21. Nucleotides

Part XLI[1])

The 2-Dansylethoxycarbonyl (= 2-{[5-(Dimethylamino)naphthalen-1-yl]sulfonyl}ethoxycarbonyl; Dnseoc) Group for Protection of the 5′-Hydroxy Function in Oligodeoxyribonucleotide Synthesis

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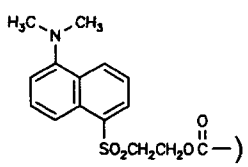
Use of the 2-dansylethoxycarbonyl (= 2-{[5-(dimethylamino)naphthalen-1-yl]sulfonyl}ethoxycarbonyl; Dnseoc) group as an intermediate 5′-OH protecting group in oligodeoxyribonucleotide synthesis using the automated phosphoramidite approach is described in a model study to an alternative strategy in RNA synthesis.

1. Introduction. – The development of an adequate protecting-group combination especially for the 2′- and 5′-OH functions is still a substantial problem in oligoribonucleotide synthesis. The use of acid-labile 2′-OH protecting groups, *e.g.* the tetrahydro-2*H*-pyranyl [2–4] and tetrahydro-4-methoxy-2*H*-pyran-4-yl groups [5–7], requires the displacement of the traditional trityl blocking groups [8–10] at the 5′-OH function due to unsatisfactory compatibility [11–13], despite the fact that recently some progress was achieved by applying the 1-(2-chloro-4-methylphenyl)- [14–16] and 1-(2-fluorophenyl)-4-methoxypiperidin-4-yl (Ctmp and Fpmp, resp.) protecting groups [17–19] in combination with the pixyl group. As base-labile functions, the levulinyl (Lev) group [20–24] and (fluoren-9-yl)methoxycarbonyl (Fmoc) group [25–27] were mainly suggested. The Fmoc group was also used in oligodeoxynucleotide synthesis to guarantee non-depurinating conditions [28–31].

To improve this alternative strategy, we have developed the 2-dansylethoxycarbonyl (= 2-{[5-(dimethylamino)naphthalen-1-yl]sulfonyl}ethoxycarbonyl; Dnseoc) group as a new base-labile 5′-OH protecting group in oligonucleotide synthesis. The Dnseoc group can easily be cleaved with dilute 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in aprotic solvents by β-elimination. The condensation yield in solid-phase syntheses can be determined by UV detection at 350 nm or, more sensitively, by fluorescence detection at 530 nm of the resulting 5-(dimethylamino)naphthalen-1-yl vinyl sulfone.

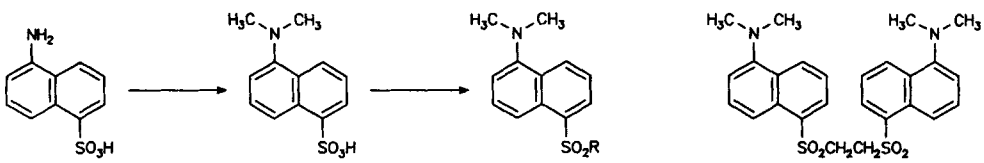


[1]) Part XL: [1].

In this paper, we wish to report the usefulness of the Dnseoc protecting group in oligodeoxyribonucleotide synthesis as a model study on the way to a new approach in oligoribonucleotide synthesis.

2. Syntheses. – To introduce the Dnseoc group into the 5′-*O*-position of a nucleoside, 2-dansylethyl chloroformate hydrochloride (**8**) was used. This reagent **8** was synthesized starting from 5-aminonaphthalene-1-sulfonic acid (**1**) by known but partially improved procedures [32–34] (*Scheme 1*). The amino function of **1** was first methylated with dimethylsulfate and the resulting 5-(dimethylamino)naphthalene-1-sulfonic acid (**2**) chlorinated with PCl_5 to yield dansyl chloride (**3**) according to *Horner* and *Lindel* [32]. After reduction of **3** with Na_2SO_3 to 5-(dimethylamino)naphthalene-1-sulfinic acid (**4**) and transformation into its corresponding sodium salt **5**, reaction with 2-chloroethanol gave 2-dansylethanol (**6**) according to a procedure of *Goya et al.* [33]. As a side product, 1,2-bis(dansyl)ethane (**7**) could be isolated in 9% yield which was not yet described and may have been formed from 5-(dimethylamino)naphthalene-1-yl vinyl sulfone and **5**. Treatment of **6** with trichloromethyl chloroformate in MeCN led to **8** of correct analytical composition, whereas the procedure of *Goya et al.* [34] turned out to be not reproducible and did not give pure material, despite the fact that these authors claim a correct elemental analysis.

Scheme 1

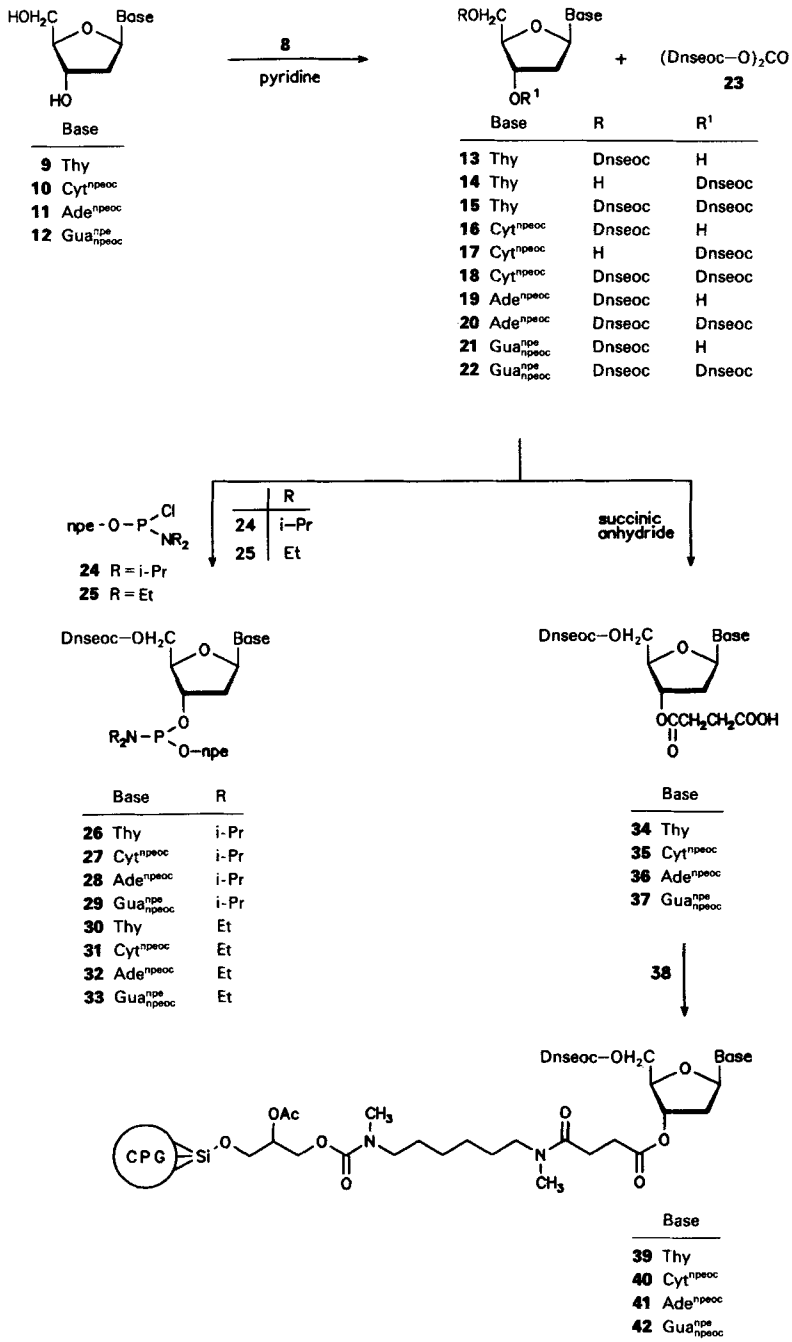


1 **2** **3** R = Cl; **4** R = H; **5** R = Na; **6** R = CH_2CH_2OH; **8** R = $CH_2CH_2OCOCl \cdot HCl$ **7**

As protecting groups for the functional residues of the nucleobases, the already established 2-(4-nitrophenyl)ethoxycarbonyl (npeoc) and 2-(4-nitrophenyl)ethyl (npe) groups were used [35] [36]. Best results to introduce the Dnseoc group were obtained by adding a slight excess of solid **8** at 0° to a pyridine solution of the 2′-deoxynucleosides **9**–**12**. The reaction was complete within 1 h, and after workup and flash chromatography, the desired 5′-*O*-Dnseoc-nucleosides **13**, **16**, **19**, and **21**, respectively, were obtained in 65–80% yield, besides small amounts of 3′,5′-di-*O*-substituted nucleosides **15**, **18**, **20**, and **22**, respectively (8–15%). The 3′-*O*-Dnseoc-nucleosides could be isolated only in case of the thymidine and cytidine derivatives (5% of **14** and 8% of **17**, resp.). A by-product in this reaction was always bis(2-dansylethyl)carbonate (**23**) which could be formed in yields up to 20%.

The 3′-phosphoramidites **26**–**33** were synthesized by phosphitylation using 2-(4-nitrophenyl)ethyl chloro(diisopropylamido)phosphite (**24**) and 2-(4-nitrophenyl)ethyl chloro-(diethylamido)phosphite (**25**) [37] [38]. The yields after workup and flash chromatography (silica gel) ranged from 45 to 68%.

Scheme 2


HOH2C
Base
HO
8
pyridine
ROH2C
Base
OR1
+
(Dnseoc–O)2CO
23
Base R R1
13 Thy Dnseoc H
14 Thy H Dnseoc
15 Thy Dnseoc Dnseoc
16 Cyt^npeoc Dnseoc H
17 Cyt^npeoc H Dnseoc
18 Cyt^npeoc Dnseoc Dnseoc
19 Ade^npeoc Dnseoc H
20 Ade^npeoc Dnseoc Dnseoc
21 Gua^npe_npeoc Dnseoc H
22 Gua^npe_npeoc Dnseoc Dnseoc
9 Thy
10 Cyt^npeoc
11 Ade^npeoc
12 Gua^npe_npeoc
npe-O-P(Cl)NR2
24 R = i-Pr
25 R = Et
R
24 i-Pr
25 Et
succinic anhydride
Dnseoc–OH2C
Base
R2N–P(O)O–npe
Base R
26 Thy i-Pr
27 Cyt^npeoc i-Pr
28 Ade^npeoc i-Pr
29 Gua^npe_npeoc i-Pr
30 Thy Et
31 Cyt^npeoc Et
32 Ade^npeoc Et
33 Gua^npe_npeoc Et
OCCH2CH2COOH
O
Base
34 Thy
35 Cyt^npeoc
36 Ade^npeoc
37 Gua^npe_npeoc
38
CPG
Si
OAc
CH3
N
O
Base
39 Thy
40 Cyt^npeoc
41 Ade^npeoc
42 Gua^npe_npeoc

Solid-phase synthesis of oligodeoxyribonucleotides *via* the npe/npeoc approach [38–40] requires a DBU-stable linkage of the starting nucleoside through a spacer molecule to a glass-bead support. Therefore, the 5′-*O*-Dnseoc-3′-*O*-succinyl-nucleosides **34–37** were synthesized by reaction of **13**, **16**, **19**, and **21** with succinic anhydride and 4-(dimethylamino)pyridine in CH_2Cl_2 [41] in almost quantitative yields. The 3′-*O*-succinyl-nucleosides **34–37** were then reacted with LCAMA-CPG (= (*l*ong-*c*hain-*a*lkyl)*m*ethyl*a*mine *c*ontrolled-*p*ore *g*lass; **38**) [38–40] using the coupling reagent *O*-{[cyano(ethoxycarbonyl)methylidene]amino}-1,1,3,3-tetramethyluronium tetrafluoroborate (TOTU) [42] and *N*-methylmorpholine in MeCN followed by a capping process with Ac_2O and 4-(dimethylamino)pyridine in pyridine (→**39–42**). Loadings of *ca.* 20 μmol/g were reached with a 500 Å-CPG material.

The assembly of oligodeoxyribonucleotides was carried out by the solid-phase phosphoramidite method similar to general procedures [43–46]. Four chemical steps and intermediate washing steps were performed using an automated DNA synthesizer by sequential passage of reagents through a column containing the nucleoside-functionalized support (**39–42**): *1*) deprotection of terminal Dnseoc groups with 0.1M DBU in MeCN for 140 s; *2*) coupling with 0.1M nucleoside phosphoramidite (**26–33**) and 0.5M 1*H*-tetrazole in MeCN for 40–60 s; *3*) capping with Ac_2O/2,6-dimethylpyridine/1-methyl-1*H*-imidazole in THF for 50 s; *4*) oxidation with 0.05M I_2 in THF/pyridine/ H_2O for 53 s. The completeness of each coupling step was checked by measurement of the absorbance at 350 nm of the eluate from the Dnseoc-deprotection step **1**. The determination of condensation yields was also possible by measuring the fluorescence at 530 nm. After the last synthesis cycle, the support was treated with 1M DBU in MeCN for 10 h to remove all npeoc and npe protecting groups. Finally, the fully deblocked oligodeoxyribonucleotide was cleaved from the support by treatment with concentrated NH_3 solution for 200 min. Thereafter, the oligonucleotide-containing ammoniacal solution from which the amount of isolated oligonucleotide was determined by measurement of the absorbance at 260 nm was lyophilized in a *Speed-vac* concentrator. The quality of the synthesized oligonucleotides was proven by reversed-phase and anion-exchange HPLC. *Table 1* shows the synthesized oligodeoxyribonucleotides and the isolated yields.

Table 1. *Synthesized Oligodeoxyribonucleotides*

Sequence	Amount of starting nucleoside [μmol]	Isolated yield [OD_{260}]
$(dT)_{10}$	0.6	39.2
(5′-3′)[d(A-A-A-A-T)]	0.45	18.0
(5′-3′)[d(A-A-A-A-A-T)]	0.56	25.0
$(dA)_{10}$	0.64	48.0
(5′-3′)[d(C-C-C-C-C-T)]	0.5	17.0
$(dC)_{10}$	0.6	22.4
(5′-3′)[d(G-G-G-G-G-G-G-T)]	0.6	28.0

The *N*,*N*-diethylphosphoramidites turned out to be more reactive than the corresponding *N*,*N*-diisopropylphosphoramidites, and, therefore, more careful handling due to a higher sensitivity to moisture was required. The efficiency of this new method is demonstrated by the anion-exchange HPLC of 'crude' $(dT)_{10}$ isolated without any further

Table 2. *Physical Data of Nucleoside Derivatives*

	UV Spectra (MeOH)	
	λ_{max} [nm]	lg ε
13	214, 257, 346	4.66, 4.32, 3.60
14	215, 258, 346	4.64, 4.36, 3.61
15	216, 255, 346	4.87, 4.55, 3.91
16	212, 246, 286 (sh), 343	4.81, 4.48, 4.19, 3.63
17	213, 246, 286 (sh), 343	4.83, 4.50, 4.21, 3.65
18	213, 249, 286 (sh), 346	5.06, 4.68, 4.25, 3.94
19	211, 263, 343	4.83, 4.54, 3.61
20	213, 259, 343	5.03, 4.70, 3.94
21	214, 262, 341	4.91, 4.63, 3.67
22	214, 256, 343	5.09, 4.76, 3.90
26	205, 260, 342	4.83, 4.49, 3.65
27	212, 254, 285 (sh), 342	4.87, 4.54, 4.37, 3.61
28	206, 265, 341	4.95, 4.67, 3.65
29	213, 264, 339	4.93, 4.69, 3.68
30	213, 260, 343	4.74, 4.47, 3.61
31	212, 255, 284 (sh), 340	4.85, 4.54, 4.38, 3.64
32	210, 264, 343	4.89, 4.66, 3.65
33	214, 264, 340	4.93, 4.70, 3.66
34	214, 257, 346	4.71, 4.36, 3.63
35	212, 247, 286 (sh), 343	4.79, 4.47, 4.18, 3.61
36	211, 263, 342	4.83, 4.57, 3.64
37	214, 262, 340	4.89, 4.62, 3.66

	^{1}H-NMR Spectra ($CDCl_3$, δ [ppm])						
	H–C(1′)	H–C(2′)	H′–C(2′)	H–C(3′)	H–C(4′)	H–C(5′)	H–C(5″)
13	6.29 (*t*)	2.38 (*m*)	2.13 (*m*)	4.32 (*m*)	4.02 (*m*)	4.20 (*m*)	
14	6.08 (*dd*)	2.46 (*m*)	2.30 (*dd*)	5.14 (*m*)	3.97 (*m*)	3.85 (*m*)	
15	6.24 (*dd*)	2.34 (*m*)	2.07 (*m*)	4.96 (*d*)	3.98 (*m*)	4.31 (*dd*)	4.22 (*dd*)
16	6.24 (*t*)	2.66 (*m*)	2.08 (*m*)	[a])	4.14 (*m*)	[4.30 to	4.19]* (*m*)
17	6.04 (*t*)	2.49 (*m*)		5.14 (*m*)	4.06 (*m*)	3.91 (*m*)	3.81 (*m*)
18	6.15 (*dd*)	2.66 (*dd*)	1.98 (*m*)	4.93 (*d*)	4.08 (*m*)	[4.35 to	4.22] (*m*)
19	6.47 (*t*)	2.82 (*m*)	2.56 (*m*)	4.61 (*m*)	4.16 (*m*)	4.22 (*m*)	
20	6.40 (*dd*)	2.86 (*m*)	2.55 (*dd*)	5.16 (*d*)	4.15 (*m*)	4.29 (*m*)	
21	6.43 (*t*)	2.84 (*m*)	2.51 (*m*)	4.77 (*t*)	4.16 (*m*)	4.32 (*dd*)	4.23 (*dd*)
22	6.23 (*t*)	3.05 (*m*)	2.44 (*m*)	5.27 (*m*)	4.14 (*m*)	[4.40 to	4.29] (*m*)
26[b])	6.12 (*t*)	2.17 (*m*)	1.92 (*m*)	4.27 (*m*)	[4.12	to	3.92] (*m*)
27[b])	6.05 (*t*)	2.44 (*m*)	1.95 (*m*)	4.25 (*m*)	[4.15	to	3.97] (*m*)
28[b])	6.32 (*m*)	2.71 (*m*)	2.46 (*m*)	4.59 (*m*)	[4.20	to	4.00] (*m*)
29[b])	6.19 (*m*)	2.81 (*m*)	2.36 (*m*)	4.70 (*m*)	[4.26	to	3.99] (*m*)
30[b])	6.10 (*t*)	2.17 (*m*)	1.93 (*m*)	4.28 (*m*)	[4.12	to	3.95] (*m*)
31[b])	6.03 (*m*)	2.41 (*m*)	1.95 (*m*)	4.25 (*m*)	[4.15	to	3.97] (*m*)
32[b])	6.30 (*t*)	2.71 (*m*)	2.45 (*m*)	4.59 (*m*)	[4.18	to	4.00] (*m*)
33[b])	6.17 (*m*)	2.79 (*m*)	2.35 (*m*)	4.75 (*m*)	[4.25	to	3.97] (*m*)
34[c])	6.14 (*t*)	2.23 (*t*)		5.09 (*m*)	4.02 (*m*)	4.15 (*m*)	
35[c])	6.09 (*t*)	2.42 (*m*)	2.17 (*m*)	5.10 (*m*)	4.16 (*m*)	4.16 (*m*)	
36[c])	6.44 (*t*)	3.07 (*m*)	2.56 (*m*)	5.35 (*m*)	[4.24	to	4.13] (*m*)
37[c])	6.32 (*t*)	3.12 (*m*)	2.49 (*m*)	5.38 (*m*)	[4.23	to	4.14] (*m*)

[a]) Chemical shift is in area marked with *. [b]) In CD_3CN. [c]) In $(D_6)DMSO$.

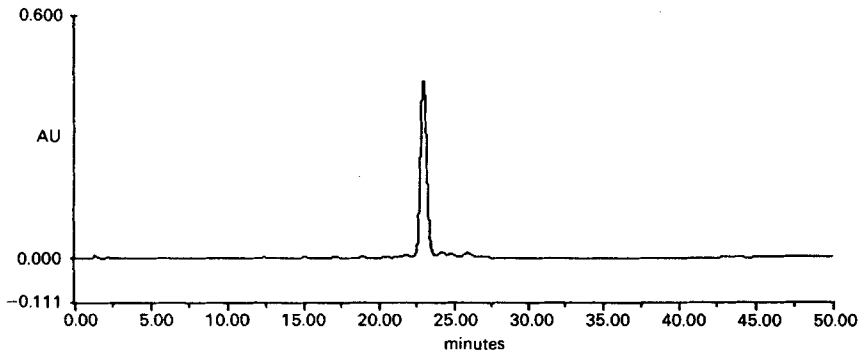


Figure. *Anion-exchange HPLC of* $(dT)_{10}$. Column: *Nucleogen 60-7 DEAE*, 7 μm, 4 × 125 mm (*Macherey-Nagel*); gradient: 0–0.6M LiCl (0–50 min) in 20% MeCN, 0.02M NaOAc pH 7.5; flow: 1 ml/min.

purification process (*Fig.*). The positive results can also be seen as an obvious encouragement to extend the strategy to RNA synthesis.

3. Physical Data. – The structural assignments of the newly synthesized nucleoside derivatives are based on elemental analyses and UV and ^{1}H-NMR spectra. The UV spectra show a new bathochromic absorption at 340 nm due to the dansyl chromophore. The ^{1}H-NMR spectra are of complex nature due to the variety of blocking groups. The characteristic sugar protons are listed in *Table 2*. A shift to lower field indicates the position of substitution.

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Experimental Part

General. Products were dried under high vacuum. TLC: Precoated silica gel thin-layer sheets *F1500 LS 254* from *Schleicher & Schuell*. Flash chromatography (FC): silica gel (*Baker*, 30–60 μm); 0.2–0.3 bar. M.p.: *Gallenkamp* melting-point apparatus; no corrections. UV/VIS: *Perkin-Elmer, Lambda 15*; λ_{max} in nm (log ε). ^{1}H-NMR: *Bruker AC 250*; in ppm rel. to TMS or $CDCl_3$ ((D_6)DMSO, CD_3CN) as internal standard. ^{31}P-NMR: *Joel 400 MHz*; in ppm rel. to H_3PO_4.

1. *5-(Dimethylamino)naphthalene-1-sulfonic Acid* (**2**) [32]. In a 3-l *Erlenmeyer* flask, 150 g (0.66 mol) of 5-aminonaphthalene-1-sulfonic acid (**1**) were added slowly in portions to 210 g (2.5 mol) of $NaHCO_3$ in 450 ml of H_2O (strong CO_2 evolution). Then, 150 ml (1.52 mol) of dimethyl sulfate were added dropwise within 30 min to the stirred ice-cooled soln. which was warmed to 80° for 30 min and after cooling acidified with 75 ml of conc. HCl soln. (pH 4). The precipitated product was filtered, washed with a small quantity of H_2O and dried to constant weight in the air and then at 120°: 148.7 g (90%) of gray powder. M.p. > 300°.

2. *5-(Dimethylamino)naphthalene-1-sulfonyl Chloride* (= *Dansyl Chloride*; **3**) [32]. Under ice-cooling (exothermic reaction), 80 g (0.32 mol) of **2** and 70 g (0.34 mol) of PCl_5 were mixed with a glass rod. To complete the reaction, the mixture was warmed to 60° for 2 h under exclusion of moisture. Then it was poured on 1 l ice/H_2O. After careful neutralization with 140 g (1.67 mol) of $NaHCO_3$, the product was extracted with Et_2O (5 × 500 ml), the org. layer dried (Na_2SO_4) and evaporated, and the residue purified by FC (silica gel, 20 × 5.5 cm, 600 ml AcOEt): 64.9 g (75%) of **3**. Orange-yellow crystals. M.p. 69° ([32]: m.p. 69°). ^{1}H-NMR ($CDCl_3$): 8.70 (*d*, H–C(2)); 8.43, 8.36 (2*d*, H–C(4), H–C(8)); 7.70, 7.58 (2*t*, H–C(3), H–C(7)); 7.27 (*d*, H–C(6)); 2.91 (*s*, Me_2N).

3. *5-(Dimethylamino)naphthalene-1-sulfinic Acid* (**4**) [33]. A suspension of 120 g (0.95 mol) of Na_2SO_3 in 200 ml of H_2O was weakly alkalinized with 1 ml of 40% NaOH, then 40 g (0.15 mol) of **3** were added. The mixture was stirred at r.t. for 2.5 h. After dilution with H_2O (200 ml) and filtration, the product was precipitated by slow addition of 28 ml of conc. H_2SO_4 soln. (pH 4). The beige crystals were recrystallized from H_2O: 31.8 g (85%) of bluish plates. M.p. 160–161° ([33]: m.p. 160°). Anal. calc. for $C_{12}H_{13}NO_2S \cdot 1\ H_2O$ (253.3): C 56.90, H 5.97, N 5.53; found: C 56.52, H 5.91, N 5.51.

4. *2-Dansylethanol* (= *2-{[5-(Dimethylamino)naphthalen-1-yl]sulfonyl}ethanol*; **6**) [33] *and 1,2-Bis(dansyl)-ethane* (= *1,2-Bis{[5-(dimethylamino)naphthalen-1-yl]sulfonyl}ethane*; **7**). To a soln. of 2.4 g (60 mmol) of NaOH in 45 ml of H_2O, 15 g (59.2 mmol) of **4** were added. Dissolution was completed with a few drops of 40% NaOH soln. Then, 15 ml of EtOH and 24 ml (0.36 mol) of 2-chloroethanol were added. The soln. was stirred at 80° for 20 h. The yellow precipitate was isolated by filtration from the hot mixture. Washing with a small quantity of MeOH and drying under high vacuum gave 1.02 g (7%) of **7**. The cooled filtrate was extracted with CH_2Cl_2 (1 × 50 ml, 2 × 25 ml), the org. layer washed with H_2O (100 ml), the aq. phase extracted with CH_2Cl_2 (50 ml), the combined org. phase dried (Na_2SO_4) and evaporated, and the resulting green oil crystallized after addition of H_2O (50 ml). The yellow-green crystals were dried in a desiccator over P_4O_{10} to give 10.71 g (65%) of **6** which was used in this form for further reactions. Recrystallization from H_2O yielded yellow needles.

6: M.p. 100° ([33]: m.p. 100–101°). $pK_a = 3.42$. UV (MeOH): 215 (4.66), 252 (4.18), 342 (3.67). ^{1}H-NMR ($CDCl_3$): 8.63 (*d*, H–C(2)); 8.33 (2*d*, H–C(4), H–C(8)); 7.61 (2*t*, H–C(3), H–C(7)); 7.22 (*d*, H–C(6)); 3.97 (*m*, CH_2O); 3.56 (*t*, SO_2CH_2); 2.90 (*s*, Me_2N); 2.88 (br., OH). Anal. calc. for $C_{14}H_{17}NO_3S$ (279.4): C 60.19, H 6.13, N 5.01; found: C 60.10, H 6.22, N 5.14.

7: M.p. 218–220°. UV ($CHCl_3$): 257 (4.45), 354 (3.91). ^{1}H-NMR ($CDCl_3$): 8.61 (*d*, 2 H, H–C(2)); 8.20 (*t*, 4 H, H–C(4), H–C(8)); 7.61–7.53 (*m*, 4 H, H–C(3), H–C(7)); 7.22 (*d*, 2 H, H–C(6)); 3.66 (*s*, CH_2CH_2); 2.91 (*s*, 2 Me_2N). Anal. calc. for $C_{26}H_{28}N_2O_4S_2$ (496.7): C 62.88, H 5.68, N 5.64; found: C 62.36, H 5.77, N 5.57.

5. *2-Dansylethyl Chloroformate Hydrochloride* (= *2-{[5-(Dimethylamino)naphthalen-1-yl]sulfonyl}ethyl Chloroformate Hydrochloride*; **8**). Under ice-cooling and stirring, 2.4 ml (19.9 mmol) of trichloromethyl chloroformate were added to 30 ml of dry MeCN. Then, a soln. of 3 g (10.7 mmol) of **6** in 15 ml of dry MeCN was added dropwise into the stirred and ice-cooled mixture within 10 min and stirring continued for another 5 h. The colourless precipitate was collected, washed with dry THF, and dried under high vacuum: 3.70 g (91%) of **8**. M.p. 154–155°. UV (MeOH): 215 (4.62), 252 (4.14), 345 (3.62). ^{1}H-NMR ((D_6)DMSO): 9.4 (br., NH); 9.06–7.84 (*d*, *t*, 3*m*, 6 arom. H); 3.66 (*m*, CH_2CH_2); 3.21 (*d*, Me_2N). Anal. calc. for $C_{15}H_{16}ClNO_4S \cdot HCl$ (378.3): C 47.63, H. 4.53, N 3.70; found: C 47.90, H 4.64, N 3.96.

6. *5′-O-(2-Dansylethoxycarbonyl)thymidine* (**13**), *3′-O-(2-Dansylethoxycarbonyl)thymidine* (**14**), *and 3′,5′-Bis-O-(2-dansylethoxycarbonyl)thymidine* (**15**). In dry pyridine (2 × 30 ml), 2 g (8.26 mmol) of thymidine (**9**) were co-evaporated and then taken up in dry pyridine (80 ml). After cooling in an ice-bath, **8** (4.06 g, 10.73 mmol) was added in solid form. The ice-cooled mixture was stirred for 1 h, then the reaction stopped with MeOH (10 ml). After evaporation, the residue was diluted with CH_2Cl_2 (100 ml) and washed with sat. $NaHCO_3$ soln. (100 ml), the aq. phase extracted with CH_2Cl_2 (2 × 50 ml), the combined org. layer dried (Na_2SO_4), evaporated, and co-evaporated with toluene (2 × 50 ml), AcOEt/EtOH 1:1 (50 ml), and CH_2Cl_2 (30 ml), and the residue purified by FC (silica gel, 25 × 4 cm, CH_2Cl_2/MeOH 100:0 (0.5 l), 99:1 (1 l), 98:2 (2 l; **15**, then **14**), 97:3 (0.5 l; **14**), and 96:4 (0.8 l; **13**)): 3.62 g (80%) of **13**, 206 mg (5%) of **14**, and 0.67 g (10%) of **15** as yellow amorphous solids.

13: UV (MeOH): 214 (4.66), 257 (4.32), 346 (3.60). ^{1}H-NMR ($CDCl_3$): 9.19 (br., NH); 8.60 (*d*, H–C(2)(Dns)); 8.33–8.28 (*m*, H–C(4)(Dns), H–C(8)(Dns)); 7.65–7.57 (*m*, H–C(3)(Dns), H–C(7)(Dns)); 7.22 (*d*, H–C(6)(Dns)); 7.21 (*s*, H–C(6)); 6.29 (*t*, H–C(1′)); 4.64–4.39 (2*m*, CH_2O); 4.32 (*m*, H–C(3′)); 4.20 (*m*, 2 H–C(5′)); 4.02 (*m*, H–C(4′)); 3.72 (*m*, SO_2CH_2); 3.60 (br., OH–C(3′)); 2.89 (*s*, Me_2N); 2.42–2.33 (*m*, H–C(2″)); 2.18–2.08 (*m*, H′–C(2″)); 1.84 (*d*, Me). Anal. calc. for $C_{25}H_{29}N_3O_9S \cdot 1\ H_2O$ (565.6): C 53.09, H 5.52, N 7.42; found: C 52.61, H 5.23, N 7.24.

14: UV (MeOH): 215 (4.64), 258 (4.36), 346 (3.61). ^{1}H-NMR ($CDCl_3$): 8.90 (br., NH); 8.64 (*d*, H–C(2)(Dns)); 8.31 (2*d*, H–C(4)(Dns), H–C(8)(Dns)); 7.62 (2*t*, H–C(3)(Dns), H–C(7)(Dns)); 7.43 (*s*, H–C(6)); 7.22 (*d*, H–C(6)(Dns)); 6.08 (*dd*, H–C(1′)); 5.14 (*m*, H–C(3′)); 4.50 (*t*, CH_2O); 3.97 (*m*, H–C(4′)); 3.85 (*m*, 2 H–C(5′)); 3.72 (*t*, SO_2CH_2); 2.90 (*s*, OH–C(5′), Me_2N); 2.51–2.40 (*m*, H–C(2″)); 2.34–2.25 (*dd*, H′–C(2″)); 1.91 (*s*, Me). Anal. calc. for $C_{25}H_{29}N_3O_9S$ (547.6): C 54.84, H 5.34, N 7.67; found: C 54.41, H 5.40, N 7.57.

15: UV (MeOH): 216 (4.87), 255 (4.55), 346 (3.91). ^{1}H-NMR ($CDCl_3$): 8.82 (br., NH); 8.63 (2*d*, 2 H, H–C(2)(Dns)); 8.33–8.28 (*m*, 4 H, H–C(4)(Dns), H–C(8)(Dns)); 7.65–7.56 (*m*, 4 H, H–C(3)(Dns), H–C(7)(Dns)); 7.20 (*d*, 2 H, H–C(6)(Dns)); 7.19 (*s*, H–C(6)); 6.24 (*dd*, H–C(1′)); 4.96 (*d*, H–C(3′)); 4.62–4.42 (*m*, 2 CH_2O); 4.33–4.20 (2*dd*, 2 H–C(5′)); 3.98 (*m*, H–C(4′)); 3.71 (*m*, 2 SO_2CH_2); 2.89 (*s*, 2 Me_2N); 2.37–2.31 (*m*,

H–C(2')); 2.13–2.01 (*m*, H'–C(2')); 1.84 (*s*, Me). Anal. calc. for $C_{40}H_{44}N_4O_{13}S_2 \cdot 1\ H_2O$ (871.0): C 55.16, H 5.32, N 6.43; found: C 55.11, H 5.19, N 6.39.

7. *5'-O-(2-Dansylethoxycarbonyl)-2'-deoxy-N⁴-[2-(4-nitrophenyl)ethoxycarbonyl]cytidine* (**16**), *3'-O-(2-Dansylethoxycarbonyl-2'-deoxy-N⁴-[2-(4-nitrophenyl)ethoxycarbonyl]cytidine* (**17**), *and 3',5'-Bis-O-(2-dansylethoxycarbonyl)-2'-deoxy-N⁴-[2-(4-nitrophenyl)ethoxycarbonyl]cytidine* (**18**). As described in *Exper.6*, with 2 g (4.76 mmol) of **10** [35] [36] and 2.34 g (6.18 mmol) of **8** in 50 ml of dry pyridine. Purification was achieved by FC (silica gel, 18 × 4 cm, CH_2Cl_2/MeOH 100:0 (0.3 l), 99:1 (1 l), 98:2 (2 l); **18**, then **17**), 97:3 (0.5 l; **17**), and 96:4 (0.5 l; **16**)) to give 2.26 g (65%) of **16**, 279 mg (8%) of **17**, and 0.73 g (15%) of **18** as yellow amorphous solids.

16: UV (MeOH): 212 (4.81), 246 (4.48), 286 (sh, 4.19), 343 (3.63). ^{1}H-NMR ($CDCl_3$): 8.59 (*d*, H–C(2)(Dns)); 8.33–8.28 (*m*, H–C(4)(Dns), H–C(8)(Dns)); 8.15 (*d*, 2 H *o* to NO_2); 8.15 (br., NH); 7.92 (*d*, H–C(6)); 7.59 (2*t*, H–C(3)(Dns), H–C(7)(Dns)); 7.40 (*d*, 2 H *m* to NO_2); 7.20 (*d*, H–C(5), H–C(6)(Dns)); 6.24 (*t*, H–C(1')); 4.59–4.40 (*m*, 2 CH_2O); 4.30–4.19 (*m*, H–C(3'), 2 H–C(5'), OH–C(3')); 4.14 (*m*, H–C(4')); 3.72 (*t*, SO_2CH_2); 3.10 (*t*, C–CH_2); 2.88 (*s*, Me_2N); 2.72–2.60 (*m*, H–C(2')); 2.13–2.02 (*m*, H'–C(2')). Anal. calc. for $C_{33}H_{35}N_5O_{12}S \cdot 1\ H_2O$ (743.8): C 53.29, H 5.01, N 9.42; found: C 53.20, H 4.79, N 9.19.

17: UV (MeOH): 213 (4.83), 246 (4.50), 286 (sh, 4.21), 343 (3.65). ^{1}H-NMR ($CDCl_3$): 8.63 (*d*, H–C(2)(Dns)); 8.31 (2*d*, H–C(4)(Dns), H–C(8)(Dns)); 8.18 (*d*, 2 H *o* to NO_2); 8.08 (*d*, H–C(6)); 7.72 (br., NH); 7.66–7.58 (*m*, H–C(3)(Dns), H–C(7)(Dns)); 7.40 (*d*, 2 H *m* to NO_2); 7.22 (*d*, H–C(6)(Dns)); 7.17 (*d*, H–C(5)); 6.04 (*t*, H–C(1')); 5.14 (*m*, H–C(3')); 4.53–4.42 (*m*, 2 CH_2O); 4.06 (*m*, H–C(4')); 3.93–3.78 (*m*, 2 H–C(5')); 3.71 (*t*, SO_2CH_2); 3.11 (*t*, C–CH_2); 3.00 (br., OH–C(5')); 2.90 (*s*, Me_2N); 2.60–2.37 (*m*, 2 H–C(2')). Anal. calc. for $C_{33}H_{35}N_5O_{12}S \cdot 1\ H_2O$ (743.8): C 53.29, H 5.01, N 9.42; found: C 52.95, H 4.77, N 9.05.

18: UV (MeOH): 213 (5.06), 249 (4.68), 286 (sh, 4.25), 344 (3.94). ^{1}H-NMR ($CDCl_3$): 8.62 (2*d*, 2 H, H–C(2)(Dns)); 8.33–8.28 (*m*, 4 H, H–C(4)(Dns), H–C(8)(Dns)); 8.16 (*d*, 2 H *o* to NO_2); 7.85 (*d*, H–C(6)); 7.65–7.55 (*m*, 5 H, NH, H–C(3)(Dns), H–C(7)(Dns)); 7.37 (*d*, 2 H *m* to NO_2); 7.22–7.18 (*m*, 3 H, H–C(5), H–C(6)(Dns)); 7.21 (*s*, H–C(6)); 6.15 (*dd*, H–C(1')); 4.93 (*d*, H–C(3')); 4.54–4.41 (*m*, 3 CH_2O); 4.28 (*m*, 2 H–C(5')); 4.08 (*m*, H–C(4')); 3.69 (*m*, 2 SO_2CH_2); 3.10 (*t*, C–CH_2); 2.89, 2.88 (2*s*, 2 Me_2N); 2.70–2.61 (*dd*, H–C(2')); 2.04–1.92 (*m*, H'–C(2')). Anal. calc. for $C_{48}H_{50}N_6O_{16}S_2 \cdot 0.5\ H_2O$ (1040.1): C 55.43, H 4.94, N 8.08; found: C 55.28, H 4.90, N 7.90.

8. *5'-O-(2-Dansylethoxycarbonyl)-2'-deoxy-N⁶-[2-(4-nitrophenyl)ethoxycarbonyl]adenosine* (**19**) *and 3',5'-Bis-O-(2-dansylethoxycarbonyl)-2'-deoxy-N⁶-[2-(4-nitrophenyl)ethoxycarbonyl]adenosine* (**20**). As described in *Exper.6*, with 2 g (4.5 mmol) of **11** [35] [36] and 2.21 g (5.85 mmol) of **8** in 40 ml of dry pyridine. Purification was achieved by FC (silica gel, 18 × 4 cm, CH_2Cl_2/MeOH 100:0 (0.3 l), 99:1 (1 l; **20**), 98:2 (0.5 l; **20**), 97:3 (1 l; **19**)) to give 2.32 g (69%) of **19** and 0.47 g (10%) of **20** as yellow amorphous solids.

19: UV (MeOH): 211 (4.83), 263 (4.54), 343 (3.61). ^{1}H-NMR ($CDCl_3$): 8.80 (br., *s*, NH); 8.67 (*s*, H–C(2)); 8.59 (*d*, H–C(2)(Dns)); 8.32–8.26 (*m*, H–C(4)(Dns), H–C(8)(Dns)); 8.13 (*s*, H–C(8)); 8.13 (*d*, 2 H *o* to NO_2); 7.63–7.55 (*m*, H–C(3)(Dns), H–C(7)(Dns)); 7.41 (*d*, 2 H *m* to NO_2); 7.20 (*d*, H–C(6)(Dns)); 6.47 (*t*, H–C(1')); 4.61 (*m*, H–C(3')); 4.56–4.35 (*m*, CH_2O); 4.53 (*t*, CH_2O); 4.22 (*m*, 2 H–C(5')); 4.16 (*m*, H–C(4')); 3.88 (br., OH–C(3')); 3.70 (*t*, SO_2CH_2); 3.14 (*t*, C–CH_2); 2.88 (*s*, Me_2N); 2.88–2.76 (*m*, H–C(2')); 2.60–2.51 (*m*, H'–C(2')). Anal. calc. for $C_{34}H_{35}N_7O_{11}S \cdot 1\ H_2O$ (767.8): C 53.19, H 4.86, N 12.77; found: C 52.84, H 4.66, N 12.46.

20: UV (MeOH): 213 (5.03), 259 (4.70), 343 (3.94). ^{1}H-NMR ($CDCl_3$): 8.72 (*s*, H–C(2)); 8.66, 8.60 (2*d*, 2 H, H–C(2)(Dns)); 8.50 (br., NH); 8.32 (*t*, 4 H, H–C(4)(Dns), H–C(8)(Dns)); 8.15 (*d*, 2 H *o* to NO_2); 8.14 (*s*, H–C(8)); 7.66–7.54 (*m*, 4 H, H–C(3)(Dns), H–C(7)(Dns)); 7.42 (*d*, 2 H *m* to NO_2); 7.19 (*t*, 2 H, H–C(6)(Dns)); 6.40 (*dd*, H–C(1')); 5.16 (*d*, H–C(3')); 4.56–4.41 (*m*, 3 CH_2O); 4.29 (*m*, 2 H–C(5')); 4.15 (*m*, H–C(4')); 3.71 (*m*, 2 SO_2CH_2); 3.15 (*t*, C–CH_2); 2.92–2.80 (*m*, H–C(2')); 2.87 (*s*, 2 Me_2N); 2.59–2.51 (*dd*, H'–C(2')). Anal. calc. for $C_{49}H_{50}N_8O_{15}S_2 \cdot 2\ H_2O$ (1091.2): C 53.94, H 4.99, N 10.27; found: C 53.79, H 4.65, N 10.11.

9. *5'-O-(2-Dansylethoxycarbonyl)-2'-deoxy-N²-[2-(4-nitrophenyl)ethoxycarbonyl]-O⁶-[2-(4-nitrophenyl)-ethyl]guanosine* (**21**) *and 3',5'-Bis-O-(2-dansylethoxycarbonyl)-2'-deoxy-N²-[2-(4-nitrophenyl)ethoxycarbonyl]-O⁶-[2-(4-nitrophenyl)ethyl]guanosine* (**22**). As described in *Exper.6*, with 2 g (3.28 mmol) of **12** [35] [36] and 1.61 g (4.27 mmol) of **8** in 30 ml of dry pyridine. Purification was achieved by FC (silica gel, 18 × 4 cm, CH_2Cl_2/MeOH 100:0 (0.3 l), 99:1 (1 l; **22**), 98:2 (1.5 l; **21**), and 97:3 (0.6 l; **21**)). After repurification of **22** (CH_2Cl_2 soln.) by FC (silica gel, 9 × 3 cm, toluene/AcOEt 2:1 (250 ml), toluene/AcOEt 1:1 (100 ml), toluene/AcOEt 1:2 (150 ml; **22**), and AcOEt (100 ml; **22**)), 2.39 g (80%) of **21** and 0.34 g (8%) of **22** were obtained as yellow amorphous solids.

21: UV (MeOH): 214 (4.91), 262 (4.63), 341 (3.67). ^{1}H-NMR ($CDCl_3$): 8.59 (*d*, H–C(2)(Dns)); 8.30 (*t*, H–C(4)(Dns), H–C(8)(Dns)); 8.15 (*m*, 4 H *o* to NO_2); 7.91 (*s*, H–C(8)); 7.64–7.55 (*m*, H–C(3)(Dns), H–C(7)(Dns)); 7.50 (br., NH); 7.49, 7.41 (*m*, 4 H *m* to NO_2); 7.20 (*d*, H–C(6)(Dns)); 6.43 (*t*, H–C(1')); 4.77 (*t*, H–C(3'), CH_2O from O^6-npe); 4.54–4.37 (*m*, 2 CH_2O); 4.35–4.18 (2*dd*, 2 H–C(5')); 4.16 (*m*, H–C(4')); 3.69 (*t*, SO_2CH_2); 3.62 (br., OH–C(5')); 3.29, 3.12 (2*t*, 2 C–CH_2); 2.89 (*s*, Me_2N); 2.89–2.78 (*m*, H–C(2')); 2.54–2.47 (*m*,

H′–C(2′)). Anal. calc. for $C_{42}H_{42}N_8O_{14}S \cdot 0.5\ H_2O$ (923.9): C 54.60, H 4.69, N 12.13; found: C 54.54, H 4.67, N 11.94.

22: UV (MeOH): 214 (5.09), 256 (4.76), 343 (3.90). ^{1}H-NMR ($CDCl_3$): 8.65, 8.59 (*2d*, 2 H, H–C(2)(Dns)); 8.34–8.27 (*m*, 4 H, H–C(4)(Dns), H–C(8)(Dns)); 8.15 (*m*, 4 H *o* to NO_2); 7.89 (*s*, H–C(8)); 7.66–7.53 (*m*, 4 H, H–C(3)(Dns), H–C(7)(Dns)); 7.52 (br., *s*, NH); 7.50, 7.42 (*m*, 4 H *m* to NO_2); 7.19 (*t*, 2 H, H–C(6)(Dns)); 6.23 (*t*, H–C(1′)); 5.27 (*d*, H–C(3′)); 4.79 (*t*, CH_2O from O^6-npe); 4.54–4.41 (*m*, 3 CH_2O); 4.35 (*m*, 2 H–C(5′)); 4.14 (*m*, H–C(4′)); 3.69 (*m*, 2 SO_2CH_2); 3.30, 3.12 (*2t*, 2 C–CH_2); 3.10–3.00 (*m*, H–C(2′)); 2.87 (*s*, 2 Me_2N); 2.49–2.42 (*m*, H′–C(2′)). Anal. calc. for $C_{57}H_{57}N_9O_{18}S_2$ (1220.3): C 56.11, H 4.71, N 10.33; found: C 55.79, H 4.76, N 10.01.

10. *Bis(2-dansylethyl) Carbonate* (**23**). In *Exper. 6–9*, **23** was formed as a by-product in variable yields up to 20% and isolated by evaporating the first eluating fractions from FC to a small volume and crystallization by addition of MeOH. Yellow crystals. M.p. 195–196°. UV ($CHCl_3$): 257 (4.44), 351 (3.88). ^{1}H-NMR ($CDCl_3$): 8.59 (*d*, 2 H, H–C(2)); 8.26 (*t*, 4 H, H–C(4), H–C(8)); 7.63–7.52 (*m*, 4 H, H–C(3), H–C(7)); 7.19 (*d*, 2 H, H–C(6)); 4.27 (*t*, 2 CH_2O); 3.58 (*t*, 2 SO_2CH_2); 2.89 (*s*, 2 Me_2N). Anal. calc. for $C_{29}H_{32}N_2O_7S_2$ (584.7): C 59.57, H 5.52, N 4.79; found: C 58.96, H 5.55, N 4.84.

11. *2-(4-Nitrophenyl)ethyl Chloro(diisopropylamido)phosphite* (**24**) [37]. Under N_2, 16.7 g (0.1 mol) of 2-(4-nitrophenyl)ethanol were added in small portions at −30° within 1.5 h to 56 ml (0.63 mol) of distilled PCl_3 in abs. Et_2O (150 ml). Thereafter, the mixture was stirred at r.t. for 3 h. Then, volatiles were removed under high vacuum. To the residue, 17.3 g (0.1 mol) of *N,N*-diisopropyl(trimethylsilyl)amine were added dropwise at 0° and under N_2. The mixture was stirred for 30 min at 0° and 20 h at r.t. Thereafter, volatiles were removed under high vacuum: 32.2 g (97%) of **24**. Slightly brownish solid which was used in this form for further reactions. ^{31}P-NMR (CH_2Cl_2): 181.6.

12. *2-(4-Nitrophenyl)ethyl Chloro(diethylamido)phosphite* (**25**) [38]. As described in *Exper. 11*, with 5 g (30 mmol) of 2-(4-nitrophenyl)ethanol and 19.2 ml (0.22 mol) of PCl_3 in abs. THF (100 ml) at −40°. The mixture was stirred at r.t. for 2 h, then evaporated. *N,N*-Diethyl(trimethylsilyl)amine (4.36 g, 30 mmol) in abs. THF (40 ml) was added dropwise at −20° to the residue in abs. THF (100 ml) and the mixture stirred for 1 h at 35° and then evaporated: 8.20 g (90%) of **25**. Slightly brownish oil which was used in this form for further reactions. ^{31}P-NMR ($CDCl_3$): 177.3.

13. *5′-O-(2-Dansylethoxycarbonyl)thymidine 3′-[2-(4-Nitrophenyl)ethyl* N,N-*Diisopropylphosphoramidite]* (**26**). To a soln. of 274 mg (0.5 mmol) of **13** in 1.5 ml of dry CH_2Cl_2, 0.52 ml (3 mmol) of abs. (i-Pr)$_2$EtN and 333 mg (1 mmol) of **24** were added. The mixture was stirred at r.t. for 1 h under Ar in the dark and then quenched with 100 µl of abs. i-PrOH. The mixture was stirred for further 10 min and then poured on CH_2Cl_2/phosphate buffer pH 1:1 (40 ml). After shaking and phase separation, the aq. layer was extracted with CH_2Cl_2 (10 ml), the combined org. layer dried (Na_2SO_4) and evaporated, and the residue dried under high vacuum for 1 h and purified by FC (silica gel, 9 × 2 cm, CH_2Cl_2/petroleum ether soln., then quickly petroleum ether/acetone 3:1 (100 ml) and 2:1 (100 ml; **26**)): 246 mg (58%) of **26**. Yellow foam. UV (MeOH): 205 (4.83), 260 (4.49), 342 (3.65). ^{1}H-NMR (CD_3CN): 9.04 (br. *s*, NH); 8.58, 8.57 (*2d*, H–C(2)(Dns)); 8.24 (*t*, H–C(4)(Dns), H–C(8)(Dns)); 8.17–8.09 (*m*, 2 H *o* to NO_2); 7.66–7.58 (*m*, H–C(3)(Dns), H–C(7)(Dns)); 7.46 (*d*, 2 H *m* to NO_2); 7.25 (*2d*, H–C(6)(Dns)); 7.13 (*m*, H–C(6)); 6.12 (*t*, H–C(1′)); 4.40 (*m*, CH_2OCO); 4.27 (*m*, H–C(3′)); 4.12–3.78 (*m*, CH_2OCO, H–C(4′), 2 H–C(5′)); 3.72 (*t*, SO_2CH_2); 3.52 (*m*, 2 Me_2CH); 2.99 (*t*, C–CH_2); 2.84 (*2s*, Me_2N); 2.23–2.12 (*m*, H–C(2′)); 2.01–1.82 (*m*, H′–C(2′)); 1.72 (*2d*, Me); 1.15–1.07 (*m*, 2 Me_2CH). ^{31}P-NMR (CD_3CN): 148.09, 148.0. Anal. calc. for $C_{39}H_{50}N_5O_{12}PS$ (843.9): C 55.51, H 5.97, N 8.30; found: C 55.12, H 6.06, N 8.39.

14. *5′-O-(2-Dansylethoxycarbonyl)-2′-deoxy-*N^4*-[2-(4-nitrophenyl)ethoxycarbonyl]cytidine 3′-[2-(4-Nitrophenyl)ethyl* N,N-*Diisopropylphosphoramidite]* (**27**). As described in *Exper. 13*, with 363 mg (0.5 mmol) of **16**. Purification by FC (silica gel, 9 × 2 cm, CH_2Cl_2/petroleum ether soln., then quickly petroleum ether/acetone 3:1 (100 ml), 2:1 (100 ml), and 1:1 (100 ml), **27**)) gave 316 mg (62%) of **27**. Yellow foam. UV (MeOH): 212 (4.87), 254 (4.54), 285 (sh, 4.37), 342 (3.61). ^{1}H-NMR (CD_3CN): 8.57 (*d*, H–C(2)(Dns)); 8.47 (br., NH); 8.23 (*t*, H–C(4)(Dns), H–C(8)(Dns)); 8.15–8.07 (*m*, 4 H *o* to NO_2); 7.76 (*2d*, H–C(6)); 7.60, 7.59 (*2t*, H–C(3)(Dns), H–C(7)(Dns)); 7.50, 7.45 (*2d*, 4 H *m* to NO_2); 7.21 (*2d*, H–C(6)(Dns)); 7.00 (*m*, H–C(5)); 6.05 (*t*, H–C(1′)); 4.40 (*2t*, 2 CH_2OCO); 4.25 (*m*, H–C(3′)); 4.15–3.76 (*m*, CH_2OP, H–C(4′), 2 H–C(5′)); 3.71 (*t*, SO_2CH_2); 3.51 (*m*, 2 Me_2CH); 3.08, 2.98 (*2t*, C–CH_2); 2.82 (*s*, Me_2N); 2.50–2.38 (*m*, H–C(2′)); 2.01–1.88 (*m*, H′–C(2′)); 1.13–1.06 (*m*, 2 Me_2CH). ^{31}P-NMR (CD_3CN): 147.91, 147.77. Anal. calc. for $C_{47}H_{56}N_7O_{15}PS$ (1022.1): C 55.23, H 5.52, N 9.59; found: C 54.81, H 5.50, N 9.67.

15. *5′-O-(2-Dansylethoxycarbonyl)-2′-deoxy-*N^6*-[2-(4-nitrophenyl)ethoxycarbonyl]adenosine 3′-[2-(4-Nitrophenyl)ethyl* N,N-*Diisopropylphosphoramidite]* (**28**). As described in *Exper. 13*, with 375 mg (0.5 mmol) of **19**. Purification by FC (silica gel, 9 × 2 cm, CH_2Cl_2/petroleum ether soln., then quickly petroleum ether/acetone 3:1

(100 ml), 2:1 (100 ml), and 1:1 (100 ml, **28**)) gave 345 mg (66%) of **28**. Yellow foam. UV (MeOH): 206 (4.95), 265 (4.67), 341 (3.65). ^{1}H-NMR (CD_3CN): 8.91 (br., NH); 8.57, 8.55 (2*s*, H–C(2)); 8.52 (2*d*, H–C(2)(Dns)); 8.23–8.02 (*m*, H–C(8), H–C(4)(Dns), H–C(8)(Dns), 4 H *o* to NO_2); 7.60–7.43 (*m*, H–C(3)(Dns), H–C(7)(Dns), 4 H *m* to NO_2); 7.19 (2*d*, H–C(6)(Dns)); 6.32 (*m*, H–C(1′)); 4.59 (*m*, H–C(3′)); 4.45, 4.44, 4.32 (3 *t*, 2 CH_2OCO); 4.20–3.78 (*m*, CH_2OP, H–C(4′), 2 H–C(5′)); 3.67 (*t*, SO_2CH_2); 3.62–3.48 (*m*, Me_2CH); 3.10, 3.00, 2.99 (3 *t*, 2 C–CH_2); 2.79 (2*s*, Me_2N); 2.79–2.63 (*m*, H–C(2′)); 2.52–2.41 (*m*, H′–C(2′)); 1.16–1.09 (*m*, 2 Me_2CH). ^{31}P-NMR (CD_3CN): 147.77, 147.69. Anal. calc. for $C_{48}H_{56}N_9O_{14}PS$ (1046.1): C 55.11, H 5.40, N 12.05; found: C 54.88, H 5.45, N 12.02.

16. *5′-O-(2-Dansylethoxycarbonyl)-2′-deoxy-*N^2*-[2-(4-nitrophenyl)ethoxycarbonyl]-*O^6*-[2-(4-nitrophenyl)-ethyl]guanosine 3′-[2-(4-Nitrophenyl)ethyl* N,N*-Diisopropylphosphoramidite]* (**29**). As described in *Exper. 13*, with 457 mg (0.5 mmol) of **21**. Purification by FC (silica gel, 9 × 2 cm, CH_2Cl_2/petroleum ether soln., then quickly petroleum ether/acetone 4:1 (100 ml) and 3:1 (100 ml, **29**)) gave 272 mg (45%) of **29**. Yellow foam. UV (MeOH): 213 (4.93), 264 (4.69), 339 (3.68). ^{1}H-NMR (CD_3CN): 8.51 (*d*, H–C(2)(Dns)); 8.31 (*s*, NH); 8.24–7.97 (*m*, H–C(4)(Dns), H–C(8)(Dns), 6 H *o* to NO_2); 7.88 (*s*, H–C(8)); 7.61–7.39 (*m*, H–C(3)(Dns), H–C(7)(Dns), 6 H *m* to NO_2); 7.19 (2*d*, H–C(6)(Dns)); 6.19 (*m*, H–C(1′)); 4.77 (*m*, CH_2O from O^6-npe); 4.70 (*m*, H–C(3′)); 4.41–4.30 (*m*, 2 CH_2OCO); 4.26–3.78 (*m*, CH_2OP, H–C(4′), 2 H–C(5′)); 3.66 (2*t*, SO_2CH_2); 3.53 (*m*, 2 Me_2CH); 3.27, 3.10, 2.97 (3 *m*, 3 C–CH_2); 2.90–2.71 (*m*, H–C(2′)); 2.79 (*s*, Me_2N); 2.42–2.30 (*m*, H′–C(2′)); 1.18–1.07 (*m*, 2 Me_2CH). ^{31}P-NMR (CD_3CN): 147.86. Anal. calc. for $C_{56}H_{63}N_{10}O_{17}PS$ (1211.2): C 55.53, H 5.24, N 11.56; found: C 55.23, H 5.35, N 11.41.

17. *5′-O-(2-Dansylethoxycarbonyl)thymidine 3′-[2-(4-Nitrophenyl)ethyl* N,N*-Diethylphosphoramidite]* (**30**). As described in *Exper. 13*, with 274 mg (0.5 mmol) of **13**, 0.52 ml (3 mmol) of abs. (i-Pr)$_2$EtN, 0.31 g (1 mmol) of **25**, and 4 ml of dry THF (1.5 h at r.t.). Purification by FC (silica gel, 6 × 2 cm, CH_2Cl_2/petroleum ether soln., then quickly petroleum ether/acetone 4:1 (60 ml), 3:1 (60 ml), and 2:1 (60 ml, **30**)) gave 277 mg (68%) of **30**. Yellow foam. UV (MeOH): 213 (4.74), 260 (4.47), 343 (3.61). ^{1}H-NMR (CD_3CN): 9.01 (br., *s*, NH); 8.58 (2*d*, H–C(2)(Dns)); 8.27–8.19 (*m*, H–C(4)(Dns), H–C(8)(Dns)); 8.11 (*d*, 2 H *o* to NO_2); 7.65–7.57 (*m*, H–C(3)(Dns), H–C(7)(Dns)); 7.46 (*d*, 2 H *m* to NO_2); 7.24 (*d*, H–C(6)(Dns)); 7.11 (*t*, H–C(6)); 6.10 (*t*, H–C(1′)); 4.40 (*m*, CH_2OCO); 4.28 (*m*, H–C(3′)); 4.22–3.79 (*m*, CH_2OP, H–C(4′), 2 H–C(5′)); 3.72 (*t*, SO_2CH_2); 3.09–2.88 (*m*, C–CH_2, 2 MeCH_2); 2.83 (2*s*, Me_2N); 2.23–2.12 (*m*, H–C(2′)); 1.99–1.86 (*m*, H′–C(2′)); 1.72, 1.70 (2*d*, Me); 1.02–0.94 (*m*, 2 *Me*CH_2). ^{31}P-NMR (CD_3CN): 148.31, 147.86. Anal. calc. for $C_{37}H_{46}N_5O_{12}PS$ (815.8): C 54.47, H 5.68, N 8.58; found: C 54.29, H 5.74, N 8.58.

18. *5′-O-(2-Dansylethoxycarbonyl)-2′-deoxy-*N^4*-[2-(4-nitrophenyl)ethoxycarbonyl]cytidine 3′-[2-(4-Nitrophenyl)ethyl* N,N*-Diethylphosphoramidite]* (**31**). As described in *Exper. 17*, with 363 mg (0.5 mmol) of **16**. Purification by FC (silica gel, 5 × 2 cm, CH_2Cl_2/petroleum ether soln., then quickly petroleum ether/acetone 3:1 (50 ml), 2:1 (50 ml), and 1:1 (50 ml, **31**)) gave 295 mg (59%) of **31**. Yellow foam. UV (MeOH): 212 (4.85), 255 (4.54), 284 (sh, 4.38), 340 (3.64). ^{1}H-NMR (CD_3CN): 8.56 (*d*, H–C(2)(Dns)); 8.41 (br., NH); 8.25–8.14 (*m*, H–C(4)(Dns), H–C(8)(Dns)); 8.15–8.08 (*m*, 4 H *o* to NO_2); 7.75, 7.74 (2*d*, H–C(6)); 7.62–7.55 (*m*, H–C(3)(Dns), H–C(7)(Dns)); 7.52–7.43 (*m*, 4 H *m* to NO_2); 7.21 (*d*, H–C(6)(Dns)); 6.99 (br., *d*, H–C(5)); 6.03 (*m*, H–C(1′)); 4.40 (*t*, 2 CH_2OCO); 4.25 (*m*, H–C(3′)); 4.15–3.75 (*m*, CH_2OP, H–C(4′), 2 H–C(5′)); 3.71 (*t*, SO_2CH_2); 3.08 (*t*, C–CH_2); 3.04–2.89 (*m*, C–CH_2, 2 MeCH_2); 2.82 (*s*, Me_2N); 2.48–2.33 (*m*, H–C(2′)); 2.02–1.87 (*m*, H′–C(2′)); 1.02–0.93 (*m*, 2 *Me*CH_2). ^{31}P-NMR (CD_3CN): 148.25, 147.83. Anal. calc. for $C_{45}H_{52}N_7O_{15}PS$ (994.0): C 54.38, H 5.27, N 9.86; found: C 54.08, H 5.39, N 9.86.

19. *5′-O-(2-Dansylethoxycarbonyl)-2′-deoxy-*N^6*-[2-(4-nitrophenyl)ethoxycarbonyl]adenosine 3′-[2-(4-Nitrophenyl)ethyl* N,N*-Diethylphosphoramidite]* (**32**). As described in *Exper. 17*, with 375 mg (0.5 mmol) of **19**. Purification by FC (silica gel, 5 × 2 cm, CH_2Cl_2/petroleum ether soln., then quickly petroleum ether/acetone 3:1 (50 ml), 2:1 (50 ml), and 1:1 (100 ml, **32**)) gave 325 mg (64%) of **32**. Yellow foam. UV (MeOH): 210 (4.89), 264 (4.66), 343 (3.65). ^{1}H-NMR (CD_3CN): 8.92 (br., *s*, NH); 8.56, 8.55 (2*s*, H–C(2)); 8.51 (*d*, H–C(2)(Dns)); 8.22–8.15 (*m*, H–C(4)(Dns), H–C(8)(Dns)); 8.11–8.04 (*m*, H–C(8), 4 H *o* to NO_2); 7.59–7.50 (*m*, H–C(3)(Dns), H–C(7)(Dns)); 7.48–7.42 (*m*, 4 H *m* to NO_2); 7.18 (*d*, H–C(6)(Dns)); 6.30 (*t*, H–C(1′)); 4.59 (*m*, H–C(3′)); 4.43 (2*t*, CH_2OCO); 4.31 (2*t*, CH_2OCO); 4.34–3.72 (*m*, CH_2OP, H–C(4′), 2 H–C(5′)); 3.66 (*t*, SO_2CH_2); 3.08 (*t*, C–CH_2); 3.02–2.93 (*m*, C–CH_2, 2 MeCH_2); 2.78 (2*s*, Me_2N); 2.77–2.64 (*m*, H–C(2′)); 2.51–2.38 (*m*, H′–C(2′)); 0.99 (*t*, 2 Me). ^{31}P-NMR (CD_3CN): 147.98, 147.77. Anal. calc. for $C_{46}H_{52}N_9O_{14}PS$ (1018.0): C 54.27, H 5.15, N 12.38; found: C 53.82, H 5.22, N 11.99.

20. *5′-O-(2-Dansylethoxycarbonyl)-2′-deoxy-*N^2*-[2-(4-nitrophenyl)ethoxycarbonyl]-*O^6*-[2-(4-nitrophenyl)-ethyl]guanosine 3′-[2-(4-Nitrophenyl)ethyl* N,N*-Diethylphosphoramidite]* (**33**). As described in *Exper. 17*, with 457 mg (0.5 mmol) of **21**. Purification by FC (silica gel, 5 × 2 cm, CH_2Cl_2/petroleum ether soln., then quickly

petroleum ether/acetone 4:1 (50 ml), 3:1 (50 ml), 2:1 (50 ml; **33**), and 1:1 (50 ml; **33**)) gave 340 mg (57%) of **33**. Yellow foam. UV (MeOH): 214 (4.93), 264 (4.70), 340 (3.66). ^{1}H-NMR (CD_3CN): 8.50 (*d*, H–C(2)(Dns)); 8.31 (*s*, NH); 8.23–7.99 (*m*, H–C(4)(Dns), H–C(8)(Dns), 6 H *o* to NO_2); 7.87 (*s*, H–C(8)); 7.60–7.38 (*m*, H–C(3)(Dns), H–C(7)(Dns), 6 H *m* to NO_2); 7.18 (*d*, H–C(6)(Dns)); 6.17 (*m*, H–C(1′)); 4.75 (*m*, CH_2O from O^6-npe, H–C(3′)); 4.40–4.28 (*m*, 2 CH_2OCO); 4.25–3.78 (*m*, CH_2OP, H–C(4′), 2 H–C(5′)); 3.66 (*t*, SO_2CH_2); 3.27/3.26 (2*t*, C–CH_2 from O^6-npe); 3.08 (*t*, C–CH_2); 3.03–2.89 (*m*, C–CH_2, MeCH_2); 2.86–2.72 (*m*, H–C(2′)); 2.78 (*s*, Me_2N); 2.39–2.31 (*m*, H′–C(2′)); 1.02–0.93 (*m*, *Me*CH_2). ^{31}P-NMR (CD_3CN): 148.03, 147.97. Anal. calc. for $C_{54}H_{59}N_{10}O_{17}PS$ (1183.2): C 54.82, H 5.03, N 11.84; found: C 54.25, H 5.12, N 11.50.

21. *5′-O-(2-Dansylethoxycarbonyl)-3′-O-succinylthymidine* (**34**). In 5 ml of dry CH_2Cl_2, 548 mg (1 mmol) of **13**, 0.2 g (2 mmol) of succinic anhydride, and 0.16 g (1.3 mmol) of 4-(dimethylamino)pyridine were stirred at r.t. for 2 h. Then, the mixture was diluted with CH_2Cl_2 (50 ml) and washed with sat. $NaHCO_3$ soln. (50 ml). To obtain a complete phase separation, 10% citric acid was added. The aq. phase was extracted with CH_2Cl_2 (2 × 25 ml), the combined org. layer washed with 10% citric acid (50 ml), the aq. phase extracted with CH_2Cl_2 (25 ml), and then the combined org. layer dried (Na_2SO_4) and evaporated: 0.61 g (94%) of **34**. Yellow amorphous solid. UV (MeOH): 214 (4.71), 257 (4.36), 346 (3.63). ^{1}H-NMR ((D_6)DMSO): 12.29 (br., COOH); 11.38 (*s*, NH); 8.53 (*d*, H–C(2)(Dns)); 8.18 (*t*, H–C(4)(Dns), H–C(8)(Dns)); 7.66 (*m*, H–C(3)(Dns), H–C(7)(Dns)); 7.34 (*s*, H–C(6)); 7.26 (*d*, H–C(6)(Dns)); 6.14 (*t*, H–C(1′)); 5.09 (*m*, H–C(3′)); 4.38 (*m*, CH_2O); 4.15 (*m*, 2 H–C(5′)); 4.02 (*m*, H–C(4′)); 3.87 (*t*, SO_2CH_2); 2.81 (*s*, Me_2N); 2.52 (*m*, CH_2CH_2); 2.23 (*t*, 2 H–C(2′)); 1.68 (*s*, Me). Anal. calc. for $C_{29}H_{33}N_3O_{12}S$ (647.7): C 53.78, H 5.14, N 6.49; found: C 53.78, H 5.34, N 6.11.

22. *5′-O-(2-Dansylethoxycarbonyl)-2′-deoxy-N^4-[2-(4-nitrophenyl)ethoxycarbonyl]-3′-O-succinylcytidine* (**35**). As described in *Exper. 21*, with 363 mg (0.5 mmol) of **16**. Workup yielded 384 mg (93%) of **35** as a yellow amorphous solid which was used in this form for reaction with the support. An anal. sample was obtained by FC (silica gel, 6 × 2 cm, CH_2Cl_2/MeOH 100:0 (50 ml), 99:1 (50 ml), 98:2 (50 ml), and 97:3 (50 ml)). UV (MeOH): 214 (4.79), 247 (4.47), 286 (sh, 4.18), 343 (3.61). ^{1}H-NMR ((D_6)DMSO): 12.20 (br., COOH); 10.90 (br., NH); 8.52 (*d*, H–C(2)(Dns)); 8.18–8.12 (*m*, H–C(4)(Dns), H–C(8)(Dns)); 8.15 (*d*, 2 H *o* to NO_2); 7.90 (*d*, H–C(6)); 7.69–7.57 (*m*, H–C(3)(Dns), H–C(7)(Dns)); 7.59 (*d*, 2 H *m* to NO_2); 7.23 (*d*, H–C(6)(Dns)); 6.98 (*d*, H–C(5)); 6.09 (*t*, H–C(1′)); 5.10 (*m*, H–C(3′)); 4.40–4.33 (*m*, 2 CH_2O); 4.16 (*m*, H–C(4′), 2 H–C(5′)); 3.86 (*t*, SO_2CH_2); 3.07 (*t*, C–CH_2); 2.79 (*s*, Me_2N); 2.58–2.38 (*m*, CH_2CH_2, H–C(2′)); 2.23–2.11 (*m*, H′–C(2′)). Anal. calc. for $C_{37}H_{39}N_5O_{15}S \cdot 0.5\ H_2O$ (834.8): C 53.23, H 4.83, N 8.39; found: C 53.25, H 4.79, N 8.49.

23. *5′-O-(2-Dansylethoxycarbonyl)-2′-deoxy-N^6-[2-(4-nitrophenyl)ethoxycarbonyl]-3′-O-succinyladenosine* (**36**). As described in *Exper. 21*, with 375 mg (0.5 mmol) of **19**. On washing with sat. $NaHCO_3$ soln., no 10% citric acid was needed to achieve complete phase separation. Further workup yielded 404 mg (95%) of **36**. Purification for anal. characterization as described in *Exper. 22*. UV (MeOH): 211 (4.83), 263 (4.57), 342 (3.64). ^{1}H-NMR ((D_6)DMSO): 12.32 (br., COOH); 10.63 (br. *s*, NH); 8.62, 8.55 (2*s*, H–C(2), H–C(8)); 8.48 (*d*, H–C(2)(Dns)); 8.17 (*t*, H–C(4)(Dns), H–C(8)(Dns)); 8.15 (*d*, 2 H *o* to NO_2); 7.66–7.58 (*m*, H–C(3)(Dns), H–C(7)(Dns)); 7.60 (*d*, 2 H *m* to NO_2); 7.23 (*d*, H–C(6)(Dns)); 6.44 (*t*, H–C(1′)); 5.35 (*m*, H–C(3′)); 4.38, 4.32 (2*t*, 2 CH_2O); 4.24–4.13 (*m*, H–C(4′), 2 H–C(5′)); 3.84 (*t*, SO_2CH_2); 3.10 (*t*, C–CH_2); 3.10–3.03 (*m*, H–C(2′)); 2.78 (*s*, Me_2N); 2.56 (*m*, CH_2CH_2, H′–C(2′)). Anal. calc. for $C_{38}H_{39}N_7O_{14}S \cdot 0.75\ H_2O$ (863.4): C 52.86, H 4.73, N 11.36; found: C 52.87, H 4.71, N 11.37.

24. *5′-O-(2-Dansylethoxycarbonyl)-2′-deoxy-N^2-[2-(4-nitrophenyl)ethoxycarbonyl]-O^6-[2-(4-nitrophenyl)-ethyl]-3′-O-succinylguanosine* (**37**). As described in *Exper. 21*, with 458 mg (0.5 mmol) of **21**. On washing with sat. $NaHCO_3$ soln., no 10% citric acid was needed to achieve complete phase separation. Further workup yielded 450 mg (89%) of **37**. Purification for anal. characterization as described in *Exper. 22*. UV (MeOH): 214 (4.89), 262 (4.62), 343 (3.66). ^{1}H-NMR ((D_6)DMSO): 12.31 (br., COOH); 10.38 (*s*, NH); 8.47 (*d*, H–C(2)(Dns)); 8.29 (*s*, H–C(8)); 8.19–8.12 (*m*, H–C(4)(Dns), H–C(8)(Dns)); 8.15 (*d*, 4 H *o* to NO_2); 7.61 (*t*, H–C(3)(Dns), H–C(7)(Dns), 4 H *m* to NO_2); 7.22 (*d*, H–C(6)(Dns)); 6.32 (*t*, H–C(1′)); 5.38 (*m*, H–C(3′)); 4.75 (*t*, CH_2O from O^6-npe); 4.39–4.26 (*m*, 2 CH_3O); 4.23–4.14 (*m*, H–C(4′), 2 H–C(5′)); 3.82 (*t*, SO_2CH_2); 3.28 (*t*, C–CH_2 from O^6-npe); 3.19–3.04 (*m*, H–C(2′)); 3.09 (*t*, C–CH_2); 2.77 (*s*, Me_2N); 2.58–2.43 (*m*, CH_2CH_2, H′–C(2′)). Anal. calc. for $C_{46}H_{46}N_8O_{17}S$ (1015.0): C 54.44, H 4.57, N 11.04; found: C 54.07, H 4.63, N 10.98.

25. *(Long-chain-alkyl)methylamine Controlled-Pore Glass* (LCAMA-CPG; **38**). A mixture of 5 g of glyceryl-CPG 500 Å (120–200 mesh, *Fluka*) and 5 g (26.3 mmol) of *N*-(phenoxycarbonyl)-1*H*-tetrazolide [47] [48] was shaken in dry CH_2Cl_2 (70 ml) at r.t. for 20 h. Then, the material was collected in a glass suction filter and washed with CH_2Cl_2 (4 ×) by taking up the CPG in CH_2Cl_2 (50 ml) and suction-filtering. Then, the CPG was reacted with 4.4 ml (25.4 mmol) of *N,N′*-dimethylhexane-1,6-diamine in dry CH_2Cl_2 (50 ml) at 60° for 2 h. The LCAMA-CPG (**38**) was isolated in a glass suction filter and washed with MeOH, DMF, MeOH, acetone, and Et_2O.

26. *Derivatives* **39–42** *of LCAMA-CPG 500 Å* (**38**) *and of 5′-O-(2-Dansylethoxycarbonyl)-2′-deoxy-3′ O-succinylnucleosides* **34–37**. To a mixture of 200 mg of **38**, 45 μmol of **34** (29 mg), **35** (37 mg), **36** (38 mg), or **37** (46 mg), and 30 mg (91.4 μmol) of TOTU, 3 ml of abs. MeCN and 19 μl (180 μmol) of *N*-methylmorpholine were added. After a short ultrasonic treatment (30 s) and 2 h standing in the dark at r.t., the CPG material was collected in a glass suction filter and washed with MeOH, DMF, MeOH, and Et_2O. Capping-procedure: The nucleoside-functionalized CPG, 50 mg (0.41 mmol) of 4-(dimethylamino)pyridine, 10 ml of abs. pyridine, and 1 ml (10.6 mmol) of Ac_2O were kept in the dark for 45 min. at r.t. Thereafter, **39–42**, resp., were collected in a glass suction filter and washed with MeOH, DMF, MeOH, and Et_2O. Determination of loading: A defined amount of **39**, **40**, **41**, or **42** (5–10 mg) was weighed in a 1-ml microcuvette (d = 1 cm). Then, 0.1M DBU in MeCN (500 μl) was added. After 1 min, the soln. was neutralized with 0.1M AcOH in MeCN (500 μl). Thereafter, the absorbance at 345 nm was measured against 0.05M DBU-acetate in MeCN. By considering log $\varepsilon = 3.63$ of the formed 5-(dimethylamino)naphthalen-1-yl vinyl sulfone, the loading L [μmol/g] can be calculated by the formula $L = 234.75 \cdot A/m$ (A = absorbance at 345 nm; m = weighed CPG (**39–42**) in mg): L(**39**) = 19, L(**40**) = 19, L (**41**) = 21, and L(**42**) = 21 μmol/g.

27. *Assembly of Oligodeoxynucleotides*. Syntheses were carried out using an *Applied Biosystems 380B DNA* synthesizer. Nucleoside-functionalized CPG material (**39–42**; 0.6 μmol) was packed into a small *ABI* column, and cycles of nucleotide addition were carried out by a programmed series of reagent and solvent washes based on recommended procedures with the following main steps: *1*) 5′-*O*-Dnseoc Deprotection: 0.1M DBU in MeCN delivered in 2 30-s and 8 10-s bursts with intermediate 1-s reverse flushes. The eluate from this step was collected and the absorbance at 350 nm measured to determine the condensation yields. *2*) Coupling: 0.1M phosphoramidite (P) and 0.5M 1*H*-tetrazole (T) in dry MeCN delivered in 5 alternating bursts (8 s T, 4 s P + T, 3 s T, 3 s P + T, 3 s T) with a subsequent wait time of 40 s. *3*) Capping: Ac_2O/2,6-dimethylpyridine/THF 1:1:8 and 1-methyl-1*H*-imidazole/THF 16:84 delivered in one 20-s burst with a subsequent wait time of 30 s. *4*) Oxidation: 0.05M I_2 in THF/H_2O/pyridine 7:2:1 delivered in one 23-s burst with a subsequent wait time of 30 s.

Then a cleavage programme was carried out: *1*) npe/npeoc Deprotection: 0.5M or 1M DBU in MeCN delivered in one 180-s burst with a consecutive wait time of 3600 s and 5 times one 120-s burst followed by another wait time of 5400 s (total wait time 10 h). *2*) Cleavage from the support: conc. NH_3 delivered in one 18-s burst with a consecutive wait time of 2400 S (5 times, total wait time 3 h 20 min). The ammoniacal oligonucleotide containing soln. was collected and, after determination of the isolated amount of oligonucleotide by measurement of the absorbance at 260 nm, was lyophilized in a *Speed-vac* concentrator under high vacuum.

REFERENCES

[1] H. Schirmeister, W. Pfleiderer, *Helv. Chim. Acta* **1994**, *77*, 10.
[2] W.E. Parham, E.L. Anderson, *J. Am. Chem. Soc.* **1948**, *70*, 4187.
[3] B.E. Griffin, C.B. Reese, *Tetrahedron Lett.* **1964**, *5*, 2925.
[4] B.E. Griffin, M. Jarman, C.B. Reese, *Tetrahedron* **1968**, *24*, 639.
[5] C.B. Reese, R. Saffhill, J.E. Sulston, *J. Am. Chem. Soc.* **1967**, *89*, 3366.
[6] D.P.L. Green, T. Ravindranathan, C.B. Reese, *Tetrahedron* **1970**, *26*, 1031.
[7] C.B. Reese, R. Saffhill, J.E. Sulston, *Tetrahedron* **1970**, *6*, 1023.
[8] M. Smith, D.H. Rammler, I.H. Goldberg, H.G. Khorana, *J. Am. Chem. Soc.* **1962**, *84*, 430.
[9] H. Schaller, G. Weimann, B. Lerch, H.G. Khorana, *J. Am. Chem. Soc.* **1963**, *85*, 3821.
[10] 'Oligonucleotide Synthesis, A Practical Approach', Ed. M.J. Gait, IRL Press, Oxford, 1984.
[11] C.B. Reese, P.A. Skone, *Nucleic Acids Res.* **1985**, *13*, 5215.
[12] C. Christodoulou, S. Agrawal, M.J. Gait, *Tetrahedron Lett.* **1986**, *27*, 1521.
[13] T. Pathak, J.B. Chattopadhyaya, *Acta Chem. Scand., Ser. B* **1985**, *39*, 799.
[14] T.S. Rao, C.B. Reese, H.T. Serafinowska, H. Takaku, G. Zappia, *Tetrahedron Lett.* **1987**, *28*, 4897.
[15] C.B. Reese, *Nucleos. Nucleot.* **1987**, *6*, 121.
[16] O. Sakatsume, M. Ohtsuki, H. Takaku, C.B. Reese, *Nucleic Acids Res.* **1989**, *17*, 3689.
[17] C.B. Reese, M.V. Rao, H.T. Serafinowska, E.A. Thompson, P.S. Yu, *Nucleos. Nucleot.* **1991**, *10*, 81.
[18] C.B. Reese, E.A. Thompson, *J. Chem. Soc., Perkin Trans. 1* **1988**, 2881.
[19] M.V. Rao, C.B. Reese, V. Schehlmann, P.S. Yu, *J. Chem. Soc., Perkin Trans. 1* **1993**, 43.
[20] E. de Vroom, H.C.P.F. Roelen, C.P. Saris, T.N.W. Budding, G.A. van der Marel, J.H. van Boom, *Nucleic Acids Res.* **1988**, *16*, 2987.

[21] C. Scalfi-Happ, E. Happ, S. Ghag, S. Chladek, *Biochemistry* **1987,** *26,* 4682.
[22] S. Iwai, E. Ohtsuka, *Nucleic Acids Res.* **1988,** *16,* 9443.
[23] T. Sasaki, S. Iwai, S. Tsuda, K. Hikichi, E. Ohtsuka, *Nucleic Acids Res. Symp. Ser.* **1990,** *22,* 43.
[24] S. Iwai, T. Sasaki, E. Ohtsuka, *Tetrahedron* **1990,** *46,* 6673.
[25] T. Fukuda, T. Hamana, R. Muramoto, *Nucleic Acids Res. Symp. Ser.* **1988,** *19,* 13.
[26] C. Lehmann, Y.-Z. Xu, C. Christodoulou, Z.-K. Tan, M.J. Gait, *Nucleic Acids Res.* **1989,** *17,* 2379.
[27] T. Ogawa, H. Hosaka, T. Makita, H. Takaku, *Chem. Lett.* **1991,** 1169.
[28] C. Gioeli, J. B. Chattopadhyaya, *J. Chem. Soc., Chem. Commun.* **1982,** 672.
[29] N. Balgobin, J. Chattopadhyaya, *Nucleos. Nucleot.* **1987,** *6,* 461.
[30] Y. Ma, E. Sonveaux, *Nucleos. Nucleot.* **1987,** *6,* 491.
[31] Y. Ma, E. Sonveaux, *Biopolymers* **1989,** *28,* 965.
[32] L. Horner, H. Lindel, *Phosphorus Sulfur* **1983,** *15,* 1.
[33] S. Goya, A. Takadate, M. Iwai, *Yakugaku Zasshi* **1981,** *101,* 1164.
[34] A. Takadate, M. Iwai, H. Fujino, K. Tahara, S. Goya, *Yakugaku Zasshi* **1983,** *103,* 962.
[35] F. Himmelsbach, B. S. Schulz, T. Trichtinger, R. Charubala, W. Pfleiderer,*Tetrahedron* **1983,** *40,* 59.
[36] F. Himmelsbach, Ph. D. Thesis, University of Konstanz, 1984.
[37] H. Schirmeister, Ph. D. Thesis, University of Konstanz, 1988.
[38] K. P. Stengele, Ph. D. Thesis, University of Konstanz, 1991.
[39] K. P. Stengele, W. Pfleiderer, *Nucleic Acids Res. Symp. Ser.* **1989,** *21,* 101.
[40] K. P. Stengele, W. Pfleiderer, *Tetrahedron Lett.* **1990,** *31,* 2549.
[41] R. Kierzek, M. H. Caruthers, C. F. Longfellow, D. Swinton, D. H. Turner, S. M. Freier, *Biochemistry* **1986,** *25,* 7840.
[42] G. Breitpohl, personal communication (Pharma Research, Fa. *Hoechst*).
[43] M. D. Matteucci, M. H. Caruthers, *Tetrahedron Lett.* **1980,** *21,* 719.
[44] S. L. Beaucage, M. H. Caruthers, *Tetrahedron Lett.* **1981,** *22,* 1859.
[45] M. A. Dorman, S. A. Noble, C. J. McBride, M. H. Caruthers, *Tetrahedron* **1984,** *40,* 95.
[46] M. D. Matteucci, M. H. Caruthers, *J. Am. Chem. Soc.* **1981,** *103,* 3185.
[47] R. W. Adamiak, J. Stawinski, *Tetrahedron Lett.* **1977,** 1935.
[48] H. Sigmund, Ph. D. Thesis, University of Konstanz, 1992.