Synthesis and Evaluation of Antiviral Activity of L-Acosamine and L-Ristosamine Nucleosides of Furanose Configuration

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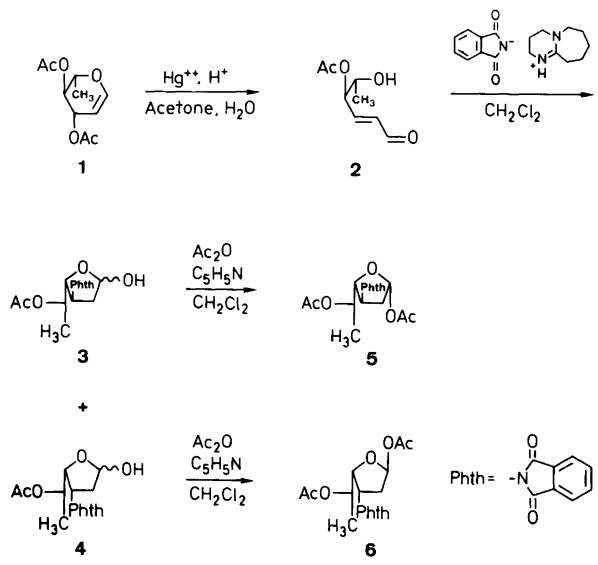
Mercuric-catalyzed hydrolysis of acetylated L-rhamnal **1** gives an α,β-unsaturated aldehyde **2**. 1,4-Addition of DBU–phthalimide salt with concomitant acetyl shift resulted in L-*ribo* and L-*arabino* isomers of 5-*O*-acetyl-2,3,6-trideoxy-3-phthalimidohexofuranose **3** and **4**. After acetylation at the anomeric center, coupling with silylated thymine resulted in three new nucleosides, with L-acosamine and L-ristosamine of furanose configuration as the carbohydrate moiety. The target compounds have been evaluated for their antiviral activity against HIV and HSV-1.

The 3-amino-2,3,6-trideoxyhexoses, L-daunosamine (*lyxo*), L-acosamine (*arabino*), L-ristosamine (*ribo*) and 3-*epi*-daunosamine (*xylo*) are distributed in nature as the glycosidic moiety of several important antibiotics, which, together with synthetic analogs, exhibit impressive anticancer activity.[1–3] In addition, synthetic 3′-amino-2′,3′-dideoxy nucleosides are described as biologically active against murine sarcoma virus 180 cells and murine L1210 cells *in vitro*[4–7] and show antiviral activity against adenovirus[8] and HSV.[9] Furthermore, 3′-amino-2′,3′-dideoxy nucleosides are reported to have moderate activity against Moloney murine leukemia (M-MULV) which is caused by a mammalian T-lymphotropic retrovirus,[10] and to inhibit the enzyme reverse transcriptase *in vitro*,[11] although the activities against HIV infected human cells are reported to be rather limited.[12]

In connection with our investigation of new 3′-amino-2′-3′-dideoxy nucleosides,[13–15] we present a new method for the preparation of protected L-acosamine **6** and L-ristosamine **5** possessing the furanose configuration. These two new carbohydrates are used for the preparation of three new thymine derivatives **11**, **12** and **13** in order to evaluate the antiviral activities of these compounds. The synthesis of new 3′-substituted 2′,3′-dideoxy nucleosides is of increasing importance in the quest to combat AIDS.[12]

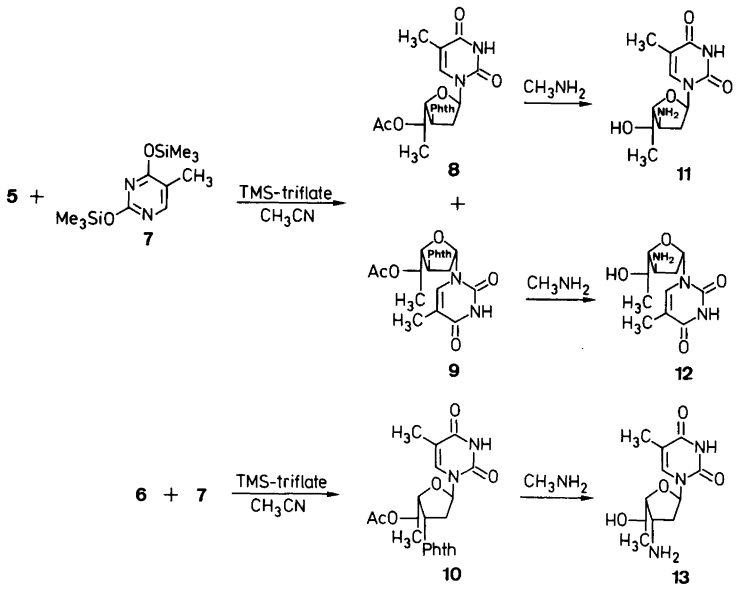
Chemistry

The L-*ribo* and L-*arabino* isomers of 5-*O*-acetyl-2,3,6-trideoxy-3-phthalimidohexofuranose **3** and **4** were obtained in two steps from commercially available acetylated L-rhamnal **1**. Mercuric-catalyzed hydrolysis[16] of L-rhamnal gave the α,β-unsaturated aldehyde **2**[17] in 91 % yield. Subsequently, 1,4-addition of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) phthalimide salt together with a concomitant acetyl shift from 4-*O* to 5-*O* of the aldehyde resulted in ring closure to give **3** and **4** in 30 and 21 % yield, respectively, after purification. Finally, acetylation of **3** and **4** gave the desired carbohydrates **5** and **6** suitable for synthesis of a new class of amino nucleosides.



Scheme 1.

Application of the reported[18,19] procedure for nucleoside synthesis using trimethylsilyl trifluoromethanesulfonate (TMS-triflate) as a Lewis acid, resulted in the protected 3′-phthalimido nucleosides **8**, **9** and **10**. When the *ribo* isomer **5** was used as the substrate in the synthesis of nucleosides, a 1:1 anomeric mixture of **8** and **9** was obtained which could be separated by means of preparative



Scheme 2.

HPLC. On the other hand, only one anomer **10** was obtained when the *arabino* isomer **6** was used as the substrate. The rather bulky β-substituents on C-3 and C-4 may explain the steric hindrance offered by the β-face of the furanose ring towards nucleophilic attack by the thymine base. Deprotection of **8**, **9** and **10** by treatment with methylamine in absolute ethanol finally gave the amino nucleosides **11**, **12** and **13** after chromatographic purification.

The configuration assignment of the carbohydrate substrates **5** and **6** as well as the nucleosides was made by comparison with similar compounds.[13–15] In particular, the β-D-*ribo* and α-D-*arabino* isomers of 1,5,6-tri-*O*-acetyl-2,3-dideoxy-3-phthalimodohexofuranoses[15,20] display very similar ^{1}H NMR shifts for the furanose ring protons when compared with **5** and **6**, respectively. Thus, in the dideoxy carbohydrates, 1-H of the β-D-*ribo* isomer is a doublet (5.0 Hz) at 6.52 ppm, very similar to 1-H of compound **5** which shows a doublet (4.9 Hz) at 6.48 ppm. On the other hand, the α-D-*arabino* isomer of the dideoxy carbohydrate is a double doublet (6.0 Hz and 3.5 Hz) at 6.60 ppm which is comparable to 1-H of compound **6** where a double doublet (6.0 Hz and 2.8 H) at 6.72 ppm is found. The ^{1}H NMR spectra of the nucleosides **8–13** are likewise very similar to the corresponding isomers from the 2,3-dideoxy nucleosides.[15]

Biological activity

The compounds **11** and **12** showed 42 and 54 % protection, respectively, at 100 μM against Herpes Simplex Virus type (HSV-1), strain McIntyre, when propagated in a continuous cell line from rabbit cornea (SIRL) which was maintained in Eagle's MEM containing 1 % fetal calf serum and antibiotics. No toxicity against the cells was observed at 100 μM. The compounds **8–13** were devoid of any activity against HVI-1 (strain HTLV-IIIB) in MT-4 cells.

Experimental

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC 250 FT NMR spectrometer. Microanalyses were carried out by NOVO Microanalytical Laboratory A/S, Novo Allé, DK-2880 Bagsværd. EI mass spectra were recorded on a Varian MAT 311A spectrometer.

(E)-*4-O-Acetyl-2,3,6-trideoxy*-aldehydo-L-erythro-*hex-2-enose* (**2**). Peracetylated L-rhamnal **1** (15.0 g, 70.0 mmol) was dissolved in acetone (150 ml). Mercuric sulfate (1.45 g, 4.8 mmol) and 5 mM sulfuric acid (250 ml) was immediately added. After 5 h at room temperature, analytical silica TLC showed a single spot (diethyl ether–hexane 4:1). The reaction mixture was extracted with chloroform (10×50 ml) and the combined organic phases washed with a saturated solution of sodium hydrogencarbonate (2×50 ml) and water (50 ml). After being dried over anhydrous magnesium sulfate, the solution was concentrated to a clear oil at reduced pressure. NMR spectroscopy showed this crude product to be sufficiently pure for the next reaction. Yield 11.2 g (91 %) of **2**. ^{1}H NMR ($CDCl_3$): δ 1.24 (d, 3 H, J = 6.5 Hz, 6-H), 2.16 (s, 3 H, OAc), 2.88 (br s, 1 H, OH), 4.02–4.08 (m, 1 H, 5-H), 5.44 (td, 1 H, J = 5.3, 1.4 Hz, 4-H), 6.25 (ddd, 1 H, J = 15.9, 7.7, 1.4 Hz, 2-H), 6.87 (dd, 1 H, J = 15.9, 5.3 Hz, 3-H), 9.57 (d, 1 H, J = 7.7 Hz, 1-H). ^{13}C NMR ($CDCl_3$): δ 18.02 (C-6), 20.45 (OAc), 68.15 (C-5), 75.89 (C-4), 132.77 (C-2), 150.40 (C-3), 192.99 (C-1).

5-O-Acetyl-2,3,6-trideoxy-3-phthalimido-L-ribo-*hexofuranose* (**3**) *and 5-O-Acetyl-2,3,6-trideoxy-3-phthalimido*-L-arabino-*hexofuranose* (**4**). A solution of α,β-unsaturated aldehyde **2** (11.0 g, 63.9 mmol) in dichloromethane (50 ml) was added dropwise, over a period of 1 h, to a cold (0 °C) solution of DBU–phthalimide salt[20] (15.0 g, 51.0 mmol) dissolved in dichloromethane (200 ml). After additional 2 h at 0 °C the reaction mixture was washed with ice-cold 1 M sulfuric acid (3×100 ml) and water (100 ml). After being dried over anhydrous magnesium sulfate the solution was concentrated to a yellow oil (14.4 g) at reduced pressure. The oil was further dried on an oil pump after which addition of dry diethyl ether (200 ml) gave a precipitate of **4** after the solution had been allowed to stand for 3 days at −18 °C. Yield 3.40 g (21 %), m.p. 117–119 °C. Pure α-isomer of **4** could be isolated by recrystallization from abs. ethanol.

α-isomer of **4**: ^{1}H NMR ($CDCl_3$): δ 1.28 (d, 3 H, J = 6.3 Hz, 6-H), 1.84 (s, 3 H, OAc), 2.36 (ddd, 1 H, J = 14.3, 9.2, 2.8 Hz, 2α-H), 2.76 (ddd, 1 H, J = 14.3, 5.8, 2.3 Hz, 2β-H), 3.08 (br s, 1 H, OH), 4.31 (dd, 1 H, J = 8.6, 5.3 Hz, 4-H), 4.83 (dq, 1 H, J = 8.6, 6.3 Hz, 5-H), 5.08 (ddd, 1 H, J = 9.2, 5.3, 2.3 Hz, 3-H), 6.02 (dd, 1 H, J = 5.8, 2.8 Hz, 1-H), 7.27–7.86 (m, 4 H, phth). ^{13}C NMR ($CDCl_3$): δ 17.06 (C-6), 20.79 (OAc), 38.33 (C-2), 50.89 (C-3), 68.08 (C-5), 81.40 (C-4), 98.52 (C-1), 123.09 (C′-4), 131.49 (C′-3a), 134.06 (C′-5), 168.04 (C′-2), 169.82 (OAc). Anal. ($C_{16}H_{17}NO_6$): C, H, N.

The mother liquid was purified by flash chromatography (Merck silica 230–400 mesh, 3×45 cm, diethyl ether–hexane 7:3) to give 6.11 g (30 %) of almost pure *ribo* isomer **3**.

1,5-Di-O-acetyl-2,3,6-trideoxy-3-phthalimido-β-L-ribo-*hexofuranose* (**5**). Compound **3** (6.0 g, 18.8 mmol) was acetylated with acetic anhydride (3.8 g, 37.2 mmol) and pyridine (3.0 g, 37.9 mmol) in dry dichloromethane (50 ml). After 3 h at 20 °C the reaction mixture was washed with ice-cold 1 M hydrochloric acid (3×15 ml) and water (15 ml). After being dried over anhydrous magnesium sulfate, the solution was evaporated to a white solid at reduced pressure. Flash chromatographic purification (Merck silica 230–400 mesh, dichloromethane–methanol 97:3) gave pure **5**. Yield 4.8 g (71 %), m.p. 108–109 °C. ^{1}H NMR ($CDCl_3$): δ 1.28 (d, 3 H, J = 6.3 Hz, 6-H), 1.96 (s, 3 H, OAc), 2.10 (s, 3 H, OAc), 2.26 (dd, 1 H, J = 13.1, 8.3 Hz, 2β-H), 3.05 (ddd, 1 H, J = 13.1, 8.0, 4.9 Hz, 2α-H), 4.43 (t, 1 H, J = 7.0 Hz, 4-H), 4.88–5.02 (m, 2 H, 3-H; 5-H), 6.48 (d, 1 H, J = 4.9 Hz, 1-H), 7.72–7.89 (m, 4 H, phth). ^{13}C NMR ($CDCl_3$): δ 16.36 (C-6), 20.81 (OAc), 21.02 (OAc), 34.80 (C-2), 50.02 (C-3), 71.71 (C-5), 82.39 (C-4), 97.87 (C-1), 123.19 (C′-4), 131.32 (C′-3a), 134.14 (C′-5), 167.70 (C′-2), 169.52 (OAc). Anal. ($C_{18}H_{19}NO_7$): C, H, N.

1,5-Di-O-acetyl-2,3,6-trideoxy-3-phthalimido-α-L-arabino-*hexofuranose* (**6**). Compound **4** (2.5 g, 7.8 mmol) was acetylated with acetic anhydride (0.8 g, 7.8 mmol) and pyridine (0.9 g, 11.4 mmol) in dichloromethane (50 ml) together with catalytic amount of 4-dimethylaminopyridine (20 mg). After 3 h at 20 °C the reaction mixture was washed with ice-cold 1 M sulfuric acid (3×15 ml) and water (15 ml). After being dried over magnesium sulfate the organic phase was concentrated to a solid at reduced pressure. Flash chromatographic purification (Merck silica 230–400 mesh, 3×40 cm, dichloromethane–methanol 97:3) gave pure **6** as a white solid. Yield 2.2 g (78 %), m.p. 154–156 °C. ^{1}H NMR ($CDCl_3$): δ 1.30 (d, 3 H, J = 6.2 Hz, 6-H), 1.84 (s, 3 H, OAc), 2.10 (s, 3 H, OAc), 2.46 (ddd, 1 H, J = 15.0, 9.0, 2.8 Hz, 2α-H), 2.94 (ddd, 1 H, J = 15.0, 6.0, 2.9 Hz, 2β-H), 4.28 (dd, 1 H, J = 8.8, 5.5 Hz, 4-H), 4.82 (dq, 1 H, J = 8.8, 6.2 Hz, 5-H), 5.10 (ddd, 1 H, J = 9.0, 5.5, 2.9 Hz, 3-H), 6.72 (dd, 1 H, J = 6.0, 2.8 Hz, 1-H), 7.71–7.84 (m, 4 H, phth). ^{13}C NMR ($CDCl_3$): δ 17.88 (C-6), 20.68 (OAc), 21.12 (OAc), 36.97 (C-2), 49.94 (C-3), 67.78 (C-5), 82.79 (C-4), 98.53 (C-1), 123.10 (C′-5), 131.29 (C′-3a), 134.12 (C′-4), 167.79 (C′-2), 169.54 (OAc), 169.88 (OAc). FAB MS *m/z* [DMSO, glycerol, NaCl] (%): 384 (M + Na^+, 40), 302 (M + H^+, 22). Anal. ($C_{18}H_{19}NO_7$): C, H, N.

1-(5-O-Acetyl-3-phthalimido-2,3,6-trideoxy-α-L-ribo-*hexofuranosyl)thymine* (**8**) and *1-(5-O-acetyl-3-phthalimido-2,3,6-trideoxy*-β-L-ribo-*hexofuranosyl)thymine* (**9**). A mixture of silylated thymine **7** (676 mg, 2.50 mmol), 1,5-di-*O*-acetyl-2,3,6-trideoxy-3-phthalimido-β-L-*ribo*-hexofuranose **5** (735 mg, 2.03 mmol) dissolved in dry acetonitrile (20 ml) was cooled to −15 °C. Trimethylsilyl trifluoromethanesulfonate (1 ml) was added dropwise and the reaction was followed by analytical silica TLC with methanol–dichloromethane (10:90) as the eluent. After 30 min, the reaction mixture was diluted with dichloromethane (100 ml) and quenched with a saturated solution of sodium hydrogencarbonate (50 ml). After 10 min the organic phase was washed successively with a saturated solution of sodium hydrogencarbonate (2×50 ml) and water (50 ml) and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave a white foam (695 mg) which was purified by flash chromatography (Merck silica 230–400 mesh, 2×30 cm, dichloromethane–methanol 95:5) to give a pure anomeric mixture of **8** and **9** (α:β ratio = 1:1, 650 mg, 75 %). Compounds **8** and **9** were separated on HPLC (Waters Delta Pak C-18, 300 Å, 15 μ, 57×300 mm, ethanol–water 32:68) to give 200 mg of analytically pure α-anomer **8** (t_R = 38 min) and 176 mg of analytically pure β-anomer **9** (t_R = 30 min).

α-Anomer **8**: m.p. 240–241 °C. ^{1}H NMR ($CDCl_3$): δ 1.25 (d, 3 H, J = 6.4 Hz, 6′-H), 2.01 (s, 3 H, CH_3), 2.06 (s, 3 H, OAc), 2.73 (dd, 2 H, J = 9.6, 7.5 Hz, 2′α-H, 2′β-H), 4.63 (dd, 2 H, J = 7.3, 5.3 Hz, 4′-H), 4.95–5.06 (m, 2 H, 3′-H, 5′-H), 6.43 (t, 1 H, J = 7.5 Hz, 1′-H), 7.78 (s, 6-H), 7.77–7.92 (m, 4 H, phth), 8.99 (br s, 1 H, NH). ^{13}C NMR ($CDCl_3$): δ 12.68 (CH_3), 15.61 (C′-6), 21.03 (OAc), 34.21 (C′-2), 49.96 (C′-3), 70.96 (C′-5), 80.84 (C′-4), 84.10 (C′-1), 111.85 (C-5), 123.55 (C″-4), 131.36 (C″-3a), 134.51 (C″-5), 135.18 (C-6), 150.36 (C-2), 163.53 (C-4), 167.47 (C″-2), 169.98 (OAc). MS: *m/z* (%): 427 (M^+, 1), 302 (64), 148 (15), 95 (100). Anal. ($C_{21}H_{21}N_3O_7$): C, H, N.

β-Anomer **9**: m.p. 271–272 °C. ^{1}H NMR ($CDCl_3$): δ 1.29 (d, 3 H, J = 6.4 Hz, 6′-H), 1.96 (s, 3 H, CH_3), 2.03 (s, 3 H, OAc), 2.30 (ddd, 1 H, J = 14.1, 11.0, 6.9 Hz, 2′β-H), 2.80 (ddd, 1 H, J = 14.1,6.9, 4.8 Hz, 2′α-H), 4.32 (t, 1 H, J = 5.7 Hz, 4′-H), 4.98 (ddd, 1 H, J = 11.0, 5.7, 4.8 Hz, 3′-H), 5.13 (dq, 1 H, J = 6.4, 5.7 Hz, 5′-H), 6.64 (t, 1 H, J = 6.9 Hz, 1′-H), 7.19 (s, 1 H, 6-H), 7.76–7.91 (m, 4 H, phth), 8.91 (br s, 1 H, NH). ^{13}C NMR ($CDCl_3$): δ 12.49 (CH_3), 16.31 (C′-6), 21.00 (OAc), 35.79 (C′-2), 48.84 (C′-3), 70.56 (C′-5), 82.14 (C′-4), 85.18 (C′-1), 111.21 (C-5), 123.49 (C″-4), 131.34 (C″-3), 134.37 (C″-5), 134.91 (C-6), 149.86 (C-2), 163.36 (C-4), 167.31 (C″-2), 169.86 (OAc). MS: *m/z* (%): 427 (M^+, 1), 302 (65), 148 (14), 95 (100). Anal. ($C_{21}H_{21}N_3O_7$): C, H, N.

*1-(5-O-Acetyl-3-phthalimido-2,3,6-trideoxy-*α*-L-*arabino*-hexofuranosyl)thymine* (**10**). A mixture of silylated thymine **7** (1.15 g, 4.25 mmol) and 1,5-di-*O*-acetyl-2,3,6-trideoxy-3-phthalimido-α-L-*arabino*-hexofuranose **6** (1.50 g, 4.15 mmol) dissolved in dry acetonitrile (50 ml) was cooled to −35 °C. Trimethylsilyl trifluoromethanesulfonate (1.5 ml) was added dropwise. After 15 min analytical silica TLC with dichloromethane–methanol (9:1) as the eluent showed the complete absence of compound **6**. The reaction mixture was diluted with dichloromethane (100 ml) and quenched with a saturated solution of sodium hydrogencarbonate (50 ml). After 10 min, the organic phase was washed successively with a saturated solution of sodium hydrogencarbonate (2×50 ml) and water (50 ml). After being dried over anhydrous magnesium sulfate, the organic solution was concentrated to a white solid at reduced pressure. Yield 1.05 g (59 %). Recrystallization from 96 % ethanol gave analytically pure **10**. Yield 0.95 g (54 %), m. p. 218–220 °C. ^{1}H NMR (DMSO-d_6): δ 1.19 (d, 3 H, J = 5.0 Hz, 6′-H), 1.76 (s, 3 H, CH_3), 1.84 (s, 3 H, OAc), 2.70 (dt, 1 H, J = 14.4, 7.0 Hz, 2′α-H), 2.85 (dd, 1 H, J = 14.4, 7.0 Hz, 2′β-H), 4.63–4.65 (m, 2 H, 4′-H, 5′-H), 5.13–5.17 (m, 1 H, 3′-H), 6.64 (t, 1 H, J = 7.0 Hz, 1′-H), 7.70 (s, 1 H, 6-H), 7.88 (s, 4 H, phth). ^{13}C NMR (DMSO-d_6): δ 12.03 (CH_3), 17.88 (C′-6), 20.39 (OAc), 35.82 (C′-2), 50.72 (C′-3), 67.52 (C′-5), 83.58 (C′-4), 86.68 (C′-1), 109.66 (C-5), 122.92 (C″-4), 131.15 (C″-3a), 134.52 (C″-5), 137.04 (C-6), 150.54 (C-2), 163.72 (C-4), 167.80 (C″-2), 168.99 (OAc). Anal. ($C_{21}H_{21}N_3O_7$): C, H, N.

General procedure for preparation of **11**, **12** and **13**. Compound **8**, **9** or **10** (0.3 mmol) was dissolved in 33 % methylamine in absolute ethanol (20 ml). The solution was stirred overnight at 20 °C. Analytical silica TLC with methanol as the eluent showed the product as the spot of lowest R_f. The solvent was evaporated off at reduced presure and the unprotected amino nucleoside was purified by flash chromatography (Merck silica, 230–400 mesh, 2×30 cm, methanol).

*1-(3-Amino-2,3,6-trideoxy-*α*-L-*ribo*-hexofuranosyl)thymine* (**11**). Yield 64 mg (83 %). Hygroscopic oil. ^{1}H NMR (DMSO-d_6): δ 1.11 (d, 3 H, J = 6.4 Hz, 6′-H), 1.78 (s, 3 H, CH_3), 1.93 (ddd, 1 H, J = 11.3, 6.5, 4.9 Hz, 2′α-H), 2.07 (dt, 1 H, J = 11.3, 6.5 Hz, 2′β-H), 3.35 (t, 1 H, J = 4.5 Hz, 4′-H), 3.52–3.58 (m, 1 H, 3′-H), 3.78 (qd, 1 H,J = 6.4, 4.5 Hz, 5′-H), 6.15 (t, 1 H, J = 6.5 Hz, 1′-H), 7.67 (s, 1 H, 6-H). ^{13}C NMR (DMSO-d_6): δ 12.18 (CH_3), 20.09 (C′-6), 40.24 (C′-2), 51.20 (C′-3), 67.22 (C′-5), 83.32 (C′-1), 90.42 (C′-4), 109.29 (C-5), 136.29 (C-6), 150.42 (C-2), 163.70 (C-4). MS: *m/z* (%): 255 (M^+, 5), 153 (8), 130 (100), 129 (25), 112 (12), 110 (10). $C_{11}H_{17}N_3O_4$: Calc. 255.12190. Found 255.12187. Anal. ($C_{11}H_{17}N_3 \cdot \frac{1}{4}H_2O$): C, H.

*1-(3-Amino-2,3,6-trideoxy-*β*-L-*ribo*-hexofuranosyl)thymine* (**12**). Yield 65 mg (85 %), m.p. 76–78 °C. ^{1}H NMR (DMSO-d_6): δ 1.07 (d, 3 H, J = 6.1 Hz, 6′-H), 1.71–1.80 (m, 1 H, 2′β-H), 1.80 (s, 1 H, CH_3), 2.43–2.55 (m, 1 H, 2α-H), 3.43–3.69 (m, 3 H, 3′-H, 4′-H, 5′-H), 6.09 (t, 1 H, J = 6.0 Hz, 1′-H), 7.98 (s, 1 H, 6-H). ^{13}C NMR (DMSO-d_6): δ 12.21 (CH_3), 19.61 (C′-6), 40.35 (C′-2), 52.10 (C′-3), 67.52 (C′-5), 84.50 (C′-1), 90.92 (C′-4), 108.88 (C-5), 137.24 (C-6), 150.51 (C-2), 163.81 (C-4). MS: *m/z* (%): 255 (M^+, 4), 153 (14), 130 (100), 129 (37), 126 (11), 112 (13), 110 (14). $C_{11}H_{17}N_3O_4$: Calc. 255.12190. Found 255.12187. Anal. ($C_{11}H_{17}N_3 \cdot \frac{1}{2}H_2O$): C, H.

*1-(3-Amino-2,3,6-trideoxy-*α*-L-*arabino*-hexofuranosyl)thymine* (**13**). Yield 60 mg (78 %). Hygroscopic, m.p. 178–180 °C. ^{1}H NMR (DMSO-d_6): δ 1.15 (d, 3 H, J = 5.7 Hz, 6′-H), 1.81 (s, 3 H, CH_3), 2.04–2.20 (m, 2 H, 2′α-H, 2β-H), 3.67–3.87 (m, 3 H, 3′-H, 4′-H, 5′-H), 6.22 (t, 1 H, J = 6.7 Hz, 1′-H), 7.50 (s, 1 H, 6-H). ^{13}C NMR (DMSO-d_6): δ 12.02 (C′-6), 21.32 (CH_3), 40.03 (C′-2), 51.96 (C′-3), 64.38 (C′-5), 84.61 (C′-1), 87.36 (C′-4), 109.55 (C-5), 136.15 (C-6), 150.37 (C-2), 163.71 (C-4). FAB MS (H_2O, glycerol): 256 (M + H^+, 100). Anal. ($C_{11}H_{17}N_3O_4$, H_2O): C, H, N.

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