

Synthesis of 5'-C- and 2'-O-(Bromoalkyl)-Substituted Ribonucleoside Phosphoramidites for the Post-synthetic Functionalization of Oligonucleotides on Solid Support

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Dedicated to Prof. Dr. Frank Seela on the occasion of his 60th birthday

The preparation of building blocks for the incorporation of 6'-O-(5-bromopentyl)-substituted β -D-allofuranosynucleosides and 2'-O-[(3-bromopropoxy)methyl]-substituted ribonucleosides into oligonucleotide sequences is presented (*Schemes 1* and *2*). These reactive building blocks can be modified with a variety of soft nucleophiles while the (fully protected) sequence is still attached to the solid support. As an example of this strategy, we carried out some preliminary solid-phase substitution and conjugation reactions with DNA sequences containing a 2'-O-[(3-bromopropoxy)methyl]-substituted ribonucleoside (*Scheme 3*) and determined the pairing properties of duplexes obtained therefrom.

1. Introduction. – Oligonucleotide conjugates and functionalized oligonucleotides are versatile tools for structural, biological, and biophysical studies. To access a variety of such oligonucleotide analogues within a short time, several solid-phase functionalization strategies have been developed. They are based on reactive, prefunctionalized building blocks that, after their incorporation into oligonucleotides, can be functionalized with a variety of different groups. The first examples of such 'convertible nucleosides' carried reactive nucleobases that, during deprotection with alkylamines, afforded *N*-alkyl-substituted nucleosides [1]. Meanwhile, a few base analogues carrying suitably protected reactive side chains have been developed; after liberation of their reactive sites, these analogues can be modified, while the sequence is still fully protected and attached to the solid support [2]. In this context, we recently reported a method for the functionalization of the sugar moiety of oligonucleotides on the solid support. Our approach was based on the incorporation of a 6'-O-(bromopentyl)-substituted allofuranosyl-cytosine phosphoramidite into sequences followed by substitution of the Br-atom with a variety of soft nucleophiles [3]. Here we describe the synthesis of the analogous 6'-O-(bromopentyl)-substituted allofuranosyl phosphoramidites containing the three other canonical nucleobases uracil, adenine, and guanosine.

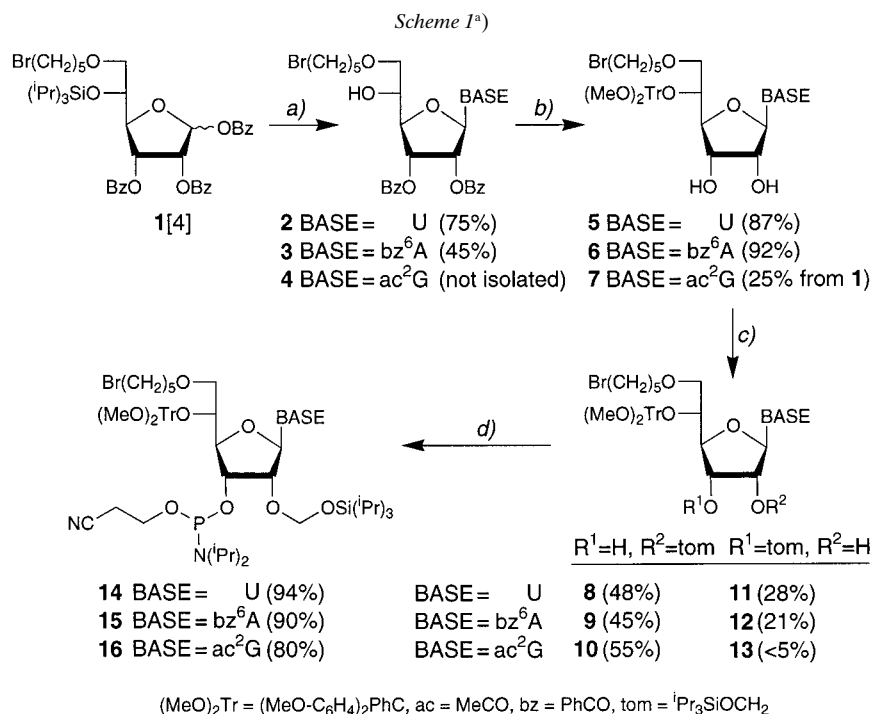
Meanwhile, we have extended our concept and have prepared reactive 2'-O-[(3-bromopropoxy)methyl]-substituted ribonucleoside building blocks that allow the introduction of additional functionalities at the 2'-O-position of oligonucleotides. In this first communication, we report the synthesis of such phosphoramidites containing the four canonical nucleobases and base-pairing properties of some derivatives obtained therefrom.

2. Results and Discussion. – 2.1. *Synthesis of 6'-O-(Bromopentyl)-Substituted Allofuranosyl Phosphoramidites.* The 6'-O-(bromopentyl)-substituted β -D-allofuranosyl nucleoside building blocks containing the nucleobases adenine, uracil, and guanine were prepared from the prefunctionalized sugar building block **1** in analogy to the synthesis of the corresponding cytosine-containing phosphoramidite that has been reported in [3][4] (*Scheme 1*).

The nucleosidation of **1** was carried out under *Vorbrüggen* conditions with the *in-situ* trimethylsilylated nucleobases uracil, *N*⁶-benzoyladenine, and *N*²-acetylguanine, respectively; after aqueous workup, the products were desilylated, affording the nucleosides **2**, **3**, and **4**, respectively. Nucleoside formation with uracil proceeded smoothly in the presence of SnCl₄ in MeCN [5], and after treatment of the crude product with HF and HCl in H₂O/MeCN according to [4], the desilylated derivative **2** was obtained in a yield of 75%. With *N*⁶-benzoyladenine, a mixture of products was obtained under a variety of nucleosidation and deprotection conditions. Nevertheless, the nucleoside **3** could be isolated in a moderate yield of 45% by performing the nucleosidation reaction with SnCl₄ in MeCN [5] and the desilylation with CF₃COOH/H₂O. The nucleosidation of **1** with *N*²-acetylguanine afforded, under various conditions, always a mixture of the two isomeric *N*⁹- and *N*⁷-connected nucleosides, which could not be separated. The best *N*⁹/*N*⁷ ratio was obtained with Me₃Si-OTf in (CH₂Cl)₂ according to [5]. After desilylation of the crude products with HF and HCl in H₂O/MeCN [4], again an unseparable mixture of isomers was obtained in a moderate yield of 40%. The dimethoxytritylation of the intermediates **2–4**, respectively, was carried out with (MeO)₂Tr-Cl in the presence of AgNO₃ and *sym*-collidine (=2,4,6-trimethylpyridine) according to [4][6]. Without purification, the intermediates were then directly *O*-debenzoylated under standard conditions with NaOH in THF/MeOH/H₂O [7]. The dimethoxytritylated uracil and adenine nucleosides **5** and **6** were obtained in good yields of 87 and 92%, respectively. At this stage, the two regioisomeric *N*⁹- and *N*⁷-connected guanine nucleosides **7** could be separated by chromatography (silica gel) and were isolated in yields of 25 and 11%, respectively (based on **1**)¹. Introduction of the 2'-*O*-[(triisopropylsilyloxy)methyl] (=tom) protecting group into the three nucleosides was carried out under our general conditions, by first forming a cyclic dibutyltin derivative with Bu₂SnCl₂/ⁱPr₂NEt and then treatment with tom-Cl at 80° [4][5][9]. Under these conditions, the three 2'-*O*-alkylated nucleosides **8–10** were obtained as major products that could be separated by chromatography (silica gel) from the corresponding 3'-*O*-alkylated regioisomers **11–13**². Finally, the nucleosides **8–10** were transformed into the phosphoramidites **14–16** according to standard procedures [5].

¹) The connection of the nucleobase was determined by ¹³C-NMR spectroscopy according to [8].

²) The correct position of the tom group was determined by ¹H-NMR spectroscopy according to [5]. Generally, within every pair of 5'-*O*-dimethoxytritylated, base-protected nucleosides with 2',3'-*O*-formaldehyde acetal-derived substituents known so far, we observed the following relationships: the 2'-*O*-alkylated nucleosides are less polar and elute faster on chromatography (silica gel) than the corresponding 3'-*O*-alkylated regioisomers; the H–C(1') signals of the former are further downfield, and the coupling constants between H–C(1')/H–C(2') are smaller than the corresponding values of the latter.

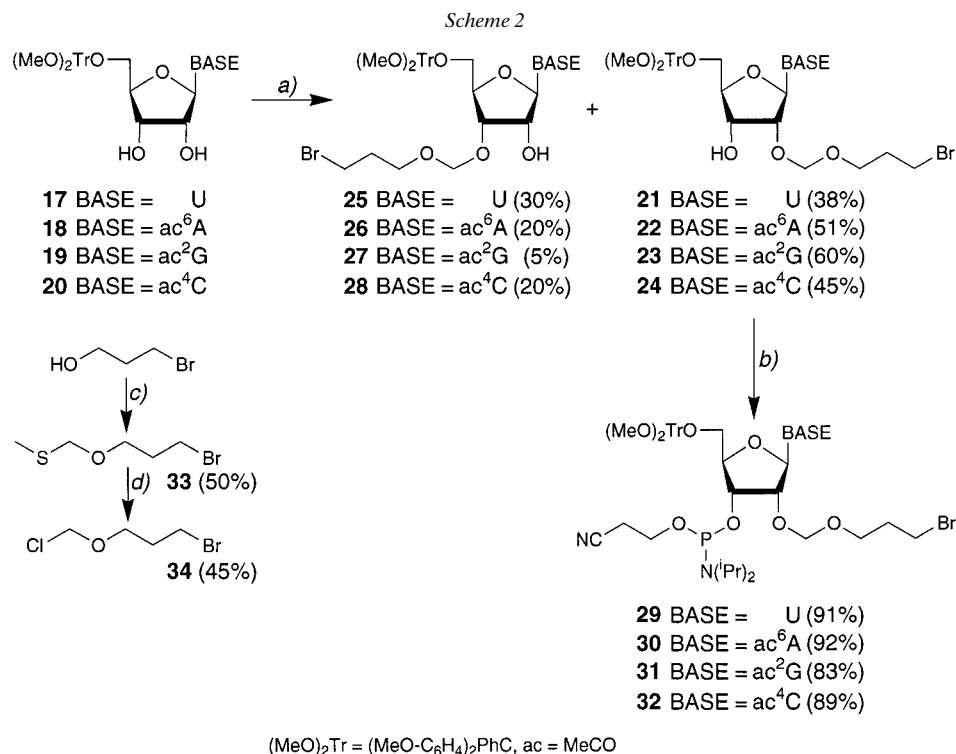


a) For **2**: 1) uracil, bis(trimethylsilyl)acetamide (BSA), then SnCl₄, 2) HF, HCl in H₂O/MeCN; for **3**: N⁶-benzoyladenine, BSA, then SnCl₄, 2) CF₃COOH, H₂O; for **4**: N²-acetylguanine, BSA, then Me₃Si-OTf, 2) HF, HCl in H₂O/MeCN. b) (MeO)₂Tr-Cl, AgNO₃, *sym*-collidine, then NaOH in THF/MeOH/H₂O. c) Bu₂SnCl₂, ⁱPr₂NEt, then tom-Cl. d) (ⁱPr₂N)₂P(O)Cl(OCH₂CH₂CN), ⁱPr₂NEt.

a) The synthesis of the analogous N⁴-acetylcytosine containing phosphoramidite is reported in [3] and [4].

2.2. *Synthesis of 2'-O-[(3-Bromopropoxy)methyl]-Substituted Ribonucleosides.* The reactive, 2'-O-substituted ribonucleosides **25**–**28** were prepared by alkylation of the 5'-O-dimethoxytritylated, base-protected nucleosides **17**–**20** with 1-bromo-3-(chloromethoxy)propane (**34**) according to the conditions we developed for the introduction of related, formaldehyde acetal based 2'-O-protecting groups [4][5][9]. The alkylating reagent **34** was prepared in two steps. From 3-bromopropanol the *O,S*-acetal **33** was prepared with DMSO, Ac₂O, and AcOH according to [10]. This intermediate was then converted to **34** with SO₂Cl₂ according to [11]. Treatment of the nucleosides **17**–**20** first with Bu₂SnCl₂/ⁱPr₂NEt and then with the alkylating agent **34** afforded mixtures of the corresponding 2'-O- and 3'-O-alkylated nucleosides **21**–**24** and **25**–**28**, respectively, which could be separated easily by chromatography (silica gel)³⁾. From the 2'-O-alkylated nucleosides **21**–**24**, the corresponding phosphoramidites **29**–**32** were prepared according to standard procedures.

³⁾ The correct position of the [(3-bromopropoxy)methyl] group was determined by ¹H-NMR spectroscopy according to [5]. See also *Footnote 2*.



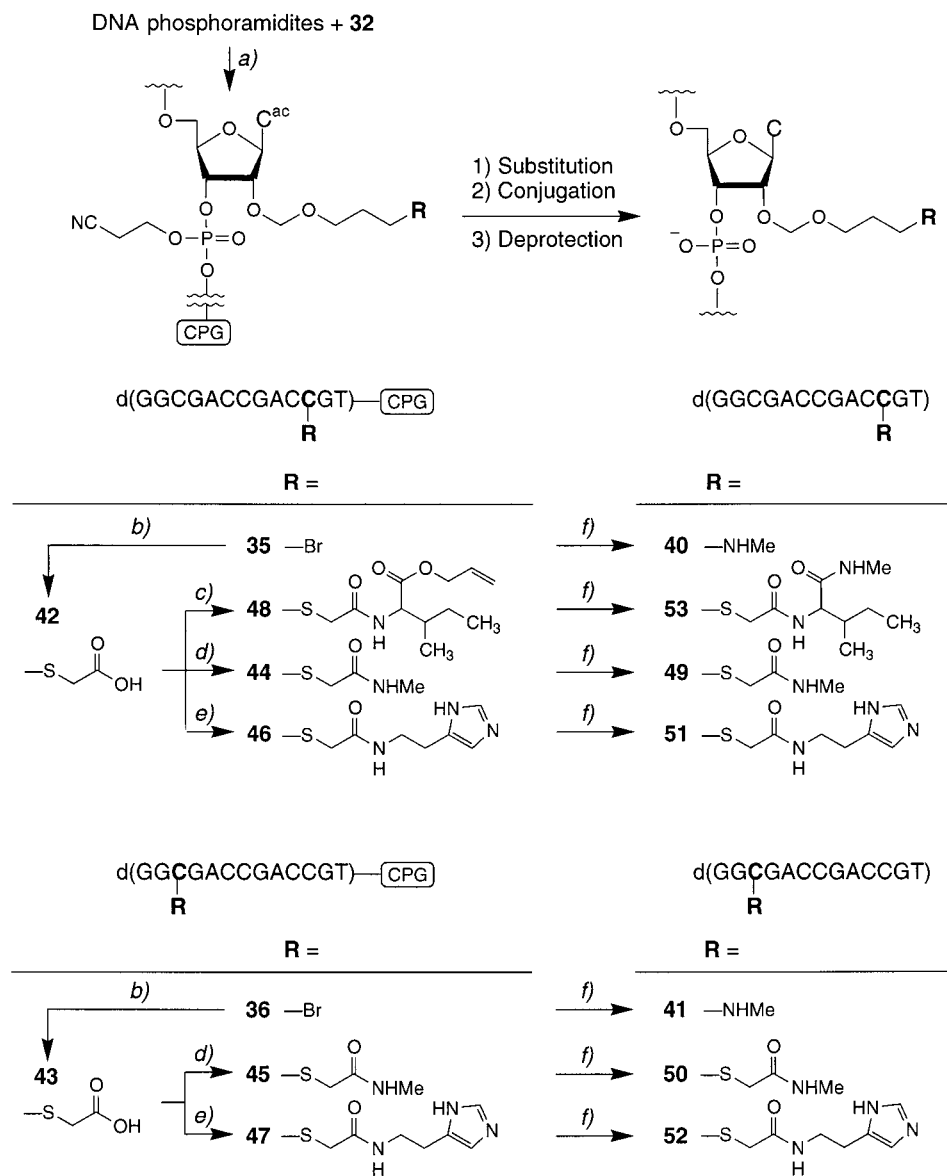
a) Bu₂SnCl₂, ⁱPr₂NEt, then **34**. b) (ⁱPr₂N)₂PCl(OCH₂CH₂CN), ⁱPr₂NEt. c) DMSO, Ac₂O, AcOH. d) SO₂Cl₂.

2.2. Solid-Phase Substitutions. Exploratory experiments were carried out to investigate the potential for solid-support functionalization of oligonucleotides containing 2'-O-[(3-bromopropoxy)methyl]substituted ribonucleosides and to collect some information about the influence of such additional substituents on the pairing behavior.

The 2'-O-[(3-bromopropoxy)methyl]-substituted cytidine phosphoramidite **32** was incorporated into a tetradecameric DNA sequence at two positions, once near the 3'-end (→**35**) and once near the 5'-end (→**36**), respectively (*Scheme 3* and *Table 1*). Under our conditions (which were developed for the assembly of RNA sequences [3][9]), the coupling yields were >99% for the standard DNA phosphoramidites and 98% for the modified phosphoramidite **32** (*Scheme 3*). As a comparison and for comparative duplex-stability studies, the corresponding DNA sequence **37** and the complementary DNA and RNA sequences **38** and **39**, respectively, were prepared as well (*Table 1*).

Small portions of the immobilized oligonucleotides **35** and **36** were then treated with 10M MeNH₂ in H₂O/EtOH 1:1 (*Scheme 3*). In *Fig. 1*, the HPLC trace of such a crude product is presented together with the chromatogram of the analogous unmodified DNA sequence **37**. According to this analysis, from sequence **35**, a dominant main product (with essentially the same retention time as the unmodified DNA sequence **37**) was formed, together with a small by-product. The main product

Scheme 3



CPG = long chain alkylamino controlled pore glass

a) Oligonucleotide assembly, see *Exper. Part*. b) HSCH₂COOH, ⁱPr₂NEt. c) HOBT, TBTU, ⁱPr₂NEt, L-isoleucine allyl ester. d) HOBT, TBTU, ⁱPr₂NEt, MeNH₂. e) HOBT, TBTU, ⁱPr₂NEt, histamine. f) MeNH₂.

Table 1. Characterization of Functionalized Oligonucleotides

Sequence ^{a)}	Product ratio ^{b)} [%]	Yield ^{c)} [%]	T_m ^{d)} [°]	[M – H] ^{-e)}	
				calc.	obs.
40 d(GGCGACCGACWGT)	90	45	67	4078	4081
41 d(GGWGACCGACCGT)	90	40	67	4078	4080
49 d(GGCGACCGACXGT)	70	40	67	4152	4153
50 d(GGXGACCGACCGT)	75	40	66	4152	4153
51 d(GGCGACCGACYGT)	75	35	68	4232	4234
52 d(GGYGACCGACCGT)	65	30	68	4232	4235
53 d(GGCGACCGACZGT)	55	25	67	4265	4265
37 d(GGCGACCGACCGT)		60	68	3960	3959
38 d(ACGGTCGGTCGCC)		55		3952	3951
39 r(ACGGUCGGUCGCC)		30		4129	4130

^{a)} For the structure of **W**, **X**, **Y**, and **Z**, see *Scheme 3*. ^{b)} Area-% (HPLC, capillary electrophoresis (CE)) of product signal. ^{c)} After purification by ion-exchange HPLC; by CE, the purity was estimated >95%. ^{d)} With the RNA sequence **39** as complement; conditions: *c* (sequences) = 1 + 1 μ M, 150 mM NaCl, 2 mM MgCl₂, 10 mM Tris · HCl (pH 7.4). ^{e)} MALDI-TOF-MS; matrix, 2,4-dihydroxyacetophenone (ammonium citrate) according to [12].

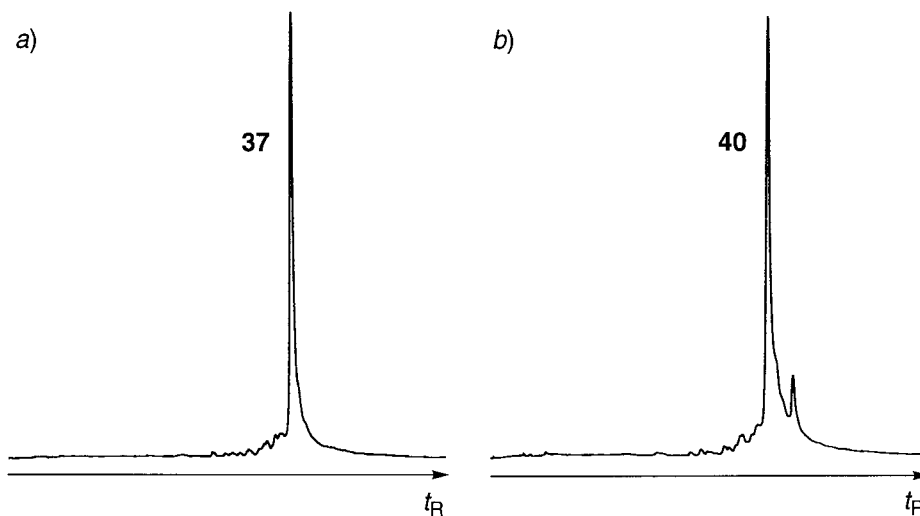


Fig. 1. Reversed-phase HPLC traces from crude sequences: a) parent DNA sequence **37**; b) (methylamino)-substituted DNA sequence **40**. Elution with A → 20% B in 30 min, measured at 260 nm (see *Exper. Part*).

was isolated by prep. HPLC and identified by MALDI-TOF mass spectrometry as the (methylamino)-substituted sequence **40** (*Table 1*).

Further solid-support functionalizations were carried out according to protocols that we developed earlier [4] (*Scheme 3*). The immobilized sequences **35** and **36** were treated with thioglycolic acid (= mercaptoacetic acid) in the presence of iPr_2NEt_3 , and the resulting intermediates **42** and **43** (now containing a reactive carboxy group) were treated under peptide-coupling conditions with MeNH₂, histamine, and L-isoleucine allyl ester, respectively. After deprotection of the intermediates **44**–**48** with MeNH₂ in EtOH/H₂O 1:1, the main products **49**–**53** were isolated by HPLC and analyzed by

MALDI-TOF-MS (Table 1). According to HPLC and capillary electrophoresis (CE) of the crude products, the efficiency of the overall functionalization procedures was in the range of 55–75%. Fig. 2 shows the CE chromatogram of the crude histamine-substituted sequence **51** (Fig. 2,a); this sequence was formed in an overall efficiency of ca. 75% and could be isolated in pure form by ion-exchange chromatography (Fig. 2,b).

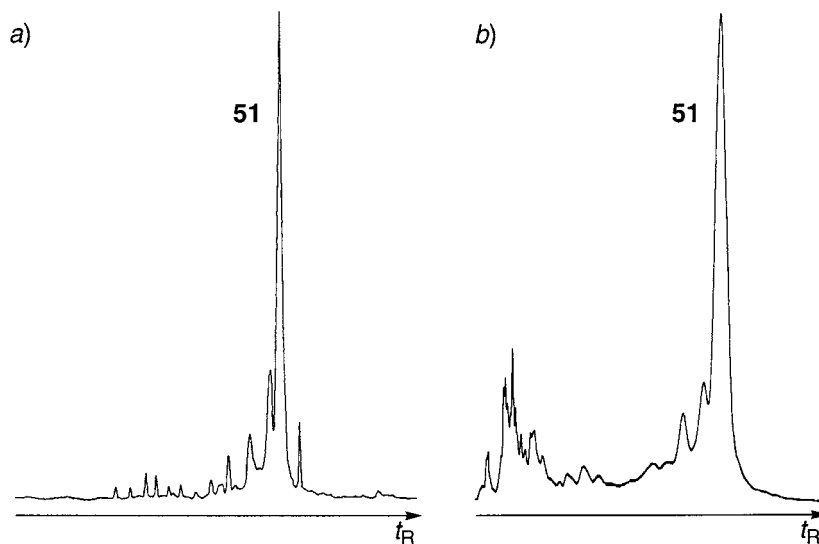


Fig. 2. a) Capillary-electrophoresis (CE) trace of crude histamine-substituted sequence **51** (conditions, see [9], measured at 260 nm); b) ion-exchange HPLC trace of crude **51** obtained from a preparative run (elution with 25% B \rightarrow 40% B in 30 min, measured at 260 nm) (see *Exper. Part*).

2.4. Thermal-Denaturation Study. In Table 1, the transition temperatures (T_m) of the duplexes formed from the functionalized sequences **40**, **41**, and **49–53** and the complementary RNA sequence **39** are presented. Under physiological conditions (150 mM NaCl, 2 mM MgCl₂, pH 7.4), the modified duplexes had similar or slightly lower T_m values than the unmodified duplex **37·39**. A more detailed study was carried out with the two histamine-substituted sequences **51** and **52** (Table 2). Their duplexes with the complementary DNA sequence were significantly destabilized (as compared to the corresponding unmodified DNA duplex **37·38**). The ΔG^0 values for duplex formation of the modified DNA·RNA duplexes **51·39** and **52·39**, respectively, were more negative ($\Delta\Delta G^0 = -0.9$ and -2.8 kcal mol⁻¹, resp.) than the corresponding value of the parent DNA·RNA duplex **37·39**. In contrast to these results, the corresponding DNA·DNA duplexes **51·38** and **52·38** showed more positive ΔG^0 values than the parent DNA·DNA duplex **37·38**.

Fig. 3 illustrates the position of the additional imidazole moieties within the DNA·RNA duplexes **51·39** and **52·39**, respectively. In duplex **51·39**, the additional functional group is near the 3'-end of the modified DNA sequence and is pointing into solution, whereas in duplex **52·39**, the additional functional group is near the 5'-end and located within the minor groove of the duplex. The T_m values and the thermodynamic data reflect a higher stability of the latter duplex, indicating a positive

Table 2. Thermodynamic Parameters of Duplex Formation^{a)}

	T_m^b [°C]	ΔH^0 [kcal mol ⁻¹]	$T\Delta S^0$ (298 K) [kcal mol ⁻¹]	ΔG^0 (298 K) [kcal mol ⁻¹]	$\Delta\Delta G^0$ (298 K) ^{c)} [kcal mol ⁻¹]
37·39	68.0	-110.8	-88.0	-22.8	
51·39	68.0	-116.9	-93.2	-23.7	-0.9
52·39	67.8	-131.9	-106.3	-25.6	-2.8
37·38	65.2	-98.1	-77.6	-20.5	
51·38	63.6	-99.3	-79.1	-20.2	+0.3
52·38	62.1	-90.7	-71.7	-19.0	+1.5

^{a)} In 150 mM NaCl, 2 mM MgCl₂, and 10 mM Tris·HCl (pH 7.4); thermodynamic parameters and transition temperatures were determined according to [13] (the exper. error was estimated to be ±5%).

^{b)} $c(\text{sequences}) = 1 + 1 \mu\text{M}$. ^{c)} Difference between the ΔG^0 value of the modified and the parent duplex.

interaction between the RNA strand **39** and the imidazole moiety on the modified DNA strand **52** (located in the minor groove). In the analogous duplexes with the complementary DNA strands, however, a duplex destabilization by the additional imidazole moieties was observed, and this destabilization was more important when the substituents were located in the minor groove. This difference is probably the

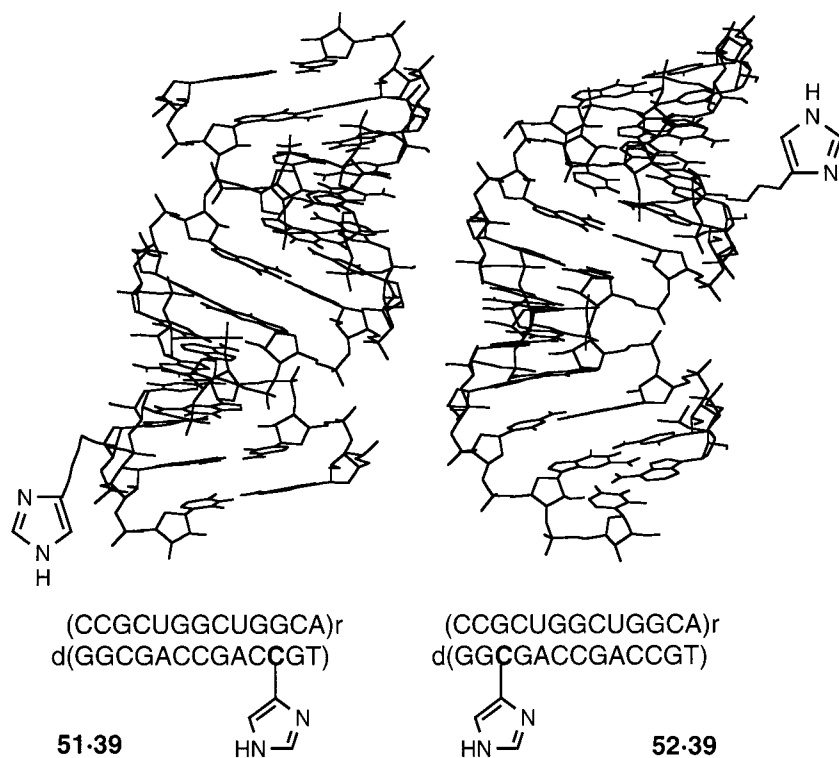


Fig. 3. Pictures of modified A-type DNA·RNA duplexes **51·39** and **52·39**, illustrating the position of the additional histamine substituent. The duplex was constructed with 'MacroModel', and the substituent was added without further minimization.

consequence of a disturbance of the hydration shell within the DNA·DNA duplex **52**·**38**⁴).

In conclusion, we present novel reactive building blocks that allow the introduction of a variety of functional groups by substitution and subsequent conjugation on the solid phase according to [3]. These building blocks are fully compatible with common procedures employed for the automated assembly of DNA and RNA oligonucleotides and can be introduced by every desired position within a sequence.

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Experimental Part

General. Reagents and solvents from *Fluka*: (MeO)₂Tr-Cl, tom-Cl, nucleosides **17**–**20**, BnSTet, and tom-phosphoramidites [9] from *Xeragon AG*; standard DNA phosphoramidites (containing thymine, *N*⁶-(phenoxyacetyl)guanine, *N*²-[4-isopropylphenoxyacetyl]guanine, and *N*⁴-acetylcytosine) and CPG supports from *Glen Research*; *N*²-acetylguanine [15] and *N*⁶-benzoyladenine [16] were prepared according to published procedures. Workup implies distribution of the reaction mixture between CH₂Cl₂ and sat. aq. NaHCO₃ soln., drying (MgSO₄) of the org. layer, and evaporation. Column chromatography (CC): silica gel from *Macherey & Nagel*, Al₂O₃ (act. III) from *Woelm*. TLC: precoated silica gel plates from *Macherey & Nagel*, stained by dipping into a soln. of anisaldehyde (10 ml; *Aldrich*), H₂SO₄ soln. (10 ml), and AcOH (2 ml) in EtOH (180 ml) and subsequent heating with a heat-gun. Reversed-phase HPLC: *Aquapore RP 300*, 4.6 × 220 mm (*Brownlee Labs*); eluent *A* 0.1M (Et₃NH)OAc in H₂O, pH 7, and eluent *B* MeCN; flow 1 ml/min; detection at 260 nm, elution at 40°. Ion-exchange HPLC: *Mono Q HR 5/5* (*Pharmacia*); eluent *A*, 10 mM sodium phosphate in H₂O, pH 11.5, and eluent *B*, 10 mM sodium phosphate/1M NaCl in H₂O, pH 11.5; flow 1 ml/min; detection at 260 nm, elution at r.t. M.p.: uncorrected. UV Spectra: λ_{max} (ε) in nm. IR Spectra: ν̄ in cm⁻¹. NMR Spectra: chemical shifts δ in ppm and coupling constants *J* in Hz. FAB-MS: positive mode; 2-nitrobenzyl alcohol (NOBA) as matrix; *m/z* (rel. %). MALDI-TOF-MS: according to [12]. Abbreviations: (MeO)₂Tr-Cl = 4,4'-dimethoxytrityl chloride, tom-Cl = (triisopropylsilyloxy)methyl chloride, BSA = bis(trimethylsilyl)acetamide, BnSTet = 1-(benzylthio)-1*H*-tetrazole, HOBT = 1-hydroxy-1*H*-benzotriazole, TBTU = *O*-(benzotriazole-1-yl)-*N,N,N',N'*-tetramethyluronium tetrafluoroborate, CPG = long-chain alkylamino controlled pore glass.

Thermal-Denaturation Studies. Absorbance vs. temperature profiles were recorded in fused quartz cuvettes at 260 nm on a *Cary Bio-1* spectrophotometer equipped with a *Peltier* temperature-controlling device. The samples were prepared under sterile conditions from stock solns. of the oligonucleotide, 1M *Tris*·HCl buffer (pH 7.4), 5M NaCl, and 50 mM MgCl₂ and subsequently degassed. A layer of silicon oil was placed on the surface of the soln. Prior to the measurements, each sample was briefly heated to 80°. The curves were obtained with both a cooling and heating ramp of 0.3°/min. The transition temperatures (*T*_m) were obtained after differentiation of the melting curves.

General Procedure (G.P.) for the Preparation of Phosphoramidites 14–16 and 29–32. At r.t., 0.3M precursor nucleoside in CH₂Cl₂ was treated consecutively with 2.5 equiv. of ³Pr₂NEt and 1.2 equiv. of (³Pr₂N)₂PCl(OCH₂CH₂CN). After 12–16 h at r.t., the mixture was subjected to CC.

1-[6'-*O*-(5-Bromopentyl)-2',3'-*di-O*-benzoyl-β-D-*allofuranosyl*]uracil (**2**). A suspension of **1** [4] (3.2 g, 4.0 mmol), uracil (0.5 g, 4.4 mmol), and BSA (2.5 ml, 10 mmol) in MeCN (12 ml) was stirred at 60° for 30 min. Then, SnCl₄ (1.7 ml, 14 mmol) was added to the clear soln., which was kept at 60° for another 20 min. After workup, the residue was dissolved in MeCN (80 ml), treated with conc. HCl soln. (0.8 ml) and 40% HF in H₂O (1.6 ml), and stirred at r.t. for 8 h. Workup and CC (silica gel, hexane/AcOEt 7:3 → 3:7) gave **2** (1.78 g, 75%). White foam. TLC (hexane/AcOEt 3:7): *R*_f 0.40. [α]_D²⁵ = –86.0 (*c* = 1.0, CHCl₃). UV (MeOH): 257 (12000), 251 (11700), 229 (29000), 216 (23300). IR (CHCl₃): 3619w, 3392w, 3014m, 2975w, 3939w, 1727s, 1700s, 1602m, 1453m, 1392w, 1317m, 1262s, 1222m, 1178w, 1126m, 1094m, 1070w, 1046m, 877w. ¹H-NMR (300 MHz, CDCl₃): 1.47–1.65 (*m*, BrCH₂(CH₂)₂); 1.82–1.89 (*m*, Br(CH₂)₃CH₂); 3.23 (*d*, *J* = 1.9, OH–C(4')); 3.39 (*t*, *J* = 6.9,

⁴) For the influence of one 2'-*O*-Me substituent within a DNA sequence on the minor-groove hydration, see [14].

BrCH₂); 3.52–3.57 (*m*, CH₂O); 3.65 (*br. d.*, *J* ≈ 5.9, 2 H–C(6')); 4.20–4.23 (*m*, H–C(5')); 4.37 (*br. s.*, H–C(4')); 5.75 (*dd*, *J* = 5.6, 7.5, H–C(2')); 5.83 (*d*, *J* = 8.1, H–C(5)); 5.89 (*dd*, *J* = 1.5, 5.6, H–C(3')); 6.50 (*d*, *J* = 7.5, H–C(1')); 7.32–7.61 (*m*, 6 arom. H); 7.90–8.04 (*m*, 4 arom. H, H–C(6)); 8.18 (*s*, NH–C(3)). ¹³C-NMR (75 MHz, CDCl₃): 24.8 (*t*, Br(CH₂)₂CH₂); 28.7 (*t*, BrCH₂CH₂); 32.5 (*t*, Br(CH₂)₃CH₂); 33.7 (*t*, BrCH₂); 71.0, 71.1 (*2t*, C(6'), CH₂O); 71.4, 71.8, 74.0 (*3d*, C(2'), C(3'), C(5')); 84.6 (*d*, C(4')); 86.3 (*br. d.*, C(1')); 103.6 (*d*, C(5)); 123.4 (*s*, C(5)); 128.4, 128.5, 128.6, 129.8, 129.9 (*5d*, arom. C); 129.0, 133.71, 133.74 (*3s*, arom. C); 140.5 (*d*, C(6)); 150.7 (*s*, C(2)); 163.0 (*s*, C(4)), 165.3, 165.5 (*2s*, CO); FAB-MS: 1263 (*26*, [M₂ + H]⁺), 633 (*10*, [M + H]⁺), 631 (*12*, [M + H]⁺), 521 (*79*), 519 (*76*). Anal. calc. for C₂₉H₃₁BrN₂O₉ (631.48): C 55.16, H 4.95, N 4.44; found: C 55.25, H 4.93, N 4.45.

*N*⁶-Benzoyl-9-[2',3'-di-O-benzoyl-6'-O-(5-bromopentyl)-β-D-allofuranosyl]adenine (**3**). A suspension of **1** [**4**] (3.2 g, 4.0 mmol), *N*⁶-benzoyladenine (1.14 g, 4.8 mmol), and BSA (3.5 ml, 14 mmol) in MeCN (12 ml) was stirred at 60° for 1 h. Then, SnCl₄ (1.9 ml, 20 mmol) was added to the clear soln., which was kept at 60° for another 20 min. After workup, the residue was dissolved in CF₃COOH/H₂O 1:1 (80 ml) and stirred at r.t. for 12 h. Workup and CC (silica gel, hexane/AcOEt 8:2 → 4:6) gave **3** (1.13 g, 45%). White foam. TLC (hexane/AcOEt 3:7): R_f 0.31. [α]_D²⁵ = –145.3 (*c* = 1.0, CHCl₃). UV (MeOH): 280 (21900), 254 (12600), 231 (32800). IR (CHCl₃): 3619w, 3014m, 2976w, 1730s, 1612m, 1590m, 1481w, 1457m, 1272s, 1245s, 1178w, 1123m, 1092m, 908w, 877w. ¹H-NMR (300 MHz, CDCl₃): 1.42–1.52, 1.57–1.66 (*m*, BrCH₂(CH₂)₂); 1.78–1.88 (*m*, Br(CH₂)₃CH₂); 3.33 (*t*, *J* = 6.8, BrCH₂); 3.55 (*t*, *J* = 6.2, CH₂O); 3.69–3.80 (*m*, 2 H–C(6')); 4.28–4.31 (*m*, H–C(5')); 4.67 (*br. s.*, H–C(4')); 6.16 (*dd*, *J* = 1.2, 5.0, H–C(3')); 6.19 (*d*, *J* = 2.5, OH–C(5')); 6.35–6.43 (*m*, H–C(1'), H–C(2')); 7.26–7.65 (*m*, 9 arom. H); 7.79–8.10 (*m*, 6 arom. H); 8.18 (*s*, H–C(2)); 8.86 (*s*, H–C(8)); 9.10 (*br. s.*, NH–C(6)). ¹³C-NMR (75 MHz, CDCl₃): 24.9 (*t*, Br(CH₂)₂CH₂); 28.7 (*t*, BrCH₂CH₂); 32.6 (*t*, Br(CH₂)₃CH₂); 33.7 (*t*, BrCH₂); 70.8, 71.9, 73.7 (*3d*, C(2'), C(3'), C(5')); 71.1, 71.5 (*2t*, C(6'), CH₂O); 87.2, 88.2 (*br. d.*, C(1'), C(4')); 123.4 (*s*, C(5)); 127.9, 128.5, 128.7, 128.9, 129.8, 133.0 (*6d*, arom. C); 128.3, 129.3, 133.5 (*3s*, arom. C); 133.7 (*d*, arom. C); 142.4 (*d*, C(8)); 150.4 (*s*, C(4)); 151.0 (*s*, C(6)); 152.6 (*d*, C(2)); 164.3, 164.8, 165.2 (*3s*, CO). FAB-MS: 761 (45, [M + H]⁺), 760 (100, M⁺), 759 (45, [M + H]⁺), 758 (87, M⁺), 519 (58), 105 (64).

1-[6'-O-(5-Bromopentyl)-5'-O-(4,4'-dimethoxytrityl)-β-D-allofuranosyl]uracil (**5**). A suspension of **2** (1.78 g, 2.8 mmol), AgNO₃ (476 mg, 2.8 mmol), and *syn*-collidine (0.93 ml, 7 mmol) in CH₂Cl₂ (10 ml) was treated with (MeO)₂Tr-Cl (1.42 g, 4.2 mmol) at r.t. for 1 h. After filtration and evaporation, the residue was dissolved in an ice-cold soln. of THF/MeOH/H₂O 5:4:1 (40 ml), treated with 10N aq. NaOH (0.8 ml), stirred at r.t. for 30 min, neutralized with AcOH (0.48 ml), and concentrated to 10 ml. Workup and CC (silica gel, CH₂Cl₂ (+2% Et₃N) → CH₂Cl₂/MeOH 97:3 (+2% Et₃N)) gave **5** (1.69 g, 87%). White foam. TLC (CH₂Cl₂/MeOH 92:8): R_f 0.45. [α]_D²⁵ = 31.8 (*c* = 1.0, CHCl₃). UV (MeOH): 269 (9500), 235 (21400), 227 (19700). IR (CHCl₃): 3622w, 3390w, 3029m, 1691s, 1608s, 1509m, 1461m, 1391w, 1302w, 1253s, 1226m, 1178m, 1107m, 1036s, 909w, 877w, 828w. ¹H-NMR (300 MHz, CDCl₃): 1.55–1.69 (*m*, BrCH₂(CH₂)₂); 1.90–1.94 (*m*, Br(CH₂)₃CH₂); 3.17–3.41 (*m*, CH₂O, 2 H–C(6'), OH); 3.45 (*t*, *J* = 6.5, BrCH₂); 3.60 (*br. s.*, H–C(5')); 3.795, 3.798 (*2s*, MeO); 4.01 (*dd*, *J* = 1.5, 7.5, H–C(4')); 4.16 (*dd*, *J* = 4.4, 5.6, H–C(2')); 4.69 (*dd*, *J* = 5.6, 7.5, H–C(3')); 4.88 (*d*, *J* = 8.1, H–C(5)); 5.86 (*d*, *J* = 4.4, H–C(1')); 6.82–6.86 (*m*, 4 arom. H); 7.22–7.53 (*m*, 9 arom. H, H–C(6)). ¹³C-NMR (75 MHz, CDCl₃): 27.7 (*t*, Br(CH₂)₂CH₂); 28.8 (*t*, BrCH₂CH₂); 32.2 (*t*, Br(CH₂)₃CH₂); 33.8 (*t*, BrCH₂); 55.3 (*q*, MeO); 70.7, 71.3, (*2t*, C(6')); 68.1, 71.5, 75.5 (*3d*, C(2'), C(3'), C(5)); 85.6 (*d*, C(4')); 87.9 (*s*, Ar₂C(Ph)); 89.2 (*d*, C(1')); 103.6 (*d*, C(5)); 113.3, 113.4 (*2d*, arom. C); 127.1, 127.7, 128.1, 128.4, 130.1, 130.6 (*6d*, arom. C); 135.6, 135.9 (*2s*, arom. C); 140.2 (*d*, C(6)); 146.3 (*s*, arom. C); 150.3 (*s*, C(2)); 158.7, 158.8 (*2s*, MeO–C); 163.1 (*s*, C(4)). FAB-MS: 747 (33), 746 (53), 727 (2, M⁺), 725 (2, M⁺), 303 (100).

*N*⁶-Benzoyl-9-[6'-O-(5-bromopentyl)-5'-O-(4,4'-dimethoxytrityl)-β-D-allofuranosyl]adenine (**6**). A suspension of **3** (1.13 g, 1.5 mmol), AgNO₃ (255 mg, 1.5 mmol), and *sym*-collidine (0.5 ml, 3.8 mmol) in CH₂Cl₂ (5 ml) was treated with (MeO)₂Tr-Cl (0.78 g, 2.3 mmol) at r.t. for 3 h. After filtration and evaporation, the residue was dissolved in an ice-cold soln. of THF/MeOH/H₂O 5:4:1 (40 ml), treated with 10N aq. NaOH (0.8 ml), stirred at 4° for 15 min, neutralized with AcOH (0.48 ml), and concentrated to 10 ml. Workup and CC (silica gel, CH₂Cl₂ (+2% Et₃N) → CH₂Cl₂/MeOH 97:3 (+2% Et₃N)) gave **6** (1.13 g, 92%). Pale yellow foam. TLC (CH₂Cl₂/MeOH 95:5): R_f 0.29. [α]_D²⁵ = –14.0 (*c* = 1.0, CHCl₃). UV (MeOH): 278 (18800), 256 (11200), 232 (29100), 224 (27900). IR (CHCl₃): 3622w, 3113w, 2975w, 1709m, 1611s, 1585w, 1509m, 1454m, 1299w, 1251s, 1179m, 1046s, 877w, 829w. ¹H-NMR (300 MHz, CDCl₃): 1.52–1.60 (*m*, BrCH₂(CH₂)₂); 1.83–1.91 (*m*, Br(CH₂)₃CH₂); 3.09–3.13 (*m*, H–C(6')); 3.18–3.25 (*m*, CH₂O, H'–C(6')); 3.43 (*t*, *J* = 6.8, BrCH₂); 3.64–3.65 (*m*, H–C(5')); 3.75, 3.76 (*2s*, MeO); 4.27 (*dd*, *J* = 3.5, 5.0, H–C(4')); 4.67 (*dd*, *J* = 4.6, 5.3, H–C(2')); 4.87 (*br. t.*, *J* ≈ 5.3, H–C(3')); 5.96 (*d*, *J* = 4.4, H–C(1')); 6.70–6.78 (*m*, 4 arom. H); 7.17–7.61 (*m*, 12 arom. H); 7.96 (*s*, H–C(2)); 8.01–8.04 (*m*, 2 arom. H); 8.72 (*s*, H–C(8)); 9.08 (*br. s.*, NH–C(6)). ¹³C-NMR (75 MHz, CDCl₃): 24.8 (*t*, Br(CH₂)₂CH₂); 28.8 (*t*, BrCH₂CH₂); 32.5 (*t*, Br(CH₂)₃CH₂); 33.7 (*t*, BrCH₂); 55.3 (*q*, MeO); 70.1, 71.1 (*2t*, C(6')); 70.0, 72.1, 74.7

(3*d*, C(2'), C(3'), C(5)); 86.3 (*d*, C(4'), CH₂O); 87.2 (*s*, Ar₂CPh); 89.3 (*d*, C(1')); 113.1 (*d*, arom. C); 123.0 (*s*, C(5)); 128.4 (*s*, arom. C); 126.9, 127.7, 127.9, 128.1, 128.9, 130.3, 130.4, 132.8 (8*d*, arom. C); 133.6, 136.2, 136.5 (3*s*, arom. C); 141.7 (*d*, C(8)); 145.9 (*s*, arom. C); 149.6 (*s*, C(4)); 151.2 (*s*, C(6)); 152.4 (*d*, C(2)); 158.6, 159.7 (2*s*, MeO–C); 164.3 (*s*, CO). FAB-MS: 855 (22, [M + H]⁺), 854 (37, M⁺), 853 (21, [M + H]⁺), 852 (33, M⁺), 303 (100).

N²-Acetyl-9-[6'-O-(5-bromopentyl)-5'-O-(4,4'-dimethoxytrityl)-β-D-allofuranosyl]guanine (N⁹-7) and N²-Acetyl-7-[6'-O-(5-bromopentyl)-5'-O-(4,4'-dimethoxytrityl)-β-D-allofuranosyl]guanine (N⁷-7). A suspension of **1** [4] (4.0 g, 5.0 mmol), N²-acetylguanine (1.6 g, 7.5 mmol), and BSA (6 ml, 25 mmol) in (CH₂)Cl₂ (15 ml) was stirred at 80° for 1 h. Then Me₃Si–OSO₂CF₃ (8.1 ml, 45 mmol) was added to the clear soln., which was kept at 80° for another 4 h. After workup, the residue was dissolved in MeCN (100 ml), treated with conc. HCl soln. (1 ml) and 40% HF in H₂O (2 ml), and stirred at r.t. for 4 h. Workup and a filtration over silica gel gave a mixture of N⁷- and N⁹-nucleoside derivatives. The mixture (1.53 g, 2.0 mmol) was dissolved in CH₂Cl₂ (12 ml) and treated with *sym*-collidine (0.67 ml, 5 mmol), AgNO₃ (340 mg, 2 mmol), and (MeO)₂Tr–Cl (1.2 g, 3.6 mmol). The suspension was stirred at r.t. for 4 h. After filtration and evaporation, the residue was dissolved in an ice-cold soln. of THF/MeOH/H₂O 5 : 4 : 1 (50 ml), treated with 10*N* aq. NaOH (1 ml), stirred at 4° for 15 min, neutralized with AcOH (0.6 ml), and concentrated to 10 ml. Workup and CC (silica gel, CH₂Cl₂ (+2% Et₃N) → CH₂Cl₂/MeOH 97:3 (+2% Et₃N)) gave **42** (0.95 g, 25%) and **43** (0.56 g, 14%) as yellow foams.

Data of N⁹-7: TLC (CH₂Cl₂/MeOH 90 : 10): R_f 0.32. [α]_D²⁵ = –26.2 (*c* = 1.0, CHCl₃). UV (MeOH): 275 (9300), 236 (19000), 225 (16700). IR (CHCl₃): 3620*w*, 3022*m*, 2937*w*, 1687*m*, 1609*s*, 1562*m*, 1509*m*, 1403*m*, 1375*w*, 1302*m*, 1252*w*, 1178*w*, 1118*w*, 1037*s*, 877*w*, 826*w*. ¹H-NMR (300 MHz, CDCl₃): 1.40–1.47 (*m*, BrCH₂(CH₂)₂); 1.80–1.84 (*m*, Br(CH₂)₃CH₂); 2.30 (*s*, Ac); 3.02–3.23 (*m*, CH₂O, 2 H–C(6')); 3.37 (*t*, *J* = 6.7, BrCH₂); 3.48–3.52 (*m*, H–C(5'), OH); 3.71, 3.73 (2*s*, MeO); 4.31–4.33 (*m*, H–C(4')); 4.51–4.54 (*m*, H–C(3')); 4.73–4.75 (*m*, H–C(2')); 5.76 (*d*, *J* = 5.6, H–C(1')); 6.70–6.76 (*m*, 4 arom. H); 7.13–7.45 (*m*, 9 arom. H); 7.58 (*s*, H–C(8)). ¹³C-NMR (75 MHz, CDCl₃): 23.5 (*q*, MeCO); 24.8 (*t*, Br(CH₂)₂CH₂); 28.7 (*t*, BrCH₂CH₂); 32.5 (*t*, Br(CH₂)₃CH₂); 33.8 (*t*, BrCH₂); 55.2 (*q*, MeO); 69.7, 70.9 (2*t*, C(6'), CH₂O); 70.6, 72.4, 74.9 (3*d*, C(2'), C(3'), C(5')); 86.5 (*d*, C(4')); 87.2 (*s*, Ar₂C(Ph)); 89.1 (*d*, C(1')); 113.0 (*d*, arom. C); 120.7 (*s*, C(5)); 126.9, 127.7, 128.2, 128.3, 130.4, 130.5 (6*d*, arom. C); 136.2, 136.4 (2*s*, arom. C); 139.1 (*d*, C(8)); 145.9 (*s*, arom. C); 147.4 (*s*, C(4)); 148.2 (*s*, C(2)); 158.6, 158.7 (2*s*, MeO–C), 172.2 (*s*, CO). FAB-MS: 809 (28, [M + H]⁺), 808 (63, M⁺), 807 (34, [M + H]⁺), 806 (54, M⁺), 303 (100).

Data of N⁷-7: TLC (CH₂Cl₂/MeOH 95 : 5): R_f 0.29. [α]_D²⁵ = 39.7 (*c* = 1.0, CHCl₃). UV (MeOH): 264 (14600), 255 (14300), 223 (32300). IR (CHCl₃): 3622*w*, 3152*w*, 3013*m*, 2936*w*, 1679*s*, 1609*s*, 1548*w*, 1509*m*, 1444*w*, 1373*m*, 1301*w*, 1252*s*, 1178*m*, 1116*m*, 1038*m*, 877*w*, 829*w*. ¹H-NMR (300 MHz, CDCl₃): 1.45–1.56 (*m*, BrCH₂(CH₂)₂); 1.83–1.87 (*m*, Br(CH₂)₃CH₂); 2.39 (*s*, Ac), 3.16–3.21 (*m*, CH₂O, H–C(6')); 3.39 (*t*, *J* = 6.7, BrCH₂); 3.36–3.41 (*m*, H'–C(6')); 3.64–3.69 (*m*, H–C(5')); 3.75, 3.77 (2*s*, MeO); 4.24 (br. *t*, *J* ≈ 5.0, H–C(4')); 4.31 (br. *t*, *J* ≈ 4.0, H–C(3')); 4.66 (br. *t*, *J* ≈ 5.3, H–C(2')); 6.13 (*d*, *J* = 4.3, H–C(1')); 6.76–6.81 (*m*, 4 arom. H); 7.18–7.50 (*m*, 9 arom. H); 7.85 (*s*, H–C(8)), 11.02 (br. *s*, NH–C(6)); 12.41 (br. *s*, H–N(1)). ¹³C-NMR (75 MHz, CDCl₃): 24.5 (*q*, MeCO); 24.8 (*t*, Br(CH₂)₂CH₂); 28.7 (*t*, BrCH₂CH₂); 32.4 (*t*, Br(CH₂)₃CH₂); 33.7 (*t*, BrCH₂); 55.2 (*q*, MeO); 69.9, 71.0 (2*t*, C(6'), CH₂O); 70.1, 72.1, 77.4 (3*d*, C(2'), C(3'), C(5')); 86.2 (*d*, C(4')); 87.3 (*s*, Ar₂CPh); 91.5 (*d*, C(1')); 111.3 (*s*, C(5)); 113.0 (*d*, arom. C); 127.0, 127.8, 128.1, 128.3, 130.4, 130.5 (6*d*, arom. C); 136.1, 136.4 (2*s*, arom. C); 141.4 (*d*, C(8)); 145.9 (*s*, arom. C); 147.9 (*s*, C(4)); 153.4 (*s*, C(2)); 157.4 (*s*, C(6)), 158.6, 158.7 (2*s*, MeO–C), 173.5 (*s*, CO). FAB-MS: 809 (9, [M + H]⁺), 808 (12, M⁺), 807 (12, [M + H]⁺), 806 (19, M⁺), 303 (100).

1-[6'-O-(5-Bromopentyl)-5'-O-(4,4'-dimethoxytrityl)-2'-O-[(triisopropylsilyl)oxy]methyl]-β-D-allofuranosyl]uracil (**8**) and 1-[6'-O-(5-Bromopentyl)-5'-O-(4,4'-dimethoxytrityl)-3'-O-[(triisopropylsilyl)oxy]methyl]-β-D-allofuranosyl]uracil (**11**). A soln. of **5** (1.68 g, 2.4 mmol) and ¹Pr₂NEt (1.5 ml, 7 mmol) in (CH₂)Cl₂ (8 ml) was treated with Bu₂SnCl₂ (729 mg, 2.4 mmol) at r.t. for 1.5 h. Then, the mixture was heated to 80°, treated with toluene (700 mg, 3.1 mmol), and stirred at 75° for 15 min. Workup and CC (silica gel, hexane/AcOEt (+2% Et₃N)) 2 : 8 → 7 : 3 (+2% Et₃N) gave **8** (1.0 g, 48%) and **11** (480 mg, 23%). White foams.

Data of **8**: TLC (hexane/AcOEt 5 : 5): R_f 0.59. [α]_D²⁵ = 31.2 (*c* = 1.0, CHCl₃). UV (MeOH): 268 (9200), 235 (22500), 226 (20700). IR (CHCl₃): 3622*w*, 3391*w*, 3013*m*, 2945*m*, 1692*s*, 1608*w*, 1509*m*, 1462*m*, 1252*s*, 1224*s*, 1177*w*, 1038*s*, 996*w*, 881*w*. ¹H-NMR (300 MHz, CDCl₃): 1.05–1.11 (*m*, ¹Pr₃Si); 1.43–1.55 (*m*, BrCH₂(CH₂)₂); 1.77–1.87 (*m*, Br(CH₂)₃CH₂); 3.12–3.25 (*m*, 2 H–C(6'), CH₂O, OH–C(3')); 3.40 (*t*, *J* = 6.7, BrCH₂); 3.49–3.50 (*m*, H–C(5')); 3.80 (*s*, MeO); 4.10 (*dd*, *J* = 2.2, 4.0, H–C(4')); 4.16 (br. *t*, *J* = 5.6, H–C(3')); 4.74–4.77 (*m*, H–C(3')); 4.97, 5.17 (2*d*, *J* = 5.0, OCH₂O); 5.06 (*d*, *J* = 8.4, H–C(5)); 5.98 (*d*, *J* = 5.6, H–C(1')); 6.81–6.85 (*m*, 4 arom. H); 7.07–7.51 (*m*, 9 arom. H, H–C(6)); 8.05 (br. *s*, H–N(3)). ¹³C-NMR (75 MHz, CDCl₃): 11.9 (*d*, Me₂CH₃Si); 17.8 (*q*, (Me₂CH₃)₃Si); 24.8 (*t*, Br(CH₂)₂CH₂); 28.7 (*t*, BrCH₂CH₂); 32.5 (*t*, Br(CH₂)₃CH₂); 33.7

(*t*, BrCH₂); 55.3 (*q*, MeO); 69.7, 70.9 (2*t*, CH₂O, C(6')); 69.3, 72.6, 81.2 (3*d*, C(2'), C(3'), C(5')); 85.8, 86.0 (2*d*, C(1'), C(4')); 87.8 (*s*, Ar₂C(Ph)); 90.5 (*t*, OCH₂O); 102.3 (*d*, C(5)); 113.2, 113.3 (2*d*, arom. C); 127.1, 128.0, 130.2, 130.6 (4*d*, arom. C); 135.8, 135.9 (2*s*, arom. C); 140.2 (*d*, C(6)); 146.3 (*s*, arom. C); 150.2 (*s*, C(6)); 158.7, 158.8 (2*s*, MeO–C); 162.9 (*s*, C(4)). FAB-MS: 913 (7, M⁺), 912 (4, [M–H]⁺), 911 (7, M⁺), 910 (4, [M–H]⁺), 303 (100).

Data of 11: TLC (hexane/AcOEt 5 : 5): R_f 0.48. [α]_D²⁵ = –41.5 (*c* = 1.0, CHCl₃). UV (MeOH): 268 (7800), 235 (21700), 227 (20200). IR (CHCl₃): 3620*w*, 3391*w*, 3018*m*, 2945*m*, 1716*m*, 1694*s*, 1608*w*, 1509*m*, 1462*m*, 1390*w*, 1299*w*, 1252*s*, 1226*m*, 1178*s*, 1076*m*, 1036*s*, 881*w*. ¹H-NMR (300 MHz, CDCl₃): 1.10–1.14 (*m*, ⁱPr₃Si); 1.44–1.54 (*m*, BrCH₂(CH₂)₂); 1.83–1.87 (*m*, Br(CH₂)₃CH₂); 3.10–3.20 (*m*, H–C(6'), CH₂O); 3.31–3.38 (*m*, H–C(5'), H'–C(6')); 3.41 (*t*, *J* = 6.8, BrCH₂); 3.79, 3.80 (2*s*, MeO); 3.80 (*d*, *J* = 7.5, OH–C(2')); 4.08–4.11 (*m*, H–C(4')); 4.18–4.19 (*m*, H–C(2')); 4.70 (*dd*, *J* = 2.2, 5.9, H–C(3')); 4.94, 5.20 (2*d*, *J* = 5.7, OCH₂O); 5.19 (*d*, *J* = 7.8, H–C(5)); 5.85 (*d*, *J* = 7.5, H–C(1')); 6.81–6.86 (*m*, 4 arom. H); 7.21–7.49 (*m*, 9 arom. H, H–C(6')); 8.44 (*br. s*, H–N(3)). ¹³C-NMR (75 MHz, CDCl₃): 11.9 (*d*, (Me₂CH)₃Si); 17.8 (*q*, (Me₂CH)₃Si); 24.8 (*t*, Br(CH₂)₂CH₂); 28.9 (*t*, BrCH₂CH₂); 32.5 (*t*, Br(CH₂)₃CH₂); 33.6 (*t*, BrCH₂); 55.3 (*q*, MeO); 69.7, 70.9 (2*t*, CH₂O, C(6)); 71.0, 72.9, 79.2 (3*d*, C(2'), C(3'), C(5')); 84.6, 87.1 (2*d*, C(4'), C(1')); 87.8 (*s*, Ar₂C(Ph)); 90.7 (*t*, OCH₂O); 102.5 (*d*, C(5)); 113.2, 113.3 (2*d*, arom. C); 127.1, 128.0, 130.3, 130.5 (4*d*, arom. C); 135.8, 136.1 (2*s*, arom. C); 140.2 (*d*, C(6)); 146.2 (*s*, arom. C); 150.5 (*s*, C(6)); 158.7, 158.8 (2*s*, MeO–C), 162.8 (*s*, C(4)). FAB-MS: 913 (3, M⁺), 912 (4, [M–H]⁺), 911 (6, M⁺), 910 (5, [M–H]⁺), 303 (100).

N⁶-Benzoyl-9-[6'-O-(5-bromopentyl)-5'-O-(4,4'-dimethoxytrityl)-2'-O-[(triisopropylsilyl)oxy]methyl]-β-D-allofuranosyl]adenine (9) and **N⁶-Benzoyl-9-[6'-O-(5-bromopentyl)-5'-O-(4,4'-dimethoxytrityl)-3'-O-[(triisopropylsilyl)oxy]methyl]-β-D-allofuranosyl]adenine (12)**. As described for **8/11**, with **6** (1.05 g, 1.0 mmol), ⁱPr₂NEt (0.7 ml, 4 mmol), (CH₂Cl)₂ (8 ml), Bu₂SnCl₂ (334 mg, 1.1 mmol), and tom-Cl (291 mg, 1.3 mmol). Workup and CC (silica gel, hexane/AcOEt (+2% Et₃N) 2 : 8 → 8 : 2 (+2% Et₃N)) gave **9** (0.45 g, 45%) and **12** (0.20 g, 20%) as pale yellow foams.

Data of 9: TLC (hexane/AcOEt 4 : 6): R_f 0.56. [α]_D²⁵ = –46.1 (*c* = 1.0, CHCl₃). UV (MeOH): 278 (19400), 257 (11900), 233 (32000), 226 (31100). IR (CHCl₃): 3620*w*, 3016*s*, 2945*m*, 2869*w*, 1708*m*, 1611*m*, 1584*w*, 1509*m*, 1456*s*, 1391*w*, 1300*m*, 1250*s*, 1177*m*, 1048*s*, 881*w*, 862*w*. ¹H-NMR (300 MHz, CDCl₃): 0.97–1.10 (*m*, ⁱPr₃Si); 1.46–1.56 (*m*, BrCH₂(CH₂)₂); 1.84–1.88 (*m*, Br(CH₂)₃CH₂); 3.05–3.18 (*m*, H–C(6'), CH₂O, OH–C(3')); 3.29 (*dd*, *J* = 4.0, 10.3, H'–C(6')); 3.43 (*t*, *J* = 6.8, BrCH₂); 3.67 (*br. s*, H–C(5')); 3.775, 3.781 (2*s*, MeO); 4.39 (*dd*, *J* = 2.3, 5.6, H–C(4')); 4.72–4.77 (*m*, H–C(2'), H–C(3')); 4.83, 5.02 (2*d*, *J* = 4.6, OCH₂O); 6.07 (*d*, *J* = 6.0, H–C(1')); 6.78–6.82 (*m*, 4 arom. H); 7.21–7.61 (*m*, 12 arom. H); 7.80 (*s*, H–C(2)); 8.01–8.03 (*m*, 2 arom. H); 8.64 (*s*, H–C(8)); 9.02 (*br. s*, NH–C(6)). ¹³C-NMR (75 MHz, CDCl₃): 11.8 (*d*, (Me₂CH)₃Si); 17.8 (*q*, (Me₂CH)₃Si); 24.9 (*t*, Br(CH₂)₂CH₂); 28.8 (*t*, BrCH₂CH₂); 32.6 (*t*, Br(CH₂)₃CH₂); 33.7 (*t*, BrCH₂); 55.3 (*q*, MeO); 69.1, 70.7 (2*t*, CH₂O, C(6)); 70.3, 72.3, 80.8 (3*d*, C(2'), C(3'), C(5')); 85.2, 86.9 (2*d*, C(1'), C(4')); 87.2 (*s*, Ar₂C(Ph)); 90.8 (*t*, OCH₂O); 113.1 (*d*, arom. C); 123.5 (*s*, C(5)); 126.9, 127.7, 127.8, 128.9; 130.3, 130.4, 132.8 (7*d*, arom. C); 133.7, 136.7, 136.8 (3*s*, arom. C); 142.4 (*d*, C(8)); 146.1 (*s*, arom. C); 149.5 (*s*, C(4)); 151.7 (*s*, C(6)); 152.6 (*d*, C(2)); 158.3 (*s*, MeO–C); 164.6 (*s*, CO). FAB-MS: 1040 (51, [M+H]⁺), 1039 (30, M⁺), 1038 (40, [M+H]⁺), 1037 (35, M⁺), 303 (100).

Data of 12: TLC (hexane/AcOEt 4 : 6): R_f 0.40. [α]_D²⁵ = –54.3. UV (MeOH): 278 (16200), 257 (10800), 233 (30000), 226 (29400). IR (CHCl₃): 3621*w*, 3014*w*, 2973*w*, 2869*w*, 1710*m*, 1611*m*, 1585*w*, 1509*m*, 1456*m*, 1390*w*, 1301*m*, 1250*s*, 1178*w*, 1038*s*, 880*w*, 829*w*. ¹H-NMR (300 MHz, CDCl₃): 1.09–1.11 (*m*, ⁱPr₃Si); 1.42–1.57 (*m*, BrCH₂(CH₂)₂); 1.84–1.88 (*m*, Br(CH₂)₃CH₂); 3.02–3.31 (*m*, 2 H–C(6'), CH₂O); 3.41 (*t*, *J* = 6.8, BrCH₂); 3.59–3.62 (*m*, H–C(5')); 3.77, 3.78 (2*s*, MeO); 3.99 (*d*, *J* = 6.9, OH–C(2')); 4.49–4.55 (*m*, H–C(3'), H–C(4')); 4.66–4.70 (*m*, H–C(2')); 4.95, 5.23 (2*d*, *J* = 4.6, OCH₂O); 5.84 (*d*, *J* = 6.9, H–C(1')); 6.78–6.84 (*m*, 4 arom. H); 7.21–7.69 (*m*, 12 arom. H); 7.82 (*s*, H–C(2)); 8.01–8.03 (*m*, 2 arom. H); 8.61 (*s*, H–C(8)); 9.02 (*br. s*, NH–C(6)). ¹³C-NMR (75 MHz, CDCl₃): 11.9 (*d*, (Me₂CH)₃Si); 17.8 (*q*, (Me₂CH)₃Si); 24.9 (*t*, Br(CH₂)₂CH₂); 28.9 (*t*, BrCH₂CH₂); 32.6 (*t*, Br(CH₂)₃CH₂); 33.7 (*t*, BrCH₂); 55.3 (*q*, MeO); 68.7, 70.7 (2*t*, CH₂O, C(6')); 72.2, 72.6, 81.0 (3*d*, C(2'), C(3'), C(5')); 83.8 (*d*, C(4')); 87.3 (*s*, Ar₂C(Ph)); 89.0 (*d*, C(1')); 91.0 (*t*, OCH₂O); 113.2 (*d*, arom. C); 123.4 (*s*, C(5)); 126.9 (*s*, arom. C); 127.7, 127.8, 128.2, 128.9, 130.3, 132.7 (6*d*, arom. C); 133.7, 136.7, 136.8 (3*s*, arom. C); 142.3 (*d*, C(8)); 146.2 (*s*, arom. C); 149.4 (*s*, C(4)); 151.8 (*s*, C(6)); 152.5 (*d*, C(2)); 158.7 (*s*, MeO–C); 164.3, 170.8 (2*s*, CO). FAB-MS: 1040 (57, [M+H]⁺), 1039 (39, M⁺), 1038 (44, [M+H]⁺), 1037 (42, M⁺), 303 (100).

N²-Acetyl-9-[6'-O-(5-bromopentyl)-5'-O-(4,4'-dimethoxytrityl)-2'-O-[(triisopropylsilyl)oxy]methyl]-β-D-allofuranosyl]guanine (10). As described for **8/11**, with **7** (0.45 g, 0.58 mmol), ⁱPr₂NEt (0.4 ml, 2.3 mmol), (CH₂Cl)₂ (2 ml), Bu₂SnCl₂ (176 mg, 0.58 mmol), and tom-Cl (130 mg, 0.58 mmol). Workup and CC (silica gel, hexane/AcOEt (+2% Et₃N) 3 : 7 → AcOEt (+2% Et₃N)) gave **10** (0.31 g, 55%). Pale yellow foam. TLC

(AcOEt): R_f 0.24. $[\alpha]_D^{25} = -15.5$ ($c = 1.0$, CHCl_3). UV (MeOH): 282 (10900), 276 (11600), 260 (13200), 246 (11600), 231 (26100). IR (CHCl_3): 3215w, 3027m, 2945w, 2868m, 1704s, 1609m, 1559m, 1509m, 1464m, 1418s, 1374w, 1298m, 1251s, 1176w, 1118s, 1037m, 996w, 831w. $^1\text{H-NMR}$ (300 MHz, CDCl_3): 1.01–1.07 (m , $^i\text{Pr}_3\text{Si}$); 1.42–1.51 (m , $\text{BrCH}_2(\text{CH}_2)_2$); 1.82–1.84 (m , $\text{Br}(\text{CH}_2)_3\text{CH}_2$); 2.12 (s , Ac); 2.95 (dd , $J = 3.1$, 10.3, $\text{H}-\text{C}(6')$); 3.13–3.17 (m , CH_2O , $\text{OH}-\text{C}(3')$); 3.24 (dd , $J = 4.3$, 10.3, $\text{H}'-\text{C}(6')$); 3.39 (t , $J = 6.8$, BrCH_2); 3.60–3.62 (m , $\text{H}-\text{C}(5')$); 3.77, 3.78 ($2s$, MeO); 4.23 (dd , $J = 3.1$, 3.4, $\text{H}-\text{C}(4')$); 4.51–4.55 (m , $\text{H}-\text{C}(2')$); 4.82–4.83 (m , $\text{H}-\text{C}(3')$); 4.89, 5.07 ($2d$, $J = 5.0$, OCH_2O); 5.85 (d , $J = 6.9$, $\text{H}-\text{C}(1')$); 6.74–6.79 (m , 4 arom. H); 7.20–7.54 (m , 9 arom. H, $\text{H}-\text{C}(8)$); 8.43 (br. s , $\text{NH}-\text{C}(6)$); 11.95 (s , $\text{H}-\text{N}(1)$). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 11.8 (d , $(\text{Me}_2\text{CH})_3\text{Si}$); 17.8 (q , $(\text{Me}_2\text{CH})_3\text{Si}$); 24.4 (q , MeCO); 24.8 (t , $\text{Br}(\text{CH}_2)_2\text{CH}$); 28.7 (t , BrCH_2CH_2); 32.5 (t , $\text{Br}(\text{CH}_2)_3\text{CH}_2$); 33.8 (t , BrCH_2); 55.3 (q , MeO); 69.9, 70.8 ($2t$, CH_2O , C(6)); 72.5, 77.2, 81.5 ($3d$, C(2'), C(3'), C(5')); 85.2, 86.1 ($2d$, C(1'), C(4')); 87.2 (s , $\text{Ar}_2\text{C}(\text{Ph})$); 90.9 (t , OCH_2O); 113.2, 113.3 ($2d$, arom. C); 121.6 (s , C(5)); 127.1, 127.9, 128.2, 128.4, 130.4, 130.5, (6d, arom. C); 136.3, 136.4 ($2s$, arom. C); 137.5 (d , C(8)); 146.1 (s , arom. C); 147.0 (s , C(4)); 148.5 (s , C(2)); 155.7 (s , C(6)); 158.7 (s , MeO–C); 171.2 (s , CO). FAB-MS: 994 (3, M^+), 992 (3, M^+), 693 (20), 691 (17), 303 (100).

1-[6'-O-(5-Bromopentyl)-5'-O-(4,4'-dimethoxytrityl)-2'-O-[[tr(isopropylsilyl)oxy]methyl]- β -D-allofuranosyl]uracil 3'-(2-Cyanoethyl Diisopropylphosphoramidite) (**14**). According to the *G.P.* with **8** (170 mg, 0.17 mmol). CC (Al_2O_3 , hexane/AcOEt 6:4 \rightarrow 3:7) gave **14** (184 mg, 94%; 1:1 mixture of diastereoisomers). White foam. TLC (hexane/AcOEt 6:4): R_f 0.39. UV (MeCN): 269 (9700), 238 (23100), 226 (19100). IR (CHCl_3): 3408w, 3019w, 2965m, 2868w, 2360w, 1719m, 1694s, 1608m, 1509m, 1462m, 1386w, 1302w, 1252m, 1218m, 1178m, 1117w, 1036m, 980w, 882w, 828w. $^1\text{H-NMR}$ (300 MHz, CDCl_3): 0.95–1.05 (m , $^i\text{Pr}_3\text{Si}$); 1.10–1.22 (m , $(\text{Me}_2\text{CH})_2\text{N}$); 1.37–1.42 (m , $\text{BrCH}_2(\text{CH}_2)_2$); 1.70–1.81 (m , $\text{Br}(\text{CH}_2)_2\text{CH}_2$); 2.53 (t , $J = 6.7$, 0.5 H, $\text{OCH}_2\text{CH}_2\text{CN}$); 2.54 (t , $J = 6.2$, 0.5 H, $\text{OCH}_2\text{CH}_2\text{CN}$); 2.62 (t , $J = 6.2$, 1 H, $\text{OCH}_2\text{CH}_2\text{CN}$); 2.97–3.11 (m , CH_2O); 3.35–3.67 (m , BrCH_2 , $\text{H}-\text{C}(5')$, 2 H–(6'), $(\text{Me}_2\text{CH})_2\text{N}$); 3.80 (s , MeO); 4.30–4.36 (m , $\text{H}-\text{C}(2')$, $\text{H}-\text{C}(4')$); 4.68–4.81 (m , $\text{H}-\text{C}(3')$); 4.87, 4.92, 4.94, 4.97 ($4d$, $J = 5.0$, OCH_2O); 5.23 (d , $J = 8.1$, $\text{H}-\text{C}(5)$); 6.00 (d , $J = 5.8$, 0.5 H, $\text{H}-\text{C}(1')$); 6.01 (d , $J = 7.5$, 0.5 H, $\text{H}-\text{C}(1')$); 6.81–6.85 (m , 4 arom. H); 7.06–7.49 (m , 9 arom. H, $\text{H}-\text{C}(6)$); 8.21 (br. s , $\text{H}-\text{N}(3)$). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 12.0 (d , $(\text{Me}_2\text{CH})_3\text{Si}$); 17.8 (q , $(\text{Me}_2\text{CH})_3\text{Si}$); 20.2, 20.4, ($2t$, $J = (\text{C,P}) = 6.1$, $\text{OCH}_2\text{CH}_2\text{CN}$); 23.5 (t , $\text{Br}(\text{CH}_2)_2\text{CH}_2$); 24.48, 24.50, 24.63, 24.69, 24.73, 24.74 ($6q$, Me_2CHN); 28.7, 28.8 ($2t$, BrCH_2CH_2); 32.4, 32.6 ($2t$, $\text{Br}(\text{CH}_2)_3\text{CH}_2$); 33.6, 33.7 ($2t$, BrCH_2); 43.4, 43.6 ($2d$, $J(\text{C,P}) = 4.9$, Me_2CHN); 55.4 (q , MeO); 57.7 (t , $(\text{C,P}) = 18.3$, $\text{OCH}_2\text{CH}_2\text{CN}$); 58.7 (t , $J(\text{C,P}) = 15.8$, $\text{OCH}_2\text{CH}_2\text{CN}$); 68.8, 69.2, 71.6, 71.7 ($4t$, CH_2O , C(6)); 70.7, 70.8, 70.9, 72.5 ($4d$, C(2'), C(3'), C(5')); 84.6, 85.6, 86.4, 87.0 ($4d$, C(1'), C(4')); 87.77, 87.81 ($2s$, $\text{Ar}_2\text{C}(\text{Ph})$); 89.3, 89.7 ($2t$, OCH_2O); 102.5 (d , C(5)); 113.4, 113.5 ($2d$, arom. C); 117.8, 118.0 ($2s$, CN); 127.3, 128.1, 128.5, 130.5, 130.8, 130.9 ($6d$, arom. C); 136.28, 136.32, 136.42 ($3s$, arom. C); 141.0 (d , C(6)); 146.2, 146.3 ($2s$, arom. C); 150.3 (s , C(4)); 162.9 ($2s$, C(6)); 159.0, 159.1 ($2s$, MeO–C). $^{31}\text{P-NMR}$ (121 MHz, CDCl_3): 150.7, 151.4. FAB-MS: 1114 (6, $[M + H]^+$), 1113 (10, M^+), 1112 (7, $[M + H]^+$), 1111 (11, M^+), 303 (100).

N^6 -Benzoyl-9-[6'-O-(5-bromopentyl)-5'-O-(4,4'-dimethoxytrityl)-2'-O-[[tr(isopropylsilyl)oxy]methyl]- β -D-allofuranosyl]adenine 3'-(2-Cyanoethyl Diisopropylphosphoramidite) (**15**). According to the *G.P.* with **9** (560 mg, 0.17 mmol). CC (Al_2O_3 , hexane/AcOEt 8:2 \rightarrow 6:4) gave **15** (605 mg, 90%; a 1:1 mixture of diastereoisomers). Pale yellow foam. TLC (hexane/AcOEt 5:5): R_f 0.52. UV (MeCN): 277 (20400), 258 (14200), 234 (33300), 224 (31400). IR (CHCl_3): 3406w, 3067w, 2945m, 2867w, 1709m, 1611s, 1545m, 1509m, 1457s, 1365w, 1300w, 1250w, 1179m, 1120m, 1082m, 980w, 932w, 828w. $^1\text{H-NMR}$ (300 MHz, CDCl_3): 0.75–0.81 (m , $^i\text{Pr}_3\text{Si}$); 1.21–1.27 (m , $(\text{Me}_2\text{CH})_2\text{N}$); 1.45–1.50 (m , $\text{BrCH}_2(\text{CH}_2)_2$); 1.72–1.84 (m , $\text{Br}(\text{CH}_2)_3\text{CH}_2$); 2.53–2.57 (m , $\text{OCH}_2\text{CH}_2\text{CN}$); 2.94–2.97 (m , 1 H, $\text{OCH}_2\text{CH}_2\text{CN}$); 3.05–3.11 (m , CH_2O); 3.25–3.28 (m , 1 H, $\text{OCH}_2\text{CH}_2\text{CN}$); 3.36–3.42 (m , 1 H, BrCH_2); 3.48–3.55 (m , 1 H, BrCH_2); 3.66–3.74 (m , 2 H–C(6'), $(\text{Me}_2\text{CH})_2\text{N}$); 3.78 (s , MeO); 3.81–3.87 (m , $\text{H}-\text{C}(5')$); 4.60–4.94 (m , $\text{H}-\text{C}(2')$, $\text{H}-\text{C}(3')$, $\text{H}-\text{C}(4')$, OCH_2O); 5.98 (d , $J = 7.4$, 0.5 H, $\text{H}-\text{C}(1')$); 6.02 (d , $J = 7.4$, 0.5 H, $\text{H}-\text{C}(1')$); 6.81–6.85 (m , 4 arom. H); 7.21–7.61 (m , 12 arom. H); 7.89, 7.91 ($2s$, $\text{H}-\text{C}(2)$); 8.00–8.02 (m , 2 arom. H); 8.58, 8.61 ($2s$, $\text{H}-\text{C}(8)$); 9.02 (br. s , $\text{NH}-\text{C}(4)$). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 11.9 (d , $(\text{Me}_2\text{CH})_3\text{Si}$); 17.5 (q , $(\text{Me}_2\text{CH})_3\text{Si}$); 20.2, 20.3 ($2t$, $J(\text{C,P}) = 6.8$, CH_2CN); 23.6 (t , $\text{Br}(\text{CH}_2)_2\text{CH}_2$); 24.51, 24.55, 24.61, 24.70, 24.72 ($5q$, Me_2CHN); 28.90, 28.96 ($2t$, BrCH_2CH_2); 32.4, 32.5 ($2t$, $\text{Br}(\text{CH}_2)_3\text{CH}_2$); 33.8, 34.0 ($2t$, BrCH_2); 43.4 (d , $J = (\text{C,P}) = 12.1$, Me_2CHN); 45.1 (d , $J(\text{C,P}) = 4.9$, Me_2CHN); 55.3 (q , MeO); 57.9, 58.4 ($2t$, $J(\text{C,P}) = 17.7$, $\text{OCH}_2\text{CH}_2\text{CN}$); 67.8, 68.0, 70.5, 70.6 ($4t$, CH_2O , C(6)); 72.0, 72.3, 72.8, 73.0, 75.9, 76.4 ($6d$, C(2'), C(3'), C(5')); 84.0, 84.7, 87.6, 88.0 ($4d$, C(1'), C(4')); 87.0 (s , $\text{Ar}_2\text{C}(\text{Ph})$); 89.1, 89.5 ($2t$, OCH_2O); 113.0 (d , arom. C); 117.7, 117.8 ($2s$, CN); 123.6 (d , C(5)); 127.0, 127.8, 128.6, 128.9, 130.2, 130.4, 130.5, 133.8 ($8d$, arom. C); 132.8, 136.8, 136.9, 137.0, 137.1 ($5s$, arom. C); 143.2, 143.3 ($2d$, C(8)); 145.8 (s , arom. C); 149.4 (s , C(4)); 151.3, 151.5 ($2s$, C(6)); 152.6 (d , C(2)); 158.6 (s , MeO–C); 164.4

(s, CO). ^{31}P -NMR (121 MHz, CDCl_3): 150.5, 151.4. FAB-MS: 1240 (5, $[M + \text{H}]^+$), 1239 (7, M^+), 1238 (6, $[M + \text{H}]^+$), 1237 (8, M^+), 303 (100).

N^2 -Acetyl-9-[6'-O-(5-bromopentyl)-5'-O-(4,4'-dimethoxytrityl)-2'-O-[[triisopropylsilyloxy]methyl]- α -D-allofuranosyl]guanine 3'-(2-Cyanoethyl Diisopropylphosphoramidite) (**16**). According to the *G.P.*, with **10** (170 mg, 0.17 mmol). CC (Al_2O_3 , hexane/AcOEt 6:4 to 3:7) gave **16** (164 mg, 80%; 1:1 mixture of diastereoisomers). Pale yellow foam. TLC (hexane/AcOEt 2:8): R_f 0.50. UV (MeCN): 276 (13500), 270 (13000), 239 (24500), 228 (22200). IR (CHCl_3): 3213w, 3012m, 2945m, 2868w, 2361w, 1695s, 1609s, 1559w, 1509m, 1464m, 1403w, 1371m, 1301m, 1252s, 1179m, 1127m, 1036s, 981w, 882w, 828w. ^1H -NMR (300 MHz, CDCl_3): 0.90–1.07 (m, $^1\text{Pr}_3\text{Si}$); 1.11–1.42 (m, $(\text{Me}_2\text{CH})_2\text{N}$, $\text{BrCH}_2(\text{CH}_2)_2$); 1.72–1.79 (m, $\text{Br}(\text{CH}_2)_3\text{CH}_2$); 2.15, 2.17 (2s, MeCO); 2.74–2.78 (m, $\text{OCH}_2\text{CH}_2\text{CN}$); 2.98–3.15 (m, CH_2O); 3.35–3.61 (m, $\text{OCH}_2\text{CH}_2\text{CN}$, BrCH_2 , 2 H–C(6'), $(\text{Me}_2\text{CH})_2\text{N}$); 3.763, 3.767, 3.774, 3.778 (4s, MeO); 3.88–3.91 (m, H–C(5')); 4.22–4.42 (m, H–C(2'), H–C(4')); 4.62–4.92 (m, H–C(3'), OCH_2O); 5.80 (d, $J = 5.3$, 0.5 H, H–C(1')); 5.96 (d, $J = 7.5$, 0.5 H, H–C(1')); 6.74–6.84 (m, 4 arom. H); 7.21–7.53 (m, 9 arom. H); 9.03–9.11 (m, NH–C(2)); 11.96–12.07 (m, H–N(1)). ^{13}C -NMR (75 MHz, CDCl_3): 11.9 (d, $(\text{Me}_2\text{CH})_3\text{Si}$); 17.9 (q, $(\text{Me}_2\text{CH})_3\text{Si}$); 20.3, 20.4 (2t, $J(\text{C,P}) = 7.2$, $\text{OCH}_2\text{CH}_2\text{CN}$); 24.3 (q, MeCO); 24.8 (t, $\text{Br}(\text{CH}_2)_3\text{CH}_2$); 24.46, 24.51, 24.59, 24.64 (4q, Me_2CHN); 28.6, 28.7 (2t, BrCH_2CH_2); 32.4, 32.6 (2t, $\text{Br}(\text{CH}_2)_3\text{CH}_2$); 33.6, 33.7 (2t, BrCH_2); 43.4, 43.5 (2d, $J(\text{C,P}) = 11.1$, Me_2CHN); 55.3 (q, MeO); 57.8 (t, $J(\text{C,P}) = 8.7$, $\text{OCH}_2\text{CH}_2\text{CN}$); 58.7 (t, $J(\text{C,P}) = 18.8$, $\text{OCH}_2\text{CH}_2\text{CN}$); 68.7, 69.2, 70.9, 71.2 (4t, CH_2O , C(6')); 74.3, 74.5, 77.2, 78.1, 87.4, 87.9 (6d, C(2'), C(3'), C(5')); 84.9, 85.3 (2d, C(4')); 87.4, 87.9 (2d, C(1')); 87.3 (s, $\text{Ar}_2\text{C}(\text{Ph})$); 90.4, 90.6 (2t, OCH_2O); 113.3 (d, arom. C); 117.7, 117.8 (2s, CN); 122.2 (d, C(5)); 127.3, 127.4, 128.1, 128.4, 128.5, 128.7, 130.4 (7d, arom. C); 135.4, 135.5, 136.1 (3s, arom. C); 137.8, 138.4 (2d, C(8)); 145.5, 146.1 (2s, arom. C); 147.7, 147.8 (2s, C(4)); 148.7, 148.9 (2s, C(2)); 155.2, 155.3 (2s, C(6)); 158.8, 158.9 (2s, MeO–C); 170.1 (s, CO). ^{31}P -NMR (121 MHz, CDCl_3): 150.4, 150.0. FAB-MS: 1195 (4, $[M + \text{H}]^+$), 1194 (6, M^+), 1193 (4, $[M + \text{H}]^+$), 1192 (5, M^+), 303 (100).

1-Bromo-3-[(methylthio)methoxy]propane (**33**). A soln. of 3-bromopropanol (8.8 g, 0.1 mol), DMSO (108 ml, 1.8 mol), Ac_2O (94 ml, 1.0 mol), and AcOH (68 ml, 1.2 mol) was kept at r.t. for 7 days. Extraction (hexane/sat. NaHCO₃ soln.) and distillation (75°/10 Torr) gave **33** (10 g, 50%). Yellow liquid. ^1H -NMR (300 MHz): 1.98–2.03 (m, CH_2); 2.14 (s, MeS); 3.37 (t, $J = 6.5$, BrCH_2); 3.51 (t, $J = 5.4$, CH_2O); 4.63 (s, OCH_2S). ^{13}C -NMR (75 MHz): 29.9 (t, CH_2); 31.6 (q, MeS); 32.2 (t, BrCH_2); 66.5 (t, CH_2O); 74.4 (t, OCH_2S).

1-Bromo-3-(chloromethoxy)propane (**34**). SO_2Cl_2 (4.3 ml, 0.1 mol) was added dropwise to a soln. of **33** (10 g, 0.05 mol) in CH_2Cl_2 (240 ml) at 0°. The soln. was stirred at r.t. for 1 h. Evaporation and distillation (53°/0.3 Torr) gave **34** (4.7 g, 42%). Yellow liquid. ^1H -NMR (300 MHz): 2.02–2.10 (m, CH_2); 3.43 (t, $J = 6.4$, BrCH_2); 3.61 (t, $J = 5.0$, CH_2O); 4.63 (s, ClCH_2O). ^{13}C -NMR (75 MHz): 30.1 (t, CH_2); 32.7 (t, BrCH_2); 66.5 (t, CH_2O); 82.0 (t, ClCH_2O).

2'-O-[(3-Bromopropoxy)methyl]-5'-O-(4,4'-dimethoxytrityl)uridine (**21**) and 3'-O-[(3-Bromopropoxy)methyl]-5'-O-(4,4'-dimethoxytrityl)uridine (**25**). A soln. of **17** (1.1 g, 2.0 mmol) and $^i\text{Pr}_2\text{NEt}$ (1.4 ml, 8 mmol) in $(\text{CH}_2\text{Cl})_2$ (6 ml) was treated with Bu_2SnCl_2 (608 mg, 2.0 mmol) at r.t. for 1 h. Then the mixture was heated to 70°, treated with **34** (488 mg, 2.6 mmol), and stirred at 70° for 15 min. Workup and CC (silica gel, hexane/AcOEt (+2% Et_3N) 5:5 → AcOEt (+2% Et_3N)) gave **21** (530 mg, 38%) and **25** (418 mg, 30%) as pale yellow foams.

Data of 21: TLC (hexane/AcOEt 7:3): R_f 0.55. $[\alpha]_D^{25} = 17.1$ ($c = 1.0$, CHCl_3). UV (MeOH): 264 (9700), 256 (9500), 233 (22900), 227 (22300). IR (CHCl_3): 3391w, 3018m, 2959w, 1691s, 1608w, 1510m, 1461w, 1390w, 1299w, 1276w, 1253m, 1221m, 1178m, 1102w, 1036m, 909w, 830w. ^1H -NMR: 2.07–2.15 (m, CH_2); 2.67 (br. s, OH–C(3')); 3.50 (t, $J = 6.4$, BrCH_2); 3.54–3.78 (m, CH_2O , 2 H–C(5')); 3.80 (s, 2 MeO); 4.07–4.09 (m, H–C(4')); 4.26 (dd, $J = 2.8$, 5.3, H–C(2')); 4.47–4.49 (m, H–C(3')); 4.90, 5.00 (2d, $J = 6.9$, OCH_2O); 5.29 (d, $J = 8.1$, H–C(5)); 6.01 (d, $J = 2.8$, H–C(1')); 6.82–6.87 (m, 4 arom. H); 7.22–7.40 (m, 9 arom. H); 7.96 (d, $J = 8.1$, H–C(6)). ^{13}C -NMR (75 MHz, CDCl_3): 30.1 (t, CH_2); 32.4 (t, BrCH_2); 55.3 (q, MeO); 62.1, 66.1 (2t, CH_2O , C(5')); 74.6, 75.4, 81.9 (3d, C(2'), C(3'), C(4')); 87.1 (s, $\text{Ar}_2\text{C}(\text{Ph})$); 89.6 (d, C(1')); 95.5 (t, OCH_2O); 102.5 (d, C(5)); 113.3 (d, arom. C); 127.3, 128.1, 128.2, 128.4, 130.1 (5d, arom. C); 135.1, 135.2 (2s, arom. C); 140.0 (d, C(6)); 144.2 (s, arom. C); 150.7 (s, C(2)); 158.8 (s, MeO–C); 163.2 (s, C(4)). FAB-MS: 699 (6, $[M + \text{H}]^+$), 698 (11, M^+), 697 (7, $[M + \text{H}]^+$), 696 (12, M^+), 303 (100).

Data of 25: TLC (hexane/AcOEt 3:7): R_f 0.43. $[\alpha]_D^{25} = 27.1$ ($c = 1.0$, CHCl_3). UV (MeOH): 264 (9700), 257 (9400), 234 (22100), 227 (21300). IR (CHCl_3): 3556w, 3390w, 2959w, 1690s, 1608w, 1510m, 1461m, 1391w, 1300w, 1253s, 1226m, 1177m, 1101m, 1036m, 909w, 830w. ^1H -NMR: 2.02–2.06 (m, CH_2); 3.37–3.70 (m, OH–C(2'), BrCH_2 , CH_2O , 2 H–C(5')); 3.80 (s, 2 MeO); 4.25–4.32 (m, H–C(2'), H–C(3'), H–C(4')); 4.74, 4.78 (2d, $J = 6.8$, OCH_2O); 5.37 (d, $J = 8.4$, H–C(5)); 5.95 (d, $J = 3.4$, H–C(1')); 6.83–6.86 (m, 4 arom. H); 7.24–7.39 (m, 9 arom. H); 7.83 (d, $J = 8.1$, H–C(6)); 8.91 (br. s, H–N(3)). ^{13}C -NMR (75 MHz, CDCl_3): 30.3 (t, CH_2); 32.4 (t, BrCH_2); 55.3 (q, MeO); 61.7, 66.4 (2t, CH_2O , C(5')); 69.0, 80.0, 83.5 (3d, C(2'), C(3'), C(4')); 87.2

(s, Ar₂C(Ph)); 87.7 (*d*, C(1')); 95.3 (*t*, OCH₂O); 102.3 (*d*, C(5)); 113.3 (*d*, arom. C), 127.2, 128.1, 128.2, 130.1, 130.2 (*5d*, arom. C); 128.4, 135.1, 135.2 (3s, arom. C); 140.0 (*d*, C(6)); 144.3 (*s*, arom. C); 150.2 (*s*, C(2)); 158.7, 158.8 (2s, MeO–C); 163.3 (*s*, C(4)). FAB-MS (NOBA, pos. mode): 699 (12, [M + H]⁺), 698 (9, M⁺), 697 (8, [M + H]⁺), 696 (14, M⁺), 303 (100).

N⁶-Acetyl-2'-O-[(3-bromopropoxy)methyl]-5'-O-(4,4'-dimethoxytrityl)adenosine (**22**) and N⁶-Acetyl-3'-O-[(3-bromopropoxy)methyl]-5'-O-(4,4'-dimethoxytrityl)adenosine (**26**). As described for **21/25**, with **18** (1.5 g, 2.5 mmol), ³Pr₂NEt (1.7 ml, 10 mmol), (CH₂Cl)₂ (10 ml), Bu₂SnCl₂ (0.75 g, 2.5 mmol), and **34** (630 mg, 3.6 mmol). Workup and CC (silica gel, hexane/AcOEt (+2% Et₃N) 8:2 → AcOEt/EtOH 9:1 (+2% Et₃N)) gave **22** (941 mg, 51%) and **26** (370 mg, 20%) as pale yellow foams.

Data of **22**: TLC (AcOEt/EtOH 9:1): R_f 0.54. [α]_D²⁵ = 1.3 (*c* = 1.0, CHCl₃). UV (MeOH): 272 (17900), 253 (12500), 234 (18400). IR (CHCl₃): 3374w, 3028w, 2934w, 1728w, 1703m, 1608s, 1588m, 1509m, 1463m, 1375w, 1297m, 1251m, 1233m, 1208s, 1177m, 1098m, 1037m, 913w, 829w. ¹H-NMR: 1.80–1.98 (*m*, CH₂); 2.16 (*s*, MeCO); 2.78 (*d*, *J* = 5.0, OH–C(3')); 3.37 (*t*, *J* = 6.5, BrCH₂); 3.41–3.67 (*m*, CH₂O, 2 H–C(5')); 3.78 (*s*, MeO); 4.25–4.28 (*m*, H–C(4')); 4.53–4.56 (*m*, H–C(3')); 4.83 (*s*, OCH₂O); 4.94 (*dd*, *J* = 5.0, 5.4, H–C(2')); 6.23 (*d*, *J* = 5.4, H–C(1')); 6.78–6.83 (*m*, 4 arom. H); 7.19–7.44 (*m*, 9 arom. H); 8.18 (*s*, H–C(2)); 8.61 (*s*, H–C(8)); 8.66 (*br. s*, NH–C(6)). ¹³C-NMR (75 MHz, CDCl₃): 25.6 (*q*, MeCO); 29.9 (*t*, CH₂); 32.2 (*t*, BrCH₂); 55.3 (*q*, MeO); 63.1, 66.3 (2*t*, CH₂O, C(5')); 78.2, 80.1, 84.1 (3*d*, C(2'), C(3'), C(4')); 87.1 (*s*, Ar₂C(Ph)); 89.5 (*d*, C(1')); 95.9 (*t*, OCH₂O); 113.4 (*d*, arom. C); 127.0, 127.9, 128.1, 130.1 (4*d*, arom. C); 128.4, 135.5, 135.6 (3s, arom. C); 141.6 (*d*, C(8)); 144.4 (*s*, arom. C); 149.4 (*s*, C(4)); 151.0 (*s*, C(6)); 152.5 (*d*, C(2)); 158.6 (*s*, MeO–C). FAB-MS: 765 (47, [M + H]⁺), 764 (100, M⁺), 763 (59, [M + H]⁺), 762 (94, M⁺), 303 (51).

Data of **26**: TLC (AcOEt/EtOH 9:1): R_f 0.43. [α]_D²⁵ = –5.7 (*c* = 1.0, CHCl₃). UV (MeOH): 271 (18200), 253 (13500), 234 (24700), 229 (24300). IR (CHCl₃): 3373w, 3016m, 2935w, 1729w, 1704m, 1609s, 1588m, 1509m, 1462m, 1375w, 1296m, 1252m, 1226m, 1206s, 1177m, 1086w, 1036m, 912w, 833w. ¹H-NMR (300 MHz, CDCl₃): 2.04–2.08 (*m*, CH₂); 2.61 (*s*, MeCO); 3.17–3.71 (*m*, BrCH₂, CH₂O, 2 H–C(5')); 3.77, 3.78 (2s, MeO); 4.09 (*br. s*, OH–C(2')); 4.37–4.39 (*m*, H–C(4')); 4.48 (*dd*, *J* = 3.4, 5.0, H–C(3')); 4.80, 4.84 (2*d*, *J* = 6.7, OCH₂O); 4.82–4.88 (*m*, H–C(2')); 6.04 (*d*, *J* = 5.6, H–C(1')); 6.73–6.82 (*m*, 4 arom. H); 7.16–7.38 (*m*, 9 arom. H); 8.19 (*s*, H–C(2)); 8.62 (*s*, H–C(8)); 8.71 (*br. s*, NH–C(6)). ¹³C-NMR (75 MHz, CDCl₃): 25.7 (*q*, MeCO); 30.1 (*t*, CH₂); 32.4 (*t*, BrCH₂); 55.2 (*q*, MeO); 63.0, 66.0 (2*t*, CH₂O, C(5')); 74.4, 77.0, 83.2 (3*d*, C(2'), C(3'), C(4')); 86.7 (*s*, Ar₂C(Ph)); 89.4 (*d*, C(1')); 95.7 (*t*, OCH₂O); 113.2 (*d*, arom. C); 122.1 (*s*, C(5)); 127.0, 127.9, 128.1, 130.1 (4*d*, arom. C); 135.5, 135.6 (2s, arom. C); 141.5 (*d*, C(8)); 144.4 (*s*, arom. C); 149.3 (*s*, C(4)); 152.3 (*s*, C(6)); 158.6 (*s*, MeO–C). FAB-MS: 765 (34, [M + H]⁺), 764 (67, M⁺), 763 (34, [M + H]⁺), 762 (64, M⁺), 303 (100).

N²-Acetyl-2'-O-[(3-bromopropoxy)methyl]-5'-O-(4,4'-dimethoxytrityl)guanosine (**23**) and N²-Acetyl-3'-O-[(3-bromopropoxy)methyl]-5'-O-(4,4'-dimethoxytrityl)guanosine (**27**). As described for **21/25**, with **19** (1.57 g, 2.5 mmol), ³Pr₂NEt (1.7 ml, 10 mmol), (CH₂Cl)₂ (10 ml), Bu₂SnCl₂ (760 mg, 2.5 mmol), and **34** (470 mg, 2.5 mmol). Workup and CC (silica gel, hexane/AcOEt (+2% Et₃N) 5:5 → AcOEt (+2% Et₃N)) gave **23** (1.18 g, 60%) as a pale yellow foam and 0.1 g of a mixture of by-products. From this mixture, **27** was isolated by prep. TLC (CH₂Cl₂/MeOH 9:1) as a pale yellow foam.

Data of **23**: TLC (AcOEt/EtOH 9:1): R_f 0.48. [α]_D²⁵ = 1.5 (*c* = 1.0, CHCl₃). UV (MeOH): 275 (13000), 271 (12900), 235 (26700), 226 (25200). IR (CHCl₃): 3369w, 3222w, 3022m, 2935w, 1703s, 1674s, 1563m, 1509m, 1463w, 1411m, 1301w, 1253m, 1226s, 1178w, 1095m, 1036m, 996w, 830w. ¹H-NMR: 1.76 (*s*, MeCO); 1.94–1.97 (*m*, CH₂); 3.18 (*br. s*, OH–C(3')); 3.22–3.73 (*m*, BrCH₂, CH₂O, 2 H–C(5')); 3.75, 3.76 (2s, MeO); 4.21 (*br. s*, H–C(4')); 4.23 (*br. s*, H–C(3')); 4.74, 4.80 (2*d*, *J* = 6.8, OCH₂O); 5.07–5.10 (*m*, H–C(2')); 5.70 (*d*, *J* = 6.2, H–C(1')); 6.75–6.84 (*m*, 4 arom. H); 7.15–7.50 (*m*, 9 arom. H); 7.87 (*s*, H–C(8)); 8.73 (*s*, NH–C(6)); 11.94 (*s*, H–N(1)). ¹³C-NMR (75 MHz, CDCl₃): 23.7 (*q*, MeCO); 30.1 (*t*, CH₂); 32.2 (*t*, BrCH₂); 55.3 (*q*, MeO); 63.8, 66.1 (2*t*, CH₂O, C(5')); 70.5, 78.9, 84.3 (3*d*, C(2'), C(3'), C(4')); 86.5 (*d*, C(1')); 87.1 (*s*, Ar₂C(Ph)); 95.7 (*t*, OCH₂O); 113.3 (*d*, arom. C); 122.0 (*s*, C(5)); 127.2, 128.1, 128.4, 130.1 (4*d*, arom. C); 135.5, 135.9 (2s, arom. C); 139.0 (*d*, C(8)); 144.9 (*s*, arom. C); 147.2 (*s*, C(4)); 148.4 (*s*, C(4)); 155.6 (*s*, C(6)); 158.8 (*s*, MeO–C); 171.9 (*s*, CO). FAB-MS: 781 (36, [M + H]⁺), 780 (52, M⁺), 779 (18, [M + H]⁺), 778 (69, M⁺), 303 (100).

Data of **27**: TLC (AcOEt/EtOH 9:1): R_f 0.40. ¹H-NMR: 1.64–1.67 (*m*, CH₂); 1.79 (*s*, MeCO); 3.11–3.16 (*m*, H–C(5')); 3.26–3.58 (*m*, BrCH₂, CH₂O, H'–C(5')); 3.74, 3.76 (2s, MeO); 4.10–4.12 (*m*, H–C(4')); 4.30–4.33 (*m*, OCH₂O); 4.45–4.48 (*m*, H–C(3')); 4.51 (*br. d*, *J* = 5.0, OH–C(2')); 4.98–5.02 (*m*, H–C(2')); 6.00 (*d*, *J* = 6.5, H–C(1')); 6.71–6.83 (*m*, 4 arom. H); 7.10–7.46 (*m*, 9 arom. H); 7.81 (*s*, H–C(8)); 8.92 (*br. s*, NH–C(6)); 11.95 (*br. s*, H–N(1)). ¹³C-NMR (75 MHz, CDCl₃): 23.6 (*q*, MeCO); 30.2 (*t*, CH₂); 31.6 (*t*, BrCH₂); 55.1 (*q*, MeO); 62.4, 64.8 (2*t*, CH₂O, C(5')); 68.7, 74.9, 82.6 (3*d*, C(2'), C(3'), C(4')); 86.9 (*d*, C(1')); 87.9 (*s*, Ar₂C(Ph)); 94.8 (*t*, OCH₂O); 113.2 (*d*, arom. C); 123.8 (*s*, C(5)); 128.0, 128.2, 128.5, 130.1 (4*d*, arom. C);

135.1, 135.6 (2s, arom. C); 138.7 (*d*, C(8)); 144.9 (s, arom. C); 147.9 (s, C(4)); 148.4 (s, C(4)); 155.5 (s, C(6)); 158.7 (s, MeO–C); 172.1 (s, CO). FAB-MS: 780 (10, M^+), 778 (8, M^+), 653 (4), 561 (5), 303 (100).

N^4 -Acetyl-2'-O-[(3-bromopropoxy)methyl]-5'-O-(4,4'-dimethoxytrityl)cytidine (**24**) and N^4 -Acetyl-3'-O-[(3-bromopropoxy)methyl]-5'-O-(4,4'-dimethoxytrityl)cytidine (**28**). As described for **21/25**, with **20** (1.47 g, 2.5 mmol), iPr_2NEt (1.7 ml, 10 mmol), $(CH_2Cl)_2$ (10 ml), Bu_3SnCl_2 (760 mg, 2.5 mmol), and **34** (610 mg, 3.3 mmol). Workup and CC (silica gel, hexane/AcOEt (+2% Et_3N) 7:3 → AcOEt/EtOH 9:1 (+2% Et_3N)) gave **24** (833 mg, 45%) and **28** (370 mg, 20%) as pale yellow foams.

Data of 24: TLC (AcOEt/EtOH 9:1): R_f 0.63. $[\alpha]_D^{25} = 40.9$ ($c = 1.0$, $CHCl_3$). UV (MeOH): 299 (6600), 290 (6100), 283 (6500), 278 (6000), 271 (5800), 236 (26700), 226 (23300). IR ($CHCl_3$): 3401w, 3011m, 2961w, 1723m, 1661s, 1610m, 1554m, 1504m, 1462s, 1362m, 1306m, 1252m, 1224s, 1206w, 1177m, 1102m, 1036m, 909w, 829w. 1H -NMR: 2.06–2.14 (*m*, CH_2); 2.22 (*s*, MeCO); 2.71 (*d*, $J = 9.3$, OH–C(3')); 3.48 (*t*, $J = 6.4$, $BrCH_2$); 3.52–3.74 (*m*, CH_2O , 2 H–C(5')); 3.81, 3.82 (2s, MeO); 4.11–4.13 (*m*, H–C(4')); 4.24 (br. *d*, $J \approx 5.0$, H–C(2')); 4.43–4.46 (*m*, H–C(3')); 4.95, 5.17 (2*d*, $J = 6.5$, OCH_2O); 5.99 (*s*, H–C(1')); 6.85–6.89 (*m*, 4 arom. H); 7.08–7.44 (*m*, 9 arom. H, H–C(5)); 8.47 (*d*, $J = 7.4$, H–C(6)); 9.21 (br. *s*, NH–C(4)). ^{13}C -NMR (75 MHz, $CDCl_3$): 24.9 (*q*, MeCO); 30.4 (*t*, CH_2); 32.5 (*t*, $BrCH_2$); 55.3 (*q*, MeO); 61.0, 66.3 (2*t*, CH_2O , C(5')); 68.0, 80.2, 83.2 (3*d*, C(2'), C(3'), C(4')); 87.1 (*s*, $Ar_2C(Ph)$); 89.5 (*d*, C(1')); 95.2 (*t*, OCH_2O); 96.7 (*d*, C(5)); 113.4 (*d*, arom. C); 127.2, 128.0, 128.1, 128.4, 130.2 (5*d*, arom. C); 135.2, 135.5, (2s, arom. C); 144.3 (*s*, arom. C); 144.7 (*d*, C(6)); 155.3 (*s*, C(2)); 158.7 (*s*, MeO–C); 162.8 (*s*, C(4)); 170.4 (*s*, CO). FAB-MS: 740 (92, $[M+H]^+$), 739 (45, M^+), 738 (74, $[M+H]^+$), 737 (14, M^+), 303 (100).

Data of 28: TLC (AcOEt/EtOH 9:1): R_f 0.53. $[\alpha]_D^{25} = 11.8$ ($c = 1.0$, $CHCl_3$). UV (MeOH): 299 (5600), 290 (5100), 284 (5400), 271 (4700), 236 (23300), 227 (20900). IR ($CHCl_3$): 3400w, 3012m, 2960w, 1724m, 1658m, 1610w, 1554m, 1510m, 1482s, 1444w, 1382m, 1307m, 1252s, 1177m, 1114m, 1036m, 909w, 830w. 1H -NMR (300 MHz, $CDCl_3$): 2.01–2.06 (*m*, CH_2); 2.24 (*s*, MeCO); 3.35–3.67 (*m*, $BrCH_2$, OCH_2 , 2 H–C(5'), OH–C(2')); 3.81 (*s*, 2 MeO); 4.27–4.39 (*m*, H–C(2'), H–C(3'), H–C(4')); 4.70, 4.77 (2*d*, $J = 6.8$, OCH_2O); 5.94 (*d*, $J = 2.8$, H–C(1')); 6.84–6.88 (*m*, 4 arom. H); 7.16–7.39 (*m*, 9 arom. H, H–C(5)); 8.31 (*d*, $J = 7.5$, H–C(6)); 9.16 (br. *s*, NH–C(4)). ^{13}C -NMR (75 MHz, $CDCl_3$): 25.0 (*q*, MeCO); 30.2 (*t*, CH_2); 32.4 (*t*, $BrCH_2$); 55.3 (*q*, MeO); 61.7, 65.9 (2*t*, CH_2O , C(5')); 74.9, 75.5, 82.4 (3*d*, C(2'), C(3'), C(4')); 87.0 (*s*, $Ar_2C(Ph)$); 92.2 (*d*, C(1')); 95.4 (*t*, OCH_2O); 96.7 (*d*, C(5)); 113.3 (*d*, arom. C); 128.0, 128.1, 128.4, 130.3 (4*d*, arom. C); 135.2, 135.3 (2s, arom. C); 144.1 (*d*, arom. C); 144.6 (*d*, C(6)); 155.7 (*s*, C(2)); 158.8 (*s*, MeO–C); 162.6 (*s*, C(4)); 170.0 (*s*, CO). FAB-MS: 740 (38, $[M+H]^+$), 739 (25, M^+), 738 (38, $[M+H]^+$), 737 (11, M^+), 303 (100).

2'-O-[(3-Bromopropoxy)methyl]-5'-O-(4,4'-dimethoxytrityl)uridine 3'-(2-Cyanoethyl Diisopropylphosphoramidite) (**29**). According to the *G.P.*, with **21** (373 mg, 0.53 mmol). CC (Al_2O_3 , hexane/AcOEt 8:2 to 3:7) gave **29** (434 mg, 91%; 1:1 mixture of diastereoisomers). Pale yellow foam. TLC (hexane/AcOEt 5:5): R_f 0.42. UV (MeCN): 265 (22300), 236 (20900), 225 (18200). IR ($CHCl_3$): 3390w, 3026s, 2973w, 2360w, 1806m, 1697s, 1608w, 1509m, 1458w, 1414w, 1395w, 1251s, 1178w, 1098w, 1034m, 1004m, 835w. 1H -NMR (300 MHz, $CDCl_3$): 1.03–1.29 (*m*, (Me_2CH_2)₂N); 2.07–2.13 (*m*, CH_2); 2.43 (*t*, $J = 6.4$, 1 H, OCH_2CH_2CN); 2.66 (*t*, $J = 6.0$, 1 H, OCH_2CH_2CN); 3.40–3.77 (*m*, 2 H–C(5'), $OCH_2CH_2CH_2Br$, OCH_2CH_2CN , (Me_2CH)₂N); 3.80, 3.83 (2s, MeO); 4.18–4.19, 4.26–4.28 (2*m*, H–C(4')); 4.37–4.39, 4.42–4.45 (2*m*, H–C(2')); 4.52–4.58 (*m*, H–C(3')); 4.82–4.93 (*m*, OCH_2O); 5.24 (*d*, $J = 8.4$, 0.5 H, H–C(5)); 5.28 (*d*, $J = 8.1$, 0.5 H, H–C(5)); 6.05 (*d*, $J = 3.7$, 0.5 H, H–C(1')); 6.09 (*d*, $J = 4.0$, 0.5 H, H–C(1')); 6.82–6.86 (*m*, 4 arom. H); 7.24–7.42 (*m*, 9 arom. H); 7.90, 7.96 (2*d*, $J = 8.1$, H–C(6)). ^{13}C -NMR (75 MHz, $CDCl_3$): 20.3 (br. *t*, CH_2CN); 24.5 (br. *q*, Me_2CHN); 30.4 (*t*, CH_2); 32.6 (*t*, $BrCH_2$); 43.2, 43.3 (2 br. *d*, Me_2CHN); 55.3 (*q*, MeO); 58.1, 58.2 (2*t*, $J(C,P) = 18.5$, OCH_2CH_2CN); 61.5, 63.9, 65.9, 66.2 (4*t*, CH_2O , C(5')); 68.0, 70.4, 73.9, 75.5, 82.7, 82.8 (6*d*, C(2'), C(3'), C(4')); 87.1, 87.2 (2*d*, C(1')); 87.7, 87.8 (2s, $Ar_2C(Ph)$); 95.0 (*t*, OCH_2O); 102.5, 102.6 (2*d*, C(5)); 113.3 (*s*, arom. C); 117.4, 117.6 (2s, CN); 127.2, 128.0, 128.2, 128.3, 130.3 (5*d*, arom. C); 134.9, 135.1, 135.2 (3s, arom. C); 140.0 (*d*, C(6)); 144.2, 144.3 (2s, arom. C); 150.06, 150.13 (2s, C(2)); 158.8 (*s*, MeO–C); 162.9 (*s*, C(4)). ^{31}P -NMR (121 MHz, $CDCl_3$): 150.5, 151.2. FAB-MS: 900 (7, $[M+H]^+$), 899 (16, M^+), 898 (8, $[M+H]^+$), 897 (21, M^+), 595 (68), 593 (64), 303 (100).

N^6 -Acetyl-2'-O-[(3-bromopropoxy)methyl]-5'-O-(4,4'-dimethoxytrityl)adenosine 3'-(2-Cyanoethyl Diisopropylphosphoramidite) (**30**). According to the *G.P.*, with **22** (705 mg, 0.87 mmol). CC (Al_2O_3 , hexane/AcOEt 6:4 to 9:1) gave **30** (760 mg, 92%; 1:1 mixture of diastereoisomers). Pale yellow foam. TLC (hexane/AcOEt 2:8): R_f 0.35. UV (MeCN): 271 (19300), 254 (14700), 236 (22300), 229 (20800). IR ($CHCl_3$): 3014m, 2974w, 2337w, 1806m, 1706w, 1610s, 1590w, 1509m, 1462m, 1412w, 1373w, 1252s, 1180m, 1097m, 1035m, 1003w, 839w. 1H -NMR (300 MHz, $CDCl_3$): 1.06–1.29 (*m*, (Me_2CH_2)₂N); 1.78–1.96 (*m*, CH_2); 2.39 (*t*, $J = 5.6$, 0.8 H, OCH_2CH_2CN); 2.60 (*s*, MeCO); 2.65 (*t*, $J = 5.6$, 1.2 H, OCH_2CH_2CN); 3.27–3.73 (*m*, 2 H–C(5'), CH_2O , $BrCH_2$, OCH_2CH_2CN , (Me_2CH)₂N); 3.77, 3.78 (2s, MeO); 4.32–4.35 (*m*, 0.6 H, H–C(4')); 4.40–4.42

(*m*, 0.4 H, H–C(4')); 4.65–4.67 (*m*, H–C(3')); 4.69–4.85 (*m*, OCH₂O); 5.08–5.13 (*m*, H–C(2')); 6.19 (*d*, *J* = 5.9, 0.4 H, H–C(1')); 6.21 (*d*, *J* = 1.5, 0.6 H, H–C(1')); 6.76–6.83 (*m*, 4 arom. H); 7.19–7.44 (*m*, 9 arom. H); 8.19, 8.20 (2*s*, 1 H, H–C(2)); 8.59, 8.61 (2*s*, 1 H, H–C(8)); 8.68 (br. *s*, NH–C(6)). ¹³C-NMR (75 MHz, CDCl₃): 20.2, 20.4 (2*t*, *J*(C,P) = 7.1, CH₂CN); 24.3, 24.4, 24.5, 24.7 (4*q*, Me₂CHN); 25.7 (*q*, MeCO); 30.1 (*t*, CH₂); 32.3 (*t*, BrCH₂); 43.1, 43.4 (2*d*, *J*(C,P) = 6.9, Me₂CHN); 55.3 (*q*, MeO); 58.1, 58.9 (2*t*, *J*(C,P) = 13.9, OCH₂CH₂CN); 63.0, 66.0 (2*t*, CH₂O, C(5')); 71.1, 71.3, 71.7, 71.9, 83.8, 83.9 (6*d*, C(2'), C(3'), C(4')); 86.7, 86.8 (2*d*, C(1')); 87.0 (*s*, Ar₂C(Ph)); 95.1, 95.2 (2*t*, OCH₂O); 113.2 (*d*, arom. C); 117.4, 117.6 (2*s*, CN); 122.2 (*s*, C(5)); 127.0 (*s*, arom. C); 127.9, 128.2, 128.3, 130.1, 130.2 (5*d*, arom. C); 135.5, 135.6 (2*s*, arom. C); 141.9 (*d*, C(8)); 144.4, 144.5 (2*s*, arom. C); 149.2 (*s*, C(4)); 151.2 (*s*, C(6)); 152.4 (*d*, C(2)); 158.6, 158.7 (*s*, MeO–C); 170.1 (*s*, CO). ³¹P-NMR (202 MHz, CDCl₃): 150.9, 151.1. FAB-MS: 965 (16, [M + H]⁺), 964 (38, M⁺), 963 (11, [M + H]⁺), 962 (37, M⁺), 787 (34), 785 (35), 303 (100).

N²-Acetyl-2'-O-[(3-bromopropoxy)methyl]-5'-O-(4,4'-dimethoxytrityl)guanosine 3'-(2-Cyanoethyl Diisopropylphosphoramidite) (**31**). According to the *G.P.* with **23** (990 mg, 1.27 mmol). CC (silica gel, hexane/AcOEt (+2% Et₃N) 6:4) → AcOEt (+2% Et₃N) gave **31** (1.03 mg, 83%; 1:1 mixture of diastereoisomers). Pale yellow foam. TLC (hexane/AcOEt 1:9): *R_f* 0.51. UV (MeCN): 281 (12900), 269 (11800), 238 (23700), 224 (19600). IR (CHCl₃): 3385*w*, 3020*s*, 2973*m*, 2241*w*, 1806*w*, 1701*s*, 1608*m*, 1560*m*, 1509*m*, 1494*w*, 1412*m*, 1301*w*, 1253*s*, 1178*m*, 1126*w*, 1094*m*, 1034*s*, 1002*w*, 835*w*. ¹H-NMR (300 MHz, CDCl₃): 1.00–1.19 (*m*, (Me₂CH)₂N); 1.59, 1.74 (2*s*, MeCO); 1.86–1.94 (*m*, CH₂); 2.31 (*t*, *J* = 6.2, 1 H, OCH₂CH₂CN); 2.72–2.78 (*m*, 1 H, OCH₂CH₂CN); 3.17–3.19 (*m*, H–C(5')); 3.26–3.29 (*m*, BrCH₂); 3.42–3.66 (*m*, H'–C(5'), CH₂O, (Me₂CH)₂N); 3.75, 3.76, 3.77 (3*s*, MeO); 4.23, 4.34 (2 br. *s*, H–C(4')); 4.52–4.61 (*m*, H–C(3')); 4.64–4.80 (*m*, OCH₂O); 5.13–5.22 (*m*, H–C(2')); 5.86 (*d*, *J* = 6.5, 0.5 H, H–C(1')); 5.98 (*d*, *J* = 8.5, 0.5 H, H–C(1')); 6.77–6.82 (*m*, 4 arom. H); 7.19–7.55 (*m*, 9 arom. H); 7.79, 7.83 (2*s*, H–C(8)); 8.60, 8.46 (2 br. *s*, NH–C(2)); 11.88 (br. *s*, H–N(1)). ¹³C-NMR (75 MHz, CDCl₃): 20.2 (*m*, CH₂CN); 23.5, 23.6 (2*q*, MeCO); 24.5, 24.6, 24.7 (3*q*, Me₂CHN); 30.1 (*t*, CH₂); 32.4, 32.5 (2*t*, BrCH₂); 43.1, 45.4 (2*d*, *J*(C,P) = 12.2, Me₂CHN); 55.4 (*q*, MeO); 57.4 (*t*, *J*(C,P) = 19.5, OCH₂CH₂CN); 59.0 (*t*, *J*(C,P) = 13.4, OCH₂CH₂CN); 63.6, 63.8 (2*t*, C(5')); 66.0, 66.2 (2*t*, CH₂O); 70.7 (*d*, *J*(C,P) = 17.1); 71.8 (*d*, *J*(C,P) = 13.4); 76.4, 76.8 (2*d*); 84.5 (*d*, C(2'), C(3'), C(4')); 86.1, 88.0 (*d*, C(1')); 86.5, 86.8 (2*s*, Ar₂C(Ph)); 95.0 (*t*, OCH₂O); 113.4, 113.5 (2*d*, arom. C); 117.7, 118.3 (2*s*, CN); 122.2, 122.9 (2*s*, C(5)); 127.35, 127.42, 128.26, 128.33, 128.4, 130.3, 130.4 (7*d*, arom. C); 135.7, 135.9, 136.0, 136.4 (4*s*, arom. C); 138.3, 139.5 (2*d*, C(8)); 144.9, 145.3 (2*s*, arom. C); 147.1, 147.5 (2*s*, C(4)); 148.4, 148.7 (2*s*, C(2)); 155.8 (*s*, C(6)); 159.0 (*s*, MeO–C); 171.8, 171.9 (2*s*, CO). ³¹P-NMR (121 MHz, CDCl₃): 150.4, 150.8. FAB-MS: 981 (16, [M + H]⁺), 980 (38, M⁺), 979 (10, [M + H]⁺), 978 (36, M⁺), 787 (40), 785 (38), 303 (100).

N²-Acetyl-2'-O-[(3-bromopropoxy)methyl]-5'-O-(4,4'-dimethoxytrityl)cytidine 3'-(2-Cyanoethyl Diisopropylphosphoramidite) (**32**). According to the *G.P.*, with **24** (566 mg, 0.77 mmol). CC (silica gel, hexane/AcOEt 6:4 → 2:8) gave **32** (639 mg, 89%; 1:1 mixture of diastereoisomers). Pale yellow foam. TLC (hexane/AcOEt 1:9): *R_f* 0.40. UV (MeCN): 304 (6600), 290 (5600), 283 (6100), 237 (27900), 226 (22700). IR (CHCl₃): 3401*w*, 3011*m*, 2969*m*, 2361*w*, 1722*m*, 1664*m*, 1609*w*, 1555*m*, 1509*m*, 1482*s*, 1383*w*, 1307*m*, 1251*m*, 1179*m*, 1120*m*, 1035*m*, 980*w*, 830*w*. ¹H-NMR (300 MHz, CDCl₃): 0.99–1.29 (*m*, (Me₂CH)₂N); 2.08–2.18 (*m*, CH₂); 2.205, 2.213 (2*s*, MeCO); 2.40, 2.61 (2*t*, *J* = 6.2, OCH₂CH₂CN); 3.41–3.76 (*m*, 2 H–C(5'), CH₂O, BrCH₂, OCH₂CH₂CN, (Me₂CH)₂N); 3.81, 3.82 (2*s*, MeO); 4.22–4.53 (*m*, H–C(2'), H–C(3'), H–C(4')); 4.89–5.01 (*m*, OCH₂O); 6.06 (*s*, 0.5 H, H–C(1')); 6.09 (*d*, *J* = 1.5, 0.5 H, H–C(1')); 6.80–6.98 (*m*, 4 arom. H); 6.95 (*d*, *J* = 7.6, 0.5 H, H–C(5)); 7.00 (*d*, *J* = 7.5, 0.5 H, H–C(5)); 7.23–7.44 (*m*, 9 arom. H); 8.42 (*d*, *J* = 7.5, 0.5 H, H–C(6)); 8.52 (*d*, *J* = 7.8, 0.5 H, H–C(6)); 9.09, 9.13 (2 br. *s*, NH–C(4)). ¹³C-NMR (75 MHz, CDCl₃): 20.2, 20.4 (2*t*, *J*(C,P) = 6.9, CH₂CN); 24.4, 24.5, 24.6, 25.0 (4*q*, Me₂CHN, MeCO); 30.7 (*t*, CH₂); 32.8 (*t*, BrCH₂); 43.1, 43.3 (2*d*, *J*(C,P) = 7.0, Me₂CHN); 55.2 (*q*, MeO); 58.2 (*t*, *J*(C,P) = 15, OCH₂CH₂CN); 60.6, 61.0, 65.2, 66.1 (4*t*, CH₂O, C(5')); 69.1, 76.6, 78.6, 79.1, 82.0, 86.4 (6*d*, C(2'), C(3'), C(4')); 87.08, 87.15 (2*s*, Ar₂C(Ph)); 89.8 (*d*, C(1')); 94.9, 95.1 (2*t*, OCH₂O); 96.4 (*d*, C(5)); 113.3 (*d*, arom. C); 117.4 (*s*, CN); 127.3, 128.0, 128.4, 130.1, 130.3 (5*d*, arom. C); 128.3, 135.1, 135.2, 135.3 (4*s*, arom. C); 144.1, 144.2 (2*s*, arom. C); 144.9 (*d*, C(6)); 155.2 (*s*, C(2)); 158.8 (*s*, MeO–C); 160.6 (*s*, C(4)); 170.1 (*s*, CO). ³¹P-NMR (202 MHz, CDCl₃): 150.2, 151.3. FAB-MS: 941 (11, [M + H]⁺), 940 (18, M⁺), 939 (11, [M + H]⁺), 938 (17, M⁺), 303 (100).

Assembly of Oligonucleotides. Automated 1.0-μmol syntheses ('trityl-off' mode) were carried out on a *Gene Assembler* (Pharmacia) by the following protocol: 1) 1.5 min detritylation with 4% CHCl₂COOH in (CH₂Cl)₂; 2) 2.5 min coupling with the appropriate phosphoramidites (0.12 ml of 0.1*M* soln. in MeCN) and BnStet (0.36 ml of a 0.35*M* soln. in MeCN); 3) 1 min capping with a 1:1 mixture of Ac₂O/2,6-lutidine/THF 1:1:8 and 16% 1-methyl-1*H*-imidazole in THF; 4) 0.5 min oxidation with I₂/H₂O/pyridine/THF 2:2:20:75. According to the trityl-assay, the average coupling yields were 99.7% for standard DNA phosphoramidites, 99.3% for tom-protected phosphoramidites [9], and ca. 98% for phosphoramidite **32**.

Oligonucleotides 37 and 38. The assembled, immobilized sequences were treated with 12M aq. MeNH₂ (0.5 ml) and 8M MeNH₂/EtOH (0.5 ml). The suspension was shaken for 2 h at r.t. After centrifugation, the supernatant was evaporated, and the resulting crude oligonucleotides were purified by ion-exchange HPLC. After desalting of the pooled product-containing fractions, 80 OD_{260nm} (60%) of **37** and 75 OD_{260nm} (55%) of **38**, resp., were obtained (*Table 1*).

Oligonucleotide 39. As described for **37** or **38**, but after the MeNH₂ treatment, the residue was treated with 1M Bu₄NF · 3H₂O/THF (0.5 ml); after 12 h at r.t., 1M aq. Tris · HCl (pH 7.4; 0.5 ml) was added, and the clear soln. was desalted on a *Sephadex G-10* column (H₂O as eluent). The product-containing fractions were collected, evaporated, and purified by ion-exchange chromatography. After desalting of the pooled product-containing fractions, 40 OD_{260nm} (30%) of **39** were obtained (*Table 1*).

Oligonucleotides 40 and 41. As described for **37** and **38**, but only with 1/10 of the solid support **35** or **36** (ca. 0.1 μmol each), resp. After ion-exchange chromatography and desalting of the pooled product-containing fractions, 6 OD_{260nm} (45%) of **40** and 5 OD_{260nm} (40%) of **41**, resp., were obtained (*Table 1*).

Oligonucleotides 49–53. Under Ar, ca. 80% of the solid support **35** or **36** (ca. 0.8 μmol each) was shaken with 1M thioglycolic acid/2M ³Pr₃NEt/DMF (1 ml). After 14 h at r.t., the solid support was collected by centrifugation and washed 3 × with DMF (→ **35** and **36**, resp.). About 1/3 of the solid support (ca. 0.25 μmol each) was treated with a soln. of HOBT (14 mg, 0.1 mmol), TBTU (32 mg, 0.1 mmol), ³Pr₃NEt (34 μl, 0.2 mmol), and 0.8 mmol of an amine (MeNH₂, histamine, or L-isoleucine allyl ester) in DMF. The suspension was shaken for 4 h at r.t., collected by centrifugation, and washed 2 × with DMF and EtOH, resp. Deprotection and purification were carried out as described for **37** and **38**. From **35**, 15 OD_{260nm} (40%) of **49**, 12 OD_{260nm} (35%) of **51**, and 9 OD_{260nm} (25%) of **53** were obtained with MeNH₂, histamine, and L-isoleucine allylester, resp. (*Table 1*). From **36**, 14 OD_{260nm} (40%) of **50** and 11 OD_{260nm} (30%) of **53** were obtained with MeNH₂ and histamine, resp. (*Table 1*).

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