SUPPLEMENTARY INFORMATION.

Synthesis and properties of DNA containing a spore photoprotein analog.

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1) SYNTHESIS OF THE SP-ISOMERS 1a/b

5’-O-tert-butyldimethylsilyl-thymidine (9). Thymidine 7 (5.00 g, 20.7 mmol) was dissolved in anhydrous DMF. Imidazole (3.09 g, 41.3 mmol) and TBDMSCl (3.42 g, 22.7 mmol) were added and the solution was stirred 6 h at room temperature. The reaction mixture was diluted with CHCl₃ (100 mL), washed with water (7 × 100 mL), dried (MgSO₄) and the solvent was removed in vacuo. Purification by flash chromatography (silica gel, CHCl₃/MeOH 20:1) provided 9 (6.35 g, 86 %) as a white solid.

1H-NMR (400 MHz, DMSO-d₆) δ: 0.07 (d, J = 1.28 Hz, 6H; Si(CH₃)₂), 0.88 (s, 9H; C(CH₃)₃), 1.77 (d, J = 1.10 Hz, 3H; C(5)CH₃), 1.90-2.16 (m, 2H; CH₂(2’)), 3.67-3.83 (m, 3H; CH(4’), CH₂(5’)), 4.09-4.35 (m, 1H; CH(3’)), 5.27 (d, J = 4.15 Hz, 1H; C(3)OH), 6.17 (dd, J = 7.59, 6.36 Hz, 1H; CH(1’)), 7.47 (s, 1H; CH(6)), 11.32 (s, 1H; NH); 13C-NMR (100 MHz, DMSO-d₆) δ: -4.98, -4.96, 12.67, 18.48, 26.26, 39.41, 63.76, 70.97, 84.34, 87.27, 109.83, 135.93, 150.82, 164.10; MS (ESI): calc. for [C₁₆H₂₈N₂O₅Si+H]+: 357.1840; found: 357.1838.

5’-O-tert-butyldimethylsilyl-3’-O-tert-butyldiphenylsilyl-thymidine (10). 9 (6.00 g, 16.8 mmol), Imidazole (3.44 g, 50.4 mmol) and TBDPSCl (6.53 mL, 25.2 mmol) were dissolved in anhydrous DMF (40 mL) and the reaction mixture was stirred overnight at room temperature. The reaction mixture was diluted with ethyl acetate (200 mL), washed with saturated aqueous sodium bicarbonate (3 × 200 mL), dried (MgSO₄) and the solvent was removed in vacuo. Purification by flash chromatography (silica gel, isohexane/ethyl acetate 7:3) provided 10 (10.19 g, 99 %) as white solid.
$^1$H-NMR (400 MHz, DMSO-d$_6$) δ: -0.14 (d, J = 11.13 Hz, 6H; Si(CH$_3$)$_2$), 0.71 (s, 9H; C(CH$_3$)$_3$), 1.01 (s, 9H; C(CH$_3$)$_3$), 1.69 (d, J = 0.92 Hz, 3H; C(5)CH$_3$), 1.85-1.96 (m, 1H; CH$_{2a}$), 2.11 (ddd, J = 12.89, 5.48, 1.27 Hz, 1H; CH$_{2b}$), 3.25 (dd, J = 11.37, 3.36 Hz, 1H; CH$_{2c}$), 3.92-3.93 (m, 1H; CH(4')), 6.26 (dd, J = 8.72, 5.58 Hz, 1H; CH(1')), 7.31 (d, J = 1.13 Hz, 1H; CH(6)), 7.38-7.69 (m, 10H; C ar), 11.32 (s, 1H; NH); $^{13}$C-NMR (100 MHz, DMSO-d$_6$) δ: -5.30, -5.14, 12.63, 18.32, 19.09, 26.09, 27.17, 39.42, 63.33, 74.26, 84.39, 87.41, 110.02, 128.43, 128.45, 130.57, 133.15, 133.21, 135.57, 135.71, 150.81, 164.00; MS (ESI): calc. for [C$_{32}$H$_{46}$N$_2$O$_5$Si$_2$Na$^+$]: 617.2837; found: 617.2825.

$^3$-trimethylsilylethoxymethyl-5'-O-tert-butydimethylsilyl-3'-O-tert-butyldiphenylsilyl-thymidine (5). A solution containing 10 (5.30 g, 8.56 mmol), iPr$_2$NEt (6.10 mL, 34.3 mmol) and SEMCl (2.36 mL, 12.9 mmol) in anhydrous CH$_2$Cl$_2$ (20 mL) was stirred for 3 d. After 2 d additional iPr$_2$NEt (6.10 mL, 34.3 mmol) and SEMCl (2.36 mL, 12.9 mmol) were added. The reaction mixture was diluted with CHCl$_3$ (30 mL), washed with saturated aqueous sodium bicarbonate (3 × 40 mL), dried (MgSO$_4$) and the solvent was removed in vacuo. Flash chromatography (silica gel, isohexane/ethyl acetate 9:1) gave 5 (5.46 g, 85 %) as a colorless oil.

$^1$H-NMR (400 MHz, DMSO-d$_6$) δ: -0.12 (s, 3H; SiCH$_3$), -0.09 (s, 3H; SiCH$_3$), -0.05 (s, 9H; Si(CH$_3$)$_3$), 0.74 (s, 9H; C(CH$_3$)$_3$), 0.80-0.85 (m, 2H; SiCH$_2$CH$_2$O), 1.05 (s, 9H; C(CH$_3$)$_3$), 1.77 (d, J = 0.44 Hz, 3H; C(5)CH$_3$), 1.94 (ddd, J = 13.60, 10.15, 5.83 Hz, 1H; CH$_{2a}$), 2.18 (ddd, J = 12.92, 5.52, 1.41 Hz, 1H; CH$_{2b}$), 3.51-3.64 (m, 4H; CH$_2$(5'), SiCH$_2$CH$_2$O), 3.93-4.14 (m, 1H; CH(4')), 4.32-4.33 (m, 1H; CH(3')), 5.21 (s, 2H; OCH$_2$N), 6.31 (dd, J = 8.45, 5.64 Hz, 1H; CH(1')), 7.40-7.67 (m, 11H; C ar, CH(6)); $^{13}$C-NMR (100 MHz, DMSO-d$_6$) δ: -5.92, -5.77, -1.54, 12.66, 17.32, 17.69, 18.47, 25.45, 26.54, 39.72, 62.67,
N³-trimethylsilylethoxymethyl-5’-O-tert-butydimethylsilyl-3’-O-tert-butyldiphenylsilyl-5-bromomethyl-2’-deoxyuridine (4). The protected thymidine 5 (1.50 g, 1.97 mmol), NBS (774 mg, 4.4 mmol) and dibenzoyl peroxide (15.0 mg, 0.06 mmol) were dissolved in carbon tetrachloride (20 mL). The reaction was heated at 70 °C for 30 min. The reaction was allowed to cool and was filtered through a sintered funnel. The solvent was removed in vacuo to yield a crude yellow oil. A quick flash chromatography (silica gel, isohexane/ethyl acetate 9:1) gave 4 (939 mg, 57 %) as a colorless oil which decomposed at room temperature but was stable at -20 °C.

1H-NMR (600 MHz, CDCl₃) δ: -0.09 (s, 3H; Si(CH₃)₃), -0.07 (s, 3H; Si(CH₃)₃), 0.00 (s, 9H; Si(CH₃)₃), 0.80 (s, 9H; C(CH₃)₃), 0.97-0.99 (m, 2H; SiCH₂CH₂O), 1.09 (s, 9H; C(CH₃)₃), 1.77-1.83 (m, 1H; CH₂a(2’)), 2.37 (dd, J = 18.23, 13.10, 5.60 Hz, 1H; CH₂b(2’)), 3.16 (dd, J = 11.58, 2.28 Hz, 1H; CH₂a(5)), 3.64 (dd, J = 11.38, 2.10 Hz, 1H; CH₂b(5)), 3.66-3.71 (m, 2H; SiCH₂CH₂O), 4.03 (bs, 1H; CH(4’)), 4.18 (d, J = 10.47 Hz, 1H; CH₂a(5’)), 4.26 (d, J = 10.51 Hz, 1H; CH₂b(5’)), 4.32-4.33 (m, 1H; CH(3’)), 5.42 (s, 2H; OCH₂N), 6.49 (dd, J = 8.82, 5.28 Hz, 1H; CH(1’)), 7.37-7.42 (m, 5H; Caryl), 7.61-7.65 (m, 5H; Caryl), 7.85 (s, 1H; CH(6)), 13C-NMR (150 MHz, CDCl₃) δ: -5.57, -5.50, -1.43, 18.10, 19.05, 25.80, 26.08, 26.55, 26.86, 41.87, 63.30, 67.64, 70.25, 74.36, 86.40, 88.42, 110.98, 127.67, 130.03, 130.05, 133.02, 133.28, 135.66, 135.70, 137.86, 150.45, 161.31; MS (MALDI): calc. for [C₃₈H₅₉BrN₂O₆Si₃+Na⁺]: 827.0; found: 827.1.

5’-O-tert-butyldiphenylsilyl-5,6-dihydrothymidine (8). Thymidine 7 (10.00 g, 0.04 mol) was dissolved in MeOH/water (200 mL, 1:1) and 600 mg Rh/Al₂O₃ (5 % Rh) was added. The suspension was stirred under an H₂-atmosphere at room temperature for 3 weeks. The reaction
mixture was filtered through celite and the solvent was removed under reduced pressure. The crude product was azeotropically dried three times with pyridine and dissolved in anhydrous DMF (50 mL). Imidazole (6.20 g, 0.09 mol) and TBDPSCl (11.40 mL, 0.05 mol) were added and the reaction mixture was stirred 6 h at room temperature. The reaction mixture was diluted with ethyl acetate (200 mL), washed with saturated aqueous sodium bicarbonate (3 × 200 mL), dried (MgSO₄) and the solvent was removed \textit{in vacuo}. Purification by flash chromatography (silica gel, CHCl₃/MeOH 20:1) provided 8 (14.00 g, 71 %) as a white solid.

$^1$H-NMR (400 MHz, DMSO-d$_6$) δ: 0.91 (d, $J = 6.97$ Hz, 3H; C(5)CH$_3$), 1.00 (s, 9H; C(CH$_3$)$_3$), 1.89 (ddd, $J = 13.24$, 6.57, 3.86 Hz, 1H; CH$_{2a}(2')$), 2.09-2.14 (m, 1H; CH$_{2b}(2')$), 2.52-2.57 (m, 1H; CH(5)), 2.92 (ddd, $J = 12.54$, 10.67 Hz, 1H; CH$_{2a}(6)$), 3.34 (dd, $J = 12.51$, 5.63 Hz, 1H; CH$_{2b}(6)$), 3.66-3.80 (m, 3H; CH(4'), CH$_2(5')$), 4.24-4.25 (m, 1H; CH(3')), 5.21 (d, $J = 4.53$ Hz, 1H; C(3')OH), 6.16 (t, $J = 7.06$ Hz, 1H; CH(1')), 7.42-7.47 (m, 5H; C$_2$H), 7.62-7.65 (m, 5H; C$_2$H), 10.22 (s, 1H; NH); $^{13}$C-NMR (100 MHz, DMSO-d$_6$) δ: 12.82, 19.31, 27.16, 35.00, 37.06, 42.03, 64.54, 70.43, 83.16, 85.60, 128.35, 128.37, 130.34, 130.39, 135.46, 135.60, 153.40, 173.43; MS (ESI): calc. for [C$_{26}$H$_{34}$N$_2$O$_5$Si$^+$Na$^+$]: 505.2129; found: 505.2121.

$5'$-O-\textit{tert}-butyldiphenylsilyl-3'-O-triethylsilyl-5,6-dihydrothymidine (11). 8 (4.90 g, 9.70 mmol), Imidazole (2.07 g, 29.1 mmol) and TESCl (2.52 mL, 14.5 mmol) were dissolved in anhydrous DMF (30 mL) and the reaction mixture was stirred overnight at room temperature. The reaction mixture was diluted with CHCl$_3$ (200 mL), washed with saturated aqueous sodium bicarbonate (6 × 150 mL), dried (MgSO$_4$) and the solvent was removed \textit{in vacuo}. Purification by flash chromatography (silica gel, isohexane/ethyl acetate 7:3) provided 11 (5.71 g, 96 %) as a colorless oil.

$^1$H-NMR (400 MHz, DMSO-d$_6$) δ: 0.56-0.58 (m, 6H; Si(CH$_2$CH$_3$)$_3$), 0.88-0.94 (m, 12H; Si(CH$_2$CH$_3$)$_3$), C(5)CH$_3$), 1.01 (s, 9H, C(CH$_3$)$_3$), 1.87 (ddd, $J = 13.12$, 6.44, 3.58 Hz, 1H;
$^{13}$C-NMR (100 MHz, DMSO-d$_6$) δ: 4.05, 6.48, 12.27, 18.66, 26.50, 34.38, 36.55, 41.45, 63.35, 71.07, 82.58, 84.94, 127.76, 127.80, 129.82, 129.91, 132.34, 132.54, 134.91, 134.95, 152.85, 172.83; MS (ESI): calc. for [C$_{32}$H$_{48}$N$_2$O$_5$Si$_2$+H]$^+$: 597.3175; found: 597.3177.

$N^3$-trimethylsilylethoxymethyl-5'-O-tert-butyldiphenylsilyl-3'-O-triethylsilyl-5,6-dihydrothymidine (3). SEM-protection was carried out as described above for 5. Product 3 (1.98 g, 79 %) was isolated as a colorless oil.

$^1$H-NMR (600 MHz, DMSO-d$_6$) δ: -0.01 (s, 9H; Si(CH$_3$)$_3$), 0.44-0.73 (m, 6H; Si(CH$_2$CH$_3$)$_3$), 0.90-0.97 (m, 11H; SiCH$_2$CH$_2$O, Si(CH$_2$CH$_3$)$_3$), 1.07-1.08 (m, 9H; C(CH$_3$)$_3$), 1.11 (d, J = 7.04 Hz, 3H; C(5)CH$_3$), 2.06-2.00 (m, 2H; CH(5), CH$_{2a}$), 2.55 (ddd, J = 8.81, 7.06, 5.26 Hz, 1H; CH$_{2b}$, 3.19 (ddd, J = 12.82, 8.92 Hz, 1H; CH$_{2a}$), 3.33 (ddd, J = 12.80, 5.22 Hz, 1H; CH$_{2b}$), 3.62 (ddd, J = 9.10, 7.45 Hz, 2H; SiCH$_2$CH$_2$O), 3.72 (ddd, J = 12.20, 3.77 Hz, 1H; CH$_{2a}$), 3.84-3.82 (m, 2H; CH$_{2b}$, CH(4')), 4.46-4.47 (m, 1H; CH(3')), 5.22 (s, 2H; OCH$_2$N), 6.38 (t, J = 7.14 Hz, 1H; CH(1')), 7.36-7.41 (m, 4H; C$_{ar}$H), 7.41-7.47 (m, 2H; C$_{ar}$H), 7.59-7.70 (m, 4H; C$_{ar}$H); $^{13}$C-NMR (150 MHz, DMSO-d$_6$) δ: -1.42, 4.71, 6.73, 13.30, 18.10, 19.26, 26.94, 35.79, 38.22, 40.80, 63.68, 66.82, 69.80, 71.69, 83.38, 86.41, 127.85, 129.88, 129.99, 132.66, 133.05, 135.41, 135.58, 152.98, 172.62; MS (ESI): calc. for [C$_{38}$H$_{62}$N$_2$O$_6$Si$_3$+Na]$^+$: 749.3808; found: 749.3830.

$N^3$-trimethylsilylethoxymethyl-5'-O-tert-butyldiphenylsilyl-5-(N$^3$-trimethylsilylethoxymethyl-3'-O-tert-butyldiphenylsilyl-thymidyl)-5,6-dihydrothymidine (2a/b). Dihydrothymidine 3 (177 mg, 0.24 mmol), azeotropically dried with anhydrous toluene, was dissolved
in anhydrous THF (1.5 mL) and cooled to -78 °C. A freshly prepared LDA-solution (diisopropylamine (51.7 μL, 0.37 mmol), BuLi (0.23 mL, 1.60 M in hexane) in anhydrous THF (0.66 mL) at 0 °C for 1 h) was slowly added and the reaction mixture was stirred at -78 °C for 2 h before addition of 4 (200 mg, 0.25 mmol), dissolved in anhydrous THF (2.3 mL). The reaction mixture was stirred at -78 °C for 1.5 h and at 0 °C for 3 h. The reaction was quenched by adding aqueous sodium bicarbonate (15 mL) and the aqueous phase was extracted with CHCl₃ (3 × 8 mL). The collected extracts were dried (MgSO₄) and the solvent was removed in vacuo. Flash chromatography (silica gel-H, isohexane/ethyl acetate 7:1) gave the fully protected dimer 12 (310 mg, 88 %) as yellow oil.

For selective deprotection of two OH-groups pTsOH (40.7 mg, 0.21 mmol) and 12 were dissolved in MeOH (40 mL). The reaction mixture was stirred at room temperature for 4 h. The mixture was neutralized with aqueous sodium bicarbonate and the solvent was removed in vacuo. The crude product was diluted with aqueous sodium bicarbonate (60 mL) and the aqueous phase was extracted with CHCl₃ (3 × 70 mL). The collected organic phases were dried (MgSO₄) and the solvent was removed in vacuo. An initial purification was achieved by flash chromatography (silica gel-H, CHCl₃/MeOH 50:1) to give 2a/b (100 mg, 35 %) as a mixture of diastereomers.

The diastereomers were separated by np-HPLC using a VP 250/21 Nucleodur 100-5-column (Macherey-Nagel) with a heptane/ethyl acetate gradient (30 → 50 % ethyl acetate in 25 min, 50 → 60 % ethyl acetate in 10 min; flow rate: 15 mL/min; detection wavelength: 250 nm). The mixture was dissolved in heptane/ethyl acetate (4 mL, 4:1) and for each separation 1 mL of the solution was injected through a rheodyne valve on the column. After HPLC purification the S-isomer 2a (68.0 mg, 24 %) and the R-isomer 2b (11.0 mg, 4 %) were isolated as white solids.

S-isomer 2a: mp 65-77 °C; IR: 3466br, 3072w, 2953m, 2932m, 2859s, 1713s, 1661s, 1589w, 1461s, 1428m, 1245m, 1192w, 1087s, 1027w, 997w, 937w, 858m, 835s, 741m, 701s cm⁻¹; ¹H-
NMR (600 MHz, DMSO-d$_6$) δ: -0.08 (s, 9H; Si(CH$_3$)$_3$), -0.06 (s, 9H; Si(CH$_3$)$_3$), 0.75-0.81 (m, 4H; 2 x SiCH$_2$CH$_2$O), 0.87 (s, 3H; C(5A)CH$_3$), 0.99 (s, 9H; C(CH$_3$)$_3$), 1.04 (s, 9H; C(CH$_3$)$_3$), 1.89-1.93 (m, 2H; CH$_2$e(2’B), CH$_2$d(2’A)), 2.02-2.06 (m, 1H; CH$_2$e(2’A)), 2.13-2.18 (m, 2H; CH$_2$a(5), CH$_2$d(2’B)), 2.70 (d, $J$ = 13.76 Hz, 1H; CH$_2$f(5)), 3.04 (d, $J$ = 13.29 Hz, 1H; CH$_2$a(5))

13C-NMR (150 MHz, DMSO-d$_6$) δ: -1.47, 17.43, 18.69, 19.61, 26.56, 28.53, 31.50, 35.95, 41.06, 44.75, 60.81, 63.91, 65.33, 66.17, 69.41, 69.62, 69.73, 73.65, 83.44, 84.97 (2C), 87.75, 107.54, 127.57, 127.75, 127.83, 134.87, 134.99, 135.10, 137.79, 149.98, 152.96, 162.46, 172.53; MS (ESI): calc. for [C$_{64}$H$_{92}$N$_4$O$_{12}$Si$_4$+Na]$^+$: 1243.5681; found: 1243.5700.

R-isomer 2b: mp 66-75 °C; IR: 3412 br, 3072 w, 2954 s, 2858 s, 1710 s, 1664 s, 1589 w, 1461 s, 1428 m, 1246 m, 1194 w, 1085 m, 1053 m, 1006 m, 937 w, 939 w, 859 w, 822 s, 742 w, 702 s cm$^{-1}$; $^1$H-NMR (600 MHz, DMSO-d$_6$) δ: -0.08 (s, 9H; Si(CH$_3$)$_3$), -0.06 (s, 9H; Si(CH$_3$)$_3$), 0.73-0.81 (m, 4H; 2 x SiCH$_2$CH$_2$O), 0.86 (s, 3H; C(5A)CH$_3$), 0.99 (s, 9H; C(CH$_3$)$_3$), 1.04 (s, 9H; C(CH$_3$)$_3$), 1.89-1.92 (m, 2H; CH$_2$e(2’B), CH$_2$d(2’A)), 2.04 (dd, $J$ = 13.6, 6.9 Hz, 1H; CH$_2$e(2’A)), 2.12-2.18 (m, 2H; CH$_2$e(5), CH$_2$d(2’B)), 2.70 (d, $J$ = 13.8 Hz, 1H; CH$_2$f(5)), 3.04 (d, $J$ = 13.2 Hz, 1H; CH$_2$a(5)), 3.11 (d, $J$ = 13.2 Hz, 1H; CH$_2$a(5)), 3.11-3.12 (m, 1H; CH$_2$a(5’B)), 3.42-3.44 (m, 3H; SiCH$_2$CH$_2$O(A), CH$_2$b(5’B)), 3.65 (dd, $J$ = 10.7, 4.7 Hz, 2H; SiCH$_2$CH$_2$O(B)), 3.71-3.72 (m, 1H; CH$_2$a(5’A)), 3.74-3.75 (m, 1H; CH$_2$a(5’A)), 3.76-3.77 (m, 1H; CH(4’A)), 3.81-3.82 (m, 1H; CH(4’A)), 4.19-4.20 (m, 1H; CH(4’A)), 4.91 (d, $J$ = 9.86 Hz, 1H; OCH$_2$N(A)), 5.13 (d, $J$ = 3.85 Hz, 2H; OCH$_2$N(B)), 5.23 (d, $J$ = 4.58 Hz, 1H; C(3’)OH), 6.25 (t, $J$ = 7.05 Hz, 1H; CH(1’A)), 6.29 (dd, $J$ = 7.80, 5.99 Hz, 1H; CH(1’B)), 7.40-7.47 (m, 10H; C$_{ar}$H), 7.59-7.65 (m, 10H; C$_{ar}$H), 7.69 (s, 1H; CH(6)); $^{13}$C-NMR (150 MHz, DMSO-d$_6$) δ: -1.47, 17.43, 18.69, 19.61, 26.56, 28.53, 31.50, 35.95, 41.06, 44.75, 60.81, 63.91, 65.33, 66.17, 69.41, 69.62, 69.73, 73.65, 83.44, 84.97 (2C), 87.75, 107.54, 127.57, 127.75, 127.83, 134.87, 134.99, 135.10, 137.79, 149.98, 152.96, 162.46, 172.53; MS (ESI): calc. for [C$_{64}$H$_{93}$N$_4$O$_{12}$Si$_4$+Na]$^+$: 1243.5681; found: 1243.5700.

Supplementary Material (ESI) for Chemical Communications
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$CH(3'\text{A}), 4.46-4.47 \ (m, 1H; CH(3'\text{B})), 4.90 \ (d, J = 9.9 \text{ Hz}, 1H; OCH_{2b}N(\text{A})), 4.99 \ (t, J = 5.2 \text{ Hz}, 1H; C(5'\text{B})O\text{H}), 5.04 \ (d, J = 9.9 \text{ Hz}, 1H; OCH_{2b}N(\text{A})), 5.13 \ (d, J = 4.0 \text{ Hz}, 2H; OCH_{2}N(\text{B})), 5.23 \ (d, J = 4.6 \text{ Hz}, 1H; C(3')O\text{H}), 6.25 \ (t, J = 7.0 \text{ Hz}, 1H; CH(1'\text{A})), 6.29 \ (dd, J = 7.8, 6.0 \text{ Hz}, 1H; CH(1'\text{B})), 7.42-7.47 \ (m, 10H; C_{\text{ar}}\text{H}), 7.59-7.69 \ (m, 10H; C_{\text{ar}}\text{H}), 7.69 \ (s, 1H; C(6)); 13C-NMR (150 MHz, DMSO-d_6) \ \delta: -1.48, 17.21, 17.44, 18.53, 18.61, 19.34, 26.46, 26.58, 31.80, 38.80, 40.83, 44.74, 60.81, 64.51, 65.21, 69.21, 69.64, 70.25, 73.64, 83.53, 84.98, 84.46, 87.69, 107.59, 127.77, 127.82, 127.84, 129.72, 129.75, 129.92, 132.64, 132.72, 134.96, 134.99, 135.10, 137.88, 151.76, 162.46, 173.10; MS (ESI): \ \text{calc. for } [C_{64}H_{92}N_4O_{12}Si_4Na]^+: 1243.5681; \ \text{found: 1243.5701.}

(5S)-N^3-$trimethylsilylethoxymethyl-5'-O-tert-butyldiphenylsilyl-5-(N^3-\text{trimethylsilyl-ethoxymethyl}-5'-O-dimethoxytrityl-3'-O-tert-butyldiphenylsilyl-thymidyrl)-5,6-dihydrothymidine (6a). The S-isomer 2a (168 mg, 0.14 mmol), azeotropically dried with pyridine, was dissolved in pyridine (0.8 mL) and stirred at room temperature over molecular sieve (4 Å). Dimethoxytrityltriflat (124 mg, 0.28 mmol) was dissolved in pyridine (0.4 mL) and stirred at room temperature over molecular sieve (4 Å). After 3 h the Dimethoxytrityl-solution was added to 2a and the reaction mixture was stirred further 6 h. The reaction was quenched by adding methanol (1 mL), filtered and the solvent was removed under reduced pressure. Purification by flash chromatography (silica gel-H, CHCl_3/MeOH/Pyr 50:1:0.1) provided 6a (176 mg, 84 %) as a pale yellow, sticky solid.

IR: 3492br, 2953s, 2859s, 1719s, 1663s, 1509m, 1460s, 1428m, 1392w, 1246s, 1182m, 1084s, 1032w, 995m, 936w, 833s, 743m, 700s, 611m cm$^{-1}$; $^1$H-NMR (400 MHz, Acetone-d$_6$) $\delta$: -0.04 (s, 9H; Si(CH$_3$)$_3$), -0.02 (s, 9H; Si(CH$_3$)$_3$), 0.76-0.93 (m, 7H; C(5A)CH$_3$, 2 x SiCH$_2$CH$_2$O), 1.05 (s, 9H; C(CH$_3$)$_3$), 1.06 (s, 9H; C(CH$_3$)$_3$), 1.93-2.03 (m, 2H; CH$_{2a}(2'B)$, CH$_{2a}(2'A)$), 2.07-2.12 (m, 2H; CH$_{2b}(2'A)$, CH$_{2a}(5)$), 2.34 (ddd, $J = 13.46, 5.79, 2.96 \text{ Hz}, 1H; CH_{2b}(2'B)$), 2.61 ($d, J = 13.89 \text{ Hz}, 1H; CH_{2b}(5)$), 2.99-3.19 (m, 4H; CH$_2$(6A), CH$_2$(5'B)), 3.48 ($t, J = 7.81 \text{ Hz},$...
2H; SiCH₂CH₂O(A)), 3.57-3.66 (m, 2H; SiCH₂CH₂O(B)), 3.75 (s, 6H; 2 x OCH₃), 3.78-3.85 (m, 2H; CH₂(5’A)), 3.87-3.88 (m, 1H; CH(4’A)), 4.21-4.24 (m, 1H; CH(4’B)), 4.41-4.46 (m, 1H; CH(3’A)), 4.49-4.50 (m, 1H; CH(3’B)), 5.00 (d, J = 9.74 Hz, 1H; OCH₂N(A)), 5.05 (d, J = 9.73 Hz, 1H; OCH₂N(A)), 5.26 (s, 2H; OCH₂N(B)), 6.36-6.41 (m, 2H; CH(1’A), CH(1’B)), 6.79-6.81 (m, 4H; CH), 7.17-7.26 (m, 6H; CH), 7.29-7.47 (m, 16H; CH), 7.13-7.27 (m, 4H; CH), 7.30-7.50 (m, 4H; CH); ¹³C-NMR (100 MHz, Acetone-δ): -0.12, 19.54, 19.66, 20.75, 21.74, 28.25, 28.33, 34.27, 40.74, 41.63, 43.34, 47.05, 56.54, 65.72, 66.23, 67.80, 68.68, 71.90, 71.95, 72.34, 75.70, 85.91, 87.35, 88.02, 88.06, 110.35, 114.94, 125.56, 129.64, 129.72, 129.79, 129.93, 129.97, 131.69, 131.71, 131.91, 131.95, 134.89, 135.00, 135.11, 135.12, 137.30, 137.49, 137.55, 139.53, 146.75, 152.46, 154.26, 160.60, 164.81, 175.51; MS (ESI+): calc. for [C₈₅H₁₁₀N₄O₁₄Si₄+NH₄]+: 1540.7434; found: 1540.7580.

(5R)-N³-trimethylsilylethoxymethyl-5’-O-tert-butyldiphenylsilyl-5-(N³-trimethylsilyl-ethoxymethyl-5’-O-dimethoxytrityl-3’-O-tert-butyldiphenylsilyl-thymidyl)-5,6-dihydrothymidine (6b). DMT-protection was carried out as described above for 6a. The R-isomer 6b (110 mg, 100 %) was isolated as a pale yellow, sticky solid.

IR: 3390 br, 2954s, 2862s, 1718s, 1660s, 1507m, 1461s, 1425m, 1390w, 1030w, 993m, 935w, 832s, 743w, 701s, 610 cm⁻¹; ¹H-NMR (400 MHz, Acetone-δ): δ: -0.03 (s, 9H; Si(CH₃)₃), -0.02 (s, 9H; Si(CH₃)₃), 0.80-0.90 (m, 4H; 2 x SiCH₂CH₂O), 0.93 (s, 3H; C(5A)CH₃), 1.05 (s, 9H; C(CH₃)₃), 1.06 (s, 9H; C(CH₃)₃), 1.84-1.92 (m, 1H; CH₂a(2’B)), 2.06-2.10 (m, 1H; CH₂a(5)), 2.11-2.12 (m, 1H; CH₂a(2’A)), 2.35 (ddd, J = 13.48, 5.99, 3.09 Hz, 1H; CH₂b(2’A)) 2.56-2.66 (m, 1H; CH₂b(2’B)), 2.85 (bs, 1H; CH₂b(5)), 3.09 (dd, J = 10.29, 4.92 Hz, 1H; CH₂b(5’B)). 3.18 (dd, J = 10.30, 4.20 Hz, 1H; CH₂b(5’B)), 3.27 (d, J = 13.34 Hz, 1H; CH₂b(6A)), 3.41 (d, J = 13.35 Hz, 1H; CH₂b(6A)), 3.53 (t, J = 7.85 Hz, 2H; SiCH₂CH₂O(A)), 3.60-3.65 (m, 2H; SiCH₂CH₂O(B)), 3.71 (dd, J = 7.80, 3.73 Hz, 2H;
(5S)-N³-trimethylsilylethoxymethyl-5’-O-tert-butyldiphenylsilyl-3’-O-β-cyanoethyl-N,N-diisopropylaminophosphanyloxy-5-(N³-trimethylsilylethoxymethyl-5’-O-dimethoxytrityl-3’-O-tert-butyldiphenylsilyl-thymidyl)-5,6-dihydrothymidine (1a). The S-isomer 6a (120 mg, 0.08 mmol) and Diisopropylamine (54 µL, 0.32 mmol) was dissolved in THF (0.6 mL), degassed 3 times and cooled to 0 °C. CEDCl (33 µL, 0.12 mmol) was added at 0 °C and the solution was stirred for 5 h. The temperature was allowed to go up to room temperature. The solvent was removed under reduced pressure. Purification by flash chromatography (deactivated silica gel, isohexane/ethyl acetate 3:1) provided 1a (100 mg, 73 %) as a white solid.

31P-NMR (200 MHz, CDCl3) δ: 149.30, 149.52; 1H-NMR (600 MHz, CDCl3) δ: -0.04 (s, 9H; Si(CH₃)₃), -0.01 (s, 9H; Si(CH₃)₃), 0.85-0.97 (m, 7H; C(5A)CH₃, 2 x SiCH₂CH₂O), 1.00-1.07 (m, 9H, C(CH₃)₃), 1.11-1.15 (m, 9H, C(CH₃)₃), 1.32-1.42 (m, 6H, NCH(CH₃)₂), 1.73-1.84 (m, 6H, NCH(CH₃)₂), 1.92-2.04 (m, 1H, CH₂(b(2’A))), 2.10-2.15 (m, 2H, CH₂(b(2’B)), CH₂(a(5))), 2.22-2.33 (m, 2H, CH₂(b(2’B)), CH₂(a(5))), 2.49-2.62 (m, 2H, CH₂aCN, CH₂(b(5))),
2.96-3.05 (m, 2H, CH$_2$a(6A), CH$_2$b(CN)), 3.08-3.16 (m, 3H, N(CH(CH$_3$)$_2$)$_2$, CH$_2$b(6A)), 3.39-3.45 (m, 1H, CH$_2$a(5’B)), 3.47-3.53 (m, 3H, SiCH$_2$CH$_2$O(A), CH$_2$b(5’B)), 3.58-3.66 (m, 4H, SiCH$_2$CH$_2$O(B), OCH$_2$CH$_2$CN), 3.75 (s, 6H; 2 x OCH$_3$), 3.83-3.84 (m, 1H, CH$_2$a(5’A)), 4.04-4.11 (m, 2H, CH$_2$b(5’A), CH(4’A)), 4.12-4.19 (m, 2H, CH(3’A), CH(4’B)), 4.32-4.42 (m, 1H, CH(3’B)), 4.98-5.04 (m, 1H, OCH$_2$N(A)), 5.09 (d, $J = 9.63$ Hz, 1H, OCH$_2$N(A)), 5.24-5.32 (m, 2H, OCH$_2$N(B)), 6.30-6.42 (m, 2H, CH(1’A), CH(1’B)), 6.65-6.75 (m, 4H, C ar), 7.09-7.20 (m, 6H, Car), 7.24-7.45 (m, 16H, Car, C ar(6)), 7.51-7.60 (m, 4H, Car); 13C-NMR (150 MHz, CDCl$_3$) δ: -1.39, -1.37, 17.59, 18.04, 18.15, 19.02, 19.23, 22.41, 22.53, 26.46, 26.87, 32.52, 38.72, 40.24, 41.87, 41.93, 43.25, 46.35, 55.15, 60.11, 63.73, 63.75, 66.57, 67.40, 70.24, 70.33, 71.01, 73.72, 84.08, 85.52, 86.33, 86.39, 108.38, 113.07, 116.59, 116.77, 123.68, 126.81, 127.88, 128.02, 128.04, 129.81, 129.83, 129.97, 129.98, 130.00, 132.72, 133.06, 133.13, 135.56, 135.61, 135.68, 139.48, 144.63, 150.62, 152.77, 158.42, 163.05, 172.97; MS (ESI): calc. for [C$_{94}$H$_{127}$N$_6$O$_{15}$PSi$_4$+NH$_4$]$^+$: 1740.8512; found: 1740.8615.

(5R)-N$_3$-trimethylsilylethoxymethyl-5’-O-tert-butyldiphenylsilyl-3’-O-β-cyanoethyl-N,N-diisopropylaminophosphanoxy-5-(N$_3$-trimethylsilylethoxymethyl-5’-O-dimethoxytrityl-3’-O-tert-butyldiphenylsilyl-thymidyl)-5,6-dihydrothymidine (1b). Phosphoramidite-synthesis was carried out as described above for 1a. The R-isomer 1b (101 mg, 89 %) was isolated as a white solid.

$^{31}$P-NMR (200 MHz, CDCl$_3$) δ: 149.44, 149.47; $^1$H-NMR (600 MHz, CDCl$_3$) δ: -0.04 (s, 9H; Si(CH$_3$)$_3$), -0.01 (s, 9H; Si(CH$_3$)$_3$), 0.86-0.95 (m, 7H; C(5A)CH$_3$, 2 x SiCH$_2$CH$_2$O), 1.04 (s, 9H; C(CH$_3$)$_3$), 1.06 (s, 9H; C(CH$_3$)$_3$), 1.12-1.26 (m, 12H; N(CH(CH$_3$)$_2$)$_2$), 1.16-1.28 (m, 2H; CH$_2$a(2’B), CH$_2$b(2’A)), 1.92-1.94 (m, 1H; CH$_2$a(5’)), 2.21-2.30 (m, 1H; CH$_2$b(2’A)), 2.36-2.40 (m, 1H; CH$_2$b(2’B)), 2.49-2.58 (m, 1H; CH$_2$b(5’)), 2.61-2.72 (m, 1H; CH$_2$CN), 2.99-3.03 (m, 1H; CH$_2$CN), 3.01 (dd, $J = 10.17$, 4.54 Hz, 1H; CH$_2$a(5’B)), 3.10-3.15 (m, 1H; CH$_2$b(5’B)),
3.17-3.27 (m, 2H; N(CH(CH₃)₂)₂), 3.37-3.45 (m, 1H; CH₂₉(6A)), 3.55-3.59 (m, 3H; CH₂₉(6A), SiCH₂CH₂O(A)), 3.59-3.70 (m, 6H; CH₂(5’A), SiCH₂CH₂O(B), OCH₂CH₂CN), 3.74 (s, 6H; 2 x OCH₃), 4.02-4.04 (m, 2H; CH(4’B), CH(4’A)), 4.40-4.42 (m, 1H; CH(3’A)), 4.50-4.65 (m, 1H; CH(3’B)), 4.98 (d, J = 9.67 Hz, 1H; OCH₂₉N(A)), 5.16 (d, J = 9.63 Hz, 1H; OCH₂₉N(A)), 5.30 (d, J = 3.99 Hz, 2H; OCH₂N(B)), 6.34-6.39 (m, 2H; CH(1’A), CH(1’B)), 6.65-6.75 (m, 4H, C₉H), 7.23-7.30 (m, 6H; C₉H), 7.30-7.44 (m, 16H; C₉H, CH(6)), 7.53-7.60 (m, 4H, C₉H), 7.64-7.70 (m, 4H, C₉H); ¹³C-NMR (150 MHz, CDCl₃) δ: -0.14, 18.15, 19.01, 19.63, 20.20, 20.62, 22.37, 22.61, 24.55, 26.84, 32.88, 38.38, 40.27, 41.77, 42.14, 43.21, 45.09, 55.15, 60.36, 63.81, 64.29, 66.45, 67.37, 70.04, 70.38, 71.01, 73.66, 81.39, 85.61, 85.67, 86.32, 108.70, 113.08, 116.94, 117.48, 123.67, 126.78, 127.78, 127.83, 128.06, 129.11, 129.80, 129.92, 130.01, 133.11, 133.14, 133.15, 135.59, 135.62, 135.64, 135.68, 139.48, 144.64, 150.69, 152.22, 158.44, 163.00, 173.27; MS (ESI): calc. for [C₉4H₁₂7N₆O₁₅PSi₄+NH₄]⁺: 1740.8512; found: 1740.8535.
2) HPLC-CHROMATOGRAMS FOR THE SEPARATED DIASTEREOMERS 2a AND 2b

Analytical HPLC-chromatograms of the separated diastereomers 2a and 2b. np-HPLC: Heptane (A), Ethyl acetate (B); gradient: 30 → 50 % B in 25 min, 50 → 60 % B in 10 min; column: CC 250/4 Nucleodur 100-3; flow rate: 0.7 mL/min; detection: 250 nm; retention times: $R_f$ (2a) 23.65 min, $R_f$ (2b) 25.45 min.
3) $^1$H-NMR SPECTRA FOR THE SEPARATED DIASTEREOMERS 2a AND 2b
$^1$H-NMR spectrums of the diastereomers 2a and 2b in DMSO-d$_6$ (600 MHz).
4) NOE DATA FOR THE ISOMERS 2a/b

Isomer 2a

NOESY crosspeaks for isomers 2a in DMSO-d$_6$ (600 MHz).
Isomer 2b

NOESY crosspeaks for isomers 2b in DMSO-d₆ (600 MHz).