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Synthesis of an AZT-HEPT Hybrid and Homologous AzddU Derivatives

Erik Larsen,[a] Krzysztof Danel,[a] Gitte B. Vaaben,[a] Ali A. El-Emam,[a] Erik B. Pedersen[a,*] and Claus Nielsen[b]

[a]Department of Chemistry, Odense University, DK-5230 Odense M, Denmark and [b]Retrovirus Laboratory, Department of Virology, Statens Seruminstitut, Artillerivej 5, DK-2300 Copenhagen, Denmark

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3′-Azido-2′,3′-dideoxyuridines **6** and their corresponding α anomers **5** were synthesized by condensation of silylated 6-alkyl and 5,6-dialkyl substituted uracils **2** with methyl 3-azido-5-*O*-*tert*-butyldiphenylsilyl-2,3-dideoxy-α,β-D-*erythro*-pentofuranoside (**4**). Compounds **5** and **6** were treated with tetrabutylammonium fluoride to obtain the deprotected nucleosides **7** and **8**, respectively.

After the discovery that human immunodeficiency virus (HIV) is the causative agent of acquired immunodeficiency syndrome (AIDS),[1,2] many 2′,3′-dideoxy nucleosides have been synthesized and investigated for their activity against HIV. In particularly, 3′-azido-3′-deoxythymidine (AZT)[3] is a useful drug against HIV, but also 6-substituted 3′-azido-2′,3′-dideoxyuridine (AZddU) derivatives have been of interest as potential drugs.[4] Recently, acyclic nucleosides of the HEPT type (1-[(2-hydroxyethoxy) methyl]-6-(phenylthio) thymine) have shown high selectivity towards HIV-1,[5] and it was found that replacement of the sulfur atom with a methylene group resulted in a new series of potent HEPT analogues, of which MKC-442 (6-benzyl-1-ethoxymethyl-5-isopropyluracil) was found to be extremely potent.[6]

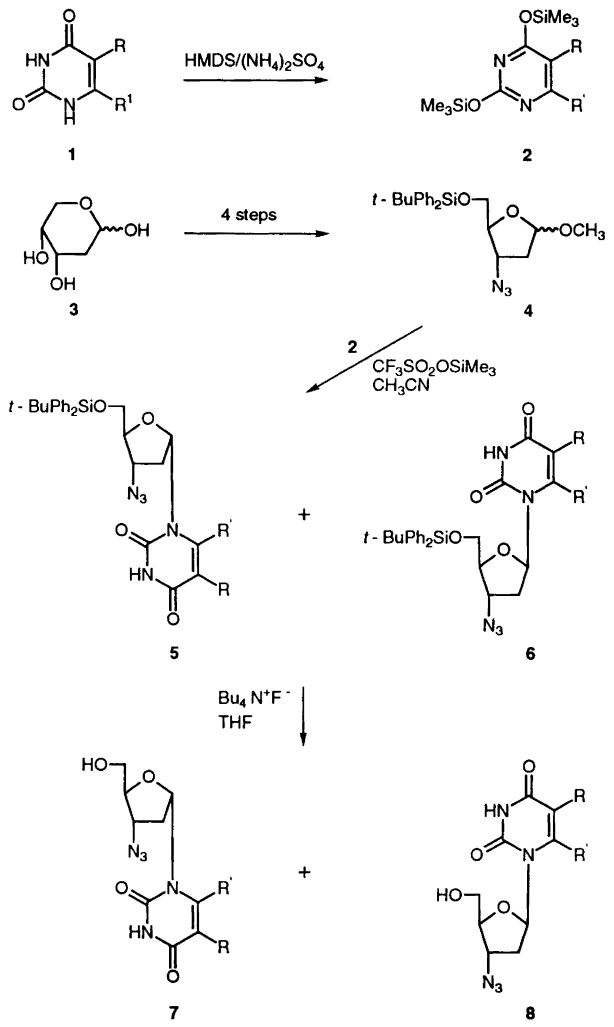
Recently, we have attempted to synthesize a hybrid between HEPT and AZT by condensing 6-phenylthiouracil with an appropriate 3-azido sugar derivative,[7] but we failed because glycosylation occured at $N-3$. Now we report that this method instead can be used successfully for the synthesis of a hybrid between AZT and the 6-benzyl analogs of HEPT. In fact, we find that 6-alkyl uracils are generally glycosylated at $N-1$ when condensed with a methyl 3-azido-2-deoxyglycoside.

Results and discussion

The starting materials 6-alkyluracils **1c,d**[8] and 5-ethyl-6-benzyluracil **1e**[9] were prepared by reaction of ethyl 3-oxovalerate, ethyl butyrylacetate and ethyl 2-ethyl-4-phenyl-3-oxobutyrate,[9,10] respectively, with thiourea and sodium ethoxide. The intermediate 2-thiouracils were finally refluxed with chloroacetic acid for 6–18 h. The uracils **1c–e** and the commercially available 6-methyluracil (**1a**) and 5,6-dimethyluracil (**1b**) were silylated[11] with 1,1,1,3,3,3-hexamethyldisilazane (HMDS) prior to condensation with methyl 3-azido-5-*O*-*tert*-butyldiphenylsilyl-2,3-dideoxy-α,β-D-*erythro*-pentofuranoside (**4**). The sugar was prepared in four steps from the commercially available 2-deoxy-D-ribose (**3**) by successive glycosidation[12] with methanolic HCl, selective 5-*O*-silylation with *tert*-butyldiphenylchlorosilane, replacement of 3-hydroxy with an iodo group in a Mitsunobu reaction[13,14] and finally treatment with sodium azide in dry *N,N*-dimethylformamide.[15] The nucleoside synthesis was accomplished by using trimethylsilyl trifluoromethanesulfonate (TMS triflate) as a Lewis acid catalyst according to the method described by Vorbrüggen *et al.*[16,17] to give an anomeric mixture of the protected nucleosides **5a,b,e** and **6a,b,e** in 43–64% yield (**5a,6a:** α/β = 1:1; **5b,6b:** α/β = 10:7; **5e,6e:** α/β = 7:10). Subsequent removal of the silyl protecting group with tetrabutylammonium fluoride followed by chromatographic purification afforded the unprotected nucleosides **7a,b,e** and **8,b,e** in 11–29 and 11–21% yields, respectively (Scheme 1).

In the case of the 6-ethyl AZddU derivative, which gave an 3:2 (α/β) anomeric mixture after the coupling reaction, the protected nucleoside was separated into the α- and β-anomers (**5c** and **6c**) by silica gel chromatography in 34 and 25% yield, respectively. Subsequent removal of the silyl protecting group with tetrabutylammonium fluoride followed by chromatographic puri-

* To whom correspondence should be addressed.



1-8	a	b	c	d	e
R	H	CH_3	H	H	C_2H_5
R'	CH_3	CH_3	C_2H_5	C_3H_7	CH_2Ph

Scheme 1.

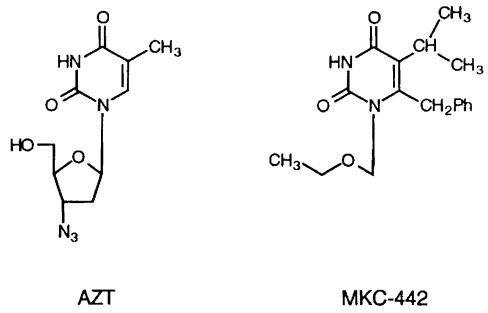


Fig. 1.

fication afforded the unprotected nucleosides **7c** and **8c** in 23 and 18% yields, respectively. Also in case of the 6-propyl AZddU derivative giving an 4:1 (α/β) anomeric mixture after the coupling reaction, the anomers were separated before deprotection. In all the nucleoside syntheses neither mono-$N-3$ glycosylation nor $N-1$, $N-3$ bisglycosylation was observed when TMS triflate was used as the catalyst in agreement with the literature observation.[16,18] The new compounds were identified by comparison of similar NMR data,[9,19] ^{1}H-COSY and ^{1}H-nuclear Overhauser effects (NOE) of the compounds **7b,e** and **8b,c,e**. NOE of **7e** confirmed it to be an α anomer. A decisive feature was irradiation of 2′-H at the β face which resulted in 9% NOE in 3′-H and 6% in 1′-H whereas irradiation of 2′-H at the α face gave 3% NOE in 3′-H, 1% in 1′-H and 2% in 4′-H. $N-1$ glycosylation was confirmed by 6% NOE in the benzylic CH_2 group when 1′-H was irradiated. NOE of **8e** proved it to be a β anomer as irradiation of 2′-H at the α site resulted in 6% NOE in 1′-H and 2% in 3′-H whereas irradiation of 2′-H at the β site gave 8% NOE in 3′-H and 2% in 1′-H. N-1 glycosylation was confirmed by 6% NOE in the benzylic CH_2 group when 1′-H was irradiated.

The nucleosides **7b,e** and **8b** did not show any significant activity in 100 μM concentration against HIV-1 in MT-4 cells. Compound **8e** showed toxicity against MT-4 cells in 10 μM concentration, but no activity against HIV-1 was observed at a lower concentration. Expression of HIV in culture medium was quantified by antigen detection ELISA. The same compounds were also devoid of any activity in 100 μM concentration against herpes simplex virus, type 1 (HSV-1), strain McIntyre when tested in African green monkey kidney cell line Vero.

Experimental

*1-(3-Azido-2,3-dideoxy-α-D-*erythro*-pentofuranosyl)-6-methyluracil* (**7a**) *and its* β*-anomer* (**8a**).

Typical procedure. 6-Methyluracil (**1a**) (0.78 g, 6.2 mmol) was dissolved in 1,1,1,3,3,3-hexamethyldisilazane (HMDS) (25 ml). $(NH_4)_2SO_4$ (50 mg, 0.37 mmol) was added and the solution was heated under reflux for 18 h. The solvent was evaporated *in vacuo* to yield the silylated base (**2**) as a colourless oil. Dry MeCN (25 ml) was added to the silylated base, followed by a solution of 3-azidofuranoside **4** (1.70 g, 4.1 mmol) in MeCN (25 ml) and the mixture was cooled to −30 °C. Trimethylsilyl trifluoromethanesulfonate (1.1 ml, 6.2 mmol) in MeCN (10 ml) was added dropwise (20 min) to the mixture with stirring. The reaction mixture was stirred at −30 °C for 2 h, diluted with CH_2Cl_2 (150 ml), neutralized with cold sat. aq. $NaHCO_3$ (75 ml), washed with cold sat. aq. $NaHCO_3$ (2 × 50 ml) and water (50 ml), dried (Na_2SO_4) and evaporated *in vacuo* to give a crude black product which was subjected to silica gel (150 g) column chromatography with MeOH–CH_2Cl_2 (1:99) to yield 900 mg (43%) of **5a/6a** as a colourless oil (α/β = 1:1). The mixture **5a/6a** (900 mg, 1.8 mmol) was dissolved in THF (30 ml) and 2 ml of 1 M Bu_4NF in THF was added slowly (10 min) at 0 °C. The reaction

mixture was stirred for 1 h and the solvent was evaporated *in vacuo*. After silica gel column chromatography with MeOH-$CHCl_3$ (2:98) afforded the products **7a** as a colourless solid and **8a** as a colourless oil.

Compound ***7a***. 0.160 g (14%); m.p. 151–153 °C. ^{1}H NMR (DMSO-d_6/TMS): δ 2.24 (s, 3 H, CH_3), 2.57–2.79 (m, 2 H, 2′-H), 3.32–3.58 (m, 2 H, 5′-H), 4.03 (q, *J* 8.7 Hz, 1 H, 3′-H), 4.21–4.27 (m, 1 H, 4′-H), 4.87 (br s, 1 H, OH), 5.50 (s, 1 H, 5-H), 5.94 (t, *J* 7.3 Hz, 1 H, 1′-H), 11.18 (br s, 1 H, NH). ^{13}C NMR (DMSO-d_6/TMS): δ 19.7 (CH_3), 33.6 (C-2′), 59.8 (C-3′), 60.9 (C-5′), 83.4 (C-4′), 85.5 (C-1′), 102.1 (C-5), 150.7 (C-2), 153.2 (C-6), 162.3 (C-4). Anal. $C_{10}H_{13}N_5O_4 \cdot 0.25\ H_2O$: C, H, N.

Compound ***8a***. 0.120 g (11%). ^{1}H NMR (DMSO-d_6/TMS): δ 2.26 (s, 3 H, CH_3), 2.79–2.90 (m, 2 H, 2′-H), 3.57 (t, *J* 5.0 Hz, 2 H, 5′-H), 3.68–3.75 (m, 1 H, 4′-H), 4.32–4.41 (m, 1 H, 3′-H), 4.90 (t, *J* 5.1 Hz, 1 H, OH), 5.50 (s, 1 H, 5-H), 6.01 (dd, *J* 4.4 and 8.8 Hz, 1 H, 1′-H), 11.17 (s, 1 H, NH). ^{13}C NMR (DMSO-d_6/TMS): δ 19.5 (CH_3), 35.0 (C-2′), 61.1 (C-3′), 61.3 (C-5′), 84.1 (C-4′), 84.4 (C-1′), 102.2 (C-5), 150.4 (C-2), 153.4 (C-6), 162.2 (C-4). Calc. for $C_{10}H_{13}N_5O_4$: 267.248. Found 267.250 (MS).

*1-(3-Azido-2,3-dideoxy-*α*-D-*erythro*-pentofuranosyl)-5,6-dimethyluracil* (**7b**) *and its* β*-anomer* (**8b**). The coupling reaction was performed at −45 °C for 3 h. α/β = 10:7 in the crude product. The deprotected nucleosides **7b** and **8b** were purified by silica gel (120 g) column chromatography with Et_2O and obtained as colourless solids.

Compound ***7b***. 0.244 g (29%); m.p. 166–168 °C. ^{1}H NMR (DMSO-d_6/TMS): δ 1.81 (s, 3 H, CH_3), 2.24 (s, 3 H, CH_3), 2.49–2.79 (m, 2 H, 2′-H), 3.41–3.57 (m, 2 H, 5′-H), 4.04 (q, *J* 8.7 Hz, 1 H, 3′-H), 4.20–4.27 (m, 1 H, 4′-H), 4.88 (t, *J* 5.6 Hz, 1 H, OH), 6.01 (t, *J* 7.4 Hz, 1 H, 1′-H), 11.17 (br s, 1 H, NH). ^{13}C NMR (DMSO-d_6/TMS): δ 10.7 (CH_3), 16.3 (CH_3), 33.6 (C-2′), 59.8, 60.9 (C-3′ and C-5′), 83.1, 85.6 (C-1′ and C-4′), 107.2 (C-5), 148.0, 150.1 (C-2 and C-6), 163.0 (C-4). Calc. for $C_{11}H_{15}N_5O_4$: 281.112. Found 281.111 (MS).

Compound ***8b***. 0.174 g (21%); m.p. 110–112 °C. ^{1}H NMR (DMSO-d_6/TMS): δ 1.88, (s, 3 H, CH_3), 2.15–2.25 (m, 1 H, 2′-H), 2.26 (s, 3 H, CH_3), 2.79–2.90 (m, 1 H, 2′-H), 3.56–3.60 (m, 2 H, 5′-H), 3.68–3.75 (m, 1 H, 4′-H), 4.34–4.43 (m, 1 H, 3′-H), 4.91 (t, *J* 5.2 Hz, 1 H, OH), 6.09 (dd, *J* 4.5 and 8.7 Hz, 1 H, 1′-H), 11.23 (s, 1 H, NH). ^{13}C NMR (DMSO-d_6/TMS): δ 10.8 (CH_3), 16.3 (CH_3), 35.1 (C-2′), 61.1, 61.3 (C-3′ and C-5′), 84.0, 84.7 (C-1′ and C-4′), 107.4 (C-5), 148.3 (C-2), 150.0 (C-6), 163.0 (C-4). FAB MS (DMSO, 3-nitrobenzylalcohol): *m/z* 282 ($M+H^+$).

*1-(3-Azido-5-*O*-*tert*-butyldiphenylsilyl-2,3-dideoxy-*α*-D-*erythro*-pentofuranosyl)-6-ethyluracil* (**5c**) *and its* β*-anomer* (**6c**). The reaction was performed at −25 °C for 4 h. α/β = 3:2 in the crude product. α and β anomers were separated by silica gel chromatography with the gradient 0–0.5 % MeOH in CH_2Cl_2.

Compound ***5c***. 0.860 g (34%). ^{1}H NMR (DMSO-d_6/TMS): δ 1.00 (s, 9 H, *t*-Bu), 1.12 (t, *J* 7.3 Hz, 3 H, CH_3), 2.48–2.87 (m, 4 H, CH_2 and 2′-H), 3.70–3.84 (m, 2 H, 5′-H), 4.16 (q, *J* 8.8 Hz, 1 H, 3′-H), 4.37–4.43 (m, 1 H, 4′-H), 5.48 (s, 1 H, 5-H), 5.92 (t, *J* 7.2 Hz, 1 H, 1′-H), 7.38–7.65 (m, 10 H, ArH), 11.25 (s, 1 H, NH). ^{13}C NMR (DMSO-d_6/TMS): δ 12.2 (CH_3), 18.7 (Me_3C), 25.3 (CH_2), 26.5 (Me_3C), 33.3 (C-2′), 59.7 (C-3′), 63.5 (C-5′), 82.7 (C-4′), 85.1 (C-1′), 100.6 (C-5), 127.7, 127.7, 129.8, 132.7, 135.0 (aryl), 150.8 (C-2), 157.9 (C-6), 162.5 (C-4).

Compound ***6c***. 0.630 g (25 %). ^{1}H NMR (DMSO-d_6/TMS): δ 0.99 (s, 9 H, *t*-Bu), 1.12 (t, *J* 7.3 Hz, 3 H, CH_3), 2.25–2.54 (m, 1 H, 2′-H), 2.59 (q, *J* 7.3 Hz, 2 H, CH_2), 2.82–2.92 (m, 1 H, 2′-H), 3.74–3.88 (m, 3 H, 4′-H and 5′-H), 4.37–4.47 (m, 1 H, 3′-H), 5.47 (s, 1 H, 5-H), 6.01 (dd, *J* 3.3 and 8.8 Hz, 1 H, 1′-H), 7.34–7.64 (m, 10 H, ArH), 11.15 (s, 1 H, NH). ^{13}C NMR (DMSO-d_6/TMS): δ 12.1 (CH_3), 18.7 (Me_3C), 25.1 (CH_2), 26.4 (Me_3C), 35.2 (C-2′), 61.3 (C-3′), 64.3 (C-5′), 84.0 (C-4′), 84.3 (C-1′), 100.4 (C-5), 127.6, 127.7, 129.3, 129.7, 132.6, 132.8, 134.9, 135.0 (aryl), 150.3 (C-2), 158.1 (C-6), 162.5 (C-4).

*1-(3-Azido-2,3-dideoxy-*α*-D-*erythro*-pentofuranosyl)-6-ethyluracil* (**7c**). *Typical procedure.* To a solution of **5c** (500 mg, 0.96 mmol) in THF (18 ml) was slowly added (10 min) 1.2 ml of 1 M Bu_4NF in THF at 0 °C. The reaction mixture was stirred for 2 h and the solvent was evaporated *in vacuo*. After silica gel (100 g) column chromatography (gradient from 0–5% MeOH in $CHCl_3$) afforded the product **7c** as a colourless solid. Yield 0.320 g (23%); m.p. 164–166 °C. ^{1}H NMR (DMSO-d_6/TMS): δ 1.13 (t, *J* 7.3 Hz, 3 H, CH_3), 2.51–2.84 (m, 4 H, CH_2 and 2′-H), 3.41–3.59 (m, 2 H, 5′-H), 4.01 (q, *J* 8.8 Hz, 1 H, 3′-H), 4.23–4.30 (m, 1 H, 4′-H), 4.85 (t, *J* 5.6 Hz, OH), 5.46 (s, 1 H, 5-H), 5.91 (d, *J* 7.3 Hz, 1 H, 1′-H), 11.19 (s, 1 H, NH). ^{13}C NMR (DMSO-d_6/TMS): δ 12.3 (CH_3), 25.3 (CH_2), 33.4 (C-2′), 59.7 (C-3′), 60.9 (C-5′), 83.3 (C-4′), 85.0 (C-1′), 100.3 (C-5), 150.8 (C-2), 158.0 (C-6), 162.5 (C-4). Anal. $C_{11}H_{15}N_5O_4$: C, H, N.

*1-(3-Azido-2,3-dideoxy-*β*-D-*erythro*-pentofuranosyl)-6-ethyluracil* (**8c**). Colourless oil. Yield 0.248 g (18%). ^{1}H NMR (DMSO-d_6/TMS): δ 1.13 (t, *J* 7.3 Hz, 3 H, CH_3), 2.18–2.30 (m, 1 H, 2′-H), 2.59 (q, *J* 7.3 Hz, 2 H, CH_2), 2.79–2.90 (m, 1 H, 2′-H), 3.58 (br s, 2 H, 5′-H), 3.73 (q, *J* 5.9 Hz, 1 H, 4′-H), 4.37 (q, *J* 7.7, 1 H, 3′-H), 4.86 (br s, 1 H, OH), 5.46 (s, 1 H, 5-H), 5.98 (dd, *J* 4.0 and 8.9 Hz, 1 H, 1′-H), 11.19 (br s, 1 H, NH). ^{13}C NMR (DMSO-d_6/TMS): δ 12.3 (CH_3), 25.2 (CH_2), 35.2 (C-2′), 61.5, 61.6 (C-3′, C-5′), 84.3, 84.4 (C-1′, C-4′), 100.4 (C-5), 150.5 (C-2), 158.1 (C-6), 162.5 (C-4). Anal. $C_{11}H_{15}N_5O_4 \cdot 1.0H_2O$: C, H, N.

*1-(3-Azido-5-*O*-tert-butyldiphenylsilyl-2,3-dideoxy-α-D-*erythro*-pentofuranosyl)-6-propyluracil* (**5d**) *and its* β-*anomer* (**6d**). Compounds **5d** and **6d** were prepared similarly to **5c** and **6c** from 6-propyluracil (**1d**) (1.15, 7.4 mmol). The reaction was performed at −25 °C for 4 h. The crude yellow product (α/β = 4:1) was subjected to silica gel (150 g) column chromatography (gradient from 0–0.75% MeOH in CH_2Cl_2) to afford the products **5d** as a colourless and **6d** as a colourless oil.

Compound ***5d***. 0.717 g (27%). ^{1}H NMR (DMSO-d_6/TMS): δ 0.91 (t, *J* 7.3 Hz, 3 H, CH_3), 1.01 (s, 9 H, *t*-Bu), 1.45–1.67 (m, 2 H, CH_2), 2.36–2.92 (m, 4 H, CH_2 and 2′-H), 3.71–3.85 (m, 2 H, 5′-H), 4.18 (q, *J* 8.8 Hz, 1 H, 3′-H), 4.38–4.44 (m, 1 H, 4′-H), 5.49 (s, 1 H, 5-H), 5.92 (t, *J* 7.3 Hz, 1 H, 1′-H), 7.39–7.67 (m, 10 H, ArH), 11.25 (s, 1 H, NH). ^{13}C NMR (DMSO-d_6/TMS): δ 13.1 (CH_3), 18.7 (Me_3C), 20.5 (CH_2), 26.4 (Me_3C), 33.2 (C-2′), 33.8 (CH_2), 59.5 (C-3′), 63.3 (C-5′), 82.7 (C-4′), 85.2 (C-1′), 101.6 (C-5), 127.7, 127.7, 129.7, 132.6, 132.7, 134.9, 134.9 (aryl), 150.8 (C-2), 156.1 (C-6), 162.3 (C-4).

Compound ***6d***. 0.163 g (6%). ^{1}H NMR (DMSO-d_6/TMS): δ 0.94 (t, *J* 7.3 Hz, 3 H, CH_3), 1.01 (s, 9 H, *t*-Bu), 1.49–1.65 (m, 2 H, CH_2), 2.27–2.67 (m, 3 H, 2′-H and CH_2), 2.88 (ddd, *J* 3.2, 3.9 and 5.7 Hz, 1 H, 2′-H), 3.79–3.94 (m, 3 H, 5′-H and 4′-H), 4.43 (q, *J* 7.6 Hz, 1 H, 3′-H), 6.01 (dd, *J* 3.3 and 8.8 Hz, 1 H, 1′-H), 7.36–7.67 (m, 10 H, ArH), 11.16 (s, 1 H, NH). ^{13}C NMR (DMSO-d_6/TMS): δ 13.1 (CH_3), 18.7 (Me_3C), 20.6 (CH_2), 26.4 (Me_3C), 33.7 (CH_2), 35.2 (C-2′), 61.3 (C-3′), 64.4 (C-5′), 84.1 (C-4′), 84.5 (C-1′), 101.4 (C-5), 127.6, 127.7, 129.7, 132.6, 132.8, 134.9, 135.0 (aryl), 150.3 (C-2), 156.3 (C-6), 162.3 (C-4).

*1-(3-Azido-2,3-dideoxy-α-D-*erythro*-pentofuranosyl)-6-propyluracil* (**7d**). Silica gel (125 g) column chromatography (gradient from 0 to 4% MeOH in $CHCl_3$) afforded a colourless solid. Yield 0.570 g (39%); m.p. 132–134 °C. ^{1}H NMR (DMSO-d_6/TMS): δ 0.93 (t, *J* 7.3 Hz, 3 H, CH_3), 1.53 (hextet, *J* 7.1 Hz, 2 H, CH_2), 2.46–2.83 (m, 4 H, CH_2 and 2′-H), 3.41–3.60 (m, 2 H, 5′-H), 4.01 (q, *J* 8.9 Hz, 1 H, 3′-H), 4.24–4.31 (m, 1 H, 4′-H), 4.85 (t, *J* 5.6 Hz, 1 H, OH), 5.46 (s, 1 H, 5-H), 5.89 (t, *J* 7.3 Hz, 1 H, 1′-H), 11.19 (s, 1 H, NH). ^{13}C NMR (DMSO-d_6/TMS): δ 13.2 (CH_3), 20.6 (CH_2), 33.5 (C-2′), 33.8 (CH_2), 59.8 (C-3′), 60.9 (C-5′), 83.4 (C-4′), 85.2 (C-1′), 101.4 (C-5), 150.8 (C-2), 156.3 (C-6), 162.4 (C-4). Calc. for $C_{12}H_{17}N_5O_4$: 295.300. Found 295.302 (MS).

*1-(3-Azido-2,3-dideoxy-β-D-*erythro*-pentofuranosyl)-6-propyluracil* (**8d**). Silica gel (50 g) column chromatography (gradient from 0 to 2% MeOH in $CHCl_3$) afforded a colourless oil. Yield 0.128 g (9%). ^{1}H NMR (DMSO-d_6/TMS): δ 0.94 (t, *J* 7.3 Hz, 3 H, CH_3), 1.46–1.61 (hextet, *J* 7.1 Hz, 2 H, CH_2), 2.19–2.31 (m, 1 H, 2′-H), 2.50–2.57 (m, 2 H, CH_2), 2.83 (ddd, *J* 4.0, 9.1 and 13.5 Hz, 1 H, 2′-H), 3.57 (t, *J* 5.5 Hz, 2 H, 5′-H), 3.74 (q, *J* 6.0 Hz, 1 H, 4′-H), 4.31–4.40 (m, 1 H, 3′-H), 4.87 (t, *J* 5.6 Hz, 1 H, OH), 5.46 (s, 1 H, 5-H), 5.96 (dd, *J* 3.9 and 8.8 Hz, 1 H, 1′-H), 11.19 (s, 1 H, NH). ^{13}C NMR (DMSO-d_6/TMS): δ 13.2 (CH_3), 20.7 (CH_2), 33.7 (CH_2), 35.2 (C-2′), 61.5 (C-3′), 61.5 (C-5′), 84.4 (C-1′ and C-4′), 101.3 (C-5), 150.4 (C-2), 156.4 (C-6), 162.3 (C-4).

*1-(3-Azido-2,3-dideoxy-α-D-*erythro*-pentofuranosyl)-6-benzyl-5-ethyluracil* (**7e**) *and its* β-*anomer* (**8e**). The coupling reaction was performed at −45 °C for 3 h. α/β = 7:10 in the crude product. The deprotected nucleosides **7e** and **8e** were purified by evaporation of the THF, dissolving in Et_2O, washing with H_2O and drying the organic phase over Na_2SO_4. Evaporation under reduced pressure and silica gel (100 g) column chromatography with 25% Et_2O in petroleum ether (b.p. 60–80 °C) afforded the nucleosides **7e** and **8e** as colourless oils.

Compound ***7e***. 0.174 g (11%). ^{1}H NMR ($CDCl_3$/TMS): δ 1.04 (t, *J* 7.3 Hz, 3 H, CH_3), 1.65–1.79 (m, 1 H, 1 H, 2a′-H), 2.36–2.83 (m, 3 H, 2b′-H, CH_2), 3.59 (dd, *J* 3.4 and 12.5 Hz, 1 H, 5a′-H), 3.79–3.94 (m, 3 H, 5b′-H, 3′-H, CH_2Ph), 4.21 (d, *J* 21.3 Hz, 1 H, CH_2Ph), 4.29–4.55 (m, 1 H, 4′-H), 5.76 (t, *J* 7.4 Hz, 1 H, 1′-H), 7.09–7.39 (m, 5 H, ArH). ^{13}C NMR ($CDCl_3$/TMS): δ 13.7 (CH_3), 19.2 (CH_2), 33.9 (C-2′), 34.5 (CH_2Ph), 59.1 (C-3′), 61.0 (C-5′), 83.9 (C-4′), 86.9 (C-1′), 116.5 (C-5), 127.4, 127.4, 129.2, 134.9 (aryl), 148.4 (C-6), 150.6 (C-2), 163.3 (C-4). FAB MS ($CHCl_3$, 3-nitrobenzylalcohol): *m/z* 372 ($M+H^+$).

Compound ***8e***. 0.234 g (15%). ^{1}H NMR ($CDCl_3$/TMS): δ 1.07 (t, *J* 7.4 Hz, 3 H, CH_3), 1.34–1.44 (m, 1 H, 2a′-H), 2.36–2.81 (m, 3 H, 2b′-H, CH_2), 3.79–3.94 (m, 4 H, 5′-H, 4′-H, CH_2Ph), 4.27 (d, *J* 17.2 Hz, 1 H, CH_2Ph), 4.43–4.50 (m, 1 H, 3′-H), 5.76 (t, *J* 6.6 Hz, 1 H, 1′-H), 7.12–7.41 (m, 5 H, ArH). ^{13}C NMR ($CDCl_3$/TMS): δ 13.6 (CH_3), 19.2 (CH_2), 34.6 (CH_2Ph), 35.1 (C-2′), 60.5 (C-3′), 62.2 (C-5′), 85.0 (C-4′), 86.7 (C-1′), 117.0 (C-5), 127.3, 127.5, 129.3, 134.7 (aryl), 148.3 (C-5), 150.9 (C-2), 163.1 (C-4). FAB MS ($CHCl_3$, 3-nitrobenzylalcohol): *m/z* 372 ($M + H^+$).

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