Electronic Supplementary Information for

A Supramolecular DNA Self-Assembly Based on β-Cyclodextrin/Adamantane Complexation as a Bioorthogonal Sticky End Motif

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Experimental Section

1. Synthetic Procedures.

General. ^{1}H and ^{13}C NMR spectra were obtained at 400 and 75 MHz, respectively, on a JEOL ECX400 spectrometer. IR spectra were measured on a JASCO-FT/IR-460 plus spectrometer. UV-vis spectra were obtained on a JASCO V-560 UV/VIS spectrophotometer. ESI-HRMS analyses were carried out on a JEOL JMS-T100LC mass spectrometer or Thermo LTQ Orbitrap XL ETD. Melting points were determined with Yanako MP-500D and not corrected. Isothermal titration calorimetry (ITC) was carried out on a MicroCal VP-ITC calorimeter.

Materials. The following compounds, mono-6-azido-6-deoxy-β-cyclodextrin (**3**),[s1] 4-(1-adamantyl)benzoic acid (**4**),[s2] and (2*R*,3*S*,5*R*)-2-(4,4'-dimethoxytrityloxymethyl)-5-ethynyl-3-hydroxytetrahydrofuran (**8**)[s3] were prepared according to literature procedures. Other materials were all commercially available.

2-Hydroxyethyl 4-(1-adamantyl)benzoate (5). To a CH_2CL_2 (5 mL) solution of **4**[s2] (100 mg, 0.390 mmol) were added $HOCH_2CH_2OH$ (484 mg, 7.80 mmol), DMAP (38 mg, 0.312 mmol), and EDC (75 mg, 0.390 mmol) at 0 ºC with a $CaCl_2$ tube. The reaction mixture was stirred at that temperature for 5 min and then at room temperature for 4 h. The reaction mixture was washed with 1 M HCl and saturated Na_2CO_3 aqueous solutions subsequently. The organic phase was dried over $MgSO_4$ and evaporated to give **5** (110 mg, 93%) as a colorless powder. Mp 124–126 ºC; IR (KBr) 3406, 2906, 1714, 1273, 767 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.99 (d, J = 8.4 Hz, 2 H), 7.43 (d, J = 8.4 Hz, 2 H), 4.45 (t, J = 4.4 Hz, 2 H), 3.95 (t, J = 4.4 Hz, 2 H), 2.11 (s, 3 H), 1.92 (s, 6 H), 1.78 ppm (dd, J = 12.0, 21.2 Hz, 6 H); ^{13}C NMR ($CDCl_3$) δ 167.0, 157.0, 129.6, 127.0, 125.0, 66.5, 61.6, 42.9, 36.6, 28.8 ppm; HRMS calcd for MNa^+, $C_{19}H_{24}O_3Na$: 323.1623; found 323.1629.

2-(*p*-Toluenesulfonyl)oxyethyl 4-(1-adamantyl)benzoate (6). To a pyridine (3 mL) solution of **5** (95 mg, 0.31 mmol) and DMAP (1.9 mg, 15.5 μmol) was added TsCl (600 mg, 3.14 mmol) at 0 ºC under an argon atmosphere. The reaction mixture was stirred for 3 h at room temperature. After removal of the solvent, the residue was diluted with AcOEt. The organic

solution was washed with 1 M HCl, saturated $NaHCO_3$, and saturated NaCl aqueous solutions subsequently. The organic phase was dried over $MgSO_4$ and concentrated. The residue was chromatographed (SiO_2; eluent, AcOEt : hexane = 1 : 9) to give **6** (128 mg, 90%) as a colorless solid. Mp 126–128 ºC; IR (KBr) 2908, 1712, 1279, 1174, 930, 768 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.87 (d, J = 8.0 Hz, 2 H), 7.78 (d, J = 8.0 Hz, 2 H), 7.40 (d, J = 8.0 Hz, 2 H), 7.25 (d, J = 8.0 Hz, 2 H), 4.46 (t, J = 4.4 Hz, 2 H), 4.34 (t, J = 4.4 Hz, 2 H), 2.38 (s, 3 H), 2.12 (s, 3 H), 1.93 (s, 6 H), 1.79 ppm (dd, J = 12.4, 21.6 Hz, 6 H); ^{13}C NMR ($CDCl_3$) δ 166.0, 157.1, 144.9, 132.7, 130.2, 129.7, 129.6, 127.82, 127.79, 126.5, 125.3, 125.2, 124.6, 67.8, 61.8, 42.9, 36.6, 28.7, 21.7 ppm; HRMS calcd for MNa^+, $C_{26}H_{30}O_5SNa$: 477.1712; found 477.1730.

2-Azidoethyl 4-(1-adamantyl)benzoate (7). A DMF (2.5 mL) solution of **6** (60.8 mg, 0.13 mmol) and NaN_3 (60.9 mg, 0.94 mmol) was stirred at 60 ºC for 30 min. The reaction mixture was diluted with H_2O and then extracted with Et_2O. The Et_2O phase was washed with saturated $NaHCO_3$, saturated NaCl aqueous solutions subsequently. The organic phase was dried over $MgSO_4$ and concentrated. The residue was chromatographed (SiO_2; eluent, AcOEt: hexane = 1 : 9) to give **7** (42.5 mg, 98%) as a colorless powder. Mp 81–83 ºC; IR (KBr) 2904, 2146, 2104, 1712, 1272, 768 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.00 (d, J = 8.0 Hz, 2 H), 7.44 (d, J = 8.0 Hz, 2 H), 4.48 (t, J = 4.8 Hz, 2 H), 3.58 (t, J = 4.8 Hz, 2 H), 2.11 (s, 3 H), 1.92 (s, 6 H), 1.78 ppm (dd, J = 12.2, 21.4 Hz, 6 H); ^{13}C NMR ($CDCl_3$) δ 166.3, 157.1, 129.8, 126.7, 124.7, 63.4, 50.0, 42.9, 36.6, 28.7 ppm; HRMS calcd for MNa^+, $C_{19}H_{23}O_2N_3Na$: 348.1688; found 348.1694.

(2*R*,3*S*,5*R*)-5-Ethynyl-3-hydroxy-2-hydroxymethyltetrahydrofuran (9). To a CH_2Cl_2 (20 mL) solution of **8**[s3] (439 mg, 0.986 mmol) was added CCl_3CO_2H (1.63 g, 9.86 mmol) at room temperature. The reaction mixture was stirred for 1.5 h at the same temperature and then to the mixture was added Et_3N (3 mL). After removal of the solvent, the residue was chromatographed (SiO_2; eluent, AcOEt) to give **9** (124 mg, 88%) as a colorless oil. IR (neat) 3388, 3291, 2941, 2884, 2119, 1348, 1093, 1045 cm^{-1}; ^1H NMR (DMSO-d_6) δ 5.04 (d, J = 4.4 Hz, 1 H), 4.70 (t, J = 6.0 Hz, 1 H), 4.54–4.59 (m, 1 H), 4.07–4.12 (m, 1 H), 3.59–3.62 (m, 1 H), 3.41 (d, J = 2.4 Hz, 1 H), 3.29–3.39 (m, 2 H), 1.92–2.00 ppm (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 87.0, 82.6, 74.1, 72.7, 67.3, 62.6, 42.3 ppm; HRMS calcd for MNa^+, $C_7H_{10}O_3Na$: 165.0528; found 165.0527.

Ad_{model} 10. To a CH_2Cl_2 (5 mL) solution of **4**[s2] (100 mg, 0.390 mmol), HO-$(CH_2CH_2O)_8$-CH_3 (140 μL, 0.390 mmol), and DMAP (38 mg, 0.312 mmol) was added EDC (75 mg, 0.390 mmol) at 0 ºC under an argon atmosphere. The reaction mixture was stirred at that temperature for 10 min and then at room temperature for 3.5 h. The reaction mixture was washed with 1 M HCl and saturated Na_2CO_3 aqueous solutions subsequently, and then dried over $MgSO_4$. After removal of the solvent, the residue was chromatographed (SiO_2; eluent, MeOH/CH_2Cl_2 = 1 : 49) to give **10** (170 mg, 70%) as a pale yellow oil. IR (KBr) 2903, 1717, 1277, 1104 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.99 (d, J = 8.4 Hz, 2 H), 7.43 (d, J = 8.4 Hz, 2 H), 4.46 (t, J = 4.8 Hz, 2 H), 3.82 (t, J = 4.8 Hz, 2 H), 3.55–3.69 (m, 28 H), 3.38 (s, 3 H), 2.11 (s, 3 H), 1.93 (s, 6 H), 1.78 ppm (dd, J = 12.8, 21.6 Hz, 6 H); ^{13}C NMR ($CDCl_3$) δ 166.6, 156.7, 129.5, 127.3, 124.9, 71.9, 70.6, 70.5, 69.3, 59.0, 42.9, 36.6, 28.8 ppm; HRMS calcd for MNa^+, $C_{34}H_{54}O_{10}Na$: 645.3615; found 645.3646.

CD_{model} 11. H_2O was degassed via argon babbling (30 min) prior to use. A mixture of **3**[s1] (30.8 mg, 0.27 μmol), **9** (3.8 mg, 0.27 μmol), and CuCl (4.55 mg, 0.31 μmol) in the degassed H_2O (10 mL) was stirred at room temperature for 1 h under an argon atmosphere. The reacton mixture was chromatographed (reverse phase C18; eluent, MeOH/H_2O = 1 : 9) to give **11** (31.3 mg, 89%) as a colorless solid. Mp >300 ºC (decomp.); IR (KBr) 3390, 2927, 1655, 1421, 1158, 1029 cm^{-1}; ^1H NMR (DMSO-d_6) δ 7.97 (s, 1 H), 5.12 (dd, J = 6.0, 9.8 Hz, 1 H), 5.01 (d, J = 3.6 Hz, 1 H), 4.77–4.86 (m, 7 H), 4.51 (dd, J = 8.8, 14.2 Hz, 1 H), 4.17–4.20 (m, 1 H), 3.99 (t, J = 8.0 Hz, 1 H), 3.51–3.75 (m, 21 H), 3.10–3.40 (m, 42 H), 2.88 (d, J = 10.4 Hz, 1 H), 2.03–2.15 ppm (m, 2 H); ^{13}C NMR (DMSO-d_6) δ 147.7, 123.3, 101.9, 87.5, 83.4, 81.8, 81.5, 81.3, 72.8, 72.7, 72.5, 72.3, 71.8, 71.5, 62.3, 59.8, 40.7 ppm; HRMS calcd for MNa^+, $C_{49}H_{79}N_3O_{37}Na$: 1324.4290; found 1324.4311.,

2. Synthesis of DNA Oligomers.

2-1. Syntehsis of precursor DNA. The single-stranded precursor ODNs including the alkynylnucleoside residue (5´-end) was prepared by using an Applied Biosystems 392 DNA/RNA synthesizer according to the literature procedure.[s4]

2-2. Synthesis of CD-linked DNA. To a H_2O (20 μL) solution of **3** (1.0 μmol) were added a solution of (+)-sodium L-ascorbate (0.40 μmol) in water (2 μL), the precursor ODN (10 nmol) in water (20 μL), and a solution of CuBr (0.40 μmol) and *tris*-(benzyltriazolylmethyl)amine (TBTA, 0.40 μmol) in a mixed solvent (H_2O:DMSO:*t*-BuOH = 4:3:1, 20 μL). The reaction mixture was stirred at room temperature for 30 min. The crude ODN was purified by reverse phase HPLC on a CHEMCOBOND 5-ODS-H column (10 x 150 mm; Chemco SCIENTIFIC, LTD., elution with 5.0 mM ammonium formate and a 0–20% (or 0–15% for **16CD**) acetonitrile linear gradient (0–40 min) at a flow rate of 2.0 mL/min) to give **1CD**, **2CD**, **12CD**, **13CD**, **14CD**, **15CD**, and **16CD**.

2-3. Synthesis of Ad-linked DNA. To a DMSO (20 μL) solution of **7** (1.0 μmol) were added a solution of (+)-sodium L-ascorbate (0.40 μmol) in water (2 μL), the precursor ODN (10 nmol) in water (20 μL), and a solution of CuBr (0.40 μmol) and *tris*-(benzyltriazolylmethyl)amine (TBTA, 0.40 μmol) in a mixed solvent (H_2O:DMSO:*t*-BuOH = 4:3:1, 20 μL). The reaction mixture was stirred at room temperature for 75 min. The crude ODN was purified by reverse phase HPLC on a CHEMCOBOND 5-ODS-H column (10 x 150 mm; Chemco SCIENTIFIC, LTD., elution with 5.0 mM ammonium formate and a 15–35% acetonitrile linear gradient (0–40 min) for **1'Ad**, **15'Ad**, and **16'Ad** and a 0–30% acetonitrile linear gradient (0–60 min) for **12'Ad**, **13'Ad**, and **14'Ad** at a flow rate of 2.0 mL/min) to give **1'Ad**, **12'Ad**, **13'Ad**, **14'Ad**, **15'Ad**, and **16'Ad**.

3. MALDI-TOF Mass Measurements. MALDI-TOF mass spectra were recorded on a Bruker-Daltonics-Autoflex mass spectrometer operating in the positive ion mode with 3-hydroxypicolinic acid as a matrix. **1CD** : calcd for MH^+, $C_{117}H_{166}N_{28}O_{80}P_7$: 3459.79; found

3461.20, **1'Ad** : calcd for MH^+, $C_{94}H_{119}N_{31}O_{46}P_7$: 2634.61; found 2634.68, **2CD** : calcd for MH^+, $C_{118}H_{167}N_{27}O_{81}P_7$: 3474.79; found 3475.28, **12CD** : calcd for MH^+, $C_{187}H_{252}N_{57}O_{121}P_{14}$: 5665.16; found 5668.50, **12'Ad** : calcd for MH^+, $C_{162}H_{206}N_{53}O_{89}P_{14}$: 4750.95; found 4750.51, **13CD** : calcd for MH^+, $C_{147}H_{203}N_{40}O_{98}P_{10}$: 4405.95; found 4408.85, **13'Ad** : calcd for MH^+, $C_{123}H_{156}N_{41}O_{64}P_{10}$: 3540.76; found 3542.19, **14CD** : calcd for MH^+, $C_{127}H_{178}N_{33}O_{85}P_8$: 3772.85; found 3774.04, **14'Ad** : calcd for MH^+, $C_{104}H_{132}N_{33}O_{53}P_8$: 2938.65; found 2939.83, **15CD** : calcd for MH^+, $C_{108}H_{154}N_{25}O_{74}P_6$: 3170.75; found 3171.20, **15'Ad** : calcd for MH^+, $C_{84}H_{107}N_{26}O_{40}P_6$: 2305.56; found 2305.46, **16CD** : calcd for MH^+, $C_{98}H_{141}N_{23}O_{67}P_5$: 2866.70; found 2867.08, **16'Ad** : calcd for MH^+, $C_{74}H_{95}N_{21}O_{35}P_5$: 1992.50; found 1992.38.

4. UV and T_m Measurements. UV-vis spectra and T_m melting curves (1.0 ºC/1.0 min) were obtained by JASCO V-560 UV/VIS spectrophotometer with a peltier and a temperature controller in a temperature range from 10 to 70 °C (10 mm pathlength). The T_m values were determined from the maxima of the first derivatives of the melting curves measured in a buffer solution: 20 mM Tris-HCl (pH 8.0), 100 mM NaCl. Errors were estimated at ± 1.0 ºC.

5. UV Titration Experiment. A titration curve in Milli-Q for **11** versus **10** (40 μM) was obtained by monitoring a specified wavelength (257 nm) of UV and was analyzed by using of "Excel Solver". UV measurement was carried out at 25 ºC with a cell of 1 cm pathlength for all the ratios of [**11**]/[**10**] = 0, 0.2, 0.4, 0.6, 0.7, 0.8, 1.0, 1.2, and 1.4.

6. ITC Measurement. A titration curve in 20 mM cacodylate (pH 8.0) with 100 mM NaCl for **11** versus **10** (10 μM) was obtained by a MicroCal VP-ITC calorimeter and analyzed by using of "One Set of Sites" model installed in the device. ITC measurement was carried out at 20 ºC with the ratios of [**11**]/[**10**] = 0.16, 0.32, 0.48, 0.64, 0.80, 0.96, 1.12, 1.28, 1.44, 1.60, 1.76, 1.92, 2.08, 2.24, 2.40, 2.56, 2.72, 2.88, 3.04, 3.20, 3.36, 3.52, 3.68, 3.84, 4.00, 4.16, 4.32, and 4.48.

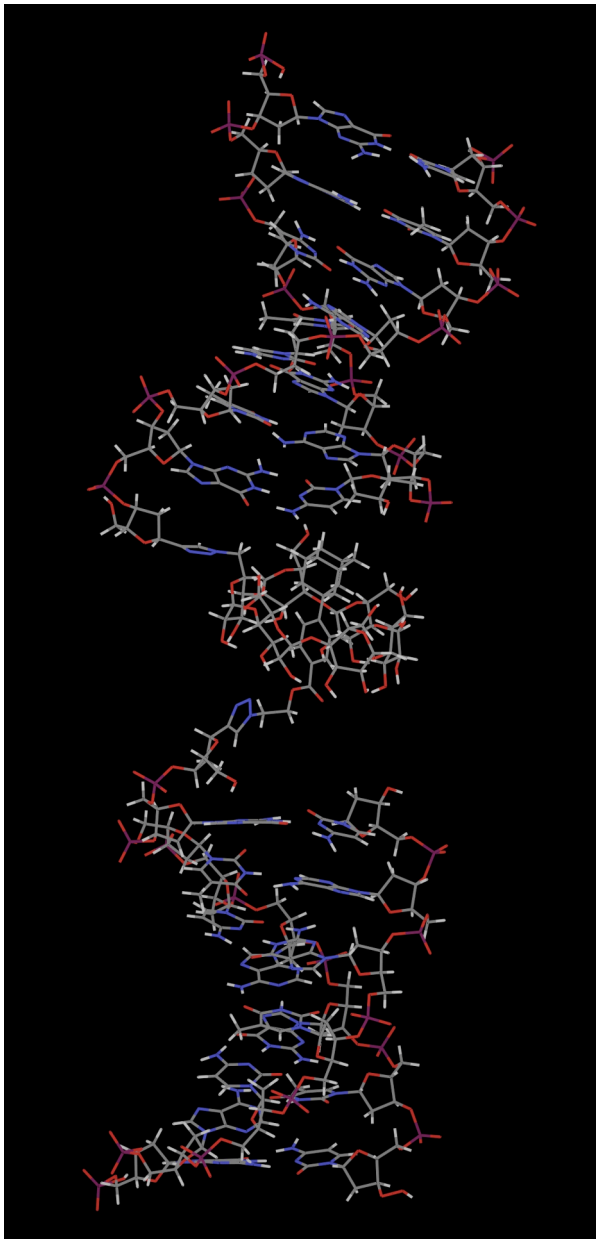

Fig. S1. A possible linear structure via CD–Ad complexation for **1CD/1'–1'Ad/1** based on MacroModel (version 9.1 with OPLS2005) calculation.

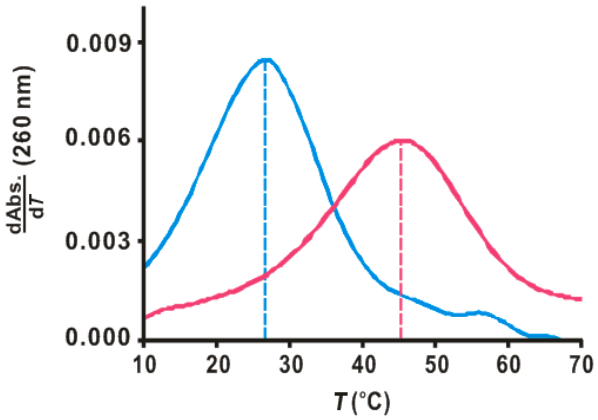

Fig. S2. The first derivative plofiles of the UV-melting curves monitored at 260 nm for the combinations of **1CD**/**1'Ad** (red) and **1**/**1'** (blue). [ssDNA] = 10 μM, 20 mM Tris-HCl (pH 8.0), 100 mM NaCl, 1 ºC/min, path length = 10 mm.

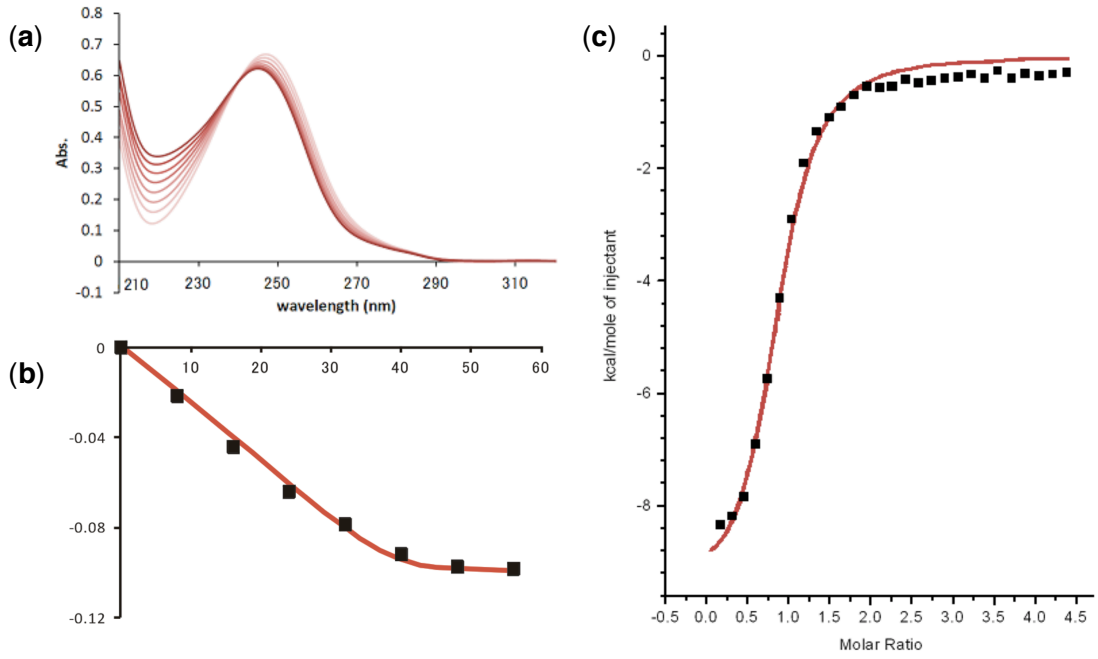

Fig. S3. (a) UV-vis spectra and (b) the titration plot at 257 nm for **10** (40 μM) and **11** in Milli-Q at 25 ºC. (c) ITC titration curve for **10** (10 mM) and **11** in 20 mM cacodylate (pH 8.0) with 100 mM NaCl at 20 ºC.

Table S1. ODN sequences.

length	abbrebiation	sequences
14 mer	**12CD**	3'-CTTAAATGAGGTCG-**X_1**-5'
	12'Ad	5'- **X_2**-GAATTTACTCCAGC-3'
	12	3'-CTTAAATGAGGTCG-5'
	12'	5'-GAATTTACTCCAGC-3'
10 mer	**13CD**	3'-TGACTGACTG- **X_1**-5'
	13'Ad	5'- **X_2**-ACTGACTGAC-3'
	13	3'-TGACTGACTG-5'
	13'	5'-ACTGACTGAC-3'
8 mer	**14CD**	3'-ACTGACTG- **X_1**-5'
	14'Ad	5'- **X_2**-TGACTGAC-3'
	14	3'-ACTGACTG-5'
	14'	5'-TGACTGAC-3'
6 mer	**15CD**	3'-TGACTG- **X_1**-5'
	15'Ad	5'- **X_2**-ACTGAC-3'
	15	3'-TGACTG-5'
	15'	5'-ACTGAC-3'
5 mer	**16CD**	3'-GACTG- **X_1**-5'
	16'Ad	5'- **X_2**-CTGAC-3'
	16	3'-GACTG-5'
	16'	5'-CTGAC-3'

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