Synthesis of Potentially Antiviral 2′,3′-Dideoxy-2′-fluoro-3′-(hydroxyamino)nucleosides

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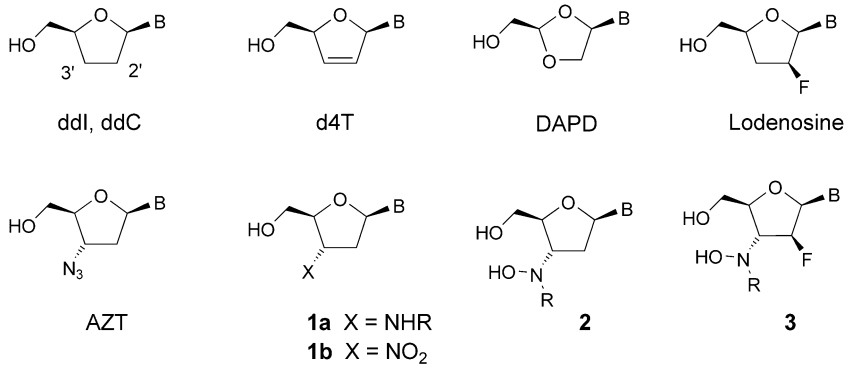
A series of novel 3′-(alkyl(hydroxy)amino)-2′-fluoronucleoside analogs were prepared *via* conjugate addition of *N*-methylhydroxylamine to various 2-fluorobutenolides. The adducts **13a** and **16** were obtained as single isomers under absolute control of stereochemistry. The crucial *N*-demethylation of **23**–**25** was readily achieved by means of DDQ oxidation, followed by nitrone/oxime exchange reaction. By this procedure, a variety of alkyl groups could be efficiently introduced at the 3′-N-atom of the nucleoside analogs, some of which might display potentially interesting anti-HIV properties.

Introduction. – Structural modifications of nucleoside analogs have been successful in the search for effective antiviral agents against human immunodeficiency virus (HIV) [1–3]. Of particular interest is the alteration of the 2′- and 3′-OH groups of ribose rings, particularly the 2′,3′-dideoxynucleoside analogs termed ddI, ddC, d4T, DAPD, and lodenosine [4–7]. It has been established that the 3′-position of 2′-deoxynucleoside analogs can tolerate various differently sized substituents, including N-containing moieties, and still maintain their antiviral activities, *e.g.*, AZT, **1a**, and **1b** [8–11]. An interesting new class of nucleoside analogs of types **2** and **3** (R = Me) possess 3′-(hydroxyamino) substituents [12][13].



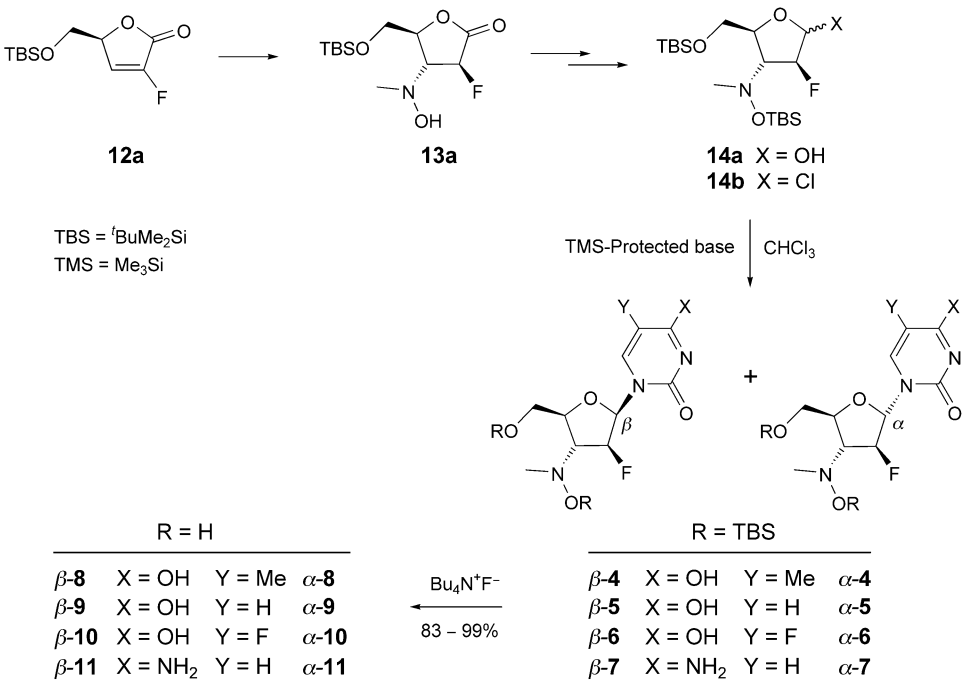
Compounds of type **3** differ from those of type **2** by an additional F-atom at the 2′β-position and by different *N*-alkyl groups. It is known that the 2′-F-atom can stabilize glycosyl bonds under both hydrolytic and enzymatic conditions [14]. As shown by

structure/activity-relationship studies, 2′β-configured compounds typically exhibit excellent antiviral activities [15] (in contrast to most 2′α-isomers), as exemplified by 2′-1-(2′-deoxy-2′-fluoro-β-L-arabinofuranosyl)uracil (L-FMAU) [16] and 1-(2′,3′-dideoxy-2-fluoro-β-D-pentofuranosyl)cytosine (F-ddA, lodenosine) [17][18].

Although nucleosides **3** with *N*-Me groups (R = Me) have been prepared by hydroxylamine-concerted addition [19], a variety of compounds with other alkyl substituents were required for antiviral studies [13]. Many synthetic approaches have been made to introduce such *N*-alkyl groups into compounds of type **3**, but without much success. Here, we report a strategy for the stereoselective preparation of 2′-fluoro-3′-(hydroxyamino)nucleosides of type **3**. The main feature of the procedure reported is that the different *N*-alkyl groups can be introduced *via* a common intermediate at a late stage of the synthesis; moreover, our approach allows for efficient preparation of many related derivatives required to study structure/activity relationships.

Results and Discussion. – To access the *N*-methylated nucleoside analogs **4**–**11**, the TBS-protected[1]) compound **12a** was prepared and converted to **13a** and **14a** (*Scheme 1*) [13]. Since the acetate derivative of **14a** (X = OAc) failed to give the coupling product with nucleoside bases in the presence of catalytic amounts of TMSOTf, the

Scheme 1



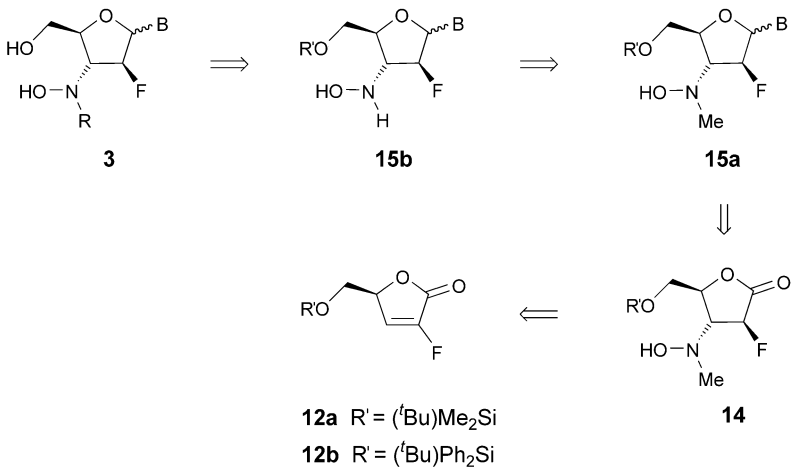
[1]) For abbreviations, see the *General* section in the *Exper. Part.*

corresponding chloride **14b** was selected as an alternative intermediate, which was easily prepared from **14a** with MsCl and 1 equiv. of Et_3N (plus a catalytic amount of Bu_3N). Glycosyl chloride **14b** was coupled with silylated uracil, thymine, 5-fluorouracil, and cytosine by refluxing in $CHCl_3$ to afford the protected nucleosides **4**–**7** (generally as *ca.* 1:1 mixtures of α/β-anomers). Then, the two TBS groups were removed with $Bu_4N^+F^-$ (TBAF) in anhydrous THF to afford **8**–**11** (83–99%), which, except for **8**, were separated into the corresponding 1′α- and 1′β-isomers by column chromatography (SiO_2).

The configuration at the anomeric center was derived from the chemical shift of H–C(4′). The β-configuration of the F-atom in 2′-position was confirmed by both ^{1}H- and ^{13}C-NMR analyses. A long-range coupling between H–C(6) and the F-atom, with J(2′-F,H–C(6)) = 1–2 Hz was observed. Also, the coupling constants observed for C(1′) and the F-atom are known to be considerably larger for the α-isomer (J(F,C(1′)) = 35–37 Hz) than for the β-isomer (J(F,C(1′)) = 16–18 Hz) [20].

We next developed a retrosynthetic strategy to access 2′-fluoro-3′-(hydroxyamino) nucleosides of type **3** with *N*-alkyl substituents other than Me (*Scheme 2*). The addition of various *N*-alkyl hydroxylamines to the 2-fluorobutenolactone **12a** was not investigated since the preparation of the corresponding starting materials would have required great synthetic efforts. An efficient method would be to demethylate **15a** to **15b** as a key intermediate[2]). This compound could then be derivatized to access a large series of products of type **3** by only a few chemical steps.

Scheme 2



The synthesis started from the TBDPS-protected[1]) butenolide **12b** (*Scheme 3*). Conjugate addition of *N*-methylhydroxylamine afforded the adduct **16** as a single isomer in 65% yield. The latter was protected with TBSCl (→**17**), reduced with DIBAL (→**18**), and chlorinated with MsCl to afford the intermediate **19**, which was then reacted with different silylated bases to the protected nucleosides **20**–**22** (as *ca.*

[2]) Direct addition of NH_2OH to **12a** afforded only low yields (<20%) of **15b**.

1:1 mixtures of α/β-anomers). The *O*-TBS group was selectively removed with 48% HF in MeCN to yield the *N*-methyl derivatives **23**–**25**.

The unique properties of hydroxylamines allow the potential replacement of *N*-Me groups (which can be regarded as 'unusual' N-protecting groups), by other alkyl groups, *i.e.*, by the sequential oxidation of the *N*-Me group, followed by alkyl exchange and reduction. In a first attempt, **23**–**25** were subjected to HgO-promoted oxidation [21] to the corresponding nitrone intermediates. However, these were contaminated with Hg-containing compounds, even after column-chromatographic purification. Finally, DDQ-mediated oxidation of **23**–**25** afforded the pure intermediate nitrones (structures not shown), in which the *N*-Me group was selectively converted to an $N{=}CH_2$ group, which was removed with $NH_2OH \cdot HCl$ by means of an exchange reaction (MeOH, 50°), affording the hydroxylamines **26**–**28**.

In the next step, compounds **26**–**28** were reductively alkylated to **29**–**35** (65–93%) by condensation with different aldehydes (butanal, 2-methylpropanal, cyclohexanecarboxaldehyde), followed by *in situ* reduction with $NaBH_3CN$ (*Scheme 4*). Then, TBDPS deprotection with TBAF finally afforded the desired nucleosides **36**–**42** in 70–96% yield.

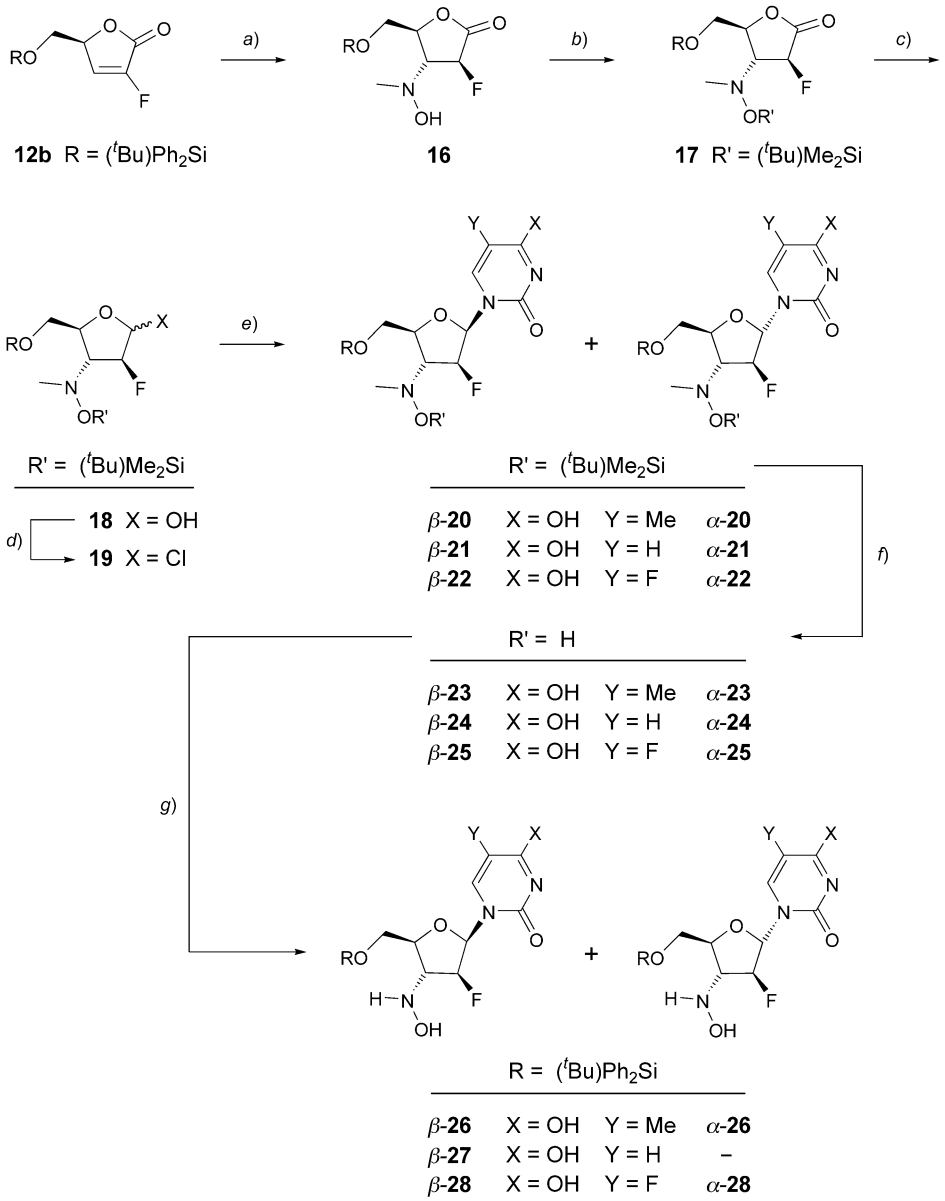
Conclusions. – We have developed a route towards the efficient synthesis of a variety of new *N*-alkylated 2′,3′-dideoxy-2′-fluoro-3′-(hydroxyamino)nucleoside analogs by stereoselective addition to α,β-unsaturated lactones (furan-1-ones). The compounds prepared were required to study their anti-HIV_{LAI} and anti-HSV-1 activities. The two anomeric cytosine derivatives α-**13** and β-**13**, indeed, showed significant anti-HIV_{LAI} activities *in vitro*; and α-**13** displayed an acceptably low cytotoxicity [19]. These compounds represent the first examples of nucleoside analogs with vicinal fluoro and amino functionalities at the 2′- and 3′-positions, respectively, of the dideoxyribose moiety and will certainly open up the way to further potentially biorelevant compounds of this type.

Experimental Part

General. Abbreviations: DDQ, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone; DIBAL, $(^i Bu)_2AlH$; Ms, $MeSO_2$; TBAF, $Bu_4N^+F^-$; TBDPS, $(^t Bu)Ph_2Si$; TBS, $(^t Bu)Me_2Si$; Tf, F_3CSO_2; TMS, Me_3Si. All reagents and solvents were purchased from *Aldrich*, *Fisher*, or *Acros Chimica*, and were used without further purification unless otherwise stated. Thin layer chromatography (TLC) was performed on *Merck* silica gel *60* F_{254} (0.25 mm; glass plates). Column and flash chromatography (CC and FC, resp.) were performed on *Mallinckrodt* silica gel *60* (230–400 mesh). ^{1}H- and ^{13}C-NMR spectra were recorded on a *Varian-200* spectrometer (200 and 50 MHz, resp.) at ambient temp.; chemical shifts δ in ppm rel. to $SiMe_4$ (=0 ppm), coupling constants *J* in Hz.

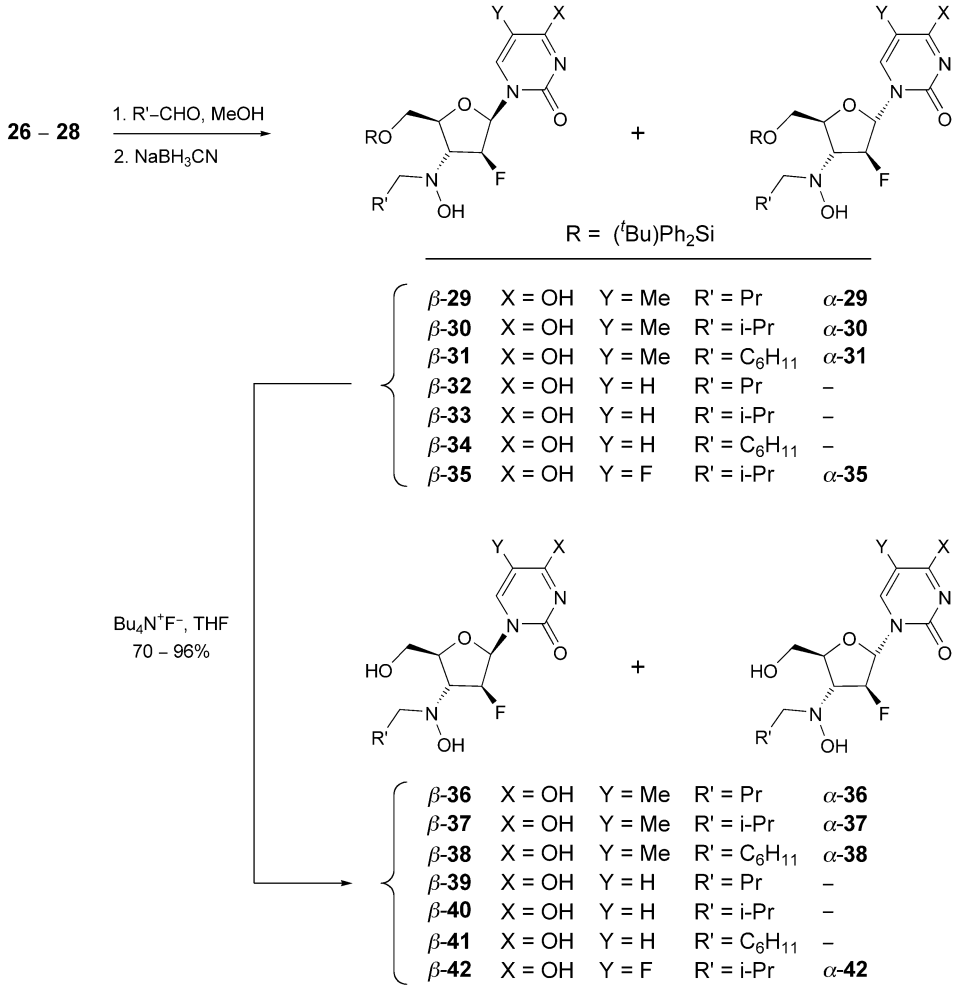
*5-*O*-[(*tert*-Butyl)dimethylsilyl]-2,3-dideoxy-2-fluoro-3-[hydroxy(methyl)amino]-*D*-arabino-1,4-lactone* (**13a**). To a soln. of *N*-methylhydroxylamine hydrochloride (12.53 g, 150 mmol) in EtOH (300 ml) was added EtONa (10.20 g, 150 mmol) portionwise. The resulting mixture was stirred at r.t. for 10 min, and *5-({[(*tert*-butyl)dimethylsilyl]oxy}methyl)-3-fluorofuran-2(5*H*)one* (**12a**; 7.38 g, 30 mmol) was added. The resulting soln. was refluxed for 5 h and concentrated under reduced pressure. Then, H_2O (100 ml) was added to the residue, and the resulting soln. was extracted with CH_2Cl_2. The org. layer was washed with brine, dried (Na_2SO_4), filtered, and concentrated. The residue was purified by FC (SiO_2; AcOEt/petroleum ether 1:3): 6.08 g (69%) of **13a**. Oil. ^{1}H-NMR ($CDCl_3$): 6.30 (br. *s*, OH); 5.53 (*dd*, *J* = 7.2, 51.4, H–C(2)); 4.51 (*dt*, *J* = 7.2, 2.4, H–C(4)); 3.85 (*m*, H–C(3), 2 H–C(5)); 2.78 (*s*, MeN); 0.89 (*s*, *t*-Bu); 0.08 (*s*, Me_2Si). ^{13}C-NMR ($CDCl_3$): 88.1, 84.3 (C(2)); 79.4, 79.3 (C(4)); 69.2, 68.8 (C(5)); 62.4 (C(3)); 47.5 (MeN); 26.3 (*Me*$_3$C); −4.8, −4.9 (Me_2Si). Anal. calc. for $C_{12}H_{24}FNO_4Si$: C 49.12, H 8.24, N 4.77; found: C 49.23, H 8.30, N 4.81.

Scheme 3



a) MeN(H)OH · HCl, EtOH, EtONa; 65%. *b*) (*t*Bu)Me$_2$SiCl, imidazole, DMF; 89%. *c*) DIBAL, CH_2Cl_2, $-78°$. *d*) $MeSO_2Cl$, Et_3N, Bu_3N (cat.), CH_2Cl_2, $-40° \rightarrow$ r.t. *e*) Me_3Si-protected base, $CHCl_3$; 65–70% (from **17**). *f*) 48% HF, MeCN; 97–99%. *g*) 1. DDQ/CH_2Cl_2; 2. $H_2NOH \cdot HCl$, MeOH; 48–57% (2 steps).

Scheme 4



*5-O-[(*tert*-Butyl)dimethylsilyl]-2,3-dideoxy-2-fluoro-3-[hydroxy(methyl)amino]-α,β-*D*-arabino-1,4-lactol* (**14a**). A mixture of **13a** (5.50 g, 18.7 mmol), TBSCl (3.10 g, 20.6 mmol), and imidazole (2.80 g, 41.2 mmol) in anh. DMF (90 ml) was stirred under Ar gas at r.t. overnight. After addition of H_2O, the resulting mixture was extracted with CH_2Cl_2. The org. layer was washed with brine, dried (Na_2SO_4), filtered, and concentrated. The residue was purified by FC (SiO_2; AcOEt/petroleum ether 5:95) to afford 5-*O*-[(*tert*-butyl)dimethylsilyl]-2,3-dideoxy-2-fluoro-3-{[(*tert*-butyl)dimethylsilyl]oxy(methyl)amino}arabino-1,4-lactone (intermediate; not shown in *Scheme 1*): 7.10 g (93%). Oil. ^{1}H-NMR ($CDCl_3$): 5.50 (br., H–C(2)); 4.38 (br. *s*, H–C(4)); 3.80 (*m*, H–C(3), 2 H–C(5)); 2.69 (*s*, MeN); 0.85 (*s*, 2 *t*-Bu); 0.08 (*m*, 2 Me_2Si). ^{13}C-NMR ($CDCl_3$): 78.6, 78.5 (C(4)); 70.1, 69.7 (C(5)); 61.1 (C(3)); 47.7 (MeN); 26.4, 26.3 (2 *Me*$_3$C); 18.8, 18.2 (2 Me$_3$*C*); −3.9, −4.1, −4.8, −4.9 (2 Me_2Si).

To a soln. of the above *O*-protected lactone (5.45 g, 13.5 mmol) in anh. CH_2Cl_2 (80 ml) was added DIBAL (14.9 ml, 1.0M soln. in hexane) at −78° under Ar gas, and the mixture was stirred at this temp. for 1 h. Then, the mixture was quenched with MeOH (10 ml) and sat. aq. NH_4Cl soln. The mixture was filtered over *Celite* to remove solid materials, and the filtrate was extracted with CH_2Cl_2. The org. layer was washed with brine, dried (Na_2SO_4), filtered, and concentrated: 5.07 g (93%) of **14a**. Colorless oil, which was directly used in the next step without further purification.

Synthesis of Nucleosides **4**–**7** (*General Procedure A*; *GPA*): MsCl (149 mg, 1.3 mmol) was added dropwise at −40° under Ar gas to a soln. of crude **14a** (409 mg, 1 mmol), Et_3N (162 mg, 1.6 mmol), and Bu_3N (37 mg, 0.2 mmol) in anh. CH_2Cl_2 (1 ml). After stirring at r.t. for 1 h, the resulting mixture was diluted with CH_2Cl_2, washed with H_2O and brine, dried (Na_2SO_4), filtered, and concentrated to afford the crude chloro derivative **14b** (yellowish oil), which was refluxed overnight in the presence of a TMS-protected nucleoside base (3 mmol) in EtOH-free $CHCl_3$ (5 ml). Then, H_2O was added, and the resulting mixture was extracted with CH_2Cl_2. The org. layer was washed with brine, dried (Na_2SO_4), filtered, and concentrated. The residue was purified by FC (SiO_2; AcOEt/petroleum ether 1:3 → 1:1).

*1-[5′-*O*-[(*tert*-Butyl)dimethylsilyl]-3′-([[(*tert*-butyl)dimethylsilyl]oxy}(methyl)amino)-2′,3′-dideoxy-2′-fluoro-α,β-*D*-arabinofuranosyl]thymine* (α,β-**4**). *GPA:* 70% (anomeric mixture). White solid. ^{1}H-NMR ($CDCl_3$): 9.97 (*m*, NH); 7.38 (*s*, H−C(6) (β)); 7.11 (*s*, H−C(6) (α)); 6.17 (*dd*, *J* = 4.4, 14.0, H−C(1′) (α)); 6.02 (*dd*, *J* = 3.7, 19.7, H−C(1′) (β)); 5.55 (br., H−C(2′)); 4.21 (br. *s*, H−C(4′) (α)); 3.75 (*m*, H−C(3′), 2 H−C(5′), H−C(4′) (β)); 2.65 (*s*, MeN); 1.89 (*s*, Me−C(5)); 0.89, 0.88 (2*s*, 2 *t*-Bu); 0.11 (*m*, 2 Me_2Si). ^{13}C-NMR ($CDCl_3$): 164.8, 164.5 (C(4)); 150.9, 150.8 (C(2)); 137.5, 135.3 (C(6)); 111.8, 110.0 (C(5)); 89.1, 85.0 (C(2′)); 88.7 (C(1′)); 81.8, 81.7 (C(4′)); 74.8, 74.3, 74.0, 73.6 (C(5′)); 47.8 (MeN); 26.5, 26.4, 18.9, 19.2, 13.0 (2 *t*-Bu); −3.8, −4.0, −4.7, −4.8 (2 Me_2Si).

*1-[5′-*O*-[(*tert*-Butyl)dimethylsilyl]-3′-([[(*tert*-butyl)dimethylsilyl]oxy}(methyl)amino)-2′,3′-dideoxy-2′-fluoro-α,β-*D*-arabinofuranosyl]uracil* (α,β-**5**). *GPA:* 68% (anomeric mixture). White solid.

Data of β-**5**: ^{1}H-NMR ($CDCl_3$): 10.00 (br. *s*, NH); 7.63 (*d*, *J* = 7.3, H−C(6)); 6.09 (*dd*, *J* = 3.7, 17.6, H−C(1′)); 5.66 (*d*, *J* = 8.1, H−C(5)); 5.55 (br., H−C(2′)); 3.80 (*m*, H−C(4′), 2 H−C(5′)); 3.50 (*dd*, *J* = 5.1, 26.3, H−C(3′)); 2.69 (*s*, MeN); 0.88 (*s*, 2 *t*-Bu); 0.15 (*m*, 2 Me_2Si). ^{13}C-NMR ($CDCl_3$): 164.1 (C(4)); 150.7 (C(2)); 141.8 (C(6)); 101.9 (C(5)); 85.1, 84.9 (C(2′)); 74.5 (C(1′)); 74.1 (C(4′)); 62.8 (C(5′)); 47.7 (MeN); 26.5, 26.4, 18.8, 18.2 (2 *t*-Bu); −3.8, −4.0, −4.8, −4.9 (2 Me_2Si).

Data of α-**5**: ^{1}H-NMR ($CDCl_3$): 9.50 (*s*, NH); 7.35 (*d*, *J* = 8.1, H−C(6)); 6.17 (*dd*, *J* = 3.9, 14.6, H−C(1′)); 5.75 (*d*, *J* = 8.1, H−C(5)); 5.55 (br., H−C(2′)); 4.23 (br. *s*, H−C(4′)); 3.88 (*dd*, *J* = 2.6, 11.4, 1 H−C(5′)); 3.74 (*dd*, *J* = 3.4, 11.4, 1 H−C(5′)); 3.62 (*dt*, *J* = 5.4, 25.0, H−C(3′)); 2.68 (*s*, MeN); 0.90, 0.87 (2*s*, 2 *t*-Bu); 0.15 (*m*, 2 Me_2Si). ^{13}C-NMR ($CDCl_3$): 163.8 (C(4)); 150.7 (C(2)); 139.8 (C(6)); 103.3 (C(5)); 90.2, 89.8 (C(2′)); 82.5, 82.4 (C(1′)); 74.4 (C(4′)); 74.0 (C(5′)); 47.9 (MeN); 26.5, 26.4, 18.9, 18.2 (2 *t*-Bu); −3.9, −4.0, −4.7, −4.8 (2 Me_2Si).

*1-[5′-*O*-[(*tert*-Butyl)dimethylsilyl]-3′-([[(*tert*-butyl)dimethylsilyl]oxy}(methyl)amino)-2′,3′-dideoxy-2′-fluoro-α,β-*D*-arabinofuranosyl]-5-fluorouracil* (α,β-**6**). *GPA:* 66% (anomeric mixture). White solid. ^{1}H-NMR ($CDCl_3$): 9.62 (br. *s*, NH); 7.79 (*d*, *J* = 6.2, H−C(6) (β)); 7.41 (*d*, *J* = 6.1, H−C(6) (α)); 6.07 (*dd*, *J* = 3.1, 17.3, H−C(1′)); 5.55 (br., H−C(2′)); 3.90 (*m*, H−C(4′), 2 H−C(5′)); 3.55 (*dd*, *J* = 4.6, 25.3, H−C(3′)); 2.63 (*s*, MeN); 0.89, 0.88 (2*s*, 2 *t*-Bu); 0.11 (*s*, 2 Me_2Si). ^{13}C-NMR ($CDCl_3$): 157.3, 157.0 (C(4)); 149.3, 142.7 (C(2)); 138.0 (C(6)); 126.5, 125.8, 124.3, 123.6 (C(5)); 85.3, 82.6 (C(2′)); 85.0, 82.5 (C(1′)); 74.4 (C(4′)); 74.0 (C(5′)); 47.7 (MeN); 26.5, 26.4, 18.9, 18.3 (2 *t*-Bu); −3.8, −4.0, −4.8, −4.9 (2 Me_2Si).

*1-[5′-*O*-[(*tert*-Butyl)dimethylsilyl]-3′-([[(*tert*-butyl)dimethylsilyl]oxy}(methyl)amino)-2′,3′-dideoxy-2′-fluoro-α,β-*D*-arabinofuranosyl]cytosine* (α,β-**7**). *GPA:* 65% (anomeric mixture). White solid. ^{1}H-NMR ($CDCl_3$): 7.65 (*dd*, *J* = 1.4, 7.5, H−C(6) (β)); 7.37 (*d*, *J* = 7.4, H−C(6) (α)); 6.10 (*m*, H−C(1′)); 5.78, 5.70 (2*d*, *J* = 7.3 and 7.4, H−C(5)); 5.40 (br., H−C(2′)); 4.22 (br. *s*, H−C(4′) (α)); 3.81 (*m*, H−C(4′) (β), 2 H−C(5′)); 3.49 (*m*, H−C(3′)); 2.63 (*m*, MeN); 0.85 (*m*, 2 *t*-Bu); 0.05 (*s*, 2 Me_2Si). ^{13}C-NMR ($CDCl_3$): 166.5, 166.3 (C(4)); 156.2, 155.9 (C(2)); 142.8, 140.6 (C(6)); 95.2, 94.2, 92.0, 91.3 (C(5)); 86.1, 83.9 (C(2′)); 85.6, 83.4 (C(1′)); 75.4, 74.9 (C(4′)); 60.3 (C(3′)); 48.0 (MeN); 26.6, 26.5, 18.7, 18.2 (2 *t*-Bu); −3.8, −3.9, −4.6, −4.7 (2 Me_2Si).

Synthesis of Nucleosides **8**–**11** (*General Procedure B*; *GPB*): Compounds **4**–**7** were treated with TBAF (2.5 equiv.) in anh. THF for 2 h at r.t. The resulting mixture was directly (without evaporation of the solvent) purified by CC (SiO_2).

*1-[2′,3′-Dideoxy-2′-fluoro-3′-[hydroxy(methyl)amino]-α,β-*D*-arabinofuranosyl]thymine* (α,β-**8**). *GPB*, with α,β-**4**: 96% (anomeric mixture). White solid. ^{1}H-NMR ((D_6)DMSO): 11.46, 11.42 (2*s*, NH); 8.45 (*dd*, *J* = 1.5, 4.7, NOH); 7.64 (*s*, H−C(6) (β)); 7.46 (*s*, H−C(6) (α)); 6.00 (*m*, H−C(1′)); 5.23 (*m*, H−C(2′)); 5.09 (*m*, C(5′)−OH); 4.39 (*m*, H−C(4′) (α)); 4.02 (*m*, H−C(4′) (β)); 3.60 (*m*, H−C(3′), 2 H−C(5′)); 2.63, 2.59 (2*s*, MeN); 1.79 (*s*, Me−C(5)). Anal. calc. for $C_{11}H_{16}FN_3O_5 \cdot 0.3\ H_2O$: C 44.83, H 5.68, N 14.26; found: C 45.08, H 5.81, N 14.30.

*1-[2′,3′-Dideoxy-2′-fluoro-3′-(hydroxy(methyl)amino)-α,β-*D*-arabinofuranosyl]uracil* (α,β-**9**). *GPB*, with β-**5** and α-**5**: 99% of β-**9** and 92% of α-**9**, resp. White solids.

Data of β-**9**: ^{1}H-NMR ((D_6)DMSO): 11.46 (*s*, NH); 8.49 (*s*, NOH); 7.76 (*d*, *J* = 8.1, H−C(6)); 5.95 (*dd*, *J* = 4.0, 19.3, H−C(1′)); 5.66 (*d*, *J* = 8.1, H−C(5)); 5.40 (*d*, *J* = 53.3, H−C(2′)); 5.08 (*t*, *J* = 6.1, C(5′)−OH); 4.06

(*m*, H–C(4′)); 3.60 (*m*, H–C(3′), 2 H–C(5′)); 2.65 (*s*, MeN). ^{13}C-NMR ((D$_6$)DMSO): 163.2 (C(4)); 150.3 (C–(2)); 141.8, 141.7 (C(6)); 101.1 (C(5)); 93.9, 90.2 (C(2′)); 84.2, 83.9 (C–(1′)); 79.8 (C(4′)); 73.0, 72.5 (C(5′)); 61.5 (C(3′)); 46.7 (MeN). Anal. calc. for $C_{10}H_{14}FN_3O_5 \cdot 0.5\ H_2O$: C 42.26, H 5.32, N 14.78; found: C 42.53, H 5.05, N 14.37.

Data of α-**9**: ^{1}H-NMR ((D$_6$)DMSO): 11.41 (*s*, NH); 8.42 (*s*, NOH); 7.58 (*d*, *J* = 8.1, H–C(6)); 6.05 (*dd*, *J* = 2.8, 16.2, H–C(1′)); 5.65 (*dd*, *J* = 1.3, 8.0, H–C(5)); 5.42 (*dt*, *J* = 51.6, 2.8, H–C(2′)); 5.09 (*t*, *J* = 5.8, C(5′)–OH); 4.39 (*m*, H–C(4′)); 3.60 (*m*, H–C(3′), H–C(5′)); 2.68 (*s*, MeN). ^{13}C-NMR ((D$_6$)DMSO): 163.4 (C(4)); 150.7 (C(2)); 140.6 (C(6)); 101.9 (C(5)); 98.9, 95.2 (C(2′)); 89.9, 89.2 (C(1′)); 83.6, 83.5 (C(4′)); 73.9, 73.4 (C(5′)); 62.5 (C(3′)); 46.9 (MeN). Anal. calc. for $C_{10}H_{14}FN_3O_5 \cdot 0.2\ H_2O$: C 43.08, H 5.21, N 15.07; found: C 43.41, H 5.26, N 14.79.

*1-{2′,3′-Dideoxy-2′-fluoro-3′-[hydroxy(methyl)amino]-*α,β*-*D*-arabinofuranosyl}-5-fluorouracil* (α,β-**10**). *GPB*, with α,β-**6**: 99% (anomeric mixture). White solid. The two anomers were partially separated by FC (SiO_2).

Data of β-**10**: ^{1}H-NMR (CD$_3$OD): 8.08 (*dd*, *J* = 1.8, 6.9, H–C(6)); 6.04 (*ddd*, *J* = 1.6, 3.9, 18.0, H–C(1′)); 5.45 (*dt*, *J* = 1.8, 52.8, H–C(2′)); 4.15 (*m*, H–C(4′)); 3.92 (*dd*, *J* = 2.8, 12.4, H–C(5′)); 3.76 (*dd*, *J* = 4.4, 12.4, H–C(5′)); 3.48 (*ddd*, *J* = 1.7, 6.2, 27.1, H–C(3′)); 2.72 (*s*, MeN). ^{13}C-NMR (CD$_3$OD): 150.7 (C(4)); 143.8 (C(2)); 139.2 (C(6)); 128.1, 127.4 (C(5)); 95.1, 91.4 (C(2′)); 86.5, 86.2 (C(1′)); 81.5 (C(4′)); 74.6, 74.1 (C(5′)); 63.1 (C(3′)); 47.4 (MeN). Anal. calc. for $C_{10}H_{13}F_2N_3O_5 \cdot 0.6\ H_2O$: C 39.50, H 4.71, N 13.82; found: C 39.23, H 4.70, N 13.99.

Data of α-**10**: ^{1}H-NMR (CD$_3$OD): 7.87 (*d*, *J* = 6.6, H–C(6)); 6.10 (*dt*, *J* = 1.6, 15.8, H–C(1′)); 5.46 (*dt*, *J* = 2.3, 50.9, H–C(2′)); 4.51 (*m*, H–C(4′)); 3.80 (*dd*, *J* = 4.0, 11.8, H–C(5′)); 3.70 (*dd*, *J* = 5.3, 12.1, H–C(5′)); 3.43 (*ddd*, *J* = 2.6, 5.1, 24.5, H–C(3′)); 2.70 (*s*, MeN). ^{13}C-NMR (CD$_3$OD): 163.6 (C(4)); 151.0 (C(2)); 144.2 (C(6)); 126.9, 126.2 (C(5)); 100.2, 96.5 (C(2′)); 92.8, 92.0 (C(1′)); 86.0 (C(4′)); 75.7, 75.3 (C(5′)); 64.2 (C(3′)); 47.6 (MeN). Anal. calc. for $C_{10}H_{13}F_2N_3O_5 \cdot 0.2\ H_2O$: C 40.46, H 4.55, N 14.16; found: C 40.61, H 4.37, N 14.43.

*1-{2′,3′-Dideoxy-2′-fluoro-3′-[hydroxy(methyl)amino]-*α,β*-*D*-arabinofuranosyl}cytosine* (α,β-**11**). *GPB*, with α,β-**7**; followed by separation by FC (SiO_2): 47% of β-**11** and 36% of α-**11**. White solids.

Data of β-**11**: ^{1}H-NMR ((D$_6$)DMSO): 8.47 (*s*, NOH); 7.69 (*d*, *J* = 6.3, H–C(6)); 7.22 (*m*, NH$_2$); 5.93 (*dd*, *J* = 3.4, 20.2, H–C(1′)); 5.75 (*d*, *J* = 7.5, H–C(5)); 5.33 (*md*, *J* = 53.0, H–C(2′)); 5.02 (*t*, *J* = 5.9, C(5′)–OH); 4.01 (*m*, H–C(4′)); 3.65 (*m*, 2 H–C(5′)); 3.35 (*m*, H–(3′)); 2.63 (*s*, MeN). ^{13}C-NMR ((D$_6$)DMSO): 165.9 (C(4)); 153.8 (C(2)); 142.3 (C(6)); 93.9, 93.8 (C(5)); 89.9, 85.2 (C(2′)); 84.9 (C(1′)); 79.5 (C(4′)); 73.6, 73.2 (C(5′)); 61.8 (C(3′)); 46.7 (MeN). Anal. calc. for $C_{10}H_{15}FN_4O_4 \cdot 0.8\ H_2O$: C 41.61, H 5.80, N 19.41; found: C 41.78, H 5.62, N 19.57.

Data of α-**11**: ^{1}H-NMR ((D$_6$)DMSO): 8.37 (*s*, NOH); 7.54 (*d*, *J* = 7.5, H–C(6)); 7.19 (*m*, NH$_2$); 6.01 (*dd*, *J* = 2.4, 16.6, H–C(1′)); 5.74 (*d*, *J* = 7.5, H–C(5)); 5.33 (*d*, *J* = 51.7, H–C(2′)); 5.06 (*t*, *J* = 5.5, C(5′)–OH); 4.34 (*m*, H–C(4′)); 3.49 (*m*, H–C(3′), 2 H–C(5′)); 2.54 (*s*, MeN). ^{13}C-NMR ((D$_6$)DMSO): 166.0 (C(4)); 155.4 (C(2)); 141.2 (C(6)); 99.3, 95.6 (C(2′)); 94.3 (C(5)); 90.6, 89.9 (C(1′)); 83.3 (C(4′)); 74.1, 73.6 (C(5′)); 62.5 (C(3′)); 47.0 (MeN). Anal. calc. for $C_{10}H_{15}FN_4O_4 \cdot 0.2\ H_2O$: C 43.23, H 5.59, N 20.16; found: C 43.43, H 5.57, N 19.97.

*5-*O*-[(*tert*-Butyl)diphenylsilyl]-2,3-dideoxy-2-fluoro-3-[hydroxy(methyl)amino]-*D*-arabino-1,4-lactone* (**16**). Prepared from **12b** in analogy to **13a**: Yield: 65% of **16**. Oil. ^{1}H-NMR (CDCl$_3$): 7.69 (*m*, 4 arom. H); 7.42 (*m*, 6 arom. H); 5.92 (br. *s*, OH); 5.57 (*dd*, *J* = 7.3, 50.9, H–C(2)); 4.51 (*m*, H–C(4)); 3.95 (*m*, H–C(3), 2 H–C(5)); 2.78 (*s*, MeN); 1.08 (*s*, *t*-Bu). ^{13}C-NMR (CDCl$_3$): 170.4; 170.0; 136.2; 136.0; 133.3; 132.9; 130.4; 128.3; 88.1; 84.2; 79.3; 79.1; 69.4; 69.1; 63.3; 47.5; 27.3; 19.9.

*5-*O*-[(*tert*-Butyl)diphenylsilyl]-3-({[(*tert*-butyl)dimethylsilyl]oxy}(methyl)amino)-2,3-dideoxy-2-fluoro-*D*-arabino-1,4-lactone* (**17**). From **16** by standard silylation methodology (TBSCl, imidiazole, DMF): 89% of **17**. Oil. ^{1}H-NMR (CDCl$_3$): 7.71 (*m*, 4 arom. H); 7.45 (*m*, 6 arom. H); 4.47 (br. *s*, H–C(4)); 3.95 (*m*, H–C(3), 2 H–C(5)); 2.72 (*s*, MeN); 1.09 (*s*, *t*-Bu); 0.90 (*s*, *t*-Bu); 0.12 (*m*, 2 MeSi). ^{13}C-NMR (CDCl$_3$): 170.4, 170.0 (C(1)); 136.2, 136.0, 133.3, 132.9, 130.4, 128.3 (2 Ph); 78.7, 78.6 (C–(4)); 70.4, 70.0 (C(5)); 62.5 (C(3)); 47.8 (MeN); 27.3, 26.5, 19.9, 18.3 (2 *t*-Bu); –3.9, –4.0 (Me$_2$Si).

*1-[5′-*O*-[(*tert*-Butyl)diphenylsilyl]-3′-({[(*tert*-butyl)dimethylsilyl]oxy}(methyl)amino)-2′,3′-dideoxy-2′-fluoro-*α,β*-*D*-arabinofuranosyl]thymine* (α,β-**20**). Prepared, in analogy to α,β-**4**, from **17** in three steps: 70% (anomeric mixture). White solid. ^{1}H-NMR (CDCl$_3$): 9.60 (*m*, NH); 7.76–7.33 (*m*, 10 arom. H, H–C(6)); 6.28 (*dd*, *J* = 4.2, 14.2, H–C(1′) (α)); 6.10 (*dd*, *J* = 3.7, 20.1, H–C(1′) (β)); 4.32 (br. *s*, H–C(4′) (α)); 3.85 (*m*, H–C(3′), 2 H–C(5′), H–C(4′) (β)); 2.67 (*s*, MeN); 1.95, 1.79 (2*s*, Me–C(5)); 1.12 (*s*, *t*-Bu); 0.90 (*m*, *t*-Bu); 0.14 (*m*, Me$_2$Si). ^{13}C-NMR (CDCl$_3$): 164.6, 164.4 (C(4)); 150.8 (C(2)); 137.6 (C(6)); 136.1, 135.9, 133.6, 133.4, 130.4,

130.3, 128.3, 128.2 (2 Ph); 111.8, 110.2 (C(5)); 85.1, 84.8 (C(2′)); 81.9, 81.8 (C(1′)); 74.9, 74.5 (C(4′)); 74.2, 73.8 (C(5′)); 47.9 (MeN); 27.4, 26.6, 26.5, 20.0, 18.3 (2 *t*-Bu); 12.8 (Me–C(5)); –3.7, –3.9 (Me_2Si).

*1-[5′-*O*-[(*tert*-Butyl)diphenylsilyl]-3′-([[(*tert*-butyl)dimethylsilyl]oxy}(methyl)amino)-2′,3′-dideoxy-2′-fluoro-α,β-*D*-arabinofuranosyl]uracil* (α,β-**21**). Prepared, in analogy to **5**, from **17** in three steps: 68% (anomeric mixture). The mixture was separated by FC (SiO_2).

Data of β-**21**: ^{1}H-NMR ($CDCl_3$): 10.12 (br. *s*, NH); 7.70 (*m*, 4 arom. H); 7.45 (*m*, 6 arom. H, H–C(6)); 6.12 (*dd*, *J* = 4.0, 18.7, H–C(1′)); 5.58 (*d*, *J* = 8.4, H–C(5)); 3.95 (*m*, H–C(4′), 2 H–C(5′)); 3.63 (*dd*, *J* = 5.6, 26.3, H–C(3′)); 2.69 (*s*, MeN); 1.11, 0.93 (2*s*, 2 *t*-Bu); 0.18 (*m*, Me_2Si). ^{13}C-NMR ($CDCl_3$): 164.2 (C(4)); 150.9 (C(2)); 141.8, 136.1 (C(5)); 136.0, 133.5, 133.3, 130.4, 128.3 (2 Ph); 102.0 (C(6)); 85.2, 84.9 (C(1′)); 74.8 (C(4′)); 74.3 (C(5′)); 47.8 (MeN); 27.4, 26.6, 19.9, 19.3 (2 *t*-Bu); –3.7, –4.0 (Me_2Si).

Data of α-**21**: ^{1}H-NMR ($CDCl_3$): 9.88 (*s*, NH); 7.71 (*m*, 4 arom. H); 7.42 (*m*, 6 arom. H, H–C(6)); 6.25 (*dd*, *J* = 3.7, 14.6, H–C(1′)); 5.78 (*d*, *J* = 8.0, H–C(5)); 4.32 (br. *s*, H–C(4′)); 3.89 (*m*, 2 H–C(5′)); 3.68 (*dd*, *J* = 4.3, 6.4, H–C(3′)); 2.65 (*s*, MeN); 1.12, 0.88 (2*s*, 2 *t*-Bu); 0.12 (*m*, Me_2Si). ^{13}C-NMR ($CDCl_3$): 163.9 (C(4)); 150.8 (C(2)); 139.9 (C(5)); 136.1, 136.0, 133.5, 133.3, 130.3, 128.3 (2 Ph); 103.3 (C(6)); 90.3, 89.6 (C(2′)); 82.6, 82.4 (C(1′)); 74.6 (C(4′)); 74.2 (C(5′)); 64.8 (C(3′)); 47.9 (MeN); 27.4, 26.6, 26.5, 19.9, 18.3 (2 *t*-Bu); –3.9 (Me_2Si).

*1-[5′-*O*-[(*tert*-Butyl)diphenylsilyl]-3′-([[(*tert*-butyl)dimethylsilyl]oxy}(methyl)amino)-2′,3′-dideoxy-2′-fluoro-α,β-*D*-arabinofuranosyl]-5-fluorouracil* (α,β-**22**). Prepared, in analogy to α,β-**6**, from **17** in three steps: 65% (anomeric mixture). White solid. ^{1}H-NMR ($CDCl_3$): 7.80–7.35 (*m*, 10 arom. H, H–C(6)); 6.22 (*m*, H–C(1′)); 4.41 (br. *s*, ½ H–C(4′)); 4.16–3.52 (*m*, H–C(3′), ½ H–C(4′), 2 H–C(5′)); 2.69 (*s*, MeN); 1.15, 0.95 (2*s*, 2 *t*-Bu); 0.21 (*m*, Me_2Si). ^{13}C-NMR ($CDCl_3$): 157.9, 157.8, 157.4, 157.3 (C(4)); 149.6 (C(2)); 143.7, 142.9 (C(5)); 138.9, 138.2 (C(6)); 136.1, 136.0, 133.5, 133.3, 130.5, 130.4, 128.4, 128.3 (2 Ph); 85.4, 85.1 (C(2′)); 82.8, 82.7 (C(1′)); 74.8 (C(4′)); 74.3 (C(5′)); 48.0 (MeN); 27.5, 26.6, 19.9, 18.3 (2 *t*-Bu); –3.7, –3.9 (Me_2Si).

Synthesis of Nucleosides **23**–**25** (*General Procedure C*; *GPC*). To a soln. of **20**–**22** (1 mmol) in MeCN (10 ml) was added 48% HF in H_2O (36 µl), and the resulting mixture was stirred at r.t. for 1 h. Then, H_2O (10 ml) was added, and the mixture was extracted with CH_2Cl_2. The org. layer was washed with sat. aq. $NaHCO_3$ soln. and brine, dried (Na_2SO_4), filtered, and concentrated. The crude products **23**–**25**, resp., were purified by FC (SiO_2).

*1-[5′-*O*-[(*tert*-Butyl)diphenylsilyl]-2′,3′-dideoxy-2′-fluoro-3′-[hydroxy(methyl)amino]-α,β-*D*-arabinofuranosyl]thymine* (α,β-**23**). *GPC*, with α,β-**20**: 99% (anomeric mixture). White solid. ^{1}H-NMR ($CDCl_3$): 10.85, 10.70 (2 br. *s*, NH); 7.71 (*m*, 4 arom. H); 7.41 (*m*, 6 arom. H, H–C(6)); 6.12 (*m*, H–C(1′)); 5.50 (*m*, H–C(2′)); 4.52 (*m*, H–C(4′) (α)); 4.24 (*m*, H–C(4′) (β)); 3.82 (*m*, H–C(3′), 2 H–C(5′)); 2.78 (*s*, MeN); 1.91, 1.75 (2*s*, Me–C(5)); 1.11 (*s*, *t*-Bu). ^{13}C-NMR ($CDCl_3$): 165.2, 165.1 (C(4)); 151.5, 151.2 (C(2)), 138.2, 136.9 (C(6)); 136.1, 135.9, 133.6, 133.5, 133.3, 130.5, 130.3, 128.3, 128.2 (2 Ph); 111.3, 110.3 (C(5)); 100.6, 96.2, 94.7, 90.3 (C(2′)); 85.2, 84.9, 83.3, 83.2 (C(1′)); 79.5, 77.8 (C(4′)); 73.9, 73.4 (C(5′)); 65.8, 63.9 (C(3′)); 47.0 (MeN); 27.5, 20.0, 19.9 (*t*-Bu); 12.9, 12.7 (C(5)–*Me*).

*1-[5′-*O*-[(*tert*-Butyl)diphenylsilyl]-2′,3′-dideoxy-2′-fluoro-3′-[hydroxy(methyl)amino]-α,β-*D*-arabinofuranosyl]uracil* (α,β-**24**). *GPC*, with β-**21** and α-**21**: 99% of β-**24** and 98% of α-**24**, resp. White solids.

Data of β-**24**: ^{1}H-NMR ($CDCl_3$): 10.68 (br. *s*, NH); 7.68 (*m*, 4 arom. H, H–C(6)); 7.42 (*m*, 6 arom. H); 6.21 (*dd*, *J* = 3.6, 19.0, H–C(1′)); 5.57 (*d*, *J* = 8.1, H–C(5)); 5.50 (*dd*, *J* = 3.0, 52.0, H–C(2′)); 4.29 (*m*, H–C(4′)); 4.07 (*dd*, *J* = 3.4, 11.4, H–C(5′)); 3.92 (*dd*, *J* = 6.0, 11.7, H–C(5′)); 3.69 (*dd*, *J* = 4.9, 25.6, H–C(3′)); 2.76 (*s*, MeN); 1.11 (*s*, *t*-Bu). ^{13}C-NMR ($CDCl_3$): 164.5 (C(4)); 151.0 (C(2)); 142.2 (C(6)); 136.1, 136.0, 133.6, 133.3, 130.4, 128.4 (2 Ph); 102.0 (C(5)); 94.5, 90.8 (C(2′)); 85.4, 85.0 (C(1′)); 79.6 (C(4′)); 73.8, 73.4 (C(5′)); 64.3 (C(3′)); 46.9 (MeN); 27.5, 19.9 (*t*-Bu).

Data of α-**24**: ^{1}H-NMR ($CDCl_3$): 11.11 (br. *s*, NH); 7.72 (*m*, 4 arom. H); 7.40 (*m*, 6 arom. H, H–C(6)); 6.05 (*dd*, *J* = 1.7, 14.7, H–C(1′)); 5.71 (*d*, *J* = 8.1, H–C(5)); 5.59 (*m*, H–C(2′)); 4.60 (*m*, H–C(4′)); 3.87 (*m*, H–C(3′), 2 H–C(5′)); 2.76 (*s*, MeN); 1.12 (*s*, *t*-Bu). ^{13}C-NMR ($CDCl_3$): 165.1 (C(4)); 151.3 (C(2)); 141.5 (C(6)); 136.1, 136.0, 133.5, 130.4, 128.3 (2 Ph); 102.2 (C(5)); 99.5, 95.7 (C(2′)); 92.5, 91.7 (C(1′)); 83.8 (C(4′)); 74.2, 73.7 (C(5′)); 65.5 (C(3′)); 47.0 (MeN); 27.5, 19.9 (*t*-Bu).

*{5′-*O*-[(*tert*-Butyl)diphenylsilyl]-2′,3′-dideoxy-2′-fluoro-3′-[hydroxy(methyl)amino]-α,β-*D*-arabinofuranosyl}-5-fluorouracil* (α,β-**25**). *GPC*, with α,β-**22**: 97% (anomeric mixture). White solid. The anomers were separated by FC (SiO_2).

Data of β-**25**: ^{1}H-NMR ($CDCl_3$): 7.72 (*m*, 4 arom. H); 7.40 (*m*, 6 arom. H, H–C(6)); 6.14 (*d*, *J* = 17.7, H–C(1′)); 5.49 (*dd*, *J* = 1.7, 52.9, H–C(2′)); 4.30 (*m*, H–C(4′)); 3.98 (*m*, 2 H–C(5′)); 3.65 (*dd*, *J* = 5.0, 26.6, H–C(3′)); 2.71 (*s*, MeN); 1.11 (*s*, *t*-Bu). ^{13}C-NMR ($CDCl_3$): 158.3, 157.7 (C(4)); 149.7 (C(2)); 142.9, 138.2

(C(5)); 136.1, 136.0, 133.3, 133.2, 130.5, 128.4 (2 Ph); 126.8, 126.1 (C(6)); 94.7, 90.9 (C(2′)); 85.6, 85.2 (C(1′)); 79.7 (C(4′)); 73.7, 73.3 (C(5′)); 64.2 (C(3′)); 46.8 (MeN); 27.4, 19.9 (*t*-Bu).

Data of α-**25**: ^{1}H-NMR ($CDCl_3$): 7.78–7.33 (*m*, 10 arom. H, H–C(6), OH); 5.90 (*d*, *J* = 14.3, H–C(1′)); 5.59 (*d*, *J* = 50.7, H–C(2′)); 4.61 (*m*, H–C(4′)); 3.81 (*m*, H–C(3′), H–C(5′)); 2.71 (*s*, MeN); 1.12 (*s*, *t*-Bu). ^{13}C-NMR ($CDCl_3$): 158.7, 158.1 (C(4)); 149.8 (C(2)); 142.9, 138.2 (C(5)); 136.1, 133.4, 130.4, 126.4, 125.7 (2 Ph); 128.3 (C(6)); 99.3, 95.6 (C(2′)); 93.0, 92.3 (C(1′)); 83.3 (C(4′)); 74.0, 73.5 (C(5′)); 65.3 (C(3′)); 46.9 (MeN); 27.5, 19.9 (*t*-Bu).

Synthesis of Nucleosides **26**–**28** (*General Procedure D*; *GPD*). To a soln. of **23**–**25** (1 mmol) in CH_2Cl_2 (10 ml) was added a soln. of DDQ (272 mg, 1.2 mmol) in CH_2Cl_2 (10 ml) in small portions, and the resulting mixture was stirred at r.t. for 30 min. Then, the mixture was diluted with CH_2Cl_2 (10 ml), washed successively with sat. aq. $NaHCO_3$ soln., brine, and H_2O, dried (Na_2SO_4), filtered, and concentrated. The resulting crude nitrone intermediate was purified by FC (short column of SiO_2; MeOH/CH_2Cl_2 1:9). To this nitrone in MeOH (10 ml) was added $NH_2OH \cdot HCl$ (104 mg, 1.5 mmol), the resulting mixture was warmed to 50° and stirred for 1 h at this temp. The solvent was evaporated, the residue, dissolved in CH_2Cl_2 (20 ml), was washed with brine, dried (Na_2SO_4), filtered, and concentrated to give the crude products **26**–**28**, resp., which were purified by FC (SiO_2).

*1-{5′-*O*-[(*tert*-Butyl)diphenylsilyl]-2′,3′-dideoxy-2′-fluoro-3′-(hydroxyamino)-*α*,*β*-*D*-arabinofuranosyl}thymine* (α,β-**26**): *GPD*, with α,β-**23**: 51% (two steps; anomeric mixture). White solid. ^{1}H-NMR ($CDCl_3$): 10.38 (br. *s*, NH); 7.75–7.30 (*m*, 10 arom. H, H–C(6)); 6.20 (*m*, H–C(1′) (*β*)); 5.82 (*m*, H–C(1′) (*α*)); 5.39 (*m*, H–C(2′)); 4.48 (*m*, H–C(4′) (*α*)); 4.00 (*m*, H–C(4′) (*β*), H–C(3′), 2 H–C(5′)); 1.85 (*s*, Me–C(5) (*α*)); 1.69 (*s*, Me–C(5) (*β*)); 1.10 (*s*, *t*-Bu).

*1-{5′-*O*-[(*tert*-Butyl)diphenylsilyl]-2′,3′-dideoxy-2′-fluoro-3′-(hydroxyamino)-β-D-arabinofuranosyl}uracil* (*β*-**27**). *GPD*, with *β*-**24**: 57% (two steps). White solid. ^{1}H-NMR ($CDCl_3$): 10.05 (br. *s*, NH); 7.70–7.30 (*m*, 10 arom. H, H–C(6)); 6.20 (*d*, *J* = 19.5, H–C(1′)); 5.56 (*d*, *J* = 8.1, H–C(5)); 5.40 (*m*, H–C(2′)); 4.01 (*m*, H–C(3′), H–C(4′), 2 H–C(5′)); 1.08 (*s*, *t*-Bu). ^{13}C-NMR ($CDCl_3$): 164.5 (C(4)); 151.0 (C(2)); 142.2 (C(6)); 136.1, 136.0, 133.4, 133.2, 130.5, 128.3 (2 Ph); 102.1 (C(5)); 95.2, 91.4 (C(2′)); 85.7, 85.5 (C(1′)); 80.1 (C(4′)); 67.9, 67.5 (C(5′)); 64.1 (C(3′)); 27.4, 19.9 (*t*-Bu).

*1-{5′-*O*-[(*tert*-Butyl)diphenylsilyl]-2′,3′-dideoxy-2′-fluoro-3′-(hydroxyamino)-β-D-arabinofuranosyl}-5-fluorouracil* (*β*-**28**). *GPD*, with *β*-**25**: 53% (2 steps). White solid. ^{1}H-NMR ($CDCl_3$): 7.72–7.31 (*m*, 10 arom. H, H–C(6), OH); 6.17 (*d*, *J* = 18.7, H–C(1′)); 5.35 (*d*, *J* = 53.0, H–C(2′)); 3.95 (*m*, H–C(3′), H–C(4′), 2 H–C(5′)); 1.11 (*s*, *t*-Bu). ^{13}C-NMR ($CDCl_3$): 158.2, 157.7 (C(4)); 149.7 (C(2)); 143.0, 138.3 (C(5)); 136.1, 136.0, 133.2, 130.5, 128.4, 126.7 (2 Ph); 125.9 (C(6)); 95.5, 91.7 (C(2′)); 85.7, 85.5 (C(1′)); 80.6 (C(4′)); 68.1, 67.6 (C(5′)); 64.0 (C(3′)); 27.4, 19.8 (*t*-Bu).

*1-{5′-*O*-[(*tert*-Butyl)diphenylsilyl]-2′,3′-dideoxy-2′-fluoro-3′-(hydroxyamino)-α-D-arabinofuranosyl}-5-fluorouracil* (*α*-**28**). *GPD*, with *α*-**25**: 48% (2 steps). White solid. ^{1}H-NMR ($CDCl_3$): 7.72–7.31 (*m*, 10 arom. H, H–C(6)); 5.92 (*d*, *J* = 15.4, H–C(1′)); 5.44 (*d*, *J* = 48.8, H–C(2′)); 4.37 (*m*, H–C(4′)); 3.90 (*m*, H–C(3′), 2 H–C(5′)); 1.11 (*s*, *t*-Bu). ^{13}C-NMR ($CDCl_3$): 158.8, 158.3 (C(4)); 149.5 (C(2)); 142.7, 138.0 (C(5)); 136.1, 133.5, 133.4, 130.4, 126.8, 126.0 (2 Ph); 128.3 (C(6)); 99.6, 96.0 (C(2′)); 93.5, 92.7 (C(1′)), 77.8 (C(4′)); 68.2 (C(5′)); 68.0 (C(5′)); 64.7 (C(3′)); 27.4, 19.8 (*t*-Bu).

Synthesis of Nucleosides **29**–**35** (*General Procedure E*; *GPE*). To a soln. of **26**–**28** (1 equiv.) in MeOH was added the aldehyde (1.2 equiv.; see *Scheme 4*), and the resulting mixture was stirred at r.t. for 10 min. Then, $NaBH_3CN$ (2 equiv.) was added in small portions, and the mixture was stirred at r.t. for another 10 min. After evaporation to dryness, the residue was dissolved in CH_2Cl_2, and the resulting soln. was washed with brine, dried (Na_2SO_4), filtered, and concentrated. The crude products were purified by FC (SiO_2).

*{5′-*O*-[(*tert*-Butyl)diphenylsilyl]-3′-[butyl(hydroxy)amino]-2′,3′-dideoxy-2′-fluoro-α,β-D-arabinofuranosyl}thymine* (α,β-**29**): *GPE*, with α,β-**26** and butanal: 84% (two steps; anomeric mixture). White solid. ^{1}H-NMR ($CDCl_3$): 10.48 (*m*, NH); 7.50 (*m*, 10 arom. H, H–C(6)); 6.20 (*m*, H–C(1′)); 5.50 (*m*, H–C(2′)); 4.48 (*m*, H–C(4′) (*α*)); 4.00 (*m*, H–C(4′) (*β*), H–C(3′), 2 H–C(5′)); 2.82 (*m*, CH_2N); 0.90–0.79 (*m*, Me–C(5), *t*-Bu, Me, 2 CH_2). ^{13}C-NMR ($CDCl_3$): 164.8 (C(4)); 151.3, 151.0 (C(2)); 138.0, 136.9 (C(6)); 136.1, 136.0, 133.6, 133.3, 130.4, 130.3, 128.3, 128.2 (2 Ph); 111.2, 110.3 (C(5)); 94.6, 90.8 (C(2′)); 85.1, 84.8, 82.9, 82.8 (C(1′)); 79.2 (C(4′)); 72.5, 72.1 (C(5′)); 65.7, 63.8 (C(3′)), 61.0, 59.0 (NCH_2); 29.4, 27.4 (2 CH_2); 20.9, 19.9 (*t*-Bu); 14.5, 12.7 (2 Me).

*1-{5′-*O*-[(*tert*-Butyl)diphenylsilyl]-2′,3′-dideoxy-2′-fluoro-3′-[hydroxy(2-methylpropyl)amino]-α,β-D-arabinofuranosyl}thymine* (α,β-**30**): *GPE*, with α,β-**26** and 2-methylpropanal: 87% (two steps; anomeric mixture). White solid. ^{1}H-NMR ($CDCl_3$): 10.01 (br. *s*, NH); 7.75–7.29 (*m*, 10 arom. H–C(6)); 6.94, 6.40 (2 br. *s*, OH); 6.12 (*m*, H–C(1′)); 5.42 (*m*, H–C(2′)); 4.49 (*m*, H–C(4′) (*α*)); 4.23 (*m*, H–C(4′) (*β*)); 3.78 (*m*, H–C(3′),

2 H–C(5′)); 2.55 (*d*, *J* = 7.0, CH_2N); 1.90 (*m*, 2.2 H, Me–C(5), CH); 1.75 (*s*, 1.8 H; Me–C(5)); 1.10 (*s*, *t*-Bu); 0.94 (*d*, *J* = 6.6, 2 Me). ^{13}C-NMR ($CDCl_3$): 164.8, 164.6 (C(4)); 151.0 (C(2)); 137.9, 136.9 (C(6)); 136.1, 135.9, 133.6, 133.4, 130.4, 130.3, 128.3 (2 Ph); 110.7, 110.4 (C(5)); 98.9, 95.2, 95.0, 91.4 (C(2′)); 91.3, 90.7, 85.3, 84.9 (C(1′)); 83.8, 79.2 (C(4′)); 73.5, 73.3, 73.0, 72.8 (C(5′)); 67.5, 66.9 (C(3′)); 65.4, 64.0 (NCH_2); 27.4, 26.7, 26.5, 19.9 (3 Me); 21.4, 21.3, 13.0, 12.8 (*t*-Bu).

*1-{5′-*O*-[(*tert*-Butyl)diphenylsilyl]-3′-[(cyclohexylmethyl)(hydroxy)amino]-2′,3′-dideoxy-2′-fluoro-α,β-*D*-arabinofuranosyl}thymine* (α,β-**31**): *GPE*, with α,β-**26** and cyclohexanecarboxaldehyde: 68% (two steps; anomeric mixture). White solid. ^{1}H-NMR ($CDCl_3$): 10.00 (*m*, NH); 7.53 (*m*, 10 arom. H, H–C(6)); 6.93 (br. *s*, OH (α)); 6.41 (br. *s*, OH (β)); 6.14 (*m*, H–C(1′)); 5.49 (*m*, H–C(2′)); 4.48 (*m*, H–C(4′) (α)); 4.26 (*m*, H–C(4′) (β)); 3.81 (*m*, H–C(3′), 2 H–C(5′)); 2.58 (*d*, *J* = 6.6, NCH_2); 1.92–0.78 (*m*, Me–C(5), 5 CH_2, CH); 1.11 (*s*, *t*-Bu). ^{13}C-NMR ($CDCl_3$): 164.9, 164.7 (C(4)); 151.3 (C(2)); 137.9, 137.3 (C(6)); 136.0, 135.9, 133.7, 133.5, 130.2, 130.1, 128.1 (2 Ph); 110.6, 110.3 (C(5)); 98.9, 95.4, 95.3, 91.5 (C(2′)); 90.5, 85.2, 84.9 (C(1′)); 84.0, 79.1 (C(4′)); 73.8, 73.6, 72.8 (C(5′)); 66.2, 65.9 (C(3′)); 65.7, 64.1 (NCH_2); 36.1, 32.2, 27.6, 26.4 (5 CH_2); 19.9, 12.8 (*t*-Bu).

*1-{5′-*O*-[(*tert*-Butyl)diphenylsilyl]-3′-[butyl(hydroxy)amino]-2′,3′-dideoxy-2′-fluoro-β-*D*-arabinofuranosyl}-uracil* (β-**32**). *GPE*, with β-**27** and butanal: 93% (two steps). White solid. ^{1}H-NMR ($CDCl_3$): 10.58 (br. *s*, NH); 7.69 (*m*, 4 arom. H, H–C(6)); 7.40 (*m*, 6 arom. H); 7.11 (br. *s*, OH); 6.20 (*dd*, *J* = 3.4, 18.5, H–C(1′)); 5.56 (*d*, *J* = 8.2, H–C(5)); 5.50 (*dd*, *J* = 3.2, 52.7, H–C(2′)); 4.28 (*m*, H–C(4′)); 3.92 (*m*, H–C(3′), 2 H–C(5′)); 2.81 (*m*, NCH_2); 1.67–0.88 (*m*, *t*-Bu, Me, 2 CH_2). ^{13}C-NMR ($CDCl_3$): 164.4 (C(4)); 150.9 (C(2)); 142.3 (C(6)); 136.1, 136.0, 133.6, 133.3, 130.4, 128.3 (2 Ph); 101.9 (C(5)); 94.6, 90.9 (C(2′)); 85.4, 85.0 (C(1′)); 79.4 (C(4′)); 72.5 (C(5′)); 72.0 (C(5′)); 64.2 (C(3′)); 58.9 (CH_2N); 29.6 (2 CH_2); 20.9, 14.6 (*t*-Bu); 19.9 (Me).

*1-{5′-*O*-[(*tert*-Butyl)diphenylsilyl]-2′,3′-dideoxy-2′-fluoro-3′-[hydroxy(2-methylpropyl)amino]-β-*D*-arabinofuranosyl}uracil* (β-**33**): *GPE*, with β-**27** and 2-methylpropanal: 92% (two steps). White solid. ^{1}H-NMR ($CDCl_3$): 10.16 (br. *s*, NH); 7.69 (*m*, 4 arom. H, H–C(6)); 7.41 (*m*, 6 arom. H); 6.51 (br. *s*, OH); 6.19 (*dd*, *J* = 3.2, 18.7, H–C(1′)); 5.58 (*d*, *J* = 8.1, H–C(5)); 5.45 (*m*, H–C(2′)); 4.27 (*m*, H–C(4′)); 4.04 (*dd*, *J* = 3.0, 11.6, 1 H–C(5′)); 3.88 (*dd*, *J* = 3.0, 11.0, 1 H–C(5′)); 3.69 (*dd*, *J* = 5.0, 26.4, H–C(3′)); 2.55 (*d*, *J* = 7.0, CH_2N); 1.91 (*m*, CH); 1.11 (*s*, *t*-Bu); 0.94 (*dd*, *J* = 1.8, 6.6, 2 Me). ^{13}C-NMR ($CDCl_3$): 164.2 (C(4)); 150.8 (C(2)); 142.1 (C(6)); 136.1, 136.0, 133.5, 133.3, 130.5, 130.4, 128.3 (2 Ph); 102.0 (C(5)); 94.9, 91.2 (C(2′)); 85.5, 85.1 (C(1′)); 79.3 (C(4′)); 73.2, 72.7 (C(5′)); 66.9 (C(3′)); 64.3 (NCH); 27.5, 26.7 (2 Me); 21.3, 19.9 (*t*-Bu).

*1-{5′-*O*-[(*tert*-Butyl)diphenylsilyl]-3′-[(cyclohexylmethyl)(hydroxy)amino]-2′,3′-dideoxy-2′-fluoro-β-*D*-arabinofuranosyl}uracil* (β-**34**): *GPE*, with β-**27** and cyclohexanecarboxaldehyde: 88% (two steps). White solid. ^{1}H-NMR ($CDCl_3$): 9.89 (br. *s*, NH); 7.53 (*m*, 10 arom. H, H–C(6)); 6.25 (br. *s*, OH); 6.17 (*dd*, *J* = 3.7, 18.8, H–C(1′)); 5.56 (*d*, *J* = 8.3, H–C(5)); 5.42 (*m*, H–C(2′)); 4.22 (*m*, H–C(4′)); 4.02 (*dd*, *J* = 3.0, 11.1, 1 H–C(5′)); 3.87 (*dd*, *J* = 3.3, 11.3, 1 H–C(5′)); 3.69 (*dd*, *J* = 4.4, 27.1, H–C(3′)); 2.59 (*d*, *J* = 6.7, CH_2N); 1.85–0.79 (*m*, CH, 5 CH_2); 1.09 (*s*, *t*-Bu). ^{13}C-NMR ($CDCl_3$): 164.1 (C(4)); 150.9 (C(2)); 142.1 (C(6)); 136.1, 136.0, 133.5, 133.3, 130.4, 128.3 (2 Ph); 102.0 (C(5)); 94.8, 91.0 (C(2′)); 85.4, 85.1 (C(1′)); 79.3 (C(4′)); 73.0, 72.5 (C(5′)); 65.8 (C(3′)); 64.2 (CH_2N); 36.1 (CH); 32.2, 27.5 (5 CH_2), 27.3, 26.6, 19.9 (*t*-Bu).

*1-{5′-*O*-[(*tert*-Butyl)diphenylsilyl]-2′,3′-dideoxy-2′-fluoro-3′-[hydroxy(2-methylpropyl)amino]-β-*D*-arabinofuranosyl]-5-fluorouracil* (β-**35**). *GPE*, with β-**28** and 2-methylpropanal: 65% (2 steps). White solid. ^{1}H-NMR ($CDCl_3$): 10.34 (br. *s*, NH); 7.71 (*m*, 4 arom. H, H–C(6)); 7.43 (*m*, 6 arom. H); 6.30 (br. *s*, OH); 6.13 (*d*, *J* = 18.0, H–C(1′)); 5.45 (*dd*, *J* = 2.4, 52.1, H–C(2′)); 4.28 (*m*, H–C(4′)); 4.02 (*dd*, *J* = 3.6, 11.4, 1 H–C(5′)); 3.84 (*dd*, *J* = 3.3, 11.4, 1 H–C(5′)); 3.64 (*dd*, *J* = 5.0, 27.0, H–C(3′)); 2.50 (*d*, *J* = 6.7, CH_2N); 1.89 (*m*, CH); 1.11 (*s*, *t*-Bu); 0.92 (*dd*, *J* = 2.5, 6.6, 2 Me). ^{13}C-NMR ($CDCl_3$): 157.9, 157.4 (C(4)); 149.5 (C(2)); 142.9, 138.2 (C(5)); 136.1, 136.0, 133.3, 130.5, 128.3, 126.6 (2 Ph); 126.0 (C(6)); 95.1, 91.4 (C(2′)); 85.7, 85.4 (C(1′)); 79.4 (C(4′)); 73.2, 72.7 (C(5′)); 66.7 (C(3′)); 64.2 (CH_2N); 27.4 (CH); 26.6, 19.8 (*t*-Bu); 21.2 (2 Me).

*1-{5′-*O*-[(*tert*-Butyl)diphenylsilyl]-2′,3′-dideoxy-2′-fluoro-3′-[hydroxy(2-methylpropyl)amino]-α-*D*-arabinofuranosyl]-5-fluorouracil* (α-**35**). *GPE*, with α-**28** and 2-methylpropanal: 83% (2 steps). White solid. ^{1}H-NMR ($CDCl_3$): 10.46 (br. *s*, NH); 7.55 (*m*, 10 arom. H, H–C(6)); 6.62 (br. *s*, OH); 6.00 (*d*, *J* = 14.6, H–C(1′)); 5.62 (*d*, *J* = 49.1, H–C(2′)); 4.49 (*m*, H–C(4′)); 3.84 (*m*, 2 H–C(5′)); 3.64 (*m*, H–C(3′)); 2.51 (*d*, *J* = 6.4, CH_2N); 1.95 (*m*, CH); 1.10 (*s*, *t*-Bu); 0.90 (*dd*, *J* = 2.3, 6.6, 2 Me). ^{13}C-NMR ($CDCl_3$): 158.5, 158.1 (C(4)); 149.2 (C(2)); 142.5, 137.8 (C(5)); 136.1, 133.4, 130.4, 128.3, 126.5 (2 Ph); 125.8 (C(6)); 99.5, 95.9 (C(2′)); 92.6, 91.8 (C(1′)); 84.9 (C(4′)); 74.1, 73.6 (C(5′)); 67.5 (C(3′)); 65.1 (CH_2N); 27.4 (CH), 26.4, 19.8 (*t*-Bu); 21.3 (2 Me).

Synthesis of Nucleosides **36**–**42** (*General Procedure F*; *GPF*). To a soln. of compounds **29**–**35**, resp., in anh. THF was added a soln of TBAF (1.2 equiv.) in THF. The mixture was stirred for 1 h at r.t., then directly (without evaporation) subjected to FC (SiO_2).

*1-{3′-[Butyl(hydroxy)amino]-2′,3′-dideoxy-2′-fluoro-α,β-*D*-arabinofuranosyl}thymine* (α,β-**36**): *GPF*, with α,β-**29**: 82% (anomeric mixture). White solid. ^{1}H-NMR (CD_3OD): 7.71 (*s*, H–C(6) (β)); 7.54 (*s*, H–C(6) (α)); 6.12 (*dd*, *J* = 2.8, 16.1, H–C(1′) (α)); 6.05 (*dd*, *J* = 3.9, 18.7, H–C(1′) (β)); 5.56 (*dt*, *J* = 2.9, 51.6, H–C(2′) (α)); 5.45 (*ddd*, *J* = 1.7, 3.7, 53.0, H–C(2′) (β)); 4.56 (*m*, H–C(4′) (α)); 4.19 (*m*, H–C(4′) (β)); 3.75 (*m*, H–C(3′), 2 H–C(5′)); 2.89 (*m*, CH_2N); 1.87 (*s*, Me–C(5)); 1.45 (*m*, 2 CH_2); 0.96 (*t*, *J* = 7.2, Me). ^{13}C-NMR (CD_3OD): 166.5, 166.4 (C(4)); 152.7, 152.6 (C(2)); 139.5, 138.5 (C(6)); 111.9, 110.8 (C(5)); 95.9, 95.1, 92.4 (C(2′)); 91.7, 91.4, 86.3, 86.0 (C(1′)); 84.9, 80.8 (C(4′)); 74.6, 74.2, 73.7, 73.2 (C(5′)); 64.2, 63.1 ((C(3′)); 59.7 (CH_2N), 30.6, 30.2, 21.6 (2 CH_2); 14.7, 12.9, 12.7 (2 Me). Anal. calc. for $C_{14}H_{22}FN_3O_5 \cdot 0.3\ H_2O$: C 49.93, H 6.77, N 12.48; found: C 50.16, H 6.75, N 12.65.

*1-{2′,3′-Dideoxy-2′-fluoro-3′-[hydroxy(2-methylpropyl)amino]-α,β-*D*-arabinofuranosyl}thymine* (α,β-**37**): *GPF*, with α,β-**30**: 95% (anomeric mixture). White solid. ^{1}H-NMR (CD_3OD): 7.72 (*s*, H–C(6) (β)); 7.54 (*s*, H–C(6) (α)); 6.13 (*dd*, *J* = 2.3, 13.7, H–C(1′) (α)); 6.04 (*dd*, *J* = 3.9, 18.7, H–C(1′) (β)); 5.45 (*dt*, *J* = 2.5, 51.3, H–C(2′) (α)); 5.32 (*ddd*, *J* = 1.8, 3.8, 53.4, H–C(2′) (β)); 4.52 (*m*, H–C(4′) (α)); 4.17 (*m*, H–C(4′) (β)); 3.97–3.29 (*m*, H–C(3′), 2 H–C(5′)); 2.72–2.38 (*m*, CH_2N); 1.89 (*m*, Me–C(5), CH); 0.92 (*m*, 2 Me). ^{13}C-NMR (CD_3OD): 166.7, 166.5 (C(4)); 152.6, 152.3 (C(2)); 139.5, 138.3 (C(6)); 111.5, 110.7 (C(5)); 100.2, 96.6, 95.4, 92.3 (C(2′)); 91.6, 86.3, 86.0, 85.7 (C(1′)); 81.2, 81.1 (C(4′)); 75.1, 74.7, 74.2, 73.8 (C(5′)); 68.2, 68.0 (C(3′)); 64.3, 63.2 (CH_2N); 27.7, 27.6 (CH); 21.5 (Me); 21.4 (Me_2CH). Anal. calc. for $C_{14}H_{22}FN_3O_5 \cdot 0.8\ H_2O$: C 48.63, H 6.88, N 12.15; found: C 48.58, H 6.62, N 12.37.

*1-{3′-[(Cyclohexylmethyl)(hydroxy)amino]-2′,3′-dideoxy-2′-fluoro-α,β-*D*-arabinofuranosyl}thymine* (α,β-**38**): *GPF*, with α,β-**31**: 96% (anomeric mixture). White solid. ^{1}H-NMR (CD_3OD): 7.72 (*s*, H–C(6) (β)); 7.54 (*s*, H–C(6) (α)); 6.09 (*m*, H–C(1′)); 5.42 (*m*, H–C(2′)); 4.51 (*m*, H–C(4′) (α)); 4.14 (*m*, H–C(4′) (β)); 3.97–3.29 (*m*, H–C(3′), 2 H–C(5′)); 2.73–2.40 (*m*, CH_2N); 2.00–0.78 (*m*, Me–C(5)), CH, 5 CH_2). ^{13}C-NMR (CD_3OD): 166.5, 164.7 (C(4)); 152.3 (C(2)); 139.5, 138.3 (C(6)); 111.4, 110.7 (C(5)); 100.4, 96.4, 95.4, 92.4 (C(2′)); 91.6, 86.3, 86.0 (C(1′)); 81.1 (C(4′)); 74.2, 73.8 (C(5′)); 66.8, 64.4 (C(3′)); 63.2 (CH_2N); 37.2, 37.1 (CH); 33.0, 32.9, 28.3, 27.6 (5 CH_2); 13.0, 12.8 (Me). Anal. calc. for $C_{17}H_{26}FN_3O_5 \cdot 0.1\ H_2O$: C 54.71, H 7.08, N 11.26; found: C 54.97, H 7.13, N 11.19.

*1-{3′-[Butyl(hydroxy)amino]-2′,3′-dideoxy-2′-fluoro-β-*D*-arabinofuranosyl}uracil* (β-**39**). *GPF*, with β-**32**: 93%. White solid. ^{1}H-NMR (CD_3OD): 7.86 (*dd*, *J* = 2.0, 8.1, H–C(6)); 6.06 (*dd*, *J* = 3.7, 18.7, H–C(1′)); 5.69 (*d*, *J* = 8.1, H–C(5)); 5.43 (*ddd*, *J* = 1.5, 3.7, 53.1, H–C(2′)); 4.19 (*m*, H–C(4′)); 3.90 (*dd*, *J* = 2.9, 12.4, 1 H–C(5′)); 3.75 (*dd*, *J* = 4.72, 12.4, 1 H–C(5′)); 3.52 (*ddd*, *J* = 1.5, 6.1, 27.5, H–C(3′)); 2.79 (*m*, CH_2N); 1.48 (*m*, 2 CH_2); 0.95 (*t*, *J* = 7.1, Me). ^{13}C-NMR (CD_3OD): 166.3 (C(4)); 152.2 (C(2)); 143.9, 143.8 (C(6)); 102.1 (C(5)); 95.4, 91.6 (C(2′)); 86.6, 86.3 (C(1′)); 81.3, 81.2 (C(4′)); 74.0, 73.5 (C(5′)); 63.3 (C(3′)); 59.6 (CH_2N); 31.1, 21.7 (2 CH_2); 14.8 (Me). Anal. calc. for $C_{13}H_{20}FN_3O_5 \cdot 0.5\ H_2O$: C 47.85, H 6.49, N 12.88; found: C 48.00, H 6.62, N 12.97.

*1-{2′,3′-Dideoxy-2′-fluoro-3′-[hydroxy(2-methylpropyl)amino]-β-*D*-arabinofuranosyl}uracil* (β-**40**): *GPF*, with β-**33**: 94%. White solid. ^{1}H-NMR (CD_3OD): 7.86 (*dd*, *J* = 2.0, 8.1, H–C(6)); 6.06 (*dd*, *J* = 3.7, 18.6, H–C(1′)); 5.69 (*d*, *J* = 8.1, H–C(5)); 5.43 (*ddd*, *J* = 1.6, 3.8, 53.2, H–C(2′)); 4.18 (*m*, H–C(4′)); 3.83 (*ddd*, *J* = 2.8, 12.2, 29.4, 2 H–C(5′)); 3.48 (*ddd*, *J* = 1.5, 6.1, 27.4, H–C(3′)); 2.67 (*dd*, *J* = 6.2, 12.1, 1 H of CH_2N); 2.46 (*dd*, *J* = 7.6, 12.2, 1 H of CH_2N); 1.90 (*m*, CH); 0.95 (*m*, 2 Me). ^{13}C-NMR (CD_3OD): 166.3 (C(4)); 152.2 (C(2)); 143.8 (C(6)); 102.1 (C(5)); 95.4, 91.7 (C(2′)); 86.6, 86.3 (C(1′)); 81.3 (C(4′)); 74.3, 73.9 (C(5′)); 67.9 (C(3′)); 63.4 (CH_2N); 27.7 (CH); 21.5, 21.4 (2 Me). Anal. calc. for $C_{13}H_{20}FN_3O_5 \cdot 0.2\ H_2O$: C 48.65, H 6.41, N 13.09; found: C 48.61, H 6.65, N 12.93.

*1-{3′-[(Cyclohexylmethyl)(hydroxy)amino]-2′,3′-dideoxy-2′-fluoro-β-*D*-arabinofuranosyl}uracil* (β-**41**): *GPF*, with β-**34**: 85%. White solid. ^{1}H-NMR (CD_3OD): 7.86 (*dd*, *J* = 2.0, 8.1, H–C(6)); 6.05 (*dd*, *J* = 3.8, 18.6, H–C(1′)); 5.68 (*d*, *J* = 8.1, H–C(5)); 5.41 (*ddd*, *J* = 1.6, 3.8, 53.2, H–C(2′)); 4.17 (*m*, H–C(4′)); 3.90 (*dd*, *J* = 3.2, 12.4, H–C(5′)); 3.74 (*dd*, *J* = 4.6, 12.2, 1 H–C(5′)); 3.46 (*ddd*, *J* = 1.7, 6.3, 27.4, H–C(3′)); 2.68 (*dd*, *J* = 5.6, 12.1, 1 H of CH_2N); 2.51 (*dd*, *J* = 7.4, 12.5, 1 H of CH_2N); 1.98–0.81 (*m*, CH, 5 CH_2). ^{13}C-NMR (CD_3OD): 166.3 (C(4)); 152.2 (C(2)); 143.8 (C(6)); 102.0 (C(5)); 95.4, 91.7 (C(2′)); 86.6, 86.3 (C(1′)); 81.4, 81.3 (C(4′)); 74.4, 73.9 (C(5′)); 66.7 (C(3′)); 63.4 (CH_2N); 37.2 (CH); 33.0, 28.3, 27.6 (5 CH_2). Anal. calc. for $C_{16}H_{24}FN_3O_5$: C 53.77, H 6.77, N 11.76; found: C 53.57, H 6.75, N 12.06.

*1-{2′,3′-Dideoxy-2′-fluoro-3′-[hydroxy(2-methylpropyl)amino]-β-*D*-arabinofuranosyl}-5-fluorouracil* (β-**42**). *GPF*, with β-**35**: 76%. White solid. ^{1}H-NMR (CD_3OD): 8.08 (*dd*, *J* = 1.8, 6.8, H–C(6)); 6.04 (*ddd*, *J* = 1.7, 3.9, 18.0, H–C(1′)); 5.44 (*ddd*, *J* = 1.7, 3.7, 53.1, H–C(2′)); 4.18 (*m*, H–C(4′)); 3.92 (*dd*, *J* = 3.6, 12.6, 1 H–C(5′)); 3.75 (*dd*, *J* = 4.4, 12.4, 1 H–C(5′)); 3.51 (*ddd*, *J* = 1.7, 6.2, 27.4, H–C(3′)); 2.67 (*dd*, *J* = 6.2, 12.8, 1 H of CH_2N); 2.46 (*dd*, *J* = 7.7, 12.4, 1 H of CH_2N); 1.89 (*m*, CH); 0.97, 0.94 (2*d*, *J* = 2.2 each, 2 Me). ^{13}C-NMR (CD_3OD): 159.8 (C(4)); 150.8 (C(2)); 143.8, 139.2 (C(5)); 128.1, 127.4 (C(6)); 95.4, 91.6 (C(2′)); 86.6, 86.3

(C(1′)); 81.5, 81.4 (C(4′)); 74.0, 73.6 (C(5′)); 67.9 (C(3′)); 63.1 (CH_2N); 27.7 (CH), 21.4, 21.3 (2 Me). Anal. calc. for $C_{13}H_{19}F_2N_3O_5 \cdot 0.5\ H_2O$: C 45.48, H 5.87, N 12.24; found: C 45.60, H 5.55, N 12.17.

*1-[2′,3′-Dideoxy-2′-fluoro-3′-[hydroxy(2-methylpropyl)amino]-α-*D*-arabinofuranosyl]-5-fluorouracil* (*α*-**42**). *GPF*, with *α*-**35**: 70%. White solid. ^{1}H-NMR (CD_3OD): 7.89 (*d*, *J* = 6.7, H–C(6)); 6.09 (*d*, *J* = 15.6, H–C(1′)); 5.45 (*dt*, *J* = 1.9, 50.5, H–C(2′)); 4.54 (*m*, H–C(4′)); 3.74 (*m*, 2 H–C(5′)); 3.44 (*ddd*, *J* = 2.0, 4.6, 24.6, H–C(3′)); 2.57 (*dd*, *J* = 6.2, 12.5, 1 H of CH_2N); 2.46 (*dd*, *J* = 7.5, 12.4, 1 H of CH_2N); 1.93 (*m*, CH); 0.93 (*dd*, *J* = 4.6, 6.6, 2 Me). ^{13}C-NMR (CD_3OD): 160.0, 159.5 (C(4)); 151.0 (C(2)); 144.2, 139.5 (C(5)); 127.0, 126.3 (C(6)); 100.5, 96.9 (C(2′)); 93.0, 92.2 (C(1′)); 86.3, 86.2 (C(4′)); 75.2, 74.7 (C(5′)); 68.1 (C(3′)); 64.2 (CH_2N); 27.6 (CH); 21.4, 21.3 (2 Me). Anal. calc. for $C_{13}H_{19}F_2N_3O_5 \cdot 0.4\ H_2O$: C 45.59, H 5.83, N 12.27; found: C 45.85, H 5.59, N 12.58.

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