Supporting Information
for DOI: 10.1055/s-0034-1380698
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Supporting Information

Synthesis of DNA-binding peptoids

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Synthesis of monomers

*General procedure for mono-Boc protection of diamines*

![Chemical structure](attachment:image.png)

Diamine 1 (100mmol) was dissolved in 50ml DCM and cooled in ice bath. Boc anhydride (12.5mmol) was dissolved in 100ml DCM added to the diamine solution over 2 hours. The reaction was slowly warmed up to room temperature and stirred overnight. The solvent was evaporated under vacuum and re-dissolved in 100ml saturated NaHCO₃ solution, the water layer was extracted with DCM 50ml×3. The organic layer was dried with Na₂SO₄, then solvent was evaporated to get 2 as an oil.

2-chloro-4,6-diamino-1,3,5-triazine (3)²

Cyanuric chloride (100mmol, 18.4g) was dissolved in 150ml acetone, then poured into 150ml ice-cold water. Ammonium hydroxide 28% solution in H₂O (53.7ml, 400mmol) was added into the reaction solution drop-wise under ice bath. The reaction was slowly warmed up to room temperature, then heat up to 50 °C in a sand bath. After reacting for another hour, the solution was cooled down to room temperature and filtered. The solid was washed with H₂O three times and dried over vacuum overnight to obtain the desired product.

Peptoid synthesis and purification

Rink Amide resin (0.71mmol/g) was swelled in N,N-dimethylformamide (DMF anhydrous) at room temperature for 0.5h. The beads were then deprotected with 20% (v/v) piperidine in DMF for 5min. The acylation step was carried in a microwave oven for 15s×2 with 2M bromoacetic acid in DMF and DIC/HOBt. After completion of this step (monitored by Kaiser test or chloranil test), 2M amine DMF solution was then subjected to the beads and react in the microwave oven for 15s×2. The above acylation and substitution steps were repeated until the desired length was achieved. The beads were then washed three times with DMF and three times with DCM, finally shrunk with MeOH and dried over vacuum. 2ml of 95% trifluoroacetic acid (TFA) in H₂O was added to the beads and incubated at room temperature for 2 hours. The slurry was filtered to remove the resin beads, the cleavage solution obtained was then evaporated under N₂. Cold diethyl ether (Et₂O) was added to precipitate the peptoid, the crude pellet was washed with cold Et₂O two times and dried over vacuum. Peptoids were purified by HPLC on a reverse phase C18 column using a gradient from 0-20% solvent B in 50min (solvent A=0.1%TFA in water, solvent B=0.1% TFA in 80% acetonitrile, 20% water). The UV detector was set at 238 nm. The purified peptoids were lyophilized to dryness. The identity of peptoid was checked by MALDI-TOF and purity checked by analytical HPLC on a C18 column.

The purified amino peptoid was then dissolved in 0.1M carbonate-bicarbonate buffer (pH=10.0) to get a final concentration of 200 μM, 500 equivalence of 2-chloro-4,6-diamino-1,3,5-triazine was subjected to the solution and reacted at 85 °C overnight. The reaction was then cooled down to room temperature and quenched with 1N HCl, passed through 0.22 μm filter and purified with HPLC to get the melamine containing peptoid.
UV-melting

UV-melting curves were measured on Carry-100 UV-vis spectrophotometer equipped with an air-circulating temperature controller. All measurements were carried out with temperature change rate of 1°C/min and monitored at 260nm. All samples are freshly annealed in 1X PBS buffer (pH=7.4) before measurements, concentration of DNAs and peptoids were both 2 μM.

Circular Dichroism(CD) spectroscopy

CD spectrums were obtained from Jasco J815 Circular Dichroism Spectrometer equipped with Peltier device and water circulator. All measurements were taken at 4 °C in a Hellma quartz cell (1mm path length) from 300-200 nm, data interval 0.5nm, band width 1nm and D.I.T. 2s. For each sample three scans were collected, averaged and corrected for blanks. All samples were freshly annealed in 1X PBS buffer (pH=7.4) before measurements.

Compound Characterization

Figure S1(a) HPLC trace of (HbM)$_6$
Figure S1(b) MALDI-TOF of (HbM)$_6$, mass calculated: [M+H]$^+$=2266.482, mass found: [M+H]$^+$=2266.247, [M+Na]$^+$=2288.207, [M+K]$^+$=2304.199
Figure S2(a) HPLC trace of (AbM)$_6$
Figure S2(b) MALDI-TOF of (AbM)_6, mass calculated: [M+H]^+=2434.542, mass found: [M+H]^+=2433.070
Figure S3(a) HPLC trace of (AbM)$_8$
Figure S3(b) MALDI-TOF of (AbM)_8, mass calculated: [M+H]^+=3167.299, mass found: [M+H]^+=3166.871

Reference:

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