Supplementary Material for Chemical Communications

Supplementary information

Photochemical DNA end capping via N^3-methyl-5-cyanovinyl-2'-deoxyuridine

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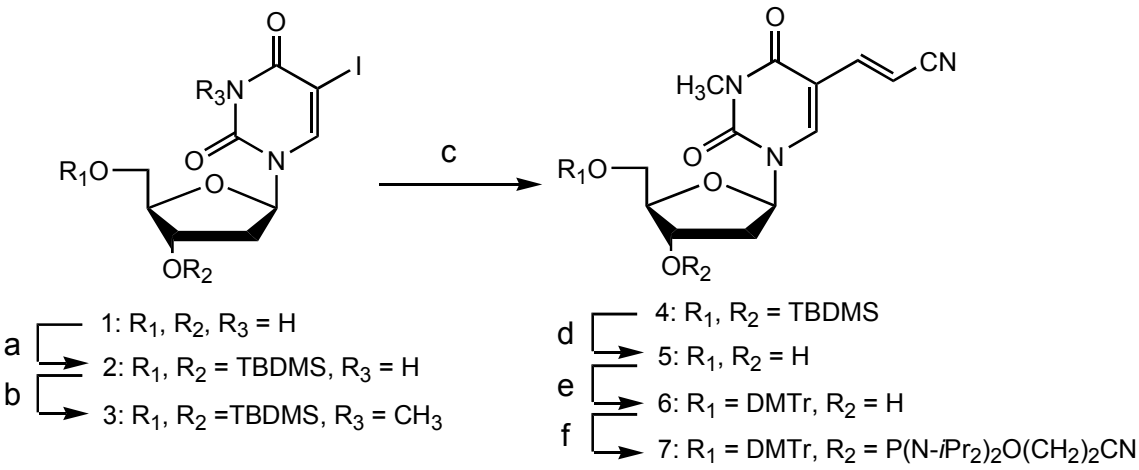
Scheme S1



3',5'-Di-O-*tert*-butyldimethylsilyl-5-iodo-2'-deoxyuridine (2).

To a solution of 5-iododeoxyuridine (**1**) (2.00 g, 5.65 mmol) and *tert*-butyldimethylsilyl chloride (4.12g, 27.3 mmol) in dry pyridine (25 mL) was added a solution of imidazole (1.86 g, 27.3 mmol) in dry pyridine and the reaction mixture was stirred for 18 h at room temperature. The reaction mixture was monitored by TLC (hexane/EtOAc, 4:1), which showed the absence of starting material. After the reaction mixture was evaporated and extracted with EtOAc (100 mL x 2) and water (100 mL). The organic layer was dried with Na_2SO_4 and evaporated. The residue was chromatographed on a silica gel using hexane/EtOAc (4:1, v/v) as eluent to give **2** (3.22 g, 95%) as a white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.04-0.14 (m, 12H, CH_3Si x 4), 0.87 (s, 9H, t-BuSi), 0.92 (s, 9H, t-BuSi), 1.90 (m, 1H, H-2'β), 2.22 (m, 1H, H-2'α), 3.67 (dd, J = 11.4, 2.4 Hz, 1H, H-5'), 3.80 (dd, J = 11.4, 2.4 Hz, 1H, H-5'), 3.89-3.91 (m, 1H, H-4'), 4.30-4.32 (m, 1H, H-3'), 6.18 (dd, J = 8.0, 5.6 Hz, 1H, H-1'), 8.01 (s, 1H, H-6), 8.21 (bs, 1H, NH).

3',5'-Di-O-*tert*-butyldimethylsilyl-N^3-methyl-5-iodo-2'-deoxyuridine (3).

3',5'-Di-O-*tert*-butyldimethylsilyl-5-iodo-2'-deoxyuridine (**2**) (120 mg, 0.21 mmol), potassium carbonate (284 mg, 0.24 mmol) and 18-crown-6 (5.0 mg, 37 μmol) was dissolved in DMF (10 mL). Dimethylcarbonate (40 μL) was added and the mixture was heated to 90 °C for 4 h. Solvent was evaporated and the residue was partitioned between EtOAc and water. Organic phase was drying with Na_2SO_4, then evaporated and applied to a column of silica. Evaporation of appropriate fractions gave **3** as a white solid with quantum yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.06-0.15 (m, 12H, CH_3Si x 4), 0.87 (s, 9H, t-BuSi), 0.92 (s, 9H, t-BuSi), 1.92-2.02 (m, 1H, H-2'β), 2.28-2.35 (m, 1H, H-2'α), 3.40 (s, 3H, NCH_3) 3.73 (dd, J = 11.4, 2.4 Hz, 1H, H-5'), 3.88 (dd, J = 11.4, 2.4 Hz, 1H, H-5'), 3.96-4.00 (m, 1H, H-4'), 4.34-4.41 (m, 1H, H-3'), 6.28 (dd, J = 8.0, 5.6 Hz, 1H, H-1'), 8.14 (s, 1H, H-6); MS (FAB) *m/e* (%) 597 [$(M+H)^+$]; HRMS (FAB) calcd. for $C_{25}H_{44}O_5N_2Si_2I$, [$(M+H)^+$], 597.1678; found, 597.1672.

3',5'-Di-O-*tert*-butyldimethylsilyl-N^3-methyl-5-cyanovinyl-2'-deoxyuridine (4).

A mixture of palladium (II) acetate (38.0 mg, 169 μmol), triphenylphosphine (88.0 mg, 336 μmol), and anhydrous triethylamine (2.43 mL, 17.4 mmol) in dry DMF (5 mL) was stirred at 70°C until an intense red color, cause by activation of the catalyst, developed. To this there was then added 3',5'-di-O-*tert*-butyldimethylsilyl-N^3-methyl-5-Iodo-2'-deoxyuridine (**3**) (1.00 g, 1.68 mmol) and acrylonitrile (4.51 mL, 67.2 mmol) in dry DMF (5 mL) and the mixture was stirred overnight at 70°C. TLC of the reaction mixture in hexane/EtOAc (8:1) showed the absence of starting material and the formation of the product. It was filtered to remove the resulting precipitate palladium, and the filtrate was evaporated to dryness in *vacuo*. The residue was dissolved in EtOAc and washed with brine. The organic layer was dried over with Na_2SO_4 and evaporated. The residue was chromatographed on silica gel using hexane/EtOAc (8:1, v/v) as eluent to give **4** (0.50 g, 57%) as yellowish oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.04-0.15 (m, 12H, CH_3Si x 4), 0.89 (s, 9H, t-BuSi), 0.92 (s, 9H, t-BuSi), 1.95-2.04 (m, 1H, H-2'β), 2.38-2.48 (m, 1H, H-2'α), 3.36 (s, 3H, NCH_3) 3.77 (dd, J = 11.6, 2.4 Hz, 1H, H-5'), 3.91 (dd, J = 11.6, 2.4 Hz, 1H, H-5'), 4.01-4.03 (m, 1H, H-4'), 4.36-4.40 (m, 1H, H-3'), 6.26 (dd, J = 6.8, 6.0 Hz, 1H, H-1'), 6.73 (d, 1H, vinylic), 6.88 (d, 1H, vinylic) 7.96 (s, 1H, H-6); MS (FAB) *m/e* (%) 522 [$(M+H)^+$]; HRMS (FAB) calcd. for $C_{25}H_{44}O_5N_3Si_2$, [$(M+H)^+$], 522.2819; found, 522.2827.

N^3-Methyl-5-cyanovinyl-2'-deoxyuridine (5).

To a THF solution of 3',5'-di-O-*tert*-butyldimethylsilyl-N^3-methyl-5-cyanovinyl-2'-deoxyuridine (**5**) (0.43 g, 0.82 mmol) was added tetrabutylammonium fluoride (2.90 mL, 2.88 mmol) and the reaction mixture was stirred at room temperature for 12 h. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel (3% EtOH/EtOAc) to give **5** (0.15 g, 63%) as a yellowish solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.10-2.26 (m, 1H, H-2'β), 2.46-2.50 (m, 1H, H-2'α), 3.16 (s, 3H, NCH_3) 3.50-3.70 (m, 1H, H-5'), 3.82 (m, 1H, H-5'), 4.20-4.26 (m, 1H, H-4'), 5.11-5.15 (m, 1H, H-3'), 6.10 (m, 1H, H-1'), 6.53 (d, 1H, vinylic), 7.24 (d, 1H, vinylic) 8.40 (s, 1H, H-6); MS (FAB) *m/e* (%) 294 [$(M+H)^+$]; HRMS (FAB) calcd. for $C_{13}H_{16}O_5N_3$, [$(M+H)^+$], 294.1011; found, 294.1092.

5'-O-Di-*p*-methoxytrityl- N^3-methyl-5-cyanovinyl-2'-deoxyuridine (6).

N^3-Methyl-5-cyanovinyl-2'-deoxyuridine (**5**) (0.11 g, 0.38 mmol) was dissolved in dry pyridine and coevaporatd three times. 4,4'-Dimethoxytrityl chloride (0.17 g, 0.49 mmol), N, N-dimethlaminopyridine (9.0 mg, 81 μmol), and triethylamine was added to a solution of N^3-methyl-5-cyanovinyl-2'-deoxyuridine (**5**) in dry pyridine (0.50 mL) and the reaction mixture was stirred at room temperature overnight. Then it was evaporated to dryness in *vacuo* and residue was extracted with EtOAc. The organic layer was collected, dried over Na_2SO_4, filtered and evaporated to dryness. The residue was chromatographed on silica gel (3% EtOH/ $CHCl_3$) to give **6** (0.16 g, 69%) as a yellowish powder; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.34-2.44 (m, 1H, H-2'β), 2.48-2.56 (m, 1H, H-2'α), 3.35 (s, 3H, NCH_3) 3.43-3.56 (m, 1H, H-5'), 3.82 (s, 6H, OCH_3), 3.82 (m, 1H, H-5'), 4.10-4.15 (m, 1H, H-4'), 4.65-4.69 (m, 1H, H-3'), 5.72 (d, 1H, vinylic), 6.42 (m, 1H, H-1'), 6.56 (d, 1H, vinylic), 7.29-7.31 (m, 9H, DMTr) 8.00 (s, 1H, H-6); MS (FAB) *m/e* (%) 595 [$(M+H)^+$]; HRMS (FAB) calcd. for $C_{34}H_{33}O_7N_3$, [$(M+H)^+$], 595.2318; found, 595.2320.

5'-O-Di-*p*-methoxytrityl-3'-O-(N,N-diisopropylamino-2-cyanoethoxyphosphinyl)-N^3-methyl-5-cyanovinyl-2'-deoxyuridine (7).

5'-O-Di-*p*-methoxytrityl- N^3-methyl-5-cyanovinyl-2'-deoxyuridine (**6**) (0.11 g) in a sealed bottle was dissolved in dry acetonitrile and coevaporated three times in *vacuo*. After substituted with argon, 2-cyanoethyl N,N,N',N'-tetraisopropylphosphorodiamidite

(100 μL) in dry acetonitrile (1.0 mL), 0.5 M tetrazole in dry acetonitrile (300 μL) were added, and the reaction mixture was stirred at ambient temperature for 2 h. Then the reaction mixture was extracted with EtOAc, which was washed with a saturated aqueous solution of sodium bicarbonate, and water. The organic layer was collected, dried over anhydrous sodium sulfate, filtered, and evaporated to dryness under reduced pressure. Then, the crude product **7** in a sealed bottle was dissolved in dry acetonitrile and coevaporated three times, and was used for automated DNA synthesizer without further purification.

Oligonucleotides synthesis.

ODNs were synthesized by the conventional phosphoramidite method by using an Applied Biosystems 3400 DNA synthesizer. The coupling efficiency was monitored with a trityl monitor. The coupling efficiency of crude mixture of **7** was 97% yield. The coupling time of crude mixture of **7** was 999 sec. They were deprotected by incubation with 28% ammonia for 4 h at 60 ˚C and were purified on a Chemcosorb 5-ODS-H column (4.6 x 150 mm) by reverse phase HPLC; elution was with 0.05 M ammonium formate containing 3-20% acetonitrile, linear gradient (30 min) at a flow rate of 1.0 mL/min, 30 ˚C. Preparation of oligonucleotides was confirmed by MALDI-TOF-MS analysis.