59. Nucleotides

Part LI[1])

Synthesis and Biological Activities of (2′–5′)Adenylate Trimer Conjugates with 2′-Terminal 3′-*O*-(ω-Hydroxyalkyl) and 3′-*O*-(ω-Carboxyalkyl) Spacers

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An efficient strategy for the synthesis of (2′–5′)adenylate trimer conjugates with 2′-terminal 3′-*O*-(ω-hydroxyalkyl) and 3′-*O*-(ω-carboxyalkyl) spacers is reported. Npeoc-protected adenosine building blocks **37**–**40** for phosphoramidite chemistry carrying a 3′-*O*-[11-(levulinoyloxy)undecyl], 3′-*O*-{2-[2-(levulinoyloxy)ethoxy]ethyl}, 3′-*O*-[5-(2-cyanoethoxycarbonyl)pentyl], and 3′-*O*-{5-[(9*H*-fluoren-9-ylmethoxy)carbonyl]pentyl} moiety, respectively, were prepared (npeoc = 2-(4-nitrophenyl)ethoxycarbonyl). Condensation with the cordycepin (3′-deoxyadenosine) dimer **1** led to the corresponding trimers **42, 43, 47,** and **48**. Whereas the levulinoyl (lev) and 9*H*-fluoren-9-ylmethyl (fm) blocking groups could be cleaved off selectively from the trimers **42, 43,** and **48** yielding the intermediates **44, 45,** and **49** for the synthesis of the 3′-*O*-(ω-hydroxyalkyl)trimers **53, 54** and the cholesterol conjugates **59**–**61**, the 2-cyanoethyl (ce) protecting group of **47**, however, could not be removed in a similar manner from the carboxy function. Trimer **47** served as precursor for the preparation of the trimer **55** with a terminal 3′-*O*-(5-carboxypentyl)adenosine moiety. The metabolically stable 3′-*O*-alkyl-(2′–5′)A derivatives were tested regarding inhibition of HIV-1 syncytia formation and HIV-1 RT activity. Only the conjugate **59** showed significant effects, whereas the trimers **53**–**55** and the conjugates **60** and **61** were less potent inhibitors, even at 100-fold larger concentrations.

1. Introduction. – Despite of the successful isolation of the AIDS-causing human immunodeficiency virus (HIV) by *Montagnier* and coworkers [2] and *Gallo* and coworkers [3] in 1983, up to now no 'cure' for AIDS could be established. All so far approved drugs belong to the 2′,3′-dideoxynucleoside class (AZT, DDI, DDC), their target being the retrovirus-specific reverse transcriptase (RT) [4], but serious toxic side effects (*e.g.* bone-marrow suppression) reinforced the search for other anti-HIV drugs [5]. Between HIV production and the level of (2′–5′)oligoadenylates ((2′–5′)A), mediators in the interferon-induced response to virus infection (2–5A synthetase/RNase L pathway [6][7]), exists an inverse correlation [8]. Therefore, extending the period during which the cellular level of (2′–5′)A is high seems a promising strategy for anti-HIV chemotherapy.

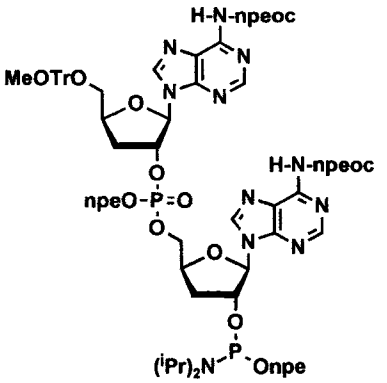
[1]) Part L: [1].

A metabolically more stable and nevertheless untoxic derivative of (2′–5′)A is the cordycepin (3′-deoxyadenosine) trimer [9], first chemically synthesized by *Charubala* and *Pfleiderer* in 1980 [10]. As expected, it inhibited virus production when encapsuled in liposomes in μM concentration [11]. Surprisingly the target of the cordycepin trimer was found to be the HIV-1 reverse transcriptase (RT) [12]. It is most likely that this inhibitory effect is caused by complexation of the cordycepin trimer with uridine residues in the anticodon domain of $tRNA^{Lys,3}$ [13], the primer of RT, thus weakening the complex formation of RT and its primer. A further 1000-fold augmentation of antiviral activity could be achieved by attaching cholesterol to the 2′- or 5′-end of cordycepin trimers *via* ester linkages [14]. In a previous publication [15], we reported on the synthesis of a new type of (2′–5′)adenylate trimer conjugates with 3′-*O*-(2-hydroxyalkyl) spacer. The synthesis was realized by phosphoramidite chemistry using the npe/npeoc blocking group strategy [16–18], (npe = 2-(4-nitrophenyl)ethyl, npeoc = 2-(4-nitrophenyl)ethoxycarbonyl) the crucial point being the selective deprotection of the spacer's OH function from the appropriately blocked trimer in order to enable the coupling of the cholesterol (cholest-5-en-3β-ol) moiety of the spacer. For protection of the spacer's OH moiety, the acetyl group was used and cleaved off from the fully blocked trimer in 60% yield. We now want to report on a strategy using the levulinoyl group [19][20] to protect 3′-*O*-(ω-hydroxyalkyl) spacers as well as on the synthesis of trimers and a cholesterol conjugate with *a* 3′-*O*-(5-carboxypentyl) spacer.

2. Syntheses. – Analogously to our previously developed method [15], npeoc-protected adenosine building blocks **37**–**40** served as intermediates, which afforded trimers on condensation with phosphoramidite **1** of a cordycepin dimer [15]. The multistep synthesis of these monomeric building blocks was based on N^6,2′-*O*,5′-*O*-tris(trityl)adenosine (**2**), prepared from adenosine by a known procedure [21–23]. As ω-hydroxyalkyl spacers appropriately protected for the alkylation (11-bromoundecyloxy)dimethyl(thexyl)silane (**3**; thexyl = 1,1,2-trimethylpropyl), (12-bromodoctecyloxy)dimethyl(thexyl)silane (**4**), and [2-(2-iodoethoxy)ethoxy]dimethyl(thexyl)silane (**6**) were obtained in 78–56% yield starting from the corresponding alcohols, with 2-(2-iodoethoxy)ethanol (**5**) resulting from *Finkelstein* reaction of the chloroprecursor (55% yield). Reaction of spacers **3**, **4**, and **6** with N^6,2′-*O*,5′-*O*-tris(trityl)adenosine (**2**) under *Williamson* conditions using NaH as base afforded the 3′-*O*-alkyl ethers **7**–**9** (90–82%), which led after removal of the silyl groups with fluoride ions to the alcohols **10**–**12** (94–87%).

Furthermore, alkylation of **2** went on more smoothly with ethyl 6-bromohexanoate than with the free acid and yielded ether **13** (71%), which gave on treatment with THF/EtOH/1M NaOH 2:2:1 acid **14** (94%).

For protection of the OH function, levulinic acid (= 4-oxopentanoic acid, levOH) was applied whereas the COOH function was blocked either with the 2-cyanoethyl(ce) or (9*H*-fluoren-9-yl)methyl (fm) group. The protecting groups were introduced in the presence of *N*-[3-(dimethylamino)propyl]-*N*′-ethylcarbodiimide (ECD) and 4-(dimethylamino)pyridine (DMAP) to give the esters **15**–**19** in 92–67% yields. The trityl groups were cleaved off with 80% $AcOH/H_2O$ at 100° yielding the 3′-*O*-alkyladenosines **20**–**24** (88–64%) and paving the way for the introduction of the 2-(4-nitrophenyl)-ethoxycarbonyl (npeoc) groups [16–18]. Transient protection of **20** and **22**–**24** using hexamethyldisilazane and subsequent reaction with 1-methyl-3-[2-(4-nitrophenyl)-



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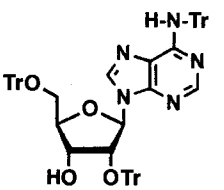


2

$X(CH_2)_n(OCH_2CH_2)_mOR$

	X	*n*	*m*	R
3	Br	11	0	Otds
4	Br	12	0	Otds
5	I	2	1	H
6	I	2	1	Otds

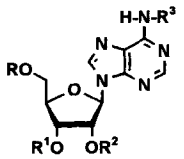
npeoc = 2-(4-nitrophenyl)ethoxycarbonyl, MeOTr = monomethoxytrityl, npe = 2-(4-nitrophenyl)ethyl, ^{i}Pr = isopropyl, tds = dimethyl(thexyl)silyl

ethoxycarbonyl]-1*H*-imidazolium chloride afforded, after desilylation with aqueous acetic acid, the N^6-npeoc derivates **25**–**28** (79–60%). Then the 5′-OH functions were selectively monomethoxytritylated leading to **29**–**32** (89–67%), and the 2′-OH positions blocked using 1-methyl-3-[2-(4-nitrophenyl)ethoxycarbonyl]-1*H*-imidazolium chloride and DMAP to give **33**–**36** (89–91%). Finally, the monomeric building blocks **37**–**40** were obtained in 92–76% yield by detritylation of their precursors **33**–**36**.

By hydrazinolysis, the levulinoyl protecting group of **33** was selectively cleaved off without harming the npeoc groups, and the alcohol **41** was isolated in 94% yield, whereas removal of the acetyl group from the previously reported corresponding 3′-*O*-(2-acetoxyethyl)-5′-*O*-(monomethoxytrityl)-N^6-[2-(4-nitrophenyl)ethoxycarbonyl]-2′-*O*-[2-(4-nitrophenyl)ethoxysulfonyl]adenosine could only be performed in 63% yield [15]. As already mentioned, the trimers **42** (93%) and **43** (94%) were synthesized by condensation of the monomeric building blocks **37** and **38** with the dimeric phosphoramidite **1** in the presence of 1*H*-tetrazole and subsequent I_2 oxidation. Cleavage of the levulinoyl groups led to the alcohols **44** in 94% and **45** in 77% yield, while the acetyl protecting group was only cleaved off in 60% yield from the corresponding trimer [15].

To study the cleavage of the terminal ester functions (COOce or COOfm) to the carboxy group, **36** was treated with piperidine affording under fm deprotection **46** (75%), whereas the removal of ce from **35** using 0.1M 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) occurred only with simultaneous loss of npeoc groups. Consequently, the free acid **49** was synthesized in 87% yield from the fm-blocked trimer **48**, which was obtained, as well as trimer **47**, by coupling of the corresponding building block **39** or **40** with phosphoramidite **1** in 89% (**47**) and 95% (**48**) yield, respectively.

The trimers **44**, **45**, and **47** were stepwise deblocked in good yields first by acid treatment (→ **50** (75%), **51** (76%), and **52** (80%), resp.) and then using DBU to give the 3′-*O*-(ω-hydroxyalkyl) trimers **53** and **54** and the 3′-*O*-(5-carboxypentyl) trimer as $HDBU^+$ salt **55** in 70, 92, and 92% yield, respectively. All these totally deprotected trimers turned out to be well H_2O-soluble.



	R	R^1	R^2	R^3
7	Tr	$(CH_2)_{11}$Otds	Tr	Tr
8	Tr	$(CH_2)_{12}$Otds	Tr	Tr
9	Tr	$(CH_2)_2O(CH_2)_2$Otds	Tr	Tr
10	Tr	$(CH_2)_{11}$OH	Tr	Tr
11	Tr	$(CH_2)_{12}$OH	Tr	Tr
12	Tr	$(CH_2)_2O(CH_2)_2$OH	Tr	Tr
13	Tr	$(CH_2)_5$COOEt	Tr	Tr
14	Tr	$(CH_2)_5$COOH	Tr	Tr
15	Tr	$(CH_2)_{11}$Olev	Tr	Tr
16	Tr	$(CH_2)_{12}$Olev	Tr	Tr
17	Tr	$(CH_2)_2O(CH_2)_2$Olev	Tr	Tr
18	Tr	$(CH_2)_5$COOce	Tr	Tr
19	Tr	$(CH_2)_5$COOfm	Tr	Tr
20	H	$(CH_2)_{11}$Olev	H	H

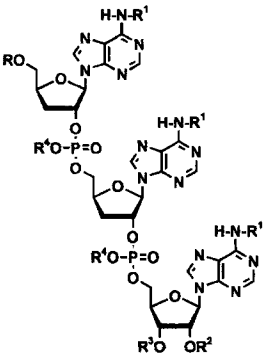
	R	R^1	R^2	R^3
21	H	$(CH_2)_{12}$Olev	H	H
22	H	$(CH_2)_2O(CH_2)_2$Olev	H	H
23	H	$(CH_2)_5$COOce	H	H
24	H	$(CH_2)_5$COOfm	H	H
25	H	$(CH_2)_{11}$Olev	H	npeoc
26	H	$(CH_2)_2O(CH_2)_2$Olev	H	npeoc
27	H	$(CH_2)_5$COOce	H	npeoc
28	H	$(CH_2)_5$COOfm	H	npeoc
29	MeOTr	$(CH_2)_{11}$Olev	H	npeoc
30	MeOTr	$(CH_2)_2O(CH_2)_2$Olev	H	npeoc
31	MeOTr	$(CH_2)_5$COOce	H	npeoc
32	MeOTr	$(CH_2)_5$COOfm	H	npeoc
33	MeOTr	$(CH_2)_{11}$Olev	npeoc	npeoc
34	MeOTr	$(CH_2)_2O(CH_2)_2$Olev	npeoc	npeoc

	R	R^1	R^2	R^3
35	MeOTr	$(CH_2)_5$COOce	npeoc	npeoc
36	MeOTr	$(CH_2)_5$COOfm	npeoc	npeoc
37	H	$(CH_2)_{11}$Olev	npeoc	npeoc
38	H	$(CH_2)_2O(CH_2)_2$Olev	npeoc	npeoc
39	H	$(CH_2)_5$COOce	npeoc	npeoc
40	H	$(CH_2)_5$COOfm	npeoc	npeoc
41	MeOTr	$(CH_2)_{11}$OH	npeoc	npeoc
46	MeOTr	$(CH_2)_5$COOH	npeoc	npeoc
62	MeOTr	$(CH_2)_5$COOH	H	npeoc
63	MeOTr	$(CH_2)_5$COOH	npes	npeoc
64	MeOTr	$(CH_2)_5$COOchol	npes	npeoc
65	H	$(CH_2)_5$COOchol	npes	npeoc

Tr = trityl, lev = levulinoyl = 1,4-dioxopentyl, ce = 2-cyanoethyl, fm = (9*H*-fluoren-9-yl)methyl, npes = 2-(4-nitrophenyl)ethoxysulfonyl, chol = cholest-5-en-3ß-yl

Next, conjugate formation was achieved by coupling of the alcohols **44** and **45** with cholesteryl chloroformate under activation with 1-methyl-1*H*-imidazole and DMAP as well as by condensation of acid **49** with cholesterol in the presence of EDC and DMAP to form the fully protected conjugates **56**–**58** (76–40%), which gave on standard deblocking with acid and DBU the conjugates **59**–**61** in 80–42% overall yield.

Another route for the preparation of the cholesterol conjugate **61** started from **31**, which gave in the first step on treatment with 0.1M DMU the acid **62** (72%). After 2′-*O*-protection with the 2-(4-nitrophenyl)ethoxysulfonyl (npes) group [24] [25] leading to **63** (86%), the cholesterol moiety was introduced already into the monomeric building block to yield conjugate **64** (60%). Detritylation afforded **65** (89%), and condensation with phosphoramidite **2** led to trimer **66** (49%). Total deprotection of trimer **66** to conjugate **61** was performed similarly to the deblocking of trimer **58** in 53% yield.



	R	R^1	R^2	R^3	R^4
42	MeOTr	npeoc	npeoc	$(CH_2)_{11}$Olev	npe
43	MeOTr	npeoc	npeoc	$(CH_2)_2O(CH_2)_2$Olev	npe
44	MeOTr	npeoc	npeoc	$(CH_2)_{11}$OH	npe
45	MeOTr	npeoc	npeoc	$(CH_2)_2O(CH_2)_2$OH	npe
47	MeOTr	npeoc	npeoc	$(CH_2)_5$COOce	npe
48	MeOTr	npeoc	npeoc	$(CH_2)_5$COOfm	npe
49	MeOTr	npeoc	npeoc	$(CH_2)_5$COOH	npe
50	H	npeoc	npeoc	$(CH_2)_{11}$OH	npe
51	H	npeoc	npeoc	$(CH_2)_2O(CH_2)_2$OH	npe
52	H	npeoc	npeoc	$(CH_2)_5$COOce	npe

	R	R^1	R^2	R^3	R^4
53	H	H	H	$(CH_2)_{11}$OH	(HDBU)
54	H	H	H	$(CH_2)_2O(CH_2)_2$OH	(HDBU)
55	H	H	H	$(CH_2)_5$COO(HDBU)	(HDBU)
56	MeOTr	npeoc	npeoc	$(CH_2)_{11}$OCOOchol	npe
57	MeOTr	npeoc	npeoc	$(CH_2)_2O(CH_2)_2$OCOOchol	npe
58	MeOTr	npeoc	npeoc	$(CH_2)_5$COOchol	npe
59	H	H	H	$(CH_2)_{11}$OCOOchol	(HDBU)
60	H	H	H	$(CH_2)_2O(CH_2)_2$OCOOchol	(HDBU)
61	H	H	H	$(CH_2)_5$COOchol	(HDBU)
66	MeOTr	npeoc	npes	$(CH_2)_5$COOchol	npe

It has also to be mentioned that conjugate **60** with a diethyleneglycol spacer could be dissolved in H_2O and trimer **61** with a pentyl spacer in various buffers, whereas, however, conjugate **59** with a undecyl spacer was only soluble in DMSO and ternary mixtures of CH_2Cl_2/MeOH/H_2O.

3. Biochemical Application. – The 3′-*O*-(ω-hydroxyalkyl) trimers **53** and **54** and the 3′-*O*-(ω-carboxyalkyl) trimer **55** as well as the corresponding cholesterol conjugates **59**–**61** were screened by the infected-centers assay to measure their ability to inhibit HIV-1-induced syncytia formation, an indicator of HIV-1 replication in T-cells. The most potent inhibitor of this series of HIV-1 replication is **59**; at 1.6 μM, this (2′–5′)A derivative inhibited HIV-1 syncytia formation 3.4-fold (*Table*). This compares with a decreased inhibition of syncytia by compounds **53**–**55**, **60**, **61**, and 3′-deoxyadenylyl-(2′–5′)-3′-deoxyadenylyl-(2′–5′)-3′-*O*-(β-hydroxyethyl)adenosine [15] shown in the *Table* at concentrations of 300 μM. The inhibition of HIV-1 replication by **59** may be attributed to the 11% inhibition of HIV-1 reverse transcriptase (RT) and/or pleiotropic activities, since, *e.g.*, alkyl derivatives of glycerol have shown inhibition of HIV-1 replication at the budding stage. With the other 3′-*O*-alkyl-(2′–5′)A derivatives, there is little inhibition of syncytia formation and little inhibition of HIV-1 RT activity. Either these (2′–5′)A derivatives are not taken up by HIV-1-infected cells, or, if taken up, they do not induce an inhibitory effect.

Table. *Inhibition of HIV-1 Replication by (2′–5′)A Trimer Analogs Carrying a Terminal 3′-O-(ω-Substituted Alkyl) Residue*

Trimer	Terminal 3′-*O*-substituent	Inhibition of syncytia formation[a]) fold	Inhibition of HIV-1 RT activity[b]) [%]
	$(CH_2)_2O(CH_2)_2OH$	0.9	0
	$(CH_2)_2O(CH_2)_2OCOOchol$	n/a[c])	64
	$(CH_2)_5COO$(HDBU)	1.3	8
	$(CH_2)_5COOchol$	n/a[c])	20
	$(CH_2)_{11}OH$	1.3	1
	$(CH_2)_{11}OCOOchol$	3.4	11
	CH_2CH_2OH [15]	0.8	0

[a]) Inhibition of HIV-1 replication was determined by HIV-1-induced syncytia formation (fold reduction). Compound **59** was tested at 1.6 μM; all the other compounds at 300 μM. The mean of triplicate determinations is shown; variance did not exceed 5–10%.

[b]) Percent inhibition of HIV-1 reverse transcriptase (HIV-1 RT) activity was measured under the same conditions as described in *Footnote a.*

[c]) Compound exhibited toxicity upon prolonged incubation with Sup T1 cells.

[d]) Compound **59** was dissolved in 0.5% DMSO.

Experimental Part

General. TLC: Precoated silica gel TLC sheets *F 1500 LS 254* from *Schleicher & Schüll.* Prep. TLC: silica gel *60 PF_{254} (Merck).* Prep. column flash chromatography (FC): silica gel for flash chromatography (*Baker*); 0.2 bar. HPLC: *Merck-Hitachi L 620, L-3000* photo diode array detector; column *RP 18, LiChrosphere* 125 × 4 mm, 5 μm, *Merck*; flow rate 1 ml/min. UV/VIS: *Perkin-Elmer Lambda 5*; λ_{max} in nm(log ε). ^{1}H-NMR: *Bruker AC 250*; δ in ppm rel. to $CHCl_3$ ((D_5)DMSO). ^{31}P-NMR: *Jeol JM 6X-400*; δ in ppm rel. to 85% H_3PO_4 soln. light petroleum ether = p.e.

Bioassay. Assays measuring HIV-1-induced syncytia formation were accomplished as described [26].

(11-Bromoundecyloxy)dimethyl(1,1,2-trimethylpropyl)silane (**3**). To a soln. of 1*H*-imidazole (7.95 g, 0.12 mol) in abs. THF (100 ml), first dimethyl(1,1,2-trimethylpropyl)silyl chloride (8.4 ml, 43 mmol), and after 10 min, 11-bromoundecanol (9.8 g, 39 mmol) were added. The mixture was stirred overnight, diluted with p.e. (100 ml), and washed with sat. NaCl soln. (3 × 100 ml). The aq. phases were re-extracted with p.e. (3 × 50 ml), the combined org. layer dried (Na_2SO_4) and evaporated, and the residue purified by FC (silica gel (100 g), *d* 6.5 cm; p.e. (100 ml), p.e./AcOEt 95:5 (500 ml)): 10.4 g (68%) of **3**. Colourless oil. ^{1}H-NMR ($CDCl_3$): 3.55 (*t*, CH_2O); 3.39 (*t*, CH_2Br); 1.86 (*m*, CH_2CH_2Br); 1.60 (*m*, CH); 1.47–1.28 (*m*, 8 CH_2); 0.85 (*m*, 4 MeC); 0.08 (*s*, 2 MeSi). Anal. calc. for $C_{19}H_{41}BrOSi$ (393.5): C 57.99, H 10.50; found: C 57.95, H 10.34.

(12-Bromododecyloxy)dimethyl(1,1,2-trimethylpropyl)silane (**4**). As described for **3**, with 1*H*-imidazole (1.95 g, 29 mmol), THF (40 ml), dimethyl(1,1,2-trimethylpropyl)silyl chloride (1.9 ml, 9.6 mmol), and 12-bromododecanol (2.8 g, 11 mmol). The crude product was destilled (185° 0.4 mbar): 2.2 g (56%) of **4**. Colourless oil. ^{1}H-NMR ($CDCl_3$): 3.56 (*t*, CH_2O); 3.38 (*t*, CH_2Br); 1.85 (*m*, CH_2CH_2Br); 1.60 (*m*, CH); 1.47–1.28 (*m*, 9 CH_2); 0.85 (*m*, 4 MeC); 0.09 (*s*, 2 MeSi). Anal. calc. for $C_{20}H_{43}BrOSi$ (407.6): C 58.94, H 10.63; found: C 58.80, H 10.58.

2-(2-Iodoethoxy)ethanol (**5**). Diethyleneglycol monochlorohydrin (= 2-(2-chloroethoxy)ethanol; 10 ml, 94 mmol) and NaI (1.5 g, 120 mmol) were refluxed in ethyl methyl keton (40 ml) for 1 d. The mixture was diluted with AcOEt (500 ml) and washed with $Na_2S_2O_3$ soln. (3 × 500 ml), the aq. phase re-extracted with AcOEt (3 × 250 ml), the combined org. layer dried (Na_2SO_4) and evaporated, and the residue submitted to vacuum destillation (64°/0.4 mbar): 11.2 g (55%) of **5**. Yellowish oil. ^{1}H-NMR ($CDCl_3$): 3.77–3.72 (*m*, 2 CH_2); 3.61–3.57 (*m*, CH_2OH); 3.24 (*t*, CH_2I); 2.20 (br. *s*, OH). Anal. calc. for $C_4H_9IO_2$ (216.0): C 22.24, H 4.20; found: C 21.87, H 4.21.

[2-(2-Iodoethoxy)ethoxy]dimethyl(1,1,2-trimethylpropyl)silane (**6**). As described for **3**, with 1*H*-imidazole (10.2 g, 150 mmol), THF (60 ml), dimethyl(1,1,2-trimethylpropyl)silyl chloride (10.8 ml, 55 mmol), and **5** (10.8 g, 50 mmol). Workup and purification by vacuum destillation (96°/0.4 mbar) yielded 14.0 g (78%) of **6**. Colourless

oil. ^{1}H-NMR ($CDCl_3$): 3.78–3.72 (*m*, 2 CH_2); 3.58–3.53 (*m*, CH_2Otds); 3.23 (*t*, CH_2I); 1.68–1.55 (*m*, CH); 0.85 (*m*, 4 MeC); 0.09 (*s*, 2 MeSi). Anal. calc. for $C_{12}H_{27}IO_2Si$ (358.3): C 40.22, H 7.59; found: C 40.38, H 7.55.

3'-O-{11-[Dimethyl(1,1,2-trimethylpropyl)silyloxy]undecyl}-N^6,2'-O,5'-O-tris(triphenylmethyl)adenosine (**7**). A mixture of *N^6,2'-O,5'-O*-tris(triphenylmethyl)adenosine (**2**) [21–23] (7.3 g, 73 mmol) and 80% oil-immersed NaH (0.85 g, 28 mmol) in abs. MeCN (160 ml) was stirred at r.t. for 10 min, then NaI (0.66 g, 4.4 mmol) and **3** (8.7 g, 22 mmol) were added. The mixture was kept overnight, then diluted with AcOEt (100 ml), and washed with phosphate buffer pH (3 × 200 ml). Then the aq. phases were re-extracted with AcOEt (3 × 100 ml). The combined org. layer was dried (Na_2SO_4) and evaporated and the residue purified by FC (silica gel (300 g), 7 × 18 cm; p.e. (250 ml), p.e./AcOEt 9:1 (500 ml), 7:1 (400 ml), 5:1 (600 ml), 3:1 (400 ml), and 2:1 (600 ml)): 8.4 g (88%) of **7**. Colourless foam. TLC (toluene/AcOEt 4:1): R_f 0.82. UV (MeOH): 274(4.32). ^{1}H-NMR $CDCl_3$): 7.67, 7.66 (2*s*, H–C(2), H–C(8)); 7.38–7.00 (*m*, 45 H of Tr); 6.9 (*s*, NH); 6.00 (*d*, *J* = 7.1, H–C(1')); 5.13 (*dd*, H–C(2')); 4.10 (*m*, H–C(4')); 3.56 (*t*, CH_2Otds); 3.25–2.85 (*m*, CH_2O–C(3'), 2 H–C(5'), H–C(3')); 1.60–1.26 (*m*, CH, 9 CH_2); 0.90–0.80 (*m*, 4 MeC); 0.06, 0.05 (2*s*, 2 MeSi, diast.). Anal. calc. for $C_{86}H_{95}N_5O_5Si$ (1306.8): C 79.04, H 7.33, N 5.36; found: C 78.69, H 7.45, N 5.19.

3'-O-{12-[Dimethyl(1,1,2-trimethylpropyl)silyloxy]dodecyl}-N^6,2'-O,5'-O-tris(triphenylmethyl)adenosine (**8**). As described for **7**, with **2** [21–23] (99 mg, 0.1 mmol), 80% oil-immersed NaH (35 mg, 1.2 mmol), abs. MeCN (5 ml), NaI (5 mg, 33 µmol) and **4** (120 mg, 0.3 mmol). Workup and purification by FC (silica gel (5 g), 1.5 × 8 cm; p.e. (50 ml), p.e./AcOEt 9:1 (50 ml), 5:1 (60 ml)) yielded 110 mg (82%) of **8**. Colourless foam. TLC (toluene/AcOEt 4:1): R_f 0.77. UV (CH_2Cl_2): 282(sh, 4.17), 274(4.33), 269(sh, 4.32). ^{1}H-NMR ($CDCl_3$): 7.67, 7.66 (2*s*, H–C(2), H–C(8)); 7.38–7.00 (*m*, 45 H of Tr); 6.89 (*s*, NH); 6.00 (*d*, *J* = 7.1, H–C(1')); 5.13 (*dd*, H–C(2')); 4.08 (*m*, H–C(4')); 3.54 (*t*, CH_2Otds); 3.30–2.85 (*m*, CH_2O–C(3'), 2 H–C(5'), H–C(3')); 1.65–1.25 (*m*, CH, H_2O, 10 CH_2); 0.85 (*m*, 4 MeC); 0.06, 0.05 (2*s*, MeSi, diast.). Anal. calc. for $C_{87}H_{97}N_5O_5Si \cdot H_2O$ (1338.8): C 78.04, H 7.45, N 5.23; found: C 77.64, H 7.53, N 5.13.

3'-O-{2-{2-[Dimethyl(1,1,2-trimethylpropyl)silyloxy]ethoxy}ethyl}-N^6,2'-O,5'-O-tris(triphenylmethyl)-adenosine (**9**). As described for **7**, with **2** [21–23] (13.3 g, 13 mmol), 80% oil-immersed NaH (2.4 g, 80 mmol), abs. MeCN (150 ml), and **6** (13.3 g, 37 mmol). After 4 h stirring at r.t., workup and purification by FC (silica gel (300 g), 7 × 16 cm; p.e. (500 ml), p.e./AcOEt 9:1 (500 ml), 7:1 (400 ml), 5:1 (300 ml), 3:1 (800 ml), 2:1 (600 ml), 1:1 (500 ml)) gave 14.3 g (90%) of **9**. Colourless foam. TLC (toluene/AcOEt 4:1): R_f 0.76. UV (MeOH): 282(sh, 4.24), 274(4.35). ^{1}H-NMR ($CDCl_3$): 7.71, 7.68 (2*s*, H–C(2), H–C(8)); 7.38–7.00 (*m*, 45 H of Tr); 6.91 (*s*, NH); 6.07 (*d*, *J* = 7.4, H–C(1')); 5.15 (*dd*, H–C(2')); 4.11 (*m*, H–C(4')); 3.68–3.50 (*m*, 3 CH_2); 3.33–3.00 (*m*, CH_2O–C(3'), 2 H–C(5')); 2.78 (*d*, H–C(3')); 1.58 (*m*, CH); 0.88–0.80 (*m*, 4 MeC); 0.07, 0.06 (2*s*, MeSi, diast). Anal. calc. for $C_{79}H_{81}N_5O_6Si$ (1224.6): C 77.48, H 6.67, N 5.71; found: C 77.18, H 6.79, N 5.76.

3'-O-(11-Hydroxyundecyl)-N^6,2'-O,5'-O-tris(triphenylmethyl)adenosine (**10**). A mixture of **7** (8.4 g, 6.5 mmol), $Bu_4NF \cdot 3\ H_2O$ (2.9 g, 9.2 mmol), and abs. THF (10 ml) was kept at r.t. overnight. Then it was diluted with AcOEt (100 ml) and washed with sat. NaCl soln. (3 × 100 ml). The aq. phases were re-extracted with AcOEt (3 × 100 ml). The combined org. layer was dried (Na_2SO_4) and evaporated and the residue purified by FC (silica gel (150 g), 5.5 × 12 cm; toluene (200 ml), toluene/AcOEt 9:1 (200 ml), 7:1 (160 ml), 6:1 (140 ml), 5:1 (360 ml), 4:1 (400 ml)): 7.1 g (94%) of **10**. Colourless foam. TLC (toluene/AcOEt 4:1): R_f 0.24. UV (MeOH): 273(4.32). ^{1}H-NMR ((D_6)DMSO): 8.36 (br. *s*, NH); 7.46, 7.45 (2*s*, H–C(2), H–C(8)); 7.37–6.99 (*m*, 45 H of Tr); 6.10 (*d*, *J* = 7.5, H–C(1')); 5.12 (*dd*, H–C(2')); 4.31 (*t*, OH); 3.92 (*m*, H–C(4')); 3.35 (*m*, CH_2OH); 3.20–2.70 (*m*, CH_2O–C(3'), 2 H–C(5')); 2.43 (*d*, H–C(3')); 1.42–1.20 (*m*, 9 CH_2). Anal. calc. for $C_{79}H_{79}N_5O_5$ (1164.5): C 80.45, H 6.66, N 6.01; found: C 79.88, H 6.66, N 5.86.

3'-O-(12-Hydroxydodecyl)-N^6,2'-O,5'-O-tris(triphenylmethyl)adenosine (**11**). As described for **10**, with **8** (1.3 g, 0.9 mmol), $Bu_4NF \cdot 3\ H_2O$ (430 mg, 1.4 mmol), and abs. THF (3 ml). After workup and purification by FC (silica gel (20 g), 3 × 9 cm; toluene (50 ml), toluene/AcOEt 9:1 (100 ml), 6:1 (70 ml), 3:1 (80 ml)), 970 mg (87%) of **11** were obtained. Colourless foam. TLC (toluene/AcOEt 4:1): R_f 0.30. UV (MeOH): 282(sh, 4.20), 273(4.34), 268(sh, 4.33). ^{1}H-NMR ((D_6)DMSO): 8.35 (br. *s*, NH); 7.48, 7.47 (2*s*, H–C(2), H–C(8)); 7.37–6.99 (*m*, 45 H of Tr); 6.12 (*d*, *J* = 7.5, H–C(1')); 5.12 (*dd*, H–C(2')); 4.32 (*t*, OH); 3.90 (*m*, H–C(4')); 3.35 (*m*, CH_2OH); 3.20–2.20 (*m*, CH_2O–C(3'), 2 H–C(5')); 2.45 (*d*, H–C(3')); 1.40–1.21 (*m*, 10 CH_2). Anal. calc. for $C_{80}H_{81}N_5O_5$ (1178.5): C 80.51, H 6.76, N 5.94; found: C 80.30, H 6.85, N 5.94.

3'-O-[2-(2-Hydroxyethoxy)ethyl]-N^6,2'-O,5'-O-tris(triphenylmethyl)adenosine (**12**). As described for **10**, with **9** (14.3 g, 12 mmol), $Bu_4NF \cdot 3\ H_2O$ (5.0 g, 16 mmol), and abs. THF (30 ml). Workup and purification by FC (silica gel (200 g), 5.5 × 17 cm; CH_2Cl_2 (500 ml), CH_2Cl_2/MeOH 99:1 (500 ml), 98:2 (500 ml), 97:3 (500 ml), 96:4 (500 ml), 95:5 (1500 ml)) gave 12.0 g (91%) of **12**. Colourless foam. TLC (CH_2Cl_2/MeOH 95:5): R_f 0.46. UV (MeOH): 282(sh, 4.23), 274(4.25), 270(sh, 4.33). ^{1}H-NMR ((D_6)DMSO): 8.37 (br. *s*, NH); 7.49, 7.46 (2*s*,

H–C(2), H–C(8)); 7.37–7.02 (*m*, 45 H of Tr); 6.13 (*d*, *J* = 7.6, H–C(1')); 5.12 (*dd*, H–C(2')); 4.56 (*t*, OH); 4.03 (*m*, H–C(4')); 3.52–3.40 (*m*, 3 CH_2O); 3.36 (*s*, H_2O); 3.32–2.88 (*m*, CH_2O–C(3'), 2 H–C(5')); 2.45 (*d*, H–C(3')). Anal. calc. for $C_{71}H_{63}N_5O_6 \cdot H_2O$ (1100.3): C 77.50, H 5.95, N 6.36; found: C 77.62, H 6.00, N 6.73.

3'-O-[5-(Ethoxycarbonyl)pentyl]-N⁶,2'-O-5'-O-tris(triphenylmethyl)adenosine (**13**). A mixture of **2** [21–23] (0.23 g, 0.23 mmol) and 80% oil-immersed NaH (40 mg, 1.3 mmol) in abs. MeCN (5 ml) was stirred at r.t. for 10 min, then a catal. amount of NaI and ethyl 6-bromohexanoate (*Fluka*; 0.12 ml, 0.67 mmol) were added. The mixture was kept overnight, then diluted with AcOEt (50 ml), and washed with 10% citric acid soln. (50 ml) and phosphate buffer pH 7 (3 × 50 ml). The aq. phases were re-extracted with AcOEt (3 × 100 ml). The combined org. layer was dried (Na_2SO_4) and evaporated and the residue purified by FC (silica gel (7 g), 2 × 8 cm; p.e. (50 ml), p.e./AcOEt 9:1 (50 ml), 7:1 (40 ml), 5:1 (60 ml), 4:1 (50 ml), 3:1 (80 ml), and 2:1 (30 ml)): 0.19 g (71%) of **13**. Colourless foam, which crystallized from EtOH/H_2O 5:1. Colourless crystals. M.p. 115°. TLC (p.e./AcOEt 3:1): R_f 0.32. UV (MeOH): 282(sh, 4.23), 274(4.29). ^{1}H-NMR ((D$_6$)DMSO): 8.37 (*s*, NH); 7.47 (2*s*, H–C(2), H–C(8)); 7.38–7.00 (*m*, 45 H of Tr); 6.12 (*d*, *J* = 7.5, H–C(1')); 5.18 (*dd*, H–C(2')); 4.07–3.99 (*q*, CH_2OCO); 3.94 (*m*, H–C(4')); 3.34–3.15, 2.90–2.70 (*m*, CH_2O–C(3'), 2 H–C(5')); 2.43 (*d*, H–C(3')); 2.22 (*t*, CH_2COO); 1.53–1.30 (*m*, 3 CH_2); 1.16 (*t*, Me). Anal. calc. for $C_{75}H_{69}N_5O_6 \cdot 0.5\ H_2O$ (1145.3): C 78.65, H 6.16, N 6.11; found: C 78.56, H 6.00, N 6.25.

3'-O-(5-Carboxypentyl)-N⁶,2'-O,5'-O-tris(triphenylmethyl)adenosine (**14**). In THF/EtOH/1M NaOH 2:2:1 (100 ml), **13** (6.4 g, 5.6 mmol) was kept at r.t. for 4 h. Then the mixture was neutralized with AcOH, diluted with $CHCl_3$ (250 ml), and washed with sat. NaCl soln. (3 × 250 ml). The aq. phases were re-extracted with $CHCl_3$ (3 × 100 ml). The combined org. layer was dried (Na_2SO_4) and evaporated and the residue purified by FC (silica gel (130 g), 5 × 20 cm; CH_2Cl_2 (250 ml), CH_2Cl_2/MeOH 98:2 (200 ml), 95:5 (200 ml), 93:7 (400 ml), 9:1 (300 ml)): 5.8 g (94%) of **14**. Colourless foam. TLC (CH_2Cl_2/MeOH 95:5): R_f 0.34. UV (MeOH): 274(4.33). ^{1}H-NMR ((D$_6$)DMSO): 12.01 (br. *s*, COOH); 8.37 (*s*, NH); 7.48, 7.47 (2*s*, H–C(2), H–C(8)); 7.35–7.00 (*m*, 45 H of Tr); 6.12 (*d*, *J* = 7.0, H–C(1')); 5.18 (*dd*, H–C(2')); 3.95 (*m*, H–C(4')); 3.20–3.10, 2.95–2.65 (2*m*, CH_2O–C(3'), 2 H–C(5')); 2.45 (*d*, H–C(3')); 2.15 (*t*, CH_2COO); 1.52–1.12 (*m*, 3 CH_2). Anal. calc. for $C_{73}H_{65}N_5O_6$ (1108.6): C 79.11, H 5.91, N 6.32; found: C 79.19, H 5.97, N 6.61.

3'-O-{11-[(1,4-Dioxopentyl)oxy]undecyl}-N⁶,2'-O,5'-O-tris(triphenylmethyl)adenosine (**15**). After stirring a soln. of **10** (7.1 g, 6.1 mmol), EDC · HCl (1.4 g, 7.4 mmol), and DMAP (1.1 g, 9.0 mmol) in abs. CH_2Cl_2 (40 ml) for 5 min at r.t., levulinic acid (1.2 g, 9.9 mmol) was added. The soln. was stirred for 3 h, then diluted with $CHCl_3$ (100 ml) and washed with sat. NaCl soln. (3 × 100 ml). The aq. phases were re-extracted with $CHCl_3$ (3 × 100 ml). The combined org. layer was dried (Na_2SO_4) and evaporated and the residue purified by FC (silica gel (160 g), 5.5 × 13 cm; toluene (200 ml), toluene/AcOEt 9:1 (200 ml), 7:1 (160 ml), 5:1 (720 ml)): 6.6 g (86%) of **15**. Colourless foam. TLC (toluene/AcOEt 4:1): R_f 0.51. UV (MeOH): 273(4.31). ^{1}H-NMR ($CDCl_3$): 7.68, 7.67 (2*s*, H–C(2), H–C(8)); 7.38–6.99 (*m*, 45 H to Tr); 6.90 (*s*, NH); 6.02 (*d*, *J* = 7.1, H–C(1')); 5.15 (*dd*, H–C(2')); 4.04–4.02 (*m*, H–C(4'), CH_2Olev); 3.28–2.85 (*m*, CH_2O–C(3'), 2 H–C(5'), H–C(3')); 2.72 (*t*, CH_2COO); 2.56 (*t*, CH_2CO); 2.17 (*s*, Me); 1.62–1.26 (*m*, 9 CH_2). Anal. calc. for $C_{83}H_{83}N_5O_7$ (1262.6): C 78.96, H 6.63, N 6.66; found: C 78.45, H 6.68, N 5.45.

3'-O-{12-[(1,4-Dioxopentyl)oxy]dodecyl}-N⁶,2'-O,5'-O-tris(triphenylmethyl)adenosine (**16**). As described for **15**, with **11** (680 mg, 580 µmol), EDC · HCl (130 mg, 720 µmol), DMAP (100 mg, 860 µmol), abs. CH_2Cl_2 (10 ml), and levulinic acid (135 mg, 810 µmol). Workup and purification by FC (silica gel (15 g), 2.5 × 10 cm; toluene (100 ml), toluene/AcOEt 9:1 (100 ml)) led to 550 mg (74%) of **16**. Colourless foam. TLC (toluene/AcOEt 4:1): R_f 0.52. UV (MeOH): 283(sh, 4.16), 274(4.32), 268(sh, 4.31). ^{1}H-NMR ($CDCl_3$): 7.68, 7.67 (2*s*, H–C(2), H–C(8)); 7.38–7.00 (*m*, 45 H of Tr); 6.89 (*s*, NH); 6.01 (*d*, *J* = 7.1, H–C(1')); 5.13 (*dd*, H–C(2')); 4.07–4.01 (*m*, H–C(4'), CH_2Olev); 3.20, 3.05, 2.85 (3*m*, CH_2O–C(3'), 2 H–C(5'), H–C(3')); 2.73 (*t*, CH_2COO); 2.57 (*t*, CH_2CO); 2.17 (*s*, Me); 1.60–1.25 (*m*, 10 CH_2). Anal. calc. for $C_{84}H_{85}N_5O_7 \cdot 0.5\ H_2O$ (1285.6): C 78.48, H 6.74, N 5.45; found: C 78.34, H 6.84, N 5.48.

3'-O-{2-{2-[(1,4-Dioxopentyl)oxy]ethoxy}ethyl}-N⁶,2'-O,5'-O-tris(triphenylmethyl) (**17**). As described for **15**, with **12** (11.4 g, 10 mmol), EDC · HCl (2.4 g, 12 mmol), DMAP (1.8 g, 14 mmol), abs. CH_2Cl_2 (60 ml), and levulinic acid (2.45 g, 21 mmol). Workup and purification by FC (silica gel (250 g), 5.5 × 23 cm, toluene/AcOEt 1:1 (1000 ml)) led to 11.0 g (92%) of **17**. Colourless foam. TLC (CH_2Cl_2/MeOH 95:5): R_f 0.78. UV (MeOH): 279(sh, 4.32), 274(4.35). ^{1}H-NMR ($CDCl_3$): 7.73, 7.67 (2*s*, H–C(2), H–C(8)); 7.36–6.99 (*m*, 45 H of Tr); 6.95 (*s*, NH); 6.05 (*d*, *J* = 7.3, H–C(1')); 5.04 (*dd*, H–C(2')); 4.12–4.08 (*m*, H–C(4'), CH_2Olev); 3.66–3.54 (*m*, 2 CH_2O); 3.32–3.00 (*m*, CH_2O–C(3'), 2 H–C(5')); 2.78 (*d*, H–C(3')); 2.63 (*t*, CH_2COO); 2.48 (*t*, CH_2CO); 2.09 (*s*, Me); 1.82 (*s*, H_2O). Anal. calc. for $C_{76}H_{69}N_5O_8 \cdot 0.5\ H_2O$ (1189.4): C 76.75, H 5.93, N 5.88; found: C 76.57, H 5.83, N 5.98.

3'-O-[5-(2-Cyanoethoxycarbonyl)pentyl]-N⁶,2'-O,5'-O-tris(triphenylmethyl) (**18**). As described for **15**, with **14** (8.3 g, 7.1 mmol), EDC · HCl (1.6 g, 8.5 mmol), DMAP (1.2 g, 9.9 mmol), abs. CH_2Cl_2 (20 ml), and 2-cyano-

ethanol (1.0 ml, 15.0 mmol). Workup and purification by FC (silica gel (200 g), 2 × 20 cm; CH_2Cl_2 (750 ml), CH_2Cl_2/MeOH 99:1 (500 ml), 98:2 (500 ml), 97:3 (500 ml), 96:4 (500 ml)) gave 7.4 g (90%) of **18**. Colourless foam. TLC (toluene/AcOEt 4:1): R_f 0.45. TLC (CH_2Cl_2/MeOH 95:5): R_f 0.73. UV (MeOH): 282(sh, 4.34), 274(4.35), 277(sh, 4.19). ^{1}H-NMR ($CDCl_3$): 7.68, 7.67 (2*s*, H–C(2), H–C(8)); 7.37–7.00 (*m*, 45 H of Tr); 6.89 (*s*, NH); 6.01 (*d*, *J* = 7.2, H–C(1')); 5.11 (*dd*, H–C(2')); 4.25 (*t*, CH_2OCO); 4.07 (*m*, H–C(4')); 3.27–2.79 (*m*, CH_2O–C(3'), 2 H–C(5'), H–C(3')); 2.60 (*t*, CH_2CN); 2.32 (*t*, CH_2COO); 1.68–1.32 (*m*, H_2O, 3 CH_2). Anal. calc. for $C_{76}H_{68}N_6O_6 \cdot 0.5\,H_2O$ (1170.4): C 77.99, H 5.94, N 7.18; found: C 77.65, H 6.04, N 7.18.

3'-O-{5-[(9H-Fluoren-9-ylmethoxy)carbonyl]pentyl}-N^6,2'-O,5'-O-tris(triphenylmethyl)adenosine (**19**). As described for **15**, with **14** (190 mg, 170 μmol), EDC · HCl (39 mg, 200 μmol), DMAP (30 mg, 250 μmol), abs. CH_2Cl_2 (5 ml), and (9*H*-fluoren-9-yl)methanol (90 mg, 460 μmol). Workup and purification by FC (silica gel (10 g, 1.5 × 13 cm; p.e. (50 ml), p.e./AcOEt 9:1 (50 ml), 7:1 (40 ml), 5:1 (120 ml), 3:1 (80 ml), and 2:1 (60 ml)) led to 150 mg (67%) of **19**. Colourless foam. TLC (toluene/AcOEt 4:1): R_f 0.58. UV (CH_2Cl_2): 300(3.83), 285(sh, 4.28), 272(sh, 4.57), 266(4.61). ^{1}H-NMR ((D$_6$)DMSO): 8.35 (*s*, NH); 7.85–8.62(2*d*, 4 H of fm); 7.46, 7.45 (2*s*, H–C(2), H–C(8)); 7.42–6.98 (*m*, 4 H of fm, 45 H of Tr); 6.03 (*d*, *J* = 7.2, H–C(1')); 5.16 (*dd*, H–C(2')); 4.42 (*d*, CH_2O of fm); 4.24 (*t*, H–C(9) of fm); 3.92 (*m*, H–C(4')); 3.30–2.65 (*m*, CH_2O–C(3'), 2 H–C(5')); 2.45 (*d*, H–C(3')); 2.21 (*t*, CH_2COO); 1.45–1.14 (*m*, 3 CH_2). Anal. calc. for $C_{87}H_{75}N_5O_6$ (1286.6): C 81.22, H 5.88, N 5.44; found: C 80.90, H 5.87, N 5.47.

3'-O-{(11-[(1,4-Dioxopentyl)oxy]undecyl}adenosine (**20**). A soln. of **15** (6.1 g, 4.9 mmol) in 80% AcOH/H_2O (30 ml) was kept at 100° for 90 min, then evaporated, co-evaporated with H_2O (3 × 5 ml) and MeOH (3 × 5 ml), and purified by FC (silica gel (100 g), 5 × 13 cm; CH_2Cl_2 (200 ml), CH_2Cl_2/MeOH 95:5 (200 ml), 9:1 (600 ml)): 2.2 g (86%) of **20**. The resulting foam crystallized from EtOH/H_2O 1:1. Colourless crystals. M.p. 137°. TLC ($CHCl_3$/MeOH 9:1): R_f 0.38. UV (MeOH): 259(4.17). ^{1}H-NMR ((D$_6$)DMSO): 8.32, 8.11 (2*s*, H–C(2), H–C(8)); 7.30 (*s*, NH_2); 5.85 (*d*, *J* = 6.2, H–C(1')); 5.42–5.39 (*m*, OH–C(2'), O–H(5')); (*dd*, H–C(2')); 4.05–3.80 (*m*, H–C(3'), H–C(4'), CH_2Olev); 3.71–3.43 (*m*, CH_2O–C(3'), 2 H–C(5')); 2.67 (*t*, CH_2CO); 2.40 (*t*, CH_2CO); 2.09 (*s*, Me); 1.52–1.25 (*m*, 9 CH_2). Anal. calc. for $C_{26}H_{41}N_5O_7$ (535.6): C 58.30, H 7.72, N 13.07; found: C 58.16, H 7.69, N 12.73.

3'-O-{12-[(1,4-Dioxopentyl)oxy]dodecyl}adenosine (**21**). As described for **20**, with **16** (0.55 g, 0.43 mmol) and 80% AcOH/H_2O (5 ml). FC (silica gel (15 g), 2.5 × 10 cm; CH_2Cl_2 (50 ml), CH_2Cl_2/MeOH 95:5 (100 ml), 9:1 (100 ml)) gave a foam which was crystallized from EtOH/H_2O 1:1 (2 ml): 0.16 g (67%) of **21**. Colourless crystals. M.p. 138°. TLC ($CHCl_3$/MeOH 9:1): R_f 0.46. UV (MeOH): 259(4.17). ^{1}H-NMR ((D$_6$)DMSO): 8.34, 8.11 (2*s*, H–C(2), H–C(8)); 7.34 (*s*, NH_2); 5.85 (*d*, *J* = 6.3, H–C(1')); 5.41–5.38 (*m*, OH–C(2'), OH–C(5')); 4.72 (*dd*, H–C(2')); 4.05–3.93 (*m*, H–C(3'), H–C(4'), CH_2Olev); 3.65–3.45 (*m*, CH_2O–C(3'), 2 H–C(5')); 2.65 (*t*, CH_2COO); 2.43 (*t*, CH_2CO); 2.08 (*s*, Me); 1.52–1.24 (*m*, 10 CH_2). Anal. calc. for $C_{27}H_{43}N_5O_7$ (549.8): C 58.99, H 7.88, N 12.74; found: C 59.00, H 7.70, N 12.83.

3'-O-{2-{2-[(1,4-Dioxopentyl)oxy]ethoxy}ethyl}adenosine (**22**). As described for **20**, with **17** (11.0 g, 9.2 mmol) and 80% AcOH/H_2O (50 ml). FC (silica gel (200 g), 5.5 × 19 cm; CH_2Cl_2 (500 ml), CH_2Cl_2/MeOH 95:5 (500 ml), 9:1 (1500 ml), 4:1 (300 ml)) yielded 3.7 g (88%) of **22**. Colourless foam. TLC ($CHCl_3$/MeOH 9:1): R_f 0.50. UV (MeOH): 258(4.17). ^{1}H-NMR ((D$_6$)DMSO): 8.33, 8.12 (2*s*, H–C(2), H–C(8)); 7.35 (*s*, NH_2); 5.86 (*d*, *J* = 6.3, H–C(1')); 5.42 (*m*, OH–C(5')); 5.39 (*d*, OH–C(2')); 4.73 (*dd*, H–C(2')); 4.12–3.98 (*m*, H–C(3'), H–C(4'), CH_2Olev); 3.84–3.55 (*m*, 2 CH_2O, CH_2O–C(3'), 2 H–C(5')); 2.68 (*t*, CH_2COO); 2.45 (*t*, CH_2CO); 2.08 (*s*, Me). Anal. calc. for $C_{19}H_{27}N_5O_8$ (453.6): C 50.33, H 6.00, N 15.44; found: C 50.09, H 6.03, N 15.06.

3'-O-[5-(2-Cyanoethoxycarbonyl)pentyl]adenosine (**23**). As described for **20**, with **18** (170 mg, 0.15 mmol) and 80% AcOH/H_2O (5 ml). Purification by FC (silica gel (5 g), 1 × 16 cm; CH_2Cl_2 (50 ml), CH_2Cl_2/MeOH 98:2 (50 ml), 96:4 (100 ml), 92:8 (50 ml)) gave 41 mg (64%) of **23**. Colourless foam. TLC ($CHCl_3$/MeOH 9:1): R_f 0.41. UV (MeOH): 258(4.19). ^{1}H-NMR ((D$_6$)DMSO): 8.34, 8.12 (2*s*, H–C(2), H–C(8)); 7.35 (br. *s*, NH_2); 5.86 (*d*, *J* = 6.3, H–C(1')); 5.50–5.39 (*m*, OH–C(5'), OH–C(2')); 4.75 (*dd*, H–C(2')); 4.22 (*m*, CH_2OCO); 4.02 (*m*, H–C(4')); 3.91 (*m*, H–C(3')); 3.71–3.42 (*m*, CH_2O–C(3'), 2 H–C(5')); 2.87 (*t*, CH_2CN); 2.35 (*t*, CH_2COO); 1.60–1.33 (*m*, 3 CH_2). Anal. calc. for $C_{19}H_{26}N_6O_6$ (434.6): C 52.53, H 6.03, N 19.34; found: C 52.31, H 6.15, N 18.88.

3'-O-{5-[(9H-Fluoren-9-ylmethoxy)carbonyl]pentyl}adenosine (**24**). As described for **20**, with **19** (2.9 g, 2.3 mmol) and 80% AcOH/H_2O (20 ml). FC (silica gel (60 g), 4 × 16 cm; CH_2Cl_2 (200 ml), CH_2Cl_2/MeOH 95:5 (200 ml), 9:1 (400 ml)) gave 0.99 g (78%) of **24** as a foam which crystallized from H_2O/EtOH 2:1. Colourless crystals. M.p. 147°. TLC ($CHCl_3$/MeOH 9:1): R_f 0.50. UV (MeOH): 299(3.77), 288(3.72), 263(4.52), 257 (sh, 4.50). ^{1}H-NMR ((D$_6$)DMSO): 8.35, 8.12 (2*s*, H–C(2), H–C(8)); 7.88–7.62, 7.42–7.29 (*m*, 8 H of fm, NH_2); 5.86 (*d*, *J* = 6.2, H–C(1')); 5.50–5.41 (*m*, OH–C(5'), OH–C(2')); 4.75 (*dd*, H–C(2')); 4.45 (*d*, CH_2O of fm); 4.28 (*t*, H–C(9) of fm); 4.02 (*m*, H–C(4')); 3.91 (*m*, H–C(3')); 3.70–3.40 (*m*, CH_2O–C(3'), 2 H–C(5')); 2.30 (*t*,

CH_2COO); 1.55–1.20 (*m*, 3 CH_2). Anal. calc. for $C_{30}H_{33}N_5O_6$ (559.6): C 64.39, H 5.94, N 12.51; found: C 63.90, H 5.94, N 12.73.

3′-O-{11-[(1,4-Dioxopentyl)oxy]undecyl}-N⁶-[2-(4-nitrophenyl)ethoxycarbonyl]adenosine (**25**). A mixture of **20** (1.6 g, 3.0 mmol), hexamethyldisilazane (7.5 ml), abs. dioxane (7.5 ml), and a catal. amount of $(NH_4)_2SO_4$ was refluxed for 3 h and then evaporated. The residue was dissolved in toluene (10 ml) and the soln. filtered and evaporated. Then 1-methyl-3-[2-(4-nitrophenyl)ethoxycarbonyl]-1*H*-imidazolium chloride [16] (1.9 g, 6.0 mmol) and abs. CH_2Cl_2 (30 ml) were added. The mixture was kept overnight, filtered, and the filtrate evaporated. To the residue, 80% AcOH/H_2O (20 ml) was added. The soln. was stirred for 1 h, then evaporated, and co-evaoprated with H_2O (3 × 5 ml) and MeOH (3 × 5 ml) and the residue purified by FC (silica gel (50 g), 4 × 20 cm; CH_2Cl_2 (200 ml), CH_2Cl_2/MeOH 99:1 (200 ml), 98:2 (200 ml), 95:5 (200 ml)): 1.7 g (79%) of **25**. Colourless foam. TLC ($CHCl_3$/MeOH 9:1): R_f 0.62. UV (MeOH): 267(4.43). ^{1}H-NMR ((D$_6$)DMSO): 10.60 (*s*, NH); 8.67, 8.61 (2*s*, H–C(2), H–C(8)); 8.15 (*d*, 2 H *o* to NO_2); 7.61 (*d*, 2 H *m* to NO_2); 5.97 (*d*, *J* = 5.7, H–C(1′)); 5.50 (*m*, OH–C(2′)); 5.16 (*t*, OH–C(5′)); 4.75 (*dd*, H–C(2′)); 4.39 (*t*, CH_2CH_2O of npeoc); 4.05–3.94 (*m*, H–C(3′), H–C(4′), CH_2Olev); 3.70–3.40 (*m*, CH_2O–C(3′), 2 H–C(5′)); 3.11 (*t*, CH_2CH_2O of npoec); 2.67 (*t*, CH_2COO); 2.40 (*t*, CH_2CO); 2.08 (*s*, Me); 1.52–1.24 (*m*, 9 CH_2). Anal. calc. for $C_{35}H_{48}N_6O_{11}$ (728.8): C 57.68, H 6.64, N 11.53; found: C 57.35, H 6.70, N 11.39.

3′-O-{2-{2-[(1,4-Dioxopentyl)oxy]ethoxy}ethyl}-N⁶-[2-(4-nitrophenyl)ethoxycarbonyl]adenosine (**26**). As described for **25**, with **22** (0.51 g, 1.1 mmol), hexamethyldisilazane (3 ml), abs. dioxane (3 ml), a catal. amount of $(NH_4)_2SO_4$, toluene (10 ml), 1-methyl-3-[2-(4-nitrophenyl)ethoxycarbonyl]-1*H*-imidazolium chloride [16] (0.72 g, 2.3 mmol), abs. CH_2Cl_2 (20 ml), and 80% AcOH/H_2O (5 ml). FC (silica gel (10 g), 2.5 × 7 cm; CH_2Cl_2 (50 ml), CH_2Cl_2/MeOH 99:1 (50 ml), 98:2 (50 ml), 97:3 (50 ml), 96:4 (50 ml)) gave 0.44 g (60%) of **26**. Colourless foam. TLC ($CHCl_3$/MeOH 95:5): R_f 0.28. UV (MeOH): 267(4.45). ^{1}H-NMR ((D$_6$)DMSO): (*s*, NH); 8.67, 8.62 (2*s*, H–C(2), H–C(8)); 8.15 (*d*, 2 H *o* to NO_2); 7.50 (*d*, 2 H *m* to NO_2); 5.99 (*d*, *J* = 5.7, H–C(1′)); 5.47 (*d*, OH–C(2′)); 5.18 (*t*, OH–C(5′)); 4.75 (*dd*, H–C(2′)); 4.39 (*t*, CH_2CH_2O of npeoc); 4.05–4.13 (*m*, H–C(3′), H–C(4′), CH_2Olev); 3.80–3.58 (*m*, 2 CH_2O, CH_2O–C(3′), 2 H–C(5′)); 3.11 (*t*, CH_2CH_2O of npeoc); 2.67 (*t*, CH_2COO); 2.46 (*t*, CH_2CO); 2.07 (*s*, Me). Anal. calc. for $C_{28}H_{34}N_6O_{12}$ (646.6): C 52.01, H 5.53, N 13.00; found: C 51.80, H 5.43, N 12.62.

3′-O-[5-(2-Cyanoethoxycarbonyl)pentyl]-N⁶-[2-(4-nitrophenyl)ethoxycarbonyl]adenosine (**27**). As described for **25** with **23** (0.40 g, 0.94 mmol), hexamethyldisilazane (2 ml), abs. dioxane (2 ml), a catal. amount of $(NH_4)_2SO_4$, 1-methyl-3-[(4-nitrophenyl)ethoxycarbonyl]-1*H*-imidazolium chloride [16] (0.58 g, 1.9 mmol), abs. CH_2Cl_2 (15 ml), and 80% AcOH/H_2O (5 ml). FC (silica gel (10 g), 2.5 × 8 cm; CH_2Cl_2 (100 ml), CH_2Cl_2/MeOH 99:1 (100 ml), 98:2 (100 ml), 97:3 (50 ml)) led to 0.4 g (70%) of **27**. Colourless foam. TLC ($CHCl_3$/MeOH 95:5): R_f 0.31. UV (MeOH): 267(4.43). ^{1}H-NMR ((D$_6$)DMSO): 10.61 (*s*, NH); 8.67, 8.61 (2*s*, H–C(2), H–C(8)); 8.15 (*d*, 2 H *o* to NO_2); 7.50 (*d*, 2 H *m* to NO_2); 5.97 (*d*, *J* = 5.7, H–C(1′)); 5.50 (*d*, OH–C(2′)); 5.17 (*t*, OH–C(5′)); 4.75 (*dd*, H–C(2′)); 4.38 (*t*, CH_2CH_2O of npeoc); 4.17 (*t*, CH_2OCO); 4.02 (*m*, H–C(4′)); 3.95 (*m*, H–C(3′)); 3.68–3.45 (*m*, CH_2O–C(3′), 2 H–C(5′)); 3.10 (*t*, CH_2CH_2O of npeoc); 2.86 (*t*, CH_2CN); 2.35 (*t*, CH_2COO); 1.60–1.35 (*m*, 3 CH_2). Anal. calc. for $C_{28}H_{33}N_7O_{10}$ (627.6): C 53.59, H 5.30, N 15.62; found: C 52.94, H 5.31, N 14.82.

3′-O-{5-[(9H-Fluoren-9-ylmethoxy)carbonyl]pentyl}-N⁶-[2-(4-nitrophenyl)ethoxycarbonyl]adenosine (**28**). As described for **27**, with **24** (0.64 g, 1.2 mmol), hexamethyldisilazane (6 ml), abs. dioxane (6 ml), a catal. amount of $(NH_4)_2SO_4$, toluene (10 ml), 1-methyl-3-[(4-nitrophenyl)ethoxycarbonyl]-1*H*-imidazolium chloride [16] (0.72 g, 2.3 mmol), abs. CH_2Cl_2 (10 ml), and 80% AcOH/H_2O (10 ml). FC (silica gel (20 g), 3 × 9 cm; CH_2Cl_2 (200 ml), CH_2Cl_2/MeOH 99:1 (200 ml), 98:2 (200 ml)) gave 0.57 g (66%) of **28**. Colourless foam. TLC ($CHCl_3$/MeOH 95:5): R_f 0.35. UV (MeOH): 298(3.84), 286(sh, 3.98), 265(4.52). ^{1}H-NMR ((D$_6$)DMSO): 10.62 (*s*, NH); 8.68, 8.62 (2*s*, H–C(2), H–C(8)); 8.17 (*d*, 2 H *o* to NO_2); 7.88 (*d*, 2 H of fm); 7.65–7.55 (*m*, 2 H of fm, 2 H *m* to NO_2); 7.42–7.28 (*m*, 4 H of fm); 5.96 (*d*, *J* = 5.7, H–C(1′)); 5.49 (*d*, OH–C(2′)); 5.17 (*t*, OH–C(5′)); 4.73 (*dd*, H–C(2′)); 4.47–4.36 (*m*, CH_2O of fm, CH_2CH_2O of npeoc); 4.25 (*t*, H–C(9) of fm); 4.08 (*m*, H–C(4′)); 3.97 (*m*, H–C(3′)); 3.70–3.40 (*m*, CH_2O–C(3′), 2 H–C(5′)); 3.02 (*t*, CH_2CH_2O of npeoc); 2.21 (*t*, CH_2COO); 1.50–1.15 (*m*, 3 CH_2). Anal. calc. for $C_{39}H_{40}N_6O_{10}$ (752.8): C 62.23, H 5.36, N 11.16; found: 62.00, H 5.44, N 10.82.

3′-O-{11-[(1,4-Dioxopentyl)oxy]undecyl}-5′-O-[(4-methoxyphenyl)diphenylmethyl]-N⁶-[2-(4-nitrophenyl)-ethoxy-carbonyl]adenosine (**29**). After co-evaporation with dry pyridine (3 × 5 ml), **25** (1.8 g, 2.5 mmol) and MeOTrCl (1.9 g, 6.2 mmol) were stirred in dry pyridine (20 ml) at r.t. for 1 d. Then the mixture was diluted with AcOEt (100 ml) and washed with sat. $NaHCO_3$ soln. (3 × 100 ml). The aq. phase was re-extracted with AcOEt (3 × 50 ml), the combined org. layer dried (Na_2SO_4), evaporated, and co-evaporated with toluene (3 × 10 ml), and the crude product purified by FC (silica gel (50 g), 4 × 12 cm; toluene/AcOEt 1:1 (400 ml), toluene/AcOEt/MeOH 50:50:1 (400 ml), 25:25:1 (200 ml)): 1.8 g (74%) of **29**. Colourless foam. TLC (toluene/AcOEt/MeOH 5:4:1): R_f

0.58. UV (MeOH): 267(4.51), 233(4.37). ^{1}H-NMR ((D$_6$)DMSO): 10.61 (*s*, NH); 8.57, 8.55 (2*s*, H–C(2), H–C(8)); 8.16 (*d*, 2 H *o* to NO$_2$); 7.60 (*d*, 2 H *m* to NO$_2$); 7.34–7.17 (*m*, 12 H of MeOTr); 6.82 (*d*, 2 H *o* to MeO); 5.99 (*d*, *J* = 4.2, H–C(1')); 5.55 (*d*, OH–C(2')); 4.90 (*dd*, H–C(2')); 4.38 (*t*, CH$_2$C*H*$_2$O of npeoc); 4.20 (*m*, H–C(3')); 4.12 (*m*, H–C(4')); 3.95 (*t*, C*H*$_2$Olev); 3.33 (*s*, MeO); 3.65–3.15 (*m*, CH$_2$O–C(3'), 2 H–C(5')); 3.09 (*t*, C*H*$_2$CH$_2$O of npeoc); 2.66 (*t*, CH$_2$COO); 2.41 (*t*, CH$_2$CO); 2.07 (*s*, Me); 1.52–1.21 (*m*, 9 CH$_2$). Anal. calc. for C$_{55}$H$_{64}$N$_6$O$_{12}$ (1001.2): C 65.98, H 6.44, N 8.39; found: C 65.49, H 6.43, N 8.26.

*3'-O-{2-{2-[(1,4-Dioxopentyl)oxy]ethoxy}ethyl}-5'-O-[(4-methoxyphenyl)diphenylmethyl]-*N^6*-[2-(4-nitrophenyl)ethoxycarbonyl]adenosine* (**30**). As described for **29**, with **26** (1.65 g, 2.6 mmol). MeOTrCl (0.96 g, 3.1 mmol), and dry pyridine (10 ml). FC (silica gel (35 g), 3 × 14 cm; CH$_2$Cl$_2$ (300 ml), CH$_2$Cl$_2$/MeOH 99:1 (300 ml), 98:2 (300 ml), 97:3 (150 ml)) gave 1.7 g (73%) of **30**. Colourless foam. TLC (CH$_2$Cl$_2$/MeOH 95:5): R_f 0.26. UV (MeOH): 267(4.49), 233(4.35). ^{1}H-NMR ((D$_6$)DMSO): 10.61 (*s*, NH); 8.56, 8.54 (2*s*, H–C(2), H–C(8)); 8.15 (*d*, 2 H *o* to NO$_2$); 7.60 (*d*, 2 H *m* to NO$_2$); 7.35–7.17 (*m*, 12 H of MeOTr); 6.82 (*d*, 2 H *o* to MeO); 6.00 (*d*, *J* = 4.6, H–C(1')); 5.55 (*d*, OH–C(2')); 4.94 (*dd*, H–C(2')); 4.48 (*t*, CH$_2$C*H*$_2$O of npeoc); 4.25 (*m*, H–C(3')); 4.15 (*m*, H–C(4')); 4.05 (*t*, C*H*$_2$Olev); 3.70 (*s*, MeO); 3.80–3.45 (*m*, 2 CH$_2$O, CH$_2$O–C(3')); 3.27–3.22 (*m*, 2 H–C(5')); 3.08 (*t*, C*H*$_2$CH$_2$O of npeoc); 2.66 (*t*, CH$_2$COO); 2.40 (*t*, CH$_2$CO); 2.06 (*s*, Me). Anal. calc. for C$_{48}$H$_{50}$N$_6$O$_{13}$ (919.0): C 62.74, H 5.48, N 9.15; found: C 62.64, H 5.72, N 9.12.

*3'-O-[5-(2-Cyanoethoxycarbonyl)pentyl]-5'-O-[(4-methoxyphenyl)diphenylmethyl]-*N^6*-[2-(4-nitrophenyl)-ethoxycarbonyl]adenosine* (**31**). As described for **29**, with **27** (165 mg, 0.26 mmol), MeOTrCl (160 mg, 0.52 mmol), and dry pyridine (5 ml). FC (silica gel (10 g), 2.5 × 8 cm; CH$_2$Cl$_2$ (100 ml), CH$_2$Cl$_2$/MeOH 99:1 (100 ml), 98:2 (100 ml)) gave 160 mg (67%) of **31**. Colourless foam. TLC (CH$_2$Cl$_2$/MeOH 95:5): R_f 0.50. UV (MeOH): 267(4.47), 233(4.32). ^{1}H-NMR ((D$_6$)DMSO): 10.62 (*s*, NH); 8.57, 8.51 (2*s*, H–C(2), H–C(8)); 8.15 (*d*, 2 H *o* to NO$_2$); 7.84 (*d*, 2 H *m* to NO$_2$); 7.35–7.17 (*m*, 12 H of MeOTr); 6.83 (*d*, 2 H *o* to MeO); 5.99 (*d*, *J* = 4.4, H–C(1')); 5.55 (*d*, OH–C(2')); 4.90 (*dd*, H–C(2')); 4.37 (*t*, CH$_2$C*H*$_2$O of npeoc); 4.18 (*t*, CH$_2$OCO); 4.15–4.10 (*m*, H–C(4'), H–C(3')); 3.71 (*s*, MeO); 3.75–3.20 (*m*, CH$_2$O–C(3'), 2 H–C(5')); 3.10 (*t*, C*H*$_2$CO of npeoc); 2.88 (*t*, CH$_2$CN); 2.31 (*t*, CH$_2$COO); 1.55–1.12 (*m*, 3 CH$_2$). Anal. calc. for C$_{48}$H$_{49}$N$_7$O$_{11}$ · H$_2$O (918.0): C 62.80, H 5.60, N 10.68; found: C 63.02, H 5.56, N 10.45.

*3'-O-{5-[(9H-Fluoren-9-ylmethoxy)carbonyl]pentyl}-5'-O-[(4-methoxyphenyl)diphenylmethyl]-*N^6*-[2-(4-nitrophenyl)ethoxycarbonyl]adenosine* (**32**). As described for **29**, with **28** (130 mg, 0.18 mmol), MeOTrCl (65 mg, 0.21 mmol), and dry pyridine (2 ml). The soln. was stirred overnight, then more MeOTrCl (27 mg, 0.09 mmol) was added. After 5 h, the mixture was worked up and the residue purified by FC (silica gel (5 g), 1.5 × 7 cm; CH$_2$Cl$_2$ (50 ml), CH$_2$Cl$_2$/MeOH 99:1 (50 ml), 98:2 (50 ml)): 160 mg (89%) of **32**. Colourless foam. TLC (CH$_2$Cl$_2$/MeOH 95:5): R_f 0.52. UV (CH$_2$Cl$_2$): 299(4.02), 288 (sh, 4.15), 271 (sh, 4.61), 266(4.68), 232(4.27). ^{1}H-NMR ((D$_6$)DMSO): 10.63 (*s*, NH); 8.59, 8.56 (2*s*, H–C(2), H–C(8)); 8.15 (*d*, 2 H *o* to NO$_2$); 7.85 (*d*, 2 H of fm); 7.65–7.57 (*m*, 2 H of fm, 2 H *m* to NO$_2$); 7.42–7.17 (*m*, 4 H of fm, 12 H of MeOTr); 6.80 (*d*, 2 H *o* to MeO); 6.00 (*t*, 4.3, H–C(1')); 5.58 (*d*, OH–C(2')); 4.92 (*dd*, H–C(2')); 4.45–4.35 (*m*, CH$_2$O of fm CH$_2$C*H*$_2$O of npeoc); 4.29–4.12 (*m*, H–C(9) of fm, H–C(4'), H–C(3')); 3.68 (*s*, MeO); 3.62–3.18 (*m*, CH$_2$O–C(3'), 2 H–C(5')); 3.09 (*t*, C*H*$_2$CH$_2$O of npeoc); 2.23 (*t*, CH$_2$COO); 1.50–1.10 (*m*, 3 CH$_2$). Anal. calc. for C$_{59}$H$_{56}$N$_6$O$_{11}$ (1025.1): C 69.13, H 5.51, N 8.20; found: 69.08, H 5.73, N 8.06.

*3'-O-{11-[(1,4-Dioxopentyl)oxy]undecyl}-5'-O-[(4-methoxyphenyl)diphenylmethyl]-*N^6*,2'-O-bis[2-(4-nitrophenyl)ethoxycarbonyl]adenosine* (**33**). A soln. of **29** (79 mg, 79 µmol), DMAP (7 mg, 57 µmol), and 1-methyl-3-[(4-nitrophenyl)ethoxycarbonyl]-1*H*-imidazolium chloride [16] (50 mg, 0.16 mmol) in abs. CH$_2$Cl$_2$ (2 ml) was kept at r.t. overnight, then diluted with CHCl$_3$ (25 ml), and washed with sat. NaCl soln. (3 × 25 ml). The aq. phase was re-extracted with CHCl$_3$ (3 × 25 ml) and the org. layer dried (Na$_2$SO$_4$) and evaporated. Purification by FC (silica gel (4 g), 1.5 × 12 cm; CH$_2$Cl$_2$ (25 ml), CH$_2$Cl$_2$/MeOH 99:1 (25 ml), 98:2 (50 ml)) gave 84 mg (89%) of **33**. Colourless foam. TLC (CH$_2$Cl$_2$/MeOH 95:5): R_f 0.63. UV (MeOH): 267(4.56), 234(4.35). ^{1}H-NMR ((D$_6$)DMSO): 10.66 (*s*, NH); 8.60, 8.59 (2*s*, H–C(2), H–C(8)); 8.15 (*d*, 2 H *o* to MeO); 6.27 (*d*, *J* = 2.9, H–C(1')); 5.92 (*dd*, H–C(2')); 4.70(2')); 4.70 (*m*, H–C(3')); 4.35 (*t*, 2 CH$_2$C*H*$_2$O of npeoc); 4.05 (*m*, H–C(4')); 3.93 (*t*, C*H*$_2$Olev); 3.70 (*s*, MeO); 3.40 (*m*, CH$_2$O–C(3')); 3.07 (*m*, 2 H–C(5'), 2 C*H*$_2$CH$_2$O of npeoc); 2.66 (*t*, CH$_2$COO); 2.40 (*t*, CH$_2$CO); 2.08 (*s*, Me); 1.53–1.13 (*m*, 9 CH$_2$). Anal. calc. for C$_{64}$H$_{71}$N$_7$O$_{16}$ (1194.3): C 64.36, H 5.99, N 8.21; found: C 63.78, H 6.00, N 8.12.

*3'-O-{2-{2-[(1,4-Dioxopentyl)oxy]ethoxy}ethyl}-5'-O-[(4-methoxyphenyl)diphenylmethyl]-*N^6*,2'-O-bis[2-(4-nitrophenyl)ethoxycarbonyl]adenosine* (**34**). As described for **33**, with **30** (250 mg, 270 µmol), DMAP (16 mg, 130 µmol), 1-methyl-3-[(4-nitrophenyl)ethoxycarbonyl]-1*H*-imidazolium chloride [12] (170 mg, 0.28 mmol), and abs. CH$_2$Cl$_2$ (10 ml). After FC (silica gel (10 g), 2.5 × 7 cm; CH$_2$Cl$_2$ (100 ml), CH$_2$Cl$_2$/MeOH 99:1 (100 ml), 98:2 (100 ml)), 275 mg (91%) of **34** were obtained. Colourless foam. TLC (CH$_2$Cl$_2$/MeOH 95:5): R_f 0.47. UV (CH$_2$Cl$_2$): 266(4.57), 236(4.36). ^{1}H-NMR ((D$_6$)DMSO): 10.66 (*s*, NH); 8.58, 8.57 (2*s*, H–C(2), H–C(8)); 8.14

(*d*, 4 H *o* to NO_2); 7.65–7.53 (*m*, 4 H *m* to NO_2); 7.30–7.15 (*m*, 12 H of MeOTr); 6.80 (*d*, 2 H *o* to MeO); 6.28 (*d*, *J* = 3.2, H–C(1')); 5.92 (*dd*, H–C(2')); 4.72 (*t*, H–C(3')); 4.40 (*t*, 2 CH_2CH_2O of npeoc); 4.11 (*m*, H–C(4')); 3.98 (*t*, CH_2Olev); 3.70 (*s*, MeO); 3.60–3.40 (*m*, 2 CH_2O, CH_2O–C(3')); 3.31–3.05 (*m*, 2 H–C(5'), 2 CH_2CH_2O of npeoc); 2.75 (*t*, CH_2COO); 2.38 (*t*, CH_2CO); 2.06 (*s*, Me). Anal. calc. for $C_{57}H_{57}N_7O_{17}$ (1112.1): C 61.56, H 5.17, N 8.82; found: C 61.58, H 5.18, N 8.72.

3'-O-[5-(2-Cyanoethoxycarbonyl)pentyl]-5'-O-[(4-methoxyphenyl)diphenylmethyl]-N⁶,2'-O-bis[2-(4-nitrophenyl)ethoxycarbonyl]adenosine (**35**). As described for **33**, with **31** (110 mg, 120 μmol), DMAP (11 mg, 90 μmol), 1-methyl-3-[(4-nitrophenyl)ethoxycarbonyl-1*H*-imidazolium chloride [16] (120 mg, 0.37 mmol), and abs. CH_2Cl_2 (5 ml). Purification by FC (silica gel (5 g), 1.5 × 10 cm; toluene/AcOEt 1:1 (100 ml), toluene/AcOEt/MeOH 25:25:1 (50 ml)) gave 110 mg (88%) of **35**. Colourless foam. TLC (CH_2Cl_2/MeOH 95:5): R_f 0.68. UV (CH_2Cl_2): 266(4.60), 237(4.38). ^{1}H-NMR ((D_6)DMSO): 10.66 (*s*, NH); 8.59, 8.58 (2*s*, H–C(2), H–C(8)); 8.14 (*d*, 4 H *o* to NO_2); 7.62–7.53 (*m*, 4 H *m* to NO_2); 7.29–7.11 (*m*, 12 H of MeOTr); 6.82 (*d*, 2 H *o* to MeO); 6.27 (*d*, *J* = 2.9, H–C(1')); 5.93 (*dd*, H–C(2')); 4.71 (*t*, H–C(3')); 4.38 (*t*, 2 CH_2CH_2O of npeoc); 4.17 (*t*, CH_2OCO); 4.05 (*m*, H–C(4')); 3.70 (*s*, MeO); 3.75–3.30 (*m*, CH_2O–C(3'), 2 H–C(5')); 3.14–3.08 (*m*, 2 CH_2CH_2O of npeoc); 2.86 (*t*, CH_2CN); 2.24 (*t*, CH_2COO); 1.50–1.15 (*m*, 3 CH_2). Anal. calc. for $C_{57}H_{56}N_8O_{15}$ (1093.1): C 62.63, H 5.16, N 10.25; found: C 62.04, H 5.31, N 9.77.

3'-O-{5-[(9H-Fluoren-9-ylmethoxy)carbonyl]pentyl}-5'-O-[(4-methoxyphenyl)diphenylmethyl]-N⁶,2'-O-bis[2-(4-nitrophenyl)ethoxycarbonyl]adenosine (**36**). As described for **33**, with **32** (76 mg, 74 μmol), DMAP (6 mg, 49 μmol), 1-methyl-3-[(4-nitrophenyl)ethoxycarbonyl]-1*H*-imidazolium chloride [16] (100 mg, 0.32 mmol), and abs. CH_2Cl_2 (1 ml). After FC (silica gel (3 g, 1.5 × 6 cm; CH_2Cl_2 (50 ml), CH_2Cl_2/MeOH 99:1 (50 ml)): 82 mg (91% of **36** were obtained. Colourless foam. TLC (CH_2Cl_2/MeOH 95:5): R_f 0.66. UV (CH_2Cl_2): 299(sh, 4.17), 287 (sh, 4.37), 266(4.77), 232(sh, 4.45). ^{1}H-NMR ((D_6)DMSO): 10.62 (*s*, NH); 8.59, 8.58 (2*s*, H–C(2), H–C(8)); 8.15–8.09 (*m*, 4 H *o* to NO_2); 7.86–7.83 (*m*, 2 H of fm); 7.62–7.40 (*m*, 2 H of fm, 4 H *m* to NO_2); 7.37–7.11 (*m*, 4 H of fm, 12 H of MeOTr); 6.78 (*d*, 2 H *o* to MeO); 6.26 (*d*, *J* = 2.5, H–C(1')); 5.94 (*dd*, H–C(2')); 4.69 (*t*, H–C(3')); 4.39–4.35 (*m*, CH_2O of fm, 2 CH_2O of npeoc); 4.21 (*t*, H–C(9) of fm); 4.03 (*m*, H–C(4')); 3.67 (*s*, MeO); 3.55–3.25 (*m*, CH_2O–C(3'), 2 H–C(5')); 3.12–3.03 (*m*, 2 CH_2CH_2O of npeoc); 2.17 (*t*, CH_2COO); 1.45–1.02 (*m*, 3 CH_2). Anal. calc. for $C_{68}H_{63}N_7O_{15}$ (1218.3): C 67.04, H 5.21, N 8.05; found: C 66.61, H 5.27, N 8.13.

3'-O-{11-[(1,4-Dioxopentyl)oxy]undecyl}-N⁶,2'-O-bis[2-(4-nitrophenyl)ethoxycarbonyl]adenosine (**37**). A soln. of **33** (350 mg, 0.29 mmol) in MeOH/$CHCl_3$ 4:1 (5 ml) containing 2% of TsOH was stirred at r.t. for 15 min. The mixture was diluted with $CHCl_3$ (20 ml) and washed with sat. $NaHCO_3$ soln. (3 × 20 ml), the aq. phase re-extracted with $CHCl_3$ (3 × 20 ml), the org. layer dried (Na_2SO_4) and evaporated, and the residue purified by FC (silica gel (10 g), 2.5 × 8 cm; CH_2Cl_2 (100 ml), CH_2Cl_2/MeOH 99:1 (100 ml), 98:2 (100 ml)): 230 mg (85%) of **37**. Colourless foam. TLC (CH_2Cl_2/MeOH 95:5): R_f 0.36. UV (MeOH): 266(4.53). ^{1}H-NMR ((D_6)DMSO): 10.64 (*s*, NH); 8.66, 8.61 (2*s*, H–C(2), H–C(8)); 8.15 (*m*, 4 H *o* to NO_2); 7.62–7.50 (*m*, 4 H *m* to NO_2); 6.23 (*d*, *J* = 4.6, H–C(1')); 5.67 (*dd*, H–C(2')); 5.25 (*t*, OH–C(5')); 4.41–4.31 (*m*, H–C(3'), 2CH_2CH_2O of npeoc); 4.04 (*m*, H–C(4')); 3.94 (*t*, CH_2Olev); 3.75–3.30 (*m*, CH_2O–C(3'), 2 H–C(5')); 3.12–3.03 (*m*, 2 CH_2CH_2O of npeoc); 2.70 (*t*, CH_2COO); 2.44 (*t*, CH_2CO); 2.08 (*s*, Me); 1.52–1.19 (*m*, 9 CH_2). Anal. calc. for $C_{44}H_{55}N_7O_{15}$ (922.0): C 57.32, H 6.01, N 10.63; found: C 57.03, H 5.96, N 10.50.

3'-O-{2-{-[(1,4-Dioxopentyl)oxy}ethoxy}ethyl}-N⁶,2'-O-bis[2-(4-nitrophenyl)ethoxycarbonyl]adenosine (**38**). As described for **37**, with **34** (120 mg, 0.11 mmol) in MeOH/$CHCl_3$ 4:1 (1 ml) containing 2% of TsOH. FC (silica gel (3 g) 1.5 × 6 cm; CH_2Cl_2 (25 ml), CH_2Cl_2/MeOH 99:1 (25 ml), 98:2 (25 ml)) gave 77 mg (83%) of **38**. Colourless foam. TLC (CH_2Cl_2/MeOH 95:5): R_f 0.38. UV (CH_2Cl_2): 273(sh, 4.46), 267(4.50). ^{1}H-NMR ((D_6)DMSO): 10.66 (*s*, NH); 8.66, 8.61 (2*s*, H–C(2), H–C(8)); 8.15 (*m*, 4 H *o* to NO_2); 7.62–7.50 (*m*, 4 H *m* to NO_2); 6.23 (*d*, 4.7, H–C(1')); 5.68 (*dd*, H–C(2')); 5.29 (*t*, OH–C(5')); 4.42–4.32 (*m*, H–C(3'), CH_2CH_2O of npeoc); 4.09–4.03 (*m*, H–C(4'), CH_2Olev); 3.75–3.42 (*m*, 2 CH_2O, CH_2O–C(3'), 2 H–C(5')); 3.13–3.01 (*m*, 2 CH_2CH_2O of npeoc); 2.65 (*t*, CH_2COO); 2.43 (*t*, CH_2CO); 2.08 (*s*, Me). Anal. calc. for $C_{37}H_{41}N_7O_{16}$ (839.8): C 52.92, H 4.92, N 11.68; found: C 52.93, H 4.98, N 11.34.

3'-O-[5-(2-Cyanoethoxycarbonyl)pentyl]-N⁶,2'-O-bis[2-(4-nitrophenyl)ethoxycarbonyl]adenosine (**39**). As described for **37**, with **35** (110 mg, 0.10 mmol) and MeOH/$CHCl_3$ 4:1 (2 ml) containing 2% of TsOH. FC (silica gel (5 g), 1.5 × 7 cm; CH_2Cl_2 (50 ml), CH_2Cl_2/MeOH 99:1 (50 ml), 98:2 (50 ml), 97:3 (50 ml)) gave 64 mg (76%) of **39**. Colourless foam. TLC (CH_2Cl_2/MeOH 95:5): R_f 0.60. UV (MeOH): 267(4.55). ^{1}H-NMR ((D_6)DMSO): 10.64 (*s*, NH); 8.66, 8.62 (2*s*, H–C(2), H–C(8)); 8.15 (*m*, 4 H *o* to NO_2); 7.62–7.58 (*m*, 4 H *m* to NO_2); 6.22 (*d*, *J* = 4.6, H–C(1')); 5.73 (*dd*, H–C(2')); 5.25 (*t*, OH–C(5')); 4.40–4.31 (*m*, H–C(3'), 2 CH_2CH_2O of npeoc); 4.17 (*t*, CH_2OCO); 4.05 (*m*, H–C(4')); 3.75–3.38 (*m*, CH_2O–C(3'), 2 H–C(5')); 3.12–3.03 (*m*, 2 CH_2CH_2O of npeoc); 2.86 (*t*, CH_2CN); 2.30 (*t*, CH_2COO); 1.56–1.21 (*m*, 3 CH_2). Anal. calc. for $C_{37}H_{40}N_8O_{14} \cdot H_2O$ (838.8): C 52.98, H 5.05, N 13.36; found: C 53.10, H 4.97, N 12.80.

3'-O-{5-[(9H-Fluoren-9-ylmethoxy)carbonyl]pentyl}-N⁶,2'-O-bis[2-(4-nitrophenyl)ethoxycarbonyl]adenosine (**40**). As described for **37**, with **36** (95 mg, 78 μmol) in MeOH/$CHCl_3$ 4:1 (1 ml) containing 2% of TsOH. FC (silica gel (3 g), 1.5 × 6 cm; CH_2Cl_2 (25 ml), CH_2Cl_2/MeOH 99:1 (25 ml), 98:2 (25 ml), 97:3 (25 ml)) gave 69 mg (92%) of **40**. Colourless foam. TLC (CH_2Cl_2/MeOH 95:5): R_f 0.52. UV (CH_2Cl_2): 298(sh, 4.16), 288(sh, 4.34), 266(4.76). ^{1}H-NMR ((D_6)DMSO): 10.64 (*s*, NH); 8.66, 8.61 (2*s*, H–C(2), H–C(8)); 8.17–8.10 (*m*, 4 H *o* to NO_2); 7.87 (*d*, 2 H of fm); 7.64–7.30 (*m*, 6 H of fm, 4 H *m* to NO_2); 6.23 (*d*, J = 4.6, H–C(1')); 5.68 (*dd*, H–C(2')); 5.28 (*t*, OH–C(5')); 4.42–4.31 (*m*, H–C(3'), CH_2O of fm, 2 CH_2CH_2O of npeoc); 4.23 (*t*, H–C(9) of fm); 4.02 (*m*, H–C(4')); 3.78–3.30 (*m*, CH_2O–C(3'), 2 H–C(5')); 3.12–3.01 (*m*, 2 CH_2CH_2O of npeoc); 2.25 (*t*, CH_2COO); 1.45–1.10 (*m*, 3 CH_2). Anal. calc. for $C_{48}H_{47}N_7O_{14} \cdot H_2O$ (964.0): C 59.80, H 5.12, N 10.17; found: C 60.01, H 5.04, N 10.08.

3'-O-(11-Hydroxyundecyl)-5'-O-[(4-methoxyphenyl)diphenylmethyl]-N⁶,2'-O-bis[2-(4-nitrophenyl)ethoxycarbonyl]adenosine (**41**). At r.t., **33** (0.11 g, 94 μmol) was treated with 0.5M hydrazine hydrate soln. in pyridine/AcOH 4:1 (2 ml) for 4 min. Then acetone (2 ml) was added, the soln. evaporated and co-evaporated with toluene (3 × 5 ml), the residue dissolved in $CHCl_3$ (50 ml), and the soln. washed with sat. NaCl soln. (3 × 50 ml). The aq. phase was re-extracted with $CHCl_3$ (3 × 50 ml), the org. layer dried (Na_2SO_4) and evaporated, and the residue purified by FC (silica gel (5 g), 1.5 × 10 cm; CH_2Cl_2 (50 ml), CH_2Cl_2/MeOH 99:1 (50 ml), 98:2 (50 ml)): 98 mg (94%) of **41**. Colourless foam. TLC (CH_2Cl_2/MeOH 95:5): R_f 0.50. UV (MeOH): 266(4.57), 234(4.36). ^{1}H-NMR ((D_6)DMSO): 10.67 (*s*, NH); 8.60, 8.59 (2*s*, H–C(2), H–C(8)); 8.15 (*d*, 4 H *o* to NO_2); 7.61–7.51 (*m*, 4 H *m* to NO_2); 7.30–7.12 (*m*, 12 H of MeOTr); 6.80 (*d*, 2 H *o* to MeO); 6.27 (*d*, J = 2.8, H–C(1')); 5.95 (*dd*, H–C(2')); 4.72 (*m*, H–C(3')); 4.40–4.34 (*m*, 2 CH_2CH_2O of npeoc, OH); 4.05 (*m*, H–C(4')); 3.70 (*s*, MeO); 3.40 (*m*, CH_2O–C(3'), CH_2OH); 3.10 (*m*, 2 H–C(5'), 2 CH_2CH_2O of npeoc); 1.36–1.13 (*m*, 9 CH_2). Anal. calc. for $C_{59}H_{65}N_7O_{14} \cdot H_2O$ (1114.2): C 63.60, H 6.06, N 8.80; found: C 63.58, H 5.94, N 8.75.

3'-Deoxy-5'-O-[(4-methoxyphenyl)diphenylmethyl]-N⁶-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'{O^P-[2-(4-nitrophenyl)ethyl]} → 5'}-3'-deoxy-N⁶-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'-{O^P-[2-(4-nitrophenyl)ethyl]} → 5'}-3'-O-{11-[(1,4-dioxopentyl)oxy]undecyl}-N⁶,2'-O-bis[2-(4-nitrophenyl)ethoxycarbonyl]adenosine (**42**). A soln. of **37** (74 mg, 80 μmol), 3'-deoxy-5'-*O*-[(4-methoxyphenyl)diphenylmethyl]-*N*⁶-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'-{*O*^P-[2-(4-nitrophenyl)ethyl]} → 5'}-3'-deoxy-*N*⁶-[2-(4-nitrophenyl)ethoxycarbonyl]adenosine 2'-[2-(4-nitrophenyl)ethyl *N,N*-diisopropylphosphoramidite] (**1**) [15] (240 mg, 0.14 mmol), and 1*H*-tetrazole (28 mg, 0.40 mmol) in abs. MeCN (7 ml) was stirred under N_2 at r.t. for 4 h. Then it was oxidized with I_2 (500 mg) in pyridine (3 ml), CH_2Cl_2 (1 ml), and H_2O (1 ml) until no colour change was detected. The mixture was stirred for 15 min, diluted with $CHCl_3$ (50 ml), and washed with sat. $Na_2S_2O_3$/NaCl soln. (3 × 50 ml). The aq. phase was re-extracted with $CHCl_3$ (3 × 50 ml), the combined org. layer dried (Na_2SO_4), evaporated, and co-evaporated with toluene (3 × 10 ml), and the residue purified by FC (silica gel (10 g), 2.5 × 8 cm; CH_2Cl_2 (100 ml), CH_2Cl_2/MeOH 99:1 (100 ml), 98:2 (100 ml), 97:3 (100 ml), 96:4 (100 ml)): 190 mg (93%) of **42**. Colourless foam. TLC (CH_2Cl_2/MeOH 95:5): R_f 0.44. UV (CH_2Cl_2): 267(5.00). ^{1}H-NMR ($CDCl_3$): 8.90–7.98 (*m*, 3 H–C(2), 3 H–C(8), 3 NH, 12 H *o* to NO_2); 7.41–7.11 (*m*, 12 H *m* to NO_2, 12 H of MeOTr); 6.77 (*d*, 2 H *o* MeO); 6.14–5.95 (*m*, 3 H–C(1')); 5.75–5.25 (*m*, 3 H–C(2')); 4.55–4.10 (*m*, 2 CH_2CH_2O of npe, H–C(3'), 3 H–C(4'), 4 CH_2CH_2O of npeoc, 4 H–C(5')); 4.04 (*t*, CH_2Olev); 3.73 (*s*, MeO); 3.50–3.25 (*m*, CH_2O–C(3'), 2 H–C(5')); 3.19–3.00 (*m*, 2 CH_2CH_2O of npe, 4 CH_2CH_2O of npeoc); 2.72 (*t*, CH_2COO); 2.56 (*t*, CH_2CO); 2.50–2.10 (*m*, 4 H–C(3')); 2.18 (*s*, Me); 1.55–1.20 (*m*, 9 CH_2). Anal. calc. for $C_{118}H_{123}N_{21}O_{38}P_2$ (2505.3): C 56.57, H 4.95, N 11.74; found: C 56.10, H 5.01, N 11.21.

3'-Deoxy-5'-O-[(4-methoxyphenyl)diphenylmethyl]-N⁶-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'{O^P-[2-(4-nitrophenyl)ethyl]} → 5'}-3'-deoxy-N⁶-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'-{O^P-[2-(4-nitrophenyl)ethyl]} → 5'}-3'-O-{2-[2-[(1,4-dioxopentyl)oxy]ethoxy}ethyl}-N⁶,2'-O-bis[2-(4-nitrophenyl)ethoxycarbonyl]adenosine (**43**). As described for **42**, with **38** (51 mg, 61 μmol), **1** [15] (180 mg, 0.11 mmol), 1*H*-tetrazole (23 mg, 0.31 mmol), and abs. MeCN (5 ml). Workup and purification by FC (silica gel (5 g), 1.5 × 10 cm; CH_2Cl_2 (50 ml), CH_2Cl_2/MeOH 99:1 (50 ml), 98:2 (50 ml), 97:3 (50 ml), 96:4 (50 ml)) yielded 140 mg (94%) of **43**. Colourless foam. TLC (CH_2Cl_2/MeOH 95:5): R_f 0.31. UV (CH_2Cl_2): 267(5.01). ^{1}H-NMR ((D_6)DMSO): 10.58–10.49 (*m*, 3 NH); 8.60–8.40 (*m*, 3 H–C(2), 3 H–C(8)); 8.13–7.95 (*m*, 12 H *o* to NO_2); 7.60–7.32 (*m*, 12 H *m* to NO_2); 7.28–7.09 (*m*, 12 H of MeOTr); 6.76 (*d*, 2 H *o* to MeO); 6.24–6.10 (*m*, 3 H–C(1')); 5.71, 5.39, 5.38 (*m*, 3 H–C(2')); 4.50–4.02 (*m*, 2 CH_2CH_2O of npe, H–C(3'), 3 H–C(4'), 4 CH_2CH_2O of npeoc, 4 H–C(5'), CH_2Olev); 3.72 (*s*, MeO); 3.63–3.40 (*m*, 2 CH_2O, CH_2O–C(3')); 3.15–2.88 (*m*, 2 H–C(5'), 2 CH_2CH_2O of npe, 4 CH_2CH_2O of npeoc); 2.63 (*t*, CH_2COO); 2.39 (*t*, CH_2CO); 2.20–2.10 (*m*, 4 H–C(3')); 2.08 (*s*, Me). Anal. calc. for $C_{111}H_{109}N_{21}O_{39}P_2$ (2423.2): C 55.02, H 4.53, N 12.14; found: C 54.74, H 4.59, N 11.92.

3'-Deoxy-5'-O-[(4-methoxyphenyl)diphenylmethyl]-N⁶-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'{O^P-[2-(4-nitrophenyl)ethyl]} → 5'}-3'-deoxy-N⁶-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'-{O^P-[2-(4-nitro-

phenyl)ethyl]} → *5'}-3'-O-(11-hydroxyundecyl)*-N^6,*2'-O-bis[2-(4-nitrophenyl)ethoxycarbonyl]adenosine* (**44**). As described for **41**, with **42** (90 mg, 36 μmol) and 0.5M hydrazine hydrate soln. in pyridine/AcOH 4:1 (1 ml). The reaction was stopped after 6 min with acetone (1 ml) and the mixture evaporated. The crude product was purified by prep. TLC (silica gel, 40 × 20 cm, CH_2Cl_2/MeOH 95:5): 81 mg (94%) of **44**. Colourless foam. TLC (CH_2Cl_2/MeOH 95:5): R_f 0.32. UV (CH_2Cl_2): 266(5.00). ^{1}H-NMR ((D$_6$)DMSO): 10.65–10.60 (*m*, 3 NH); 8.58–8.45 (*m*, 3 H–C(2), 3 H–C(8)); 8.15–7.98 (*m*, 12 H *o* to NO_2); 7.60–7.33 (*m*, 12 H *m* to NO_2); 7.24–7.08 (*m*, 12 H of MeOTr); 6.77 (*d*, 2 H *o* to MeO); 6.28–6.08 (*m*, 3 H–C(1')); 5.74, 5.59, 5.37 (*m*, 3 H–C(2')); 4.50–4.15 (*m*, 2 CH_2CH_2O of npe, H–C(3'), 3 H–C(4'), 4CH_2CH_2O of npeoc, 4 H–C(5'), OH); 3.78 (*s*, MeO); 3.40–3.30 (*m*, CH_2OH, CH_2O–C(3')); 3.15–2.90 (*m*, 2 H–C(5'), 2 CH_2CH_2O of npe, 4 CH_2CH_2O of npeoc); 2.60–2.15 (*m*, 4 H–C(3')); 1.39–1.11 (*m*, 9 CH_2). Anal. calc. for $C_{113}H_{117}N_{21}O_{36}P_2$ (2407.2): C 56.38, H 4.90, N 12.22; found: C 55.62, H 5.19, N 11.83.

3'-Deoxy-5'-O-[(4-methoxyphenyl)diphenylmethyl]-N^6*-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'{O*^{P}*-[2-(4-nitrophenyl)ethyl]}* → *5'}-3'-deoxy*-N^6*-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'-{O*^{P}*-[2-(4-nitrophenyl)ethyl]}* → *5'}-3'-O-[2-(2-hydroxyethoxy)ethyl]*-N^6,*2'-O-bis[2-(4-nitrophenyl)ethoxycarbonyl]adenosine* (**45**). As described for **41**, with **43** (100 mg, 42 μmol) and 0.5M hydrazine hydrate soln. in pyridine/acetic acid 4:1 (2 ml). The crude product was dissolved in CH_2Cl_2 (50 ml) and washed with phosphate buffer pH 7 (3 × 50 ml). Then the aq. phases were re-extracted with CH_2Cl_2 (3 × 50 ml). The combined org. layer was dried (Na_2SO_4) and evaporated and the residue purified by FC (silica gel (5 g), 1.5 × 8 cm; CH_2Cl_2 (50 ml), CH_2Cl_2/MeOH 99:1 (50 ml), 98:2 (50 ml), 97:3 (50 ml), 96:4 (50 ml)): 75 mg (77%) of **45**. Colourless foam. TLC (CH_2Cl_2/MeOH 95:5): R_f 0.24. UV (CH_2Cl_2): 267(5.01). ^{1}H-NMR ((D$_6$)DMSO): 10.64–10.56 (*m*, 3 NH); 8.60–8.42 (*m*, 3 H–C(2), 3 H–C(8)); 8.15–7.98 (*m*, 12 H *o* to NO_2); 7.60–7.09 (*m*, 12 H *m* to NO_2, 12 H of MeOTr); 6.76 (*d*, 2 H *o* to MeO); 6.27–6.10 (*m*, 3 H–C(1')); 5.72, 5.50, 5.38 (3*m*, 3 H–C(2')); 4.56–4.15 (*m*, 2 CH_2CH_2O of npe, H–C(3'), 3 H–C(4'), 4 CH_2CH_2O of npeoc, 4 H–C(5'), OH); (*s*, MeO); 3.58–3.35 (*m*, 2 CH_2O, CH_2OH, CH_2O–C(3')); 3.15–2.90 (*m*, 2 H–C(5'), 2 CH_2CH_2O of npe, 4 CH_2CH_2O of npeoc); 2.62–2.15 (*m*, 4 H–C(3')). Anal. calc. for $C_{106}H_{103}N_{21}O_{37}P_2$ (2325.1): C 54.76, H 4.47, N 12.65; found: C 54.25, H 4.66, N 12.34.

3'-O-(5-Carboxypentyl)-5'-O-[(4-methoxyphenyl)diphenylmethyl]-N^6,*2'-O-bis[2-(4-nitrophenyl)ethoxycarbonyl]adenosine Triethylammonium Salt* (**46** · Et_3N). At r.t., **36** (40 mg, 33 μmol) was treated with 3% piperidine/DMF (1 ml) for 10 min, then dissolved in AcOEt (20 ml), and washed with phosphate buffer pH 7 (3 × 20 ml). The aq. phase was re-extracted with AcOEt (3 × 20 ml), the org. layer dried (Na_2SO_4) and evaporated, and the residue purified by FC (silica gel (3 g), 1.5 × 6 cm; CH_2Cl_2/Et_3N 99:1 (50 ml), CH_2Cl_2/MeOH/Et_3N 98:1:1 (50 ml), 97:2:1 (50 ml), 96:3:1 (50 ml)): 28 mg (75%) of **46**. Colourless foam. TLC (CH_2Cl_2/MeOH 9:1): R_f 0.71. UV (CH_2Cl_2): 267(4.57), 233(4.37). ^{1}H-NMR ((D$_6$)DMSO): 10.60 (br. *s*, NH); 8.62, 8.61 (2*s*, H–C(2), H–C(8)); 8.15 (*d*, 4 H *o* to NO_2); 7.61–7.52 (*m*, 4 H *m* to NO_2); 7.30–7.12 (*m*, 12 H of MeOTr); 6.89 (*d*, 2 H *o* to MeO); 6.28 (*d*, *J* = 2.4, H–C(1')); 5.94 (*dd*, H–C(2')); C(2')); 4.70 (*m*, H–C(3')); 4.41–4.35 (*m*, 2CH_2CH_2O of npeoc); 4.05 (*m*, H–C(4')); 3.70 (*s*, MeO); 3.50–3.30 (*m*, CH_2O–C(3'), 2 H–C(5')); 3.15–3.03 (*m*, 2 CH_2CH_2O of npeoc); 2.62 (*q*, 3 $MeCH_2$); 2.12 (*t*, CH_2COO); 1.50–1.12 (*m*, 3 CH_2); 1.02 (*t*, 3 $MeCH_2$). Anal. calc. for $C_{54}H_{53}N_7O_{15}$ · Et_3N (1141.2): C 63.15, H 6.01, N 9.82; found: C 63.05, H 6.52, N 9.30.

3'-Deoxy-5'-O-[(4-methoxyphenyl)diphenylmethyl]-N^6*-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'{O*^{P}*-[2-(4-nitrophenyl)ethyl]}* → *5'}-3'-deoxy*-N^6*-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'-{O*^{P}*-[2-(4-nitrophenyl)ethyl]}* → *5'}-3'-O-[5-(2-cyanoethoxycarbonyl)pentyl]*-N^6,*2'-O-bis[2-(4-nitrophenyl)ethoxycarbonyl]-adenosine* (**47**). As described for **42**, with **39** (53 mg, 63 μmol), **1** [15] (190 mg, 0.11 mmol), 1*H*-tetrazole (24 mg, 0.34 mmol), and abs. MeCN (5 ml). Workup and purification by FC (silica gel (10 g), 2 × 13 cm; CH_2Cl_2 (100 ml), CH_2Cl_2/MeOH 99:1 (100 ml), 98:2 (100 ml), 97:3 (100 ml), 96:4 (100 ml)) gave 144 mg (95%) of **47**. Colourless foam. TLC ($CHCl_3$/MeOH 9:1): R_f 0.66. UV (CH_2Cl_2): 267(5.02). ^{1}H-NMR ((D$_6$)DMSO): 10.62–10.58 (*m*, 3 NH); 8.59–8.44 (*m*, 3 H–C(2), 3 H–C(8)); 8.17–7.88 (*m*, 12 H *o* to NO_2); 7.60–7.35 (*m*, 12 H *m* to NO_2); 7.25–7.10 (*m*, 12 H of MeOTr); 6.76 (*d*, 2 H *o* to MeO); 6.25–6.10 (*m*, 3 H–C(1')); 5.75, 5.59, 5.38 (*m*, 3 H–C(2')); 4.40–4.10 (*m*, 2 CH_2CH_2O of npe, H–C(3'), 3 H–C(4'), 4 CH_2CH_2O of npeoc, 4 H–C(5'), CH_2OCO); 3.79 (*s*, MeO); 3.45–3.35 (*m*, CH_2O–C(3')); 3.13–2.89 (*m*, 2 H–C(5'), 2 CH_2CH_2O of npe, 4 CH_2CH_2O of npeoc); 2.84 (*t*, CH_2CN); 2.30–2.10 (*m*, 4 H–C(3'), CH_2COO); 1.50–1.10 (*m*, 3 CH_2). Anal. calc. for $C_{111}H_{108}N_{22}O_{37}P_2$ (2404.2): C 55.45, H 4.53, N 12.82; found: C 55.35, H 4.79, N 11.99.

3'-Deoxy-5'-O-[(4-methoxyphenyl)diphenylmethyl]-N^6*-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'{O*^{P}*-[2-(4-nitrophenyl)ethyl]}* → *5'}-3'-deoxy*-N^6*-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'-{O*^{P}*-[2-(4-nitrophenyl)ethyl]}* → *5'}-3'-O-{[(9H-fluoren-9-ylmethoxy)carbonyl]pentyl}*-N^6,*2'-O-bis[2-(4-nitrophenyl)ethoxycarbonyl]adenosine* (**48**). As described for **42**, with **40** (46 mg, 48 μmol), **1** [15] (133 mg, 80 μmol), 1*H*-tetrazole (13 mg, 0.19 mmol), and abs. MeCN (3 ml). Workup and purification by FC (silica gel (5 g) 1.5 × 10 cm; (50 ml), CH_2Cl_2/MeOH 99:1 (50 ml), 98:2 (50 ml), 97:3(50 ml), 96:5(50 ml)) yielded 110 mg (89%) of **48**. Colourless

foam. TLC (CH_2Cl_2/MeOH 95:5): R_f 0.30. UV (CH_2Cl_2): 297(sh, 4.57), 267(5.11). ^{1}H-NMR ((D_6)DMSO): 10.72–10.58 (*m*, 3 NH); 8.60–8.42 (*m*, 3 H–C(2), 3 H–C(8)); 8.15–7.98 (*m*, 12 H *o* to NO_2); 7.75 (*d*, 2 H of fm); 7.60–7.10 (*m*, 12 H *m* to NO_2, 8 H of fm, 12 H of MeOTr); 6.78 (*d*, 2 H *o* to MeO); 6.26–6.10 (*m*, 3 H–C(1')); 5.74, 5.48, 5.38 (*m*, 3 H–C(2')); 4.44–4.10 (*m*, 2CH_2CH_2O of npe, H–C(3'), 3 H–C(4'), 4 CH_2CH_2O of npeoc, 4 H–C(5'), CH_2O of fm, H–C(9) of fm); 3.78 (*s*, MeO); 3.40–2.88 (*m*, CH_2O–C(3'), 2 H–C(5'), 2 CH_2CH_2O of npe, 4 CH_2CH_2O of npeoc); 2.60–2.10 (*m*, 4 H–C(3'), CH_2COO); 1.40–1.02 (*m*, 3 CH_2). Anal. calc. for $C_{122}H_{115}N_{21}O_{37}P_2$ (2529.3): C 57.93, H 4.58, N 11.63; found: C 57.43, H 4.84, N 11.38.

*3'-Deoxy-5'-O-[(4-methoxyphenyl)diphenylmethyl]-*N^6*-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'{O^P-[2-(4-nitrophenyl)ethyl]} → 5'}-3'-deoxy-*N^6*-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'-{O^P-[2-(4-nitrophenyl)ethyl]} → 5'}-3'-O-(5-carboxypentyl)-*N^6*,2'-O-bis[2-(4-nitrophenyl)ethoxycarbonyl]adenosine* (**49**). As described for **46**, with **48** (255 mg, 100 μmol) and 3% piperidine/DMF (2.5 ml). Workup and purification by FC (silica gel (5 g), 1.5 × 7 cm; CH_2Cl_2 (50 ml), CH_2Cl_2/MeOH 99:1 (50 ml), 98:2 (50 ml), 97:3 (50 ml), 96:4 (50 ml), 95:5 (50 ml), 94:6 (50 ml)) gave 210 mg (87%) of **49**. Colourless foam. TLC (CH_2Cl_2/MeOH 9:1): R_f 0.58. UV (CH_2Cl_2): 267(5.01), 271(sh, 493). ^{1}H-NMR ((D_6)DMSO): 12.00 (br. *s*, COOH); 10.60 (*m*, 3 NH); 8.61–8.44 (*m*, 3 H–C(2), 3 H–C(8)); 8.13–7.98 (*m*, 12 H *o* to NO_2); 7.61–7.08 (*m*, 12 H *m* to NO_2, 12 H of MeOTr); 6.77 (*d*, 2 H *o* to MeO); 6.26–6.09 (*m*, 3 H–C(1')); 5.73, 5.48, 5.36 (3*m*, 3 H–C(2')); 4.44–4.13 (*m*, 2 CH_2CH_2O of npe, H–C(3'), 3 H–C(4'), 4CH_2CH_2O of npeoc, 4 H–C(5')); 3.69 (*s*, MeO); 3.50–3.40 (*m*, CH_2O–C(3')); 3.17–2.90 (*m*, 2 H–C(5'), 2 CH_2CH_2O of npe, 4 CH_2CH_2O of npeoc); 2.62–2.10 (*m*, 4 H–C(3'), CH_2COO); 1.46–1.15 (*m*, 3 CH_2). Anal. calc. for $C_{108}H_{105}N_{21}O_{37}P_2$ (2351.1): C 55.17, H 4.50, N 12.51; found: C 55.28, H 4.79, N 12.01.

*3'-Deoxy-*N^6*-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'{O^P-[2-(4-nitrophenyl)ethyl]} → 5'}-3'-deoxy-*N^6*-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'-{O^P-[2-(4-nitrophenyl)ethyl]} → 5'}-3'-O-(11-hydroxyundecyl)-*N^6*,2'-O-bis[2-(4-nitrophenyl)ethoxycarbonyl]adenosine* (**50**). A soln. of **44** (53 mg, 22 μmol) in 80% AcOH/H_2O (1 ml) was stirred at r.t. for 1 d, then evaporated, and co-evaporated with H_2O (3 × 5 ml) and MeOH (3 × 5 ml). The residue was purified by FC (silica gel (3 g) 1.5 × 5 cm; CH_2Cl_2 (25 ml), CH_2Cl_2/MeOH 99:1 (25 ml), 98:2 (25 ml), 97:3 (25 ml) 96:4 (25 ml), 95:5 (25 ml), 94:6 (25 ml)): 35 mg (75%) of **50**. Colourless foam. TLC (CH_2Cl_2/MeOH 9:1): R_f 0.52. UV (CH_2Cl_2): 266(5.02). ^{1}H-NMR ((D_6)DMSO): 10.69 (*m*, 3 NH); 8.63–8.45 (*m*, 3 H–C(2), 3 H–C(8)); 8.14–7.99 (*m*, 12 H *o* to NO_2); 7.59–7.35 (*m*, 12 H *m* to NO_2); 6.25–6.15 (*m*, 3 H–C(1')); 5.76, 5.42, 5.25 (*m*, 3 H–C(2')); 5.12 (*t*, OH–C(5')); 4.40–4.15 (*m*, 2 CH_2CH_2O of npe, H–C(3'), 3 H–C(4'), 4 CH_2CH_2O of npeoc, 4 H–C(5'), OH); 3.72–3.31 (*m*, CH_2OH, CH_2O–C(3'), 2 H–C(5')); 3.13–2.90 (*m*, 2 CH_2CH_2O of npe, 4 CH_2CH_2O of npeoc); 2.50–1.90 (*m*, 4 H–C(3')); 1.48–1.13 (*m*, 9 CH_2). Anal. calc. for $C_{93}H_{101}N_{21}O_{35}P_2$ (2134.9): C 52.32, H 4.77, N 13.78; found: C 51.94, H 4.98, N 13.09.

*3'-Deoxy-*N^6*-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'{O^P-[2-(4-nitrophenyl)ethyl]} → 5'}-3'-deoxy-*N^6*-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'-{O^P-[2-(4-nitrophenyl)ethyl]} → 5'}-3'-O-[2-(2-hydroxyethoxy)ethyl]-*N^6*,2'-O-bis[2-(4-nitrophenyl)ethoxycarbonyl]adenosine* (**51**). As described for **37**, with **45** (240 mg, 100 μmol) in MeOH/$CHCl_3$ 4:1 (1 ml) containing 2% of TsOH. Workup and FC (silica gel (5 g), 1.5 × 10 cm; CH_2Cl_2 (50 ml), CH_2Cl_2/MeOH 99:1 (50 ml), 98:2 (50 ml), 97:3 (50 ml), 96:4 (50 ml), 95:5 (50 ml), 94:6 (50 ml)) gave 160 mg (76%) of **51**. Colourless foam. TLC (CH_2Cl_2/MeOH 95:5): R_f 0.35. UV (CH_2Cl_2): 267(5.02). ^{1}H-NMR ((D_6)DMSO): 10.68–10.65 (*m*, 3 NH); 8.73–8.47 (*m*, 3 H–C(2), 3 H–C(8)); 8.16–8.01 (*m*, 12 H *o* to NO_2); 7.62–7.44 (*m*, 12 H *m* to NO_2); 6.25–6.15 (*m*, 3 H–C(1')); 5.72, 5.40, 5.26 (3*m*, 3 H–C(2')); 5.11 (*t*, OH–C(5')); 4.60–410 (*m*, 2 CH_2CH_2O of npe, H–C(3'), 3 H–C(4'), 4 CH_2CH_2O of npeoc, 4 H–C(5'), OH); 3.70–3.32 (*m*, 2 CH_2O, CH_2OH, CH_2O–C(3'), 2 H–C(5')); 3.12–2.89 (*m*, 2 CH_2CH_2O of npe, 4 CH_2CH_2O of npeoc); 2.45–2.00 (*m*, 4 H–C(3')). Anal. calc. for $C_{86}H_{87}N_{21}O_{36}P_2$ (2052.7): C 50.32, H 4.27, N 14.33; found: C 49.86, H 4.38, N 13.64.

*3'-Deoxy-*N^6*-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'{O^P-[2-(4-nitrophenyl)ethyl]} → 5'}-3'-deoxy-*N^6*-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'-{O^P-[2-(4-nitrophenyl)ethyl]} → 5'}-3'-O-[5-(2-cyanoethoxycarbonyl)pentyl]-*N^6*,2'-O-bis[2-(4-nitrophenyl)ethoxycarbonyl]adenosine* (**52**). As described for **37**, with **47** (120 mg, 52 μmol) in MeOH/$CHCl_3$ 4:1 (1 ml) containing 2% of TsOH. Workup after 2 h reaction time and FC (silica gel (5 g), 1.5 × 10 cm; CH_2Cl_2 (50 ml), CH_2Cl_2/MeOH 99:1 (50 ml), 98:2 (50 ml), 97:3 (50 ml), 96:4 (50 ml), 95:5 (50 ml)) gave 88 mg (80%) of **52**. Colourless foam. TLC (CH_2Cl_2/MeOH 9:1): R_f 0.48. UV (CH_2Cl_2): 267(5.02). ^{1}H-NMR ((D_6)DMSO): 10.57–10.53 (*m*, 3 NH); 8.60–8.45 (*m*, 3 H–C(2), 3 H–C(8)); 8.16–7.99 (*m*, 12 H *o* to NO_2); 7.61–7.46 (*m*, 12 H *m* to NO_2); 6.25–6.14 (*m*, 3 H–C(1')); 5.74, 5.40, 5.26 (*m*, 3 H–C(2')); 5.08 (*t*, OH–C(5')); 4.45–4.15 (*m*, 2 CH_2CH_2O of npe, H–C(3'), 3 H–C(4'), 4 CH_2CH_2O of npeoc, 4 H–C(5'), CH_2OCO); 3.70–3.39 (*m*, CH_2O–C(3'), 2 H–C(5')); 3.15–2.90 (*m*, 2 $CH_2CH_2Cl_2O$ of npe, 4 CH_2CH_2O of npeoc); 2.87 (*t*, CH_2CN); 2.45–2.03 (*m*, 4 H–C(3'), CH_2COO); 1.50–1.20 (*m*, 3 CH_2). Anal. calc. for $C_{91}H_{92}N_{22}O_{36}P_2$ (2131.8): C 51.27, H 4.35, N 14.45; found: C 50.89, H 4.47, N 14.16.

3'-Deoxyadenylyl-(2' → 5')-3'-deoxyadenylyl-(2' → 5')-3'-O-(11-hydroxyundecyl)adenosine Bis(1.8-diazabicyclo[5.4.0]undec-7-enium) Salt (**53**). After co-evaporation with dry pyridine (3 × 5 ml), **50** (32 mg, 15 μmol) was dissolved in 0.5M DBU/pyridine (1 ml) and stirred at r.t. for 3 d, then neutralized with 1M AcOH, evaporated, and co-evaporated with toluene (3 × 5 ml). The residue was washed and centrifugated several times with MeCN: 19 mg (70%) of **53**. Colourless powder. HPLC: (*A* 0.1M $(Et_3NH)OAc$ buffer (pH 7), *B* 0.1M $(Et_3NH)OAc$ buffer/MeCN 1:1, *C* MeCN; gradient: 0–20 min 90% *A* in *B* → 100% *B*, 20–40 min 100% *B* → 100% *C*): t_R 14.40 min. ^{1}H-NMR (D_2O): 8.12, 8.03, 7.98, 7.93, 7.83, 7.75 (6*s*, 3 H–C(2), 3 H–C(8)); 6.02, 5.79 (2*s*, 2 H–C(1')); 5.72 (*d*, *J* = 5.7, H–C(1')); 5.10 (br. *s*, H–C(2')); 4.67–4.00 (*m*, 2 H–C(2'), H–C(3'), 3 H–C(4'), 4 H–C(5')); 4.07–3.45 (*m*, CH_2OH, CH_2O–C(3'), 2 H–C(5'), 4 H–C(2), of DBU, 4 H–C(11) of DBU); 3.29 (*t*, 4 H–C(9) of DBU); 2.60 (*m*, 4 H–C(6) of DBU); 2.50–2.33 (*m*, 4 H–C(3')); 2.00 (*m*, 4 H–C(10) of DBU); 1.75–1.48 (*m*, 4 H–C(3) of DBU, 4 H–C(4) of DBU, 4 H–C(5)); 1.25 (br. *s*, 9 CH_2).

3'-Deoxyadenylyl-(2' → 5')-3'-deoxyadenylyl-(2' → 5')-3'-O-[2-(2-hydroxyethoxy)ethyl]adenosine Bis(1.8-diazabicyclo[5.4.0]undec-7-enium) Salt (**54**). As described for **53**, with **51** (135 mg, 66 μmol) and 0.5M DBU/pyridine (4 ml). The crude product was washed and centrifugated several times with MeCN: 100 mg (92%) of **54**. Colourless powder. HPLC: (see **53** for *A*, and *B*; gradient: 0–2 min 98% *A* in *B*, 2–20 min 98% *A* in *B* → 100% *B*, 20–25 min 100% *B*): t_R 10.55 min. ^{1}H-NMR (D_2O): 8.11, 8.01, 7.99, 7.88, 7.82, 7.74 (6*s*, 3 H–C(2), 3 H–C(8)); 6.02, 5.78 (2*s*, 2 H–C(1')); 5.69 (*d*, *J* = 5.8, H–C(1')); 5.05 (*m*, H–C(2')); 4.65–4.10 (*m*, 2 H–C(2'), H–C(3'), 3 H–C(4'), 4 H–C(5')); 3.84–3.40 (*m*, 2 CH_2O, CH_2OH, CH_2O–C(3'), 2 H–C(5'), 4 H–C(2) of DBU, 4 H–C(11) of DBU); 3.28 (*t*, 4 H–C(9) of DBU); 2.57–2.62 (*m*, 4 H–C(6) of DBU); 2.48–2.30 (*m*, 4 H–C(3')); 1.94–2.04 (*m*, 4 H–C(10) of DBU); 1.68 (*m*, 4 H–C(3) of DBU, 4 H–C(4) of DBU, 4 H–C(5)).

3'-Deoxyadenylyl-(2' → 5')-3'-deoxyadenylyl-(2' → 5')-3'-O-(5-carboxypentyl)adenosine Tris(1.8-diazabicyclo[5.4.0]undec-7-enium) Salt (**55**). As described for **53**, with **52** (11 mg, 5.2 μmol) and 0.5M DBU/pyridine (0.36 ml). The crude product was washed and centrifugated several times with MeCN: 8.3 mg (92%) of **55**. Colourless powder. HPLC: (see **53** for *A*–*C*; gradient: 0–20 min 90% *A* in *B* → 100% *B*, 20–40 min 100% *B* → 100% *C*): t_R 7.73 min. ^{1}H-NMR (D_2O): 8.10, 8.00, 7.97, 7.88, 7.80, 7.77 (6*s*, 3 H–C(2), 3 H–C(8)); 6.00, 5.77 (2*s*, 2 H–C(1')); 5.66 (*d*, *J* = 5.7, H–C(1')); 5.05 (br. *s*, H–C(2')); 4.65–4.00 (*m*, 2 H–C(2'), H–C(3'), 3 H–C(4'), 4 H–C(5')); 3.80–3.55 (*m*, CH_2O-C(3'), 2 H–C(5')); 3.52–3.40 (*m*, 6 H–C(2) of DBU, 6 H–C(C11) of DBU); 3.19 (*t*, 6 H–C(9) of DBU); 2.55 (*m*, 6 H–C(6) of DBU); 2.44–2.30 (*m*, 4 H–C(3')); 2.25 (*t*, CH_2COO); 1.95 (*m*, 6 H–C(10) of DBU); 1.63 (*m*, 6 H–C(3) of DBU, 6 H–C(4) of DBU, 6 H–C(5)); 1.60–1.30 (br. *s*, 3 CH_2).

3'-Deoxy-5'-O-[(4-methoxyphenyl)diphenylmethyl]-N^6-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'-{O^P-[2-(4-nitrophenyl)ethyl]} → 5'}-3'-deoxy-N^6-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'-{O^P-[2-(4-nitrophenyl)ethyl]} → 5'}-3'-O-[11-(cholest-5-en-3β-yloxycarbonyloxy)undecyl]-N^6,2'-O-bis[2-(4-nitrophenyl)-ethoxycarbonyl]adenosine (**56**). A mixture of **44** (64 mg, 27 μmol), DMAP (29 mg, 240 μmol), cholesteryl chloroformate (= cholest-5-en-3β-yl carbonochloridate; *Fluka*, 24 mg, 53 μmol), 1-methyl-1*H*-imidazole (4 μl, 50 μmol), and abs. CH_2Cl_2 (5 ml) was stirred at r.t. for 1 d, then more cholesteryl chloroformate (25 mg, 56 μmol) and 1-methyl-1*H*-imidazole (4 μl, 50 μmol) were added. The soln. was kept at r.t. for 8 h, then diluted with CH_2Cl_2 (50 ml), and washed with sat. NaCl soln. (3 × 50 ml). The aq. phase was re-extracted with CH_2Cl_2 (3 × 20 ml), the combined org. layer dried (Na_2SO_4) and evaporated, and the residue purified by FC (silica gel (10 g), 2 × 13 cm; CH_2Cl_2 (100 ml), CH_2Cl_2/MeOH 99:1 (100 ml), 98:2 (100 ml)); 55 mg (73%) of **56**. Colourless foam. TLC (CH_2Cl_2/MeOH 95:5): R_f 0.42. UV (CH_2Cl_2): 267(5.01). ^{1}H-NMR ((D$_6$)DMSO): 10.61–10.57 (*m*, 3 NH); 8.68–8.42 (*m*, 3 H–C(2), 3 H–C(8)); 8.10–7.95 (*m*, 12 H *o* to NO_2); 7.68–7.34 (*m*, 12 H *m* to NO_2); 7.25–7.08 (*m*, 12 H of MeOTr); 6.85 (*d*, 2 H *o* to MeO); 6.24–6.10 (*m*, 3 H–C(1')); 5.73, 5.49, 5.36 (*m*, 3 H–C(2')); 5.29 (*m*, H–C(6) of chol); 4.40–4.15 (*m*, 2 CH_2CH_2O of npe, H–C(3'), 3 H–C(4'), 4 CH_2CH_2O of npeoc, 4 H–C(5'), H–C(3) of chol); 3.99 (*t*, $CH_2OCOOchol$); 3.78 (*s*, MeO); 3.30–3.40 (*m*, CH_2O–C(3')); 3.13–2.80 (*m*, 2 H–C(5'), 2 CH_2CH_2O of npe, 4 CH_2CH_2O of npeoc); 2.30–0.60 (*m*, 4 H–C(3'), 43 H of chol, 9 CH_2). Anal. calc. for $C_{141}H_{161}N_{21}O_{38}P_2$ (2819.9): C 60.06, H 5.75, N 10.43; found: C 60.47, H 6.06, N 10.20.

3'-Deoxy-5'-O-[(4-methoxyphenyl)diphenylmethyl]-N^6-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'-{O^P-[2-(4-nitrophenyl)ethyl]} → 5'}-3'-deoxy-N^6-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'-{O^P-[2-(4-nitrophenyl)ethyl]} → 5'}-3'-O-{2-[2-(cholest-5-en-3β-yloxycarbonyloxy)ethoxy]ethyl}-N^6,2'-O-bis[2-(4-nitrophenyl)-ethoxycarbonyl]adenosine (**57**). As described for **56**, with **45** (570 mg, 250 μmol), DMAP (28 mg, 230 μmol), cholesteryl chloroformate (280 mg, 620 μmol), 1-methyl-1*H*-imidazole (50 μl, 630 μmol), and abs. CH_2Cl_2 (5 ml). After 16 h, more cholesteryl chloroformate (100 mg, 220 μmol) and 1-methyl-1*H*-imidazole (18 μl, 220 mmol) were added. The soln. was kept at r.t. for 8 h, then worked up and purified by FC (silica gel (20 g), 3 × 9 cm; CH_2Cl_2 (200 ml), CH_2Cl_2/MeOH 99:1 (200 ml), 98:2 (200 ml), 97:3 (200 ml)): 510 mg (76%) of **57**.

Colourless foam. TLC (CH_2Cl_2/MeOH 95:5): R_f 0.36. UV (CH_2Cl_2): 267(5.01). ^{1}H-NMR ((D_6)DMSO): 10.65–10.60 (*m*, 3 NH); 8.60–8.45 (*m*, 3 H–C(2), 3 H–C(8)); 8.15–7.98 (*m*, 12 H *o* to NO_2); 7.60–7.12 (*m*, 12 H *m* to NO_2, 12 H of MeOTr); 6.78 (*d*, 2 H *o* to MeO); 6.26–6.12 (*m*, 3 H–C(1')): 5.75, 5.50, 5.39 (*m*, 3 H–C(2')); 5.22 (*m*, H–C(6) of chol); 4.55–4.12 (*m*, 2 CH_2CH_2O of npe, H–C(3'), 3 H–C(4'), 4 CH_2CH_2O of npeoc, 4 H–C(5'), $CH_2OCOOchol$, H–C(3) of chol); 3.68 (*s*, MeO); 3.65–3.47 (*m*, 2 CH_2O, CH_2O–C(3')); 3.16–2.91 (*m*, 2 H–C(5'), 2 CH_2CH_2O of npe, 4 CH_2CH_2O of npeoc); 2.65–0.55 (*m*, 4 H–C(3), 43 H of chol). Anal. calc. for $C_{134}H_{147}N_{21}O_{39}P_2$ (2737.7): C 58.79, H 5.41, N 10.74; found: C 58.27, H 5.62, N 10.10.

3'-Deoxy-5'-O-[(4-methoxyphenyl)diphenylmethyl]-N^6-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'-{O^P-[2-(4-nitrophenyl)ethyl]} → 5'}-3'-deoxy-N^6-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'-{O^P-[2-(4-nitrophenyl)ethyl]} → 5'}-3'-O-[5-(cholest-5-en-3β-yloxycarbonyl)pentyl]-N^6,2'-O-bis[2-(4-nitrophenyl)ethoxycarbonyl]adenosine (**58**). As described for **15**, with **49** (10.5 mg, 4.5 μmol), EDC · HCl (6.1 mg, 32 μmol), DMAP (9.8 mg, 80 μmol), abs. CH_2Cl_2 (0.5 ml), and cholesterol (12 mg, 31 μmol). After 3 h reaction time, the soln. was worked up with CH_2Cl_2 (4 × 20 ml) and phosphate buffer pH 7 (3 × 20 ml). Purification by prep. TLC (silica gel, 20 × 20 cm, CH_2Cl_2/MeOH 95:5) gave 4.7 mg (40%) of **58**. Colourless foam. TLC (CH_2Cl_2/MeOH 95:5): R_f 0.55. UV (CH_2Cl_2): 267(5.00). ^{1}H-NMR ((D_6)DMSO): 10.62–10.55 (*m*, 3 NH); 8.60–8.44 (*m*, 3 H–C(2), 3 H–C(8)); 8.12–7.95 (*m*, 12 H *o* to NO_2); 7.57–7.10 (*m*, 12 H *m* to NO_2, 12 H of MeOTr); 6.75 (*d*, 2 H *o* to MeO); 6.26–6.10 (*m*, 3 H–C(1')); 5.72, 5.49, 5.38 (*m*, 3 H–C(2')); 5.67 (*s*, CH_2Cl_2); 5.21 (*m*, H–C(6) of chol); 4.44–4.14 (*m*, 2 CH_2CH_2O of npe, H–C(3'), 3 H–C(4'), 4 CH_2CH_2O of npeoc, 4 H–C(5'), H–C(3) of chol); 3.68 (*s*, MeO); 3.15–2.88 (*m*, CH_2O–C(3'), 2 H–C(5'), 2 CH_2CH_2O of npe, 4 CH_2CH_2). Anal. calc. for C of npeoc); 2.60–0.59 (*m*, CH_2COO, 4 H–C(3'), 43 H of chol, 3 CH_2). Anal. calc. for $C_{135}H_{149}N_{21}O_{37}P_2 \cdot 0.5\ CH_2Cl_2$ (2762.2): C 58.92, H 5.47, N 10.65; found: C 58.29, H 5.56, N 10.36.

3'-Deoxyadenylyl-(2' → 5')-3'-deoxyadenylyl-(2' → 5')-3'-O-[11-(cholest-5-en-3β-yloxycarbonyloxy)undecyl]adenosine Bis(1,8-diazobicyclo[5.4.0]undec-7-enium) Salt (**59**). A soln. of **56** (56 mg, 20 μmol) in MeOH/$CHCl_3$ 4:1 (1 ml) containing 2% of TsOH was stirred at r.t. for 60 min. The mixture was diluted with CH_2Cl_2 (20 ml) and washed with sat. $NaHCO_3$ soln. (3 × 20 ml), the aq. phase re-extracted with CH_2Cl_2 (3 × 20 ml), the org. layer dried (Na_2SO_4) and evaporated and the residue dissolved in CH_2Cl_2 and treated with Et_2O. A colourless powder was obtained on centrifugation. After co-evaporation with dry pyridine (3 × 5 ml), this solid was dissolved in 0.5M DBU/MeCN (0.7 ml) and the soln. stirred at r.t. for 3 d, then neutralized with 1M AcOH, evaporated, and co-evaporated with toluene (3 × 5 ml). The residue was washed and centrifugated several times with MeCN: 10 mg (42%) of **59**. Colourless powder. TLC (CH_2Cl_2/H_2O/MeOH 50:20:4) R_f 0.40. HPLC (0.1M (Et_3NH)OAc buffer (pH 7)/THF/MeCN 15:10:75): t_R 9.04 min. ^{1}H-NMR ((D_6)DMSO with little $CDCl_3$): 8.50–8.10 (*m*, 3 H–C(2), 3 H–C(8)); 7.20–7.10 (*m*, 3 NH_2); 6.15, 5.99 (2*s*, 2 H–C(1')); 5.90 (*d*, *J* = 5.5, H–C(1')); 5.46, 5.22, 5.02 (*m*, 3 H–C(2')); 5.31 (*m*, H–C(6) of chol); 4.71 (*m*, H–C(3')); 4.33 (*m*, 3 H–C(4'), H–C(3) of chol); 4.02 (*t*, CH_2OCOO); 3.95–3.33 (*m*, 6 H–C(5'), CH_2O–C(3'), 4 H–C(2) of DBU, 4 H–C(11) of DBU, 4 H–C(9) of DBU); 2.40–0.64 (*m*, 4 H–C(6) of DBU, 4 H–C(10) of DBU, 4 H–C(3'), 43 H of chol, 9 CH_2, 4 H–C(3) of DBU, 4 H–C(4) of DBU).

3'-Deoxyadenylyl-(2' → 5')-3'-deoxyadenylyl-(2' → 5')-3'-O-{2-[2-(cholest-5-en-3β-yloxycarbonyloxy)ethoxy]ethyl}adenosine Bis(1,8-diazobicyclo[5.4.0]undec-7-enium) Salt (**60**). As described for **59**, with **57** (470 mg, 170 μmol) in MeOH/$CHCl_3$ 4:1 (5 ml) containing 2% of TsOH. After workup, the residue was treated with 0.5M DBU/MeCN (10 ml), the soln. at r.t. for 3 d, then neutralized with 1M AcOH, and evaporated, and the residue washed and centrifugated several times with MeCN: 220 mg (80%) of **60**. Colourless powder. TLC (CH_2Cl_2/H_2O/MeOH 50:20:4): R_f 0.35. HPLC (0.1M (Et_3NH)OAc buffer (pH 7)/THF/MeCN 15:10:75) (HPLC (see **53** for *A*–*C*; gradient: 0–20 min 90% *A* in *B* → 100% *B*, 20–40 min 100% *B* → 100% *C*): t_R 36.80 min.

3'-Deoxyadenylyl-(2' → 5')-3'-deoxyadenylyl-(2' → 5')-3'-O-[5-(cholest-5-en-3β-yloxycarbonyl)pentyl]-adenosine Bis(1,8-diazobicyclo[5.4.0]undec-7-enium) Salt (**61**). *a*) A soln. of **58** (16 mg, 5.8 μmol) in MeOH/$CHCl_3$ 4:1 (1 ml) containing 2% of TsOH was stirred at r.t. for 20 min. The mixture was diluted with CH_2Cl_2 (20 ml) and washed with sat. $NaHCO_3$ soln. (3 × 20 ml) and the aq. phase re-extracted with CH_2Cl_2 (3 × 20 ml). The org. layer was dried (Na_2SO_4) and evaporated and the residue dissolved in CH_2Cl_2 and treated with Et_2O. A colourless powder was obtained on centrifugation. After co-evaporation with dry pyridine (3 × 5 ml), this solid was dissolved in 0.5M DBU/MeCN (0.35 ml) and the soln. stirred at r.t. for 3 d, then neutralized with 1M AcOH, evaporated, and co-evaporated with toluene (3 × 5 ml). The residue was washed and centrifugated several times with MeCN: 6.0 mg (67%) of **61**. Colourless powder. TLC (CH_2Cl_2/H_2O/MeOH 50:20:4): R_f 0.31. HPLC (0.1M (Et_3NH)OAc buffer (pH 7)/THF/MeCN 15:10:75): t_R 3.60 min.

b) As described before, with **66** (14 mg, 5.1 μmol) in MeOH/$CHCl_3$ 4:1 (1 ml) containing 2% of TsOH. After workup, the residue was treated with 0.5M DBU/MeCN (0.33 ml), the soln. at r.t. for 3 d, then neutralized with 1M AcOH; and evaporated, and the residue washed and centrifugated several times with MeCN: 4.6 mg (53%) of **61**. Colourless powder.

3'-O-(5-Carboxypentyl)-5'-O-[(4-methoxyphenyl)diphenylmethyl]-N⁶-[2-(4-nitrophenyl)ethoxycarbonyl]-adenosine (**62**). A soln. of **31** (81 mg, 88 μmol) in 0.1M DBU/MeCN (4:5) was stirred at r.t. for 3 h, then neutralized with 1M AcOH, and evaporated. The residue was dissolved in $CHCl_3$ (20 ml) and the soln. washed with H_2O (3 × 20 ml). The aq. phase was re-extracted with $CHCl_3$ (3 × 20 ml), the combined org. layer dried (Na_2SO_4), and evaporated, and the residue purified by FC (silica gel (5 g), 1.5 × 9 cm; CH_2Cl_2 (100 ml), CH_2Cl_2/MeOH 95:5 (100 ml)): 54 mg (72%) of **62**. Colourless foam. TLC ($CHCl_3$/MeOH 9:1): R_f 0.38. UV (MeOH): 266(4.48), 232(4.35). ^{1}H-NMR ((D_6)DMSO): 12.01 (br. *s*, COOH); 10.63 (*s*, NH); 8.58, 8.55 (2*s*, H–C(2), H–C(8)); 8.15 (*d*, 2 H *o* to NO_2); 7.60 (*d*, 2 H *m* to NO_2); 7.34–7.17 (*m*, 12 H of MeOTr); 6.83 (*d*, 2 H *o* to MeO); 5.99 (*d*, *J* = 4.4, H–C(1')); 5.98 (*d*, OH–C(2')); 4.91 (*dd*, H–C(2')); 4.37 (*t*, CH_2CH_2O of npeoc); 4.20–4.08 (*m*, H–C(4'), H–C(3')); 3.71 (*s*, MeO); 3.65–3.18 (*m*, CH_2O–C(3'), 2 H–C(5')); 3.09 (*t*, CH_2CH_2O of npeoc); 2.16 (*t*, CH_2COO); 1.68–1.20 (*m*, 3 CH_2). Anal. calc. for $C_{45}H_{46}N_6O_{11}$ (846.9): C 63.82, H 5.47, N 9.92; found: C 63.35, H 5.72, N 9.58.

3'-O-(5-Carboxypentyl)-5'-O-[(4-methoxyphenyl)diphenylmethyl]-N⁶-[2-(4-nitrophenyl)ethoxycarbonyl]-2'-O-[2-(4-nitrophenyl)ethoxysulfonyl]adenosine (**63**). To **62** (56 mg, 66 μmol), which was co-evaporated in abs. pyridine (2 × 5 ml), 2-(4-nitrophenyl)ethoxysulfonyl chloride [25] (40 mg, 0.16 mmol) and dry pyridine (5 ml) were added. The mixture was kept at r.t. for 4 h and then evaporated and co-evaporated with toluene (3 × 10 ml). The residue was dissolved in $CHCl_3$ (10 ml), the soln. washed with sat. NaCl soln. (3 × 20 ml), and the aq. phase re-extracted with $CHCl_3$ (3 × 20 ml). The org. layer was dried (Na_2SO_4) and evaporated and the residue purified by FC (silica gel (5 g), 1.5 × 8 cm; CH_2Cl_2 (50 ml), CH_2Cl_2/MeOH 99:1 (50 ml), 98:2 (50 ml)): 60 mg (86%) of **63**. Colourless foam. TLC ($CHCl_3$/MeOH 9:1): R_f 0.69. UV (CH_2Cl_2): 266(4.59), 237(4.39). ^{1}H-NMR ((D_6)DMSO): 11.97 (br. *s*, COOH); 10.66 (*s*, NH); 8.60, 8.50 (2*s*, H–C(2), H–C(8)); 8.18–8.11 (*m*, 4 H *o* to NO_2); 7.61–7.46 (*m*, 4 H *m* to NO_2); 7.32–7.13 (*m*, 12 H of MeOTr); 6.81 (*d*, 2 H *o* to MeO); 6.38 (*d*, *J* = 3.1, H–C(1')); 6.02 (*dd*, H–C(2')); 4.71 (*t*, H–C(3')); 4.38 (*t*, CH_2CH_2O of npeoc); 4.14 (*m*, H–C(4')); 3.92–3.84 (*m*, CH_2CH_2O of npes); 3.71 (*s*, MeO); 3.63–3.15 (*m*, CH_2O–C(3'), 2 H–C(5')); 3.15–3.08 (*m*, CH_2CH_2O of npeoc, CH_2CH_2O of npes); 2.11 (*t*, CH_2COO); 1.50–1.16 (*m*, 3 CH_2). Anal. calc. for $C_{53}H_{53}N_7O_{15}S$ (1060.1): C 60.05, H 5.04, N 9.25; found: 60.02, H 5.30, N 8.53.

3'-O-[5-(Cholest-5-en-3β-yloxycarbonyl)pentyl]-5'-O-[(4-methoxyphenyl)diphenylmethyl]-N⁶-[2-(4-nitrophenyl)ethoxycarbonyl]-2'-O-[2-(4-nitrophenyl)ethoxysulfonyl]adenosine (**64**). As described for **15**, with **63** (31 mg, 29 μmol), EDC · HCl (17 mg, 89 μmol), DMAP (12 mg, 98 μmol), abs. CH_2Cl_2 (2 ml), and cholesterol (34 mg, 88 μmol). Workup and purification by FC (silica gel (5 g), 1.5 × 8 cm; toluene (25 ml), toluene/AcOEt 9:1 (25 ml), 7:1 (40 ml), 5:1 (30 ml), 1:1 (40 ml)) led to 24 mg (60%) of **64**. Colourless foam. TLC (toluene/AcOEt 1:1): R_f 0.50. UV (CH_2Cl_2): 266(4.57), 237(4.41). ^{1}H-NMR ((D_6)DMSO): 10.69 (*s*, NH); 8.61, 8.52 (2*s*, H–C(2), H–C(8)); 8.15–8.10 (*m*, 4 H *o* to NO_2); 7.60–7.46 (*m*, 4 H *m* to NO_2); 7.30–7.13 (*m*, 12 H of MeOTr); 6.82 (*d*, 2 H *o* to MeO); 6.38 (*d*, *J* = 3.1, H–C(1')); 6.00 (*dd*, H–C(2')); 5.29 (*m*, H–C(6) of chol); 4.72 (*m*, H–C(3')); 4.39 (*m*, CH_2CH_2O of npeoc, H–C(3) of chol); 4.12 (*m*, H–C(4')); 3.85 (*m*, CH_2CH_2O of npes); 3.73 (*s*, MeO); 3.60–3.08 (*m*, CH_2O–C(3'), 2 H–C(5'), CH_2CH_2O of npeoc, CH_2CH_2O of npes); 2.22–0.63 (*m*, CH_2COO, 43 H of chol, 3 CH_2). Anal. calc. for $C_{80}H_{97}N_7O_{15}S$ (1428.8): C 67.25, H 6.84, N 6.86; found: C 67.62, H 7.40, N 5.83.

3'-O-[5-(Cholest-5-en-3β-yloxycarbonyl)pentyl]-N⁶-[2-(4-nitrophenyl)ethoxycarbonyl]-2'-O-[2-(4-nitrophenyl)ethoxysulfonyl]adenosine (**65**). As described for **37**, with **64** (71 mg, 50 μmol) in MeOH/$CHCl_3$ 4:1 (1 ml) containing 2% of TsOH. Workup and FC (silica gel (5 g), 1.5 × 6 cm; CH_2Cl_2 (50 ml), CH_2Cl_2/MeOH 99:1 (50 ml), 98:2 (50 ml)) gave 51 mg (89%) of **65**. Colourless foam. TLC (CH_2Cl_2/MeOH 95:5): R_f 0.51. UV (MeOH): 272(sh, 4.51), 267(4.55), 251(sh, 4.45). ^{1}H-NMR ((D_6)DMSO): 10.66 (*s*, NH); 8.69, 8.56 (2*s*, H–C(2), H–C(8)); 8.16 (*m*, 4 H *o* NO_2); 7.60–7.45 (*m*, 4 H *m* to NO_2); 6.34 (*d*, *J* = 4.3, H–C(1')); 5.73 (*dd*, H–C(2')); 5.31 (*m*, OH–C(5'), H–C(6) of chol); 4.40 (*m*, H–C(3'), CH_2CH_2O of npeoc, H–C(3) of chol); 4.11 (*m*, H–C(4')); 3.90–3.50 (*m*, CH_2O–C(3'), 2 H–C(5'), CH_2CH_2O of npes); 3.10 (*m*, CH_2CH_2O of npeoc, CH_2CH_2O of npes); 2.24–0.61 (*m*, CH_2COO, 43 H of chol, 3 CH_2). Anal. calc. for $C_{60}H_{81}N_7O_{14}S$ (1153.4): C 62.32, H 7.06, N 8.48; found: C 61.97, H 7.50, N 7.87.

3'-Deoxy-5'-O-[(4-methoxyphenyl)diphenylmethyl]-N⁶-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'-{O^P-[2-(4-nitrophenyl)ethyl]} → 5'}-3'-deoxy-N⁶-[2-(4-nitrophenyl)ethoxycarbonyl]adenylyl-{2'-{O^P-[2-(4-nitrophenyl)ethyl]} → 5'}-3'-O-[5-(cholest-5-en-3β-yloxycarbonyl)pentyl]-N⁶-[2-(4-nitrophenyl)ethoxycarbonyl]-2'-O-[2-(4-nitrophenyl)ethoxysulfonyl]adenosine (**66**). As described for **42**, with **65** (36 mg, 31 μmol), **1** [15] (95 mg, 57 μmol), 1*H*-tetrazole (11 mg, 0.16 mmol), and abs. MeCN (2 ml) mixed with abs. CH_2Cl_2 (1 ml). Workup and purification by FC (silica gel (5 g), 1.5 × 10 cm; CH_2Cl_2 (50 ml), CH_2Cl_2/MeOH 99:1 (50 ml), 98:2 (50 ml)) yielded 42 mg (49%) of **66**. Colourless foam. TLC (CH_2Cl_2/MeOH 95:5): R_f 0.38. UV (CH_2Cl_2): 266(5.00). ^{1}H-NMR ($CDCl_3$): 8.62–8.48, 8.20–7.95 (2*m*, 3 H–C(2), 3 H–C(8), 12 H *o* to NO_2); 7.41–7.13 (*m*, 12 H *m* to NO_2, 12 H of MeOTr); 6.78 (*d*, 2 H *o* to MeO); 6.18–6.00 (*m*, 3 H–C(1')); 5.72–5.30 (*m*, 3 H–C(2'), H–C(6)

of chol); 4.60–4.15 (*m*, 2 CH_2CH_2O of npe, H–C(3'), 3 H–C(4'), 3 CH_2CH_2O of npeoc, 4 H–C(5'), H–C(3) of chol); 3.73 (*s*, MeO); 3.65–2.95 (*m*, CH_2CH_2O of npes, CH_2O–C(3'), 2 H–C(5'), 2 CH_2CH_2O of npe, 3 CH_2CH_2O of npeoc, CH_2CH_2O of npes); 2.48–0.65 (*m*, CH_2COO, 4 H–C(3'), 43 H of chol, 3 CH_2). Anal. calc. for $C_{134}H_{149}N_{21}O_{37}P_2S$ (2739.8): C 58.74, H 5.48, N 10.74; found: C 59.13, H 5.45, N 9.95.

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