137. An Efficient Total Synthesis of Carbocyclic 2′-Deoxyribonucleosides

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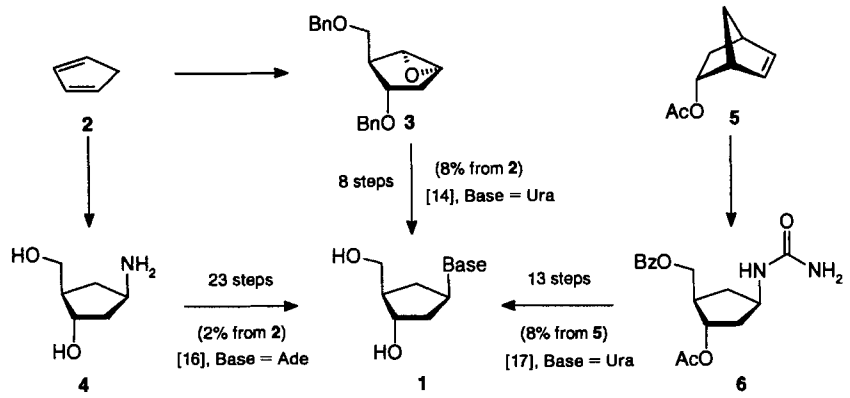
(30.V.94)

The present work describes a new and efficient method for the preparation of either racemic or enantiomerically pure carbocyclic 2′-deoxyribonucleosides **1**. Key steps are the efficient assembly of the racemic carbocyclic 2′-deoxyribose core (±)-**12**, its enzymatic resolution, and a new approach to covalently link the purine and pyrimidine bases with the cyclopentane moiety *via* the cyclic sulfate (+)-**19**. This total synthesis of enantiomerically pure and racemic carbocyclic 2′-deoxyribonucleosides **1** represents one of the most efficient approaches reported to date. Starting from cyclopentadiene, the four carbocyles corresponding to the naturally occurring 2′-deoxyribonucleosides could be prepared in 12 steps and 9–12% overall yield. For the corresponding racemic compounds, 10 steps were used with overall yields between 22 and 30%.

Introduction. – Antisense oligonucleotides were proposed by *Zamecnik* and *Stephenson* as a new class of potential therapeutics that – in principle – should act in a rational way on the m-RNA of a disease-related protein [1], thereby specifically inhibiting its synthesis. However, naturally occurring oligonucleotides (DNA or RNA) do not possess the properties required for potential drugs: they are too labile intra- and extracellularly, poorly penetrate cellular membranes, and have inadequate pharmacokinetic behavior. Therefore, research activities have currently been focused on chemical modifications of nucleosides aiming at improving the properties of the corresponding oligonucleotides [2–7].

When we started our activities in this area, our focus was drawn to carbocyclic oligodeoxyribonucleotides which were unknown at that time but meanwhile were described in the literature [8–11]. Compared to DNA oligomers, we expected almost identical RNA binding affinities considering the structural similarities, improved nuclease resistance due to a more electron-rich phosphodiester group, increased stability of the nucleosides against depurination, and better cellular uptake due to increased lipophilicity. In the field of antitumor and antiviral drug discovery, carbocyclic nucleosides are well known, and biological activities as well as synthetic efforts were recently excellently reviewed [12] [13]. Three different syntheses were reported to give enantiomerically pure carbocyclic 2′-deoxyribonucleosides **1** (*Scheme 1*) [14–17]. Starting from cyclopentadiene **2**, the first synthesis used the bicyclic oxirane **3** as key intermediate to link the base by nucleophilic ring opening of the epoxide with the deprotonated base. The two other syntheses both made use of the amine **4** or its derivative **6** (from **5**) as precursors from which the bases were built up by using published procedures [18] [19]. The requirement to produce reasonable quantities of at least the four carbocycles corresponding to the naturally occurring 2′-deoxyribonucleosides urged us to look for a new and simpler strategy to prepare these compounds in enantiomerically pure form.

Scheme 1



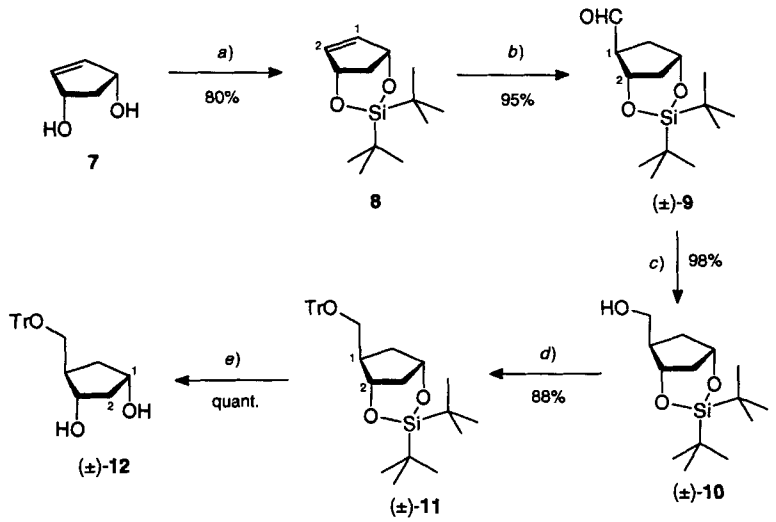
Results. – Our synthetic strategy for the synthesis of carbocyclic 2′-deoxyribonucleosides included two key steps. We wanted to prepare in a first step the carbocyclic core without attached base by introducing the extra C-atom to an appropriately functionalized cyclopentene derivative *via* stereospecific hydroformylation. Secondly, we had in mind to activate the carbocyclic sugar analog as a cyclic sulfate that should serve as common precursor for the direct introduction of the purine and pyrimidine bases.

Our synthesis started from the known cyclopentenediol **7** (*Scheme 2*) which can be obtained in 59% yield from cyclopentadiene (**2**) by $^1O_2$ addition under reducing conditions [20]. Originally, our idea was to protect both OH functions by acetalization or ketalization and thereby sterically shielding the lower face of the double bond in the subsequent hydroformylation step. Unfortunately, all attempts to prepare the acetal of benzaldehyde or the ketal of acetone with diol **7** failed with a variety of methods examined, presumably due to steric constraints of the desired bicyclic products. Preliminary experiments with different protecting groups at the OH functions of **7** indicated that silyl groups (Me_3Si or (t-Bu)Me_2Si) were well tolerated under the hydroformylation conditions; as expected, however, a 2–3:1 ratio of the corresponding diastereoisomeric aldehydes was obtained (data not shown). The use of the bifunctional di(*tert*-butyl)silanediyl protecting group finally turned out to be almost ideal. Diol **7** was smoothly converted to the silanediyl derivative **8** in 80% yield by using the bis(triflate) reagent[1]) [21]. Hydroformylation of **8** was carried out under pressurized H_2/CO atmosphere in the presence of a Rh-catalyst to give a single diastereoisomer as a pair of enantiomers (±)-**9** in quantitative yield. The relative configuration of (±)-**9** could be verified by ^{1}H-NMR spectroscopy based on the lack of coupling between H–C(1) and H–C(2) (see *Exper. Part*), as expected for the perpendicular orientation of these two bonds in the *trans*-aldehyde (±)-**9**. Reduction of (±)-**9** with $NaBH_4$ (→(±)-**10**), tritylation with (chloro)triphenylmethane (→(±)-**11**), and removal of the silanediyl group by treatment with Bu_4NF gave the racemic trityloxy-diol (±)-**12** in excellent yield, for which the relative configuration was established by X-ray crystallography. Later, we found that an

[1]) Only the di(*tert*-butyl)silanediyl bis(triflate) gave the desired product **8**. The corresponding dichloride reagent even failed to produce traces of **8**.

analogous reaction sequence (**8**→**12**) can be performed in almost identical yields with the 1,1,3,3-tetraisopropyldisiloxane-1,3-diyl group introduced by *Markiewicz* [22]. For both protecting groups, this four-step reaction sequence could be carried out on up to a 50- to 200-g scale without intermediate workup to give the crystalline trityloxy-diol (±)-**12** in 90% overall yield (4 steps).

Scheme 2

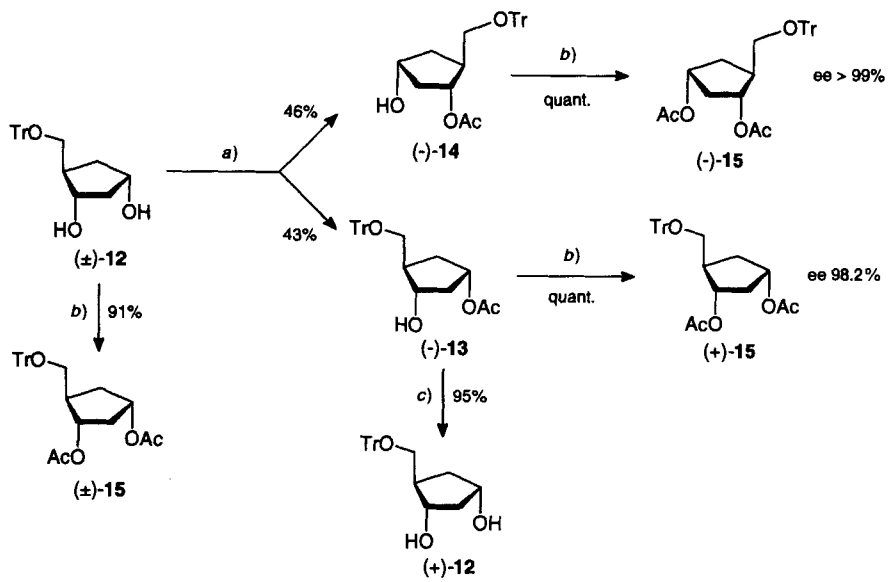


a) 1.1 equiv. of $(t\text{-Bu})_2Si(OSO_2CF_3)_2$, 3 equiv. of 2,3-lutidine, CH_2Cl_2; 0°, 30 min. *b*) 0.4 mol-% of $[RhCl(PPh_3)_3]$, THF, H_2/CO 1:1 at 80 bar; 80°, 5 h. *c*) 0.5 equiv. of $NaBH_4$, THF/H_2O 9:1; r.t., 10 min. *d*) 1.3 equiv. of TrCl, 0.1 equiv. of DMAP, 3 equiv. of Et_3N, CH_2Cl_2; r.t., 18 h. *e*) 2.2 equiv. of $Bu_4NF \cdot 3\ H_2O$, THF; r.t., 5 h.

This racemic diol (±)-**12** could easily be resolved by enzymatic transesterification [23] (*Scheme 3*). *Pseudomonas fluorescens* lipase (PFL) in vinyl acetate catalyzed the acetylation of (±)-**12** to give, in excellent yield, roughly equal amounts of two compounds which were identified by their 500-MHz ^{1}H-NMR COSY spectra to be the regioisomeric monoacetates (−)-**13** and (−)-**14**. Both compounds were converted separately in Ac_2O/pyridine to the corresponding diacetates (+)-**15** and (−)-**15**, respectively, whose enantiomeric excess (ee) could be determined by HPLC on *Chiralcel OD* (verified with the racemic diacetate (±)-**15**). Whereas in the diacetate (−)-**15**, corresponding to the 'unnatural' L-enantiomer of deoxyribose (*vide infra* for the determination of the absolute configuration), the other enantiomer was not detectable (ee ≥ 99%), the diacetate (+)-**15** contained 0.9% of its optical antipode (ee = 98.2%). This rather unexpected result that the acetylation of a racemic diol is catalyzed with high enantioselectivity by a lipase to furnish regioisomeric monoacetates gave rise to the assumption that the size of the bulky trityl group played an essential role in obtaining such a high stereodifferentiation [23]. For further conversion to the cyclic sulfate, monoacetate (−)-**13** could easily be deprotected with ethylenediamine to give the trityloxy-diol (+)-**12**.

As we initially could not assign the absolute configuration of monoacetates (−)-**13** and (−)-**14**, we converted the ideally protected monoacetate (−)-**14**, by activation and nucleophilic displacement, to the carbocyclic 2′-deoxyadenosine of known absolute con-

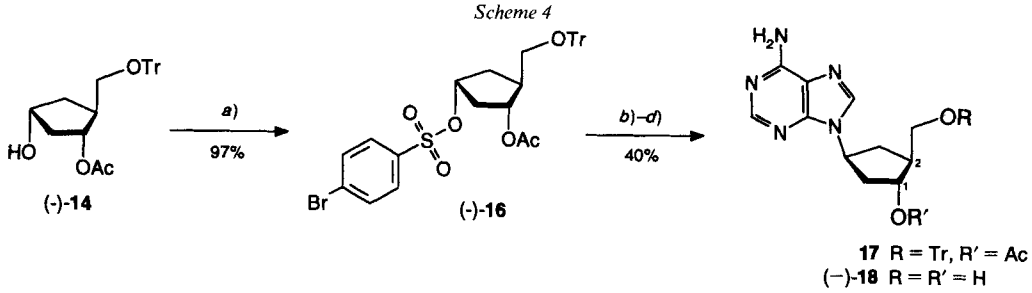
Scheme 3



a) 20 weight-% of PFL, vinyl acetate; r.t., 50 h. *b*) 2.5 equiv. of Ac_2O, 0.1 equiv. of DMAP, 3 equiv. of Et_3N, CH_2Cl_2; 0°, 30 min. *c*) 20 equiv. of ethylenediamine, MeOH; 50°, 15 h.

figuration [16]. Sulfonylation of the free OH group with 4-bromobenzenesulfonyl chloride (= brosyl chloride) in pyridine gave, after extractive purification, the crude intermediate (−)-**16** (*Scheme 4*). Displacement of the brosyl group with the potassium salt of adenine in DMSO under inversion of configuration gave the protected carbocyclic 2′-deoxyadenosine **17** in 55% yield over both steps. Deprotection with concentrated aqueous HCl in EtOH afforded the crystalline carbocyclic 2′-deoxyadenosine (−)-**18** with an optical rotation opposite to the one described [15]. Therefore, the absolute configuration of the five-membered ring of (−)-**18** corresponded to the unnatural or L-series of 2′-deoxyribonucleosides. In analogy to the conversion (−)-**14**→(−)-**18**, the monoacetate (−)-**13** of the 'natural series' could be converted, after (*t*-Bu)Me_2Si-protection of the free OH group and cleavage of the acetate in a similar way, to the carbocyclic 2′-deoxyribonucleosides **1** (data not shown).

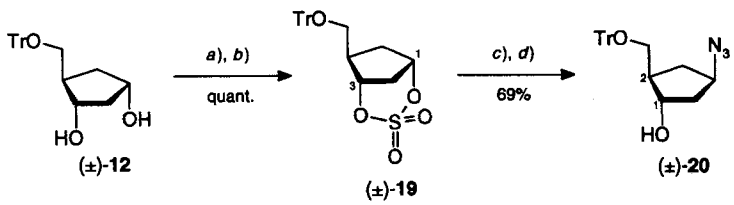
Scheme 4



a) 1.5 equiv. of 4-bromobenzenesulfonyl chloride, pyridine; 0°, 24 h. *b*) 2 equiv. of potassio-adenine, DMSO; r.t., 4 d (57%). *c*) EtOH/aq. HCl soln. 4:1; r.t., 3 h (77%). *d*) *Amberlite IRA 93* (OH^- form), MeOH (92%).

After the absolute configuration of our compounds had been established, we focused our attention on the initial plan to build up the carbocyclic nucleosides *via* the cyclic sulfate as intermediate. According to a published procedure by *Sharpless* and *Kim* [24] to convert vicinal diols to the corresponding cyclic sulfates, we successfully prepared the intermediate (±)-**19**: the racemic diol (±)-**12** was treated with a slight excess of $SOCl_2$ in CH_2Cl_2/Et_3N to furnish a mixture of the diastereoisomeric cyclic sulfites which were subsequently oxidized with $RuCl_3/NaIO_4$ using phase-transfer catalysis to give, after extraction, the crude cyclic sulfate (±)-**19** in almost quantitative yield (*Scheme 5*). This reactive intermediate could be stored under anhydrous conditions for several weeks at −18° without detectable degradation; however, even neat DMF was able to form – according to ^{1}H-NMR – a quite insoluble 1:1 adduct. Unfortunately, we were not able to detect the molecular-ion peak of this compound by different MS techniques and, therefore, the structure remains not fully established[2]). As a consequence of this lability of (±)-**19** in DMF, we performed our substitution reactions in MeCN. In a first experiment, we treated (±)-**19** with NaN_3/[15]crown-5 in MeCN at 0°: after 4 h, TLC indicated complete consumption of the starting material and the formation of a polar product, presumably the charged monoalkyl sulfate. This crude product was dried and hydrolyzed at room temperature in anhydrous THF with 1 equiv. of H_2SO_4 and H_2O according to the procedure published by *Sharpless* and coworkers [24]. After chromatography, 69% of azide (±)-**20** could be isolated for which the configuration at C(4) was not proven but is assumed to be as shown for mechanistic reasons and based on analogous conversions with purine and pyrimidine bases (*vide infra*). Even though the azide anion is a rather small nucleophile, we were not able to detect any of the possible regioisomeric compound carrying the azide function vicinal to the CH_2OTr group.

Scheme 5

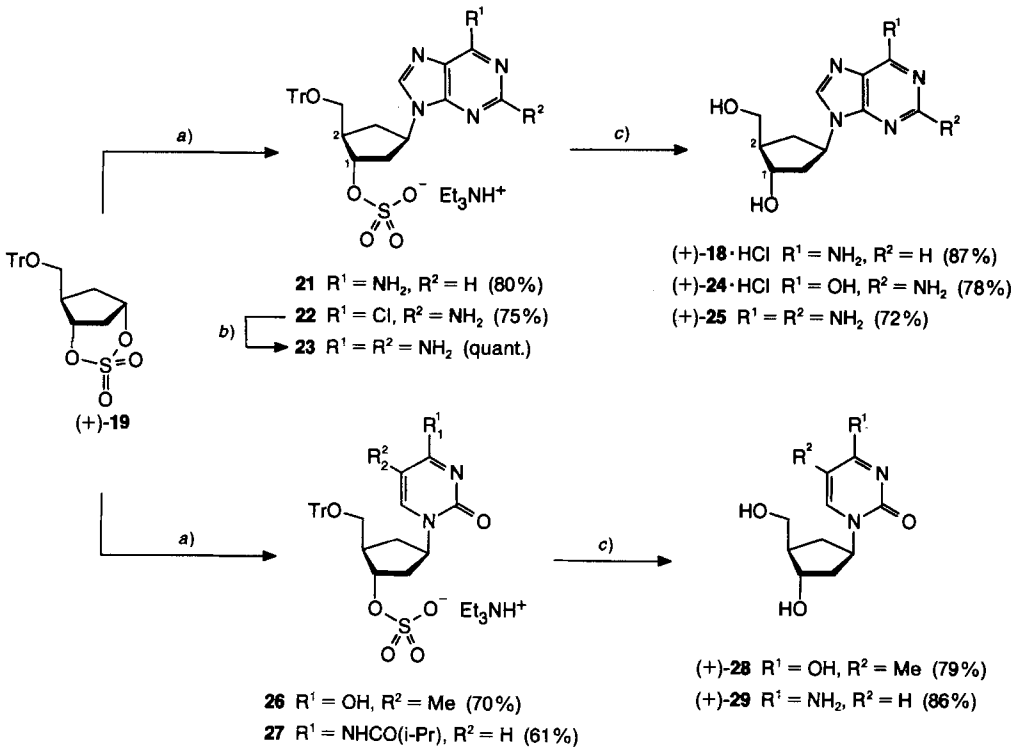


a) 1.5 equiv. of $SOCl_2$, 4 equiv. of Et_3N, CH_2Cl_2; 0°, 19 min. *b*) MeCN/CCl_4 1:1, H_2O, 1.5 mol-% of $RuCl_3$, 2 equiv. of $NaIO_4$; 0°, 1 h. *c*) 1.15 equiv. of NaN_3, 1 equiv. of [15]crown-5, MeCN; 0°, 4 h. *d*) 1 equiv. of H_2O, 1 equiv. of H_2SO_4, anh. THF; r.t., 4 h.

Encouraged by this smooth and regiospecific addition of azide to (±)-**19**, we optimized the reactions of purine and pyrimidine bases with the enantiomerically pure cyclic sulfate (+)-**19** which can be prepared in analogy to the racemic compound (±)-**19** from diol (+)-**12**. For the preparation of carbocyclic 2′-deoxyadenosine (+)-**18**, adenine was deprotonated with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in MeCN and reacted with the intermediate (+)-**19** to give, *via* nucleophilic substitution at C(1) under inversion of configuration, the adenine derivative **21** in 80% yield (*Scheme 6*). Due to the high

[2]) According to the H-NMR spectrum of this 1:1 adduct, the carbonyl O-atom of DMF attacks C(4) of the five-membered ring under opening of the cyclic sulfate to give a zwitterion.

Scheme 6



a) 1.05–1.1 equiv. of purine or pyrimidine base and DBU, MeCN; **21**: 40°, 2 d; **22**: r.t., 3 h; **26** and **27**: reflux, 1 h. *b*) MeOH/NH_3; 130°, 15 h. *c*) MeOH/aq. HCl 50:1; (+)-**18** and (+)-**25**: 65°, 15 h; (+)-**24** and (+)-**29**: 65°, 20 h; (+)-**28**: 45°, 15 h.

polarity of **21** (insoluble in THF) and the basic properties of adenine, the hydrolysis protocol using 1 equiv. of H_2SO_4 and H_2O (see *Scheme 5*) was unsuccessful. After evaluating different acids, H_2O percentages, and solvents to perform the hydrolytic cleavage of different monoalkyl sulfates, we found the use of 2% conc. aqueous HCl in MeOH at 65° overnight to be most convenient. By applying these conditions to **21**, cleavage of the trityl and sulfate groups occurred concomitantly, and crystalline carbocyclic 2′-deoxyadenosine (+)-**18**·HCl was isolated in 87% yield. The preparation of the guanosine nucleoside could easily be realized by using 2-amino-6-chloro-9*H*-purine as base precursor according to a published procedure [25]. Reaction of the DBU salt in MeCN afforded, after chromatographic purification, 75% of the desired monoalkyl sulfate **22**, besides 11% of the N^7-alkylated purine derivative. Hydrolysis as described above directly yielded the carbocyclic 2′-deoxyguanosine (+)-**24**·HCl in 78% yield due to Cl → O exchange under the hydrolytic conditions. In addition, intermediate **22** could also be used as precursor for the synthesis of the 2-aminoadenosine derivative (+)-**25**: quantitative Cl → NH_2 exchange was achieved in NH_3/MeOH at 130° (→ **23**) followed by acid-catalyzed hydrolysis to afford (+)-**25**·HCl in 83% overall yield.

The carbocyclic pyrimidine nucleosides (+)-**28** and (+)-**29** were prepared in similar yields according to the procedure outlined above (*Scheme 6*). Whereas deprotonated thymine could directly be used as nucleophile, cytosine had to be protected at the exocyclic NH_2 function. We preferred the use of the isobutyryl *N*-protecting group [26] due to its better solubility as compared to the corresponding benzoyl group. Nevertheless, reaction of the deprotonated N^4-isobutyryl-1*H*-cytosine with cyclic sulfate (+)-**19** in refluxing MeCN afforded, in addition to 61% of the desired cytidine derivative **27**, 35% of the product formed O^2-alkylation of the *N*-protected cytosine. Performing the same reaction at lower temperature shifted the product ratio in favor of the undesired side product which we were not able to convert to compound **27**. Both, the thymidine and cytidine derivatives **26** and **27** were treated with HCl in MeOH to give the carbocyclic thymidine (+)-**28** and 2′-deoxycytidine (+)-**29**, respectively, in good yields.

The synthesis and biophysical properties of the corresponding oligonucleotides were already partially published [10] and will be described in full detail elsewhere.

The support by Dr. *Tammo Winkler* for the skillful interpretation of numerous NMR spectra and by Mrs. *Grety Rihs* for resolution of the X-ray structure of diol (±)-**12** is greatly appreciated. The critical review of this manuscript by Dr. *Karl-Heinz Altmann* is acknowledged.

Experimental Part

General. If not otherwise indicated, anh. solvents were purchased from *Fluka*. Prep. chromatography: silica gel *60*, 230–240 mesh (*Merck*) as described [27]. TLC: Silica gel glass plates ('Kieselgel' *60 F_{254}, Merck*); visualization by UV light and/or dipping in a staining soln. (2.5 g of phosphormolybdic acid and 0.6 g of cerium(IV) sulfate in 1 l of 1M H_2SO_4) followed by heating the plates with an air gun. IR Spectra: *Perkin-Elmer 298*; in cm^{-1}. ^{1}H-NMR Spectra: *Bruker BZH 250/52* (250 MHz) or *Varian Unity 500* (500 MHz); chemical shifts δ in ppm *vs.* $SiMe_4$ (= 0 ppm) and coupling constants *J* in Hz. ^{13}C-NMR Spectra: *Bruker BZH 250/2* (62.5 MHz) or *Varian XL-300* (75 MHz); chemical shifts δ in ppm *vs.* $SiMe_4$ (= 0 ppm). MS Spectra: *Finnigan MAT 212/SS300* with ionization energy of 70 eV or *ZAB HF* mass spectrometer (*Fisons Instruments*) for fast-atom bombardment (FAB) with thioglycerol as matrix; instrument and Xe gun at accelerating voltages of 8 and 10 kV, resp. Optical rotations: *Perkin-Elmer 241/241MC*; 1-ml cuvette with 10-cm path length; wavelengths given in parentheses.

cis-*3,5-[Di(* tert-*butyl)silanediyldioxy]cyclopent-1-ene* (**8**). *cis*-Cyclopent-4-ene-1,3-diol (**7**; 910 mg, 9.1 mmol) and anh. CH_2Cl_2 (20 ml; filtered through basic aluminium oxid, act I) were combined under Ar, and the stirred heterogeneous mixture was cooled to 0°. Then, 2,6-lutidine (= 2,6-dimethylpyridine; dest. from CaH_2; 3.17 ml, 27.3 mmol) was added *via* syringe followed by di(*tert*-butyl)silanediyl bis(triflate) (4.42 g, 10.0 mmol; *Aldrich*) within 10 min. Stirring at 0° was continued for another 10 min before the ice bath was removed. After 30 min (TLC (hexane/AcOEt 9:1): R_f 0.57; almost no **7** left), the mixture was evaporated and the resulting oil taken up in hexane (20 ml) with vigorous stirring. After crystallization of the by-product (lutidinium triflate), the mixture was filtered and the filtrate evaporated. The crude product was chromatographed (hexane/Et_2O 20:1) to give, after evaporation and drying (30 min at r.t./0.01 Torr), **8** (1.41 g, 65%)[3]. Colorless oil. IR (neat): 3065*w*, 2975*vs*, 2895*s*, 2865*vs*, 1700*w*, 1478*s*, 1465 (sh), 1438*m*, 1395*m*, 1385*m*, 1362*m*, 1342*s*, 1278*w*, 1230*m*, 1100*m*, 1078*vs*, 1012*w*, 1002*m*, 985*vs*, 968*s*, 935*m*, 890*m*, 870*vs*, 830*s*, 823*vs*, 792*w*, 758*vs*, 717*vs*, 640*s*. ^{1}H-NMR (250 MHz, $CDCl_3$): 0.96, 1.04 (2*s*, 2 *t*-Bu); 1.81 (*dt*, *J* = 12, 3, 1 H–C(4)); 2.49 (*d*, *J* = 12, 1 H–C(4)); 4.79 (*m*, H–C(3), H–C(5)); 6.47 (*s*, H–C(1), H–C(2)). MS: 240 (3.0, M^+), 183 (33, $[M - C_4H_9]^+$), 141 (100). Anal. calc. for $C_{13}H_{24}O_2Si$: C 64.95, H 10.06, Si 11.69; found: C 65.04, H 10.07, Si 11.62.

*(±)-*t*-2,*t*-4-[Di(* tert-*butyl)silanediyldioxy]cyclopentane-*r*-1-carbaldehyde* ((±)-**9**). Cyclopentene **8** (1.00 g, 4.16 mmol), $[RhCl(PPh_3)_3]$ (15.4 mg, 0.4 mol-%), and THF (30 ml) were placed in a 50-ml Au-coated autoclave and heated under H_2/CO 1:1 atmosphere of 80 bar to 80° for 5 h. The crude product, according to GC (*Chirasil L-Val*, 50 m, 150°, carrier 50 kPa; t_R 21.2 min) > 99% pure, was filtered through a short silica-gel column (hexane/AcOEt

[3]) Following this protocol, 80% of pure **8** was obtained on a 5-fold larger scale.

9:1, R_f 0.28) to remove the catalyst[4]). After evaporation and drying at r.t./0.01 Torr (1 h), pure (±)-**9** (1.07 g, 95%) was obtained. IR (neat): 2970*s*, 2945*vs*, 2895*s*, 2865*vs*, 2730 (sh), 2710*w*, 1725*vs*, 1478*s*, 1465*m*, 1440*m*, 1395*w*, 1388*m*, 1365*m*, 1302*w*, 1267*w*, 1227*m*, 1207*w*, 1173*s*, 1145*w*, 1102*vs*, 1074*m*, 1062*m*, 1010*m*, 980*vs*, 937*w*, 885*w*, 860*m*, 824*vs*, 803*w*, 758*s*, 730*m*, 690*w*, 643*s*. ^{1}H-NMR (250 MHz, $CDCl_3$): 1.05, 1.06 (2*s*, 2 *t*-Bu); 1.24 (*ddd*, *J* = 3, 3, 14, 1 H–C(3)); 2.24 (*m*, 3 main peaks, 2 H–C(5)); 2.44 (br. *d*, *J* = 14, 1 H–C(3)); 3.45 (br. *dd*, *J* = 7, 7, H–C(1)); 4.67 (br. *s*, H–C(2)); 4.81 (*m*, H–C(4)); 9.79 (*s*, CHO). MS: 286 (1.5), 270 (0.5, M^+), 229 (29), 187 (99), 171 (33), 77 (100), 57 (29), 45 (44), 41 (51). Anal. calc. for $C_{14}H_{26}O_3Si$: C 62.18, H 9.69, Si 10.39; found: C 61.45, H 9.63, Si 10.31.

*(±)-*t*-2,*t*-4-[Di(*tert*-butyl)silanediyldioxy]cyclopentane-*r*-1-methanol* ((±)-**10**). A soln. of (±)-**9** (491 mg, 1.82 mmol) in THF/H_2O 9:1[5]) (10 ml) was cooled to 0° under stirring and $NaBH_4$ (34.5 mg, 0.91 mmol) was added at once. After 10 min (TLC (hexane/AcOEt 2:1): R_f 0.34; no (±)-**9** left), the mixture was evaporated, the residue taken up in AcOEt (2 × 30 ml), the soln. washed with 2.5% aq. $NaHCO_3$ soln. (20 ml) and brine, the combined org. phase dried (Na_2SO_4) and evaporated, and the residue dried at r.t./0.01 Torr (1 h): (±)-**10** (485 mg, 98%). Colorless oil containing a small amount of AcOEt. IR (neat): 3420*m* (br.), 2970 (sh), 2940*vs*, 2895*m*, 2860*vs*, 1476*s*, 1462 (sh), 1438*m*, 1392*m*, 1385*m*, 1362*m*, 1343*w*, 1307*w*, 1290*w*, 1268*w*, 1250*w*, 1226*m*, 1205*m*, 1183*s*, 1142*w*, 1100*vs*, 1058*vs*, 1040*s*, 1018*m*, 1000 (sh), 980*vs*, 943 (sh), 935*m*, 890*s*, 874*m*, 845*m*, 822*vs*, 798*m*, 762*s*, 728*m*, 713*m*, 639*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.04, 1.05 (2*s*, 2 *t*-Bu); 1.38 (*ddd*, *J* = 5, 5, 14.5), 1.47 (*ddd*, *J* = 3.5, 3.5, 13.5), 2.30 (*ddd*, *J* = 3, 8.5, 14.5), 2.42 (br. *d*, *J* = 13.5, 2 H–C(3), 2 H–C(5)); 1.59 (br. *s*, OH); 2.65 (*m*, H–C(1)); 3.36 (*dd*, *J* = 8.5, 10.5, 1 H, CH_2OH); 3.51 (*dd*, *J* = 6, 10.5, 1 H, CH_2OH); 4.45, 4.58 (2*m*, H–C(2), H–C(4)). MS: 272 (1, M^+), 215 (29), 173 (100), 79 (21), 77 (82). Anal. calc. for $C_{14}H_{28}O_3Si$: C 61.72, H 10.36, Si 10.31; found: C 61.19, H 10.27, Si 9.67.

*(±)-*t*-2,*t*-4-[Di(*tert*-butyl)silanediyldioxy]-*t*-1-*r*-[(triphenylmethoxy)methyl]cyclopentane* ((±)-**11**). To a soln. of (±)-**10** (397 mg, 1.46 mmol), 4-(dimethylamino)pyridine (DMAP; *Merck* 'z.S.'; 17.8 mg, 0.15 mmol), and Et_3N (405 µl, 2.91 mmol) under Ar in anh. CH_2Cl_2 (5 ml; filtered through basic aluminium oxid, act. I), (chloro)triphenylmethane (528 mg, 1.89 mmol) was added at r.t. and the reaction monitored by TLC (hexane/AcOEt 19:1: R_f ((±)-**11**) 0.40). After 18 h, the solvent was evaporated, the residue taken up in hexane/AcOEt 1:1 (2 × 50 ml), the soln. washed with 6% aq. $NaHCO_3$ soln. (30 ml) and brine (30 ml), the combined org. phase dried (Na_2SO_4) and evaporated, and the residue dried at r.t./0.01 Torr overnight: (±)-**11** (657 mg, 88%). Colorless foam. IR (CH_2Cl_2): 3080*w*, 3040*w* (br.), 2935*s*, 2890*m*, 2855*s*, 1593*w*, 1487*m*, 1475*s*, 1460*m*, 1445*s*, 1392*w*, 1384*w*, 1360*w*, 1310*w*, 1290*w*, 1217*m*, 1205*w*, 1187*m*, 1148*w*, 1112*s*, 1087*m*, 1060*vs*, 1028*m*, 987*s*, 946*w*, 935*w*, 897 (sh), 887*m*, 874*w*, 850*w*, 822*s*. ^{1}H-NMR (250 MHz, $CDCl_3$): 1.04, 1.05 (2*s*, 2 *t*-Bu); 1.32–1.50 (*m*), 2.22 (*ddd*, *J* = 3.0, 9.0, 14.5), 2.35 (br. *d*, *J* = 13.5, 2 H–C(3), 2 H–C(5)); 2.66 (*m*, H–C(1)); 2.84 (*t*-like *m*, *J* = 8.5), 3.05 (*dd*, *J* = 5.5, 9.5, CH_2OTr); 4.43–4.58 (*m*, H–C(2), H–C(4)); 7.17–7.47 (*m*, 15 arom. H). MS: 457 (28, $[M - C_4H_9]^+$), 415 (23), 243 (100), 165 (52), 77 (39). Anal. calc. for $C_{33}H_{42}O_3Si$: C 77.00, H 8.22, Si 5.46; found: C 77.62, H 8.43, Si 5.21.

*(±)-*t*-4-[(Triphenylmethoxy)methyl]cyclopentane-*r*-1,*c*-3-diol* ((±)-**12**). A soln. of $Bu_4NF \cdot 3\ H_2O$ (752 mg, 2.39 mmol; *Fluka purum*) in THF (10 ml)[6]) (*Merck*, 'z.A.') was added to (±)-**11** (558 mg, 1.08 mmol) and left at r.t. After 5 h (TLC (AcOEt/hexane 2:1): R_f 0.29; no (±)-**11** left), chromatography (AcOEt/hexane 2:1) afforded, after evaporation and drying at 0.01 Torr (18 h), (±)-**12** (409 mg, quant.)[7]) as a colorless resin which crystallized upon standing. For the anal. data, recrystallized material (hexane/AcOEt 2:1) was used. M.p. 116–117°. IR (CH_2Cl_2): 3700–3300 (br.), 3680*w*, 3605*m*, 3550 (sh), 3090*w*, 3055*m*, 3035*m*, 2960*m*, 2930*m*, 2870*w*, 1595*w*, 1490*s*, 1447*vs*, 1315*w*, 1220*m*, 1183*m*, 1152*m*, 1087*s*, 1056*vs*, 1040*s*, 1001*m*, 980*m*. ^{1}H-NMR (250 MHz, $CDCl_3$): 1.48 (*ddd*, *J* = 5.5, 8.8, 14), 1.78 (*m*, 2 main peaks), 1.88–2.08 (*m*, 2 H–C(2), 2 H–C(5)); 2.51 (*m*, H–C(4)); 2.03 (*d*, *J* = 5), 2.58 (*d*, *J* = 5, OH–C(1), OH–C(3)); 2.93 (*dd*, *J* = 8.5, 8.5, 1 H, CH_2OTr); 3.21 (*dd*, *J* = 5.5, 9.0, 1 H, CH_2OTr); 4.09, 4.32 (2*m*, H–C(1), H–C(3)); 7.18–7.46 (*m*, arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 37.7 (C(5)); 43.2 (C(2)); 47.2 (C(4)); 65.9 (C(6)); 73.0 (C(1)); 76.9 (C(3)); 86.7 (Ph_3C); 127.1, 127.9, 128.7 (arom. CH); 144.0 (arom. C). MS: 374 (M^+), 356 ($[M - H_2O]^+$), 259 (23), 244 (32), 243 (100, PhC^+), 183 (55), 165 (66), 105 (83), 77 (38), 41 (22). Anal. calc. for $C_{25}H_{26}O_3$: C 80.18, H 7.00; found: C 79.76, H 6.96.

*(1S,3S,4R)-1-O-Acetyl-4-[(triphenylmethoxy)methyl]cyclopentane-*r*-1,*c*-3-diol* (= *(1S,3S,4R)-c-3-Hydroxy-*t*-4-[(triphenylmethoxy)methyl]cyclopent-*r*-1-yl Acetate*; (–)-**13**) *and (1R,3R,4S)-3-O-Acetyl-4-[(tri-*

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[4]) There is no need for working up (±)-**9**. Preferably, to the THF soln. obtained directly after the hydroformylation, H_2O and $NaBH_4$ are added directly as described in the following step.

[5]) THF/H_2O 9:1 as solvent mixture is extremely well suited for $NaBH_4$ reductions. The same reduction in MeOH is not as clean and requires several h at r.t. for completion.

[6]) THF can also be replaced by CH_2Cl_2/MeOH 9:1; in this case, the reaction is run overnight.

[7]) The synthesis was repeated on a ten-fold larger scale. Starting from **8**, (±)-**12** was prepared in 90% overall yield in 4 steps. The intermediate products were not purified and used for the next step as obtained.

phenylmethoxy)methyl]cyclopentane-r-*1*,c-*3*-*diol* (= *(1*R,*2*S,*4*R)-c-*4*-*Hydroxy*-t-*2*-*[(triphenylmethoxy)methyl]-cyclopent*-r-*1*-*yl Acetate*; (−)-**14**). Diol (±)-**12** (6.22 g, 16.6 mmol) was dissolved in vinyl acetate (63 ml) and *Pseudomonas fluorescens* lipase (PFL; 1.24 g; *Biocatalyst*) added. The heterogeneous mixture was stirred at r.t. for 50 h (TLC (AcOEt/hexane 1:1): R_f 0.33 and 0.48; no (±)-**12** left). The mixture was evaporated and chromatographed (AcOEt/hexane 1:2) to give, besides diacetate **15** (250 mg, 3.3%), pure (−)-**13** (3.00 g, 43.4%) and (−)-**14** (3.15 g, 45.4%) as slightly yellow oils. The same reaction was also carried out on a 30-fold larger scale to give similar results.

(−)-**13**: HPLC (*Chiralcel OD* (*Daicel*), hexane/i-PrOH 9:1, flow 1 ml/min): t_R 11.1 (99.1%) and 19.7 min (0.9%), ee 98.2%. $[\alpha]_{589} = -18.0$ ($c = 2.21$, $CHCl_3$). IR (neat): 3460*m* (br.), 3090*w*, 3060*m*, 3035*w*, 2975*m*, 2930*m*, 2870*m*, 2255*w*, 1965*w* (br.), 1820*w* (br.), 1734*vs*, 1598*w*, 1491*s*, 1448*s*, 1375*s*, 1318*m*, 1247*vs*, 1183*m*, 1154*m*, 1087*s*, 1060*s* (br.), 1022*s*, 1002*m*, 988*m*, 935*w*, 900*m*, 835*w* (br.), 776*s*, 764*s*, 747*s*, 706*vs*, 647*w*, 632*s*. ^{1}H-NMR (250 MHz, $CDCl_3$)[8]: 1.54 (*m*, 1 H–C(5)); 1.74 (*m*, 1 H–C(2)); 1.89 (*m*, 1 H–C(5)); 2.05 (*s*, Ac); 2.40 (*m*, 1 H–C(2), H–C(4)); 2.52 (*d*, $J = 4$, OH–C(3)); 2.98 (*t*, $J = 8.5$, 1 H, CH_2OTr); 3.34 (*dd*, $J = 9$, 5, 1 H, CH_2OTr); 3.95 (*dq*, $J = 3$, 7, H–C(3)); 5.07 (*m*, H–C(1)); 7.21–7.35 (*m*, H_p, H_m); 7.39–7.45 (*m*, H_o). MS: 416 (2.7, M^+), 356 (4.4, $[M - AcOH]^+$), 339 (7.2, $[M - Ph]^+$), 259 (25), 244 (39), 243 (100, $[Ph_3C]^+$), 183 (42), 165 (45), 105 (66), 97 (20), 77 (21), 43 (43).

(−)-**14**: $[\alpha]_{589} = -22.1$ ($c = 2.31$, $CHCl_3$). ^{1}H-NMR (250 MHz, $CDCl_3$): 1.61–1.78 (*m*, 1 H–C(2), 1 H–C(5), OH–C(1)); 1.95 (*m*, 1 H–C(5)); 2.03 (*s*, Ac); 2.30 (*ddd*, $J = 14.5$, 7.5, 5.5, 1 H–C(2)); 2.60 (*m*, H–C(4)); 3.12 (*ABM*, CH_2OTr); 4.34 (*m*, H–C(1)); 5.05 (*m*, H–C(3)); 7.18–7.34 (*m*, H_p, H_m); 7.38–7.45 (*m*, H_o).

The racemate (±)-**14** was inseparable by HPLC on the chiral columns examined, thus (−)-**14** was converted to diacetate (−)-**15** for the ee determination (*vide infra*).

(±)-t-*4*-*[(Triphenylmethoxy)methyl]cyclopentane*-r-*1*,c-*3*-*diyl Diacetate* ((±)-**15**). Diol (±)-**12** (200 mg, 534 μmol) was dissolved under Ar in anh. CH_2Cl_2 (2 ml) and cooled to 0°. DMAP (6.5 mg, 53 μmol) and Et_3N (162 mg, 1.60 mmol) were added under stirring followed by Ac_2O (136.3 mg, 1.34 mmol). After 30 min at 0° (TLC (AcOEt/hexane 1:1): R_f 0.73; no (±)-**12** left), the soln. was diluted with CH_2Cl_2 and extracted twice with 0.5M citric acid, once with sat. aq. $NaHCO_3$, and once with brine. The combined org. phase was dried (Na_2SO_4) and evaporated. Crystallization from hexane/AcOEt yielded, after drying under high vacuum, (±)-**15** (222.4 mg, 91%). Colorless crystals. M.p. 127°. HPLC (*Chiralcel OD* (*Daicel*), hexane/i-PrOH 49:1, flow 0.5 ml/min): t_R 23.5 (49%; (+)-enantiomer, (1*S*,3*S*,4*R*)) and 26.4 min (51%; (−)-enantiomer, (1*R*,3*R*,4*S*)). IR (KBr): 3440*m* (br., H_2O), 3085*w*, 3060*w*, 3025*m*, 3005*m*, 2975*w*, 2945*m*, 2900*w*, 2880*m*, 1735*vs*, 1598*w*, 1494*s*, 1478*m*, 1453*s*, 1447*s*, 1435*m*, 1373*s*, 1360*s*, 1312*w*, 1296*m*, 1280*m*, 1243*vs*, 1226*vs*, 1173*m*, 1150*m*, 1136 (sh), 1124*s*, 1080*s*, 1057*s*, 1043*m*, 1018*s*, 1001*s*, 978*m*, 957*m*, 944*m*, 932*m*, 923*m*, 905*m*, 884*w*, 856*w*, 834*w*, 810*w*, 873*s*, 770*s*, 756*s*, 729*m*, 706*vs*, 642*m*, 630*s*, 610*m*. ^{1}H-NMR (500 MHz, $CDCl_3$): 1.71–1.82 (*m*, 1 H–C(2), 1 H–C(5)); 1.97–2.05 (*m*, partially covered by 2*s*, 1 H–C(5)); 2.01, 2.04 (2*s*, 2 Ac); 2.44–2.55 (*m*, 1 H–C(2), H–C(4)); 3.11 (*ABM*, CH_2OTr); 4.98 (*ddd*, $J = 7.5$, 6.0, 4.5, H–C(3)); 5.12 (*sept.*-like *m*, H–C(1)); 7.20–7.31 (*m*, 3 H_p, 6 H_m); 7.38–7.43 (*m*, 6 H_o). ^{13}C-NMR (62.5 MHz, $CDCl_3$): 21.2, 21.3 (2 *Me*CO); 34.4 (C(5)); 39.0 (C(2)); 44.0 (C(4)); 63.6 (CH_2OTr); 74.3, 76.4 (C(1), C(3)); 86.4 (Ph_3C); 127.0, 127.8, 128.6 (arom. CH); 143.9 (arom. C); 170.7 (MeCO). MS: 458 (0.7, M^+), 398 (0.5, $[M - AcOH]^+$), 381 (1.2, $[M - Ph]^+$), 321 (1.1, $[M - Ph - AcOH]^+$), 259 (26), 243 (100, $[Ph_3C]^+$), 215 (14, $[M - Ph_3C]^+$), 199 (40), 165 (40), 155 (22), 105 (43), 96 (21), 95 (38), 79 (35), 43 (91). Anal. calc. for $C_{29}H_{30}O_5$: C 75.96, H 6.59; found: C 75.95, H 6.67.

*(1*S,*3*S,*4*R)-*Enantiomer* (+)-**15**. As described for (±)-**15**, a small sample of (−)-**13** was converted in quantitative yield to pure (+)-**15**. TLC and ^{1}H-NMR: identical with (±)-**15**. $[\alpha]^{25} = +25.6$ (589), +26.7 (578), +30.2 (546), +50.1 (436), +75.4 (365; $c = 2.19$, $CHCl_3$). HPLC (*Chiralcel OD*, hexane/i-PrOH 49:1, flow 0.5 ml/min): t_R 23.9 (99.1%) and 27.6 min (0.9%); ee 98.2%.

*(1*R,*3*R,*4*S)-*Enantiomer* (−)-**15**. As described for (±)-**15**, a small sample of (−)-**14** was converted in quantitative yield to pure (−)-**15**. TLC and ^{1}H-NMR: identical with (±)-**15**. $[\alpha]^{25} = -26.4$ (589), −27.5 (578), −30.9 (546), −51.1 (436), −77.0 (365; $c = 2.28$, $CHCl_3$). HPLC (*Chiralcel OD*, hexane/i-PrOH 49:1, flow 0.5 ml/min): t_R 25.8 min (100%); ee 100%.

*(1*S,*3*S,*4*R)-*4*-*[(Triphenylmethoxy)methyl]cyclopentane*-*1*,*3*-*diol* ((+)-**12**). To a soln. of (−)-**13** (100 g, 240 mmol) under Ar in anh. MeOH (600 ml), ethylenediamine (288.5 g, 4.80 mol; *Fluka*, freshly dist. over CaH_2) was added (temp. rise from r.t. to *ca.* 50°). After stirring the soln. for 15 h at 50° (TLC (AcOEt/hexane 1:1): R_f 0.22, no (−)-**13** (R_f 0.39) left), the solvents were removed under high vacuum, and the residue was dissolved 3 times in MeCN followed by evaporation. The resulting oil was dissolved in AcOEt (500 ml) and H_2O (300 ml) added. Under

[8]) Each proton of (−)-**13** and (−)-**14** was assigned with the help of the corresponding 500-MHz 2D COSY spectra.

stirring, the pH of the aq. phase was adjusted to 5 with 10% aq. citric acid. After addition of AcOEt (500 ml), the aq. layer was extracted and washed twice with AcOEt (150 ml). The combined org. layer was dried ($NaHCO_3$) and evaporated and the residue dissolved twice in MeCN followed by evaporation: crude (+)-**12** (90.5 g, quant.). Recrystallization from cyclohexane (550 ml; kinetically very slow, 1 week at 8–10°) gave, after drying at 0.1 Torr (16 h), (+)-**12** (85.2 g, 95%). Colorless crystals. M.p. 105–106°. $[\alpha]^{25} = +24.1$ (589), +26.3 (578), +28.8 (546), +48.2 (436), +73.7 (365; $c = 1.00$, MeOH). HPLC (*Chiralcel OD*, hexane/i-PrOH 9:1, flow 0.75 ml/min): t_R 16.0 (98.5%) and 22.4 min (1.5%); ee 97.0%. ^{1}H- and ^{13}C-NMR: identical with those of (±)-**12**. Anal. calc. for $C_{25}H_{26}O_3$: C 80.18, H 7.00; found: C 80.06, H 6.92.

*(1R,3R,4S)-3-*O*-Acetyl-1-*O*-[(4-bromophenyl)sulfonyl]-4-[(triphenylmethoxy)methyl]cyclopentane-1,3-diol* (= *(1R,2S,4R)-4-[(Bromophenyl)sulfonyloxy]-2-[(triphenylmethoxy)methyl]cyclopent-1-yl Acetate*; (−)-**16**). A soln. of (−)-**14** (10.0 g, 24.0 mmol) in anh. pyridine (30 ml; *Fluka puriss.*, stored over 4 Å molecular sieves) under Ar was cooled to 0° and 4-bromobenzenesulfonyl chloride (9.2 g, 36.0 mmol; *Fluka purum*) added under stirring at a rate to maintain the temp. < 2°. After roughly 2 h, the yellow soln. became heterogeneous and pyridinium hydrochloride started to crystallize. TLC (hexane/AcOEt 3:1) indicated complete formation of the product (R_f 0.37) after 24 h at 0°. Thus, 2-(dimethylamino)ethanol (3 ml) was added and the mixture stirred for another 30 min at 0° (conversion of excess reagent to an extractable form). The solvent was removed under high vacuum (bath temp. ≤ 10°) and the residue dissolved in Et_2O. The org. phase was washed with 10% aq. citric acid (3 ×), dried ($NaHCO_3$), and evaporated and the residue dried at 0.01 Torr overnight: crude (−)-**16** (14.85 g, 97%). Slightly yellowish amorphous solid. $[\alpha]^{20} = -14.1$ (589), −14.3 (578), −16.6 (546), −27.1 (436), −41.5 (365; $c = 1.24$, MeOH). ^{1}H-NMR (250 MHz, $CDCl_3$): 1.73 (*ddd*, $J = 14.5, 9, 4.5, 1$ H–C(2)); 1.84–2.17 (partially overlapping *m*, 2 H–C(5)); 1.99 (*s*, Ac); 2.36, 2.55 (*m*, 1 H–C(2), H–C(4)); 3.04 (*dd*, $J = 9.5, 9$), 3.17 (*dd*, $J = 9, 5$, *ABM*, CH_2OTr); 4.97 (*m*, H–C(1), H–C(3)); 7.20–7.40 (*m*, Ph_3C); 7.71 (*q*-like *m*, $BrC_6H_4SO_3$). ^{13}C-NMR (62.5 MHz, $CDCl_3$): 21.1 (*Me*COO); 35.1 (C(5)); 39.5 (C(2)); 43.8 (C(4)); 63.3 (CH_2OTr); 75.8 (C(3)); 82.9 (C(1)); 86.6 (Ph_3C); 127.1, 127.8, 128.6, 143.8 (*Ph*$_3$C); 128.9, 129.2, 132.6, 136.0 ($BrC_6H_4SO_3$); 170.7 (MeCOO). Anal. calc. for $C_{33}H_{31}BrO_6S$: C 62.36, H 4.92, Br 12.57, S 5.05; found: C 62.46, H 5.05, Br 12.71, S 4.77.

(1R,2S,4S)-4-(9H-Adenin-9-yl)-2-[(triphenylmethoxy)methyl]cyclopent-1-yl Acetate (= *9-{(1S,3R,4S)-3-Acetoxy-4-[(triphenylmethoxy)methyl]cyclopent-1-yl}-9H-adenine*; **17**). To a soln. of (−)-**16** (125 mg, 197 µmol) in anh. DMSO (3 ml; *Fluka puriss.*, stored over 4 Å molecular sieves) under Ar potassio-adenine[9]) (67 mg, 389 µmol) was added. The heterogeneous mixture was stirred for 4 days at r.t. (TLC (AcOEt/MeOH 9:1): R_f 0.3; no (−)-**16** left). The mixture was transferred to a 50-ml centrifugation tube, and BuOH (25 ml) and H_2O (20 ml) were added. After vortexing and centrifugation, the org. phase (upper) was evaporated and the crude product purified by chromatography (AcOEt/MeOH 9:1) to give, after drying at 0.1 Torr (16 h), **17** (60 mg, 57%). Amorphous, colorless solid. ^{1}H-NMR (250 MHz, $CDCl_3$): 1.90–2.05 (partially overlapping *m*), 2.17–2.59 (*m*, 2 H–C(5), CH_2OTr, H–C(2)); 2.05 (*s*, Ac); 3.30 (*ABM*, 2 H–C(3)); 5.07 (*m*, H–C(4)); 5.25 (*quint.*-like *m*, H–C(1)); 5.76 (br. *s*, NH_2); 7.19–7.51 (*m*, Ph_3C); 7.70, 8.34 (2*s*, 2 H of Ade). ^{13}C-NMR (62.5 MHz, $CDCl_3$): 21.2 (Ac); 34.3 (CH_2OTr); 38.6 (C(5)); 44.8 (C(2)); 53.5 (C(4)); 63.9 (C(3)); 75.8 (C(1)); 86.7 (Ph_3C); 127.1, 127.9, 128.7, 143.9 (*Ph*$_3$C); 120.1, 138.5, 150.1, 152.8, 155.4 (C of Ade); 170.5 (MeCOO).

(1R,2S,4S)-4-(9H-Adenin-9-yl)-2-(hydroxymethyl)cyclopentan-1-ol (= *9-[(1S,3R,4S)-3-Hydroxy-4-(hydroxymethyl)cyclopent-1-yl]-9H-adenine*; (−)-**18**). A soln. of **17** (1.00 g, 1.87 mmol) in 15 ml conc. HCl/EtOH 1:4 was stirred for 3 h at r.t. (after 2.5 h, the homogeneous soln. became heterogeneous, probably due to the separation of crystalline trityl derivatives). H_2O (9 ml) was added and stirring continued for another 5 min. The precipitate was filtered off and the filtrate evaporated (high vacuum). The crude product was recrystallized from MeOH/AcOMe: (−)-**18**·HCl (412 mg, 77%). Colorless crystals. M.p. 185–186° (dec.). $[\alpha]^{25} = -10.2$ (589), −10.6 (578), −11.8 (546), −18.6 (436), −27.8 (365; $c = 0.50$, MeOH). $[\alpha]^{25} = -10.2$ (589), −9.0 (578), −10.2 (546), −17.8 (436), −28.4 (365; $c = 0.50$, H_2O). (−)-**18**·HCl (400 mg, 1.40 mmol) was dissolved in MeOH and filtered with MeOH through a column containing *Amberlite IRA 93* (10 g; *Fluka*, OH^- form). The product fractions were evaporated, twice dissolved in MeCN, and evaporated under high vacuum. Crystallization from MeOH/AcOMe and drying afforded (−)-**18** (320 mg, 92%). Colorless crystals. Negative chloride test. M.p. 186–187° (dec.). $[\alpha]^{25} = -11.2$ (589), −11.6 (578), −13.2 (546), −21.2 (436), −31.4 (365; $c = 0.50$, H_2O). $[\alpha]^{25} = -10.6$ (589), −11.4 (578), −13.0 (546), −22.0 (436), −34.2 (365; $c = 0.50$, MeOH). ^{1}H-NMR (250 MHz, CD_3OD): 1.93 (*dt*, $J = 12.5, 9.5$), 2.11–2.30 (*m*, 2 H), 2.35–2.61 (*m*, 2 H, 2 H–C(5), CH_2OH, H–C(2)); 3.67 (*dd*, $J = 10.5, 6$), 3.75 (*dd*, $J = 11, 5.5$, *ABM*, 2 H–C(3)); 4.31 (*dt*, $J = 6.5, 4$, H–C(4)); 5.14 (*quint.*-like *m*, H–C(1)); 8.19, 8.24 (2*s*, 2 H of Ade).

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[9]) Equimolar amounts of adenine and KOMe were refluxed in MeOH for 24 h. The solvent was removed and the residue dried at 80°/high vacuum overnight.

(±)-t-4-[(Triphenylmethoxy)methyl]cyclopentane-r-1,c-3-diyl Sulfate ((±)-**19**). A soln. of (±)-**12** (1.049 g, 2.80 mmol) in anh. CH_2Cl_2 (20 ml; filtered through basic Alox, act. I) and Et_3N (1.56 ml, 11.4 mmol; *Fluka puriss.*, stored over 4 Å molecular sieves) under Ar was cooled to 0° and $SOCl_2$ (302 µl, 4.2 mmol; *Fluka puriss.*, dest.) added dropwise under stirring within 5 min (→ yellow after addition of roughly half of the $SOCl_2$, then brownish). After 10 min, a precipitate started to separate (TLC (hexane/AcOEt 4:1): R_f 0.32 and 0.40; no (±)-**12** left). The mixture was extracted twice with ice-cold H_2O (25 ml) and finally with ice-cold brine (18% *w/v*; 30 ml). The combined org. phase was dried ($MgSO_4$) and evaporated (bath temp. 15°), the residue twice dissolved in MeCN and evaporated, and the brownish product dried at 0.01 Torr (10 min): crude diastereoisomeric cyclic sulfites (1.34 g, 113%; containing Et_3N and MeCN). These crude sulfites (8.50 g; obtained from 5.00 g of (±)-**12**; 13.4 mmol) were dissolved in MeCN/CCl_4 1:1 (160 ml) and cooled to 0°. H_2O (120 ml) was added followed by $RuCl_3 \cdot H_2O$ (47 mg, 200 µmol; *Engelhard*) and $NaIO_4$ (5.71 g, 26.7 mmol; *Merck*, 'z.A.'). The mixture was vigorously stirred at 0° (TLC (hexane/AcOEt 3:1): R_f 0.32). After complete conversion (1 h), Et_2O (300 ml) was added, the org. phase washed 3 times with ice-cooled brine, dried ($MgSO_4$), and evaporated (bath temp. 15°), and the residue dried at 0.01 Torr: (±)-**19** (5.80 g; quant. over two steps). Colorless amorphous solid. IR (CH_2Cl_2): 3065*w*, 2990*w*, 2800*w*, 1600*w*, 1493*m*, 1450*m*, 1423*w*, 1380*vs*, 1340*w*, 1317*w*, 1299*w*, 1208*vs*, 1187*s*, 1155*w*, 1110*w*, 1092*w*, 1076*m*, 1043*m*, 1034*m*, 1020*m*, 1005*w*, 967*vs*, 920*m*, 894*s*, 833*w*, 820*w*, 788*s*, 649*w*, 634*m*, 605*w*. ^{1}H-NMR (250 MHz, $CDCl_3$): 1.61 (*dt*, J = 13.5, 4), 1.77 (*dt*, J = 12.5, 2.5), 2.69 (br. *d*, J = 12.5), 2.80–2.92 (*m*, partially overlapping signal, 2 H–C(2), 2 H–C(5)); 3.39 (*m*, H–C(4)); 2.84 (*dd*, J = 8.5, 7, partially overlayed signal), 3.29 (*dd*, J = 8.5, 4.5, CH_2OTr); 5.09 (br. *s*), 5.22 (br. *s*, H–C (1), H–C(3)); 7.21–7.45 (*m*, arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 33.5, 34.1 (C(2), C(5)); 42.4 (C(4)); 63.8 (CH_2OTr); 87.2 (Ph_3C); 89.7, 91.6 (C(1), C(3)); 127.4, 128.1, 128.5 (arom. CH); 143.4 (arom. C). MS: 436 (6.5, M^+), 359 (4.2, $[M - Ph]^+$), 243 (28, $[Ph_3C]^+$), 105 (21), 71 (21), 70 (32), 57 (33), 55 (69), 44 (100).

(1S,3S,4R)-4-[(Triphenylmethoxy)methyl]cyclopentane-1,3-diyl Sulfate ((+)-**19**). As described for (±)-**19**. Yield 98%. $[\alpha]^{25} = +9.2$ (589), +10.4 (578), +10.7 (546), +16.6 (436), +22.5 (365; c = 1.05, $CHCl_3$). ^{1}H- and ^{13}C-NMR: identical with those of (±)-**19**.

(±)-t-4-Azido-t-2-[(Triphenylmethoxy)methyl]cyclopentan-r-1-ol ((±)-**20**). To the soln. of (±)-**19** (500 mg, 1.15 mmol) in anh. MeCN (*Baker*) under Ar at 0°, [15]crown-5 (242 mg, 1.10 mmol; *Fluka*) was added followed by NaN_3 (90 mg, 1.38 mmol; *Fluka*). The homogeneous mixture was stirred at 0°. After 90 min, a white solid started to precipitate. After 4 h (TLC (hexane/AcOEt 2:1): no (±)-**19** (R_f 0.47) left), the mixture was evaporated and dried at 0.01 Torr. Anh. THF (10 ml; dest. from Na/benzophenone) was added under Ar followed by H_2O (19.8 µl, 1.10 mmol) and conc. H_2SO_4 (107 mg, 1.09 mmol; *Fluka*) to achieve the hydrolysis of the monoalkyl sulfate [24]. The mixture was vigorously stirred at r.t. and after 4 h (TLC (hexane/AcOEt 2:1): no polar sulfate (R_f 0) left; R_f 0.58), excess $NaHCO_3$ was added and the mixture stirred for further 2 h and filtered through 5 g of SiO_2 (washing with AcOEt). The solvents were evaporated, the residue chromatographed (hexane/AcOEt 5:1), and the product fractions evaporated, twice co-evaporated with MeCN and dried under high vacuum: honey-like (±)-**20** (316 mg, 69%)[10]. IR ($CHCl_3$): 3600, 3250*w*, 3075*w*, 3050*m*, 3015 (sh), 2995*m*, 2950*m*, 2915*m*, 2855*m*, 2470*w* (br.), 2100*vs*, 1955*w* (br.), 1817*w* (br.), 1725*w* (br.), 1595*w*, 1488*s*, 1447*s*, 1395*w*, 1372*w*, 1317*m*, 1255*s*, 1151*s*, 1136*s*, 1123*s*, 1105*s*, 1085 (sh), 1070*vs*, 1031*s*, 1002*m*, 995 (sh), 984*m*, 946*w*, 900*m*, 863*w*, 702*vs*, 665*w*, 633*m*. ^{1}H-NMR (500 MHz, $CDCl_3$; assignment by 500-MHz COSY): 1.26 (*ddd*, J = 13, 9.5, 6.5, 1 H–C(3)); 1.89–2.01 (*m*, 2 H–C(5)); 2.08–2.16 (*m*, H–C(2)); 2.20 (*dt*, J = 13, 7.5, 1 H–C(3)); 2.32 (*d*, J = 2.5, OH–C(1)); 3.06 (*t*, J = 8.5, 1 H, CH_2OTr); 3.34 (*dd*, J = 9, 5, 1 H, CH_2OTr); 4.04 (*m*, H–C(4)); 4.10 (*dq*, J = 2.5, 7, H–C(1)); 7.23–7.27 (*m*, 3 H_p); 7.29–7.34 (*m*, 6 H_m); 7.39–7.43 (*m*, 6 H_o). ^{13}C-NMR (62.5 MHz, $CDCl_3$): 33.4 (C(3)); 40.1 (C(5)); 46.8 (C(2)); 59.3 (C(4)); 66.1 (CH_2OTr); 75.4 (C(1)); 87.0 (Ph_3C); 127.2, 127.9, 128.6 (arom. CH); 143.7 (arom. C).

(1S,2R,4R)-4-(9H-Adenin-9-yl)-2-[(triphenylmethoxy)methyl]cyclopent-1-yl Triethylammonium Sulfate (**21**). Adenine (3.76 g, 27.8 mmol; finely ground and dried under high vacuum for 16 h) was suspended under Ar in anh. MeCN (200 ml; *Baker*) and DBU (4.23 g, 27.8 mmol) added. After 15 min stirring at r.t., a clear soln. was obtained to which (+)-**19** (11.50 g, 26.3 mmol) was added. The soln. was heated to 40° and kept at this temp. After 2 days (TLC (hexane/AcOEt 3:1): no (+)-**19** (R_f 0.32) left; new product), the mixture was evaporated and the residue purified by chromatography (column diameter 11 cm, CH_2Cl_2/MeOH/Et_3N 30:3:1, R_f 0.32). Pure product fractions were evaporated, co-evaporated with MeCN (4 × 50 ml), and dried at 0.1 Torr (16 h): **21** (14.3 g, 80%). Amorphous solid. ^{1}H-NMR (250 MHz, CD_3OD): 1.31 (*t*, J = 7, $(MeCH_2)_3NH^+$); 1.64–2.66 (*m*, 2 H–C(5),

[10]) Comparison of the ^{13}C-NMR data of (±)-**12** and (±)-**20** lead to the conclusion that the configuration at the CH_2OTr- and the vicinal OH-substituted C-atoms were identical in both compounds. However, the configuration at C(4) of (±)-**20** could not directly be verified and is assumed in analogy to similar substitution experiments with the cyclic sulfate **19**.

CH_2OTr, H–C(2)); 3.20 (*q*, $J = 7$, $(MeCH_2)_3NH^+$); 3.15–3.40 (*m*, 2 H–C(3) partially overlapping with $(CH_3CH_2)_3NH^+$ and CD_2HOD); 5.02–5.17 (*m*, H–C(1), H–C(4)); 7.18–7.51 (*m*, Ph_3C); 8.15 (*s*, 2 H of Ade).

(1S,2R,4R)-4-(6-Amino-2-chloro-9H-purin-9-yl)-2-[(triphenylmethoxy)methyl]cyclopent-1-yl Triethylammonium Sulfate (**22**). To a suspension of 2-amino-6-chloro-9*H*-purine (9.82 g, 57.9 mmol; *Sigma*; finely ground and dried under high vacuum for 16 h) in anh. MeCN (350 ml; *Baker*) under Ar, DBU (8.83 g, 58 mmol) was added. After 15 min stirring at r.t., a clear soln. was obtained to which (+)-**19** (23 g, 52.7 mmol) in anh. MeCN (90 ml; *Baker*) was added. After stirring for 3 h at r.t. (TLC (hexane/AcOEt 3:1): no (+)-**19** (R_f 0.32) left; 2 products), the mixture was evaporated and the residue separated by chromatography (column diameter 11 cm, CH_2Cl_2/MeOH/Et_3N 50:3:1, R_f 0.36 (major) and 0.29 (minor)). Fractions containing the pure (major) product were evaporated, co-evaporated with MeCN (4 × 50 ml), and dried at 0.1 Torr (16 h): **22** (28.1 g, 75%). Amorphous solid. ^{1}H-NMR (250 MHz, CD_3OD): 1.30 (*t*, $J = 7$, $(MeCH_2)_3NH^+$); 1.92 (*q*-like *m*), 2.33–2.63 (*m*, 2 H–C(5), CH_2OTr, H–C(2)); 3.19 (*q*, $J = 7$, $(MeCH_2)_3NH^+$); 3.34 (*m*, 2 H–C(3), partially overlapping with $(MeCH_2)_3NH^+$ and CD_2HOD); 4.93–5.12 (*m*, H–C(1), H–C(4), partially overlapping with CD_3OH); 7.17–7.51 (*m*, Ph_3C); 8.06 (*s*, H–C(8) of Pur).

In addition to **22**, the N^7-alkylated purine isomer was isolated as well (4.2 g, 11%).

(1S,2R,4R)-4-(2,6-Diamino-9H-purin-9-yl)-2-[(triphenylmethoxy)methyl]cyclopent-1-yl Triethylammonium Sulfate (**23**). The soln. of **22** (10.0 g, 14.1 mmol) in MeOH (500 ml) was placed in an autoclave and saturated with NH_3 (36°, 11 bar). After 15 h at 130° (TLC (AcOEt/MeOH 7:3): no **22** (R_f 0.73) left; R_f 0.30), the mixture was evaporated and co-evaporated 3 times with MeCN: **23** (9.91 g, 102%). Yellowish solid which was used in the next step without further purification. A small sample was purified by chromatography (CH_2Cl_2/MeOH/Et_3N 50:3:1) for anal. purposes. ^{13}C-NMR (75 MHz, CD_3OD): 9.3 ($(MeCH_2)_3NH^+$); 34.9 (CH_2OTr); 39.2 (C(5)); 46.9 (C(2)); 48.0 ($(MeCH_2)_3NH^+$); 54.7 (C(4)); 65.3 (C(3)); 81.0 (C(1)); 88.0 (Ph_3C); 114.6 (C(3)); 128.1, 128.9, 130.0, 145.6 (Ph_3C); 138.3 (C(8) of Pur); 153.0 (C(4) of Pur); 157.1 (C(6) of Pur); 161.0 (C(2) of Pur).

(1R,2R,4R)-4-(9H-Adenin-9-yl)-2-(hydroxymethyl)cyclopentan-1-ol Hydrochloride ((+)-**18**·HCl). A soln. of **21** (14.0 g, 20.8 mmol) in MeOH containing 2% (*v*/*v*) of 37% aq. HCl soln. (510 ml) was heated to 65°. After 15 h, the mixture was evaporated and the residue purified by chromatography (AcOEt/MeOH 1:1; R_f 0.42). Recrystallization from hot MeOH/AcOEt afforded (+)-**18**·HCl (5.21 g, 87%). Light brownish crystals. M.p. 196–197° (dec.). $[\alpha]^{25} = +8.5$ (589), +9.4 (578), +10.4 (546), +17.5 (436), +26.9 (365; $c = 1.00$, MeOH). ^{1}H-NMR (250 MHz, CD_3OD): 1.95 (*dt*, $J = 12.5, 9.5$), 2.11–2.64 (*m*, 4 H, 2 H–C(5), CH_2OTr, H–C(2)); 3.70 (*m*, 2 H–C(3)); 4.31 (*m*, H–C(1)); 5.22 (*quint.*-like *m*, H–C(4)); 8.40, 8.48 (2*s*, 2 H of Ade). ^{13}C-NMR (75 MHz, CD_3OD): 35.0 (CH_2OH); 41.5 (C(5)); 50.5 (C(2)); 55.7 (C(4)); 64.1 (C(3)); 73.6 (C(1)); 120.1 (C(5) of Ade); 144.2 (C(8) of Ade); 144.5 (C(2) of Ade); 150.1 (C(4) of Ade); 151.5 (C(6) of Ade).

As described for (–)-**18**·HCl, (+)-**18**·HCl (300 mg, 1.05 mmol) was converted to crystalline (+)-**18** (231 mg, 89%). TLC and ^{1}H-NMR: identical to those of (–)-**18**. M.p. 185–186°. $[\alpha]^{25} = +10.9$ (589), +11.1 (578), +13.0 (546), +20.6 (436), +30.8 (365; $c = 0.50$, MeOH).

(1S,2R,4R)-4-(9H-Guanin-9-yl)-2-(hydroxymethyl)cyclopentan-1-ol Hydrochloride ((+)-**24**·HCl). A soln. of **22** (18.0 g, 25.4 mmol) in MeOH containing 2% (*v*/*v*) of 37% aq. HCl soln. (1.02 l) was kept for 20 h at 65°. After evaporation, the residue was purified by chromatography (AcOEt/MeOH/*N*-methylmorpholine 25:25:1; R_f 0.36). The product was dissolved in MeOH (100 ml) and 37% aq. HCl soln. (20 ml) and evaporated (conversion to the hydrochloride). Recrystallization from hot MeOH/AcOMe 3:11 (380 ml) afforded (+)-**24**·HCl (6.02 g, 78%). Colorless crystals. M.p. 247–248° (dec.). $[\alpha]^{25} = +11.9$ (589), +12.7 (578), +13.0 (546), +19.2 (436), +27.8 (365; $c = 1.01$, MeOH). ^{1}H-NMR (500 MHz, (D_6)DMSO): 1.64 (*dt*, $J = 13, 9.5$), 1.98 (*m*), 2.05 (*m*), 2.16 (*m*), 2.37 (*dt*, $J = 13, 7.5$, 2 H–C(5), CH_2OH, H–C(2)); 3.41, 3.50 (*AB* of *ABM*, each $J = 10.5, 6.5$, 2 H–C(3)); 4.07 (*quint.*-like *m*, $J = 3.5$, H–C(1)); 4.89 (*m*, H–C(4)); 7.06 (br. *s*, NH_2); 8.95 (*s*, H–C(8) of Gua); 11.45 (*s*, H–N(1) of Gua). ^{13}C-NMR (75 MHz, (D_6)DMSO): 33.5 (CH_2OH); 49.1 (C(2)); 54.1 (C(4)); 62.5 (C(3)); 71.2 (C(1)); 108.4; 135.6; 149.7; 153.5; 155.3. FAB-MS: 288 (10, $[M + Na]^+$), 266 (100, $[M + H]^+$), 152 (17, [guanine + H]$^+$). Anal. calc. for $C_{11}H_{15}N_5O_3 \cdot HCl \cdot 0.5\,H_2O$: C 42.51, H 5.19, Cl 11.41, N 23.53; found: C 42.39, H 5.17, Cl 12.12, N 22.32.

(1S,2R,4R)-4-(2,6-Diamino-9H-purin-9-yl)-2-(hydroxymethyl)cyclopentan-1-ol ((+)-**25**). A soln. of **23** (9.69 g, 14.1 mmol) in MeOH containing 2% (*v*/*v*) of 37% aq. HCl soln. (510 ml) was kept for 15 h at 65°. After evaporation, the residue was purified by chromatography (AcOEt/MeOH 7:3; R_f 0.36). Recrystallization from hot MeOH (50 ml) afforded **25**·HCl (3.51 g, 83%) as light brownish crystals which contained, according to ^{1}H-NMR, 5–10% impurities. A sample of **25**·HCl (500 mg, 1.66 mmol) was dissolved in hot MeOH/H_2O 5:1 (12 ml), and the pH was adjusted to 8 by the addition of 1M aq. NH_3. The mixture was evaporated, the residue dried under high vacuum overnight and recrystallized from hot MeOH (10 ml), and the product dried: (+)-**25** (380 mg, 87%). Colorless crystals. Negative chloride test. M.p. 214–215° (dec.). $[\alpha]^{25} = +7.2$ (589), +7.8 (578), +9.2 (546), +14.6 (436), +20.2 (365; $c = 1.00$, MeOH). ^{1}H-NMR (250 MHz, (D_6)DMSO): 1.62 (*dt*, $J = 12.5, 9.5$), 1.90–2.20 (*m*),

2.28 (*dt*, J = 12.5, 7.5, 2 H–C(5), CH_2OH, H–C(2)); 3.37–3.58 (*m*, 2 H–C(3)); 4.06 (*m*, H–C(1)); 4.66 (*t*, J = 5, CH_2OH); 4.76 (*d*, J = 4, OH–C(1)); 4.85 (*m*, H–C(4)); 5.75, 6.65 (2 br. *s*, 2 NH_2); 7.82 (*s*, H–C(8) of Pur). ^{13}C-NMR (75 MHz, (D_6)DMSO): 34.0 (CH_2OH); 40.7 (C(5)); 49.3 (C(2)); 51.8 (C(4)); 62.9 (C(3)); 71.6 (C(1)); 113.5 (C(5) of Pur); 135.6 (C(8) of Pur); 151.8 (C(4) of Pur); 156.2 (C(6) of Pur). FAB-MS: 265 (100, $[M + H]^+$), 237 (10), 197 (13), 151 (23, [2,6-diaminopurine + H]$^+$).

(1S,2R,4R)-4-(1H-Thymin-1-yl)-2-[(triphenylmethoxy)methyl]cyclopent-1-yl Triethylammonium Sulfate (**26**). To a suspension of thymine (6.71 g, 53.1 mmol; finely ground and dried under high vacuum for 16 h) in anh. MeCN (400 ml; *Baker*) under Ar, DBU (8.1 g, 53.1 mmol) was added. This mixture was refluxed (→ clear soln.) and (+)-**19** (22 g, 50.4 mmol) in MeCN (50 ml) added. After 1 h at reflux (TLC (hexane/AcOEt 3:1): no (+)-**19** (R_f 0.32) left; new, major product), the mixture was evaporated and the crude product purified by chromatography (column diameter 7.5 cm, CH_2Cl_2/MeOH/Et_3N 60:3:1, R_f 0.29). Pure product fractions were evaporated and co-evaporated with MeCN (3 × 50 ml) to give, after drying at 0.1 Torr (16 h), **26** (23.6 g, 70%). Amorphous solid. ^{1}H-NMR (250 MHz, CD_3OD): 1.29 (*t*, J = 7, $(MeCH_2)_3NH^+$); 1.52 (*q*-like *m*), 2.10–2.54 (*m*, 2 H–C(5), CH_2OTr, H–C(2)); 1.76 (*s*, Me–C(5) of Thy); 3.19 (*q*, J = 7, $(MeCH_2)_3NH^+$); 3.00–3.38 (*m*, 2 H–C(3), partially overlapping with $(MeCH_2)_3NH^+$ and CD_2HOD); 4.64–5.10 (*m*, H–C(1), H–C(4), partially overlayed by CD_3OH); 7.10–7.50 (*m*, arom. H). FAB-MS: 765 (30, $[M + Et_3NH]^+$), 686 (8, $[M + Et_3NH - SO_3]^+$), 243 (100, $[Ph_3C]^+$).

(1S,2R,4R)-4-[N^4-(2-Methylpropanoyl)-1H-cytosin-1-yl]-2-[(triphenylmethoxy)methyl]cyclopent-1-yl Triethylammonium Sulfate (**27**). N^4-(2-Methylpropanoyl)-1H-cytosine [26] (5.23 g, 28.9 mmol; finely ground and dried under high vacuum for 16 h) was suspended under Ar in anh. MeCN (200 ml; *Baker*). DBU (4.39 g, 28.9 mmol) was added, the soln. heated to reflux, and (+)-**19** (11.5 g, 26.3 mmol) in MeCN (100 ml) added. After 1 h at reflux (TLC (hexane/AcOEt 3:1): no (+)-**19** (R_f 0.32) left; two major products), the mixture was evaporated and the residue separated by chromatography (column diameter 11 cm, CH_2Cl_2/MeOH/Et_3N 90:3:1, R_f 0.19 and 0.40). Pure product fractions were evaporated and co-evaporated with MeCN (4 × 40 ml) to give, after drying at 0.1 Torr (16 h), **27** (11.6 g, 61%) as an amorphous solid, along with the less polar O^2-alkylation product (7.2 g, 35%), as determined by ^{1}H-NMR (data not shown). **27**: ^{1}H-NMR (250 MHz, CD_3OD): 1.16 (*d*, J = 7, Me_2CH); 1.29 (*t*, J = 7, $(MeCH_2)_3NH^+$); 1.58 (*q*-like *m*), 2.18–2.58 (*m*, 2 H–C(5), CH_2OTr, H–C(2)); 2.66 (*sept.*, J = 7, Me_2CH); 3.18 (*q*, J = 7, $(MeCH_2)_3NH^+$); 3.1–3.4 (*m*, 2 H–C(3), partially overlayed by $(MeCH_2)_3NH^+$ and CD_2HOD); 4.8–5.15 (*m*, H–C(1), H–C(4), partially overlayed by CD_3OH); 7.15–7.50 (*m*, arom. H); 7.95 (*d*, J = 8, H–C(5) of Cyt).

Note: The ratio of O- *vs.* N-alkylation was temp.-dependent: at 0°, O-alkylation was kinetically preferred over N-alkylation, and **27** could be isolated in only 33% yield along with the O^2-alkylation product (51%; data not shown).

(1S,2R,4R)-2-(Hydroxymethyl)-4-(1H-thymin-1-yl)cyclopentan-1-ol ((+)-**28**). A soln. of **26** (23.5 g, 35.4 mmol) in MeOH containing 2% (*v*/*v*) of 37% aq. HCl soln. (510 ml) was kept for 15 h at 45°. After evaporation, the residue was purified by chromatography (AcOEt/MeOH 7:1; R_f 0.32). Recrystallization from hot MeOH/Et_2O 1:1 afforded (+)-**28** (6.73 g, 79%). Colorless crystals. M.p. 175–176°. $[\alpha]^{25}$ = +7.3 (589), +7.4 (578), +8.0 (546), +8.2 (436), −4.1 (365; c = 1.00, MeOH). ^{1}H-NMR (250 MHz, CD_3OD): 1.59 (*dt*, J = 12, 10), 1.90–2.32 (*m*, 2 H–C(5), CH_2OH, H–C(2)); 1.89 (*s*, Me–C(5) of Thy); 3.56–3.73 (*m*, 2 H–C(3)); 4.17 (*m*, H–C(1)); 5.06 ('*quint.*', J = 7, H–C(4)); 7.51 (*s*, H–C(6) of Thy). ^{13}C-NMR (75 MHz, CD_3OD): 12.4 (Me–C(5) of Thy); 33.5 (CH_2OH); 40.0 (C(5)); 50.3 (C(2)); 55.9 (C(4)); 64.3 (C(3)); 73.7 (C(1)); 111.6 (C(5) of Thy); 139.9 (C(6) of Thy); 153.0 (C(2) of Thy); 166.5 (C(4) of Thy). FAB-MS: 241 (100, $[M + H]^+$), 127 (16, [thymine + H]$^+$). Anal. calc. for $C_{11}H_{16}N_2O_4 \cdot 0.5\ H_2O$: C 53.00, H 6.87, N 11.23; found: C 53.31, H 6.65, N 11.28.

(1S,2R,4R)-4-(1H-Cytosin-1-yl)-2-(hydroxymethyl)cyclopentan-1-ol ((+)-**29**). A soln. of **27** (11.0 g, 15.3 mmol) in MeOH containing 2% (*v*/*v*) of 37% aq. HCl soln. (408 ml) was kept for 20 h at 65°. After evaporation, the residue was purified by chromatography (first AcOEt/MeOH 1:1 (R_f 0.32), then AcOEt/MeOH/aq. NH_3 soln. 7:3:1 (R_f 0.31)). Recrystallization from hot MeOH/AcOEt afforded (+)-**29** (2.98 g, 86%). Colorless crystals. M.p. 204–205°. $[\alpha]^{25}$ = +5.3 (589), +5.7 (578), +6.0 (546), +5.6 (436), −8.2 (365; c = 0.997, MeOH). ^{1}H-NMR (250 MHz, CD_3OD): 1.59 (*dt*, J = 12.5, 10), 1.93–2.17 (*m*, 3 H), 2.31 (*dt*, J = 12.5, 8, 2 H–C(5), CH_2OH, H–C(2)); 3.55–3.73 (*m*, 2 H–C(3)); 4.18 (*q*, J = 5, H–C(1)); 5.08 (*quint.*, J = 9, H–C(4)); 5.99 (*d*, J = 8, H–C(5) of Cyt); 7.85 (*d*, J = 8, H–C(6) of Cyt). ^{13}C-NMR (75 MHz, CD_3OD): 33.7 (CH_2OH); 40.2 (C(5)); 50.3 (C(2)); 57.5 (C(4)); 64.2 (C(3)); 73.6 (C(1)); 95.7 (C(5) of Cyt); 146.3 (C(6) of Cyt); 154.6 (C(2) of Cyt); 164.2 (C(4) of Cyt). FAB-MS: among other peaks 451 (19, $[2\ M + H]^+$), 226 (100, $[M + H]^+$), 112 (22, [cytosine + H]$^+$), 91 (46).

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