2. Nucleotides

Part XXXIV[1])

Synthesis of Modified Oligomeric 2′–5′A Analogues: Potential Antiviral Agents

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A series of new 2′–5′-oligonucleotide trimers carrying a 9-(2′,3′-anhydro-β-D-ribofuranosyl)- (**59**), 9-(3′-deoxy-β-D-*glycero*-pent-3-enofuranosyl)-(**63**), 9-(3′-azido-3′-deoxy-β-D-xylofuranosyl)-(**62**), and 9-(3′-halo-3′-deoxy-β-D-xylofuranosyl)adenine (**60** and **61**) moiety at the 2′-terminal end have been synthesized *via* the phosphotriester method. The properly protected, modified monomeric building blocks (**6**, **9**, **16**, **19**, **27**, **33**, **36**, **37**, and **43**) were obtained, in general, by a sequence of reactions, introducing the protecting groups into the right positions. Their condensations with the intermediary dimeric 2′-terminal phosphodiesters **48** and **49** led to the fully protected 2′–5′-trimers **50–58** which were deblocked to form the free 2′–5′-trimers **59–63**. Easy elimination of HBr on deprotection did not allow to form the trimeric (3′-bromo-3′-deoxy-β-D-xylofuranosyl)adenine analogue but only **63** carrying an unsaturated sugar moiety instead. The newly synthesized compounds have been characterized by UV and NMR spectra as well as by elemental analysis.

1. Introduction. – More detailed studies on the 'antiviral activity' of interferon revealed that this protein functions as an inducer to enhance antiviral resistance in virally infected cells by a cascade of reactions. This resistance is typically characterized by induced activity of several enzymes, a protein kinase, a (2′–5′)pppA(pA)$_n$ synthetase, a specific exoribonuclease-2′-phosphodiesterase, and an endoribonuclease, RNase L [2–4]. The biological function of the interferon-induced synthetase is the oligomerization of ATP to various (2′–5′)pppA(pA)$_n$ oligomers, of which the trimer showed so far the highest activity in subsequent activation of RNase L. Chemically synthesized (2′–5′)ApApA ('core'), which is also formed naturally in mouse L-cells following treatment with interferon [5], can mimic the antimitogenic effect of interferon and seems to play a separate role in the inhibition of DNA synthesis and cellular reactions. Since the 2′-phosphodiesterase activity is also triggered 4–6 fold in interferon-treated cells, enhanced cleavage of the naturally occurring 2′–5′-oligoadenylate molecules is noticed. This fact led to several attempts to synthesize chemically modified structural analogues lacking enzymatic degradation but still activating the latent endoribonuclease L [6–18]. Since the presence of a 3′-*O*-methyl group at the 2′-terminal end of (2′–5)ApApA induced a higher biological index, obviously due to greater enzymatic stability [6], we decided to continue our efforts [17] [18] in synthesizing some additional 2′–5′A_3 analogues in which the

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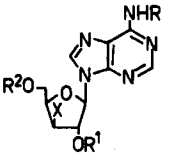
2′-terminal adenosine moiety has been replaced by a 3′-substituted 9-(β-D-xylofuranosyl)adenine or the 9-(2′,3-anhydro-β-D-ribofuranosyl)adenine (= 2′,3′-anhydroadenosine) residue. The introduced 3′-substituents are located in the β(up)-configuration, and they vary in electronegativity and bulkiness.

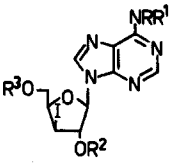
It can be seen from the coupling constants $J(1',2')$ of the starting nucleosides 9-(β-D-xylofuranosyl)adenine (2.0 Hz) [19], its 3′-fluoro- (2.3 Hz), 3′-methoxy- (2.7 Hz), 3′-chloro- (4.0 Hz), 3′-bromo- (4.5 Hz), 3′-iodo- (5.5 Hz), and 3′-azido-3′-deoxy derivatives (6.0 Hz) that there is already a conformational change in the puckering of the sugar moiety which may also affect the fine structure of the anticipated oligonucleotides and their interactions with other biomolecules.

2. Syntheses. – The provision for a successful synthesis of oligonucleotides is the preparation of appropriately protected monomeric building blocks. Starting from adenosine the 9-(3′-chloro-3′-deoxy-β-D-xylofuranosyl)adenine (**1**) [20] [21] and its 3′-bromo (**10**) [21], 3′-iodo (**20**) [21], 3′-fluoro [22], and 3′-azido [22] analogue as well as the 2′,3′-anhydroadenosine [20] [23] have been synthesized by known or slightly modified procedures.

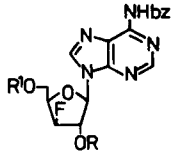


	R	R^1	R^2	X
1	H	H	H	Cl
2	bz	H	H	Cl
3	bz	H	MeOTr	Cl
4	bz	tbds	MeOTr	Cl
5	H	tbds	MeOTr	Cl
6	bz	tbds	H	Cl
7	bz	H	tbds	Cl
8	bz	MeOTr	tbds	Cl
9	bz	MeOTr	H	Cl

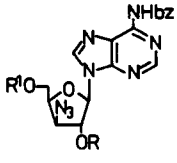
	R	R^1	R^2	X
10	H	H	H	Br
11	H	ac	H	Br
12	bz	H	H	Br
13	bz	H	MeOTr	Br
14	bz	tbds	MeOTr	Br
15	H	tbds	MeOTr	Br
16	bz	tbds	H	Br
17	bz	H	tbds	Br
18	bz	MeOTr	MeOTr	Br
19	bz	MeOTr	H	Br



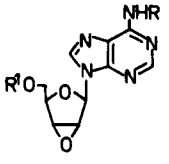
	R	R^1	R^2	R^3
20	H	H	H	H
21	bz	bz	H	H
22	bz	bz	H	MeOTr
23	bz	H	H	H
24	bz	H	H	MeOTr
25	bz	H	tbds	MeOTr
26	H	H	tbds	MeOTr
27	bz	H	tbds	H
28	npeoc	H	H	H
29	npeoc	H	H	MeOTr
30	npeoc	H	tbds	MeOTr



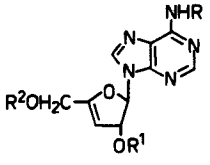
	R	R^1
31	H	H
32	H	MeOTr
33	tbds	H



	R	R^1
34	H	H
35	H	MeOTr
36	tbds	H



	R	R^1
37	bz	H
38	bz	MeOTr
39	H	MeOTr



	R	R^1	R^2
40	bz	tbds	MeOTr
41	bz	H	MeOTr
42	H	tbds	MeOTr
43	bz	tbds	H

bz = benzoyl; MeOTr = monomethoxytrityl; tbds = (*tert*-butyl)dimethylsilyl; ac = acetyl; npe = 2-(4-nitrophenyl)ethyl; npeoc = [2-(4-nitrophenyl)ethoxy]carbonyl.

The protection of the amino group of **1** and **10**, of the 3′-fluoro-3′-deoxy and 3′-azido-3′-deoxy analogue, and of 2′,3′-anhydroadenosine by a benzoyl (bz) group was carried out by the transient-protection method [24] giving good yields of **2**, **12**, **31**, **34**, and **37**, respectively. In the case of 9-(3′-iodo-3′-deoxy-β-D-xylofuranosyl)adenine (**20**), the usual workup after benzoylation could not be applied, since desilylation and removal of one benzoyl group with ammonia led to 2′,3′-epoxide formation (→**37**) due to the high reactivity of the I-substituent and easy intramolecular nucleophilic displacement. Therefore, the N^6,N^6-dibenzoyl derivative **21** was isolated and then hydrolysed under very mild conditions (MeOH in presence of imidazole) to the N^6-monobenzoyl compound **23**. Selective protection of the 5′-OH groups was achieved by monomethoxytritylation in the usual manner (MeOTrCl) forming **3**, **13**, **22**, **24**, **32**, **35**, and **38**, respectively. These compounds were then silylated at the 2′-OH group using (*tert*-butyl)dimethylsilyl chloride (*t*-Bu)Me_2SiCl to give either the corresponding silyl ether **4**, **14**, and **25**, which were subsequently detritylated to **6**, **16**, and **24**, respectively, or to give directly in an one-pot reaction the 5′-OH deprotected derivatives **33** and **36**.

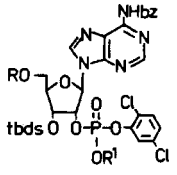
The interesting features of the [2-(4-nitrophenyl)ethoxy]carbonyl residue (npeoc) [25] as a superior amino-protecting group encouraged us to synthesize from **11** in an analogous sequence of reactions the 9-(3′-iodo-3′-deoxy-β-D-xylofuranosyl)-N^6-([2-(4-nitrophenyl)ethoxy]carbonyl)adenine (**28**) and its 5′-*O*-monomethoxytrityl-(**29**) as well as the corresponding 2′-*O*-(*tert*-butyl)dimethylsilyl derivative **30**.

The lability of 3′-iodo-3′-deoxy derivative **20** under basic reaction conditions (→**37**) prompted us to test the stability of the protected 3′-halo-3′-deoxy building blocks **4**, **14**, and **25** under deprotection conditions to see, whether the appropriate protected oligonucleotides can finally be converted into their free forms without structural modifications. On treatment with conc. ammonia at room temperature, **4**, **14**, and **25** were debenzoylated to **5**, **15**, and **26**, respectively, and detritylation of **4**, **14**, and **25** with 80% AcOH gave **6**, **16**, and **27**, respectively without affecting the halo atoms. On treatment with 0.5M DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) in pyridine **4** was still stable, but the 3′-bromo- (**14**) and 3′-iodo analogue (**25**) showed *trans*-1,2-elimination to form N^6-benzoyl-9-{2′-*O*-[(*tert*-butyl)dimethylsilyl]-3′-deoxy-5′-*O*-(monomethoxytrityl)-β-D-*glycero*-pent-3′-enofuranosyl}adenine (**40**) and its desilylated analogue **41** in 80 and 15% and 49 and 32% yield, respectively. Bu_4NF in tetrahydrofuran (THF) caused the expected desilylation and was accompanied by simultaneous intramolecular displacement to form the 2′,3′-anhydro-N^6-benzoyl-5′-*O*-(monomethoxytrityl)adenine (**38**) in high yields.

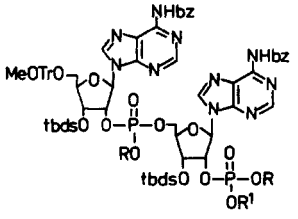
The unsaturated nucleoside **40** reacted with conc. ammonia under debenzoylation to **42**, which was also obtained on DBU treatment of **30** in two simultaneous elimination processes. Finally, **40** was detritylated in the usual manner with 80% AcOH to give **43** in 74% yield. Also, the anhydro derivative **38** was debenzoylated to **17** with conc. ammonia.

These results indicated an obvious change in the blocking-group strategy, since the desilylation from the 2′-*O*-position is accompanied by a side reaction leading to concomitant oxirane formation, when the adjacent halo atom is Cl, Br, or I. We tried, therefore, to introduce an acid-labile protecting group into the 2′-OH position by converting **2** and **12** first into their 5′-*O*-(*tert*-butyl)dimethylsilyl derivatives **7** and **16**, respectively. The following monomethoxytritylation turned out to be rather difficult. After 5 days at 50°, only a 66% yield of the N^6-benzoyl-9-[5′-*O*-[(*tert*-butyl)dimethylsilyl]-3′-chloro-3′-deoxy-2′-*O*-(monomethoxytrityl)-β-D-xylofuranosyl]adenine (**8**) was obtained, while 20% of **7**

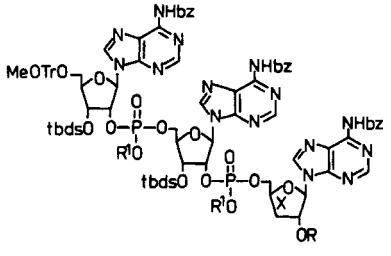
could still be recovered. Removal of the (*tert*-butyl)dimethylsilyl group from **8** proceeded without difficulties with Bu_4NF in THF to give **9** in 97% yield. The same reaction sequence, however, was not applicable to the 3′-bromo analogue **17**, since treatment with MeOTrCl in pyridine for 7 days at 50° led to a mixture of the expected N^6-benzoyl-9-{5′-*O*-[(*tert*-butyl)dimethylsilyl]-3′-bromo-3′-deoxy-2′-*O*-(monomethoxytrityl)-β-D-xylofuranosyl}adenine and the corresponding 2′,5′-bis-*O*-monomethoxytrityl derivative **18**, which could not be separated cleanly. This mixture reacted in 80% AcOH at 4° for 12 h



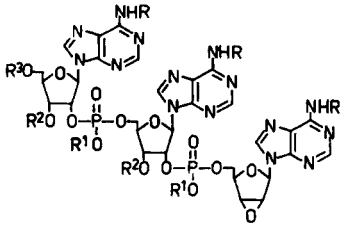
	R	R^1
44	MeOTr	CH_2CH_2CN
45	MeOTr	$HNEt_3$
46	H	CH_2CH_2CN



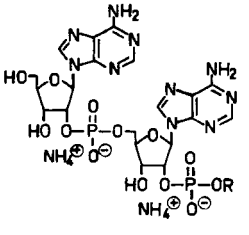
	R	R^1
47	2,5-Cl_2-C_6H_3	CH_2CH_2CN
48	2,5-Cl_2-C_6H_3	$HNEt_3$
49	npe	$HNEt_3$

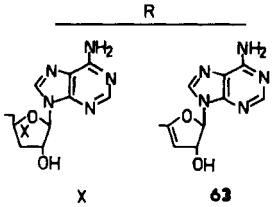


	R	R^1	X
50	tbds	npe	Cl
51	MeOTr	2,5-Cl_2-C_6H_3	Cl
52	tbds	npe	Br
53	tbds	2,5-Cl_2-C_6H_3	Br
54	MeOTr	2,5-Cl_2-C_6H_3	Br
55	tbds	2,5-Cl_2-C_6H_3	I
56	tbds	npe	F
57	tbds	npe	N_3



	R	R^1	R^2	R^3
58	bz	2,5-Cl_2-C_6H_3	tbds	MeOTr
59	H	NH_4	H	H





	X
60	Cl
61	F
62	N_3

63

with partial detritylation and allowed the isolation of 70% of **19**. Due to the difference in reactivity of the 2′-*O*- and 5′-*O*-monomethoxytrityl group, **19** was then synthesized more straightforwardly from **12** by bis-tritylation (→**18**) followed by selective removal of the 5′-*O*-MeOTr group (→**19** in 71% yield). It should also be mentioned that all attempts to protect N^6-benzoyl-9-(3′-iodo-3′-deoxy-β-D-xylofuranosyl)adenine (**23**) in a similar manner have so far failed.

The synthesis of the various anticipated fully protected 2′–5′ trimers **50–58** was achieved by routine condensations of the triethylammonium dinucleoside diphosphates **48** or **49** with the 5′-OH free nucleosides **6**, **9**, **16**, **19**, **27**, **33**, **36**, and **37**, respectively, under activation by 2,4,6-triisopropylbenzenesulfonyl chloride and *N*-methylimidazole as condensing agents in pyridine. The use of different blocking groups for the phosphate functions and especially the very bulky 2′-*O*-monomethoxytrityl residue did not alter the yields very much and the products were isolated after column chromatography in moderate to good (55–77%) yield. The starting dimer **49** was described earlier [18], whereas **48** had to be synthesized by a series of reactions from N^6-benzoyl-3′-*O*-[(*tert*-butyl)-dimethylsilyl]-5′-*O*-(monomethoxytrityl)adenosine [26] [27] first by conversion into the 2′-(2,5-dichlorophenyl, 2-cyanoethyl)phosphotriester **44**. Treatment either with Et_3N in pyridine or with 2% TsOH in CH_2Cl_2/MeOH led to the two components **45** and **46**, respectively, which were then condensed to the fully protected dimer **47** in 81% yield. Elimination of the 2-cyanoethyl group at the 2′-terminal phosphotriester function was performed in the usual manner to give **48** in 80% isolated yield.

The crucial point of all the synthetic efforts was then encountered during the deprotection steps to form the free 2′–5′ trimers **59–63**. Deblocking of **56** and **57** to the free trimers **61** and **62** in 86 and 80% yield, respectively, proceeded as expected in four successive steps, first by elimination of the phosphate-protecting groups with DBU in pyridine, second by cleavage of the silyl groups with Bu_4NF, third by debenzoylation with conc. ammonia, and finally by AcOH-catalyzed detritylation (see *Table*), and purification by *DEAE-Sephadex* chromatography. Subsequent paper chromatography yielded, after lyophilisation, the pure ammonium salts **61** and **62** as checked by HPLC on a reverse-phase column (*RP 18*, 0.1M a NH_4OAc/MeCN 95:5). Analogously, the deprotection of **58** proceeded smoothly to **59** in 78% yield, after incubation with conc. ammonia for 3 days at r.t., followed by Bu_4NF treatment in THF, final detritylation with 80% AcOH, and purification.

Table. *Deprotection of 2′-5′ Trimers*

Starting material	Conditions[a])	Resulting trimer
50	1, 3, 2, 4	**59**
51	3, 2, 4	**60**
52	1, 3, 2, 4	**59/63**
53	3, 2, 4	**59**
54	3, 2, 4	–
55	3, 2, 4	**59/63**
56	1, 2, 3, 4	**61**
57	1, 2, 3, 4	**62**
58	3, 2, 4	**59**

[a]) 1) DBU in pyridine; 2) Bu_4NF in THF; 3) conc. NH_3; 4) 80% AcOH.

More problems were encountered, as expected, on deprotection of the halo trimers **50–55** (see *Table*). Compound **51** still worked fine on successive treatment with conc. ammonia, Bu_4NF in THF, and 80% AcOH, giving a 87% yield of **60** and thus proving that the monomethoxytrityl group for 2′-OH protection was the correct choice. On the contrary, **50** gave, after the deprotection sequence DBU in pyridine, conc. ammonia, Bu_4NF in THF, and 80% AcOH a trimer which was identical with **59** carrying the 2′,3′-anhydroadenosine moiety at the 2′-terminal end. Of the Br-containing trimers **52–54**, only **53** reacted uniformly to give again **59**, whereas from **52** the two trimers **59** and **63** were isolated. Unfortunately, the deprotection of **54** led to an intractable mixture which could not be separated into pure components. Finally, the I-containing trimer **55** led again to the mixture **59**/**63**.

3. Spectral Data. – All new compounds were characterized in the usual manner by elemental analyses and UV and ^{1}H-NMR spectra. Comparisons of the UV spectra indicate that the long-wavelength absorption of the adenine chromophor at 259 nm is shifted bathochromically by 20 nm on N^6-benzoylation and by *ca.* 10 nm on introduction of the [2-(4-nitrophenyl)ethoxy]carbonyl group. In the fully protected trimers **50–58**, the presence of three adenine moieties is reflected in the extinctions which are highly additive revealing no or very little base-stacking and a more linear conformation.

In the complex ^{1}H-NMR spectra, the chemical shifts of the anomeric protons of the monomeric building blocks show characteristic deviations which are due to special structural features. Thus, the presence of a 2′-*O*-(*tert*-butyl)dimethylsilyl group and the simultaneous absence of the 5′-*O*-(monomethoxytrityl) group, like in **6**, **16**, **27**, and **36**, causes an upfield shift of 0.3–0.4 ppm from the normal anomeric-proton region (5.9–6.1 ppm) and a substantial increase of $J(1',2')$. Furthermore, introduction of a 2′-*O*-(monomethoxytrityl) group (**8**, **9**, **18**, **19**) is associated with a down-field shift of H–C(1′) which is, as expected, also observed with the unsaturated nucleosides **40–43**. The fully deprotected 2′–5′ trimers **59–63** show three distinct ^{1}H-NMR signals (D_2O) for the anomeric protons, which are difficult to assign to the various nucleoside moieties due to an interfering influence of the substituents in the 2′-terminal unit. It should be mentioned that the assignments of H–C(2) and H–C(8) of all new compounds have not been corroborated by further experiments and are, therefore, tentative.

We thank the *Alexander von Humboldt Foundation* for a research fellowship, the *Fonds der chemischen Industrie* for financial support, and Mrs. *M. Bischler* for the measurements of the UV spectral data.

Experimental Part

General. See [18]. HPLC: *SP-8000-B* chromatograph, *Spectra Physics;* column: *Lichrosorb RP-18* and *Lichrophor RP-18* (*Merck*). OD measured at 260 nm.

1. *9-(3′-Chloro-3′-deoxy-β-*D*-xylofuranosyl)adenine* (**1**) [20] [21]. A suspension of 3.34 g (12.5 mmol) of dry adenosine and 8.25 g (50 mmol) of freshly distilled 2-acetoxyisobutyryl chlorid in dry MeCN (125 ml) was heated to 80° for 1 h. After cooling to r.t., the precipitate (adenine) was filtered off and the filtrate evaporated. The residue was dissolved in AcOEt (150 ml) and washed subsequently with 10% $NaHCO_3$ soln. (3 × 50 ml) and H_2O (2 × 50 ml). The org. layer was dried (Na_2SO_4) and evaporated. The solid foam was treated with 1% HCl/MeOH (200 ml) at r.t. for 7 days. The soln. was then neutralized by addition of Ag_2CO_3 (8.5 g) and stirring for 4 h, filtered, and evaporated and the residue chromatographed (silica gel (24 × 6 cm), $CHCl_3$/MeOH 95:5). The main fraction was collected after 700 ml of eluant and gave, on coevaporation and recrystallization from acetone/AcOEt 2.0 g (56%)

of **1**. Colorless crystals. M.p. 193° ([21]: 194°). UV (MeOH): 259 (4.18). ^{1}H-NMR ((D$_6$)DMSO): 8.25 (*s*, H–C(8)); 8.14 (*s*, H–C(2)); 7.37 (br. *s*, NH$_2$); 6.37 (*d*, OH–C(2′)); 5.86 (*d*, H–C(1′)); 5.33 (*t*, OH–C(5′)); 4.81 (*m*, H–C(2′)); 4.53 (*m*, H–C(3′)); 4.40 (*m*, H–C(4′)); 3.74 (*m*, 2 H–C(5′)).

2. N^6-*Benzoyl-9-(3′-chloro-3′-deoxy-β-*D*-xylofuranosyl)adenine* (**2**). A mixture of 0.45 g (1.56 mmol) of **1** and 1 ml (7.8 mmol) of Me$_3$SiCl in pyridine (8 ml) was stirred for 15 min at r.t. After addition of 0.9 ml (7.8 mmol) of benzoyl chloride, the mixture was further stirred for 3 h at r.t. and then cooled to 0°. H$_2$O (1.6 ml) was added and after 10 min, conc. NH$_3$ (3.1 ml). The mixture was stirred for another 30 min. After dilution with H$_2$O (23 ml) and extraction with AcOEt (3 × 15 ml), the combined org. layer was evaporated, coevaporated with toluene, and purified by column chromatography (silica gel, CHCl$_3$/MeOH 95:5). Recrystallization from AcOEt gave 0.425 g (70%). Colorless crystals. M.p. 149°. UV (MeOH): 279 (4.28). ^{1}H-NMR ((D$_6$)DMSO): 8.77 (*s*, H–C(8)); 8.59 (*s*, H–C(2)); 8.04 (*m*, 2 H, bz); 7.59 (*m*, 3 H, bz); 6.49 (*d*, OH–C(2′)); 6.03 (*d*, *J* = 3.7, H–C(1′)); 5.16 (*t*, OH–C(5′)); 4.86 (*m*, H–C(2′)); 4.58 (*m*, H–C(3′)); 4.47 (*m*, H–C(4′)); 3.83–3.70 (*m*, 2 H–C(5′)). Anal. calc. for C$_{17}$H$_{16}$ClN$_5$O$_4$ (389.8): C 52.38, H 4.74, N 17.96; found: C 52.76, H 4.37, N 18.15.

3. N^6-*Benzoyl-9-[3′-chloro-3′-deoxy-5′-*O*-(monomethoxytrityl)-β-*D*-xylofuranosyl]adenine* (**3**). A mixture of 0.7 g (1.8 mmol) of **2** and 0.67 g (2.16 mmol) of MeOTrCl in dry pyridine (10 ml) was stirred for 48 h at r.t. MeOH (3 ml) and CHCl$_3$ (20 ml) were added, and the mixture was washed with phosphate buffer pH 7 (2 × 50 ml). The org. layer was dried, filtered, evaporated, coevaporated with toluene, and purified by column chromatography (silica gel, CHCl$_3$/CH$_2$Cl$_2$ 1:1, then CHCl$_3$/MeOH 98:2). The residue of the main fraction was precipitated from CHCl$_3$/hexane: 0.96 g (81%). Colorless solid. UV (MeOH): 279 (4.39). ^{1}H-NMR (CHCl$_3$): 8.98 (*s*, NH); 8.77 (*s*, H–C(8)); 8.19 (*s*, H–C(2)); 7.98, 7.17–7.59 (*m*, 19 arom. H); 6.80 (*d*, 2 H, *o* to MeO); 6.09 (*d*, *J* = 1.2, H–C(1′)); 4.88 (*m*, OH–C(2′), H–C(2′)); 4.76 (*m*, H–C(4′)); 4.43 (*m*, H–C(3′)); 3.77 (*s*, MeO); 3.65–3.40 (*m*, 2 H–C(5′)). Anal. calc. for C$_{37}$H$_{32}$ClN$_5$O$_5$ (662.2): C 67.11, H 4.87, N 10.57; found: C 66.62, H 4.66, N 10.62.

4. N^6-*Benzoyl-9-{2′-*O*-[(*tert*-butyl)dimethylsilyl]-3′-chloro-3′-deoxy-5′-*O*-(monomethoxytrityl)-β-*D*-xylofuranosyl}adenine* (**4**). A mixture of 3.0 g (4.5 mmol) of **3**, 0.92 g (13.5 mmol) of imidazole, and 1.02 g (6.75 mmol) of (*t*-Bu)Me$_2$SiCl in dry pyridine (20 ml) was stirred at r.t. for 40 h. After addition of CHCl$_3$ (100 ml) and washing with H$_2$O (2×50 ml), the org. layer was dried, evaporated, and coevaporated with toluene. Purification by column chromatography (silical gel, CH$_2$Cl$_2$/CHCl$_3$ 2:1) and reprecipitation from CHCl$_3$/hexane gave 3.72 g (89%) o **4**. Amorphous solid. UV (MeOH): 279 (4.36). ^{1}H-NMR (CDCl$_3$): 9.12 (br. *s*, NH); 8.77 (*s*, H–C(8)); 8.20 (*s*, H–C(2)); 8.02 (2 H, bz); 7.21–7.60 (*m*, 17 arom. H); 6.84 (*d*, 2 H, *o* to MeO); 6.12 (*d*, H–C(1′)); 4.73 (*m*, H–C(2′), H–C(4′)); 4.13 (*m*, H–C(3′)); 3.79 (*s*, MeO); 3.73 (*dd*, 1 H–C(5′)); 3.42 (*dd*, 1 H–C(5′)); 0.92 (*s*, *t*-Bu); 0.19 (*s*, MeSi). Anal. calc. for C$_{43}$H$_{46}$ClN$_5$O$_5$Si (776.4): C 66.52, H 5.97, N 9.02; found: C 66.56, H 6.15, N 9.21.

5. *9-{2′-*O*-[(*tert*-Butyl)dimethylsilyl]-3′-chloro-3′-deoxy-5′-*O*-(monomethoxytrityl)-β-*D*-xylofuranosyl}-adenine* (**5**). A soln. of 0.562 g (0.72 mmol) of **4** in conc. NH$_3$ (10 ml) and dioxane (8 ml) was stirred at r.t. for 48 h. After evaporation, the residue in CH$_2$Cl$_2$/CHCl$_3$ 1:1 was chromatographed (silica gel (38×2 cm), CH$_2$Cl$_2$/CHCl$_3$ 1:1 (500 ml), CHCl$_3$ (300 ml), and CHCl$_3$/MeOH 50:1 (500 ml)). The last fraction gave a colorless foam which was precipitated from little CHCl$_3$/hexane (50 ml) under stirring. The amorphous solid was dried under high vacuum at 40°: 0.46 g (95%). UV (MeOH): 233 (4.23), 258 (4.20). ^{1}H-NMR (CDCl$_3$): 8.31 (*s*, H–C(8)); 8.01 (*s*, H–C(2)); 7.50, 7.31 (2*m*, 12 arom. H); 6.83 (*d*, 2 H, *o* to MeO); 6.03 (*d*, *J* = 1.0, H–C(1′)); 5.90 (br. *s*, NH$_2$); 4.69 (*m*, H–C(2′), H–C(4′)); 4.11 (*m*, H–C(3′)); 3.79 (*s*, MeO); 3.70 (*dd*, 1 H–C(5′)); 3.39 (*dd*, 1 H–C(5′)); 0.90 (*s*, *t*-Bu); 0.16 (*s*, CH$_3$); 0.12 (*s*, CH$_3$). Anal. calc. for C$_{36}$H$_{42}$ClN$_5$O$_4$Si (672.3): C 64,31, H 6.30, N 10.42; found: C 64.17, H 6.69, N 10.11.

6. N^6-*Benzoyl-9-{2′-*O*-[(*tert*-butyl)dimethylsilyl]-3′-chloro-3′-deoxy-β-*D*-xylofuranosyl}adenine* (**6**). A soln. of 0.233 g (0.3 mmol) of **5** in 80% aq. AcOH (10 ml) was kept at r.t. for 16 h. The mixture was partitioned between CHCl$_3$ (100 ml) and H$_2$O (100 ml). The org. layer was dried, evaporated, and coevaporated with toluene and the residue purified by column chromatography (silica gel, CHCl$_3$): 0.139 g (92%). Amorphous solid. UV (MeOH): 279 (4.35). ^{1}H-NMR (CDCl$_3$): 9.01 (*s*, NH); 8.82 (*s*, H–C(8)); 8.09 (*s*, H–C(2)); 8.01 (2 H, bz); 7.49–7.61 (*m*, 3 H, bz); 5.78 (*d*, *J* = 5.8, H–C(1′)); 5.01–5.11 (*m*, OH–C(5′), H–C(2′)); 4.54 (*m*, H–C(4′)); 4.41 (*m*, H–C(3′)); 4.03 (*m*, 2 H–C(5′)); 0.79 (*s*, *t*-Bu); 0.02 (*s*, MeSi); −0.36 (*s*, MeSi). Anal. calc. for C$_{23}$H$_{30}$ClN$_5$O$_4$Si (504.1): C 54.80, H 6.00, N 13.89; found: C 54.30, H 5.97, N 13.75.

7. N^6-*Benzoyl-9-{5′-*O*-[(*tert*-butyl)dimethylsilyl]-3′-chloro-3′-deoxy-β-*D*-xylofuranosyl}adenine* (**7**). A mixture of 0.9 g (2.31 mmol) of **2** and 0.435 g (2.88 mmol) of (*t*-Bu)Me$_2$SiCl in dry pyridine (5 ml) was stirred at r.t. for 3 h. After addition of MeOH (5 ml) the mixture was diluted with CHCl$_3$ (50 ml) and washed with H$_2$O (2 × 50 ml). The org. layer was dried, filtered, evaporated, and purified by column chromatography (silica gel, CHCl$_3$/MeOH 99:1, then CHCl$_3$/MeOH 98:2): 0.93 g (80%). Amorphous solid. UV (MeOH): 279 (4.13). ^{1}H-NMR (CDCl$_3$): 9.08

(*s*, NH); 8.69 (*s*, H–C(8)); 8.31 (*s*, H–C(2)); 7.99–7.96 (*m*, 2 H, bz); 7.61–7.46 (*m*, 3 H, bz); 6.05 (*d*, $J = 3.7$, H–C(1′)); 5.66 (*d*, OH–C(2′)); 4.88 (*m*, H–C(2′)); 4.60 (*m*, H–C(4′)); 4.50 (*m*, H–C(3′)); 4,04–3.91 (*m*, 2 H–C(5′)); 0.79 (*s*, *t*-Bu); 0.03 (*s*, Me_2Si). Anal. calc. for $C_{23}H_{30}ClN_5O_4Si$ (504.1): C 54.80, H 6.00, N 13.89; found: C 54.34, H 6.10, N 13.64.

8. N^6-*Benzoyl-9-*{5′-O-*[*(tert-*butyl)dimethylsilyl*]-3′-chloro-3′-deoxy-2′-*O-*(monomethoxytrityl)-β-*D*-xylofuranosyl*}adenine* (**8**). A soln. of 0.66 g (1.31 mmol) of **7** and 0.97 g (3.14 mmol) of MeOTrCl in pyridine (8 ml) was heated for 5 days at 50°. The mixture was cooled, MeOH (5 ml) added, the mixture evaporated, coevaporated with toluene (3 × 10 ml), diluted with $CHCl_3$ (50 ml), and washed with H_2O (3 × 50 ml), the org. layer dried and evaporated, and the residue purified, by column chromatography (silica gel, $CH_2Cl_2/CHCl_3$ 2:1, $CHCl_3$, and $CHCl_3$/MeOH 99:1): 0.67 g (66%). Amorphous solid. An anal. pure sample was obtained after prep. TLC ($CHCl_3$/MeOH 99:1). UV (MeOH): 278 (4.33). ^{1}H-NMR ($CDCl_3$): 8.96 (br. *s*, NH); 8.90 (*s*, H–C(8)); 8.31 (*s*, H–C(2)); 8.02–7.99 (*m*, 2 H, bz); 7.63–7.17 (*m*, 15 H, bz, MeO*Tr*); 6.72 (*d*, 2 H, *o* to MeO); 6.66 (*d*, H–C(1′)); 4.43 (*m*, H–C(4′), H–C(3′)); 3.91–3.77 (*m*, H–C(5′)); 3.72 (*s*, MeO); 3.15 (*m*, H–C(2′)); 0.83 (*s*, *t*-Bu); 0.01 (Me_2Si). Anal. calc. for $C_{43}H_{46}ClN_5O_5Si$ (776.4): C 66.52, H 5.97, N 9.02; found: C 66.03, H 6.01, N 8.87.

9. N^6-*Benzoyl-9-[3′-chloro-3′-deoxy-2′-*O-*(monomethoxytrityl)-β-*D*-xylofuranosyl]adenine* (**9**). A soln. of 0.23 g (0.3 mmol) of **8** in 0.5M Bu_4NF (20 ml) in THF was kept for 30 min at r.t. and was then evaporated. The residue was diluted with $CHCl_3$ (50 ml) and washed with H_2O (4 × 50 ml). The org. layer was dried, evaporated, and purified by column chromatography (silica gel, $CHCl_3$, then $CHCl_3$/MeOH 99:1): 0.175 g (88%). UV (MeOH): 279 (4.34). ^{1}H-NMR ($CDCl_3$): 8.97 (*s*, NH); 8.86 (*s*, H–C(8)); 8.22 (*s*, H–C(2)); 8.02–7.99 (*m*, 2 H, bz); 7.61–7.48 (*m*, 3 H, bz); 7.41–7.12 (*m*, 12 H, MeO*Tr*); 6.68 (*d*, 2 H, *o* to MeO); 6.57 (*d*, $J = 2.1$, H–C(1′)); 4.57–4.51 (*m*, H–C(4′), H–C(3′)); 3.94 (*dd*, H–C(5′)); 3.80 (*dd*, 1 H–C(5′)); 3.71 (*s*, MeO); 3.42 (*m*, H–C(2′)); 2.23 (*t*, OH–C(5′)). Anal. calc. for $C_{37}H_{32}ClN_5O_5$ (662.2): C 67.11, H 4.87, N 10.57; found: C 66.61, H 5.19, N 10.29.

10. *9-(3′-Bromo-3′-deoxy-β-*D*-xylofuranosyl)adenine* (**10**). As described in *Exper. 1*, with 6.675 g (25 mmol) of adenosine, 15.7 g (75 mmol) of freshly distilled 2-acetoxyisobutyryl bromide, and MeCN (75 ml), at r.t. for 40 min; workup (no filtration) with AcOEt (250 ml), sat. $NaHCO_3$ soln. (3 × 125 ml), and H_2O (2 × 100 ml); HCl/MeOH treatment at r.t. for 8 days and Ag_2CO_3 (12.5 g) treatment for 4 h; after chromatography (silica gel (30 × 6 cm), $CHCl_3$/MeOH 95:5 (1.5 l)), the first fraction gave, on recrystallization from MeOH, 1.31 g (14%) of *9-(2′-*O*-acetyl-3′-bromo-3′-deoxy-β-*D*-xylofuranosyl)adenine* (**11**). M.p. 207° ([21]: 206–207°).

The second fraction gave, on recrystallization, 1.91 g (23%) of **10**. Colorless crystals. M.p. 134° ([21]: 133°). UV (MeOH): 259 (4.17). ^{1}H-NMR ((D_6)DMSO): 8.29 (*s*, H–C(8)); 8.15 (*s*, H–C(2)); 7.37 (br. *s*, NH_2); 6.37 (*d*, OH–C(2′)); 5.83 (*d*, $J = 4.3$, H–C(1′)); 5.40 (*t*, OH–C(5′)); 4.90 (*m*, H–C(2′)); 4.55 (*m*, H–C(3′)); 4.32 (*m*, H–C(4′)); 3.75 (*m*, 2 H–C(5′)).

From the last fraction were isolated 2.1 g (25%) of *9-(2′-bromo-2′-deoxy-β-*D*-arabinofuranosyl)adenine*. M.p. 215° ([20]: 215–216°).

11. N^6-*Benzoyl-9-(3′-bromo-3′-deoxy-β-*D*-xylofuranosyl)adenine* (**12**). As described in *Exper. 2*, with 0.46 g (1.4 mmol) of **10**. The crude product was purified by prep. TLC (silica gel (40 × 20 × 0.2 cm), $CHCl_3$/MeOH 9:1; elution of the main band (R_f 0.35) with $CHCl_3$/MeOH 4:1) and recrystallization from AcOEt (20 ml): 0.48 g (75%) of colorless crystals. M.p. 165°. UV (MeOH): 230 (sh, 4.12), 260 (sh, 4.06), 279 (4.28). ^{1}H-NMR ((D_6)DMSO): 11.15 (br. *s*, NH); 8.76 (*s*, H–C(8)); 8.62 (*s*, H–C(2)); 8.04 (*m*, 2 H, bz); 7.67–7.51 (*m*, 3 H, bz); 6.44 (*d*, OH–C(2′)); 6.02 (*d*, $J = 3.9$, H–C(1′)); 5.14 (*t*, OH–C(5′)); 4.99 (*m*, H–C(2′)); 4.59 (*m*, H–C(3′)); 4.39 (*m*, H–C(4′)); 3.85–3.70 (*m*, 2 H–C(5′)).

12. N^6-*Benzoyl-9-[3′-bromo-3′-deoxy-5′-*O-*(monomethoxytrityl)-β-*D*-xylofuranosyl]adenine* (**13**). Dry pyridine (10 ml) and 0.978 g (2.25 mmol) of **12** were coevaporated to remove any moisture. Treatment, as described in *Exper. 3*, with pyridine (10 ml) and 0.832 g (2.7 mmol) of MeOTrCl; workup with $CHCl_3$ (50 ml; no MeOH) and phosphate buffer (2 × 50 ml); chromatography (silica gel (27 × 3 cm), CH_2Cl_2 (2 l), $CHCl_3$ (0.7 l), and $CHCl_3$/MeOH 50:1) and drying under high vacuum gave 1.275 g (80%) of amorphous foam. UV (MeOH): 279 (4.38). ^{1}H-NMR ($CDCl_3$): 9.03 (br. *s*, NH); 8.74 (*s*, H–C(8)); 8.24 (*s*, H–C(2)); 7.98 (*m*, 2 H, bz); 7.61–7.22 (*m*, 15 H, bz MeO*Tr*); 6.79 (*d*, 2 H, *o* to MeO); 6.09 (*d*, H–C(1′)); 5.36 (br. *s*, OH–C(2′)); 4.97 (*m*, H–C(2′)); 4.66 (*m*, H–C(4′)); 4.41 (*m*, H–C(3′)); 3.76 (*s*, MeO); 3.76–3.37 (2*dd*, 2 H–C(5′)). Anal. calc. for $C_{37}H_{32}BrN_5O_5$ (706.6): C 62.89, H 4.56, N 9.91; found: C 69.39, H 4.50, N 9.73.

13. N^6-*Benzoyl-9-*{3′-*bromo-2′-*O-*[*(tert-*butyl)dimethylsilyl*]-3′-deoxy-5′-*O-*(monomethoxytrityl)-β-*D*-xylofuranosyl*}adenine* (**14**). As described in *Exper. 4*, with pyridine (9 ml), 1.3 g (1.84 mmol) of **13**, 0.376 g (5.52 mmol) of imidazole, and 0.416 g (2.76 mmol) of (*t*-Bu)Me_2SiCl, 2 days. MeOH (5 ml) was added and evaporated. Coevaporation with toluene (2 × 20 ml), partition between $CHCl_3$ (30 ml) and phosphate buffer pH 7 (2 × 30 ml)

drying (Na_2SO_4) of the org. layer, evaporation, and chromatography (silica gel (31 × 4 cm), $CH_2Cl_2/CHCl_3$ 2:1), gave, after reprecipitation from little $CHCl_3$ hexane and drying under high vacuum at 40°, 1.231 g (81%) of amorphous powder. UV (MeOH): 279 (4.35). ^{1}H-NMR ($CDCl_3$): 8.77 (*s*, H–C(8)); 8.25 (*s*, H–C(2)); 8.03 (*m*, 2 H, bz); 7.62–7.28 (*m*, 15 H, bz MeO*Tr*); 6.84 (*d*, 2 H, *o* to MeO); 6.10 (*d*, H–C(1′)); 4.86 (*m*, H–C(2′)); 4.61 (*m*, H–C(4′)); 4.10 (*m*, H–C(3′)); 3.79 (*s*, MeO); 3.75–3.68 (*dd*, 1 H–C(5′)); 3.40–3.35 (*dd*, 1 H–C(5′)); 0.92 (*s*, *t*-Bu); 0.18 (*s*, MeSi); 0.14 (*s*, MeSi). Anal. calc. for $C_{43}H_{46}BrN_5O_5Si$ (820.9): C 62.92, H 5.65, N 8.53; found: C 62.63, H 5.39, N 8.42.

14. *9-{3′-Bromo-2′-O-[(*tert*-butyl)dimethylsilyl]-3′-deoxy-5′-O-(monomethoxytrityl)-β-*D*-xylofuranosyl}-adenine* (**15**). As described in *Exper. 5*, with dioxane (8 ml), conc. NH_3 (10 ml), and 0.115 g (0.14 mmol) of **14**; after evaporation coevaporation with toluene (2 × 10 ml), and prep. TLC (silica gel (40 × 20 × 0.2 cm), $CHCl_3$/MeOH 50.1 (2 developments); elution with AcOEt (300 ml) 0.09 g (90%) of amorphous solid were obtained. UV (MeOH): 233 (4.25), 258 (4.23). ^{1}H-NMR ($CDCl_3$): 8.29 (*s*, H–C(8)); 8.10 (*s*, H–C(2)); 7.47–7.51, 7.26–7.38 (2*m*, 12 H, MeO*Tr*); 6.84 (*d*, 2 H, *o* to MeO); 6.70 (br. *s*, NH_2); 6.01 (*d*, H–C(1′)); 4.82 (*m*, H–C(2′)); 4.58 (*m*, H–C(4′)); 4.09 (*m*, H–C(3′)); 3.79 (*s*, MeO); 3.70 (*dd*, 1 H–C(5′)); 3.37 (*dd*, 1 H–C(5′)); 0.90 (*s*, *t*-Bu); 0.15 (*s*, MeSi); 0.13 (*s*, MeSi). Anal. calc. for $C_{36}H_{42}BrN_5O_4Si$ (716.8): C 60.33, H 5.91, N 9.77; found: C 60.49, H 5.78, N 9.94.

15. *N^6-Benzoyl-9-{3′-bromo-2′-O-[(*tert*-butyl)dimethylsilyl]-3′-deoxy-β-*D*-xylofuranosyl}adenine* (**16**). As described in *Exper. 6*, with 80% AcOH (10 ml) and 0.246 g (0.3 mmol) of **14**; workup with $CHCl_3$ (100 ml) and phosphate buffer pH 7 (2 × 100 ml); chromatography (silica gel (42 × 2 cm), $CHCl_3$/MeOH 100:1) gave 0.142 g (86%) of amorphous solid. UV (MeOH): 232 (sh, 4.18), 260 (sh, 4.14), 279 (4.35). ^{1}H-NMR ($CDCl_3$): 9.03 (br. *s*, NH); 8.81 (*s*, H–C(8)); 8.09 (*s*, H–C(2)); 8.02–7.99 (*m*, 2 H, bz); 7.63–7.48 (*m*, 3 H, bz); 5.73 (*d*, J = 5.8, H–C(1′)); 5.21 (*t*, OH–C(5′)); 5.16 (*m*, H–C(2′)); 4.50 (*m*, H–C(4′)); 4.40 (*m*, H–C(3′)); 4.04 (*m*, 2 H–C(5′)); 0.79 (*s*, *t*-Bu); 0.03 (*s*, MeSi); −0.42 (*s*, MeSi). Anal. calc. for $C_{23}H_{30}BrN_5O_4Si$ (548.5): C 50.36, H 5.51, N 12.77; found: C 50.22, H 5.78, N 12.53.

16. *N^6-Benzoyl-9-{3′-bromo-5′-O-[(*tert*-butyl)dimethylsilyl]-3′-deoxy-β-*D*-xylofuranosyl}adenine* (**17**). As described in *Exper. 7*, with 0.4 g (0.9 mmol) of **12**, 0.164 g (1.08 mmol) of (*t*-Bu)Me_2SiCl, and pyridine (3 ml); after evaporation and coevaporation with toluene, workup with $CHCl_3$ (50 ml) and phosphate buffer pH 7 (2 × 50 ml); chromatography (silica gel, $CHCl_3$, then $CHCl_3$/MeOH 99:1) and prep. TLC (silica gel, $CHCl_3$/MeOH 97:3 (2 developments)) gave 0.465 g (94%) of amorphous solid. UV (MeOH): 230 (sh, 4.15), 259 (sh, 4.08), 279 (4.32). ^{1}H-NMR ($CDCl_3$): 9.02 (br. *s*, NH); 8.72 (*s*, H–C(8)); 8.31 (*s*, H–C(2)); 8.01–7.98 (*m*, 2 H, bz); 7.60–7.48 (*m*, 3 H, bz); 6.02 (*d*, J = 4.0, H–C(1′)); 5.40 (*d*, OH–C(2′)); 4.99 (*m*, H–C(2′)); 4.53 (*m*, H–C(4′)); 4.47 (*m*, H–C(3′)); 4.09–3.92 (2*dd*, 2 H–C(5′)); 0.74 (*s*, *t*-Bu); −0.04 (*s*, MeSi); −0.14 (*s*, MeSi). Anal. calc. for $C_{23}H_{30}BrN_5O_4Si$ (548.5): C 50.36, H 5.51, N 12.77; found: C 50.45, H 6.11, N 12.61.

17. *N^6-Benzoyl-9-[3′-bromo-3′-deoxy-2′,5′-bis-O-(monomethoxytrityl)-β-*D*-xylofuranosyl]adenine* (**18**). As described in *Exper. 3*, with 0.434 g (1 mmol) of **12**, 0.74 g (2.4 mmol) of MeOTrCl and pyridine (8 ml), 7 days at 50°; after addition of MeOH (5 ml) and evaporation, workup with $CHCl_3$ and phosphate buffer pH 7 (2 × 50 ml); chromatography (silica gel, $CH_2Cl_2/CHCl_3$ 4:1, $CH_2Cl_2/CHCl_3$ 1:1, and $CHCl_3$) and prep. TLC ($CHCl_3$/MeOH 99.5:0.5) of the product fraction gave 0.30 g (43%) of **13** and 0.524 g (54%) of **18** as amorphous solid. **18**: UV (MeOH): 231 (4.62), 260 (sh, 4.20), 279 (4.39). ^{1}H-NMR ($CDCl_3$): 9.07 (br. *s*, NH); 8.89 (*s*, H–C(8)); 8.36 (*s*, H–C(2)); 8.01 (*m*, 2 H, bz); 7.59–7.14, 6.80–6.72 (2 *m*, 27 H, bz, MeO*Tr*); 6.80 (*d*, 2 H, *o* to MeO); 6.72 (*d*, 2 H, *o* to MeO); 6.63 (*d*, J = 1.2, H–C(1′)); 4.57 (*m*, H–C(3′)); 4.19 (*m*, H–C(4′)); 3.76 (*s*, MeO); 3.72 (*s*, MeO); 3.61–3.54 (*dd*, 1 H–C(5′)); 3.20–3.15 (*dd*, 1 H–C(5′)); 3.13 (*m*, H–C(2′)). Anal. calc. for $C_{57}H_{48}BrN_5O_6$ (978.9): C 69.93, H 4.94, N 7.15; found: C 69.67, H 5.03, N 7.21.

18. *N^6-Benzoyl-9-[3′-bromo-3′-deoxy-2′-O-(monomethoxytrityl)-β-*D*-xylofuranosyl]adenine* (**19**). As described in *Exper. 6*, with 0.216 g (0.22 mmol) of **18** and 80% AcOH (10 ml), 18 h at 4°; workup with $CHCl_3$ (50 ml), H_2O (2 × 50 ml), and $CHCl_3$ (50 ml); chromatography ($CHCl_3$) gave 0.11 g (71%) of amorphous solid. UV (MeOH): 231 (4.44), 279 (4.34). ^{1}H-NMR ($CDCl_3$): 9.18 (br. *s*, NH); 8.84 (*s*, H–C(8)); 8.32 (*s*, H–C(2)); 8.03–8.00 (*m*, 2 H, bz); 7.59–7.13 (*m*, 15 H, bz, MeO*Tr*); 6.68 (*d*, 2 H, *o* to MeO); 6.55 (*s*, H–C(1′)); 4.67 (*m*, H–C(4′)); 4.37 (*m*, H–C(3′)); 3.95–3.88 (*m*, H–C(5′)); 3.75–3.63 (*m*, 1 H–C(5′)); 3.71 (*s*, MeO); 3.45 (*m*, H–C(2′)); 2.56 (br. *s*, OH–C(5′)). Anal. calc. for $C_{37}H_{32}BrN_5O_5$ (706.6): C 62.89, H 4.56, N 9.91; found: C 62.36, H 4.60, N 9.73.

19. *9-(3′-Deoxy-3′-iodo-β-*D*-xylofuranosyl)adenine* (**20**). To a soln. of 15 g (0.1M) of NaI in dry MeCN (100 ml) were added with stirring 5.2 ml (37 mmol) of freshly distilled 2-acetoxyisobutyryl chloride and 2.67 g (10 mmol) of adenosine. The mixture was stirred for 30 min at r.t. and then poured into a sat. soln. of $Na_2S_2O_3$ (150 ml) and $NaHCO_3$ (250 ml; →decoloration). The soln. was extracted with CH_2Cl_2 (2 × 100 ml) and washed with H_2O the

org. layer dried (Na_2SO_4) and evaporated, and the amorphous solid dissolved in 1.5% HCl/MeOH (200 ml) and kept at r.t. for 8 days in the dark. The mixture was then neutralized with $PbCO_3$ (10 g) in little $CHCl_3$/MeOH 4:1 and separated by column chromatography (silica gel (40 × 6 cm), $CHCl_3$/MeOH 95:5, then $CHCl_3$/MeOH 9:1) into 0.65 g (16%) of *9-(2'-O-acetyl-3'-deoxy-3'-iodo-β-D-ribofuranosyl)adenine* and, after recrystallization from MeOH, 1.5 g (40%) of **20**. Colorless crystals. M.p. 172° ([21]: 173°). UV (MeOH): 258 (4.21). ^{1}H-NMR ((D$_6$)DMSO): 8.32 (*s*, H–C(8)); 8.14 (*s*, H–C(2)); 7.38 (br. *s*, NH_2); 6.23 (*d*, OH–C(2')); 5.75 (*d*, *J* = 5.5, H–C(1')); 5.61 (*t*, OH–C(5')); 4.94 (*m*, H–C(2')); 4.48 (*m*, H–C(3')); 4.08 (*m*, H–C(4')); 3.85 (*m*, 2 H–C(5)).

20. N^6,N^6-*Dibenzoyl-9-(3'-deoxy-3'-iodo-β-D-xylofuranosyl)adenine* (**21**). As described in *Exper. 2*, with 0.76 g (2 mmol) of **20**, 1.28 ml (10 mml) of Me_3SiCl, pyridine (10 ml; 10 min at r.t.), and 1.2 ml (12 mmol) of benzoyl chloride (2.5 h at r.t.); MeOH (5 ml) was added and the mixture further stirred for 3 h; workup with H_2O (40 ml) and AcOEt (2 × 40 ml); chromatography ($CHCl_3$/MeOH 99:1) and prep. TLC ($CHCl_3$/MeOH 99:1) gave 0.78 g (66%) of **21**. Amorphous solid. UV (MeOH): 249 (4.37), 271 (sh, 4.28). ^{1}H-NMR ((D$_6$)DMSO): 8.86 (*s*, H–C(8)); 8.72 (*s*, H–C(2)); 7.77 (*m*, 4 H, bz); 7.62–7.43 (*m*, 6 H, bz); 6.38 (*t*, OH–C(2')); 5.95 (*d*, *J* = 4.9, H–C(1')); 5.19 (*t*, OH–C(5')); 5.05 (*m*, H–C(2')); 4.50 (*m*, H–C(3')); 4.11 (*m*, H–C(4')); 3.75 (*m*, 2 H–C(5')). Anal. calc. for $C_{24}H_{20}IN_5O_5$ (585.4): C 49.24, H 3.44, N 11.96; found: C 48.89, H 3.32, N 11.78.

21. N^6,N^6-*Dibenzoyl-9-[3'-deoxy-3'-iodo-5'-O-(monomethoxytrityl)-β-D-xylofuranosyl]adenine* (**22**). As described in *Exper. 3*, with pyridine (3.5 ml), 0.4 g (0.68 mmol) of **21**, and 0.222 g of MeOTrCl, 70 h; after evaporation and coevaporation with toluene (2×), workup with $CHCl_3$ (20 ml) and phosphate buffer pH 7 (2 × 20 ml); chromatography (silica gel (28 × 4 cm), $CHCl_3$/CH_2Cl_2 1:1 (1 l), then $CHCl_3$ (100 ml)), prep. TLC (plate 40 × 20 × 0.2 cm, AcOEt), and reprecipitation from $CHCl_3$/hexane gave 0.51 g (87%) of **22**. Amorphous powder. UV (MeOH): 231 (4.52), 250 (sh, 4.42), (270 (4.32)). ^{1}H-NMR ($CDCl_3$): 8.63 (*s*, H–C(8)); 8.35 (*s*, H–C(2)); 7.80 (*m*, 4 H, bz); 7.30 (*m*, 18 H, bz, MeO*Tr*); 6.79 (*d*, 2 H, *o* to MeO); 5.95 (*d*, *J* = 2.7, H–C(1')); 5.13 (*m*, H–C(2')); 4.35 (*m*, H–C(3')); 4.23 (*m*, OH–C(2'), H–C(4')); 3.76 (*s*, MeO); 3.43 (2*dd*, 2 H–C(5')). Anal. calc. for $C_{44}H_{36}IN_5O_6$ (857.7): C 61.61, H 4.23, N 8.16; found: C 61.29, H 4.43, N 8.11

22. N^6-*Benzoyl-9-(3'-deoxy-3'-iodo-β-D-xylofuranosyl)adenine* (**23**). A soln. of 0.45 g (0.77 mmol) of **21** and 0.64 g (9.2 mmol) of imidazole in MeOH (50 ml) was kept for 7 days at r.t. The mixture was evaporated, diluted with AcOEt (200 ml), washed with phosphate buffer pH 7 (2 × 200 ml), dried, and evaporated. The residue was purified by prep. TLC ($CHCl_3$/MeOH 95:5 (two developments)) and recrystallization from AcOEt: 0.35 g (94%) of **23** Colorless crystals. M.p. 186°. UV (MeOH): 279 (4.34). ^{1}H-NMR ((D$_6$)DMSO): 11.25 (*s*, NH); 8.77 (*s*, H–C(8)); 8.68 (*s*, H–C(2)); 8.04 (*s*, 2 H, bz); 7.60 (*m*, 3 H, bz); 6.36 (*d*, OH–C(2')); 5.95 (*d*, *J* = 4.9, H–C(1')); 5.28 (*t*, OH–C(5')); 5.04 (*m*, H–C(2')); 4.52 (*m*, H–C(3')); 4.12 (*m*, H–C(4')); 3.88 (*m*, 2 H–C(5')). Anal. calc. for $C_{17}H_{16}IN_5O_4$ (481.2): C 42.43, H 3.35, N 14.55; found: C 42.45, H 3.12, N 14.28.

23. N^6-*Benzoyl-9-[3'-deoxy-3'-iodo-5'-O-(monomethoxytrityl)-β-D-xylofuranosyl]adenine* (**24**). As described in *Exper. 3*, with 0.53 g (1.1 mmol) of **23**, 0.407 g (1.32 mmol) of MeOTrCl, and pyridine (6 ml), 41 h; workup with $CHCl_3$ (50 ml, no MeOH) and H_2O (2 × 50 ml); chromatography (CH_2Cl_2/$CHCl_3$ 1:1, then $CHCl_3$) gave 0.694 g (84%) of **24**. Amorphous solid. UV (MeOH): 279 (4.30). ^{1}H-NMR ($CDCl_3$): 8.80 (*s*, H–C(8)); 8.31 (*s*, H–C(2)); 8.02 (*s*, 2 H, bz); 7.60–7.21 (*m*, 18 arom. H); 6.78 (*d*, 2 H, *o* to MeO); 5.99 (*d*, H–C(1')); 5.14 (*m*, H–C(2')); 4.42 (*m*, H–C(4')); 4.30 (*m*, H–C(3')); 3.77 (*s*, MeO); 3.59–3.41 (*m*, 2 H–C(5')). Anal. calc. for $C_{37}H_{32}IN_5O_5$ (753.6): C 58.97, H 4.28, N 9.29; found: C 58.49, H 4.20, N 9.22.

24. N^6-*Benzoyl-9-{2'-O-[(*tert*-butyl)dimethylsilyl]-3'-deoxy-3'-iodo-5'-O-(monomethoxytrityl)-β-D-xylofuranosyl}adenine* (**25**). As described in *Exper. 4*, with 0.555 g (0.74 mmol) of **24**, 0.166 g of of (*t*-Bu)Me_2SiCl, 0.15 g (2.21 mmol) of imidazole, and pyridine (4 ml) 29 h; after evaporation, workup with $CHCl_3$ (50 ml) and H_2O (50 ml); chromatography (silica gel (42 × 2 cm), CH_2Cl_2/$CHCl_3$ 2:1) gave 0.561 g (88%) of **25**. Amorphous solid. UV (MeOH): 280 (4.37). ^{1}H-NMR ($CDCl_3$): 8.77 (*s*, H–C(8)); 8.31 (*s*, H–C(2)); 8.05 (*s*, 2 H, bz); 7.60–7.28 (*m*, 15 arom. H); 6.85 (*d*, 2 H, *o* to MeO); 6.06 (*d*, H–C(1')); 5.08 (*m*, H–C(2')); 4.09 (*m*, H–C(3'), H–C(4')); 3.79 (*s*, MeO); 3.68–3.95 (*m*, 2 H–C(5')); 0.91 (*s*, *t*-Bu); 0.15 (*s*, MeSi); 0.14 (*s*, MeSi). Anal. calc. for $C_{43}H_{46}IN_5O_5$ (867.9): C 59.51, H 5.34, N 8.07; found: C 59.65, H 5.55, N 8.10.

25. *9-{2'-O-[(*tert*-Butyl)dimethylsilyl]-3'-deoxy-3'-iodo-5'-O-(monomethoxytrityl)-β-D-xylofuranosyl}adenine* (**26**). As described in *Exper. 5*, with dioxane (8 ml) conc. NH_3 (10 ml), and 0.1 g (0.115 mmol) of **25**, 22 h. The residue was purified by prep. TLC (silica gel (40 × 20 × 0.2 cm), $CHCl_3$/MeOH 50:1) and reprecipitation from little $CHCl_3$/hexane: 0.082 g (93%) of **26**. Amorphous powder. UV (MeOH): 233 (**4**.23), 259 (4.22). ^{1}H-NMR ($CDCl_3$): 8.30 (*s*, H–C(8)); 8.07 (*s*, H–C(2)); 7.52–7.21 (*m*, 12 arom. H); 6.84 (*d*, 2 H, *o* to MeO); 5.97 (*d*, *J* = 1.8, H–C(1')); 5.06 (*m*, H–C(2')); 4.08 (*m*, H–C(3'), H–C(4')); 3.79 (*s*, MeO); 3.64 (*dd*, 1 H–C(5')); 3.27 (*dd*,

1 H–C(5′)); 3.27 (*dd*, 1 H–C(5′)); 0.89 (*s*, *t*-Bu); 0.13 (*s*, MeSi); 0.08 (*s*, MeSi). Anal. calc. for $C_{36}H_{42}IN_5O_4Si$ (763.8): C 56.61, H 5.54, N 9.17; found: C 56.90, H 5.82, N 8.88.

26. N^6-*Benzoyl-9-{2′-O-[(*tert*-butyl)dimethylsilyl]-3′-deoxy-3′-iodo-β-*D*-xylofuranosyl}adenine* (**27**). As described in *Exper. 6*, with 0.32 g (0.37 mmol) of **25** in 80% aq. AcOH (10 ml); workup with $CHCl_3$ (100 ml) and H_2O (2 × 100 ml); chromatography (silica gel (32 × 2 cm), $CHCl_3$/MeOH 100:1) gave 0.213 g (95%) of **27**. Amorphous solid. UV (MeOH): 229 (sh, 4.16), 279 (4.34). ^{1}H-NMR ($CDCl_3$): 9.20 (*s*, NH); 8.79 (*s*, H–C(8)); 8.07 (*s*, H–C(2)); 8.00 (*s*, 2 H, bz); 7.55 (*m*, 3 H, bz); 5.73 (*t*, OH–C(5′)); 5.63 (*d*, J = 6.1, H–C(1′)); 5.20 (*m*, H–C(2′)); 4.64–4.32 (*m*, H–C(3′), H–C(4′)); 4.09 (*m*, 2 H–C(5′)); 0.78 (*s* tert-Bu); 0.04 (*s*, MeSi); –0.55 (*s*, MeSi). Anal. calc. for $C_{23}H_{30}IN_5O_4Si$ (595.5): C 46.39, H 5.08, N 11.76; found: C 46.27, H 5.07, N 11.84.

27. N^6-{*[2-(4-Nitrophenyl)ethoxy]carbonyl*}-*9-(3′-deoxy-3′-iodo-β-*D*-xylofuranosyl)adenine* (**28**). After evaporation of a soln. of **20** (1.9 g, 5 mmol) in dry pyridine (30 ml), the residue was redissolved in 30 ml of dry pyridine and treated with Me_3SiCl for 15 min at r.t. with stirring. Then, 3.11 g (10 mmol) of 1-methyl-3-{[2-(4-nitrophenyl)ethoxy]carbonyl}imidazolium chloride [25] were added and stirred for 4 days. MeOH (20 ml) was added and after another 4 h stirring, the soln. evaporated and coevaporated with toluene (2 × 20 ml). The residue was dissolved in AcOEt (250 ml) and extracted with H_2O (250 ml). The org. layer was dried (Na_2SO_4) and evaporated and the solid purified by chromatography (silica gel (35 × 3 cm), $CHCl_3$/MeOH 50:1) and recrystallization from MeOH: 2.06 g (72%) of **28**. Colorless crystals. M.p. 117°. UV (MeOH): 267 (4.44). ^{1}H-NMR ((D_6)DMSO): 10.57 (br. *s*, NH); 8.63 (*s*, H–C(8), H–C(2)); 8.16 (*d*, 2 H, *o* to NO_2); 7.62 (*d*, 2 H *m* to NO_2); 6.30 (*d*, OH–C(2′)); 5.90 (*d*, J = 4.9, H–C(1′)); 5.25 (*t*, OH–C(5′)); 5.03 (*m*, H–C(2′)); 4.50 (*m*, H–C(3′)); 4.38 (*t*, CH_2CH_2O); 4.10 (*m*, H–C(4′)); 3.77 (*m*, 2 H–C(5′)); 3.11 (*t*, CH_2CH_2O). Anal. calc. for $C_{19}H_{19}IN_6O_7 \cdot H_2O$ (588.3): C 38.79, H 3.59, N 14.28; found: C 38.94, H 3.43, N 14.14.

28. N^6-{*[2-(4-Nitrophenyl)ethoxy]carbonyl*}-*9-[3′-deoxy-3′-iodo-5′-O-(monomethoxytrityl)-β-*D*-xylofuranosyl]adenine* (**29**). As described in *Exper. 3*, with pyridine (6 ml), 0.57 g (1 mmol) of **28** and 0.37 (1.2 mmol) of MeOTrCl 26 h; chromatography (silica gel (40 × 2 cm), CH_2Cl_2/$CHCl_3$ 1:1) gave 0.71 g (84%) of **29**. Amorphous solid. UV (MeOH): 235 (4.29), 267 (4.49), 273 (sh, 4.42). ^{1}H-NMR ($CDCl_3$): 8.72 (*s*, H–C(8)); 8.18 (*m*, H–C(2), 2 H, *o* to NO_2); 7.39–7.19 (*m*, 14 arom. H); 6.77 (*d*, 2 H, *o* to MeO); 5.92 (*s*, H–C(1′)); 5.13 (*m*, H–C(2′)); 4.52 (*t*, CH_2CH_2), 4.41 (*m*, H–C(3′)); 4.30 (*m*, H–C(4′)); 3.77 (*s*, MeO); 3.48 (2*dd*, 2 H–C(5′)); 3.14 (*t*, CH_2CH_2O). Anal. calc. for $C_{39}H_{35}IN_6O_8$ (842.6): C 55.59, H 4.19, N 9.97; found: C 55.38, H 4.23, N 9.64.

29. N^6-{*[2-(4-Nitrophenyl)ethoxy]carbonyl*}-*9-{2′-O-[(*tert*-butyl)dimethylsilyl]-3′-deoxy-3′-iodo-5′-O-(monomethoxytrityl)-β-*D*-xylofuranosyl}adenine* (**30**). As described in *Exper. 4*, with pyridine (3 ml), 0.548 g (0.65 mmol) of **29**, 0.133 g (1.95 mmol) of imidazole, and 0.147 g (0.98 mmol) of (*t*-Bu)Me_2SiCl, 31 h; after addition of MeOH (5 ml) and evaporation, workup with $CHCl_3$ (30 ml) and phosphate buffer pH 7; purification by chromatography (silica gel (34 × 2 cm), CH_2Cl_2/$CHCl_3$ 2:1): 0.53 g (85%) of **30**. Solid foam. UV (MeOH): 235 (4.34), 267 (4.54), 275 (sh, 4.46). ^{1}H-NMR ($CDCl_3$): 8.71 (*s*, H–C(8)); 8.18 (*m*, H–C(2), 2 H, *o* to NO_2); 7.50–7.27 (*m*, 14 arom. H); 6.84 (*d*, 2 H, *o* to MeO); 6.01 (*d*, H–C(1′)); 5.06 (*m*, H–C(2′)); 4.51 (*t*, CH_2CH_2O); 4.09 (*m*, H–C(3′), H–C(4′)); 3.79 (*s*, MeO); 3.67–3.26 (2*dd*, 2 H–C(5′)); 3.14 (*t*, CH_2CH_2O); 0.89 (*s*, *t*-Bu); 0.13 (*s*, MeSi); 0.10 (*s*, MeSi). Anal. calc. for $C_{45}H_{49}IN_6O_8Si$ (956.9): C 56.48, H 5.16, N 8.78; found: C 56.67, H 4.96, N 8.71.

30. N^6-*Benzoyl-9-(3′-fluoro-3′-deoxy-β-*D*-xylofuranosyl)adenine* (**31**). As described in *Exper. 2*, with 0.228 g (0.85 mmol) of 9-(3′-deoxy-3′-fluoro-β-D-xylofuranosyl)adenine [22], pyridine (4 ml), Me_3SiCl (0.6 ml), benzoyl chloride (0.5 ml; 2 h), H_2O (0.85 ml; 5 min), and conc. NH_3 (1.7 ml). The mixture was stirred at r.t. for 30 min, evaporated, and the product purified by chromatography ($CHCl_3$/MeOH 95:5) and recrystallization from MeOH/Et_2O: 0.247 g (78%) of **31**. Colorless crystals. M.p. 189–190°. UV (MeOH): 279 (4.36). ^{1}H-NMR ((D_6)DMSO): 11.23 (*s*, NH); 8.77 (*s*, H–C(8)); 8.43 (*s*, H–C(2)); 8.02 (*m*, 2 arom. H); 7.59 (*m*, 3 arom. H); 6.38 (*d*, OH–C(2′)); 6.1 (*d*, J = 2.4, H–C(1′)); 5.13 (*m*, J(3′,F) = 52, H–C(3′)); 5.07 (*t*, OH–C(5′)); 4.83 (*m*, J(2′,F) = 15, H–C(2′)); 4.35 (*m*, J(4′,F) = 29, H–C(4′)); 3.76 (*m*, 2 H–C(5′)). Anal. calc. for $C_{17}H_{16}FN_5O_4$ (373.3): C 54.96, H 4.32, N 18.76; found: C 54.68, H 4.54, N 18.61.

31. N^6-*Benzoyl-9-[3′-deoxy-3′-fluoro-5′-O-(monomethoxytrityl)-β-*D*-xylofuranosyl]adenine* (**32**). As described in *Exper. 3*, with 0.187 g (0.5 mmol) of **31**, 0.193 g (0.625 mmol) of MeOTrCl and pyridine (10 ml); after addition of MeOH (1 ml), evaporation, and coevaporation with toluene, the product was purified by chromatography (silica gel, $CHCl_3$, then $CHCl_3$/MeOH 98.5:1.5) and precipitation from $CHCl_3$/Et_2O: 0.274 g (85%) of **32**. Amorphous solid. UV (MeOH): 278 (4.34). ^{1}H-NMR ($CDCl_3$): 8.95 (*s*, NH); 8.75 (*s*, H–C(8)); 8.06 (*s*, H–C(2)); 7.56–7.97 (*m*, 5 H, Ph); 7.18–7.50 (*m*, 12 H, MeO*Tr*); 6.82 (*d*, 2 H, *o* to MeO); 6.14 (*d*, J = 1.8, H–C(1′)); 5.13 (*m*, J(3′,F) = 52, H–C(3′)); 4.74 (*m*, J(2′,F) = 16, H–C(2′)); 4.66 (*m*, J(4′,F) = 26, H–C(4′)); 3.78 (*s*, MeO); 4.44 (*d*,

OH–C(2')); 3.60 (*m*, 1 H–C(5')); 3.49 (*m*, 1 H–C(5')). Anal. calc. for $C_{37}H_{32}FN_5O_5$ (645.7): C 68.83, H 5.00, N 10.85; found: C 68.68, H 5.33, N 10.41.

32. *N^6-Benzoyl-9-{2'-O-[(tert-butyl)dimethylsilyl]-3'-deoxy-3'-fluoro-β-D-xylofuranosyl}adenine* (**33**). As described in *Exper. 4*, with 0.226 g (0.35 mmol) of **32**, 80 mg (0.52 mmol) of (*t*-Bu)Me_2SiCl, 72 mg (1.05 mmol) of imidazole, and pyridine (5 ml), 48 h; after evaporation and coevaporation with toluene, workup with $CHCl_3$ (20 ml) and phosphate buffer pH 7.0 (2 × 20 ml). The resulting oil in CH_2Cl_2/MeOH 4:1 (5 ml) was treated with 0.1 g of TsOH · H_2O. After 30 min, the mixture was diluted with $CHCl_3$ (10 ml), washed with phosphate buffer pH 7 (3 × 20 ml), dried, and evaporated. The resulting oil was purified by prep. TLC ($CHCl_3$/MeOH 95:5) and reprecipitated from Et_2O/hexane: 130 mg (76%) of **33**. Amorphous solid. UV (MeOH): 278 (4.33). ^{1}H-NMR ($CDCl_3$): 8.94 (*s*, NH); 8.81 (*s*, H–C(8)); 8.13 (*s*, H–C(2)); 8.52–8.00 (*m*, 5 H, Ph); 6.00 (*d*, *J* = 4.0, H–C(1')); 5.08 (*m*, *J*(3',F) = 56, H–C(3')); 4.94 (*m*, *J*(2',F) = 14, H–C(2')); 4.53 (*m*, *J*(4',F) = 20, H–C(4')); 4.04 (*m*, 2 H–C(5')); 3.46 (*t*, OH–C(5')); 0.84 (*s*, *t*-Bu); 0.04 (*s*, MeSi); –0.04 (*s*, MeSi). Anal. calc. for $C_{23}H_{30}FN_5O_4Si \cdot 0.5\ H_2O$ (497.5): C 55.52, H 6.28, N 14.08; found: C 55.73, H 6.28, N 14.03.

33. *9-(3'-Azido-3'-deoxy-β-D-xylofuranosyl)-N^6-benzoyladenine* (**34**). As described in *Exper. 2*, with 0.292 g (1 mmol) of 9-(3'-azido-3'-deoxy-β-D-xylofuranosyl)adenine [22], pyridine (5 ml), 0.7 ml of Me_3SiCl, benzoyl chloride (0.6 ml; 2 h), H_2O (1 ml; 5 min), conc. NH_3 (2 ml). The mixture was stirred at r.t. for 30 min and evaporated and the product purified by chromatography (silica gel, $CHCl_3$/MeOH 95:5) and recrystallization from MeOH/H_2O: 0.32 g (76%) after drying at 50° *in vacuo*. Colorless crystals. M.p. 168° (soften), 178° (dec.). UV (MeOH): 280 (4.35). ^{1}H-NMR ((D_6)DMSO): 11.24 (*s*, NH); 8.77 (*s*, H–C(8)); 8.64 (*s*, H–C(2)); 8.04–7.59 (*m*, 5 H, bz); 6.31 (*d*, OH–C(2')); 6.01 (*d*, *J* = 4.6, H–C(1')); 5.17 (*t*, OH–C(5')); 4.84 (*m*, H–C(2')); 4.39 (*m*, H–C(3'), H–C(4')); 3.70 (*m*, 2 H–C(5')). Anal. calc. for $C_{17}H_{16}N_8O_4 \cdot 0.5\ H_2O$ (405.4): C 50.37, H 4.22, N 27.64; found: C 50.38, H 4.00, N 27.54.

34. *9-[3'-Azido-3'-deoxy-5'-O-(monomethoxytrityl)-β-D-xylofuranosyl]-N^6-benzoyladenine* (**35**). As described in *Exper. 3*, with 0.243 g (0.6 mmol) of **34**, 0.222 g (0.72 mmol) of MeOTrCl, and pyridine (10 ml); after addition of MeOH (1 ml), evaporation, and coevaporated with toluene, the product was purified by chromatography (silica gel, $CHCl_3$, then $CHCl_3$/MeOH 99:1) and reprecipitation from Et_2O/hexane: 0.355 g (88%) of **35**. Amorphous solid. UV (MeOH): 279 (4.33). ^{1}H-NMR ($CDCl_3$): 8.88 (*s*, NH); 8.79 (*s*, H–C(8)); 8.13 (*s*, H–C(2)); 7.97–7.52 (*m*, 5 H, Ph); 7.15–7.35 (*m*, 12 H, MeO*Tr*); 6.75 (*d*, 2 H, *o* to MeO); 5.96 (*d*, *J* = 4.3, H–C(1')); 5.09 (*d*, OH–C(2')); 4.95 (*m*, H–C(2')); 4.57 (*m*, H–C(4')); 4.39 (*m*, H–C(3')); 3.77 (*s*, MeO); 3.46 (*m*, H–C(5')); 3.32 (*m*, H–C(5")). Anal. calc. for $C_{37}H_{32}N_8O_4$ (668.7): C 66.46, H 4.82, N 16.76; found: C 66.05, H 4.86, N 16.06.

35. *9-{3'-Azido-2'-O-[(tert-butyl)dimethylsily]-3'-deoxy-β-D-xylofuranosyl}-N^6-benzoyladenine* (**36**). As described in *Exper. 4*, with 0.267 g (0.4 mmol) of **35**, 90 mg (0.6 mmol) of (*t*-Bu)MeSiCl, 82 mg (1.2 mmol) of imidazole, and pyridine (5 ml), 48 h; after evaporation and coevaporation with toluene, workup with $CHCl_3$ (20 ml) and phosphate buffer pH 6.0 (2 × 20 ml). The residue was treated with TsOH · H_2O as described in *Exper. 32*; recrystallization from Et_2O gave 0.159 g (78%) of **36**. Colorless crystals. M.p. 145–146°. UV (MeOH): 279 (4.36). ^{1}H-NMR ($CDCl_3$): 8.96 (*s*, NH); 8.82 (*s*, H–C(8)); 8.04 (*s*, H–C(2)); 7.99–7.55 (*m*, 5 H, Ph); 5.74 (*d*, *J* = 6.7, H–C(1')); 5.42 (*t*, OH–C(5')); 5.08 (*m*, H–C(2')); 4.44 (*m*, H–C(4')); 4.25 (*m*, H–C(3')); 3.94 (*m*, 2 H–C(5')); 0.79 (*s*, *t*-Bu); 0.00 (*s*, MeSi); –0.50 (*s*, MeSi). Anal. calc. for $C_{23}H_{30}N_8O_4Si$ (510.6): C 54.10, H 5.92, N 21.94; found: C 54.20, H 5.90, N 21.61.

36. *2',3'-Anhydro-N^6-benzoyladenosine* (**37**). As described in *Exper. 2*, with 0.43 g (1.73 mmol) of 2',3'-anhydroadenosine [22] [23], 1.1 ml (8.63 mmol) of Me_3SiCl, pyridine (9 ml), benzoyl chloride (1 ml, 8.63 mmol; 2 h); H_2O (1.8 ml; 5 min) and aq. NH_3 (3.4 ml; 30 min); after evaporation, workup with AcOEt (100 ml) and H_2O (2 × 100 ml), coevaporation with toluene, and chromatography ($CHCl_3$/MeOH 95:5): 0.464 g (76%) of **37**. M.p. 186–187°. UV (MeOH): 230 (sh, 4.11), 258 (sh, 4.06), 279 (4.29). ^{1}H-NMR ((D_6)DMSO): 11.21 (*s*, NH); 8.76 (*s*, H–C(8)); 8.64 (*s*, H–C(2)); 8.03 (*m*, 2 H, bz); 7.64–7.51 (*m*, 3 H, bz); 6.33 (*s*, H–C(1')); 5.06 (*t*, OH–C(5')); 4.55 (*m*, H–C(2')); 4.24 (*m*, H–C(3')); 4.21 (*m*, H–C(4')); 3.53 (*m*, 2 H–C(5')). Anal. calc. for $C_{17}H_{15}N_5O_4$ (353.3): C 57.79, H 4.28, N 19.82; found: C 57.74, H 4.30, N 19.67.

37. *2',3'-Anhydro-N^6-benzoyl-5'-O-(monomethoxytrityl)adenosine* (**38**). As decribed in *Exper. 9*, with 1M Bu_4NF in THF (35 ml) and 0.15 mmol of *N^6*-benzoyl-9-{2'-*O*-[(*tert*-butyl)dimethylsilyl]-3'-deoxy-3'-halo-5'-*O*-(monomethoxytrityyl)-β-D-xylofuranosyl}adenine (**4**, **14**, or **25**), 48 h; workup with $CHCl_3$ (50 ml) and H_2O (50 ml); purification by prep. TLC (silica gel (40 × 20 × 0.2 cm), $CHCl_3$/MeOH 50:1; elution with AcOEt) and reprecipitation from $CHCl_3$/hexane: 92% (from **4**), 85% (from **14**), and 83% (from **25**) of **38**. Amorphous powder. UV (MeOH): 229 (4.49), 260 (sh, 4.14), 280 (4.32). ^{1}H-NMR ($CDCl_3$): 9.11 (br. *s*, NH); 8.72 (*s*, H–C(8)); 8.08 (*m*, 3 H, H–C(2), bz); 7.65 (*m*, 3 H, bz); 7.30 (*m*, 12 H, MeO*Tr*); 6.79 (*d*, 2 H, *o* to MeO); 6.18 (*d*, H–C(1')); 4.53 (*m*,

H–C(2'), H–C(3')); 4.13 (*m*, H–C(4')); 3.75 (*s*, MeO); 3.44 (*dd*, 1 H–C(5')); 3.30 (*dd*, 1 H–C(5')). Anal. calc. for $C_{37}H_{31}N_5O_5$ (625.7): C 71.03, H 4.99, N 11.19; found: C 70.84, H 5.07, N 10.98.

38. *2',3'-Anhydro-5'-O-(monomethoxytrityl)adenosine* (**39**). As described in *Exper. 5*, with dioxane (2 ml), 64 mg (0.1 mmol) of **38**, and conc. NH_3 (8 ml). After evaporation and coevaporation with toluene (2 × 10 ml), the product was purified by prep. TLC (silica gel (40 × 20 × 0.2 cm), $CHCl_3$/MeOH 100:3 (two developments); elution with AcOEt) and reprecipitation from $CHCl_3$/hexane: 43 mg (81%) of **39**. Amorphous powder. UV (MeOH): 233 (4.22), 259 (4.13). ^{1}H-NMR ($CDCl_3$): 8.23 (*s*, H–C(8)); 7.86 (*s*, H–C(2)); 7.30 (*m*, 12 H, MeO*Tr*); 6.82 (*d*, 2 H, *o* to MeO); 6.20 (*s*, H–C(1')); 5.76 (br. *s*, NH_2); 4.56 (*m*, H–C(2')); 4.51 (*m*, H–C(3')); 4.17 (*m*, H–C(4')); 3.84 (*s*, MeO); 3.44 (*dd*, 1 H–C(5')); 3.28 (*dd*, 1 H–C(5')). Anal. calc. for $C_{30}H_{27}N_5O_4$ (521.6): C 69.09, H 5.22, N 13.43; found: C 68.92, H 5.25, N 13.22.

39. N^6-*Benzoyl-9-{2'-O-[(*tert*-butyl)dimethylsilyl]-3'-deoxy-5'-O-(monomethoxytrityl)-β*-D-glycero-*pent-3'-enofuranosyl}adenine* (**40**) *and* N^6-*Benzoyl-9-[3'-deoxy-5'-O-(monomethoxytrityl)-β*-glycero-*pent-3'-enofuranosyl]adenine* (**41**). A soln. of 0.33 g (0.4 mmol) of **14** or of 0.416 g (0.48 mmol) of **25** in dry pyridine (20 ml) was evaporated and the residue treated with 0.5M DBU in dry pyridine (130 ml) with stirring at r.t. for 24 h. After neutralization with AcOH (3.75 ml) in dry pyridine (66 ml), each solution was evaporated and the residue partitioned thrice between $CHCl_3$ (50 ml) and 0.15M KH_2PO_4 (50 ml). The org. layers were dried (Na_2SO_4) and evaporated and each residue chromatographed (silica gel (27 × 4 cm)), **40** eluting with CH_2Cl_2/$CHCl_3$ 2:1, and after 1 l of eluat, **41** with $CHCl_3$/MeOH 100:1: 0.236 g (80%) of **40** and 0.04 g (15%) of **41** from **14**; 0.204 g (49%) of **40** and 0.103 g (32%) of **41** from **25**. Amorphous solids.

Compound **40**: UV (MeOH): 230 (4.47), 279 (4.35). ^{1}H-NMR ($CDCl_3$): 8.91 (br. *s*, NH); 8.81 (*s*, H–C(8)); 8.10 (*s*, H–C(2)); 8.04 (*m*, 2 H, bz); 7.60–7.24 (*m*, 15 H, bz, MeO*Tr*); 6.82 (*d*, 2 H, *o* to MeO); 6.48 (*d*, *J* = 1.5, H–C(1')); 5.37 (*s*, H–C(3')); 5.17 (*m*, H–C(2')); 3.77 (*s*, MeO, 2 H–C(5')); 0.88 (*s*, *t*-Bu); 0.09 (*s*, MeSi); 0.07 (*s*, MeSi). Anal. calc. for $C_{43}H_{45}N_5O_5Si$ (739.9): C 69.80, H 6.13, N 9.46; found: C 69.87, H 5.95, N 9.65.

Compound **41**: UV (MeOH): 230 (4.46), 279 (4.34). ^{1}H-NMR ($CDCl_3$): 9.05 (br. *s*, NH); 8.78 (*s*, H–C(8)); 8.03 (*m*, 2 H, bz); 7.99 (*s*, H–C(2)); 7.60–7.20 (*m*, 15 H, bz, MeO*Tr*); 6.83 (*d*, 2 H, *o* to MeO); 6.52 (*d*, *J* = 1.5 Hz, H–C(1')); 5.46 (*s*, H–C(3')); 5.20 (*m*, H–C(2')); 3.82 (*s*, 2 H–C(5')); 3.78 (*s*, MeO). Anal. calc. for $C_{37}H_{31}N_5O_5$ (625.7): C 71.03, H 4.99, N 11.19; found: C 70.81, H 5.05, N 11.09.

40. *9-{2'-O-[(*tert*-Butyl)dimethylsilyl]-3'-deoxy-5'-O-(monomethoxytrityl)-β*-D-glycero-*pent-3'-enofuranosyl}adenine* (**42**). 40.1. As described in *Exper. 5*, with dioxane (1.5 ml), 54 mg (0.07 mmol) of **40**, and conc. NH_3 (6 ml), 4 days. The product was purified by prep. TLC (silica gel (40 × 20 × 0.2 cm), $CHCl_3$/MeOH 50:1; elution with $CHCl_3$/MeOH 4:1) and reprecipitation from little $CHCl_3$/hexane (50 ml): 35 mg (75%) of **40**. Amorphous powder.

40.2. As described in *Exper. 39*, with 0.144 g (0.15 mmol) of **30**, pyridine (20 ml), 0.5M DBU in pyridine (50 ml), 21 h; workup with AcOH (1.4 ml) in pyridine (25 ml), evaporation and coevaporation with toluene (2×), $CHCl_3$ (50 ml) and 0.15M K_2HPO_4; chromatography (silica gel (33 × 2 cm), $CHCl_3$ (300 ml), $CHCl_3$/MeOH 100:1 (200 ml), and $CHCl_3$/MeOH 50:1 (100 ml)) gave 0.09 g (84%) of **40**. Solid foam. UV (MeOH): 233 (4.26), 259 (4.21). ^{1}H-NMR ($CDCl_3$): 8.36 (*s*, H–C(8)); 7.86 (*s*, H–C(2)); 7.46–7.20 (*m*, 12 H, MeO*Tr*); 6.82 (*d*, 2 H, *o* to MeO); 6.40 (*d*, *J* = 1.8, H–C(1')); 5.81 (br. *s*, NH_2); 5.35 (*s*, H–C(3')); 5.17 (*m*, H–C(2')); 3.77 (*s*, MeO); 3.75 (*s*, 2 H–C(5')); 0.88 (*s*, *t*-Bu); 0.08 (*s*, MeSi); 0.06 (*s*, MeSi). Anal. calc. for $C_{36}H_{41}N_5O_4Si$ (635.8): C 68.00, H 6.50, N 11.01; found: C 68.10, H 6.20, N 10.96.

41. N^6-*Benzoyl-9-{2'-O-[(*tert*-butyl)dimethylsilyl]-3'-deoxy-β*-D-glycero-*pent-3'-enofuranosyl}adenine* (**43**). As described in *Exper. 6*, with 80% AcOH (16 ml) and 0.26 g (0.35 mmol) of **40**, at 4°; workup with $CHCl_3$ (50 ml) and phosphate buffer pH 7 (50 ml), coevaporation with pyridine and then toluene; chromatography (silica gel (38 × 2 cm), $CHCl_3$ (300 ml), $CHCl_3$/MeOH 100:1) and reprecipitation from $CHCl_3$/hexane gave 0.12 g (74%). Amorphous powder. UV (MeOH): 232 (sh, 4.33), 278 (4.59). ^{1}H-NMR ($CDCl_3$): 9.23 (br. *s*, NH); 8.77 (*s*, H–C(8)); 8.02 (*m*, 3 H, H–C(2); bz); 7.62–7.47 (*m*, 3 H, bz); 6.44 (*d*, *J* = 1.8, H–C(1')); 5.28 (*s*, H–C(3')); 5.20 (*m*, H–C(2')); 4.28 (*s*, 2 H–C(5')); 0.89 (*s*, *t*-Bu); 0.05–0.03 (*m*, Me_2Si).

42. N^6-*Benzoyl-3'-O-[(*tert*-butyl)dimethylsilyl]-5'-O-(monomethoxytrityl)adenosine 2'-(2,5-Dichlorophenyl 2-Cyanoethyl Phosphate)* (**44**). A mixture of 1.175 g (16 mmol) of 1,2,4-triazole and 2.1 g (7.5 mmol) of 2,5-dichlorophenyl dichlorophosphate in dry pyridine (20 ml) was stirred for 10 min and then cooled to 0°. A soln. of 3.79 g (5 mmol) of N^6-benzoyl-3'-*O*-[(*tert*-butyl)dimethylsily]-5'-*O*-(monomethoxytrityl)adenosine [26] [27] in dry pyridine (20 ml) was added dropwise. After stirring for 30 min at 0°, 2.04 g (30 mmol) of 3-hydroxypropanenitrile were added. The mixture was warmed to r.t., stirred 12 h, then diluted with $CHCl_3$ (200 ml), and treated twice with phosphate buffer pH 7 (200 ml). The aq. layer was extracted again with $CHCl_3$, the combined org. phase dried (Na_2SO_4), evaporated, and coevaporated with toluene, and the residue chromatographed (silica gel (37 × 4 cm),

CH_2Cl_2 (2 l) and CH_2Cl_2/MeOH 50:1). The product fraction was rechromatrographed ($CHCl_3$ (1 l), $CHCl_3$/MeOH 100:1): 4.37 g (84%) of a solid foam.

43. N^6-*Benzoyl-3'-*O*-[(*tert*-butyl)dimethylsily]-5'-*O*-(monomethoxytrityl)adenosine 2'-(2,5-Dichlorophenyl Triethylammonium Phosphate)* (**45**). A mixture of pyridine (12.5 ml), Et_3N (12.5 ml), H_2O (0.25 ml) and 1.25 g (1.2 mmol) of **44** was stirred for 1.5 h at r.t., then evaporated, and coevaporated with toluene (2 × 30 ml). The residue was chromatographed (silica gel (24 × 4 cm), $CHCl_3$/MeOH 50:1 (500 ml), then $CHCl_3$/MeOH 25:1): 1.14 g (87%) of solid foam.

44. N^6-*Benzoyl-3'-*O*-[(*tert*-butyl)dimethylsilyl]adenosine 2'-(2,5-Dichlorophenyl 2-Cyanoethyl Phosphate)* (**46**). To 0.96 g of TsOH·H_2O in CH_2Cl_2 (38 ml) and MeOH (10 ml), 2.28 g (2.2 mmol) of **44** were added and stirred at r.t. for 30 min. The mixture was diluted with $CHCl_3$ (100 ml) and washed twice with phosphate buffer pH 7 (100 ml), the org. layer dried (Na_2SO_4) and evaporated, and the residue purified by chromatography (silica gel (38 × 4 cm), $CHCl_3$ (2 l), $CHCl_3$/MeOH 50:1): 1.5 g (89%) of solid foam.

45. N^6-*Benzoyl-3'-*O*-[(*tert*-butyl)dimethylsilyl]-5'-*O*-(monomethoxytrityl)adenylyl-{2'-[*O*^{P}-(2,5-dichlorophenyl)]→5'}-N^6-benzoyl-3'-*O*-[(*tert*-butyl)dimethylsilyl]adenosine 2'-(2,5-Dichlorophenyl 2-Cyanoethyl Phosphate)* (**47**). A mixture of 1.074 g (0.99 mmol) of **45** and 0.685 g (0.94 mmol) of **46** was coevaporated twice with dry pyridine (10 ml) and the residue dissolved in dry pyridine (12 ml). Then, 0.57 g (0.19 mmol) of 2,4,6-triisopropylbenzenesulfonyl chloride and 0.473 g (5.76 mmol) of *N*-methylimidazole were added and stirred at r.t. for 26 h. The mixture was diluted with $CHCl_3$ (100 ml) and shaken twice with phosphate buffer pH 7 (50 ml), the org. layer dried (Na_2SO_4), evaporated, and coevaporated with toluene (2 × 30 ml), and the residue purified by chromatography (silica gel, $CHCl_3$ (800 ml), then $CHCl_3$/MeOH 100:1): 1.3 g (81%) of a solid foam, after drying.

46. N^6-*Benzoyl-3'-*O*-[(*tert*-butyl)dimethylsilyl]-5'-*O*-(monomethoxytrityl)adenylyl-{2'-[*O*^{P}-(2,5-dichlorophenyl)]→5'}-N^6-benzoyl-3'-*O*-[(*tert*-butyl)dimethylsilyl]adenosine 2'-(2,5-Dichlorophenyl Triethylammonium Phospate)* (**48**). A mixture of 0.3 g (0.174 mmol) of **47** in pyridine (6 ml), Et_3N (6 ml), and H_2O (0.5 ml) was stirred at r.t. for 2 h, then evaporated, and coevaporated with toluene (2 × 20 ml). The residue was chromatographed (silica gel (16 × 2 cm), $CHCl_3$/MeOH 50:1): 0.247 g (79%) of a solid foam, after drying.

47. N^6-*Benzoyl-3'-*O*-[(*tert*-butyl)dimethylsilyl]-5'-*O*-(monomethoxytrityl)adenylyl-{2'-{*O*^{P}-[2-(4-nitrophenyl)ethyl]}→5'}-N^6-benzoyl-3'-*O*-[(*tert*-butyl)dimethylsilyl]adenylyl-{2'-{*O*^{P}-[2-(4-nitrophenyl)ethyl]}→5'}-N^6-benzoyl-9-{2'-*O*-[(*tert*-butyl)dimethylsilyl]-3'-chloro-3'-deoxy-β-D-xylofuranosyl}adenine* (**50**). A mixture of 0.23 g (0.13 mmol) of phosphodiester **49** [18], 0.06 g (0.12 mmol) of **6**, 0.07 ml (0.86 mmol) of *N*-methylimidazole, and 0.09 g (0.31 mmol) of 2,4,6-triisopropylbenzenesulfonyl chloride in dry pyridine (2 ml) was stirred for 37 h at r.t. The mixture was diluted with $CHCl_3$ (25 ml) and washed with H_2O (2 × 25 ml), the org. layer dried, evaporated, and coevaporated with toluene, and the resulting oil purified by prep. TLC (silica gel, $CHCl_3$/MeOH 99:1): 0.145 g (56%) of **50**. Amorphous powder. UV (MeOH): 229 (sh, 4.76), 260 (sh, 4.73), 278 (4.88). ^{1}H-NMR ($CDCl_3$): 9.13–9.06 (br. *s*, 3 H, NH); 8.74–8.61 (*m*, 3 H, H–C(8)); 8.24–7.94 (*m*, 13 arom. H); 7.57–7.10 (*m*, 25 arom. H); 6.76 (*d*, 2 H, *o* to MeO); 6.18 (*m*, 2 H, H–C(1')); 5.96 (*d*, 1 H, H–C(1')); 3.72 (*s*, MeO); 0.87–0.74 (*m*, 27 H, *t*-Bu); 0.09 to −0.09 (*m*, 18 H, MeSi). Anal. calc. for $C_{105}H_{120}ClN_{17}O_{23}P_2Si_3$ (2169.9): C 58.12, H 5.57, N 10.97; found: C 57.58, H 5.77, N 10.82.

48. N^6-*Benzoyl-3'-*O*-[(*tert*-butyl)dimethylsilyl]-5'-*O*-(monomethoxytrityl)adenylyl-{2'-[*O*^{P}-(2,5-dichlorophenyl)]→5'}-N^6-benzoyl-3'-*O*-[(*tert*-butyl)dimethylsilyl]adenylyl-{2'-[*O*^{P}-(2,5-dichlorophenyl)]→5'}-N^6-benzoyl-9-[3'-chloro-3'-deoxy-2'-*O*-(monomethoxytrityl)-β-D-xylofuranosyl]adenine* (**51**). As described in *Exper. 49*, 0.247 g (0.15 mmol) of phosphodiester **48** and 2.07 g (0.14 mmol) of **9** were reacted for 18 h at r.t.; prep. TLC ($CHCl_3$/MeOH 99:1 (3 developments)) gave 0.24 g (74%) of **51**. Amorphous powder. UV (MeOH): 255 (sh, 4.92), 260 (sh, 4.59), 280 (4.79). ^{1}H-NMR ($CDCl_3$): 9.10–9.02 (br. *s*, 3 H, NH); 8.89 (*m*, 1 H, H–C(8)); 8.56 (*m*, 2 H, H–C(8)); 8.56 (*m*, 2 H, H–C(8)); 8.22–8.09 (*m*, 3 H, H–C(2)); 8.00–7.95 (*m*, 6 arom. H); 7.59–6.87 (*m*, 39 arom. H); 3.73, 3.69 (2*s*, MeO); 0.88–0.76 (*m*, 18 H, *t*-Bu); 0.12 to −0.05 (*m*, 12 H, MeSi). Anal. calc. for $C_{115}H_{112}Cl_5N_{15}O_{20}P_2Si_2$ (2319.6): C 59.55, H 4.87, N 9.06; found: C 59.17, H 5.08, N 8.88.

49. N^6-*Benzoyl-3'-*O*-[(*tert*-butyl)dimethylsilyl]-5'-*O*-(monomethoxytrityl)adenylyl-{2'-{*O*^{P}-[2-(4-nitrophenyl)ethyl]}→5'}-N^6-benzoyl-3'-*O*-[(*tert*-butyl)dimethylsilyl]adenylyl-{2'-{*O*^{P}-[2-(4-nitrophenyl)ethyl]}→5'}-N^6-benzoyl-9-{3'-bromo-2'-*O*-[(*tert*-butyl)dimethylsilyl]-3'-deoxy-β-D-xylofuranosyl}adenine* (**52**). As described in *Exper. 47*, with 0.3 g (0.17 mmol) of **49**, 0.084 g (0.15 mmol) of **16**, 0.09 ml (1.12 mmol) of *N*-methylimidazole, 0.114 g (0.38 mmol) of 2,4,6-triisopropylbenzenesulfonyl chloride, and pyridine (2 ml), 40 h; prep. TLC (silica gel (40 × 20 × 0.2 cm), $CHCl_3$/MeOH 99:1) gave 0.182 g (55%) of **52**. Amorphous solid. UV (MeOH): 229 (sh, 4.78), 260 (4.75), 276 (4.89). ^{1}H-NMR ($CDCl_3$): 9.15 (br. *s*, 3 H, NH); 8.75 (br. *s*, 1 H, H–C(8)); 8.67 (*m*, 2 H, H–C(8)); 8.30–8.01 (*m*, 13 arom. H); 7.57–7.15 (*m*, 27 arom. H); 6.80 (*d*, 2 H, *o* to MeO); 6.20 (*m*, 2 H, H–C(1')); 5.96 (br. *s*,

1 H, H–C(1')); 3.74 (*s*, MeO); 0.91–0.82 (*m*, 27 H, *t*-Bu); 0.12 to –0.04 (*m*, 18 H, MeSi). Anal. calc. for $C_{105}H_{120}BrN_{17}O_{23}P_2Si_3$ (2214.3): C 56.95, H 5.46, N 10.75; found: C 56.99, H 5.36, N 10.65.

50. N^6-*Benzoyl-3'*-O-*[(*tert*-butyl)dimethylsilyl]-5'*-O-*(monomethoxytrityl)adenylyl-{2'-[*O^P*-(2,5-dichlorophenyl)]→5'}-*N^6*-benzoyl-3'*-O-*[(*tert*-butyl)dimethylsilyl]adenylyl-{2'-[*O^P*-(2,5-dichlorophenyl)]→5'}-*N^6*-benzoyl-9-{3'-bromo-2'*-O-*[(*tert*-butyl)dimethylsilyl]-3'-deoxy-β-*D*-xylofuranosyl}adenine* (**53**). As described in *Exper. 49*, with 0.28 g (0.17 mmol) of **48** and 0.084 g (0.15 mmol) of **16**, 22 h; prep. TLC gave 0.256 g (77%) of **53**. UV (MeOH): 279 (4.75). ^{1}H-NMR ($CDCl_3$): 9.10 (*m*, 3 H, NH); 8.73–8.53 (*m*, 3 H, H–C(8)); 8.30–8.05 (*m*, 3 H, H–C(2)); 7.98 (br. *s*, 6 arom. H); 7.57–6.94 (*m*, 27 arom. H); 6.74 (*d*, 2 H, *o* to MeO); 6.31–6.10 (*m*, 2 H, H–C(1')); 5.93 (*m*, 1 H, H–C(1')); 3.72 (*s*, MeO); 0.90–0.75 (*m*, 27 H, *t*-Bu); 0.14 to –0.06 (*m*, 18 H, MeSi). Anal. calc. for $C_{101}H_{110}Br\,Cl_4N_{15}O_{19}P_2Si_3$ (2216.1): C 55.20, H 5.00, N 9.48; found: C 54.97, H 5.10, N 8.98.

51. N^6-*Benzoyl-3'*-O-*[(*tert*-butyl)dimethylsilyl]-5'*-O-*(monomethoxytrityl)adenylyl-{2'-[*O^P*-(2,5-dichlorophenyl)]→5'}-*N^6*-benzoyl-3'*-O-*[(*tert*-butyl)dimethylsilyl]adenylyl-{2'-[*O^P*-(2,5-dichlorophenyl)]→5'}-*N^6*-benzoyl-9-[3'-bromo-3'-deoxy-2'*-O-*(monomethoxytrityl)-β-*D*-xylofuranosyl]adenine* (**54**). As described in *Exper. 49*, with 0.28 g (0.17 mmol) of **48** and 0.106 g (0.15 mmol) of **19**, 20 h; prep. TLC gave 0.266 g (75%) of **54**. Amorphous powder. UV (MeOH): 228 (sh, 4.92), 260 (sh, 4.58), 279 (4.76). ^{1}H-NMR ($CDCl_3$): 9.03 (*m*, 3 H, NH); 8.83 (*s*, 1 H, H–C(8)); 8.57 (*m*, 2 H, H–C(8)); 8.32–7.97 (*m*, 9 H, H–C(2), arom. H); 7.53–6.90 (*m*, 39 arom. H); 6.76 (*d*, 4 H, *o* to MeO); 6.52 (*m*, 1 H, H–C(1')); 6.19 (*m*, 2 H, H–C(1')); 3.73 (*s*, 1 MeO); 3.69 (*s*, 1 MeO); 0.88–0.76 (*m*, 18 H, *t*-Bu); 0.09 to –0.05 (*m*, 12 H, MeSi). Anal. calc. for $C_{115}H_{112}BrCl_4N_{15}O_{20}P_2Si_2$ (2364.1): C 58.43, H 4.78, N 8.89; found: C 58.04, H 4.88, N 8.80.

52. N^6-*Benzoyl-3'*-O-*[(*tert*-butyl)dimethylsilyl]-5'*-O-*(monomethoxytrityl)adenylyl-{2'-[*O^P*-(2,5-dichlorophenyl)]→5'}-*N^6*-benzoyl-3'*-O-*[(*tert*-butyl)dimethylsilyl]adenylyl-{2'-[*O^P*-(2,5-dichlorophenyl)]→5'}-*N^6*-benzoyl-9-{2'*-O-*[(*tert*-butyl)dimethylsilyl]-3'-deoxy-3'-iodo-β-*D*-xylofuranosyl}adenine* (**55**). As described in *Exper. 47*, with 0.06 g (0.1 mmol) of **27**, 0.17 g (0.1 mmol) of **48**, 0.05 ml (0.6 mmol) of *N*-methylimidazole, 0.06 g (0.2 mmol) of 2,4,6-triisopropylbenzenesulfonyl chloride, and pyridine (2 ml), 22 h; workup with $CHCl_3$ (50 ml) and H_2O (3 × 50 ml); column chromatography (silica gel, $CHCl_3$/MeOH 99:1) gave 0.170 g (75%) of **55**. Colorless solid. UV (MeOH): 227 (sh, 4.82), 260 (sh, 4.54), 279 (4.75). ^{1}H-NMR ($CDCl_3$): 9.13–8.98 (*m*, 3 H, NH); 8.73 (*s*, 1 H, H–C(8)); 8.60 (*s*, 1 H, H–C(8)); 8.55 (*s*, 1 H, H–C(8)); 8.32–8.03 (*m*, 3 H, H–C(2)); 8.01–7.96 (*m*, 6 arom. H); 7.60–7.45 (*m*, 9 arom. H); 7.35–6.90 (*m*, 18 arom. H); 6.75 (*d*, 2 H, *o* to MeO); 6.22 (*m*, 2 H, H–C(1')); 5.86 (*m*, 1 H, H–C(1')); 3.73 (*s*, MeO); 0.90–0.78 (*m*, 27 H, *t*-Bu); 0.13 to –0.06 (*m*, 18 H, MeSi). Anal. calc. for $C_{101}H_{110}Cl_4IN_{15}O_{19}P_2Si_3$ (2263.1): C 54.05, H 4.90, N 9.28; found: C 53.97, H 5.16, N 8.87.

53. N^6-*Benzoyl-3'*-O-*[(*tert*-butyl)dimethylsilyl]-5'*-O-*(monomethoxytrityl)adenylyl-{2'-{*O^P*-[2-(4-nitrophenyl)ethyl]}→5'}-*N^6*-benzoyl-3'*-O-*[(*tert*-butyl)dimethylsilyl]adenylyl-{2'-{*O^P*[2-(4-nitrophenyl)ethyl]}→5'}-*N^6*-benzoyl-9-{2'*-O-*[(*tert*-butyl)dimethylsilyl]-3'-deoxy-3'-fluoro-β-*D*-xylofuranosyl}adenine* (**56**). As described in *Exper. 47*, with 0.33 g (0.185 mmol) of **49**, 0.073 g (0.15 mmol) of **33**, pyridine (3 ml), 0.09 ml (1.12 mmol) of *N*-methylimidazole, and 0.112 g (0.37 mmol) of 2,4,6-triisopropylbenzenesulfonyl chloride, overnight; workup with $CHCl_2$ (20 ml) and H_2O (3 × 20 ml); column chromatography (silica gel, $CHCl_3$, then $CHCl_3$/MeOH 97:3) followed by prep. TLC (silica gel, $CHCl_3$/MeOH 95:5 (two developments)) yielded 0.168 g (52%) of **56**. Solid foam. UV (MeOH): 276 (4.87). ^{1}H-NMR ($CDCl_3$): 9.11–9.17 (*m*, 3 H, NH); 8.56–8.73 (*m*, 3 H, H–C(8)); 7.94–8.24 (*m*, 13 H, H–C(2), arom. H); 7.10–7.54 (*m*, 25 arom. H); 6.75 (*d*, 2 H, *o* to MeO); 6.04–6.20 (*m*, 3 H, H–C(1')); 3.70 (*s*, MeO); 0.86 (br. *s*, 27 H, *t*-Bu); 0.08 (br. *s*, 18 H, MeSi). Anal. calc. for $C_{105}H_{120}FN_{17}O_{23}P_2Si_3 \cdot 0.3\ CHCl_3$ (2184.2): C 57.50, H 5.53, N 10.86; found: C 57.65, H 5.38, N 10.75.

54. N^6-*Benzoyl-3'*-O-*[(*tert*-butyl)dimethylsilyl]-5'*-O-*(monomethoxytrityl)adenylyl-{2'-{*O^P*-[2-(4-nitrophenyl)ethyl]}→5'}-*N^6*-benzoyl-3'*-O-*[(*tert*-butyl)dimethylsilyl]adenylyl-{2'-{*O^P*-[2-(4-nitrophenyl)ethyl]}→5'}-*N^6*-benzoyl-9-{3'-azido-2'*-O-*[(*tert*-butyl)dimethylsilyl]-3'-deoxy-β-*D*-xylofuranosyl}adenine* (**57**). As described in *Exper. 53*, with 0.33 g (0.185 mmol) of **49** and 0.077 g (0.15 mmol) of **36**; column chromatography (silica gel, $CHCl_3$, then $CHCl_3$/MeOH 97:3) and prep. TLC ($CHCl_3$/MeOH 96:4) gave 0.22 g (67%) of **57** as solid foam, slightly contaminated by a trace of **49**. UV (MeOH): 276 (4.86). IR (KBr): 2100 (N_3). ^{1}H-NMR ($CDCl_3$): 9.15–9.20 (*m*, 3 H, NH, H–C(8)); 8.58–8.72 (*m*, 3 H, H–C(2)); 7.92–8.24 (*m*, 13 arom. H); 7.09–7.55 (*m*, 25 arom. H); 6.75 (*d*, 2 H, *o* to MeO); 6.20 (*m*, 1 H, H–C(1')); 5.90 (*m*, 2 H, H–C(1')); 3.72 (*s*, MeO); 0.86 (*m*, 27 H, *t*-Bu); 0.06 (*m*, 18 H, MeSi). Anal. calc. for $C_{105}H_{120}N_{20}O_{23}Si_3P_2$ (2176.4): C 57.95, H 5.56, N 12.87; found: C 57.42, H 5.48, N 12.60.

55. N^6-*Benzoyl-3'*-O-*[(*tert*-butyl)dimethylsilyl]-5'*-O-*(monomethoxytrityl)adenylyl-{2'-[*O^P*-(2,5-dichlorophenyl)]→5'}-*N^6*-benzoyl-3'*-O-*[(*tert*-butyl)dimethylsilyl]adenylyl-{2'-[*O^P*-(2,5-dichlorophenyl)]→5'}-2',3'-anhydro-*N^6*-benzoyladenosine* (**58**). As described in *Exper. 47*, with 0.083 g (0.23 mmol) of **37**, 0.4 g (0.23 mmol) of **48**, 0.11 ml (1.4 mmol) of *N*-methylimidazole, 0.142 g (0.47 mmol) of 2,4,6-triisopropylbenzenesulfonyl chloride,

and pyridine (4 ml), 23 h; after evaporation, and coevaporation with toluene (10 ml), workup with $CHCl_3$ (50 ml) and H_2O (2 × 50 ml); column chromatography (silica gel, $CHCl_3$/MeOH 99:1) and subsequent prep. TLC ($CHCl_3$/MeOH 49:1) gave 0.35 g (76%) of **58**. Solid foam. UV (MeOH): 224 (sh, 4.84), 260 (sh, 4.56), 280 (4.76). ^{1}H-NMR ($CDCl_3$): 9.25–9.01 (*m*, 3 H, NH); 8.69–8.53 (*m*, 3 H, H–C(8)); 8.23–8.11 (*m*, 3 H, H–C(2)); 8.01–7.96 (*m*, 6 arom. H); 7.57–6.95 (*m*, 27 arom. H); 6.76 (*d*, 2 H, *o* to MeO); 6.31 (*m*, 1 H, H–C(1′)); 6.23–6.04 (*m*, 2 H, H–C(1′)); 3.72 (*s*, MeO); 0.85–0.75 (*m*, 18 H, *t*-Bu); 0.07 to −0.05 (*m*, 12 H, MeSi). Anal. calc. for $C_{95}H_{95}Cl_4N_{15}O_{19}P_2Si_2$ (2010.8): C 56.74, H 4.76, N 10.45; found: C 56.14, H 4.88, N 10.24.

56. *Adenylyl-(2′→5′)-adenylyl-(2′→5′)-2′,3′-anhydroadenosine* (ammonium salt; **59**). 56.1. A soln. of 40 mg (20 μM) of **58** in dioxane (3 ml) was diluted with conc. NH_3 (17 ml) and kept for 3 days at r.t. After evaporation and coevaporation with pyridine (3 × 5 ml), the residue was diluted with 1M Bu_4NH in THF (20 ml) and again kept for 3 days at r.t. Evaporation and coevaporation with toluene gave a solid which was stirred at r.t. for 17 h in 80% AcOH (25 ml). After another evaporation and coevaporation with H_2O (3 × 10 ml), the residue was purified by *DEAE-Sephadex* column chromatography (linear gradient of 0–0.3M Et_3NHHCO_3) the trimer **59** being eluted with 0.165M Et_3NHHCO_3. Evaporation and several coevaporations with H_2O yielded 520 *OD* (78%) of **59** (triethylammonium salt). This material was transformed into the ammonium salt by paper chromatography using i-PrOH/conc. NH_3/H_2O 55:10:35. Elution with 1% NH_3 soln. and lyophilization yielded 447 *OD* (67%) of **59**·2NH_3 as amorphous powder. TLC (cellulose; i-PrOH/conc. NH_3/H_2O 55:10:35): R_f 0.41. UV (H_2O): 258; hypochromicity: 20.6%. ^{1}H-NMR (D_2O): 8.04, 7.96, 7.93 (3*s*, 3 H, H–C(8)); 7.70, 7.67, 7.56 (3*s*, 3 H, H–C(2)); 5.95 (*s*, 1 H, H–C(1′)); 5.88 (*d*, J = 3.4, H–C(1′)); 5.57 (*s*, H–C(1′)).

56.2. A soln. of 21.7 mg (10 μM) of **52** in 0.5N DBU in dry pyridine (6.6 ml) was stirred at r.t. for 24 h. The mixture was neutralized with 1M AcOH in pyridine (3.3 ml) and then evaporated. The residue was dissolved in conc. NH_3 (5 ml) and dioxane (2 ml) and stirred at r.t. for 2 days. After evaporation and coevaporation with dry pyridine (3 × 5 ml), the residue was treated with 1M Bu_4NF in THF (8 ml) for 3 days at r.t. with stirring. Evaporation and coevaporation with toluene (2 × 10 ml) gave solid residue coevaporation with toluene (2 × 10 ml) gave a solid residue which was treated with 80% AcOH (8 ml) at r.t. for 16 h. The mixture was again evaporated and several times coevaporated with H_2O (5 × 5 ml). The residue was dissolved in H_2O (20 ml), extracted with $CHCl_3$ (2 × 20 ml), and the aq. phase separated by *DEAE-Sephadex-A-25* column chromatography (H_2O (500 ml), then linear gradient of 0–0.3M Et_3NHHCO_3), the product being eluted with 0.165M Et_3NHHCO_3. Evaporation, several coevaporations with H_2O, and final lyophilization from H_2O (10 ml) yielded 273 *OD* (91%) of **59** (triethylammonium salt). Amorphous powder. The product was chromatographically and spectrophotometrically identical with the preceding material.

57. *Adenylyl-(2′→5′)-adenylyl-(2′→5′)-9-(3′-chloro-3′-deoxy-β-*D*-xylofuranosyl)adenine* (triethylammonium salt; **60**). A soln. of 35 mg (15 μM) of **51** in dioxane (25 ml) was triturated with conc. NH_3 (7.5 ml) at r.t. for 2 days. The mixture was evaporated and coevaporated with pyridine and THF and the residue treated with 1M Bu_4NF in THF (12 ml) for 48 h at r.t. After evaporation, the mixture was kept in 80% AcOH (3 ml) at r.t. for 48 h. The solvent was evaporated and the residue dissolved in H_2O (20 ml) and extracted with $CHCl_3$ (20 ml). Purification was performed on a *DEAE-Sephadex-A-25* column (linear gradient of 0–0.3M Et_3NHHCO_3), the product being eluted with 0.156M Et_3NHHCO_3. Evaporation and final lyophilization from H_2O gave 398 *OD* (87%) of **60**. Amorphous powder. UV (H_2O): 258; hypochromicity: 18.7%. ^{1}H-NMR (D_2O): 8.05 (*s*, 1 H, H–C(8)); 7.98 (*s*, 2 H, H–C(8)); 7.84 (*s*, 1 H, H–C(2)); 7.79 (*s*, 1 H, H–C(2)); 7.64 (*s*, 1 H, H–C(2)); 5.94 (*d*, J = 3.97, H–C(1′)); 5.79 (*d*, J = 2.74, H–C(1′)); 5.65 (*d*, J = 4.9, H–C(1′)).

58. *Adenylyl-(2′→5′)adenylyl-(2′→5′)-9-(3′-deoxy-3′-fluoro-β-*D*-xylofuranosyl)adenine* (ammonium salt; **61**). A soln. of 42 mg (20 μM) of **56** in 0.5M DBU in pyridine (16 ml) was stirred at r.t. for 24 h, then neutralized with 1M AcOH in pyridine (8 ml), evaporated, and coevaporated with pyridine. The oily residue in 1M Bu_4NF in THF (10 ml) was stirred for 48 h. After evaporation, treatment with conc. NH_3 (20 ml) for 48 h at r.t., evaporation, treatment with 80% AcOH (10 ml) at r.t. for 20 h, and evaporation, the residue in H_2O was chromatographed on a *DEAE-Sephadex-A-25* column (H_2O (500 ml), then linear gradient of 0–0.3M Et_3NHHCO_3). The main fraction was evaporated and coevaporated with H_2O (3 × 10 ml): 527 *OD* (80%) of **61** (triethylammonium salt) as solid. Further purification by paper chromatography in i-PrOH/conc. NH_3/H_2O 6:1:3, elution with H_2O, and lyophilization yielded the ammonium salt **61** as amorphous powder. UV (H_2O): 258; hypochromicity: 8.7%. ^{1}H-NMR (D_2O): 8.14 (*s*, 1 H, H–C(8)); 8.11 (*s*, 1 H, H–C(8)); 8.03 (*s*, 1 H, H–C(8)); 8.00 (*s*, 1 H, H–C(2)); 7.97 (*s*, 1 H, H–C(2)); 7.78 (*s*, 1 H, H–C(2)); 6.05 (*d*, J = 4.0, H–C(1′)); 5.96 (*d*, J = 3.67, H–C(1′)); 5.80 (*d*, J = 1.8, H–C(1′)).

59. *Adenylyl-(2′→5′)-adenylyl-(2′→5′)-9-(3′-azido-3′-deoxy-β-*D*-xylofuranosyl)adenine* (ammonium salt; **62**). Analogous to *Exper. 58*, 30 mg (14 μM) of **57** were treated subsequently with DBU, Bu_4NF, conc. NH_3, and

AcOH. *DEAE-Sephadex-A-25* chromatography in the usual manner gave 367 *OD* (86%) of **62** (triethylammonium salt). Conversion into the ammonium salt was performed by paper chromatography in i-PrOH/conc. NH_3H_2O 6:1:3, elution with 1% NH_3, and lyophilization: colorless powder. TLC (cellulose; i-PrOH/NH_3/H_2O 6:1:3): R_f 0.40. UV (H_2O): 258; hypochromicity: 18%. ^{1}H-NMR (D_2O): 7.96 (*s*, 1 H, H–C(8)); 7.88 (*s*, 2 H, H–C(8)); 7.73 (*s*, 1 H, H–C(2)); 7.67 (*s*, 1 H, H–C(2)); 7.54 (*s*, 1 H, H–C(2)); 5.86 (*d*, J = 3.97, H–C(1′)); 5.70 (*d*, J = 2.74, H–C(1′)); 5.58 (*d*, J = 5.5, H–C(1′)).

60. *Adenylyl-(2′→5′)-adenylyl-(2′→5′)-9-(3′-deoxy-β-*D-glycero-*pent-3′-enofuranosyl)adenine* (triethylammonium salt; **63**) *and Adenylyl-(2′→5′)-adenylyl-(2′→5′)-2′,3′-anhydroadenosine* (triethylammonium salt; **59**). A soln. of 22 mg (10 μM) of **52** in 0.5M DBU in dry pyridine (6.6 ml) was stirred at r.t. for 24 h, neutralized with 1M AcOH in pyridine (3.3 ml), and evaporated. The residue was treated with conc. NH_3 (5 ml) and dioxane (2 ml) for 28 h. After evaporation and coevaporation with pyridine (2 × 5 ml), the residue in 1M Bu_4NF in THF (8 ml) was stirred at r.t. for 48 h, the mixture again evaporated, the residue treated in 80% AcOH (8 ml) for 16 h, and the AcOH removed by evaporation and several coevaporations with H_2O (5 × 10 ml). The residue was dissolved in H_2O (20 ml) and extracted with $CHCl_3$ (2 × 20 ml) and the aq. phase separated by *DEAE-Sephadex-A-25* column chromatography (H_2O (1 l), then linear gradient of 0.03M Et_3NHHCO_3). The first product was eluted with 0.15M Et_3NHHCO_3, yielding 100 *OD* (36%) of **59** (triethylammonium salt), whereas the second product appeared with 0.165M Et_3NHHCO_3, giving 195 *OD* (54%) of **63** (triethylammonium salt). ^{1}H-NMR (D_2O): 7.96 (*s*, 1 H, H–C(8)); 7.91 (*s*, 1 H, H–C(8)); 7.71 (*s*, 1 H, H–C(2)); 7.57 (*s*, 1 H, H–C(2)); 7.54 (*s*, 1 H, H–C(2)); 5.97 (*s*, 1 H, H–C(1′)); 5.86 (*d*, J = 3.97, 1 H, H–C(1′)); 5.77 (*d*, J = 3.36, 1 H, H–C(1′)).

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