New Journal of Chemistry

Supporting Information

Thermal Responsiveness and Binding Affinity of Cucurbit[7]uril Terminal Poly(*N*-isopropylacrylamide)

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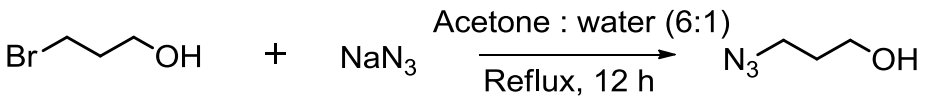
Materials

CB[7], 3,3'-(octane-1,8-diyl)-bis-(1-ethyl-imidazolium) dibromide (C_8bim) and CuAAC catalyst (THPTM·CuCl) were synthesized following literature procedures.[1-4] 3-Bromo-1-propanol, 2-chloropropionyl chloride, *N*-isopropyl acrylamide (NIPAM), tris[2-(dimethylamino)ethyl]amine (Me_6TREN), 3-bromo-1-propyne, 1,8-dibromooctane, 4,4'-dipyridyl, L-phenylalanine, hydroxymethylferrocene, (ferrocenylmethyl)trimethyl ammonium iodide and 1-adamantanamine hydrochloride were purchased from J&K Scientific. 1-Ethylimidazole was received from Strem Chemical Inc.. Spermine tetrahydrochloride and 1,6-diaminohexane dihydrochloride were received from TCI. Sodium azide and CuCl were obtained from Sinopharm Chemical Reagent Co., Ltd. NIPAM was recrystallized twice from benzene/hexane prior to use. CuCl was washed with acetic acid and methanol, desiccated under vacuum to obtain white purified compound before use. All other chemicals were used without further purification.

Instruments

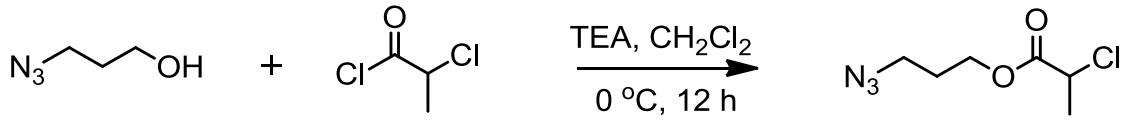
NMR tests were conducted by using a Bruker Avance 400 NMR spectrometer at 298 K. Mass spectrometry was performed on Agilent 6520 accurate mass Q-TOF. GPC experiments were carried out at 40 ^{o}C using a Waters 515 liquid chromatograph (Milford, MA) equipped with three Styragel columns (HR-3, HR-4, and HR-6) and a refractive-index detector. THF was used as the mobile phase (1.0 mL/min), and the system was calibrated with narrow-disperse polystyrene standards. Cloud points were measured on Persee TU1901 ultraviolet spectrophotometer (Beijing, China). ITC experiments were performed on MicroCal iTC200 at 298 K.

Synthesis of 3-azido-1-propanol



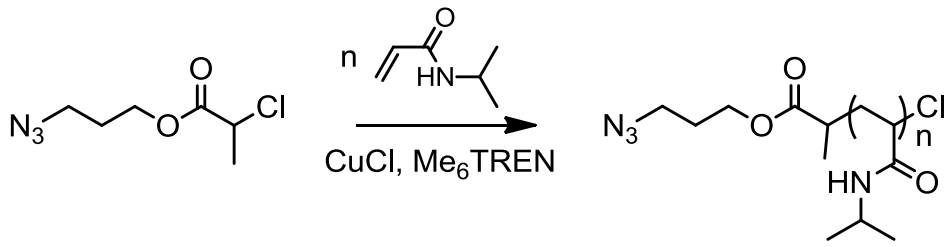
Sodium azide (2.8 g, 43.0 mmol) was added to a solution of 3-bromo-1-propanol (2.8 g, 20 mmol) in 30 mL acetone and 15 mL deionized water, and the solution was heated to 80 ^{o}C to reflux for 12 h. Acetone was removed through rotate evaporation and the rest of the solution was washed twice with 30 mL of diethyl ether. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo to afford the product (1.627 g, 80.0%). ^{1}H NMR (400 MHz, $CDCl_3$): δ=3.74 (t, J = 6.0 Hz, 2H), 3.45 (t, J = 6.6 Hz, 2H), 2.26 (s, 1H), 1.83 (p, J = 6.3 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ=59.93, 48.50, 31.44. HRMS: $[M\text{-}N_2+H^+]^+$ calculated for C_3H_8NO: 74.0606, found: 74.0595.

Synthesis of 3-azidopropyl 2-chloropropanoate



A solution of acryloyl chloride (675 μL, 6.86 mmol) in 15 mL of CH_2Cl_2 was added dropwise to a solution of 3-azido-1-propanol (0.461 g, 4.56 mmol) and trimethylamine (950 μL, 6.85 mmol) in 20 mL of CH_2Cl_2 at 0 ^{o}C, and the resulting solution slowly recovered to room temperature and reacted for 12 h. The solution was washed with saturated $NaHCO_3$ solution, dried over Na_2SO_4, filtered, concentrated in vacuo. Purification by flash chromatography on a short pack of silica gel eluting with petroleum ether and ethyl acetate 19:1 afforded 3-azidopropyl 2-chloropropanoate (0.553g, 63.3%). ^{1}H NMR (400 MHz, $CDCl_3$): δ=4.41 (q, J = 6.9 Hz, 1H), 4.34-4.20 (m, 2H), 3.43 (t, J = 6.6 Hz, 2H), 1.96 (p, J = 6.4 Hz, 2H), 1.70 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ=169.97, 62.80, 52.34, 47.97, 27.99, 21.39. HRMS: $[M\text{-}N_2+H^+]^+$ calculated for $C_6H_{11}ClNO_2$: 164.0178, 166.0449, found: 164.0475, 166.0567.

Typical synthesis procedure of azido terminal PNIPAM (N_3-PNIPAM)



The synthesis procedure of N_3-PNIPAM with target degree of polymerization of 150 was used as a typical example. NIPAM (15.00 g, 132.6 mmol) was dissolved in 30 mL 2-propanol, degassed under vacuum and purged with nitrogen for three cycles at -78 ℃. CuCl (87.5 mg, 0.884 mmol) was added under nitrogen atmosphere. Me_6TREN (226 μL, 0.884 mmol) was added *via* a nitrogen-purged syringe, and the solution was stirred for 30 min at room temperature to allow the formation of the CuCl/Me_6TREN complex. 3-Azidopropyl 2-chloropropanoate (169 mg, 0.884mmol) was then added using a syringe to begin the polymerization. The reaction was carried out at room temperature under nitrogen atmosphere for 24 h, and concentrated to 5 mL after the reaction. CuCl/Me_6TREN complex was removed by flash chromatography on a short pack of silica gel eluting with CH_2Cl_2. Unreacted monomer can be removed through dialysis with a MWCO 500 semi-permeable membrane in pure water for 3 days. N_3-PNIPAM was obtained as a white solid through freeze-drying the solution.

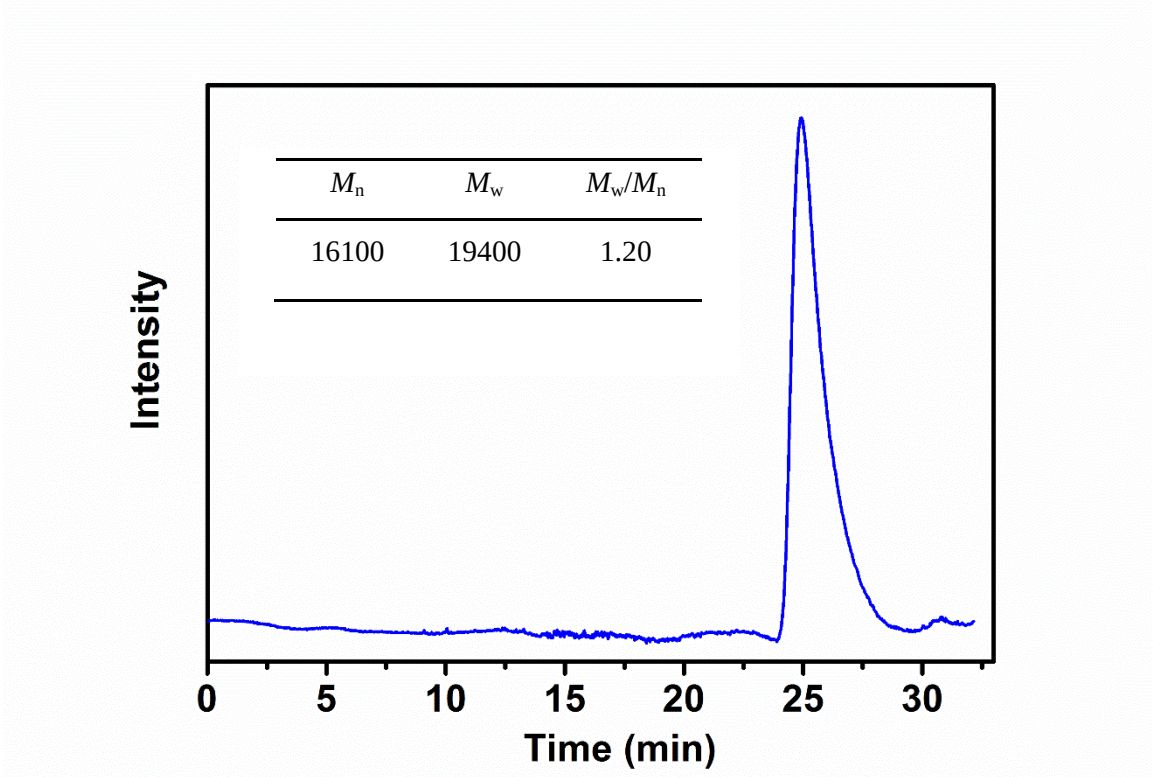


Figure S-1 Gel permeation chromatograms of N_3-PNIPAM-1.

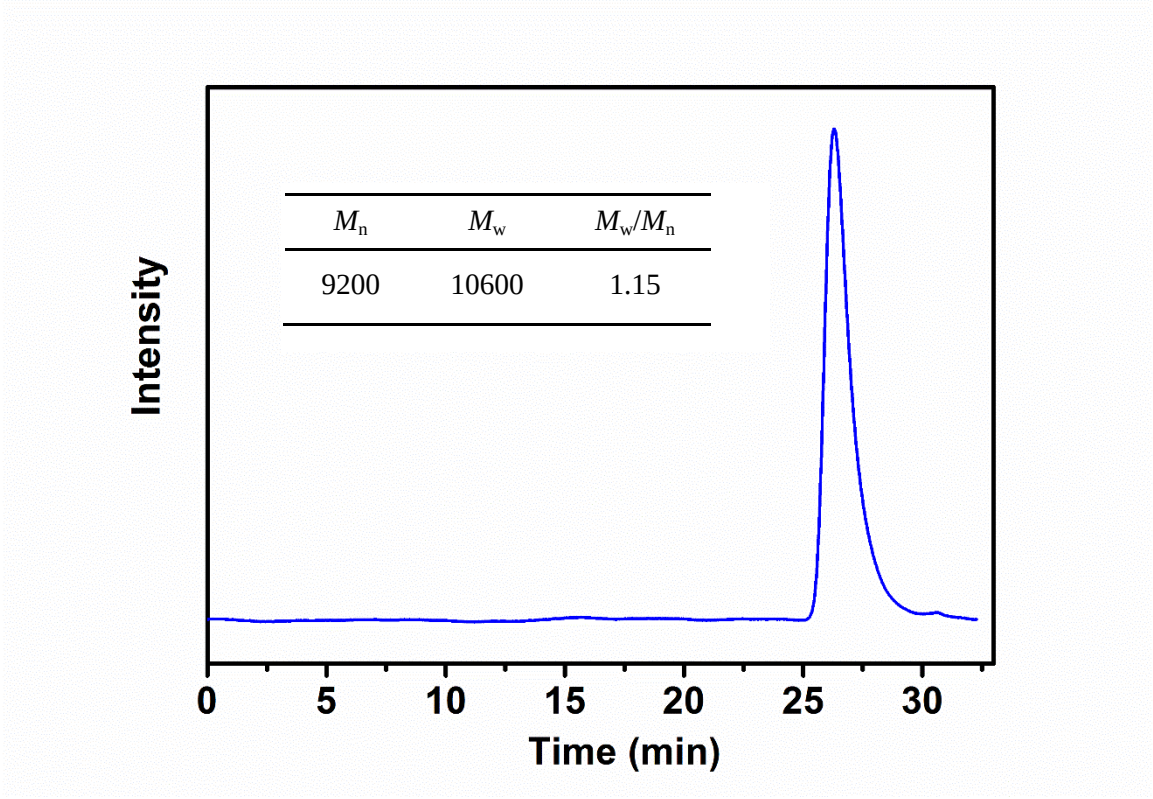


Figure S-2 Gel permeation chromatograms of N_3-PNIPAM-2.

Synthesis of monopropargylated CB[7]

Monohydroxy CB[7] (HOCB[7]) was synthesized and obtained as a host-guest complex with C_8bim following literature procedure. C_8bim⊣HOCB[7] (0.326 g, 0.193 mmol) was dispersed in 5 mL anhydrous DMF, then 15 mL anhydrous DMSO was slowly added and the suspension could be dissolved under stirring. NaH (0.35 g, 14.6 mmol) was added under nitrogen atmosphere and the mixture was stirred for 2 h. Then 3-bromo-1-propyne (80% in toluene, 2.5 mL, 16.8 mmol) was added after the solution cooled down to 0 ℃. The solution slowly recovered to room temperature and reacted for 5 h. Monopropargylated C_8bim⊂CB[7] can be obtained with firstly precipitated with 150 mL methanol and then washed with 3 × 50 mL methanol. HRMS: $[C_8\text{bim}⊣\text{HOCB[7]-2Br}^-]^{2+}$ calculated for $C_{60}H_{74}N_{32}O_{15}^{2+}$: 741.3005, 741.8022, found: 741.1472, 741.6467.

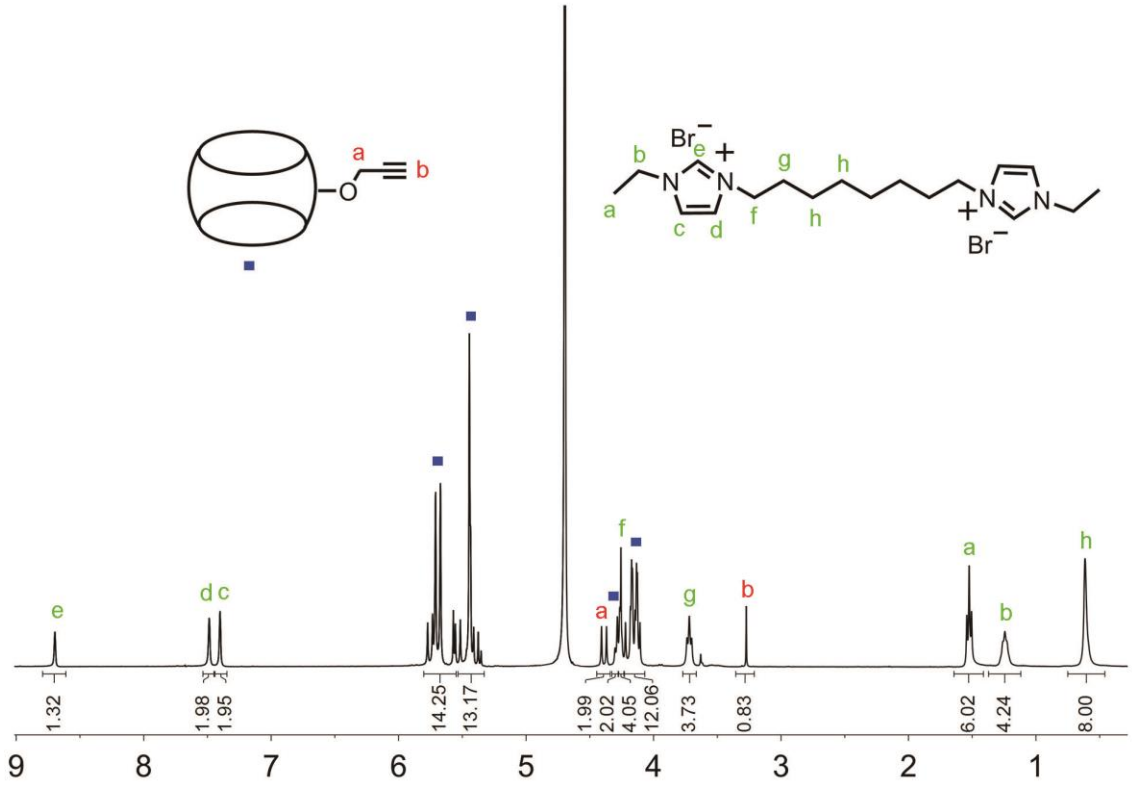
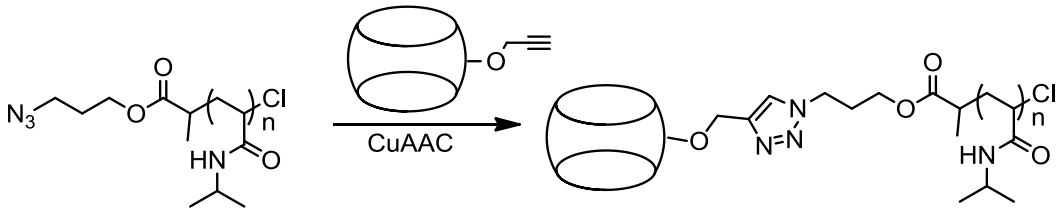


Figure S-3 ^{1}H NMR spectrum of monopropargylated C_8bim CB[7] in D_2O.

Typical synthesis procedure of CB[7] terminal PNIPAM (CB[7]-PNIPAM)



Monopropargylated C_8bim CB[7] (0.1545g, 0.0834 mmol) and N_3-PNIPAM (0.832 g, 0.0693 mmol) were dissolved in 15 mL deionized water. The solution was degassed under vacuum and purged with nitrogen for three cycles. THPTM CuCl (0.7 mg, 1.39 μmol) was added under nitrogen atmosphere. The solution was stirred at room temperature for 36 h. Unreacted monopropargylated C_8bim CB[7] and THPTM CuCl can be removed through dialysis with a MWCO 500 semi-permeable membrane in pure water for 3 days. The mixture of N_3-PNIPAM and C_8bim CB[7]-PNIPAM was obtained through freeze-drying the solution. Purification by flash chromatography on a short pack of silica gel eluting with dichloromethane and methanol 5:1 afforded C_8bim CB[7]-PNIPAM. C_8bim can be removed through dialysis with a MWCO 500

semi-permeable membrane in 0.2% CB[7] solution for 3 days and in pure water for another 3 days. The target product CB[7] terminal PNIPAM (CB[7]-PNIPAM) was obtained as a white solid through freeze-drying the solution.

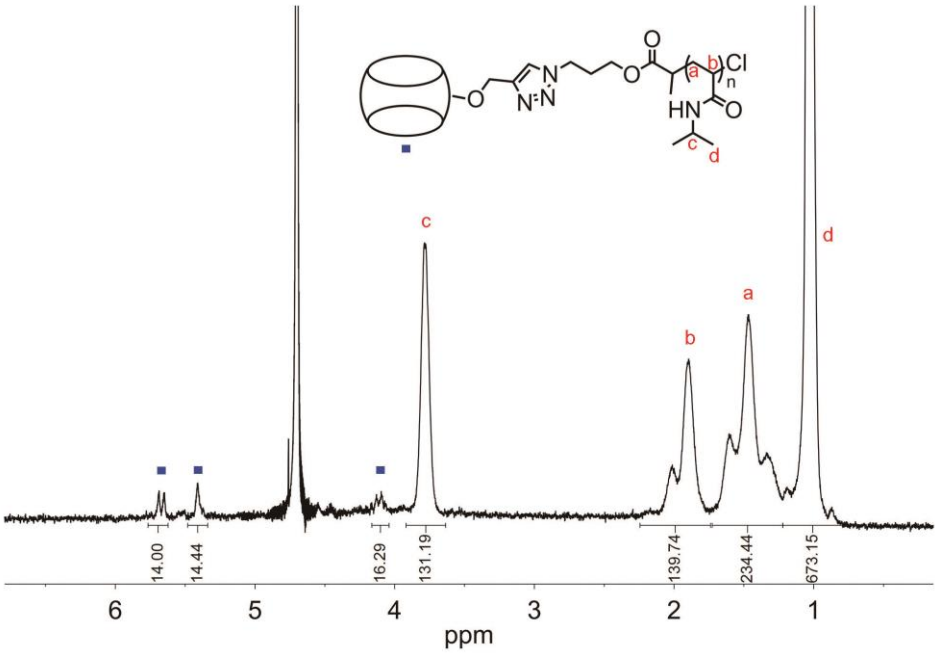


Figure S-4 ^{1}H NMR spectrum of CB[7]-PNIPAM-1 in D_2O (blue squares represent the signal of [7]).

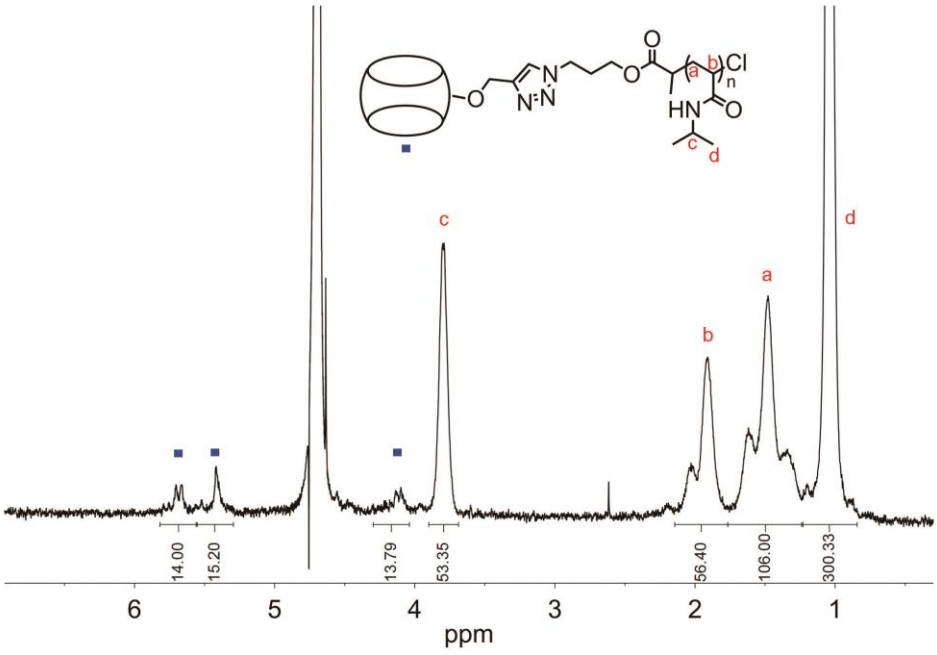


Figure S-5 ^{1}H NMR spectrum of CB[7]-PNIPAM-2 in D_2O (blue squares represent the signal of [7]).

Isothermal titration calariemetry (ITC) experiments

In ITC experiments, solution of guest molecules were used as titrant with the concentration of 1 mM to titrate 0.1 mM CB[7]-PNIPAM-1. The spinning speed of the needle is set as 600 rpm and all the experiments were conducted at 298 K in pure water. All the data were fitted with 1:1 binding model.

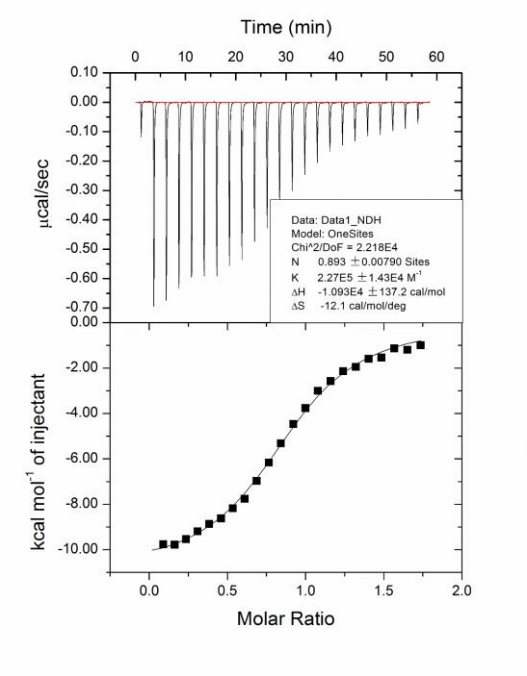


Figure S-6 ITC plots of CB[7]-PNIPAM-1 titrated with L-phenylalanine.

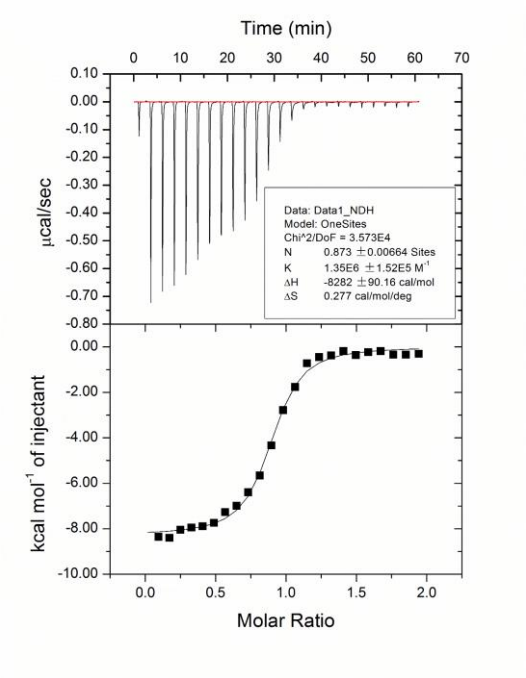


Figure S-7 ITC plots of CB[7]-PNIPAM-1 titrated with dimethyl viologen dichloride.

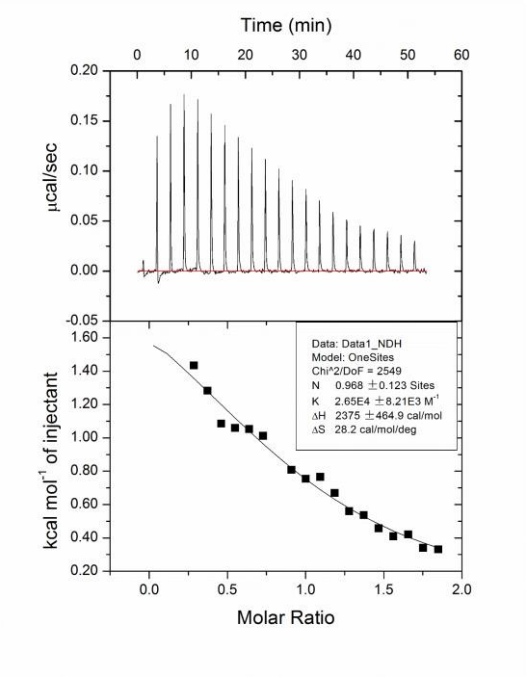


Figure S-8 ITC plots of CB[7]-PNIPAM-1 titrated with spermine (compete with 10 mM L-phenylalanine).

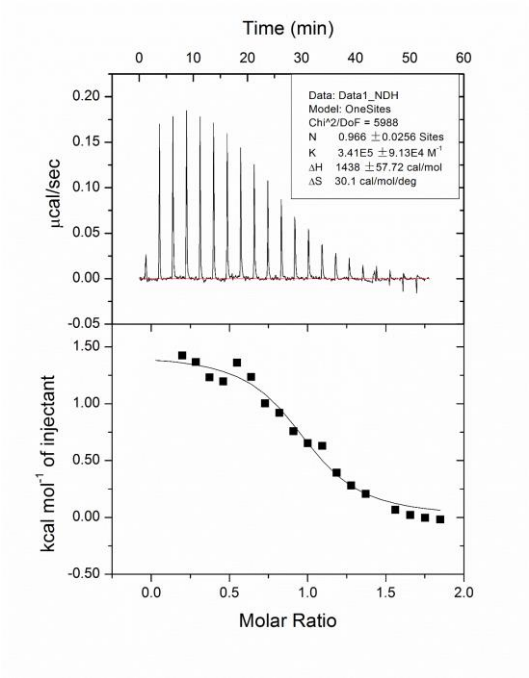


Figure S-9 ITC plots of CB[7]-PNIPAM-1 titrated with 1,6-diaminohexane dihydrochloride (compete with 10 mM L-phenylalanine).

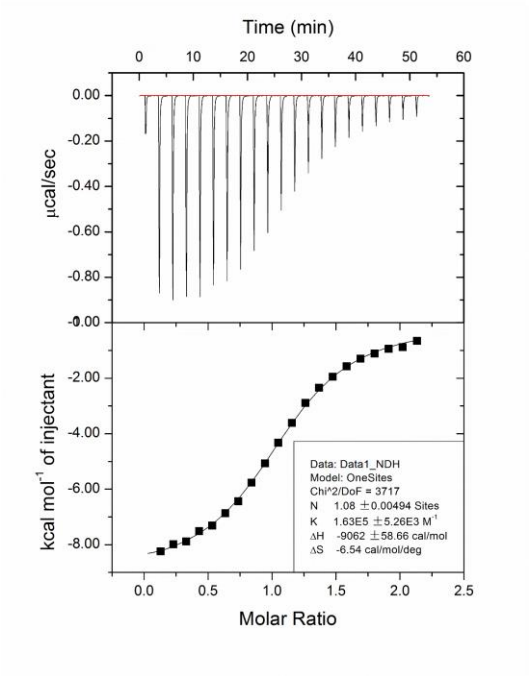


Figure S-10 ITC plots of CB[7]-PNIPAM-1 titrated with hydroxymethylferrocene (compete with 10 mM L-phenylalanine).

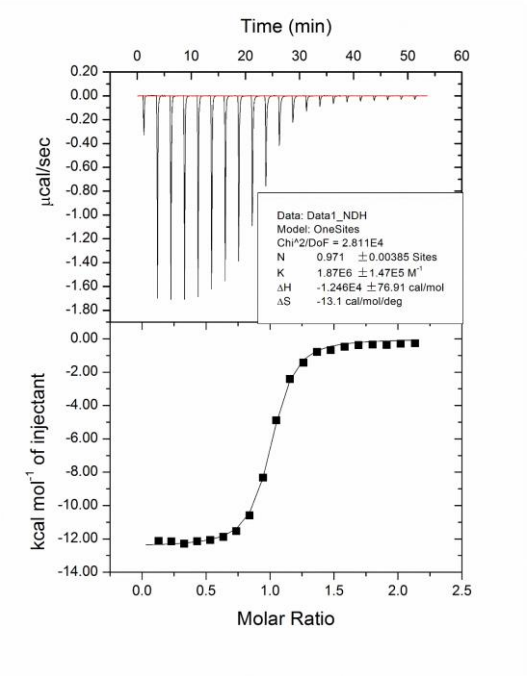


Figure S-11 ITC plots of CB[7]-PNIPAM-1 titrated with (ferrocenylmethyl)trimethylammonium iodide (compete with 10 mM dimethyl viologen dichloride).

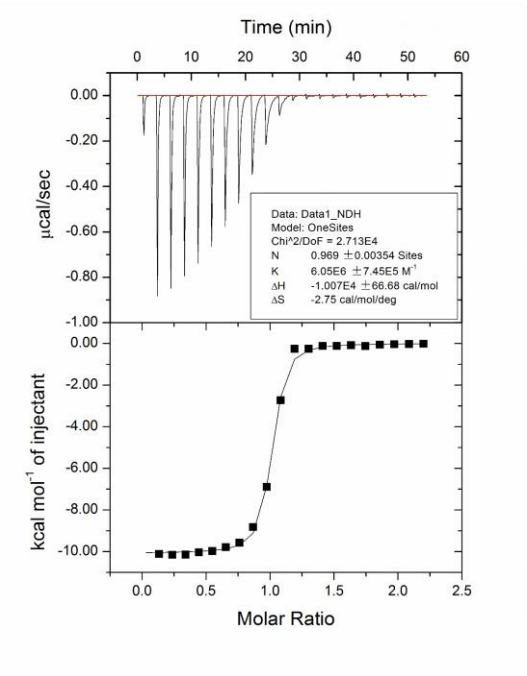


Figure S-12 ITC plots of CB[7]-PNIPAM-1 titrated with 1-adnmantanamine hydrochloride (compete with 10 mM dimethyl viologen dichloride).

References

1. J. Kim, I.-S. Jung, S.-Y. Kim, E. Lee, J.-K. Kang, S. Sakamoto, K. Yamaguchi and K. Kim, *J. Am. Chem. Soc.*, 2000, **122**, 540-541.
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