Supplementary Information

New imidazopyridopyrimidine:naphthyridine base-pairing motif, ImN^{N}:NaO^{O}, consisting of a DAAD:ADDA hydrogen bonding pattern, markedly stabilize DNA duplexes

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Synthesis of phosphoramidite units.

3-(3,5-Di-*O*-acetyl-2-deoxy-β-D-ribofuranosyl)-2-(*N*,*N*-dibutylaminomethylidene)amino-7-hydroxy-1,8-naphthyridine (2). To a solution of **1**[5] (1.0 g, 2.4 mml) in DMF (24 mL) containing Et_3N (0.74 mL, 5.3 mmol) and DMAP (catalytic) was added Ac_2O (0.5 mL, 5.3 mmol), and the whole mixture was stirred for 20 h at room temperature. The reaction was quenched by addition of EtOH, and the reaction mixture was partitioned between AcOEt and H_2O. The separated organic layer was washed with saturated $NaHCO_3$ and brine. The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by a silica gel column, eluted with hexane/AcOEt (7:1–1:5) to give **2** (1.1 g, 92% as a yellow foam): EI-LRMS *m/z* 500 (M^+); EI-HRMS (M^+) Calcd for $C_{26}H_{36}N_4O_6$ 500.2634, found 500.2639; ^{1}H-NMR ($CDCl_3$) δ: 11.58 (br s, 1 H), 8.56 (s, 1 H), 7.83 (s, 1 H), 7.75 (d, 1 H, *J* = 9.5 Hz), 6.26 (d, 1 H, *J* = 9.5 Hz), 5.34 (dd, 1 H, *J* = 4.6, 10.6 Hz), 5.12 (m, 1 H), 4.30–4.17 (m, 3 H), 3.50–3.31 (m, 4 H), 2.49 (m, 1 H), 2.05, 2.02 (each s, each 3 H), 1.81 (m, 1 H), 1.56 (m, 4 H), 1.31 (m, 4 H), 0.92 (m, 6 H); ^{13}C-NMR ($CDCl_3$) δ: 170.9, 170.6, 163.8, 159.5, 155.2, 148.0, 139.7, 132.6, 126.5, 118.5, 110.0, 82.4, 77.3, 77.0, 64.5, 52.3, 46.1, 40.1, 31.4, 29.3, 21.1, 21.0, 20.5, 19.9, 14.0, 13.8.

3-(3,5-Di-*O*-acetyl-2-deoxy-β-D-ribofuranosyl)-2-(*N*,*N*-dibutylaminomethylidene)amino-7-chloro-1,8-naphthyridine (3). A solution of **2** (1.1 g, 2.2 mmol) in $POCl_3$ (22 mL) was stirred for 1 h at room temperature. The solvent was removed *in vacuo*, and the residue was diluted

with $CHCl_3$. The organic solvent was poured into ice water, and the mixture was stirred for 30 min. The separated organic layer was washed with saturated $NaHCO_3$ and brine. The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by a silica gel column, eluted with 0–3% MeOH in $CHCl_3$ to give **3** (970 mg, 85% as a yellow oil): EI-LRMS *m/z* 518 (M^+); EI-HRMS (M^+) Calcd for $C_{26}H_{35}ClN_4O_5$ 518.2296, found 518.2188; ^{1}H-NMR ($CDCl_3$) δ: 8.78 (s, 1 H), 8.28 (d, 1 H, *J* = 8.6 Hz), 8.14 (s, 1 H), 7.36 (d, 1 H, *J* = 9.5 Hz), 5.39 (dd, 1 H, *J* = 5.3, 10.6 Hz), 5.14 (d, 1 H, *J* = 6.0 Hz), 4.32–4.20 (m, 3 H), 3.56–3.30 (m, 4 H), 2.64 (dd, 1 H, *J* = 5.3, 13.9 Hz), 2.05, 1.99 (each s, each 3 H), 1.84 (m, 1 H), 1.60 (m, 4 H), 1.33 (m, 4 H), 0.93 (m, 6 H); ^{13}C-NMR ($CDCl_3$) δ: 170.8, 170.6, 161.6, 156.6, 154.8, 152.6, 138.7, 133.3, 132.1, 120.0, 118.6, 82.6, 77.4, 76.9, 64.4, 52.5, 46.2, 39.9, 31.5, 29.4, 21.1, 21.0, 20.5, 20.0, 14.0, 13.8.

2-Amino-7-chloro-3-(2-deoxy-β-D-ribofuranosyl)-1,8-naphthyridine (4). A solution of **3** (1.3 g, 2.5 mmol) in methanolic ammonia (saturated at 0 °C, 25 mL) was heated at 80 °C for 13 h in a steel container. The solvent was removed *in vacuo*, and the residue was purified by a silica gel column, eluted with 0–10% MeOH in $CHCl_3$ to give **4** (740 mg, quant. as a white foam): FAB-LRMS *m/z* 295 (M^+); FAB-HRMS (M^+) Calcd for $C_{13}H_{14}ClN_3O_3$ 295.0724, found 295.0727; ^{1}H-NMR (DMSO-d_6) δ: 8.07 (d, 1 H, *J* = 8.3 Hz), 8.03 (s, 1 H), 7.17 (d, 1 H, *J* = 8.3 Hz), 6.98 (br s, 2 H), 5.15–5.02 (m, 3 H), 4.24 (m, 1 H), 3.83 (m, 1 H), 3.57 (m, 2 H), 2.06 (m, 2 H); ^{13}C-NMR (DMSO-d_6) δ: 158.9, 155.5, 150.9, 139.4, 134.3, 124.4, 117.3, 115.6, 87.9, 77.2, 71.8, 61.4, 40.0.

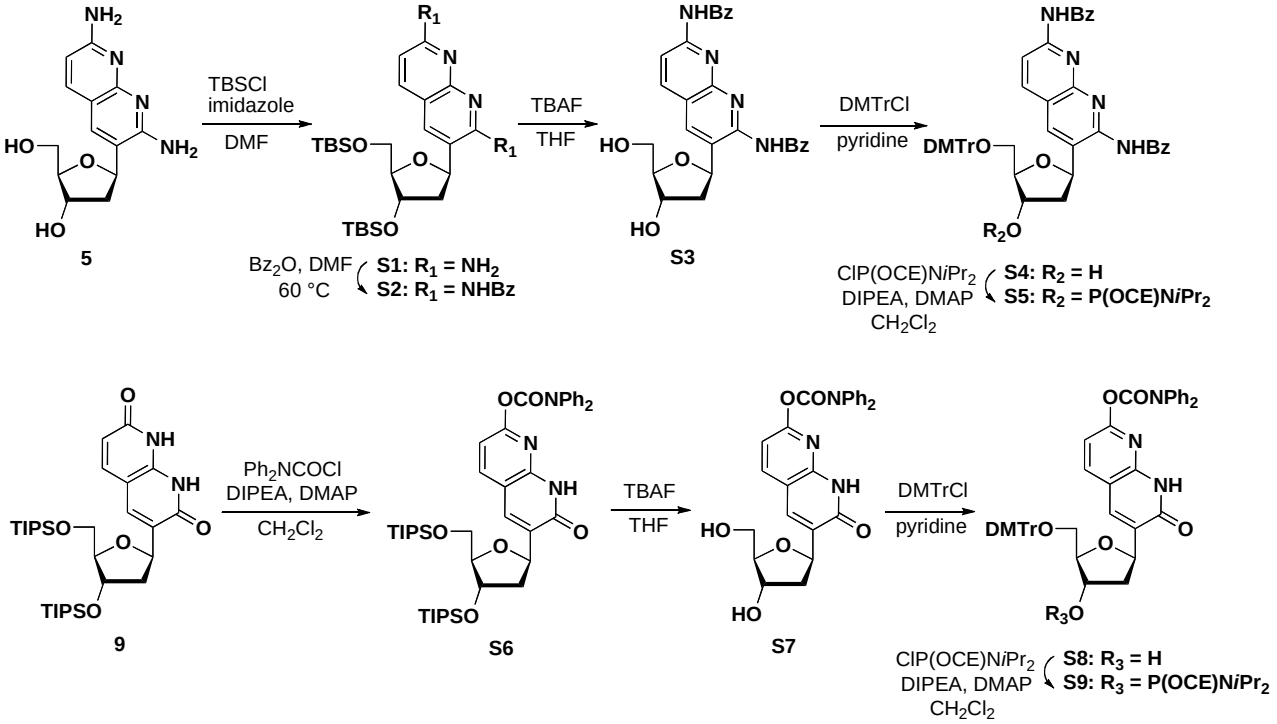
2,7-Diamino-3-(2-deoxy-β-D-ribofuranosyl)-1,8-naphthyridine (5). A solution of **4** (740 mg, 2.5 mmol) in methanolic ammonia (saturated at 0 °C, 25 mL) was heated at 120 °C for 4 days in a steel container. The solvent was removed *in vacuo*, and the residue was purified by a silica gel column, eluted with 5–30% MeOH in $CHCl_3$ to give **5** (590 mg, 88% as a yellow solid): FAB-LRMS *m/z* 277 (MH^+); FAB-HRMS (M^+) Calcd for $C_{13}H_{17}N_4O_3$ 277.1300, found 277.1309; ^{1}H-NMR (DMSO-d_6) δ: 7.76 (s, 1 H), 7.72 (d, 1 H, *J* = 8.6 Hz), 6.95, 6.87 (each br s, each 2 H) 6.48 (d, 1 H, *J* = 8.6 Hz), 5.13–5.02 (m, 3 H), 4.25 (m, 1 H), 3.80 (m, 1 H), 3.55 (m, 2 H), 2.02 (m, 2 H); ^{13}C-NMR (DMSO-d_6) δ: 159.7, 157.5, 153.1, 138.2, 135.6, 117.7, 108.7, 107.4, 87.9, 77.4, 72.0, 61.5, 40.0.

2-(*N*,*N*-Dibutylaminomethylidene)amino-3-[2-deoxy-3,5-di-*O*-(triisopropylsilyl)-*β*-D-ribofuranosyl]-7-hydroxy-1,8-naphthyridine (6). To a solution of **1** (1.0 g, 2.4 mmol) in DMF (48 mL) containing imidazole (980 mg, 14 mmol) was added TIPSCl (1.5 mL, 7.2 mmol), and the whole mixture was stirred at 55 °C. After being stirred for 16 h, additional imidazole (1.31 g, 18.8 mmol) and TIPSCl (2.0 mL, 9.6 mmol) were added and the mixture was stirred further 8 h at the same temperature. The reaction was quenched by addition of EtOH, and the reaction mixture was partitioned between AcOEt and H_2O. The separated organic layer was washed with saturated $NaHCO_3$, followed by brine. The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by a silica gel column, eluted with hexane/AcOEt (3:1–1:3) to give **6** (1.8 g, quant. as a yellow oil): FAB-LRMS *m/z* 729 (MH^+); FAB-HRMS Calcd for $C_{40}H_{73}N_4O_4Si_2$ (MH^+) 729.5182, found 729.5176; ^{1}H-NMR ($CDCl_3$) δ: 9.13 (br s, 1 H), 8.54 (s, 1 H), 7.96 (s, 1 H), 7.55 (d, 1 H, *J* = 9.6 Hz), 6.44 (d, 1 H, *J* = 9.6 Hz), 5.58 (dd, 1 H, *J* = 5.3, 10.2 Hz), 4.58 (m, 1 H), 4.06 (m, 1 H), 3.92 (dd, 1 H, *J* = 10.6, 3.6 Hz), 3.84 (dd, 1 H, *J* = 10.6, 4.6 Hz), 3.55 (m, 2 H), 3.34 (m, 2 H), 2.48 (dd, 1 H, *J* = 12.5, 5.3 Hz), 1.71 (m, 1 H), 1.61 (m, 4 H), 1.35 (m, 4 H), 1.08 (m, 42 H), 0.95 (m, 6 H); ^{13}C-NMR ($CDCl_3$) δ: 163.8, 160.1, 155.5, 147.8, 139.7, 133.2, 128.2, 118.2, 110.1, 88.3, 76.1, 74.8, 64.5, 51.8, 45.2, 44.0, 31.2, 29.5, 20.4, 20.0, 18.2, 14.1, 13.9, 12.3, 12.1.

2-Amino-3-[2-deoxy-3,5-di-*O*-(triisopropylsilyl)-*β*-D-ribofuranosyl]-7-hydroxy-1,8-naphthyridine (7). A solution of **6** (1.8 g, 2.4 mmol) in methanolic ammonia (saturated at 0 °C, 25 mL) was heated at 80 °C for 19 h in a steel container. The solvent was removed *in vacuo*, and the residue was purified by a silica gel column, eluted with $CHCl_3$ to give **7** (1.4 g, quant. as a white oil): EI-LRMS *m/z* 589 (M^+); EI-HRMS (M^+) Calcd for $C_{31}H_{55}N_3O_4Si_2$ 589.3731, found 589.3738; ^{1}H-NMR ($CDCl_3$) δ: 12.85 (br s, 1 H), 7.52–7.50 (m, 4 H), 6.32 (d, 1H, *J* = 9.3 Hz), 5.10 (dd, 1 H, *J* = 11.2, 4.6 Hz), 4.65 (m, 1 H), 4.05 (m, 1 H), 3.85 (m, 1 H), 2.27 (m, 1 H), 2.07 (dd, 1 H, *J* = 12.6, 4.6), 1.09 (m, 42 H); ^{13}C-NMR ($CDCl_3$) δ: 165.7, 159.6, 150.0, 139.9, 135.0, 116.3, 115.7, 105.9, 89.1, 78.3, 74.2, 64.0, 41.0, 18.2, 18.1, 12.3, 12.1.

3-[2-Deoxy-3,5-di-*O*-(triisopropylsilyl)-β-D-ribofuranosyl]-2,7-dihydroxy-1,8-naphthyridine (9). To a solution of **7** (1.4 g, 2.4 mmol) in AcOH (50 mL) was added sodium nitrite (500 mg, 7.2 mmol), and the reaction mixture was stirred for 3 h at room temperature. The reaction mixture was diluted with $CHCl_3$, and the organic layer was washed with H_2O. Then the organic layer was neutralized with saturated aqueous Na_2CO_3, and washed with brine. The organic layer was dried (Na_2SO_4) and concentrated *in vacuo* to give crude **8**. The resulting **8** was then heated in methanolic ammonia (saturated at 0 °C, 25 mL) at 60 °C for 5 h in a steel container. The solvent was removed *in vacuo*, and the residue was purified by a silica gel column, eluted with $CHCl_3$ to give **9** (1.2 g, 88% as a white solid). An analytical sample was crystallized from MeOH–AcOEt: mp 160–161 °C; EI-LRMS *m/z* 591 (M^+); ^{1}H-NMR ($CDCl_3$) δ: 15.35 (br s, 1 H), 12.79 (br s, 1 H), 8.06 (s, 1 H), 7.77 (d, 1 H, *J* = 9.2 Hz), 6.64 (d, 1 H, *J* = 9.2 Hz), 5.37 (dd, 1 H, *J* = 5.6, 9.9 Hz), 4.60 (m, 1 H), 4.09 (m, 1 H), 3.86 (m, 2 H), 2.58 (dd, 1 H, *J* = 5.6, 12.6 Hz), 1.78 (m, 1 H), 1.09 (m, 42 H); ^{13}C-NMR ($CDCl_3$) δ: 165.9, 164.1, 147.1, 140.1, 134.8, 108.8, 88.3, 75.0, 74.7, 64.3, 42.6, 18.1, 12.2, 12.0. *Anal*. Calcd. for $C_{31}H_{54}N_7O_3Si_2$: C, 63.01; H, 9.21; N, 4.74. Found: C, 62.96; H, 9.32; N, 4.71.

3-[2-Deoxy-β-D-ribofuranosyl]-2,7-dihydroxy-1,8-naphthyridine (10). To a solution of **9** (150 mg, 0.26 mmol) in THF (10 mL) was added TBAF (1 M, 0.78 mL, 0.78 mmol) at 0 °C, and the mixture was stirred at room temperature. After 24 h, the resulting precipitate was collected to give **10** (36 mg, 50% as a white solid): FAB-LRMS *m/z* 279 (MH^+); FAB-HRMS (M^+) Calcd for $C_{13}H_{14}N_2O_5$ 278.0903, found 278.0922; ^{1}H-NMR (DMSO-d_6) δ: 8.53 (s, 1 H), 8.50 (d, 1 H, *J* = 8.9 Hz), 8.08 (br s, 1 H), 7.42 (br s, 1 H), 6.70 (d, 1 H, *J* = 8.9 Hz), 5.75 (dd, 1 H, *J* = 5.6 and 9.6 Hz), 4.87 (m, 1 H), 4.50 (m, 1 H), 4.19 (m, 1 H), 2.94 (dd, 1 H, *J* = 5.6, 12.2 Hz), 2.40 (m, 1 H); ^{13}C-NMR (DMSO-d_6) δ: 171.6, 163.8, 162.0, 146.7, 139.4, 133.6, 87.2, 74.7, 72.3, 62.4, 41.2.



Scheme S1

2,7-Diamino-3-[3,5-di-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-*β*-D-ribofuranosyl]-1,8-naphthyridine (S1). To a solution of **5** (140 mg, 0.51 mmol) in DMF (10 mL) containing imidazole (210 mg, 3.1 mmol) was added TBSCl (230 mg, 1.5 mmol), and the whole mixture was stirred at room temperature for overnight. The reaction was quenched by addition of EtOH, and the reaction mixture was concentrated *in vacuo*. The residue was purified by a silica gel column, eluted with 0–3% MeOH in $CHCl_3$ to give **S1** (220 mg, 87% as a brown foam): EI-LRMS *m/z* 504 (M^+); EI-HRMS (M^+) Calcd for $C_{25}H_{44}N_4O_3Si_2$ 504.2952, found 504.2947; ^{1}H-NMR (DMSO-d_6) δ: 7.62 (s, 1 H), 7.56 (d, 1 H, *J* = 8.6 Hz), 6.39 (d, 1 H, *J* = 8.3 Hz), 6.27, 6.07 (each br s, each 2 H), 5.04 (m, 1 H), 4.36 (m, 1 H), 3.80 (m, 1 H), 3.72 (m, 2 H), 2.06 (m, 2 H), 0.88, 0.87 (each s, each 9 H), 0.07 (s, 12 H); ^{13}C-NMR ($CDCl_3$) δ: 159.6, 158.3, 156.2, 137.5, 135.7, 117.0, 110.9, 107.1, 88.3, 79.8, 73.5, 62.9, 40.4, 25.8, 25.7, 18.3, 17.9, –4.7, –4.8, –5.6, –5.6.

2,7-Dibenzoylamino-3-[3,5-di-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-*β*-D-ribofuranosyl]-1,8-naphthyridine (S2). To a solution of **S1** (180 mg, 0.36 mmol) in DMF (8 mL) was added Bz_2O (410 mg, 1.8 mmol), and the whole mixture was heated at 60 °C. After being stirred for 5 h, additional Bz_2O (410 mg, 1.8 mmol) was added and the reaction mixture was heated for more 4 h

at the same temperature. The reaction was quenched by addition of EtOH, and the reaction mixture was partitioned between AcOEt and H_2O. The separated organic layer was washed with saturated $NaHCO_3$ and brine. The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by a silica gel column, eluted with hexane/AcOEt (15:1–10:1) to give **S2** (220 mg, 89% as a yellow oil): FAB-LRMS *m/z* 713 (MH^+); FAB-HRMS (M^+) Calcd for $C_{39}H_{53}N_4O_5Si_2$ 713.3554, found 713.3547; ^{1}H-NMR ($CDCl_3$) δ: 8.90 (br s, 1 H), 8.52 (d, 1 H, *J* = 8.3 Hz), 8.30 (br s, 1 H), 8.21 (s, 1 H), 8.13–7.43 (m, 11 H), 5.66 (m, 1 H), 4.44 (m, 1 H), 4.08 (m, 1 H), 3.83–3.66 (m, 2 H), 2.69 (m, 1 H), 0.97, 0.90 (each s, each 9 H), 0.14–0.10 (m, 12 H).

2,7-Dibenzoylamino-3-(2-deoxy-β-D-ribofuranosyl)-1,8-naphthyridine (S3). In the similar manner as described for **10**, **S2** (200 mg, 0.28 mmol) in THF (6 mL) was treated with TBAF (1M, 0.84 mL, 0.84 mmol) to give **S3** (140 mg including tetrabutylammonium salt): FAB-LRMS *m/z* 485 (MH^+); FAB-HRMS (MH^+) Calcd for $C_{27}H_{25}N_4O_5$ 485.1847, found 485.1836; ^{1}H-NMR (DMSO-d_6) δ: 11.34 (br s, 1 H), 10.78 (br s, 1 H), 8.55–7.53 (m, 13 H), 5.37 (m, 1 H), 5.10 (br s, 1 H), 4.85 (br s, 1 H), 4.19 (m, 1 H), 3.83 (m, 1 H), 3.55 (m, 2 H), 2.32 (m, 1 H), 1.83 (m, 1 H).

2,7-Dibenzoylamino-3-[2-deoxy-5-*O*-(4,4'-dimethoxytrityl)-β-D-ribofuranosyl]-1,8-naphthyridine (S4). To a solution of **S3** (140 mg, crude) in pyridine (10 mL) was added 4,4'-dimethoxytrityl chloride (120 mg, 0.34 mmol), and the mixture was stirred for 20 h at room temperature. The reaction was quenched by addition of EtOH, and the reaction mixture was concentrated *in vacuo*. The residue was partitioned between $CHCl_3$ and H_2O. The separated organic layer was washed with saturated $NaHCO_3$ and brine. The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by a silica gel column, eluted with 0–2% MeOH in $CHCl_3$ to give **S4** (160 mg, 75% from **S2** as a yellow foam): FAB-LRMS *m/z* 787 (MH^+); FAB-HRMS (MH^+) Calcd for $C_{48}H_{43}N_4O_7$ 787.3152, found 787.3142; ^{1}H-NMR (DMSO-d_6) δ: 15.55 (br s, 0.2 H), 11.34 (br s, 1 H), 10.85 (br s, 0.8 H), 8.52–6.82 (m, 26 H), 5.56 (m, 0.2 H), 5.38 (m, 0.8 H), 5.26 (d, 0.2 H, *J* = 3.3 Hz), 5.12 (d, 0.8 H, *J* = 3.3 Hz), 4.17 (m, 1 H), 4.03 (m, 0.2 H), 3.97 (m, 0.8 H), 3.72 (s, 1.2 H), 3.70 (s, 4.8 H), 3.24 (m, 0.4 H), 3.17 (m, 1.6 H),

2.31 (m, 1 H), 1.98 (m, 1 H).

2,7-Dibenzoylamino-3-{2-deoxy-3-*O*-[(*N*,*N*-diisopropylamino)-2-cyanoethoxyphosphino]-5-*O*-(4,4'-dimethoxytrityl)-β-D-ribofuranosyl}-1,8-naphthyridine (S5). To a solution of **S4** (150 mg, 0.19 mmol) in CH_2Cl_2 (7 mL) containing *N*,*N*-diisopropylethylamine (100 μL, 0.57 mmol) and DMAP (catalytic) was added 2-cyanoethyl *N*,*N*-diisopropylchlorophosphoramidite (85 μL, 0.38 mmol), and the whole mixture was stirred for 3 h at room temperature. The reaction mixture was diluted with $CHCl_3$, and the organic layer was washed with saturated $NaHCO_3$ and brine. The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by a silica gel column (neutralized), eluted with hexane/AcOEt (5:1–1:1) to give **S5** (140 mg, 74% as a yellow foam): FAB-LRMS *m/z* 987 (MH^+); FAB-HRMS (MH^+) Calcd for $C_{57}H_{60}N_6O_8P$ 987.4218, found 987.4214; ^{31}P-NMR ($CDCl_3$) δ: 149.1, 148.2.

3-[2-Deoxy-3,5-di-*O*-(triisopropylsilyl)-β-D-ribofuranosyl]-2-hydroxy-7-diphenylcarbamoyloxy-1,8-naphthyridine (S6). To a solution of **9** (870 mg, 1.48 mmol) in CH_2Cl_2 (50 mL) containing *N*,*N*-diisopropylethylamine (390 μL, 2.21 mmol) and DMAP (catalytic) was added diphenylcarbamoyl chloride (513 mg, 2.21 mmol), and the whole mixture was stirred for 3 h at room temperature. The reaction was quenched by addition of EtOH, and the reaction mixture was partitioned between AcOEt and H_2O. The separated organic layer was washed with saturated $NaHCO_3$ and brine. The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by a silica gel column, eluted with hexane/AcOEt (9:1–1:1) to give **S6** (880 mg, 76% as a white foam): FAB-LRMS *m/z* 786 (MH^+); FAB-HRMS (MH^+) Calcd for $C_{44}H_{64}N_3O_6Si_2$ 786.4340, found 786.4337; ^{1}H-NMR ($CDCl_3$) δ: 8.94 (br s, 1 H), 7.85 (s, 1 H), 7.77 (d, 1 H, *J* = 8.6 Hz), 7.31–7.18 (m, 10 H), 6.87 (d, 1 H, *J* = 8.6 Hz), 5.24 (dd, 1 H, *J* = 5.3 and 9.9 Hz), 4.51 (m, 1 H), 4.01 (m, 1 H), 3.81 (dd, 1 H, *J* = 10.6 and 4.0 Hz), 3.71 (dd, 1 H, *J* = 10.6 and 4.6 Hz), 2.53 (dd, 1 H, *J* = 5.3 and 11.2 Hz), 1.67 (m, 1 H), 1.00 (m, 42 H); ^{13}C-NMR ($CDCl_3$) δ: 161.4, 157.9, 151.8, 147.4, 141.8, 139.0, 136.4, 131.9, 129.2, 126.9, 113.0, 110.9, 88.3, 75.5, 74.5, 64.2, 42.4, 18.0, 12.2, 12.0.

3-(2-Deoxy-β-D-ribofuranosyl)-2-hydroxy-7-diphenylcarbamoyloxy-1,8-naphthyridine (S7). In the similar manner as described for **10**, **S6** (480 mg, 0.61 mmol) in THF (20 mL) was treated with TBAF (1 M, 1.3 mL, 1.3 mmol) to give **S7** (150 mg, including tetrabutylammonium salt): FAB-LRMS *m/z* 473 (MH^+); FAB-HRMS (MH^+) Calcd for $C_{26}H_{23}N_3O_6$ 473.1586, found 473.1584; ^{1}H-NMR ($CDCl_3$) δ: 9.68 (br s, 1 H), 7.92 (d, 1 H, *J* = 8.6 Hz), 7.83 (s, 1 H), 7.39–7.26 (m, 10 H), 6.94 (d, 1 H, *J* = 8.6 Hz), 5.23 (dd, 1 H, *J* = 6.6, 9.9 Hz), 4.52 (m, 1 H), 4.10 (m, 1 H), 3.87 (dd, 1 H, *J* = 11.9, 3.3 Hz), 3.77 (dd, 1 H, *J* = 11.9, 3.3 Hz), 2.31 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ: 161.1, 158.0, 151.8, 147.3, 141.7, 139.7, 134.2, 133.9, 129.1, 126.8, 112.7, 110.9, 87.5, 76.8, 73.3, 63.1, 40.9.

3-[2-Deoxy-5-*O*-(4,4'-dimethoxytrityl)-β-D-ribofuranosyl]-2-hydroxy-7-diphenylcarbamoyloxy-1,8-naphthyridine (S8). In the similar manner as described for **S4**, **S7** (150 mg, crude) in pyridine (10 mL) was treated with 4,4'-dimethoxytrityl chloride (130 mg, 0.39 mmol) to give **S8** (190 mg, 45% from **S6** as a white foam): FAB-LRMS *m/z* 776 (MH^+); FAB-HRMS (MH^+) Calcd for $C_{47}H_{42}N_3O_8$ 776.2972, found 776.2968; ^{1}H-NMR ($CDCl_3$) δ: 9.13 (br s, 1 H), 7.96 (s, 1 H), 7.62 (d, 1 H, *J* = 8.3 Hz), 7.47–6.79 (m, 23 H), 6.88 (d, 1 H, *J* = 8.3 Hz), 5.32 (m, 1 H), 4.39 (m, 1 H), 4.10 (m, 1 H), 3.77 (s, 6 H), 3.35 (m, 2 H), 2.31 (ddd, 1 H, *J* = 6.6, 13.2, 3.3 Hz), 1.95 (m, 1 H), 1.90 (m, 1 H); ^{13}C-NMR ($CDCl_3$) δ: 161.7, 158.5, 158.0, 151.7, 147.3, 144.8, 141.8, 139.2, 136.0, 135.9, 132.3, 130.0, 129.2, 128.2, 127.8, 126.8, 113.1, 112.8, 110.8, 86.2, 85.4, 75.0, 73.7, 64.0, 55.2, 41.6.

3-{2-Deoxy-3-*O*-[(*N*,*N*-diisopropylamino)-2-cyanoethoxyphosphino]-5-*O*-(4,4'-dimethoxytrityl)-β-D-ribofuranosyl}-2-hydroxy-7-diphenylcarbamoyloxy-1,8-naphthyridine (S9). In the similar manner as described for **S5**, **S8** (150 mg, 0.19 mmol) in CH_2Cl_2 (7 mL) containing *N*,*N*-diisopropylethylamine (68 μL, 0.39 mmol) and DMAP (catalytic) treated with 2-cyanoethyl *N*,*N*-diisopropylchlorophosphoramidite (87 μL, 0.39 mmol) to give **S9** (130 mg, 70% as a white foam): FAB-LRMS *m/z* 976 (MH^+); FAB-HRMS (MH^+) Calcd for $C_{56}H_{59}N_5O_9P$ 976.4050, found 976.4042; ^{31}P-NMR ($CDCl_3$) δ: 149.1, 148.4.

Synthesis and characterization of ODNs.

ODN I, III, and V containing NaN^N and NaO^O were synthesized on a DNA/RNA synthesizer (Applied Biosystem Model 3400) by the phosphoramidite method. The other ODNs had already been prepared in our previous studies.[4,5] For the incorporation of the NaN^N and NaO^O into the ODNs, a 0.12 M solution of each phosphoramidite in CH_3CN and a coupling time of 600s was used. The fully protected ODNs were then deblocked and purified by the same procedure as for the purification of normal ODNs. Thus each ODN linked to the resin (1 μmol) was treated with concentrated NH_4OH at 55 °C for 16 h, and the released ODN protected by a DMTr group at the 5'-end was chromatographed on a C-18 silica gel column (1 x 12 cm, Waters) with a linear gradient of CH_3CN from 0 to 50% in 0.1 M TEAA buffer (pH 7.0). The fractions were concentrated, and the residue was treated with aqueous 80% AcOH at room temperature for 20 min, then the solution was concentrated, and the residue was coevaporated with H_2O. The residue was dissolved in H_2O and the solution was washed with Et_2O, then the H_2O layer was concentrated to give the deprotected ODN. The ODN was further purified by reverse-phase HPLC, using a J'sphere ODN M80 column (4.6 × 150 mm, YMC) with a linear gradient of CH_3CN (from 10 to 25% over 30 min) in 0.01 M TEAA buffer (pH 7.0) to give highly purified ODNs.

Characterization of each ODN was done by complete hydrolysis according to our previous method and the nucleoside composition was analyzed by HPLC. Hyperchromicity of each ODN was determined by comparing UV absorbances at 260 nm of the solutions before and after hydrolyses. The extinction coefficient (at 260 nm) of each ODN was determined using the following equation: ε_{ODN} = the sum of $\varepsilon_{nucleoside}$/hyperchromicity. The extinction coefficients (at 260 nm) of the natural nucleosides used for calculations were as follows: dA, 15400; dC, 7300; dG, 11700; T, 8800. The extinction coefficients for the NaN^N and NaO^O at 260 nm were determined to be the following: NaN^N, 2,622; NaO^O, 815. Hyperchromicities, extinction coefficients and nucleoside composition of each ODN are listed in Table S1.

Table S1. Characterization of ODNs containing NaN^N and NaO^O

ODN	hyperchromicity	extinction coefficiency ($M^{-1}cm^{-1}$)	nucleoside composition
ODN I : X = Na-N^N	1.40	1.33 x 10^5	C : G : A : X = 5.9 : 3.1 : 6.5 : 0.9 (6 : 3 : 7 : 1)
Na-O^O	1.57	1.19 x 10^5	6.1 : 3.2 : 6.8 : 0.8
ODN III : X = Na-N^N	1.35	1.13 x 10^5	C : G : A : X = 5.9 : 2.4 : 4.7 : 3.0 (6 : 3 : 5 : 3)
Na-O^O	1.39	1.12 x 10^5	6.4 : 2.8 : 5.1 : 3.0
ODN V : X = Na-N^N	1.45	1.18 x 10^5	C : G : A : X = 5.9 : 2.4 : 4.7 : 3.0 (6 : 3 : 5 : 3)
Na-O^O	1.41	1.22 x 10^5	6.4 : 2.8 : 5.1 : 3.0

Thermal Denaturation. Each sample contained appropriate ODNs (6 μM) in a buffer of 0.01 M sodium cacodylate (pH 7.0) containing 1.0 mM NaCl was heated at 95 °C for 5 min, cooled gradually to an appropriate temperature, and used for the thermal denaturation study. Thermal-induced transitions of each mixture of ODNs were monitored at 260 nm on a Beckman DU650 spectrophotometer. Sample temperature was increased 0.5 °C/min. The hybridization data for all possible combinations were given in Tables S2, S3 and S4.

Table S2. Hybridization data of all possible combinations for ODN I:ODN II.

		X	Y	T_m (°C)	ΔT_m (°C)
		A	T	48.6	–
		G	C	49.9	+1.3
		ImO^N	NaN^O	56.4	+7.8
		ImN^O	NaN^O	53.3	+4.7
		ImO^O	NaN^O	51.0	+2.4
		ImN^N	NaN^O	51.5	+2.9
		ImO^N	NaO^N	50.4	+1.8
		ImN^O	NaO^N	56.1	+7.5
ODN I	5'-GCACCGAA**X**AAACCACG-3'	ImO^O	NaO^N	49.3	+0.7
ODN II	3'-CGTGGCTT**Y**TTTGGTGC-5'	ImN^N	NaO^N	48.6	0
		ImO^N	NaN^N	50.9	+2.3
		ImN^O	NaN^N	50.4	+1.8
		ImO^O	NaN^N	56.5	+7.9
		ImN^N	NaN^N	53.4	+4.8
		ImO^N	NaO^O	53.1	+4.5
		ImN^O	NaO^O	54.6	+6.0
		ImO^O	NaO^O	51.8	+3.2
		ImN^N	NaO^O	60.0	+11.4

The blue/red pairs are the matched, while all the others are mismatches.

Table S3. Hybridization data of all possible combinations for ODN III:ODN IV.

	X	Y	T_m (°C)	ΔT_m (°C)
	A	T	48.6	–
	G	C	56.7	+8.1
	ImO^N	NaN^O	81.4	+32.8
	ImN^O	NaN^O	66.7	+18.1
	ImO^O	NaN^O	58.8	+10.2
	ImN^N	NaN^O	61.7	+13.2
	ImO^N	NaO^N	65.8	+17.2
	ImN^O	NaO^N	79.6	+31.0
ODN III 5'-GC**X**CCGAA**X**AAACC**X**CG-3'	ImO^O	NaO^N	57.5	+8.9
ODN IV 3'-CG**Y**GGCTT**Y**TTTGG**Y**GC-5'	ImN^N	NaO^N	58.3	+9.7
	ImO^N	NaN^N	68.0	+19.4
	ImN^O	NaN^N	64.7	+16.1
	ImO^O	NaN^N	80.5	+31.9
	ImN^N	NaN^N	70.7	+22.1
	ImO^N	NaO^O	72.7	+24.1
	ImN^O	NaO^O	70.5	+21.9
	ImO^O	NaO^O	65.8	+17.2
	ImN^N	NaO^O	88.0	+39.4

The blue/red pairs are the matched, while all the others are mismatches.

Table S4. Hybridization data of all possible combinations for ODN V:ODN VI.

		X	Y	T_m (°C)	ΔT_m (°C)
		A	T	48.6	–
		G	C	55.2	+6.6
		ImO^N	NaN^O	79.0	+30.2
		ImN^O	NaN^O	67.2	+18.6
		ImO^O	NaN^O	61.6	+13.0
		ImN^N	NaN^O	59.1	+10.5
		ImO^N	NaO^N	64.6	+16.0
		ImN^O	NaO^N	80.1	+31.5
ODN V	5'-GCACCGA**XXX**AACCACG-3'	ImO^O	NaO^N	56.5	+7.9
ODN VI	3'-CGTGGCT**YYY**TTGGTGC-5'	ImN^N	NaO^N	55.5	+6.9
		ImO^N	NaN^N	64.1	+15.5
		ImN^O	NaN^N	62.8	+14.2
		ImO^O	NaN^N	81.3	+32.7
		ImN^N	NaN^N	70.0	+21.4
		ImO^N	NaO^O	70.7	+22.1
		ImN^O	NaO^O	76.8	+28.2
		ImO^O	NaO^O	69.7	+21.1
		ImN^N	NaO^O	88.9	+40.3

The blue/red pairs are the matched, while all the others are mismatches.

Thermodynamic parameters. Thermodynamic parameters were determined from thermal denaturation studies via construction of van't Hoff plots (see E. O. Otokiti and R. D. Sheardy, *Biophys. J.*, **1997**, *73*, 3135–3141). The T_ms were measured at duplex concentrations of 1.0, 2.0, 3.0, 4.0, and 5.0 μM in a buffer of 10 mM Na cacodylate (pH 7.0) containing 1.0 mM NaCl. The resulting thermodynamic parameters for ODN I:ODN II were given in Table S5.

Table S5. Thermodynamic parameters for ODN I:ODN II.

		X	Y	$-\Delta H^0$ (kcal/mol)	$-\Delta S^0$ (cal/mol•K)	$-\Delta G^0$ (kcal/mol)
		A	T	68.01	183.58	13.28
		G	C	88.58	246.82	14.99
ODN I	5'-GCACCGAA**X**AAACCACG-3'	ImO^N	NaN^O	98.33	269.68	17.93
ODN II	3'-CGTGGCTT**Y**TTTGGTGC-5'	ImN^O	NaO^N	96.93	265.90	17.64
		ImO^O	NaN^N	91.38	249.24	17.07
		ImN^N	NaO^O	126.48	351.62	21.64

Measurement of aromatic stacking ability of a series of naphthyridine (Na) and imidazopyridopyrimidine (Im) bases. According to the method reported by Guckian et al. (*J. Am. Chem. Soc.*, **1996**, *118*, 8182), a series of duplexes, where Z was added at the end of each paired duplex (dangling end), were prepared and the T_m values were determined to evaluate the stacking ability. All measurements were carried out using an ODN (5'-ZCGCGCG-3', 5 μM) in a buffer of 0.01 M sodium cacodylate (pH 7.0) containing 1.0 M NaCl. As a comparison, the T_m data for nondangling and natural bases (A, G, C, and T) at the dangling end listed in Table S6.

Table S6. Measurements of aromatic stacking ability.

	Z	T_m (°C)	ΔT_m / Z (°C)	Z	T_m (°C)	ΔT_m / Z (°C)
5'-**Z**-CGCGCG + GCGCGC-**Z**-5' ⇌ 5'-**Z** CGCGCG GCGCGC **Z**-5'	none	40.8	–			
	NaN^N	59.5	+9.4	NaN^O	61.0	+10.1
	NaO^O	56.9	+8.1	NaO^N	56.7	+8.0
	ImN^N	57.0	+8.1	ImN^O	58.8	+9.0
	ImO^O	52.5	+5.9	ImO^N	57.4	+8.3
	A	54.9	+7.1	C	49.1	+4.2
	G	54.6	+6.9	T	49.1	+4.2