Nucleotides

Part LXVIII[1])

Acetals as New 2′-*O*-Protecting Functions for the Synthesis of Oligoribonucleotides: Synthesis of Monomeric Building Units and Oligoribonucleotides

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For the efficient synthesis of oligoribonucleotides by the 5′-*O*-(4,4′-dimethoxytrityl) phosphoramidite approach, the 2′-*O*-[1-(benzyloxy)ethyl]acetals **56**–**67** were investigated. Studies with the 2′-*O*-[1-(benzyloxy)-ethyl]-5′-*O*-(dimethoxytrityl)ribonucleoside 3′-phosphoramidites **56**–**59** gave, however, only reasonable results. The oligoribonucleotides obtained showed some impurities since the acid stabilities of the acetal and dimethoxytrityl functions are too close to guarantee a high selectivity. A combination of new acid-labile *protected* 2′-*O*-protecting groups with the 2-(4-nitrophenyl)ethyl/[2-(4-nitrophenyl)ethoxy]carbonyl (npe/npeoc) strategy for base protection was more successful. The synthesis and physical properties of the monomeric building units and their intermediates **8**–**67** and the conditions for the automated generation of homo- and mixed oligoribonucleotides is described. The new 2′-acetal protecting group could be cleaved off in a two step procedure and was designed for levelling their stability with regard to the attached nucleobase as well. Therefore, we used the 1-{{3-fluoro-4-{{[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}benzyl}oxy}ethyl (fnebe) moiety for the protection of 2′-OH of uridine, and for that of 2′-OH of A, C, and G, the 1-{{4-{{[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}benzyl}oxy}ethyl (nebe) residue. After selective deprotection by β-elimination induced by a strong organic base like DBU, the remaining activated acetal was hydrolyzed under very mild acidic protic conditions, which reduced 2′-3′ isomerization and chain cleavage. Also storage, handling, and purification of the chemically and enzymatically sensitive oligomers was simplified by this approach.

1. Introduction. – The chemical synthesis of oligoribonucleotides is still a big challenge due to the fact that a perfect combination of compatible protecting groups for the nucleobase, the sugar moiety, and the phosphate function has not yet been found. There are practical solutions of the problem leading to longer RNA sequences [2–6] since, for 2′-OH protection, the **tbds** ((*tert*-butyl)dimethylsilyl group) [7–9] or the **fpmp** (1-(2-fluorophenyl)-4-methoxypiperidin-4-yl) [6][10] residue can be used. Still, some side reactions [10][11] have to be overcome, especially when other blocking groups such as the 2-nitrobenzyl (**nbn**) [12], the dianisoyltrichloroethyl (**date**) [13], the 4,4′-dinitrobenzhydryl (**dnbh**) [14], the [2-(4-nitrophenyl)ethyl]sulfonyl (**npes**) [15], or the acetal functions tetrahydro-2*H*-pyran-2-yl (**thp**) [16], tetrahydro-4-methoxy-2*H*-pyran-2-yl (**mthp**) [17], [(trimethylsilyl)ethoxy]ethyl (**see**) [18], 3-methoxy-1,5-bis(methoxycarbonyl)pentan-3-yl (**mdmp**) [19–21], 1-alkoxyethyl- and 1-(2-chloroethoxy)ethyl (**cee**) [22] are applied.

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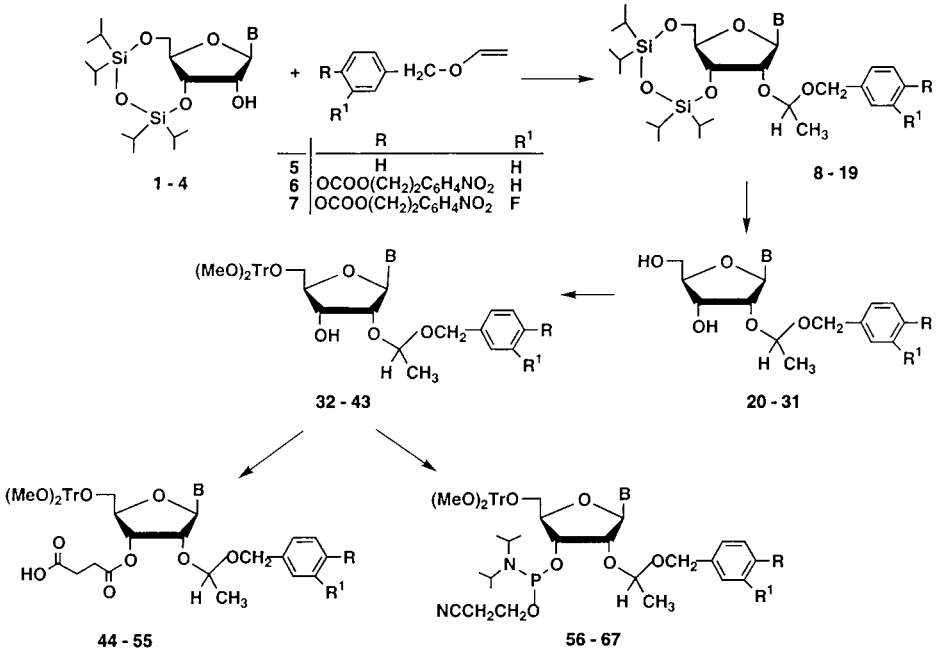
In our previous publication [23], we reported about the synthesis of new 2′-acetal-protected uridine building units and their relative acid stability. From the kinetic data, we were able to select a set of benzyl acetals that possess the stabilities needed to protect the 2′-OH function during synthesis and that can be cleaved off under very mild acidic conditions thereafter. First synthetic tests towards the machine-aided assembly of oligoribonucleotides by the well-established 4,4′-dimethoxytrityl/2-(4-nitrophenyl)-ethyl/[2-(4-nitrophenyl)ethoxy]carbonyl ($(MeO)_2$Tr/npe/npeoc) approach [24–26] were done with the uridine phosphoramidites 2′-O-protected by the 1-{{4-{{[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}benzyl}oxy}ethyl residue (**nebe**) and by the corresponding 3-fluoro residue (**fnebe** = 1-{{3-fluoro-4-{{[2-(4-nitrophenyl)ethoxy]carbonyl}-oxy}benzyl}oxy}ethyl).

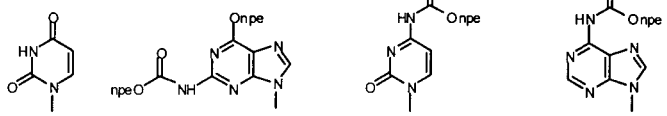
An overview of the synthesis steps and all monomeric building units is shown in the *Scheme*. The advantage of this new type of protecting group is the two-step procedure for the liberation of the 2′-OH function. The first step goes parallel with the cleavage of the base-labile protecting groups at the P-atom (cyanoethoxy) and the nucleobase-blocking groups (npe and npeoc) by a strong base like DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) in MeCN. In the presence of the 2′-acetal protecting group, DBU induces β-elimination of the npeoc residue, the acetal protecting group itself remaining untouched. Therefore, on the solid support, only oligonucleotides with the 1-[(4-hydroxybenzyl)oxy]ethyl (**hboe**) residue still attached at the 2′-*O*-position are present and covalently bound *via* a succinate bridge, while all deprotection products can be washed away. Hydrolysis with aqueous ammonia leads to 2′-*O*-protected oligoribonucleotides free of contamination and without other cleavage products. After standard workup procedures, these partially protected oligomers can be stored for several months at $-20°$ and are fully deprotected just before their use with highly diluted AcOH. A similar strategy was established by others involving the 2′-*O*-bis(2-acetoxyethoxy)methyl (**ace**) orthoester function in combination with a 5′-*O*-alkoxy-bis[(trimethylsilyl)oxy]silyl group [27] and the 2′-*O*-[(triisopropylsilyl)oxy]methyl (**tom**) group [28][29], which is structurally related to the tbdms group and can also be cleaved off by fluoride ions, but which is more stable towards 2′ → 3′ phosphodiester migration due to the acetal nature of the protecting group. Despite the mild cleavage conditions, the use of fluoride salts still leads to additional workup procedures, which is not necessary in the protocols we have developed in our strategy.

2. Synthesis of the Monomers. – The monomeric building units were synthesized by protocols more or less analogous to the procedures described before [23] (*Scheme*). Starting from the corresponding 3′,5′-*O*-silyl-protected uridine or 3′,5′-*O*-silyl/npe and/or npeoc-protected guanosine, cytidine, and adenosine derivatives **1**–**4**, the corresponding acetal protecting groups derived from **5**–**7** were introduced by an acid-catalyzed reaction, giving **8**–**19** in yields of 65–95%. Fluoride-ion-induced desilylation liberating the 3′-OH and 5′-OH groups (→ **20**–**31**) was followed by selective reaction of the primary OH function with 4,4′-dimethoxytrityl chloride in toluene/pyridine to give **32**–**43** in very good yields. Then, either the corresponding succinate derivatives **44**–**55** or the phosphoramidites **56**–**67** were synthesized by standard procedures in expectedly satisfying yields. All the different derivatives were characterized by TLC, HPLC, ^{1}H- or ^{19}F-NMR, and elementary analysis (see *Exper. Part*).

Scheme



	B	R	R^1				
1	U						
2	$^{npeoc}G^{npe}$						
3	C^{npeoc}						
4	A^{npeoc}						
8	U	H	H	20	32	44	56
9	$^{npeoc}G^{npe}$	H	H	21	33	45	57
10	C^{npeoc}	H	H	22	34	46	58
11	A^{npeoc}	H	H	23	35	47	59
12	U	OCOOnpe	H	24	36	48	60
13	U	OCOOnpe	F	25	37	49	61
14	$^{npeoc}G^{npe}$	OCOOnpe	H	26	38	50	62
15	$^{npeoc}G^{npe}$	OCOOnpe	F	27	39	51	63
16	C^{npeoc}	OCOOnpe	H	28	40	52	64
17	C^{npeoc}	OCOOnpe	F	29	41	53	65
18	A^{npeoc}	OCOOnpe	H	30	42	54	66
19	A^{npeoc}	OCOOnpe	F	31	43	55	67

B = 

3. Simulated Synthesis on Solid Support. – First, we synthesized a series of oligoribonucleotides (*Table 1*) starting with the 2′-*O*-[1-(benzyloxy)ethyl]nucleoside 3′-phosphoramidites **56**–**59**, and noticed, after deprotection and HPLC analysis, that the oligomers are not pure enough to meet our standards. To investigate the stability of the 2′-acetal protecting groups, in general, under standard synthesis conditions, we simulated the condensation cycle with the 2′-*O*-protected uridine monomer **37** attached to the resin LCAMA-CPG *via* a 3′-succinate linker. Thus, 0.2 μmol of the corresponding loaded solid support was first treated several times under the detritylation conditions shown in *Table 2*, and second, optionally, a DBU cleavage step was implemented to remove the npeoc residue from the 2′-protecting group. After standard ammonia cleavage and workup the resulting reaction products were analyzed by reversed-phase HPLC. The results shown in *Fig. 1*,*a* and *b*, establish the detritylation of **25** (attached at the solid support) on $CHCl_2COOH$ treatment, and subsequent cleavage of **25** from the support and concomitant breaking of the 2-(4-nitrophenyl)ethyl carbonate bridge with formation of 2′-*O*-{1-[(3-fluoro-4-hydroxybenzyl)oxy]ethyl}uridine (**68**) and 2-(4-nitrophenyl)ethyl carbamate on DBU and NH_3 treatment. Thus,

Table 1. *Synthesis of Oligoribonucleotides Carrying Various 2′*-O-*Protecting Groups*

2′-*O*-Protected Sequence	Number of monomers	2′-*O*-Blocking group[a])
5′-UUU-3′	3	fnebe
5′-UUU U-3′	4	fnebe
5′-UUU UUU-3′	6	fnebe
5′-UUU UUU-3′	6	npee
5′-CCC CCC-3′	6	boe
5′-CCC CCC-3′	6	fnebe
5′-CCC CCC CCC C-3′	10	boe
5′-CCC CCC CCC C-3′	10	nebe
5′-CCC CCC CCC C-3′	10	fnebe
5′-AAA AAA AAA A-3′	10	boe
5′-AAA AAA AAA A-3′	10	nebe
5′-AAA AAA AAA A-3′	10	fnebe
5′-GGG GGG GGG G-3′	10	boe
5′-GGG GGG GGG G-3′	10	nebe
5′-GGG GGG GGG G-3′	10	fnebe
5′-GGA GA-3′	5	fnebe
5′-CGC GCG-3′	6	boe
5′-UAC CUA-3′	6	nebe + fnebe
5′-UAA UUU U-3′	7	nebe + fnebe
5′-CCU GCG AUG A-3′	10	boe
5′-AAA AAU UUU U-3′	10	boe
5′-UGC AUG CAU GCA-3′	12	nebe + fnebe
5′-UAA UCC UAA UUA UAA-3′	15	nebe + fnebe
5′-AGG GUA CAG GUG GCC GGC-3′	18	nebe + fnebe
5′-GCG GGG GUC CAU GGG GGU CG-3′	20	boe
5′-GGA GAG GUC UCC GGU UCG UCG AUU CCG GAC UCG ACC A-3′	37	boe nebe + fnebe

[a]) npee = 1-[2-(4-nitrophenyl)ethoxy]ethyl; boe = 1-(benzyloxy)ethyl; fnebe = 1-{{3-fluoro-4-{{[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}benzyl}oxy}ethyl; nebe = 1-{{4-{{[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}benzyl}oxy}-ethyl.

Table 2. *Timetable of the Synthesis Cycle Applied*

Synthesis step	Reagents	Time/s
Detritylation	1.3% $CHCl_2COOH$ in CH_2Cl_2	75 (2×20, 2×10, 3×5)
Washing	MeCN	45
Activation and condensation	0.075–0.1M phosphoramidite solution	700–1200
Capping	Ac_2O, 2,6-lutidine (= 2,6-dimethylpyridine) in THF, and 1-methyl-1*H*-imidazole in THF	30
Oxidation	0.05M I_2 solution in THF/H_2O/pyridine	30
Washing	MeCN	40
Total cycle time	inclusive all waiting steps	1020–1500 (= 17–25 min)

detritylation with $CHCl_2COOH$ and subsequent treatment with DBU and NH_3 led to very pure **68** (*Fig. 1,c*).

Two conclusions could be drawn from these experiments. First, there is no significant loss of the fnebe moiety, even after 10 repeats of the detritylation step. Second, when the stabilizing npeoc residue was cleaved off with DBU after the first $CHCl_2COOH$ treatment and then the $CHCl_2COOH$ treatment was repeated 9 further times, only little uridine (2–5%) was detectable (*Fig. 1,d*). This effect was expected and verified our results from kinetic studies in diluted protic acids, which established that the electron-donating effect of the aromatic 4-hydroxy function reduces the acid stability of the ketal significantly.

4. Synthesis of Oligoribonucleotides. – To optimize the reaction conditions in the synthesizer, the more easily accessible uridine phosphoramidite **61** was applied first. In

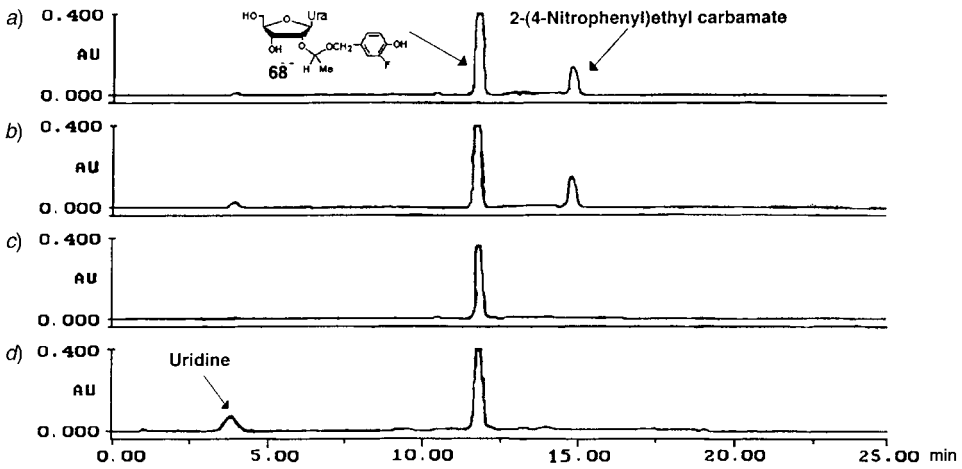


Fig. 1. *HPLC Traces of the crude reaction products from* **37** *after the following treatments:* a) *1 × $CHCl_2COOH/NH_3$*, b) *10 × $CHCl_2COOH/NH_3$*, c) *1 × $CHCl_2COOH/DBU/NH_3$, and* d) *1 × $CHCl_2COOH/DBU$, then 9 × $CHCl_2COOH/NH_3$*. Column: *LiChrospher 100 RP-18*, 4 × 125 mm) (*Merck*): gradient: 0% MeCN (0–2 min) 0–50% MeCN (2–32 min), 50% MeCN (32–40 min) in 0.1M $(Et_3NH)OAc$ (pH 7.0); flow rate: 1 ml/min.

comparison to a DNA-oligomer synthesis, the condensation time had to be increased significantly because of the steric hindrance by the bulky acetal moiety in the phosphoramidates. We compared the quality of hexameric and decameric homouridylates with regard to the condensation times, 600 s *vs.* 1200 s, and found no significant difference in purity by measuring the concentration of the dimethoxytrityl cation at 498 nm and by HPLC analysis of the 2′-acetal-protected oligomers.

Additional experiments showed that the same reaction conditions also worked well with the C, A, and G phosphoramidites **62**–**67**, leading to high average condensation yields of 97.8–99.1% with the pyrimidine, of 97.1–97.7% with the adenosine, and of 95.3–97.1% with the guanine building blocks, respectively. A large variety of homo- and mixed oligoribonucleotides (*Table 1*) were synthesized by the npe/npeoc approach, which turned out, after partial deprotection to the corresponding 2′-acetal derivatives, to be of very good quality.

Another very important outcome was the orthogonality of the 5′-*O*-(dimethoxytrityl) and the new 2′-acetal protecting groups. Therefore, the detritylation step was investigated thoroughly and in great detail. We found that 1.3–2% $CHCl_2COOH$ in CH_2Cl_2 worked best for fast and selective deprotection of the 5′-$(MeO)_2$Tr group without harming the nebe and the fnebe groups at all. However, to minimize undesired loss of the 2′-protecting group, it is absolutely necessary to use anhydrous reagents.

From these and other investigations (data not shown), we could also see that, in the case of the C, A, and G nucleosides, the nebe protecting group was more stable in acidic environment than in the case of the corresponding uridine. A similar observation was already made by *Reese et al.* [30] for the mthp blocking group. Such differences can be explained by the different nature of the nucleobases and their electronic influence, which is also the reason for the different stabilities of substituted acetals under acidic conditions, as demonstrated earlier [23].

In general, after workup and isolation of the crude 2′-acetal-protected oligomers, it was noticed that these products are rather lipophilic, which makes the usually applied 'trityl-on' adsorption-purification procedure to get rid of failure sequences less efficient compared to the DNA series. Another characteristic of these racemic acetal protecting groups is peak broadening, observed mainly for poly(G) strands when reversed-phase HPLC was applied for analysis. We isolated, therefore, pure diastereoisomeric monomers, repeated the synthesis, and found the expected sharp peaks, thus confirming the conclusion that broad product signals are caused by the various diastereoisomeric units of the synthesized 2′-*O*-protected RNA sequence.

5. Isolation of Partially and Fully Deprotected Oligoribonucleotides. – Partial deprotection of the oligoribonucleotides still bound to the solid support was achieved by acid treatment to remove the dimethoxytrityl group, followed by DBU treatment to eliminate the 2-cyanoethyl groups from the phosphotriester function and the npe/npeoc groups from the nucleobases and the acetal functions. Final acidic deprotection of the acetal groups was achieved with dilute AcOH (0.3–3%) at room temperature. Normally, the reaction was complete within 2 h. The progress of the cleavage was easily monitored by HPLC analysis of aliquots.

The quality of crude homouridylate still carrying – after ammonia treatment – the $(MeO)_2$Tr group at the 5′-O and the fnebe group at the 2′-*O* position is demonstrated

by the HPLC analysis of *Fig. 2*, and that of the completely deprotected crude homouridylate by the HPLC trace of *Fig. 3*.

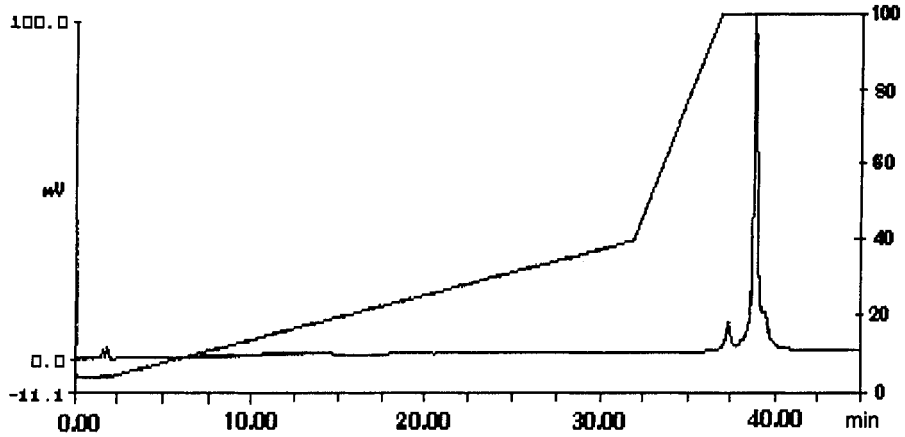


Fig. 2. *HPLC Trace of crude undecameric homouridylate after ammonia treatment, having the 2′-*O*-function blocked by the fnebe moiety and the 5′-*O*-function by the ((MeO)$_2$Tr) group.* Column: *LiChrospher 100 RP-18*, 4 × 125 mm (*Merck*); gradient: 2.5% MeCN (0–2 min), 0–20% MeCN (2–32 min), 20–50% MeCN (32–37 min), 50% MeCN (37–45 min) in 0.1M (Et_3NH)OAc buffer (pH 7.0); flow rate: 1 ml/min.

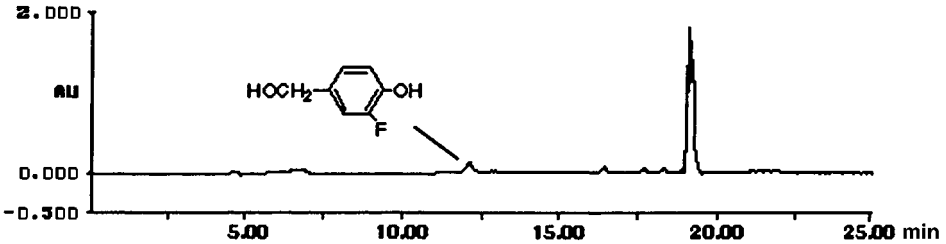


Fig. 3. *HPLC Trace of undecameric homouridylate, after deprotection of {2′-O-[1-[(3-fluoro-4-hydroxybenzyl)-oxy]ethyl]}$_{10}U_{11}$ by treatment with 3% AcOH for 180 min.* Gradient: 0% MeCN (0–2 min), 0–50% MeCN (2–32 min), 50% MeCN (32–37 min), 50% MeCN (37–45 min).

There is obviously a big difference in acetal stability under aprotic and protic acidic conditions, which is the main reason for the orthogonality of the two acid-sensitive protecting groups ((MeO)$_2$Tr and 2′-acetal). In the case of longer (> 12) homouridylate oligomers, it was quite surprising that treatment with very dilute acids led to significant side reactions involving cleavage and isomerization of the RNA strand, whereas the same conditions applied to homomers of C, A, or G did not show any degradation at all, even after several hours or days. This instability of adjacent uridine units may be due to a special sugar puckering, which could enhance the nucleophilic attack of the 2′-OH group at the central P-atom and would lead to an increased 2′ → 3′isomerization and strand cleavage.

To obtain protecting groups that allow efficient deprotection and have similar kinetics for all four nucleoside units, we decided to combine the fnebe group for uridine

with the nebe group for the three other building blocks. After studies of various preliminary oligomer syntheses, we then started the assembly of longer mixed sequences. The results are shown by the HPLC traces in *Fig. 4*, which demonstrate the quality of crude products after full deprotection.

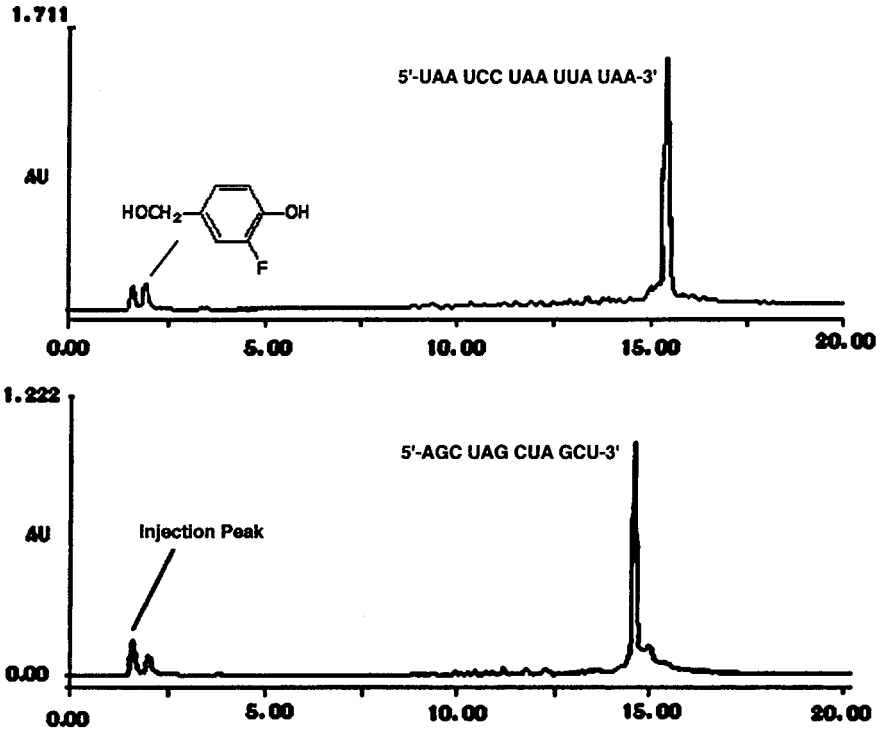


Fig. 4. *HPLC Traces of crude mixed oligoribonucleotide sequences, obtained after final acetal deprotection by treatment with 3% AcOH at room temperature.* Column: *Nucleopak Pa-100* (*Dionex*), 25 μm, 4 × 250 mm; gradient: 0% *B* (0–2 min), 0–40% *B* (2–32 min), 40–100% *B* (32–37 min), 100% *B* (37–47 min); *A* 25 mM *Tris*/0.5% MeCN (pH 8; low salt conc.), *B* = 25 mM *Tris*/800 mM NH_4Cl/0.5% MeCN (pH 8, hight salt conc.), flow rate: 1 ml/min.

Because of the equalized stabilities of the acetal protecting groups after DBU treatment, the complete deprotection with 1–3% AcOH/H_2O could be achieved in a few hours at room temperature. After lyophilization, the oligoribonucleotides were obtained in very good quality and nearly free of salt contamination. The final test for the applicability of the new approach based on protected protecting groups was the synthesis of a 37-mer (exchanging rT and Ψ against U), found as the 3′-terminus of t-RNA^{Ala} from *Saccharomyces cerevisae*. The result was, however, disappointing since a denaturating 20% PAGE electropherogram showed distinctive signals of the expected failure sequences around a major product band, but we failed to get reliable ion-exchange HPLCs of the fully deprotected RNA sequence. This may be due to strong intramolecular base pairing, which leads to stable secondary structures, as expected for an intact RNA single strand.

Conclusion and Discussion. – We have developed a new type of protecting group for the 2′-OH function of oligoribonucleotides following automated standard synthesis protocols. These acetal protecting groups were stable enough under standard solid-phase conditions applied for 5′-*O*-$(MeO)_2$Tr- and npe/npeoc-protected phosphoramidites. After the final synthesis cycle, detritylation was performed first, followed by cleavage of the 2-cyanoethyl and all npe/npeoc protecting groups by DBU-induced β-elimination. Simultaneously, the 2′-acetal protecting group was converted to a more acid-labile form, which was still stable under basic or neutral conditions, but was cleaved off under very mild acidic conditions. Synthesis and physical properties of all of the monomeric building units are described, and solid-phase built-up of homomeric and mixed oligoribonucleotides was successfully achieved. We determined the average condensation yields with the trityl-cation assay and controlled the quality of the oligomers with reversed-phase ion-exchange HPLC and PAGE.

There are still analytical problems for longer sequences, but the quality of the oligoribonucleotides generated and analyzed so far is excellent. It will be an exciting challenge for the future to synthesize longer RNA fragments of high quality using these new 'protected protecting groups', approach and the corresponding easy workup procedures.

Experimental Part

1. *General*. Org. solvents were purchased from *Fluka*, Buchs, Switzerland. Oligomer synthesis was done on a *ABI-392-DNA* synthesizer and with standard reagents. Products were dried under high vacuum or in a desiccator over $CaCl_2$. TLC: Precoated silica gel thin-layer sheets *F1500 LS 254* from *Schleicher & Schüll*. Flash column chromatography (FC): silica gel, *Baker* (30–60 mm), 0.3–0.5 bar. HPLC: *L-6200-Intelligent* pump, UV integrator *L4000*, autosampler *AS 4000*, software *HPLC-Manager/Merck-Hitachi*; UV detector *Uvikon 820* (Fa. *Kontron*), detection at 260 nm. M.p.: *Gallenkamp* or *Büchi*. Melting-point apparatus, model *Dr. Tottoli*; no corrections. UV/VIS: *Perkin-Elmer Lambda 5*; λ_{max} in nm (log ε). ^{1}H-NMR: *Bruker WM-250*; δ in ppm rel. to $SiMe_4$. ^{31}P-NMR: *Bruker AC-250*, *Jeol JM GX 400*; in ppm rel. to 85% phosphoric acid; $CDCl_3$ or (D_6)DMSO as internal standard.

2. *Acetalization of* **1**–**4** *to* **8**–**19**. 2.1. *General Procedure.* See [23].

2.2. *2′*-O-*[1-(Benzyloxy)ethyl]-3′,5′*-O-*(1,1,3,3-tetraisopropyldisiloxan-1,3-diyl)uridine* (**8**) [23].

2.3. *2′*-O-*[1-(Benzyloxy)ethyl]*-N^2-*{[2-(4-nitrophenyl)ethoxy]carbonyl}*-O^6-*[2-(4-nitrophenyl)ethyl]-3′,5′*-O-*(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)guanosine* (**9**). According to *2.1*, from **2**. Yield 91%. Colorless foam. TLC (hexane/AcOEt 1:1): R_f 0.67, 0.69. UV (MeOH): 203 (4.71), 216 (4.67), 268 (4.57), 276 (sh, 4.46). ^{1}H-NMR ($CDCl_3$): 8.22–8.07 (*m*, H–C(8), 2 H *o* to NO_2 (npeoc), 2 H *o* to NO_2 (npe)); 7.50 (*m*, 2 H *m* to NO_2 (npeoc); 7.40–7.31 (*m*, 2 H *m* to NO_2 (npe)); 7.28–7.02 (*m*, 2 arom. H, H–N(2)); 6.03 (*d*, H–C(1′)); 5.28, 5.13 (2*q*, Me*CH*$(O)_2$); 4.94–3.97 (*m*, 11 H, H–C(2′), H–C(3′), H–C(4′), 3 CH_2CH_2O, ArCH_2, 2 H–C(5′)); 3.30 (*t*, CH_2CH_2O (npeoc)); 3.13–3.00 (*m*, CH_2CH_2O (npeoc)); 1.50 (2*d*, *Me*CH$(O)_2$); 1.14–0.88 (*m*, 28 h, 4 Me_2CH). Anal. calc. for $C_{48}H_{63}N_7O_{13}Si_2$ (1002.1): C 57.52, H 6.34, N 9.78; found: C 57.64, H 6.39, N 9.75.

2.4. *2′*-O-*[1-(Benzyloxy)ethyl]*-N^4-*{[2-(4-nitrophenyl)ethoxy]carbonyl}-3′,5′*-O-*(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)cytidine* (**10**). According to *2.1*, from **3**. Yield 84%. Colorless foam. TLC (toluene/AcOEt 1:2): R_f 0.48, 0.52. UV (MeOH): 212 (4.49), 225 (sh, 4.32), 244 (4.26), 278 (4.19). ^{1}H-NMR ($CDCl_3$): 8.40–8.28 (*m*, H–C(6)); 8.18 (*d*, 2 H *o* to NO_2 (npeoc)); 8.08 (br. *s*, H–N(4)); 7.45–7.11 (*m*, 2 H *m* to NO_2 (npeoc), H–C(5), 5 arom. H); 5.80 (*m*, H–C(1′)); 5.27, 5.09 (2*q*, Me*CH*$(O)_2$); 4.93–4.57 (*m*, PhCH_2); 4.40 (*t*, CH_2CH_2O); 4.33–3.92 (*m*, H–C(2′), H–C(3′), H–C(4′), 2 H–C(5′)); 3.09 (*t*, CH_2CH_2O (npeoc)); 1.49 (2*d*, *Me*CH$(O)_2$); 1.17–0.85 (*m*, 4 Me_2CH). Anal. calc. for $C_{39}H_{56}N_4O_{11}Si_2$ (813.1): C 57.61, H 6.94, N 6.89; found: C 57.42, H 6.97, N 6.84.

2.5. *2′*-O-*[1-(Benzyloxy)ethyl]*-N^6-*{[2-(4-nitrophenyl)ethoxy]carbonyl}-3′,5′*-O-*(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)adenosine* (**11**). According to *2.1*, from **4**. Yield 63%. Colorless foam. TLC (toluene/AcOEt 1:2): R_f 0.48, 0.53. ^{1}H-NMR ($CDCl_3$): 8.66, 8.62 (2*s*, H–C(2)); 8.28, 8.19 (2*s*, H–C(8)); 8.17 (*d*, 2 H *o* to NO_2

(npeoc)); 8.10 (br. *s*, H–N(6)); 7.43 (*d*, 2 H *m* to NO_2 (npeoc)); 7.32–7.18 (*m*, 5 arom. H); 6.03 (*m*, H–C(1′)); 5.20, 5.14 (2*q*, MeC*H*(O)$_2$); 4.99–4.46 (*m*, PhCH_2, CH_2CH_2O, H–C(2′)); 4.30–3.97 (*m*, H–C(3′), H–C(4′), 2 H–C(5′)); 3.13 (*t*, CH_2CH_2O (npeoc)); 1.51 (2*d*, *Me*CH(O)$_2$); 1.13–0.88 (*m*, 4 Me_2CH). Anal. calc. for $C_{40}H_{56}N_6O_{10}Si_2$ (837.1): C 57.39, H 6.74, N 10.04; found: C 57.19, H 6.62, N 9.86.

2.6. *2′-*O*-{1-{[4-{[[2-(4-Nitrophenyl)ethoxy]carbonyl}oxy}benzyl}oxy}ethyl}-3′,5′-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)uridine* (**12**) [23].

2.7. *2′-*O*-{1-{[3-Fluoro-4-{[[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}benzyl}oxy}ethyl}-3′,5′-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)uridine* (**13**) [23].

2.8. *2′-*O*-{1-{[4-{[[2-(4-Nitrophenyl)ethoxy]carbonyl}oxy}benzyl}oxy}ethyl}-*N^2*-{[2-(4-nitrophenyl)ethoxy]carbonyl}-*O^6*-[2-(4-nitrophenyl)ethyl]-3′,5′-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)guanosine* (**14**). According to *2.1*, from **2** with **6**. Yield 87%. Colorless foam. TLC (toluene/AcOEt 1:1): R_f 0.53, 0.55. UV (MeOH): 203 (4.68), 214 (4.67), 268 (4.65), 284 (sh, 4.42). ^{1}H-NMR ($CDCl_3$): 8.22–8.10 (*m*, 4 H *o* to NO_2 (npeoc), 2 H *o* to NO_2 (npe), H–C(8)); 7.48 (*d*, 2 H *m* to NO_2 (npeoc)); 7.45–7.20 (*m*, 4 H *m* to NO_2 (npe, npeoc), 2 arom. H, H–N(2)); 7.70–6.93 (*m*, 2 arom. H); 6.03 (*d*, H–C(1′)); 5.22 (2*q*, MeC*H*(O)$_2$); 4.93–3.88 (*m*, H–C(2′), H–C(3′), H–C(4′), 3 CH_2CH_2O, ArCH_2, 2 H–C(5′)); 3.29 (*t*, CH_2CH_2O (npeoc)); 3.18–2.98 (*m*, CH_2CH_2O (npeoc), CH_2CH_2O (npe)); 1.50 (2*d*, *Me*CH(O)$_2$); 1.14–0.83 (*m*, 4 Me_2CH). Anal. calc. for $C_{57}H_{70}N_8O_{18}Si_2$ (1211.4): C 56.52, H 5.82, N 9.25; found: C 56.43, H 5.85, N 8.99.

2.9. *2′-*O*-{1-{[3-Fluoro-4-{[[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}benzyl}oxy}ethyl}-*N^2*-{[2-(4-nitrophenyl)ethoxy]carbonyl}-*O^6*-[2-(4-nitrophenyl)ethyl]-3′,5′-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)guanosine* (**15**). According to *2.1*, from **2** with **7**. Yield 81%. Colorless foam. TLC (toluene/AcOEt 1:1): R_f 0.55, 0.57. UV (MeOH): 203 (4.72), 216 (4.71), 268 (4.68), 275 (sh, 4.64). ^{1}H-NMR ($CDCl_3$): 8.22–8.08 (*m*, 4 H *o* to NO_2(npeoc), 2 H *o* to NO_2(npe), H–C(8)); 7.48 (*d*, 4 H *m* to NO_2 (npeoc)); 7.46–6.96 (*m*, 2 H *m* to NO_2(npe), 3 arom. H, H–N(2)); 6.04 (*d*, H–C(1′)); 5.32, 5.19 (2*q*, MeC*H*(O)$_2$); 4.94–3.97 (*m*, H–C(2′), H–C(3′), H–C(4′), 3 CH_2CH_2O (npeoc, npe), ArCH_2, 2 H–C(5′)); 3.29 (*t*, CH_2CH_2O (npeoc)); 3.20–2.98 (*m*, CH_2CH_2O (npeoc), CH_2CH_2O (npe)); 1.50 (2*d*, *Me*CH(O)$_2$); 1.17–0.89 (*m*, 4 Me_2CH). Anal. calc. for $C_{57}H_{69}FN_8O_{18}Si_2$ (1229.4): C 55.69, H 5.66, N 9.11; found: C 55.83, H 5.72, N 9.06.

2.10. *2′-*O*-{1-{[4-{[[2-(4-Nitrophenyl)ethoxy]carbonyl}oxy}benzyl}oxy}ethyl}-*N^4*-{[2-(4-nitrophenyl)ethoxy]carbonyl}-3′,5′-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)cytidine* (**16**). According to *2.1*, from **3** with **6**. Yield 70%. Colorless foam. TLC (toluene/AcOEt 1:1): R_f 0.40, 0.43. UV (MeOH): 203 (4.64), 212 (4.63), 246 (sh, 4.42), 271 (4.43). ^{1}H-NMR ($CDCl_3$): 8.37–8.29 (*m*, H–C(6)); 8.21–8.11 (*m*, 4 H *o* to NO_2 (npeoc)); 7.98–7.64 (br. *s*, H–N(4)); 7.48–7.27 (*m*, 4 H *m* to NO_2 (npeoc), 2 arom. H); 7.14–7.02 (*m*, H–C(5), 3 arom. H); 5.85, 5.73 (2*s*, H–C(1′)); 5.27, 5.08 (2*q*, MeC*H*(O)$_2$); 4.92–3.93 (*m*, H–C(2′), H–C(3′), H–C(4′), 2 CH_2CH_2O (npeoc), ArCH_2, 2 H–C(5′)); 3.18–3.05 (*m*, 2 CH_2CH_2O (npeoc)); 1.50 (2*d*, *Me*CH(O)$_2$); 1.13–0.80 (*m*, 4 Me_2CH). Anal. calc. for $C_{48}H_{63}N_5O_{16}Si_2$ (1022.2): C 56.40, H 6.21, N 6.85; found: C 55.88, H 6.22, N 6.80.

2.11. *2′-*O*-{1-{[3-Fluoro-4-{[[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}benzyl}oxy}ethyl}-*N^4*-{[2-(4-nitrophenyl)ethoxy]carbonyl}-3′,5′-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)cytidine* (**17**). According to *2.1*, from **3** with **7**. Yield 75%. Colorless foam. TLC (toluene/AcOEt 1:1): R_f 0.42, 0.45. UV (MeOH): 204 (4.67), 211 (4.65), 248 (sh, 4.40), 269 (4.35), 274 (sh, 3.37). ^{1}H-NMR ($CDCl_3$): 8.38–8.27 (*m*, H–C(6)); 8.21–8.12 (*m*, 2 H *o* to NO_2 (npeoc)); 8.04–7.80 (br. *s*, H–N(4)); 7.49–7.01 (*m*, 2 H *m* to NO_2 (npeoc), H–C(5), 3 arom. H); 5.87, 5.73 (2*s*, H–C(1′)); 5.27, 5.09 (2*m*, MeC*H*(O)$_2$); 4.92–3.92 (2*d*, *m*, H–C(2′), H–C(3′), H–C(4′), 2 CH_2CH_2O (npeoc), ArCH_2), 2 H–C(5′)); 3.19–3.05 (*m*, 2 CH_2CH_2O (npeoc)); 1.50 (2*d*, *Me*CH(O)$_2$); 1.13–0.80 (*m*, Me_2CH). Anal. calc. for $C_{48}H_{62}FN_5O_{16}Si_2$ (1040.2): C 55.42, H 6.01, N 6.73; found: C 55.18, H 6.02, N 6.71.

2.12. *2′-*O*-{1-{[4-{[[2-(4-Nitrophenyl)ethoxy]carbonyl}oxy}benzyl}oxy}ethyl}-*N^6*-{[2-(4-nitrophenyl)ethoxy]carbonyl}-3′,5′-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)adenosine* (**18**). According to *2.1*, from **4** with **6**. Yield 52%. Colorless foam. TLC (toluene/AcOEt 1:1): R_f 0.46, 0.48. UV (MeOH): 205 (4.70), 267 (4.58), 272 (sh, 4.54). ^{1}H-NMR ($CDCl_3$): 8.67, 8.62 (2*s*, H–C(2)); 8.31, 8.24 (2*s*, H–C(8)); 8.18 (*m*, 4 H *o* to NO_2 (npeoc)); 7.96 (*s*, H–N(6)); 7.46–7.38 (*m*, 4 H *m* to NO_2 (npeoc)); 7.36–7.27 (*m*, 2 arom. H); 7.08–6.98 (*m*, 2 arom. H); 6.08, 6.06 (2*s*, H–C(1′)); 5.18 (*m*, MeC*H*(O)$_2$); 4.98–4.43 (2*m*, H–C(2′), H–C(3′), H–C(4′), 2 CH_2CH_2O (npeoc), ArCH_2); 4.32–3.97 (*m*, 2 H–C(5′)); 3.14 (2*t*, 2 CH_2CH_2O (npeoc)); 1.52 (2*d*, *Me*CH(O)$_2$); 1.15–0.89 (*m*, Me_2CH). Anal. calc. for $C_{49}H_{63}N_7O_{15}Si_2$ (1046.3): C 56.25, H 6.07, N 9.37; found: C 56.31, H 6.04, N 9.19.

2.13. *2′-*O*-{1-{[3-Fluoro-4-{[[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}benzyl}oxy}ethyl}-*N^6*-{[2-(4-nitrophenyl)ethoxy]carbonyl}-3′,5′-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)adenosine* (**19**). According to *2.1*, from **4** with **7**. Yield 66%. Colorless foam. TLC (toluene/AcOEt 1:1): R_f 0.46, 0.48. UV (MeOH): 209 (4.61), 267 (4.56), 272 (sh, 4.52). ^{1}H-NMR ($CDCl_3$): 8.68, 8.62 (2*s*, H–C(2)); 8.32, 8.28 (2*s*, H–C(8)); 8.18 (*m*, 4 H *o* to NO_2 (npeoc)); 8.04 (br. *s*, H–N(6)); 7.46–7.37 (*m*, 4 H *m* to NO_2 (npeoc)); 7.21–7.11 (*m*, H–C(2) (Ar)); 7.10–7.02 (*m*, 2 arom. H); 6.08 (*d*, H–C(1′)); 5.19 (*m*, MeC*H*(O)$_2$); 4.98–4.43 (2*m*, H–C(2′), H–C(3′), H–C(4′),

2 CH_2CH_2O (npeoc), ArCH_2)); 4.32–3.98 (*m*, 2 H–C(5′)); 3.17 (2*t*, 2 CH_2CH_2O (npeoc)); 1.53 (2*d*, *Me*CH$(O)_2$); 1.15–0.89 (*m*, 4 Me_2CH). Anal. calc. for $C_{49}H_{62}FN_7O_{15}Si_2$ (1064.2): C 55.30, H 5.87, N 9.21; found: C 55.36, H 5.93, N 9.18.

3. *Desilylation of* **8**–**19**. 3.1. *General Procedure* [23].

3.2. *2′*-O-*[1-(Benzyloxy)ethyl]uridine* (**20**) [23].

3.3. *2′*-O-*[1-(Benzyloxy)ethyl]*-N^2-*{[2-(4-nitrophenyl)ethoxy]carbonyl}*-O^6-*[2-(4-nitrophenyl)ethyl]guanosine* (**21**). According to *3.1*, from **9**. Yield 84%. Colorless foam. TLC (toluene/AcOEt/MeOH 5:4:1): R_f 0.27, 0.30. UV (MeOH): 212 (4.88), 268 (4.55), 278 (sh, 4.48). ^{1}H-NMR ((D_6)DMSO): 10.35 (br. *s*, H–N(2)); 8.45 (*m*, H–C(8)); 8.20–8.05 (*m*, 4 H *o* to NO_2); 7.60 (*m*, 4 H *m* to NO_2); 7.25–7.08 (*m*, 5 arom. H); 6.04 (*d*, H–C(1′)); 5.27 (*m*, OH–C(3′)); 5.06 (*m*, OH–C(5′)); 5.03 (*m*, Me*CH*$(O)_2$); 4.87–4.72 (*m*, Me*CH*$(O)_2$, CH_2CH_2OCO, H–C(2′)); 4.43–3.92 (2*m*, ArCH_2, CH_2CHO_2, H–C(3′), H–C(4′)); 3.64 (*m*, 2 H–C(5′)); 3.29 (*t*, CH_2CH_2OCO); 3.10 (*t*, CH_2CH_2O); 1.20 (*m*, *Me*CH$(O)_2$). Anal. calc. for $C_{36}H_{37}N_7O_{12}$ (759.7): C 56.91, H 4.91, N 12.91; found: C 56.59, H 4.93, N 12.66.

3.4. *2′*-O-*[1-(Benzyloxy)ethyl]*-N^4-*{[2-(4-nitrophenyl)ethoxy]carbonyl}cytidine* (**22**). According to *3.1*, from **10**. Yield 68%. Colorless foam. TLC (toluene/AcOEt/MeOH 5:4:1): R_f 0.46, 0.50. UV (MeOH): 212 (4.49), 225 (4.32), 244 (4.26), 278 (4.15). ^{1}H-NMR ((D_6)DMSO): 10.79 (br. *s*, H–N(4)); 8.41 (*m*, H–C(6)); 8.18 (*d*, 2 H *o* to NO_2); 7.50 (*d*, 2 H *m* to NO_2); 7.33–7.17 (*m*, 5 arom. H)); 6.94 (*d*, H–C(5)); 5.97, 5.89 (2*d*, H–C(1′)); 5.30–5.14 (*m*, OH–C(3′), OH–C(5′)); 5.03 (*m*, Me*CH*$(O)_2$); 4.72–4.28 (*m*, ArCH_2, CH_2CH_2O); 4.20 (*m*, H–C(2′)); 4.07 (*m*, H–C(3′)); 3.93 (*m*, H–C(4′)); 3.81–3.56 (*m*, 2 H–C(5′)); 3.07 (*t*, CH_2CH_2O); 1.32 (*m*, *Me*CH$(O)_2$). Anal. calc. for $C_{27}H_{30}N_4O_{10}$ (570.6): C 56.84, H 5.30, N 9.82; found: C 56.56, H 5.46, N 9.65.

3.5. *2′*-O-*[1-(Benzyloxy)ethyl]*-N^6-*{[2-(4-nitrophenyl)ethoxy]carbonyl}adenosine* (**23**). According to *3.1*, from **11**. Yield 97%. Colorless foam. TLC (toluene/AcOEt/MeOH 5:4:1): R_f 0.39, 0.42. UV (MeOH): 208 (4.59), 267 (4.42), 272 (sh, 4.39). ^{1}H-NMR ((D_6)DMSO): 10.63 (*s*, H–N(6)); 8.72, 8.60 (2*d*, H–C(2), H–C(8)); 8.17 (*d*, 2 H *o* to NO_2); 7.62 (*d*, 2 H *m* to NO_2); 7.28–7.10 (*m*, 3 arom. H); 6.98 (*m*, 2 arom. H); 6.18 (*d*, H–C(1′)); 5.41–5.19 (*m*, OH–C(3′), OH–C(5′)); 4.95–4.80 (*m*, Me*CH*$(O)_2$, H–C(2′)); 4.48–3.95 (*m*, ArCH_2, CH_2CH_2O, H–C(3′), H–C(4′)); 3.80–3.53 (*m*, 2 H–C(5′)); 3.13 (*t*, CH_2CH_2O); 1.26 (*m*, *Me*CH$(O)_2$). Anal. calc. for $C_{28}H_{30}N_6O_9 \cdot 0.5\ H_2O$ (603.6): C 55.72, H 5.18, N 13.92; found: C 54.48, H 5.12, N 13.85.

3.6. *2′*-O-*[1-{[4-{[[2-(4-Nitrophenyl)ethoxy]carbonyl}oxy}benzyl]oxy}ethyl]uridine* (**24**). According to *3.1*, from **12**. Yield 76%. Colorless foam. TLC (toluene/AcOEt/MeOH 5:4:1): R_f 0.38, 0.40. UV (MeOH): 204 (4.42), 209 (sh, 4.22), 264 (4.29). ^{1}H-NMR ((D_6)DMSO): 11.36 (br. *s*, H–N(3)); 8.19 (*d*, 2 H *o* to NO_2); 7.95 (*d*, H–C(6)); 7.59 (*d*, 2 H *m* to NO_2); 7.26 (*d*, 2 H *o* to OCO); 7.11 (*d*, 2 H *m* to OCO); 5.92 (*m*, H–C(1′)); 5.62 (*dd*, H–C(5)); 5.28–5.12 (*m*, OH–C(3′), OH–C(5′)); 4.92 (*m*, Me*CH*$(O)_2$); 4.69–4.35 (*m*, ArCH_2, CH_2CH_2O); 4.24 (*m*, H–C(2)); 4.09 (*m*, H–C(3′)); 3.88 (*m*, H–C(4′)); 3.60 (*m*, 2 H–C(5′)); 3.15 (*t*, CH_2CH_2O); 1.30 (*m*, *Me*CH$(O)_2$). Anal. calc. for $C_{27}H_{29}N_3O_{12}$ (587.5): C 55.20, H 4.97, N 7.15; found: C 54.91, H 5.02, N 7.13.

3.7. *2′*-O-*[1-{[3-Fluoro-4-{[[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}benzyl]oxy}ethyl]uridine* (**25**). According to *3.1*, from **13**. Yield 89%. Colorless foam. TLC (toluene/AcOEt/MeOH 5:4:1): R_f 0.45, 0.47. UV (MeOH): 205 (4.38), 212 (sh, 4.28), 264 (4.31). ^{1}H-NMR ((D_6)DMSO): 11.28 (br. *s*, H–N(3)); 8.18 (*m*, 2 H *o* to NO_2); 7.95–7.80 (*m*, H–C(6)); 7.63–7.09 (*m*, 2 H *m* to NO_2, H–C(2) (Ar), H–C(6) (Ar), H–C(5) (Ar)); 5.91 (*m*, H–C(1′)); 5.53 (*m*, H–C(5)); 5.29–5.09 (*m*, OH–C(3′), OH–C(5′)); 4.95 (*m*, Me*CH*$(O)_2$); 4.70–4.36 (*m*, ArCH_2, CH_2CH_2O); 4.26 (*t*, H–C(2′)); 4.06 (*m*, H–C(3′)); 3.87 (*m*, H–C(4′)); 3.78–3.48 (*m*, 2 H–C(5′)); 3.12 (*t*, CH_2CH_2O); 1.46, 1.38 (2*d*, *Me*CH$(O)_2$). Anal. calc. for $C_{27}H_{28}FN_3O_{12} \cdot 0.5\ H_2O$ (614.5): C 53.56, H 4.66, N 6.94; found: C 52.86, H 4.83, N 6.91.

3.8. *2′*-O-*[1-{[4-{[[2-(4-Nitrophenyl)ethoxy]carbonyl}oxy}benzyl]oxy}ethyl]*-N^2-*{[2-(4-nitrophenyl)ethoxy]carbonyl}*-O^6-*[2-(4-nitrophenyl)ethyl]guanosine* (**26**). According to *3.1*, from **14**. Yield 96%. Colorless foam. TLC (toluene/AcOEt/MeOH 5:5:2): R_f 0.58, 0.60. UV (MeOH): 205 (4.73), 214 (sh, 4.73), 269 (4.63), 284 (sh, 4.46). ^{1}H-NMR ((D_6)DMSO): 10.34 (br. *s*, H–N(2)); 8.48, 8.44 (2*s*, H–C(8)); 8.20–8.08 (*m*, 4 H *o* to NO_2 (npeoc), 2 H *o* to NO_2 (npe)); 7.66–7.52 (*m*, 4 H *m* to NO_2 (npeoc), 2 H *m* to NO_2 (npe)); 7.09–6.96 (*m*, 4 arom. H); 6.06–5.98 (*m*, H–C(1′)); 5.31, 5.27 (2*d*, OH–C(5′)); 5.04 (*m*, OH–C(3′)); 4.94–4.79 (*m*, Me*CH*$(O)_2$, H–C(2′)); 4.77–4.64 (*m*, CH_2CH_2O (npeoc)); 4.51–4.03 (*m*, CH_2CH_2O (npeoc), CH_2CH_2O(npe), ArCH_2, H–C(3′)); 3.97 (*m*, H–C(4′)); 3.77–3.64, 3.63–3.51 (2*m*, 2 H–C(5′)); 3.27 (*t*, CH_2CH_2O (npeoc)); 3.18–3.04 (*m*, CH_2CH_2O (npeoc), CH_2CH_2O (npe)); 1.26, 1.18 (2*d*, *Me*$(CH(O)_2)$. Anal. calc. for $C_{45}H_{44}N_8O_{17}$ (968.9): C 55.79, H 4.58, N 11.57; found: C 55.38, H 4.61, N 11.39.

3.9. *2′*-O-*[1-{[3-Fluoro-4-{[[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}benzyl]oxy}ethyl]*-N^2-*{[2-(4-nitrophenyl)ethoxy]carbonyl}*-O^6-*[2-(4-nitrophenyl)ethyl]guanosine* (**27**). According to *3.1*, from **15**. Yield 86%. Colorless

foam. TLC (toluene/AcOEt/MeOH 5:4:1): R_f 0.38, 0.41. UV (MeOH): 203 (4.68), 214 (4.67), 268 (4.65), 274 (sh, 4.55). ^{1}H-NMR ((D$_6$)DMSO): 10.53, 10.35 (2 br. *s*, H–N(2)); 8.46, 8.43 (2*s*, H–C(8)); 8.20–8.08 (*m*, 4 H *o* to NO$_2$ (npeoc), 2 H *o* to NO$_2$ (npe)); 7.66–7.51 (*m*, 4 H *m* to NO$_2$ (npeoc), 2 H *m* to NO$_2$ (npe)); 7.23–7.10 (*m*, H–C(2) (Ar)); 7.06–6.94 (*m*, H–C(5)); 6.90–6.82 (*m*, H–C(6)); 6.06–5.98 (*m*, H–C(1′)); 5.31, 5.28 (2*d*, OH–C(5′)); 5.04 (*m*, OH–C(3′)); 4.94–4.80 (*m*, MeC*H*(O)$_2$, H–C(2′)); 4.77–4.65 (*m*, C*H*$_2$CH$_2$O (npeoc)); 4.55–4.05 (*m*, C*H*$_2$CH$_2$O (npeoc), C*H*$_2$CH$_2$O (npe), ArC*H*$_2$, H–C(3′)); 3.96 (*m*, H–C(4′)); 3.78–3.63, 3.63–3.51 (2*m*, 2 H–C(5′)); 3.25 (*m*, CH$_2$C*H*$_2$O (npeoc)); 3.18–3.05 (*m*, CH$_2$C*H*$_2$O (npeoc), CH$_2$C*H*$_2$O (npe)); 1.26, 1.19 (2*d*, *Me*CH(O)$_2$). Anal. calc. for C$_{45}$H$_{43}$FN$_8$O$_{17}$ · 0.5 H$_2$O (995.9): C 54.27, H 4.45, N 11.25; found: C 54.09, H 4.48, N 11.16.

3.10. *2′-*O*-{1-{{4-{{[2-(4-Nitrophenyl)ethoxy]carbonyl}oxy}benzyl}oxy}ethyl}-*N^4*-{[2-(4-nitrophenyl)ethoxy]carbonyl}cytidine* (**28**). According to *3.1*, from **16**. Yield 92%. Colorless foam. TLC (toluene/AcOEt/MeOH 5:4:1): R_f 0.41, 0.44. UV (MeOH): 204 (4.63), 210 (4.61), 269 (4.37). ^{1}H-NMR ((D$_6$)DMSO): 10.78 (br. *s*, H–N(4)); 8.46–8.38 (*m*, H–C(6)); 8.24–8.09 (*m*, 4 H *o* to NO$_2$ (npeoc)); 7.65–7.53 (*m*, 4 H *m* to NO$_2$ (npeoc)); 7.35–7.22 (*m*, H–C(3) (Ar), H–C(5) (Ar)); 7.15–7.04 (*m*, H–C(2) (Ar), H–C(6) (Ar)); 6.94 (*d*, H–C(5)); 5.93, 5.86 (2*d*, H–C(1′)); 5.28–5.14 (*m*, OH–C(5′), OH–C(3′)); 5.08, 4.98 (2*q*, MeC*H*(O)$_2$); 4.71–4.41 (*m*, 2 CH$_2$CH$_2$O (npeoc), ArC*H*$_2$); 4.33 (*t*, 2 C*H*$_2$CH$_2$O (npeoc)); 4.18 (*m*, H–C(2′)); 4.05 (*m*, H–C(3′)); 3.94 (*m*, H–C(4′)); 3.82–3.69, 3.68–3.54 (2 *m*, 2 H–C(5′)); 3.19, 3.02 (2*t*, 2 CH$_2$C*H*$_2$O (npeoc)); 1.35, 1.29 (2*d*, *Me*CH(O)$_2$). Anal. calc. for C$_{36}$H$_{35}$N$_5$O$_{15}$ · H$_2$O (786.7): C 54.96, H 4.61, N 8.90; found: C 55.04, H 4.85, N 8.88.

3.11. *2′-*O*-{1-{{3-Fluoro-4-{{[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}benzyl}oxy}ethyl}-*N^4*-{[2-(4-nitrophenyl)-ethoxy]carbonyl}cytidine* (**29**). According to *3.1*, from **17**. Yield 90%. Colorless foam. TLC (toluene/AcOEt 1:1): R_f 0.40, 0.44. UV (MeOH): 203 (4.61), 210 (sh, 4.67), 268 (4.41), 274 (sh, 4.39). ^{1}H-NMR ((D$_6$)DMSO): 10.77 (br. *d*, H–N(4)); 8.42 (*m*, H–C(6)); 8.22–8.12 (*m*, 4 H *o* to NO$_2$ (npeoc)); 7.65–7.51 (*m*, 4 H *m* to NO$_2$ (npeoc)); 7.32–7.19 (*m*, H–C(2) (Ar), H–C(5) (Ar)); 7.12 (*t*, H–C(6) (Ar)); 6.94 (*d*, H–C(5)); 5.91, 5.86 (2*d*, H–C(1′)); 5.29, 5.18 (2*m*, OH–C(5′), OH–C(3′)); 5.11, 5.00 (2*q*, MeC*H*(O)$_2$); 4.72–4.40 (*m*, C*H*$_2$CH$_2$O (npeoc), ArC*H*$_2$); 4.35 (*t*, C*H*$_2$CH$_2$O (npeoc)); 4.18 (*m*, H–C(2′)); 4.07 (*m*, H–C(3′)); 3.93 (*m*, H–C(4′)); 3.82–3.70, 3.69–3.55 (2*m*, 2 H–C(5′)); 3.17, 3.07 (2*t*, 2 CH$_2$C*H*$_2$O (npeoc)); 1.36, 1.30 (2*d*, *Me*CH(O)$_2$). Anal. calc. for C$_{36}$H$_{34}$FN$_5$O$_{15}$ · H$_2$O (813.7): C 53.14, H 4.46, N 8.61; found: C 53.32, H 4.56, N 8.59.

3.12. *2′-*O*-{1-{{4-{{[2-(4-Nitrophenyl)ethoxy]carbonyl}oxy}benzyl}oxy}ethyl}-*N^6*-{[2-(4-nitrophenyl)ethoxy]carbonyl}adenosine* (**30**). According to *3.1*, from **18**. Yield 87%. Colorless foam. TLC (toluene/AcOEt/MeOH 5:4:1): R_f 0.50, 0.52. UV (MeOH): 207 (4.64), 267 (4.56), 273 (sh, 4.52). ^{1}H-NMR ((D$_6$)DMSO): 10.59 (br. *d*, H–N(6)); 8.71 (2*s*, H–C(2′)); 8.60 (2*s*, H–C(8)); 8.22–8.11 (*m*, 4 H *o* to NO$_2$ (npeoc)); 7.64–7.52 (*m*, 4 H *m* to NO$_2$ (npeoc)); 7.04–6.98 (*m*, 4 arom. H); 6.15 (*d*, H–C(1′)); 5.39, 5.32 (2*d*, OH–C(5′)); 5.31–5.18 (*m*, OH–C(3′)); 4.95–4.83 (*m*, MeC*H*(O)$_2$), H–C(2)); 4.46 (*t*, C*H*$_2$CH$_2$O (npeoc)); 4.38 (*t*, C*H*$_2$CH$_2$O (npeoc)); 4.40–3.98 (*m*, ArC*H*$_2$, H–C(3′), H–C(4′)); 3.79–3.67, 3.66–3.54 (2*m*, 2 H–C(5′)); 3.18–3.04 (*m*, 2 C*H*$_2$CH$_2$O (npeoc)); 1.25, 1.19 (2*d*, *Me*CH(O)$_2$). Anal. calc. for C$_{37}$H$_{37}$N$_7$O$_{14}$ (803.7): C 55.29, H 4.64, N 12.20; found: C 55.32, H 4.68, N 12.00.

3.13. *2′-*O*-{1-{{3-Fluoro-4-{{[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}benzyl}oxy}ethyl}-*N^6*-{[2-(4-nitrophenyl)ethoxy]carbonyl}adenosine* (**31**). Not isolated. TLC (toluene/AcOEt/MeOH 5:4:2): R_f 0.60, 0.62.

4. *Tritylation to* **32**–**43**. 4.1. *General Procedure.* Predried 2′-acetal-protected monomer **20**–**31** (2.0 mmol, *ca.* 1.2–2.0 g) was co-evaporated with abs. toluene (2 × 100 ml) and taken up in abs. pyridine (30 ml). Then, (MeO)$_2$TrCl (850 mg, 2.51 mmol) was added, the soln. stirred at r.t. overnight, and then the reaction stopped by adding MeOH (1 ml). After 5 min, the soln. was evaporated *in vacuo*, the oil taken up in AcOEt (200 ml) and extracted with NaHCO$_3$ soln. (50 ml) and sat. NaCl soln. (50 ml), the aq. phase back-extracted with AcOEt (150 ml), and the combined org. phase dried (Na$_2$SO$_4$) and evaporated. The crude oil was purified by FC (silica gel, toluene/AcOEt). The product fractions were evaporated and co-evaporated several times with MeOH (10 ml) and CH$_2$Cl$_2$. The resulting colorless foam was dried in a desiccator under high vacuum.

4.2. *2′-*O*-[1-(Benzyloxy)ethyl]-5′-*O*-(4,4′-dimethoxytriphenylmethyl)uridine* (**32**). According to *4.1*, from **20**. Yield 88%. Colorless foam. TLC (toluene/AcOEt/MeOH 5:4:1): R_f 0.86, 0.88. UV (MeOH): 209 (4.73), 233 (4.36), 265 (4.04). ^{1}H-NMR (CDCl$_3$): 8.50 (br. *s*, H–N(3)); 7.92, 7.83 (2*d*, H–C(6)); 7.40–7.18 (*m*, 4 H *m* to MeO, 5 arom. H); 6.82 (*m*, 4 H *o* to MeO); 6.07, 5.97 (2*d*, H–C(1′)); 5.24 (*d*, H–C(5)); 5.06 (*m*, MeC*H*(O)$_2$); 4.78–4.31 (*m*, ArC*H*$_2$, H–C(2′), H–C(3′)); 4.08 (*m*, H–C(4′)); 3.79 (*s*, 2 MeO); 3.48 (*m*, 2 H–C(5′)); 2.91, 2.73 (2*d*, OH–C(3′)); 1.45, 1.38 (2*m*, *Me*CH(O)$_2$). Anal. calc. for C$_{39}$H$_{40}$N$_2$O$_9$ (680.8): C 68.81, H 5.92, N 4.12; found: C 68.55, H 6.07, N 4.07.

4.3. *2′-*O*-[1-(Benzyloxy)ethyl]-5′-*O*-(4,4′-dimethoxytriphenylmethyl)-*N^2*-{[2-(4-nitrophenyl)ethoxy]carbonyl}-*O^6*-[2-(4-nitrophenyl)ethyl]guanosine* (**33**). According to *4.1*, from **21**. Yield 89%. Colorless foam.

TLC (toluene/AcOEt 1:3): R_f 0.56, 0.59. UV (MeOH): 203 (4.99), 214 (4.80), 236 (4.48), 269 (4.57). ^{1}H-NMR ($CDCl_3$): 8.13 (*m*, 4 H *o* to NO_2 (npe)); 7.92, 7.82 (2*s*, H–C(8)); 7.55–7.45 (*m*, 2 H *m* to NO_2 (npeoc)); 7.40 (*m*, 2 H *m* to NO_2 (npe)); 7.35–7.07 (*m*, H–N(2), 10 arom. H, 4 H *m* to MeO); 6.74 (*m*, 4 H *o* to MeO); 6.03 (*d*, H–C(1′)); 5.05 (*m*, acetal-H, H–C(2′)); 4.78 (*t*, CH_2CH_2OCO); 4.70–4.13 (*m*, CH_2CH_2O, $ArCH_2$, H–C(3′)); 4.20 (*m*, H–C(4′)); 3.73 (2*s*, 2 MeO); 3.49–3.24 (*m*, 2 H–C(5′), CH_2CH_2OCO); 3.03 (*t*, CH_2CH_2O); 2.85, 2.65 (2*d*, OH–C(3′)); 1.39, 1.25 (2*d*, *Me*$CH(O)_2$). Anal. calc. for $C_{57}H_{55}N_7O_{14}$ (1062.1): C 64.46, H 5.21, N 9.23; found: C 64.39, H 5.30, N 9.18.

4.4. *2′-O-[1-(Benzyloxy)ethyl]-5′-O-(4,4′-dimethoxytriphenylmethyl)-*N^4*-{[2-(4-nitrophenyl)ethoxy]carbonyl}cytidine* (**34**). According to *4.1*, from **22**. Yield 97%. Colorless foam. TLC (toluene/AcOEt/MeOH 5:4:1): R_f 0.58, 0.60. UV (MeOH): 204 (4.96), 235 (4.54), 275 (4.23). ^{1}H-NMR ($CDCl_3$): 8.45 (*m*, H–C(6)); 8.17 (*m*, 2 H *o* to NO_2); 7.92, 7.82 (2*s*, H–N(4)); 7.55–7.45 (*m*, 2 H *m* to NO_2 (npeoc)); 7.40 (*m*, 2 H *m* to NO_2 (npe)); 7.51 (br. *s*, H–N(4)); 7.44–7.18 (*m*, 10 arom. H, 4 H *m* to MeO, 2 H *o* to NO_2); 6.82 (*m*, 4 H *o* to MeO, H–C(5)); 6.00 (*d*, H–C(1′)); 5.34 (*m*, acetal-H); 4.88–4.53 (*m*, $ArCH_2$); 4.46–4.03 (*m*, CH_2CH_2O, H–C(2′), H–C(3′), H–C(4′)); 3.79 (*s*, 2 MeO); 3.62–3.47 (*m*, 2 H–C(5)); 3.08 (*m*, CH_2CH_2O); 2.97, 2.67 (2*d*, OH–C(3′)); 1.43, 1.38 (2*d*, *Me*$CH(O)_2$). Anal. calc. for $C_{48}H_{49}N_4O_{13}$ (889.9): C 66.05, H 5.54, N 6.42; found: C 66.20, H 5.60, N 6.23.

4.5. *2′-O-[1-(Benzyloxy)ethyl]-5′-O-(4,4′-dimethoxytriphenylmethyl)-*N^6*-{[2-(4-nitrophenyl)ethoxy]carbonyl}adenosine* (**35**). According to *4.1*, from **23**. Yield 90%. Colorless foam. TLC (toluene/AcOEt/MeOH 5:4:1): R_f 0.66, 0.68. UV (MeOH): 204 (4.93), 235 (4.54), 275 (4.25), 288 (sh, 4.15). ^{1}H-NMR ($CDCl_3$): 8.64, 8.62 (2*d*, H–C(2)); 8.20–8.11 (*m*, H–N(6), H–C(8), 2 H *o* to NO_2); 7.48–7.03 (*m*, 2 H *m* to NO_2, 4 H *m* to MeO, 10 arom. H); 6.82–6.71 (*m*, 4 H *o* to MeO); 6.16 (2*d*, H–C(1′)); 4.98 (*m*, Me*CH*$(O)_2$, H–C(2′)); 4.60–4.19 (*m*, H–C(3′), H–C(4′), CH_2CH_2O, $ArCH_2$); 3.75 (*s*, 2 MeO); 3.56–3.32 (*m*, 2 H–C(5′)); 3.15 (*t*, CH_2CH_2O); 2.93, 2.72 (2*d*, OH–C(3′)); 1.39, 1.21 (2*d*, *Me*$CH(O)_2$). Anal. calc. for $C_{48}H_{48}N_6O_{11}$ (897.0): C 65.62, H 5.39, N 9.37; found: C 66.00, H 5.54, N 9.10.

4.6. *5′-O-(4,4′-Dimethoxytriphenylmethyl)-2′-O-{1-[{4-[{[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}benzyl}-oxy}ethyl]uridine* (**36**). According to *4.1*, from **24**. Yield 84%. Colorless foam. TLC (toluene/AcOEt/MeOH 5:4:1): R_f 0.86, 0.88. UV (MeOH): 207 (4.78), 235 (4.42), 265 (4.32). ^{1}H-NMR ($CDCl_3$): 8.46, 8.39 (2 br. *s*, H–N(3)); 8.18 (*m*, 2 H *o* to NO_2 (npeoc)); 7.93, 7.83 (2*d*, H–C(6)); 7.48–7.18 (*m*, 4 H *m* to MeO, 5 arom. H, 2 H *m* to NO_2 (npeoc), H–C(2) (Ar), H–C(6) (Ar)); 7.08 (*m*, C(3) (Ar), H–C(5) (Ar)); 6.80 (*m*, 4 H *o* to MeO); 6.04, 5.91 (2*d*, H–C(1′)); 5.24 (*d*, H–C(5)); 5.10 (*m*, Me*CH*$(O)_2$); 4.80–4.27 (*m*, CH_2CH_2O (npeoc), $ArCH_2$, H–C(2′), H–C(3′)); 4.06 (*m*, H–C(4′)); 3.79 (*s*, 2 MeO); 3.50 (*m*, 2 H–C(5′)); 3.17 (*m*, CH_2CH_2O (npeoc)); 2.81, 2.67 (2*d*, OH–C(3′)); 1.45, 1.40 (2*d*, *Me*$CH(O)_2$). Anal. calc. for $C_{48}H_{47}N_3O_{14}\cdot 0.5\ H_2O$ (898.9): C 64.14, H 5.38, N 4.68; found: C 64.15, H 5.39, N 4.68.

4.7. *5′-O-(4,4′-Dimethoxytriphenylmethyl)-2′-O-{1-{[3-fluoro-4-{[[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}-benzyl}oxy}ethyl]uridine* (**37**). According to *4.1*, from **25**. Yield 98%. Colorless foam. TLC (toluene/AcOEt/MeOH 5:4:1): R_f 0.78, 0.80. UV (MeOH): 205 (4.90), 235 (4.40), 265 (4.31), 279 (sh, 3.90). ^{1}H-NMR ($CDCl_3$): 8.50 (br. *s*, H–N(3)); 8.18 (*m*, 2 H *o* to NO_2 (npeoc)); 7.96, 7.87 (2*d*, H–C(6)); 7.42–7.02 (*m*, 5 arom. H, 4 H *m* to MeO, 2 H *m* to NO_2 (npeoc), H–C(2) (Ar), H–C(5) (Ar), H–C(6) (Ar)); 6.88–6.79 (*m*, 4 H *o* to MeO); 6.04, 5.90 (2*d*, H–C(1′)); 5.27 (*m*, H–C(5)); 5.13 (*m*, Me*CH*$(O)_2$); 4.78–4.29 (*m*, $ArCH_2$, CH_2CH_2O (npeoc), H–C(2′), H–C(3′)); 4.07 (*m*, H–C(4′)); 3.78 (*s*, 2 MeO); 3.51 (*m*, 2 H–C(5′)); 3.15 (*m*, CH_2CH_2O (npeoc)); 2.72, 2.58 (2*d*, OH–C(3′)); 1.46, 1.40 (2*d*, *Me*$C(O)_2$). Anal. calc. for $C_{48}H_{46}FN_3O_{14}$ (907.9): C 63.50, H 5.11, N 4.63; found: C 63.83, H 5.20, N 4.54.

4.8. *5′-O-(4,4′-Dimethoxytriphenylmethyl)-2′-O-{1-{[4-{[[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}benzyl}-oxy}ethyl}-*N^2*-{[2-(4-nitrophenyl)ethoxy]carbonyl}-*O^6*-[2-(4-nitrophenyl)ethyl]guanosine* (**38**). According to *4.1*, from **26**. Yield 96%. Colorless foam. TLC (toluene/AcOEt/MeOH 5:4:1): R_f 0.67, 0.69. UV (MeOH): 204 (5.01), 211 (4.90), 236 (4.51), 269 (4.66), 289 (sh, 4.31). ^{1}H-NMR ($CDCl_3$): 8.18–8.06 (*m*, 4 H *o* to NO_2 (npeoc), 2 H *o* to NO_2 (npe)); 7.98, 7.86 (2*s*, H–C(8)); 7.53–7.44 (*m*, 2 H *m* to NO_2 (npeoc)); 7.43–7.08 (*m*, 2 H *m* to NO_2 (npeoc), H–N(2), 5 arom. H, 4 H *m* to MeO, 2 H *m* to NO_2 (npe), H–C(2) (Ar), H–C(6) (Ar)); 7.03–6.96 (*m*, H–C(3) (Ar), H–C(5) (Ar)); 6.78–6.69 (*m*, 4 H *o* to MeO); 6.03 (*m*, H–C(1′)); 5.13, 5.06–4.97 (2*m*, Me*CH*$(O)_2$), H–C(2′)); 4.77 (*t*, CH_2CH_2O (npeoc)); 4.63–4.28 (*m*, CH_2CH_2O (npeoc), CH_2CH_2O (npe), $ArCH_2$, H–C(3′)); 4.23–4.12 (*m*, H–C(4′)); 3.73 (*s*, 2 MeO); 3.50–3.24 (*m*, 2 H–C(5′)), CH_2CH_2O (npeoc)); 3.14 (*t*, CH_2CH_2O (npeoc)); 3.03 (*t*, CH_2CH_2O (npeoc)); 2.78, 2.62 (2*d*, OH–C(3′)); 1.39, 1.26 (2*d*, *Me*$CH(O)_2$). Anal. calc. for $C_{66}H_{62}N_8O_{19}$ (1271.3): C 62.36, H 4.92, N 8.81; found: C 62.01, H 4.93, N 8.56.

4.9. *5′-O-(4,4′-Dimethoxytriphenylmethyl)-2′-O-{1-{[3-fluoro-4-{[[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}-benzyl}oxy}ethyl}-*N^2*-{[2-(4-nitrophenyl)ethoxy]carbonyl}-*O^6*-[2-(4-nitrophenyl)ethyl]guanosine* (**39**). According to *4.1*, from **27**. Yield 94%. Colorless foam. TLC (toluene/AcOEt/MeOH 5:4:1): R_f 0.68, 0.70. UV

(MeOH): 204 (5.14), 211 (4.92), 236 (4.54), 269 (4.67), 287 (sh, 4.36). ^{1}H-NMR ($CDCl_3$): 8.18–8.06 (*m*, 4 H *o* to NO_2 (npeoc), 2 H *o* to NO_2 (npe)); 7.98, 7.90 (2*s*, H–C(8)); 7.52–7.44 (*m*, 2 H *m* to NO_2 (npeoc)); 7.43–7.11 (*m*, 2 H *m* to NO_2 (npeoc), H–N(2), 5 arom. H, 4 H *m* to MeO, 2 H *m* to NO_2 (npe), H–C(2) (Ar), H–C(6) (Ar)); 7.03–6.93 (*m*, H–C(5) (Ar)); 6.79–6.69 (*m*, 4 H *o* to MeO); 6.03 (*m*, H–C(1′)); 5.15, 5.04 (2*m*, MeC*H*$(O)_2$), H–C(2′)); 4.75 (*t*, CH_2CH_2O (npeoc)); 4.63–4.24 (*m*, CH_2CH_2O (npeoc), CH_2CH_2O (npe), ArCH_2, H–C(3′)); 4.23–4.12 (*m*, H–C(4′)); 3.74 (*s*, 2 MeO); 3.51–3.32 (*m*, 2 H–C(5′)); 3.28 (*t*, CH_2CH_2O (npeoc)); 3.17 (*t*, CH_2CH_2O (npeoc)); 3.03 (*t*, CH_2CH_2O (npe)); 2.74, 2.59 (2*d*, OH–C(3′)); 1.41, 1.28 (2*d*, *Me*CH$(O)_2$). Anal. calc. for $C_{66}H_{61}FN_8O_{19}$ (1289.3): C 61.49, H 4.77, N 8.69; found: C 61.45, H 4.86, N 8.59.

4.10. *5′-O-(4,4′-Dimethoxytriphenylmethyl)-2′-O-{1-{{4-{{[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}benzyl}-oxy}ethyl}-*N^4*-[[2-(4-nitrophenyl)ethoxy]carbonyl]cytidine* (**40**). According to *4.1*, from **28**. Yield 88%. Colorless foam. TLC (toluene/AcOEt/MeOH 5 : 4 : 1): R_f 0.58, 0.61. UV (MeOH): 205 (4.92), 236 (4.59), 271 (4.46), 282 (sh, 4.42). ^{1}H-NMR ($CDCl_3$): 8.52–8.42 (*m*, H–C(6)); 8.21–8.13 (*m*, 4 H *o* to NO_2 (npeoc)); 7.45–7.13 (*m*, H–N(4), 5 arom. H, 4 H *m* to NO_2 (npeoc), 4 H *m* to MeO, H–C(2) (Ar), H–C(6) (Ar)); 6.88–6.78 (*m*, 4 H *o* to MeO, H–C(3) (Ar), H–C(5)); 6.03, 5.90 (2*s*, H–C(1′)); 5.41–5.30 (*m*, MeC*H*$(O)_2$); 4.87–4.27 (*m*, ArCH_2, H–C(2′), H–C(3′), 2 CH_2CH_2O (npeoc)); 4.14–4.03 (*m*, H–C(4′)); 3.78 (*s*, 2 MeO); 3.63–3.47 (*m*, 2 H–C(5′)); 3.18–3.04 (*m*, 2 CH_2CH_2O (npeoc)); 2.83, 2.58 (2*d*, OH–C(3′)); 1.46–1.37 (2*d*, *Me*CH$(O)_2$). Anal. calc. for $C_{57}H_{53}N_5O_{17}$ (1080.1): C 63.39, H 4.95, N 6.48; found: C 63.01, H 5.19, N 6.32.

4.11. *5′-O-(4,4′-Dimethoxytriphenylmethyl)-2′-O-{1-{{3-fluoro-4-{{[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}-benzyl}oxy}ethyl}-*N^4*-[[2-(4-nitrophenyl)ethoxy]carbonyl]cytidine* (**41**). According to *4.1*, from **29**. Yield 88%. Colorless foam. TLC (toluene/AcOEt/MeOH 5 : 4 : 1): R_f 0.58, 0.61. UV (MeOH): 205 (4.90), 236 (4.56), 270 (4.42), 287 (sh, 4.31). ^{1}H-NMR ($CDCl_3$): 8.52–8.41 (*m*, H–C(6)); 8.21–8.13 (*m*, 4 H *o* to NO_2 (npeoc)); 7.45–7.03 (*m*, H–N(4), 5 arom. H, 4 H *m* to NO_2 (npeoc), 4 H *m* to MeO, H–C(2) (Ar), H–C(5) (Ar), H–C(6) (Ar)); 6.88–6.77 (*m*, 4 H *o* to MeO); 6.02, 5.90 (2*s*, H–C(1′)); 5.41, 5.32 (2*q*, MeC*H*$(O)_2$); 4.87–4.28 (*m*, ArCH_2, H–C(2′), H–C(3′), 2 CH_2CH_2O (npeoc)); 4.14–4.01 (*m*, H–C(4′)); 3.78 (*s*, 2 MeO); 3.64–3.45 (*m*, 2 H–C(5′)); 3.18–3.04 (*m*, 2 CH_2CH_2O (npeoc)); 2.70, 2.49 (2*d*, OH–C(3′)); 1.48–1.39 (2*d*, *Me*CH$(O)_2$). Anal. calc. for $C_{57}H_{52}FN_5O_{17}$ (1098.1): C 62.35, H 4.77, N 6.38; found: C 62.18, H 5.07, N 6.42.

4.12. *5′-O-(4,4′-Dimethoxytriphenylmethyl)-2′-O-{1-{{4-{{[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}benzyl}-oxy}ethyl}-*N^6*-[[2-(4-nitrophenyl)ethoxy]carbonyl]adenosine* (**42**). According to *4.1*, from **30**. Yield 98%. Colorless foam. TLC (toluene/AcOEt/MeOH 5 : 4 : 1): R_f 0.58, 0.60. UV (MeOH): 205 (4.94), 236 (4.46), 267 (4.58), 272 (sh, 4.55). ^{1}H-NMR ($CDCl_3$): 8.63 (*d*, H–C(2)); 8.22–8.14 (*m*, 4 H *o* to NO_2 (npeoc)); 8.06, 7.97 (2*s*, H–C(8)); 7.97 (br. *s*, H–N(6)); 7.46–7.35 (*m*, 4 H *m* to NO_2 (npeoc), H–C(2) (Ar), H–C(6) (Ar)); 7.34–6.94 (*m*, 5 arom. H, 4 H *m* to MeO, H–C(3) (Ar), H–C(5) (Ar)); 6.83–6.74 (*m*, 4 H *o* to MeO)); 6.17 (2*d*, H–C(1′)); 5.12–4.93 (*m*, MeC*H*$(O)_2$, H–C(2′)); 4.57–4.38 (*m*, H–C(3′), 2 CH_2CH_2O (npeoc)); 4.35–4.21 (*m*, ArCH_2, H–C(4′)); 3.75 (*s*, 2 MeO); 3.56–3.45, 3.44–3.33 (2*m*, 2 H–C(5′)); 3.14 (*t*, 2 CH_2CH_2O (npeoc)); 2.84, 2.67 (2*d*, OH–C(3′)); 1.40, 1.26 (2*d*, *Me*CH$(O)_2$). Anal. calc. for $C_{58}H_{55}N_7O_{16}$ (1106.1): C 62.98, H 5.01, N 8.86; found: C 62.91, H 5.09, N 8.65.

4.13. *5′-O-(4,4′-Dimethoxytriphenylmethyl)-2′-O-{1-{{3-fluoro-4-{{[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}-benzyl}oxy}ethyl}-*N^6*-[[2-(4-nitrophenyl)ethoxy]carbonyl]adenosine* (**43**). According to *4.1*, from **31**. Yield 92%. Colorless foam. TLC (toluene/AcOEt/MeOH 5 : 4 : 1): R_f 0.59, 0.62. UV (MeOH): 206 (4.92), 236 (4.49), 267 (4.60), 275 (sh, 4.53). ^{1}H-NMR ($CDCl_3$): 8.62 (*d*, H–C(2)); 8.22–8.10 (*m*, 4 H *o* to NO_2 (npeoc)); 8.07, 7.98 (2*s*, H–C(8)); 7.46–7.33, 7.32–7.17 (*m*, 5 arom. H, 4 H *m* to NO_2 (npeoc), 4 H *m* to MeO, H–C(2) (Ar), H–N(6)); 7.06–6.95 (*m*, H–C(5) (Ar)); 6.94–6.84 (*m*, H–C(6) (Ar)); 6.83–6.72 (*m*, 4 H *o* to MeO); 6.17 (*m*, H–C(1′)); 5.13–4.93 (*m*, MeC*H*$(O)_2$, H–C(2′)); 4.58–4.38 (*m*, H–C(3′), 2 CH_2CH_2O (npeoc)); 4.35–4.17 (*m*, ArCH_2, H–C(4′)); 3.74 (*s*, 2 MeO); 3.56–3.44, 3.43–3.31 (2*m*, 2 H–C(5′)); 3.14 (*t*, 2 CH_2CH_2O (npeoc)); 2.77, 2.53 (2*d*, OH–C(3′)); 1.41, 1.28 (2*d*, *Me*CH$(O)_2$). Anal. calc. for $C_{58}H_{54}FN_7O_{16}$ (1124.1): C 61.97, H 4.84, N 8.72; found: C 62.00, H 4.91, N 8.64.

5. *Succinylation to* **44**–**55**. 5.1. *General Procedure*. To 5′-*O*-(4,4′-dimethoxytriphenylmethyl)-2′-acetal-protected monomer **32**–**43** (0.1 mmol; *ca.* 90–130 mg) were added succinic anhydride (0.15–0.3 mmol, 15–30 mg) and *N,N*-dimethylpyridin-4-amine (DMAP; 0.02–0.04 mmol, 2.5–5.0 mg). The mixture was taken up in abs. CH_2Cl_2 (10 ml) and stirred at r.t. for 2–4-h. The reaction was stopped by dilution with AcOEt (100 ml) and shaken with 1N phosphate buffer (100 ml, pH 7). The extraction was repeated once and the combined org. phase dried (Na_2SO_4) and evaporated. The crude oil was purified by FC (silica gel, toluene/AcOEt/MeOH). The product fractions were evaporated and co-evaporated with MeOH (2 × 5 ml) and CH_2Cl_2 (2 × 5 ml). The resulting colorless foam was dried in a desiccator under high vacuum. *Note:* For solid-phase coupling, a chromatographic purification is not necessary in most cases.

5.2. *2′-O-[1-(1-Benzyloxy)ethyl]-5′-O-(4,4′-dimethoxytriphenylmethyl)uridine 3′-(Hydrogen Butanedioate)* (**44**). According to *5.1*, from **32**. Yield 93%. Colorless foam. TLC (toluene/AcOEt/MeOH 5 : 4 : 1): R_f 0.60. UV (MeOH): 204 (4.85), 234 (4.34), 260 (4.01). ^{1}H-NMR ($CDCl_3$): 9.40 (br. *s*, H–N(3)); 7.87, 7.69 (2*d*, H–C(6)); 7.40–7.12 (*m*, 4 H *m* to MeO, 5 arom. H); 6.80 (*m*, 4 H *o* to MeO); 6.08 (2*d*, H–C(1′)); 5.52–5.40 (*d*, H–C(5)); 5.13 (*m*, H–C(3′)); 4.98 (*m*, MeC*H*$(O)_2$); 4.72–4.36 (*m*, ArCH_2, H–C(2′)); 4.22 (*m*, H–C(4′)); 3.78 (*s*, 2 MeO); 3.46 (*m*, 2 H–C(5′)); 2.68 (*m*, CH_2CH_2); 1.42, 1.28 (2*m*, *Me*CH$(O)_2$). Anal. calc. for $C_{43}H_{44}N_2O_{10}$ (680.8): C 66.19, H 5.58, N 3.59; found: C 66.12, H 5.78, N 3.54.

5.3. *2′-O-[1-(1-Benzyloxy)ethyl]-5′-O-(4,4′-dimethoxytriphenylmethyl)-N^2-{[2-(4-nitrophenyl)ethoxy]carbonyl}-O^6-[2-(4-nitrophenyl)ethyl]guanosine 3′-(Hydrogen Butanedioate)* (**45**). According to *5.1*, from **33**. Yield 93%. Colorless foam. TLC (toluene/AcOEt/MeOH 5 : 4 : 1): R_f 0.49, 0.54. UV (MeOH): 203 (4.96), 235 (4.38), 260 (4.30). ^{1}H-NMR ((D$_6$)DMSO): 12.24 (br. *s*, H–N(2)); 11.47 (*d*, COOH); 8.18 (*m*, 2 H *o* to NO_2 (npeoc)); 7.69, 7.61 (2*d*, H–C(6)); 7.58 (*m*, 2 H *m* to NO_2 (npeoc)); 7.40–7.18 (*m*, 5 arom. H, 2 H *m* to NO_2 (npeoc), H–C(2) (Ar), 4 H *m* to MeO)); 6.86 (*m*, 4 H *o* to MeO); 5.91 (2*d*, H–C(1′)); 5.38 (*dd*, H–C(5)); 5.23 (*m*, H–C(3′)); 4.92, 4.86 (2*q*, MeC*H*$(O)_2$); 4.68 (*m*, H–C(2′)); 4.57–4.29 (*m*, 2 CH_2CH$_2$O (npeoc), ArCH_2); 4.16 (*m*, H–C(4′)); 3.75 (*s*, 2 MeO); 3.43–3.19 (*m*, 2 H–C(5′)); 3.16 (*t*, 2 CH_2CH_2O (npeoc)); 2.67–2.42 (*m*, 4 H (succ.)); 1.28, 1.20 (2*d*, *Me*CH$(O)_2$). Anal. calc. for $C_{52}H_{51}N_3O_{17}\cdot H_2O$ (1008.0): C 61.96, H 5.30, N 4.16; found: C 61.98, H 5.29, N 4.14.

5.4. *2′-O-[1-(1-Benzyloxy)ethyl]-5′-O-(4,4′-dimethoxytriphenylmethyl)-N^4-{[2-(4-nitrophenyl)ethoxy]carbonyl}cytidine 3′-(Hydrogen Butanedioate)* (**46**). According to *5.1*, from **34**. Yield 98%. Colorless foam. TLC (toluene/AcOEt/MeOH 5 : 4 : 1): R_f 0.50, 0.52. UV (MeOH): 203 (4.94), 236 (4.51), 270 (4.22). ^{1}H-NMR ($CDCl_3$): 8.42, 8.29 (2*d*, H–C(6)); 8.12 (*m*, 2 H *o* to NO_2); 7.41–7.13 (*m*, 2 H *m* to NO_2, H–N(4), 4 H *m* to MeO, 10 arom. H); 7.44–7.18 (*m*, 10 arom. H, 4 H *m* to MeO, 2 H *o* to NO_2); 6.82 (*m*, 4 H *o* to MeO, H–C(5)); 5.99 (2*d*, H–C(1′)); 5.30 (*m*, H–C(3′)); 5.15 (*m*, acetal-H); 4.70–4.20 (*m*, ArCH_2, CH_2CH_2O, H–C(2′), H–C(4′)); 3.75 (*s*, 2 MeO); 3.59–3.42 (2*m*, 2 H–C(5′)); 2.97 (*m*, CH_2CH$_2$O); 2.74–2.46 (*m*, CH_2CH_2); 1.41, 1.28 (2*d*, *Me*CH$(O)_2$). Anal. calc. for $C_{52}H_{53}N_4O_{16}$ (990.0): C 63.09, H 5.40, N 5.66; found: C 63.82, H 5.50, N 5.64.

5.5. *2′-O-[1-(1-Benzyloxy)ethyl]-5′-O-(4,4′-dimethoxytriphenylmethyl)-N^6-{[2-(4-nitrophenyl)ethoxy]carbonyl}adenosine 3′-(Hydrogen Butanedioate)* (**47**). According to *5.1*, from **35**. Yield 79%. Colorless foam. TLC (toluene/AcOEt/MeOH 5 : 4 : 1): R_f 0.60. UV (MeOH): 203 (4.97), 235 (4.43), 267 (4.47), 272 (sh, 4.43). ^{1}H-NMR ($CDCl_3$): 8.62, 8.58 (2*d*, H–C(2)); 8.53–8.36 (br. *s*, H–N(6)); 8.18, 8.02 (2*m*, 2 H *o* to NO_2, H–C(8)); 7.49–6.87 (*m*, 2 H *m* to NO_2, 4 H *m* to MeO, 8 arom. H); 6.93 (*m*, 2 H (*Ar*CH_2)); 6.84–6.71 (*m*, 4 H *o* to MeO); 6.21, 6.12 (2*d*, H–C(1′)); 5.56 (*m*, H–C(3′)); 5.27 (2*m*, H–C(2′)); 4.86, 4.79 (2*q*, MeC*H*$(O)_2$); 4.60–4.29 (*m*, CH_2CH_2O, H–C(4′)); 4.03 (*m*, ArCH_2); 3.75 (*s*, 2 MeO); 3.52–3.37 (*m*, 2 H–C(5′)); 3.12 (*t*, 2 CH_2CH$_2$O); 2.70 (*m*, CH_2CH_2); 1.32, 1.10 (2*d*, *Me*CH$(O)_2$). Anal. calc. for $C_{53}H_{52}N_6O_{14}$ (997.0): C 63.85, H 5.26, N 8.43; found: C 63.63, H 5.41, N 8.29.

5.6. *5′-O-(4,4′-Dimethoxytriphenylmethyl)-2′-O-{1-{[4-{[[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}benzyl}-oxy}ethyl}uridine 3′-(Hydrogen Butanedioate)* (**48**). According to *5.1*, from **36**. Yield 96%. Colorless foam. TLC (toluene/AcOEt/MeOH 5 : 4 : 1): R_f 0.30–0.42. UV (MeOH): 203 (4.96), 235 (4.38), 260 (4.30). ^{1}H-NMR ((D$_6$)-DMSO): 12.24 (br. *s*, H–N(3)); 11.47 (*s*, COOH); 8.18 (*m*, 2 H *o* to NO_2); 7.65 (*d*, H–C(6)); 7.58 (*m*, 2 H *m* to NO_2); 7.40–7.18 (*m*, 5 arom. H, 2 H *o* to C_6H_4OCO, 4 H *m* to MeO); 7.08 (*d*, 2 H *m* to C_6H_4OCO); 6.86 (*m*, 4 H *o* to MeO); 5.91 (2*d*, H–C(1′)); 5.38 (*m*, H–C(5)); 5.23 (*m*, H–C(3′)); 4.89 (*m*, MeC*H*$(O)_2$); 4.68 (*m*, H–C(2′)); 4.57–4.29 (*m*, ArCH_2, CH_2CH_2O); 4.16 (*m*, H–C(4′)); 3.75 (*s*, 2 MeO); 3.43–3.19 (*m*, 2 H–C(5′)); 3.16 (*t*, CH_2CH$_2$O); 2.67–2.42 (*m*, CH_2CH_2); 1.28, 1.20 (2*d*, *Me*CH$(O)_2$). Anal. calc. for $C_{52}H_{51}N_3O_{17}\cdot H_2O$ (1008.0): C 61.96, H 5.30, N 4.16; found: C 61.98, H 5.29, N 4.14.

5.7. *5′-O-(4,4′-Dimethoxytriphenylmethyl)-2′-O-{1-{[3-fluoro-4-{[[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}-benzyl}oxy}ethyl}uridine 3′-(Hydrogen Butanedioate)* (**49**). According to *5.1*, from **37**. Yield 56%. Colorless foam. TLC (toluene/AcOEt/MeOH 5 : 4 : 1): R_f 0.35–0.45. UV (MeOH): 205 (4.89), 235 (4.39), 264 (4.31), 279 (sh, 4.11). ^{1}H-NMR ($CDCl_3$): 9.51, 9.41 (2 br. *s*, H–N(3)); 8.16 (*m*, 2 H *o* to NO_2 (npeoc)); 7.92, 7.73 (2*d*, H–C(6)); 7.44–7.02 (*m*, 5 arom. H, 2 H *m* to NO_2 (npeoc), H–C(2) (Ar), 4 H *m* to MeO, H–C(5) (Ar), H–C(6) (Ar)); 6.87–6.77 (*m*, 4 H *o* to MeO); 6.05, 5.98 (2*d*, H–C(1′)); 5.44 (*m*, H–C(5)); 5.21 (*d*, H–C(3′)); 4.99 (*m*, MeC*H*$(O)_2$); 4.66–4.37 (*m*, ArCH_2, CH_2CH$_2$O (npeoc), H–C(2′)); 4.27 (*m*, H–C(4′)); 3.77 (*s*, 2 MeO); 3.58–3.39 (*m*, 2 H–C(5′)); 3.14 (*t*, CH_2CH_2O (npeoc)); 2.94, 2.88 (2*s*, COOH); 2.73, 2.56 (2*m*, CH_2CH_2); 1.42, 1.30 (2*d*, *Me*CH$(O)_2$). Anal. calc. for $C_{52}H_{50}FN_3O_{17}\cdot H_2O$ (1008.0): C 61.96, H 5.00, N 4.17; found: C 62.00, H 5.23, N 4.55.

5.8. *5′-O-(4,4′-Dimethoxytriphenylmethyl)-2′-O-{1-{[4-{[[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}benzyl}-oxy}ethyl}-N^2-{[2-(4-nitrophenyl)ethoxy]carbonyl}-O^6-[2-(4-nitrophenyl)ethyl]guanosine-3′-(Hydrogen Butane-*

dioate) (**50**). According to *5.1*, from **38**. Yield 85%. Colorless foam. TLC (toluene/AcOEt/MeOH 5:4:1): R_f 0.34–0.46. UV (MeOH): 203 (4.97), 210 (sh, 4.92), 237 (4.54), 268 (4.67), 279 (sh, 4.11). ^{1}H-NMR ((D$_6$)DMSO): 12.29 (br. *s*, COOH); 10.22 (2*s*, H–N(2)); 8.37, 8.32 (2*s*, H–C(8)); 8.18–8.10 (*m*, 4 H *o* to NO$_2$ (npeoc), 2 H *o* to NO$_2$ (npe)); 7.66–7.53 (*m*, 4 H *m* to NO$_2$ (npeoc), 2 H *m* to NO$_2$ (npe)); 7.34–7.26 (*m*, H–C(3) (Ar), H–C(5) (Ar)); 7.24–7.12 (*m*, 5 arom. H, 4 H *m* to MeO); 6.98, 6.93 (2*s*, H–C(2) (Ar), H–C(6) (Ar)); 6.79–6.66 (*m*, 4 H *m* to MeO); 6.08 (*m*, H–C(1′)); 5.57–5.48 (*m*, H–C(3′)); 5.39–5.32 (*m*, H–C(2′)); 4.86–4.65 (*m*, MeC*H*(O$_2$), C*H*$_2$CH$_2$O (npeoc)); 4.50–4.42 (*m*, C*H*$_2$CH$_2$O (npeoc)); 4.40–3.97 (*m*, C*H*$_2$CH$_2$O (npe), ArC*H*$_2$, H–C(4′)); 3.68 (*s*, 2 MeO); 3.76–3.49 (2*m*, 2 H–C(5′)); 3.37–3.21 (*m*, CH$_2$C*H*$_2$O (npeoc)); 3.18–3.02 (*m*, CH$_2$C*H*$_2$O (npeoc), CH$_2$C*H*$_2$O (npe)); 2.68–2.44 (*m*, 4 H (succ.)); 1.15, 1.08 (2*d*, *Me*CH(O$_2$). Anal. calc. for $C_{70}H_{66}N_8O_{22}$ (1371.3): C 61.31, H 4.85, N 8.17; found: C 60.93, H 4.93, N 7.98.

5.9. *5′-*O*-(4,4′-Dimethoxytriphenylmethyl)-2′-*O*-{1-{{3-fluoro-4-{{[2-(4-nitrophenyl)-ethoxy]carbonyl}oxy}-benzyl}oxy}ethyl}-*N^2*-{[2-(4-nitrophenyl)ethoxy]carbonyl}-*O^2*-[2-(4-nitrophenyl)ethyl]guanosine 3′-(Hydrogen Butanedioate)* (**51**). According to *5.1*, from **39**. Yield 91%. Colorless foam. TLC (toluene/AcOEt/MeOH 5:4:1): R_f 0.43–0.49. UV (MeOH): 203 (4.97), 211 (sh, 4.58), 237 (4.59), 268 (4.74). ^{1}H-NMR (CDCl$_3$): 8.20–8.04 (*m*, 4 H *o* to NO$_2$ (npeoc), 2 H *o* to NO$_2$ (npe)); 8.03, 7.88 (2*s*, H–C(8)); 7.52–7.43 (*m*, 2 H *m* to NO$_2$ (npeoc)); 7.43–7.13 (*m*, 2 H *m* to NO$_2$ (npeoc), H–N(2), 5 arom. H, 4 H *m* to MeO, 2 H *m* to NO$_2$ (npe), H–C(2) (Ar)); 6.89–6.84 (*m*, H–C(5) (Ar)); 6.83–6.64 (*m*, H–C(6) (Ar), 4 H *o* to MeO); 6.20, 6.14 (2*d*, H–C(1′)); 5.55–5.48 (*m*, H–C(3′)); 5.28, 5.15 (2*m*, H–C(2′)); 4.89, 4.78 (2*q*, MeC*H*(O$_2$)); 4.68 (*t*, C*H*$_2$CH$_2$O (npeoc)); 4.52–4.43 (*m*, C*H*$_2$CH$_2$O (npeoc)); 4.42–3.85 (*m*, C*H*$_2$CH$_2$O (npe), ArC*H*$_2$, H–C(4′)); 3.72 (*s*, 2 MeO); 3.52–3.32 (*m*, 2 H–C(5′)); 3.27 (*t*, CH$_2$C*H*$_2$O (npeoc)); 3.14 (*t*, CH$_2$C*H*$_2$O (npeoc)); 3.05 (*t*, CH$_2$C*H*$_2$O (npe)); 2.81–2.60 (*m*, 4 H (succ.)); 1.32, 1.12 (2*d*, *Me*CH(O$_2$). Anal. calc. for $C_{70}H_{65}FN_8O_{22}$ (1389.3): C 60.52, H 4.72, N 8.07; found: C 60.66, H 4.90, N 7.87.

5.10. *5′-*O*-(4,4′-Dimethoxytriphenylmethyl)-2′-*O*-{1-{{4-{{[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}benzyl}-oxy}ethyl}-*N^4*-{[2-(4-nitrophenyl)ethoxy]carbonyl}cytidine 3′-(Hydrogen Butanedioate)* (**52**). According to *5.1*, from **40**. Yield 87%. Colorless foam. TLC (toluene/AcOEt/MeOH 5:4:1): R_f 0.34–0.38. UV (MeOH): 204 (4.92), 209 (sh, 4.88), 236 (4.58), 270 (4.45), 284 (sh, 4.38). ^{1}H-NMR ((D$_6$)DMSO): 12.28 (br. *s*, COOH); 10.85 (br. *s*, H–N(4)); 8.23–8.05 (*m*, H–C(6), 4 H *o* to NO$_2$(npeoc)); 7.63–7.52 (*m*, 4 H *m* to NO$_2$ (npeoc)); 7.40–7.15 (*m*, 5 arom. H, 4 H *m* to MeO, 2 H *m* to NO$_2$ (npe), H–C(3) (Ar), H–C(5) (Ar)); 7.10–7.02 (*m*, H–C(2) (Ar), H–C(6) (Ar)); 6.94–6.84 (*m*, 4 H *o* to MeO); 6.78 (*m*, H–C(5)); 5.97 (*d*, H–C(1′)); 5.28 (*m*, H–C(3′)); 5.05, 4.88 (2*m*, MeC*H*(O$_2$)); 4.64–4.18 (*m*, 2 C*H*$_2$CH$_2$O (npeoc), ArC*H*$_2$, H–C(2′), H–C(4′)); 3.73 (*s*, 2 MeO); 3.43–3.25 (*m*, 2 H–C(5′)); 3.18–3.02 (*m*, 2 CH$_2$C*H*$_2$O (npeoc)); 2.64–2.48 (*m*, 4 H (succ.)); 1.30, 1.19 (2*d*, *Me*CH(O$_2$). Anal. calc. for $C_{61}H_{57}N_5O_{20}\cdot H_2O$ (1198.2): C 61.15, H 4.96, N 5.85; found: C 61.21, H 5.09, N 5.85.

5.11. *5′-*O*-(4,4′-Dimethoxytriphenylmethyl)-2′-*O*-{1-{{3-fluoro-4-{{[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}-benzyl}oxy}ethyl}-*N^4*-{[2-(4-nitrophenyl)ethoxy]carbonyl}cytidine 3′-(Hydrogen Butanedioate)* (**53**). According to *5.1*, from **41**. Yield 87%. Colorless foam. TLC (toluene/AcOEt/MeOH 5:4:1): R_f 0.34–0.38. UV (MeOH): 205 (4.93), 236 (4.54), 269 (4.43), 287 (sh, 4.30). ^{1}H-NMR (CDCl$_3$): 8.49, 8.41 (2*d*, H–C(6)); 8.17–8.08 (*m*, 4 H *o* to NO$_2$ (npeoc)); 7.42–7.18 (*m*, H–N(4), 5 arom. H, 4 H *m* to MeO, H–C(2) (Ar), 4 H *m* to NO$_2$ (npeoc)); 7.08–6.95 (*m*, H–C(5) (Ar), H–C(6) (Ar)); 6.94–6.77 (*m*, H–C(5), 4 H *o* to MeO); 6.00, 5.92 (2*s*, H–C(1′)); 5.34–5.23, 5.22–5.10 (2*m*, H–C(3′), MeC*H*(O$_2$)); 4.78–4.17 (*m*, 2 C*H*$_2$CH$_2$O (npeoc), ArC*H*$_2$, H–C(2′), H–C(4′)); 3.75 (*s*, 2 MeO); 3.66–3.55, 3.47–3.35 (*m*, 2 H–C(5′)); 3.09 (*t*, CH$_2$C*H*$_2$O (npeoc)); 2.93 (*t*, CH$_2$C*H*$_2$O (npeoc)); 2.72–2.48 (*m*, 4 H (succ.)); 1.41, 1.29 (2*d*, *Me*CH(O$_2$). Anal. calc. for $C_{61}H_{56}FN_5O_{20}\cdot H_2O$ (1216.2): C 60.25, H 4.81, N 5.76; found: C 60.45, H 4.95, N 5.59.

5.12. *5′-*O*-(4,4′-Dimethoxytriphenylmethyl)-2′-*O*-{1-{{4-{{[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}benzyl}-oxy}ethyl}-*N^6*-{[2-(4-nitrophenyl)ethoxy]carbonyl}adenosine 3′-(Hydrogen Butanedioate)* (**54**). According to *5.1*, from **42**. Yield 76%. Colorless foam. TLC (toluene/AcOEt/MeOH 5:4:1): R_f 0.38–0.43. UV (MeOH): 203 (5.00), 235 (4.47), 267 (4.57), 272 (sh, 4.54). ^{1}H-NMR (CDCl$_3$): 8.62, 8.58 (2*d*, H–C(2)); 8.51–8.37 (br. *s*, H–N(6)); 8.19–8.10, 8.04 (2*m*, 4 H *o* to NO$_2$ (npeoc), H–C(8)); 7.47–7.33 (*m*, 4 H *m* to NO$_2$ (npeoc), H–C(3) (Ar), H–C(5) (Ar)); 7.32–7.13 (*m*, 4 H *m* to MeO, H–C(2) (Ar), H–C(6) (Ar), 4 arom. H); 6.82–6.72 (*m*, 4 H *o* to MeO); 6.21, 6.12 (2*d*, H–C(1′)); 5.54 (*m*, H–C(3′)); 5.37, 5.18 (2*m*, H–C(2′)); 4.88, 4.81 (2*q*, MeC*H*(O$_2$)); 4.53–4.40 (*m*, 2 C*H*$_2$CH$_2$O (npeoc)); 4.38–4.24, 4.10–3.92 (2*m*, ArC*H*$_2$, H–C(4′)); 3.74 (*s*, 2 MeO); 3.57–3.47, 3.46–3.35 (*m*, 2 H–C(5′)); 3.12 (*t*, 2 CH$_2$C*H*$_2$O (npeoc)); 2.80–2.51 (*m*, 4 H (succ.)); 1.32, 1.12 (2*d*, *Me*CH(O$_2$). Anal. calc. for $C_{62}H_{59}N_7O_{19}$ (1206.2): C 61.74, H 4.93, N 8.13; found: C 61.56, H 5.00, N 7.86.

5.13. *5′-*O*-(4,4′-Dimethoxytriphenylmethyl)-2′-*O*-{1-{{3-fluoro-{{4-[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}-benzyl}oxy}ethyl}-*N^6*-{[2-(4-nitrophenyl)ethoxy]carbonyl}adenosine 3′-(Hydrogen Butanedioate)* (**55**). Accord-

ing to *5.1*, from **43**. Yield 78%. Colorless foam. TLC (toluene/AcOEt/MeOH 5:4:1): R_f 0.33–0.41. UV (MeOH): 203 (5.98), 235 (4.44), 267 (4.55), 272 (sh, 4.52). ^{1}H-NMR ($CDCl_3$): 8.62, 8.58 (2*d*, H–C(2)); 8.66–8.49 (br. *s*, H–N(6)); 8.18–8.10, 8.04 (2*m*, 4 H *o* to NO_2 (npeoc), H–C(8)); 7.47, 7.33 (2*m*, 4 H *m* to NO_2 (npeoc), 4 H *m* to MeO); 7.33–7.18 (*m*, 4 arom. H, H–C(2) (Ar)); 7.00–6.88 (*m*, H–C(5) (Ar)); 6.84–6.58 (*m*, H–C(6) (Ar), 4 H *o* to MeO); 6.20, 6.13 (2*d*, H–C(1′)); 5.53 (*m*, H–C(3′)); 5.31–5.21 (2*m*, H–C(2′)); 4.89, 4.81 (2*q*, MeC*H*$(O)_2$); 4.54–4.41 (*m*, 2 CH_2CH_2O (npeoc)); 4.38–3.86 (*m*, ArCH_2, H–C(4′)); 3.74 (*s*, 2 MeO); 3.60–3.49, 3.48–3.35 (2*m*, 2 H–C(5′)); 3.12 (*t*, 2 CH_2CH_2O (npeoc)); 2.78–2.57 (*m*, 4 H (succ.)); 1.33, 1.14 (2*d*, *Me*CH$(O)_2$). Anal. calc. for $C_{62}H_{58}FN_7O_{19}$ (1224.1): C 60.83, H 4.78, N 8.01; found: C 60.44, H 4.65, N 7.58.

6. *Phosphitylation to* **56**–**67**. 6.1. *General Procedure.* The 5′-*O*-(4,4′-dimethoxytriphenylmethyl)-2′-acetal-protected monomer **32**–**43** (0.5 mmol, 450–640 mg) was co-evaporated with abs. CH_2Cl_2 (2 × 30 ml). Subsequently, 4–8 ml (0.6–1.2 mmol, 181–362 mg) of a stock soln. of 2-cyanoethyl tetraisopropylphosphorodiamidite (0.15M in abs. CH_2Cl_2) were added in portions of 1–2 ml. The mixture was evaporated, the oil taken up with MeCN (10 ml), and 1*H*-tetrazole (0.5–0.7 mmol, 35–50 mg) was added. The soln. was stirred at r.t. for 1–4 h. The reaction was stopped by pouring into sat. $NaHCO_3$ soln. (150 ml) after dilution with AcOEt (100 ml). The aq. phase was extracted with AcOEt (50 ml), the combined org. phase washed with twice with sat. NaCl soln. (50 ml), dried (Na_2SO_4), and evaporated, and the crude oil purified by FC (silica gel (20 g), toluene/AcOEt/MeOH). *Note: It is very important that chromatographic purification takes place rapidly.* The product fractions were evaporated and co-evaporated with MeOH (2 × 5 ml) and CH_2Cl_2 (2 × 5 ml). The resulting colorless foam was dried in a desiccator under high vacuum.

6.2. *2′-*O*-[1-(Benzyloxy)ethyl]-5′-*O*-(4,4′-dimethoxytriphenylmethyl)uridine 3′-(2-Cyanoethyl Diisopropylphosphoramidite)* (**56**). According to *6.1*, from **32**. Yield 85%. Colorless foam. TLC (toluene/AcOEt/MeOH 5:4:1): R_f 0.64, 0.68. UV (MeOH): 204 (4.84), 234 (4.40), 260 (4.06). ^{1}H-NMR ($CDCl_3$): 8.60 (br. *s*, H–N(3)); 7.93–7.77 (*m*, H–C(6)); 7.40–7.18 (*m*, 4 H *m* to MeO, 10 arom. H); 6.81 (*m*, 4 H *o* to MeO); 6.09 (2*d*, H–C(1′)); 5.27–5.01 (*m*, H–C(5), MeC*H*$(O)_2$); 4.80–4.42 (*m*, H–C(2′), H–C(3′), ArCH_2); 4.24 (*m*, H–C(4′)); 3.99–3.33 (*s*, 12 H, 2 MeO), 2 H–C(5′), CH_2CH_2CN, 2 Me_2C*H*); 2.63–2.32 (*m*, CH_2CH_2CN); 1.40 (*m*, *Me*CH$(O)_2$); 1.24–0.98 (2*m*, 2 *Me*$_2$CH). Anal. calc. for $C_{48}H_{57}N_4O_{10}P$ (881.0): C 65.44, H 6.52, N 6.36; found: C 65.52, H 6.53, N 6.01.

6.3. *2′-*O*-[1-(Benzyloxy)ethyl]-5′-*O*-(4,4′-dimethoxytriphenylmethyl)-*N^2*-{[2-(4-nitrophenyl)ethoxy]carbonyl}-*O^6*-[2-(4-nitrophenyl)ethyl]guanosine 3′-(2-Cyanoethyl Diisopropylphosphoramidite)* (**57**). According to *6.1*, from **33**. Yield 80%. Colorless foam. TLC (hexane/AcOEt 1:3): R_f 0.57, 0.63. UV (MeOH): 205 (4.96), 236 (4.47), 269 (4.56). ^{1}H-NMR ($CDCl_3$): 8.18–7.85 (*m*, 4 H *o* to NO_2 (npe), H–C(8)); 7.55–6.95 (*m*, 2 H *m* to NO_2 (npeoc), 2 H *m* to NO_2 (npe)), 8 arom. H, 4 H *m* to MeO, H–N(2)); 6.80–6.65 (*m*, 4 H *o* to MeO); 6.18–5.92 (*m*, H–C(1′)); 5.41–4.72 (*m*, acetal-H, H–C(2′), CH_2CH_2OCO); 4.60–3.81 (*m*, 10 H, CH_2CH_2O, ArCH_2, CH_2CH_2CN, H–C(3′), H–C(4′)); 3.70 (2*s*, 2 MeO); 3.77–3.83 (*m*, 2 H–C(5′)); 3.35–3.21 (*m*, CH_2CH_2OCO); 3.07–2.93 (*m*, CH_2CH_2O); 2.72–2.61, 2.30–2.19 (2*m*, CH_2CH_2CN); 1.39–0.95 (3*m*, *Me*CH$(O)_2$, 2 *Me*$_2$CH). Anal. calc. for $C_{66}H_{72}N_9O_{15}P$ (1262.3): C 62.80, H 5.75, N 9.99; found: C 62.69, H 5.86, N 9.85.

6.4. *2′-*O*-[1-(Benzyloxy)ethyl]-5′-*O*-(4,4′-dimethoxytriphenylmethyl)-*N^4*-{[2-(4-nitrophenyl)ethoxy]carbonyl}cytidine 3′-(2-Cyanoethyl Diisopropylphosphoramidite)* (**58**). According to *6.1*, from **34**. Yield 85%. Colorless foam. TLC (toluene/AcOEt 1:3): R_f 0.52, 0.57. UV (MeOH): 204 (4.92), 235 (4.53), 277 (4.23), 288 (sh, 4.17). ^{1}H-NMR ($CDCl_3$): 8.45 (*m*, H–C(6)); 8.17 (*m*, 2 H *o* to NO_2); 7.72–7.53 (br. *s*, H–N(4)); 7.48–7.13 (*m*, 2 H *m* to NO_2, 4 H *m* to MeO, 10 arom. H); 6.90–6.75 (*m*, 4 H *o* to MeO); 6.72–6.61 (*m*, H–C(5)); 6.17–6.01 (*m*, H–C(1′)); 5.44–5.18 (*m*, acetal-H); 4.88–4.23 (*m*, ArCH_2, CH_2CH_2O, H–C(2′), H–C(3′), H–C(4′)); 3.90–3.37 (*m*, 2 MeO, 2 H–C(5′), CH_2CH_2CN, 2 MeC*H*); 3.06 (*t*, CH_2CH$_2$O); 2.35 (*m*, CH_2CH_2CN); 1.40 (2*d*, *Me*CH$(O)_2$); 1.35 (*m*, 2 *Me*$_2$CH). Anal. calc. for $C_{57}H_{65}N_6O_{13}P$ (1073.2): C 63.80, H 6.11, N 7.83; found: C 63.29, H 6.23, N 7.63.

6.5. *2′-*O*-[1-(Benzyloxy)ethyl]-5′-*O*-(4,4′-dimethoxytriphenylmethyl)-*N^6*-{[2-(4-nitrophenyl)ethoxy]carbonyl}adenosine 3′-(2-Cyanoethyl Diisopropylphosphoramidite)* (**59**). According to *6.1*, from **35**. Yield 78%. Colorless foam. TLC (hexane/AcOEt 1:3): R_f 0.59, 0.64. UV (MeOH): 204 (5.00), 235 (4.43), 267 (4.47), 22 (sh, 4.44). ^{1}H-NMR ($CDCl_3$): 8.65, 8.59 (2*d*, H–C(2)); 8.24 (*m*, H–N(6)); 8.20–8.04 (*m*, H–C(8), 2 H *o* to NO_2); 7.48–7.10 (*m*, 2 H *m* to NO_2, 4 H *m* to MeO, 8 arom. H); 7.09–6.95 (*m*, 2 arom. H); 6.82–6.71 (*m*, 4 H *o* to MeO); 6.23–6.12 (*m*, H–C(1′)); 5.33–4.82 (3*m*, MeC*H*$(O)_2$, H–C(2′)); 4.70–3.79 (*m*, H–C(3′), H–C(4′), CH_2CH_2O, ArCH_2); 3.72 (*m*, 2 MeO); 3.68–3.25 (*m*, 2 H–C(5′), CH_2CH_2CN, Me_2C*H*); 3.10 (*t*, CH_2CH$_2$O); 2.64–2.28 (*m*, CH_2CH_2CN); 1.31–0.95 (*m*, *Me*CH$(O)_2$, 2 *Me*$_2$CH). Anal. calc. for $C_{57}H_{65}N_8O_{12}P$ (1085.2): C 63.08, H 6.04, N 10.32; found: C 62.93, H 6.16, N 10.06.

6.6. *5′-O-(4,4′-Dimethoxytriphenylmethyl)-2′-O-{1-{{4-{{[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}benzyl}-oxy}ethyl}uridine 3′-(2-Cyanoethyl Diisopropylphosphoramidite)* (**60**). According to *6.1*, from **36**. Yield 89%. Colorless foam. TLC (toluene/AcOEt 1:1): R_f 0.38, 0.44. UV (MeOH): 205 (4.92), 235 (4.38), 265 (4.30), 279 (sh, 4.13). ^{1}H-NMR ($CDCl_3$): 8.18 (*m*, 2 H *o* to NO_2 (npeoc)); 8.08 (br. *s*, H–N(3)); 7.99–7.82 (*m*, H–C(6)); 7.44–7.00 (*m*, 5 arom. H, 4 H *m* to MeO, 2 H *m* to NO_2 (npeoc)), H–C(2) (Ar), H–C(5) (Ar), H–C(6) (Ar)); 6.87–6.75 (*m*, 4 H *o* to MeO); 6.05, 5.94 (2*m*, H–C(1′)); 5.25–5.06 (*m*, MeC*H*$(O)_2$, H–C(5)); 4.73–4.40 (*m*, ArCH_2, CH_2CH_2O (npeoc), H–C(2′), H–C(3′)); 4.30–4.13 (*m*, H–C(4′)); 3.97–3.35 (*m*, 2 MeO, 2 H–C(5′), CH_2CH_2CN, 2 Me_2CH); 3.15 (*t*, CH_2CH_2O (npeoc)); 2.63–2.49, 2.44–2.35 (2*m*, CH_2CH_2CN); 1.49–1.34 (*m*, *Me*CH$(O)_2$); 1.27–0.94 (*m*, 2 *Me*$_2$CH). ^{31}P-NMR ($CDCl_3$): 151.21, 150.94, 150.73, 150.49 (4 *s*). Anal. calc. for $C_{57}H_{64}FN_5O_{15}P$ (1109.1): C 61.73, H 5.82, N 6.31; found: C 61.56, H 5.82, N 5.67.

6.7. *5′-O-(4,4′-Dimethoxytriphenylmethyl)-2′-O-{1-{{3-fluoro-{{4-[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}-benzyl}oxy}ethyl}uridine 3′-(2-Cyanoethyl Diisopropylphosphoramidite)* (**61**). According to *6.1*, from **37**. Yield 89%. Colorless foam. TLC (toluene/AcOEt 1:1): R_f 0.38, 0.44. UV (MeOH): 205 (4.92), 235 (4.38), 265 (4.30), 279 (sh, 4.13). ^{1}H-NMR ($CDCl_3$): 8.18 (*m*, 2 H *o* to NO_2 (npeoc)); 8.08 (br. *s*, H–N(3)); 7.99–7.82 (*m*, H–C(6)); 7.44–7.00 (*m*, 5 arom. H, 4 H *m* to MeO, 2 H *m* to NO_2(npeoc), H–C(2) (Ar), H–C(5) (Ar), H–C(6) (Ar)); 6.87–6.75 (*m*, 4 H *o* to MeO); 6.05, 5.94 (2*m*, H–C(1′)); 5.25–5.06 (*m*, MeC*H*$(O)_2$, H–C(5)); 4.73–4.40 (*m*, ArCH_2, CH_2CH_2O (npeoc), H–C(2′), H–C(3′)); 4.30–4.13 (*m*, H–C(4′)); 3.97–3.35 (*m*, 2 MeO, CH_2CH_2CN, 2 H–C(5′), 2 Me_2CH); 3.15 (*t*, CH_2CH_2O (npeoc)); 2.63–2.49, 2.44–2.35 (2*m*, CH_2CH_2CN); 1.49–1.34 (*m*, *Me*CH$(O)_2$); 1.27–0.94 (*m*, 2 *Me*$_2$CH). ^{31}P-NMR ($CDCl_3$): 151.21, 150.94, 150.73, 150.49 (4 *s*). Anal. calc. for $C_{57}H_{64}FN_5O_{15}P$ (1109.1): C 61.73, H 5.82, N 6.31; found: C 61.56, H 5.82, N 5.67.

6.8. *5′-O-(4,4′-Dimethoxytriphenylmethyl)-2′-O-{1-{{4-{{[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}benzyl}-oxy}ethyl}-*N^2*-{[2-(4-nitrophenyl)ethoxy]carbonyl}-*O^6*-[2-(4-nitrophenyl)ethyl]guanosine 3′-(2-Cyanoethyl Di-isopropylphosphoramidite)* (**62**). According to *6.1*, from **38**. Yield 72%. Colorless foam. TLC (toluene/AcOEt/MeOH 5:6:1): R_f 0.80, 0.83. UV (MeOH): 204 (5.05), 236 (4.51), 269 (4.62), 278 (sh, 4.56). ^{1}H-NMR ($CDCl_3$): 8.20–8.07 (*m*, 4 H *o* to NO_2 (npeoc), 2 H *o* to NO_2 (npe)); 8.06, 7.95 (2*m*, H–C(8)); 7.50–7.14 (*m*, H–N(2), 5 arom. H, 4 H *m* to NO_2 (npeoc), 2 H *m* to NO_2 (npe), 4 H *m* to MeO); 7.04–6.99 (*m*, H–C(3) (Ar), H–C(5) (Ar)); 6.98–6.88 (*m*, H–C(2) (Ar), H–C(6) (Ar)); 6.80–6.68 (*m*, 4 H *o* to MeO); 6.09, 5.98 (2*d*, H–C(1′)); 5.40–5.12 (*m*, H–C(2′)); 5.06–4.92, 4.90–4.82 (2*m*, MeC*H*$(O)_2$); 4.81–4.70 (*m*, CH_2CH_2O (npeoc)); 4.60–4.39, 4.38–3.79 (2*m*, CH_2CH_2O (npeoc), CH_2CH_2O (npe), ArCH_2, H–C(3′), H–C(4′), CH_2CH_2CN)); 3.72 (2*s*, 2 MeO); 3.66–3.39 (*m*, 2 H–C(5′), 2 Me_2CH); 3.13 (*t*, CH_2CH_2O (npeoc)); 2.99 (*m*, CH_2CH_2O (npeoc), CH_2CH_2O (npe)); 2.72–2.61, 2.30–2.18 (2*m*, CH_2CH_2CN); 1.43–1.31 (*m*, *Me*CH$(O)_2$); 1.30–0.94 (*m*, 2 *Me*$_2$CH). ^{31}P-NMR ($CDCl_3$): 151.63, 151.23, 150.77, 150.43 (4 *s*). Anal. calc. for $C_{75}H_{79}N_{10}O_{20}P$ (1471.5): C 61.22, H 5.41, N 9.52; found: C 60.97, H 5.44, N 9.32.

6.9. *5′-O-(4,4′-Dimethoxytriphenylmethyl)-2′-O-{1-{{3-fluoro-4-{{[2-(4-nitrophenyl)-ethoxy]carbonyl}oxy}-benzyl}oxy}ethyl}-*N^4*-{[2-(4-nitrophenyl)ethoxy]carbonyl}-*O^6*-[2-(4-nitrophenyl)ethyl]guanosine 3′-(2-Cyanoethyl Diisopropylphosphoramidite)* (**63**). According to *6.1*, from **39**. Yield 70%. Colorless foam. TLC (toluene/AcOEt/MeOH 10:8:1): R_f 0.76, 0.80. UV (MeOH): 203 (4.96), 237 (4.49), 269 (4.63), 279 (sh, 4.56). ^{1}H-NMR ($CDCl_3$): 8.20–8.06 (*m*, 4 H *o* to NO_2 (npeoc), 2 H *o* to NO_2 (npe)); 8.04,7.96 (2*m*, H–C(8)); 7.54–7.10 (*m*, H–N(2), 5 arom. H, 4 H *m* to NO_2 (npeoc), 2 H *m* to NO_2 (npe), 4 H *m* to MeO, H–C(2) (Ar)); 7.05–6.83 (*m*, H–C(5) (Ar), H–C(6) (Ar)); 6.82–6.66 (*m*, 4 H *o* to MeO); 6.09, 5.97 (2*m*, H–C(1′)); 5.42–5.13 (*m*, H–C(2′)); 5.08–4.82 (*m*, MeC*H*$(O)_2$); 4.80–4.68 (*m*, CH_2CH_2O (npeoc)); 4.60–3.78 (*m*, CH_2CH_2O (npeoc), CH_2CH_2O (npe), ArCH_2, H–C(3′), H–C(4′), CH_2CH_2CN)); 3.72 (*s*, 2 MeO); 3.68–3.41 (*m*, 2 H–C(5′), 2 Me_2CH); 3.35–3.20 (*m*, CH_2CH_2O (npeoc); 3.18–3.09 (*t*, CH_2CH_2O (npeoc)); 3.05–2.92 (*m*, CH_2CH_2O (npe)); 2.72–2.61, 2.30–2.20 (2*m*, CH_2CH_2CN); 1.39, 1.37 (2*d*, *Me*CH$(O)_2$); 1.30–0.94 (*m*, 2 *Me*$_2$CH). ^{31}P-NMR ($CDCl_3$): 151.61, 151.18, 150.78, 150.49 (4 *s*). Anal. calc. for $C_{75}H_{78}FN_{10}O_{20}P$ (1489.4): C 60.48, H 5.28, N 9.40; found: C 60.53, H 5.32, N 9.23.

6.10. *5′-O-(4,4′-Dimethoxytriphenylmethyl)-2′-O-{1-{{4-{{[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}benzyl}-oxy}ethyl}-*N^4*-[[2-(4-nitrophenyl)ethoxy]carbonyl}cytidine 3′-(2-Cyanoethyl Diisopropylphosphoramidite)* (**64**). According to *6.1*, from **40**. Yield 86%. Colorless foam. TLC ($CHCl_3$/MeOH 100:1): R_f 0.43,0.46. UV (MeOH): 204 (4.92), 235 (4.54), 272 (4.39), 289 (sh, 4.28). ^{1}H-NMR ($CDCl_3$): 8.56–8.38 (*m*, H–C(6)); 8.20–8.09 (*m*, 4 H *o* to NO_2(npeoc)); 7.56–7.47 (br. *s*, H–N(4)); 7.46–7.12 (*m*, 5 arom. H, 4 H *m* to NO_2 (npeoc), 4 H *m* to MeO, H–C(3) (Ar), H–C(5) (Ar)); 7.08–6.99 (*m*, H–C(2) (Ar), H–C(6) (Ar)); 6.88–6.78 (*m*, 4 H *o* to MeO); 6.72, 6.61 (2*m*, H–C(5)); 6.13–5.98 (2*m*, H–C(1′)); 5.47–5.15 (*m*, MeC*H*$(O)_2$); 4.87–4.64 (*m*, H–C(2′)); 4.62–4.20 (*m*, 2 CH_2CH_2O (npeoc), ArCH_2, H–C(3′), H–C(4′)); 3.77 (*s*, 2 MeO); 3.74–3.37 (*m*, Me_2CH, CH_2CH_2CN, 2 H–C(5′)); 3.18–3.02 (*m*, 2 CH_2CH_2O (npeoc)); 2.73, 2.34 (2*m*, CH_2CH_2CN); 1.43,

1.38 (2*d*, *Me*CH(O)$_2$); 1.30–0.89 (*m*, 2 *Me*$_2$CH). ^{31}P-NMR ($CDCl_3$): 151.54, 151.67, 150.35, 149.81 (4 *s*). Anal. calc. for $C_{66}H_{70}N_7O_{18}P$ (1280.3): C 61.92, H 5.51, N 7.66; found: C 61.75, H 5.87, N 5.78.

6.11. *5′-*O*-(4,4′-Dimethoxytriphenylmethyl)-2′-*O*-{1-{{3-fluoro-4-{{[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}-benzyl}oxy}ethyl}-*N^4*-{[2-(4-nitrophenyl)ethoxy]carbonyl}cytidine 3′-(2-Cyanoethyl Diisopropylphosphoramidite)* (**65**). According to *6.1*, from **41**. Yield 94%. Colorless foam. TLC (toluene/AcOEt/MeOH 5:4:1): R_f 0.76, 0.80. UV (MeOH): 205 (4.98), 235 (4.59), 272 (4.43), 288 (sh, 4.32). ^{1}H-NMR ($CDCl_3$): 8.57–8.39 (*m*, H–C(6)); 8.21–8.12 (*m*, 4 H *o* to NO_2 (npeoc)); 7.63–7.35 (br. *s*, H–N(4)); 7.45–7.02 (*m*, 5 arom. H, 4 H *m* to NO_2 (npeoc), 4 H *m* to MeO, H–C(3) (Ar), H–C(5) (Ar), H–C(6) (Ar)); 6.87–6.78 (*m*, 4 H *o* to MeO); 6.74, 6.62 (2*m*, H–C(5)); 6.08, 5.99 (2*d*, H–C(1′)); 5.47–5.16 (*m*, MeC*H*(O)$_2$); 4.88–4.21 (*m*, 2 CH_2CH$_2$O (npeoc), ArCH_2, H–C(2′), H–C(3′), H–C(4′)); 3.79 (*d*, 2 MeO); 3.73–3.38 (*m*, 2 Me$_2$C*H*, CH_2CH$_2$CN, 2 H–C(5′)); 3.18–3.00 (*m*, 2 CH$_2$CH_2O (npeoc)); 2.78–2.31 (*m*, CH$_2$CH_2CN); 1.45–1.36 (*m*, *Me*CH(O)$_2$); 1.31–0.91 (*m*, 2 *Me*$_2$CH). ^{31}P-NMR ($CDCl_3$): 151.69, 150.87, 150.21, 149.73 (4 *s*). Anal. calc. for $C_{66}H_{69}FN_7O_{18}P$ (1298.3): C 61.06, H 5.36, N 7.55; found: C 61.76, H 5.63, N 7.95.

6.13. *5′-*O*-(4,4′-Dimethoxytriphenylmethyl)-2′-*O*-{1-{{4-{{[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}benzyl}-oxy}ethyl}-*N^6*-{[2-(4-nitrophenyl)ethoxy]carbonyl}adenosine 3′-(2-Cyanoethyl Diisopropylphosphoramidite)* (**66**). According to *6.1*, from **42**. Yield 82%. Colorless foam. TLC ($CHCl_3$/MeOH 100:1): R_f 0.65, 0.69. UV (MeOH): 204 (5.01), 235 (4.46), 267 (4.58), 273 (sh, 4.55). ^{1}H-NMR ($CDCl_3$): 8.60 (*dd*, H–C(2)); 8.23–8.08 (*m*, 4 H *o* to NO_2 (npeoc), H–C(8)); 8.02 (br. *s*, H–N(6)); 7.48–7.36 (*m*, 4 H *m* to NO_2 (npeoc), H–C(3) (Ar), H–C(5) (Ar)); 7.35–7.12 (*m*, 5 arom. H, H–C(2) (Ar), H–C(6) (Ar)); 7.08–6.88 (*m*, 4 H *m* to MeO); 6.82–6.72 (*m*, 4 H *o* to MeO); 6.23–6.08 (2*d*, H–C(1′)); 5.35–4.82 (*m*, H–C(2′), MeC*H*(O)$_2$); 4.68–3.05 (*m*, ArCH_2, 2 CH_2CH$_2$O (npeoc), 2 Me$_2$C*H*, 2 MeO, H–C(3′), H–C(4′), CH_2CH$_2$CN, 2 H–C(5′)); 2.67–2.53, 2.38–2.26 (2*m*, CH_2CH$_2$CN); 1.40, 1.35 (2*d*, *Me*CH(O)$_2$); 1.31–0.97 (*m*, 2 *Me*$_2$CH). ^{31}P-NMR ($CDCl_3$): 151.69, 151.14, 150.81, 150.48 (4 *s*). Anal. calc. for $C_{67}H_{72}N_9O_{17}P$ (1306.3): C 61.60, H 5.56, N 9.65; found: C 61.18, H 5.71, N 9.48.

6.14. *5′-*O*-(4,4′-Dimethoxytriphenylmethyl)-2′-*O*-{1-{{3-fluoro-4-{{[2-(4-nitrophenyl)ethoxy]carbonyl}oxy}-benzyl}oxy}ethyl}-*N^6*-{[2-(4-nitrophenyl)ethoxy]carbonyl}-adenosine 3′-(2-Cyanoethyl Diisopropylphosphoramidite)* (**67**). According to *6.1*, from **43**. Yield 88%. Colorless foam. TLC (toluene/AcOEt/MeOH 5:4:1): R_f 0.78, 0.82. UV (MeOH): 203 (4.97), 236 (4.44), 269 (4.56), 274 (sh, 4.56). ^{1}H-NMR ($CDCl_3$): 8.62, 8.58 (2*d*, H–C(2)); 8.20–8.11, 8.07 (2*m*, 4 H *o* to NO_2 (npeoc), H–C(8)); 8.06–7.95 (br. *s*, H–N(6)); 7.47, 7.15 (*m*, 4 H *m* to NO_2 (npeoc), H–C(2) (Ar), 4 H *m* to MeO, 5 arom. H); 7.02–6.67 (*m*, H–C(5) (Ar), H–C(6) (Ar), 4 H *o* to MeO); 6.22–6.11 (*m*, H–C(1′)); 5.33–4.85 (*m*, H–C(2′), MeC*H*(O)$_2$); 4.66–3.79 (*m*, H–C(3′), ArCH_2, 2 CH_2CH$_2$O (npeoc), 2 MeO, H–C(3′), H–C(4′), CH_2CH$_2$CN)); 3.74 (*s*, 2 MeO); 3.72–3.24 (*m*, 2 H–C(5′), Me$_2$C*H*); 3.19–3.07 (*m*, 2 CH$_2$CH_2O (npeoc)); 2.67–2.55, 2.37–2.28 (2*m*, CH$_2$CH_2CN); 1.42, 1.38 (2*d*, *Me*CH(O)$_2$); 1.32–0.98 (*m*, 2 *Me*$_2$CH). ^{31}P-NMR ($CDCl_3$): 151.65, 151.07, 150.83, 150.64 (4 *s*). Anal. calc. for $C_{67}H_{71}FN_9O_{17}P$ (1324.3): C 60.77, H 5.40, N 9.52; found: C 60.76, H 5.59, N 9.56.

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