Electronic Supplementary Material (ESI) for ChemComm.

Cyclodextrin-based Switchable DNA Condenser

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Experimental Section

Materials. All solvents and reagents were commercially available and used without further purification unless otherwise noted. Anhydrous N,N-dimethylformamide (DMF) was dried and distilled over CaH_2 under reduced pressure. All aqueous solutions were prepared with distilled water. *β*-CD of reagent grade (Shanghai Reagent Factory) was recrystallized twice from water and dried in vacuum at 95°C for 24 h prior to use. I_2, PPh_3 and ethyl bromoacetate were purchased from Tianjin FuChen Chemical Reagents Factory. Ethyl 6-bromohexanoate was purchased from J&K chemical Co. Ltd. Im_7-*β*CD was prepared according to a reported method[S1].

Instruments. NMR spectra were recorded in D_2O on a Bruker AV 400 spectrometer, and two-dimensional NMR spectra were recorded in D_2O in the presence of 1% DMF-d_6 on a Varian Mercury VX-300 spectrometer. Mass spectra were recorded on a Varian 7.0T FTICR mass spectrometer (MALDI). Elemental analysis was performed by using a Vario EL Cube

elemental analyzer (Elementar Ltd. Corp., Germany). UV/Vis spectra were recorded in a quartz cell (light path 10 mm) on a Shimadzu UV-3600 spectrophotometer equipped with a PTC-384WI temperature controller. AFM images were examined with a Nanoscope IIIa Multimode 8 AFM (Bruker). Samples were prepared by dropping the solution on mica. The mica samples were then air-dried, and the samples were examined in tapping mode. The zeta potential was recorded with a Zeta-Plus z potential analyzer (Zetapals/BI-200SM, Brookhaven, USA).

Synthesis of 1.

Ethyl 6-bromohexanoate (2.1 mmol, 468 mg) was added to a solution of Im_7-*β*CD (0.1 mmol, 149 mg) in DMF (5 mL). The mixture was stirred at 80°C for 48 h, and then was poured into excess Et_2O (300 mL) to give a white precipitate. The precipitate was dissolved in the minimum amount of cold water, and then poured into acetone (400 mL). The product was collected by filtration with a yield of 145 mg (48 %). ESI-MS, *m/z* (caculated) = 355.33 (**1**-7Br^-), *m/z* (found) = 355.19 (**1**-7Br^-); Elemental analysis calculated for $C_{119}H_{211}Br_7N_{14}O_{53}$ (**1**·11H_2O) (%): C 44.04, H 6.55, N 6.04. Found (%): C 43.96, H 6.43, N 6.38; ^{1}H NMR (D_2O, 400 MHz) *δ* 8.97 (m, 7H, Im-H-2), 7.57-7.55 (d, 14H, J = 8.0 Hz, Im-H-4,5), 5.1 (m, 7H, CD-H-1), 4.50-4.47 (m, 14H, CH_2), 4.10-3.99 (m, 42H), 3.55-3.51 (m, 7H), 3.35-3.29 (m, 7H), 2.30-2.25 (t, 14H, J = 10.0 Hz), 1.77-1.72 (m, 14H), 1.54-1.49 (m, 14H), 1.24-1.11 (m, 35H). ^{13}C NMR (d_6-DMSO, 100 MHz) *δ* 173.20, 137.85, 124.01, 122.99, 102.33, 82.74, 72.70, 72.03, 69.29, 60.21, 49.15, 33.69, 31.17, 29.66, 25.51, 24.25, 14.59.

Synthesis of 2.

2 was prepared in 71% yield from Im_7-*β*CD and EtAcBr as a white solid according to the

procedures described above. ESI-MS, *m/z* (caculated) = 299.12 (**2**-7Br^{-}), *m/z* (found) = 229.13 (**2**-7Br^{-}); Elemental analysis calculated for $C_{91}H_{143}Br_7N_{14}O_{47}$ (**2**·5H_2O) (%): C 39.82, H 5.25, N 7.15. Found (%): C 39.73, H 5.02, N 7.18; ^{1}H NMR (D_2O, 400 MHz) δ H: 8.90 (s, 7H, Im-H-2), 7.71 (s, 7H, Im-H-4,5), 7.42 (s, 7H, Im-H-4,5), 5.06-5.04 (m, 21H), 4.50 (s, 7H), 4.33-4.29 (m, 7H), 4.14-4.12 (m, 21H), 4.00-3.98 (m, 7H), 3.56-3.53 (m, 7H) , 3.37-3.35 (m, 7H) , 1.17-1.16 (m, 21H). ^{13}C NMR (d_6-DMSO, 100 MHz) δ 167.48, 138.94, 124.35, 123.62, 102.35, 82.94, 72.59, 72.03, 69.20, 62.43, 50.29, 14.46.

General Agarose Gel Electrophoresis.

Agarose gels (1%) were prepared by heating agarose (250 mg) in TAE buffer (25 mL; 4.0 x 10^{-2} M Tris, 2.0 x 10^{-2} M acetic acid, 2 x 10^{-3} M ethylenediaminetetraacetic acid from Dingguo Changsheng Biotechnology Co. Ltd.). Sample solutions containing pBR322 DNA were prepared by adding an appropriate volume of DNA solution into Eppendorf tubes with different compounds, which were then diluted to a total volume of 15 μL. After incubation at 4 °C for 30 min, the sample solutions were subjected to electrophoresis at 60 V for 40 min and visualized by ethidium bromide staining. The DNA bands were visualized and photographed with a UV transilluminator and WD-9413B gel documentation system (Beijing Liuyi Instrument Factory, P.R. China).

The determination of critical aggregate concentration (CAC) of 1.

The original stored solution of **1** (20 mM) in water is diluted to 5 - 750 μM by Tris buffer (0.1 M, pH = 7.5). The transmittance (%) of these samples at λ = 400 nm are used to calculate the CAC of **1** following the reported method [S2].

2D ^{1}H-ROESY.

The solutions containing cationic CDs (10^{-3}M) are perpared in D_2O, and about 1% DMF is added to improve the solubility.

AFM Measurement.

Samples were prepared by dropping the solution on mica. The mica samples were then air-dried and the samples were examined in tapping mode

The preparation of "Switch off" CD derivates.

The ester-hydrolyzed cationic CDs are prepared from mixing the cationic CD and NaOH in a molar ratio of 1:7. The solutions are stored at room temperature for 3 days and then diluted by Tris buffer (0.1 M, pH = 7.5). The samples for ^{1}H NMR spectra are prepared using the similar method, but buffer is instead by D_2O. The concentrations of cationic CD and NaOH are 1 mM and 7 mM in these samples, respectively. The concentrations marked in Fig.3 were calculated according to the original concentrations of **1** or **2** in the samples.

Switch off in a mimicking psychological condition.

To measure the time dependence of the hydrolysis of CDs in buffer, the solutions of CDs (0.2 mM, 100 μL) in pH = 7.3 HEPES buffer ([HEPES] = 50 mM, ion strength is maintained at 0.1 M with NaCl) are filled in Eppendorf tubes and sealed with polytetrafluoroethylene tapes in water bath (37 °C). Each day 5 μL of solution is corrected from each samples and then rapidly frozen at -20 °C. After 7 days all the samples in freezer are melted for the further experiment to detect their DNA condensation abilities.

Switch off induced by esterase.

The solutions ([AChE] = 100 or 200 U ml^{-1}, [**1**] or [**2**] = 100 μM) were prepared with

redistilled water. These samples were filled in Eppendrof tubes and sealed with polytetrafluorethylene tapes in water bath (37 ^{o}C). About 20 μL of solutions were corrected at every 6 h then rapidly frozen at -20 ^{o}C. The reactions were stopped at 24 h. The samples for gel analysis were prepared at V_{DNA} = 6 μL, $V_{samples}$ = 1.5 and 3 μL. Tris buffer was added to keep the final volume of 15 μL. (The concentration of DNA store solution was 25 ng μL^{-1}.)

Cytotoxicity assay.

The cytotoxicity was investigated by means of a 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT; Sigma, St. Louis, MO, USA) viability test on the 293T and HeLa cell line. Generally, cells were plated at a density of 2 x 10^4 cells per well in 96 wells. After 24 h of incubation, cells were treated with **1** at indicated concentrations for 24 h, then the medium was removed and fresh medium (200 mL) plus MTT reagent (20 mL; 2.5 mg dissolved in 50 mL of dimethylsulfoxide (DMSO) were added to each well. After incubation for 4 h at 37 ^{o}C, the culture medium containing MTT was withdrawn and DMSO (200 mL) was added, followed by shaking for 10 min until the crystals dissolved. Viable cells were detected by measuring the absorbance at λ=490 nm by using a Bio-tekELx800 absorbance reader (BioTek Instruments, Inc, USA). Cell growth was expressed as a percentage of absorbance in cells treated with **1** to that in cells without **1** treatment (100%). The survival rate (IR) was calculated as follows: IR= (A value of **1** well/A value of control well) *100%.[S3]

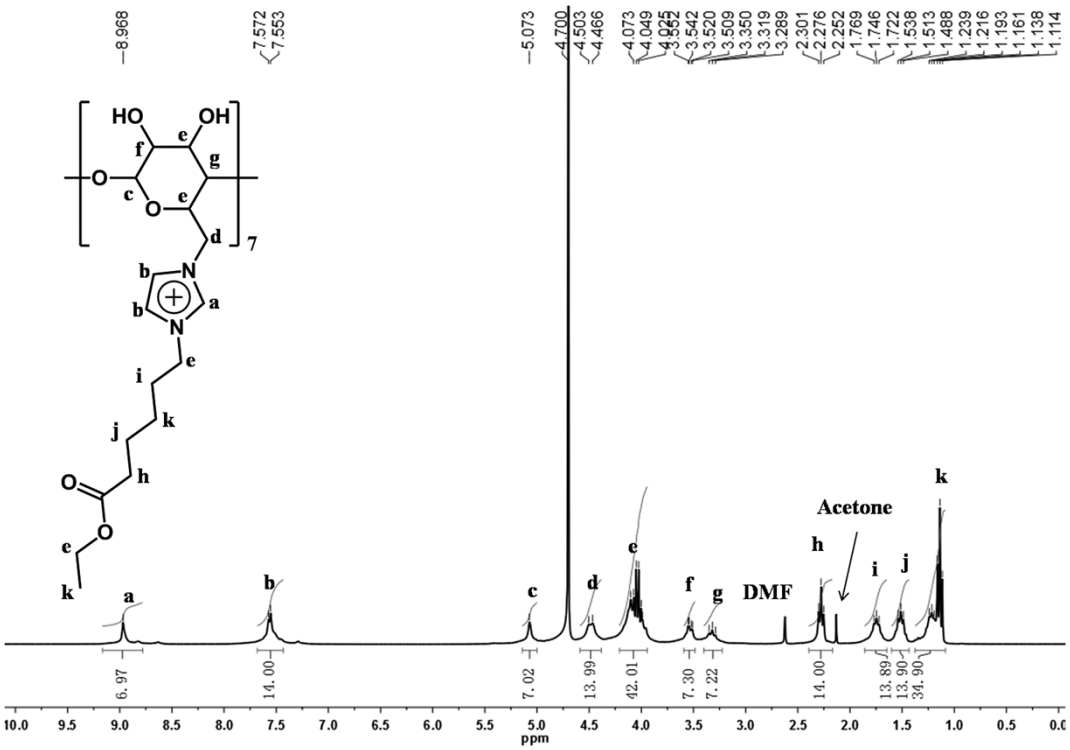


Figure S1 ^{1}H-NMR (400 MHz) spectrum of **1** in D_2O.

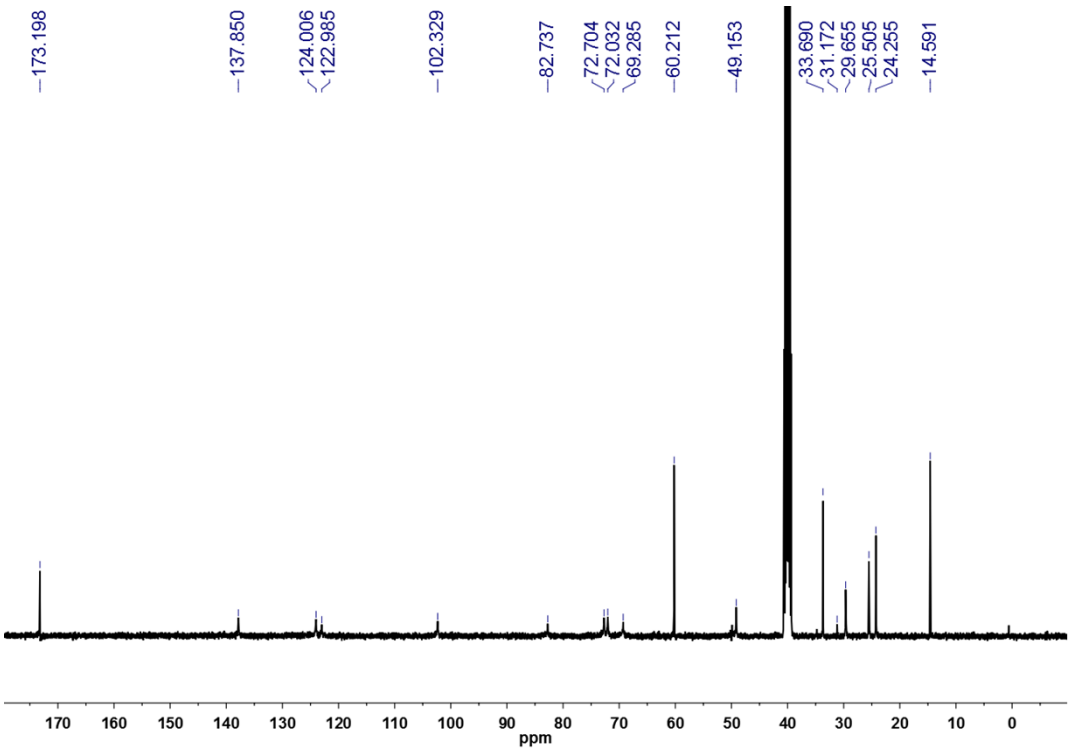


Figure S2 ^{13}C-NMR (100 MHz) spectrum of **1** in d^6-DMSO.

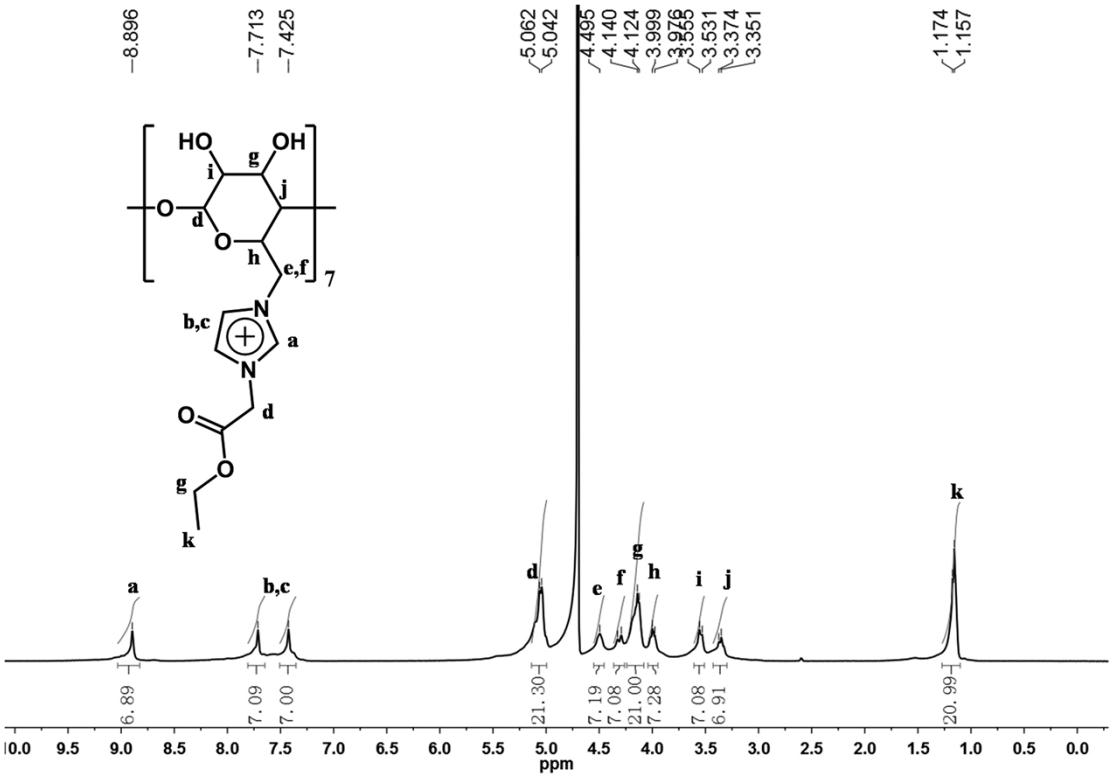


Figure S3 ^{1}H-NMR (400 MHz) spectrum of **2** in D_2O.

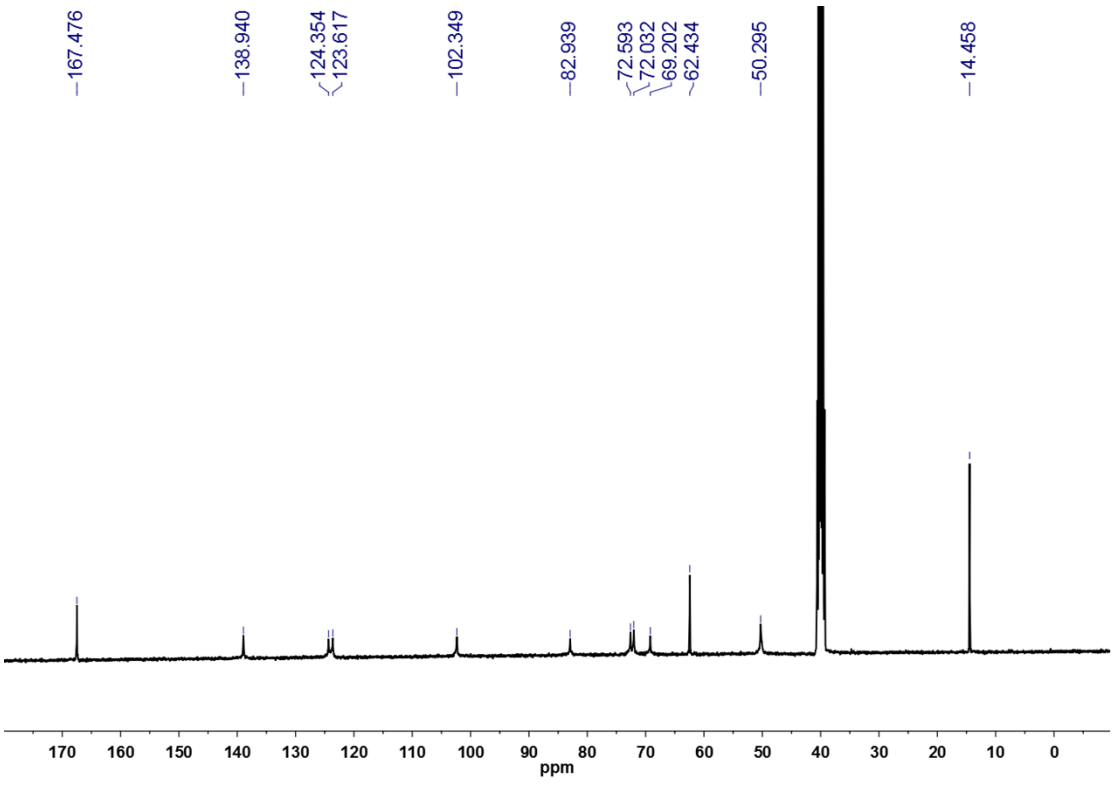


Figure S4 ^{13}C-NMR (100 MHz) spectrum of **2** in d^6-DMSO.

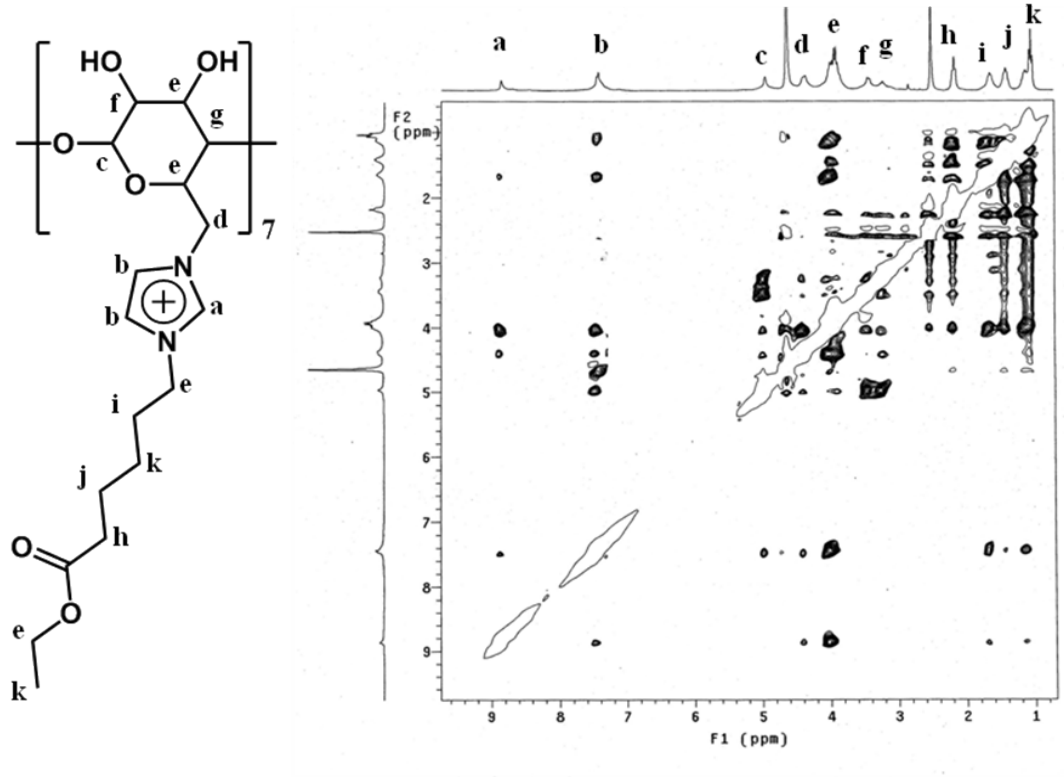


Figure S5 2D ^{1}H-^{1}H ROESY (300 MHz) spectrum of **1** in D_2O with less 1% DMF.

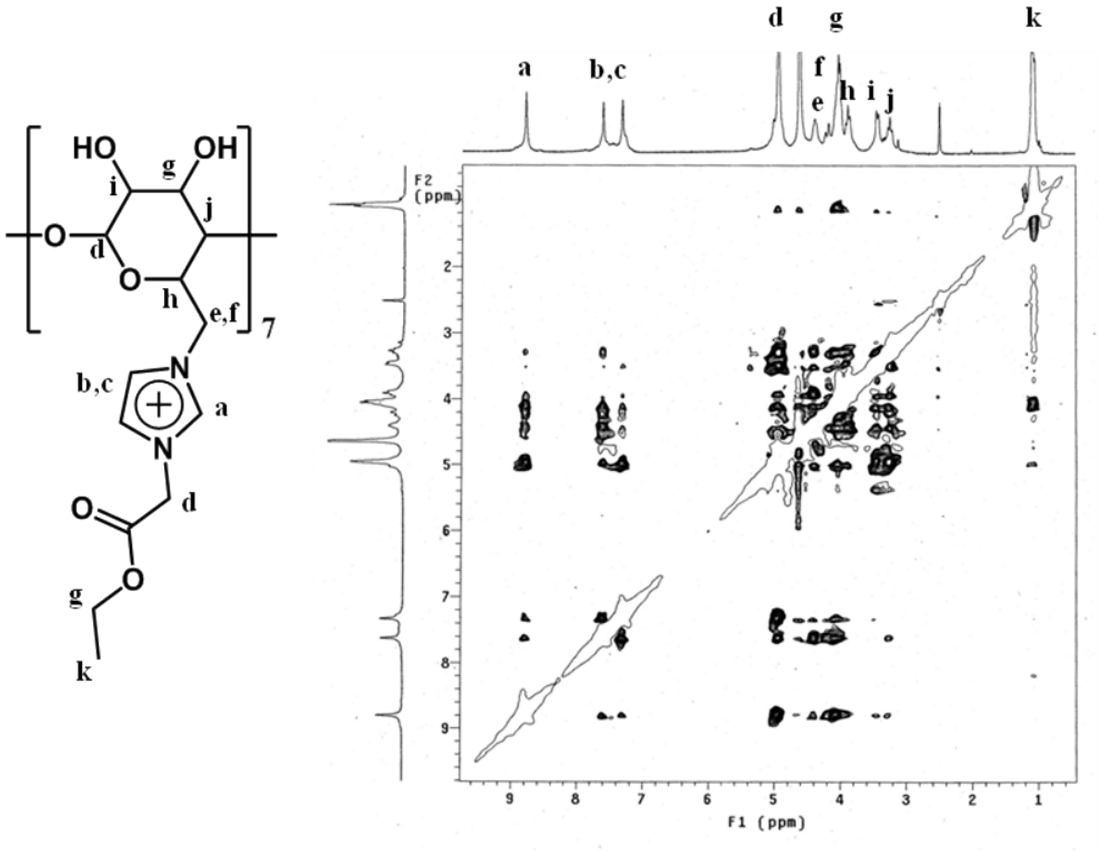
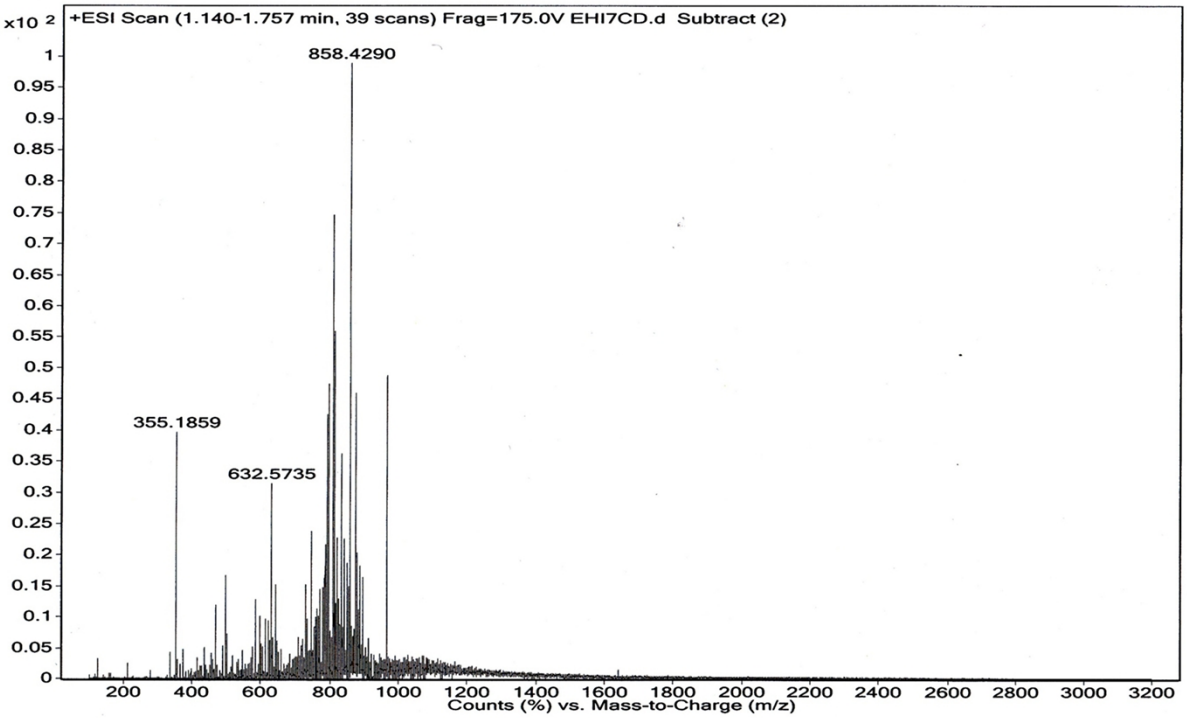
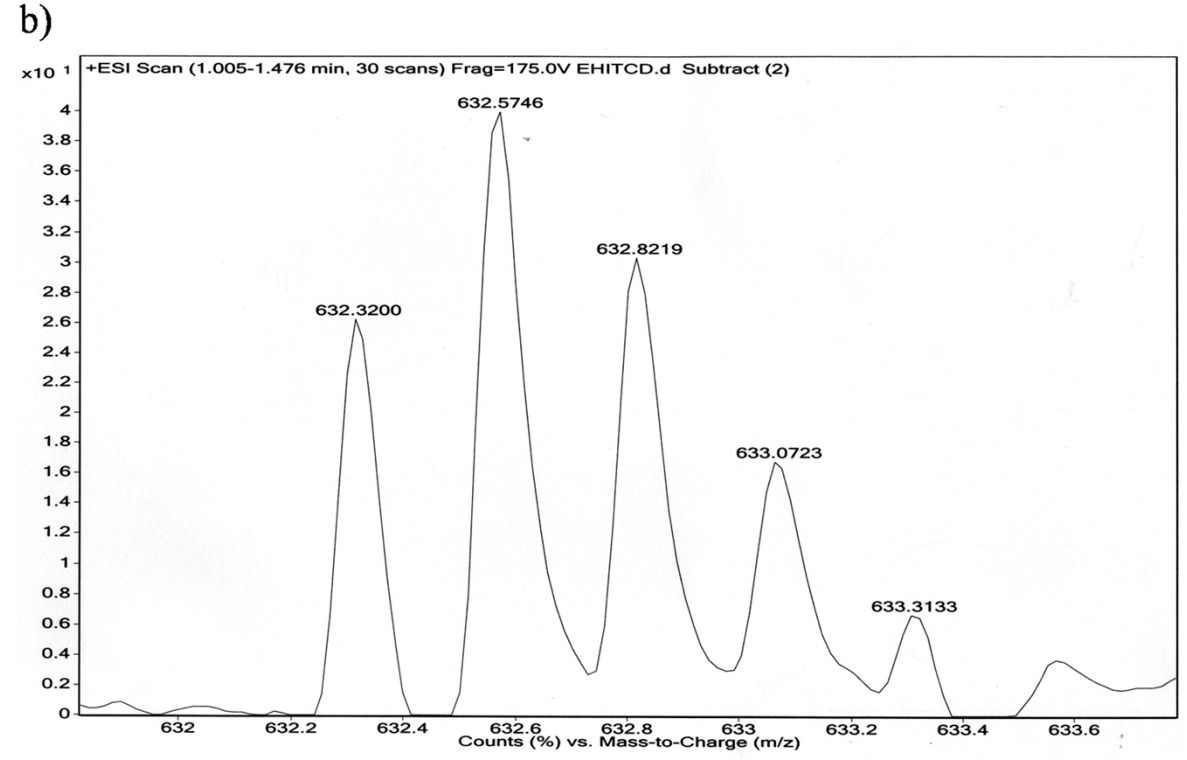


Figure S6 ^{1}H-^{1}H ROESY (300 MHz) spectrum of **2** in D_2O with <1% DMF.

a)


+ESI Scan (1.140-1.757 min, 39 scans) Frag=175.0V EHI7CD.d Subtract (2)
x10 2
858.4290
355.1859
632.5735
Counts (%) vs. Mass-to-Charge (m/z)

b)


+ESI Scan (1.005-1.476 min, 30 scans) Frag=175.0V EHITCD.d Subtract (2)
x10 1
632.5746
632.8219
632.3200
633.0723
633.3133
Counts (%) vs. Mass-to-Charge (m/z)

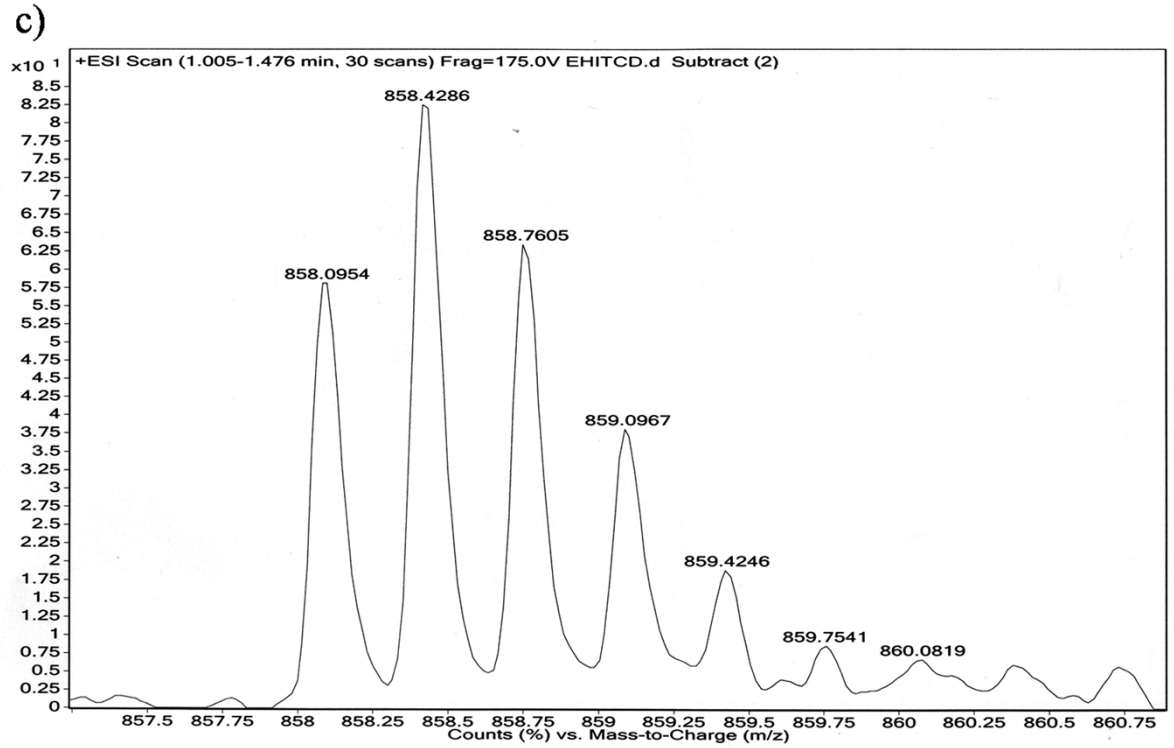
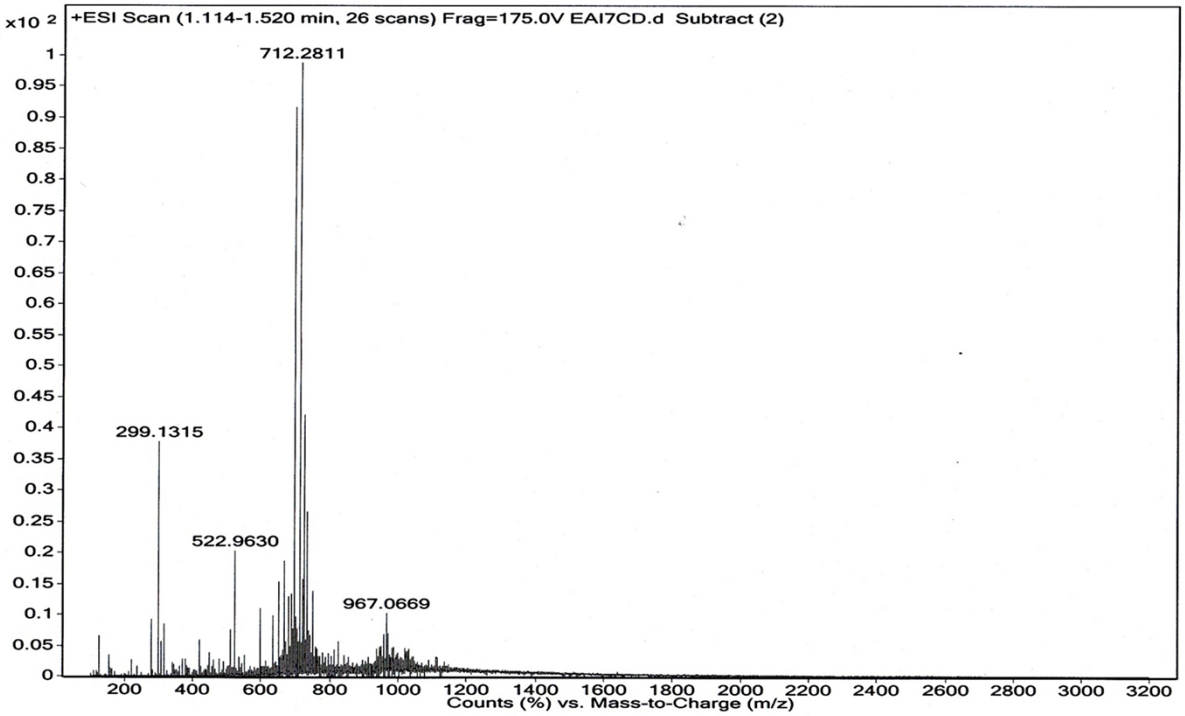
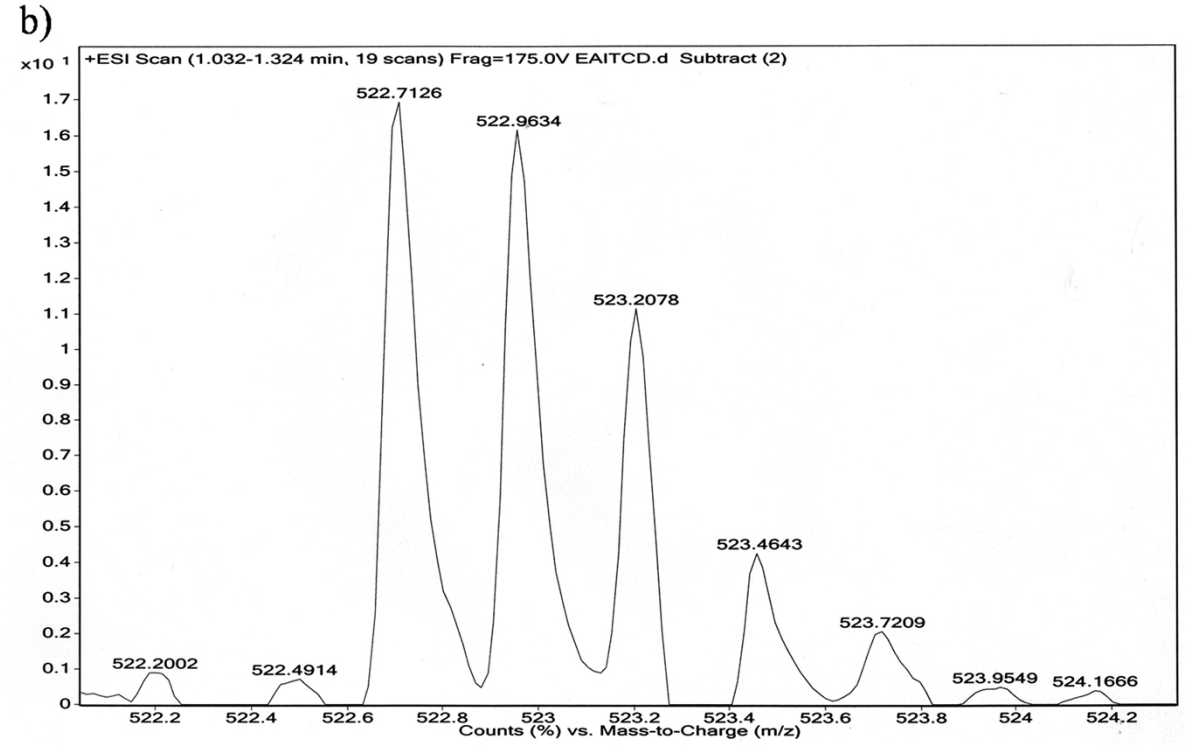


Figure S7 (a) ESI-MS of **1** in EtOH. (b)*m/z* (caculated) = 632.58 (**1**-7Br$^-$-3H$^+$ +EtOH), *m/z* (found) = 632.57 (**1**-7Br$^-$-3H$^+$ +EtOH); (c) *m/z* (caculated) = 858.45 (**1**-7Br$^-$-4H$^+$+EtOH), *m/z* (found) = 858.43 (**1**-7Br$^-$-4H$^+$+EtOH).

a)


+ESI Scan (1.114-1.520 min, 26 scans) Frag=175.0V EAI7CD.d Subtract (2)
x10 2
712.2811
299.1315
522.9630
967.0669
Counts (%) vs. Mass-to-Charge (m/z)

b)


+ESI Scan (1.032-1.324 min, 19 scans) Frag=175.0V EAITCD.d Subtract (2)
x10 1
522.7126
522.9634
523.2078
523.4643
523.7209
522.2002
522.4914
523.9549
524.1666
Counts (%) vs. Mass-to-Charge (m/z)

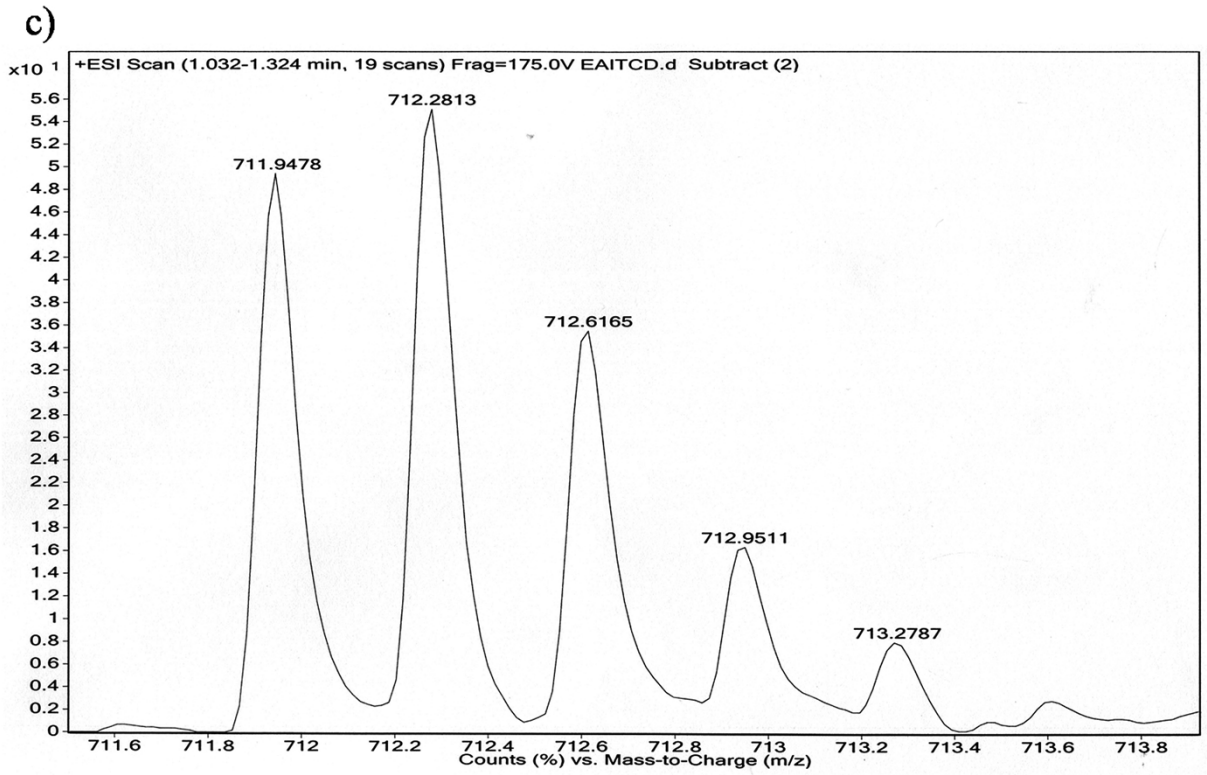


Figure S8 (a) ESI-MS of **2** in EtOH. (b) *m/z* (caculated) = 522.71 (**2**-7Br$^-$-3H$^+$), *m/z* (found) = 522.71 (**2**-7Br$^-$-3H$^+$); (c) *m/z* (caculated) = 712.29 (**2**-7Br$^-$-4H$^+$ +EtOH), *m/z* (found) = 712.28 (**2**-7Br$^-$-4H$^+$ +EtOH).

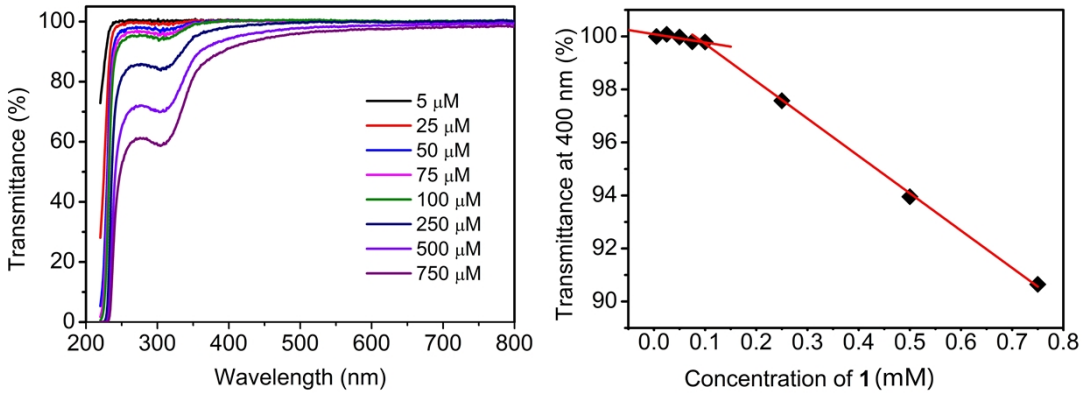


Figure S9 Optical transmittance spectra (left) of **1** and the transmittance change at λ = 400 nm (right) at various concentrations ([**1**] = 5-750 μM, pH = 7.5, Tris-HCl 0.1M, 25 °C).

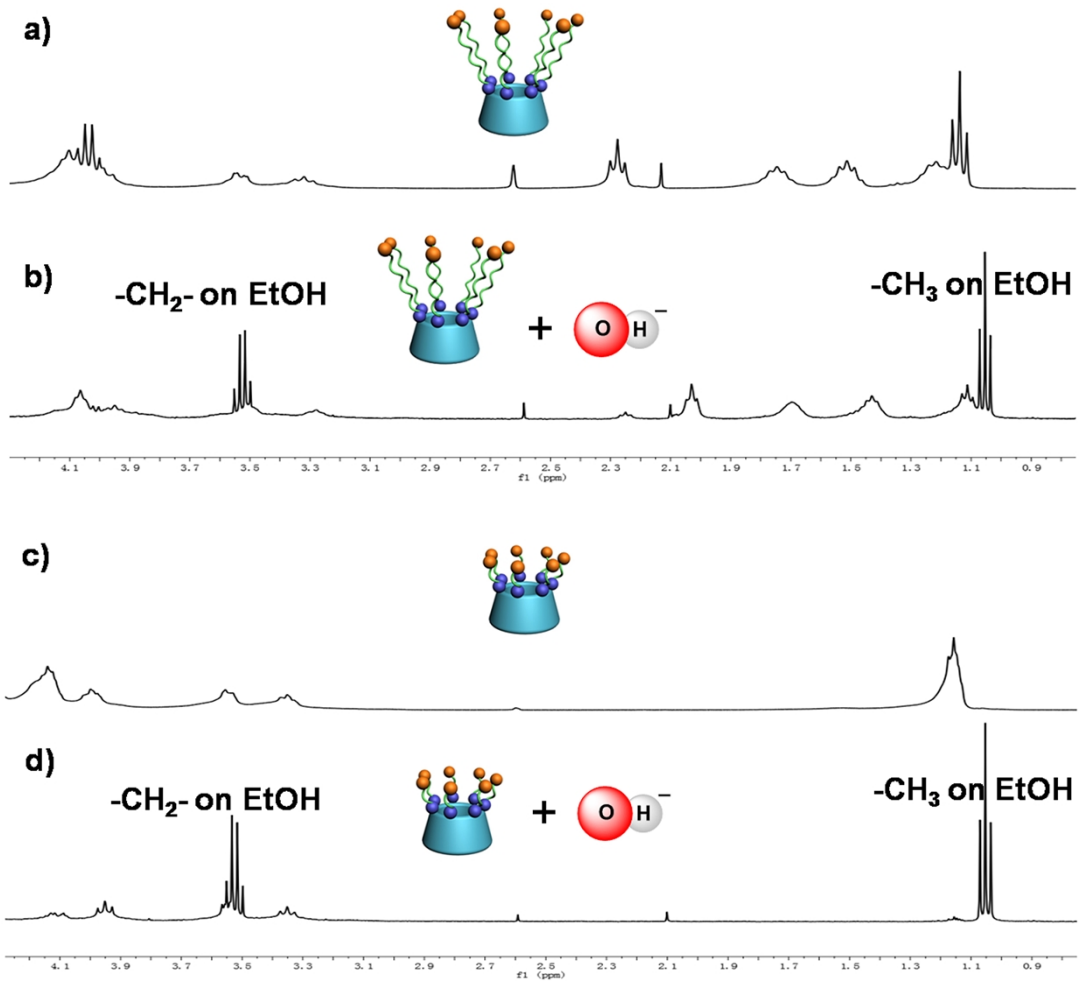


Figure S10 ^{1}H NMR spectra of **1** (a and b) and **2** (c and d) in D_2O before and after the hydrolysis induced by NaOH ([**1**]:[NaOH] = [**2**]:[NaOH] = 1:7).

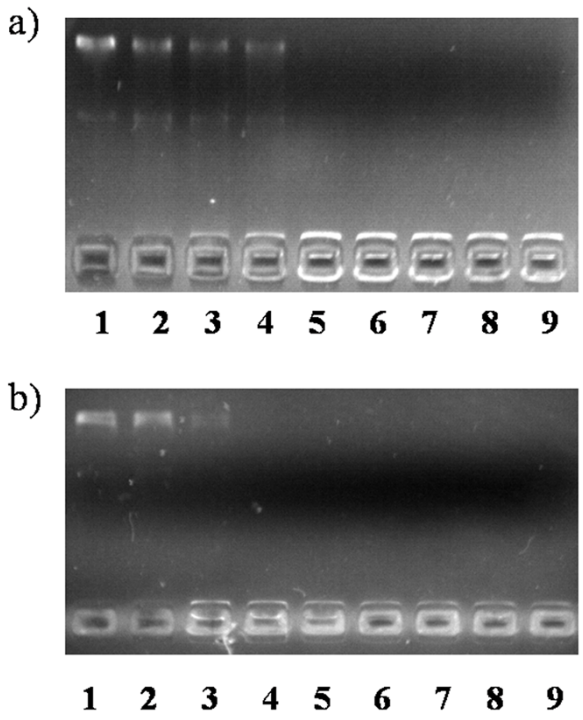


Figure S11**.** Agarose gel electrophoresis assay to investigate the DNA condensation induced by **1**(a) and **2**(b). Lane 1, DNA only (10 ng μL^{-1}); Lane 2 to 9, DNA + **1** (or **2**) (5 - 40 μM)

Table S1 Original MTT datas (OD_{490}) in the cytotoxicity assay. The holes located at the edge were filled with PBS (white background).

a) 293T

[1]/M	0	1.0×10^{-7}	1.0×10^{-6}	5.0×10^{-6}	1.0×10^{-5}	5.0×10^{-5}	1.0×10^{-4}	1.0×10^{-3}	PBS
	1	2	3	4	5	6	7	8	9	10
A	0.041	0.04	0.042	0.041	0.04	0.04	0.04	0.042	0.042	0.04
B	0.04	0.333	0.331	0.331	0.322	0.321	0.331	0.324	0.229	0.044
C	0.041	0.334	0.335	0.326	0.326	0.325	0.327	0.311	0.235	0.042
D	0.04	0.336	0.335	0.332	0.324	0.325	0.315	0.322	0.228	0.041
E	0.042	0.332	0.334	0.329	0.327	0.324	0.327	0.321	0.235	0.041
F	0.042	0.338	0.339	0.328	0.322	0.324	0.316	0.328	0.233	0.045
G	0.041	0.339	0.331	0.331	0.325	0.326	0.325	0.328	0.239	0.041
H	0.041	0.043	0.043	0.043	0.042	0.044	0.046	0.041	0.042	0.048

b) HeLa

[1]/M	0	1.0×10^{-7}	1.0×10^{-6}	5.0×10^{-6}	1.0×10^{-5}	5.0×10^{-5}	1.0×10^{-4}	1.0×10^{-3}	PBS
	1	2	3	4	5	6	7	8	9	10
A	0.042	0.042	0.042	0.041	0.042	0.041	0.041	0.041	0.041	0.041
B	0.041	0.606	0.601	0.598	0.595	0.588	0.585	0.581	0.425	0.042
C	0.043	0.607	0.602	0.599	0.593	0.587	0.586	0.584	0.426	0.043
D	0.041	0.608	0.602	0.601	0.596	0.588	0.587	0.582	0.425	0.042
E	0.041	0.605	0.603	0.598	0.594	0.591	0.584	0.583	0.426	0.041
F	0.042	0.604	0.604	0.597	0.597	0.586	0.586	0.582	0.424	0.042
G	0.043	0.604	0.607	0.602	0.594	0.589	0.589	0.583	0.423	0.043
H	0.042	0.041	0.041	0.041	0.042	0.043	0.043	0.042	0.042	0.041

Reference

S1 Vizitiu, D.; Walkinshaw, C. S.; Gorin, B. I.; Thatcher, G. R. J. *J. Org. Chem.* **1997**, *62*, 8760-8766.

S2 Guo, D. S.; Wang, K.; Wang, Y. X.; Liu, Y. *J. Am. Chem. Soc.* **2012**, *134*, 10244-10250.

S3 a) A. Schlegel, C. Largeau, P. Bigey, M. Bessodes, K. Lebozec, D. Scherman and V. Escriou. *J. Controlled Release*, **2011**, *152*, 393-401. b) H. Wang, Y. Chen, X.-Y. Li and Y. Liu. *Mol. Pharm.*, **2007**, *4*, 189-198.