (±)-**6**



Entry	R	% Yield (% ee)	
1	Me	59 (63)	30 (91)
2	C_9H_{19}	75 (40)	20 (96)
3	Bn	63 (43)	21 (91)

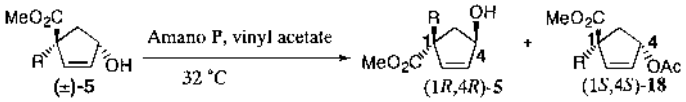
with 1 N NaOH to provide the target compounds **4a**—**c** in 34—39% yield. The relative stereochemistry of **15a** was determined by NOE experiments and the observed NOE enhancements of each proton signal, upon irradiation of H_b and H_c in **15a** are listed in Fig. 4. On irradiation of H_b, C_8-H and the methylene protons of the hydroxymethyl group were enhanced. Furthermore, H_a and the methyl proton were enhanced on irradiation of H_c. The NOE enhancement patterns of **15b** and **15c** were very similar to those of **15a**. Thus, the β-configuration for the C_1 of **15** was established as shown in Fig. 4. The attachment of the carbo-sugar to the base at N_9 is confirmed by the heteronuclear multiple-bond correlation (HMBC) experiment of **15a**, **15b** and **4c**. The important part of the HMBC correlations of **15a** is shown in Fig. 5. The C_4 and C_5 of the 2-amino-6-chloropurine fragment could be assigned as δ 154.7 and 125.1 based on long range coupling with C_8-H, respectively. Furthermore the spectra showed a long range coupling between the $C_{1'}$-H and the purine carbons C_4 and C_8.

Next we tried the enantioselective acetylation of the racemic secondary alcohol (±)-**5a**—**c** and (±)-**6a**—**c** with a quaternary carbon. The substrates (±)-**5a**—**c** and (±)-**6a**—**c** were prepared by following steps (Chart 4). Treatment of (±)-**17a**—**c** with trimethylsilyl trifluoromethanesulfonate (TMSOTf) and triethylamine followed by Pd-catalyzed oxidation[14] gave (±)-**12** in 87—91% yield. The cyclopentenones (±)-**12a**—**c** were converted to (±)-**5a**—**c** and (±)-**6a**—**c** according to the above mentioned procedure (Chart 2). Then the enantioselective acetylation of (±)-**5a**—**c** and (±)-**6a**—**c**, using lipase "Amano P" from *Pseudomonas* sp. in vinyl acetate, was carried out and the results are shown in Tables 1 and 2. The enantiomeric excess (ee) of the products was determined based on the ^{1}H-NMR spectra of the corresponding (*R*)-α-methoxy-α-trifluoromethylphenylacetyl (MTPA) esters. The absolute configuration of the enzymatic reaction products was assigned by comparison with authentic samples. Enzymatic acetylation of (±)-**6a**—**c** gave the acetate (2*R*)-**13a**—**c** (21—30%, 91—96% ee) and the recovered (2*S*)-**6a**—**c** (59—75%, 40—63% ee) (Table 1, entry 1—3). Although the ee of (2*R*)-**13a**—**c** was generally high, the reaction rate was slow.

Enzymatic acetylation of (±)-**5a**—**c** gave the acetate (1*S*,4*S*)-**18a**—**c** (42—57%, 53—92% ee) and the unchanged (1*R*,4*R*)-**5a**—**c** (39—52%, 69—83% ee) (Table 2, entry 1—3). The recovered (1*R*,4*R*)-**5a**—**c**, having 69—83% ee, were again subjected to the enzymatic reaction to give 91—96% ee of (1*R*,4*R*)-**5a**—**c** (Table 2, entry 4—6). Enrichment of ee of (1*S*,4*S*)-**18a**—**c** (84—99% ee) was also achieved by the repeated enzymatic acetylation of (1*S*,4*S*)-**5a**—**c** (53—92% ee) (Table 2, entry 7—9). Treatment of (1*S*,4*S*)-**18a**—**c** (84—99% ee) with K_2CO_3 in MeOH gave (1*S*,4*S*)-**5a**—**c** (84—99% ee). Thus, both enantiomers of the key intermediate **5a**—**c** ((1*R*,4*R*)-**5a**—**c** (91—96% ee) and (1*S*,4*S*)-**5a**—**c** (84—99% ee)) were obtained in high optical purity. The enantioselective acetylation was explained by Cygler's model[15] (Fig. 6). This empirical rule generalizes the observed enantioselectivity of lipases in both hydrolysis reactions and transesterifications. The importance of substituent size was reported in studies which showed that lipases resolve secondary alcohols with two similarly-sized substituents poorly, but they resolve these secondary alcohols efficiently when the size of one substituent is increased.[15] In our cases, the great difference between the large substituent (quaternary carbon side) and the medium substituent (olefinic carbon side) in (±)-**6a**—**c** provided a high enantiomeric excess of the acetylated products (1*R*,2*R*)-**13a**—**c**. In comparison with (±)-**6a**—**c**, the great distance between the quaternary carbon and the reaction site led to lower enantioselectivity, especially in (±)-**5a**.

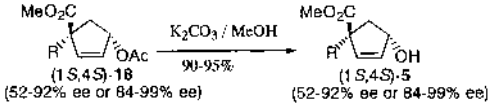
In conclusion, the enantioselective synthesis of 4′-α-alkylcarbovir derivatives **4a**—**c** was achieved based on the following two methods. One is asymmetric alkylation of the β-keto ester, the other is enzymatic resolution of the racemic inter-

Table 2. Enantioselective Acetylation of (±)-**5**



Entry	Substrate (% ee)	R	Time (d)	Products	
				% (% ee)	% (% ee)
1	(±)-**5a**	Me	2	(1*R*,4*R*)-**5a**; 39 (77)	(1*S*,4*S*)-**18a**; 57 (53)
2	(±)-**5b**	C_9H_{19}	7	(1*R*,4*R*)-**5b**; 52 (69)	(1*S*,4*S*)-**18b**; 42 (92)
3	(±)-**5c**	Bn	7	(1*R*,4*R*)-**5c**; 45 (83)	(1*S*,4*S*)-**18c**; 49 (87)
4	(1*R*,4*R*)-**5a** (77)	Me	1	(1*R*,4*R*)-**5a**; 62 (96)	(1*S*,4*S*)-**18a**; 19 (42)
5	(1*R*,4*R*)-**5b** (69)	C_9H_{19}	7	(1*R*,4*R*)-**5b**; 75 (91)	(1*R*,4*R*)-**18b**; 20 (12)
6	(1*R*,4*R*)-**5c** (83)	Bn	7	(1*R*,4*R*)-**5c**; 72 (92)	(1*R*,4*R*)-**18c**; 8 (1)
7	(1*S*,4*S*)-**5a** (53)[a]	Me	1	(1*R*,4*R*)-**5a**; 24 (33)	(1*S*,4*S*)-**18a**; 66 (84)
8	(1*S*,4*S*)-**5b** (92)[a]	C_9H_{19}	7	(1*S*,4*S*)-**5b**; 30 (77)	(1*S*,4*S*)-**18b**; 68 (99)
9	(1*S*,4*S*)-**5c** (87)[a]	Bn	7	(1*S*,4*S*)-**5c**; 45 (73)	(1*S*,4*S*)-**18c**; 49 (99)

a) The substrates (1*S*,4*S*)-**5** (53—92% ee) were obtained by deacetylation of (1*S*,4*S*)-**18** (53—92% ee).



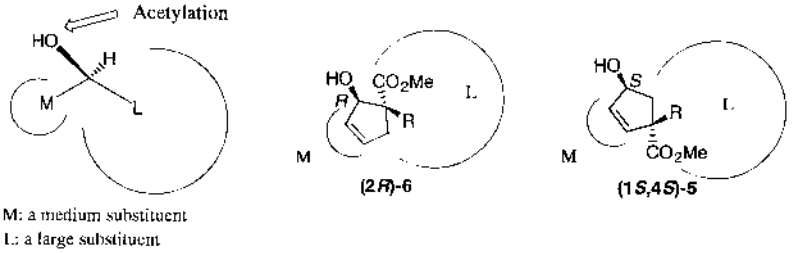


Fig. 6

mediate. The optically active cyclopentene derivatives (2*S*)-**6a**—**c** obtained by enzymatic resolution were converted to the target molecules **4a**—**c** in the same way as the asymmetric synthesis. On the other hand, deprotection of the asymmetric acetylation products (1*S*,4*S*)-**18a**—**c** gave the optically active cyclopentene derivatives **5a**—**c**, which were also converted to the target molecules **4a**—**c**. Although no antiviral activity against HIV-1 was exhibited by the carbocyclic nucleosides **4a**—**c**, the effects of further structural modifications on the antiviral activity in this series need to be investigated.

Experimental

All melting points were measured on a Yanaco MP-3S micro melting point apparatus and are uncorrected. ^{1}H- and ^{13}C-NMR spectra were measured at 23 °C (internal standard, Me_4Si) with a JEOL GX 400 or JEOL LA 500 spectrometer. The fast atom bombardment mass spectra (FAB-MS) were obtained with a JEOL JMS-SX 102A or JEOL JMS-DX 303 spectrometer. IR spectra were recorded on a JASCO IR-810 spectrometer. Optical rotations were measured with a JASCO DIP-140 digital polarimeter. UV spectra were recorded on a JASCO Ubest-55 spectrophotometer. For column chromatography, silica-gel (Kieselgel 60) was employed.

Methyl (1*R*)-1-Benzyl-2-[(1′*R*,2′*R*)-2-hydroxycycloheptan-1′-yl]oxy-2-cyclopenten-1-carboxylate (9c) Chromatographed on a Florisil column (hexane/ethyl acetate=30 : 1) afforded **9c** (1.51 g, 90%) as a colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 7.25—7.18 (5H, m), 4.48 (1H, t, J=2.4 Hz), 3.76—3.63 (2H, m), 3.72 (3H, s), 3.62 (1H, br s), 3.08 (2H, s), 2.28—2.08 (2H, m), 2.02—1.94 (4H, m), 1.78—1.49 (8H, m). ^{13}C-NMR ($CDCl_3$) δ: 175.9 (s), 155.7 (s), 137.1 (s), 130.4 (d), 127.8 (d), 126.4 (d), 98.5 (d), 87.1 (d), 75.8 (d), 50.9 (s), 52.3 (q), 40.0 (t), 31.4 (t), 31.3 (t), 28.4 (t), 27.3 (t), 26.1 (t), 22.3 (t), 22.2 (t). FAB-MS m/z: 345 (M^++H). IR (neat, cm^{-1}) 3500, 2930, 1730, 1650. $[\alpha]_D^{25}$ −60.5 (c=0.92, $CHCl_3$). HRMS (FAB) m/z: 345.2072 (M^++H, Calcd for $C_{21}H_{29}O_4$ 345.2066).

General Procedure for the Preparation of 10 A solution of I_2 (2.31 g, 9.1 mmol) in THF (7 ml) was added dropwise to a stirred solution of triethylamine (0.66 ml, 4.8 mmol) and **9** (4.55 mmol) in THF (25 ml) at −40 °C under an Ar atmosphere. After being stirred for 12 h at −40 °C and for an additional 12 h at −20 °C, the reaction was quenched with aqueous 3% sodium thiosulfate, followed by extraction with ethyl acetate. The extracts were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by column chromatography on silica-gel, the fraction eluted with hexane/ethyl acetate (40 : 1—30 : 1) afforded **10** as a colorless oil.

Methyl (1*S*,3*S*)-2,2-[(1′*R*,2′*R*)-Cycloheptane-1′,2′-dioxy]-3-iodo-1-methylcyclopentane-carboxylate (10a) 98% yield. ^{1}H-NMR ($CDCl_3$) δ: 4.52 (1H, dd, J=12, 8 Hz, C_3-H), 4.17 (1H, dt, J=14, 5 Hz, $C_{1'}$-H), 3.79 (1H, dt, J=14, 5 Hz, $C_{2'}$-H), 3.68 (3H, s, OMe), 2.41 (1H, dt, J=13, 9 Hz, C_5-H_β), 2.30—2.22 (2H, m, C_4-H_β and $C_{3'}$-H), 2.15—2.07 (2H, m, C_4-H_α and $C_{7'}$-H), 1.64—1.48 (9H, m, C_5-H_α and other-H), 1.33 (3H, s, C_1-Me). ^{13}C-NMR ($CDCl_3$) δ: 175.2 (s, CO), 115.5 (s, C_2), 82.6, 81.9 (each as d, $C_{1'}$ and $C_{2'}$), 52.3 (s, C1), 52.1 (q, OMe), 35.7 (t, C_5), 33.8 (d, C_3), 33.0 (t, C_4), 29.2 (t), 28.5 (t), 25.0 (t), 25.0 (t), 24.9 (t), 21.4 (q). FAB-MS m/z 433 (M^++K). IR (neat, cm^{-1}) 2980, 1730. $[\alpha]_D^{20}$ +63.2 (c=0.96, $CHCl_3$). HRMS (FAB) m/z: 520.9686 (M^++I, Calcd for $C_{15}H_{23}O_4I_2$ 520.9687).

Methyl (1*S*,3*S*)-2,2-[(1′*R*,2′*R*)-Cycloheptane-1′,2′-dioxy]-3-iodo-1-nonylcyclopentane-carboxylate (10b) 88% yield. ^{1}H-NMR ($CDCl_3$) δ: 4.39 (1H, dd, J=9, 7 Hz, C_3-H), 4.09 (1H, dt, J=14, 5 Hz, $C_{1'}$-H), 3.75 (1H, dt, J=14, 5 Hz, $C_{2'}$-H), 3.68 (3H, s, OMe), 2.39 (1H, dt, J=13, 8 Hz, C_5-H_β), 2.31—2.22 (2H, m, C_4-H_β and $C_{3'}$-H), 2.12—2.03 (2H, m, C_4-H_α and $C_{7'}$-H), 1.98 (1H, dt, J=12, 4 Hz, C<u>H$_2$</u>-C_8H_{17}), 1.72 (1H, m, C_5-H_α), 1.66—1.46 (9H, m), 1.31—1.05 (14H, m), 0.87 (3H, t, J=7 Hz, C_8H_{16}<u>Me</u>); ^{13}C-NMR ($CDCl_3$) δ: 174.3 (s, CO), 115.5 (s, C_2), 82.4, 81.9 (each as d, $C_{1'}$ and $C_{2'}$), 57.1 (s, C_1), 51.8 (q, OMe), 34.9 (t, C_5), 34.5 (d, C_3), 32.9 (t, C_4), 31.9 (t), 31.7 (t), 30.2 (t), 29.5 (t), 29.5 (t), 29.4 (t), 29.3 (t), 28.4 (t), 25.7 (t), 25.0

(t), 24.9 (t), 24.9 (t), 22.6 (t), 14.1 (q). FAB-MS *m/z* 545 (M^++K). IR (neat, cm^{-1}) 2930, 1740. $[\alpha]_D^{26}$ +41.4 (*c*=0.82, $CHCl_3$). HRMS (FAB) *m/z*: 545.1536 (M^++K, Calcd for $C_{23}H_{39}O_4IK$ 545.1530).

Methyl (1*R*,3*S*)-1-Benzyl-2,2-[(1′*R*,2′*R*)-Cycloheptane-1′,2′-dioxy]-3-iodo-1-cyclopentane-carboxylate (10c) 99% yield. ^{1}H-NMR ($CDCl_3$) δ: 7.26—7.11 (5H, m), 4.40 (1H, t, *J*=8 Hz, C_3-H), 4.15 (1H, dt, *J*=15, 5 Hz, $C_{1'}$-H), 3.82 (1H, dd, *J*=15, 5 Hz, $C_{2'}$-H), 3.70 (3H, s, OMe), 3.50 (1H, d, *J*=14 Hz, C$\underline{H}_2$Ph), 2.95 (1H, d, *J*=14 Hz, C$\underline{H}_2$Ph), 2.33—2.27 (2H, m), 2.18—2.08 (3H, m), 1.86 (1H, m), 1.72—1.48 (8H, m). ^{13}C-NMR ($CDCl_3$) δ: 173.6 (s, CO), 138.1 (s), 129.7 (d), 128.2 (d), 126.4 (d), 115.4 (s, C_2), 82.5, 82.0 (each as d, $C_{1'}$ and $C_{2'}$), 57.9 (s, C_1), 51.8 (q, OMe), 39.5 (t), 34.3 (d, C_3), 33.0 (t, C_4), 31.0 (t), 29.5 (t), 28.5 (t), 25.0 (t), 24.9 (t), 24.9 (t). FAB-MS *m/z* 471 (M^++H). IR (neat, cm^{-1}) 2940, 1730. $[\alpha]_D^{22}$ +42.4 (*c*=0.95, $CHCl_3$). HRMS (FAB) *m/z*: 471.1014 (M^++H, Calcd for $C_{21}H_{28}O_4I$ 471.1032).

General Procedure for the Preparation of 11 A solution of **10** (4.55 mmol) in DBU (5 ml) was heated at 95—100 °C for 1 h. The product was purified by column chromatography on silica-gel, and the fraction eluted with hexane/ethyl acetate (30 : 1—20 : 1) afforded **11** as a colorless oil.

Methyl (1*S*)-2,2-[(1′*R*,2′*R*)-Cycloheptane-1′,2′-dioxy]-1-methyl-3-cyclopentenecarboxylate (11a) 94% yield. ^{1}H-NMR ($CDCl_3$) δ: 6.04 (1H, dt, *J*=6, 2 Hz, C_3-H or C_4-H), 5.54 (1H, dt, *J*=6, 2 Hz, C_3-H or C_4-H), 3.68 (3H, s, OMe), 3.74 (1H, m, $C_{1'}$-H), 3.63 (1H, m, $C_{2'}$-H), 3.23 (1H, dt, *J*=17, 2 Hz, C_5-H), 2.19—2.09 (3H, m), 1.67—1.35 (8H, m), 1.34 (3H, s, C_1-Me). ^{13}C-NMR ($CDCl_3$) δ: 174.5 (s, CO), 134.5 (d), 130.1 (d), 119.3 (s, C_2), 81.0, 81.9 (each as d, $C_{1'}$ and $C_{2'}$), 54.4 (s, C_1), 51.6 (q, OMe), 41.9 (t), 29.7 (t), 28.8 (t), 25.2 (t), 24.9 (t), 24.8 (t), 21.7 (q). FAB-MS *m/z* 305 (M^++K). IR (neat, cm^{-1}) 2940, 1740, 1630. $[\alpha]_D^{25}$ −58.1 (*c*=0.82, $CHCl_3$).

Methyl (1*S*)-2,2-[(1′*R*,2′*R*)-Cycloheptane-1′,2′-dioxy]-1-nonyl-3-cyclopentenecarboxylate (11b) 96% yield. ^{1}H-NMR ($CDCl_3$) δ: 6.01 (1H, dt, *J*=6, 2 Hz, C_3-H or C_4-H), 5.53 (1H, dt, *J*=6, 2 Hz, C_3-H or C_4-H), 3.68 (3H, s, OMe), 3.74 (1H, m, $C_{1'}$-H), 3.64 (1H, m, $C_{2'}$-H), 3.14 (1H, dt, *J*=17, 2 Hz, C_5-H), 2.24 (1H, dt, *J*=17, 2 Hz, C_5-H), 2.21—2.03 (2H, m), 1.63—1.24 (24H, m), 0.86 (3H, t, *J*=7 Hz, $C_8H_{16}\underline{Me}$). ^{13}C-NMR ($CDCl_3$) δ: 173.7 (s, CO), 134.5, 130.2 (each as d, C3 and C4), 119.4 (s, C_2), 81.9, 80.9 (each as d, $C_{1'}$ and $C_{2'}$), 59.2 (s, C_1), 51.4 (q, OMe), 38.3 (t), 34.4 (t), 31.9 (t), 30.2 (t), 29.8 (t), 29.5 (t), 29.5 (t), 29.3 (t), 28.8 (t), 26.0 (t), 25.2 (t), 24.9 (t), 24.8 (t), 22.6 (t), 21.7 (q). FAB-MS *m/z* 417 (M^++K). IR (neat, cm^{-1}) 2930, 1740, 1635. $[\alpha]_D^{25}$ −70.7 (*c*=0.75, $CHCl_3$).

Methy (1*S*)-1-Benzyl-2,2-[(1′*R*,2′*R*)-cycloheptane-1′,2′-dioxy]-1-3-cyclopentenecarboxylate (11c) 95% yield. ^{1}H-NMR ($CDCl_3$) δ: 7.25—7.15 (5H, m), 6.04 (1H, dt, *J*=6, 3 Hz, C_3-H or C_4-H), 5.59 (1H, dt, *J*=6, 3 Hz, C_3-H or C_4-H), 3.71 (3H, s, OMe), 3.85—3.70 (2H, m, $C_{1'}$-H and $C_{2'}$-H), 2.96 (1H, dt, *J*=17, 3 Hz, C_5-H), 2.66 (1H, d, *J*=14 Hz, C$\underline{H}_2$Ph), 2.61 (1H, d, *J*=14 Hz, C$\underline{H}_2$Ph), 2.35 (1H, dt, *J*=17, 3 Hz, C_5-H), 2.26 (1H, m), 2.15 (1H, m), 1.76—1.3 (8H, m). ^{13}C-NMR ($CDCl_3$) δ: 173.3 (s, CO), 138.8 (s, Ph), 134.4, 129.9, 129.8, 128.1, 126.3 (each as d, Ph, C_3 and C_4), 119.6 (s, C_2), 82.1, 81.1 (each as d, $C_{1'}$ and $C_{2'}$), 59.9 (s, C_1), 51.6 (q, OMe), 39.3 (t), 36.7 (t), 29.9 (t), 28.9 (t), 25.2 (t), 24.9 (t), 24.8 (t). FAB-MS *m/z* 343 (M^++H). IR (neat, cm^{-1}) 2930, 1730, 1620. $[\alpha]_D^{25}$ +0.2 (*c*=0.86, $CHCl_3$).

General Procedure for the Preparation of 12 Aqueous 10% HCl (3.5 ml) was added to a stirred solution of **11** (3.85 mmol) in MeOH (20 ml) at r.t. After being stirred for 8 h, the reaction was quenched with $NaHCO_3$, and the solution was concentrated *in vacuo*. The crude product was purified by column chromatography on silica-gel. The fractions eluted with hexane/ethyl acetate (30 : 1—10 : 1) afforded **12** (colorless oil) and the fractions eluted with ethyl acetate afforded (1*R*,2*R*)-cycloheptane-1,2-diol (355—405 mg, 71—81%).

Methyl (1*S*)-1-Methyl-2-oxo-3-cyclopentenecarboxylate (12a) 85% yield. ^{1}H-NMR ($CDCl_3$) δ: 7.74 (1H, dt, *J*=6, 3 Hz, C_4-H), 6.18 (1H, dt, *J*=6, 3 Hz, C_3-H), 3.70 (3H, s, OMe), 3.28 (1H, dt, *J*=19, 3 Hz, C_5-H), 2.55 (1H, dt, *J*=19, 3 Hz, C_5-H), 1.42 (3H, s, Me). ^{13}C-NMR($CDCl_3$) δ: 206.5 (s, CO), 172.0 (s, CO), 163.1 (d, C_4), 131.6 (d, C_3), 53.3 (s, C_1), 52.7 (q, OMe), 42.7 (t, C_5), 20.7 (q, Me). IR (neat, cm^{-1}): 2975, 1750, 1720, 1600. FAB-MS *m/z*: 155 (M^++H). $[\alpha]_D^{28}$ −59.1 (*c*=0.95, $CHCl_3$). *Anal*. Calcd for $C_8H_{10}O_3$: C, 62.33; H, 6.54. Found: C, 62.30; H, 6.81.

Methyl (1*S*)-1-Nonyl-2-oxo-3-cyclopentenecarboxylate (12b) 91% yield. ^{1}H-NMR ($CDCl_3$): δ: 7.75 (1H, dt, *J*=6, 3 Hz, C_4-H), 6.15 (1H, dt, *J*=6, 3 Hz, C_3-H), 3.70 (3H, s, OMe), 3.28 (1H, dt, *J*=19, 3 Hz, C_5-H), 2.61 (1H, dt, *J*=19, 3 Hz, C_5-H), 1.98 (1H, m), 1.74 (1H, m), 1.24 (14H, m), 0.88 (3H, t, *J*=7 Hz, Me). ^{13}C-NMR ($CDCl_3$) δ: 205.8 (s, CO), 171.2 (s, CO), 163.7 (d, C_4), 132.2 (d, C_3), 58.1 (s, C_1), 52.7 (q, OMe), 39.3 (t, C_5), 34.5 (t), 31.8 (t), 29.8 (t), 29.5 (t), 29.3 (t), 29.2 (t), 24.6 (t), 22.6 (t), 14.1 (q, Me). IR (neat, cm^{-1}): 2930, 1750, 1718, 1600. FAB-MS *m/z*: 267 (M^++H). $[\alpha]_D^{20}$ −64.4 (*c*=0.77, $CHCl_3$). HRMS (FAB) *m/z*: 267.1962 (M^++H, Calcd for $C_{16}H_{27}O_3$ 267.1960).

Methyl (1*R*)-1-Benzyl-2-oxo-3-cyclopentenecarboxylate (12c) 100% yield. ^{1}H-NMR ($CDCl_3$) δ: 7.58 (1H, dt, *J*=6, 3 Hz, C_4-H), 7.25—7.09 (5H, m), 6.06 (1H, dt, *J*=6, 2 Hz, C_3-H), 3.74 (3H, s, OMe), 3.26 (2H, s, C$\underline{H}_2$Ph), 3.17 (1H, dt, *J*=19, 3 Hz, C_5-H), 2.72 (1H, dt, *J*=19, 2 Hz, C_5-H). ^{13}C-NMR ($CDCl_3$) δ: 205.4 (s, CO), 170.9 (s, CO), 164.3 (d, C_4), 136.0 (s), 132.3 (d, C_3), 130.0 (d), 128.3 (d), 126.9 (d), 58.6 (s, C_1), 52.8 (q, OMe), 39.3 (t, C_5), 38.0 (t). IR (neat, cm^{-1}): 2950, 1740, 1708, 1590. FAB-MS *m/z*: 231 (M^++H). $[\alpha]_D^{22}$ −100.4 (*c*=0.77, $CHCl_3$). HRMS (FAB) *m/z*: 231.1002 (M^++H, Calcd for $C_{14}H_{15}O_3$ 231.1021).

General Procedure for Preparation of 6 $NaBH_4$ (427 mg, 11.3 mmol) was slowly added to a stirred solution of **12** (7.52 mmol) and $CeCl_3$ (1.85 g, 7.52 mmol) in MeOH (60 ml) at −40 °C. After 15 min, the reaction was quenched with acetone and H_2O, and the mixture was diluted with ethyl acetate. The mixture was filtered through celite and the filtrate was concentrated in vacuo. The crude product was purified by column chromatography on silica-gel. The fractions eluted with hexane/ethyl acetate (10 : 1—5 : 1) afforded **6** as a colorless oil.

Methyl (1*S*,2*S*)-2-Hydroxy-1-methyl-3-cyclopentenecarboxylate (6a) 86% yield. ^{1}H-NMR ($CDCl_3$): δ: 5.84 (1H, m, C_3-H or C_4-H), 5.68 (1H, dt, *J*=6, 3 Hz, C_3-H or C_4-H), 5.05 (1H, br s, C_2-H), 3.72 (3H, s, OMe), 2.88 (1H, ddd, *J*=17, 4, 3 Hz, C_5-H), 2.29 (1H, ddd, *J*=17, 4, 3 Hz, C_5-H), 1.95 (1H, br s, OH), 1.28 (3H, s, Me). ^{13}C-NMR ($CDCl_3$): δ: 177.9 (s, CO), 131.8 (d, C_3 or C_4), 131.6 (d, C_3 or C_4), 80.9 (d, C_2), 52.9 (s, C_1), 52.1 (q, OMe), 42.9 (t, C_5), 19.0 (q, Me). IR (neat, cm^{-1}): 3430, 2950, 1730. FAB-MS *m/z*: 157 (M^++H). $[\alpha]_D^{27}$ +56.4 (*c*=0.76, $CHCl_3$).

Methyl (1*S*,2*S*)-2-Hydroxy-1-nonyl-3-cyclopentenecarboxylate (6b) 82% yield. ^{1}H-NMR ($CDCl_3$) δ: 5.91 (1H, m, C_3-H or C_4-H), 5.75 (1H, m, C_3-H or C_4-H), 4.93 (1H, d, *J*=5 Hz, C_2-H), 3.70 (3H, s, OMe), 2.92 (1H, d, *J*=17 Hz, C_5-H), 2.31 (1H, ddd, *J*=17, 6, 2 Hz, C_5-H), 1.85 (1H, m), 1.62—1.54 (2H, m, OH and C$\underline{H}_2$-C_8H_{17}), 1.25 (14H, m), 0.88 (3H, t, *J*=7 Hz, Me). ^{13}C-NMR ($CDCl_3$) δ: 177.0 (s, CO), 133.6 (d, C_3 or C_4), 131.7 (d, C_3 or C_4), 80.6 (d, C_2), 57.5 (s, C_1), 52.0 (q, OMe), 39.3 (t, C_5), 32.7 (t), 31.8 (t), 30.1(t), 29.5 (t), 29.4 (t), 29.3 (t), 25.8 (t), 22.6 (t), 14.1 (q, Me). IR (neat, cm^{-1}): 3440, 2920, 1725. FAB-MS *m/z*: 269 (M^++H), 251 (M^++H−H_2O). $[\alpha]_D^{23}$ +24.3 (*c*=0.76, $CHCl_3$).

Methyl (1*R*,2*S*)-1-Benzyl-2-hydroxy-3-cyclopentenecarboxylate (6c) 91% yield. ^{1}H-NMR ($CDCl_3$) δ: 7.26—7.10 (5H, m, Ph), 5.94 (1H, m, C_3-H or C_4-H), 5.81 (1H, m, C_3-H or C_4-H), 4.98 (1H, br s, C_2-H), 3.63 (3H, s, OMe), 3.31 (1H, d, *J*=14 Hz, C$\underline{H}_2$Ph), 2.87 (1H, d, *J*=14 Hz, C$\underline{H}_2$Ph), 2.77(1H, dd, *J*=17, 1 Hz, C_5-H), 2.64 (1H, ddd, *J*=17, 4, 2 Hz, C_5-H), 1.92 (1H, br s, OH). ^{13}C-NMR ($CDCl_3$) δ: 176.2 (s, CO), 138.2 (s), 133.5, 131.7, 129.6, 128.2, 126.5 (each as d, C_3, C_4 and Ph), 80.9 (d, C_2), 59.0 (s, C_1), 51.9 (q, OMe), 38.1, 37.9 (each as t, $\underline{C}H_2$Ph and C_5). IR (neat, cm^{-1}): 3450, 2950, 1720. FAB-MS *m/z*: 233 (M^++H), 215 (M^++H−H_2O). $[\alpha]_D^{23}$ +78.0 (*c*=0.94, $CHCl_3$).

General Procedure for Preparation of Diol 16 $LiAlH_4$ (94.9 mg, 2.5 mmol) was slowly added to a stirred solution of **6** (1 mmol) in THF (10 ml) at 0 °C. After 15 min, the reaction was quenched with ethyl acetate and H_2O. The mixture was filtered through celite and the filtrate was concentrated *in vacuo*. The crude product was purified by column chromatography on silica-gel. The fractions eluted with $CHCl_3$/MeOH (80 : 1—40 : 1) afforded **16** as a colorless oil.

(1*S*,5*R*)-5-Hydroxymethyl-5-methyl-2-cyclopentenol (16a) 95% yield. ^{1}H-NMR ($CDCl_3$) δ: 5.86 (1H, m, C_3-H), 5.72 (1H, m, C_2-H), 4.57 (1H, br s, C_1-H), 3.52 (1H, d, *J*=10 Hz, C$\underline{H}_2$OH), 3.49 (1H, d, *J*=10 Hz, C$\underline{H}_2$OH), 2.22 (1H, d, *J*=17, C_4-H), 2.13 (1H, ddd, *J*=17, 5, 2 Hz, C_4-H), 1.85 (1H, br s, OH), 1.74 (1H, br s, OH), 1.09 (3H, s, Me). ^{13}C-NMR ($CDCl_3$) δ: 132.9 (d, C_3), 132.6 (d, C_2), 80.8 (d, C_1), 70.4 (t, $\underline{C}H_2$OH), 47.2 (s, C_5), 40.2 (t, C_4), 17.9 (q, Me). IR (neat, cm^{-1}): 3350, 2930, 1620. FAB-MS *m/z*: 167 (M^++K). $[\alpha]_D^{20}$ +64.0 (*c*=0.3, $CHCl_3$).

(1*S*,5*R*)-5-Hydroxymethyl-5-nonyl-2-cyclopentenol (16b) 97% yield. ^{1}H-NMR ($CDCl_3$) δ: 5.86 (1H, m, C_3-H), 5.76 (1H, m, C_2-H), 4.54 (1H, br s, C_1-H), 3.55 (1H, d, *J*=11 Hz, C$\underline{H}_2$OH), 3.40 (1H, d, *J*=11 Hz, C$\underline{H}_2$OH), 2.21 (1H, ddd, *J*=17, 4, 2 Hz, C_4-H), 2.02 (1H, d, *J*=17 Hz, C_4-H), 1.82 (1H, br s, OH), 1.68 (1H, br s, OH), 1.58 (1H, dt, *J*=13, 4 Hz, C$\underline{H}_2$-C_8H_{17}), 1.45 (1H, dt, *J*=13, 3 Hz, C$\underline{H}_2$-C_8H_{17}), 1.29 (14H, br s), 0.87 (3H, t, *J*=7 Hz, Me). ^{13}C-NMR ($CDCl_3$) δ: 133.5 (d, C_3), 132.5 (d, C_2), 80.8 (d, C_1), 67.4 (t, $\underline{C}H_2$OH), 49.4 (s, C_5), 39.9 (t, C_4), 31.9 (t), 30.7 (t), 30.2 (t), 29.7 (t), 29.6 (t), 29.3 (t), 25.0 (t), 22.6 (t), 14.1 (q, Me). IR (neat, cm^{-1}): 3440, 2920, 1725. FAB-MS *m/z*: 279 (M^++K). $[\alpha]_D^{23}$ +41.5 (*c*=0.5, $CHCl_3$).

(1*S*,5*S*)- 5-Benzyl-5-hydroxymethyl-2-cyclopentenol (16c) 98% yield.

^{1}H-NMR ($CDCl_3$) δ: 7.31—7.20 (5H, m, Ph), 5.91 (1H, m, C_3-H), 5.85 (1H, m, C_2-H), 4.65 (1H, br s, C_1-H), 3.43 (1H, d, J=11 Hz, C$\underline{H}_2$OH), 3.28 (1H, d, J=11 Hz, C$\underline{H}_2$OH), 3.12 (1H, d, J=14 Hz, C$\underline{H}_2$Ph), 2.73 (1H, d, J=14 Hz, C$\underline{H}_2$Ph), 2.42 (1H, ddd, J=17, 4, 2 Hz, C_4-H), 1.84 (1H, d, J=17 Hz, C_4-H), 1.56 (1H, br s, OH), 1.45 (1H, br s, OH). ^{13}C-NMR ($CDCl_3$) δ: 139.2 (s), 133.5 (d, C_3), 132.6 (d, C_2), 130.3, 128.2, 126.1 (each as d, Ph), 80.8 (d, C_1), 66.5 (t, $\underline{C}H_2$OH), 50.9 (s, C_5), 38.8 (t, C_4), 35.5 (t, $\underline{C}H_2$Ph). IR (neat, cm^{-1}): 3330, 2920, 1627, 1603. FAB-MS m/z: 205 (M^++H). $[\alpha]_D^{25}$ +149.5 (c=0.59, MeOH).

General Procedure for the Acetylation of 6 Ac_2O (1.35 g, 13.2 mmol) was added to a stirred solution of 4-dimethylaminopyridine (134 mg, 1.1 mmol), pyridine (1.6 ml, 13.2 mmol) and **6** (6.6 mmol) at r.t. After being stirred for 1 h, the reaction was quenched with H_2O and the solution was extracted with ethyl acetate. The extract was washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by column chromatography on silica-gel, and the fraction eluted with hexane/ethyl acetate (30 : 1—20 : 1) afforded the acetate **13** as a colorless oil.

Methyl (1*S*,2*S*)-2-Acetoxy-1-methyl-3-cyclopentenecarboxylate (13a) 100% yield. ^{1}H-NMR ($CDCl_3$) δ: 6.00 (1H, br s, C_2-H), 5.96 (1H, m, C_3-H or C_4-H), 5.67 (1H, m, C_3-H or C_4-H), 3.73 (3H, s, OMe), 2.92 (1H, ddd, J=17, 4, 2 Hz, C_5-H), 2.35 (1H, ddd, J=17, 4, 2 Hz, C_5-H), 2.07 (3H, s, COMe), 1.23 (3H, s, C_1-Me). ^{13}C-NMR ($CDCl_3$) δ: 176.8 (s, CO), 170.6 (s, CO), 133.7 (d, C_3 or C_4), 128.6 (d, C_3 or C_4), 82.9 (d, C_2), 52.3 (q, OMe), 51.5 (s, C_1), 44.6 (t, C_5), 20.8 (q, CO$\underline{Me}$), 18.9 (q, Me). IR (neat, cm^{-1}): 2940, 1735, 1235. FAB-MS m/z: 237 (M^++K). $[\alpha]_D^{24}$ +114.8 (c=0.93, $CHCl_3$). *Anal*. Calcd for $C_{10}H_{14}O_4$: C, 60.58; H, 7.12. Found: C, 60.44; H, 7.22.

Methyl (1*S*,2*S*)-2-Acetoxy-1-nonyl-3-cyclopentenecarboxylate (13b) 100% yield. ^{1}H-NMR ($CDCl_3$) δ: 6.03 (1H, m, C_3-H or C_4-H), 5.95 (1H, br s, C_2-H), 5.75 (1H, m, C_3-H or C_4-H), 3.70 (3H, s, OMe), 3.00 (1H, dt, J=17, 3 Hz, C_5-H), 2.34 (1H, ddd, J=17, 4, 2 Hz, C_5-H), 2.06 (3H, s, COMe), 1.79 (1H, m, C$\underline{H}_2$-C_8H_{17}), 1.63 (1H, m, C$\underline{H}_2$-C_8H_{17}), 1.25 (14H, m), 0.88 (3H, t, J=7 Hz, C_8H_{16}-$\underline{Me}$). ^{13}C-NMR ($CDCl_3$) δ: 175.9 (s, CO), 170.4 (s, CO), 136.2 (d, C_3 or C_4), 128.8 (d, C_3 or C_4), 85.4 (d, C_2), 56.5 (s, C_1), 52.2 (q, OMe), 40.6 (t, C_5), 33.0 (t), 31.9 (t), 30.1(t), 29.5 (t), 29.4 (t), 29.3 (t), 25.7 (t), 22.6 (t), 21.0 (q, CO$\underline{Me}$), 14.1 (q, C_8H_{16}-Me). IR (neat, cm^{-1}): 2920, 1735, 1230. FAB-MS m/z: 311 (M^++H). $[\alpha]_D^{22}$ +120.7 (c=0.75, $CHCl_3$). HRMS (FAB) m/z: 311.2213 (M^++H, Calcd for $C_{18}H_{31}O_4$ 311.2223).

Methyl (1*R*,2*S*)-2-Acetoxy-1-benzyl-3-cyclopentenecarboxylate (13c) 100% yield. ^{1}H-NMR ($CDCl_3$) δ: 7.24—7.07 (5H, m, Ph), 6.06 (1H, m, C_3-H or C_4-H), 5.95 (1H, br s, C_2-H), 5.80 (1H, m, C_3-H or C_4-H), 3.63 (3H, s, OMe), 3.24 (1H, d, J=14 Hz, C$\underline{H}_2$Ph), 2.95 (1H, d, J=14 Hz, C$\underline{H}_2$Ph), 2.89 (1H, br d, J=17 Hz, C_5-H), 2.52 (1H, ddd, J=17, 4, 2 Hz, C_5-H), 2.11 (3H, s, CO$\underline{Me}$). ^{13}C-NMR ($CDCl_3$) δ: 174.9 (s, CO), 170.3 (s, CO), 137.6 (s), 136.5, 129.4, 128.7, 128.3, 126.7 (each as d, C_3, C_4 and Ph), 81.8 (d, C_2), 58.0 (s, C_1), 52.2 (q, OMe), 39.3, 38.2 (each as t, $\underline{C}H_2$Ph and C_5), 21.1 (q, CO$\underline{Me}$). IR (neat, cm^{-1}): 2945, 1735, 1235. FAB-MS m/z: 275 (M^++H), 215 (M^++H−H_2O). $[\alpha]_D^{20}$ +162.9 (c=0.89, $CHCl_3$). HRMS (FAB) m/z: 275.1264 (M^++H, Calcd for $C_{16}H_{19}O_4$ 275.1283).

General Procedure for Preparation of 5 A stirred mixture of the above acetate **13** (5.87 mmol), 1,4-benzoquinone (317 mg, 2.94 mmol) and bis(acetonitrile)dichloropalladium (85 mg, 0.29 mmol) in THF (20 ml) was refluxed for 3—10 h. The reaction mixture was diluted with aqueous 3% sodium thiosulfate and extracted with ethyl acetate. The extract was washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. To a solution of the crude product in MeOH (8 ml) was added K_2CO_3 (811 mg, 5.87 mmol) and the entire mixture was stirred at r.t. for 1 h. The reaction mixture was diluted with brine and extracted with ethyl acetate. The extracts were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by column chromatography on silica-gel, and the fractions eluted with hexane/ethyl acetate (10 : 1—6 : 1) afforded **5** as a colorless oil and unreacted **6** (**6a**: 40%, **6b**: 12%, **6c**: 15%).

Methyl (1*S*,4*S*)-4-Hydroxy-1-methyl-2-cyclopentenecarboxylate (5a) 42% yield. ^{1}H-NMR ($CDCl_3$) δ: 5.86 (2H, s, C_2-H and C_3-H), 4.97 (1H, dd, J=7, 4 Hz, C_4-H), 3.67 (3H, s, OMe), 2.84 (1H, dd, J=14, 7 Hz, C_5-H$_\beta$), 1.88 (1H, br s, OH), 1.56 (1H, dd, J=14, 4 Hz, C_5-H$_\alpha$), 1.44 (3H, s, C_1-Me). ^{13}C-NMR ($CDCl_3$) δ: 176.5 (s, CO), 138.1, 134.6 (each as d, C_3 and C_4), 77.0 (d, C_4), 55.2 (s, C_1), 52.1 (q, OMe), 45.4 (t, C_5), 25.9 (q, C_1-Me). IR (neat, cm^{-1}): 3400, 2950, 1730. FAB-MS m/z: 157 (M^++H). $[\alpha]_D^{18}$ −197.8 (c=0.68, $CHCl_3$).

Methyl (1*S*,4*S*)-4-Hydroxy-1-nonyl-2-cyclopentenecarboxylate (5b) 75% yield. ^{1}H-NMR ($CDCl_3$) δ: 5.88 (1H, br d, J=6 Hz, C_2-H), 5.84 (1H, dd, J=6, 2 Hz, C_3-H), 4.95 (1H, br s, C_4-H), 3.66 (3H, s, OMe), 2.84 (1H, dd, J=14, 7 Hz, C_5-H$_\beta$), 1.84 (1H, m, C$\underline{H}_2$-C_8H_{17}), 1.62—1.68 (2H, m, OH and C$\underline{H}_2$-C_8H_{17}), 1.58 (1H, dd, J=14, 4 Hz, C_5-H$_\alpha$), 1.25 (14H, m), 0.88 (3H, t, J=7 Hz, C_8H_{16}-$\underline{Me}$). ^{13}C-NMR ($CDCl_3$) δ: 175.9 (s, CO), 137.3 (d, C_2), 134.6 (d, C_3), 76.8 (d, C_4), 59.9 (s, C_1), 52.0 (q, OMe), 43.1 (t, C_5), 39.6 (t), 31.9 (t), 29.9 (t), 29.5 (t), 29.5 (t), 29.3 (t), 25.4 (t), 22.7 (t), 14.1 (q, C_8H_{16}-$\underline{Me}$). IR (neat, cm^{-1}): 3400, 2930, 1740. FAB-MS m/z: 307 (M^++K), 269 (M^++H). $[\alpha]_D^{15}$ −99.8 (c=0.83, $CHCl_3$).

Methyl (1*S*,4*S*)-1-Benzyl-4-hydroxy-2-cyclopentenecarboxylate (5c) 69% yield. ^{1}H-NMR ($CDCl_3$) δ: 7.31—7.12 (5H, m, Ph), 5.93 (1H, d, J=6 Hz, C_2-H), 5.83 (1H, dd, J=6, 2 Hz, C_3-H), 4.74 (1H, br s, C_4-H), 3.68 (3H, s, OMe), 3.12 (1H, d, J=13 Hz, C$\underline{H}_2$Ph), 3.07 (1H, d, J=13 Hz, C$\underline{H}_2$Ph), 2.70 (1H, dd, J=14, 8 Hz, C_5-H$_\beta$), 1.75 (1H, dd, J=14, 3 Hz, C_5-H$_\alpha$), 0.65 (1H, d, J=8 Hz, OH). ^{13}C-NMR ($CDCl_3$) δ: 175.5 (s, CO), 137.0 (s), 136.6, 135.2, 130.3, 128.2, 127.0 (each as d, C_2, C_3 and Ph), 76.4 (d, C_4), 60.8 (s, C_1), 52.1 (q, OMe), 44.3, 41.5 (each as t, $\underline{C}H_2$Ph and C_5). IR (neat, cm^{-1}): 3400, 2950, 1730. FAB-MS m/z: 271 (M^++K). $[\alpha]_D^{22}$ −89.8 (c=0.94, $CHCl_3$).

General Procedure for Preparation of 14 A mixture of **5** (2.52 mmol), 3,4-dihydro-2*H*-pyran (276 mg, 3.28 mmol) and pyridinium *p*-toluenesulfonate (63 mg, 0.25 mmol) in CH_2Cl_2 (15 ml) was stirred for 1 h at r.t. The reaction mixture was diluted with brine, and extracted with ethyl acetate. The extract was dried over $MgSO_4$, and concentrated *in vacuo*. To a solution of the crude product in THF (10 ml) was added $LiAlH_4$ (96 mg, 2.52 mmol) at 0 °C and the entire mixture was stirred at r.t. for 0.5 h. The reaction was quenched with ethyl acetate and H_2O, the mixture was filtered and the filtrate was concentrated *in vacuo.* A mixture of the crude product, imidazole (515 mg, 7.56 mmol) and TBDPS-Cl (0.98 ml, 3.78 mmol) in DMF (10 ml) was stirred at r.t. for 2 h. The crude mixture was diluted with 5% $NaHCO_3$ and extracted with ethyl acetate. The extracts were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. A mixture of the crude product and pyridinium *p*-toluenesulfonate (63 mg, 0.25 mmol) in MeOH (25 ml) was stirred at r.t. for 3 h. The crude mixture was diluted with 5% $NaHCO_3$ and extracted with ethyl acetate. The extract was washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by column chromatography on silica-gel, and the fractions eluted with hexane/ethyl acetate (40 : 1—30 : 1) afforded **14** as a colorless oil.

(1*S*,4*S*)-4-(*tert*-Butyldiphenylsilyloxymethyl)-4-methyl-2-cyclopentenol (14a) 80% yield. ^{1}H-NMR ($CDCl_3$) δ: 7.64—7.61 (4H, m), 7.43—7.35 (6H, m), 5.79—5.75 (2H, m, C_2-H and C_3-H), 4.87 (1H, br s, C_1-H), 3.39 (2H, s, CH_2OSi), 2.34 (1H, dd, J=14, 7 Hz, C_5-H), 1.49 (1H, br s, OH), 1.38 (1H, dd, J=14, 4 Hz, C_5-H), 1.16 (3H, s, C_4-Me), 1.04 (9H, s, CMe_3). ^{13}C-NMR ($CDCl_3$) δ: 133.7, 133.6 (each as s), 141.5, 135.7, 135.6, 133.2, 129.6, 129.6, 127.6, 127.6 (each as d, C_2, C_3 and Ph), 77.6 (d, C_1), 71.2 (t, CH_2OSi), 51.1 (s, C_4), 44.9 (t, C_5), 26.8 (q, C$\underline{Me}_3$), 24.9 (q, C_4-$\underline{Me}$), 19.3 (q, $\underline{C}Me_3$). IR (neat, cm^{-1}): 3310, 2850, 1430, 1115. FAB-MS m/z: 405 (M^++K). $[\alpha]_D^{24}$ −66.9 (c=0.82, $CHCl_3$). HRMS (FAB) m/z: 405.1614 (M^++K, Calcd for $C_{23}H_{30}O_2SiK$405.1652).

(1*S*,4*S*)-4-(*tert*-Butyldiphenylsilyloxymethyl)-4-nonyl-2-cyclopentenol (14b) 97% yield. ^{1}H-NMR ($CDCl_3$) δ: 7.62—7.60 (4H, m), 7.43—7.34 (6H, m), 5.78 (1H, dd, J=6, 2, C_2-H or C_3-H), 5.74 (1H, d, J=6, C_2-H or C_3-H), 4.84 (1H, br s, C_1-H), 3.40 (2H, s, CH_2OSi), 2.20 (1H, dd, J=14, 7, C_5-H), 1.52 (1H, br s, OH), 1.48—1.40 (3H, m, C$\underline{H}_2$-C_8H_{17} and C_5-H), 1.25 (14H, br s), 1.03 (9H, s, CMe_3), 0.88 (3H, t, J=7 Hz, C_8H_{16}-$\underline{Me}$). ^{13}C-NMR ($CDCl_3$) δ: 133.7, 133.6 (each as s), 140.5, 135.7, 135.7, 133.6, 129.6, 129.6, 127.6, 127.6 (each as d, C_2, C_3 and Ph), 77.5 (d, C_1), 70.0 (t, $\underline{C}H_2OSi$), 54.8 (s, C_4), 42.4 (t, C_5), 36.7 (t), 31.9 (t), 30.5 (t), 29.7 (t), 29.7 (t), 29.4 (t), 26.9 (q, C$\underline{Me}_3$), 24.8 (t), 22.7 (t), 19.4 (s, $\underline{C}Me_3$), 14.2 (q, C_8H_{16}-$\underline{Me}$). IR (neat, cm^{-1}): 3340, 2930, 1430, 1150. FAB-MS m/z: 517 (M^++K). $[\alpha]_D^{24}$ −36.7° (c=0.88, $CHCl_3$). *Anal*. Calcd. for $C_{31}H_{46}O_2Si$: C, 77.77; H, 9.69. Found: C, 77.81; H, 9.39.

(1*S*,4*S*)-4-Benzyl-4-(*tert*-butyldiphenylsilyloxymethyl)-2-cyclopentenol (14c) 98% yield. ^{1}H-NMR ($CDCl_3$) δ: 7.66—7.63 (4H, m, Ph), 7.44—7.36 (6H, m, Ph), 7.28—7.11 (5H, m, Ph), 5.84 (1H, d, J=6 Hz, C_2-H or C_3-H), 5.71 (1H, dd, J=6, 2 Hz, C_2-H or C_3-H), 4.52 (1H, dt, J=8, 2 Hz, C_1-H), 3.49 (2H, s, CH_2OSi), 2.97 (1H, d, J=13 Hz, C$\underline{H}_2$Ph), 2.74 (1H, d, J=13 Hz, C$\underline{H}_2$Ph), 2.05 (1H, dd, J=14, 8 Hz, C_5-H), 1.54—1.51 (2H, m, OH and C_5-H), 1.09 (1H, s, CMe_3). ^{13}C-NMR ($CDCl_3$) δ: 138.5, 133.5, 133.5 (each as s), 139.5, 135.7, 135.6, 134.1, 130.7, 129.7, 129.7, 129.6, 127.9, 127.6, 126.5 (each as d, C_2, C_3 and Ph), 76.9 (d, C_1), 70.7 (t, CH_2OSi), 56.1 (s, C_4), 42.4, 40.5 (each as t, C_5 and $\underline{C}H_2$Ph), 26.9 (q, C$\underline{Me}_3$), 19.4 (s, $\underline{C}Me_3$). IR (neat, cm^{-1}): 3350, 2860, 1430, 1110. FAB-MS m/z: 481 (M^++K). $[\alpha]_D^{20}$ −31.2 (c=0.88, $CHCl_3$). HRMS (FAB) m/z: 481.1945 (M^++K, Calcd for $C_{29}H_{34}O_2SiK$481.1965).

General Procedure for Preparation of 15 A solution of Ph_3P (444 mg,

1.69 mmol) in THF (10 ml) was added dropwise to a stirred solution of 2-amino-6-chloropurine (287 mg, 1.69 mmol) and diethyl azodicarboxylate (295 mg, 1.72 mmol) in THF (10 ml) at r.t. After 10 min, substrate **14** (0.85 mmol) in THF (7 ml) was slowly added and the mixture was stirred for 2 h. 2-Amino-6-chloropurine (144 mg, 0.85 mmol) and diethyl azodicarboxylate (147 mg, 0.85 mmol) were added to the reaction mixture and stirred for an additional 12 h. The mixture was diluted with AcOEt, filtered and the filtrate was concentrated *in vacuo*. The crude product was purified by column chromatography on silica-gel, and the fraction eluted with hexane/ethyl acetate (3 : 1—2 : 1) afforded an amorphous solid. A mixture of the above amorphous solid in THF (5 ml) and tetrabutylammonium fluoride (1 M in THF, 1.69 ml, 1.69 mmol) was stirred for 12 h at r.t. The mixture was purified by column chromatography on silica-gel, and the fraction eluted with $CHCl_3$/MeOH (80 : 1—70 : 1) afforded **15** as an amorphous solid.

2-Amino-6-chloro-9-[(1′*R*,4′*S*)-4′-hydroxymethyl-4′-methyl-2′-cyclopenten-1′-yl]-9H-purine (15a) 36% yield. m.p. 208—212 °C (dec.). ^{1}H-NMR (MeOH-d_4) δ: 8.11 (1H, s, C_8-H), 6.02 (1H, dd, J=6, 2 Hz, $C_{3'}$-H), 5.81 (1H, dd, J=6, 2 Hz, $C_{2'}$-H), 5.68 (1H, m, $C_{1'}$-H), 3.52 (1H, d, J=11 Hz, C$\underline{H}_2$-OH), 3.39 (1H, d, J=11 Hz, C$\underline{H}_2$-OH), 2.31 (1H, dd, J=14, 9 Hz, $C_{5'}$-H_α), 2.03 (1H, dd, J=14, 5 Hz, $C_{5'}$-H_β), 1.13 (3H, s, $C_{4'}$-Me). ^{13}C-NMR (MeOH-d_4) δ: 161.1 (s, C_2 or C_6), 154.7 (s, C_4), 151.3 (s, C_2 or C_6), 145.7 (d, $C_{3'}$), 142.7 (d, C_8), 128.6 (d, $C_{2'}$), 125.1 (s, C_5), 69.7 (t, C$\underline{H}_2$-OH), 61.0 (d, $C_{1'}$), 52.5 (s, $C_{4'}$), 42.3 (t, $C_{5'}$), 24.1 (q, $C_{4'}$-Me). IR (KBr, cm^{-1}): 3470, 3300, 3200, 1625. FAB-MS m/z: 280 (M^++H). $[\alpha]_D^{24}$ −48.2 (c=0.71, MeOH). λ_{max}^{MeOH}/nm (ε): 222 (17783), 247 (4263), 310 (5903). *Anal*. Calcd. for $C_{12}H_{14}N_5OCl$ 1/2H_2O: C, 49.98; H, 5.25; N, 24.30. Found: C, 50.25; H, 5.20; N, 24.41.

2-Amino-6-chloro-9-[(1′*R*,4′*S*)-4′-hydroxymethyl-4′-nonyl-2′-cyclopenten-1′-yl]-9H-purine (15b) 42% yield. m.p. 115—118 °C (dec.). ^{1}H-NMR ($CDCl_3$) δ: 7.92 (1H, s, H_8), 5.94 (1H, dd, J=5, 2 Hz, $C_{3'}$-H), 5.74 (1H, dd, J=5, 2 Hz, $C_{2'}$-H), 5.53 (1H, m, $C_{1'}$-H), 5.15 (2H, br s, NH_2), 3.82 (1H, br s, CH_2-O$\underline{H}$), 3.69 (1H, d, J=11 Hz, C$\underline{H}_2$-OH), 3.59 (1H, d, J=11 Hz, C$\underline{H}_2$-OH), 2.42 (1H, dd, J=14, 9 Hz, $C_{5'}$-H_α), 2.25 (1H, dd, J=14, 6 Hz, $C_{5'}$-H_β), 1.45—1.36 (2H, m, C$\underline{H}_2$-C_8H_{17}), 1.27 (14H, m), 0.89 (3H, t, J=7 Hz, C_8H_{16}-C$\underline{H}_3$). ^{13}C-NMR ($CDCl_3$) δ: 158.4 (s, C_2 or C_6), 152.9 (s, C_4), 151.5 (s, C_2 or C_6), 142.9 (d, $C_{3'}$), 141.9 (d, C_8), 129.1 (d, $C_{2'}$), 125.9 (s, C_5), 69.3 (t, C$\underline{H}_2$-OH), 61.4 (d, $C_{1'}$), 55.9 (s, $C_{4'}$), 37.9 (t, $C_{5'}$), 37.1, 31.9, 30.3, 29.6, 29.6, 29.3, 24.5, 22.7 (each as t), 14.1 (q, C_8H_{16}-C$\underline{H}_3$). IR (KBr, cm^{-1}): 3300, 3200, 2920, 1625, 1560. FAB-MS m/z: 392 (M^++H). $[\alpha]_D^{20}$ +26.0 (c=0.56, MeOH). λ_{max}^{MeOH}/nm (ε): 222 (20782), 248 (5042), 310 (6228). *Anal*. Calcd. for $C_{20}H_{30}N_5OCl$ 3/2H_2O: C, 57.38; H, 7.95; N, 16.74. Found: C, 57.46; H, 7.82; N, 16.78.

2-Amino-6-chloro-9-[4′-benzyl-(1′*R*,4′*S*)-4′-hydroxymethyl-2′-cyclopenten-1′-yl]-9H-purine (15c) 36% yield. m.p. 103—105 °C. ^{1}H-NMR ($CDCl_3$) δ: 7.82 (1H, s, C_8-H), 7.31— 7.14 (5H, m, Ph), 6.02 (1H, dd, J=6, 2 Hz, $C_{3'}$-H), 5.69 (1H, dd, J=6, 2 Hz, $C_{2'}$-H), 5.27 (2H, br s, NH_2), 5.03 (1H, m, $C_{1'}$-H), 4.38 (1H, br s, CH_2-O$\underline{H}$), 3.75 (1H, d, J=11 Hz, C$\underline{H}_2$-OH), 3.69 (1H, d, J=11 Hz, C$\underline{H}_2$-OH), 2.83 (1H, d, J=13 Hz, C$\underline{H}_2$-Ph), 2.71 (1H, d, J=13 Hz, C$\underline{H}_2$-Ph), 2.52 (1H, dd, J=14, 9 Hz, $C_{5'}$-H_α), 2.25 (1H, dd, J=14, 5 Hz, $C_{5'}$-H_β). ^{13}C-NMR ($CDCl_3$) δ: 158.4 (s, C_2 or C_6), 152.8 (s, C_4), 151.3 (s, C_2 or C_6), 142.4 (d, $C_{3'}$), 141.9 (d, C_8), 137.1 (s, Ph), 130.4, 128.1, 126.5 (each as d, Ph), 129.9 (d, $C_{2'}$), 125.6 (s, C_5), 68.9 (t, CH_2-OH), 60.9 (d, $C_{1'}$), 56.8 (s, $C_{4'}$), 43.0 (t, C$\underline{H}_2$-Ph), 37.3 (t, $C_{5'}$). IR (KBr, cm^{-1}): 3460, 3320, 1620. FAB-MS m/z: 356 (M^++H). $[\alpha]_D^{27}$ +90.5° (c=0.61, MeOH). λ_{max}^{MeOH}/nm (ε): 223 (20695), 248 (4231), 309 (5985). *Anal*. Calcd. for $C_{18}H_{18}N_5OCl$ 1/2H_2O: C, 59.32; H,5.26; N, 19.23. Found: C, 59.61; H, 5.03; N, 19.28.

General Procedure for Preparation of 4 A stirred solution of **15** (0.2 mmol) in 1 M aqueous NaOH (20 ml) was refluxed for 1—3 h. Evaporation of the solvent under reduced pressure provided a crude product which was purified by column chromatography on silica-gel, and the fractions eluted with $CHCl_3$/MeOH (10 : 1—8 : 1) afforded **4** as an amorphous solid.

2-Amino-9-[(1′*R*,4′*S*)-4′-hydroxymethyl-4′-methyl-2′-cyclopenten-1′-yl]-9H-purine-6(1H)-one (4a) 94% yield. m.p. 287—290 °C (dec.). ^{1}H-NMR(DMSO-d_6) δ: 10.54 (1H, s, N_1-H), 7.59 (1H, s, C_8-H), 6.39 (2H, br s, N$\underline{H}_2$), 5.93 (1H, dd, J=6, 2 Hz, $C_{3'}$-H), 5.73 (1H, dd, J=6, 2 Hz, $C_{2'}$-H), 5.43 (1H, m, $C_{1'}$-H), 4.72 (1H, s, CH_2-OH), 3.34 (1H, d, J=11 Hz, C$\underline{H}_2$-OH), 3.26 (1H, d, J=11 Hz, C$\underline{H}_2$-OH), 2.12 (1H, dd, J=13, 9 Hz, $C_{5'}$-H_α), 1.87 (1H, dd, J=13, 6 Hz, $C_{5'}$-H_β), 1.05 (3H, s, Me). ^{13}C-NMR (DMSO-d_6) δ: 156.6 (s, C_2 or C_6), 153.4 (s, C_2 or C_6), 150.6 (s, C_4), 143.6 (d, $C_{3'}$), 134.7 (s, C_8), 127.7 (d, $C_{2'}$), 116.4 (s, C_5), 68.2 (t, C$\underline{H}_2$-OH), 58.3 (d, $C_{1'}$), 50.9 (s, $C_{4'}$), 41.5 (t, $C_{5'}$), 23.4 (q, Me). IR (KBr, cm^{-1}): 3400, 3150, 2920, 1680, 1610, 1530. FAB-MS m/z: 262 (M^++H). $[\alpha]_D^{22}$ −4.7 (c=0.2, MeOH). λ_{max}^{MeOH}/nm (ε): 206.0 (19310), 253.4 (10211). Anal. Calcd. for $C_{12}H_{15}N_5O_2$ 1H_2O: C, 51.59; H, 6.14; N, 25.08. Found: C, 51.88; H, 5.98; N, 24.95.

2-Amino-9-[(1′*R*,4′*S*)-4′-hydroxymethyl-4′-nonyl-2′-cyclopenten-1′-yl]-9H-purine-6(1H)-one (4b) 92% yield. m.p. 287—290 °C (dec.). ^{1}H-NMR (DMSO-d_6) δ: 10.90 (1H, s, N_1-H), 7.57 (1H, s, H_8), 6.77 (2H, s, NH_2), 5.87 (1H, dd, J=6, 2 Hz, $C_{3'}$-H), 5.75 (1H, dd, J=6, 2 Hz, $C_{2'}$-H), 5.35 (1H, m, $H_{1'}$), 4.79 (1H, t, J=5 Hz, CH_2-O$\underline{H}$), 3.38 (1H, dd, J=10, 5 Hz, C$\underline{H}_2$-OH), 3.28 (1H, dd, J=10, 5 Hz, C$\underline{H}_2$-OH), 2.19 (1H, dd, J=14, 9 Hz, $C_{5'}$-H_α), 1.79 (1H, dd, J=14, 5 Hz, $C_{5'}$-H_β), 1.36 (2H, t, J=7.9 Hz, C$\underline{H}_2$-C_8H_{17}), 1.25 (14H, m), 0.87 (3H, t, J=7 Hz, C_8H_{16}-C$\underline{H}_3$). ^{13}C-NMR (DMSO-d_6) δ: 156.6 (s, C_2), 153.7 (s, C_6), 150.6 (s, C_4), 142.2 (d, $C_{3'}$), 134.7 (d, C_8), 128.6 (d, $C_{2'}$), 116.5 (s, C_5), 67.2 (t, C$\underline{H}_2$-OH), 58.5 (d, $C_{1'}$), 54.8 (s, $C_{4'}$), 39.3 (t, $C_{5'}$), 35.9, 31.2, 29.8, 29.0, 29.0, 28.7, 23.9, 22.0 (each as t), 13.9 (q, C_8H_{16}-C$\underline{H}_3$). IR (KBr, cm^{-1}): 3420, 2930, 1680, 1610, 1530. FAB-MS m/z: 374 (M^++H). $[\alpha]_D^{23}$ +59.9 (c=0.2, MeOH). λ_{max}^{MeOH}/nm (ε): 206.2 (18953), 254.8 (9731). *Anal*. Calcd. for $C_{20}H_{31}N_5O_2$ 1H_2O: C, 61.35; H, 8.50; N, 17.89. Found: C, 61.52; H, 8.34; N, 17.65.

2-Amino-9-[(1′*R*,4′*S*)-4′-benzyl-4′-hydroxymethyl-2′-cyclopenten-1′-yl]-9H-purine-6(1H)-one (4c) 95% yield. m.p. 292—295 °C. ^{1}H-NMR (DMSO-d_6) δ: 10.83 (1H, s, N_1-H), 7.55 (1H, s, C_8-H), 7.30—7.15 (5H, m, Ph), 6.71 (2H, s, N$\underline{H}_2$), 5.93 (1H, dd, J=5, 2 Hz, $C_{3'}$-H), 5.71 (1H, dd, J=5, 2 Hz, $C_{2'}$-H), 4.93—4.98 (2H, m, $C_{1'}$-H and CH_2-O$\underline{H}$), 3.41 (1H, dd, J=11, 5 Hz, C$\underline{H}_2$-OH), 3.34 (1H, dd, J=11, 5 Hz, C$\underline{H}_2$-OH), 2.77 (1H, d, J=13 Hz, C$\underline{H}_2$-Ph), 2.67 (1H, d, J=13 Hz, C$\underline{H}_2$-Ph), 2.31 (1H, dd, J=14.0, 9.0 Hz, $C_{5'}$-H_α), 1.78 (1H, dd, J=14, 5 Hz, $C_{5'}$-H_β). ^{13}C-NMR (DMSO-d_6) δ: 156.7 (s, C_2 or C_6), 153.6 (s, C_2 or C_6), 150.6 (s, C_4), 141.8 (d, $C_{3'}$), 138.1 (s, Ph), 134.8 (d, C_8), 130.3, 127.7, 125.9 (each as d, Ph), 129.4 (d, $C_{2'}$), 116.5 (s, C_5), 67.0 (t, C$\underline{H}_2$-OH), 58.2 (d, $C_{1'}$), 55.9 (s, $C_{4'}$), 41.4 (t, C$\underline{H}_2$-Ph), 38.3 (t, $C_{5'}$). IR (KBr, cm^{-1}): 3330, 1687, 1625. FAB-MS m/z: 376 (M^++K). $[\alpha]_D^{23}$ +112.0 (c=0.41, MeOH). λ_{max}^{MeOH}/nm (ε): 207 (23555), 255 (9222). *Anal*. Calcd. for $C_{18}H_{19}N_5O_2$ 1/2H_2O: C, 62.40; H,5.82; N, 20.23. Found: C, 62.49; H, 5.79; N, 19.96.

General Procedure for Preparation of (±)-12 Trimethylsilyl trifluoromethanesulfonate (3.3 ml, 19.0 mmol) was added dropwise to a stirred solution of (±)-**17** (11.1 mmol) and triethylamine (7.7 ml, 55.2 mmol) in CH_2Cl_2 (20 ml) at 0 °C. After being stirred for 0.5 h at r.t., the reaction was quenched with aqueous saturated $NaHCO_3$ at 0 °C. The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was dissolved in hexane (100 ml) which was washed with H_2O, dried over $MgSO_4$ and concentrated *in vacuo*. A mixture of crude product and $Pd(OAc)_2$ (125 mg, 0.56 mmol) in dimethyl sulfoxide (DMSO) (15 ml) was stirred for 24 h at r.t.under an atmosphere of O_2. The reaction mixture was diluted with H_2O and extracted with ethyl acetate. The extract was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by column chromatography on silica-gel. The fractions eluted with hexane/ethyl acetate (30 : 1—10 : 1) afforded (±)-**12** as a colorless oil.

General Procedure for Enantioselective Esterification of (±)-5 and (±)-6 A mixture of substrate (250 mg) and lipase "Amano P" (250 mg) in vinyl acetate (25 ml) was shaken at 33 °C for a suitable period. The mixture was filtered and the filtrate was concentrated *in vacuo*. The crude product was purified by column chromatography on silica-gel, and the fractions eluted with hexane/ethylacetate (30 : 1—20 : 1) afforded acetate **13** and **18** as a colorless oil while the fractions eluted with hexane/ethylacetate (10 : 1—5 : 1) afforded **6** and **5** as a colorless oil.

General Procedure for Hydrolysis of Acetate 13 and 18 A mixture of substrate **13** or **18** (1 mmol) and K_2CO_3 (138 mg, 1 mmol) in MeOH (15 ml) was stirred at r.t. for 1 h. The reaction mixture was diluted with brine and extracted with ethyl acetate. The extracts were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by column chromatography on silica-gel, and the fraction eluted with hexane/ethyl acetate (10 : 1—5 : 1) afforded **6** or **5** (90—95%) , respectively as a colorless oil.

General Procedure for Preparation of (*R*)-MTPA Ester A mixture of substrate **6a**—**c** or **5a**—**c** (7 mg, 0.045 mmol—0.026 mmol), 4-*N*,*N*-dimethylaminopyridine (20 mg, 0.16 mmol) and (*S*)-MTPACl (20 mg, 0.079 mmol) in CH_2Cl_2 (1 ml) was stirred at r.t. for 0.5 h. The mixture was purified by column chromatography on silica-gel. The fractions eluted with hexane/ethyl acetate (20 : 1—10 : 1) afforded (*R*)-MTPA ester (97—99%) as a colorless oil.

Methyl (1*R*,2*R*)-2-Acetoxy-1-methyl-3-cyclopentenecarboxylate (13a) $[\alpha]_D^{23}$ −104.5 (c=0.95, $CHCl_3$) (91% ee). (*R*)-MTPA ester of (1*R*,2*R*)-**6a**: ^{1}H-NMR ($CDCl_3$) (major diastereomer) δ: 7.54—7.39 (5H, m, Ph), 6.15 (1H, br s, C_2-H), 6.00 (1H, m, C_3-H or C_4-H), 5.74 (1H, m, C_3-H or C_4-H), 3.75 (3H, s, OMe), 3.53 (3H, s, OMe), 2.95 (1H, dd, J=17, 2 Hz, C_5-H), 2.35 (1H, dd, J=17, 2 Hz, C_5-H), 1.27 (3H, s, C_1-Me). FAB-MS m/z: 373

(M^++1).

Methyl (1*S*,2*S*)-2-Hydroxy-1-methyl-3-cyclopentenecarboxylate (6a) $[\alpha]_D^{23}$ +36.5 (c=0.6, $CHCl_3$) (63% ee). (*R*)-MTPA ester of (1*S*,2*S*)-**6a**: ^{1}H-NMR ($CDCl_3$) (major diastereomer) δ: 7.53—7.34 (5H, m, Ph), 6.19 (1H, br s, C_2-H), 6.05 (1H, m, C_3-H or C_4-H), 5.79 (1H, m, C_3-H or C_4-H), 3.73 (3H, s, OMe), 3.56 (3H, s, OMe), 2.96 (1H, d, J=16 Hz, C_5-H), 2.36 (1H, d, J=16 Hz, C_5-H), 1.16 (3H, s, C_1-Me). FAB-MS m/z: 373 (M^++H).

Methyl (1*R*,2*R*)-2-Acetoxy-1-nonyl-3-cyclopentenecarboxylate (13b) $[\alpha]_D^{27}$ −115.9 (c=0.75, $CHCl_3$) (96% ee). (*R*)-MTPA ester of (1*R*,2*R*)-**6b**: ^{1}H-NMR ($CDCl_3$) (major diastereomer) δ: 7.52—7.34 (5H, m, Ph), 6.06 (1H, m, C_3-H or C_4-H), 6.05 (1H, br s, C_2-H), 5.86 (1H, m, C_3-H or C_4-H), 3.72 (3H, s, OMe), 3.51 (3H, s, OMe), 2.98 (1H, d, J=17 Hz, C_5-H), 2.34 (1H, dd, J=17, 2 Hz, C_5-H), 1.74 (1H, m, C$\underline{H}_2$-C_8H_{17}), 1.63 (1H, m, C$\underline{H}_2$-C_8H_{17}), 1.28—1.15 (14H, m), 0.88 (3H, t, J=7 Hz, C_8H_{16}-$\underline{Me}$). FAB-MS m/z: 485 (M^++H).

Methyl (1*S*,2*S*)-2-Hydroxy-1-nonyl-3-cyclopentenecarboxylate (6b) $[\alpha]_D^{27}$ +9.7 (c=0.51, $CHCl_3$) (40% ee). (*R*)-MTPA ester of (1*S*,2*S*)-**6b**: ^{1}H-NMR ($CDCl_3$) (major diastereomer) δ: 7.52—7.37 (5H, m, Ph), 6.13 (1H, m, C_3-H or C_4-H), 6.09 (1H, br s, C_2-H), 5.92 (1H, m, C_3-H or C_4-H), 3.70 (3H, s, OMe), 3.56 (3H, s, OMe), 3.00 (1H, d, J=17 Hz, C_5-H), 2.36 (1H, d, J=17 Hz, C_5-H), 1.65—1.49 (2H, m, C$\underline{H}_2$-C_8H_{17}), 1.28—1.15 (14H, m), 0.88 (3H, t, J=7 Hz, C_8H_{16}-$\underline{Me}$). FAB-MS m/z: 485 (M^++H).

Methyl (1*S*,2*R*)-2-Acetoxy-1-benzyl-3-cyclopentenecarboxylate (13c) $[\alpha]_D^{26}$ −148.2 (c=0.77, $CHCl_3$) (91% ee). (*R*)-MTPA ester of (1*S*,2*R*)-**6c**: ^{1}H-NMR ($CDCl_3$) (major diastereomer) δ: 7.57—7.18 (8H, m, Ph), 7.00 (2H, m, Ph), 6.11—6.08 (2H, m, C_2-H and C_3-H or C_4-H), 5.88 (1H, m, C_3-H or C_4-H), 3.64 (3H, s, OMe), 3.56 (1H, d, J=1 Hz, OMe), 3.19 (1H, d, J=14 Hz, C$\underline{H}_2$Ph), 2.89 (1H, d, J=14 Hz, C$\underline{H}_2$Ph), 2.87 (1H, d, J=17 Hz, C_5-H), 2.50 (1H, dd, J=17, 4 Hz, C_5-H). FAB-MS m/z: 449 (M^++H).

Methyl (1*R*,2*S*)-1-Benzyl-2-hydroxy-3-cyclopentenecarboxylate (6c) $[\alpha]_D^{27}$ +33.3 (c=0.71, $CHCl_3$) (43% ee). (*R*)-MTPA ester of (1*R*,2*S*)-**6c**: ^{1}H-NMR ($CDCl_3$) (major diastereomer) δ: 7.59—7.17 (8H, m, Ph), 6.92 (2H, m, Ph), 6.18 (1H, m, C_3-H or C_4-H), 6.09 (1H, br s, C_2-H), 5.96 (1H, m, C_3-H or C_4-H), 3.60 (3H, s, OMe), 3.59 (1H, d, J=1 Hz, OMe), 3.08 (1H, d, J=14 Hz, C$\underline{H}_2$Ph), 2.92 (1H, d, J=17 Hz, C_5-H), 2.79 (1H, d, J=14 Hz, C$\underline{H}_2$Ph), 2.53 (1H, dd, J=17, 2 Hz, C_5-H). FAB-MS m/z: 449 (M^++H).

Methyl (1*S*,4*S*)-4-Acetoxy-1-methyl-2-cyclopentenecarboxylate (18a) $[\alpha]_D^{26}$ −184.5 (c=0.67, $CHCl_3$) (84% ee). ^{1}H-NMR ($CDCl_3$) δ: 5.99 (1H, dd, J=6, 1 Hz, C_2-H or C_3-H), 5.87 (1H, dd, J=6, 2 Hz, C_2-H or C_3-H), 5.74 (1H, m, C_4-H), 3.68 (3H, s, OMe), 2.86 (1H, dd, J=14, 8 Hz, C_5-H), 2.04 (3H, s, Ac), 1.67 (1H, dd, J=14, 4 Hz, C_5-H), 1.43 (3H, s, C_1-$\underline{Me}$). ^{13}C-NMR ($CDCl_3$) δ: 176.1, 170.8 (each as s, CO), 140.7, 130.5 (each as d, C_2 and C_3), 79.5 (d, C_4), 55.1 (s, C_1), 52.3 (q, OMe), 41.8 (t, C_5), 25.6 (q, CO$\underline{Me}$), 21.2 (q, C_1-Me). IR (neat, cm^{-1}): 2960, 1740, 1245. FAB-MS m/z: 199 (M^++H). (1*S*,4*S*)-**5a**: $[\alpha]_D^{29}$ −164.3 (c=0.95, $CHCl_3$) (84% ee). (*R*)-MTPA ester of (1*S*,4*S*)-**5a**: ^{1}H-NMR ($CDCl_3$) (major diastereomer) δ: 7.51—7.26 (5H, m, Ph), 6.08 (1H, d, J=6 Hz, C_2-H or C_3-H), 5.94 (1H, m, C_4-H), 5.91 (1H, dd, J=6, 2 Hz, C_2-H or C_3-H), 3.69 (3H, s, OMe), 3.53 (3H, d, J=1 Hz, OMe), 2.89 (1H, dd, J=14, 7 Hz, C_5-H), 1.83 (1H, dd, J=14, 3 Hz, C_5-H), 1.36 (3H, s, C_1-Me) . FAB-MS m/z: 373 (M^++H).

Methyl (1*R*,4*R*)-4-Hydroxy-1-methyl-2-cyclopentenecarboxylate (5a) $[\alpha]_D^{27}$ +189.9 (c=0.66, $CHCl_3$) (96% ee). (*R*)-MTPA ester of (1*R*,4*R*)-**5a**: ^{1}H-NMR ($CDCl_3$) (major diastereomer) δ: 7.51—7.26 (5H, m, Ph), 6.11 (1H, d, J=5 Hz, C_2-H or C_3-H), 5.96—5.93 (2H, m, C_4-H and C_2-H or C_3-H), 3.67 (3H, s, OMe), 3.55 (3H, d, J=1 Hz, OMe), 2.85 (1H, dd, J=15, 7 Hz, C_5-H), 1.76 (1H, dd, J=15, 2 Hz, C_5-H), 1.32 (3H, s, C_1-Me) . FAB-MS m/z: 373 (M^++H).

Methyl (1*S*,4*S*)-4-Acetoxy-1-nonyl-2-cyclopentenecarboxylate (18b) $[\alpha]_D^{27}$ −124.0 (c=0.81, $CHCl_3$) (99% ee). ^{1}H-NMR ($CDCl_3$) δ: 6.01 (1H, dd, J=6, 1 Hz, C_2-H or C_3-H), 5.85 (1H, dd, J=6, 2 Hz, C_2-H or C_3-H), 5.71 (1H, m, C_4-H), 3.67 (3H, s, OMe), 2.85 (1H, dd, J=14, 8 Hz, C_5-H$_\beta$), 2.04 (3H, s, CO$\underline{Me}$), 1.81 (1H, m, C$\underline{H}_2$-C_8H_{17}), 1.71 (1H, dd, J=14, 4 Hz, C_5-H$_\alpha$), 1.67 (1H, m, C$\underline{H}_2$-C_8H_{17}), 1.26 (14H, m), 0.88 (3H, t, J=7 Hz, C_8H_{16}-$\underline{Me}$). ^{13}C-NMR ($CDCl_3$). δ: 175.5, 170.8 (s, CO), 139.6, 130.6 (each as d, C_2 and C_3), 79.2 (d, C_4), 59.7 (s, C_1), 52.1 (q, OMe), 39.4 (t, C_5), 39.3 (t), 31.9 (t), 29.9 (t), 29.5 (t), 29.4 (t), 29.3 (t), 25.3 (t), 22.7 (t), 21.2 (q, CO$\underline{Me}$), 14.1 (q, C_8H_{16}-$\underline{Me}$). IR (neat, cm^{-1}): 2927, 1737, 1239. FAB-MS m/z: 311 (M^++H). (1*S*,4*S*)-**5b**: $[\alpha]_D^{25}$ −100.0 (c=0.81, $CHCl_3$) (99% ee). (*R*)-MTPA ester of (1*S*,4*S*)-**5b**: ^{1}H-NMR ($CDCl_3$) (major diastereomer) δ: 7.52—7.38 (5H, m, Ph), 6.10 (1H, d, J=6 Hz, C_2-H or C_3-H), 5.93—5.89 (2H, m, C_4-H and C_2-H or C_3-H), 3.68 (3H, s, OMe), 3.54 (3H, d, J=1 Hz, OMe), 2.87 (1H, dd, J=14, 4 Hz, C_5-H), 1.85 (1H, dd, J=14, 2 Hz, C_5-H), 1.76—1.56 (2H, m, CH_2-C_8H_{17}), 1.31—1.14 (14H, m), 0.88 (3H, t, J=7 Hz, C_8H_{16}-$\underline{Me}$). FAB-MS m/z: 485 (M^++H).

Methyl (1*R*,4*R*)-4-Hydroxy-1-nonyl-2-cyclopentenecarboxylate (5b) $[\alpha]_D^{28}$ +90.4 (c=0.93, $CHCl_3$) (91% ee). (*R*)-MTPA ester of (1*S*,4*S*)-**5b**: ^{1}H-NMR ($CDCl_3$) (major diastereomer) δ: 7.52—7.38 (5H, m, Ph), 6.13 (1H, d, J=5 Hz, C_2-H or C_3-H), 5.94—5.91 (2H, m, C_4-H and C_2-H or C_3-H), 3.68 (3H, s, OMe), 3.55 (3H, d, J=1 Hz, OMe), 2.83 (1H, dd, J=15, 8 Hz, C_5-H), 1.78 (1H, dd, J=15, 3 Hz, C_5-H), 1.75—1.54 (2H, m, C$\underline{H}_2$-C_8H_{17}), 1.31—1.11 (14H, m), 0.88 (3H, t, J=7 Hz, C_8H_{16}-$\underline{Me}$). FAB-MS m/z: 485 (M^++H).

Methyl (1*S*,4*S*)-4-Acetoxy-1-benzyl-2-cyclopentenecarboxylate (18c) $[\alpha]_D^{29}$ −123.3 (c=0.77, $CHCl_3$) (99% ee). ^{1}H-NMR ($CDCl_3$) δ: 7.28—7.09 (5H, m, Ph), 6.04 (1H, dd, J=6, 1 Hz, C_2-H or C_3-H), 5.89 (1H, dd, J=6, 2 Hz, C_2-H or C_3-H), 5.67 (1H, m, C_4-H), 3.65 (3H, s, OMe), 3.13 (1H, d, J=13 Hz, C$\underline{H}_2$Ph), 3.07 (1H, d, J=13 Hz, C$\underline{H}_2$Ph), 2.73 (1H, dd, J=15, 8 Hz, C_5-H), 2.00 (3H, s, CO$\underline{Me}$), 1.90 (1H, dd, J=15, 4 Hz, C_5-H). ^{13}C-NMR ($CDCl_3$) δ: 174.9, 170.7 (s, CO), 137.2 (s), 139.3, 131.1, 129.8, 128.2, 126.8 (each as d, C_2, C_3 and Ph), 78.9 (d, C_4), 60.7 (s, C_1), 52.1 (q, OMe), 45.1, 39.2 (each as t, $\underline{C}H_2$Ph and C_5), 21.2 (q, CO$\underline{Me}$). IR (neat, cm^{-1}): 2950, 1735, 1242. FAB-MS m/z: 275 (M^++H). (1*S*,4*S*)-**5c**: $[\alpha]_D^{24}$ −89.6 (c=0.66, $CHCl_3$) (99% ee). (*R*)-MTPA ester of (1*S*,4*S*)-**5c**: ^{1}H-NMR ($CDCl_3$) (major diastereomer) δ: 7.53—6.96 (10H, m, Ph), 6.10 (1H, d, J=6 Hz, C_2-H or C_3-H), 5.97 (1H, dd, J=6, 2 Hz, C_2-H or C_3-H), 5.89 (1H, dt, J=7, 2 Hz, C_4-H), 3.66 (3H, s, OMe), 3.52 (3H, d, J=1 Hz, OMe), 3.00 (2H, s, C$\underline{H}_2$Ph), 2.74 (1H, dd, J=15, 7 Hz, C_5-H), 2.04 (1H, dd, J=15, 2 Hz, C_5-H). FAB-MS m/z: 449 (M^++H).

Methyl (1*R*,4*R*)-1-Benzyl-4-hydroxy-2-cyclopentenecarboxylate (5c) $[\alpha]_D^{29}$ +82.3 (c=0.9, $CHCl_3$) (92% ee). (*R*)-MTPA ester of (1*R*,4*R*)-**5c**: ^{1}H-NMR ($CDCl_3$) (major diastereomer) δ: 7.53—6.95 (10H, m, Ph), 6.15 (1H, d, J=6 Hz, C_2-H or C_3-H), 5.99 (1H, dd, J=6, 2 Hz, C_2-H or C_3-H), 5.92 (1H, dt, J=8, 2 Hz, C_4-H), 3.65 (3H, s, OMe), 3.54 (3H, d, J=1 Hz, OMe), 3.01 (1H, d, J=14 Hz, C$\underline{H}_2$Ph), 2.97 (1H, d, J=14 Hz, C$\underline{H}_2$Ph), 2.72 (1H, dd, J=15, 8 Hz, C_5-H), 1.97 (1H, dd, J=15, 2 Hz, C_5-H). FAB-MS m/z: 449 (M^++H).

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References and Notes

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