

9. Nucleotides

Part XXXIX¹⁾

Synthesis of Arabinonucleoside Phosphoramidite Building Blocks

by Matthias Resmini and Wolfgang Pfeleiderer*

Fakultät für Chemie, Universität Konstanz, Universitätsstrasse 10, D-7750 Konstanz

(8.IX.92)

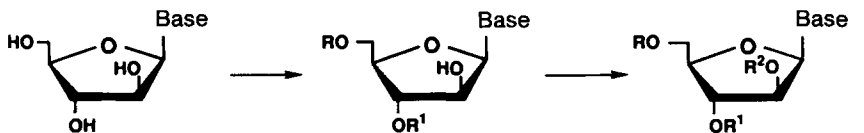
High-yield chemical syntheses of phosphoramidite building blocks of the four arabinonucleosides aUrd (1), aCyd (2), aAdo (3), and aGuo (4), suitable for (3'–5')oligoarabinonucleotide synthesis are described. The problem of 2'-hydroxy group protection was solved by introduction of the versatile 2-(4-nitrophenyl)ethoxycarbonyl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

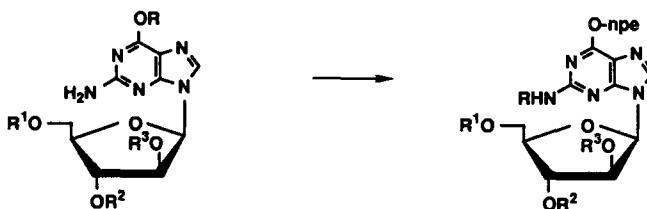
¹⁾ Part XXXVIII: [1].



	Base
1	Ura
2	Cyt
3	Ade
4	Gua

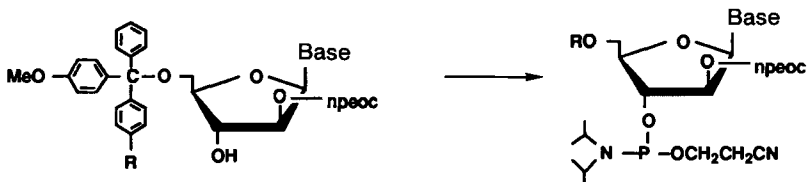
	Base	R	R ¹
5	Ura	tds	tds
6	Ura	tds	H
7	Cyt	tds	tds
8	Cyt	tds	H
9	Ade	tipds	

	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

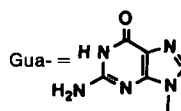
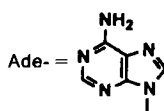
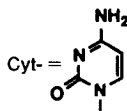
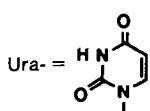
	R	R ¹	R ²	R ³
21	H	tipds		npeoc
22	npeoc	tipds		H
23	npeoc	tipds		npeoc
24	npeoc	H	H	npeoc



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

	Base	R
33	Ura	MeOTr
34	Cyt ^{npeoc}	MeOTr
35	Ade ^{npeoc}	MeOTr
36	Gua ^{npe}	MeOTr
37	Ura	(MeO) ₂ Tr
38	Cyt ^{npeoc}	(MeO) ₂ Tr
39	Ade ^{npeoc}	(MeO) ₂ Tr
40	Gua ^{npe}	(MeO) ₂ Tr

ac = acetyl; tds = thxyldimethylsilyl; tipds = tetraisopropylsiloxane-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 AgNO₃ 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-tetraisopropylidisiloxan (*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 CH₂Cl₂ 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 ((Bu₄N)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 Ac₂O 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 NH₃ in MeOH/dioxan/H₂O 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 (\rightarrow **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 ¹H-NMR spectra. The UV spectra encounter no peculiarities and have their corresponding counterparts in the 2′-deoxy- and ribonucleoside series [13]. The ¹H-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). ¹H-NMR: Bruker AC 250; in ppm rel. to TMS. ³¹P-NMR: Jeol 400 MHz; in ppm rel. to H₃PO₄. 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 AgNO₃ 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 CHCl₃ (100 ml), washed with H₂O (3 × 100 ml), dried (Na₂SO₄), 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 C₂₅H₄₈N₂O₆Si₂ (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 C₁₇H₃₀N₂O₆Si (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 C₂₅H₄₉N₃O₅Si₂ (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 C₁₇H₃₁N₃O₅Si (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-Tetraisopropylidisiloxane-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-tetraisopropylidisiloxane. After stirring for 5 h at r.t. the clear soln. was evaporated and the residue partitioned between AcOEt (200 ml) and H₂O (200 ml). The org. layer was washed subsequently with 0.2M HCl (2 × 150 ml), sat. NaHCO₃ soln. (150 ml), and NaCl soln. (150 ml), dried (Na₂SO₄), 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 C₂₂H₃₉N₅O₅Si₂ (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. CH₂Cl₂ (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. CH₂Cl₂ (150 ml) was added and the mixture washed with H₂O (3 × 150 ml), dried (Na₂SO₄), and evaporated. CC (toluene/AcOEt 10:1, then toluene/AcOEt 3:1) of the

Table. Physical Data of Arabinucleoside 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')	H-C(5')	H-C(4')	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)	4.42	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	282	4.26	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)	4.39	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	4.18	6.10 (d, J = 4.2) ^a	4.06 (m)	3.73 (m)	3.61 (m)			
20	278	4.15	6.05 (d, J = 6.5) ^a	4.43 (dd)	4.30 (t)	3.75 (m)	3.93 (m)		
21	254	4.30	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	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	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)	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)	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	264	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	273	4.42	6.37 (d, J = 4.9)	5.43 (dd)	4.22 (m)	4.12 (m)	3.43 (m)	3.76 (s)	
31	266	4.51	6.65 (d, J = 5.4)	5.22 (dd)	4.64 (m)	4.08 (m)	3.49 (m)	3.75 (s)	
32	268	4.49	6.55 (d, J = 5.3)	5.15 (t)	4.75 (m) ^{b)}	4.12 (m)	3.46 (m)	3.73 (s)	
33	263	4.21	6.26 (d, J = 4.7)	5.27 (m)	4.60 (m), 4.50 (m)	4.06 (m)	3.38 (m) ^{c)}	3.78 (s), 3.77 (s)	
34	273	4.45	6.31 (d, J = 4.4)	5.42 (t)	4.45 (m)	4.34 (m) ^{b)}	3.44 (m) ^{c)}	3.77 (s), 3.76 (s)	
35	266	4.33	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) ^{c)}	3.76 (s)	
36	236 (sh)	4.35	6.44 (m, J = 5.0)	5.31 (t), 5.20 (t)	4.62 (m) ^{b)}	4.15 (m) ^{b)}	3.50 (m) ^{c)}	3.74 (s)	
37	264	4.39	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	273	4.54	6.31 (d, J = 3.2)	5.43 (t)	4.53 (m) ^{b)}	4.33 (m) ^{b)}	3.45 (m) ^{c)}	3.77 (s), 3.76 (s)	
39	266	4.41	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	268	4.54	6.43 (m, J = 4.9)	5.30 (t), 5.19 (t)	4.62 (m) ^{b)}	4.17 (m) ^{b)}	3.51 (m) ^{c)}	3.74 (s)	

^{a)} In (D₂O)DMSO. ^{b)} Overlapping with O-CH₂CH₂. ^{c)} Together with OH-C(3'). ^{d)} Together with OH-C(3'). ^{e)} Together with CH₂OP. (i-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 \times 28 cm, toluene/AcOEt 10:1 \rightarrow 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-tetraiso-propyldisiloxane-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 \times 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 \times 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-tetraisopropylidisiloxane-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-tetraisopropylidisiloxane in abs. pyridine (90 ml) was stirred at r.t. overnight. After evaporation, the residue was partitioned between AcOEt (200 ml) and H₂O (200 ml). The org. layer was washed with 0.2M HCl, NaHCO₃ soln., and NaCl soln. (each 150 ml), dried (MgSO₄), 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 C₃₀H₄₆N₆O₈Si₂ (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-tetraisopropylidisiloxane-1,3-diyl)- β -D-arabinofuranosyl}-O⁶-[2-(4-nitrophenyl)ethyl]guanine (**21**). As described in *Exper. 4*, with 1.49 g (2.21 mmol) of **20**, abs. CH₂Cl₂ (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 CH₂Cl₂ (150 ml), 0.2M HCl, NaHCO₃ soln., NaCl soln. (each 70 ml), and (MgSO₄). FC (2.5 × 12 cm, toluene/AcOEt 10:1, then toluene/AcOEt 6:1) gave 1.57 g (82%) of **21**. Anal. calc. for C₃₉H₅₃N₇O₁₂Si₂ (868.1): C 53.96, H 6.15, N 11.29; found: C 54.26, H 6.27, N 10.91.

15. N²-[2-(4-Nitrophenyl)ethoxycarbonyl]-O⁶-[2-(4-nitrophenyl)ethyl]-9-[3',5'-O-(1,1,3,3-tetraisopropylidisiloxane-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 CH₂Cl₂ (30 ml), the soln. washed with H₂O, 0.2M HCl, and NaHCO₃ soln. (each 20 ml), dried (MgSO₄), 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 C₃₉H₅₃N₇O₁₂Si₂ (868.1): C 53.96, H 6.15, N 11.29; found: C 53.88, H 6.26, N 11.14.

16. N²-[2-(4-Nitrophenyl)ethoxycarbonyl]-9-{2'-O-[2-(4-nitrophenyl)ethoxycarbonyl]-3',5'-O-(1,1,3,3-tetraisopropylidisiloxane-1,3-diyl)- β -D-arabinofuranosyl}-O⁶-[2-(4-nitrophenyl)ethyl]guanine (**23**). a) As described in *Exper. 4*, with 2.9 g (3.3 mmol) of **22**, CH₂Cl₂ (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 CH₂Cl₂ (200 ml), 0.2M HCl, NaHCO₃ soln., NaCl soln. (150 ml of each), and MgSO₄. 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. CH₂Cl₂ (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 CH₂Cl₂ (100 ml), 0.2M HCl, NaHCO₃ soln., NaCl soln. (each 70 ml), and MgSO₄. 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 H₂O and AcOEt (200 ml of each), 0.2M HCl, NaHCO₃ soln., NaCl soln. (each 100 ml), and MgSO₄. 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 C₄₈H₆₀N₈O₁₆Si₂ (1061.2): C 54.32, H 5.69, N 10.58; found: C 54.38, H 5.67, N 10.37.

17. N²-[2-(4-Nitrophenyl)ethoxycarbonyl]-9-{2'-O-[2-(4-nitrophenyl)ethoxycarbonyl]- β -D-arabinofuranosyl}-O⁶-[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 (Bu₄N)F · 3 H₂O (3.5 h at r.t.). Workup with AcOEt (200 ml), H₂O, sat. NaHCO₃ soln., sat. NaCl soln. (200 ml of each), and MgSO₄. Purification by FC (CH₂Cl₂/MeOH 97:3) gave 1.9 g (68%) of a colourless foam. Anal. calc. for C₃₆H₃₄N₈O₁₅ (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 H₂O (200 ml of each), the org. layer washed with sat. NaCl soln. (150 ml), dried (MgSO₄), 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 CH₂Cl₂ gave 4.31 g (87%) of a colourless foam. Anal. calc. for C₃₈H₂₅N₃O₁₁ · H₂O (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}-N⁴-[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 C₄₇H₄₃N₅O₁₄ (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 \times 20 cm) with toluene/AcOEt 1:1 gave 7.62 g (82%) of solid foam. Anal. calc. for C₄₈H₄₃N₇O₁₃·H₂O (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 \times 11 cm) with toluene/AcOEt 5:1, then toluene/AcOEt 2:1, gave 1.0 g (92%) of solid foam. Anal. calc. for C₅₆H₄₈N₈O₁₆ (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 CH₂Cl₂ (200 ml) and washed with H₂O (2 \times 100 ml) and sat. NaCl soln. (100 ml), dried (MgSO₄), and evaporated. The resulting oil was purified by FC (3 \times 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 C₃₉H₃₇N₃O₁₂ (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 \times 20 cm) with toluene/AcOEt 2:1, then toluene/AcOEt 1:1, gave 2.83 g (72%) of solid foam. Anal. calc. for C₄₈H₄₅N₅O₁₅ (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 \times 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 C₄₉H₄₅N₇O₁₄ (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-[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 CH₂Cl₂ was purified by FC (2 \times 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 C₅₇H₅₀N₈O₁₇ (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 N₂, to 0.709 g (1 mmol) of **25** and 35 mg (0.5 mmol) of 1H-tetrazole were added 6 ml of 0.25M (2-cyanoethoxy)bis(diisopropylamino)phosphane in CH₂Cl₂ (1.5 mmol). The mixture was stirred at r.t. for 15 h, diluted with CH₂Cl₂ to 30 ml, washed with sat. NaHCO₃ soln. (30 ml) and sat. NaCl soln., dried (MgSO₄), and evaporated. The crude foam was purified by FC (2.5 \times 8 cm, toluene/AcOEt 1:2 with addition of 0.3% of Et₃N). The product fractions were co-evaporated with CH₂Cl₂: 0.802 g (88%) of **33**. Colourless foam. ³¹P-NMR (CDCl₃): 152.18, 151.86. Anal. calc. for C₄₇H₅₂N₃O₁₂P (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 1H-tetrazole, and 6 ml of 0.25M (2-cyanoethoxy)bis(diisopropylamino)phosphane in CH₂Cl₂ (1.5 mmol). FC (2.5 \times 9 cm, toluene/AcOEt 1:1 with addition of 0.3% of Et₃N) gave 1.005 g (91%) of **34**. Colourless foam. ³¹P-NMR (CDCl₃): 152.12, 152.04. Anal. calc. for C₅₆H₅₉N₇O₁₅P (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 1H-tetrazole, and 12 ml of 0.25M (2-cyanoethoxy)bis(diisopropylamino)phosphane in CH₂Cl₂ (3 mmol). FC (2.5 \times 18 cm, toluene/AcOEt 1:1 with addition of 0.3% of Et₃N) gave 2.065 g (92%) of **35**. Colourless foam. ³¹P-NMR (CDCl₃): 152.15, 151.91. Anal. calc. for C₅₇H₆₀N₉O₁₄P (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 1H-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 $\text{C}_{65}\text{H}_{65}\text{N}_{10}\text{O}_{17}\text{P}$ (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, petroleum ether/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 $\text{C}_{48}\text{H}_{54}\text{N}_5\text{O}_{13}\text{P}$ (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, petroleum ether/acetone 2:1, petroleum ether/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 $\text{C}_{57}\text{H}_{62}\text{N}_7\text{O}_{16}\text{P}$ (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, petroleum ether/acetone 2:1, petroleum ether/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 $\text{C}_{58}\text{H}_{62}\text{N}_9\text{O}_{15}\text{P}$ (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, petroleum ether/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 $\text{C}_{66}\text{H}_{67}\text{N}_{10}\text{O}_{18}\text{P}$ (1319.3): C 60.09, H 5.12, N 10.62; found: C 60.07, H 5.82, N 10.43.

REFERENCES

- [1] Part XXXVIII: R. Charubala, W. Pfeleiderer, *Helv. Chim. Acta* **1992**, 75, 471.
- [2] R. J. Suhadolnik, 'Nucleoside Antibiotics', J. Wiley & Sons, New York, 1970.
- [3] E. Uhlmann, A. Peyman, *Chem. Rev.* **1990**, 90, 543.
- [4] C. Gioeli, J. B. Chattopadhyaya, A. F. Drake, B. Öberg, *Chem. Scr.* **1982**, 19, 13.
- [5] J. L. Barascut, H. B. Lazrek, J. L. Imbach, *Nucleos. Nucleot.* **1984**, 3, 423.
- [6] M. J. Damha, N. Usman, K. K. Ogilvie, *Can. J. Chem.* **1989**, 67, 831.
- [7] K. P. Stengele, W. Pfeleiderer, *Tetrahedron Lett.* **1990**, 31, 2549.
- [8] H. Wetter, K. Oertle, *Tetrahedron Lett.* **1985**, 26, 5515.
- [9] K. K. Ogilvie, D. P. C. McGee, S. M. Boisvert, G. H. Hakimelahi, Z. A. Proba, *Can. J. Chem.* **1983**, 61, 1204.
- [10] T. L. Chwang, R. D. Williams, J. E. Schieber, *Tetrahedron Lett.* **1983**, 24, 3183.
- [11] M. J. Robins, J. S. Wilson, L. Sawyer, M. N. G. James, *Can. J. Chem.* **1983**, 61, 1911.
- [12] W. T. Markiewicz, *J. Chem. Res. (S)* **1979**, 24.
- [13] F. Himmelsbach, B. S. Schulz, T. Trichtinger, R. Charubala, W. Pfeleiderer, *Tetrahedron* **1984**, 40, 59.
- [14] H. Morisawa, T. Utagawa, T. Miyoshi, F. Yoshinaga, A. Yamazaki, K. Mitsugi, *Tetrahedron Lett.* **1980**, 21, 479.
- [15] A. Kraszewski, K. E. Norris, *Nucleic Acids Res. Symp. Ser.* **1987**, 18, 177.