SUPPLEMENTARY INFORMATION.

1) SYNTHESIS OF THE SP-ISOMERS **8a/b**

3',5'-*O*-Di-triethylsilyl-5,6-dihydrothymidine (10). Thymidine **1** (2.00 g, 8.26 mmol) was dissolved in MeOH/water (50 mL, 1:1) and 100 mg Rh/Al_2O_3 (5 % Rh) was added. The suspension was stirred under an H_2-atmosphere at room temperature for 3 d. 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 (20 mL). Imidazole (3.00 g, 44.1 mmol) and TESCl (4.16 mL, 24.8 mmol) were added and the reaction mixture was stirred overnight at room temperature. 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*. Purification by flash chromatography (silica gel, pentane/ethyl acetate 7:3) provided **10** (3.45 g, 88 %) as a white solid.

^{1}H-NMR (300 MHz, DMSO-d_6) δ: 0.52-0.62 (*m*, 12 H; 2× $Si(CH_2CH_3)_3$), 0.87-0.96 (*m*, 18 H; 2× $Si(CH_2CH_3)_3$), 1.05 (*d*, *J* = 6.6 Hz, 3 H; $C(5)CH_3$), 1.73-1.82 (*m*, 1 H; $CH_2(2')$), 2.11-2.22 (*m*, 1 H; $CH_2(2')$), 2.55-2.64 (*m*, 1 H; *CH*(5)), 2.91-2.99 (*m*, 1 H; $CH_2(6)$), 3.35-3.40 (*m*, 1 H; $CH_2(6)$), 3.55-3.68 (*m*, 3 H; *CH*(4'), $CH_2(5')$), 4.22-4.33 (*m*, 1 H; *CH*(3')), 6.11 (*t*, *J* = 6.6 Hz, 1 H; *CH*(1')), 10.23 (*s*, 1 H; N*H*); ^{13}C-NMR (75 MHz, DMSO-d_6) δ: 3.99, 4.33, 6.75, 12.69, 34.76, 36.48, 41.53, 62.65, 72.06, 83.06, 85.63, 153.17, 173.26; MS (FAB$^+$): 495 (20, M+Na$^+$), 443 (13), 413 (6), 311 (10), 213 (18), 145 (40), 115 (93), 87 (100), 59 (36).

N^3-Trimethylsilylethoxymethyl-3',5'-*O*-di-triethylsilyl-5,6-dihydrothymidine (3). A solution containing **10** (3.64 g, 7.70 mmol), iPr_2NEt (5.27 mL, 30.8 mmol) and SEMCl (2.04 mL, 11.6 mmol) in anhydrous CH_2Cl_2 (20 mL) was stirred for 4 d. After 24 h additional iPr_2NEt (5.27 mL, 30.8 mmol) and SEMCl (2.04 mL, 11.6 mmol) were added. The reaction mixture was diluted with $CHCl_3$ (30 mL), washed with saturated aqueous sodium bicarbonate (3 × 50 mL), dried ($MgSO_4$) and the solvent was removed *in vacuo*. Flash chromatography (silica gel, pentane/ethyl acetate 10:1) gave **3** (3.89 g, 84 %) as a colorless oil.

^{1}H-NMR (300 MHz, DMSO-d_6) δ: -0.04 (*s*, 9 H; Si(C*H*$_3$)$_3$), 0.54-0.63 (*m*, 12 H; 2× Si(C*H*$_2$CH$_3$)$_3$), 0.81 (*t*, *J* = 7.8 Hz, 2 H; SiC*H*$_2$CH$_2$O), 0.90-0.96 (*m*, 18 H; 2× Si(CH$_2$C*H*$_3$)$_3$), 1.11 (*d*, *J* = 7.0 Hz, 3 H; C(5)C*H*$_3$), 1.81-1.88 (*m*, 1 H; C*H*$_{2a}$(2')), 2.15-2.24 (*m*, 1 H; C*H*$_{2b}$(2')), 2.72-2.79 (*m*, 1 H; C*H*(5)), 2.99 (*dd*, *J* = 12.3 Hz, 10.3 Hz, 1 H; C*H*$_{2a}$(6)), 3.41 (*dd*, *J* = 12.9, 5.6 Hz, 1 H; C*H*$_{2b}$(6)), 3.50 (*t*, *J* = 8.0 Hz, 2 H; SiCH$_2$C*H*$_2$O), 3.60-3.62 (*m*, 2 H; C*H*$_2$(5')), 3.66-3.68 (*m*, 1 H; C*H*(4')), 4.30-4.32 (*m*, 1 H; C*H*(3')), 5.05 (*s*, 2 H; OC*H*$_2$N), 6.17 (*t*, *J* = 7.3 Hz, 1 H; C*H*(1')); ^{13}C-NMR (75 MHz, DMSO-d_6) δ: -1.21, 3.98, 4.33, 6.74, 13.08, 17.59, 35.09, 36.67, 40.40, 62.56, 65.75, 69.25, 71.96, 83.98, 85,75, 152.92, 172.57; MS (FAB$^+$): 625 (8, *M*+Na$^+$), 603 (3, *M*+H$^+$), 573 (5), 427 (5), 213 (13), 145 (48), 116 (100), 87 (71), 73 (53), 59 (23), 44 (11).

3',5'-*O*-Di-*tert*-butyldimethylsilyl-thymidine (11). Thymidine **1** (2.00 g, 8.26 mmol) was dissolved in anhydrous DMF. Imidazole (3.38 g, 49.6 mmol) and TBDMSCl (3.74 g, 24.8 mmol) were added and the solution was stirred overnight at room temperature. The reaction mixture was diluted with $CHCl_3$ (200 mL), washed with water (3 × 200 mL), dried ($MgSO_4$) and the solvent was removed *in vacuo*. Purification by flash chromatography (silica gel, pentane/ethyl acetate 1:1) provided **11** (3.70 g, 95 %) as a white foam.

^{1}H-NMR (300 MHz, DMSO-d_6) δ: 0.06 (*s*, 6 H; Si(C*H*$_3$)$_2$), 0.07 (*s*, 6 H; Si(C*H*$_3$)$_2$), 0.86 (*s*, 9 H; C(C*H*$_3$)$_3$), 0.87 (*s*, 9 H; C(C*H*$_3$)$_3$), 1.76 (*s*, 3 H; C(5)C*H*$_3$), 2.00-2.09 (*m*, 1 H; C*H*$_{2a}$(2')), 2.12-2.22 (*m*, 1 H; C*H*$_{2b}$(2')), 3.67-3.74 (*m*, 2 H; C*H*$_2$(5')), 3.75-3.79 (*m*, 1 H; C*H*(4')), 4.32-4.38 (*m*, 1 H; C*H*(3')), 6.14 (*t*, *J* = 6.3 Hz, 1 H; C*H*(1')), 7.41 (*s*, 1 H; C*H*(6)), 11.33 (*s*, 1 H; N*H*); ^{13}C-NMR (75 MHz, DMSO-d_6) δ: -5.34, -5.31, -4.78, -4.62, 12.38, 17.85, 18.16, 25.82, 25.92, 39.30, 62.85, 72.20, 83.84, 86.84, 109.71, 135.70, 150.55, 163.78; MS (FAB$^+$): 493 (35, *M*+Na$^+$), 471 (17, *M*+H$^+$), 281 (10), 213 (13), 145 (46), 127 (15), 115 (16), 89 (40), 73 (100).

***N*^{3}-Trimethylsilylethoxymethyl-3',5'-*O*-di-*tert*-butydimethylsilyl-thymidine (4).** SEM-protection was carried out as described above for **3**. Product **4** (3.34 g, 72 %) was isolated as a colorless oil.

^{1}H-NMR (500 MHz, DMSO-d$_6$) δ: -0.04 (*s*, 9 H; Si(CH_3)$_3$), 0.08 (*s*, 6 H; Si(CH_3)$_2$), 0.09 (*s*, 6 H; Si(CH_3)$_2$), 0.81-0.85 (*m*, 2 H; SiCH_2CH$_2$O), 0.88 (*s*, 9 H; C(CH_3)$_3$), 0.89 (*s*, 9 H; C(CH_3)$_3$), 1.84 (*s*, 3 H; C(5)CH_3), 2.12 (*ddd*, *J* = 13.3, 6.3, 3.4 Hz, 1 H; CH_{2a}(2')), 2.17-2.22 (*m*, 1 H; CH_{2b}(2')), 3.57 (*t*, *J* = 8.0 Hz, 2 H; SiCH$_2$CH_2O), 3.72 (*dd*, *J* = 11.4, 3.8 Hz, 1 H; CH_{2a}(5')), 3.78 (*dd*, *J* = 11.5, 4.2 Hz, 1 H; CH_{2b}(5')), 3.81-3.85 (*m*, 1 H; C*H*(4')), 4.35-4.40 (*m*, 1 H; C*H*(3')), 5.22 (*s*, 2 H; OCH_2N), 6.18 (*t*, *J* = 6.5 Hz, 1 H; C*H*(1')), 7.51 (*s*, 1 H; C*H*(6)); ^{13}C-NMR (125 MHz, DMSO-d$_6$) δ: -5.35 (2C), -4.80, -4.66, -1.25, 12.99, 17.63, 17.81, 18.13, 25.78, 25.88, 39.59, 62.76, 66.49, 69.79, 72.05, 85.05, 87.07, 108.85, 135.06, 150.62, 162.79; MS (FAB$^+$): 601 (17, *M*+H$^+$), 543 (15), 229 (34), 213 (30), 199 (47), 145 (100), 115 (21).

***N*^{3}-Trimethylsilylethoxymethyl-3',5'-*O*-di-*tert*-butydimethylsilyl-5-bromomethyl-2'-deoxyuridine (5).** The protected thymidine **4** (1.00 g, 1.66 mmol), NBS (621 mg, 3.49 mmol) and benzoyl peroxide (12.0 mg, 0.05 mmol) were dissolved in carbon tetrachloride (20 mL). The reaction was heated at 70 °C for 1 h. 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, pentane/ethyl acetate 9:1) gave **5** (683 mg, 60 %) as a colorless oil which decomposed at room temperature but was stable at -20 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.00 (*s*, 9 H; $Si(CH_3)_3$), 0.07 (*s*, 6 H; $Si(CH_3)_2$), 0.13 (*s*, 6 H; $Si(CH_3)_2$), 0.89 (*s*, 9 H; $C(CH_3)_3$), 0.91 (*s*, 2 H; $SiCH_2CH_2O$), 0.94 (*s*, 9 H; $C(CH_3)_3$), 1.92-2.04 (*m*, 1 H; CH_{2a}(2’)), 2.34 (*ddd*, *J* = 8.6, 5.6, 2.7 Hz, 1 H; CH_{2b}(2’)), 3.64-3.72 (*m*, 2 H; $SiCH_2CH_2O$), 3.77 (*dd*, *J* = 11.3, 2.6 Hz, 1 H; CH_{2a}(5’)), 3.89 (*dd*, *J* = 11.6, 2.6 Hz, 1 H; CH_{2b}(5’)), 4.27 (*d*, *J* = 10.3 Hz, 1 H; $CH_{2a}Br$), 4.30 (*d*, *J* = 10.3 Hz, 1 H; $CH_{2b}Br$), 4.35-4.41 (*m*, 1 H; *CH*(3’)), 5.41 (*s*, 2 H; OCH_2N), 6.30 (*dd*, *J* = 7.6, 5.6 Hz, 1 H; *CH*(1’)), 7.88 (*s*, 1 H; *CH*(6)); ^{13}C-NMR (75 MHz, $CDCl_3$) δ: -5.36, -4.86, -4.66, -1.46, 17.96, 18.09, 18.44, 25.70, 25.97, 26.14, 41.91, 62.98, 67.66, 70.22, 72.21, 86.21, 88.17, 110.91, 137.81, 150.40, 161.32; MS (FAB$^+$): 751 (25), 679 (8, M+H$^+$), 653 (13), 623 (18), 599 (13), 543 (6), 287 (10), 213 (23), 145 (100).

***N*^{3}(A/B)-Di-trimethylsilylethoxymethyl-5-(α-thymidyl)-5,6-dihydrothymidine (7a/b).** Dihydrothymidine **3** (446 mg, 0.74 mmol), azeotropically dried with anhydrous toluene, was dissolved in anhydrous THF (4 mL) and cooled to -78 °C. A freshly prepared LDA-solution (diisopropylamine (156 µL, 1.11 mmol), BuLi (0.70 mL, 1.60 M in hexane) in anhydrous THF (2 mL) at 0 °C for 1 h) was slowly added and the reaction mixture was stirred at -78 °C for 2 h before the addition of **5** (500 mg, 0.74 mmol), dissolved in anhydrous THF (6 mL). The reaction mixture was stirred at -78 °C for 1.5 h and at 0 °C for 1.5 h. The reaction was quenched by adding aqueous sodium bicarbonate (12 mL) and the aqueous phase was extracted with $CHCl_3$ (3 × 20 mL). The collected extracts were dried ($MgSO_4$) and the solvent was removed *in vacuo*.

For deprotection of the OH-groups a TBAF solution was prepared by dissolving TBAF (2.33 g, 7.40 mmol) in anhydrous THF (10 mL) and adding molecular sieves (4 Å). The solution was stirred at room temperature for 1.5 h to remove traces of water. The crude mixture of the coupling was dissolved in anhydrous THF (20 mL) and added to the TBAF solution. The reaction mixture was stirred at room temperature for 1.5 h until all starting material had reacted. The mixture was filtered, diluted with $CHCl_3$ (100 mL), washed with aqueous sodium bicarbonate (150 mL) and the aqueous phase was extracted with $CHCl_3$ (3 × 100 mL). The collected organic phases were dried ($MgSO_4$) and the solvent was removed *in vacuo*. An initial purification was achieved by flash chromatography (silica gel, $CHCl_3$/MeOH 10:1) to give **7a/b** (328 mg, 60 %) as a mixture of diastereomers.

The diastereomers were separated by rp-HPLC using a 250/10 Nucleosil 120-3 C8-column (*Macherey-Nagel*) with a water/acetonitrile gradient (0 → 6 % acetonitrile in 20 min, 6 → 9 % acetonitrile in 30 min, 9 → 100 % acetonitrile in 5 min; flow rate: 3 mL/min; detection wavelength: 250 nm). The mixture was dissolved in water/acetonitrile (30 mL, 1:1) and for each separation 1 mL of the solution was injected through a *rheodyne* valve on the column. After HPLC purification the *S*-isomer **7a** (82.0 mg, 15 %) and the *R*-isomer **7b** (58.0 mg, 11 %) were isolated as colorless oils.

S-isomer **7a**: IR (film): 3400, 2952, 1710, 1666, 1465, 1394, 1365, 1338, 1279, 1247, 1199, 1091, 998, 917, 860, 837, 766, 694, 619 cm^{-1}; ^{1}H-NMR (500 MHz, DMSO-d_6) δ: -0.06 (*s*, 9 H; $Si(CH_3)_3$), -0.05 (*s*, 9 H; $Si(CH_3)_3$), 0.73-0.84 (*m*, 4 H; 2× $SiCH_2CH_2O$), 1.03 (*s*, 3 H; C(5A)CH_3), 1.81 (*ddd*, *J* = 13.1, 6.0, 2.5 Hz, 1 H; CH_{2a}(2’A)), 1.96-2.08 (*m*, 2 H; CH_{2b}(2’A), CH_{2a}(2’B)), 2.15 (*ddd*, *J* = 13.1, 6.0, 3.3 Hz, 1 H; CH_{2b}(2’B)), 2.32 (*d*, *J* = 13.9 Hz, 1 H; C(5B)CH_{2a}), 2.78 (*d*, *J* = 13.7 Hz, 1 H; C(5B)CH_{2b}), 3.14 (*d*, *J* = 13.3 Hz, 1 H; CH_{2a}(6A)), 3.19 (*d*, *J* = 13.3 Hz, 1 H; CH_{2b}(6A)), 3.38-3.41 (*m*, 3 H; CH_2(5’A), H_2O), 3.43-3.48 (*m*, 2 H; $SiCH_2CH_2O$(A)), 3.50-3.55 (*m*, 2 H; $SiCH_2CH_2O$(B)), 3.56-3.59 (*m*, 2 H; CH_2(5’B)), 3.61-3.64 (*m*, 1 H; C*H*(4’A)), 3.79-3.83 (*m*, 1 H; C*H*(4’B)), 4.11-4.15 (*m*, 1 H; C*H*(3’A)), 4.23-4.27 (*m*, 1 H; C*H*(3’B)), 4.96 (*d*, *J* = 9.6 Hz, 1 H; $OCH_{2a}N$(A)), 5.04 (*d*, *J* = 9.9 Hz, 1 H; $OCH_{2b}N$(A)), 5.15 (*d*, *J* = 9.9 Hz, 1 H; $OCH_{2a}N$(B)), 5.17 (*d*, *J* = 9.9 Hz, 1 H; $OCH_{2b}N$(B)), 6.15-6.22 (*m*, 2 H; 2× C*H*(1’)), 7.84 (*s*, 1 H; C*H*(6B)); ^{13}C-NMR (125 MHz, DMSO-d_6) δ: -1.17 (2C), 17.56, 17.75, 20.00, 31.72, 36.15, 40.11, 41.39, 44.38, 61.42, 62.01, 65.65, 66.51, 69.66, 69.95, 70.57, 70.85, 84.00, 85.30, 86.28, 87.82, 107.64, 138.62, 150.38, 152.35, 162.97, 173.47; MS (MALDI$^+$): 783 (17, *M*+K$^+$), 767 (86, *M*+Na$^+$), 306 (27), 284 (100), 215 (17), 175 (12); HR-MS (ESI$^+$): calc. for $[C_{32}H_{56}N_4O_{12}Si_2+Na]^+$: 767.3331; found: 767.3296.

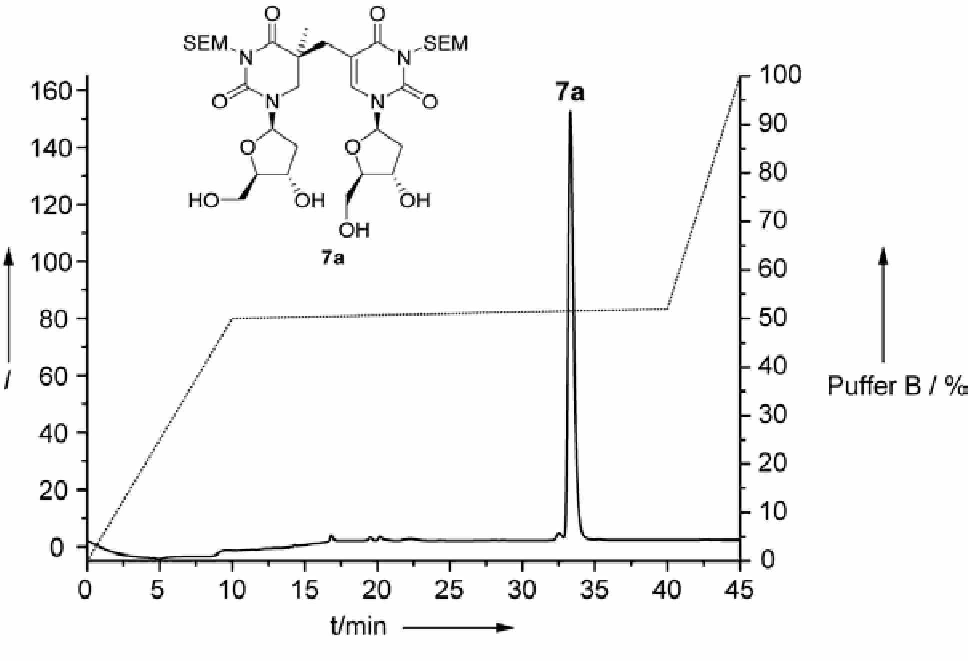
R-isomer **7b**: IR (film): 3442, 2952, 1653, 1465, 1364, 1278, 1247, 1200, 1091, 916, 860, 836, 760, 694, 667 cm^{-1}; ^{1}H-NMR (500 MHz, DMSO-d$_6$) δ: -0.06 (*s*, 9 H; Si(C*H$_3$*)$_3$), -0.04 (*s*, 9 H; Si(C*H$_3$*)$_3$), 0.76-0.85 (*m*, 4 H; 2× SiC*H$_2$*CH$_2$O), 1.02 (*s*, 3 H; C(5A)C*H$_3$*), 1.77-1.84 (*m*, 1 H; C*H$_{2a}$*(2'A)), 1.96-2.04 (*m*, 1 H; C*H$_{2b}$*(2'A)), 2.07-2.14 (*m*, 2 H; C*H$_2$*(2'B)), 2.19 (*d*, *J* = 14.2 Hz, 1 H; C(5B)C*H$_{2a}$*), 2.83 (*d*, *J* = 13.9 Hz, 1 H; C(5B)C*H$_{2b}$*), 3.11 (*d*, *J* = 13.2 Hz, 1 H; C*H$_{2a}$*(6A)), 3.31 (*d*, *J* = 13.1 Hz, 1 H; C*H$_{2b}$*(6A)), 3.41-3.48 (*m*, 4 H; C*H$_2$*(5'A), SiCH$_2$C*H$_2$*O(A)), 3.49-3.61 (*m*, 4 H; C*H$_2$*(5'B), SiCH$_2$C*H$_2$*O(B)), 3.63-3.68 (*m*, 1 H; C*H*(4'A)), 3.77-3.82 (*m*, 1 H; C*H*(4'B)), 4.11-4.16 (*m*, 1 H; C*H*(3'A)), 4.22-4.27 (*m*, 1 H; C*H*(3'B)), 4.75 (*t*, *J* = 5.4 Hz, 1 H; O*H*(5'A)), 4.92 (*d*, *J* = 9.8 Hz, 1 H; OC*H$_{2a}$*N(A)), 4.98 (*t*, *J* = 5.0 Hz, 1 H; O*H*(5'B)), 5.07 (*d*, *J* = 9.9 Hz, 1 H; OC*H$_{2b}$*N(A)), 5.10-5.19 (*m*, 3 H; O*H*(3'A), OC*H$_2$*N(B)), 5.26 (*d*, *J* = 4.1 Hz, 1 H; O*H*(3'B)), 6.17-6.20 (*m*, 2 H; 2× C*H*(1')), 7.73 (*s*, 1 H; C*H*(6B)); ^{13}C-NMR (125 MHz, DMSO-d$_6$) δ: -1.16 (2C), 17.52, 17.81, 19.57, 32.19, 36.13, 41.27, 44.70, 61.54, 62.15, 65.55, 66.51, 69.56, 69.98, 70.63, 71.02, 83.93, 85.14, 86.38, 87.72, 107.86, 138.45, 150.47, 152.12, 162.85, 173.25; MS (MALDI$^+$): 783 (3, *M*+K$^+$), 767 (29, *M*+Na$^+$), 306 (30), 253 (6), 242 (100), 197 (5); HR-MS (ESI$^+$): calc. for $[C_{32}H_{56}N_4O_{12}Si_2+Na]^+$: 767.3331; found: 767.3343.

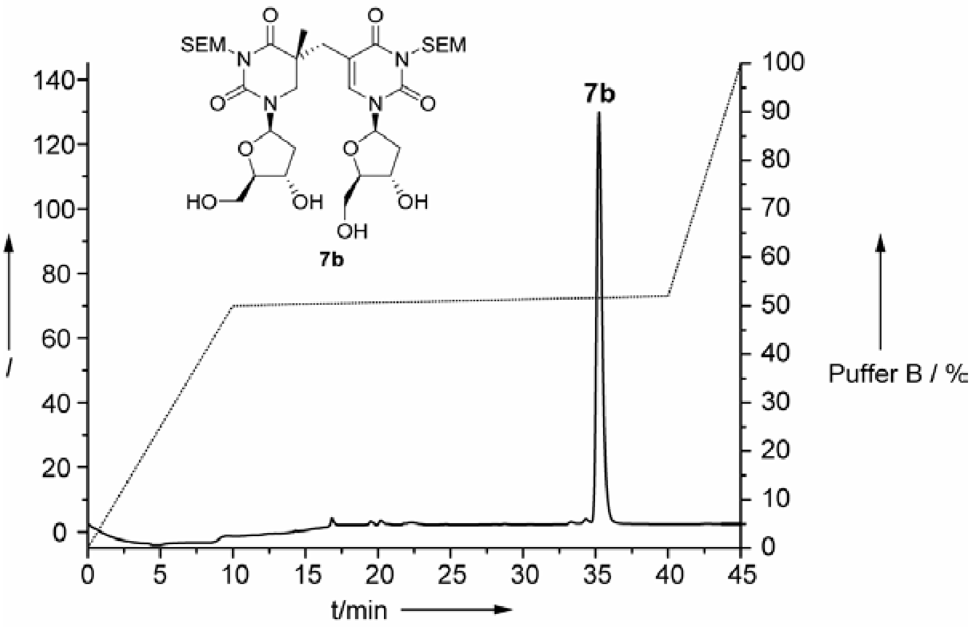
5*R*-(α-thymidyl)-5,6-dihydrothymidine (8b). The *R*-isomer **7b** (59.0 mg, 0.08 mmol) was dissolved in anhydrous CH_2Cl_2 (7 mL) and cooled to 0 °C. A $SnCl_4$ solution (0.80 mL, 1 M in CH_2Cl_2) was added dropwise. The reaction mixture was stirred at 0 °C for 1 h. The reaction was quenched by adding methanolic sodium hydroxide (3 mL, 4 % NaOH). The solvent was removed under reduced pressure. The crude product was suspended in methanol (4 mL), centrifugated and decanted to remove the tin salts. This procedure was repeated twice. The solvent was removed from the collected solutions *in vacuo*. Purification by flash chromatography (silica gel, $CHCl_3$/MeOH 4:1) provided **8b** (27.0 mg, 75 %) as a white solid. mp 155-158 °C; IR (KBr): 3419, 2924, 2854, 1697, 1476, 1389, 1278, 1205, 1091, 1050, 766 cm^{-1}; ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 0.98 (*s*, 3 H; C(5A)CH_3), 1.77 (*ddd*, J = 12.8, 6.2, 2.5 Hz, 1 H; CH_{2a}(2'A)), 1.94-2.01 (*m*, 1 H; CH_{2b}(2'A)), 2.05-2.11 (*m*, 2 H; CH_2(2'B)), 2.25 (*d*, J = 14.2 Hz, 1 H; C(5B)CH_{2a}), 2.73 (*d*, J = 13.3 Hz, 1 H; C(5B)CH_{2b}), 3.05 (*d*, J = 13.1 Hz, 1 H; CH_{2a}(6A)), 3.23 (*d*, J = 13.1 Hz, 1 H; CH_{2b}(6A)), 3.41 (*t*, J = 5.3 Hz, 2 H; CH_2(5'A)), 3.51-3.57 (*m*, 2 H; CH_2(5'B)), 3.59-3.63 (*m*, 1 H; C*H*(4'A)), 3.74-3.79 (*m*, 1 H; C*H*(4'B)), 4.07-4.12 (*m*, 1 H; C*H*(3'A)), 4.21-4.27 (*m*, 1 H; C*H*(3'B)), 4.81 (*t*, J = 5.5 Hz, 1 H; O*H*(5'A)), 5.02 (*t*, J = 5.3 Hz, 1 H; O*H*(5'B)), 5.30 (*d*, J = 4.1 Hz, 1 H; O*H*(3'A)), 5.30 (*d*, J = 4.1 Hz, 1 H; O*H*(3'B)), 6.08-6.17 (*m*, 2 H; 2× C*H*(1')), 7.65 (*s*, 1 H; C*H*(6B)), 10.05 (*s*, 1 H; N*H*(A)), 11.22 (*s*, 1 H; N*H*(B)); ^{13}C-NMR (125 MHz, DMSO-d_6) δ: 19.49, 31.12, 36.03, 41.16, 46.03, 61.65, 62.16, 70.79, 70.99, 83.11, 84.25, 86.15, 87.60, 108.80, 139.08, 150.42, 152.42, 163.67, 174.19; MS (MALDI$^+$): 507 (100, M+Na$^+$), 444 (5), 412 (5), 390 (6), 314 (10), 306 (46), 288 (29), 284 (35), 268 (15), 254 (12), 165 (13); HR-MS (ESI$^+$): calc. for $[C_{20}H_{28}N_4O_{10}+Na]^+$: 507.1703; found: 507.1694; calc. for $[C_{20}H_{28}N_4O_{10}+K]^+$: 523.1443; found: 523.1434.

5*S*-(α-thymidyl)-5,6-dihydrothymidine (8a). SEM-deprotection was carried out as described above for **8b**. The *S*-isomer **8a** (27.0 mg, 55 %) was isolated as a white solid. mp 155-158 °C; IR (KBr): 3393, 2918, 2253, 1693, 1474, 1389, 1278, 1232, 1093, 1051, 1026, 1002, 827, 766, 574 cm^{-1}; ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 0.99 (*s*, 3 H; C(5A)CH_3), 1.77 (*ddd*, J = 13.2, 6.2, 2.8 Hz, 1 H; CH_{2a}(2'A)), 1.94-2.06 (*m*, 2 H; CH_{2b}(2'A), CH_{2a}(2'B)), 2.10 (*ddd*, J = 13.2, 5.9, 3.1 Hz, 1 H; CH_{2b}(2'B)), 2.30 (*d*, J = 13.8 Hz, 1 H; C(5B)CH_{2a}), 2.72

(*d*, J = 14.0 Hz, 1 H; C(5B)CH_{2b}), 3.05 (*d*, J = 12.9 Hz, 1 H; CH_{2a}(6A)), 3.17 (*d*, J = 13.0 Hz, 1 H; CH_{2b}(6A)), 3.36 (*s*, 13 H; CH_2(5’A), H_2O), 3.51-3.59 (*m*, 3 H; CH_2(5’B), C*H*(4’A)), 3.75-3.79 (*m*, 1 H; C*H*(4’B)), 4.08-4.13 (*m*, 1 H; C*H*(3’A)), 4.23-4.28 (*m*, 1 H; C*H*(3’B)), 4.77 (*t*, J = 5.5 Hz, 1 H; O*H*(5’A)), 5.14 (*t*, J = 5.1 Hz, 1 H; O*H*(5’B)), 5.19 (*d*, J = 4.2 Hz, 1 H; O*H*(3’A)), 5.34 (*d*, J = 4.2 Hz, 1 H; O*H*(3’B)), 6.09 (*dd*, J = 7.9, 6.2 Hz, 1 H; C*H*(1’A)), 6.13 (*t*, J = 7.2 Hz, 1 H; C*H*(1’B)), 7.72 (*s*, 1 H; C*H*(6B)), 10.11 (*s*, 1 H; N*H*(A)), 11.23 (*s*, 1 H; N*H*(B)); ^{13}C-NMR (125 MHz, DMSO-d$_6$) δ: 20.16, 30.75, 35.85, 41.11, 45.52, 61.50, 62.03, 70.73, 70.79, 83.01, 84.18, 85.98, 87.61, 108.71, 139.11, 150.37, 152.53, 163.75, 174.43; MS (ESI$^+$): 523 (57, *M*+K$^+$), 407 (16), 336 (12), 303 (100), 257 (17), 122 (45); HR-MS (ESI$^+$): calc. for [$C_{20}H_{28}N_4O_{10}$+K]$^+$: 523.1443; found: 523.1450.

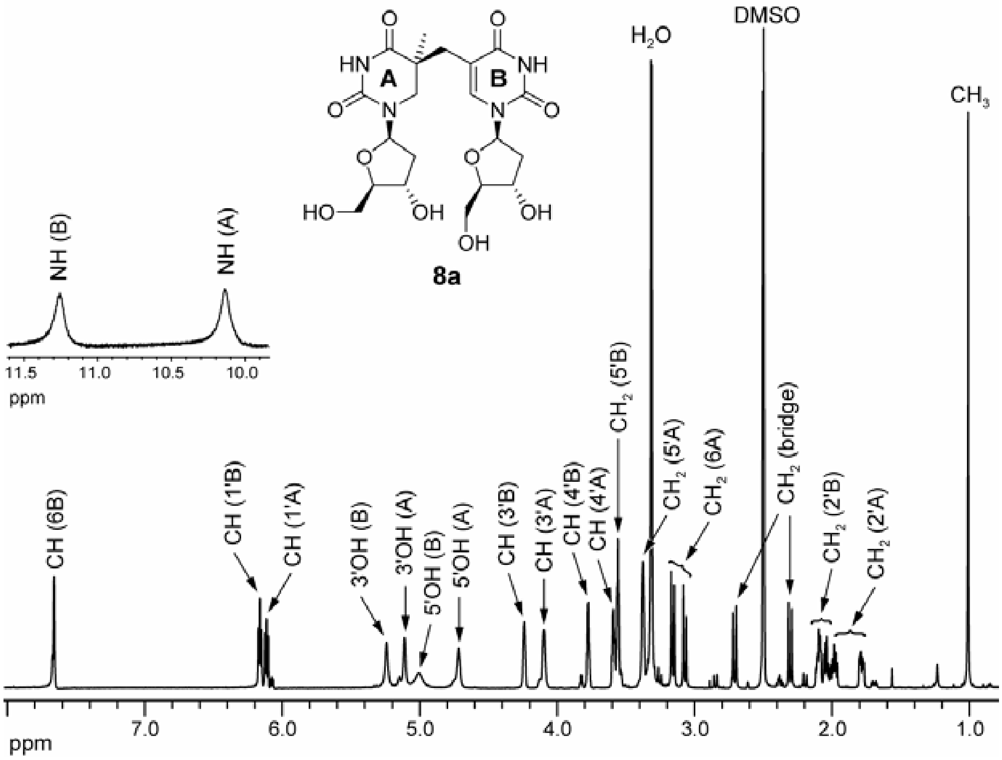
2) HPLC-CHROMATOGRAMS FOR THE SEPARATED DIASTEREOMERS **7a** AND **7b**

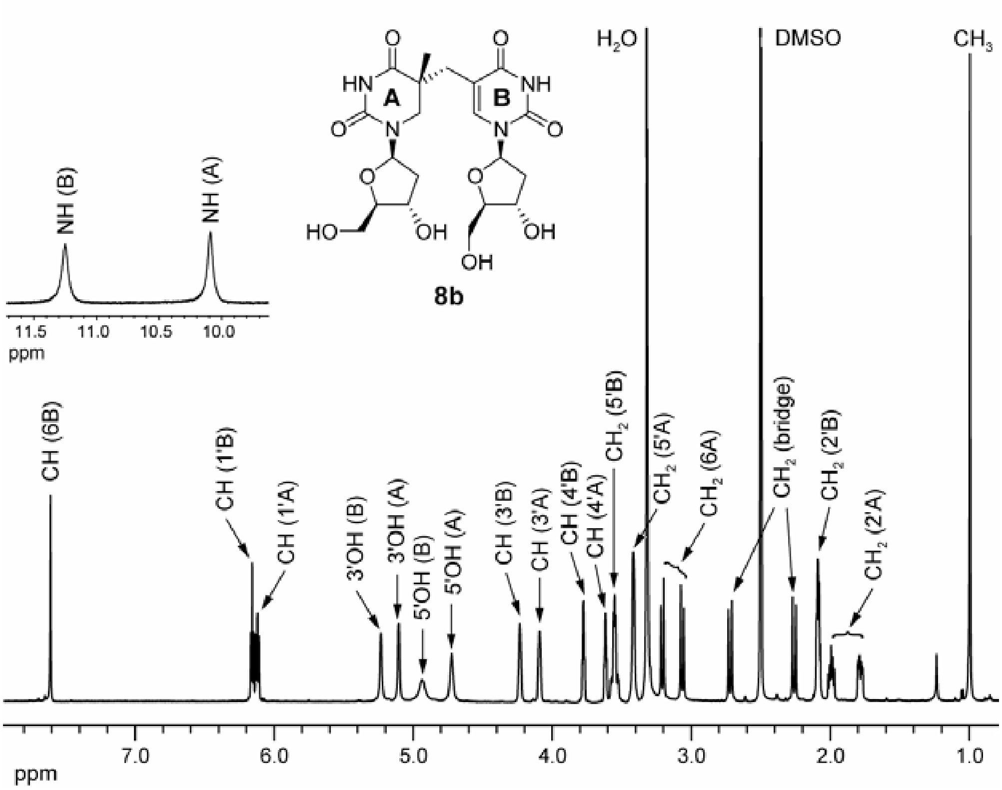




Analytical HPLC-chromatograms of the separated diastereomers **7a** and **7b**. *rp*-HPLC: 0.1 M NEt_3/AcOH in water (A), 0.1 M NEt_3/AcOH in 80 % acetonitrile (B); gradient: 0 → 50 % B in 10 min, 50 → 52 % B in 30 min, 52 → 100 % B in 5 min; column: 120 A, 3 µm, C8; flow rate: 0.7 mL/min; detection: 250 nm; retention times: R_f (**7a**) 33.3 min, R_f (**7b**) 35.3 min.

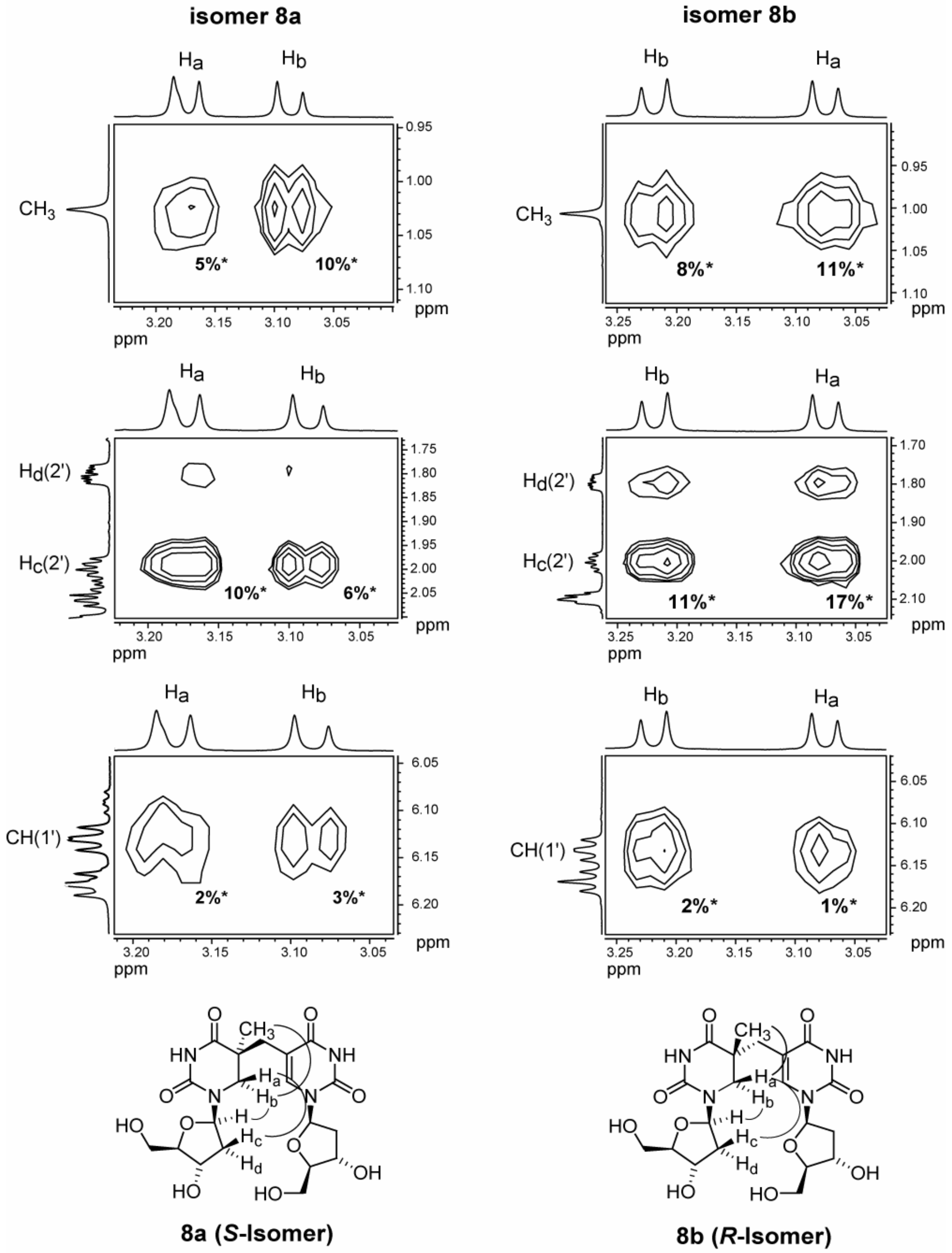
3) ^{1}H-NMR SPECTRA FOR THE SEPARATED DIASTEREOMERS **8a** AND **8b**





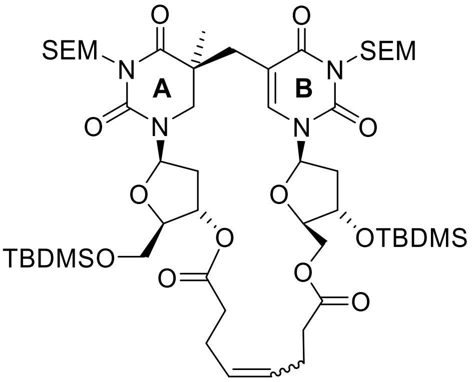
^{1}H-NMR spectrums of the diastereomers **8a** and **8b** in DMSO-d_6 (600 MHz).

4) NOE DATA FOR THE ISOMERS **8a/b**

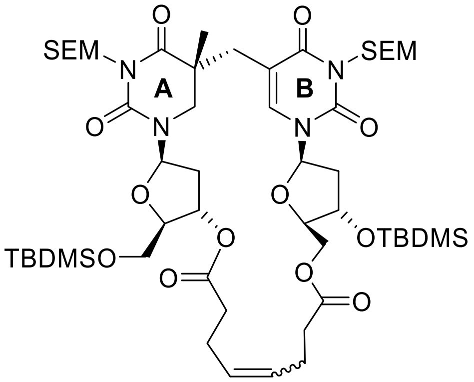


NOESY crosspeaks for isomers 8a and 8b in DMSO-d_6 (600 MHz). Quantification in comparison to the crosspeak of the CH_2-bridge (=100 %) between the bases.

5) ANALYTICAL DATA OF THE BRIDGED SP-ISOMERS **9a/b**



9a



9b

***N*^{3}(A/B)-Di-trimethylsilylethoxymethyl-5'(A),3'(B)-*O*-di-*tert*-butyldimethylsilyl-3'(A),5'(B)-*O*-oct-4-endiyl-5*S*-(α-thymidyl)-5,6-dihydrothymidine (9a).**

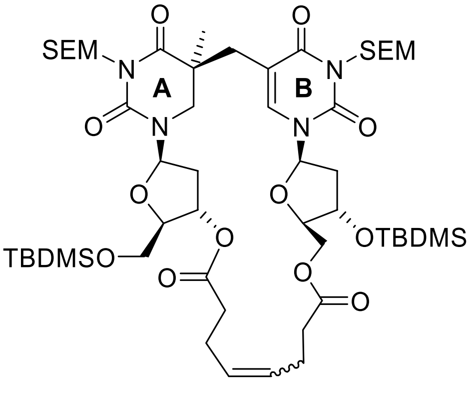
IR (Film): 2927, 2854, 1737, 1667, 1461, 1360, 1249, 1089, 860, 835, 778 cm^{-1}; ^{1}H-NMR (600 MHz, CDCl$_3$) δ: -0.01 (*s*, 9 H; Si(C*H*$_3$)$_3$), 0.00 (*s*, 9 H; Si(C*H*$_3$)$_3$), 0.03 (*s*, 3 H; SiC*H*$_3$), 0.04 (*s*, 3 H; SiC*H*$_3$), 0.10 (*s*, 3 H; SiC*H*$_3$), 0.11 (*s*, 3 H; SiC*H*$_3$), 0.86-0.93 (*m*, 20 H; 2× C(C*H*$_3$)$_3$, SiC*H*$_2$CH$_2$O), 0.96-0.99 (*m*, 2 H; SiC*H*$_2$CH$_2$O), 1.24 (*s*, 3 H; C(5A)C*H*$_3$), 1.85-1.90 (*m*, 2 H; C*H*$_{2a}$(2'A), C*H*$_{2a}$(2'B)), 2.12-2.18 (*m*, 1 H; C*H*$_{2b}$(2'A)), 2.19-2.24 (*m*, 1 H; 1× CH=CHC*H*$_2$CH$_2$), 2.27 (*d*, *J* = 13.8 Hz, 1 H; C(5B)C*H*$_{2a}$), 2.35-2.49 (*m*, 8 H; 2× CH=CHC*H*$_2$C*H*$_2$, C*H*$_{2b}$(2'B)), 2.68 (*d*, *J* = 13.8 Hz, 1 H; C(5B)C*H*$_{2b}$), 3.24 (*d*, *J* = 13.8 Hz, 1 H; C*H*$_{2a}$(6A)), 3.33 (*d*, *J* = 13.8 Hz, 1 H; C*H*$_{2b}$(6A)), 3.57 (*t*, *J* = 8.4 Hz, 2 H; SiCH$_2$C*H*$_2$O(A)), 3.67 (*t*, *J* = 8.4 Hz, 2 H; SiCH$_2$C*H*$_2$O(B)), 3.74 (*dd*, *J* = 11.4, 2.4 Hz, 1 H; C*H*$_{2a}$(5'A)), 3.77 (*dd*, *J* = 11.4, 2.4 Hz, 1 H; C*H*$_{2b}$(5'A)), 4.03-4.06 (*m*, 1 H; C*H*(4'B)), 4.09-4.12 (*m*, 1 H; C*H*(4'A)), 4.18-4.21 (*m*, 2 H; C*H*$_{2a}$(5'B), C*H*(3'B)), 4.40 (*dd*, *J* = 12.6, 3.0 Hz, 1 H; C*H*$_{2b}$(5'B)), 5.14 (*d*, *J* = 9.6 Hz, 1 H; OC*H*$_{2a}$N(A)), 5.18-5.21 (*m*, 2 H; OC*H*$_{2b}$N(A), C*H*(3'A)), 5.36 (*d*, *J* = 9.6 Hz, 1 H; OC*H*$_{2a}$N(B)), 5.41 (*d*, *J* = 9.6 Hz, 1 H; OC*H*$_{2b}$N(B)), 5.44-5.50 (*m*, 1 H; C*H*=CH), 5.52-5.57 (*m*, 1 H; C*H*=CH), 6.07 (*t*, *J* = 6.0 Hz, 1 H; C*H*(1'B)), 6.37 (*dd*, *J* = 10.2, 4.8 Hz, 1 H; C*H*(1'A)), 7.09 (*s*, 1 H; C*H*(6B)); ^{13}C-NMR (150 MHz, MeOH-d_4) δ: -5.21, -5.14, -4.77, -4.59, -1.25 (2C), 18.84, 18.91, 19.04, 19.31, 20.99, 26.25, 26.56, 29.13, 29.65, 33.56, 34.38, 34.66, 36.34, 42.64, 44.85, 47.06, 64.30, 64.90, 67.91, 68.50, 71.12, 71.39, 72.86, 76.65, 83.80, 85.48, 86.97, 87.45, 109.81, 130.79, 131.04, 138.39, 151.94, 154.43, 164.87, 174.14, 174.43, 174.55; MS (FAB$^+$): 1131 (4, *M*+Na$^+$), 154 (19), 136 (27), 89 (26), 81 (29), 73 (100); HR-MS (ESI$^+$): calc. for [$C_{52}H_{92}N_4O_{14}Si_4$+Na]$^+$: 1131.5585; found: 1131.5577.

N^3(A/B)-Di-trimethylsilylethoxymethyl-5'(A),3'(B)-*O*-di-*tert*-butyldimethylsilyl-3'(A),5'(B)-*O*-oct-4-endiyl-5*R*-(α-thymidyl)-5,6-dihydrothymidine (9b).

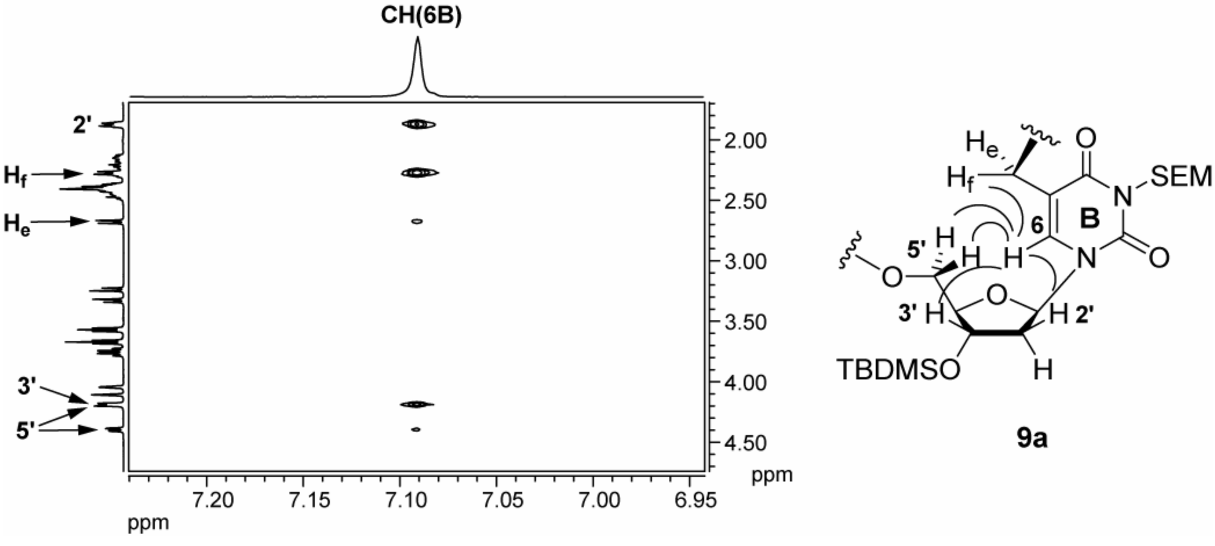
IR (Film): 2953, 2929, 2857, 1732, 1682, 1461, 1361, 1248, 1080, 936, 860, 835, 778 cm^{-1}; ^{1}H-NMR (600 MHz, MeOH-d_4) δ: 0.02 (*s*, 9 H; Si(C*H₃*)₃), 0.03 (*s*, 9 H; Si(C*H₃*)₃), 0.14 (*s*, 3 H; SiC*H₃*), 0.15 (*s*, 3 H; SiC*H₃*), 0.17 (*s*, 6 H; Si(C*H₃*)₂), 0.87-0.91 (*m*, 4 H; 2× SiC*H₂*CH₂O), 0.95 (*s*, 18 H; 2× C(C*H₃*)₃), 1.34 (*s*, 3 H; C(5A)C*H₃*), 2.09-2.14 (*m*, 2 H; C*H₂ₐ*(2'A), C*H₂ₐ*(2'B)), 2.18-2.23 (*m*, 1 H; C*H₂b*(2'A)), 2.28-2.41 (*m*, 5 H; C*H₂b*(2'B), 2× CH=CHC*H₂*CH₂), 2.43-2.50 (*m*, 4 H; 2× CH=CHCH₂C*H₂*), 2.72 (*d*, *J* = 13.8 Hz, 1 H; C(5B)C*H₂ₐ*), 2.78 (*d*, *J* = 13.8 Hz, 1 H; C(5B)C*H₂b*), 3.19 (*d*, *J* = 12.6 Hz, 1 H; C*H₂ₐ*(6A)), 3.56-3.60 (*m*, 2 H; SiCH₂C*H₂*O(A)), 3.64-3.73 (*m*, 3 H; C*H₂b*(6A), SiCH₂C*H₂*O(B)), 3.93-3.98 (*m*, 2 H; C*H₂*(5'A)), 4.01-4.03 (*m*, 1 H; C*H*(4'A)), 4.04-4.07 (*m*, 1 H; C*H*(4'B)), 4.12 (*dd*, *J* = 12.0, 6.0 Hz, 1 H; C*H₂ₐ*(5'B)), 4.28 (*dd*, *J* = 12.0, 5.4 Hz, 1 H; C*H₂b*(5'B)), 4.40-4.42 (*m*, 1 H; C*H*(3'B)), 5.03 (*d*, *J* = 9.6 Hz, 1 H; OC*H₂ₐ*N(A)), 5.15 (*d*, *J* = 9.0 Hz, 1 H; OC*H₂b*N(A)), 5.19-5.21 (*m*, 1 H; C*H*(3'A)), 5.36 (*s*, 2 H; OC*H₂*N(B)), 5.50-5.60 (*m*, 2 H; C*H*=C*H*), 6.25 (*dd*, *J* = 7.8, 6.0 Hz, 1 H; C*H*(1'B)), 6.37 (*dd*, *J* = 10.2, 4.8 Hz, 1 H; C*H*(1'A)), 7.44 (*s*, 1 H; C*H*(6B)); ^{13}C-NMR (100 MHz, MeOH-d_4) δ: -5.21, -5.18, -4.58, -4.43, -1.24, -1.22, 18.89, 19.01, 19.12, 19.32, 22.27, 26.30, 26.60, 28.58, 28.72, 34.30, 34.35, 34.68, 34.82, 41.17, 43.33, 46.77, 64.68, 65.15, 67.90, 68.56, 71.16, 71.43, 73.98, 77.49, 86.22, 86.39 (2C), 87.25, 111.05, 130.66, 131.31, 138.69, 152.17, 154.37, 164.63, 174.22, 174.35, 174.58; MS (FAB$^+$): 1131 (5, *M*+Na$^+$), 154 (19), 136 (28), 89 (30), 81 (30), 73 (100); HR-MS (ESI$^+$): calc. for $[C_{52}H_{92}N_4O_{14}Si_4+Na]^+$: 1131.5585; found: 1131.5568.

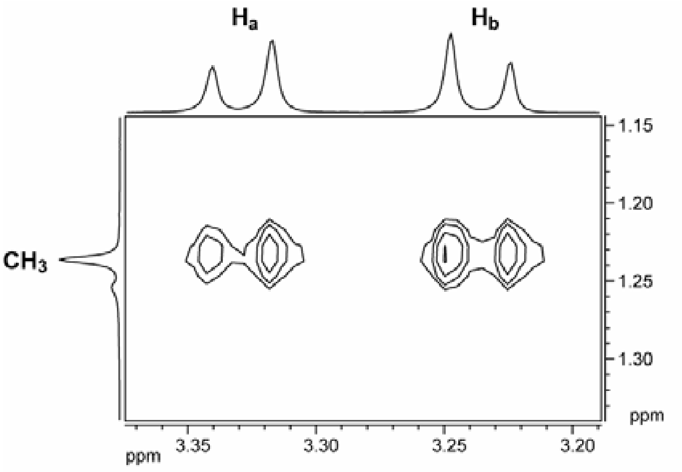
The synthesis of compounds **9a/b** will be published elsewhere.

6) NOE DATA FOR THE ISOMER **9a**



9a

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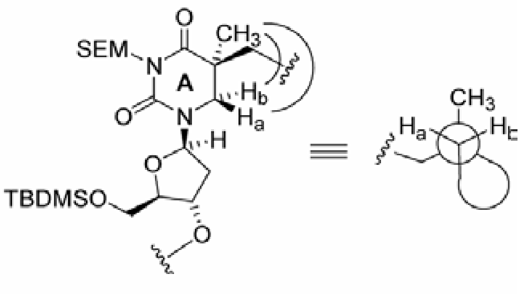
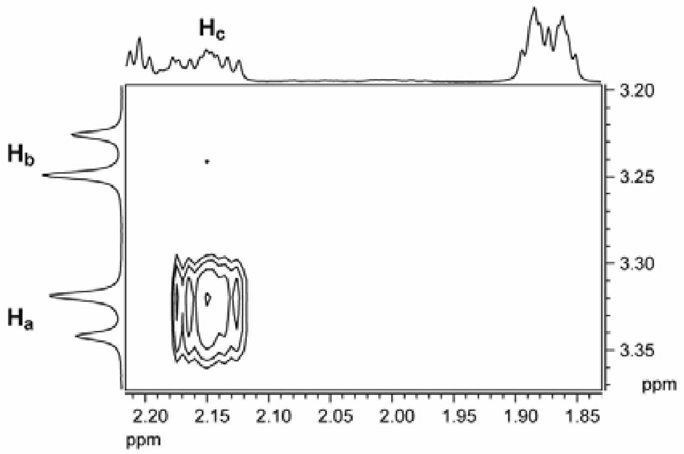
ppm
3.35
3.30
3.25
3.20
ppm


SEM
O
CH_3
N
A
H_b
H_a
H
O
TBDMSO
O
H_a
H_b
CH_3

9a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H_c
H_b
H_a
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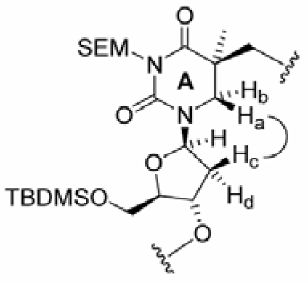
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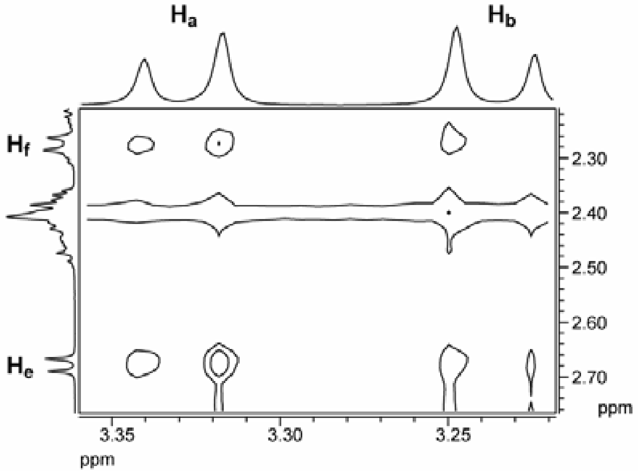
O
N
A
H_b
H_a
H
H_c
H_d
O
TBDMSO
O

9a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H_b
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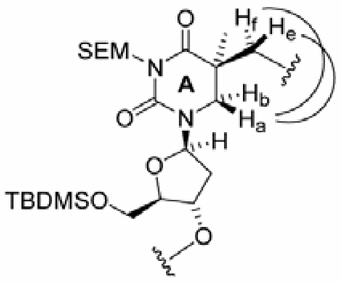
ppm


SEM
O
H_f
H_e
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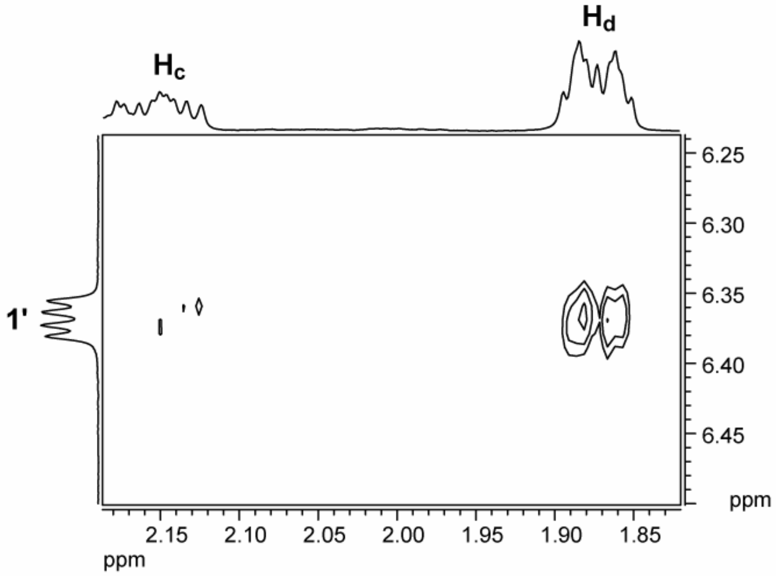
A
H_b
H_a
H
O
TBDMSO
O

9a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ppm
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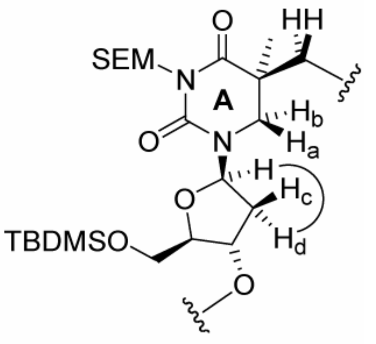
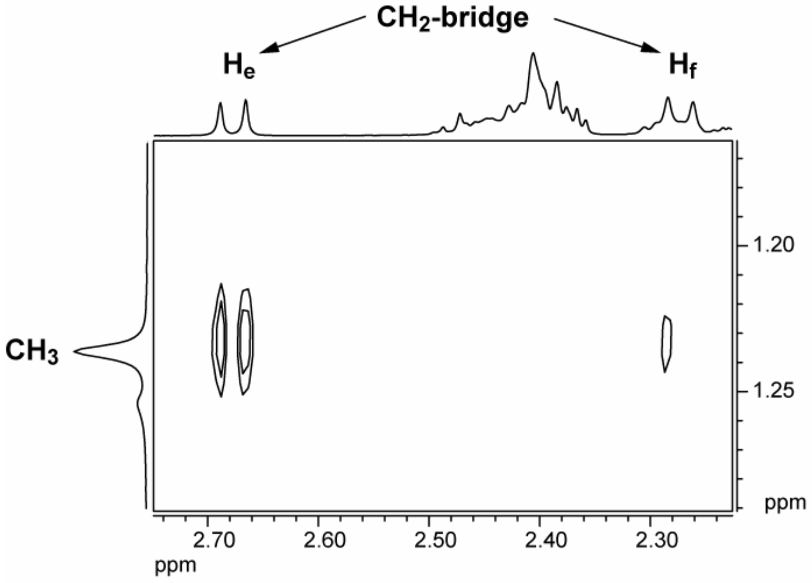

SEM
N
O
HH
A
Hb
Ha
N
O
H
Hc
Hd
TBDMSO
O

9a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Hf
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ppm
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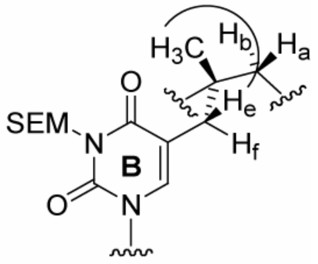
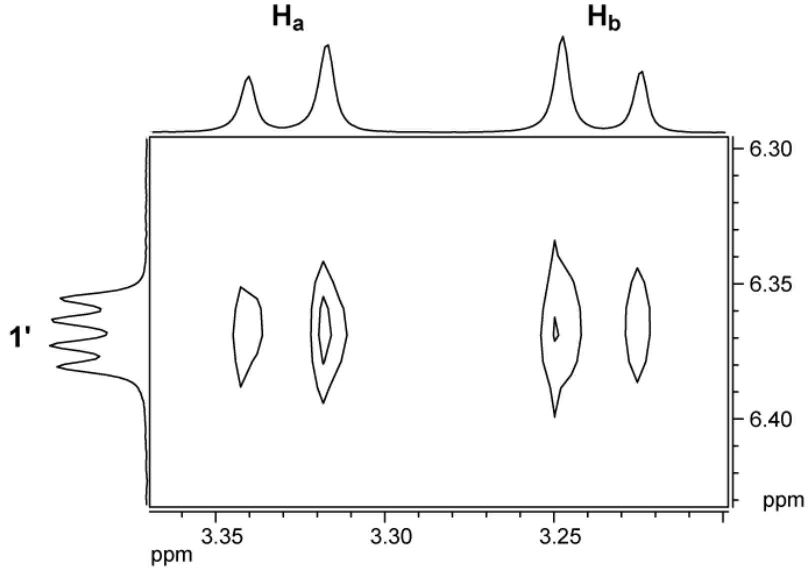
2.50
2.40
2.30
ppm


H3C
Hb
Ha
He
Hf
SEM
N
O
B
N
O

9a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Hb
1'
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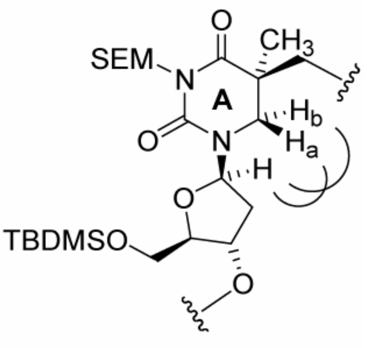
6.35
6.40
ppm
3.35
3.30
3.25
ppm


SEM
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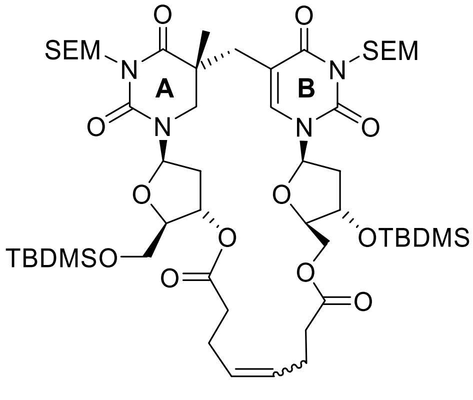
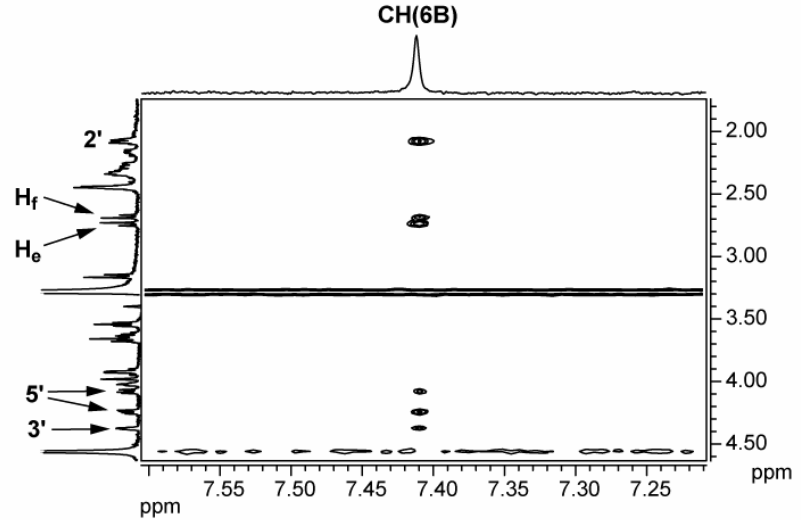
CH3
A
Hb
Ha
N
O
H
TBDMSO
O

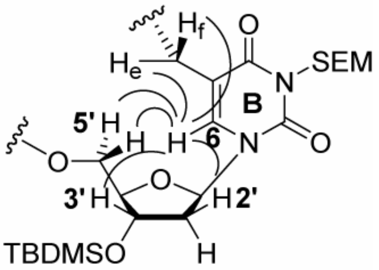
9a

7) NOE DATA FOR THE ISOMER **9b**

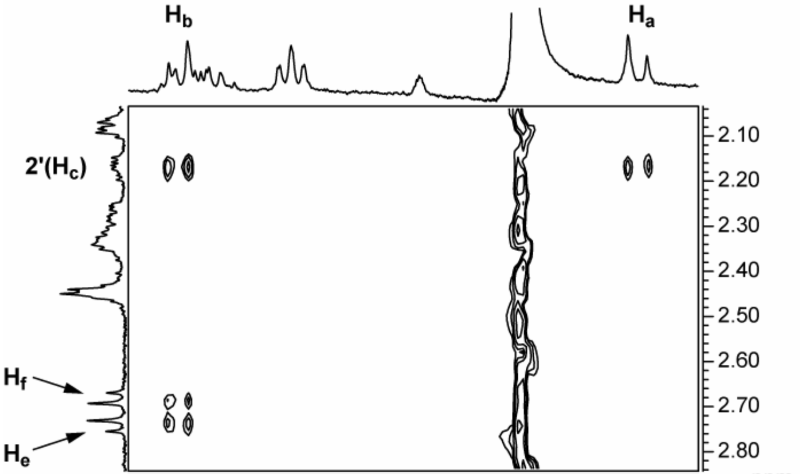


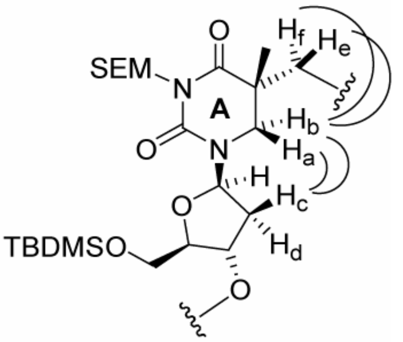
9b



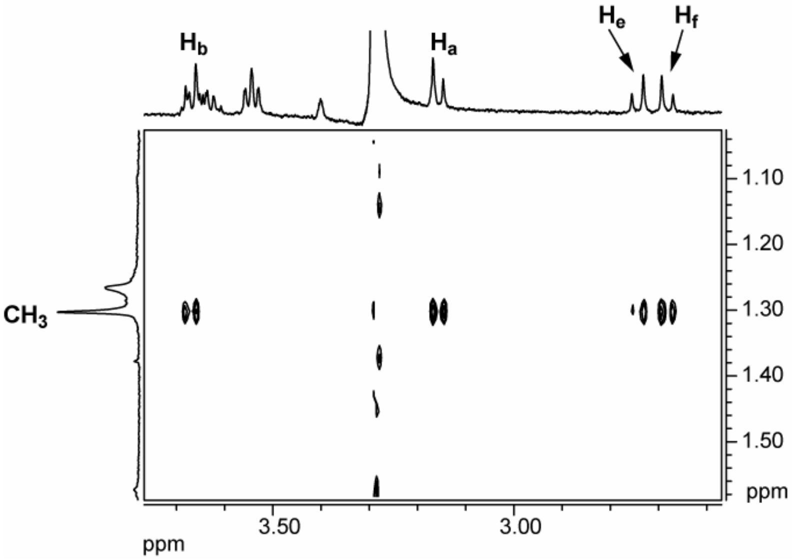


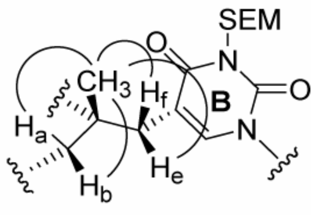
9b





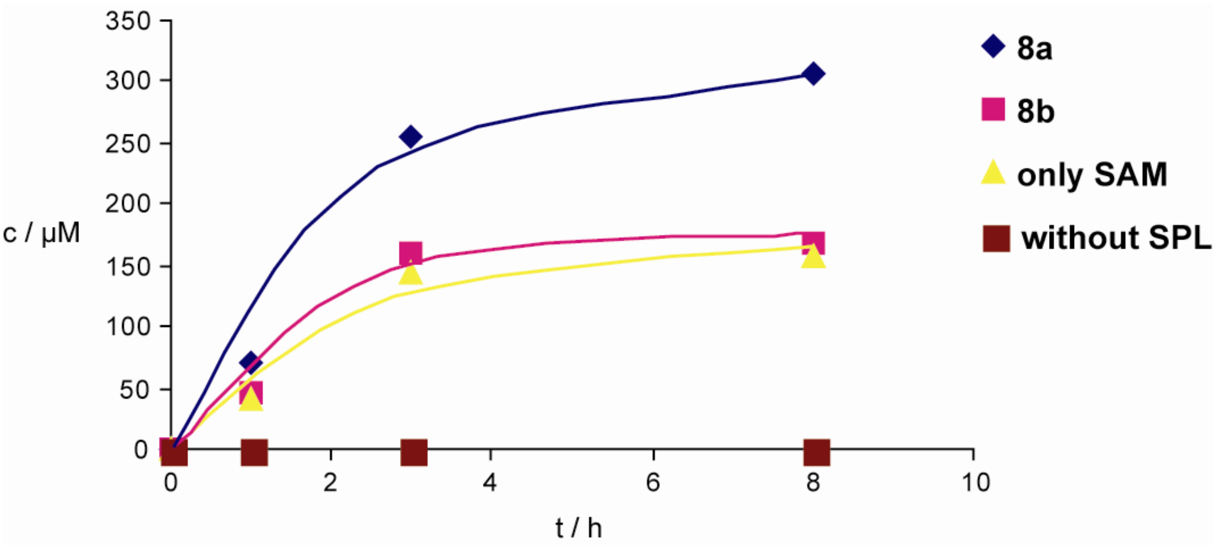
9b





9b

8) 5'-dAdoH PRODUCTION WITH SUBSTRATES **8a/b**



In the presence of the 5-*S* compound **8a** a clear increase of 5'-dAdoH formation is observed.