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Supporting Information

A Chiroptical Photoswitchable DNA Complex

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Scheme 1-2: Synthesis

S1: Extinction Coefficients

S2: Absorption spectra for the titration of **1o** with poly(dGdC)₂

S3: Absorption spectra for the titration of **1c** with poly(dGdC)₂

S4: Calculation of the binding constant for the poly(dGdC)₂-**1o** complex

S5: Absorption spectra at different pH and pKa plots of switches **1o** and **1c**

S6: Absorption spectra at different pH and plots of poly(dGdC)₂-**1o** and the poly(dGdC)₂-**1c** complexes

S7: Changes in the absorption spectra of poly(dGdC)₂-**1o** and the poly(dGdC)₂-**1c** complexes upon irradiation with UV or visible light.

S8: Calculation of the binding constant for the poly(dAdT)₂-**1o** and the poly(dAdT)₂-**1c** complexes

S9: CD and absorption spectra for the titration of **1o** with poly(dAdT)₂

S10: CD spectra for the poly(dAdT)₂-**1o** and the poly(dAdT)₂-**1c** complexes at different ratios

S11: Irradiation cycles of a solution of poly(dAdT)₂-**1c** complex

Experimental

General Comments

Both lyophilized synthetic polynucleotides poly(deoxyguanylic-deoxycytidylic) acid sodium salt, poly(dGdC)₂, and poly(deoxyadenylic-thymidylic) acid sodium salt, poly(dAdT)₂, were purchased from Sigma-Aldrich and stored at -20°C. Stock solutions of polynucleotides were prepared in MOPS buffer (20 mM, pH 6.5). The concentration in base-pairs was calculated from the UV-Vis absorption spectrum using the following extinction coefficients: $\epsilon = 8400 \text{ M}^{-1}\text{cm}^{-1}$ at 259 nm for poly(dGdC)₂ and $\epsilon = 6800 \text{ M}^{-1}\text{cm}^{-1}$ at 262 nm for poly(dAdT).¹

Instrumental Measurements

Circular dichroism (CD) spectroscopy was performed with a JASCO J-815 circular dichroism spectropolarimeter. UV-Vis absorption spectroscopy was performed with a JASCO V630 spectrophotometer. Measurements were performed in a quartz cuvette with a 1 cm pathlength. All solutions were prepared in a MOPS buffer (20 mM, pH 6.5). Mass spectra (HRMS) were recorded on an AEI MS-902. ¹H and ¹³C NMR spectra were recorded on a Varian VXR-300.

Photochemical Experiments

For UV irradiation, solutions were irradiated through a 340 nm cut-off filter with a Spectroline UV lamp ($\lambda_{\text{max}} = 365 \text{ nm}$). For visible irradiation, solutions were irradiated through a 520 nm cut-off filter with a microscope lamp equipped with a fiber optic. Samples were irradiated for 20 min. with UV light and 30 min. with visible light.

134.7 (s), 135.8 (s), 136.9 (s), 137.2 (s), 138.5 (s), 157.5 (s), 167.3 (s) Maldi-Tof of $C_{43}H_{52}N_4O_6S_2$ (M⁺) 784.3

Scheme S2 Synthesis of compound **3H**

To a solution of compound **2H** (0.178 g, 0.22 mmol), and TFA (10 ml) in CH_2Cl_2 (10 ml) was stirred at room temperature for 6h. The solvent was evaporated in vacuo. To the remaining oil was added a small amount of demi water (3 ml) and subsequently 50 ml of aqueous NaOH (2 M) was added while stirring the reaction mixture. The mixture was filtered through a sintered glass funnel (p4) and the residue washed with H_2O . Pure compound **3H**, 0.10 g (75% yield), was obtained without further purification.

1H NMR (400 MHz, $CDCl_3$) δ 1.81 (s, 6H), 2.00 (m, 2H), 2.71 (m, 8H), 3.20 (m, 2H), 3.32 (m, 2H), 7.11 (s, 2H), 7.46 (d, J = 8.43 Hz, 4H), 7.69 (d, J =8.43 Hz, 4H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5 (q), 24.0 (t), 39.3 (t), 41.9 (t), 42.8 (t), 125.9 (d), 126.6 (d), 133.6 (s), 136.3 (s), 137.0 (s), 138.5 (s), 138.9 (s), 139.8 (s), 170.1 (s) Maldi-Tof of $C_{43}H_{52}N_4O_6S_2$ (M+Na) 607.2

Extinction coefficient

The extinction coefficients were calculated by preparing solutions of **1o** in MOPS buffer (pH = 6.5) containing a known concentration. Solutions were prepared directly in a quartz cuvette to avoid inaccurate concentrations due to transfer from one vial to another as both the switch **1o** and **1c** were found to stick tenaciously to glass. The most concentrated solution was subsequently diluted.

The absorption spectra of each solution were recorded. The extinction coefficients were calculated by plotting the absorption intensity versus the concentration (fig. S1).

S1: Plot of the absorption intensity of the diamino switch open form **1o** in MOPS buffer (20 mM pH 6.5) at 303 nm **(a)** and 331 nm **(b)** versus the molar concentration of the switch.

For the diamino switch in the open form the following values were obtained:

$$\epsilon_{\lambda_{303}} = 23\,254\, M^{-1}cm^{-1}$$

$$\epsilon_{\lambda_{331}} = 23\,836\, M^{-1}cm^{-1}$$

S2: Titration of **1o** (34 μM in MOPS buffer 20 mM pH 6.5) with poly(dGdC)₂ shows a hypochromic effect in the absorption spectra **a)** 0 μM < [poly]_{bp} < 43 μM ; **b)** Further addition of poly(dGdC)₂ (43 μM < [poly]_{bp} < 61 μM) produces no further hypochromic effect but only an increase of the polynucleotide band at 254 nm.

S3: Titration of **1c** (35 μM in MOPS buffer 20 mM pH 6.5) with poly(dGdC)₂ shows a hypochromic effect in the absorption spectra **a)** 0 μM < [poly]_{bp} < 42 μM ; **b)** Further addition of poly(dGdC)₂ (42 μM < [poly]_{bp} < 64 μM) produces no further hypochromic effect but only an increase of the polynucleotide band at 254 nm.

Binding Constant

Under conditions where the ratio of bound complex : DNA base pairs approaches zero, the K_b can be determined using :

$$\frac{D}{\Delta\epsilon_{ap}} = \frac{1}{\Delta\epsilon} D + \frac{1}{\Delta\epsilon K_b} \quad \text{Eq. 1}$$

where

$$\Delta\epsilon_{ap} = |\epsilon_a - \epsilon_f|$$

$$\Delta\epsilon = |\epsilon_b - \epsilon_f|$$

ϵ_a , ϵ_f and ϵ_b are the apparent, free and bound extinction coefficients for the complex, respectively

D is the DNA concentration in base-pairs.

In a plot of $D/\Delta\epsilon_{ap}$ vs. D, K_b is given by the ratio of the slope to the y intercept.

Diamino switch open form with poly(dGdC)₂:

$$K_b = \text{slope} / \text{intercept} = 0,0002 / 1E-9 = \mathbf{2,0 \text{ E}5}$$

S4: Calculation of binding constant of **1o** to poly(dGdC)₂.

S5: UV-Vis absorption spectra of pH titration (6.5-11) of **a) 1o** (34.6 μM) and **b) 1c** (40 μM) without poly(nucleotide) in MOPS buffer (20 mM). UV-Vis spectra were obtained after adding aliquots of NaOH (1 M). **c)** Plot of the absorption of **1o** at 331 nm vs. pH. From the inflection point of the sigmoidal curve a pKa of 7.45 is deduced. **d)** Plot of the absorption of **1c** at 555 nm vs. pH. From the inflection point of the sigmoidal curve a pKa of 7.45 is deduced, which is the same value found for **1o**.

S6: UV-Vis absorption spectra of pH titration (6.5-11) of **a)** poly(dGdC)₂ (45.5 μM)-**1o** (38 μM) and **b)** poly(dGdC)₂ (43 μM)-**1c** (36 μM). UV-Vis spectra were obtained after adding aliquots of NaOH (1 M) to a solution of switch-polynucleotide in MOPS buffer (20 mM). **c)** Plot of the absorption of poly(dGdC)₂ -**1o** at 331 nm vs. pH. There is a quasi-inflexion point at 9.9 which could signify either the pKa or a dissociation of the DNA-switch complex. **d)** Plot of the absorption of poly(dGdC)₂ -**1c** at 555 nm vs. pH.

S7: Irradiation of a solution of poly(dGdC)₂ (45 μM) -**1o** (38 μM) (**a**) and poly(dGdC)₂ (45 μM) -**1c** (38 μM) (**b**) in MOPS buffer (20 mM, pH 6.5) for varying amounts of time with UV light (>340 nm) (**a**) and visible light (>520 nm) (**b**) is accompanied by characteristic changes in the absorption spectra signifying ring opening and closing photochemical reactions.

Binding Constant

See above (**Eq.1**)

Diamino switch open form with poly(dAdT)₂:

$$K_b = \text{slope} / \text{intercept} = 0,0002 / 9\text{E-}10 = \mathbf{2,2\ E5}$$

Diamino switch closed form with poly(dAdT)₂:

$$K_b = \text{slope} / \text{intercept} = 0,0003 / 1\text{E-}10 = \mathbf{30\ E5}$$

S8: Calculation of binding constant of **a) 1o** and **b) 1c** to poly(dAdT)₂

S9: Titration of **1o** (37 μM in MOPS buffer 20 mM pH 6.5) with poly(dAdT)₂ shows:

- a)** 0 μM < $[\text{poly}]_{\text{bp}}$ < 49.3 μM a hypochromic effect in the absorption spectra and the appearance of an ICD corresponding to the absorption of the switch;
- b)** 49.3 μM < $[\text{poly}]_{\text{bp}}$ < 60.5 μM no further hypochromic effect in the switch absorption spectrum but an increase of both the switch band at 331 nm and the poly(dAdT)₂ band at 262 nm together with the CD signals corresponding to the switch and to the DNA;

c) $60.5 \mu\text{M} < [\text{poly}]_{\text{bp}} < 82.4 \mu\text{M}$) no further increase of the ICD relative to the switch but only an increase of both the UV-Vis and CD signals corresponding to the poly(dAdT)₂.

S10: CD spectra of four solutions of **1o** (left) and **1c** (right) (40 μM) with poly(dAdT)₂ (52/65/90 μM) at different ratios.

S11 Irradiation cycles of a solution of poly(dAdT)₂ (90 μM) -**1c** (40 μM) in MOPS buffer 20 mM pH 6.5.

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