Nucleotides

Part LXXIX[1])

New Building Blocks for Photolithographic Syntheses of Oligoribonucleotides

by **Christoph Hermann**, **Evgeny Kvassiouk**, and **Wolfgang Pfleiderer***

Fachbereich Chemie, Universität Konstanz, Postfach 5560, D-78457 Konstanz
(phone: +49-7531-882279; fax: +49-7531-883138; e-mail: Wolfgang.Pfleiderer@uni-konstanz.de)

Two series of new ribonucleoside 3′-phosphoramidites (see **36**–**42**) carrying the photolabile [2-(2-nitrophenyl)propoxy]carbonyl group at the 5′-*O*-position were synthesized and characterized as monomeric building blocks for photolithographic syntheses of RNA chips. Base protection was achieved in the well-known manner by the 2-(4-nitrophenyl)ethyl (npe) and the [2-(4-nitrophenyl)ethoxy]carbonyl (npeoc) group. The carbohydrate moiety carried in addition the 2′-*O*-(tetrahydro-4-methoxy-2*H*-pyran-4-yl) group for blocking the 2′-OH function.

1. Introduction. – Based upon the photolability of the 2-nitrobenzyl group [2] and its derivatives, their use in nucleic acid [3–10], carbohydrate [11], and peptide [12–14] chemistry is common practise. More recently, photolabile 5′-protection of 2′-deoxyribonucleoside 3′-phosphoramidites have also successfully been employed in the solid-phase synthesis of DNA probe arrays [15–18]. There are numerous publications describing the photolabile protection of OH, COOH, NH_2, SH, and C=O functions [19]. Since the quantum yield of photodeprotection is highly influenced by substitutions at the benzene ring or the CH_2 C-atom [20] of the 2-nitrobenzyl group, a large variety of structural modifications is known.

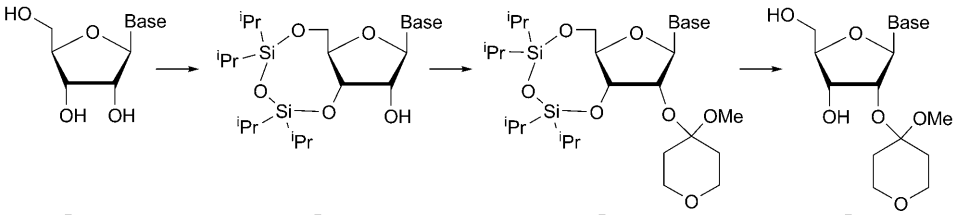
The reported photochemical reactions of the *o*-NO_2 groups with C(β) atoms [21][22] suggested that the homologous 2-(2-nitrophenyl)ethyl group [23] might also be useful as a photocleavable protecting function. We developed new types of very efficient photolabile protecting groups based upon the [2-(2-nitrophenyl)propoxy]carbonyl [nppoc] moiety [24], determined the mechanism of cleavage [25], and could improve the cleavage rate by intramolecular sensitization [26–28]. Caged nucleosides [29] have also been applied, and the use of new building blocks for photolithographic oligonucleotide array formation was very successful [29][30].

2. Syntheses. – Two new types of building blocks for photolithographic oligoribonucleotide synthesis were obtained based on two series of nucleobase-protected starting materials carrying either the phenoxyacetyl (pac) (see **2**–**4** [30][31]) or the [2-(4-nitrophenyl)ethoxy]carbonyl (npeoc) group (see **5**–**7** [32]) at the amino functions

[1]) Part LXXVIII: [1].

of the ribonucleosides. Guanosine was further protected at the O^6-position by the 2-(4-nitrophenyl)ethyl group (see **7**) for solubility reasons (*Scheme*).

Scheme

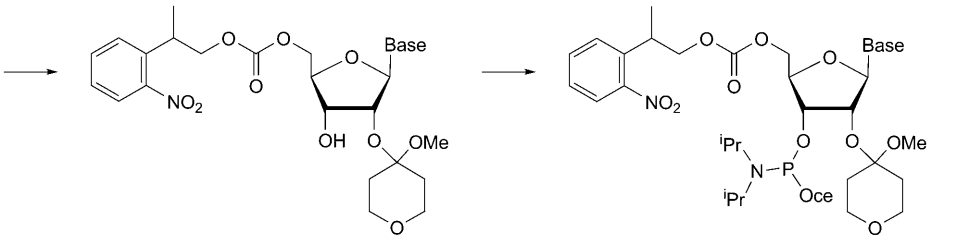


	Base
1	Ura
2	Cyt^{pac}
3	Ade^{pac}
4	Gua_{pac}
5	Cyt^{npeoc}
6	Ade^{npeoc}
7	Gua^{npe}_{npeoc}

	Base
8	Ura
9	Cyt^{pac}
10	Ade^{pac}
11	Gua_{pac}
12	Cyt^{npeoc}
13	Ade^{npeoc}
14	Gua^{npe}_{npeoc}

	Base
15	Ura
16	Cyt^{pac}
17	Ade^{pac}
18	Gua_{pac}
19	Cyt^{npeoc}
20	Ade^{npeoc}
21	Gua^{npe}_{npeoc}

	Base
22	Ura
23	Cyt^{pac}
24	Ade^{pac}
25	Gua_{pac}
26	Cyt^{npeoc}
27	Ade^{npeoc}
28	Gua^{npe}_{npeoc}



	Base
29	Ura
30	Cyt^{pac}
31	Ade^{pac}
32	Gua_{pac}
33	Cyt^{npeoc}
34	Ade^{npeoc}
35	Gua^{npe}_{npeoc}

	Base
36	Ura
37	Cyt^{pac}
38	Ade^{pac}
39	Gua_{pac}
40	Cyt^{npeoc}
41	Ade^{npeoc}
42	Gua^{npe}_{npeoc}

The next steps included the 3′,5′-protection by *Markiewicz*'s 1,1,3,3-tetraisopropyldisiloxane-1,3-diyl group (see **8**–**14** [33–36]) and was followed by the introduction of the tetrahydro-4-methoxy-2*H*-pyran-4-yl residue at the 2′-OH position leading to **15**–**21**. Deprotection of the silyl group by fluoride ion proceeded well and led to the modified ribonucleosides **22**–**28**. Several compounds of these two series have been described before [32][33][36], and the new types have been prepared by similar procedures.

The interconversion of compounds **22**–**28** into the 5′-*O*-{[2-(2-nitrophenyl)propoxy]carbonyl} (=5′-[2-(2-nitrophenyl)propyl carbonate]) derivatives **29**–**35** proceeded well on acylation with [2-(2-nitrophenyl)propoxy]carbonyl chloride (=2-(2-nitrophenyl)propyl carbonochloridate) in pyridine. The final phosphitylation to **36**–**42** was

achieved by 2-cyanoethyl *N*,*N*,*N*′,*N*′-tetraisopropylphosphorodiamidite in good to excellent yields. The newly synthesized compounds were characterized by UV and ^{1}H- and ^{31}P-NMR spectra as well as elemental analyses.

Experimental Part

General. Products were dried under high vacuum. All solvents used were of anh. grade. TLC: precoated silica gel (SiO_2) thin-layer sheets *60 F_{254}* from *Merck*. Flash Chromatography (FC): SiO_2 (30–60 μm, *Baker*); 0.2–0.3 bar. M.p.: *Büchi* melting-point apparatus *B-545*; uncorrected. UV/VIS: *Perkin-Elmer Lambda 5*; λ_{max} ($\log \varepsilon$) in nm. ^{1}H-NMR: *Bruker AC 250*; δ in ppm rel. to Me_4Si or $CDCl_3$ ((D_6)DMSO) as internal standard, *J* in Hz. ^{31}P-NMR: *Jeol JMN-GX400*.

N^4-*(Phenoxyacetyl)cytidine* (**2**) [31]. A mixture of cytidine (30.0 g, 0.12 mol) and hexamethyldisilazane (300 ml) was refluxed for 4 h and then evaporated, and the residue was dissolved in pyridine (200 ml). A suspension of 3-methyl-1-(phenoxyacetyl)-1*H*-imidazol-3-ium chloride (MPIC), prepared from phenoxyacetyl chloride (pac-Cl; 30.7 g, 0.18 mol) and 1-methyl-1*H*-imidazole (MeIm; 16.4 g, 0.2 mol), in CH_2Cl_2 (400 ml) was added at 4° by portions within 30 min. The mixture was stirred at r.t. for 20 h, the CH_2Cl_2 distilled off, and ice (15 g) added. The soln. was cooled with ice, then conc. $NH_3 \cdot H_2O$ (15 ml) was added dropwise, and after stirring for 4 h at r.t., the precipitate was washed with pyridine (2×100 ml) and CH_2Cl_2 (2×100 ml). The combined filtrates were concentrated and then treated with CH_2Cl_2 (200 ml) in a ultrasonic bath for 5 min. The precipitate was collected by suction and washed with CH_2Cl_2, and the solid treated with H_2O (200 ml) in an ultrasonic bath again. The precipitate was filtered off, washed with H_2O (3×100 ml), and dried (P_4O_{10}) in a vacuum desiccator: 28.3 g (61%) of **2**. Colorless solid. M.p. 180–182°. ^{1}H-NMR ((D_6)DMSO): 10.99 (*s*, NH); 8.45 (*d*, H–C(6)); 7.28 (*d*, 2 arom. H); 7.10 (*d*, H–C(5)); 6.92 (*m*, 3 arom. H); 5.77 (*d*, H–C(1′)); 5.49 (*d*, HO–C(2′)); 5.16 (*t*, HO–C(5′)); 5.05 (*d*, HO–C(3′)); 4.81 (*s*, CH_2O); 3.95 (*m*, H–C(2′,3′,4′)); 3.71 (*m*, 1 H–C(5′)); 3.60 (*m*, 1 H–C(5′)).

N^6-*(Phenoxyacetyl)adenosine* (**3**) [31]. As described for **2**, with adenosine (32.0 g, 0.12 mol) in pyridine (200 ml) and chlorotrimethylsilane (Me_3Si-Cl) (98.0 g, 0.9 mol) and stirring at r.t. for 2 h. After cooling to 4°, a suspension of MPIC (from pac-Cl (30.7 g, 0.18 mol) and MeIm (16.4 g, 0.2 mol)) in CH_2Cl_2 (400 ml) was added within 30 min. After stirring for 18 h at r.t., analog workup gave 39.0 g (81%) of **3**. Colorless solid. M.p. 110–112° (from EtOH/H_2O 1:1). ^{1}H-NMR ((D_6)DMSO): 10.96 (*s*, NH); 8.73 (*s*, H–C(2)); 8.68 (*s*, H–C(8)); 7.37–6.90 (*m*, 5 arom. H); 6.01 (*d*, H–C(1′)); 5.55 (*d*, HO–C(2′)); 5.25 (*d*, HO–C(3′)); 5.13 (*t*, HO–C(5′)); 5.03 (*s*, CH_2O); 4.61 (*m*, H–C(2′)); 4.17 (*m*, H–C(3′)); 3.97 (*m*, H–C(4′)); 3.66 (*m*, 1 H–C(5′)); 3.58 (*m*, 1 H–C(5′)).

N^2-*(Phenoxyacetyl)guanosine* (**4**) [31]. As described for **3**, with guanosine (28.3 g, 0.1 mol) and Me_3Si-Cl (81.6 g, 95 ml, 0.74 mol) in pyridine (300 ml), MPIC (from pac-Cl (25.6 g, 0.15 mol) and MeIm (13.9 g, 0.17 mol)) in CH_2Cl_2 (400 ml): 35.0 g (84%) of **4**. Colorless solid. M.p. 128–133° (dec.). ^{1}H-NMR ((D_6)DMSO): 11.85, 11.78 (2*s*, 2 NH); 7.33–6.92 (*m*, 5 arom. H); 5.81 (*d*, H–C(1′)); 5.49 (*d*, HO–C(2′)); 5.18 (*d*, HO–C(3′)); 5.03 (*t*, HO–C(5′)); 4.86 (*s*, CH_2O); 4.44 (*m*, H–C(2′)); 4.12 (*m*, H–C(3′)); 3.90 (*m*, H–C(4′)); 3.59 (*m*, 2 H–C(5′)).

N^4-*{[2-(4-Nitrophenyl)ethoxy]carbonyl}cytidine* (**5**) [32].

N^6-*{[2-(4-Nitrophenyl)ethoxy]carbonyl}adenosine* (**6**) [32].

N^2-*{[2-(4-Nitrophenyl)ethoxy]carbonyl}*-O^6-*[2-(4-nitrophenyl)ethyl]guanosine* (**7**) [32].

3′,5′-O-*(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)uridine* (**8**) [33]. A soln. of uridine (9.8 g, 40 mmol) in pyridine (100 ml) was treated with 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (tipdsCl_2) (14.0 g, 44 mmol) for 18 h at r.t. Then, MeOH (2 ml) was added with stirring, and after 10 min, the soln. diluted with $CHCl_3$ (200 ml) and washed with $NaHCO_3$ soln. (2×150 ml). The org. layer was dried (Na_2SO_4) and concentrated and the residue co-concentrated with toluene (2×100 ml) and $CHCl_3$ (2×150 ml): 19.0 g (97%) of **8**. Amorphous solid foam which was used for the next step to **15** without further purification. ^{1}H-NMR ((D_6)DMSO): 11.36 (*s*, NH); 7.68 (*d*, H–C(6)); 5.59 (*d*, HO–C(2′)); 5.52 (*d*, H–C(1′)); 5.50 (*d*, H–C(5)); 4.20–3.85 (*m*, H–C(2′,3′,4′), CH_2(5′)); 1.03–0.95 (*m*, 4 i-Pr).

N^4-*(Phenoxyacetyl)-3′,5′*-O-*(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)cytidine* (**9**). As described for **8**, with **2** (20.0 g, 53 mmol) and tipdsCl_2 (18.3 g, 58 mmol) in pyridine (150 ml): 32.1 g (97%) of **9**.

Amorphous foam, pure enouph for the next step. ^{1}H-NMR ((D$_6$)DMSO): 11.01 (*s*, NH); 8.14 (*d*, H–C(6)); 7.28 – 6.92 (*m*, 5 arom. H); 7.13 (*d*, H–C(5)); 5.79 (*d*, HO–C(2′)); 5.60 (*d*, H–C(1′)); 4.81 (*s*, CH_2O); 4.40 (*s*, H–C(3′); 4.06 (*m*, H–C(2′,4′), CH_2(5′)); 1.04 – 0.94 (*m*, 4 i-Pr).

N^6-*(Phenoxyacetyl)-3′,5′*-O-*(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)adenosine* (**10**) [34]. As described for **9**, with **3** (20.0 g, 50 mmol) and tipdsCl$_2$ (17.3 g, 55 mmol) in pyridine (150 ml): 30.9 g (98%) of **10**. Amorphous solid. ^{1}H-NMR ((D$_6$)DMSO): 10.98 (*s*, NH); 8.59 (*s*, H–C(2)); 8.54 (*s*, H–C(8)); 7.32 – 6.93 (*m*, 5 arom. H); 5.98 (*d*, H–C(1′)); 5.71 (*d*, HO–C(2′)); 5.02 (*s*, CH_2O); 4.77 (*s*, H–C(3′); 4.59 (*m*, H–C(2′)); 4.04 (*m*, H–C(4′), CH_2(5′)); 1.03 – 0.94 (*m*, 4 i-Pr).

N^2-*(Phenoxyacetyl)-3′,5′*-O-*(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)guanosine* (**11**) [35]. As described for **9**, with **4** (20.8 g, 50 mmol) and tipdsCl$_2$ (17.3 g, 55 mmol) in pyridine (150 ml): crude **11** which was purified by CC (SiO_2 (8 × 15 cm), hexane/AcOEt 4 : 1 and hexane/AcOEt/acetone 4 : 1 : 1): 27.6 g (84%) of **11**. Amorphous foam. ^{1}H-NMR ((D$_6$)DMSO): 11.90, 11.80 (2*s*, 2 NH); 8.06 (*s*, H–C(8)); 7.35 – 6.90 (*m*, 5 arom. H); 5.79 (*d*, H–C(1′)); 5.73 (*d*, HO–C(2′)); 4.86 (*s*, CH_2O); 4.33 (*m*, H–C(2′,3′)); 4.00 (*m*, H–C(4′), CH_2(5′)); 1.04 – 0.94 (*m*, 4 i-Pr).

N^4-*{[2-(4-Nitrophenyl)ethoxy]carbonyl}-3′,5′*-O-*(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)cytidine* (**12**) [36].

N^6-*{[2-(4-Nitrophenyl)ethoxy]carbonyl}-3′,5′*-O-*(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)adenosine* (**13**) [36].

N^2-*{[2-(4-Nitrophenyl)ethoxy]carbonyl}*-O^6-*[2-(4-nitrophenyl)ethyl]-3′,5′*-O-*(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)guanosine* (**14**) [36].

2′-O-*(Tetrahydro-4-methoxy-2*H*-pyran-4-yl)-3′,5′*-O-*(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)uridine* (*= 1-{Tetrahydro-2,2,4,4-tetraisopropyl-9-[(tetrahydro-4-methoxy-2*H*-pyran-4-yl)oxy]-6*H*-furo[3,2-f][1,3,5,2,4]trioxadisilocin-8-yl}uracil*; **15**) [36].

N^4-*(Phenoxyacetyl)-2′*-O-*(tetrahydro-4-methoxy-2*H*-pyran-4-yl)-3′,5′*-O-*(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)cytidine* (**16**). A mixture of **9** (16.6 g, 26.8 mmol), (−)-camphor-10-sulfonic acid (CSA; 2.0 g, 8.9 mmol), molecular sieves (MS; 4.5 g), and 3,6-dihydro-4-methoxy-2*H*-pyran (5.0 g, 43.8 mmol) in CH_2Cl_2 (100 ml) was stirred at r.t. for 18 h and then neutralized by pyridine (2 ml). The molecular sieves were filtered off and washed with $CHCl_3$ (200 ml). The combined filtrate was washed with $NaHCO_3$ soln., the org. phase dried (Na_2SO_4), concentrated and co-concentrated with toluene (100 ml), and the residue purified by CC (SiO_2 (5 × 15 cm), hexane/acetone 9 : 1 and 6 : 1): 2.3 g of **9** and 10.7 g (60%) of **16**. Amorphous foam. ^{1}H-NMR ((D$_6$)DMSO): 11.05 (*s*, NH); 8.24 (*d*, H–C(6)); 7.28 – 6.92 (*m*, 5 arom. H); 7.13 (*d*, H–C(5)); 5.94 (*d*, H–C(1′)); 4.81 (*s*, CH_2O); 4.44 (*d*, H–C(2′)); 4.16 (*m*, H–C(3,'4′), 1 H–C(5′)); 3.95 (*dd*, 1 H–C(5′)); 3.65, 3.50 (2*m*, CH_2OCH_2); 3.23 (*s*, MeO); 1.98, 1.78 (2*m*, CH_2CCH_2); 1.04 – 0.95 (*m*, 4 i-Pr).

N^6-*(Phenoxyacetyl)-2′*-O-*(4-tetrahydro-4-methoxy-2*H*-pyran-4-yl)-3′,5′*-O-*(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)adenosine* (**17**). As described for **16**, with **10** (10.0 g, 15.5 mmol), CSA (1.0 g, 4.3 mmol), MS (3.5 g), and 3,6-dihydro-4-methoxy-2*H*-pyran (5.0 g, 43.8 mmol) in CH_2Cl_2 (70 ml). Neutralization by pyridine (1 ml), workup and CC gave 2.3 g of **10** and 6.5 g (76%) of **17**. Amorphous foam. ^{1}H-NMR ((D$_6$)DMSO): 10.97 (*s*, NH); 8.58 (*s*, H–C(2.8)); 7.32 – 6.93 (*m*, 5 arom. H); 6.11 (*d*, H–C(1′)); 5.02 (*s*, CH_2O); 4.98 (*d*, H–C(2′); 4.90 (*m*, H–C(3′)); 4.15 – 3.90 (*m*, H–C(4′), 1 H–C(5′)); 3.95 (*dd*, 1 H–C(5′)); 3.70, 3.42 (2*m*, CH_2OCH_2); 3.17 (*s*, MeO); 1.77 (*m*, CH_2CCH_2); 1.03 – 0.99 (*m*, 4 i-Pr).

N^2-*(Phenoxyacetyl)-2′*-O-*(tetrahydro-4-methoxy-2*H*-pyran-4-yl)-3′,5′*-O-*(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)guanosine* (**18**). As described for **16**, with **11** (6.0 g, 0.9 mmol), CSA (0.2 g, 0.9 mmol), MS (2.0 g), and 3,6-dihydro-4-methoxy-2*H*-pyran (8.3 g, 72.7 mmol) in CH_2Cl_2 (30 ml) for 8 h. Neutralization by pyridine (1 ml), workup, and CC gave 5.5 g (78%) of **18**. Colorless solid. M.p. 173 – 174° (from EtOH). ^{1}H-NMR ((D$_6$)DMSO): 11.84, 11.50 (2*s*, 2 NH); 8.18 (*s*, H–C(8)); 7.33 – 6.95 (*m*, 5 arom. H); 5.88 (*d*, H–C(1′)); 4.85 (*s*, CH_2O); 4.71 (*d*, H–C(2′)); 4.47 (*m*, H–C(3′)); 4.05 (*m*, H–C(4′), 1 H–C(5′)); 3.95 (*m*, 1 H–C(5′)); 3.69, 3.40 (2*m*, CH_2OCH_2); 3.04 (*s*, MeO); 1.78 (*m*, CH_2CCH_2); 1.01 – 1.01 (*m*, 4 i-Pr).

N^4-*{[2-(4-Nitrophenyl)ethoxy]carbonyl}-2′*-O-*(tetrahydro-4-methoxy-2*H*-pyran-4-yl)-3′,5′*-O-*(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)cytidine* (**19**) [36].

N^6-*{[2-(4-Nitrophenyl)ethoxy]carbonyl}-2′*-O-*(tetrahydro-4-methoxy-2*H*-pyran-4-yl)-3′,5′*-O-*(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)adenosine* (**20**) [36].

N^2-*{[2-(4-Nitrophenyl)ethoxy]carbonyl}*-O^6-*[2-(4-nitrophenyl)ethyl]-2′*-O-*(tetrahydro-4-methoxy-2*H-*pyran-4-yl)-3′,5′*-O-*(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)guanosine* (**21**) [36].

2′-O-*(Tetrahydro-4-methoxy-2*H-*pyran-4-yl)uridine* (**22**) [36].

N^4-*(Phenoxyacetyl)-2′*-O-*(tetrahydro-4-methoxy-2*H-*pyran-4-yl)cytidine* (**23**). To a soln. of **16** (10.5 g, 14.3 mmol) in THF (80 ml) was added $Bu_4NF \cdot 3\ H_2O$ (12.2 g, 38.6 mmol) in THF (50 ml) with stirring. After 10 min, the mixture was neutralized by AcOH (9.2 ml, 154.4 mmol) in THF (30 ml) and concentrated. The residue was dissolved in $CHCl_3$ (500 ml), the soln. washed with $NaHCO_3$ soln. (200 ml) and H_2O (100 ml), dried (Na_2SO_4), and concentrated, and the residue crystallized from EtOH: 6.2 g (88%) of **23**. Colorless crystals. M.p. 150–152°. ^{1}H-NMR ((D$_6$)DMSO): 11.02 (*s*, NH); 8.40 (*d*, H–C(6)); 7.32–6.90 (*m*, 5 arom. H); 7.16 (*d*, H–C(5)); 6.09 (*d*, H–C(1′)); 5.17 (*m*, HO–C(3′), HO–C(5′)); 4.81 (*s*, CH_2O); 4.34 (*d*, H–C(2′)); 3.96 (*m*, H–C(3′,4′)); 3.95 (*dd*, 1 H–C(5′)); 3.70–3.30 (*m*, 1 H–C(5′), CH_2OCH_2); 2.90 (*s*, MeO); 1.67 (*m*, CH_2CCH_2).

N^6-*(Phenoxyacetyl)-2′*-O-*(tetrahydro-4-methoxy-2*H-*pyran-4-yl)adenosine* (**24**). As described for **23**, with **17** (8.0 g, 10.5 mmol) in THF (70 ml) and Bu_4NF (8.0 g, 25.4 mmol) in THF (80 ml) and stirring at r.t. for 10 min. Neutralization with AcOH (5.7 ml) in THF (10 ml), evaporation, and purification of the residue by CC (SiO_2 (5 × 25 cm), $CHCl_3$ and $CHCl_3$/MeOH 20:1) gave 4.7 g (87%) of **24**. Amorphous foam. ^{1}H-NMR ((D$_6$)DMSO): 10.97 (*s*, NH); 8.79 (*s*, H–C(2)); 8.70 (*s*, H–C(8)); 7.32–6.94 (*m*, 5 arom. H); 6.16 (*d*, H–C(1′)); 5.32 (*d*, HO–C(3′)); 5.26 (*t*, HO–C(5′)); 5.03 (*s*, CH_2O); 4.96 (*d*, H–C(2′)); 4.16 (*m*, H–C(3′)); 4.03 (*m*, H–C(4′)); 3.68–3.19 (*m*, CH_2(5′), CH_2OCH_2); 2.57 (*s*, MeO); 1.72, 1.51 (2*m*, CH_2CCH_2).

N^2-*(Phenoxyacetyl)-2′*-O-*(tetrahydro-4-methoxy-2*H-*pyran-4-yl)guanosine* (**25**). As described for **24**, with **18** (7.9 g, 9.4 mmol), THF (50 ml), and Bu_4NF (8.3 g, 26 mmol) in THF (35 ml): 4.4 g (87%) of **25**. Amorphous foam. ^{1}H-NMR ((D$_6$)DMSO): 11.84, 11.79 (2*s*, 2 NH); 8.32 (*s*, H–C(8)); 7.34–6.95 (*m*, 5 arom. H); 5.79 (*d*, H–C(1′)); 5.21 (*d*, HO–C(3′)); 5.15 (*t*, HO–C(5′)); 4.85 (*s*, CH_2O); 4.72 (*dd*, H–C(2′)); 4.10 (*m*, H–C(3′)); 3.97 (*m*, H–C(4′)); 3.95 (*m*, 1 H–C(5′)); 3.70–3.40 (*m*, 1 H–C(5′), CH_2OCH_2); 2.60 (*s*, MeO); 1.70, 1.52 (2*m*, CH_2CCH_2).

N^4-*{[2-(4-Nitrophenyl)ethoxy]carbonyl}-2′*-O-*(tetrahydro-4-methoxy-2*H-*pyran-4-yl)cytidine* (**26**) [36].

N^6-*{[2-(4-Nitrophenyl)ethoxy]carbonyl}-2′*-O-*(tetrahydro-4-methoxy-2*H-*pyran-4-yl)adenosine* (**27**) [36].

N^2-*{[2-(4-Nitrophenyl)ethoxy]carbonyl}*-O^6-*[2-(4-nitrophenyl)ethyl]-2′*-O-*(tetrahydro-4-methoxy-2*H-*pyran-4-yl)guanosine* (**28**) [36].

2′-O-*(Tetrahydro-4-methoxy-2*H-*pyran-4-yl)uridine 5′-[2-(2-Nitrophenyl)propyl Carbonate]* (**29**). To a soln. of **22** (4.9 g, 13.7 mmol) in abs. pyridine (60 ml) was added slowly, at −30° under Ar and stirring, 2-(2-nitrophenyl)propyl carbonochloridate [24] (nppoc-Cl; 5.0 g, 20.5 mmol) in CH_2Cl_2 (20 ml). After 5 h, the temp. was raised to −10°, then MeOH (1 ml) added, and the mixture stirred at r.t. for 1 h. The mixture was diluted with $CHCl_3$ (20 ml), the soln. washed with $NaHCO_3$ soln. (100 ml), dried (Na_2SO_4), concentrated and co-concentrated with toluene (2 × 50 ml), and the residue purified by CC (SiO_2 (6.5 × 10 cm), $CHCl_3$ and $CHCl_3$/MeOH 50:1): first 3.96 g (37%) of the 3′,5′-di-*O*-acylated derivative and then 4.1 g (53%) of **29**. Amorphous foam. UV (MeOH): 206 (4.29), 257 (4.08). ^{1}H-NMR ((D$_6$)DMSO): 11.41 (*s*, NH); 7.81–7.44 (*m*, H–C(6), 4 arom. H); 5.93 (*d*, H–C(1′)); 5.62 (*d*, H–C(5)); 5.34 (*d*, HO–C(3′)); 4.28 (*m*, H–C(4′), CH_2(5′), CH_2O); 3.99 (*d*, H–C(2′)); 3.91 (*m*, H–C(3′)); 3.47 (*m*, Me*CH*CH_2O, CH_2OCH_2); 2.96 (*s*, MeO); 1.66 (*m*, CH_2CCH_2); 1.27 (*d*, *Me*$CHCH_2O$). Anal. calc. for $C_{25}H_{31}N_3O_{12}$ (565.5): C 53.09, H 5.52, N 7.43; found: C 52.80, H 5.53, N 7.27.

N^4-*(Phenoxyacetyl)-2′*-O-*(tetrahydro-4-methoxy-2*H-*pyran-4-yl)cytidine 5′-[2-(2-Nitrophenyl)propyl Carbonate]* (**30**). As described for **29**, with **23** (6.9 g, 14 mmol), pyridine (100 ml), and nppoc-Cl (4.14 g, 17 mmol) in CH_2Cl_2 (40 ml). Purification by CC (SiO_2 (6.5 × 12 cm), $CHCl_3$, $CHCl_3$/MeOH 50:1) gave 5.3 g (60%) of **30**. Amorphous foam and 2.0 g (18%) of the di-*O*-acylated derivative. UV (MeOH): 208 (4.56), 248 (4.30), 300 (3.91). ^{1}H-NMR ((D$_6$)DMSO): 11.06 (*s*, NH); 8.09–6.90 (*m*, H–C(6), H–C(5), 9 arom. H); 6.02 (*d*, H–C(1′)); 5.37 (*d*, HO–C(3′)); 4.83 (*s*, CH_2OCO); 4.38 (*d*, H–C(2′)); 4.27 (*m*, CH_2(5′), CH_2O); 4.05 (*m*, H–C(3′)); 3.96 (*m*, H–C(4′)); 3.46 (*m*, Me*CH*CH_2O, CH_2OCH_2); 2.91 (*s*, MeO); 1.65 (*m*, CH_2CCH_2); 1.26 (*d*, *Me*$CHCH_2O$). Anal. calc. for $C_{33}H_{38}N_4O_{13} \cdot H_2O$ (716.7): C 55.30, H 5.62, N 7.81; found: C 55.33, H 5.41, N 7.56.

N^6-*(Phenoxyacetyl)-2′*-O-*(tetrahydro-4-methoxy-2*H*-pyran-4-yl)adenosine 5′-[2-(2-Nitrophenyl)-propyl Carbonate]* (**31**). As described for **29**, with **24** (4.9 g, 9.5 mmol), pyridine (50 ml), and nppoc-Cl (3.4 g, 14 mmol) in CH_2Cl_2 (20 ml). Purification by CC (SiO_2 (5 × 15 cm), $CHCl_3$, $CHCl_3$/MeOH 50:1) gave 4.3 g (61%) of **31**. Amorphous foam. UV (MeOH): 206 (4.57), 269 (4.40). ^{1}H-NMR ((D$_6$)DMSO): 10.96 (*s*, NH); 8.70, 8.66 (2*s*, H–C(2), H–C(8)); 7.84–6.92 (*m*, 9 arom. H); 6.16 (*d*, H–C(1′)); 5.52 (*d*, HO–C(3′)); 5.03 (*m*, H–C(2′), CH_2OCO); 4.29 (*m*, H–C(3′,4′), CH_2(5′), CH_2O); 3.60–3.20 (*m*, Me*C*HCH_2O, CH_2OCH_2); 2.57 (*s*, MeO); 1.72, 1.52 (2*m*, CH_2CCH_2); 1.25 (*d*, *Me*CHCH_2O). Anal. calc. for $C_{34}H_{38}N_6O_{12}\cdot H_2O$ (740.7): C 55.13, H 5.44, N 11.34; found: C 55.33, H 5.38, N 11.21.

N^2-*(Phenoxyacetyl)-2′*-O-*(tetrahydro-4-methoxy-2*H*-pyran-4-yl)guanosine 5′-[2-(2-Nitrophenyl)-propyl Carbonate]* (**32**). As described for **29**, with **25** (4.6 g, 8.65 mmol) in pyridine (50 ml) and nppoc-Cl (2.95 g, 14 mmol) in CH_2Cl_2 (20 ml). Purification by CC (SiO_2 (6.5 × 10 cm), $CHCl_3$, $CHCl_3$/MeOH 50:1) gave 4.85 g (76%) of **32**. Amorphous foam. UV (MeOH): 204 (4.61), 254 (4.26), 275 (sh, 4.14). ^{1}H-NMR ((D$_6$)DMSO): 11.79, 11.72 (2*s*, 2 NH); 8.22 (*s*, H–C(8)); 7.68–6.94 (*m*, 9 arom. H); 5.97 (*d*, H–C(1′)); 5.41 (*d*, HO–C(3′)); 4.85 (*s*, CH_2OCO); 4.79 (*m*, H–C(2′)); 4.31 (*m*, H–C(3′,4′), CH_2O); 4.12 (*m*, CH_2(5′)); 3.60 (*m*, Me*C*HCH_2O); 3.40 (*m*, CH_2OCH_2); 2.68 (*s*, MeO); 1.72, 1.52 (2*m*, CH_2CCH_2); 1.27 (*d*, *Me*CHCH_2O). Anal. calc. for $C_{34}H_{38}N_6O_{13}\cdot H_2O$ (756.7): C 55.96, H 5.32, N 11.10; found: C 56.26, H 5.30, N 10.99.

N^4-*{[2-(4-Nitrophenyl)ethoxy]carbonyl}-2′*-O-*(tetrahydro-4-methoxy-2*H*-pyran-4-yl)cytidine 5′-[2-(2-Nitrophenyl)propyl Carbonate]* (**33**). As described for **29**, with **26** (6.0 g, 10.6 mmol), pyridine (60 ml), and nppoc-Cl (3.08 g, 12.6 mmol) in CH_2Cl_2 (20 ml). Isolation and purification by FC (SiO_2 (6.5 × 12 cm), CH_2Cl_2 (200 ml), CH_2Cl_2/MeOH 100:1 → 100:3) gave 4.21 g (53%) of **33**. Colorless foam. UV (MeOH): 205 (4.57), 246 (4.34), 281 (sh, 4.19). ^{1}H-NMR ((D$_6$)DMSO): 10.86 (*s*, NH); 8.16 (*d*, 2 H *o* to NO_2); 8.00 (*m*, 1 H *o* to NO_2 (nppoc)); 7.81 (*d*, H–C(6)); 7.68 (*m*, 2 arom H (nppoc)); 7.60 (*d*, 2 H *m* to NO_2); 7.48 (*m*, 1 arom.H (nppoc)); 7.00 (*m*, H–C(5)); 6.00 (*d*, H–C(1′)); 5.35 (*d*, HO–C(3′)); 4.39–4.26 (*m*, 7 H, CH_2OCO (npeoc), CH_2OCO (nppoc), H–C(2′), CH_2(5′)); 4.03 (*m*, H–C(3′)); 3.95 (*m*, H–C(4′)); 3.67–3.41 (*m*, Me*C*HCH_2O, CH_2OCH_2); 3.08 (*t*, Ar*CH*$_2$); 2.89 (*s*, MeO); 1.70 (*m*, CH_2CCH_2); 1.27 (*d*, *Me*CHCH_2O). Anal. calc. for $C_{34}H_{39}N_5O_{15}$ (757.7): C 53.90, H 5.19, N 9.24; found: C 54.08, H 5.27, N 9.09.

N^6-*{[2-(4-Nitrophenyl)ethoxy]carbonyl}-2′*-O-*(tetrahydro-4-methoxy-2*H*-pyran-4-yl)adenosine 5′-[2-(2-Nitrophenyl)propyl Carbonate]* (**34**). As described for **29**, with **27** (6.0 g, 10.13 mmol), pyridine (60 ml), and nppoc-Cl (2.94 g, 12.15 mmol) in CH_2Cl_2 (30 ml), all at −30°. Isolation by FC (SiO_2 (6.5 × 12 cm), CH_2Cl_2 (300 ml), CH_2Cl_2/MeOH 100:1 → 100:3) gave 5.0 g (63%) of **34**. Colorless foam. UV (MeOH): 206 (4.64), 266 (4.48). ^{1}H-NMR ($CDCl_3$): 8.73 (*s*, H–C(2)); 8.34 (br. *s*, NH); 8.17 (*m*, H–C(8), 2 H *o* to NO_2); 8.00 (*m*, 1 H *o* to NO_2 (nppoc)); 7.61–7.34 (*m*, 3 arom. H of nppoc, 2 H *m* to NO_2); 6.18 (*d*, H–C(1′)); 5.06 (*m*, H–C(2′)); 4.54 (*t*, CH_2OCO (npeoc)); 4.49–4.23 (*m*, H–C(3′,4′), CH_2(5′), CH_2OCO (nppoc)); 3.85–3.36 (*m*, Me*C*HCH_2O, CH_2OCH_2); 3.16 (*t*, Ar*CH*$_2$); 2.95 (*s*, HO–C(3′)); 2.81 (*s*, MeO); 1.80 (*m*, CH_2CCH_2); 1.38 (*d*, *Me*CHCH_2O). Anal. calc. for $C_{35}H_{39}N_7O_{14}\cdot 0.5\ H_2O$ (790.7): C 53.16, H 4.97, N 12.40; found: C 53.08, H 5.02, N 12.09.

N^2-*{[2-(4-Nitrophenyl)ethoxy]carbonyl}*-O^6-*[2-(4-nitrophenyl)ethyl]-2′*-O-*(tetrahydro-4-methoxy-2*H*-pyran-4-yl)guanosine 5′-[2-(2-Nitrophenyl)propyl Carbonate]* (**35**). As described for **29**, with **28** (6.0 g, 8.1 mmol), pyridine (60 ml), and nppoc-Cl (2.57 g, 10.56 mmol) in CH_2Cl_2 (60 ml). Isolation by FC (SiO_2 (6.5 × 12 cm), CH_2Cl_2 (300 ml), CH_2Cl_2/MeOH 100:1 → 100:3) gave 6.3 g (82%) of **35**. Colorless foam. UV (MeOH): 204 (sh, 4.66), 214 (4.68), 268 (4.57). ^{1}H-NMR ($CDCl_3$): 8.16 (*m*, 4 H *o* to NO_2); 7.92 (*d*, H–C(8)); 7.75 (*d*, 1 H *o* to NO_2 (nppoc)); 7.60–7.32 (*m*, 3 arom. H of nppoc, 4 H *m* to NO_2, NH); 6.00 (*d*, H–C(1′)); 5.20 (*m*, H–C(2′)); 4.80 (*t*, CH_2OCO (npe)); 4.47–4.20 (*m*, H–C(3′,4′), CH_2(5′), CH_2OCO (nppoc), CH_2O); 3.77–3.37 (*m*, Me*C*HCH_2O, CH_2OCH_2); 3.31 (*t*, Ar*CH*$_2$ (npe)); 3.12 (*t*, Ar*CH*$_2$ (npeoc)); 2.87 (*s*, MeO); 2.79 (*s*, OH–C(3′)); 1.80 (*m*, CH_2CCH_2); 1.36 (*d*, *Me*CHCH_2O). Anal. calc. for $C_{43}H_{46}N_8O_{17}$ (946.9): C 54.54, H 4.90, N 11.83; found: C 54.45, H 4.95, N 11.43.

2′-O-*Tetrahydro-4-methoxy-2*H*-pyran-4-yl)uridine 3′-(2-Cyanoethyl* N,N-*Diisopropylphosphoramidite) 5′-[2-(2-Nitrophenyl)propyl Carbonate]* (**36**). A mixture of **29** (6.1 g, 10.8 mmol), 2-cyanoethyl *N*,*N*,*N*′,*N*′-tetraisopropylphosphorodiamidite (ceOP(N^{i}Pr$_2$)$_2$) (4.87 g, 16.18 mmol), and 1*H*-tetrazole (0.38 g, 5.4 mmol) in CH_2Cl_2 (50 ml) was stirred at r.t. for 20 h. After dilution with $CHCl_3$ (200 ml), the

mixture was washed with $NaHCO_3$ soln. (2 × 100 ml), the org. layer dried (Na_2SO_4) and concentrated, the residue dissolved in CH_2Cl_2 (20 ml), and then the soln. dropwise added into hexane (800 ml). The precipitate was filtered off and dissolved again in CH_2Cl_2 (100 ml), and the soln. concentrated: 8.2 g (99%) of **36**. Colorless foam. UV (MeOH): 204 (4.42), 258 (4.09). ^{31}P-NMR ($CHCl_3$): 152.2401; 152.1958; 150.0892; 150.0302. Anal. calc. for $C_{34}H_{48}N_5O_{13}P$ (765.7): C 53.33, H 6.32, N 9.14; found: C53.61, H 6.74, N 9.21.

N^4-*(Phenoxyacetyl)-2′*-O-*(tetrahydro-4-methoxy-2*H*-pyran-4-yl)cytidine 3′-(2-Cyanoethyl* N,N-*Diisopropylphosphoramidite) 5′-[2-(2-Nitrophenyl)propyl Carbonate]* (**37**). As described for **36**, with **30** (5.08 g, 7.27 mmol), ceOP(N^{i}Pr$_2$)$_2$ (3.06 g, 10.17 mmol), and 1*H*-tetrazole (0.24 g, 3.4 mmol): 6.4 g (98%) of **37**. Colorless foam. UV (MeOH): 217 (4.32), 249 (4.28), 300 (3.90). ^{31}P-NMR ($CHCl_3$): 152.0044, 151.9308, 150.2807, 150.1923. Anal. calc. for $C_{42}H_{55}N_6O_{16}P$ (898.9): C 56.12, H 6.17, N 9.35; found: C55.91, H 6.36, N 9.21.

N^6-*(Phenoxyacetyl)-2′*-O-*(tetrahydro-4-methoxy-2*H*-pyran-4-yl)adenosine 3′-(2-Cyanoethyl* N,N-*Diisopropylphosphoramidite) 5′-[2-(2-Nitrophenyl)propyl Carbonate]* (**38**). As described for **36**, with **31** (6.0 g, 8.3 mmol), ceOP(N^{i}Pr$_2$)$_2$ (3.25 g, 10.8 mmol), and 1*H*-tetrazole (0.25 g, 3.6 mmol): 7.4 g (96%) of **38**. Colorless foam. UV (MeOH): 215 (4.44), 258 (sh, 4.24), 270 (4.33). ^{31}P-NMR ($CHCl_3$): 152.4466, 150.2218, 150.1628. Anal. calc. for $C_{43}H_{55}N_8O_{13}P$ (922.9): C 55.96, H 6.00, N 12.14; found: C 56.10, H 6.24, N 12.15.

N^2-*(Phenoxyacetyl)-2′*-O-*(tetrahydro-4-methoxy-2*H*-pyran-4-yl)guanosine 3′-(2-Cyanoethyl* N,N-*Diisopropylphosphoramidite) 5′-[2-(2-Nitrophenyl)propyl Carbonate]* (**39**). As described for **36**, with **32** (4.57 g, 6.18 mmol), ceOP(N^{i}Pr$_2$)$_2$ (2.8 g, 9.2 mmol), and 1*H*-tetrazole (0.22 g, 3.1 mmol): 5.68 g (98%) of **39**. Colorless foam. UV (MeOH): 207 (4.54), 254 (4.25), 275 (sh, 4.12). ^{31}P-NMR ($CHCl_3$): 152.4317; 152.3875; 150.2954; 150.2660. Anal. calc. for $C_{43}H_{55}N_8O_{14}P$ (930.9): C 55.00, H 5.90, N 11.93; found: C 54.56, H 6.36, N 11.82.

N^4-*{[2-(4-Nitrophenyl)ethoxy]carbonyl}-2′*-O-*(tetrahydro-4-methoxy-2*H*-pyran-4-yl)cytidine 3′-(2-Cyanoethyl* N,N-*Diisopropylphosphoramidite) 5′-[2-(2-Nitrophenyl)propyl Carbonate]* (**40**). To a mixture of **33** (5.66 g, 7.47 mmol) and 1*H*-tetrazole (0.24 g, 3.34 mmol) in CH_2Cl_2 (60 ml) was dropwise added ceOP(N^{i}Pr$_2$)$_2$ (3.2 g, 10.6 mmol) under N_2 and then stirred at r.t. for 22 h. The mixture was diluted with CH_2Cl_2 (100 ml) and washed with $NaHCO_3$ soln. (2 × 100 ml), the org. layer dried (Na_2SO_4) and concentrated, and the residue purified by FC (SiO_2 (5 × 12 cm), toluene (100 ml), toluene/AcOEt 7:3 → 1:4). The product fractions were concentrated and finally co-concentrated with CH_2Cl_2: 6.69 g (93%) of **40**. Colorless foam. UV (MeOH): 205 (4.69), 246 (4.42), 281 (sh, 4.25). ^{1}H-NMR ($CDCl_3$): 8.18 (*d*, 2 H *o* to NO_2); 7.92–7.83 (*m*, NH, 1 H *o* to NO_2(nppoc)); 7.77 (*d*, H–C(6)); 7.59 (*m*, 1 arom. H); 7.48 (*m*, 1 arom. H); 7.41 (*m*, 2 H *m* to NO_2, 1 arom. H); 7.15 (*d*, H–C(5)); 6.25 (*m*, H–C(1′)); 4.50–4.20 (*m*, CH_2O(npeoc), CH_2O, H–C(2′,3′,4′), CH_2(5′)); 4.00–3.40 (*m*, CH_2OCH_2, MeC*H*CH_2O, CH_2OP, 2 Me$_2$C*H*); 3.12 (*t*, ArC*H*$_2$); 3.0 (*s*, MeO); 2.67–2.57 (*m*, CH_2CN); 1.9–1.70 (*m*, CH_2CCH_2); 1.39 (*d*, *Me*$CHCH_2O$); 1.30–1.10 (*m*, 2 *Me*$_2$CH). ^{31}P-NMR ($CDCl_3$): 151.89; 151.82; 150.18; 150.12. Anal calc. for $C_{43}H_{56}N_7O_{16}P$ (957.9): C 53.92, H 5.89, N 10.24; found: C 53.68, H 6.16, 10.28.

N^6-*{[2-(4-Nitrophenyl)ethoxy]carbonyl}-2′*-O-*(tetrahydro-4-methoxy-2*H*-pyran-4-yl)adenosine 3′-(2-Cyanoethyl* N,N-*Diisopropylphosphoramidite) 5′-[2-(2-Nitrophenyl)propyl Carbonate]* (**41**). As described for **40**, with **34** (2.13 g, 2.72 mmol), 1*H*-tetrazole (0.12 g, 1.71 mmol), and ceOP(N^{i}Pr$_2$)$_2$ (1.6 g, 5.3 mmol) in CH_2Cl_2 (30 ml). FC (SiO_2, toluene/AcOEt 7:3 → 4:3) gave 2.04 g (76%) of **41**. Colorless foam. UV (MeOH): 206 (4.77), 266 (4.55). ^{1}H-NMR ($CDCl_3$): 8.75 (*s*, H–C(2)); 8.30–8.16 (*m*, H–C(8), NH, 2 H *o* to NO_2); 7.78 (*m*, 1 H *o* to NO_2(nppoc)); 7.58 (*m*, 1 arom. H); 7.50–7.30 (*m*, 3 arom. H, 2 H *m* to NO_2); 6.16 (*t*, H–C(1′)); 5.30–5.10 (*m*, H–C(2′)); 4.56–4.30 (*m*, CH_2O(npeoc), CH_2O, H–C(3′,4′), CH_2(5′)); 4.00–3.29 (*m*, CH_2OCH_2, MeC*H*CH_2O, CH_2OP, 2 MeC*H*); 3.16 (*t*, ArC*H*$_2$); 2.69 (*m*, CH_2CN); 2.60 (*s*, MeO); 1.9–1.60 (*m*, CH_2CCH_2); 1.35 (*d*, *Me*$CHCH_2O$); 1.30–1.10 (*m*, 2 *Me*$_2$CH). ^{31}P-NMR ($CDCl_3$): 152.37; 152.34; 150.15; 150.10. Anal calc. for $C_{44}H_{56}N_9O_{15}P$ (981.95): C 53.82, H 5.75, N 12.87; found: C 53.64, H 6.20, 12.38.

N^2-*{[2-(4-Nitrophenyl)ethoxy]carbonyl}*-O^6-*[2-(4-nitrophenyl)ethyl]-2′*-O-*(tetrahydro-4-methoxy-2*H*-pyran-4-yl)guanosine 3′-(2-Cyanoethyl* N,N-*Diisopropylphosphoramidite) 5′-[2-(2-Nitrophenyl)-propyl Carbonate]* (**42**). As described for **40**, with **35** (2.84 g, 3.0 mmol), 1*H*-tetrazole (0.12 g, 1.71 mmol), and ceOP(N^{i}Pr$_2$)$_2$ (1.8 g, 5.7 mmol) in CH_2Cl_2 (40 ml). FC (SiO_2, toluene (200 ml),

toluene/AcOEt 7:3 → 2:3) gave 2.53 g (74%) of **42**. Colorless foam. UV (MeOH): 204 (4.70), 268 (4.53). ^{1}H-NMR ($CDCl_3$): 8.15 (*m*, 4 H *o* to NO_2); 7.94 (*s*, H–C(8)); 7.75 (*m*, 1 H *o* to NO_2(nppoc)); 7.60–7.40 (*m*, NH, 4 H *m* to NO_2, 3 arom. H); 6.00 (*d*, H–C(1′)); 5.50 (*m*, H–C(2′)); 4.82 (*t*, CH_2CH_2O(npe)); 4.50–4.27 (*m*, CH_2O(npeoc), CH_2O, H–C(3′,4′), CH_2(5′)); 4.10–3.29 (*m*, CH_2OCH_2, $MeCHCH_2O$, CH_2OP, 2 Me_2CH, $ArCH_2$(npe)); 3.13 (*t*, $ArCH_2$(npeoc)); 2.72 (*m*, CH_2CN); 2.60 (*s*, MeO); 1.9–1.60 (*m*, CH_2CCH_2); 1.35 (*d*, $MeCHCH_2O$); 1.28–1.10 (*m*, 2 Me_2CH). ^{31}P-NMR ($CDCl_3$): 152.56; 152.43; 150.38; 150.16. Anal calc. for $C_{52}H_{63}N_{10}O_{18}P$ (1147.1): C 54.44, H 5.54, N 12.21; found: C 54.72, H 5.74, N 11.87.

REFERENCES

[1] T. Maier, W. Pfleiderer, *Helv. Chim. Acta* **2010**, *93*, 2365.
[2] A. Patchornik, B. Amit, R. B. Woodward, *J. Am. Chem. Soc.* **1970**, *92*, 6333.
[3] E. Ohtsuka, S. Tanaka, M. Ikehara, *Nucleic Acid Res.* **1974**, *1*, 1351; E. Ohtsuka, S. Tanaka, M. Ikehara, *Chem. Pharm. Bull.* **1977**, *25*, 949; E. Ohtsuka, S. Tanaka, M. Ikehara, *Synthesis* **1977**, 453; E. Ohtsuka, S. Tanaka, M. Ikehara, *J. Am. Chem. Soc.* **1978**, *100*, 8210; E. Ohtsuka, S. Tanaka, M. Ikehara, *Nucleic Acid Res.* **1978**, *1*, 410.
[4] E. Ohtsuka, T. Tanaka, S. Tanaka, M. Ikehara, *J. Am. Chem. Soc.* **1978**, *100*, 4580.
[5] D. G. Bartholomev, A. D. Broom, *J. Chem. Soc., Chem. Commun.* **1975**, 38.
[6] T. Tanaka, M. Orita, S. Uesugi, M. Ikehara, *Tetrahedron* **1988**, *44*, 4331.
[7] J. H. Kaplan, B. Forbush III, J. F. Hoffman, *Biochemistry* **1978**, *17*, 1929.
[8] J. A. McCray, L. Herbette, T. Kihara, D. R. Trentham, *Proc. Natl. Acad. Sci. U.S.A.* **1980**, *77*, 7237.
[9] J. M. Nerbonne, S. Richard, J. Nargeot, H. A. Lester, *Nature (London)* **1984**, *310*. 74.
[10] J. W. Walker, G. P. Reid, J. A. McCray, D. R. Trentham, *J. Am. Chem. Soc.* **1988**, *110*, 7170.
[11] U. Zehavi, B. Amit, A. Patchornik, *J. Org. Chem.* **1972**, *37*, 2281.
[12] D. H. Rich, S. K. Gurwara, *J. Am. Chem. Soc.* **1975**, *97*, 1575.
[13] C. P. Holmes, D. G. Jones, *J. Org. Chem.* **1995**, *60*, 2318.
[14] P. Lloyd-Williams, F. Albericio, E. Giralt, *Tetrahedron* **1993**, *49*, 11065.
[15] S. P. A. Fodor, J. L. Reed, M. C. Pirrung, L. Stryer, A. T. Liu, D. Solas, *Science (Washington, DC, U.S.)* **1991**, *251*, 767.
[16] A. C. Pease, D. Solas, E. J. Sullivan, M. T. Cronin, C. P. Holmes, S. P. A. Fodor, *Proc. Natl. Acad. Sci. U.S.A.* **1994**, *91*, 5022.
[17] M. C. Pirrung, J.-C. Bradley, *J. Org. Chem.* **1995**, *60*, 6270.
[18] M. C. Pirrung, L. Fallon, D. C. Lever, S. W. Shuey, *J. Org. Chem.* **1996**, *61*, 2129.
[19] V. N. R. Pillai, *Synthesis* **1980**, 1; V. N. R. Pillai, *Org. Photochem.* **1987**, *9*, 225.
[20] E. Reichmanis, B. C. Smith, R. J. Gooden, *J. Polymer Sci.* **1985**, *23*, 1.
[21] D. Döpp, *Chem. Commun.* **1968**, 1284.
[22] J. Bakke, *Acta Chem. Scand.* **1970**, *24*, 2650.
[23] A. Hasan, K.-P. Stengele, H. Giegrich, P. Cornwell, K. R. Isham, R. A. Sachleben, W. Pfleiderer, R. S. Foote, *Tetrahedron* **1997**, *53*, 4247.
[24] S. Bühler, I. Lagoja, H. Giegrich, K.-P. Stengele, W. Pfleiderer, *Helv. Chim. Acta* **2004**, *87*, 620.
[25] S. Walbert, W. Pfleiderer, U. E. Steiner, *Helv. Chim. Acta* **2001**, *84*, 1601.
[26] D. Wöll, J. Smirnova, W. Pfleiderer, U. E. Steiner, *Angew. Chem.* **2006**, *45*, 2975.
[27] D. Wöll, S. Laimgruber, M. Galetskaya, J. Smirnova, W. Pfleiderer, B. Heinz, P. Gilch, U. E. Steiner, *J. Am. Chem. Soc.* **2007**, *129*, 12148.
[28] D. Wöll, J. Smirnova, M. Galetskaya, T. Prykota, J. Bühler, K.-P. Stengele, W. Pfleiderer, U. E. Steiner, *Chem.–Eur. J.* **2008**, *14*, 6490.
[29] D. Wöll, S. Walbert, K. P. Stengele, T. J. Albert, T. Richmond, J. Norton, M. Singer, R. D. Green, W. Pfleiderer, U. E. Steiner, *Helv. Chim. Acta* **2004**, *87*, 28.
[30] K.-P. Stengele, J. Bühler, S. Bühler, E. Kvassiouk, R. Green, T. Prykota, W. Pfleiderer, *Nucleosides, Nucleotides Nucleic Acids* **2005**, *24*, 891.
[31] K. K. Singh, P. Nahar, *Synth. Commun.* **1995**, *25*, 1997.

[32] F. Himmelsbach, B. S. Schulz, T. Trichtinger, R. Charubala, W. Pfleiderer, *Tetrahedron* **1984**, *40*, 59.
[33] W. Markiewicz, *J. Chem. Res., Synop.* **1979**, 24.
[34] A. Karpeisky, C. Gonzales, A. B. Burgin, N. Usman, L. Beigelman, *Nucleosides Nucleotides* **1997**, *16*, 955.
[35] R. T. Pon, S. Yu, T. Prabhavalkar, T. Mishra, B. Kulkani, Y. S. Sanghvi, *Nucleosides, Nucleotides Nucleic Acids* **2005**, *24*, 777.
[36] F. Bergmann, W. Pfleiderer, *Helv. Chim. Acta* **1994**, *77*, 481.

Received October 29, 2010