Supporting Information

Right-handed and left-handed G-quadruplexes from the same DNA sequence：distinct conformations induced by organic small molecule and potassium

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Materials Methods and Instrumentation. The following solvents, compounds and reagents were commercially available: p-Aminophenol, phenol was bought from SCRC (Shanghai, China). 2-Piperidinoethylchloridehydrochloride was bought from Aladdin (Beijing, China). Methyl iodide, KCl and other organic solvent were bought from SCRC (Shanghai, China). All stock and buffer solutions were prepared using water purified with the RU Water Purification Sys-tem (Millipore, Billerica, MA, USA). ^{1}H and ^{13}C NMR spectra were recorded on Varian Mercury 300 spectrometers, respectively. API-ES were recorded on Agilent LC/MS 6120B (Agilent, USA).

The Synthesis of Razo. Compound Razo was prepared by the literature methods reported in our previous reseach[1].

Circular Dichroic Studies. The circular dichroism spectra were collected on Chirascan™ CD spectroscopy (Applied Photophysics, Leatherhead, United Kingdom). CD spectra from 220 to 350 nm were collected and scanning speed was 200 nm/min. The bandwidth was 5 nm. The response time was 2 s. Baseline-corrected was carried out to avoid the signal contributions due to the buffer after scanning. Every sample ran at least two times. All scanning was processed at ambient temperature unless otherwise specified.

Thermodynamic Melting Studies. For the Z-G4 study, a solution of AS-M (10 μM) was prepared in 100 K^+ mM. And the B-G4 solution contain 10 μM AS-M and 50μM Razo. The *trans*-conformation of Razo was affirmed by the NMR (figure S1). The CD absorbance was monitored on a Chirascan™ CD spectroscopy (Applied Photophysics, Leatherhead, United Kingdom) equipped with a temperature controller. The temperature was increased from 4 to 90 °C and the speed is about 0.5–1.5 °C/min. The

bandwidth is 1 nm. Melting curves were obtained by monitoring absorbance at the indicated nm (277nm). Melting profiles were analyzed by fitting them to a concerted two-state model.

The Dimethylsulfate (DMS) Footprinting Experiment. The G reaction tube contained 1 μl DNA (100 μM), 10 μl Tris-EDTA buffer (100 mM, pH 7.8) and 89 μl distilled water. Then 2 μl DMS was added to the G reaction tube. After vortex, the tube was incubated at room temperature for eight minutes. The DMS stop buffer containing 20 μl CH_3COONa-CH_3COOH buffer (1 M, pH 5.0), and 40 μl ethanethiol was add to the G reaction tube to stop alkylation. 100% ethanol having been prechilled to −20°C to the G reaction tube and mixing. The mixture was freezed at −80°C for 2 hours, and centrifuged for 20 minutes at 4°C. After piperidine treatment finished, the DNA was precipitated once again as the step mentioned above.

Titration Experiments. The detail of experiments solution condition have been showed in the cutline under the figure. (Figure S3, S4, S5, S6) K^+ and *trans*-Razo was added to the solution containing the oligonucleotide in single strand or preconceived secondary structure. All experiments were carried out at ambient temperature. The titration binding data were analyzed quantitatively by Scatchard equation[4]. In the Scatchard equation, r/Cf= K(n - r), where r is the number of moles of Razo bound to 1 mol of G-quadruplex, n is the number of equivalent binding sites, and K is the affinities of binding constant. Cf is the concentration of free compound Razo.

Visualization of Crystal Structure and G-quart stacking model. Visualization was achieved by using UCSF Chimera[5]. The structure model was built from crystal structure (PDB: 4U5M[2], 2GKU[6])

Table S1 Sequences of oligomers used in the study.

Oligomer	Sequence(from 5'to 3')
AS-M	TGGTGGTGGTGGTTGTGGTGGTGGTGTT
T95-2T	TTGGGTGGGTGGGTGGGT
AS-M-Fam	Fam-TGGTGGTGGTGGTTGTGGTGGTGGTGTT

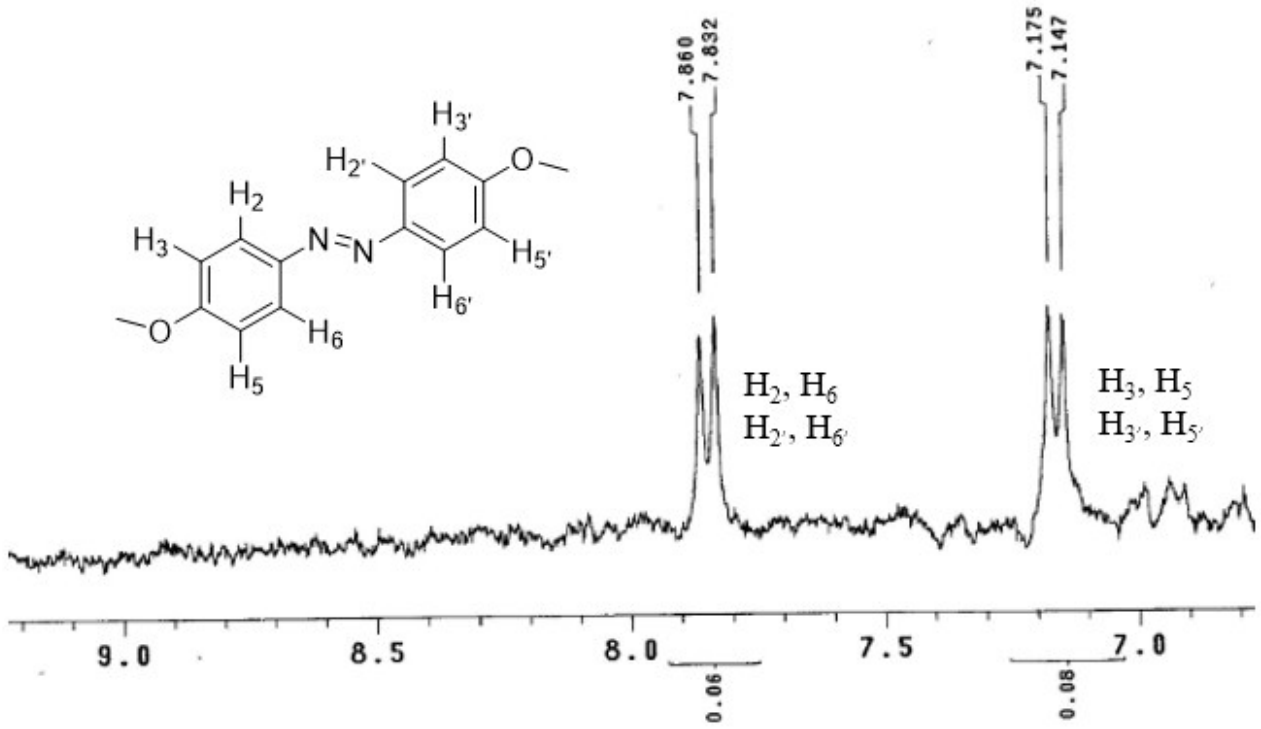

Figure S1. ^{1}H NMR spectra of 5mM in 10% H_2O/90% D_2O solution. The chemical shift of H_6 /$H_{6'}$ and H_5/$H_{5'}$ indicated there is long distance with two kinds of hydrogen. That means the Razo in the *trans*conformation.

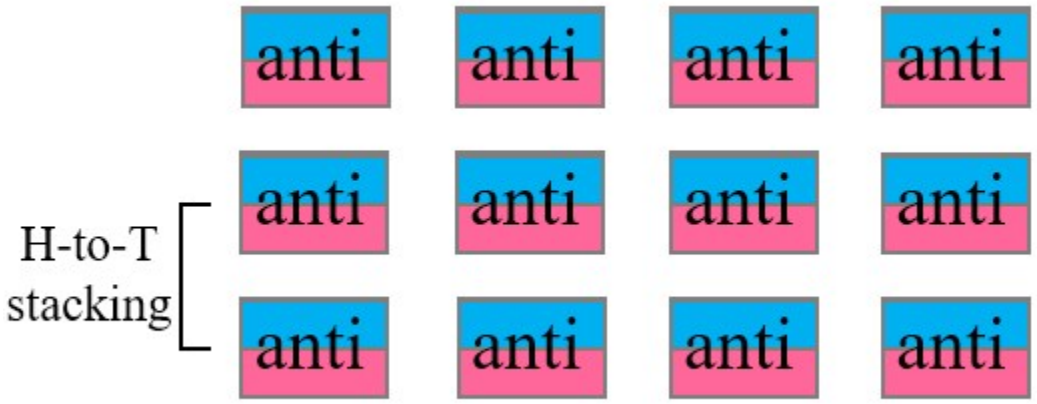

Figure S2. The sketch of the stacking arrangement of the G-quadruplex from T95-2T[3].

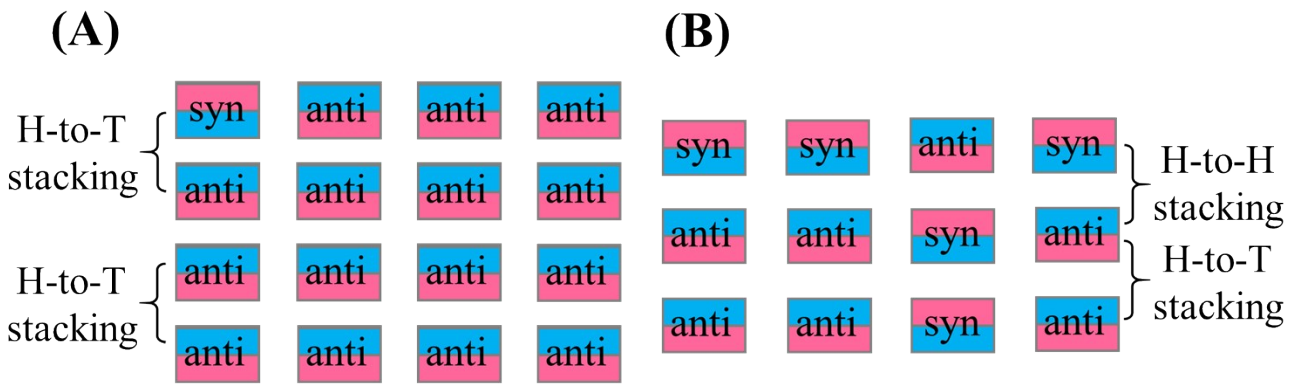

Figure S3 (A) The sketch of the stacking arrangement of G-quartets in Z-G4 induced by K^+. (B) A sketch of the stacking arrangement of G-quartets in Z-G4 induced by Razo. The conformation contained both homopolarity stacking (H-to-T) and heteropolarity stacking (H-to-H), which meant that the G-quartet polarity also alternated

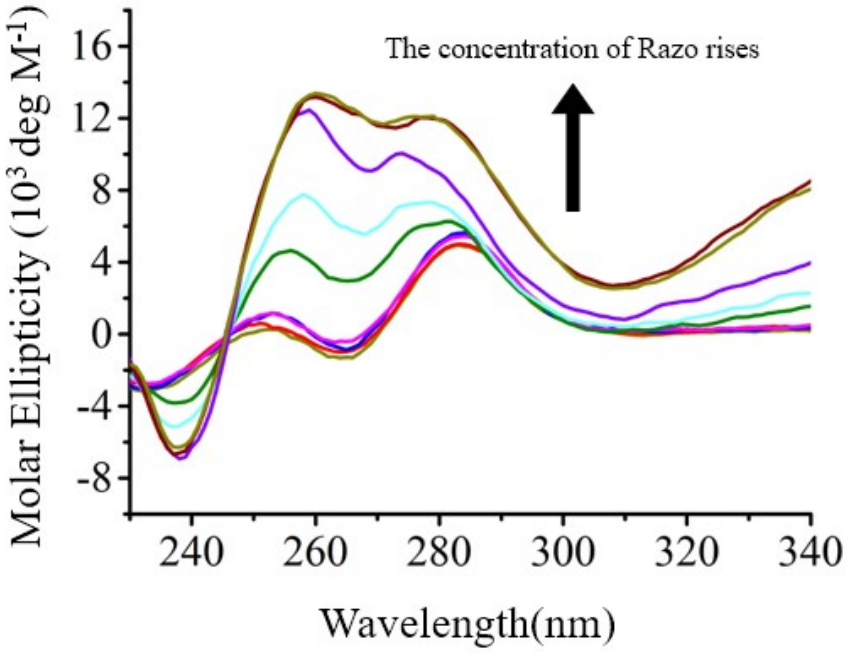

Figure S4. The Circular dichroism spectra of titration between AS-M and Razo.

(AS-M =10μM, Razo = 0μM, 1μM, 3μM, 5μM, 10μM, 30μM, 50μM, 100μM, 500μM)

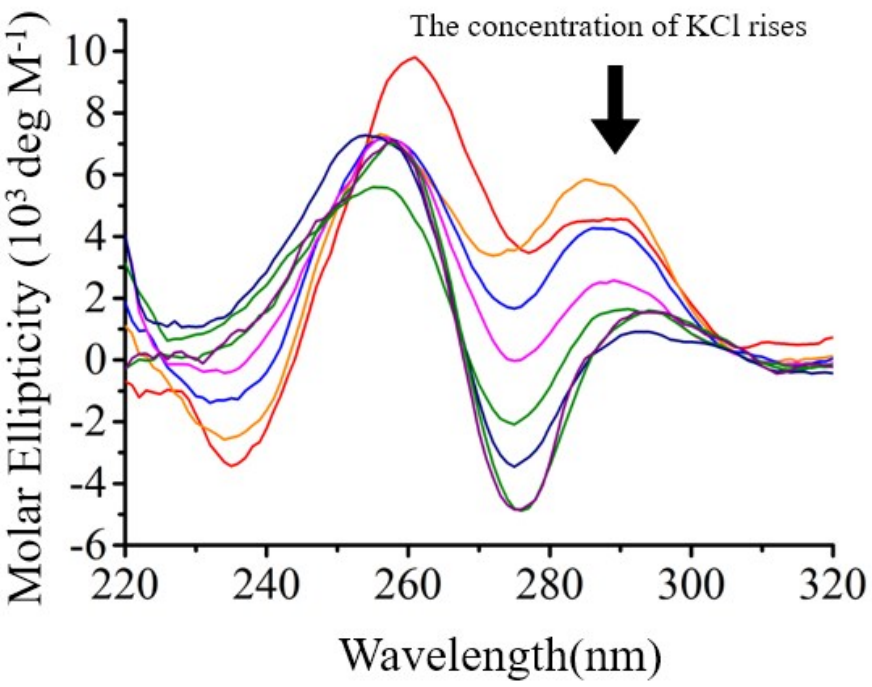

Figure S5. The Circular dichroism spectra of titration between AS-M and KCl.

(AS-M =10μM, KCl = 0μM, 1mM, 5mM, 10mM, 30mM, 50mM, 100mM, 500mM)

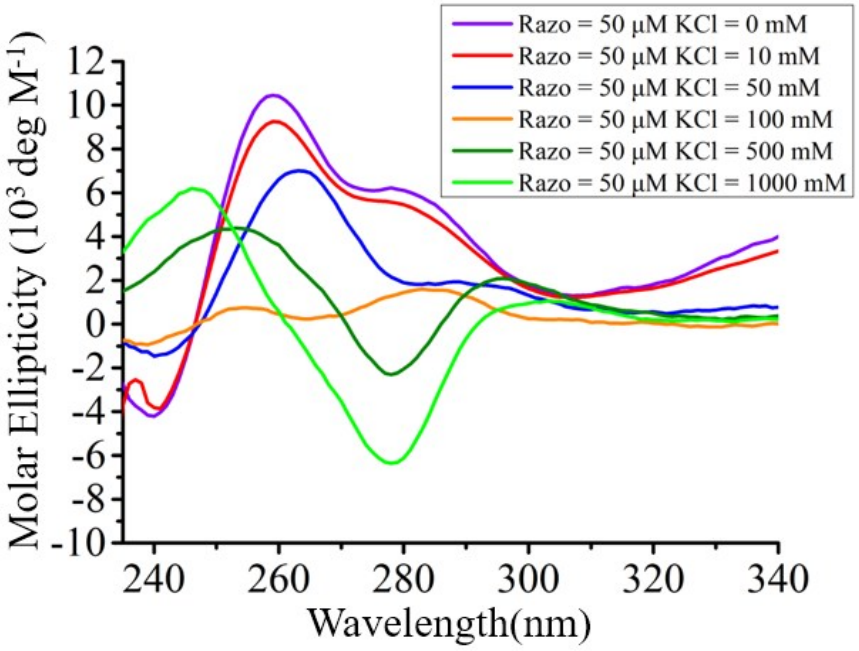

Figure S6. The Circular dichroism spectra of the competition titration. The initiating structure of AS-M (The concentration of AS-M =10μM) is the left-handed formation in the present of 100mM K^+.

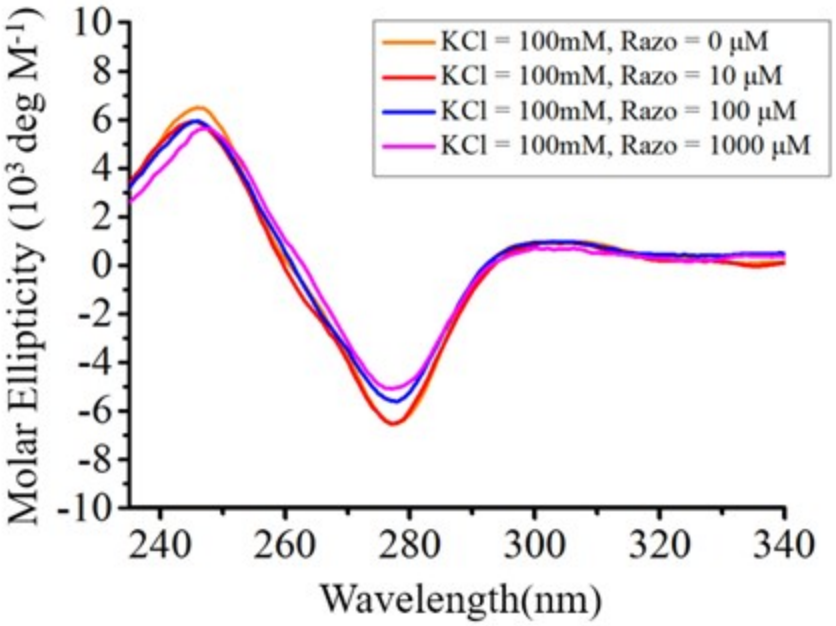

Figure S7. The Circular dichroism spectra of the competition titration. The initiating structure of AS-M (The concentration of AS-M =10μM) is the right-handed formation in the present of 100μM Razo.

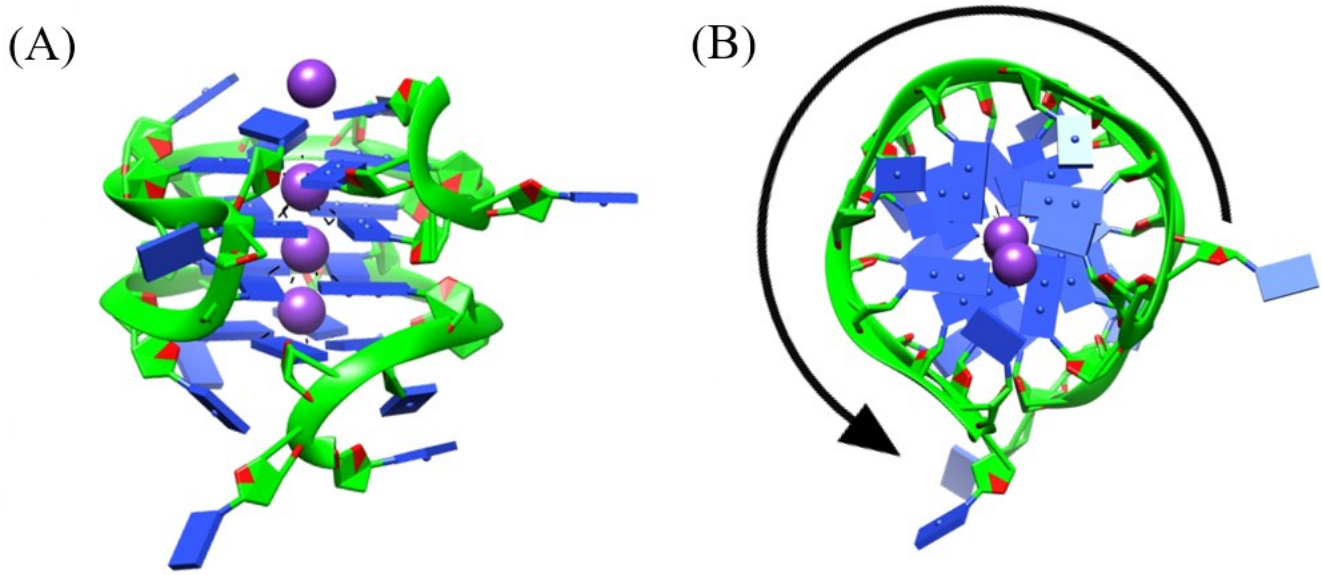

Figure S8. The crystal structure of left-handed G-quadruplex. (PDB: 4U5M[2]) (A) Mainview. (B) Topview.

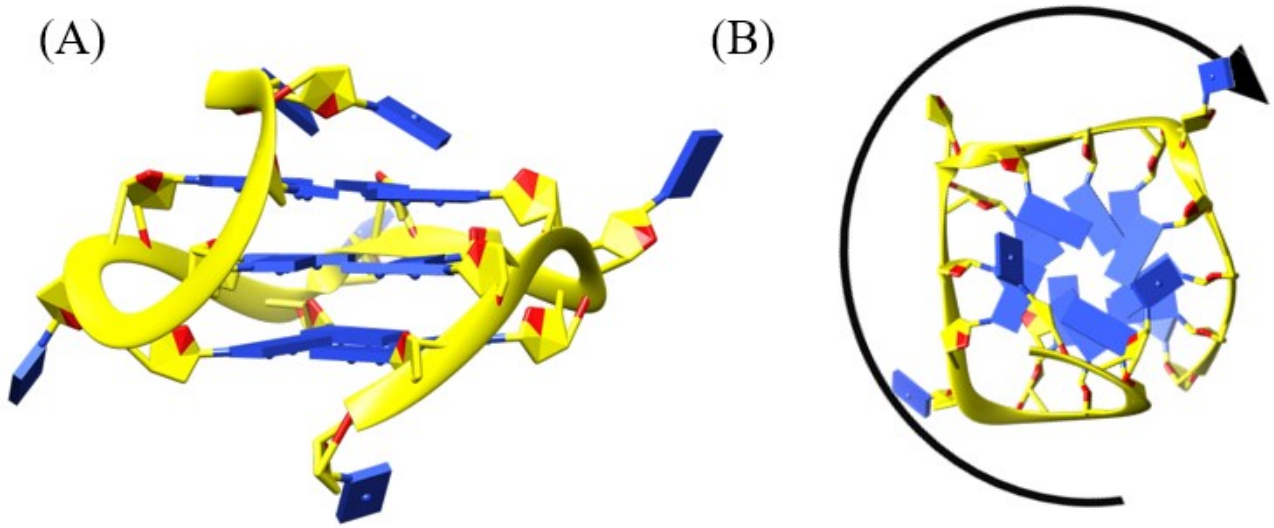

Figure S9 The crystal structure of right-handed G-quadruplex from T95-2T. (PDB: 2lk7[3]) (A) Mainview. (B) Topview.

Reference

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