9. Nucleotides

Part XXXIX[1])

Synthesis of Arabinonucleoside Phosphoramidite Building Blocks

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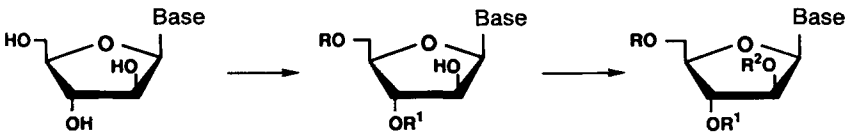
High-yield chemical syntheses of phosphoramidite building blocks of the four arabinonucleosides aUrd (**1**), aCyd (**2**), aAdo (**3**), and aGuo (**4**), suitable for (3′–5′)oligoarabinonucleotide synthesis are described. The problem of 2′-hydroxy group protection was solved by introduction of the versatile 2-(4-nitrophenyl)ethoxycarbonyl (npeoc) residue, which was also used for aglycon protection.

1. Introduction. – Arabinonucleosides and -nucleotides, especially 9-(β-D-arabinofuranosyl)adenine (aAdo) and 1-(β-D-arabinofuranosyl)cytosine (aCyd), are well known as antiviral and antitumor agents [2]. To increase these effects, short chains of arabinonucleic acids may be of interest. Furthermore, in recent years the biological activity of synthetic oligonucleotides as inhibitors of gene expression ('antisense' oligonucleotides) has become more and more evident. But apart from a sufficient hybridization to the sense strand, the two main problems are the poor penetration ability through membranes and the rapid enzymatic digestion of antisense oligonucleotides [3]. From this point of view, oligoarabinonucleotides may have advantageous and interesting properties.

Therefore, we wish to report in this paper a straightforward synthetic strategy to obtain suitably protected arabinonucleoside phosphoramidite building blocks (derived from the corresponding nucleosides **1**–**4**) for rapid and high-yield syntheses of (3′–5′)-linked oligomers. A fundamental question in this respect is the adequate choice of compatible blocking groups. In recent years, some short oligomers of aAdo and aUrd were prepared *via* the phosphotriester [4] [5] and phosphoramidite [6] approach using various combinations of protecting groups. The excellent results with the 2-(4-nitrophenyl)ethyl (npe) and 2-(4-nitrophenyl)ethoxycarbonyl (npeoc) blocking groups in oligodeoxynucleotide synthesis, demonstrated in conjunction with a stable new solid-support material [7], prompted us to extend this concept of β-eliminating protecting groups to arabinonucleotides.

2. Syntheses. – A fundamental requirement for a successful synthesis of oligonucleotides is a defined and selective reaction sequence for the preparation of appropriately protected monomeric building blocks. Starting from the unprotected nucleosides 1-(β-D-arabinofuranosyl)uracil (**1**) and 1-(β-D-arabinofuranosyl)cytosine (**2**; see *Scheme*), a

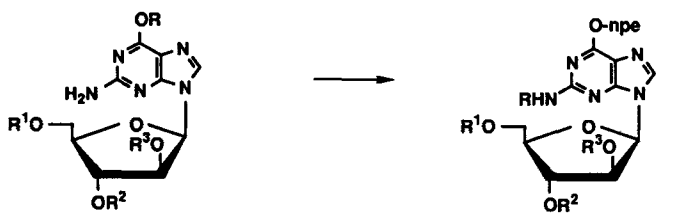
[1]) Part XXXVIII: [1].



	Base
1	Ura
2	Cyt
3	Ade
4	Gua

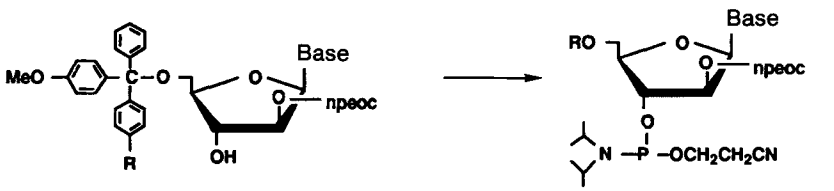
	Base	R	R^1
5	**Ura**	tds	tds
6	**Ura**	tds	H
7	**Cyt**	tds	tds
8	**Cyt**	tds	H
9	**Ade**	tipds	

	Base	R	R^1	R^2
10	**Ura**	tds	tds	npeoc
11	**Cyt**^{npeoc}	tds	tds	npeoc
12	**Ade**^{npeoc}	tipds		npeoc
13	**Cyt**^{npeoc}	tds	tds	H
14	**Ura**	H	H	npeoc
15	**Cyt**^{npeoc}	H	H	npeoc
16	**Ade**^{npeoc}	H	H	npeoc



	R	R^1	R^2	R^3
17	H	ac	ac	ac
18	npe	ac	ac	ac
19	npe	H	H	H
20	npe	tipds		H

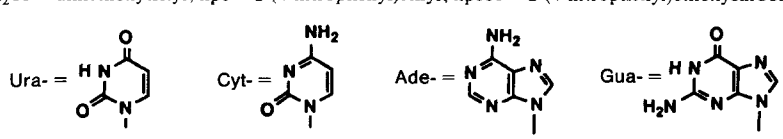
	R	R^1	R^2	R^3
21	H	tipds		npeoc
22	npeoc	tipds		H
23	npeoc	tipds		npeoc
24	npeoc	H	H	npeoc



	Base	R
25	**Ura**	H
26	**Cyt**^{npeoc}	H
27	**Ade**^{npeoc}	H
28	**Gua**$^{npe}_{npeoc}$	H
29	**Ura**	MeO
30	**Cyt**^{npeoc}	MeO
31	**Ade**^{npeoc}	MeO
32	**Gua**$^{npe}_{npeoc}$	MeO

	Base	R
33	**Ura**	MeOTr
34	**Cyt**^{npeoc}	MeOTr
35	**Ade**^{npeoc}	MeOTr
36	**Gua**$^{npe}_{npeoc}$	MeOTr
37	**Ura**	$(MeO)_2Tr$
38	**Cyt**^{npeoc}	$(MeO)_2Tr$
39	**Ade**^{npeoc}	$(MeO)_2Tr$
40	**Gua**$^{npe}_{npeoc}$	$(MeO)_2Tr$

ac = acetyl; tds = thexyldimethylsilyl; tipds = tetraisopropyldisiloxane-1,3-diyl; MeOTr = monomethoxytrityl; $(MeO)_2Tr$ = dimethoxytrityl; npe = 2-(4-nitrophenyl)ethyl; npeoc = 2-(4-nitrophenyl)ethoxycarbonyl



selective blocking of the 3′-OH and 5′-OH functions was achieved by reaction with thexyldimethylsilyl chloride [8] in presence of 3-methylpyridine *N*-oxide as base and $AgNO_3$ in THF following an analogous procedure described by *Ogilvie et al.* for (*tert*-butyl)dimethylsilyl chloride [9]. Apart from the desired products **5** and **7**, which were obtained in 87 and 83% yield, respectively, a small amount of the corresponding 5′-monosilylated compounds **6** and **8** were also isolated. In the case of purine arabinosides, this protection procedure showed much less selectivity, therefore, **9** [10] [11] was synthesized by action of 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxan (*Markiewicz*'s reagent) [12] in pyridine on 1-(β-D-arabinofuranosyl)adenine (**3**).

The subsequent introduction of the 2-(4-nitrophenyl)ethoxycarbonyl (npeoc) residues worked best with 1-methyl-3-[2-(4-nitrophenyl)ethoxycarbonyl]imidazolium chloride [13] as acylating agent. In CH_2Cl_2 solution with addition of 4-(dimethylamino)pyridine as activator, the 2′-*O*-unsubstituted components **5**, **7**, and **9** were converted into the totally protected nucleosides **10**, **11**, and **12**, respectively. By this reaction, both the amino group of the aglycon moiety as well as the 2′-OH group of the aCyd and aAdo derivatives **7** and **9**, respectively, were blocked in the same step. Reaction of **7** with 2-(4-nitrophenyl)ethyl chloroformate [13] in pyridine gave, with high selectivity, a product bearing only one npeoc group. It was identified as 1-[3′,5′-bis-*O*-(thexyldimethylsilyl)-β-D-arabinofuranosyl]-N^4-[2-(4-nitrophenyl)ethoxycarbonyl]cytosine (**13**).

Cleavage of the silyl groups of **10**–**12** with fluoride ions ($(Bu_4N)F$)-deactivated by AcOH – in THF solution afforded, without harming the npeoc groups, **14**, **15**, and **16**, respectively, in yields of 87–92% as crystalline products.

In the case of 9-(β-D-arabinofuranosyl)guanine (**4**), an additional protection of the amide function of the guanine moiety is highly desirable. Acylation of **4** with Ac_2O in pyridine/*N*,*N*-dimethylformamide gave **17** [14] in 94% yield. O^6-Alkylation under *Mitsunobu*'s conditions [13] with diethyl azodicarboxylate, triphenylphosphane, and 2-(4-nitrophenyl)ethanol followed by deacetylation of the intermediate **18** with NH_3 in MeOH/dioxan/H_2O led to 9-{O^6-[2-(4-nitrophenyl)ethyl]-β-D-arabinofuranosyl}guanine (**19**), which was protected at the 3′- and 5′-OH group with *Markiewicz*'s reagent giving **20** in high yield. The anticipated simultaneous protection of the aglycon amino and the 2′-OH function with the 2-(4-nitrophenyl)ethoxycarbonyl residue could not be achieved in this case. Instead, **21** was obtained as the only product using 1-methyl-3-[2-(4-nitrophenyl)ethoxycarbonyl]imidazolium chloride as acylating agent. On the other hand, a selective blocking of the amino function could be observed, when **20** was reacted with 2-(4-nitrophenyl)ethyl chloroformate in pyridine (→ **22**). The fully protected nucleoside **23** finally was obtained by subsequent application of both acylating procedures. Desilylation with deactivated fluoride ions led to the partially blocked N^2-[2-(4-nitrophenyl)ethoxy-carbonyl]-9-{2′-*O*-[2-(4-nitrophenyl)ethoxycarbonyl]-β-D-arabinofuranosyl}-O^6-[2-(4-nitrophenyl)ethyl]guanine (**24**).

Reaction of the 3′-*O*- and 5′-*O*-unsubstituted building blocks **14**–**16** and **24** with monomethoxytrityl chloride or dimethoxytrityl chloride in pyridine formed the appropriate 5′-*O*-tritylated compounds **25**–**32**. Conversion into the corresponding arabinonucleoside 3′-(2-cyanoethyl, *N*,*N*-diisopropylphosphoramidites) **33**–**40** was achieved by reaction with (2-cyanoethoxy)bis(diisopropylamino)phosphane [15] under 1*H*-tetrazole activation in high yields. Purification of the phosphoramidite building blocks was performed by flash chromatography on silica gel giving colourless foams suitable for the

synthesis of (3′–5′)-linked oligoarabinonucleotides in solution or on a solid support by a repetitive cycle.

3. Physical Data. – The structural assignments of the newly synthesized arabinonucleoside derivatives are based on elemental analyses, UV and ^{1}H-NMR spectra. The UV spectra encounter no peculiarities and have their corresponding counterparts in the 2′-deoxy- and ribonucleoside series [13]. The ^{1}H-NMR spectra are of complex nature due to the variety of the various blocking groups showing overlapping regions which are not informative at all. We listed, therefore, in the *Table* only the signals of the MeO and sugar protons, of which the chemical shifts of the anomeric H–C(1′) are the most characteristic ones. They appear expectedly as *d* with coupling constants $J(1',2')$ between 3 and 6 Hz and, in more rare cases, as *m* due to the presence of diastereoisomeric mixtures in the phosphoramidites.

Experimental Part

General. TLC: precoated silica-gel thin-layer sheets *60 F 254* from *Merck*. Prep. column chromatography (CC): silica gel (*Merck 60*, 0.063–0.2 mesh). Flash chromatography (FC): silica gel (*Baker*, 30–60 μm); 0.2–0.3 bar. M.p.: *Gallenkamp* melting point apparatus; no corrections. UV/VIS: *Perkin Elmer*, *Lambda 15*; λ_{max} in nm (log ε). ^{1}H-NMR: *Bruker AC 250*; in ppm rel. to TMS. ^{31}P-NMR: *Jeol 400 MHz*; in ppm rel. to H_3PO_4. Products were dried under high vacuum.

1. *1-{3′,5′-Bis-O-[dimethyl(1,1,2-trimethylpropyl)silyl]-β-D-arabinofuranosyl}uracil* (**5**) *and 1-{5′-O-[dimethyl(1,1,2-trimethylpropyl)silyl]-β-D-arabinofuranosyl}uracil* (**6**). To a suspension of 1.87 g (11 mmol) of $AgNO_3$ and molecular sieves (4 Å; 10 g) in abs. THF (100 ml) were added 1.42 g (13 mmol) of 3-methylpyridine *N*-oxide, and the mixture was stirred for 10 min. After addition of 2.16 ml (11 mmol) of dimethyl(1,1,2-trimethylpropyl)silyl chloride (= dimethyl(thexyl)silyl chloride), stirring was continued for 3 h. Then 1.22 g (5 mmol) of 1-(β-D-arabinofuranosyl)uridine (**1**) were added and stirred for 5 d. The mixture was filtered, the filtrate diluted with $CHCl_3$ (100 ml), washed with H_2O (3 × 100 ml), dried (Na_2SO_4), and evaporated. Separation of the two products by CC (4 × 15 cm) gave **5** and **6**.

5: 2.32 g (87%), eluted with toluene/AcOEt 1:1. Colourless foam. Anal. calc. for $C_{25}H_{48}N_2O_6Si_2$ (528.8): C 56.78, H 9.15, N 5.29; found: C 56.43, H 9.15, N 5.44.

6: 0.20 g (10%), eluted with toluene/AcOEt/MeOH 5:5:1. Colourless needles. M.p. 157°. Anal. calc. for $C_{17}H_{30}N_2O_6Si$ (336.5): C 52.83, H 7.82, N 7.25; found: C 52.34, H 7.80, N 7.23.

2. *1-{3′,5′-Bis-O-[dimethyl(1,1,2-trimethylpropyl)silyl]-β-D-arabinofuranosyl}cytosine* (**7**) *and 1-{5′-O-[dimethyl(1,1,2-trimethylpropyl)silyl]-β-D-arabinofuranosyl}cytosine* (**8**). As described in *Exper. 1*, with 1.21 g (5 mmol) of 1-(β-D-arabinofuranosyl)cytosine (**2**). Separation of the two products by CC (4 × 15 cm) gave **7** and **8**.

7: 2.18 g (83%), eluted with toluene/AcOEt/MeOH 4:4:1. Colourless foam. Anal. calc. for $C_{25}H_{49}N_3O_5Si_2$ (527.8): C 56.88, H 9.36, N 7.96; found: C 56.26, H 9.29, N 7.59.

8: 0.19 g (10%), eluted with toluene/AcOEt/MeOH 2:2:1. M.p. 191–192°. Anal. calc. for $C_{17}H_{31}N_3O_5Si$ (385.5): C 52.96, H 8.10, N 10.89; found: C 52.22, H 7.99, N 10.60.

3. *9-[3′,5′-O-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)-β-D-arabinofuranosyl]adenine* (**9**). To a suspension of 2.67 g (10 mmol) of 9-(β-D-arabinofuranosyl)adenine (**3**) in abs. pyridine (100 ml) were added 3.2 ml (10 mmol) of 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane. After stirring for 5 h at r.t. the clear soln. was evaporated and the residue partitioned between AcOEt (200 ml) and H_2O (200 ml). The org. layer was washed subsequently with 0.2M HCl (2 × 150 ml), sat. $NaHCO_3$ soln. (150 ml), and NaCl soln. (150 ml), dried (Na_2SO_4), and evaporated. Purification by CC (4.5 × 10 cm; toluene, toluene/AcOEt 1:1, toluene/AcOEt/MeOH 10:10:1) gave 4.45 g (87%) of colourless foam. Anal. calc. for $C_{22}H_{39}N_5O_5Si_2$ (509.7): C 51.83, H 7.71, N 13.74; found: C 51.62, H 7.68, N 13.59.

4. *1-{3′,5′-Bis-O-[dimethyl(1,1,2-trimethylpropyl)silyl]-2′-O-[2-(4-nitrophenyl)ethoxycarbonyl]-β-D-arabinofuranosyl}uridine* (**10**). To a soln. of 9.11 g (17.2 mmol) of **5** in abs. CH_2Cl_2 (150 ml) were added 2.1 g (17 mmol) of 4-(dimethylamino)pyridine and 10.7 g (34 mmol) of 1-methyl-3-[2-(4-nitrophenyl)ethoxycarbonyl]imidazolium chloride. The suspension was stirred at r.t. overnight. CH_2Cl_2 (150 ml) was added and the mixture washed with H_2O (3 × 150 ml), dried (Na_2SO_4), and evaporated. CC (toluene/AcOEt 10:1, then toluene/AcOEt 3:1) of the

Table. *Physical Data of Arabinonucleoside Derivatives*

	UV Spectra (MeOH)					^{1}H-NMR Spectra ($CDCl_3$, δ [ppm], $J(1',2')$ [Hz])					
	λ_{max} [nm]			lg ε		H–C(1′)	H–C(2′)	H–C(3′)	H–C(4′)	H–C(5′)	MeO
5		262			4.04	6.06 (*d*, *J* = 3.1)	4.13 (*m*)		3.89 (*m*)	3.75 (*m*)	
6		262			4.02	6.10 (*d*, *J* = 4.3)	4.56	4.29 (*m*)	3.88 (*m*)		
7		273			3.96	6.06 (*d*, *J* = 3.7)	4.21 (*t*)	4.13 (*t*)	3.79 (*m*)		
8		272			3.98	6.01 (*d*, *J* = 4.4)[a]	4.03 (*dd*)	3.87 (*m*)	3.75 (*m*)		
9	258			4.20		6.15 (*d*, *J* = 6.1)	4.61 (*m*)		3.82 (*m*)	4.01 (*m*)	
10		262			4.28	6.23 (*d*, *J* = 5.1)	5.12 (*t*)	4.33 (*m*)[b]	3.79 (*m*)		
11	247 (sh)	272		4.42	4.43	6.26 (*d*, *J* = 5.0)	5.29 (*t*)	4.43 (*m*)[b]	3.92 (*m*)	3.77 (*m*)	
12		266			4.56	6.15 (*d*, *J* = 3.6)	4.16 (*m*)	4.17 (*t*)	3.38 (*m*)[c]		
13	242	282		4.26	4.18	6.49 (*d*, *J* = 6.2)	5.48 (*dd*)	4.85 (*t*)	3.96 (*m*)	4.15 (*m*)[c]	
14		262			4.27	6.18 (*d*, *J* = 5.2)[a]	5.09 (*m*)[d]	4.11 (*dd*)	3.78 (*m*)	3.61 (*m*)	
15	250 (sh)	272		4.39	4.41	6.28 (*d*, *J* = 4.8)[a]	5.29 (*t*)	4.35 (*m*)	3.97 (*m*)	3.77 (*m*)	
16		267			4.55	6.53 (*d*, *J* = 6.0)[a]	5.29 (*t*)	4.43 (*m*)[b]	3.81 (*m*)	3.70 (*m*)	
17	253			4.05		6.24 (*d*, *J* = 4.7)[a]	5.40 (*m*)		4.31 (*m*)		
19	250	278		4.18	4.26	6.10 (*d*, *J* = 4.2)[a]	4.06 (*m*)		3.73 (*m*)	3.61 (*m*)	
20	250	278		4.15	4.25	6.05 (*d*, *J* = 6.5)[a]	4.43 (*dd*)	4.30 (*t*)	3.75 (*m*)	3.93 (*m*)	
21	254	275		4.30	4.39	6.31 (*d*, *J* = 6.1)	5.41 (*dd*)	4.68 (*m*)[b]	3.86 (*m*)	4.06 (*m*)	
22		268			4.55	6.05 (*d*, *J* = 5.8)	4.70 (*m*)[b]	4.54 (*t*)	3.86 (*m*)	3.96 (*m*)	
23		268			4.61	6.36 (*d*, *J* = 6.2)	5.39 (*dd*)	4.96 (*m*)[b]	3.88 (*m*)	4.13 (*m*)	
24		268			4.63	6.43 (*d*, *J* = 6.2)	5.35 (*t*)	5.16 (*t*)	3.96 (*m*)		
25	233	263		4.26	4.26	6.30 (*d*, *J* = 5.6)	5.16 (*t*)	4.37 (*m*)[b]	3.95 (*m*)	3.54 (*m*)	3.79 (*s*)
26	235	273		4.53	4.45	6.38 (*d*, *J* = 5.0)	5.42 (*t*)	4.22 (*t*)	4.17 (*m*)	3.48 (*m*)	3.79 (*s*)
27	235 (sh)	266		4.37	4.57	6.58 (*d*, *J* = 5.4)	5.23 (*t*)	4.65 (*m*)	4.08 (*m*)	3.52 (*m*)	3.78 (*s*)
28	236 (sh)	268		4.43	4.66	6.61 (*d*, *J* = 5.0)	5.16 (*t*)	4.75 (*m*)[b]	4.16 (*m*)	3.47 (*m*)	3.73 (*s*)

Table (cont.)

	UV Spectra (MeOH)				^{1}H-NMR Spectra ($CDCl_3$, δ [ppm], $J(1',2')$ [Hz])					
	λ_{max} [nm]		lg ε		H–C(1′)	H–C(2′)	H–C(3′)	H–C(4′)	H–C(5′)	MeO
29	235	264	4.39	4.29	6.28 (*d*, *J* = 5.5)	5.14 (*dd*)	4.83 (*m*)[b]	3.95 (*m*)	3.45 (*m*)	3.76 (*s*)
30	235	273	4.59	4.42	6.37 (*d*, *J* = 4.9)	5.43 (*dd*)	4.22 (*m*)	4.12 (*m*)	3.43 (*m*)	3.76 (*s*)
31	235	266	4.51	4.58	6.65 (*d*, *J* = 5.4)	5.22 (*dd*)	4.64 (*m*)	4.08 (*m*)	3.49 (*m*)	3.75 (*s*)
32	237	268	4.49	4.62	6.55 (*d*, *J* = 5.3)	5.15 (*t*)	4.75 (*m*)[b]	4.12 (*m*)	3.46 (*m*)	3.73 (*s*)
33	233	263	4.21	4.24	6.26 (*d*, *J* = 4.7)	5.27 (*m*)	4.60 (*m*), 4.50 (*m*)	4.06 (*m*)	3.38 (*m*)[e]	3.78 (*s*), 3.77 (*s*)
34	235	273	4.45	4.39	6.31 (*d*, *J* = 4.4)	5.42 (*t*)	4.45 (*m*)	4.34 (*m*)[b]	3.44 (*m*)[e]	3.77 (*s*), 3.76 (*s*)
35	235	266	4.33	4.56	6.58 (*d*, *J* = 4.6)	5.35 (*t*), 5.29 (*t*)	4.66 (*m*), 4.75 (*m*)	4.14 (*m*)[b]	3.47 (*m*)[e]	3.76 (*s*)
36	236 (sh)	268	4.35	4.61	6.44 (*m*, *J* = 5.0)	5.31 (*t*), 5.20 (*t*)	4.62 (*m*)[b]	4.15 (*m*)[b]	3.50 (*m*)[e]	3.74 (*s*)
37	235	264	4.39	4.30	6.26 (*d*, *J* = 4.8)	5.27 (*m*)	4.59 (*m*), 4.50 (*m*)	4.06 (*m*)	3.36 (*m*)	3.77 (*s*), 3.76 (*s*)
38	236	273	4.54	4.39	6.31 (*d*, *J* = 3.2)	5.43 (*t*)	4.53 (*m*)[b]	4.33 (*m*)[b]	3.45 (*m*)[e]	3.77 (*s*), 3.76 (*s*)
39	236	266	4.41	4.54	6.58 (*d*, *J* = 4.6)	5.35 (*t*), 5.29 (*t*)	4.65 (*m*), 4.75 (*m*)	4.16 (*m*)[b]	3.42 (*m*)	3.76 (*s*), 3.75 (*s*)
40	236	268	4.54	4.65	6.43 (*m*, *J* = 4.9)	5.30 (*t*), 5.19 (*t*)	4.62 (*m*)[b]	4.17 (*m*)[b]	3.51 (*m*)[e]	3.74 (*s*)

[a]) In (D_6)DMSO. [b]) Overlapping with O–CH_2CH_2. [c]) Together with OH–C(2′). [d]) Together with OH–C(3′). [e]) Together with CH_2OP, $(i\text{-}Pr)_2N$.

residue gave an oil which, after addition of hexane, crystallized slowly: 10.3 g (81%) of **10**. M.p. 110°. Anal. calc. for $C_{34}H_{55}N_3O_{10}Si_2$ (722.0): C 56.56, H 7.68, N 5.82; found: C 56.42, H 7.58, N 5.86.

5. *1-{3',5'-Bis-O-[dimethyl(1,1,2-trimethylpropyl)silyl]-2'-O-[2-(4-nitrophenyl)ethoxycarbonyl]-β-D-arabinofuranosyl}-N⁴-[2-(4-nitrophenyl)ethoxycarbonyl]cytosine* (**11**). As described in *Exper. 4*, with 5.1 g (9.6 mmol) of **7**, abs. CH_2Cl_2 (100 ml), 1.22 g (10 mmol) of 4-(dimethylamino)pyridine, and 12.14 g (39 mmol) of 1-methyl-1-[2-(4-nitrophenyl)ethoxycarbonyl]imidazolium chloride (40 h at r.t.). Workup with CH_2Cl_2 (200 ml), H_2O (200 ml), sat. NaCl soln. (200 ml), and $MgSO_4$. FC (4.5 × 28 cm, toluene/AcOEt 10:1 → 1:1) and co-evaporation of the product fractions with EtOH, MeOH, and CH_2Cl_2 gave 7.57 g (86%) of **11**. Anal. calc. for $C_{43}H_{63}N_5O_{13}Si_2$ (914.2): C 56.49, H 6.95, N 7.66; found: C 56.34, H 6.97, N 7.65.

6. *N⁶-[2-(4-Nitrophenyl)ethoxycarbonyl]-9-{2'-O-[2-(4-nitrophenyl)ethoxycarbonyl]-3',5'-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-D-arabinofuranosyl}adenine* (**12**). As described in *Exper. 4*, with 7.65 g (15 mmol) of **9**, abs. CH_2Cl_2 (150 ml), 1.83 g (15 mmol) of 4-(dimethylamino)pyridine, and 14.03 g (45 mmol) of 1-methyl-3-[2-(4-nitrophenyl)ethoxycarbonyl]imidazolium chloride (48 h at r.t.). Workup with CH_2Cl_2 (200 ml), H_2O (200 ml), sat. NaCl soln. (200 ml), and Na_2SO_4. FC (4.5 × 16 cm, toluene/AcOEt 10:1, then toluene/AcOEt 1:1) gave 12.25 g (91%) of colourless foam. Anal. calc. for $C_{40}H_{53}N_7O_{13}Si_2$ (896.1): C 53.61, H 5.96, N 10.94; found: C 53.53, H 6.03, N 10.65.

7. *1-{3',5'-Bis-O-[dimethyl(1,1,2-trimethylpropyl)silyl]-β-D-arabinofuranosyl}-N⁴-[2-(4-nitrophenyl)ethoxycarbonyl]-β-D-arabinofuranosyl}cytosine* (**13**). A mixture of 0.527 g (1 mmol) of **7** and 0.528 g (2.3 mmol) of 2-(4-nitrophenyl)ethyl chloroformate was stirred for 2.5 h in abs. pyridine (5 ml). The mixture was partitioned between H_2O (50 ml) and AcOEt (50 ml), the org. layer washed with H_2O (2 × 30 ml) and sat. NaCl soln. (30 ml), dried (Na_2SO_4), and evaporated, and the residue submitted to CC (toluene/AcOEt 10:1, AcOEt): 0.576 g (79%) of crystalline solid. M.p. 161°. Anal. calc. for $C_{34}H_{56}N_4O_9Si_2$ (721.0): C 56.64, H 7.83, N 7.77; found: C 56.64, H 7.86, N 7.82.

8. *1-{2'-O-[2-(4-Nitrophenyl)ethoxycarbonyl]-β-D-arabinofuranosyl}uridine* (**14**). To a mixture of 7.22 g (10 mmol) of **10** and 2.85 ml (50 mmol) of AcOH in THF (110 ml) were added 6.31 g (20 mmol) of $(Bu_4N)F \cdot 3\ H_2O$ and stirred at r.t. for 5 d. The mixture was diluted with AcOEt (400 ml), washed successively with H_2O, sat. $NaHCO_3$ soln., and sat. NaCl soln. (each 200 ml), dried ($MgSO_4$), and evaporated. The residue was dissolved in CH_2Cl_2 (50 ml), and shortly thereafter, the product crystallized: 3.8 g (87%) of **14**. M.p. 144°. Anal. calc. for $C_{18}H_{19}N_3O_{10} \cdot 0.5\ H_2O$ (446.4): C 48.43, H 4.52, N 9.41; found: C 48.08, H 4.52, N 9.23.

9. *N⁴-[2-(4-Nitrophenyl)ethoxycarbonyl]-1-{2'-O-[2-(4-nitrophenyl)ethoxycarbonyl]-β-D-arabinofuranosyl}cytosine* (**15**). As described in *Exper. 8*, with 3.66 g (4 mmol) of **11**, 1.14 ml (20 mmol) of AcOH, THF (40 ml), and 3.0 g (9.5 mmol) of $(Bu_4N)F \cdot 3\ H_2O$ (6 h at r.t.). Workup with AcOEt (200 ml), H_2O, sat. $NaHCO_3$ soln., and sat. NaCl soln. (each 150 ml). Crystallization from CH_2Cl_2 (15 ml): 1.808 g (72%) of **15**. M.p. 114°. Anal. calc. for $C_{27}H_{27}N_5O_{13}$ (629.5): C 51.51, H 4.32, N 11.12; found: C 51.30, H 4.36, N 11.15.

10. *N⁶-[2-(4-Nitrophenyl)ethoxycarbonyl]-9-{2'-O-[2-(4-nitrophenyl)ethoxycarbonyl]-β-D-arabinofuranosyl}adenine* (**16**). As described in *Exper. 8*, with 12.25 g (13.6 mmol) of **13**, 7.47 ml (130.6 mmol) of AcOH, THF (150 ml), and 10.72 g (34 mmol) of $(Bu_4N)F \cdot 3\ H_2O$ (5 h at r.t.). Workup with AcOEt (400 ml), H_2O, sat. $NaHCO_3$ soln. and NaCl soln. (each 300 ml). Evaporation to *ca.* 70 ml gave the crystallized product: 10.2 g (92%). M.p. 92°. Anal. calc. for $C_{28}H_{27}N_7O_{12}$ (653.6): C 51.46, H 4.16, N 15.00; found: C 51.98, H 4.45, N 14.42.

11. *9-(2',3',5'-Tri-O-acetyl-β-D-arabinofuranosyl)guanine* (**17**). A suspension of 6 g (21 mmol) of *9-(β-D-arabinofuranosyl)guanine* (**4**) in abs. Ac_2O (14 ml), abs. DMF (17 ml), and abs. pyridine (8.5 ml) was stirred at r.t. for 5 h. From the clear soln., a crystalline precipitate separated which was filtered off by suction, washed with i-PrOH and Et_2O, and dried. The mother liquor was evaporated and the residue crystallized from i-PrOH: 5.38 g. Total yield of **17**: 8.09 g (94%). M.p. 196°. Anal. calc. for $C_{16}H_{19}N_5O_8$ (409.4): C 46.94, H 4.68, N 17.11; found: C 46.84, H 4.96, N 17.08.

12. *9-(β-D-Arabinofuranosyl)-O⁶-[2-(4-nitrophenyl)ethyl]guanine* (**19**). A mixture of 5.5 g (13.4 mmol) of **17**, 5.27 g (20.1 mmol) of Ph_3P, and 3.34 g (20 mmol) of 2- (4- nitrophenyl)ethanol in abs. dioxan (90 ml) was stirred at r.t. for 45 min. Then 3.15 ml (20.1 mmol) of diethyl azodicarboxylate were added and stirred for another 4 h. The soln. was evaporated, the residue dissolved in CH_2Cl_2 (20 ml) and kept overnight at 4°. The separated diethyl hydrazinedicarboxylate was filtered off by suction and washed with 5 ml of cold CH_2Cl_2. The filtrate was evaporated leaving an oil, which was dissolved in MeOH/dioxan/25% NH_3 soln. 1:1:1 (60 ml) and kept for 48 h at 4°. On evaporation to *ca.* 30 ml, the product crystallized: 2.93 g (51%) of yellowish crystals. M.p. 202°. Anal. calc. for $C_{18}H_{19}N_6O_7$ (431.4): C 50.12, H 4.44, N 19.48; found: C 49.60, H 4.58, N 19.80.

13. O^6-*[2-(4-Nitrophenyl)ethyl]-9-[3′,5′-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-*D*-arabinofuranosyl]guanine* (**20**). A mixture of 5 g (11.5 mmol) of **19** and 3.75 ml (12 mmol) of 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane in abs. pyridine (90 ml) was stirred at r.t. overnight. After evaporation, the residue was partitioned between AcOEt (200 ml) and H_2O (200 ml). The org. layer was washed with 0.2M HCl, $NaHCO_3$ soln., and NaCl soln. (each 150 ml), dried ($MgSO_4$), and evaporated to give 7.3 g (94%) of colourless foam. An anal. sample was further purified by FC (toluene/AcOEt 2:1). Anal. calc. for $C_{30}H_{46}N_6O_8Si_2$ (674.9): C 53.39, H 6.87, N 12.45; found: C 53.22, H 6.96, N 12.21.

14. *9-{2′-O-[2-(4-Nitrophenyl)ethoxycarbonyl]-3′,5′-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-*D*-arabinofuranosyl}-O^6-[2-(4-nitrophenyl)ethyl]guanine* (**21**). As described in *Exper. 4*, with 1.49 g (2.21 mmol) of **20**, abs. CH_2Cl_2 (30 ml), 0.27 g (2.21 mmol) of 4-(dimethylamino)pyridine, and 2.07 g (6.63 mmol) of 1-methyl-3-[2-(4-nitrophenyl)ethoxycarbonyl]imidazolium chloride (22 h at r.t.). Workup with CH_2Cl_2 (150 ml), 0.2M HCl, $NaHCO_3$ soln., NaCl soln. (each 70 ml), and ($MgSO_4$). FC (2.5 × 12 cm, toluene/AcOEt 10:1, then toluene/AcOEt 6:1) gave 1.57 g (82%) of **21**. Anal. calc. for $C_{39}H_{33}N_7O_{12}Si_2$ (868.1): C 53.96, H 6.15, N 11.29; found: C 54.26, H 6.27, N 10.91.

15. N^2-*[2-(4-Nitrophenyl)ethoxycarbonyl]-O^6-[2-(4-nitrophenyl)ethyl]-9-[3′,5′-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-*D*-arabinofuranosyl]guanine* (**22**). To a soln. of 337 mg (0.5 mmol) of **20** in abs. pyridine (4 ml) were added 343 mg (1.5 mmol) of 2-(4-nitrophenyl)ethyl chloroformate, and the mixture was stirred at r.t. for 20 h. After evaporation, the residue was dissolved in CH_2Cl_2 (30 ml), the soln. washed with H_2O, 0.2M HCl, and $NaHCO_3$ soln. (each 20 ml), dried ($MgSO_4$), and evaporated, and the crude product purified by FC (2 × 10 cm, toluene/AcOEt 10:1 → 2:1); 245 mg (56%) of **22**. Colourless foam. Anal. calc. for $C_{39}H_{33}N_7O_{12}Si_2$ (868.1): C 53.96, H 6.15, N 11.29; found: C 53.88, H 6.26, N 11.14.

16. N^2-*[2-(4-Nitrophenyl)ethoxycarbonyl]-9-{2′-O-[2-(4-nitrophenyl)ethoxycarbonyl]-3′,5′-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-*D*-arabinofuranosyl}-O^6-[2-(4-nitrophenyl)ethyl]guanine* (**23**). *a*) As described in *Exper. 4*, with 2.9 g (3.3 mmol) of **22**, CH_2Cl_2 (40 ml), 0.36 g (3 mmol) of 4-(dimethylamino)pyridine, and 2.85 g (9.2 mmol) of 1-methyl-3-[2-(4-nitrophenyl)ethoxycarbonyl]imidazolium chloride (22 h at r.t.). Workup with CH_2Cl_2 (200 ml), 0.2M HCl, $NaHCO_3$ soln., NaCl soln. (150 ml of each), and $MgSO_4$. FC (3 × 20 cm, toluene/AcOEt 10:1, then toluene/AcOEt 4:1): 2.74 g (78%) of **23**.

b) As described in *Exper. 4*, with 4.26 g (6.3 mmol) of **20**, abs. CH_2Cl_2 (80 ml), 0.86 g (7.0 mmol) of 4-(dimethylamino)pyridine, and 4.9 g (15.7 mmol) of 1-methyl-3-[2-(4-nitrophenyl)ethoxycarbonyl]imidazolium chloride (overnight at r.t.). Workup with CH_2Cl_2 (100 ml), 0.2M HCl, $NaHCO_3$ soln., NaCl soln. (each 70 ml), and $MgSO_4$. Rough purification by FC (2.5 × 13 cm, toluene/AcOEt 15:1, then toluene/AcOEt 5:1) gave an oil which was treated as described in *Exper. 15*: in abs. pyridine (60 ml), with 2.0 g (8.7 mmol) of 2-(4-nitrophenyl)ethyl chloroformate (24 h at r.t.). Workup with H_2O and AcOEt (200 ml of each), 0.2M HCl, $NaHCO_3$ soln., NaCl soln. (each 100 ml), and $MgSO_4$. FC (3.5 × 16 cm, toluene/AcOEt 15:1, then toluene/AcOEt 6:1) gave 4.27 g (64%) of **23**. Colourless foam. Anal. calc. for $C_{48}H_{60}N_8O_{16}Si_2$ (1061.2): C 54.32, H 5.69, N 10.58; found: C 54.38, H 5.67, N 10.37.

17. N^2-*[2-(4-Nitrophenyl)ethoxycarbonyl]-9-{2′-O-[2-(4-nitrophenyl)ethoxycarbonyl]-β-*D*-arabinofuranosyl}-O^6-[2-(4-nitrophenyl)ethyl]guanine* (**24**). As described in *Exper. 8*, with 3.61 g (3.4 mmol) of **23** and 1.64 ml (25.5 mmol) of AcOH, abs. THF (35 ml), and 2.15 g (6.8 mmol) of $(Bu_4N)F \cdot 3\ H_2O$ (3.5 h at r.t.). Workup with AcOEt (200 ml), H_2O, sat. $NaHCO_3$ soln., sat. NaCl soln. (200 ml of each), and $MgSO_4$. Purification by FC (CH_2Cl_2/MeOH 97:3) gave 1.9 g (68%) of a colourless foam. Anal. calc. for $C_{36}H_{34}N_8O_{15}$ (818.7): C 52.81, H 4.18, N 13.68; found: C 52.36, H 4.29, N 13.57.

18. *1-{5′-O-(Monomethoxytrityl)-2′-O-[2-(4-nitrophenyl)ethoxycarbonyl]-β-*D*-arabinofuranosyl}uridine* (**25**). To a soln. of 3.06 g (7 mmol) of **14** in abs. pyridine (50 ml), 2.37 g (7.7 mmol) of MeOTrCl were added and stirred at r.t. for 24 h. The mixture was evaporated and co-evaporated with toluene (2 × 50 ml). The residue was partitioned between AcOEt and H_2O (200 ml of each), the org. layer washed with sat. NaCl soln. (150 ml), dried ($MgSO_4$), and evaporated. Purification by FC (4.5 × 13 cm, toluene/AcOEt 10:1, then toluene/AcOEt 1.5:1) and co-evaporation of the product with MeOH and CH_2Cl_2 gave 4.31 g (87%) of a colourless foam. Anal. calc. for $C_{38}H_{25}N_3O_{11} \cdot H_2O$ (727.7): C 62.72, H 5.12, N 5.77; found: C 62.69, H 5.06, N 5.84.

19. *1-{5′-O-(Monomethoxytrityl)-2′-O-[2-(4-nitrophenyl)ethoxycarbonyl]-β-*D*-arabinofuranosyl}-N^4-[2-(4-nitrophenyl)ethoxycarbonyl]cytosine* (**26**). As described in *Exper. 18*, with 3.14 g (5 mmol) of **15** and 1.85 g (6 mmol) of MeOTrCl. FC (3.5 × 14 cm) with toluene/AcOEt 1:1 gave 4.29 g (94%) of solid foam. Anal. calc. for $C_{47}H_{43}N_5O_{14}$ (901.9): C 62.59, H 4.81, N 7.76; found: C 62.50, H 4.88, N 7.76.

20. *9-{5'-O-(Monomethoxytrityl)-2'-O-[2-(4-nitrophenyl)ethoxycarbonyl]-β-D-arabinofuranosyl}-N⁶-[2-(4-nitrophenyl)ethoxycarbonyl]adenine* (**27**). As described in *Exper. 18*, with 6.53 g (10 mmol) of **16** and 3.39 g (11 mmol) of MeOTrCl. FC (4.5 × 20 cm) with toluene /AcOEt 1:1 gave 7.62 g (82%) of solid foam. Anal. calc. for $C_{48}H_{43}N_7O_{13} \cdot H_2O$ (943.9): C 61.07, H 4.81, N 10.38; found: C 60.70, H 4.86, N 10.05.

21. *9-{5'-O-(Monomethoxytrityl)-2'-O-[2-(4-nitrophenyl)ethoxycarbonyl]-β-D-arabinofuranosyl}-N²-[2-(4-nitrophenyl)ethoxycarbonyl]-O⁶-[2-(4-nitrophenyl)ethyl]guanine* (**28**). As described in *Exper. 18*, with 0.818 g (1 mmol) of **24** in abs. pyridine (10 ml) and 0.4 g (1.3 mmol) of MeOTrCl. FC (2.5 × 11 cm) with toluene/AcOEt 5:1, then toluene/AcOEt 2:1, gave 1.0 g (92%) of solid foam. Anal. calc. for $C_{56}H_{48}N_8O_{16}$ (1089.0): C 61.76, H 4.44, N 10.29; found: C 61.82, H 4.83, N 9.88.

22. *1-{5'-O-(Dimethoxytrityl)-2'-O-[2-(4-nitrophenyl)ethoxycarbonyl]-β-D-arabinofuranosyl}uridine* (**29**). In abs. pyridine (40 ml), 2.186 g (5 mmol) of **14** and 2.03 g (6 mmol) of $(MeO)_2TrCl$ were dissolved and stirred at r.t. for 24 h. The soln. was evaporated, the residue dissolved in CH_2Cl_2 (200 ml) and washed with H_2O (2 × 100 ml) and sat. NaCl soln. (100 ml), dried ($MgSO_4$), and evaporated. The resulting oil was purified by FC (3 × 20 cm, toluene/AcOEt 2.5:1, toluene/AcOEt 1:1, toluene/AcOEt/MeOH 5:5:1): 3.05 g (83%) of colourless foam. Anal. calc. for $C_{39}H_{37}N_3O_{12}$ (739.7): C 63.32, H 5.04, N 5.68; found: C 63.17, H 5.20, N 5.45.

23. *1-{5'-O-(Dimethoxytrityl)-2'-O-[2-(4-nitrophenyl)ethoxycarbonyl]-β-D-arabinofuranosyl}-N⁴-[2-(4-nitrophenyl)ethoxycarbonyl]cytosine* (**30**). As described in *Exper. 22*, with 2.65 g (4.2 mmol) of **15** and 1.72 g (5.1 mmol) of $(MeO)_2TrCl$. FC (3 × 20 cm) with toluene/AcOEt 2:1, then toluene/AcOEt 1:1, gave 2.83 g (72%) of solid foam. Anal. calc. for $C_{48}H_{45}N_5O_{15}$ (931.90): C 61.86, H 4.87, N 7.26; found: C 61.75, H 5.07, N 7.26.

24. *9-{5'-O-(Dimethoxytrityl)-2'-O-[2-(4-nitrophenyl)ethoxycarbonyl]-β-D-arabinofuranosyl}-N⁶-[2-(4-nitrophenyl)ethoxycarbonyl]adenine* (**31**). As described in *Exper. 22*, with 6.53 g (10 mmol) of **16** and 3.5 g (10.35 mmol) of $(MeO)_2TrCl$. FC (4.5 × 16 cm) with toluene/AcOEt 10:1, toluene/AcOEt 2:1, then toluene/AcOEt 1:1. gave 6.67 (70%) of solid foam. Anal. calc. for $C_{49}H_{45}N_7O_{14}$ (955.9): C 61.57, H 4.74, N 10.25; found: C 61.49, H 4.90, N 10.00.

25. *9-{5'-O-(Dimethoxytrityl)-2'-O-[2-(4-nitrophenyl)ethoxycarbonyl]-β-D-arabinofuranosyl}-N²-[2-(4-nitrophenyl)ethoxycarbonyl]-O⁶-2-[(4-nitrophenyl)ethyl]guanine* (**32**). As described in *Exper. 22*, with 0.818 g (1 mmol) of **24**, 0.373 (1.1 mmol) of $(MeO)_2TrCl$. The oil in little CH_2Cl_2 was purified by FC (2 × 15 cm) with toluene/AcOEt 5:1, toluene/AcOEt 2:1, then toluene/AcOEt 1:1, giving 1.01 g (89%) of solid foam. Anal. calc. for $C_{57}H_{50}N_8O_{17}$ (1119.1): C 61.18, H 4.50, N 10.01; found: C 61.43, H 4.87, N 9.81.

26. *1-{5'-O-(Monomethoxytrityl)-2'-O-[2-(4-nitrophenyl)ethoxycarbonyl]-β-D-arabinofuranosyl}uridine 3'-(2-Cyanoethyl N,N-Diisopropylphosphoramidite)* (**33**). Under N_2, to 0.709 g (1 mmol) of **25** and 35 mg (0.5 mmol) of 1*H*-tetrazole were added 6 ml of 0.25M (2-cyanoethoxy)bis(diisopropylamino)phosphane in CH_2Cl_2 (1.5 mmol). The mixture was stirred at r.t. for 15 h, diluted with CH_2Cl_2 to 30 ml, washed with sat. $NaHCO_3$ soln. (30 ml) and sat. NaCl soln., dried ($MgSO_4$), and evaporated. The crude foam was purified by FC (2.5 × 8 cm, toluene/AcOEt 1:2 with addition of 0.3% of Et_3N). The product fractions were co-evaporated with CH_2Cl_2: 0.802 g (88%) of **33**. Colourless foam. ^{31}P-NMR ($CDCl_3$): 152.18, 151.86. Anal. calc. for $C_{47}H_{52}N_5O_{12}P$ (909.9): C 62.04, H 5.76, N 7.69; found: C 61.68, H 5.82, N 7.60.

27. *1-{5'-O-(Monomethoxytrityl)-2'-O-[2-(4-nitrophenyl)ethoxycarbonyl]-β-D-arabinofuranosyl}-N⁴-[2-(4-nitrophenyl)ethoxycarbonyl]cytosine 3'-(2-Cyanoethyl N,N-Diisopropylphosphoramidite)* (**34**). As described in *Exper. 26*, with 0.901 g (1 mmol) of **26**, 35 mg (0.5 mmol) of 1*H*-tetrazole, and 6 ml of 0.25M (2-cyanoethoxy)bis(diisopropylamino)phosphane in CH_2Cl_2 (1.5 mmol). FC (2.5 × 9 cm, toluene/AcOEt 1:1 with addition of 0.3% of Et_3N) gave 1.005 g (91%) of **34**. Colourless foam. ^{31}P-NMR ($CDCl_3$): 152.12, 152.04. Anal. calc. for $C_{56}H_{59}N_7O_{15}P$ (1101.1): C 61.08, H 5.40, N 8.90; found: C 60.98, H 5.68, N 8.85.

28. *9-{5'-O-(Monomethoxytrityl)-2'-O-[2-(4-nitrophenyl)ethoxycarbonyl]-β-D-arabinofuranosyl}-N⁶-[2-(4-nitrophenyl)ethoxycarbonyl]adenine 3'-(2-Cyanoethyl N,N-Diisopropylphosphoramidite)* (**35**). As described in *Exper. 26*, with 1.85 g (2 mmol) of **27**, 70 mg (1 mmol) of 1*H*-tetrazole, and 12 ml of 0.25M (2-cyanoethoxy)bis(diisopropylamino)phosphane in CH_2Cl_2 (3 mmol). FC (2.5 × 18 cm, toluene/AcOEt 1:1 with addition of 0.3% of Et_3N) gave 2.065 g (92%) of **35**. Colourless foam. ^{31}P-NMR ($CDCl_3$): 152.15, 151.91. Anal. calc. for $C_{57}H_{60}N_9O_{14}P$ (1126.1): C 60.79, H 5.37, N 11.19; found: C 60.59, H 5.71, N 11.08.

29. *9-{5'-O-(Monomethoxytrityl)-2'-O-[2-(4-nitrophenyl)ethoxycarbonyl]-β-D-arabinofuranosyl}-N²-[2-(4-nitrophenyl)ethoxycarbonyl]-O⁶-[2-(4-nitrophenyl)ethyl]guanine 3'-(2-Cyanoethyl N,N-Diisopropylphosphoramidite)* (**36**). As described in *Exper. 26*, with 0.42 g (0.388 mmol) of **28**, 13.4 mg (0.194 mmol) of 1*H*-tetrazole, and

2.3 ml of 0.25M (2-cyanoethoxy)bis(diisopropylamino)phosphane in CH_2Cl_2 (0.575 mmol). FC (2 × 9 cm, toluene/AcOEt 4:1 with addition of 0.3% of Et_3N) gave 0.394 g (79%) of **35**. Colourless foam. ^{31}P-NMR ($CDCl_3$): 151.94, 151.58. Anal. calc. for $C_{65}H_{65}N_{10}O_{17}P$ (1289.3): C 60.55, H 5.08, N 10.86; found: C 61.03, H 5.44, N 10.52.

30. *1-{5'-O-(Dimethoxytrityl)-2'-O-[2-(4-nitrophenyl)ethoxycarbonyl]-β-D-arabinofuranosyl}uridine 3'-(2-Cyanoethyl* N,N-*Diisopropylphosphoramidite)* (**37**). As described in *Exper. 26*, with 0.739 g (1 mmol) of **29**, 35 mg (0.5 mmol) of 1*H*-tetrazole, 6 ml of 0.25M (2-cyanoethoxy)bis(diisopropylamino)phosphane, and CH_2Cl_2 (1.5 mmol). FC (2 × 12 cm, petroleumether/acetone 2:1 with addition of 0.3% of Et_3N) of the solid foam in little CH_2Cl_2 gave a colourless foam: 0.87 g (92%) of **37**. ^{31}P-NMR ($CDCl_3$): 152.07, 151.67. Anal. calc. for $C_{48}H_{54}N_5O_{13}P$ (940.0): C 61.33, H 5.79, N 7.45; found: C 60.96, H 6.09, N 7.40.

31. *1-{5'-O-(Dimethoxytrityl)-2'-O-[2-(4-nitrophenyl)ethoxycarbonyl]-β-D-arabinofuranosyl}-N^4-[2-(4-nitrophenyl)ethoxycarbonyl]cytosine 3'-(2-Cyanoethyl* N,N-*Diisopropylphosphoramidite)* (**38**). As described in *Exper. 26*, with 0.931 g (1 mmol) of **30**, 35 mg (0.5 mmol) of 1*H*-tetrazole, 6 ml of 0.25M (2-cyanoethoxy)bis(diisopropylamino)phosphane, and CH_2Cl_2 (1.5 mmol). FC (2 × 16 cm, petroleumether/acetone 2:1, petroleumether/acetone 1.5:1 with addition of 0.3% of Et_3N) gave 1.04 g (92%) of **38**. Colourless foam. ^{31}P-NMR ($CDCl_3$): 151.95, 151.89. Anal. calc. for $C_{57}H_{62}N_7O_{16}P$ (1132.2): C 60.47, H 5.52, N 8.66; found: C 60.35, H 5.67, N 8.34.

32. *9-{5'-O-(Dimethoxytrityl)-2'-O-[2-(4-nitrophenyl)ethoxycarbonyl]-β-D-arabinofuranosyl}-N^6-[2-(4-nitrophenyl)ethoxycarbonyl]adenine 3'-(2-Cyanoethyl* N,N-*Diisopropylphosphoramidite)* (**39**). As described in *Exper. 26*, with 0.955 g (1 mmol) of **31**, 35 mg (0.5 mmol) of 1*H*-tetrazole, 6 ml of 0.25M (2-cyanoethoxy)bis(diisopropylamino)phosphane, and CH_2Cl_2 (1.5 mmol). FC (2 × 16 cm, petroleumether/acetone 2:1, petroleumether/acetone 1.5:1 with addition of 0.3% of Et_3N) gave 1.077 g (93%) of **39**. Colourless foam. ^{31}P-NMR ($CDCl_3$): 151.98, 151.77. Anal. calc. for $C_{58}H_{62}N_9O_{15}P$ (1156.2): C 60.25, H 5.40, N 10.90; found: C 60.03, H 6.48, N 10.65.

33. *9-{5'-O-(Dimethoxytrityl)-2'-O-[2-(4-nitrophenyl)ethoxycarbonyl]-β-D-arabinofuranosyl}-N^2-[2-(4-nitrophenyl)ethoxycarbonyl]-O^6-[2-(4-nitrophenyl)ethyl]guanine 3'-(2-Cyanoethyl* N,N-*Diisopropylphosphoramidite)* (**40**). As described in *Exper. 26*, with 1.02 g (0.91 mmol) of **31**, 35 mg (0.5 mmol) of 1*H*-tetrazole, 6 ml of 0.25M (2-cyanoethoxy)bis(diisopropylamino)phosphane, and CH_2Cl_2 (1.5 mmol). FC (2 × 16 cm, petroleumether/acetone 2:1, with addition of 0.3% of Et_3N) gave 0.925 g (77%) of **40**. Colourless foam. ^{31}P-NMR ($CDCl_3$): 151.87, 151.56. Anal. calc. for $C_{66}H_{67}N_{10}O_{18}P$ (1319.3): C 60.09, H 5.12, N 10.62; found: C 60.07, H 5.82, N 10.43.

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