Supporting Information

Modular DNA-based Hybrid Catalysts as a Toolbox for Enantioselective Hydration of α,β-unsaturated Ketones

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Materials

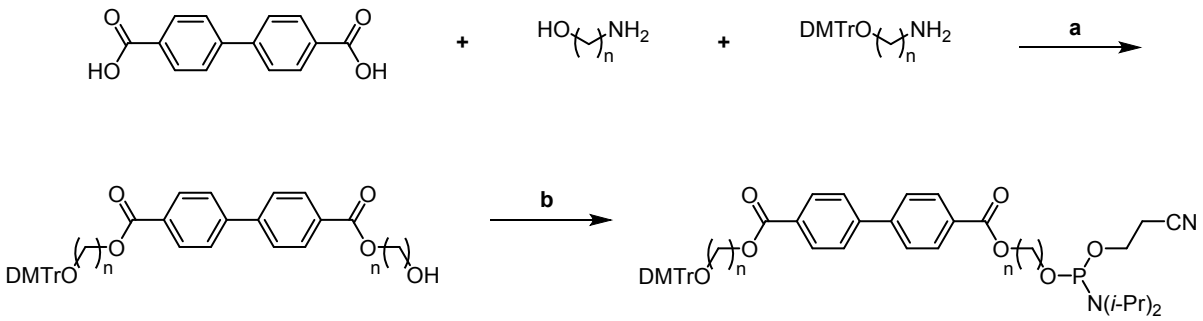
N,N-Dimethylformamide dimethyl acetal, potassium phthalimide, 4,4'-dimethoxytrityl chloride, triethylamine, *N,N*-dimethyl-4-aminopyridine, 3-chloro-1-propanol, 3-amino-1-propanol were received from Wako Chemicals and used without further purification. 2-cyanoethyl *N,N*-diisopropylchloro phosphoramidite, D-threoninol (97%), hydrazine monohydrate, 2,2'-bipyridine-5,5'-dicarboxylic acid, 4-amino-1-butanol were purchased from Sigma-Aldrich Chemicals Co. and used as received. *N,N*-Diisopropylethylamine was purchased from Nacalai and used as received. 6-Amino-1-hexanol, 6-chloro-1-hexanol were obtained from TCI. Glen-Pak™ DNA and RNA cartridges columns are purchased at Glen research and used. All other chemicals and solvents were purchased from Sigma-Aldrich Chemicals Co., Wako Pure Chemical Ind. Ltd., TCI, or Kanto Chemical Co. Inc. and used without further purification and synthetic oligonucleotides were obtained from Sigma Genosys. Water was deionized (specific resistance of $\geq$ 18.0 MW cm at 25^{o}C) by a Milli-Q system (Millipore Corp.).

Methods and Equipment

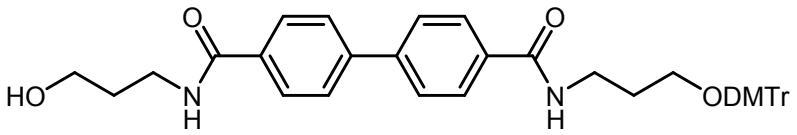
NMR spectra were obtained on a JEOL JNM ECA-600 spectrometer operating at 600 MHz for ^{1}H NMR and 150 MHz for ^{13}C NMR in $CDCl_3$ unless otherwise noted. Flash column chromatography was performed employing Silica Gel 60 (70–230 mesh, Merck Chemicals). Silica-gel preparative thin-layer chromatography (PTLC) was performed using plates from Silica gel 70 PF_{254} (Wako Pure Chemical Ind. Ltd.). Enantiomeric excess (*ee*) determinations were performed by HPLC analysis (Chiralcel AD-H, OD-H) using UV-detection. DNA concentrations were measured by Nanodrop ND-1000 spectrophotometer. Rotary mixing of reaction suspension was performed by Intelli-Mixer RM-2 (Elmi).

Synthetic routes for intrastrand bipyridine ligands and non-binding steric moieties

Synthesis of bi-linker conjugated bipyridine ligand derivatives (^{n}X, n=3, 6) and triethylene glycol linkers (**E**) were followed by previous reported papers[1,2]

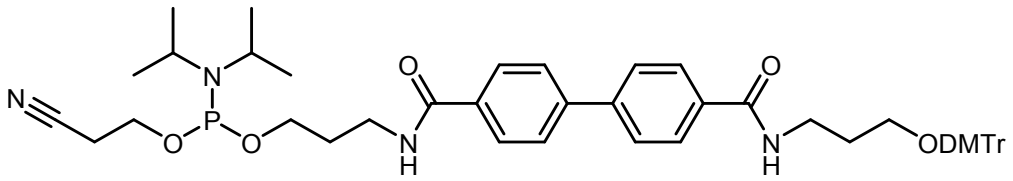


Scheme S1. Synthesis bi(propyl)-linker conjugated biphenyl derivative (**^{3}P**). Reagents and conditions: (a) 3.0 equiv of PyBOP, 5.0 equiv of *i*Pr_2NEt, DMF, rt, 4 h, 76% yield; (b) 1.5 equiv of 2-cyanoethyl *N,N*-diisopropylchlorophosphoramidite, 3.0 equiv of *i*Pr_2NEt, DCM, rt, 1 h. This product was used in the subsequent step without further purification.



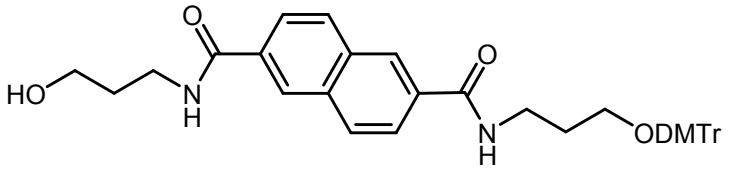
1,1'-biphenyl-4,4'-dicarboxamide 4-(({3-[4,4'-dimethoxytrityl]-oxy}-propyl)-amide)-4'-[(3-hydroxy-propyl)amide]

^{1}H NMR ($CDCl_3$): δ 7.86 (d, J_{HH} = 8.3 Hz, 2H), 7.63 (d, J_{HH} = 7.1 Hz, 4H), 7.49 (d, J_{HH} = 8.3 Hz, 2H), 7.42 (d, J_{HH} = 7.7 Hz, 2H), 7.31 (d, J_{HH} = 8.9 Hz, 4H), 7.29-7.26 (m, 5H), 7.22 (t, J_{HH} = 7.4 Hz, 1H), 6.94 (d, J_{HH} = 4.8 Hz, 1H), 6.81 (d, J_{HH} = 8.9 Hz, 4H), 3.77-3.75 (m, 8H), 3.69 (q, J_{HH} = 5.9 Hz, 2H), 3.59 (q, J_{HH} = 5.5 Hz, 2H), 3.35 (t, J_{HH} = 5.1 Hz, 2H), 1.92 (q, J_{HH} = 5.6 Hz, 2H), 1.84 (q, J_{HH} = 5.6 Hz, 2H). ^{13}C NMR ($CDCl_3$): δ 167.9, 167.0, 158.5, 144.5, 142.9, 142.5, 135.9, 133.8, 133.5, 128.1, 127.9, 127.6, 127.1, 127.0, 126.9, 113.2, 86.7, 62.9, 60.0, 55.1, 39.3, 37.4, 31.39, 28.8 HRMS (ESI-TOF) calculated for $C_{41}H_{42}N_2NaO_6$ $[M+Na]^+$ 681.2900, found 681.2935.



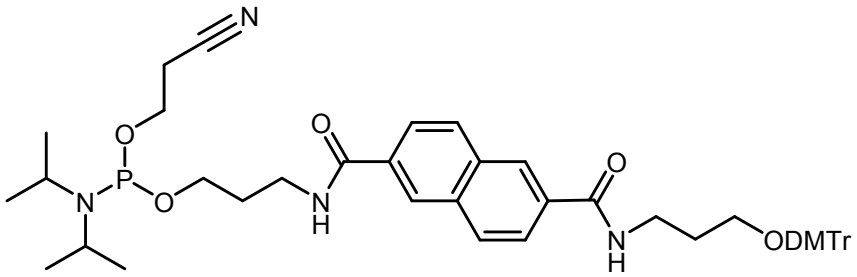
1,1'-biphenyl-4,4'-dicarboxamide 4-(({3-[4,4'-dimethoxytrityl]-oxy}-propyl)-amide)-4'-(({3'-[(2-cyanoethyl)-diisopropyl]}-propyl)-amide phosphoramidite

^{1}H NMR ($CDCl_3$): δ 7.89 (dd, J_{HH} = 8.3 Hz, 1.8 Hz, 2H), 7.66 (m, 4H), 7.52 (dd, J_{HH} = 8.9 Hz, 2.4 Hz, 2H), 7.43 (dd, J_{HH} = 7.4 Hz, 1.5 Hz, 2H), 7.32 (dd, J_{HH} = 8.9 Hz, 2.4 Hz, 4H), 7.29-7.28 (m, 2H), 7.22 (t, J_{HH} = 7.1 Hz, 1H), 6.92 (s, J_{HH} = 4.8 Hz, 2H), 6.81 (dd, J_{HH} = 8.9 Hz, 2.4 Hz, 4H), 3.89-3.85 (m, 2H), 3.84-3.78 (m, 2H), 3.75 (s, 6H), 3.65-3.61 (m, 2H), 3.59 (q, J_{HH} = 3.2 Hz, 2H), 3.36-3.48 (m, 2H), 2.77-2.73 (m, 2H), 2.62 (td, J_{HH} = 6.5 Hz, 2.4 Hz, 2H), 1.99-1.92 (m, 4H), 1.18 (t, J_{HH} = 7.4 Hz, 12H).^{13}C NMR ($CDCl_3$): δ 166.9, 166.7, 158.5, 144.5, 142.5, 135.9, 133.9, 133.8, 129.9, 128.1, 127.9, 127.5, 127.1, 127.0, 126.8, 117.7, 113.1, 86.6, 62.7, 58.3, 58.1, 55.1, 45.3, 43.1, 38.1, 30.3, 28.9, 24.6, 20.0. ^{31}P NMR ($CDCl_3$): δ 148.84. ESI-TOF Mass calculated for $C_{50}H_{59}O_7N_4NaP$ $[M+Na]^+$ 881.40, found 859.39



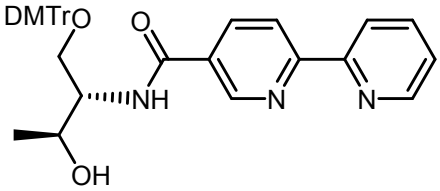
Naphthalene-2,6-dicarboxamide 2-(({3-[4,4'-dimethoxytrityl]-oxy}-propyl)-amide)-6-[(3-hydroxy-propyl)amide]

Synthesis of bi(propyl)-linker conjugated naphthalene derivative (**^{3}N**) was followed by the synthetic procedure for a bi(propyl)-linker conjugated biphenyl derivative (**^{3}P**). 50% yield. ^{1}H NMR ($CDCl_3$): δ 8.26 (s, 1H), 8.09 (s, 1H), 7.79 (dd, J_{HH} = 8.9 Hz, 1.2 Hz, 1H), 7.77 (d, J_{HH} = 8.9 Hz, 1H), 7.69-7.67 (m, 2H), 7.43 (d, J_{HH} = 7.1 Hz, 2H), 7.32 (d, J_{HH} = 8.9 Hz, 5H), 7.26-2.23 (m, 4H), 7.2 (t, J_{HH} = 7.1 Hz, 1H), 7.02 (t, $^{3}J_{HH}$ = 5.1 Hz, 1H), 6.98 (t, $^{3}J_{HH}$ = 5.6 Hz, 1H), 6.77 (d, J_{HH} = 8.3 Hz, 4H), 3.79 (t, J_{HH} = 5.6, 2H), 3.72-3.69 (m, 8H), 3.63 (q, J_{HH} = 5.7 Hz, 2H), 3.35 (t, J_{HH} = 5.3 Hz, 2H), 1.95 (q, J_{HH} = 5.8 Hz, 2H), 1.86 (q, J_{HH} = 5.8 Hz, 2H). ^{13}C NMR ($CDCl_3$): δ 168.1, 167.1, 158.5, 144.6, 135.9, 133.9, 133.7, 133.5, 132.9, 129.97, 129.6, 129.3, 128.1, 127.9, 127.1, 126.99, 126.91, 124.6, 124.1, 113.2, 86.7, 62.8, 60.1, 55.2, 39.3, 37.5, 32.1, 28.9 HRMS (ESI-TOF) calculated for $C_{39}H_{40}N_2NaO_6$ $[M+Na]^+$ 655.2779, found 655.2755.



Naphthalene-2,6-dicarboxamide 4-(({3-[4,4'-dimethoxytrityl]-oxy}-propyl)-amide)-4'-(({3'-[(2-cyanoethyl)-diisopropyl]}-propyl)-amide phosphoramidite

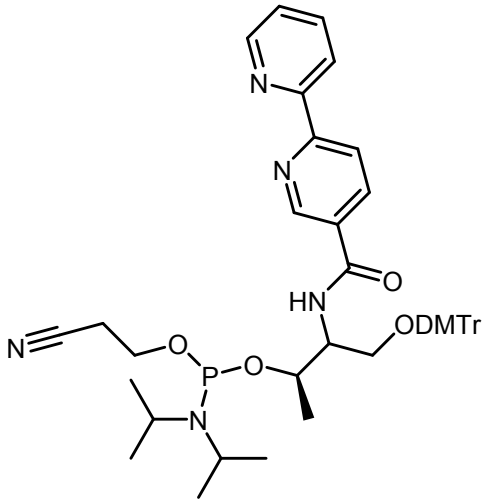
^{1}H NMR ($CDCl_3$): δ 8.31 (s, 1H), 8.13 (s, 1H), 7.86 (dd, J_{HH} = 8.6 Hz, 1.5 Hz, 1H), 7.83 (d, J_{HH} = 8.3 Hz, 1H), 7.75 (d, J_{HH} = 8.9 Hz, 2H), 7.72 (dd, J_{HH} = 8.6 Hz, 1.5 Hz, 1H), 7.44 (d, J_{HH} = 1.2 Hz, 2H), 7.32 (dt, J_{HH} = 7.6 Hz, 4.9 Hz, 1.3 Hz, 4H), 7.25 (t, J_{HH} = 7.4 Hz, 2H), 7.19 (t, J_{HH} = 7.1 Hz, 1H), 6.99 (t, J_{HH} = 5.3 Hz , 1H), 6.97 (t, J_{HH} = 5.1 Hz, 1H), 6.78 (q, J_{HH} = 4.95 Hz, 4H), 3.92-3.85 (m, 2H), 3.81-3.77 (m, 2H), 3.72 (s, 6H), 3.69-3.57 (m, 4H), 3.34 (t, J_{HH} = 5.3 Hz, 2H), 2.77-2.63 (m, 2H), 2.57 (t, J_{HH} = 6.2 2H), 2.01-1.99 (m, 2H), 1.97-1.93 (m, 2H), 1.16 (t, J_{HH} = 7.1 Hz, 12H).^{13}C NMR ($CDCl_3$): δ 167.1, 167.0, 158.5, 144.7, 135.9, 133.8, 133.5, 133.47, 129.9, 129.4, 129.2, 128.1, 127.9, 127.7, 126.96, 126.86. 124.6, 124.3, 117.7, 113.2, 86.6, 62.6, 60.99, 58.3, 55.1, 47.6, 43.1, 39.2, 38.3, 30.4, 28.9, 24.6, 20.4. ^{31}P NMR ($CDCl_3$): δ 147.86. ESI-TOF Mass calculated for $C_{48}H_{57}O_7N_4NaP$ $[M+Na]^+$855.39, found 855.38.



2,2'-bipyridine-5-carboxamide *N*-((2S,3S)-1-({4,4'-dimethoxytrityl-oxy})-3-hydroxybutan-2-ol)

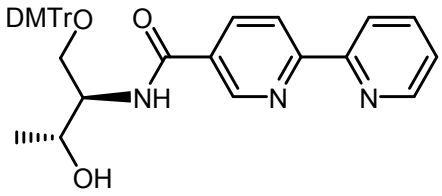
DMTr-protected D-threoninol backbone was synthesized based on the previous report by Asanuma and co-workers.[5] To a 2,2'-bipyridine-5-carboxylic acid (130 mg, 0.65 mmol) in DMF (dehydrated, 4 mL), (2S,3S)-3-amino-4-{4,4'-dimethoxytrityl-oxy}-3-hydroxybutan-2-ol 397 mg, 0.98 mmol) in DMF (dehydrated, 7 mL) and DIEA (559 μL, 3.3 mmol) was added PyBOP (774 mg, 1.4 mmol) and the resulting mixture was stirred for 3 days at the room temperature. The mixture was evaporated and purified by column chromatography with CH_2Cl_2:MeOH = 100:1 to CH_2Cl_2:MeOH = 10:1 to afford a brown oil. (240 mg, 46% yield)

^{1}H NMR ($CDCl_3$): δ 9.09 (d, J_{HH} = 2.2 Hz, 1H), 8.72 (d, J_{HH} = 4.8 Hz, 1H), 8.53 (d, J_{HH} = 8.1 Hz, 1H), 8.48 (d, J_{HH} = 7.8 Hz, 1H), 8.21 (dd, J_{HH} = 8.3, 2.2 Hz, 1H), 7.86 (td, J_{HH} = 7.6, 1.7 Hz, 1H), 7.39 (dd, J_{HH} = 8.5, 1.0 Hz, 2H), 7.36 (m, 1H), 7.28 (m, 5H), 7.20 (t, J_{HH} = 7.3 Hz, 1H), 6.85 (d, J_{HH} = 8.9 Hz, 1H), 6.81 (t, J_{HH}= 8.7, 4H), 4.25 (qd, J_{HH} = 6.3, 1.8 Hz, 1H), 4.15 (m, 1H), 3.764 (s, 3H), 3.756 (s, 3H), 3.60 (dd, J_{HH} = 9.7, 4.2 Hz, 1H), 3.43 (dd, J_{HH} = 9.9, 3.4 Hz, 1H), 3.10 (s, 1H), 1.23 (d, J_{HH} = 6.5 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 165.9, 158.8, 158.7, 155.2, 149.5, 147.9, 144.4, 137.2, 135.9, 135.5, 135.3, 130.04, 130.00, 129.7, 128.1, 128.0, 127.2, 124.5, 121.8, 120.8, 113.5, 87.1, 68.8, 65.5, 55.3, 54.1, 20.3. HRMS (ESI-TOF) calculated for $C_{36}H_{35}N_3NaO_5$ $[M+Na]^+$ 612.2469, found 612.2455. $[\alpha]_D$ value D-^{t}X was -8.5 (c 1.30, $CHCl_3$)



2,2'-bipyridine-5-carboxamide *N*-((2S,3S)-1-({4,4'-dimethoxytrityl-oxy})-3-[(2-cyanoethyl)-diisopropyl]butan-2-yl phosphoramidite

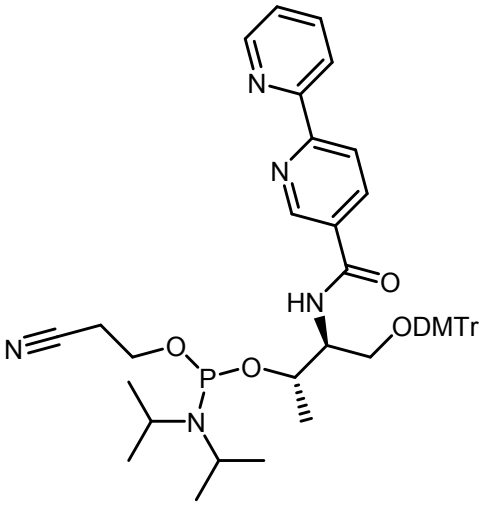
^{1}H NMR ($CDCl_3$): δ 9.04 (dd, J_{HH} = 21 Hz, 1.8 Hz, 1H), 8.70 (ddd, J_{HH} = 4.0 Hz, 1.5 Hz, 0.89 Hz, 1H), 8.49 (dd, J_{HH} = 8.6 Hz, 4.5 Hz, 1H), 8.47 (dd, J_{HH} = 8.0 Hz, 3.9 Hz 1H), 8.18 (ddd, J_{HH} = 20 Hz, 8.3 Hz, 2.1 Hz, 1H), 7.84 (td, J_{HH} = 7.9 Hz, 1.6 Hz, 1H), 7.43 (d, J_{HH} = 8.3 Hz, 2H), 7.35 (ddd, J_{HH} = 7.6 Hz, 4.9 Hz, 1.3 Hz, 1H), 7.31 (dd, J_{HH} = 8.9, 1.2 Hz, 7H), 7.29-7.26 (m, 5H), 7.20 (t, J_{HH} = 7.1 Hz, 1H), 6.86 (d, J_{HH} = 8.5 Hz, 1H), 6.81 (q, J_{HH}= 4.2 Hz, 4H), 4.42-4.36 (m, 1H), 4.12 (q, J_{HH} = 7.1 Hz, 1H), 3.93-3.81 (m, 2H), 3.78 (d, J_{HH} = 1.8 Hz, 6H), 3.66-3.62 (m, 2H), 3.43 (d, J_{HH} = 6.5 Hz, 1H), 2.69-2.59 (m, 4H), 1.26 (t, J_{HH} = 7.1 Hz, 3H), 1.15 (dd, J_{HH} = 6.8 Hz, 2.7 Hz, 12H). ^{13}C NMR ($CDCl_3$): δ 165.3, 158.5 (overlapped), 155.2, 149.3, 147.7, 144.7, 137.1. 136.9, 135.9, 135.7, 130.1, 129.9, 128.2, 127.8, 126.8, 124.2, 121.6, 120.6, 117.7, 113.1, 86.1, 69.0, 62.6, 60.3, 58.2, 55.2, 43.3, 24.6, 20.1, 14.2. ^{31}P NMR ($CDCl_3$): δ 139.65, 139.9, 148.78, 149.14. ESI-TOF Mass calculated for $C_{45}H_{53}O_6N_5P$ $[M+H]^+$ 790.37, found 790.37



2,2'-bipyridine-5-carboxamide *N*-((2R,3R)-1-({4,4'-dimethoxytrityl-oxy})-3-hydroxybutan-2-ol)

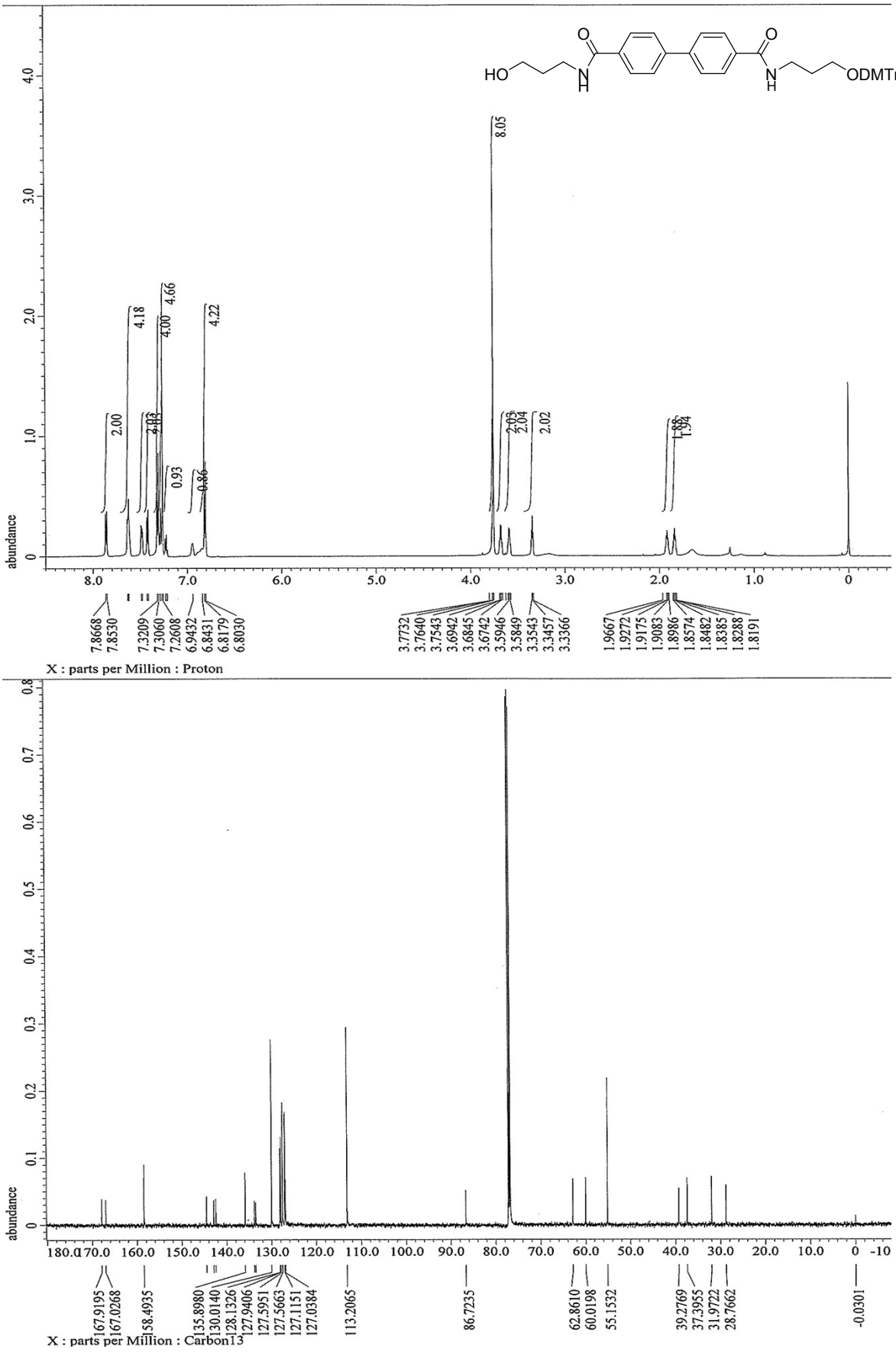
DMTr-protected L-threoninol backbone was synthesized based on the previous report by Asanuma and co-workers.[6] To a 2,2'-bipyridine-5-carboxylic acid (130 mg, 0.65 mmol) in DMF (dehydrated, 4 mL), (2S,3S)-3-amino-4-{4,4'-dimethoxytrityl-oxy}-3-hydroxybutan-2-ol 397 mg, 0.98 mmol) in DMF (dehydrated, 7 mL) and DIEA (559 μL, 3.3 mmol) was added PyBOP (774 mg, 1.4 mmol) and the resulting mixture was stirred for 2 days at the 80 °C. The mixture was evaporated and purified by column chromatography with CH_2Cl_2:MeOH = 100:1 to CH_2Cl_2:MeOH = 10:1 to afford a brown oil. (240 mg, 64% yield)

^{1}H NMR ($CDCl_3$): δ 9.09 (d, J_{HH} = 1.2 Hz, 1H), 8.72 (dd, J_{HH} = 4.8 Hz, J_{HH} = 0.59 Hz, 1H), 8.53 (dd, J_{HH} = 7.7 Hz, J_{HH} = 0.59 Hz, 1H), 8.48 (dt, J_{HH} = 8.3 Hz, J_{HH} = 1.2 Hz, 1H), 8.21 (dd, J_{HH} = 8.3, J_{HH} = 2.4 Hz, 1H), 7.86 (td, J_{HH} = 7.7, J_{HH} = 1.8 Hz, 1H), 7.4-7.35 (m, 3H), 7.29 (dd, J_{HH} = 8.9 Hz, J_{HH} = 2.4 Hz, 5H), 7.27-7.26 (m, 1H), 7.20 (t, J_{HH} = 7.1 Hz, 1H), 6.86 (d, J_{HH} = 8.3 Hz, 1H), 6.81 (t, J_{HH}= 8.3, 4H), 4.25 (dd, J_{HH} = 5.9, J_{HH} = 2.4 Hz, 1H), 4.16 (dd, J_{HH} = 8.3 Hz, J_{HH} = 2.4 Hz, 1H), 3.76 (d, J_{HH} = 4.8 Hz, , 6H), 3.60 (dd, J_{HH} = 9.5, J_{HH} = 4.2 Hz, 1H), 3.43 (dd, J_{HH} = 10 Hz, J_{HH} = 3.6 Hz, 1H), 2.66 (q, J_{HH} = 7.1 Hz, 1H), 1.23 (d, J_{HH} = 5.95 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 165.7, 158.7, 158.6, 155.1, 149.3, 147.8, 144.2, 137.0, 135.5, 135.4, 135.2, 129.9, 129.8, 129.5, 128.1, 127.8, 127.1, 124.1, 124.4, 121.6, 113.4, 87, 68.7, 65.3, 55.2, 53.9, 26.7, 20.1. HRMS (ESI-TOF) calculated for $C_{36}H_{36}N_3NaO_5$ $[M+Na+H]^+$ 613.2547, found 613.2455. $[\alpha]_D$ value L-^{t}X was +7.8 (c 1.10, $CHCl_3$)



2,2'-bipyridine-5-carboxamide *N*-((2R,3R)-1-({4,4'-dimethoxytrityl-oxy})-3-[(2-cyanoethyl)-diisopropyl]butan-2-yl phosphoramidite

^{1}H NMR ($CDCl_3$): δ 9.02 (dd, J_{HH} = 20.5 Hz, J_{HH} = 1.5 Hz, 1H), 8.68 (dd, J_{HH} = 4.8 Hz, J_{HH} = 1.8 Hz, 1H), 8.47-8.43 (m, 2H), 8.19 (ddd, J_{HH} = 20 Hz, J_{HH} = 8.3 Hz, J_{HH} = 2.4 Hz, 1H), 7.82 (td, J_{HH} = 7.6 Hz, J_{HH} = 1.8 Hz, 1H), 7.41 (d, J_{HH} = 8.3 Hz, 2H), 7.32 (q, J_{HH} = 3.96 Hz, 1H), 7.29 (dd, J_{HH} = 8.3, J_{HH} = 1.8 Hz, 5H), 7.26-7.23 (m, 1H), 7.18 (t, J_{HH} = 5.9 Hz, 1H), 6.79-6.77 (m, 5H), 4.48-4.43 (m, 1H), 4.40-4.34 (m, 1H), 4.01 (q, J_{HH} = 7.7 Hz, 2H), 3.75 (q, J_{HH} = 1.8 Hz, 6H), 3.73-3.71 (m, 2H), 3.29 (q, J_{HH} = 6.4 Hz, 1H), 2.77-2.67 (m, 4H), 1.24-1.22 (m, 3H), 1.15 (t, J_{HH} = 6.5 Hz, 12H). ^{13}C NMR ($CDCl_3$): δ 165.4, 158.6, 158.5, 155.3, 149.4, 147.97, 147,79, 144,8, 137.1, 136.1, 135,9, 135.8, 130.2, 130.1, 128.3, 127.9, 126.9, 124.4, 121.7, 120.7, 117.4, 113.2, 86.3, 62.7, 59.4, 58.5, 55.2, 43.0, 24.6, 20.4, 17.1. ^{31}P NMR ($CDCl_3$): δ 147.47, 139.59. ESI-TOF Mass calculated for $C_{45}H_{53}O_6N_5P$ $[M+H]^+$ 790.3728, found 790.3712.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O
N
H
O
N
H
ODMTr
abundance
8.05
4.18
4.66
4.00
4.22
2.00
2.03
2.04
2.02
0.93
0.86
1.94
7.8668
7.8530
7.3209
7.3060
7.2608
6.9432
6.8431
6.8179
6.8030
3.7732
3.7640
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3.6942
3.6845
3.6742
3.5946
3.5849
3.3543
3.3457
3.3366
1.9667
1.9272
1.9175
1.9083
1.8986
1.8574
1.8482
1.8385
1.8288
1.8191
X : parts per Million : Proton
abundance
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167.0268
158.4935
135.8980
130.0140
128.1326
127.9406
127.5951
127.5663
127.1151
127.0384
113.2065
86.7235
62.8610
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55.1532
39.2769
37.3955
31.9722
28.7662
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X : parts per Million : Carbon13

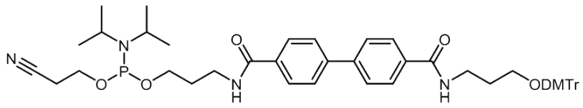
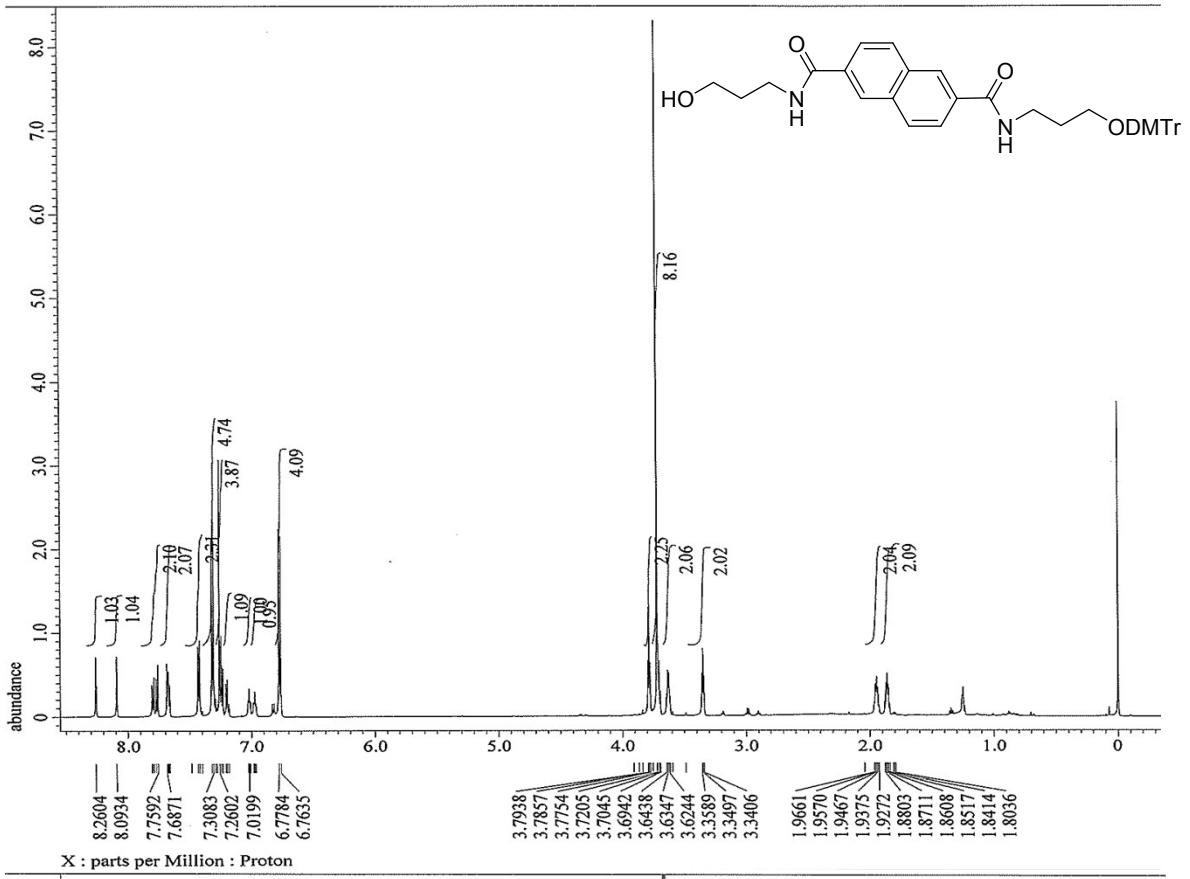


Figure S1. ^{1}H NMR, ^{13}C NMR, and ^{31}P NMR spectra of biphenyl derivative (**^{3}P**)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O
N
H
O
N
H
ODMTr
abundance
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4.74
3.87
4.09
2.10
2.07
2.31
2.25
2.06
2.02
2.04
2.09
1.03
1.04
1.09
8.2604
8.0934
7.7592
7.6871
7.3083
7.2602
7.0199
6.7784
6.7635
3.7938
3.7857
3.7754
3.7205
3.7045
3.6942
3.6438
3.6347
3.6244
3.3589
3.3497
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1.9661
1.9570
1.9467
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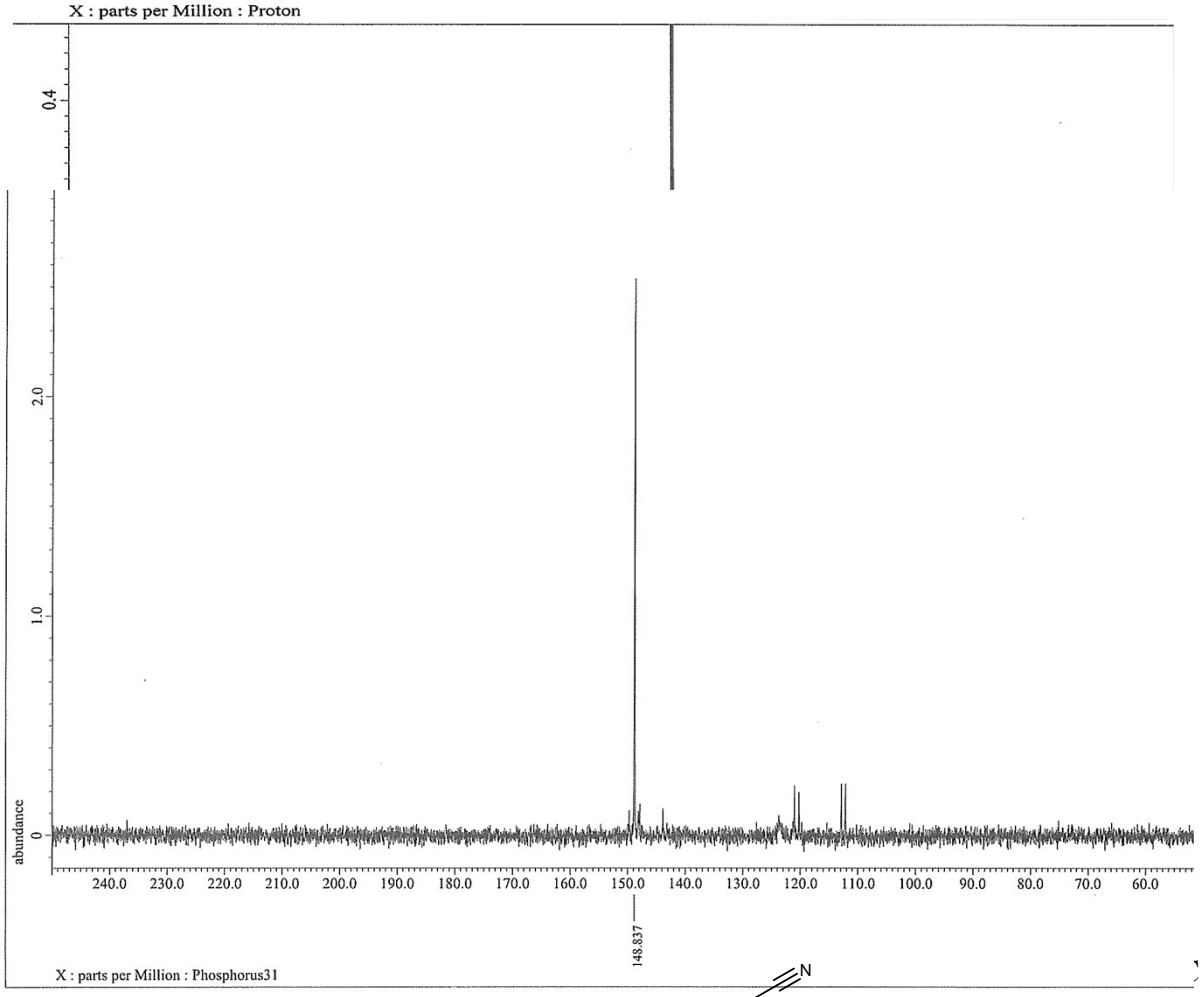
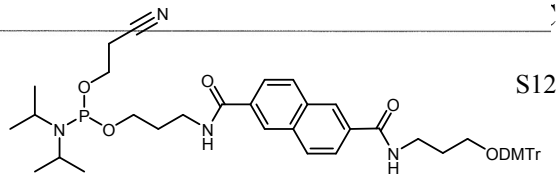
1.8608
1.8517
1.8414
1.8036
X : parts per Million : Proton


abundance
148.837
X : parts per Million : Phosphorus31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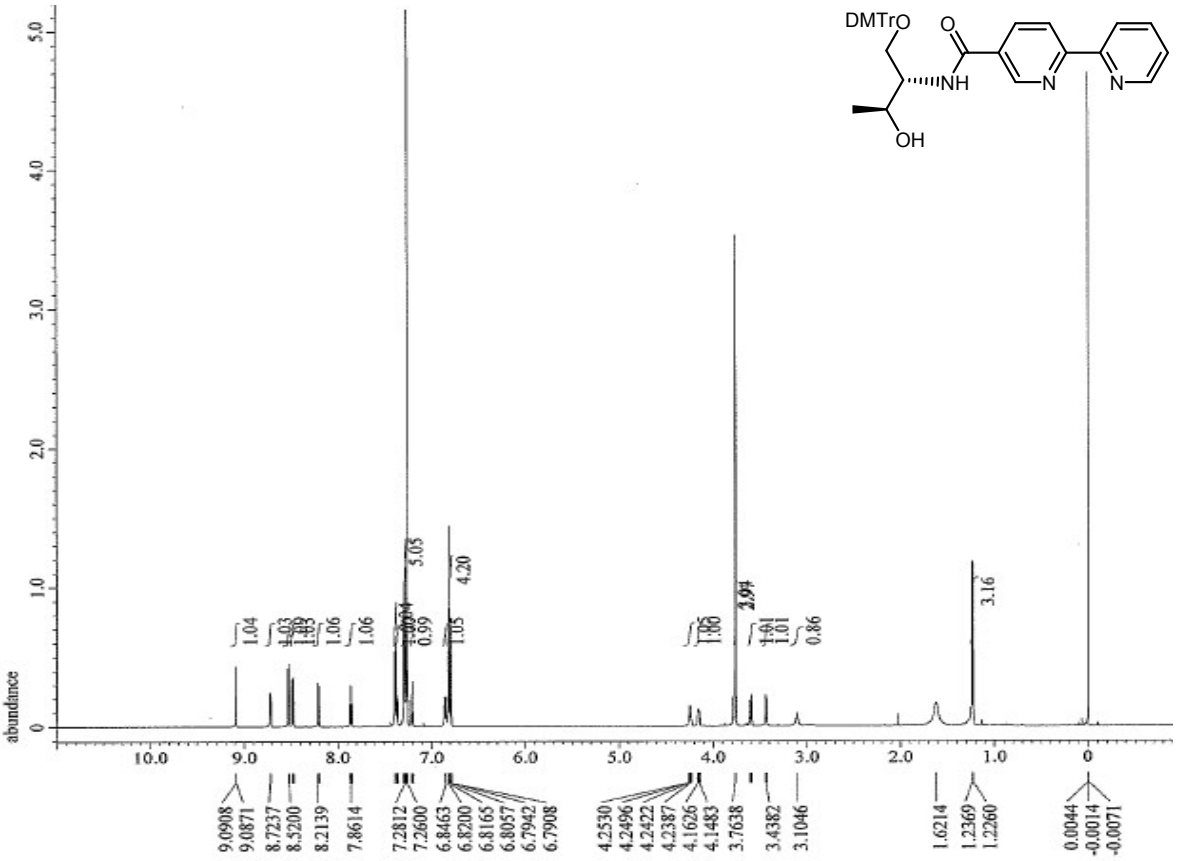
O
P
N
O
O
N
H
O
N
H
ODMTr

NMR, and ^{31}P NMR spectra of naphthalene derivative (**^{3}N**)


DMTrO
O
NH
N
N
OH
abundance
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1.03
1.05
1.06
1.06
5.03
1.00
0.99
4.20
1.05
1.06
1.00
1.01
1.01
0.86
3.16
9.0908
9.0871
8.7237
8.5200
8.2139
7.8614
7.2812
7.2600
6.8463
6.8200
6.8165
6.8057
6.7942
6.7908
4.2530
4.2496
4.2422
4.2387
4.1626
4.1483
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3.4382
3.1046
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1.2369
1.2260
0.0044
-0.0014
-0.0071

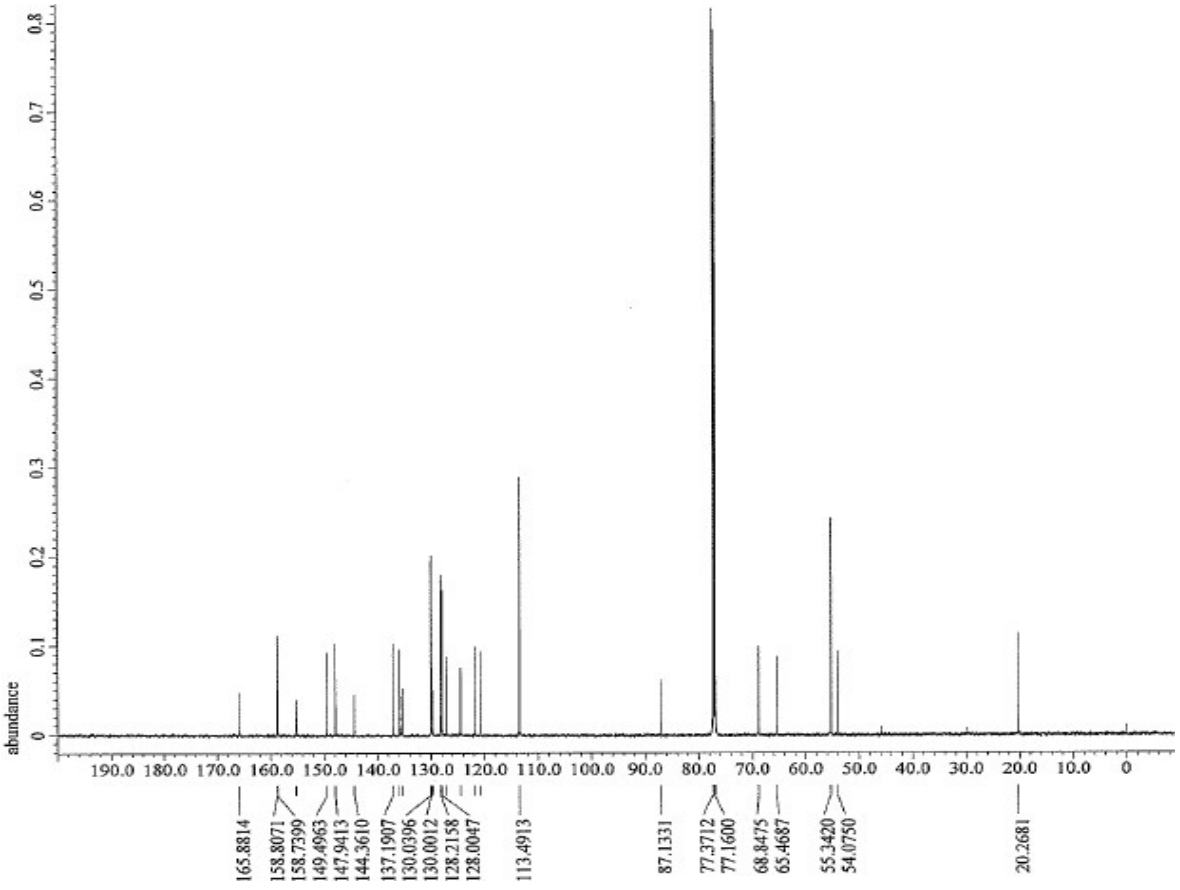
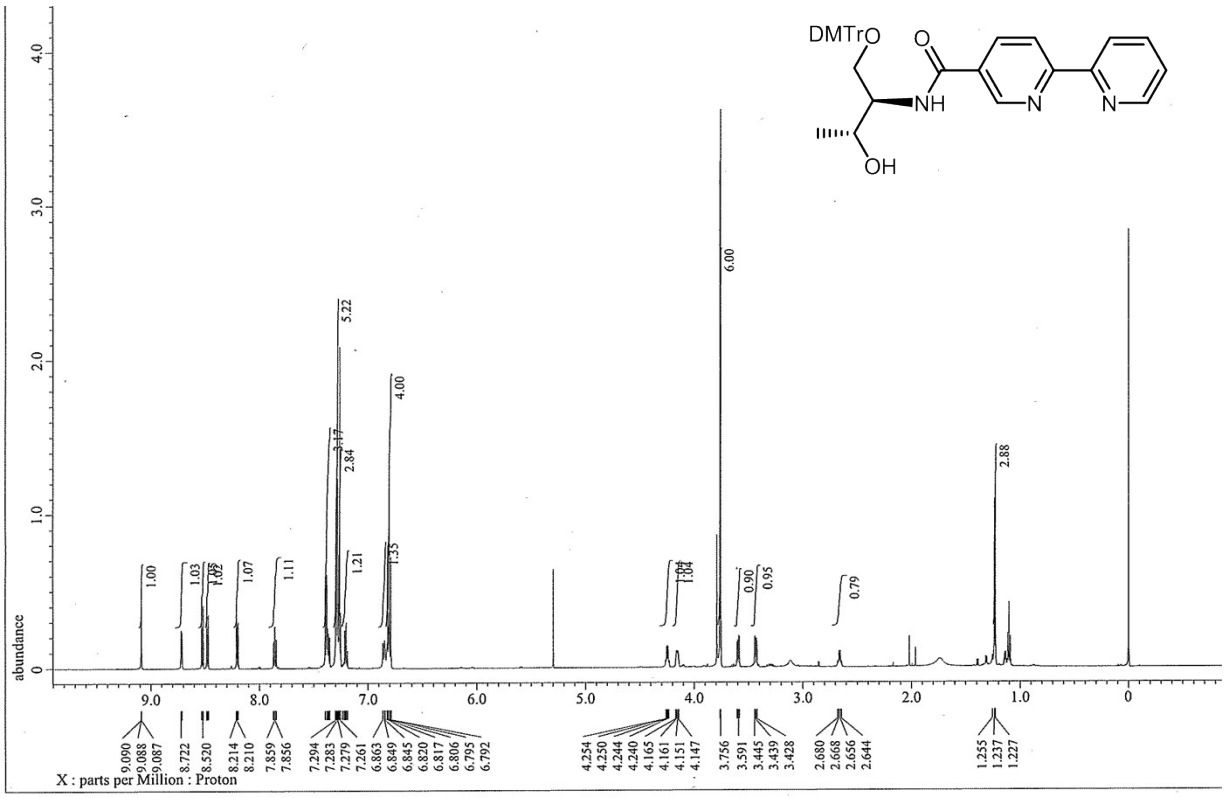
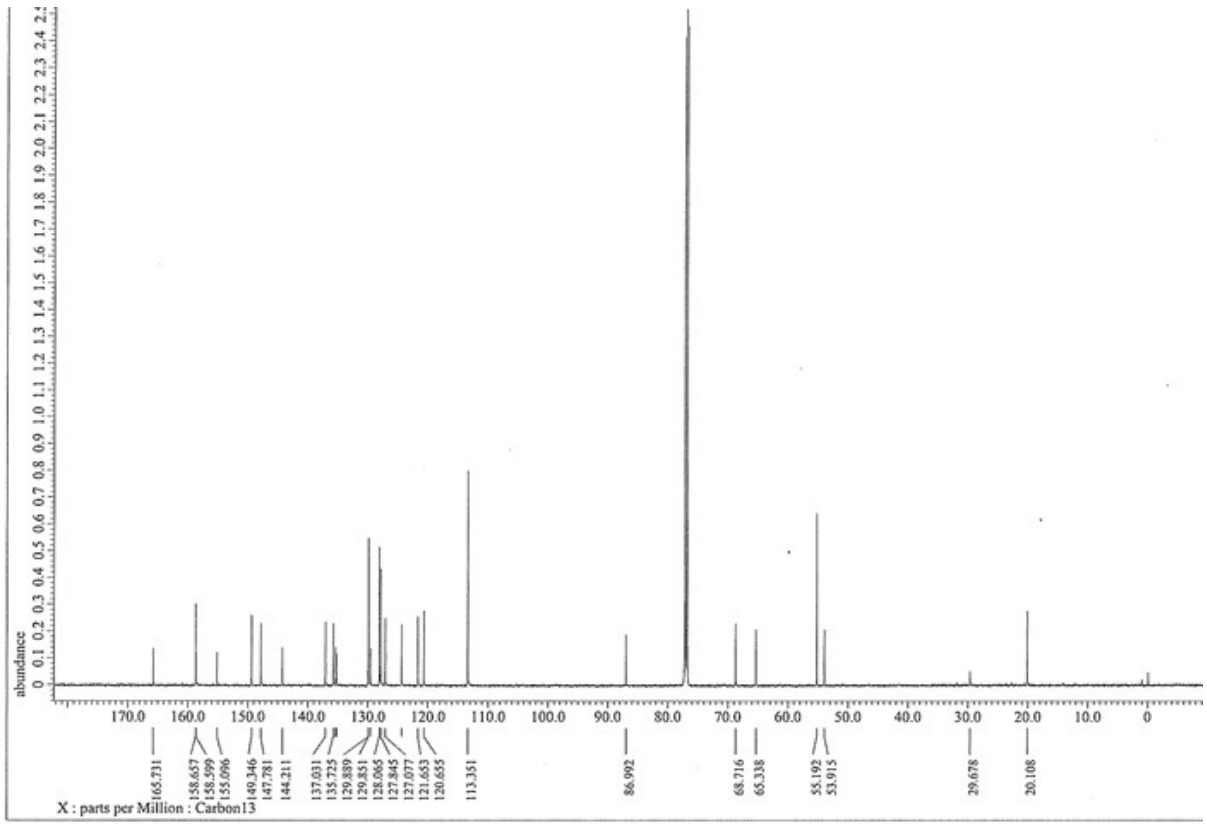

abundance
165.8814
158.8071
158.7399
149.4963
147.9413
144.3610
137.1907
130.0396
130.0012
128.2158
128.0047
113.4913
87.1331
77.3712
77.1600
68.8475
65.4687
55.3420
54.0750
20.2681

Figure S3. ^{1}H NMR, ^{13}C NMR, ^{31}P NMR, and enlarged spectra of the ^{31}P NMR spectra of the bipyridine-conjugated threoninol derivatives (**^{Dt}X**) [7-8]


DMTrO
O
NH
N
N
OH
abundance
X : parts per Million : Proton


abundance
X : parts per Million : Carbon13

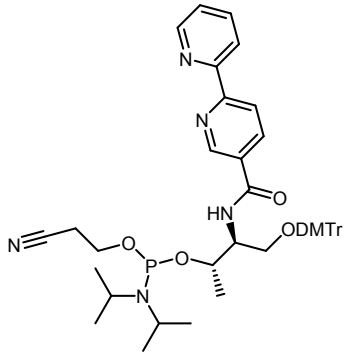
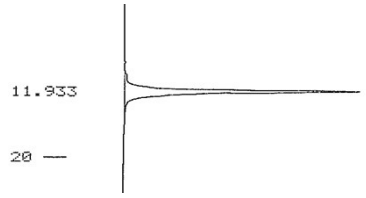
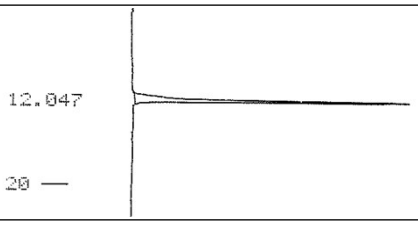
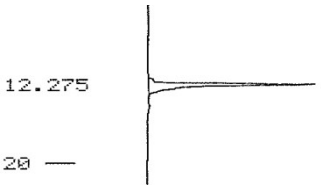
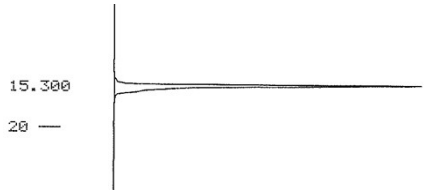
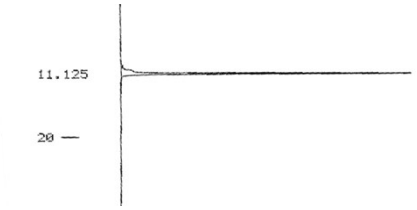


Figure S4. ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra of the bipyridine-conjugated threoninol derivatives (**^{Lt}X**) (^{1}H NMR ($CDCl_3$): δ 5.3 (s) indicates solvent peak of CH_2Cl_2)

ODN No.	Analytical HPLC profile
ODN8	
ODN12	
ODN13	
ODN15	
ODN16	
ODN17	

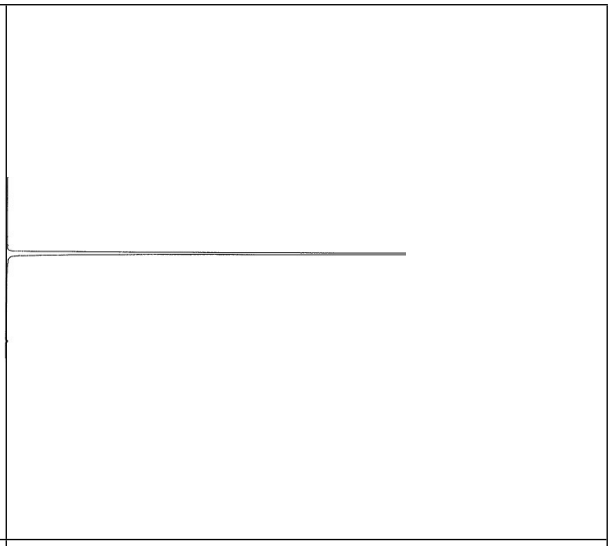
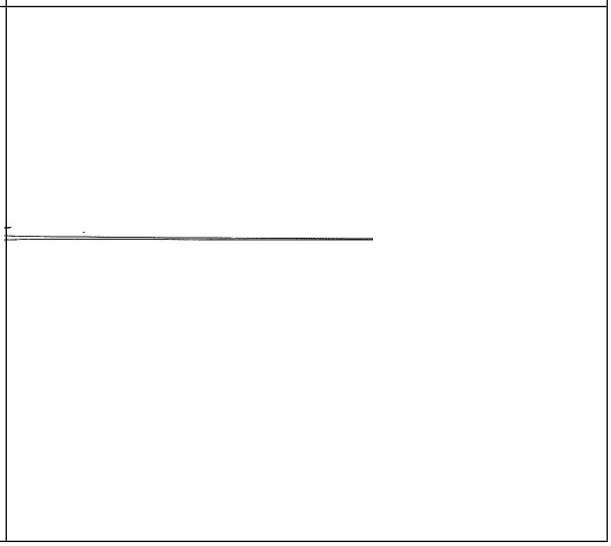
ODN18	
ODN19	

Table S1. Analytical HPLC profile of newly synthesized oligonucleotides (**ODN8, ODN12, ODN13, ODN15, ODN16, ODN17)**; For HPLC analysis, COSMOSIL 5C18 AR-II (Nacalai Tesque, Inc., Kyoto, 150 × 10 mm id), a linear gradient of 3 to 30% acetonitrile over 30 min at a flow rate of 3.0 mL/min. 50 mM ammonium formate (pH 6.6) was used as a buffer on 254 nm.

Table S2. MALDI-TOF-Mass data of ODNs.

Other DNA oligomers were purchased from Sigma Genosys or JBios.

DNA oligomer	Calcd.	Found.

5’-ACCGTG**dS**CCATGC-3’ (**ODN8**)	3784.7	3785.2
5’-ACCGTG^{3}**N**CCATGC-3’ (**ODN12**)	3996.8	3996.9
5’-ACCGTG^{3}**P**CCATGC-3’ (**ODN13**)	4022.8	4022.1
5'-GCATGA^{t}**X**TACGGT-3' (**ODN15**)	4032.7	4031.3
5'-GCATGG^{t}**X**CACGGT-3' (**ODN16**)	4033.7	4032.9
5'-GCATGG^{Lt}**X**CACGGT-3' (**ODN17**)	4033.7	4033.7
5’-CAAAAA^{t}**X**TTTTTG-3’ (**ODN18**)	3990.7	3991.2
5’-GCGCGC^{t}**X**GCGCGC-3’ (**ODN19**)	3995.7	3994.6

Enantioselective hydration of α,β-unsaturated ketones

The *ee* of the product was determined on a Daicel Chiralcel AD-H, OD-H column with a solvent mixture of suitable polarity. Various ratios of Hexane and 2-propanol mixed solution was used with a flow rate of 1.0 mL/min or 0.5 mL/min.[3-4] The conversion of the chiral products was calculated based on the below formula

$$\text{conversion (\%)} = \frac{A(\text{v.s.})_{pd}}{\frac{A(\text{v.s.})_{sm}}{C} + A(\text{v.s.})_{pd}} \times 100$$

Here, $A(v.s.)_{pd}$ is the total peak area of the product of the reaction, $A(v.s.)_{sm}$ is the peak area of the starting material and ***C*** is the correction factor determined from a calibration curve.

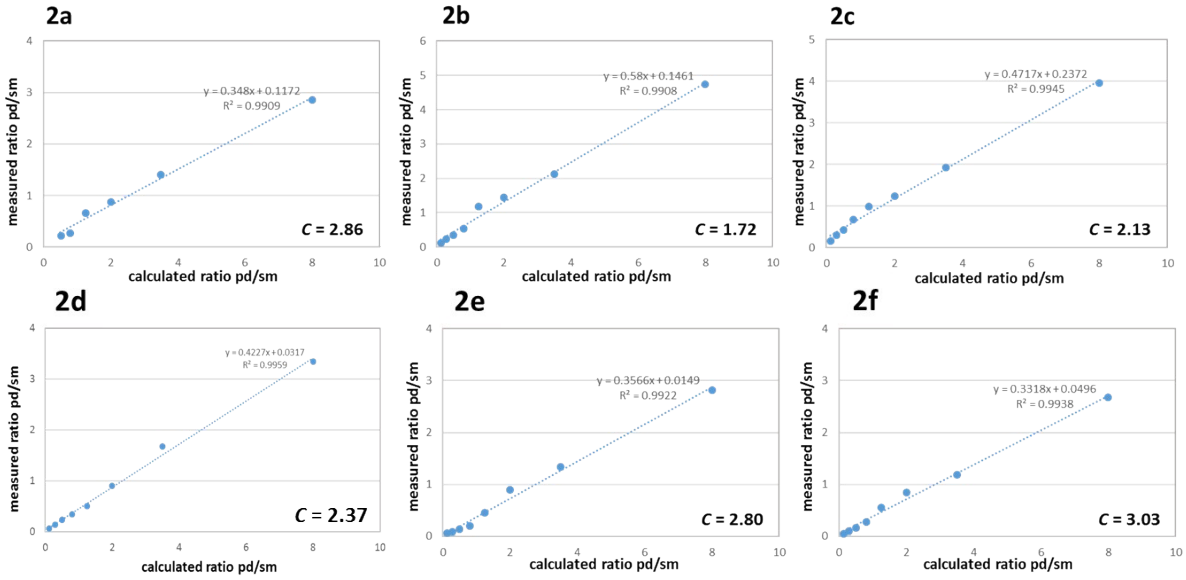
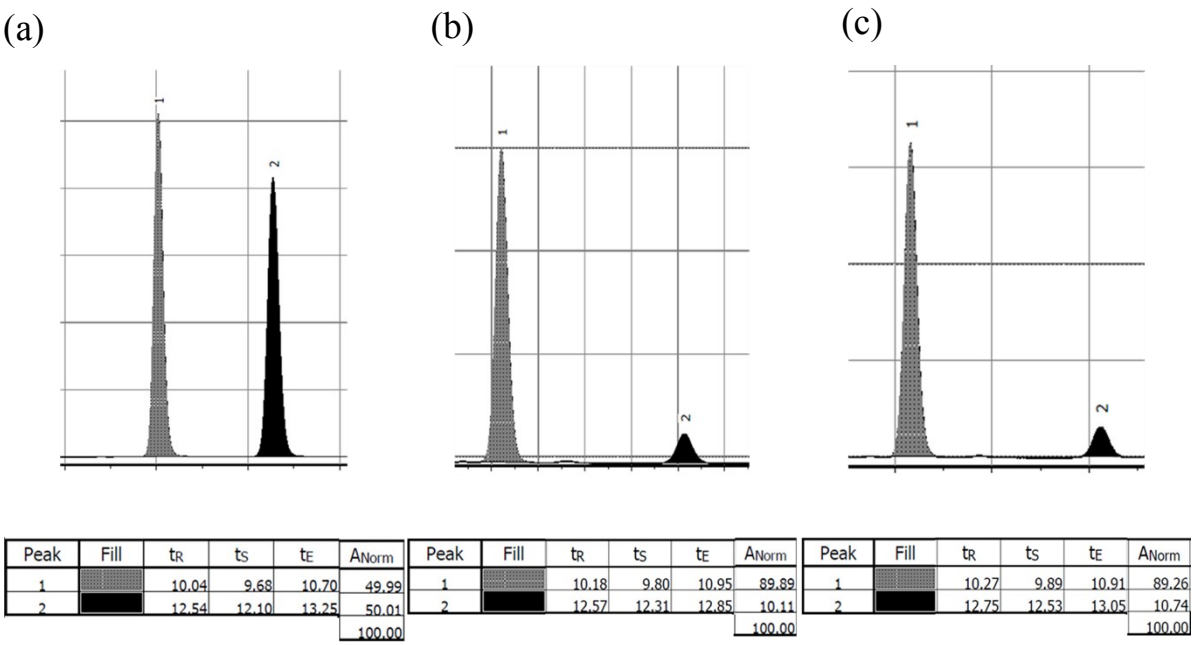


Figure S5. Calibration curves for the determination of the correction factor of 2a-2f



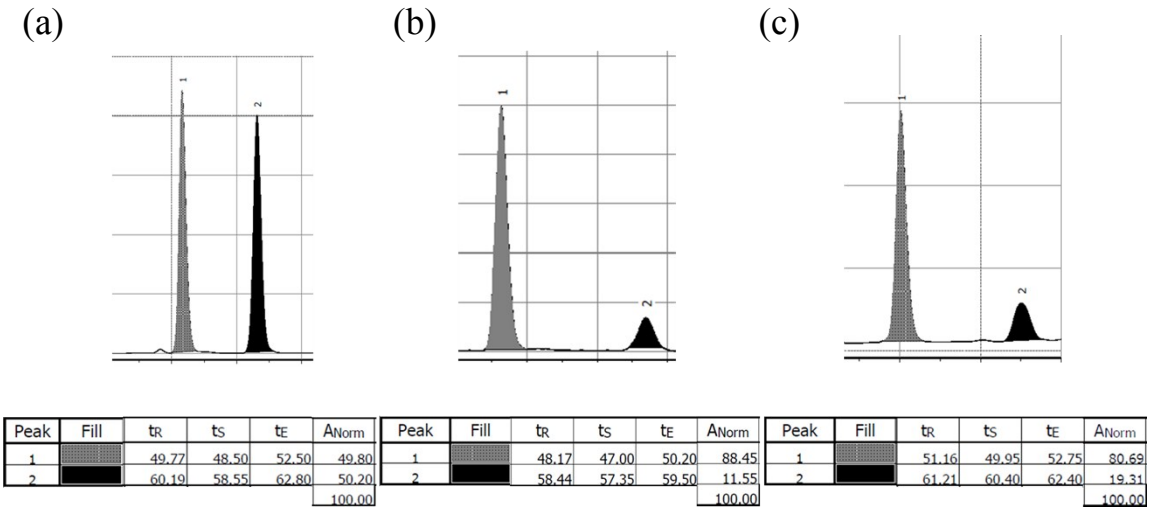
Peak	Fill	tR	tS	tE	ANorm
1		10.04	9.68	10.70	49.99
2		12.54	12.10	13.25	50.01
					100.00

Peak	Fill	tR	tS	tE	ANorm
1		10.18	9.80	10.95	89.89
2		12.57	12.31	12.85	10.11
					100.00

Peak	Fill	tR	tS	tE	ANorm
1		10.27	9.89	10.91	89.26
2		12.75	12.53	13.05	10.74
					100.00

Figure S6. HPLC analysis of the R_1=*N*-methylimidazole, R_2=*tert*-butyl substituted α,β-unsaturated ketone product. a) racemic mixture of **2a** (Coefficient *C*= 2.86), b) enantioenriched **2a** by **ODN14/ODN13** (-G^{6}**X**C-/C^{3}**P**G-), c) enantioenriched **2a** by **ODN16/ODN13** (-G^{t}**X**C-/C^{3}**P**G-) (entry 1 in **Scheme 1**). Chiral HPLC analysis conditions: CHIRALPAK® AD-H (DAICEL Corporation, 4.6 × 250 mm, 5 μm particle size), Hexane/2-propanol=90/10 mixed

solution at a flow rate of 1.0 mL/min, rt, 275 nm.

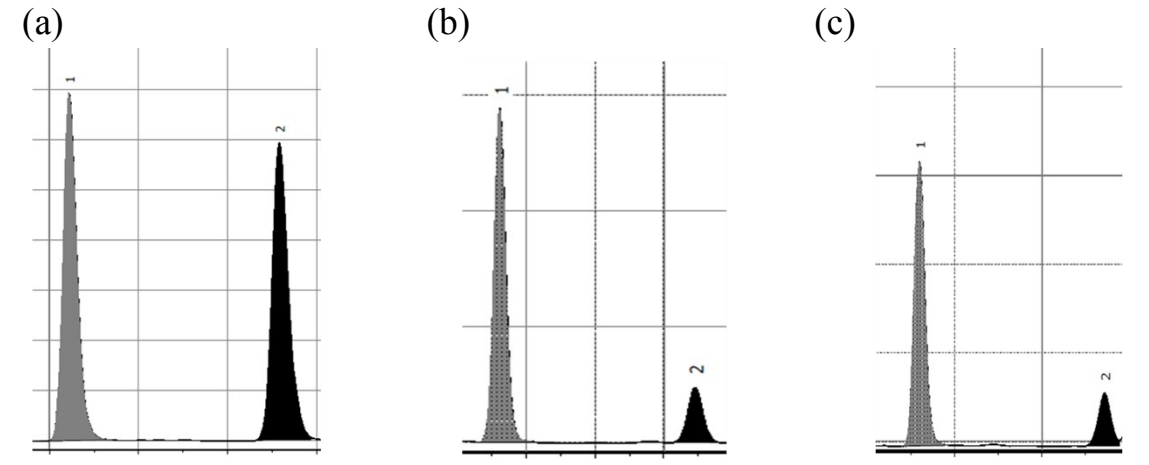


Peak	Fill	t_R	t_S	t_E	A_{Norm}
1		49.77	48.50	52.50	49.80
2		60.19	58.55	62.80	50.20
					100.00

Peak	Fill	t_R	t_S	t_E	A_{Norm}
1		48.17	47.00	50.20	88.45
2		58.44	57.35	59.50	11.55
					100.00

Peak	Fill	t_R	t_S	t_E	A_{Norm}
1		51.16	49.95	52.75	80.69
2		61.21	60.40	62.40	19.31
					100.00

Figure S7. HPLC analysis of the R_1=*N*-methylimidazole, R_2=cyclohexyl substituted α,β-unsaturated ketone product. a) a) racemic mixture of **2b** (Coefficient *C*= 1.76), b) enantioenriched **2b** by **ODN14/ODN13** (-G^{6}**X**C-/C^{3}**P**G-), c) enantioenriched **2b** by **ODN16/ODN13** (-G^{t}**X**C-/C^{3}**P**G-) (**Scheme 1**). (The time interval between two peaks is identical.) Chiral HPLC analysis conditions: CHIRALPAK® AD-H (DAICEL Corporation, 4.6 × 250 mm, 5 μm particle size), Hexane/2-propanol=95/5 mixed solution at a flow rate of 0.5 mL/min, rt, 275 nm.

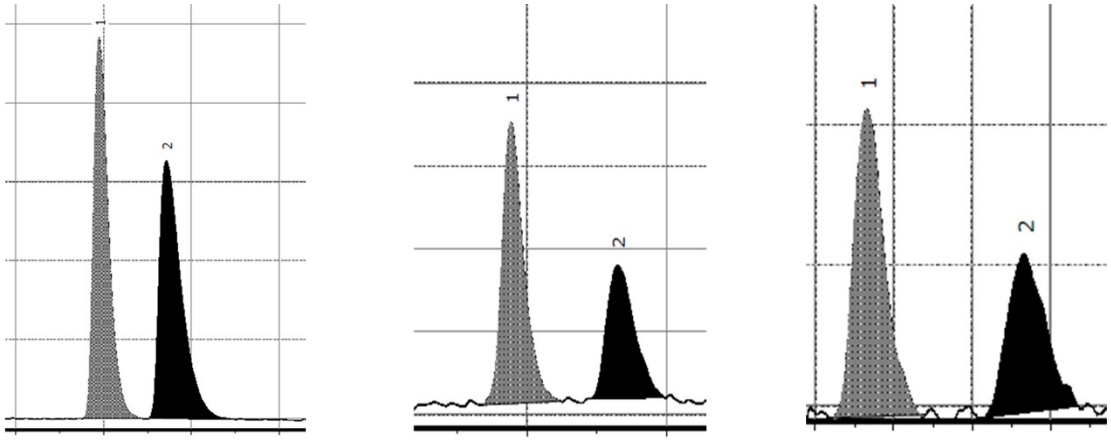


Peak	Fill	t_R	t_S	t_E	A_{Norm}
1		36.11	34.50	38.62	49.93
2		47.89	46.62	50.00	50.07
					100.00

Peak	Fill	t_R	t_S	t_E	A_{Norm}
1		38.35	37.60	39.70	83.76
2		49.24	48.33	49.98	16.24
					100.00

Peak	Fill	t_R	t_S	t_E	A_{Norm}
1		37.97	36.85	39.75	82.82
2		48.59	47.60	49.45	17.18
					100.00

Figure S8. HPLC analysis of the R_1=*N*-methylimidazole, R_2=*i*-propyl substituted α,β-unsaturated ketone product. a) racemic mixture of **2c** (Coefficient *C*= 2.13), b) enantioenriched **2c** by **ODN14/ODN13** (-G^{6}**X**C-/C^{3}**P**G-), c) enantioenriched **2c** by **ODN16/ODN13** (-G^{t}**X**C-/C^{3}**P**G-) (**Scheme 1**). Chiral HPLC column analysis conditions: CHIRALPAK® AD-H (DAICEL Corporation, 4.6 × 250 mm, 5 μm particle size), Hexane/2-propanol=95/5 mixed solution at a flow rate of 0.5 mL/min, rt, 275 nm.

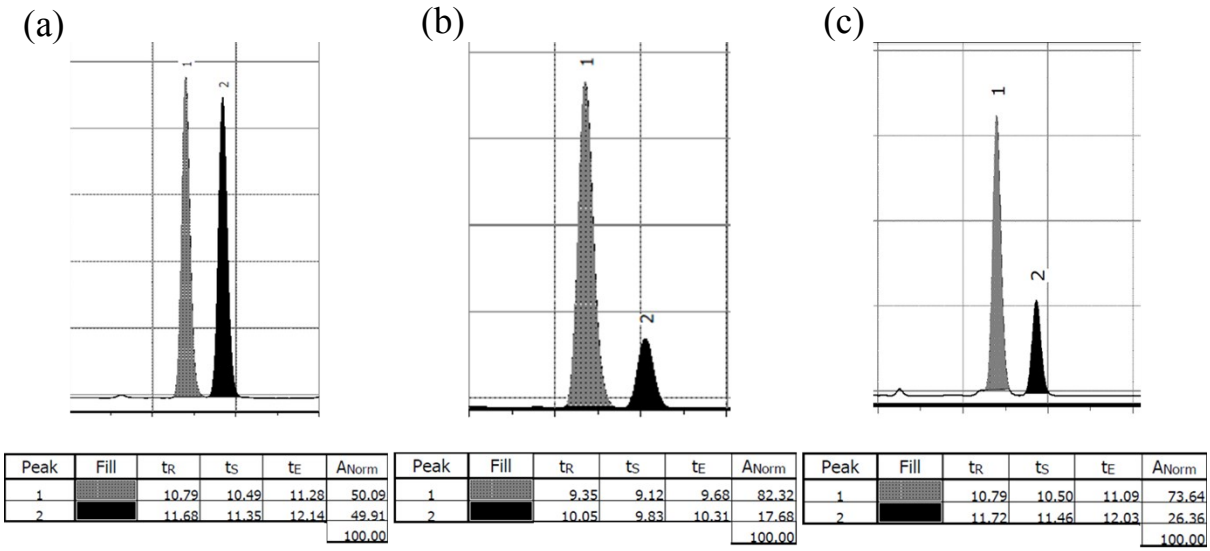


Peak	Fill	t_R	t_S	t_E	ANorm
1		34.73	33.80	37.20	50.25
2		38.57	37.55	42.15	49.75
					100.00

Peak	Fill	t_R	t_S	t_E	ANorm
1		34.43	33.40	36.20	62.19
2		38.24	37.20	39.95	37.81
					100.00

Peak	Fill	t_R	t_S	t_E	ANorm
1		35.31	34.40	36.80	65.80
2		39.33	38.40	40.30	34.20
					100.00

Figure S9. HPLC analysis of the R_1=*N*-methylimidazole, R_2=methyl substituted α,β-unsaturated ketone product. a) racemic mixture of **2d** (Coefficient *C*= 2.37), b) enantioenriched **2d** by **ODN14/ODN13** (-G^{6}**X**C-/C^{3}**P**G-), c) enantioenriched **2d** by **ODN16/ODN13** (-G^{t}**X**C-/C^{3}**P**G-) (**Scheme 1**). For chiral HPLC analysis, CHIRALPAK® AS-H (DAICEL Corporation, 4.6 × 250 mm, 5 μm particle size), Hexane/2-propanol=95/5 mixed solution at a flow rate of 1.0 mL/min, rt, 254 nm.

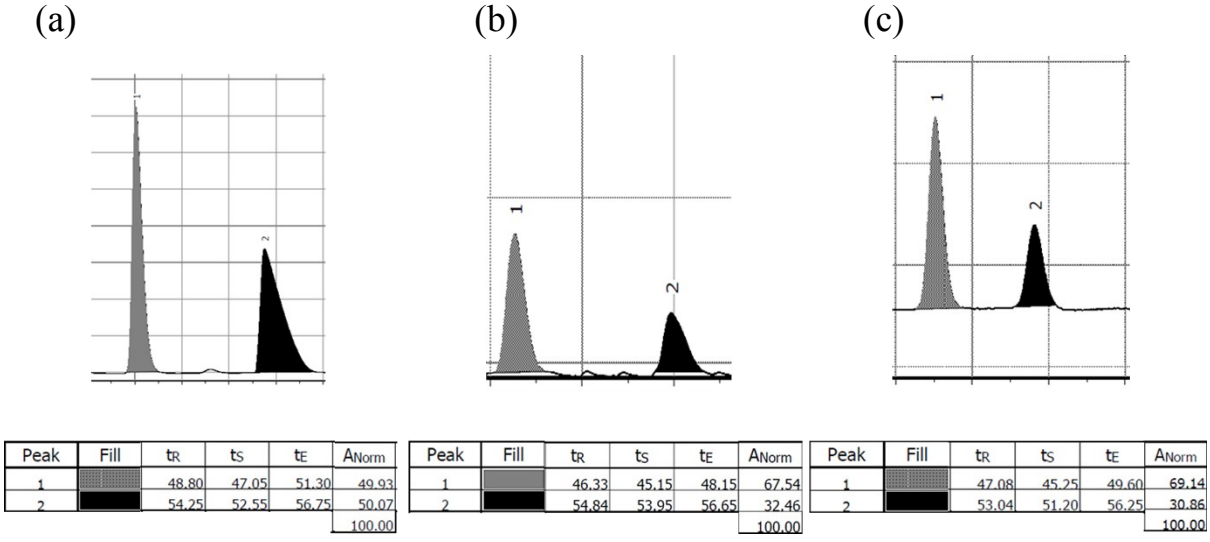


Peak	Fill	t_R	t_S	t_E	ANorm
1		10.79	10.49	11.28	50.09
2		11.68	11.35	12.14	49.91
					100.00

Peak	Fill	t_R	t_S	t_E	ANorm
1		9.35	9.12	9.68	82.32
2		10.05	9.83	10.31	17.68
					100.00

Peak	Fill	t_R	t_S	t_E	ANorm
1		10.79	10.50	11.09	73.64
2		11.72	11.46	12.03	26.36
					100.00

Figure S10. HPLC analysis of the R_1=pyridine, R_2=*tert*-butyl substituted α,β-unsaturated ketone product. a) racemic mixture of **2e** (Coefficient *C*= 2.80), b) enantioenriched **2e** by **ODN14/ODN13** (-G^6**X**C-/C^3**P**G-), c) enantioenriched **2e** by **ODN16/ODN13** (-G^t**X**C-/C^3**P**G-) (**Scheme 1**). Chiral HPLC analysis conditions, CHIRALPAK® AD-H (DAICEL Corporation, 4.6 × 250 mm, 5 μm particle size), Hexane/2-propanol=90/10 mixed solution at a flow rate of 1.0 mL/min, rt, 275 nm.

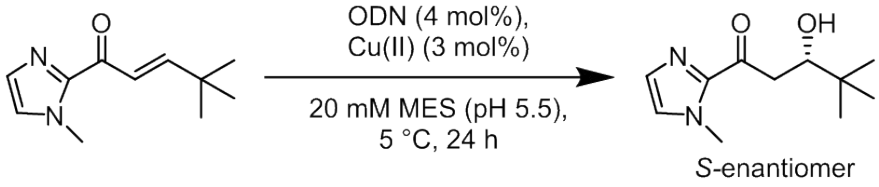


Peak	Fill	t_R	t_S	t_E	ANorm
1		48.80	47.05	51.30	49.93
2		54.25	52.55	56.75	50.07
					100.00

Peak	Fill	t_R	t_S	t_E	ANorm
1		46.33	45.15	48.15	67.54
2		54.84	53.95	56.65	32.46
					100.00

Peak	Fill	t_R	t_S	t_E	ANorm
1		47.08	45.25	49.60	69.14
2		53.04	51.20	56.25	30.86
					100.00

Figure S11. HPLC analysis of the R_1=pyridine, R_2=pentane substituted α,β-unsaturated ketone product. a) racemic mixture of **2f** (Coefficient *C*= 3.03), b) enantioenriched **2f** by **ODN14/ODN13** (-G^6**X**C-/C^3**P**G-), c) enantioenriched **2f** by **ODN16/ODN13** (-G^t**X**C-/C^3**P**G-) (**Scheme 1**). For chiral HPLC analysis, CHIRALPAK® OD-H (DAICEL Corporation, 4.6 × 250 mm, 5 μm prticle size), Hexane/2-propanol=99/1 mixed solution at a flow rate of 0.5 mL/min, rt, 254 nm.



entry[a]	DNA sequences	ee [conv.] /%
1[b]	5'-GCATG**G^{6}XC**ACGGT-3' (**ODN14**)	30[6]
2[b]	5'-GCATG**G^{t}XC**ACGGT-3' (**ODN16**)	17[6]
3	5'-CAAAA**A^{t}XT**TTTTG-3' (**ODN18**) 3'-GTTTT**T^{t}XA**AAAAC-5' (**ODN18**)	18[13]
4	5'-GCGCG**C^{t}XG**CGCGC-3' (**ODN19**) 3'-CGCGC**G^{t}XC**GCGCG-5' (**ODN19**)	11[18]
5[c]	5'-GCATG**GGC**ACGGT-3' (**ODN20**) 3'-CGTAC**CCG**TGCCA-5' (**ODN21**)	racemate [20]

Table S3. Enatioselective hydration reaction of **1a** α,β-unsaturated ketone catalyzed by the DNA-based hybrid catalysts

[a] Experiments were carried out using 3.3 mM α,β-unsaturated 2-acyl imidazole, 0.13 mM DNA, and 0.1 mM $CuSO_4$ (or 0.1mM Cu(dmbpy) complex) at 5 °C in 20 mM MES buffer (pH 5.5) for 1 day. The conversion and enantioselectivities were determined by chiral HPLC analysis. [b] Optimized reaction conditions with 4 mol% of single-strand modified DNA and 3 mol% of Cu(II) ion in 20 mM MES buffer (pH 5.5). [c] Reaction conditions with 4 mol% of DNA and 4 mol% of Cu(dmbpy) complexes in 20 mM MES buffer (pH 5.5).

UV Spectroscopy study

1) CD Spectroscopy.

CD spectra of oligonucleotide solutions collected in 0.5-nm steps from 360 to 220 nm were measured using JASCO J-805LST Spectrometer in a 1-cm quartz cuvette. The buffer and concentrations of MES were the same as for Fluorescence measurement. Each spectrum shown is the average of two individual scans.

2) T_m Measurement (UV-melting)

Melting temperature was determined by measuring changes in absorbance at 260 nm as a function of temperature using a JASCO V-650 UV/VIS spectrophotometer. JASCO PAC-743R equipped with a high performance temperature controller and micro auto eight-cell holder.

Absorbance was recorded in the forward and reverse direction at temperatures from 5 to 95 °C at a rate of 0.5 °C/min. The melting samples were denatured at 95 °C for 3 min and annealed slowly to RT then stored at 5 °C until experiments were initiated. All melting samples were prepared in a total volume of 150 µl containing 3.3 µM of each strand oligonucleotide, 2.5 µM $CuSO_4$, 20 mM MES buffer (pH 5.5) and 100 mM NaCl.

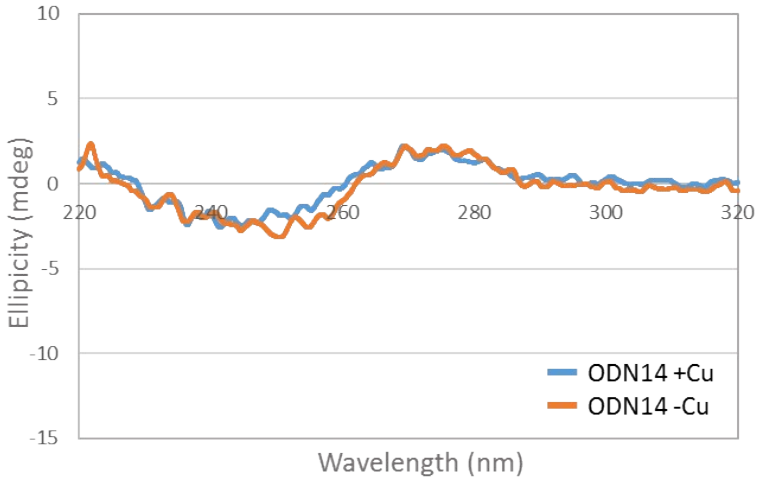


Figure S12. CD spectra of the single-strand ODN14 (-G^{6}**X**C-) in 20 mM MES buffer (pH 5.5) with 100 mM NaCl in the presence and absence of 2.5 µM copper (II) ion

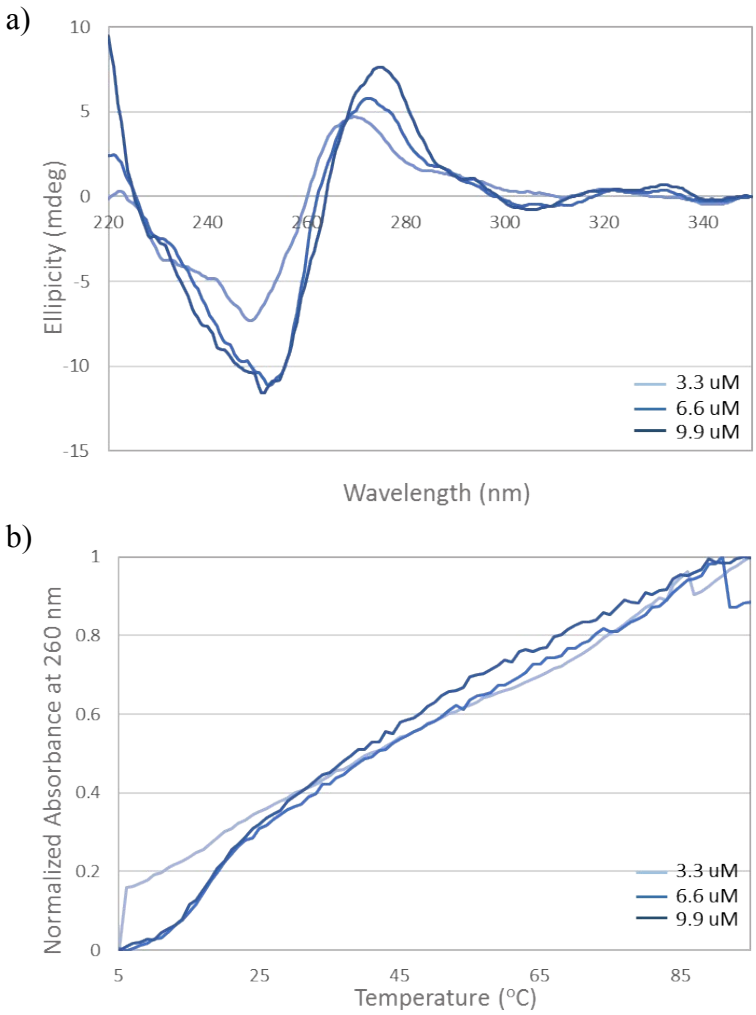


Figure S13. Spectroscopic studies of the various concentration of **ODN14/ODN13** (-G^{6}**X**C-/-C^{3}**P**G-) in the absence of salt. a) CD spectra of the various concentration of DNA oligomer (**ODN13**/**ODN14**) and 2.5 μM of copper(II) in 20 mM MES buffer (pH 5.5). b) UV melting curve of the various concentration of **ODN14/ODN13** (-G^{6}**X**C-/-C^{3}**P**G-) and 2.5 μM of copper(II) in 20 mM MES buffer (pH 5.5)

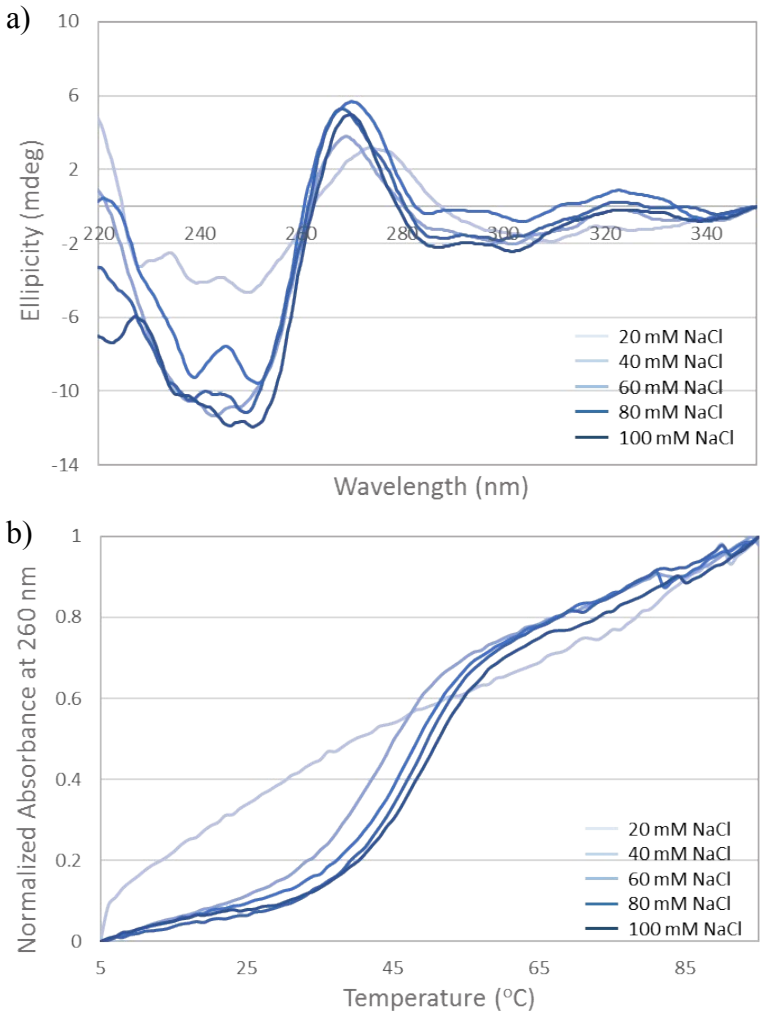


Figure S14. Spectroscopic studies of 3.3 μM **ODN14/ODN13** (-G^{6}**X**C-/-C^{3}**P**G-) with the various salt conditions. a) CD spectra of 3.3 μM DNA oligomer (**ODN13**/**ODN14**) and 2.5 μM of copper(II) in 20 mM MES buffer (pH 5.5) with the various salt conditions. b) UV melting curve of 3.3 μM DNA oligomer (**ODN13**/**ODN14**) and 2.5 μM of copper(II) in 20 mM MES buffer (pH 5.5) with the various salt conditions.

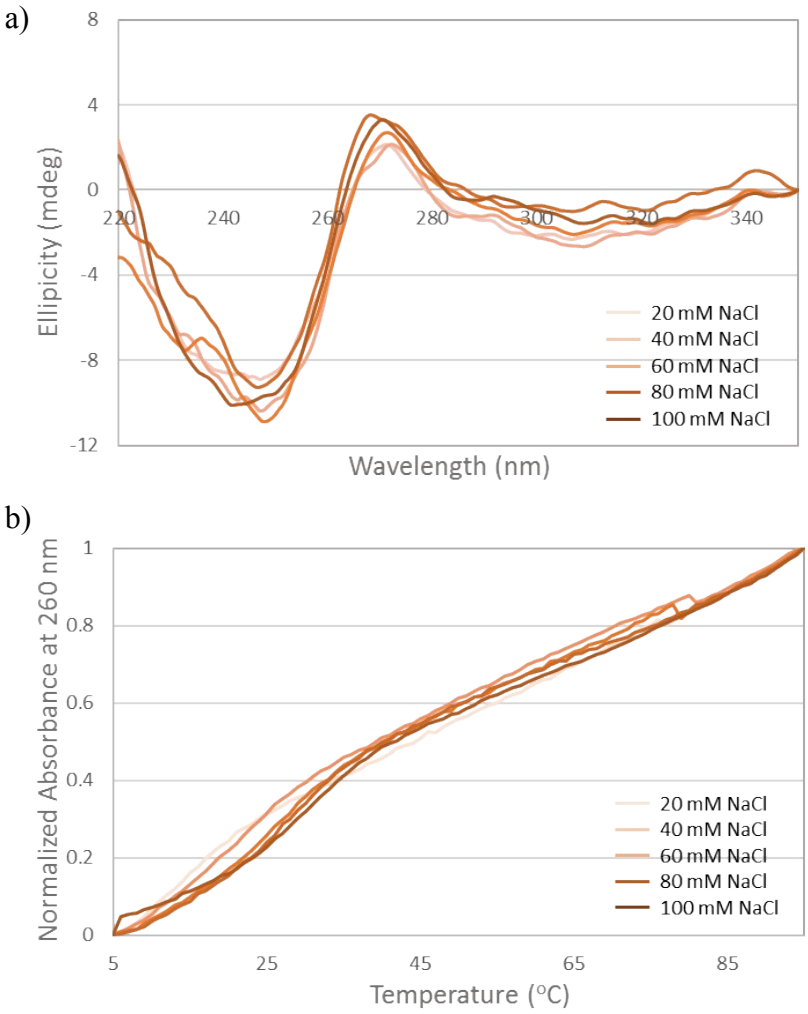


Figure S15. Spectroscopic studies of 3.3 µM **ODN16/ODN13** (-G^{t}**X**C-/-C^{3}**P**G-) with the various salt conditions. a) CD spectra of 3.3 µM DNA oligomer (**ODN16**/**ODN13**) and 2.5 µM of copper(II) in 20 mM MES buffer (pH 5.5) with the various salt conditions. b) UV melting curve of 3.3 µM DNA oligomer (**ODN16**/**ODN13**) and 2.5 µM of copper(II) in 20 mM MES buffer (pH 5.5) with the various salt conditions.

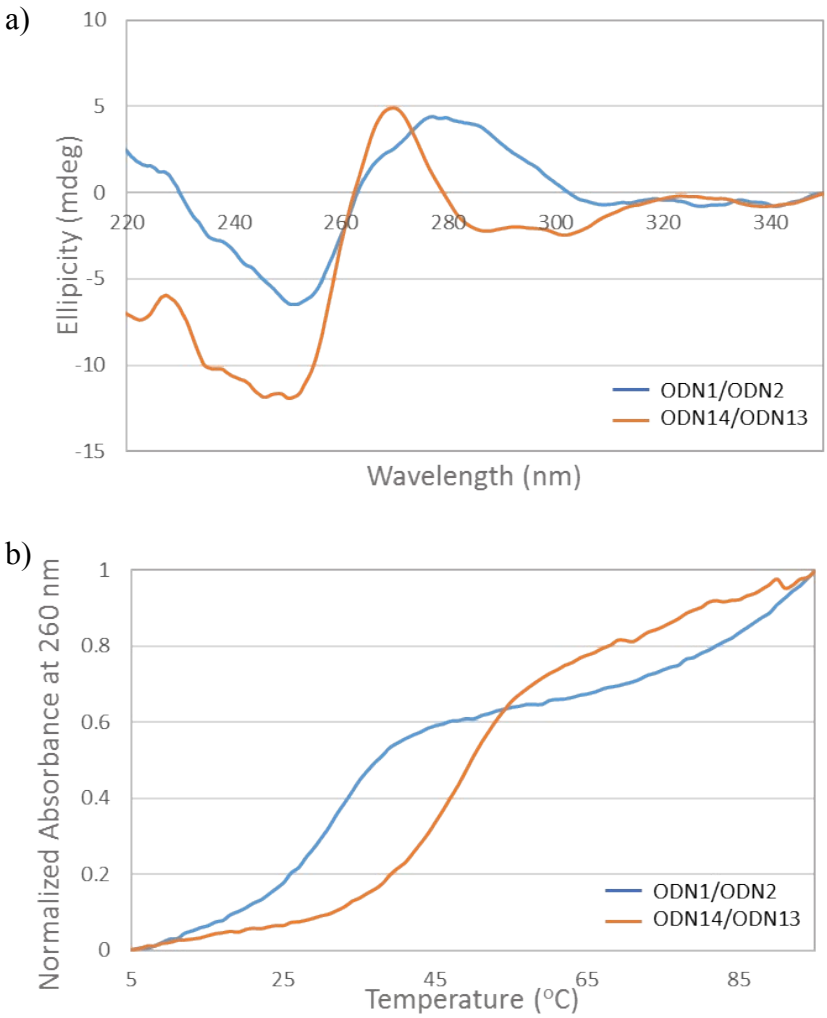


Figure S16. Spectroscopic studies of **ODN1/ODN2** (-A^{3}**X**T-/-TCA-) and **ODN14/ODN13** (-G^{6}**X**C-/-C^{3}**P**G-). a) CD spectra of 3.3 µM DNA oligomer **ODN1/ODN2** (-A^{3}**X**T-/-TCA-) and **ODN14/ODN13** (-G^{6}**X**C-/-C^{3}**P**G-) and 2.5 µM of copper(II) in 20 mM MES buffer (pH 5.5) in the presence of 100 mM NaCl. b) UV melting curve of 3.3 µM DNA oligomer **ODN1/ODN2** (-A^{3}**X**T-/-TCA-) and **ODN14/ODN13** (-G^{6}**X**C-/-C^{3}**P**G-) and 2.5 µM of copper(II) in 20 mM MES buffer (pH 5.5) in the presence of 100 mM NaCl.

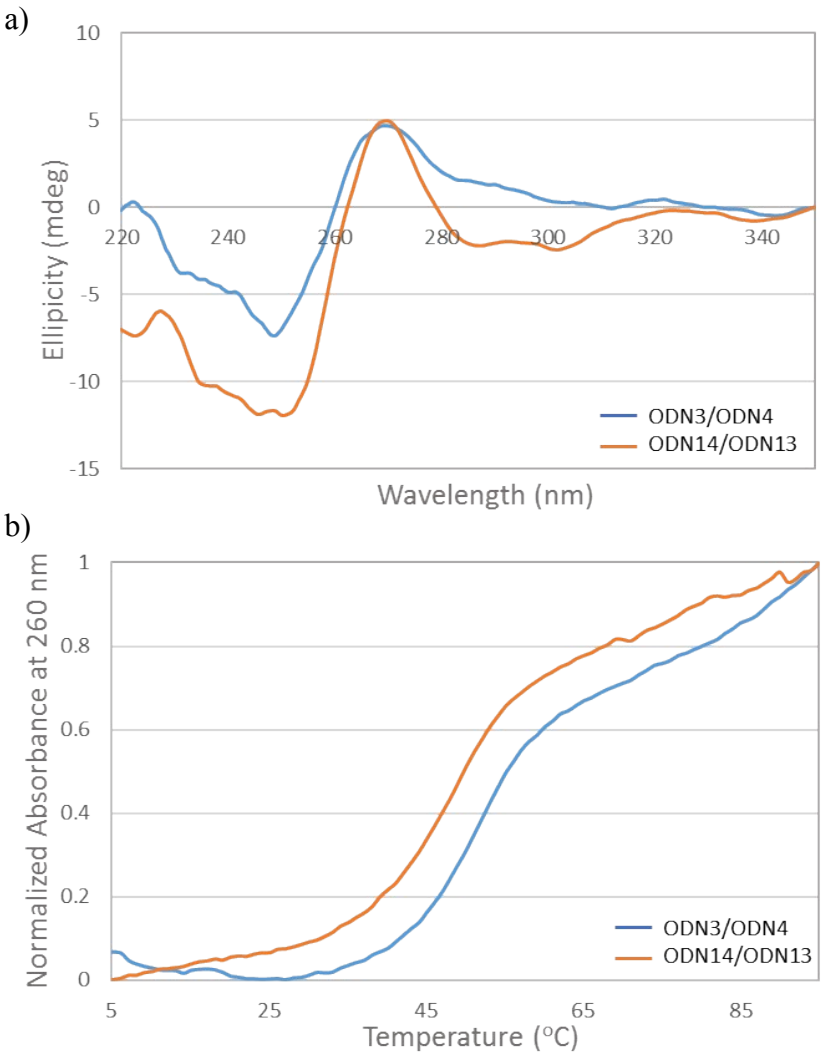


Figure S17. Spectroscopic studies of **ODN3/ODN4** (-G^{3}**X**C-/-CCG-) and **ODN14/ODN13** (-G^{6}**X**C-/-C^{3}**P**G-). a) CD spectra of 3.3 µM DNA oligomer **ODN3/ODN4** (-G^{3}**X**C-/-CCG-) and **ODN14/ODN13** (-G^{6}**X**C-/-C^{3}**P**G-) and 2.5 µM of copper(II) in 20 mM MES buffer (pH 5.5) in the presence of 100 mM NaCl. b) UV melting curve of 3.3 µM DNA oligomer **ODN3/ODN4** (-G^{3}**X**C-/-CCG-) and **ODN14/ODN13** (-G^{6}**X**C-/-C^{3}**P**G-) and 2.5 µM of copper(II) in 20 mM MES buffer (pH 5.5) in the presence of 100 mM NaCl.

Molecular Modeling Studies

Molecular modeling was carried out using the MOE (Molecular Operating Environment) software package. DNA duplexes containing an intrastrand bipyridine ligand were constructed and minimized with amber force field parameters, a distance-dependent dielectric constant of ε = 4r (where, r is the distance between two atoms) and convergence criteria having an RMS gradient of less than 0.001 kcal mol^{-1} Å. For energy minimization water molecules were added to produce distance of 10 Å from the solute to droplet sphere boundaries and sodium counter ions were added to neutralize the system.

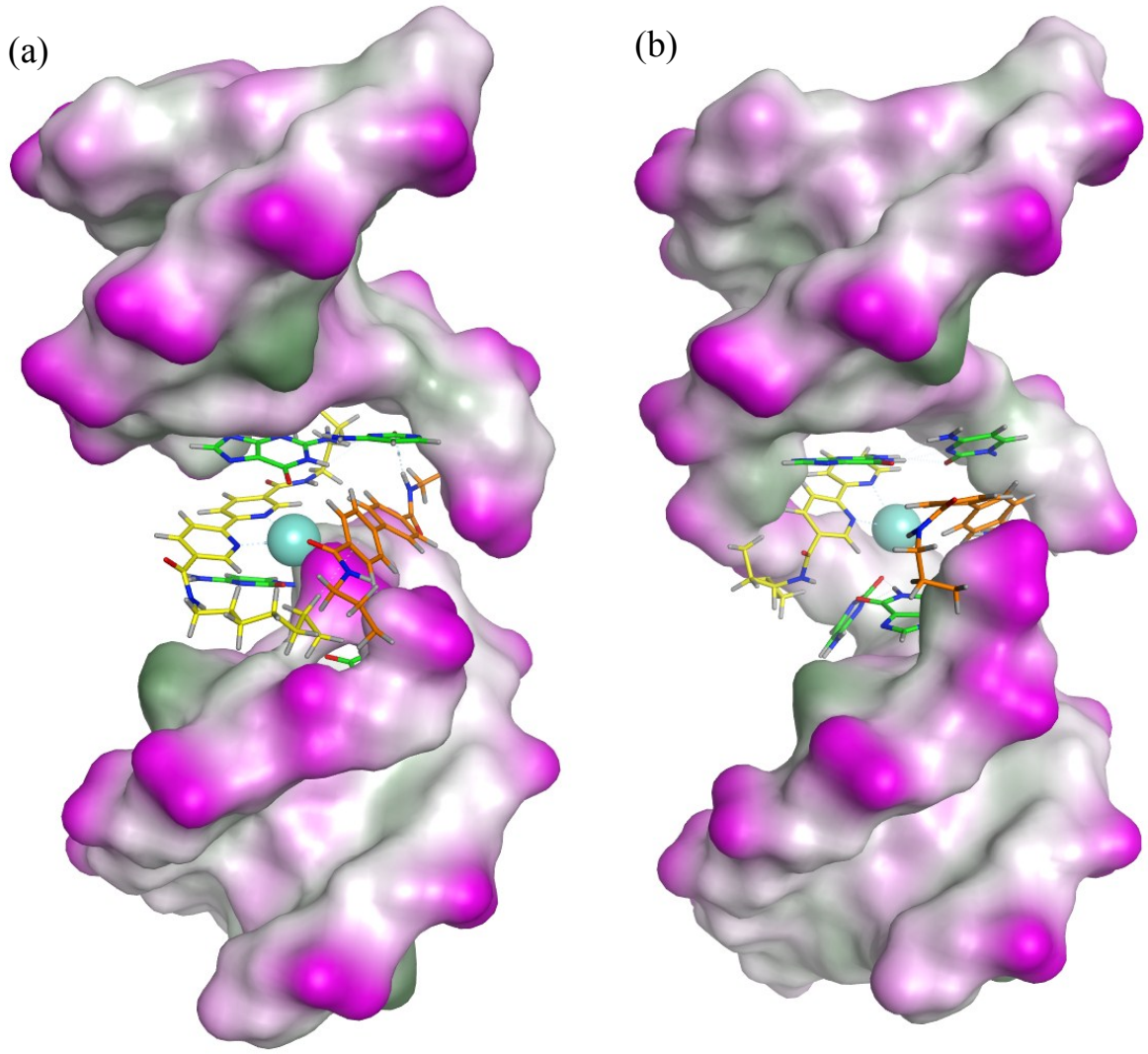


Figure S18. The energy-minimized model between DNA. a) 5′–d(GCATGG^{6}**X**CACGGT)–3′/5′–d(ACCGTG^{3}**P**CCATGC)–3′ (**ODN14**/**ODN13**) and the copper (II) complex. b) 5’–d(GCATGG^{t}**X**CACGGT)–3′/5′–d(ACCGTG^{3}**P**CCATGC)–3′ (**ODN16**/**ODN13**) and copper (II) complex. The yellow structure represents intrastrand bipyridine ligand. The orange color

means bi(propyl)-linker conjugated biphenyl derivative (^{3}P) as a non-binding steric moiety in the complementary strand.

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