Supporting Information

Solution Structure of Ternary Complex of Berberine Bound to a dGMP-Fill-in Vacancy G-Quadruplex Formed in the PDGFR-β Promoter

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Table S1. Proton chemical shifts of berberine-dGMP-Pu19m2 ternary complex at 25 °C in pH 7, 50 mM K^+-containing solution.

Base	H1/H2/H5	H6/H8	H1′	H2′, H2″	H3′	H4′	H5′, H5″*
dGMP	11.36	7.97	6.09	2.49, 2.80	4.70	4.21	3.95, 4.00
A1	7.44	7.68	5.86	2.24, 2.34	4.63	3.91	3.30, 3.42
A2	7.86	8.18	6.20	2.61, 2.71	4.92	4.04	3.91, 3.72
G3	11.59	8.13	6.10	2.79, 3.05	5.00	4.50	4.13, 4.21
G4	11.16	7.65	6.14	2.61, 2.99	5.02	4.56	4.31, 4.32
G5	10.8	7.75	6.40	2.79, 2.69	5.18	4.66	4.39, 4.32
A6	8.33	8.57	6.69	2.94, 2.94	5.24	4.68	4.32, 4.32
G7	11.21	8.00	6.11	2.39, 2.91	5.18	4.51	4.31, 4.39
G8	11.21	7.88	6.06	2.66, 2.79	5.09	4.55	4.22, 4.30
G9	11.03	7.64	6.35	2.68, 2.68	5.08	4.62	4.32, 4.31
C10	6.20	8.05	6.49	2.42, 2.77	4.99	4.58	4.32, 4.41
G11	11.05	7.53	6.19	2.85, 2.94	4.87	4.57	4.31, 4.41
G12	10.84	7.94	6.47	2.77, 2.70	5.13	4.69	4.29, 4.35
C13	6.20	8.04	6.52	2.42, 2.77	5.11	4.62	4.31, 4.41
G14	11.28	7.90	6.03	2.33, 2.85	5.16	4.50	4.29, 4.37
G15	11.3	7.89	5.98	2.68, 2.68	5.11	4.53	4.29, 4.21
G16	10.83	7.50	6.15	2.35, 2.54	5.04	4.52	4.30, 4.21
A17	7.80	8.33	6.17	2.75, 2.63	4.99	4.43	4.21, 4.21
C18	5.67	7.44	5.84	1.72, 2.11	4.59	3.99	3.99, 3.95
A19	7.75	8.00	5.98	2.41, 2.26	4.45	3.92	3.82, 3.76

Note: *Assignments are not stereospecific

Table S2. Proton chemical shifts of free-dGMP (dGMPb) and bound-dGMP (dGMPa) at 25 °C in pH 7, 50 mM K^+-containing solution.

Proton	Free-dGMP	Bound-dGMP
H1	N.D.	11.36
H8	8.14	7.97
H1′	6.30	6.09
H2′	2.49	2.49
H2″	2.80	2.80
H3′	4.70	4.70
H4′	4.21	4.21
H5′, H5″	3.95, 4.00	3.95, 4.00

Table S3. Proton chemical shifts of free-berberine and bound-berberine at 25 °C in pH 7, 50 mM K^+-containing solution.

Proton	Free-berberine	Bound-berberine
H51	3.18	2.70
H52	3.18	2.78
H61	4.93	4.62
H62	4.93	4.57
HA	4.04	3.75
HB	4.08	3.85
HC1	6.06	5.81
HC2	6.06	5.85
H1	7.37	6.71
H4	6.91	6.10
H8	9.60	9.01
H11	7.98	7.47
H12	7.85	7.24
H13	8.36	7.85

Table S4. Intermolecular NOEs between the Pu19m2 DNA and dGMP.

	G11	G7
dGMP	**H8**	**H1**
H1		W
H8	W	W
H1′	M	
H2′	M	
H2″	S	
H3′	W	
H4′	W	

Note: S = strong, M = Medium intensity, W = weak intensity, VW = very weak intensity.

Table S5. Intermolecular NOEs between the berberine and dGMP-Pu19m2 DNA.

5′-end Berberine

	G3	G14		A1		A2	G7	dGMP	
BER	**H1**	**H1**	**H8**	**H8**	**H2**	**H2**	**H8**	**H8**	**H1′**
H8	VW	W							
H4	M				M				
H51		M							
H52		M							
H61	W	M				W			
H62	VW	W				M			
HA			VW	M					
HB								M	W
HC1							W		
HC2							M		
H11								M	
H12								W	

3′-end Berberine

	G9			G12	G5		G16	A19		A17
BER	**H1**	**H8**	**H1′**	**H1**	**H1**	**H8**	**H1**	**H2**	**H8**	**H2**
H8	W			M	W			W		W
H51				M						
H52									OL	
H61	W			M	W		W			
H62	M			M	W		W			
HA								W		
HB		M	W					OL		
HC1						M				
HC2						M				
H11								W		
H12								W		

Note: M = Medium intensity, W = weak intensity, VW = very weak intensity, OL = overlapped.

Table S6. Inter-residue NOEs of the 5′-end capping structure.

	A2	
A1	**H8**	**H2**
H2		OL
H8	W	
H1′	M	
H2′	VW	
H2″	W	
H3′	W	
H4′	OL	
H5′	VW	
H5″	VW	

	G3		**G14**
A2	**H1**	**H8**	**H1**
H2	W		W
H8			W
H1′		M	
H2′		W	
H2″		M	
H3′		W	
H4′		M	
H5′		VW	
H5″		VW	

Note: M = Medium intensity, W = weak intensity, VW = very weak intensity, OL = overlapped.

Table S7. Inter-residue NOEs of the 3′-end capping structure.

	C18					G16						G12
A17	**H5**	**H6**	**H4'**	**H5′**	**H5″**	**H1**	**H8**	**H1′**	**H2′**	**H2″**	**H3′**	**H1**
H8	W	W					W	M	M	S	M	
H2						W						W
H1′		W	M	M	W							
H2′		M										
H2″		S										
H3′		M										
H4′		W										
H5′								M				
H5″								M				

	A19		
C18	**H8**	**H5′**	**H5″**
H1′	M	W	W
H2′	W		
H2″	M		
H3′	M		
H4′	W		

Note: S = Strong intensity, M = Medium intensity, W = weak intensity, VW = very weak intensity.

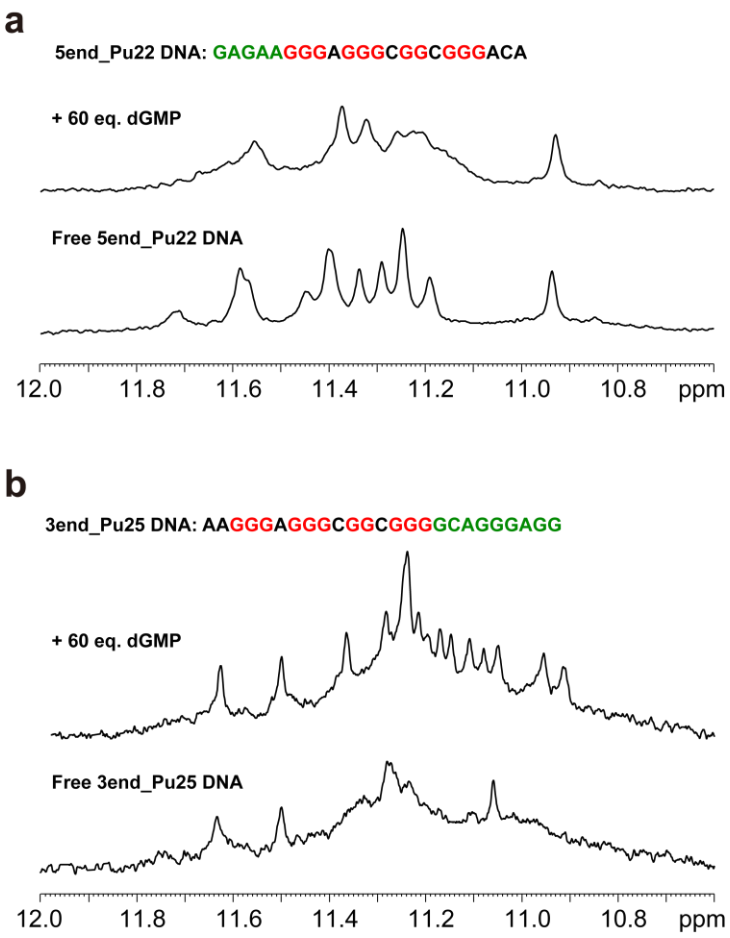

Figure S1. 1D ^{1}H NMR spectra of 5end_Pu22 (a) and 3end_Pu25 (b) DNA in the absence and presence 60 eq. dGMP. DNA sequences are shown at top. Conditions: 150 μM DNA, pH 7, 50 mM K^+ solutions, 25 °C.

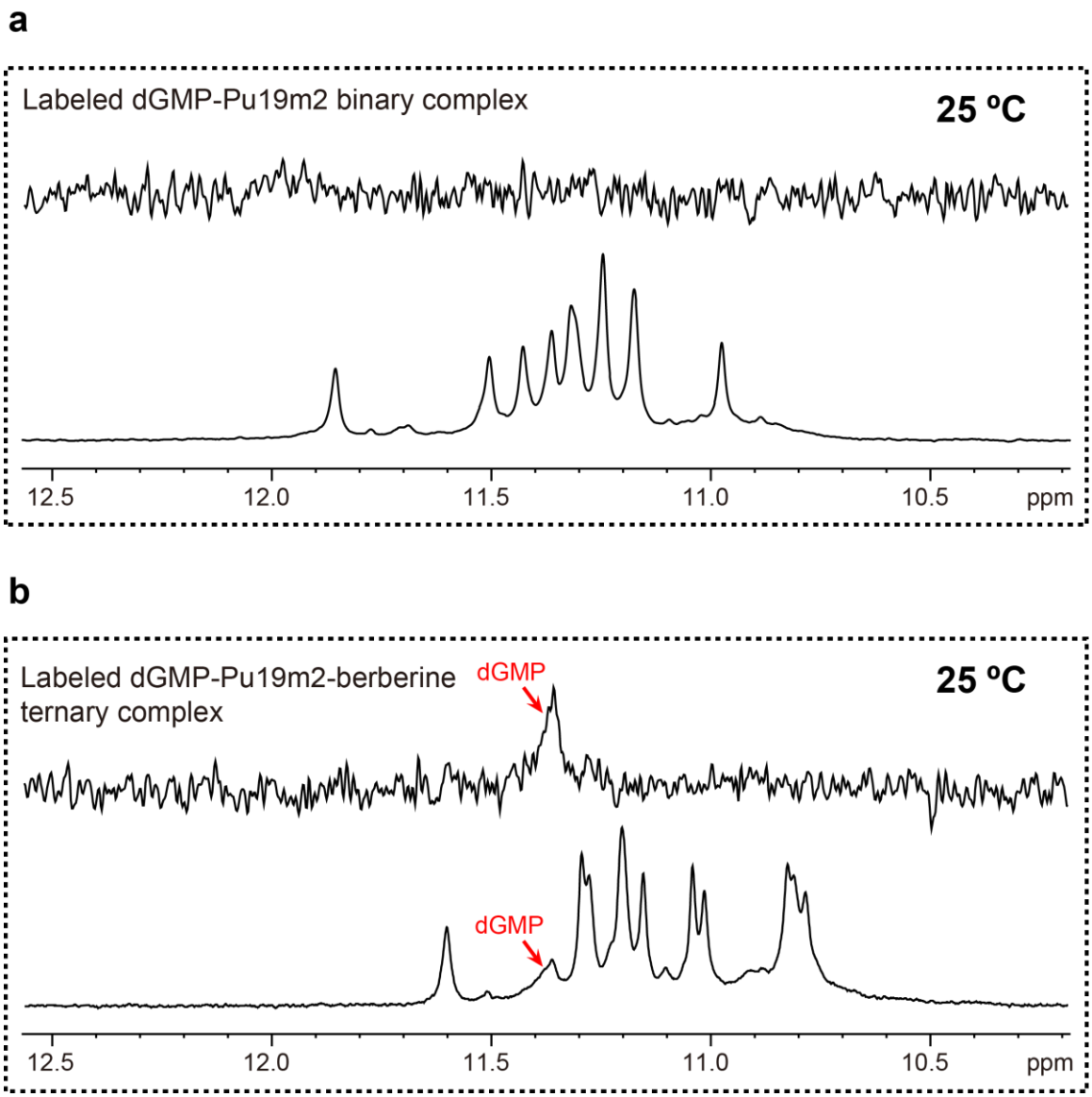

Figure S2. dGMP H1 proton assignments of dGMP-vG4 binary complex (a) and berberine-dGMP-vG4 ternary complex (b) by 1D ^{15}N-edited experiments using ^{13}C-^{15}N-labeled dGMP. The upper spectrum corresponds to the ^{15}N-edited experiments, whereas the lower spectrum is ^{1}H 1D experiment of the same sample. Conditions: 150 μM Pu19m2 DNA, 15:1 labeled dGMP:Pu19m2, 2:1 drug:DNA, pH 7, 50 mM K^+ solution, 25 °C.

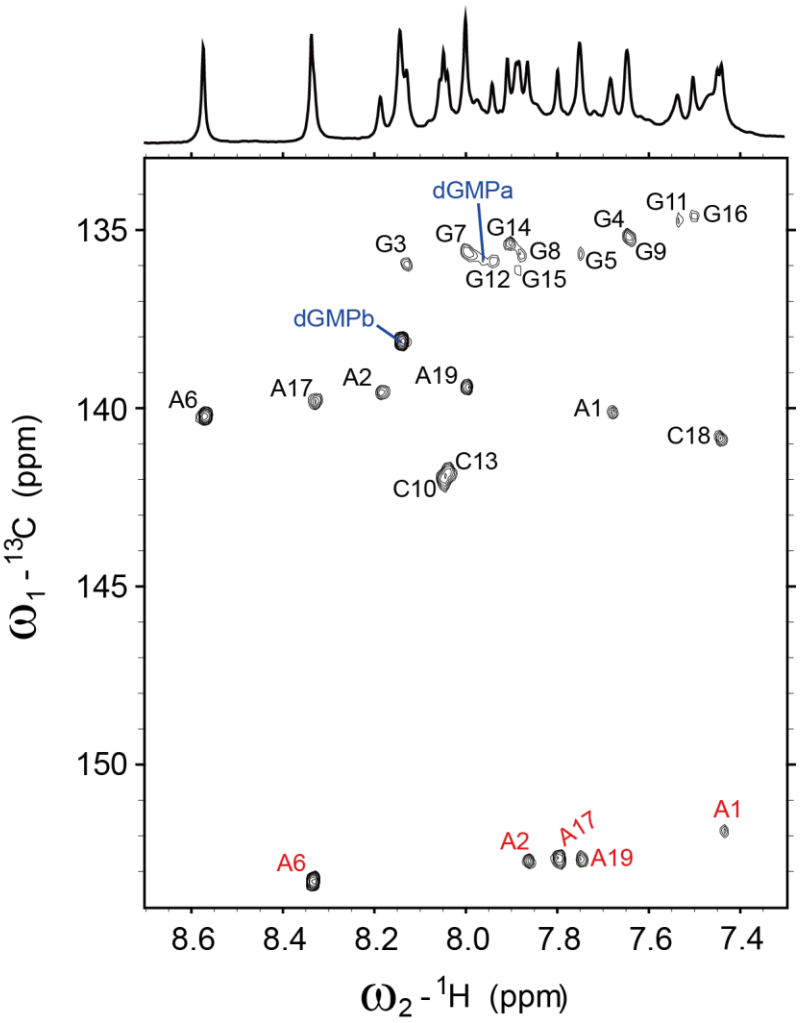

Figure S3. H6−C6/H8−C8 cross-peaks for all bases (black label) and the adenine H2-C2 contacts (red label) assignments for berberine-dGMP-vG4 ternary complex by HSQC experiments. The H8−C8 cross-peaks of free-dGMP (dGMPb) and bound-dGMP (dGMPa) are labeled in blue. Conditions: 1.5 mM Pu19m2 DNA, 3:1 dGMP:DNA, 2:1 drug:DNA, pH 7, 25 °C, 50 mM K^+ solution.

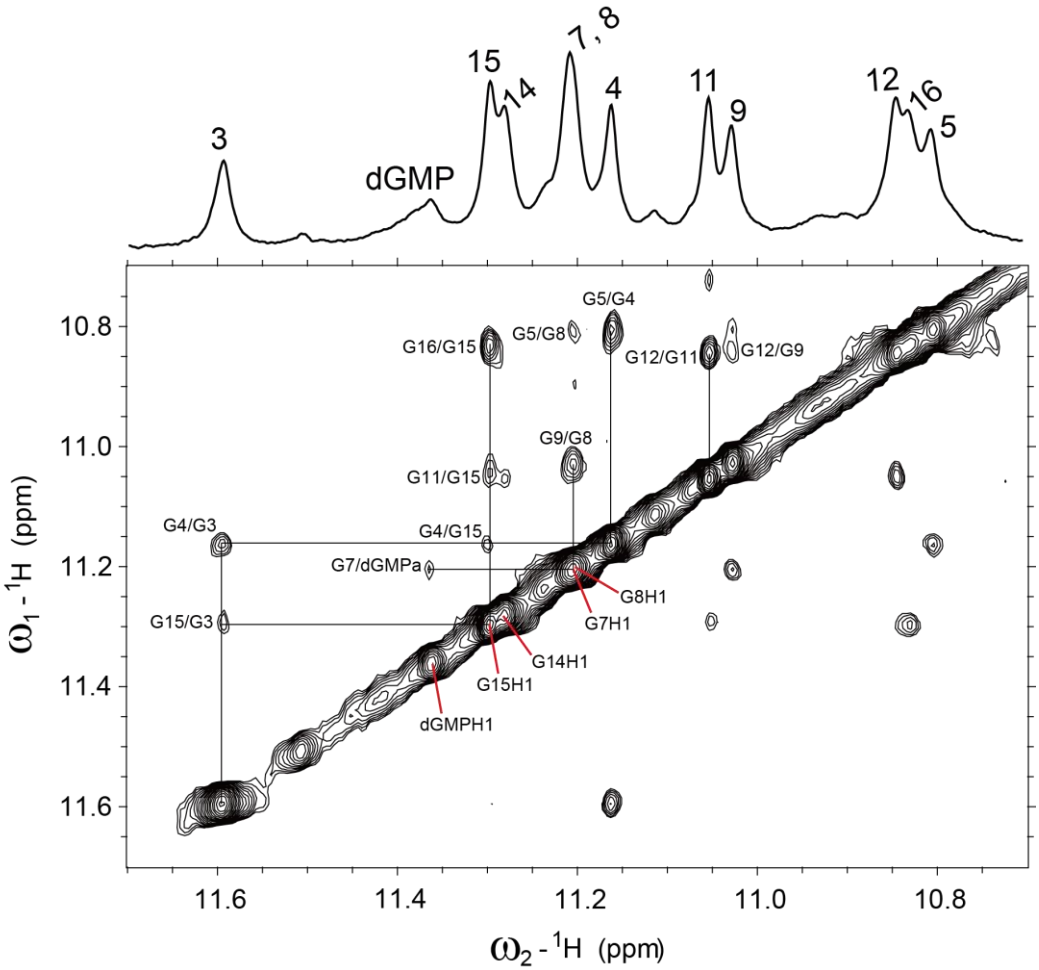

Figure S4. The H1–H1 region of the 2D-NOESY spectrum of berberine-dGMP-vG4 ternary complex in H_2O with sequential assignment pathway. Conditions: 1.5 mM Pu19m2 DNA, 3:1 dGMP:DNA, 2:1 drug:DNA, pH 7, 25 °C, 50 mM K^+ solution, mixing time of 300 ms.

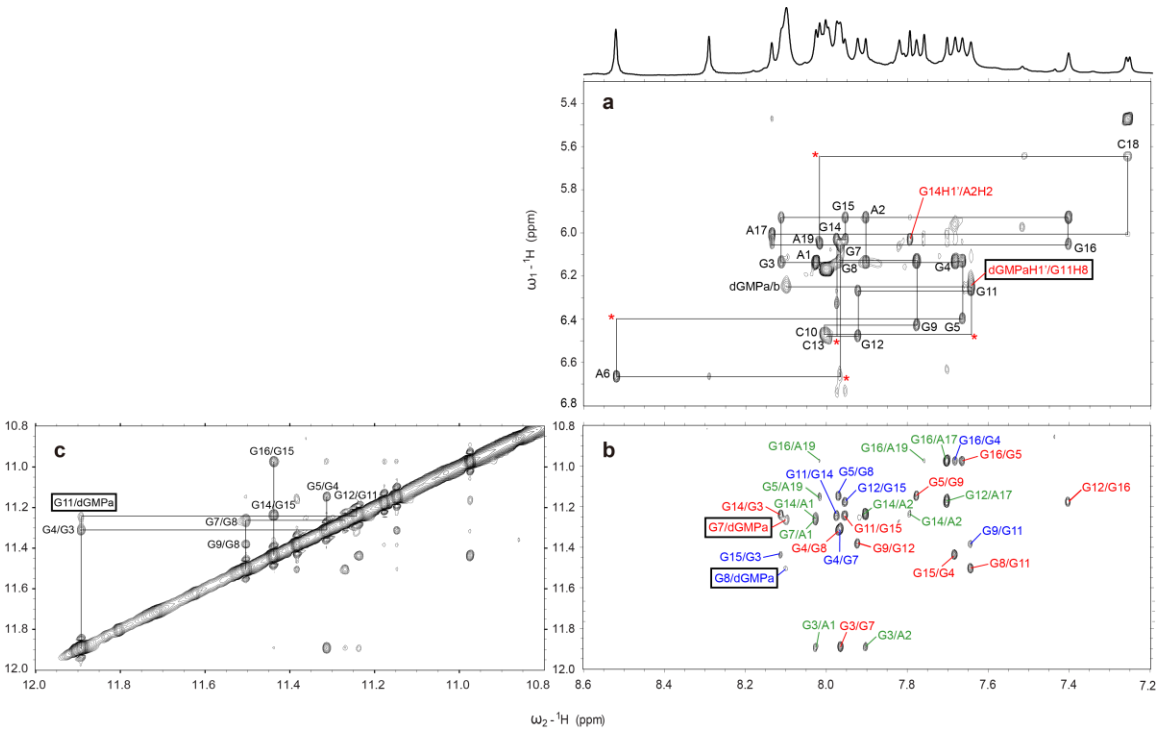

Figure S5. (a) The H1′-H8 region, (b) H8-H1 region, and (c) H1–H1 region of the 2D-NOESY spectrum of dGMP-vG4 binary complex in H_2O with sequential assignment pathway. The NOE cross-peaks that involved in bound-dGMP (dGMPa) are marked by black boxes. Conditions: 2.8 mM Pu19m2 DNA, 3:1 dGMP:DNA, pH 7, 15 °C, 50 mM K^+ solution, mixing time of 250 ms.

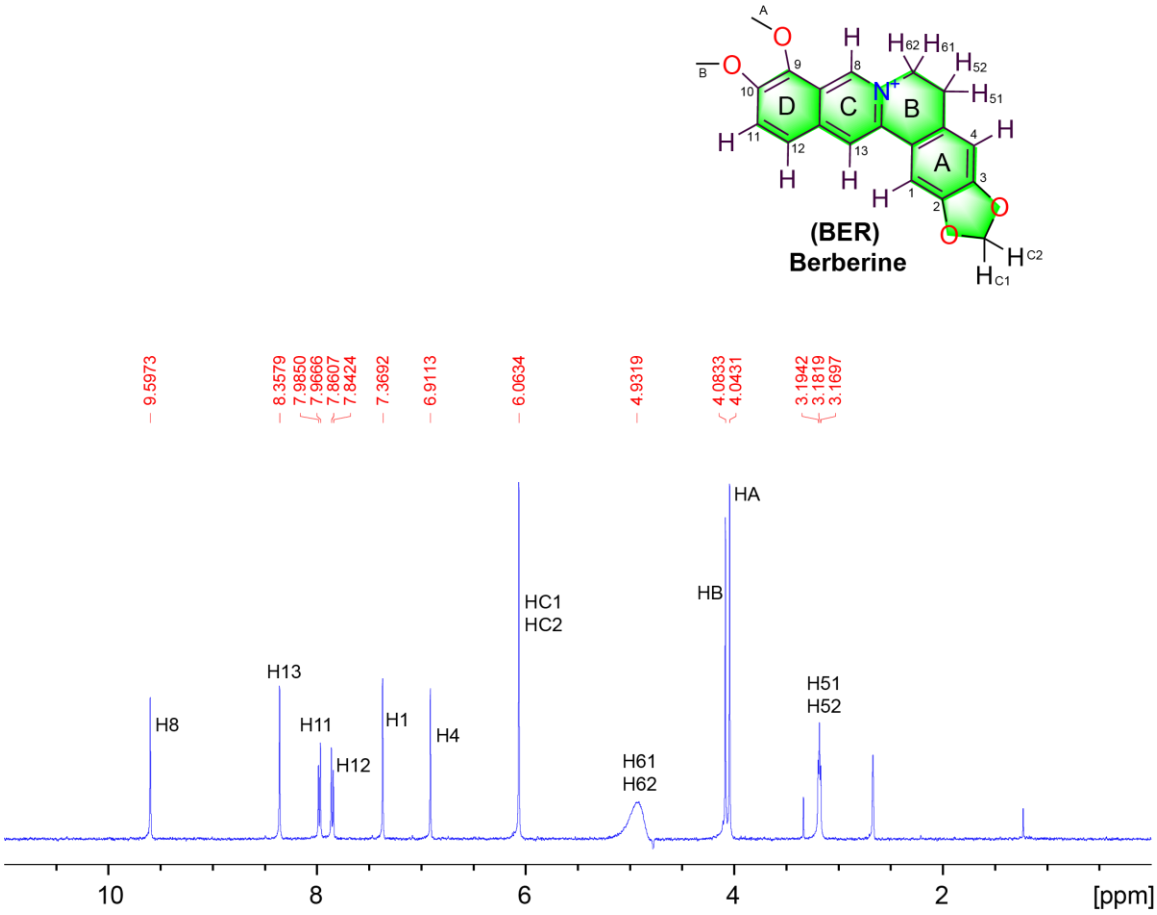

Figure S6. 1D ^{1}H NMR spectrum of the free berberine in pH 7, 50 mM K^{+} at 25 °C with peak assignments and corresponding chemical structure.

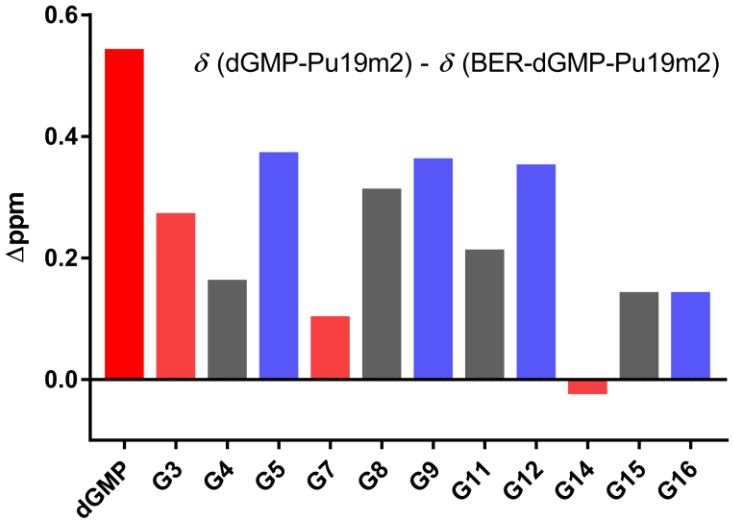

Figure S7. The H1 proton chemical shift difference between the dGMP-Pu19m2 G4 and its berberine ternary complex at 25 °C. The residue numbers of dGMP-Pu19m2 G4 are shown. 5′-end, mid-, and 3′-end G-tetrad guanines are colored in red, gray, and blue, respectively.

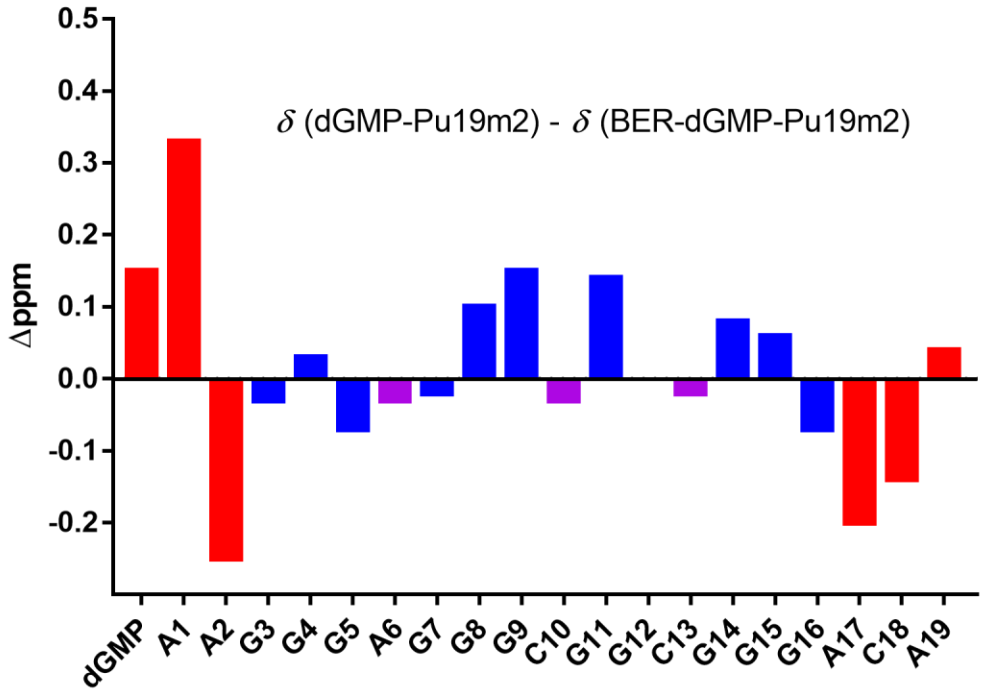

Figure S8. The H8/H6 proton chemical shift difference between the dGMP-Pu19m2 G4 and its berberine ternary complex at 25 °C. The residue numbers of dGMP-Pu19m2 G4 are shown. dGMP and flanking bases, G-tetrad guanines, and loop bases are colored in red, blue, and purple, respectively.

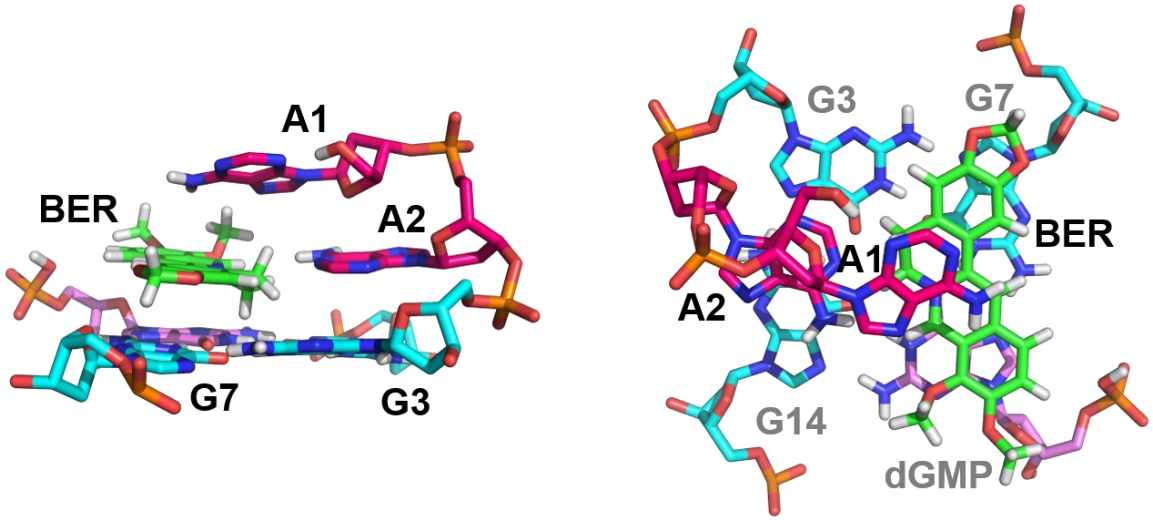

Figure S9. Side (left) and top (right) view of the 5′-end capping structure.

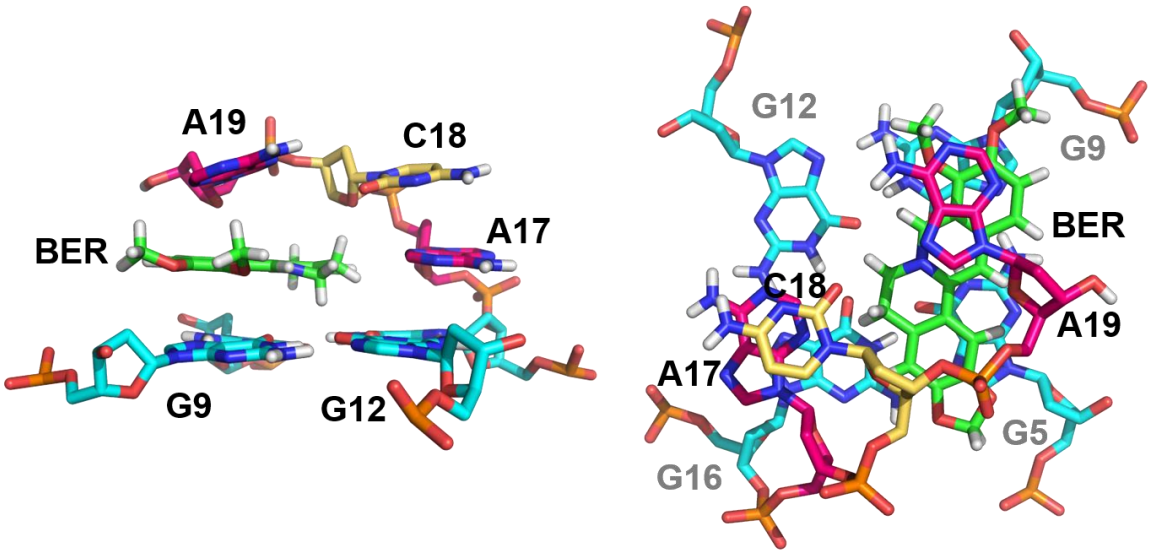

Figure S10. Side (left) and top (right) view of the 3′-end capping structure.

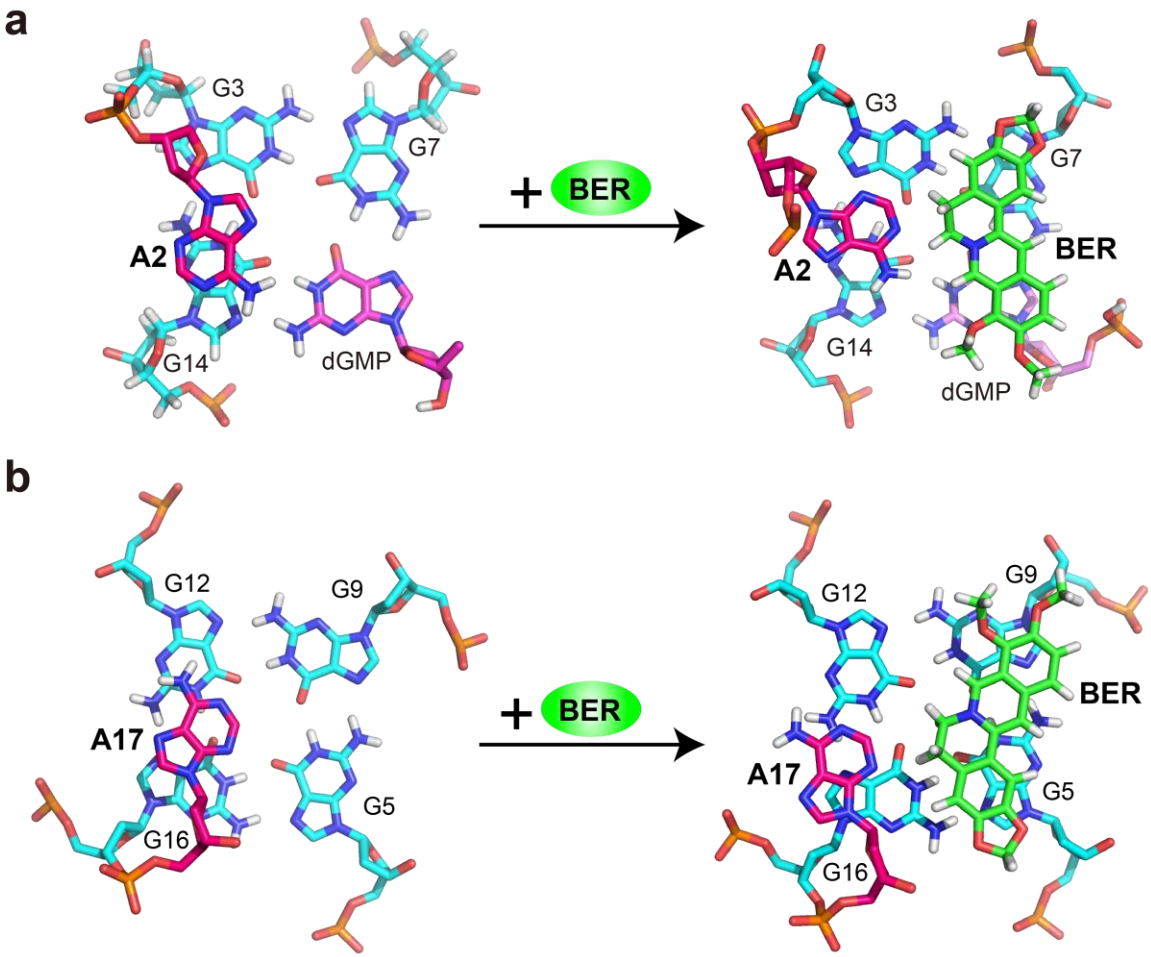

Figure S11. (a) 5′-end and (b) 3′-end top views of the berberine:A2 and berberine:A17 “quasi-triad” planes formation process.