Supporting Information

Analogues of Locked Nucleic Acid with three carbon 2´,4´-linkages; Synthesis by ring-closing metathesis and influence on nucleic acid duplex stability and structure

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Experimental Section

General. Reactions were performed under an atmosphere of nitrogen when anhydrous solvents were used. Column chromatography was carried out on glass columns using silica gel 60 (0.040 – 0.063 mm). NMR spectra were recorded at 300 MHz for ^{1}H NMR, 75 MHz for ^{13}C NMR and 121.5 MHz for ^{31}P NMR. The δ values are in ppm relative to tetramethylsilane as internal standard (for ^{1}H and ^{13}C NMR) and relative to 85% H_3PO_3 as external standard (for ^{31}P NMR). Assignments of NMR spectra are based on 2D spectra and follow standard carbohydrate and nucleoside style; *i.e.*

the carbon atom next to a nucleobase is assigned C-1′, etc. Compound names given in this section for the bicyclic compounds are given according to the von Baeyer nomenclature. HRMALDI and ESI mass spectra were recorded in positive-ion mode except for the oligonucleotides where these were recorded in negative-ion mode.

Synthesis of 2´-*O*-phenoxythiocarbonyl-3´,5´-di-*O*-(*tert*-butyldimethylsilyl)uridine (11). To a stirred solution of **10** (6.401 g, 13.5 mmol) in anhydrous CH_3CN (100 mL) were added DMAP (7.719 g, 63.2mmol) and a solution of PhOC(S)Cl (2.0 mL, 14.4 mmol) in CH_3CN (20 mL). The reaction mixture was stirred for 17 hours and more PhOC(S)Cl (0.15 mL, 1.08 mmol) was added. After additional 2 hours the reaction was quenched with H_2O (100 mL) and extracted with EtOAc (2 × 200 mL). The combined extracts were washed with a saturated aqueous solution of $NaHCO_3$ (80 mL) and brine (80 mL) and then dried ($MgSO_4$). The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (EtOAc – petroleum ether 1:4 v/v) to give the product **11** (6.488 g, 79%) as a colourless oil: R_f 0.6 (EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (s, 1H, NH), 7.84 (d, *J* = 8.2 Hz, H-6), 7.40 (m, 2H, Ph), 7.26 (m, 1H, Ph), 7.10 (m, 2H, Ph), 6.42 (d, 1H, *J* = 6.3 Hz, H-1´), 5.74 (dd, 1H, *J* = 2.2 Hz, *J* = 8.2 Hz, H-5), 5.66 (dd, 1H, *J* = 5.2 Hz, *J* = 6.3 Hz, H-2´), 4.61 (dd, 1H, *J* = 2.5 Hz, *J* = 5.2 Hz, H-3´), 4.15 (m, 1H, H-4´), 3.94 (dd, 1H, *J* = 2.0 Hz, *J* = 11.5 Hz, H-5´), 3.77 (dd, 1H, *J* = 1.6 Hz, *J* = 11.5 Hz, H-5´), 0,95 (s, 9H, $SiC(CH_3)_3$), 0.94 (s, 9H, $SiC(CH_3)_3$), 0,15 (s, 3H, $SiCH_3$), 0.14 (s, 3H, $SiCH_3$), 0.13 (s, 3H, $SiCH_3$), 0.12 (s, 3H, $SiCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.3 (CS), 162.8 (C-4), 153.4 (Ph), 150.1 (C-2), 140.0 (C-6), 129.5 (Ph), 126.7 (Ph), 121.7 (Ph), 103.0 (C-5), 86.8 (C-4´), 85.6 (C-1´), 82.9 (C-2´), 70.4 (C-3´), 63.0 (C-5´), 26.0 ($C(\mathit{C}H_3)_3$), 25.7($C(\mathit{C}H_3)_3$), 18.4 ($\mathit{C}(CH_3)_3$), 18.1 ($\mathit{C}(CH_3)_3$), −4.7 (CH_3Si), −4.9 (CH_3Si), −5.4 (CH_3Si), −5.6 (CH_3Si); HRMALDI MS *m/z* (631.2274 $[M + Na]^+$, $C_{28}H_{44}O_7N_2Si_2S\text{-}Na^+$ calcd 631.2300).

Synthesis of 2´-deoxy-2´-*C*-allyl-3´,5´-di-*O*-(*tert*-butyldimethylsilyl)uridine (12). To a stirred solution of **11** (2.538 g, 4.17 mmol) in anhydrous toluene (100 mL) was added allyltributyltin (6.5 mL, 21.0 mmol). N_2 was continuously bobbled through the reaction mixture and after 45 min, a suspension of AIBN (0.142 g, 0.86 mmol) in anhydrous toluene (5 mL) was added slowly. The reaction mixture was stirred at reflux for 3 hours, and then the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc - petroleum ether 1:4 v/v) to give the product **12** (1.341 g, 65%) as a colourless oil: R_f 0.4 (EtOAc - petroleum ether 1:1); (Found: C, 57.98; H, 9.17; N, 5.46. $C_{24}H_{44}O_5N_2Si_2$ requires C, 58.02; H, 8.93; N, 5.64%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (s, 1H, NH), 7.81 (d, 1H, *J* = 8.4 Hz, H-6), 6.09 (d, 1H, *J* = 8.4 Hz, H-1´), 5.71-5.61 (m, 2H, H-5, C*H*=CH_2), 5.08-4.97 (m, 2H, CH=CH_2), 4.29 (d, 1H, *J* = 5.3 Hz, H-3´), 3.98 (m, 1H, H-4´), 3.84 (dd, 1H, *J* = 2.6 Hz, *J* = 11.4 Hz, H-5´), 3.74 (dd, 1H, *J* = 2.0 Hz, *J* = 11.4 Hz, H-5´), 2.43 (m, 1H, CH_2CH=CH_2), 2.28-2.05 (m, 2H, H-2´, CH_2CH=CH_2), 0,93 (s, 9H, $SiC(CH_3)_3$), 0.92 (s, 9H, $SiC(CH_3)_3$), 0.11 (s, 6H, $SiCH_3$), 0.08 (s, 3H, $SiCH_3$), 0.07 (s, 3H, $SiCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.1 (C-4), 150.5 (C-2), 140.3 (C-6), 135.2 (*C*H=CH_2), 116.5 (CH=*C*H_2), 102.6 (C-5), 88.3, 87.4 (C-1´, C-4´), 73.9 (C-3´), 63.7 (C-5´), 49.6 (C-2´), 28.3 (*C*H_2CH=CH_2), 25.8 (C(*C*H_3)$_3$), 25.7(C(*C*H_3)$_3$), 18.3 (*C*(CH_3)$_3$), 18.0 (*C*(CH_3)$_3$), −4.4 (CH_3Si), −4.9 (CH_3Si), −5.6 (CH_3Si), −5.6 (CH_3Si); HRESI MS *m/z* (519.2659 $[M + Na]^+$, $C_{24}H_{44}O_5N_2Si_2$-Na^+ calcd 519.2681).

Reference

Tronchet, J. M. J.; Grand, E.; Zsely, M.; Giovannini, R.; Geoffroy, M. *Carbohydrate Lett.* **1998**, *3*, 161-168.