Supporting Information for

Synthesis of 2′-*O*-monohaloethoxymethyl-modified RNAs and their duplex formation ability

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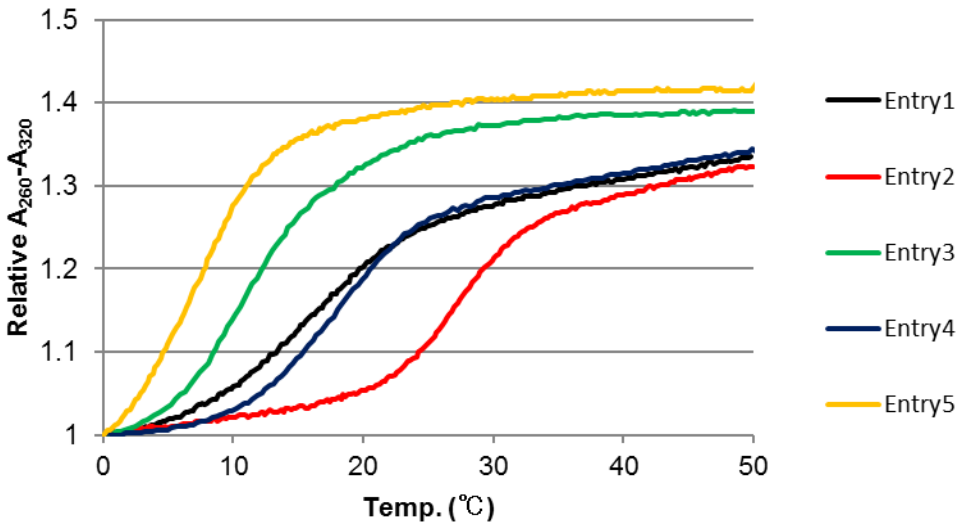


Fig. S1 UV melting curves of rU_{12}/rA_{12}, 2′-*O*-modified rU_{12}/rA_{12}, and rU_{12}/2′-*O*-modified rA_{12} (Corresponding to Entries1–5 in Table 1)

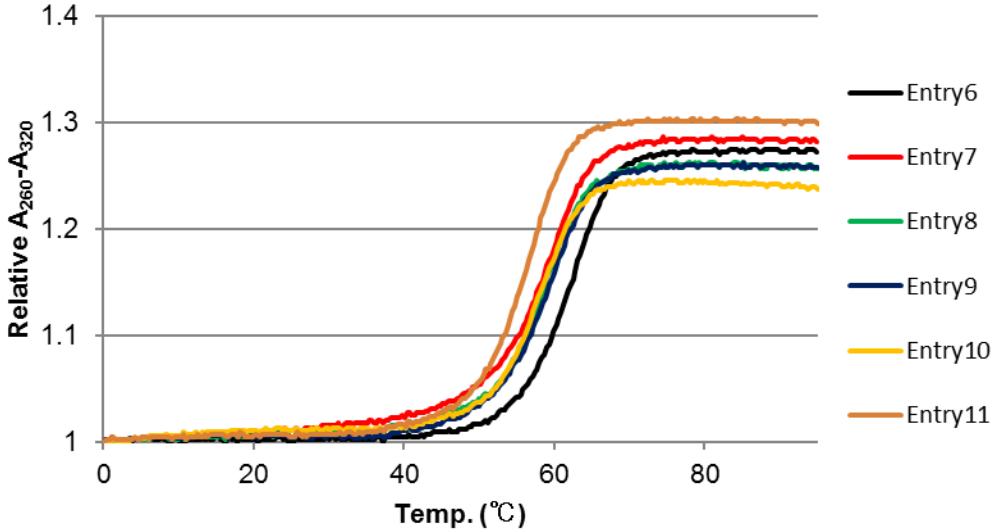


Fig. S2 UV melting curves of $r(GUCA)_3/r(UGAC)_3$ and 2′-*O*-MCEM-modified $r(GUCA)_3$/ $r(UGAC)_3$ (Corresponding to Entries 6–11 in Table 1)

Table S1 melting temperature of rU_{12}/rA_{12}, 2′-*O*-EOM rU_{12}/rA_{12}, and 2’-*O*-MCEM rU_{12}/rA_{12} of various concentrations.

$C_{tot}/\mu M$	unmodified	EOM	MCEM
16	-	16.8	30.1
11	19.6	15.9	29.2
8.0	18.0	15.1	28.4
5.7	17.4	14.4	27.5
4.0	16.4	13.6	26.8
2.8	15.1	12.9	26.3
2.0	-	12.1	25.8
1.4	12.7	-	

Compound **2**

Compound **1** (1.65g, 3.0 mmol) was dried with repeated coevaporation with pyridine and toluene, and dissolved in THF (11 mL). 2-Fluoroethanol (1.65 mL, 30 mmol) was added and the mixture was cooled to -40 °C. *N*-Iodosuccinimide (0.81 g, 3.6 mmol, in 8.1 mL of THF) was added, followed by trifluoromethanesulfonic acid (528 μL, 6.0 mmol in 7.3 mL of THF) added dropwise to the mixture. After 1 h, the reaction was quenched with triethylamine (7 mL). The resulting solution was diluted with dichloromethane (100 mL), and washed with 10% solution of $Na_2S_2O_3$ (80 mL × 3) and a saturated aqueous solution of $NaHCO_3$ (80 mL × 3). The water layers were combined and extracted with dichloromethane (50 mL × 3). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude product was purified with silica gel column chromatography [hexane–ethyl acetate (2:1, v/v)] to afford **2** (1.49 g, 2.64 mmol, 88%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.57 (1H, br), 7.90 (1H, *J* = 8.1 Hz), 5.76 (1H, s), 5.69 (1H, d, *J* = 8.1), 5.05-4.99 (2H, m), 4.68-4.53 (2H, m), 4.29-3.86 (7H, m), 1.10-0.91 (28H, m)

Compound **3**

Compound **2** (1.12 g, 2.0 mmol) was dried with repeated coevaporation with pyridine and toluene, and dissolved in methanol (9.5 mL). Ammonium fluoride (291 mg, 8 mmol) was added, and the solution was heated to 50 °C. After 19 h, the reaction was quenched with methoxytrimethylsilane (1 mL), and the mixture was concentrated. Acetonitrile (100 mL) was added and insoluble solid was removed by filtration. The residue was washed with hexane (60 mL × 3) and the resulting solution was extracted with acetonitrile (50 mL × 2). All acetonitrile solutions were combined and concentrated. The mixture was dried with repeated coevaporation with pyridine, and dissolved in pyridine (20 mL). 4,4′-dimethoxytritylchloride (714 mg, 2.1 mmol) was added and the solution was stirred for 20 h. The reaction was quenched with methanol (1 mL). The solution was diluted with chloroform (150 mL) and then washed with a saturated aqueous solution of $NaHCO_3$ (100 mL × 3). The water layers were combined and extracted with chloroform (80 mL × 3). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude product was purified with silica gel column chromatography [dichloromethane–methanol–pyridine (99.5:0:0.5 to 98.5:1:0.5, v/v/v)] to afford **3** (908 mg, 1.46 mmol, 73%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (1H, br), 7.93 (1H, d, *J* = 8.4 Hz), 7.39-7.16 (9H, m), 6.87-6.82 (4H, m), 6.02 (1H, d, *J* = 3.3 Hz), 5.29 (1H, dd, *J* = 8.1, 2.4 Hz), 5.04 (1H, d, *J* = 6.6 Hz), 4.93 (1H, d, *J* = 6.6 Hz), 4.67-4.64 (1H, m), 4.52-4.46 (2H, m), 4.36-4.34 (1H, m), 4.10-4.08 (1H, m), 3.94-3.80 (8H, m), 3.53-3.52 (2H, m), 2.61 (1H, d, *J* = 6.9 Hz).

Compound **4**

Compound **3** (908 mg, 1.46 mmol) was dried with repeated coevaporation with pyridine and toluene, and dissolved in dichloromethane (8.0 mL). To the solution, *N*,*N*-diisopropylethylamine (744 μL, 4.4 mmol) was added followed by 2-cyanoethyl *N*,*N*-diisopropylchlorophosphoramidite (325 μL, 2.92 mmol, in 7 mL of dichloromethane) added dropwise. After 1.5 h, the reaction was quenched with ethanol (2 mL). The solution was diluted with dichloromethane (80 mL), and washed with a saturated aqueous solution of $NaHCO_3$ (80 mL × 3). The water layers were combined and extracted with chloroform (80 mL × 3). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude product was purified with silica gel column chromatography [hexane-ethyl acetate (7:3 to 0:10, v/v)] to afford **4** (918 mg, 1.12 mmol, 77%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.80-8.20 (1H, br), 7.95-7.90 (1H, m), 7.41-6.84 (13H, m), 6.06 (1H, d, J = 3.6 Hz), 5.26 (1H, dd, J = 12.6, 7.8 Hz), 5.01-4.86 (2H, m), 4.67-4.43 (4H, m), 4.28-4.20 (1H, m), 3.97-3.40 (14H, m), 2.68-2.41 (2H, m), 1.28-1.03 (12H, m).

^{31}P NMR (121 MHz, $CDCl_3$) δ 151.1, 150.8.

MALDI-TOF MS: calcd for $C_{42}H_{52}FKN_4O_{10}P$ m/z $[M + K]^+$ 861.30 Found 861.49.

Compound **6**

Compound **5** (1.83 g, 3.0 mmol) was dried with repeated coevaporation with pyridine and toluene, and then dissolved in THF (11 mL). 2-Fluoroethanol (825 μL, 15 mmol) was added and the mixture cooled to –40 °C. *N*-Iodosuccinimide (0.81 g, 3.6 mmol, in 8.1 mL of THF) was added, and then trifluoromethanesulfonic acid (351 μL in 7 mL of THF) added in a dropwise manner. After 1 h, the reaction was quenched with triethylamine (7 mL). The resulting solution was diluted with dichloromethane (100 mL), and washed with 10% solution of $Na_2S_2O_3$ (100 mL × 2) and a saturated aqueous solution of $NaHCO_3$ (100 mL × 3). The water layers were combined and extracted with dichloromethane (50 mL × 3). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude product was purified with silica gel column chromatography [hexane–ethyl acetate (2:1, v/v)] to afford **6** (1.19 g, 1.90 mmol, 63%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.63 (2H, s), 8.30 (1H, s), 6.10 (1H, s), 5.05 (2H, s), 4.78-4.73 (1H, m), 4.68-4.66 (1H, m), 4.55-4.50 (2H, m), 4.26 (1H, d, J = 13.5 Hz), 4.17 (1H, d, J = 9.3 Hz), 4.06-3.80 (3H, m), 2.62 (3H, s), 1.11-0.99 (28H, m).

Compound **7**

Compound **6** (0.885 g, 1.41 mmol) was dissolved in THF (15 mL) and triethylammonium trifluoride (345 μL, 2.1 mmol) was added. The solution was stirred at 50 °C for 6 h and the reaction was quenched with methoxytrimethylsilane (0.3 mL), and the mixture was then

concentrated. Acetonitrile was added and the insoluble solid was removed by filtration. The residue was washed with hexane and the resulting solution extracted with acetonitrile. All the acetonitrile solutions were combined and concentrated. The mixture was dissolved in THF (6 mL), and the solution was added to hexane (300 mL) in a dropwise manner. The solid obtained by reprecipitation was dried with repeated coevaporation with pyridine, and dissolved in pyridine (11 mL). 4,4′-Dimethoxytritylchloride (434 mg, 1.1 mmol) was added and the solution stirred for 16 h. The reaction was quenched with methanol (1 mL). The solution was diluted with chloroform (150 mL) and washed with a saturated aqueous solution of $NaHCO_3$ (100 mL × 3). The water layers were combined and extracted with chloroform (80 mL × 3). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude product was purified with silica gel column chromatography [dichloromethane–methanol–pyridine (99.5:0:0.5 to 97.5:2:0.5, v/v/v)] to afford **7** (758 mg, 1.08 mmol, 76%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.60 (1H, s), 8.37 (1H, s), 8.15 (1H, s), 7.44-7.11 (9H, m), 6.80 (4H, d, *J* = 8.7 Hz), 6.23 (1H, d, J = 4.8 Hz), 4.97 (1H, t, *J* = 5.1 Hz), 4.88 (2H, s), 4.59-4.54 (2H, m), 4.40-4.39 (1H, m), 4.29-4.25 (1H, m), 3.81-3.68 (8H, m), 3.53-3.41 (4H), 2.69-2.67 (1H, m), 2.63 (3H, s).

Compound **8**

Compound **7** (726 mg, 1.03 mmol) was dried with repeated coevaporation with pyridine and toluene, and dissolved in dichloromethane (8.0 mL). To the solution, *N*,*N*-diisopropylethylamine (600 μL, 3.5 mmol) was added, followed by 2-cyanoethyl *N*,*N*-diisopropylchlorophosphoramidite (390 μL, 1.75 mmol, in 3.6 mL of dichloromethane) added in a dropwise manner. After 3 h, the reaction was quenched with ethanol (2 mL). The solution was diluted with dichloromethane (80 mL), and washed with a saturated aqueous solution of $NaHCO_3$ (80 mL × 3). The water layers were combined and extracted with dichloromethane (50 mL × 3). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude product was purified with silica gel column chromatography [dichloromethane-methanol–pyridine (99.5:0:0.5 to 98:1.5:0.5, v/v/v)], and then with reprecipitation (5 mL dichloromethane/ 300 mL ice cold hexane) to afford **8** (342 mg, 378 μmol, 37%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.60 (1H, s), 8.49 (1H, s), 8.18 (1H, s), 7.42-7.18 (9H, s), 6.82-6.75 (4H, m), 6.24-6.19 (1H, m), 5.12 (1H, t, *J* = 5.4 Hz), 4.92-4.69 (3H, m), 4.48-4.31 (3H, m) 3.95-3.34 (14H, m), 2.67-2.34 (5H, m), 1.20-1.06 (12H, m)

^{31}P NMR (121 MHz, $CDCl_3$) δ 151.8, 151.3.

MALDI-TOF MS: calcd for $C_{45}H_{55}FKN_7O_9P$ m/z $[M + K]^+$: 926.34 Found 926.55.

Compound **9**

Compound **5** (3.68 g, 6.0 mmol) was dried with repeated coevaporation with pyridine and

toluene, and then dissolved in THF (20 mL). 2-Chloroethanol (4.04 mL, 60 mmol) was added and the mixture was cooled to −40 °C. *N*-Iodosuccinimide (1.62 g, 7.2 mmol, in 16.2 mL of THF) was added and trifluoromethanesulfonic acid (1.05 mL in 21 mL of THF) was added dropwise to the mixture. After 5.5 h, the reaction was quenched with triethylamine (10 mL). The resulting solution was diluted with chloroform (300 mL), and washed with 10% solution of $Na_2S_2O_3$ (150 mL × 2) and a saturated aqueous solution of $NaHCO_3$ (120 mL × 3). The water layers were combined and extracted with chloroform (100 mL × 3). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude product was purified with silica gel column chromatography [hexane-ethyl acetate (2:1, v/v), and dichlromethane−methanol (99:1, v/v)] to afford **9** (1.53 g, 2.38 mmol, 40%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.65 (2H, m), 8.31 (1H, s), 6.10 (1H, s), 5.08-5.02 (2H, m), 4.74-4.70 (1H, m), 4.54-4.53 (1H, m), 4.55-4.50 (2H, m), 4.26 (1H, d, *J* = 13.2 Hz), 4.17 (1H, m), 4.08-4.01 (2H, m), 3.93-3.85 (1H, m), 2.62 (3H, s), 1.11-0.97 (28H, m).

Compound **10**

Compound **9** (1.53 g, 2.38 mmol) was dissolved in THF (25 mL) and triethylammonium trifluoride (715 μL, 4.4 mmol) was added. The solution was stirred at 50 °C for 6 h and the reaction was quenched with methoxytrimethylsilane (1 mL), followed by concentration of the mixture. The mixture was dissolved in THF (5 mL), and the solution was added to hexane (400 mL) in a dropwise manner. The solid obtained by the reprecipitation was dried with repeated coevaporation with pyridine, and dissolved in pyridine (20 mL). 4,4'-Dimethoxytritylchloride (850 mg, 2.50 mmol) was added. After 2 h, another 4,4'-dimethoxytritylchloride (120 mg) was added again and the solution was stirred for 12 h. The reaction was quenched with methanol (3 mL). The solution was diluted with chloroform (200 mL) and washed with a saturated aqueous solution of $NaHCO_3$ (140 mL × 3). The water layers were combined and extracted with chloroform (50 mL × 3). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude product was purified with silica gel column chromatography [dichloromethane−methanol−pyridine (99.5:0:0.5 to 98.5:1:0.5, v/v/v)] to afford **10** (1.68 g, 2.38 mmol, quant).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.61 (1H, s), 8.56 (1H, s), 8.17 (1H, s), 7.43-7.22 (9H, m), 6.84-6.79 (4H, m), 6.24 (1H, d, *J* = 5.1 Hz), 4.97 (1H, t, *J* = 5.1 Hz), 4.88 (2H, s), 4.59-4.57 (1H, m), 4.28-4.27 (1H, m), 3.80-3.43 (12H, m), 2.70 (1H, d, J = 4.8 Hz), 2.62 (3H, s).

Compound **11**

Compound **10** (1.68 g, 2.38 mmol) was dried with repeated coevaporation with pyridine and toluene, and dissolved in dichloromethane (15 mL). To the solution, *N*,*N*-diisopropylethylamine (1.4 mL, 8.2 mmol) was added, followed by 2-cyanoethyl *N*,*N*-

diisopropylchlorophosphoramidite (802 μL, 3.6 mmol, in 9.5 mL of dichloromethane) was added in a dropwise manner. After 5 h, the reaction was quenched with ethanol (1 mL). The solution was diluted with chloroform (150 mL), and washed with a saturated aqueous solution of $NaHCO_3$ (100 mL × 3). The water layers were combined and extracted with chloroform (50 mL × 3). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude product was purified with silica gel column chromatography [dichloromethane−methanol−pyridine (99.5:0:0.5 to 98:1.5:0.5, v/v/v), and ethyl acetate-hexane (3:1, v/v, containing 0.5% of triethylamine)] to afford **11** (1.04 g, 1.15 mmol, 48%).
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.60 (1H, s), 8.49 (1H, s), 8.18 (1H, s), 7.43-7.21 (9H, s), 6.82-6.78 (4H, m), 6.24-6.20 (1H, m), 5.10 (1H, t, *J* = 6.0 Hz), 4.92-4.62 (3H, m), 4.42-4.33 (1H, m) 3.95-3.35 (16H, m), 2.67-2.37 (5H, m), 1.20-1.06 (12H, m)
^{31}P NMR (121 MHz, $CDCl_3$) δ 151.3, 150.9.
MALDI-TOF MS: calcd for $C_{45}H_{55}ClKN_7O_9P$ m/z $[M + K]^+$: 942.31 Found 942.49.

Compound **13**

Compound **12** (3.53 g, 6.0 mmol) was dried with repeated coevaporation with pyridine and toluene, and then dissolved in THF (44 mL). 2-Chloroethanol (2.0 mL, 30 mmol) was added and the mixture was cooled to -40 °C. *N*-Iodosuccinimide (1.62 g, 7.2 mmol) was added, followed by trifluoromethanesulfonic acid (1.05 mL in 21 mL of THF) in a dropwise manner. After 2.5 h, the reaction was quenched with triethylamine (6 mL). The resulting solution was diluted with chloroform (150 mL), and washed with 10% solution of $Na_2S_2O_3$ (100 mL × 2) and a saturated aqueous solution of $NaHCO_3$ (100 mL × 3). The water layers were combined and extracted with chloroform (100 mL × 3). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude product was purified with silica gel column chromatography [hexane−ethyl acetate (4:1 to 2:1, v/v)] to afford **13** (2.73 g, 4.4 mmol, 73%).
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.53 (1H, br), 8.30 (1H, d, *J* = 7.5 Hz), 7.38 (1H, d, *J* = 7.5), 5.80 (1H, s), 5.14 (1H, d, *J* = 6.9), 5.01 (1H, d, *J* = 6.6), 4.32-4.19 (4H, m), 4.03-3.89 (3H, m), 3.70 (2H, m). 2.23 (3H, s), 1.11-0.94 (28H, m).

Compound **14**

Compound **13** (2.42 g, 3.9 mmol) was dissolved in THF (10 mL) and triethylammonium trifluoride (956 μL, 5.9 mmol) was added. The solution was stirred at 50 °C for 23 h and the reaction was quenched with methoxytrimethylsilane (1 mL), followed by concentration of the mixture. The mixture was washed with hexane and acetonitrile. The insoluble solid was dried with repeated coevaporation with pyridine, and dissolved in pyridine (30 mL). 4,4'-dimethoxytritylchloride (1.2 g, 3.5 mmol) was added. After 21 h, the reaction was quenched with methanol (6 mL). The solution was diluted with chloroform (100 mL) and washed with a

saturated aqueous solution of $NaHCO_3$ (150 mL × 3). The water layers were combined and extracted with chloroform (50 mL × 2). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude product was purified with silica gel column chromatography [dichloromethane−methanol−pyridine (99.5:0:0.5 to 98.5:1:0.5, v/v/v)] to afford **14** (1.91 g, 2.80 mmol, 73%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.47 (1H, d, J = 7.5 Hz), 8.18 (1H, br), 7.43-7.16 (9H, m), 7.06 (1H, d, *J* = 7.2 Hz), 6.89-6.85 (4H, m), 6.00 (1H, s), 5.22 (1H, d, *J* = 6.6 Hz), 5.01 (1H, d, *J* = 6.6 Hz), 4.50-4.40 (1H, m), 4.29-4.27 (1H, m), 4.09 (1H, d, *J* = 8.7 Hz), 3.93-3.88 (2H, m), 3.81 (6H, s), 3.66 (2H, t, *J* = 5.7 Hz), 3.60-3.50 (2H, m), 2.55 (1H, d, *J* = 9.0 Hz), 2.21 (3H, s)

Compound **15**

Compound **14** (1.91 g, 2.80 mmol) was dried with repeated coevaporation with pyridine and toluene, and dissolved in dichloromethane (28 mL). To the solution, *N*,*N*-diisopropylethylamine (1.4 mL, 8.2 mmol) was added, followed by 2-cyanoethyl *N*,*N*-diisopropylchlorophosphoramidite (940 μL, 4.2 mmol) in a dropwise manner. After 4.5 h, the reaction was quenched with ethanol (1 mL). The solution was diluted with chloroform (120 mL) and washed with a saturated aqueous solution of $NaHCO_3$ (100 mL × 3). The water layers were combined and extracted with chloroform (50 mL × 2). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude product was purified with silica gel column chromatography [ethyl acetate−hexane (3:7 to 10:0, v/v, containing 0.5% of pyridine)] to afford **15** (1.79 g, 2.03 mmol, 73%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.53-8.44 (1H, m), 8.38-8.24 (1H, m), 7.44-7.26 (9H, m), 6.99-6.84 (5H, m), 6.05 (1H, s), 5.09-4.96 (2H, m), 4.59-4.53 (1H, m), 4.38-4.24 (2H, m), 4.17-3.99 (1H, m), 3.87-3.44 (15H, m), 2.62-2.40 (2H, m), 2.19 (3H, s), 1.17-0.99 (12H, m).

^{31}P NMR (121 MHz, $CDCl_3$) δ 152.1, 150.7.

MALDI-TOF MS: calcd for $C_{44}H_{55}ClKN_5O_{10}P$ m/z $[M + K]^+$: 918.30 Found 918.48.

Compound **17**

Compound **16** (4.32 g, 6.0 mmol) was dried with repeated coevaporation with pyridine and toluene and dissolved in THF (40 mL). 2-Chloroethanol (4.02 mL, 60 mmol) was added and the mixture was cooled to -40 °C. *N*-Iodosuccinimide (1.62 g, 7.2 mmol) was added, and then trifluoromethanesulfonic acid (1.05 mL in 21 mL of THF) in a dropwise manner to the mixture. After 1 h, the reaction was quenched with triethylamine (5 mL). The resulting solution was diluted with chloroform (300 mL), and washed with 10% solution of $Na_2S_2O_3$ (200 mL × 2) and a saturated aqueous solution of $NaHCO_3$ (150 mL × 3). The water layers were combined and extracted with chloroform (50 mL × 3). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude product was purified with silica gel column

chromatography [dichloromethane−methanol (100:0 to 99:1, v/v)] to afford **17** (2.91 g, 3.87 mmol, 65%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 11.81 (1H, br), 9.02 (1H, br), 8.07 (1H, s), 7.41-7.36 (2H, m), 7.11 (1H, t, *J* =7.2 Hz), 7.01-6.96 (2H, m), 5.96 (1H, s), 5.07-4.99 (2H, d × 2, *J* = 6.6, 6.9 Hz), 4.70 (2H, s), 4.57-4.52 (1H, m), 4.33-3.89 (6H, m), 3.63 (2H, t, *J* = 6.0 Hz), 1.11-0.94 (28H, m).

Compound **18**

Compound **17** (2.53 g, 3.36 mmol) was dissolved in THF (16.8 mL) and triethylammonium trifluoride (920 μL, 5.65 mmol) was added. The solution was stirred at 50 °C for 5 h, and then the reaction was quenched with methoxytrimethylsilane (1 mL). The mixture was then stirred overnight and concentrated. The mixture was dissolved in THF (16.8 mL), and then the solution was added to hexane (400 mL) in a dropwise manner. The solid obtained with reprecipitation was dried with repeated coevaporation with pyridine, and dissolved in pyridine (30 mL). 4,4′-Dimethoxytritylchloride (1.2 g, 3.5 mmol) was added. After 18 h, the reaction was quenched with methanol (3 mL). The solution was diluted with chloroform (300 mL) and washed with a saturated aqueous solution of $NaHCO_3$ (150 mL × 3). The water layers were combined and extracted with chloroform (50 mL × 2). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude product was purified with silica gel column chromatography [dichloromethane-methanol-pyridine (99.5:0:0.5 to 98.5:1:0.5, v/v/v)] to afford **18** (0.82 g, 0.84 mmol, 25%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50-7.43 (3H, m), 7.34-7.11 (18H, m), 6.80-6.71 (8H, m), 5.65 (1H, d, *J* = 4.2 Hz), 4.63-4.50 (3H, m), 4.20 (1H, br), 4.09 (1H, d, *J* = 3.0 Hz), 3.72-3.38 (17 H), 3.28-3.23 (1H, m), 2.69 (1H, br).

Compound **19**

Compound **18** (727 mg, 741 μmol) was dried with repeated coevaporation with pyridine and toluene, and dissolved in dichloromethane (9 mL). To the solution, *N*,*N*-diisopropylethylamine (457 μL, 2.69 mmol) was added, followed by 2-cyanoethyl *N*,*N*-diisopropylchlorophosphoramidite (299 μL, 1.34 mmol) was added in a dropwise manner. After 5 h, the reaction was quenched with ethanol (1 mL). The solution was diluted with chloroform (150 mL), and washed with a saturated aqueous solution of $NaHCO_3$ (100 mL × 3). The water layers were combined and extracted with chloroform (50 mL × 2). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude product was purified with silica gel column chromatography [ethyl acetate–hexane (5:5 to 8:2, v/v, containing 0.5% of pyridine)], and then reprecipitation (4 mL dichloromethane/ 400 mL hexane, 5 times) to afford

19 (329 mg, 283 μmol, 38%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73-6.91 (20H, m), 6.80-6.70 (8H, m), 6.05-5.98 (1H, m), 5.93-5.80 (1H, m), 5.20-5.10 (1H, m), 4.85-4.78 (1H, m), 4.70-4.64 (1H, m), 4.58-4.50 (1H, m), 4.33-4.24 (1H, m), 3.97-3.40 (21H, m), 3.18-3.10 (1H, m), 2.68-2.26 (2H, m), 1.27-0.99 (12H, m).
^{31}P NMR (121 MHz, $CDCl_3$) δ 151.8, 151.3.
MALDI-TOF MS: calcd for $C_{64}H_{71}ClKN_7O_{11}P$ m/z $[M + K]^+$: 1218.43 Found 1218.64.

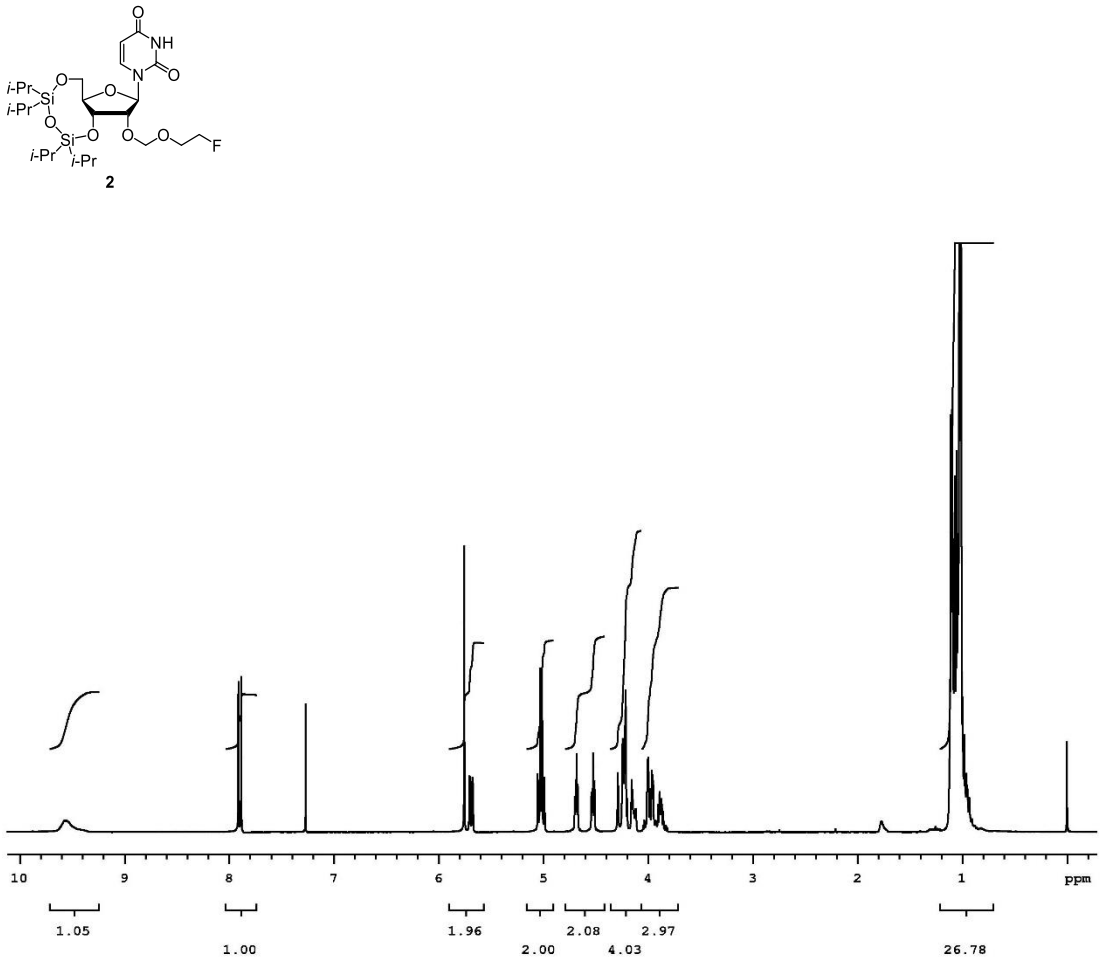
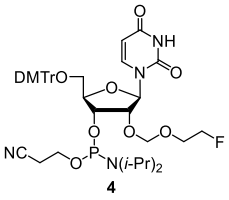


Fig. S3 ^{1}H-NMR spectra of compound **2** in $CDCl_3$.



4

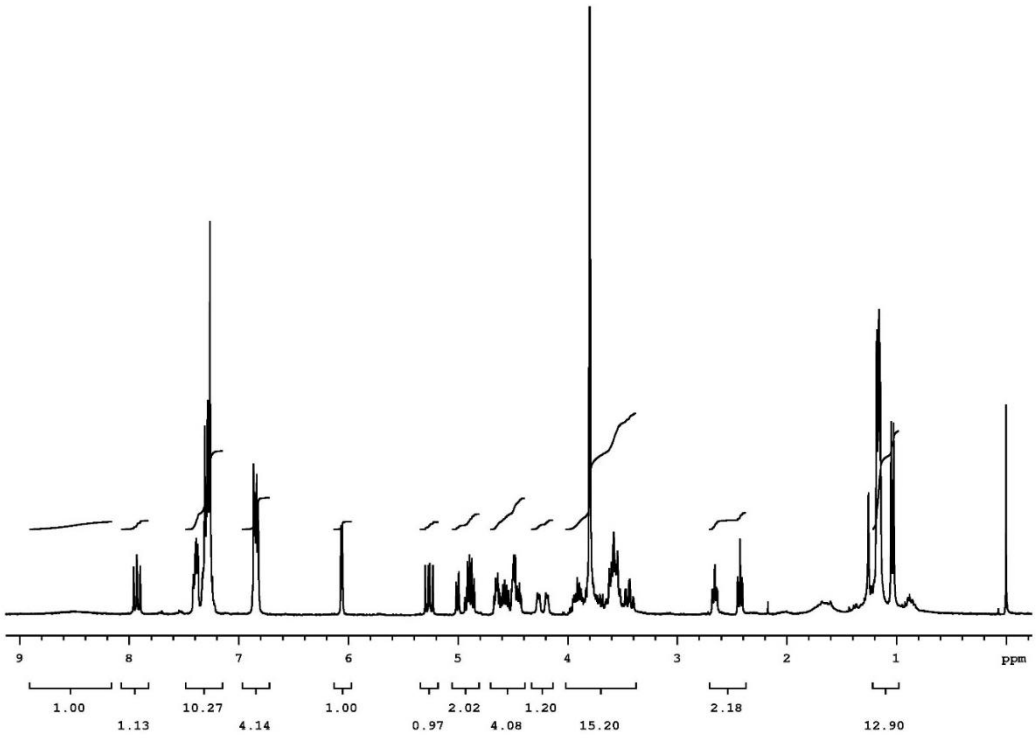


Fig. S4 ^{1}H-NMR spectra of compound **4** in $CDCl_3$.

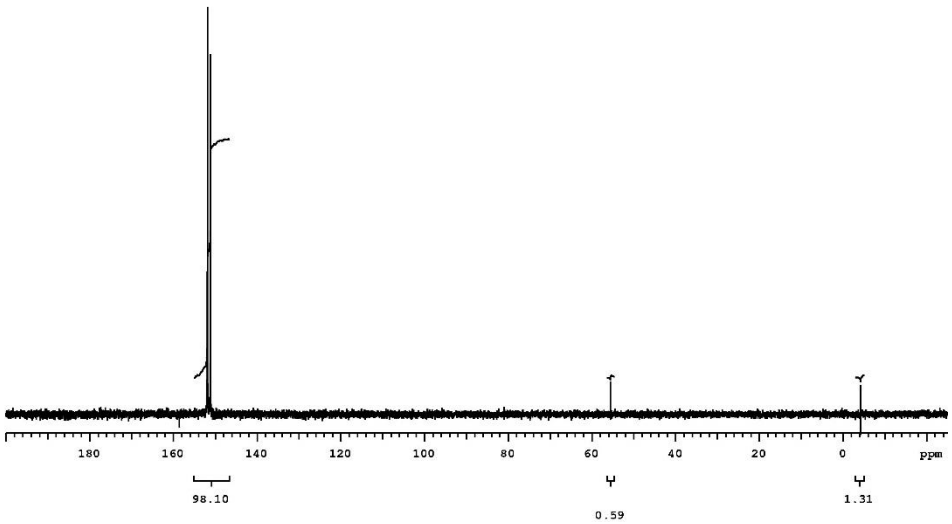


Fig. S5 ^{31}P-NMR spectra of compound **4** in $CDCl_3$.

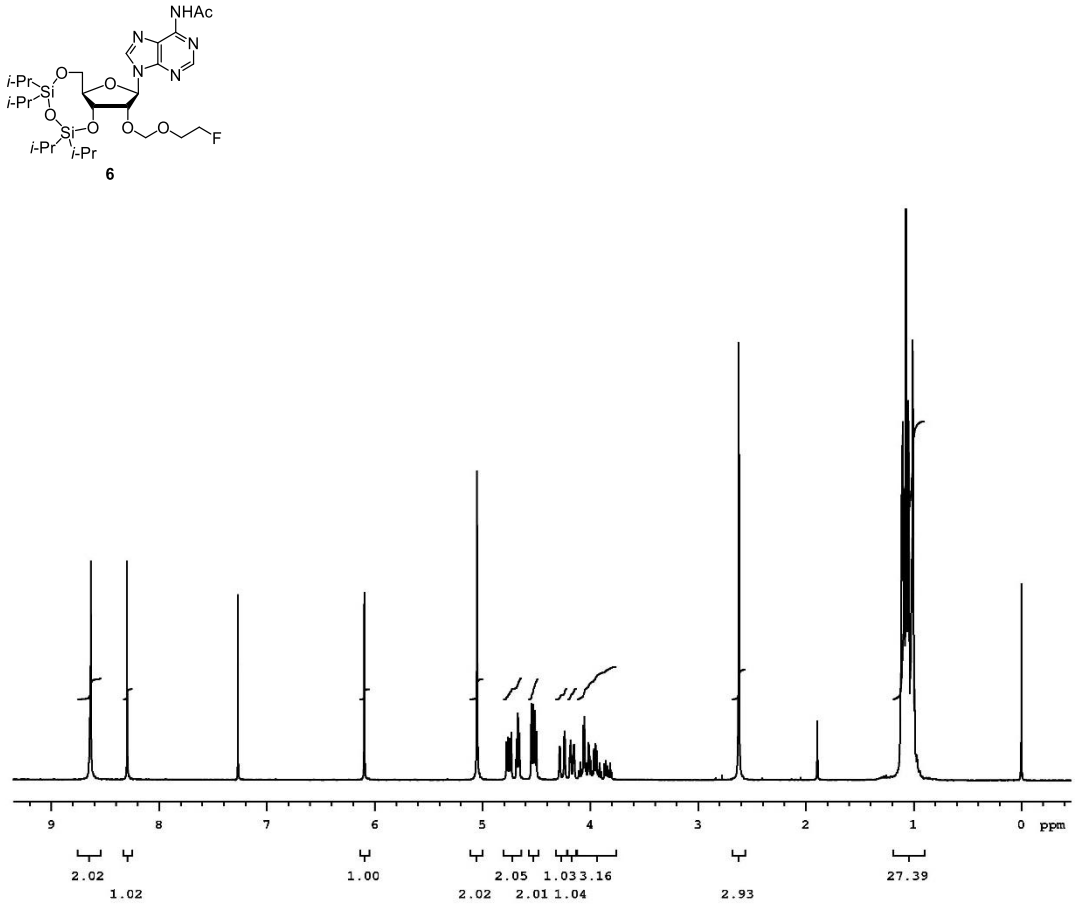
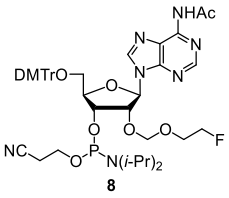


Fig. S6 ^{1}H-NMR spectra of compound **6** in $CDCl_3$.



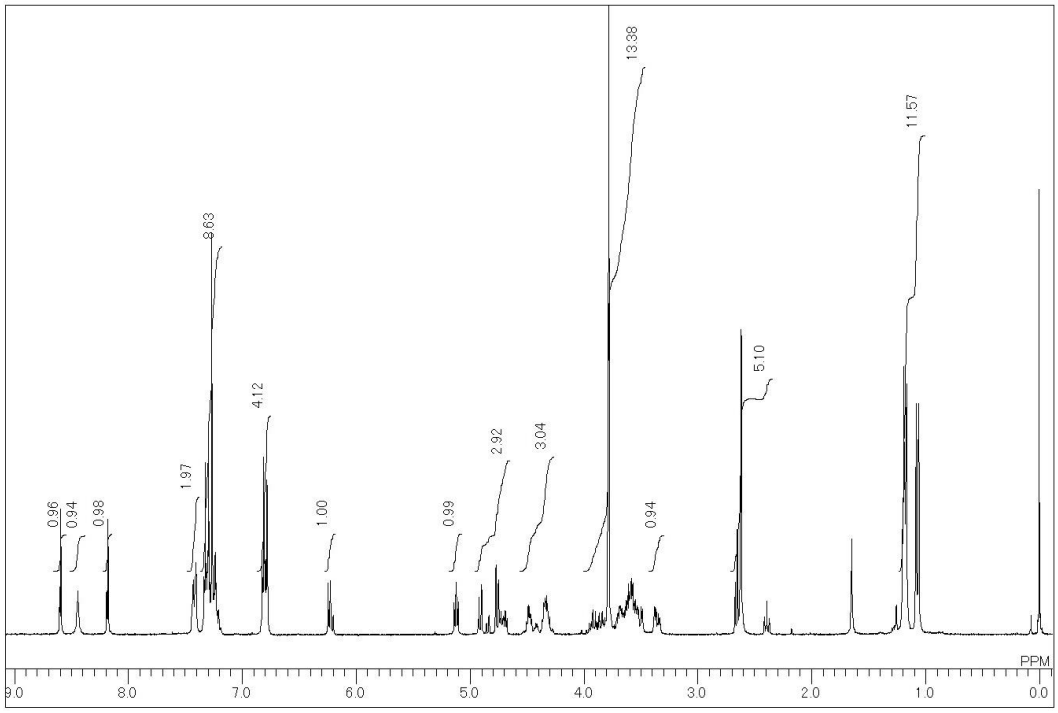


Fig. S7 ^{1}H-NMR spectra of compound **8** in $CDCl_3$.

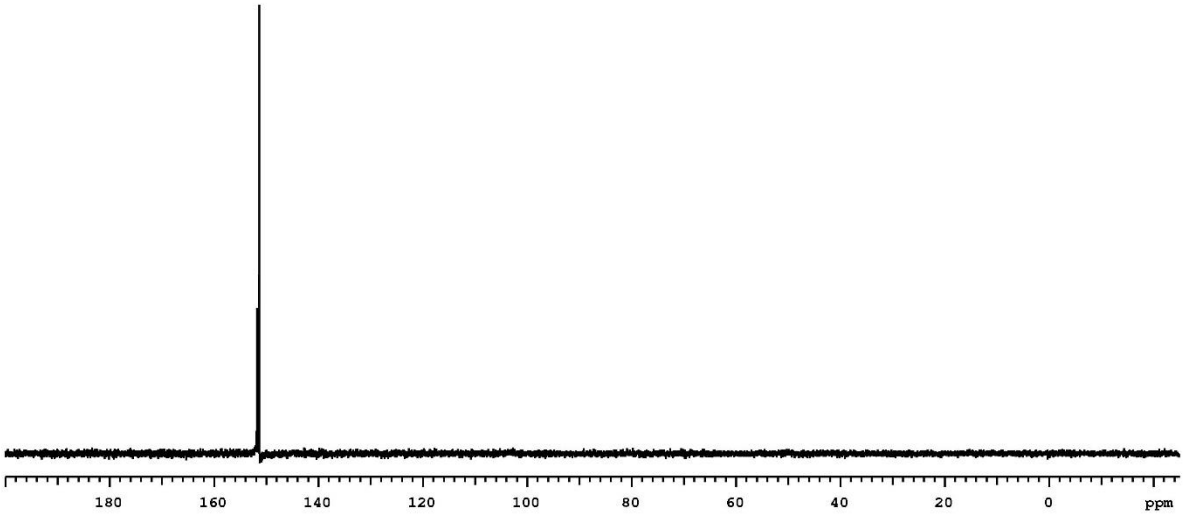


Fig. S8 ^{31}P-NMR spectra of compound **8** in $CDCl_3$.

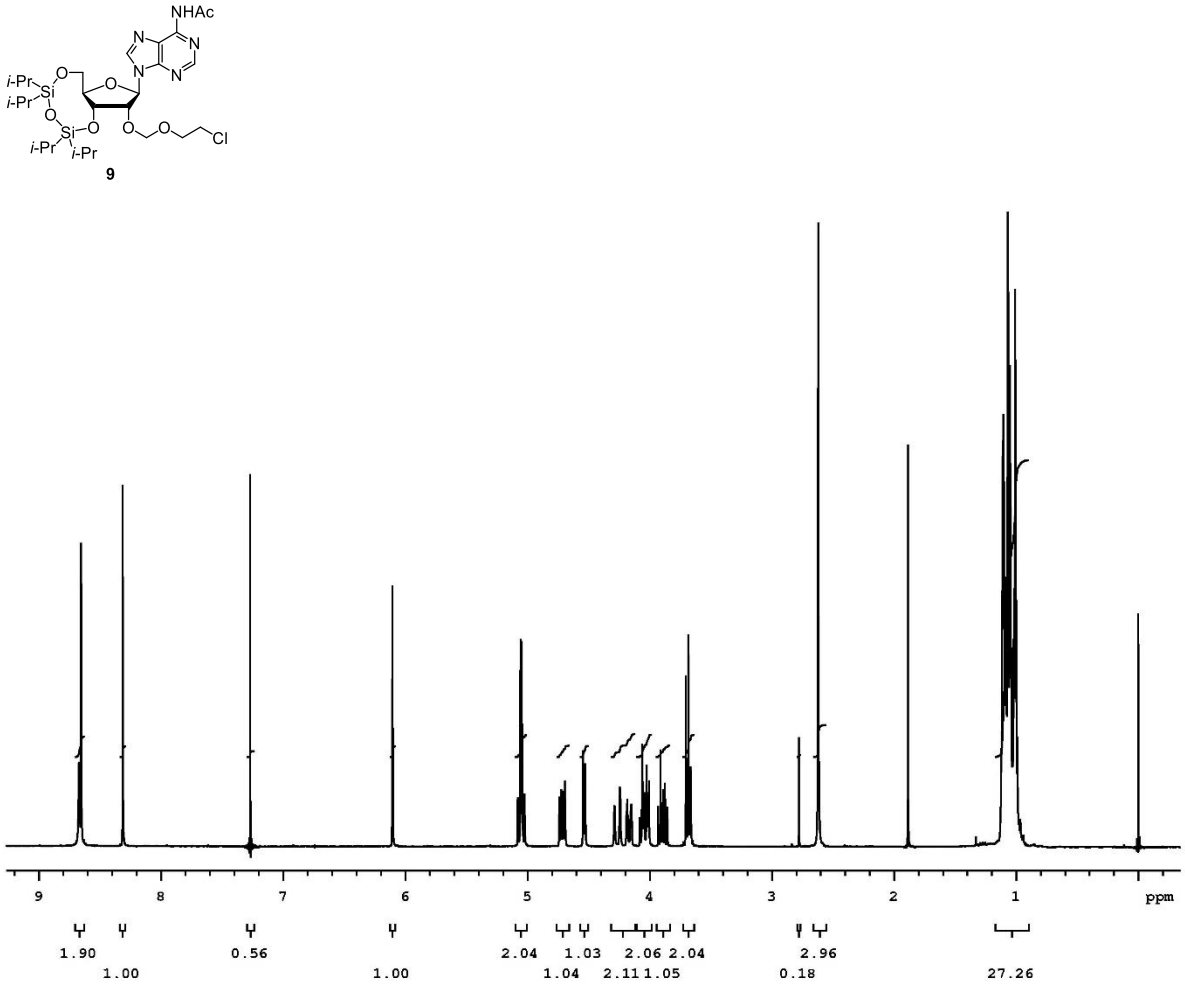
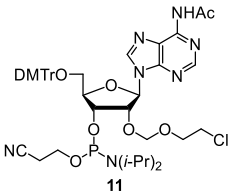


Fig. S9 ^{1}H-NMR spectra of compound **9** in $CDCl_3$.



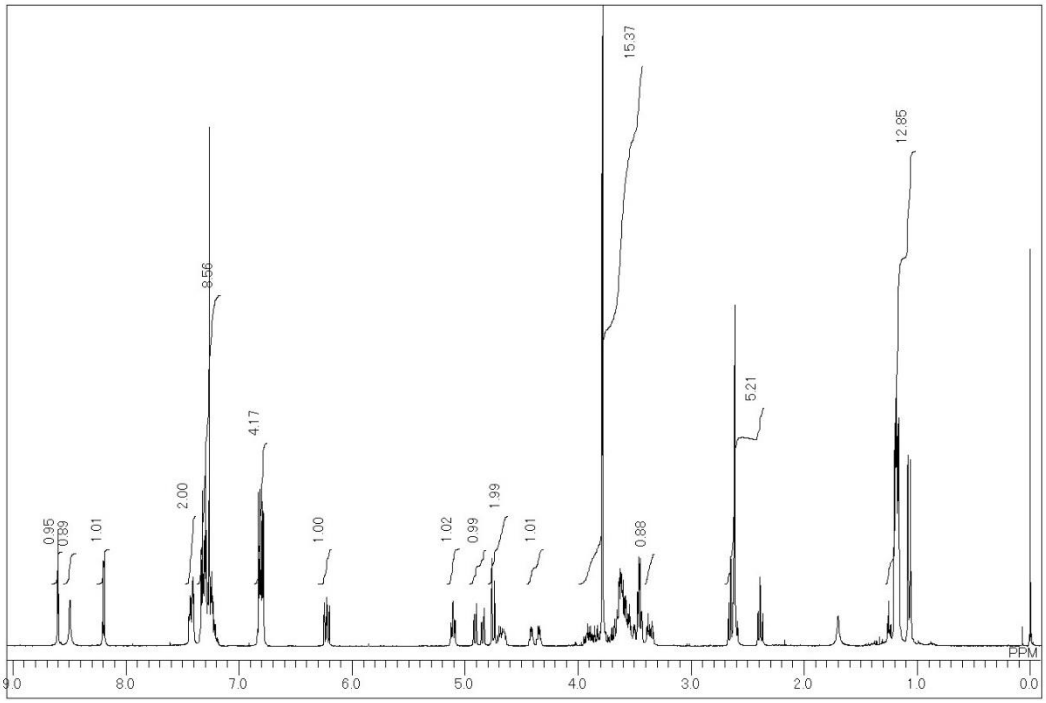


Fig. S10 ^{1}H-NMR spectra of compound **11** in $CDCl_3$.

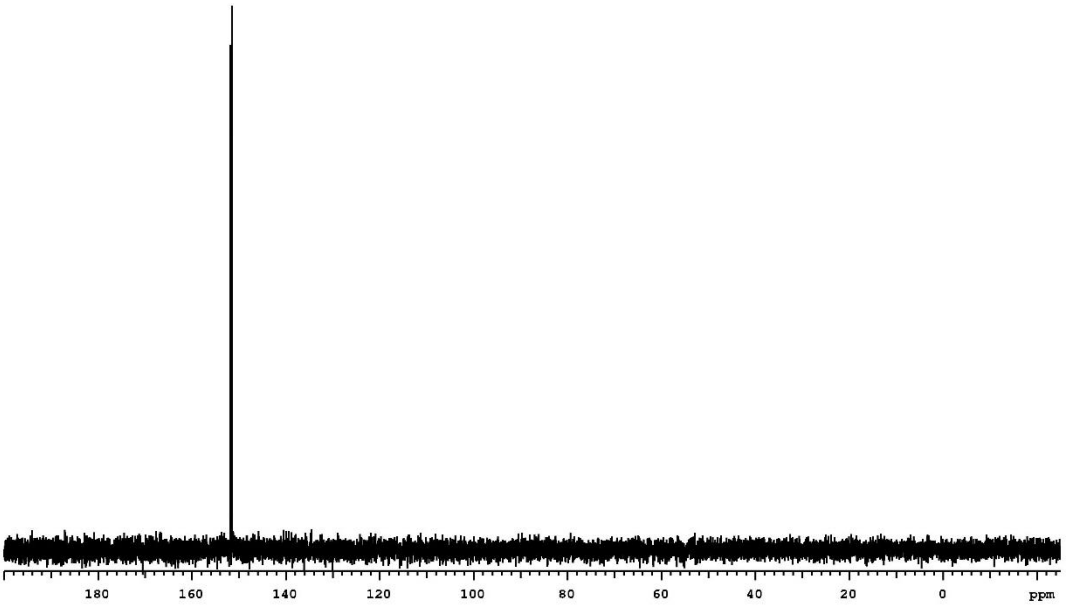
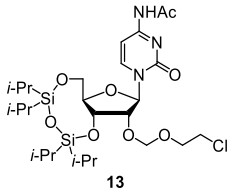


Fig. S11 ^{31}P-NMR spectra of compound **11** in $CDCl_3$.



13

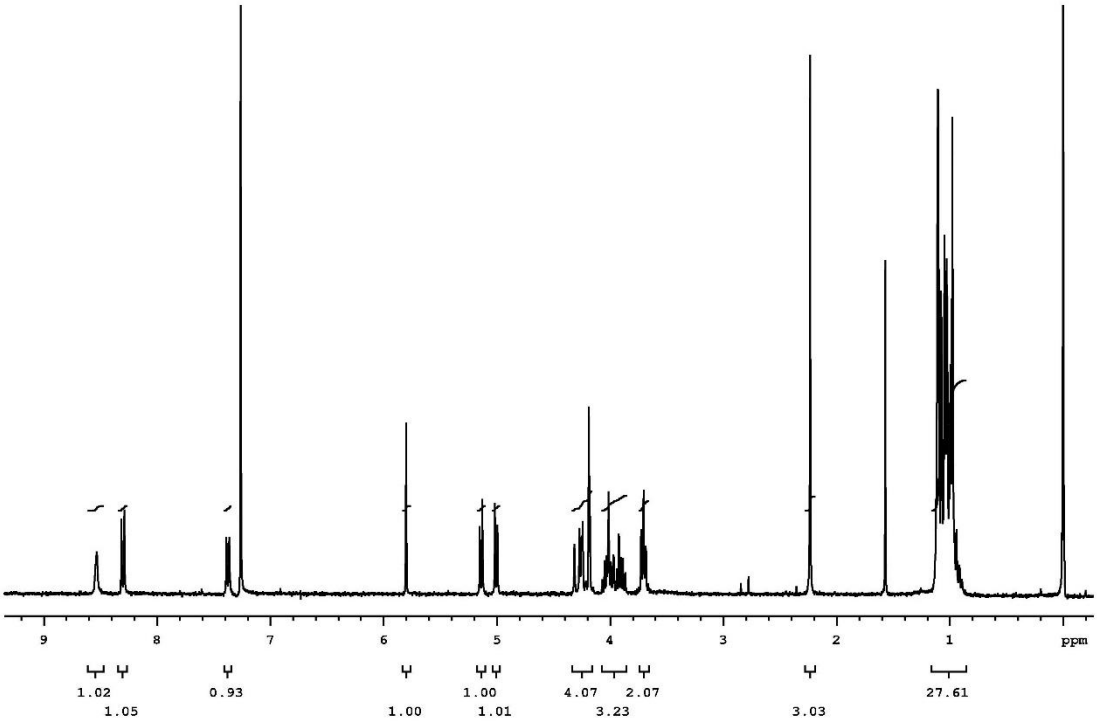
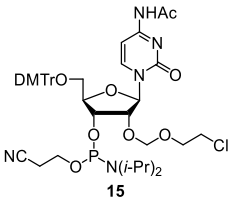


Fig. S12 ^{1}H-NMR spectra of compound **13** in $CDCl_3$.



15

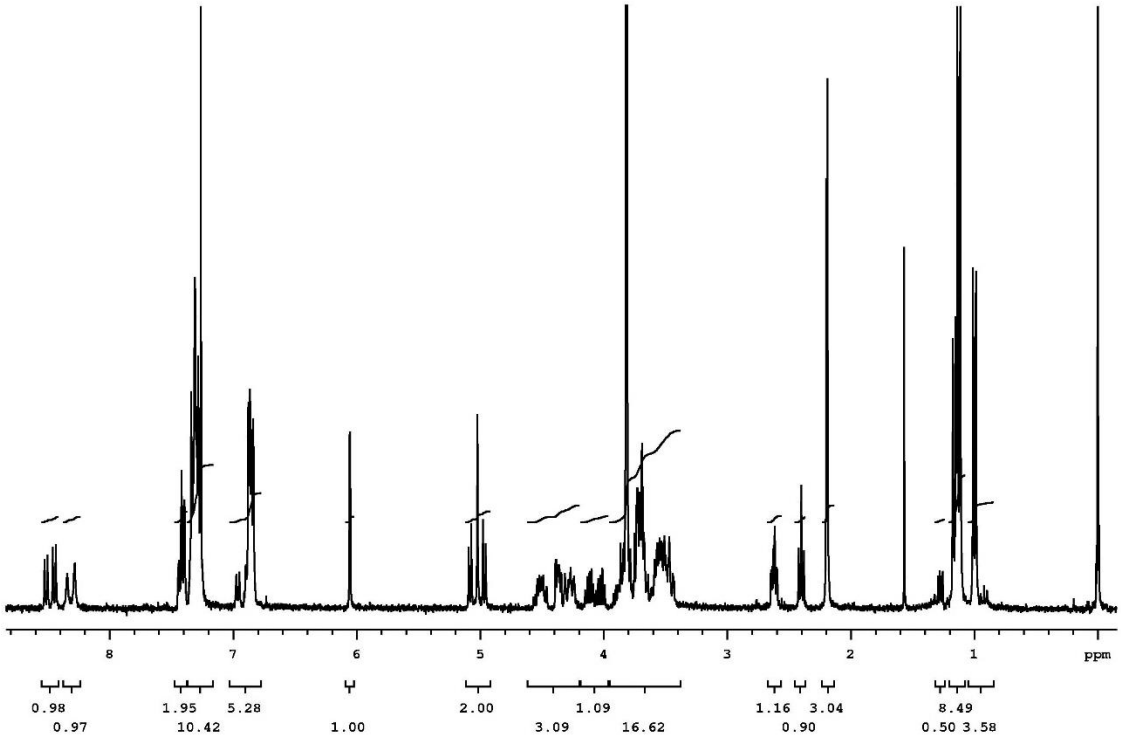


Fig. S13 ^{1}H-NMR spectra of compound **15** in $CDCl_3$.

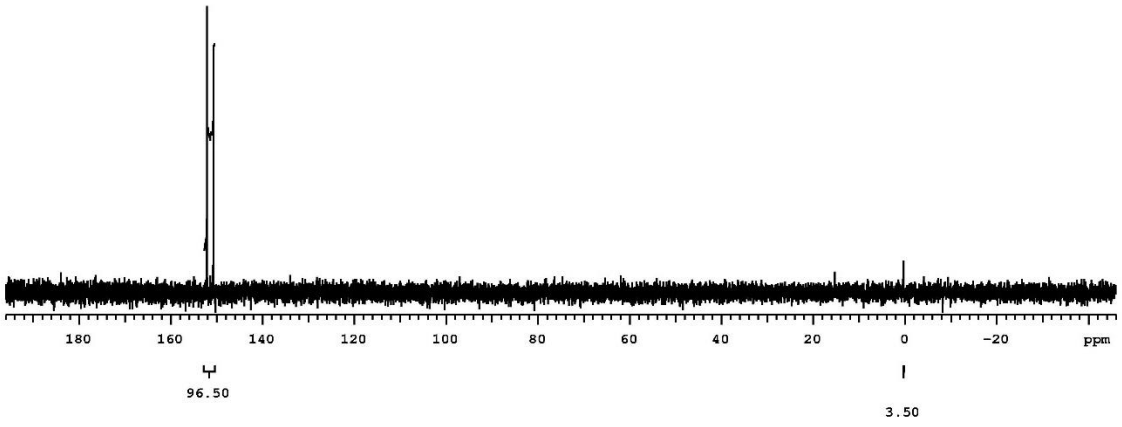


Fig. S14 ^{31}P-NMR spectra of compound **15** in $CDCl_3$.

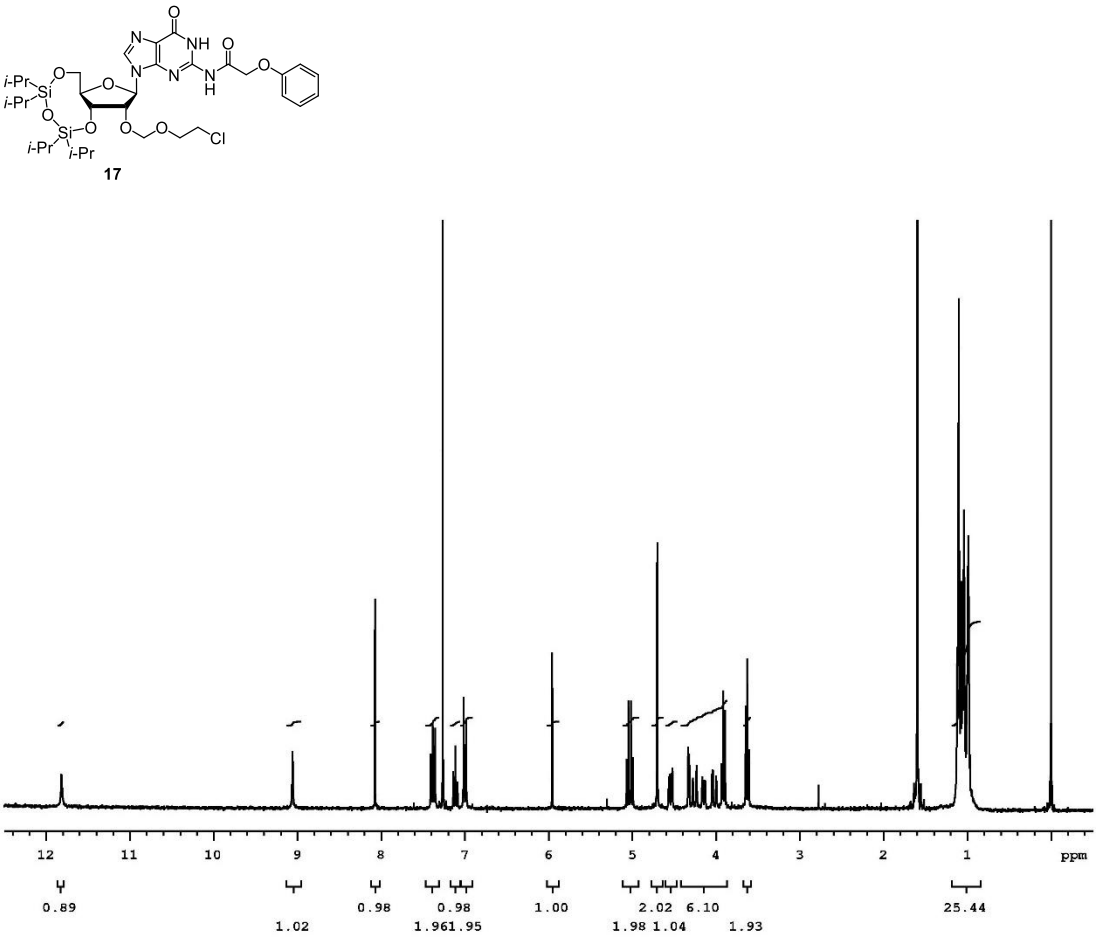
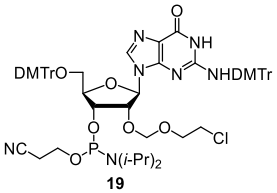


Fig. S15 ^{1}H-NMR spectra of compound **17** in $CDCl_3$.



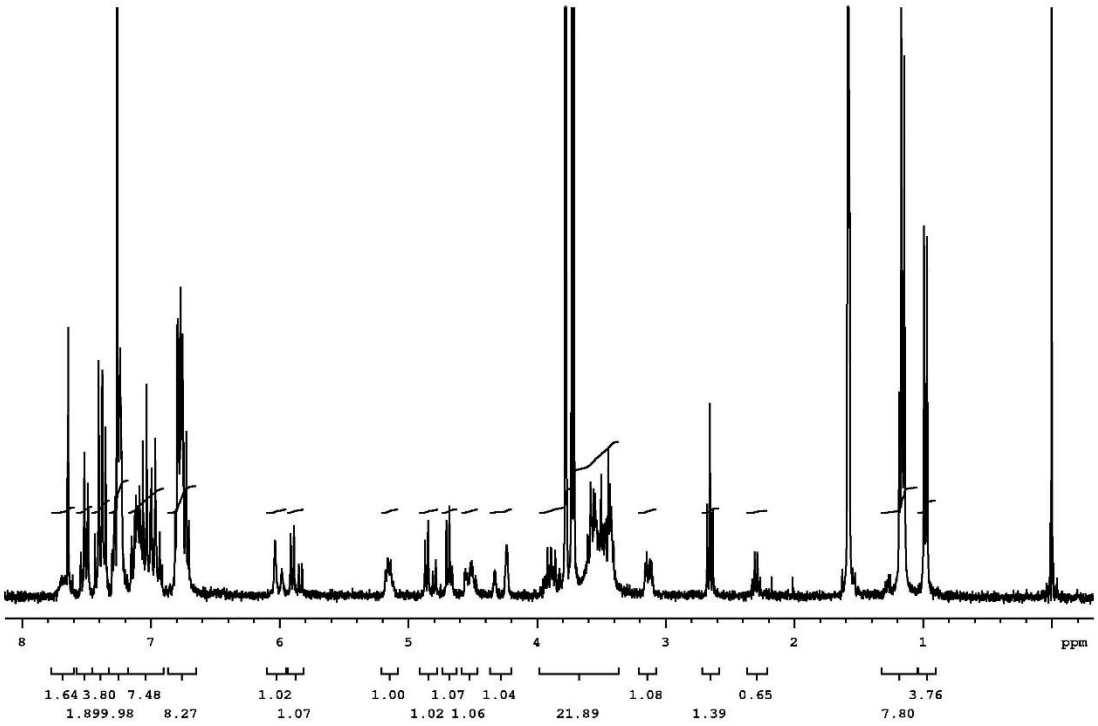


Fig. S18 ^{1}H-NMR spectra of compound **19** in $CDCl_3$.

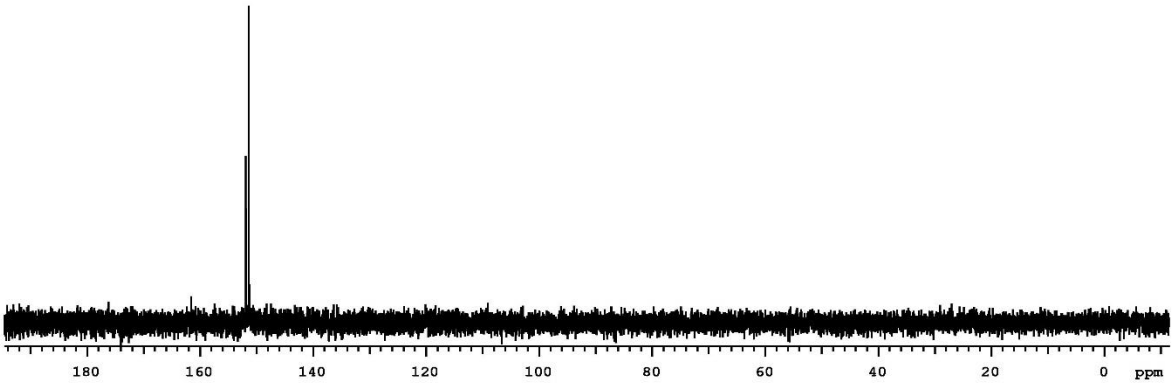


Fig. S20 ^{31}P-NMR spectra of compound **19** in $CDCl_3$.