Supplementary Information

Thermoresponsive Cyclodextrins with Switchable Inclusion Abilities

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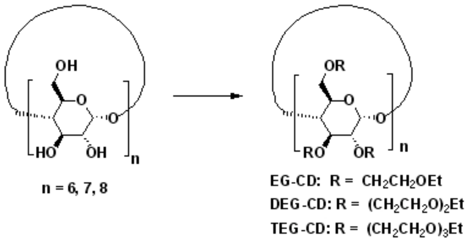
Content

Experimental Sections

Materials. Tosylated ethylene glycol monoethyl ether (EG-Ts), Tosylated diethylene glycol monoethyl ether (DEG-Ts) and tosylated triethylene glycol monoethyl ether (TEG-Ts) were synthesized according to literature method.[s1] N, N-Dimetylformamide (DMF) was distilled from CaH_2 for drying. Pure water was redistilled. Other reagents and solvents were purchased at reagent grade and used without further purification. All reactions were run under a nitrogen atmosphere. Macherey-Nagel precoated TLC plates (silica gel 60 G/UV254, 0.25 mm) were used for thin-layer chromatography (TLC) analysis. Silica gel 60 M (Macherey-Nagel, 0.04~0.063 mm, 200~300 mesh) was used as the stationary phase for column chromatography.

Instrumentation and Measurements. ^1H and ^{13}C NMR spectra were recorded on a Bruker AV 500 (^1H: 500 MHz, ^{13}C: 125 MHz) spectrometer. High resolution MALDI-TOF-MS analyses were performed on IonSpec Ultra instruments. UV/vis turbidity measurements were carried out for determination cloud points (T_c) on a PE UV/vis spectrophotometer Lambda 35 equipped with a thermostatically regulated bath. Aqueous OEG-modified CDs solutions were placed in the spectrophotometer (path length 1 cm) and heated or cooled at a rate of 0.2 $°C \cdot min^{-1}$. The absorptions of the solution at λ = 500 nm were recorded every five seconds. The T_c is determined the one at which the transmittance at λ= 500 nm had reached 50% of its initial value. Circular dichroism measurements were performed on a JASCO J-815 spectropolarimeter with a thermo-controlled 1-mm quartz cell (10 accumulations, continues scanning mode, scanning speed 100 $nm \cdot min^{-1}$, data pitch: 0.5 nm, response: 1 sec, band width: 2.0 nm).



General procedure for synthesis of OEG-modified cyclodextrin derivatives. Sodium hydride was added into a mixture of cyclodextrin and potassium iodide in dry DMF at 0 °C. After stirring for 30 minutes, tosylated oligo(ethylene glycol) monoethyl ether in DMF was dropped slowly. The reaction temperature was then allowed to rise to room temperature. After stirring for 24 h, methanol was added to terminate the unreacted sodium hydride. The solvents were evaporated *in vacuo*, and the residue was dissolved with DCM. The organic phase was washed with brine for three times, and then dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography afforded the title compounds as colorless liquids.

EG-α-CD. According to the general procedure from α-CD (0.50 g, 0.51 mmol), KI (0.77 g, 4.64 mmol), NaH (0.66 g, 27.50 mmol), EG-Ts (7.50 g, 30.70 mmol) and dry DMF (30 mL), **EG-α-CD** was yielded as colorless oil (0.50 g, 43%). ^1H NMR ($CDCl_3$): δ = 1.15-1.19 (m, 9H, CH_3), 3.29-3.32 (m, 1H, CH), 3.48-3.70 (m, 17H, CH_2+CH), 3.78-3.93 (m, 4H, CH_2), 4.03-4.06 (m, 1H, CH), 4.13-4.17 (m, 1H, CH), 5.21 (d, 1H, CH). MS: m/z calcd. for $C_{108}H_{204}O_{48}Na$ $[M+Na]^+$ 2292.34, found 2293.41.

DEG-α-CD. According to the general procedure from α-CD (1.00 g, 1.03 mmol), KI (1.54 g, 9.28 mmol), NaH (1.33 g, 55.40 mmol), DEG-Ts (13.34 g, 46.30 mmol) and dry DMF (50 mL), **DEG-α-CD** was yielded as colorless oil (2.20 g, 70%). ^1H NMR ($CDCl_3$): δ = 1.18-1.22 (m, 9H, CH_3), 3.26-3.31 (m, 1H, CH), 3.45-3.71 (m, 29H, CH_2+CH), 3.77-3.90 (m, 4H, CH_2), 3.97-4.04 (m, 1H, CH), 4.10-4.13 (m, 1H, CH), 5.14 (d, 1H, CH). HR-MS: m/z calcd. for $C_{144}H_{276}O_{66}Na$ $[M+Na]^+$ 3084.8138, found 3086.0993.

EG-β-CD. According to the general procedure from β-CD (1.00 g, 0.88 mmol), KI (1.55 g, 9.34 mmol), NaH (1.46 g, 60.80 mmol), EG-Ts (12.13 g, 49.70 mmol) and dry DMF (80 mL), **EG-β-CD** was yielded as colorless oil (0.60 g, 26%). ^1H NMR ($CDCl_3$): δ = 1.17-1.19 (m, 9H, CH_3), 3.28-3.31 (m, 1H, CH), 3.47-3.71 (m, 17H, CH_2+CH), 3.78-3.89 (m, 4H, CH_2), 4.01-4.12 (m, 2H, CH), 5.27 (d, 1H, CH). HR-MS: m/z calcd. for $C_{126}H_{238}O_{56}Na$ $[M+Na]^+$ 2670.5673, found 2671.1519.

DEG-β-CD. According to the general procedure from β-CD (1.00 g, 0.88 mmol), KI (1.54 g, 9.28 mmol), NaH (1.50 g, 62.50 mmol), DEG-Ts (16.30 g, 56.50 mmol) and dry DMF (80 mL), **DEG-β-CD** was yielded as colorless oil (0.80 g, 25%). ^1H NMR ($CDCl_3$): δ = 1.18-1.22 (m, 9H, CH_3), 3.27-3.30 (m, 1H, CH), 3.44-3.73 (m, 29H, CH_2+CH), 3.73-3.92 (m, 4H, CH_2), 3.94-4.13 (m, 2H, CH), 5.22 (d, 1H, CH). HR-MS: m/z calcd. for $C_{168}H_{322}O_{77}Na$ $[M+Na]^+$ 3595.1179, found 3596.1685.

TEG-β-CD. This compound was synthesized through two-step Williamson etherification to ensure the 100% grafting ratio. Firstly, according to the general procedure from β-CD (1.00 g, 0.88 mmol), KI (1.17 g, 7.05 mmol), NaH (1.10 g, 45.80 mmol), TEG-Ts (11.70 g, 35.20 mmol) and dry DMF (80 mL), partially TEG-modified β-CD derivative with about 70% grafting ratio was yielded (1.60 g). Then, this compound was further reacted with TEG-Ts (2.23 g, 6.71 mmol) in the presence of NaH (0.32 g, 13.30 mmol), KI (0.14 g, 0.84 mmol) and 15-crown-5 (0.45 g, 2.04 mmol) for 24 h at room temperature to afford the title compound **TEG-β-CD** (0.90 g, 23%). ^{1}H NMR ($CDCl_3$): δ = 1.19-1.22 (m, 9H, CH_3), 3.25-3.27 (m, 1H, CH), 3.40-3.70 (m, 41H, CH_2+CH), 3.73-3.86 (m, 4H, CH_2), 3.91-4.10 (m, 2H, CH), 5.20 (d, 1H, CH). HR-MS: m/z calcd. for $C_{210}H_{406}O_{98}Na$ $[M+Na]^+$ 4519.6684, found 4521.1063.

DEG-γ-CD. Similar to the general procedure from γ-CD (0.50 g, 0.39 mmol), KI (0.80 g, 4.82 mmol), NaH (1.20 g, 50.00 mmol), DEG-Ts (10.70 g, 37.10 mmol) and dry DMF (40 mL), but the reaction temperature was kept at 50 ^{o}C for 16 h. **DEG-γ-CD** was yielded as colorless liquid (0.1 g, 6%). ^{1}H NMR ($CDCl_3$): δ = 1.18-1.22 (m, 9H, CH_3), 3.27-3.30 (m, 1H, CH), 3.47-3.89 (m, 33H, CH_2+CH), 3.92-4.02 (m, 1H, CH), 4.02-4.13 (m, 1H, CH), 5.25 (d, 1H, CH). MS: m/z calcd. for $C_{192}H_{368}O_{88}Na$ $[M+Na]^+$ 4105.43, found 4109.80.

(S1) M. Ouchi, Y. Inoue, Y. Liu, S. Nagamune, S. Nakamura, K. Wada, T. Hakushi, *Bull. Chem. Soc. Jpn.* **1990**, *63*, 1260.

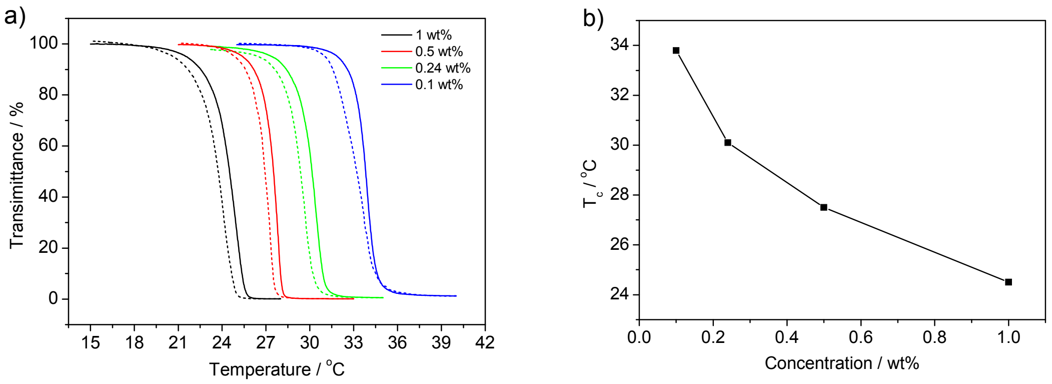


Figure S1. a) Plots of transmittance versus temperature for EG-α-CD aqueous solution at different concentrations. b) T_c dependence of EG-α-CD on solution concentrations.

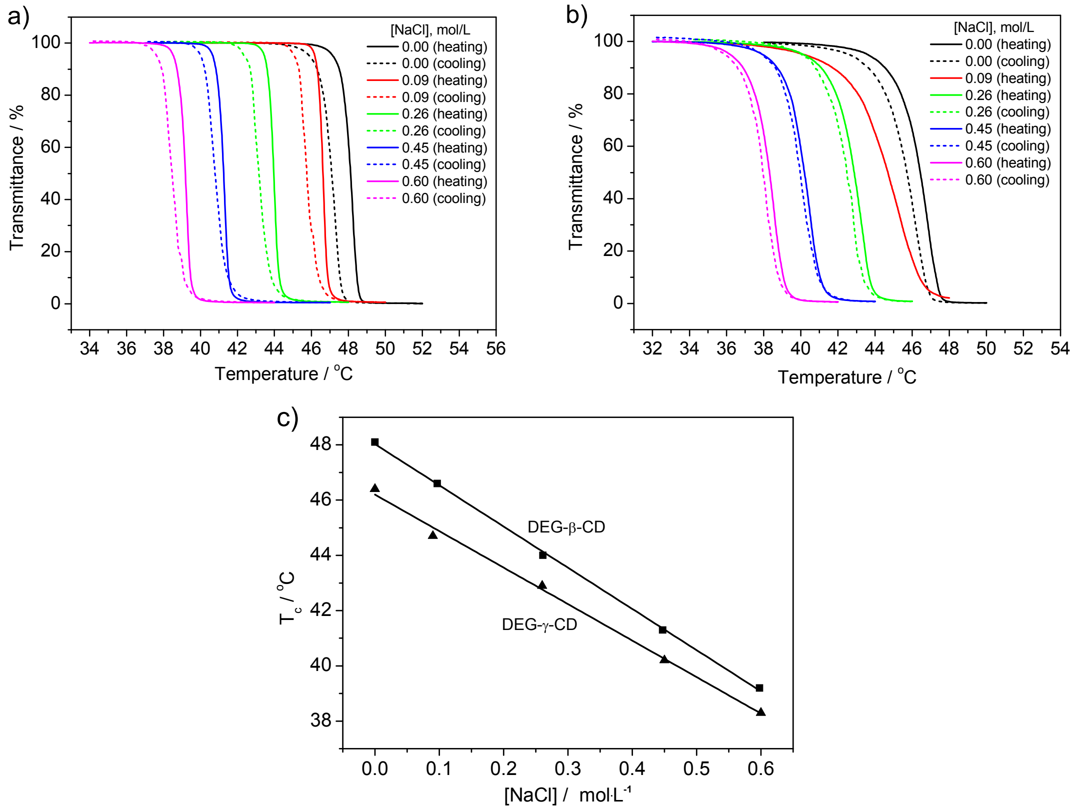


Figure S2. Plots of transmittance *vs* temperature for 0.5 wt% aqueous solution of DEG-β-CD (a) and DEG-γ-CD (b) with different NaCl concentrations. c) T_c dependence of DEG-β-CD and DEG-γ-CD on NaCl concentrations.

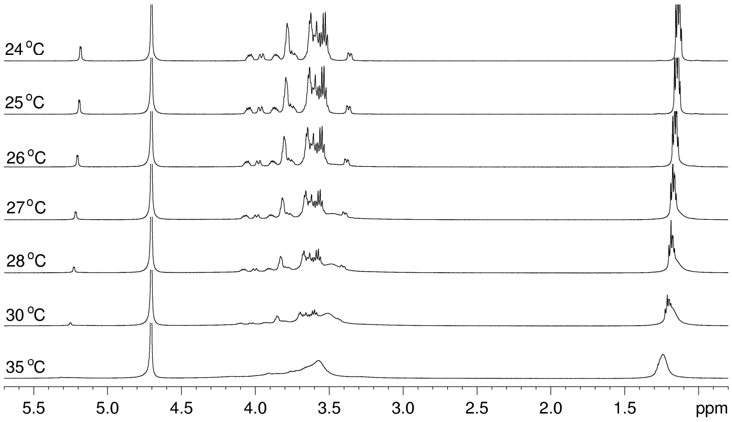


Figure S3. Temperature-varied ^{1}H NMR spectra for EG-α-CD in D_2O (0.5 wt%).

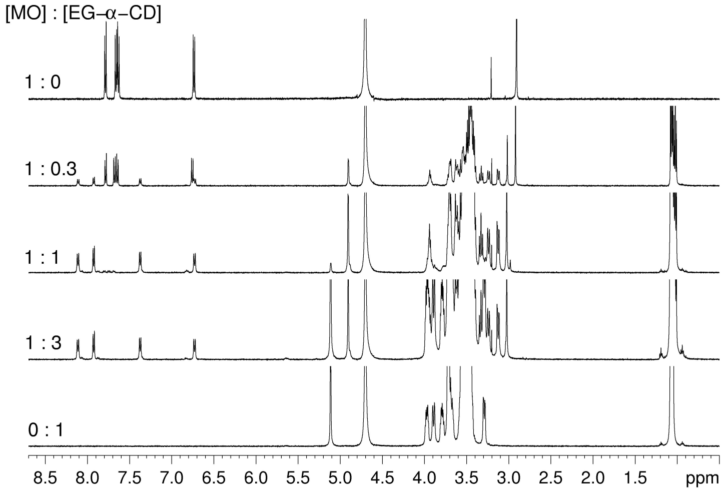


Figure S4. ^{1}H NMR spectra of MO, EG-α-CD and their mixture with different ratios (1:0.3 to 1:3) in D_2O.

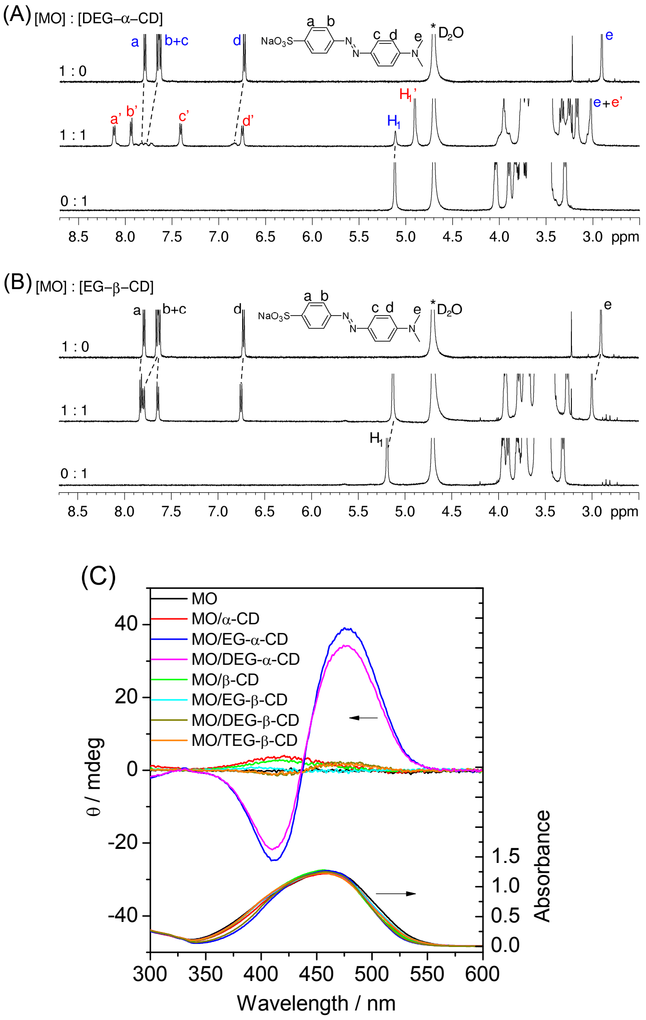


Figure S5. ^{1}H NMR spectra of MO, DEG-α-CD (A) or EG-β-CD (B), and their mixture with equivalent molar ratio in D_2O, respectively; CD and UV spectra of MO and equivalent mixture of MO with α-CD, EG-α-CD, DEG-α-CD, β-CD, EG-β-CD, DEG-β-CD, and TEG-β-CD, respectively (C). Signals a, b, c, d, e, and H_1 correspond to free MO and DEG-α-CD or EG-β-CD, and a′, b′, c′, d′, e′ and H_1′ to complexed state, respectively.

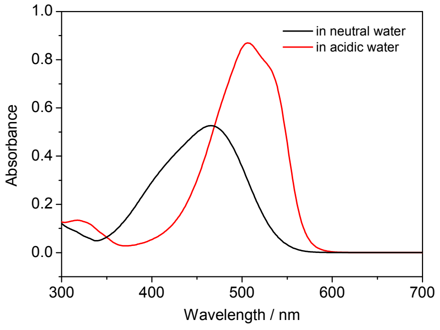


Figure S6. UV/vis spectra for 0.02 mM MO in neutral and acidic (2 mM HCl) solutions.

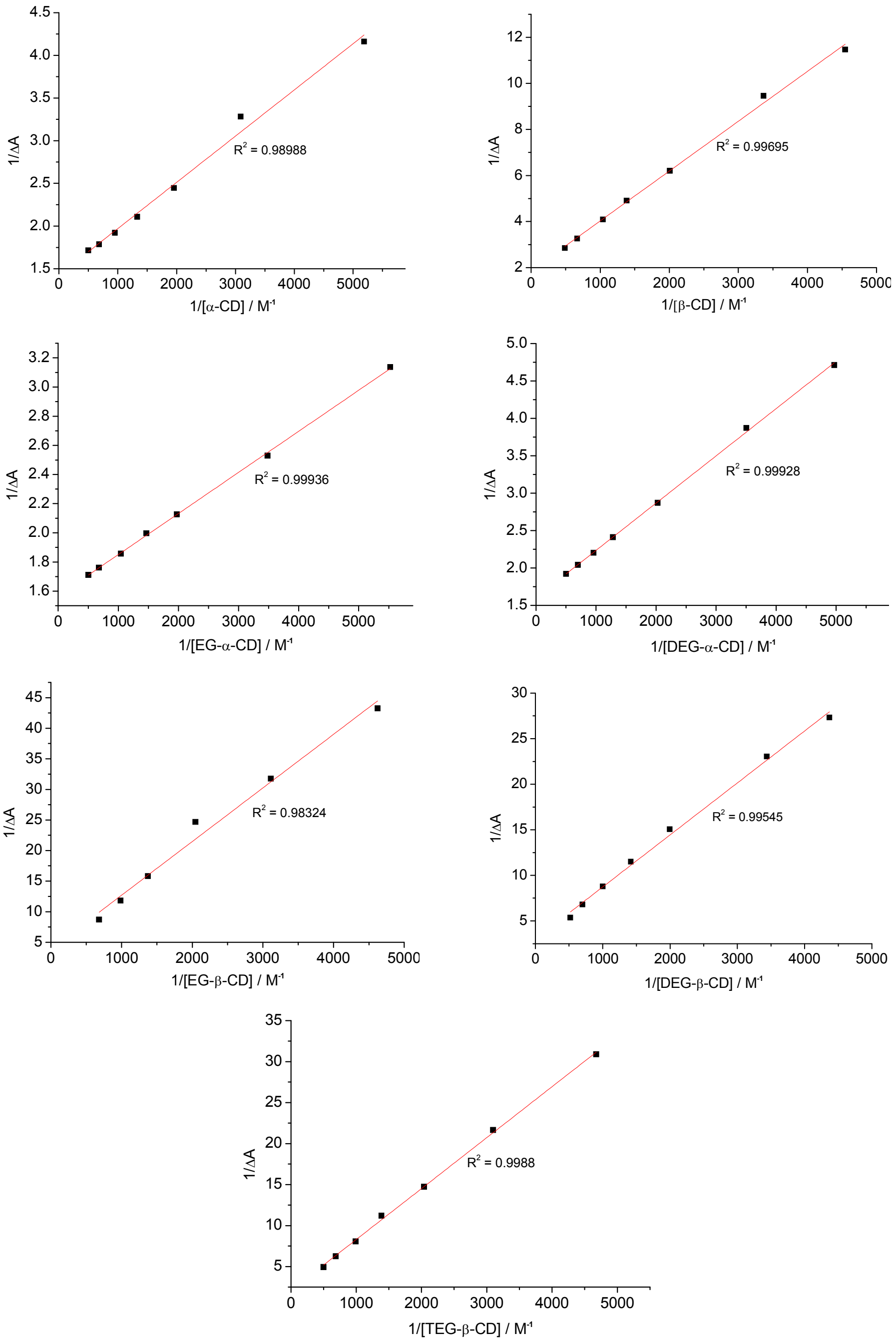


Figure S7. Benesi-Hildebrand plots obtained from the UV/vis titrations of native and OEG-modified CDs with MO guest at room temperature. ΔA represents the change in absorbance of MO at 506 nm. [MO] = 0.02 mM, [HCl] = 2 mM.

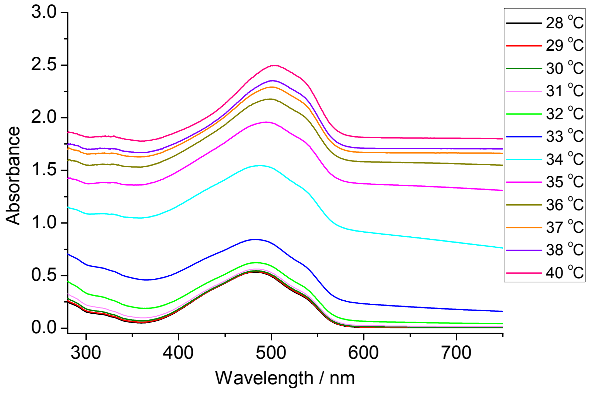


Figure S8. Temperature-varied UV/vis spectra of MO acidic solution in the presence of 0.47 mM EG-α-CD. [MO] = 0.02 mM, [HCl] = 2 mM.

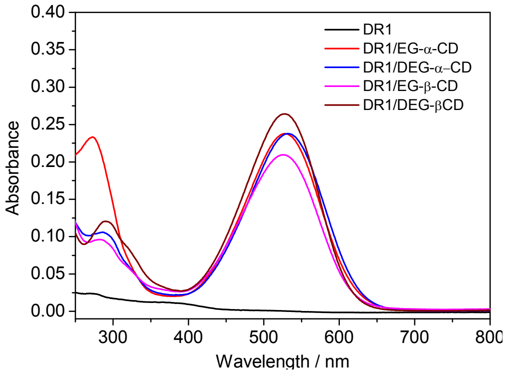


Figure S9. UV/vis spectra of saturated DR1 in neutral water before or after addition of 0.5 wt% OEG-modified CDs at room temperature.

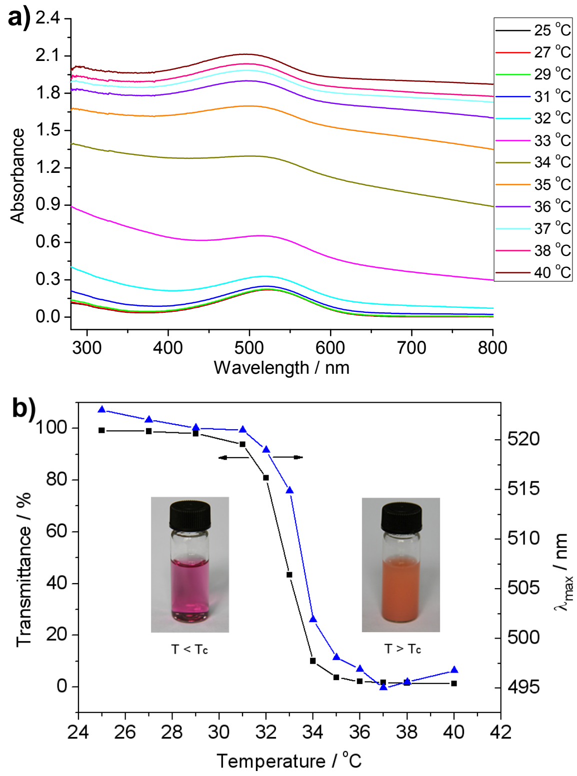


Figure S10. a) Temperature-varied UV/vis spectra of neutral disperse red 1 (DR1) solution in the presence of 0.467 mM EG-α-CD. b) Plot of transmittance and λ_{max} (DR1) versus temperature for DR1/EG-α-CD solution. Photographs of DR1/EG-α-CD neutral solution below and above T_c were included.

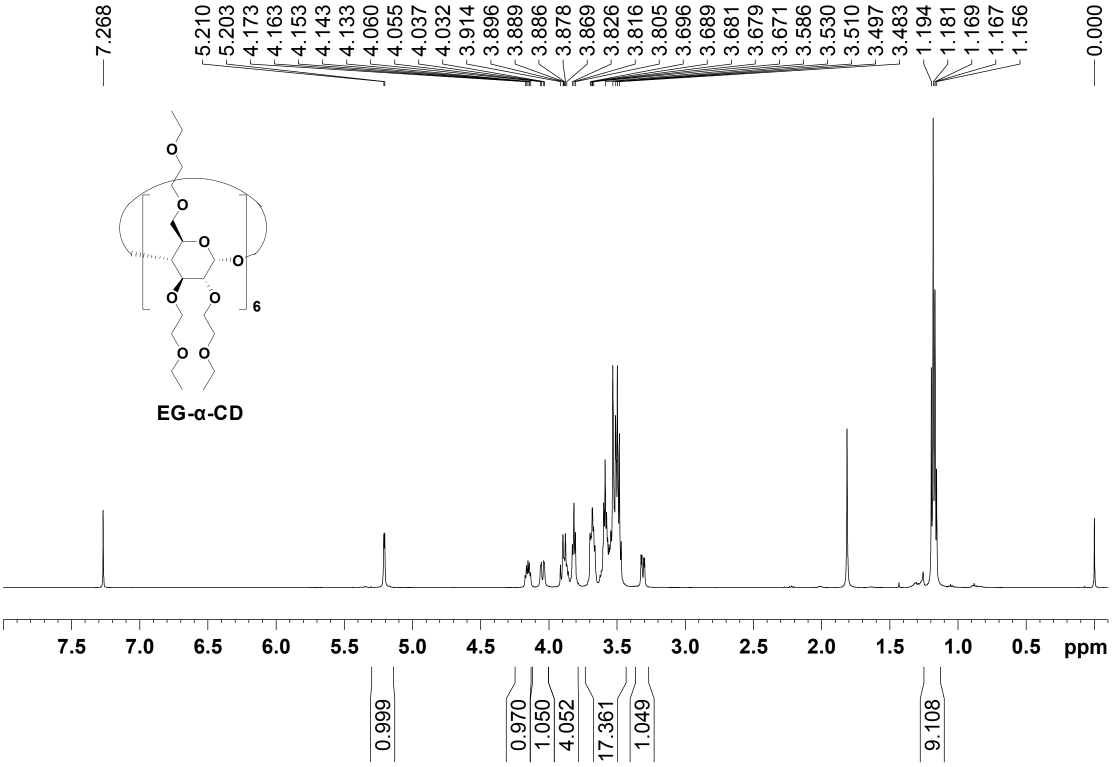


Figure S11. ^{1}H NMR spectrum of EG-α-CD in $CDCl_3$.

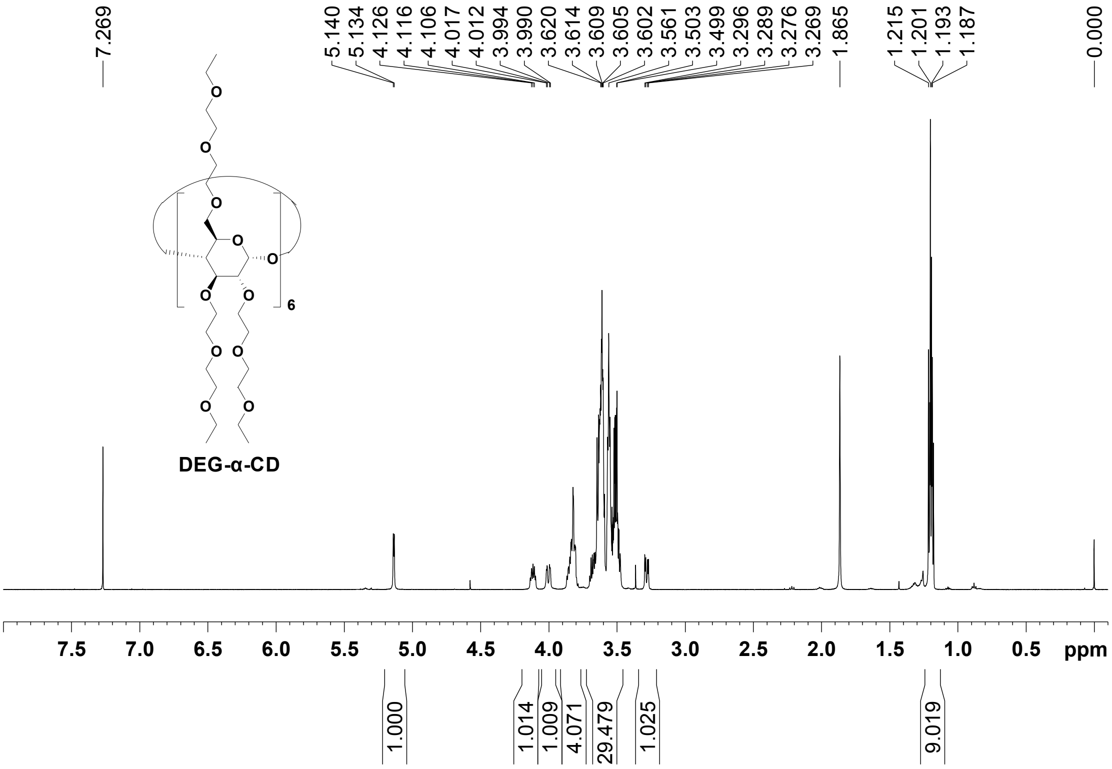


Figure S12. ^{1}H NMR spectrum of DEG-α-CD in $CDCl_3$.

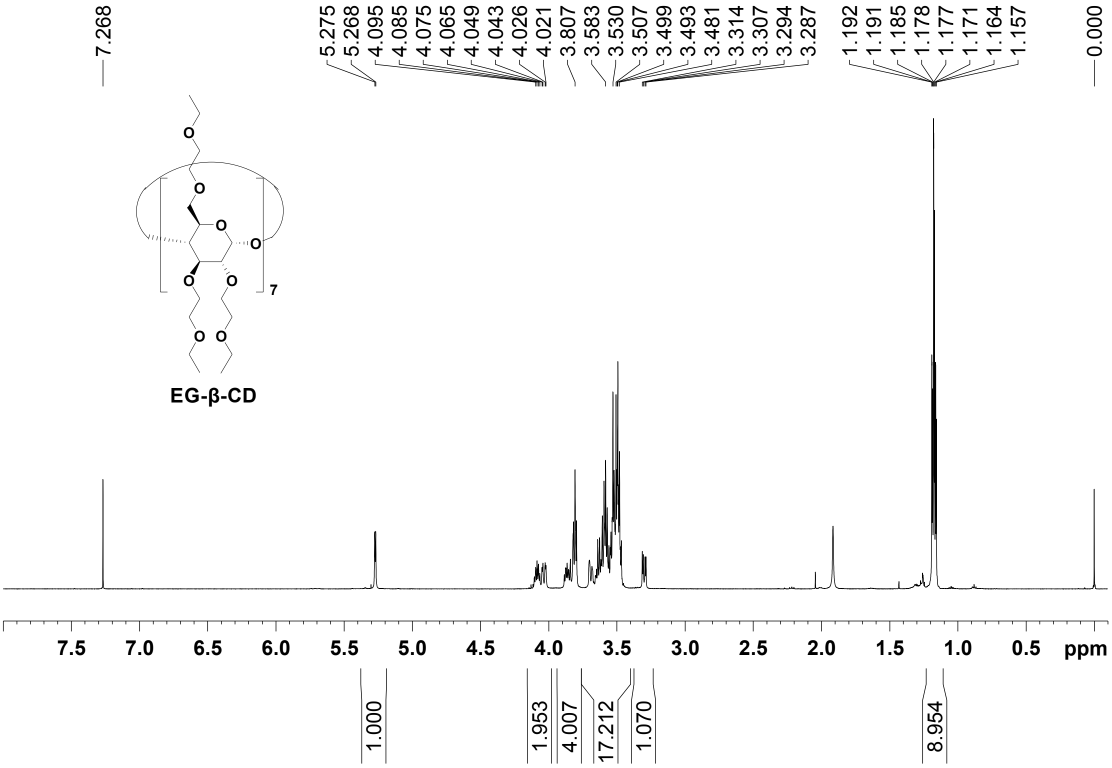


Figure S13. ^{1}H NMR spectrum of EG-β-CD in $CDCl_3$.

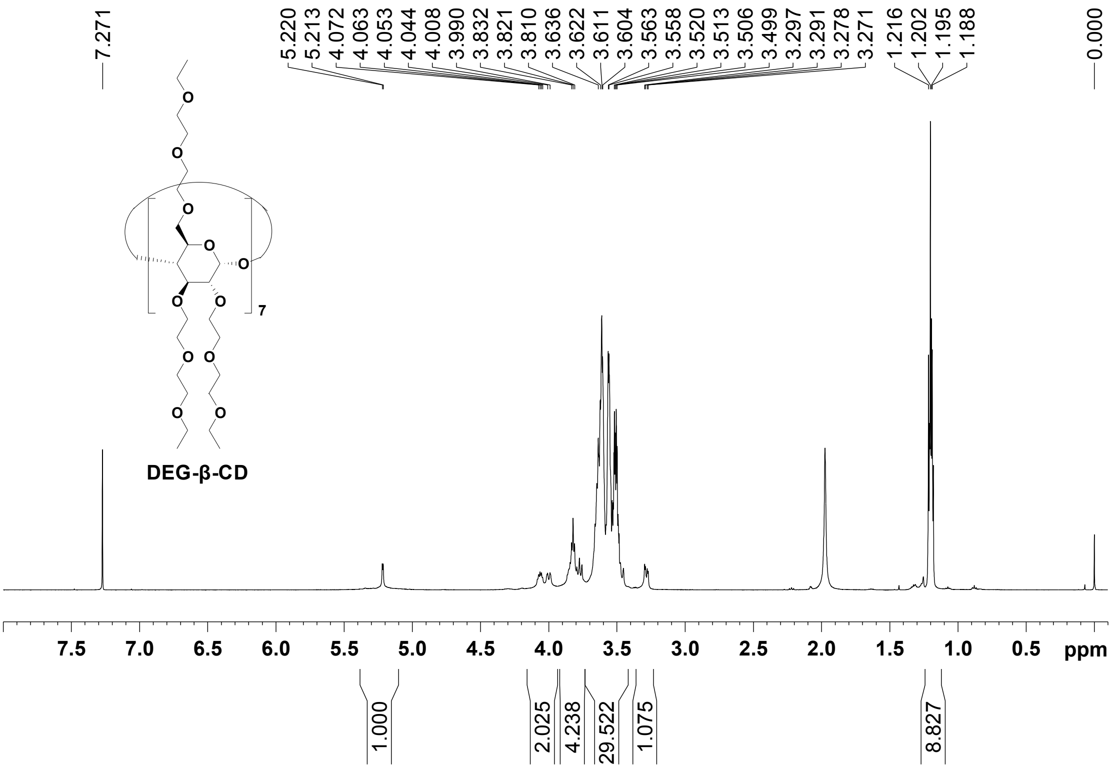


Figure S14. ^{1}H NMR spectrum of DEG-β-CD in $CDCl_3$.

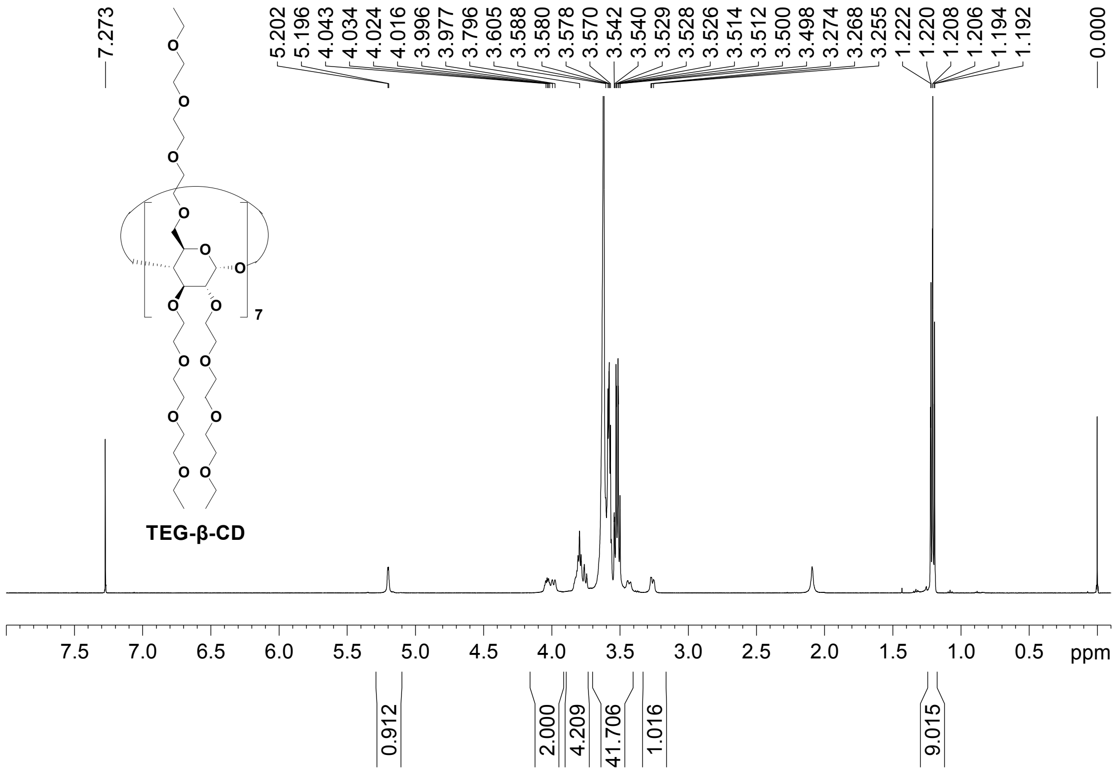


Figure S15. ^{1}H NMR spectrum of TEG-β-CD in $CDCl_3$.

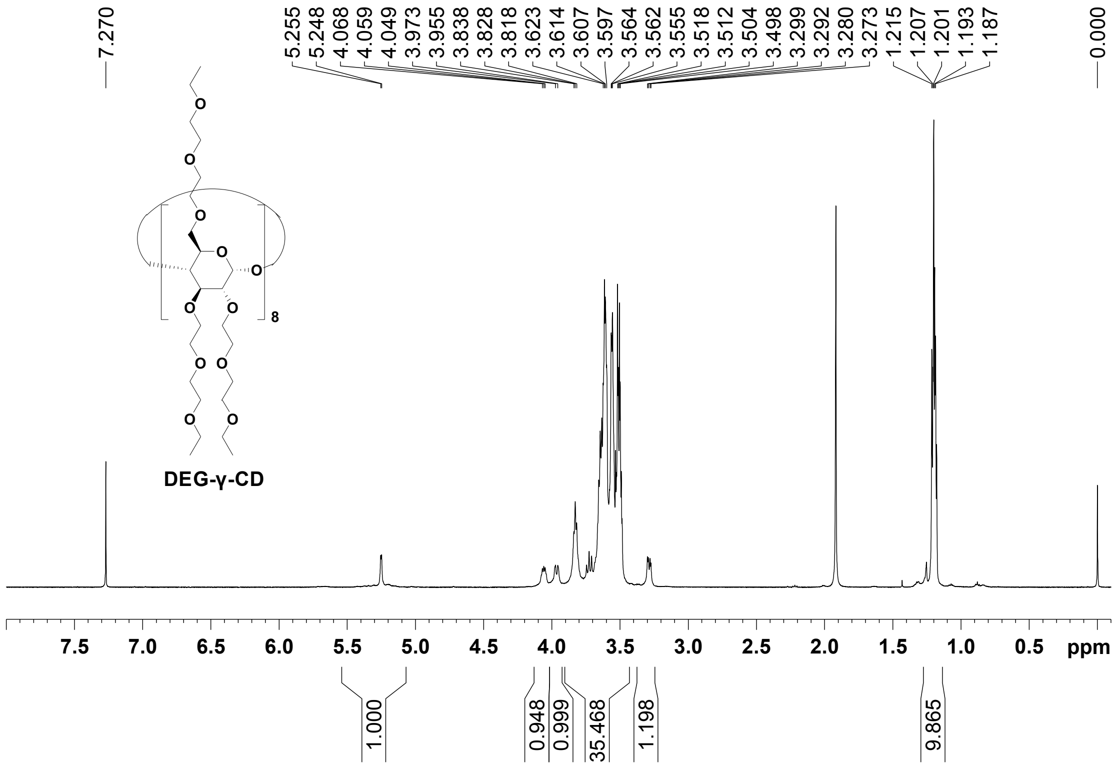


Figure S16. ^{1}H NMR spectrum of DEG-γ-CD in $CDCl_3$.