Synthesis of 1-(3-Alkyl-2,3-dideoxy-D-pentofuranosyl)uracils with Potential Anti-HIV Activity

Krzysztof Walczak and Erik B. Pedersen

Department of Chemistry, Odense University, DK-5230 Odense M, Denmark

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1-(3-Alkyl-2,3-dideoxy-α,β-D-*erythro*-pentofuranosyl)uracils and 1-(3-alkyl-2,3-dideoxy-α,β-D-*threo*-pentofuranosyl)uracils have been prepared from (*E*)-4,5-di-*O*-acetyl-2,3-dideoxy-*aldehydo*-D-*glycero*-pent-2-enose by a Michael addition reaction of the appropriate organocopper reagent followed in subsequent order by glycosidation of the resulting 3-alkyl-4,5-diacetoxypentanal with methanolic hydrogen chloride, protection with *p*-methoxybenzoyl chloride, and trimethylsilyl triflate catalyzed coupling with 2,4-di-*O*-(trimethylsilyl)uracil. The nucleosides were deprotected by treatment with 33 % methylamine in absolute ethanol and separated by reversed-phase HPLC.

The interest in modifying the carbohydrate moiety of nucleosides increased tremendously after the report on 3′-azido-3′-deoxythymidine as a potent antiviral agent against human immunodeficiency virus (HIV).[1-3] From the great number of modified nucleosides synthesized, attempts have been made to establish relationships between molecular structure and biological activity.[4] From these studies, the best suggestion is to modify the natural nucleosides at carbon C-2′ abnd C-3′, but there seems to be very few structural possibilities which retain the anti-HIV activity.

For the preparation of 3′-alkyl-2′,3′-dideoxynucleosides one possibility would be to use a convergent route in which the carbohydrate is first synthesized and then coupled to an independently prepared nucleobase. Although a copper-catalyzed conjugate addition of an appropriate Grignard reagent to an α,β-unsaturated aldehyde is well known,[5-8] nobody seems to have used the corresponding sugar aldehydes to build up a 3-alkyl-carbohydrate in spite of the fact that α,β-unsaturated *aldehydo*-carbohydrates are easily synthesized.[9-11]

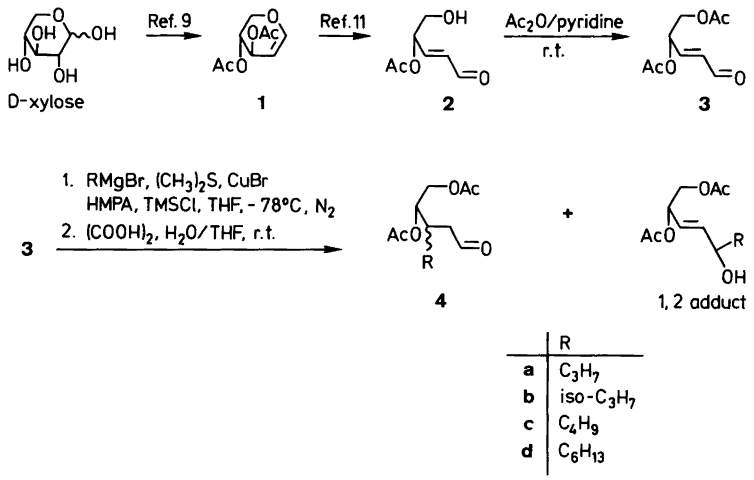
In this investigation we report on the copper-catalyzed conjugate 1,4-addition of Grignard reagents to (*E*)-4,5-di-*O*-acetyl-2,3-dideoxy-*aldehydo*-D-glycero-pent-2-enose **3** and utilization of the resulting 1,4-adducts in the synthesis of 3′-alkyl-2′,3′-dideoxynucleosides.

Results and discussion

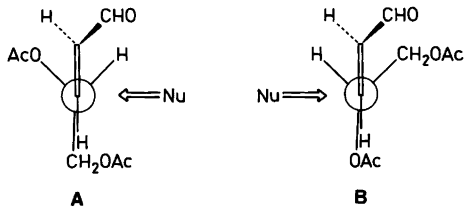
D-Xylose was used as a cheap starting material to prepare 3,4-di-*O*-acetyl-D-xylal **1** by a known procedure.[9] Xylal **1** is easily hydrolyzed to (*E*)-4-*O*-acetyl-2,3-dideoxy-*aldehydo*-D-*glycero*-pent-2-enose **2** in 95 % yield.[11] Protection of the free hydroxy group with acetic anhydride in pyridine solution gave, after purification on a silica gel column, the acetyl-protected aldehyde **3** in 79 % yield. The conjugate 1,4-addition to **3** of the Grignard reagent, prepared *in situ* from magnesium and appropriate alkyl halide, was performed in the presence of CuBr, dimethyl sulfide, hexamethylphosphoric triamide (HMPA) and trimethylsilyl chloride (TMSCI) under the same conditions as described by Horiguchi *et al.*[12] After work-up the expected product **4** was found as an isomeric mixture of 3*S*/4*S* and 3*R*/4*S* diastereomers in a ratio close to 1:1 in a 52–65 % yield, but accompanied by a concurrent 1,2-addition reaction in 9–11 % yield.

The combination of HMPA and TMSCl is known to be an accelerator for the copper-catalyzed conjugate addition of the Grignard reagent.[12] These additions show high anti-selectivities on certain unsaturated aldehydes.[12-14] Treatment of the *E*-unsaturated aldehyde **3** under these conditions gave low stereoselectivity. It is assumed that the reagent attacks from the less-hindered site of the conformer **A** or **B** (Scheme 2). However, the bulkiness of the methylene group and the oxygen atom is comparable and no preference for either of the two conformers should be expected. This explains the non-selectivity of the 1,4-addition reaction to the α,β-unsaturated sugar aldehyde **3**. Conformations due to chelation of the metal to one of the acetyl groups and to the aldehyde group can be excluded with the *E*-configuration of the double bond.

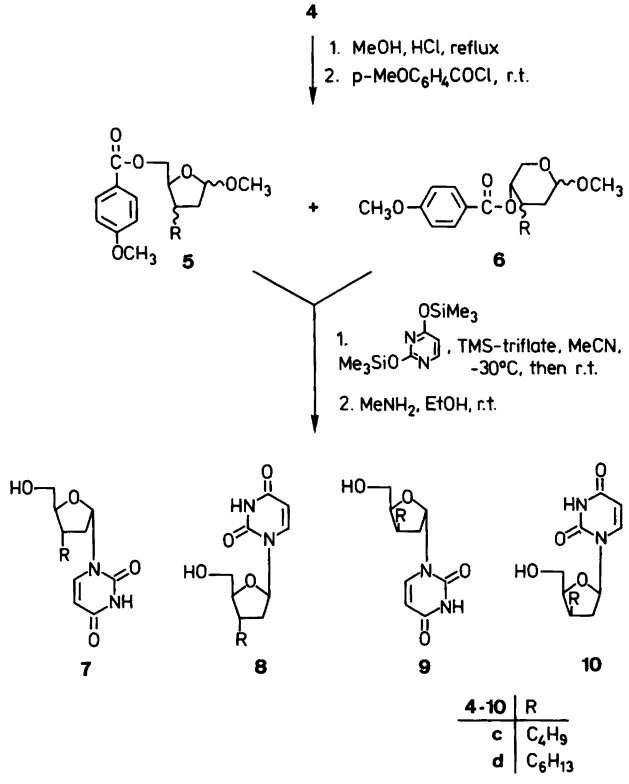
The resulting 1,4-adducts **4c** and **4d** were used in the synthesis of C−3′-alkyl branched nucleosides. Glycosidation of **4c** or **4d** with hydrogen chloride in methanol followed by reaction with *p*-methoxybenzoyl chloride in dry pyridine at room temperature for 24 h, gave *erythro* and *threo* isomers as a mixture of the methyl 3-alkyl-2,3-dideoxy-α,β-D-pentofuranoside **5** and the methyl 3-alkyl-2,3-dideoxy-α,β-D-pentopyranoside **6** in 71 and 63 % overall yield for **5c–6c** and **5d–6d**, respectively; the ratio of



Scheme 1.



Scheme 2.



Scheme 3.

pentofuranosides **5** to pentopyranosides **6** was approximately 3:1.

Reaction of the isomeric mixture of **5** and **6** with silylated uracil in the presence of trimethylsilyl trifluoromethanesulfonate (TMS-triflate) as the catalyst[15,16] followed by deprotection with methylamine gave, after chromatographic purification, the corresponding nucleosides **7c–10c** and **7d–10d** in 38 and 33 % yield, respectively, as an isomeric mixture. Owing to the lower reactivity of pyranosides, products of coupling with **6** were not detected. The isomeric mixtures of nucleosides were separated by means of preparative reversed-phase HPLC.

The structural assignment of the nucleosides **7c** and **8c** was made by comparison with the NMR data of recently described 1-[3-(2-cyanoethyl)-2,3-dideoxy-β-D-*erythro*-pentofuranosyl]uracil and its α-anomer[17] and they are in close agreement. For compounds **9c** and **10c** configurational assignment was based on the deshielding effect of the nucleobase which generates a considerable downfield shift of proton H−5′a and H−5′b when the position of the nucleobase is changed from the α- to the β-side of the furanose ring. Similarly, H−4′ is shifted downfield when the nucleobase is changed from the β- to the α-side of the furanose ring. Such downfield shifts have previously been observed for 2-deoxy nucleosides.[17,18] For the 3′-hexyl derivatives **7d–10d** the structural assignment was made by comparison with appropriate isomers from the 3′-butyl series **7c–10c**.

The anti-HIV activity of compounds **7–10** is currently under investigation.

Experimental

NMR spectra were recorded on a Bruker AC 250 FT NMR spectrometer at 250 MHz for ^{1}H and 62.5 MHz for ^{13}C. Microanalyses were carried out at NOVO Microanalytical Laboratory A/S, Novo Allé, DK-2880 Bagsværd. EI mass spectra were recorded on a Varian MAT 311 A spectrometer. The column chromatography was carried out using Merck silica gel (230–400 mesh ASTM).

(4S),(E)-4,5-Diacetoxy-2-pentenal **3**. To 4-acetoxy-5-hydroxy-2-pentenal **2** (20.2 g, 0.13 mol), cooled in an ice bath, was added a mixture of pyridine (54 ml, 0.67 mol) and acetic anhydride (80 ml, 0.85 mol) with stirring. Stirring was continued at room temperature and the reaction was monitored by TLC (CH_2Cl_2−MeOH, 97:3). When the starting material had disapeared, the reaction mixture was evaporated under reduced pressure and coevaporated twice with xylene. The residue was purified on a silica column (230 g, CH_2Cl_2−MeOH, 97:3) to give **3** (23.5 g, 79 %) as a colourless oil. ^{1}H NMR ($CDCl_3$/TMS): δ 9.58 (d, 1 H, *J* 7.7 Hz, H−1), 6.80 (dd, 1 H, *J* 4.6, 15.8 Hz, H−3), 6.30 (ddd, 1 H, *J* 1.7, 7.7, 15.8 Hz, H−2), 5.78–5.72 (m, 1 H, H−4), 4.40–4.18 (m, 2 H, H−5), 2.16 (s, 3 H, C*H*$_3$CO), 2.08 (s, 3 H, C*H*$_3$CO). ^{13}C NMR ($CDCl_3$/TMS): δ 192.27 (C−1), 170.11 (C=O), 169.35 (C=O), 148.87 (C−3), 132.77 (C−2), 69.81 (C−4), 63.29 (C−5), 20.38 (*C*H$_3$CO), 20.26 (*C*H$_3$CO).

(4S)-3-Alkyl-4,5-diacetoxypentanal **4a–d**. *General procedure.* HMPA (5.4 g, 5.25 ml, 30 mmol, carcinogenic), CuBr (0.09 g, 0.62 mmol) and dimethyl sulfide (0.05 ml, 0.62 mmol) were added at −45 °C to a solution of alkylmagnesium bromide prepared from alkyl bromide (17.5 mmol) and magnesium (18.75 mmol) in dry THF (30 ml) under nitrogen. After being stirred for several minutes, the reaction mixture was cooled to −78 °C and a mixture of **3** (2.5 g, 12.5 mmol) and trimethylsilyl chloride (3.2 ml, 25 mmol) in THF (10 ml) was added dropwise. After 3 h, triethylamine (3.5 ml, 25 mmol) and petroleum ether (b.p. 60–80 °C) (50 ml) were added. After a few minutes, the reaction mixture was quenched with saturated NH_4Cl (50 ml) and filtered. The organic layer was washed with water (5×5 ml) and the water layer was extracted with petroleum ether (b.p. 60–80 °C) (30 ml). The combined organic layers were washed with a saturated solution of NaCl (20 ml) and dried (Na_2SO_4). The solvent was evaporated under reduced pressure and the residue was stirred for 1 h with 50 % solution of THF in water (60 ml) containing oxalic acid (0.01 mol). After separation, the water layer was extracted with ethyl ether (4×10 ml). The combined organic layers were dried over Na_2SO_4. After filtration and evaporation, the residue was purified on a silica gel column (230 g, CH_2Cl_2−MeOH 97:3) to give the title compounds **4a–d** and 1,2-adducts. The latter showed typical NMR data as follows: ^{1}H NMR ($CDCl_3$/TMS): δ 5.89–5.60 (m, 2 H, H−2, H−3), 5.56–5.47 (m, 1 H, H−4), 4.27–4.06 (m, 2 H, H−5), 2.71 (br, 1 H, OH), 2.09 (s, 3 H, C*H*$_3$CO), 2.06 (s, 3 H, C*H*$_3$CO). ^{13}C NMR ($CDCl_3$/TMS): δ 170.40 (C=O), 169.80 (C=O), 136.15 (C−3), 124.81 (C−2), 72.50 (C−5), 71.50 (C−4), 65.07 (C−1), 20.73 (*C*H$_3$CO).

(4S)-4,5-Diacetoxy-3-propylpentanal **4a**. Yield 60 %. ^{1}H NMR ($CDCl_3$/TMS): δ 9.75 (br s, 1 H, H−1), 5.22–5.10 (m, 1 H, H−4), 4.35–4.01 (m, 2 H, H−5a, H−5b), 2.49–2.28 (m, 3 H, H−2a, H−2b, H−3), 2.06 (s, 3 H, C*H*$_3$CO), 2.05 (s, 3 H, C*H*$_3$CO), 1.44–1.31 [m, 4 H, $(CH_2)_2$], 0.94–0.91 (m, 3 H, CH_3). ^{13}C NMR ($CDCl_3$/TMS): δ 201.12, 200.89 (C–1), 170.62 (C=O), 170.28 (C=O), 72.65 (C−4), 63.57, 62.87 (C−5), 44.45 (C−2), 35.62, 34.57 (C−3), 33.54, 32.29 (C−1′), 20.6 (*C*H$_3$CO), 20.55 (*C*H$_3$CO), 19.89, 19.45 (C−2′), 13.81 (C−3′). MS: *m/z* (%) 201 [M^+−43 (CH_3CO), 0.6], 127 (24), 43 (100).

(4S)-4,5-Diacetoxy-3-isopropylpentanal **4b**. Yield 58 %. ^{1}H NMR ($CDCl_3$/TMS): δ 9.76–9.73 (m, 1 H, H−1), 5.23–5.12 (m, 1 H, H−4), 4.36–4.27 (m, 1 H, H−5a), 4.06–3.97 (m, 1 H, H−5b), 2.46–2.30 (m, 3 H, H−2a, H−2b, H−3), 2.06 (s, 3 H, C*H*$_3$CO), 2.05 (s, 3 H, C*H*$_3$CO), 1.90–1.74 (m, 1 H, H−1′), 0.97 (2 × d, 3 H, *J* 6.8 Hz, CH_3), 0.86 (2 × d, 3 H, *J* 6.8 Hz, CH_3). ^{13}C NMR ($CDCl_3$/TMS): δ 201.03, 200.57 (C−1), 170.32 (C=O), 169.89 (C=O), 71.99 (C−4), 63.78, 63.10 (C−5), 41.25,

41.06 (C−2), 39.45, 39.16 (C−3), 28.34, 27.81 (C−1'), 20.67 (CH_3CO), 20.54 (CH_3CO), 18.67, 17.79 (C−2'). MS: *m/z* (%) 201 [M^+−43 (CH_3CO), 0.7], 111 (12), 43 (100).

(4S)-3-Butyl-4,5-diacetoxypentanal **4c**. Yield 52%. ^{1}H NMR ($CDCl_3$/TMS): δ 9.75–9.74 (m, 1 H, H−1), 5.20–5.06 (m, 1 H, H−4), 4.34–4.25 (m, 1 H, H−5a), 4.13–4.02 (m, 1 H, H−5b), 2.46–2.34 (m, 3 H, H−2a, H−2b, H−3), 2.06 (s, 3 H, CH_3CO), 2.05 (s, 3 H, CH_3CO), 1.33–1.22 [m, 6 H, $(CH_2)_3$], 0.92–0.88 (m, 3 H, CH_3). ^{13}C NMR ($CDCl_3$/TMS): δ 200.99, 200.78 (C−1), 170.50 (C=O), 170.13 (C=O), 72.83, 72.58 (C−4), 63.63, 62.89 (C−5, 44.56 (C−2), 33.83 (C−3), 30.69, 30.57 (C−1'), 28.59, 27.60 (C−2', C−3'), 20.60 (CH_3CO), 20.52 (CH_3CO), 13.68 (C−4'). MS: *m/z* (%) 215 [M^+−43 (CH_3CO), 0.5], 141 (32), 95 (10), 43 (100).

(4S)-4,5-Diacetoxy-3-hexylpentanal **4d**. Yield 65%. ^{1}H NMR ($CDCl_3$/TMS): δ 9.74 (br s, 1 H, H−1), 5.19–5.13 (m, 1 H, H−4), 4.33–4.24 (m, 1 H, H−5a), 4.08–4.01 (m, 1 H, H−5b), 2.60–2.32 (m, 3 H, H−2a, H−2b, H−3), 2.06 (s, 3 H, CH_3CO), 2.05 (s, 3 H, CH_3CO), 1.43–1.26 [m, 10 H, $(CH_2)_5$], 0.88 (t, 3 H, *J* 6.4 Hz, CH_3). ^{13}C NMR ($CDCl_3$/TMS): δ 200.81, 200.60 (C−1), 170.37 (C=O), 169.98 (C=O), 72.72, 72.61 (C−4), 63.39, 62.79 (C−5), 44.50 (C−2), 34.27, 33.77 (C−3), 31.39, 30.95 (C−1'), 30.13, 29.11, 26.79, 22.44 (C−2', C−3', C−4', C−5'), 20.66 (CH_3CO), 20.54 (CH_3CO), 13.85 (C−6'). MS: *m/z* (%) 243 [M^+−43 (CH_3CO), 1.8], 180 (10), 153 (24), 43 (100). Anal. $C_{15}H_{26}O_5 \cdot {}^1/_3\,H_2O$: C, H.

*Methyl 3-alkyl-2,3-dideoxy-5-*O-p-*methoxybenzoyl-α,β-*D-erythro,threo-*pentofuranoside* **5** and *methyl 3-alkyl-2,3-dideoxy-4-*O-p-*methoxybenzoyl-α,β-*D-erythro,threo-*pentopyranoside* **6**. *General procedure.* To the aldehyde (**4c** or **4d**) (3.2 mmol) dissolved in methanol (11 ml) was added 1% methanolic HCl (1.4 ml). The mixture was refluxed for 3 h and evaporated under reduced pressure. The residual oil was dissolved in CH_2Cl_2 (10 ml) and mixed with pyridine (10 ml) and *p*-methoxybenzoyl chloride (5.2 mmol). The reaction mixture was stirred overnight at room temperature. The solvent was evaporated under reduced pressure and the residue was chromatographed on silica gel (80 g) eluting with petroleum ether (b.p. 60–80 °C) – ethyl ether (1:5).

5c and **6c**: Yield 0.73 g (71%). Anal.: $C_{18}H_{26}O_5$: C, H.

5d and **6d**: Yield 0.70 g (63%). Anal.: $C_{20}H_{30}O_5$: C, H.

*1-(3-Alkyl-2,3-dideoxy-α,β-*D-erythro,threo-*pentofuranosyl)uracil* **7–10**. *General procedure.* Trimethylsilyl trifluoromethanesulfonate (0.16 ml, 0.9 mmol) was added to an isomeric mixture of **5** and **6** (0.9 mmol) and silylated uracil[15] in anhydrous acetonitrile (6 ml) cooled to −30 °C with stirring. After 2 h at −30 °C the temperature was increased to ambient. After 16 h, the reaction mixture was diluted with CH_2Cl_2 (50 ml) and quenched with cold saturated aq. $NaHCO_3$ (20 ml). The organic phase was washed with cold water (20 ml) and dried (Na_2SO_4). After filtration, the solvent was evaporated and the residual oil purified on a silica gel column (15 g) using CH_2Cl_2−MeOH (97:3) as the eluent. The combined fraction of nucleosides **7–10** was collected and evaporated. The residue was dissolved in a 33% solution of $MeNH_2$ in EtOH (10 ml) and stirred at room temperature for 24 h. The solvent was removed and the residue purified on a silica gel column (15 g) eluting with CH_2Cl_2−MeOH (97:3) to give pure nucleosides **7–10** as an isomeric mixture. Yield **7c–10c** 0.092 g (38%) and **7d–10d** 0.087 g (33%). The isomeric mixture **7–10** was separated by reversed-phase HPLC (Waters Delta Pak 300 Å, 15 μ, RP18, 57×300 mm) with isocratic EtOH−H_2O (20:80 for **7c–10c** and 32:68 for **7d–10d**, respectively) to give pure nucleosides **7–10**.

*1-(3-Butyl-2,3-dideoxy-α-*D-erythro-*pentofuranosyl)uracil* **7c**. Retention time 62 min, yield 17 mg. ^{1}H NMR (DMSO-d_6/TMS): δ 7.68 (d, 1 H, *J* 8.0 Hz, H−6), 5.98 (dd, 1 H, *J* 6.0, 7.6 Hz, H−1'), 5.58 (d, 1 H, *J* 8.0 Hz, H−5), 3.87 (ddd, 1 H, *J* 3.2, 4.5, 8.0 Hz, H−4'), 3.53 (dd, 1 H, *J* 3.2, 12.0 Hz, H−5'a), 3.38 (dd, 1 H, *J* 4.5, 12.0 Hz, H−5'b), 2.42 (dd, 1 H, *J* 6.2, 13.0 Hz, H−2'β), 2.11–1.96 (m, 1 H, H−3'), 1.70–1.58 (m, 1 H, H−2'α), 1.47–1.27 [m, 6 H, $(CH_2)_3$], 0.86 (t, 3 H, *J* 6.4 Hz, CH_3). ^{13}C NMR (DMSO-d_6/TMS): δ 164.03 (C−4), 150.99 (C−2), 146.41 (C−6), 101.64 (C−5), 85.69 (C−1'), 84.94 (C−4'), 62.20 (C−5'), 37.92 (C−3'), 36.38 (C−2'), 30.99, 29.83, 22.14, 13.78 (butyl). MS: *m/z* (%) 268 (M^+, 3.2), 157 (100), 113 (72), 95 (30), 69 (32), 57 (50), 55 (28), 40 (26). Found 268.140. Calc. for $C_{13}H_{20}N_2O_4$ 268.142.

*1-(3-Butyl-2,3-dideoxy-β-*D-erythro-*pentofuranosyl)uracil* **8c**. Retention time 68 min, yield 45 mg. ^{1}H NMR (DMSO-d_6/TMS): δ 8.02 (d, 1 H, *J* 8.0 Hz, H−6), 5.92 (dd, 1 H, *J* 2.1, 6.6 Hz, H−1'), 5.56 (d, 1 H, *J* 8.0 Hz, H−5), 3.73–3.51 (m, 3 H, H−4', H−5'a, H−5'b), 2.15–1.97 (m, 3 H, H−3', H−2'α, H−2'β), 1.46–1.24 [m, 6 H, $(CH_2)_3$], 0.86 (t, 3 H, *J* 6.4 Hz, CH_3). ^{13}C NMR (DMSO-d_6/TMS): δ 163.37 (C−4), 150.43 (C−2), 140.51 (C−6), 100.76 (C−5), 86.59 (C−4'), 84.27 (C−1'), 60.46 (C−5'), 38.76 (C−3'), 36.30 (C−2'), 30.90, 29.66, 22.19, 13.78 (butyl). MS: *m/z* (%) 268 (M^+, 4.6), 157 (100), 113 (60), 95 (22), 69 (20), 57 (39), 55 (20), 41 (16). Found 268.145. Calc. for $C_{13}H_{20}N_2O_4$ 268.142.

*1-(3-Butyl-2,3-dideoxy-α-*D-threo-*pentofuranosyl)uracil* **9c**. Retention time 52 min, yield 20 mg. ^{1}H NMR (DMSO-d_6/TMS): δ 7.58 (d, 1 H, *J* 8.0 Hz, H−6), 6.03 (dd, 1 H, *J* 2.4, 6.7 Hz, H−1'), 5.55 (d, 1 H, *J* 8.0 Hz, H−5), 4.22 (ddd, 1 H, *J* 3.6, 4.0, 7.6 Hz, H−4'), 3.50 (dd, 1 H, *J* 3.6, 12.0 Hz, H−5'a), 3.42 (dd, 1 H, *J* 4.0, 12.0 Hz, H−5'b), 2.28–2.26 (m, 1 H, H−3'), 2.16 (td, 1 H, *J* 6.7, 12.9 Hz, H−2'β), 2.02 (dd, 1 H, *J* 2.4, 12.9 Hz, H−2α), 1.46–1.28 [m, 6 H, $(CH_2)_3$], 0.87 (t, 3 H, *J* 6.4 Hz, CH_3). ^{13}C NMR (DMSO-d_6/TMS): δ 163.79 (C−4), 150.62 (C−2), 140.27 (C−6), 101.06 (C−5), 85.41 (C−1'), 83.21 (C−4'), 60.96

(C–5'), 38.44 (C–3'), 37.80 (C–2'), 30.36, 27.46, 22.25, 13.83 (butyl). MS: *m/z* (%) 268 (M^+, 2.8), 157 (100), 113 (66), 95 (30), 69 (34), 57 (46), 55 (32), 40 (26), 28 (12). Found 268.137. Calc. for $C_{13}H_{20}N_2O_4$ 268.142.

*1-(3-Butyl-2,3-dideoxy-β-*D-threo-*pentofuranosyl)uracil* **10c**. Retention time 84 min, yield 10 mg. ^{1}H NMR (DMSO-d_6/TMS): δ 8.0 (d, 1 H, *J* 8.0 Hz, H–6), 5.95 (dd, 1 H, *J* 5.5, 9.0 Hz, H–1'), 5.56 (d, 1 H, *J* 8.0 Hz, H–5), 4.0–3.94 (m, 1 H, H–4'), 3.61 (dd, 1 H, *J* 3.3, 11.8 Hz, H–5'a), 3.51 (dd, 1 H, *J* 4.0, 11.8 Hz, H–5'b), 2.50–2.40 (m, 1 H, H–3'), 2.20 (dd, 1 H, *J* 6.0, 12.0 Hz, H–2'α), 1.70 (dd, 1 H, *J* 9.0, 12.0 Hz, H–2'β), 1.47–1.28 [m, 6 H, $(CH_2)_3$], 0.87 (t, 3 H, *J* 6.5 Hz, CH_3). ^{13}C NMR (DMSO-d_6/TMS): δ 163.24 (C–4), 150.36 (C–2), 140.50 (C–6), 100.77 (C–5), 86.57 (C–1'), 84.29 (C–4'), 60.54 (C–5'), 38.53 (C–3'), 36.40 (C–2'), 30.94, 29.63, 22.16, 13.76 (butyl). MS: *m/z* (%) 268 (M^+, 3.6), 157 (100), 125 (18), 113 (86), 95 (44), 69 (56), 57 (66), 55 (54), 41 (66), 29 (26). Found 268.140. Calc. for $C_{13}H_{20}N_2O_4$ 268.142.

*1-(2,3-Dideoxy-3-hexyl-α-*D-erythro-*pentofuranosyl)uracil* **7d**. Retention time 189 min, yield 17 mg. ^{1}H NMR (DMSO-d_6/TMS): δ 7.60 (d, 1 H, *J* 8.0 Hz, H–6), 5.98 (dd, 1 H, *J* 6.0, 7.6 Hz, H–1'), 5.54 (d, 1 H, *J* 8.0 Hz, H–5), 3.90–3.84 (m, 1 H, H–4'), 3.53 (dd, 1 H, *J* 3.0, 12.0 Hz, H 5'a), 3.45 (dd, 1 H, *J* 4.0, 12.0 Hz, H–5'b), 2.42 (dd, 1 H, *J* 6.0, 12.0 Hz, H–2'β), 2.11–2.07 (m, 1 H, H–3'), 1.68–1.55 (m, 1 H, H–2'α), 1.46–1.26 [m, 10 H, $(CH_2)_5$], 0.86 (t, 3 H, *J* 6.1 Hz, CH_3). ^{13}C NMR (DMSO-d_6/TMS): δ 164.03 (C–4), 150.08 (C–2), 139.80 (C–6), 101.64 (C–5), 85.54 (C–1'), 84.87 (C–4'), 62.18 (C–5'), 37.91 (C–3'), 36.37 (C–2'), 31.36, 30.99, 28.59, 27.47, 21.85, 13.74 (Hexyl). MS: *m/z* (%) 296 (M^+, 1.25), 185 (100), 167 (10), 141 (22), 113 (14), 85 (70), 81 (22), 69 (38), 66 (96), 57 (48), 55 (46), 43 (40), 41 (46), 29 (20), 18 (40).

*1-(2,3-Dideoxy-3-hexyl-β-*D-erythro-*pentofuranosyl)uracil* **8d**. Retention time 222 min, yield 40 mg. ^{1}H NMR (DMSO-d_6/TMS): δ 8.0 (d, 1 H, *J* 8.1 Hz, H–6), 5.94 (dd, 1 H, *J* 2.0, 6.6 Hz, H–1'), 5.54 (d, 1 H, *J* 8.1 Hz, H–5), 3.73–3.51 (m, 3 H, H–4', H–5', H–5'b), 2.15–1.97 (m, 3 H, H–3', H–2'α, H–2'β), 1.45–1.25 [m, 10 H, $(CH_2)_5$], 0.86 (t, 3 H, *J* 6.5 Hz, CH_3). ^{13}C NMR (DMSO-d_6/TMS): δ 163.62 (C–4), 150.64 (C–2), 140.64 (C–6), 100.91 (C–5), 86.73 (C–4'), 84.44 (C–1'), 60.63 (C–5'), 38.60 (C–3'), 36.54 (C–2'), 31.43, 31.25, 28.91, 27.56, 16.06, 14.00 (hexyl). MS: *m/z* (%) 296 (M^+, 2.4), 185 (10), 141 (40), 113 (26), 83 (18), 81 (28), 69 (32), 57 (40), 55 (34), 43 (24), 41 (28), 29 (12). Found 296.173. Calc. for $C_{15}H_{24}N_2O_4$ 296.176.

*1-(2,3-Dideoxy-3-hexyl-α-*D-threo-*pentofuranosyl)uracil* **9d**. Retention time 265 min, yield 20 mg. ^{1}H NMR (DMSO-d_6/TMS: δ 7.57 (d, 1 H, *J* 8.1 Hz, H–6), 6.02 (dd, 1 H, *J* 2.5, 6.5 Hz, H–1'), 5.54 (d, 1 H, *J* 8.1 Hz, H–5), 4.33–4.30 (m, 1 H, H–4'), 3.46 (dd, 2 H, *J* 3.9, 8.5 Hz, H–5'a, H–5'b), 2.28–1.99 (m, 3 H, H–3', H–2'α, H–2'β), 1.47–1.26 [m, 10 H, $(CH_2)_5$], 0.86–0.83 (m, 3 H, CH_3). ^{13}C NMR (DMSO-d_6/TMS): δ 163.90 (C–4), 150.46 (C–2), 140.28 (C–6), 101.02 (C–5), 85.39 (C–1'), 83.18 (C–4'), 60.98 (C–5'), 38.44 (C–3'), 37.77 (C–2'), 31.07, 28.81, 28.05, 27.77, 21.84, 13.86 (hexyl). MS: *m/z* (%) 296 (M^+, 1.6), 185 (10), 141 (42), 123 (20), 113 (34), 83 (26), 81 (44), 69 (44), 67 (36), 55 (50), 43 (40), 41 (54), 29 (24).

*1-(2,3-Dideoxy-3-hexyl-β-*D-threo-*pentofuranosyl)uracil* **10d**. Retention time 165 min, yield 10 mg. ^{1}H NMR (DMSO-d_6/TMS): δ 8.13 (d, 1 H, *J* 8.1 Hz, H–6), 6.03 (dd, 1 H, *J* 5.5, 8.6 Hz, H–1'), 5.69 (d, 1 H, *J* 8.1 Hz, H–5), 4.09–4.06 (m, 1 H, H–4'), 3.80–3.67 (m, 2 H, H–5'a, H–5'b), 2.57–2.52 (m, 2 H, H–3', H–2'α), 1.84–1.70 (m, 1 H, H–2'β), 1.54–1.32 [m, 10 H, $(CH_2)_5$], 0.94–0.91 (m, 3 H, CH_3). ^{13}C NMR (DMSO-d_6/TMS): δ 163.50 (C–4), 150.61 (C–2), 140.77 (C–6), 101.55 (C–5), 84.37 (C–1'), 81.23 (C–4'), 61.41 (C–5'), 36.81 (C–2'), 31.28, 28.96, 28.20, 28.03, 22.16, 14.05 (hexyl). MS: *m/z* (%) 296 (M^+, 2.5), 185 (100), 141 (36), 113 (34), 83 (22), 81 (28), 69 (34), 67 (22), 55 (38), 43 (32), 31 (40). Found 296.175. Calc. for $C_{15}H_{24}N_2O_4$ 296.176.

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