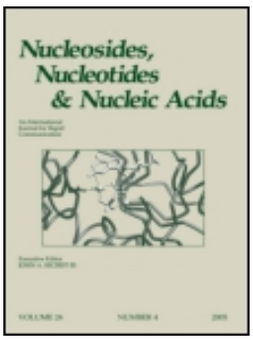

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SYNTHESIS AND BIOLOGICAL EVALUATION OF ISONUCLEOSIDES DERIVED FROM METHYL 3,5-ANHYDRO-2-*O*-(2-FLUOROBENZYL)-D-XYLOFURANOSIDES

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ABSTRACT

New isonucleosides [methyl 5-(1-pyrimidinyl)furanosides] are prepared by nucleophilic opening of the oxetane ring of methyl 3,5-anhydro-2-*O*-(2-fluorobenzyl)-D-xylofuranoside with silylated pyrimidine bases in the presence of trimethylsilyl triflate. Structures, configurations and conformations were determined by NMR techniques and several X-ray diffraction analyses. seven of the isonucleosides were tested for cytotoxicity and activity against HIV, HSV and several other viruses.

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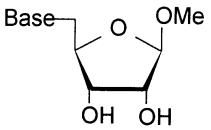
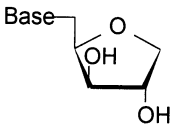
INTRODUCTION

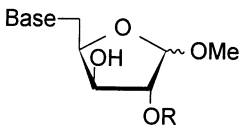
Since the mid-seventies the so-called isonucleosides in which the nucleobase is linked to the primary carbon atom (C-5) of a pentofuranose instead to the anomeric centre have found considerable scientific interest[1]. Two general ways for the preparation of such compounds have been described in the literature. One is to couple the sodium salt of a pyrimidine or purine base with a sugar, which bears a good leaving group at C-5 (e.g., a tosyl group). Using this method, Holý[1] synthesised adenine and thymine derivatives of type **A**. The second route to isonucleosides consists in the reaction of a 3,5-anhydro-1-deoxypentofuranose with a nucleobase under base-catalysis. In this way Ioannisyan et al.[2] prepared 1′-deoxy-isonucleosides of type **B**. The synthesis of isonucleosides carrying an anomeric hydroxy or methoxy group according to this method has, however, not been reported in the literature. In our paper we describe the synthesis of pyrimidine isonucleosides of type **C** from 3,5-anhydro-D-xylofuranosides by use of the well established triflate method[3]. Besides the question of the regioselectivity of the oxetane ring opening reaction also the biological properties of the products seemed to be interesting in our view.



A



B

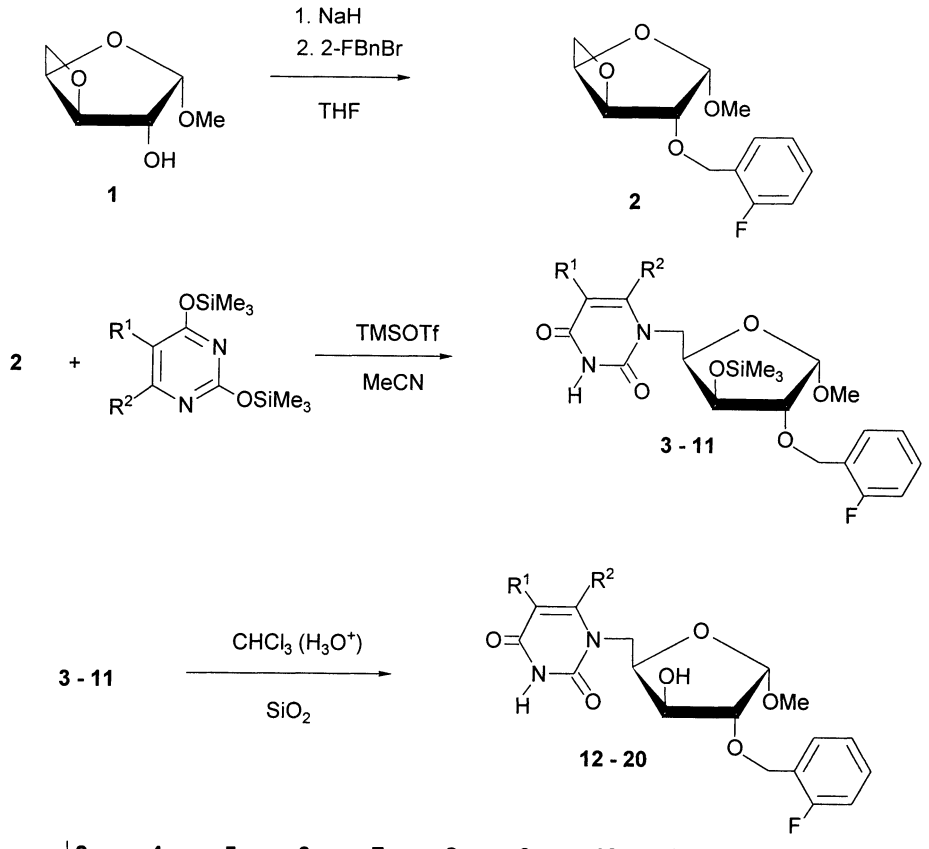


C

RESULTS AND DISCUSSION

The preparation of the 2-*O*-(fluorobenzyl) substituted derivative **2** was achieved by reaction of methyl 3,5-anhydro-α-D-xylofuranoside[4] with 2-fluorobenzyl bromide with a yield of 94%. The 2-*O*-(2-fluorobenzyl) substituent of **2** represents a substructure, which, in combination with the nucleoside analogous structure of **C**, could induce interesting biological activity[5]. Coupling of **2** with silylated uracil[6] in the presence of trimethylsilyl trifluoromethanesulfonate (TMSOTf)[3] led to the 3′-silylated isonucleoside **3** with a low yield of 8%. An isomer of **3** with the nucleobase linked to C-3 and a trimethylsilyl group at O-5, which could have been formed by attack of the base on C-3 under opening of the oxetane ring, was not detectable. Neither was a regular uridine type nucleoside formed where the nucleobase is linked to the anomeric centre C-1. The position of the nucleobase at the sugar moiety of **3** was proved by its ^{13}C NMR-spectrum. The chemical shift of the C-5′ atom (49.6 ppm) is typical for a C-N bond, in contrast to the chemical shift of the C-3′ atom (75.0 ppm) which is in accordance with a C-O bond. We also measured the HMBC spectrum of **3** in which we observed interactions between one of

the H-5′ protons of the furanose with the C-2 atom and the C-6 atom of the nucleobase. This is only possible if the base is linked to the C-5 atom of the sugar moiety. Desilylation of the 3′-position was achieved by stirring **3** in chloroform, which, due to spontaneous hydrolysis and photooxidation, contains traces of hydrochloric acid. Under these mild conditions it was possible to obtain the uracil derivative **12** with a yield of 34%. The corresponding silylated thymine isonucleoside **4** was obtained from **2** and 2,4-bis-*O*-trimethylsilylthymine[6] with a low yield of 10%. Cleavage of the 3′-*O*-silyl group by hydrolysis led to the deprotected isothymine **13** with 64% yield. Analogously we prepared the 3′-silylated 5-halouracil isonucleosides **5–8** with yields between 64% and 76%. Removal of the trimethylsilyl group led to the unprotected target molecules **14–17** with high yields of 82%–90% (Sch. 1).



	3	4	5	6	7	8	9	10	11
	12	13	14	15	16	17	18	19	20
R^1	H	Me	F	Cl	Br	I	H	Me	NO_2
R^2	H	H	H	H	H	H	Me	Me	H

Scheme 1. (2-FBnBr = 2-fluorobenzylbromide).

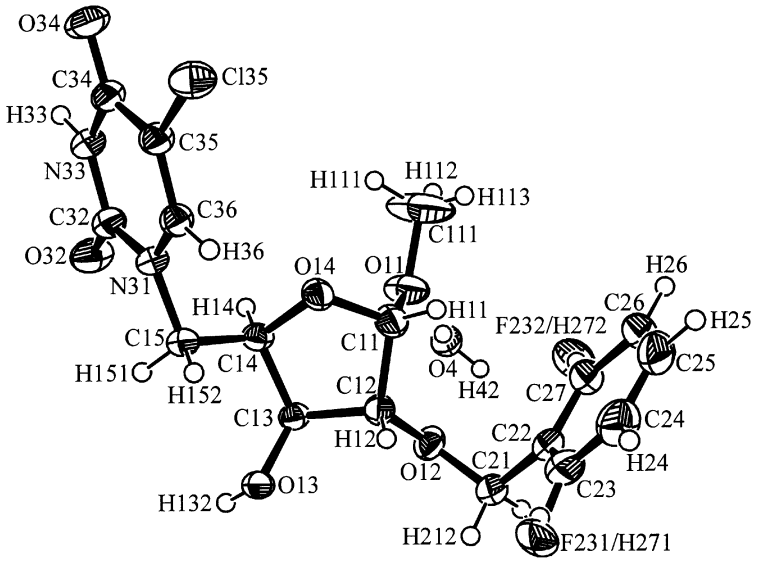


Figure 1. ORTEP view of the X-ray diffraction structure of **15** with one molecule of crystal water. Thermal ellipsoids are drawn at the 50% probability level.

The isonucleosides **15–17** were crystallised and investigated by X-ray structural analyses. An ORTEP view of the 5-chloro derivative **15** is shown as example in Fig. 1. The furanose ring of **15** exhibits the usual envelope conformation (E_1). In the case of **16** and **17** each two conformers occur in the crystal. The furanose rings of **16** exhibit two different envelope conformations E_1 and ^2E whereas both the two different molecules of **17** exhibit ^2E envelopes. The orientation of the nucleobase, i.e., the torsion angle C14-C15-N31-C32 is almost identical in **15–17**. (cf. Table 1).

We obtained the silylated 6-methyluracil isonucleoside **9** and its 5,6-dimethyl analogue **10** from silylated 6-methyluracil[7] and 5,6-dimethyluracil[7]

Table 1. Selected Torsion Angles in **15–17** and **19**

	Torsion Angles [°]		
Nucleoside	C14-C15-N31-C32	C12-O12-C21-C22	O12-C21-C22-C23
15	82	− 59	120
16, conformer 1	91	176	160
16, conformer 2	86	− 176	− 130
17, conformer 1	92	− 176	− 144
17, conformer 2	91	− 174	20
19, conformer 1	84	176	− 159
19, conformer 2	79	− 168	− 154

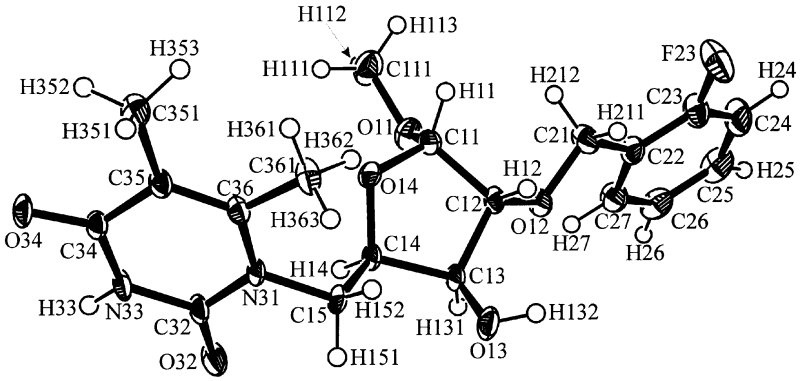


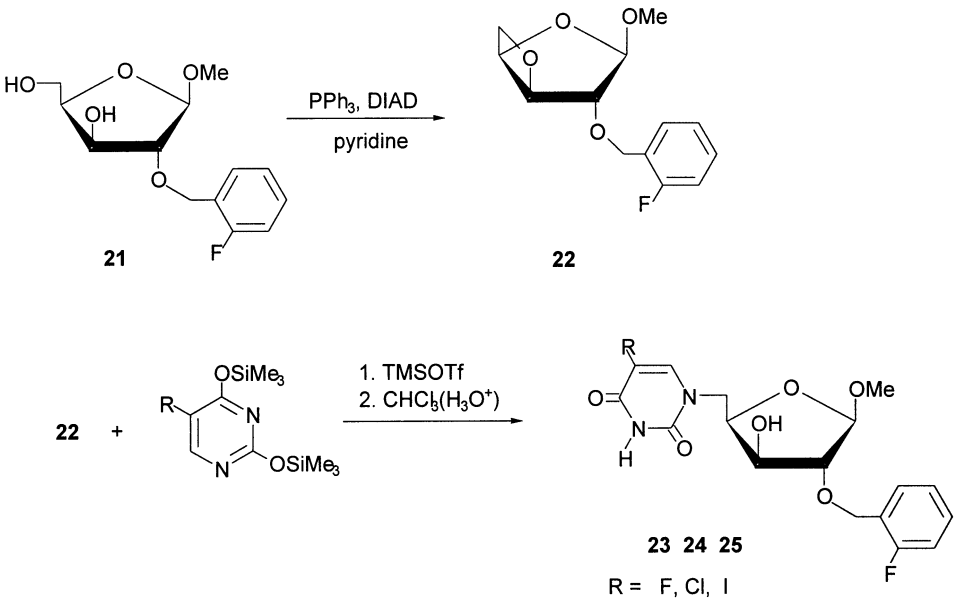
Figure 2. ORTEP view of one of the two conformers of **19**. Thermal ellipsoids are drawn at the 50% probability level.

with significantly higher yields (80% and 71%) as compared with **3** and **4**. Deprotection with acidic chloroform led to 65% of the 6-methyluracil derivative **18** and 70% of the 5,6-dimethyluracil derivative **19** (Sch. 1). The 5,6-dimethyluracil derivative **19** could be crystallised from water-acetonitrile. A single crystal was suitable for an X-ray diffraction analysis. As in the case of **16** and **17** two different conformers ($^0T_1$) were found for **19** (cf. Fig. 2 and Table 1).

Coupling of **2** with silylated 5-nitrouracil[8] in the presence of TMSOTf and subsequent chromatography on silica gel directly led to 8% of the unprotected 5-nitrouracil isonucleoside **20**. The intermediate 3′-*O*-silyl derivative **11** could only be detected by TLC (PE/EA 1:3, **11**: $R_f = 0.58$; **20**: $R_f = 0.19$).

The β-anomer **22** was prepared in a different way compared to the α-anomer **2**. Methyl 2-*O*-(2-fluorobenzyl)-β-D-xylofuranoside **21**, which is conveniently obtained from methyl β-D-xylofuranoside in three steps[9], was cyclised by an intramolecular Mitsunobu reaction to form the oxetane **22** with an acceptable yield of 69%. The reaction of **22** with silylated pyrimidine bases in the presence of trimethylsilyl triflate led to the corresponding isonucleosides **23–25** with β-configuration (Sch. 2). As in the case of the nitrocompound **20**, no silylated intermediates were isolated. Again, no isomers, e.g., regular nucleosides, were obtained. Possibly due to steric hindrance of the attack of the nucleobase on the β-anomer, the yields were low.

The isonucleosides **12** and **14–19** were tested for antiviral activity against HIV-1, HIV-2, HSV-1, HSV-2, Vaccinia virus, Vesicular stomatitis virus, Parainfluenza-3 virus, Reovirus-1, Sindbis virus, Coxsackie virus B4, Punta Toro virus and Respiratory syncytial virus cell cultures. With the exception of **12**, which reduced the virus-induced cytopathogenicity of



Scheme 2.

HSV-1 (KOS) in E_6SM cell cultures by 50% at a concentration of 9.6 μg/mL, none of the isonucleosides exhibited a significant antiviral activity against one of the evaluated viruses. The 5-haloisonucleosides **15–17** and the methyl derivative **18** were weakly cytotoxic (IC_{50}: 100–250 μg/mL). Only **19** was more inhibitory to human tumor cell proliferation (IC_{50}: 12–30 μg/mL). Selected details are given in Table 2.

Table 2. Inhibitory Effects of **15–19** on the Proliferation of Murine Leukemia Cells (L1210) and Human T-lymphocyte Cells (Molt4/C8, CEM/0 and CEM/TK^-)

	IC_{50} [μM][a]			
Compound	L1210	Molt4/C8	CEM/0	CEM/TK-
15	> 250	134 ± 6	135 ± 9	106 ± 3
16	> 250	102 ± 13	112 ± 3	84 ± 4
17	175 ± 8	126 ± 11	122 ± 3	99 ± 1
18	≥250	155 ± 11	218 ± 18	165 ± 5
19	104 ± 3	30 ± 1	24 ± 1	12 ± 2

[a] 50% inhibitory concentration or compound concentration required to inhibit tumor cell proliferation by 50%.

EXPERIMENTAL SECTION

Melting points were determined by the use of an Electrothermal apparatus (values are corrected). IR spectra (KBr pellets) were measured with an ATI Mattson Genesis spectrometer. NMR spectra were recorded with Bruker AMX 400 and DRX 500 spectrometers. Chemical shifts (ppm) are related to Me_4Si (^1H and ^{13}C), coupling constants are given in Hz. Standard correlation techniques were used for assignments. Mass spectra were measured on Varian CH 7 (EI, 70 eV) and VG Analytical 70–250 S (HRMS, FAB) apparatus. Optical rotations were measured on a Perkin Elmer Polarimeter 341. TLC was carried out on E. Merck PF_{254} foils (detection: UV light, iodine vapour, EtOH-H_2SO_4 spray/200°C), and column chromatography on E. Merck Kieselgel 60 (70–230 mesh). Solvents (EA = ethyl acetate, PE = petroleum ether) were purified and dried according to standard laboratory procedures[10].

X-ray Structure Analyses

The crystal data for **15** and **16** were collected on an Enraf-Nonius CAD4 diffractometer in the $2\theta/\omega$ scan mode with graphite monochromated Cu K_α radiation (1.54178 Å) at a temperature of 173 K. For **17** data collection was performed on a Kappa CCD Nonius diffractometer with graphite monochromated Mo K_α radiation (0.71073 Å) in the Rotation Φ scan mode at a temperature of 293 K. The X-ray diffraction of **19** was measured on a Hilger & Watts Y290 diffractometer with graphite monochromated Mo K_α radiation (0.71073 Å) in the 2/ scan mode at a temperature of 153 K. The structures were solved by direct methods using the SIR-97 program[11], and refined by full-matrix-block least-squares on F^2 using all data and the SHELXL-97 program[12]. The full crystallographic details, excluding structure features, have been deposited with the Cambridge Crystallographic Data Centre. These data may be obtained, on request, from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK. Tel. +44-1223-336408, Fax +44-1223-336033, E-mail deposit@ccdc.cam.ac.uk. Deposition number CCDC 144157 (**15**), 148803 (**16**), 148998 (**17**) and 145046 (**19**).

Methyl 3,5-Anhydro-2-*O*-(2-fluorobenzyl)-α-D-xylofuranoside (2). Sodium hydride (60% dispersion in mineral oil, 370 mg, 9.17 mmol) was added to a solution of methyl 3,5-anhydro-α-D-xylofuranoside[4] (1320 mg, 9.04 mmol), in dry THF (30 mL). After 5 min 2-fluorobenzyl bromide (1.20 mL, 1870 mg, 9.89 mmol) was added. After 1 h the reaction mixture was filtered, the solvent was evaporated and the crude product was purified by column chromatography (PE/EA 2:1, $R_f = 0.35$) to yield **2** (2170 mg, 94%) as colourless oil. $[\alpha]_D^{20} = +111.9$ (c = 1.0 in $CHCl_3$). ^1H

NMR ($CDCl_3$): δ 3.47 (s, 3H, OCH_3), 4.24 (dd, 1H, H-2), 4.28 (dd, 1H, H-5_{endo}), 4.68 (dd, 1H, H-5_{exo}), 4.70 (s, 2H, $CH_2C_6H_4F$), 4.92 (ddd, 1H, H-4), 5.15 (dd, 1H, H-3), 5.26 (d, 1H, H-1), 7.02 (ddd, 1H, H_{ar}-3), 7.11 (ddd, 1H, H_{ar}-5), 7.23–7.30 (m, 1H, H_{ar}-4), 7.43 (ddd, 1H, H_{ar}-6). $J_{1,2} = 3.9$, $J_{2,3} = 1.8$, $J_{3,4} = 4.6$, $J_{4,5endo} = 2.7$, $J_{4,5exo} = 4.6$, $J_{5endo,5exo} = 7.7$, $J_{3ar,4ar} = 9.9$, $J_{3ar,5ar} = 0.9$, $J_{3ar,F} = 9.1$, $J_{4ar,5ar} = 7.5$, $J_{4ar,6ar} = 1.8$, $J_{5ar,6ar} = 7.5$, $J_{6ar,F} = 7.5$. ^{13}C NMR ($CDCl_3$): δ 56.0 (OCH_3), 66.1 (d, $CH_2C_6H_4F$), 75.4 (C-4), 76.4 (C-5), 84.7 (C-2), 88.6 (C-3), 105.2 (C-1), 115.0 (d, C_{ar}-3), 123.8 (d, C_{ar}-5), 124.2 (d, C_{ar}-1), 129.4 (d, C_{ar}-4), 130.2 (d, C_{ar}-6), 160.8 (d, C_{ar}-2). $J_{CH2,F} = 3.8$, $J_{1ar,F} = 14.6$, $J_{2ar,F} = 247.0$, $J_{3ar,F} = 21.5$, $J_{4ar,F} = 8.2$, $J_{5ar,F} = 3.6$, $J_{6ar,F} = 4.1$. EI MS m/z (%): 254 (0.1) [$M^{+\bullet}$], 253 (0.2), 223 (0.8) [$M^{+\bullet}$-OCH_3], 195 (0.4), 194 (0.2), 193 (0.3), 192 (0.2), 163 (1), 135 (1), 123 (4), 115 (4), 110 (10), 109 (100) [$C_7H_6F^{+\bullet}$], 87 (5), 85 (10), 83 (8), 71 (3), 69 (9), 68 (4), 61 (4), 59 (4), 57 (3). *Anal*. Calcd. for $C_{13}H_{15}FO_4$: C, 61.41; H, 5.95. Found: C, 61.14; H, 6.03.

Reaction of 2 with silylated nucleobases (*General procedure A*). A solution of **2** (0.4–0.6 mmol), the corresponding silylated uracil derivative (1.6–2.4 mmol), and molecular sieves A4 (40-60 mg) in dry MeCN (5–6 mL) was cooled to −18°C. Then, TMSOTf (0.2–0.3 mL, 1.1–1.7 mmol) was added. the mixture was stirred for 90 min, whereat the temperature was allowed to rise to 20 °C. when the reaction was complete satd aq $NaHCO_3$ solution (20 mL) was added and stirring was continued for 30 min. After filtration the aq phase was extracted with $CHCl_3$, the organic phase was dried with $MgSO_4$ and evaporated. The products were obtained as white solids after purification by column chromatography. Appropriate eluents are given with the melting points (M.p.).

Methyl 5-Deoxy-2-*O*-(2-fluorobenzyl)-3-*O*-trimethylsilyl-5-*N*-(uracil-1-yl)-α-D-xylofuranoside (3). 21 mg (8%), from 2 (150 mg, 0.59 mmol) and 2,4-bis-*O*-trimethylsilyluracil[6] (621 mg, 2.24 mmol). M.p. 122–125 °C (PE/EA 1:2, $R_f = 0.16$, decomp.). $[\alpha]_D^{20} = +95.0$ (c = 1.0 in $CHCl_3$). IR: ν 3192 (NH), 1680 (C = O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.14 [s, 9H, $SI(CH_3)_3$], 3.33 (s, 3H, OCH_3), 3.41 (dd, 1H, H-$5'_a$), 3.81 (dd, 1H, H-2′), 4.26 (dd, 1H, H-$5'_b$), 4.33 (ddd, 1H, H-4′), 4.48 (dd, 1H, H-3′), 4.65, 4.69 (AB-system, 2H, $CH_2C_6H_4f$), 4.83 (d, 1H, H-1′), 5.65 (dd, 1H, H-5), 7.05 (ddd, 1H, H_{ar}-3), 7.14 (ddd, 1H, H_{ar}-5), 7.26–7.32 (m, 1H, H_{ar}-4), 7.28 (d, 1H, H-6), 7.44 (ddd, 1H, H_{ar}-6), 8.97 (bs, 1H, NH). $J_{1',2'} = 4.1$, $J_{2',3'} = 5.6$, $J_{3',4'} = 6.7$, $J_{4',5'a} = 9.4$, $J_{4',5'b} = 2.8$, $J_{5'a,5'b} = 14.5$, $J_{AB} = 12.3$, $J_{AB,F} = 0.8$, $J_{5,6} = 7.9$, $J_{5,NH} = 2.2$, $J_{3ar,4ar} = 8.4$, $J_{3ar,5ar} = 1.1$, $J_{3ar,F} = 9.9$, $J_{4ar,5ar} = 7.5$, $J_{4ar,6ar} = 1.8$, $J_{5ar,6ar} = 7.5$, $J_{6ar,F} = 7.5$. ^{13}C NMR ($CDCl_3$): δ − 0.1 [$Si(CH_3)_3$], 49.6 (C-5′), 55.6 (OCH_3), 66.2 (d, $CH_2C_6H_4F$), 75.0 (C-3′), 75.3 (C-4′), 85.4 (C-2′), 100.8 (C-1′), 101.4 (C-5), 115.2 (d, C_{ar}-3), 124.2 (d, C_{ar}-5), 124.6 (d, C_{ar}-1), 129.8 (d, C_{ar}-4), 130.4 (d, C_{ar}-6), 145.9 (C-6), 150.7 (2-CO),

160.7 (d, C_{ar}-2), 163.7 (4-CO). $J_{1ar,F} = 14.8$, $J_{2ar,F} = 247.0$, $J_{3ar,F} = 21.6$, $J_{4ar,F} = 8.1$, $J_{5ar,F} = 3.6$, $J_{6ar,F} = 4.1$, $J_{CH2,F} = 3.7$.

Methyl 5-Deoxy-2-*O*-(2-fluorobenzyl)-5-*N*-(thymine-1-yl)-3-*O*-trimethylsilyl-α-D-xylofuranoside (4). 26 mg (10%), from **2** (100 mg, 0.39 mmol) and 2,4-bis-*O*-trimethylsilylthymine[6] (454 mg, 1.68 mmol). M.p. 98–100 °C (PE/EA 1:1, $R_f = 0.20$, decomp.). $[\alpha]_D^{20} = +66.3$ (c = 1.0 in $CHCl_3$). IR: ν 3180 (NH), 1690 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.02 [s, 9H, $Si(CH_3)_3$], 1.83 (d, 3H, CH_3), 3.33 (s, 3H, OCH_3), 3.44 (dd, 1H, H-5′$_a$), 3.78 (dd, 1H, H-2′), 4.24 (ddd, 1H, H-4′), 4.28 (dd, 1H, H-5′$_b$), 4.38 (dd, 1H, H-3′), 4.74 (s, 2H, $CH_2C_6H_4F$), 4.83 (d, 1H, H-1′), 6.93 (ddd, 1H, H_{ar}-3), 7.05 (q, 1H, H-6), 7.08 (ddd, 1H, H_{ar}-5), 7.21–7.23 (m, 1H, H_{ar}-4), 7.39 (ddd, 1H, H_{ar}-6), 9.65 (bs, 1H, NH). $J_{1',2'} = 4.0$, $J_{2',3'} = 5.0$, $J_{3',4'} = 5.5$, $J_{4',5'a} = 6.1$, $J_{4',5'b} = 5.5$, $J_{5'a,5'b} = 14.2$, $J_{6,Me} = 1.2$, $J_{3ar,4ar} = 8.3$, $J_{3ar,5ar} = 1.2$, $J_{3ar,F} = 9.8$, $J_{4ar,5ar} = 7.3$, $J_{4ar,6ar} = 2.0$, $J_{5ar,6ar} = 7.5$, $J_{6ar,F} = 7.5$. ^{13}C NMR ($CDCl_3$): δ −0.1 [$Si(CH_3)_3$], 10.6 (CH_3), 46.2 (C-5′), 53.9 (OCH_3), 64.4 (d, $CH_2C_6H_4F$), 72.4 (C-3′), 74.2 (C-4′), 82.8 (C-2′), 99.7 (C-1′), 109.0 (C-5), 114.1 (d, C_{ar}-3), 122.3 (d, C_{ar}-5), 122.7 (d, C_{ar}-1), 128.0 (d, C_{ar}-4), 128.6 (d, C_{ar}-6), 139.5 (C-6), 149.8 (2-CO), 158.9 (d, C_{ar}-2), 162.2 (4-CO). $J_{1ar,F} = 14.4$, $J_{2ar,F} = 245.7$, $J_{3ar,F} = 21.4$, $J_{4ar,F} = 8.5$, $J_{5ar,F} = 3.5$, $J_{6ar,F} = 4.1$, $J_{CH2,F} = 3.6$.

Methyl 5-Deoxy-2-*O*-(2-fluorobenzyl)-5-*N*-(5-fluorouracil-1-yl)-3-*O*-trimethylsilyl-α-D-xylofuranoside (5). 179 mg (64%), from **2** (156 mg, 0.61 mmol) and 5-fluoro-2,4-bis-*O*-trimethylsilyluracil[13] (678 mg, 2.47 mmol). M.p. 133°C (PE/EA 1:3, $R_f = 0.52$). $[\alpha]_D^{20} = +138.1$ (c = 1.0 in $CHCl_3$). IR: ν 3179 (NH), 1691 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.15 [s, 9H, $Si(CH_3)_3$], 3.33 (s, 3H, OCH_3), 3.51 (dd, 1H, H-5′$_a$), 3.88 (dd, 1H, H-2′), 4.30 (ddd, 1H, H-4′), 4.37 (dd, 1H, H-5′$_b$), 4.56 (dd, 1H, H-3′), 4.75 (s, 2H, $CH_2C_6H_4F$), 4.81 (d, 1H, H-1′), 7.03 (ddd, 1H, H_{ar}-3), 7.14 (ddd, 1H, H_{ar}-5), 7.27–7.30 (m, 1H, H_{ar}-4), 7.42 (d, 1H, H-6), 7.46 (ddd, 1H, H_{ar}-6), 9.52 (d, 1H, NH). $J_{1',2'} = 4.1$, $J_{2',3'} = 5.5$, $J_{3',4'} = 6.5$, $J_{4',5'a} = 7.4$, $J_{4',5'b} = 3.7$, $J_{5'a,5'b} = 14.0$, $J_{6,F} = 5.6$, $J_{NH,F} = 4.7$, $J_{3ar,4ar} = 8.5$, $J_{3ar,5ar} = 1.2$, $J_{3ar,F} = 9.8$, $J_{4ar,5ar} = 7.7$, $J_{4ar,6ar} = 1.5$, $J_{5ar,6ar} = 7.5$, $J_{6ar,F} = 7.5$. ^{13}C NMR ($CDCl_3$): δ − 0.2 [$Si(CH_3)_3$], 49.1 (C-5′), 55.6 (OCH_3), 66.2 (d, $CH_2C_6H_4F$), 74.4 (C-3′), 75.6 (C-4′), 85.0 (C-2′), 101.1 (C-1′), 115.3 (d, C_{ar}-3), 124.3 (d, C_{ar}-5), 124.7 (d, C_{ar}-1), 129.8 (d, C_{ar}-4), 130.3 (d, C-6), 130.6 (d, C_{ar}-6), 140.2 (d, C-5), 150.1 (2-CO), 157.3 (d, 4-CO), 160.4 (d, C_{ar}-2). $J_{4,F} = 26.2$, $J_{5,F} = 237.5$, $J_{6,F} = 33.0$, $J_{1ar,F} = 14.7$, $J_{2ar,F} = 246.8$, $J_{3ar,F} = 21.5$, $J_{5ar,F} = 3.7$, $J_{6ar,F} = 4.2$, $J_{CH2,F} = 3.5$.

Methyl 5-*N*-(5-Chlorouracil-1-yl)-5-deoxy-2-*O*-(2-fluorobenzyl)-3-*O*-trimethylsilyl-α-D-xylofuranoside (6). 183 mg (68%), from **2** (145 mg, 0.57 mmol) and 5-chloro-2,4-bis-*O*-trimethylsilyluracil[13] (712 mg, 2.45 mmol). M.p. 115°C (PE/EA 1:3, $R_f = 0.50$, decomp.). $[\alpha]_D^{20} = +122.0$ (c = 1.0 in

$CHCl_3$). IR: ν 3187 (NH), 1671 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.06 [s, 9H, $Si(CH_3)_3$], 3.32 (s, 3H, OCH_3), 3.54 (dd, 1H, H-5′$_a$), 3.95 (dd, 1H, H-2′), 4.31 (ddd, 1H, H-4′), 4.44 (dd, 1H, H-5′$_b$), 4.46 (dd, 1H, H-3′), 4.75 (s, 2H, $CH_2C_6H_4F$), 4.87 (d, 1H, H-1′), 7.03 (ddd, 1H, H_{ar}-3), 7.11 (ddd, 1H, H_{ar}-5), 7.25–7.29 (m, 1H, H_{ar}-4), 7.45 (ddd, 1H, H_{ar}-6), 7.56 (s, 1H, H-6), 8.76 (bs, 1H, NH). $J_{1',2'} = 4.1$, $J_{2',3'} = 5.7$, $J_{3',4'} = 6.5$, $J_{4',5'a} = 8.3$, $J_{4',5'b} = 3.5$, $J_{5'a,5'b} = 14.5$, $J_{3ar,4ar} = 8.5$, $J_{3ar,5ar} = 1.2$, $J_{3ar,F} = 9.9$, $J_{4ar,5ar} = 7.5$, $J_{4ar,6ar} = 1.8$, $J_{5ar,6ar} = 7.5$, $J_{6ar,F} = 7.5$. ^{13}C NMR ($CDCl_3$): δ; −0.1 [$Si(CH_3)_3$], 49.6 (C-5′), 55.6 (OCH_3), 66.2 (d, $CH_2C_6H_4F$), 74.6 (C-3′), 75.3 (C-4′), 84.7 (C-2′), 101.0 (C-1′), 108.6 (C-5), 115.2 (d, C_{ar}-3), 124.2 (d, C_{ar}-5), 124.6 (d, C_{ar}-1), 129.9 (d, C_{ar}-4), 130.5 (d, C_{ar}-6), 142.6 (C-6), 150.6 (2-CO), 159.5 (4-CO), 160.6 (d, C_{ar}-2). $J_{1ar,F} = 14.6$, $J_{2ar,F} = 247.2$, $J_{3ar,F} = 21.4$, $J_{4ar,F} = 8.3$, $J_{5ar,F} = 3.6$, $J_{6ar,F} = 4.2$, $J_{CH2,F} = 3.6$.

Methyl 5-*N*-(5-Bromouracil-1-yl)-5-deoxy-2-*O*-(2-fluorobenzyl)-3-*O*-trimethylsilyl-α-D-xylofuranoside (7). 211 mg (73%), from **2** (142 mg, 0.56 mmol) and 5-bromo-2,4-bis-*O*-trimethylsilyluracil[13] (792 mg, 2.07 mmol). M.p. 129°C (PE/EA 1:3, $R_f = 0.54$). $[\alpha]_D^{20} = +109.0$ (c = 1.0 in $CHCl_3$). IR: ν; 3208 (NH), 1695 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.01 [s, 9H, $Si(CH_3)_3$], 3.32 (s, 3H, OCH_3), 3.60 (dd, 1H, H-5′$_a$), 3.94 (dd, 1H, H-2′), 4.22 (ddd, 1H, H-4′), 4.35 (dd, 1H, H-5′$_b$), 4.54 (dd, 1H, H-3′), 4.77 (s, 2H, $CH_2C_6H_4F$), 4.89 (d, 1H, H-1′), 7.02 (ddd, 1H, H_{ar}-3), 7.12 (ddd, 1H, H_{ar}-5), 7.26–7.29 (m, 1H, H_{ar}-4), 7.46 (ddd, 1H, H_{ar}-6), 7.65 (s, 1H, H-6), 9.66 (bs, 1H, NH). $J_{1',2'} = 4.2$, $J_{2',3'} = 6.0$, $J_{3',4'} = 6.0$, $J_{4',5'a} = 9.2$, $J_{5'a,5'b} = 14.3$, $J_{3ar,4ar} = 8.3$, $J_{3ar,5ar} = 1.1$, $J_{3ar,F} = 9.9$, $J_{4ar,5ar} = 7.5$, $J_{4ar,6ar} = 1.8$, $J_{5ar,6ar} = 7.5$, $J_{6ar,F} = 7.5$. ^{13}C NMR ($CDCl_3$): δ −0.1 [$Si(CH_3)_3$], 48.1 (C-5′), 55.8 (OCH_3), 66.3 (d, $CH_2C_6H_4F$), 74.3 (C-3′), 74.9 (C-4′), 84.8 (C-2′), 96.3 (C-5), 101.0 (C-1′), 115.3 (d, C_{ar}-3), 124.2 (d, C_{ar}-5), 124.5 (d, C_{ar}-1), 129.9 (d, C_{ar}-4), 130.5 (d, C_{ar}-6), 145.2 (C-6), 150.7 (2-CO), 160.8 (d, C_{ar}-2), 164.1 (4-CO). $J_{1ar,F} = 14.5$, $J_{2ar,F} = 247.4$, $J_{3ar,F} = 21.4$, $J_{4ar,F} = 8.1$, $J_{5ar,F} = 3.6$, $J_{6ar,F} = 4.2$, $J_{CH2,F} = 3.7$.

Methyl 5-Deoxy-2-*O*-(2-fluorobenzyl)-5-*N*-(5-iodouracil-1-yl)-3-*O*-trimethylsilyl-α-D-xylofuranoside (8). 269 mg (76%), from **2** (160 mg, 0.63 mmol) and 5-iodo-2,4-bis-*O*-trimethylsilyluracil[13] (920 mg, 2.41 mmol). M.p. 156–158°C (PE/EA 1:3, $R_f = 0.50$, decomp.). $[\alpha]_D^{20} = +90.0$ (c = 1.0 in $CHCl_3$). IR: ν 3205 (NH), 1679 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.10 [s, 9H, $Si(CH_3)_3$], 3.37 (s, 3H, OCH_3), 3.61 (dd, 1H, H-5′$_a$), 3.84 (dd, 1H, H-2′), 4.14–4.21 (m, 2H, H-4′, H-5′$_b$), 4.40 (dd, 1H, H-3′), 4.66 (s, 2H, $CH_2C_6H_4F$), 4.90 (d, 1H, H-1′), 7.03 (ddd, 1H, H_{ar}-3), 7.11 (ddd, 1H, H_{ar}-5), 7.25–7.29 (m, 1H, H_{ar}-4), 7.45 (ddd, 1H, H_{ar}-6), 7.73 (s, 1H, H-6), 8.75 (bs, 1H, NH). $J_{1'2'} = 4.1$, $J_{2',3'} = 5.7$, $J_{3'4'} = 6.0$, $J_{4',5'a} = 9.2$, $J_{5'a,5'b} = 14.6$, $J_{3ar,4ar} = 8.5$, $J_{3ar,5ar} = 1.1$, $J_{3ar,F} = 9.9$, $J_{4ar,5ar} = 7.5$, $J_{4ar,6ar} = 1.8$, $J_{5ar,6ar} = 7.5$, $J_{6ar,F} = 7.5$. ^{13}C NMR ($CDCl_3$): δ −0.1 [$Si(CH_3)_3$], 48.3 (C-5′), 55.6

(OCH_3), 66.2 (d, $CH_2C_6H_4F$), 67.2 (C-5), 73.0 (C-3′), 74.9 (C-4′), 85.1 (C-2′), 101.0 (C-1′), 115.2 (d, C_{ar}-3), 124.2 (d, C_{ar}-5), 124.6 (d, C_{ar}-1), 129.8 (d, C_{ar}-4), 130.4 (d, C_{ar}-6), 150.4 (C-6), 151.1 (2-CO), 160.9 (d, C_{ar}-2), 162.1 (4-CO). $J_{1ar,F} = 14.5$, $J_{2ar,F} = 246.8$, $J_{3ar,F} = 21.5$, $J_{4ar,F} = 8.3$, $J_{5ar,F} = 3.7$, $J_{6ar,F} = 4.4$, $J_{CH2,F} = 3.6$.

Methyl 5-Deoxy-2-*O*-(2-fluorobenzyl)-5-*N*-(6-methyluracil-1-yl)-3-*O*-trimethylsilyl-α-D-xylofuranoside (9). 153 mg (80%), from **2** (107 mg, 0.42 mmol) and 6-methyl-2,4-bis-*O*-trimethylsilyluracil[7] (430 mg, 1.59 mmol). M.p. 153–156°C (EA, $R_f = 0.36$, decomp.). $[\alpha]_D^{20} = +129.4$ (c = 1.0 in $CHCl_3$). IR: ν 3192 (NH), 1688 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.14 [s, 9H, $Si(CH_3)_3$], 2.26 (s, 3H, CH_3), 3.37 (s, 3H, OCH_3), 3.67 (dd, 1H, H-5′$_a$), 3.82 (dd, 1H, H-2′), 4.12 (dd, 1H, H-5′$_b$), 4.41 (ddd, 1H, H-4′), 4.48 (dd, 1H, H-3′), 4.64, 4.68 (AB-system, 2H, $CH_2C_6H_4F$), 4.82 (d, 1H, H-1′), 5.52 (s, 1H, H-5), 7.02 (ddd, 1H, H_{ar}-3), 7.12 (ddd, 1H, H_{ar}-5), 7.27 (dddd, 1H, H_{ar}-4), 7.44 (ddd, 1H, H_{ar}-6), 9.65 (bs, 1H, NH). $J_{1',2'} = 4.1$, $J_{2'3'} = 5.5$, $J_{3',4'} = 6.7$, $J_{4',5'a} = 9.9$, $J_{4',5'b} = 2.4$, $J_{5'a,'b} = 14.9$, $J_{AB} = 12.4$, $J_{A,B,F} = 0.8$, $J_{3ar,4ar} = 8.4$, $J_{3ar,5ar} = 1.2$, $J_{3ar,F} = 9.9$, $J_{4ar,5ar} = 7.6$, $J_{4ar,6ar} = 1.8$, $J_{5ar,6ar} = 7.5$, $J_{6ar,F} = 7.5$. ^{13}C NMR ($CDCl_3$): δ − 0.2 [$Si(CH_3)_3$], 22.8 (CH_3), 45.7 (C-5′), 55.5 (OCH_3), 66.1 (d, $CH_2C_6H_4F$), 74.8 (C-4′), 75.3 (C-3′), 85.5 (C-2′), 100.6 (C-1′), 101.8 (C-5), 115.1 (d, C_{ar}-3), 124.1 (d, C_{ar}-5), 124.7 (d, C_{ar}-1), 129.6 (d, C_{ar}-4), 130.3 (d, C_{ar}-6), 151.5, 155.1 (2-CO, C-6), 163.2 (d, C_{ar}-2), 163.8 (4-CO). $J_{1ar,F} = 14.5$, $J_{2ar,F} = 246.8$, $J_{3ar,F} = 21.4$, $J_{4ar,F} = 8.2$, $J_{5ar,F} = 3.6$, $J_{6ar,F} = 4.2$, $J_{CH2,F} = 3.8$.

Methyl 5-Deoxy-5-*N*-(5,6-dimethyluracil-1-yl)-2-*O*-(2-fluorobenzyl)-3-*O*-tri-methylsilyl-α-D-xylofuranoside (10). 129 mg (71%), from **2** (104 mg, 0.41 mmol) and 5,6-dimethyl-2,4-bis-*O*-trimethylsilyluracil[7] (448 mg, 1.57 mmol). M.p. 169°C (PE/EA 1:6, $R_f = 0.57$). $[\alpha]_D^{20} = +145.9$ (c = 1.0 in $CHCl_3$). IR: ν 3178 (NH), 1674 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.14 [s, 9H, $Si(CH_3)_3$], 1.95 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 3.31 (s, 3H, OCH_3), 3.75 (dd, 1H, H-5′$_a$), 3.83 (dd, 1H, H-2′), 4.15 (dd, 1H, H-5′$_b$), 4.42 (ddd, 1H, H-4′), 4.49 (dd, 1H, H-3′), 4.65, 4.69 (AB-system, 2H, $CH_2C_6H_4F$), 4.82 (d, 1H, H-1′), 7.03 (ddd, 1H, H_{ar}-3), 7.13 (ddd, 1H, H_{ar}-5), 7.27 (dddd, 1H, H_{ar}-4), 7.44 (ddd, 1H, H_{ar}-6), 9.64 (bs, 1H, NH). $J_{1',2'} = 4.1$, $J_{2',3'} = 5.5$, $J_{3',4'} = 6.8$, $J_{4',5'a} = 9.7$, $J_{4',5'b} = 2.4$, $J_{5'a,5'b} = 15.1$, $J_{AB} = 12.3$, $J_{3ar,4ar} = 8.5$, $J_{3ar,5ar} = 0.9$, $J_{3ar,F} = 9.8$, $J_{4ar,5ar} = 7.6$, $J_{4ar,6ar} = 1.8$, $J_{5ar,6ar} = 7.5$, $J_{6ar,F} = 7.5$. ^{13}C NMR ($CDCl_3$): δ − 0.2 [$Si(CH_3)_3$], 11.2 (CH_3), 17.0 (CH_3), 45.9 (C-5′), 55.4 (OCH_3), 66.1 (d, $CH_2C_6H_4F$), 75.0 (C-4′), 75.3 (C-3′), 85.5 (C-2′), 100.5 (C-1′), 107.5 (C-5), 115. (1, C_{ar}-3), 124.1 (d, C_{ar}-5), 124.7 (d, C_{ar}-1), 129.6 (d, C_{ar}-4), 130.3 (d, C_{ar}-6), 149.9, 151.0 (2-CO, C-6), 160.6 (d, C_{ar}-2), 163.8 (4-CO). $J_{1ar,F} = 14.6$, $J_{2ar,F} = 246.8$, $J_{3ar,F} = 21.5$, $J_{4ar,F} = 8.1$, $J_{5ar,F} = 3.7$, $J_{6ar,F} = 4.2$, $J_{CH2,F} = 3.8$.

Desilylation of 3–10 ***(General procedure B).*** A solution of the 3-*O*-trimethylsilyl-isonucleoside (5–50 mmol) in $CHCl_3$ (10–100 mL) containing traces of HCl due to spontaneous hydrolysis was stirred at 20°C for 24–100 h. When the reaction was complete (TLC control) the $CHCl_3$ was removed in vacuo. The products were obtained as colourless crystals by recrystallisation from H_2O/MeCN (20:1) or as white solids (**13**, **18**, and **20**) by column chromatography. In the latter cases, appropriate eluents are given with the melting points (M.p.).

Methyl 5-Deoxy-2-*O*-(2-fluorobenzyl)-5-*N*-(uracil-1-yl)-α-D-xylofuranoside (12). 6 mg (34%), from **3** (21 mg, 0.05 mmol, 100 h). M.p. 127°C. $[\alpha]_D^{20} = +73.2$ (c = 0.6 in $CHCl_3$). IR: ν 3443 (OH), 1691 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 3.36 (s, 3H, OCH_3), 3.56 (dd, 1H, H-5′$_a$), 3.89 (dd, 1H, H-2′), 4.30 (ddd, 1H, H-4′), 4.36 (dd, 1H, H-5′$_b$), 4.49 (dd, 1H, H-3′), 4.74 (s, 2H, $CH_2C_6H_4F$), 4.87 (d, 1H, H-1′), 5.69 (d, 1H, H-5), 7.03 (ddd, 1H, H_{ar}-3), 7.13 (ddd, 1H, H_{ar}-5), 7.25–7.31 (m, 1H, H_{ar}-4), 7.29 (d, 1H, H-6), 7.45 (ddd, 1H, H_{ar}-6), 9.54 (bs, 1H, NH). $J_{1',2'} = 4.2$, $J_{2',3'} = 5.5$, $J_{3',4'} = 5.7$, $J_{4',5'a} = 7.1$, $J_{4',5'b} = 4.4$, $J_{5'a,5'b} = 14.1$, $J_{5,6} = 7.9$, $J_{3ar,4ar} = 8.4$, $J_{3ar,5ar} = 1.2$, $J_{3ar,F} = 9.9$, $J_{4ar,5ar} = 7.5$, $J_{4ar,6ar} = 1.8$, $J_{5ar,6ar} = 7.5$, $J_{6ar,F} = 7.5$. ^{13}C NMR ($CDCl_3$): δ 48.7 (C-5′), 55.7 (OCH_3), 66.2 (d, $CH_2C_6H_4F$), 74.3 (C-3′), 75.8 (C-4′), 84.8 (C-2′), 101.2 (C-1′), 102.2 (C-5), 115.3 (d, C_{ar}-3), 124.2 (d, C_{ar}-5), 124.6 (d, C_{ar}-1), 129.8 (d, C_{ar}-4), 130.5 (d, C_{ar}-6), 145.7 (C-6), 151.4 (2-CO), 160.8 (d, C_{ar}-2), 163.7 (4-CO). $J_{1ar,F} = 14.6$, $J_{2ar,F} = 247.0$, $J_{3ar,F} = 21.5$, $J_{4ar,F} = 8.4$, $J_{5ar,F} = 3.7$, $J_{6ar,F} = 4.2$, $J_{CH2,F} = 3.7$. FAB MS (*m*NBA) *m*/*z*: 367 [M + H]. FAB HRMS (*m*NBA) calcd 367.1305 ($C_{17}H_{20}FN_2O_6$); found 367.1348.

Methyl 5-Deoxy-2-*O*-(2-fluorobenzyl)-5-*N*-(thymine-1-yl)-α-D-xylofuranoside (13). 14 mg (64%), from **4** (25 mg, 0.06 mmol, 48 h). M.p. 118°C (PE/EA 1:3, $R_f = 0.17$). $[\alpha]_D^{20} = +84.4$ (c = 1.0 in $CHCl_3$). IR: ν 3441 (OH), 1678 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.85 (d, 3H, CH_3), 3.32 (s, 3H, OCH_3), 3.46 (dd, 1H, H-5′$_a$), 3.80 (dd, 1H, H-2′), 4.24 (ddd, 1H, H-4′), 4.29 (dd, 1H, H-5′$_b$), 4.38 (dd, 1H, H-3′), 4.68 (s, 2H, $CH_2C_6H_4F$), 4.84 (d, 1H, H-1′), 6.97 (ddd, 1H, H_{ar}-3), 7.03 (q, 1H, H-6), 7.07 (ddd, 1H, H_{ar}-5), 7.22 (dddd, 1H, H_{ar}-4), 7.40 (ddd, 1H, H_{ar}-6), 9.24 (bs, 1H, NH). $J_{1',2'} = 4.1$, $J_{2',3'} = 5.0$, $J_{3',4'} = 5.5$, $J_{4',5'a} = 6.0$, $J_{4',5'b} = 5.4$, $J_{5'a,5'b} = 14.0$, $J_{6,Me} = 1.2$, $J_{3ar,4ar} = 8.4$, $J_{3ar,5ar} = 1.2$, $J_{3ar,F} = 9.9$, $J_{4ar,5ar} = 7.5$, $J_{4ar,6ar} = 1.8$, $J_{4ar,F} = 5.6$, $J_{5ar,6ar} = 7.5$, $J_{6ar,F} = 7.5$. ^{13}C NMR ($CDCl_3$): δ 10.4 (CH_3), 46.3 (C-5′), 53.9 (OCH3), 64.4 (d, $CH_2C_6H_4F$), 72.4 (C-3′), 74.3 (C-4′), 82.7 (C-2′), 99.7 (C-1′), 109.1 (C-5), 113.3 (d, C_{ar}-3), 122.3 (d, C_{ar}-5), 122.8 (d, C_{ar}-1), 127.8 (d, C_{ar}-4), 128.6 (d, C_{ar}-6), 139.5 (C-6), 149.7 (2-CO), 158.9 (d, C_{ar}-2), 162.1 (4-CO). $J_{1ar,F} = 14.5$, $J_{2ar,F} = 246.9$, $J_{3ar,F} = 21.4$, $J_{4ar,F} = 8.3$, $J_{5ar,F} = 3.6$, $J_{6ar,F} = 4.1$, $J_{CH2,F} = 3.8$. FAB MS (*m*NBA) *m*/*z* 381 [M + H]. FAB HRMS (*m*NBA) calcd 381.1462 ($C_{18}H_{22}FN_2O_6$); found 381.1485.

Methyl 5-Deoxy-2-*O*-(2-fluorobenzyl)-5-*N*-(5-fluorouracil-1-yl)-α-D-xylofuranoside (14). 129 mg (88%), from **5** (175 mg, 0.38 mmol, 48 h). M.p. 151–152°C. $[\alpha]_D^{20} = +124.8$ (c = 1.0 in $CHCl_3$). IR: ν 3439 (OH), 3203 (NH), 1693 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 3.36 (s, 3H, OCH_3), 3.51 (dd, 1H, H-5′$_a$), 3.89 (dd, 1H, H-2′), 4.32 (ddd, 1H, H-4′), 4.37 (dd, 1H, H-5′$_b$), 4.54 (dd, 1H, H-3′), 4.74 (s, 2H, CH_2C$_6$H$_4$F), 4.87 (d, 1H, H-1′), 7.04 (ddd, 1H, H$_{ar}$-3), 7.14 (ddd, 1H, H$_{ar}$-5), 7.29 (dddd, 1H, H$_{ar}$-4), 7.42 (d, 1H, H-6), 7.45 (ddd, 1H, H$_{ar}$-6), 9.68 (d, 1H, NH). $J_{1',2'} = 4.2$, $J_{2',3'} = 5.8$, $J_{3',4'} = 6.5$, $J_{4',5'a} = 7.4$, $J_{4',5'b} = 3.8$, $J_{5'a,5'b} = 14.1$, $J_{6,F} = 5.6$, $J_{NH,F} = 4.8$, $J_{3ar,4ar} = 8.4$, $J_{3ar,5ar} = 1.2$, $J_{3ar,F} = 9.9$, $J_{4ar,5ar} = 7.6$, $J_{4ar,6ar} = 1.9$, $J_{4ar,F} = 5.5$, $J_{5ar,6ar} = 7.5$, $J_{6ar,F} = 7.5$. ^{13}C NMR ($CDCl_3$): δ 49.1 (C-5′), 55.7 (OCH_3), 66.2 (d, CH_2C$_6$H$_4$F), 74.4 (C-3′), 75.5 (C-4′), 84.9 (C-2′), 101.1 (C-1′), 115.3 (d, C$_{ar}$-3), 124.2 (d, C$_{ar}$-5), 124.5 (d, C$_{ar}$-1), 129.9 (d, C$_{ar}$-4), 130.1 (d, C-6), 130.6 (d, C$_{ar}$-6), 140.2 (d, C-5), 150.0 (2-CO), 157.3 (d, 4-CO), 160.8 (d, C$_{ar}$-2). $J_{4,F} = 26.2$, $J_{5,F} = 237.1$, $J_{6,F} = 32.9$, $J_{1ar,F} = 14.7$, $J_{2ar,F} = 247.1$, $J_{3ar,F} = 21.5$, $J_{4ar,F} = 8.2$, $J_{5ar,F} = 3.6$, $J_{6ar,F} = 4.1$, $J_{CH2,F} = 3.6$. ^{19}F NMR ($CDCl_3$): δ −166.58 (dd, 1F, F-5, $J = 5.3$, 5.3 Hz), −119.11 (m, 1F, $CH_2C_6H_4F$). FAB MS (*m*NBA) *m/z* 385 [M + H]. FAB HRMS (*m*NBA) calcd 385.1211 ($C_{17}H_{19}F_2N_2O_6$); found 385.1104.

Methyl 5-*N*-(5-Chlorouracil-1-yl)-5-deoxy-2-*O*-(2-fluorobenzyl)-α-D-xylofuranoside (15). 138 mg (90%), from **6** (181 mg, 0.38 mmol, 48 h). M.p. 166°C. $[\alpha]_D^{20} = +115.2$ (c = 1.0 in $CHCl_3$). IR: ν 3421 (OH), 3192 (NH), 1680 (C=O), 1623 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 3.35 (s, 3H, OCH_3), 3.54 (dd, 1H, H-5′$_a$), 3.92 (dd, 1H, H-2′), 4.32 (ddd, 1H, H-4′), 4.39 (dd, 1H, H-5′$_b$), 4.57 (dd, 1H, H-3′), 4.74 (s, 2H, CH_2C$_6$H$_4$F), 4.86 (d, 1H, H-1′), 7.03 (ddd, 1H, H$_{ar}$-3), 7.12 (ddd, 1H, H$_{ar}$-5), 7.28 (dddd, 1H, H$_{ar}$-4), 7.45 (ddd, 1H, H$_{ar}$-6), 7.54 (s, 1H, H-6), 10.00 (bs, 1H, NH). $J_{1',2'} = 4.2$, $J_{2',3'} = 6.0$, $J_{3',4'} = 6.5$, $J_{4',5'a} = 8.2$, $J_{4'5'b} = 3.5$, $J_{5'a,5'b} = 14.4$, $J_{3ar,4ar} = 8.5$, $J_{3ar,5ar} = 1.1$, $J_{3ar,F} = 9.8$, $J_{4ar,5ar} = 7.6$, $J_{4ar,6ar} = 1.9$, $J_{4ar,F} = 5.7$, $J_{5ar,6ar} = 7.5$, $J_{6ar,F} = 7.5$. ^{13}C NMR ($CDCl_3$): δ 49.5 (C-5′), 55.7 (OCH_3), 66.2 (d, CH_2C$_6$H$_4$F), 74.3 (C-3′), 75.3 (C-4′), 84.7 (C-2′), 100.9 (C-1′), 108.6 (C-5), 115.3 (d, C$_{ar}$-3), 124.2 (d, C$_{ar}$-5), 124.5 (d, C$_{ar}$-1), 129.8 (d, C$_{ar}$-4), 130.5 (d, C$_{ar}$-6), 142.7 (C-6), 150.6 (2-CO), 159.6 (4-CO), 160.8 (d, C$_{ar}$-2). $J_{1ar,F} = 14.5$, $J_{2ar,F} = 236.1$, $J_{3ar,F} = 21.4$, $J_{4ar,F} = 8.3$, $J_{5ar,F} = 3.7$, $J_{6ar,F} = 5.0$, $J_{CH2,F} = 3.6$. FAB MS (*m*NBA) *m/z*: 401 [M + H]. FAB HRMS (*m*NBA) calcd 401.0916 ($C_{17}H_{19}ClFN_2O_6$); found 401.0840.

Methyl 5-*N*-(5-Bromouracil-1-yl)-5-deoxy-2-*O*-(2-fluorobenzyl)-α-D-xylofuranoside (16). 146 mg (82%), from **7** (206 mg, 0.40 mmol, 72 h). M.p. 169°C. $[\alpha]_D^{20} = +100.5$ (c = 1.0 in $CHCl_3$). IR: ν 3442 (OH), 3196 (NH), 1690 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 3.37 (s, 3H, OCH_3), 3.59 (dd, 1H, H-5′$_a$), 3.90 (dd, 1H, H-2′), 4.37–4.37 (m, 2H, H-4′, H-5′$_b$), 4.54 (dd, 1H, H-3′), 4.74 (s, 2H, CH_2C$_6$H$_4$F), 4.88 (d, 1H, H-1′), 7.04 (ddd, 1H, H$_{ar}$-3), 7.14

(ddd, 1H, H_{ar}-5), 7.29 (dddd, 1H, H_{ar}-4), 7.45 (ddd, 1H, H_{ar}-6), 7.65 (s, 1H, H-6), 9.43 (bs, 1H, NH). $J_{1',2'} = 4.2$, $J_{2',3'} = 5.8$, $J_{3',4'} = 6.0$, $J_{4',5'a} = 9.1$, $J_{5'a,5'b} = 14.5$, $J_{3ar,4ar} = 8.3$, $J_{3ar,5ar} = 1.2$, $J_{3ar,F} = 9.9$, $J_{4ar,5ar} = 7.5$, $J_{4ar,6ar} = 1.9$, $J_{4ar,F} = 5.4$, $J_{5ar,6ar} = 7.5$, $J_{6ar,F} = 7.5$. ^{13}C NMR ($CDCl_3$): δ 49.3 (C-5′), 55.7 (OCH_3), 66.3 (d, $CH_2C_6H_4F$), 74.4 (C-3′), 75.3 (C-4′), 84.8 (C-2′), 96.3 (C-5), 101.0 (C-1′), 115.3 (d, C_{ar}-3), 124.2 (d, C_{ar}-5), 124.5 (d, C_{ar}-1), 129.9 (d, C_{ar}-4), 130.6 (d, C_{ar}-6), 145.1 (C-6), 150.6 (2-CO), 160.8 (d, C_{ar}-2), 164.2 (4-CO). $J_{1ar,F} = 14.6$, $J_{2ar,F} = 247.2$, $J_{3ar,F} = 21.5$, $J_{4ar,F} = 8.1$, $J_{5ar,F} = 3.6$, $J_{6ar,F} = 4.2$, $J_{CH2,F} = 3.8$. FAB MS (*m*NBA) *m/z*: 445 [M + H for ^{79}Br], 447 [M + H for ^{81}Br]. FAB HRMS (*m*NBA) calcd 445.0411 ($C_{17}H_{19}{}^{79}BrFN_2O_6$), 447.0390 ($C_{17}H_{19}{}^{81}BrFN_2O_6$); found 445.0398, 447.0451.

Methyl 5-Deoxy-2-*O*-(2-fluorobenzyl)-5-*N*-(5-iodouracil-1-yl)-α-D-xylo-furanoside (17). 205 mg (88%), from **8** (266 mg, 0.47 mmol, 24 h). M.p. 203°C. $[\alpha]_D^{20} = +82.0$ (c = 1.0 in $CHCl_3$). IR: ν 3446 (OH), 3188 (NH), 1690 (C=O), 1614 (C=O) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 3.32 (s, 3H, OCH_3), 3.53 (dd, 1H, H-5′$_a$), 3.84 (dd, 1H, H-2′), 4.14–4.21 (m, 2H, H-4′, H-5′$_b$), 4.41 (dd, 1H, H-3′), 4.67, 4.71 (AB-system, 2H, $CH_2C_6H_4F$), 4.84 (d, 1H, H-1′), 7.01 (ddd, 1H, H_{ar}-3), 7.10 (ddd, 1H, H_{ar}-5), 7.26 (dddd, 1H, H_{ar}-4), 7.41 (ddd, 1H, H_{ar}-6), 7.74 (s, 1H, H-6), 9.78 (bs, 1H, NH). $J_{1',2'} = 4.2$, $J_{2',3'} = 5.7$, $J_{3',4'} = 5.9$, $J_{4',5'a} = 9.1$, $J_{5'a,5'b} = 15.3$, $J_{AB} = 12.3$, $J_{AB,F} = 1.0$, $J_{3ar,4ar} = 8.4$, $J_{3ar,5ar} = 1.2$, $J_{3ar,F} = 9.9$, $J_{4ar,5ar} = 7.5$, $J_{4ar,6ar} = 1.9$, $J_{4ar,F} = 5.6$, $J_{5ar,6ar} = 7.5$, $J_{6ar,F} = 7.5$. ^{13}C NMR ($CDCl_3$): δ 49.2 (C-5′), 55.6 (OCH_3), 66.2 (d, $CH_2C_6H_4F$), 67.4 (C-5), 72.8 (C-3′), 75.8 (C-4′), 84.9 (C-2′), 101.0 (C-1′), 115.2 (d, C_{ar}-3), 124.1 (d, C_{ar}-5), 124.4 (d, C_{ar}-1), 129.8 (d, C_{ar}-4), 130.4 (d, C_{ar}-6), 150.2 (C-6), 151.0 (2-CO), 160.7 (d, C_{ar}-2), 161.5 (4-CO). $J_{1ar,F} = 14.6$, $J_{2ar,F} = 247.2$, $J_{3ar,F} = 21.5$. $J_{4ar,F} = 8.3$, $J_{5ar,F} = 3.7$, $J_{6ar,F} = 4.2$, $J_{CH2,F} = 3.8$. FAB MS (*m*NBA) *m/z*: 493 [M + H]. FAB HRMS (*m*NBA) calcd 493.0272 ($C_{17}H_{19}FIN_2O_6$); found 493.0295.

Methyl 5-Deoxy-2-*O*-(2-fluorobenzyl)-5-*N*-(6-methyluracil-1-yl)-α-D-xylo-furanoside (18). 82 mg (65%), from **9** (149 mg, 0.33 mmol, 24 h). M.p. 169°C (EtOAc, $R_f = 0.10$). $[\alpha]_D^{20} = +101.5$ (c = 1.0 in $CHCl_3$). IR: ν 3424 (OH), 3218 (NH), 1679 (C=O) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 2.31 (s, 3H, CH_3), 3.36 (s, 3H, OCH_3), 3.74 (dd, 1H, H-5′$_a$), 3.96 (dd, 1H, H-2′), 4.33 (ddd, 1H, H-4′), 4.39 (dd, 1H, H-5′$_b$), 4.44 (dd, 1H, H-3′), 4.75 (s, 2H, $CH_2C_6H_4F$), 4.90 (d, 1H, H-1′), 5.59 (s, 1H, H-5), 7.02 (ddd, 1H, H_{ar}-3), 7.12 (ddd, 1H, H_{ar}-5), 7.26 (dddd, 1H, H_{ar}-4), 7.47 (ddd, 1H, H_{ar}-6), 10.02 (bs, 1H, NH). $J_{1',2'} = 4.2$, $J_{2',3'} = 4.9$, $J_{3',4'} = 5.3$, $J_{4',5'a} = 6.9$, $J_{4',5'b} = 4.6$, $J_{5'a,5'b} = 14.6$, $J_{3ar,4ar} = 8.5$, $J_{3ar,5ar} = 1.2$, $J_{3ar,F} = 9.9$, $J_{4ar,5ar} = 7.5$, $J_{4ar,6ar} = 1.9$, $J_{5ar,6ar} = 7.5$, $J_{6ar,F} = 7.8$. ^{13}C NMR ($CDCl_3$): δ 20.6 (CH_3), 44.6 (C-5′), 55.8 (OCH_3), 66.2 (d, $CH_2C_6H_4F$), 74.3 (C-3′), 76.4 (C-4′), 84.8 (C-2′), 101.4 (C-1′), 102.6 (C-5), 115.2 (d, C_{ar}-3), 124.1 (d, C_{ar}-5), 124.8

(d, C_{ar}-1), 129.6 (d, C_{ar}-4), 130.4 (d, C_{ar}-6), 152.3, 155.0 (2-CO, C-6), 160.7 (d, C_{ar}-2), 163.0 (4-CO). $J_{1ar,F} = 14.6$, $J_{2ar,F} = 247.0$, $J_{3ar,F} = 21.4$, $J_{4ar,F} = 8.1$, $J_{5ar,F} = 3.6$, $J_{6ar,F} = 4.2$, $J_{CH2,F} = 3.7$. FAB MS (*m*NBA) *m/z* 381 [M+H]. FAB HRMS (*m*NBA) calcd 381.1462 ($C_{18}H_{22}FN_2O_6$); found 381.1411.

Methyl 5-Deoxy-5-*N*-(5,6-dimethyluracil-1-yl)-2-*O*-(2-fluorobenzyl)-α-D-xylofuranoside (19). 73 mg (70%), from **10** (123 mg, 0.26 mmol, 100 h). M.p. 188°C. $[\alpha]_D^{20} = +110.7$ (c = 1.0 in $CHCl_3$). IR: ν 3426 (OH), 3218 (NH), 1679 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.96 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 3.38 (s, 3H, OCH_3), 3.78 (dd, 1H, H-5′$_a$), 3.98 (dd, 1H, H-2′), 4.31 (ddd, 1H, H-4′), 4.38 (dd, 1H, H-3′), 4.45 (dd, 1H, H-5′$_b$), 4.75 (s, 2H, $CH_2C_6H_4F$), 4.93 (d, 1H, H-1′), 7.01 (ddd, 1H, H_{ar}-3), 7.11 (ddd, 1H, H_{ar}-5), 7.26 (dddd, 1H, H_{ar}-4), 7.47 (ddd, 1H, H_{ar}-6), 10.00 (bs, 1H, NH). $J_{1',2'} = 4.1$, $J_{2',3'} = 4.5$, $J_{3',4'} = 5.3$, $J_{4',5'a} = 6.5$, $J_{4',5'b} = 5.5$, $J_{5'a,5'b} = 15.1$, $J_{3ar,4ar} = 8.5$, $J_{3ar,5ar} = 1.0$, $J_{3ar,F} = 9.8$, $J_{4ar,5ar} = 7.6$, $J_{4ar,6ar} = 1.8$, $J_{5ar,6ar} = 7.5$, $J_{6ar,F} = 7.5$. ^{13}C NMR ($CDCl_3$): δ 11.3 (CH_3), 16.8 (CH_3), 44.4 (C-5′), 55.9 (OCH_3), 66.3 (d, $CH_2C_6H_4F$), 74.3 (C-3′), 76.9 (C-4′), 84.6 (C-2′), 101.8 (C-1′), 108.8 (C-5), 115.2 (d, C_{ar}-3), 124.1 (d, C_{ar}-5), 124.8 (d, C_{ar}-1), 129.5 (d, C_{ar}-4), 130.4 (d, C_{ar}-6), 149.5, 151.9 (2-CO, C-6), 160.7 (d, C_{ar}-2), 163.5 (4-CO). $J_{1ar,F} = 14.6$, $J_{2ar,F} = 246.8$, $J_{3ar,F} = 21.5$, $J_{4ar,F} = 8.1$, $J_{5ar,F} = 3.6$, $J_{6ar,F} = 4.2$, $J_{CH2,F} = 3.8$. FAB MS (mNBA) *m/z* 395 [M + H]. FAB HRMS (*m*NBA) calcd 395.1618 ($C_{19}H_{24}FN_2O_6$); found 395.1584.

Methyl 5-Deoxy-2-*O*-(2-fluorobenzyl)-5-*N*-(5-nitrouracil-1-yl)-α-D-xylofuranoside (20). The nitro derivative **20** was obtained directly according to the ***General procedure A*** from **2** (96 mg, 0.38 mmol) and 5-nitro-2,4-bis-*O*-trimethylsilyluracil[8] (460 mg, 1.53 mmol). Yield: 13 mg (8%). M.p. 164–166°C (PE/EA 1:3, $R_f = 0.19$, decomp.). $[\alpha]_D^{20} = +73.7$ (c = 1.0 in MeOH). IR: ν 3476 (OH), 1706 (C=O), 1614 (C=O), 1513 (NO_2), 1370 (NO_2) cm^{-1}. ^1H NMR ($CDCl_3$): δ 3.31 (s, 3H, OCH_3), 3.80 (dd, 1H, H-5′$_a$), 3.93 (dd, 1H, H-2′), 4.30–4.36 (m, 2H, H-4′, H-5′$_b$), 4.41 (dd, 1H, H-3′), 4.67, 4.71 (AB-system, 2H, $CH_2C_6H_4F$), 4.90 (d, 1H, H-1′), 7.02 (ddd, 1H, H_{ar}-3), 7.12 (ddd, 1H, H_{ar}-5), 7.28–7.31 (m, 1H, H_{ar}-4), 7.45 (ddd, 1H, H_{ar}-6), 9.06 (s, 1H, H-6). $J_{1',2'} = 4.2$, $J_{2',3'} = 5.6$, $J_{3',4'} = 6.2$, $J_{4',5'a} = 9.7$, $J_{5'a,5'b} = 15.1$, $J_{AB} = 12.0$, $J_{3ar,4ar} = 8.6$, $J_{3ar,5ar} = 1.1$, $J_{3ar,F} = 9.9$, $J_{4ar,5ar} = 7.5$, $J_{4ar,6ar} = 1.6$, $J_{5ar,6ar} = 7.5$, $J_{6ar,F} = 7.5$. ^{13}C NMR ($CDCl_3$): δ 51.4 (C-5′), 56.2 (OCH_3), 67.4 (d, $CH_2C_6H_4F$), 75.0 (C-3′), 75.7 (C-4′), 86.3 (C-2′), 102.6 (C-1′), 116.2 (d, C_{ar}-3), 125.3 (d, C_{ar}-5), 126.0 (d, C_{ar}-1), 126.2 (C-5), 131.0 (d, C_{ar}-4), 131.8 (d, C_{ar}-6), 152.3 (C-6), 150.8 (2-CO), 157.2 (4-CO), 162.2 (d, C_{ar}-2). $J_{1ar,F} = 14.5$, $J_{2ar,F} = 246.5$, $J_{3ar,F} = 21.6$, $J_{4ar,F} = 8.3$, $J_{5ar,F} = 3.6$, $J_{6ar,F} = 4.2$, $J_{CH2,F} = 3.9$. FAB MS (*m*NBA) *m/z*: 412 [M + H].

Methyl 3,5-Anhydro-2-*O*-(2-fluorobenzyl)-β-D-xylofuranoside (22). Diisopropyl azodicarboxylate (730 mg, 3.61 mmol) and, shortly after that, a

solution of methyl 2-*O*-(2-fluorobenzyl)-β-D-xylofuranoside[9] (**21**) (450 mg, 1.65 mmol) in dry pyridine (1 mL) were added to a solution of triphenylphosphine (880 mg, 3.35 mmol) in dry pyridine (10 mL) under N_2. The reaction mixture was heated to 80°C for 16 h. The solvent was removed under vacuum. The residue was dissolved in EA and filtered over silica gel (50 g). Repeated column chromatography over silica gel (50 g; 1.: PE/EA 1:1, 2.: EA) gave **22** (290 mg, 69%) as a colourless syrup containing traces of diisopropyl hydrazodicarboxylate. R_f(EA) = 0.73, R_f(EA/PE) = 0.56. ^{1}H NMR ($CDCl_3$): δ 3.52 (s, 3H, CH_3), 4.13 (s, 1H, H-2), 4.44 (dd, 1H, H-5_{endo}), 4.62 (d, 1H, CH_2Ar), 4.65 (d, 1H, CH_2Ar), 4.79 (dd, 1H, H-5_{exo}), 5.12 (ddd, 1H, H-4), 5.23 (d, 1H, H-3), 5.33 (d, 1H, H-1), 7.04 (ddd, 1H, H-3_{ar}), 7.12 (ddd, 1H, H-5_{ar}), 7.28 (dddd, 1H, H-4_{ar}), 7.36 (ddd, 1H, H-6_{ar}). $J_{1,2} = 0.6$, $J_{3,4} = 4.6$, $J_{4,5endo} = 2.8$, $J_{4,5exo} = 4.9$, $J_{5endo,5exo} = 7.5$, $J_{CH2Ar} = 12.3$. ^{13}C NMR ($CDCl_3$): δ 55.8 (CH_3), 65.8 (CH_2Ar), 78.9 (C-4), 79.6 (C-5), 85.6 (C-2), 88.9 (C-3), 111.6 (C-1), 115.4 (d, C_{ar}-3), 124.2 (d, C_{ar}-5), 124.4 (d, C_{ar}-1), 129.9 (d, C_{ar}-4), 130.2 (d, C_{ar}-6), 160.8 (d, C_{ar}-2). $J_{CH2,F} = 3.1$, $J_{3ar,F} = 21.4$, $J_{5ar,F} = 4.1$, $J_{1ar,F} = 15.1$, $J_{4ar,F} = 8.1$, $J_{6ar,F} = 4.1$, $J_{2ar,F} = 247.2$. EI MS m/z (%): 254 (0.1) [$M^{+\bullet}$], 253 (0.2), 223 (0.2) [$M^{+\bullet}$-OCH_3], 195 (0.5), 194 (0.4), 193 (0.3), 192 (0.1), 165 (0.5), 164 (2), 163 (3), 153 (1), 136 (1), 135 (2.5), 134 (1), 129 (2), 126 (1), 125 (3), 124 (1), 123 (8.5), 115 (10), 110 (15), 109 (100) [$C_7H_6F^{+\bullet}$], 87 (7), 85 (16), 83 (10), 71 (5), 69 (18), 68 (5), 61 (5), 59 (4.5), 57 (4), 45 (8).

Methyl 5-Deoxy-2-*O*-(2-fluorobenzyl)-5-*N*-(5-fluorouracil-1-yl)-β-D-xylofuranoside (23). Compound **23** was obtained directly according to the ***General procedure A*** from **22** (50 mg, 0.20 mmol) and 5-fluoro-2,4-bis-*O*-trimethylsilyluracil[13] (168 mg, 0.61 mmol). Yield: 10 mg (13%). M.p. 182°C (PE/EA 1:3, $R_f = 0.12$). $[a]_D^{20} = -40.0$ (c = 1.0, $CHCl_3$). IR: ν 3443 (OH), 3188 (NH), 1696 (C=O) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 3.42 (s, 3H, CH_3), 3.76 (dd, 1H, H-$5_{a'}$), 3.97 (d, 1H, H-2′), 4.20–4.22 (m, 2H, H-3′, H-$5_{b'}$), 4.42 (ddd, 1H, H-4′), 4.63, 4.66 (AB-system, 2H, C$H_2C_6H_4F$), 4.94 (s, 1H, H-1′), 7.03 (ddd, 1H, H_{ar}-3), 7.12 (ddd, 1H, H_{ar}-5), 7.29 (dddd, 1H, H_{ar}-4), 7.42 (ddd, 1H, H_{ar}-6), 7.46 (d, 1H, H-6), 8.86 (bs, 1H, NH). $J_{1',2'} = 0$, $J_{2',3'} = 1.1$, $J_{3',4'} = 4.1$, $J_{4',5a'} = 8.2$, $J_{4',5b'} = 4.1$, $J_{5a',5b'} = 14.3$, $J_{AB} = 11.7$, $J_{6,F} = 5.6$, $J_{3ar,4ar} = 8.4$, $J_{3ar,5ar} = 1.1$, $J_{3ar,F} = 9.9$, $J_{4ar,5ar} = 7.5$, $J_{4ar,6ar} = 1.9$, $J_{4ar,F} = 5.7$, $J_{5ar,6ar} = 7.5$, $J_{6ar,F} = 7.5$. ^{13}C NMR ($CDCl_3$): δ 49.17 (C-5′), 55.8 (CH_3), 65.8 (d, $CH_2C_6H_4F$), 73.5 (C-3′), 80.5 (C-4′), 86.3 (C-2′), 107.3 (C-1′), 115.4 (d, C_{ar}-3), 124.3 (d, C_{ar}-5), 124.7 (d, C_{ar}-1), 130.0 (d, C_{ar}-4), 130.1 (d, C_{ar}-6), 130.3 (d, C-6), 140.4 (d, C-5), 149.4 (2-CO), 157.0 (4-CO), 160.6 (d, C_{ar}-2). $J_{5,F} = 236.8$, $J_{6,F} = 32.8$, $J_{1ar,F} = 14.8$, $J_{2ar,F} = 245.7$, $J_{3ar,F} = 21.2$, $J_{4ar,F} = 8.0$, $J_{5ar,F} = 3.5$, $J_{6ar,F} = 4.2$, $J_{CH2F} = 3.9$.

Methyl 5-*N*-(5-Chlorouracil-1-yl)-5-deoxy-2-*O*-(2-fluorobenzyl)-β-D-xylo-furanoside (24). Compound **24** was obtained directly according to the ***General procedure A*** from **22** (50 mg, 0.20 mmol) and 5-chloro-2,4-bis-trimethylsilyluracil[13] (148 mg, 0.67 mmol). Yield: 9 mg (11%). M.p. 186°C (PE/EA 1:4, $R_f = 0.09$). $[\alpha]_D^{20} = -31.4$ (c = 0.9, $CHCl_3$). IR: ν 3434 (OH), 3206 (NH), 1688 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): 3.43 (s, 3H, CH_3), 3.81 (dd, 1H, H-$5_{a'}$), 3.98 (d, 1H, H-2′), 4.22 (dd, 1H, H-3′), 4.25 (dd, 1H, H-$5_{b'}$), 4.43 (ddd, 1H, H-4′), 4.63–4.66 (AB system, 2H, $CH_2C_6H_4F$), 4.94 (s, 1H, H-1′), 7.04 (ddd, 1H, H_{ar}-3), 7.12 (ddd, 1H, H_{ar}-5), 7.29 (dddd, 1H, H-4_{ar}), 7.34 (ddd, 1H, H_{ar}-6), 7.58 (s, 1H, H-6), 8.70 (bs, 1H, NH). $J_{1',2'} = 0$, $J_{2',3'} = 1.5$, $J_{3',4'} = 4.2$, $J_{4',5a'} = 8.2$, $J_{4',5b'} = 4.4$, $J_{5a',5b'} = 14.5$, $J_{AB} = 12.3$, $J_{AB,F} = 1.3$, $J_{3ar,4ar} = 8.5$, $J_{3ar,5ar} = 1.3$, $J_{3ar,F} = 9.9$, $J_{4ar,5ar} = 7.5$, $J_{4ar,6ar} = 1.8$, $J_{4ar,F} = 5.7$, $J_{5ar,6ar} = 7.5$, $J_{6ar,F} = 7.4$. ^{13}C NMR: δ 49.3 (C-5′), 55.9 (CH_3), 65.8 (d, $CH_2C_6H_4F$, 73.6 (C-3′), 80.3 (C-4′), 86.4 (C-2′), 107.3 (C-1′), 108.5 (C-5), 115.3 (d, C_{ar}-3), 124.1 (d, C_{ar}-1), 124.3 (d, C_{ar}-5), 130.0 (d, C_{ar}-4), 130.1 (d, C_{ar}-6), 142.2 (C-6), 149.9 (2-CO), 160.6 (d, C-2_{ar}), 162.8 (4-CO). $J_{1ar,F} = 14.5$, $J_{2ar,F} = 238.0$, $J_{3ar,F} = 21.5$, $J_{4ar,F} = 8.3$, $J_{5ar,F} = 3.7$, $J_{6ar,F} = 4.9$, $J_{CH2,F} = 3.8$.

Methyl 5-Deoxy-2-*O*-(2-fluorobenzyl)-5-*N*-(5-iodouracil-1-yl)-β-D-xylo-furanoside (25). Compound **25** was obtained directly according to the ***General procedure A***. from **22** (50 mg, 0.20 mmol) and 5-iodo-2,4-bis-trifluorouracil[13] (230 mg, 0.60 mmol). Yield: 7 mg (7%). M.p. 167–170°C (PE/EA 1:5, $R_f = 0.13$, decomp.). $[\alpha]_D^{20} = -16.1$ (c = 0.7, $CHCl_3$). IR: ν 3435 (OH), 3192 (NH), 1689 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 3.45 (s, 3H, CH_3), 3.83 (dd, 1H, H-$5_{a'}$), 3.97 (d, 1H, H-2′), 4.22 (dd, 1H, H-3′), 4.24 (dd, 1H, H-$5_{b'}$), 4.44 (ddd, 1H, H-4′), 4.63, 4.67 (AB system, 2H, $CH_2C_6H_4F$), 4.95 (s, 1H, H-1′), 7.04 (ddd, 1H, H_{ar}-3), 7.12 (ddd, 1H, H_{ar}-5), 7.25–7.28 (m, 1H, H_{ar}-4), 7.39 (ddd, 1H, H_{ar}-6), 7.69 (s, 1H, H-6), 8.53 (bs, 1H, NH). $J_{1',2'} = 0$, $J_{2',3'} = 1.3$, $J_{3',4'} = 4.1$, $J_{4',5a'} = 8.4$, $J_{4',5b'} = 4.2$, $J_{5a',5b'} = 14.3$, $J_{AB} = 12.1$, $J_{3ar,4ar} = 8.4$, $J_{3ar,5ar} = 1.1$, $J_{3ar,F} = 9.9$, $J_{4ar,5ar} = 7.4$, $J_{4ar,6ar} = 1.8$, $J_{5ar,6ar} = 7.5$, $J_{6ar,F} = 7.5$. ^{13}C NMR ($CDCl_3$): δ 49.3 (C-5′), 55.9 (CH_3), 65.6 (d, $CH_2C_6H_4F$), 67.5 (C-5), 73.4 (C-3), 80.2 (C-4′), 86.3 (C-2′), 107.3 (C-1′), 115.2 (d, C_{ar}-3), 124.1 (d, C_{ar}-1), 124.4 (d, C_{ar}-5), 130.1 (d, C_{ar}-4), 130.2 (d, C_{ar}-6), 149.8 (C-6), 150.7 (2-CO), 160.6 (d, C_{ar}-2), 161.6 (4-CO). $J_{1ar,F} = 14.5$, $J_{2ar,F} = 237.3$, $J_{3ar,F} = 21.4$, $J_{4ar,F} = 8.3$, $J_{5ar,F} = 3.8$, $J_{6ar,F} = 4.8$, $J_{CH2,F} = 3.7$.

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