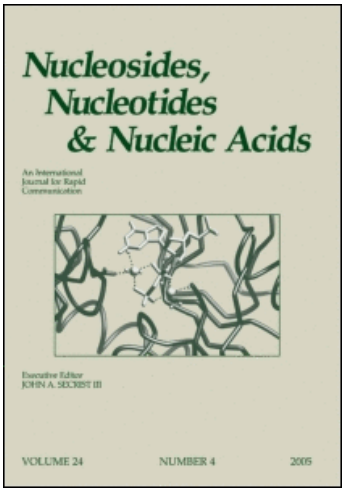

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3'-Deoxy-3'-*C*-trifluoromethyl Nucleosides: Synthesis and Antiviral Evaluation

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3'-DEOXY-3'-*C*-TRIFLUOROMETHYL NUCLEOSIDES : SYNTHESIS AND ANTIVIRAL EVALUATION

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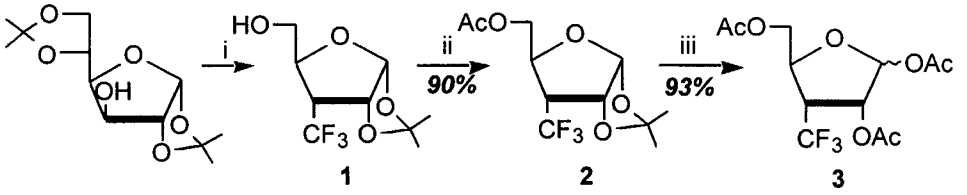
Abstract: 2',3'-Dideoxy-3'-*C*-trifluoromethylthymidine **9a** and -uridine **9b** and 3'-*C*-trifluoromethyl-d_4T **11** were prepared in a few steps from 3'-deoxy-3'-*C*-trifluoromethyl-D-ribose, which synthesis was recently reported. The biological assessment of these nucleoside analogues did not reveal interesting antiviral properties against HIV-1, HSV-1, CMV, Vaccine, and Cox B4.

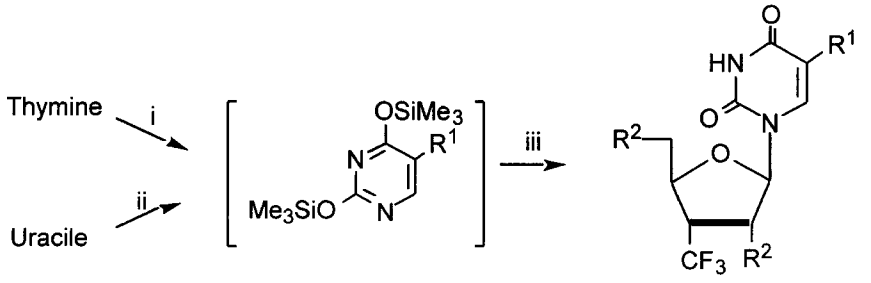
Nucleoside analogues are among the most potent antiviral agents. The derivatives with good reverse transcriptase inhibition properties belong generally to the 2',3'-dideoxy-3'-substituted family.[1] For example, one of the best anti HIV agent today is the 2',3'-didehydro-2',3'-dideoxy-thymidine (d_4T).[2] On the other hand, fluorinated derivatives often exhibit enhanced activity owing to the specific properties of fluorine atom or of the fluorinated group.[3] For example, 3'-fluorodeoxythymidine was reported to have a higher efficiency than AZT as anti-HIV.[4] Very few trifluoromethylnucleosides have been described until now.[5] We recently reported the synthesis of 3-deoxy-3-*C*-trifluoromethyl-D-ribose.[6] We report in this paper its coupling with thymine and uracile and the derivatisation of the corresponding nucleosides toward the 2',3'-dideoxy analogues. Owing to the high electron withdrawing power of a trifluoromethyl group, we have also considered the 2',3'-didehydroanalogue, where the vinylic trifluoromethyl group was able to stabilize the glycosydic junction. The results of anti-viral assessment of these dideoxy trifluoromethyl derivatives are also reported.

3-Deoxy-1,2-*O*-isopropylidene-3-*C*-trifluoromethyl-α-D-ribofuranose **1** was obtained from diacetone-D-glucose as described earlier.[6] The last step of this preparation involves an oxidative cleavage of the C-5-C-6 bond. Taking into account a recently reported improvement of the sequence deprotection of the 5,6-*O*-isopropylidene-oxidative cleavage-reduction of the carbonyl group which can be carried out efficiently in a one-pot process,[7] the synthesis of **1** can be accomplished with an overall yield of about 70 % from diacetone-D-glucose. Compound **1** was converted into the corresponding tri-*O*-acetyl derivative according to the reaction sequence described in Scheme 1. To preserve the furanose structure, an acetylation with acetic anhydride-pyridine gave compound **2** which was hydrolysed with 80 % aqueous trifluoroacetic acid. The resulting crude compound was acetylated with an excess of acetic anhydride in pyridine in the presence of a catalytic amount of dimethylaminopyridine to yield quantitatively the peracetylated derivative **3** (α/β = 5/95). The overall yield of the three steps is 84 %.



(i) ref 5. (ii) 1.4 eq. pyridine, 1.2 eq. Ac_2O, CH_2Cl_2, 0°C, 18 h.
(iii) 1/ CF_3COOH 80%, r. t., 3 h.; 2/ Pyridine, Ac_2O, cat. DMAP, r. t., 2 h.

Scheme 1



(i) Et_3N, TMSCl, benzène, Δ□
(ii) HMDS, pyridine, Δ
(iii) **3**, TMSOTf, CH_3CN, r.t.
(iv) 1/ NaOMe, MeOH; 2/ IRN 77 H^+

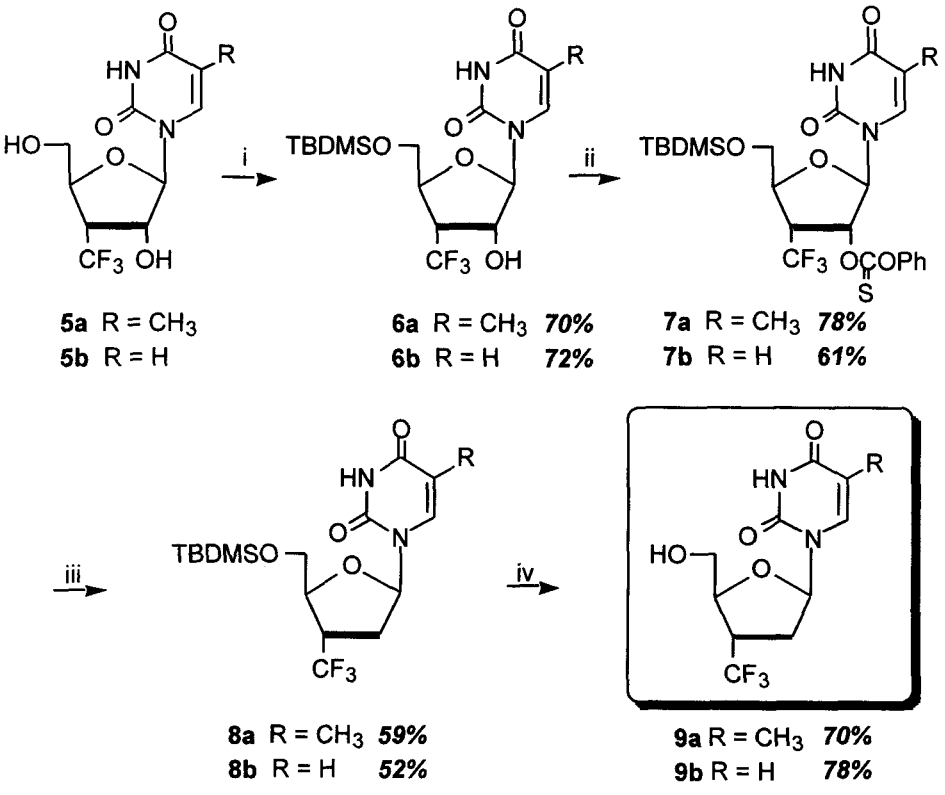
iv

4a R^1 = Me, R^2 = OAc **95 %**
4b R^1 = H, R^2 = OAc **95 %**
5a R^1 = Me, R^2 = OH **91 %**
5b R^1 = H, R^2 = OH **76 %**

Scheme 2

The Vorbrüggen method was used for nucleosides formation.[8] Silylation of the bases and coupling with **3** were performed in essentially quantitative yield following the procedure described by Johnson et al.[5b] (Scheme 2). The di-*O*-acetyl nucleosides **4a** (thymine derivative) and **4b** (uracile derivative) were deacetylated by treatment with sodium methanolate and then with a weakly acidic resin,[9] to give the nucleosides **5a** and **5b** with 91 and 76 % yield, respectively.

The synthesis of the dideoxy derivatives from compounds **5** is depicted in Scheme 3. Protection of the hydroxyl at C-5 as a TBDMS ether gave compounds **6** whose radical deoxygenation at C-2 was performed via the thionocarbonates **7**.[10] The deoxygenated compounds **8** were deprotected with *n*-tetrabutylammonium fluoride to give the target 2',3'-dideoxy-3'-*C*-trifluoromethyl thymidine **9a** and uridine **9b**. Compound **9a** had previously been synthesized by a completely different strategy,



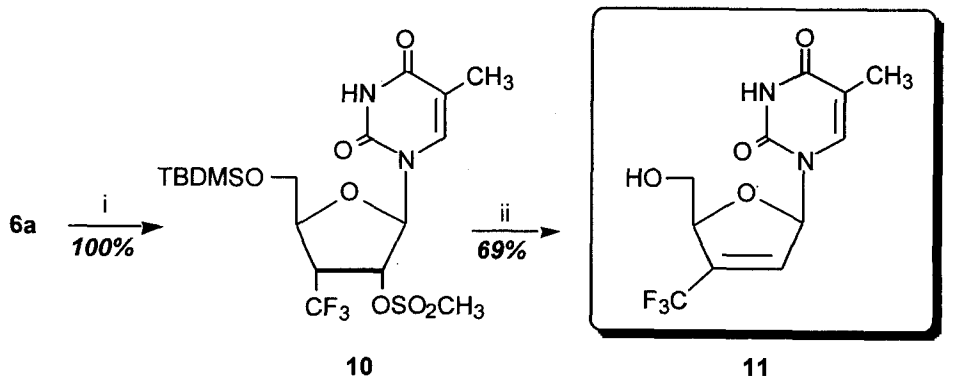
(i) TBDMSCl, pyridine, cat. DMAP, CH_2Cl_2, 0°C to r.t. (ii) PhOCSCl, cat. DMAP, CH_3CN, r.t. (iii) Bu_3SnH, AIBN, toluene, 100°C. (iv) TBAF, THF-H_2O, r.t.

Scheme 3

starting from protected 2',3'-dideoxy-3'-*C*-trifluoromethyl-D-ribose, itself being synthesized in twelve steps from 4,4,4-trifluoromethylbutane-1,3-diol.[5a] Our strategy is advantageous owing to the starting material (diacetone D-glucose) and the effective synthesis of the intermediate 3-*C*-trifluoromethyl-D-ribose **1**. Moreover, the base coupling prior to deoxygenation, with subsequent easy and classical reactions allowed a completely stereoselective access to the β-derivatives.

The didehydro derivative **11** was prepared as described in Scheme 4, by a sequence similar to the one recently reported for the synthesis of d_4T from thymidine,[11] except for the last elimination step. The silyl protected compound **6a** was converted quantitatively into the 3'-mesyloxy analogue **10**. Elimination using potassium *tert*-butylate, as described for d_4T, failed, leading to the decomposition of the product. This elimination step was performed smoothly with *n*-tetrabutylammonium fluoride which induces desilylation and subsequent elimination,[12] leading to 3'-*C*-trifluoromethyl d_4T **11**.

Compounds **9a**, **9b**, and **11** were tested against various viruses: HIV-1, Herpes simplex virus-1 (HSV1), Human cytomegalovirus (CMV), vaccine and coxsackie B4 (Cox-B4) in human MRC 5 cells.[13] The cytotoxicity of all the trifluoromethylated nucleosides was assessed by a MTT test. Activity against HIV-1 was assessed in two different cellular systems (CEM-SS cells, MT4 cells). The results, reported in Table 1, indicate a poor or no activity for any of the compounds assessed, at non toxic



(i) CH_3SO_2Cl, pyridine, CH_2Cl_2, 0°C to r.t. (ii) TBAF, THF, 50°C.

Scheme 4

Table 1. Results of the anti-HIV activity assessment. [a]

	HIV 1 Lai / CEM-SS		HIV 1 III B / MT4	
	IC 50 (μM)[b]	CC 50 (μM)[c]	IC 50 (μM)[b]	CC 50 (μM)[c]
AZT	$2.4 \pm 1.2\ 10^{-3}$		$1.65 \pm 0.2\ 10^{-2}$	
9a	32.5 ± 31	79 ± 1	> 100	23.5 ± 8
9b	> 100	> 100	> 100	40 ± 19
11	> 100	> 100	> 100	69.5 ± 9

a/ values are expressed as mean ± SD (standard deviation) of two experiments.
b/ 50% inhibitory concentration or concentration required to inhibit the replication of HIV1 by 50%.
c/ 50% cytotoxic concentration or concentration required to reduce the viability of uninfected cells by 50%

concentrations. Compounds **9a**, **9b** and **11** are ineffective on replication of HSV-1, CMV, vaccine and Cox-B4 viruses.

EXPERIMENTAL SECTION

General methods: synthesis and characterization. All reactions were performed under a constant flow of dry argon. Toluene and benzene were dried over CaH_2 and then distilled directly before use. Commercial dichloromethane (Fluka puriss) and acetonitrile (SDS synthesis grade) were used without further purification. Merck silica gel F_{254} (0.2 nm) was used for TLC plates, detection being carried out by spraying with an alcoholic solution of phosphomolybdic acid, followed by heating. Flash column chromatography was performed on silica gel Merck Art. 9385 Kieselgel 60 (0.04-0.063 μm). Melting points were determined with a Buchi apparatus. IR spectra were recorded with an IR^{TM} plus MIDAC spectrophotometer and are expressed in cm^{-1}. NMR spectra were recorded on a Brücker AC 250 spectrometer (250 MHz for ^1H, 62.5 MHz for ^{13}C and 235.36 MHz for ^{19}F). Chemical shifts are expressed in parts per million from TMS (^1H and ^{13}C) or $CFCl_3$ as internal reference. Coupling constants are in Hz and splitting pattern abbreviations are : s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Optical rotations were determined with a Perkin-Elmer 241 polarimeter. Elemental analyses were performed with a Perkin-Elmer CHN 2400 apparatus. Mass spectra were recorded on a Fison VG Autospec spectrometer.

General methods: biological assays. The inhibitory properties of the compounds were evaluated according to previously published procedures (HIV-1[14], other viruses[15]). The effect of each compound on cell metabolism was tested on uninfected CEM-SS, MT4 and MRC5 cells.[16]

5-*O*-Acetyl-3-deoxy-1,2-*O*-isopropylidene-3-*C*-trifluoromethyl-α-D-ribofuranose (2). To a solution of **1** (3.11 g, 12.8 mmol) in CH_2Cl_2 (15 mL) was added, at 0°C, pyridine (1.87 mL, 20.5 mmol) and acetic anhydride (1.36 mL, 16.0 mmol). After stirring at room temperature (18 h), aqueous NH_4Cl was added. The aqueous solution was extracted twice with CH_2Cl_2 and the organic layer was dried over $MgSO_4$, filtered and evaporated. After flash chromatography (petroleum ether/AcOEt 9/1), compound **2** was obtained (3.23 g, 90%) as a colorless solid. m.p. 46°C; $[\alpha]^{20}_D$ + 41.3 (*c* 0.8, $CHCl_3$); IR (KBr): 2997, 2947, 1775, 1391, 1228, 1028, 688, MS (CI) m/z: 285 (M+1, 24); 284 (12); 269 (100); 227 (79); 167 (69); 149 (68); ^1H NMR ($CDCl_3$) δ: 1.35 and 1.55 (2 x (s, 3H, CH_3)); 2.08 (s, 3H, $COCH_3$); 2.75 (ddq, 1H, $J_{3,4}$ = 10.3 Hz, $J_{3,F}$ = 8.6 Hz, $J_{3,2}$ = 4.9 Hz, H-3); 4.11(dd, 1H, $J_{5,5'}$ = 12.2 Hz, $J_{5,4}$ = 4.6 Hz, H-5); 4.46 (dd, 1H, $J_{5',5}$ = 12.2 Hz, $J_{5',4}$ = 2.6 Hz, H-5'); 4.53 (ddd, 1H, $J_{4,3}$ = 10.3 Hz, $J_{4,5}$ = 4.6 Hz, $J_{4,5'}$ = 2.6 Hz, H-4); 4.86 (dd, 1H, $J_{2,3}$ = 4.9 Hz, $J_{2,1}$ = 3.8 Hz, H-2); 5.87 (d, 1H, $J_{1,2}$ = 3.8 Hz, H-1); ^{13}C NMR ($CDCl_3$) δ: 20.6 and 26.4 (2 x CH_3); 48.6 (q, $^2J_{C,F}$ = 27.7 Hz, C-3); 60.6 (C-5); 74.3 (C-4); 78.2 (C-2); 104.8 (C-1); 113.3 (Cq isopropylidene); 124.0 (q, $^2J_{C,F}$ = 278.0 Hz, CF_3); 170.3 (CO); ^{19}F NMR ($CDCl_3$) δ: -62.51 (d, 3F, $J_{F,H}$ = 8.6 Hz, CF_3). Anal. calcd for $C_{11}H_{15}O_5F_3$ (284.23): C, 46.48; H, 5.32. Found: C, 46.28; H, 5.14.

1,2,5-Tri-*O*-acetyl-3-deoxy-3-*C*-trifluoromethyl-α,β-D-ribofuranose (3). A solution of **2** (2.2 g, 7.75 mmol) in 80% aqueous trifluoroacetic acid (20 mL) was stirred for 3 h. Trifluoroacetic acid was removed under vacuo, and then co-evapored with toluene (2 x 10 mL). To the crude product obtained was added pyridine (53 mL), DMAP (100 mg) and acetic anhydride (10 mL, 106 mmol). The reaction mixture was stirred for 2 h and pyridine was removed under vacuo and co-evapored with toluene. The residue diluted in diethyl ether (50 mL) was washed with H_2O. The organic solution was dried over $MgSO_4$, filtered and the solvent evaporated to give crude **3**. Flash chromatography (petroleum ether/EtOAc 4/1) gave **3** (**3**α + **3**β = 2.38 g, 93 %, α/β = 5/95). IR (KBr): 3015, 2947, 1747, 1379, 1267, 1028, 864; MS (CI) m/z: 285 (5); 269 (100); 255 (12); 213 (32); 183 (29); 166 (24); 149 (25); 136 (22); β anomer: m.p. 85°C; ^1H NMR ($CDCl_3$) δ: 2.08, 2.09 (2 x (s, 3H, $COCH_3$)); 2.12 (s, 3H, $COCH_3$); 3.20 (ddq, 1H, $J_{3,4}$ = 8.7 Hz, $J_{3,F}$ = 7.6 Hz, $J_{3,2}$ = 5.3 Hz, H-3); 4.16 (dd, 1H, $J_{5,5'}$ = 12.2 Hz, $J_{5,4}$ = 5.3 Hz, H-

5); 4.35 (dd, 1H, $J_{5',5}$ = 12.2 Hz, $J_{5',4}$ = 3.4 Hz, H-5'); 4.71 (ddd, 1H, $J_{4,3}$ = 8.7 Hz, $J_{4,5}$ = 5.3 Hz, $J_{4,5'}$ = 3.4 Hz, H-4); 5.49 (d, $J_{2,3}$ = 5.3 Hz, H-2); 6.11 (s, 1H, H-1); ^{13}C NMR ($CDCl_3$) δ: 20.2 and 20.3 (2 x CH_3); 20.6 (CH_3); 45.5 (q, $^2J_{C,F}$ = 29.5 Hz, C-3); 64.1 (C-5); 74.1 (C-4); 76.2 (C-2); 98.1 (C-1); 124.0 (q, $^2J_{C,F}$ = 277.6 Hz, CF_3); 168.2 (CO); 168.8 (CO); 169.9 (CO); ^{19}F NMR ($CDCl_3$) δ: -63.64 (d, 3F, $J_{F,H}$ = 7.6 Hz, CF_3); α anomer: oil. ^{13}C NMR ($CDCl_3$) δ: 43.2 (q, $^2J_{C,F}$ = 27.6 Hz, C-3); ^{19}F NMR ($CDCl_3$) δ: -65.59 (d, 3F, $J_{F,H}$ = 7.8 Hz, CF_3).

1-(2,5-Di-*O*-acetyl-3-deoxy-3-*C*-trifluoromethyl-β-D-ribofuranosyl)-thymine (4a). The reaction was carried out according to Johnson et al.[5b] from compound **3** (0.55 g, 1.67 mmol). The intermediate silylated base was obtained by treatment of thymine by TMS-Cl and triethylamine in benzene. Stirring was continued for 12 h. After treatment and flash chromatography (petroleum ether/EtOAc 3/2) **4a** was obtained (0.63 g, 95%). m.p. 63-65°C; IR (KBr): 3211, 3086, 2835, 1755, 1693, 1379, 1228, 1178, 1053; ^{1}H NMR ($CDCl_3$) δ: 1.92 (s, 3H, CH_3); 2.13 (s, 3H, $COCH_3$); 2.14 (s, 3H, $COCH_3$); 3.53 (m, 1H, H-3'); 4.26 (dd, 1H, $J_{5',5''}$ = 12.6 Hz, $J_{5',4'}$ = 4.6 Hz, H-5'); 4.49 (dd, 1H, $J_{5'',5'}$ = 12.6 Hz, $J_{5'',4'}$ = 2.3 Hz, H-5"); 4.59 (ddd, 1H, $J_{4',3'}$ = 7.6 Hz, $J_{4',5'}$ = 4.6 Hz, $J_{4',5''}$ = 2.3 Hz, H-4'); 5.63-5.68 (m, 2H, H-1', H-2'); 7.07 (d, 1H, J = 1.1 Hz, H-6); 9.38 (s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ: 12.4 (CH_3); 20.4 and 20.6 (2 x $COCH_3$); 45.3 (q, $^2J_{C,F}$ = 27.6 Hz, C-3'); 63.5 (C-5'); 73.5 (C-4', C-2'); 92.0 (C-1'); 111.7 (C-5); 124.3 (q, $^2J_{C,F}$ = 279.6 Hz, CF_3); 136.6 (C-6); 149.9 (C-2); 163.5 (C-4); 169.8 (CO); 170.1 (CO); ^{19}F NMR ($CDCl_3$) δ: -64.54 (d, 3F, $J_{F,H}$ = 9.1 Hz, CF_3).

1-(2,5-Di-*O*-acetyl-3-deoxy-3-*C*-trifluoromethyl-β-D-ribofuranosyl)- uracile (4b). The reaction was carried out according to Johnson et al.[5b] from compound **3** (0.55 g, 1.67 mmol). The intermediate silylated base was obtained by treatment of uracile by hexamethyldisilazane and pyridine. Stirring was continued for 12 h. After treatment and flash chromatography (petroleum ether/EtOAc 1/1) compound **4b** was obtained (0.71 g, 95%). m.p. 53-55°C; IR (KBr): 3223, 3098, 1755, 1705, 1390, 1228, 1053, 814; MS (CI) m/z: 381 (M+1, 47); 380 ($M^{+\circ}$, 25); 321 (9); 270 (100); 149 (17); 113 (20); ^{1}H NMR ($CDCl_3$) δ: 2.12 and 2.15 (2 x (s, 3H, $COCH_3$)); 3.50 (ddq, 1H, $J_{3',F}$ = 8.7 Hz, $J_{3',4'}$ = 7.6 Hz, $J_{3',2'}$ = 5.3 Hz, H-3'); 4.26 (dd, 1H, $J_{5',5''}$ = 12.6 Hz, $J_{5',4'}$ = 4.6 Hz, H-5'); 4.49 (dd, 1H, $J_{5'',5'}$ = 12.6 Hz, $J_{5'',4'}$ = 2.6 Hz, H-5"); 4.61 (ddd, 1H, $J_{4',3'}$ = 7.6 Hz, $J_{4',5'}$ = 4.6 Hz, $J_{4',5''}$ = 2.6 Hz, H-4'); 5.61-5.66 (m, 2H, H-1', H-2'); 5.76 (d, 1H, $J_{5,6}$ = 8.0 Hz, H-5); 7.26 (d, 1H, $J_{6,5}$ = 8.0 Hz, H-6); 8.62 (s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ: 20.4 and 20.6 (2 x ($COCH_3$)); 45.3 (q, $^2J_{C,F}$ = 27.6 Hz, C-3'); 63.5 (C-5'); 73.4 (C-4'); 76.7 (C-2'); 92.4 (C-1'); 103.1 (C-5); 124.2 (q, $^2J_{C,F}$ = 277.6 Hz, CF_3); 140.9 (C-6);

149.9 (C-2); 163.4 (C-4); 169.7 (CO); 170.1 (CO); ^{19}F NMR ($CDCl_3$) δ: -64.37 (d, 3F, $J_{F,H}$ = 8.7 Hz, CF_3).

1-(3-Deoxy-3-*C*-trifluoromethyl-β-D-ribofuranosyl)-thymine (5a). To a solution of **4a** (0.56 g, 1.4 mmol) in methanol (6 mL) was added 1.15 equivalent of sodium methanolate (87 mg, 1.6 mmol) and the reaction mixture was stirred for 12 h at room temperature. Then Amberlite IRN-77 resin (H^+, 0.56 g) was added and slowly stirred for 15 mn. The resin was filtered and the solvent evaporated under vacuo. The crude product was purified by flash chromatography (petroleum ether/EtOAc 3/2) to give **5a** as a white solid (0.4 g, 91%). m.p. 70°C; IR (KBr): 3398, 3323, 3061, 1693, 1404, 1265, 1128; ^1H NMR ($CDCl_3$) δ: 1.80 (d, 3H, J = 1.1 Hz, CH_3); 3.31 (m, 1H, H-3'); 3.75 (ddd, 1H, $J_{5',5}$ = 12.2 Hz, $J_{5',4'}$ = 5.3 Hz, $J_{5',OH}$ = 2.7 Hz, H-5'); 4.06 (m, 1H, H-5"); 4.51 (m, 2H, H-4', OH); 4.78 (ddd, 1H, $J_{2',3'}$ = 6.2 Hz, $J_{2',OH}$ = 5.3 Hz, $J_{2',1'}$ = 3.4 Hz, H-2'); 5.28 (d, 1H, $J_{OH,2'}$ = 5.3 Hz, OH); 5.85 (d, 1H, $J_{1',2'}$ = 3.4 Hz, H-1'); 7.91 (q, 1H, J = 1.1 Hz, H-6); 10.06 (s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ: 12.5 (CH_3); 45.6 (q, $^2J_{C,F}$ = 25.6 Hz, C-3'); 61.9 (C-5'); 75.1 (C-4'); 75.1 (C-2'); 92.3 (C-1'); 110.4 (C-5); 126.6 (q, $^2J_{C,F}$ = 277.6 Hz, CF_3); 137.1 (C-6); 151.6 (C-2); 164.5 (C-4); ^{19}F NMR ($CDCl_3$) δ: -62.57 (d, 3F, $J_{F,H}$ = 9.6 Hz, CF_3). MS (CI) m/z: 311 (M+1, 17); 206 (13); 155 (19); 127 (100); 113 (33); HRMS calcd for $C_{11}H_{13}O_5N_2F_3$: 310.0773. Found: 310.0776.

1-(3-Deoxy-3-*C*-trifluoromethyl-β-D-ribofuranosyl)-uracile (5b). Product **5b** was obtained by a similar method, starting from **4b** (0.6 g, 1.6 mmol), as a white solid (0.35 g, 76%). IR (KBr): 3412, 3098, 1693, 1400, 1265, 1140; ^1H NMR (CD_3COCD_3) δ: 3.31 (m, 1H, H-3'); 3.76 (ddd, 1H, $J_{5',5"}$ = 12.6 Hz, $J_{5',4'}$ = 5.3 Hz, $J_{5',OH}$ = 3.0 Hz, H-5'); 4.07 (m, 1H, H-5"); 4.55 (m, 2H, H-4', OH); 4.78 (ddd, 1H, $J_{2',3'}$ = 8.8 Hz, $J_{2',OH}$ = 5.0 Hz, $J_{2',1'}$ = 3.0 Hz, H-2'); 5.35 (d, 1H, $J_{OH,2'}$ = 5.0 Hz, OH); 5.58 (d, 1H, J = 8.0 Hz, H-5); 5.84 (d, 1H, $J_{1',2'}$ = 3.0 Hz, H-1'); 8.08 (d, 1H, J = 8.0 Hz, H-6); 10.20 (s, 1H, NH); ^{13}C NMR (CD_3COCD_3) δ: 45.6 (q, $^2J_{C,F}$ = 25.6 Hz, C-3'); 61.9 (C-5'); 75.2 (C-4'); 80.5 (C-2'); 92.5 (C-1'); 102.2 (C-5); 126.6 (q, $^2J_{C,F}$ = 277.6 Hz, CF_3); 141.3 (C-6); 151.6 (C-2); 163.9 (C-4); ^{19}F NMR (CD_3COCD_3) δ: -62.36 (d, 3F, $J_{F,H}$ = 9.5 Hz, CF_3). MS (EI) m/z: 296 ($M^{+\circ}$, 8); 278 (49); 247 (26); 204 (28); 185 (30); 165 (80); 113 (100).

1-(5-*O*-*tert*-Butyldimethylsilyl-3-deoxy-3-*C*-trifluoromethyl-β-D-ribofuranosyl)-thymine (6a). To compound **5a** (0.81 g, 2.6 mmol) in CH_2Cl_2 (10 mL) was added, at 0°C, pyridine (0.42 mL, 5.2 mmol), DMAP (31 mg, 0.26 mmol) and *tert*-butyldimethylsilyl chloride (0.59 g, 3.9 mmol). The reaction mixture was stirred for 4 h

at room temperature and washed with water (2x10 mL). The aqueous layer was extracted with CH_2Cl_2 (2x5 mL). The organic layer was dried over $MgSO_4$, filtered and the solvent was evaporated to give the crude product which was flash chromatographed (petroleum ether/EtOAc 3/2). Compound **6a** was obtained as a white solid (0.78 g, 70%). m.p. 160°C; $[\alpha]^{25}_D$ - 5.0 (*c* 0.43, $CHCl_3$); IR (KBr): 3425, 3186, 2936, 2860, 1705, 1479, 1404, 1265, 1128, 839; ^{1}H NMR ($CDCl_3$) δ: 0.14, 0.15 (2 x (s, 3H, $SiCH_3$)); 0.95 (s, 9H, $(CH_3)_3$); 1.90 (d, 3H, J = 1.1 Hz, CH_3); 3.02 (m, 1H, H-3'); 3.82 (dd, 1H, $J_{5',5''}$ = 12.2 Hz, $J_{5',4'}$ = 1.9 Hz, H-5'); 4.20 (d, 1H, $J_{5'',5'}$ = 12.2 Hz, H-5''); 4.67 (m, 2H, H-2', H-4'); 5.10 (s, 1H, OH); 5.78 (s, 1H, H-1'); 7.69 (q, 1H, J = 1.1 Hz, H-6); 10.40 (s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ: -5.3 ($SiCH_3$); -5.6 ($SiCH_3$); 12.6 (CH_3); 18.6 (Cq *tert*-butyl); 26.0 (*tert*-butyl); 43.9 (q, $^2J_{C,F}$ = 25.6 Hz, C-3'); 61.8 (C-5'); 75.4 (C-2'); 80.2 (C-4'); 92.0 (C-1'); 110.4 (C-5); 124.8 (q, $J_{C,F}$ = 277.6 Hz, CF_3); 139.5 (C-6); 151.1 (C-2); 164.4 (C-4); ^{19}F NMR ($CDCl_3$) δ: -62.80 (d, 3F, $J_{F,H}$ = 9.0 Hz, CF_3); MS (EI) m/z: 426 (M+2, 2); 368 (62); 241 (100); 183 (55); 149 (21); 127 (41); 117 (67). Anal. calcd for $C_{17}H_{27}O_5N_2F_3Si$ (424.28): C, 48.12; H, 6.41; N, 6.60. Found: C, 48.23; H, 6.26; N, 6.24.

1-(5-*O*-*tert*-Butyldimethylsilyl-3-deoxy-3-*C*-trifluoromethyl-β-D-ribofuranosyl)-uracile (6b). Compound **6b** was similarly obtained from **5b** (340 mg, 1.15 mmol) in 72% yield (0.34 g) as a white solid. m.p. 185°C; $[\alpha]^{25}_D$ + 9.8 (*c* 0.47, $CHCl_3$); IR (KBr): 3425, 3173, 2936, 2680, 1705, 1466, 1265, 1140, 839; ^{1}H NMR ($CDCl_3$) δ: 0.13, 0.14 (2 x (s, 3H, $SiCH_3$)); 0.94 (s, 9H, $(CH_3)_3$); 3.04 (m, 1H, H-3'); 3.82 (d, 1H, $J_{5',5''}$ = 11.8 Hz, H-5'); 4.22 (d, 1H, $J_{5'',5'}$ = 11.8 Hz, H-5''); 4.69 (m, 2H, H-2', H-4'); 5.37 (d, 1H, J = 3.4 Hz, OH); 5.65 (d, 1H, $J_{5,6}$ = 8.0 Hz, H-5); 5.80 (s, 1H, H-1'); 8.18 (d, 1H, $J_{6,5}$ = 8.0 Hz, H-6); 10.74 (s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ: -5.7 (2 x ($SiCH_3$)); 18.3 (Cq *tert*-butyl); 25.8 (*tert*-butyl); 43.5 (q, $^2J_{C,F}$ = 27.6 Hz, C-3'); 61.4 (C-5'); 75.6 (C-2'); 80.5 (C-4'); 92.3 (C-1'); 102.0 (C-5); 124.7 (q, $J_{C,F}$ = 277.6 Hz, CF_3); 139.9 (C-6); 151.1 (C-2); 163.8 (C-4); ^{19}F NMR ($CDCl_3$) δ: -62.70 (d, 3F, $J_{F,H}$ = 8.3 Hz, CF_3); MS (CI) m/z: 411 (M+1, 100); 353 (34); 299 (11); 241 (56); 169 (14); 113 (22). Anal. calcd for $C_{16}H_{25}O_5N_2F_3Si$ (410.47): C, 46.81; H, 6.13; N, 6.82. Found: C, 46.57; H, 6.26; N, 6.58.

1-(5-*O*-*tert*-Butyldimethylsilyl-3-deoxy-2-*O*-(phenoxy)-thionocarbonyl-3-*C*-trifluoromethyl-β-D-ribofuranosyl)-thymine (7a). To a solution of **6a** (220 mg, 0.53 mmol) in CH_3CN (10 mL) was added DMAP (320 mg, 2.65 mmol) and phenylchlorothionocarbonate (0.11 mL, 0.82 mmol). The reaction mixture was stirred for 12 h. at room temperature and the solvent was evaporated. The crude product was

purified by flash chromatography (petroleum ether/EtOAc 4/1) to give **7a** as an oil (231 mg, 78%). ^{1}H NMR ($CDCl_3$) δ: 0.11 (s, 6H, $Si(CH_3)_2$); 0.92 (s, 9H, $(CH_3)_3$); 1.90 (d, 1H, J = 1.1 Hz, CH_3); 3.60 (m, 1H, H-3'); 3.71 (dd, 1H, $J_{5',5''}$ = 11.4 Hz, $J_{5',4'}$ = 2.3 Hz, H-5'); 4.01 (d, 1H, $J_{5'',5'}$ = 11.4 Hz, H-5''); 4.49 (m, 1H, H-4'); 5.99 (dd, 1H, $J_{2',3'}$ = 8.0 Hz, $J_{2',1'}$ = 5.7 Hz, H-2'); 6.25 (d, 1H, $J_{1',2'}$ = 5.7 Hz, H-1'); 6.81-7.38 (m, 6H, H-6, Ph); 9.53 (s, 1H, NH).

1-(5-*O*-*tert*-Butyldimethylsilyl-3-deoxy-2-*O*-(phenoxy)-thionocarbonyl-3-*C*-trifluoromethyl-β-D-ribofuranosyl)-uracile (7b). Similarly, **6b** (160 mg, 0.39 mmol) was transformed into **7b** (oil, 130 mg, 61%). ^{1}H NMR ($CDCl_3$) δ: 0.14 (s, 6H, $Si(CH_3)_2$); 0.95 (s, 9H, $(CH_3)_3$); 3.48 (m, 1H, H-3'); 3.68 (dd, 1H, $J_{5',5''}$ = 11.8 Hz, $J_{5',4'}$ = 2.3 Hz, H-5'); 4.00 (d, 1H, $J_{5'',5'}$ = 11.8 Hz, H-5''); 4.50 (m, 1H, H-4'); 5.67 (d, 1H, J = 8.4 Hz, H-5); 5.99 (dd, 1H, $J_{2',3'}$ = 7.2 Hz, $J_{2',1'}$ = 5.3 Hz, H-2'); 6.21 (d, 1H, $J_{1',2'}$ = 5.3 Hz, H-1'); 7.19-7.37 (m, 5H, Ph); 7.69 (d, 1H, J = 8.4 Hz, H-6); 8.98 (s, 1H, NH).

1-(5-*O*-*tert*-Butyldimethylsilyl-2,3-dideoxy-3-*C*-trifluoromethyl-β-D-*erythro*-pentofuranosyl)-thymine (8a). To a solution of **7a** (231 mg, 0.41 mmol) in anhydrous toluene (15 mL) was added *n*-tributyltin hydride (*n*-Bu_3SnH, 0.22 mL, 0.84 mmol) and AIBN (36 mg, 0.22 mmol). The mixture was refluxed for 3 h and toluene was evaporated. The crude product was purified by flash chromatography with a mixture silica gel/florisil 1/1 to eliminate tin salts (petroleum ether/EtOAc 4/1). The deoxygenated product **8a** was obtained as a syrup (120 mg, 59%). $[\alpha]^{24}_D$ + 2.2 (*c* 0.45, $CHCl_3$); IR (Film): 3186, 3061, 2936, 2860, 1693, 1466, 1265, 1128, 827; ^{1}H NMR ($CDCl_3$) δ: 0.14 (s, 6H, $Si(CH_3)_2$); 0.95 (s, 9H, $(CH_3)_3$); 1.93 (d, 3H, J = 1.1 Hz, CH_3); 2.15 (ddd, 1H, $J_{2'\alpha,2'\beta}$ = 14.1 Hz, $J_{2',3'}$ = 9.9 Hz, $J_{2',1'}$ = 6.5 Hz, H-2'α); 2.62 (ddd, 1H, $J_{2'\alpha,2'\beta}$ = 14.1 Hz, $J_{2',1'}$ = 6.5 Hz, $J_{2',3'}$ = 5.0 Hz, H-2'β); 3.15 (dddq, 1H, $J_{3',2'}$ = 9.9 Hz, $J_{3',F}$ = 9.3 Hz, $J_{3',4'}$ = 6.1 Hz, $J_{3',2'}$ = 5.3 Hz, H-3'); 3.75 (dd, 1H, $J_{5',5''}$ = 11.8 Hz, $J_{5',4'}$ = 1.9 Hz, H-5'); 4.04 (dd, 1H, $J_{5'',5'}$ = 11.8 Hz, $J_{5'',4'}$ = 1.9 Hz, H-5''); 4.27 (dt, 1H, $J_{4',3'}$ = 6.1 Hz, $J_{4',5'}$ = $J_{4',5''}$ = 1.9 Hz, H-4'); 6.16 (t, 1H, $J_{1',2'\alpha}$ = $J_{1',2'\beta}$ = 6.5 Hz, H-1'); 7.46 (d, 1H, J = 1.1 Hz, H-6); 8.64 (s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ: -5.5 ($Si\underline{C}H_3$); -5.4 ($Si\underline{C}H_3$); 12.5 (CH_3); 17.5 (Cq *tert*-butyl); 25.9 (*tert*-butyl); 32.9 (C-2'); 42.5 (q, $^2J_{C,F}$ = 27.6 Hz, C-3'); 63.4 (C-5'); 79.4 (C-4'); 84.8 (C-1'); 111.0 (C-5); 126.5 (q, $J_{C,F}$ = 277.6 Hz, CF_3); 134.8 (C-6); 150.1 (C-2); 163.5 (C-4); ^{19}F NMR ($CDCl_3$) δ: -70.74 (d, 3F, $J_{F,H}$ = 9.3 Hz, CF_3); MS (CI) m/z: 409 (M+1, 4); 351 (99); 283 (41); 225 (100); 215 (22); 183 (42); 127 (32); 107 (31).

1-(5-*O*-*tert*-Butyldimethylsilyl-2,3-dideoxy-3-*C*-trifluoromethyl-β-D-*erythro*-pentofuranosyl)-uracile (8b). A similar procedure was applied to **7b** (130 mg,

0.23 mmol) to give **8b** (80 mg, 52%) as a paste. $[\alpha]^{24}_D$ + 18.2 (*c* 0.19, $CHCl_3$); IR ($CHCl_3$): 3387, 3011, 1693, 1265, 1140, 788; ^1H NMR ($CDCl_3$) δ: 0.09 and 0.13 (2 x (s, 3H, $SiCH_3$)); 0.94 (s, 9H, $(CH_3)_3$); 2.24 (ddd, 1H, $J_{2'\alpha,2'\beta}$ = 14.1 Hz, $J_{2',3'}$ = 9.1 Hz, $J_{2',1'}$ = 5.0 Hz, H-2'α); 2.68 (dt, 1H, $J_{2'\alpha,2'\beta}$ = 14.1 Hz, $J_{2',1'}$ = $J_{2',3'}$ = 6.9 Hz, H-2'β); 3.15 (dtq, 1H, $J_{3',F}$ = 9.3 Hz, $J_{3',2'}$ = 9.1 Hz, $J_{3',2'}$ = $J_{3',4'}$ = 6.9 Hz, H-3'); 3.77 (dd, 1H, $J_{5',5''}$ = 11.8 Hz, $J_{5',4'}$ = 1.9 Hz, H-5'); 4.08 (dd, 1H, $J_{5'',5'}$ = 11.8 Hz, $J_{5'',4'}$ = 1.9 Hz, H-5''); 4.30 (dt, 1H, $J_{4',3'}$ = 6.9 Hz, $J_{4',5'}$ = $J_{4',5''}$ = 1.9 Hz, H-4'); 5.70 (d, 1H, $J_{5,6}$ = 8.0 Hz, H-5); 6.18 (dd, 1H, $J_{1',2'\beta}$ = 6.9 Hz, $J_{1',2'\alpha}$ = 5.0 Hz, H-1'); 7.94 (d, 1H, $J_{6,5}$ = 8.0 Hz, H-6); 8.80 (s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ: -5.7 ($SiCH_3$); -5.6 ($SiCH_3$); 18.3 (Cq *tert*-butyl); 25.8 (*tert*-butyl); 33.8 (C-2'); 41.8 (q, $^2J_{C,F}$ = 27.6 Hz, C-3'); 63.1 (C-5'); 80.4 (C-4'); 85.2 (C-1'); 102.3 (C-5); 126.2 (q, $J_{C,F}$ = 278.0 Hz, CF_3); 139.7 (C-6); 150.1 (C-2); 163.0 (C-4); ^{19}F NMR ($CDCl_3$) δ: -70.42 (d, 3F, $J_{F,H}$ = 9.3 Hz, CF_3).

1-(2,3-Dideoxy-3-*C*-trifluoromethyl-β-D-*erythro*-pentofuranosyl)-thymine (9a). To a solution of **8a** (100 mg, 0.24 mmol) in THF (5 mL) was added *n*-tetrabutyl ammonium fluoride (1M solution in THF, 0.24 mL, 0.24 mmol). The reaction mixture was stirred for 2 h. at room temperature and the solvent was evaporated under vacuo. The crude product was filtered over silica gel (petroleum ether/EtOAc 2/3) to give **9a** as a paste (50 mg, 70%). $[\alpha]^{24}_D$ + 17.2 (*c* 0.14, CH_3COCH_3); IR (CH_3COCH_3): 3524, 3399, 2961, 2922, 1755, 1454; ^1H NMR (CD_3OD) δ: 1.87 (d, 3H, J = 1.1 Hz, CH_3); 2.34 (ddd, 1H, $J_{2'\alpha,2'\beta}$ = 14.1 Hz, $J_{2',3'}$ = 9.1 Hz, $J_{2',1'}$ = 6.5 Hz, H-2'α); 2.55 (dt, 1H, $J_{2'\alpha,2'\beta}$ = 14.1 Hz, $J_{2',1'}$ = $J_{2',3'}$ = 6.5 Hz, H-2'β); 3.31 (m, 1H, H-3'); 3.68 (dd, 1H, $J_{5',5''}$ = 12.6 Hz, $J_{5',4'}$ = 3.0 Hz, H-5'); 3.90 (dd, 1H, $J_{5'',5'}$ = 12.6 Hz, $J_{5'',4'}$ = 2.7 Hz, H-5''); 4.22 (ddd, 1H, $J_{4',3'}$ = 6.1 Hz, $J_{4',5'}$ = 3.0 Hz, $J_{4',5''}$ = 2.7 Hz, H-4'); 6.13 (t, 1H, $J_{1',2'}$ = 6.5 Hz, H-1'); 7.83 (d, 1H, J = 1.1 Hz, H-6). ^1H NMR (CD_3COCD_3) δ: 1.87 (d, 3H, J = 1.1 Hz, CH_3); 2.41-2.63 (m, 2H, H-2'α; H-2'β); 3.35 (m, 1H, H-3'); 3.75 (d, 1H, $J_{5',5''}$ = 11.8 Hz, H-5'); 3.96 (d, 1H, $J_{5'',5'}$ = 11.8 Hz, H-5''); 4.27 (dt, 1H, $J_{4',3'}$ = 5.7 Hz, $J_{4',5'}$ = $J_{4',5''}$ = 3.0 Hz, H-4'); 4.48 (s, 1H, OH); 6.18 (dd, 1H, $J_{1',2'\alpha}$ = 6.8 Hz, $J_{1',2'\beta}$ = 6.5 Hz, H-1'); 7.79 (q, 1H, J = 1.1 Hz, H-6); 9.88 (s, 1H, NH); ^{13}C NMR (CD_3COCD_3) δ: 12.5 (CH_3); 32.7 (C-2'); 43.3 (q, $^2J_{C,F}$ = 27.5 Hz, C-3'); 63.0 (C-5'); 79.4 (C-4'); 84.8 (C-1'); 110.8 (C-5); 128.1 (q, $J_{C,F}$ = 277.6 Hz, CF_3); 136.9 (C-6); 151.3 (C-2); 164.2 (C-4); ^{19}F NMR (CD_3COCD_3) δ: -70.07 (d, 3F, $J_{F,H}$ = 9.7 Hz, CF_3); MS (CI) m/z: 294 ($M^{+\circ}$, 9); 263 (6); 215 (9); 180 (7); 169 (58); 151 (14); 126 (100); HRMS calcd for $C_{11}H_{13}O_4N_2F_3$: 294.0824. Found: 294.0827.

1-(2,3-Dideoxy-3-*C*-trifluoromethyl-β-D-*erythro*-pentofuranosyl)-uracile (9b). The same method applied to **8b** (70 mg, 0.17 mmol) gave **9b** (39 mg, 78%) as a white solid.

m.p. 183°C; IR (CH_3COCH_3): 3524, 3399, 2961, 2922, 1755; ^1H NMR (CD_3COCD_3) δ: 2.46 (ddd, 1H, $J_{2'\alpha,2'\beta}$ = 14.1 Hz, $J_{2',3'}$ = 9.5 Hz, $J_{2',1'}$ = 6.1 Hz, H-2'α); 2.61 (dt, 1H, $J_{2'\alpha,2'\beta}$ = 14.1 Hz, $J_{2',1'}$ = $J_{2',3'}$ = 6.1 Hz, H-2'β); 3.43 (dddq, 1H, $J_{3',F}$ = 9.8 Hz, $J_{3',2'}$ = 9.1 Hz, $J_{3',2'}$ = 6.1 Hz, $J_{3',4'}$ = 5.7 Hz, H-3'); 3.74 (dd, 1H, $J_{5',5''}$ = 12.2 Hz, $J_{5',4'}$ = 2.7 Hz, H-5'); 3.96 (dd, 1H, $J_{5'',5'}$ = 12.2 Hz, $J_{5'',4'}$ = 2.7 Hz, H-5''); 4.28 (dt, 1H, $J_{4',3'}$ = 5.7 Hz, $J_{4',5}$ = $J_{4',5''}$ = 2.7 Hz, H-4'); 4.50 (s, 1H, OH); 5.59 (d, 1H, $J_{5,6}$ = 8.0 Hz, H-5); 6.16 (t, 1H, $J_{1',2'}$ = 6.1 Hz, H-1'); 7.97 (d, 1H, $J_{6,5}$ = 8.0 Hz, H-6); 10.00 (s, 1H, NH); ^{13}C NMR (CD_3COCD_3) δ: 33.0 (C-2'); 43.2 (q, $^2J_{C,F}$ = 27.6 Hz, C-3'); 62.9 (C-5'); 80.8 (C-4'); 86.1 (C-1'); 102.6 (C-5); 128.0 (q, $J_{C,F}$ = 277.6 Hz, CF_3); 141.2 (C-6); 151.3 (C-2); 163.6 (C-4); ^{19}F NMR (CD_3COCD_3) δ: -69.73 (d, 3F, $J_{F,H}$ = 9.8 Hz, CF_3); HRMS calcd for $C_{10}H_{11}O_4N_2F_3$: 280.0668. Found: 280.0670.

1-(5-*O*-*tert*-Butyldimethylsilyl-3-deoxy-2-*O*-methanesulfonyl-3-*C*-trifluoromethyl-β-D-ribofuranosyl)-thymine (10). To a solution of **6a** (170 mg, 0.4 mmol) in CH_2Cl_2 (3 mL), at 0°C, was added pyridine (0.2 mL, 2.4 mmol) and methanesulfonyl chloride (0.1 mL, 1.2 mmol). The reaction mixture was stirred for 2 days at room temperature. Then, water was added and the aqueous layer was extracted with CH_2Cl_2 (2x5 mL). The organic layer was dried over $MgSO_4$, filtered and the solvent was evaporated. After purification by flash chromatography (petroleum ether/EtOAc 7/3), compound **10** was obtained as a syrup (195 mg, 100%). $[\alpha]^{22}_D$ + 17.4 (*c* 0.19, $CHCl_3$); IR (KBr): 3186, 3036, 2961, 2860, 1705, 1365, 1265, 1078, 839; ^1H NMR ($CDCl_3$) δ: 0.12 and 0.13 (2 x (s, 3H, $SiCH_3$)); 0.95 (s, 9H, $(CH_3)_3$); 1.92 (d, 3H, J = 1.1 Hz, CH_3); 3.21 (s, 3H, SO_2CH_3); 3.42 (m, 1H, H-3'); 3.79 (dd, 1H, $J_{5',5''}$ = 12.2 Hz, $J_{5',4'}$ = 2.6 Hz, H-5'); 4.12 (d, 1H, $J_{5'',5'}$ = 12.2 Hz, H-5''); 4.52 (m, 1H, H-4'); 5.46 (dd, 1H, $J_{2',3'}$ = 6.5 Hz, $J_{2',1'}$ = 3.0 Hz, H-2'); 5.92 (d, 1H, $J_{1',2'}$ = 3.0 Hz, H-1'); 7.39 (q, 1H, J = 1.1 Hz, H-6); 9.48 (s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ: -5.5 (2 x $Si\underline{C}H_3$); 12.5 (CH_3); 18.4 (Cq *tert*-butyl); 25.8 (*tert*-butyl); 38.8 ($SO_2\underline{C}H_3$); 44.1 (q, $^2J_{C,F}$ = 27.6 Hz, C-3'); 61.9 (C-5'); 79.6 (C-2' and C-4'); 89.9 (C-1'); 111.6 (C-5); 123.9 (q, $J_{C,F}$ = 279.6 Hz, CF_3); 135.0 (C-6); 150.6 (C-2); 163.8 (C-4); ^{19}F NMR ($CDCl_3$) δ: -63.56 (d, 3F, $J_{F,H}$ = 8.4 Hz, CF_3); MS (EI) m/z: 503 (M+1, trace); 487 (10); 445 (55); 349 (71); 183 (61); 153 (100); 137 (85); 117 (60).

1-(2,3-Dideoxy-3-*C*-trifluoromethyl-β-D-*glycero*-pent-2-enofuranosyl)-thymine (11). To a solution of **10** (159 mg, 0.31 mmol) in THF (6 mL) was added *n*-tetrabutylammonium fluoride (1M solution in THF, 0.31 mL, 0.31 mmol). The reaction mixture was stirred for 3 h at 50°C. The solvent was evaporated and the crude product was purified by flash chromatography (petroleum ether/EtOAc 1/1) to give **11** as a white solid (63 mg, 69%). m.p. 53-55°C; $[\alpha]^{23}_D$ + 4.6 (*c* 0.21, $CHCl_3$); IR ($CHCl_3$): 3624,

3387, 3022, 2961, 1693, 1466, 1265, 1140; ^{1}H NMR ($CDCl_3$) δ: 1.84 (d, 3H, J = 1.1 Hz, CH_3); 3.04 (s, 1H, OH); 3.91 (d, 1H, $J_{5',5''}$ = 12.6 Hz, H-5'); 3.91 (d, 1H, $J_{5'',5'}$ = 12.6 Hz, H-5''); 5.03 (m, 1H, H-4'); 6.43 (d, 1H, $J_{2',1'}$ = 1.9 Hz, H-2'); 7.07 (m, 1H, H-1'); 7.58 (d, 1H, J = 1.1 Hz, H-6); 9.36 (s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ: 12.2 (CH_3); 61.8 (C-5'); 84.8 (C-4'); 88.3 (C-1'); 111.2 (C-5); 120.5 (q, $J_{C,F}$ = 270.0 Hz, CF_3); 130.9 (C-2'); 136.4 (C-6); 136.6 (q, $^2J_{C,F}$ = 35.5 Hz, C-3'); 150.7 (C-2); 164.1 (C-4); ^{19}F NMR ($CDCl_3$) δ: -64.03 (s, 3F, CF_3); MS (CI) m/z: 293 (M+1, 7); 292 ($M^{+\circ}$, 36); 201 (83); 126 (100); HRMS calcd for $C_{11}H_{11}O_4N_2F_3$: 292.0668. Found: 292.0671.

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