Supplementary Information

One-pot synthesis of water-soluble β-cyclodextrin-based polyrotaxanes in a homogeneous water system and its use in bio-applications

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Synthesis and characterization of Mono-(6-azido-6-desoxy)-β-cyclodextrin (β-CD-N_3)

Mono-6-deoxy-6-(p-tolylsulfonyl)-β-cyclodextrin (β-CD-OTs) was synthesized using the following reported procedure,[1] β-CD (50.00 g, 44.05 mmol) was suspended in 400 mL of deionized water and NaOH solution (34.20 mL 4 M) was added dropwise slowly over 1 h. Then a TsCl acetonitrile solution (25 mL, 2 mol/L) was added dropwise over 1.5 h as a white solid gradually appeared. The mixture was filtered to remove the insoluble solid after stirring for 5 h, the filtrate was collected and neutralized with HCl water solution (7.6%) to a pH of 6 producing a white solid. The mixture was placed at 4 °C overnight, then filtered and the white solid was collected, washed five times with acetone and finally washed with ether. The filter cake was dried under vacuum at room temperature for 24 h to obtain the final product, β-CD-OTs. Yield: 16.5 %, 9.37 g, mp 178.3~179.1 °C (yield 11%, mp 179 °C), ^{1}H NMR (DMSO-d_6, δ, ppm): 2.43 (s, 3H, CH_3), 3.20-3.66 (br overlapped, 42H, H-2,3,4,5,6), 4.17-4.52 (m, 6H, OH-6), 4.77-4.84 (m, 7H, H-1), 5.64-5.84 (br overlapped, 14H, OH-2,3), 7.43 (d, J = 8 Hz, 2H, H of benzene ring close to -SO_3-), 7.75 (d, J = 8 Hz, 2H, H of benzene ring close to -CH_3).

Our NMR results confirmed that β-CD-N_3 was prepared as described previously.[2] The β-CD-OTs obtained from the above reaction (9.00 g, 6.98 mmol) was suspended in 320 mL of deionized water with sodium azide (2.26 g, 34.8 mmol) and the reaction system was heated to 80 ºC and stirred for 16 h. Then TLC (isopropyl

alcohol：ethyl acetate：water：ammonia water =7：7：5：4) was used to check whether the reaction was complete. Finally, the solution was concentrated under reduced pressure, and the residue was precipitated with 450 mL of acetone to obtain a white solid. The white solid was then collected by centrifugation and dried under vacuum. Yield: 7.16 g, 88.5 % [yield 85% in the literature 2], mp 208.9~209.6 °C [209 °C (dec) in the literature 3]. ^{1}HNMR (DMSO-d_6, δ, ppm): 3.31-3.39 (br overlapped, 14H, H -2,4), 3.47-3.63 (br overlapped, 28H, H-3,5,6), 4.48 (br, 6H, OH-6), 4.83 (s, 7H, H-1), 5.65-5.87 (br overlapped, 14H, OH-2,3).

Synthesis and characterization of dialk-PPG

The synthesis of dialk-PPG followed the reference [4]. Propiolic acid (0.45 mL 7.3 mmol) was added to a solution of N,N'-dicyclohexylcarbodiimide (DCC) (1.55 g, 7.51 mmol) in dichloromethane (DCM, 60 mL) and the reaction system was stirred for 1 h at -20 ºC. A solution of PPG (Mn = 2000, 6.81 g, 3.41 mmol) in DCM (20 mL) was then added to the reaction system, dropwise over 35 min. The resulting mixture was stirred at -5~5 ºC for 1.5 h and allowed to warm slowly to room temperature. After stirring for 16 h, the precipitate was removed. Then the filtrate was concentrated under reduced pressure, and the product was isolated by column chromatography with an eluent of CH_2Cl_2/CH_3OH (99/1, v:v). Finally, the dialk-PPG was obtained as an oil-like liquid (6.24 g, 87.2 %). ^{1}H NMR (500 MHz, DMSO-d_6, δ, ppm) (Figure S2) δ: 1.13 (d, J=5, 3H, -CH_3), 3.39-3.42 (m, 1H, -CH-), 3.46-3.59 (m, 2H, -CH_2-).

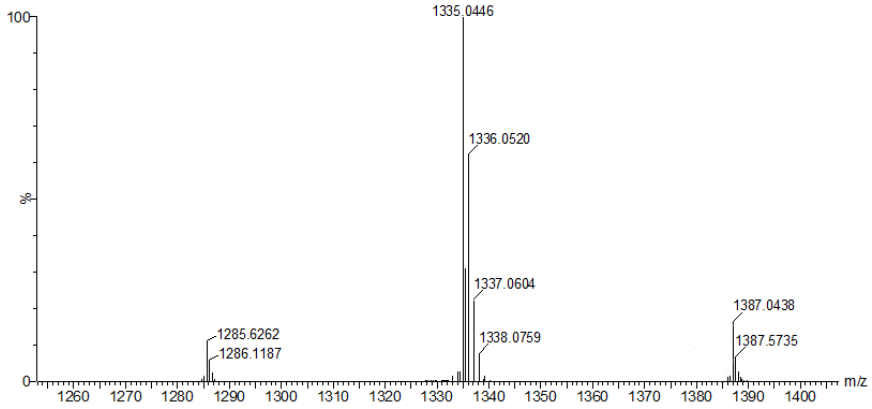

Figure S1. The high resolution mass spectrometric of β-Cyclodextrin-$(COOH)_2$.

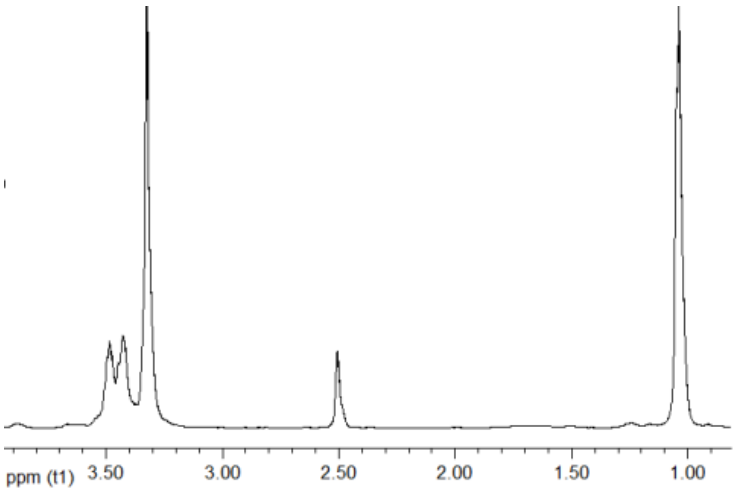

Figure S2. The ^{1}H NMR spectrum of dialk-PPG in DMSO-d_6.

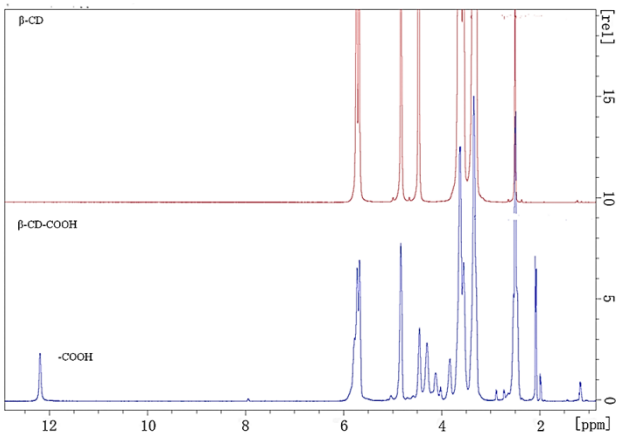

Figure S3. ^{1}H NMR spectra of β-CD-$(COOH)_2$ and β-CD in DMSO-d_6.

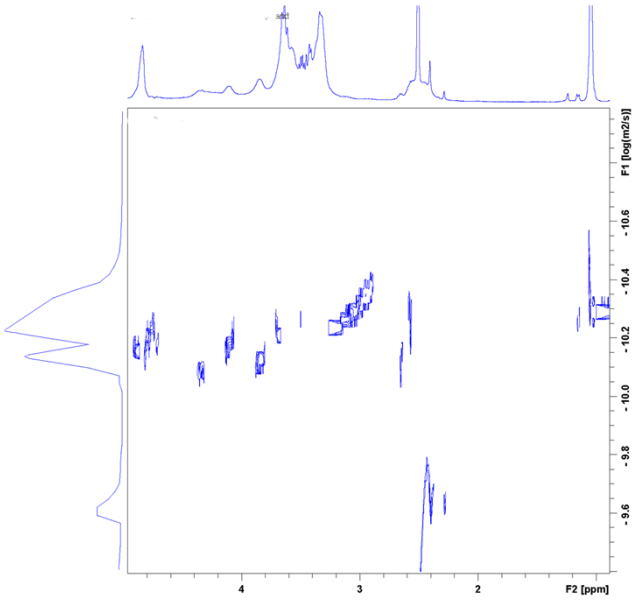

Figure S4. 2D DOSY spectrum of the pseudo-polyrotaxane in DMSO-d_6.

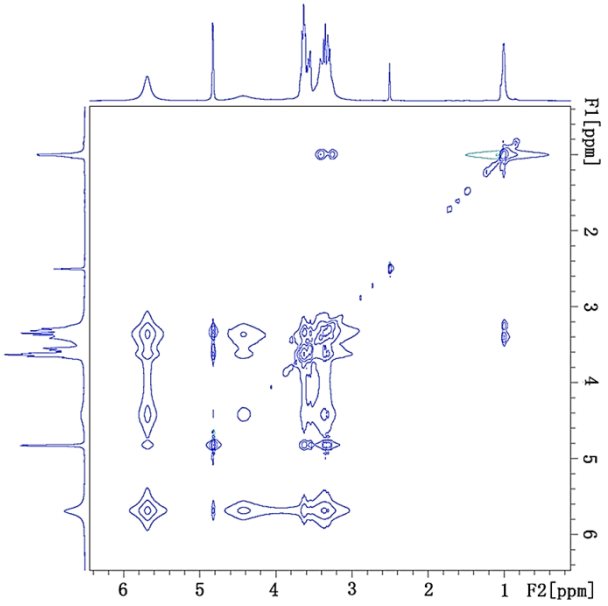

Figure S5. 2D NOESY spectrum of the β-CD-$(COOH)_2$ and dialk-PPG physical blend in DMSO-d_6.

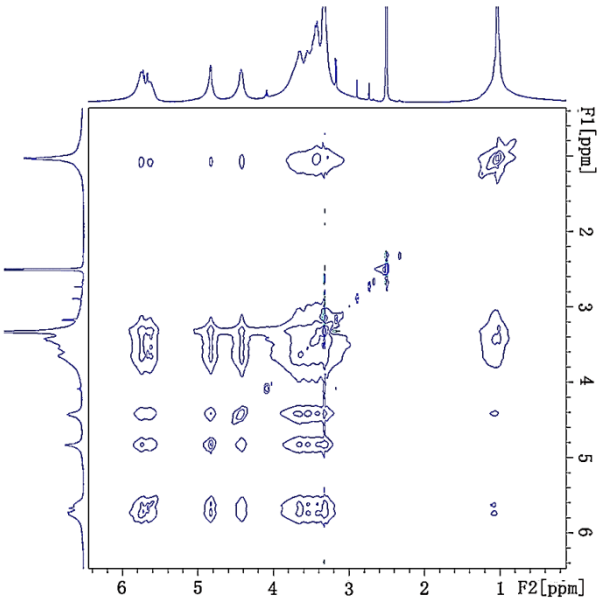

Figure S6. 2D NOESY spectrum of the PR in DMSO-d_6.

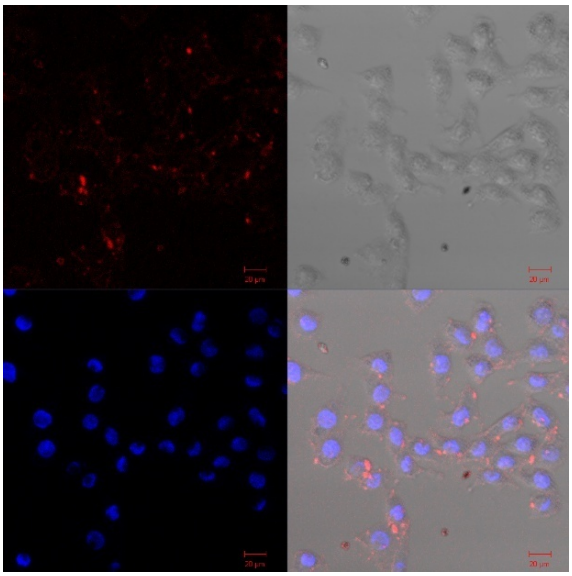

Figure S7. Typical CLSM image of SH-SY5Y cells incubated with rhodamin-labeled PR for 4 h at 4 ºC.

Reference

[1] R. C. Petter, J. S. Salek, C. T. Sikorski, G. Kumaravel, and F. T. Lin, *J. Am. Chem. SOC.,* 1990, **112**, 3860–3868.

[2] S. Amajjahe, S. Choi, M. Munteanu, and H. Ritter, *Angew. Chem. Int. Ed.,* 2008, **47**, 3435–3437.

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[4] S. Yu, Y. Zhang, X. Wang, X. Zhen, Z. Zhang, W. Wu, and X. Jiang, *Angew. Chem. Int. Ed.,* 2013, **52**, 7272–7277.