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Oligonucleotide synthesis under mild deprotection conditions

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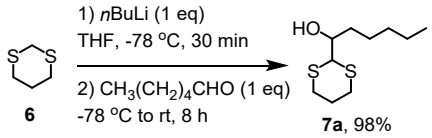
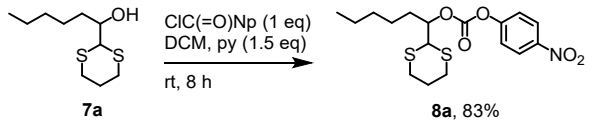
Experimental Details

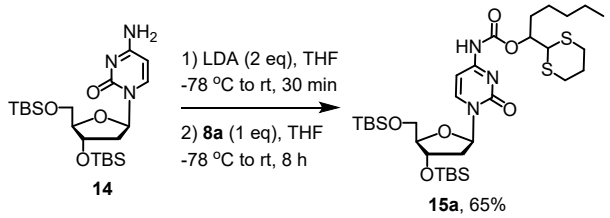
General. All the reactions were performed in oven-dried glassware under nitrogen atmosphere using standard Schlenk techniques. All reagents and solvents from commercial sources were used as received with the following exceptions. DCM, pyridine, ACN, diethyl ether and diisopropylamine were distilled over CaH_2 under nitrogen. THF was distilled over CaH_2 and then Na/benzophenone under nitrogen. Sigma-Aldrich TLC plates, silica gel 60F-254 over glass support, 0.25 μm thickness, were used for thin-layer chromatography (TLC). Selecto Scientific silica gel, particle size 32-63μm, was used for flash column chromatography. ^{1}H, ^{13}C and ^{31}P NMR spectra were measured on a Varian UNITYINOVA spectrometer at 400, 100 and 162 MHz, respectively. Chemical shifts (δ) were reported in reference to solvent peaks, residue $CHCl_3$ at 7.24 ppm for ^{1}H, $CDCl_3$ at 77.00 ppm for ^{13}C, and H_3PO_4 at 0.00 ppm for ^{31}P. ODN syntheses were performed on a MerMade 6 solid phase synthesizer. RP HPLC was performed on a JASCO LC-2000Plus System: pump, PU-2089Plus Quaternary Gradient; detector, UV-2075Plus. Column: C-18 reversed phase, analytical, 5 μm diameter, 100 Å, 250 × 4.60 mm. Solvent A: 0.1 M triethylammonium acetate, 5% ACN. Solvent B: 90% ACN. All profiles were generated by detecting absorbance at 260 nm using the linear gradient solvent system: solvent B (0%-45%) in solvent A over 60 min followed by solvent B (45%-100%) in solvent A over 20 min at a flow rate of 1.0 mL/min. Additionally, ODN **29j**, which contains N^4-acetylcytidine, was also analyzed under denatured RP HPLC conditions.[1] Capillary electrophoresis (CE) was carried out on an Agilent 7100 CE system with UV-Visible diode-array detector (190–600 nm). Capillary: PVA coated 25 cm × 100 μm (40 cm was cut to 25 cm). Buffer solution: 200 mM Bis-Tris and 200 mM boric acid in CE water, pH 7.2. Sieving solution: 27% or 30% (w/v) PEG 35,000 in buffer solution. Flush regimen: High pressure flush from outlet −8 bar for 5 min. Injection: 0.02-0.07 μM 19- to 22-mer ODNs in buffer solution, −10 KV for 10 sec. Run: −25 KV, 30 °C for 40 min. Detection: alignment interface for standard capillary with 75 μm ID, detected at 260 ± 8 nm. HRMS was obtained on a Thermo HR-Orbitrap Elite Mass Spectrometer. LRMS was obtained on a Thermo Finnigan LCQ Advantage Ion Trap Mass Spectrometer. Both MS were calibrated using the Pierce™ ESI Positive/Negative Ion Calibration Solutions and the semi-automatic procedure provided by the instrument software. The HRMS was further checked at *m/z* 138.06619, 195.08765, and 524.26496 (for positive mode) and *m/z* 112.98559, 265.14790, and 514.28440 (for negative mode). MALDI-TOF MS were obtained on Bruker's microflex™ LRF MALDI-TOF System. The negative mode of the system was calibrated using unmodified standard ODNs synthesized in house using standard methods as external standards. More details regarding MALDI MS conditions can be found in reference.[2]



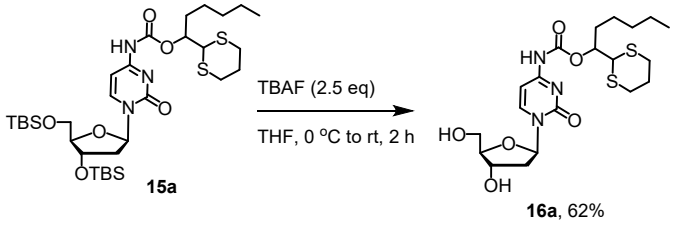
*1-(1,3-Dithian-2-yl)hexan-1-ol (**7a**):* To a solution of 1,3-dithiane (**6**, 7.5 g, 62.5 mmol, 1.0 equiv.) in dry THF (100 mL) was slowly added *n*BuLi (2.5 M in hexanes, 25 mL, 62.5 mmol, 1.0 equiv.) at -78 °C under nitrogen. The mixture was stirred at the same temperature for 30 min. *n*-Hexanal (7.68 mL, 62.5 mmol, 1.0 equiv.) was added. The mixture was stirred for 8 h while warming to rt gradually. The reaction was quenched with sat. NH_4Cl (75 mL) and extracted with EtOAc (50 mL × 3). The extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated. Product **7a** was purified with flash column chromatography (SiO_2, hexanes/EtOAc 5:1): 13.47 g, 98%; colorless oil; TLC R_f = 0.5 (SiO_2, hexanes/EtOAc 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (t, J = 7.0 Hz, 3H), 1.26-1.31 (m, 4H), 1.46-1.55 (m, 2H), 1.73-1.81 (m, 1H), 1.87-1.91 (m, 1H), 2.01-2.09 (m, 1H), 2.41 (t, J = 2.6 Hz, 1H), 2.68-2.78 (m, 2H), 2.86-2.93 (m, 2H), 3.79-3.85 (m, 1H), 3.88 (d, J = 6.4 Hz, 1H), 5.27 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 22.8, 25.7, 25.9, 28.2, 28.7, 31.9, 34.3, 52.7, 72.4; HRMS (ESI) *m/z* calcd for $C_{10}H_{20}OS_2Na$ $[M + Na]^+$ 243.0853, found 243.0840.



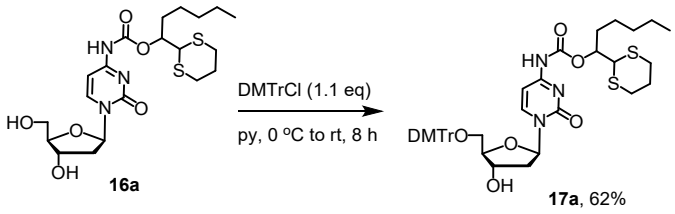
*1-(1,3-Dithian-2-yl)hexyl (4-nitrophenyl) carbonate (**8a**):* To a solution of **7a** (7.0 g, 36.4 mmol, 1.0 equiv.) in dry DCM (100 mL) under nitrogen was added distilled pyridine (4.39 mL, 54.6 mmol, 1.5 equiv.). After cooling to 0 °C, 4-nitrophenol chloroformate (7.34 g, 36.4 mmol, 1.0 equiv.) was added. The mixture was stirred overnight while warming to rt gradually. The reaction was quenched with sat. NH_4Cl (75 mL) and extracted with DCM (50 mL × 3). The extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated. Product **8a** was precipitated from DCM by hexanes: 10.18 g, 83%; yellow foam; TLC R_f = 0.6 (SiO_2, hexanes/EtOAc 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84 (t, J = 6.8 Hz, 3H), 1.27-1.29 (m, 4H), 1.33-1.44 (m, 2H), 1.72-1.81 (m, 1H), 1.91-2.04 (m, 3H), 2.67-2.76 (m, 2H), 2.86-2.96 (m, 2H), 4.01 (d, J = 7.0 Hz, 1H), 5.05-5.09 (m, 1H), 7.36 (d, J = 9.3 Hz, 2H), 8.22 (d, J = 9.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 22.6, 25.1, 25.6, 28.3, 28.6, 31.6, 31.9, 48.7, 80.1, 122.0, 125.4, 145.5, 152.5, 155.8; HRMS (ESI) *m/z* calcd for $C_{17}H_{23}NO_5S_2Na$ $[M + Na]^+$ 408.0915, found 408.0900.



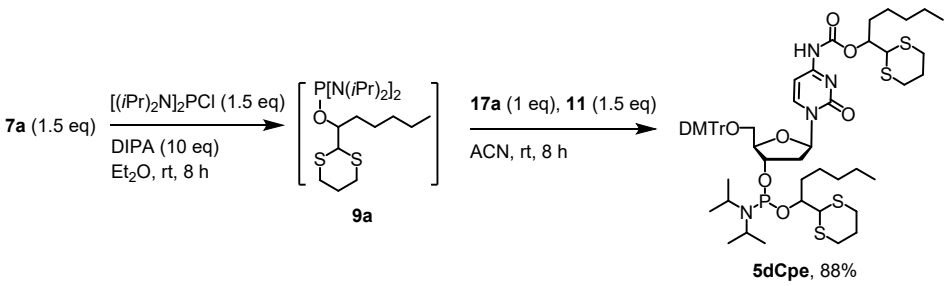
*Compound **15a**:* To a solution of diisopropylamine (4.51 mL, 32.02 mmol, 2.0 equiv.) in THF (200 mL) at −78 °C was added *n*BuLi (2.5 M in hexanes, 12.8 mL, 32.02 mmol, 2.0 equiv.). After stirring for 30 min, the freshly prepared LDA solution was added via a cannula to a solution of **14** (7.28 g, 16.01 mmol, 1.0 equiv.) in THF (50 mL) at −78 °C. The mixture was stirred at the same temperature for 30 min, and compound **8a** (16.01 mmol, 1.0 equiv.) was then added under positive nitrogen pressure. The mixture was stirred for 8 h while warming to rt gradually. The contents were poured into a separatory funnel and partitioned between EtOAc (50 mL) and sat. NaCl (50 mL). The aqueous layer was extracted with EtOAc (40 mL × 3). The combined organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated. Product **15a** was purified with flash column chromatography (SiO_2, hexanes/EtOAc 1:1): 7.26 g, 65%; white foam; TLC R_f = 0.55 (SiO_2, hexanes/EtOAc 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.02 (s, 6H), 0.08 (d, J = 4.0 Hz , 6H), 0.84 (s, 10H), 0.89 (s, 8H), 1.15-1.35 (m, 6H), 1.66-1.75 (m, 1H), 1.81-1.93 (m, 2H), 1.99-2.13 (m, 2H), 2.45-2.52 (m, 1H), 2.65-2.77 (m, 2H), 2.83-2.90 (m, 2H), 3.74 (dd, J = 9.4, 2.6 Hz, 1H), 3.90-3.93 (m, 2H), 4.06 (dd, J = 4.6, 1.6 Hz, 1H), 4.33-4.37 (m, 1H), 5.06-5.10 (m, 1H), 6.21 (t, J = 5.5 Hz, 1H), 7.18 (d, J = 7.2 Hz, 1H), 8.36 (d, J = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.3, -5.2, -4.7, -4.4, 14.2, 18.1, 18.6, 22.6, 25.2, 25.8, 25.9, 26.1, 28.97, 29.00, 29.18, 29.22, 31.6, 31.8, 42.5, 49.72, 49.77, 61.94, 61.98, 70.15, 70.24, 87.03, 87.10, 87.0, 87.99, 88.03, 95.2, 116.1, 126.2, 140.7, 144.7, 152.2, 155.6, 162.4, 164.0; HRMS (ESI) *m/z* calcd for $C_{32}H_{59}N_3O_6S_2Si_2H$ [M + H]$^+$ 702.3462, found 702.3426.



*Compound **16a**:* To a solution of **15a** (1.95 g, 2.77 mmol, 1.0 equiv.) in THF (50 mL) at 0 °C was added TBAF (1 M in THF, 6.94 mL, 6.94 mmol, 2.5 equiv.). The mixture was stirred for 2 h while warming to rt. THF was evaporated under reduced pressure and the residue was loaded onto a column for flash column chromatography (SiO_2, EtOAc/MeOH 10:1). Compound **16a**: 815 mg, 62%; yellow foam; TLC R_f = 0.4 (SiO_2, EtOAc/MeOH 10:1); ^{1}H NMR (400 MHz, CD_3OD) δ 0.85-0.88 (m, 3H), 1.22-1.37 (m, 6H), 1.62-1.75 (m, 1H), 1.85-1.91 (m, 2H), 1.97-2.04 (m, 1H), 2.12-2.20 (m, 1H), 2.44-2.50 (m, 1H), 2.71-2.95 (m, 4H), 3.71-3.84 (m, 2H), 3.97-4.00 (m, 1H), 4.13 (dd, J = 6.4, 1.4 Hz, 1H), 4.34-4.38 (m, 1H), 5.09-5.13 (m, 1H), 6.19 (t, J = 6.2 Hz, 1H), 7.26 (d, J = 7.5 Hz, 1H), 8.42 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 13.2, 22.3, 24.9, 25.8, 28.24, 28.51, 28.53, 31.4, 31.7, 41.3, 49.4, 61.3, 70.5, 76.0, 87.4, 88.2, 95.6, 144.7, 153.3, 156.4, 163.6, 164.3; HRMS (ESI) *m/z* calcd for $C_{20}H_{31}N_3O_6S_2Na$ [M + Na]$^+$ 496.1552, found 496.1566.

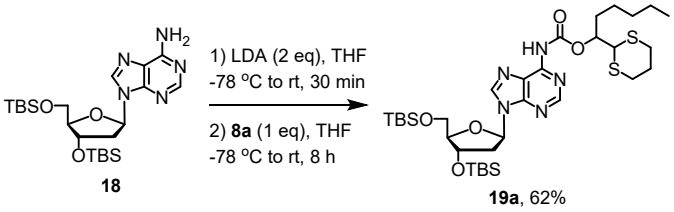


*Compound **17a***: To a solution of **16a** (534 mg, 1.13 mmol, 1.0 equiv.) in pyridine (10 mL) at 0 °C was added DMTrCl (402.02 mg, 1.18 mmol, 1.1 equiv.) under positive nitrogen pressure. The mixture was stirred for 8 h while warming to rt. The volume of the mixture was reduced to about 2 mL under vacuum from an oil pump (the remaining pyridine can help to retain the DMTr group in the product). The residue was poured into a separatory funnel and partitioned between 5% Na_2CO_3 (10 mL) and EtOAc (10 mL). The aqueous layer was extracted with EtOAc (10 mL × 3). The combined organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated to dryness. Product **17a** was purified with flash column chromatography (SiO_2, EtOAc/MeOH 9:1 with 5% Et_3N): 549.6 mg, 62%; white foam; TLC R_f = 0.6 (SiO_2, EtOAc/MeOH 9:1 with 5% Et_3N); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.80-0.89 (m, 3H), 1.06-1.24 (m, 6H), 1.68-1.73 (m, 1H), 1.85-1.92 (m, 2H), 2.13-2.21 (m, 1H), 2.60-2.76 (m, 2H), 2.84-2.91 (m, 2H), 3.35 (dd, J = 10.6, 3.6 Hz, 1H), 3.45 (dd, J = 10.4, 2.3 Hz, 1H), 3.76 (s, 6H), 4.02-4.11 (m, 2H), 4.15-4.16 (m, 1H), 4.47-4.48 (m, 1H), 5.05-5.11 (m, 1H), 6.25 (t, J = 5.8 Hz, 1H), 6.81 (d, J = 8.3 Hz, 4H), 7.00 (d, J = 7.5 Hz, 1H), 7.17-7.27 (m, 7H), 7.37 (d, J = 7.5 Hz, 2H), 8.20 (d, J = 5.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 14.4, 22.6, 25.2, 25.8, 28.8, 29.0, 29.1, 29.2, 31.6, 31.8, 31.9, 42.3, 49.6, 49.8, 55.5, 60.6, 63.0, 71.1, 86.7, 87.1, 87.5, 95.2, 113.5, 127.2, 128.2, 128.4, 130.2, 135.6, 135.7, 144.5, 152.2, 158.8, 162.4; HRMS (ESI) *m/z* calcd for $C_{41}H_{49}N_3O_8S_2H$ $[M + H]^+$ 776.3039, found 776.3063.

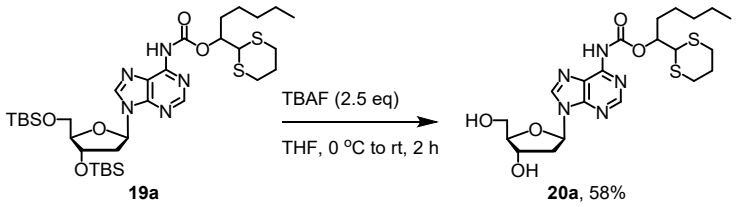


*Compound **5dCpe***: To a solution of **7a** (851.4 mg, 3.87 mmol, 1.5 equiv.) and freshly distilled diisopropyl amine (DIPA, 3.63 mL, 25.8 mmol, 10 equiv.) in dry diethyl ether (30 mL) was added bis(diisopropylamino)chlorophosphine (1.03 g, 3.87 mmol, 1.5 equiv.) at rt under nitrogen. After stirring overnight, a cloudy solution containing the soluble intermediate **9a** and insoluble diisopropylamine hydrochloride side product was formed. The intermediate **9a** in the supernatant was transferred into a solution of **17a** (2.00 g, 2.58 mmol, 1 equiv.) and diisopropylammonium tetrazolide (**11**, 661.7 mg, 3.87 mmol, 1.5 equiv.) in dry ACN (60 mL) via a cannula with its inflow

end wrapped with a copper wire-secured cotton to avoid transferring of insoluble salts. After stirring overnight, the mixture was concentrated to dryness. The residue was dissolved in the solvent mixture of hexanes/EtOAc 1:1 with 5% Et_3N and loaded onto a column (SiO_2). Eluting with the same solvent mixture gave **5dCpe**: mixture of diastereomers; 2.55 g, 2.27 mmol, 88%; white foam; TLC R_f = 0.3 and 0.4 (SiO_2, hexanes/EtOAc 1:1 with 5% Et_3N); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.76-0.81 (m, 6H), 0.98-1.22 (m, 22H), 1.55-1.60 (m, 1H), 1.63-1.70 (m, 1H), 1.78-1.88 (m, 2H), 1.94-2.00 (m, 2H), 2.18-2.29 (m, 1H), 2.67-2.75 (m, 6H), 2.80-2.86 (m, 2H), 3.39-3.52 (m, 3H), 3.72 (s, 6H), 3.83-3.86 (m, 1H), 4.00 (t, J = 7.2 Hz, 1H), 4.15-4.18 (m, 1H), 4.49-4.59 (m, 1H), 5.01-5.06 (m, 1H), 6.15-6.22 (m, 1H), 6.75-6.79 (m, 4H), 6.83-6.85 (m, 1H), 7.13-7.25 (m, 7H), 7.33 (t, J = 8.2 Hz, 2H), 7.54 (brs, 1H), 8.18-8.23 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 14.4, 22.7, 22.8, 22.90, 22.92, 23.94, 23.96, 24.90, 24.94, 25.01, 25.07, 25.3, 25.91, 26.6, 29.04, 29.17, 29.30, 30.6, 30.9, 31.7, 31.9, 33.4, 43.4, 43.6, 44.7, 44.8, 49.7, 49.8, 53.8, 55.5, 62.5, 76.51, 76.54, 76.64, 76.7, 87.0, 87.2, 87.3, 94.7, 113.4, 127.1, 128.1, 128.3, 130.17, 130.19, 135.47, 135.53, 144.2, 144.30, 144.5, 152.0, 154.9, 158.7, 162.1; ^{31}P NMR (162 MHz, $CDCl_3$) δ 148.8, 149.0, 149.3; HRMS (ESI) *m/z* calcd for $C_{57}H_{81}N_4O_9PS_4H$ $[M + H]^+$ 1125.4702, found 1125.4691.

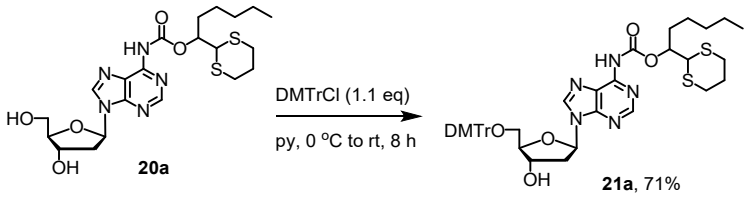


*Compound **19a***: Synthesized using the procedure for **15a**. Diisopropylamine (4.65 mL, 33.05 mmol, 2.0 equiv.), THF (200 mL), *n*BuLi (2.5 M in hexanes, 13.2 mL, 33.05 mmol, 2.0 equiv.), **18** (7.91 g, 16.52 mmol, 1.0 equiv.), THF (50 mL) and **8a** (16.52 mmol, 1.0 equiv.) were used. Product **19a** was purified with flash column chromatography (SiO_2, hexanes/EtOAc 1:1): 7.56 g, 62%; light yellow foam; TLC R_f = 0.45 (SiO_2, hexanes/EtOAc 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.06 (d, J = 3.4 Hz, 12H), 0.72-0.82 (m, 3H), 0.87 (s, 18H), 1.22-1.24 (m, 3H), 1.33-1.36 (m, 1H), 1.70-1.73 (m, 1H), 1.89-1.91 (m, 1H), 1.98-2.02 (m, 1H), 2.41-2.46 (m, 1H), 2.56-2.62 (m, 1H), 2.66-2.75 (m, 1H), 2.82-2.95 (m, 2H), 3.76 (dd, J = 11.1, 2.7 Hz, 1H), 3.87 (dd, J = 11.3, 3.6 Hz, 1H), 4.10 (d, J = 6.0 Hz, 1H), 4.57-4.59 (m, 1H), 5.17-5.21 (m, 1H), 6.47 (t, J = 6.1 Hz, 1H), 6.94 (d, J = 9.0 Hz, 1H), 8.37 (s, 1H), 8.69 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.1, -5.0, -4.5, -4.3, 14.3, 18.3, 18.7, 22.7, 25.4, 26.0, 26.2, 29.00, 29.04, 29.4, 31.7, 31.9, 41.8, 41.9, 50.0, 62.9, 71.95, 71.98, 76.24, 76.28, 85.0, 88.3, 122.2, 141.0, 141.52, 141.55, 149.4, 150.73, 150.79, 152.7, 162.9; HRMS (ESI) *m/z* calcd for $C_{33}H_{59}N_5O_5S_2Si_2H$ $[M + H]^+$ 726.3574, found 726.3597.



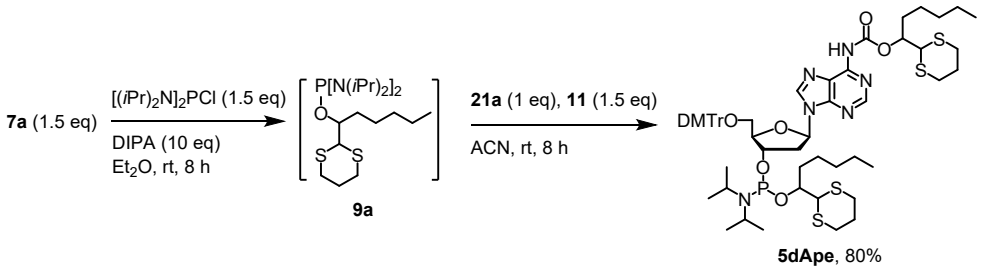
19a **20a**, 58%

*Compound **20c***: Synthesized using the procedure for **16a**. Compound **19a** (554 mg, 0.75 mmol, 1.0 equiv.), THF (50 mL), and TBAF (1 M in THF, 1.87 mL, 1.87 mmol, 2.5 equiv.) were used. Product **20a** was purified with flash column chromatography (SiO_2, EtOAc/MeOH 10:1): 222.4 mg, 58%; light yellow foam; TLC R_f = 0.3 (SiO_2, EtOAc/MeOH 10:1); ^{1}H NMR (400 MHz, CD_3OD) δ 0.86 (t, J = 6.9 Hz, 3H), 1.22-1.33 (m, 4H), 1.35-1.41 (m, 2H), 1.69-1.76 (m, 1H), 1.81-1.93 (m, 2H), 1.96-2.04 (m, 1H), 2.42-2.47 (m, 1H), 2.72-2.88 (m, 4H), 3.73 (dd, J = 8.8, 3.8 Hz, 1H), 3.82 (dd, J = 8.4, 3.3 Hz, 1H), 4.04 (dd, J = 6.4, 3.3 Hz, 1H), 4.20 (dd, J = 6.2, 1.9 Hz, 1H), 4.56-4.59 (m, 1H), 5.15-5.20 (m, 1H), 6.49 (t, J = 6.8 Hz, 1H), 8.52 (d, J = 1.7 Hz, 1H), 8.55 (d, J = 1.8 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 13.3, 22.5, 25.1, 26.0, 28.5, 28.8, 31.5, 31.8, 40.4, 49.7, 62.3, 71.6, 75.9, 85.6, 88.6, 122.6, 142.8, 149.8, 150.8, 151.6, 151.8, 164.2; HRMS (ESI) *m/z* calcd for $C_{21}H_{31}N_5O_5S_2H$ $[M + H]^+$ 498.1845, found 498.1836.

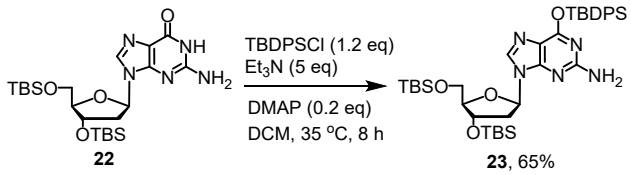


20a **21a**, 71%

*Compound **21a***: Synthesized using the procedure for **17a**. Compound **20a** (220 mg, 0.43 mmol, 1.0 equiv.), pyridine (10 mL) and DMTrCl (160.5 mg, 0.47 mmol, 1.1 equiv.) were used. Product **21a** was purified with flash column chromatography (SiO_2, EtOAc/MeOH 9:1 with 5% Et_3N): 240.5 mg, 71%; white foam; TLC R_f = 0.55 (SiO_2, EtOAc/MeOH 9:1 with 5% Et_3N); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (t, J = 5.4 Hz, 3H), 1.08-1.26 (m, 4H), 1.31-1.41 (m, 2H), 1.70-1.79 (m, 1H), 1.86-1.92 (m, 2H), 2.53-2.59 (m, 1H), 2.65-2.77 (m, 2H), 2.79-2.88 (m, 2H), 2.90-2.97 (m, 1H), 3.38 (d, J = 4.5 Hz, 2H), 3.73 (s, 6H), 4.14-4.19 (m, 2H), 4.69-4.70 (m, 1H), 5.18-5.23 (m, 1H), 6.45 (t, J = 5.4 Hz, 1H), 6.75 (d, J = 8.7 Hz, 4H), 7.15-7.25 (m, 7H), 7.34 (d, J = 7.1 Hz, 2H), 8.09 (d, J = 0.9 Hz, 1H), 8.66 (d, J = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 14.5, 22.8, 25.4, 26.1, 29.1, 29.5, 31.8, 31.9, 40.56, 40.60, 50.2, 55.5, 64.0, 72.67, 72.70, 76.1, 84.9, 86.5, 86.8, 113.3, 122.4, 127.1, 128.0, 128.2, 130.1, 135.70, 135.72, 141.4, 144.6, 149.5, 150.6, 150.8, 152.9, 158.7; HRMS (ESI) *m/z* calcd for $C_{42}H_{49}N_5O_7S_2Na$ $[M + Na]^+$ 822.2971, found 822.2999.

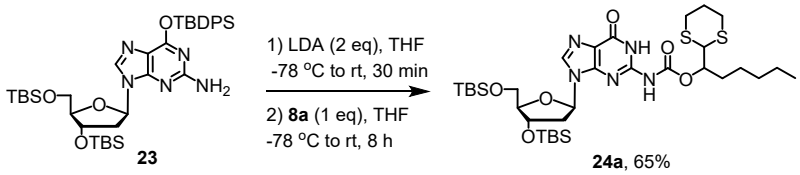


*Compound **5dApe***: Synthesized using the procedure for **5dCpe**. Compound **7a** (853.6 mg, 3.88 mmol, 1.5 equiv.), diisopropylamine (3.64 mL, 25.9 mmol, 10 equiv.), diethyl ether (30mL), bis(diisopropylamino)chlorophosphine (1.03 g, 3.88 mmol, 1.5 equiv.), **21a** (2.00 g, 2.59 mmol, 1.0 equiv.), diisopropylammonium tetrazolide (**11**, 663.5 mg, 3.88 mmol, 1.5 equiv.) and ACN (60 mL) were used. Product **5dApe** was purified with flash chromatography by dissolving the sample in the solvent mixture of hexanes/EtOAc 1:1 with 5% Et_3N, loading onto a column (SiO_2), and eluting with the same solvent mixture: mixture of diastereomers; 1.04 g, 80%; white foam; TLC R_f = 0.4 and 0.5 (SiO_2, hexanes/EtOAc 1:1 with 5% Et_3N); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.77-0.79 (m, 6H), 0.94-1.27 (m, 25H), 1.27-1.37 (m, 3H), 1.61-1.74 (m, 3H), 1.81-1.86 (m, 2H), 1.95-2.02 (m, 2H), 2.54-2.92 (m, 10H), 3.29-3.36 (m, 2H), 3.49-3.60 (m, 2H), 3.70 (s, 6H), 3.78-3.90 (m, 1H), 4.12 (t, J = 7.0 Hz, 1H), 4.16-4.19 (m, 0.5H), 4.23-4.26 (m, 1H), 4.29-4.34 (m, 0.5H), 4.66-4.76 (m, 1H), 5.15-5.18 (m, 1H), 6.41 (t, J = 6.4 Hz, 1H), 6.69-6.72 (m, 4H), 7.09-7.22 (m, 7H), 7.32 (d, J = 7.3 Hz, 2H), 8.12-8.14 (m, 1H), 8.64-8.65 (m, 1H), 8.69 (brs, 0.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.9, 14.3, 14.4, 22.7, 22.9, 24.9, 25.0, 25.04, 25.3, 25.4, 25.5, 26.1, 26.6, 29.1, 29.47, 29.51, 30.64, 30.74, 30.85, 30.97, 31.7, 31.85, 31.9, 33.4, 43.5, 43.6, 46.5, 50.1, 50.14, 53.7, 53.75, 53.83, 53.87, 55.4, 63.77, 63.85, 76.0, 76.6, 76.7, 85.1, 85.2, 86.6, 113.2, 122.5, 127.0, 127.9, 128.2, 130.13, 130.16, 135.7, 135.8, 141.6, 144.57, 144.64, 149.5, 150.6, 150.97, 151.0, 152.8, 158.5; ^{31}P NMR (162 MHz, $CDCl_3$) δ 149.2, 148.5; HRMS (ESI) *m/z* calcd for $C_{58}H_{81}N_6O_8PS_4H$ $[M + H]^+$ 1149.4815, found 1149.4797.

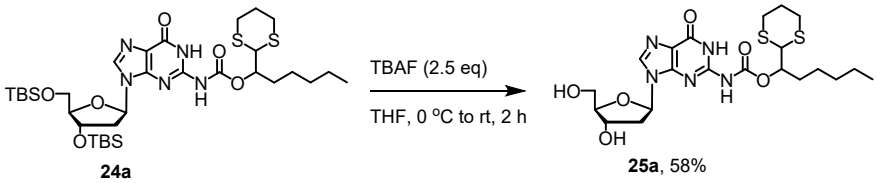


*Compound **23***: To a solution of TBDPSCl (3.14 mL, 12.12 mmol, 1.2 equiv.), Et_3N (4.82 mL, 50.50 mmol, 5.0 equiv.), 4-dimethylaminopyridine (246.78 mg, 2.02 mmol, 0.2 equiv.) in DCM (150 mL) at 35 °C was added **22** (5.0 g, 10.10 mmol, 1.0 equiv.) under positive nitrogen pressure. The mixture was stirred at the same temperature overnight. The crude product was partitioned between DCM (150 mL) and NaH_2PO_4/Na_2HPO_4 buffer (pH 7, 50 mL). The organic phase was washed with the same buffer two times, dried over anhydrous Na_2SO_4, filtered and concentrated to dryness. Product **23** was purified with flash column chromatography (SiO_2, hexanes/ EtOAc

4:1): 4.57 g, 65%; white foam; TLC R_f = 0.5 (SiO_2, hexanes/ EtOAc 4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.04 (d, J = 3.8 Hz, 6H), 0.06 (d, J = 2.9 Hz, 6H), 0.87 (d, J = 2.6 Hz, 18H), 1.15 (s, 9H), 2.23-2.29 (m, 1H), 2.51-2.58 (m, 1H), 3.73 (t, J = 4.3 Hz, 1.5H), 3.91-3.93 (m, 1H), 4.00-4.05 (m, 0.5H), 4.58 (m, 2H), 6.20 (t, J = 6.6 Hz, 1H), 7.22-7.32 (m, 6H), 7.72 (dd, J = 9.0, 2.6 Hz, 4H), 7.83 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.1, -4.9, -4.4, -4.3, 18.3, 18.7, 19.9, 26.1, 26.3, 27.4, 40.7, 63.1, 72.3, 83.8, 87.8, 117.4, 127.57, 127.59, 129.72, 129.75, 133.0, 135.6, 137.9, 154.5, 159.1, 159.5; HRMS (ESI) *m/z* calcd for $C_{38}H_{59}N_5O_4Si_3H$ $[M + H]^+$ 734.3953, found 734.3955.

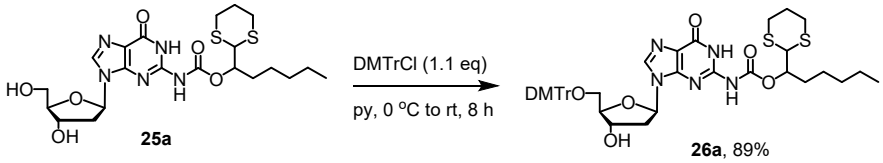


*Compound **24a***: Synthesized using the procedure for **15a**. Diisopropylamine (0.95 mL, 0.71 mmol, 2.0 equiv.), THF (100 mL), *n*BuLi (2.5 M in hexanes, 0.271 mL, 0.68 mmol, 2.0 equiv.), **23** (0.249 g, 0.34 mmol, 1.0 equiv.), THF (mL) and **8a** (0.13g, 0.34 mmol, 1.0 equiv.) were used. The product was partitioned between EtOAc (50 mL) and NH_4Cl (50 mL). The aqueous layer was extracted with EtOAc (40 mL × 3). The combined organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated. Product **24a** was purified with flash column chromatography (SiO_2, DCM/MeOH, 19:1): 0.16 g, 65%; white foam; TLC R_f = 0.3 (SiO_2, DCM/MeOH 19:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.06 (d, J = 5.2 Hz, 8H), 0.83-0.93 (m, 21H), 1.24-1.37 (m, 6H), 1.87-1.96 (m, 2H), 2.00-2.06 (m, 1H), 2.31-2.42 (m, 2H), 2.67-2.77 (m, 2H), 2.87-2.97 (m, 2H), 3.74 (d, J = 3.5 Hz, 1H), 3.94-3.97 (m, 2H), 4.53-4.54 (m, 1H), 5.15-5.21 (m, 1H), 6.19-6.24 (m, 1H), 7.77-7.78 (m, 0.5H), 7.92 (d, J = 4.0 Hz, 0.5H), 11.19 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.1, -5.0, -4.4, -4.3, 14.3, 18.3, 18.7, 22.72, 22.74, 25.24, 25.31, 25.8, 26.0, 26.3, 28.44, 28.55, 28.75, 28.83, 31.6, 32.0, 41.7, 41.9, 49.00, 49.13, 63.05, 63.09, 72.17, 72.21, 84.07, 84.08, 88.16, 88.19, 94.6, 121.29, 121.34, 136.80, 136.86, 146.5, 148.1, 153.2, 155.6; HRMS (ESI) *m/z* calcd for $C_{33}H_{59}N_5O_6S_2Si_2H$ $[M + H]^+$ 742.3524, found 742.3554.

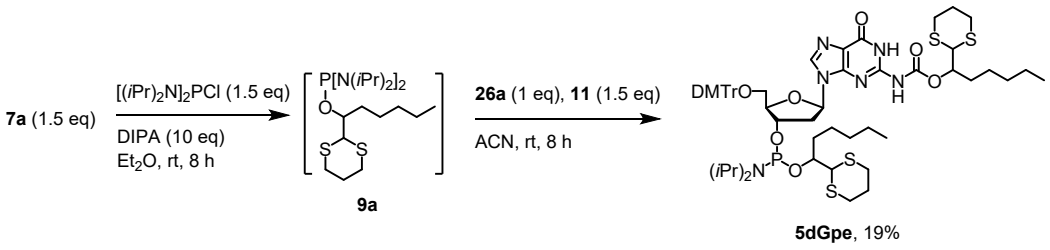


*Compound **25a***: Synthesized using the procedure for **16a**. Compound **24a** (0.48 g, 0.65 mmol, 1.0 equiv.), THF (20 mL) and TBAF (1 M in THF, 1.63 mL, 1.63 mmol, 2.5 equiv.) were used. Product **25a** was purified with flash column chromatography (SiO_2, DCM/MeOH 9:1): 222.4 mg, 58%; white foam; TLC R_f = 0.3 (SiO_2, DCM/MeOH 9:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.70-0.78 (m, 3H), 1.15-1.23 (m, 2H), 1.78-1.87 (m, 1.5H), 1.90-1.97 (m, 1H), 2.48-2.53 (m, 1.5H), 2.57-2.66

(m, 2H), 2.77-2.89 (m, 2H), 3.72-3.82 (m, 1H) 3.90-3.96 (m, 1H), 4.79-4.84 (m, 1H), 5.03-5.09 (m, 1H) , 6.17-6.19 (m, 1H), 7.85 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 22.7, 24.5, 25.2, 25.7, 28.4, 28.7, 31.6, 32.0, 40.4, 40.5, 48.7, 62.0, 70.36, 70.41, 84.94, 84.96, 87.8, 121.4, 138.0, 138.1, 146.83, 146.88, 148.0, 153.8, 155.8; HRMS (ESI) *m/z* calcd for $C_{21}H_{31}N_5O_6S_2H$ $[M + H]^+$ 514.1794, found 514.1809.

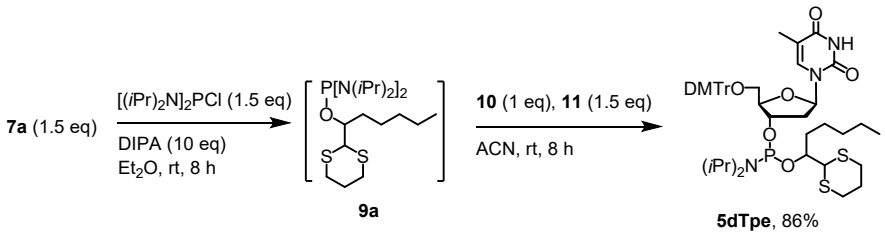


*Compound **26a***: Synthesized using the procedure for **17a**. Compound **25a** (0.419 g, 0.81 mmol, 1.0 equiv.), pyridine (20 mL) and DMTrCl (0.30 g, 0.89 mmol, 1.1 equiv.) were used. Product **26a** was purified with flash column chromatography (SiO_2, DCM/MeOH 19:1 with 5% Et_3N): 588 mg, 89%; white foam; TLC R_f = 0.5 (SiO_2, DCM/MeOH 19:1 with 5% Et_3N); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.79-0.85 (m, 3H), 1.22-1.26 (m, 4H), 1.62-1.70 (m, 1H), 1.86-2.00 (m, 4H), 2.53-2.71 (m, 4H), 2.85-2.93 (m, 2H), 3.21-3.33 (m, 2H), 3.69 (s, 6H), 3.94 (d, J = 7.2 Hz, 1H), 4.19-4.22 (m, 1H), 4.68-4.74 (m, 1H), 5.13-5.21 (m, 1H), 6.27-6.31 (m, 1H), 6.70-6.72 (m, 4H), 7.08-7.26 (m, 7H), 7.30-7.36 (m, 2H), 7.78 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.1, 14.31, 14.34, 15.1, 22.7, 25.38, 25.40, 25.8, 28.17, 28.23, 28.47, 28.54, 31.7, 32.05, 32.11, 34.8, 40.83, 40.96, 46.2, 48.62, 48.76, 55.5, 64.5, 72.26, 72.34, 84.59, 84.75, 86.52, 86.56, 86.67, 86.71, 113.3, 120.96, 121.05, 127.0, 127.9, 128.3, 130.1, 135.9, 137.5, 137.6, 144.66, 144.68, 146.96, 146.99, 148.53, 148.56, 153.95, 154.02, 155.85, 155.88, 158.5; HRMS (ESI) *m/z* calcd for $C_{42}H_{49}N_5O_8S_2H$ $[M + H]^+$ 816.3101, found 816.3132.

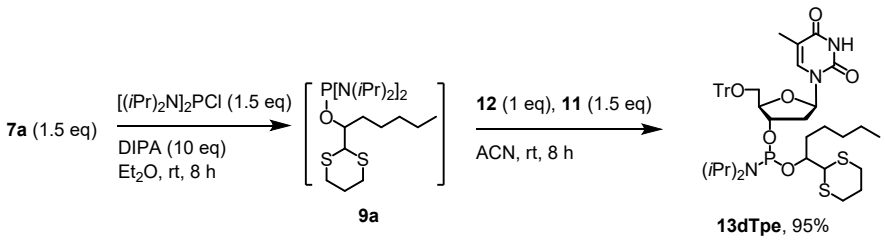


*Compound **5dGpe***: Synthesized using the procedure for **5dCpe**. Compound **7a** (0.128 g, 0.581 mmol, 1.5 equiv.), diisopropyl amine (0.547 mL, 3.88 mmol, 10 equiv.), diethyl ether (10 mL), bis(diisopropylamino)chlorophosphine (0.155 g, 0.581 mmol, 1.5 equiv.), **26a** (0.815 g, 0.388 mmol, 1.0 equiv.), diisopropylammonium tetrazolide (**11**, 0.099 g, 0.581 mmol, 1.5 equiv.) and ACN (10 mL) were used. Product **5dGpe** was purified by dissolving the sample in the solvent mixture of DCM/acetone 19:1 with 5% Et_3N, loading onto a flash chromatography column (SiO_2) and eluting with the same solvent mixture: mixture of diastereomers; 0.224 g, 19%; white foam; TLC R_f = 0.5 and 0.55 (SiO_2, DCM/acetone 19:1 with 5% Et_3N); ^{1}H NMR (400 MHz, $CDCl_3$) δ

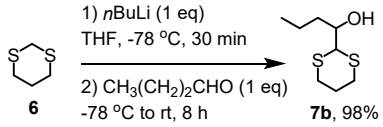
0.78-0.83 (m, 6H), 1.01 (t, J = 7.2 Hz, 9H), 1.10 (dd, J = 6.6, 1.4 Hz, 3H), 1.14-1.23 (m, 16H), 1.61-1.71 (m, 2H), 1.85-1.93 (m, 2H), 1.96-2.04 (m, 2H), 2.72-2.80 (m, 4H), 2.84- 2.94 (m, 2H), 3.22-3.27 (m, 2H), 3.50-3.58 (m, 2H), 3.71 (s, 6H), 3.86-3.92 (m, 1H), 4.17-4.26 (m, 2H), 4.55-4.66 (m, 1H), 5.08-5.15 (m, 1H), 6.13-6.17 (m, 1H), 6.71-6.74 (m, 4H), 7.11-7.26 (m, 7H), 7.33-7.37 (m, 2H), 7.69-7.70 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.30, 14.33, 14.41, 22.70, 22.73, 22.86, 22.93, 23.93, 24.9, 25.2, 25.3, 25.4, 25.7, 26.6, 28.2, 28.4, 28.7, 30.7, 30.79, 31.0, 31.6, 31.9, 32.0, 33.37, 33.42, 43.4, 43.6, 44.71, 44.77, 45.9, 48.9, 53.7, 53.9, 55.5, 63.91, 63.94, 76.7, 76.8, 84.6, 84.9, 86.5, 86.6, 113.3, 127.0, 128.0, 128.2, 128.3, 130.05, 130.10, 130.16, 135.70, 135.8, 144.56, 144.63, 146.41, 146.49, 148.4, 153.2, 155.7, 158.6; ^{31}P NMR (162 MHz, $CDCl_3$) δ 148.6, 148.5; HRMS (ESI) *m/z* calcd for $C_{58}H_{81}N_6O_9PS_4H$ $[M + H]^+$ 1165.4764, found 1165.4756.



*Compound **5dTpe***: Synthesized using the procedure for **5dCpe**. Compound **7a** (1.21 g, 5.50 mmol, 1.5 equiv.), diisopropyl amine (5.17 mL, 36.7 mmol, 10 equiv.), diethyl ether (30 mL), bis(diisopropylamino)chlorophosphine (1.47 g, 5.50 mmol, 1.5 equiv.), **10** (2.00 g, 3.67 mmol, 1 equiv.), diisopropylammonium tetrazolide (**11**, 0.941 g, 5.50 mmol, 1.5 equiv.) and ACN (60 mL) were used. Product **5dTpe** was purified with flash chromatography by dissolving the sample in the solvent mixture of hexanes/EtOAc 1:1 with 5% Et_3N, loading onto a column (SiO_2), and eluting with the same solvent mixture: mixture of diastereomers; 2.82 g, 86%; white foam; TLC R_f = 0.4 and 0.5 (SiO_2, hexanes/EtOAc 1:1 with 5% Et_3N); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.78-0.83 (m, 3H), 0.99 (d, J = 6.7 Hz, 3H), 1.11-1.19 (m, 12H), 1.22-1.25 (m, 3H), 1.34 (d, J = 4.1 Hz, 4H), 1.58-1.62 (m, 1H), 1.68-1.81 (m, 2H), 1.99-2.05 (m, 1H), 2.22-2.33 (m, 1H), 2.42-2.53 (m, 1H), 2.74-2.81 (m, 4H), 3.25-3.33 (m, 1H), 3.40-3.45 (m, 1H), 3.48-3.58 (m, 2H), 3.74 (s, 6H), 3.84-3.91 (m, 1H), 4.17 (d, J = 4.2 Hz, 0.5H), 4.23 (d, J = 4.2 Hz, 0.5H), 4.58-4.67 (m, 1H), 6.35-6.40 (m, 1H), 6.76-6.80 (m, 4H), 7.16-7.26 (m, 7H), 7.34-7.37 (m, 2H), 7.57 (s, 0.5H), 7.61 (s, 0.5H), 8.98 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.0, 14.4, 22.8, 24.88, 24.95, 25.3, 25.4, 26.6, 30.7, 30.9, 31.83, 31.89, 33.38, 33.49, 43.43, 43.55, 43.60, 53.76, 53.80, 55.5, 63.61, 63.69, 73.49, 73.61, 73.78, 84.9, 85.1, 86.07, 87.1, 111.2, 113.4, 127.2, 128.1, 128.30, 128.31, 130.3, 135.39, 135.48, 135.9, 144.38, 144.46, 150.4, 158.74, 158.76, 164.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ 149.1, 148.6; HRMS (ESI) *m/z* calcd for $C_{47}H_{64}N_3O_8PS_2Na$ $[M + Na]^+$ 916.3770, found 916.3755.

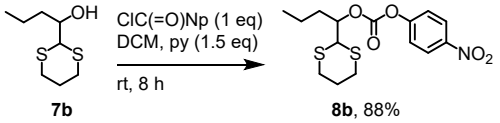


*Compound **13dTpe***: Synthesized using the procedure for **5dCpe**. Compound **7a** (1.36 g, 6.19 mmol, 1.5 equiv.), diisopropyl amine (5.82 mL, 41.3 mmol, 10 equiv.), diethyl ether (30 mL), bis(diisopropylamino)chlorophosphine (414.73 mg, 6.19 mmol, 1.5 equiv.), **12** (2.00 g, 4.13 mmol, 1 equiv.), diisopropylammonium tetrazolide (**11**, 1.06 g, 6.19 mmol, 1.5 equiv.) and ACN (60 mL) were used. Product **13dTpe** was purified with flash chromatography by dissolving the sample in the solvent mixture of hexanes/EtOAc 2:1 with 5% Et_3N, loading onto a column (SiO_2), and eluting with the same solvent mixture: mixture of diastereomers; 3.27 g, 95%; white foam; TLC R_f = 0.5 and 0.6 (SiO_2, hexanes/EtOAc 2:1 with 5% Et_3N); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.80-0.85 (m, 3H), 1.01 (d, J = 7.2 Hz, 3H), 1.14-1.27 (m, 18H), 1.38 (dd, J = 3.9, 1.1 Hz, 3H), 1.61-1.64 (m, 1H), 1.78-1.87 (m, 1H), 2.03-2.08 (m, 1H), 2.24-2.35 (m, 1H), 2.52 (m, 1H), 2.75-2.85 (m, 4H), 3.31 (dd, J = 10.4, 2.8 Hz, 0.5H), 3.36 (dd, J = 10.5, 2.8 Hz, 0.5H), 3.41-3.47 (m, 1H), 3.48-3.61 (m, 2.5H), 3.76-3.94 (m, 1H), 4.10-4.12 (m, 0.5H), 4.18 (d, J = 4.3 Hz, 0.5H), 4.25 (d, J = 4.0 Hz, 0.5H), 4.61-4.70 (m, 1H), 6.33-6.41 (m, 1H), 7.21-7.31 (m, 9H), 7.37-7.41 (m, 6H), 7.55 (d, J = 1.2 Hz, 0.5H), 7.60 (d, J = 1.2 Hz, 0.5H), 8.64 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.8, 12.03, 12.04, 14.4, 22.8, 22.9, 23.2, 23.5, 23.97, 23.99, 24.81, 24.89, 24.96, 25.02, 25.3, 25.5, 26.61, 26.64, 30.7, 30.9, 31.85, 31.90, 33.4, 33.5, 40.30, 40.37, 40.57, 40.61, 43.46, 43.51, 43.58, 43.63, 44.70, 44.79, 46.4, 53.78, 53.81, 63.87, 63.94, 73.46, 73.62, 73.73, 76.5, 76.6, 76.8, 84.9, 85.1, 85.57, 85.62, 86.01, 86.05, 87.7, 111.2, 127.5, 128.1, 128.84, 128.86, 135.8, 143.41, 143.47, 150.3, 163.82, 163.85; ^{31}P NMR (162 MHz, $CDCl_3$) δ 149.2, 148.6; HRMS (ESI) *m/z* calcd for $C_{45}H_{60}N_3O_6PS_2H$ $[M + H]^+$ 834.3739, found 834.3729.



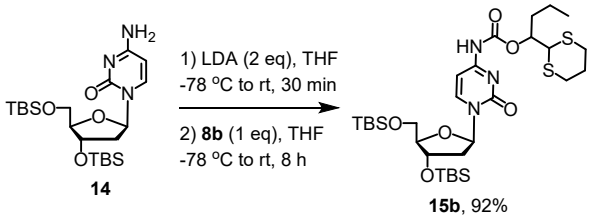
*1-(1,3-Dithian-2-yl)butan-1-ol (**7b**)*: Synthesized using the procedure for **7a**. 1,3-Dithiane (**6**, 7.5 g, 62.5 mmol, 1.0 equiv.), THF (100 mL), *n*BuLi (2.5 M in hexanes, 25 mL, 62.5 mmol, 1.0 equiv.) and *n*-butyraldehyde (5.59 mL, 62.5 mmol, 1.0 equiv.) were used. Product **7b** was purified with flash column chromatography (SiO_2, hexanes/EtOAc 5:1): 7.01 g, 98%; colorless oil; TLC R_f = 0.45 (SiO_2, hexanes/EtOAc 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (td, J = 7.2, 1.4 Hz, 3H), 1.32-1.41 (m, 1H), 1.46-1.54 (m, 2H), 1.71-1.78 (m, 1H), 1.87-1.96 (m, 1H), 2.00-2.09 (m, 1H), 2.43 (t, J = 3.5 Hz, 1H), 2.68-2.77 (m, 2H), 2.86-2.93 (m, 2H), 3.80-3.85 (m, 1H), 3.88 (d, J = 6.3

Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 19.3, 26.1, 28.5, 28.9, 36.5, 52.9, 72.3; HRMS (ESI) *m/z* calcd for $C_8H_{16}OS_2H$ $[M + H]^+$ 193.0721, found 193.0712.



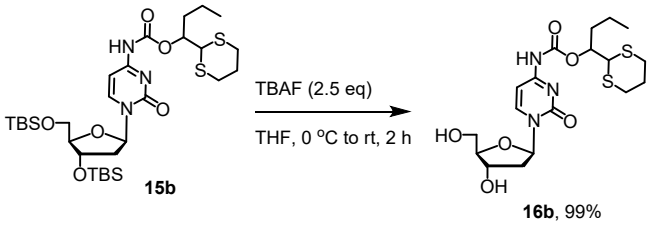
7b **8b**, 88%

*1-(1,3-Dithian-2-yl)butyl (4-nitrophenyl) carbonate (**8b**)*: Synthesized using the procedure for **8a**. Compound **7b** (7.0 g, 36.4 mmol, 1.0 equiv.), DCM (100 mL), pyridine (4.39 mL, 54.6 mmol, 1.5 equiv.) and 4-nitrophenol chloroformate (7.34 g, 36.4 mmol, 1.0 equiv.) were used. Product **8b** was purified by precipitating from DCM by hexanes: 11.40 g, 88%; white foam; TLC R_f = 0.5 (SiO_2, hexanes/EtOAc 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96 (td, J = 7.4, 1.8 Hz, 3H), 1.37-1.55 (m, 2H), 1.75-1.83 (m, 1H), 1.93-2.00 (m, 2H), 2.03-2.10 (m, 1H), 2.70-2.78 (m, 2H), 2.90-3.00 (m, 2H), 4.03 (d, J = 6.9 Hz, 1H), 5.09-5.14 (m, 1H), 7.38 (dd, J = 9.3, 1.4 Hz, 2H), 8.25 (dd, J = 9.1, 1.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 19.0, 25.7, 28.4, 28.7, 34.2, 36.5, 42.9, 48.8, 79.9, 122.0, 125.4, 145.5, 152.5, 155.7; HRMS (ESI) *m/z* calcd for $C_{15}H_{19}NO_5S_2H$ $[M + H]^+$ 358.0783, found 358.0789.

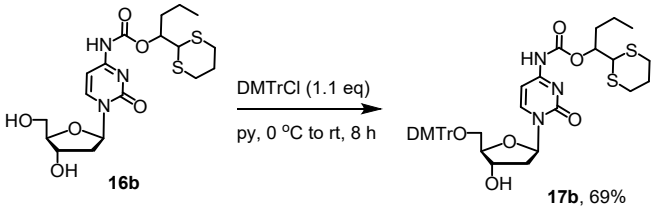


14 **15b**, 92%

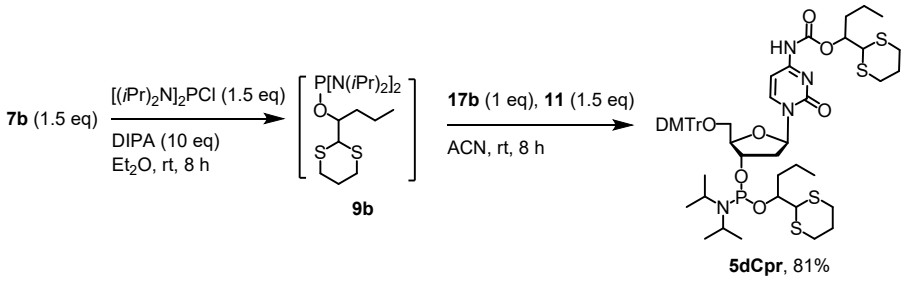
*Compound **15b***: Synthesized using the procedure for **15a**. Diisopropylamine (4.51 mL, 32.02 mmol, 2.0 equiv.), THF (200 mL), *n*BuLi (2.5 M in hexanes, 12.8 mL, 32.02 mmol, 2.0 equiv.), **14** (7.28 g, 16.01 mmol, 1.0 equiv.), THF (50 mL) and **8b** (16.01 mmol, 1.0 equiv.) were used. Product **15b** was purified with flash column chromatography (SiO_2, hexanes/EtOAc 1:1): 9.93 g, 92%; white foam; TLC R_f = 0.3 (SiO_2, hexanes/EtOAc 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ -0.001 (s, 6H), 0.06 (dd, J = 2.1, 1.6 Hz, 6H), 0.82 (d, J = 1.8 Hz, 9H), 0.87 (d, J = 1.6 Hz, 9H), 1.17-1.21 (m, 3H), 1.26-1.39 (m, 2H), 1.64-1.74 (m, 1H), 1.78-1.89 (m, 2H), 2.03-2.10 (m, 2H), 2.40-2.49 (m, 1H), 2.67-2.75 (m, 2H), 2.82-2.91 (m, 2H), 3.72 (d, J = 11.1 Hz, 1H), 3.89 (d, J = 11.4 Hz, 2H), 4.02-4.08 (m, 3H), 4.30-4.34 (m, 1H), 5.06-5.11 (m, 1H), 6.17 (t, J = 5.4 Hz, 1H), 7.10 (d, J = 7.0 Hz, 1H), 7.73 (brs, 0.5H), 8.29 (d, J = 6.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.3, -4.7, -4.3, 14.0, 14.4, 18.1, 18.6, 18.9, 21.2, 25.9, 26.1, 28.8, 29.1, 34.0, 42.4, 49.6, 60.4, 61.9, 70.1, 70.2, 76.2, 86.7, 87.73, 87.77, 94.6, 144.2, 152.3, 154.8, 162.3, 170.9; HRMS (ESI) *m/z* calcd for $C_{30}H_{55}N_3O_6S_2Si_2H$ $[M + H]^+$ 674.3149, found 674.3143.



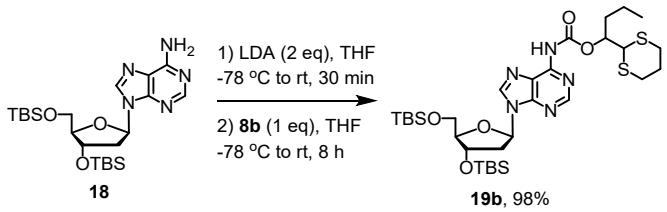
*Compound **16b***: Synthesized using the procedure for **16a**. Compound **15b** (13.8 g, 20.5 mmol, 1.0 equiv.), THF (150 mL) and TBAF (1 M in THF, 51.3 mL, 51.25 mmol, 2.5 equiv.) were used. Product **16b** was purified with flash column chromatography (SiO_2, EtOAc/MeOH 10:1): 9.0 g, 99%; light yellow foam; TLC R_f = 0.3 (SiO_2, EtOAc/MeOH 10:1); ^{1}H NMR (400 MHz, CD_3OD) δ 0.88 (t, J = 7.3, 3H), 1.24-1.42 (m, 2H), 1.62-1.71 (m, 1H), 1.80-1.85 (m, 2H), 1.93-2.00 (m, 1H), 2.12-2.19 (m, 1H), 2.43-2.49 (m, 1H), 2.68-2.92 (m, 4H), 3.77 (dd, J = 12.1, 3.3 Hz, 2H), 3.97-4.00 (m, 1H), 4.09 (d, J = 6.4 Hz, 1H), 4.34-4.38 (m, 1H), 5.08-5.11 (m, 1H), 6.18 (t, J = 6.1 Hz, 1H), 7.24 (d, J = 7.5 Hz, 1H), 8.42 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 13.3, 13.6, 18.7, 25.9, 28.4, 28.7, 29.9, 34.0, 41.4, 49.3, 49.5, 60.5, 61.3, 70.4, 70.5, 75.6, 75.8, 87.3, 87.5, 88.1, 88.3, 95.5, 95.7, 144.8, 153.0, 156.3, 163.5, 171.6; HRMS (ESI) *m/z* calcd for $C_{18}H_{27}N_3O_6S_2H$ $[M + H]^+$ 446.1420, found 446.1410.



*Compound **17b***: Synthesized using the procedure for **17a**. Compound **16b** (12 g, 26.93 mmol, 1.0 equiv.), pyridine (50 mL) and DMTrCl (10.04 g, 29.62 mmol, 1.1 equiv.) were used. Product **17b** was purified with flash column chromatography (SiO_2, EtOAc/MeOH 9:1 with 5% Et_3N): 13.9 g, 69%; white foam; TLC R_f = 0.5 (SiO_2, EtOAc/MeOH 9:1 with 5% Et_3N); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (td, J = 7.4, 2.1 Hz, 3H), 1.32-1.44 (m, 2H), 1.65-1.76 (m, 4H), 2.18-2.23 (m, 1H), 2.62-2.69 (m, 1H), 2.69-2.78 (m, 2H), 2.84-2.93 (m, 2H), 3.37 (dd, J = 10.7, 3.4 Hz, 1H), 3.47-3.51 (m, 1H), 3.73-3.75 (m, 1H), 3.78 (s, 6H), 4.10 (d, J = 7.1 Hz, 1H), 4.44-4.47 (m, 1H), 5.09-5.12 (m, 1H), 6.22 (t, J = 5.8 Hz, 1H), 6.83 (d, J = 8.8 Hz, 4H), 7.18-7.28 (m, 7H), 7.37 (d, J = 7.6 Hz, 2H), 8.21 (d, J = 7.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 19.0, 26.0, 28.9, 29.1, 29.3, 31.2, 34.07, 34.13, 42.3, 49.7, 49.9, 55.5, 63.0, 70.99, 71.04, 76.47, 76.49, 86.7, 87.1, 87.4, 95.2, 113.5, 127.2, 128.1, 128.3, 135.57, 135.66, 144.3, 144.4, 152.2, 155.4, 158.7, 162.4; HRMS (ESI) *m/z* calcd for $C_{39}H_{45}N_3O_8S_2H$ $[M + H]^+$ 748.2726, found 748.2722.

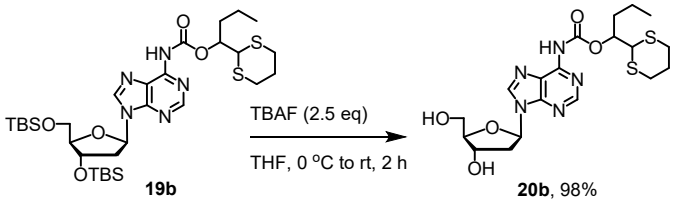


*Compound **5dCpr***: Synthesized using the procedure for **5dCpe**. Compound **7b** (769.36 mg, 4.0 mmol, 1.5 equiv.), diisopropyl amine (3.76 mL, 26.7 mmol, 10 equiv.), diethyl ether (30mL); bis(diisopropylamino)chlorophosphine (1.06 g, 4.0 mmol, 1.5 equiv.), **17b** (2.00 g, 2.67 mmol, 1.0 equiv.), diisopropylammonium tetrazolide (**11**, 684 mg, 4.0 mmol, 1.5 equiv.) and ACN (60mL) were used. Product **5dCpr** was purified with flash chromatography by dissolving the sample in the solvent mixture of hexanes/EtOAc 2:1 with 5% Et_3N, loading onto a column (SiO_2), and eluting with the same solvent mixture: mixture of diastereomers; 2.29 g, 81%; white foam; TLC R_f = 0.3 and 0.4 (SiO_2, hexanes/EtOAc 2:1 with 5% Et_3N); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.69-0.83 (m, 6H), 1.04-1.15 (m, 12H), 1.20-1.36 (m, 4H), 1.56-1.64 (m, 2H), 1.69-1.77 (m, 2H), 1.89-1.97 (m, 2H), 2.14-2.26 (m, 1H), 2.58-2.71 (m, 8H), 2.74-2.84 (m, 2H), 3.28 (td, J = 13.5, 3.2 Hz, 1H), 3.36-3.53 (m, 4H), 3.67 (s, 6H), 3.94 (t, J = 6.6 Hz, 1H), 4.03-4.15 (m, 2H), 4.45-4.57 (m, 1H), 4.98-5.04 (m, 1H), 6.12-6.18 (m, 1H), 6.73 (t, J = 7.8 Hz, 4.5H), 7.09-7.22 (m, 7H), 7.29 (t, J = 6.2 Hz, 2.5H), 8.14 (t, J = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.8, 14.0, 14.19, 14.23, 14.3, 18.5, 18.91, 19.1, 22.9, 23.1, 23.3, 23.9, 24.7, 24.8, 24.9, 25.0, 25.9, 26.2, 26.6, 28.8, 28.9, 29.1, 29.2, 29.5, 30.6, 30.9, 34.0, 34.1, 35.55, 35.59, 35.64, 41.2, 41.6, 43.4, 43.5, 44.65, 44.70, 45.2, 45.3, 46.3, 49.6, 49.7, 51.4, 53.73, 53.76, 53.39, 55.4, 62.5, 71.4, 71.6, 71.9, 76.1, 76.2, 76.23, 76.4, 85.6, 85.7, 86.1, 86.2, 87.0, 87.2, 95.1, 95.2, 113.4, 127.1, 128.0, 128.3, 130.1, 130.2, 135.3, 135.5, 144.1, 144.2, 144.3, 155.5, 158.6, 158.7, 162.2, 162.3; ^{31}P NMR (162 MHz, $CDCl_3$) δ 149.1; MS (ESI) *m/z* calcd for $C_{53}H_{73}N_4O_9PS_4Na$ $[M + Na]^+$ 1091.39, found 1091.58.

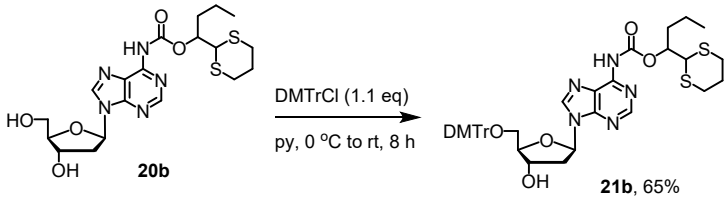


*Compound **19b***: Synthesized using the procedure for **15a**. Diisopropylamine (4.65 mL, 33.05 mmol, 2.0 equiv.), THF (200 mL), *n*BuLi (2.5 M in hexanes, 13.2 mL, 33.05 mmol, 2.0 equiv.), **18** (7.91 g, 16.52 mmol, 1.0 equiv.), THF (50 mL) and **8b** (16.52 mmol, 1.0 equiv.) were used. Product **19b** was purified with flash column chromatography (SiO_2, hexanes/EtOAc 1:2): 7.71 g, 98%; light yellow foam; TLC R_f = 0.47 (SiO_2, hexanes/EtOAc 1:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.07 (d, J = 5.2 Hz, 12H), 0.89 (d, J = 1.4 Hz, 18H), 0.92 (t, J = 7.3 Hz, 3H), 1.35-1.46 (m, 2H),

1.74-1.76 (m, 2H), 1.85-1.93 (m, 2H), 2.41-2.47 (m, 1H), 2.58-2.66 (m, 1H), 2.71-2.79 (m, 2H), 2.86-2.99 (m, 2H), 3.75 (dd, J = 11.4, 3.1 Hz, 1H), 3.86 (dd, J = 10.9, 3.9 Hz, 1H), 4.00-4.01 (m, 1H), 4.15 (d, J = 6.2 Hz, 1H), 4.57-4.61 (m, 1H), 5.21-5.25 (m, 1H), 6.47 (t, J = 6.4 Hz, 1H), 8.29 (d, J = 2.5 Hz, 1H), 8.73 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.12, -5.05, -4.5, -4.3, 14.06, 14.08, 18.3, 18.7, 19.0, 19.1, 26.0, 26.2, 29.1, 29.5, 40.0, 41.4, 41.5, 50.1, 63.0, 72.1, 75.69, 75.64, 84.9, 88.2, 122.5, 141.6, 149.6, 150.8, 150.9, 152.8; HRMS (ESI) *m/z* calcd for $C_{31}H_{55}N_5O_5S_2Si_2H$ $[M + H]^+$ 698.3261, found 698.3258.

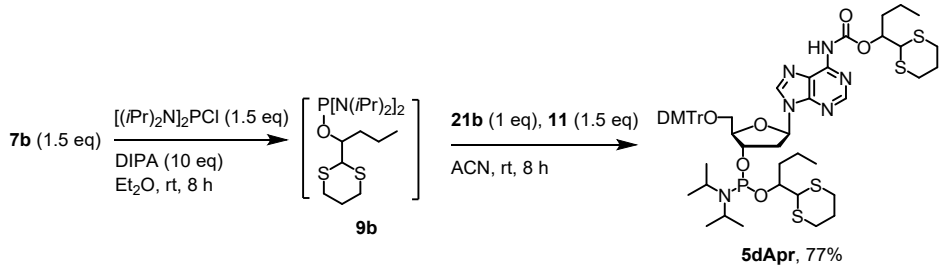


*Compound **20b***: Synthesized using the procedure for **16a**. Compound **19b** (7.71 g, 11.05 mmol, 1.0 equiv.), THF (50 mL) and TBAF (1 M in THF, 27.62 mL, 27.62 mmol, 2.5 equiv.) were used. Product **20b** was purified with flash column chromatography (SiO_2, EtOAc/MeOH 10:1): 5.08 g, 98%; pale yellow foam; TLC R_f = 0.3 (SiO_2, EtOAc/MeOH 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88-0.89 (m, 3H), 1.44-1.51 (m, 1H), 1.71-1.79 (m, 1H), 1.84-1.93 (m, 2H), 2.02-2.08 (m, 1H), 2.50-2.56 (m, 1H), 2.70-2.77 (m, 3H), 2.86-2.97 (m, 2H), 3.84-3.90 (m, 2H), 4.06-4.08 (m, 1H), 4.15 (d, J = 6.1 Hz, 1H), 4.71-4.72 (m, 1H), 5.19-5.22 (m, 1H), 6.50 (t, J = 6.1 Hz, 1H), 8.41 (s, 1H), 8.67 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 19.1, 26.1, 29.1, 29.4, 34.1, 41.0, 50.1, 62.5, 70.8, 71.0, 75.8, 77.5, 85.9, 89.0, 122.9, 142.6, 150.4, 152.3; HRMS (ESI) *m/z* calcd for $C_{19}H_{27}N_5O_5S_2H$ $[M + H]^+$ 470.1532, found 470.1534.

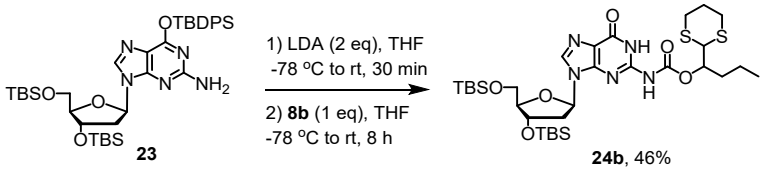


*Compound **21b***: Synthesized using the procedure for **17a**. Compound **20b** (8.71g, 18.65 mmol, 1.0 equiv.), pyridine (40 mL) and DMTrCl (6.95 g, 20.51 mmol, 1.1 equiv.) were used. Product **21b** was purified with flash column chromatography (SiO_2, EtOAc/MeOH 9:1 with 5% Et_3N): 9.30 g, 65%; white foam; TLC R_f = 0.62 (SiO_2, EtOAc/MeOH 9:1 with 5% Et_3N); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (td, J = 7.3, 3.1 Hz, 3H), 1.33-1.46 (m, 2H), 1.71-1.79 (m, 1H), 1.82-1.91 (m, 2H), 2.52-2.58 (m, 1H), 2.68-2.77 (m, 2H), 2.79-2.87 (m, 2H), 2.90-2.99 (m, 2H), 3.38 (d, J = 4.6 Hz, 2H), 3.73 (s, 6H), 4.13-4.18 (m, 2H), 4.67-4.70 (m, 1H), 5.20-5.24 (m, 1H), 6.45 (td, J = 6.4, 1.6 Hz, 1H), 6.75 (d, J = 8.9 Hz, 4H), 7.13-7.25 (m, 7H), 7.34 (dd, J = 8.0, 1.2 Hz, 2H), 8.09 (s, 1H), 8.66 (d, J = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 19.0, 19.1, 26.0, 29.1, 29.5, 34.0,

40.6, 50.2, 55.4, 64.0, 72.4, 75.8, 85.1, 86.7, 113.3, 122.32, 122.34, 127.0, 127.9, 128.2, 130.1, 135.7, 141.57, 141.61, 144.6, 149.6, 150.8, 152.7, 158.6; HRMS (ESI) *m/z* calcd for $C_{40}H_{45}N_5O_7S_2H$ $[M + H]^+$ 772.2839, found 772.2842.

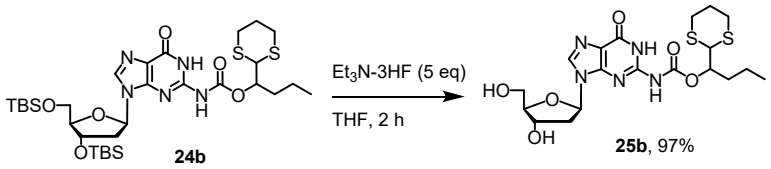


*Compound **5dApr***: Synthesized using the procedure for **5dCpe**. Compound **7b** (750.12 mg, 3.9 mmol, 1.5 equiv.), diisopropyl amine (3.66 mL, 26 mmol, 10 equiv.), diethyl ether (30 mL), bis(diisopropylamino)chlorophosphine (1.04 g, 3.9 mmol, 1.5 equiv.), **21b** (2.00 g, 2.6 mmol, 1.0 equiv.), diisopropylammonium tetrazolide (**11**, 666.9 mg, 3.9 mmol, 1.5 equiv.) and ACN (60 mL) were used. Product **5dApr** was purified with flash chromatography by dissolving the sample in the solvent mixture of hexanes/EtOAc 1:1 with 5% Et_3N, loading onto a column (SiO_2), and eluting with the same solvent mixture: mixture of diastereomers; 2.18 g, 77%; white foam; TLC R_f = 0.5 and 0.6 (SiO_2, hexanes/EtOAc 1:1 with 5% Et_3N); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.78-0.87 (m, 6H), 1.09-1.20 (m, 12H), 1.25-1.44 (m, 4H), 1.56-1.83 (m, 6H), 1.90-2.00 (m, 2H), 2.53-2.79 (m, 8H), 2.81-2.90 (m, 2H), 3.42-3.58 (m, 3H), 3.65 (s, 6H), 3.81-3.90 (m, 1H), 4.05-4.10 (m, 1H), 4.19 (dd, J = 16.2, 4.1 Hz, 1.5H), 4.29-4.30 (m, 0.5H), 4.64-4.74 (m, 1H), 5.12-5.17 (m, 1H), 6.39 (t, J = 7.3 Hz, 1H), 6.66-6.68 (m, 4H), 7.07-7.19 (m, 7H), 7.29 (d, J = 6.1 Hz, 2H), 8.15 (d, J = 2.6 Hz, 1H), 8.62 (d, J = 3.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.9, 14.1, 14.2, 14.4, 18.9, 19.06, 19.11, 22.9, 23.1, 23.4, 23.9, 24.0, 24.9, 26.1, 26.6, 29.1, 29.2, 29.3, 29.5, 29.6, 30.0, 30.6, 30.7, 30.9, 31.0, 33.9, 35.6, 35.7, 43.4, 43.6, 44.67, 44.72, 45.2, 45.3, 46.4, 50.15, 50.23, 53.78, 53.82, 53.9, 55.4, 63.77, 63.80, 75.6, 76.2, 76.3, 76.4, 85.1, 85.2, 86.2, 86.6, 113.2, 122.6, 126.9, 127.9, 128.2, 130.1, 135.6, 135.7, 141.7, 141.8, 144.60, 144.64, 149.7, 150.9, 151.0, 152.8, 158.5; ^{31}P NMR (162 MHz, $CDCl_3$) δ 149.2, 148.5 ppm; MS (ESI) *m/z* calcd for $C_{54}H_{73}N_6O_8PS_4Na$ $[M + Na]^+$ 1115.40, found 1115.58.

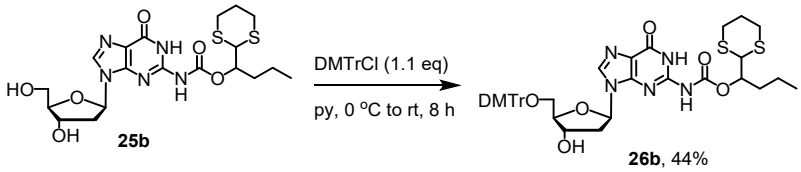


*Compound **24b***: Synthesized using the procedure for **24a**. Diisopropylamine (0.76 mL, 5.44 mmol, 2.0 equiv.), THF (100 mL), *n*BuLi (2.5 M in hexanes, 2.17 mL, 5.44 mmol, 2.0 equiv.), **23** (2.0 g, 2.72 mmol, 1.0 equiv.), THF (mL) and **8b** (972.2 mg, 2.72 mmol, 1.0 equiv.) were used. Product

24b was purified with flash column chromatography (SiO_2, hexanes/EtOAc 1:3): 2.73 g, 46%; light yellow foam; TLC R_f = 0.3 (SiO_2, hexanes/EtOAc 1:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.05 (d, J = 3.9 Hz, 12H), 0.86 (d, J = 2.2 Hz, 18H), 0.89-0.92 (m, 3H), 1.28-1.42 (m, 2H), 1.63-1.72 (m, 1H), 1.85-1.93 (m, 2H), 1.99-2.04 (m, 1H), 2.33-2.40 (m, 2H), 2.65-2.75 (m, 2H), 2.84-2.92 (m, 2H), 3.72-3.74 (m, 2H), 3.91-3.96 (m, 2H), 4.50-4.52 (m, 1H), 5.14-5.21 (m, 1H), 6.23 (dt, J = 9.9, 6.5 Hz, 1H), 7.03 (d, J = 8.0 Hz, 0.5H), 7.97 (d, J = 2.9 Hz, 1H), 8.05 (d, J = 8.0 Hz, 0.5H), 8.19 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.2, -5.1, -4.5, -4.4, 14.0, 18.2, 18.7, 18.8, 18.9, 25.7, 25.9, 26.2, 28.4, 28.6, 28.8, 28.82, 34.1, 41.9, 42.1, 48.9, 49.2, 63.0, 63.1, 72.0, 72.1, 76.8, 84.2, 88.1, 88.2, 116.2, 120.8, 126.1, 137.1, 140.2, 147.0, 148.20, 148.22, 153.6, 155.8, 164.4; HRMS (ESI) *m/z* calcd for $C_{31}H_{55}N_5O_6S_2Si_2Na$ $[M + Na]^+$ 736.3030, found 736.3027.

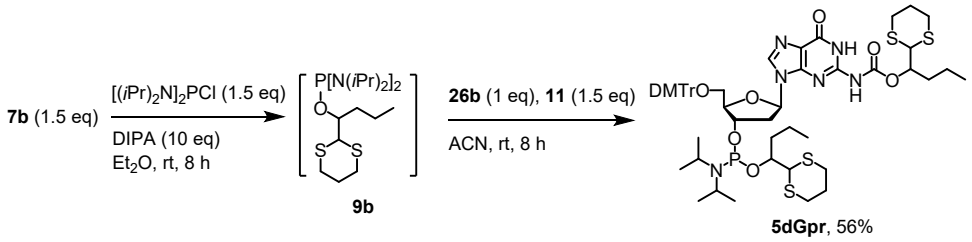


*Compound **25b***: To the solution of **24b** (2.4 g, 2.52 mmol, 1.0 equiv.) in THF (50 mL) was added triethylamine trihydrogen fluoride (2.05 mL, 12.6 mmol, 5.0 equiv.) at rt. After stirring for 2 h, the reaction was quenched with trimethylmethoxy silane (1.74 mL, 12.6 mmol, 5.0 equiv.). Volatiles were evaporated under reduced pressure. Product **25b** was purified with flash chromatography by dissolving the crude product in the solvent mixture of DCM/MeOH 10:1, loading onto a column (SiO_2) and eluting with the same solvent mixture: 1.18 g, 97%; pale yellow foam; TLC R_f = 0.3 (SiO_2, DCM/MeOH 10:1); ^{1}H NMR (400 MHz, CD_3OD) δ 0.97 (t, J = 7.4 Hz, 3H), 1.38-1.45 (m, 2H), 1.71-1.79 (m, 1H), 1.89-1.95 (m, 2H), 1.97-2.04 (m, 1H), 2.38-2.43 (m, 1H), 2.62-2.68 (m, 1H), 2.72-2.83 (m, 2H), 2.88-2.97 (m, 2H), 3.69-3.78 (m, 2H), 3.95-3.97 (m, 1H), 4.13 (d, J = 6.6 Hz, 1H), 4.50-4.53 (m, 1H), 5.21-5.26 (m, 1H), 6.33 (t, J = 6.7 Hz, 1H), 8.16-8.18 (m, 0.5H), 8.19 (d, J = 1.0 Hz, 0.5H); ^{13}C NMR (100 MHz, CD_3OD) δ 13.2, 18.6, 25.9, 28.2, 28.5, 29.8, 34.0, 40.5, 49.1, 62.1, 71.3, 76.6, 84.4, 88.2, 119.7, 138.39, 138.40, 148.1, 149.3, 155.1, 156.4; HRMS (ESI) *m/z* calcd for $C_{19}H_{27}N_5O_6S_2H$ $[M + H]^+$ 486.1481, found 486.1474.

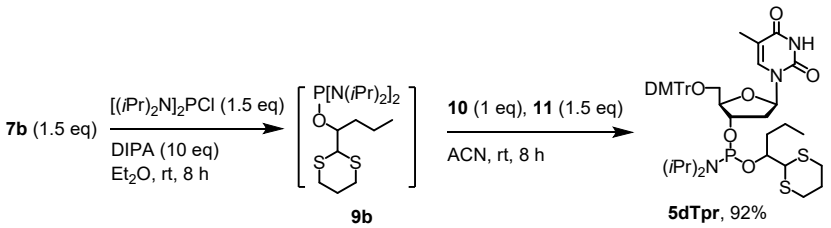


*Compound **26b***: Synthesized using the procedure for **17a**. Compound **25b** (3.09 g, 6.38 mmol, 1.0 equiv.), pyridine (50 mL) and DMTrCl (2.37 g, 7.02 mmol, 1.1 equiv.) were used. Product **26b** was purified with flash column chromatography (SiO_2, EtOAc/MeOH 20:1 with 5% Et_3N): 2.20 g, 44%; pale yellow foam; TLC R_f = 0.4 (SiO_2, EtOAc/MeOH 20:1 with 5% Et_3N); ^{1}H NMR (400

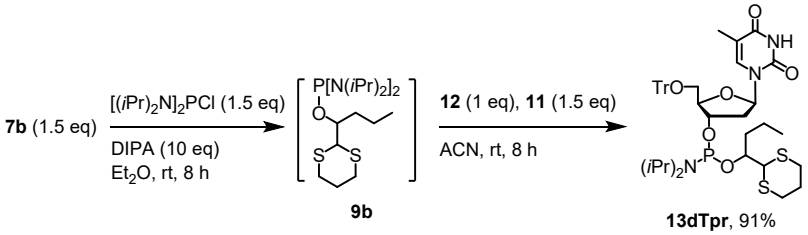
MHz, $CDCl_3$) δ 0.89 (td, J = 7.3, 2.5 Hz, 3H), 1.30-1.35 (m, 2H), 1.66-1.70 (m, 1H), 1.85-1.92 (m, 2H), 2.01 (s, 1H), 2.44-2.51 (m, 1H), 2.83-2.95 (m, 3H), 3.25-3.34 (m, 2H), 3.71 (s, 6H), 3.99 (dd, J = 6.8, 2.4 Hz, 1H), 4.13 (m, 1H), 4.67-4.71 (m, 1H), 5.16-5.19 (m, 1H), 6.22 (td, J = 6.5, 1.7 Hz, 1H), 6.72 (d, J = 8.8 Hz, 4H), 7.12-7.25 (m, 7H), 7.34 (dd, J = 5.3, 1.7 Hz, 2H), 7.73 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5, 19.1, 25.9, 28.4, 28.6, 28.7, 28.8, 34.2, 40.7, 40.8, 49.2, 49.4, 55.5, 64.5, 72.0, 76.1, 84.4, 84.5, 86.48, 86.50, 86.7, 113.2, 120.6, 120.7, 127.0, 127.9, 128.3, 130.1, 130.2, 135.9, 137.1, 137.2, 144.7, 148.8, 149.10, 149.14, 155.35, 155.4, 156.4, 158.52, 158.54; HRMS (ESI) *m/z* calcd for $C_{40}H_{45}N_5O_8S_2H$ $[M + H]^+$ 788.2788, found 788.2800.



*Compound **5dGpr***: Synthesized using the procedure for **5dCpe**. Compound **7b** (432.7 mg, 2.25 mmol, 1.5 equiv.), diisopropyl amine (2.11 mL, 15.0 mmol, 10.0 equiv.), diethyl ether (20 mL), bis(diisopropylamino)chlorophosphine (600.75 mg, 2.25 mmol, 1.5 equiv.), **26b** (1.17 g, 1.5 mmol, 1.0 equiv.), diisopropylammonium tetrazolide (**11**, 384.75 mg, 2.25 mmol, 1.5 equiv.) and ACN (40 mL) were used. Product **5dGpr** was purified with flash chromatography by dissolving the sample in the solvent mixture of hexanes/DCM 1:2 with 5% Et_3N, loading onto a column (SiO_2), and eluting with the same solvent mixture: 924.5 mg, 56%; white foam; mixture of diastereomers; TLC R_f = 0.2 and 0.3 (SiO_2, hexanes/DCM 1:2 with 5% Et_3N); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.76-0.83 (m, 6H), 1.09-1.18 (m, 12H), 1.23-1.33 (m, 4H), 1.50-1.58 (m, 2H), 1.67-1.72 (m, 2H), 1.75-1.82 (m, 2H), 1.91-1.98 (m, 2H), 2.53-2.63 (m, 4H), 2.67-2.78 (m, 8H), 3.16-3.25 (m, 2H), 3.38-3.54 (m, 4H), 3.64 (s, 6H), 3.73-3.76 (m, 1H), 3.79-3.87 (m, 2H), 4.09-4.22 (m, 2H), 4.51-4.62 (m, 1H), 5.01-5.10 (m, 1H), 6.13-6.16 (m, 1H), 6.66-6.68 (m, 4H), 7.06-7.13 (m, 3H), 7.18-7.24 (m, 4H), 7.28-7.34 (m, 2H), 7.71 (d, J = 6.8 Hz, 1H), 7.81 (d, J = 5.8 Hz, 0.5H), 8.04 (d, J = 6.9 Hz, 0.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 14.2, 14.39, 14.4, 18.5, 18.9, 19.0, 19.1, 19.2, 19.3, 22.9, 23.1, 23.4, 23.5, 23.9, 23.93, 24.8, 24.9, 25.0, 25.7, 26.1, 26.6, 26.7, 28.2, 28.3, 28.7, 29.0, 29.9, 30.6, 30.7, 30.9, 31.0, 34.1, 34.7, 35.2, 35.6, 35.9, 36.5, 43.3, 43.4, 43.5, 43.6, 44.7, 45.2, 45.3, 48.9, 49.0, 51.5, 53.2, 53.8, 53.9, 54.0, 55.4, 63.8, 63.9, 72.4, 76.3, 76.5, 76.6, 84.4, 84.7, 86.4, 86.5, 94.6, 113.2, 121.25, 121.27, 121.5, 125.6, 125.7, 127.0, 127.9, 128.2, 130.1, 130.13, 131.7, 135.7, 135.8, 137.1, 137.4, 137.5, 144.6, 146.9, 147.0, 147.1, 148.5, 153.6, 153.7, 155.9, 158.5; ^{31}P NMR (162 MHz, $CDCl_3$) δ 149.2, 148.2 ppm; MS (ESI) *m/z* calcd for $C_{54}H_{73}N_6O_9PS_4Na$ $[M + Na]^+$ 1131.40, found 1131.50.

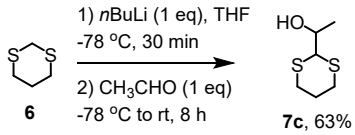


*Compound **5dTpr***: Synthesized using the procedure for **5dCpe**. Compound **7b** (1.06 g, 5.50 mmol, 1.5 equiv.), diisopropyl amine (5.17 mL, 36.7 mmol, 10 equiv.), diethyl ether (30 mL), bis(diisopropylamino)chlorophosphine (1.47 g, 5.50 mmol, 1.5 equiv.), **10** (2.00 g, 3.67 mmol, 1 equiv.), diisopropylammonium tetrazolide (**11**, 0.941 g, 5.50 mmol, 1.5 equiv.) and ACN (60 mL) were used. Product **5dTpr** was purified with flash chromatography by dissolving the sample in the solvent mixture of hexanes/EtOAc 1:1 with 5% Et_3N, loading onto a column (SiO_2), and eluting with the same solvent mixture: mixture of diastereomers; 2.92 g, 92%; white foam; TLC R_f = 0.4 and 0.5 (SiO_2, hexanes/EtOAc 1:1 with 5% Et_3N); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.78 (t, J = 7.5 Hz, 1H), 0.85 (t, J = 7.3 Hz, 2H), 1.09-1.22 (m, 12H), 1.33 (d, J = 5.6 Hz, 3H), 1.38-1.46 (m, 1H), 1.50-1.79 (m, 4H), 1.94-2.00 (m, 1H), 2.20-2.31 (m, 1H), 2.39-2.51 (m, 1H), 2.68-2.78 (m, 4H), 3.23-3.32 (m, 1H), 3.38-3.44 (m, 1H), 3.49-3.56 (m, 2H), 3.77 (s, 6H), 3.73-3.81 (m, 1H), 3.85-3.91 (m, 0.5H), 4.05-4.09 (m, 0.5H), 4.14 (d, J = 4.2 Hz, 0.5H), 4.20 (d, J = 3.9 Hz, 0.5H), 4.56-4.65 (m, 1H), 6.33-6.40 (m, 1H), 6.76 (dd, J = 8.0, 4.0 Hz, 4H), 7.19-7.23 (m, 2H), 7.25-7.27 (m, 5H), 7.34 (dd, J = 7.7, 3.0 Hz, 2H), 7.58 (s, 0.5H), 7.62 (s, 0.5H), 9.9 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.0, 14.3, 14.4, 18.9, 19.2, 19.3, 24.9, 25.0, 25.1, 26.1, 26.7, 28.8, 30.7, 30.9, 31.1, 35.7, 35.8, 36.6, 40.3, 43.3, 43.5, 43.6, 53.9, 55.5, 63.7, 63.8, 73.7, 73.9, 85.0, 85.1, 85.7, 86.1, 87.1, 92.2, 111.2, 113.4, 127.3, 128.1, 128.31, 128.35, 130.3, 135.4, 135.5, 135.9, 144.4, 150.2, 158.79, 158.80, 163.6; ^{31}P NMR (162 MHz, $CDCl_3$): δ 149.4, 148.5; MS (ESI) *m/z* calcd for $C_{45}H_{60}N_3O_8PS_2Na$ $[M + Na]^+$ 888.35, found 888.50.

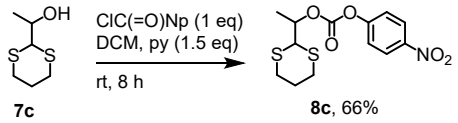


*Compound **13dTpr***: Synthesized using the procedure for **5dCpe**. Compound **7b** (1.19 g, 6.19 mmol, 1.5 equiv.), diisopropyl amine (5.82 mL, 41.3 mmol, 10 equiv.), diethyl ether (30 mL), bis(diisopropylamino)chlorophosphine (414.73 mg, 6.19 mmol, 1.5 equiv.), **12** (2.00 g, 4.13 mmol, 1 equiv.), diisopropylammonium tetrazolide (**11**, 1.06 g, 6.19 mmol, 1.5 equiv.) and ACN (60 mL) were used. Product **5dTpr** was purified with flash chromatography by dissolving the sample in the solvent mixture of hexanes/EtOAc 2:1 with 5% Et_3N, loading onto a column (SiO_2),

and eluting with the same solvent mixture: mixture of diastereomers; 3.02 g, 91%; white foam; TLC R_f = 0.2 and 0.3 (SiO_2, hexanes/EtOAc 2:1 with 5% Et_3N); ^1H NMR (400 MHz, $CDCl_3$) δ 0.82 (t, J = 7.4 Hz, 1H), 0.90 (dt, J = 10.0, 7.4 Hz, 3H), 1.18-1.26 (m, 12H), 1.37 (dd, J = 7.1, 1.1 Hz, 3H), 1.41-1.49 (m, 1H), 1.58-1.73 (m, 2H), 1.76-1.84 (m, 2H), 2.00-2.10 (m, 1H), 2.24-2.35 (m, 1H), 2.75-2.84 (m, 4H), 2.87-2.96 (m, 1H), 3.32 (td, J = 7.3, 2.9 Hz, 1H), 3.38 (dd, J = 16.8, 2.5 Hz, 1H), 3.44-3.62 (m, 4H), 3.77-3.95 (m, 1H), 4.18 (d, J = 4.3 Hz, 0.5H), 4.24 (d, J = 4.1 Hz, 0.5H), 4.60-4.68 (m, 1H), 6.35-6.40 (m, 1H), 7.20-7.31 (m, 9H), 7.33-7.41 (m, 6H), 7.55 (d, J = 1.2 Hz, 0.5H), 7.59 (d, J = 1.2 Hz, 0.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.0, 14.2, 14.3, 18.5, 18.9, 19.1, 22.9, 23.2, 23.4, 23.9, 24.0, 24.8, 24.9, 25.0, 26.2, 26.6, 29.3, 29.5, 30.7, 30.9, 35.6, 35.8, 36.0, 40.3, 40.6, 43.5, 43.6, 44.8, 45.3, 51.4, 53.8, 53.9, 63.9, 64.0, 73.6, 73.7, 76.2, 76.3, 76.5, 84.9, 85.1, 85.5, 86.0, 87.6, 111.2, 111.3, 127.5, 128.1, 128.81, 128.84, 135.8, 143.4, 143.5, 150.4, 150.5, 164.08, 164.1; ^{31}P NMR (162 MHz, $CDCl_3$) δ 149.3, 148.5; MS (ESI) *m/z* calcd for $C_{43}H_{56}N_3O_6PS_2Na$ $[M + Na]^+$ 828.32, found 828.58.

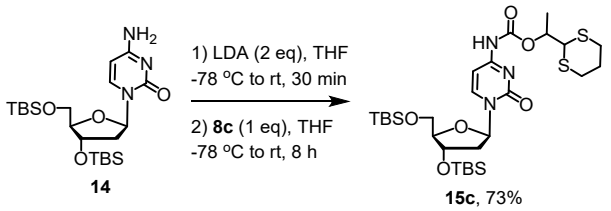


*1-(1,3-Dithian-2-yl)ethan-1-ol (**7c**)*: Synthesized using the procedure for **7a**. 1,3-Dithiane (**6**, 7.51 g, 62.5 mmol, 1.0 equiv.), THF (100 mL), *n*BuLi (2.5 M in hexanes, 25 mL, 62.5 mmol, 1.0 equiv.) and acetaldehyde (2.7 mL, 62.5 mmol, 1.0 equiv.) were used. was added to the reaction mixture. Product **7c** was purified with flash column chromatography (SiO_2, hexanes/EtOAc 4:1): 6.29 g, 63%; colorless oil; TLC R_f = 0.3 (SiO_2, hexanes/EtOAc 4:1); ^1H NMR (400 MHz, $CDCl_3$) δ 1.21 (dd, J = 5.2, 1.0 Hz, 3H), 1.73-1.96 (m, 2H), 2.55-2.63 (m, 2H), 2.73-2.81 (m, 2H), 2.87 (d, J = 3.4 Hz, 1H), 3.70 (d, J = 6.8 Hz, 1H), 3.88-3.92 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7, 25.9, 28.2, 28.5, 53.7, 68.6; HRMS (ESI) *m/z* calcd for $C_6H_{12}OS_2Na$ $[M + Na]^+$ 187.0227, found 187.0218.

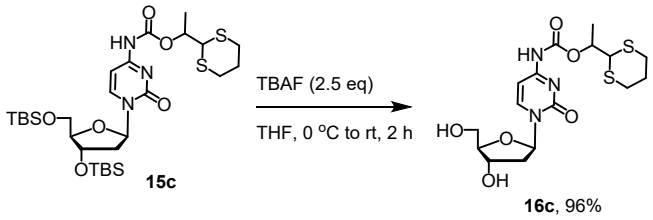


*1-(1,3-Dithian-2-yl)ethyl (4-nitrophenyl) carbonate (**8c**)*: Synthesized using the procedure for **8a**. Compound **7c** (4.51 g, mmol, 1.0 equiv.), DCM (75 mL), pyridine (3.32 mL, 41.25 mmol, 1.5 equiv.) and 4-nitrophenol chloroformate (5.54 g, 27.5 mmol, 1.0 equiv.) were used. Product **8c** was purified by precipitating from DCM with hexanes: 4.31 g, 66%; pale white powder; TLC R_f = 0.5 (SiO_2, hexanes/EtOAc 5:1); ^1H NMR (400 MHz, $CDCl_3$) δ 1.47 (dd, J = 5.6, 0.8 Hz, 3H), 1.84-2.04 (m, 2H), 2.65-2.73 (m, 2H), 2.83-2.93 (m, 2H), 3.98 (d, J = 6.8 Hz, 1H), 5.08-5.15 (m, 1H), 7.31 (d, J = 9.4 Hz, 2H), 8.17 (d, J = 9.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.3, 25.7,

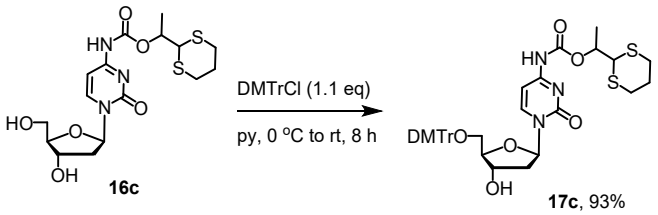
28.4, 28.8, 49.9, 76.8, 122.0, 125.4, 145.4, 152.0, 155.6; HRMS (ESI) *m/z* calcd for $C_{13}H_{15}NO_5S_2H$ $[M + H]^+$ 330.0470, found 330.0467.



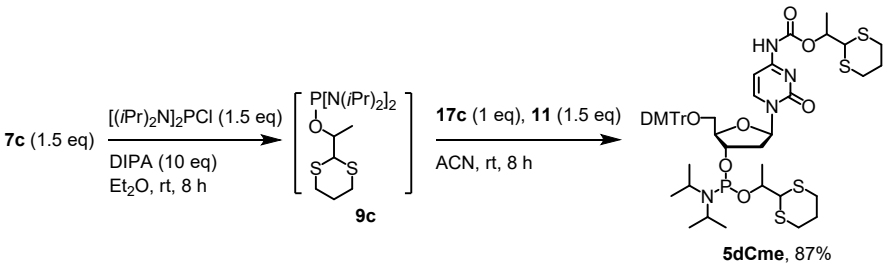
*Compound **15c***: Synthesized using the procedure for **15a**. Diisopropylamine (1.62 mL, 11.5 mmol, 2.0 equiv.), THF (50 mL), *n*BuLi (2.5 M in hexanes, 4.39 mL, 10.98 mmol, 2.0 equiv.), **14** (2.5 g, 5.49 mmol, 1.0 equiv.), THF (50 mL) and **8c** (1.80 g, 5.49 mmol, 1.0 equiv.) were used. Product **15c** were purified with flash column chromatography (SiO_2, hexanes/EtOAc 1:1): 2.60 g, 73%; white foam; TLC R_f = 0.5 (SiO_2, hexanes/EtOAc 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.02 (d, J = 1.5 Hz, 6H), 0.08 (d, J = 4.2 Hz, 6H), 0.84 (s, 9H), 0.89 (s, 9H), 1.44 (d, J = 8.0 Hz, 3H), 1.86-1.95 (m, 1.5H), 2.01-2.13 (m, 2.5H), 2.69-2.78 (m, 2H), 2.84-2.93 (m, 2H), 3.74 (dd, J = 9.5, 2.9 Hz, 1H), 3.90-3.93 (m, 2H), 4.05 (d, J = 6.2 Hz, 1H), 4.32-4.37 (m, 1H), 5.15-5.22 (m, 1H), 6.18-6.21 (m, 1H), 7.12 (d, J = 7.5 Hz, 1H), 8.33 (d, J = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.25, -5.30, -4.7, -4.4, 18.1, 18.6, 25.8, 25.9, 26.1, 28.8, 29.2, 42.5, 50.6, 61.9, 62.0, 70.1, 70.2, 73.6, 86.9, 87.0, 87.9, 88.0, 94.6, 94.61, 116.1, 126.2, 144.6, 151.9, 155.2, 162.2; HRMS (ESI) *m/z* calcd for $C_{28}H_{51}N_3O_6S_2Si_2H$ $[M + H]^+$ 646.2836, found 646.2817.



*Compound **16c***: Synthesized using the procedure for **16a**. Compound **15c** (2.4 g, 3.72 mmol, 1.0 equiv.), THF (50 mL) and TBAF (1 M in THF, 9.3 mL, 9.3 mmol, 2.5 equiv.) were used. Product **16c** was purified with flash column chromatography (SiO_2, EtOAc/MeOH 19:1): 1.5 g, 96%; white foam; TLC R_f = 0.4 (SiO_2, EtOAc/MeOH 19:1); ^{1}H NMR (400 MHz, CD_3OD) δ 1.43 (dd, J = 6.4, 0.6 Hz, 3H), 1.81-1.91 (m, 1H), 2.01-2.08 (m, 1H), 2.12-2.19 (m, 1H), 2.44-2.50 (m, 1H), 2.74-2.84 (m, 2H), 2.78-2.97 (m, 2H), 3.72 (dd, J = 12.1, 3.8 Hz, 1H), 3.81 (dd, J = 12.1, 3.8 Hz, 1H), 3.96-3.99 (m, 1H), 4.15 (dd, J = 6.3, 2.0 Hz, 1H), 4.35 (dt, J = 6.2, 3.9 Hz, 1H), 5.15-5.22 (m, 1H), 6.19 (t, J = 6.2 Hz, 1H), 7.26 (d, J = 7.6 Hz, 1H), 8.42 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 17.2, 25.8, 28.1, 28.5, 41.3, 50.3, 53.3, 61.3, 70.4, 73.00, 73.02, 87.4, 88.2, 95.5, 144.7, 152.8, 156.5, 163.6; HRMS (ESI) *m/z* calcd for $C_{16}H_{23}N_3O_6S_2H$ $[M + H]^+$ 418.1107, found 418.1107.

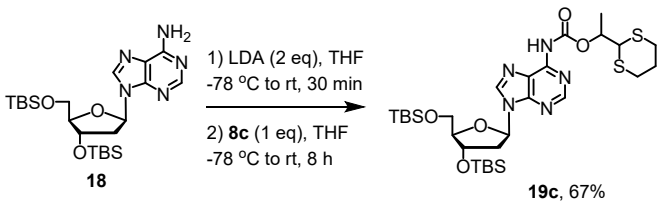


*Compound **17c***: Synthesized using the procedure for **17a**. Compound **16c** (1.5 g, 3.5 mmol, 1.0 equiv.), pyridine (30 mL) and DMTrCl (1.54 g, 3.9 mmol, 1.1 equiv.) were used. Product **17c** was purified with flash column chromatography (SiO_2, EtOAc/MeOH 19:1 with 5% Et_3N): 2.3 g, 93%; white foam; TLC R_f = 0.5 (SiO_2, EtOAc/MeOH 19:1 with 5% Et_3N); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44 (dd, J = 6.4, 1.0 Hz, 3H), 1.84-1.91 (m, 1.5H), 2.03-2.08 (m, 1H), 2.16-2.24 (m, 1.5H), 2.67-2.79 (m, 2H), 2.83-2.91 (m, 2H), 3.37 (dd, J = 10.8, 3.8 Hz, 1H), 3.46 (dd, J = 11.0, 2.6 Hz, 1H), 3.77 (s, 6H), 4.02-4.10 (m, 2H), 4.12-4.15 (m, 1H), 4.46-4.50 (m, 1H), 5.12-5.20 (m, 1H), 6.24 (t, J = 5.8 Hz, 1H), 6.82 (d, J = 8.8, 4H), 6.93-6.98 (m, 1H), 7.00-7.28 (m, 7H), 7.37 (d, J = 8.0 Hz, 2H), 7.76 (brs, 1H), 8.21 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.1, 18.2, 25.8, 28.8, 28.9, 29.1, 29.2, 31.1, 42.2, 50.6, 50.7, 55.4, 55.5, 62.9, 71.0, 73.4, 86.6, 87.1, 87.4, 95.0, 113.5, 127.3, 128.2, 128.4, 130.2, 135.6, 135.7, 144.4, 144.5, 158.8, 162.4; HRMS (ESI) *m/z* calcd for $C_{37}H_{41}N_3O_8S_2H$ $[M + H]^+$ 720.2413, found 720.2403.

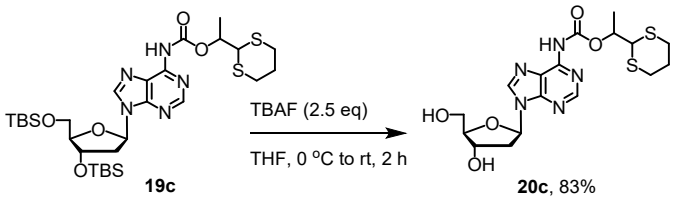


*Compound **5dCme***: Synthesized using the procedure for **5dCpe**. Compound **7c** (0.64 g, 3.9 mmol, 1.5 equiv.), diisopropyl amine (3.6 mL, 26.2 mmol, 10 equiv.), diethyl ether (15 mL), bis(diisopropylamino)chlorophosphine (1.04 g, 3.9 mmol, 1.5 equiv.), **17c** (1.89 g, 2.62 mmol, 1 equiv.), diisopropylammonium tetrazolide (**11**, 0.67 g, 3.9 mmol, 1.5 equiv.) and ACN (10 mL) were used. Product **5dCme** was purified with flash chromatography by dissolving the sample in the solvent mixture of hexanes/EtOAc 1:2 with 5% Et_3N, loading onto a column (SiO_2), and eluting with the same solvent mixture: mixture of diastereomers; 2.28 g, 87%; white foam; TLC R_f = 0.3 and 0.4 (SiO_2, hexanes/EtOAc 1:2 with 5% Et_3N); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.99-1.05 (m, 3H), 1.10-1.25 (m, 12H), 1.35-1.37 (m, 1H), 1.43-1.46 (m, 3H), 1.78-1.96 (m, 3H), 2.18-2.36 (m, 2H), 2.70-2.92 (m, 10H), 3.35-3.47 (m, 2H), 3.50-3.65 (m, 3H), 3.78 (s, 6H), 3.81-3.85 (m, 1H), 4.03-4.05 (m, 1H), 4.14-4.19 (m, 1H), 4.55-4.64 (m, 1H), 5.13-5.20 (m, 1H), 6.21-6.25 (m, 1H), 6.80-6.84 (m, 4H), 7.19-7.31 (m, 7H), 7.35-7.39 (m, 2H), 8.23-8.26 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.9, 14.6, 18.3, 18.4, 20.31, 20.34, 24.85, 24.9, 25.0, 25.9, 26.5, 28.7, 29.3, 29.4, 30.2,

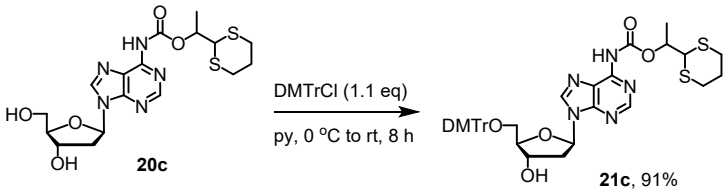
30.3, 30.5, 30.6, 43.4, 43.5, 46.5, 50.7, 50.8, 55.5, 62.5, 62.6, 71.8, 72.5, 73.3, 87.0, 113.4, 127.2, 128.1, 128.3, 128.4, 130.2, 130.3, 135.4, 135.6, 136.7, 139.9, 144.3, 146.0, 158.7; ^{31}P NMR (162 MHz, $CDCl_3$) δ 149.1, 148.1, 148.0; MS (ESI) *m/z* calcd for $C_{49}H_{65}N_4O_9PS_4Na$ $[M + Na]^+$ 1035.33, found 1035.50.



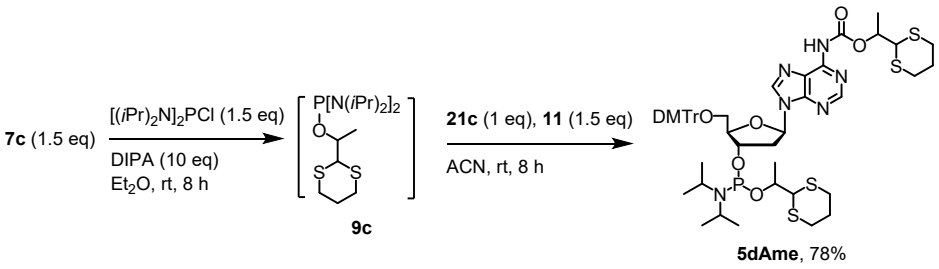
*Compound **19c***: Synthesized using the procedure for **15a**. Diisopropylamine (1.79 mL, 12.77 mmol, 2.0 equiv.), THF (100 mL), *n*BuLi (2.5 M in hexanes, 4.8 mL, 12.0 mmol, 2.0 equiv.), **18** (2.9 g, 6.08 mmol, 1.0 equiv.), THF (50 mL) and **8c** (2.0 g, 6.08 mmol, 1.0 equiv.) were used. Product **19c** was purified with flash column chromatography (SiO_2, hexanes/EtOAc 1:1): 2.72 g, 67%; white foam; TLC R_f = 0.5 (SiO_2, hexanes/EtOAc 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.06 (d, J = 3.4 Hz, 12H), 1.46 (dd, J = 6.4, 1.4 Hz, 3H), 1.86-1.97 (m, 2H), 2.42-2.61 (m, 2H), 2.67-2.77 (m, 4H), 3.73-3.78 (m, 1H), 3.85-3.89 (m, 1H), 4.05-4.15 (m, 2H), 5.27 (m, 1H), 6.47 (t, J = 6.6 Hz, 1H), 8.37 (d, J = 2.2 Hz, 1H), 8.68 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.0, -4.5, -4.3, 18.2, 18.3, 18.7, 20.6, 25.9, 26.0, 26.2, 27.9, 28.3, 29.0, 29.4, 41.9, 51.0, 53.5, 62.9, 68.6, 72.0, 73.1, 73.14, 85.0, 88.3, 117.5, 122.2, 126.3, 141.6, 149.3, 150.5, 150.8, 152.7, 162.9; HRMS (ESI) *m/z* calcd for $C_{29}H_{51}N_5O_5S_2Si_2H$ $[M + H]^+$ 670.2948, found 670.2937.



*Compound **20c***: Synthesized using the procedure for **16a**. Compound **19c** (2.6 g, 3.88 mmol, 1.0 equiv.), THF (50 mL) and TBAF (1 M in THF, 8.5 mL, 8.5 mmol, 2.5 equiv.) were used. Product **20c** was purified with flash column chromatography (SiO_2, DCM/MeOH 25:1): 1.10 g, 83%; light yellow foam; TLC R_f = 0.5 (SiO_2, DCM/MeOH 25:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (d, J = 6.4 Hz, 3H), 1.85-1.91 (m, 1H), 1.99-2.04 (m, 1H), 2.71-2.91 (m, 4H), 3.57 (m, 1H), 2.92-2.99 (m, 2H), 3.79 (t, J = 12.0 Hz, 1H), 3.93 (d, J =12.0 Hz, 1H), 4.17 (d, J = 5.8 Hz, 1H), 4.23 (m, 1H), 5.24-5.30 (m, 1H), 6.39-6.43 (m, 1H), 8.18 (s, 1H), 8.69 (s, 1H), 9.36 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 18.16, 18.9, 20.5, 25.5, 26.0, 29.2, 29.7, 41.1, 51.3, 52.5, 63.4, 73.0, 73.20, 73.24, 87.6, 89.6, 123.43, 123.44, 142.75, 142.77, 150.3, 150.4, 152.3; HRMS (ESI) *m/z* calcd for $C_{17}H_{23}N_5O_5S_2H$ $[M + H]^+$ 442.1219, found 442.1195.

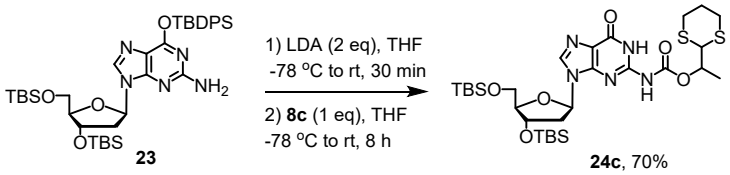


*Compound **21c***: Synthesized using the procedure for **17a**. Compound **20c** (2.2 g, 4.9 mmol, 1.0 equiv.), pyridine (30 mL) and DMTrCl (2.19 g, 5.63 mmol, 1.1 equiv.) were used. Product **21c** was purified with flash column chromatography (SiO_2, DCM/MeOH 19:1 with 5% Et_3N): 3.38 g, 91%; white foam; TLC R_f = (SiO_2, DCM/MeOH 19:1 with 5% Et_3N); ^1H NMR (400 MHz, $CDCl_3$) δ 1.38 (t, J = 6.4 Hz, 3H), 1.71-1.79 (m, 1H), 1.89-1.96 (m, 2H), 2.53-2.57 (m, 1H), 2.60-2.68 (m, 2H), 2.73-2.81 (m, 2H), 3.33 (d, J = 3.7 Hz, 2H), 3.64 (s, 6H), 4.07-4.11 (m, 1H), 4.19-4.21 (m, 1H), 4.68-4.69 (m, 1H), 5.18-5.25 (m, 1H), 6.44 (t, J = 5.6 Hz, 1H), 6.66 (d, J = 8.8 Hz, 4H), 7.03-7.19 (m, 7H), 7.28 (d, J = 7.0 Hz, 2H), 8.13 (d, J = 2.5 Hz, 1H), 8.62 (d, J = 2.7 Hz, 1H), 9.45 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5, 18.2, 26.0, 29.1, 29.5, 40.58, 40.63, 51.2, 55.4, 60.7, 64.0, 72.4, 72.9, 85.05, 85.1, 86.7, 113.3, 122.4, 127.0, 128.0, 128.2, 130.1, 135.7, 141.6, 141.7, 144.6, 149.5, 150.6, 150.9, 152.7, 158.5; HRMS (ESI) *m/z* calcd for $C_{38}H_{41}N_5O_7S_2$ $[M + H]^+$ 744.2526, found 744.2507.

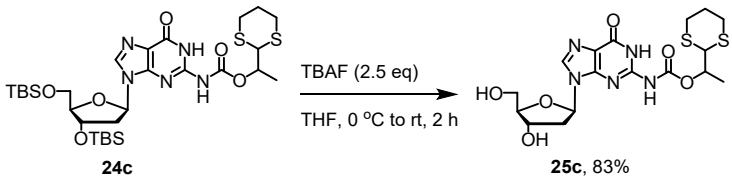


*Compound **5dAme***: Synthesized using the procedure for **5dCpe**. Compound **7c** (0.48 g, 2.97 mmol, 1.5 equiv.), diisopropyl amine (2.8 mL, 19.8 mmol, 10 equiv.), diethyl ether (15 mL), bis(diisopropylamino)chlorophosphine (0.78 g, 2.97 mmol, 1.5 equiv.), **21c** (1.47 g, 1.98 mmol, 1.0 equiv.), diisopropylammonium tetrazolide (**11**, 0.5 g, 2.97 mmol, 1.5 equiv.) and ACN (10 mL) were used. Product **5dAme** was purified with flash chromatography by dissolving the sample in the solvent mixture of hexanes/EtOAc 1:2 with 5% Et_3N, loading onto a column (SiO_2), and eluting with the same solvent mixture: mixture of diastereomers; 0.96 g, 78%; white foam; TLC R_f = 0.3 and 0.4 (SiO_2, hexanes/EtOAc 1:2 with 2% Et_3N); ^1H NMR (400 MHz, $CDCl_3$) δ 1.05-1.16 (m, 12H), 1.32-1.40 (m, 6H), 1.69-1.84 (m, 2H), 1.95-1.99 (m, 2H), 2.63-2.89 (m, 12H), 3.26-3.36 (m, 2H), 3.48-3.58 (m, 1.5H), 3.71 (s, 6H), 3.99-4.04 (m, 1.5H), 4.08-4.11 (m, 2H), 4.65-4.72 (m, 1H), 5.20-5.26 (m, 1H), 6.40 (t, J = 6.7 Hz, 1H), 6.67-6.70 (m, 4H), 7.06-7.21 (m, 7H), 7.30 (d, J = 7.0 Hz, 2H), 8.16-8.18 (m, 1H), 8.64 (t, J = 3.1 Hz, 1H), 9.26 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.0, 18.1, 18.14, 18.2, 20.2, 20.3, 24.7, 24.8, 24.9, 25.0, 26.0, 26.4, 26.6, 29.1,

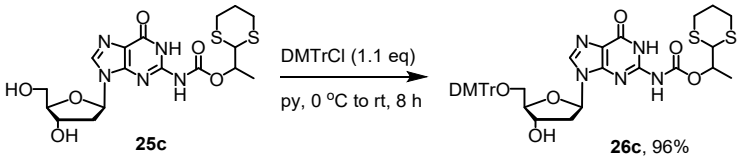
30.2, 30.3, 30.6, 43.4, 43.5, 51.0, 51.2, 54.6, 54.7, 54.73, 55.3, 55.5, 63.8, 72.3, 72.6, 72.7, 72.9, 85.1, 86.6, 113.1, 113.3, 122.6, 122.7, 126.7, 127.1, 127.8, 128.1, 128.3, 130.0, 130.3, 135.7, 135.8, 144.6, 149.6, 150.5, 151.1, 152.6, 152.8, 158.5; ^{31}P NMR (162 MHz, $CDCl_3$): δ 148.7, 148.6, 148.0; MS (ESI) *m/z* calcd for $C_{50}H_{65}N_6O_8PS_4Na$ $[M + Na]^+$ 1059.34, found 1059.53.



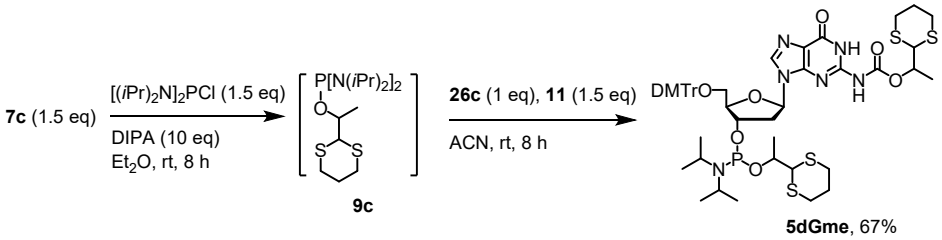
*Compound **24c***: Synthesized using the procedure for **24a**. Diisopropylamine (2.49 mL, 17.7 mmol, 2.0 equiv.), THF (75 mL), *n*BuLi (2.5 M in hexanes, 6.7 mL, 16.8 mmol, 2.0 equiv.), **23** (6.18 g, 8.4 mmol, 1.0 equiv.), THF (50 mL) and **8c** (2.77 g, 8.4 mmol, 1.0 equiv.) were used. Product **24c** was purified with flash column chromatography (SiO_2, hexanes/EtOAc, 1:1): 3.80 g, 70%; white foam; TLC R_f = 0.4 (SiO_2, hexanes/EtOAc, 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.06 (d, J = 6.4 Hz, 12H), 0.87-0.88 (m, 18H), 1.47 (d, J = 6.3 Hz, 3H), 1.90-2.05 (m, 2H), 2.27-2.42 (m, 2H), 2.69-2.77 (m, 2H), 2.86-2.97 (m, 2H), 3.58 (dd, J = 10.5, 3.6 Hz, 0.5H), 3.67 (dd, J = 11.7, 3.8 Hz, 0.5H), 3.94-3.99 (m, 2H), 4.49-4.55 (m, 1H), 5.23-5.32 (m, 1H), 6.17-6.23 (m, 1H), 7.92 (s, 0.5H), 8.16 (s, 0.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.1, -5.0, -4.4, -4.3, 18.3, 18.4, 18.7, 25.7, 26.0, 26.3, 28.6, 29.0, 41.8, 41.9, 50.2, 50.3, 63.1, 72.1, 74.1, 84.1, 88.2, 94.6, 127.8, 131.7, 136.9, 146.6, 148.1, 152.8, 155.7; HRMS (ESI) *m/z* calcd for $C_{29}H_{51}N_5O_6S_2Si_2H$ $[M + H]^+$ 686.2898, found 686.2883.



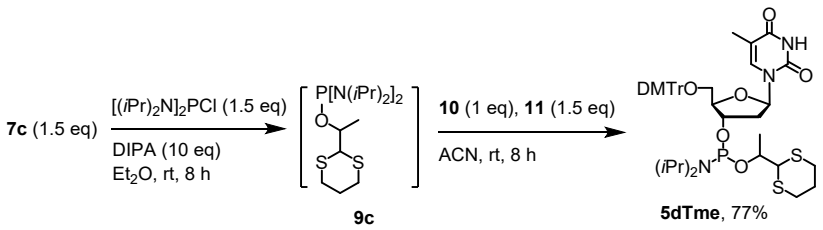
*Compound **25c***: Synthesized using the procedure for **16a**. Compound **24c** (2.6 g, 8.5 mmol, 1.0 equiv.), THF (50 mL) and TBAF (8.5 mL, 8.5 mmol, 5.0 equiv.) were used. Product **25c** was purified with flash column chromatography (SiO_2, DCM/MeOH 19:1): 1.1 g, 83%; white foam; TLC R_f = 0.4 (SiO_2, DCM/MeOH 19:1); ^{1}H NMR (400 MHz, CD_3OD) δ 1.44 (d, J = 6.4 Hz, 3H), 1.81-1.89 (m, 1H), 1.96-2.01 (m, 1H), 2.35-2.41 (m, 1H), 2.59-2.67 (m, 1H), 2.70-2.78 (m, 2H), 2.86-2.96 (m, 2H), 3.66-3.75 (m, 2H), 3.91-3.94 (m, 1H), 4.09 (d, J = 6.5 Hz, 1H), 4.48-4.52 (m, 1H), 5.22-5.29 (m, 1H), 6.29 (t, J = 6.6 Hz, 1H), 8.15 (d, J = 1.5 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 17.3, 25.8, 27.9, 28.4, 40.48, 40.49, 49.9, 61.9, 71.2, 73.8, 84.3, 88.0, 119.62, 119.64, 138.2, 138.3, 147.8, 149.2, 154.4, 156.2; HRMS (ESI) *m/z* calcd for $C_{17}H_{23}N_5O_6S_2H$ $[M + H]^+$ 458.1168, found 458.1154.



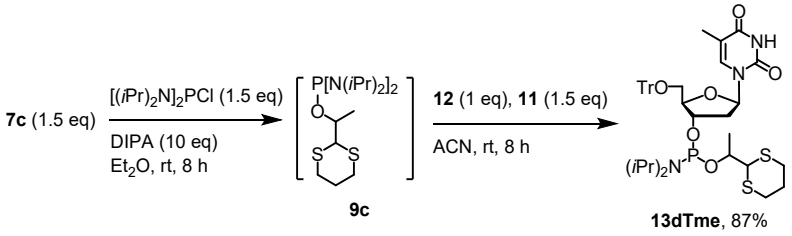
*Compound **26a***: Synthesized using the procedure for **17a**. Compound **25c** (1.19 g, 2.6 mmol, 1.0 equiv.), pyridine (30 mL) and DMTrCl (1.16 g, 2.99 mmol, 1.1 equiv.) were used. Product **26c** was purified with flash column chromatography (SiO_2, DCM/MeOH 19:1 with 5% Et_3N): 1.9 g, 96%; white foam; TLC R_f = 0.5 (SiO_2, DCM/MeOH 19:1 with 5% Et_3N); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (t, J = 5.7 Hz, 3H), 1.62-1.71 (m, 1H), 1.83-1.91 (m, 1H), 2.45-2.61 (m, 2H), 2.66-2.71 (m, 2H), 3.09-3.14 (m, 1H), 3.35-3.41 (m, 1H), 3.55 (s, 6H), 3.95-3.97 (m, 1H), 4.05-4.11 (m, 1H), 4.53-4.56 (m, 1H), 4.98-5.04 (m, 1H), 6.15-6.19 (m, 1H), 6.56 (d, J = 8.4 Hz, 4H), 6.94-7.09 (m, 7H), 7.19 (d, J = 7.5 Hz, 2H), 7.60 (d, J = 3.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.1, 18.2, 26.0, 29.1, 29.46, 29.5, 41.2, 41.4, 51.3, 53.0, 55.4, 64.5, 71.8, 72.3, 84.1, 86.3, 86.4, 113.1, 126.8, 127.8, 128.2, 130.1, 135.8, 136.2, 144.7, 150.1, 156.9, 158.4; HRMS (ESI) *m/z* calcd for $C_{38}H_{41}N_5O_8S_2H$ $[M + H]^+$ 760.2475, found 760.2453.



*Compound ***5dGme***: Synthesized using the procedure for **5dCpe**. Compound **7c** (0.32 g, 1.97 mmol, 1.5 equiv.), diisopropyl amine (1.85 mL, 13.1 mmol, 10 equiv.), diethyl ether (15 mL), bis(diisopropylamino)chlorophosphine (0.52 g, 1.97 mmol, 1.5 equiv.), **26c** (1.0 g, 1.31 mmol, 1.0 equiv.), diisopropylammonium tetrazolide (**11**, 0.34 g, 1.97 mmol, 1.5 equiv.) and ACN (10 mL) were used. Product **5dGme** was purified with flash chromatography by dissolving the sample in the solvent mixture of hexanes/EtOAc 1:5 with 5% Et_3N, loading onto a column (SiO_2), and eluting with the same solvent mixture: mixture of diastereomers; 1.0 g, 67%; white foam; TLC R_f = 0.2 and 0.3 (SiO_2, hexanes/EtOAc 1:5 with 5% Et_3N); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.11-1.19 (m, 12H), 1.35-1.46 (m, 6H), 1.77-1.94 (m, 2H), 1.99-2.06 (m, 2H), 2.70-2.87 (m, 10H), 3.23-3.30 (m, 2H), 3.55-3.61 (m, 3.5H), 3.74 (s, 6H), 3.97-4.02 (m, 1.5H), 4.18-4.28 (m, 1H), 4.56-4.66 (m, 1H), 5.20-5.24 (m, 1H), 6.19 (t, J = 6.3 Hz, 1H), 6.73-6.77 (m, 4H), 7.21-7.29 (m, 7H), 7.34-7.40 (m, 2H), 7.71 (d, J = 1.4 Hz, 0.5H), 7.74 (d, J = 2.6 Hz, 0.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.1, 18.4, 20.3, 22.9, 24.8, 24.9, 25.1, 26.0, 26.4, 26.5, 28.8, 29.2, 30.2, 30.4, 30.5, 30.6, 43.5, 43.6, 45.8, 50.75, 50.8, 53.1, 55.5, 64.0, 72.5, 84.2, 86.6, 113.1, 113.3, 127.0, 128.0, 128.3, 130.1, 130.2, 131.7, 135.8, 144.3, 144.6, 149.0, 158.5, 158.6; ^{31}P NMR (162 MHz, $CDCl_3$) δ 148.6, 148.5; MS (ESI) *m/z* calcd for $C_{50}H_{65}N_6O_9PS_4Na$ $[M + Na]^+$ 1075.33, found 1075.42.

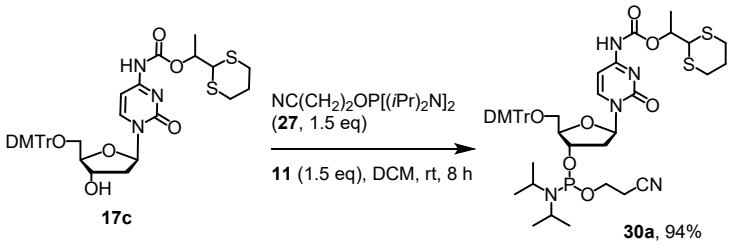


*Compound **5dTme***: Synthesized using the procedure for **5dCpe**. Compound **7c** (0.2 g, 1.2 mmol, 1.5 equiv.), diisopropyl amine (1.7 mL, 8.0 mmol, 10 equiv.), diethyl ether (15 mL), bis(diisopropylamino)chlorophosphine (0.26 g, 1.2 mmol, 1.5 equiv.), **10** (0.44 g, 0.80 mmol, 1 equiv.), diisopropylammonium tetrazolide (**11**, 0.26 g, 1.2 mmol, 1.5 equiv.) and ACN (10 mL) were used. Product **5dTme** was purified with flash chromatography by dissolving the sample in the solvent mixture of hexanes/EtOAc 1:1 with 5% Et_3N, loading onto a column (SiO_2), and eluting with the same solvent mixture: mixture of diastereomers; 0.78 g, 77%; white foam; TLC R_f = 0.5 and 0.55 (SiO_2, hexanes/EtOAc 1:1 with 5% Et_3N); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.17-1.26 (m, 12H), 1.48 (dd, J = 4.1, 2.3 Hz, 3H), 1.86-1.93 (m, 2H), 2.66-2.98 (m, 11H), 3.28-3.41 (m, 2H), 3.75 (s, 6H), 4.05-4.10 (m, 1H), 4.12-4.16 (m, 1H), 4.24-4.29 (m, 0.5H), 4.34-4.38 (m, 0.5H), 4.67-4.76 (m, 1H), 5.27-5.33 (m, 1H), 6.45 (t, J = 7.1 Hz, 1H), 6.73-6.77 (m, 4H), 7.14-7.27 (m, 7H), 7.35 (d, J = 8.5 Hz, 2H), 8.14 (d, J = 8.1 Hz, 1H), 8.41 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.2, 20.3, 23.0, 23.1, 23.4, 24.0, 24.9, 25.0, 25.1, 26.1, 26.5, 29.1, 29.6, 30.4, 30.6, 30.7, 43.5, 43.6, 44.8, 45.4, 51.1, 55.5, 63.7, 72.85, 72.88, 85.0, 85.1, 86.1, 86.7, 94.6, 113.27, 113.29, 127.0, 128.0, 128.3, 130.18, 130.20, 135.7, 135.8, 141.5, 144.6, 149.4, 150.2, 151.0, 152.8, 158.6; ^{31}P NMR (162 MHz, $CDCl_3$) δ 148.6, 148.5; MS (ESI) *m/z* calcd for $C_{43}H_{56}N_3O_8PS_2Na$ $[M + Na]^+$ 860.31, found 860.50.

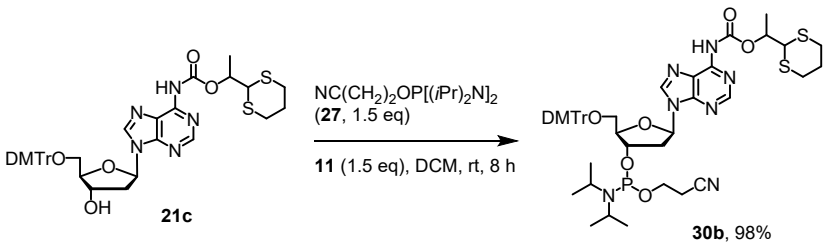


*Compound **13dTme***: Synthesized using the procedure for **5dCpe**. Compound **7c** (0.64 g, 3.9 mmol, 1.5 equiv.), diisopropyl amine (3.6 mL, 26.2 mmol, 10 equiv.), diethyl ether (15 mL), bis(diisopropylamino)chlorophosphine (1.04 g, 3.9 mmol, 1.5 equiv.), **12** (1.89 g, 2.62 mmol, 1 equiv.), diisopropylammonium tetrazolide (**11**, 0.67 g, 3.9 mmol, 1.5 equiv.) and ACN (10 mL) were used. Product **13dTme** was purified with flash chromatography by dissolving the sample in the solvent mixture of hexanes/EtOAc 1:2 with 5% Et_3N, loading onto a column (SiO_2), and eluting with the same solvent mixture: mixture of diastereomers; 2.28 g, 87%; white foam; TLC R_f = 0.3 and 0.4 (SiO_2, hexanes/EtOAc 1:2 with 5% Et_3N); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.13-1.20 (m,

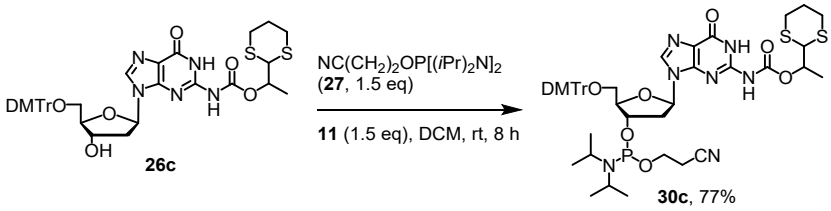
12H), 1.36-1.40 (m, 3H), 1.78-1.91 (m, 2H), 2.03-2.10 (m, 1.5H), 2.25-2.36 (m, 1H), 2.43-2.55 (m, 1.5H), 2.71-2.91 (m, 5H), 3.31 (dd, J = 10.5, 3.0 Hz, 0.5H), 3.35 (dd, J = 11.6, 2.9 Hz, 0.5H), 3.41-3.61 (m, 4H), 4.02-4.06 (m, 1H), 4.09-4.15 (m, 1H), 4.60-4.67 (m, 1H), 6.38 (dt, J = 7.7, 2.0 Hz, 1H), 7.22-7.31 (m, 9H), 7.38-7.36 (m, 6H), 7.56 (d, J = 1.2 Hz, 0.5H), 7.62 (d, J = 1.2 Hz, 0.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.1, 20.2, 20.3, 20.4, 23.0, 23.1, 23.4, 24.0, 24.9, 25.0, 25.02, 26.1, 26.4, 26.5, 29.1, 30.3, 30.5, 40.5, 40.6, 43.3, 43.5, 43.6, 43.64, 44.8, 45.4, 54.65, 54.71, 63.8, 63.9, 72.3, 72.5, 72.8, 73.5, 73.7, 73.9, 84.9, 85.1, 85.5, 86.1, 87.7, 111.27, 111.28, 127.6, 128.2, 128.8, 128.9, 135.9, 143.4, 143.5, 150.3, 163.7; ^{31}P NMR (162 MHz, $CDCl_3$) δ 148.7, 148.5; MS (ESI) *m/z* calcd for $C_{41}H_{52}N_3O_6PS_2Na$ $[M + Na]^+$ 800.29, found 800.58.



*Compound **30a***: To a solution of **17c** (1.0 g, 1.39 mmol, 1.0 equiv.) in dry DCM (30mL) was added diisopropylammonium tetrazolide (**11**, 356.6 mg, 2.08 mmol, 1.5 equiv.) and 2-cyanoethyl *N*,*N*,*N*′,*N*′-tetraisopropylphosphorodiamidite (**27**, 0.66 mL, 2.08 mmol, 1.5 equiv.) at rt under nitrogen. After stirring overnight, the mixture was concentrated to dryness. Product **30a** was purified by dissolving the sample in the solvent mixture of hexanes/EtOAc 1:3 with 5% Et_3N, loading onto a column (SiO_2), and eluting with the same solvent mixture: mixture of diastereomers; 1.20 g, 94%; white foam; TLC R_f = 0.4 and 0.45 (SiO_2, hexanes/EtOAc 1:3 with 5% Et_3N); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01-1.14 (m, 12H), 1.30 (t, J = 5.7 Hz, 3H), 1.66-1.75 (m, 1H), 1.82-1.90 (m, 1H), 2.31 (t, J = 6.2 Hz, 0.5H), 2.47 (t, J = 6.1 Hz, 1H), 2.55-2.64 (m, 4H), 2.67-2.79 (m, 2H), 3.06-3.14 (m, 0.5H), 3.20-3.28 (m, 1H), 3.31-3.47 (m, 4H), 3.64 (s, 6H), 3.92 (t, J = 5.6 Hz, 1H), 4.00-4.10 (m, 2H), 4.44-4.51 (m, 1H), 5.02-5.07 (m, 1H), 6.02 (s, 0.25H), 6.09-6.14 (m, 1H), 6.69-6.74 (m, 4H), 6.78 (brs, 0.5H), 7.06-7.18 (m, 6H), 7.25-7.28 (m, 2H), 7.62 (s, 0.25H), 8.08 (d, J = 7.4 Hz, 0.6H), 8.16 (d, J = 6.7 Hz, 0.4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.7, 14.45, 14.49, 20.28, 20.43, 20.64, 22.5, 23.1, 23.2, 23.2, 23.4, 24.78, 24.84, 24.9, 25.6, 26.3, 28.0, 28.1, 29.1, 41.1, 43.31, 43.35, 43.47, 44.7, 45.42, 46.2, 55.4, 58.4, 58.6, 59.5, 60.5, 62.1, 65.3, 71.53, 71.7, 74.2, 74.39, 85.7, 86.9, 95.3, 113.3, 117.5, 117.7, 117.8, 127.2, 128.1, 128.3, 130.2, 135.25, 135.29, 135.4, 144.07, 144.2, 154.6, 158.6, 162.5, 162.7; ^{31}P NMR (162 MHz, $CDCl_3$) δ 149.7, 150.25, 150.28; HRMS (ESI) *m/z* calcd for $C_{46}H_{58}N_5O_9PS_2H$ $[M + H]^+$ 920.3492, found 920.3477.

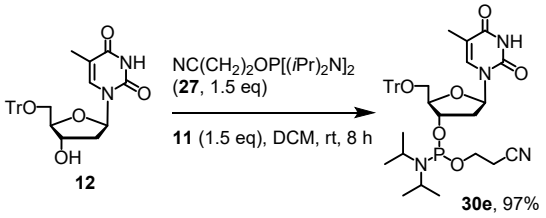


*Compound **30b***: Synthesized using the procedure for **30a**. Compound **21c** (1.0 g, 1.34 mmol, 1.0 equiv.), DCM (30 mL), diisopropylammonium tetrazolide (**11**, 356.6 mg, 2.08 mmol, 1.5 equiv.) and 2-cyanoethyl *N*,*N*,*N*′,*N*′-tetraisopropylphosphorodiamidite (**27**, 0.66 mL, 2.08 mmol, 1.5 equiv.) were used. Product **30b** was purified by dissolving the sample in the solvent mixture of hexanes/EtOAc 1:3 with 5% Et_3N, loading onto a column (SiO_2), and eluting with the same solvent mixture: mixture of diastereomers; 1.24 g, 98%; white foam; TLC R_f = 0.3 and 0.4 (SiO_2, hexanes/EtOAc 1:3 with 5% Et_3N); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.99 (d, J = 6.8 Hz, 3H), 1.04-1.15 (m, 12H), 1.68-1.75 (m, 1H), 1.87-1.90 (m, 1H), 2.33 (t, J = 6.3 Hz, 1H), 2.46-2.49 (m, 2H), 2.57-2.60 (m, 2H), 2.70-2.80 (m, 2H), 2.84-2.90 (m, 1H), 3.21-3.25 (m, 1H), 3.29-3.42 (m, 2H), 3.34-3.52 (m, 3H), 3.61 (d, J = 2.2 Hz, 6H), 3.68-3.74 (m, 0.5H), 3.93-3.99 (m, 1H), 4.01-4.05 (m, 1.5H), 4.17-4.20 (m, 1H), 4.65-4.70 (m, 1H), 5.14-5.20 (m, 1H), 6.33-6.36 (m, 1H), 6.61-6.65 (m, 4H), 7.02-7.16 (m, 7H), 7.24-7.26 (m, 2H), 7.61 (s, 0.3H), 8.17 (dd, J = 8.4, 2.9 Hz, 1H), 8.57-8.59 (m, 1H), 9.72 (brs, 0.7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5, 18.0, 18.1, 20.2, 20.3, 20.4, 20.5, 20.6, 20.7, 22.5, 23.11, 23.19, 23.2, 23.7, 24.74, 24.81, 24.88, 25.9, 29.0, 29.5, 29.6, 39.3, 39.4, 43.4, 43.5, 45.4, 45.5, 45.8, 46.3, 51.05, 51.14, 55.4, 58.3, 58.5, 58.6, 58.7, 60.5, 63.5, 63.7, 72.7, 73.6, 73.7, 74.2, 74.4, 85.02, 85.06, 85.88, 85.96, 86.12, 86.15, 86.51, 86.52, 94.61, 113.2, 117.2, 117.6, 117.8, 122.8, 126.9, 127.9, 128.12, 128.15, 130.05, 130.09, 135.7, 142.0, 142.1, 144.6, 149.8, 150.7, 151.08, 151.12, 152.6, 158.5; ^{31}P NMR (162 MHz, $CDCl_3$) δ 149.6, 149.7; HRMS (ESI) *m/z* calcd for $C_{47}H_{58}N_7O_8PS_2H$ $[M + H]^+$ 944.3604, found 944.3589.



*Compound **30c***: Synthesized using the procedure for **30a**. Compound **26c** (1.0 g, 1.32 mmol, 1.0 equiv.), DCM (30 mL), diisopropylammonium tetrazolide (**11**, 338.58 mg, 1.98 mmol, 1.5 equiv.) and 2-cyanoethyl *N*,*N*,*N*′,*N*′-tetraisopropylphosphorodiamidite (**27**, 0.63 mL, 1.98 mmol, 1.5 equiv.) were used. Product **30c** was purified by dissolving the sample in the solvent mixture of hexanes/acetone 1:1 with 5% Et_3N, loading onto a column (SiO_2), and eluting with the same solvent mixture: mixture of diastereomers; 945 mg, 77%; pale yellow foam; TLC R_f = 0.2 and 0.25

(SiO_2, hexanes/acetone 1:1 with 5% Et_3N); ^1H NMR (400 MHz, $CDCl_3$) δ 0.92-1.09 (m, 12H), 1.26 (d, J = 4.9 Hz, 3H), 1.65-1.81 (m, 2H), 1.95 (s, 1H), 2.19-2.39 (m, 2H), 2.45-2.56 (m, 4H), 2.66-2.75 (m, 2H), 3.05-3.23 (m, 2H), 3.30-3.47 (m, 3H), 3.58 (d, J = 5.4 Hz, 6H), 3.90-4.13 (m, 1H), 4.42-4.60 (m, 1H), 5.06-5.10 (m, 1H), 6.08-6.13 (m, 0.5H), 6.18-6.26 (m, 0.5H), 6.64 (dd, J = 11.2, 8.0 Hz, 4H), 7.01-7.16 (m, 7H), 7.24-7.33 (m, 2.5H), 7.60 (s, 0.15H), 7.67 (s, 0.5H), 8.01 (d, J = 7.6 Hz, 0.35H), 10.28 (brs, 0.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.3, 15.0, 18.2, 20.2, 20.5, 20.6, 23.1, 23.2, 23.4, 24.6, 24.8, 25.7, 28.4, 28.7, 28.8, 29.5, 29.8, 31.1, 34.6, 43.3, 43.4, 45.3, 45.4, 45.5, 50.1, 50.3, 55.4, 58.2, 58.50, 58.55, 63.85, 63.86, 73.40, 73.42, 86.5 , 113.2, 113.3, 117.7, 117.9, 120.5, 126.9, 127.86, 127.94, 128.1, 130.1, 135.65, 135.72, 144.58, 144.6, 144.7, 147.9, 148.8, 153.96, 154.1, 156.4, 158.50, 158.52; ^{31}P NMR (162 MHz, $CDCl_3$) δ 149.38, 149.46, 149.50, 149.68, 149.98; HRMS (ESI) *m/z* calcd for $C_{47}H_{58}N_7O_9PS_2H$ $[M + H]^+$ 960.3553, found 960.3528.



*Compound **30e***: Synthesized using the procedure for **30a**. Compound **12** (2.00 g, 4.13 mmol, 1 equiv.), DCM (30 mL), diisopropylammonium tetrazolide (1.06 g, 6.19 mmol, 1.5 equiv.), and 2-cyanoethyl *N*,*N*,*N*′,*N*′-tetraisopropylphosphorodiamidite (**27**, 1.96 mL, 6.19 mmol, 1.5 equiv.) were used. Product **30e** was purified by dissolving the sample in the solvent mixture of hexanes/EtOAc 1:2 with 5% Et_3N, loading onto a column (SiO_2), and eluting with the same solvent mixture: mixture of diastereomers; 2.74 g, 97%; white foam; TLC R_f = 0.5 and 0.6 (SiO_2, hexanes/EtOAc 1:2 with 5% Et_3N); ^1H NMR (400 MHz, $CDCl_3$) δ 1.10-1.16 (m, 12H), 1.41 (d, J = 4.1 Hz, 3H), 2.27-2.35 (m, 2H), 2.49-2.57 (m, 2H), 3.26-3.31 (m, 1H), 3.46-3.61 (m, 4H), 3.66-3.77 (m, 1H), 4.09-4.14 (m, 1H), 4.59-4.66 (m, 1H), 6.35-6.41 (m, 1H), 7.17-7.27 (m, 9H), 7.35-7.38 (m, 6H), 7.52 (s, 0.5H), 7.58 (s, 0.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.17, 2.49, 20.57, 20.8, 24.79, 24.83, 24.86, 24.90, 24.98, 40.3, 43.4, 43.5, 58.3, 58.5, 58.7, 63.5, 63.7, 73.4, 73.6, 73.9, 74.1, 84.80, 84.86, 85.3, 85.7, 87.6, 94.6, 111.5, 111.6, 117.6, 117.8, 127.6, 128.2, 128.3, 135.7, 143.34, 143.37, 150.8, 150.9, 164.37, 164.42; ^{31}P NMR (162 MHz, $CDCl_3$) δ 149.5, 149.9; HRMS (ESI) *m/z* calcd for $C_{38}H_{45}N_4O_6PH$ $[M + H]^+$ 685.3155, found 685.3144.

References

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(2) A. Apostle, S. Fang. Dissolve-Spin: Desalting Oligonucleotides for MALDI MS Analysis. *Journal of Mass Spectrometry* **2022**, *57*, e4893. doi:10.1002/jms.4893.