168. Nucleic-Acid Analogs with Constraint Conformational Flexibility in the Sugar-Phosphate Backbone 'Tricyclo-DNA'

Part 1

Preparation of [(5′*R*,6′*R*)-2′-Deoxy-3′,5′-ethano-5′,6′-methano-β-D-ribofuranosyl]thymine and -adenine, and the Corresponding Phosphoramidites for Oligonucleotide Synthesis

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Dedicated to Professor *Dieter Seebach* on the occasion of his 60th birthday

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The synthesis of the tricyclo-deoxynucleoside analogs **1** and **2** and of the corresponding cyanoethyl phosphoramidite building blocks **16** and **21** for oligonucleotide synthesis is described. These tricyclic deoxynucleoside analogs differ from the recently introduced bicyclo-deoxynucleosides by an additional cyclopropane unit joined to the centers C(5′) and C(6′) of the latter (see *Fig. 1*), and thus represent a further member of the class of nucleoside analogs with constraint conformational flexibility. The synthesis of the tricyclo-deoxynucleosides was achieved by a diastereoselective carbene addition to the enantiomerically pure silyl enol either **8**/**9** and a *Vorbrüggen* condensation of the tricyclic carbohydrate unit **10**/**11** with *in situ* persilylated thymine and N^6-benzoyladenine. Selective tritylation of the tertiary OH–C(5′) and phosphinylation of OH–C(3′) of **1** and **2** afforded the corresponding phosphoramidites **16** and **21**. The '*exo*'-configuration of the newly introduced cyclopropane ring was confirmed by ^{1}H-NMR-NOE spectroscopy. The α-D- and β-D-configuration at C(1′) of the nucleoside analogs **1** and **14** (**2** and **19**, resp.) was assigned by ^{1}H-NMR-NOE spectroscopy and NOESY. Modeling studies of the β-D-anomeric nucleoside analog **1** indicate a preference for the 2′-*endo*-conformation of the furanose ring and a partial correction of the torsion angle γ to the *anti*-clinal range compared to bicyclo-deoxynucleosides.

1. Introduction. – Due to their molecular recognition properties, oligonucleotide analogs are of interest in medicinal chemistry as potential antisense and antigene drugs [1]. *Via* specific and strong association with natural RNA or DNA, oligonucleotide analogs also play an important role as tools for the modulation of gene regulation processes, *e.g.*, as potential gene activators and transcription promoters *in vitro* [2]. Furthermore, pairing systems based on oligonucleotides with defined complexation patterns are of interest in materials science [3], *e.g.*, as molecular scaffolds for the precise spatial positioning of metal clusters and nanocrystals [4] or as numerical functional units in computer technology [5]. Oligonucleotide analogs with well-defined structural alterations in their sugar-phosphate backbone can also contribute to the rationalization of the base-pairing properties of natural DNA. Hence, there exists considerable interest in the development of such oligonucleotide analogs.

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[1]) Part of the planned Ph.D. Thesis of *R.S.*

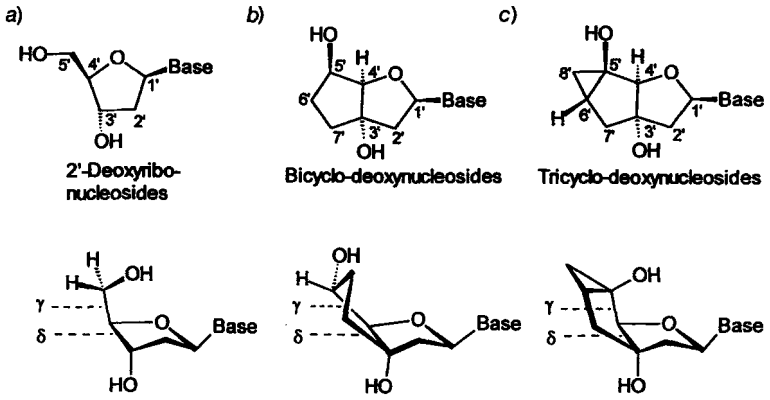


Fig. 1. a) *2'-Deoxyribonucleosides containing the nucleobases adenine, thymine, guanine, and cytosine.* b) *Bicyclo-deoxynucleosides* [6]. c) *Tricyclo-deoxynucleosides* (= 2'-deoxy-3'5'-ethano-5',6'-methano-β-D-ribonucleosides (or 2'-deoxy-3',5',5'-propane[1,2,3]triyl-β-D-ribonucleosides), see *Footnote 2*) *of the natural nucleobase thymine and the* N^6*-benzoyl-protected adenine*

The recently introduced 'bicyclo-DNA' [6] is an analog that differs from natural DNA by an additional ethylene bridge between the centres C(3') and C(5') (*Fig. 1,b*). This change in the carbohydrate moiety results in a locked 1'-*exo*-conformation which corresponds to the repeating nucleotide unit in DNA duplexes of the B-form. The torsion angle γ (*Fig. 1*) is restricted to the *anti*-periplanar range (140–160°) and deviates from that observed in natural A- or B-DNA by *ca.* + 100°. This shift of γ from the *syn*-clinal in the natural system to the *anti*-periplanar range in bicyclic oligonucleotides altered the relative stability of duplexes and triplexes and strongly influenced the preferences of the base-pairing modes. It has been shown that homopurine and homopyrimidine sequences of bicyclo-DNA preferentially select the *Hoogsteen*- and reversed-*Hoogsteen* base-pairing mode [7]. Meanwhile, several other bicyclic nucleoside analogs were synthesized and incorporated into oligonucleotides, the most important ones having been reviewed recently [8].

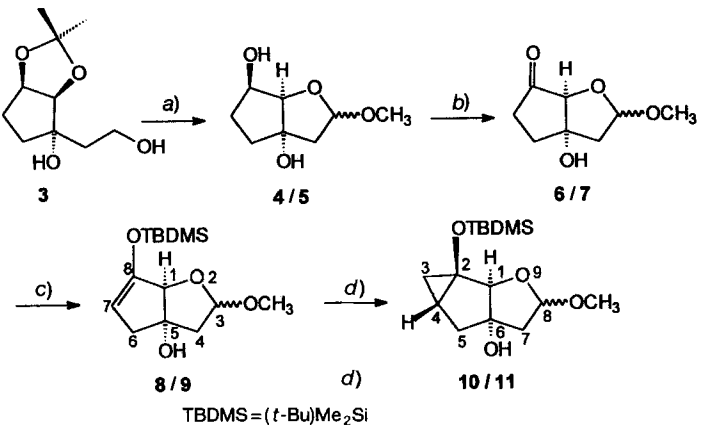
Tricyclo-DNA[2]) is designed to give rise to a further restriction in the conformational flexibility of the sugar-phosphate backbone compared to bicyclo-DNA. Specifically, the backbone torsion angle γ (*Fig. 1,c*) is rendered rigid and positioned in the *anti*-clinal range (110–130°). This corresponds to a partial correction, relative to that found in bicyclo-DNA, towards values for γ observed in A- and B-DNA (40–60°). Therefore, an improvement in affinity to complementary RNA and DNA is expected. Furthermore, tricyclo-DNA with its double tertiary phosphodiester functions should be more resistant

[2]) In extension of the bicyclo-DNA nomenclature (see [6], *Footnote 3*), the name tricyclo-DNA and, correspondingly, tricyclo-deoxynucleosides was chosen to denominate this type of nucleotide and nucleoside analog. The numbering scheme as depicted in *Fig. 1* for nucleosides was chosen in order to be able to use the structural descriptors and notions common in natural nucleotide chemistry (an alternative numbering scheme results when 3',5',5'-bridging by a propane-1,2,3-triyl moiety is assumed; see *Exper. Part*, names of **1**, **2**, **14**, **16**, **19**, and **21**). For sugar intermediates **3**–**11**, the systematic IUPAC nomenclature with the numbering scheme depicted in *Fig. 1* was used.

towards nucleases, and, due to the enlarged alkyl moiety of the tricyclo-nucleotides, an increase in lipophilicity of the corresponding oligodeoxynucleotides and, therefore, enhanced cell permeability is expected.

2. Synthesis of the Tricyclic Carbohydrate Unit. – In our synthetic plan, we envisaged the assembly of the tricyclic carbohydrate building block **10/11** by stereoselective cyclopropanation of the enol ether **8/9**, which is easily available from the enantiomerically pure diol **3**, prepared earlier in our laboratory [6]. Starting from **3**, the synthesis of the carbohydrate unit **10/11** could be achieved in four steps (*Scheme 1*).

Scheme 1



a) 1. *Dess-Martin* reagent (1.3 equiv.), CH_2Cl_2, r.t., 2 h; 2. *Amberlyst 15*, MeOH, r.t., 18 h; 77%. *b*) *Dess-Martin* reagent (1.3 equiv.), CH_2Cl_2, r.t., 2 h; 67%. *c*) 1. LDA (1.5 equiv.), THF, −74°; 15 min; 2. (*t*-Bu)Me_2SiCl, THF, −74°, 2 h; 92%. *d*) CH_2I_2/Ag-Zn, Et_2O, 34°, 3 h; 58%.

Oxidation of the primary alcohol group of (−)-**3** with the *Dess-Martin* reagent [9] to the corresponding aldehyde followed by an acid-catalyzed deketalization/acetalization step in MeOH yielded 77% of the bicyclic diol **4/5** as a 2:1 anomer mixture (α/β)[3]. Formation of the ketones **6/7** in a 2:1 ratio (α/β)[4] was again achieved by *Dess-Martin* oxidation of the secondary OH group of **4/5** in 67% yield. After regioselective deprotonation of **6/7** using lithium diisopropylamide (LDA) at −74° and (*tert*-butyl)dimethylsilyl-protection of the enolate, the silyl enol ether **8/9** became available as a 2:1 mixture (α/β) in 92% yield. For the introduction of the cyclopropane ring at the centers C(7) and C(8) of **8/9**, we envisaged a cyclopropanation according to an improved *Simmons-Smith* procedure [10]. Reaction of the carbene formed by CH_2I_2 and the

[3]) The ratio of isomers with α-D- and β-D-configuration at the anomeric center was determined for the mixtures **4/5**, **6/7**, **8/9**, and **10/11** by ^{1}H-NMR. The mixture **4/5** can be separated by column chromatography. As this separation is not necessary for the preparation of the tricyclic carbohydrate precursor, the anomer mixture was employed for the next reaction step. The β-D-configuration at the anomeric center of **5** was assigned on the basis of the ^{1}H-NMR difference NOE spectra of **5**.

[4]) All anomer mixtures **6/7**, **8/9**, and **10/11** can be separated by column chromatography; however, separation into the pure anomers was only done for analytical purposes.

Ag-Zn couple yielded the tricyclic compound **10/11** in 58% yield as a 2:1 mixture (α/β), besides 23% of non-converted starting material. The reaction seems to be stereospecific as no products arising from an attack from the β-face to the double bond could be isolated[5]). The diastereoselectivity can be explained in terms of a preferred attack to the double bond from the convex side of the bicyclo[3.3.0] system ('*exo*' product) and by a directing effect of the homoallylic OH group[6]) at C(5) in **8/9** both working in concert.

The '*exo*'-configuration of the products **10/11** was confirmed by ^{1}H-NMR difference NOE spectra of a desilylated sample of the α-D-isomer **10** (see *Exper. Part*). A strong and mutual NOE between H–C(1) and H_α–C(3) and no NOE between H–C(1) and H–C(4) or between H_β–C(3) and H_β–C(5) or H_β–C(7) clearly indicate the '*exo*'-configuration (all ^{1}H-NMR signals were unambiguously assigned by a ^{1}H-COSY spectrum).

3. Synthesis of the Tricyclic Nucleoside Analogs and the Corresponding Phosphoramidites. – For the formation of the tricyclic nucleoside analogs **12/13** and **17/18** (*Scheme 2*) from the sugar derivative **10/11**, we chose the *Lewis*-acid-induced formation of the nucleosidic bond between the silylated compound **10/11** and the persilylated thymine and N^6-benzoyladenine according to the method of *Vorbrüggen* [13].

The use of trimethylsilyl trifluoromethanesulfonate (Me_3SiOTf) as *Lewis* acid proved to be advantageous over the use of $SnCl_4$, which afforded lower yields and substantial amounts of N^3-nucleosides in the case of thymine. Me_3SiOTf-Catalyzed condensation of the mixture **10/11**[7]) with persilylated thymine in MeCN and in the presence of *N,O*-bis(trimethylsilyl)acetamide (BSA) afforded only the N^1-tricyclo-thymidine **12/13** in a ratio of 1.7:1 (α/β) in 65% yield. After the selective removal of the Me_3Si group at OH–C(3′) with 1 equiv. of Bu_4NF, the mixture **12/13** could be separated into the pure α-D- and β-D-isomers by chromatography. In the case of the purine base, condensation of **10/11** with N^6-benzoyladenine was performed in $ClCH_2CH_2Cl$ and in the presence of BSA, and yielded 72% of the N^9-nucleosides **17/18** in a ratio of 1.4:1 (α/β). The mixture **17/18** could be chromatographically separated into the pure isomers. Both α-D-anomers **12** and **17**, could be equilibrated under the corresponding nucleosidation conditions into the α/β-D-mixtures, thus providing additional access to the desired β-D-anomers **13** and **18**. After deprotection using Bu_4NF in THF, the nucleoside analogs **1**, **14**, **2**, and **19** bearing free OH groups at the centers C(3′) and C(5′) became available. The relative configuration of C(1′) of the thymidine and adenosine analgos **1**, **14**, **2**, and **19** was unambiguously assigned by their ^{1}H-NMR difference NOE spectra.

Irradiation at the resonance of H–C(1′) resulted in the case of the β-D-anomers **1** and **2** in a strong NOE on H–C(4′), which was weak or absent in the case of the α-D-anomers **14** and **19**.

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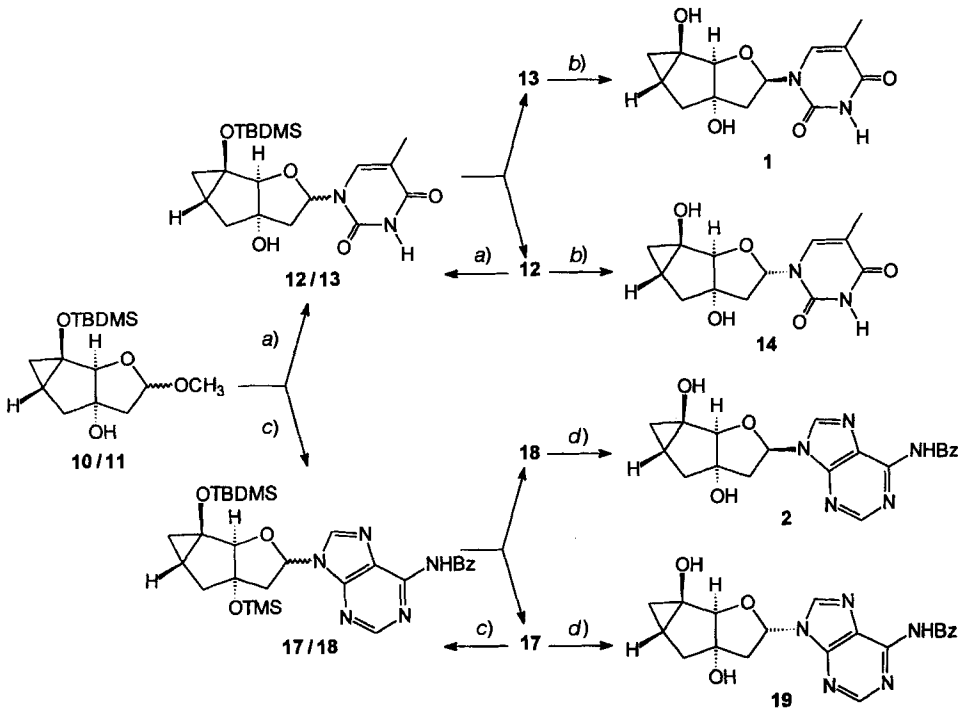
[5]) Longer reaction times and the use of THF instead of Et_2O as solvent for the carbene addition did not lead to higher yields but to a substantial amount of decomposition. As the only by-product under these conditions, the ethyl glycoside of **10** could be isolated in yields of up to 12%. This product most likely arises from carbene insertion into the C–H bond of the methyl glycoside [11].

[6]) Cyclopropanations of cyclopentenes with allylic or homoallylic OH groups are known to lead to stereospecific *cis* introduction of the methylene group [12].

[7]) The use of anomerically pure **10** or **11** in the nucleosidation reaction did not alter the product ratio **12/13** (or **17/18**).

Scheme 2

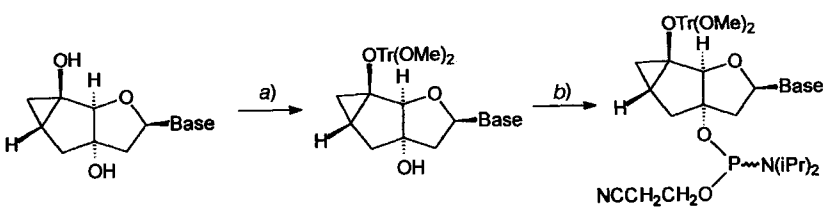


TBDMS = (*t*-Bu)Me_2Si, TMS = Me_3Si, Bz = PhCO

a) 1. Thymine (2 equiv.), BSA (4 equiv.), Me_3SiOTf (0.1 equiv.), MeCN, r.t. (17 h) → 81° (6 h); 65% (α/β 1.7:1); 2. Bu_3NF (1.0 equiv.), THF, r.t., 1 min; 87%. *b*) Bu_4NF (2.0 equiv.), THF, r.t., 5 h; 93%. *c*) N^6-Benzoyladenine (2 equiv.), BSA (4 equiv.), Me_3SiOTf (0.1 equiv.), $ClCH_2CH_2Cl$, 83° (7 h); 72% (α/β 1.4:1); *d*) Bu_4NF (2.5 equiv.), THF, r.t. (4 h) → 50° (1 h); 95%.

Selective tritylation of the OH group at C(5′) could be achieved with 4,4′-dimethoxytrityl trifluoromethane sulfonate ($(MeO)_2TrOTf$) in pyridine (*Scheme 3*). The position of the trityl group at the less hindered tertiary OH group at C(5′) was proven by a ^{1}H-NMR NOESY experiment on compound **15** [14].

Scheme 3



1 Base = Thy
2 Base = Bz^6Ade
15 Base = Thy
20 Base = Bz^6Ade
16 Base = Thy
21 base = Bz^6Ade

a) $(MeO)_2TrOTf$ (2 equiv.), pyridine, r.t., 4 h; 70% (**15**), 58% (**20**). *b*) $(NCCH_2CH_2O)(i\text{-}Pr_2N)PCl$ (1.5 equiv.), $Et(i\text{-}Pr)_2N$ (6 equiv.), MeCN, r.t., 1 h; 92% (**16**), 89% (**21**).

Cross-peaks in the ^{1}H-NMR NOESY of **15** between the resonances of the aromatic protons of the $(MeO)_2Tr$ group and H–C(6'), but no cross-peaks to H–C(1') correspond to a 5'-*O*-derivatized trityl compound. A further cross-peak between the base proton H–C(6) and the protons of the trityl group confirms its 5'-*O* attachment. Besides this, the cross-peak between H_α–C(8') and H–C(4') in the spectrum again confirms the '*exo*'-configuration of the cyclopropyl unit in **15**.

The phosphoramidite building blocks **16** and **21** were obtained by standard reaction of the tritylated tricyclo-deoxynucleosides **15** and **20** with chloro(2-cyanoethoxy)-(diisopropylamino)phosphine (= 2-cyanoethyl diisopropylphosphoramidochloridite) in MeCN in yields of 92% (**16**) and 89% (**21**). As determined by ^{1}H- and ^{31}P-NMR, the phosphoramidites **16** and **21** were formed as 1:1 diastereoisomeric mixtures which proved to be stable under normal workup conditions, and which did not show any decomposition over several months when stored at −20°.

4. Modeling Studies. – In bicyclo-DNA, the sugar pucker of the furanose part is restricted to an *S*-type (2'-*endo*,1'-*exo*) conformation with an excellent structural agreement for the torsion angles δ and χ with that of the repeating nucleotide unit in B-DNA [6]. The dihedral torsion angle γ (*Fig. 1*), however, adopts an *anti*-periplanar (*ap*) orientation which stays in contrast to the corresponding *syn*-clinal (+ *sc*) orientation of γ in natural DNA duplexes of the A- or B-type. Compared to bicyclo-nucleosides, the additional methylene bridge in tricyclo-nucleosides (*Fig. 1*) is expected to enforce the torsion angle γ from the + *ap* towards the + *ac* orientation.

A conformational search of tricyclo-thymidine **1** and tricyclo-deoxyadenosine was performed using the AMBER force field [15] as implemented in the molecular-modeling system Insight II (95.0)/Discover (3.0) from *Molecular Simulations*, San Diego, CA, USA[8]). As a result of the energy minimizations, the most stable conformers in both cases show a 2'-*endo* conformation in the furanose moiety (*Fig. 2*; structure for tricyclo-deoxyadenosine not shown). The values for the dihedral torsion angles γ(O-(5')–C(5')–C(4')–C(3')), δ(C(5')–C(4')–C(3')–O(3')), and χ(O(4')–C(1')–N(1)–C(2) for pyrimidines and O(4')–C(1')–N(9)–C(4) for purines) are summarized and compared with that of bicyclo-thymidine in the *Table*.

As the next most stable structures for each nucleoside were identified a O(4')-*endo*-conformer in the case of the pyrimidine nucleoside and a 3'-*endo*-conformer in the case of the purine nucleoside. They deviate by only 0.27 kcal/mol and 0.17 kcal/mol, respectively in energy, compared to the absolute minimum[9]). This contrasts with results in the bicyclo-deoxynucleoside series, in which *S*-conformers are considerably more stable than *N*-conformers and thus indicates the subtle influence of the cyclopropane unit to the conformational equilibria of the furanose unit.

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[8]) Explicit water was neglected and a distance-dependent dielectric constant of $\varepsilon = 4r$ was used to simulate an aqueous environment. No cut-off distance was applied for nonbonded interactions. *Van der Waals* and electrostatic 1–4 interactions were scaled by 0.5. The structures were minimized up to a gradient of 0.0001 kcal mol$^-$ K^{-1}. The minimizations involved successively the following algorithms: steepest descent, *Polak-Ribiere* conjugated gradient, and finally *BFGS Quasi-Newton-Raphson*.

[9]) The values for the torsion angles γ, δ, and χ obtained by molecular modeling of a O(4')-*endo*-conformation of the tricyclic thymidine analog are $\gamma = 142.7°$, $\delta = 97.8°$, and $\chi = -143.2°$. The 3'-*endo*-conformation in the tricyclic deoxyadenosine analog gives rise to $\gamma = 142.9°$, $\delta = 99.4°$, and $\chi = -166.4°$

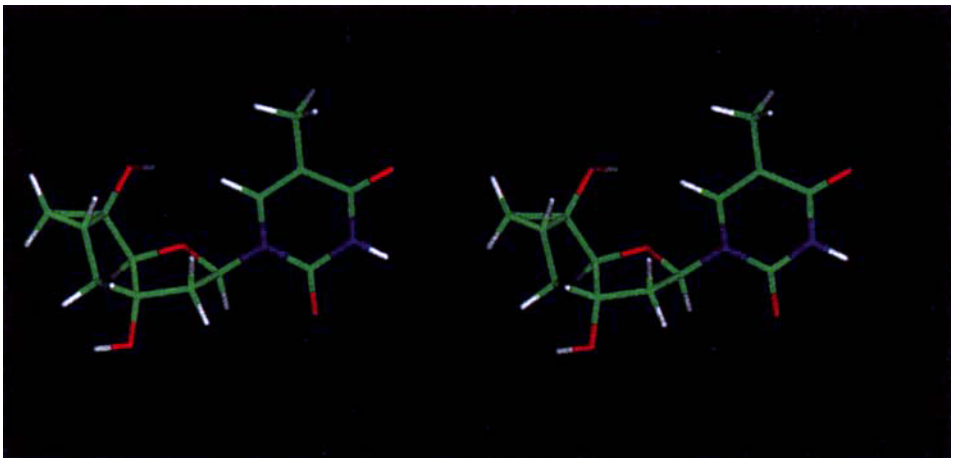

Fig. 2. *Stereoscopic view of the energy-minimized* (Insight II (95.0)/Discover (3.0)) *conformer of the tricyclo-thymidine* **1**

Table. *Values of Selected Torsion Angles in the Sugar Moiety Obtained by Molecular Modeling for B-DNA, Bicyclo-thymidine, Tricyclo-thymidine* **1**, *and Tricyclo-deoxyadenosine*

	γ	δ	χ	ν_1
B-DNA [17][a])	54°	123°	−117°	
Bicyclo-thymidine[a]) [6]	149.3°	126.5°	−112.7°	43.1°
Tricyclo-thymidine **1**	118.3°	140.0°	−137.6°	33.7°
Tricyclo-deoxyadenosine	115.8°	143.3°	−151.0	33.2°

[a]) Crystal structure.

The furanose pucker in solution can be determined experimentally by NMR from vicinal coupling constants of H-atoms (^3J(H,H)) [16]. In the case of the tricyclo-deoxynucleosides **1** and **2**, the absence of protons at the centers C(3′) and C(5′) only allows the calculation of the dihedral angle ν_1 from the ^{1}H-NMR coupling constants. For both **1** and **2**, the experimentally determined value of 32.3° for the dihedral angle ν_1 is in excellent agreement with the corresponding value of the 2′-*endo*-conformer of the tricyclo-thymidine and tricyclo-deoxyadenosine obtained by molecular modeling (*Table*).

The dihedral torsion angle γ in the most stable conformations of the tricyclo-nucleoside analogs is shifted, compared to bicyclo-thymidine, by *ca.* 30° from the + *ap* to the + *ac* region, but still deviates from that in natural DNA of the B-type (being in the + *sc* range) by *ca.* + 70°. The increase of *ca.* 15° of torsion angle δ can be attributed to the preferred 2′-*endo*-conformation of the tricyclo-nucleosides compared to the 1′-*exo* conformation of the bicyclo-nucleosides, whereas χ deviates by *ca.* −20° from the one observed in a natural B-type DNA.

In conclusion we have presented here an efficient synthesis of the tricyclo-nucleosides containing the bases adenine and thymine as well as their building blocks for oligonucle-

otide synthesis. In a following communication we will report about their successful incorporation into oligonucleotides as well as about their complementary base-pairing properties.

We thank the *Swiss National Science Foundation* for financial support and Dr. *C. Müller* for help with the 2D-NMR experiments.

Experimental Part

General. Solvents for extraction: technical grade, distilled. Solvents for reactions: reagent grade, distilled over CaH_2 (MeCN, CH_2Cl_2, pyridine), $LiAlH_4$ (Et_2O), or Na (THF). Reagents: if not otherwise stated from *Fluka*, highest quality available. Melting points: *Büchi 510*; uncorrected. Optical rotations: *Perkin-Elmer-241* polarimeter, 10-mm cell. IR: *Perkin-Elmer FTIR 1600;* ($\tilde{\nu}$ in cm^{-1}). NMR: *Bruker AC-300*, *DRX500*; δ in ppm, ^{13}C multiplicities from DEPT spectra, *J* in Hz, internal Me_4Si. MS: *Varian MAT CH-7A*; ionizing voltage 70 eV; *m/z* (intensity in %); fast-atom bombardment (FAB), pos., matrix dithioerythrol/dithio-DL-threitol). TLC: *Merck SiL G-25 UV_{254}*; compounds not detectable by UV/VIS were stained by dipping the plate in a mixture of EtOH (180 ml), 4-methoxybenzaldehyde (10 ml), conc. H_2SO_4 (10 ml), and AcOH (2 ml) followed by heating with a heat gun. Flash column chromatography (FC): silica gel (30–60 μm) from *Baker*. Medium-pressure liquid chromatography (MPLC): *Büchi-688* chromatography pump equipped with a *Büchi-684* fraction collector; silica gel (30 μm) from *Baker*.

*(1*R*,3*RS*,5*S*,8*R*)-3-Methoxy-2-oxabicyclo[3.3.0]octane-5,8-diol* (= *(2*RS*,3a*S*,6*R*,6a*R*)-Hexahydro-2-methoxy-3a*H*-cyclopenta[*b*]furan-3a,6-diol*; **4**/**5**). To a soln. of diol (–)-**3** (2.22 g, 11.0 mmol; ee (GC) > 97%, prepared according to [6]) in CH_2Cl_2 (7 ml), a suspension of 1,1,1-triacetoxy-1,1-dihydro-1,2-benziodoxol-3-(1*H*)-one (6.1 g, 14.3 mmol; *Dess-Martin* reagent, prepared according to [9]) in CH_2Cl_2 (7 ml) was added under stirring and cooling to r.t. After stirring for 2 h, the suspension was diluted with Et_2O (35 ml), sat. $NaHCO_3$ soln. (35 ml), and 20% $Na_2S_2O_3$ soln. (7 ml). The mixture was stirred for 30 min, the white solid filtered off, and the filtrate extracted with CH_2Cl_2 (3 × 20 ml) and Et_2O (5 × 15 ml). The combined org. phases were dried ($MgSO_4$) and evaporated and the residual white gel diluted with MeOH (25 ml). After addition of *Amberlyst 15* (0.75 g, H^+ form), the mixture was stirred for 16 h at r.t. and 2 h at reflux. After neutralization with sat. $NaHCO_3$, soln. the *Amberlyst* was filtered off, and the solvents were evaporated. FC (silica gel (50 g), AcOEt/hexane 3:1) of the residue afforded **4**/**5** (1.48 g, 77%) in a ratio of 2:1 (α/β; ^1H-NMR). Colorless oil. R_f (AcOEt/hexane 3:1) 0.13. IR ($CHCl_3$): 3667*w*, 3557*s*, 2836*m*, 1778*s*, 1460*w*, 1355*m*, 1317*m*, 1105*m*, 986*s*, 899*m*, 865*w*. ^1H-NMR (300 MHz, $CDCl_3$): 5.15 (*m*, 0.33 H, H_β–C(3)); 5.10 (*d*, *J* = 4.4, 0.67 H, H_α–C(3)); 4.00–4.15 (*m*, 2 H, H–C(1), H–C(8)); 3.38, 3.30 (2*s*, 3 H, MeO); 2.75 (br. *s*, 1 H, OH); 2.20 (br. *s*, 1 H, OH); 1.80–2.12, 1.45–1.65 (2*m*, 6 H, CH_2(4), CH_2(6), CH_2(7)). ^{13}C-NMR (75 MHz, $CDCl_3$): 107.82, 107.21 (2*d*, C(3) (α/β)); 88.91 (*d*, C(1)); 86.76 (*s*, C(5)); 71.35 (*d*, C(8)); 54.81 (*q*, MeO); 47.97, 33.57, 32.45 (3*t*, C(4), C(6), C(7)). EI-MS (70 eV): 174 (0.9, M^+), 156 (44), 143 (52), 124 (100), 113 (74), 100 (95).

*(1*S*,3*RS*,5*S*)-5-Hydroxy-3-methoxy-2-oxabicyclo[3.3.0]octan-8-one* (= *(2*RS*,3a*S*,6a*S*)-Hexahydro-3a-hydroxy-2-methoxy-6*H*-cyclopenta[*b*]furan-6-one*; **6**/**7**). To a soln. of **4**/**5** (1.48 g, 8.5 mmol) in CH_2Cl_2 (12 ml), a suspension of *Dess-Martin* reagent (4.7 g, 11 mmol) in CH_2Cl_2 (9 ml) was added dropwise within 5 min under cooling to r.t., and the resulting suspension was stirred for 2 h. After dilution with AcOEt/hexane 1:1 (11 ml), the mixture was adsorbed to silica gel (2.5 g) and purified by FC (silica gel (50 g), AcOEt/hexane 1:1 + 5% Et_2N): **6**/**7** (0.98 g, 67%) in a ratio of 2:1 (α/β; ^1H-NMR) as pale yellow crystals. A sample of **6**/**7** was separated by FC (silica gel, AcOEt/hexane 1:1 + 5% Et_3N) for anal. purposes.

Data of **6**: R_f (Et_2O) 0.45. IR ($CHCl_3$): 3533*s*, 2914*w*, 2839*m*, 1747*s*, 1602*w*, 1458*w*, 1359*m*, 1105*m*, 969*s*, 903*m*, 866*w*. ^1H-NMR (300 MHz, $CDCl_3$): 5.11 (*d*, *J* = 4.4, H–C(3)); 4.19 (*s*, H–C(1)); 3.51 (*s*, OH); 3.39 (*s*, MeO); 2.13–2.64 (*m*, CH_2(7), 1 H–C(4), CH_2(6)); 1.97 (*dd*, *J* = 13.8, 4.4, 1 H–C(4)). ^{13}C-NMR (75 MHz, $CDCl_3$): 213.11 (*s*, C(8)); 107.09 (*d*, C(3)); 88.90 (*d*, C(1)); 83.95 (*s*, C(5)); 55.23 (*q*, MeO); 44.65, 36.32, 28.37 (3*t*, C(4), C(6), C(7)). EI-MS (70 eV): 172 (23, M^+), 154 (17), 141 (30), 114 (48), 99 (27), 95 (15), 83 (100).

Data of **7**: R_f (Et_2O) 0.41. IR ($CHCl_3$): 3688*w*, 3598*m*, 2933*w*, 2837*m*, 1751*s*, 1603*w*, 1445*w*, 1358*m*, 1226*s*, 1110*m*, 1053*s*, 1029*s*. ^1H-NMR (300 MHz, $CDCl_3$): 5.10 (*d*, *J* = 5.5, H–C(3)); 3.99 (*s*, H–C(1)); 3.16 (*s*, MeO); 3.04 (*s*, OH); 2.10–2.58 (*m*, CH_2(7), CH_2(4), CH_2(6)). ^{13}C-NMR (75 MHz, $CDCl_3$): 215.25 (*s*, C(8)); 106.75 (*d*, C(3)); 87.58 (*d*, C(1)); 83.90 (*s*, C(5)); 54.54 (*q*, MeO); 48.90, 36.31, 33.38 (3*t*, C(4), C(6), C(7)). EI-MS (70 eV): 172 (27, M^+), 154 (24), 141 (34), 114 (27), 99 (33), 83 (100).

*(1*S*,3*RS*,5*S*)-8{[(*tert*-Butyl)dimethylsilyl]oxy}-3-methoxy-2-oxabicyclo[3.3.0]oct-7-en-5-ol* (= *(2*RS*,3a*S*,6a*S*)-6-{[(*tert*-Butyl)dimethylsilyl]oxy}-2,3,4,6a-tetrahydro-2-methoxy-3a*H*-cyclopenta[*b*]furan-3a-ol*; **8**/**9**). To a

soln. of LDA prepared *in situ* from BuLi (16 mmol in THF (19 ml)) and i-Pr_2N (2.4 ml) at −74° under Ar, a soln. of **6**/**7** (0.98 g, 5.7 mmol) in THF (12 ml) was added dropwise within 30 min. After stirring the suspension for 15 min at −74°, a soln. of (*t*-Bu)Me_2SiCl (1.54 g, 10.2 mmol) in THF (6 ml) and Et_3N (0.3 ml) was added and the mixture stirred for another 20 min before it was allowed to warm up to r.t. After 2 h the mixture was diluted with Et_2O (40 ml) and the org. phase washed with sat. $NaHCO_3$ soln. (3 × 40 ml). The aq. phases were extracted with Et_2O (30 ml) and the combined org. phase dried ($MgSO_4$) and evaporated. The resulting oil was purified by FC (silica gel (40 g), hexane/AcOEt/Et_2O 7:2:1) to give, after drying (r.t. 0.01 Torr, 3 h), **8**/**9** (1.5 g, 92%) in a ratio of 2:1 (α/β; ^{1}H-NMR) as a colorless oil. A sample of **8**/**9** was separated for analysis of FC (silica gel, hexane/AcOEt/Et_2O 7:2:1).

Data of **8**: R_f (Et_2O) 0.81. IR ($CHCl_3$): 4212*w*, 3673*w*, 3528*m*, 2914*w*, 2854*m*, 2399*w*, 1724*w*, 1643*m*, 1461*w*, 1360*m*, 1103*m*, 947*m*, 900*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.88 (*d*, *J* = 4.8, H–C(3)); 4.43, 4.49 (2*s*, H–C(1), H–C(7)); 3.20 (*s*, MeO); 3.02 (br. *s*, OH); 2.25 (*s*, CH_2(6)); 2.03 (*d*, *J* = 13.5, 1 H–C(4)); 1.83 (*dd*, *J* = 13.5, 4.8, 1 H–C(4)); 0.77 (*s*, Me_3C); 0.00–0.10 (2*s*, Me_2Si). ^{13}C-NMR (75 MHz, $CDCl_3$): 152.73 (*s*, C(8)); 106.29 (*d*, C(3)); 101.76 (*d*, C(7)); 92.47 (*d*, C(1)); 85.21 (*s*, C(5)); 54.02 (*q*, MeO); 49.56, 42.23 (2*t*, C(4), C(6)); 25.70 (*q*, *Me*$_3$C); 18.21 (*s*, Me_3C); −4.63, −4.73 (2*q*, Me_2Si). EI-MS (70 eV): 286 (7, M^+), 255 (20), 229 (88), 212 (72), 197 (100), 185 (27), 179 (18), 169 (72), 155 (65).

Data of **9**: R_f (Et_2O) 0.61. IR ($CHCl_3$): 3572*w*, 3440*m*, 2924*m*, 2858*m*, 2400*w*, 1649*s*, 1460*w*, 1260*m*, 1110*m*, 1030*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.98 (*d*, *J* = 4.8, H–C(3)); 4.33, 4.38 (2*s*, H–C(1), H–C(7)); 3.15 (*s*, MeO); 1.96–2.54 (*m*, CH_2(6), CH_2(4), OH); 0.76 (*s*, Me_3C); 0.00 (*s*, Me_2Si). ^{13}C-NMR (75 MHz, $CDCl_3$): 154.64 (*s*, C(8)); 108.19 (*d*, C(3)); 103.64 (*d*, C(7)); 94.37 (*d*, C(1)); 87.17 (*s*, C(5)); 56.91 (*q*, MeO); 51.43, 44.18 (2*t*, C(4), C(6)); 27.58 (*q*, *Me*$_3$C); 20.06 (*s*, Me_3C); −2.76, −2.85 (2*q*, Me_2Si). EI-MS (70 eV): 286 (1, M^+), 229 (40), 212 (25), 197 (80), 169 (43), 155 (38), 143 (58).

*(1S,2R,4R,6S,8RS)-2-{[(*tert*-Butyl)dimethylsilyl]oxy}-8-methoxy-9-oxatricyclo[4.3.0^{1,6}.0^{2,4}]nonane-6-ol* (= *(2RS,3aS,4aR,5aR,5bS)-5a-{[(*tert*-Butyl)dimethylsilyl]oxy}octahydro-2-methoxycyclopropa[4,5]cyclopenta-[1,2-b]furan-3a-ol*; **10**/**11**). AgOAc (60 mg) was dissolved in conc. AcOH (60 ml) at 70° and Zn (10 g; grain size *ca.* 0.5 mm, shortly corroded with 0.1M HCl, washed with H_2O and EtOH, and dried at r.t./0.01 Torr for 15 min) was added at once. The mixture was stirred for 1 min, decanted, and washed with AcOH (40 ml) and dry Et_2O (3 × 40 ml). The now dark grey Ag-Zn couple was stored over Ag-wool in abs. Et_2O. To the Ag-Zn couple (6.3 g) in Et_2O (11 ml), CH_2I_2 (8.41 g, 31.4 mmol) was added through a syringe, and the mixture was stirred under Ar for 1 h at r.t. A soln. of **8**/**9** (1.5 g, 5.23 mmol) in dry Et_2O (11 ml) was added dropwise to the carbene soln. within 10 min, and the mixture was refluxed under Ar for 3 h. The grey suspension was then cooled to 0° and diluted with Et_2O (30 ml) before pyridine (6.6 ml) was added dropwise at 0°. The white precipitate was filtered off over *Celite*, the filtrate washed with sat. $NaHCO_3$ soln. (2 × 50 ml), and the aq. phases extracted with Et_2O (50 ml). The combined org. phase was dried ($MgSO_4$) and evaporated and the residue purified by FC (silica gel (50 g), Et_2O/hexane 1:1), dried (r.t./0.01 Torr, 3 h): **10**/**11** (908 mg, 58%) in a ratio of 2:1 (α/β; ^{1}H-NMR) as a colorless oil. A sample of **10**/**11** was separated by FC (silica gel, hexane/AcOEt/Et_2O 7:2:1) for spectroscopic analysis.

Data of **10**: R_f (Et_2O/hexane 1:1) 0.38. IR ($CHCl_3$): 3552*m*, 2884*s*, 1644*m*, 1441*s*, 1360*s*, 1132*s*, 1089*m*, 1042*w*, 934*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 5.06 (*dd*, *J* = 5.3, 1.8, H–C(8)); 4.08 (*s*, H–C(1)); 3.37 (*s*, MeO); 2.40 (*dd*, *J* = 13.8, 5.3, 1 H–C(7)); 2.21 (*dd*, *J* = 13.8, 5.0, 1 H–C(5)); 2.08 (*s*, OH); 1.99 (*dd*, *J* = 13.8, 1.8, 1 H–C(7)); 1.62 (*d*, *J* = 13.8, 1 H–C(5)); 1.48 (*m*, H–C(4)); 0.93 (*m*, 1 H–C(3)); 0.85 (*s*, Me_3C); 0.75 (*dd*, *J* = 5.8, 4.5, 1 H–C(3)); 0.02, 0.00 (2*s*, Me_2Si). ^{13}C-NMR (75 MHz, $CDCl_3$): 105.40 (*d*, C(8)); 89.16 (*d*, C(1)); 87.56 (*s*, C(6)); 64.92 (*s*, C(2)); 54.68 (*q*, MeO); 49.82, 41.34 (2*t*, C(5), C(7)); 25.69 (*q*, *Me*$_3$C); 24.47 (*d*, C(4)); 18.29 (*t*, C(3)); 17.88 (*s*, Me_3C); −3.81, −3.85 (2*q*, Me_2Si). EI-MS (70 eV): 300 (0.1, M^+), 243 (13), 225 (26), 211 (100), 193 (17), 183 (35), 169 (30), 157 (16), 143 (40).

Data of **11**: R_f (Et_2O/hexane 1:1) 0.33. ^{1}H-NMR (300 MHz, $CDCl_3$): 5.06 (*dd*, *J* = 5.3, 1.8, H–C(8)); 4.07 (*s*, H–C(1)); 3.36 (*s*, MeO); 2.41 (*dd*, *J* = 13.8, 5.3, 1 H–C(7)); 2.24 (*s*, OH); 2.20 (*dd*, *J* = 13.8, 5.0, 1 H–C(5)); 1.98 (*dd*, *J* = 13.8, 1.8, 1 H–C(7)); 1.62 (*d*, *J* = 13.8, 1 H–C(5)); 1.48 (*m*, H–C(4)); 0.93 (*m*, 1 H–C(3)); 0.85 (*s*, Me_3C); 0.75 (*dd*, *J* = 5.8, 4.5, 1 H–C(3)); 0.14, 0.12 (2*s*, Me_2Si).

Desilylation of a Sample of the α-D-*Anomer* **10**. For spectroscopic purpose, a sample of **10** (78 mg, 0.26 mmol) was desilylated by treatment with HF/pyridine (0.12 g; 60–70% HF) in pyridine (81 ml) for 14 h at r.t. After addition of silica gel (0.5 g), FC (silica gel (5 g), Et_2O/hexane 2:1) yielded 40 mg (83%) of the desilylated compound. R_f (Et_2O) 0.3. ^{1}H-NMR (500 MHz, $CDCl_3$): 5.08 (*dd*, *J* = 4.8, 1.2, H–C(8)); 4.13 (*s*, H–C(1)); 3.35 (*s*, MeO); 2.83 (*s*, OH); 2.60 (*s*, OH); 2.26 (*dd*, *J* = 13.8, 4.8, H_β–C(7)); 2.21 (*dd*, *J* = 14.0, 5.8 H_α–C(5)); 2.10 (*dd*, *J* = 13.8, 1.2, H_α–C(7)); 1.44 (*d*, *J* = 14.0, H_β–C(5)); 1.42 (*m*, H–C(4)); 1.16 (*m*, H_β–C(3)); 0.56 (*dd*, *J* = 6.1, 4.2, H_α–C(3)). Difference NOE (500 MHz, $CDCl_3$): 4.13 (H–C(1)) → 0.56 (H_α–C(3)); 2.26

(H_β–C(7)) → 1.44 (H_β–C(5)); 1.44 (H–C(4), H_β–C(5)) → 2.26 (H_β–C(7)), 1.16 (H_β–C(3)), 0.56 (H_α–C(3)); 0.56 (H_α–C(3)) → 1.16 (H_β–C(3)).

*(5'R,6'R)-1-{5'-O-[(tert-Butyl)dimethylsilyl]-2'deoxy-3',5'-ethano-5',6'-methano-α- and-β-*D*-ribofuranosyl}-thymine* (**12**/**13**). Dried (r.t./0.01 Torr, 15 H) thymine (734 mg, 5.8 mmol) was mixed under Ar at r.t. with MeCN (6.8 ml) and BSA (*N,O*-bis(trimethylsilyl)acetamide; 2.1 ml, 11.5 mmol). After 30 min (→ homogeneous mixture), a soln. of **10**/**11** (864 mg, 2.876 mmol) in MeCN (6.5 ml) and $CF_3SO_3SiMe_3$ (70 µl) were added. After 17 h stirring at r.t., the mixture was refluxed for 6 h, cooled to r.t., diluted with AcOEt (30 ml), and washed with sat. $NaHCO_3$ soln. (30 ml). The combined org. phase was dried ($MgSO_4$) and evaporated. FC (silica gel (55 g), AcOEt/hexane 1:2) afforded 710 mg (53%) of 3'-*O*-Me_3Si-**12**/**13** and 390 mg (36%) of recovered, 3'-*O*-silylated starting material. Recyclation of the unreacted starting material led to a combined yield of 65% (922 mg, 1.975 mmol) of 3'-*O*-Me_3Si-**12**/**13** (R_f (hexane/AcOEt 2:1) 0.33) as a white foam in a ratio of 1.7:1 (α/β; ^{1}H-NMR). To a soln. of 3'-*O*-Me_3Si-**12**/**13** (898 mg, 1.924 mmol) in THF (11 ml), a soln. of Bu_4NF (1.96 ml, 2.15 mmol; 1.1M in hexane) was added and the mixture stirred at r.t. for 1 min. Silica gel (1 g) was added and the solvent evaporated. FC (silica gel (40 g), AcOEt/hexane 2:1) of the residue afforded 664 mg (87%) of **12**/**13** as a white foam in a ratio of 1.7:1 (α/β). MPLC (silica gel (100 g), i-PrOH/hexane 5:95) of **12**/**13** yielded 409 mg (53%) of the α-D-anomer **12** and 241 mg (31%) of the β-D-isomer **13**, both as white foams.

Data of **12**: R_f (AcOEt/hexane 2:1) 0.29. IR ($CHCl_3$): 3500*m*, 2929*m*, 2360*s*, 2341*m*, 1684*s*, 1360*s*, 1472*m*, 1362*m*, 1271*m*, 1103*w*, 1049*m*, 984*w*, 832*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 8.87 (br. *s*, H–N(3)); 7.25 (*d*, *J* = 1.1, H–C(6)); 5.90 (*dd*, *J* = 7.0, 5.9, H–C(1')); 4.28 (*s*, H–C(4')); 2.71 (*dd*, *J* = 13.8, 7.0, 1 H–C(2')); 2.32 (*m*, 1 H–C(2'), 1 H–C(7')); 1.91 (*d*, *J* = 1.1, Me–C(5)); 1.70 (*d*, *J* = 13.9, 1 H–C(7')); 1.62 (br. *s*, OH); 1.53 (*m*, H–C(6')); 1.00 (*m*, 1 H–C(8')); 0.88 (*s*, Me_3C, 1 H–C(8')); 0.12, 0.09 (2*s*, Me_2Si). EI-MS (70 eV): 377 (6), 338 (40), 320 (16), 251 (27), 225 (17), 211 (100), 193 (36), 183 (79), 167 (17), 153 (22), 143 (10), 127 (23).

Data of **13**: R_f (AcOEt/hexane 2:1) 0.29. ^{1}H-NMR (300 MHz, $CDCl_3$): 8.87 (br. *s*, H–N(3)); 8.03 (*d*, *J* = 1.1, H–C(6)); 6.03 (*dd*, *J* = 5.9, 2.6, H–C(1')); 4.24 (*s*, H–C(4')); 2.51 (*m*, CH_2(2')); 2.00 (*dd*, *J* = 14.3, 4.8, 1 H–C(7')); 1.90 (*d*, *J* = 1.1, Me–C(5)); 1.69 (br. *s*, OH); 1.68 (*d*, *J* = 14.3, 1 H–C(7')); 1.37 (*m*, H–C(6')); 1.09 (*m*, 1H–C(8')); 0.88 (*s*, Me_3C); 0.79 (*m*, 1H–C(8')); 0.18, 0.10 (2*s*, Me_2Si). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.58 (*s*, C(4)); 150.46 (*s*, C(2)); 136.58 (*d*, C(6)); 109.52 (*s*, C(5)); 92.33, 88.70 (2*d*, C(4'), C(1')); 86.59 (*s*, C(3')); 65.30 (*s*, C(5')); 48.27, 42.04 (2*t*, C(7'), C(2')); 25.63 (*q*, *Me*$_3$C); 24.73 (*d*, C(6')); 17.76 (*s*, Me_3C); 16.63 (*t*, C(8')); 12.40 (*q*, *Me*–C(5)); –3.83 (*q*, Me_2Si).

*(5'R,6'R)-1-(2'-Deoxy-3',5'-ethano-5',6'-methano-α-*D*-ribofuranosyl)thymine* (= *(5'R,7'R)-1-(2'-Deoxy-3',5',5'-propane[1,2,3]triyl-α-*D*-ribofuranosyl)thymine*; (+)-**14**). To a soln. of **12** (118 mg, 0.3 mmol) in THF (2.7 ml), a soln. of Bu_4NF (0.7 ml, 0.77 mmol; 1.1M in hexane) was added and the mixture stirred at r.t. for 5 h. Silica gel (0.7 g) was added and the solvent evaporated. FC (silica gel (7 g), hexane/i-PrOH 3:1) afforded (+)-**14** (73 mg, 87%). White solid. M.p. > 220° (dec.). R_f (hexane/i-PrOH 3:1) 0.2. $[\alpha]_D^{22}$ = + 11.4 (*c* = 0.5, MeOH). UV: 265 (8900). IR ($CHCl_3$): 3020*m*, 2361*m*, 1690*s*, 789*m*. ^{1}H-NMR (300 MHz, CD_3OD): 7.50 (*d*, *J* = 1.1, H–C(6)); 6.08 (*dd*, *J* = 7.7, 5.9, H–C(1')); 4.17 (*s*, H–C(4')); 2.42 (*dd*, *J* = 13.1, 5.9, 1 H–C(2')); 2.16 (*dd*, *J* = 14.1, 5.0, 1 H–C(7')); 2.08 (*dd*, *J* = 13.1, 7.7, 1 H–C(2')); 1.82 (*d*, *J* = 1.1, Me–C(5)); 1.61 (*d*, *J* = 14.1, 1 H–C(7)); 1.42 (*m*, H–C(6')); 0.86 (*m*, 1H–C(8')); 0.78 (*m*, 1H–C(8')). Difference-NOE (500 MHz, CD_3OD): 7.50 (H–C(6)) → 6.05 (H–C(1')), 4.17 (H–C(4')), 2.10 (H_α–C(2')), 1.83 (Me–C(5)); 6.05 (H–C(1')) → 7.50 (H–C(6)), 2.42 (H_β–C(2')), 2.10 (H_α–C(2')); 4.17 (H–C(4')) → 7.50 (H–C(6)), 0.78 (H–C(8')). ^{13}C-NMR (75 MHz, CD_3OD): 166.38 (*s*, C(4)); 152.33 (*s*, C(2)); 137.79 (*d*, C(6)); 111.86 (*s*, C(5)); 90.50, 86.60 (2*d*, C(1'), C(4')); 86.54 (*s*, C(3')); 65.13 (*s*, C(5')); 47.35 (*t*, C(7')); 41.35 (*t*, C(2')); 25.38 (*d*, C(6')); 17.43 (*t*, C(7')); 12.49 (*q*, *Me*–C(5)). EI-MS (70 eV): 280 (1, M^+), 278 (15), 262 (11), 200 (10), 170 (10), 152 (13), 135 (56), 126 (100). Anal. calc. for $C_{13}H_{16}N_2O_3 \cdot 0.25\ H_2O$: C 54.83, H 5.84, N 9.84; found: C 54.90, H 5.99, N 9.74.

*(5'R,6'R)-1-(2'-Deoxy-3',5'-ethano-5',6'-methano-β-*D*-ribofuranosyl)thymine* (= *(5'R,7'R)-1-(2'-Deoxy-3',5',5'-propane[1,2,3]triyl-β-*D*-ribofuranosyl)thymine*; (+)-**1**). To a soln. of **13** (240 mg, 0.608 mmol) in THF (4 ml), a soln. of Bu_4NF (1.15 ml, 1.26 mmol; 1.1M in hexane) was added, and the soln. was stirred for 3 h at r.t. The white precipitate was dissolved by addition of hexane/i-PrOH 3:1 (2 ml). Silica gel (0.7 g) was added and the solvent evaporated. FC (silica gel (15 g), hexane/i-PrOH 3:1) of the residue afforded (+)-**1** (159 mg, 93%). White foam. R_f (hexane/AcOEt 1:2) 0.29. $[\alpha]_D^{22}$ = + 86.9 (*c* = 0.68, MeOH). UV: 265 (9000). IR ($CHCl_3$): 3391*m*, 1691*s*, 1356*w*, 1300*w*, 1106*w*, 975*w*, 895*w*. ^{1}H-NMR (300 MHz, CD_3OD): 7.80 (*d*, *J* = 1.1, H–C(6)); 5.98 (*dd*, *J* = 6.6, 4.8, H–C(1')); 4.00 (*s*, H–C(4')); 2.37 (*dd*, *J* = 13.6, 6.6, 1 H–C(2')); 2.26 (*dd*, *J* = 13.6, 4.8, 1 H–C(2')); 2.00 (*dd*, *J* = 14.2, 4.8, 1 H–C(7')); 1.78 (*d*, *J* = 1.1, Me–C(5)); 1.51 (*d*, *J* = 14.2, 1 H–C(7')); 1.39 (*m*, H–C(6')); 0.91 (*m*, 1 H–C(8')); 0.68 (*m*, 1 H–C(8')). Difference-NOE (500 MHz, CD_3OD): 7.80 (H–C(6)) → 6.00 (H–C(1')), 2.25 (H_β–C(2')), 2.02 (H–C(7')), 1.78 (Me–C(5)), 1.40 (H–C(6')); 6.00 (H–C(1')) → 7.80 (H–C(6)), 4.00 (H–C(4')), 2.37 (H_α–C(2')); 4.00 (H–C(4')) → 6.00 (H–C(1')), 2.37 (H_α–C(2')), 0.68 (H–C(8')). ^{13}C-NMR

(75 MHz, CD_3OD): 166.86 (*s*, C(4)); 152.46 (*s*, C(2)); 138.30 (*d*, C(6)); 111.07 (*s*, C(5)); 92.48, 88.97 (2*d*, C(1'), C(4')); 87.41 (*s*, C(3')); 64.86 (*s*, C(5')); 48.94 (*t*, C(7')); 42.51 (*t*, C(2')); 25.51 (*d*, C(6')); 18.72 (*t*, C(8')); 12.80 (*q*, *Me*–C(5)). EI-MS (70 eV): 280 (8, M^+), 252 (4), 154 (18), 136 (28), 127 (100). Anal. calc. for $C_{13}H_{16}N_2O_3 \cdot 0.25\ H_2O$: C 54.83, H 5.84, N 9.84; found: C 54.84, H 6.17, N 9.57.

*(5'R,6'R)-1-{5'-O-[Bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-3',5'-ethano-5',6'-methano-β-*D*-ribofuranosyl}thymine* (**15**). To a soln. of (+)-**1** (159 mg, 0.567 mmol) in pyridine (2 ml) was added $(MeO)_2Tr(CF_3SO_3)$ (515 mg, 1.13 mmol) [18] under Ar and r.t. After 2 h, a further portion of $(MeO)_2Tr(CF_3SO_3)$ (257 mg, 0.570 mmol) was added and the mixture stirred at r.t. until all starting material had disappeared (TLC control). After 4 h, CH_2Cl_2 (10 ml) was added and the soln. washed with sat. $NaHCO_3$ soln. (7 ml). The org. phase was dried (Na_2SO_4) and evaporated and the crude product purified by FC (silica gel (15 g), hexane/AcOEt 1:9). **15** (231 mg, 70%). White foam. R_f (hexane/AcOEt 1:9) 0.39. UV: 233 (18260), 269 (19170). IR ($CHCl_3$): 3683*w*, 3415*m*, 3170*w*, 2939*w*, 2841*w*, 1687*s*, 1612*m*, 1466*w*, 1370*m*, 1320*m*, 1120*m*, 915*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 9.18 (br. *s*, H–N(3)); 8.29 (*d*, J = 1.1, H–C(6)); 7.54 (*d*, J = 7.0, arom. H); 7.32–7.40, 7.18–7.28 (2*m*, 7 arom. H); 6.82 (*m*, 4 arom. H); 5.82 (*dd*, J = 5.7, 3.1, H–C(1')); 3.78 (*s*, 2 MeO): 3.77 (*s*, H–C(4')); 2.34 (*m*, CH_2(2')); 2.06 (*d*, J = 1.1, Me–C(5)); 1.95 (*dd*, J = 14.5, 5.1, 1 H–C(7')); 1.57 (br. *s*, OH); 1.64 (*d*, J = 14.5, 1 H–C(7')); 1.63 (*m*, H–C(6')); 1.31 (*m*, 1 H–C(8')); 0.50 (*m*, 1 H–C(8')). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.54 (*s*, C(4)); 158.69, 158.75 (2*s*, arom. C); 150.46 (*s*, C(2)); 146.17, 136.93, 136.83 (3*s*, arom. C); 136.34 (*d*, C(6)); 130.90, 128.47, 127.65, 126.99, 112.87 (5*d*, arom. C); 109.45 (*s*, C(5)); 91.33, 88.34 (2*d*, C(4'), C(1')); 88.03, 86.22 (2*s*, C(3'), Ar_2CPh); 67.36 (*s*, C(5')); 55.25 (*q*, MeO); 48.49, 41.32 (2*t*, C(7'), C(2')); 25.44 (*d*, C(6)); 17.16 (*t*, C(8')); 12.65 (*q*, *Me*–C(5)). EI-MS (70 eV): 438 (1), 408 (1), 320 (17), 304 (100), 273 (41), 243 (40), 213 (13), 197 (22), 181 (15), 165 (15), 153 (13), 136 (37), 126 (45).

*(5'R,6'S)-1-{5'-O-[Bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-3',5'-ethano-5',6'-methano-β-*D*-ribofuranosyl}thymine 3'-(2-Cyanoethyl Diisopropylphosphoramidite)* (= *(5'R,7'S)-1-{5'-O-[Bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-3',5',5'-propane[1,2,3]triyl-β-*D*-ribofuranosyl}thymine 3'-(2-Cyanoethyl Diisopropylphosphoramidite)*; **16**). To a soln. of **15** (231 mg, 0.396 mmol) in dry MeCN (2 ml), $(i\text{-}Pr)_2NEt$ (0.4 ml, 2.4 mmol) and 2-cyanoethyl diisopropylphosphoramidochloridite (0.25 ml, 1.2 mmol; *Aldrich*) were added under Ar and r.t. After 1 h, the soln. was diluted with AcOEt (20 ml) and washed with sat. $NaHCO_3$ soln. (20 ml). The org. phase was dried (Na_2SO_4), silica gel (2.5 g) added, and the solvent evaporated. FC (silica gel (21 g), hexane/AcOEt/Et_3N 10:20:1) of the residue afforded, after drying (r.t./0.01 Torr, 15 h), **16** (285 mg, 92%). Pale yellow foam (diastereoisomer mixture). R_f (hexane/AcOEt 1:4) 0.65, 0.57. ^{1}H-NMR (300 MHz, CD_3OD): 8.93 (br. *s*, H–N(3)); 8.28 (*d*, J = 1.1, H–C(6)); 7.44 (*m*, 2 arom. H); 7.32–7.40, 7.17–7.28 (*m*, 7 arom. H); 6.80 (*m*, 4 arom. H); 5.87, 5.84 (2*m*, H–C(1')); 3.78, 3.77 (2*s*, 2 MeO); 3.76 (*s*, H–C(4')); 3.35–3.70 (*m*, 2 Me_2(C*H*, OCH_2CH_2CN); 2.68 (*m*, H–C(2')); 2.50 (*m*, OCH_2CH_2CN); 2.46, 2.36 (2*d*, J = 14.5, 1 H–C(2')); 2.22 (*d*, J = 14.7, 1 H–C(7')); 2.07 (*d*, J = 1.1, Me–C(5)); 1.81 (*d*, J = 14.7, 1 H–C(7')); 1.68 (*m*, H–C(6')); 1.24 (*m*, H–C(8')); 1.00–1.08 (*m*, 2 Me_2CH); 0.60, 0.53 (2*m*, 1 H–C(8')). ^{13}C-NMR (75 MHz, $CDCl_3$): 163.93 (*s*, C(4)); 158.77, 158.71 (2*s*, arom. C); 149.81 (*s*, C(2)); 146.14, 136.92, 136.92; 136.83 (4*s*, arom. C); 136.30 (*d*, C(6)); 130.87, 130.71, 128.49, 127.63, 126.98, 112.88, 112.85 (7*d*, arom. C); 117.46 (*s*, CN); 109.19 (*s*, C(5)); 91.96 (*d*, J(C,P) = 4, C(4')); 88.99 (2*d*, C(1')); 89.40 (*s*, C(3')); 88.08, 88.04 (2*s*, Ar_2CPh); 67.02, 66.99 (2*s*, C(5')); 57.92, 57.66 (2*t*, OCH_2CH_2CN); 55.20, 55.15 (2*q*, MeO); 46.37 (*t*, C(2')); 43.21, 43.04 (2*d*, Me_2CH); 39.29 (*t*, C(7')); 25.41 (*d*, C(6')); 24.45, 24.35, 24.42, 24.23, 24.20, 24.12 (6*q*, Me_2CH); 20.21, 20.30 (2*t*, OCH_2CH_2CN); 16.80 (*t*, C(8')); 12.62 (*q*, *Me*–C(5)). ^{31}P-NMR (161.9 MHz, $CDCl_3$, 85% H_3PO_4 (= 0 ppm)): 144.75, 143.01. FAB-MS: 853 (1.2, $[M + 70]^+$), 821 (0.8, $[M + 38]^+$), 783 (0.3, M^+), 560 (1.7), 507 (2.7), 475 (4.7), 455 (2), 419 (3), 303 (100).

*(5'R,6'R)-N^6-Benzoyl-9-{5'-O-[(*tert*-butyl)dimethylsilyl]-2'-deoxy-3'-O-(trimethylsilyl)-3',5'-ethano-5',6'-methano-α- and -β-*D*-ribofuranosyl}adenine* (**17**/**18**). To a suspension of N^6-benzoyladenine (1.53 g, 6.4 mmol) in CH_2ClCH_2Cl (7.5 ml; freshly distilled under P_2O_5), BSA (2.33 ml, 12.8 mmol) was added and the mixture stirred under Ar for 15 min. Then a soln. of **10**/**11** (961 mg, 3.2 mmol) in CH_2ClCH_2Cl (7 ml) and $CF_3SO_3SiMe_3$ (0.1 ml) were added, and the mixture was held under reflux for 7 h. The slightly yellow soln. was diluted with AcOEt (50 ml) and washed with sat. $NaHCO_3$ soln. (50 ml). The aq. phase was extracted with AcOEt (50 ml) and the combined org. phase dried ($MgSO_4$) and evaporated. FC (silica gel (150 g), hexane/AcOEt 2:1) yielded 128 mg (10%) of silylated starting material, 557 mg (30%) of the β-D-anomer **18** and 790 mg (42%) of the α-D-anomer **17**. Recyclation of the unreacted silylated starting material and equilibration of **17** under the same conditions to the anomer mixture **17**/**18** (α/β 4:3) led to a total yield of 768 mg (41%) of **18**.

Data of **17**: R_f (AcOEt/hexane 1:1) 0.44. IR ($CHCl_3$): 2954*s*, 2856*m*, 2360*w*, 1700*s*, 1610*m*, 1580*m*, 1512*m*, 1455*m*, 1363*m*, 1299*m*, 1253*s*, 1120*s*, 1066*m*, 1005*m*, 969*w*, 839*s*, 778*m*, 709*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 9.11 (br. *s*, NH–C(6)); 8.77, 8.27 (2*s*, H–C(2), H–C(8)); 8.01 (*d*, J = 7, 2 arom. H); 7.50 (*m*, 3 arom. H); 6.42

(*t*, *J* = 6.6, H–C(1′)); 4.40 (*s*, H–C(4′)); 2.86 (*dd*, *J* = 12.8, 6.6, 1 H–C(2′)); 2.66 (*dd*, *J* = 12.8, 5.9, 1 H–C(2′)); 2.31 (*dd*, *J* = 13.6, 4.8, 1 H–C(7′)); 1.81 (*d*, *J* = 13.6, 1 H–C(7′)); 1.57 (*m*, H–C(6′)); 0.95 (*m*, 1H–C(8′)); 0.83 (*s*, Me_3C, 1 H–C(8′)); 0.12, 0.08 (2*s*, Me_2Si, Me_3SiO–C(3′)). ^{13}C-NMR (75 MHz, $CDCl_3$): 152.47 (*d*, C(2)); 151.37, 149.41 (2*s*, C(4), C(6)); 141.12 (*d*, C(8)); 132.67, 128.76, 127.86 (3*d*, arom. C); 90.89, 85.05 (2*d*, C(1′), C(4′)); 87.94 (*s*, C(3′)); 64.91 (*s*, C(5′)); 47.27, 40.16 (2*t*, C(7′), C(2′)); 25.66 (*q*, *Me*$_3$C); 23.85 (*d*, C(6′)); 18.23 (*t*, C(8′)); 17.80 (*s*, Me_3C); 1.87 (*q*, Me_3Si); −3.78, −3.82 (2*q*, Me_2Si). EI-MS (70 eV): 522 (8), 489 (38), 432 (8), 338 (10), 299 (75), 297 (42), 283 (36), 266 (10), 257 (14), 250 (22), 240 (100), 211 (10), 193 (28), 167 (10), 147 (26).

Data of **18**: R_f (AcOEt/hexane 1:1) 0.50. IR ($CHCl_3$): 2954*s*, 2856*m*, 2360*w*, 1700*s*, 1608*m*, 1580*m*, 1512*m*, 1451*m*, 1363*m*, 1314*m*, 1295*m*, 1253*s*, 1135*m*, 1074*s*, 1009*m*, 995*w*, 839*s*, 778*m*, 709*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 9.07 (br. *s*, NH–C(6)); 8.77 (2*s*, H–C(2), H–C(8)); 8.01 (*d*, *J* = 7, 2 arom. H); 7.50 (*m*, 3 arom. H); 6.44 (*d*, *J* = 6.6, H–C(1′)); 4.35 (*s*, H–C(4′)); 2.95 (*d*, *J* = 13.2, 1 H–C(2′)); 2.75 (*dd*, *J* = 13.2, 6.6, 1 H–C(2′)); 1.66 (*d*, *J* = 13.9, 1 H–C(7′)); 1.40 (*m*, 1 H–C(7′), H–C(6′)); 1.04 (*m*, 1 H–C(8′)); 0.90 (*s*, Me_3C); 0.76 (*m*, 1 H–C(8′)); 0.21, 0.11, 0.10 (3*s*, Me_2Si, Me_3SiO–C(3′)). ^{13}C-NMR (75 MHz, $CDCl_3$): 152.26 (*d*, C(2)); 151.05, 149.30 (2*s*, C(4), C(6)); 141.96 (*d*, C(8)); 133.70 (*s*, arom. C); 132.66, 128.77, 127.84 (3*d*, arom. C); 93.55, 88.14 (2*d*, C(1′), C(4′)); 88.60 (*s*, C(3′)); 65.25 (*s*, C(5′)); 47.47, 42.04 (2*t*, C(7′), C(2′)); 25.68 (*q*, *Me*$_3$C); 24.63 (*d*, C(6′)); 17.79 (*s*, Me_3C); 17.12 (*t*, C(8′)); 1.93 (*q*, Me_3Si); −3.75 (*q*, Me_2Si). EI-MS (70 eV): 522 (6), 489 (10), 432 (10), 299 (98), 297 (90), 283 (40), 250 (10), 240 (60), 211 (16), 193 (17), 185 (13), 169 (14), 154 (10), 147 (29).

*(5′*R*,6′*R*)-*N*^{6}-Benzoyl-9-(2′-deoxy-3′,5′-ethano-5′-6′-methano-*α*-*D*-ribofuranosyl)adenine* (= *(5′*R*,7′*R*)-*N*^{6}-Benzoyl-9-(2′-deoxy-3′,5′,5′-propane[1,2,3]triyl-*α*-*D*-ribofurano-syl)adenine*; (+)-**19**). To a soln. of **17** (83 mg, 143 μmol) in THF (2 ml), a soln. of Bu_4NF (0.33 ml, 0.36 mmol; 1.1M in hexane) was added. After stirring for 2.5 h at r.t. and 1.5 h at 50°, NH_4Cl (50 mg, 0.93 mmol) was added and the mixture adsorbed at silica gel (0.5 g) and purified by FC (silica gel (7 g), CH_2Cl_2/MeOH 9:1). The product-containing fractions were evaporated. Addition of H_2O (0.8 ml) afforded a white solid which was filtered off and purified again by FC (silica gel (7 g), CH_2Cl_2/MeOH 9:1). Crystallization from EtOH/H_2O 1:2 (1 ml) yielded, after drying (r.t./0.01 Torr, 48 h), 43 mg (76%) of (+)-**19**. M.p. 126–128°. R_f (CH_2Cl_2/MeOH 9:1) 0.48. $[\alpha]_D^{22}$ = + 49.4 (*c* = 0.58, MeOH). UV: 279 (20290). IR (KBr): 3600–3000*s* (br.), 1701*m*, 1616*s*, 1576*m*, 1456*s*, 1302*s*, 1250*s*, 1098*m*, 1048*m*, 1011*w*, 980*w*, 894*w*, 796*m*, 707*m*, 643*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 11.23 (br. *s*, NH–C(6)); 8.77, 8.69 (2*s*, H–C(2), H–C(8)); 8.03 (*d*, *J* = 7, 2arom. H); 7.54 (*m*, 3 arom. H); 6.45 (*t*, *J* = 6.6, H–C(1′)); 5.60 (*s*, OH); 5.41 (*s*, OH); 4.26 (*s*, H–C(4′)); 2.82 (*dd*, *J* = 13.2, 6.9, 1 H–C(2′)); 2.71 (*dd*, *J* = 13.1, 6.6, 1 H–C(2′)); 2.26 (*dd*, *J* = 13.6, 5.1, 1 H–C(7′)); 1.66 (*d*, *J* = 13.6, 1 H–C(7′)); 1.40 (*m*, H–C(6′)); 0.87 (*m*, 1 H–C(8′)); 0.78 (*m*, 1H–C(8′)). Difference-NOE (500 MHz, (D_6)DMSO): 6.45 (H–C(1′)) → 8.69 (H–C(8)), 2.71 (H_β–C(2′)); 4.26 (H–C(4′)) → 8.69 (H–C(8)), 5.41 (OH), 2.82 (H_α–C(2′)), 0.87 (H–C(8′)); 2.26 (H–C((7′)) → 6.45 (H–C(1′)), 1.66 (H–C(7′)). ^{13}C-NMR (75 MHz, (D_6)DMSO): 152.15 (*s*, C(4)); 151.82 (*d*, C(2)); 150.59 (*s*, C(6)); 143.33 (*d*, C(8)); 133.59 (*s*, arom. C); 132.67, 128.70 (*d*, arom. C); 126.01 (*s*, C(5)); 89.00 (*d*, C(4′)); 85.07 (*s*, C(3′)); 83.55 (*d*, C(1′)); 63.53 (*s*, C(5′)); 45.97, 40.39 (2*t*, C(7′), C(2′)); 23.72 (*d*, C(6′)); 16.76 (*t*, C(8′)). EI-MS (70 eV): 393 (4, M^+), 364 (6), 239 (65), 217 (10), 211 (56), 162 (13), 155 (18), 136 (82), 122 (18), 113 (14), 108 (46), 105 (100). Anal. calc. for $C_{13}H_{16}N_2O_3 \cdot 0.25\ H_2O$: C 60.37, H 4.94, N 17.60; found: C 60.54, H 5.08, N 17.67.

*(5′*R*,6′*R*)-*N*^{6}-Benzoyl-9-(2′-deoxy-3′,5′-ethano-5′,6′-methano-β-*D*-ribofuranosyl)adenine* (= *(5′*R*,7′*R*)-*N*^{6}-Benzoyl-9-(2′-deoxy-3′,5′,5′-propane[1,2,3]triyl-β-*D*-ribofurnosyl)adenine*; (+)-**2**). To a soln. of **18** (768 mg, 1.325 mmol) in THF (18 mol) a soln. of Bu_4NF (3.0 ml, 3.3 mmol; 1.1M in hexane) was added and stirred for 4 h at r.t. and 1 h at 50°. After addition of NH_4Cl (550 mg, 10 mmol) and stirring for 30 min at r.t., the mixture was adsorbed at silica gel (2.5 g) and purified by FC (silica gel (40 g), CH_2Cl_2/MeOH 9:1). The isolated product was dissolved in CH_2Cl_2/MeOH 9:1 (4 ml). Addition of H_2O (15 ml) led to the formation of a white solid which was purified by FC (silica gel (40 g), CH_2Cl_2/MeOH 9:1): 496 mg (95%) of (+)-**2**. White foam. R_f (CH_2Cl_2/MeOH 9:1) 0.48. $[\alpha]_D^{22}$ = + 14.0 (*c* = 0.60, MeOH). UV: 280 (19540). IR (KBr): 3600–3000*s* (br.), 2933*m*, 1702*s*, 1619*w*, 1582*s*, 1456*s*, 1354*m*, 1303*m*, 1262*s*, 1119*w*, 1058*m*, 1037*w*, 963*w*, 898*w*, 850*w*, 828*w*, 800*m*, 756*w*, 712*m*, 640*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 11.20 (br. *s*, NH–C(6)); 8.75, 8.74 (2*s*, H–C(2), H–C(8)); 8.03 (*d*, *J* = 7, 2 arom. H); 7.54 (*m*, 3 arom. H); 6.47 (*dd*, *J* = 6.6, 5.1, H–C(1′)); 5.96 (*s*, OH); 5.35 (*s*, OH); 4.09 (*s*, H–C(4′)); 2.87 (*dd*, *J* = 13.2, 4.8, 1 H–C(2′)); 2.57 (*dd*, *J* = 13.4, 6.6, 1 H–C(2′)); 1.93 (*dd*, *J* = 13.1, 4.8, 1 H–C(7′)); 1.48 (*d*, *J* = 13.6, 1 H–C(7′)); 1.34 (*m*, H–C(6′)); 0.89 (*m*, 1 H–C(8′)); 0.69 (*m*, 1H–C(8′)). Difference-NOE (500 MHz, (D_6)DMSO): 8.75 (H–C(8), H–C(2)) → 5.96 (OH), 2.87 (H_β–C(2′)), 1.93 (H–C(7′)), 1.34 (H–C(6′)); 6.47 (H–C(1′)) → 4.09 (H–C(4′)), 2.57 (H_α–C(2′)); 4.09 (H–C(4′)) → 6.47 (H–C(1′)), 5.96 (OH), 5.35 (OH), 0.69 (H–C(6′)). ^{13}C-NMR (75 MHz, (D_6)DMSO): 165.79 (*s*, CO); 151.67 (*s*, C(4)); 151.62 (*d*, C(2)); 150.50 (*s*, C(6)); 142.84 (*d*, C(8)); 133.57 (*s*, arom. C); 132.60, 128.64 (2*d*, arom. C); 126.45 (*s*, C(5)); 90.80 (*d*, C(4′)); 86.00 (*s*, C(3′)); 85.98 (*d*, C(1′)); 63.43 (*s*, C(5′)); 46.43, 40.95 (2*t*, C(7′), C(2′)); 23.90 (*d*, C(6′)); 17.78

(*t*, C(8')). EI-MS (70 eV): 393 (3, M^+), 364 (5), 239 (99), 211 (69), 162 (10), 154 (11), 142 (24), 136 (100). Anal. calc. for $C_{13}H_{16}N_2O_3 \cdot 1.5\ H_2O$: C 57.14, H 5.27, N 16.66; found: C 57.04, H 5.38, N 16.55.

*(5'R,6'R)-N⁶-Benzoyl-9-{5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-3',5'-ethano-5'-6'-methano-β-*D*-ribofuranosyl}adenine* (**20**). To a soln. of (+)-**2** (472 mg, 1.20 mmol) in pyridine (5 ml) was added $(MeO)_2Tr(CF_3SO_3)$ (1092 mg, 2.4 mmol) under Ar at r.t. After 3 h, a further portion of $(MeO)_2Tr(CF_3SO_3)$ (596 mg, 1.2 mmol) was added, and the mixture was stirred until all starting material had disappeared (TLC control with Et_3N-treated TLC plates). After 6 h, AcOEt was added (50 ml) and the soln. washed with sat. $NaHCO_3$ soln. (2 × 30 ml). The aq. phases were extracted with AcOEt (50 ml) and CH_2Cl_2 (30 ml) and the combined org. phases dried ($MgSO_4$) and evaporated. FC (silica gel (35 g) AcOEt + 5% Et_3N) of the residue yielded **20** (487 mg, 58%). White foam. R_f (CH_2Cl_2/MeOH 9:1) 0.54. UV: 232 (21030), 279 (31240). IR ($CHCl_3$): 3729*w*, 3175–3525*m* (br.), 2935*w*, 2361*s*, 2337*s*, 1698*m*, 1607*m*, 1577*m*, 1508*s*, 1454*m*, 1295*m*, 1250*s*, 1176*m*, 1066*w*, 1033*m*, 995*w*, 910*w*, 830*m*, 730*m*, 670*m*, 645*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 9.01 (br. *s*, NH–C(6)); 9.07, 8.75 (2*s*, H–C(2), H–C(8)); 8.03 (*d*, *J* = 7, 2 arom. H); 7.38–7.65 (*m*, 9 arom. H); 7.15–7.20 (*m*, 3 arom. H); 6.80 (*m*, 4 arom. H); 6.29 (*d*, *J* = 6.3, H–C(1')); 3.78, 3.78 (2*s*, 2 MeO, H–C(4')); 3.19, 2.83, 2.60, 2.50, 1.24–1.73 (5*m*, OH, CH_2(2'), H–C(6'), CH_2(7')); 0.98 (*m*, 1 H–C(8')); 0.46 (*m*, 1 H–C(8')). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.80 (*s*, CO); 158.62, 158.55 (2*s*, arom. C); 152.08 (*d*, C(2)); 150.46 (*s*, C(6)); 149.25 (*s*, C(4)); 146.05 (*s*, arom. C); 141.79 (*d*, C(8)); 136.99, 136.83, 133.61 (3*s*, arom. C); 132.71, 130.85, 130.67, 128.75, 128.57, 127.83, 127.55, 126.89 (8*d*, arom. C); 123.93 (*s*, C(5)); 112.80 (*d*, arom. C); 91.38, 87.75 (2*d*, C(4'), C(1')); 88.11, 86.44 (2*s*, C(3'), Ar_2CPh); 67.71 (*s*, C(5')); 55.12 (*q*, MeO); 47.69, 41.36 (2*t*, C(7'), C(2')); 25.35 (*d*, C(6')); 17.19 (*t*, C(8')). FAB-MS: 696 (5, M^+), 633 (5), 303 (11), 242 (100), 184 (6), 142 (11).

*(5'R,6'S)-N⁶-Benzoyl-9-{5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-3',5'-ethano-5',6'-methano-β-*D*-ribofuranosyl}adenine 3'-(2-Cyanoethyl Diisopropylphosphoramidite)* (= *(5'R,7'S)-N⁶-Benzoyl-9-{5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-3',5'-propane[1,2,3]triyl-β-*D*-ribofuranosyl}adenine 3'-(2-Cyanoethyl Diisopropylphosphoramidite*); **21**). To a soln. of **20** (481 mg, 0.825 mmol) in dry MeCN (4 ml) was added under Ar at r.t. $(i\text{-}Pr)_2NEt$ (0.83 ml, 4.9 mmol) and 2-cyanoethyl diisopropylphosphoramidochloridite (0.43 ml, 2.06 mmol; *Aldrich*). After 45 min, the soln. was diluted with AcOEt (40 ml) and washed with sat. $NaHCO_3$ soln. (40 ml). The org. phase was dried (Na_2SO_4) and evaporated. FC (silica gel (40 g), hexane/AcOEt/Et_3N 10:20:1) of the residue afforded, after drying (r.t./0.01 Torr, 15 h), **21** (577 mg, 89%). Pale yellow foam (1:1 diastereoisomer mixture). R_f (hexane/AcOEt 1:4) 0.60, 0.50. ^{1}H-NMR (300 MHz, $CDCl_3$): 9.04 (br. *s*, NH–C(6)); 9.05, 8.77 (2*s*, H–C(2), H–C(8)); 8.03 (*d*, *J* = 7, 2 arom. H); 7.40–7.62 (*m*, 9 arom. H); 7.19–7.28 (*m*, 3 arom. H); 6.80 (*m*, 4 arom. H); 6.34 (*m*, H–C(1')); 3.78, 3.77, 3.76, 3.75 (4*s*, 2 MeO, H–C(4')); 3.36–3.70 (*m*, 4 H, 2 Me_2CH, OCH_2CH_2CN); 2.76–2.96, 2.08, 1.86 (3*m*, CH_2(2'), CH_2(7')); 2.54, 2.48 (2*t*, *J* = 6, OCH_2CH_2CN); 1.73 (*m*, H–C(6')); 1.25 (*m*, 1 H–C(8')); 1.01–1.12 (*m*, 2 Me_2CH); 0.58, 0.51 (2*m*, 1 H–C(8')). ^{13}C-NMR (75 MHz, $CDCl_3$): 164.48 (*s*, CO); 158.68, 158.61 (2*s*, arom. C); 152.25 (*d*, C(2)); 150.66 (*s*, C(6)); 149.21 (*s*, C(4)); 146.19, 146.16 (2*s*, arom. C); 141.77 (*d*, C(8)); 137.08, 137.07, 136.87 (3*s*, arom. C); 133.69 (*s*, arom. C); 132.69, 130.94, 130.73, 128.81, 128.57, 127.80, 127.60, 126.87, 126.81 (9*d*, arom. C); 124.21 (*s*, C(5)); 117.42, 117.29 (2*s*, CN); 112.84 (*d*, arom. C); 92.06, 91.76, 91.76 (2*d*, *J*(C,P) = 6, C(4')); 89.64, 89.62 (2*s*, C(3')); 88.14, 88.10 (2*s*, Ar_2CPh); 88.26, 88.05 (2*d*, C(1')); 67.48, 67.46, 67.42, 67.39 (4*s*, C(5')); 57.86, 57.60, 57.33 (3*t*, OCH_2CH_2CN); 55.16, 55.15, 55.12, 55.11 (4*q*, MeO); 45.70 (*t*, C(2')); 43.30, 43.16, 43.14, 43.0 (4*d*, Me_2CH); 39.40, 39.26 (2*t*, C(7')); 25.34, 25.30 (2*d*, C(6')); 24.41, 24.33, 24.20, 24.09 (4*q*, Me_2CH); 20.29, 20.25, 20.19, 20.15 (4*t*, OCH_2CH_2CN); 16.85, 16.69 (2*t*, C(8')). ^{31}P-NMR (161.9 MHz, $CDCl_3$, 85% H_3PO_4 (= 0 ppm)): 150.07, 148.33. FAB-MS: 896 (1, M^+), 306 (4), 303 (100).

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