Altering the Electrostatic Potential in the Major Groove: Thermodynamic and Structural Characterization of 7-Deaza-2'-deoxyadenosine•dT Base Pairing in DNA

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Supporting Information

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Table S1. Parameters used to calculate differential water binding for dodecamers.[a]

Oligodeoxynucleotide	NaCl (mM)	$\Delta H_{cal}/RT_M^2$ (°C)	$\partial T_M/\partial \log a_w$ (°C)	Δn_w (mol^{-1}) DNA
DDD	10	0.62		
	100	0.50	7.49	-53.0 ± 5.0
	100 (EG)	0.40		
7-deaza-dA DDD	10	0.40		
	100	0.32	7.41	-26.0 ± 4.0
	100 (EG)	0.28		

[a]The slopes of T_M vs log a_w were obtained by least-square analysis. The values of $\Delta H/RT_M^2$ represent an average of three determinations in each salt concentration while $\partial T_M/\log a_w$ was determined at 100mM sodium phosphate buffer (pH 7.0)

EG : 1.4 m ethylene glycol

Table S2. Parameters Used to Calculate Differential Counterion Binding for Dodecamers.[a]

Oligodeoxynucleotide	NaCl (mM)	$\Delta H_{cal}/RT_M^2$ (°C)	$\partial T_M/\partial \log[Na^+]$ (°C)	Δn_{Na+} (mol^{-1}) DNA
DDD	10	0.62	7.49	-2.3 ± 0.15
	100	0.50		-1.8 ± 0.12
7-deaza-dA DDD-1	10	0.40	7.41	-1.4 ± 0.14
	100	0.32		-1.1 ± 0.12

[a] Data obtained in 10 mM sodium phosphate at pH 7.0 adjusted to the desired ionic strength with NaCl.

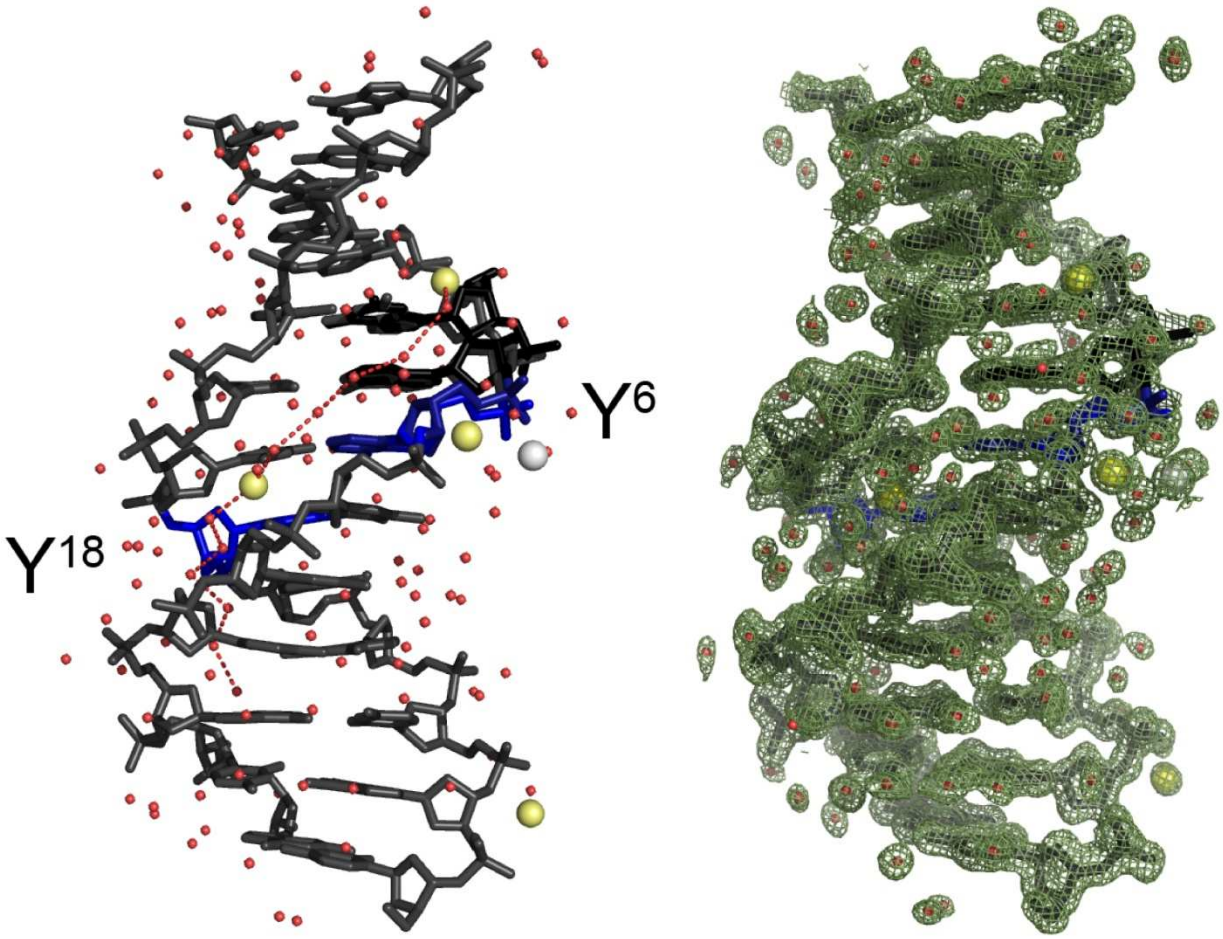


Figure S1. Stick model of the crystal structure of 7-deaza-dA modified DDD-1 (left side) and electron density shown at 1.0 σ level around the duplex (right side). Modified bases Y^6 and Y^{18} are shown in blue, Mg^{2+} ion is shown as white sphere, 133 water molecules are shown as red spheres and four Na^+ ions as yellow spheres. Red dash line shows water inner spine in the minor groove of DNA duplex. It contains water and sodium molecules (from the bottom end): HOH 426, HOH 444, HOH 438, HOH 442, HOH 412, HOH 441, NA 400, HOH 450, HOH 413, HOH 451, HOH 432, HOH 519, NA 402.

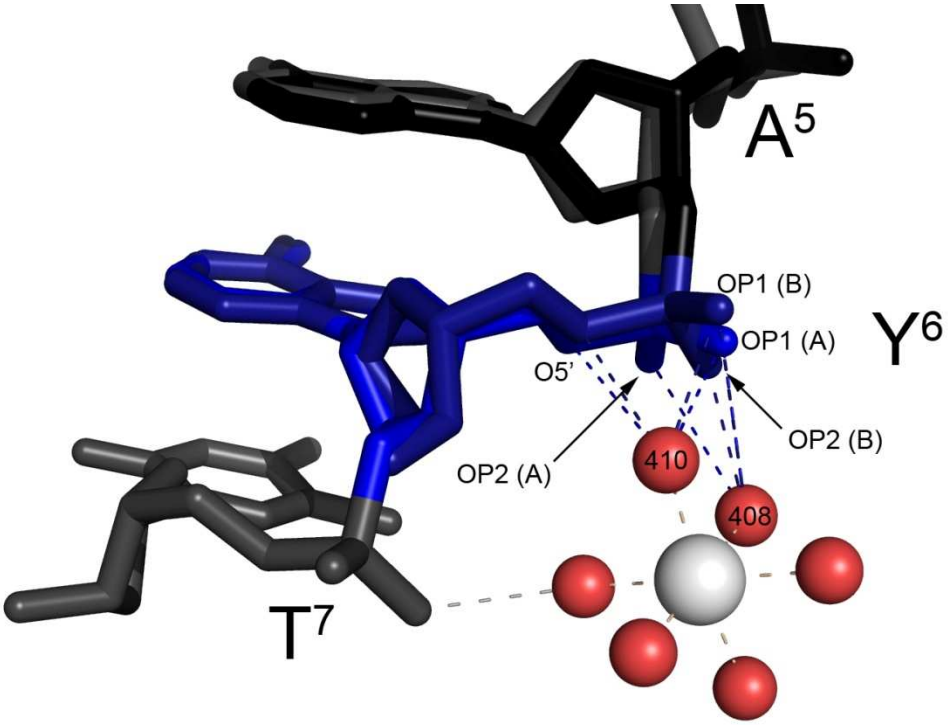


Figure S2. Interactions between Mg^{2+} ion and DDD-1 duplex are indicated by dash lines. Modified base Y^6 is in blue (one phosphate conformation, A) and navy (second phosphate group conformation, B). Mg^{2+} ion (white sphere) is coordinated by six water molecules (red spheres). The Mg^{2+} ion interacts via coordinated waters with phosphate oxygens of two conformers of Y^6 and T^7 nucleotides. Distances between water molecules coordinated to Mg^{2+} ion and Y^6 nucleotide are shown below:

HOH 410	OP1 (A)	3.55Å
HOH 410	OP1 (B)	2.73 Å
HOH 410	O5’ (A)	4.06 Å
HOH 410	O5’ (B)	3.44 Å
HOH 408	OP1 (A)	2.85 Å
HOH 408	OP1 (B)	3.53 Å
HOH 408	OP2 (A)	4.04 Å

HOH 408	OP2 (B)	2.77 Å

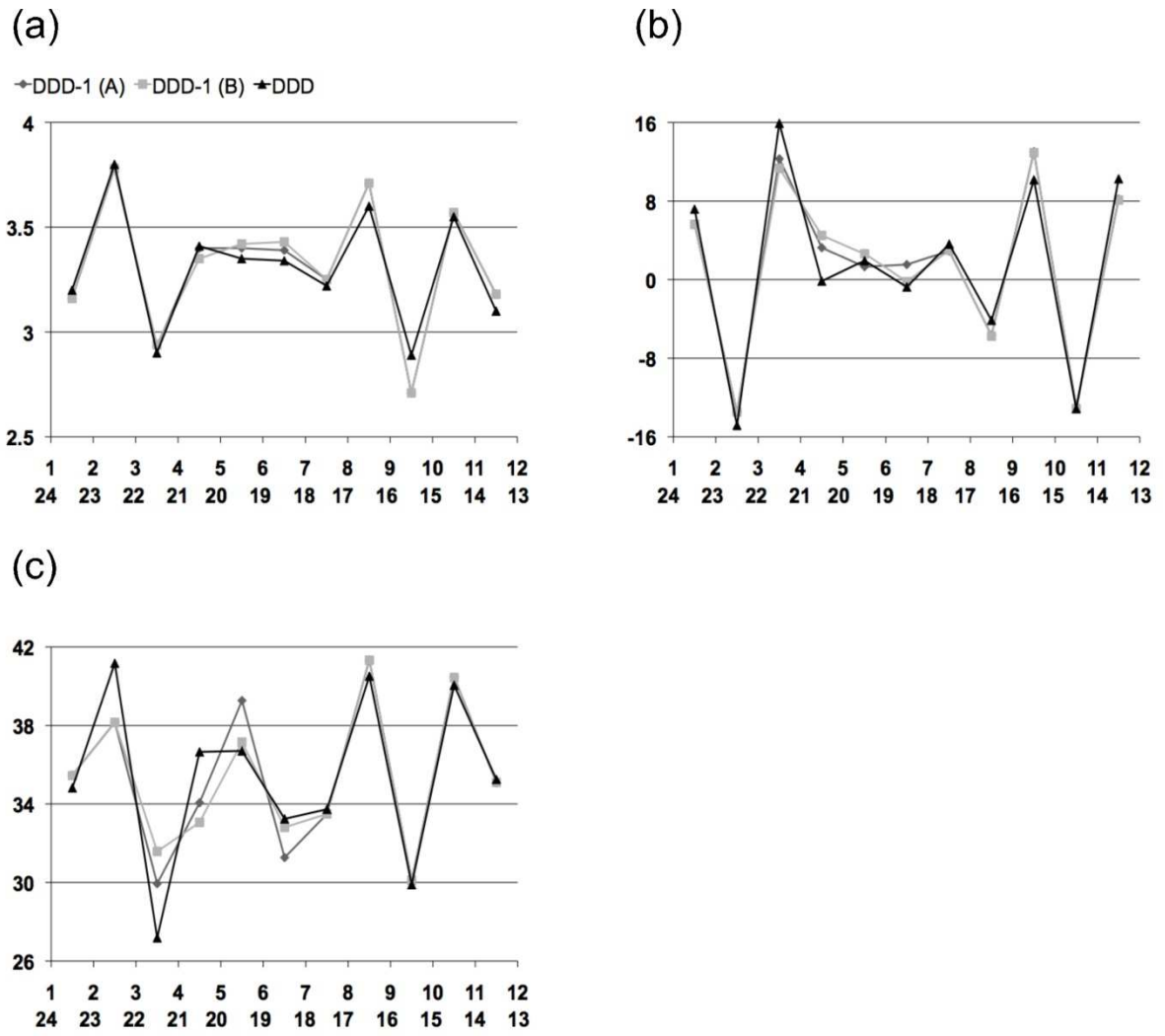


Figure S3. Interbase pair parameters: (a) helical rise, (b) roll and (c) twist for the DDD-1(A) (with one phosphate backbone conformation for the G^4, A^5 and Y^6), DDD-1 (B) (with second phosphate conformation for the G^4, A^5 and Y^6), DDD (PDB entry 355D) duplexes.

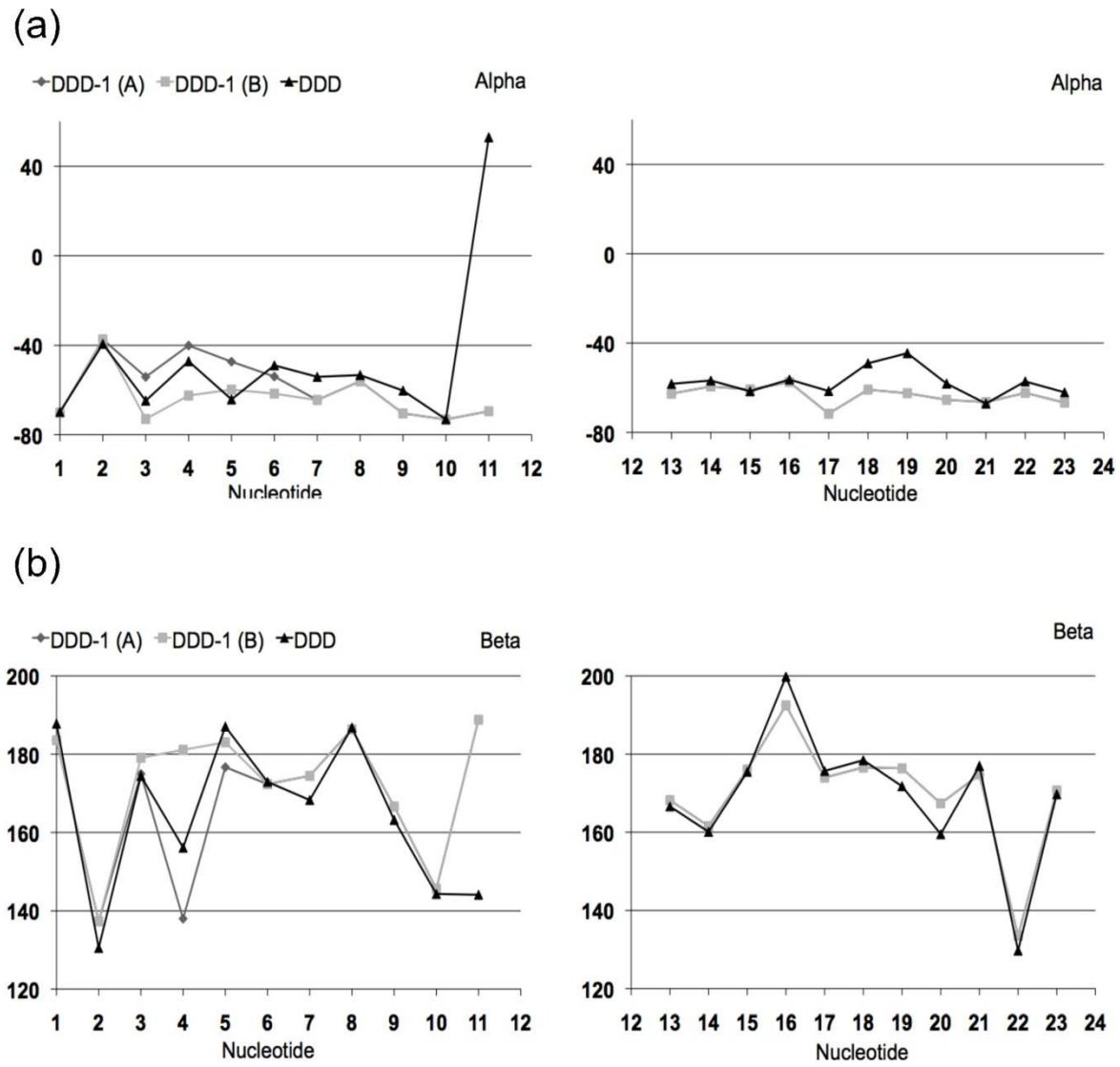
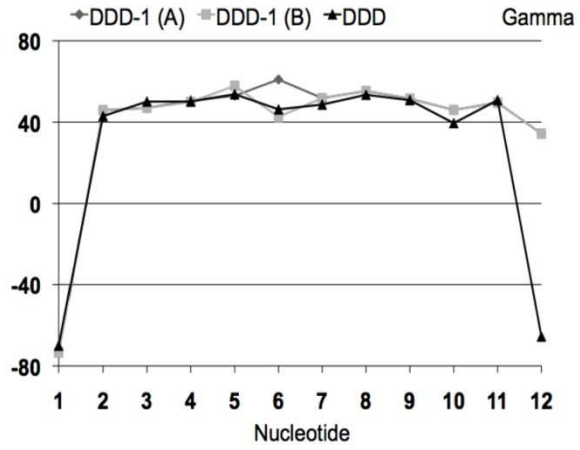
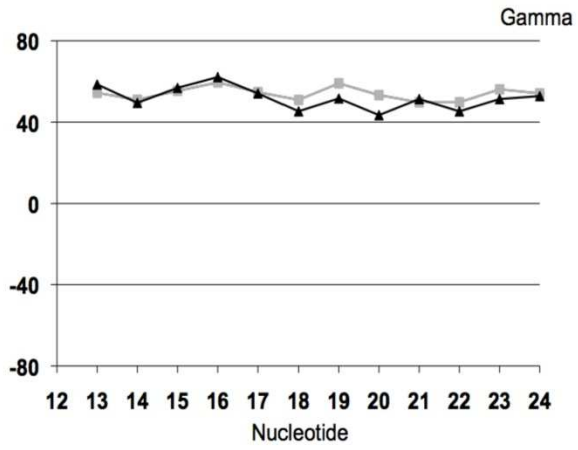


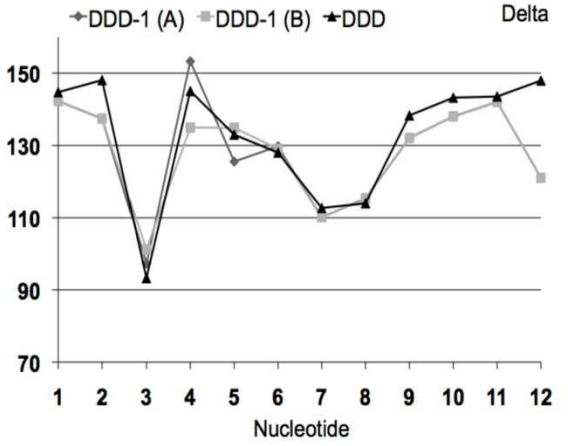
Figure S4. Comparison of backbone torsion angles (a) Alpha and (b) Beta in the crystal structures of the DDD-1(A) (with one phosphate backbone conformation for the G^4, A^5 and Y^6), DDD-1 (B) (with second phosphate conformation for the G^4, A^5 and Y^6), DDD (PDB entry 355D) duplexes.

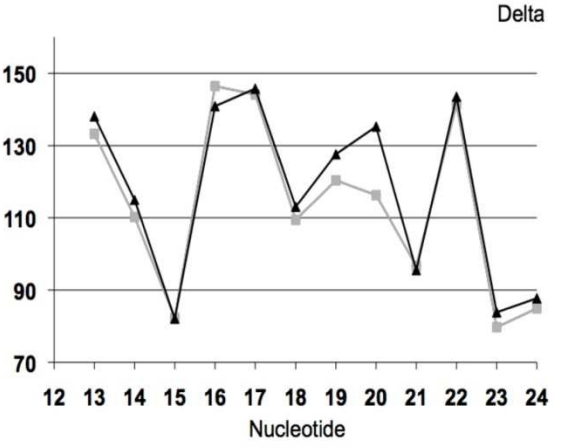
(a)


DDD-1 (A)
DDD-1 (B)
DDD
Gamma
80
40
0
-40
-80
1 2 3 4 5 6 7 8 9 10 11 12
Nucleotide

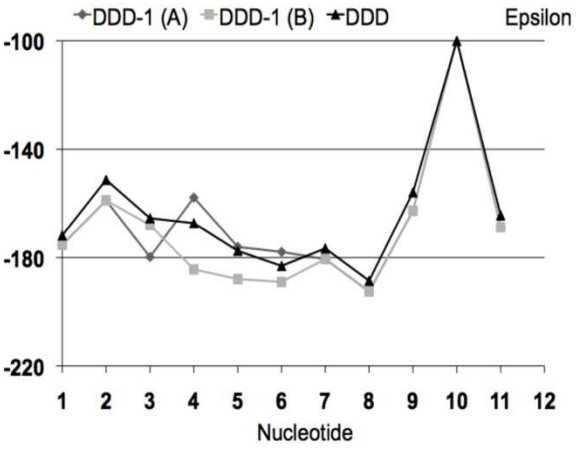

Gamma
80
40
0
-40
-80
12 13 14 15 16 17 18 19 20 21 22 23 24
Nucleotide

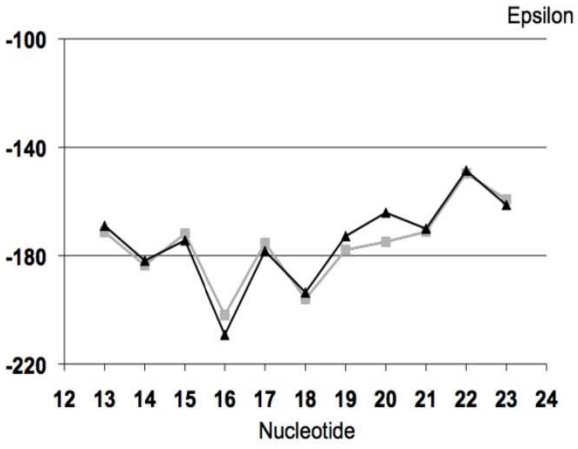
(b)


DDD-1 (A)
DDD-1 (B)
DDD
Delta
150
130
110
90
70
1 2 3 4 5 6 7 8 9 10 11 12
Nucleotide


Delta
150
130
110
90
70
12 13 14 15 16 17 18 19 20 21 22 23 24
Nucleotide

(c)


DDD-1 (A)
DDD-1 (B)
DDD
Epsilon
-100
-140
-180
-220
1 2 3 4 5 6 7 8 9 10 11 12
Nucleotide


Epsilon
-100
-140
-180
-220
12 13 14 15 16 17 18 19 20 21 22 23 24
Nucleotide

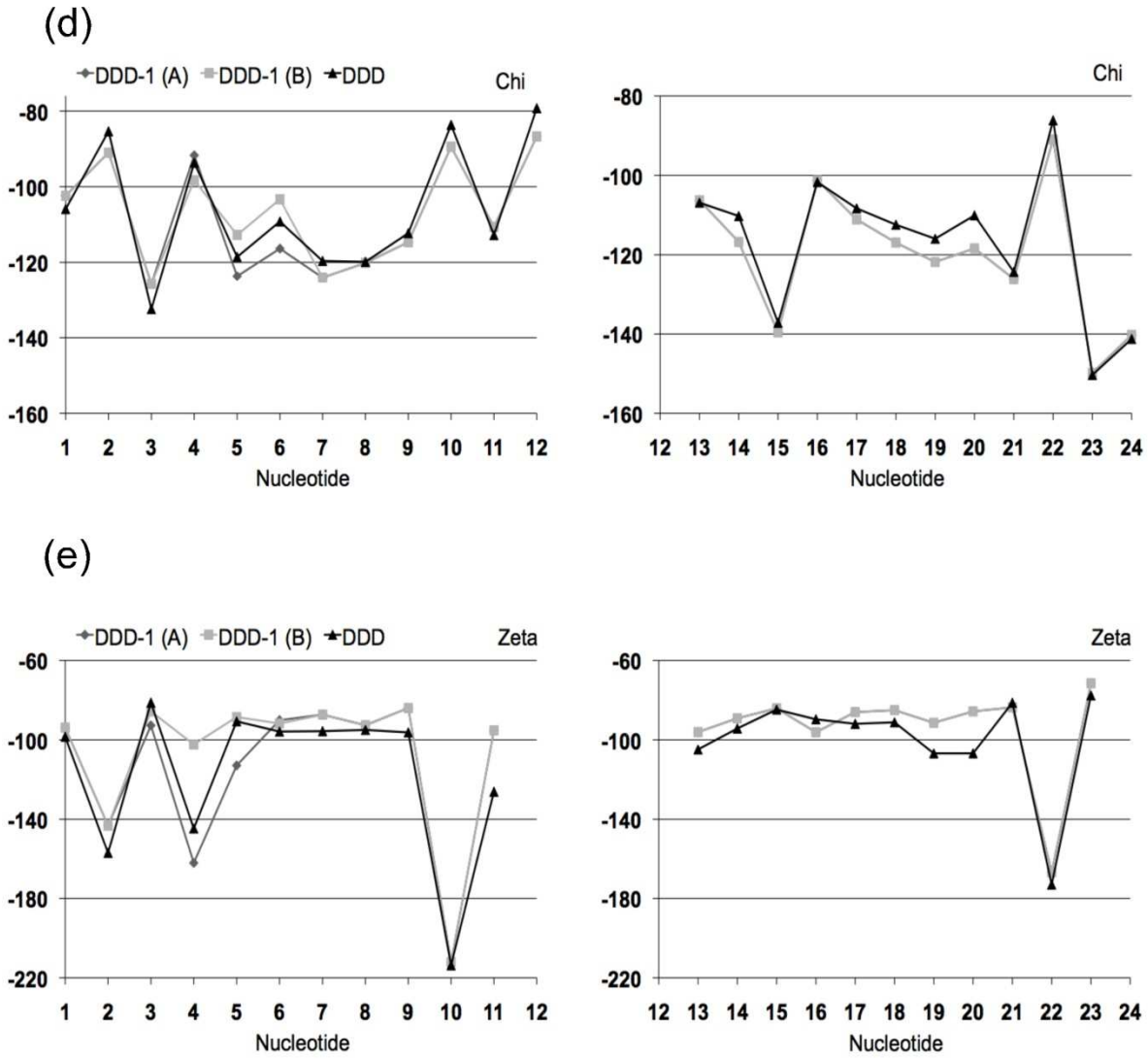


Figure S5. Comparison of (a) Gamma, (b) Delta, (c) Epsilon, (d) Chi and (e) Zeta angles in the crystal structures of the DDD-1(A) (with one phosphate backbone conformation for the G^4, A^5 and Y^6), DDD-1 (B) (with second phosphate conformation for the G^4, A^5 and Y^6), DDD (PDB entry 355D) duplexes.

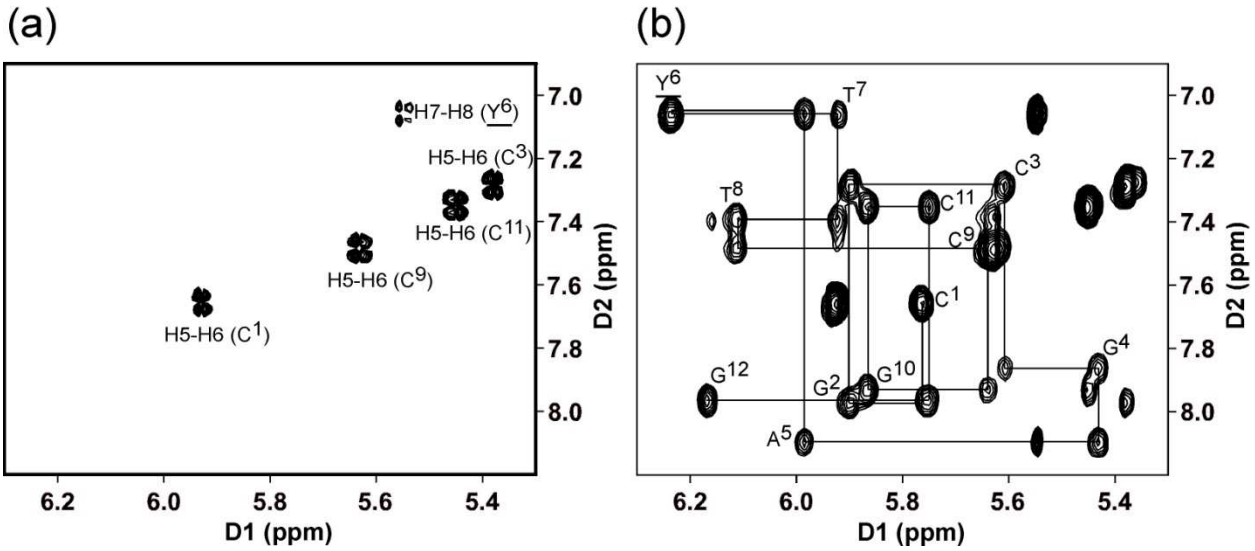


Figure S6. The 7-deaza-dA modified DDD-1 duplex. (a) The expanded plot of a DQF-COSY spectrum of DDD-1 duplex shows four cross peaks corresponding to four cytosine H5-H6 proton interactions (C^1, C^3, C^9, C^{11}) and one cross peak corresponding to the H7-H8 proton interactions of the 7-deaza-dA (b) The expanded plot of the NOESY spectrum of the DDD-1 duplex showing sequential NOEs between the aromatic and anomeric protons.