159. An Efficient Synthesis of Enantiomeric Ribonucleic Acids from D-Glucose

by **Stefan Pitsch**

Organisch-chemisches Laboratorium der Eidgenössischen Technischen Hochschule, Universitätstr. 16, CH-8092 Zürich

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Enantiomeric oligoribonucleotides (= *ent*-RNA) up to a sequence length of thirty-five and consisting of the (L-configurated) nucleosides *ent*-adenosine, *ent*-guanosine, *ent*-cytidine, *ent*-uridine, and 1-(β-L-ribofuranosyl)thymine were prepared by automated synthesis from appropriate building blocks, carrying a known photolabile 2′-*O*-protecting group. A simple large-scale synthesis of the new, prefunctionalized L-ribose derivative **5** from D-glucose (*Scheme 1*) and its straightforward conversion into the five phosphoramidites **28**–**32** and five solid supports **38**–**42**, respectively, were elaborated (*Scheme 4*). Within this project, a novel, superior strategy for the synthesis of the 2′-*O*-{[(2-nitrobenzyl)oxy]methyl}-substituted key intermediates **18**–**22** by regioselective alkylation of their 5′-*O*-dimethoxytritylated precursors **13**–**17** was developed. Furthermore, an improved set-up for the final light-induced cleavage of the 2′-*O*-protecting groups from the oligonucleotide sequences was designed (*Scheme 5* and *Fig. 1*). The correct composition of all *ent*-oligoribonucleotides prepared was established by their MALDI-TOF mass spectra. The ^{1}H-NMR-spectroscopic data of a dodecameric *ent*-RNA sequence was in excellent agreement with the published data of its natural counterpart, synthesized by conventional methods. The known specific cleavage of a tetradecamer sequence by a 35mer ribozyme structure could be reproduced by *ent*-oligoribonucleotides, synthesized by the presented methods (*Fig. 4*).

Introduction. – Currently, we are working on the synthesis of RNA analogues and congeners [1] [2]. This introductory publication summarizes the work carried out to create a solid methodological basis for the preparation of such analogues, and, consequently, deals with a synthesis of RNA itself.

The known instability of oligoribonucleotides due to ubiquitous RNA-cleaving enzymes [3] [4] led to the decision to first synthesize enantiomeric oligoribonucleotides (*ent*-RNA, consisting of L-ribose) as 'model system' to test the critical final deprotection steps without possible interference of enzymatic cleavage (thus avoiding tedious sterilization protocols)[1]).

In different contexts, enantiomeric oligodeoxyribonucleotides [5] [6] and enantiomeric oligoribonucleotides [3] [4] have been prepared already. *ent*-DNA hybridizes only very weakly with DNA and RNA [6], whereas *ent*-RNA forms at least stable triplex structures with RNA [3]. *ent*-Aptamers ('Spiegelmere') have interesting features and potential applications in therapy [4]. Furthermore, it is recommended to perform screening tests of potential RNA-binding drugs, of which only one enantiomer is available, with both enantiomeric forms of the oligonucleotide target.

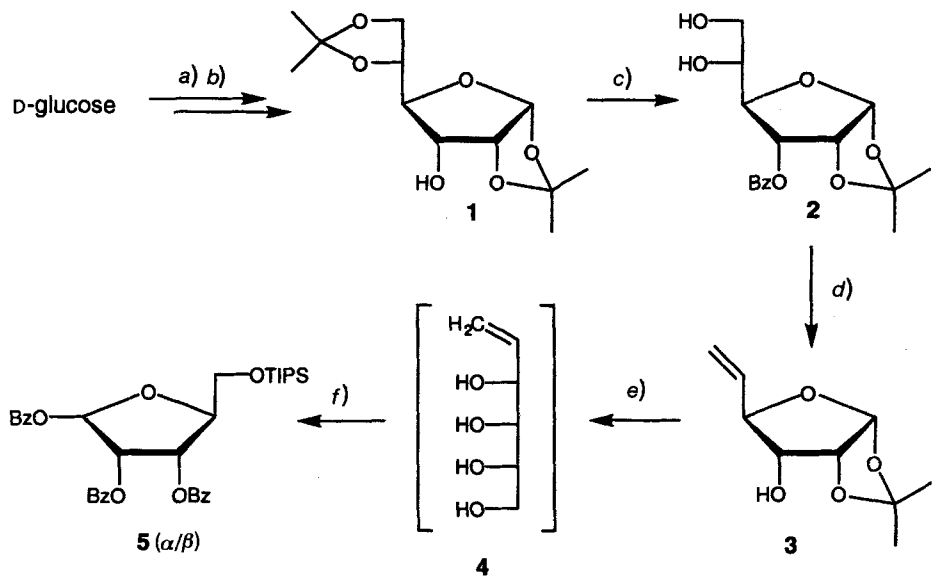
[1]) This property makes *ent*-RNA in general a superior material for all investigations where no enzymes, cells, or organisms are involved, such as physicochemical or structural studies.

Herein, an efficient large-scale preparation of a new, prefunctionalized L-ribose derivative, its transformation into phosphoramidite building blocks, and the synthesis of *ent*-oligoribonucleotides derived therefrom is described.

Results and Discussion. – 1. *Synthesis of the Monomers.* Among the few known preparations of L-ribonucleosides, the most straightforward is certainly the metal-catalyzed epimerization of L-arabinose to L-ribose, followed by its conversion into a peracylated ribofuranose derivative and subsequent nucleosidation with a protected nucleobase [7][2]). This method, however, suffers from the low yield and a cumbersome purification step.

Hence, a simple, cheap, and unambitious large-scale synthesis of an appropriately protected L-*ribo*-configurated sugar building block **5** (an immediate precursor for nucleoside formation) starting from D-glucose was developed (*Scheme 1*). The synthesis was carried out on a 0.1- to 0.5-mol scale and required only five very simple purification steps (four crystallizations and one filtration on silica gel).

Scheme 1



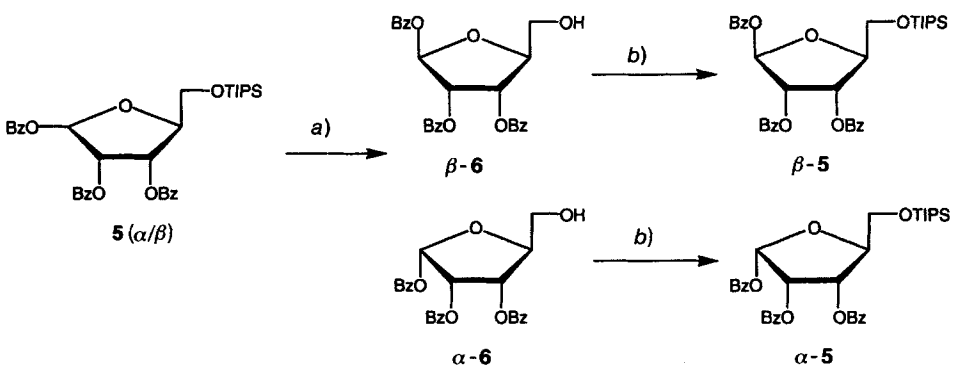
a) Acetone, $ZnCl_2$, H_3PO_4, r.t., 30 h; 91% of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (cryst.) [10]. *b*) 1) Pyridinium dichromate, Ac_2O, CH_2Cl_2, 50°, 2 h; 2) $NaBH_4$, H_2O/EtOH, r.t., 2 h; 90% (cryst.). *c*) 1) BzCl, DMAP, Py, CH_2Cl_2, r.t., 2 h (extr.); 2) AcOH, HCOOH, H_2O, r.t., 1 h; 88% (cryst.). *d*) 1) $MeSO_2Cl$, Et_3N, CH_2Cl_2, 4°, 20 min (extr.); 2) NaI, pentan-3-one, 100°, 2.5 h (extr.); 3) NaOH, MeOH, r.t., 30 min; 83% (cryst.), *e*) 1) Ion-exchange resin (H^+ form), H_2O/THF, 80°, 3.5 h; 2) $NaBH_4$, H_2O, r.t., 2 h. *f*) 1) TIPS-Cl/1*H*-imidazole, DMF, 4° → r.t., 2 h (extr.); 2) O_3, MeOH, −78°, then Me_2S/MeOH, 4°, 14 h; 3) BzCl, Py, CH_2Cl_2, r.t., 14 h; 81% (SiO_2).

[2]) For different approaches, see [3] [4] [8] [9].

Benzoylation and selective cleavage of the primary ketal group of 1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (**1**) (prepared in two steps from D-glucose according to [10] [11]) provided the crystalline diol **2**. This diol was transformed into the corresponding di-*O*-mesylate, from which the crystalline olefin **3** was obtained by treatment with NaI (according to [12]) followed by debenzoylation[3]). Acid-catalyzed hydrolysis of the remaining ketal group in **3**, followed by reduction of the resulting hemiacetal, yielded the hexenitol **4** which was selectively *O*-triisopropylsilylated at the primary OH group. Ozonization of the resulting intermediate, followed by reductive workup and perbenzoylation, led to an α-L/β-L-mixture of the differentially protected L-ribose derivative **5** in an overall yield of 48% (based on D-glucose).

It was impossible to separate the two anomers of **5** by flash chromatography on silica gel. However, after acid-catalyzed hydrolytic removal of the triisopropylsilyl (TIPS, $(i\text{-}Pr)_3Si$) group, a partial separation of the anomers α- and β-**6** by chromatography was achieved; resilylation of the two anomers afforded samples of both α- and β-**5**, respectively (*Scheme 2*).

Scheme 2



a) HCl, H_2O/THF, 20 h, r.t., 93% (SiO_2). *b*) TIPS-Cl, 1*H*-imidazole, CH_2Cl_2, 3 h, r.t.; *ca.* 85% (SiO_2).

This new approach led not to L-ribose, but to an appropriately protected, immediate precursor of L-ribonucleosides. The selective introduction of the $(i\text{-}Pr)_3Si$ group prior to ozonolysis prevented the formation of pyranose isomers, hence no additional purification or derivatizing steps were required to obtain the pure furanose form. No tedious purifications of polar intermediates had to be carried out, since the lipophilic character of the $(i\text{-}Pr)_3Si$ group allowed an easy isolation by conventional extraction.

The *Vorbrüggen* nucleosidation reactions [14] of L-ribofuranose **5**(α/β) with the *in situ* trimethylsilylated pyrimidine bases uracil, thymine, and N^4-benzoylcytosine proceeded smoothly in the presence of $SnCl_4$ (*Scheme 3*). The reactions were carried out at 60° in MeCN and went to completion within 30 min. After extractive workup, the crude products were desilylated with aqueous HCl in THF to give the nucleosides **7**, **8**, and **9**, respectively, in excellent yields.

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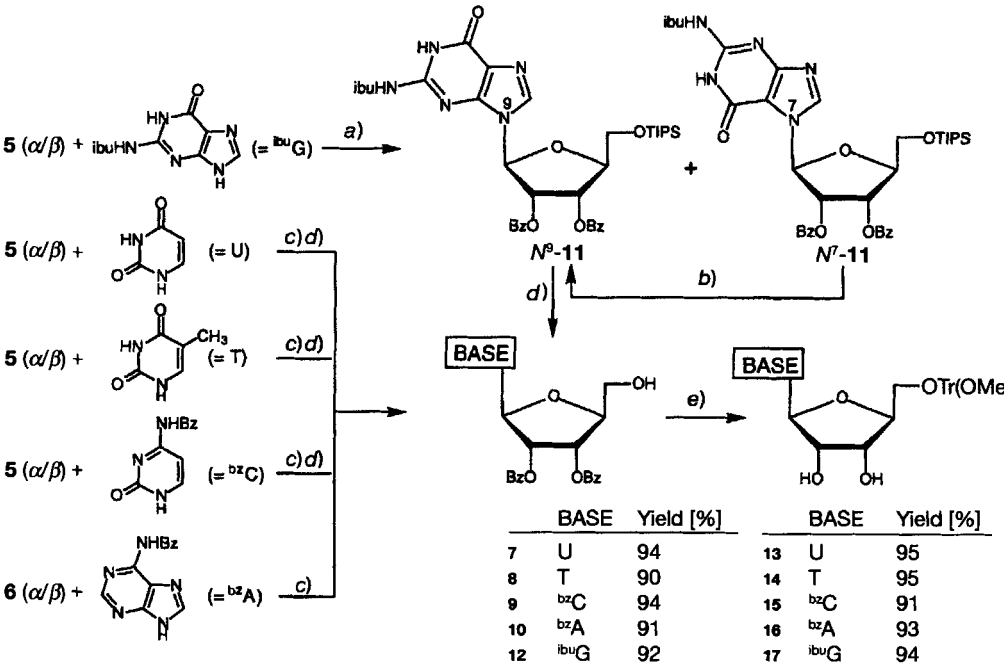
[3]) Alternatively, olefin **3** could be prepared in similar yields from diol **2** by formation of the corresponding 5,6-carbonothioate followed by treatment with $P(OMe)_3$ [13]. Nevertheless, the cheaper reagents and the easier workup make the first route more favorable.

Scheme 3



	BASE	Yield [%]		BASE	Yield [%]
7	U	94	13	U	95
8	T	90	14	T	95
9	bzC	94	15	bzC	91
10	bzA	91	16	bzA	93
12	ibuG	92	17	ibuG	94

Bz = bz = benzoyl TIPS = triisopropylsilyl
ibu = isobutyryl $(MeO)_2Tr$ = 4,4′-dimethoxytrityl

a) Bis(trimethylsilyl)acetamide (BSA), trimethylsilyl triflate, $(CH_2Cl)_2$, 80°, 2.5 h; 58% of N^9-**11** + 36% of N^7-**11**. *b*) Conditions as in *a*); 50% of N^9-**11** + 26% of N^7-**11**. *c*) BSA, $SnCl_4$, MeCN, 65°, 0.5–1 h, *d*) HCl, THF/H_2O, r.t., 1–2 h. *e*) $(MeO)_2TrCl$/*Hünig*'s base, CH_2Cl_2, r.t., 30 min, then NaOH, THF/MeOH/H_2O, 4°, 30 min.

Application of similar conditions to N^6-benzoyladenine yielded only 65% of nucleoside **10** together with 30% of the corresponding N^7-isomer. This ratio could neither be improved by prolonging the reaction time nor by changing the solvent (dichloroethane, 70°) or the *Lewis* acid ($CF_3SO_3SiMe_3$). In contrast, an almost quantitative yield of the adenine nucleoside **10** was obtained by nucleosidation of the *in situ* *O*-trimethylsilylated L-ribofuranose derivative **6**(α/β) with *in situ* *O*-trimethylsilylated N^6-benzoyladenine.

The nucleosidation of **5**(α/β) with *in situ* *O*-trimethylsilylated N^3-isobutyrylguanine afforded a mixture of the two isomeric N^9- and N^7-connected nucleosides N^9-**11** and N^7-**11**, respectively[4]). The ratio of the two products depended strongly on the *Lewis* acid and, to a smaller extent, on the solvent. With $SnCl_4$ in MeCN, the formation of N^7-**11** predominated (N^7/N^9 *ca.* 2:1, yield 90%), whereas with $CF_3SO_3SiMe_3$ in dichloroethane, the desired regioisomer N^9-**11** was the major product. Fortunately, the two products could be easily separated by flash chromatography. Applying similar reaction conditions, the N^7-isomer of **11** could be equilibrated again into a 2:1 mixture

[4]) The structure of the two isomers was assigned by ^{13}C-NMR spectroscopy [15].

of N^9- and N^7-**11**, and the first was isolated in a yield of 50%. Subsequent desilylation of N^9-**11** with aqueous HCl in THF afforded the nucleoside **12**.

The transformation of the five partially protected nucleosides **7**–**10** and **12** into the corresponding 5′-*O*-dimethoxytritylated compounds **13**–**17** proceeded smoothly with 1.1 equiv. of dimethoxytrityl chloride ($(MeO)_2TrCl$)/*Hünig*'s base ($(i\text{-}Pr)_2NEt$) in CH_2Cl_2 within 30 min at room temperature. Without isolation, these intermediates were directly *O*-debenzoylated, and the five nucleosides **13**–**17**, which are common intermediates[5]) in nucleoside chemistry, could be isolated in excellent yields by simple filtration on silica gel. The analytical data of these products were identical to those of their enantiomers, synthesized by known procedures[6]).

It was found that nucleosidations of the two L-configurated ribofuranose derivatives **5** and **6** were much faster than the analogous reactions of the usually employed peracylated derivatives. This result is attributed to the more favorable formation of the intermediate oxycarbenium ion from a 5′-*O*-trialkylsilylated than from a 5′-*O*-acylated precursor.

The protecting-group pattern of the nucleosides obtained from the partially prefunctionalized ribose derivatives **5** and **6** allowed a straightforward preparation and purification of the dimethoxytritylated nucleosides **13**–**17**[7]). The conventional two-step procedure for the preparation of these key intermediates from a peracylated nucleoside derivative (involving *O*-deacylation followed by dimethoxytritylation) requires the tedious purification of very polar, only base-protected intermediates and results in a mixture of different dimethoxytritylated regioisomers, which have to be separated by careful chromatography.

For reasons concerning mainly the stability, alternatives to the commonly used 2′-*O*-protecting groups of the silyl-ether [16] or acetal type [20] were investigated. The most attractive was the [(2-nitrobenzyl)oxy]methyl (nbm) protecting group, introduced by *Gough* and coworkers, which is cleavable under mild photochemical conditions and allows good coupling yields due to its minimal steric hindrance [21]. However, the reported introduction of this group into ribonucleosides and the final photochemical cleavage was not satisfactory for our purposes and was, therefore, improved.

The [(2-nitrobenzyl)oxy]methyl protecting group was introduced at a late stage of the synthesis, with all other protecting groups already in place[8]). From the many reaction conditions tried, first with the uridin nucleoside **13**, formation of a cyclic 2′,3′-di-*O*-stannyl derivative with dibutyltin dichloride/*Hünig*'s base in 1,2-dichloroethane for 90 min at room temperature, followed by addition of 1.05 equiv. of the alkylating agent [(2-nitrobenzyl)oxy]methyl chloride (nbm-Cl) [21] [23], and further heating for 15 min at 80° was superior with respect to selectivity and yield (*Scheme 4*). Other tin reagents (Me_2SnCl_2, Ph_2SnCl_2), bases (Et_3N, DBU, NaH, collidine), solvents (MeCN, DMF,

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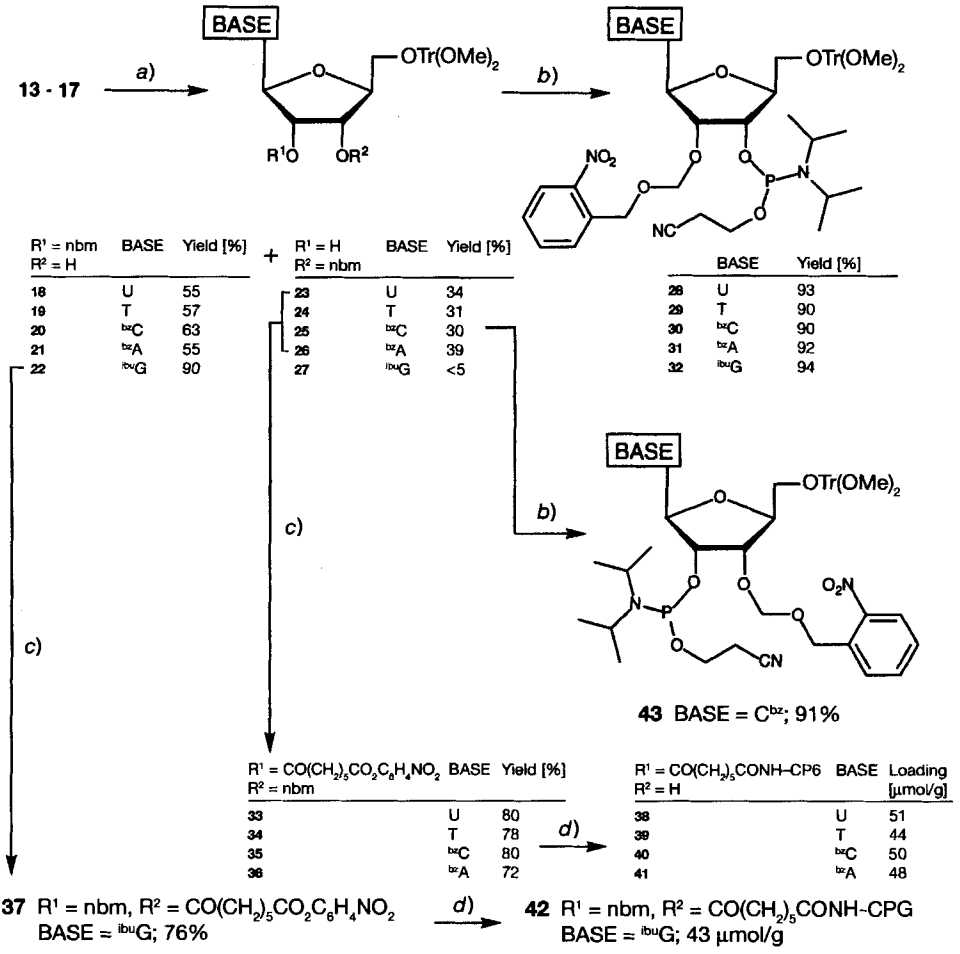
[5]) The enantiomers of these compounds serve as starting materials in the synthesis of the usually employed and commercially available 2′-*O*-trialkylsilylated RNA building blocks [16].

[6]) Prepared from authentic D-nucleosides by protection of the base moieties [17] followed by dimethoxytritylation [18].

[7]) A similar protecting-group strategy was used by *Usman* and coworkers for the synthesis of 5′-methyl-substituted ribonucleosides [19].

[8]) A similar strategy was employed in a synthesis of 2′-*O*-methylated ribonucleosides by *Cramer* and *Pfleiderer* [22].

Scheme 4



nbm = (*ortho*-nitrobenzyloxy)methyl
CPG = aminoalkyl-functionalized controlled pore glass

a) Bu_2SnCl_2/*Hünig*'s base, $(CH_2Cl)_2$, r.t., 1.5 h, then [(*ortho*-nitrobenzyl)oxy] methyl chloride (nbm-Cl), 80°, 20 min. *b*) 2-Cyanoethyl diisopropylphosphoramidochloridite, *Hünig*'s base, CH_2Cl_2, r.t., 3 h. *c*) Bis(4-nitrophenyl) pimelate, DMAP, Py, r.t., 16 h. d) Aminoalkyl-CPG, *Hünig*'s base, DMF, r.t., 24 h.

dioxan, THF, toluene, benzene), or additives (Bu_4N^+/I^-, Br^-, Cl^-, F^-) led to a lower selectivity and/or lower yield. The high temperature favored the formation of the 2′-*O*-alkylated isomer to a small extent (**18**/**23** *ca.* 1:1 at room temperature; *ca.* 3:2 at 80°). The short reaction time and the presence of an excess of base completely prevented the loss of the (thermolabile) dimethoxytrityl group. Under these optimized reaction conditions, side reactions (alkylation of the base moieties) could be observed only to a very small extent (< 5%). The same reaction conditions proved to be suitable for the other four nucleosides **19**–**22** as well, leading to similar (adenosine and thymine nucleosides),

to slightly better (cytosine nucleoside), and to excellent (guanosine nucleoside) yields of the corresponding 2′-*O*-alkylated product. The separation of the two regioisomers could be achieved readily by flash chromatography[9]). In all cases, the less polar, predominant isomer was the 2′-*O*-alkylated compound.

The reported preparation of the ribonucleosides *ent*-**18**–**27** [21] has been carried out by alkylation of the completely unprotected or only base-protected nucleosides (after formation of the cyclic 2′,3′-di-*O*-dibutyl-stannyl derivatives with dibutyltin oxide), followed by base protection and dimethoxytritylation. This protocol has given only moderate regioselectivities in favor of the desired 2′-*O*-alkylated compounds, accompanied by medium-to-low yields. Due to the high polarity of intermediates and products, their isolation has been tedious. Applying the alternative strategy presented herein (dimethoxytritylation followed by alkylation), uniformly higher overall yields were obtained, and all products could be isolated easily.

The unambiguous identification of the products was carried out by ^{1}H-NMR spectroscopy (*Table 1*). Irradiation experiments provided the identification of the signals from the sugar-bound protons and the remaining OH protons. By irradiation of the latter (or D_2O exchange), their connection to either C(3′) or C(2′) could be established, and, therefore, the alkylation sites were identified. Due to signal overlapping, the alkylation sites in **19**, **24**, and **25** could not be determined in this way. After formation of the acyl derivative from **24**, however, the position of the new acyl group (which corresponds to the position of the OH group in **24**) could be easily determined, since it caused the expected downfield-shift of the H–C(3′) signal. The structure of **25** was determined analogously. Furthermore, the two uridin nucleosides **18** and **23** had the same ^{1}H-NMR

Table 1. *^{1}H-NMR Data* (300 MHz, $CDCl_3$) *of Key Intermediates*. Chemical shifts δ in ppm rel. to $SiMe_4$.

	H–C(1′)	H–C(2′)	H–C(3′)	H–C(4′)	H–C(5′)	H′–C(5′)	OH
13	5.91	4.34	4.44	4.16	3.49	3.53	
18	6.04	4.38	4.55	4.10	3.52	3.55	2.67
23	5.93	4.10	4.42	4.26	3.41	3.60	4.10
14	5.94	4.38	4.38	4.19	3.38	3.48	
19	6.10	4.49	4.49	4.10	3.43	3.53	2.73
24	5.99	4.45	4.45	4.25	3.32	3.57	3.61
15	5.91	4.4	4.4	4.4	3.48	3.68	
20	6.06	4.38	4.51	4.13	3.57	3.62	2.70
25	5.96	4.4	4.4	4.4	3.41	3.62	4.29
16	6.09	4.93	4.49	4.38	3.31	3.44	
21	6.24	5.11	5.55	4.28	3.42	3.53	2.89
26	6.07	4.20	4.59	4.37	3.32	3.49	4.20
17	5.91	5.01	4.50	4.33	3.20	3.42	
22	5.98	5.22	4.51	4.23	3.20	3.50	2.83
27	5.71	5.36	4.61	4.19	2.99	3.50	5.42

[9]) The ΔR_f values within the pairs of regioisomers are as follows: **18**/**23** 0.35, **19**/**24** 0.15, **20**/**25** 0.3, **21**/**26** 0.35 (hexane/AcOEt 1:9); **22**/**27** 0.15 (CH_2Cl_2/MeOH 19:1).

data as reported in [21]. The signals of the anomeric protons of all pairs of regioisomers followed the rule of *Reese* and coworkers [24], which states that, in such compounds, the H–C(1′) signal of the 2′-*O*-alkylated isomer is further downfield than that of the corresponding 3′-*O*-alkylated isomer, and the coupling constants between H–C(1′) and H–C(2′) of the former isomers are smaller than those of the latter. The OH signals of all 2′-*O*-alkylated compounds were further upfield than those of the corresponding 3′-*O*-alkylated isomers, which suggests a much stronger H-bond from *H*O–C(2′) to O–C(3′) than from *H*O–C(3′) to O–C(2′).

Following standard procedures, the protected nucleosides **18**–**22** were converted into the phosphoramidite building blocks **28**–**32**, which were suitable for the synthesis of corresponding oligonucleotides on a DNA synthesizer [25] [26]. Additionally, the phosphoramidite building block **43** was prepared from **25**, which was required for the synthesis of oligonucleotides with unnatural 5′ → 2′ phosphodiester linkages (*Scheme 4*).

The solid supports **38**–**42** loaded with the five L-nucleosides were synthesized using known protocols, by first preparing the 2′-*O*-(nitrophenyl pimelates) **33**–**36** from the 3′-*O*-alkylated nucleosides **23**–**26** and the 3′-*O*-(nitrophenyl pimelate) **37** from the 2′-*O*-alkylated nucleoside **22**, and then immobilizing these activated esters on aminoalkyl-functionalized CPG (*c*ontrolled *p*ore *g*lass; *Sigma*) (*Scheme 4*) [27]. By preparing the solid supports from the 3′-*O*-alkylated nucleosides **23**–**26**, these alkylation by-products were not lost, and the main isomers from the alkylation reaction, the 2′-*O*-alkylated nucleosides **18**–**21**, could be entirely used for the preparation of phosphoramidite building blocks.

2. *Synthesis of Ribonucleic Acids.* The synthesis of L(and D)-configurated oligoribonucleotides[10]) from the phosphoramidite building blocks **28**–**32** and **43** and the solid supports **38**–**42** was carried out on 1.5- and 10-μmol scales on a *Pharmacia Gene Assembler* using essentially the protocol which was developed for the synthesis of p-RNA (p = pyranosyl) [28]. The coupling step was carried out in the presence of a mixture of 1*H*-tetrazole and 5-(4-nitrophenyl)-1*H*-tetrazole. To save precious starting materials, only 7 equiv. (1.5-μmol scale) or 1.5 equiv. (10-μmol scale) of phosphoramidites were used for each coupling step; as a consequence, the coupling time had to be adjusted to 12 min for optimal results. The coupling yields obtained under these conditions were > 98% (detritylation assay[11])) and could not be increased further by using more equiv. of phosphoramidites or longer reaction times[12]).

The removal of the base- and phosphate-protecting groups and the cleavage from the solid support was carried out by ammonolysis for 24 h using a 2:1 mixture of saturated aqueous NH_3 solution/MeOH at 50° (*Scheme 5*). Much longer exposure or higher temperatures resulted in a substantial degradation of the oligonucleotide strands. The crude

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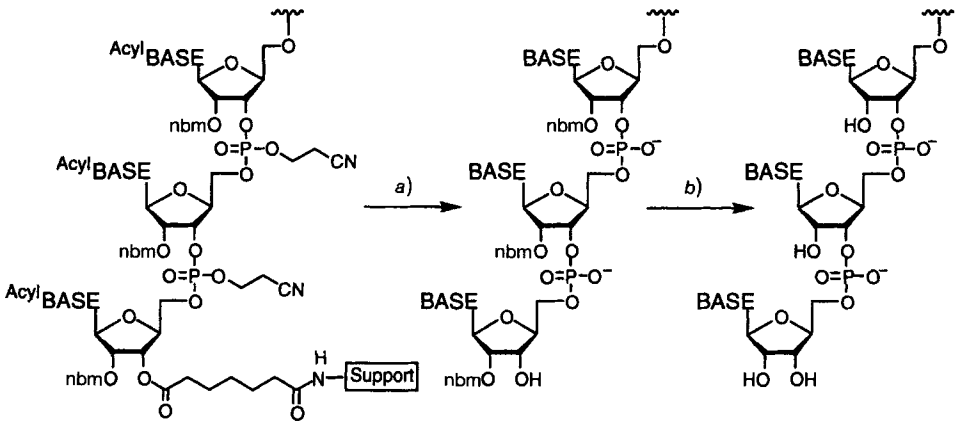
[10]) The D-configurated phosphoramidites *ent*-**28**–**32** and solid supports *ent*-**38**–**42** were prepared from the corresponding 5′-*O*-dimethoxytritylated, base-protected D-nucleosides (see *Footnote 6*), using the presented methods.

[11]) Each chain-elongation cycle begins with an acid-promoted cleavage of the dimethoxytrityl group from the growing chain. By comparison of the spectrophotometrically determined amount of dimethoxytrityl group (ε = 70000 l mol^{-1} cm^{-1}), the efficiency for each coupling step can be calculated.

[12]) The same yield is reported by *Gough* and coworkers [21]: using conventional 20-fold excesses of phosphoramidites, only a 2-min coupling time was required.

Scheme 5



a) NH_3/H_2O/MeOH, 50°, 24 h. *b*) *Pyrex*-filtered light (slide projector), H_2O (10 mM sodium phosphate, 10 mM sodium citrate pH 3.9), $(CH_2Cl)_2$, r.t., 5–9 h.

products were analyzed by reversed-phase HPLC and showed a composition as expected from the detritylation assay[11]).

Initially, the photolytic removal of the remaining 2′-*O*-{[(2-nitrobenzyl)oxy]methyl} protecting groups from the oligonucleotide was carried out as reported in [21] ($c \approx 10$ μM in *t*-BuOH/H_2O 1:1, pH 3.7, *ca.* 5 h) using *Pyrex*-filtered light from a mercury lamp. The deprotections were followed by HPLC; a very fast deprotection was observed in the beginning, which almost ceased after *ca.* 1 h and continued only very slowly. Obviously, this nonlinear behavior was due to inhibition by the by-product 2-nitrosobenzaldehyde (and its degradation products), which, after having built up, absorbed the light used for activation of the remaining nitrobenzyl groups. To circumvent this effect, a different set-up was designed.

Efficient removal of 2-nitrosobenzaldehyde could be achieved by continuous extraction of the aqueous, buffered reaction mixture with 1,2-dichloroethane. This simple modification allowed the photolytical deprotection to be performed under much milder conditions, using more concentrated (up to $c \approx 500$ μM) and less acidic (pH 3.9) solutions. As a light source, a commercial slide projector was employed. Under these conditions, the deprotection was finished after 5–9 h (depending on the sequence length of the oligonucleotide) (*Scheme 5*). The UV spectra (*Fig. 1,a*) of the aqueous and the organic phases of such a reaction confirm the initial expectation: After completion of the reaction, the aqueous phase contains essentially only the oligoribonucleotide (as deduced from the typical spectrum). The by-products which absorb strongly around 320 nm – the position of the relevant n → π* transition – are collected in the organic phase, where they do not interfere with the deprotection process. The time course of a typical deprotection is documented by HPLC plots that were collected during photolysis of a protected tetradecamer sequence (*Fig. 1,b*).

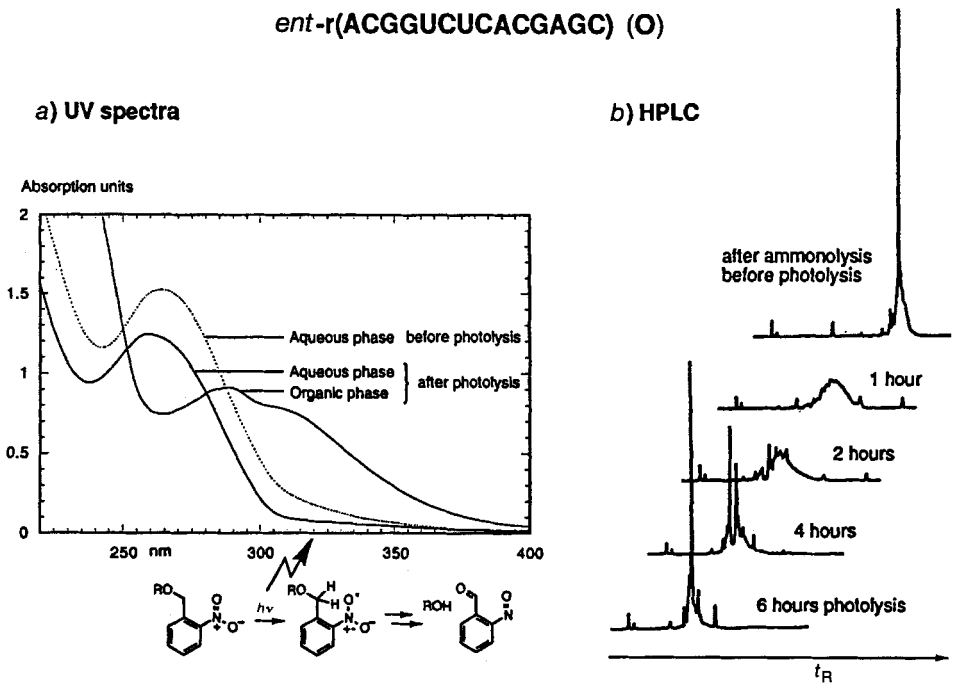


Fig. 1. *Photolytic deprotection of the tetradecamer sequence* **O** *in a two-phase system* (for details, see text, *Scheme 5* and *Exper. Part*: a) *UV spectra* (1-cm cell) *of both phases* (strongly absorbing (at *ca.* 320 nm) by-products in the organic phase); b) *reversed-phase HPLC monitoring* (0 → 40% buffer *B* within 30 min; see *Exper. Part* for details) *of the aqueous phase* (t_R (deprotected oligomer) < t_R (nbm-protected oligomer))

Short- to medium-length oligomers were prepared in the 'trityl-off'[13]) mode. The crude products, obtained after ammonolysis and photolysis were purified by reversed-phase HPLC. With some guanosin-rich sequences, additional purification was carried out by anion-exchange chromatography under denaturing conditions (pH 11.5, see *Exper. Part*). For an easier purification of long sequences, they were prepared in the 'trityl-on'[13]) mode. After ammonolysis, the trityl-containing sequences were isolated by reversed-phase HPLC. Subsequent cleavage of the trityl groups with 50% aqueous formic acid and photolysis provided crude products which could again be purified by HPLC. Depending on the efficiency of separation from shorter or still partially protected sequences, the oligonucleotides were obtained in isolated yields between 10 and 40%. The relatively low yields were obtained from sequences which were purified by more than one chromatography and from self-complementary sequences which exhibited broad peaks.

[13]) 'Trityl-off' and 'trityl-on' mean that the last dimethoxytrityl group is cleaved at the end of the synthesis or is left on the sequence, respectively. After ammonolysis, the latter procedure allows an easier separation of the long sequences from contaminating shorter sequences. An additional step, however, is then required to cleave the remaining dimethoxytrityl group.

Table 2. *Synthesis and Characterization of* ent-*Oligonucleotides* **A**–**S**

Sequence[a])	Synthesis scale [μmol]	Purification[b])	Yield[c])		$[M-H^+]^-$[d]		
			[abs.u.]	[%]	calc.	obs.	Δ[‰]
A *ent*-5′-r(GGGCp)-3′	10	*a*, *b*	65	15	1358	1360	+1.5
B *ent*-5′-r(GCCCp)-3′	10	*a*	90	38	1278	1278	0
C *ent*-5′-r(GGGCGGGCp)-3′	10	*a*, *b*	120	14	2698	2699	+0.4
D *ent*-5′-r(GGGC*GGGCp)-3′	1.5	*a*, *b*	30	25	2698	2695	−1.1
E *ent*-5′-r(GCCCGCCCp)-3′	10	*a*	160	24	2538	2539	+0.4
F *ent*-5′-r(GCCC*GCCCp)-3′	1.5	*a*	35	35	2538	2537	−0.4
G *ent*-5′-r(AAAAUUUAUAUUAUUA)-3′	1.5	*a*	60	20	5020	5019	−0.2
H *ent*-5′-r(UUUUAAAUAUAAUAAU)-3′	1.5	*a*	65	23	5020	5019	−0.2
I *ent*-5′-r(AUUAUUAUAUUUAAAA)-3′	1.5	*a*	65	23	5020	5022	+0.4
J *ent*-5′-r(AAAATTTATATTATTA)-3′	1.5	*a*	65	23	5132	5127	−1.0
K *ent*-5′-r(TTTTAAATATAATAAT)-3′	1.5	*a*	75	25	5132	5128	−0.8
L *ent*-5′-r(ATTATTATATTTAAAA)-3′	1.5	*a*	60	20	5132	5127	−1.0
M *ent*-5′-r(ACGGUCUCp)-3′	1.5	*a*	45	35	2564	2562	−0.8
N *ent*-5′-r(ACGAGC)-3′	1.5	*a*	40	40	1896	1894	−0.8
O *ent*-5′-r(ACGGUCUCACGAGC)-3′	1.5	*a*	55	24	4444	4439	−1.1
P *ent*-5′-r(ACGGUCUC*ACGAGC)-3′	1.5	*a*	60	26	4444	4438	−1.4
Q *ent*-5′-r(GCUCGUCUGAUGAGUCC GUGAGGACGAAAGACCGU)-3′[e])	1.5	*a*, *b*	55	10	11298	11297	−0.1
R *ent*-5′-r(CGCGAAUUCGCG)-3′	10	*a*	250	20	3809	3805	−1.0
S *ent*-5′-r(CGCGAAUUCGCG)-3′	10	*a*	260	21	3809	3804	−1.3

[a]) C* stands for an (unnatural) C2′p5′X phosphodiester junction (prepared by incorporating phosphoramidite **43**); the terminal 3′-monophosphate containing sequences **A**–**F** and **M** were prepared from a special solid support [29]. [b]) *Method a*: purification by reversed-phase HPLC; *Method b*: purification by ion-exchange chromatography at pH 11.5 (for conditions, see *Exper. Part*). [c]) One absorption unit (1 abs.u.) is equivalent to the amount of oligonucleotide which, after dissolution in 1 ml and measured with a 1-cm cell, has an extinction of 1; the yields were calculated using the extinction values given in *Exper. Part.* [d]) Determined by MALDI-TOF mass spectrometry according to [30]. [e]) This oligonucleotide was prepared in the 'trityl-on' mode (see *Footnote 13*).

3. *Structural and Functional Characterization of* ent-*Oligoribonucleotides*. Employing the presented methods, the *ent*-oligoribonucleotides **A**–**S** were synthesized (*Table 2*). All sequences exceeded a purity of 97% as analyzed by reversed-phase and ion-exchange HPLC and exhibited the correct mass in MALDI-TOF spectra (*Table 2*).

In *Fig. 2*, transition curves ('melting curves') and CD spectra of the self-complementary enantiomeric RNA sequences **R** and **S** are shown. The (racemic) mixture of both enantiomers at $c = 6 + 6$ μM displays the same transition temperature and the same hyperchromicity as the individual enantiomers alone at $c = 6$ μM each. As a comparison, the same curve of one enantiomer alone but at $c = 2 \times 6$ μM is shown which differs from the others by a higher transition temperature and a lower hyperchromicity (*Fig. 2,a*). These measurements demonstrate that there is no interaction between the two enantiomeric strands. The CD spectra of both enantiomers are identical but mirror-symmetrical, whereas their 1:1 (racemic) mixture shows no CD spectrum (*Fig. 2,b*).

Additionally, the sequence **R** was characterized by ^{1}H-NMR spectroscopy since such data of its enantiomer **S** were reported [31] and could be used for comparison. A first

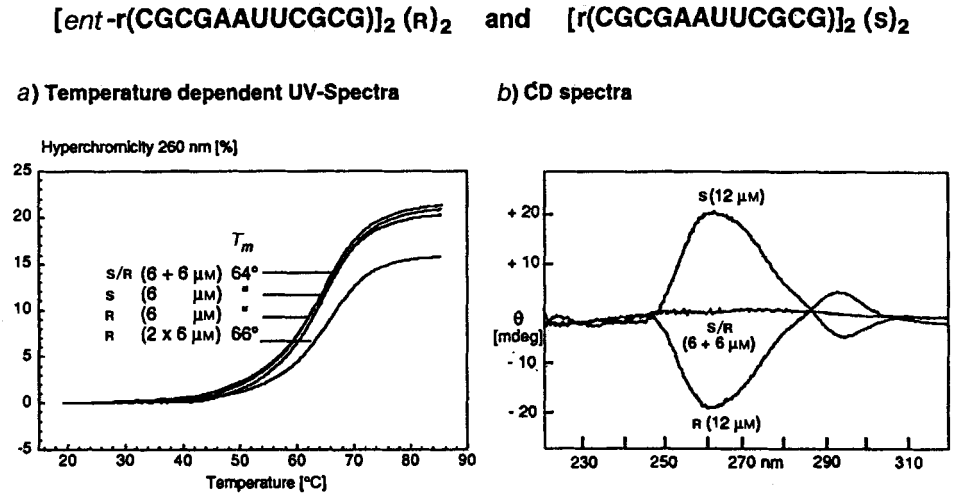


Fig. 2. a) *Transition curves* ('melting curves') *and* b) *CD spectra* (1-cm cell, 25°) *of both enantiomers* **R** *and* **S** *and the racemate* **S**/**R** *of a self-complementary dodecamer RNA sequence.* These measurements illustrate the constitutional identity and the enantiomorphic character of both sequences **R** and **S** and show the absence of any base-pairing interaction between the two enantiomeric oligonucleotides (conditions: 0.15M NaCl, 0.01M phosphate, pH 7.0).

inspection of the 500-MHz ^{1}H-NMR spectrum measured in D_2O (*Fig. 3,a*) revealed the high purity of the material: apart from the expected *s* and *d* from the C-bound base protons and the *s* from the anomeric protons[14]) (only the signal of the terminal guanosin nucleoside G12 appears as a *d*), no other signals, which could be attributed to shorter, isomeric, or still partially protected sequences can be detected in the resolved regions from 4.9–6.0 and 7.1–8.1 ppm; the relative integral intensities within the three separate regions fully agree with the expected number of non-exchangeable protons. In *Table 3*, the ^{1}H-NMR chemical shifts of the H–C(1′) and H–C(2′) signals are shown[15]). The values obtained agree very well with the reported ones [31], which are uniformly *ca.* 0.08 ppm lower. Larger differences can be found only for the values of the first residue C1 and of residues G10 and C11. The chemical-shift differences for the terminal, relatively weakly paired C1 residue can be attributed to differences in the dynamic behavior, which could result from different measurement conditions (concentration of oligonucleotide and salts, pH). The differences for residues G10 and C11, however, originate from an opposite assignment.

A further proof of the correct structure of the presented *ent*-oligoribonucleotides was achieved by synthesizing the mirror image of a ribozyme structure; *i.e.*, **Q**, together with its substrate **O** and comparing the course of the known phosphodiester-cleaving reaction with corresponding published data [33]. In *Fig. 4*, HPLC plots of such a reaction are

[14]) Sharp *s* for the anomeric protons are compatible with a dihedral angle of H–C(1′)/H–C(2′) of *ca.* 90°, which is typical of an A-type (3′-*endo*) sugar conformation [31] [32].

[15]) They were extracted from a NOESY spectrum, of which a selected region, showing the inter- and intra-nucleoside cross-peaks between the anomeric and the base protons, is displayed (*Fig. 3,b*).

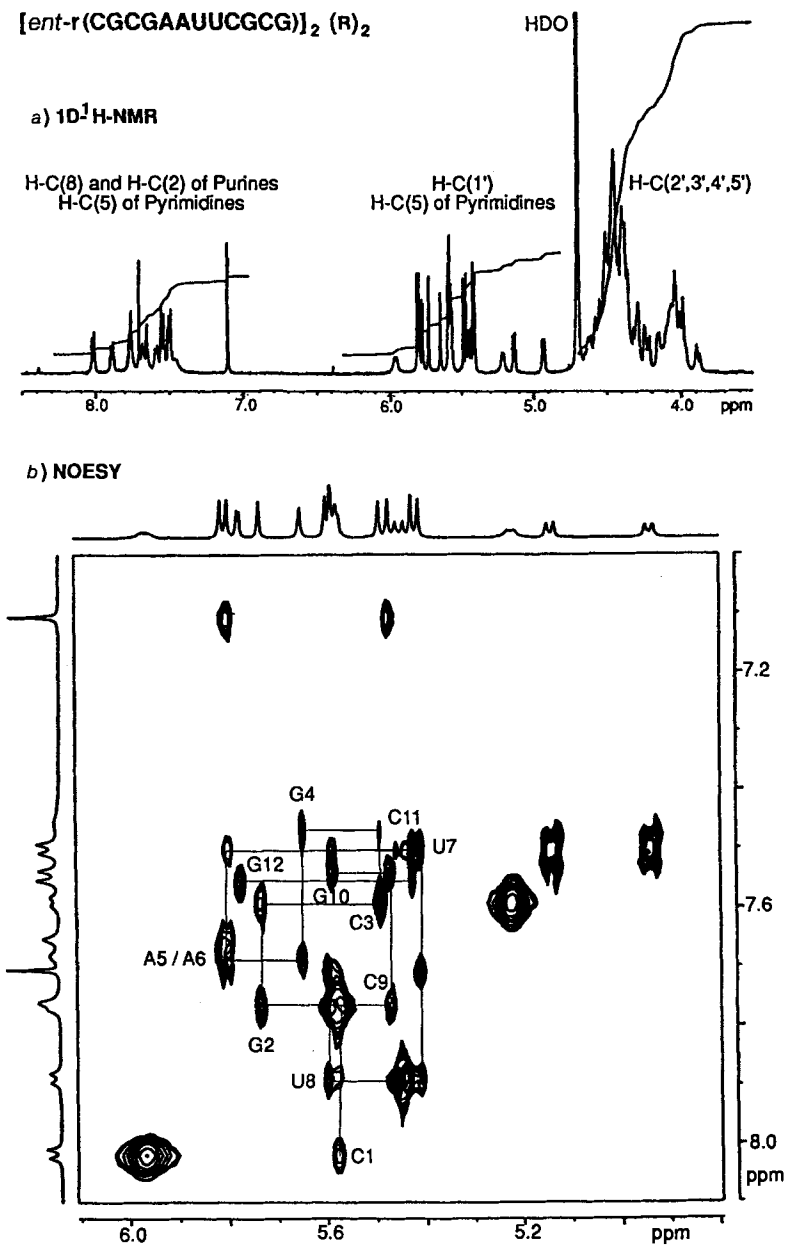


Fig. 3. *^{1}H-NMR Spectra* (500 MHz) *of the self-complementary dodecamer sequence* **R** (10 mg of oligonucleotide in 1 ml of D_2O). a) *1D NMR spectrum*; b) *NOESY spectrum with sequential assignment of the anomeric and the base protons*. The intranucleoside cross-peaks are labeled with their residue number.

Table 3. *Selected ^{1}H-NMR Data of Sequence* **R**[a])

Residue	H–C(1′)		H–C(2′)		H–C(8) (Purines) H–C(6) (Pyrimidines)		H–C(5) (Pyrimidines) H–C(2) (Adenines)	
	δ [ppm]	Δ[b]) [ppm]	δ [ppm]	Δ[b])	δ [ppm]	Δ[b])	δ [ppm]	Δ[b])
C1	5.56	+0.26	4.51	+0.12	8.02	+0.22	5.96	+0.16
G2	5.73	+0.09	4.55	+0.13	7.76	+0.14		
C3	5.50	+0.11	4.52	+0.10	7.59	+0.09	5.22	+0.12
G4	5.65	+0.10	4.53	+0.08	7.45	+0.10		
A5	5.82	+0.08	4.58	+0.12	7.68	+0.07	7.10	+0.09
A6	5.80	+0.06	4.41	+0.16	7.65	+0.04	7.71	+0.10
U7	5.41	+0.07	4.29	+0.12	7.49	+0.03	4.93	+0.07
U8	5.60	+0.08	4.40	+0.12	7.89	+0.09	5.44	+0.07
C9	5.45	+0.06	4.39	+0.11	7.76	+0.08	5.57	+0.07
G10	5.58[c]	+0.23[c])	4.30[c])	+0.05[c])	7.54	+0.11		
C11	5.42[c])	−0.08[c])	4.25[c])	−0.07[c])	7.50	+0.11	5.13	+0.08
G12	5.78	+0.10	4.04	+0.10	7.55	+0.13		

[a]) Extracted from a NOESY spectrum (*Fig. 3,b*); comparison with published data of the same, naturally configurated sequence, prepared by established methods [31]. [b]) Deviation from the values reported in [31]. [c]) Interchanged assignment.

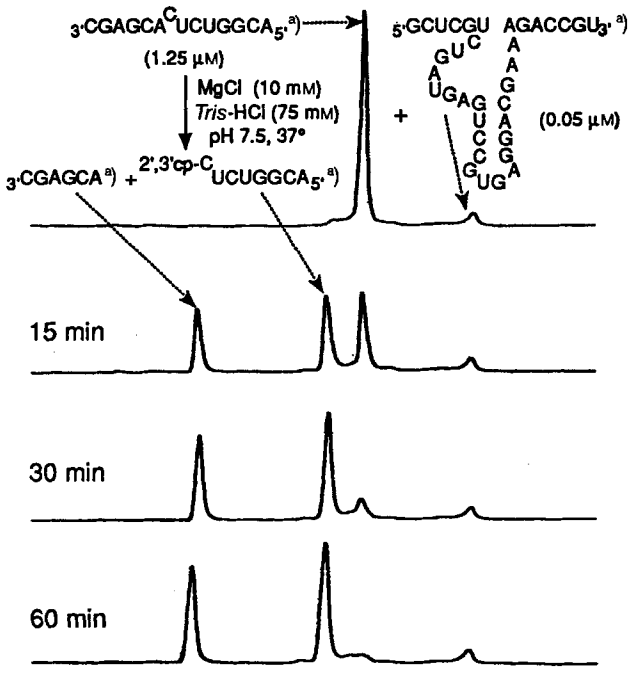
shown: after 1 h, only traces of the starting tetradecamer substrate **O** were still present. This *ent*-oligonucleotide was selectively cleaved into two pieces which were unambiguously identified by coinjection with authentic samples[16]). This result is completely identical to the course of the reaction published in [33], which was followed by gel electrophoresis.

Conclusion. – The sum of structural and functional data collected from the presented *ent*-oligoribonucleotides confirmed unambiguously their structure and their purity. A novel method for the introduction of a photolabile sugar-protecting group allowed the efficient preparation of phosphoramidite building blocks derived from a new, easily synthesized prefunctionalized L-ribose derivative. Improved conditions for the final photolytic deprotection step allowed the synthesis of relatively large amounts of *ent*-oligoribonucleotides and of relatively long sequences using photolabile protection.

A number of *ent*-oligoribonucleotides prepared by the presented methods were employed successfully in two studies, dealing with functional and structural properties of p-RNA (p = pyranosyl) [29] [34]. The enantiomeric sequences **R** and **S** were prepared for a study with Dr. *Martin Egli* (Northwestern Medical School Chicago). We are about to explore the crystallization properties of racemic RNA [35] and to investigate whether this class of important biopolymers follows '*Wallach*'s rule' [36], originally formulated for small molecules and stating that, generally, crystals formed from a racemic mixture are more stable (and thus more likely to be formed) then crystals formed from one enantiomer alone.

[16]) The *ent*-oligonucleotide **P**, having the same sequence as the substrate **O**, but a 5′ → 2′ connection at the potential cleaving site, resisted cleavage completely, even after incubation for 24 h.

ent-5'-r(GCUCGUCUGAUGAGUCCGUGAGGACGAAAGACCGU)-3' (Q)



a) The *ent*-sequence is meant.

Fig. 4. *Functional analysis of the 35mer* ent-*oligonucleotide* **Q**. Its known function as catalyst in the selective cleaving of the tetradecamer sequence **O** was followed by ion-exchange HPLC (conditions, see *Exper. Part*); the reaction was carried out according to [33] and could be completely reproduced. The identity of the two produced *ent*-oligonucleotides was unambiguously confirmed by coinjection with authentic samples (the octamer cyclophosphate sequence was synthesized from *ent*-oligonucleotide **M** under conditions described in [29]).

Using the strategy and the methods presented herein, the first syntheses of some functionalized oligoribonucleotides, containing a 1-[6'-*O*-(ω-aminopropyl)-β-D-allofuranosyl]cytosine residue could be completed successfully and efficiently [1] [2].

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Experimental Part

General. All reagents and solvents from *Fluka* (exceptions mentioned); N^2-isobutyrylguanine monohydrate [37], N^6-benzoyladenine [38], N^4-benzoylcytosine [39], 1-[(chloromethoxy)methyl]-2-nitrobenzene (nbm-Cl) [21] [23] 2-cyanoethyl diisopropylphosphoramidochloridite [26] [40], bis(4-nitrophenyl) pimelate (bis(4-nitrophenyl) heptanedioate) [27], and 5-(4-nitrophenyl)-1*H*-tetrazole [41] were prepared according to published procedures. Usual workup implies distribution of the reaction mixture between the indicated org. solvent and the indicated

aq. soln. and drying ($MgSO_4$) and evaporation of the org. phase. Column chromatography (CC): silica gel from *Macherey & Nagel*. TLC: precoated silica gel plates from *Macherey & Nagel*; detection by a soln. of anisaldehyde (10 ml; *Aldrich*), conc. H_2SO_4 soln. (10 ml), and AcOH (2 ml) in EtOH (180 ml) and subsequent heating. Reversed-phase HPLC (*Method a*): anal.: *Aquapore RP 300* (4.6 × 220 mm; *Brownlee Labs*), flow 1 ml/min; prep.: *Nucleosil 5 C18* (10 × 220 mm; *Macherey & Nagel*), flow 5 ml/min; eluent *A*, 0.1M (Et_3NH)OAc in H_2O (pH 7); eluent *B* MeCN; detection at 260 nm, elution at 40°. Ion-exchange HPLC (*Method b*): *Mono Q HR 5/5* (*Pharmacia*), flow 1 ml/min; eluent *A*, 10 mM Na_3PO_4 in H_2O (pH 11.5); eluent *B*, 10 mM Na_3PO_4/1M NaCl in H_2O (pH 11.5); detection at 260 nm, elution at r.t., desalting of oligonucleotides by prep. HPLC using for 5 min eluent *A*, then for 10 min H_2O, then $H_2O \rightarrow H_2O$/MeCN 1:1 within 10 min. For the determination of oligonucleotide concentrations, the following extinction coefficients (260 nm) [$l\ mol^{-1}\ cm^{-1}$] were used: adenosine 15300; guanosine 11700; cytosine 7400; uridine 9900; 1-(β-D-ribofuranosyl)thymine 9000. Abbreviations: DMAP = 4-(*N,N*-dimethylamino)pyridine; BSA = bis(trimethylsilyl)acetamide. M.p.: uncorrected. UV Spectra: $\lambda_{max}/\lambda_{min}$ (ε) in nm. IR Spectra: $\tilde{\nu}$ in cm^{-1}. NMR: chemical shift δ in ppm and coupling constants J in Hz. MS: matrix indicated (NOBA = 3-nitrobenzyl alcohol); *m/z* (rel. intensity in %); CI (chemical ionization). ES (electrospray), FAB (fast-atom bombardment); MALDI-TOF (matrix-assisted time-of-flight) spectra measured according to [30].

1,2:5,6-Di-O-isopropylidene-α-D-allofuranose (**1**) [11]. To a suspension of pyridinium dichromate (108 g, 0.288 mol) and Ac_2O (110 ml, 1 mol) in CH_2Cl_2 (750 ml), 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (prepared from D-glucose according to [10]; 100 g, 0.38 mol) in CH_2Cl_2 (250 ml) was added. After 2 h reflux, the mixture was evaporated, the residue taken up in AcOEt, and the soln. filtered through a pad of silica gel and *Celite*. The filtrate was evaporated, the residue dissolved in EtOH/H_2O 24:19 (430 ml) and treated with $NaBH_4$ (18 g, 0.5 mol) in H_2O (260 ml). The mixture was stirred for 3 h at r.t. and extracted with CH_2Cl_2, the extract dried ($MgSO_4$) and evaporated, and the residue crystallized from Et_2O: **1**, 90 g (90%). Colorless prisms. TLC (hexane/Et_2O 1:5): R_f 0.29. M.p. 76°. $[\alpha]_D^{25°} = +37$ ($c = 1.00$, $CHCl_3$). IR ($CHCl_3$): 3550*m*, 2990*m*, 2930*m*, 1480*w*, 1455*m*, 1435*s*, 1385*s*, 1375*s*, 1315*m*, 1285*m*, 1260*m*, 1235*s*, 1165*s*, 1115*s*, 1095*m*, 1065*s*, 1020*s*, 870*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.38, 1.39, 1.47, 1.59 (4*s*, 4 Me); 2.56 (*d*, $J = 8.3$, OH); 3.82 (*dd*, $J = 4.6$, 8.5, 1 H–C(6)); 4.00–4.11 (*m*, H–C(3), H–C(4), 1 H–C(6)); 4.32 (*dt*, $J = 4.6$, 6.5, H–C(5)); 4.62 (*dd*, $J = 4.1$, 3.8, H–C(2)); 5.82 (*d*, $J = 3.8$, H–C(1)). ^{13}C-NMR (75 MHz, $CDCl_3$): 25.2, 26.3, 26.5 (3*q*, Me); 65.8 (*t*, C(6)); 72.4, 75.5, 78.9, 79.7 (4*d*, C(2), C(3), C(4), C(5)); 103.9 (*d*, C(1)); 112.8, 119.8 (2*s*, Me_2C). EI-MS: 245 (70, $[M - Me]^+$), 159 (21), 127 (26), 101 (80), 59 (72), 43 (100).

3-O-Benzoyl-1,2-O-isopropylidene-α-D-allofuranose (**2**). To a soln. of **1** (70 g, 0.27 mol) and DMAP (3.3 g, 27 mmol) in pyridine/CH_2Cl_2 1:2 (600 ml), benzoyl chloride (34.2 ml, 0.3 mol) was slowly added. The mixture was stirred 1 h at r.t., treated with MeOH (100 ml) and stirred 30 min at r.t. The org. phase, obtained after addition of H_2O (200 ml) was evaporated, treated twice with H_2O (200 ml), and evaporated again. The residue was dissolved in CH_2Cl_2 (400 ml) and extracted twice with 1M aq. H_2SO_4 (200 ml). The org. phase was dried ($MgSO_4$) and evaporated. The residue was dissolved in AcOH/HCOOH/H_2O 10:4:3 (850 ml), stirred 1 h at r.t., evaporated, treated with H_2O (3 × 200 ml), and evaporated again. The residue was dissolved in CH_2Cl_2 (400 ml). Usual workup (CH_2Cl_2/sat. aq. $NaHCO_3$ soln.) afforded a residue which was dissolved in hot AcOEt (200 ml). After addition of hexane (200 ml) and slow cooling to r.t., 65.5 g of **2** were obtained as colorless crystals. The mother liquor was evaporated, the residue dissolved in CH_2Cl_2 (150 ml) and adsorbed on SiO_2 (20 g). CC (silica gel, 60 g, hexane → hexane/AcOEt 1:2) and crystallization (hexane/AcOEt) gave a further crop of **2** (12 g; combined yield 88%). TLC (hexane/AcOEt 7:13): R_f 0.33. M.p. 98°. $[\alpha]_D^{25°} = +114$ ($c = 1.22$, $CHCl_3$). IR ($CHCl_3$): 3600*m*, 3000*m*, 1730*s*, 1600*w*, 1460*m*, 1390*m*, 1280*s*, 1130*m*, 1100*m*, 1070*m*, 1050*m*, 1020*m*, 870*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.31, 1.54 (2*s*, 2 Me); 2.48, 2.97 (2 br. *s*, 2 OH); 3.64 (*dd*, $J = 7.2$, 11.2, 1 H–C(6)); 3.73 (br. *d*, $J \approx 11$, 1 H–C(6)); 4.07 (br. *m*, H–C(5)); 4.32 (*dd*, $J = 3.7$, 9.0, H–C(2)); 4.96 (*dd*, $J = 4.0$, 5.0, H–C(3)); 5.87 (*d*, $J = 3.7$, H–C(1)); 7.45 (*m*, 2 arom. H); 7.58 (*m*, 1 arom. H); 8.05 (*m*, 2 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 26.73, 26.76 (2*q*, Me); 62.9 (*t*, C(6)); 71.4, 72.3, 78.0, 78.5 (4*d*, C(2), C(3), C(4), C(5)); 104.5 (*d*, C(1)); 113.5 (*s*, Me_2C); 128.8 (*d*, arom. C); 129.5 (*s*, arom. C); 130.1, 133.7 (2*d*, arom. C); 166.2 (*s*, CO). CI-MS (NH_3): 325 (1, $[M + H]^+$), 309 (13), 267 (100), 205 (31), 105 (44).

(4R)-4-Vinyl-1,2-O-isopropylidene-α-D-erythrofuranose (**3**). A soln. of **2** (50 g, 0.154 mol) in CH_2Cl_2 (400 ml) was cooled to 4° and treated consecutively with Et_3N (50 ml, 0.39 mol) and $MeSO_2Cl$ (27 ml, 0.34 mol). The suspension was stirred for 20 min at 4°, and then H_2O (200 ml) was added. After usual workup (CH_2Cl_2/sat. aq. $NaHCO_3$ soln.) and drying *in vacuo*, a voluminous yellow foam was obtained (di-*O*-mesyl derivative of **2**). This crude product was dissolved in pentan-3-one (1.2 l), and solid NaI (150 g, 1.0 mol) was added. The suspension was purged with Ar and heated under reflux for 2.5 h. The dark red mixture was then poured into sat. aq. $Na_2S_2O_3$ soln. (1 l). The aq. layer was washed with CH_2Cl_2, the combined org. phase washed with sat. aq. $NaHCO_3$ soln., dried ($MgSO_4$), and evaporated, and the residue dissolved in MeOH (300 ml), treated with 10N aq. NaOH (3 ml),

and stirred for 30 min at r.t. After addition of NH_4Cl (3 g) and evaporation, the mixture was suspended in CH_2Cl_2 and absorbed on silica gel (100 g). CC (silica gel (200 g), hexane → hexane/AcOEt 3:7) and crystallization (hexane/AcOEt) gave **3** (23.5 g, 83%). Colorless crystals. TLC (hexane/AcOEt 3:2): R_f 0.45. $[\alpha]_D^{25°} = +40$ ($c = 1.11$, $CHCl_3$). IR ($CHCl_3$): 3560*m*, 2995*m*, 1650*w*, 1400*m*, 1170*m*, 1130*s*, 1070*s*, 1030*s*, 950*m*, 880*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.37, 1.57 (2*s*, 2 Me); 2.42 (*d*, $J = 10.6$, OH); 3.69 (*ddd*, $J = 5.0$, 8.7, 10.6, H–C(3)); 4.14 (br. *dd*, $J = 6.5$, 7.6, H–C(4)); 4.57 (*dd*, $J = 4.2$, 4.8, H–C(2)); 5.28 (*dt*, $J = 10.6$, 1.3, 1 H–C(6)); 5.43 (*dt*, $J = 17.4$, 1.3, 1 H–C(6)); 5.83 (*d*, $J = 3.7$, H–C(1)); 5.87 (*ddd*, $J = 6.5$, 10.6, 17.2, H–C(5)). ^{13}C-NMR (75 MHz, $CDCl_3$): 26.5, 26.6 (2*q*, Me); 76.8, 78.6, 81.2 (3*d*, C(2), C(3), C(4)); 103.9 (*d*, C(1)); 112.8 (*s*, Me_2C); 118.9 (*t*, C(6)); 134.5 (*d*, C(5)). CI-MS (NH_4): 186 (1, M^+), 146 (37), 129 (79), 115 (36), 111 (26), 83 (14), 71 (19), 69 (64), 59 (100).

5,6-Dideoxy-D-ribo-*hex-5-enitol* (**4**). A mixture of **3** (21.3 g, 0.115 mol) and ion-exchange resin *IR 120* (H^+ form; 50 g) in THF/H_2O 1:1 (600 ml) was heated 3.5 h at 80°. The resin was filtered off and washed with THF/H_2O 1:1. The colorless filtrate was concentrated to 200 ml and treated with $NaBH_4$ (2.2 g, 0.06 mol). After 2 h at r.t., the soln. was acidified (pH paper) by addition of *IR 120* (H^+ form). The resin was filtered off and washed carefully with H_2O. The filtrate was evaporated and treated with 1% HCl in MeOH (2 × 150 ml), followed by evaporation. The residue was dissolved in H_2O (100 ml), and ion-exchange resins *IR 120* (H^+ form) and *A27* (OH^- form) were added in small portions until the pH of the soln. was neutral (pH paper). The resins were filtered off and washed with H_2O. The filtrate was evaporated and the residue dried *in vacuo*: crude **4** (15.8 g; *ca.* 95% pure by ^{1}H-NMR). White solid. TLC (CH_2Cl_2/MeOH 4:1): R_f 0.45. $[\alpha]_D^{25°} = +7$ ($c = 0.73$, MeOH). ^{1}H-NMR (300 MHz, CD_3OD): 3.53–3.64 (*m*, 3 H); 3.73–3.80 (*m*, 1 H); 4.24 (*m*, 1 H); 5.20 (*ddd*, $J = 1.3$, 2.0, 10.6, 1 H–C(6)); 5.32 (*ddd*, $J = 1.3$, 1.8, 17.1, 1 H–C(6)); 6.00 (*ddd*, $J = 6.5$, 10.6, 17.1, H–C(5)). ^{13}C-NMR (75 MHz, $CDCl_3$): 64.9 (*t*, C(1)); 74.1, 75.3, 75.9 (3*d*, C(2), C(3), C(4)); 117.3 (*t*, C(6)); 138.9 (*d*, C(5)). ES-MS (NH_4OAc): 166 (100, $[M + NH_4]^+$).

1,2,3-Tri-O-*benzoyl-5*-O-*(triisopropylsilyl)*-α/β-L-*ribose* (**5**(α/β)). A soln. of **4** (crude product; 15.7 g, *ca.* 0.1 mol) and 1*H*-imidazole (16 g, 0.23 mol) in DMF (200 ml) was cooled to 4° and treated with (chloro)triisopropylsilane (24.5 ml, 0.11 mol). After 1.5 h at 4° and 30 min at r.t., the mixture was poured on H_2O/hexane/Et_2O 5:4:8 (1700 ml). After stirring for 15 min, the org. layer was dried ($MgSO_4$) and evaporated. The residue was dissolved in MeOH (600 ml), cooled to –78°, and purged with O_3/O_2 until the soln. turned blue. Then it was treated with Me_2S (15 ml, 0.2 mol) and stored at 4° overnight. The soln. was evaporated and poured on H_2O/hexane/Et_2O 1:1:2 (800 ml). The org. phase was dried ($MgSO_4$), evaporated, and dried *in vacuo*. The residue was dissolved in pyridine CH_2Cl_2 1:2 (600 ml) and treated slowly with benzoyl chloride (50 ml, 0.43 mol). The suspension was stirred at r.t. overnight, then mannitol (20 g) was added at once. After stirring for 2 h at r.t., the mixture was diluted with H_2O (200 ml) and extracted (CH_2Cl_2/sat. aq. $NaHCO_3$ soln.). The org. phase was dried ($MgSO_4$) and evaporated, the pyridine removed by co-evaporation with toluene, and the residue dissolved in CH_2Cl_2 (400 ml) and adsorbed on silica gel (200 g). Chromatography (silica gel (400 g), hexane → hexane/AcOEt 6:4) afforded **5**(α/β) (57.2 g, 81%; α/β 1:2 by ^{1}H-NMR). Colorless, viscous liquid. TLC (hexane/AcOEt 9:1): R_f 0.45. IR ($CHCl_3$): 3065*w*, 3038*w*, 2945*m*, 2895*m*, 2870*m*, 1730*s*, 1600*w*, 1450*m*, 1315*m*, 1115*s*, 1095*s*, 1065*s*, 1025*m*, 950*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.00 (*m*, 7 H, Me_2CH); 1.15 (*m*, 14 H, Me_2CH); 4.00 (*d*, $J = 4.0$, 0.65 H, H–C(5)(α),H′–C(5)(α)); 4.00 (*dd*, $J = 2.6$, 10.9, 0.65 H, H–C(5)(β)); 4.14 (*dd*, $J = 2.2$, 10.9, 0.65 H, H′–C(5)(β)); 4.60 (*m*, 0.35 H, H–C(4)(α)); 4.64 (br. *q*, $J \approx 2$, 0.65 H, H–C(4)(β)); 5.70 (*dd*, $J = 4.3$, 6.2, 0.65 H, H–C(2)(β)); 5.92 (*dd*, $J = 1.6$, 6.2, 0.65 H, H–C(3)(β)); 5.95 (*m*, 0.65 H, H–C(2)(α), H–C(3)(α)); 6.65 (*d*, $J = 1.2$, 0.35 H, H–C(1)(α)); 6.91 (*d*, $J = 4.3$, 0.65 H, H–C(1)(β)); 7.14–7.64 (*m*, 9 arom. H); 7.84–8.19 (*m*, 6 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 11.9, 12.0 (2*d*, Me_2CH); 17.91, 17.96, 18.03, 18.06 (4*q*, Me); 63.5, 63.9 (2*t*, C(5)); 71.6, 72.0, 72.1, 75.4, 83.6, 86.4 (6*d*, C(2), C(3), C(4)); 95.6, 99.4 (2*d*, C(1)); 128.57, 128.67, 128.70 (3*d*, arom. C); 129.18, 129.28, 129.40, 129.52, 129.90 (5*s*, arom. C); 130.00, 130.07, 130.11, 130.19, 130.30, 133.55, 133.63, 133.75, 133.84 (9*d*, arom. C); 165.3, 165.4, 165.8, 166.3 (4*s*, CO). EI-MS: 497 (20, $[M - OBz]^+$), 235 (21), 201 (40), 105 (100).

1,2,3-Tri-O-*benzoyl*-α-L-*ribose* (α-**6**) *and 1,2,3-tri*-O-*benzoyl*-β-L-*ribose* (β-**6**). An emulsion of **5**(α/β) (8.15 g, 13 mmol) in THF/conc. aq. HCl soln. 9:1 (40 ml) was stirred at r.t. overnight. It was then diluted with H_2O/CH_2Cl_2 1:2 (750 ml) and extracted. The org. phase was washed with sat. aq. $NaHCO_3$ soln., dried ($MgSO_4$), and evaporated. The residue was subjected to chromatography (silica gel (200 g), hexane/AcOEt 7:3 → 2:3): 0.83 g of α-**6**, 0.65 g of β-**6**, and 4.15 g of α/β-**6** (93%) as colorless foams.

Data of α-**6**: TLC (hexane/AcOEt 1:1): R_f 0.70. $[\alpha]_D^{25°} = +30$ ($c = 0.51$, $CHCl_3$). IR ($CHCl_3$): 3600*w*, 3522*w* (br.), 2933*w*, 1728*s*, 1600*m*, 1444*m*, 1311*m*, 1261*s*, 1122*m*, 1095*m*, 1067*m*, 1022*m*, 944*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.2 (br. *s*, OH); 3.84 (*dd*, $J = 3.0$, 12.4, H–C(5)); 4.02 (*dd*, $J = 3.1$, 12.4, H′–C(5)); 4.60 (*m*, H–C(4)); 5.92 (*m*, H–C(2), H–C(3)); 6.67 (*s*, H–C(1)); 7.32–7.64 (*m*, 9 arom. H); 8.02–8.12 (*m*, 6 arom. H). ^{13}C-NMR

(75 MHz, $CDCl_3$): 62.3 (*t*, C(5')); 71.0, 75.6, 83.4, (3*d*, C(2), C(3), C(4)); 99.1 (*d*, C(1')); 128.7, 128.8, 128.9 (3*d*, arom. C); 129.2 (*s*, arom. C); 130.0, 130.1, 130.3, 133.8, 133.9, 134.0 (6*d*, arom. C); 165.1, 165.4, 166.0 (3*s*, CO). FAB-MS (NOBA, pos. mode): 341 (100, $[M - OBz]^+$), 105 (45).

Data of β-**6**: TLC (hexane/AcOEt 1:1): R_f 0.60. $[\alpha]_D^{25°} = -65$ ($c = 0.671$, $CHCl_3$). IR ($CHCl_3$): 3600*w*, 3520*w* (br.), 2944*w*, 1728*s*, 1600*m*, 1450*m*, 1317*m*, 1283*s*, 1255*s*, 1139*m*, 1094*m*, 1061*m*, 1022*m*, 878*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.29 (*t*, $J = 6.2$, OH); 4.02 (br. *dd*, $J \approx 3.1$, 6.2, 2 H–C(5')); 4.65 (*q*, $J = 2.7$, H–C(4')); 5.63 (*dd*, $J = 4.3$, 6.9, H–C(2')); 5.83 (*dd*, $J = 2.1$, 6.9, H–C(3')); 6.93 (*d*, $J = 4.3$, H–C(1')); 7.16–7.63 (*m*, 9 arom. H); 7.85–8.09 (*m*, 6 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 62.5 (*t*, C(5')); 71.2, 71.9, 85.8, (3*d*, C(2), C(3), C(4)); 95.2 (*d*, C(1')); 128.6, 128.7, 128.9 (2*d*, arom. C); 129.7 (*s*, arom. C); 130.0, 130.1, 130.2, 133.7, 133.8 (5*d*, arom. C); 165.4, 165.6, 166.2 (3*s*, CO). FAB-MS (NOBA, pos. mode): 341 (100, $[M - OBz]^+$), 105 (70).

*1,2,3-Tri-*O*-benzoyl-5-*O*-(triisopropylsilyl)-*α*-*L*-ribose* (α-**5**). A soln. of α-**6** (0.46 g, 1 mmol) and 1*H*-imidazole (0.16 g, 2.3 mol) in CH_2Cl_2 (3 ml) was treated with (chloro)triisopropylsilane (0.25 ml, 1.1 mmol) and stirred for 1.5 h at r.t. Usual workup (sat. aq. $NaHCO_3$ soln./CH_2Cl_2) and chromatography (silica gel (10 g), hexane → hexane/AcOEt 6:4) afforded α-**5** (0.55 g, 89%). Colorless, viscous liquid. TLC (hexane/AcOEt 9:1): R_f 0.45. $[\alpha]_D^{25°} = +22$ ($c = 1.00$, $CHCl_3$). IR ($CHCl_3$): 2944*m*, 2866*m*, 1728*s*, 1600*m*, 1450*m*, 1317*m*, 1261*s*, 1117*m*, 1022*m*, 950*m*, 877*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.00 (*m*, 21 H, Me_2CH); 4.00 (*d*, $J = 4.0$, 2 H–C(5')); 4.60 (*m*, H–C(4')); 5.95 (*m*, H–C(2), H–C(3')); 6.65 (*d*, $J = 1.2$, H–C(1')); 7.26–7.64 (*m*, 9 arom. H); 7.93–8.11 (*m*, 6 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 11.9 (*d*, Me_2CH); 17.91 (*q*, Me); 63.9 (*t*, C(5')); 72.0, 75.4, 83.6 (3*d*, C(2), C(3), C(4)); 99.4 (*d*, C(1')); 128.65, 128.70 (2*d*, arom. C); 129.28, 129.41, 129.54 (3*s*, arom. C); 29.98, 130.11, 130.30, 133.62, 133.75, 133.83 (6*d*, arom. C); 165.4, 165.8 (2*s*, CO).

*1,2,3-Tri-*O*-benzoyl-5-*O*-(triisopropylsilyl)-*α*-*L*-ribose* (β-**5**). As described for α-**5**, from β-**6** (0.46 g, 1 mmol): β-**5** (0.52 g, 84%). Colorless, viscous liquid. TLC (hexane/AcOEt 9:1): R_f 0.45. $[\alpha]_D^{25°} = -53$ ($c = 1.02$, $CHCl_3$). IR ($CHCl_3$): 2933*m*, 2867*m*, 1728*s*, 1600*m*, 1444*m*, 1317*m*, 1283*s*, 1255*s*, 1117*m*, 1061*m*, 1017*m*, 883*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.15 (*m*, 14 H, Me_2CH); 4.00 (*dd*, $J = 2.6$, 10.9, H–C(5')); 4.14 (*dd*, $J = 2.2$, 10.9, H'–C(5')); 4.64 (br. *q*, $J \approx 2$, H–C(4')); 5.70 (*dd*, $J = 4.3$, 6.2, H–C(2')); 5.92 (*dd*, $J = 1.6$, 6.2, H–C(3')); 6.91 (*d*, $J = 4.3$, H–C(1')); 7.23–7.61 (*m*, 9 arom. H); 7.84–8.10 (*m*, 6 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 11.9 (*d*, Me_2CH); 18.03 (*q*, Me); 63.5 (*t*, C(5')); 71.6, 72.1, 86.4 (3*d*, C(2), C(3), C(4)); 95.6 (*d*, C(1')); 128.57, 128.67 (2*d*, arom. C); 129.2 (*s*, arom. C); 130.00, 130.07, 130.19, 133.54, 133.63 (5*d*, arom. C); 165.8, 166.2 (2*s*, CO).

*1-(2',3'-Di-*O*-benzoyl-β-L-ribofuranosyl)uracil* (**7**). A suspension of **5**(α/β) (7.15 g, 11.5 mmol) and uracil (1.4 g, 13 mmol) in MeCN (35 ml) was heated to 60° and treated with BSA (6.5 ml, 26 mmol). After stirring for 30 min at 60°, $SnCl_4$ (4.0 ml, 34 mmol) was added to the clear soln. After 30 min, the mixture was poured into a mixture of $NaHCO_3$ (20 g) and sat. aq. $NaHCO_3$ soln./AcOEt 1:1 (700 ml). The residue obtained after usual workup (sat. aq. $NaHCO_3$/AcOEt) was dissolved in THF/conc. aq. HCl soln. 4:1 (200 ml) and stirred for 1 h at r.t. The clear soln. was diluted with CH_2Cl_2/H_2O 2:1 (600 ml). Usual workup (sat. aq. $NaHCO_3$ soln./CH_2Cl_2) and CC (silica gel (80 g), CH_2Cl_2 → CH_2Cl_2/MeOH 19:1) afforded **7** (4.9 g, 94%). Colorless foam. TLC (hexane/AcOEt 3:7): R_f 0.40. $[\alpha]_D^{25°} = +107$ ($c = 1.16$, MeOH). UV (MeOH): 258 (12400), 251 (12000), 229 (28000), 212 (16800). ^{1}H-NMR (300 MHz, (D_6)DMSO): 3.75 (br. *s*, 2 H–C(5')); 4.43 (*d*, $J \approx 2.5$, H–C(4')); 5.49 (br. *s*, OH–C(5')); 5.71 (*m*, H–C(2'), H–C(3')); 5.75 (*d*, $J = 8.1$, H–C(5)); 6.26 (*d*, $J = 5.3$, H–C(1')); 7.35–8.02 (*m*, 10 arom. H, H–C(6)); 11.40 (br. *s*, H–N(3)). ^{13}C-NMR (75 MHz, (D_6)DMSO): 60.9 (*t*, C(5')); 72.1, 73.5, 83.3 (3*d*, C(2'), C(3'), C(4')); 86.2 (*d*, C(1')); 102.7 (*d*, C(5)); 128.5, 128.9 (2*d*, arom. C); 129.0 (*s*, arom. C); 129.1, 129.4, 129.5, 134.0, 134.1 (5*d*, arom. C); 140.7 (*d*, C(6)); 150.8 (*s*, C(2)); 163.2 (*s*, C(4)); 164.7, 165.0 (2*s*, CO). FAB-MS (NOBA, pos. mode): 453 (87, $[M + H]^+$), 341 (100), 136 (55), 105 (35).

*1-(2',3'-Di-*O*-benzoyl-β-L-ribofuranosyl)thymine* (**8**). As described for **7**, with **5**(α/β) (7.15 g, 11.5 mmol), thymine (1.64 g, 13 mmol), MeCN (35 ml), BSA (6.5 ml, 26 mmol; 30 min at 60°), $SnCl_4$ (4.0 ml, 34 mmol), $NaHCO_3$ (20 g), sat. aq. $NaHCO_3$ soln./AcOEt 1:1 (700 ml), usual workup (sat. aq. $NaHCO_3$ soln./AcOEt), THF/conc. aq. HCl soln. 4:1 (200 ml; 1 h at r.t.), CH_2Cl_2/H_2O 2:1 (600 ml), usual workup (sat. aq. $NaHCO_3$ soln./CH_2Cl_2), and CC (silica gel (70 g), CH_2Cl_2 → CH_2Cl_2/MeOH 19:1): **8** (4.84 g, 90%). Colorless foam. TLC (hexane/AcOEt 1:1): R_f 0.40. $[\alpha]_D^{25°} = +133$ ($c = 0.98$, acetone). UV (MeOH): 264 (12300), 251 (10800), 228 (27700), 212 (20000). ^{1}H-NMR (300 MHz, $CDCl_3/CD_3OD$ 1:1): 1.92 (*d*, $J = 1.2$, Me); 3.92 (*dd*, $J = 2.6$, 10.5, H–C(5')); 3.97 (*dd*, $J = 2.5$, 10.5, H'–C(5')); 4.44 (br. *q*, $J \approx 2.5$, H–C(4')); 5.75 (*t*, $J = 5.6$, H–C(2')); 5.82 (*dd*, $J = 2.8$, 5.6, H–C(3')); 6.42(*d*, $J = 6.4$, H–C(C1')); 7.30–7.99 (*m*, 10 arom. H, H–C(6)). ^{13}C-NMR (75 MHz, $CDCl_3/CD_3OD$ 1:1): 13.0 (*q*, Me); 62.8 (*t*, C(5')); 73.8, 75.5, 85.4 (3*d*, C(2'), C(3'), C(4')); 88.2 (*d*, C(1')); 113.0 (*s*, C(5)); 130.0, 130.1 (2*d*, arom. C); 130.2, 130.3 (2*s*, arom. C); 131.1, 131.2, 135.2 (3*d*, arom. C); 138.2 (*d*, C(6)); 153.0 (*s*, C(2)); 166.6 (*s*, C(4)); 167.1, 167.4 (2*s*, CO). FAB-MS (NOBA, pos. mode): 467 (80, M^+), 341 (100).

N^4*-Benzoyl-1-(2',3'-di-*O*-benzoyl-β-L-ribofuranosyl)cytosine* (**9**). As described for **7**, with **5**(α/β) (6.8 g, 11.0 mmol), N^4-benzoylcytosine (2.8 g, 13.2 mmol), MeCN (50 ml), BSA (7 ml, 28.4 mmol; 1 h at 60°), $SnCl_4$

(2.6 ml, 22 mmol), $NaHCO_3$ (20 g), sat. aq. $NaHCO_3$ soln./AcOEt 1:1 (700 ml), usual workup (sat. aq. $NaHCO_3$ soln./AcOEt), THF/conc. aq. HCl soln. 9:1 (200 ml; 2 h at r.t.), CH_2Cl_2/H_2O 2:1 (600 ml), usual workup (sat. aq. $NaHCO_3$ soln./CH_2Cl_2), and CC (silica gel (80 g), hexane/AcOEt 1:1 → 1:5): **9** (5.4 g, 94%). Colorless powder. TLC (hexane/AcOEt 1:4): R_f 0.55. $[\alpha]_D^{25°} = +119$ ($c = 1.40$, $CHCl_3$). UV (MeOH): 303 (10000), 291 (9100), 261 (28300), 247 (22600), 229 (34800), 213 (25200). IR ($CHCl_3$): 3699*w*, 3622*w*, 3400*w* (br.), 3000*w*, 1728*s*, 1667*s*, 1622*m*, 1550*m*, 1478*s*, 1317*s*, 1267*s*, 1106*s*, 1067*m*, 1028*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.00 (br. *dd*, $J \approx 2$, 11, H–C(5')); 4.07 (br. *dd*, $J \approx 2$, 11, H'–C(5')); 4.10 (br. *s*, OH–C(5')); 4.52 (br. *q*, $J \approx 2$, H–C(4')); 5.98 (*m*, H–C(2'), H–C(3')); 6.47 (*d*, $J = 5.4$, H–C(1')); 7.28–7.93 (*m*, 15 arom. H, H–C(5)); 8.46 (*d*, $J = 7.5$, H–C(6)); 9.08 (br. *s*, NH–C(4)). ^{13}C-NMR (75 MHz, $CDCl_3$): 61.7 (*t*, C(5')); 72.0, 75.2, 84.5 (3*d*, C(2'), C(3'), C(4')); 94.1 (*d*, C(1')); 98.0 (br. *d*, C(5)); 128.0, 128.7, 128.8 (3*d*, arom. C); 129.0, 129.1 (2*s*, arom. C); 129.1, 130.1, 130.2, 133.4, 133.8, 133.9 (6*d*, arom. C); 136.3 (*d*, C(6)); 155.8 (br. *s*, C(2)); 163.2, 165.6, 166.1 (3*s*, CO); 167.1 (*s*, C(4)). FAB-MS (NOBA, pos. mode): 556 (64, $[M + H]^+$), 341 (100), 154 (22), 105 (86).

N^6-*Benzoyl-9-(2',3'-di-*O*-benzoyl-β-*L*-ribofuranosyl)adenine* (**10**). A suspension of 3.5 g **6**(α/β) (7.6 mmol) and 2.2 g N^6-benzoyladenine (9.1 mmol) in MeCN (30 ml) was heated to 60° and treated with BSA (7 ml, 28.4 mmol). After stirring for 1 h at 60°, $SnCl_4$ (3.8 ml, 32 mmol) was added to the clear soln. One hour later, the mixture was poured into a mixture of $NaHCO_3$ (15 g) and sat. aq. $NaHCO_3$ soln./AcOEt 1:1 (500 ml). Usual workup (sat. aq. $NaHCO_3$ soln./AcOEt) and CC (silica gel (70 g), CH_2Cl_2 → CH_2Cl_2/MeOH 19:1) afforded **10** (4.0 g, 91%). White powder. TLC (hexane/AcOEt 1:4): R_f 0.30. $[\alpha]_D^{25°} = +227$ ($c = 1.30$, $CHCl_3$). UV (MeOH): 280 (20800), 255 (12000), 229 (36400), 215 (26400). IR ($CHCl_3$): 3689*w*, 3403*w*, 3289*w* (br.), 3000*w*, 1730*s*, 1612*s*, 1590*m*, 1481*m*, 1457*s*, 1273*s*, 1123*m*, 1094*s*, 1070*m*, 1026*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.03 (br. *td*, $J \approx 13$, 2, H–C(5')); 4.10 (br. *dt*, $J \approx 14$, 2, H'–C(5')); 4.62 (br. *q*, $J \approx 5.5$, H–C(4')); 5.98 (br. *dd*, $J \approx 14$, 3, OH–C(5')); 6.07 (*dd*, $J = 1.6$, 4.7, H–C(3')); 6.39 (*m*, H–C(1'), H–C(2')); 7.26–7.38 (*m*, 9 arom. H); 7.41–8.08 (*m*, 6 arom. H); 8.18 (*s*, H–C(2)); 8.84 (*s*, H–C(8)); 9.23 (br. *s*, NH–C(6)). ^{13}C-NMR (75 MHz, $CDCl_3$): 62.7 (*t*, C(5')); 73.5, 73.7, 86.6 (3*d*, C(2'), C(3'), C(4')); 89.9 (*d*, C(1')); 124.7 (*s*, C(5)); 128.2 (*d*, arom. C); 128.6 (*s*, arom. C); 128.7, 128.9, 129.1, (3*d*, arom. C); 129.4 (*s*, arom. C); 130.0 (*d*, arom. C); 133.2, 133.7 (2*s*, arom. C); 134.0 (*d*, arom. H); 142.7 (*d*, C(8)); 150.7 (*s*, C(4)); 151.3 (*s*, C(6)); 152.8 (*d*, C(2)); 164.9, 165.1, 165.7 (3*s*, CO). FAB-MS (NOBA, pos. mode): 580 (100, $[M + H]^+$), 413 (26), 341 (23), 307 (28), 154 (62), 137 (52), 105 (98).

*9-[2',3'-Di-*O*-benzoyl-5'-*O*-(triisopropylsilyl)-β-*L*-ribofuranosyl]-*N^3*-isobutyrylguanine* (N^9-**11**) *and 7-(2',3'-Di-*O*-benzoyl-5'-*O*-(triisopropylsilyl)-β-*L*-ribofuranosyl)-*N^3*-isobutyrylguanine* (N^7-**11**). A suspension of **5**(α/β) (9.1 g, 14.6 mmol) and N^3-isobutyrylguanine monohydrate (5.2 g, 22 mmol) in $(CH_2Cl)_2$ (45 ml) was heated to 80° and treated with BSA (18.6 ml, 76 mmol). After stirring for 1 h at 80°, trimethylsilyl triflate (16 ml, 88 mmol) was added to the clear soln. After 2.5 h, the mixture was poured into a mixture of $NaHCO_3$ (20 g) and sat. aq. $NaHCO_3$ soln./CH_2Cl_2 1:1 (700 ml). Usual workup (sat. aq. $NaHCO_3$ soln./CH_2Cl_2) and CC (silica gel (300 g), hexane/AcOEt 1:1 → 1:5) afforded N^7-**11** (3.8 g, 36%) as white powder and N^9-**11** (6.1 g, 58%) as colorless foam.

Data of N^7-**11**: TLC (hexane/AcOEt/MeOH 6:24:1): R_f 0.60. $[\alpha]_D^{25°} = -14$ ($c = 1.00$, $CHCl_3$). IR ($CHCl_3$): 3412*w*, 3167*m*, 2945*m*, 2868*m*, 1730*s*, 1689*m*, 1610*s*, 1600*w*, 1551*m*, 1452*m*, 1395*m*, 1370*m*, 1320*m*, 1273*s*, 1125*s*, 1106*s*, 1070*m*, 883*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.12–1.30 (*m*, 27 H, Me_2CHCO, Me_2CHSi); 3.04 (*sept.*, $J = 6.8$, Me_2CHCO); 4.12 (*dd*, $J = 2.5$, 11.5, H–C(5')); 4.18 (*dd*, $J = 2.2$, 11.5, H'–C(5)); 4.55 (*q*, $J = 2.2$, H–C(4')); 5.87 (*t*, $J = 5.9$, H–C(2')); 5.95 (*dd*, $J = 3.1$, 5.5, H–C(3')); 6.95 (*d*, $J = 5.9$, H–C(1')); 7.34–7.41 (*m*, 4 arom. H); 7.50–7.58 (*m*, 2 arom. H); 7.95–8.00 (*m*, 4 arom. H); 8.45 (*s*, H–C(8)); 10.47 (br. *s*, NH–C(6)); 12.40 (br. *s*, H–N(1)). ^{13}C-NMR (75 MHz, $CDCl_3$): 12.0 (*d*, Me_2CHSi); 18.1 (*q*, Me_2CHSi); 19.0, 19.2 (2*q*, Me_2CHCO); 36.0 (*d*, Me_2CHCO); 63.3 (*t*, C(5')); 71.8, 76.4, 84.7 (3*d*, C(2'), C(3'), C(4')); 87.9 (*d*, C(1')); 112.1 (*s*, C(5)); 128.7, 128.8 (2*d*, arom. C); 128.9, 129.2 (2*s*, arom. C); 130.0, 130.2, 133.8 (3*d*, arom. C); 141.5 (*d*, C(8)); 148.4 (*s*, C(4)); 153.1 (*s*, C(2)); 157.4 (*s*, C(6)); 165.3, 165.9, 180.5 (3*s*, CO). FAB-MS (NOBA, pos. mode): 718 (14, $[M + H]^+$), 674 (32), 497 (88), 222 (16), 145 (25), 105 (100).

Data of N^9-**11**: TLC (hexane/AcOEt/MeOH 6:24:1): R_f 0.48. $[\alpha]_D^{25°} = +36$ ($c = 0.92$, $CHCl_3$). IR ($CHCl_3$): 3415*w*, 3221*w*, 3065*m*, 3007*m*, 2946*m*, 2868*m*, 1727*s*, 1698*s*, 1605*s*, 1561*m*, 1470*m*, 1452*m*, 1373*m*, 1316*m*, 1273*s*, 1095*s*, 1070*m*, 883*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.99–1.23 (*m*, 21 H, Me_2CHSi); 1.26 (2*d*, $J = 6.8$, Me_2CHCO); 2.63 (*sept.*, $J = 6.8$, Me_2CHCO); 4.01 (*dd*, $J = 2.8$, 11.5, H–C(5')); 4.07 (*dd*, $J = 2.5$, 11.5, H'–C(5')); 4.53 (*m*, H–C(4')); 6.22 (*m*, H–C(1'), H–C(2'), H–C(3')); 7.36–7.42 (*m*, 4 arom. H); 7.52–7.60 (*m*, 2 arom. H); 7.92–7.96 (*m*, 4 arom. H); 8.00 (*s*, H–C(8)); 8.78 (br. *s*, NH–C(6)); 12.05 (br. *s*, H–N(1)): ^{13}C-NMR (75 MHz, $CDCl_3$): 11.9 (*d*, Me_2CHSi); 17.9 (*q*, Me_2CHSi); 18.9, 19.0 (2*q*, Me_2CHCO); 36.6 (*d*, Me_2CHCO); 62.6 (*t*, C(5')); 71.5, 74.6, 76.8 (3*d*, C(2'), C(3'), C(4')); 86.4 (*d*, C(1')); 121.9 (*s*, C(5)); 128.8 (*d*, arom. C); 129.0, 129.3 (2*s*, arom. C); 129.9, 130.1, 133.9, 134.0 (4*d*, arom. C); 137.8 (*d*, C(8)); 147.7 (*s*, C(4)); 148.2 (*s*, C(2)); 155.9 (*s*, C(6)); 165.2, 166.0, 178.5 (3*s*, CO). Pos. FAB-MS (NOBA, pos. mode): 718 (13, $[M + H]^+$), 497 (100), 222 (16), 145 (30), 105 (80).

N^9-**11** *by Equilibration of* N^7-**11**. A suspension of N^9-**11** (3.0 g, 4.2 mmol) and N^3-isobutyrylguanine monohydrate (0.5 g, 2.1 mmol) in $(CH_2Cl)_2$ (15 ml) was heated to 80° and treated with BSA (5.5 ml, 22 mmol). After stirring for 1 h at 80°, trimethylsilyl triflate (4.6 ml, 25 mmol) was added to the clear soln. After 1.5 h, the mixture was poured into a mixture of $NaHCO_3$ (5 g) and sat. aq. $NaHCO_3$ soln./CH_2Cl_2 1:1 (300 ml). Usual workup (sat. aq. $NaHCO_3$ soln./CH_2Cl_2) and CC (silica gel (100 g), hexane/AcOEt 1:1 → 5:1) afforded N^7-**11** (0.8 g, 26%) as white powder and N^9-**11** (1.5 g, 50%) as colorless foam.

9-(2',3'-Di-O-benzyol-N^3*-isobutyryl-β-*L*-ribofuranosyl)guanine* (**12**). A suspension of N^9-**11** (6.9 g, 9.5 mmol) in THF/conc. aq. HCl soln. 9:1 (80 ml) was stirred for 1 h at r.t. The clear soln. was diluted with CH_2Cl_2/H_2O 2:1 (600 ml). Usual workup (sat. aq. $NaHCO_3$ soln./CH_2Cl_2) and CC (silica gel (80 g), CH_2Cl_2 → CH_2Cl_2/MeOH 9:1) afforded **12** (4.9 g, 92%). Colorless foam. TLC (CH_2Cl_2/MeOH 19:1): R_f 0.40. $[\alpha]_D^{25°} = +163$ ($c = 1.16$, $CHCl_3$). UV (MeOH): 275 (13100), 272 (12500), 254 (17500), 249 (16900), 229 (30000), 216 (20600). IR ($CHCl_3$): 3411*w*, 3222*w* (br.), 3000*w*, 1724*s*, 1704*s*, 1605*s*, 1565*m*, 1411*m*, 1316*m*, 1274*s*, 1124*s*, 1095*s*, 1025*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.26 (*2d*, $J = 6.8$, Me_2CHCO); 2.78 (*sept.*, $J = 6.8$, Me_2CHCO); 3.93 (br. *dt*, $J \approx 1, 10$, H–C(5')); 4.07 (br. *td*, $J \approx 1, 10$, H'–C(5')); 4.50 (br. *q*, $J \approx 2$, H–C(4')); 5.04 (br. *dd*, $J \approx 2, 10$, OH–C(5')); 6.03 (*dd*, $J = 2.8, 5.8$, H–C(3')); 6.20 (*d*, $J = 6.5$, H–C(1')); 6.32 (*t*, $J = 6.1$, H–C(2')); 7.28–7.38 (*m*, 4 arom. H); 7.40–7.58 (*m*, 2 arom. H); 7.83–7.94 (*m*, 4 arom. H); 7.96 (*s*, H–C(8)); 9.51 (br. *s*, NH–C(6)); 12.26 (br. *s*, H–N(1)). ^{13}C-NMR (75 MHz, $CDCl_3$): 19.0 (*q*, Me_2CHCO); 36.4 (*d*, Me_2CHCO); 62.1 (*t*, C(5')); 72.3, 73.3, 84.8 (3*d*, C(2'), C(3'), C(4')); 88.1 (*d*, C(1')); 122.8 (*s*, C(5)); 128.6, 128.7, 128.8 (3*d*, arom. C); 129.1 (*s*, arom. C); 130.0, 133.9, 134.0 (3*d*, arom. C); 139.4 (*d*, C(8)); 147.8 (*s*, C(4)); 148.4 (*s*, C(2)); 155.6 (*s*, C(6)); 165.3, 165.8, 179.6 (3*s*, CO). FAB-MS (NOBA, pos. mode): 562 (32, $[M + H]^+$), 497 (35), 341 (66), 222 (18), 105 (100).

*1-[5'-O-(4,4'-Dimethoxytrityl)-β-*L*-ribofuranosyl]uracil* (**13**)[17]. A soln. of **7** (3.87 g, 8.56 mmol) and $(i\text{-}Pr)_2NEt$ (2.2 ml, 13 mmol) in CH_2Cl_2 (25 ml) was treated with dimethoxytrityl chloride (3.5 g, 10.3 mmol). The soln. was stirred for 30 min at r.t. and poured into a stirred, ice-cold soln. of THF/MeOH/H_2O 5:4:1 (400 ml). After addition of 10N aq. NaOH (8 ml), the soln. was stirred at 4° for 25 min, treated with AcOH (4.8 ml), and concentrated to 50 ml. Usual workup (CH_2Cl_2/sat. aq. $NaHCO_3$ soln.) and CC (silica gel (80 g), CH_2Cl_2 (+ 2% Et_3N) → CH_2Cl_2/MeOH 9:1 (+ 2% Et_3N)) afforded **13** (4.4 g, 95%). Yellow foam. TLC (CH_2Cl_2/MeOH 19:1): R_f 0.30. $[\alpha]_D^{25°} = -3$ ($c = 0.73$, $CHCl_3$). UV (MeOH): 264 (11600), 256 (11000), 234 (24500), 225 (22500). IR ($CHCl_3$): 3389*m* (br.), 3233*w* (br.), 2978*w*, 1689*s*, 1606*m*, 1506*s*, 1461*m*, 1400*w*, 1106*m*, 1033*m*, 906*m*, 828*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 3.49 (*dd*, $J = 2.8, 11.5$, H–C(5')); 3.53 (*dd*, $J = 1.9, 11.2$, H'–C(5')); 3.77 (*s*, 2MeO); 4.16 (*m*, H–C(4')); 4.34 (*dd*, $J = 2.5, 5.0$, H–C(2')); 4.44 (br. *t*, $J \approx 6$, H–C(3')); 5.35 (*d*, $J = 8.1$, H–C(5)); 5.91 (*d*, $J = 2.5$, H–C(1')); 6.84 (*d*, $J = 8.7$, 4 arom. H); 7.19–7.40 (*m*, 9 arom. H); 8.03 (*d*, $J = 8.4$, H–C(6)). ^{13}C-NMR (75 MHz, $CDCl_3$): 55.3 (*q*, MeO); 61.9 (*t*, C(5')); 69.9, 75.6, 83.8 (3*d*, C(2'), C(3'), C(4')); 87.2 (*s*, Ar_2CPh); 90.7 (*d*, C(1')); 102.4 (*d*, C(5)); 113.5 (*d*, arom. C); 127.4, 128.3, 128.4, 130.3, 130.4 (5*d*, arom. C); 135.6, 135.8 (2*s*, arom. C); 140.8 (*d*, C(6)); 144.7 (*s*, arom. C); 151.5 (*s*, C(2)); 158.9, 159.0 (2*s*, MeO–*C*); 164.3 (*s*, C(4)). FAB-MS (NOBA, pos. mode): 546 (67, M^+), 303 (100).

*1-[5'-O-(4,4'-Dimethoxytrityl)-β-*L*-ribofuranosyl]thymine* (**14**). As described for **13**, with **8** (4.72 g, 10.4 mmol), $(i\text{-}Pr)_2NEt$ (3.6 ml, 20.8 mmol), CH_2Cl_2 (25 ml), dimethoxytrityl chloride (4.2 g, 12.5 mmol), THF/MeOH/H_2O 5:4:1 (400 ml), 10N aq. NaOH (8 ml), and AcOH (4.8 ml). **14** (5.2 g, 95%). Yellow foam. TLC (CH_2Cl_2/MeOH 19:1): R_f 0.45. $[\alpha]_D^{25°} = +3$ ($c = 0.67$, $CHCl_3$). UV (MeOH): 279 (sh, 7600), 269 (9500), 255 (8200), 232 (20400), 227 (20100). IR ($CHCl_3$): 3340*m* (br.), 3180*w* (br.), 2972*w*, 1689*s*, 1608*m*, 1509*s*, 1465*m*, 1367*w*, 1107*m*, 1036*m*, 906*m*, 830*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.42 (*d*, $J = 0.9$, Me); 3.38 (*dd*, $J = 2.8, 10.9$, H–C(5')); 3.48 (*dd*, $J = 2.2, 10.9$, H'–C(5')); 3.78 (*s*, 2 MeO); 4.19 (*m*, H–C(4')); 4.38 (*m*, H–C(2'), H–C(3')); 5.94 (*d*, $J = 3.1$, H–C(1')); 6.82 (*d*, $J = 8.7$, 4 arom. H); 7.19–7.41 (*m*, 9 arom. H); 7.69 (*d*, $J = 0.9$, H–C(6)). ^{13}C-NMR (75 MHz, $CDCl_3$): 11.9 (*q*, Me); 55.4 (*q*, MeO); 62.8 (*t*, C(5')); 70.6, 75.5, 84.4 (3*d*, C(2'), C(3'), C(4')); 87.0 (*s*, Ar_2CPh); 90.2 (*d*, C(1')); 111.2 (*s*, C(5)); 113.5 (*d*, arom. C); 127.3, 128.3, 128.4, 130.3 (4*d*, arom. C); 135.6, 135.7, 136.0 (3*s*, arom. C); 144.6 (*d*, C(6)); 151.5 (*s*, C(2)); 159.0 (*s*, MeO–*C*); 164.3 (*s*, C(4)). FAB-MS (NOBA, pos. mode): 561 (50, $[M + H]^+$), 303 (100).

N^4*-Benzoyl-1-[5'-O-(4,4'-dimethoxytrityl)-β-*L*-ribofuranosyl]cytosine* (**15**)[17]. As described for **13**, with **9** (5.17 g, 9.6 mmol), $(i\text{-}Pr)_2NEt$ (2.5 ml, 14.5 mmol), CH_2Cl_2 (25 ml), dimethoxytrityl chloride (3.9 g, 11.5 mmol), THF/MeOH/H_2O 5:4:1 (400 ml), 10N aq. NaOH (8 ml), and AcOH (4.8 ml): **15** (5.6 g, 91%). Yellow foam. TLC (CH_2Cl_2/MeOH 19:1): R_f 0.35. $[\alpha]_D^{25°} = -49$ ($c = 1.27$, $CHCl_3$). UV (MeOH): 305 (7700), 294 (7000), 279 (sh, 10900), 260 (17200), 254 (19800), 233 (33000), 222 (30500). IR ($CHCl_3$): 3700*w*, 3627*w*, 3403*w* (br.), 3000*w*, 1728*s*,

[17]) A synthesis of the (natural) D-configurated enantiomer is reported in [18].

1667*s*, 1628*m*, 1600*m*, 1550*m*, 1478*s*, 1317*m*, 1267*s*, 1106*s*, 1067*m*, 1022*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 3.42 (*dd*, *J* = 3.1, 10.9, H–C(5')); 3.48 (*dd*, *J* = 2.5, 10.9, H'–C(5')); 3.68 (br. *s*, OH); 3.76, 3.78 (2*s*, 2 MeO); 4.39–4.47 (*m*, H–C(2'), H–C(3'), H–C(4')); 5.89 (br. *s*, OH); 5.91 (*d*, *J* = 2.5, H–C(1')); 6.82–6.87 (*m*, 4 arom. H); 7.20–7.62 (*m*, 12 arom. H, H–C(5)); 7.87–7.90 (*m*, 2 arom. H); 8.32 (*d*, *J* = 7.5, H–C(6)); 8.93 (br. *s*, NH–C(4)). ^{13}C-NMR (75 MHz, $CDCl_3$): 55.3 (*q*, MeO); 62.7 (*t*, C(5')); 71.4, 76.9, 85.7 (3*d*, C(2'), C(3'), C(4')); 87.2 (*s*, Ar_2CPh); 93.5 (*d*, C(1')); 97.0 (*d*, C(5)); 113.5 (*d*, arom. C); 127.4, 127.9, 128.3, 128.4, 129.3, 130.4 (6*d*, arom. C); 135.4 (*d*, arom. C); 135.8, 144.3 (2*s*, arom. C); 145.1 (*d*, C(6)); 156.8 (*s*, C(2)); 158.9 (*s*, MeO–*C*); 159.0 (*s*, arom. C); 162.9 (*s*, CO); 166.5 (*s*, C(4)). FAB-MS (NOBA, pos. mode): 650 (41, $[M + H]^+$), 303 (100).

*N^6-Benzoyl-1-[5'-O-(4,4'-dimethoxytrityl)-β-*L*-ribofuranosyl]adenine* (**16**)[17]. As described for **13**, with **10** (4.7 g, 8.1 mmol) $(i\text{-}Pr)_2NEt$ (2.1 ml, 12.2 mmol), CH_2Cl_2 (30 ml), dimethoxytrityl chloride (3.3 g, 9.7 mmol), THF/MeOH/H_2O 5:4:1 (400 ml), 10N aq. NaOH (8 ml), and AcOH (4.8 ml): **16** (5.0 g, 93%). Yellow foam. TLC (CH_2Cl_2/MeOH 19:1): R_f 0.30. $[\alpha]_D^{25°} = +9$ (*c* = 1.23, $CHCl_3$). UV (MeOH): 280 (17800), 257 (11000), 233 (27600), 222 (25400). IR ($CHCl_3$): 3544*w*, 3400*w* (br.), 2933*w*, 2833*w*, 1705*m*, 1606*s*, 1588*m*, 1506*s*, 1456*s*, 1294*m*, 1083*m*, 1028*m*, 905*w*, 828*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 3.31 (*dd*, *J* = 3.7, 10.6, H–C(5')); 3.44 (*dd*, *J* = 3.1, 10.6, H'–C(5')); 3.73 (*s*, 2 MeO); 4.38 (br. *q*, *J* ≈ 2.5, H–C(4')); 4.49 (*dd*, *J* = 2.5, 5.0, H–C(3')); 4.93 (*t*, *J* = 5.3, H–C(2')); 6.09 (*d*, *J* = 5.9, H–C(1')); 6.74 (*d*, *J* = 9.0, 4 arom. H); 7.14–7.60 (*m*, 12 arom. H); 7.97–8.00 (*m*, 2 arom. H); 8.23 (*s*, H–C(2)); 8.62 (*s*, H–C(8)); 9.25 (br. *s*, NH–C(6)). ^{13}C-NMR (75 MHz, $CDCl_3$): 55.3 (*q*, MeO); 63.7 (*t*, C(5')); 72.5, 75.6, 85.8 (3*d*, C(2'), C(3'), C(4')); 86.8 (*s*, Ar_2CPh); 90.2 (*d*, C(1')); 113.4 (*d*, arom. C); 123.1 (*s*, C(5)); 127.1, 128.1, 128.2, 129.1, 130.2 (5*d*, arom. C); 133.2 (*d*, arom. C); 133.7, 135.7, 135.8 (3*s*, arom. C); 142.0 (*d*, C(8)); 144.7 (*s*, arom. C); 149.7 (*s*, C(4)); 151.3 (*s*, C(6)); 152.5 (*d*, C(2)); 158.8 (*s*, MeO–*C*); 165.1 (*s*, CO). FAB-MS (NOBA, pos. mode): 674 (67, $[M + H]^+$), 303 (100), 240 (21), 154 (20).

*9-[5'-O-(4,4'-Dimethoxytrityl)-β-*L*-ribofuranosyl]-N^3-guanine* (**17**)[17]. As described for **13**, with **12** (4.66 g, 8.32 mmol), $(i\text{-}Pr)_2NEt$ (2.2 ml, 12.9 mmol), CH_2Cl_2 (25 ml), dimethoxytrityl chloride (3.4 g, 10 mmol), THF/MeOH/H_2O 5:4:1 (400 ml) 10N aq. NaOH (8 ml), and AcOH (4.8 ml): **17** (5.15 g, 94%). Yellow foam. TLC (CH_2Cl_2/MeOH 9:1): R_f 0.20. $[\alpha]_D^{25°} = +48$ (*c* = 1.27, $CHCl_3$). UV (MeOH): 298 (sh, 6900), 276 (14300), 272 (14100), 258 (sh, 18000), 250 (sh, 18800), 236 (24300), 224 (20000). IR ($CHCl_3$): 3544*w*, 3400*w* (br.), 2990*w*, 2933*w*, 1700*m*, 1644*s*, 1611*m*, 1550*m*, 1511*s*, 1478*s*, 1388*m*, 1300*w*, 1106*m*, 1033*m*, 828*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.91, 1.04 (2*d*, *J* = 6.6, Me_2CH); 2.48 (br. *sept.*, *J* ≈ 6.5, Me_2CH); 3.20 (br. *d*, *J* ≈ 7, H–C(5')); 3.42 (br. *d*, *J* ≈ 8, H'–C(5')); 3.71, 3.72 (2*s*, 2 MeO); 4.33 (br. *s*, H–C(4')); 4.50 (br. *d*, *J* ≈ 5, H–C(3')); 5.01 (*t*, *J* = 5.3, H–C(2')); 5.91 (*d*, *J* = 5.6, H–C(1')); 6.73–6.77 (*m*, 4 arom. H); 7.10–7.39 (*m*, 9 arom. H); 7.84 (*s*, H–C(8)). ^{13}C-NMR (75 MHz, $CDCl_3$): 18.8, 18.9 (2 *q*, Me_2C); 46.2 (*d*, Me_2C); 55.3 (*q*, MeO); 64.0 (*t*, C(5')); 72.1, 75.0, 85.5 (3*d*, C(2'), C(3'), C(4')); 86.5 (*s*, Ar_2CPh); 90.4 (*d*, C(1')); 113.4 (*d*, arom. C); 121.1 (*s*, C(5)); 127.2, 128.1, 128.3, 130.2, 130.3 (5*d*, arom. C); 135.9, 136.2 (2*d*, arom. C); 138.9 (*d*, C(8)); 144.9 (*s*, arom. C); 148.1 (*s*, C(4)); 148.7 (*s*, C(2)); 156.8 (*s*, C(6)); 158.9 (*s*, MeO–*C*); 180.4 (*s*, CO). FAB-MS (NOBA, pos. mode): 656 (45, $[M + H]^+$), 303 (100).

*1-{5'-O-(4,4'-Dimethoxytrityl)-2'-O-{[(2-nitrobenzyl)oxy]methyl}-β-*L*-ribofuranosyl}uracil* (**18**) *and 1-{5'-O-(4,4'-Dimethoxytrityl)-3-O-{[(2-nitrobenzyl)oxy]methyl}-β-*L*-ribofuranosyl}uracil* (**23**)[18]. A soln. of **13** (4.16 g, 7.60 mmol) and $(i\text{-}Pr)_2NEt$ (6.5 ml, 38 mmol), in $(CH_2Cl)_2$ (30 ml) was treated with Bu_2SnCl_2 (2.77 g, 9.1 mmol). The soln. was stirred for 90 min at r.t., heated to 80°, treated with 1-[(chloromethoxy)methyl]-2-nitrobenzene (nbm-Cl; 1.60 g, 8.0 mmol), and stirred for 20 min at 80°. Usual workup (CH_2Cl_2/sat. aq. $NaHCO_3$) and CC (silica gel (80 g) hexane/AcOEt 3:2 (+ 2% Et_3N)Pr → hexane/AcOEt 1:9 (+ 2% Et_3N)) afforded **18** (2.97 g, 55%) and **23** (1.83 g, 34%) as yellow foams.

Data of **18**: TLC (hexane/AcOEt 1:9): R_f 0.60. $[\alpha]_D^{25°} = -33$ (*c* = 1.00, $CHCl_3$). UV (MeOH): 279 (sh, 9700), 261 (15900), 255 (15600), 234 (26900), 227 (25600). IR ($CHCl_3$): 3555*w*, 3389*w*, 2944*w*, 1689*s*, 1606*m*, 1528*m*, 1505*m*, 1456*m*, 1344*m*, 1300*m*, 1094*m*, 1033*m*, 828*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.67 (br. *d*, *J* ≈ 7, OH–C(3')); 3.52 (*dd*, *J* = 2.5, 11.2, H–C(5')); 3.55 (*dd*, *J* = 2.1, 11.2, H'–C(5')); 3.79 (*s*, 2 MeO); 4.10 (br. *dt*, *J* ≈ 8, 1, H–C(4')); 4.38 (*dd*, *J* = 5.3, 2.8, H–C(2')); 4.55 (br. *q*, *J* ≈ 6, H–C(3')); 5.03, 5.09 (2*d*, *J* = 14.0, OCH_2O); 5.04, 5.18 (2*d*, *J* = 6.8, $ArCH_2O$); 5.29 (*d*, *J* = 8.1, H–C(5)); 6.04 (*d*, *J* = 2.5, H–C(1')); 6.82–6.87 (*m*, 4 arom. H); 7.21–7.76 (*m*, 12 arom. H); 7.94 (*d*, *J* = 8.1, H–C(6)); 8.06–8.09 (*m*, 1 arom. H); 9.02 (br. *s*, H–N(3)). ^{13}C-NMR (75 MHz, $CDCl_3$): 55.4 (*q*, MeO); 61.8 (*t*, C(5')); 67.5 (*t*, $ArCH_2$); 69.2, 80.3, 83.6 (3*d*, C(2'), C(3'), C(4')); 87.3 (*s*, Ar_2CPh); 87.9 (*d*, C(1')); 95.3 (*t*, OCH_2O); 102.5 (*d*, C(5)); 113.6 (*d*, arom. C); 125.1, 127.4, 128.3, 128.4, 128.6, 129.0, 130.3, 130.4 (8*d*, arom. C); 134.0, 134.1, 135.3, 135.5 (4*s*, arom. C); 140.3 (*d*, C(6)); 144.6, 147.4 (2*s*, arom. C); 150.4 (*s*, C(2)); 159.0, 159.1 (2*s*, MeO–*C*); 163.4 (*s*, C(4)). FAB-MS (NOBA, pos. mode): 711 (84, M^+), 634 (19), 604 (19), 303 (100).

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[18]) A synthesis of the (natural) D-configurated enantiomer is reported in [21].

Data of **23**: TLC (hexane/AcOEt 1:9): R_f 0.25. $[\alpha]_D^{25°} = -41$ ($c = 0.97$, $CHCl_3$). IR ($CHCl_3$): 3555*w*, 3389*w*, 2956*w*, 1689*s*, 1606*m*, 1528*m*, 1505*m*, 1456*m*, 1344*m*, 1094*m*, 1039*m*, 911*w*, 828*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 3.41 (*dd*, $J = 2.5, 11.2$, H–C(5′)); 3.60 (*dd*, $J = 2.5, 11.2$, H′–C(5′)); 3.770, 3.774 (2*s*, 2 MeO); 4.10 (br. *d*, $J \approx 6$, OH–C(2′)); 4.26 (*m*, H–C(4′)); 4.38 (*m*, H–C(2′)); 4.42 (*t*, $J \approx 5.3$, H–C(3′)); 4.87, 4.94 (2*d*, $J = 6.8$, ArCH_2O); 4.45, 5.03 (2*d*, $J = 14.9$, OCH_2O); 5.36 (*d*, $J = 8.1$, H–C(5)); 5.93 (*d*, $J = 3.4$, H–C(1′)); 6.80–6.86 (*m*, 4 arom. H); 7.22–7.69 (*m*, 12 arom. H); 7.90 (*d*, $J = 8.1$, H–C(6)); 8.04–8.07 (*m*, 1 arom. H); 9.64 (br. *s*, H–N(2)). ^{13}C-NMR (75 MHz, $CDCl_3$): 55.3 (*q*, MeO); 62.0 (*t*, C(5′)); 67.5 (*t*, ArCH_2); 74.7, 75.3, 81.9 (3*d*, C(2′), C(3′), C(4′)); 87.2 (*s*, Ar_2CPh); 90.0 (*d*, C(1′)); 95.5 (*t*, OCH_2O); 102.7 (*d*, C(5)); 113.5 (*d*, arom. C); 125.1, 127.4, 128.3, 128.4, 128.6, 129.1, 130.3, 130.4 (8*d*, arom. C); 133.9, 134.0, 135.3, 135.4 (4*s*, arom. C); 140.3 (*d*, C(6)); 144.5, 147.6 (2*s*, arom. C); 151.1 (*s*, C(2)); 159.0 (*s*, MeO–*C*); 163.6 (*s*, C(4)). FAB-MS (NOBA, pos. mode): 711 (27, M^+), 303 (100).

*1-{5′-*O*-(4,4′-Dimethoxytrityl)-2′-*O*-{[(2-nitrobenzyl)oxy]methyl}-β-*L*-ribofuranosyl}thymine* (**19**) *and 1-{5′-*O*-(4,4′-Dimethoxytrityl)-3′-*O*-{[(2-nitrobenzyl)oxy]methyl}-β-*L*-ribofuranosyl}thymine* (**24**). As described for **18**/**23**, with **14** (4.85 g, 8.60 mmol), (i-Pr)$_2$NEt (7.4 ml, 43 mmol), $(CH_2Cl)_2$ (30 ml), Bu_2SnCl_2 (3.16 g, 10.4 mmol), and nbm-Cl (1.60 g, 8.0 mmol). **19** (3.55 g, 57%) and **24** (1.92 g, 31%) as colorless foams.

Data of **19**: TLC (hexane/AcOEt 1:4): R_f 0.25. $[\alpha]_D^{25°} = -14$ ($c = 0.81$, $CHCl_3$). UV (MeOH): 279 (sh, 12000), 266 (16000), 254 (14800), 232 (27700), 229 (26100). IR ($CHCl_3$): 3540*w*, 3380*w*, 2934*w*, 1689*s*, 1609*m*, 1528*m*, 1509*m*, 1464*m*, 1344*m*, 1253*m*, 1098*m*, 1037*m*, 830*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.32 (*s*, Me); 2.73 (*d*, $J = 5.3$, OH–C(3′)); 3.43 (*dd*, $J = 2.8, 10.9$, H–C(5′)); 3.53 (*dd*, $J = 1.9, 10.9$, H′–C(5′)); 3.78 (*s*, 2 MeO); 4.10 (*m*, H–C(4′)); 4.49 (*m*, H–C(2′), H–C(3′)); 5.03, 5.12 (2*m*, OCH_2O); 5.04 (*s*, ArCH_2O); 6.10 (*d*, $J = 4.0$, H–C(1′)); 6.80–6.86 (*m*, 4 arom. H); 7.23–7.72 (*m*, 12 arom. H, H–C(6)); 8.06–8.10 (*m*, 1 arom. H); 8.62 (br. *s*, H–N(3)). ^{13}C-NMR (75 MHz, $CDCl_3$): 11.7 (*q*, Me); 55.3 (*q*, MeO); 62.7 (*t*, C(5′)); 67.5 (*t*, ArCH_2); 70.0, 79.9, 83.8 (3*d*, C(2′), C(3′), C(4′)); 87.2 (*s*, Ar_2CPh); 87.3 (*d*, C(1′)); 95.3 (*t*, OCH_2O); 111.4 (*s*, C(5)); 113.5 (*d*, arom. C); 125.1, 127.4, 128.3, 128.4, 128.6, 128.7, 128.9, 130.4 (8*d*, arom. C); 133.9, 134.0, 135.5 (3*s*, arom. C); 135.6 (*d*, C(6)); 144.5, 147.5 (2*s*, arom. C); 150.6 (*s*, C(2)); 159.0 (*s*, MeO–*C*); 163.8 (*s*, C(4)). FAB-MS (NOBA, pos. mode): 726 (86, $[M + H]^+$), 303 (100).

Data of **24**: TLC (hexane/AcOEt 1:4): R_f 0.10. $[\alpha]_D^{25°} = -4$ ($c = 0.63$, $CHCl_3$). IR ($CHCl_3$): 3425*w*, 3280*w*, 2925*w*, 1689*s*, 1608*m*, 1528*m*, 1509*m*, 1465*m*, 1344*m*, 1177*m*, 1037*m*, 830*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.32 (*d*, $J = 1.0$, Me); 3.32 (*dd*, $J = 2.5, 10.9$, H–C(5′)); 3.57 (*dd*, $J = 2.8, 10.9$, H′–C(5′)); 3.62 (br. *s*, OH–C(2′)); 3.778, 3.784 (2*s*, 2 MeO); 4.25 (*m*, H–C(4′)); 4.45 (*m*, H–C(2′), H–C(3′)); 4.88, 4.94 (2*d*, $J = 6.8$, ArCH_2O); 4.95, 5.03 (2*d*, $J = 14.0$, OCH_2O); 5.99 (*d*, $J = 4.4$, H–C(1′)); 6.80–6.84 (*m*, 4 arom. H); 7.20–7.69 (*m*, 13 arom. H, H–C(6)); 8.04–8.08 (*m*, 1 arom. H); 8.95 (br. *s*, H–N(3)). ^{13}C-NMR (75 MHz, $CDCl_3$): 11.8 (*q*, Me); 55.4 (*q*, MeO); 62.8 (*t*, C(5′)); 67.5 (*t*, ArCH_2); 74.6, 76.4, 82.2 (3*d*, C(2′), C(3′), C(4′)); 87.2 (*s*, Ar_2CPh); 89.2 (*d*, C(1′)); 95.6 (*t*, OCH_2O); 111.6 (*s*, C(5)); 113.5 (*d*, arom. C); 125.1, 127.4, 128.3, 128.4, 128.7, 128.9, 130.3 (7*d*, arom. C); 133.9, 135.5, 135.6 (3*s*, arom. C); 135.7 (*d*, C(6)); 144.5, 147.6 (2*s*, arom. C); 151.0 (*s*, C(2)); 159.1 (*s*, MeO–*C*); 163.9 (*s*, C(4)). FAB-MS (NOBA, pos. mode): 726 (55, $[M + H]^+$), 303 (100).

*N^4-Benzoyl-1-{5′-*O*-(4,4′-dimethoxytrityl)-2′-*O*-{[(2-nitrobenzyl)oxy]methyl}-β-*L*-ribofuranosyl}cytosine* (**20**) *and N^4-Benzoyl-1-[5′-*O*-(4,4′-dimethoxytrityl)-3′-*O*-{[(2-nitrobenzyl)oxy]methyl}-β-*L*-ribofuranosyl]-cytosine* (**25**)[18]. As described for **18**/**23**, with **15** (4.04 g, 6.20 mmol), (i-Pr)$_2$NEt (5.5 ml, 32 mmol), $(CH_2Cl)_2$ (25 ml), Bu_2SnCl_2 (2.45 g, 8.0 mmol), and nbm-Cl (1.31 g, 6.5 mmol). CC (silica gel (80 g), hexane/AcOEt 1:1 (+ 2% Et_3N) → AcOEt (+ 2% Et_3N)) afforded **20** (3.18 g, 63%) and **25** (1.50 g, 30%) as yellow foams.

Data of **20**: TLC (hexane/AcOEt 1:9): R_f 0.45. $[\alpha]_D^{25°} = -62$ ($c = 0.95$, $CHCl_3$). UV (MeOH): 303 (10200), 293 (9600), 280 (sh, 13300), 261 (25000), 251 (23700), 235 (30900), 226 (29100). IR ($CHCl_3$): 3555*w*, 3400*w*, 2967*w*, 1700*m*, 1661*s*, 1605*m*, 1550*m*, 1528*m*, 1505*m*, 1478*s*, 1378*m*, 1344*m*, 1300*m*, 1094*m*, 1033*m*, 905*m*, 833*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.70 (br. *d*, $J \approx 7$, OH–C(3′)); 3.57 (*dd*, $J = 2.5, 11.2$, H–C(5′)); 3.62 (*dd*, $J = 2.2, 11.4$, H′–C(5′)); 3.821, 3.823 (2*s*, 2 MeO); 4.13 (br. *dt*, $J = 8.7, 1$, H–C(4′)); 4.38 (*d*, $J = 5.0$, H–C(2′)); 4.51 (br. *m*, H–C(3′)); 5.04, 5.14 (2*d*, $J = 14.9$, OCH_2O); 5.13, 5.43 (2*d*, $J = 6.5$, ArCH_2O); 6.06 (*s*, H–C(1′)); 6.85–6.89 (*m*, 4 arom. H); 7.19–7.90 (*m*, 17 arom. H, H–C(5)); 8.06–8.09 (*m*, 1 arom. H); 8.55 (*s*, H–C(6)); 8.72 (br. *s*, NH–C(4)). ^{13}C-NMR (75 MHz, $CDCl_3$): 55.3 (*q*, MeO); 61.0 (*t*, C(5′)); 67.4 (*t*, ArCH_2); 68.1, 80.3, 83.3 (3*d*, C(2′), C(3′), C(4′)); 87.3 (*s*, Ar_2CPh); 89.7 (*d*, C(1′)); 95.2 (*t*, OCH_2O); 96.9 (*d*, C(5)); 113.6 (*d*, arom. C); 125.0, 127.4, 127.8, 128.3, 128.4, 128.5, 129.1, 129.3, 130.3, 130.4 (10*d*, arom. C); 133.4, 134.1 (2*d*, arom. C); 134.4, 135.6, 135.9, 144.4 (4*s*, arom. C); 145.2 (*d*, C(6)); 147.3 (*s*, arom. C); 155.1 (*s*, C(2)); 159.0 (*s*, MeO–*C*); 162.7 (*s*, CO); 166.4 (*s*, C(4)). FAB-MS (NOBA, pos. mode): 815 (22, $[M + H]^+$), 303 (100).

Data of **25**: TLC (hexane/AcOEt 1:9): R_f 0.15. $[\alpha]_D^{25°} = -41$ ($c = 0.97$, $CHCl_3$). IR ($CHCl_3$): 3555*w*, 3400*w*, 2911*w*, 1700*m*, 1665*s*, 1605*m*, 1556*m*, 1528*m*, 1505*m*, 1478*s*, 1378*m*, 1344*m*, 1300*m*, 1111*m*, 1044*m*, 905*m*, 833*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 3.41 (*dd*, $J = 2.2, 10.6$, H–C(5′)); 3.62 (*dd*, $J = 2.0, 10.5$, H′–C(5′)); 3.78, 3.79

(2*s*, 2 MeO); 4.29 (br. *s*, OH–C(2')); 4.42 (*m*, H–C(2'), H–C(3'), H–C(4')); 4.84, 4.96 (2*d*, J = 7.2, ArCH_2O); 4.94, 4.99 (2*d*, J = 17.5, OCH$_2$O); 5.96 (*d*, J = 1.5, H–C(1')); 6.83 (*d*, J = 8.7, 4 arom. H); 7.24–7.68 (*m*, 16 arom. H); 7.88–7.91 (*m*, 2 arom. H); 8.04–8.07 (*m*, 1 arom. H); 8.41 (*d*, J = 7.5, H–C(6)); 8.80 (br. *s*, NH–C(4)). ^{13}C-NMR (75 MHz, $CDCl_3$): 55.3 (*q*, MeO); 61.8 (*t*, C(5')); 67.4 (*t*, ArCH_2); 75.2, 75.7, 82.6 (3*d*, C(2'), C(3'), C(4')); 87.2 (*s*, Ar$_2$*C*Ph); 92.6 (*d*, C(1')); 95.6 (*t*, OCH$_2$O); 96.9 (*d*, C(5)); 113.5 (*d*, arom. C); 125.1, 127.4, 127.8, 128.3, 128.4, 128.6, 129.2, 129.3, 130.3, 130.4, (10*d*, arom. C); 133.4, 134.0 (2*d*, arom. C); 134.2, 135.5, 135.6, 144.2 (4*s*, arom. C); 145.0 (*d*, C(6)); 147.6 (*s*, arom. C); 155.8 (*s*, C(2)); 159.0 (*s*, MeO–*C*); 162.7 (*s*, CO); 166.6 (*s*, C(4)). FAB-MS (NOBA, pos. mode): 815 (43, $[M + H]^+$), 303 (100).

N^6-*Benzoyl-9-{5'-O-(4,4'-dimethoxytrityl)-2'-O-{[(2-nitrobenzyl)oxy]methyl}-β-*L*-ribofuranosyl}adenine* (**21**) *and* N^6-*Benzoyl-9-{5'-O-(4,4'-dimethoxytrityl)-3'-O-{[(2-nitrobenzyl)oxy]methyl}-β-*L*-ribofuranosyl}adenine* (**26**)[18]. As described for **18**/**23**, with **16** (3.54 g, 5.26 mmol), (i-Pr)$_2$NEt (5.0 ml, 29 mmol), $(CH_2Cl)_2$ (20 ml), Bu_2SnCl_2 (2.11 g, 6.9 mmol), and nbm-Cl (1.11 g, 5.5 mmol). CC (silica gel (60 g), hexane/AcOEt 6:4 (+ 2% Et_3N) → hexane/AcOEt 1:9 (+ 2% Et_3N)) afforded **21** (2.41 g, 55%) and **26** (1.73 g, 39%) as yellow foams.

Data of **21**: TLC (hexane/AcOEt 1:9): R_f 0.40. $[\alpha]_D^{25°} = +17$ (c = 1.09, $CHCl_3$). UV (MeOH): 277 (20700), 257 (15700), 233 (31700), 223 (30700). IR ($CHCl_3$): 3556*w*, 3400*w*, 2944*w*, 1705*m*, 1611*s*, 1583*m*, 1528*s*, 1510*s*, 1478*m*, 1456*s*, 1344*m*, 1300*m*, 1039*s*, 905*m*, 828*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.89 (br. *d*, $J \approx 4$, OH–C(3')); 3.42 (*dd*, J = 4.4, 10.6, H–C(5')); 3.53 (*dd*, J = 3.7, 10.6, H'–C(5')); 3.77 (*s*, 2 MeO); 4.28 (*q*, J = 2.7, H–C(4')); 4.55 (br. *q*, $J \approx 4$, H–C(3')); 4.83, 4.85 (2*d*, J = 10.4, OCH$_2$O); 5.11 (*s*, ArCH_2O); 5.11 (*t*, J = 5.3, H–C(2')); 6.24 (*d*, J = 5.3, H–C(1')); 6.80 (*d*, J = 8.4, 4 arom. H); 7.20–7.61 (*m*, 15 arom. H); 8.01–8.04 (*m*, 3 arom. H); 8.16 (*s*, H–C(2)); 8.62 (*s*, H–C(8)); 9.00 (br. *s*, NH–C(6)). ^{13}C-NMR (75 MHz, $CDCl_3$): 55.3 (*q*, MeO); 63.3 (*t*, C(5')); 67.3 (*t*, ArCH_2); 70.8, 80.0, 84.4 (3*d*, C(2'), C(3'), C(4')); 87.2 (*s*, Ar$_2$*C*Ph); 92.6 (*d*, C(1')); 95.7 (*t*, OCH$_2$O); 113.4 (*d*, arom. C); 123.5 (*s*, C(5)); 125.0, 127.2, 128.1, 128.2, 128.4, 128.6, 129.2, 130.3 (8*d*, arom. C); 133.1 (*d*, arom. C); 133.6 (*s*, arom. C); 134.1 (*d*, arom. C); 135.8 (*s*, arom. C); 142.0 (*d*, C(8)); 144.7 (*s*, arom. C); 147.1 (*s*, arom. C); 149.7 (*s*, C(4)); 151.7 (*s*, C(6)); 153.0 (*d*, C(2)); 158.9 (*s*, MeO–*C*); 164.7 (*s*, CO). FAB-MS (NOBA, pos. mode): 839 (100, $[M + H]^+$), 303 (20).

Data of **26**: TLC (hexane/AcOEt 1:9): R_f 0.20. $[\alpha]_D^{25°} = +11$ (c = 1.05, $CHCl_3$). IR ($CHCl_3$): 3544*w*, 3400*w*, 2933*w*, 1705*m*, 1611*s*, 1583*m*, 1528*s*, 1505*s*, 1456*s*, 1344*m*, 1294*m*, 1033*s*, 828*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 3.32 (*dd*, J = 3.7, 10.6, H–C(5')); 3.49 (*dd*, J = 4.1, 10.6, H'–C(5')); 3.75 (*s*, 2 MeO); 4.20 (br. *d*, $J \approx 5$, OH–C(2')); 4.37 (*q*, J = 3.7, H–C(4')); 4.59 (*dd*, J = 3.7, 5.3, H–C(3')); 4.94–5.02 (*m*, H–C(2'), OCH$_2$O, ArCH_2O); 6.07 (*d*, J = 5.6, H–C(1')); 6.76 (*d*, J = 9.0, 4 arom. H); 7.19–7.69 (*m*, 15 arom. H); 8.00–8.11 (*m*, 3 arom. H); 8.22 (*s*, H–C(2)); 8.72 (*s*, H–C(8)); 9.10 (br. *s*, NH–C(6)). ^{13}C-NMR (75 MHz, $CDCl_3$): 55.3 (*q*, MeO); 63.1 (*t*, C(5')); 67.4 (*t*, ArCH_2); 74.5, 77.6, 83.4 (3*d*, C(2'), C(3'), C(4')); 86.8 (*s*, Ar$_2$*C*Ph); 89.7 (*d*, C(1')); 95.7 (*t*, OCH$_2$O); 113.4 (*d*, arom. C); 123.5 (*s*, C(5)); 125.1, 127.2, 128.1, 128.3, 128.6, 129.0, 129.1, 130.2 (8*d*, arom. C); 133.1, 134.0 (2*d*, arom. C); 135.7, 135.8 (2*s*, arom. C); 142.0 (*d*, C(8)); 144.7 (*s*, arom. C); 147.5 (*s*, arom. C); 149.9 (*s*, C(4)); 151.7 (*s*, C(6)); 152.9 (*d*, C(2)); 158.9 (*s*, MeO–*C*); 164.9 (*s*, CO). FAB-MS (NOBA, pos. mode): 839 (100, $[M + H]^+$), 303 (56).

*9-{5'-O-(4,4'-Dimethoxytrityl)-2'-O-{[(2-nitrobenzyl)oxy]methyl}-β-*L*-ribofuranosyl}-*N*^{2}-isobutyrylguanine* (**22**)[18]. As described for **18**/**23**, with **17** (4.80 g, 7.3 mmol), (i-Pr)$_2$NEt (6.1 ml, 36 mmol), $(CH_2Cl)_2$ (30 ml), Bu_2SnCl_2 (2.66 g, 8.8 mmol), and nbm-Cl (1.54 g, 7.7 mmol). CC (silica gel (60 g), CH_2Cl_2 (+ 2% Et_3N) → CH_2Cl_2/MeOH 85:15 (+ 2% Et_3N)) afforded **22** (4.9 g, 90%). Yellow foam. TLC (CH_2Cl_2/MeOH 19:1): R_f 0.50. $[\alpha]_D^{25°} = +17$ (c = 0.64, $CHCl_3$). UV (MeOH): 281 (sh, 15500), 269 (sh, 18800), 261 (21700), 247 (20300), 235 (23700), 230 (22900), 220 (28500). IR ($CHCl_3$): 3400*w*, 3211*w*, 2966*m*, 2933*m*, 2811*w*, 1695*s*, 1605*s*, 1555*m*, 1528*s*, 1506*m*, 1461*m*, 1372*m*, 1338*m*, 1300*m*, 1094*m*, 1038*m*, 833*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.83, 0.99 (2*d*, J = 6.8, *Me*$_2$CH); 1.81 (*sept.*, J = 6.8, Me$_2$*CH*); 2.83 (br. *s*, OH–C(3')); 3.20 (*dd*, J = 3.1, 10.6, H–C(5')); 3.50 (*dd*, J = 2.2, 10.6, H'–C(5')); 3.76, 3.77 (2*s*, 2 MeO); 4.23 (br. *q*, $J \approx 2$, H–C(4')); 4.51 (br. *d*, $J \approx 4$, H–C(3')); 4.78, 4.85 (2*d*, J = 14.6, OCH$_2$O); 4.92, 4.95 (2*d*, J = 6.9, ArCH_2O); 5.22 (*dd*, J = 5.0, 7.1, H–C(2')); 5.98 (*d*, J = 7.1, H–C(1')); 6.78–6.82 (*m*, 4 arom. H); 7.19–7.56 (*m*, 12 arom. H); 7.79 (br. *s*, NH–C(2)); 7.98 (*s*, H–C(8)); 8.00 (*d*, 1 arom. H); 11.75 (br. *s*, H–N(1)). ^{13}C-NMR (75 MHz, $CDCl_3$): 18.5, 18.8 (2*q*, *Me*$_2$CHCO); 36.1 (*d*, Me$_2$*C*HCO); 55.4 (*q*, MeO); 63.9 (*t*, C(5')); 67.4 (*t*, ArCH_2); 70.8, 79.9, 84.5 (3*d*, C(2'), C(3'), C(4')); 86.3 (*d*, C(1')); 86.7 (*s*, Ar$_2$*C*Ph); 95.8 (*t*, OCH$_2$O); 113.5 (*d*, arom. C); 122.1 (*s*, C(5)); 124.9, 127.4, 128.3, 128.8, 130.3 (5*d*, arom. C); 133.4 (*s*, arom. C); 134.2 (*d*, arom. C); 135.8, 136.1 (2*s*, arom. C); 138.8 (*d*, C(8)); 145.0, 147.0 (2*s*, arom. C); 147.6 (*s*, C(4)); 148.4 (*s*, C(2)); 155.5 (*s*, C(6)); 159.0 (*s*, MeO–*C*); 179.0 (*s*, CO). FAB-MS (NOBA, pos. mode): 821 (58, $[M + H]^+$), 675 (62), 303 (100).

*9-{5'-O-(4,4'-Dimethoxytrityl)-3'-O-{[(2-nitrobenzyl)oxy]methyl}-β-*L*-ribofuranosyl}-*N*^{2}-isobutyrylguanine* (**27**)[18]. A soln. of **17** (1.2 g, 1.8 mmol) and (i-Pr)$_2$NEt (1.5 ml, 9 mmol) in MeCN (7.5 ml) was treated with Bu_2SnCl_2 (0.67 g, 2.2 mmol). The soln. was stirred for 90 min at r.t., cooled to 4°, treated with nbm-Cl (0.385 g,

1.9 mmol), and stirred for 3 h at 4°. Usual workup (CH_2Cl_2/sat. aq. $NaHCO_3$ soln.) and CC (silica gel (18 g), CH_2Cl_2 (+ 2% Et_3N) → CH_2Cl_2/MeOH 85:15 (+ 2% Et_3N)) afforded **22** (1.08 g, 80%) and 0.1 g of a mixture of different by-products. From this mixture, pure **27** (10 mg) was obtained by repeated prep. TLC (CH_2Cl_2/MeOH 9:1 and then 19:1). TLC (CH_2Cl_2/MeOH 19:1): R_f 0.45. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.48, 0.82 (*2d*, $J \approx 6.8$, Me_2CH); 1.25 (*sept.*, $J = 6.8$, Me_2CH); 2.99 (*dd*, $J = 2.2, 10.6$, H–C(5')); 3.50 (*dd*, $J = 2.2, 10.6$, H'–C(5')); 3.75, 3.77 (*2s*, 2 MeO); 4.19 (br. *q*, $J \approx 2$, H–C(4')); 4.61 (*dd*, $J = 2.2, 5.6$, H–C(3')); 4.95, 5.12 (*2d*, = 12.6, OCH_2O); 4.94 (*s*, $ArCH_2O$); 5.36 (br. *t*, $J \approx 6.0$, H–C(2')); 5.42 (br. *s*, OH–C(2')); 5.71 (*d*, $J = 7.5$, H–C(1')); 6.77–6.85 (*m*, 4 arom. H); 7.16–7.67 (*m*, 12 arom. H, NH–C(2)); 7.98 (*s*, H–C(8)); 8.02–8.09 (*m*, 1 arom. H); 11.88 (br. *s*, H–N(1)).

*1-{5'-O-(4,4'-Dimethoxytrityl)-2'-O-{[(2-nitrobenzyl)oxy]methyl}-β-*L*-ribofuranosyl}uracil 3'-[(2-Cyanoethyl) Diisopropylphosphoramidite]* (**28**)[18]. A soln. of **18** (2.8 g, 3.9 mmol) in CH_2Cl_2 (15 ml) was treated consecutively with (i-Pr)$_2$NEt (1.35 ml, 7.8 mmol) and 2-cyanoethyl diisopropylphosphoramidochloridite (1.10 g, 4.6 mmol). After stirring for 3 h at r.t., the mixture was subjected to CC (silica gel (50 g), hexane/AcOEt 7:3 (+ 2% Et_3N) → hexane/AcOEt 2:3 (+ 2% Et_3N)): **28** (3.30 g, 93%). Colorless foam (mixture of diastereoisomers). TLC (hexane/AcOEt 2:3): R_f 0.50, 0.40. UV (MeCN): 254 (sh, 17000), 236 (25600), 227 (23800). IR ($CHCl_3$): 3389*w*, 2967*m*, 2933*m*, 1689*s*, 1606*m*, 1528*m*, 1511*m*, 1456*m*, 1367*w*, 1344*m*, 1033*s*, 978*m*, 828*w*. ^{1}H-NMR (500 MHz, $CDCl_3$): 1.02, 1.11, 1.13 (*3d*, $J = 6.8$, 12 H, Me_2CH); 2.44, 2.61 (*2t*, $J = 6.7$, 2 H, OCH_2CH_2CN); 3.41–3.74 (*m*, 5 H, Me_2CH, H–C(5'), OCH_2CH_2CN); 3.78, 3.79 (*2s*, 6 H, MeO); 3.91 (*m*, 1 H, OCH_2CH_2ON); 4.21 (*dt*, $J = 5.4, 2.7, 0.5$ H, H–C(4')); 4.27 (*dt*, $J = 6.4, 3.6, 0.5$ H, H–C(4')); 4.45 (*dd*, $J = 3.4, 4.8, 0.5$ H, H–C(2')); 4.51 (br. *t*, $J \approx 4, 0.5$ H, H–C(2')); 4.53–4.58 (*m*, 1 H, H–C(3')); 5.00–5.07 (*m*, 4 H, OCH_2O, $ArCH_2$); 5.19, 5.23 (*2d*, $J = 8.1$, 1 H, H–C(5)); 6.06 (*d*, $J = 3.3$, 0.5 H, H–C(1')); 6.10 (*d*, $J = 3.8$, 0.5 H, H–C(1')); 6.81–6.85 (*m*, 4 arom. H); 7.22–7.45 (*m*, 10 arom. H); 7.60, 7.78 (*2m*, 2 arom. H); 7.87, 7.95 (*2d*, $J = 8.1$, 1 H, H–C(6)); 8.06 (*m*, 1 arom. H); 8.68 (br. *s*, 1 H, H–N(2)). ^{13}C-NMR (125 MHz, $CDCl_3$): 20.2, 20.4 (*2t*, *J*(CP) = 7, CH_2CN); 24.44, 24.49, 24.54, 24.60, 24.64, 24.70 (*6q*, Me_2CH); 43.2, 43.3 (*2d*, *J*(CP) = 9, Me_2CH); 55.2 (*q*, MeO); 58.1, 58.3 (*2t*, *J*(CP) = 18, CH_2O); 61.4, 61.8, (*2t*, C(5')); 67.0, 67.1 (*2t*, $ArCH_2$); 70.2 and 70.5 (*2d*, *J*(CP) = 14), 78.6 and 78.8 (*2d*), 82.7 (*d*, C(2'), C(3'), C(4')); 87.2, 87.3 (*2s*, Ar_2CPh); 87.8, 88.0 (*2d*, C(1')); 94.8 (*t*, OCH_2O); 102.2, 102.3 (*2d*, C(5)); 113.1, 113.2, 113.3, 113.4 (*4d*, arom. C); 117.4, 117.7 (*2s*, CN); 124.7, 124.8, 127.2, 127.9, 128.0, 128.1, 128.2, 128.3, 128.4, 128.8, 128.9, 130.2, 130.3, 133.6, 133.7 (*15d*, arom. C); 134.3, 134.4, 134.9, 135.0, 135.1, 135.2 (*6s*, arom. C); 140.0 (*d*, C(6)); 144.1, 144.3, 147.2, 147.3 (*4s*, arom. C); 150.1, 150.2 (*2s*, C(2)); 158.7, 158.8 (*2s*, arom. C); 162.9, 163.0 (*2s*, C(4)). ^{31}P-NMR (202 MHz, $CDCl_3$): 150.3, 151.1. FAB-MS (NOBA, pos. mode): 912 (31, $[M + H]^+$), 608 (16), 303 (100).

*1-{5'-O-(4,4'-Dimethoxytrityl)-2'-O-{[(2-nitrobenzyl)oxy]methyl}-β-*L*-ribofuranosyl}thymine 3'-[(2-Cyanoethyl) Diisopropylphosphoramidite]* (**29**). As described for **28**, with **19** (2.8 g, 3.9 mmol), CH_2Cl_2 (15 ml), (i-Pr)$_2$NEt (1.35 ml, 7.8 mmol), and (i-Pr)$_2$NPCl(OCH_2CH_2CN) (1.10 g, 4.6 mmol): **29** (3.15 g, 90%). Colorless foam (mixture of diastereoisomers). TLC (hexane/AcOEt 2:3): R_f 0.40. UV (MeCN): 264 (18400), 256 (17900), 235 (28600), 229 (28000). IR ($CHCl_3$): 3350*w*, 2967*m*, 2933*m*, 1691*s*, 1606*m*, 1528*m*, 1510*m*, 1464*m*, 1365*w*, 1344*m*, 1253*m*, 1122*m*, 1036*s*, 980*m*, 830*w*. ^{1}H-NMR (500 MHz, $CDCl_3$): 0.98, 1.13, 1.14 (*3d*, $J = 6.8$, 12 H, Me_2CH); 1.28, 1.30 (*2d*, $J \approx 1.1$, Me–C(5)); 2.38, 2.64 (*2t*, $J = 6.3$, 2 H, OCH_2CH_2CN); 3.30–3.67 (*m*, 5 H, Me_2CH, H–C(5'), OCH_2CH_2CN); 3.774, 3.775, 3.782 (*3s*, 6 H, MeO); 3.79–3.96 (*m*, 1 H, OCH_2CH_2CN); 4.19, 4.28 (2 br. *dt*, $J \approx 2$, 4, 1 H, H–C(4')); 4.51 (*m*, 1 H, H–C(3')); 4.56, 4.62 (*2t*, $J = 5.2$, 1 H, H–C(2')); 4.97–5.03 (*m*, 4 H, OCH_2O, $ArCH_2$); 6.14 (*d*, $J = 5.1$, 0.5 H, H–C(1')); 6.18 (*d*, $J = 5.6$, 0.5 H, H–C(1')); 6.80–6.84 (*m*, 4 arom. H); 7.22–7.47 (*m*, 10 arom. H); 7.55–7.72 (*m*, 3 arom. H); 8.05–8.07 (*m*, 1 arom. H); 8.41 (br. *s*, H–N(2)). ^{13}C-NMR (125 MHz, $CDCl_3$): 11.5, 11.6 (*2q*, *Me*–C(5')); 20.2, 20.4 (*2t*, *J*CP = 7, OCH_2CH_2CN); 24.51, 24.55, 24.59, 24.65 (*4q*, Me_2CH); 43.1, 43.3 (*2d*, *J*(CP) = 13, Me_2CH); 55.3 (*q*, MeO); 57.9, 58.8 (*2t*, *J*(CP) = 18, OCH_2CH_2CN); 62.5, 62.8 (*2t*, C(5')); 66.9, 67.0 (*2t*, $ArCH_2$); 70.8 and 71.3 (*2d*, *J*(CP) = 14), 78.0 and 78.4 (*2d*), 83.2 and 83.4 (*2d*, C(2'), C(3'), C(4')); 86.8, 87.0 (*2s*, Ar_2CPh); 87.1, 87.2 (*2d*, C(1')); 94.7, 94.8 (*2t*, OCH_2O); 111.2, 111.3 (*2d*, C(5)); 113.1, 113.2, 113.3, 113.4 (*4d*, arom. C); 117.4, 117.7 (*2s*, CN); 124.7, 124.8, 127.2, 127.9, 128.0, 128.1, 128.2, 128.3, 128.7, 128.8, 130.1, 130.2, 130.3, 133.6, 133.7 (*15d*, arom. C); 134.0, 134.2, 135.1, 135.2 (*4s*, arom. C); 135.3, 135.5 (*2d*, C(6)); 144.1, 144.2, 147.2, 147.3 (*4s*, arom. C); 150.3, 150.4 (*2s*, C(2)); 158.8 (*s*, arom. C)); 163.4, 163.5 (*2s*, C(4)). ^{31}P-NMR (202 MHz, $CDCl_3$): 150.7, 151.0. FAB-MS (NOBA, pos. mode): 926 (31, $[M + H]^+$), 800 (20), 622 (16), 303 (100).

N^4*-Benzoyl-1-{5'-O-(4,4'-dimethoxytrityl)-2'-O-{[(2-nitrobenzyl)oxy]methyl}-β-*L*-ribofuranosyl}cytosine 3'-[(2-Cyanoethyl) Diisopropylphosphoramidite]* (**30**)[18]. As described for **28**, with **20** (3.10 g, 3.8 mmol) CH_2Cl_2 (15 ml), (i-Pr)$_2$NEt (1.3 ml, 7.6 mmol), (i-Pr)$_2$NPCl(OCH_2CH_2CN) (1.08 g, 4.6 mmol). CC (silica gel (50 g), hexane/AcOEt 4:1 (+ 2% Et_3N) → hexane/AcOEt 1:1 (+ 2% Et_3N)) afforded **30** (3.48 g, 90%). Colorless foam (mixture of diastereoisomers). TLC (hexane/AcOEt 2:3): R_f 0.40, 0.30. UV (MeCN): 310 (9800), 293

(8900), 254 (30000), 252 (29000), 236 (38200), 225 (35800). IR ($CHCl_3$): 3400*w*, 2955*m*, 2922*m*, 1700*m*, 1661*s*, 1605*s*, 1550*m*, 1528*m*, 1505*m*, 1478*s*, 1383*m*, 1300*m*, 1106*m*, 1033*m*, 978*m*, 829*w*. ^{1}H-NMR (500 MHz, $CDCl_3$): 0.99, 1.06, 1.07 (3*d*, J = 6.8, 12 H, Me_2CH); 2.44, 2.54 (2*t*, J = 6.5, 2 H, OCH_2CH_2CN); 3.45–3.86 (*m*, 6 H, OCH_2CH_2CN, Me_2CH, H–C(5′)); 3.817, 3.818, 3.827, 3.828 (4*s*, 6 H, MeO); 4.31, 4.34 (2*dt*, J = 8.4, 2.0, 1 H, H–C(4′)); 4.43 (*dd*, J = 1.0, 4.6, 0.5 H, H–C(2′)); 4.48 (*dd*, J = 1.9, 4.6, 0.5 H, H–C(2′)); 4.54 (*ddd*, J = 4.6, 8.5, 10.6, 1 H, H–C(3′)); 5.1–5.29 (*m*, 4 H, OCH_2O, $ArCH_2$); 6.11 (*d*, J = 1.0, 0.5 H, H–C(1′)); 6.15 (*d*, J = 1.9, 0.5 H, H–C(1′)); 6.85–6.89 (*m*, 4 arom. H); 7.27–7.64 (*m*, 13 arom. H); 7.81–8.06 (*m*, 3 arom. H); 8.46, 8.49 (2br. *d*, $J \approx 7$, 2 H, NH–C(4), H–C(6)). ^{13}C-NMR (125 MHz, $CDCl_3$): 20.2, 20.3 (2*t*, J(CP) = 7, OCH_2CH_2CN); 24.38, 24.43, 24.49, 24.55, 24.59, 24.67, 24.73 (7*q*, Me_2CH); 43.1, 43.2 (2*d*, J(CP) = 7, Me_2CH); 55.2, 55.3 (2*q*, MeO); 58.2, 58.4 (2*t*, J(CP) = 15, OCH_2CH_2CN); 60.6, 61.0 (2*t*, C(5′)); 67.2 (*t*, $ArCH_2$); 68.8 and 70.0 (2*d*, J(CP) = 14), 78.9 (*d*), 82.0 (*d*, C(2′), C(3′), C(4′)); 87.1, 87.2 (2*s*, Ar_2CPh); 89.8, 89.9 (2*d*, C(1′)); 94.7, 94.8 (2*t*, OCH_2O); 96.5 (br. *d*, C(5)); 113.28, 113.29, 113.32, 113.38 (4*d*, arom. C); 117.4, 117.5 (2*s*, CN); 124.6, 127.3, 127.5, 127.8, 128.0, 128.3, 128.5, 129.0, 129.1, 129.4, 130.3, 130.4, 133.0, 133.7 (14*d*, arom. C); 134.6, 134.8, 135.1, 135.2, 135.3, 135.4 (6*s*, arom. C); 143.9, 144.0 (2*s*, arom. C); 144.9 (br. *d*, C(6)); 147.1, 147.3 (2*s*, arom. C); 154.5 (*s*, C(2)); 158.8 (*s*, arom. C); 162.2 (*s*, CO); 165.5 (*s*, C(4)). ^{31}P-NMR (202 MHz, $CDCl_3$): 150.1, 151.3. FAB-MS (NOBA, pos. mode): 1015 (26, $[M + H]^+$), 801 (23), 303 (100).

N^6-*Benzoyl-9-{5′-O-(4,4′-dimethoxytrityl)-2′-O-{[(2-nitrobenzyl)oxy]methyl}-β-*L*-ribofuranosyl}adenine 3′-[(2-Cyanoethyl) Diisopropylphosphoramidite]* (**31**)[18]. As described for **28**, with **21** (2.20 g, 2.6 mmol), CH_2Cl_2 (10 ml), (i-Pr)$_2$NEt (0.9 ml, 5.25 mmol), (i-Pr)$_2$NPCl(OCH_2CH_2CN) (0.74 g, 3.1 mmol). CC (silica gel (50 g), hexane/AcOEt 7:3 (+ 2% Et_3N) → hexane/AcOEt 1:2 (+ 2% Et_3N)) afforded **31** (2.48 g, 92%). Colorless foam (mixture of diastereoisomers). TLC (hexane/AcOEt 2:3): R_f 0.35. UV (MeCN): 276 (22400), 258 (17500), 232 (35100), 226 (34700). IR ($CHCl_3$): 3400*w*, 2967*m*, 1706*m*, 1611*s*, 1583*m*, 1528*m*, 1505*m*, 1456*m*, 1344*m*, 1300*m*, 1033*m*, 978*m*, 828*w*. ^{1}H-NMR (500 MHz, $CDCl_3$): 1.06, 1.17, 1.20 (3*d*, J = 6.8, 12 H, Me_2CH); 2.39 (*t*, J = 6.4, 0.67 H, OCH_2CH_2CN); 2.65 (*dt*, J = 1.4, 6.2, 1.33 H, OCH_2CH_2CN); 3.36 (*m*, 0.67 H, OCH_2CH_2CN); 3.55–3.76 (*m*, 4.33 H, OCH_2CH_2CN, Me_2CH, H–C(5′)); 3.763, 3.765, 3.770, 3.772 (4*s*, 6 H, MeO); 3.83–3.98 (*m*, 1 H, H–C(5′)); 4.36, 4.41 (2*q*, J = 2.7, 1 H, H–C(4′)); 4.65 (*m*, 1 H, H–C(3′)); 4.72, 4.73, 4.81, 4.82 (4*d*, J = 15.0, 2 H, OCH_2O); 4.89, 4.96, 5.00 (3*d*, J = 7.0, 2 H, $ArCH_2$); 5.26 (*m*, 1 H, H–C(2′)); 6.18, 6.21 (2*d*, J = 6.0, 1 H, H–C(1′)); 6.75–6.81 (*m*, 4 arom. H); 7.18–7.63 (*m*, 15 arom. H); 7.99–8.07 (*m*, 3 arom. H); 8.15, 8.16 (2*s*, 1 H, H–C(2)); 8.55, 8.57 (2*s*, 1 H, H–C(8)); 8.94 (br. *s*, 1 H, NH–C(6)). ^{13}C-NMR (125 MHz, $CDCl_3$): 20.2, 20.4 (2*t*, J(CP) = 7, OCH_2CH_2CN); 24.54, 24.60, 24.65, 24.72 (4*q*, Me_2CH); 43.16, 43.26, 43.35, 43.45 (4*d*, Me_2CH); 55.23, 55.24 (2*q*, MeO); 58.0, 58.8 (2*t*, J(CP) = 15, OCH_2CH_2CN); 62.8, 63.0 (2*t*, C(5′)); 66.7 (*t*, $ArCH_2$); 71.2 and 71.8 (2*d*, J(CP) = 15), 77.4 and 77.9 (2*d*, J(CP) = 5), 84.0 and 84.3 (2*d*, C(2′), C(3′), C(4′)); 86.7, 86.8 (2*s*, Ar_2CPh); 87.1, 87.2 (2*d*, C(1′)); 94.8, 94.9 (2*t*, OCH_2O); 113.2 (*d*, arom. C); 117.4, 117.7 (2*s*, CN); 123.3, 124.6 (2*s*, C(5)); 127.0 (*s*, arom. C); 127.8, 128.1, 128.2, 128.3, 128.4, 128.9, 130.1, 130.2 (8*d*, arom. C); 132.78, 133.76, 133.81, 133.84, 133.88 (5*d*, arom. C); 135.56, 135.61, 135.66 (3*s*, arom. C); 142.1 (*d*, C(8)); 144.4, 144.5, 146.7 (3*s*, arom. C); 149.4 (*s*, C(4)); 151.47, 151.51 (2*s*, C(6)); 152.7 (*d*, C(2)); 158.60, 158.62 (2*s*, arom. C)); 164.3 (*s*, CO). ^{31}P-NMR (202 MHz, $CDCl_3$): 150.9, 151.1. FAB-MS (NOBA, pos. mode): 1039 (54, $[M + H]^+$), 800 (23), 303 (100), 239 (20).

*9-{5′-O-(4,4′-Dimethoxytrityl)-2′-O-{[(2-nitrobenzyl)oxy]methyl}-β-*L*-ribofuranosyl}*N^2*-isobutyrylguanine 3′-[(2-Cyanoethyl) Diisopropylphosphoramidite]* (**32**)[18]. As described for **28**, with **22** (4.1 g, 5 mmol), CH_2Cl_2 (20 ml), (i-Pr)$_2$NEt (1.7 ml, 10 mmol), and (i-Pr)$_2$NPCl(OCH_2CH_2CN) (1.42 g, 6 mmol). CC (silica gel (50 g), hexane/AcOEt 1:1 (+ 2% Et_3N) → hexane/AcOEt 1:9 (+ 2% Et_3N)) afforded **32** (4.79 g, 94%). Colorless foam (mixture of diastereoisomers). TLC (hexane/AcOEt 2:3): R_f 0.15. UV (MeCN): 275 (15000), 272 (14500), 257 (sh, 19700), 248 (sh, 22000), 236 (26000), 226 (24400). IR ($CHCl_3$): 3367*w*, 3200*w*, 2967*m*, 2933*m*, 1694*s*, 1606*s*, 1555*m*, 1528*m*, 1505*m*, 1461*m*, 1406*m*, 1367*m*, 1339*m*, 1300*m*, 1122*w*, 1089*m*, 1038*m*, 978*m*, 917*w*, 828*w*. ^{1}H-NMR (500 MHz, $CDCl_3$): 0.72, 0.90, 0.93, 0.99, 1.02 1.16, 1.17, 1.20 (8*d*, J = 6.8, 18 H, Me_2CH); 1.62, 1.93 (2*sept.*, J = 6.9, Me_2CHCO); 2.76 (*m*, 2 H, OCH_2CH_2CN), 3.45–3.67 (*m*, 4 H, Me_2CH, H–C(5′)); 3.755, 3.759, 3.762, 3.766 (4*s*, 6 H, MeO); 3.94–4.24 (*m*, 2 H, OCH_2CH_2CN); 4.21, 4.32 (2 br. *s*, 1 H, H–C(4′)); 4.58 (*m*, 1 H, H–C(3′)); 4.71–4.94 (*m*, 4 H, OCH_2O, $ArCH_2$); 5.16, 5.32 (2*dd*, J = 4.7, 7.6, 1 H, H–C(2′)); 5.87, 6.00 (2*d*, J = 7.6, 1 H, H–C(1′)); 6.77–6.81 (*m*, 4 arom. H); 7.19–7.54 (*m*, 12 arom. H); 7.77, 7.81 (2*s*, 1 H, H–C(8)); 8.00 (*m*, 1 arom. H); 7.65, 8.15 (2 br. *s*, 1 H, NH–C(2)); 11.68 (br. *s*, 1 H, H–N(1)). ^{13}C-NMR (125 MHz, $CDCl_3$): 18.38, 18.43, 18.58, 18.82 (4*q*, Me_2CHCO); 20.1, 20.3 (2*t*, J(CP) = 7, OCH_2CH_2CN); 24.49, 24.55, 24.59, 24.64 (4*q*, Me_2CH); 35.9, 36.0 (2*d*, Me_2CHCO); 43.1, 43.3 (2*d*, J(CP) = 12, Me_2CH); 55.29 (*q*, MeO); 58.1 (*t*, J(CP) = 6, OCH_2CH_2CN); 59.1 (*t*, J(CP) = 15, OCH_2CH_2CN); 63.4 (*t*, C(5′)); 67.0, 67.1 (2*t*, $ArCH_2$); 71.0 and 71.7 (2*d*, J(CP) = 15), 79.6 (*d*), 84.0 and 84.3 (2*d*, C(2′), C(3′), C(4′)); 85.6, 86.4 (2*d*, C(1′)); 86.7, 86.9 (2*s*, Ar_2CPh); 95.1, 95.6 (2*t*, OCH_2O); 113.3, 113.4 (2*d*, arom. C); 117.3, 118.0 (2*s*, CN); 121.8, 122.5 (2*s*, C(5));

124.6, 127.2, 128.0, 128.1, 128.2, 128.4, 128.5, 130.0, 130.1, 133.4, 133.5 (11*d*, arom. C); 135.5, 135.6, 135.7, 136.1 (4*s*, arom. C); 137.7, 139.0 (2*d*, C(8)); 144.5, 144.8, 146.8, 147.0 (4*s*, arom. C); 147.2, 147.4 (2*s*, C(4)); 148.0, 148.3 (2*s*, C(2)); 155.2, 155.3 (2*s*, C(6)); 158.8 (*s*, arom. C); 178.4, 178.6 (2*s*, CO). ^{31}P-NMR (202 MHz, $CDCl_3$): 150.5, 150.8. FAB-MS (NOBA, pos. mode): 1021 (86, $[M + H]^+$), 800 (24), 303 (100).

N^4-*Benzoyl-1-{5'-O-(4,4'-Dimethoxytrityl)-3'-{[(2-nitrobenzyl)oxy]methyl}-β-*L*-ribofuranosyl}cytosine 2'-[(2-Cyanoethyl) Diisopropylphosphoramidite]* (**43**). As described for **28**, with **25** (1.65 g, 1.9 mmol), CH_2Cl_2 (7 ml), $(i\text{-}Pr)_2NEt$ (0.65 ml, 3.8 mmol), and $(i\text{-}Pr)_2NPCl(OCH_2CH_2CN)$ (0.51 g, 2.4 mmol), CC (silica gel (30 g), hexane/AcOEt 4:1 (+ 2% Et_3N) → hexane/AcOEt 1:1 (+ 2% Et_3N)) afforded **43** (1.80 g, 91%). Colorless foam (mixture of diastereoisomers). TLC (hexane/AcOEt 2:3): R_f 0.30, 0.25. IR ($CHCl_3$): 3400*w*, 2956*m*, 2923*m*, 1700*m*, 1661*s*, 1607*s*, 1550*m*, 1528*m*, 1478*s*, 1385*m*, 1300*m*, 1102*m*, 1033*m*, 978*m*, 826*w*. ^{1}H-NMR (500 MHz, $CDCl_3$): 1.17, 1.18, 1.23 (3*d*, J = 6.9, 12 H, Me_2CH); 2.59–2.77 (*m*, 2 H, OCH_2CH_2CN); 3.47 (*dt*, J = 2.3, 11.2, 2 H, OCH_2CH_2CN); 3.66 (*m*, 2 H, Me_2CH); 3.80, (*s*, 6 H, MeO); 3.83 (*m*, 1 H, H–C(5')); 3.94–4.07 (*m*, 1 H, H'–C(5')); 4.33, 4.37 (2*dt*, J = 8.7, 2.0, 1 H, H–C(4')); 4.50 (*m*, 1 H, H–C(3')); 4.58 (*m*, 1 H, H–C(2')); 4.73, 4.78, 4.85, 4.94 (4*d*, J = 7.0, 2 H, $ArCH_2$); 4.88 (*s*, 1 H, OCH_2O); 4.89, 4.98 (2*d*, J = 15.0, 1 H, OCH_2O); 6.129, 6.133 (2*s*, 1 H, H–C(1')); 6.80–6,84 (*m*, 4 arom. H); 7.22–7.70 (*m*, 15 arom. H); 7.87 (*m*, 2 arom. H); 8.05 (*m*, 1 arom. H); 8.64 (br. *s*, 2 H, NH–C(4), H–C(6)). ^{13}C-NMR (125 MHz, $CDCl_3$): 20.2, 20.3 (2*t*, J(CP) = 8, OCH_2CH_2CN); 24.44, 24.48, 24.51, 24.53, 24.56, 24.63, 24.65, 24.70 (8*q*, Me_2CH); 43.4, 43.6 (2*d*, J(CP) = 13, Me_2CH); 55.2 (*q*, MeO); 58.5, 58.6 (2*t*, J(CP) = 20, OCH_2CH_2CN); 60.7, 60.8 (2*t*, C(5')); 67.2, 67.3 (2*t*, $ArCH_2$); 71.6 (*d*, J(CP) = 5); 74.5 and 75.7 (2*d*, J(CP) = 14); 80.9 and 81.0 (2*d*, C(2'), C(3'), C(4')); 72.1 (*d*, C(3')); 87.1 (*s*, Ar_2CPh); 90.7 (*d*, C(1')); 94.4, 94.7 (2*t*, OCH_2O); 96.4 (br. *d*, C(5)); 113.28, 113.30 (2*d*, arom. C); 117.9, 118.3 (2*s*, CN); 124.7, 124.8, 127.3, 127.5, 128.0, 128.1, 128.2, 128.3, 128.4, 128.7, 129.0, 130.1, 130.2, 133.1 (14*d*, arom. C); 133.1, 133.7, 133.8, 134.1, 134.3, 135.1, 135.2, 135.3 (8*s*, arom. C); 143.8, 143.9 (2*s*, arom. C); 145.1 (br. *d*, C(6)); 147.1 (*s*, arom. C); 154.8 (*s*, C(2)); 158.8 (*s*, arom. C); 162.2 (*s*, CO); 165.8 (*s*, C(4)). ^{31}P-NMR (202 MHz, $CDCl_3$): 150.1, 151.3. FAB-MS (NOBA, pos. mode): 1015 (11, $[M + H]^+$), 914 (51), 797 (55), 303 (100).

*1-{5'-O-(4,4'-Dimethoxytrityl)-3'-O-{[(2-nitrobenzyl)oxy]methyl}-β-*L*-ribofuranosyl}uracil 2'-[(4-Nitrophenyl) Heptanedioate]* (**33**). A soln. of **23** (0.36 g, 0.5 mmol) in pyridine (3 ml) was added slowly (3 h) to a soln. of bis(4-nitrophenyl) pimelate (1.6 g, 4 mmol) and DMAP (65 mg, 0.5 mmol) in pyridine (5 ml). After stirring for 14 h at r.t., the mixture was evaporated, treated twice with toluene (10 ml), evaporated again, and subjected to CC (silica gel (15 g), hexane/AcOEt 1:1 → hexane/AcOEt 1:4): **33** (0.39 g, 80%). Colorless foam. TLC (hexane/AcOEt 3:7): R_f 0.40. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.46 (*m*, 1 CH_2); 1.65–1.82 (*m*, 2 CH_2); 2.44 (*m*, 1 CH_2); 2.61 (*t*, J = 7.2, 1 CH_2); 3.44 (*dd*, J = 2.5, 11.2, H–C(5')); 3.67 (*dd*, J = 2.2, 11.2, H'–C(5')); 3.76, 3.77 (2*s*, 2 MeO); 4.20 (*td*, J = 2.5, 6.2, H–C(4')); 4.65 (*t*, J = 5.8, H–C(3')); 4.69, 4.84 (2*d*, J = 7.1, 2 H, $ArCH_2O$); 4.78, 4.85 (2*d*, J = 15.2, OCH_2O); 5.27 (*d*, J = 8.1, H–C(5)); 5.42 (*dd*, J = 3.7, 5.0, H–C(2')); 6.12 (*d*, J = 3.7, H–C(1')); 6.76–6.81 (*m*, 4 arom. H); 7.18–7.34 (*m*, 11 arom. H); 7.44 (*m*, 1 arom. H); 7.56–7.67 (*m*, 2 arom. H); 7.87 (*d*, J = 8.1, H–C(6)); 8.07–8.10 (*m*, 1 arom. H); 8.12–8.27 (*m*, 2 arom. H); 8.61 (br. *s*, H–N(2)). ^{13}C-NMR (75 MHz, $CDCl_3$): 24.3, 24.4, 28.4, 33.7, 34.1 (5*t*, CH_2); 55.3 (*q*, MeO); 61.8 (*t*, C(5')); 67.4 (*t*, $ArCH_2$); 73.2, 74.4, 82.1 (3*d*, C(2'), C(3'), C(4')); 87.3 (*s*, Ar_2CPh); 87.4 (*d*, C(1')); 95.5 (*t*, OCH_2O); 102.7 (*d*, C(5)); 113.5 (*d*, arom. C); 122.7, 125.1, 125.4, 127.5, 128.2, 128.5, 128.7, 130.4, 130.5, 134.0 (10*d*, arom. C); 134.4, 135.1, 135.2 (3*s*, arom. C); 140.1 (*d*, C(6)); 144.3, 147.3 (2*s*, arom. C); 150.2 (*s*, C(2)); 155.7 (*s*, arom. H); 159.1 (*s*, MeO–*C*); 163.1 (*s*, C(4)); 171.4, 172.6 (2*s*, CO). FAB-MS (NOBA, pos. mode): 975 (50, $[M + H]^+$), 897 (14), 867 (15), 810 (20), 303 (100), 154 (20), 136 (20).

*1-{5'-O-(4,4'-Dimethoxytrityl)-3'-O-{[(2-nitrobenzyl)oxy]methyl}-β-*L*-ribofuranosyl}thymine 2'-[(4-Nitrophenyl) Heptanedioate]* (**34**). As described for **33**, with **24** (0.36 g, 0.5 mmol): **34** (0.39 g, 78%). Colorless foam. TLC (hexane/AcOEt 2:3): R_f 0.35. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.22 (*s*, Me–C(5)); 1.46 (*m*, 1 CH_2); 1.65–1.82 (*m*, 2 CH_2); 2.44 (*m*, 1 CH_2); 2.61 (*t*, J = 7.2, 1 CH_2); 3.35 (*dd*, J = 2.5, 11.2, H–C(5')); 3.62 (*dd*, J = 2.2, 11.2, H'–C(5')); 3.76, 3.77, 3.78 (3*s*, 2 MeO); 4.21 (*td*, J = 2.5, 5.2, H–C(4')); 4.65 (*t*, J = 5.3, H–C(3')); 4.72, 4.82 (2*d*, J = 6.8, $ArCH_2O$); 4.83, 4.85 (2*d*, J = 16, OCH_2O); 5.48 (*t*, J = 5.1, H–C(2')); 6.18 (*d*, J = 5.0, H–C(1')); 6.77–6.81 (*m*, 4 arom. H); 7.23–7.44 (*m*, 13 arom. H); 7.56–7.64 (*m*, 2 arom. H); 8.05–8.10 (*m*, 1 arom. H); 8.13–8.27 (*m*, 2 arom. H); 8.64 (br. *s*, H–N(2)). ^{13}C-NMR (75 MHz, $CDCl_3$): 11.6 (*q*, *Me*–C(5)); 24.3, 28.4, 33.7, 34.1 (4*t*, CH_2); 55.4 (*q*, MeO); 62.6 (*t*, C(5')); 67.3 (*t*, $ArCH_2$); 74.0, 74.2, 82.5 (3*d*, C(2'), C(3'), C(4')); 86.8 (*d*, C(1')); 87.3 (*s*, Ar_2CPh); 95.2 (*t*, OCH_2O); 111.8 (*s*, C(5)); 113.5, 115.9 (*d*, arom. C); 122.7, 125.1, 125.4, 126.4, 127.5, 128.2, 128.5, 128.8, 130.4, 133.9 (10*d*, arom. C); 134.3, 135.3, 135.4, 135.7 (4*s*, arom. C); 144.3 (*d*, C(6)); 145.5, 147.4 (2*s*, arom. C); 150.4 (*s*, C(2)); 155.7 (*s*, arom. H); 159.1 (*s*, MeO–*C*); 163.8 (*s*, C(4)); 171.4, 172.8 (2*s*, CO). FAB-MS (NOBA, pos. mode): 989 (60, $[M + H]^+$), 303 (100).

N^4-*Benzoyl-1-{5'-O-(4,4'-dimethoxytrityl]-3'-O-{[(2-nitrobenzyl)oxy]methyl}-β-*L*-ribofuranosyl}cytosine 2'-[(4-Nitrophenyl Heptanedioate]* (**35**). As described for **33**, with **25** (0.41 g, 0.5 mmol). CC (silica gel (15 g),

hexane/AcOEt 1:1 → hexane/AcOEt 1:3) afforded **35** (0.43 g, 80%). Colorless foam. TLC (hexane/AcOEt 3:7): R_f 0.35. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.46 (*m*, 1 CH_2); 1.65–1.81 (*m*, 2 CH_2); 2.45 (*td*, *J* = 6.8, 2.5, 1 CH_2); 2.60 (*t*, *J* = 7.2, 1 CH_2); 3.50 (*dd*, *J* = 2.5, 10.9, H–C(5')); 3.79 (*s*, 2 MeO); 3.80 (*m* (partially hidden), H'–C(5')); 4.28 (br. *dt*, *J* = 8.1, 2.5, H–C(4')); 4.60, 4.84 (2*d*, *J* = 7.2, 2 H, ArCH_2O); 4.64 (*dd*, *J* = 4.7, 8.1, H–C(3')); 4.72, 4.79 (2*d*, *J* = 15.2, OCH_2O); 5.54 (*dd*, *J* = 1.6, 4.7, H–C(2')); 6.18 (*d*, *J* = 1.5, H–C(1')); 6.81 (*d*, *J* = 8.7, 4 arom. H); 6.95–7.66 (*m*, 15 arom. H); 7.86–7.89 (*m*, 2 arom. H); 8.06–8.13 (*m*, 2 arom. H); 8.21–8.26 (*m*, 2 arom. H); 8.51 (*d*, *J* = 7.5, H–C(6)); 9.04 (br. *s*, NH–C(4)). ^{13}C-NMR (75 MHz, $CDCl_3$): 24.3, 24.4, 28.3, 33.7, 34.1 (5*t*, CH_2); 55.3 (*q*, MeO); 61.1 (*t*, C(5')); 67.4 (*t*, ArCH_2); 72.1, 74.4, 81.6 (3*d*, C(2'), C(3'), C(4')); 87.4 (*s*, Ar_2CPh); 89.4 (*d*, C(1')); 95.1 (*t*, OCH_2O); 97.2 (*d*, C(5)); 113.4, 116.1 (2*d*, arom. C); 122.7, 125.1, 125.4, 126.4, 127.6, 127.8, 128.3, 128.4, 128.6, 128.7, 129.3, 130.4, 130.5 (13*d*, arom. C); 133.2 (*s*, arom. C); 133.5, 134.0 (2*d*, arom. C); 134.5, 135.2 (2*s*, arom. C); 135.3 (*d*, C(6)); 141.0, 144.0, 145.0, 145.5, 147.2 (5*s*, arom. C); 155.8 (*s*, C(2)); 159.1 (*s*, MeO–*C*); 162.8 (*s*, CO); 163.5 (*s*, C(4)); 171.4, 172.3 (2*s*, CO). FAB-MS (NOBA, pos. mode): 1078 (25, $[M + H]^+$), 711 (10), 303 (100).

*N^6-Benzoyl-{5'-O-(4,4'-dimethoxytrityl)-3'-O-{[(2-nitrobenzyl)oxy]methyl}-β-*L*-ribofuranosyl}adenine 2'-[(4-Nitrophenyl) Heptanedioate]* (**36**). As described for **33**, with **26** (0.42 g, 0.5 mmol): **36** (0.40 g, 72%). Colorless foam. TLC (hexane/AcOEt 3:7): R_f 0.30. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.43 (*m*, 1 CH_2); 1.65 (*m*, 1 CH_2); 1.73 (*m*, 1 CH_2); 2.42 (*t*, *J* = 7.5, 1 CH_2); 2.58 (*t*, *J* = 7.5, 1 CH_2); 3.38 (*dd*, *J* = 4.0, 10.9, H–C(5')); 3.57 (*dd*, *J* = 3.4, 10.6, H'–C(5')); 3.75 (*s*, 2 MeO); 4.34 (br. *q*, *J* ≈ 4, H–C(4')); 4.82, 4.86 (2*d*, *J* = 6.8, ArCH_2O); 4.91 (*s*, OCH_2O); 4.93 (*t* (partially hidden), *J* ≈ 5, H–C(3')); 5.95 (*t*, *J* = 5.0, H–C(2')); 6.28 (*d*, *J* = 4.7, H–C(1')); 6.75 (*d*, *J* = 8.1, 4 arom. H); 7.20–7.70 (*m*, 16 arom. H); 7.99–8.24 (*m*, 6 arom. H); 8.25 (*s*, H–C(2)); 8.75 (*s*, H–C(8)); 9.02 (br. *s*, NH–C(6)). ^{13}C-NMR (75 MHz, $CDCl_3$): 24.2, 28.3, 33.6, 34.0 (4*t*, CH_2); 55.3 (*q*, MeO); 62.7 (*t*, C(5')); 67.2 (*t*, ArCH_2); 74.3, 74.5, 82.8 (3*d*, C(2'), C(3'), C(4')); 86.8 (*s*, Ar_2CPh); 86.9 (*d*, C(1')); 95.2 (*t*, OCH_2O); 113.4 (*d*, arom. C); 122.7 (*s*, C(5)); 125.0, 125.4, 126.3, 127.2, 128.1, 128.4, 128.7, 129.1, 130.3 (9*d*, arom. C); 133.1 (*d*, arom. C); 133.8 (*s*, arom. C); 134.1 (*d*, arom. C); 134.5, 135.7 (2*s*, arom. C); 141.9 (*d*, C(8)); 144.5 (*s*, arom. C); 147.2 (*s*, arom. C); 149.9 (*s*, C(4)); 151.8 (*s*, C(6)); 153.2 (*d*, C(2)); 155.7 (*s*, arom. C); 158.9 (*s*, MeO–*C*); 164.9, 171.4, 172.7 (3*s*, CO). FAB-MS (NOBA, pos. mode): 1102 (100, $[M + H]^+$), 937 (17), 798 (11), 303 (97), 240 (16), 154 (23), 137 (40), 105 (23).

*9-{5'-O-(4,4'-Dimethoxytrityl)-N^2-isobutyryl-2'-O-{[(2-nitrobenzyl)oxy]methyl}-β-*L*-ribofuranosyl}guanine 3'-[(4-Nitrophenyl) Heptanedioate]* (**37**). As described for **33**, with **22** (0.41 g, 0.5 mmol): **37** (0.41 g, 76%). Colorless foam. TLC (hexane/AcOEt 3:7): R_f 0.15. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.71, 0.90 (2*d*, *J* = 6.9, Me_2CH); 1.53 (*m*, 1 CH_2); 1.73 (*m*, 1 CH_2); 1.82 (*m*, 1 CH_2); 2.45 (*m*, 1 CH_2); 2.65 (*t*, *J* = 7.5, 1 CH_2); 3.16 (*dd*, *J* = 2.8, 10.6, H–C(5')); 3.52 (*dd*, *J* = 1.9, 10.6, H'–C(5')); 3.75, 3.77 (2*s*, 2 MeO); 4.26 (br. *s*, H–C(4')); 4.58, 4.73 (2*d*, *J* = 15.0, OCH_2O); 4.71, 4.89 (2*d*, *J* = 7.1, ArCH_2O); 5.49 (*dd*, *J* = 5.3, 7.8, H–C(2')); 5.61 (*dd*, *J* = 1.6, 5.3, H–C(3')); 5.84 (*d*, *J* = 7.8, H–C(1')); 6.77–6.82 (*m*, 4 arom. H); 7.20–7.54 (*m*, 14 arom. H); 7.78 (*s*, H–C(8)); 7.96–7.99 (*m*, 1 arom. H); 8.24–8.27 (*m*, 2 arom. H); 11.69 (br. *s*, NH–C(2)). ^{13}C-NMR (75 MHz, $CDCl_3$): 18.4, 18.6 (2*q*, Me_2CH); 24.3, 24.5, 28.4, 33.9, 34.2 (5*t*, CH_2); 36.1 (*d*, Me_2CH); 55.4 (*q*, MeO); 63.7 (*t*, C(5')); 67.0 (*t*, ArCH_2); 71.6, 77.0, 82.4 (3*d*, C(2'), C(3'), C(4')); 86.4 (*d*, C(1')); 86.8 (*s*, Ar_2C); 95.5 (*t*, OCH_2O); 113.6 (*d*, arom. C); 122.4 (*s*, C(5)); 122.7, 124.9, 125.4, 127.5, 128.1, 128.3, 128.8, 130.2, 130.3 (9*d*, arom. C); 133.4 (*d*, arom. C); 133.9, 135.7, 136.1 (3*s*, arom. C); 139.0 (*d*, C(8)); 145.0, 145.6, 147.0 (3*s*, arom. C); 147.3 (*s*, C(4)); 148.3 (*s*, C(2)); 155.3 (*s*, C(6)); 155.7 (*s*. arom. C); 159.2 (*s*, MeO–*C*); 171.6, 172.9, 178.5 (3*s*, CO). FAB-MS (NOBA, pos. mode): 1084 (64, $[M + H]^+$), 303 (100).

Procedure for the Immobilization of the Nucleoside 2'- or 3'-[(4-Nitrophenyl) Hexanedioates] on Solid Support. To a soln. of 0.25 mmol of the nucleosides 2' or 3'-[(4-nitrophenyl) hexanedioate] **33**–**37** in DMF (8 ml) were added 2 g of 'long-chain-alkylamino-controlled pore glass' (*Sigma*) and then (i-Pr)$_2$NEt (0.8 ml). The mixture was shaken 20 h at r.t. After filtration, the solid was washed with DMF and CH_2Cl_2, dried *in vacuo*, suspended in pyridine (5 ml) and Ac_2O (3 ml), and shaken 2 h at r.t. After filtration, the solid was washed with DMF and CH_2Cl_2 and dried *in vacuo*. Photometric determinations[11]) revealed the following loading of the solid supports: **38** (U nucleoside) 51 μmol/g, **39** (T nucleoside) 44 μmol/g, **40** (C nucleoside) 50 μmol/g, **41** (A nucleoside) 48 μmol/g, and **42** (G nucleoside) 43 μmol/g.

Procedure for the Synthesis of Ribonucleic Acids. a) *Chain Elongation, 1.5-μmol Scale.* Detritylation: 1.2 min (3% $CH_2ClCOOH$ in $(CH_2Cl)_2$). Coupling: 12 min (0.16 ml of 0.06M phosphoramidite soln. + 0.36 ml of 0.35M 1*H*-tetrazole/0.15M 5-(4-nitrophenyl)-1*H*-tetrazole soln. in MeCN). Capping and oxidation under standard conditions [42].

b) *Chain Elongation, 10-μmol Scale.* Detritylation: 2.5 min (3% $CH_2ClCOOH$ in $(CH_2Cl)_2$). Coupling: 20 min (0.32 ml of 0.06M phosphoramidite soln. + 0.6 ml of 0.35M 1*H*-tetrazole/0.15M 5-(4-nitrophenyl)-1*H*-tetrazole soln. in MeCN). Capping and oxidation under standard conditions [42].

c) *Deprotection and Purification* (*'trityl-off'*). The solid support was suspended in conc. aq. NH_3 soln./MeOH 3:1 (4 ml) and heated 24 h to 50°. After filtration, the soln. was evaporated. The residue was taken up in aq. buffer soln. (10 mM sodium citrate/10 mM sodium phosphate (pH 3.9); 50–200 ml) and transferred to a *Pyrex* bottle (diameter 3–5 cm), and then the same volume of $(CH_2Cl)_2$ was added. The gently stirred two-phase system was purged with Ar, the back and the sides of the bottle wrapped in Al-foil and the upper phase was irradiated with a slide projector placed in a distance of 2 cm. When HPLC analysis of samples (0.1 ml) taken showed complete deprotection (5–9 h), the yellow org. phase was removed and the aq. phase neutralized with 1M NaOH. After evaporation, the crude products were purified by HPLC and desalted.

d) *Deprotection and Purification* (*'trityl-on'*). After ammonolysis and evaporation, the trityl-containing products were isolated by reversed-phase HPLC and desalted. The materials were taken up in H_2O/HCOOH 1:1 (10 ml). After 5 min at r.t., the solvents were evaporated and the residues subjected to photolysis. The following steps were as described above.

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