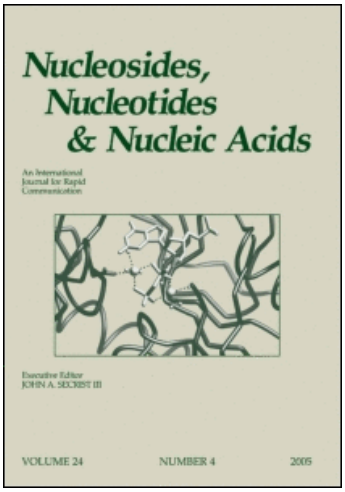

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Synthesis of 2'-Deoxy-2' -Fluoro-D-Arabinopyranopyranosyl Nucleosides and Their 3',4'-Seco analogues

P. Herdewijn[a]; A. Van Aerschot[a]; R. Busson[a]; P. Claes[a]; E. De Clercq[a]
[a] Rega Institute for Medical Research, Laboratory of Pharmaceutical Chemistry and Laboratory of Chemotherapy, Katholieke Universiteit Leuven, Leuven, Belgium

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SYNTHESIS OF 2'-DEOXY-2'-FLUORO-D-ARABINOPYRANOSYL NUCLEOSIDES AND THEIR 3',4'-SECO ANALOGUES

P. Herdewijn*, A. Van Aerschot, R. Busson, P. Claes and E. De Clercq

Rega Institute for Medical Research, Laboratory of Pharmaceutical Chemistry and Laboratory of Chemotherapy, Katholieke Universiteit Leuven, Minderbroedersstraat 10, B-3000 Leuven, Belgium

Abstract. 2'-Deoxy-2'-fluoro-D-arabinopyranosyl nucleosides were synthesized by condensation of 1,3,4-tri-O-benzoyl-2-deoxy-2-fluoro-D-arabinopyranose with the appropriate silylated bases in the presence of trimethylsilyl triflate. Scission of the 3',4'-bond by periodate oxidation followed by sodium borohydride reduction resulted in the formation of the 3',4'-seco analogues of the 2'-deoxy-2'-fluoro-D-arabinofuranosyl nucleosides.

Pyrimidine nucleosides with a 2-deoxy-2-fluoro-D-arabinofuranose moiety rank among the most active antiherpetic agents[1]. They show potent activity against the multiplication of herpes simplex virus type 1 (HSV-1), herpes simplex virus type 2 (HSV-2), varicella zoster virus (VZV) and cytomegalovirus. From *in vivo* studies with 2'-fluoro-5-iodo-1-β-D-arabinofuranosylcytosine (FIAC)[2] and 2'-fluoro-5-methyl-1-β-D-arabinofuranosyluracil (FMAU)[3], FMAU appeared to be superior to FIAC. However, FMAU is neurotoxic[4,5], and both FIAC and FMAU are incorporated into viral as well as cellular DNA[6]. The 5-ethyl analogue of FMAU, i.e. 2'-fluoro-5-ethyl-1-β-D-arabinofuranosyluracil (FEAU), is less active but also less toxic than FMAU[7,8]. In contrast to FIAC and FMAU, FEAU could not be detected in host cell DNA[9]. The selectivity of these compounds is based on the presence of a virus-specific thymidine kinase which converts them to the corresponding 5'-monophosphate derivatives[10]. The monophosphate derivatives are further phosphorylated by cellular enzymes to the triphosphates which then inhibit the viral DNA polymerase[11].

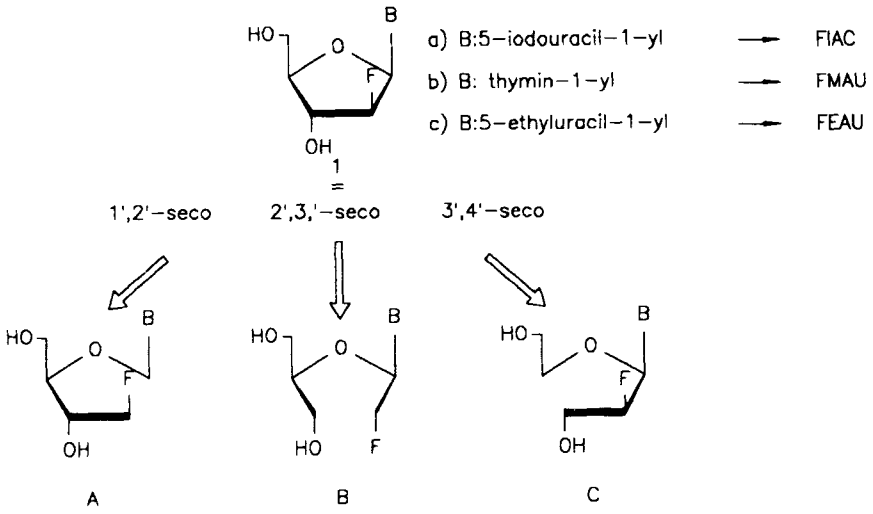
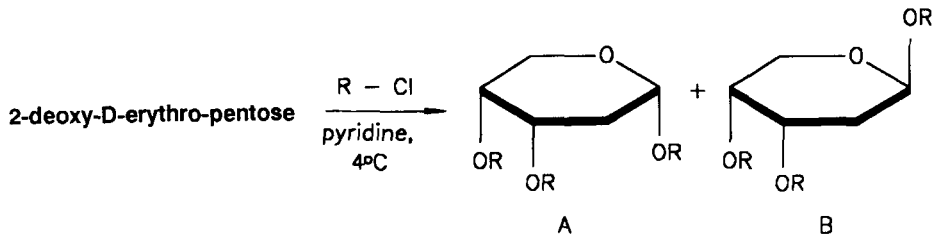


Figure 1

Acyclic fluorinated nucleosides have not been the subject of extensive studies[12]. Assuming that the hydroxyethoxymethyl ($HOCH_2CH_2OCH_2$) group contains important recognition sites for metabolic enzymes involved in the phosphorylation of the compound (as is the case for acyclovir), we could envisage three types of acyclic fluorinated nucleosides (Figure 1). Of these three possible "seco" structures, two (A and B) have a fluorine substituent on a primary carbon atom. In order to mimic the 2-fluoro-β-D-arabinofuranosyl nucleosides, the fluorinated carbon atom for type C structures should be in the (S)-configuration.

A possible problem with acyclic fluorinated compounds is that when metabolized in vivo, they could release the highly toxic fluoroacetate. Such a metabolite could be easily formed from structure B. Structure C could give rise to 2-fluoro-3-hydroxypropanoic acid, which likewise may be converted to fluoroacetate. However, 2-fluoro-3-hydroxypropanoic acid can be formed only after cleavage of the glycosyl bond. It has been shown that 2-fluoro-β-D-arabinofuranosyl nucleosides are resistant to nucleoside phosphorylases[9] and 2'-fluorinated 3',4'-seconucleoside analogues (structure C) may also be expected to resist degradation by nucleoside phosphorylases.



A B

2 R: benzoyl	40 %	60 %
3 R: 4 tert–butylbenzoyl	25 %	75 %

Scheme 1

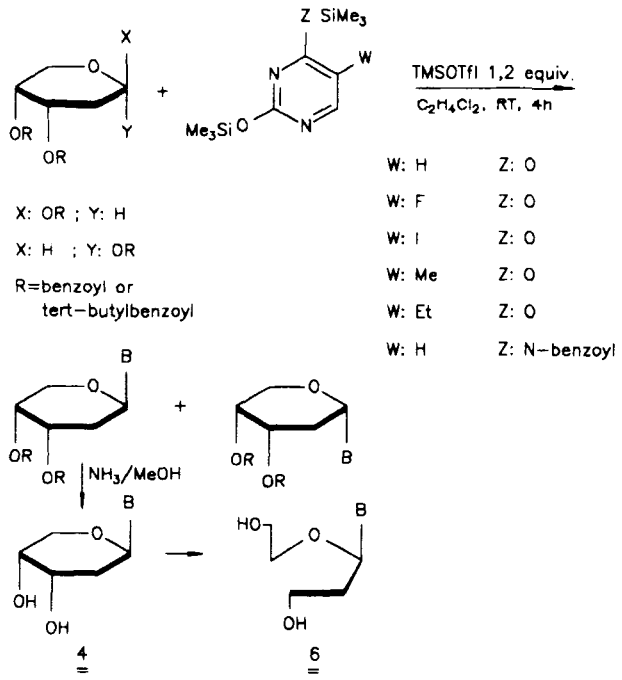
CHEMISTRY

Our synthetic strategy consisted of the condensation of a purine or pyrimidine base with the appropriately fluorinated pentopyranose followed by oxidative scission of the C_3-C_4 bond. The feasibility of this approach was first tried on 2-deoxy-D-ribopyranose nucleosides.

1,3,4-Tri-O-benzoyl-2-deoxy-α-D-ribopyranose (2A) (mp 151-152°C) and 1,3,4-tri-O-benzoyl-2-deoxy-β-D-ribopyranose (2B) (mp 157-158°C) were synthesized as described by Pedersen et al[13] (Scheme 1). Both anomers were separated by column chromatography (eluent : CH_2Cl_2) and crystallized from EtOH. The α/β ratio was 2/3. Using the more bulky 4-tert-butylbenzoyl protecting group, 1,3,4-tri-O-(4-tert-butylbenzoyl)-2-deoxy-α-D-ribopyranose (3A) and 1,3,4-tri-O-(4-tert-butylbenzoyl)-2-deoxy-β-D-ribopyranose (3B) were obtained in an α/β ratio of 1/3.

Condensation reactions with the silylated bases were carried out in dichloroethane at room temperature with 1.2 equiv. of trimethylsilyl trifluoromethanesulphonate (TMSOTfl) as catalyst (Scheme 2). The results are summarized in Table I. The condensation reaction can be followed by HPLC. Therefore, a sample of the reaction mixture was diluted with $CHCl_3$, washed with 5% sodium bicarbonate solution, dried on Na_2SO_4 and analyzed on an Lichrosorb Si 60 10 μ column (eluent : CH_2Cl_2-CH_3CN 90:10).

Figure 2 gives the HPLC profile of the crude reaction mixture of the condensation of 3 different pyrimidine bases with 1,2,4-tri-O-



a) B: uracil-1-yl b) B: thymin-1-yl c) B: 5-iodouracil-1-yl
d) B: 5-fluorouracil-1-yl e) B: 5-ethyluracil-1-yl
f) B: cytosin-1-yl

Scheme 2

TABLE 1. Yields and α/β ratio of the condensation reaction of silylated pyrimidine bases with protected 2-deoxy-D-ribopyranose

Base	Protecting group			
	Benzoyl (2A,2B)		tert butyl benzoyl (3A,3B)	
	Ratio α/β	Total Yield %	Ratio α/β	Total Yield %
Thymine	80/20	93	75/25	94
5-Fluoro-uracil	68/32	90	58/42	94
5-Iodo-uracil	76/24	90	63/37	93
N-benzoyl-cytosine	80/20	94	71/29	95
5-Ethyl-uracil	73/27	93	ND	ND
Uracil	66/34	91	ND	ND

ND : not determined

Figure 2. HPLC profile of the crude reaction mixture of the condensation of 2 with silylated 5-fluorouracil, 5-iodouracil and thymine. Lichrosorb Si60 10 μ (CH_2Cl_2-CH_3CN 90:10).

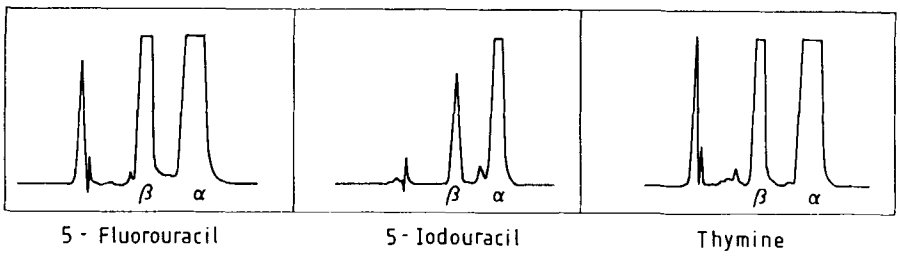


Figure 2

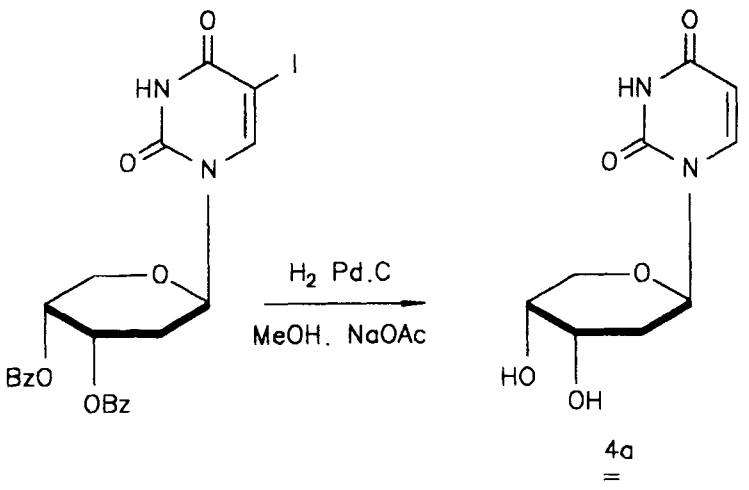
benzoyl-2-deoxy-D-ribopyranose. These chromatograms also show that negligible amounts of side compounds are formed during the condensation reaction.

The α-anomer always predominated. A slight increase in the amount of the β-anomer was obtained with the 4-tert-butylbenzoyl protecting group. The obtained ratios were independent of the use of pure α (2A,3A) or pure β (2B,3B) isomers as the starting material.

Because of the predominant formation of the thermodynamic more stable α isomer, neighboring group participation of the 3-O-benzoyl-group to direct the glycosylation reaction could only be of minor influence. Starting from the pure silylated α-nucleoside, however, an anomerization could be performed by stirring the compounds in acetonitrile at room temperature in the presence of TMSOTfl. An equilibration was reached after 48 h with the formation of 20-30% of the β isomer.

The α and β anomers of the 2-deoxyribopyranose nucleosides could be separated when still protected. This separation was more difficult after removal of the benzoyl protecting groups.

The reaction with silylated uracil gave a mixture of α and β 1-(3,4-di-O-benzoyl-2-deoxy-D-ribopyranosyl)uracil in 91% total yield (Table I). Although both isomers could be separated by HPLC (CH_2Cl_2-CH_3CN 95:5), the separation of the anomeric compounds on a preparative scale with usual laboratory chromatographic equipment is a very



Scheme 3

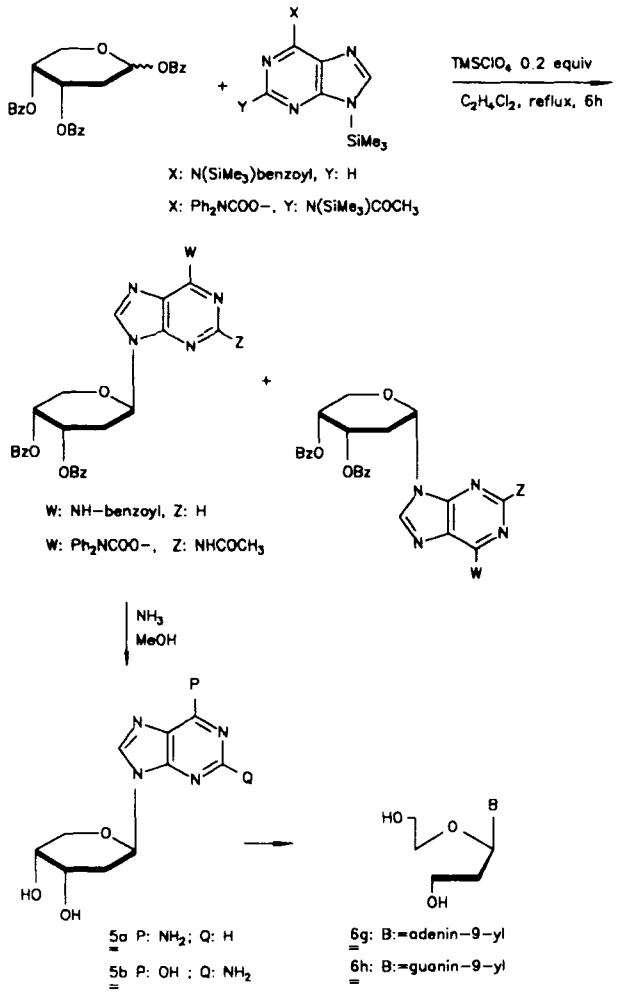
laborious task. Therefore, pure 1-(2-deoxy-β-D-ribopyranosyl)uracil was synthesized from the 5-iodo analogue as depicted in Scheme 3. The anomers with a 5-iodouracil base moiety are better separated by chromatography than those with the uracil base. Catalytic hydrogenation overnight in the presence of Pd/C in MeOH containing sodium acetate, not only reduced the 5-position but also removed the benzoyl protecting groups (by transesterification) yielding 1-(2-deoxy-β-D-ribopyranosyl)uracil in 66%.

As can be seen from Table 2, the α and β anomer of the benzoylated nucleosides can be clearly distinguished by ^{1}H NMR. H-1' resonates at higher field for the α-anomer . The signals of the 3'- and 4'-protons are well separated for the β-isomer but are more close to each other for the α-isomer. The 5'-protons of the β-isomer appear as a doublet at δ values between 4.20 and 4.30 ppm while these signals for the 5'-protons of the α-isomer are clearly separated, showing two distinct doublets at δ values of ± 4.10 and 4.40 ppm. These values are in agreement with previously published data on the thymine analogue[14,15].

The reaction with protected silylated purine bases ($\underline{N}^6$-benzoyladenine[16] and $\underline{N}^2$-acetyl-$\underline{O}^6$-diphenylcarbamoylguanine[17]) in the presence of TMSOTfl at room temperature gave an intractable mixture of com-

TABLE 2. ^{1}H NMR data of the α and β anomers of 3,4-di-O-benzoyl-2-deoxy-D-ribopyranose nucleosides

	α-anomer				β-anomer			
Base	H-1'	H-3';H-4'	H-5'	H-5"	H-1'	H-3'	H-4'	H-5';H-5"
Thymin-1-yl	5.90	5.50	3.90	4.35	6.12	5.90	5.30	4.20
5-Iodouracil-1-yl	5.96	5.55	4.04	4.38	6.25	5.88	5.25	4.18
5-Fluorouracil-1-yl	5.97	5.56	4.04	4.46	6.18	5.95	5.32	4.20
N^4-benzoylcytosin-1-yl	6.05	5.57	4.06	4.47	6.34	5.97	5.37	4.27
N^6-benzoyladenin-9-yl	6.15	5.69	4.15	4.52	6.34	6.04	5.53	4.31
O^6-diphenylcarbamoyl-N^2-acetylguanin-9-yl	5.91	5.49	4.01	4.40	6.18	5.96	5.46	4.23



Scheme 4

pounds. However, the use of 0.2 eq of trimethylsilyl perchlorate at reflux for 6 h gave a clean reaction mixture from which the α and β nucleosides could be isolated after column chromatography. The catalyst was added in two portions : 0.1 equivalent at the start and another 0.1 equivalent after 3 h reflux. The N-benzoyladenine analogue was obtained in 62% yield in an α/β ratio of 55/45, the guanine analogue in 55% yield in an α/β ratio of 65/35 (Scheme 4). Debenzoylation was carried out with ammonia in methanol.

9-(2-Deoxy-β-D-ribopyranosyl)adenine was synthesized previously by Zinner and Wittenburg[18], Robins et al[19] and Nagasawa et al[20]. They

described a compound with a mp of 266-267°C as the β-anomer and a compound with a mp of 232-235°C as the α-anomer. The assignment of the configuration was based on an extensive ^{1}H NMR study[21]. However, the mp we obtained for the α isomer was the higher one. Also the ^{1}H NMR values we obtained were not in agreement with the above assignment. The physical data for the 2-deoxy-β-D-ribopyranosyl nucleosides are described in Table 3. Therefore we undertook an X-ray analysis study of the β-adenine analogue and of the β-5-iodouracil analogue[22].

These structures derived from the crystallographic analysis are in agreement with the configurations proposed by us. This again indicates that determination of anomeric configuration by ^{1}H NMR studies should be pursued with extreme caution.

Periodate oxidation cleaved the C3'-C4' bond, and the dialdehyde was reduced with sodium borohydride providing the corresponding acyclic nucleosides[23]. The compound with the adenine base, 9-[1-(2-hydroxyethoxy)-3-hydroxypropyl]adenine[26], with the thymine base 1[1-(2-hydroxyethoxy)-3-hydroxypropyl]thymine[27] and with the guanine base 9-[1-(2-hydroxyethoxy)-3-hydroxypropyl]guanine[28] have also been described previously as a racemic mixture. Table 4 describes the physical data for the acyclic nucleosides which are in good agreement with a recent Russian publication describing the adenine, guanine, thymine and cytosine analogues[29].

2-Deoxy-2-fluoro-D-arabinose was synthesized as previously described by Fox et al[30,31]. Both protecting groups were removed with methanolate in methanol. Reaction of 2-deoxy-2-fluoro-D-arabinose with benzoyl chloride in pyridine at 0°C afforded 26% of crystalline 1,3,4-tri-O-benzoyl-2-deoxy-2-fluoro-β-D-arabinopyranose and 31% of crystalline 1,3,4-tri-O-benzoyl-2-deoxy-2-fluoro-α-D-arabinopyranose. The most probable conformation of these anomers (Scheme 5) could be deduced from their ^{1}H NMR coupling constants and chemical shift values (Table 5).

The β-anomer shows a large trans-diaxial $J_{2,3}$ coupling constant of 10 Hz, a small $J_{1,2}$ coupling constant (3.6 Hz) and two clearly distinguishable H-5 protons (4.05 and 4.44 ppm). Also typical is the zero value of $J_{1,F}$. The same values were previously reported for 1,3,4-tri-O-acetyl-2-deoxy-2-fluoro-β-D-arabinopyranose[32]. The α-anomer shows coupling constants for H-1/H-2 of 7.0 Hz and for H-2/H-3 of 8.5 Hz. The chemical shift values for the two H-5 protons are similar.

TABLE 3. Physical data for 2-deoxy-β-D-ribopyranosyl nucleosides

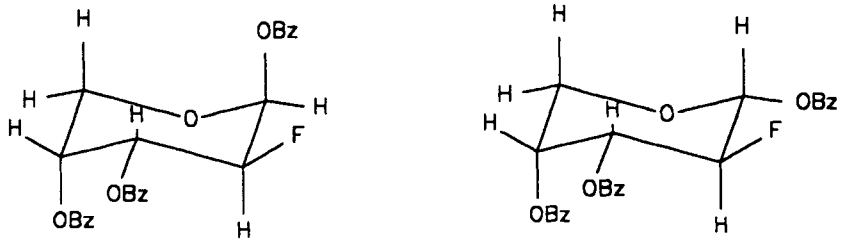
B	mp (°C)	UV		MS	^{1}H NMR[b]				
		λ_{max} (nm)	log ε	m/z (M)	H-1'	H-2' H-2"	H-3'	H-4'/H-5'	Base protons
Thymin-1-yl	220-221[c]	266	3.99	242	5.85	2.01	4.00	3.61	7.56
5-Iodouracil-1-yl	190-192[d]	284	3.92	354	5.89	1.93	4.01	3.64	8.09
Uracil-1-yl	200-202[e]	260	4.00	228	5.84	2.06	4.01	3.62	5.62;7.69
5-Fluorouracil-1-yl	200-202[d]	267	3.94	246	5.91	2.10	4.29	3.88	7.97; $J_{6,F}$=6.4Hz
5-Ethyluracil-1-yl	180-185	267	4.00	256	5.96	2.00	4.00	3.63	7.95
Cytosin-1-yl	237-239[d]	272	3.93	227	5.90	1.90	4.00	3.58	5.75;7.60
Adenin-9-yl	223-225	260	4.18	251	6.00	2.33	4.10	3.76	8.20;8.37
Guanin-9-yl	>300	254	4.13	-	5.80	2.18	4.08	3.68	7.91

[a]All spectra were taken in DMSO-d_6 with tetramethylsilane as internal standard (δ values are given).
[b]The resonance signal of the OH protons is seen as an overlapping double doublet between δ 4.7 and 4.9.
[c]Ref. 24 : 224-225°C.
[d]With decomposition.
[e]Ref. 25 : 200-202°C.

TABLE 4. Physical data for the acyclic nucleosides (generated from the β-D-ribopyranosyl congeners)

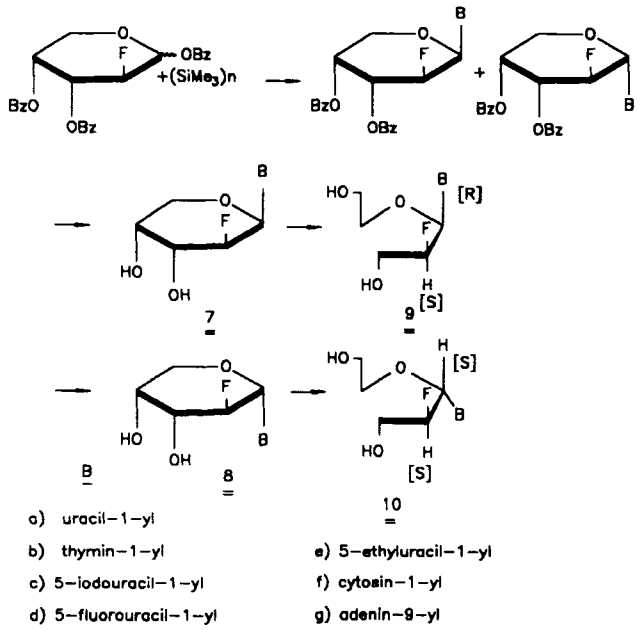
B	UV		MS	^{1}H NMR[a]				Analysis					
								Calculated			Found		
	λ max (nm)	log ε	m/z (M^+)	H-1'[b]	H-2' H-2"	H-3'/H-4' H-5'/H-5"	Base protons	C	H	N	C	H	N
Thymin-1-yl	267	3.96	244	5.77	2.00	3.49	7.48				[c]		
5-Iodouracil-1-yl	283	3.91	-	5.73	1.90	3.58	7.83	30.36	3.68	7.87	29.97	3.59	7.58
Uracil-1-yl	260	4.00	230	5.78	1.87	3.80	5.65; 7.59	46.95	6.13	12.17	46.63	6.10	11.97
5-Fluorouracil-1-yl	268	3.92	248	5.74	1.87	3.50	7.80 ($J_{6,F}$=6.8Hz)	43.55	5.28	11.29	43.71	5.14	11.18
5-Ethyluracil-1-yl	267	3.99	258	5.76	1.87	3.40	7.37	51.16	7.02	10.85	51.42	6.83	10.93
Cytosin-1-yl	271	3.94	-	5.80	1.87	3.51	5.80;7.56				[c]		
Adenin-9-yl	260	4.18	-	5.85	2.28	3.53	8.00;8.30				[c]		
Guanin-9-yl	254	4.14	-	5.64	2.05	3.40	7.77				[c]		

[a]All spectra were taken in DMSO-d_6 with tetramethylsilane as internal standard (δ values are given)
[b]H-1' appears as a triplet with coupling instants between 6.5 and 7 Hz.
[c]Compounds already described in reference 29.



Scheme 5

Condensation reactions with the silylated bases were carried out on the α/β mixture at reflux temperature in dichloroethane and TMS-triflate as condensing agent (Scheme 6). The α and β anomers were separated by column chromatography and deprotected with ammonia in methanol. Here too, the α anomer always predominated (Table 6). X ray crystallographic analysis of 1-(2-deoxy-2-fluoro-β-D-arabinopyranosyl)thymine and of 1-(2-deoxy-2-fluoro-β-D-arabinopyranosyl)-5-ethyluracil confirmed the proposed configuration[22].



Scheme 6

TABLE 5. ^{1}H NMR values for 1,3,4-tri-O-benzoyl-2-deoxy-2-fluoro-D-arabinose

	H-1	$J_{1,F}$ $J_{1,2}$	H-2	$J_{2,F}$ $J_{2,3}$	H-3	$J_{3,4}$ $J_{3,F}$	H-4	$J_{4,5}$ $J_{4,5'}$	H-5 H-5'	$J_{5,5'}$
β-isomer	6.77	0 Hz and 3.6 Hz	5.54	48 Hz and 10.0 Hz	5.98	0 Hz and 3.1 Hz	5.81	2x0 Hz	4.05 and 4.44	13.4 Hz
α-isomer	6.32	5.0 Hz and 7.0 Hz	5.25	50.0 Hz and 8.5 Hz	5.93	3.5 Hz and 12.5 Hz	5.64	2.1 Hz and 1.5 Hz	4.24	12 Hz

Spectra were taken in DMSO-d_6 (δ : 2.49) which was used as internal standard. δ values in ppm. Coupling constants in Hertz

Finally the C_3'-C_4' bond was opened by reaction with periodate and the intermediary formed dialdehyde was reduced with sodium borohydride to give the acyclic fluorinated nucleosides. These compounds were purified by preparative thin layer chromatography and characterized by ^1H NMR, UV, MS and ^{13}C NMR. Purity of all β-isomers and of key intermediates was also verified by elemental analysis. Because of the presence of several overlapping multiplets, ^1H NMR is of little value for the characterization of the compounds. ^{13}C NMR proved to be much more reliable. The ^{13}C NMR data are summarized in Table 7.

TABLE 6. Yields of the α en β anomers of the fluorinated nucleosides after deprotection

B	α	β
5-Iodouracil-1-yl	42%	30%
Thymin-1-yl	50%	35%
5-Ethyluracil-1-yl	37%	30%
Uracil-1-yl	51%	37%
5-Fluorouracil-1-yl	47%	32%
Cytosin-1-yl	41%	22%
Adenin-9-yl	48%	35%

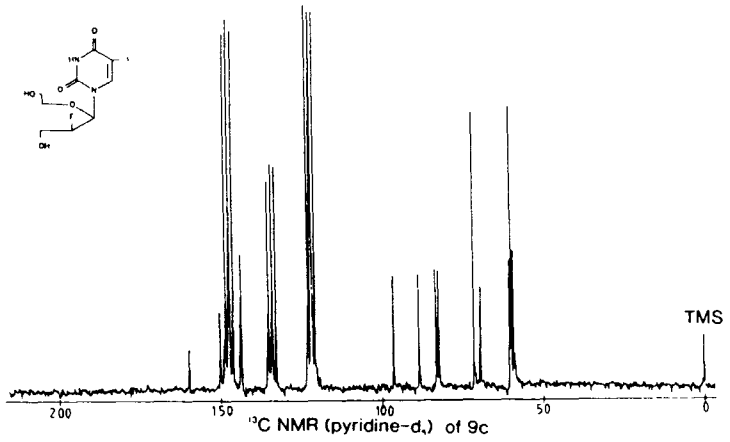
The UV spectra showed the expected maxima and extinction values. The MS spectra show the molecular ion except for the cytosine analogues.

The H-1' of the pyrimidine acyclic nucleoside β-anomers always resonates at higher field than the H-1' of the α-anomers. This is opposite to what is found for the closed (pyranose) precursors where the H-1' of the β-anomers always resonates at lower yield. The H-1' of the β-anomer appear as double doublets with $J_{1',F}$ values of about 20 Hz, while the H-1' of the α-anomers appear as triplets. Also the chemical shifts of the carbon atoms are very characteristic as can be concluded from Table VII. The $J_{C,F}$ values are higher for C-1' (α) than for C-1' (β), lower for C-2' (α) than for C-2' (β) and also lower for C-3' (α) than for C-3' (β). A ^{19}F NMR spectrum (ref: $CFCl_3$) of 9b (δ : -205.6 ppm), 9c (δ : -206.6 ppm) and 9e (δ : -206.0 ppm) was taken in order to be able to exclude the possibility that an epimerization at C-2' occurred during opening of the C_3'-C_4' bond. Coupling constants of 47.4 Hz ($J^2_{F,H}$) and of 19.5 Hz ($J^3_{F,H}$) are in agreement with the proposed structures.

Table 7. ^{13}C NMR values of the acyclic fluorinated nucleosides[a]

B	C-1'	$J_{1',F}$	C-2'	$J_{2',F}$	C-3'	$J_{3',F}$	C-4'	C-5'	Others
5-Iodouracil-1-yl (β)	84.3	18.3	94.5	181.9	60.5	24.4	72.5	60.7	70.3; 145.7 ($J_{6,F}$=3.7Hz); 152.2; 162.0
5-Iodouracil-1-yl (α)	83.1	25.6	93.1	178.2	60.3	19.5	71.9	60.0	71.1; 145.4; 152.7; 161.8
Thymin-1-yl (β)	83.6	19.5	94.3	181.9	60.6	24.4	72.1	60.7	12.5; 110.9; 136.9 ($J_{6,F}$=3.7Hz); 152.2; 165.1
Thymin-1-yl (α)	82.4	25.6	93.2	178.2	61.0	19.5	71.5	60.7	12.4; 111.7; 136.0; 152.7; 165.1
5-Ethyluracil-1-yl (β)	83.6	18.3	94.3	181.9	60.6	23.2	72.1	60.7	13.2; 20.4; 116.7; 136.2 ($J_{6,F}$=3.6Hz); 152.1; 164.8
5-Ethyluracil-1-yl (α)	82.9	25.8	93.4	177.3	61.5	19.5	71.9	61.1	13.7; 20.9; 117.8; 135.6; 153.3; 165.1
Uracil-1-yl (β)	84.5	18.3	94.6	180.7	61.1	23.2	72.7	61.3	103.3; 142.1 ($J_{6,F}$=3.6Hz); 152.6; 165.7
Uracil-1-yl (α)	82.6	26.8	92.8	177.0	61.0	19.5	71.5	60.6	103.3. 141.0; 152.6; 164.8
5-Fluorouracil-1-yl (β)	84.1	19.5	94.0	181.9	60.4	24.0	72.3	60.7	Values for the base could not be exactly determined because of overlapping with the pyridine-d_5 signals
5-Fluorouracil-1-yl (α)	81.8	25.6	91.4	178.2	59.4	19.5	70.4	59.3	
Cytosin-1-yl (β)	84.5	18.3	94.6	181.9	61.1	24.4	72.3	61.0	95.2; 142 ($J_{6,F}$=3.5Hz); 157.4; 167.3
Cytosin-1-yl (α)	82.9	23	94.1	178.2	61.4	19.0	71.7	61.0	95.8; 141.8; 158.0; 167.0
Adenin-9-yl (β)	82.4	22	93.0	180.7	59.6	23.6	71.7	59.8	139.1 ($J_{8,F}$=3.7Hz); 152.7
Adenin-9-yl (α)	81.9	26	92.0	177.0	60.0	20	70.8	59.9	139.4; 152.8

[a]All spectra were taken in pyridine-d_5-D_2O.



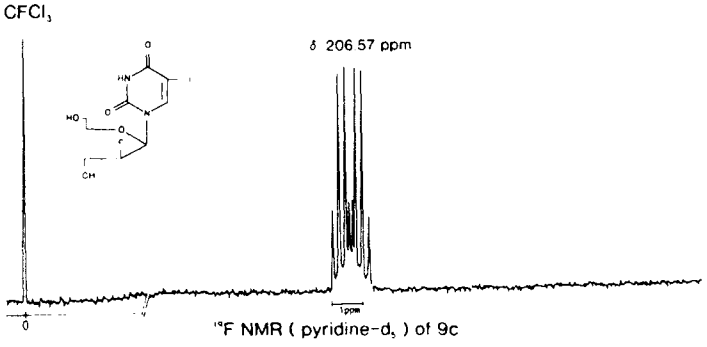
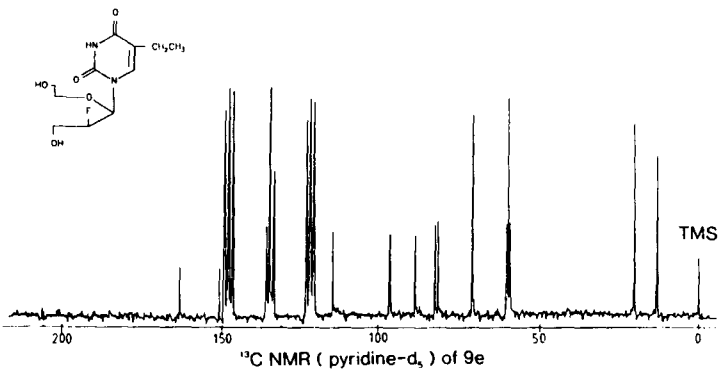
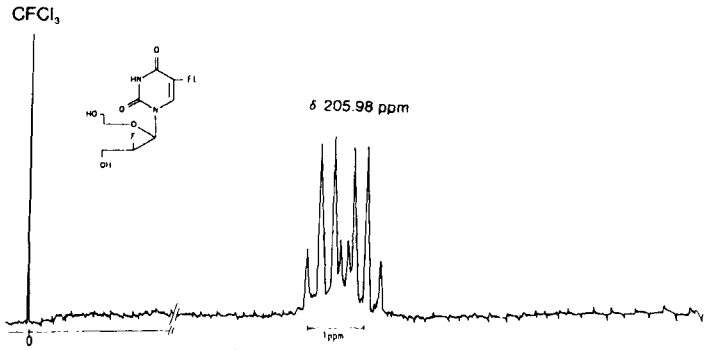


FIG. 3. ^{13}C NMR and ^{19}F NMR spectrum of the acyclic nucleosides with a 5-ethyluracil (9e) and 5-iodouracil (9c) base moiety.

(Continued)



^{13}C NMR (pyridine-d_5) of 9e



^{19}F NMR (pyridine-d_5) of 9e

Figure 3 Continued

BIOLOGICAL ACTIVITY

None of the compounds showed antiviral activity when evaluated against HSV-1, HSV-2 or vaccinia virus in human embryonic skin muscle (E_6SM) fibroblast cultures at the highest concentration tested (400 μg/ml).

EXPERIMENTAL SECTION

Melting points were determined in capillary tubes with a Büchi-Tottoli apparatus and are uncorrected. Ultraviolet spectra were recorded with a Philips PU 8700 UV/Vis spectrophotometer. The ^{1}H NMR and ^{13}C NMR spectra were determined with a JEOL FX 90Q spectrometer with tetramethylsilane as internal standard (s = singlet, d = doublet, t = triplet, br s = broad signal, m = multiplet). Mass spectra were determined with an AEI MS-12 apparatus. Precoated Merck silica gel F254 plates were used for TLC, and the spots were examined with UV light and sulfuric acid-anisaldehyde spray. Column chromatography was performed on Merck silica gel (0.063-0.200 mm). Anhydrous solvents were obtained as follows: acetonitrile was obtained by distillation after reflux overnight with calcium hydride. Dichloroethane was stored for 1 week on anhydrous calcium chloride, filtered and distilled.

1,3,4-Tri-O-(4-tert-butylbenzoyl)-2-deoxy-α-D-erythro-pentopyranose 3A

^{1}H NMR ($CDCl_3$): 1.31-1.36 (3 x tert butyl); 2.41-2.61 (m,H-2',H-2"); 3.96 (dd) and 4.43 (dd) (H-5',H-5"); 5.43 (m,H-4'); 5.73 (m,H-3'); 6.36 (H-1'); 7.22-7.54 and 7.84-8.16 (aromatic H) ppm.
mp 141-142°C.
Elemental analysis : ($C_{38}H_{46}O_7$): calculated C: 74.23, H: 7.54; found: C: 74.23, H: 7.53.

1,3,4-Tri-O-(4-tert-butylbenzoyl)-2-deoxy-β-D-erythro-pentopyranose 3B

^{1}H NMR ($CDCl_3$): 1.30-1.36 (3 x tert butyl); 2.15-2.84 (m,H-2',H-2"); 4.12 (m,H-5',H-5"); 5.67 and 5.85 (2 x m, H-3', H-4'); 6.64 (H-1'); 7.29-7.58 and 7.79-8.13 (aromatic H) ppm.
mp 158-160°C.
Elemental analysis : ($C_{38}H_{46}O_7$): calculated C: 74.24, H: 7.54; found C: 73.89, H:7.42.

Reaction of silylated pyrimidines with 1,3,4-tri-O-benzoyl-2-deoxy-D-erythro-pentopyranose

A mixture of 450 mg (1 mmol) of 1,3,4-tri-O-benzoyl-2-deoxy-D-erythro-pentopyranose and 1 mmol of the silylated base (obtained by refluxing the pyrimidine base overnight in 5 ml of hexamethyldisilazane in the presence of 0.1 ml trimethylsilyl chloride or a spatula point of ammonium sulfate, followed by evaporation and coevaporation with xylene) in 2.5 mL of dichloroethane and 2.5 mL of 0.5 M trimethylsilyl triflate (1.25 mmol) in dichloroethane was stirred at room temperature for 3 h. The reaction mixture was poured into $CHCl_3$ (50 mL), washed with 5 % sodium bicarbonate (2 x 20 mL), dried and evaporated. The residual oil was purified by column chromatography (CH_2Cl_2-CH_3CN 90:10). The β-isomer, which eluted first from the column, was debenzoylated with ammonia in methanol at room temperature overnight, followed by chromatographic purification ($CHCl_3$-MeOH 90:10).

1-(2-deoxy-β-D-ribopyranosyl)uracil 4a

565 mg (1 mmol) of 1-(3,4-di-O-benzoyl-2-deoxy-β-D-ribopyranosyl)-5-iodouracil and 160 mg (2 mmol) of sodium acetate in 10 mL of MeOH was hydrogenated overnight at 35 psi in the presence of 50 mg of 10% Pd/C. The reaction mixture was filtered, evaporated and purified by column chromatography ($CHCl_3$-MeOH 80:20) affording 155 mg (66%) of the title compound. The physical data are described in Table III.

Reaction of silylated, protected purines with 1,3,4-tri-O-benzoyl-2-deoxy-D-erythro-pentopyranose

1 mmol of 1,3,4-tri-O-benzoyl-2-deoxy-D-erythro-pentopyranose, 1 mmol of silylated base (N^6-benzoyladenine silylated with HMDS-TMSCl as previously described; N^2-acetyl-O^6-diphenycarbamoylguanine silylated with BSA at 80°C for 15 min) and 1 mL of a stock solution of 0.1 M (0.1 mmol) of trimethylsilyl perchlorate in benzene in 10 mL of dichloroethane was refluxed for 3 h. Another 1 mL of the same stock solution of $TMSClO_4$ was added and the mixture was refluxed further for 3 h. Workup and debenzoylation was carried out as described for the pyrimidine analogues.

Periodate oxidation and sodium borohydride reduction

To a solution of 100 mg (0.4 mmol) of 1-(2-deoxy-β-D-ribopyranosyl)thymine (4b) in 5 mL of H_2O-dioxane (1:1) was added 0.8 mL of a stock solution of sodium periodate (0.4 mmol) in H_2O and the mixture was stirred for 90 min at room temperature. EtOH was added, the precipitate was filtered off, 14 mg (0.4 mmol) of sodium borohydride was added and the mixture was stirred at room temperature for 30 min. The reaction mixture was filtered, neutralized with dilute acetic acid (10%) and the compound was precipitated from EtOH:Et_2O affording 60 mg (60% yield) of 6b. This modus operandi was used for the opening of all pyrimides and purine pyranoses.

1,3,4-Tri-O-benzoyl-2-deoxy-2-fluoro-D-arabinose

To a solution of 15 g (100 mmol) of 2-deoxy-2-fluoro-D-arabinose in 300 mL pyridine at 0°C, was added dropwise a solution of 56 g (400 mmol) of benzoylchloride in 200 mL pyridine and the mixture was stirred overnight at room temperature. The reaction mixture was concentrated, diluted with H_2O (300 mL) and $CHCl_3$ (300 mL), and the organic layer was separated, dried and evaporated. The resulting oil was purified on silica column (eluent : 1) benzene 2) CH_2Cl_2).

12.1 g (26 mmol) 26% of 1,3,4-tri-O-benzoyl-2-deoxy-2-fluoro-β-D-arabinose : mp 151-152°C. MS (m/z) : 464 (M^+). $[\alpha]_D$ = -116.35 (C=1,$CHCl_3$). ^1H NMR ($CDCl_3$): 7.40-7.84 and 8.00-8.31 (m,3xbenzoyl) ppm. Elem. anal. ($C_{26}H_{21}O_7F$): calculated C: 67.24, H: 4.56; found C: 67.20, H: 4.66.

14.4 g (30 mmol) 30% of 1,3,4-tri-O-benzoyl-2-deoxy-2-fluoro-α-D-arabinose : mp 124-125°C. MS (m/z) : 464 (M^+). $[\alpha]_D$ = -74.50 (C=1, $CHCl_3$). ^1H NMR ($CDCl_3$): 7.41-7.76 and 7.86-8.31 (m,3xbenzoyl) ppm. Elem. anal. ($C_{26}H_{21}O_7F$): calculated C: 67.24, H:4.56; found C: 67.20, H:4.68.

1-(2-deoxy-2-fluoro-β-D-arabinopyranosyl)-5-iodouracil 7c and 1-(2-deoxy-2-fluoro-α-D-arabinopyranosyl)-5-iodouracil 8c

A mixture of 3.05 g (4 mmol) of 1,3,4-tri-O-benzoyl-2-deoxy-2-fluoro-D-arabinose, 1.19 g (5 mmol) of 5-iodouracil (silylated with HMDS-TMS at reflux, evaporated and coevaporated with xylene) and 5 mL of a stock solution of TMSOTfl (0.5 M) in 10 mL of dichloroethane was refluxed for 60 h. The reaction mixture was poured into 20 mL of 5% aqueous sodium bicarbonate, extracted with $CHCl_3$, evaporated and purified by column chromatography ($CHCl_3$-MeOH 99:1) to give the protected α and β-isomers.

α-isomer : ^1H NMR ($CDCl_3$): 4.16 (m,H-5',H-5"); 5.07 (m, $J_{2',F}$=50.4Hz,H-2'); 5.56-5.79 (m,H-3',H-4'); 6.01 (dd,J=3.7 and 8.8Hz,H-1'); 7.07-7.58 and 7.70-8.07 (2xm,benzoyl and H-6); 9.80 (brs,NH) ppm.

β-isomer : ^{1}H NMR ($CDCl_3$): 3.89-4.41 (m,H-5',H-5"); 4.85 (m,$J_{2',F}$= 45.5 Hz,H-2'); 5.51 (m,H-4'); 5.90 (m,H-3'); 6.07 (dd,$J_{1',F}$=25.0Hz,H-1'); 7.09-7.57 and 7.60-8.07 (2xm,benzoyl and H-6); 9.80 (brs,NH) ppm.

These compounds were treated overnight with ammonia in methanol, evaporated and purified by column chromatography ($CHCl_3$-MeOH 90:10) giving 450 mg (1.2 mmol,30%) of the β-isomer and 630 mg (1.7 mmol,42%) of the α-isomer. The β-isomer crystallized from EtOH.

β-isomer : mp : 124-126°C. MS (m/z) : 372 (M^+), UV (MeOH) λ_{max} : 280 nm ($\log \varepsilon$: 3.88).

^{1}H NMR (DMSO-d_6): 3.77 and 4.03 (2xm,H-3',H-4',H-5,H-5"); 4.67 (dm, $J_{2',F}$=48Hz,H-2'); 4.95 (OH); 5.68 (OH); 5.82 (m,$J_{1',F}$=26.4Hz,H-1'); 7.78 (d,H-6); 11.78 (brs,NH) ppm.

Elem. anal. ($C_9H_{10}N_2O_5FI.EtOH$): calculated: C 31.59, H: 3.86, N: 6.70; found C: 31.49, H: 3.81, N: 6.54.

α-isomer : UV (MeOH) λ_{max} 282 nm ($\log \varepsilon$ 3.91).

^{1}H NMR (DMSO-d_6): 3.77 (m,H-3',H-4',H-5',H-5"); 4.74 (dt,$J_{2',F}$=51Hz,H-2'); 4.88 (OH); 5.38 (OH); 5.60 (dd,J=4 and 9Hz, H-1'); 8.20 (H-6); 11.72 (brs,NH) ppm.

Elem. anal. ($C_9H_{10}N_2O_5FI$): calculated C: 29.05, H: 2.71, N: 7.53; found C: 29.10, H: 2.65, N: 7.33.

1-[1-(R)-(2-hydroxyethoxy)-2-(S)-fluoro-3-hydroxypropyl]-5-iodouracil 9c

To a solution of 125 mg (0.34 mmol) of the β-isomer (7c) in 6 mL of H_2O-dioxane (1/1) was added 73 mg (0.34 mmol) of sodium periodate and the mixture was stirred for 6 h at 60°C. The reaction mixture was cooled, EtOH was added and the mixture was filtered. After addition of 14 mg (0.34 mmol) of $NaBH_4$, the reaction was further stirred for 10 min at room temperature, filtered, neutralized (pH 7) with acetic acid and evaporated. The title compound was purified by preparative thin layer chromatography ($CHCl_3$-MeOH 80-20) : 60 mg (50% yield, 0.17 mmol). UV (MeOH) λ_{max} : 282 nm ($\log \varepsilon$ 3.88). MS (m/e) : 374 (M^+). ^{1}H NMR (pyridine-d_5): 6.40 (dd,$J_{1',F}$=20.2Hz,H-1') ppm. Elem. anal. ($C_9H_{12}N_2O_5FI$): calculated C: 28.90, H: 3.23, N: 7.49; found C: 28.80, H: 3.26, N: 7.19.

1-[1-(S)-(2-hydroxyethoxy)-2-(S)-fluoro-3-hydroxypropyl]-5-iodouracil 10c

The α-isomer was synthesized in the same way as described for the β-isomer.

UV (MeOH) λ_{max} 282 nm ($\log \varepsilon$ 3.85). MS (m/z) : 374 (M^+). ^{1}H NMR (pyridine-d_5): 6.64 (t,H-1') ppm. Elem. anal. ($C_9H_{12}N_2O_5FI$): calculated C: 28.90, H: 3.23, N: 7.49; found C: 28.74, H: 3.32, N: 7.19.

The other compounds were synthesized in the same way as the 5-iodouracil analogue. However, 24 h reflux was sufficient for the condensation reaction and purification of the deprotected compounds was carried out with CH_2Cl_2-MeOH 95:5. Yields of the deprotected α and β isomers are given in Table VI. For the adenine analogue, refluxing the mixture for 5 days was necessary to complete the reaction. The ^{13}C NMR spectra of all compounds are given in Table VII. Only characteristic complementary data are given in the experimental section. Numbering of the acyclic nucleosides is the same as for the normal nucleosides, for the sake of clarity.

1-(2-deoxy-2-fluoro-β-D-arabinopyranosyl)thymine 7b
mp : 265-268°C (dec). UV (MeOH) λ_{max} 264 nm (log ε 4.00). ^{1}H NMR (pyr-d_5): 1.96 (s,CH_3); 4.37 and 4.71 (2xm,H-3',H-4',H-5'); 5.49 (m,1/2 of H-2' - other part is hidden by HOD); 6.65 (m, H-1', $J_{1',F}$=26Hz); 7.67 (H-6) ppm.
Elem. Anal. ($C_{10}H_{13}N_2O_5F$): calculated C: 46.16, H: 5.04, N: 10.77; found C: 46.06, H: 5.05, N: 10.52.

1-(2-deoxy-2-fluoro-α-D-arabinopyranosyl)thymine 8b
UV(MeOH) λ_{max} 264 nm (log ε 4.00). ^{1}H NMR (pyr-d_5): 1.86 (s,CH_3); 4.40 (m,H-3',H-4',H-5'); 5.55 (dt,$J_{2',F}$=49Hz,H-2'); 6.36 (dd,H-1'); 7.72 (H-6) ppm.

1-[1- (R)-(2-hydroxyethoxy)-2-(S)-fluoro-3-hydroxypropyl]thymine 9b
UV (MeOH) λ_{max} : 265 nm (log ε 3.99). ^{1}H NMR : (pyridine-d_5): 6.45 (dd, $J_{1',F}$=20.3Hz,H-1') ppm. Elem. Anal. ($C_{10}H_{15}N_2O_5F$): calculated C: 45.80, H: 5.77, N: 10.68; found C: 45.47, H: 5.92, N: 10.83.

1-[1-(S)-(2-hydroxyethoxy)-2-(S)-fluoro-3-hydroxypropyl]thymine 10b
UV (MeOH) λ_{max} : 264 nm (log ε 3.97)
^{1}H NMR (pyr-d_5-D_2O): 6.61 (t,H-1') ppm.

1-(2-deoxy-2-fluoro-β-D-arabinopyranosyl)-5-ethyluracil 7e
mp 190-197°C. UV (MeOH) λ_{max} 264 nm (log ε 4.04). MS (m/z) 274 (M^+). ^{1}H NMR (DMSO-d_6): 1.05 (t,CH_3); 2.23 (q,CH_2); 3.78 and 4.06 (2xm,H-3',H-4',H-5',H-5"); 4.68 (dm,$J_{2',F}$=49Hz,H-2'); 4.95 (OH); 5.67 (OH); 5.86 (m,$J_{1',F}$=27Hz,H-1'); 7.30 (H-6); 11.36 (NH) ppm.
^{13}C NMR (DMSO-d_6) δ : 13.2 (CH_3); 19.8 (CH_2); 63.1 (C-5'); 66.1 (C-4'); 67.3 (J=25.6Hz, C-3'); 77.3 (J=14.6Hz,C-1'); 89.8 (J=184.3Hz,C-2'); 114.8 (C-5); 136.3 (J=7.3Hz,C-6); 150.0 (CO); 163.2 (CO).
Elem. Anal. ($C_{11}H_{15}N_2O_5F$): calculated C: 48.18, H: 5.51, H: 10.21; found C: 48.10, H: 5.43; N: 10.10

1-(2-deoxy-2-fluoro-α-D-arabinopyranosyl)-5-ethyluracil 8e
UV (MeOH) λ_{max} 264 nm (log ε 4.00).
^{1}H NMR (DMSO-d_6): 1.05 (t,CH_3): 2.33 (q,CH_2); 3.80 (m,H-3',H-4',H-5',H-5"); 4.74 (dm, $J_{2',F}$=49Hz,H-2'); 4.98 (OH); 5.43 (OH); 5.60 (dd,H-1'); 7.50 (H-6); 11.20 (NH) ppm.

1-[1-(R)-(2-hydroxyethoxy)-2-(S)-fluoro-3-hydroxypropyl]-5-ethyluracil 9e
UV (MeOH) λ_{max} : 264 nm (log ε 3.98). MS (m/z) : 276 (M^+).
^{1}H NMR (pyr-d_5-D_2O): 6.44 (dd,$J_{1,F}$=20Hz,H-1') ppm.
Elem. anal. $C_{11}H_{17}N_2O_5F.0.4CHCl_3$: calculated C: 42.26, H: 5.41, N: 8.65; found C: 42.54, H: 5.71, N: 8.59.

1-[1-(S)-(2-hydroxyethoxy)-2-(S)-fluoro-3-hydroxypropyl]-5-ethyluracil 10e
UV (MeOH) λ_{max} 264 nm (log ε 3.98) MS (m/z) : 276 (M^+) ^{1}H NMR (pyr-d_6-D_2O): 6.66 (t,H-1') ppm.

1-(2-deoxy-2-fluoro-β-D-arabinopyranosyl)uracil 7a
mp : 214-216°C UV (MeOH) λ_{max} 260 nm (log ε 4.02) MS (m/z) : 246 (M^+) ^{1}H NMR (DMSO-d_6): 3.77 and 4.03 (2xm,H-3',H-4',H-5',H-5"); 4.65 (dm,$J_{2',F}$=49Hz,H-2'); 5.64 (d,H-5); 5.84 (m,$J_{1',F}$=27Hz,H-1');7.50 (d,H-

6) ppm. Elem. anal. $C_9H_{11}N_2O_5F$: calculated C: 43.91, H: 4.50, N: 11.38; found: 43.72, H: 4.53, N: 11.17.

1-(2-deoxy-2-fluoro-α-D-arabinopyranosyl)uracil 8a
UV (MeOH) λ_{max} 260 nm (log ε 4.00)
^{1}H NMR (DMSO-d_6): 3.77 (m,H-3',H-4',H-5',H-5"); 4.71 (dt,$J_{2',F}$=51Hz,H-2'); 5.06 (2xOH); 5.53 (dd,H-1'); 5.77 (d,H-5); 7.76 (d,H-6) ppm.

1-[1-(R)-(2-hydroxyethoxy)-2-(S)-fluoro-3-hydroxypropyl)uracil 9a
UV (MeOH) λ_{max} 260 nm (log ε 4.00) MS (m/z) 248 (M^+)
^{1}H NMR (pyr-d_5-D_2O): 6.33 (dd,$J_{1',F}$=20Hz,H-1') ppm.
Elem. anal. $C_9H_{13}N_2O_5F$: calculated C: 43.55, H: 5.28, N: 11.29; found C: 48.82, H: 5.07, N: 10.92.

1-[1-(S)-(2-hydroxyethoxy)-2-(S)-fluoro-3-hydroxypropyl]uracil 10a
UV (MeOH) λ_{max} 260 nm (log ε 4.02) MS (m/z) 248 (M^+)
^{1}H NMR (pyr-d_5-D_2O)): 6.57 (t,H-1') ppm.

1-(2-deoxy-2-fluoro-β-D-arabinopyranosyl)-5-fluorouracil 7d
mp 228-231°C UV (MeOH) λ_{max} : 266 nm (log ε 3.98) MS (m/z) 264 (M^+)
^{1}H NMR (DMSO-d_6): 3.75 and 4.08 (2xm,H-3',H-4',H-5',H-5"); 4.71 (dm,$J_{2',F}$=48Hz,H-2'); 5.82 (m,$J_{1',F}$=26.1Hz,H-1'); 7.68 (d,$J_{6,F}$=6Hz, H-6) ppm. Elem. anal. ($C_9H_{10}N_2O_5F_2$): calculated C: 40.92, H: 3.82, N: 10.60; found C: 40.89, H: 3.77, N: 10.48.

1-(2-deoxy-2-fluoro-α-D-arabinopyranosyl)-5-fluorouracil 8d
UV (MeOH) λ_{max} : 266 nm (log ε 3.96) ppm. ^{1}H NMR (DMSO-d_6): 3.72 (m,H-3',H-4',H-5',H-5"); 4.72 (dt,$J_{2',F}$=51Hz,H-2'); 5.60 (dd,H-1'); 7.94 (d,J=6Hz,H-6).

1-[1-(R)-(2-hydroxyethoxy)-2-(S)-fluoro-3-hydroxypropyl]-5-fluorouracil 9d
UV (MeOH) λ_{max} 268 nm (log ε 3.96) MS (m/z) : 266 (M^+)
^{1}H NMR (pyr-d_5-D_2O): 6.38 (dd,$J_{1',F}$=20Hz,H-1') ppm.
Elem. anal. ($C_9H_{12}N_2O_5F_2$): calculated C: 40.61, H: 4.54, N: 10.52; found C: 40.59, H: 4.44, N: 10.22.

1-[1-(S)-(2-hydroxyethoxy)-2-(S)-fluoro-3-hydroxypropyl]-5-fluorouracil 10d
UV (MeOH) λ_{max} 267 nm (log ε 3.97) MS (m/z) 266 (M^+)
^{1}H NMR (pyr-d_5-D_2O): 6.59 (t,H-1') ppm.

1-(2-deoxy-2-fluoro-β-D-arabinopyranosyl)cytosine 7f
mp 278-281°C (dec) UV (MeOH) λ_{max} : 271 nm (log ε 3.95) MS (m/z) 245 (M^+) ^{1}H NMR (DMSO-d_6): 3.75 and 4.05 (2xm,H-3',H-4',H-5',H-5"); 4.59 (dm,$J_{2',F}$=47Hz,H-2'); 4.96 (OH); 5.7 (OH); 5.77 (H-5); 5.90 (m, $J_{1',F}$=27Hz,H-1'); 7.48 (H-6) ppm.
Elem. anal. (C-$9H_{12}N_3O_4F$): calculated C: 44.08, H: 4.93, N: 17.14; found 43.82, H: 5.01, N: 16.92.

1-(2-deoxy-2-fluoro-α-D-arabinopyranosyl)cytosine 8f
UV (MeOH) λ_{max} 269 nm (log ε 3.93)
^{1}H NMR (DMSO-d_6): 3.77 (m,H-3',H-4',H-5',H-5"); 4.66 (dt,$J_{2',F}$=51Hz,H-2'); 5.70 (H-1'); 5.82 (d,H-5); 7.35 (NH_2); 7.66 (d,H-6) ppm.

1-[1-(R)-(2-hydroxyethoxy)-2-(S)-fluoro-3-hydroxypropyl]cytosine 9f
UV (MeOH) λ_{max} 270 nm (log ε 3.94)
^{1}H NMR (pyr-d_5-D_2O): 3.70-4.40 (H-3',H-4',H-5',H-5"); 5.12 (H-2'); 6.20 (H-5); 6.41 (dd,H-1'); 7 77 (H-6) ppm.
Elem. anal. ($C_9H_{14}N_3O_4F$): calculated C: 43.77, H: 5.71, N: 17.00; found: 43.52, H: 5.59, N: 17.25.

1-[1-(S)-(2-hydroxyethoxy)-2-(S)-fluoro-3-hydroxypropyl)cytosine 10f
UV (MeOH) λ_{max} : 269 nm (log ε 3.96)
^{1}H NMR (pyr-d_5-D_2O): 3.80-4.50 (H-3',H-4',H-5'); 4.89 (1/2 of H-2'; other part hidden by HOD); 6.18 (H-5); 6.77 (H-1'); 7.86 (H-6) ppm.

9-(2-deoxy-2-fluoro-β-D-arabinopyranosyl)adenine 7g
mp 230-233° (dec) UV (MeOH) λ_{max} 259 nm (log ε 4.16) MS (m/z) 269 (M^+) ^{1}H NMR (DMSO-d_6): 3.83 and 4.17 (2xm,H-3',H-4',H-5',H-5") 4.85 (dm, $J_{2',F}$=47Hz,H-2'); 5.10 (OH); 5.75 (OH); 6.07 ($J_{1',F}$=27Hz,H-1'); 7.32 (NH_2); 8.02 (d,H-8); 8.17 (H-2) ppm. Elem. anal. ($C_{10}H_{12}N_5O_3F$): calculated C: 44.61, H: 4.49, N: 26.01; found C: 44.41, H: 4.62, N: 25.73.

9-(2-deoxy-2-fluoro-α-D-arabinopyranosyl)adenine 8g
UV (MeOH) λ_{max} 259 nm (log ε 4.16) ^{1}H NMR (DMSO-d_6): 3.86 (m,H-3',H-4',H-5',H-5"); 5.32 (d,$J_{2',F}$=50Hz,H-2'); 5.69 (t,H-1'); 7.35 (NH_2); 8.44 and 8.18 (H-8 and H-2) ppm.

9-[1-(R)-(2-hydroxyethoxy)-2-(S)-fluoro-3-hydroxypropyl]adenine 9g
UV (MeOH) λ_{max} 260 nm (log ε 4.18) MS (m/z) 271 (M^+).
^{1}H NMR (pyr-d_5-D_2O): 6.69 (dd, $J_{1',F}$=18Hz, H-1') ppm
Elem. anal. ($C_{10}H_{14}N_5O_3F$): calculated C: 44.28, H: 5.20, N: 25.82; found C: 44.57, H: 5.27, N: 25.98.

9-[1-(S)-(2-hydroxyethoxy)-2-(S)-fluoro-3-hydroxypropyl]adenine 10g
UV (MeOH) λ_{max} 259 nm (log ε 4.16) MS (m/z) 271 (M^+).
^{1}H NMR (pyr-d_5-D_2O): 6.58 (t,H-1') ppm.

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