31. Nucleic-Acid Analogues with Constraint Conformational Flexibility in the Sugar-Phosphate Backbone ('Bicyclo-DNA')

Part 1[1])

Preparation of (3'*S*,5'*R*)-2'-Deoxy-3',5'-ethano-α,β-D-ribonucleosides ('Bicyclonucleosides')

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We describe the synthesis of 2'-deoxy-3',5'-ethano-D-ribonucleosides **1–8** (= (5',8'-dihydroxy-2'-oxabicyclo-[3.3.0]oct-3'-yl)purines or -pyrimidines) of the nucleobases adenine, thymine, cytosine, and guanine. They differ from natural 2'-deoxyribonucleosides only by an additional ethylene bridge between the centers C(3') and C(5'). The configuration at these centers (3'*S*,5'*R*) was chosen as to match the geometry of a repeating nucleoside unit in duplex DNA as close as possible. These nucleosides were designed to confer, as constituents of an oligonucleotide chain, a higher degree of preorganization of a single strand for duplex formation with respect to natural DNA, thus leading to an *entropic* advantage for the pairing process. The synthesis of these 'bicyclonucleosides' was achieved by construction of an enantiomerically pure carbohydrate precursor **18**/**19** (*Scheme 1*), which was then converted to the corresponding nucleosides by known methods in nucleoside synthesis (*Schemes 2* and *3*). In all cases, both anomeric forms of the nucleosides were obtained in pure crystalline form, the relative configuration of which was established by ^{1}H-NMR-NOE spectroscopy. A conformational analysis of the nucleosides with β-configuration at the anomeric center by means of X-ray and ^{1}H-NMR (including NOE) spectroscopy show the furanose part of the molecules to adopt uniformly a 1'-*exo*-conformation with the base substituents preferentially in the *anti*-range in the pyrimidine nucleosides (*anti*/*syn ca.* 2:1) and in an almost equal *anti*/*syn* distribution in the purine nucleosides (in solution).

1. Introduction. – Synthetic oligonucleotides that form stable complexes with natural DNA and RNA according to the *Watson-Crick* base-pairing rules recently gained enormous interest as specific inhibitors of protein biosynthesis. By hybridization of a complementary ('antisense') oligonucleotide to a ('sense') RNA, the expression of a target gene sequence can be arrested on the level of translation [1]. Similarly, oligonucleotides that specifically pair to double-stranded DNA forming local triplex structures may block gene expression at the level of transcription as well as DNA replication itself [2]. The specificity of such oligonucleotides towards a target sequence is defined by their base sequence and length. In this context, an extensive search for oligonucleotide analogues showing stronger binding to complementary DNA and RNA and/or higher enzymatic resistance towards cellular nucleases evolved over the last decade [3].

[1]) Presented in part by *C. L.* at the autumn meeting of the Swiss Chemical Society, Berne, October 18, 1991.

[2]) Taken in part from the planned Ph. D. theses of *M. T.* and *M. B.*

Stronger binding of an oligonucleotide to complementary DNA or RNA can, in principle, be achieved either by increasing the enthalpy and/or decreasing the entropy of duplexation. Enthalpic stabilization of duplexation was addressed by substituting the negatively charged phosphate groups in natural oligonucleotides with charge-neutral nucleoside linking groups, such as phosphotriester [4], methyl phosphonate [5], phosphoramidate [6], sulfonate [7], and acetal groups [8] or, most recently, by replacing the sugar-phosphate backbone by an amide backbone [9], thus eliminating interstrand phosphate repulsion in duplexes. Substitution of 2,6-diaminopurine for adenine as the nucleobase in DNA oligomers [10] stands as an example of enhanced enthalpic stabilization of the resulting duplexes due to an additional H-bond in the diaminopurine-thymine base pair with respect to the parent adenine-thymine base pair.

Entropic stabilization of duplexation is one of the unprecedented pairing properties exhibited by oligonucleotides consisting of 2′,3′-dideoxyglucopyranonucleosides ('homo DNA'), prepared and characterized in the laboratories of *Eschenmoser* at ETH [11]. In comparable oligomer sequences, homo-DNA always shows a slightly smaller (less negative) enthalpy change (ΔH) and a distinctly smaller (less negative) entropy change (ΔS) upon duplexation with respect to natural DNA. This generally leads to more negative free enthalpies of pairing (ΔG) in homo-DNA. Empirically, the difference in the entropy term can be attributed in part to the conformationally locked six-membered pyranose ring of homo-DNA, compared to the more flexible furanose ring of natural nucleosides. Homo-DNA represents an autonomous pairing system with its own base-pairing rules and does not form mixed duplexes with natural DNA. On the other hand, oligonucleotides incorporating nucleosides based on acyclic, glycerol-derived sugar substitutes, show a drastic reduction in binding energy or no binding at all to their DNA complements [12]. This may be interpreted as a consequence of an unfavorable pairing entropy, due to the higher flexibility of these modified nucleotides with respect to natural DNA.

Inspired by the work on homo-DNA, we wished to extend the concept of entropic duplex stabilization, as outlined above, to oligonucleotides that pair to complementary DNA and RNA, and, therefore, designed the nucleosides **1**–**8**. These nucleosides differ from natural 2′-deoxy-α- and -β-D-ribonucleosides only by an additional ethylene bridge between the centers C(5′) and C(3′)[3]). This additional bridge brings about that two torsion angles (γ and δ) relevant for the description of the repeating nucleotide unit in duplex DNA (*Fig. 2*) are restricted in their rotational freedom. The configuration at the centers C(5′) and C(3′) is chosen so as to match the conformation of the natural nucleosides in a duplex state as close as possible. From oligomers of such nucleosides, one can expect a higher degree of preorganisation of single strands, which should lead to less entropy change upon duplexation with natural complementary DNA and RNA and,

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[3]) To express the structural similarities of the nucleosides **1**–**8** with the natural nucleosides and to be able to use the IUPAC abbreviations and symbols for the description of conformations of polynucleotide chains [13], we propose to maintain the same carbohydrate nomenclature and numbering scheme [14] as for ribonucleosides and to use the prefix 'ethano' for the additional C_2-bridge, in analogy to the notation for bridged fused aromatic (hetero)cycles [15]. The numbering of the ethano substituent is given by extension of that of the ribose chain (*Fig. 1*). Accordingly, nucleoside **1** would be named (3′*S*,5′*R*)-1-(2′-deoxy-3′,5′-ethano-β-D-ribofuranosyl)thymine and compound **39** (see below, *Scheme 3*), as another example, (3′*S*,5′*R*)-N^6-Benzoyl-9-(2′-deoxy-3′,5′-ethano-α-D-ribofuranosyl)adenine.

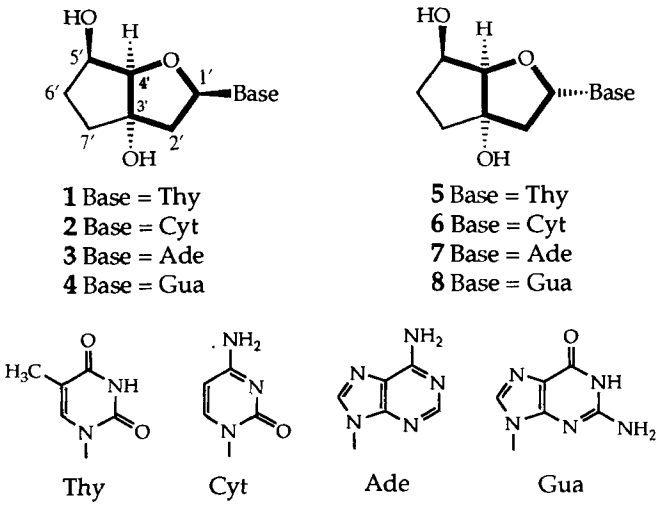


Fig. 1. *The (5′,8′-dihydroxy-2′-oxabicyclo[3.3.0]oct-3′-yl)nucleobases* (= (2′-deoxy-3′,5′-ethano-D-ribonucleosides, 'bicyclonucleosides') *of the four natural nucleobases thymine, cytosine, adenine, and guanine*

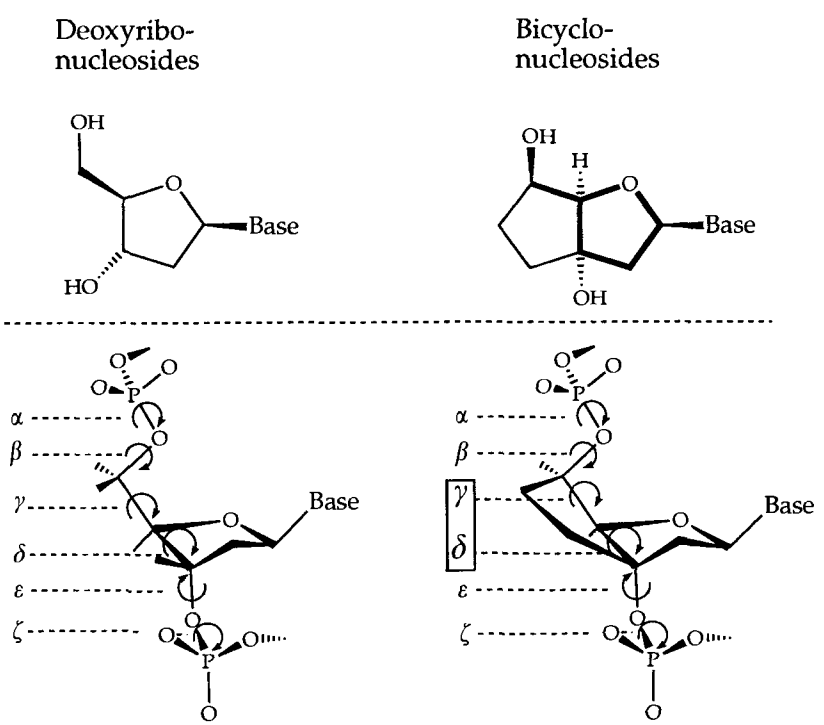
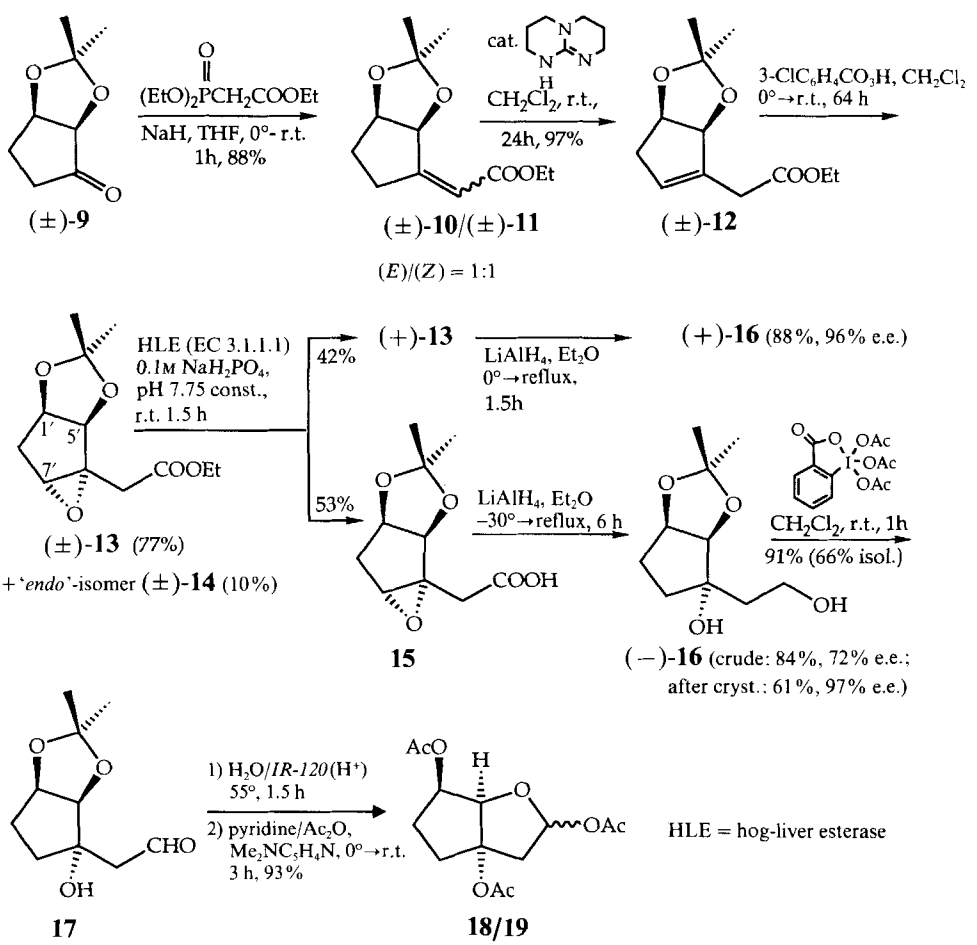


Fig. 2. *The six torsion angles α–ζ describing the conformation of the repetitive nucleotide unit in a duplex: natural DNA* (left) *and 'bicyclo-DNA'* (right)

eventually, to thermodynamically more stable duplexes. Furthermore, oligonucleotides consisting of β-D-nucleosides **1–4** show secondary and tertiary phosphodiester groups and were expected to be more resistant towards enzymatic degradation by phosphodiesterases with respect to their natural counterpart. In this communication, the first in a series, we present the synthesis of the bicyclonucleosides **1–8** and a conformational analysis of the β-D-nucleosides **1–4**.

2. Synthesis of the Bicyclic Carbohydrate Unit. – In our synthetic plan, we envisaged a convergent access to the nucleosides **1–8**, starting from a common bicyclic carbohydrate precursor, rather than a route *via* modification of the natural 2′-deoxyribonucleosides. We decided to build up the C-framework of this bicyclic precursor **18/19** (*Scheme 1*) by a *Horner-Wittig* reaction of a suitably protected *cis*-2,3-dihydroxycyclopentanone with (diethoxyphosphoryl)acetate as the C_2 unit. While the resulting double bond was used as

Scheme 1



an anchor for the introduction of the tertiary OH group at the bridgehead, the O-atoms of the secondary OH group and of the furanose ring in **18**/**19** were already incorporated in the chiral cyclopentanone derivative. Since we started with racemic material, separation of enantiomers was achieved by kinetic resolution of an intermediate by an esterase.

Reaction of racemic ketone (±)-**9** (*Scheme 1*), which was already described by *Posternak* and coworkers [16], with the anion of ethyl (diethoxyphosphoryl)acetate in THF resulted in the almost quantitative formation of the corresponding α,β-unsaturated (*E*)/(*Z*)-esters (±)-**10**/(±)-**11**[4]) in slightly varying ratios of (*E*)/(*Z*) (1:2 to 2:1), depending upon the nature of the base used[5]). Treatment of the mixture (±)-**10**/(±)-**11** with a catalytic amount of a strong organic base such as 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) or 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in CH_2Cl_2 or benzene resulted in spontaneous tautomerization to the thermodynamically more stable, *deconjugated* β,γ-unsaturated ester (±)-**12**[6]) and thus eliminated the configurational heterogeneity around the double bond. The transformation (±)-**9** → (±)-**12** could also be performed directly in one pot with yields of up to 90% by using 2 equiv. of TBD as the base in the *Horner-Wittig* reaction [18].

Introduction of the tertiary OH function was realized by an epoxidation/reduction pathway. Epoxidation of (±)-**12** with 3-chloroperbenzoic acid in CH_2Cl_2 proceeded, as expected, stereoselectively from the convex side of the bicyclic ring system and afforded the desired *'exo'*-epoxy-ester (±)-**13** in 77% yield, together with 10% of the corresponding *'endo'*-diastereoisomer (±)-**14**, which was easily separated by CC. The relative configuration of the epoxy group in (±)-**13** and (±)-**14** was determined by NOE (*Exper. Part*)[7]).

Tamm and coworkers [19] showed that racemic β,γ-epoxy-esters can readily and efficiently be resolved into their enantiomerically pure constituents by the action of an esterase. Thus, we subjected β,γ-epoxy-ester (±)-**13** to partial ester hydrolysis catalyzed by hog-liver esterase (EC 3.1.1.1): titration of an emulsion of (±)-**13** and esterase in 0.1M sodium-phosphate buffer with 1M NaOH at a constant pH of 7.75 was stopped after 50% of the stoichiometric amount of base was added. Extractive workup yielded 42% of ester

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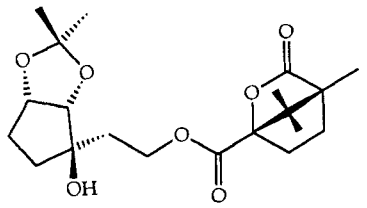
[4]) The mixture (±)-**10**/(±)-**11** can be separated by column chromatography (CC), although it is not necessary for the following synthetic transformations. The relative configuration of the double bond in (±)-**10** and (±)-**11** was assigned by NOE measurements on pure samples (*Exper. Part*). Irradiation at the resonance of the proton at the sp^2-C-atom gave a strong effect at the signal of the bridgehead proton in the case of (±)-**10** and at the signal of the neighboring ring CH_2 group in the case of (±)-**11**.

[5]) If NaH was used, we generally obtained a 1:1 ratio of diastereoisomers (±)-**10**/(±)-**11**. Addition of 1 equiv. of LiCl resulted in a slight preference for the (*Z*)-isomer ((±)-**10**/(±)-**11** 1:2). With the Li salt of hexamethyldisilazane (HMDS) as base, however, a slight predominance of the (*E*)-isomer ((±)-**10**/(±)-**11** 1.75:1) was observed (all ratios determined by isolation). Therefore, Li cations seem to play a minor role in determining the stereochemical outcome of the reaction (for salt effects in *Wittig* reactions, see [17]).

[6]) In all experiments, product (±)-**12** still contained traces of starting material (±)-**10**/(±)-**11** (Σ *ca.* 5% by ^{1}H-NMR) which persisted even after prolonged reaction time or increased base concentration. We, therefore, believe that the observed ratio of (±)-**10**/(±)-**11** to (±)-**12** corresponds to the equilibrium mixture of the tautomeric forms under the given reaction conditions with $\Delta G^{25°} \approx -2.0$ kcal/mol for the equilibrium (±)-**10**/(±)-**11** ⇆ (±)-**12**.

[7]) Irradiation at the resonance of the epoxide-ring proton in both (±)-**13** and (±)-**14** showed, besides enhancement of the signals of the adjacent CH_2 group of the carbocyclic ring and that of the side chain, a strong effect on H–C(5') in the case of (±)-**14**, while no such effects was observed in the case of (±)-**13**.



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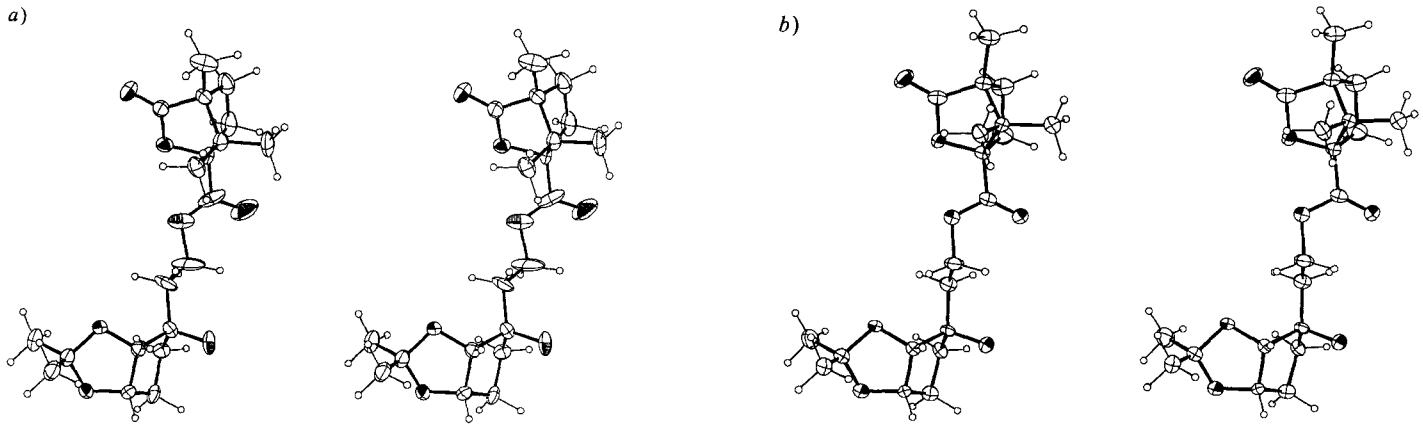


Fig. 3. *ORTEP plots* (stereoscopic views, 25%-probability thermal ellipsoids) *of the two symmetrically independent molecules in the asymmetric unit of crystals of* **20**[8])

(+)-**13**, together with 53% of the corresponding acid **15**. The enantiomeric excess (e.e.) of the unreacted ester (+)-**13** was directly determined by GLC on chiral phase (*Exper. Part*) and that of the hydrolysis product **15** indirectly by GLC of its reduction product (−)-**16**. While the e.e. of (+)-**13** (96%) was quite attractive, the e.e. of the hydrolysis product **15** (72%) was somewhat low, probably mainly due to incomplete extractive separation of unreacted ester. However, crystallization of crude diol (−)-**16** (72% e.e.), which was obtained stereospecifically in 84% chemical yield by standard $LiAlH_4$ reduction of acid **15**, furnished crystals of racemate (±)-**16** and allowed the isolation of diol (−)-**16** from the mother liquor in 61% chemical yield and 97% e.e. Using this resolution procedure, we repeatedly prepared diol (−)-**16** in quantities of 7–10 g/batch in reproducible optical purities of 97–98% e.e. and chemical yields of 30–33% starting from racemic ester (±)-**13**.

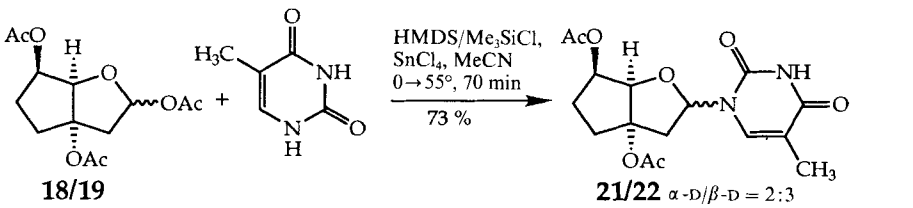
From (−)-**16**, having the desired absolute configuration (1*R*,5*R*,6*S*) (see below), the synthesis of the bicyclic derivatives **18**/**19** was accomplished in three steps. Selective oxidation of the primary OH function of (−)-**16** worked best using the *Dess-Martin* reagent [20] in CH_2Cl_2 and furnished the crude, somewhat labile aldol **17** in 91% yield. Isolation of **17** generally lead to partial degradation: only a 66% yield was obtained after distillation *in vacuo*. Treatment of crude **17** with a strongly acidic ion-exchange resin in H_2O at 55° resulted in the cleavage of the acetal function followed by spontaneous intramolecular cyclization, thus providing the desired bicyclic carbohydrate framework. Peracetylation of the crude product with Ac_2O in pyridine, using 4-(dimethylamino)pyridine as a catalyst, finally gave **18**/**19** (93%) as a 1:1 mixture of anomers (^{1}H-NMR) which was directly used in the following nucleosidation reactions. In routine reactions where the sequence (−)-**16** → **17** → **18**/**19** was performed on scales of 2–5 g without isolation of intermediates, **18**/**19** was obtained in yields of 68–73%.

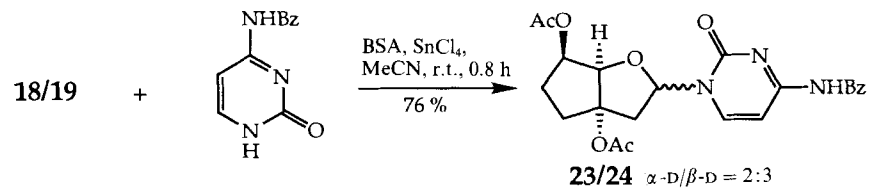
The absolute configuration of (+)-**16** was assigned by X-ray analysis (*Fig. 3*) of its crystalline (−)-(*S*)-camphanic-acid derivative **20**[8]) which was obtained by standard esterification of (+)-**16** (96% e.e, from $LiAlH_4$ reduction of (+)-**13**) with (−)-(*S*)-camphanoyl chloride. Thus, (+)-**16** has (1*S*,5*S*,6*R*)-configuration.

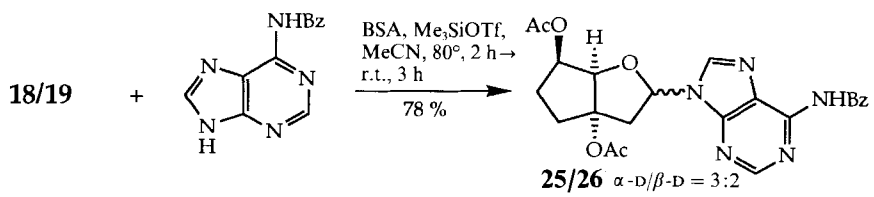
3. Synthesis of 'Bicyclonucleosides'. – The remaining task in the synthesis of the bicyclonucleosides **1**–**8** was the formation of the nucleosidic bond between the bicyclic sugar derivatives **18**/**19** and the four nucleobases adenine, guanine, cytosine, and thymine. From the wide variety of methods of nucleoside synthesis [22], we chose the variant of *Vorbrüggen* and coworkers [23], which is based on a *Lewis*-acid-induced formation of the nucleosidic bond between a sugar component and a persilylated (and where necessary acyl-protected) nucleobase. This procedure, a variant of the *Hilbert-Johnson* reaction [24], does not require a specially activated leaving group at the anomeric center of the sugar component and was successfully used in the past for the preparation of

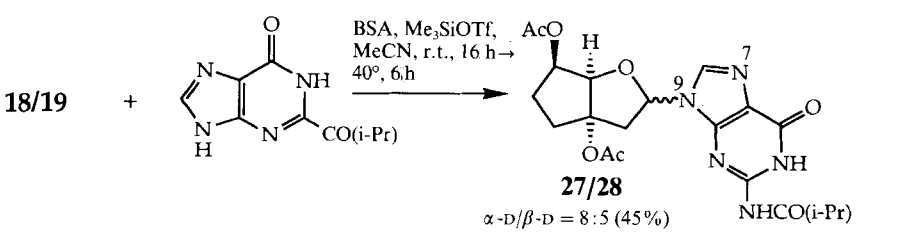
[8]) In the asymmetric unit of crystals of **20**, two symmetrically independent molecules, virtually only differring in the conformation of the short acyloxy chain linking the two bicyclic units, are observed. The torsion angle C(O)–O–C–C of the ester group in the first molecule (141.5°; *Fig. 3a*) is not in an energetically favorable range (180 and 80° [21]), in contrast to that of the second molecule (−77.1°; *Fig. 3b*). This may explain the high degree of disorder of the ester-group atoms in the former case.

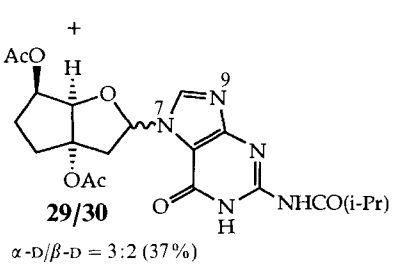
Scheme 2











HMDS = $(Me_3Si)_2NH$
BSA = $MeC(OSiMe_3) = N(SiMe_3)$

a wide variety of nucleoside analogues [25]. One-pot reactions [23i] of the mixture **18/19** with the nucleobase thymine, N^4-benzoylcytosine, N^6-benzoyladenine, or N^2-isobutyrylguanine in MeCN in the presence of the silylating agents hexamethyldisilazane HMDS/Me_3SiCl or *N,O*-bis(trimethylsilyl)acetamide (BSA) and either $SnCl_4$ (in the case of the pyrimidine bases) or trimethylsilyl trifluoromethanesulfonate (Me_3SiOTf; in the case of the purine bases) furnished the bicyclonucleosides as anomeric mixtures **21/22**, **23/24**, **25/26**, **27/28**, and **29/30**, respectively, in yields of 73–82% (*Scheme 2*).

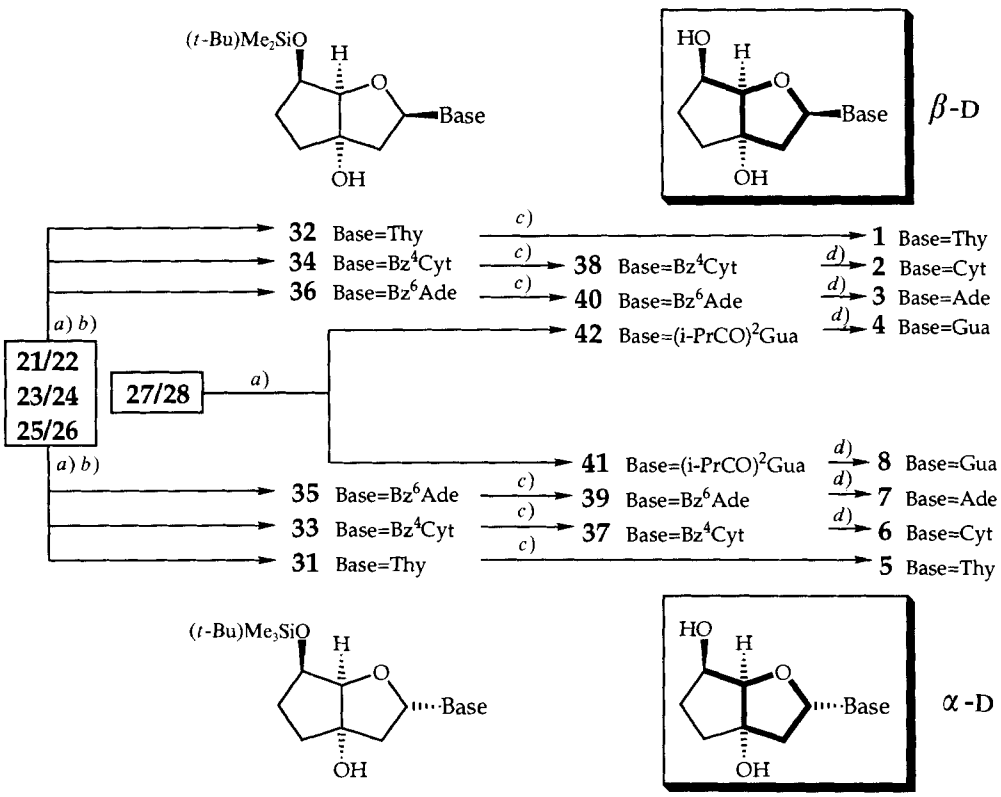
In the case of the pyrimidine bases, only the nucleoside pairs **21/22** and **23/24**, respectively, with N(1) as the point of attachement at the base were obtained after the indicated reaction time. In both cases, the β-D-nucleosides were formed in a slight excess (α-D/β-D 2:3, as determined by ^{1}H-NMR). In the purine series, the nucleosidation was smooth in the case of adenine furnishing only the anomeric mixture **25/26** with the base bound to the sugar *via* N(9). Somewhat more difficult was the preparation of the corresponding guanine nucleosides, since not only the desired N^9-nucleosides **27/28** (45%), but also the N^7-nucleosides **29/30** (37%) were isolated. The formation of mixtures of N^7- and N^9-isomers in nucleosidations with N^2-isobutyrylguanine according to the *Vorbrüggen* procedure is well documented in the literature (see, *e.g.* [26] [27]). In the anomeric mixture of the purine nucleosides **25/26**, **27/28**, and **29/30**, a slight excess of the α-D-form was observed. However, we were not able to separate the four nucleoside pairs of interest (**21/22**, **23/24**, **25/26**, **27/28**) into their anomerically pure components.

After selective saponification of the ester groups of **21/22**, **23/24**, **25/26**, and **27/28** with dilute NaOH in THF/MeOH/H_2O according to standard protocols in nucleoside chemistry [28], we only succeeded to isolate the nucleosides **41** and **42** (from **27/28**) in pure form by CC (*Scheme 3*). In the three remaining cases, the formed anomeric mixtures **1/5**, **37/38**, and **39/40** were, in our hands, inseparable by conventional CC (*Scheme 3*). At this point came to our rescue the observation that introduction of a bulky silyl group at the secondary OH function of these nucleosides leads to substantial chromatographic differentiation of the corresponding α- and β-D-forms[9]). Thus, treatment of each mixture **1/5**, **37/38**, and **39/40** with (*tert*-butyl)dimethylsilyl trifluoromethanesulfonate in pyridine, followed by separation of the silylated mixtures **31/32**, **33/34**, and **35/36**, respectively, into their pure α- and β-D-forms by CC and desilylation with Bu_4NF in THF afforded all nucleosides **1**, **5**, and **37–40** in anomerically pure, crystalline form and overall yields of 48–73% for the two steps (*Scheme 3*). The relative configuration at the anomeric center and the point of attachement of the base (N(1) for pyrimidine and N(9) for purine bases) in **1**, **5**, and **37–42** was determined by spectroscopic methods.

The relative configuration at the anomeric center in the nucleosides **1**, **5**, and **37–42** was assigned by ^{1}H-NMR difference NOE spectroscopy (for individual NOE experiments, see *Exper. Part*). Irradiation at the resonance of the anomeric proton in the series **1**, **38**, **40**, and **42** resulted in a strong positive NOE at the signal of H–C(4′). The corresponding NOE in the series **5**, **37**, **39**, and **41** was either very weak or absent. Irradiation of H–C(4′) in the latter series resulted in a strong positive NOE at the signal of the base protons H–C(6) (pyrimidines) or H–C(8) (purines), while no such NOE was observed in the former series. One can, therefore, unambiguously assign the β-D-configuration to **1**, **38**, **40**, and **42**, and the α-D-configuration to **5**, **37**, **39**, and **41**. For the pyrimidine

[9]) It is worth to note that introduction of the bulky (4,4′-dimethoxytriphenyl)methyl group at the secondary OH function of **1/5**, **37/38**, and **39/40** did not lead to enhanced chromatographic separability of the α/β-D-mixtures.

Scheme 3



a) 0.2M NaOH in THF/MeOH/H_2O 5:4:1, 0–2°, 30–75 min, 72-94%. *b*) (*t*-Bu)$Me_2Si(CF_3SO_3)$, pyridine, 0°, 30–45 min, 87–90%. *c*) $Bu_4NF \cdot 3\,H_2O$, 55°, 17 h–17 d, 50–81%. *d*) Conc. NH_3, 55–60°, 2–5 h, 55–92%.

nucleosides **1**, **5** and **37**, **38**, N(1) is the point of attachement of the base because of a strong NOE between H–C(1) and H–C(6). An independent proof for the correct structural assignment was obtained for **1** by X-ray analysis (*vide infra*). The assignment of the N^9-attachment in the purine bicyclonucleosides **39**, **40** and **41**, **42** was achieved indirectly by comparison of the ^{13}C-NMR spectra (signals of the nucleobase C-atoms) and UV spectra of the corresponding free nucleosides **3**, **7** of adenine and **4**, **8** of guanine with those of known N^7- and N^9-derivatives of adenine [29] and of guanine [26] [27].

The nucleoside derivatives **1**, **5**, and **37**–**42** were directly used in the preparation of phosphoramidite building blocks for oligonucleotide synthesis according to the method of *Letsinger* and *Caruthers* [30]. The preparation of the free α- and β-D-bicyclonucleosides **2**–**4** and **6**–**8** (*Scheme 3*) was performed by standard ammonolysis [28] of the base-protecting groups of the corresponding precursors **37**–**42**. Thus, the synthesis and isolation in anomerically pure form of the complete set of α- and β-D-bicyclonucleosides **1**–**8**, incorporating the four standard DNA bases, was achieved.

4. Conformational Analysis of β-D-Bicyclonucleosides. – 4.1. *General.* In ribonucleosides and 2′-deoxyribonucleosides, generally two types of sugar pucker in the five-mem-

bered furanose ring are energetically preferred, namely the 2′-*endo*- and the 3′-*endo*-conformation (*Fig. 4*)[10]). In DNA duplexes, a 2′-*endo*-conformation of the repeating nucleoside unit is responsible for a double helix of the B-conformation (only observed in DNA duplexes), whereas the 3′-*endo*-conformation leads to a helix of the A-conformation (observed in DNA and RNA duplexes). In 2′-deoxy-β-D-ribonucleosides, both the 2′-*endo*- and 3′-*endo*-conformations are almost equal in energy. This is the result of calculations [32] and is adequately reflected by the occurrence of both conformational types in a large number of X-ray structures [33].

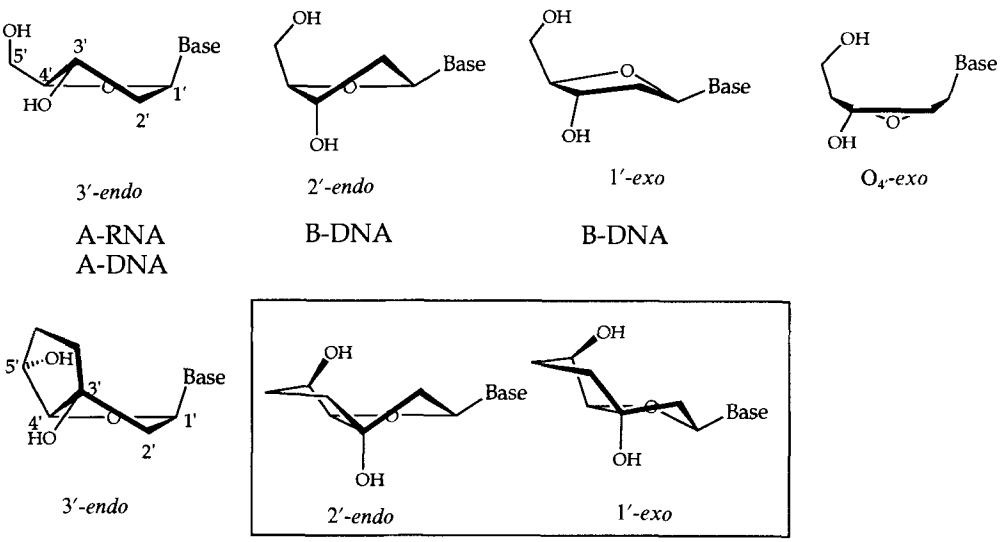


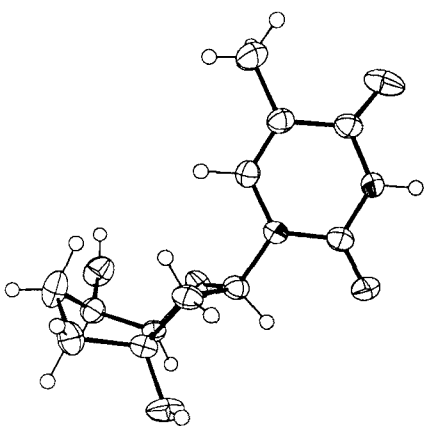
Fig. 4. *Selected conformations of natural nucleosides and 'bicyclonucleosides'*

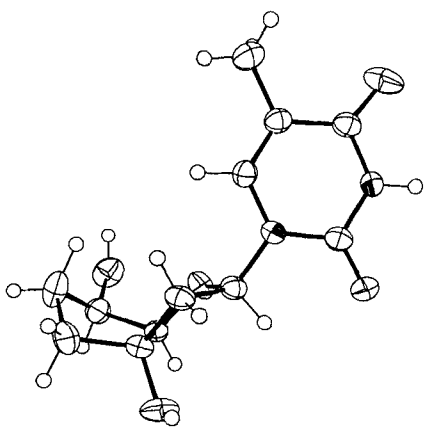
A qualitative analysis of the conformation of the furanose part in the β-D-bicyclonucleosides, however, suggests that this should *not* be the case here. Because of steric interaction of the pseudoaxially arranged base and C-substituents at the centers C(1′) and C(3′), respectively, in the N-type (3′-*endo*)-conformation of the bicyclonucleosides (*Fig. 4*), the S-type conformation (2′-*endo*,1′-*exo*) should be energetically more favored. This argument is corroborated by calculations of the total energy as a function of the pseudorotation phase angle *P* in the natural 2′-deoxyribonucleoside series by *Warshel* [32a] and *Olson* [32b], which showed that the 4′-*exo*-conformation, having a pseudodiaxial arrangement of the base and the hydroxymethyl substituent at the centers C(1′) and C(4′), respectively (*Fig. 4*), is considerably higher in energy (2.5–5.8 kcal·mol^{-1}) than the 2′-*endo*- or 3′-*endo*-conformation. Here, we restrict our conformational analysis to the β-D-bicyclonucleosides **1**–**4**, **38**, **40**, and **42**. The somewhat more subtle discussion of the preferred conformations of the α-D-bicyclonucleosides **5**–**8**, **37**, **39**, and **41** will be the subject of a further communication.

[10]) For a discussion of conformations in ribonucleosides and 2′-deoxyribonucleosides and for an explanation of the terminology in the conformational description of nucleosides and oligonucleotides, see [31].

4.2. *X-Ray Structure of β-D-Bicyclothymidine* (**1**). To check our structural hypothesis, we subjected crystals of β-D-bicyclothymidine **1** to X-ray analysis (*Fig. 5*)[11]). Inspection of the structure reveals that the furanose part in **1** adopts an almost perfect 1′-*exo* sugar pucker (pseudorotation phase angle $P = 128.4°$) with an eclipsed conformation around the C(3′)–C(4′) bond (endocyclic torsion angle ν_3(C(2′)–C(3′)–C(4′)–O(4′)) = 3.2°), the torsion angle δ(O(3′)–C(3′)–C(4′)–C(5′)) thus being 126.5° (*Fig. 5a*). The OH–C(5′) bond in **1** adopts a pseudoantiperiplanar arrangement to the C(3′)–C(4′) bond, which leads to 149.3° for the torsion angle γ(C(3′)–C(4′)–

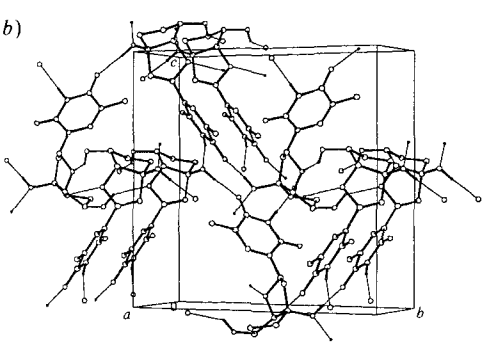
a)





γ(O(5′)–C(5′)–C(4′)–C(3′)) =	149.3°	ν_1(O(4′)–C(1′)–C(2′)–C(3′) =	43.1°
δ(C(5′)–C(4′)–C(3′)–O(3′)) =	126.5°	ν_2(C(1′)–C(2′)–C(3′)–C(4′) =	–27.3°
χ(O(4′)–C(1′)–N(1)–C(2)) =	–112.7°	ν_3(C(2′)–C(3′)–C(4′)–O(4′) =	3.2°
ν_0(C(4′)–O(4′)–C(1′)–C2′)) =	–42.4°	ν_4(C(3′)–C(4′)–O(4′)–C(1′) =	23.9°

b)



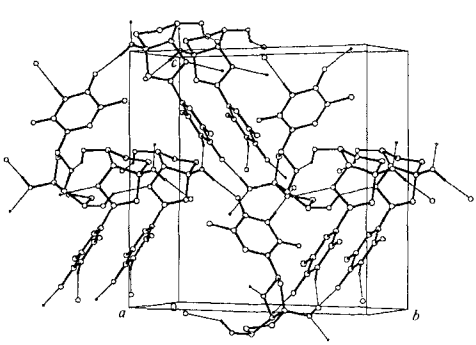


Fig. 5. *X-Ray structure of bicyclothymidine* **1**: a) *ORTEP plot* (stereoscopic view, 50%-probability thermal ellipsoids) *including selected torsion angles and* b) *stereoscopic view of the asymmetric unit*

[11]) Crystal data and coordinates were deposited in the *Cambridge Data File*.

C(5′)–O(5′)). The orientation of the base substituent is in the *anti*-range (torsion angle χ (O(4′)–C(1′)–N(1)–C(2)) = −112.8°). Neither intramolecular H-bonds nor such between two base residues of adjacent molecules are observed. Intermolecular contacts arise from H-bonds between sugar-sugar (O(4′)···HO(5′)) and sugar-base units (O(3′)···HN, O(4)···HO(3′)) of neighboring molecules (*Fig. 5b*).

4.3. *Conformation of β-D-Bicyclonucleosides in Solution.* The conformation of the furanose ring in ribonucleosides and 2′-deoxyribonucleosides in solution can be determined by ^{1}H-NMR spectroscopy as shown by *Altona* and *Sundaralingam* [34]. Calculation of dihedral angles from experimental vicinal H,H coupling constants (^3J(H,H)) of the H-atoms at the furanose unit according to the *Karplus* relation [35], in its optimized form for nucleosides and nucleotides [36] allows the determination of the sugar pucker and also the quantification of the equilibrium mixture of the two preferred conformational states (2′-*endo*,3′-*endo*) in nucleosides [34] and single-stranded oligonucleotides [37].

In the case of the bicyclonucleosides, it is not possible to completely describe the sugar pucker of their furanose units in an analogous way because of the H-coupling barrier at C(3′). However, the torsion angles ν_1 and γ in **1**–**3**, **38**, **40**, and **42** were obtained by determination of the dihedral angles between the protons at C(1′) and C(2′), which were calculated from the experimental coupling constants ^3J(1′,2′α), ^3J(1′,2′β), and ^3J(4′,5′) according to the modified *Karplus* relation of *Davies* [36] (*Table*, torsion angles in parentheses).

In all considered β-D-nucleosides, almost conserved values for the endocyclic torsion angle ν_1 (O(4′)–C(1′)–C(2′)–C(3′)) in the range of 38–42° were determined. These values are fully consistent with the 1′-*exo*-conformation as observed in the X-ray structures of **1**

Table. *Selected Chemical Shifts* (in ppm) *and Coupling Constants* J (in Hz) *of Protons of the β-D-Bicyclonucleosides* **1**–**4** *and Derivatives* **38**, **40**, *and* **42**. Numbers in parentheses represent torsion angles calculated from the corresponding coupling constants.

	δ [ppm]				
	H–C(1′)	H_α–C(2′)	H_β–C(2′)	H–C(4′)	H–C(5′)
1	6.24	2.49	2.15	4.09	4.19
2	6.26	2.52	1.90	4.03	4.10
3	6.26	2.63	2.50	4.16–4.22	
4	6.08	2.36		3.87	3.92
38	6.27	2.73	1.94	4.14	4.16
40	6.55	2.63	2.70	4.12–4.17	
42	6.32	2.57	2.50	4.09–4.13	
	^3J(1′,2′α) (torsion angle)	^3J(1′,2′β) (torsion angle)	^2J(2′α,2′β)	^3J(4′,5′) (torsion angle)	ν_1 [°]
1	5.2 (41°)	10.1 (163°)	14.1	5.3 (40°)	42
2	5.2 (41°)	9.6 (158°)	13.5	5.6 (38°)	40
3	5.3 (40°)	10.0 (162°)	13.9	–	41
4	7.3		–	5.4 (±40°)	–
38	5.2 (41°)	9.2 (155°)	13.4	–	38
40	5.6 (38°)	9.6 (158°)	13.3	–	38
42	5.4 (40°)	9.7 (159°)	13.2	–	39

(*Fig. 5*)[12]). In the same way, the dihedral angle between H–C(4′) and H–C(5′) was determined from the coupling constant $^3J(4',5')$ in **1**, **2**, and **4** to be in the range of ±40°. Signal overlap for H–C(4′) and H–C(5′) prevented the determination of $^3J(4',5')$ in the remaining β-D-nucleosides. Unfortunately, the ambiguity of the sign (±) of the torsion angle and the difficulty to derive coupling constants from H–C(5′) to one of the H–C(6′) because of signal overlap did not allow a conclusive assignment of a value for the torsion angle γ in **4**. Only in **1** and **2**, where a large $J(5',6'\alpha)$ (9.5 and 8.3 Hz, resp.) was observed, it was possible to determine γ to be in the antiperiplanar (*ap*) range (160 and 158°, resp.), again in agreement with the value for γ (149.3°) in the X-ray structure of **1**.

For the purpose of detecting a possible equilibrium between different conformational states (as observed in most ribonucleosides [34] [38]), we recorded ^{1}H-NMR spectra of **1** (as an example of a β-D-bicyclonucleoside) in CD_3OD at temperature intervals of 20° between +40° and −80° (*Fig. 6*). Besides a general line broadening at lower temperatures, due to enhanced viscosity of the solvent, we could not find any relevant changes in chemical shift or coupling constants between the high- and low-temperature spectra, showing that no change in population of different conformers occurred under these conditions. This is a strong indication, that the sugar pucker of the bicyclonucleosides is monophasic and rigid.

The preferred conformation around the glycosidic bond χ in the free β-D-bicyclonucleosides **1**–**4** was investigated by ^{1}H-NMR difference NOE spectroscopy in D_2O or CD_3OD. NOE methods were already successfully used for this purpose in the series of the natural deoxyribonucleosides [39]. Positive NOE's between the base proton H–C(6) (pyrimidine nucleosides **1** and **2**) or H–C(8) (purine nucleoside **3**) and both H–C(1′) and H_β–C(2′) in each were observed. An analogous NOE on H_α–C(2′) was weak and negative, most likely due to an indirect NOE through H_β–C(2′). These facts corroborate the 1′-*exo*-conformation of the furanose unit in **1**–**3** and are indicative for the tendency of the base substituents to occur in both, the *syn*- and *anti*-conformation in solution (*Fig. 7*). The bicycloguanosine **4** (for solubility reasons in (D_6)DMSO) showed strong positive NOE's between H–C(8) and the secondary OH, H–C(2′), and H–C(1′). Since the signals of H_α–C(2′) and H_β–C(2′) are essentially isochronic, the NOE observed at this signal can not be interpreted in terms of a preference for H_β–C(2′) rather than for H_α–C(2′).

From the comparison of the NOE-intensity ratios H–C(1′)/H_β–C(2′) in the pyrimidine nucleosides **1** and **2** (*ca.* 0.6), and in the purine nucleoside **3** (*ca.* 1.0), one can estimate the population of *syn*- and *anti*-forms using the relation of *Rosemeyer et al.* [40]. Thus, **1** and **2** show a higher propensity for the *anti*-conformation (*ca.* 60–70%), whereas in **3** an almost equal distribution of the *syn*- and *anti*-form occurs.

4.4. *Modeling of Bicyclothymidine* **1**. In addition to the structural investigations of the sugar part of the β-D-bicyclonucleosides, as outlined above, we modeled the thymine nucleoside **1** with the molecular-modeling system *MacroModel* (Vers. 3.0) [41]. Energy minimizations were performed using the implemented MM2 force field [42]. A search for low-energy conformations of the sugar residue was done with the base substituent

[12]) The free β-D-bicycloguanosine **4** (but *not* its base-protected derivative **42**) seems to deviate in the β-D-series in that $J(1',2'\alpha)$ and $J(1',2'\beta)$ (*Table*) indicate a conformation of the furanose moiety slightly different from that of the other β-D-nucleosides. The reason for this different conformational behavior remains open so far.

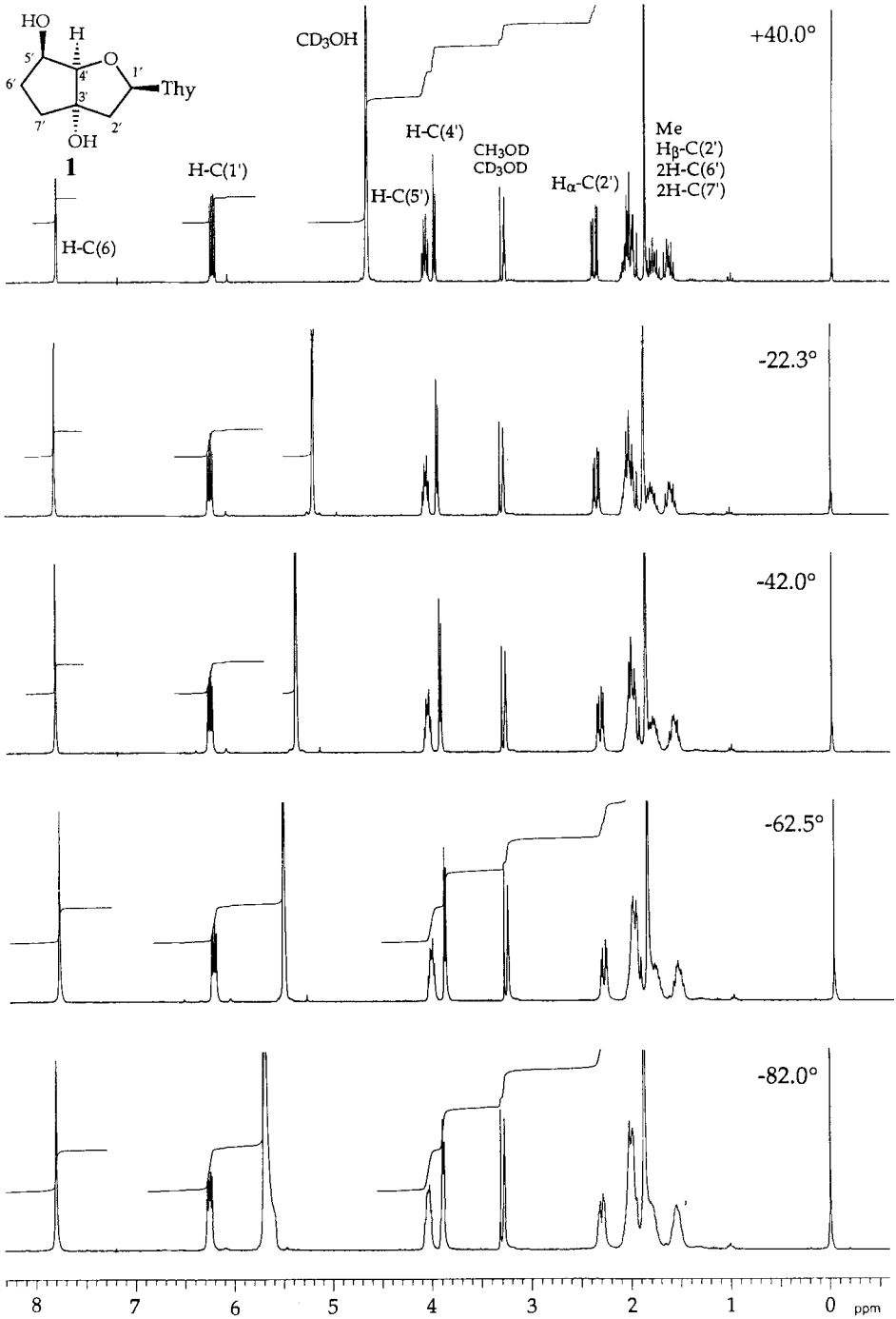
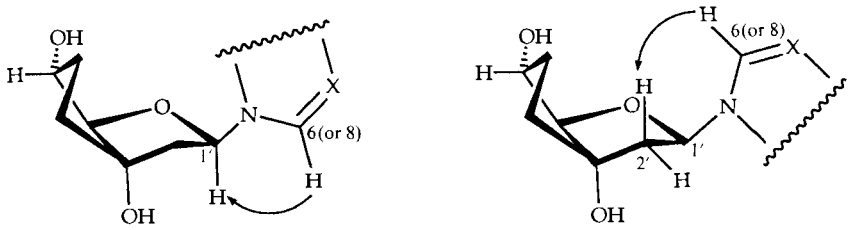


Fig. 6. *^{1}H-NMR spectra* (400 MHz, CD_3OD) *of bicyclothymidine* **1** *at temperatures between +40 and −82°*



syn *anti*

Fig. 7. *Relevant NOE's in* syn- *and* anti-*conformers of the bicyclonucleosides* **1**–**4**

restricted to the *anti*-range[13]). Only two conformers **A** and **B**, corresponding to local energy minima were found this way (*Fig. 8*). Conformer **A** (*Fig. 8a*) almost matches the structure found in the X-ray analysis of **1** (*Fig. 5*), showing the furanose part in the 1'-*exo*-conformation with values for the torsion angles δ and γ of 118.8 and 149.2°,

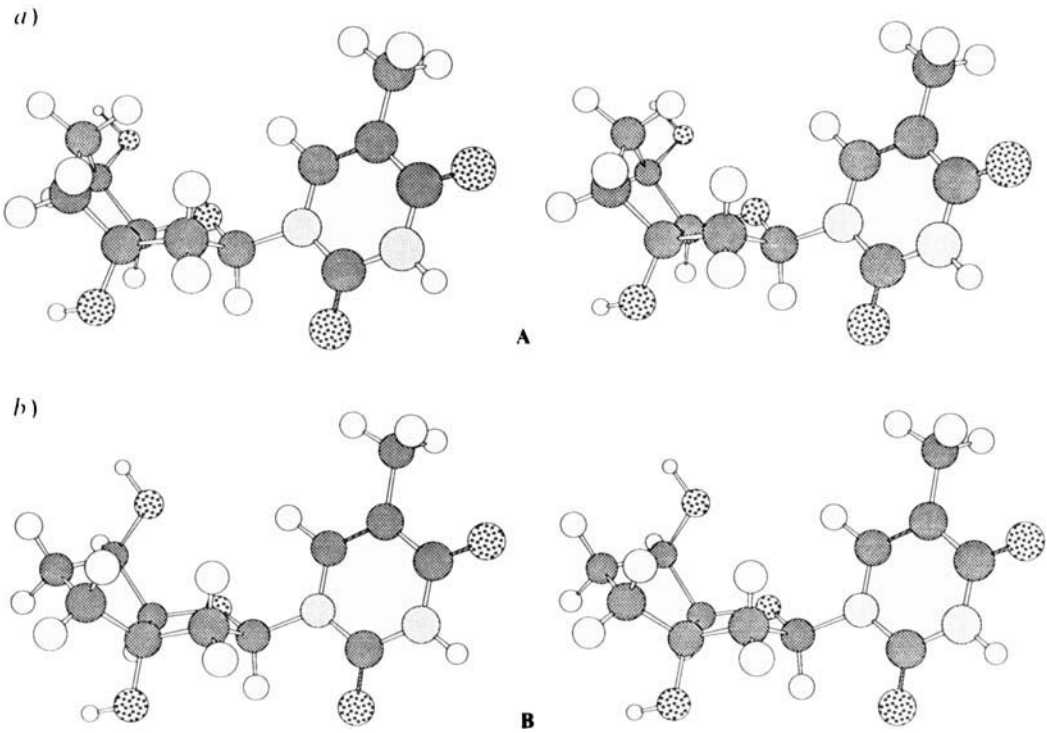


Fig. 8. *Stereoscopic views of energy-minimized* (*MacroModel* V3.0, MM2) *conformers of bicyclothymidine* **1**: a) *conformer* **A** *and* b) *conformer* **B**

[13]) A first energy-minimized conformer was created starting from a structure with a planar bicyclic sugar system and the base substituent oriented in the *anti*-range ($\chi = -90°$). This conformer was then subjected to a multiconformational search using the BATCHMIN program. In this way, 12 structures were generated and each energy-minimized with the MM2 force field using the block diagonal *Newton-Raphson* (BDNR) mode to an RMS gradient of < 0.01 (max. 350 iterations).

respectively. Conformer **B** (*Fig. 8b*) has a 2′-*endo*-type of sugar pucker in the furanose ring with torsion angle $\delta = 136.2°$, thus resembling **A** in this part of the structure. However, **B** clearly differs from **A** in the conformation of the carbocyclic ring, showing the torsion angle γ (81.0°) in the synclinal (+*sc*) range (and not in the antiperiplanar (*ap*) range as in **A**). The two structures differ by 1.47 kJ·mol^{-1} in energy, molecule **A** being the more stable conformer.

5. Discussion. – In contrast to natural nucleosides, the β-D-bicyclonucleosides described herein show a less flexible, uniform sugar pucker restricted to the S-type conformation in their furanose part, regardless of the base attached to it. This was confirmed by X-ray and NMR experiments and was also the result of molecular modeling. In terms of a qualitative conformational analysis, the preference for the S-type furanose pucker can be rationalized as the consequence of the presence of a substituent in β-position at C(3′), that clearly disfavors the 3′-*endo*-conformation because of steric interaction with the base substituent. The same situation occurs also in ribonucleosides and 2′-deoxyribonucleosides bearing a Me group in β-position at C(3′), as in the case of 3′-methylsangivamycin [43] and 3′-methylthymidine [44]. In both cases, the 2′-*endo*-conformation was observed (X-ray). Both the 1′-*exo* and 2′-*endo* sugar pucker occurs in the nucleotide units in DNA duplexes of the B-type, as shown by X-ray analysis of a DNA dodecamer [45]. If one compares the torsion angles γ (149.3°), δ (126.5°), and χ (−112.7°) of **1** (from its X-ray structure) with the corresponding (averaged) values of the repeating nucleotide unit in this B-DNA duplex ($\gamma = 54°$, $\delta = 123°$, $\chi = -117°$) [45], there is an excellent structural agreement for δ and χ. The torsion angle γ of **1**, however, implies an *ap*-orientation, in contrast to its corresponding exclusive +*sc*-conformation in DNA duplexes of the A- and B-type. Molecular modeling of **1** (*Fig. 8*) suggests the energy difference between the two conformers of **1**, showing γ for an *ap*- and +*sc*-spatial arrangement, to be *ca.* 0.4 kcal/mol, the former being more stable. ^{1}H-NMR experiments at different temperatures (for **1**, see *Fig. 6*), however, indicate this energy difference to be too small. The inherent preference of the secondary OH group in **1** (and presumably in all bicyclonucleosides) to be in a pseudoequatorial position (γ corresponding to *ap*) may be amplified by the fact that in its pseudoaxial position (γ corresponding to +*sc*), an unfavorable steric interaction with the C(2′)–C(3′) bond of the furanose unit results (*Fig. 9a*)[14]). In a bicyclonucleoside model containing a six-instead of the five-membered carbocyclic ring (*Fig. 9b*), the same interaction should be even more pronounced. This is adequately demonstrated by molecular modeling, showing the 4′-*endo*-conformer to be more stable than the 2′-*endo*-form by 4.55 kJ·mol^{-1}. In the context of 3′,5′-bridged nucleosides, the sugar bicyclo[3.3.0] framework (*Fig. 9a*) seems to be better than the bicyclo[4.3.0] system (*Fig. 9b*) in matching the geometric requirements of a natural nucleoside in its duplexed form. According to the rationalization of the backbone conformation of nucleic acids by *Eschenmoser* and *Dobler* [46], the *ap*-range for the torsion angle γ belongs to one of the 'allowed' conformational states, although it leads to a least-strained single strand which

[14]) One should also mention, that the same steric arrangement between the O–C(5′) group and the C(2′)–C(3′) bond occurs in duplexed natural nucleotides of the 2′-*endo*-conformation (*Fig. 9c*). The fact, however, that the CH_2OH substituent is not part of a second ring system, seems to be responsible for the relaxation of steric strain. In crystal structures of ribonucleosides and deoxyribonucleosides, both types of conformers (*Fig. 9c*) occur in almost equal distribution [49].

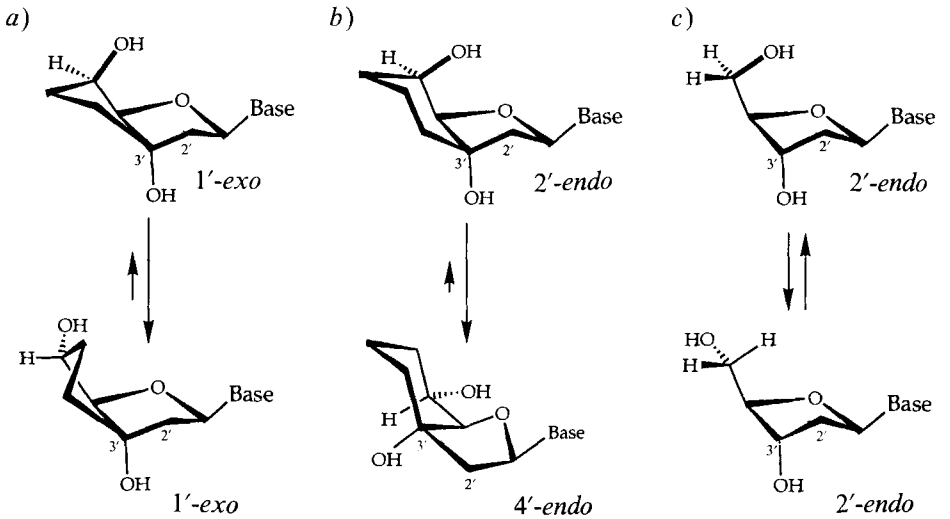


Fig. 9. *Conformational drawings of nucleosides with torsion angle γ corresponding to a* +sc- (upper) *and* ap-*conformation* (lower): a) *bicyclonucleosides with a five-membered carbocyclic ring* (this communication), b) *bicyclonucleosides with a six-membered carbocyclic ring, and* c) *natural 2'-deoxyribonucleosides*

does not show a repetitive mononucleotide conformation and, therefore, does not fulfill the structural prerequisites for base-pairing with a complementary strand. The structural details of 'bicyclo-DNA' single strands and duplexes will, therefore, be of interest, particularly also with respect to the conformation of the inherently more strained secondary and tertiary phosphodiester groups. In natural nucleic acids, torsion angles γ are known to have values for an *ap*-orientation in Z-DNA duplexes (G-nucleotides) [47] and at the intercalation site in DNA-intercalator complexes [48].

Having found an efficient synthetic access to the bicyclonucleosides described herein, our next task was to prepare oligonucleotides from **1**–**4** and to explore their binding properties to natural DNA and RNA, as well as their resistance against the activity of phosphodiesterases. This will be the subject of a following communication [50].

We are very grateful to Prof. *A. Eschenmoser* for having teached us a new and unprecedented way of analyzing nucleic-acid structure and for his ongoing interest in our work. Furthermore, we thank PD Dr. *B. Jaun* for help with NMR-spectroscopic problems and Dr. *D. Felix* for assistance with GLC on chiral columns. We also acknowledge generous financial support from the *Stipendienfonds der Basler Chemischen Industrie* and from ETH (grant No. 41-2514.5).

Experimental Part

General. Solvents for extraction: technical grade, distilled. Solvents for reactions: reagent grade, distilled over CaH_2 (MeCN, CH_2Cl_2, pyridine) or Na (THF). Reagents: if not otherwise stated, from *Fluka*, highest quality available. TLC: silica gel *60* F_{254} glass plates, *Merck*; visualization by dipping in a soln. of anisaldehyde (10 ml), conc. sulfuric acid (10 ml), AcOH (2 ml), and EtOH (280 ml), followed by heating with a heat gun. Flash column chromatography (CC): silica gel *60* (220–440 mesh ASTM, *Merck*). GLC: *Carlo-Erba, Fractovap 4160*, FI detection, mobile phase H_2, integrator *HP3380*. M.p.: not corrected. Optical rotation: at 25°; d = 10 cm, c in g/100 ml. UV: λ_{max} (ε) in nm. IR: $\tilde{\nu}$ in cm^{-1}. NMR: δ in ppm rel. to TMS as internal standard (in D_2O, rel. to HDO = 4.769 (^1H) or sodium 3-(trimethylsilyl)propane-1-sulfonate as external standard (^{13}C)), J in Hz; ^{13}C: multiplicities from DEPT spectra. MS: m/z (intensities in %); EI, ionization energy 70 eV; FAB (positive), matrix solvent NOBA (= 3-nitrobenzyl alcohol).

Ethyl (1'RS,5'RS,6'RS,7'RS)-6',7'-Epoxy-3',3'-dimethyl-2',4'-dioxabicyclo[3.3.0]oct-6'-yl)acetate ((±)-**13**). Resolution on 10% permethylated β-cyclodextrin in *OV 1701-Vi* [51], column 52 m × 0.28 mm, 1.6 bar, initial temp. 120°, heating rate 0.3°/min, injection of 1 µl of a 1‰ (*w*/*v*) soln. in CH_2Cl_2: t_R 41.96 min ((+)-**13**), 41.57 min ((−)-**13**).

(1RS,5RS,6SR)-6-(2'-Hydroxyethyl)-3,3-dimethyl-2,4-dioxabicyclo[3.3.0]octan-6-ol ((±)-**16**). Resolution on octakis(3-*O*-butyryl-2,6-di-*O*-pentyl)-γ-cyclodextrin [52] in *OV 1701-Vi* (ratio 1:2), column 46 m × 0.25 mm, initial temp. 80°, heating rate 1°/min. A soln. of (±)-**16** (1 mg) in CH_2Cl_2 (500 µl) and $(CF_3CO)_2O$ (50 µl) was evaporated after 16 h of reaction time at r.t. The residue was dissolved in CH_2Cl_2 (1 ml) and 1 µl of this soln. injected: t_R 31.63 min (derivative of (+)-**16**), 30.57 min (derivative of (−)-**16**).

Ethyl (E and Z,1'RS,5'SR)-(3',3'-Dimethyl-2',4'-dioxabicyclo[3.3.0]oct-6'-ylidene)acetate ((±)-**10** and (±)-**11**, resp.). To a mechanically stirred suspension of NaH (5.1 g, 0.21 mol; washed with pentane) in THF (200 ml) was added at 0° under N_2 ethyl (diethoxy phosphoryl) acetate (42.3 ml, 0.21 mol) within 40 min. To the brownish, clear soln. was added a soln. of (*1RS,5RS*)-3,3-dimethyl-2,4-dioxabicyclo[3.3.0]octan-6-one [16] ((±)-**9**; 33 g, 0.21 mol) in THF (150 ml). After 1 h at r.t., the solvent was evaporated, the residual gel diluted with aq. 1M KH_2PO_4 (400 ml), and the mixture extracted with Et_2O (2 × 500 ml). The combined org. phase was dried ($MgSO_4$) and evaporated and the residual oil distilled at 76–80°/0.05 Torr: (±)-**10**/(±)-**11** (41.0 g, 88%), colorless oil, ratio 1:1 (^{1}H-NMR).

Samples for analyses were obtained from an experiment (3.28 mmol), which was performed essentially in the same way, but using Li-HMDS instead of NaH as base, and where (±)-**10** and (±)-**11** were separated by CC (silica gel, hexane/Et_2O 3:1) and isolated in a ratio of 1.75:1 in a combined yield of 92%.

*Data of (±)-***10**: TLC (hexane/Et_2O 3:1): R_f 0.43. ^{1}H-NMR (300 MHz, C_6D_6): 0.97 (*t*, *J* = 7.1, CH_3CH_2); 1.19, 1.36 (2*s*, Me_2C); 1.15–1.27, 1.85–1.93, 2.89–3.02 (3*m*, 3 H, H–C(8'), H–C(7')); 3.22 (*ddt*, *J* = 1.9, 8.3, 18.3, 1 H, H–C(7'), H–C(8')); 4.00 (*q*, *J* = 7.1, CH_3CH_2); 4.19 (*t*, *J* = 5.0, H–C(1')); 4.34 (*d*, *J* = 5.3, H–C(5')); 6.14 (br. *s*, H–C(2)). Difference NOE: 6.14 (H–C(2)) → 4.34 (H–C(5')). ^{13}C-NMR (75 MHz, C_6D_6): 14.31 (*q*, CH_3CH_2); 25.15, 27.22 (2*q*, Me_2C); 28.26, 29.46 (2*t*, C(7'), C(8')); 59.82 (*t*, CH_3CH_2); 79.54, 83.32 (2*d*, C(5'), C(1')); 111.23 (*s*, Me_2C); 117.64 (*d*, C(2)); 163.76, 166.23 (2*s*, C(1), C(6')). EI-MS: 227 (1.4, $[M + 1]^+$), 212 (12), 211 (60), 181 (17), 161 (49), 141 (10), 123 (31), 122 (14), 112 (15), 95 (22), 77 (12), 67 (17), 66 (12), 65 (10), 59 (15), 55 (16), 43 (100), 41 (20), 39 (19), 29 (28), 27 (17), 18 (17).

*Data of (±)-***11**: TLC (hexane/Et_2O 3:1): R_f 0.34. ^{1}H-NMR (300 MHz, C_6D_6): 0.99 (*t*, *J* = 7.1, CH_3CH_2); 1.23, 1.41 (2*s*, Me_2C); 0.94–1.10, 1.71–1.81, 2.58–2.65 (3*m*, 2 H–C(7'), 2 H–C(8')); 3.97–4.06 (*dq*, *J* = 1.3, 7.1, CH_3CH_2); 4.33 (*t*, *J* = 5.2, H–C(1')); 5.70 (*d*, *J* = 5.5, H–C(5')); 5.81 (*t*, *J* = 1.3, H–C(2)). Difference NOE: 5.82 (H–C(2)) → 1.71–1.81 (H–C(7')). ^{13}C-NMR (75 MHz, C_6D_6): 14.28 (*q*, CH_3CH_2); 25.54, 26.84 (2*q*, Me_2C); 29.16, 31.21 (2*t*, C(7'), C(8')); 59.83 (*t*, CH_3CH_2); 77.89, 80.41 (2*d*, C(5'), C(1')); 110.45 (*s*, Me_2C); 116.79 (*d*, C(2)); 161.51, 165.22 (2*s*, C(1), C(6')). EI-MS: 227 (5.2, $[M + 1]^+$), 212 (17), 211 (75), 181 (23), 169 (59), 168 (22), 151 (53), 141 (28), 124 (17), 123 (100), 122 (53), 112 (34), 107 (17), 95 (29), 94 (18), 83 (15), 81 (16), 77 (19), 67 (26), 66 (21), 65 (16), 59 (19), 55 (26), 53 (15), 43 (84), 41 (31), 39 (32), 29 (40), 27 (28).

Ethyl (1'RS,5'SR)-(3',3'-Dimethyl-2',4'-dioxabicyclo[3.3.0]oct-6'-enyl)acetate ((±)-**12**). To a soln. of (±)-**10**/(±)-**11** (42.0 g, 0.18 mol) in CH_2Cl_2 (250 ml) was added 1,5,7-triazabicyclo[4.4.0]dec-5-ene (2.6 g, 18.6 mmol). After standing over night at r.t., the mixture was diluted with 0.5M aq. NaH_2PO_4 (250 ml), the aq. layer extracted with CH_2Cl_2 (250 ml), the combined org. phase dried ($MgSO_4$), and evaporated, and the residual oil distilled at 76–79°/0.05 Torr: (±)-**12** (40.9 g, 97%) containing 5% of (±)-**10**/(±)-**11**, as determined by ^{1}H-NMR. Colorless oil. B.p. 59–60°/0.01 Torr. TLC (hexane/AcOEt 3:1): R_f 0.64. IR ($CHCl_3$): 2988*m*, 2936*m*, 1730*s*, 1456*w*, 1372*m*, 1330*w*, 1312*w*, 1295*w*, 1280*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.27 (*t*, *J* = 7.5, CH_3CH_2); 1.36, 1.38 (2*s*, Me_2C); 2.48 (*dd*, *J* = 17.8, 1.0, H–C(8')); 2.59 (*dd*, *J* = 17.8, 5.4, H–C(8')); 3.17 (*d*, *J* = 16.3, H–C(2)); 3.22 (*d*, *J* = 16.3, H–C(2)); 4.15 (*q*, *J* = 7.15, CH_3CH_2); 4.75 (*t*, *J* = 5.5, H–C(1')); 5.07 (*d*, *J* = 5.7, H–C(5')); 5.61 (br. *s*, H–C(7')). ^{13}C-NMR (100 MHz, $CDCl_3$): 14.12 (*q*, CH_3CH_2); 26.1, 27.5 (2*q*, Me_2C); 33.9, 37.8 (2*t*, C(2), C(8')); 60.7 (*t*, CH_3CH_2); 78.3 (*d*, C(1')); 85.9 (*d*, C(5')); 110.2 (*s*, Me_2C); 128.5 (*d*, C(7')); 136.6 (*s*, C(6')); 171.0 (*s*, C(1)). EI-MS: 211 (74, $[M - 15]^+$), 181 (15), 169 (72), 168 (10), 151 (15), 123 (51), 122 (13), 109 (13), 95 (51), 94 (20), 79 (35), 78 (32), 77 (11), 67 (30), 66 (14), 65 (13), 43 (100), 41 (35), 39 (33), 29 (76), 28 (29), 27 (35).

Ethyl (1'RS,5'RS,6'RS,7'RS)- and (1'RS,5'RS,6'SR,7'SR)-6',7'-Epoxy-3',3'-dimethyl-2',4'-dioxabicyclo-[3.3.0]oct-6'-yl)acetate ((±)-**13** and (±)-**14**, resp.).To a stirred soln. of 55% 3-chloroperbenzoic acid (70.0 g, 223 mmol) in CH_2Cl_2 (700 ml) was added at 0° (±)-**12** (33.7 g, 149 mmol). After stirring for 22 h at r.t., the resulting suspension was evaporated to half of its volume and filtered and the filtrate extracted with 20% aq. $Na_2S_2O_3$ soln. (200 ml) and sat. $NaHCO_3$ soln. (2 × 200 ml). The aq. phases were again extracted with hexane (2 × 200 ml), the combined org. phases dried ($MgSO_4$) and evaporated, and the crude (±)-**13**/(±)-**14** separated by CC (silica gel (800 g), hexane/AcOEt 4:1): (±)-**13** (27.8 g, 77%) and (±)-**14** (3.8 g, 10%), both as colorless oils.

Data of (±)-**13**: B.p. 73°/0.01 Torr. TLC (hexane/AcOEt 3:1): R_f 0.40. IR ($CHCl_3$): 2986*m*, 2938*m*, 1740*s*, 1373*m*, 1260*m*, 1210*m*, 1160*m*, 1076*m*, 1051*m*, 982*w*, 867*w*. ^{1}H-NMR (300 MHz, C_6D_6): 0.92 (*t*, *J* = 7.1, CH_3CH_2); 1.12, 1.37 (2*s*, Me_2C); 1.75 (*dt*, *J* = 15.2, 2.1, H–C(8′)); 1.95 (*dd*, *J* = 6.4, 15.2, H–C(8′)); 2.56 (*d*, *J* = 16.4, H–C(2)); 3.09 (*d*, *J* = 16.3, H–C(2)); 3.20 (*dd*, *J* = 1.0, 2.2, H–C(7′)); 3.93 (*q*, *J* = 7.1, CH_3CH_2); 4.28 (*m* ('*t*'), H–C(1′)); 4.74 (*d*, *J* = 5.6, H–C(5′)). Difference NOE: 3.20 (H–C(7′)) → 1.76 (H–C(8′)), 1.96 (H–C(8′)), 2.57 (H–C(2)). ^{13}C-NMR (75 MHz, C_6D_6): 14.15 (*q*, CH_3CH_2); 24.64, 27.19 (2*q*, Me_2C); 34.35, 35.64 (2*t*, C(2), C(8′)); 60.50 (*t*, CH_3CH_2); 63.71 (*d*, C(7′)); 65.35 (*s*, C(6′)); 81.38, 81.51 (2*d*, C(5′), C(1′)); 111.62 (*s*, Me_2C); 169.43 (*s*, C(1)). EI-MS: 243 (57, $[M + 1]^+$), 228 (32), 227 (100), 197 (52), 185 (31), 167 (66), 139 (80), 138 (14), 111 (33), 110 (21), 97 (59), 95 (17), 94 (14), 85 (15), 83 (17), 81 (14), 69 (17), 68 (16), 67 (10), 59 (19), 55 (27), 43 (84), 41 (24), 39 (21), 29 (44), 27 (18).

Data of (±)-**14**: TLC (hexane/AcOEt 3:1): R_f 0.18. IR (neat): 2982*m*, 2936*m*, 1736*s*, 1443*w*, 1372*s*, 1336*m*, 1322*m*, 1253*s*, 1211*s*, 1159*s*, 1101*s*, 1071*s*, 1055*s*, 991*w*, 972*w*, 926*w*, 872*m*, 800*w*, 676*w*. ^{1}H-NMR (300 MHz, C_6D_6): 0.89 (*t*, *J* = 7.1, CH_3CH_2); 1.20, 1.66 (2*s*, Me_2C); 1.45 (*ddd*, *J* = 1.7, 6.9, 15.6, H–C(8′)); 2.10 (*d*, *J* = 15.6, H–C(8′)); 2.43 (*d*, *J* = 16.1, H–C(2)); 2.93 (*d*, *J* = 16.1, H–C(2)); 3.22 (*t*, *J* = 1.4, H–C(7′)); 3.87 (*q*, *J* = 7.1, CH_3CH_2); 4.26 (*t*, *J* = 7.0, H–C(1′)); 4.52 (*d*, *J* = 6.8, H–C(5′)). Difference NOE: 3.24 (H–C(7′)) → 4.51 (H–C(5′)), 2.50 (H–C(2)), 2.11 (H–C(8′)). ^{13}C-NMR (75 MHZ, C_6D_6): 14.08 (*q*, CH_3CH_2); 25.74, 27.00 (2*q*, Me_2C); 32.60, 35.87 (2*t*, C(2), C(8′)); 60.53 (*t*, CH_3CH_2); 64.13 (*d*, C(7′)); 64.80 (*s*, C(6′)); 79.95, 81.58 (2*d*, C(5′), C(1′)); 112.81 (*s*, Me_2C); 169.69 (*s*, C(1)). EI-MS: 243 (66, $[M + 1]^+$), 228 (39), 227 (100), 197 (14), 185 (34), 168 (15), 167 (86), 139 (66), 111 (28), 110 (13), 97 (66), 95 (20), 94 (17), 73 (16), 69 (19), 59 (17), 55 (29), 43 (86), 41 (31), 39 (30), 29 (64), 27 (26).

(1′R,5′R,6′R,7′R)-(6′,7′-Epoxy-3′,3′-dimethyl-2′,4′-dioxabicyclo[3.3.0]oct-6′-yl)acetic Acid (**15**). To a vigorously stirred emulsion of (±)-**13** (10.1 g, 41.3 mmol) in 0.1M Na_2HPO_4/NaH_2PO_4 buffer (pH 7.85; 500 ml) was added a suspension of hog-liver esterase (1.1 ml; 10 mg protein/ml) in 3.2M $(NH_4)_2SO_4$ (*Fluka* num. 46063) at r.t. The pH of the resulting emulsion was kept constant at pH 7.75 by gradual addition of 1M aq. NaOH using a *Metrohm Impulsomate®*. After addition of 1M NaOH (20 ml, 20 mmol, 49 mol-%; *ca.* 4 h); the clear mixture was brought to pH 9.0 with 2N NaOH and immediately extracted with Et_2O (4 × 250 ml). The combined Et_2O phases were dried ($MgSO_4$) and evaporated: unreacted (+)-**13** (4.2 g, 42%; 96% ee, $[\alpha]_D^{25°} = +28.4$ (*c* = 1.09, MeOH)). The aq. phase was acidified to pH 2.0 with 1N HCl, saturated with NaCl (solid), and extracted with CH_2Cl_2 (6 × 250 ml). The combined CH_2Cl_2 phases were dried (Na_2SO_4) and evaporated: **15** (4.7 g, 53%; 72%ee, by GLC of the corresponding **16** see below) as a colorless oil which solidified upon standing at −20°. For analyses, a small probe of **15** was crystallized from Et_2O/pentane (racemate as determined by GLC of the corresponding **16**). M.p. 121–123°. IR ($CHCl_3$): 3600–2400*m* (br.), 1711*s*, 1436*m*, 1385*m*, 1376*m*, 1344*m*, 1328*m*, 1277*s*, 1231*s*, 1213*s*, 1163*m*, 1086*m*, 1066*s*, 1048*s*, 982*m*, 962*w*, 934*m*, 892*w*, 852*m*, 798*w*, 753*w*, 722*w*, 672*w*, 651*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.32, 1.47 (2*s*, 2 Me); 2.01 (*dt*, *J* = 15.5, 2.0, H–C(8′)); 2.28 (*dd*, *J* = 6.2, 15.6, H–C(8′)); 2.71, 3.17 (2*d*, *J* = 16.7, 2 H–C(2)); 3.60 (*t*, *J* = 1.1, H–C(7′)); 4.55–4.60 (*m*, ('*t*'), H–C(1′)); 4.63 (*d*, *J* = 5.5, H–C(5′)). ^{13}C-NMR (75 MHz, $CDCl_3$): 24.67, 26.93 (2*q*, 2 Me); 33.99, 35.22 (2*t*, C(2), C(8′)); 64.22 (*d*, C(7′)); 65.10 (*s*, C(6′)); 80.77, 81.35 (2*d*, C(5′), C(1′)); 111.95 (*s*, Me_2C); 175.58 (*s*, COOH). EI-MS: 215 (0.2, $[M + 1]^+$), 200 (10), 199 (100), 157 (3), 155 (4), 140 (3), 139 (34), 121 (4), 111 (8), 110 (4), 97 (32), 95 (4), 87 (3), 85 (5), 83 (4), 81 (5), 69 (6), 68 (4), 67 (3), 59 (7), 55 (5), 43 (30), 39 (5), 28 (3).

(1R,5R,6S)-6-(2′-Hydroxyethyl)-3,3-dimethyl-2,4-dioxabicyclo[3.3.0]octan-6-ol ((−)-**16**). To a suspension of $LiAlH_4$ (4.2 g, 110.7 mmol) in Et_2O (60 ml) was added at −30° under N_2 a soln. of crude **15** (4.7 g, 21.9 mmol) in Et_2O/CH_2Cl_2 4:1 (100 ml) within 20 min. The mixture was refluxed for 6 h, then cooled to r.t. After the addition of H_2O (20 ml) and 2M NaOH (10 ml), the mixture was filtered over *Celite*, the white solid washed thoroughly with CH_2Cl_2 (400 ml), the combined filtrate evaporated, and the residual oil purified by CC (silica gel (200 g), hexane/AcOEt 1:2, 1:3, and 1:5): (−)-**16** (3.7 g, 84%; 72%ee). Crystallization from refluxing hexane (80 ml/g; 4d) led to crystals of the racemate (±)-**16**. After filtration, (−)-**16** (2.7 g, 61%; 97%ee) was obtained from the filtrate as a colorless, slowly solidifying oil. TLC (hexane/AcOEt 1:2) R_f 0.27. $[\alpha]_D^{25°} = -47.0$ (*c* = 1.0, MeOH). IR ($CHCl_3$): 3606*w*, 3600–3200*m* (br.), 2993*s*, 2938*s*, 1434*m*, 1383*s*, 1374*s*, 1301*w*, 1272*m*, 1164*m*, 1064*s*, 1040*s*, 1021*s*, 994*w*, 965*w*, 912*w*, 871*m*, 848*w*. ^{1}H-NMR (400 MHz, C_6D_6): 1.17, 1.39 (2*s*, 2 Me); 1.54–1.59, 1.71–1.90, 2.01–2.10 (3*m*, 7 H, OH, H–C(2′), H–C(8), H–C(7)); 3.39 (br. *s*, OH); 3.59, 3.81 (2*s*, ('*m*'), 2 H–C(1′)); 4.24 (*dd*, *J* = 1.4, 5.5, H–C(5)); 4.68 (*t*, *J* = 5.3, H–C(1)). ^{13}C-NMR (100 MHz, C_6D_6): 24.00, 26.58 (2*q*, 2 Me); 30.16 (*t*, C(8)); 35.31, 36.79 (2*t*, C(2′), C(7)); 61.10 (*t*, C(1′)); 81.31 (*d*, C(1)); 83.27 (*s*, C(6)); 86.42 (*d*, C(5)); 109.88 (*s*, Me_2C). EI-MS: 203 (14, M^+), 187 (50), 185 (16), 144 (35), 127 (52), 126 (64), 109 (70), 108 (28), 102 (10), 101 (41), 99 (32), 98 (18), 97 (22), 96 (15), 95 (15), 88 (77), 85 (13), 83 (37), 82 (16), 81 (100), 79 (36), 73 (39), 71 (39), 70 (70), 69 (19), 67 (16), 60 (12), 59 (60), 58 (36), 57 (36), 55 (54), 53 (16).

(1S,5S,6R)-6-(2'-Hydroxyethyl)-3,3-dimethyl-2,4-dioxabicyclo[3.3.0]octan-6-ol ((+)-**16**). To a suspension of $LiAlH_4$ (3.30 g, 86.96 mmol) in Et_2O (100 ml) was slowly added at 0° a soln. of (+)-**13** (4.2 g, 17.34 mmol) in Et_2O (20 ml). The ice-bath was removed and the mixture refluxed for 90 min. At r.t., H_2O (3.3 ml) 15% aq. NaOH soln. (3.3 ml) and H_2O (9.9 ml) were added. The white alumina salts were then filtered off. The filtrate was evaporated and the crude material submitted to CC (silica gel, hexane/AcOEt 1:3): (+)-**16** (3.1 g, 88%; 96%ee) as a colorless oil, which slowly solidified at r.t. $[\alpha]_D^{25°} = +44.3$ ($c = 0.56$, MeOH). ^{1}H- and ^{13}C-NMR and IR: identical with those of (−)-**16**.

(1'R,5'R,6'S)-(6'-Hydroxy-3',3'-dimethyl-2',4'-dioxabicyclo[3.3.0]oct-6'-yl)acetaldehyde (**17**). To a stirred soln. of 1,1,1-triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1*H*)-one (7.18 g, 16.93 mmol; *Dess-Martin* reagent, prepared according to [20a]) in CH_2Cl_2 (68 ml) was added a soln. of (−)-**16** (2.74 g, 13.55 mmol) in CH_2Cl_2 (54 ml) within 5 min. After stirring for 2 h, 20% aq. $Na_2S_2O_3$ (50 ml) and aq. $NaHCO_3$ soln. (150 ml) were added. The resulting mixture was extracted with Et_2O (4 × 300 ml), the combined org. phase dried ($MgSO_4$) and evaporated: crude **17** (2.49 g, 91%). Filtration over a short pad of silica gel with AcOEt followed by distillation at 72–75° 0.02 Torr (partial dec.) afforded **17** (1.78 g, 66%) as a colorless oil. In routine reactions, crude **17** was used without purification in the next step. TLC (hexane/AcOEt 1:3): R_f 0.56. IR ($CHCl_3$): 3600–3300*w* (br.), 3005m*w*, 2992*m*, 2937*m*, 2836*w*, 2742*w*, 1715*s*, 1601*w*, 1445*w*, 1383*m*, 1273*m*, 1165*m*, 1069*m*, 1039*s*, 988*w*, 965*w*, 922*w*, 871*m*. ^{1}H-NMR (300 MHz, C_6D_6): 1.09, 1.33 (2*s*, 2 Me); 1.51–1.62, 1.70–1.77, 1.85–1.98 (3*m*, 2 H–C(7'), 2 H–C(8')); 2.23 (*dd*, $J = 0.9$, $J = 18.0$, H–C(2)); 2.55 (*dd*, $J = 1.0$, 18.0, H–C(2)); 2.70 (br. *s*, OH); 4.18 (*dd*, $J = 1.3$, 5.5, H–C(5')); 4.52 (*t*, $J = 5.2$, H–C(1')); 9.33 (*t*, $J = 1.0$, CHO). ^{13}C-NMR (75 MHz, C_6D_6): 23.86, 26.39 (2*q*, 2 Me); 29.79, 34.97 (2*t*, C(7'), C(8')); 49.18 (*t*, C(2)); 80.38 (*s*, C(6')); 81.00 (*d*, C(1')); 86.31 (*d*, C(5')); 109.97 (*s*, Me_2C); 202.52 (*d*, CHO). EI-MS: 200 (1, M^+), 185 (36), 143 (19), 142 (18), 125 (34), 124 (30), 107 (32), 101 (10), 100 (12), 99 (28), 98 (24), 97 (33), 96 (19), 95 (25), 86 (37), 85 (24), 83 (15), 81 (38), 79 (36), 71 (50), 70 (49), 69 (38), 68 (14), 67 (25), 61 (10), 60 (17), 59 (56), 58 (38), 57 (41), 55 (48), 54 (11), 53 (25), 45 (18), 44 (44), 43 (92), 42 (100), 41 (52), 40 (28), 39 (45), 31 (40), 29 (91), 28 (63), 27 (42), 26 (13), 18 (37), 15 (28).

(1R,3RS,5S,8R)-2-Oxabicyclo[3.3.0]octane-3,5,8-triyl Triacetate (**18**/**19**). To a stirred emulsion of aldehyde **17** (1.64 g, 8.19 mmol) in H_2O (40 ml) was added *Amberlite IR-120* (H^+ form; 3.3 g), and the mixture was heated to 55° for 90 min. After cooling to r.t., the resin was filtered off and washed with H_2O and the combined aq. filtrate adjusted to pH 8.0 with sat. $NaHCO_3$ soln. and evaporated. Residual H_2O was coevaporated with pyridine (20 ml) and the remaining yellow gum dissolved in pyridine (25 ml). To this soln. were added at 0° Ac_2O (5.4 ml, 57.13 mmol) and 4-(dimethylamino)pyridine (250 mg, 2.05 mmol). Then the mixture was stirred for 3 h at r.t., cooled again to 0°, diluted with sat. $NaHCO_3$ soln. (100 ml), and extracted with CH_2Cl_2 (3 × 150 ml). The combined org. phase was dried ($MgSO_4$) and evaporated, residual pyridine coevaporated with toluene (2 × 100 ml), and the slightly brownish oil purified by CC (silica gel, hexane/AcOEt 2:1) to give, after 2 d drying at r.t./0.01 Torr, 2.19 g (93%) of **18**/**19** 1:1 as a viscous, slightly yellow oil. Bulb-to-bulb distillation at 124°–132°/0.01 Torr yielded a sample for analysis. TLC (hexane/AcOEt 1:1): R_f 0.40. IR ($CHCl_3$): 3032*w*, 1737*s*, 1430*w*, 1369*m*, 1117*m*, 1054*m*, 997*m*, 955*w*, 847*w*, 812*w*, 612*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.73–2.67 (*m*, 2 H–C(4), 2 H–C(6), 2 H–C(7)); 2.04, 2.05, 2.061, 2.063, 2.08, 2.09 (6*s*, 3 Me); 4.73 (*d*, $J = 5.8$, 0.5 H, H–C(1)); 4.79 (*d*, $J = 5.3$, 0.5 H, H–C(1)); 5.01 (*ddd*, $J = 5.8$, 7.5, 9.8, 0.5 H, H–C(8)); 5.08 (*dt*, $J = 10.8$, 5.4, 0.5 H, H–C(8)); 6.34 (*dd*, $J = 2.2$., 5.3, 0.5 H, H–C(3)); 6.40 (*d*, $J = 5.0$, 0.5 H, H–C(3)). ^{13}C-NMR (100 MHz, $CDCl_3$): 20.74, 20.91, 21.23, 21.31, 21.39, 21.55 (6*q*, Me); 27.86, 28.00, 33.98, 34.00 (4*t*, C(6), C(7)); 46.02, 46.11 (2*t*, C(4)); 72.38, 72.85 (2*d*, C(8)); 86.25, 87.30 (2*d*, C(1)); 91.11, 91.73 (2*s*, C(5)); 99.02, 99.33 (2*d*, C(3)); 169.74, 169.99, 170.12, 170.25, 170.43, 170.47 (6*s*, CO). EI-MS: 286 (0.7, M^+), 227 (22), 168 (11), 167 (82), 166 (9), 137 (10), 125 (18), 124 (13), 108 (13), 107 (100), 81 (7), 79 (8).

(3'S,5'R)-1-(3',5'-Di-O-acetyl-2'-deoxy-3',5'-ethano-αβ-D-ribofuranosyl)thymine (**21**/**22**). To a suspension of thymine (1.25 g, 9.91 mmol) in CH_2Cl_2 (100 ml) were added under Ar at 0° $(Me_3Si)_2NH$ (1.65 ml, 7.91 mmol), Me_3SiCl (1.0 ml, 7.89 mmol), $SnCl_4$ (1.39 ml, 11.83 mmol), and a soln. of **18**/**19** (2.83 g, 9.89 mmol) in CH_2Cl_2 (20 ml). After removal of the ice bath, the now clear soln. was stirred for 35 min at r.t. and for 35 min at 50°. The mixture was then cooled to r.t., diluted with sat. $NaHCO_3$ soln. (300 ml), and extracted with AcOEt (2 × 300 ml). The combined org. phase was filtered over cotton wool and evaporated. The remaining slightly brownish foam was purified by CC (silica gel, hexane/AcOEt 1:3): 2.55 g (73%) of **21**/**22** 2:3 (^{1}H-NMR). Colorless foam. TLC (AcOEt): R_f 0.50. IR ($CHCl_3$): 3393*w*, 3032*w*, 1740*s*, 1710*s* (sh), 1692*s*, 1465*w*, 1371*m*, 1288*m*, 1110*w*, 1059*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.84–2.53 (*m*, 4 H, H–C(6'), H–C(7')); 1.95, 1.96 (2*d*, $J = 1.2$, 3 H, Me–C(5)); 2.05, 2.08, 2.115, 2.119 (4*s*, 6 H, 2 Ac); 2.81 (*dd*, $J = 6.6$, 14.7, 0.32 H, H–C(2')); 2.97 (*dd*, $J = 5.4$, 14.6, 0.68 H, H–C(2')); 4.64 (*d*, $J = 5.6$, 0.67 H, H–C(4')); 4.91 (*d*, $J = 5.5$, 0.33 H, H–C(4')); 5.05–5.15 (*m*, 1 H, H–C(5')); 6.21–6.29 (*m*, 1 H, H–C(1')); 7.29, 7.31 (2*d*, $J = 1.2$, 1 H, H–C(6)); 8.73 (br. *s*, 1 H, NH). EI-MS: 352 (7, M^+), 227 (25), 168 (13), 167 (89), 127 (13), 126 (22), 125 (27), 108 (15), 107 (100), 106 (10), 83 (13), 81 (12), 43 (66).

(3'S,5'R)-N⁴-Benzoyl-1-(3',5'-di-O-acetyl-2'-deoxy-3',5'-ethano-αβ-D-ribofuranosyl)cytosine (**23/24**). To a suspension of N^4-benzoylcytosine (1.48 g, 6.88 mmol) in MeCN (55 ml) were added *N,O*-bis(trimethylsilyl)-acetamide (BSA; 3.4 ml, 13.8 mmol) and, after stirring for 1 h at r.t. (clear soln.), a soln. of **18/19** (1.57 g, 5.5 mmol) in MeCN (28 ml), followed by $SnCl_4$ (2.1 ml, 17.9 mmol). After 50 min, the dark green mixture was evaporated, diluted with $CHCl_3$ (200 ml), and extracted with sat. $NaHCO_3$ (2 × 200 ml) and sat. NaCl soln. (2 × 200 ml). The aq. layers were extracted with CH_2Cl_2 (3 × 200 ml). The combined org. phase was dried ($MgSO_4$) and evaporated and the resulting viscous oil purified by CC (silica gel (150 g), CH_2Cl_2/MeOH 30:1) to give, after precipitation from pentane and 1 h drying at r.t./0.01 Torr, **23/24** 2:3 (^{1}H-NMR; 1.84 g, 76%). White powder. TLC (CH_2Cl_2/MeOH 20:1): R_f 0.44. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.88 (*dd*, *J* = 8.6, 15.0, 0.6 H, H–C(2')); 1.79–2.10, 2.21–2.32, 2.34–2.41 (3*m*, 4 H, H–C(6'), H–C(7')); 1.95, 2.08, 2.12, 2.13 (4*s*, 6 H, 2 Ac); 2.72 (*dd*, *J* = 3.7, 15.2, 0.4 H, H–C(2')); 2.89 (*dd*, *J* = 6.3, 15.2, 0.4 H, H–C(2')); 3.35 (*dd*, *J* = 5.5, 14.9, 0.6 H, H–C(2')); 4.78 (*d*, *J* = 5.7, 0.6 H, H–C(4')); 5.07 (*d*, *J* = 5.8, 0.4 H, H–C(4')); 5.10 (*dd*, *J* = 5.1, 9.8, 0.6 H, H–C(5')); 5.16 (*dd*, *J* = 5.9, 12.7, 0.4 H, H–C(5')); 6.21–6.26 (*m*, 1 H, H–C(1')); 7.50–7.54, 7.60–7.65 (2*m*, 3 arom. H); 7.615 (*d*, *J* = 7.5, 0.4 H, H–C(5)); 7.619 (*d*, *J* = 7.5, 0.6 H, H–C(5)); 7.89 (*d*, *J* = 8.0, 2 arom. H); 7.97 (*d*, *J* = 7.5, 0.4 H, H–C(6)); 8.14 (*d*, *J* = 7.5, 0.6 H, H–C(6)); 8.71 (br. *s*, 1 H, NH). EI-MS: 441 (1.0, M^+), 186 (12), 167 (13), 124 (27), 107 (46), 106 (26), 105 (63), 95 (13), 86 (10), 78 (10), 77 (42), 60 (17), 51 (13), 43 (100).

(3'S,5'R)-N⁶-Benzoyl-9-(3',5'-di-O-acetyl-2'-deoxy-3',5'-ethano-αβ-D-ribofuranosyl)adenine (**25/26**). To a suspension of N^6-benzoyladenine (3.86 g, 16.1 mmol) in MeCN (20 ml) were added BSA (5.86 ml, 32.3 mmol) and, after stirring for 30 min at r.t. (clear soln.), a soln. of **18/19** (2.31 g, 8.1 mmol) in MeCN (15 ml) followed by $CF_3SO_3SiMe_3$ (200 µl, 1.1 mmol). After refluxing for 2 h and stirring for another 3 h at r.t., the dark brown mixture was diluted with sat. $NaHCO_3$ (100 ml) and sat. NaCl soln. (100 ml) and extracted with CH_2Cl_2 (2 × 200 ml). The combined org. phase was dried ($MgSO_4$) and evaporated and the resulting viscous oil purified by CC (silica gel, AcOEt) to give, after 1 h drying at r.t./0.01 Torr, **25/26** 3:2 (^{1}H-NMR; 2.94 g, 78%). Pale-yellow foam. TLC (AcOEt): R_f 0.37. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.90–2.19, 2.20–2.30, 2.41–2.48 (3*m*, 4 H, H–C(6'), H–C(7')); 1.94, 2.04, 2.11, 2.13 (4*s*, 6 H, 2 Ac); 2.84 (*dd*, *J* = 8.9, 14.6, 0.4 H, H–C(2')); 2.91 (*dd*, *J* = 6.8, 15.1, 0.6 H, H–C(2')); 3.14 (*dd*, *J* = 5.8, 14.6, 0.4 H, H–C(2')); 3.32 (*dd*, *J* = 3.5, 15.0, 0.6 H, H–C(2')); 4.77 (*d*, *J* = 5.4, 0.4 H, H–C(4')); 4.98 (*d*, *J* = 5.3, 0.6 H, H–C(4')); 5.05 (*dt*, *J* = 9.7, 6.2, 0.4 H, H–C(5')); 5.17 (*dt*, *J* = 8.4, 5.8, 0.6 H, H–C(5')); 6.48 (*dd*, *J* = 5.8, 9.0, 0.4 H, H–C(1')); 6.54 (*dd*, *J* = 3.5, 6.7, 0.6 H, H–C(1')); 7.51–7.63 (*m*, 3 arom. H); 8.02 (*d*, *J* = 7.2, 2 arom. H); 8.24, 8.25, 8.78, 8.79 (4*s*, 2 H, H–C(2), H–C(8)); 9.10 (br. *s*, 1 H, NH). ^{13}C-NMR (100 MHz, $CDCl_3$): 20.84, 20.92, 21.38, 21.60 (4*q*, 2 Me); 28.12, 28.57, 33.49, 33.74 (4*t*, C(6'), C(7')); 44.91, 45.01 (2*t*, C(2')); 72.69, 72.78 (2*d*, C(5')); 84.94, 85.60 (2*d*, C(1')); 86.67, 87.18 (2*d*, C(4')); 97.76, 97.94 (2*s*, C(3')); 123.25, 123.60 (2*s*, C(5)); 127.89, 128.90, 132.83 (3*d*, arom. C); 133.59, 133.62 (2*s*, arom. C); 140.94, 141.16 (2*d*, C(8)); 149.56, 149.63 (2*s*, C(4)); 151.54, 151.74 (2*s*, C(6)); 152.73 (*d*, C(2)); 164.61 (*s*, CONH); 170.03, 170.28, 170.39 (3*s*, COO). FAB-MS (pos.): 467 (19), 466 (49), 465 (3.6, M^+), 241 (27), 240 (100), 154 (13), 137 (11), 136 (17), 107 (33), 105 (47).

(3'S,5'R)-9- and -7-(3',5'-Di-O-acetyl-2'-deoxy-3',5'-ethano-αβ-D-ribofuranosyl)-N²-isobutyrylguanine (**27/28** and **29/30** resp.). To a suspension of N^2-isobutyrylguanine (4.69 g, 76.3 mmol) in MeCN (150 ml) were added BSA (19.0 ml, 76.3 mmol) and, after stirring for 1 h at r.t. and 30 min at 40° (clear soln.), a soln. of **18/19** (3.03 g, 10.6 mmol) in MeCN (15 ml) followed by $CF_3SO_3SiMe_3$ (4.2 ml, 23.3 mmol). After stirring for 16 h at r.t. and for another 6 h at 40°, the mixture was evaporated, diluted with CH_2Cl_2 (250 ml), and extracted with sat. $NaHCO_3$ soln. (2 × 250 ml). The aq. layers were reextracted with CH_2Cl_2 (3 × 250 ml). The combined org. phase was dried ($MgSO_4$) and evaporated and the resulting viscous oil separated by CC (silica gel, CH_2Cl_2/MeOH 39:1; 2× rechromatography of mixed fractions) to give, after 1 h drying at r.t./0.01 Torr, **27/28** 8:5 (^{1}H-NMR; 2.13 g, 45%) as the more polar component and **29/30** 3:2 (^{1}H-NMR; 1.75 g, 37%) as the more apolar component, both as colorless foams.

Data of **27/28**: TLC (CH_2Cl_2/MeOH 9:1): R_f 0.58. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.23–1.28 (*m*, Me_2CHCO); 1.82–2.03, 2.18–2.28, 2.31–2.41 (3*m*, H–C(6'), H–C(7')); 1.98, 2.06, 2.04, 2.10 (4*s*, Ac); 2.45 (*dd*, *J* = 9.1, 14.6, H–C(2')); 2.70, 2.71 (2 *sept.*, *J* = 6.9, Me_2CHCO); 2.81 (*dd*, *J* = 7.0, 15.2, H–C(2')); 3.03 (*dd*, *J* = 5.7, 14.6, H–C(2')); 3.10 (*dd*, *J* = 3.2, 15.2, H–C(2')); 4.68 (*d*, *J* = 5.6, H–C(4')); 4.90 (*d*, *J* = 5.2, H–C(4')); 4.98–5.03 (*m*, H–C(5')); 5.10–5.15 (*m*, H–C(5')); 6.20 (*dd*, *J* = 5.7, 9.0, H–C(1')); 6.26 (*dd*, *J* = 3.2, 6.9, H–C(1')); 7.86, 7.90 (2*s*, H–C(8)); 8.87, 8.93 (br. *s*, NH); 12.07 (br. *s*, NH). ^{13}C-NMR (100 MHz, $CDCl_3$): 18.93, 18.95, 19.03, 20.8, 20.9, 21.4, 21.6 (7*q*, *Me*CO, Me_2CHCO); 28.2, 28.5, 33.4, 33.9 (4*t*, C(6'), C(7')); 36.5 (*d*, Me_2*C*HCO); 45.3, 45.4 (2*t*, C(2')); 72.6, 72.8 (2*t*, C(5')); 84.6, 84.9, 86.3, 87.0 (4*t*, C(1'), C(4')); 91.78, 91.80 (2*s*, C(3')); 121.4, 121.6 (2*s*, C(5)); 136.2, 136.6 (2*d*, C(8)); 147.,5, 147.7, 147.8, 148.1 (4*s*, C(2), C(4)); 155.5, 155.6 (2*s*, C(6)); 170.16, 170.20, 170.3, 170.5, 178.5, 178.6 (6*s*, CO). FAB-MS (pos.): 895 (10, $[2M + H]^+$), 449 (11), 448 (36, $[M + H]^+$), 447 (4.4), 223 (20), 222 (100), 221 (14), 167 (15), 152 (28), 107 (41).

Data of **29/30**: TLC (CH_2Cl_2/MeOH 9:1): R_f 0.71. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.22–1.25 (*m*, Me_2CHCO); 1.92, 2.102, 2.105, 2.13 (4*s*, Ac); 1.94–2.07, 2.23–2.29, 2.31–2.41, 2.89–3.00 (4*m*, H–C(2'), H–C(6'), H–C(7'), Me_2CHCO); 3.28 (*dd*, *J* = 5.7, 14.7, H–C(2')); 4.77 (*d*, *J* = 5.5, H–C(4')); 5.05–5.10 (*m*, H–C(4'), H–C(5')); 5.15–5.20 (*m*, H–C(5')); 6.59 (*dd*, *J* = 5.7, 8.6, H–C(1')); 6.68 (*dd*, *J* = 3.7, 6.0, H–C(1')); 8.04, 8.18 (2*s*, H–C(8)). ^{13}C-NMR (100 MHz, $CDCl_3$): 19.06, 19.08, 19.11, 20.87, 20.92, 21.4, 21.6 (7*q*, Me_2CHCO, *Me*CO); 28.3, 28.7, 33.2, 33.4 (4*t*, C(6'), C(7')); 36.1, 36.2 (2*d*, Me_2CHCO); 47.1, 47.7 (2*t*, C(2')); 72.69, 72.73 (2*d*, C(5')); 85.4, 87.6, 87.9, 89.4 (4*d*, C(1'), C(4')); 91.7, 92.1 (2*s*, C(3')); 111.1, 111.3 (2*s*, C(5)); 140.6, 140.8 (2*d*, C(8)); 147.8, 147.9 (2*s*, C(2)); 152.8, 153.0 (2*s*, C(6)); 157.5, 157.6 (2*s*, C(4)); 170.0, 170.2, 170.3, 179.56, 179.63 (5*s*, CO). FAB-MS (pos.): 448 (19, $[M + H]^+$), 447 (2.8, M^+), 223 (17), 222 (100), 221 (13), 152 (26), 107 (21).

Deacylation: General Procedure. A soln. (9–22 mM) of the corresponding anomeric mixture **21/22–27/28** in 0.2M NaOH in (THF/MeOH/H_2O 5:4:1) was stirred at 0–2° for 30–75 min. Then NH_4Cl (1.25–1.5 equiv. rel. to NaOH) was added and the ice-bath removed. After all solid had dissolved, the mixture was evaporated and the residue adsorbed on silica gel with MeOH and purified by CC to give the anomeric mixture of the deacylated nucleosides.

Silylation: General Procedure. The deacylated anomeric mixture (see above) was dissolved in pyridine to give a 0.1–0.2M soln., to which (*tert*-butyl)dimethylsilyl trilfuoromethanesulfonate (1.3–1.6 equiv.) was added at 0°. After 30–45 min, the reaction was quenched with sat. $NaHCO_3$ soln. and the resulting mixture extracted with AcOEt or Et_2O. The org. phase was dried ($MgSO_4$) and evaporated and the crude anomeric mixture of silylated nucleosides separated by CC.

*(3'S,5'R)-1-{5'-O-[(*tert*-Butyl)dimethylsilyl]-2'-deoxy-3',5'-ethano-α- and -β-*D*-ribofuranosyl}thymine* (**31** and **32**, resp.). From **21/22** (2.30 g, 6.53 mmol, 22 mM; 75 min) was obtained **5/1** (1.65 g, 94%), after deacylation, CC (silica gel, CH_2Cl_2/MeOH 5:1), and precipitation from hexane. Silylation of **5/1** yielded, after separation by CC (silica gel, 5% Me_2CO in Et_2O; 2× rechromatography of mixed fractions) and drying at r.t./0.01 Torr, **31** (655 mg, 28%) as the apolar and **32** (1.47 g, 62%) as the polar component, both as white foams.

Data of **31**: TLC (Et_2O (sat. H_2O)/Me_2CO 95:5): R_f 0.19. IR ($CHCl_3$). 3392*w*, 2956*m*, 1710*s* (sh), 1688*s*, 1471*m*, 1360*w*, 1261*m*, 1114*m*, 1070*m*, 989*w*, 915*w*, 864*w*, 837*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.09, 0.10 (2*s*, MeSi); 0.91 (*s*, *t*-Bu); 1.70–1.93, 1.83–1.93, 1.98–2.07, 2.12–2.19 (4*m*, 2 H–C(6'), 2 H–C(7')); 1.89 (*s*, Me–C(5)); 2.49 (*d*, *J* = 14.5, H–C(2')); 2.61 (*dd*, *J* = 7.9, 14.6, H–C(2')); 3.85 (br. *s*, OH); 4.15 (*dd*, *J* = 4.2, 8.7, H–C(5')); 4.45 (*d*, *J* = 4.6, H–C(4')); 6.05 (*dd*, *J* = 2.5, 7.8, H–C(1')); 7.37 (*s*, H–C(6)); 9.35 (br. *s*, NH). ^{13}C-NMR (100 MHz, $CDCl_3$): –5.03, –4.69 (2*q*, MeSi); 12.46 (*q*, *Me*–C(5)); 18.23 (*s*, Me_3C); 25.88 (*q*, Me_3C); 32.36, 36.45 (2*t*, C(6'), C(7')); 48.06 (*t*, C(2')); 73.56 (*d*, C(5')); 86.42 (*s*, C(3')); 92.20, 94.54 (2*d*, C(1'), C(4')); 110.05 (*s*, C(5)); 138.35 (*d*, C(6)); 150.48 (*s*, C(2)); 164.18 (*s*, C(4)). FAB-MS (pos.): 384 (21), 383 (75, $[M + H]^+$), 382 (3, M^+), 325 (29), 258 (16), 257 (87), 241 (18), 240 (14), 239 (68), 213 (34), 199 (49), 183 (11), 181 (10), 155 (15), 154 (25), 153 (21), 138 (12), 137 (12), 136 (30), 129 (14), 127 (73), 125 (12), 115 (12), 110 (15), 107 (38).

Data of **32**: TLC (Et_2O (sat. H_2O)/Me_2CO 95:5): R_f 0.12. IR ($CHCl_3$): 3600*w*, 3398*w*, 2956*m*, 2931*m*, 2858*w*, 1687*s*, 1471*m*, 1369*w*, 1282*m*, 1144*m*, 1094*m*, 997*w*, 940*w*, 904*w*, 838*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.10, 0.12 (2*s*, MeSi); 0.91 (*s*, *t*-Bu); 1.63–2.12 (*m*, 2 H–C(6'), 2 H–C(7'), H–C(2')); 1.92 (*d*, *J* = 1.1, Me–C(5)); 2.67 (*dd*, *J* = 5.0, 13.6, H–C(2')); 3.85 (br. *s*, OH); 4.08 (*d*, *J* = 6.0, H–C(4')); 4.19 (*dd*, *J* = 6.1, 14.1, H–C(5')); 6.39 (*dd*, *J* = 4.9, 9.3, H–C(1')); 7.66 (*d*, *J* = 1.2, H–C(6)); 9.55 (br. *s*, NH). ^{13}C-NMR (75 MHz, $CDCl_3$): –4.92, –4.60 (2*q*, MeSi); 12.53 (*q*, Me–C(5)); 18.30 (*s*, Me_3C); 25.90 (*q*, Me_3C); 33.43, 34.46 (2*t*, C(6'), C(7')); 47.39 (*t*, C(2')); 72.34 (*d*, C(5')); 85.92 (*d*, C(1')); 86.68 (*s*, C(3')); 89.34 (*d*, C(4')); 111.13 (*s*, C(5)); 135.41 (*d*, C(6)); 150.62 (*s*, C(2)); 163.89 (*s*, C(4)). FAB-MS (pos.): 406 (11), 405 (40, $[M + Na]^+$), 383 (37, $[M + H]^+$), 325 (16), 257 (46), 241 (11), 239 (34), 213 (22), 199 (29), 153 (12), 127 (34), 107 (12).

*(3'S,5'R)-N^4-Benzoyl-1-{5'-O-[(*tert*-butyl)dimethylsilyl]-2'-deoxy-3',5'-ethano-α- and -β-*D*-ribofuranosyl}-cytosine* (**33** and **34**, resp.). From **23/24** (1.89 g, 4.29 mmol, 10 mM; 20 min) was obtained **37/38** (1.29 g, 84%), after deacylation and CC (silica gel, CH_2Cl_2/MeOH 15:1). Silylation of **37/38** yielded, after separation by CC (silica gel, AcOEt), **33** (677 mg, 38%; polar isomer) as a white amorphous solid and **34** (865 mg, 49%; apolar isomer) as a white foam.

Data of **33**: TLC (AcOEt): R_f 0.17. $[\alpha]_D^{25°} = -40.7$ (*c* = 0.95, MeOH). UV (MeOH): 257 (21 900), 302 (10 600). IR ($CHCl_3$): 3403*m*, 3005*m*, 2955*s*, 2930*s*, 2857*m*, 1702*s*, 1655*s*, 1557*s*, 1483*s*, 1428*m*, 1385*s*, 1327*s*, 1309*s*, 1256*s*, 1152*m*, 1112*s*, 1072*s*, 1005*s*, 986*m*, 938*m*, 910*m*, 857*m*, 838*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.09 (*s*, MeSi); 0.91 (*s*, *t*-Bu); 1.73–1.86, 2.01–2.09, 2.13–2.20 (3*m*, 2 H–C(6'), 2 H–C(7')); 2.61–2.69 (*m*, 2 H–C(2')); 4.15–4.18 (*m*, H–C(5')); 4.25 (*s*, OH–C(3')); 4.53 (*d*, *J* = 4.6, H–C(4')); 6.06 (*dd*, *J* = 3.2, 5.7, H–C(1')); 7.47–7.51, 7.58–7.62 (2*m*, 3 arom. H, H–C(5)); 7.89 (*d*, *J* = 7.4, 2 arom. H); 7.95 (*d*, *J* = 7.4, H–C(6)); 8.89 (br. *s*, NH). ^{13}C-NMR (100 MHz, $CDCl_3$): –5.0, –4.7 (2*q*, MeSi); 18.2 (*s*, Me_3C); 25.9 (*q*, Me_3C); 32.9, 36.2 (2*t*, C(6'), C(7')); 48.0 (*t*, C(2')); 73.2 (*d*, C(5')); 86.5 (*s*, C(3')); 94.4 (*d*, C(1')); 95.3 (*d*, C(4')); 96.0 (*d*, C(5)); 127.7, 129.0, 133.1 (3*d*, arom. C); 146.3

(*d*, C(6)); 162 (*s*, C(4)). FAB-MS (pos.): 494 (23, $[M + Na]^+$), 472 (14, $[M + H]^+$), 239 (13), 238 (46), 217 (18), 216 (100), 213 (15), 105 (52), 99 (19).

Data of **34**: TLC (AcOEt): R_f 0.40. $[\alpha]_D^{25°} = +139.4$ ($c = 0.92$, MeOH). UV (MeOH): 259 (22 700), 303 (11 100). IR ($CHCl_3$): 3403*m*, 3002*m*, 2955*m*, 2858*m*, 1702*s*, 1651*s*, 1620*s*, 1557*s*, 1481*s*, 1430*m*, 1395*s*, 1309*s*, 1254*s*, 1120*m*, 1072*m*, 1004*m*, 940*w*, 902*m*, 864*m*, 838*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.12, 0.13 (2*s*, MeSi); 0.93 (*s*, *t*-Bu); 1.57–1.71, 1.91–2.12 (2*m*, 2 H–C(6′), 2 H–C(7′)); 1.77 (*dd*, $J = 8.6$, 14.0, H–C(2′)); 3.15 (*dd*, $J = 5.5$, 14.0, H–C(2′)); 4.16–4.21 (*m*, H–C(5′)); 4.24 (*d*, $J = 5.4$, H–C(4′)); 6.47 (*dd*, $J = 5.4$, 8.5, H–C(1′)); 7.48–7.52, 7.58–7.62, 7.91–7.93 (3*m*, 5 arom. H, H–C(5)); 8.59 (*d*, $J = 7.4$, H–C(6)); 8.96 (br. *s*, NH). ^{13}C-NMR (100 MHz, $CDCl_3$): –4.9, –4.6 (2*q*, MeSi); 18.3 (*s*, Me_3C); 25.9 (*q*, Me_3C); 33.2, 34.6 (2*t*, C(6′), C(7′)); 49.0 (*t*, C(2′)); 72.6 (*d*, C(5′)); 87.0 (*s*, C(3′)); 88.7 (*d*, C(1′)); 90.4 (*d*, C(4′)); 96.8 (*d*, C(5)); 127.7, 129.0, 133.2 (3*d*, arom. C); 133.0 (*s*, arom. C); 145.0 (*d*, C(6)); 162.5 (*s*, C(4)). FAB-MS (pos.): 494 (13, $[M + Na]^+$), 472 (24, $[M + H]^+$), 471 (3.5, M^+), 414 (18), 257 (14), 238 (16), 217 (24), 216 (100), 213 (19), 105 (61), 99 (20).

(3′S,5′R)-N^6-Benzoyl-9-{5′-O-[(tert-butyl)dimethylsilyl]-2′-deoxy-3′,5′-ethano-α- and -β-D-ribofuranosyl}-adenine (**35** and **36**, resp.). From **25**/**26** (3.37 g, 7.24 mmol, 22 mM; 30 min) was obtained **39**/**40** (1.98 g, 72%), after deacylation and CC (silica gel, CH_2Cl_2/MeOH 9:1). Silylation of **39**/**40** yielded, after separation by CC (silica gel, Et_2O (sat. H_2O)/Me_2CO 83:17; 1× rechromatography of mixed fractions), **35** (1.452 g, 57%) as the apolar and **36** (0.864 g, 33%) as the polar component, both as white foams.

Data of **35**: TLC (Et_2O (sat. H_2O)/Me_2CO 85:15): R_f 0.51. IR (KBr): 3600–3100*m* (br.), 2950*s*, 2930*s*, 2860*m*, 1700*s*, 1610*s*, 1580*s*, 1510*s*, 1485*s*, 1470*s* (sh), 1455*s*, 1400*m*, 1330*s*, 1295*s*, 1255*s*, 1215*s*, 1180*m*, 1155*m*, 1090*s* (sh), 1070*s*, 1030*w*, 1005*w*, 985*w*, 940*m*, 910*m*, 840*s*, 800*m*, 780*s*, 710*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.11 (*s*, MeSi); 0.92 (*s*, *t*-Bu); 1.75–1.83, 1.94–2.08, 2.12–2.19 (3*m*, 2 H–C(6′), 2 H–C(7′)); 2.82–2.92 (*m*, 2 H–C(2′)); 4.18 (*dt*, $J = 6.1$, 4.8, H–C(5′)); 4.39 (*d*, $J = 4.8$, H–C(4′)); 6.34 (*dd*, $J = 3.8$, 7.3, H–C(1′)); 7.11 (*s*, OH); 7.53 (*t*, $J = 7.5$, 2 arom. H); 7.62 (*t*, $J = 7.4$, 1 arom. H); 8.02 (*d*, $J = 7.1$, 2 arom. H); 8.08 (*s*, H–C(8)); 8.80 (*s*, H–C(2)); 9.13 (br. *s*, NH). ^{13}C-NMR (100 MHz, $CDCl_3$): –4.91, –4.69 (2*q*, MeSi); 18.32 (*s*, Me_3C); 25.93 (*q*, Me_3C); 31.55, 36.25 (2*t*, C(6′), C(7′)); 48.23 (*t*, C(2′)); 74.04 (*d*, C(5′)); 86.00 (*s*, C(3′)); 88.68 (*d*, C(1′)); 93.63 (*d*, C(4′)); 124.25 (*s*, C(5)); 127.89, 128.95, 132.95 (3*d*, arom. C); 133.52 (*s*, arom. C); 143.76 (*d*, C(8)); 149.95 (*s*, C(4)); 150.22 (*s*, C(6)); 151.84 (*d*, C(2)); 164.47 (*s*, CO). FAB-MS (pos.): 497 (20), 496 (43, $[M + H]^+$), 438 (10), 266 (20), 241 (29), 240 (10), 213 (10), 136 (14), 105 (43).

Data of **36**: TLC (Et_2O (sat. H_2O)/Me_2CO 85:15): R_f 0.33. IR (KBr): 3600–3100*m*, 2950*m*, 2930*m*, 2860*m*, 1700*m*, 1610*s*, 1580*s*, 1510*m*, 1485*m* (sh), 1460*s*, 1405*m*, 1320*m*, 1300*m*, 1250*s*, 1220*m*, 1185*m*, 1145*m*, 1095*s*, 1075*s*, 1005*w*, 980*w*, 940*w*, 905*m*, 865*m*, 835*s*, 710*m*, 690*m*, 645*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.06, 0.10 (2*s*, MeSi); 0.88 (*s*, *t*-Bu); 1.67–1.86, 2.08–2.14 (2*m*, 2 H–C(6′), 2 H–C(7′)); 2.37 (*dd*, $J = 9.1$, 13.6, H–C(2′)); 2.84 (*dd*, $J = 5.4$, 13.5, H–C(2′)); 3.08 (br. *s*, OH); 4.18–4.23 (*m*, H–C(4′), H–C(5′)); 6.57 (*dd*, $J = 5.3$, 9.0, H–C(1′)); 7.50–7.54 (*m*, 2 arom. H); 7.58–7.63 (*m*, 1 arom. H); 8.04 (*d*, $J = 7.2$, 2 arom. H); 8.47 (*s*, H–C(8)); 8.79 (*s*, H–C(2)); 9.23 (br. *s*, NH). ^{13}C-NMR (100 MHz, $CDCl_3$): –4.93, –4.46 (2*q*, MeSi); 18.32 (*s*, Me_3C); 25.92 (*q*, Me_3C); 33.34, 35.41 (2*t*, C(6′); C(7′)); 48.60 (*t*, C(2′)); 72.49 (*d*, C(5′)); 86.13 (*d*, C(1′)); 87.08 (*s*, C(3′)); 90.58 (*d*, C(4′)); 123.02 (*s*, C(5)); 127.94, 128.86, 132.79 (3*d*, arom. C); 133.78 (*s*, arom. C); 141.23 (*d*, C(8)); 149.45 (*s*, C(4)); 151.29 (*s*, C(6)); 152.66 (*d*, C(2)); 164.74 (*s*, CO). FAB-MS (pos.): 497 (22), 496 (51, $[M + H]^+$), 495 (2.3, M^+), 438 (16), 266 (19), 241 (26), 240 (100), 154 (12), 137 (10), 136 (17), 105 (39).

(3′S,5′R)-9-(2′-Deoxy-3′,5′-ethano-α- and -β-D-ribofuranosyl)-N^2-isobutyryl guanine (**41** and **42**, resp.). From **27**/**28** 7:9 (^{1}H-NMR; 1.13 g, 2.53 mmol, 9 mM; 25 min) was obtained deacylated **41**/**42** which was directly separated by CC (silica gel, CH_2Cl_2/MeOH 10:1, 2× rechromatography of mixed fractions) to give **41** (254 mg, 28%) as the polar and **42** (427 mg, 47%) as the apolar component. For analysis, **41** was crystallized from H_2O and **42** from MeOH/H_2O 4:1.

Data of **41**: M.p. > 160° (dec.). TLC (CH_2Cl_2/MeOH 10:1): R_f 0.20. $[\alpha]_D^{25°} = +53.2$ ($c = 1.02$, MeOH). UV (MeOH): 260 (12 300). IR (KBr): 3380*s* (br.), 3220*s* (sh), 3120*s* (sh), 2970*m*, 2940*m*, 2870*m*, 1680*s*, 1605*s*, 1565*s*, 1470*s*, 1400*s*, 1320*m*, 1250*m*, 1200*m*, 1160*m*, 1105*m*, 1070*m*, 910*m*, 785*m*. ^{1}H-NMR (400 MHz, CD_3OD): 1.25 (*d*, $J = 6.8$, Me_2CH); 1.69–1.80, 2.02–2.11 (2*m*, 2 H–C(6′), 2 H–C(7′)); 2.65 (*dd*, $J = 7.2$, 14.4, H–C(2′)); 2.73–2.78 (*m*, H–C(2′), Me_2CH); 4.11–4.16 (*m*, H–C(5′)); 4.34 (*d*, $J = 5.2$, H–C(4′)); 6.42 (*dd*, $J = 2.8$, 7.1, H–C(1′)); 8.38 (*s*, H–C(8)). Difference-NOE (300 MHz, CD_3OD): 4.34 (H–C(4′)) → 4.11–4.16 (H–C(5′)), 8.38 (H–C(8)); 6.42 (H–C(1′)) → 2.65 (H–C(2′)), 2.73–2.78 (H–C(2′)), 4.34 (H–C(4′), weak); 8.38 (*s*, H–C(8)). ^{13}C-NMR (100 MHz, CD_3OD): 19.5 (*q*, Me_2CH); 32.2, 37.1 (2*t*, C(6′), C(7′)); 37.1 (*d*, Me_2CH); 48.5 (*t*, C(2′)); 73.3 (*d*, C(5′)); 87.1 (*s*, C(3′)); 87.8, 92.0 (2*d*, C(1′), C(4′)); 120.8 (*s*, C(5)); 140.4 (*d*, C(8)); 150.5, 150.9 (2*s*, C(2), C(4)); 181.5 (*s*, CO). FAB-MS (pos.): 545 (10), 520 (11), 519 (43), 481 (16), 387 (13), 386 (59), 364 (23), 363 (6.1, M^+), 270 (11), 260 (57), 248 (10), 244 (51), 223 (15), 222 (100), 221 (16), 178 (11), 176 (26), 173 (14), 125 (12), 120 (11), 107 (26), 105 (15). Anal. calc. for $C_{16}H_{21}N_5O_5$: C 52.89, H 5.83, N 19.27; found: C 52.61, H 5.89, N 19.16.

Data of **42**: M.p. > 180° (dec.). TLC (CH_2Cl_2/MeOH 10:1): R_f 0.27. $[\alpha]_D^{25°} = +21.7$ ($c = 0.91$, MeOH). UV (MeOH): 259 (15400), 279 (11400). IR (KBr): 3640*m*, 3480*s*, 3430*s*, 3180*s*, 3040*m*, 2970*s*, 2920*s*, 2880*m*, 1730*s*, 1670*s*, 1610*s*, 1560*s*, 1540*s*, 1480*m*, 1470*m*, 1420*s*, 1400*s*, 1370*m*, 1315*m*, 1255*s*, 1215*s*, 1125*m*, 1100*s*, 1070*s*, 1045*m*, 980*s*, 960*m*, 905*m*, 800*m*, 775*m*. ^{1}H-NMR (400 MHz, CD_3OD): 1.22 (*d*, $J = 6.9$, Me_2CH); 1.65–1.72, 1.86–1.97, 2.06–2.15 (3*m*, 2 H–C(6′), 2 H–C(7′)); 2.50 (*dd*, $J = 9.7$, 13.2, H–C(2′)); 2.57 (*dd*, $J = 5.4$, 13.3, H–C(2′)); 2.72 (*sept.*, $J = 6.9$, Me_2CH); 4.09–4.13 (*m*, H–C(4′), H–C(5′)); 6.32 (*dd*, $J = 5.4$, 9.6, H–C(1′)); 8.30 (*s*, H–C(8)). Difference-NOE (300 MHz, CD_3OD): 4.09–4.13 (H–C(4′), H–C(5′)) → 1.65–1.72 (H–C(6′), H–C(7′)), 2.06–2.15 (H–C(6′), H–C(7′)), 6.32 (H–C(1′)); 6.32 (H–C(1′)) → 2.50 (H–C(2′)), 2.57 (H–C(2′)), 4.10 (H–C(4′)), 8.31 (H–C(8)). ^{13}C-NMR (100 MHz, CD_3OD): 19.36, 19.37 (2*q*, Me_2CH); 33.0, 36.5 (2*t*, C(6′), C(7′)); 37.0 (*d*, Me_2CH); 48.5 (*t*, C(2′)); 72.8 (*d*, C(5′)); 86.7, 91.7 (2*d*, C(1′), C(4′)); 87.2 (*s*, C(3′)); 121.3 (*s*, C(5)); 139.6 (*d*, C(8)); 149.8 (*s*, C(4)); 150.4 (*s*, C(2)); 157.5 (*s*, C(6)); 181.8 (*s*, CO). FAB-MS (pos.): 386 (25, $[M + Na]^+$), 364 (38, $[M + H]^+$), 363 (12.9, M^+), 248 (15), 244 (19), 223 (26), 222 (100), 221 (24), 178 (12), 152 (38), 151 (16). Anal. calc. for $C_{16}H_{21}N_5O_5 \cdot H_2O$: C 50.39, H 6.08, N 18.36; found: C 50.20, H 5.97, N 18.29.

Desilylation: General Procedure. To a 0.08–0.14M soln. of the corresponding silylated nucleoside **31**–**36** in THF was added at r.t. $Bu_4NF \cdot 3\ H_2O$ 1.2–2.3 equiv. and the mixture stirred for 17 h to 17 d at r.t. to 55°. Then, silica gel (3–10 g) was added, the mixture evaporated, and the adsorbed crude material purified by CC. Residual Bu_4N-salts which coeluted with the products were eliminated by crystallization of the desilylated nucleosides **1**, **5**, and **37**–**42**.

*(3′S,5′R)-1-(2′-Deoxy-3′,5′-ethano-α-*D*-ribofuranosyl)thymine* (**5**). Desilylation of **31** (638 mg, 1.67 mmol; 0.11M) with $Bu_4NF \cdot 3\ H_2O$ (740 mg, 2.34 mmol) for 17 d at r.t. afforded **5** (345 mg, 77%), after CC (silica gel, CH_2Cl_2/MeOH 6:1) and crystallization (from MeOH/Et_2O 4:1, pentane). Colorless prisms. M.p. > 220° (dec.). TLC (CH_2Cl_2/MeOH 6:1): R_f 0.36. $[\alpha]_D^{25°} = +35.1$ ($c = 0.8$, MeOH), +25.0 ($c = 0.7$, H_2O). UV (H_2O): 267 (9900). IR (KBr): 3600–3400*m* (br.), 3165*w*, 3040*w*, 2950*w*, 2820*w*, 1685*s*, 1470*m*, 1275*m*, 1115*m*, 1075*m*, 1065*m*, 1000*w*, 965*w*, 765*w*. ^{1}H-NMR (300 MHz, D_2O): 1.57–1.75, 1.99–2.08 (2*m*, 2 H–C(6′), 2 H–C(7′)); 1.84 (*d*, $J = 1.2$, Me–C(5)); 2.38 (*dd*, $J = 4.3$, 14.7, H–C(2′)); 2.58 (*dd*, $J = 7.0$, 14.7, H–C(2′)); 4.10–4.17 (*m*, H–C(5′)); 4.37 (*d*, $J = 5.3$, H–C(4′)); 6.15 (*dd*, $J = 4.3$, 7.0, H–C(1′)); 7.69 (*d*, $J = 1.2$, H–C(6)). Difference-NOE (300 MHz, D_2O): 6.15 (H–C(1′)) → 7.69 (H–C(6)), 2.58 (H–C(2′)); 4.37 (H–C(4′)) → 7.69 (H–C(6)), 4.10–4.17 (H–C(5′)). ^{13}C-NMR (100 MHz, D_2O): 14.21 (*q*, *Me*–C(5)); 32.89, 37.91 (2*t*, C(6′), C(7′)); 48.82 (*t*, C(2′)); 74.39 (*d*, C(5′)); 88.31 (*s*, C(3′)); 91.25, 92.74 (2*d*, C(1′), C(4′)); 113.63 (*s*, C(5)); 142.31 (*d*, C(6)); 154.30 (*s*, C(2)); 169.26 (*s*, C(4)). EI-MS: 268 (1.7, M^+), 143 (79), 127 (39), 126 (54), 125 (39), 124 (10), 113 (10), 110 (16), 99 (100). Anal. calc. for $C_{12}H_{16}N_2O_5$: C 53.73, H 6.01, N 10.44; found: C 53.52, H 6.01, N 10.43.

*(3′S,5′R)-1-(2′-Deoxy-3′,5′-ethano-β-*D*-ribofuranosyl)thymine* (**1**). Desilylation of **32** (1.07 g, 2.80 mmol; 0.14M) with $Bu_4NF \cdot 3\ H_2O$ (1.76 g, 5.58 mmol) for 4 d at r.t. afforded **1** (521 mg, 69%), after CC (silica gel, CH_2Cl_2/MeOH 6:1) and crystallization (from MeOH/Et_2O 4:1, pentane). Colorless cubes. M.p. > 210° (dec.). TLC (CH_2Cl_2/MeOH 6:1): R_f 0.36. $[\alpha]_D^{25°} = +61.6$ ($c = 1.5$, H_2O). UV (H_2O): 265 (9700). IR (KBr): 3520*m*, 3500–3200*m*, 3170*m*, 3040*m*, 2940*m*, 2840*w*, 1710*s*, 1670*s*, 1480*s*, 1465*m*, 1440*m*, 1410*m*, 1390*m*, 1375*m*, 1360*w*, 1335*w*, 1305*m*, 1290*s*, 1280*s*, 1265*s*, 1215*m*, 1195*w*, 1155*w*, 1130*m*, 1110*m*, 1075*s*, 1050*s*, 1015*w*, 980*s*, 965*s*, 950*m*, 905*w*, 895*w*, 850*m*, 825*m*, 780*w*, 755*w*, 675*m*, 660*w*, 615*w*, 600*w*. ^{1}H-NMR (400 MHz, D_2O): 1.61–1.69, 1.75–1.85, 2.06–2.14 (3*m*, 2 H–C(6′), 2 H–C(7′)); 1.89 (*d*, $J = 1.2$, Me–C(5)); 2.15 (*dd*, $J = 10.0$, 14.0, H–C(2′)); 2.49 (*dd*, $J = 5.2$, 14.1, H–C(2′)); 4.09 (*d*, $J = 5.3$, H–C(4′)); 4.19 (*dt*, $J = 9.5$, 5.6, H–C(5′)); 6.24 (*dd*, $J = 5.2$, 10.1, H–C(1′)); 7.67 (*d*, $J = 1.2$, H–C(6)). Difference-NOE (300 MHz, D_2O): 7.67 (H–C(6)) → 6.24 (H–C(1′)), 2.49 (H_α–C(2′), neg.), 2.15 (H_β–C(2′)), 1.89 (Me–C(5)), intensity ratio H–C(1′)/H_β–C(2′) *ca.* 0.6; 6.24 (H–C(1′)) → 7.67 (H–C(6)), 4.09 (H–C(4′)), 2.49 (H_α–C(2′)); 4.09 (H–C(4′)) → 6.24 (H–C(1′)), 4.19 (H–C(5′)). ^{13}C-NMR (100 MHz, D_2O): 14.17 (*q*, *Me*–C(5)); 33.40, 37.39 (2*t*, C(6′), C(7′)); 47.80 (*t*, C(2′)); 73.70 (*d*, C(5′)); 87.52 (*d*, C(1′)); 88.07 (*s*, C(3′)); 90.58 (*d*, C(4′)); 114.25 (*s*, C(5)); 139.85 (*d*, C(6)); 154.32 (*s*, C(2)); 169.11 (*s*, C(4)). EI-MS: 268 (0.5, M^+), 143 (21), 127 (11), 126 (14). Anal. calc. for $C_{12}H_{16}N_2O_5$: C 53.68, H 6.01, N 10.44; found: C 53.22, H 6.02, N 10.41.

*(3′S,5′R)-N⁴-Benzoyl-1-(2′-deoxy-3′,5′-ethano-α-*D*-ribofuranosyl)cytosine* (**37**). Desilylation of **33** (806 mg, 2.25 mmol; 0.11M) with $Bu_4NF \cdot 3\ H_2O$ (1.42 g, 4.50 mmol) for 4.5 d at r.t. afforded **37** (398 mg, 50%), after CC (silica gel, CH_2Cl_2/MeOH 10:1) and crystallization (MeOH/Et_2O 1:1, pentane). White needles. M.p. 175° (dec.). TLC (CH_2Cl_2/MeOH 10:1): R_f 0.28. $[\alpha]_D^{25°} = -67.7$ ($c = 0.94$, MeOH). UV (MeOH): 258 (23500), 303 (11000). IR (KBr): 3400*m* (br.), 3280*m* (sh), 3060*w*, 2950*m*, 2875*w*, 2600*w*, 1805*s*, 1705*s*, 1615*s*, 1605*s*, 1560*s*, 1490*s*, 1425*m*, 1395*s*, 1365*m*, 1325*s*, 1315*s*, 1305*s*, 1270*s*, 1250*s*, 1200*m*, 1180*m*, 1135*m*, 1115*s*, 1080*s*, 1065*s*, 995*m*, 965*m*, 930*w*, 785*m*, 700*m*. ^{1}H-NMR (400 MHz, CD_3OD): 1.67–1.81, 2.01–2.15 (2*m*, 2 H–C(6′), 2 H–C(7′)); 2.40 (*dd*, $J = 2.6$, 14.4, H–C(2′)); 2.65 (*dd*, $J = 7.0$, 14.5, H–C(2′)); 4.11–4.15 (*m*, H–C(5′)); 4.51 (*d*, $J = 5.2$, H–C(4′)); 6.23 (*dd*, $J = 2.6$, 6.9, H–C(1′)); 7.51–7.56, 7.61–7.66, 7.96–7.99 (3*m*, 5 arom. H); 7.62 (*d*, $J = 7.4$, H–C(5)); 8.30 (*d*, $J = 7.5$,

H–C(6)). Difference-NOE (300 MHz, (D_6)DMSO): 4.37 (H–C(4′)) → 1.52–1.68, 1.86–2.00 (H–C(6′), H–C(7′)), 3.88–4.02 (H–C(5′)), 4.75 (OH–C(5′)), 5.25 (*s*, OH–C(3′)), 6.14 (H–C(1′)), 8.25 (H–C(6)); 6.14 (H–C(1′)) → 1.52–1.68, 1.86–2.00 (H–C(6′), H–C(7′)), 2.48 (H–C(2′)), 3.88–4.02 (H–C(5′)), 4.37 (H–C(4′)), 4.75 (OH–C(5′)), 8.25 (H–C(6)). ^{13}C-NMR (100 MHz, CD_3OD): 32.5, 36.7 (2*t*, C(6′), C(7′)); 49.0 (*t*, C(2′)); 73.1 (*d*, C(5′)); 86.9 (*s*, C(3′)); 92.9, 94.2 (2*d*, C(1′), C(4′)); 98.0 (*d*, C(5)); 129.2, 129.8, 134.1 (3*d*, arom. C); 134.7 (*s*, arom. C); 146.7 (*d*, C(6)); 157.9 (*s*, C(2)); 164.8 (*s*, C(4)); 169.0 (*s*, CO). FAB-MS (pos.): 359 (11), 358 (39, $[M + H]^+$), 357 (3.6, M^+), 243 (11), 242 (46), 217 (25), 216 (100), 154 (14), 137 (10), 136 (14), 104 (51), 99 (22). Anal. calc. for $C_{18}H_{19}N_3O_5 \cdot 0.24\ H_2O$: C 59.77, H 5.43, N 11.62; found: C 59.91, H 5.63, N 11.72.

*(3′S,5′R)-*N^4*-Benzoyl-1-(2′-deoxy-3′,5′-ethano-β-*D*-ribofuranosyl)cytosine* (**38**). Desilylation of **38** (992 mg, 2.8 mmol; 0.11M) with $Bu_4NF \cdot 3\ H_2O$ (1.75 g, 5.50 mmol) for 3.5 d at r.t. afforded **38** (488 mg, 61%), after CC (silica gel, CH_2Cl_2/MeOH 10:1) and crystallization (H_2O). Fine, white needles. M.p. 194° (dec.). TLC (CH_2Cl_2/MeOH): R_f 0.28. $[\alpha]_D^{25°} = +114.1$ (*c* = 0.92, MeOH). UV (MeOH): 259 (17600), 304 (7300). IR ($CHCl_3$): 3402*m*, 3006*m*, 2941*w*, 1699*m*, 1651*s*, 1557*s*, 1482*s*, 1400*m*, 1312*s*, 1251*s*, 1120*m*, 1068*m*, 984*m*, 893*w*, 651*w*, 619*w*. ^{1}H-NMR (400 MHz, CD_3OD): 1.62–1.69, 1.74–1.83, 1.99–2.05, 2.06–2.13 (4*m*, 2 H–C(6′), 2 H–C(7′)); 1.94 (*dd*, *J* = 9.2, 13.4, H–C(2′)); 2.73 (*dd*, *J* = 5.2, 13.4, H–C(2′)); 4.12–4.17 (*m*, H–C(4′), H–C(5′)); 6.27 (*dd*, *J* = 5.2, 9.2, H–C(1′)); 7.52–7.56, 7.62–7.66, 7.96–7.98 (3*m*, 5 arom. H, H–C(5)); 8.62 (*d*, *J* = 7.5, H–C(6)). Difference-NOE (300 MHz, (D_6)DMSO): 3.98 (H–C(4′), H–C(5′)) → 1.50–1.60, 1.66–1.76, 1.90–2.00 (H–C(6′), H–C(7′)), 4.97 (OH–C(5′)), 5.40 (OH–C(3′)), 6.18 (H–C(1′)), 11.25 (NH); 6.18 (H–C(1′)) → 2.52 (H–C(2′)), 3.92–4.02 (H–C(4′), H–C(5′)), 5.40 (OH–C(3′)), 8.58 (H–C(6)). ^{13}C-NMR (100 MHz, CD_3OD): 33.1, 36.4 (2*t*, C(6′), C(7′)); 49.2 (*t*, C(2′)), 72.8 (*d*, C(5′)); 87.3 (*s*, C(3′)); 89.5, 91.6 (2*d*, C(1′), C(4′)); 98.5 (*d*, C(5)); 129.2, 129.8, 134.1 (3*d*, arom. C); 134.7 (*s*, arom. C); 146.6 (*d*, C(6)); 157.7 (*s*, C(2)); 164.9 (*s*, C(4)); 169.1 (*s*, CO). FAB-MS (pos.): 380 (12, $[M + Na]^+$), 358 (26.0, $[M + H]^+$), 254 (13), 243 (15), 242 (70), 217 (18), 216 (100), 138 (21), 137 (26), 136 (37), 112 (50), 107 (19), 106 (11), 105 (60), 99 (22). Anal. calc. for $C_{18}H_{19}N_3O_5 \cdot 0.12\ H_2O$: C 60.13, H 5.39, N 11.69; found: C 60.07, H 5.41, N 11.76.

*(3′S,5′R)-*N^6*-Benzoyl-9-(2′-deoxy-3′,5′-ethano-α-*D*-ribofuranosyl)adenine* (**39**). Desilylation of **35** (1.22 g, 2.47 mmol; 0.10M) with $Bu_4NF \cdot 3\ H_2O$ (936 mg, 2.97 mmol; after 96 h, additional 886 mg, 2.81 mmol) and AcOH (169 µl, 2.96 mmol) for 96 h at r.t. and 48 h at 55° afforded **39** (765 mg, 81%), after CC (silica gel, CH_2Cl_2/MeOH 9:1), crystallization (CH_2Cl_2/Et_2O/MeOH 10:2:2), and recrystallization (MeOH/Et_2O 4:1, pentane). White plates. M.p. 91–93°. TLC (CH_2Cl_2/MeOH 9:1): R_f 0.37. $[\alpha]_D^{25°} = +52.8$ (*c* = 1.08, MeOH). UV (MeOH): 280 (19100). IR (KBr): 3600–3000*s* (br.), 2950*m*, 1705*s*, 1610*s*, 1580*s*, 1510*s*, 1485*s*, 1455*s*, 1415*m*, 1400*m*, 1355*m*, 1335*s*, 1300*s*, 1250*s*, 1230*s*, 1200*m*, 1160*w*, 1130*m*, 1070*s*, 1025*m*, 1000*w*, 985*w*, 965*w*, 930*w*, 900*w*, 800*m*, 750*w*, 710*s*, 690*m*, 670*m*, 645*m*. ^{1}H-NMR (400 MHz, CD_3OD): 1.71–1.81, 2.02–2.15 (2*m*, 2 H–C(6′), 2 H–C(7′)); 2.75 (*dd*, *J* = 7.4, 14.7, H–C(2′)); 2.84 (*dd*, *J* = 2.5, 14.7, H–C(2′)); 4.11 (*dt*, *J* = 8.4, 5.4, H–C(5′)); 4.35 (*d*, *J* = 5.0, H–C(4′)); 6.63 (*dd*, *J* = 2.5, 7.3, H–C(1′)); 7.53–7.58 (*m*, '*t*', 2 arom. H); 7.63–7.67 (*m*, 1 arom. H); 8.08 (*d*, *J* = 8.3, 2 arom. H); 8.71 (*s*, H–C(2)); 8.76 (*s*, H–C(8)). Difference-NOE (300 MHz, CD_3OD): 4.35 (H–C(4′)) → 8.76 (H–C(8)), 4.11 (H–C(5′)); 6.63 (H–C(1′)) → 8.76 (*s*, H–C(8)), 2.75 (H–C(2′)). ^{13}C-NMR (100 MHz, CD_3OD): 32.11, 37.25 (2*t*, C(6′), C(7′)); 48.52 (*t*, C(2′)); 73.37 (*d*, C(5′)); 87.22 (*s*, C(3′)); 88.34, 92.64 (2*d*, C(1′), C(4′)); 125.24 (*s*, C(5)); 129.47, 129.80, 133.94 (3*d*, arom. C); 135.03 (*s*, arom. C); 144.96 (*d*, C(8)); 151.22 (*s*, C(6), C(4)); 153.01 (*d*, C(2)); 168.14 (*s*, CO). FAB-MS (pos.): 763 (4, $[2M + H]^+$), 383 (20), 382 (64, $[M + H]^+$), 381 (5.8, M^+), 266 (13), 241 (24), 240 (100), 154 (25), 137 (18), 136 (25), 105 (47), 99 (12). Anal. calc. for $C_{19}H_{19}N_5O_4 \cdot 1.1$ MeOH: C 57.88, H 5.68, N 16.75; found: C 57.65, H 5.51, N 16.97.

*(3′S,5′R)-*N^6*-Benzoyl-9-(2′-deoxy-3′,5′-ethano-β-*D*-ribofuranosyl)adenine* (**40**). Desilylation of **36** (852 mg, 1.72 mmol; 0.09M) with $Bu_4NF \cdot 3\ H_2O$ (651 mg, 2.1 mmol) for 12 h at r.t. and 5 h at 50° afforded **40** (530 mg, 81%), after quenching with NH_4Cl (500 mg), CC (silica gel, CH_2Cl_2/MeOH 9:1), and crystallization from H_2O. Colorless needles. M.p. > 125° (dec.). TLC (CH_2Cl_2/MeOH 9:1): R_f 0.47. $[\alpha]_D^{25°} = +16.8$ (*c* = 1.19, MeOH). UV (MeOH): 279 (19400). IR (KBr): 3600–3000*s* (br.), 2950*w*, 1700*s*, 1660*w*, 1610*s*, 1590*s*, 1525*m*, 1480*m* (sh), 1455*s*, 1440*m*, 1360*m*, 1320*m* (sh), 1305*m*, 1250*s*, 1190*w*, 1160*w*, 1120*m*, 1095*m*, 1075*m*, 1050*m*, 1040*w*, 1010*w*, 985*w*, 960*w*, 900*w*, 820*w*, 800*w*, 755*w*, 710*m*, 700*m*, 640*w*. ^{1}H-NMR (400 MHz, CD_3OD): 1.66–1.75, 1.90–2.02, 2.10–2.16 (3*m*, 2 H–C(6′), 2 H–C(7′)); 2.63 (*dd*, *J* = 5.6, 13.4, H–C(2′)); 2.70 (*dd*, *J* = 9.6, 13.3, H–C(2′)); 4.12–4.17 (*m*, H–C(4′), H–C(5′)); 6.55 (*dd*, *J* = 5.6, 9.6, H–C(1′)); 7.53–7.57 (*m*, 2 arom. H); 7.63–7.67 (*m*, 1 arom. H); 8.08 (*d*, *J* = 7.2, 1 arom. H); 8.67 (*s*, H–C(8)); 8.69 (*s*, H–C(2)). Difference-NOE (300 MHz, CD_3OD): 4.12–4.17 (H–C(4′), H–C(5′)) → 6.55 (H–C(1′)), 2.10–2.16, 1.90–2.02, 1.66–1.75 (H–C(6′), H–C(7′)); 6.55 H–C(1′)) → 8.67 (H–C(8)), 4.12–4.17 (H–C(4′)), 2.63 (H–C(2′)). ^{13}C-NMR (100 MHz, CD_3OD): 33.10, 36.26 (2*t*, C(6′), C(7′)); 48.00 (*t*, C(2′)); 72.86 (*d*, C(5′)); 87.33 (*s*, C(3′)); 87.65 (*d*, C(1′)); 91.65 (*d*, C(4′)); 125.33 (*s*, C(5)); 129.47, 129.80, 133.94 (3*d*, arom. C); 135.01 (*s*, arom. C); 144.34 (*d*, C(8)); 151.22 (*s*, C(4)); 153.18 (*s*, C(6)); 153.21 (*d*, C(2)); 168.12 (*s*, CO). FAB-MS (pos.): 383 (12), 382 (36, $[M + H]^+$), 381 (3.1, M^+), 266 (13), 242 (11), 241 (27), 240 (100), 136

(16), 105 (61), 99 (17). Anal. calc. for $C_{19}H_{19}N_5O_4 \cdot H_2O$: C 57.14, H 5.30, N 17.53; found: C 57.29, H 5.18, N 17.56.

General Procedure for the Deprotection of Nucleosides **37**–**42**. A 0.06–0.2M soln. of the corresponding nucleoside **37**–**42** in conc. aq. NH_3 soln. was heated for 2–5 h to 55–60°. After cooling to r.t. and evaporation, the residual crude product was dissolved in MeOH, if possible, adsorbed on silica gel (0.2–1.0 g) and purified by CC, followed by crystallization, to give the corresponding pure free nucleoside **2**–**4** or **6**–**8**.

*(3'S,5'R)-1-(2'-Deoxy-3',5'-ethano-α-*D*-ribofuranosyl)cytosine* (**6**). From **37** (200 mg, 0.56 mmol; 0.19M) was obtained **6** (131 mg, 92%), after 2 h at 55°, CC (silica gel, CH_2Cl_2/MeOH 10:1 → 1:1), and crystallization (MeOH/Me_2CO 1:2, pentane). White needles. M.p. 223° (dec.). TLC (CH_2Cl_2/MeOH 1:1): R_f 0.57. $[\alpha]_D^{25°} = -35.1$ (c = 1.03, MeOH). UV (MeOH): 272 (8500). IR (KBr): 3370*s*, 3310*s*, 3200*s* (br.), 3120*s* (br.), 2960*m*, 2940*m*, 2930*m*, 2870*m*, 1670*s*, 1650*s*, 1630*s* (sh), 1605*s*, 1520*s*, 1495*s*, 1435*m*, 1405*m*, 1370*m*, 1355*m*, 1335*m*, 1310*m*, 1290*s*, 1280*s*, 1245*m*, 1190*s*, 1130*s*, 1115*s*, 1105*s*, 1070*s*, 1055*s*, 1000*m*, 960*m*, 940*m*, 835*w*, 790*s*, 720*m*. ^{1}H-NMR (400 MHz, CD_3OD): 1.64–1.76, 1.90–2.09 (2*m*, 2 H–C(6'), 2 H–C(7')); 2.29 (*dd*, J = 3.6, 14.3, H–C(2')); 2.57 (*dd*, J = 7.1, 14.3, H–C(2')); 4.06–4.12 (*m*, H–C(5')); 4.36 (*d*, J = 5.2, H–C(4')); 5.89 (*d*, J = 7.5, H–C(5)); 6.20 (*dd*, J = 3.6, 7.0, H–C(1')); 7.85 (*d*, J = 7.5, H–C(6)). ^{13}C-NMR (100 MHz, CD_3OD): 32.4, 37.1 (2*t*, C(6'), C(7')); 49.1 (*t*, C(2')); 73.5 (*d*, C(5')); 87.0 (*s*, C(3')); 91.5, 93.2 (2*d*, C(1'), C(4')); 95.6 (*d*, C(5)); 143.1 (*d*, C(6)); 158.4 (*s*, C(2)); 167.9 (*s*, C(4)). FAB-MS (pos.): 508 (120), 507 (36, $[2M + H]^+$), 276 (12, $[M + Na]^+$), 255 (13), 254 (70 $[M + H]^+$), 253 (6.1, M^+), 155 (35), 154 (94), 153 (10), 152 (12), 124 (15), 121 (11), 120 (17), 113 (10), 112 (100), 108 (11), 107 (32), 105 (10), 99 (13).

*(3'S,5'R)-1-(2'-Deoxy-3',5'-ethano-β-*D*-ribofuranosyl)cytosine* (**2**). From **38** (106 mg, 0.30 mmol; 0.06M) was obtained **2** (60 mg, 80%), after 2 h at 55°, CC (silica gel, CH_2Cl_2/MeOH 10:1 → 4:1 → 1:1), and crystallization (MeOH/Me_2CO 1:5, pentane). White needles. M.p. 218–220° (dec.). $[\alpha]_D^{25°} = +121.9$ (c = 0.51, MeOH). UV (MeOH): 271 (8300). IR (KBr): 3450*s* (sh), 3360*s* (br.), 3200*m*, 3120*s*, 2970*m*, 2950*m*, 2870*m*, 2810*m*, 1655*s*, 1630*s*, 1605*s* (sh), 1530*s*, 1485*s*, 1410*s*, 1370*s*, 1340*m*, 1305*s*, 1290*s*, 1245*m*, 1215*m*, 1175*m*, 1120*m*, 1085*m*, 1060*s*, 1045*s*, 990*m*, 960*m*, 915*m*, 900*w*, 805*m*, 795*m*, 785*m*, 725*m*, 640*m*. ^{1}H-NMR (400 MHz, CD_3OD): 1.59–1.66, 1.72–1.82, 1.97–2.15 (3*m*, 2 H–C(6'), 2 H–C(7')); 1.90 (*dd*, J = 9.6, 13.4, H–C(2')); 2.52 (*dd*, J = 5.2, 13.5, H–C(2')); 4.03 (*d*, J = 5.6, H–C(4')); 4.10 (*dt*, J = 8.3, 5.5, H–C(5')); 5.91 (*d*, J = 7.4, H–C(5)); 6.26 (*dd*, J = 5.1, J = 9.6, H–C(1')); 8.26 (*d*, J = 7.4, H–C(6)). Difference-NOE (300 MHz, CD_3OD): 8.26 (H–C(6)) → 6.26 (H–C(1')), 5.91 (H–C(5)), 2.52 (H_α–C(2'), neg.), 1.90 (H_β–C(2')), intensity ratio H–C(1')/H_β–C(2') *ca.* 0.6; 6.26 (H–C(1')) → 8.26 (H–C(6)), 5.91 (H–C(5), neg.), 4.03 (H–C(4')), 2.52 (H_α–C(2')); 4.03 (H–C(4')) → 6.26 (H–C(1')), 4.10 (H–C(5')). ^{13}C-NMR (100 MHz, CD_3OD): 33.1, 36.5 (*t*, C(6'), C(7')); 48.5 (*t*, C(2')); 72.8 (*d*, C(5')), 87.1 (*s*, C(3')), 88.4, 90.8 (2*d*, C(1'), C(4')); 96.2 (*d*, C(5)); 142.8 (*d*, C(6)); 158.2 (*s*, C(2)); 167.7 (*s*, C(4)). FAB-MS (pos.): 276 (12, $[M + Na]^+$), 254 (52, $[M + H]^+$), 253 (5.0, M^+), 176 (7), 112 (64).

*(3'S,5'R)-9-(2'-Deoxy-3',5'-ethano-α-*D*-ribofuranosyl)adenine* (**7**). From **39** (125 mg, 0.328 mmol; 0.11M) was obtained **7** (62 mg, 68%), after 3.75 h at 50°, CC (silica gel, CH_2Cl_2/MeOH 3:1), and crystallization (MeOH/pentane). White plates. M.p. 109–111°. TLC (CH_2Cl_2/MeOH 3:1): R_f 0.47. $[\alpha]_D^{25°} = +69.8$ (c = 0.46, H_2O). UV (H_2O): 259 (14000). IR (KBr): 3600–2600*s* (br.), 2960*m*, 2940*m*, 1685*s*, 1645*s*, 1610*s*, 1575*m*, 1475*m*, 1420*m*, 1370*m*, 1335*s*, 1300*s*, 1245*m*, 1225*m*, 1200*s*, 1105*s*, 1060*s*, 995*w*, 960*w*, 930*w*, 910*w*, 795*w*, 735*w*, 710*w*, 650*m*. ^{1}H-NMR (400 MHz, D_2O): 1.64–1.76, 2.04–2.13 (2*m*, 2 H–C(6'), 2 H–C(7')); 2.73–2.90 (*m*, 2 H–C(2')); 4.13–4.18 (*m*, H–C(5')); 4.32 (*d*, J = 5.2, H–C(4')); 6.32 (*dd*, J = 3.9, 6.1, H–C(1')); 8.02 (*s*, H–C(2)); 8.25 (*s*, H–C(8)). ^{13}C-NMR (100 MHz, D_2O): 32.65, 37.93 (2*t*, C(6'), C(7')); 49.01 (*t*, C(2')); 74.34 (*d*, C(5')); 88.66 (*s*, C(3')); 89.27, 92.41 (2*d*, C(1'), C(4')); 121.26 (*s*, C(5)); 143.70 (*d*, C(8)); 150.31 (*s*, C(4)); 154.74 (*d*, C(2)); 157.90 (*s*, C(6)). FAB-MS (pos.): 370 (7), 279 (11), 278 (35, $[M + H]^+$), 277 (21, M^+), 186 (10), 136 (21).

*(3'S,5'R)-9-(2'-Deoxy-3',5'-ethano-β-*D*-ribofuranosyl)adenine* (**3**). From **40** (198 mg, 0.519 mmol; 0.13M) was obtained **3** (122 mg, 85%), after 2.5 h at 55°, CC (silica gel, CH_2Cl_2/MeOH 3:1), and crystallization (MeOH/Et_2O 1:4, pentane). White cubes. M.p. > 175° (dec.). TLC ($MeCl_2$/MeOH 3:1): R_f 0.57. $[\alpha]_D^{25°} = +9.3$ (c = 0.53, H_2O). UV (H_2O): 258 (14000). IR (KBr): 3600–2500*s* (br.), 1640*s*, 1600*s*, 1575*s*, 1475*m*, 1420*m*, 1370*m*, 1330*m*, 1300*m*, 1250*m*, 1210*m*, 1165*m*, 1155*m*, 1010*m*, 980*w*, 960*w*, 895*w*, 835*w*, 810*w*, 800*w*, 730*w*, 650*m*. ^{1}H-NMR (400 MHz, D_2O): 1.64–1.72, 1.80–1.90, 2.08–2.16 (3*m*, 2 H–C(6'), 2 H–C(7')); 2.50 (*dd*, J = 10.0, 13.9, H–C(2')); 2.63 (*dd*, J = 5.3, 13.9, H–C(2')); 4.16–4.22 (*m*, H–C(4'), H–C(5')); 6.26 (*dd*, J = 5.3, 10.0, H–C(1')); 8.04 (*s*, H–C(2)); 8.21 (*s*, H–C(8)). Difference-NOE (300 MHz, D_2O): 8.21 (H–C(8)) → 6.26 (H–C(1')), 2.63 (H_α–C(2'), neg.), 2.50 (H_β–C(2')), intensity ratio H–C(1')/H_β–C(2') *ca.* 1.0; 6.26 (H–C(1')) → 8.04 (H–C(8)), 4.16–4.22 (H–C(4'), H–C(5')), 2.63 (H_α–C(2')); 4.16–4.22 (H–C(4'), H–C(5')) → 6.26 (H–C(1')), 2.08–2.16 (H–C(6'), H–C(7')), 1.64–1.72 (H–C(6'), H–C(7')). ^{13}C-NMR (100 MHz, D_2O): 33.60, 36.92 (2*t*, C(6'), C(7')); 48.35 (*t*, C(2')); 73.70 (*d*, C(5')); 87.57 (*d*, C(1')); 88.60 (*s*, C(3')); 91.35 (*d*, C(4')); 121.04 (*s*, C(5)); 142.45 (*d*, C(8)); 150.88 (*s*, C(4)); 155.03 (*d*, C(2)); 157.84 (*s*, C(6)). FAB-MS (pos.): 370 (12), 279 (21), 278 (63, $[M + H]^+$), 277 (21, M^+), 242 (16), 186 (10), 136 (40).

(3'S,5'R)-9-(2'-Deoxy-3',5'-ethano-α-D-ribofuranosyl)guanine (**8**). From **41** (300 mg, 0.826 mmol; 0.2M) was obtained, **8** (133 mg, 55%), after 4.5 h at 60° as a white solid, which was suspended in MeOH (40 ml), refluxed for 30 min, and filtered. White amorphous solid. $[\alpha]_D^{25°} = +113.6$ ($c = 0.51$, DMSO). UV (10 mM Na_2HPO_4, pH 7): 252 (14000), 269 (10100, sh). IR (KBr): 3440*s*, 3390*s*, 3310*s*, 3150*s*, 2920*s*, 2740*m*, 2650*m* (br.), 1900*w* (br.), 1745*s*, 1690*s*, 1650*s*, 1630*s*, 1590*s*, 1550*s*, 1485*s*, 1390*s*, 1360*s*, 1325*s*, 1260*m*, 1180*m*, 1110*m*, 1080*m*, 1060*m*, 1000*w*, 910*m*, 830*w*, 780*m*, 695*m*. ^{1}H-NMR (400 MHz, (D_6)DMSO): 1.51–1.67, 1.82–1.88, 1.90–1.95 (3*m*, 2 H–C(6'), 2 H–C(7')); 2.34–2.67 (*m*, 2 H–C(2')); 3.90–3.97 (*m*, H–C(5')); 4.09 (*d*, $J = 4.9$, H–C(4')); 4.65–4.66 (*m*, OH–C(5')); 5.57 (*s*, OH–C(3')); 6.17 (*dd*, $J = 4.3, 6.4$, H–C(1')); 6.46 (*s*, NH_2–C(2)); 8.03 (s, H–C(8)); 10.65 (*s*, H–N(1)). ^{13}C-NMR (100 MHz, (D_6)DMSO): 30.9, 36.4 (2*t*, C(6'), C(7')); 47.1 (*t*, C(2')); 71.4 (*t*, C(5')); 84.1, 90.0 (2*d*, C(1'), C(4')); 85.0 (*s*, C(3')); 116.4 (*s*, C(5)); 135.7 (*d*, C(8)); 150.7 (*s*, C(4)); 153.5 (*s*, C(2)); 156.7 (*s*, C(6)).

(3'S,5'R)-9-(2'-Deoxy-3',5'-ethano-β-D-ribofuranosyl)guanine (**4**). From **42** (83 mg, 0.228 mmol; 0.08M) was obtained **4** (53 mg, 80%), after 5 h at 55° and crystallization from hot H_2O (6 ml). White needles. M.p. > 240°. $[\alpha]_D^{25°} = +14.4$ ($c = 0.48$, DMSO). UV (10 mM Na_2HPO_4, pH 7): 252 (13000), 269 (9400, sh). IR (KBr): 3400*s* (sh), 3330*s*, 3200*s*, 2930*m*, 2720*m*, 1725*s*, 1690*s*, 1630*s*, 1600*s*, 1570*s*, 1535*s*, 1415*m*, 1390*s*, 1365*m*, 1320*s*, 1280*m*, 1250*m*, 1180*s*, 1120*m*, 1065*s*, 985*m*, 965*m*, 945*w*, 930*w*, 900*w*, 865*w*, 780*m*, 730*w*, 680*m*, 630*m*. ^{1}H-NMR (400 MHz, (D_6)DMSO): 1.48–1.55, 1.71–1.80, 1.87–1.96 (3*m*, 2 H–C(6'), 2 H–C(7')); 2.36 (*d*, $J = 7.3$, 2 H–C(2')); 3.87 (*d*, $J = 5.4$, H–C(4')); 3.92 (*m*, H–C(5')); 4.74 (*d*, $J = 5.9$, OH–C(5')); 5.35 (*s*, OH–C(3')); 6.08 (*m* '*t*', H–C(1')); 6.45 (br. *s*, NH_2–C(2)); 8.02 (*s*, H–C(8)); 10.65 (br. *s*, H–N(1)). Difference-NOE (300 MHz, (D_6)DMSO): 8.02 (H–C(8)) → 6.08 (H–C(1')), 4.74 (OH–C(5')), 2.36 (H–C(2')). ^{13}C-NMR (100 MHz, (D_6)DMSO): 31.7, 35.1 (2*t*, C(6'), C(7')); 46.5 (*t*, C(2')); 70.7 (*d*, C(5')); 83.4, 89.4 (2*d*, C(1'), C(4')); 85.0 (*s*, C(3')); 116.5 (*s*, C(5)); 135.2 (*d*, C(8)); 150.8 (*s*, C(4)); 153.6 (*s*, C(2)); 156.6 (*s*, C(6)).

2-{(1'S,5'S,6'R)-6'-Hydroxy-3',3'-dimethyl-2',4'-dioxabicyclo[3.3.0]oct-6'-yl}ethyl (S)-Camphanoate (**20**). To a soln. of (+)-**16** (36.5 mg, 0.180 mmol; 96%ee) in CH_2Cl_2 (1 ml) and pyridine (0.5 ml) was added a soln. of (−)-(*S*)-camphanoyl chloride (59 mg, 0.272 mmol) in CH_2Cl_2 (1 ml) at 0°. After 5 min, the ice-bath was removed and the mixture stirred for 1 h at r.t. After addition of 1M aq. $NaHCO_3$ (5 ml), the aq. layer was extracted with CH_2Cl_2 (2 × 5 ml), the combined org. phase evaporated, residual pyridine removed by coevaporation with CCl_4 (2 × 5 ml) and the crude product purified by CC (silica gel, hexane/AcOEt 1:2): 70 mg of a colorless oil, which crystallized upon drying at r.t./0.01 Torr. Twofold recrystallization from Et_2O/hexane afforded **20** (53 mg, 77%) as colorless prisms which could directly be used for X-ray crystal-structure determination. M.p. 97°. TLC (hexane/AcOEt 1:2): R_f 0.59. IR (KBr): 3470*m* (br.), 2970*m*, 2940*m*, 1790*s*, 1730*s*, 1450*w*, 1400*w*, 1375*m*, 1350*m*, 1325*m*, 1270*s*, 1210*m*, 1190*m*, 1165*s*, 1110*s*, 1065*s*, 1040*s*, 1025*w*, 995*m*, 970*w*, 955*w*, 940*w*, 930*m*, 900*w*, 870*m*, 830*w*, 820*w*, 795*w*, 785*w*, 740*w*, 620*w*. ^{1}H-NMR (300 MHz, C_6D_6): 0.69 (*s*, Me–C(4'')); 0.82, 0.83 (2*s*, 2 Me–C(7'')); 1.15, 1.37 (2*s*, Me_2C); 1.20–1.25, 1.34–1.40, 1.68–1.79, 1.82–1.95, 2.00–2.15 (5*m*, H–C(2), H–C(7'), H–C(8'), H–C(5''), H–C(6'')); 1.47 (*s*, OH); 4.03 (*dd*, $J = 1.6, 3.9$, H–C(5')); 4.37–4.53 (*m*, 2 H–C(1)); 4.56–4.59 (*m* '*t*', H–C(1')). ^{13}C-NMR (75 MHz, C_6D_6): 9.78 (*q*, Me–C(4'')); 16.51, 16.80 (2*q*, 2 *Me*–C(7'')); 23.99, 26.54 (2*q*, *Me*$_2$C); 28.81, 30.11, 30.91, 35.03, 35.45 (5*t*, C(2), C(7'), C(8'), C(5''), C(6'')); 54.00, 54.71 (2*s*, C(4''), C(7'')); 62.97 (*t*, C(1)); 81.19 (*d*, C(1'), C(5')); 81.28 (*s*, C(6')); 86.40 (*d*, C(1'), C(5')); 90.87 (*s*, C(1'')); 109.96 (*s*, Me_2C); 167.84, 177.30 (2*s*, CO). EI-MS: 382 (6.0, M^+), 368 (28), 367 (68), 325 (11), 324 (52), 307 (15), 268 (20), 185 (27), 181 (19), 169 (22), 154 (15), 153 (65), 152 (16), 151 (20), 137 (54), 136 (28), 135 (39), 134 (31), 127 (54), 126 (59), 125 (58), 121 (20), 110 (39), 109 (100), 108 (78), 107 (76), 106 (21), 101 (44). Anal. calc. for $C_{20}H_{30}O_7$: C 62.81, H 7.91; found: C 62.92, H 8.10.

X-Ray Structure of **20**. $C_{20}H_{30}O_7$; orthorombic space group $P2_12_12$, $Z = 8$; $a = 15.509$, $b = 21.812$, $c = 12.137$ Å. Intensities were measured with an *Enraf-Nonius-CAD4* diffractometer equipped with a graphite monochromator (MoK_α, $\lambda = 0.7107$ Å). Of the 4015 independent reflections ($\theta < 25°$), 1924 with $I > 3\,\sigma(I)$ were used in the refinement. The structure was solved using direct methods with SHELXS 86 [53] and refined by full-matrix least-squares analysis (SHELXS 76 [54]). Non-H-atoms were refined anisotropically. The positions of the H-atoms (with the exception of the H-atom of the tertiary OH group) were calculated and included in the final structure factor calculation. The weighting scheme used was $\sigma(F)^{-2}$. The refinement converged at $R = 0.052$, $R_w = 0.043$.

X-Ray Structure of **1**. $C_{12}H_{16}N_2O_5$; orthorhombic space group $P2_12_12_1$, $Z = 4$; $a = 5.970$, $b = 14.265$, $c = 14.368$ Å. From a crystal of approximate size 0.3 × 0.3 × 0.2 mm, 1713 independent reflexions were measured. The structure was solved by direct methods with SHELXS-86 [53]. Non-H-atoms were refined anisotropically and H-atoms isotropically with full-matrix least-squares analysis (SHELX76 [54] using 1387 reflexions with $I > 3\,\sigma(I)$. The weighting scheme applied was $\sigma(F)^{-2}$. Final agreement factors are $R = 0.031$ and $R_w = 0.028$.

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