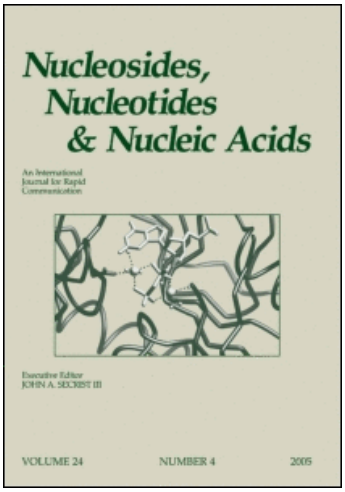


Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Effective Anomerisation of 2'-Deoxyadenosine Derivatives During Disaccharide Nucleoside Synthesis

Irina V. Gulyaeva[a]; Kari Neuvonen[b]; Harri Lönnberg[b]; Andrei A. Rodionov[a]; Elena V. Shcheveleva[a]; Georgii V. Bobkov[a]; Ekaterina V. Efimtseva[a]; Sergey N. Mikhailov[a]
[a] Engelhardt Institute of Molecular Biology, Russian Academy of Sciences, Moscow, Russia [b] Department of Chemistry, University of Turku, Turku, Finland

Online publication date: 30 November 2004

To cite this Article Gulyaeva, Irina V. , Neuvonen, Kari , Lönnberg, Harri , Rodionov, Andrei A. , Shcheveleva, Elena V. , Bobkov, Georgii V. , Efimtseva, Ekaterina V. and Mikhailov, Sergey N.(2004) 'Effective Anomerisation of 2'-Deoxyadenosine Derivatives During Disaccharide Nucleoside Synthesis', Nucleosides, Nucleotides and Nucleic Acids, 23: 12, 1849 — 1864
To link to this Article: DOI: 10.1081/NCN-200040627
URL: http://dx.doi.org/10.1081/NCN-200040627

NUCLEOSIDES, NUCLEOTIDES & NUCLEIC ACIDS
Vol. 23, No. 12, pp. 1849–1864, 2004

Effective Anomerisation of 2′-Deoxyadenosine Derivatives During Disaccharide Nucleoside Synthesis

Irina V. Gulyaeva,[1] Kari Neuvonen,[2] Harri Lönnberg,[2] Andrei A. Rodionov,[1] Elena V. Shcheveleva,[1] Georgii V. Bobkov,[1] Ekaterina V. Efimtseva,[1] and Sergey N. Mikhailov[1,*]

[1]Engelhardt Institute of Molecular Biology, Russian Academy of Sciences, Moscow, Russia
[2]Department of Chemistry, University of Turku, Turku, Finland

ABSTRACT

The formation of a disaccharide nucleoside (**11**) by *O*3′-glycosylation of 5′-*O*-protected 2′-deoxyadenosine or its N^6-benzoylated derivative has been observed to be accompanied by anomerisation to the corresponding α-anomeric product (**12**). The latter reaction can be explained by instability of the *N*-glycosidic bond of purine 2′-deoxynucleosides in the presence of Lewis acids. An independent study on the anomerisation of partly blocked 2′-deoxyadenosine has been carried out. Additionally, transglycosylation has been utilized in the synthesis of 3′-*O*-β-D-ribofuranosyl-2′-deoxyadenosines and its α-anomer.

Key Words: Disaccharide nucleosides; Synthesis; Anomerisation; 2′-Deoxyadenosine derivatives.

*Correspondence: Sergey N. Mikhailov, Engelhardt Institute of Molecular Biology, Russian Academy of Sciences, Vavilov St. 32, Moscow 119991, Russia; Fax: +7-095-135-1405; E-mail: smikh@eimb.ru.

DOI: 10.1081/NCN-200040627
1525-7770 (Print); 1532-2335 (Online)

INTRODUCTION

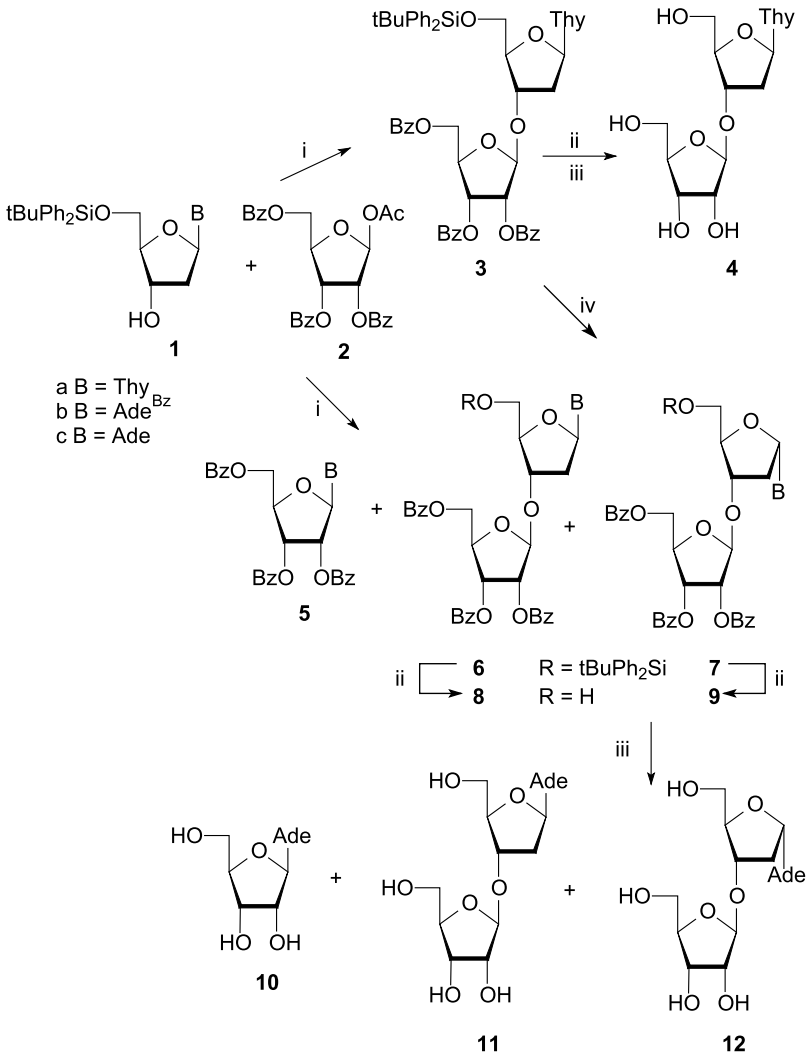
Disaccharide nucleosides belong to an important group of natural substances found in tRNAs and poly(ADP-ribose), or characterised as antibiotics and other physiologically active compounds.[1,2] To date about a hundred disaccharide nucleosides have been isolated from various natural sources.[3] These compounds contain an extra carbohydrate residue linked to one of the nucleoside hydroxyl groups via an *O*-glycosidic bond. The presence of an *O*- and *N*-glycosidic bond in disaccharide nucleosides makes their properties similar to those of both carbohydrates and nucleosides.

Disaccharide nucleosides have been prepared either by coupling of an appropriately blocked disaccharide with a heterocyclic base or by condensation of a protected nucleoside with a monosaccharide using classical procedures of *O*- and *N*-glycosylation.[4,5] The use of a natural nucleoside as a starting material simplifies the synthesis. Many examples of the formation of an *O*-glycosidic bond between a partially protected nucleoside and sugar have been reviewed.[2] In several cases side reactions occur and substantial amounts of by-products are formed. During the past decade, the scope and limitations of nucleoside *O*-glycosylation have been examined.[1,2] As part of our investigations, we now present our recent results on the *O*-ribosylation reaction of 2′-deoxyadenosine derivatives.

RESULTS AND DISCUSSION

A simple and effective method for the preparation of 2′-*O*-(β-D-ribofuranosyl)nucleosides starting from readily available 3′,5′-*O*-blocked *N*-acylribonucleosides and 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (**2**) preactivated with tin tetrachloride in 1,2-dichloroethane, has been recently developed.[6–8] The condensation proceeds by stereospecific formation of the β-D-glycosidic bond and gives a high yield. Several other fully acylated monosaccharide derivatives of D- and L-arabinofuranoses, D-erythrofuranose and D-ribopyranose have been successfully used in the same reaction.[9] This general methodology has additionally been extended to the synthesis of pyrimidine 3′-*O*-(β-D-ribofuranosyl)-2′-deoxynucleosides.[10] The coupling of 5′-*O*-(*tert*-butyldiphenylsilyl)thymidine (**1a**) with fully acylated sugar (**2**) in the presence of tin tetrachloride under standard conditions (1,2-dichloroethane, 0°C, under nitrogen) gave the desired product (**3**) in 79% yield[10] (Scheme 1). After deblocking, disaccharide nucleoside **4** was obtained without difficulties. It has been, however, shown that *O*-glycosylation of purine 2′-deoxynucleosides results in a complex mixture of products.[10] Therefore we now report on a detailed investigation of this condensation reaction, including structural studies of the main products and mechanistic considerations of their formation.

Two nucleoside substrates, *viz.* 5′-*O*-(*tert*-butyldiphenylsilyl)-2′-deoxyadenosine (**1c**) and its N^6-benzoyl derivative (**1b**), were tested in the *O*-ribosylation reaction (Scheme 1). The starting materials (**1b,c**) were prepared by selective silylation[11,12] of N^6-benzoyl-2′-deoxyadenosine[13] and 2′-deoxyadenosine, respectively. Condensation of **1b** with a small excess of **2**, activated with tin tetrachloride in 1,2-dichloroethane for 1.5 h at 0°C under nitrogen, gave a complex mixture of products. Prolonged treatment resulted in darkening of the reaction mixture and lowered the yield of the disaccharide nucleoside. After standard work-up and silica gel column chromatography, two main products were isolated: nucleoside tetra-*O*-benzoate **5b**[14,15] (39%) and disaccharide nucleoside **7b**



Reagents and conditions: (i) $SnCl_4$, $ClCH_2CH_2Cl$, 0 °C, 1.5 - 3 h; (ii) Bu_4NF/THF, r.t., 40 min; (iii) NH_3/MeOH, r.t., 2 days; (iv) Ade^{Bz}, BSA, TMSOTf, MeCN, reflux 2.5 h.

Scheme 1.

(12%). The same condensation with **1c** resulted in formation of nucleoside tri-*O*-benzoate **5c** (31%) and disaccharide nucleoside **6c** (18%). Deprotection with tetrabutylammonium fluoride in THF gave the desilylated products (**8c**, **9b**) and, after subsequent treatment with ammonia in methanol, the free disaccharide nucleosides **11** and **12** were obtained. The ^1H NMR spectra of the disaccharide nucleosides (Tables 1 and 2) indicated the presence of two furanose residues linked by a β-glycosidic bond ($J_{1',2'} < 0.5$ Hz). The principal difference was observed in $J_{1',2'a}$ and $J_{1',2'b}$ of the nucleoside moiety. For β-series, the sum of these coupling constants is greater than that for the corresponding α-nucleosides[16,17] (Table 2). The assignment of anomeric

Table 1. Chemical shifts δ (ppm) of the prepared disaccharide nucleosides.[a]

	Nucleoside moiety[b,c]							Ribofuranosyl moiety					
Compd	1′	2′a	2′b	3′	4′	5′a	5′b	1′	2′	3′	4′	5′a	5′b
6b	6.34 dd	2.87 ddd	2.66 ddd	4.77 m	4.24 m	3.90 dd	3.80 dd	5.41 s	5.69 d	5.89 dd	4.77 m		4.60 dd
7b	6.54 dd	2.80 ddd	2.67 dd	4.68 d	4.58 dd	3.80 dd	3.71 dd	5.36 s	5.52 d	5.55 dd	4.63 ddd	4.44 dd	4.30 dd
6c	6.30 dd	2.82 ddd	2.66 ddd	4.76 m	4.22 m	3.89 dd	3.81 dd	5.40 s	5.69 d	5.88 dd	4.76 m		4.61 dd
8b	6.29 dd	2.99 ddd	2.64 dd	4.77 m	4.33 brs	4.00 d	3.81 d	5.44 s	5.72 d	5.88 dd	4.77 m		4.68 dd
9b	6.56 dd	2.82 ddd	2.68 dd	4.51–4.67 m		3.82 dd	3.75 dd	5.40 d	5.59 dd	5.63 dd	4.51–4.67 m		4.36 dd
8c	6.19 dd	2.98 ddd	2.57 dd	4.76 m	4.31 brs	3.97 d	3.78 d	5.43 s	5.71 d	5.88 dd	4.76 m		4.66 dd
11	6.21 dd	2.67 ddd	2.57 ddd	4.47 ddd	4.13 ddd	3.68 dd	3.62 dd	5.02 d	3.98 dd	4.11 dd	3.90 ddd	3.71 dd	3.54 dd
12	6.24 dd	2.63 ddd	2.49 dd	4.30 dd	4.41 ddd	3.59 dd	3.55 dd	4.90 d	3.75 dd	3.57 dd	3.73 ddd	3.31 dd	2.88 dd

[a]The ^{1}H NMR spectra of compds **6–8** were measured in CDCl3 and those of compounds **11** and **12** in D_2O at 25°C.
[b]H2′a and H2′b were assigned as up (pro-*S*) and down (pro-*R*) protons, respectively.
[c]Typical chemical shifts of the other signals, for example in **7b**: 1.06 (9 H, s, *t*-Bu), 7.28–8.10 (30 H, m, Bz, Ph), 8.33 (1 H, s, H-2), 8.77 (1 H, s, H-8), 9.18 (1 H, br s, NH); in **6c**:1.05 (9 H, s, *t*-Bu), 6.43 (2 H, br s, NH_2), 7.29–7.64 (19 H, m, Ph, Bz), 7.91–8.06 (6 H, m, Bz), 7.97 (1 H, s, H-2), 8.22 (1 H, s, H-8).

Table 2. Vicinal ^{1}H, ^{1}H coupling constants J (Hz) of the prepared disaccharide nucleosides.

	Nucleoside moiety									Ribofuranosyl moiety					
Compd	1′,2′a	1′,2′b	2′a,2b	2′a,3′	2′b,3′	3′,4′	4′,5′a	4′,5′b	5′a,5′b	1′,2′	2′,3′	3′,4′	4′,5′a	4′,5′b	5′a,5′b
6b	7.5	5.9	−13.7	6.2	3.1	–	5.7	3.9	−11.1	<0.5	4.9	6.5	–	5.9	−12.0
7b	6.8	1.6	−14.4	6.9	<0.5	<0.5	3.4	5.3	−11.2	<0.5	5.1	6.4	4.3	5.6	−11.8
6c	6.5	5.8	−13.6	7.0	3.3	–	5.4	3.9	−11.2	<0.5	4.9	6.7	–	5.2	−11.9
8b	9.6	5.3	−13.7	5.3	<0.5	<0.5	<0.5	<0.5	−11.8	<0.5	5.0	6.5	–	5.6	−11.8
9b	7.0	2.5	−14.4	6.8	<0.5	–	4.1	3.9	−12.0	0.9	5.0	6.5	–	5.4	−12.0
8c	9.6	5.3	−13.7	5.0	<0.5	<0.5	<0.5	<0.5	−12.6	<0.5	5.0	6.5	–	5.6	−11.8
11	7.5	6.3	−14.0	6.2	3.0	2.4	3.6	4.1	−12.6	1.1	4.6	6.8	3.5	6.5	−12.3
12	6.4	0.8	−14.2	6.6	<0.5	1.1	4.4	4.6	−12.3	0.9	4.5	7.0	3.4	6.8	−12.0

Table 3. NOE-data (%) of compounds **11** and **12** upon irradiation of 1′-H.[a]

Nucleoside moiety[b]	β-Anomer **11**	α-Anomer **12**
H-4′	2.1	
H-3′	[c]	
H-2′a	[c]	3.6
H-2′b	5.0	0.9

[a]The NOE enhancements expressed as percentage integrated with respect to the irradiated spin (set to −100%).
[b]H2′a and H2′b were assigned as up (pro-*S*) and down (pro-*R*) protons respectively.
[c]Intensity enhancement less than 0.5%.

configuration was based on NOE difference spectroscopy.[18] Saturation of H-1′ of the β-anomer (**11**) resulted in a characteristic NOE (2.1%) at the H-4′, while no effect was observed at the signal H-3′ of the nucleoside moiety[18] (Table 3). With both anomers, the NOE effects on H-2′a and H-2′b signals were in agreement with the published data:[18] the *cis* oriented protons exhibited a greater enhancement. As the table shows, the α-anomer (**12**) exhibited only a weak enhancement at H-3′. With α-2′-deoxynucleosides, the corresponding enhancement at H-3′ has been reported to be less then 1%.[18] In addition, **11** had a negative Cotton effect on the B_{2u} band, similarly to natural 2′-deoxyadenosine, while **12** exerted a positive effect.

In order to determine the number of major products formed upon the *O*-ribosylation of 2′-deoxyadenosines **1b** and **1c** and to quantify their yields, a HPLC analysis was carried. The products obtained by the condensation of **1b** with **2** in the presence of tin tetrachloride under the above-mentioned conditions were isolated by extraction with methylene chloride and the blocking groups were removed. According to HPLC analysis, the mixture consisted of adenine, adenosine **10** and disaccharide nucleosides **12** and **11**, and several unidentified UV absorbing products. The ratio of **10**:**12**:**11** was 51:13:3. Similar products, but with predominant formation of the β-anomer (**11**) were formed upon the analogous condensation of **1c** with **2**. The ratio of **10**:**12**:**11** was 39:4:31. It should be noted that in both cases the main product was adenosine **10**.

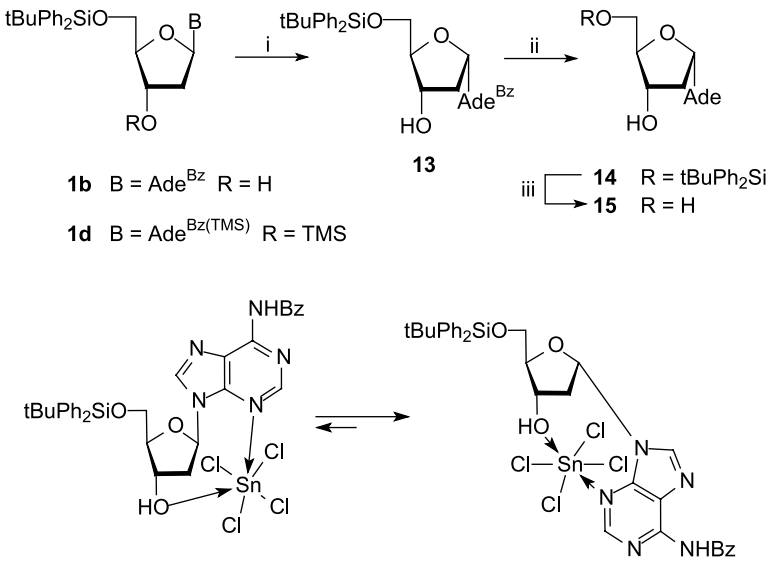
The formation of adenosine (**10**) and the α-anomer (**12**) as the main by-products may be attributed to instability of the *N*-glycosidic bond of purine nucleosides (**1b**,**c** and/or those in disaccharide **6b**) in the presence of a Lewis acid. Previously it has been shown that analogous condensation of N^6-benzoyl-2′,3′-di-*O*-acyladenosines with **2** results in formation of the desired disaccharide together with substantial amounts of nucleoside **5b** and a trisaccharide.[15] It is known that the *N*-glycosidic bond of N^6-acylated 2′-deoxyadenosine is in acid less stable than that of its unprotected derivative.[19,20] This may explain the predominant cleavage of the *N*-glycosidic bond during ribosylation of **1b**.

To get a deeper insight into the anomerisation process, we decided to examine the behavior of **1b** in the presence of tin tetrachloride in 1,2-dichloroethane. It was shown that the reaction was completed in about 1 h at 0°C. According to TLC, **1b** ($R_f = 0.30$ in methylene chloride—ethanol 95:5) was converted to its α-anomer (**13**; $R_f = 0.47$) and

N^6-benzoyladenine. Prolonged treatment resulted in decomposition of nucleosides and exclusive formation of N^6-benzoyladenine. The yield of **13** was increased up to 50% by addition of N^6-benzoyladenine to the reaction mixture. The separation of **13** was easily achieved by silica gel column chromatography. Stepwise deblocking of **13** gave **14** and finally **15**. The UV and CD spectra of **15** were consistent with the literature data.[21]

Much more drastic conditions were needed for the previously described[21] anomerisation of fully acylated pyrimidine 2′-deoxyribonucleosides, *viz.* heating in acetonitrile in the presence of bis(trimethylsilyl)acetamide (BSA) and trimethylsilyl trifluoromethanesulfonate (TMSOTf) for 2–3 h at 70°C. α-2′-Deoxyriboadenosine was synthesised by transglycosylation under similar conditions.[21] It should be mentioned that the separation of the anomeric mixtures was rather complicated and the yields of α-2′-deoxyribonucleosides ranged from 27 to 51%.[21]

To learn more about the mechanism of anomerisation, the stability of the 3′-*O*-trimethylsilyl derivative **1d** in the presence of tin tetrachloride in 1,2-dichloroethane was investigated. The compound turned out to be stable for 3 h at 0°C. It may be concluded that the presence of unprotected 3′-OH group destabilised the *N*-glycosidic bond of **1b**. Evidently the anomerisation took place with nucleoside **1b** but not with disaccharide **6b**. It is known that tin tetrachloride may form complexes with nitrogen atoms of heterocyclic bases and with hydroxyl groups.[22,23] The proposed mechanism for the anomerisation is depicted in Scheme 2. For steric reasons, the complex of the β-anomer presumably is less stable than that of the α-anomer and the equilibrium is shifted towards the more stable product.



Reagents and conditions: (i) Ade^{Bz}, $SnCl_4$, $ClCH_2CH_2Cl$, 0°C, 1 h; (ii) NH_3/MeOH, r.t., 2 days; (iii) Bu_4NF/THF, r.t., 40 min.

Scheme 2.

Preparation of the desired compounds from a disaccharide building block was also attempted. Unfortunately condensation of methyl 5-*O*-toluoyl-2-deoxy-D-*erythro*-pentofuranoside (5-*O*-toluoyl-2-deoxy-D-ribofuranoside) with **2** in the presence of tin tetrachloride in 1,2-dichloroethane resulted in only decomposition of the starting material, which may be taken as an indication of instability of 3-*O*-unprotected 2-deoxy-D-ribofuranosides under the reaction conditions.

Preparation of 3′-*O*-(β-D-ribofuranosyl)-2′-deoxyadenosine (**11**) was additionally attempted by the previously described method of transglycosylation.[24] Easily available 3′-*O*-glycosylated thymidine (**3**) was chosen as the glycosyl donor and N^6-benzoyl-adenine as the glycosyl acceptor. The reaction catalysed by trimethylsilyl triflate gave a mixture of α- (**7b**) and β-anomers (**6b**) (Scheme 1). This mixture was difficult to separate by silica gel column chromatography, due to rather similar R_f values of **6b** and **7b**, but after removal of the 5′-*O*-silyl groups, the separation could be carried out without difficulties and **8b** and **9b** were obtained in 22% and 45% yields, respectively. Subsequent saponification gave the free anomeric disaccharide nucleosides (**11**, **12**).

The NMR spectra (Tables 1 and 2) of disaccharide nucleosides are rather complicated due to the presence of two ribofuranose residues. Chemical shifts of H1′, H2′ and H3′ of the ribose moiety and H1′, H2′a and H2′b of the 2-deoxyribose residue along with the corresponding coupling constants could be calculated directly from the NMR spectra. The other protons were assigned by comparison with the ^{1}H NMR spectra of related disaccharide nucleosides[7,10,15] and making use of double resonance and COSY spectra. With α-anomers, the chemical shifts of H1′ and H4′ of the 2-deoxyribose residue are located in a lower field than with β-anomers (Table 1). The ^{13}C NMR spectra were analyzed in the similar fashion using ^{1}H–^{13}C correlation spectra. An upfield shift of C1′ of the 3′-*O*-ribosyl residue to 105–107 ppm is typical for β-linked disaccharide nucleosides.[7,10,15]

In summary, the facile anomerization of 2′-deoxyadenosine derivatives during disaccharide nucleoside synthesis can be explained by the instability of the protected purine nucleosides in the presence of Lewis acids. Consistent with this, trans-glycosylation has been successfully used for the preparation of 3′-*O*-(β-D-ribofur-anosyl)-2′-deoxyadenosine and its α-anomer (**12**).

EXPERIMENTAL PART

NMR spectra were recorded on a Bruker AMX 400 or a JEOL JNM-L-400 spectrometer at 298 K. The deuterium of the solvent was used as a lock signal and the chemical shifts were measured relative to the solvent signals. The 2D homonuclear H,H-correlation experiments were acquired using double quantum filtered COSY. The 2D heteronuclear one-bond correlation experiments were acquired using carbon detected CH-shift correlation with partial homonuclear decoupling in the f1 dimension. The spectral widths of 2D spectra were optimised from ID spectra. NOE difference experiments were acquired using saturation times of 6–8 sec and the reported enhancements were expressed as percentage integrated with respect to the irradiated spin (set to −100%). Prior to NOE measurements, samples were deoxygenated by nitrogen bubbling. The UV spectra were recorded on a Cary-300 UV/VIS spectro-photometer (Varian) and the CD spectra on a JASCO J-715 spectropolarimeter. The

liquid secondary ion mass spectra (FAB-LSIMS, Cs^+ ion bombardment) were recorded on a VG Zab Autospec mass spectrometer (VG Analytical, Manchester, UK) using positive-ion mode and a polyethylene glycol matrix. Column chromatography was performed on silica gel (0.063–0.200 mm, Merck). TLC was carried out on Kieselgel 260 F (Merck) using UV-detection and the following solvent systems (compositions expressed as *v/v*): methylene chloride (A), methylene chloride—ethanol 95:5 (B), methylene chloride—ethanol 9:1 (C), methylene chloride—ethanol 7:3 (D) and isopropanol—aq. ammonia—water 7:1:2 (E).

5′-*O*-(*tert*-Butyldiphenylsilyl)-N^6-benzoyl-2′-deoxyadenosine (1b). To a solution of N^6-benzoyl-2′-deoxyadenosine (10 mmol) and imidazole (10 mmol) in dry pyridine (20 ml), *tert*-butyldiphenylsilyl chloride (11 mmol) was added and the solution was kept at 20°C for 3–5 h, *i. e.* until the reaction was complete according to TLC. The solution was evaporated to dryness, the residue was dissolved in methylene chloride and the organic layer was washed with water, 10% aqueous solution of sodium bicarbonate and again with water. The organic layer was dried with Na_2SO_4, filtered, evaporated to dryness and evaporated with toluene. The residue was purified by silica gel chromatography using eluent B. Yield (4.45 g, 75%) as a foam; R_f 0.3 (B); δ_H(400 MHz; $CDCl_3$) 1.05 (9 H, s, *t*-Bu), 2.57 (1 H, ddd, $J_{2'b1'}$ 6.5, $J_{2'b,3'}$ 3.7, $J_{2'b,2'a}$ −13.4, H-2′b), 2.79 (1 H, ddd, $J_{2'a,1'}$ 6.5, $J_{2'a,3'}$ 6.2, H-2′a), 2.88 (1 H, br s,OH), 3.84 (1 H, dd, $J_{5'a,4'}$ 4.0, $J_{5'a,5'b}$ −11.2, H-5′a), 3.93 (1 H, dd, $J_{5'b,4'}$ 5.0, H-5′b), 4.12(1 H, ddd, $J_{4',3'}$ 2.8, H-4′), 4.76 (1 H, m, H-3′), 6.49 (1 H, t, H-1′), 7.33–8.03 (15 H, m, Bz, Ph), 8.20 (1 H, s, H-2), 8.74 (1 H, s, H-8), 9.21 (1 H, br s, NH); δ_C(100 MHz; $CDCl_3$) 19.20 (Si*C*Me_3), 26.91 (Me_3), 40.44 (C-2′), 63.89 (C-5′), 72.05 (C-3′), 84.59 (C-1′), 87.14 (C-4′), 123.23 (C-5), 127.86, 128.82, 129.97, 132.73, 133.72, 135.45, 135.52, (Bz, Ph), 141.29 (C-8), 149.47 (C-4), 151.28 (C-2), 152.62 (C-6), 164.66 (C = O). LSIMS (FAB): [$C_{33}H_{33}N_5O_5Si$ + H^+] requires 594.2536, found 594.2540.

5′-*O*-*tert*-Butyldiphenylsilyl-2′-deoxyadenosine (1c). Compound **1c** was prepared from 2′-deoxyadenosine as described above for **1b**. The residue obtained by evaporation of the reaction solution to dryness was, however, dissolved in ethyl acetate instead of methylene chloride and the product was purified by recrystallisation from a mixture of methylene chloride—hexane 1:1, not by chromatography. Yield (4.1 g, 84%); R_f 0.11 (B); mp 138–140°C (from methylene chloride—hexane); δ_H(400 MHz; $CDCl_3$) 1.06 (9 H, s, *t*-Bu), 2.53 (1 H, ddd, $J_{2'b,1'}$ 6.5, $J_{2'b,3'}$ 3.8, $J_{2'b,2'a}$ −13.3, H-2′b), 2.75 (1 H, ddd, $J_{2'a,1'}$ 6.5, $J_{2'a,3'}$ 6.4, H-2′a), 3.08 (1 H, br s, OH), 3.85 (1 H, dd, $J_{5'a,4'}$ 4.1, $J_{5'a,5'b}$ −11.1, H-5′a), 3.91 (1 H, dd, $J_{5'b,4'}$ 4.7, H-5′b), 4.08 (1 H, ddd, $J_{4',3'}$ 3.5, H-4′), 4.73 (1 H, m, H-3′), 5.79 (2 H, br s, NH2), 6.46 (1 H, t, H-1′), 7.20–7.70 (10 H, m, Bz), 8.02 (1 H, s, H-2), 8.30 (1 H, s, H-8); δ_C(100 MHz; $CDCl_3$) 19.23 (Si*C*Me_3), 26.93 (Me_3), 40.52 (C-2′), 63.98 (C-5′), 72.07 (C-3′), 84.22 (C-1′), 86.96 (C-4′), 123.21 (C-5), 127.86, 129.98, 132.78, 135.51 (Ph), 138.80 (C-8), 148.50 (C-4), 152.97 (C-2), 155.40 (C-6). LSIMS (FAB): [$C_{26}H_{31}N_5O_3Si$ + H^+] requires 490.2274, found 490.2270.

N^6-benzoyl-9-[5-*O*-tert-butyldiphenylsilyl-3-*O*-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-2-deoxy-α-D-*erythro*-pentofuranosyl]adenine 7b. To a cold solution (0°C) of 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose **2** (605 mg, 1.2 mmol) in 1,2-dichloroethane (15 ml) under nitrogen, tin tetrachloride (0.18 ml, 1.5 mmol) was

added and the solution was kept at 0°C for 10 min. Nucleoside **1b** (594 mg, 1 mmol) was added and the resulting solution was kept for 1.5 h at 0°C. Then 10% aqueous solution of sodium bicarbonate (10 ml) was added and the suspension was stirred for 20 min at 0°C. The suspension was diluted with methylene chloride (20 ml), filtered through Hyflo Super Cel, the organic layer was separated, washed with water (15 ml), dried over Na_2SO_4, filtered and evaporated to dryness. The residue was applied onto a silica gel column (50 g). The column was washed with system A, and then eluted with a mixture of methylene chloride—ethanol 99:1 to give N^6-benzoyladenosine 2,3,5-tri-*O*-benzoate (**5b**)[14,15] (266 mg, 39%) as a foam. R_f 0.72 (B). Further elution with the same system yielded **7b** (125 mg, 12%) as a foam. R_f 0.63 (B). LSIMS (FAB): $[C_{59}H_{55}N_5O_{11}Si + H^+]$ requires 1038.3745, found 1038.3738.

9-[5-*O*-*tert*-Butyldiphenylsilyl-3-*O*-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-2-deoxy-β-D-*erythro*-pentofuranosyl]adenine 6c. An analogous condensation of **2** (605 mg, 1.2 mmol) with **1c** (490 mg, 1 mmol) in the presence of tin tetrachloride (0.18 ml, 1.5 = mmol) in 1,2-dichloroethane (15 ml) for 3 h at 0°C, followed by silica gel chromatography (50 g) using a mixture of methylene chloride—ethanol 98:2 as an eluent, gave **6c** (170 mg, 18%) as a foam. R_f 0.51 (B); δ_C(100 MHz; $CDCl_3$) 19.14 ($SiCMe_3$), 26.83 (Me_3), 38.17 (C-2′ dAdo), 63.47, 64.68 (C-5′ dAdo, C-5′ Rib), 72.06 (C-3′ Rib), 75.72 (C-2′ Rib), 78.19, 79.34 (C-3′ dAdo, C-4′ Rib), 84.71, 85.03 (C-1′ dAdo, C-4′ dAdo), 104.86 (C-1′ Rib), 119.86 (C-5), 127.79, 128.39, 128.52, 128.80, 129.54, 129.74, 129.91, 132.58, 133.27, 133.59, 135.47 (Bz, Ph), 139.77 (C-8), 149.22 (C-4), 150.14 (C-2), 154.07 (C-6), 165.15, 165.35, 166.09 (C = O). LSIMS (FAB): $[C_{52}H_{51}N_5O_{10}Si + H^+]$ requires 934.3483, found 934.3478.

Further elution with the same system yielded adenosine 2′,3′,5′-tri-*O*-benzoate (**5c**) (180 mg, 31%) as a foam. R_f 0.46 (B); δ_H(400 MHz; $CDCl_3$) 4.72 (1 H, dd, $J_{5'a,4'}$ 4.4, $J_{5'a,5'b}$ −12.1, H-5′a), 4.83 (1 H, ddd, $J_{4',3'}$ 5.0, $J_{4',5'b}$ 3.1, H-4′), 4.90 (1 H, dd, H-5′b), 6.28 (1 H, dd, $J_{3',2'}$ 5.9, H-3′), 6.36 (2 H, br s, NH_2), 6.38 (1 H, dd, $J_{2',1'}$ 5.0, H-2′), 6.43 (1 H, d, H-1′), 7.34–7.59 (9 H, m, Bz), 7.93–8.10 (7 H, m, H-2, Bz), 8.24 (1 H, s, H-8); δ_C(100 MHz; $CDCl_3$) 63.57 (C-5′), 71.48 (C-3′), 74.05 (C-2′), 80.71 (C-4′), 86.96 (C-1′), 119.91 (C-5), 128.48, 128.77, 129.39, 129.79, 129.82, 133.34, 133.62, 133.70 (Bz), 139.08 (C-8), 149.68 (C-4), 153.08 (C-2), 155.69 (C-6), 165.11, 165.26, 166.12 (C = O).

N^6-Benzoyl-9-[3-*O*-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-2-deoxy-α-D-*erythro*-pentofuranosyl]adenine (9b). Nucleoside **7b** (104 mg, 0.10 mmol) was dissolved in tetrahydrofuran (0.5 ml) and 0.5 M tetrabutylammonium fluoride trihydrate in tetrahydrofuran (0.28 ml) was added. The solution was kept for 45 min at 20°C, evaporated to dryness, coevaporated with chloroform (2 ml) and applied onto a silica gel column (10 g). The column was washed with system A and eluted with a mixture of methylene chloride-ethanol 97:3 to give **9b** (64 mg, 80%) as a foam. R_f O.32 (B). δ_C(100 MHz; $CDCl_3$) 39.19 (C-2′ dAdo), 62.50, 64.32 (C-5′ dAdo, C-5′ Rib), 71.89 (C-3′ Rib), 75.72 (C-2′ Rib), 78.29, 79.47 (C-3′ dAdo, C-4′ Rib), 85.09, 85.98 (C-1′ dAdo, C-4′ dAdo), 105.10 (C-1′ Rib), 122.81 (C-5), 128.38, 129.77, 132.59, 133.21, 133.48, 133.62 (Bz), 141.47 (C-8), 149.52 (C-4), 151.27 (C-2), 152,61 (C-6), 165.30, 166.02 (C = O). LSIMS (FAB): $[C_{43}H_{37}N_5O_{11} + H^+]$ requires 800.2567, found 800.2574.

9-[3-*O*-(2,3,5-Tri-*O*-benzoyl-β-D-ribofuranosyl)-2-deoxy-β-D-*erythro*-pentofutanosyl]adenine (8c). An anlogous desilylation of **6c** (100 mg, 0.107 mmol) gave **8c** (57 mg, 77%) as a foam. R_f 0.29 (B); δ_C(100 MHz; $CDCl_3$) 38.61 (C-2′ dAdo), 63.65, 64.84 (C-5′ dAdo, C-5′ Rib), 71.99 (C-3′ Rib), 75.96 (C-2′ Rib), 79.51, 81.30 (C-3′ dAdo, C-4′ Rib), 87.20, 87.86 (C-1′ dAdo, C-4′ dAdo), 105.68 (C-1′ Rib), 120.91 (C-5), 128.41, 128.53, 128.83, 129.75, 129.80, 132.58, 133.41, 133.53, 133.62 (Bz), 140.48 (C-8), 148.82 (C-4), 152.09 (C-2), 156.04 (C-6), 165.29, 165.44, 166.20 (C = O). LSIMS (FAB): [$C_{36}H_{33}N_5O_{10}$+ H^+] requires 696.2305, found 696.2311

9-(3-*O*-β-D-ribofuranosyl-2-deoxy-β-D-*erythro*-pentofuranosyl)adenine (11). A solution of nucleoside **8c** (97 mg, 0.14 mmol) in 5 M ammonia in methanol (5 ml) was kept for 3 days at 20°C and then evaporated to dryness in vacuo. The residue was partitioned between methylene chloride (5 ml) and water (10 ml), and the water layer was washed with methylene chloride (2 × 5 ml). The aqueous layer was evaporated and purified on a Silasorb C-18 reversed-phase HPLC column (10 × 150 mm, 13 μm) by isocratic elution with 5% acetonitrile in 0.01 M triethylammonium acetate at a flow rate of 4 ml × min^{-1}. The main UV absorbing peak (t_R=10.0 min) was desalted on the same column, washed initially with water and eluted with 20% aq. acetonitrile. The fraction was evaporated and freeze-dried to give 11 (43 mg, 81%). R_f 0.12 (D), 0.81 (E); CD (water): λ_{max} 262 nm (Δε − 0.85). λ_{max} (H_2O) 261 (pH 7–13) (ε 14400), 259 nm (pH 2) (ε 14000). δ_C(100 MHz; D_2O) 38.55 (C-2′ dAdo), 62.55 (C-5′ dAdo), 63.48 (C-5′ Rib), 71.46 (C-3′ Rib), 75.38 (C-2′ Rib), 78.87 (C-3′ dAdo), 83.72 (C-4′ Rib), 85.58 (C-1′ dAdo), 86.25 (C-4′ dAdo), 107.26 (C-1′ Rib), 119.64 (C-5), 141.00 (C-8), 149.04 (C-4), 153.13 (C-2), 156.21 (C-6). LSIMS (FAB): [$C_{15}H_{21}N_5O_5$+ H^+] requires 384.1519, found 384.1526.

9-(3-*O*-β-D-Ribofuranosyl-2-deoxy-α-D-*erythro*-pentofuranosyl) adenine (12). Analogous debenzoylation of **9b** (104 mg, 0.13 mmol) gave **12** (39 mg, 79%). R_f 0.09 (D), 0.78 (E); CD (water): λ_{max} 261 nm (Δε + 3.80). λ_{max} (H_20) 261 nm (pH 7–13) (ε 14300), 259 nm (pH 2) (ε 14000). δ_C(100 MHz; D_2O) 39.78 (C-2′ dAdo), 62.52 (C-5′ dAdo), 63.40 (C-5′ Rib), 71.50 (C-3′ Rib), 75.43 (C-2′ Rib), 79.22 (C-3′ dAdo), 83.43 (C-4′ Rib), 86.77 (C-1′ dAdo), 88.32 (C-4′ dAdo), 107.49 (C-1′ Rib), 119.36 (C-5), 141.13 (C-8), 148.63 (C-4), 153.14 (C-2), 155.84 (C-6). LSIMS (FAB): [$C_{15}H_{21}N_5O_7$+ H^+] requires 384.1519, found 384.1515.

***O*-Ribosylation of 5′-*O*-(*tert*-butyldiphenylsilyl)-N^6-benzoyl-2′-deoxyadenosine (1b).** To a cold solution (0°C) of 2 (303 mg, 0.6 mmol) in 1,2-dichloroethane (7 ml) under nitrogen, tin tetrachloride (0.084 ml, 0.72 mmol) was added and the solution was kept for 10 min at 0°C. After addition of nucleoside **1b** (297 mg, 0.5 mmol), the solution was kept for 1.5 h at 0°C. Then 10% aqueous solution of sodium bicarbonate (10 ml) was added and the suspension was stirred for 20 min at 0°C. The suspension was diluted with methylene chloride (10 ml), filtered through Hyflo Super Cel, the organic layer was separated, washed with water (2 × 10 ml), dried and evaporated to dryness. The residue (550 mg) was co-evaporated with tetrahydrofuran (3 ml), and dissolved in tetrahydrofuran (1.5 ml), 0.5 M tetrabutylammonium fluoride trihydrate in tetrahydrofuran (1.3 ml) was added. After 45 min at 20°C, water (0.5 ml) and Dowex-50 (Na^+ form; 0.7 ml) were added, and the mixture was stirred for 30 min at 20°C. The

resin was filtered off and washed with ethyl acetate and the filtrate was washed with water (2 × 10 ml). The organic layer was dried over Na_2SO_4, evaporated to dryness. The residue was dissolved in 5 mol dm^{-3} ammonia in methanol (10 ml), kept for 3 days at 20°C and concentrated to dryness in vacuo. The residue was partitioned between methylene chloride (10 ml) and water (30 ml), and the aqueous layer was washed with methylene chloride (2 × 10 ml). The aqueous layer was concentrated to dryness. The total yield 54% was estimated by UV spectra (A_{260} 4000 o.u.). The mixture was analysed by reversed-phase HPLC on a Nucleosil C-18 column (4 × 250 mm, 5 μm) using a concentration gradient 0–15% of acetonitrile in 0.05 M sodium acetate pH 4.2, the flow rate was 1 ml × min^{-1}. The following UV absorbing (254 nm) peaks were observed: t_R (integral in %, assignment), 9.40 min (4.8%, adenine), 11.46 min (5.5%, unidentified), 12.96 min (51.0%, adenosine **10**), 13.82 min (9.4%, benzamide), 14.30 min (13.0%, **12**), 15.57 min (11.9%, unidentified), 17.63 min (2.9%, **11**), 18.57 min (1.4%, unidentified). The concentration ratio of **10**:**12**:**11** was 51:13:3.

***O*-Ribosylation of 5′-*O*-(*tert*-butyldiphenylsilyl)-2′-deoxyadenosine (1c).** The condensation of **2** (303 mg, 0.6 mmol) with **1c** (245 mg, 0.5 mmol) in the presence of tin tetrachloride (0.084 ml, 0.72 mmol) in 1,2-dichloroethane (7 ml) was performed analogously. According to the UV spectra (A_{260} 3900 o.u.), the total yield was 52%. The mixture was analysed analogously as with **1b**. The following UV absorbing (254 nm) peaks were observed: t_R in min (integral in %, assignment), 9.40 min (4.1%, adenine), 10.15 min (3.8%, unidentified), 12.97 min (38.6%, adenosine **10**), 13.89 min (6.5%, benzamide), 14.30 min (4.3%, **12**), 15.52 min (1.3%, unidentified), 16.11 min (10.3%, unidentified), 17.68 min (31.0%, **11**). The concentration ratio of **10**:**12**:**11** was 39:4:31.

N^6-Benzoyl-9-[3-*O*-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-2-deoxy-β-D-*erythro*-pentofuranosyl]adenine (8b) and N^6-benzoyl-9-[3-*O*-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-2-deoxy-α-D-*erythro*-pentofuranosyl]adenine (9b). A mixture of 3 (925 mg, 1 mmol), N^6-benzoyladenine (478 mg, 2 mmol) and BSA (1.23 ml, 5 mmol) in dry acetonitrile (6 ml) was refluxed for 10 min and 0.5 M trimethylsilyl triflate (0.6 ml, 1.2 mmol) in 1,2-dichloroethane was added. After refluxing for 2.5 h, the mixture was cooled to 20°C, diluted with methylene chloride (70 ml) and washed with 10% aqueous solution of sodium bicarbonate (20 ml). The organic layer was washed with water (2 × 10 ml), dried over Na_2SO_4 and evaporated to dryness. The residue (1.15 g) could be partly separated on silica gel in system A to give **6b** (79 mg) R_f 0.68 (B), the mixture of **6b** and **7b** (515 mg) and **7b** (183 mg). The mixture of **6b** and **7b** was dissolved in tetrahydrofuran (2 ml) and 0.5 M tetrabutylammonium fluoride trihydrate in tetrahydrofuran (2.6 ml) was added. The solution was kept for 45 min at 20°C, evaporated to dryness, coevaporated with chloroform (10 ml) and applied onto a silica gel column (30 g). The column was washed with system A and eluted with a mixture of methylene chloride—ethanol 97:3 to give **8b** (176 mg, 22%) as a foam. R_f 0.49 (B). δ_C(100 MHz; $CDCl_3$) 38.61 (C-2′ dAdo), 63.38, 64.76 (C-5′ dAdo, C-5′ Rib), 71.94 (C-3′ Rib), 75.89 (C-2′ Rib), 79.52, 81.86 (C-3′ dAdo, C-4′ Rib), 86.99, 87.60 (C-1′ dAdo, C-4′ dAdo), 105.62 (C-1′ Rib), 124.32 (C-5), 127.89, 128.38, 128.52, 128.77, 129.69, 129.74, 132.77, 133.38, 133.50, 133.59 (Bz), 142.78 (C-8), 149.81 (C-4), 152.60 (C-2), 152.04 (C-6), 164.62, 165.25, 165.40, 166.16 (C = O).

Further elution with system B gave **9b** (362 mg 45%) as a foam. R_f 0.32 (B).

N^6-Benzoyl-9-(5′-*O*-*tert*-butyldiphenylsilyl-2′-deoxy-α-D-*erythro*-pentofuranosyl-fladenine (13). N^6-Benzoyladenine (120 mg, 0.5 mmol) was suspended in 1,2-dichloroethane (10 ml), tin tetrachloride (0.16 ml, 1.37 mmol) was added and the solution was kept for 10 min at 0°C. After addition of nucleoside **1b** (297 mg, 0.5 mmol), the mixture was kept for 1 h at 0°C. Then 10% aqueous solution of sodium bicarbonate (15 ml) was added and the suspension was stirred for 20 min at 0°C. The suspension was diluted with methylene chloride (20 ml) and filtered through Hyflo Super Cel. The organic layer was separated, washed with water (15 ml), dried over Na_2SO_4, filtered and evaporated to dryness. The residue was applied onto silica gel column (20 g). The column was washed with system A, and then eluted with a mixture of methylene chloride—ethanol 98:2 to give 13 (149 mg, 50%) as a foam. R_f 0.47 (B); δ_H(400 MHz; $CDCl_3$) 1.02 (9 H, s, t-Bu), 2.59 (1 H, dd, $J_{2'b1'}$ 1.6, $J_{2'b,2'a}$ −14.9, H2′b), 3.09(1 H, ddd, $J_{2'a,1'}$ 8.2, $J_{2'a,3'}$ 7.6, H-2′a), 3.78 (1 H, dd, $J_{5'a,4'}$ 3.0, $J_{5'a,5'b}$ −11.3, H-5′a), 3.82 (1 H, dd, $J_{5'b,4'}$ 3.2, H-5′b), 4.53 (1 H, dd, H-4′), 4.65 (1 H, d, H-3′), 6.32 (1 H, dd, H-1′), 7.29-8.01 (15 H, m, Bz, Ph), 8.43 (1 H, s, H-2), 8.78 (1 H, s, H-8), 9.42(1 H, br s, NH); δ_C(100 MHz; $CDCl_3$) 19.16 ($SiCMe_3$), 26.76 (Me_3), 41.32 (C-2′), 65.11 (C-5′), 73.02 (C-3′), 87.18 (C-1′), 90.54 (C-4′), 123.10 (C-5), 127.72, 127.87, 128.83, 129.93, 129.99, 132.74, 132.94, 133.26, 135.53, (Bz, Ph), 143.24 (C-8), 149.63 (C-4), 150.06 (C-2), 151.96 (C-6), 164.82 (C = O). LSIMS (FAB): [$C_{33}H_{35}N_5O_4Si + h^+$] requires 594.2536, found 594.2532.

9-(2-Deoxy-α-D-*erythro*-pentofuranosyl)adenine (15). A solution of protected nucleoside 13 (100 mg, 0.17 mmol) in 5 mol dm^{-3} methanolic ammonia (5 ml) was kept for 3 days at 20°C and then evaporated to dryness in vacuo. The residue was crystallized from a mixture of methylene chloride—hexane 1:1 to give 9-(5′-*O*-*tert*-butyldiphenylsilyl-α-D-*erythro*-pentofuranosyl)adenine (**14**). R_f 0.22 (B); mp 113–115°C (from methylene chloride—hexane); δ_H(400 MHz; DMSO-d_6) 1.02 (9 H, s, *t*-Bu), 2.39 (1 H, ddd, $J_{2'b,1'}$ 2.8, $J_{2'b,3'}$ 1.0, $J_{2'b,2'a}$ −14.3, H-2′b), 2.78 (1 H, ddd, $J_{2'a,1'}$ 7.8, $J_{2'a,3'}$ 6.8, H-2′a), 3.70 (1 H, dd, $J_{5'a,4'}$ 4.0, $J_{5'a,5'b}$ −11.2, H-5′a), 3.74(1 H, dd, $J_{5'b,4'}$ 3.4, H-5′b), 4.28 (1 H, ddd, $J_{4',3'}$ 2.9, H-4′), 4.45 (1 H, dddd, $J_{3',OH}$ 4.7, H-3′), 5.85 (1 H, d, OH), 6.39 (1 H, dd, H-1′), 7.29 (2 H, br s, NH_2), 7.43–7.69 (10 H, m, Bz), 8.17(1 H, s, H-2), 8.40(1 H, s, H-8); δ_C(100 MHz; DMSO-d_6) 18.74 (Si*C*Me_3), 25.60 (Me_3), 40.42 (C-2′), 64.22 (C-5′), 70.74 (C-3′), 83.72 (C-1′), 87.93 (C-4′), 118.90 (C-5), 127.88, 129.86, 132.70, 135.05 (Ph), 139.57 (C-8), 148.86 (C-4), 152.39 (C-2), 156.01 (C-6).

The residue (**14**) was evaporated with tetrahydrofuran (3 ml), dissolved in tetrahydrofuran (1 ml) and 0.5 M tetrabutylammonium fluoride trihydrate in tetrahydrofuran (0.48 ml) was added. After 45 min at 20°C, water (0.5 ml) and Dowex-50 (Na^+ form; 0.5 ml) were added, and the mixture was stirred for 30 min at 20°C. The resin was filtered off and washed with water. The filtrate was washed with ethyl acetate (3 × 5 ml) and evaporated in vacuo. The residue was purified on a Silasorb C-18 semi-preparative reversed-phase HPLC column (10 × 250 mm, 13 μm) by isocratic elution with 5% acetonitrile in 0.01 M triethylammonium acetate at a flow rate of 4 ml × min^{-1}. The peak eluted at t_R=6.0 min was collected and concentrated. The residue was desalted on the same column, washed initially with water and eluted with 20% aq. acetonitrile. The main fraction was evaporated and freeze-dried to give 15 (22 mg, 51%). CD (water): λ_{max} 262 nm (Δε + 0.35). λ_{max} (H_2O) 261 nmn (pH 7–13) (ε 14600), 260 nm (pH 2) (ε 14300). R_f 0.28 (D). δ_H(400 MHz; D_2O) 2.49(1 H, dd,

$J_{2'b,1'}$ 1.2, $J_{2'b,2'a}$ −14.0, H-2′b), 2.90 (1 H, ddd, $J_{2'a,1'}$ 8.0, $J_{2'a,3'}$ 7.2, H-2′a), 3.67 (1 H, dd, $J_{5'a,4'}$ 5.2, $J_{5'a,5'b}$ −12.4, H-5′a), 3.74 (1 H, dd, $J_{5'b,4'}$ 3.6, H-5′b), 4.35 (1 H, ddd, $J_{4',3'}$ 2.4, H-4′), 4.51(1 H, dd, H-3′), 6.36 (1 H, dd, H-1′), 8.07 (1 H, s, H-2), 8.29 (1 H, s, H-8); δ_C(100 MHz; D_2O) 39.23 (C-2′), 61.33 (C-5′), 70.90 (C-3′), 84.78 (C-1'), 87.23 (C-4′), 118.36 (C-5), 140.48 (C-8), 147.63 (C-4), 151.85 (C-2), 154.94 (C-6). LSIMS (FAB): [$C_{10}H_{13}N_5O_3$+ H^+] requires 252.1096, found 252.1094.

Attempt of anomerization of *N,O*-bis(trimethylsilyl)-5′-*O*-*tert*-butyldiphenylsilyl-N^6-benzoyl-2-deoxyadenosine (1d). A solution of nucleoside **1b** (297 mg, 0.5 mmol), BSA (0.25 ml, 1mmol) in 1,2-dichloroethane (7 ml) was refluxed for 10 min. After cooling to 0°C, tin tetrachloride (0.12 ml, 1 mmol) was added and the solution was kept for 3 h at 0°C. Then 10% aqueous solution of sodium bicarbonate (15 ml) was added and the suspension was stirred for 20 min at 0°C. According to TLC, no changes were observed. The suspension was diluted with methylene chloride (20 ml) and filtered through Hyflo Super Cel. The organic layer was separated, washed with water (15 ml), dried over Na_2SO_4, filtered and evaporated to dryness. The residue was dissolved in 5 M methanolic ammonia (5 ml) and kept for 3 days at 20°C, and then evaporated to dryness in vacuo. The residue was dissolved in ethyl acetate (30 ml) and washed with water (10 ml). The organic layer was dried with Na_2SO_4, filtered and evaporated to dryness. According to TLC and NMR spectroscopy, the product was identical with nucleoside **1c**.

ACKNOWLEDGMENTS

Authors thank the Russian Foundation for Basic Research and the Academy of Finland for financial support.

REFERENCES

1. Mikhailov, S.N.; Efimtseva, E.V. Disaccharide nucleosides and oligonucleotides of their basis. Collect. Symp. Ser. **2002**, *5*, 181–194.
2. Efimtseva, E.V.; Mikhailov, S.N. Disaccharide nucleosides. Russ. Chem. Rev. **2004**, *73*, 401–414.
3. *Dictionary of Natural Products on CD-ROM Version 9.2*; Chapman&Hall/CRC, February 2001.
4. Toshima, K.; Tatsuta, K. Recent progress in *O*-glycosylation methods and its Application to natural products synthesis. Chem. Rev. **1993**, *93*, 1503–1531.
5. Vorbruggen, H. Adventures in silicon—organic chemistry. Acc. Chem. Res. **1995**, *28*, 509–520.
6. Niewczyk, A.; Krzyzaniak, A.; Barciszewski, J.; Markiewicz, W.T. Studies on the synthesis of *O*-ribosyl-adenosine—a new minor nucleoside of tRNA. Nucleosides Nucleotides **1991**, *10*, 635–638.
7. Mikhailov, S.N.; Efimtseva, E.V.; Gurskaya, G.V.; Zavodnik, V.E.; De Bruyn, A.; Janssen, G.; Rozenski, J.; Herdewijn, P. An efficient synthesis and physico-

chemical properties of 2′-*O*-β-D-ribofuranosyl-nucleosides, minor tRNA components. J. Carbohydr. Chem. **1997**, *16*, 75–92.
8. Markiewicz, W.T.; Niewczyk, A.; Gdaniec, Z.; Adamiak, D.A.; Dauter, Z.; Rypniewski, W.; Chmielewski, M. Studies on synthesis and structure of *O*-β-D-ribofuranosyl(1″-->2″)ribonucleosides and oligonucleotides. Nucleosides Nucleotides **1998**, *17*, 411–424.
9. Efimtseva, E.V.; Bobkov, G.V.; Mikhailov, SN.; Van Aerschot, A.; Schepers, G.; Busson, R.; Rozenski, J.; Herdewijn, P. Oligonucleotides containing disaccharide nucleosides. Helv. Chim. Acta **2001**, *84*, 2387–2397.
10. Mikhailov, S.N.; De Clercq, E.; Herdewijn, P. Ribosylation of pyrimidine 2′-deoxynucleosides. Nucleosides Nucleotides **1996**, *15*, 1323–1334.
11. Hanessian, S.; Lavallee, P. The preparation and synthetic utility of tert-butyldiphenylsilyl ethers. Can. J. Chem. **1977**, *53*, 2975–2977.
12. Larsen, E.; Jorgensen, P.T.; Sofan, M.A.; Pedersen, E.B. A new and easy synthesis of silylated furanoid glycals in one step from nucleosides. Synthesis **1994**, 1037–1038.
13. Ti, G.S.; Gaffney, B.L.; Jones, R.A. Transient protection: efficient one-flask syntheses of protected deoxynucleosides. J. Am. Chem. Soc. **1982**, *104*, 1316–1319.
14. Vorbruggen, H.; Krolikiewicz, K.; Bennua, B. Nucleoside synthesis with trimethylsilyl triflate and perchlorate as catalyst. Chem. Ber. **1981**, *114*, 1234–1255.
15. Mikhailov, S.N.; Rodionov, A.A.; Efimtseva, E.V.; Ermolinsky, B.S.; Fomitcheva, M.V.; Padyukova, N.Sh.; Rothenbacher, K.; Lescrinier, E.; Herdewijn, P. Formation of trisaccharide nucleoside during disaccharide nucleoside synthesis. Eur. J. Org. Chem. **1998**, 2193–2199.
16. Robins, M.J.; Robins, R.K. The synthesis of 2′-deoxy-9-α- and β-D-ribofuranosylpurines and the correlation of their anomeric structure with proton magnetic resonance spectra. J. Am. Chem. Soc. **1965**, *87*, 4934–4940.
17. Raap, J.; van Boom, J.H.; van Lieshout, H.C.; Haasnoot, C.A. Conformations of methyl 2′-deoxy-α-D-ribofuranoside and methyl 2′-deoxy-β-D-ribofuranoside. A proton magnetic resonance spectroscopy and molecular mechanics study. J. Am. Chem. Soc. **1988**, *110*, 2736–2743.
18. Rosemeyer, H.; Seela, F.; Toth, G. Assignment of anomeric configuration of D-ribo-, arabino-, 2′-deoxyribo-, and 2′,3′-dideoxyribonucleosides by NOE difference spectroscopy. Nucleosides Nucleotides **1989**, *8*, 587–597.
19. Remaud, G.; Zhou, X.-X.; Chattopadhyaya, J.; Oivanen, M.; Lonnberg, H. The effect of protecting groups of the nucleobase and the sugar moieties on the acidic hydrolysis of the glycosidic bond of 2′-deoxyadenosine: a kinetic and 15 N NMR spectroscopic study. Tetrahedron **1987**, *43*, 4453–4461.
20. Oivanen, M.; Hovinen, J.; Lehikoinen, P.; Lonnberg, H. Hydrolysis of the N-glycosidic bond of nucleosides and nucleotides. Trends Org. Chem. **1993**, *4*, 397–412.
21. Yamaguchi, T.; Saneyoshi, M. Synthetic nucleosides and nucleotides. XXI. On the synthesis and biological evalutions of 2′-deoxy-α-D-ribofuranosyl nucleosides and nucleotides. Chem. Pharm. Bull. **1984**, *32*, 1441–1450.
22. Blunden, S.J.; Cusack, P.A.; Smith, P.J. The use of tin compounds in carbohydrate and nucleoside chemistry. J. Organomet. Chem. **1987**, *325*, 141–152.

23. Vorbruggen, H.; Ruh-Pohlenz, C. Synthesis of nucleosides. In *Organic Reactions*; Paquette, L.A., Ed.; Wiley: New York, 2000; Vol. 55, 1–630.
24. Imazawa, M.; Eckstein, F. Synthesis of 3′-azido-2′,3′-dideoxyribofuranosylpurines. J. Org. Chem. **1978**, *43*, 3044–3048.

Received April 28, 2004
Accepted August 25, 2004