Synthesis and Properties of 3′-Deoxypsiconucleosides: Anomeric 1-(3-Deoxy-D-*erythro*-2-hexulofuranosyl)thymines and 9-(3-Deoxy-D-*erythro*-2-hexulofuranosyl)adenines

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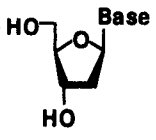
Anomeric 1-(3-deoxy-D-*erythro*-2-hexulofuranosyl)thymines and 9-(3-deoxy-D-*erythro*-2-hexulofuranosyl)adenines were prepared by tin(IV) chloride catalyzed *N*-glycosylation of trimethylsilylated thymine and N^6-benzoyladenine with methyl 3-deoxy-D-*erythro*-2-hexulofuranoside triacetate or tribenzoate, respectively. These *O*-glycosides used as starting materials were obtained by deoxygenation of 1,2:4,5-di-*O*-isopropylidene-β-D-fructopyranose and subsequent acid-catalyzed methanolysis of the resulting 3-deoxy derivative. The anomeric configuration of the nucleosides prepared was assigned by a combination of X-ray crystallography and 2D ^{1}H NMR spectroscopy. The conformation and hydrolytic stability of these new nucleoside analogous are discussed.

The chemical modification of nucleic acid fragments offers a continuous challenge for organic chemists. Usually the base residues or internucleotidic phosphodiester bonds are modified to enable attachment of various conjugate groups, such as chemically reactive groups, chemiluminescent markers or groups promoting intermolecular interactions.[1-4] This brings about distortion of ionic and/or tautomeric properties of the structural units and thus affects the behavior of the entire modified oligomer. Therefore nucleoside analogs which possess the ionic and tautomeric properties and all functional groups of the natural 2′-deoxyribonucleosides (**1**), but display additional functionalities for further derivatization, are of interest. We have focused our attention to 3′-deoxypsiconucleosides (**2**), which fulfil all these requirements. Appropriately protected 4′-phosphoroamidites of **2** may be introduced into oligonucleotides by standard phosphoroamidite strategy[5] and subsequently labeled at 1′-OH. The phosphoroamidites of **2** may also be utilized in the assembly of branched oligonucleotides, multiprobes for hybridization diagnostics. 6′-Triphosphates of **2** are potential substrates of DNA polymerases.



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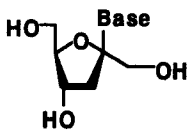

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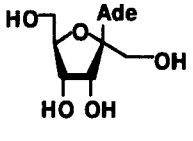

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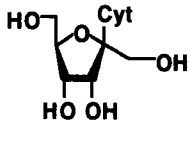

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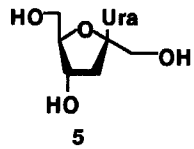

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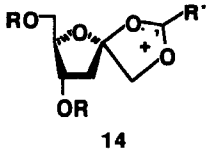

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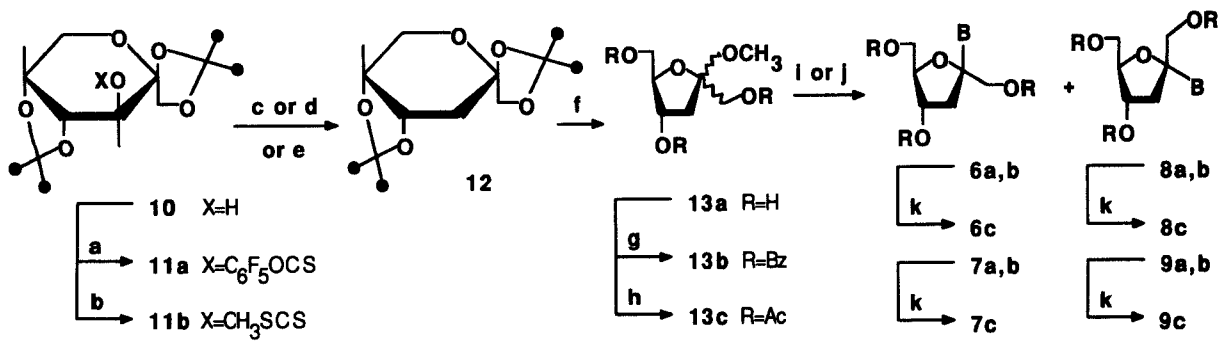
Psiconucleosides **3** and **4**, having a *cis*-diol system analogous to ribonucleosides, have been previously prepared[6,7] starting from D-fructose. The only 3′-deoxypsiconucleoside known is 1-(3-deoxy-β-D-*erythro*-2-hexulofuranosyl)uracil (**5**).[8] The synthetic route applied involves conversion of D-fructose to **5** via 2-amino-β-D-fructofuro[2′,3′:3,4]-2-oxazoline, 2,3′-anhydro-1-(β-D-fructofuranosyl)uracil and 1-(1,4,6-tri-*O*-benzoyl-3-chloro-3-deoxy-β-D-psicofuranosyl)uracil. Accordingly, only uracil nucleosides may be obtained by this method. We now report on a more general procedure, which allows the synthesis of 3′-deoxypsiconucleosides derived from normal DNA bases, such as adenine and thymine. Conformation and hydrolytic stability of these nucleosides **6c**, **7c**, as well as their α-anomers **8c**, **9c**, are discussed.

The synthetic route applied to the preparation of 3′-deoxypsiconucleosides is depicted in Scheme 1. 1,2:4,5 Di-*O*-isopropylidene-β-D-fructopyranose[7] (**10**) was first deoxygenated to the corresponding 3-deoxy derivative **12**, the acid-catalyzed methanolysis of which gave a mixture of anomeric methyl 3-deoxy-D-*erythro*-2-hexulofuranosides (**13a**) and -pyranosides. This mixture was subsequently either peracetylated or perbenzoylated and then fractionated on silica gel to acylated furanosides **13b,c** and pyranosides. The furanoid products **13b,c** were used for *N*-glycosylation of trimethylsilylated thymine or N^6-benzoyladenine and tin(IV) chloride as catalyst. The α- and β-anomers obtained were separated by adsorption chromatography and finally deprotected with methanolic ammonia. The reactions utilized are discussed hereafter.

Three alternative methods of Barton et al.[9-11] were employed to reduce **10** to **12**. Firstly, 1,2: 4,5-di-*O*-isopropylidene-3-*O*-pentafluorophenoxythiocarbonyl-β-D-fructopyranose (**11a**), prepared from **10** according to Robins,[12] was deoxygenated to **12** in triethylsilane in the presence of benzoylperoxide.[9] Secondly, **10** was first converted to its 3-*O*-methylxanthate (**11b**) as described previously,[13] and deoxygenated with tributyltin hydride in the presence of AIBN.[10] Thirdly, **11b** was treated with the *N*-ethylpiperidinium salt of hypophosphorous acid and AIBN in boiling dioxane to give **12**.[11] All these methods gave an overall yield of about 90%. By contrast, treatment of **11b** with benzoyl peroxide in triethylsilane proved to be less efficient, the yield of **12** being only about 30%. Inexpensive and nonexplosive reagents, high yield and convenient work-up made deoxygenation of **11b** with the *N*-ethylpiperidinium salt of hypophosphorous acid the method of choice. 3-Deoxy-1,2:4,5-di-*O*-isopropylidene-β-D-*erythro*-hexulopyranose (**12**) prepared by this method was converted into a furanoside-rich mixture of unprotected methyl glycosides with acid-catalyzed methanolysis. The highest yield of furanoid forms was ob-



	R	B		R	B
6a	Bz	N^6-benzoyladenin-9-yl	**8a**	Bz	N^6-benzoyladenin-9-yl
6b	Ac	N^6-benzoyladenin-9-yl	**8b**	Ac	N^6-benzoyladenin-9-yl
6c	H	adenin-9-yl	**8c**	H	adenin-9-yl
7a	Bz	thymin-1-yl	**9a**	Bz	thymin-1-yl
7b	Ac	thymin-1-yl	**9b**	Ac	thymin-1-yl
7c	H	thymin-1-yl	**9c**	H	thymin-1-yl

[a] C_6F_5OCSCl/4-(dimethylamino)pyridine, r.t., 6 h (**11a**, 83%)
[b] $NaH/CS_2/CH_3I$/dioxane (**11b**, 91%)
[c] Method A: Et_3SiH/BzOOBz, reflux, 3 h (**12** from **11a**, 87%); **12** from **11b**, 31%)
[d] Method B: Bu_3SnH/AIBN/toluene, reflux, 4 h (**12** from **11b**, 91%)
[e] Method C: *N*-ethylpiperidine – hypophosphorous acid/AIBN/dioxane, reflux, 4 h (**12** from **11b**, 94%)
[f] H_2SO_4/MeOH, r.t., 5 h
[g] BzCl/Py, r.t., 6 h (**13b** from **12**, 66%)
[h] Ac_2O/Py, r.t., 10 h (**13c** from **12**, 45%)
[i] silylated BzAde/$SnCl_4$/MeCN or $ClCH_2CH_2Cl$, from −20°C to r.t., 1 h
[j] silylated thymine/$SnCl_4$/MeCN or $ClCH_2CH_2Cl$, from −20°C to r.t., 1 h
[k] NH_3/MeOH, r.t., 24 h (Table 1)

Scheme 1

tained when **12** was treated for 5 h with 0.25% methanolic sulfuric acid at room temperature. The overall yield of anomeric methyl 3-deoxy-D-*erythro*-2-hexulofuranosides, isolated by column chromatography as tribenzoates **13b** or triacetates **13c**, fell in the range 40 to 60% starting from **10**.

The method of Vorbrüggen[14] was applied to *N*-glycosylation of trimethylsilylated thymine and N^6-benzoyladenine with **13b** and **13c** to give rise to the mixtures of protected anomeric nucleosides **6a,b**, **8a,b** and **7a,b**, **9a,b**. The latter were subsequently separated by column chromatography and finally deblocked to give **6c–9c**. Table 1 records the yield and α/β-ratio obtained under various experimental conditions. The highest yields (60%) were achieved by using the tin(V) chloride catalyst in excess. Attempts to use a catalytic amount of tin(IV) chloride or trimethylsilyl trifluoromethanesulfonate were not successful. The ratio of the α- and β-anomers obtained depended on both the attacking nucleobase and the nature of the acyl protecting groups on the sugar moiety. When the methyl glycoside tribenzoate **13b** was used as the

Table 1. *N*-Glycosidation of Anomeric Methyl 1,4,6-Tri-*O*-benzoyl-3-deoxy-D-*erythro*-2-hexulofuranosides (**13b**) and Methyl 1,4,6-Tri-*O*-acetyl-3-deoxy-D-*erythro*-2-hexulofuranosides (**13c**) with Trimethylsilylated Thymine and N^6-Benzoyladenine

Base	Sugar	Catalyst	Solvent	B/S/C[a]	Products	Yield[b]	α/β[c]
A[d]	**13b**	$SnCl_4$	MeCN	2:1:0.1	–	–	–
A	**13b**	$SnCl_4$	MeCN	2:1:1	**6c + 8c**	7	14:1
A	**13b**	$SnCl_4$	MeCN	2:1:5	**6c + 8c**	61	11:1
A	**13b**	TMSOTf[e]	MeCN	2:1:0.1	–	–	–
A	**13b**	TMSOTf[e]	MeCN	2:1:5	–	–	–
A	**13b**	$SnCl_4$	$ClCH_2CH_2Cl$	2:1:5	**6c + 8c**	64	30:1
A	**13c**	$SnCl_4$	MeCN	2:1:5	**6c + 8c**	37	1:3
T[f]	**13b**	$SnCl_4$	MeCN	2:1:0.1	–	–	–
T	**13b**	$SnCl_4$	MeCN	2:1:1	**7c + 9c**	12	1:3
T	**13b**	$SnCl_4$	MeCN	2:1:5	**7c + 9c**	62	1:3
T	**13b**	TMSOTf[e]	MeCN	2:1:5	–	–	–
T	**13b**	$SnCl_4$	$ClCH_2CH_2Cl$	2:1:5	**7c + 9c**	58	1:5
T	**13c**	$SnCl_4$	MeCN	2:1:5	**7c + 9c**	41	1:2

[a] Molar ratio of the base, sugar and catalyst.
[b] After deprotection and isolation.
[c] Determined by RP HPLC.
[d] Trimethylsilylated N^6-benzoyladenine.
[e] Trimethylsilyl trifluoromethanesulfonate.
[f] Trimethylsilylated thymine.

Table 2. Chromatographic Retention Times, UV Absorption Maxima, and Vicinal and Geminal $^1H,^1H$-Coupling Constants of the Sugar Moiety of the 3′-Deoxypsiconucleosides **6c–9c**

Compound	t_R/min[a]	UV_{max}/nm[b]	^1H NMR coupling constants/Hz[c] 3′,4′	3″,4′	4′,5′	5′,6′	5′,6″	1′,1″	3′,3″	6′,6″
6c	4.9	259 (15.3)	6.7	3.7	[d]	3.8[e]	8.1	[d]	14.9	11.8
8c	5.3	259 (15.5)	6.4	1.5	[d]	4.0	5.6	12.4	14.0	12.4
7c	5.1	267 (9.9)	6.8	3.5	3.8	3.7	5.7	12.3	14.9	12.4
9c	4.8	267 (9.8)	6.3	3.3	3.1	4.2	6.6	12.2	14.7	12.2

[a] RP column (Spherisorb ODS-2, 5 μm, 4.6 × 250 nm), 7.5% MeCN in 0.1 M NH_4OAc, flow rate 1 mL min^{-1}.
[b] In MeOH $\varepsilon/10^3$ given in parentheses.
[c] In D_2O.
[d] Could not be obtained owing to overlapping.
[e] The assignment of H6′ and H6″ is tentative.

starting material, the α-anomer predominated with N^6-benzoyladenine and the β-anomer with thymine. By contrast, *N*-glycosidation of the methyl glycoside triacetate **(13c)** gave predominantly the β-anomer with both bases. Evidently the attack on the 1,2-acyloxonium ion **14** from either α- or β-side is possible, and hence the product distribution is sensitive to structural changes of the reactants.

One of the anomers of adenine 3′-deoxypsiconucleosides prepared **8c** gave crystals that enabled determination of the molecular structure by X-ray diffraction. The anomeric configuration was shown to be α.[15]

The 2D NOESY ^1H NMR spectrum of the same compound showed distinct cross peaks of the well separated H1′ and H6′ methylene resonances in D_2O [δ H1′ d 3.82 and d 3.98; δ H6′ dd 3.61 and dd 3.70]. One of the anomers of thymine 3′-deoxypsiconucleoside **9c** exhibited very similar spectroscopic characteristics: H1′ resonances at d 3.72 and d 3.91 showed distinct cross peaks with the H6′ resonances at dd 3.47 and dd 3.59. Consequently, this nucleoside may also be assigned as the α-anomer, and hence the two other nucleosides, **6c** and **7c**, must have β-configuration. Unfortunately, with the latter compounds H1′ and H6′ resonances overlap, which hampered the interpretation of their 2D NOESY spectra. The assignment of the anomeric configuration, however, receives additional support from the fact that the sugar moiety 1D spectrum of **9c** closely resembles that of **8c** (shown to be α by X-ray crystallography), and differs from that of **6c**. In fact the only marked difference between the 1D spectra of **8c** and **9c** is that with the adenine nucleoside **8c** the H3′ resonates at a higher field than the H3″, while with the thymine nucleoside **9c** the situation is opposite. The 1D spectrum of **7c**, in turn, closely resembles that of **6c**. Again the only difference is the opposite order of the H3′ and H3″ resonances. Similarly, with 2′-deoxyribonucleosides the order of the H2′ and H2″ resonances is changed on going from adenine to thymine nucleosides.[16]

Table 2 records the vicinal and geminal ^1H, ^1H coupling constants for the 3′-deoxypsiconucleosides prepared. The coupling constant *J*(H4′,H5′), corresponding to *J*(H3′,4′) of 2′-deoxyribonucleosides, may be employed to estimate the mole fraction of the sugar-ring conformers,[17] when the two state model, *N*(3′-*exo*-4′-*endo*)⇔*S* (3′-*endo*-4′-*exo*), of Altona and Sundaralingam is used to describe the ring puckering.[18] The values of 3.1 and 3.8 Hz observed for the α- and β-nucleosides of thymine suggest that the *S* conformer prevails, x(*S*) falling in the range 0.6 to 0.8. In other words, the ring puckering is similar to that of 2′-deoxyribonucleosides. The X-ray structure of the α-nucleoside of adenine exhibits the following typical conformational features: (i) the ring puckering is of *S*-type ($P = 168°$ and $\phi_m = 35°$), (ii) the base moiety is *anti* ($O^{5'}$–C2′–N9–C4 180°), (iii) C1′-hydroxymethyl group is *gg* ($O^{1'}$–C1′–C2′–C3′–51°) and (iv) C6′-hydroxymethyl group is *gt* ($O^{6'}$–C6′–C5′–C4′ 166°).

Table 3 records the first-order rate constants and the activation parameters for the acid-catalyzed hydrolysis of the 3′-deoxypsiconucleosides prepared. The anomeric configuration has only a minor effect on the hydrolytic stability. The adenine derivatives, **6c** and **8c**, are hydro-

Table 3. First-order Rate Constants and the Enthalpies and Entropies of Activation for the Hydrolysis of the *N*-Glycosidic Bond of 3′-Deoxypsiconucleosides at 333.2 K[a]

Compound	$[H^+]$/M	$k_{obs}/10^{-3}\ s^{-1}$	$\Delta H^{\neq}$/kJ mol^{-1}	$\Delta S^{\neq}$/JK^{-1} mol^{-1}
6c	0.0010	10.2 ± 0.1	95.6 ± 1.9	50 ± 7
8c	0.0010	12.5 ± 0.1	94.3 ± 1.5	58 ± 5
7c	0.10	0.0317 ± 0.0003	123.9 ± 1.5	59 ± 4
9c	0.10	0.0255 ± 0.0004	124.8 ± 0.6	60 ± 2

[a] In aqueous HCl; ionic strength adjusted to 0.1 M with NaCl. Reference state of activation parameters is a dilute solution of the substrate in 1 M aq acid.

lyzed about two orders of magnitude as fast as 2′-deoxyadenosine.[19] This is expected, since purine 2′-deoxyribonucleosides are known to hydrolyze by rate-limiting formation of a cyclic glycosyl oxocarbenium ion.[19,20] The tertiary ionic intermediate derived from 3′-deoxypsiconucleosides is undoubtedly markedly more stable than the secondary ion derived from 2′-deoxyribonucleosides. The thymine 3′-deoxypsiconucleosides are, in turn, hydrolyzed 250 times as rapidly as thymidine.[19] No anomerization of the starting material was observed, in contrast to thymidine[21] and its 3′-*O*-substituted derivatives,[16] but analogously with 3′-deoxythymidine.[16] One may tentatively assume that thymine nucleosides are hydrolyzed via a cyclic glycosyl oxocarbenium ion only when this intermediate is exceptionally stable, but otherwise via an acyclic Schiff base intermediate, as suggested by Cadet and Teoule.[21] Anyway, the reactivity difference between 3′-deoxypsiconucleosides and 2′-deoxyribonucleosides is comparable with adenine and thymine nucleosides. With all the 3′-deoxypsiconucleosides the entropies of activation are slightly positive, consistent with the unimolecular nature of the rate-limiting step.

The melting points reported are uncorrected. The TLC separations were carried out on silica gel plates (Merck, F_{254}) and column chromatography on Silica gel 60 (Merck). Merck Lichroprep RP-18 column (40–63 μm, 25 × 250 mm) was employed for the preparative RP chromatography. The ^{1}H NMR spectra were recorded on a 400 or 500 MHz spectrometer. The assignment of nucleoside sugar protons were based on 2D COSY measurements, where the matrix size was 1024 × 256. A sineball window function was applied to both axes before FFT. The assignment of the anomeric configuration of nucleosides **6c–9c** was based on 2D NOESY experiments. The matrix size and the window function was equal to the COSY experiment. The mixing time applied in NOESY was 1000 ms. After assignment of the anomeric configuration the 3′- and 3″-protons were assigned on the basis of the cross peaks of their resonances with the 1′-hydroxymethyl resonance.

First-order rate constants of the hydrolysis of **6c–9c** were obtained by the HPLC technique described previously.[20] All new compounds gave satisfactory microanalysis, C ± 0.25, H ± 0.25, N ± 0.2.

3-Deoxy-1,2:4,5-di-*O*-isopropylidene-β-D-*erythro*-2-hexulopyranose (12):

Method A: 1,2:4,5-Di-*O*-isopropylidene-β-D-fructopyranose[7] (**10**; 3.22 g, 12.38 mmol) was converted to its 3-*O*-pentafluorophenoxythiocarbonyl derivative **11a** as described by Robins.[12] The crude **11a** was dissolved in triethylsilane (30 mL) under argon, the solution was brought to boil and treated with 70% benzoyl peroxide (2.00 g, 5.78 mmol) in 3 portions at 30 min intervals. When the reaction was complete (2 h), the solvent was evaporated, and **12** was isolated by short-column chromatography on silica gel (benzene/EtOAc 6:1, v/v). The pure fractions were pooled and evaporated to dryness, and the residue was distilled (bp 80–84 °C/1 Torr) to give pale yellow crystals. Recrystallization from MeOH gave 2.63 g (87%) of white crystalline **12**.

Method B: Compound **10** (33.0 g, 126.9 mmol) was converted to 3-methylxanthate **11b** as described previously.[13] The crude product was treated with Bu_3SnH according to Barton and McCombie,[10] and the radical reaction was initiated by adding AIBN (0.50 g, 3.04 mmol). After the reaction was completed, the mixture was diluted with hexane (300 mL), and the product was extracted with MeCN (3 × 100 mL). The extracts were combined, evaporated to dryness, and the residue was distilled and crystallized as described above to give 28.2 g (91%) of white crystalline **12**.

Method C: Crude **11b** obtained from **10** (14.56 g, 56.0 mmol)[13] was dissolved in dioxane (420 mL) and treated with the *N*-ethylpiperidinium salt of hypophosphorous acid (100.8 g, 560 mmol) and a solution of AIBN (6.00 g, 36.54 mmol) in dioxane (80 mL).[11] Distillation and crystallization from MeOH gave **12** 12.85 g (94%) as white crystals; mp 72–74 °C; $[\alpha]_D^{25} = -105°$ (c = 1.09, $CHCl_3$); R_F 0.29 (TLC; benzene/EtOAc 6:1).

^{1}H NMR ($CDCl_3$) δ = 1.34, 1.38, 1.48, 1.50 (each 3 H, s, *i*-Pr); (1 H, dd, J = 12.7, 4.5 Hz, H3); 2.08 (1 H, dd, J = 12.7, 5.7 Hz, H3); 3.83 (1 H, d, J = 9.2 Hz, H1); 3.90 (2 H, d, J = 1.8 Hz, H6); 4.07 (1 H, d, J = 9.2 Hz, H1); 4.14 (1 H, dt, J = 6.7, 1.8 Hz, H5); 4.48 (1 H, m, H4).

Methyl 1,4,6-Tri-*O*-benzoyl-3-deoxy-α- and -β-D-*erythro*-2-hexulofuranosides (13b) and Methyl 1,4,6-Tri-*O*-acetyl-3-deoxy-α- and -β-D-*erythro*-2-hexulofuranosides (13c):

Compound **12** (23.6 g, 96.7 mmol) was dissolved in MeOH (1000 mL) containing 0.25% (v/v) sulfuric acid, and the solution was kept 5 h at r. t. The acidic solution was neutralized with conc. aq ammonia and evaporated to dryness. The residue was extracted with EtOAc (5 × 100 mL) and evaporated to dryness. The residue was coevaporated with pyridine (2 × 100 mL), dissolved in the same solvent (300 mL), and the solution was divided into two equal parts. One part was benzoylated and the other acetylated in a conventional manner. Compounds **13b** and **13c** were isolated as colorless oils by column chromatography on silica gel, using a mixture of cyclohexane and EtOAc (9:1, v/v) as eluant. The yield of anomeric mixture (0.85:1) **13b** was 15.64 g (66%); R_F 0.60 (TLC; benzene/EtOAc 9:1).

^{1}H NMR ($CDCl_3$): δ = 2.44 (2 H, dd, J = 14.7, 3.4 Hz, H3); 2.54 (1 H, dd, J = 14.2, 5.4 Hz, H3); 2.73 (2 H, dd, J = 14.7, 8.3 Hz, H3); 2.80 (1.7 H, dd, J = 14.2, 7.3 Hz, H3); 3.37 (2.6 H, s, OMe); 3.44 (3 H, s, OMe); 4.37–4.67 (9.3 H, m, H1, H5, H6); 5.54 (1 H, m, H4); 5.68 (0.85 H, m, H4); 7.30–8.15 (28 H, m, benzoyl).

The yield of anomeric mixture (1:1) **13c** was 6.62 g (45%); R_F 0.28 (TLC; benzene/EtOAc 6:1).

^{1}H NMR ($CDCl_3$): δ = 1.9–2.2 (4 H, m, H3); 2.01, 2.02, 2.11, 2.12, 2.13 and 2.14 (each 3 H, s, OAc); 3.25 (6 H, br. s, OMe); 3.82–4.27 (8 H, m, H1, H6); 5.19 (2 H, m, H5); 5.28 (1 H, m, H4); 5.31 (1 H, m, H4).

3′-Deoxypsiconucleosides (6c–9c):

N^6-Benzoyladenine (4.78 g, 20.0 mmol) or thymine (2.52 g, 20.0 mmol) was heated under reflux in a mixture of hexamethyldisilazane (50 mL) and Me_3SiCl (5 mL) until the solid had dissolved. The mixture was evaporated and the residue was dissolved in MeCN or $ClCH_2CH_2Cl$ (100 mL) containing **13b** (4.90 g, 10.0 mmol) or **13c** (3.04 g, 10.0 mmol). The solution was cooled to −20 °C. $SnCl_4$ (13.0 g, 50 mmol) was added, and the mixture was allowed to warm to r.t. After 1 h the mixture was poured into sat. aq. $NaHCO_3$ (500 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The extracts were washed with H_2O (2 × 100 mL), dried (Na_2SO_4) and evaporated to dryness. An analytical sample was deblocked with NH_3/MeOH (24 h) and analyzed by RP HPLC (Table 1). The anomeric mixture of protected nucleosides was separated on a silica gel column, using a mixture containing from 10 to 20% EtOAc in benzene as eluant. Fractions containing the separated protected anomers were pooled, evaporated, deblocked with NH_3/MeOH (24 h) and evaporated to dryness. The residue was dissolved in H_2O and applied onto a column containing 10 mL of Dowex 1X8 (OH^-). The resin was washed with H_2O and the nucleosides were eluted with either 30% aq EtOH (adenine derivatives) or 0.1 M NH_4HCO_3 (thymine derivatives). The eluates were concentrated to a volume of 1 to 2 mL and applied onto a preparative RP column. Fractions of pure nucleosides obtained by elution with 5% aq MeCN were pooled, evaporated to dryness, coevaporated with EtOH (3 × 25 mL) and finally dried in vacuo to give **6c–9c** as colorless foams.

8c (from **13b** in $ClCH_2CH_2Cl$) was crystallized from MeOH/acetone to give 1.80 g (64%) of white crystals; mp 199–201 °C.

^{1}H NMR (D_2O) δ = 2.52 (1 H, dd, H3′); 2.81 (1 H, dd, H3″); 3.61 (1 H, dd, H6″); 3.70 (1 H, dd, H6′); 3.82 and 3.98 (each 1 H, d, H1′

and H1″); 4.25 (1 H, m, H5′); 4.34 (1 H, m, H4′); 8.02 (1 H, s, H2); 8.12 (1 H, s, H8).

Crystals of **8c** were monoclinic, space group $P2_1$ with a = 6222(2) Å, b = 9861.1(1) Å, c = 10797(1) Å, V = 639.0(2) å^3, Z = 2, $d_{calc.}$ = 1.462 g cm^{-3}, F(000) = 296, μ(MoKα) = 1.07 cm^{-1}. Listing of final data is deposited with Cambridge Crystallographic Data Centre.

The yield of **6c** (from **13c** in MeCN) was 0.78 g (28 %).

^{1}H NMR (D_2O) δ = 2.30 (1 H, dd, H3″); 2.91 (1 H, dd, H3′); 3.72 (1 H, dd, H6″); 3.78 (1 H, dd, H6′); 3.83–3.90 (3 H, m, H1′, H1″ and H5′); 4.11 (1 H, m, H4′); 8.10 (1 H, s, H8); 8.21 (1 H, s, H2).

The yield of **9c** (from **13c** in MeCN) was 0.37 g (14 %).

^{1}H NMR (D_2O) δ = 1.80 (3 H, d, J = 1.1 Hz, Me); 2.33 (1 H, dd, H3″); 2.76 (1 H, dd, H3′); 3.47 (1 H, dd, H6″); 3.59 (1 H, dd, H6′); 3.72 and 3.91 (each 1 H, d, H1′ and H1″); 4.15 (1 H, m, H5′); 4.20 (1 H, dt, H4′); 7.87 (1 H, d, J = 1.1 Hz, H6).

The yield of **7c** (from **13b** in $ClCH_2CH_2Cl$) was 1.32 g (48 %).

^{1}H NMR (D_2O) δ = 1.83 (3 H, d, J = 1.1 Hz, Me); 2.54 (1 H, dd, H3′); 2.79 (1 H, dd, H3″); 3.69 (1 H, dd, H6″); 3.81 (1 H, dd, H6′); 3.76 and 4.00 (each 1 H, d, H1′ and H1″); 4.13 (1 H, m, H5′); 4.33 (1 H, dt, H4′); 7.84 (1 H, d, H6).

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