Electronic Supplementary Information

Cucurbit[7]uril-driven modulation of ligand-DNA interactions by ternary assembly

Ekaterina Y. Chernikova,*[a] Anna Y. Ruleva,[a] Vladimir B. Tsvetkov,[b,c,d] Yuri V. Fedorov,[a] Valentin V. Novikov,[e] Tseimur M. Aliyeu,[f] Alexander A. Pavlov,[e] Nikolay E. Shepel[a] and Olga A. Fedorova*[a]

[a.] *Laboratory of Photoactive Supramolecular Systems, A.N. Nesmeyanov Institute of Organoelement Compounds of Russian Academy of Sciences, Russia, 119991, Moscow, Vavilova St. 28*

[b.] *Computational oncology group, I.M. Sechenov First Moscow State Medical University, Trubetskaya str, 8/2, Moscow, 119146 Russia;*

[c.] *Biophysics Department, Research and Clinical Center for Physical Chemical Medicine, Malaya Pirogovskaya str. 1a, Moscow 119435, Russia;*

[d.] *Polyelectrolytes and Biomedical Polymers Laboratory, A.V. Topchiev Institute of Petrochemical Synthesis, Russian Academy of Sciences, Leninsky prospect str. 29, Moscow, 119991, Russia*

[e.] *Laboratory of Nuclear Magnetic Resonances, A.N. Nesmeyanov Institute of Organoelement Compounds of Russian Academy of Sciences, Russia, 119991, Moscow, Vavilova St. 28*

[f.] *Center for molecule composition studies, A.N. Nesmeyanov Institute of Organoelement Compounds of Russian Academy of Sciences, Russia, 119991, Moscow, Vavilova St. 28*

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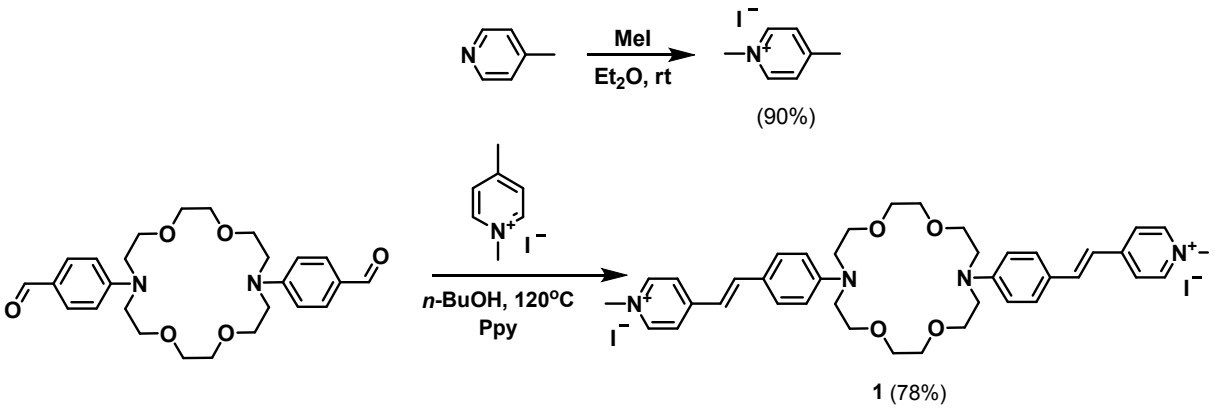
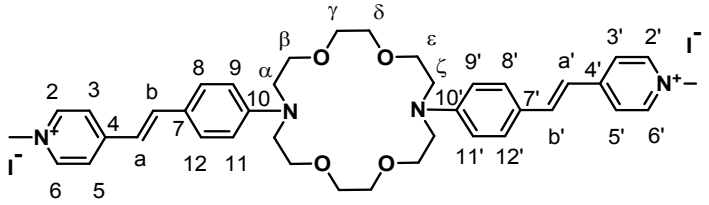
1. Synthesis and characterization

1,4-Dimethylpyridinium iodide was prepared according to literature procedures.[1]



4,4'-(1E,1'E)-2,2'-(4,4'-(1,4,10,13-tetraoxa-7,16-diazacyclooctadecane-7,16-diyl)bis(4,1-phenylene))bis(ethene-2,1-diyl)bis(1-methylpyridinium) iodide (L)



1,4-Dimethylpyridinium iodide (62.4 mg, 0.27 mmol) and 4,4′-dibenzaldehyde-diaza-18-crown-6 ether (50 mg, 0.11 mmol) were dissolved in *n*-BuOH (5 mL) with addition of piperidine (0.04 mL). The mixture was stirred at 120 °C under argon during 11.5 h. The reaction mixture was cooled to −10 °C, and the precipitate was filtered off, thoroughly washed with hot benzene and dried in air. Dye **1** was obtained as dark red crystals in 78% yield (75 mg, 0.08 mmol). Mp. 209–211 °C with decomposition, ^{1}H NMR (400 MHz; DMSO-d_6): 3.61-3.52 (br.s, 8H, H-α, H-ζ), 3.71-3.61 (br.s, 16H, H-β, H-γ, H-δ, H-ε), 4.16 (s, 6H, 2CH_3), 6.78 (d, 4H, H-9, H-9', H-11, H-11', J = 8.9), 7.13 (d, 2H, H-a, H-a', J_{trans} = 16.1), 7.56 (d, 4H, H-8, H-8', H-12, H-12', J = 8.9), 7.88 (d, 2H, H-b, H-b', J_{trans} = 16.1), 8.03 (d, 4H, H-3, H-3', H-5, H-5', J = 6.8), 8.68 (d, 4H, H-2, H-2', H-6, H-6', J = 6.8). ^{13}C NMR (126 МГц, DMSO-d_6, δ м.д.): 46.38 (2C, CH_3), 50.59 (4C, C-α, C-ζ), 68.14 (4C, H-β, H-ε), 70.26 (4C, H-γ, H-δ), 111.67 (4C, C-9, C-9', C-11, C-11'), 117.05 (2C, C-a, C-a'), 122.13 (4C, C-3, C-3', C-5, C-5'), 122.41 (2C, C-7, C-7'), 130.43 (4C, C-8, C-8', C-12, C-12'), 141.78 (2C, C-b, C-b'), 144.35 (4C, C-2, C-2', C-6, C-6'), 149.89 (2C, C-10, C-10'), 153.37 (2C, C-4, C-4'). Anal. calcd. for $C_{40}H_{50}N_4I_2O_4$: C, 53.11; H, 5.57; N, 6.19; found: C, 52.61; H, 5.58; N, 6.22. ESI-MS **1** in H_2O, *m/z*: found $[\mathbf{1}]^{2+}$ 325.20 for $C_{40}H_{50}N_4O_4^{2+}$ calcd. 325.19.

2. Optical spectroscopy data

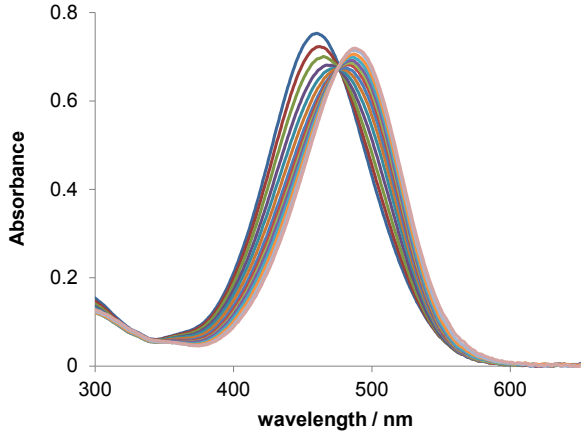


Figure S1. UV-Vis spectra of bis-styryl dye (1.5×10^{-5} M) with increasing CB[7] concentration (0-1.2×10^{-3} M), H_2O.

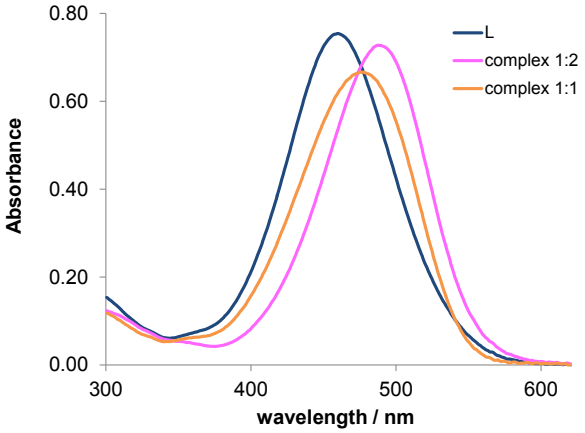


Figure S2. Electronic absorption spectra obtained by a global fit of the spectrophotometric titration data using the SpecFit/32 program for bis-styryl dye (blue curve) and its complexes dye-CB[7] (orange curve) and dye-$(CB[7])_2$ (pink curve), H_2O.

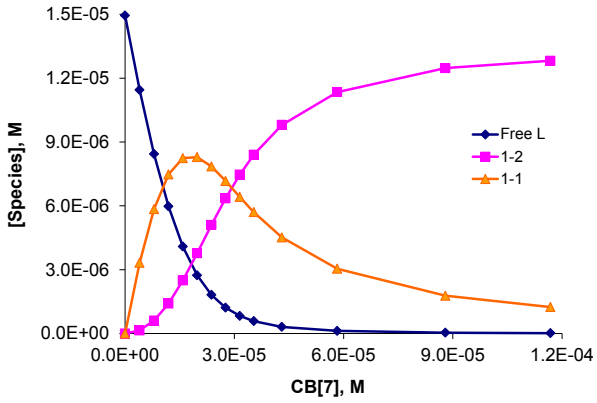


Figure S3. Concentrations of the solution components: bis-styryl dye (blue curve) and its complexes dye-CB[7] (orange curve) and dye-$(CB[7])_2$ (pink curve), depending on the CB[7] concentration, H_2O.

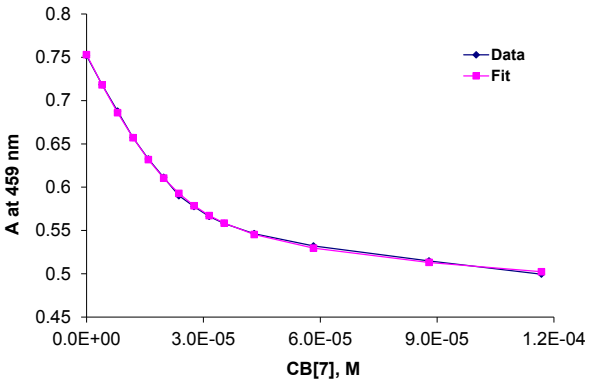


Figure S4. Changes in absorption spectra of bis-styryl dye at 459 nm depending on the CB[7] concentration: experimental data and obtained by a global fit of the spectrophotometric titration data using the SpecFit/32 program, H_2O.

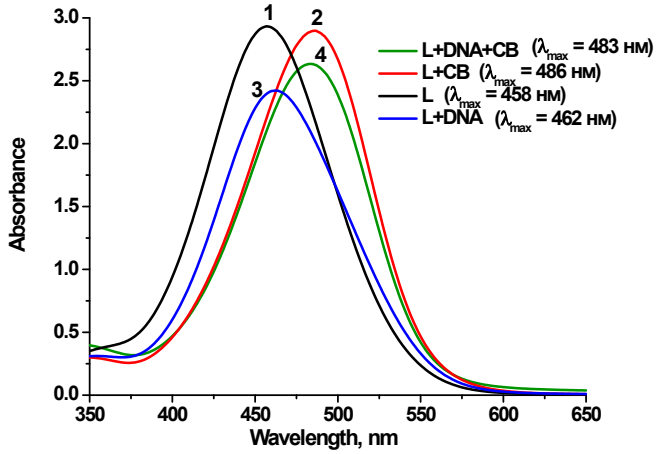


Figure S5. Absorption spectra of free **L** and in the presence of DNA and/or CB[7]: (1) $C_{\mathbf{L}}$ =6·10^{-5} M (black); (2) $C_{\mathbf{CB[7]}}$ = 6·10^{-4} M, $C_{\mathbf{L}}$ = 6·10^{-5} M (red); (3) C_{DNA} = 10^{-4} M, $C_{\mathbf{L}}$ = 6·10^{-5} M (blue); (4) $C_{\mathbf{CB[7]}}$ = 6·10^{-4} M, $C_{\mathbf{L}}$ = 6·10^{-5} M, C_{DNA} = 10^{-4} M (green).

3. Molecular modeling data

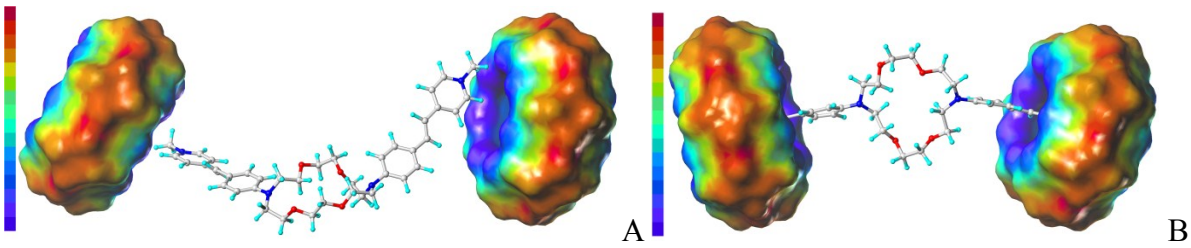


Figure S6. Snapshots of arrangement of dye and cucurbiturils molecules relative to each other. (A) – the starting position of components, (B) - after 14 picoseconds MD simulations. The cucurbiturils are covered with a Connolly surface, which is colored depending on the distribution of the electrostatic potential from negative (blue) to positive (red).

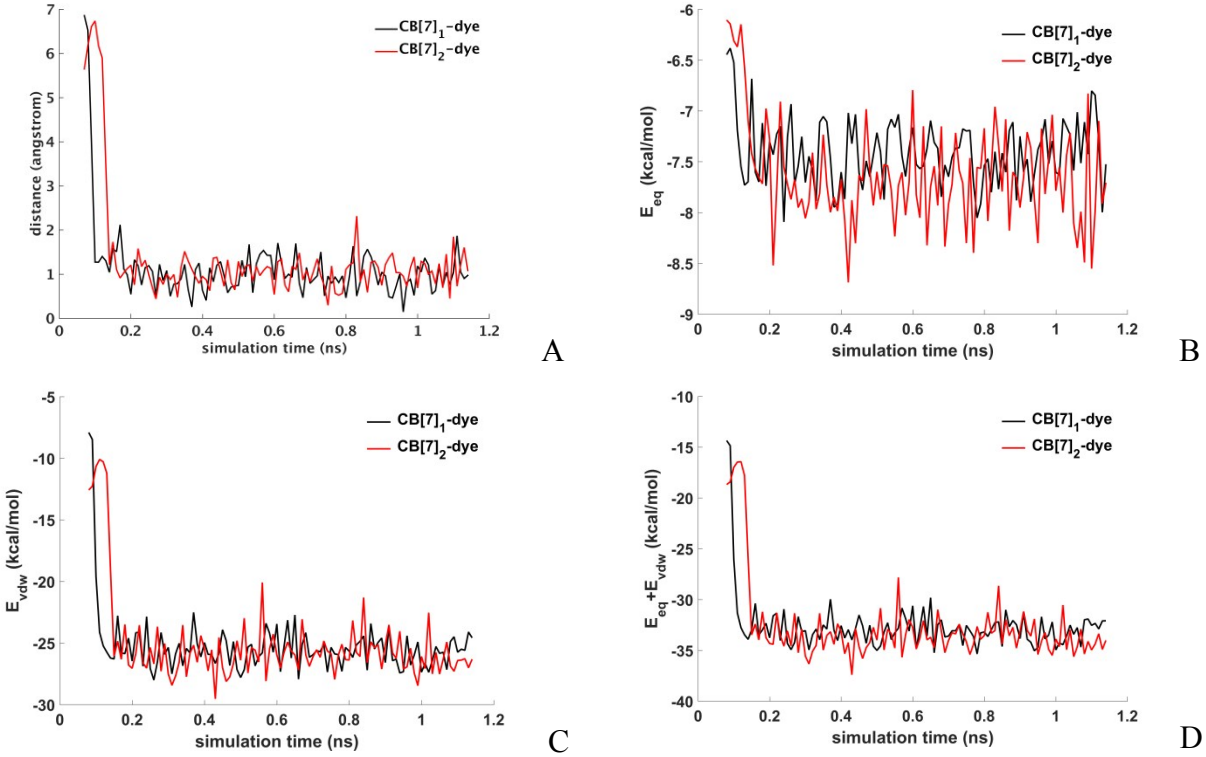


Figure S7. The evolution of the distance between pyridinium N-atom of dye and center of carbonyl portal of CB[7] farthest from this N-atom (A). Evolution of the Coulomb (Eeq) (B), van der Waals (Evdw) (C) and their sum (Eeq + Evdw) (D) contributions to the interaction energy of bis-styryl dye with one (black) or two (red) CB[7] molecules.

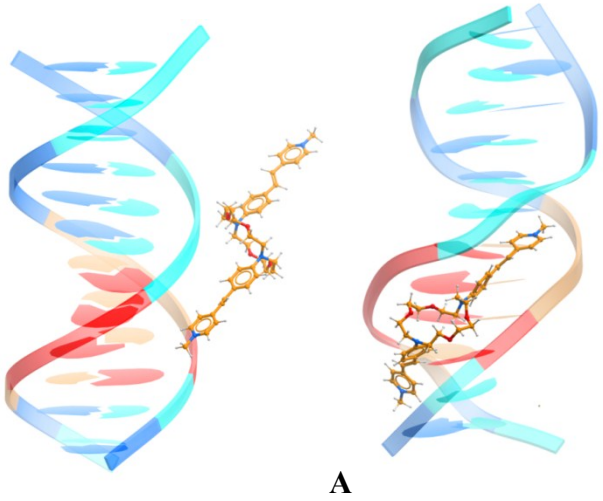


Figure S8. Snapshots of arrangement of dye and DNA molecules relative to each other. (A) – the starting position of components, (B) - after 38 nanoseconds MD simulation.

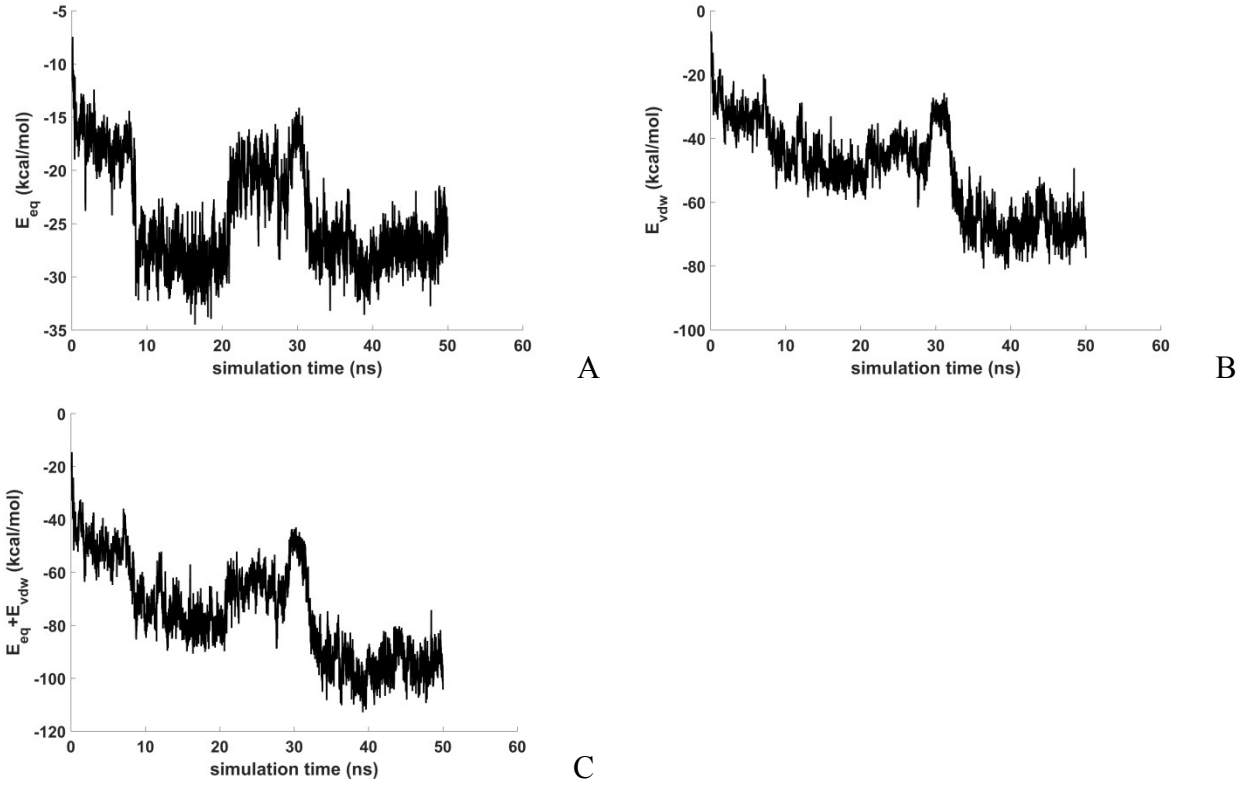


Figure S9. Evolution of the Coulomb (Eeq) (A), van der Waals (Evdw) (B) and their sum (Eeq + Evdw) (C) contributions to the interaction energy of bis-styryl dye with DNA.

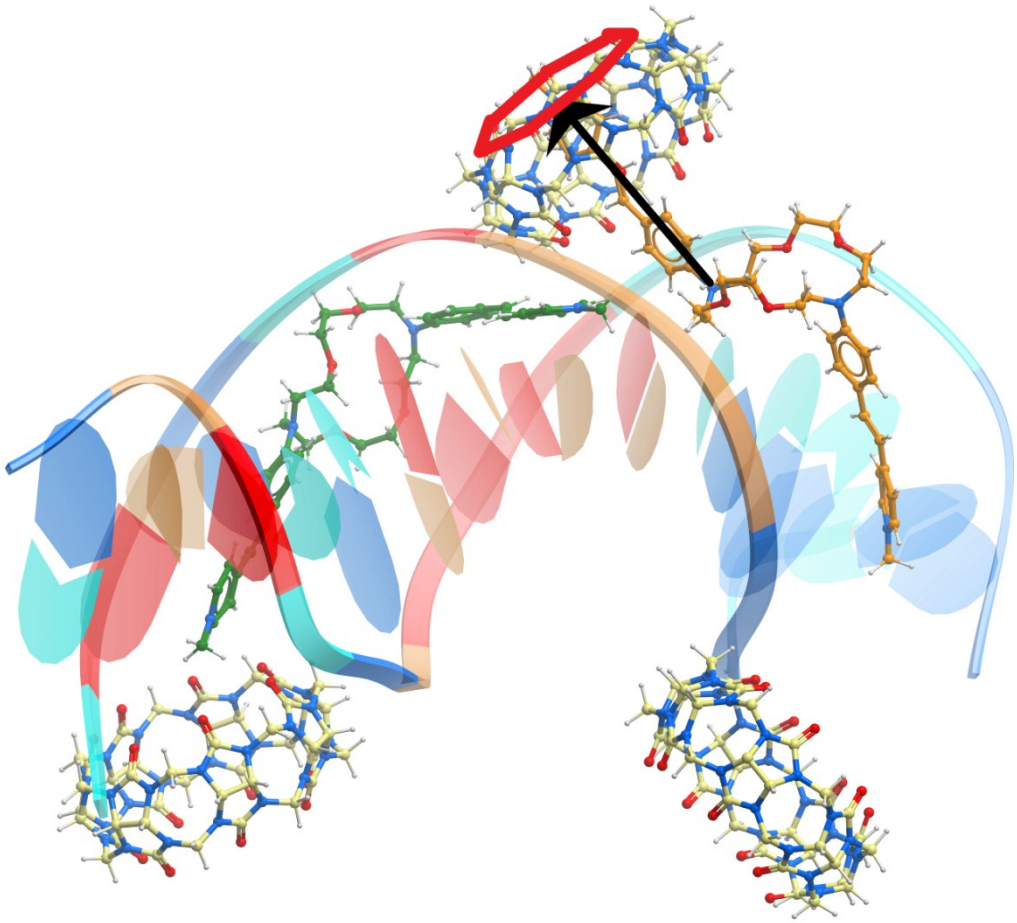


Figure S10. Locations of the DNA, bis-styryl dye and cucurbiturils in the final stages of MD calculations: A - start, B - final. The DNA shown by rendering with the nucleotides colored as follows: G - blue, A - red, T - light brown, C - cyan. Atoms are represented by the following colors: cucurbituril carbon - yellow, bis-styryl dye carbon - beige and green, oxygen - red, nitrogen - blue, hydrogen - white. A black vector is a vector connecting the aliphatic and pyridinium N-atoms of dye molecule. The red closed line marks the plane of carbonyl portal of CB[7].

4. NMR spectroscopy data

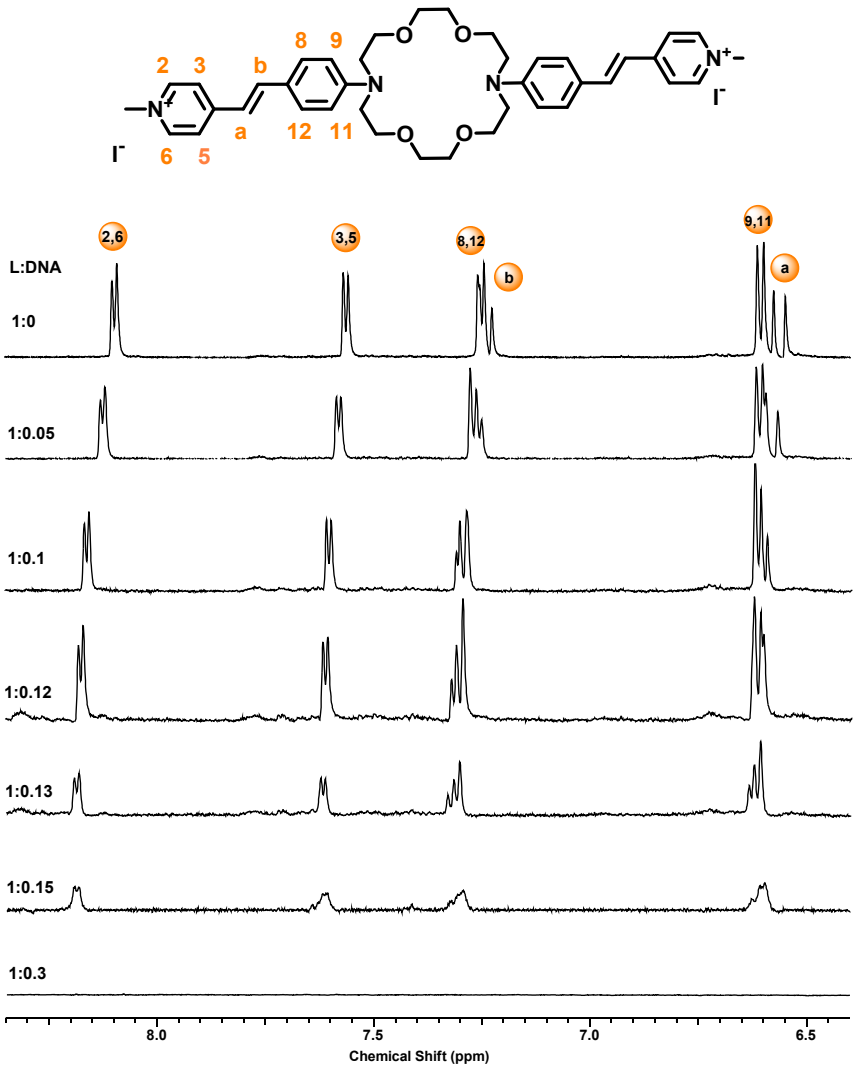


Figure S11. Aromatic part of ^{1}H NMR spectra (600 MHz, 298 K, sodium phosphate buffer/D_2O 9:1, 1mM) of free ligand **L** and in the presence of different amounts of Dickerson dodecamer.

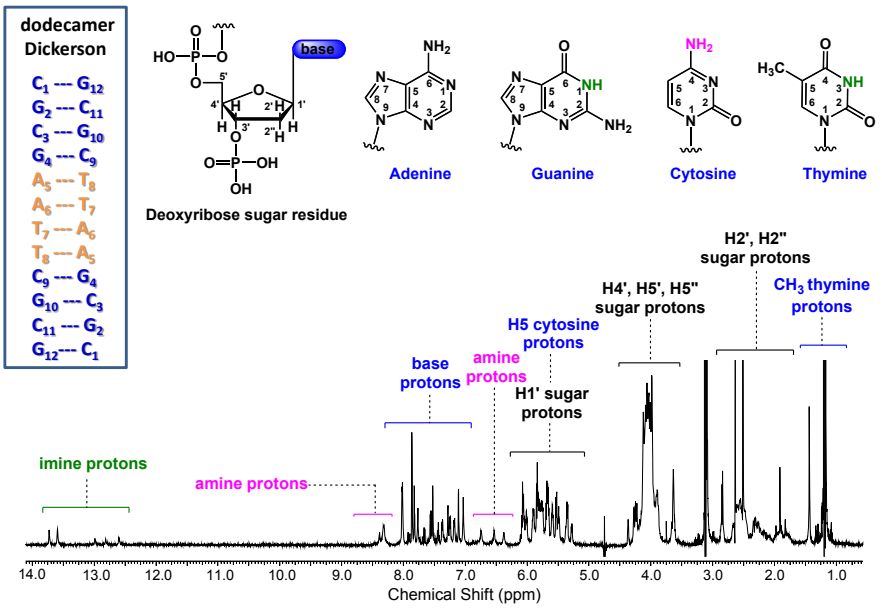


Figure S12. Assignment of dodecamer Dickerson protons. Green and pink color display visible exchangeable protons such as NH of guanines and thymines and NH_2 of cytosines.

Table S1. Assignment of the ^{1}H NMR spectrum of the oligonucleotide d(CGCGAATTCGCG)$_2$ in D_2O.

Residue	C8H	C6H	C5H	C2H	CH3	C1'H	C2'H/C2''H	C4'H
C1		7.56	5.84			5.68	2.27/1.85	4.15
G2	7.86					5.79	2.56/2.52	4.31
C3		7.17	5.28			5.49	2.13/1.7	4.17
G4	7.77					5.38	2.63/2.52	4.29
A5	8.02			7.11		5.90	2.82/2.57	4.44
A6	8.02			7.53		6.05	2.79/2.42	4.44
T7		7.03			1.20	5.82	2.42/1.87	4.24
T8		7.28			1.44	6.01	2.44/2.05	4.24
C9		7.37	5.53			5.59	2.30/1.94	4.20
G10	7.82					5.76	2.56/2.52	4.35
C11		7.24	5.35			5.66	2.19/1.79	4.20
G12	7.86					6.08	2.50/2.23	4.20

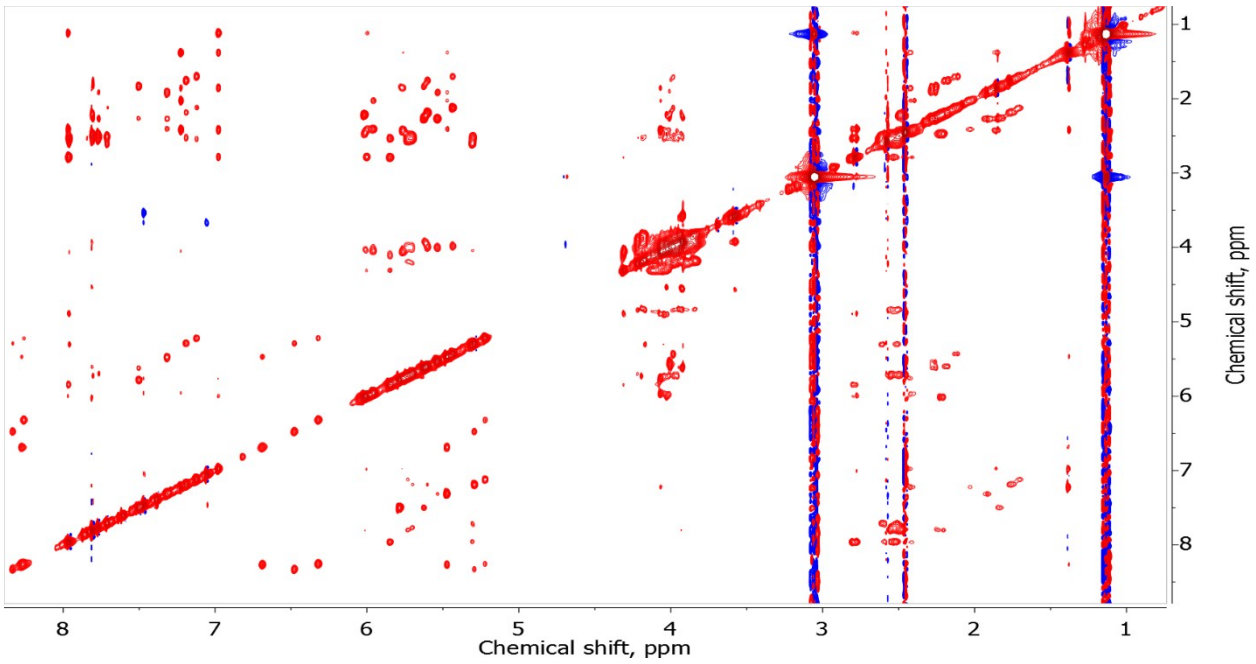


Figure S13. 600 MHz NOESY of 1mM DD in 10mM phosphate buffer:D_2O 9:1 (pH=7.0).

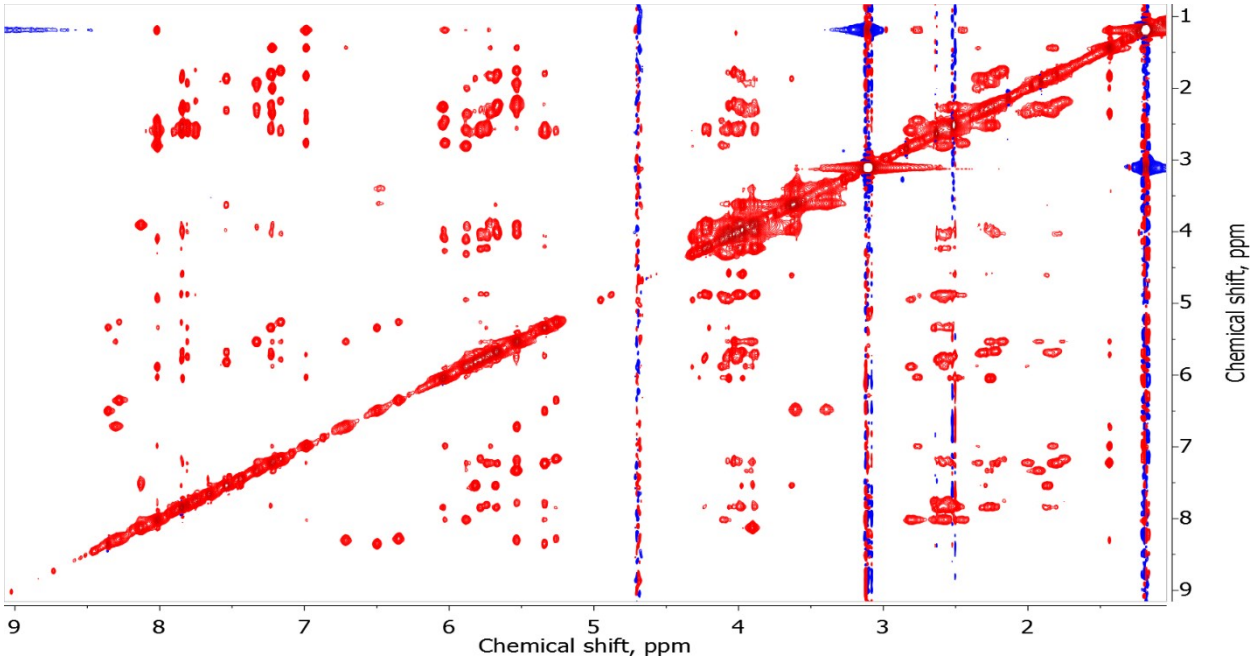


Figure S14. 600 MHz NOESY of **L**-DD (0.3-1) mixture in 10mM phosphate buffer:D_2O 9:1 (pH=7.0).

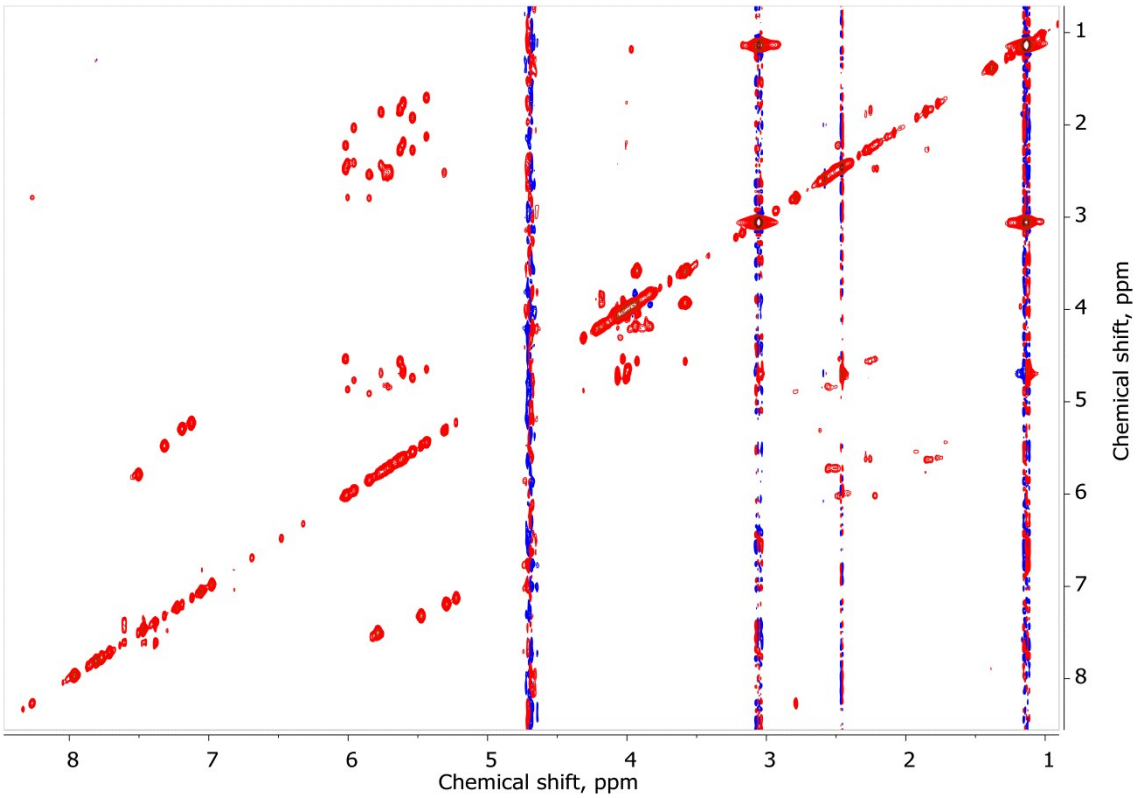


Figure S15. 600 MHz TOCSY of 1mM DD in 10mM phosphate buffer:D_2O 9:1 (pH=7.0).

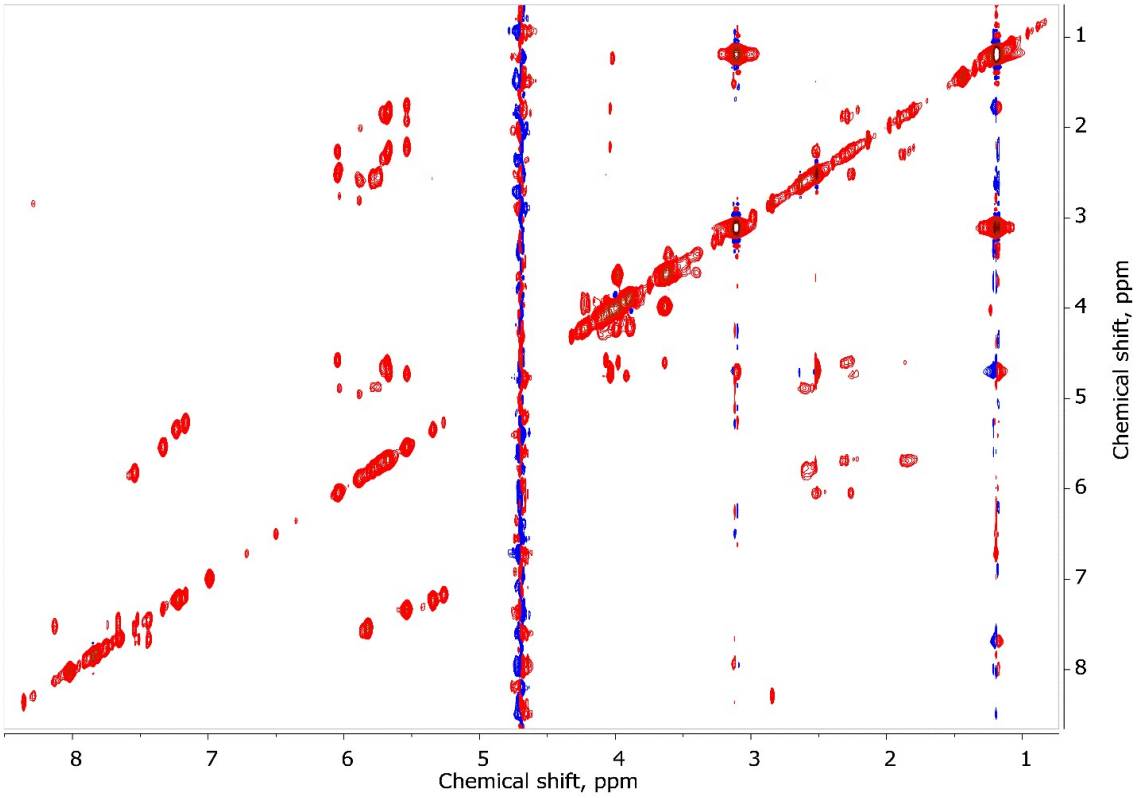


Figure S16. 600 MHz TOCSY of **L**-DD (0.3-1) mixture in 10mM phosphate buffer:D_2O 9:1 (pH=7.0).

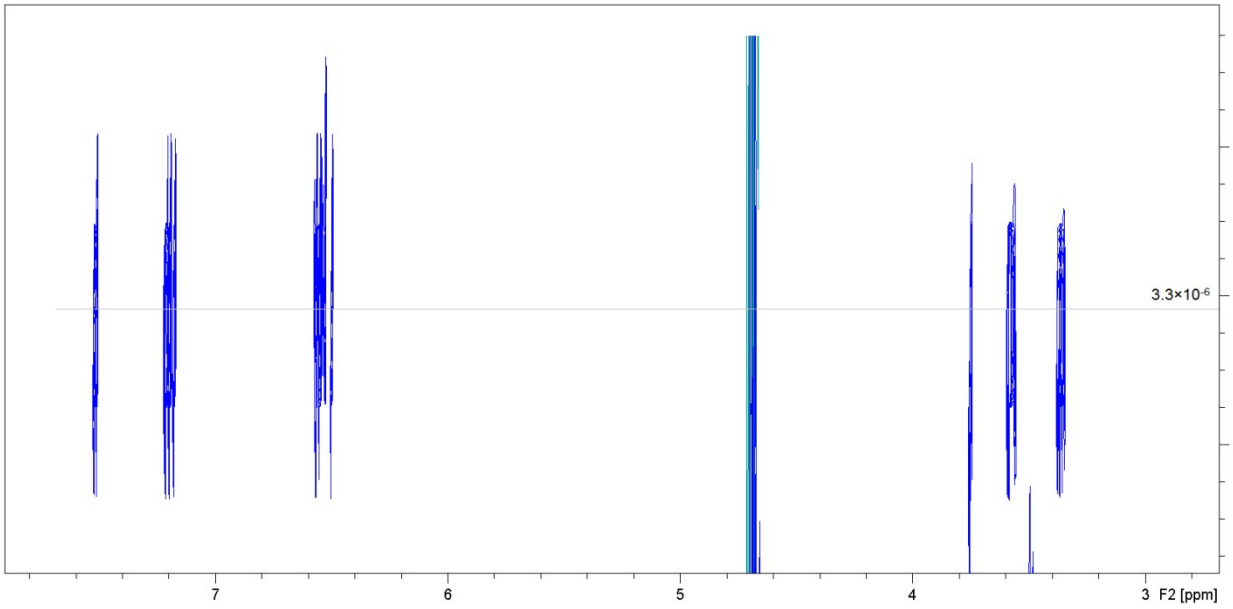


Figure S17. 600 MHz DOSY of **L** in 10mM phosphate buffer:D_2O 9:1 (pH=7.0).

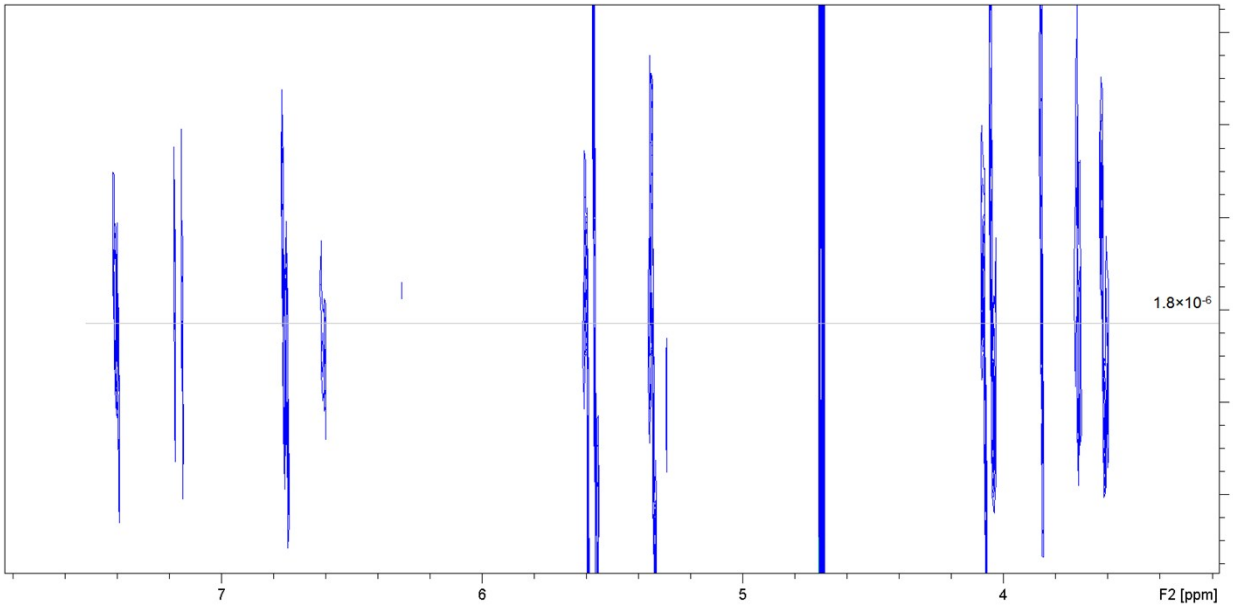


Figure S18. 600 MHz DOSY of **L**-CB[7] (1:2) mixture in 10mM phosphate buffer:D_2O 9:1 (pH=7.0).

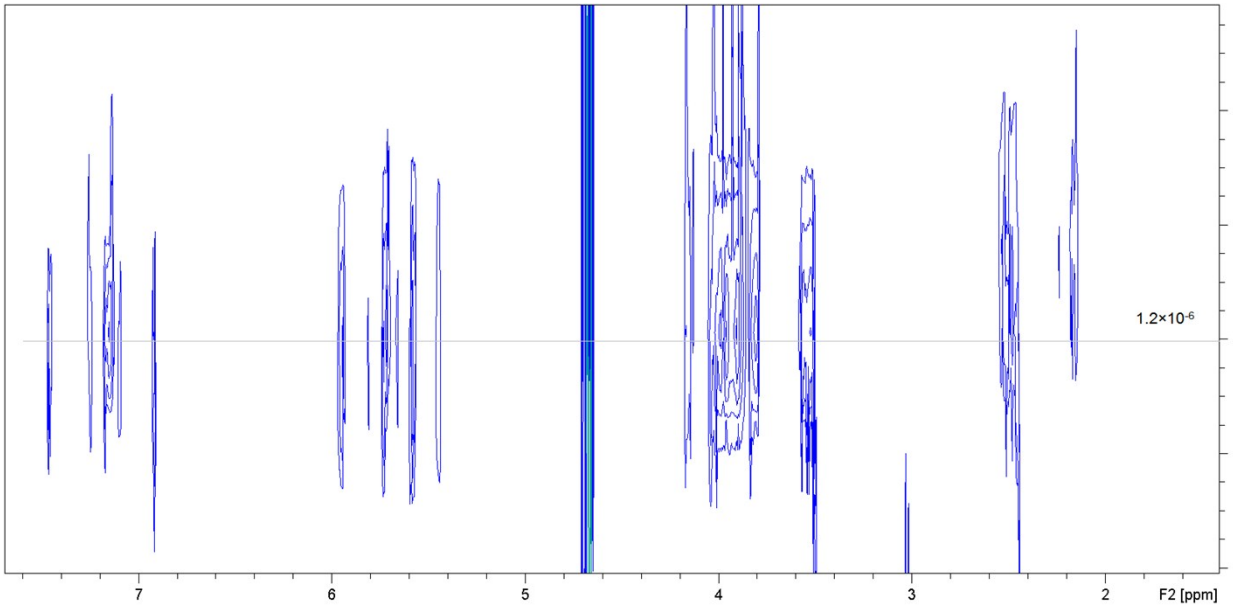


Figure S19. 600 MHz DOSY of **L**-DD (0.3-1) mixture in 10mM phosphate buffer:D_2O 9:1 (pH=7.0).

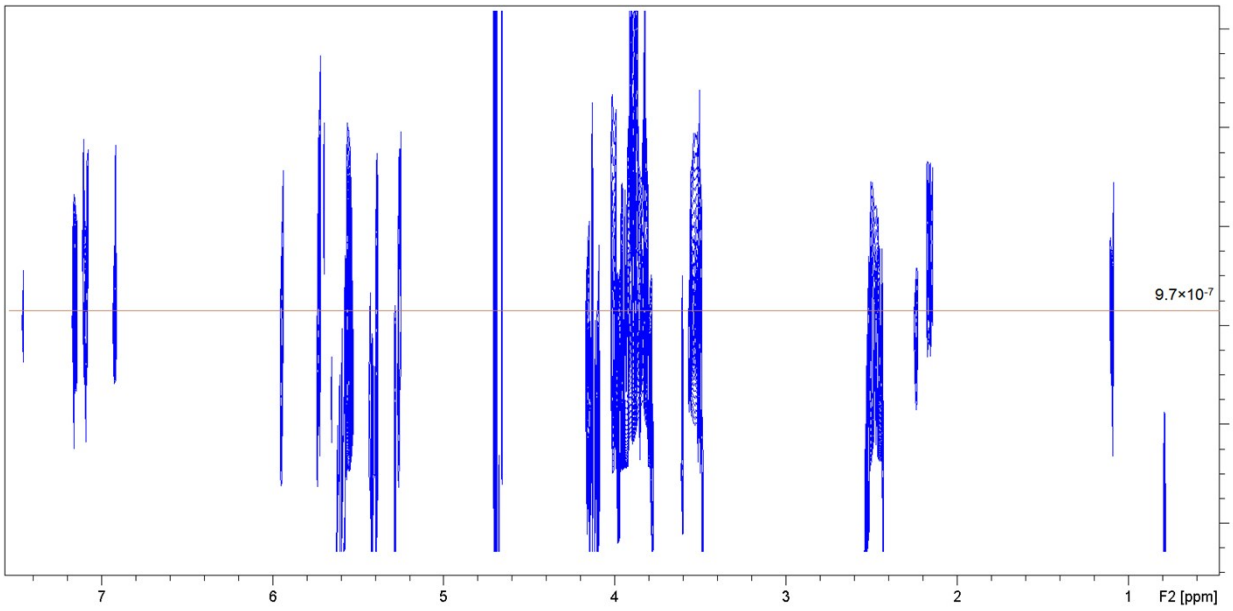


Figure S20. 600 MHz DOSY **L**-DD-CB[7] mixture (1:1.5:3) in 10mM phosphate buffer:D_2O 9:1 (pH=7.0).

5. References

(1) Usoltsev, A. N. et al. (2018) Mononuclear bromotellurates (IV) with pyridinium-type cations: Structures and thermal stability. *Polyhedron 151*, 498-502.