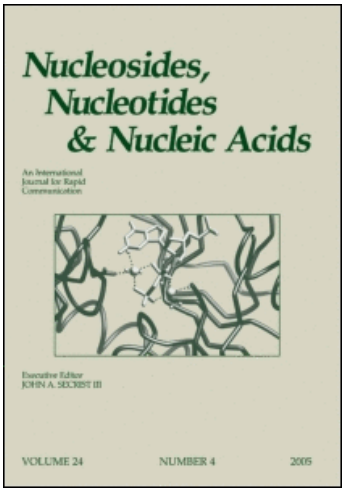

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Christoph Henke[a]; Wolfgang Pfleiderer[a]
[a] Fachbereich Chemie, Universität Konstanz, Konstanz, Germany

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NUCLEOTIDES. LXXIV* SYNTHESIS OF α-D-ARABINO-OLIGONUCLEOTIDES

Christoph Henke and Wolfgang Pfleiderer □ *Fachbereich Chemie, Universität Konstanz, Konstanz, Germany*

□ *The 5 α-D-arabinofuranosylnucleosides α-araU (***15***), α-araT (***18***), α-araC (***22***), α-araA (***25***), and α-araG (***28***) have been synthesized by the modified silyl-method. The amino groups at the nucleobases and the 2′-hydroxy group at the sugar moiety were protected by the 2-(4-nitrophenyl)ethoxycarbonyl (npeoc) group (***37-40***) and the amide function in α-araG was additionally blocked by the 2-(4-nitrophenyl)ethyl group (***63***) to improve solubility in organic solvents. Mono- and dimethoxytritylation of the 5′-OH group was performed in the usual manner to give* **41-48**, **64**, *and* **65** *in high yields and further substitution of the 3′-OH group led to the monomeric building blocks* **66-75** *as well as the 3′-O-succinoyl derivatives* **76-85** *functioning as starting units in solid-support oligonucleotide synthesis. A large number of oligo-α-arabinonucleotides have been prepared on modified CPG-material applying the npeoc/npe strategy as a very efficient synthetic tool for highly purified, homogenous oligomers. Hybridizations between α-arabinonucleotide strands revealed in analogy to earlier findings an antiparallel orientation whereas the combination of an oligo-α-D-arabinonucleotide with a complementary oligo-2′-deoxy-β-D-ribofuranosylnucleotide showed base-pairing only if a parallel polarity was present. The advantages in oligo-α-arabinonucleotide synthesis were furthermore demonstrated by the synthesis of the tα-ANA^{his} a structural analog of the natural tRNA^{his} of the phage T5.*

Keywords α-D-arabinonucleosides; Glycosylation reactions; npeoc/npe protection; 3′-phosphoramidites; Oligo-α-arabinonucleotides; Hybridizations; tα-ANA^{his} synthesis

INTRODUCTION

The most common 5 natural nucleobases thymine, uracil, cytosine, adenine, and guanine are linked to pentose-sugar derivatives by β-glycosidic bonds. Besides the nucleic acid components various β-D-arabinofu-

In honor and celebration of the life and career of John A. Montgomery.

*See Münch and Pfleiderer.

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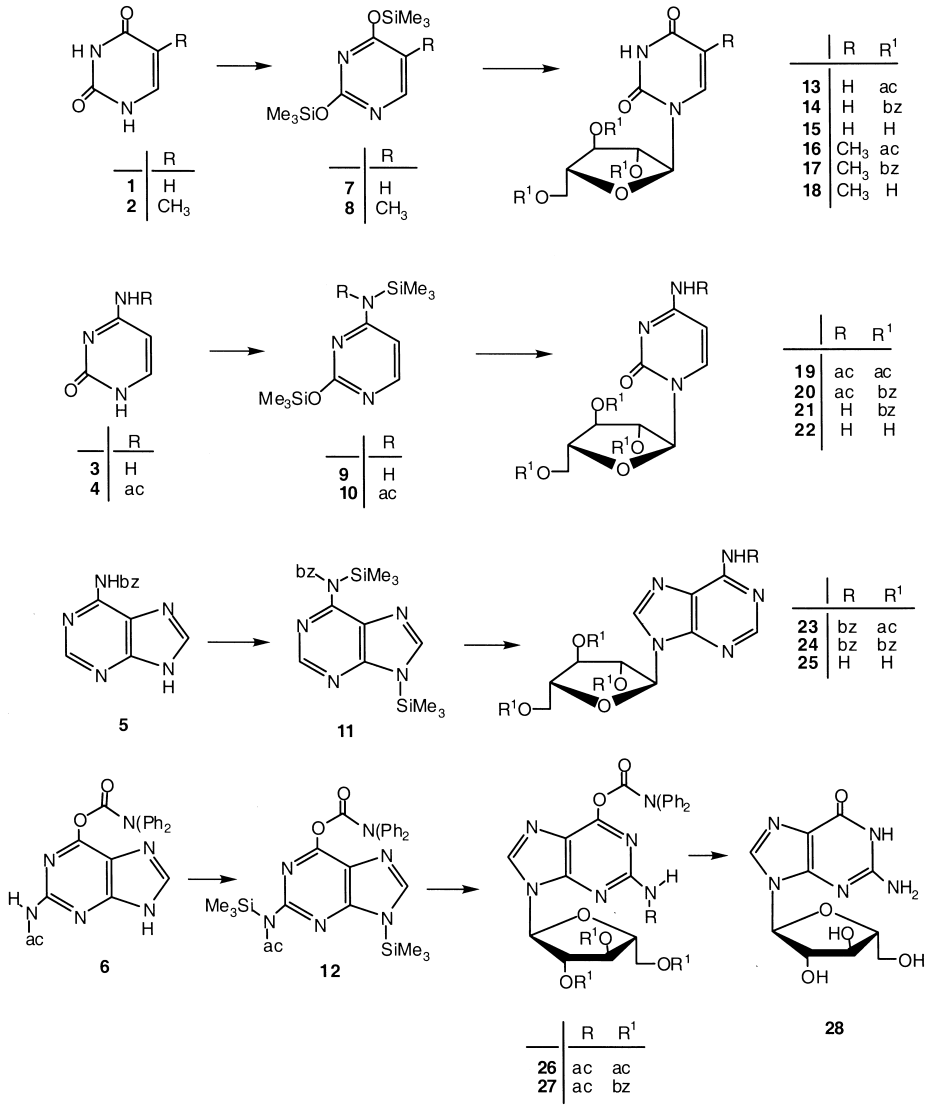
Address correspondence to Wolfgang Pfleiderer, Fachbereich Chemie, Universität Konstanz, Postfach 5560, 78457 Konstanz, Germany. Fax: 0049-7531-883138; E-mail: wolfgang.pfleiderer@uni-konstanz.de

ranosyl-nucleosides have been found in nature or resulted from synthetic approaches. 9-β-D-Arabinofuranosyladenine (ara-A)[2], 1-β-D-arabino-furanosylcytosine (araC), and 9-β-D-arabinofuranosylhypyxanthine (ara-H) show antiviral activities[3,4] and araATP inhibit DNA-polymerase and ribonucleotide-reductase.[5] From extracts of the sponge *Cryptothetica crypta*[6] spongouridine (1-β-D-arabinofuranosyluracil) and spongothymidine (1-β-D-arabinofuranosylthymidine) have been isolated showing antibiotic activities. α-Arabinofuranosyl-nucleosides have sofar not been found in nature but synthetically this type of compounds has been investigated by different methods based upon mainly on classical glycosylation reactions and leading often to α,β-anomeric mixtures. We describe here a direct general approach to α-arabino-nucleosides in high yields using Vorbrüggen's silyl method,[7–10] which forms in a stereospecific manner by the neighboring participation effect of the 2-acyloxy function almost exclusively an α-glycosidic linkage. The arabino-nucleosides have been converted into the corresponding fully protected nucleoside-3′-phosphoramidites which have then been applied as building blocks to form by solid-phase synthesis various α-arabino-oligonucleotides.

SYNTHESES OF α-D-ARABINOFURANOSYL-NUCLEOSIDES

The Vorbrüggen approach afforded in the first step of the synthesis the silylation of uracil (**1**), thymine (**2**), cytosine (**3**), N^4-acetylcytosine (**4**), and N^6-benzoyladenine (**5**) by heating in hexamethyldisilazene (HMDS) under reflux to give **7-11**. In the case of N^2-acetyl-O^6-diphenylcarbamoylguanine (**6**) the more reactive N,O-*bis*-trimethylsilylacetamide was used in boiling CH_2Cl_2 to get fast silylation in 15 min to **12**. Glycosylation of **7** and **8**, respectively, with 1,2,3,5-tetra-O-acetyl-D-arabinofuranose[11,12] as well as 1-O-acetyl-2,3,5-tri-O-benzoyl-D-arabinofuranose[13,14] in CH_2Cl_2 under trimethylsilyl trifluorosulfonate (TMS-triflate) activation giving high yields of **13** (62%), **14**[13] (87%), **16** (73%), and **17**[15] (91%) after chromatographical isolation and purification. In a similar manner reacted N^4-acetylcytosine via **7** to 1-(N^4-,2′,3′,5′-tetracetyl-α-D-arabinofuranosyl)cytosine (**19**) in 76% yield and silylated cytosine **8** could be converted with 1-O-acetyl-2,3,5-tri-O-benzoyl-D-arabinofuranose into 1-(2′,3′,5′-tri-O-benzoyl-α-D-arabinofuranosyl)cytosine (**20**) in 80% yield. N^6-Benzoyladenine (**5**) and N^2-acetyl-O^6-diphenylcarbamoylguanine (**6**) worked with both sugar derivatives under the same reaction conditions to **23** (83%) and **24**[16] (69%), respectively, as well as to **26**[17] (72%) and **27** (79%) (Scheme 1).

Treatment of the various acylated α-D-arabinofuranosyl-nucleosides by sodium methoxide in MeOH or by methanolic ammonia led to free 1-α-D-arabinofuranosyluracil (**15**) (82%),[15] 1-α-D-arabinofuranosylthymine (**18**) (88%),[15] 1-α-D-arabinofuranosylcytosine (**22**) (66%),[18] 1-α-D-arabinofu-



SCHEME 1

ranosyladenine (**25**) (67%),[16] and 1-α-D-arabinofuranosyl-guanine (**28**) (74%),[17] all of which have been prepared earlier with variable success.

The characterization and structural assignment of all α-D-arabinofuranosyl-nucleosides has been achieved by determination of the UV- and ^{1}H-NMR spectra listed in the experimental part and their comparisons with the corresponding natural ribofuranosyl-nucleosides. It is worth mentioning that all sugar protons in the O-benzoyl series are shifted to lower field comparing with the O-acetyl analogs. Furthermore a comparison of the

α- and β-arabinofuranosyladenine and the α- and β-arabinofuranosylguanine, respectively, revealed that in D_6-DMSO the H-1′- and H-3′-signals resonate in the β-anomer at lower field than the α-anomer whereas the H-2′- and H-4′-signals shift in opposite directions (Table 1).

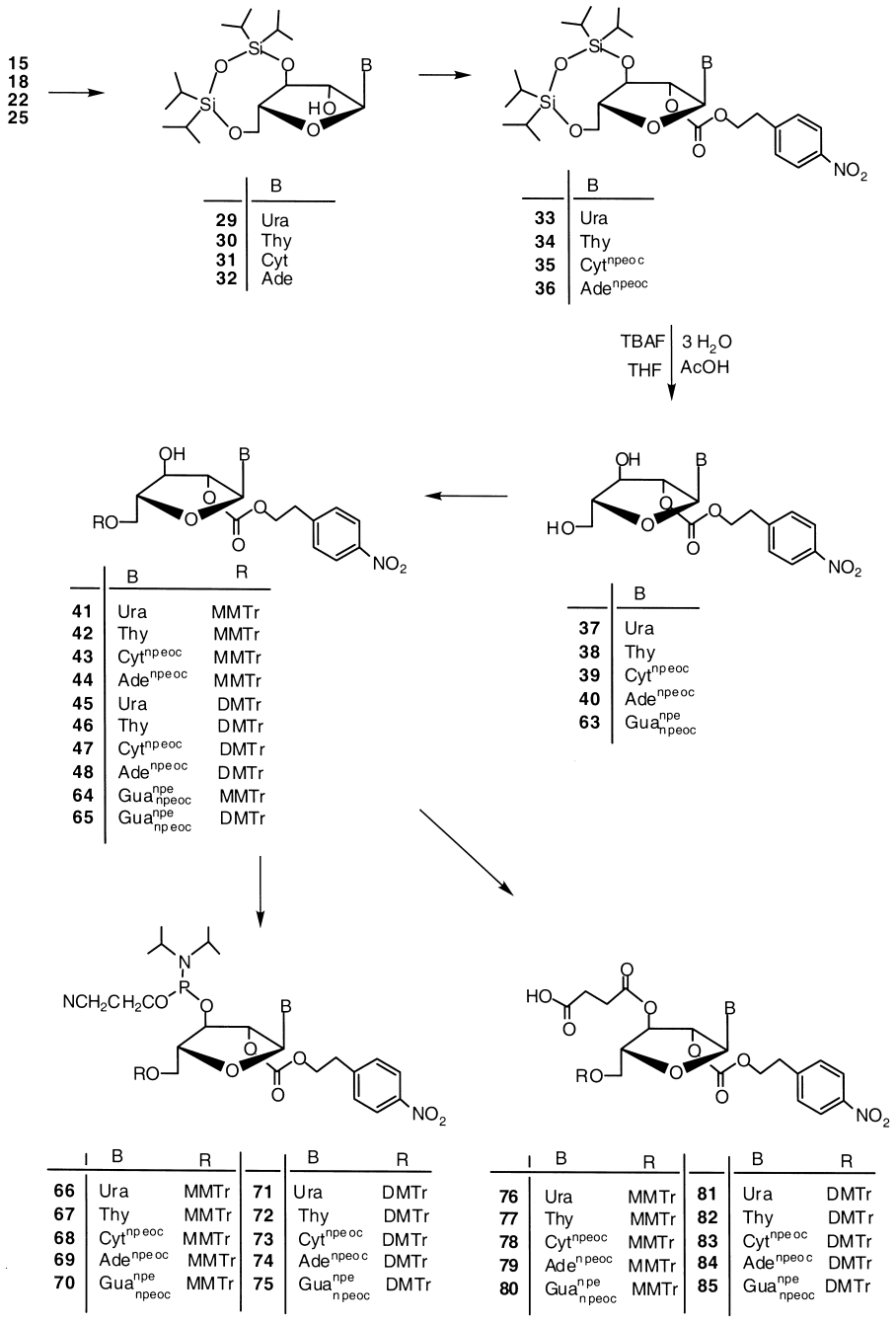
The next chapter of our investigations was concerned with the synthesis of the appropriate building blocks for the α-arabino-oligonucleotides. We decided to use the 2-(4-nitrophenyl)ethyl- (npe) and the 2-(4-nitrophenyl) ethoxycarbonyl- (npeoc) group for base protection[19,20] according to their advanced properties in ribo-, 2′-deoxyribo- and β-arabino-nucleoside and nucleotide chemistry.[21,22] The sequence of protection started with the introduction of the 3′,5′-O-(1,1,3,3-tetraisopropyl-1,3-disiloxan-1,3-yl) (tipds) group[23] into α-araU (**15**), α-araT (**18**), α-araC (**21**), and α-araA (**25**) to give **29-32** in 80–90% yield. Subsequent acylation with an excess of 1-methyl-3-[2-(4-nitrophenyl)ethoxycarbonyl]-imidazolium chloride in CH_2Cl_2 and in presence of 4-dimethylaminopyridine afforded not only reaction at the 2′-OH group[24] but blocked also the amino function in **31** and **32** and gave isolated yields of 88–97% of **33-36**. The selective cleavage of the Markiewicz blocking group in **33-36** and **62** afforded special reaction conditions, applying tetrabutylammonium fluoride trihydrate in THF and in presence of AcOH, since fluoride ions in aprotic solvents are too basic and cause slow β-elimination of the npeoc functionality. Isolation of **37-40** and **63** was achieved by chromatographical means and gave high yields of 82–93% (Scheme 2).

The mono- and dimethoxytritylation of **37-40** and **63** worked in the usual manner in pyridine forming **41-48**, **64**, and **65** with yields between 82 and 95%.

TABLE 1 ^{1}H-NMR Data of α- and β-araA and α- and β-araG in D_6-DMSO

Compound	α-AraA	β-AraA	α-araG	β-AraG
H-1′	5.85 (d, 1)	6.26 (d, 1)	5.64 (d, 1)	6.04 (d, 1)
H-2′	4.67 (dd, 1)	4.13 (m, 1)	4.44 (dd, 1)	4.08 (m, 1)
H-3′	3.98 (dd, 1)	4.13 (m, 1)	3.95 (dd, 1)	4.08 (m, 1)
H-4′	4.14 (m, 1)	3.78 (m, 1)	4.05 (m, 1)	3.77 (m, 1)
H-5′, 5″	3.50 (m, 2)	3.65 (m, 2)	3.54 (m, 2)	3.65 (m, 2)
2′-OH	5.76 (d, 1)	5.63 (d, 1)	5.72 (d, 1)	5.61 (d, 1)
3′-OH	5.62 (d, 1)	5.53 (d, 1)	5.52 (d, 1)	5.45 (d, 1)
5′-OH	4.87 (t, 1)	5.11 (t, 1)	4.87 (t, 1)	5.05 (t, 1)
H-2	8.14 (s, 1)	8.13 (s.1)		
H-8	8.32 (s, 1)	8.18 (s, 1)	7.90 (s, 1)	7.80 (s, 1)
NH_2	7.29 (bs, 2)	7.26 (bs, 2)	6.45 (bs, 2)	6.49 (bs, 2)
NH			10.63 (s, 1)	11.62 (s, 1)

s = singlet, bs = broad singlet, d = doublet, dd = double doublet, t = triplet, m = multiplet.



	B
29	Ura
30	Thy
31	Cyt
32	Ade

	B
33	Ura
34	Thy
35	Cyt^{npeoc}
36	Ade^{npeoc}

	B
37	Ura
38	Thy
39	Cyt^{npeoc}
40	Ade^{npeoc}
63	Gua^{npe}_{npeoc}

	B	R
41	Ura	MMTr
42	Thy	MMTr
43	Cyt^{npeoc}	MMTr
44	Ade^{npeoc}	MMTr
45	Ura	DMTr
46	Thy	DMTr
47	Cyt^{npeoc}	DMTr
48	Ade^{npeoc}	DMTr
64	Gua^{npe}_{npeoc}	MMTr
65	Gua^{npe}_{npeoc}	DMTr

I	B	R
66	Ura	MMTr
67	Thy	MMTr
68	Cyt^{npeoc}	MMTr
69	Ade^{npeoc}	MMTr
70	Gua^{npe}_{npeoc}	MMTr

	B	R
71	Ura	DMTr
72	Thy	DMTr
73	Cyt^{npeoc}	DMTr
74	Ade^{npeoc}	DMTr
75	Gua^{npe}_{npeoc}	DMTr

I	B	R
76	Ura	MMTr
77	Thy	MMTr
78	Cyt^{npeoc}	MMTr
79	Ade^{npeoc}	MMTr
80	Gua^{npe}_{npeoc}	MMTr

	B	R
81	Ura	DMTr
82	Thy	DMTr
83	Cyt^{npeoc}	DMTr
84	Ade^{npeoc}	DMTr
85	Gua^{npe}_{npeoc}	DMTr

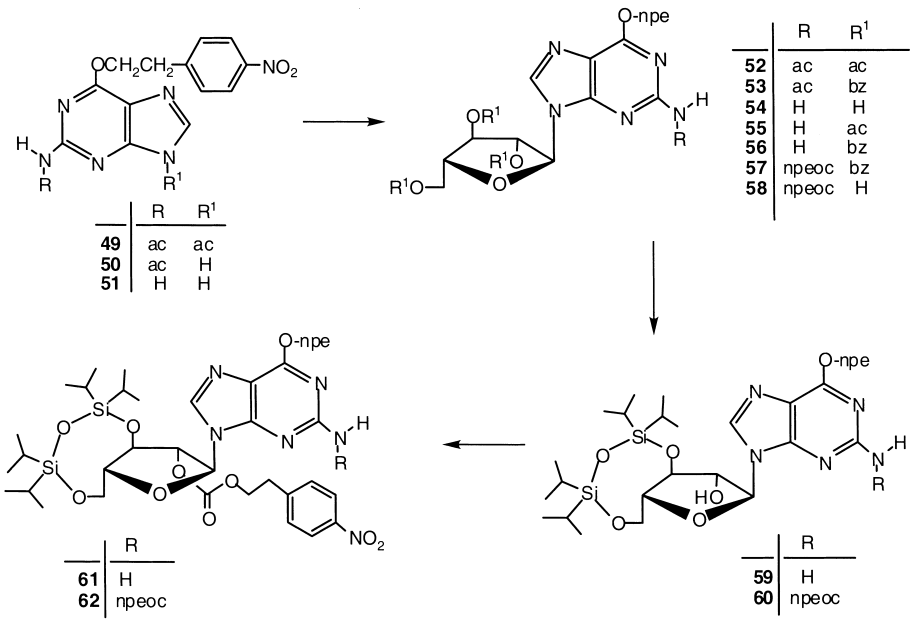
SCHEME 2

According to our experience with β-arabinofuranosylguanine[22] showing that O^6-protection is essential from solubility reasons we started first from N^2-acetyl-O^6-2-(4-nitrophenyl)ethylguanine (**50**) which was glycosylated with 1,2,3,5-tetra-O-acetyl-D-arabinofuranose[11,12] as well as 1-O-acetyl-2,3,5-tri-O-benzoyl-D-arabinofuranose[13,14] under Vorbrüggen conditions leading to N^2-acetyl-O^6-npe-9-(2,3,5-tri-O-acetyl-)- (**52**) and N^2-acetyl-O^6-npe-9-(2,3,5-tri-O-benzoyl-α-D-arabinofuranosyl)guanine (**53**) in 55% and 75% yield, respectively. Selective cleavage of the sugar-acyl-groups caused, however, difficulties and proceeded to **54** under a variety of reaction conditions such as NH_3/MeOH, Et_3N/MeOH, MeONa/MeOH, K_2CO_3/MeOH, and dioxan/MeOH/NH_3 only in moderate yields. More straightforward were the analogous glycosylations of O^6-2(4-nitrophenyl)ethylguanine (**51**) to **55** and **56** in 52% and 73% yield. Deacylation proceeded best with K_2CO_3 in MeOH to give **54** in yields >80%. **56** was then converted by 2-(4-nitrophenyl)ethoxycarbonyl chloride into O^6-npe-N^2-npeoc-9-(2,3,5-tri-O-benzoyl-α-D-arabinofuranosyl)guanine (**57**) in 93% yield and followed by debenzoylation in MeOH/dioxane/aqueous NH_3 forming **58** in 83% yield. The subsequent Markiewicz protection of **56** and **58** gave under the usual reaction conditions **59** and **60** which were then treated by 1-methyl-3-[2-(4-nitrophenyl)ethoxycarbonyl]-imidazolium chloride reacting at the 2′-OH group to the corresponding carbonates **61** and **62**. The expected concerted acylation of **59** also at the 2-amino group did not take place and afforded a second step applying 2-(4-nitrophenyl)ethoxycarbonyl chloride to form **62** (Scheme 3).

The last step of the synthesis of the fully protected α-arabino-nucleoside-3′-phosphor-amitides **66-75** was performed with **41-48**, **64**, and **65** under anhydrous conditions and under N_2-atmosphere with *bis*-(N,N-diisopropylamino)-2-cyanoethoxyphosphane and sublimed tetrazole as activator in CH_3CN and a reaction time of 8–18 h at room temperature. Work-up was best achieved by flash chromatography on silica gel with toluene/ethyl acetate and n-hexane/acetone gradients, respectively, isolating solid foams of **66-75** in 70–90% yield. Finally, the 3′-O-succinoyl-α-arabinonucleoside **76-85** were also prepared from **41-48**, **64**, and **65** with succinic anhydride and 4-dimethylaminopyridine in CH_2Cl_2 in yields >90% (Scheme 2).

All newly synthesized compounds have been characterized and proven in their structures by UV-, ^{1}H- and ^{31}P-NMR spectra as well as by elemental analysis. All data are reported in the experimental part.

The high purity and long-time stability of the 5 fully protected 5′-O-dimethoxytrityl-α-arabinofuranosylnucleoside-3′-phosphoramidites **71-75** have been chosen as the appropriate building blocks for the synthesis of a broad variety of homogenous and mixed oligo-α-arabinonucleotides. The synthetic cycle performed in an Applied Biosystem 392 synthesizer was based upon our experiences with the corresponding 2′-deoxy-



SCHEME 3

and ribonucleoside-3′-phosphoramidites[26–28] applying optimized reaction conditions for the oligo-α-arabinonucleotide synthesis. The applied npe/npeoc strategy[29] afforded the long-chain-N-methylaminoalkyl-CPG (LCMAA-CPG) solid-support material (500 Å),[30] which was prepared from dry glyceryl-CPG by subsequent treatment with 1,1′-carbonyldiimidazole and N,N′-dimethylhexane-1,6-diamine, followed by either one of the 3′-O-succinates **81-85** as 3′-terminal α-arabinofuranosylnucleoside and a final capping step (Figure 1).

The synthesis of the oligonucleotides was performed in the usual manner with a slightly modified cycle starting with the detritylation, coupling with the phosphoramidite, a capping step and the final oxidation of the phosphite ester to the phosphate stage. The time scale of 20 min per cycle is reported in the experimental part. The advantage of the npe/npeoc strategy is seen during deprotection of the blocking groups of which the 2-(4-nitrophenyl)ethyl-, the 2-(4-nitrophenylethoxy-carbonyl-, and the 2-cyanoethyl group can be removed in one step by DBU treatment quantitatively by a β-elimination process. During this procedure the oligonucleotide is still attached to the support and can after washing be cleaved by ammonia treatment, yielding 5′-protected oligomers, which can further be purified by ion-pair reverse-phase HPLC before final acid-catalyzed detritylation. An alternative workup starts with detritylation of the fully protected oligonucleotide, followed by DBU treatment, and, finally, ammonia cleavage leading to

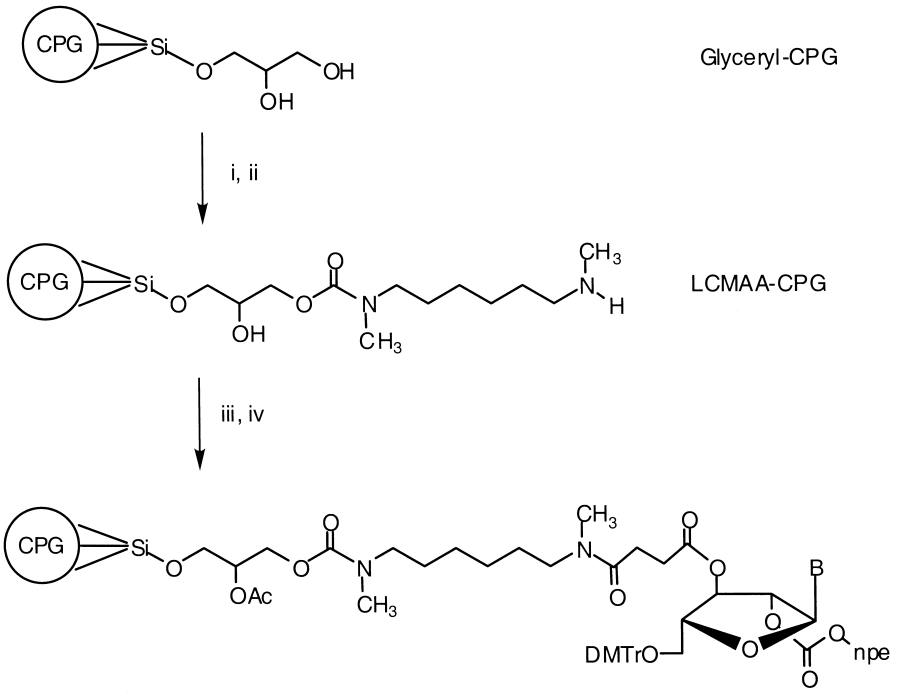


FIGURE 1 Synthesis and loading of LCMAA-CPG solid-support. i) Carbonyldiimidazole, CH_2Cl_2, 2h, RT; ii) 1,6-N.N-dimethyl-hexane-diamine, 6 h. RT; iii) nucleoside-succinate, N-methylmorpholine, TOTU, 2 h, CH_3CN; iv) Ac_2O, DMAP, pyridine, RT.

the free oligomers, which were characterized by anion-exchange HPLC on a NucleoPak column and in most cases showed a high purity, which did not need further purification or separation from failure sequences.

We first synthesized from the 5 fully protected phosphoramidites **71-75** homo-α-arabinooligonucleotides which gave the best results if a condensation time of 10 min was applied. The average stepwise yield was surprisingly very high, in general >99%, except with α-araG whereby the purity of the phosphoramidte **75** had an enormous influence on the yield in the condensation step. Chromatographical purification by FC on siliga-gel with toluene/EtOAc applying a 6:1-3:1 proportion afforded the anticipated purity.

Mixed oligomers (Table 2, 12–14) with 2′-deoxy-β-D-ribonucleoside-3′-phosphoramidites have been prepared in the same manner and showed the same purity like the oligo-2′-deoxyribonucleotides.

In order to study the hybridization properties of the α-arabinooligonucleotides a series of combinations have been prepared (Table 3) and the melting temperatures of the duplexes determined. The homo- and mixed oligomers were compared with the corresponding oligo-2′-deoxyribonucleo-

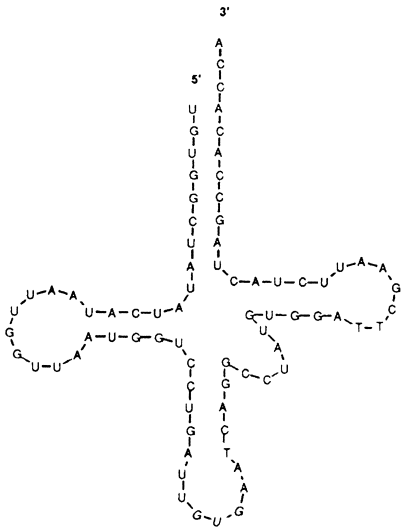


FIGURE 2 Structure of tα-ANA^{his}.

TABLE 2 Homo-α-arabino- and Mixed α-Arabino-2′-deoxy-β-ribo-oligonucleotides

Sequence	Average coupling yield %
1. 5′-α-ara-CCC CCC CCC-3′	98.4
2. 5′-α-ara-AAA AAA AAA-3′	97.2
3. 5′-α-ara-TTT TTT TTT T-3′	99.8
4. 5′-α-ara-UUU UUU UUU U-3′	99.9
5. 5′-α-ara-CCC CCC CCC C-3′	98.7
6. 5′-α-ara-AAA AAA AAA A-3′	99.9
7. 5′-d-TTT TTT TTT TTT TTT TTT-3′	99.5
8. 5′-d-AAA AAA AAA AAA AAA AAA-3′	99.4
9. 5′-α-ara-TTT TTT TTT TTT TTT TTT-3′	99.9
10. 5′-α-ara-AAA AAA AAA AAA AAA AAA-3′	99.2
11. 5′-d-GGT TCC ATG CAT GGA ACC-3′	98.8
12. 5′-α-ara-(GGT T)-d-CC ATG CAT GGA ACC-3′	98.6
13. 5′-d-GGT TCC TAG CAT GG-α-ara-(A ACC)-3′	99.9
14. 5-'d-GGT TCC A-α-ara-(TG CA)-d-T GGA ACC-3′	98.9
15. 5′-α-araGCT GGG GGT ACC TCG GGG CG-3′	99.9
16. 5′-α-araCGC CCC GAG GTA CCC CCA GC-3′	99.9
17. 5′-α-araCGG CCG GTG GAC ATG GGA CC-3′	99.8
18. 5′-α-araGGT CCC ATG TCC ACC GGC CG-3′	99.5
19. 5′-α-araCGG AGG AGT CGT AGG AGG ACG-3′	99.6
20. 5′-α-araCCG GCC GGT GGA CAT GGG ACC-3′	99.1
21. 5′-α-araCGT CCT CCT ACG ACT CCT CCG-3′	99.9
22. 5′-α-araGGT CCC ATG TCC ACC GGC CGG-3′	99.9

TABLE 3 Melting Temperature of DNA/α-ANA Hybridizations

Sequence	$[Na^+]$ mM	T_m (°C)
15. 5′-d(TTT TTT TTT TTT TTT TTT T)-3′ 3′-d(AAA AAA AAA AAA AAA AAA A)-5′	150	41.8
16. 5′-d(TTT TTT TTT TTT TTT TTT T)-3′ 3′-α-ara(AAA AAA AAA AAA AAA AAA A)-5′	150	36.2
17. 5′-α-ara (TTT TTT TTT TTT TTT TTT T)-3′ 3′-α-ara(AAA AAA AAA AAA AAA AAA A)-5′	150	23.8
18. 5′-α-ara(TTT TTT TTT TTT TTT TTT T)-3′ 3′-d(AAA AAA AAA AAA AAA AAA A)-5′	150	18.6
19. 5′-d(GGT TCC ATG CAT GGA ACC)-3′ 3′-d(CCA AGG TAC GTA CCT TGG)-5′	30	60.8
20. 5′-d(GGT TCC A)α-ara(TG CA)d(T GGA ACC)-3′ 3′-d(CCA AGG T)α-ara(AC GT)d(A CCT TGG)-5′	30	54.2
21. 5′-d(GGT TCC ATG CAT GG)α-ara(A ACC)-3′ 3-α-ara(CCA A)d(GG TAC GTA CCT TGG)-5′	30	40.0
22. 5′-α-ara(GGT T)d(CC ATG CAT GGA ACC)-3′ 3′-d(CCA AGG TAG GTA CC)α-ara(T TGG)-5′	30	35.3

tides under the same salt concentrations showing that in all combinations the presence of α-arabinonucleotides is associated with a substantial drop in the T_m, showing that the normal Watson-Crick base pairing is functioning but in a highly disturbed manner. It is interesting to note that the duplex 16 reveals a much higher stabilization than the counterpart duplex 18 but no simple explanation of this effect can be offered. The self-complementary mixed sequences 20–22 show a strong dependence regarding the site of the α-ara-tetrameric part in the oligonucleotide chain. The deviation is expectedly lowest in the duplex 20 where the α-ara-oligo-strip is located in the middle of the chain creating a reduced fit of only 4 base pairs, whereas the introduction of the α-ara-tetrameric sequence at either end causes a much stronger disturbance.

These results can be better understood on the basis of earlier findings in the α- and β-2′-deoxyoligoribonucleotide series[31–34] showing that duplexes are only formed if an α-strand is combined with the complementary β-strand in a parallel orientation whereas the combination of two α-sequences afford an antiparallel polarity for base pairing.

Similar observations have been noticed with the duplexes 23–32. The α-strands 24 and 29 show in the antiparallel orientation a slightly lower stability than the corresponding reference sequence and the parallel polarity of the α-ara- and β-deoxyribo still reveal substantial base pairing, whereas in an antiparallel arrangement of such strands no interaction is observed (Table 4).

As model sequences for antisense studies various oligo-2′-deoxy-β-D-ribonucleotides have been modified at the 3′- and 5′-terminal end with α-arabinonucleosides (34–37, 41–43) forming duplexes, which show a small

TABLE 4 DNA/α-ANA Hybridization Experiments

Sequence	G/C pairs	T_m (°C)
23. 5′-d(CAG CGT GGA GGA GGT GGT GGA)-3′ 3′-d(GTC GCA CCT CCT CCA CCA CCT)-5′	14	57.3
24. 5′-α-ara(GTC GCA CCT CCT CCA CCA CCT)-3′ 3′-α-ara(CAG CGT GGA GGA GGT GGT GGA)-5′	14	55.3
25. 5′-d(TCC ACC ACC TCC TCC ACG CTA)-3′ 5′-α-ara(AGG TGG TGG AGG AGG TGC GAC)-3′	14	49.3
26. 5′-d(CAG CGT GGA GGA GGT GGT GGA)-3′ 5′-α-ara(GTC GCA CCT CCT CCA CCA CCT)-5′	14	40.3
27. 5′-d(CAG CGT GGA GGA GGT GGT GGA)-3′ 3′-α-ara(GTC GCA CCT CCT CCA CCA CCT)-5′	14	—
28. 5′-d(AAG CCC CAA GCC GAA GGA TTT)-3′ 3′-d(TTC GGG GTT CGG CTT CCT AAA)-5′	11	52.4
29. 5′-α-ara(TTC GGG GTT CGG CTT CCT AAA)-3′ 3′-α-ara(AAG CCC CAA GCC GAA GGA TTT)-5′	11	48.2
30. 5′-d(AAA TCC TTC GGC TTG GGG CTT)-3′ 5′-α-ara(TTT GGG GTT CGG CTT CCT AAA)-3′	11	42.9
31. 5′-d(AAG CCC CAA GCC GAA GGA TTT)-3′ 5′-α-ara(TTC GGG GTT CGG CTT CCT AAA)-3′	11	38.3
32. 5′-d(AAG CCC CAA GCC GAA GGA TTT)-3′ 3′-α-ara(TTC GGG GTT CGG CTT CCT AAA)-5′	11	—

decrease in T_m with ara-T, ara-C, and ara-A and a slightly higher T_m on introduction of ara-G. The other duplexes fit well in the accepted picture of strand orientation (Table 5).

A general goal for testing a special oligonucleotide chemistry is the synthesis of longer oligonucleotide sequences. We decided to prove our method by synthesizing the α-ara-analog (tα-ANA^{his}) of the histidine tRNA of the phage T5 consisting of 78 nucleotide units (Figure 2). The rare nucleobases pseudouridine in position 41 and 57 and the ribothymidine in position 56 have been replaced by α-arabinothymidine. The synthesis worked, to our surprise, very well on LCMAA-CPG-1000 Å solid-support material with an average condensation yield in every step of 99.7% and a total reaction time of 26 h. After cleavage of the protective groups by DBU and acid, followed by a washing step and final removal from the solid-support by ammonia gave a perfect looking product of high purity. The HPLC analysis on a Dionex NucleoPac PA-100 column gave one main peak (Figure 3), the polyacrylamide-gel-electrophoresis (Figure 4), and especially the capillary gel electrophoresis (Figure 5) proved the homogenicity of the probe. Furthermore, an electrospray mass spectrum offered a molecular mass of 25,065.72 ± 22.42 lying in good agrement with the calculated mass of 25,039.59 for $C_{742}H_{994}N_{282}O_{549}P_{77}$ and an actual counting error of ±0.2 DA/1000 DA and without taking into account the isotope distribution.

The enzymatic stability of the α-arabinonucleotide unit was tested with the exonuclease snake venom phosphodiesterase degrading in 3′-5′-direc-

TABLE 5 DNA/α-ANA Hybridization Experiments

Sequence	T_m (°C)
33. 5′-CGA CCC CCA TGG AGC CCC GC-3′ 3′-GCT GGG GGT ACC TCG GGG CG-5′	65.2
34. 5′-CGA CCC CCA TGG AGC CCC GC-3′ 3′-α-araT-d(GCT GGG GGT ACC TCG GGG CG)α-araT-5′	64.5
35. 5′-CGA CCC CCA TGG AGC CCC GC-3′ 3′-α-araC-d(GCT GGG GGT ACC TCG GGG CG)α-araC-5′	62.9
36. 5′-CGA CCC CCA TGG AGC CCC GC-3′ 3′-α-araA-d(GCT GGG GGT ACC TCG GGG CG)α-araA-5′	64.0
37. 5′-CGA CCC CCA TGG AGC CCC GC-3′ 3′-α-araG-d(GCT GGG GGT ACC TCG GGG CG)αα-araG-5′	65.2
38. 5′-CGA CCC CCA TGG AGC CCC GC-3′ 5′-α-ara-GCT GGG GGT ACC TCG GGG CG-5′	52.4
39. 3′-α-araCGA CCC CCA TGG AGC CCC GC-3′ 5′-α-araGCT GGG GGT ACC TCG GGG CG-5′	59.4
40. 5′-GCC GGC CAC CTG TAC CCT GG-3′ 3′-CGG CCG GTG GAC ATG GGA CC-5′	64.0
41. 5′-GCC GGC CAC CTG TAC CCT GG-3′ 3′-α-araCd(CGG CCG GTG GAC ATG GGA CC)α-araC-5′	62.6
42. 5′-GCC GGC CAC CTG TAC CCT GG-3′ 3′-α-araAd(CGG CCG GTG GAC ATG GGA CC)α-araA-5′	62.7
43. 5′-GCC GGC CAC CTG TAC CCT GG-3′ 3′-α-araGd(CGG CCG GTG GAC ATG GGA CC)αα-araG-5′	64.5
44. 5′-GCC GGC CAC CTG TAC CCT GG-3′ 5′-α-araCGG CCG GTG GAC ATG GGA CC-3′	50.3
45. 3′-α-araGCC GGC CAC CTG TAC CCT GG-3′ 5′-α-araCGG CCG GTG GAC ATG GGA CC-3′	59.2
46. 5′-α-araCGG AGG AGT AGT AGG AGG ACG-3′ 3′-α-araGCC TCC TCA GCA TCC TCC TGC-5′	54.5
47. 5′-α-araCCG GCC GGT GGA CAT GGG ACC-3′ 3′-α-araGGC CGG CCA CCT GTA CCC TGG-5′	62.6

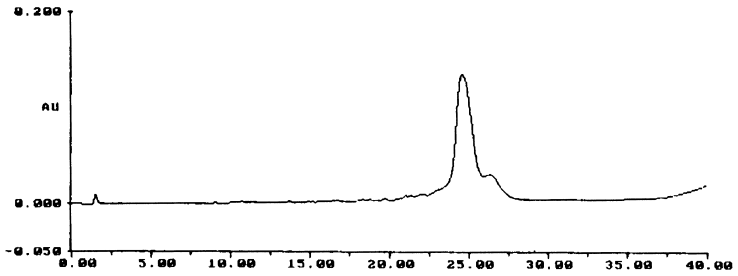


FIGURE 3 HPLC of tα-ANA^{his} on NucleoPak PA-100, 4 × 250 mm (Dionex).

tion and followed by alkaline phosphatase for HPLC analysis of the resulting nucleosides. Expectedly, the oligo-2′-deoxyribonucleotide sequences were degraded completely within a few minutes whereas the presence of an α-arabinonucleotide unit at the 3′-end prevents enzymatic hydrolysis to a large extent showing only partial cleavage after 24 h.

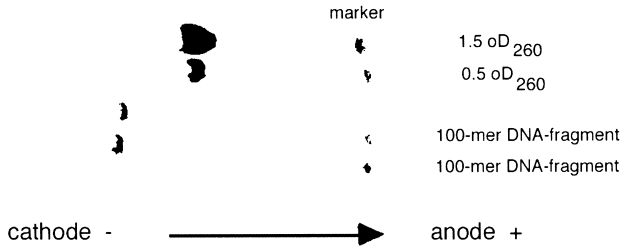


FIGURE 4 Polyacrylaminde-gel-electrophoresis of tα-ANA^{his}.

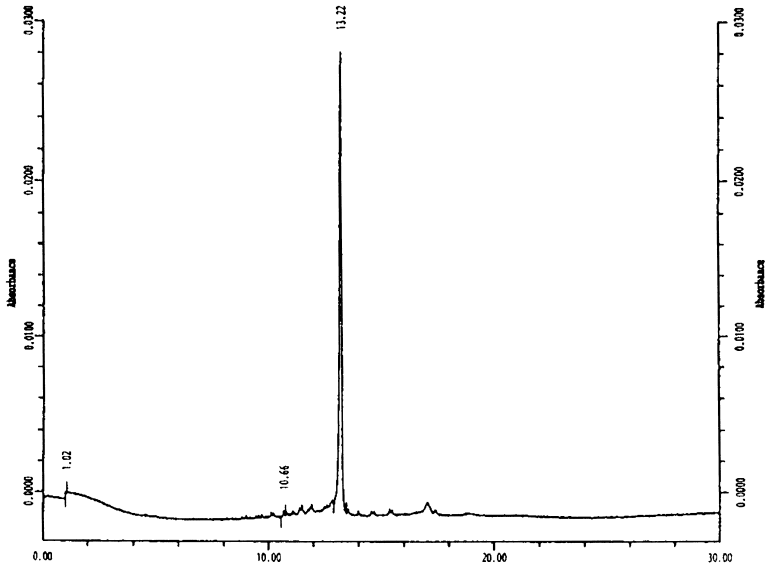


FIGURE 5 Capillary-gel-electrophoresis of tα-ANA^{his}.

EXPERIMENTAL

All melting points are uncorrected. Products were dried under high vacuum. TLC: precoated silica gel thin-layer sheets 60 F 254 from Merck and cellulose sheets F 1440 LS 254 from Schleicher & Schüll. Column chromatography (CC): silica gel 60 from Merck and flash chromatography (FC): silica gel (30–60 μm) from Baker. UV/VIS: Perkin-Elmer Lambda 5; λ_{max} in nm (log ε). ^{1}H-NMR: Bruker AC 250; δ in ppm rel. to $SiMe_4$ or $CDCl_3$ (DMSO-d_6) as internal standard. HPLC: Merck-Hitachi L 6200, UV-detector L 400. Oligonucleotide syntheses: DNA-synthesizer from Applied Biosystems, Model 392. Lyophilizations with Speed-Vac-Concentrator from Savant. All solvents used were of anhydrous grade. The pK_a-values were determined by the spectrophotometric method.[25] Elemental analyses were

performed by the analytical lab of the department of chemistry, Konstanz University.

1-(2,3,5-Tri-O-acetyl-α-D-arabinofuranosyl)uracil (13). Under anhydrous conditions uracil (**1**) (0.336 g, 3 mmol) and $(NH_4)_2SO_4$ (5 mg) were suspended in hexamethyldisilazane (HMDS) (10 mL) and then heated under reflux for 20 h. It was evaporated, the resulting oil dissolved in dry toluene (15 mL) and combined with a solution of 1,2,3,5-tetra-acetyl-arabinofuranose (1.14 g, 3.6 mmol) in toluene (15 mL). Under stirring a solution of TMS-triflate (0.9 mL, 5 mmol) in toluene (5 mL) was added dropwise and then the mixture heated in an oilbath to 80°C for 1 h. The reaction solution was diluted with EtOAc (100 mL) and treated with a saturated aqueous solution of $NaHCO_3$ (100 mL). The aqueous phasae was reextracted with EtOAc (100 mL), the organic layers united, dried over Na_2SO_4, and evaporated. The resulting solid foam was purified by CC (4 × 13 cm, silica gel) with toluene/EtOAc 1:5 to give 0.68 g (62% of a solid foam. R_f: 0.5 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 208(3.99), 258 (3.99). ^{1}H-NMR ($CDCl_3$): 9.21 (s, 1H, NH); 7.32 (d, 1H, H-C(6)); 5.97 (d, 1H, H-C(1′)); 5.78 (d, 1H, H-C(5)); 5.49 (pt, 1H, H-C(2′)); 5.22 (pt, 1H, H-C(3′)); 4.59 (q, 1H, H-C(4′)); 4.28 (m, 2H, H-C(5′, 5″)); 2.16 (s, 3H, Oac); 2.15 (s, 3H, Oac); 2.14 (s, 3H, Oac). Anal. for $C_{15}H_{18}N_2O_9$ (370.3). Calcd: C 48.65, H 4.90, N 7.56. Found: C 48.63, H 5.05, N 7.32.

1-(2,3,5-Tri-O-benzoyl-α-D-arabinofuranosyl)uracil (14). Analogous to the preceding procedure with uracil (**1**) (0.56 g, 5 mmol) and 1-O-acetyl-2,3,5-tri-O-benzoyl-arabinofuranose (2.52 g, 5 mmol) in CH_2Cl_2 (15 mL). Addition of TMS-triflate (0.9 mL, 5 mmol) in CH_2Cl_2 (5 mL) and stirring at room temperature for 18 h. Purification by CC (35 g silica gel) with toluene/EtOAc 10:1 (500 mL) and then toluene/4:1 (600 mL) to give 2.3 g (87%) of a colorless solid foam. R_f: 0.35 (toluene/EtOAc 1:1). UV (MeOH): 201 (4.39), 230 (4.62), 256 (sh 3.92). ^{1}H-NMR ($CDCl_3$): 9.17 (s, 1H, NH); 8.05 (m, 6H, arom. H); 7.48 (m, 10H, H-C(6), arom. H); 6.21 (d, 1H, H-C(1′)); 5.96 (pt, 1H, H-C(2′)); 5.81 (d, 1H, H-C(5)); 5.76 (pt, 1H, H-C(3′)); 4.98 (q, 1H, H-C(4′)); 4.72 (m, 2H, H-C(5′, 5″)). Anal. for $C_{30}H_{24}N_2O_9$ (556.5). Calcd: C 64.75, H 5.03, N 7.56. Found: C 64.36, H 4.60, N 4.79.

1-α-D-Arabinofuranosyl)uracil (15)[15]. In MeOH (35 mL) Na (80 mg, 3.5 mmol) was dissolved, then 1-(2,3,5-tri-O-benzoyl-α-D-arabinofuranosyl) uracil (**14**) (1.67 g, 3 mmol) added and stirred for 45 min whereby a precipitate separated out. The suspension was evaporated, dissolved in H_2O (30 mL), and then neutralized with Dowex ion-exchange resin H^+-form. The water phase was extracted with CH_2Cl_2 (3 × 30 mL), filtered from the resin, and then evaporated to an oily residue. Purification was done by

FC (16 g silica gel) with CH_2Cl_2(MeOH 15:1 (250 mL) and 12:1 (450 mL). The product fractions were evaporated, and coevaporated subsequently with EtOH, MeOH and CH_2Cl_2 (2×) to give 0.6 g (82%) of a colorless solid, which was dried in high vacuum at 40°C. R_f: 0.67 ($CHCl_3$/MeOH 1:1). pK_a = 9.36. UV (H_2O): pH 7: 202 (4.01), 262 (4.00); pH 12: 204 (4.11,), 223 (sh 3.93), 260 (3.87). ^{1}H-NMR (DMSO-d_6): 11.28 (s, 1H, NH); 7.68 (d, 1H, H-C(6)); 5.69 (m, 2H, H-C(1′), H-O (2′)); 5.60 (m, 2H, H-C(5), H-O(3′)); 4.93 (t, 1H, H-O(5′)); 4.09 (m, 1H, H-C(2′)); 4.05 (m, 1H, H-C(4′)); 3.92 (m, 1H, H-C(3′)); 3.50 (m, 2H, H-C(5′, 5″)). Anal. for $C_9H_{12}N_2O_9 \times 0.5\ H_2O$ (253.2). Calcd: C 42.69, H 5.18, N 11.06. Found: C 42.29, H 5.14, N 10.95.

1-(2,3,5-Tri-O-acetyl-α-D-arabinofuranosyl)thymine (16). Analogous to **13** with thymine (**2**) (0.378 g, 3 mmol). Purification by FC (4 × 15 cm, silica gel) with toluene/EtOAc 2:5 (1 L) to give 0.84 g (73% of a colorless solid foam. R_f: 0.62 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 210 (3.87), 263 (3.979. ^{1}H-NMR ($CDCl_3$): 8.93 (s, 1H, NH); 7.13 (d, 1H, H-C(6)); 5.99 (d, 1H, H-C(1′)); 5.50 (pt, 1H, H-C(2′)); 5.25 (pt, 1H, H-C(3′)); 4.58 (q, 1H, H-C(4′)); 4.30 (m, 2H, H-C(5′, 5″)); 2.15 (s, 3H, Oac); 2.13 (s, 3H, Oac); 2.12 (s, 3H, Oac); 1.96 (s, 3H, H_3C-(5)). Anal. for $C_{16}H_{20}N_2O_9$ (384.4). Calcd: C 50.00, H 5.25, N 7.28. Found: C 50.15, H 5.47, N 7.02.

1-(2,3,5-Tri-O-benzoyl-α-D-arabinofuranosyl)thymine (17). Analogous to **14** with thymine (**2**) (3.1 g, 24 mmol) and $(NH_4)_2SO_4$ (10 mg) in HMDS (20 mL). Followed by 1-O-acetyl-2,3,5-tri-O-benzoylarabinofuranose (10.9 g, 22 mmol) in CH_3CN (60 mL) and TMS-triflate (3.75 mL, 22 mmol) in CH_3CN (10 mL). Work-up in CH_2Cl_2 gave a solid foam, which was coevaporated subsequently with EtOH, MeOH, and CH_2Cl_2 to give 11.4 g (91%) of a chromatographically pure solid. R_f: 0.5 (toluene/EtOAc 1:1). UV (MeOH): 201 (4.56), 230 (4.63), 265 (4.09), 282 (sh 3.79). ^{1}H-NMR ($CDCl_3$): 9.21 (s, 1H, NH); 8.06 (m, 6H, arom. H); 7.48 (m, 9H, arom. H); 7.27 (s, 1H, H-C(6)); 6.28 (d, 1H, H-C(1′)); 5.93 (pt, 1H, H-C(2′)); 5.76 (pt, 1H, H-C(3′)); 4.97 (q, 1H, H-C(4′)); 4.69 (m, 2H, H-C(5′, 5″)); 1.92 (s, 3H, H_3C-(5). Anal. for $C_{31}H_{26}N_2O_9$ (570.6). Calcd: C 65.26, H 4.59, N 4.91. Found: C 65.11, H 4.61, N 4.71.

1-α-D-Arabinofuranosyl)thymine (18)[15]. Analogous to **15** with **17** (2 g, 3.5 mmol) in MeOH (70 mL) and Na (150 mg). Purification by FC (2 × 10 cm, silica gel) with CH_2Cl_2/MeOH 8:1 to give 0.8 g (88%) of a colorless solid. R_f: 0.78 ($CHCl_3$/MeOH 1:1). pK_a 10.43, UV (H_2O): pH 7: 205 (3.97), 266 (3.98); pH 12: 210 (4.01), 224 (3.95), 266 (3.85). ^{1}H-NMR (DMSO-d_6): 11.28 (s, 1H, NH); 7.59 (d, 1H, H-C(6)); 5.67 (m, 2H, H-C(1′), H-O (2′)); 5.45 (d, 1H, H-O(3′)); 4.90 (t, 1H, H-O(5′)); 4.06 (m, 2H, H-C(2′), H-C(4′)); 3.92 (m, 1H, H-C(3′)); 3.50 (m, 2H, H-C(5′, 5″)); 1.78 (s, 3H, H_3C-C(5).

Anal. for $C_{10}H_{14}N_2O_9 \times 0.5\ H_2O$ (267.2). Calcd: C 44.95, H 5.66, N 10.48. Found: C 45.06, H 5.70, N 10.04.

N^4-Acetyl-1-(2,3,5-tri-O-acetyl-α-D-arabinofuranosyl)cytosine (19). Analogous to **13** with N^4-acetylcytosine (**4**) (0.92 g, 6 mmol) and 1,2,3,5-tetra-O-acetylarabinnofuranose (3.1 g, 6.3 mmol) and TMS-triflate (1.1 mL, 6 mmol) in CH_3CN by stirring 6 h at room temperature. After extraction with EtOAc and washing the resulting solid was disoolved in a mixture of EtOH (2 mL), isopropanol (2 mL), and ether (2 mL) by heating. On cooling in the icebox overnight 1.23 g (50%) of colorless crystals of m.p. 177–178°C were obtained. R_f: 0.41 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 211 (4.32), 247 (4.21), 296 (3.85). ^{1}H-NMR ($CDCl_3$): 9.43 (s, 1H, NH); 7.74 (d, 1H, H-C(6)); 7.48 (d, 1H, H.C(5)); 6.04(d, 1H, H-C(1′)); 5.51 (pt, 1H, H-C(2′)); 5.15 (pt, 1H, H-C(3′)); 4.68 (m, 1H, H-C(4′)); 4.31 (m, 2H, H-C(5′, 5″)); 2.27 (s, 3H, N-ac); 2.16 (s, 3H, Oac); 2.14 (s, 3H, Oac); 2.03 (s, 3H, Oac). Anal. for $C_{17}H_{21}N_3O_9$ (411.4). Calcd: C 49.64, H 5.14, N 10.22. Found: C 49.55, H 5.20, N 10.05.

N^4-Acetyl-1-(2,3,5-tri-O-benzoyl-α-D-arabinofuranosyl)cytosine (20). Analogous to the preceeding procedure with **4** (0.92 g, 6 mmol) and 1-O-acetyl-2,3,5-tri-O-benzoylarabinofuranose (3.1 g, 6.3 mmol) and TMS-triflate (1.1 mL, 6 mmol) in CH_3CN by stirring 20 h at room temperature. Work-up with CH_2Cl_2 gave a solid foam which was recrystallized from EtOH (10 mL) to give 2.54 g (76%) of colorless crystals of m.p. 184–185°C. R_f: 0.59 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 218 (sh 4.57), 232 (4.69), 282 (3.89), 296 (3.87). ^{1}H-NMR ($CDCl_3$): 9.34 (s, 1H, NH); 8.07 (m, 4H, arom. H); 7,78 (m, 3H, H-C(6), arom. H); 7.48 (m, 10H, H-C(6), arom. H); 6.26 (d, 1H, H-C(1′)); 6.02 (pt, 1H, H-C(2′)); 5.71 (pt, 1H, H-C(3′)); 5.06 (m, 1H, H-C(4′)); 4.70 (m, 2H, H-C(5′, 5″)); 2,26 (s, 3H, N-ac). Anal. for $C_{32}H_{27}N_3O_9$ (597.6). Calcd: C 64.32, H 4.55, N 7.03. Found: C 64.08, H 4.54, N 7.09.

1-(2,3,5-Tri-O-benzoyl-α-D-arabinofuranosyl)cytosine (21). Analogous to **13** with **3** (0.35 g, 3.15 mmol) and after silylation addition of 1-O-acetyl-2,3,5-tri-O-benzoylarabinofuranosose (1.56 g, 3.1 mmol) and TMS-triflate (1.1 mL, 6 mmol) in CH_3CN by stirring and heating to 65°C for 8 h. Work-up with CH_2Cl_2 gave a solid foam which was recrystallized from EtOH (5 mL) to give 1.37 g (80%) of colorless crystals of m.p. 129–132°C. R_f: 0.48 (toluene/EtOAc/MeOH 5:5:2). UV (MeOH): 201 (4.71), 231 (4.68), 271 (4.04), 278 (sh 3.97). ^{1}H-NMR ($CDCl_3$): 8.55 (bd, 2H, NH_2); 8.05 (m, 4H, arom. H); 7,81 (d, 2H, arom. H); 7.40 (m, 10H, H-C(6), arom. H); 6.15 (d, 1H, H-C(1′)); 6.01 (pt, 1H, H-C(2′)); 5.84 (d, 1H, H-C(5)); 5.62 (pt, 1H, H-C(3′)); 4.90 (m, 1H, H-C(4′)); 4.65 (m, 2H, H-C(5′, 5″)). Anal. for $C_{30}H_{25}N_3O_9$ (555.5). Calcd: C 64.86, H 4.54, N 7.56. Found: C 64.77, H 4.30, N 7.44.

1-α-D-Arabinofuranosylcytosine (22)[18]. In a saturated solution of methanolic ammonia (15 mL) **20** (0.5 g, 0.87 mmol) was stirred at room temperature for 28 h. It was evaporated, the residue dissolved in H_2O (20 mL), and then extracted with CH_2Cl_2 (10 mL). The CH_2Cl_2 phase was separated and then treated again with H_2O. The united H_2O layers were evaporated and the resulting syrup recrystallized from MeOH (5 mL) to give 0.135 g (66%) of colorless crystals of m.p. 198–200°C. R_f: 0.38 ($CHCl_3$/MeOH 1:1). pK_a = 3.89. UV (H_2O): pH 1: 212 (3.99), 279 (4.13); pH 6: 214 (sh 3.99), 227 (3.91), 270 (3.95). ^{1}H-NMR (DMSO-d_6): 7.58 (d, 1H, H-C(6)); 7.11(s, 2H, NH_2); 5.67 (m, 2H, H-C(1′), H-C(5)); 5.58 (d, 1H, H-O(2′)); 5.31 (d, 1H, H-O(3′)); 4.91 (t, 1H, H-O(5′)); 4.09 (m, 1H, H-C(2′)); 4.00 (m, 1H, H-C(4′)); 3.88 (m, 1H, H-C(3′)); 3.50 (m, 2H, H-C(5′, 5″)). Anal. for $C_9H_{13}N_3O_5$ (243.2). Calcd: C 44.44, H 5.39, N 17.28. Found: C 44.25, H 5.35, N 17.08.

N^6-Benzoyl-9-(2,3,5-tri-O-acetyl-α-D-arabinofuranosyl)adenine (23). N^6-Benzoyl-adenine (**5**)[26] (0.72 g, 3 mmol) and N,O-*bis*-trimethylsilylacetamide (1.5 mL) were heated in 1,2-dichloroethane (15 mL) to 80°C in an oilbath under anhydrous conditions for 15 min. It was evaporated, coevaporated with toluene, the resulting oil dissolved in toluene (15 mL), TMS-triflate (0.8 mL, 3.8 mmol) added and the mixture heated to 80°C. A solution of 1,2,3,5-tetraacetylarabinofuranose (1.14 g, 3.6 mmol) in abs. toluene (15 mL) was then added dropwise with stirring. After 1 h heating, the mixture was cooled with EtOAc (100 mL), diluted, washed with $NaHCO_3$ solution (100 mL), dried over Na_2SO_4, and evaporated. The oil was purified by FC (4 × 15 cm, silica gel) with toluene/EtOAc/MeOH 10:10:1 (1.2 L) to give 1.25 g (83%) of a colorless solid. R_f: 0.38 (toluene/EtOAc/MeOH 10:10:1). UV (MeOH): 202 (4.47), 232 (sh 4.12), 254 (sh 4.05), 279 (4.29).^{1}H-NMR ($CDCl_3$): 9.00 (s, 1H, NH); 8.83 (s, 1H, H-C(8)); 8.19 (s, 1H, H-C(2)); 8.05 (d, 2H, arom. H); 7.55 (m, 3H, arom. H); 6.32 (d, 1H, H-C(1′)); 6.04 (pt, 1H, H-C(2′)); 5.38 (pt, 1H, H-C(3′)); 4.77 (m, 1H, H-C(4′)); 4.39 (m, 2H, H-C(5′, 5″)); 2.17 (s, 3H, Oac); 2.13 (s, 3H, Oac); 2.10 (s, 3H, Oac). Anal. for $C_{23}H_{23}N_5O_8$ (497.5). Calcd: C 55.53, H 4.66, N 14.08. Found: C 55.51, H 4.95, N 14.03.

N^6-Benzoyl-9-(2,3,5-tri-O-benzoyl-α-D-arabinofuranosyl)adenine (24)[16]. A suspension of **5**[26] (0.753 g, 3.15 mmol) and $(NH_4)_2SO_4$ (10 mg) in HMDS (15 mL) was heated in an oilbath under reflux for 20 h. It was evaporated, the residue dissolved in CH_3CN (30 mL), then united with a solution of 1-O-acetyl-2,3,5-tri-O-benzoylarabinofuranose (1.86 g, 3.6 mmol) in CH_3CN (30 mL) and finally under stirring $SnCl_4$ (0.9 mL, 7.56 mmol) added dropwise. After reaction at room temperature for 20 h was diluted with CH_2Cl_2 (100 mL), washed with saturated aqueous $NaHCO_3$ solution and twice with NaCl solution. The organic phase was dried over Na_2SO_4,

evaporated, and purified by FC (4 × 15 cm, silica gel) with toluene/EtOAc 3:2 (1 L) to give 1.48 g (69%) of a colorless solid. R_f: 0.37 (toluene/EtOAc 3:2). UV (MeOH): 201 (4.78), 231 (4.73), 278 (4.36). ^{1}H-NMR ($CDCl_3$): 9.06 (s, 1H, NH); 8.83 (s, 1H, H-C(8)); 8.30 (s, 1H, H-C(2)); 8.08 (d, 2H, arom. H); 8.02 (m, 6H, arom. H); 7.45 (m, 12H, arom. H); 6.55 (m, 2H, H-C(1′), H-C(2′)); 5.93 (q, 1H, H-C(3′)); 5.12 (q, 1H, H-C(4′)); 4.80 (m, 2H, H-C(5′, 5″)). Anal. for $C_{38}H_{29}N_5O_8$ (683.7). Calcd: C 66.76, H 4.28, N 10.24. Found: C 66.16, H 4.32, N 10.00.

9–α-D-Arabinofuranosyl)adenine (25)[16]. Analogous to **22** with **24** (0.4 g, 0.6 mmol). The crude syrup was crystallized from MeOH (4 mL) to give 98 mg (67%) of colorless crystals of m.p. 209–211°C. R_f: 0.57 ($CHCl_3$/MeOH 1:1). pK_a = 4.16. UV (H_2O): pH 1: 206 (4.31), 256 (4.15), 260 (sh 4.12); pH 7: 204 (4.34), 258 (4.16). ^{1}H-NMR (DMSO-d_6): 8.32 (s, 1H, H-C(8)); 8.14 (s, 1H, H-C(2)); 7.29 (s, 2H, NH_2); 5.85 (d, 2H, H-C(1′)); 5.76 (t, 1H, H-O(2′)); 5.62 (d, 1H, H-O(3′)); 4.87 (t, 1H, (H-O(5′)); 4.67 (q, 1H, H-C(2′)); 4.14 (m, 1H, H-C(4′)); 3.98 (q, 1H, H-C(3′)); 3.50 (m, 2H, H-C(5′, 5″)). Anal. for $C_{10}H_{13}N_5O_4$ (267.3). Calcd: C 44.94, H 4.90, N 26.21. Found: C 44.90, H 4.92, N 26.61.

N^2-Acetyl-1-(2,3,5-tri-O-acetyl-α-D-arabinofuranosyl)-O^6-diphenylcarbamoylguanine (26). A mixture of N^2-acetyl-O^6-diphenylcarbamoylguanine (**6**) (1.17 g, 3 mmol) and N,O-*bis*-trimethylsilylacetamide (1.5 mL) in CH_2Cl_2 (15 mL) was stirred at 80°C in an oil bath for 15 min. It was evaporated, coevaporated with toluene, dissolved in toluene (15 mL), and then TMS-triflate (0.8 mL, 3.8 mmol) was added dropwise. The mixture was heated to 80°C and then a solution of 1,2,3,5-tetraacetylarabinofuranose (1.02 g, 3.2 mmol) in toluene (15 mL) again added dropwise with stirring for 1 h. After cooling was diluted with EtOAc (150 mL), washed with saturated aqueous $NaHCO_3$ solution, the aqueous phase reextracted with EtOAc (75 mL), and then the organic layers united. After drying over Na_2SO_4, the mixture was evaporated and the resulting foam purified by FC (4 × 15 cm, silica gel) with toluene/EtOAc 1:3 to give 1.4 g (72%) of a colorless solid. R_f: 0.6 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 202 (4.63), 226 (4.53), 254 (sh 4.22), 277 (4.10). ^{1}H-NMR ($CDCl_3$): 8.04 (s, 1H, H-C(8)); 8.08 (m, 4H, arom. H); 8.02 (s, 1H, NH); 7.40 (m, 10H, arom. H); 6.16 (m, 2H, H-C(1′)); 6.02 (d, 1H, H-C(2′)); 5.34 (dd, 1H, H-C(3′)); 4.74 (m, 1H, H-C(4′)); 4.34 (m, 2H, H-C(5′, 5″)); 2.56 (s, 3H, N-ac); 2.15 (s, 3H, O-ac); 2.13 (s, 3H, O-ac); 2.07 (s, 3H, O-ac). Anal. for $C_{31}H_{30}N_6O_{10}$ (646.6). Calcd: C 57.58, H 4.68, N 13.00. Found: C 57.61, H 4.91, N 12.98.

N^2-Acetyl-1-(2,3,5-tri-O-benzoyl-α-D-arabinofuranosyl)-O^6-diphenylcarbamoylguanine (27). Analogous to the preceeding procedure with **6** (1.17

g, 3 mmol) and 1-O-acetyl-2,3,5-tri-O-benzoylarabinofuranose (1.86 g, 3.6 mmol). Purification by FC (4 × 15 cm, silica gel) with toluene/EtOAc 5:2 (1.1 L) to give 1.96 g (79%) of a colorless solid. R_f: 0.79 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 201 (4.86), 228 (4.86), 257 (sh 4.24), 276 (4.19). ^{1}H-NMR ($CDCl_3$): 8.21 (s, 1H, H-C(8)); 8.08 (m, 4H, arom. H); 8.02 (m, 6H, arom. H); 7.90 (s, 1H, NH); 7.82 (m, 2H, arom. H); 7.45–7.40 (m, 19H, arom. H); 6.48 (m, 2H, H-C(1′)); 6.41 (d, 1H, H-C(2′)); 5.88 (dd, 1H, H-C(3′)); 5.13 (m, 1H, H-C(4′)); 4.79 (m, 2H, H-C(5′, 5″)); 2.44 (s, 3H, N-ac). Anal. for $C_{46}H_{36}N_6O_{10}$ (832.8). Calcd: C 66.34, H 4.36, N 10.09. Found: C 66.54, H 4.53, N 9.84.

9–α-D-Arabinofuranosyl)guanine (28). Analogous to **22** in $MeOH/NH_3$ (40 mL) with **27** by stirring for 36 h. After evaporation was dissolved in H_2O (150 mL) and CH_2Cl_2 (150 mL). The organic phase was washed with H_2O (70 mL) and then the united H_2O layer extracted with CH_2Cl_2 (3 × 80 mL). The H_2O extract was evaporated to a small volume until crystallization started. It was heated till a clear solution was obtained, then cooled and kept in the icebox overnight to give 0.25 g (74%) colorless crystals of m.p. >300°C (decomp.). R_f: 0.26 (2-BuOH, 2.PrOH, H_2O, conc. NH_4OH 30:45:25:2). $pK_a = 9.78$. UV (H_2O): pH 7: 252 (4.12), 274 (sh 3.92); pH 12: 210 (4.36), 258 (sh 4.05), 263 (4.05). ^{1}H-NMR (DMSO-d_6): 10.63 (s, 1H, NH); 7.90 (s, 1H, H-C(8)); 6.45 (s, 2H, NH_2); 5.72 (t, 1H, H-O(2′)); 5.64 (d, 2H, H-C(1′)); 5.52 (d, 1H, H-O(3′)); 4.87 (t, 1H, (H-O(5′)); 4.44 (q, 1H, H-C(2′)); 4.05 (m, 1H, H-C(4′)); 3.95 (q, 1H, H-C(3′)); 3.54 (m, 2H, H-C(5′, 5″)). Anal. for $C_{10}H_{13}N_5O_5$ (283.2). Calcd: C 42.41, H 4.63, N 24.72. Found: C 42.34, H 4.87, N 24.33.

1-[3,5-O-(1,1,3,3-Tetraisopropyldisiloxan-1,3-diyl)-α-D-arabinofuranosyl] uracil (29). 1-α-Arabinofuranosyluracil (**15**) (2.9 g, 12 mmol) was twice coevaporated with abs. pyridine and then with 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (4.4 mL, 14.1 mmol) in pyridine (80 mL) 15 h stirred at room temperature. It was dilute with EtOAc (80 mL), then treated with 0.2 M HCl (80 mL), the aqueous layer separated and reextracted with EtOAc. The united EtOAc phases were washed with saturated $NaHCO_3$ solution (80 mL) and saturated NaCl solution (80 mL), dried over Na_2SO_4, evaporated, and the residue purified by FC (3 × 8 cm, silica gel) with toluene (100 mL) and toluene/EtOAc 1:2. The product fraction was evaporated, coevaporated with CH_2Cl_2 and dried under high vacuum to give 4.97 g (85%) of a colorless solid foam. R_f: 0.66 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 207 (3.95), 260 (4.00). ^{1}H-NMR (DMSO-d_6): 11.35 (bs, 1H, NH); 7.85 (d, 1H, H-C(6)); 5.70 (d, 1H, H-C(5)); 5.61 (m, 2H, H-C(1′), H-O(2′)); 4.45 (dd, 1H, H-C(2′)); 4.15 (m, 2H, H-C(3′), H-C(4′)); 3.85 (2H, H-C(5′, 5″)); 1.15-0.9 (m, 28H, 4 × Me_2CH). Anal. for $C_{12}H_{38}N_2O_7Si_2$ (486.7). Calcd: C 51.82, H 7.87, N 5.76. Found: C 52.17, H 8.05, N 5.37.

1-[3,5-O-(1,1,3,3-Tetraisopropyldisiloxan-1,3-diyl)-α-D-arabinofuranosyl] thymine (30). Analogous to **29** with **18** (6.6 g, 25.6 mmol) and 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (9.3 mL, 29.7 mmol) in pyridine (180 mL). Purification by FC with toluene (400 mL) and toluene/EtOAc 1:1 (600 mL) to give 11.37 g (89%) of a colorless solid. R_f: 0.68 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 209 (3.97), 265 (3.97). ^{1}H-NMR (DMSO-d_6): 11.35 (bs, 1H, NH); 7.75 (d, 1H, H-C(6)); 5.75 (d, 1H, H-O(2′)); 5.65 (m, 2H, H-C(1′), H-O(2′)); 4.40 (dd, 1H, H-C(2′)); 4.21 (m, 2H, H-C(3′), H-C(4′)); 3.85 (2H, H-C(5′, 5″)); 1.15–0.9 (m, 28H, 4 × Me_2CH). Anal. for $C_{13}H_{40}N_2O_7Si_2$ (500.7). Calcd: C 52.77, H 8.05, N 5.59. Found: C 52.67, H 8.17, N 5.53.

1-[3,5-O-(1,1,3,3-Tetraisopropyldisiloxan-1,3-diyl)-α-D-arabinofuranosyl]-cytosine (31). Analogous to **29** with **22** (8.0 g, 32.8 mmol) and 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (11.4 mL, 36.2 mmol) in pyridine (180 mL). Purification by FC with toluene (300 mL), toluene/EtOAc 1:1 (1000 mL + 10 mL MeOH) and toluene/EtOAc 1:1 (750 mL + 20 mL MeOH) to give 13.0 g (83%) of a colorless solid. R_f: 0.24 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 203 (4.19), 236 (sh 3.90), 271 (3.93). ^{1}H-NMR (DMSO-d_6): 7.75 (d, 1H, H-C(6)); 7.20 (bs, 2H NH_2); 5.65 (m, 2H, H-C(5),H-O(2′)); 5.55 (d, 2H, H-C(1′), H-O(2′)); 4.45 (dd, 1H, H-C(2′)); 4.15 (m, 2H, H-C(3′), H-C(4′)); 3.85 (2H, H-C(5′, 5″)); 1.15-0.9 (m, 28H, 4 × Me_2CH). Anal. for $C_{21}H_{39}N_3O_6Si_2$ (485.7). Calcd: C 51.93, H 8.09, N 8.65. Found: C 51.50, H 8.13, N 8.45.

9-[3,5-O-(1,1,3,3-Tetraisopropyldisiloxan-1,3-diyl)-α-D-arabinofuranosyl] adenine (32). Analogous to **29** with **25** (1.2 g, 4.6 mmol) and 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (1.65 mL, 5.1 mmol) in pyridine (35 mL). Purification by FC (3 × 8 cm, silica gel) with toluene (200 mL) and toluene/EtOAc/MeOH 15:15:2 to give 1.98 g (83%) of a colorless solid. R_f: 0.37 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 206 (4.30), 258 (4.13). ^{1}H-NMR (DMSO-d_6): 8.40 (s, 1H, H-C(8)); 8.15 (s, 1H, H-C(2)); 7.30 (bs, 2H NH_2); 5.92 (d, 1H, H-O(2′)); 5.75 (d, 2H, H-C(1′)); 5.05 (dd, 1H, H-C(2′)); 4.25 (m, 2H, H-C(3′), H-C(4′)); 3.85 (2H, H-C(5′, 5″)); 1.2–0.9 (m, 28H, 4 × Me_2CH). Anal. for $C_{22}H_{39}N_5O_5Si_2$ (509.8). Calcd: C 51.84, H 7.71, N 13.74. Found: C 51.69, H 7.72, N 13.94.

1-{2-O-[2-(4-Nitrophenyl)ethoxycarbonyl]-3,5-O-(1,1,3,3-tetraisopropyldisiloxan-1,3-diyl)-α-D-arabinofuranosyl}uracil (33). A cooled solution (0–5°C) of **29** (5.8 g, 12 mmol) in abs. CH_2Cl_2 (120 mL) was treated with 1-methyl-3-[2-(4-nitrophenyl)ethoxycarbonylimidazolium chloride (9.4 g, 30 mmol) and 4-dimethylaminopyridine (1.5 g, 12 mmol) and stirred at 5°C for 18 h. It was evaporated, the residue treated with EtOAc (200 mL), 0.2 M HCl (200 mL), and extracted. The organic layer was washed subsequently

with saturated $NaHCO_3$ and NaCl solution and then dried over $MgSO_4$. After evaporation was purified by FC (5 × 12 cm, silica gel) with toluene (200 mL), toluene/EtOAc 10:1 (200 mL), toluene/EtOAc 4:1 (300 mL) and toluene/AcOEt 2:1 (600 mL) to give 7.2 g (88%) of a colorless solid foam. R_f: 0.71 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 203 (4.31), 262 (4.30). ^{1}H-NMR ($CDCl_3$): 8.60 (bs, 1H, NH); 8.15 (d, 2H, *o* to NO_2); 7.41 (d, 2H, *m* to NO_2); 7.30 (d, 1H, H-C(6)); 5.71 (m, 2H, H-C(5), H-C(1′)); 5.45 (pt, 1H, H-C(2′)); 4.55 (m, 2H, H-C(3′)); 4.40 (m, 2H, O*CH*$_2$CH$_2$); 4.20 (m, 1H, H-C(4′)); 3.95 (d, 2H, H-C(5′, 5″)); 3.12 (t, 2H, OCH$_2$*CH*$_2$); 1.2–0.9 (m, 28H, 4 × Me_2CH). Anal. for $C_{30}H_{45}N_3O_{11}Si_2$ (679.9). Calcd: C 53.00, H 6.67, N 6.18. Found: C 52.66, H 6.72, N 5.96.

1-{2-O-[2-(4-Nitrophenyl)ethoxycarbonyl]-3,5-O-(1,1,3,3-tetraisopropyldisiloxan-1,3-diyl)-α-D-arabinofuranosyl}thymine (34). Analogous to **33** with **30** (1.5 g, 3 mmol), 1-methyl-3[2-(4-nitrophenyl)ethoxycarbonylimidazolium chloride (2.5 g, 8 mmol) and 4-dimethylaminopyridine (0.38 g, 3 mmol) in CH_2Cl_2 (60 mL) to give 1.94 g (93%) of a colorless solid. R_f: 0.82 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 204 (4.29), 266 (4.32). ^{1}H-NMR ($CDCl_3$): 8.60 (bs, 1H, NH); 8.15 (d, 2H, *o* to NO_2); 7.41 (d, 2H, *m* to NO_2); 7.10 (d, 1H, H-C(6)); 5.75 (s, 1H, H-C(1′)); 5.45 (pt, 1H, H-C(2′)); 4.55 (m, 2H, H-C(3′)); 4.41 (m, 2H, O*CH*$_2$CH$_2$); 4.19 (m, 1H, H-C(4′)); 3.95 (d, 2H, H-C(5′, 5″)); 3.11 (t, 2H, OCH$_2$*CH*$_2$); 1.95 (s, 3H, H_3C-C(5)); 1.2-0.9 (m, 28H, 4 × Me_2CH). Anal. for $C_{31}H_{47}N_3O_{11}Si_2$ (693.9). Calcd: C 53.66, H 6.83, N 6.06. Found: C 53.58, H 6.87, N 6.20.

N^4-[2-(4-Nitrophenyl)ethoxycarbonyl]-1-{2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-3,5-O-(1,1,3,3-tetraisopropyldisiloxan-1,3-diyl)-α-D-arabinofuranosyl}cytosine (35). Analogous to **33** with **30** (11.66 g, 24 mmol), 1-methyl-3[2-(4-nitrophenyl)ethoxycarbonylimidazolium chloride (19.0 g, 61 mmol) and 4-dimethylaminopyridine (3.2 g, 25 mmol) in CH_2Cl_2 (250 mL). Purification by FC (8 × 20 cm, silica gel) with toluene/EtOAc 10:1 (1 L), toluene/EtOAc 2:1 (1 L) and toluene/EtOAc (2 L) to give 20.5 g (97%) of a colorless solid. R_f: 0.85 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 211 (4.53), 246 (4.37), 270 (sh 4.36). ^{1}H-NMR ($CDCl_3$): 10.85 (bs, 1H, NH); 8.15 (d, 5H, 4H, *o* to NO_2, H-C(6)); 7.55 (m, 4H, *m* to NO_2); 6.95 (d, 1H, H-C(5)); 5.75 (s, 1H, H-C(1′)); 5.65 (pt, 1H, H-C(2′)); 4.45 (m, 2H, H-C(3′), H-C(4′)); 4.30 (m, 4H, O*CH*$_2$CH$_2$); 3.91 (d, 2H, H-C(5′, 5″)); 3.11 (q, 4H, OCH$_2$*CH*$_2$); 1.1–0.8 (m, 28H, 4 × Me_2CH). Anal. for $C_{39}H_{53}N_5O_{14}Si_2$ × 0.5 H_2O (881.1). Calcd: C 53.17, H 6.18, N 7.94. Found: C 53.16, H 6.25, N 7.44.

N^6-[2-(4-Nitrophenyl)ethoxycarbonyl]-1-{2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-3,5-O-(1,1,3,3-tetraisopropyldisiloxan-1,3-diyl)-α-D-arabinofuranosyl}adenine (36). Analogous to **33** with **32** (1.54 g, 3 mmol), 1-methyl-3[2-(4-nitrophenyl)ethoxycarbonylimidazolium chloride (6.0 g, 18 mmol)

and 4-dimethylaminopyridine (0.36 g, 3 mmol) in abs. CH_2Cl_2 (70 mL). Purification by FC (3 × 10 cm, silica gel) with toluene (200 mL), toluene/EtOAc 10.1 (220 mL), toluene/EtOAc (4:1) and toluene/EtOAc 1:1 (400 mL) to give 2.47 g (92%) of a colorless solid. R_f: 0.80 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 209 (4.62), 266 (4.57). ^{1}H-NMR ($CDCl_3$): 10.6 (bs, 1H, NH); 8.55 + 8.50 (2s, 2H, H-C(8), H-C(2)); 8.15 (d, 4H, 4H, *o* to NO_2); 7.60 + 7.45 (2d, 4H, *m* to NO_2); 6.25 (d, 1H, H-C(1′)); 6.15 (m, 1H, H-C(2′)); 4.55 (m, 2H, H-C(3′), H-C(4′)); 4.40 + 4.25 (2t, 4H, O*CH*$_2$CH$_2$); 3.91 (q, 2H, H-C(5′, 5″)); 3.1 + 2.9 (2t, 4H, OCH$_2$*CH*$_2$); 1.1–0.8 (m, 28H, 4 × Me_2CH). Anal. for $C_{40}H_{53}N_7O_{13}Si_2$ (896.1). Calcd: C 53.62, H 5.96, N 10.94. Found: C 53.48, H 5.93, N 11.23.

1-{2-O-[2-(4-Nitrophenyl)ethoxycarbonyl]-α-D-arabinofuranosyl}uracil (37). A solution of **33** (10.2 g, 15 mmol) in abs. THF (150 mL) and AcOH (10 mL, 45 mmol) was treated with tetrabutylammonium fluoride × 3 H_2O (TBAF) (14 g) and stirred for 12 h at room temperature. It was diluted with AcOEt (400 mL) and extracted with saturated $NaHCO_3$ solution. The aqueous phase was reextracted with AcOEt, then the organic layer united and further washed with saturated NaCl solution. The AcOEt extract was dried over Na_2SO_4, evaporated, and the residue purified by FC (3 × 13 cm, silica gel) with toluene/EtOAc 1:1 (500 mL), toluene/EtOAc 1:1 + MeOH (10 mL) (250 mL) and toluene/EtOAc 1:1 + MeOH (40 mL) (500 mL) to give 5.75 g (88%) of a colorless solid. R_f: 0.30 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 203 (4.66), 262 (4.34). ^{1}H-NMR (DMSO-d_6): 11.35 (bs, 1H, NH); 8.15 (d, 2H, *o* to NO_2); 7.75 (d, 1H, H-C(6)); 7.55 (d, 2H, *m* to NO_2); 5.80 (m, 2H, H-C(1′), H-O(3′)); 5.65 (m, 2H, H-C(5)); 5.15 (pt, 1H, H-C(2′)); 4.90 (t, 1H, H-O(5′)); 4.35 (m, 2H, O*CH*$_2$CH$_2$); 4.15 (m, 2H, H-C(3′), H-C(4′)); 3.52 (m, 2H, H-C(5′, 5″)); 3.05 (t, 2H, OCH$_2$*CH*$_2$). Anal. for $C_{18}H_{19}N_3O_{10}$ (437.4). Calcd: C 49.42, H 4.38, N 9.61. Found: C 49.59, H 4.60, N 9.14.

1-{2-O-[2-(4-Nitrophenyl)ethoxycarbonyl]-α-D-arabinofuranosyl}thymine (38). Analogous to **37** with **34** (10.4 g, 15 mmol) and crystallization from CH_2Cl_2 yielded 6.4 g (93%) of colorless crystals. R_f: 0.27 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 203 (4.66), 262 (4.34). ^{1}H-NMR (DMSO-d_6): 11.35 (bs, 1H, NH); 8.15 (d, 2H, *o* to NO_2); 7.65 (d, 1H, H-C(6)); 7.55 (d, 2H, *m* to NO_2); 5.85 (m, 2H, H-C(1′), H-O(3′)); 5.15 (pt, 1H, H-C(2′)); 4.90 (t, 1H, H-O(5′)); 4.35 (m, 2H, O*CH*$_2$CH$_2$); 4.20 (m, 2H, H-C(3′), H-C(4′)); 3.51 (m, 2H, H-C(5′, 5″)); 3.05 (t, 2H, OCH$_2$*CH*$_2$), 1.80 (s, 3H, H_3C-C(5)). Anal. for $C_{19}H_{21}N_3O_{10}$ (446.4). Calcd: C 48.44, H 4.52, N 9.41. Found: C 48.59, H 4.60, N 9.14.

N^4-[2-(4-Nitrophenyl)ethoxycarbonyl]-1-{2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-α-D-arabinofuranosyl}cytosine (39). Analogous to **37** with **35**

(13.1 g, 15 mmol). Purification by FC (6 × 15 cm, silica gel) with toluene/EtOAc 4:1 (500 mL), toluene/EtOAc 1:1 (500 mL), toluene/EtOAc 1:1 + MeOH (10 mL) (500 mL), toluene/EtOAc 1:1 + MeOH (20 mL) (500 mL) and toluene/EtOAc 1:1 + MeOH (50 mL) (1 L) to give 8.15 g (86%) of a colorless solid. R_f: 0.27 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 203 (4.81), 232 (4.44), 273 (4.39). ^{1}H-NMR (DMSO-d_6): 10.80 (bs, 1H, NH); 8.15 (d, 2H, *o* to NO_2); 8.05 (d, 1H, H-C(6)); 7.55 (m, 4H, *m* to NO_2); 7.00 (m, 2H, H-C(5)); 5.80 (m, 2H, H-C(1′), H-O(3′)); 5.15 (pt, 1H, H-C(2′)); 4.95 (t, 1H, H-O(5′)); 4.45 (m, 5H, O*CH*$_2$CH$_2$), H-C(4′)); 4.15 (m, 2H, H-C(3′)); 3.52 (m, 2H, H-C(5′, 5″)); 3.05 (t, 4H, OCH$_2$*CH*$_2$). Anal. for $C_{27}H_{27}N_5O_{13}$ (629.5). Calcd: C 51.51, H 4.32, N 11.13. Found: C 51.02, H 4.55, N 10.72.

N^6-[2-(4-Nitrophenyl)ethoxycarbonyl]-1-{2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-α-D-arabinofuranosyl}adenine (40). Analogous to **37** with **36** (13.4 g, 15 mmol). Purification by FC (6 × 15 cm, silica gel) with toluene/EtOAc 4:1 (500 mL), toluene/EtOAc 1:1 (600 mL), toluene/EtOAc 1:1 + MeOH (5 mL) (500 mL), toluene/EtOAc 1:1 + MeOH (15 mL) (500 mL), toluene/EtOAc 1:1 + MeOH (20 mL) (1 L) and toluene/EtOAc 1:1 + MeOH (30 mL) (1 L) to give 8.03 g (82%) of a colorless solid. R_f: 0.19 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 205 (4.61), 266 (4.55). ^{1}H-NMR (DMSO-d_6): 10.6 (bs, 1H, NH); 8.65 (s, 1H, H-C(8)); 8.80 (s, 1H, H-C(2)); 8.15 (d, 4H, *o* to NO_2); 7.60 + 7.45 (2d, 4H, *m* to NO_2); 6.20 (d, 2H, H-C(1′)); 6.00 (d, 1H, H-O(3′)); 5.75 (pt, 1H, H-C(2′)); 4.90 (t, 1H, H-O(5′)); 4.44–4.20 (m, 6H, 2 × O*CH*$_2$CH$_2$), H-C(3′), H-C(4′)); 3.55 (m, 2H, H-C(5′, 5″)); 3.10 + 2.95 (m, 4H, 2 × OCH$_2$*CH*$_2$). Anal. for $C_{28}H_{27}N_7O_{12}$ (653.6). Calcd: C 51.46, H 4.16, N 15.00. Found: C 51.26, H 4.33, N 14.75.

1-{5-O-Monomethoxytrityl-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-α-D-arabinofuranosyl}uracil (41). The 1-{2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-α-D-arabinofuranosyl}uracil (**37**) (2.8 g, 6.4 mmol) was coevaporated with toluene, then dissolved in abs. pyridine (60 mL), monomethoxytritylchloride (Mmtr-Cl) (2.4 g, 7.7 mmol) added and stirred at room temperature for 20 h. The reaction solution was poured slowly into ice-water (300 mL) and then extracted with EtOAc (3 × 100 mL), washed with saturated NaCl solution, and then dried over Na_2SO_4. It was evaporated, twice coevaporated with toluene to remove traces of pyridine and purified by FC with toluene/EtOAc 10:1 (200 mL), toluene/EtOAc 4:1 (500 mL), and toluene/EtOAc 1:1 (500 mL) to give 3.7 g (82%) of a colorless solid foam. R_f: 0.54 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 204 (4.88), 232 (sh 4.38), 262 (4.39). ^{1}H-NMR (DMSO-d_6): 11.4 (bs, 1H, NH); 8.15 (d, 2H, *o* to NO_2); 7.75 (d, 1H, H-C(6)); 7.50 (d, 2H, *m* to NO_2); 7.4–7.2 (m, 12H, trityl); 6.85 (d, 2H, *o* to OCH_3); 5.85 (m, 2H, H-C(1′), H-O(3′)); 5.65 (m, 2H, H-C(5)); 5.10 (pt, 1H,

H-C(2′)); 4.31 (m, 3H, H-C(4′), O*CH*$_2$CH$_2$); 4.20 (m, 1H, H-C(3′)); 3.70 (s, 3H, OCH$_3$); 3.10 (m, 4H, H-C(5′, 5″),OCH$_2$*CH*$_2$). Anal. for $C_{38}H_{36}N_3O_{11} \times 0.5\ H_2O$ (719.7). Calcd: C 63.42, H 5.83, N 5.83. Found: C 63.65, H 5.25, N 5.46.

1-{5-O-Monomethoxytrityl-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-α-D-arabinofuranosyl}thymine (42). Analogous to **41** with **38** (2.91 g, 6.4 mmol) in 8 h to give 4.13 (89%) of a colorless foam. R_f: 0.58 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 208 (4.84), 234 (sh 4.38), 265 (4.32). ^{1}H-NMR (DMSO-d$_6$): 11.35 (bs, 1H, NH); 8.15 (d, 2H, *o* to NO$_2$); 7.71 (d, 1H, H-C(6)); 7.50 (d, 2H, *m* to NO$_2$); 7.4–7.2 (m, 12H, trityl); 6.85 (d, 2H, *o* to OCH$_3$); 5.90 (m, 2H, H-C(1′), H-O(3′)); 5.15 (pt, 1H, H-C(2′)); 4.45-4.20 (m, 4H, H-C(3′), H-C(4′), O*CH*$_2$CH$_2$); 3.70 (s, 3H, OCH$_3$); 3.10 (m, 4H, H-C(5′, 5″), OCH$_2$*CH*$_2$); 1.81 (s, 3H, H$_3$C-C(5)). Anal. for $C_{39}H_{38}N_3O_{11}$ (724.7). Calcd: C 64.63, H 5.29, N 5.80. Found: C 64.75, H 5.42, N 5.44.

N^4-[2-(4-Nitrophenyl)ethoxycarbonyl]-1-{5-O-monomethoxytrityl-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-α-D-arabinofuranosyl}cytosine (43). Analogous to **41** with **39** (4.0 g, 6.4 mmol) in 28 h. Purification by FC with toluene/EtOAc 10:1 (200 mL), toluene/EtOAc 2:1 (500 mL) and toluene/EtOAc 1:2 (500 mL) to give 5.46 g (95%) of a colorless foam. R_f: 0.79 (toluene/EtOAc/MeOH 1:1:1). UV (MeOH): 204 (5.12), 232 (sh 4.71), 273 (4.48). ^{1}H-NMR (DMSO-d$_6$): 10.85 (bs, 1H, NH); 8.15 (m, 5H, 4H, *o* to NO$_2$), H-C(6)); 7.60 + 7.50 (2d, 4H, *m* to NO$_2$); 7.4–7.2 (m, 12H, trityl); 7.00 (d, 1H, H-C(5)); 6.85 (d, 2H, *o* to OCH$_3$); 5.81 (m, 2H, H-C(1′), H-O(3′)); 5.15 (pt, 1H, H-C(2′)); 4.55 (m, 3H, H-C(3′)); 4.35 (m, 4H, O*CH*$_2$CH$_2$); 4.15 (dd, 1H, H-C(4′)); 3.70 (s, 3H, OCH$_3$); 3.10 (m, 6H, H-C(5′, 5″),OCH$_2$*CH*$_2$). Anal. for $C_{47}H_{43}N_5O_{14}$ (901.9). Calcd: C 62.59, H 4.81, N 7.76. Found: C 62.30, H 4.99, N 7.32.

N^6-[2-(4-Nitrophenyl)ethoxycarbonyl]-1-{5-O-monomethoxytrityl-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-α-D-arabinofuranosyl}adenine (44). Analogous to **41** with **40** (1.25 g, 1.9 mmol), Mmtr-Cl (0.7 g, 2.28 mmol) in pyridine (20 mL) in 40 h. FC with toluene/EtOAc 4:1 (400 mL), toluene/EtOAc 2:1 (300 mL) toluene/EtOAc 1:2 (300 mL) and toluene/EtOAc 1:3 (600 mL) to give 1.63 g (92%) of a colorless solid foam. R_f: 0.80 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 203 (5.00), 229 (sh 4.47), 266 (4.56). ^{1}H-NMR (DMSO-d$_6$): 10.6 (bs, 1H, NH); 8.65(s, 1H, H-C(8)); 8.15 (m, 4H, *o* to NO$_2$)); 7.60 + 7.45 (2d, 4H, *m* to NO$_2$); 7.4–7.2 (m, 12H, trityl); 6.90 (d, 2H, *o* to OCH$_3$); 6.31 (d, 1H, H-O(3′)); 6.11 (m, 2H, H-C(1′), 5.75 (pt, 1H, H-C(2′)); 4.55 (m, 3H, H-C(4′)); 4.32 (m, 5H, H-C(3′), O*CH*$_2$CH$_2$); 3.70 (s, 3H, OCH$_3$); 3.25 (m, 6H, H-C(5′, 5″)); 3.00 (m, 4H, OCH$_2$*CH*$_2$). Anal. for $C_{48}H_{43}N_7O_{13}$ (925.9). Calcd: C 62.20, H 4.78, N 10.58. Found: C 61.91, H 4.88, N 10.23.

1-{5-O-Dimethoxytrityl-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-α-D-arabinofuranosyl}uracil (45). Analogous to **41** with **37** (1.18 g, 3 mmol) with dimethoxytrityl chloride (1.15 g, 3.45 mmol) in abs. pyridine (30 mL) in 20 h. Purification by FC with toluene/EtOAc 3:1 (400 mL) and tolune/EtOAc 1:1 + MeOH (5 mL) (500 mL) to give 1.98 g (88%) of a colorless foam. R_f: 0.34 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 204 (4.88), 235 (4.44), 263 (4.35). ^{1}H-NMR (DMSO-d_6): 11.4 (bs, 1H, NH); 8.15 (d, 2H, *o* to NO_2); 7.80 (d, 1H, H-C(6)); 7.50 (d, 2H, *m* to NO_2); 7.4–7.2 (m, 9H, trityl); 6.85 (d, 4H, *o* to OCH_3); 5.90 (m, 2H, H-C(1′), H-O(3′)); 5.65 (m, 2H, H-C(5)); 5.15 (pt, 1H, H-C(2′)); 4.35 (m, 3H, H-C(4′), O*CH*$_2$CH$_2$); 4.20 (m, 1H, H-C(3′)); 3.70 (s, 6H. 2 × OCH_3); 3.05 (m, 4H, H-C(5′, 5″),OCH_2*CH*$_2$). Anal. for $C_{39}H_{37}N_3O_{12} \times 0.5\ H_2O$ (748.7). Calcd: C 62.56, H 5.61, N 5.61. Found: C 62.51, H 5.05, N 5.65.

1-{5-O-Dimethoxytrityl-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-α-D-arabinofuranosyl}thymine (46). Analogous to **45** with **38** (1.35 g, 3 mmol) and Dmtr-Cl (1.16 g, 3.45 mmol) in 20 h to give 2.1 g (91%) of a colorless foam. R_f: 0.33 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 204 (4.87), 235 (4.43), 266 (4.36). ^{1}H-NMR (DMSO-d_6): 11.4 (bs, 1H, NH); 8.15 (d, 2H, *o* to NO_2); 7.70 (d, 1H, H-C(6)); 7.50 (d, 2H, *m* to NO_2); 7.4–7.2 (m, 9H, trityl); 6.85 (d, 4H, *o* to OCH_3); 5.90 (m, 2H, H-C(1′), H-O(3′)); 5.15 (pt, 1H, H-C(2′)); 4.45–4.20 (m, 4H, H-C(3′), H-C(4′), O*CH*$_2$CH$_2$); 3.70 (s, 6H. 2 × OCH_3); 3.10 (m, 4H, H-C(5′, 5″),OCH_2*CH*$_2$); 1.81 (s, 3H, H_3C-C(5). Anal. for $C_{40}H_{39}N_3O_{12} \times 0.5\ H_2O$ (762.8). Calcd: C 62.98, H 5.28, N 5.50. Found: C 62.87, H 5.11, N 5.78.

N^4-[2-(4-Nitrophenyl)ethoxycarbonyl]-1-{5-O-dimethoxytrityl-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-α-D-arabinofuranosyl}cytosine (47). Analogous to **45** with **39** (1.88 g, 3 mmol) and Dmtr-Cl (1.22 g, 3.6 mmol) in 28 h. Purification by FC (4 × 12 cm, silica gel) with toluene/EtOAc 10:1 (200 mL), toluene/EtOAc (3:1 (400 mL), toluene/EtOAc 1:1 (400 mL) and toluene/EtOAc 2:3 (500 mL) to give 2.7 g (96%) of a colorless foam. R_f: 0.67 (toluene/EtOAc/MeOH 1:1:1). UV (MeOH): 204 (4.97), 236 (4.63), 273 (4.43). ^{1}H-NMR (DMSO-d_6): 10.8 (bs, 1H, NH); 8.15 (m, 5H, 4H, *o* to NO_2, H-C(6)); 7.60 + 7.50 (2d, 4H, *m* to NO_2); 7.4–7.2 (m, 9H, trityl); 6.85 (d, 4H, *o* to OCH_3); 5.85 (m, 2H, H-C(1′), H-O(3′)); 5.15 (pt, 1H, H-C(2′)); 4.55 (m, 3H, H-C(3′)); 4.35 (m, 4H, 2 × O*CH*$_2$CH$_2$); 4.15 (m, 1H, H-C(4′)); 3.70 (s, 6H. 2 × OCH_3); 3.05 (m, 4H, HC(5′, 5″), OCH_2*CH*$_2$). Anal. for $C_{48}H_{45}N_5O_{15}$ (931.9). Calcd: C 61.86, H 4.87, N 7.26. Found: C 61.96, H 5.01, N 7.29.

N^6-[2-(4-Nitrophenyl)ethoxycarbonyl]-1-{5-O-dimethoxytrityl-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-α-D-arabinofuranosyl}adenine (48). Analo-

gous to **45** with **40** (1.96 g, 3 mmol) and Dmtr-Cl (1.1 g, 3.3 mmol) in 40 h. Purification by FC with toluene/EtOAc 4:1 (500 mL), toluene/EtOAc 1:1 (500 mL) and toluene/EtOAc 1:1 + MeOH (10 mL) (500 mL) to give 2.72 g (95%) of a colorless solid. R_f: 0.64 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 204 (4.98), 236 (4.49), 267 (4.61). ^{1}H-NMR (DMSO-d_6): 10.6 (bs, 1H, NH); 8.65 (2s, 2H, H-C(8), H-C(2)); 8.15 (m, 4H, *o* to NO_2, H-C(6))); 7.60 + 7.45 (2d, 4H, *m* to NO_2); 7.4–7.2 (m, 9H, trityl); 6.89 (d, 4H, *o* to OCH_3); 6.30 (d, 1H, H-O(3′)); 6.12 (m, 2H, H-C(1′)); 5.75 (pt, 1H, H-C(2′)); 4.55 (m, 3H, H-C(4′)); 4.30 (m, 5H, H-C(3′), 2 × O*CH*$_2$CH$_2$); 3.70 (s, 6H. 2 × OCH_3); 3.25 (m, 4H, H-C(5′, 5″)); 3.05 (m, 4H, 2 × OCH_2*CH*$_2$). Anal. for $C_{49}H_{45}N_7O_{14}$ (955.9). Calcd: C 61.57, H 4.74, N 10.25. Found: C 61.24, H 4.81, N 10.18.

N^2,N^9-Diacetyl-O^6-2-(4-nitrophenyl)ethylguanine (49). To a suspension of N^2,N^9-diacetylguanine[17] (9.6 g, 40 mmol) in abs. dioxane (200 mL) were subsequently added under stirring triphenylphosphane (13.5 g, 50 mmol) and 2-(4-nitrophenyl)ethanol (14.0 g, 80 mmol). After 10 min ethyl azodicarboxylate (12.5 mL, 80 mmol) dissolved in dioxane (20 mL) was added slowly dropwise and the mixture then stirred for 24 h. The precipitate was collected, washed with ether and dried at 100°C to give 12.3 g (80%) of colorless crystals of m.p. 215–219°C. UV (MeOH): 217 (4.47), 268 (4.40). ^{1}H-NMR (DMSO-d_6): 10.55 (bs, 1H, NH); 8.60 (s, 1H, H-C(8)); 8.15 (d, 2H, *o* to NO_2); 7.65 (d, 2H, *m* to NO_2); 4.75 (t, 2H, O*CH*$_2$CH$_2$); 3.31 (t, 2H, OCH_2*CH*$_2$); 2.85 (s, 3H, Ac-N(9)); 2.25 (s, 3H, ac-N(2)). Anal. for $C_{17}H_{16}N_6O_5$ (384.4). Calcd: C 53.13, H 4.20, N 21.87. Found: C 52.88, H 4.16, N 21.88.

N^2-Acetyl-O^6-2-(4-nitrophenyl)ethylguanine (50). N^2,N^9-Diacetyl-O^6-2-(4-nitro-phenyl)ethylguanine **(49)** (12.3 g, 32 mmol) was heated in DMF (180 mL) and H_2O (60 mL) under reflux for 4 h. After 10 min boiling a clear solution was obtained from which crystals separated during heating. The precipitate was collected after cooling, washed with cold EtOH and ether and dried at 100°C to give 10.1 g (92%) of colorless crystals of m.p. 275–277°C. UV (MeOH): 217 (4.43), 268 (4.36). ^{1}H-NMR (DMSO-d_6): 13.15 (bs, 1H, NH); 10.55 (bs, 1H, NH); 8.60 (s, 1H, H-C(8)); 8.15 (d, 3H, *o* to NO_2, H-C(8)); 7.65 (d, 2H, *m* to NO_2); 4.75 (t, 2H, O*CH*$_2$CH$_2$); 3.30 (t, 2H, OCH_2*CH*$_2$); 2.22 (s, 3H, ac-N(2)). Anal. for $C_{15}H_{14}N_6O_4$ (384.4). Calcd: C 52.63, H 4.12, N 24.55. Found: C 52.50, H 4.14, N 24.51.

O^6-2-(4-Nitrophenyl)ethylguanine (51). A) A suspension of **49** (1.15 g, 3 mmol) in methanolic HCl (25 mL) was stirred at room temperature for 2 days. Under cooling was neutralized by 5% aqueous NaOH, the precipitate collected, washed with H_2O and dried at 100°C to give 0.81 g (90%) impure

solid. Purification was done by FC. 0.8 g were dissolved in hot MeOH (80 mL), then silica gel (12 g) added, evaporated, filled into a column, and eluted with toluene/EtOAc 1:1 (600 mL) and toluene/EtOAc/MeOH 5:4:1 (600 mL) to give 0.62 g (69%) of a colorless solid. B) Analogous to A with **50** (0.69 g, 2 mmol) to give 0.485 g (81%) of a colorless powder of m.p. >300°C (decomp.). UV (MeOH): 205 (4.57), 245 (4.10), 278 (4.26). ^{1}H-NMR (DMSO-d_6): 12.4 (bs, 1H, NH); 8.15 (d, 2H, *o* to NO_2); 7.80 (s, 1H, H-C(8)); 7.62 (d, 2H, *m* to NO_2); 6.75 (bs, 2H, NH_2); 4.60 (t, 2H, O*CH*$_2$CH$_2$); 3.25 (t, 2H, OCH$_2$*CH*$_2$). Anal. for $C_{13}H_{12}N_6O_3$ (300.3). Calcd: C 52.00, H 4.03, N 27.98. Found: C 52.25, H 3.99, N 27.49.

N^2-Acetyl-O^6-[2-(4-nitrophenyl)ethyl]-9-(2,3,5-tri-O-acetyl-α-D-arabinofuranosyl)guanine (52). A mixture of **50** (1.72 g, 5 mmol) and N,O-*bis*-trimethylsilylacetamide (3 mL) in CH_2Cl_2 (25 mL) was heated in an oilbath at 80°C for 2 h with stirring. After 20 min a clear solution was obtained. It was cooled, evaporated, and coevaporated with toluene. The resulting oil was dissolved in toluene (30 mL), TMS-triflate (2 mL) added and followed by dropwise addition of a solution of 1,2,3,4-tetra-O-acetyl-D-arabinofuranose (2.0 g, 6.25 mmol) in toluene (35 mL) and heated for 3 h at 80°C. After cooling was diluted with EtOAc (150 mL), extracted subsequently with saturated $NaHCO_3$ (150 mL) and NaCl solution (150 mL), dried over Na_2SO_4, and evaporated. Purification by FC (3 × 12 cm, silica gel) with toluene/EtOAc 8:1 (400 mL), toluene/EtOAc 4:1 (400 mL), toluene/EtOAc 1:1 (400 mL) and toluene/EtOAc 1:2 (300 mL) to give 1.62 g (55%) of a colorless foam. R_f = 0.39 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 204 (4.44), 217 (4.54), 268 (4.48). ^{1}H-NMR ($CDCl_3$): 8.15 (d, 2H, *o* to NO_2); 7.90 (s, 1H, H-C(8)); 7.85 (bs, 1H, NH); 7.45 (d, 2H, *m* to NO_2); 6.10 (d, 1H, H-C(1′)); 6.00 (pt, 1H, H-C(2′)); 5.31 (pt, 1H; H-C(3′)); 4.75 (m, 3H, H-C(4′), O*CH*$_2$CH$_2$); 4,32 (m, 2H, H-C(5′, 5″)); 3.30 (t, 2H, O*CH*$_2$CH$_2$); 2.55 (s, 3H, ac-N(2)); 2.15–2.00 (3s, 9H, 3 × ac-O). Anal. for $C_{26}H_{28}N_6O_{11}$ (600.5). Calcd: C 52.00, H 4.70, N 13.99. Found: C 52.37 H 5.09, N 13.58.

N^2-Acetyl-O^6-[2-(4-nitrophenyl)ethyl]-9-(2,3,5-tri-O-benzoyl-α-D-arabinofuranosyl)guanine (53). Analogous to **52** with **50** (1.72 g, 5 mmol) and 1-O-acetyl-2,3,5-tri-O-benzoyl-D-arabinofuranose (2.8 g, 5.6 mmol) to give 2.95 g (75%) of a colorless solid foam. R_f = 0.75 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 202 (4.66), 222 (4.73), 231 (sh 4.67), 269 (4.48). ^{1}H-NMR ($CDCl_3$): 8.15 (d, 2H, *o* to NO_2); 8.05 + 7.85 (2m, 8H, 3 × 2H, *o* to bz), H-C(8), NH); 7.55–7.30 (m, 11H, 2H, *m* to NO_2, 3 × 3H bz); 6.50 (pt, 1H, H-C(2′)); 6.41 (d, 1H, H-C(1′)); 5.89 (pt, 1H; H-C(3′)); 5.05 (m, 1H, H-C(4′), 4,81 (m, 4H, H-C(5′, 5″), O*CH*$_2$CH$_2$); 3.30 (t, 2H, OCH$_2$*CH*$_2$); 2.50

(s, 3H, ac-N(2)). Anal. for $C_{41}H_{34}N_6O_{11}$ (786.8). Calcd: C 62.59, H 4.46, N 10.68. Found: C 62.53, H 4.45, N 10.71.

O^6-[2-(4-Nitrophenyl)ethyl]-9-α-D-arabinofuranosylguanine (54). To a suspension of **56** (0.7 g, 0.94 mmol) in MeOH (20 mL) was added K_2CO_3 (25 mg) and stirred under gentle warming for 2 h. It was neutralized by a few drops of AcOH, the precipitate collected, washed with ether and dried at 100°C to give 0.345 g, (85%) of a crystalline powder of m.p. 144–146°C. R_f = 0.67 (toluene/EtOAc/MeOH 1:1:1). UV (MeOH): 212 (4.52), 252 (4.17), 278 (4.25). ^{1}H-NMR (DMSO-d_6): 8.15 (d, 2H, *o* to NO_2); 8.05 (s, 1H, H-C(8)); 7.65 (d, 2H, *m* to NO_2); 6.45 (s, 2H, NH_2); 5.75 (d, 2H, H-C(1′), H-O(2′)); 5.55 (d, 1H, H-O(3′)); 4.90 (t 1H, H-O(5′)); 4.70 (t, 2H, O*CH*$_2$CH$_2$); 4.50 (dd, 1H, H-C(2′)); 4,12 (m, 1H, H-C(4′)); 3.95 (dd, 1H, H-C(3′)); 3.55 (m, 2H, H-C(5′, 5″)); 3.25 (t, 2H, OCH$_2$*CH*$_2$); Anal. for $C_{18}H_{20}N_6O_7$ (432.4). Calcd: C 50.00, H 4.66, N 19.44. Found: C 49.63, H 4.92, N 19.23.

O^6-[2-(4-Nitrophenyl)ethyl]-9-(2,3,5-tri-O-acetyl-α-D-arabinofuranosyl) guanine (55). A suspension of **51** (0.92 g, 3 mmol) and N,O-*bis*-trimethylsilylacetamide (2 mL) in CH_2Cl_2 (30 mL) was stirred at 80°C for 2 h. It was evaporated, the residue coevaporated with toluene and then dissolved in toluene (30 mL). After addition of TMS-triflate (0.6 mL) a solution of 1,2,3,5-tetra-O-acetyl-D-arabinofuranose (1.28 g, 4 mmol) in toluene (12 mL) was dropwise added followed by heating to 80°C for 18 h. The reaction solution was diluted with EtOAc (120 mL) and subsequently washed with saturated aqueous $NaHCO_3$ (100 mL) and NaCl solution (100 mL). The organic layer was dried over Na_2SO_4, evaporated, and then purified by FC (3 × 10 cm) with toluene/EtOAc 4:1 (400 mL), toluene/EtOAc 2:1 (400 mL), and toluene/EtOAc/MeOH 20:20:1 (300 mL) to give 0.46 mg (52%) of a colorless foam. R_f = 0.22 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 209 (4.49), 253 (4.17), 277 (4.22). ^{1}H-NMR ($CDCl_3$): 8.20 (d, 2H, *o* to NO_2); 7.72 (s, 1H, H-C(8)); 7.45 (d, 2H, *m* to NO_2); 6.05 (d, 1H, H-C(1′)); 5.92 (pt, 1H, H-C(2′)); 5.25 (pt, 1H; H-C(3′)); 4.90 (bs, 2H, NH_2); 4.65 (m, 3H, H-C(4′), O*CH*$_2$CH$_2$); 4,25 (m, 2H, H-C(5′, 5″)); 3.20 (t, 2H, OCH$_2$CH$_2$); 2.10 (3s, 9H, 3 × ac-O). Anal. for $C_{24}H_{26}N_6O_{10}$ (558.5). Calcd: C 51.61, H 4.69, N 15.05. Found: C 51.35 H 4.93, N 15.50.

O^6-[2-(4-Nitrophenyl)ethyl]-9-(2,3,5-tri-O-benzoyl-α-D-arabinofuranosyl)guanine (56). Analogous to **55** with **51** (9.2 g, 30 mmol) and N,O-*bis*-trimethylsilylacetamide (15 mL) in CH_2Cl_2 (30 mL) at 80°C for 2 h. Followed by TMS-triflate (5.5 mL) and 1-O-acetyl-2,3,5-tri-O-benzoyl-D-arabinofuranose (14.1 g, 27 mmol) in toluene and heating to 80°C for 8 h. The crude material was purified by FC (6 × 15 cm, silica gel) using toluene/EtOAc 6:1 (700 mL), toluene/EtOAc 4:1 (400 mL), toluene/EtOAc 2:1

(1.5 L) and toluene/EtOAc 1:1 (600 mL) to give 14.6 g (73%) of a colorless solid. $R_f = 0.63$ (toluene/EtOAc 1:2). UV (MeOH): 212 (4.55), 231 (4.64), 276 (4.28). ^{1}H-NMR ($CDCl_3$): 8.20 (m, 3H, *o* to NO_2, H-C(8)); 8.00 (d, (m, 6H, 3 × 2H, *o* to bz)); 7.55–7.40 (m, 11H, 2H, *m* to NO_2, 3 × 3H bz); 6.58 (bs, 2H, NH_2); 6.45 (m, 2H, H-C(1′), H-C(2′)); 5.95 (pt, 1H; H-C(3′)); 5.15 (m, 1H, H-C(4′); 4,65 (m, 4H, H-C(5′, 5″), O*CH*$_2$CH$_2$); 3.25 (t, 2H, OCH$_2$*CH*$_2$). Anal. for $C_{39}H_{32}N_6O_{10}$ (744.7). Calcd: C 62.90, H 4.33, N 11.28. Found: C 62.21, H 4.23, N 10.99.

O^6-[2-(4-Nitrophenyl)ethyl]-N^2-[2-(4-nitrophenyl)ethoxycarbonyl]-9-(2,3,5-tri-O-benzoyl-α-D-arabinofuranosyl)guanine (57). Compound **56** (4.5 g, 6.5 mmol) was coevaporated with abs. pyridine (15 mL), then dissolved in pyridine (50 mL), cooled to 5–8°C, 2-(4-nitrophenyl)ethoxycarbonyl chloride (2.7 g, 12 mmol) added and kept for 2 days in the icebox. It was evaporated, coevaporated with toluene (3 × 20 mL), and then the residue dissolved in CH_2Cl_2 (10 mL) for FC (4 × 10 cm, silica gel) with toluene/EtOAc 8:1 (650 mL), toluene/EtOAc 4:1 (500 mL), and toluene/EtOAc 3:1 (800 mL) to give 5.96 g (93%) of a colorless solid foam. $R_f = 0.63$ (toluene/EtOAc 1:2). UV (MeOH): 201 (4.73), 217 (4.72), 231 (4.65), 270 (4.52). ^{1}H-NMR ($CDCl_3$): 10.45 (s, 1H, NH); 8.40 (s, 1H, H-C(8)); 8.20 (m, 4H, *o* to NO_2, H-C(8)); 8.00 (d, (m, 6H, 3 × 2H, *o* to bz)); 7.7–7.3 (m, 13H, 4H, *m* to NO_2, 3 × 3H bz); 6.55 (d, 1H, H-C(1′)); 6.45 (m, 1H, H-C(2′)); 6.00 (m, 1H; H-C(3′)); 5.60 (dd, 1H, H-C(4′); 4,65 (m, 4H, O*CH*$_2$CH$_2$); 4.25 (m, 2H, H-C(5′, 5″), 3.3 + 3.0 (2t, 4H, OCH$_2$*CH*$_2$). Anal. for $C_{48}H_{39}N_7O_{14}$ (937.9). Calcd: C 61.47, H 4.19, N 10.45. Found: C 61.42, H 4.31, N 10.32.

O^6-[2-(4-Nitrophenyl)ethyl]-N^2-[2-(4-nitrophenyl)ethoxycarbonyl]-9-α-D-arabinofuranosyl)guanine (58). In a mixture of MeOH (100 mL), dioxane (100 mL), and conc. aqueous NH_3 (100 mL) compound **57** (7.45 g, 10 mL) was dissolved and then stirred at room temperature for 2 days in a closed bottle. It was evaporated and the residue crystallized from MeOH to give 3.5 g (81%) of colorless crystals of m.p. 123–130°C. $R_f = 0.30$ (CH_2Cl_2/MeOH 8:1). UV (MeOH): 206 (4.77), 268 (4.58). ^{1}H-NMR (DMSO-d_6): 10.35 (bs, 1H, NH); 8.40 (s, 1H, H-C(8)); 8.20 (m, 4H, *o* to NO_2); 7.60 (m, 4H, *m* to NO_2); 5.85 (d, 1H, H-C(1′)); 5.75 (d, 1H, H-O(2′)); 5.45 (d, 1H, H-O(3′)); 4.90 (t, 1H, H-O(5′)); 4.75 (t, 2H, O*CH*$_2$CH$_2$); 4.60 (dd, 1H, H-C(2′)); 4.22 (m, 1H, H-C(3′)); 4.05 (m, 1H, H-C(4′)); 3.55 (m, 2H, H-C(5′, 5″)); 3.3 + 3.1 (2t, 4H, OCH$_2$*CH*$_2$). Anal. for $C_{27}H_{27}N_7O_{10}$, × 0.5 H_2O (634.6). Calcd: C 51.11, H 4.30, N 15.45. Found: C 51.24, H 4.46, N 15.38.

O^6-[2-(4-Nitrophenyl)ethyl]-9-[3,5-O-(1,1,3,3-tetraisopropyldisiloxan-1,3-diyl)-α-D-arabinofuranosyl]guanine (59). Analogous to **29** with **54** (3.45 g, 8 mmol) and 1,3-di-chloro-1,1,3,3-tetraisopropyldisiloxane (1.6 mL, 9.6

mmol) in abs. pyridine (100 mL) and 18 h stirring at room temperature. Dilution by EtOAc (250 mL) and washing with 250 mL each 0.2 M HCl, saturated $NaHCO_3$, and NaCl solution. Purification by FC (5 × 10 cm, silica gel) with toluene/EtOAc 4:1 (500 mL) and toluene/EtOAc 2:1 (1.2 L) to give 4.17 g (77%) of a colorless foam. $R_f = 0.60$ (toluene/EtOAc 1:2). UV (MeOH): 210 (4.53), 251 (4.24), 278 (4.31). ^{1}H-NMR (DMSO-d_6): 8.15 (d, 3H, *o* to NO_2, H-C(8)); 7.65 (d, 2H, *m* to NO_2); 6.48 (s, 2H, NH_2); 5.90 (d, 1H, H-C(1′)); 5.65 (d, 1H, H-O(2′)); 4.90 (dd, 1H, H-C(2′)); 4.65 (t, 2H, O*CH*$_2$CH$_2$); 4.25 (m, 2H, H-C(3′), H-C(4′)); 3.85 (m, 2H, H-C(5′, 5″)); 3.25 (t, 2H, OCH$_2$*CH*$_2$); 1.15-0.9 (m, 28H, CH(CH$_3$)$_2$). Anal. for $C_{30}H_{46}N_6O_8Si_2$ (674.9). Calcd: C 53.39, H 6.87, N 12.45. Found: C 53.56, H 7.04, N 12.08.

O^6-[2-(4-Nitrophenyl)ethyl]-N^2-[2-(4-nitrophenyl)ethoxycarbonyl]-9-[3,5-O-(1,1,3,3-tetraisopropyldisiloxan-1,3-diyl)-α-D-arabinofuranosyl]guanine (60). Analogous to the preceeding procedure with **58** (5.0 g, 8 mmol) and 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (1.6 mL, 9.6 mmol) in abs. pyridine (180 mL) and 24 h stirring at room temperature. Purification by FC with toluene/EtOAc 10:1 (300 mL), toluene/EtOAc 5:1 (400 mL), toluene/EtOAc 4:1 (300 mL), toluene/EtOAc 3:1 (500 mL), and toluene/EtOAc 2:1 (400 mL) to give 5.76 g (83%) of a colorless foam. $R_f = 0.65$ (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 210 (4.80), 268 (4.57). ^{1}H-NMR (DMSO-d_6): 11.35 (s, 1H, NH); 8.40 (s, 1H, H-C(8)); 8.15 (d, 4H, *o* to NO_2); 7.65 (m, 4H, *m* to NO_2); 5.90 (d, 1H, H-C(1′)); 5.75 (d, 1H, H-O(2′)); 5.00 (dd, 1H, H-C(2′)); 4.75 (t, 2H, O*CH*$_2$CH$_2$); 4.55 (m, 1H, H-C(3′)); 4.35 (t, 2H, O*CH*$_2$CH$_2$); 4.25 (m, 1H, H-C(4′)); 3.85 (m, 2H, H-C(5′, 5″)); 3.3 + 3.1 (t, 4H, OCH$_2$*CH*$_2$); 1.1–0.9 (m, 28H, CH(CH$_3$)$_2$). Anal. for $C_{39}H_{53}N_7O_{12}$ Si_2(868.1). Calcd: C 53.96, H 6.15, N 11.29. Found: C 53.99, H 6.17, N 10.85.

O^6-[2-(4-Nitrophenyl)ethyl]-9-{3,5-O-(1,1,3,3-tetraisopropyldisiloxan-1,3-diyl)-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-α-D-arabinofuranosyl}guanine (61). Analogous to **33** with **59** (0.675 g, 1 mmol) and 1-methyl-3-[2-(4-nitrophenyl)ethoxycarbonyl]imidazolium chloride (0.73 g, 2 mmol) in CH_2Cl_2 (20 mL) and 4-dimethylaminopyridine (0.17 g) at 5°C for 18 h. Purification by FC (2 × 8 cm), silica gel) with toluene/EtOAc 10:1 (220 mL) and toluene/EtOAc 1:1 (300 mL) to give 0.815 g (94%) of a colorless foam. $R_f = 0.67$ (toluene/EtOAc 1:2). UV (MeOH): 205 (4.56), 253 (4.42), 276 (4.31). ^{1}H-NMR (DMSO-d_6): 8.15 (d, 5H, *o* to NO_2, H-C(8)); 7.65 + 7.45 (2d, 4H, *m* to NO_2); 6.48 (s, 2H, NH_2); 5.95 (m, 2H, H-C(1′), H-C(2′)); 4.65 (t, 2H, O*CH*$_2$CH$_2$); 4.50 (m, 2H, H-C(3′), H-C(4′)); 4.32 (t, 2H, O*CH*$_2$CH$_2$); 3.88 (m, 2H, H-C(5′, 5″)); 3.25 + 3.00 (2t, 4H, OCH$_2$*CH*$_2$); 1.1–0.8 (m, 28H, CH(CH$_3$)$_2$). Anal. for $C_{39}H_{53}N_7O_{12}Si_2$ (868.1). Calcd: C 53.96, H 6.87, N 11.29. Found: C 54.13, H 6.24, N 10.91.

O^6-[2-(4-Nitrophenyl)ethyl]-N^2-[2-(4-nitrophenyl)ethoxycarbonyl]-9-{3,5-O-(1,1,3,3-tetraisopropyldisiloxan-1,3-diyl)-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-α-D-arabinofuranosyl}guanine (62). Analogous to the preceeding procedure with **61** (0.87 g, 1 mmol) and purification by FC (3 × 10 cm) with toluene/EtOAc 10:1 (250 mL), toluene/EtOAc 4:1 (200 mL), and toluene/EtOAc 1:1 (400 mL) to give 1.0 g (94%) of a colorless foam. R_f = 0.53 (toluene/EtOAc 1:1). UV (MeOH): 214 (4.65), 268 (4.60). ^{1}H-NMR ($CDCl_3$): 8.15 (m, 6H, *o* to NO_2); 7.90 (m, 1H, H-C(8)); 7.55–7.33 (m, 6H, *m* to NO_2); 6.05 (m, 1H, H-C(2′)); 5.90 (d, 1H, H-C(1′)); 4.75 (t, 3H, O*CH*$_2$CH$_2$, H-C(3′)); 4.60 (m, 1H, H-C(4′)); 4.45 + 4.30 (2t, 4H, O*CH*$_2$CH$_2$); 4.00 (m, 2H, H-C(5′, 5″)); 3.3 + 3.1 + 3.0 (3t, 6H, OCH$_2$*CH*$_2$); 1.15–0.9 (m, 28H, CH(CH$_3$)$_2$). Anal. for $C_{48}H_{60}N_8O_{16}Si_2$ (1061.2). Calcd: C 54.33, H 5.70, N 10.56. Found: C 54.27, H 5.81, N 10.64.

O^6-[2-(4-Nitrophenyl)ethyl]-N^2-[2-(4-nitrophenyl)ethoxycarbonyl]-9-{2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-α-D-arabinofuranosyl}guanine (63). Analogous to **37** with **62** (3.9 g, 3.7 mmol) in THF (60 mL), AcOH (4 mL), and TBAF ×3 H_2O (4.7 g, 15 mmol) and stirring for 3 h. Purification by FC (4 × 10 cm, silica gel) with toluene/EtOAc 1:1 (300 mL), toluene/EtOAc 1:1 + MeOH (5 mL) (300 mL), toluene/EtOAc 1:1 + MeOH (15 mL) (500 mL), toluene/EtOAc 1:1 + MeOH (20 mL) (500 mL), and toluene/EtOAc 1:1 + MeOH (30 mL) (500 mL) to give 2.45 g (80%) of a colorless solid. R_f: 0.61 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 204 (4.61), 214 (4.69), 268 (4.64). ^{1}H-NMR (DMSO-d_6): 10.4 (bs, 1H, NH); 8.35 (s, 1H, H-C(8)); 8.15 (m, 6H, *o* to NO_2); 7.65 (m, 4H, *m* to NO_2); 7.45 (d, 2H, *m* to NO_2); 6.05 (d, 1H, H-C(1′)); 5.65 (m, 1H, H-C(2′), H-O(3′)); 4.95 (t, 1H, H-O(5′)); 4.75 (m, 2H, O*CH*$_2$CH$_2$)); 4.45–4.20 (m, 6H, H-C(3′),H-C(4′), 2 × OCH$_2$*CH*$_2$); 3.55 (m, 2H, H-C(5′, 5″)); 3.30 + 3.10 + 3.00 (3t, 6H, 3 × OCH$_2$*CH*$_2$). Anal. for $C_{36}H_{34}N_8O_{15}$ (817.7). Calcd: C 52.80, H 4.19, N 13.69. Found: C 52.82, H 4.31, N 13.58.

O^6-[2-(4-Nitrophenyl)ethyl]-N^2-[2-(4-nitrophenyl)ethoxycarbonyl]-9-{5-O-monomethoxytrityl-2-O-[2-(4-nitrophenyl)-ethoxycarbonyl]-α-D-arabinofuranosyl}guanine (64). Analogous to **41** with **63** (5.26 g, 6.4 mmol) in 20 h. Purification by FC with toluene/EtOAc 4:1 (600 mL) and toluene/EtOAc 1:1 (1 L) to give 6.28 g (90%) of a colorless foam. R_f: 0.88 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 204 (5.03), 236 (4.50), 268 (4.72). ^{1}H-NMR (DMSO-d_6): 10.4 (bs, 1H, NH); 8.35 (s, 1H, H-C(8)); 8.15 (m, 6H, *o* to NO_2); 7.65, 7.55 + 7.45 (3d, 6H, *m* to NO_2); 7.35–7.10 (m, 12H, trityl); 6.85 (d, 2H, *o* to OCH_3); 6.22 (d, 1H, H-C(1′)); 5.75 (m, 1H, H-C(2′)); 5.65 (t, 1H, H-O(3′)); 4.75 (m, 3H, H-C(3′), O*CH*$_2$CH$_2$); 4.4–4.2 (m, 5H, H-C(4′), 2 × O*CH*$_2$CH$_2$)); 3.72 (s, 3H, OCH_3); 3.25 (m, 4H, H-C(5′, 5″), OCH$_2$*CH*$_2$); 3.05 + 2.95 (2t, 4H, 2 × OCH$_2$*CH*$_2$). Anal. for

$C_{56}H_{50}N_8O_{16}$ (1091.1). Calcd: C 61.59, H 4.71, N 10.26. Found: C 61.52, H 4.71, N 9.91.

O^6-[2-(4-Nitrophenyl)ethyl]-N^2-[2-(4-nitrophenyl)ethoxycarbonyl]-9-{5-O-dimethoxytrityl-2-O-[2-(4-nitrophenyl)-ethoxycarbonyl]-α-D-arabinofuranosyl}guanine (65). Analogous to **45** with **63** (3.0 g, 3 mmol) and Dmtr-Cl (1.2 g, 3,6 mmol) in 20 h. Purification by FC with toluene/EtOAc 3:1 (500 mL), toluene/EtOAc 1:1 (500 mL), and toluene/EtOAc 1:1 + MeOH (10 mL) (500 mL) to give 2.96 g (88%) of a colorless solid. R_f: 0.48 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 204 (5.01), 237 (4.54), 269 (4.66). ^{1}H-NMR (DMSO-d_6): 10.4 (bs, 1H, NH); 8.35 (s, 1H, H-C(8)); 8.15 (m, 6H, *o* to NO_2); 7.65, 7.55 + 7.45 (3d, 6H, *m* to NO_2); 7.35–7.10 (m, 9H, trityl); 6.85 (d, 2H, *o* to OCH_3); 6.21 (d, 1H, H-C(1′)); 5.75 (m, 1H, H-C(2′)); 5.65 (t, 1H, H-O(3′)); 4.75 (m, 3H, H-C(3′), O*CH*$_2$CH$_2$); 4.4–4.2 (m, 5H, H-C(4′), 2 × O*CH*$_2$CH$_2$)); 3.72 (s, 6H, 2 × OCH_3); 3.25 (m, 4H, H-C(5′, 5″), OCH_2*CH*$_2$); 3.05 + 2.95 (2t, 4H, 2 × OCH_2*CH*$_2$). Anal. for $C_{57}H_{52}N_8O_{17}$ (1121.1). Calcd: C 61.07, H 4.67, N 9.99. Found: C 60.80, H 4.69, N 9.84.

General Procedure for the Synthesis of α-D-Arabinonucleoside-3′-phosphoramidites (A)

The protected nucleoside (1 mmol) was dissolved in CH_3CN (15 mL), then 1*H*-tetrazole (0.5 mmol) and *bis*-(N,N-diisopropylamino)-2-cyanoethoxyphosphane (1.5–2.0 mmol) added under N_2 or Ar atmosphere. The reaction mixture was stirred at room temperature for 8–24 h and then dilute with EtOAc (50 mL). It was washed subsequently with each 50 mL of saturated $NaHCO_3$ and NaCl solution. The organic phase was dried over Mg_2SO_4, evaporated, and the residue purified by FC using toluene/EtOAc mixtures for separation. In most cases the addition of small amounts of Et_3N was not necessary. The product containing fractions were evaporated, coevaporated with toluene and CH_2Cl_2 to give a colorless solid foam. The resulting colorless phosphoramidite was dried under high vacuum for 24 h before use in the DNA-synthesizer.

1-{5-O-Monomethoxytrityl-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-α-D-arabinofuranosyl}uracil-3′-(2-cyanoethyl,-N,N-diisopropyl)phosphoramidite (66). According to the general procedure A with **41** (0.72 g, 1 mmol), tetrazole (40 mg) and *bis*-(N,N-diisopropylamino)-2-cyanoethoxyphosphane (0.5 g). Purification by FC (2.5 × 8 cm, silica gel) with toluene/EtOAc 4:1 (500 mL) and toluene/EtOAc 3:1 (200 mL) to give 0.736 g (81%). R_f: 0.55 and 0.68 (toluene/EtOAc 1:2). UV (MeOH): 204 (4.99), 232 (4.35), 263 (4.29). ^{1}H-NMR ($CDCl_3$): 8.3 (bs, 1H, NH); 8.15 (d, 2H, *o* to NO_2); 7.5–7.1 (m, 15H, H-C(6), *m* to NO_2, trityl); 6.80 (d, 2H, *o* to OCH_3); 6.11 + 6.02

(2d, 1H, H-C(1′)); 5.25 (2d, 1H, H-C(5)); 5.30 + 5.15 (2pt, 1H, H-C(2′)); 4.6–4.3 (m, 4H, H-C(3′), H-C(4′), O*CH*$_2$CH$_2$); 3.80 (s, 3H, OCH$_3$); 3.7–3.4 (m, 4H, *H*C(CH$_3$)$_2$, O*CH*$_2$CH$_2$CN); 3.30 (m, 2H, H-C(5′, 5″)); 3.05 (t, 2H, OCH$_2$*CH*$_2$); 2.55 + 2.40 (2t, 2H, OCH$_2$*CH*$_2$); 1.15–1.0 (m, 12H, HC(*CH*$_3$)$_2$). ^{31}P-NMR (CDCl$_3$): 152.23/152.50. Anal. for $C_{47}H_{52}N_5O_{12}P$ (909.0). Calcd: C 62.04, H 5.76, N 7.69. Found: C 61.84, H 5.95, N 7.80.

1-{5-O-Monomethoxytrityl-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-α-D-arabinofuranosyl}thymine-3′-(2-cyanoethyl,-N,N-diisopropyl)phosphoramidite (67). According to the general procedure A with **42** (0.725 g, 1 mmol), tetrazole (40 mg), and *bis*-(N,N-diisopropylamino)-2-cyanoethoxyphosphane (0.5 g). Purification by FC (2.5 × 8 cm, silica gel) with toluene/EtOAc 5:1 (500 mL), toluene/EtOAc 4:1 (250 mL), and toluene/EtOAc 3:1 (200 mL) to give 0.84 g (91%). R_f: 0.50 and 0.61 (toluene/EtOAc 1:2). UV (MeOH): 203 (4.93), 230 (4.40), 266 (4.35). ^{1}H-NMR (CDCl$_3$): 8.5 (bs, 1H, NH); 8.15 (d, 2H, *o* to NO$_2$); 7.4–7.1 (m, 15H, H-C(6), *m* to NO$_2$, trityl); 6.80 (d, 2H, *o* to OCH$_3$); 6.10 + 6.05 (2d, 1H, H-C(1′)); 5.30 + 5.15 (2pt, 1H, H-C(2′)); 4.65–4.25 (m, 4H, H-C(3′), H-C(4′), O*CH*$_2$CH$_2$); 3.80 (s, 3H, OCH$_3$); 3.7–3.45 (m, 4H, *H*C(CH$_3$)$_2$, O*CH*$_2$CH$_2$CN); 3.20 (m, 2H, H-C(5′, 5″)); 3.11 (t, 2H, OCH$_2$*CH*$_2$); 2.55 + 2.40 (2t, 2H, OCH$_2$*CH*$_2$CN); 1.90 (bs, 3H, H$_3$C-C(5); 1.15–1.0 (m, 12H, HC(*CH*$_3$)$_2$). ^{31}P-NMR (CDCl$_3$): 152.53/152.70. Anal. for $C_{48}H_{54}N_5O_{12}P$ (924.0). Calcd: C 62.39, H 5.89, N 7.58. Found: C 62.00, H 6.04, N 7.66.

N^4-[2-(4-Nitrophenyl)ethoxycarbonyl]-1-{5-O-monomethoxytrityl-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-α-D-arabinofuranosyl}cytosine-3′-(2-cyanoethyl,-N,N-diisopropyl)phosphoramidite (68). According to the general procedure A with **43** (0.9 g, 1 mmol), tetrazole (40 mg) and *bis*-(N,N-diisopropylamino)-2-cyanoethoxyphosphane (0.75 g). Purification by FC (2.5 × 8 cm, silica gel) with toluene/EtOAc 4:1 (250 mL), toluene/EtOAc 3:1 (200 mL), toluene/EtOAc 2:1 (200 mL), and toluene/EtOAc 1:1 (200 mL) to give 1.0 g (91%). R_f: 0.21 and 0.38 (toluene/EtOAc 1:2). UV (MeOH): 204 (5.00), 234 (4.47), 273 (4.39). ^{1}H-NMR (CDCl$_3$): 8.15 (d, 4H, *o* to NO$_2$); 7.85 (m, 1H, H-C(6))); 7.55 (bs, 1H, NH); 7.5–7.15 (m, 17H, H-C(5), *m* to NO$_2$, trityl); 6.80 (d, 2H, *o* to OCH$_3$); 6.1 + 6.0 (2s, 1H, H-C(1′)); 5.4 + 5.2 (2bs, 1H, H-C(2′)); 4.6–4.3 (m, 6H, H-C(3′), H-C(4′), O*CH*$_2$CH$_2$); 3.80 (s, 3H, OCH$_3$); 3.65–3.20 (m, 6H, *H*C(CH$_3$)$_2$, O*CH*$_2$CH$_2$CN, H-C(5′, 5″)); 3.11 (t, 4H, OCH$_2$*CH*$_2$); 2.60 + 2.40 (2m, 2H, OCH$_2$*CH*$_2$CN); 1.15–1.0 (m, 12H, HC(*CH*$_3$)$_2$). ^{31}P-NMR (CDCl$_3$): 152.83/152.91. Anal. for $C_{48}H_{54}N_5O_{12}P$ (924.0). Calcd: C 62.39, H 5.89, N 7.58. Found: C 62.00, H 6.04, N 7.66.

N^6-[2-(4-Nitrophenyl)ethoxycarbonyl]-1-{5-O-monomethoxytrityl-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-α-D-arabinofuranosyl}adenine-3′-(2-cyanoethyl,-N,N-diisopropyl)phosphoramidite (69). Accordingto the general

procedure A with **44** (0.926 g, 1 mmol), tetrazole (40 mg) and *bis*-(N,N-diisopropylamino)-2-cyanoethoxyphosphane (0.7 g). Purification by FC (2.5 × 8 cm, silica gel) with toluene/EtOAc 4:1 (500 mL), toluene/EtOAc 2:1 (800 mL), and toluene/EtOAc 1:1 (200 mL) to give 0.96 g (85%). R_f: 0.30 and 0.42 (toluene/EtOAc 1:2). UV (MeOH): 205 (4.98), 232 (4.40), 266 (4.58). ^{1}H-NMR ($CDCl_3$): 8.75 (bs, 1H, NH); 8.3–8.05 (m, 6H, H-C(8), H-C(2), *o* to NO_2); 7.5–7.15 (m, 16H, *m* to NO_2, trityl); 6.80 (d, 2H, *o* to OCH_3); 6.35 (d, 1H, H-C(1′)); 5.75 + 5.65 (2pt, 1H, H-C(2′)); 4.75 (m, 1H, H-C(3′)); 4.55 (m, 3H, H-C(4′), O*CH*$_2$CH$_2$); 3.80 (s, 3H, OCH_3); 3.65–3.25 (m, 6H, *H*C(CH$_3$)$_2$, O*CH*$_2$CH$_2$CN, H-C(5′, 5″)); 3.15 + 3.05 (2m, 4H, OCH$_2$*CH*$_2$); 2.5 + 2.35 (2t, 2H, OCH$_2$*CH*$_2$CN); 1.15–0.9 (m, 12H, HC(*CH*$_3$)$_2$). ^{31}P-NMR ($CDCl_3$): 151.91/152.30. Anal. for $C_{57}H_{60}N_9O_{14}P$ (1126.3). Calcd: C 60.79, H 5.37, N 11.19. Found: C 60.58, H 5.43 N 11.08.

O^6-[2-(4-Nitrophenyl)ethyl]-N^2-[2-(4-nitrophenyl)ethoxycarbonyl]-9-{5-O-monomethoxytrityl-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-α-D-arabinofuranosyl}guanine-3′-(2-cyanoethyl,-N,N-diisopropyl)phosphoramidite (70). According to the general procedure A with **64** (1.1 g, 1 mmol), tetrazole (40 mg) and *bis*-(N,N-diisopropylamino)-2-cyanoethoxy-phosphane (0.6 g). Purification by FC (2.5 × 8 cm, silica gel) with toluene/EtOAc 6:1 (300 mL), toluene/EtOAc 4:1 (500 mL), and toluene/EtOAc 3:1 (200 mL) to give 1.05 g (81%). R_f: 0.57 and 0.63 (toluene/EtOAc 1:2). UV (MeOH): 205 (5.02), 235 (4.45), 268 (4.63). ^{1}H-NMR ($CDCl_3$): 8.2–8.05 (m, 7H, NH, *o* to NO_2); 7.5–7.15 (m, 18H, *m* to NO_2, trityl); 6.80 (d, 2H, *o* to OCH_3); 6.15 (pt, 1H, H-C(1′)); 5.7 + 5.6 (2pt, 1H, H-C(2′)); 4.70 (m, 3H, H-C(3′), O*CH*$_2$CH$_2$); 4.42 (m, 5H, H-C(4′), O*CH*$_2$CH$_2$); 3.75 (s, 3H, OCH_3); 3.45 (m, 4H, *H*C(CH$_3$)$_2$, O*CH*$_2$CH$_2$CN); 3.30 (2m, 4H, H-C(5′, 5″), OCH$_2$*CH*$_2$); 3.05 (m, 4H, OCH$_2$*CH*$_2$CN); 2.5 + 2.3 (2t, 2H, OCH$_2$*CH*$_2$CN); 1.15–0.9 (m, 12H, HC(*CH*$_3$)$_2$). ^{31}P-NMR ($CDCl_3$): 151.88/152.48. Anal. for $C_{65}H_{67}N_{10}O_{17}P$ (1291.2). Calcd: C 60.46, H 5.23, N 10.84. Found: C 60.67, H 5.44, N 11.51.

1-{5-O-Dimethoxytrityl-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-α-D-arabinofuranosyl}uracil-3′-(2-cyanoethyl,-N,N-diisopropyl)phosphoramidite (71). Analogous to **66** with **45** (0.75 g, 1 mmol), *bis*-(N,N-diisopropylamino)-2-cyanoethyl-phosphane (0.6 g), and tetrazole (40 mg). Purification by FC (2.5 × 9 cm, silica gel) with toluene/EtOAc 4:1 (300 mL), toluene/EtOAc 3:1 (400 mL), and toluene/EtOAc 1:1 (200 mL) to give 0.835 g (89%) of a colorless foam. R_f: 0.52 and 0.62 (toluene/EtOAc 1:1). UV (MeOH): 204 (4.93), 235 (4.46), 263 (4.37). ^{1}H-NMR ($CDCl_3$): 8.7 (bs, 1H, NH); 8.15 (d, 2H, *o* to NO_2); 7.55 (d, 1H, H-C(6)); 7.45–7.15 (m, 11H, 2H, *m* to NO_2, trityl); 6.80 (d, 4H, *o* to OCH_3); 6.11 + 6.02 (2d, 1H, H-C(1′)); 5.25 (2d, 1H, H-C(5)); 5.30 + 5.15 (2pt, 1H, H-C(2′)); 4.65–4.3 (m, 4H, H-C(3′), H-C(4′), O*CH*$_2$CH$_2$); 3.80 (s, 6H. OCH_3); 3.75–3.4

(m, 4H, *H*C(CH_3)$_2$, O*C*H_2CH_2CN); 3.30 (m, 2H, H-C(5′, 5″)); 3.05 (t, 2H, OCH_2*C*H_2); 2.55 + 2.40 (2t, 2H, OCH_2*C*H_2CN); 1.15-1.0 (m, 12H, HC(*C*H_3)$_2$). ^{31}P-NMR ($CDCl_3$): 152.02/152.42. Anal. for $C_{48}H_{54}N_5O_{13}P$ (940.0). Calcd: C 61.33, H 5.79, N 7.45. Found: C 61.56, H 5.90, N 7.21.

1-{5-O-Dimethoxytrityl-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-α-D-arabinofuranosyl}thymine-3′-(2-cyanoethyl,-N,N-diisopropyl)phosphoramidite (72). Analogous to **67** with **47** (0.76 g, 1 mmol), *bis*-(N,N-diisopropylamino)-2-cyanoethyl-phosphane (0.6 g) and tetrazole (40 mg). Purification by FC (2.5 × 9 cm, silica gel) with toluene/EtOAc 4:1 (300 mL), toluene/EtOAc 3:1 (300 mL), and toluene/EtOAc 1:1 (300 mL) to give 0.715 g (75%) of a colorless foam. R_f: 0.42 and 0.55 (toluene/EtOAc 1:1). UV (MeOH): 203 (4.90), 234 (4.41), 267 (4.33). ^{1}H-NMR ($CDCl_3$): 8.7 (bs, 1H, NH); 8.15 (d, 2H, *o* to NO_2); 7.45–7.15 (m, 12H, H-C(6), 2H, *m* to NO_2, trityl); 6.80 (d, 4H, *o* to OCH_3); 6.11 + 6.05 (2d, 1H, H-C(1′)); 5.30 + 5.15 (2pt, 1H, H-C(2′)); 4.65–4.25 (m, 4H, H-C(3′), H-C(4′), O*C*H_2CH_2); 3.80 (s, 6H, OCH_3); 3.70–3.45 (m, 4H, *H*C(CH_3)$_2$, O*C*H_2CH_2CN); 3.25 (m, 2H, H-C(5′, 5″)); 3.10 (t, 2H, OCH_2*C*H_2); 2.55 + 2.40 (2t, 2H, OCH_2*C*H_2CN); 1.90 (s, 3H, H_3C-C(5); 1.15–1.0 (m, 12H, HC(*C*H_3)$_2$). ^{31}P-NMR ($CDCl_3$): 152.16/152.51. Anal. for $C_{49}H_{56}N_5O_{13}P$ (954.0). Calcd: C 61.69, H 5.92, N 7.34. Found: C 61.68, H 6.00, N 7.04.

N^4-[2-(4-Nitrophenyl)ethoxycarbonyl]-1-{5-O-dimethoxytrityl-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-α-D-arabinofuranosyl}cytosine-3′-(2-cyanoethyl,-N,N-diisopropyl)phosphoramidite (73). Analogous to **68** with **47** (0.932 g, 1 mmol), *bis*-(N,N-diisopropylamino)-2-cyanoethyl-phosphane (0.6 g) and tetrazole (40 mg). Purification by FC (2.5 × 9 cm, silica gel) with toluene/EtOAc 3:1 (300 mL), toluene/EtOAc 2:1 (200 mL), toluene/EtOAc 3:2 (300 mL), and toluene/EtOAc 1:1 (300 mL) to give 0.82 g (73%) of a colorless foam. R_f: 0.2 and 0.31 (toluene/EtOAc 1:1). UV (MeOH): 203 (4.98), 236 (4.59), 273 (4.41). ^{1}H-NMR ($CDCl_3$): 8.15 (d, 2H, *o* to NO_2); 7.85 (m, 1H, H-C(6)); 7.45–7.15 (m, 15H, H-C(6), 4H, *m* to NO_2, trityl, NH); 6.80 (d, 4H, *o* to OCH_3); 6.11 + 6.05 (2d, 1H, H-C(1′)); 5.4 + 5.2 (2bs, 1H, H-C(2′)); 4.6–4.3 (m, 6H, H-C(3′), H-C(4′), O*C*H_2CH_2); 3.80 (s, 6H, OCH_3); 3.7–3.2 (m, 6H, *H*C(CH_3)$_2$, O*C*H_2CH_2CN, H-C(5′, 5″)); 3.10 (t, 4H, OCH_2*C*H_2); 2.6 + 2.4 (2m, 2H, OCH_2*C*H_2CN); 1.15–0.95 (m, 12H, HC(*C*H_3)$_2$). ^{31}P-NMR ($CDCl_3$): 151.88/152.90. Anal. for $C_{57}H_{62}N_7O_{16}P$ (1132.2). Calcd: C 60.47, H 5.52, N 8.66. Found: C 60.47, H 5.84, N 8.49.

N^6-[2-(4-Nitrophenyl)ethoxycarbonyl]-1-{5-O-dimethoxytrityl-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-α-D-arabinofuranosyl}adenine-3′-(2-cyanoethyl,-N,N-diisopropyl)phosphoramidite (74). Analogous to **69** with **48** (0.956 g, 1 mmol), *bis*-(N,N-diisopropylamino)-2-cyanoethyl-phosphane (0.6 g) and tetrazole (40 mg). Purification by FC (2.5 × 9 cm, silica gel) with

toluene/EtOAc 4:1 (300 mL), toluene/EtOAc 2:1 (300 mL), toluene/EtOAc 3:2 (300 mL), toluene/EtOAc 1:1 (300 mL), and toluene/EtOAc 1:2 (200 mL) to give 0.91 g (79%) of a colorless foam. R_f: 0.16 and 0.25 (toluene/EtOAc 1:1). UV (MeOH): 204 (5.01), 236 (4.49), 267 (4.60). ^{1}H-NMR ($CDCl_3$): 8.65 (s, 1H, H-C(8)); 8.2 (s, 1H, H-C(2)); 8.05 (d, 4H, *o* to NO_2); 7.4–7.05 (m, 13H, 4H, *m* to NO_2, trityl); 6.85 (d, 4H, *o* to OCH_3); 6.30 (m, 1H, H-C(1′)); 5.7 + 5.6 (2bs, 1H, H-C(2′)); 4.65 (m, 1H, H-C(3′)); 4.5 (m, 3H, H-C(4′), O*CH*$_2$$CH_2$); 4.30 (m, 2H, O*CH*$_2$$CH_2$); 3.70 (s, 6H, OCH_3); 3.65–3.2 (m, 6H, *H*C(CH_3)$_2$, O*CH*$_2$$CH_2$CN, H-C(5′, 5″)); 3.05 + 2.95 (2m, 4H, OCH_2*CH*$_2$); 2.4 + 2.25 (2t, 2H, OCH_2*CH*$_2$CN); 1.1–0.9 (m, 12H, HC(*CH*$_3$)$_2$). ^{31}P-NMR ($CDCl_3$): 151.88/152.26. Anal. for $C_{58}H_{62}N_9O_{15}P$ (1156.2). Calcd: C 60.25, H 5.40, N 10.90. Found: C 60.33, H 5.62, N 10.56.

O^6-[2-(4-Nitrophenyl)ethyl]-N^2-[2-(4-nitrophenyl)ethoxycarbonyl]-9-{5-O-dimethoxytrityl-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-α-D-arabinofuranosyl}guanine-3′-(2-cyanoethyl,-N,N-diisopropyl)phosphoramidite (75). Analogous to **70** with **65** (1.12 g, 1 mmol), *bis*-(N,N-diisopropylamino)-2-cyanoethyl-phosphane (0.6 g) and tetrazole (40 mg). Purification by FC (2.5 × 9 cm, silica gel) with toluene/EtOAc 6:1 (300 mL), toluene/EtOAc 5:1 (300 mL), toluene/EtOAc 4:1 (300 mL), and toluene/EtOAc 3:1 (300 mL) to give 0.95 g (72%) of a colorless foam. R_f: 0.46 and 0.57 (toluene/EtOAc 1:1). UV (MeOH): 203 (5.04), 236 (4.55), 269 (4.67). ^{1}H-NMR ($CDCl_3$): 8.2–8.05 (m, 7H, H-C(8), 6H, *o* to NO_2); 7.5–7.2 (m, 15H, 6H, *m* to NO_2, trityl); 6.85 (d, 4H, *o* to OCH_3); 6.15 (m, 1H, H-C(1′)); 5.7 + 5.6 (2bs, 1H, H-C(2′)); 4.70 (m, 3H, H-C(3′), O*CH*$_2$$CH_2$); 4.4 (m, 5H, H-C(4′), O*CH*$_2$$CH_2$); 3.75 (s, 6H, OCH_3); 3.50 (m, 4H, *H*C(CH_3)$_2$, O*CH*$_2$$CH_2$CN); 3.32 (m, 4H, H-C(5′, 5″), OCH_2*CH*$_2$); 3.05 (m, 4H, OCH_2*CH*$_2$); 2.5 + 2.3 (2t, 2H, OCH_2*CH*$_2$CN); 1.15–0.95 (m, 12H, HC(*CH*$_3$)$_2$). ^{31}P-NMR ($CDCl_3$): 151.81/152.44. Anal. for $C_{66}H_{67}N_{10}O_{18}P$ (1319.3). Calcd: C 60.09, H 5.12, N 10.62. Found: C 59.86, H 5.39, N 10.17.

General Procedure for the Synthesis of 3′-O-Succinoyl-α-D-arabinonucleosides (B)

The protected nucleoside (1 mmol) was dissolved in CH_2Cl_2 (4 mL), then succinic acid anhydride (0.2 g, 2 mmol) and 4-dimethylaminopyridine (0.16 g, 1.3 mmol) added and stirred at room temperature 2–4 h until all educt has disappeared. It was diluted with EtOAc (50 mL) and extracted with phosphate-buffer pH 4 (3 × 30 mL) and saturated NaCl solution (30 mL). The organic layer was dried over $MgSO_4$, evaporated, and coevaporated with CH_2Cl_2 to give a colorless solid foam pure enough for solid support derivatization.

1-{5-O-Monomethoxytrityl-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-3-O-succinoyl-α-D-arabinofuranosyl}uracil (76). According to the general procedure B with **41** (0.715 g) to give 0.81 g (98%) of **76**. R_f: 0.33 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 206 (4.88), 233 (4.35), 265 (4.32). ^{1}H-NMR ($CDCl_3$): 9.6 (bs, 1H, NH); 8.12 (d, 2H, *o* to NO_2); 7.45–7.15 (m, 15H, H-C(6), 2H, *m* to NO_2, trityl); 6.85 (d, 2H, *o* to OCH_3); 5.95 (d, 2H, H-C(1′)); 5.75 (d, 1H, H-C(5)); 5.30 (m, 2H, H-C(2′), H-C(3′)); 4.51 (m, 1H, H-C(4′)); 4.35 (m, 2H, O*CH*$_2$CH$_2$); 3.80 (s, 3H, OCH_3); 3.35 (m, 2H, H-C(5′, 5″)); 3.05 (t, 2H, OCH_2*CH*$_2$); 2.8–2.45 (m, 4H, *CH*$_2$*CH*$_2$). Anal. for $C_{42}H_{39}N_3O_{14} \times H_2O$ (827.8). Calcd: C 60.94, H 4.99, N 5.07. Found: C 60.74, H 5.03, N 4.78.

1-{5-O-Monomethoxytrityl-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-3-O-succinoyl-α-D-arabinofuranosyl}thymine (77). According to the general procedure B with **42** (0.725 g) to give 0.825 g (98%) of **77**. R_f: 0.26 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 204 (4.76), 232 (4.32), 266 (4.29). ^{1}H-NMR ($CDCl_3$): 9.7 (bs, 1H, NH); 8.15 (d, 2H, *o* to NO_2); 7.6–7.2 (m, 15H, H-C(6), 2H, *m* to NO_2, trityl); 6.85 (d, 2H, *o* to OCH_3); 6.10 (d, 1H, H-C(1′)); 5.40 (m, 2H, H-C(2′), H-C(3′)); 4.61 (m, 1H, H-C(4′)); 4.44 (m, 2H, O*CH*$_2$CH$_2$); 3.7 (s, 3H, OCH_3); 3.38 (m, 2H, H-C(5′, 5″)); 3.12 (t, 2H, OCH_2*CH*$_2$); 2.8–2.6 (m, 4H, *CH*$_2$*CH*$_2$); 1.95 (s, 3H, H_3C-C(5)). Anal. for $C_{43}H_{41}N_3O_{14} \times H_2O$ (841.8). Calcd: C 61.35, H 5.15, N 4.99. Found: C 61.64, H 5.27, N 4.55.

N^4-[2-(4-Nitrophenyl)ethoxycarbonyl]-1-{5-O-monomethoxytrityl-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-3-O-succinoyl-α-D-arabinofuranosyl}cytosine (78). According to the general procedure B with **43** (0.9 g) to give 0.97 g (97%) of **78**. R_f: 0.29 (toluene/EtOAc/MeOH 1:1:1). UV (MeOH): 204 (4.90), 236 (4.49), 273 (4.39). ^{1}H-NMR ($CDCl_3$): 8.12 (m, 4H, *o* to NO_2); 7.75 (d, 1H, H-C(6)); 7.45–7.15 (m, 17H, H-C(5), 4H, *m* to NO_2, trityl); 6.85 (d, 2H, *o* to OCH_3); 5.95 (d, 1H, H-C(1′)); 5.40 (m, 2H, H-C(2′), H-C(3′)); 4.55 (m, 1H, H-C(4′)); 4.35 (m, 4H, O*CH*$_2$CH$_2$); 3.75 (s, 3H, OCH_3); 3.35 (m, 2H, H-C(5′, 5″)); 3.05 (m, 4H, OCH_2*CH*$_2$); 2.55 (m, 4H, *CH*$_2$*CH*$_2$). Anal. for $C_{51}H_{47}N_5O_{17}$ (1002.0). Calcd: C 61.14, H 4.73, N 6.99. Found: C 61.08, H 4.84, N 6.69.

N^6-[2-(4-Nitrophenyl)ethoxycarbonyl]-9-{5-O-monomethoxytrityl-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-3-O-succinoyl-α-D-arabinofuranosyl}adenine (79). According to the general procedure B with **44** (0.925 g) to give 1.0 g (98%) of **79**. R_f: 0.26 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 204 (4.85), 235 (sh 4.29), 266 (4.55). ^{1}H-NMR ($CDCl_3$): 8.7 (s, 1H, H-C(8)); 8.25 (s, 1H, H-C(2)); 8.12 (m, 4H, *o* to NO_2); 7.5–7.15 (m, 16H, 4H, *m* to NO_2, trityl); 6.82 (d, 2H, *o* to OCH_3); 6.45 (d, 1H, H-C(1′)); 5.85 (m, 1H, H-C(2′)); 5.50 (m, 1H, H-C(3′)); 4.58 (m, 1H, H-C(4′)); 4.5 + 4.35 (m, 4H, 2 ×

O*CH*$_2$CH$_2$); 3.8 (s, 3H, OCH$_3$); 3.4 (m, 2H, H-C(5′, 5″)); 3.15 + 3.05 (m, 4H, 2 × OCH$_2$*CH*$_2$); 2.65 + 2.55 (2m, 4H, *CH*$_2$*CH*$_2$). Anal. for $C_{52}H_{47}N_7O_{16}$ (1027.0). Calcd: C 60.82, H 4.71, N 9.55. Found: C 60.40, H 5.17, N 9.25.

O^6-[2-(4-Nitrophenyl)ethyl]-N^2-[2-(4-nitrophenyl)ethoxycarbonyl]-9-{5-O-monomethoxytrityl-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-3-O-succinoyl-α-D-arabinofuranosyl}guanine (80). According to the general procedure B with **64** (1.09 g) to give 1.17 g (98%) of **80**. R$_f$: 0.55 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 204 (4.85), 213 (sh 4.73), 268 (4.56). ^{1}H-NMR (CDCl$_3$): 8.15 (m, 6H, *o* to NO$_2$); 7.7 (s, 1H, H-C(8)); 7.5–7.15 (m, 18H, 6H, *m* to NO$_2$, trityl); 6.82 (d, 2H, *o* to OCH$_3$); 6.2 (d, 1H, H-C(1′)); 5.85 (m, 1H, H-C(2′)); 5.55 (m, 1H, H-C(3′)); 4.75 (m, 2H, O*CH*$_2$CH$_2$); 4.58 (m, 1H, H-C(4′)); 4.5 + 4.3 (m, 4H, 2 × O*CH*$_2$CH$_2$); 3.75 (s, 3H, OCH$_3$); 3.45–3.2 (m, 4H, H-C(5′, 5″), OCH$_2$*CH*$_2$); 3.05 (m, 4H, 2 × OCH$_2$*CH*$_2$); 2.65 (m, 4H, *CH*$_2$*CH*$_2$). Anal. for $C_{60}H_{54}N_8O_{19}$ ×2 H$_2$O (1191.1). Calcd: C 58.72, H 4.76, N 9.13. Found: C 58.76, H 4.83, N 8.87.

1-{5-O-Dimethoxytrityl-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-3-O-succinoyl-α-D-arabinofuranosyl}uracil (81). According to the general procedure B with **45** (0.75 g) to give 0.775 g (92%) of **76**. R$_f$: 0.36 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 203 (4.84), 235 (4.43), 263 (4.33). ^{1}H-NMR (CDCl$_3$): 9.75 (bs, 1H, NH); 8.12 (d, 2H, *o* to NO$_2$); 7.45 (m, 3H, H-C(6), 2H, *m* to NO$_2$); 7.35–7.15 (m, 9H, trityl); 6.85 (d, 4H, *o* to OCH$_3$); 6.00 (d, 1H, H-C(1′)); 5.75 (d, 1H, H-C(5)); 5.35 (m, 2H, H-C(2′), H-C(3′)); 4.51 (m, 1H, H-C(4′)); 4.35 (m, 2H, O*CH*$_2$CH$_2$); 3.75 (s, 6H, 2 × OCH$_3$); 3.35 (m, 2H, H-C(5′, 5″)); 3.05 (t, 2H, OCH$_2$*CH*$_2$); 2.65 + 2.55 (m, 4H, *CH*$_2$*CH*$_2$). Anal. for $C_{43}H_{41}N_3O_{15}$ (839.8). Calcd: C 61.42, H 5.03, N 4.99. Found: C 61.59, H 5.20, N 5.03.

1-{5-O-Dimethoxytrityl-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-3-O-succinoyl-α-D-arabinofuranosyl}thymine (82). According to the general procedure B with **46** (0.75 g) to give 0.8 g (93%) of **77**. R$_f$: 0.28 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 203 (4.86), 235 (4.43), 263 (4.33). ^{1}H-NMR (CDCl$_3$): 9.6 (bs, 1H, NH); 8.1 (d, 2H, *o* to NO$_2$); 7.45 (d, 2H, *m* to NO$_2$); 7.35–7.15 (m, 10H, H-C(6), trityl); 6.85 (dd, 4H, *o* to OCH$_3$); 6.03 (d, 1H, H-C(1′)); 5.4 + 5.35 (2pt, 2H, H-C(2′), H-C(3′)); 4.50 (m, 1H, H-C(4′)); 4.35 (m, 2H, O*CH*$_2$CH$_2$); 3.75 (s, 6H, 2 × OCH$_3$); 3.35 (m, 2H, H-C(5′, 5″)); 3.05 (t, 2H, OCH$_2$*CH*$_2$); 2.65 + 2.55 (2m, 4H, *CH*$_2$*CH*$_2$); 1.91 (s, 3H, H$_3$C-C(5)). Anal. for $C_{44}H_{43}N_3O_{11}$ (853.8). Calcd: C 61.80, H 5.18, N 4.91. Found: C 61.89, H 5.31, N 4.66.

N^4-[2-(4-Nitrophenyl)ethoxycarbonyl]-1-{5-O-dimethoxytrityl-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-3-O-succinoyl-α-D-arabinofuranosyl}cytosine (83). According to the general procedure B with **47** (0.95 g) to give 0.95 g

(92%) of **83**. R_f: 0.31 (toluene/EtOAc/MeOH 1:1:1). UV (MeOH): 203 (4.94), 237 (4.58), 273 (4.38). ^{1}H-NMR ($CDCl_3$): 8.15 (m, 4H, *o* to NO_2); 7.75 (d, 1H, H-C(6)); 7.45–7.15 (m, 14H, 4H, *m* to NO_2, trityl); 6.85 (d, 4H, *o* to OCH_3); 5.95 (d, 1H, H-C(1′)); 5.40 (m, 1H, H-C(2′), H-C(3′)); 4.55 (m, 1H, H-C(4′)); 4.35 (m, 4H, O*CH*$_2$CH$_2$); 3.75 (s, 6H, 2 × OCH_3); 3.35 (m, 2H, H-C(5′, 5″)); 3.05 (m, 4H, OCH_2*CH*$_2$); 2.55 (m, 4H, *CH*$_2$*CH*$_2$). Anal. for $C_{52}H_{49}N_5O_{18}$ (1032.0). Calcd: C 60.52, H 4.88, N 6.78. Found: C 60.81, H 5.15, N 6.31.

N^6-[2-(4-Nitrophenyl)ethoxycarbonyl]-9-{5-O-dimethoxytrityl-2-O-[2-(4-nitrophenyl)ethoxycarbonyl]-3-O-succinoyl-α-D-arabinofuranosyl}adenine (84). According to the general procedure B with **48** (0.975 g) to give 0.95 g (90%) of **84**. R_f: 0.29 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 204 (4.98), 237 (4.48), 267 (4.60). ^{1}H-NMR ($CDCl_3$): 8.7 (s, 1H, H-C(8)); 8.25 (s, 1H, H-C(2)); 8.12 (m, 4H, *o* to NO_2); 7.5–7.15 (m, 13H, 4H, *m* to NO_2, trityl); 6.82 (d, 4H, *o* to OCH_3); 6.35 (d, 1H, H-C(1′)); 5.75 (m, 1H, H-C(2′)); 5.50 (m, 1H, H-C(3′)); 4.6 (m, 1H, H-C(4′)); 4.45 + 4.35 (m, 4H, 2 × O*CH*$_2$CH$_2$); 3.8 (s, 6H. OCH_3); 3.4 (m, 2H, H-C(5′, 5″)); 3.15 + 3.05 (m, 4H, 2 × OCH_2*CH*$_2$); 2.65 + 2.55 (bs, 4H, *CH*$_2$*CH*$_2$). Anal. for $C_{53}H_{49}N_7O_{17}$ (1056.0). Calcd: C 60.28, H 4.68, N 9.27. Found: C 60.30, H 4.99, N 8.72.

O^6-[2-(4-Nitrophenyl)ethyl]-N^2-[2-(4-nitrophenyl)ethoxycarbonyl]-9-{5-O-dimethoxytrityl-2-O-[2-(4-nitrophenyl)-ethoxycarbonyl]-3-O-succinoyl-α-D-arabinofuranosyl}guanine (85). According to the general procedure B with **65** (1.125 g) to give 1.14 g (93%) of **85**. R_f: 0.59 (toluene/EtOAc/MeOH 5:4:1). UV (MeOH): 203 (5.02), 236 (sh 4.53), 269 (4.63). ^{1}H-NMR ($CDCl_3$): 8.15 (m, 6H, *o* to NO_2); 7.8 (s, 1H, H-C(8)); 7.5–7.15 (m, 15H, 6H, *m* to NO_2, trityl); 6.82 (d, 4H, *o* to OCH_3); 6.2 (d, 1H, H-C(1′)); 5.95 (m, 1H, H-C(2′)); 5.55 (m, 1H, H-C(3′)); 4.82 (m, 2H, O*CH*$_2$CH$_2$); 4.58 (m, 1H, H-C(4′)); 4.5 + 4.3 (m, 4H, 2 × O*CH*$_2$CH$_2$); 3.75 (s, 6H, OCH_3); 3.45–3.2 (m, 4H, H-C(5′, 5″), OCH_2*CH*$_2$); 3.05 (m, 4H, 2 × OCH_2*CH*$_2$); 2.65 (bs, 4H, *CH*$_2$*CH*$_2$). Anal. for $C_{61}H_{56}N_8O_{20}$ × H_2O (1238.2). Calcd: C 59.17, H 4.64, N 9.05. Found: C 59.17, H 4.87, N 8.28.

Amino-derivatization of Glyceryl-CPG-500 Å Material

Under N_2-atmosphere 1,1′-carbonyldiimidazole (2.0 g) was dissolved in a two-necked flask in abs. CH_2Cl_2 (80 mL) by shaking (no stirrer). Then Bioran Glyceryl-CPG (2.0 g), dried in high vacuum, was added and the mixture shaken slowly mechanically for 2–5 h. It was decanted from the solid under N_2-atmosphere, CH_2Cl_2 (30 mL) added and this washing process repeated two more times. The activated solid-support material was suspended in CH_2Cl_2 (80 mL), 1,6-N,N′-dimethylhexane-diamine (2 mL)

added and then the mixture shaken again 6 h. The modified solid-support was collected, washed with 80 mL each of DMF, H_2O, MeOH, acetone, and ether and dried in high vacuum at 40°C for 2 h.

Loading and Capping of LCMAA-CPG-500 Å Solid Support Material

To the amino-protected solid support (100 mg) in a 10-mL flask was added subsequently 3′-O-succinoyl-nucleoside (6 μmol), N-methylmorpholine (5 mL, 45 μmol), CH_3CN (3 mL), and O-[cyano-(ethoxycarbonyl)methylidene)amino-1,1,3,3-tetramethyl]uronium tetrafluoroborate (TOTU) (6 mg, 18 μmol) and gently shaken mechanically for 3–4 h. The solid was collected, washed with 15 mL each of DMF, MeOH, acetone and ether and dried at room temperature in high vacuum. Capping of free hydroxy- and amino-groups was achieved by treatment with acetic anhydride (0.75 mL) and 4-dimethylaminopyridine (25 mg) in abs. pyridine (2 mL) for 30 min. The solid was collected and washed by the same procedure described before.

Automated Oligonucleotide Synthesis

The normal automated cycle in the DNA-synthesizer was only slightly modified for the built up of oligo-α-arabinonucleotides in 1 μmol scale. Detritylation was done with 3% trichloroacetic acid in CH_2Cl_2 (5 × 10 s), washing with CH_3CN (40 s), condensation with 0.1 M phosphoramidite/0.5 M tetrazole (600 s) in CH_3CN, capping: Ac_2O/2,6-lutidine/THF 1:1:8 and N-methylimidazole/THF 16:84 (10 s), waiting: 5 s, oxidation: 0.05 M iodine in THF/H_2O/pyridine 7:2:1 (10 s), waiting 15 s, and followed by washing with CH_3CN (30 s). The deprotection of the blocking groups was achieved with 0.5–1 M DBU-solution in CH_3CN at room temperature for 10–12 h. After washing with CH_3CN was treated with conc. aqueous ammonia for 30 min. The reaction solution was evaporated in a Speed-Vac concentrator to give a colorless solid of the appropriate oligonucleotide.

REFERENCES

1. Münch, U; Pfleiderer, W. Oligoribonucleotide synthesis with the (2-cyano-1-phenylethoxy)carbonyl (2c1peoc) group for the 5′-hydroxy protection. Helv. Chim. Acta **2003**, 86, 2546–2565.
2. Lee, W.W.; Benitz, A.; Goodman, L.; Baker, B.R. Potential anticancer agents. XL. Synthesis of the β-anomer of 9-(D-arabinofuranosyl)adenine. J. Am. Chem. Soc. **1960**, 82, 2648–2649.
3. Creasey, W.A. Arabinosylcytosine in "Antineoplastic and immunosuppressive agents." Part II. Handbook of Exper. Pharmacology. Sartorelli, A.C., Johns, D.G., Eds.; Springer Verlag: Berlin, 1975; 232–256.
4. Perigaud, C.; Gosselin, G.; Imbach, J.-L. Nucleoside analogues as chemotherapeutic agents: A review. Nucleosides and Nucleotides, **1992**, 11, 903–943.

5. Furth, J.J.; Cohen, S.S. Inhibition of mammalian DNA polymerase by the 5′-triphosphate of 1-β-D-arabinofuranosylcytosine and the 5′-triphosphate of 9-β-D-arabinofuranosyladenine. Cancer Res. **1968**, 28, 2061–2067.
6. Bergmann, W.; Burke, D.C. Contributions to the study of marine products. XXXIX. The nucleosides of sponges. III. Spongothymidine and spongouridine. J. Org. Chem. **1955**, 20, 1501–1507. Angew. Chem. **1955**, 67, 127.
7. Niedballa, U.; Vorbrüggen, H. A general synthesis of N-glycosides. I. Synthesis of pyrimidine nucleosides. J. Org. Chem. **1974**, 39, 3654–3663.
8. Niedballa, U.; Vorbrüggen, H. A general synthesis of N-glycosides. III. A simple synthesis of pyrimidine disaccharide nucleosides. J. Org. Chem. **1974**, 39, 3664–3671.
9. Vorbrüggen, H.; Krolikiewicz, K. Neue Katalysatoren für die Nucleosid-Synthese. Angew. Chem. **1975**, 87, 417.
10. Vorbrüggen, H.; Höfle, G. On the mechanism of nucleoside synthesis. Chem. Ber. **1981**, 114, 1256–1268.
11. Wright, R.S.; Khorana, H.G. Phosphorylated sugars. V. Syntheses of arabinofuranose and arabinopyranose 1-phosphates. J. Am. Chem. Soc. **1958**, 80, 1994–1998.
12. Kam, B.; Barascut, L.; Imbach, J.L. A general method of synthesis and isolation, and an N.M.R.-spectroscopic study, of tetra-o-acetyl-D-aldopentofuranoses. Carbohydr. Res. **1979**, 69, 135–142.
13. Tolman, R.L.; Baker, D.A. 1-O-Acetyl-2,3,5-tri-O-benzoyl-D-arabinofuranose and its use in glycosylation by fusion. Methods of Carbohydr. Chem. **1978**, 7, 59–62.
14. Korbukh, I.A.; Abramova, L.N.; Preobrazhenskaya, M.N. Anomers of 1-O-acetyl-2,3,5-tri-O-benzoyl-D-arabinose. Nucleic Acid Chem. **1978**, 1, 151–153.
15. Nishimura, T.; Shimizu, B. Studies on synthetic nucleosides. V. Anomeric pyrimidine nucleosides of D-arabinose and D-lyxose. Chem. Pharm. Bull. **1965**, 13, 803–810.
16. Revankar, G.R.; Huffman, J.H.; Allen, L.B.; Sidwell, R.W.; Robins, R.K.; Tolman, R.L. Synthesis and antiviral activity of certain 5′-monophosphates of 9-D-arabinofuranosyladenine and 9-D-arabinofuranosylhypoxanthine. J. Med. Chem. **1975**, 7, 721–726.
17. Zou, R.; Robins, M.J. High-yield regioselective synthesis of 9-glycosyl guanine nucloeosides and analogues via coupling with 2-N-acetyl-6-O-diphenylcarbamoyl-guanine. Can. J. Chem. **1987**, 65, 1436–1437.
18. Montgomery J.A.; Thomas, H.J. Arabinonucleosides. J. Heterocycl. Chem. **1979**, 16, 353–357.
19. Himmelsbach, F.; Schulz, B.S.; Trichtinger, T.; Charubala, R.; Pfleiderer, W. The p-nitrophenyl (NPE) Group. A versatile new blocking group for phosphate and aglycone protection in nucleosides and nucleotides. Tetrahedron **1984**, 40, 59–72.
20. Lang, H.; Gottlieb, M.; Schwarz, M.; Farkas, S.; Schulz, B.S.; Himmelsbach, F.; Charubala, R.; Pfleiderer, W. New 2-(4-nitrophenyl)ethyl (Npe)- and 2-(4-nitro-phenyl)ethoxycarbonyl (Npeoc)-protected 2′-deoxyribonucleosides and their 3′-phosphoramidites—Versatile building blocks for oligonucleotide synthesis. Helv. Chim. Acta **1999**, 82, 2172–2185.
21. Resmini, M.; Pfleiderer, W. Synthesis of arabinonucleoside phosphoramidite building blocks. Helv. Chim. Acta **1993**, 76, 158–167.
22. Resmini, M.; Pfleiderer, W. Efficient synthesis of arabinoguanosine building blocks. Helv. Chim. Acta **1994**, 77, 429–434.
23. Markiewicz, W.T. Tetraisopropyldisiloxane-1,3-diyl, a group of simultanous protection of the 3′- and 5′-hydroxy functions in nucleosides. J. Chem. Res. **1979**, 24–25.
24. Schirmeister, H.; Himmelsbach, F.; Pfleiderer, W. The 2-(4-nitrophenyl)ethoxycarbonyl (npeoc) and 2-(2,4-dinitrophenyl)ethoxycarbonyl (dnpeoc) group for protection of hydroxy functions in ribonucleosides and their 2′-deoxyribonucleosides. Helv. Chim. Acta **1993**, 76, 385–401.
25. Albert, A.; Serjeant, E.P. *The Determination of Ionization Constants*; Chapman and Hall, Ltd.: London, 1962; 44.
26. Visser, G.M.; van Westrenen, J.; van Boeckel, C.C.A.; van Boom, J.H. Synthesis of the mirror image of the RNA fragment D-CAAGG: A model compound to study interactions between oligonucleotides of opposite handedness. Recl. Trav. Chim. Pays-Bas **1986**, 105, 528–537.
27. Pfleiderer, W.; Matysiak, S.; Bergmann, F.; Schnell, R. Recent progress in oligonucleotide synthesis. Acta Biochim. Polon. **1996**, 43, 37–44.
28. Walcher, G.; Pfleiderer, W. Synthesis of 2′-amino-2′-deoxyarabinonucleoside phosphoramidite building blocks. Helv. Chim. Acta **1996**, 79, 1067–1074.

29. Stengele, K.-P.; Pfleiderer, W. Improved synthesis of oligodeoxyribonucleotides. Tetrahedron Lett. **1990**, 31, 2549–2552.
30. Stengele, K.-P.; Pfleiderer, W. Improved synthesis of oligodeoxyribonucleotides. Nucleic Acids Res., Symp. Ser. **1989**, 21, 101–102.
31. Morvan, F.; Rayner, B.; Imbach, J.-L.; Chang, D.D.-K.; Lown, J.W. α-DNA. III. Characterization by high field ^{1}H-NMR, anti-parallel self-recognition and conformation of the unnatural hexadeoxyribonucleotides α-[d(CpApTpGpCpG)] and α-[d(CpGpCpApTpG)]. α-Oligodeoxynucleotides as potential cellular probes for gene control. Nucleic Acids Res. **1987**, 15, 4241–4255.
32. Sun, J.; Asseline U.; Rouzaud, D.; Montenay-Garestier, T.; Thuong, N.T.; Helene, C. Oligo-[α]-deoxynucleotides covalently linked to an intercalating agent. Double helices with parallel strands are formed with complementary oligo-[β]-deoxynucleotides. Nucleic Acids Res. **1987**, 15, 6149–6158.
33. Morvan, F.; Rayner, B.; Imbach, J.-L.; Lee, M.; Hartley, J.A.; Chang, D.-K.; Lown, J.W. α-DNA. V. Parallel annealing, handedness and conformation of the duplex of the unnatural α-hexadeoxyribonucleotide α-[d(CpApTpGpCpG)] with its β-complement β-[d(GpTpApCpGpC)] deduced from high field ^{1}H-NMR. Nucleic Acids Res. **1987**, 15, 7027–7044.
34. Seela, F.; Amberg, S.; Melenewski, A.; Rosemeyer, H. 5-Aza-7-deazaguanine DNA: Recognition and strand orientation of oligonucleotides incorporating anomeric imidazo[1,2-*a*]-1,3,5-triazine nucleosides. Helv. Chim. Acta **2001**, 84, 1996–2014.