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Supporting Information

Anti-flavivirus Activity of Different Tritylated Pyrimidine and Purine Nucleoside Analogues

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Supporting Information

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General procedure 1

A mixture of a nucleoside (1.0 eq/mol), an appropriate trityl chloride (2.2 eq/mol) and DMAP (2.8 mol/eq, unless stated otherwise) in anhydrous pyridine (4.5 mL/mmol) was heated at 80 ºC under an argon atmosphere for 18 h. The reaction was quenched by addition of methanol (2 mL/mmol) at room temperature, and kept stirring at room temperature for 30 min. The solution was then concentrated and diluted in dichloromethane. The organic solution was washed with saturated solution of $NaHCO_3$ (3 x 20 mL) and the combined aqueous layers were extracted with dichloromethane. Combined organic layers were dried over Na_2SO_4, filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel (eluent system gradient methanol in dichloromethane = 1-3% containing 0.5% triethylamine).

General biological procedures

Antiviral assay. Trityl compounds were prepared as stock solution of 100mM in DMSO and then were diluted to a final assay concentration of 20, 10, 5µM. Dilutions were made by adding the appropriate amount of DMSO to lyophilized compound to achieve stock concentrations of 10 to 100mM. Dissolved compounds were stored at -20 ˚C and brought to room temperature prior to assay. All compounds were well dissolved in DMSO, and precipitates were not observed upon thawing.

Cell culture. Vero cells were grown in DMEM with 10% FBS. Cells were plated into 96wp at a density of 10e4 cells per well.

Virus Culture. Cells were then infected with Dengue virus (serotype D2, ATCC), and Yellow fever vaccine (17D strain of Asibi) at a moi of 1, or left uninfected to determine compound toxicity.

Cell viability was determined at day seven using CellTiterGlo ®PROMEGA, following the manufacturers instructions. Toxicity was determined as cell viability at day seven in the presence of drug. Antiviral effect was determined as cell viability at day seven in the presence of drug and virus and compared to vehicle (DMSO). Cells were pretreated with compounds 30 minutes prior to infection. All experiments were performed in triplicate.

5',3',2'-Tri-*O*-tritylribavirin (5A) was obtained as a white solid (0.160 g, 8%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.34 (s, 1H, *H*-3), 7.29 – 7.25 (m, 13H, *H*-Ph), 7.25 – 7.18 (m, 13H, *H*-Ph), 7.16 – 7.13 (m, 6H, *H*-Ph), 7.10 – 7.05 (m, 13H, *H*-Ph), 6.52 (d, *J* = 6.6 Hz, 1H, *H*-1'), 6.12 (br s, 1H, NH_2), 5.23 (br s, 1H, NH_2), 4.94 (dd, *J* = 6.6, 4.5 Hz, 1H, *H*-2'), 4.11 – 4.07 (m, 1H, *H*-4'), 3.25 (dd, *J* = 4.3, 1.4 Hz, 1H, *H*-3'), 2.92 (dd, *J* = 10.9 Hz, 2.6 1H, *H*-5'), 1.82 (dd, *J* = 10.9, 3.1 Hz, 1H, *H*-5'); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 160.29 (*C*=O), 156.95 (*C*-5), 145.64 (*C*-3), 144.32, 143.80, 143.54 (*C*-Ph), 129.16, 128.94, 128.60, 127.86, 127.75, 127.55, 127.27, 127.13, 126.98 (*C*H-Ph), 91.55 (*C*-1'), 87.77, 87.28, 87.12 (*C*$(Ph)_3$), 83.42 (*C*-4'), 77.82 (*C*-2'), 74.87 (*C*-3'), 63.74 (*C*-5'); MS (ES+) Found: *m/z* 994.3 (M + Na^+); Calculated for [$C_{65}H_{54}N_4O_5$]: *m/z* 971.15; Reverse-phase HPLC (H_2O/CH_3CN from 80/20 to 0/100 in 15 minutes, 0/100 for other 15 minutes), flow = 1ml/min, λ = 245 nm, t_R = 22.81 min.

5',2'-Bis-*O*-tritylribavirin (5C) was obtained as a white solid (1.0 g, 66%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.38 (s, 1H, *H*-3), 7.45 – 7.40 (m, 6H, *H*-Ph), 7.37 – 7.32 (m, 6H, *H*-Ph), 7.31 – 7.26 (m, 3H, *H*-Ph), 7.23 – 7.15 (m, 15H, *H*-Ph), 6.41 (br s, 1H, NH_2), 5.99 (d, *J* = 6.1 Hz, 1H, *H*-1'), 5.85 (br s, 1H, NH_2), 5.07 (dd, *J* = 6.1, 4.8 Hz, 1H, *H*-2'), 4.18 – 4.12 (m, 1H, *H*-4'), 3.40 (dd, *J* = 10.7, 2.2 Hz, 1H, *H*-5'), 3.05 – 3.00 (m, 1H, *H*-3'), 2.85 (dd, *J* =10.7, 2.6 Hz, 1H, *H*-5'), 2.47 –2.41 (m, 1H, O*H*-5'); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 160.58 (*C*=O), 156.32 (*C*-5), 145.83 (*C*-3), 143.63, 143.13 (*C*-Ph), 128.60, 128.33, 127.93, 127.77, 127.22 (*C*H-Ph), 90.93 (*C*-1'), 88.06, 87.28 (*C*$(Ph)_3$), 85.26 (*C*-4'), 78.25 (*C*-2'), 71.04 (*C*-3'), 64.22 (*C*-5'). MS (ES+) Found: *m/z* 751.3 (M + Na^+); Calculated for [$C_{46}H_{40}N_4O_5$]: *m/z* 728.83; Reverse-phase HPLC (H_2O/CH_3CN from 100/10 to 0/100 in 30 minutes), flow = 1ml/min, λ = 245 nm, t_R = 26.70 min.

Dimethoxytritylated derivatives of ribavirin (**5**) were prepared according to the general procedure **1** from **5** (0.500 g, 2.05 mmol) 4,4′-dimethoxytrityl chloride (1.94 g, 5.74 mmol) and DMAP (0.700 g, 5.74 mmol). Column purification with a gradient of

methanol/triethylamine (1% : 0.5% to 2% : 0.5%) in CH_2Cl_2 as an eluent yielded 5',3',2'-tri-*O*-dimetoxytritylribavirin **(5E)** and 5',2'-bis-*O*-dimethoxytritylribavirin **(5G)**.

5',3',2'-Tri-*O*-dimetoxytritylribavirin (5E) was obtained as a white solid (0.306 g, 13%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.39 (s, 1H, *H*-3), 7.38 – 7.03 (m, 28H, *H*-Ph), 6.70 – 6.53 (m, 11H, *H*-Ph), 6.49 (d, *J* = 6.5 Hz, 1H, *H*-1'), 6.18 (br s, 1H, N*H*$_2$), 5.34 (br s, 1H, N*H*$_2$), 4.91 (dd, *J* = 6.5, 4.5 Hz, 1H, *H*-2'), 4.17 – 4.14 (m, 1H, *H*-4'), 3.80 (s, 3H, OC*H*$_3$), 3.79 (s, 3H, OC*H*$_3$), 3.78 (s, 3H, OC*H*$_3$), 3.77 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3). MS (ES+) Found: *m/z* 1173.5 (M + Na^+); Calculated for [$C_{71}H_{66}N_4O_{11}$]: *m/z* 1151.30. Reverse-phase HPLC (H_2O/CH_3CN from 80/20 to 10/90 in 15 minutes, then to CH_3CN 100% in 25 min), flow 1ml/min, λ = 245 nm, t_R = 20.29 min.

5',2'-Bis-*O*-dimethoxytritylribavirin (5G) was obtained as a white solid (0.991 g, 57%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.46 (s, 1H, *H*-3), 7.44 – 7.40 (m, 2H, *H*-Ph), 7.32 – 7.29 (m, 5H, *H*-Ph), 7.27 – 7.11 (m, 11H, *H*-Ph), 6.73 – 6.67 (m, 8H, *H*-Ph), 6.28 (br s, 1H, N*H*$_2$), 6.07 (d, *J* = 6.5 Hz, 1H, *H*-1'), 5.23 (br s, 1H, N*H*$_2$), 5.06 (dd, *J* = 6.5, 4.5 Hz, 1H, *H*-2'), 4.17 – 4.11 (m, 2H, *H*-4', O*H*-3'), 3.38 (dd, *J* = 11.0, 2.5 Hz, 1H, *H*-5'), 2.92 – 2.89 (m, 1H, *H*-3'), 2.79 (dd, *J* = 11.0, 2.5 Hz, 1H, *H*-5'). MS (ES+) Found: *m/z* 871.3 (M + Na^+); Calculated for [$C_{50}H_{48}N_4O_9$]: *m/z* 848.94; Reverse-phase HPLC (H_2O/CH_3CN from 80/20 to 10/90 in 15 minutes, then to CH_3CN 100% in 25 min), flow 1ml/min, λ = 245 nm, t_R = 15.56 min.

5',3'-Bis-*O*-trityl-5-fluorouridine (**6B**) was obtained as a white solid (0.068 g, 8%). ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 7.78 (d, $J_{H\text{-}F}$ = 5.0 Hz, 1H, *H*-6), 7.44 – 7.42 (m, 6H, *H*-Ph), 7.26 – 7.21 (m, 24H, *H*-Ph), 6.06 – 6.02 (m, 2H, *H*-1', C-2'-O*H*), 4.26 – 4.20 (m, 1H, *H*-2'), 3.97 – 3.94 (m, 1H, *H*-3'), 2.89 – 2.87 (m, 1H, *H*-4'), 2.69 (apparent d, *J* = 10.5 Hz, 1H, *H*-5'), 2.57 (dd, *J* = 10.5, 1.0 Hz, 1H, *H*-5'); ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 163.64 (*C*=O, C-2), 149.56 (*C*=O, *C*-4), 144.08, 143.10 (*C*-Ph), 140.14 (d, $^1J_{C\text{-}F}$ = 230.3 Hz, *C*-5), 128.47, 128.14, 127.90, 127.88, 127.18 (*C*H-Ph), 109.52 (*C*-6), 87.19 (*C*-1'), 86.85 (*C*(Ph)$_3$), 84.79 (*C*-4'), 79.16 (*C*-2'), 72.13 (*C*-3'), 63.50 (*C*-5'). ^{19}F-NMR (DMSO-d_6, 470 MHz): δ_F –167.67. MS (ES+) Found: *m/z* 769.3 (M + Na^+, 100%); Calculated for [$C_{47}H_{39}FN_2O_6$]: *m/z* 746.82; Reverse phase $HPLC_b$ (H_2O/CH_3CN from 90/10 to 0/50 in 30 min), flow = 1ml/min, λ = 245 nm, t_R = 29.29 min.

5',2'-Bis-*O*-trityl-5-fluorouridine (6C) was obtained as a white solid (0.09 g, 11%). ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 7.53 (d, $J_{H\text{-}F}$ = 7.0 Hz, 1H, *H*-6), 7.49 – 7.46 (m, 6H, *H*-Ph), 7.33 – 7.29 (m, 4H, *H*-Ph), 7.28 – 7.20 (m, 20H, *H*-Ph), 6.14 (dd, *J* = 7.5, 2.0 Hz, 1H, *H*-1'), 5.00 (d, *J* = 5.5 Hz, C-3'-O*H*), 4.32 – 4.29 (m, 1H, *H*-2'), 3.92 – 3.90 (m, 1H, *H*-4'), 3.08 (dd, *J* = 10.5, 3.5 Hz, 1H, *H*-5'), 3.04 – 3.01 (m, 1H, *H*-3'), 2.88 (dd, *J* = 10.5, 3.0 Hz, 1H, *H*-5'); ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 163.64 (*C*=O, C-2), 150.35 (*C*=O, C-4), 143.87, 142.99 (*C*-Ph), 139.12 (d, $^{1}J_{C\text{-}F}$ = 232.5 Hz, *C*-5), 128.46, 128.06, 127.87, 127.82, 127.23 (*C*H-Ph), 109.54 (*C*-6), 86.35 (*C*(Ph)$_3$), 86.43 (C-1'), 84.79 (*C*-4'), 75.88 (*C*-2'), 69.87 (*C*-3'), 63.96 (*C*-5'); ^{19}F NMR (DMSO-d_6, 470 MHz): δ = –166.49. MS (ES+) Found: *m/z* 769.26 (M + Na^+, 100%); Calculated for [$C_{47}H_{39}FN_2O_6$]: *m/z* 746.82; Reverse phase HPLC$_b$ (H_2O/CH_3CN from 90/10 to 0/50 in 30 min), flow = 1ml/min, λ = 245 nm, t_R = 27.04 min.

5',3'-Bis-*O*-dimethoxytrityl-5-fluorouridine (6F) was obtained as a yellowish solid (0.078 g, 8%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.64 (d, $J_{H\text{-}F}$ = 6.0 Hz, 1H, *H*-6), 7.32 (dd, *J* = 8.5, 2.0 Hz, 2H, *H*-Ph), 7.22 – 7.11 (m, 14H, *H*-Ph), 7.09 – 7.06 (m, 4H, *H*-Ph), 6.70 – 6.63 (m, 6H, *H*-Ph), 6.01 (dd, *J* = 6.5, 1.5 Hz, 1H, *H*-1'), 4.27 (dd, *J* = 5.0, 2.5 Hz, 1H, *H*-3'), 3.98 (t, *J* = 6.0 Hz, 1H, *H*-2'), 3.693 (s, 3H, OC*H*$_3$), 3.69 (s, 3H, OC*H*$_3$), 3.67 (s, 3H, OC*H*$_3$), 3.66 (s, 3H, OC*H*$_3$), 3.55 (q, *J* = 2.5 Hz, 1H, *H*-4'), 3.10 (dd, *J* = 10.5, 2.5 Hz, 1H, *H*-5'), 2.80 (dd, *J* = 10.5, 2.5 Hz, 1H, *H*-5'); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 158.92, 158.89, 158.68, 158.62 (CH_3O-*C*-Ph), 157.30 (d, $^{2}J_{C\text{-}F}$ = 25.6 Hz, *C*-4), 149.83 (*C*-2), 144.58, 144.07 (*C*-Ph), 140.80 (d, $^{1}J_{C\text{-}F}$ = 237.4 Hz, *C*-5), 135.64, 135.54, 135.32, 135.19 (*C*-Ph), 130.35, 130.30, 129.98, 129.97, 129.36, 129.17, 128.28, 128.14, 128.09, 127.99, 127.98, 127.81, 127.80, 127.34, 127.11 (*C*H-Ph), 124.09 (d, $^{2}J_{C\text{-}F}$ = 33.6 Hz, *C*-6), 113.49, 113.46, 113.32 (*C*H-Ph), 89.44 (*C*-1'), 87.88, 87.37 (*C*(Ph)$_3$), 83.42 (*C*-4'), 75.09 (*C*-2'), 73.49 (*C*-3'), 63.35 (*C*-5'), 55.26 (O*C*H$_3$); ^{19}F NMR ($CDCl_3$, 470 MHz): δ = –164.25. MS (ES+) Found: *m/z* 889.5 (M + Na^+, 100%); Calculated for [$C_{51}H_{47}FN_2O_{10}$] 866.92; Reverse phase HPLC$_b$ (H_2O/CH_3CN from 90/10 to 0/50 in 30 min), flow = 1ml/min, λ = 245 nm, t_R = 28.89 min.

5',2'-Bis-*O*-dimethoxytrityl-5-fluorouridine (6G) was obtained as a yellowish solid (0.06 g, 6%). ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 7.53 (d, $J_{H\text{-}F}$ = 7.0 Hz, 1H, *H*-6), 7.49 – 7.47 (m, 2H, *H*-Ph), 7.39 – 7.33 (m, 4H, *H*-Ph), 7.30 – 7.19 (m, 8H, *H*-Ph), 7.12 – 7.07

(m, 5H, *H*-Ph), 6.85 – 6.83 (m, 2H, *H*-Ph), 6.81 – 6.77 (m, 5H, *H*-Ph), 6.08 (dd, *J* = 7.0, 1.5 Hz, 1H, *H*-1'), 4.94 (d, *J* = 6.0 Hz, 1H, C-3'-O*H*), 4.28 – 4.26 (m, 1H, *H*-2'), 3.95 – 3.91 (q, *J* = 2.5 Hz, 1H, *H*-4'), 3.746 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3), 3.18 – 3.14 (m, 1H, *H*-3'), 3.08 (dd, *J* = 10.5, 3.5 Hz, 1H, *H*-5'), 2.93 (dd, *J* = 10.5, 3.5 Hz, 1H, *H*-5'); ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 158.28, 158.14, 158.12, 157.80 (CH_3O-*C*-Ph), 156.82 (d, $^2J_{C\text{-}F}$ = 25.4 Hz, *C*-4), 148.33 (*C*-2), 145.27, 144.09 (*C*-Ph), 140.02 (d, $^1J_{C\text{-}F}$ = 232.02 Hz, *C*-5), 135.69, 135.61, 135.14, 134.82 (*C*-Ph), 130.04, 130.09, 129.62, 129.49, 129.68, 128.89, 127.86, 127.78, 127.72, 127.62, 127.56, 127.39, 126.85, 126.78, 126.72 (*C*H-Ph), 124.24 (d, $^2J_{C\text{-}F}$ = 33.1 Hz, *C*-6), 113.14, 113.10, 113.05, 112.75 (*C*H-Ph), 86.48 (*C*-1'), 86.48, 86.22 (*C*$(Ph)_3$), 84.84 (*C*-4'), 75.59 (*C*-2'), 70.03 (*C*-3'), 63.84 (*C*-5'), 55.03, 54.99 (O*C*H_3); ^{19}F NMR (DMSO-d_6, 470 MHz): δ_F –164.18. MS (ES+) Found: *m/z* 889.3 (M + Na^+, 100%); Calculated for [$C_{51}H_{47}FN_2O_{10}$] 866.92. Reverse phase HPLC$_b$ (H_2O/CH_3CN from 90/10 to 0/50 in 30 min), flow = 1ml/min, λ = 245 nm, t_R = 22.16 min.

Tritylated derivatives of 5-bromouridine (**7**) were prepared according to the general procedure **1** from 5-bromouridine **7** (0.50 g, 1.55 mmol), trityl chloride (0.95 g, 3.40 mmol) in anhydrous pyridine (10 mL). After work-up, the crude was purified by column chromatography eluting with dichloromethane/methanol/triethylamine (97% : 2% : 1%) as an eluent to give 5',3'-bis-*O*-trityl-5-bromo-uridine (**7B**) and 5',2'-bis-*O*-trityl-5-bromo-uridine (**7C**).

5',3'-Bis-*O*-trityl-5-bromo-uridine (7B) was obtained as a white solid (0.06 g, 5%). ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 8.00 (s, 1H, *H*-6), 7.41 – 7.39 (m, 6H, *H*-Ph), 7.25 – 7.23 (m, 24H, *H*-Ph), 6.12 – 6.11 (m, 1H, *H*-1'), 6.08 (d, *J* = 7.9 Hz, OH-2'), 4.39 – 4.35 (m, 1H, *H*-2'), 4.05 – 4.04 (m, 1H, *H*-3'), 2.86 – 2.73 (m, 2H, *H*-4', *H*-5'), 2.46 –2.43 (m, 1H, *H*-5'). ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 158.94 (*C*-4), 150.23 (*C*-2), 144.09, 143.11 ('ipso' *C*-Ph), 138.97 (*C*-6), 128.42, 128.08, 128.00, 127.91, 127.18, (*C*H-Ph), 96.73 (*C*-5), 87.06 (*C*$(Ph)_3$), 86.91 (*C*-1'), 86.70 (*C*$(Ph)_3$), 82.36 (*C*-4'), 73.58 (*C*-3'), 72.63 (*C*-2'), 63.18 (*C*-5'). MS (ES+) Found: *m/z* 853.12 (M + 2Na^+); Calculated for [$C_{47}H_{39}BrN_2O_6$]: *m/z* 807.73 (M); Reverse-phase HPLC (H_2O/CH_3CN from 50/50 to 0/100 in 30 min), flow = 1 mL/min, λ = 254 nm, t_R = 23.89 min.

5',2'-Bis-*O*-trityl-5-bromo-uridine (7C) was obtained as a white solid (0.10 g, 8%). ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 7.64 (s, 1H, *H*-6), 7.48 – 7.47 (m, 6H, *H*-Ph), 7.31 – 7.22 (m, 24H, *H*-Ph), 6.15 (d, *J* = 7.4 Hz, 1H, *H*-1'), 5.05 (d, *J* = 5.7 Hz, 1H, O*H*-3'), 4.35 (dd, *J* = 7.2, 5.3 Hz, 1H, *H*-2'), 3.94 – 3.92 (m, 1H, *H*-4'), 3.17 – 3.15 (m, 1H, *H*-3'), 3.03 – 3.00 (m, 1H, *H*-5'), 2.94 – 2.93 (m, 1H, *H*-5'); ^{13}C NMR (DMSO-d_6, 125 MHz) δ = 158.87 (*C*-4), 149.91 (*C*-2), 143.86, 143.04 ('ipso' *C*-Ph), 139.16 (*C*-6), 128.40, 128.10, 127.91, 127.82, 127.20 (*C*H-Ph), 97.29 (*C*-5), 86.99, 86.76 (*C*(Ph)$_3$), 86.28 (*C*-1'), 84.76 (*C*-4'), 76.00 (*C*-2'), 69.81 (*C*-3'), 63.89 (*C*-5'). MS (ES+) Found: *m/z* 853.12 (M + 2Na$^+$); Calculated for [$C_{47}H_{39}BrN_2O_6$]: *m/z* 807.73 (M). Reverse-phase HPLC (H_2O/CH_3CN from 50/50 to 0/100 in 30min), flow = 1 mL/min, λ = 254 nm, t_R = 20.12 min.

Tritylated derivatives of 4'-azidouridine (**8**) were prepared according to the general procedure **1** from **8** (0.5 g, 1.76 mmol), trityl chloride (1.46 g, 5.23 mmol) in anhydrous pyridine (10 mL). After work-up, the crude was purified by column chromatography eluting with a gradient of methanol (0% to 4%) in CH_2Cl_2 to give compounds 5',3'-bis-*O*-trityl-4'-azido-uridine (**8B**), 5',2'-bis-*O*-trityl-4'-azido-uridine (**8C**) and 5'-*O*-trityl-4'-azido-uridine (**8D**).

5',3'-Bis-*O*-Trityl-4'-azido-uridine (8B) was obtained as a white solid (0.147 g, 17%). ^{1}H NMR (CD_3OD, 500 MHz): δ = 7.56 – 7.53 (m, 5H, *H*-Ph), 7.32 (d, 1H, *J* = 8.0 Hz *H*-6), 7.30 – 7.23 (m, 25H, *H*-Ph), 6.20 (d, *J* = 6.0 Hz, 1H, *H*-1'), 5.22 (d, *J* = 8.0 Hz, *H*-5), 4.65 (dd, *J* = 6.0, 3.5 Hz, 1H, *H*-2'), 3.53 (d, *J* = 5.5 Hz, 1H, *H*-3'), 3.08 (d, *J* = 10.5 Hz, 1H, *H*-5'a), 3.02 (d, *J* = 10.5 Hz, 1H, *H*-5'b). MS (ES+) Found: *m/z* 792.3 (M + Na$^+$); Calculated for [$C_{47}H_{39}N_5O_6$]: *m/z* 769.2900 (M); Reverse-phase HPLC (H_2O/CH_3CN from 80/20 to 0/100 in 30 minutes), flow = 1ml/min, λ = 254 nm, t_R = 27.25 min.

5',2'-Bis-*O*-trityl-4'-azido-uridine (8C) was obtained as a white solid (0.13 g, 15%). ^{1}H NMR (CD_3OD, 500 MHz): δ = 7.52 – 7.49 (m, 5H, *H*-Ph), 7.30 – 7.18 (m, 26H, *H*-Ph, *H*-6), 5.82 (d, *J* = 1.5 Hz, 1H, *H*-1'), 5.10 (d, *J* = 8.0 Hz, *H*-5), 4.48 (d, *J* = 6.0 Hz, 1H, *H*-3'), 3.43 (d, *J* = 10.5 Hz, 1H, *H*-5'a), 3.23 (d, *J* = 10.5 Hz, 1H, *H*-5'b), 2.98 (dd, *J* = 6.0, 1.5 Hz, 1H, *H*-2'). MS (ES+) Found: *m/z* 792.3 (M + Na$^+$); Calculated for [$C_{47}H_{39}N_5O_6$]: *m/z* 769.2900 (M). Reverse-phase HPLC (H_2O/CH_3CN from 80/20 to

0/100 in 30 minutes), flow = 1ml/min, λ = 254 nm, t_R = 28.22 min.

5'-*O*-Trityl-4'-azido-uridine (8D) was obtained as a white solid (0.369 g, 40%). ^{1}H NMR (CD_3OD, 500 MHz): δ = 7.73 (d, 1H, *J* = 8.0 Hz, *H*-6), 7.46 – 7.44 (m, 6H, *H*-Ph), 7.37 – 7.34 (m, 6H, *H*-Ph), 7.32 – 7.29 (m, 3H, *H*-Ph), 6.09 (d, *J* = 4.0 Hz, 1H, *H*-1'), 5.40 (d, *J* = 8.0 Hz, *H*-5), 4.47 (d, *J* = 6.0 Hz, 1H, *H*-3'), 4.41 (dd, *J* = 6.0, 3.5 Hz, 1H, *H*-2'), 3.42 (d, *J* = 10.5 Hz, 1H, *H*-5'a), 3.34 (d, *J* = 10.5 Hz, 1H, *H*-5'b). MS (ES+) Found: *m/z* 550.18 (M + Na^+); Calculated for [$C_{28}H_{25}N_5O_6$]: *m/z* 527.1805 (M); Reverse-phase HPLC (H_2O/CH_3CN from 90/10 to 0/100 in 30 minutes), flow = 1ml/min, λ = 254 nm, t_R = 19.7 min.

5',2'-Bis-*O*-dimetoxytrityl-4'-azido-uridine (8G) was prepared according to the general procedure **1** from 4'-azidouridine (**8**) (0.5g, 1.75 mmol), 4,4'-dimethoxytrityl chloride (1.3g, 3.83 mmol) in anhydrous pyridine (10 mL). After work-up, the crude was purified by column chromatography eluting with dichloromethane/methanol/triethylamine (95.5% : 4% : 0.5) to give compound **8G** as a white solid (0.343 g, 22%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.95 (bs, 1H, N*H*), 7.50 – 7.48 (m, 2H, *H*-Ph), 7.43 – 7.30 (m, 10H, *H*-Ph, *H*-6), 7.22 – 7.19 (m, 4H, *H*-Ph), 7.13 – 7.10 (m, 3H, *H*-Ph), 6.87 – 6.72 (m, 8H, *H*-Ph), 6.28 (d, *J* = 6.0 Hz, 1H, *H*-1'), 4.71 (dd, *J* = 6.0, 5.5 Hz, *H*-2'), 3.83, 3.82, 3.81, 3.80 (4 x s, 12H, OCH_3), 3.40 (d, *J* = 5.0, 3.5 Hz, 1H, *H*-3'), 3.15, 3.11 (AB system, *J* = 10.0 Hz, 2H, *H*-5'), 2.78 (d, *J* = 4.0 Hz, 1H, O*H*-3'). MS (ES+) Found: *m/z* 912.33 (M + Na^+); Calculated for [$C_{51}H_{47}N_5O_{10}$]: *m/z* 889.9464 (M); Reverse-phase HPLC (H_2O/CH_3CN from 80/20 to 0/100 in 30 minutes), flow = 1ml/min, λ = 254 nm, t_R = 22.03 min.

Tritylated derivatives of uridine (**9**) were prepared according to the general procedure **1** from **9** (0.535 g, 2.19 mmol), trityl chloride (1.71 g, 6.13 mmol) in anhydrous pyridine (10 mL). After work-up, the crude was purified by column chromatography with a gradient of methanol/triethylamine (1% : 0.5% to 3% : 0.5%) in CH_2Cl_2 as an eluent to give compounds **2** and **3**.

5',2'-Bis-*O*-trityluridine (2) was obtained as a white solid (0.49 g, 31%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 11.47 (br s, N*H*), 7.50 – 7.45 (m, 6H, *H*-Ph), 7.39 (d, *J* = 8.16 Hz, 1H, *H*-6), 7.33 – 7.17 (m, 24H, *H*-Ph), 6.15 (d, *J* = 7.5 Hz, 1H, *H*-1'), 5.16 (d, *J* = 8.16 Hz, 1H, *H*-5), 4.82 (d, *J* = 4.28 Hz, 1H, O*H*-3'), 4.31 (dd, *J* = 7.5, 5.0 Hz, 1H, *H*-2'), 3.91

– 3.84 (m, 1H, *H*-4'), 3.00 (dd, *J* = 10.8, 3.0 Hz, 1H, *H*-5'), 2.92 (dd, *J* = 10.8, 3.0 Hz, 1H, *H*-5'), 2.89 – 2.83 (m, 1H, *H*-3'); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 162.86 (*C*-2), 150.66 (*C*-4), 143.82, 142.94 (*C*-Ph), 140.36 (*C*-6), 128.40, 128.12, 127.88, 127.86, 127.24, 127.22 (*C*H-Ph), 102.10 (*C*-5), 86.87, 86.66 ($C(Ph)_3$), 86.29 (*C*-1'), 84.53 (*C*-4'), 76.26 (*C*-2'), 69.75 (*C*-3'), 63.83 (*C*-5'). (ES+) Found: *m/z* 751.3 ($M + Na^+$); Calculated for [$C_{47}H_{40}N_2O_6$]: *m/z* 728.83 (M); Reverse-phase HPLC (H_2O/CH_3CN from 90/10 to 0/100 in 30 minutes), flow 1ml/min, λ = 254 nm, t_R = 28.20 min.

5',3'-Bis-*O*-trityluridine (3) was obtained as a white solid (0.22 g, 14%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 11.46 (br s, N*H*), 7.56 (d, *J* = 8.15 Hz, 1H, *H*-6), 7.44 – 7.40 (m, 6H, *H*-Ph), 7.31 – 7.18 (m, 24H, *H*-Ph), 6.06 – 5.98 (m, 2H, *H*-1', O*H*-2'), 5.53 (d, *J* = 8.15 Hz, 1H, *H*-5), 4.15 – 4.10 (m, 1H, *H*-2'), 3.95 (dd, *J* = 5.22, 1.26 Hz, 1H, *H*-3'), 2.94 – 2.89 (m, 1H, *H*-4'), 2.82 – 2.76 (m, 1H, *H*-5'), 2.55 (dd, *J* = 10.71, 4.24 Hz, 1H, *H*-5'). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 162.86 (*C*-2), 150.89 (*C*-4), 144.10 (*C*-Ph), 143.09 (*C*-Ph), 139.77 (*C*-6), 128.48, 128.21, 127.92, 127.86, 127.15 (*C*H-Ph), 101.98 (*C*-5), 86.78 (*C*-1'), 86.75, 86.69 ($C(Ph)_3$), 82.06 (*C*-4'), 73.48 (*C*-3'), 72.10 (*C*-2'), 63.28 (*C*-5'). (ES+) Found: *m/z* 751.3 ($M + Na^+$); Calculated for [$C_{47}H_{40}N_2O_6$]: *m/z* 728.83 (M); Reverse-phase HPLC (H_2O/CH_3CN from 100/10 to 0/100 in 30 minutes), flow 1ml/min, λ = 254 nm, t_R = 29.33 min.

5',2'-Bis-*O*-dimethoxytrityluridine (9G) was obtained as a white solid (0.119 g, 23%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.39 (brs, 1H, N*H*), 7.75 (d, *J* = 8.0 Hz, *H*-6), 7.53 – 7.49 (m, 2H, *H*-Ph), 7.46 – 7.41 (m, 4H, *H*-Ph), 7.32 – 7.27 (m, 4H, *H*-Ph), 7.21 – 7.18 (m, 4H, *H*-Ph), 7.12 – 7.07 (m, 4H, *H*-Ph), 6.85 – 6.80 (m, 4H, *H*-Ph), 6.77 – 6.69 (m, 4H, *H*-Ph), 6.55 (d, *J* = 7.5 Hz, *H*-1'), 5.17 (d, *J* = 8.0 Hz, *H*-5), 4.50 (dd, *J* = 7.5, 4.5 Hz, *H*-2'), 4.04 – 4.01 (m, 1H, *H*-4'), 3.82 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 3.809 (s, 3H, OCH_3), 3.804 (s, 3H, OCH_3), 3.19 (dd, *J* = 11.0, 2.0 Hz, 1H, *H*-5'), 3.14 (dd, *J* = 11.0, 2.0 Hz, 1H, *H*-5'), 2.92 (d, *J* = 4.5 Hz, 1H, *H*-3'), 2.36 (s, 1H, O*H*-3'). (ES+) Found: *m/z* 871.3 ($M + Na^+$); Calculated for [$C_{51}H_{48}N_2O_{10}$]: *m/z* 848.93 (M); Reverse-phase HPLC (H_2O/CH_3CN from 80/20 to 10/90 in 15 minutes, then to CH_3CN 100% in 25 min), flow 1ml/min, λ = 245 nm, t_R = 16.46 min.

Tritylated derivatives of ara-uridine (**10**) were prepared according to the general procedure **1** from **10** (0.207 g, 0.848 mmol), trityl chloride (0.756 g, 2.71 mmol) and DMAP (0.207 g, 1.69 mmol) in anhydrous pyridine (10 mL). After work-up, the crude was purified by column chromatography eluting with a gradient of methanol (1% to 4%) in CH_2Cl_2 to give compounds 5',3'-bis-*O*-trityl-ara-uridine (**10B**), 5',2'-bis-*O*-trityl-ara-uridine (**10C**) and 5'-*O*-trityl-ara-uridine (**10D**).

5',3'-Bis-*O*-trityl-ara-uridine (10B) was obtained as a white solid (0.141 g, 23%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.45 (bs, 1H, N*H*), 7.84 (bs, 1H, *H*-6), 7.45 – 7.43 (m, 5H, *H*-Ph), 7.33 – 7.28 (m, 25H, *H*-Ph), 6.22 (bs, 1H, *H*-1'), 5.69 (d, *J* = 8.0 Hz, 1H, *H*-5), 4.27 (dd, *J* = 5.5, 3.5 Hz, 1H, *H*-2'), 3.78 – 3.72 (m, 1H, *H*-4'), 3.54 (bs, 1H, *H*-3'), 3.42 (dd, *J* = 10.5, 5.5 Hz, 1H, *H*-5'a), 3.24 (dd, *J* = 10.5, 4.0 Hz, 1H, *H*-5'b). MS (ES+) Found: *m/z* 751.3 (M + Na^+); Calculated for [$C_{47}H_{40}N_2O_6$]: *m/z* 728.8303 (M); Reverse-phase HPLC (H_2O/CH_3CN from 80/20 to 0/100 in 30 minutes), flow = 1ml/min, λ = 254 nm, t_R = 27.78 min.

5',2'-Bis-*O*-trityl-ara-uridine (10C) was obtained as a white solid (0.159 g, 26%). ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 8.4 (bs, 1H, N*H*), 7.61 (d, *J* = 8.0 Hz, 1H, *H*-6), 7.37 – 7.35 (m, 5H, *H*-Ph), 7.32 – 7.25 (m, 25H, *H*-Ph), 6.15 (d, *J* = 3.0 Hz, 1H, *H*-1'), 5.61 (d, *J* = 8.0 Hz, 1H, *H*-5), 3.95 – 3.93 (m, 1H *H*-4'), 3.68 (dd, *J* = 9.0, 3.0 Hz, 1H *H*-2'), 3.44 (dd, *J* = 10.5, 2.5 Hz, 1H, *H*-5'a), 3.13 (d, *J* = 8.5 Hz, 1H, *H*-3'), 3.04 (dd *J* = 10.5, 4.0 Hz, 1H, *H*-5'b). MS (ES+) Found: *m/z* 751.3 (M + Na^+); Calculated for [$C_{47}H_{40}N_2O_6$]: *m/z* 728.8303 (M); Reverse-phase HPLC (H_2O/CH_3CN from 80/20 to 0/100 in 30 minutes), flow = 1ml/min, λ = 254 nm, t_R = 30.89 min.

5'-*O*-Trityl-ara-uridine (10D) was obtained as a white solid (0.221 g, 54%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 10.2 (bs, 1H, N*H*), 7.88 (d, *J* = 8.5 Hz, 1H, *H*-6), 7.44 – 7.43 (m, 5H, *H*-Ph), 7.30 – 7.27 (m, 7H, *H*-Ph), 7.24 – 7.21 (m, 3H, *H*-Ph), 6.13 (d, *J* = 5.0 Hz, 1H, *H*-1'), 5.35 (d, *J* = 8.0,Hz, 1H, *H*-5), 4.79 (bs, 1H, O*H*-2'), 4.45 (t, *J* = 5.0 Hz, 1H, *H*-2'), 4.34 (t, *J* = 5.5 Hz, 1H, *H*-3'), 3.99 – 3.96 (m, 1H, *H*-4'), 3.51 – 3.49 (m, 2H, *H*-5'). MS (ES+) Found: *m/z* 509.2 (M + Na^+); Calculated for [$C_{28}H_{26}N_2O_6$]: 486.5158 (M); Reverse-phase HPLC (H_2O/CH_3CN from 80/20 to 0/100 in 30 minutes), flow = 1ml/min, λ = 254 nm, t_R = 16.40 min.

Dimethoxytritylated derivatives of ara-uridine (**10**) were prepared according to the general procedure **1** from ara-uridine **10** (0.218 g, 0.892 mmol), 4,4'-dimethoxytrityl chloride (0.968g, 2.86 mmol) in anhydrous pyridine (10 mL). After work-up, the crude was purified by column chromatography eluting with dichloromethane/methanol/triethylamine (95% : 5% : 1%) to give compounds 5',3',2'-tri-*O*-dimetoxytrityl-ara-uridine **(10E**) and 5',3'-bis-*O*-dimetoxytrityl-ara-uridine (**10F**).

5',3',2'-Tri-*O*-dimetoxytrityl-ara-uridine (10E) was obtained as a white solid (0.625 g, 61%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.76 (bs, 1H, N*H*), 7.81 (d, *J* = 8.5 Hz, 1H, *H*-6), 7.44 – 7.42 (m, 2H, *H*-Ph), 7.33 – 7.25 (m, 7H, *H*-Ph), 7.19 – 7.11 (m, 6H, *H*-Ph), 7.06 – 6.99 (m, 6H, *H*-Ph), 6.94 – 6.92 (m, 2H, *H*-Ph), 6.87 – 6.80 (m, 8H, *H*-Ph), 6.68 – 6.65 (m, 4H, *H*-Ph), 6.54 – 6.52 (m, 2H, *H*-Ph), 6.46 – 6.42 (m, 3H, *H*-Ph, *H*-1'), 5.58 (d, *J* = 8.0 Hz, 1H, *H*-5), 4.38 (m, 1H, *H*-2'), 3.82 – 3.71 (m, 18H, 6 x OC*H*$_3$), 3.60 – 3.58 (m, 1H *H*-5'a), 3.60 – 3.55 (m, 2H, *H*-5'b, *H*-4'), 2.13 – 2.11 (m, 1H *H*-3'); MS (ES+) Found: *m/z* 1173.5 (M + Na^+); Calculated for [$C_{72}H_{66}N_2O_{12}$]: *m/z* 1150.46 (M); Reverse-phase HPLC (H_2O/CH_3CN from 80/20 to 0/100 in 30 minutes), flow = 1ml/min, λ = 254 nm, t_R = 25.76 min.

5',3'-Bis-*O*-dimetoxytrityl-ara-uridine (10F) was obtained as a white solid (0.189 g, 25%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.22 (bs, 1H, N*H*), 7.63 (d, *J* = 8.5 Hz, 1H, *H*-6), 7.37 – 7.17 (m, 18H, *H*-Ph), 6.86 – 6.81 (m, 8H, *H*-Ph), 6.14 (d, *J* = 3.0 Hz 1H, *H*-1'), 5.61 (d, *J* = 8.0 Hz, 1H, *H*-5), 4.07 (s, 1H *H*-3'), 3.97 (s, 1H, *H*-4'), 3.81, 3.80, 3.79, 3.78 (4s, 12H, 4 x OC*H*$_3$), 3.68 (d, *J* = 11.5 Hz, 1H, *H*-2'), 3.45 (dd, *J* = 11.0, 2.5 Hz, 1H, *H*-5'b), 3.30 (d, *J* = 9.0 Hz, 1H, O*H*-3'), 3.04 (dd, *J* = 11.0, 3.0, Hz 1H, *H*-5'a). MS (ES+) *m/z*: Found: 871.3 (M + Na^+) $C_{51}H_{48}N_2O_5$ required: 848.3309 (M).

5'-*O*-Trityl-*N*-trityl-lamivudine (11D-NHTr) was prepared according to the general procedure **2** from lamivudine (**11**) (0.5 g, 2.18 mmol), trityl chloride (1.95 g, 6.98 mmol) and DMAP (0.53 g, 4.36 mmol) in anhydrous pyridine (10 mL). After work-up, the crude was purified by column chromatography eluting with a gradient of methanol (1% to 3%) in CH_2Cl_2 to give compound **11D** as a white solid (1.1 g, 71%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.89 (d, *J* = 7.5Hz, 1H, *H*-6), 7.35 – 7.12 (m, 30H, *H*-Ph), 6.72 (bs, 1H, N*H*), 6.31 (dd, *J* = 5.3, 2.4 Hz, *H*-1'), 5.23 (t, *J* = 4.0 Hz, 1H, *H*-4'), 4.74 (d, *J* = 7.5 Hz, 1H, *H*-

5), 3.56 (dd, *J* = 11.1, 3.8 Hz, 1H, *H*-5'a), 3.54 (dd, *J* = 12.2, 4.8 Hz, 1H, *H*-2'a), 3.49 (dd *J* = 11.1, 2.6 Hz, 1H, *H*-5'b), 3.26 (dd, *J* = 12.5, 2.2 Hz, *H*-2'b); MS (ES+) Found: *m/z* 736.31 (M + Na^+); Calculated for [$C_{46}H_{39}N_3O_3S$]: *m/z* 713.2712 (M); Reverse-phase HPLC (H_2O/CH_3CN from 90/10 to 0/100 in 30 minutes), flow = 1ml/min, λ = 263 nm, t_R = 30.79 min.

5'-*O*-Trityl-*N*-acetyl-lamivudine (12D) was prepared according to the general procedure **1** from *N*-acetyl-lamivudine (**12**) (0.5 g, 1.84 mmol), trityl chloride (1.61 g, 5.90 mmol) and DMAP (0.225 g, 1.84 mmol) in anhydrous pyridine (10 mL). After work-up, the crude was purified by column chromatography eluting with dichloromethane/methanol (97% : 3%) to give compound **12D** as a white solid (0.396 g, 42%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 9.73 (bs, 1H, N*H*), 8.43 (d, *J* = 7.5 Hz, 1H, *H*-6), 7.50 – 7.48 (m, 6H, *H*-Ph), 7.38 – 7.32 (m, 9H, *H*-Ph), 7.22 (d, *J* = 7.5 Hz, *H*-5), 6.37 (dd, *J* = 5.5, 2.0 Hz 1H, *H*-1'), 5.35 (t, *J* = 4.0 Hz, 1H, *H*-4'), 3.67 (dd, *J* = 11.0, 3.0 Hz, 1H, *H*-5'a), 3.66 (dd, *J* = 11.0, 4.0 Hz, 1H, *H*-5'b), 3.62 (dd, *J* = 12.5, 5.0 Hz, 1H, *H*-2'a), 3.29 (dd, *J* = 12.5, 1.5 Hz, *H*-2'b), 2.29 (s, 3H, C*H*$_3$). MS (ES+) Found: *m/z* 536.2 (M + Na^+); Calculated for [$C_{29}H_{27}N_3O_4S$]: 513.6074 (M); Reverse-phase HPLC (H_2O/CH_3CN from 80/20 to 0/100 in 30 minutes), flow = 1ml/min, λ = 254 nm, t_R = 22.77 min.

5'-*O*-Trityl-2',3'-didehydro-2',3'-dideoxythymidine (13D) was prepared according to the general procedure **1** from 2',3'-didehydro-2',3'-dideoxythymidine (0.250 g, 1.11 mmol), trityl chloride (0.621 g, 2.23 mmol) in anhydrous pyridine (10 mL). After work-up, the crude was purified by column chromatography eluting with dichloromethane/methanol (97% : 3%) to give compound **13D** as a white solid (0.415 g, 80%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = – 2H, 6H, *H*-Ph and *H*-6), 7.33 – 7.27 (m, 10H, *H*-Ph), 7.01 – 7.00 (m, 1H, *H*-1'), 6.51 (dt, *J* = 6.0, 1.5 Hz, C*H*=), 6.01 (ddd, *J* = 6.0, 2.0, 1.5 Hz, C*H*=), 5.03 – 5.01 (m, 1H, *H*-4'), 3.40 (dd, *J* = 10.5, 2.5 Hz, 1H, *H*-5'a), 3.37 (dd, *J* = 10.5, 4.0 Hz, 1H, *H*-5'b), 1.97 (d, *J* = 1.5 Hz, 3H, C*H*$_3$). MS (ES+) Found: *m/z* 489.19 (M + Na^+); Calculated for [$C_{29}H_{26}N_2O_4$]: *m/z* 466.1893 (M); Reverse-phase HPLC (H_2O/CH_3CN from 80/20 to 0/100 in 30 minutes), flow = 1ml/min, λ = 265 nm, t_R = 20.35 min.

Tritylated derivatives of 5-fluoro-2'-deoxyuridine (**15**) were prepared according to the general procedure **1** from **15** (0.30 g, 1.22 mmol), trityl chloride (0.75 g, 2.68 mmol) in pyridine (6 mL). Column chromatography purification using gradient of methanol/triethylamine (1% : 0.5% to 2% : 0.5%) in CH_2Cl_2 as an eluent gave 5',3'-bis-*O*-trityl-5-fluoro-2'-deoxyuridine (**4**) and 5'-*O*-trityl-5-fluoro-2'-deoxyuridine (**15D**).

5',3'-Bis-*O*-trityl-5-fluoro-2'-deoxyuridine (4) was obtained as a white solid (0.13 g, 22%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 9.1 (bs, 1H, N*H*), 7.74 (d, $J_{H\text{-}F}$ = 6.0 Hz, 1H, *H*-6), 7.48 (dd, *J* = 8.0, 2.0 Hz, 6H, *H*-Ph), 7.31 – 7.25 (m, 24H, *H*-Ph), 6.41 – 6.38 (m, 1H, *H*-1'), 4.46 (apparent d, *J* = 6.0 Hz, 1H, *H*-3'), 3.95 – 3.93 (m, 1H, *H*-4'), 3.20 (dd, *J* = 11.0, 2.5 Hz, 1H, *H*-5'), 3.06 (dd, *J* = 11.0, 2.5 Hz, 1H, *H*-5'), 2.03 (dd, *J* = 13.5, 5.5 Hz, 1H, *H*-2'), 1.89 – 1.84 (m, 1H, *H*-2'); ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 163.62 (*C*=O, C-2), 154.10 (*C*=O, C-4), 145.56, 144.79 (*C*-Ph), 142.51 (d, $^1J_{C\text{-}F}$ = 236.3 Hz, *C*-5), 130.01, 129.78, 129.19, 129.05, 128.56, 128.42 (*C*H-Ph), 124.75 (d, $^2J_{C\text{-}F}$ = 34.3 Hz, *C*-6), 89.23, 88.84 (*C*(Ph)$_3$), 87.42 (C-1'), 86.68 (*C*-4'), 76.83 (*C*-3'), 65.13 (*C*-5'), 41.01 (*C*-2'); ^{19}F NMR (DMSO-d_6, 470 MHz): δ = –166.71. MS (ES+) Found: *m/z* 753.30 (M + Na^+, 100%); Calculated for [$C_{47}H_{39}FN_2O_5$]: *m/z* 730.82 (M); Reverse phase HPLC (H_2O/CH_3CN from 90/10 to 0/50 in 30 min), flow = 1ml/min, λ = 245 nm, t_R = 30.21 min.

5'-*O*-Trityl-5-fluoro-2'-deoxyuridine (15D) was obtained as a white solid (0.29 g, 49%). ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 7.88 (d, $J_{H\text{-}F}$ = 6.5 Hz, 1H, *H*-6), 7.49 – 7.46 (m, 6H, *H*-Ph), 7.36 – 7.33 (m, 3H, *H*-Ph), 7.29 – 7.26 (m, 3H, *H*-Ph), 6.25 (td, 1H, *J* = 6.5 Hz, *H*-1'), 4.52 (q, *J* = 4.0 Hz, 1H, *H*-3'), 4.05 – 4.03 (m, 1H, *H*-4'), 3.43 (dd, *J* = 10.5, 4.5 Hz, 1H, *H*-5'), 3.37 (dd, *J* = 10.5, 4.5 Hz, 1H, *H*-5'), 2.42 – 2.38 (m, 1H, *H*-2'), 2.34 – 2.28 (m, 1H, *H*-2'); ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 161.62 (*C*=O, C-2), 157.74 (*C*=O, C-4), 144.62 (*C*-Ph), 142.41 (d, $^1J_{C\text{-}F}$ = 242.5 Hz, *C*-5), 129.86, 128.99, 128.37 (*C*H-Ph), 125.32 (d, $^2J_{C\text{-}F}$ = 33.8 Hz, *C*-6), 88.67 (*C*(Ph)$_3$), 87.68 (C-1'), 87.00 (*C*-4'), 72.30 (*C*-3'), 64.87 (*C*-5'), 41.68 (*C*-2'); ^{19}F NMR (DMSO-d_6, 470 MHz): δ = –167.73. MS (ES+) Found: *m/z* 511.50 (M + Na^+); Calculated for [$C_{28}H_{25}FN_2O_5$]: *m/z* 488.50; Reverse phase $HPLC_b$ (H_2O/CH_3CN from 90/10 to 0/50 in 30 min), flow = 1ml/min, λ = 245 nm, t_R = 18.49 min.

5',3'-Bis-*O*-dimethoxytrityl-5-fluoro-2'-deoxyuridine (15F) was obtained as a yellowish solid (0.15 g, 15%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 9.5 (bs, 1H, N*H*), 7.74 (d, $J_{H\text{-}F}$ = 6.0 Hz, 1H, *H*-6), 7.47 (dd, *J* = 7.0, 1.5 Hz, 2H, *H*-Ph), 7.36 – 7.34 (m, 6H, *H*-Ph), 7.30 – 7.24 (m, 14H, *H*-Ph), 6.86 – 6.79 (m, 4H, *H*-Ph), 6.41 – 6.38 (m, 1H, *H*-1'), 4.51 (apparent d, *J* = 5.5 Hz, 1H, *H*-3'), 4.07 – 4.05 (m, 1H, *H*-4'), 3.817 (s, 3H, OCH_3), 3.815 (s, 6H, 2 x OCH_3), 3.80 (s, 3H, OCH_3), 3.21 (dd, *J* = 11.0, 2.5 Hz, 1H, *H*-5'), 3.14 (dd, *J* = 11.0, 2.5 Hz, 1H, *H*-5'), 1.96 (dd, *J* = 13.5, 5.5 Hz, 1H, *H*-2'), 1.87 – 1.82 (m, 1H, *H*-2'). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 158.78, 158.75, 158.67, 157.62 (CH_3O-*C*-Ph), 156.97 ($^{2}J_{C\text{-}F}$ = 26.8 Hz, *C*-4), 148.94 (*C*-2), 145.02, 144.29 (*C*-Ph), 140.53 (d, $^{1}J_{C\text{-}F}$ = 236.4 Hz, *C*-5), 136.15, 136.11, 135.35, 135.14 (*C*-Ph), 130.28, 130.20, 129.96, 129.92, 128.28, 128.07, 127.99, 127.95, 127.15, 127.05 (*C*H-Ph), 124.75 (d, $^{2}J_{C\text{-}F}$ = 33.5 Hz, *C*-6), 113.46, 113.43, 113.34, 113.31 (*C*H-Ph), 89.23, 88.84 (*C*$(Ph)_3$), 85.79 (C-1'), 85.75 (*C*-4'), 74.98 (*C*-3'), 65.87 (*C*-5'), 55.24 (O*C*H_3), 40.04 (*C*-2'); ^{19}F NMR ($CDCl_3$, 470 MHz): δ = –164.72. MS (ES+) Found: *m/z* 873.30 (M + Na^+, 100%); Calculated for [$C_{51}H_{47}FN_2O_9$]: *m/z* 850.92; Reveres phase $HPLC_b$ (H_2O/CH_3CN from 90/10 to 0/50 in 30 min), flow = 1ml/min, λ = 254 nm, t_R = 28.67 min.

5',3'-Bis-*O*-trityl 2'-fluoro-2'-deoxyuridine (16B) was obtained as a white solid (0.26 g, 18%). ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 11.36 (bs, 1H, N*H*), 7.52 (d, *J* = 8.1 Hz, *H*-6), 7.33 – 7.17 (m, 30H, *H*-Ph), 5.81 – 5.77 (m, 1H, *H*-1'), 5.33 (d, *J* = 8.1 Hz, *H*-5), 4.27 – 4.21 (m, 1H, *H*-3'), 4.17 – 4.16 (m, 0.5H, *H*-2'), 4.12 – 4.09 (m, 1H, *H*-4'), 4.07 – 4.06 (m, 0.5H, *H*-2'), 3.18 – 3.16 (m, 1H, *H*-5'), 2.98 – 2.94 (m, 1H, *H*-5'). ^{13}C NMR (DMSO-d_6, 125 MHz): δ_C 162.94 (*C*-4), 149.90 (*C*-2), 143.26, 143.22 ('ipso' *C*-Ph), 141.69 (*C*-6), 128.87, 128.54, 128.29, 128.18, 127.86, 127.80, 127.48, 127.12 (*C*H-Ph), 101.61 (*C*-5), 91.46 (d, J_{C-F} = 186.9 Hz, *C*-2'), 89.64 (d, J_{C-F} = 37.0 Hz, *C*-1'), 87.08, 86.54, (*C*$(Ph)_3$), 80.78 (*C*-4'), 71.00 (d, J_{C-F} = 15.6 Hz, *C*-3'), 62.99 (*C*-5'); ^{19}F NMR (DMSO-d_6, 470 MHz): δ = –193.04. MS (ES+) Found: *m/z* 753.20 (M + Na^+); Calculated for [$C_{47}H_{39}FN_2O_5$]: *m/z* 730.82 (M); Reverse-phase HPLC (H_2O/CH_3CN from 50/50 to 0/100 in 30 min), flow = 1 mL/min, λ = 254 nm, t_R = 23.08 min.

5',3'-Bis-*O*-dimethoxytrityl-2'-fluoro-2'-deoxyuridine (16F) was obtained as a white solid (0.241 g, 35%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 9.03 (br s, N*H*), 7.64 (d, *J* = 8.5

Hz, 1H, *H*-6), 7.47 – 7.42 (m, 2H, *H*-Ph), 7.36 – 7.20 (m, 13H, *H*-Ph), 7.16 – 7.12 (m, 4H, *H*-Ph), 6.84 – 6.74 (m, 8H, *H*-Ph), 6.07 (dd, $^{3}J_{H\text{-}F}$ = 15.0 Hz, *J* = 2.5 Hz, 1H, *H*-1'), 5.19 (d, *J* = 8.0 Hz, 1H, *H*-5), 4.26 – 4.05 (m, 3H, *H*-2', *H*-3', *H*-4'), 3.824 (s, 3H, OC*H*$_3$), 3.823 (s, 3H, OC*H*$_3$), 3.80 (s, 3H, OC*H*$_3$), 3.79 (s, 3H, OC*H*$_3$), 3.57 (dd, *J* = 11.5, 2.5 Hz, 1H, *H*-5'), 3.32 (dd, *J* = 11.5, 3.5 Hz, 1H, *H*-5'); MS (ES+) Found: *m/z* 873.3 (M + Na^+); Calculated for [$C_{51}H_{47}FN_2O_9$]: *m/z* 850.93 (M); Reverse-phase HPLC (H_2O/CH_3CN from 80/20 to 10/90 in 15 minutes, then to CH_3CN 100% in 25 min), flow 1ml/min, λ = 245 nm, t_R = 17.60 min.

5'-*O*-Trityl-5-Aza-C (17D) was prepared according to the general procedure **1** from 5-Aza-C **(17)** (0.5 g, 2.04 mmol), trityl chloride (1.71 g, 6.14 mmol) in anhydrous pyridine (10 mL). After work-up, the crude was purified by column chromatography eluting with a gradient of methanol (1% to 4%) in CH_2Cl_2 to give compound **17D** as a white solid (0.119 g, 12%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = □8.36 (s, 1H, *H*-6), 7.59 (bs, 2H, N*H*$_2$), 7.41 – 7.26 (m, 15H, *H*-Ph), 5.67 (d, *J* = 3.0 Hz, 1H, *H*-1'), 5.51 (d, *J* = 3.0 Hz, 1H, O*H*-2'), 5.09 (d, *J* = 6.5 Hz, 1H, O*H*-3'), 4.16 – 4.14 (m, 1H, *H*-2'), 4.11 – 4.10 (m, 1H, *H*-3'), 4.00 – 3.99 (m, 1H, *H*-4'), 3.27 (dd, *J* = 10.5, 5.5 Hz, 1H, *H*-5'a), 3.37 (dd, *J* = 10.5, 2.5 Hz, 1H, H-*5*'b). MS (ES+) Found: *m/z* 509.22 (M + Na^+); Calculated for [$C_{27}H_{26}N_4O_5$]: *m/z* 486.1903 (M); Reverse-phase HPLC (H_2O/CH_3CN from 90/10 to 0/100 in 30 minutes), flow = 1ml/min, λ = 254 nm, t_R = 16.50 min.

5'-*O*-Trityl-azidothymidine (18D) was prepared according to the general procedure from, azidothymidine (**18**) (0.50 g, 1.87 mmol), trityl chloride (1.04 g, 3.74 mmol) in anhydrous pyridine (8.5 mL). After work-up, the crude was purified by column chromatography with a gradient of methanol/triethylamine (1% : 0% to 1% : 1%) in CH_2Cl_2 to give **18D** as a white solid (0.86 g, 90%). ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 11.39 (bs, 1H, N*H*), 7.54 (bs, 1H, *H*-6), 7.42 – 7.24 (m, 15H, *H*-Ph), 6.14 (dd, *J* = 7.0, 5.7 Hz, 1H, *H*-1'), 4.62 – 4.58 (m, 1H, *H*-3'), 3.90 – 3.87 (m, 1H, *H*-4'), 3.26 – 3.25 (m, 1H, *H*-4'), 2.54 – 2.34 (m, 2H, *H*-2'), 1.57 (d, *J* = 1.1 Hz, 3H, C*H*$_3$); ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 163.63 (*C*-4), 150.34 (*C*-2), 143.34 ('ipso' *C*-Ph), 135.85 (*C*-6), 128.22, 127.99, 127.20 (*C*H-Ph), 109.71 (*C*-5), 86.46 (*C*(Ph)$_3$), 83.25 (*C*-1'), 81.90 (*C*-4'), 63.08

(*C*-5'), 59.67 (*C*-3'), 35.94 (*C*-2'), 11.86 (*C*H_3); MS (ES+) Found: *m/z* 554.15 (M + 2Na^+); Calculated for [$C_{29}H_{27}N_5O_4$]: *m/z* 509.26 (M); Reverse-phase HPLC (H_2O/CH_3CN from 50/50 to 0/100 in 30 min), flow = 1 mL/min, λ= 254 nm, t_R = 12.21 min.

5',3'-Bis-*O*-trityl-5-methyl-uridine (19B) was obtained as a white solid (0.53 g, 37%). ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 11.47 (bs, 1H, N*H*), 7.45 – 7.22 (m, 31H, *H*-Ph, *H*-6), 6.11 – 6.09 (m, 2H, *H*-1', O*H*-2'), 4.42 – 4.38 (m, 1H, *H*-2'), 4.09 – 4.08 (m, 1H, *H*-3'), 2.82 – 2.81 (m, 1H, *H*-4'), 2.70 – 2.67 (m, 1H, *H*-5'), 2.40 – 2.37 (m, 1H, *H*-5'), 1.45 (d, *J* = 0.9 Hz, 3H, C*H*$_3$). ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 163.53 (*C*-4), 151.01 (*C*-2), 144.15, 143.09 ('ipso' *C*-Ph), 135.13 (*C*-6), 128.48, 128.07, 127.98, 127.89, 127.24, 127.17 (*C*H-Ph), 109.84 (*C*-5), 86.83, 86.72, (*C*(Ph)$_3$), 86.26 (*C*-1'), 82.10 (*C*-4'), 73.74 (*C*-3'), 72.14 (*C*-2'), 63.37 (*C*-5'), 11.69 (*C*H_3); MS (ES+) Found: *m/z* 765.29 (M + Na^+); Calculated for [$C_{48}H_{42}N_2O_6$]: *m/z* 742.86 (M); Reverse-phase HPLC (H_2O/CH_3CN from 50/50 to 0/100 in 30min), flow = 1 mL/min, λ = 254 nm, t_R = 22.35 min.

5',2'-Bis-*O*-trityl-5-methyl-uridine (19C) was obtained as a white solid (0.09 g, 6%). ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 11.51 (bs, 1H, N*H*), 7.48 – 7.46 (m, 6H, *H*-Ph), 7.33 – 7.19 (m, 25H, *H*-Ph, *H*-6), 6.29 – 6.28 (m, 1H, *H*-1'), 4.74 – 4.73 (m, 1H, O*H*-3'), 4.34 - 4.32 (m, 1H, *H*-2'), 3.87 – 3.86 (m, 1H, *H*-4'), 2.98 – 2.89 (m, 2H, *H*-5'), 2.81 –2.79 (m, 1H, *H*-2'), 1.17 (s, 3H, C*H*$_3$); ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 163.59 (*C*-4), 150.81 (*C*-2), 143.83, 143.03, ('ipso' *C*-Ph), 135.30 (*C*-6), 128.38, 128.06, 127.91, 127.82, 127.30, 127.19 (*C*H-Ph), 110.36 (*C*-5), 86.80 (*C*(Ph)$_3$), 85.34 (*C*-1'), 84.65 (*C*-4'), 76.15 (*C*-2'), 69.78 (*C*-3'), 64.02 (*C*-5'), 11.17 (*C*H_3); MS (ES+) Found: *m/z* 765.29 (M + Na^+); Calculated for [$C_{48}H_{42}N_2O_6$]: *m/z* 742.86 (M); Reverse-phase HPLC (H_2O/CH_3CN from 60/40 to 0/100 in 40 min), flow = 1 mL/min, λ = 254 nm, t_R = 19.51 min.

5',3'-Bis-*O*-trityl-fludarabine (20B) was obtained as a white solid (0.042 g, 5%). ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 7.91 (bs, 2H, NH_2), 7.87 (s, 1H, *H*-8), 7.38 – 7.35 (m, 6H, *H*-Ph), 7.34 – 7.31 (m, 6H, *H*-Ph), 7.30 – 7.23 (m, 18H, *H*-Ph), 6.25 (d, *J* = 3.0 Hz, 1H, *H*-1'), 5.54 (d, *J* = 4.0 Hz, 1H, C-2'-O*H*), 4.00 (apparent m, 1H, *H*-4'), 3.89 (apparent broad s, 1H, *H*-3'), 3.64 (apparent t, *J* = 4.0 Hz, 1H, *H*-2'), 3.47 (dd, *J* = 10.5,

3.5 Hz, 1H, *H*-5'), 2.97 (dd, *J* = 10.5, 3.5 Hz, 1H, *H*-5'); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 159.10 ($^1J_{C\text{-}F}$ = 209.40 Hz, *C*-2), 156.86 ($^3J_{C\text{-}F}$ = 19.8 Hz, *C*-6), 151.39 ($^3J_{C\text{-}F}$ = 19.1 Hz, *C*-4), 143.64, 142.80 (*C*-Ph), 140.83 (*C*H-8), 128.69, 128.68, 128.16, 128.05, 127.57, 127.49 (*C*H-Ph), 117.15 ($^4J_{C\text{-}F}$ = 3.6 Hz, *C*-5), 88.53, 88.21 ($C(Ph)_3$), 85.17 (*C*-1'), 83.68 (*C*-4'), 80.29 (*C*-3'), 75.24 (*C*-2'), 63.41 (*C*-5'); ^{19}F NMR (DMSO-d_6, 470 MHz): δ = –51.02. MS (ES+) Found: *m/z* 792.3 (M + Na^+, 100%); Calculated for [$C_{48}H_{40}FN_5O_4$]: *m/z* 769.86 (M); Reverse phase $HPLC_b$ (H_2O/CH_3CN from 90/10 to 0/50 in 30 min), flow = 1ml/min, λ = 245 nm, t_R = 29.29 min.

5'-*O*-Dimetoxytrityl-fludarabine (20H) was prepared according to the general procedure **1** from fludarabine (**20**) (0.5 g, 1.75 mmol), 4,4'-dimethoxytrityl (1.3 g, 3.8 mmol) in anhydrous pyridine (7 mL). Column chromatography purification using a gradient of methanol/triethylamine (1% : 0.5% to 2% : 0.5%) in CH_2Cl_2 as eluent gave **20H** as a yellowish solid (0.371 g, 36%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.05 (s, 1H, *H*-8), 7.38 – 7.26 (m, 5H, *H*-Ph), 7.24 (d, *J* = 9.0 Hz, 4H, *H*-Ph), 6.80 (d, *J* = 9.0 Hz, 4H, *H*-Ph), 6.24 (d, *J* = 4.0 Hz, 1H, *H*-1'), 4.43 (m, 1H, *H*-3'), 4.20 – 4.19 (m, 1H, *H*-2'), 4.09 – 3.97 (m, 1H, *H*-4'), 3.78 (s, 6H, O*CH*$_3$), 3.96 (dd, *J* = 12.5, 3.5 Hz, 1H, *H*-5'a), 3.65 (d, *J* = 12.5 Hz, 1H, *H*-5'a); MS (ES+) Found: *m/z* 610.21 (M + Na^+); Calculated for [$C_{31}H_{30}FN_5O_6$]: *m/z* 587.5982 (M); Reverse-phase HPLC (H_2O/CH_3CN from 80/20 to 0/100 in 30 minutes), flow = 1ml/min, λ = 254 nm, t_R = 18.23 min.

5',3'-*O*-Bis-trityl penciclovir (22B) was obtained as a white solid (0.15 g, 9%). ^{1}H NMR (DMSO-d_6, 500 MHz) δ = 10.56 (bs, 1H, N*H*), 7.39 (s, 1H, *H*-8), 7.33 – 7.24 (m, 30H, *H*-Ph), 6.37 (bs, 2H, NH_2), 3.67 (t, *J* = 6.9 Hz, 2H, *H*-1'), 3.15 – 3.12 (m, 2H, *H*-4'), 3.08 – 3.05 (m, 2H, *H*-5'), 1.79 – 1.78 (m, 1H, *H*-3'), 1.74 – 1.70 (m, 2H, *H*-2'); ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 156.77 (*C*-6), 153.37 (*C*-2), 150.97 (*C*-4), 143.78 ('ipso' *C*-Ph), 136.98 (*C*-8), 128.51, 128.17, 127.81, 127.46, 126.91 (*C*H-Ph), 116.71 (*C*-5), 85.80 ($C(Ph)_3$), 62.58 (*C*-4', *C*-5'), 40.87 (*C*-1'), 36.85 (*C*-3'), 28.44 (*C*-2'). MS (ES+) Found: *m/z* 760.43 (M + Na^+); Calculated for [$C_{48}H_{43}N_5O_3$]: *m/z* 737.89 (M); Reverse-phase HPLC (H_2O/CH_3CN from 50/50 to 0/100 in 30 min), flow = 1 mL/min, λ = 254 nm, t_R = 18.64 min.

2',5'-Bis-*O*-trityl-3'-deoxyadenosine (23C) was prepared according to the general procedure **1** from 3'-deoxyadenosine (**23**) (0.200 g, 0.80 mmol) and trityl chloride (0.624 g, 2.24 mmol) in anhydrous pyridine (10 mL). Column purification with a gradient of methanol/triethylamine (1% : 0.5% to 2% : 0.5%) in CH_2Cl_2 as eluent yielded **23C** as a white solid (0.222 g, 38%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.06 (s, 1H, *H*-8), 8.00 (s, 1H, *H*-2), 7.44 – 7.37 (m, 12H, *H*-Ph), 7.32 – 7.25 (m, 18H, *H*-Ph), 5.88 (d, *J* = 2.9 Hz, 1H, *H*-1'), 5.73 (br s, 1H, N*H*$_2$), 4.80 – 4.76 (m, 1H, *H*-2'), 4.72 – 4.66 (m, 1H, *H*-4'), 3.44 (dd, *J* = 10.5, 3.2 Hz, 1H, *H*-5'), 3.28 (dd, *J* = 10.5, 4.5 Hz, 1H, *H*-5'), 2.40 (br s, 1H, N*H*$_2$), 2.26 – 2.12 (m, 2H, *H*-3'); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 154.21 (*C*-6), 151.75 (*C*-2), 147.64 (*C*-4), 144.95, 143.71 (*C*-Ph), 137.97 (*C*-8), 129.13, 128.75, 128.01, 127.95, 127.28, 127.00 (*C*H-Ph), 121.39 (*C*-5), 93.24 (*C*-1'), 87.06 (*C*(Ph)$_3$), 80.55 (*C*-4'), 76.05 (*C*-2'), 71.60 (*C*(Ph)$_3$), 65.17 (*C*-5'), 33.92 (*C*-3'); MS (ES+) Found: *m/z* 733.3 (M + Na^+); Calculated for [$C_{46}H_{41}N_5O_3$]: *m/z* 711.85 (M); Reverse-phase HPLC (H_2O/CH_3CN from 80/20 to 0/100 in 50 minutes), flow 1ml/min, λ = 245 nm, t_R = 30.27 min.

Tritylated derivatives of 3-(2′-deoxy-β-D-ribofuranosyl)-6-(4-n-pentylphenyl)-2,3-dihydrofuro-[2,3-d]pyrimidin-2-one (**24**) were prepared according to the general procedure **1** from BCNA (**Cf1743, 24**) (0.50 g, 1.25 mmol), trityl chloride (1.05 g, 3.76 mmol) in anhydrous pyridine (10 mL). After work-up, the crude was purified by column chromatography eluting with dichloromethane/methanol/triethylamine (96% : 3 % : 1%) to give compounds **24B** and **24D**. Further re-purification of impure **24B** by preparative TLC eluting with dichloromethane/methanol/triethylamine (96% : 3 % : 1%) afforded pure **24B**.

5',3'-Di-*O*-trityl-3-(2′-deoxy-β-D-ribofuranosyl)-6-(4-n-pentylphenyl)-2,3-dihydrofuro-[2,3-d]pyrimidin-2-one (24B) was obtained as a white solid (0.06 g, 5%). ^{1}H NMR (DMSO, 500 MHz): δ = 8.65 (s, 1H, *H*-4), 7.69 (d, *J* = 8.2 Hz, 2H), 7.32 – 7.12 (m, 32H, *H*-Ph), 6.78 (s, 1H, *H*-5), 6.19 (t, *J* = 6.6 Hz, 1H, *H*-1'), 3.98 – 3.97 (m, 1H, *H*-3'), 3.62 – 3.61 (m, 1H, *H*-4'), 3.31 – 3.25 (m, 1H, H-5'), 2.90 – 2.87 (m, 1H, *H*-5'), 2.61 (t, *J* = 7.5 Hz, 2H, α-C*H*$_2$), 2.47-2.40 (m, 1H, *H*-2'), 1.92 – 1.87 (m, 2H, *H*-2'), 1.61 – 1.54 (m, 2H, C*H*$_2$), 1.33 – 1.21 (m, 4H, C*H*$_2$), 0.86 (t, *J* = 6.7 Hz, 3H, C*H*$_3$); ^{13}C NMR

(DMSO, 125 MHz): δ = 13.87 (CH_3), 21.90, 30.36, 30.77, 34.86 (C_4H_8), 40.68 (C-2'), 62.98 (C-5'), 74.78 (C-3'), 85.31 (C-4'), 86.92, 87.13 (*C*$(Ph)_3$), 88.87 (C-1'), 98.08 (C-5), 106.82 (C-4a), 124.50 (Ph), 125.64 ('*ipso*'-Ph), 127.11, 127.30, 127.91, 128.05, 128.29, 129.02 (Ph), 137.39 (C-4), 143.15, 143.78 ('ipso' Ph), 144.17 (*Ph*-CH_2), 153.62 (C-6), 154.01 (C-2), 171.10 (C-7a); MS (ES+) Found: *m/z* 905.06 (M + Na^+); Calculated for [$C_{60}H_{54}N_2O_5$]: *m/z* 882.40 (M); Reverse-phase HPLC (H_2O/CH_3CN from 60/40 to 0/100 in 40 min), flow = 1 mL/min, λ = 254 nm, t_R = 28.65 min.

5'-*O*-Trityl-3-(2′-deoxy-β-D-ribofuranosyl)-6-(4-n-pentylphenyl)-2,3-dihydrofuro-[2,3-d]pyrimidin-2-one (24D) was obtained as a white solid (0.26 g, 33%). ^{1}H NMR (DMSO, 500 MHz): δ = 8.65 (s, 1H, *H*-4), 7.66 (d, *J* = 8.3 Hz, 2H), 7.44 – 7.29 (m, 17H, *H*-Ph), 6.40 (s, 1H, *H*-5), 6.18 (t, *J* = 5.0 Hz, 1H, *H*-1'), 5.45 (t, *J* = 4.9 Hz, 1H, 3'-O*H*), 4.42-4.38 (m, 1H, *H*-3'), 4.05 – 4.03 (m, 1H, *H*-4'), 3.43 – 3.40 (m, 1H, *H*-5'), 3.32 – 3.30 (m, 1H, *H*-5'), 2.62 (t, *J*= 7.6 Hz, 2H, CH_2), 2.49 – 2.44 (m, 1H, *H*-2'), 2.27 – 2.22 (m, 2H, *H*-2'), 1.63 – 1.57 (m, 2H, CH_2), 1.34 – 1.23 (m, 4H, CH_2), 0.87 (t, *J* = 6.9 Hz, 3H, CH_3); ^{13}C NMR (DMSO, 125 MHz): δ = 13.88 (CH_3), 21.91, 30.36, 30.67, 34.88 (C_4H_8), 40.99 (C-2'), 62.80 (C-5'), 68.99 (C-3'), 85.84 (C-4'), 86.61 (*C*$(Ph)_3$), 87.39 (C-1'), 98.00 (C-5), 106.74 (C-4a), 124.45 (Ph), 125.67 ('*ipso*'-Ph), 127.19, 128.08, 128.30, 128.68, 129.04, 129.33 (Ph), 137.34 (C-4), 143.35 ('ipso' Ph), 144.15 (*Ph*-CH_2), 153.62 (C-6), 153.83 (C-2), 170.98 (C-7a); MS (ES+) Found: *m/z* 663.21 (M + Na^+); Calculated for [$C_{41}H_{40}N_2O_5$]: *m/z* 640.29 (M); Reverse-phase HPLC (H_2O/CH_3CN from 50/50 to 0/100 in 30min), flow = 1 mL/min, λ = 254 nm, t_R = 24.67 min.