Oligonucleotide Analogues with a Nucleobase-Including Backbone:

Part 6

2-Deoxy-D-erythrose-Derived Phosphoramidites: Synthesis and Incorporation into 14-Mer DNA Strands

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Two modified DNA 14-mers have been prepared, containing either a 2-deoxy-D-erythrose-derived adenosine analogue carrying a C(8)–CH_2O group (deA*), or a 2-deoxy-D-erythrose-derived uridine analogue, possessing a C(6)–CH_2O group (deU*). These nucleosides are linked *via* a phosphinato group between O–C(3′) (deA* and deU*) and O–C(5′) of one neighbouring nucleotide, and between C(8)–CH_2O (deA*), or C(6)–CH_2O (deU*) and O–C(3′) of the second neighbour. N^6-Benzoyl-9-(β-D-erythrofuranosyl)adenine (**3**) and 1-(β-D-erythrofuranosyl)uracil (**4**) were prepared from D-glucose, deoxygenated at C(2′), and converted into the required phosphoramidites **1** and **2**. The modified tetradecamers **31** and **32** were prepared by solid-phase synthesis. Pairing studies show a decrease in the melting temperature of 7 to 8 degrees for the duplexes **31** · **30** and **32** · **29**, as compared to the unmodified DNA duplex **29** · **30**. A comparison with the pairing properties of tetradecamers similarly incorporating deoxyribose- instead of the deoxyerythrose-derived nucleotides evidences that the CH_2OH substituent at C(4′) has no significant effect on the pairing.

Introduction. – Oligonucleotide analogues with a nucleobase-including backbone should allow to answer the question whether the structural differentiation between nucleobase and backbone in DNA, RNA, and their analogues is a necessary prerequisite for the formation of stable homo- and/or heteroduplexes [1–5]. We have already described oligonucleotide analogues with a phosphinato group between O–C(3′) and either a C(8)–CH_2O group of 2′-deoxyadenosine (dA^{*}_{n}[1]); *Fig. 1*), or a C(6)–CH_2O group of 2′-deoxyuridine (dU^{*}_{n}[1]); *Fig. 1*) [5]. Force-field calculations [6] and *Maruzen* model studies suggested that these analogues may form autonomous pairing systems, and that the incorporation of single modified dA* or dU* units into DNA 14-mers is compatible with duplex formation. Pairing studies of singly modified tetradecamers, however, showed that the introduction of dA* or dU* units into a 14-mer DNA duplex lowered the melting temperature by 6–7°, as compared to the unmodified DNA duplex [5]. This destabilization may be due to a distortion of the DNA duplex caused by the *syn*-conformation [7] of the dA* or dU* units, as enforced by an unfavourable interaction between the *C(8)*- or *C(6)*-substituent and the carbohydrate moiety – presumably the O–C(5′) group – of dA* and dU*. To reduce this steric interaction, we decided to remove the CH_2OH substituent at C(4′) of dA*

[1]) The repeating units of B-DNA are denoted dA, dT, dG, and dC. 2-Deoxyribose-derived units linked *via* O–C(3′) and O(10), or O(7) are denoted dA* and dU*, respectively, and 2-deoxy-D-erythrose-derived units linked *via* O–C(3′) and O(10), or O(7), deA* and deU*, respectively (*Fig. 1*).

and dU*, and to introduce the 2-deoxyerythrose-derived units deA*[1]) and deU*[1]) (*Fig. 1*) into a DNA duplex.

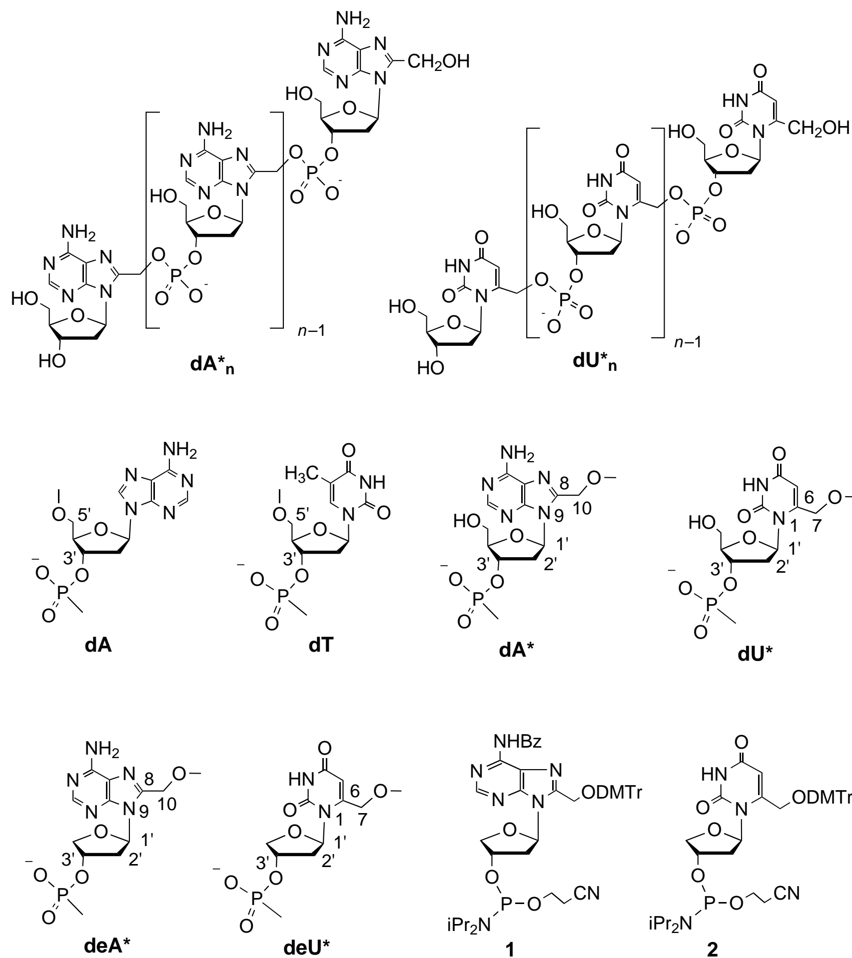


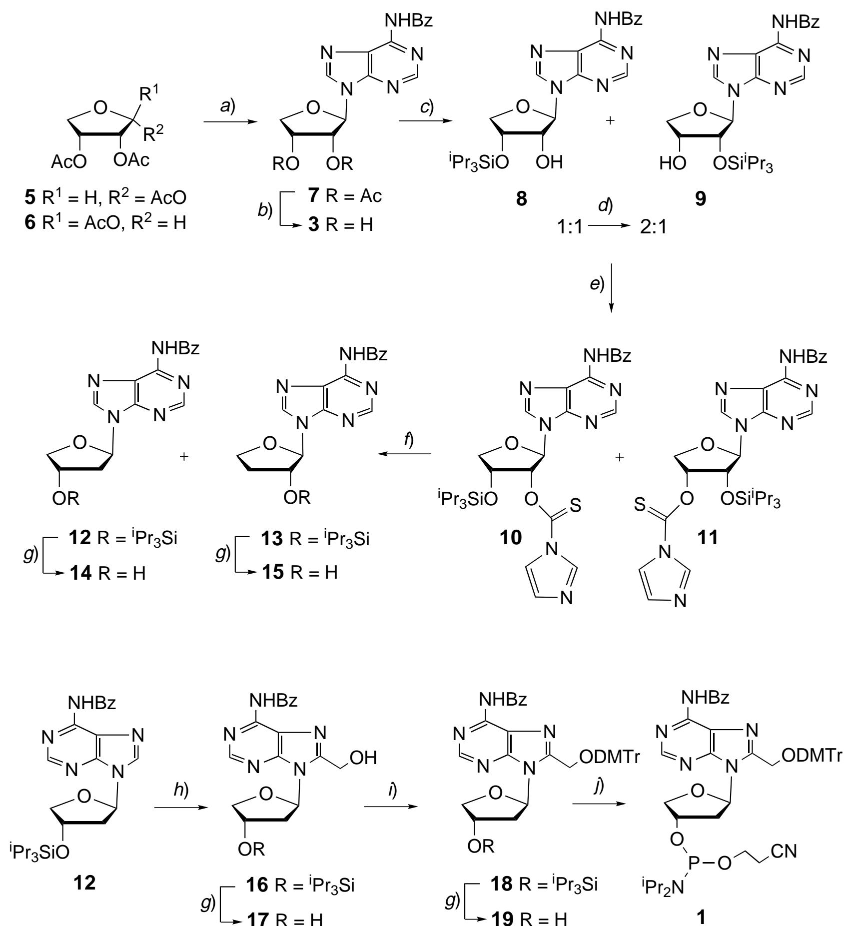
Fig. 1. *2-Deoxyribose-derived oligonucleotide analogues* dA^*_n *and* dU^*_n, *DNA units dA and dT*, *2-deoxyribose-derived units dA* and dU**, *2-deoxyerythrose-derived units deA* and deU**, *and the phosphoramidites* **1** *and* **2**

We report on the syntheses of the deA*- and deU*-derived phosphoramidites **1** and **2** (*Fig. 1*), the incorporation of a single deA*, or deU* unit into a tetradecamer, and on the pairing of these tetradecamers with an unmodified complementary strand.

Results and Discussion. – 1. *Synthesis of the Phosphoramidites* **1** *and* **2**. Nucleosidation of 2-deoxy-D-erythrose derivatives with thymine [8] and uracil [9] proceeds with a low selectivity, affording 2:1 to 1:1 mixtures of anomers, while nucleosidation of anomeric mixtures of triacetyl erythrofuranose with N^6-benzoyladenine or uracil afforded diastereoselectively the β-D-nucleosides **3** and **4** (*Schemes 1* and *2*) after deprotection [10]. For this reason, we decided to prepare the phosphoramidites

1 and **2** from the 1,2,3-tri-*O*-acetyl-α,β-D-erythroses **5**/**6** (*Scheme 1*) rather than from 2-deoxy-D-erythrose, and to subsequently remove the OH group at C(2'). Triacetylerythrose is readily accessible by degradation of D-glucose with $Pb(OAc)_4$ [11] [12] and acetylation [13][2]). Deoxygenation of **3** and **4**, followed by hydroxymethylation, protection, and phosphitylation, should lead to the phosphoramidites **1** and **2**.

Scheme 1



a) 1. N^6-Benzoyladenine, *N*,*O*-bis(trimethylsilyl)acetamide (BSA); 2. $SnCl_4$; 80%. *b*) 1. NaOH, H_2O/MeOH/THF 5:4:1; 2. NH_4Cl; 80%. *c*) $^iPr_3SiOTf$, pyridine, DMF; 92%. *d*) SiO_2, Et_3N. *e*) *N*,*N*-(thiocarbonyl)diimidazole, CH_2Cl_2. *f*) Bu_3SnH, 2,2'-azobis(isobutyronitrile) (AIBN), toluene; 44% of **12** and 20% of **13** (from **8**/**9** 2:1). *g*) $Bu_4NF \cdot 3\ H_2O$, THF; **14** (74%); **15** (89%); **19** (76%). *h*) 1. LDA/THF; 2. DMF; 3. AcOH; 4. $NaBH_4$/EtOH; 88%. *i*) Dimethoxytrityl chloride (= bis(4-methoxyphenyl)(phenyl)methyl chloride; DMTrCl), EtN^iPr_2, 4-(dimethylamino)pyridine (DMAP), CH_2Cl_2; 89%. *j*) $(NCCH_2CH_2O)P(^iPr_2N)Cl$, CH_2Cl_2, EtN^iPr_2; 80% of 2 diastereoisomers (1:1).

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[2]) 2-Deoxy-D-erythrose has been prepared from 3-deoxy-D-erythropentose [14], dimethyl (*S*)-malate [15], D-isoascorbic acid [16], and (*S*)-solketal [16].

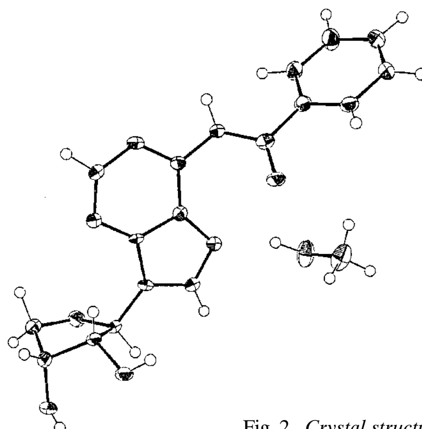


Fig. 2. *Crystal structure of* **3** · MeOH

Nucleosidation of the anomeric mixture **5/6** with N^6-benzoyladenine in the presence of $SnCl_4$ and *N,O*-bis(trimethylsilyl)acetamide (BSA) at 60° (*cf.* [17][18]) gave the β-D-configured nucleoside **7** (80%), which was deacetylated with 2M NaOH to yield 80% of the nucleoside **3**. Stannylation of **3** with Bu_2SnO in toluene [19], followed by treatment of the crude Sn-acetal with Et_3SiCl, led to a 1:1 mixture of regioisomeric silyl ethers. Regioselective silylation of **3** at HO−C(3′) with various trialkylchlorosilanes in the presence of Ag salts and DABCO as reported for ribonucleosides [20] led again to unsatisfactory results. Finally, we treated **3** with a 2.5-fold excess of $^iPr_3SiOTf$ in DMF/pyridine 16:1 at 23° to obtain 92% of a 1:1 mixture of the 3′- and 2′-*O*-$^iPr_3Si$-protected nucleosides **8** and **9**. Treatment of this mixture with silica gel in Et_3N led to partial migration of the $^iPr_3Si$ group from O(2′) to O(3′), resulting in a 2:1 mixture **8/9** after 24 h. This mixture was converted to the thiocarbamates **10/11** (2:1). Treatment of the crude mixture with Bu_3SnH and 2,2′-azobis(isobutyronitrile) (AIBN) in refluxing toluene yielded a mixture **12/13** (2:1; 64% from **8/9**). The nucleosides **12/13** were readily separated by FC. Desilylation of **12** and **13** yielded **14** and **15** (80% each), respectively. Deprotonation of **12** by LDA [21], addition of DMF, and reduction with $NaBH_4$ gave 88% of the *C(8)*-CH_2OH nucleoside **16** that was desilylated to **17** (80%). Dimethoxytritylation of **16** gave **18** (89%) that was desilylated to **19** (80%). The alcohol **19** was converted to the phosphoramidite **1** in the usual way [22]; **1** is stable at −15° for several months.

The configuration of **3** was established by X-ray crystal-structure analysis of **3** · MeOH[3]) (*Fig. 2*). The erythrofuranosyl moiety adopts the $^2T_3$ conformation, similarly to the conformation deduced for **3** in D_2O solution [10]. HO−C(3′) forms a weak intramolecular H-bond to O−C(2′) (distance O(2′)···O(3′) 2.77 Å); intermolecular H-bonds are found between HO−C(3′) and N(1), H−N(6) and O−C(2′), MeOH and

[3]) The crystallographic data have been deposited with the *Cambridge Crystallographic Data Centre* (deposition No. CCDC-158435 (**3**), CCDC-158436 (**4**), and CCDC-158437 (**25**)). Copies of the data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44(1223)336033; e-mail: deposit@ccdc.cam.ac.uk).

N(7), and between HO–C(2′) and MeOH. The nucleobase adopts the *syn*-conformation.

The structures of **8** and **9** were assigned on the basis of the ^{1}H-NMR spectra of **8/9** (2:1). The signals of H–C(2′) and H–C(3′) of **8/9** were assigned on the basis of their multiplicity and coupling constants (see *Table 3*). In $CDCl_3$, H–C(2′) of the major compound appears as a *dt* with $J(2',3') = 5.0$, $J(1',2') = 4.1$, and $J(H,OH) = 5.3$ Hz. Upon addition of D_2O, this signal collapsed to a *dd*, while the H–C(3′) *q* remained unchanged, evidencing that the major compound possesses structure **8**. The broad H–C(3′) signal of the minor compound (**9**) collapsed to a *ddd* upon addition of D_2O, while the H–C(2′) *t* remained unchanged. The structure determination was corroborated by the ^{1}H-NMR spectra of a 2:1 mixture of the thiocarbamates **10/11**. The H–C(2′) and H–C(3′) signals of **10/11** were assigned on the basis of their multiplicity and coupling constants (see *Table 3*). Carbamoylation of O–C(2′) of the major compound **8**, leading to **10**, induced a 1.6-ppm downfield shift for H–C(2′), while carbamoylation of O–C(3′) of the minor compound **9**, leading to **11**, resulted in a 1.67-ppm downfield shift for H–C(3′). As expected, H–C(1′) of **12** appears as a *t* at 6.46 ppm with $J(1',2') = 6.6$ Hz (see *Table 3* in *Exper. Part*). The $H_{pro\text{-}S}$–C(2′) of **12** gives rise to a *ddd* at 2.97 ppm, while $H_{pro\text{-}R}$–C(2′) appears at 2.60 ppm as a *dddd* (W coupling to H–C(4′), $J(2',4') = 1.0$ Hz). The signals of H–C(1′), H–C(2′), H–C(3′), and H–C(4′) of **13** were assigned on the basis of irradiation experiments. H–C(1′) of **13** resonates at 6.00 ppm as a *d*, $J(1',2') = 1.6$ Hz, $H_{pro\text{-}S}$–C(3′) of **13** at 2.32 ppm as a *dtd*, and $H_{pro\text{-}R}$–C(3′) at 2.12 ppm as a *dddd*. As a rule, the shift from the *anti*- to the *syn*-conformation is indicated by a downfield shift for $H_{pro\text{-}S}$–C(2′) and an upfield shift for C(2′) [23]. The significant downfield shifts for $H_{pro\text{-}S}$–C(2′) ($\Delta\delta = 0.18 - 0.30$ ppm) and the upfield shifts for C(2′) ($\Delta\delta = -1.1$ to -2.6 ppm) of the nucleosides **16**, **18**, **19**, and the phosphoramidite **1**, as compared to the corresponding signals of **12**, evidence that all *C(8)*-substituted nucleosides adopt predominantly the *syn*-conformation (*Table 1*).

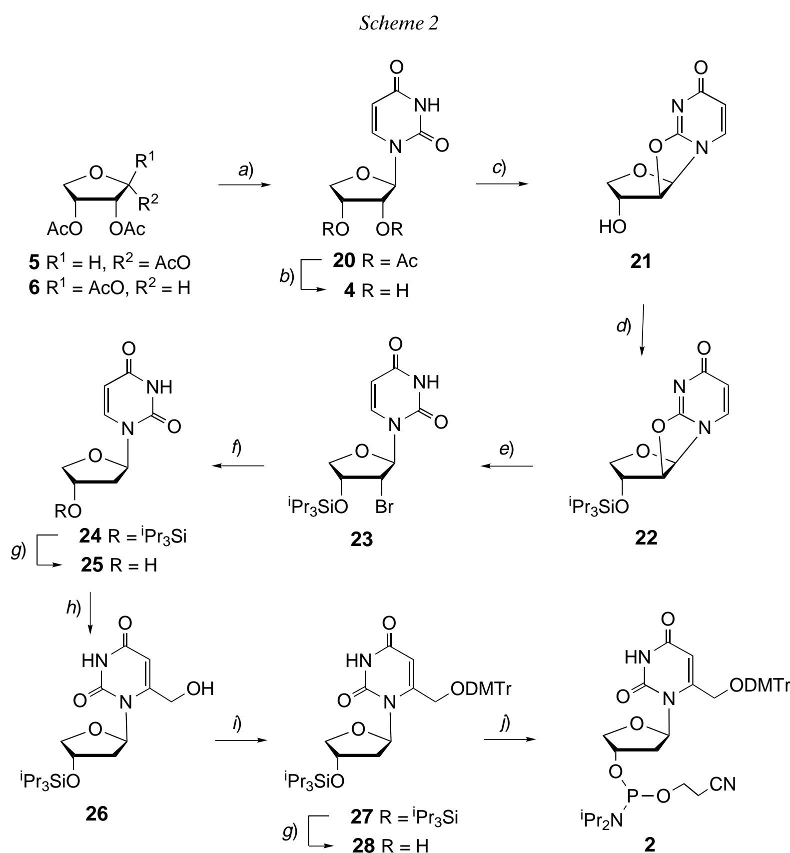
The ratio $J(1',2'_{pro\text{-}S})/J(3'_{pro\text{-}R},4')$ is considered a measure of the position of the equilibrium between the *S*- (sugar-pucker $_3E - {}^2T_1$) and *N*-conformers (sugar-pucker $^3T_2 - {}^3T_4$) [24]. The $J(1',2'_{pro\text{-}S})$ (6.6 Hz) and $J(3',4')$ ($\leqslant 2.1$ Hz) values (*Table 1*) evidence a predominance of the *S*-conformer of the nucleosides **1**, **12**, **14**, **16**, **18**, and **19**.

Table 1. *^{1}H- and ^{13}C-NMR Shift Differences $\Delta\delta$(H–C(2′)), and $\Delta\delta$(C(2′))* [ppm] *for the Nucleosides* **16**, **18**, **19**, *and* **1** *as Compared to* **12**, *and for* **24**, **26**–**28**, *and for* **2** *as Compared to* **24**, *and Ratio of* S/N-*Conformers of these Nucleosides, as Deduced from* J*(1′,2′)*/J*(3′,4′)* [Hz]

Nucleoside	$\Delta\delta$(H–C(2′$_{pro\text{-}S}$))	$\Delta\delta$(C(2′))	J(1′,2′)	J(3′,4′)	Ratio S/N
12	–	–	6.6	2.1	76/24
16	0.18	−1.1	6.6	< 1.0	> 87/13
18	0.23	−1.1	6.6	< 1.0	> 87/13
19	0.23	−1.8	6.6	< 1.0	> 87/13
1	0.30	−2.6	6.6	< 1.0	> 87/13
24	–	–	6.5	2.2	75/25
26	0.79	−2.0	6.6	< 1.0	> 87/13
27	0.74	−2.1	7.0	< 1.0	> 88/12
28	0.71	−3.1	7.0	< 1.0	> 88/12
2	0.77	−4.1	6.5	< 1.0	> 87/13

To prepare the phosphoramidite **2** (*Scheme 2*), the anomeric mixture **5**/**6** was treated with uracil in the presence of BSA and $SnCl_4$ in MeCN at 60° (*cf.* [17][18]). We obtained 80% of the *β*-D-configured nucleoside **20**, which was deacetylated with 2M NaOH to yield 80% of **4**. To deoxygenate **4** at C(2′), we planned to convert **4** to the corresponding 2,2′-anhydronucleoside [25], to cleave the C(2′)–O bond with LiBr and $BF_3 \cdot Et_2O$ [26], and to reductively debrominate the resulting 2′-bromo-2′-deoxynucleoside. The 2,2′-anhydro-1-(*β*-D-threofuranosyl)uracil (**21**) was prepared from **4** by treatment with diphenyl carbonate and $NaHCO_3$ in DMF [25]. However, all attempts to convert **21** to the 2′-deoxynucleoside **25** failed. Silylation of the 2,2′-anhydronucleoside **21** with a 5-fold excess of $^iPr_3SiOTf$ yielded **22** (61% from **4**). Treatment of **22** with LiBr and $BF_3 \cdot Et_2O$ gave the 2′-bromo-2′-deoxynucleoside **23** (88%) that was debrominated in 97% yield with Bu_3SnH and AIBN. The resulting 2′-deoxynucleoside

Scheme 2



a) 1. Uracil, *N*,*O*-bis(trimethylsilyl)acetamide (BSA); 2. $SnCl_4$; 80%. *b*) 1. NaOH, H_2O/MeOH/THF 5:4:1; 2. NH_4Cl; 80%. *c*) 1. Diphenyl carbonate, DMF; 2. $NaHCO_3$. *d*) $^iPr_3SiOTf$, pyridine, DMF; 62% (from **4**). *e*) LiBr, $BF_3 \cdot Et_2O$, 1,4-dioxane; 88%. *f*) Bu_3SnH, AIBN, toluene; > 97%. *g*) $Bu_4NF \cdot 3\,H_2O$, THF; **25** (88%), **28** (96%). *h*) 1. LDA/THF; 2. DMF; 3. AcOH; 4. $NaBH_4$/EtOH; 51%. *i*) DMTrCl, $^iPr_2NEt$, DMAP, CH_2Cl_2; 77%. *j*) $(NCCH_2CH_2O)P(^iPr_2N)Cl$, CH_2Cl_2, $^iPr_2NEt$; 69% of 2 diastereoisomers (2:1).

24 was desilylated to **25** (80%). Hydroxymethylation of **24** to **26** was accomplished in 52% yield similarly as described above for **12**. Dimethoxytritylation of **26** to **27** and desilylation of **27** yielded 73% of the alcohol **28**, which was converted to the phosphoramidite **2** in the usual way (70%); at $-15°$, **2** is stable for several months.

The β-D-configuration of 1-(β-D-erythrofuranosyl)uracil (**4**) was established by X-ray crystal-structure analysis (*Fig. 3,a*).

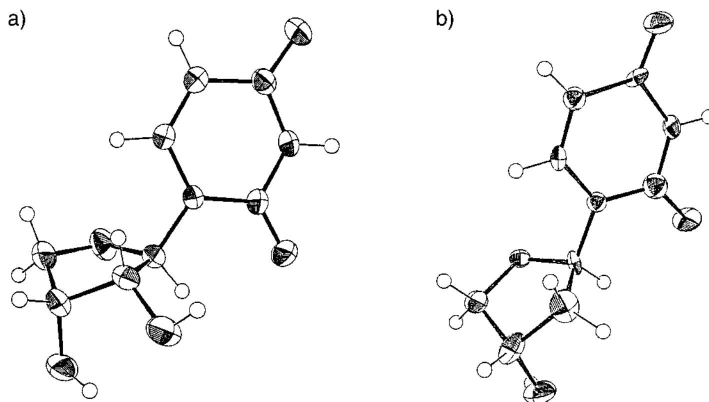


Fig. 3. *Crystal structures of* a) **4** *and* b) **25**

Similarly to N^6-benzoyl-9-(β-D-erythrofuranosyl)adenine (**3**), the erythrofuranosyl moiety of **4** adopts the $_3E$-conformation. There is a (weak?) intramolecular H-bond between HO–C(3′) and O–C(2′) (distance O(2′)···O(3′) 2.69 Å), while intermolecular H-bonds are found between HO–C(2′) and O–C(2′), HO–C(3′) and O–C(4′), and H–N(3) and O–C(4′). Unlike **3**, the uracil derivative **4** adopts the *anti*-conformation.

The H-atoms H–C(1′), H–C(2′), H–C(3′), H–C(5), and H–C(6) of the 2,2′-anhydronucleoside **21** (*Table 5* in *Exper. Part*) resonate at almost the same field as the corresponding signals of 2,2′-anhydrouridine ($\Delta\delta = \pm 0.04$ ppm) [27]. As observed for 5′-protected 2,2′-anhydrouridines [28][29], C(2), C(4), C(5), C(1′), and C(2′) of **21** are shifted significantly downfield, as compared to **4**: C(4) and C(2) give rise to two *s* at 178.7 and 164.2 ppm (**4**: two *s* at 163.5 and 151.0 ppm), C(5) resonates as a *d* at 112.1 ppm (**4**: *d* at 102 ppm), and C(1′) and C(2′) as two *d* at 93.4 and 90.6 ppm (**4**: two *d* at 88.8 and 74.1 ppm). Bromination of **22** to **23** is indicated by a strong upfield shift for C(2′) of **23** ($\delta = 52.4$ as compared to $\delta = 74.1$ ppm in **4**), and the $[M + H]^+$ peak in the FAB-MS of **23** shows the typical isotope pattern for Br compounds.

As expected, H–C(1′) of **24** appears at 6.15 ppm as a *t* with $J(1′,2′) = 6.5$ Hz. The $H_{pro\text{-}R}$–C(2′) of **24** gives rise to a *ddd* at 2.50, and $H_{pro\text{-}S}$–C(2′) to a *dt* at 2.11 ppm. The ratio $J(1′,2′)/J(3′,4′)$ indicates that the 2-deoxy-D-erythrofuranosyl moiety of **24** adopts predominantly the *S*-conformation (*Table 1*).

The structure of **25** was established by X-ray crystal-structure analysis (*Fig. 3,b*). Two symmetrically independent molecules in the elementary cell form a dimer with intermolecular H-bonds between H–N(3) and O–C(4), and between H–N(3) and O–C(2). Both independent molecules adopt the $^2T_3$- and the *anti*-conformations.

Similarly to the adenine series, the downfield shift for $H_{pro\text{-}S}$–C(2′) ($\Delta\delta = 0.71 - 0.79$ ppm) and the upfield shift for C(2′) of **2** and **26**–**28**, as compared to **24** ($\Delta\delta = -2.0$ to -4.1 ppm), show the predominance of the *syn*-conformation for the *C(6)*-substituted nucleosides (*Table 1*). The equilibrium between the *S*- and the *N*-conformers of **2** and **26**–**28** is clearly in favour of the *S*-conformer (> 88/12), as indicated by $J(1',2'_{pro\text{-}S})$ and $J(3',4')$ values of **2** and **26**–**28** (*Table 1*).

2. *Solid-Phase Synthesis of 14-Mer DNA Strands Containing deA* or deU*, and of the Complementary DNA Strands. Table 2* shows the 14-mer DNA strands **29** and **30** possessing a random sequence with an internal dA or dT unit flanked by dG or dC units. Replacement of the internal dA of **29** by deA* (derived from **1**) led to the modified 14-mer **31**, while replacement of the internal dT of **30** by deU* (from **2**) led to the modified 14-mer **32**. The solid-phase synthesis of the oligomers **29**–**32** was carried out on a DNA-synthesizer using essentially the protocol for the synthesis of pRNA [30]. The coupling time for the attachment of **1**, **2**, and the DNA phosphoramidites following the incorporation of **1** and **2** was arbitrarily set to 30 min; it led to coupling yields of 82% [4]) for **1** and *ca.* 80–90% for the DNA-phosphoramidites following **1**, and of *ca.* 90% for **2** (99% for all other couplings). Longer coupling times did not improve yields. The DNA 14-mers **29** and **30** were deprotected and cleaved off the solid support by ammonolysis with saturated aqueous NH_3/MeOH 1:1 at 50° within 20 h, while **31** was deprotected under the same conditions within 3.5 h. Prolonged heating of the modified DNA strand **32** (incorporating deU*) at 50° led to degradation; this strand was deprotected at 35°. The crude products were analyzed by RP-HPLC. The DNA strands **29** and **30** were pure, the modified tetradecamer **32** was *ca.* 70–80% pure, while crude **31** contained three major products A, B, and C in a *ca.* 1:2:1 ratio. The products were purified by RP-HPLC, desalted, and analyzed by RP-HPLC and MALDI-TOF mass spectroscopy; only fraction C (from crude **31**) exhibited a molecular ion in agreement with structure **31** [5]). The yield of the oligomers, as determined from the detritylation assay, and their molecular masses are shown in *Table 2*.

Table 2. *Total Yields, and Calculated and Experimental Molecular Masses of the Oligodeoxynucleotides* **29**–**32**

Sequence	Total yield [%] [a])	Calc. mass	Exper. mass (MALDI-TOF)
29 5′-d(CGTAAGCTCGATAG)-3′	94	4287.8	4287.4
30 5′-d(CTATCGAGCTTACG)-3′	99	4238.8	4239.1
31 5′-d(CTATCG**eA***GCTTACG)-3′	27	4238.8	4237.7
32 5′-d(CGTAAGC**eU***CGATAG)-3′	75	4273.8	4276.6

[a]) Calculated from the yield of the coupling steps, as determined by the detritylation assay.

3. *Pairing Studies.* The modified 14-mer **31** (*Table 2*) was hybridized with the complementary 14-mer **30** at a concentration of (2 + 2) μM and at pH 7 (10 mM NaH_2PO_4/Na_2HPO_4 in H_2O) in 0.1M aqueous NaCl. The modified duplex **31** · **30**

[4]) Each chain elongation cycle began with an acid promoted cleavage of the dimethoxytrityl group. The efficiency of each coupling step was calculated by UV-determination of the amount of $DMTr^+$ ($\varepsilon = 70000$ l · $mol^{-1} \cdot cm^{-1}$).

[5]) In agreement with this assignment, the fractions A and B did not pair with **30**.

showed a decrease of the melting temperature by 8°, as compared to the non-modified duplex **29** · **30** (see *Fig. 4* for the melting curves).

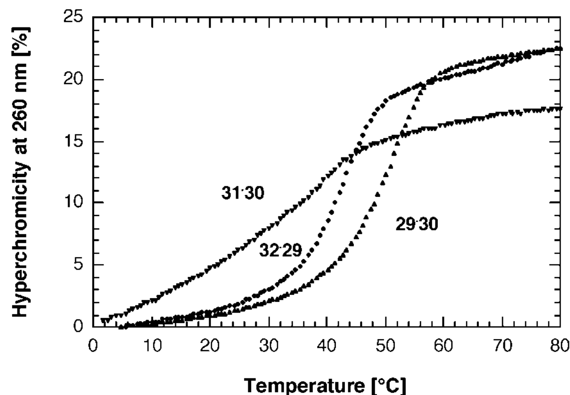


Fig. 4. *Temperature-dependent UV spectra* ('melting curves') *of the duplexes* **29** · **30**, **31** · **30**, *and* **32** · **29**

Similarly, the modified 14-mer **32** (*Table 2*) incorporating one deU* unit was hybridized with the complementary 14-mer **29** at a concentration of (2 + 2) μM and at pH 7 (10 mM NaH_2PO_4/Na_2HPO_4 in H_2O) in 0.1M aqueous NaCl. Again, the modified duplex **32** · **29** melted 7° lower than the non-modified DNA duplex **29** · **30** (see *Fig. 4* for the melting curves). Since the modified 14-mer **32** is degraded during prolonged heating, the melting process for the duplex **32** · **29** was irreversible.

Similarly as reported for the incorporation of the 2-deoxyribose-derived units dA* and dU* [5], the introduction of the 2-deoxy-D-erythrose-derived units deA* and deU* into a DNA duplex causes a decrease in melting temperature by 7–8°, as compared to the unmodified duplex. A comparison of the duplex destabilization imposed by dA*, dU*, deA*, and deU* shows that this destabilization is independent of the CH_2OH substituent at C(4′).

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Experimental Part

General. Solvents were distilled before use: THF from K/benzophenone, toluene from Na, CH_2Cl_2, DMF, pyridine, 1,4-dioxane, and EtN^iPr_2 from CaH_2. Reactions were run under Ar. Qual. TLC: precoated silica-gel plates (*Merck* silica gel *60 F_{254}*); detection by spraying with 'mostain' (400 ml of 10% aq. H_2SO_4, 20 g of $(NH_4)_6Mo_7O_{24} \cdot H_2O$, 0.4 g of $Ce(SO_4)_2$) and heating. Flash chromatography (FC): silica gel *Merck 60* (0.04–0.063 mm). Reversed-Phase High-Performance Liquid Chromatography (RP-HPLC): analytical RP column: *Macherey-Nagel*; *LiChroCart®250-4 HPLC Cartridge* filled with *LiChrospher®100*, *RP-18e* (5 μm); prep. RP column: *Macherey-Nagel*, *Hibar® RT250-10*, customized packing: *LiChrospher®100*, *RP-18e* (5 μm), eluents: 0.1M aq. Et_3NHOAc, MeCN, H_2O. Optical rotations: 1-dm cell at 25° and 589 nm. FT-IR: 1–2% soln. in the indicated solvent. ^1H-, ^{13}C-, and ^{31}P-NMR: at 200, 300, or 400 MHz, 50 or 75 MHz, or 121 MHz, resp. MS: fast-atom bombardment (FAB), matrix-assisted laser-desorption ionization (MALDI), high-resolution (HR). NOBA: 3-nitrobenzyl alcohol.

N^6-Benzoyl-9-(2′,3′-di-O-acetyl-β-D-erythrofuranosyl)adenine (**7**). A suspension of **5/6** (1:4) [11–13] (4.16 g, 16.9 mmol) and *N^6-benzoyladenine* (4.4 g, 18.4 mmol) in MeCN (18 ml) was treated dropwise with *N,O*-bis(trimethylsilyl)acetamide (10 ml, 41 mmol) at 60°. The mixture was stirred for 30 min, treated with $SnCl_4$

(8 ml, 68 mmol), stirred for 20 min, poured into a stirred mixture of AcOEt (300 ml) and sat. aq. $NaHCO_3$ (300 ml), and stirred for 15 min. The org. layer was dried (Na_2SO_4) and evaporated. FC (AcOEt/MeOH 100 : 1) gave **7** (5.7 g, 80%). Colourless powder. R_f(AcOEt/hexane 6 : 1) 0.40. $[\alpha]_D^{25} = -90.1$ ($c = 0.75$, $CHCl_3$). IR ($CHCl_3$): 3375*w* (br.), 3007*m*, 1750*s*, 1709*s*, 1612*s*, 1587*s*, 1504*m*, 1480*s*, 1469*s*, 1374*s*, 1072*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): see *Table 3*; additionally, 9.22 (br. *s*, NH); 8.05 – 7.95 (*m*, 2 arom. H); 7.63 – 7.40 (*m*, 3 arom. H); 2.16 (*s*, AcO); 2.05 (*s*, AcO). ^{13}C-NMR (50 MHz, $CDCl_3$): see *Table 4*; additionally, 170.0, 169.5 (2*s*, 2 O–C=O); 164.9 (*s*, N–C=O); 133.0 (*s*); 132.9 (*d*); 128.9 (*d*, 2 C); 128.0 (*d*, 2 C); 20.7 (*q*, Me); 20.4 (*q*, Me). FAB-MS (NOBA): 426 (69, M^+), 427 (25, $[M + H]^+$). HR-MALDI-MS: 448.123 ($C_{20}H_{19}N_5NaO_6$, $[M + Na]^+$; calc. 448.123).

Table 3. *Selected* ^{1}*H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *for the Nucleosides* **7** – **13**, **16** – **19**, and **1** *in* $CDCl_3$, *for* **3** *in* (D_6)*DMSO, and for* **14** *and* **15** *in* CD_3OD

	7	**3**	**8**	**9**	**10**	**11**	**12**	**13**
H–C(1′)	6.1 – 6.2	5.97	5.94	5.90	6.33	6.00	6.46	6.00
H–C(2′$_{pro-S}$)	6.1 – 6.2	4.86	4.83	5.56	6.42	5.90	2.97	5.10
H–C(2′$_{pro-R}$)	–	–	–	–	–	–	2.60	–
H_a–C(3′)	5.74	4.28	5.00	4.45	5.47	6.12	4.93	2.32
H_b–C(3′)	–	–	–	–	–	–	–	2.12
H_a–C(4′)	4.73	4.40	4.50	4.58	4.62	4.88	4.43	4.42
H_b–C(4′)	4.17	3.84	4.00	4.15	4.00	4.37	4.03	4.32
H–C(2)	8.75	8.75	8.76	8.80	8.71	8.76	8.82	8.80
H–C(8)	8.10	8.68	8.08	8.00	8.35	8.45	8.13	8.05
J(1′,2′)	[a]	6.6	4.2	5.3	4.1	6.2	6.6	1.6
J(2′,2′)	–	–	–	–	–	–	13.7	–
J(2′$_{pro-S}$,3′)	5.1	4.1	5.0	5.0	4.4	4.4	6.6	4.4
J(2′$_{pro-R}$,3′)	–	–	–	–	–	–	2.5	2.4
J(3′,3′)	–	–	–	–	–	–	–	13.0
J(3′,4′a)	4.1	3.7	5.0	3.4	5.0	3.0	4.0	8.4, 4.0
J(3′,4′b)	2.1	1.2	4.1	< 1.0	5.0	< 1.0	2.1	8.7, 6.2
J(4′a,4′b)	10.4	9.1	9.3	10.0	9.1	11.5	9.1	8.4
	14	**15**	**16**	**17**	**18**	**19**	**1**	
H–C(1′)	6.57	6.10	6.50	6.68	6.47	6.37	6.46	
H–C(2′$_{pro-S}$)	2.95	4.84	3.15	3.25	3.20	3.20	3.27	
H–C(2′$_{pro-R}$)	2.58	–	2.39	2.50	2.43	2.35	2.60, 2.51	
H_a–C(3′)	4.77	2.40	4.95	4.82	4.94	4.87	4.85	
H_b–C(3′)	–	2.10	–	–	–	–	–	
H_a–C(4′)	4.42	4.42	4.36	4.57	4.55	4.50	4.53	
H_b–C(4′)	3.96	4.28	3.89	3.96	3.92	3.92	4.08, 4.04	
H_a–C(10)	–	–	4.90	4.95	4.55	4.52	4.53, 4.50	
H_b–C(10)	–	–	4.90	4.90	4.40	4.45	4.45, 4.42	
H–C(2)	8.70	8.70	8.68	8.66	8.80	8.76	8.78	
H–C(8)	8.50	8.42	–	–	–	–	–	
J(1′,2′)	6.6	1.9	6.6	6.8	6.6	6.6	6.6	
J(2′,2′)	14.0	–	13.7	14.0	13.3	14.0	13.3	
J(2′$_{pro-S}$,3′)	5.6	5.6	6.8	5.6	6.6	6.0	6.4	
J(2′$_{pro-R}$,3′)	1.2	3.1	1.0	1.3	< 1.0	< 1.0	< 1.0	
J(3′a,3′b)	–	14.0	–	–	–	–	–	
J(3′,4′a)	3.7	8.4, 4.3	4.0	3.7	3.3	3.7	3.3	
J(3′,4′b)	1.2	8.4, 7.1	< 1.0	< 1.0	< 1.0	< 1.0	< 1.0	
J(4′a,4′b)	9.3	8.4	8.7	9.0	8.7	9.3	9.3	
J(10_a,10_b)	–	–	[a]	14.3	11.8	11.8	12.1	

[a]) Not assigned.

Table 4. *Selected* ^{13}*C-NMR Chemical Shifts* [ppm] *for* **7**–**13**, **16**–**19**, *and* **1** *in* $CDCl_3$, *for* **14** *and* **15** *in* CD_3OD, *and for* **3** *in* $(D_6)DMSO$

	C(1′)	C(2′)	C(3′)	C(4′)	C(10)	C(2)	C(4)	C(5)	C(6)	C(8)
7	87.3	74.2	71.6	72.7	–	151.8	149.9	124.1	152.9	142.1
3	88.0	74.5	70.4	74.0	–	151.9	150.6	126.3	152.6	144.0
8	91.4	75.2	71.7	74.7	–	152.9	150.2	124.1	151.5	142.5
9	91.2	75.9	71.9	74.7	–	153.2	150.2	124.1	151.5	143.1
10	87.7	83.4	70.4	74.4	–	152.6	150.3	124.2	151.7	142.3
11	91.0	74.3	82.4	72.0	–	152.7	150.3	124.2	151.7	143.0
12	86.2	41.7	72.6	77.3	–	152.8	149.9	124.2	151.8	142.2
13	92.9	76.4	33.8	69.3	–	152.5	149.6	123.8	151.2	141.3
14	87.2	41.7	73.0	78.0	–	153.0	151.3	125.6	153.1	144.8
15	93.8	76.7	33.8	70.5	–	153.0	151.0	125.6	152.8	144.0
16	85.6	40.6	73.0	77.6	57.8	154.8	149.3	122.0	153.0[a])	152.4[a])
17	87.2	40.7	73.3	78.2	58.3	156.5	150.5	124.2	154.5[a])	152.9[a])
18	86.1	40.6	73.2	77.8	59.7	152.0	149.5	122.5	152.7[a])	152.6[a])
19	85.7	39.9	72.7	77.4	59.5	152.0	149.4	122.5	152.6[a])	152.5[a])
1	85.9	39.2	74.4	76.5	59.9	152.2	149.7	122.7	152.7[a])	152.6[a])
	85.8	39.0	74.2	76.2		152.1	149.6			

[a]) Assignment may be interchanged.

N^6*-Benzoyl-9-(β-*D*-erythrofuranosyl)adenine · MeOH* (**3**). At 23°, a soln. of **7** (5.2 g, 12.2 mmol) in THF (190 ml), MeOH (152 ml), and H_2O (38 ml) was treated with 2M NaOH in H_2O (25 ml, 50 mmol), stirred at 23° for 10 min, treated with NH_4Cl (5.26 g, 98.3 mmol), and evaporated after addition of SiO_2 (46 g). The resulting powder was dried at 0.1 mbar for 14 h, filled in a column, and eluted with $CHCl_3$/MeOH 10:1. The colourless crystals obtained from a few pooled fractions were submitted to X-ray analysis. Evaporation of the residual fractions gave **3** (3.2 g, 78%). Colourless powder. R_f ($CHCl_3$/MeOH 10:1) 0.20. IR (KBr): 3407*s* (br.), 3237*s* (br.), 1685*s*, 1608*m*, 1572*s*, 1518*s*, 1466*m*, 1428*m*, 1396*m*, 1325*m*, 1294*m*, 1248*m*, 1194*m*, 1146*m*, 1107*m*, 1070*s*,1025*s*. ^{1}H-NMR (200 MHz, (D_6)DMSO): see *Table 3*; additionally, 11.17 (br. *s*, NH); 8.06–7.97 (*m*, 2 arom. H); 7.69–7.47 (*m*, 3 arom. H); 5.56 (*d*, J = 6.2, HO–C(2′)); 5.29 (*d*, J = 3.7, HO–C(3′)); 4.01 (*q*, J = 5.5, MeO*H*); 3.16 (*d*, J = 5.5, *Me*OH). ^{13}C-NMR (50 MHz, (D_6)DMSO): see *Table 4*; additionally, 165.9 (*s*, C=O); 133.6 (*s*); 132.6 (*d*); 128.7 (*d*, 4 C); 48.6 (*q*, MeOH). FAB-MS (NOBA): 342 (100, $[M+H]^+$).

N^6*-Benzoyl-9-(3′-*O*-(triisopropylsilyl)-β-*D*-erythrofuranosyl)adenine* (**8**) *and* N^6*-Benzoyl-9-(2′-*O*-(triisopropylsilyl)-β-*D*-erythrofuranosyl)adenine* (**9**). A soln. of **3** (3.2 g, 9.4 mmol) in pyridine (4.1 ml, distilled from CaH_2) and DMF (64 ml, distilled from CaH_2) was treated with $^iPr_3SiOTf$ (3.2 ml, 12 mmol) at 23°, stirred for 4 h, treated with $^iPr_3SiOTf$ (3 ml, 11 mmol), stirred for 4 h at 23°, and evaporated. FC (AcOEt/hexane 6:1) gave **8/9** 1:1 (4.3 g, 92%). A soln. of this mixture in 150 ml of Et_3N was treated with SiO_2 (60 g), stirred at 23° for 16 h, and evaporated. FC (CH_2Cl_2/MeOH 10:1) gave **8/9** 2:1. Colourless foam.

Data of **8/9**: R_f(AcOEt/hexane 6:1) 0.41. $[\alpha]_D^{25} = -58.4$ (c = 1.135, $CHCl_3$, **8/9** 2:1). IR ($CHCl_3$, **8/9** 2:1): 3411*w* (br.), 3003*m*, 2947*s*, 2893*m*, 2869*s*, 1708*s*, 1671*m*, 1612*s*, 1585*s*, 1503*m*, 1457*s*, 1387*m*, 1354*m*, 1328*m*, 1141*m*, 1112*m*. ^{1}H-NMR (300 MHz, $CDCl_3$, **8/9** 2:1): see *Table 3*; additionally, 9.13 (br. *s*, 0.33 H), 9.10 (br. *s*, 0.67 H) (NH); 8.05–7.95 (*m*, 2 arom. H); 7.65–7.40 (*m*, 3 arom. H); 3.45 (*d*, J = 5.6, 0.67 H, exch., HO–C(2′) of **8**); 3.02–2.96 (*m*, 0.33 H, exch., HO–C(3′) von **9**); 1.20–0.80 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$, **8/9** 2:1): see *Table 4*; additionally, 165.9 (*s*, C=O); 134.0 (*s*); 133.1 (*d*); 129.0 (*d*, 2 C); 128.4 (*d*, 2 C); 17.9–17.5 (4*q*, $(Me_2CH)_3Si$); 12.4–12.0 (3*d*, $(Me_2CH)_3Si$). FAB-MS (NOBA, **8/9** 2:1): 498 (100, $[M+H]^+$). HR-MALDI-MS (**8/9** 2:1): 498.254 ($C_{25}H_{36}N_5O_4Si$, $[M+H]^+$; calc. 498.254); 520.236 ($C_{25}H_{35}N_5NaO_4Si$, $[M+Na]^+$; calc. 520.236).

N^6*-Benzoyl-9-{2′-*O*-[(imidazol-1-yl)thiocarbonyl]-3′-*O*-(triisopropylsilyl)-β-*D*-erythrofuranosyl}adenine* (**10**) *and* N^6*-Benzoyl-9-{3′-*O*-[(imidazol-1-yl)thiocarbonyl)-2′-*O*-(triisopropylsilyl)-β-*D*-erythrofuranosyl}adenine* (**11**). A soln. of **8/9** 2:1 (2 g, 4 mmol) in CH_2Cl_2 (20 ml) was treated with 1,1′-(thiocarbonyl)diimidazole (4.6 g, 26 mmol), stirred at 23° for 3 d, extracted once with H_2O and brine, and dried (Na_2SO_4). Evaporation gave a yellow oil (3.8 g), consisting of **10/11** (2:1) and 1,1′-(thiocarbonyl)diimidazole. It was used without

further purification. R_f(AcOEt/hexane 6 : 1, **10/11** 2 : 1) 0.33. ^{1}H-NMR (300 MHz, $CDCl_3$, **10/11** 2 : 1): see *Table 3*; additionally, 9.40 (br. *s*, 0.67 H), 9.37 (br. *s*, 0.33 H) (NH); 8.20 – 7.80 (*m*, 3 arom. H); 7.80 – 7.30 (*m*, 3 arom. H); 7.20 – 6.95 (*m*, 2 arom. H); 1.20 – 0.80 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 4*; additionally, 183.0, 182.9 (2*s*, C=S); 165.3, 165.1 (2*s*, C=O); 137.0 (*d*); 133.7 (*s*); 133.6 (*s*); 132.8 – 128.0 (several *d*); 118.1 (*d*); 17.8 – 17.4 (several *q*, $(Me_2CH)_3Si$), 12.1, 11.9 (2*d*, $(Me_2CH)_3Si$). FAB-MS (NOBA, **10/11** 2 : 1): 608 (63, $[M+H]^+$).

N^6*-Benzoyl-9-[2′-deoxy-3′-*O*-(triisopropylsilyl)-β-*D-glycero*-tetrofuranosyl]adenine* (**12**) *and* N^6*-Benzoyl-9-[3′-deoxy-2′-*O*-(triisopropylsilyl)-β-*D-glycero*-tetrofuranosyl]adenine* (**13**). A suspension of **10/11** 2 : 1 (3.8 g) in toluene (20 ml) and a mixture of Bu_3SnH (6 ml, 22.6 mmol) and AIBN (3.5 g, 21 mmol) in toluene (10 ml) were each degassed. The suspension of **10/11** was heated to 110°, treated with the soln. of AIBN and Bu_3SnH in 6 portions over 40 min, and stirred at 110° for 2 h. The soln. was diluted with $CHCl_3$ (200 ml), extracted once with H_2O and brine, dried (Na_2SO_4), and evaporated. FC (AcOEt/hexane 1 : 1) gave **12** (850 mg, 44% from **8/9**) and **13** (385 mg, 20% from **8/9**) as colourless foams.

Data of **12**: R_f(AcOEt/hexane 6 : 1) 0.51. $[\alpha]_D^{25} = -40.8$ ($c = 1.07$, $CHCl_3$). IR ($CHCl_3$): 3406*w* (br.), 3003*m*, 2946*m*, 2892*w*, 2868*m*, 1708*m*, 1612*s*, 1583*s*, 1503*m*, 1457*s*, 1386*w*, 1346*w*, 1328*m*, 1071*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): see *Table 3*; additionally, 9.00 (br. *s*, NH); 8.10 – 8.00 (*m*, 2 arom. H); 7.65 – 7.50 (*m*, 3 arom. H); 1.20 – 1.00 (*m*, $Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 4*; additionally, 165.2 (*s*, C=O); 134.0 (*s*); 133.1 (*d*); 129.2 (*d*, 2 C); 128.3 (*d*, 2 C); 17.9 (*q*, $(Me_2CH)_3Si$);12.0 (*d*, $(Me_2CH)_3Si$). FAB-MS (NOBA): 482 (77, $[M+H]^+$). HR-FAB-MS: 482.2585 ($C_{25}H_{36}N_5O_3Si$, $[M+H]^+$; calc. 482.2587).

Data of **13**: R_f(AcOEt/hexane 6 : 1) 0.57. $[\alpha]_D^{25} = -51.1$ ($c = 1.065$, $CHCl_3$). IR ($CHCl_3$): 3403*w* (br.), 3002*m*, 2946*m*, 2892*w*, 2868*m*, 1707*m*, 1612*s*, 1584*m*, 1501*m*, 1455*s*, 1327*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 3*; additionally, 9.00 (br. *s*, NH); 8.07 – 7.98 (*m*, 2 arom. H); 7.65 – 7.45 (*m*, 3 arom. H); 1.20 – 1.00 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 4*; additionally, 165.0 (*s*, C=O); 133.7 (*s*); 132.7 (*d*); 128.7 (*d*, 2 C); 128.0 (*d*, 2 C); 17.9 (*q*, $(Me_2CH)_3Si$); 12.0 (*d*, $(Me_2CH)_3Si$). FAB-MS (NOBA): 482 (55, $[M+H]^+$). HR-MALDI-MS: 504.240 ($C_{25}H_{35}N_5NaO_3Si$, $[M+Na]^+$; calc. 504.240).

N^6*-Benzoyl-9-(2′-deoxy-β-*D-glycero*-tetrofuranosyl)adenine* (**14**). A soln. of **12** (20 mg, 0.042 mmol) in THF (2 ml) was treated with 1M Bu_4NF in THF (0.24 ml, 0.24 mmol) at 23° for 3 h and evaporated after addition of SiO_2 (0.5 g). The resulting powder was dried at 0.1 mbar for 14 h and filled in a column. Elution ($CHCl_3$/MeOH 20 : 1) gave **14** (10 mg, 74%) as colourless powder. R_f($CHCl_3$/MeOH 10 : 1) 0.29. ^{1}H-NMR (300 MHz, CD_3OD): see *Table 3*; additionally, 8.10 – 8.00 (*m*, 2 arom. H); 7.70 – 7.50 (*m*, 3 arom. H). ^{13}C-NMR (75 MHz, CD_3OD): see *Table 4*; additionally, 168.0 (*s*, C=O); 135.0 (*s*); 134.0 (*d*); 130.0 (*d*, 2 C); 129.8 (*d*, 2 C). FAB-MS (NOBA): 326 (56, $[M+H]^+$), 348 (16, $[M+Na]^+$).

N^6*-Benzoyl-9-(3′-deoxy-β-*D-glycero*-tetrofuranosyl)adenine* (**15**). A soln. of **13** (100 mg, 0.208 mmol) in THF (2 ml) was treated with 1M Bu_4NF in THF (0.62 ml, 0.62 mmol) at 23° for 3 h and evaporated after addition of SiO_2 (0.5 g). The resulting powder was dried at 0.1 mbar for 14 h and filled in a column. Elution ($CHCl_3$/MeOH 20 : 1) gave **15** (60 mg, 89%) as colourless powder. R_f($CHCl_3$/MeOH 10 : 1) 0.42.^{1}H-NMR (300 MHz, CD_3OD): see *Table 3*; additionally, 8.10 – 8.00 (*m*, 2 arom. H); 7.70 – 7.50 (*m*, 3 arom. H). ^{13}C-NMR (75 MHz, CD_3OD): see *Table 4*; additionally, 168.0 (*s*, C=O); 135.0 (*s*); 134.0 (*d*); 129.9 (*d*, 2 C); 129.5 (*d*, 2 C). FAB-MS (NOBA): 326 (65, $[M+H]^+$).

N^6*-Benzoyl-9-(2-deoxy-3-*O*-(triisopropylsilyl)-β-*D*-erythrofuranosyl)-8-(hydroxymethyl)adenine* (**16**). At −70°, a soln. of **12** (800 mg, 1.663 mmol) in THF (20 ml) was treated dropwise with 2M LDA in THF (4.2 ml, 8.4 mmol), stirred at −70° for 2 h, treated with DMF (3.3 ml, 42.8 mmol), stirred at −70° for 2.5 h, treated with AcOH (1.4 ml), allowed to warm to 23°, and diluted with EtOH (30 ml). The resulting soln. was treated with $NaBH_4$ (220 mg, 5.8 mmol) for 25 min and evaporated. The residue was taken up in CH_2Cl_2 (100 ml), washed once with H_2O (50 ml) and brine (50 ml), dried (Na_2SO_4), and evaporated. FC (AcOEt/hexane 6 : 1) gave **16** (748 mg, 88%). Colourless foam. R_f(AcOEt/hexane 6 : 1) 0.34. $[\alpha]_D^{25} = -40.4$ ($c = 1.095$, $CHCl_3$). IR ($CHCl_3$): 3404*m* (br.), 3006*m*, 2945*s*, 2892*m*, 2868*s*, 1706*s*, 1655*m*, 1614*s*, 1585*s*, 1462*s*, 1436*s*, 1384*m*, 1336*s*, 1072*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 3*; additionally, 9.60 (br. *s*, NH); 8.10 – 7.90 (*m*, 2 arom. H); 7.60 – 7.40 (*m*, 3 arom. H); 4.15 (br. *s*, exch., OH); 1.20 – 0.80 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 4*; additionally, 165.5 (*s*, C=O); 134.2 (*s*); 132.8 (*d*); 129.0 (*d*, 2 C); 128.3 (*d*, 2 C); 17.9 (*q*, $(Me_2CH)_3Si$); 12.0 (*d*, $(Me_2CH)_3Si$). FAB-MS (NOBA): 512 (35, $[M+H]^+$). HR-MALDI-MS: 512.268 ($C_{26}H_{38}N_5O_4Si$, $[M+H]^+$; calc. 512.269), 534.251 ($C_{26}H_{37}N_5NaO_4Si$, $[M+Na]^+$; calc. 534.251).

N^6*-Benzoyl-9-(2-deoxy-β-*D*-erythrofuranosyl)-8-(hydroxymethyl)adenine* (**17**). A soln. of **16** (20 mg, 0.039 mmol) in THF (1 ml) was treated with 1M Bu_4NF in THF (0.12 ml, 0.12 mmol) at 23° for 3 h and evaporated after addition of SiO_2 (0.4 g). The resulting powder was dried at 0.1 mbar for 14 h and filled in a column. Elution ($CHCl_3$/MeOH 20 : 1 to 10 : 1) gave **17** (11 mg, 80%) as colourless powder. R_f($CHCl_3$/MeOH

6 : 1) 0.51. ^{1}H-NMR (300 MHz, CD_3OD): see *Table 3*; additionally, 8.10 – 8.00 (*m*, 2 arom. H); 7.70 – 7.50 (*m*, 3 arom. H). ^{13}C-NMR (75 MHz, CD_3OD): see *Table 4*; additionally, 168.3 (*s*, C=O); 135.2 (*s*); 134.0 (*d*); 129.8 (*d*, 2 C); 129.5 (*d*, 2 C). FAB-MS (NOBA): 356 (78, $[M+H]^+$), 378 (41, $[M+Na]^+$).

*N^6-Benzoyl-9-[2′-deoxy-3′-O-(triisopropylsilyl)-β-*D*-*glycero*-tetrofuranosyl]-8-[(4,4′-dimethoxytrityloxy)methyl]adenine* (**18**). A soln. of **16** (748 mg, 1.46 mmol), EtN(i-Pr)$_2$ (1.03 ml, 6 mmol) and DMAP (50 mg, 0.4 mmol) in CH_2Cl_2 (15 ml) was treated with DMTrCl (2 g, 5.91 mmol) at 0°. The mixture was stirred at 23° for 16 h, and evaporated. The residue was diluted with CH_2Cl_2, washed once with H_2O and brine, dried (Na_2SO_4), and evaporated. FC (AcOEt/hexane 1 : 2) gave **18** (1056 mg, 89%). Colourless foam. R_f(AcOEt/hexane 2 : 1) 0.61. $[\alpha]^{25}_D = -15.2$ ($c = 2.32$, $CHCl_3$). IR ($CHCl_3$): 3409*w* (br.), 3007*m*, 2960*m*, 2867*w*, 1706*m*, 1610*s*, 1584*m*, 1509*s*, 1463*m*, 1447*m*, 1428*m*, 1070*m*, 1034*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): see *Table 3*; additionally, 9.06 (br. *s*, NH); 8.10 – 8.00 (*m*, 2 arom. H); 7.69 – 7.20 (*m*, 12 arom. H); 6.92 – 6.80 (*m*, 4 arom. H); 3.78 (*s*, 2 MeO); 1.20 – 1.00 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 4*; additionally, 165.0 (*s*, C=O); 159.2 (*s*, 2 C); 144.4 (*s*); 135.6 (*s*); 135.3 (*s*); 134.4 (*s*); 132.8 (*d*); 130.2 – 127.2 (several *d*); 113.3 (*d*, 4 C); 87.9 (*s*, Ar_3C); 55.3 (*q*, 2 MeO); 18.0 (*q*, $(Me_2CH)_3Si$), 12.0 (*d*, $(Me_2CH)_3Si$). FAB-MS (NOBA): 814 (38, $[M+H]^+$), 303 (100, DMTr$^+$). HR-MALDI-MS: 836.382 ($C_{47}H_{55}N_5NaO_6Si$, $[M+Na]^+$; calc. 836.381).

*N^6-Benzoyl-9-[2′-deoxy-β-*D*-*glycero*-tetrofuranosyl]-8-[(4,4′-dimethoxytrityloxy)methyl]adenine* (**19**). A soln. of **18** (976 mg, 1.2 mmol) in THF (15 ml) was treated dropwise with 1M Bu_4NF in THF (3.55 ml, 3.55 mmol) at 23° for 1.5 h and evaporated. FC (AcOEt/hexane 2 : 1) gave **19** (600 mg, 76%). Colourless foam. R_f(AcOEt/hexane 2 : 1) 0.13. $[\alpha]^{25}_D = -12.5$ ($c = 1.69$, $CHCl_3$). IR ($CHCl_3$): 3405*m* (br.), 3007*s*, 2839*w*, 1707*m*, 1613*s*, 1585*m*, 1509*s*, 1462*s*, 1448*s*, 1428*s*, 1409*m*, 1336*s*, 1302*s*, 1065*s*, 1036*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 3*; additionally, 9.20 (br. *s*, NH); 8.05 – 7.95 (*m*, 2 arom. H); 7.60 – 7.10 (*m*, 12 arom. H); 6.85 – 6.75 (*m*, 4 arom. H); 3.75 (*s*, 2 MeO); 2.60 – 2.40 (br. *s*, exch., HO–C(3′)). ^{13}C-NMR (50 MHz, $CDCl_3$): see *Table 4*; additionally, 164.9 (*s*, C=O); 159.0 (*s*, 2 C); 144.3 (*s*); 135.3 (*s*); 135.2 (*s*); 134.2 (*s*); 132.9 (*d*); 130.2 – 127.3 (several *d*); 113.6 (*d*, 4 C); 88.0 (*s*, Ar_3C); 55.3 (*q*, 2 MeO). FAB-MS (NOBA): 659 (2, $[M+H]^+$), 303 (100, DMTr$^+$). HR-FAB-MS (NOBA): 658.2663 ($C_{38}H_{36}N_5O_6$, $[M+H]^+$; calc. 658.2666).

*N^6-Benzoyl-9-(2′-deoxy-β-*D*-*glycero*-tetrofuranosyl)-8-[(4,4′-dimethoxytrityloxy)methyl]adenine 3′-[(2-Cyanoethyl)diisopropylphosphoramidite]* (**1**). A soln. of **19** (395 mg, 0.601 mmol) and EtN(i-Pr)$_2$ (2 ml) in CH_2Cl_2 (20 ml) was treated with 2-cyanoethyl diisopropylchlorophosphoramidite (184 mg, 0.77 mmol) at 23°, stirred for 3 h, and evaporated. FC (AcOEt/hexane 2 : 1) gave **1** (413 mg, 80%, 2 diastereoisomers (1 : 1)). Colourless foam. R_f(AcOEt/hexane 2 : 1, 2 diastereoisomers (1 : 1)) 0.34; 0.45. IR ($CHCl_3$, 2 diastereoisomers (1 : 1)): 3404*w* (br.), 3007*m*, 2970*m*, 2935*m*, 1707*m*, 1613*s*, 1585*m*, 1509*s*, 1462*m*, 1448*m*, 1428*w*, 1408*m*, 1365*m*, 1337*m*, 1063*m*, 1036*m*. ^{1}H-NMR (300 MHz, $CDCl_3$, 2 diastereoisomers (1 : 1)): see *Table 3*; additionally, 9.00 (br. *s*, NH); 8.10 – 7.95 (*m*, 2 arom. H); 7.70 – 7.20 (*m*, 12 arom. H); 6.90 – 6.80 (*m*, 4 arom. H); 3.90 – 3.50 (*m*, OCH_2CH_2CN, $(Me_2CH)_2N$); 3.78 (*s*, 2 MeO); 2.63 (*t*, $J = 6.3$), 2.55 (*t*, $J = 6.1$) (CH_2CN); 1.30 – 1.10 (*m*, $(Me_2CH)_2N$). ^{13}C-NMR (75 MHz, $CDCl_3$, 2 diastereoisomers (1 : 1)): see *Table 4*; additionally, 165.1 (*s*, N–C=O); 159.2 (*s*, 2 C); 144.5, 144.4 (2*s*, 1 C); 135.6, 135.5, 135.4, 134.4 (several *s*, 3 C); 132.9 – 127.5 (several *d*); 117.8 (*s*, CN); 113.7 (*d*, 4 C); 88.1 (*s*, Ar_3C); 58.5 (*dt*, ^2J(C,P) = 19.0, OCH_2CH_2CN); 55.4 (*q*, 2 MeO); 43.4 (*dd*, ^2J(C,P) = 12.0, $(Me_2CH)_2N$); 24.8 – 24.5 (several *q*, $(Me_2CH)_2N$); 20.5 – 20.3 (*m*, OCH_2CH_2CN). ^{31}P-NMR (121.5 MHz, $CDCl_3$): 148.9; 148.6. FAB-MS (NOBA): 858 (49, $[M+H]^+$), 303 (100, DMTr$^+$). HR-MALDI-MS: 880.356 ($C_{47}H_{52}N_7NaO_7P$, $[M+Na]^+$; calc. 880.356).

*1-(2′,3′-Di-O-acetyl-β-*D*-erythrofuranosyl)uracil* (**20**). A suspension of **5**/**6** 1 : 4 (1.8 g, 7.3 mmol) and uracil (0.92 g, 8.2 mmol) in MeCN (18 ml) was treated dropwise with *N,O*-bis(trimethylsilyl)acetamide (4.32 ml, 17.7 mmol) at 60°, stirred at 60° for 30 min, and treated with $SnCl_4$ (3.47 ml, 29.5 mmol). The mixture was stirred at 60° for 20 min, poured into a stirred mixture of AcOEt (300 ml) and sat. aq. $NaHCO_3$ (300 ml), and stirred for 15 min. The org. layer was dried (Na_2SO_4) and evaporated. FC (AcOEt/hexane 10 : 1) gave **20** (1.74 g, 80%). Colourless powder. R_f(AcOEt/hexane 6 : 1) 0.38. ^{1}H-NMR (200 MHz, $CDCl_3$): see *Table 5*; additionally, 9.48 (br. *s*, NH); 2.14 (*s*, AcO); 2.09 (*s*, AcO). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 6*; additionally, 170.4, 170.2 (2*s*, 2 O–C=O); 20.7, 20.5 (2*q*, 2 Me).

*1-(β-*D*-Erythrofuranosyl)uracil* (**4**). At 23°, a soln. of **20** (1.1 g, 3.7 mmol) in a mixture of THF (94 ml), MeOH (75 ml), and H_2O (19 ml) was treated with 2M NaOH in H_2O (12.4 ml, 25 mmol), stirred at 23° for 8 min, treated with NH_4Cl (2.6 g, 48.6 mmol), treated with SiO_2 (22.8 g), and evaporated. The resulting colourless powder was dried at 0.1 mbar for 14 h, filled in a column, and eluted ($CHCl_3$/MeOH 6 : 1). The colourless crystals obtained from a few pooled fractions were submitted to X-ray analysis. Evaporation of the residual fractions gave **4** (0.63 g, 80%). Colourless crystals. R_f ($CHCl_3$/MeOH 6 : 1) 0.16. $[\alpha]^{25}_D = -41.2$ ($c = 0.9$, H_2O). IR (KBr): 3385*s* (br.), 3186*s*, 1693*s*, 1470*m*, 1404*s*, 1262*m*, 1130*m*, 1065*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO): see

Table 5. *Selected* ^{1}*H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *for* **20**, **22**–**24**, **26**–**28**, *and* **2** *in* $CDCl_3$, *for* **4** *in* $(D_6)DMSO$, *and for* **21** *and* **25** *in* D_2O

	2	**4**	**20**	**22**	**23**	**24**	**26**	**27**	**28**	**21**	**25**
H–C(1′)	5.87	5.70	5.86	6.27	5.90	6.15	6.11	5.90	5.85	6.56	6.18
H–C($2'_{pro\text{-}S}$)	2.88	4.18	5.5–5.6	5.13	4.64	2.11	2.90	2.85	2.82	5.45	2.19
H–C($2'_{pro\text{-}R}$)	2.32, 2.25	–	–	–	–	2.50	2.23	2.18	2.12	–	2.40
H–C(3′)	4.72	4.08	5.4–5.5	4.64	4.53	4.65	4.83	4.73	4.65	4.70	4.53
H_a–C(4′)	4.34	4.21	4.52	4.04	4.35	4.20	4.42	4.38	4.34	4.16	4.25
H_b–C(4′)	3.4–3.9	3.67	4.06	3.80	4.02	3.87	3.83	3.73	3.73	3.93	3.88
H_a–C(7)	3.98, 3.97	–	–	–	–	–	4.52	3.96	4.02	–	–
H_b–C(7)	3.98, 3.97	–	–	–	–	–	4.45	3.96	3.95	–	–
H–C(5)	5.76, 5.73	5.60	5.77	6.06	5.76	5.73	5.80	5.80	5.80	6.22	5.69
H–C(6)	–	7.65	7.22	7.38	7.20	7.32	–	–	–	7.94	7.61
J(1′,2′)	6.5	6.2	5.3	5.0	5.6	6.5	6.6	7.0	7.0	5.3	7.0
J(2′,2′)	13.7	–	–	–	–	14.0	12.8	13.0	13.4	–	14.0
$J(2'_{pro\text{-}S},3')$	6.5	4.4	[a])	< 1.0	4.7	6.2	6.5	6.5	6.5	< 1.0	5.3
$J(2'_{pro\text{-}R},3')$	[a])	–	–	–	–	2.3	< 1.0	< 1.0	< 1.0	–	1.6
J(3′,4′a)	4.4	4.0	4.5	< 1.0	4.4	4.2	4.4	4.1	4.0	< 1.0	3.7
J(3′,4′b)	< 1.0	2.2	2.0	2.5	3.7	2.2	< 1.0	< 1.0	< 1.0	2.8	1.5
J(4′a,4′b)	8.7	9.1	10.3	10.6	9.0	9.0	8.5	8.4	9.0	11.2	9.3
J(5,6)	–	8.1	8.1	7.5	8.1	8.1	–	–	–	7.5	8.1
$J(7_a,7_b)$	[a])	–	–	–	–	–	14.7	[a])	13.4	–	–

[a]) Not assigned.

Table 6. *Selected* ^{13}*C-NMR Chemical Shifts* [ppm] *for* **20**, **22**–**24**, **26**–**28**, *and* **2** *in* $CDCl_3$, *for* **4** *in* $(D_6)DMSO$, *and for* **21** *and* **25** *in* D_2O

	C(1′)	C(2′)	C(3′)	C(4′)	C(7)	C(6)	C(2)	C(4)	C(5)
20	89.9	73.8	71.1	72.4	–	140.7	150.7	163.4	103.4
4	88.8	74.1	70.0	73.6	–	141.8	151.0	163.5	102.0
21	93.4[a])	90.6[a])	75.7[b])	75.7[b])	–	141.7	164.2	178.7	112.1
22	90.3[a])	87.7[a])	75.0[b])	74.0[b])	–	135.2	160.3	172.0	110.8
23	95.4	52.4	71.7	74.8	–	141.4	150.1	163.8	102.9
24	88.0	42.4	72.0	77.2	–	140.0	150.8	164.0	102.6
25	88.4	41.9	72.3	77.5	–	142.3	152.1	166.0	102.6
26	87.7	40.4	73.6	78.7	61.2	156.0	151.2	164.0	101.6
27	88.1	40.3	73.5	78.5	62.8	153.5	151.2	163.8	102.5
28	88.1	39.3	73.0	78.0	62.5	153.3	151.2	163.6	102.6
2	88.2	38.4	74.5	79.8	62.8	153.3	150.6	162.6	102.6
		38.3	74.3	79.6			150.5		102.5

[a]) [b]) Assignments may be interchanged.

Table 5; additionally, 11.22 (br. *s*, NH); 5.34 (*d*, $J = 6.2$, exch., HO–C(2′)); 5.07 (*d*, $J = 3.7$, exch., HO–C(3′)). ^{13}C-NMR (50 MHz, (D_6)DMSO): see *Table 6*. FAB-MS (NOBA): 215 (100, $[M+H]^+$).

*2,2′-Anhydro-1-(β-*D*-threofuranosyl)uracil* (**21**). A suspension of **4** (1 g, 4.67 mmol) and diphenyl carbonate (1.29 g, 0.61 mmol) in DMF (25 ml) was stirred at 80° for 30 min, treated with $NaHCO_3$ (390 mg) at 80°, stirred at 150° for 2 h, and evaporated. The residue was diluted with AcOEt and H_2O. Evaporation of the aq. layer gave 998 mg of a colourless powder containing **21** and Na salts. R_f(AcOEt/MeOH 3:2) 0.57. $[\alpha]_D^{25} = -44$ ($c = 1.05$, H_2O). IR (KBr): 2923*m*, 1662*s*, 1620*m*, 1533*s*, 1482*s*, 1272*w*, 1241*w*, 1190*w*, 1113*w*, 1062*m*, 1041*m*. ^{1}H-NMR (300 MHz, D_2O): see *Table 5*. ^{13}C-NMR (75 MHz, D_2O): see *Table 6*. FAB-MS (NOBA): 219 (100, $[M+Na]^+$), 197 (24, $[M+H]^+$). HR-MALDI-MS: 219.037 ($C_8H_8N_2NaO_4$, $[M+Na]^+$; calc. 219.038).

*2,2′-Anhydro-1-[3′-*O*-(triisopropylsilyl)-β-D-threofuranosyl]uracil* (**22**). A soln. of **21** (1 g, 5.1 mmol) in DMF (16 ml) and pyridine (12.5 ml) was treated with $^iPr_3SiOTf$ (7 ml, 26 mmol), stirred at 23° for 24 h, and evaporated. FC (AcOEt/MeOH 30 : 1) gave **22** (790 mg, 61.5% from **4**). Colourless foam. R_f(AcOEt/MeOH 10 : 1) 0.37. $[\alpha]_D^{25} = -40.6$ ($c = 0.9$, $CHCl_3$). IR ($CHCl_3$): 2944*s*, 1672*s*, 1644*s*, 1544*m*, 1468*s*, 1387*w*, 1134*m*, 1072*m*, 1042*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): see *Table 5*; additionally, 1.20 – 0.90 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 6*; additionally, 18.0 (*q*, $(Me_2CH)_3Si$); 12.0 (*d*, $(Me_2CH)_3Si$). FAB-MS (NOBA): 353 (100, $[M + H]^+$), 705 (8, $[2M + H]^+$). HR-MALDI-MS: 353.189 ($C_{17}H_{29}N_2O_4Si$, $[M + H]^+$; 353.189).

*1-[2′-Bromo-2′-deoxy-3′-*O*-(triisopropylsilyl)-β-D-erythrofuranosyl]uracil* (**23**). A suspension of **22** (670 mg, 1.9 mmol) and LiBr (215 mg, 2.47 mmol) in 1,4-dioxane (20 ml) was heated to 60° and treated dropwise with $BF_3 \cdot Et_2O$ (0.62 ml, 4.9 mmol). The mixture was stirred at 60° for 6 h, and taken to dryness. The residue was diluted with $CHCl_3$ (50 ml), washed once with H_2O (20 ml) and brine (20 ml), dried (Na_2SO_4), and evaporated. FC (AcOEt/hexane 1 : 1) gave **23** (720 mg, 88%). Colourless foam. R_f(AcOEt/hexane 1 : 1) 0.34. $[\alpha]_D^{25} = -29.9$ ($c = 1.15$, $CHCl_3$). IR ($CHCl_3$); 3391*w* (br.), 2940*m*, 2868*m*, 1695*s*, 1633*w*, 1457*m*, 1384*m*, 1143*m*, 1108*m*, 1068*m*, 1017*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 5*; additionally, 8.60 (br. *s*, NH); 1.15 – 1.03 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 6*; additionally, 18.0 (*q*, $(Me_2CH)_3Si$); 12.0 (*d*, $(Me_2CH)_3Si$). FAB-MS (NOBA): 433, 435 (23, 24; $[M + H]^+$). HR-MALDI-MS: 375.173 ($C_{17}H_{28}N_2NaO_4Si$, $[M - HBr + Na]^+$; calc. 375.172).

*1-[2′-Deoxy-3′-*O*-(triisopropylsilyl)-β-D-*glycero*-tetrofuranosyl]uracil* (**24**). A suspension of **23** (696 mg, 1.61 mmol) in toluene (10 ml) and a mixture of Bu_3SnH (0.43 ml, 1.62 mmol) and AIBN (100 mg, 0.61 mmol) in toluene (5 ml) were each degassed. The suspension of **23** was heated to 80° and treated with the soln. of AIBN and Bu_3SnH over 20 min. The mixture was heated to 110°, stirred for 30 min, diluted with $CHCl_3$ (200 ml), washed with H_2O and brine, dried (Na_2SO_4), and evaporated. FC (AcOEt/hexane 1 : 1) gave **24** (556 mg, 97%). Colourless foam. R_f(AcOEt/hexane 1 : 1) 0.30. IR ($CHCl_3$): 3391*w* (br.), 2946*m*, 1690*s*, 1633*w*, 1461*m*, 1390*m*, 1135*m*, 1073*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 5*; additionally, 9.67 (br. *s*, NH); 1.17 – 0.94 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 6*; additionally, 18.0 (*q*, $(Me_2CH)_3Si$); 12.0 (*d*, $(Me_2CH)_3Si$). FAB-MS (NOBA): 355 (18, $[M + H]^+$). HR-FAB-MS: 355.2052 ($C_{17}H_{31}N_2O_4Si$, $[M + H]^+$; calc. 355.2053).

*1-(2′-Deoxy-β-D-*glycero*-tetrofuranosyl)uracil* (**25**). A soln. of **24** (91 mg, 0.258 mmol) in THF (2 ml) was treated with 1M $Bu_4NF \cdot 3 H_2O$ in THF (0.76 ml, 0.76 mmol) at 23° for 3 h, and evaporated after addition of SiO_2 (0.5 g). The resulting powder was dried at 0.1 mbar for 14 h, filled in a column, and eluted ($CHCl_3$/MeOH 20 : 1). Evaporation gave **25** (45 mg, 88%) as white powder. Recrystallization in MeOH gave colourless crystals used for X-ray analysis. R_f($CHCl_3$/MeOH 10 : 1) 0.28. ^{1}H-NMR (300 MHz, CD_3OD): see *Table 5*. ^{13}C-NMR (75 MHz, CD_3OD): see *Table 6*. FAB-MS (NOBA): 199 (28, $[M + H]^+$).

*1-[2′-Deoxy-3′-*O*-(triisopropylsilyl)-β-D-*glycero*-tetrofuranosyl]-6-(hydroxymethyl)uracil* (**26**). At −70°, 2M LDA in THF/heptane/ethylbenzene (*FLUKA*; 1.63 ml, 3.26 mmol) was treated with a soln. of **24** (230 mg, 0.652 mmol) in THF (4 ml). The mixture was stirred at −70° for 30 min, treated with DMF (1.7 ml, 16.5 mmol), stirred at −70° for 2.5 h, and treated with AcOH (0.55 ml). The mixture was allowed to warm to 23°, diluted with EtOH (4 ml), and treated with $NaBH_4$ (83 mg, 2.17 mmol) for 25 min. After evaporation, a soln. of the residue in CH_2Cl_2 was washed with H_2O and brine, dried (Na_2SO_4), and evaporated. FC (AcOEt/hexane 4 : 1) gave **26** (128 mg, 51%). Colourless foam. R_f(AcOEt/hexane 1 : 1) 0.15. $[\alpha]_D^{25} = -82.2$ ($c = 0.4$, $CHCl_3$). IR ($CHCl_3$): 3390*m* (br.), 2946*s*, 2867*s*, 1697*s*, 1602*m*, 1462*m*, 1377*m*, 1094*s*, 1015*s*. ^{1}H-NMR (300 MHz, $CDCl_3/CD_3OD$): see *Table 5*; additionally, 1.16 – 0.94 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 6*; additionally, 18.0 (*q*, $(Me_2CH)_3Si$); 12.0 (*d*, $(Me_2CH)_3Si$). FAB-MS (NOBA): 385 (21, $[M + H]^+$).

*1-[2′-Deoxy-3′-*O*-(triisopropylsilyl)-β-D-*glycero*-tetrofuranosyl]-6-[(4,4′-dimethoxytrityloxy)methyl]uracil* (**27**). A soln. of **26** (117 mg, 0.305 mmol), $EtN(i\text{-}Pr)_2$ (0.24 ml, 1.39 mmol) and DMAP (10 mg, 0.4 mmol) in CH_2Cl_2 (5 ml) was treated with DMTrCl (413 mg, 1.26 mmol) at 0°, stirred at 23° for 16 h, and evaporated. A soln. of the residue in CH_2Cl_2 (50 ml) was washed once with H_2O (20 ml) and brine (20 ml), dried (Na_2SO_4), and evaporated. FC (AcOEt/hexane/Et_3N 1 : 1 : 0.02) gave **27** (161 mg, 77%). Colourless foam. R_f(AcOEt/hexane 1 : 1) 0.36. $[\alpha]_D^{25} = -25$ ($c = 0.1$, $CHCl_3$). IR ($CHCl_3$): 3389*m* (br.), 2975*m*, 1695*s*, 1607*m*, 1509*s*, 1457*w*, 1045*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 5*; additionally, 9.75 (br. *s*, NH); 7.50 – 7.10 (*m*, 9 arom. H); 6.93 – 6.70 (*m*, 4 arom. H); 3.80 (*s*, 2 MeO); 1.15 – 0.75 (*m*, $(Me_2CH)_3Si$). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 6*; additionally, 159.4 (*s*, 2 C); 144.3 (*s*); 135.5 (*s*); 135.1 (*s*); 130.1 – 127.6 (several *d*); 113.6, 113.5 (2*d*, 4 C); 88.6 (*s*, Ar_3C); 55.4 (*q*, 2 MeO); 18.0 (*q*, $(Me_2CH)_3Si$); 12.0 (*d*, $(Me_2CH)_3Si$). FAB-MS (NOBA): 686 (7, $[M + H]^+$); 303 (100, $DMTr^+$).

*1-(2′-Deoxy-β-D-*glycero*-tetrofuranosyl)-6-[(4,4′-dimethoxytrityloxy)methyl]uracil* (**28**). A soln. of **27** (161 mg, 0.235 mmol) in THF (6 ml) was treated dropwise at 23° with 1M Bu_4NF in THF (0.7 ml, 0.7 mmol)

for 1.5 h, and evaporated. FC (AcOEt/hexane/Et_3N 10:1:0.02) gave **28** (120 mg, 96%). Colourless foam. R_f(AcOEt/hexane 10:1) 0.24. $[\alpha]_D^{25} = -17.9$ ($c = 0.9$, $CHCl_3$). IR ($CHCl_3$): 3390*m* (br.), 2961*m*, 1692*s*, 1608*m*, 1584*w*, 1509*s*, 1464*s*, 1410*m*, 1378*m*, 1302*m*, 1066*s*, 1035*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): see *Table 5*; additionally, 9.60 (br. *s*, NH); 7.50–7.20 (*m*, 9 arom. H); 6.90–6.70 (*m*, 4 arom. H); 3.75 (*s*, 2 MeO). ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 6*; additionally, 159.2 (*s*, 2 C); 144.2 (*s*); 135.2 (*s*, 2 C); 130.1–127.7 (several *d*); 114.0 (*d*, 4 C); 88.2 (*s*, Ar_3C); 55.3 (*q*, 2 MeO). FAB-MS (NOBA): 530 (12, $[M+H]^+$, 303 (100, $DMTr^+$). HR-FAB-MS: 530.2053 ($C_{30}H_{30}N_2O_7$, M^+; calc. 530.2053).

*1-(2′-Deoxy-β-*D*-*glycero*-tetrofuranosyl)-6-[(4,4′-dimethoxytrityloxy)methyl]uracil 3′-[(2-Cyanoethyl)diisopropylphosphoramidite]* (**2**). A soln. of **28** (108 mg, 0.204 mmol) and EtN(i-Pr)$_2$ (0.12 ml, 0.69 mmol, distilled from CaH_2) in CH_2Cl_2 (2 ml) was treated with 2-cyanoethyl diisopropylchlorophosphoramidite (46 µl, 0.206 mmol) at 23°, stirred for 3 h, and evaporated. FC (AcOEt/hexane 2:1) gave **2** (102 mg, 69%, 2 diastereoisomers (2:1)). Colourless foam. R_f(AcOEt/hexane 1:1, 2 diastereoisomers (2:1)) 0.26. IR ($CHCl_3$, 2 diastereoisomers (2:1)): 3391*w* (br.), 2967*s*, 2929*s*, 1693*s*, 1608*s*, 1509*s*, 1463*s*, 1378*s*, 1064*m*, 1035*m*. ^{1}H-NMR (300 MHz, $CDCl_3$, 2 diastereoisomers (2:1)): see *Table 5*; additionally, 8.30–8.20 (br. *s*, NH); 7.45–7.20 (*m*, 9 arom. H); 6.90–6.80 (*m*, 4 arom. H); 3.90–3.45 (*m*, $(Me_2CH)_2N$, OCH_2CH_2CN, H–C(4′)); 3.80 (*s*, 2 MeO); 2.62 (*t*, $J = 6.5$, 0.67 H), 2.52 (*t*, $J = 6.5$, 1.33 H) (CH_2CN); 1.36–1.00 (*m*, $(Me_2CH)_2N$). ^{13}C-NMR (75 MHz, $CDCl_3$, 2 diastereoisomers (2:1)): see *Table 6*; additionally, 159.3 (*s*, 2 C); 144.2, 144.1 (2*s*, 1 C); 135.2, 135.0 (2*s*, 2 C); 130.2–127.7 (several *d*); 113.9 (*d*, 4 C); 111.3 (*s*, CN); 88.4 (*s*, Ar_3C); 58.5 (*t*, ^2J(C,P) = 18, OCH_2CH_2CN); 55.5 (*q*, 2 MeO); 43.3 (*dd*, ^2J(C,P) = 13.0, $(Me_2CH)_2N$); 24.8–24.4 (several *q*, $(Me_2CH)_2N$); 20.5, 20.4 (2*t*, OCH_2CH_2CN). ^{31}P-NMR (121.5 MHz, $CDCl_3$, 2 diastereoisomers (2:1)): 148.7, 148.2. FAB-MS (NOBA, 2 diastereoisomers (2:1)): 513 (40, $[M-OPR_2]^+$), 303 (100, $DMTr^+$). HR-MALDI-MS: 535.184 ($C_{30}H_{28}N_2NaO_6$, $[M - HOP(OCH_2CH_2CN)N^iPr_2 + Na]^+$; calc. 535.185), 449.156 ($C_{18}H_{27}N_4NaO_6P$, $[M - DMTrH + Na]^+$; calc. 449.157), 303.138 ($C_{21}H_{19}O_2$, $DMTr^+$; calc. 303.139), 241.108 ($C_9H_{19}N_2NaO_2P$, $[HOP(OCH_2CH_2CN)N^iPr_2 + Na]^+$; calc. 241.108).

Oligonucleotide Synthesis. Oligonucleotide syntheses were performed on a *Pharmacia Gene Assembler* on a 1.3-µmol scale. The commercial phosphoramidites and the CPG solid-supports were from *Glen Research*. Solvents and reagents were prepared according to the protocol for the synthesis of pRNA [30]. Detritylation was accomplished within 2 min with 3% $Cl_2CHCOOH$ in $(CH_2Cl)_2$. Couplings (0.16 ml of 0.1M phosphoramidite soln. + 0.36 ml of 0.25M 1-(benzylthio)-1*H*-tetrazole soln. in MeCN) were performed within 6–10 min (DNA-phosphoramidites coupled on unmodified nucleotides), or 30 min (modified phosphoamidites, and DNA-phosphoramidites coupled on modified nucleotides, resp.). Capping and oxidation were accomplished under standard conditions [31].

Deprotection and Purification of Oligonucleotides. Removal of the protecting groups and detachment from the solid support was effected in conc. aq. NH_3 soln./MeOH 1:1 (2.5 ml) at 50° within 20 h (oligomers **29** and **30**), or 3.5 h (oligomer **31**), or at 35° within 3.5 h (oligomer **32** containing dU*, see *Results and Discussion*). After filtration and evaporation of the resulting mixture, the crude oligomers were dissolved in aq. buffer soln. (0.1M AcOH, 0.1M Et_3N), purified by RP-HPLC, and desalted by RP-HPLC. Their compositions were confirmed by MALDI-TOF mass spectroscopy.

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