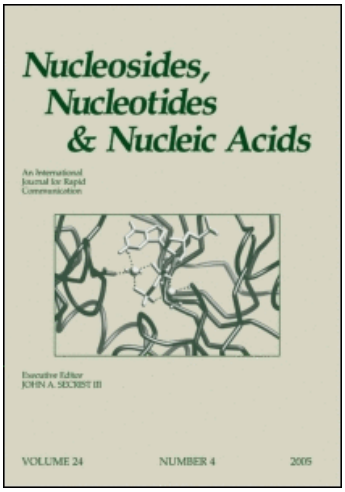

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3'-*C*-Trifluoromethyl Ribonucleosides

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3'-*C*-TRIFLUOROMETHYL RIBONUCLEOSIDES

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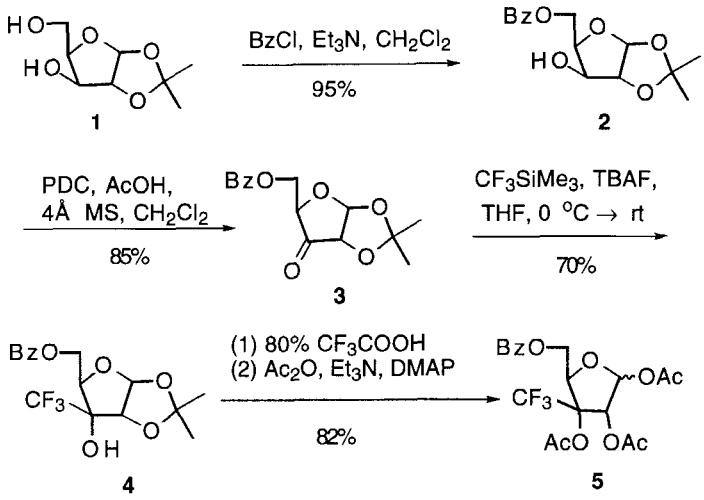
Abstract: (3-*C*-trifluoromethyl-β-D-ribofuranosyl) nucleosides of thymine, uracil and adenine were synthesized from 5-*O*-benzoyl-1,2,3-tri-*O*-acetyl-3-*C*-trifluoromethyl-β-D-ribofuranoside, prepared by addition of CF_3SiMe_3 to 5-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-*erythro*-pentos-3-ulose. 9-(3-*C*-Trifluoromethyl-β-D-ribofuranosyl)adenine was active against HSV-1.

Fluorinated nucleosides have generated considerable interest recently.[1] A fluoro substituent in a biologically active molecule may cause inhibition of metabolism at or near an active site, increase lipophilicity or alter reactivity and stability of functional groups by electron withdrawing effect.[2] In spite of comparatively close inductive effects of F and CF_3 (σ, F = 0.50, CF_3 = 0.45) only a few carbohydrate and nucleoside derivatives incorporating a CF_3 group are known.[3] A number of 3'-*C*-branched nucleosides are known including 3'-*C*-methyl adenosine,[4] 3'-*C*-hydroxymethyl-2',3'-dideoxyadenosine,[5] and 3'-*C*-fluoromethyl-3'-deoxy nucleosides.[6] It has been reported that 1-(3-*C*-methyl-β-D-ribofuranosyl)uracil-5'-phosphate is an effective terminator of the synthesis of RNA catalyzed by *E. coli* RNA polymerase and could be used in sequencing nucleic acids.[7] With the above matters in mind we decided to focus our attention on the synthesis of 3'-*C*-trifluoromethylribose and its conversion to nucleosides. A procedure for the introduction of trifluoromethyl group to carbonyl compounds was reported by Olah and co-workers.[8] The method involves the use of Ruppert's reagent (CF_3SiMe_3), a source of a nucleophilic trifluoromethyl group.[9] Very little work has been reported in which this reagent was applied to carbohydrate area and none with cyclic carbohydrates.[3a-d]

The 3-*C*-trifluoromethyl derivative **5** was synthesized as shown in Scheme 1. 1,2-*O*-Isopropylidene-α-D-xylofuranose (**1**) was converted to the 5-*O*-benzoyl derivative **2** by reaction with benzoyl chloride and triethylamine. Oxidation of compound **2** with PDC/AcOH in dichloromethane in the presence of molecular sieves (4Å) yielded the 3-keto derivative **3**.

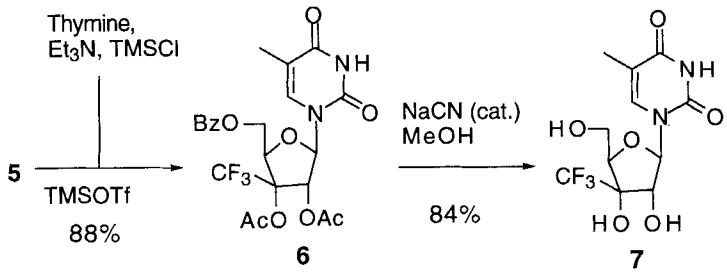


Scheme 1

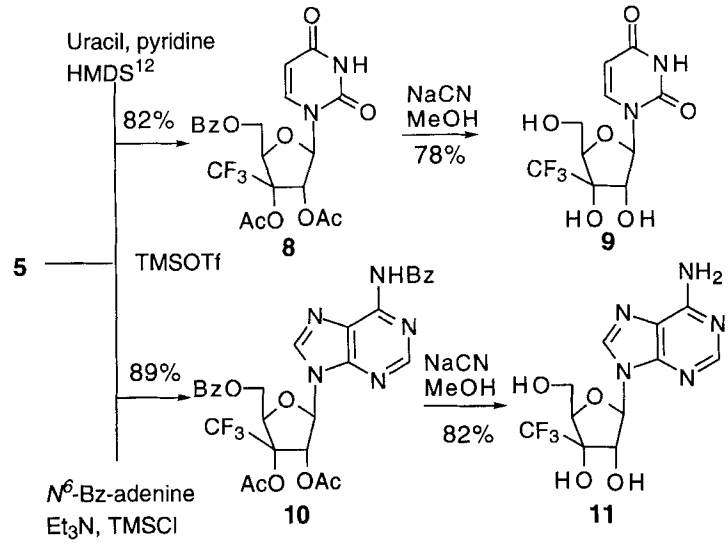
Compound **3** was converted to the trifluoromethyl derivative **4** as the only isomer in 70% yield by reaction with 1.5 equiv. of CF_3SiMe_3 in THF at room temperature in the presence of tetrabutylammonium fluoride (TBAF) (1.5 equiv.). The reaction is catalytic in F^- but more than one equivalent of TBAF was used to generate **4** without the isolation of its TMS protected derivative. The ^{19}F NMR showed a singlet at -75.07 ppm. Compound **4** was exposed to 80% trifluoroacetic acid to generate the triol which was immediately treated with acetic anhydride and triethylamine in the presence of catalytic 4-dimethylaminopyridine (DMAP) in dichloromethane to afford the triacetate **5** as a anomeric mixture in overall 82% yield (Scheme 1).

The Vorbrüggen method was used for nucleoside formation.[10] In a typical procedure thymine was silylated with triethylamine and TMSCl in benzene.[11] To the silylated base in acetonitrile were added **5** and TMSOTf; the reaction mixture was stirred for 24 h at room temperature. Work up and purification by column chromatography gave **6** in 88% yield. The deprotection was carried out by the treatment of **6** with NaCN in methanol for 36 h to give **7** (Scheme 2).

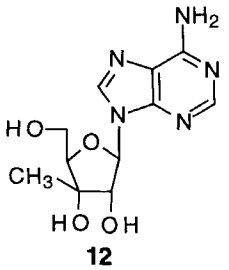
Similar Vorbrüggen reactions with uracil and N^6-benzoyladenine were carried out to give nucleoside derivatives **8** and **10** which upon treatment with NaCN in methanol gave nucleosides **9** and **11,** respectively (Scheme 3).



Scheme 2



Nucleosides **7**, **9** and **11** were evaluated for antiviral activity (Table 1). Only nucleoside **11** showed activity [herpes simplex virus-1 (KOS), Junin virus and Tacaribe virus] at concentrations ≥ 10 fold lower than cytotoxic concentration. For perspective, known nucleoside **12**[4,13] with a 3'-methyl group was prepared and included in the antiviral screens. It is interesting to note that the 3'-methyl nucleoside **12** exhibited considerably higher cytotoxicity than the trifluoromethyl nucleosides **7**, **9** and **11**.



Scheme 3

Table 1. Anti-viral activity of nucleosides **7, 9, 11** and **12.**

Compound :	**7**		**9**		**11**		**12**	
	Activity (μg/mL)[a]							
Virus	IC_{50} (MIC)	CC_{50} (MTC)	IC_{50} (MIC)	CC_{50} (MTC)	IC_{50} (MIC)	CC_{50} (MTC)	IC_{50} (MIC)	CC_{50} (MTC)
Parainfluenza-3 virus in Vero cells	(>200)	(≥400)	(>400)	(>400)	(300)	(≥400)	(40)	(≥200)
Reovirus-1 in Vero cells	(>200)	(≥400)	(>400)	(>400)	(>200)	(≥400)	(20)	(≥200)
Sindbis virus in Vero cells	(>200)	(≥400)	(>400)	(>400)	(>200)	(≥400)	(>100)	(≥200)
Coxsackie virus B4 in Vero cells	(>200)	(≥400)	(>400)	(>400)	(>200)	(≥400)	(>100)	(≥200)
Semliki forest virus in Vero cells	(>200)	(≥400)	(>400)	(>400)	(>200)	(≥400)	(>100)	(≥200)
Herpes simplex virus-1 (KOS) in E_6SM cells	(300)	(>400)	(200)	(>400)	(20)	(>400)	(10)	(200)
Herpes simplex virus-2 (G) in E_6SM cells	(100)	(>400)	(>400)	(>400)	(400)	(>400)	(20)	(200)
Vaccinia virus in E_6SM cells	(>400)	(>400)	(>400)	(>400)	(100)	(>400)	(4)	(200)
Vesicular stomatis virus in E_6SM cells	(150)	(>400)	(>400)	(>400)	(400)	(>400)	(7)	(200)
Polio virus-1 in HeLa cells	(>400)	(>400)	(>400)	(>400)	(>400)	(>400)	(>40	(100)
HIV-1 in CEM/O cells	>200	>200	>200	>200	>40	>200	>1.6	4.2
HIV-2 in CEM/O cells	>200	>200	>200	>200	>40	76	>1.6	4.2
Junin virus in Vero cells	(>50)	(200)	(>200)	(>200)	(10)	(>200)	(10)	(50)
Tacaribe virus in Vero cells	(>50)	(200)	(>200)	(>200)	(14)	(>200)	(10)	(50)
Varicella zoster virus[b] in Vero cells	>50	>200	>50	>200	>50	>200	>5	20
Cytomeglovirus AD-169 in Vero cells	>50	>200	>50	>200	>50	>200	>5	20
Cycomegalovirus (Davis) in Vero cells	>50	>200	>50	>200	>50	>200	>5	20

[a] IC_{50} = 50% inhibitory concentration, concentration required to reduce virus plaque formation by 50% or, in the cases of HIV, to protect CEM cells against cytopathogenicity by 50%. CC_{50} = 50% cytotoxic concentration or concentration required to reduce cell growth or viability by 50%. MIC = Minimum inhibitory concentration required to reduce virus-induced cytopathogenicity by 50%. MTC = Minimum toxic concentration to cause microscopically detectable change in morphology of normal uninfected cells. [b] Data were identical for the following strains: TK^+ VZV OKA and YS strains; TK^- VZV 07/1 and YS/R strains.

Experimental Section

5-*O*-Benzoyl-1,2-*O*-isopropylidene-α-D-xylofuranose (2). To a solution of 1,2-*O*-isopropylidene-α-D-xylofuranose (**1**) (0.51 g, 3 mmol) in dichloromethane (10 mL) at 0 °C was added triethylamine (1.25 mL, 9 mmol). To this cooled mixture was added dropwise benzoyl chloride (0.38 mL, 3.3 mmol); the reaction was monitored by TLC. After the disappearance of the starting material, water (10 mL) was added to the reaction mixture. The organic layer was separated, washed with sat. aq. $NaHCO_3$ (1 x 5 mL), water (2 x 5 mL) and dried over Na_2SO_4. The solvent was removed under vacuo and the residue was flash chromatographed (9 : 1, petroleum ether : EtOAc) to give **2** (0.84 g, 95%) as a colorless solid: mp 82-84 °C (lit.[14] mp 83.5-84.5 °C); ^1H NMR ($CDCl_3$) δ: 8.05-7.41 (m, 5 H , Ar), 5.95 (d, J = 4.8 Hz, 1 H, 1 - H), 4.75 (m, 1 H, 2 - H), 4.59 (d, J = 3.6 Hz, 1 H, 5 - Ha), 4.39 (m, 2 H, 3- and 4 - H), 4.17 (br s, 1 H, 5 - Hb), 3.40 (br s, 1 H, OH), 1.49 (s, 3 H), 1.31 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ: 167.3, 133.5, 129.8, 128.4, 104.6, 84.9, 78.4, 74.3, 61.2, 26.7, 26.1.

5-*O*-Benzoyl-1,2-*O*-isopropylidene-α-D-*erythro*-pentos-3-ulose (3). To a suspension of **2** (4 g, 1.3 mmol), PDC (14 g, 4 mmol) and 15 g of crushed molecular sieves (4Å) in dichloromethane (30 mL) was added dropwise acetic acid (1.4 mL, 2.5 mmol) at 0 °C. The reaction mixture was brought to room temperature and stirred for 12 h. Diethyl ether (20 mL) was added and the reaction mixture was stirred for 15 min. The ethereal mixture was applied to a silica gel column and the column was washed with diethyl ether; all the fractions were collected and the solvents were removed under vacuo to afford **3** (3.25 g, 85%) as a colorless crystalline solid: mp 90-93 °C (lit.[15] mp 93 - 95 °C); R_f 0.61 (1 : 1, EtOAc : petroleum ether); ^1H NMR ($CDCl_3$) δ: 7.94-7.39 (m, 5 H), 6.13 (d, J = 4.2 Hz, 1 H, 1 - H), 4.69 (m, 2 H), 4.49 (m, 2 H), 1.49 (s, 3 H), 1.41 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ: 207.6, 165.6, 133.4, 133.3, 129.4, 129.3, 129.1, 114.2, 76.0, 63.3, 27.3, 26.9.

5-*O*-Benzoyl-1,2-*O*-isopropylidene-3-*C*-trifluoromethyl-α-D-ribofuranose (4). To a solution of **3** (0.64 g, 2.19 mmol) and (trifluoromethyl)trimethylsilane (0.54 mL, 2.84 mmol) in THF (5 mL) was added dropwise a solution of TBAF in THF (1M, 2.84 mL, 2.84 mmol) under argon at 0 °C. The reaction mixture was brought to room temperature and stirred for 2 h. THF was removed under vacuo, dichloromethane (10 mL) was added and the mixture was washed with water (2 x 10 mL). The organic layer was dried over Na_2SO_4 and concentrated to give the crude product, which was flash chromatographed (7 : 3, petroleum ether : EtOAc) to afford **4** (0.55 g, 70%) as a white crystalline solid: mp 127-129 °C (recrystallized with EtOAc and petroleum ether); R_f 0.7 (7 : 3, petroleum ether : EtOAc); $[\alpha]_D^{25}$ + 22.49 (*c* 0.85, $CHCl_3$); IR (KBr): 3414, 2999, 1728, 1379, 1254, 1107, 869, 710, 690 cm^{-1}; ^1H NMR ($CDCl_3$)δ: 8.07-7.40 (m, 5 H), 5.98 (d, J = 4.2 Hz, 1 H, 1' - H), 4.78-4.73 (dd, J = 2.8 Hz, 1 H, 4' - H), 4.62 (d, J = 4.2 Hz, 1 H, 2' - H), 4.52-4.34 (m, 2 H, 5' - Ha and Hb), 3.54 (s, 1 H, -OH), 1.61 (s, 3 H), 1.41 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ:

162.1, 133.1, 129.7, 129.5, 128.3, 122.3 (q, J = 282 Hz), 113.7, 104.2, 80.4, 79.0 (q, J = 28 Hz), 77.4, 61.5, 26.6, 26.2; ^{19}F NMR ($CDCl_3$) δ: -75.07 (s); MS (CI) m/z: 363, 347, 305, 240, 165, 105. Anal. Calcd for $C_{16}H_{15}F_3O_6$: C, 53.04; H, 4.72. Found: C, 52.98; H, 4.64.

5-*O*-Benzoyl-1,2,3-tri-*O*-acetyl-3-*C*-trifluoromethyl-β-D-ribofuranoside (5). A solution of **4** (0.07 g, 0.193 mmol) in 80% trifluoroacetic acid (5 mL)was stirred for 15 h. Trifluoroacetic acid was removed under vacuo, and then coevaporated with toluene (2 x 10 mL) to give the crude triol. The triol was dissolved in dichloromethane (3 mL) to which was added DMAP (5 mg), triethylamine (0.16 mL, 1.15 mmol) and acetic anhydride (0.09 mL, 0.965 mmol) dropwise; after the reaction mixture was stirred for 2 h, dichloromethane (5 mL) was added and the mixture was washed with water (2 x 10 mL), sat. aq. $NaHCO_3$ (2 x 10 mL) and then again water (1 x 10 mL). The organic layer was dried over Na_2SO_4 and concentrated under vacuo to give crude **5** which was flash chromatographed (8 : 2, petroleum ether : EtOAc) to give an anomeric mixture of **5** (0.07 g, 82%).

β-Anomer: mp 54-56 °C (recrystallized with EtOAc and petroleum ether); R_f 0.56 (8:2, petroleum ether: EtOAc); $[\alpha]_D^{25}$ +50.19 (*c* 1.4, $CHCl_3$); IR (KBr): 3500, 3407, 3015, 2975, 1762, 1717, 724, 664, 603 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 8.03-7.37 (m, 5 H), 6.47 (d, J = 4.8 Hz, 1 H, 1' - H), 5.71 (d, J = 4.8 Hz, 1 H, 2' - H), 5.11 (d, J = 6.6 Hz, 1 H, 4' - H), 4.96 (dd, J = 9.6, 2.4 Hz, 1 H, 5' - Ha), 4.58 (dd, J = 8.4, 3.3 Hz, 1 H, 5' - Hb), 2.15 (s, 3 H), 2.09 (s, 3 H), 2.06 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ:168.8, 167.2, 167.5, 165.7, 133.1, 129.6, 129.3, 128.8, 128.2, 125.0, 92.8, 81.6, 80.6, 70.5, 62.0, 20.8, 20.5, 19.9; ^{19}F NMR ($CDCl_3$) δ: -70.78(s); MS (EI) m/z: 389, 286, 266, 224, 165, 123, 105, 77, 57; HRMS calcd for $C_{19}H_{19}F_3O_9$-$OCOCH_3$ 389.0847. Found: 389.0835. Anal. Calcd for $C_{19}H_{19}F_3O_9$: C, 50.90; H, 4.26. Found: C, 50.98, H, 4.26.

α-Anomer: oil; R_f 0.52 (8:2, petroleum ether: EtOAc); ^{1}H NMR ($CDCl_3$) δ: 8.09-7.44 (m, 5 H), 6.23 (d, J = 3.3 Hz, 1 H, 1' - H), 5.96 (d, J = 3.3 Hz, 1 H, 2' - H), 5.11 (t, J = 3.0 Hz, 1 H, 4' - H), 4.86 (m, 1 H, 5' - Ha), 4.55 (dd, J = 6.9, 5.4 Hz, 1 H, 5' - Hb), 2.18 (s, 3 H), 2.12 (s, 3 H), 2.01 (s, 3 H); ^{19}F NMR ($CDCl_3$) δ: -69.20 (s).

1-(5-*O*-Benzoyl-2,3-di-*O*-acetyl-3-*C*-trifluoromethyl-β-D-ribofuranosyl)thymine (6). To a well stirred suspension of thymine (0.28 g, 2.23 mmol) and TMSCl (0.58 mL, 4.5 mmol) in dry benzene (10 mL) was added dropwise triethylamine (0.65 mL, 4.5 mmol) under anhydrous conditions at room temperature. After the addition, stirring was continued for 10 h. The precipitated mixture of triethylamine hydrochloride and thymine was filtered off and washed with dry benzene (3 x 5 mL), the filtrate and washings were collected and the solvent removed under vacuo to give a viscous oily silylated thymine which was then treated with a solution of **5** (0.25 g , 0.55 mmol) in dry acetonitrile (5 mL) followed by TMSOTf (0.46 mL, 2.2 mmol) to give a clear solution. The reaction mixture was stirred at room temperature for 20 h and then sat. aq. $NaHCO_3$ (10 mL) and dichloromethane (10 mL) were added. The organic layer was washed with water (2 x 10 mL), dried over Na_2SO_4 and concentrated under vacuo to give the crude product

which was flash chromatographed (1 : 1, petroleum ether : EtOAc) to give **6** (0.24 g, 88%): mp 75-76 °C (recrystallized with EtOAc and petroleum ether); R_f 0.28 (1 : 1, petroleum ether : EtOAc); $[\alpha]_D^{25}$ -9.79 (*c* 0.35, $CHCl_3$); IR (KBr): 3204, 3065, 2963, 1771, 1722, 1452, 1265, 1120, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 9.29 (s, 1 H, NH), 8.06-7.43 (m, 5 H), 7.11 (s, 1 H, 6 - H), 6.43 (d, *J* = 7.2 Hz, 1 H, 1' - H), 5.68 (d, *J* = 7.2 Hz, 1 H, 2' - H), 5.11 (d, *J* = 6.6 Hz, 1 H, 4' - H), 4.91 (dd, *J* = 12.0, 1.8 Hz, 1 H, 5' - Ha), 4.68 (dd, *J* = 11.7, 7.8 Hz, 1 H, 5' - Hb), 2.26 (s, 3 H), 2.13 (s, 3 H), 1.82 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ: 168.8, 168.3, 165.8, 163.2, 150.51, 133.7, 135.5, 129.0, 128.7, 128.5, 128.5 (q, *J* = 285 Hz), 112.5, 84.7, 82.3 (q, *J* = 30 Hz), 72.7, 71.4, 62.1, 21.1, 20.2, 12.4; ^{19}F NMR ($CDCl_3$) δ: -72.04 (s); MS (FAB) m/z: 515 (M^+ + H), 389, 347, 273, 207, 165, 126, 105, 77. Anal. Calcd for $C_{22}H_{21}F_3N_2O_9$: C, 50.36; H, 4.11; N, 5.44. Found: C, 50.53; H, 4.23; N, 5.04.

1-(3-*C*-Trifluoromethyl-β-D-ribofuranosyl)thymine (7). To a solution of **6** (0.16 g, 0.31 mmol) in methanol (3 mL) were added several crystals of NaCN and the reaction mixture was stirred at room temperature for 30 h. The solvent was removed under vacuo and the crude residue was flash chromatographed (EtOAc) to give **7** as a colorless solid (83 mg, 84%): mp 111-113 °C (recrystallized with methanol and petroleum ether); R_f 0.57 (EtOAc); $[\alpha]_D^{25}$ -1.70 (*c* 1.0, MeOH); IR (KBr): 3411, 1696, 1668, 1257, 1157, 1048, 710 cm^{-1}; ^1H NMR (CD_3OD) δ: 7.79 (s, 1 H, 6 - H), 5.98 (d, *J* = 7.5 Hz, 1 H, 1' - H), 4.52 (d, *J* = 7.5 Hz, 1 H, 2' - H), 4.05 (m, 1 H, 4' - H), 3.80 (m, 2 H, 5'a- and 5'b - H), 1.86 (s, 3 H); ^{13}C NMR (CD_3OD) δ: 164.9, 151.6, 137.1, 126.6 (q, *J* = 285 Hz), 110.9, 87.1, 85.2, 77.9 (q, *J* = 29 Hz), 72.4, 60.1, 11.1; ^{19}F NMR (CD_3OD) δ: -76.26 (s); MS (EI) m/z: 326, 246, 155, 126, 97, 81, 69, 55. HRMS calcd. for $C_{11}H_{13}F_3N_2O_6$, 326.0725. Found, 326.0730. Anal. Calcd for $C_{11}H_{13}F_3N_2O_6.0.5H_2O$: C, 39.41; H, 4.23. Found: C, 39.84; H, 4.23.

1-(5-*O*-Benzoyl-2,3-di-*O*-acetyl-3-*C*-trifluoromethyl-β-D-ribofuranosyl)uracil (8). A mixture of uracil (0.24 g, 2.2 mmol), 1,1,1,3,3,3-hexamethyldisilazane (3 mL) and dry pyridine (3 mL) was refluxed under anhydrous conditions for 3 h. The solvents were evaporated under vacuo and then coevaporated with toluene (2 x 5 mL) to give a viscous silylated uracil, which was then treated with a solution of **5** (0.25 g, 0.55 mmol) in dry acetonitrile (5 mL) followed by TMSOTf (0.42 mL, 2.2 mmol) to give a clear solution. The reaction mixture was stirred at room temperature for 20 h and then sat. aq. $NaHCO_3$ (10 mL) and dichloromethane (10 mL) were added. The organic layer was washed with water (2 x 10 mL), dried over Na_2SO_4 and concentrated under vacuo to give the crude product which was flash chromatographed (1 : 1, petroleum ether : EtOAc); to give **8** (0.23 g, 82%): mp 87-89 °C (recrystallized with EtOAc and petroleum ether); R_f 0.22 (1 : 1, petroleum ether : EtOAc); $[\alpha]_D^{25}$ -36.03 (*c* 0.8, $CHCl_3$); IR (KBr): 3191, 3065, 1770, 1656, 1452, 1374, 1275, 1207, 1117, 1070, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 9.86 (s, 1 H, NH), 8.02-7.41 (m, 5 H), 7.33 (d, *J* = 8.1 Hz, 1 H, 6 - H), 6.39 (d, *J* = 6.6 Hz, 1 H, 1' -

H), 5.77 (d, J = 8.1 Hz, 1 H, 5 - H), 5.62 (d, J = 6.6 Hz, 1 H, 2' - H), 5.26 (d, J = 6.9 Hz, 1 H, 4' - H), 4.88 (d, J = 12.0 Hz, 1 H, 5'a - H), 4.66 (m, 1 H, 5'b - H), 2.23 (s, 3 H), 2.10 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ: 168.6, 168.2, 165.7, 162.8, 150.3, 138.3, 133.7, 129.6, 128.4, 125.0 (q, J = 283.Hz), 103.8, 85.2, 82.5 (q, J = 30 Hz), 77.9, 71.6, 61.9, 21.0, 20.0; ^{19}F NMR ($CDCl_3$) δ: -72.69 (s); MS (FAB) m/z: 501 (M^+ + H), 389, 347, 259, 216, 165, 113, 105, 77. Anal. Calcd for $C_{21}H_{19}F_3N_2O_9$: C, 50.40; H, 3.82; N, 5.59. Found: C, 50.61; H, 3.98; N, 5.44.

1-(3-*C*-Trifluoromethyl-β-D-ribofuranosyl)uracil (9). The deprotection of **8** was carried out by a similar method as described for **7**, starting from 0.21 g (0.43 mmol) to give **9** (0.10 g , 78%): mp >250 °C; R_f 0.65 (EtOAc); $[\alpha]_D^{25}$ -3.83 (*c* 0.6, MeOH); IR (KBr): 3380, 1695, 1646, 1473, 1267, 1189, 989, 708 cm^{-1}; ^{1}H NMR (d_6 - DMSO,) δ: 11.39 (s, 1 H, NH), 7.91 (d, J = 8.1 Hz, 1 H, 6 - H), 6.09 (d, 1 H, -OH), 5.86 (d, J = 7.8 Hz, 1 H, 1' - H), 5.69 (d, J = 8.1 Hz, 1 H, 5 - H), 5.16 (s, 1 H, 2' - H), 4.38 (t, J = 4.6 Hz, 1 H, 4' - H), 3.93 (s, 1 H, -OH), 3.58 (m, 2 H, 5'a- and 5'b - H); ^{13}C NMR (DMSO, d_6) δ: 163.5, 151.5, 141.4, 127.1 (q, J = 283 Hz), 103.1, 86.1 85.3, 78.5 (q, J = 30 Hz), 72.3, 60.2; ^{19}F NMR (DMSO, d_6) δ: -73.52 (s); MS (EI) m/z: 312, 257, 225, 141, 113, 98, 83, 69, 55. Anal. Calcd for $C_{10}H_{11}F_3N_2O_6$: C, 38.46; H, 3.55; N, 8.97. Found: C, 38.45; H, 3.61; N, 8.81.

***N*^{6}-Benzoyl-9-(5-*O*-Benzoyl-2,3-di-*O*-acetyl-3-*C*-trifluoromethyl-β-D-ribofuranosyl)-adenine (10)** was synthesized by a similar method as described for **6**, starting from **5** (0.35 g, 0.78 mmol) and *N*^{6}-benzoyladenine (0.93 g, 3.9 mmol). Yield 0.44 g (89%): mp 73-75 °C; R_f 0.37 (2 : 8, petroleum ether : EtOAc); $[\alpha]_D^{25}$ -13.44 (*c* 0.7, $CHCl_3$); IR (KBr): 3228, 3121, 3055, 2975, 1767, 1369, 1116, 738 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 9.56 (s, 1 H, NH), 8.66 (s, 1 H, 8 - H), 8.14 (s, 1 H, 2 - H), 7.96-7.30 (m, 10 H), 6.53 (d, J = 6.9 Hz, 1 H, 1' - H), 6.43 (d, J = 6.9 Hz, 1 H, 2' - H), 5.31 (d, J = 6.9 Hz, 1 H, 5' - Ha), 4.89 (d, J = 11.7 Hz, 1 H, 5' - Hb), 4.68 (m, 1 H, 4' - H), 2.24 (s, 3 H), 1.99 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ: 168.4, 167.8, 165.6, 164.8, 152.6, 151.7, 149.6, 140.9, 133.2, 133.1, 132.3, 129.4, 128.8, 128.1, 127.3, 127.1, 123.2, 121.1 (q, J = 285 Hz), 85.3, 83.0 (q, J = 30 Hz), 78.3, 71.0, 62.0, 20.9, 19.8; ^{19}F NMR ($CDCl_3$) δ: -72.47 (s); MS (FAB) m/z: 628 (M^+ + H), 389, 330, 240, 207, 165, 113, 105. Anal. Calcd for $C_{29}H_{24}F_3N_5O_8$: C, 55.50; H, 3.85. Found: C, 54.97; H, 3.90.

9-(3-*C*-Trifluoromethyl-β-D-ribofuranosyl)adenine (11) was synthesized by a similar method as described for **7**, starting from **10** (0.26 g, 0.41 mmol). Yield 0.12 g (82%): mp >250 °C; R_f 0.14 (EtOAc); $[\alpha]_D^{25}$ -34.36 (*c* 0.3, MeOH); IR (KBr): 3360, 2928, 1638, 1371, 1179, 860, 713 cm^{-1}; ^{1}H NMR (CD_3OD) δ: 8.37 (s, 1 H, 8 - H), 8.18 (s, 1 H, 2 - H), 6.01 (d, J = 7.5 Hz, 1 H, 1' - H), 5.19 (d, J = 7.5 Hz, 1 H, 2' - H), 4.20 (br s, 1 H, 4' - H), 3.89 (br s, 2 H, 5' - Ha and Hb); ^{13}C NMR (CD_3OD) δ: 156.0, 152.2, 149.0, 140.8, 126.4, 103.6, 87.8, 86.2, 78.7, 72.5, 60.4; ^{19}F NMR ($CDCl_3$) δ: -75.99 (s); MS (FAB) m/z: 336 (M^+ + H), 178, 136, 73. Anal. Calcd for $C_{11}H_{12}F_3N_5O_4.0.5H_2O$: C, 38.37, H, 3.80. Found: C, 38.16; H, 3.56.

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