SUPPLEMENTARY INFORMATION

Supramolecular Glycopolymers with Thermo-Responsive Self-Assembly and Lectin Binding

Nese Cakir[1,2], Gurkan Hizal[2], Remzi Becer[1*]

[1]School of Engineering and Materials Science, Queen Mary University of London, Mile End Road, E1 4NS London, United Kingdom

[2]Department of Polymer Science and Technology, Istanbul Technical University, 34469 Maslak, Istanbul, Turkey

Corresponding author: r.becer@qmul.ac.uk

Content:

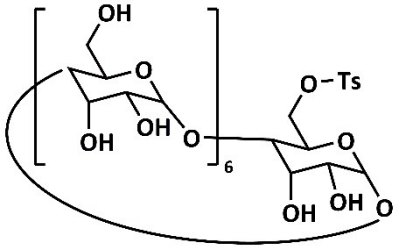
A. Experimental procedures:

A.1. Chemicals.

β-Cyclodextrin (β-CD; Sigma-Aldrich, 97%) was recrystallized twice from water and dried in a vacuum oven at 100 °C for two days before use. 2,2' -azobis(isobutyronitrile) (AIBN; Fluka, 99%) was purified by recrystallization twice from methanol. *N*-isopropylacrylamide (NIPAAm; Sigma-Aldrich, ≥99%) was recrystallized from hexane and *N,N*-Dimethylacrylamide (DMAAm; Sigma-Aldrich, 99%) was passed over a short column of basic alumina prior to use. Copper (I) Bromide (CuBr; Sigma-Aldrich, 98%) was washed sequentially with acetic acid and ethanol and dried under vacuum. H_2SO_4-silica catalyst was prepared according to the literature procedure[1]. The RAFT agent, 2-(((dodecylthio)carbonothioyl)thio)propan-2-yl pentanoate, kindly provided by Lubrizol. Sodium methoxide (CH_3ONa; Sigma-Aldrich, 25 wt. % in methanol), triphenylphosphine (Ph_3P; Sigma-Aldrich, ≥95.0%), *N*-bromosuccinimide (NBS, Sigma-Aldrich, 99%), *p*-toluenesulfonyl chloride (TsCl; Sigma-Aldrich, ≥99%), sodium azide (NaN_3; Sigma-Aldrich, ≥99.5%), propargyl alcohol (Sigma-Aldrich, 99%), triethylamine (Et_3N; Acros, 99%), acryloyl chloride (Sigma-Aldrich, 97%), Concanavalin A (Con A; Sigma-Aldrich), tris[2-(dimethylamino)ethyl]amine (Me_6TREN; Sigma-Aldrich, 97%), Methyl α-D-mannopyranoside (Sigma-Aldrich, ≥99%), and D-(+)-mannose (Sigma-Aldrich, ≥99%),) were used as received. All chemicals were used as received unless stated otherwise. All solvents used were of analytical grade, except DMSO and dioxane. Distilled water from Ultrapure was used throughout this work.

A.2. Synthesis of Monoazide functional Cyclodextrin.[2]

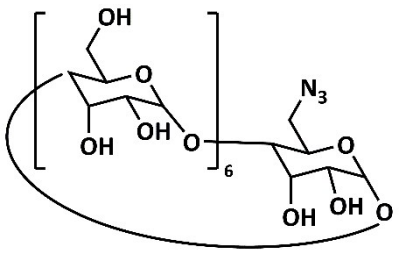
A.2.1. Synthesis of Mono-6-deoxy-6-(p-tolylsulfonyl)-β-cyclodextrin (β-CD-OTs).



Based on a literature procedure, in a 500 mL round bottom flask *β*-cyclodextrin (20.0 g, 17.6 mmol) was suspended in 250 mL 0.4 M sodium hydroxide (NaOH) aqueous solution. The flask was cooled to 0°C in ice bath. TsCl (13.4 g, 70.3 mmol) was added in slow portions over 10 min. After 45 min of stirring at 0°C, the precipitate was removed by filtration and the pH of the filtrate was adjusted to 8.5 by dropping HCl aqueous solution. Then the mixture was stirred for 1 h at room temperature. The resulting white precipitate was recovered by filtration and washed three times with water. The final product was dried in a vacuum oven at 60°C, yielding a white solid (8.8

g, yield: 40%). ^{1}H NMR (DMSO-d_6): δ 7.76 (d, J= 8.3 Hz, 2H, H-7), 7.45 (d, J= 8.2 Hz, 2H, H-8), 5.69 (br, 14H, OH-2,3), 4.83 (t, 5H, H-1), 4.77 (t, 2H, H-1), 4.47 (d, J = 26.3 Hz, 6H, OH-6), 4.37 (br, 2H, H-6'), 4.35 (br, 1H, H-5'), 3.81-3.08 (br, 26H, H-2,3,4,5,6 overlap with H_2O), 2.43 (s, 3H, H-9). FT-IR ν: 3316 (OH), 2924 (CH), 2160 (CH), 2030, 1358 (S=O), 1152 (S-O), 1077 (OH), 1023 (CH), 945, 841, 756 (OH), 684 (CH) cm^{-1}. ESI-MS: m/z 1312.2 [M + Na^+].

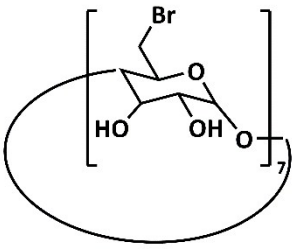
A.2.2. Synthesis of Mono-6-deoxy-6-azido-β-cyclodextrin (β-CD-N_3).



β-CD-OTs (8.0 g, 6.2 mmol) was suspended in 100 mL water. After heating to 80°C, NaN_3 (2.0 g, 31.0 mmol) was added. The reaction mixture was stirred at 80°C for overnight. The reaction solution was cooled to room temperature and precipitated in 800 mL acetone. The resulting white precipitate was recovered by filtration and redissolved in 50 mL of water and precipitated again in acetone. The white solid was dried under vacuum at 60°C for 2 days (6.8 g, yield: 95%). ^{1}H NMR (DMSO-d_6): δ 5.72 (br, 14H, OH-2,3), 4.88 (s, H, H-1), 4.83 (d, 6H, H-1), 4.57-4.40 (br, 6H, OH-6), 3.86-3.50 (br, 28H, H-3,5,6,6'), 3.32 (br, 14H, H-2,4 overlap with H_2O). FT-IR ν: 3316 (OH), 2924 (CH), 2160 (C-C), 2102 (N=N), 1644 (C=C), 1364 (OH), 1152 (CN), 1077 (OH), 1025 (CH), 945, 853, 756 (NH), 704 (CH) cm^{-1}. ESI-MS: m/z 1182.3 [M + Na^+].

A.3. Synthesis of Heptaazide functional Cyclodextrin.[3]

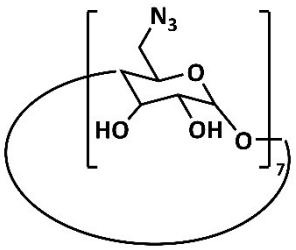
A.3.1. Synthesis of Heptkis-(6-deoxy-6-bromine)-β-cyclodextrin (β-CD-$(Br)_7$)



Based on a literature procedure, in a 500 mL round bottom flask Ph_3P (16.2 g, 61.7 mmol) was dissolved in anhydrous DMF (60 mL). The flask was cooled to 0°C in ice bath. NBS (11.0 g, 61.7 mmol) was dissolved in anhydrous DMF (20 mL) and added dropwise to Ph_3P solution and stirred 30 min. at room temperature. *β*-CD (5.0 g, 4.4 mmol) was dissolved in anhydrous DMF (60 mL) and added dropwise to Ph_3P/NBS solution under N_2 atmosphere. Reaction temperature was maintained at 80 °C for overnight. The reaction mixture was then cooed to -15 °C and the pH was adjusted to 9 with sodium methoxide (5.4 M in methanol), while stirring for further1 h. It was then poured into stirred ice-water (1 L) resulting in the formation of a precipitate which was filtered, washed with MeOH, obtained as white solids and dried under vacuum for 2 days (5.2 g, 75%). ^{1}H NMR (DMSO-d_6): δ 6.01 (d, J=6.6 Hz, 7H, OH-2), 5.88 (d, J=2.1 Hz, 7H, OH-3), 4.98 (d, J=3.4 Hz, 7H, H-1), 4.00

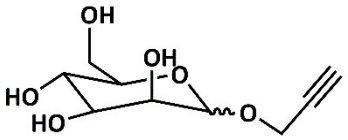
(d, J=9.6 Hz, 7H, H-6a), 3.82 (t, J=9.4 Hz, 7H, H-5), 3.72-3.54 (m, 14H, H-3, H-6'), 3.46-3.29 (m, 14H, H-2, H-4, overlap with H_2O). FT-IR ν: 3334(OH); 2916 (CH) cm^{-1}.

A.3.2. Synthesis of Heptkis-(6-deoxy-6-azido)-β-cyclodextrin (β-CD-$(N_3)_7$)



β-CD-$(Br)_7$ (4.7 g, 3.0 mmol) was dissolved in anhydrous DMF (20 ml) and NaN_3 (2.7 g, 41.8 mmol) was added. The resulting suspension was stirred at 70 °C under N_2 atmosphere for 24h. The reaction solution was cooled to room temperature and precipitated in 600 mL water. The precipitate was filtered and washed two times with water. The obtained white powder was dried under vacuum at ambient temperature for 24 h (3.5 g, 90%). ^{1}H NMR (DMSO-d_6): δ 5.88 (d, J=6.8 Hz, 7H, OH-2), 5.75 (d, J=2.1 Hz, 7H, OH-3), 4.90 (d, J=3.5 Hz, 7H, H-1), 3.91-3.67 (m, 14H, H-5, H-6), 3.65-3.50 (m, 14H, H-3, H-6'), 3.45-3.25 (m, 14H, H-2, H-4, overlap with H_2O). FT-IR ν: 3334(OH); 2922 (CH); 2098 (N_3) cm^{-1}.

A.4. Synthesis of 1-(2′-Propargyl) D-Mannose



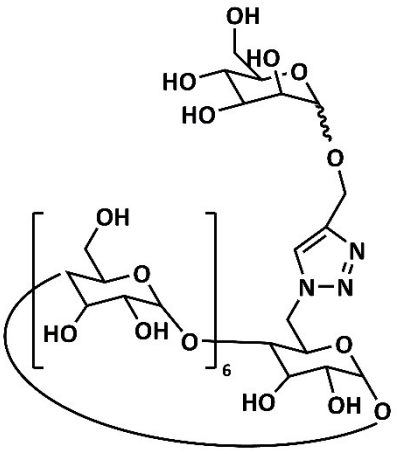
Based on a literature procedure,[4] the solution of D-mannose (6.0 g, 33.4 mmol), propargyl alcohol (9.7 mL, 166.5 mmol) and H_2SO_4-silica (166 mg) was stirred at 65 °C for overnight. After cooling to room temperature, reaction mixture was transferred to a silica gel column and eluted with $CHCl_3$–MeOH (8:1) to remove the excess propargyl alcohol. The product was obtained as white solid after drying under vacuum (1.8 g, yield: 57%).

FT-IR ν: 3347 (OH), 3285 (C≡C–H), 2118 (C≡C) cm^{-1}. ESI-MS: m/z 241.2 [M + Na^+].

For detailed characterization, a part of the product was per-*O*-acetylated using acetic anhydride (8 equiv) and catalytic H_2SO_4–silica. ^{1}H NMR spectroscopy of the per-O-acetylated product revealed formation of the desired glycoside in a 6:1 (α/β) ratio. ^{1}H NMR ($CDCl_3$): δ 5.32 (dd, J=3.3, 1H, H-3), 5.30–5.25 (m, 2H, H-2, H-4), 5.02 (s, 1H, H-1), 4.28 (dd, J=5.2, 1H, H-6a), 4.27 (d, J=2.4 Hz, 2H, C*H*$_2$–C≡CH), 4.10 (dd, J=2.5 Hz, 1H, H-6b), 4.04-3.98 (m, 1H, H-5), 2.47 (t, 1H, CH_2–C≡C*H*), 2.16, 2.10, 2.03, 1.98 (4s, 12H, 4 x COC*H*$_3$).

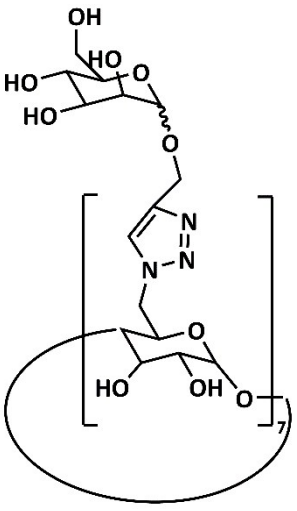
A.5. Synthesis of monosubstituted cyclodextrin-based mannose via CuAAC (CD_1)

β-CD-N_3 (1.0 g, 0.86 mmol), 1-(2′-Propargyl) D-Mannose (0.4 g, 1.72 mmol, α/β=6/1) were dissolved in DMSO (5 mL) in a Schlenk tube. Me_6TREN (230 μL, 0.86 mmol) and CuBr (0.12 g, 0.86 mmol) were added, and the reaction mixture was evacuated and filled with nitrogen, then stirred at 50 ºC for 24 h. When the reaction was completed, it was precipitated into methanol (no need to remove the DMSO), filtered and upper solution concentrated under reduced pressure and precipitated again into methanol. All precipitates were carefully collected, washed with methanol and dissolved in water, cuprisorb (copper chelating agent from Seachem Laboratories) was added into the solution and stirred overnight. After that the clear solution was separated from cuprisorb via filter for freeze drying (Yield= 0.8 g, 67%). ^{1}H NMR (DMSO-d_6): δ 7.95 (s, 1H, NC*H*=C), 6.10-5.85 (m, 14H, OH-2, 3 of CD), 5.10 (s, 7H, H-1), 4.99-3.00 (m, CD & mannose residues, overlap with H_2O). FT-IR ν: 3351 (OH), 2927 (CH), 1331 (OH), 1153 (C-N), 1078 (OH), 1026 (CH), 946 (C=C) cm^{-1}.

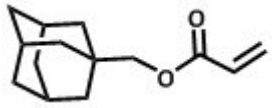


A.6. Synthesis of persubstituted cyclodextrin-based mannose via CuAAC (CD_7)

β-CD-$(N_3)_7$ (0.3 g, 0.23 mmol), 1-(2′-Propargyl) D-Mannose (1.0 g, 4.81 mmol, α/β=6/1) were dissolved in DMSO (2 mL) in a Schlenk tube. Me_6TREN (429 μL, 1.61 mmol) and CuBr (0.23 g, 1.61 mmol) were added, and the reaction mixture was evacuated and filled with nitrogen, then stirred at 50 ºC for 24 h. When the reaction was completed, it was precipitated into methanol. When the reaction was completed, due to low amount of DMSO, solvent wasn't removed from reaction medium. It was precipitated into methanol, filtered and upper solution concentrated under reduced pressure and precipitated again into methanol. All precipitates were carefully collected and dissolved in water, cuprisorb (copper chelating agent from Seachem Laboratories) was added into the solution and stirred overnight. After that the clear solution was separated from cuprisorb via filter for freeze drying (Yield= 0.44 g, 69%). ^{1}H NMR (DMSO-d_6): δ 7.95 (s, 7H, NC*H*=C), 6.12-5.84 (m, 14H, OH-2, 3 of CD), 5.11 (s, 7H, H-1), 4.98-3.00 (m, CD & mannose residues, overlap with H_2O). FT-IR ν: 3326 (OH), 2910 (CH), 1261 (OH), 1150 (C-N), 1075 (OH), 1027 (CH), 950 (C=C) cm^{-1}.



A.7. Synthesis of adamantane acrylate monomer



1-Adamantane methanol (3.0 g, 18.0 mmol) as dissolved in 80 mL of THF and Et_3N (6.3 mL, 45.0 mmol) was added. The reaction mixture was then cooled to 0 ºC. Acryloyl chloride (1.7 mL, 21.6 mmol) in THF (20 mL) was added dropwise within 30 minutes. The reaction mixture was stirred for 15 min. at 0 ºC then over night at room tempeature. The reaction was filtered off, solvent evaporated and was added CH_2Cl_2, then extracted with HCl (1 M, 2×30 mL), deionized water (2×30 mL) in sequence. After removing the solvents by a rotary evaporator, the crude product was purified by column chromatography over silica gel eluting with hexane/EtOAc (9/1). (Yield=2.9 g, 73%). ^{1}H NMR ($CDCl_3$): δ 6.33 (d, *J* = 16.9 Hz, 1H, H-c), 6.06 (dd, *J* = 17.3 Hz, 1H, H-b), 5.74 (d, *J* = 10.4 Hz, 1H, H-c'), 3.89 (s, 2H, H-a) 1.92 (m, 3H, H-e), 1.70 and 1.65 (d, 6H, H-d), 1.60 (d, 6H, H-d').

A.8.Triblock Copolymer Preparation by Iterative Reversible Addition−Fragmentation Chain Transfer (RAFT) Polymerization. ***Typical Synthesis of the First Block.*** Chain transfer agent (CTA), monomer(s), initiator and solvent are introduced in a flask equipped with a magnetic stirrer and sealed with a rubber septum (Table S2 for the quantity of reagents needed for the triblock coopolymer). The flask is degassed by bubbling argon through the solution for 15 min, then the RAFT polymerization is performed in a thermostated oil bath at 65 °C and removed after nearly full monomer conversion. The tube was subsequently cooled with liquid nitrogen to stop the reaction. The residue was precipitated in hexane. During polymerization samples are withdrawn from the polymerization medium using a degassed syringe for GC instrument for monitor monomer conversions. Before each new block, a sample is withdrawn from the polymerization medium using a degassed syringe for ^{1}H NMR and SEC analysis.

Typical Synthesis of the Following Blocks. For the iterative chain extension, a further mixture of degassed monomer, initiator and solvent is added via gastight syringe to the polymerization medium and the polymerization mixture is allowed to polymerize at the same temperature for desired time with stirring (Table S2 for the quantity of reagents needed for the triblock copolymer). Importantly, the amount of initiator remaining after each cycle is taken into account for the following blocks.

A.9. Supramolecular interaction and self-assembly of micelles.

The Solutions of **P1** triblock copolymer and CD derivatives dissolved in Milli-Q water at an 1 $mg.mL^{-1}$ concentration. After waiting a sufficient time period to allow for complex formation

(approx.30 min), the solutions were filtered with 0.2μm regenerated cellulose syringe filter (Roth, Rotilabo) to remove the particle impurities and placed in a microquartz cuvette. The cuvette was placed in a dynamic light scattering (DLS) particle size analyzer. Every measurement was performed at least five times both 10 °C and 40 °C. The change of the average particles diameters or mean count rate vs temperature was then observed. For the temperature sequenced measurements the sample was equilibrated at the specific temperature for 3 minutes, then the DLS measurement was performed 2 times for 5 minutes and the temperature changed again. The entire procedure was performed 2 times and the data points were finally averaged. All hydrodynamic diameters (D_h) in the text are the averages of the number weighted distributions.

A.10. Sugar lectin interaction

All experiments were conducted with HEPES-buffered saline (HBS) (0.10 M HEPES, 0.9 M NaCl, 1 mM $MgCl_2$, 1 mM $CaCl_2$, and 1 mM $MnCl_2$ adjusted to pH 7.4 and filtered with 0.2μm regenerated cellulose syringe filter.

Turbidimetry Assay

Sugar-lectin binding activities were investigated by the increasing absorbance at λ=420 nm after addition of glycomacromolecule to a concentrated Con A solution. A solution of 40 μM ConA in HBS buffer solution was made fresh before the assay. The exact concentration of Con A was determined by measuring the absorbance at 280 nm (A_{280} = 1.37 × [mg/mL Con A]). Turbidity measurements were performed by adding 350 μL of the ConA solution to a dry quartz microcuvette (700 μl, 1 cm pathlength) and put into the holder of UV-visible spectrophotometry at a certain temperature for 1 min. A solution of the ligand in HBS buffer was then added (350 μL at 320μM of the polymer with CD derivatives). Upon addition, the solution was mixed vigorously for 5 s using a pipette. Absorbance data were recorded at 420 nm for 15 min at 1.2 Hz.

Competitive binding to 1-methyl-D-mannopyranoside

After conjugation of polymer with CD derivatives with ConA, 30 μL of 5 $mg.ml^{-1}$ 1-methyl-D-mannopyranoside were added and the absorbance was recorded over 15 min at 40 ^oC.

Quantitative Precipitation Assay

Con A was dissolved in the HBS buffer solution to make fresh stock solution and the concentration was 60 μM (assuming Con A tetramers with a molecular weight of 104 kDa.)

Polymer with CD derivative solutions in HBS buffer (512 μM) were also prepared with a series of different concentration. Then Con A solution and the glycopolymer solution were mixed (1:1, v/v) energetically and incubated for 5 h at 40 °C. So the final concentration of Con A was 30 μM. White precipitates were separated from solution by centrifugation at 5000 x *g* for 5 min, followed by removal of the supernatants very carefully using pipette. Then the pellets were resuspended in cold buffer again. These washing steps were repeated twice. After removal of the supernatants, the precipitates were dissolved in a HBS buffer solution of methyl-α-D-mannopyranoside (1 mL, 100 mM). With complete dissolution, the Con A content was determined by measuring the absorbance at 280 nm.

B. <u>Measurements and analysis:</u>

Size exclusion chromatography (SEC). Gel permeation chromatography was used to determine the molecular weight and molecular weight distribution of polymers. A Varian 390-LC system in DMF (1 g/L LiBr) at 50 °C, equipped with refractive index and viscometry detectors, 2 × PLgel 5 mm mixed-D columns (300 × 7.5 mm), 1 × PLgel 5 mm guard column (50 × 7.5 mm) and autosampler. Narrow linear poly (methyl methacrylate) standards in range of 200 to 1.0×10^6 g·mol^{-1} were used to calibrate the system. All samples were passed through 0.45 μm PTFE filter before analysis.

Nuclear Magnetic Resonance (NMR) spectroscopy. ^{1}H NMR spectra were recorded using a Bruker Avance 400 spectrometer (400 MHz); samples were analyzed in $CDCl_3$ and DMSO-d_6 at 25°C. 2D NOESY (nuclear Overhauser enhancement spectroscopy) were performed on a Bruker AV600 (IconNMR) spectrometer at both room temperature and 70°C.

FT-IR Spectroscopy. The FT-IR spectra were recorded on a Bruker FT-IR spectrometer TENSOR II with Diamond-ATR module. The scanning range was 600-4000 cm^{-1} and the resolution was 1 cm^{-1}.

Electrospray ionization-mass spectrometry (ESI-MS). Mass spectra were recorded on a Thermo Finnigan LCQ Decaquadrupole ion trap mass spectrometer (Thermo Finnigan, San Jose, CA), equipped with an atmospheric pressure ionization source operating in the nebulizer assisted electrospray mode and was used in positive ion mode.

Dynamic light scattering (DLS). Dynamic light scattering (DLS) measurements were carried out in a Malvern Instrument Nano ZS using a He–Ne laser with a 633 nm wavelength, at an angle of 173°.

UV-visible spectrophotometry. UV-visible spectra were recorded on a PerkinElmer Lamda 25 UV/VIS spectrometer equipped with a (PTP-1) temperature control unit at a certain temperatures in the range of 200 nm and 600 nm using quartz microcuvettes.

C. Additional data and Figures:

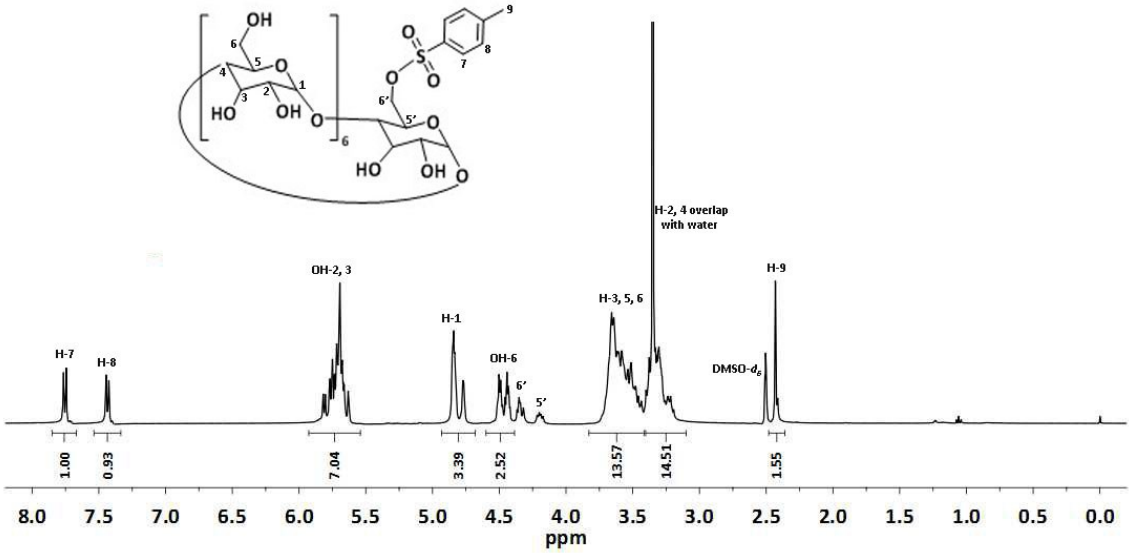


Figure S1. ^{1}H NMR spectrum of β-CD-OTs in DMSO-d_6 at room temperature.

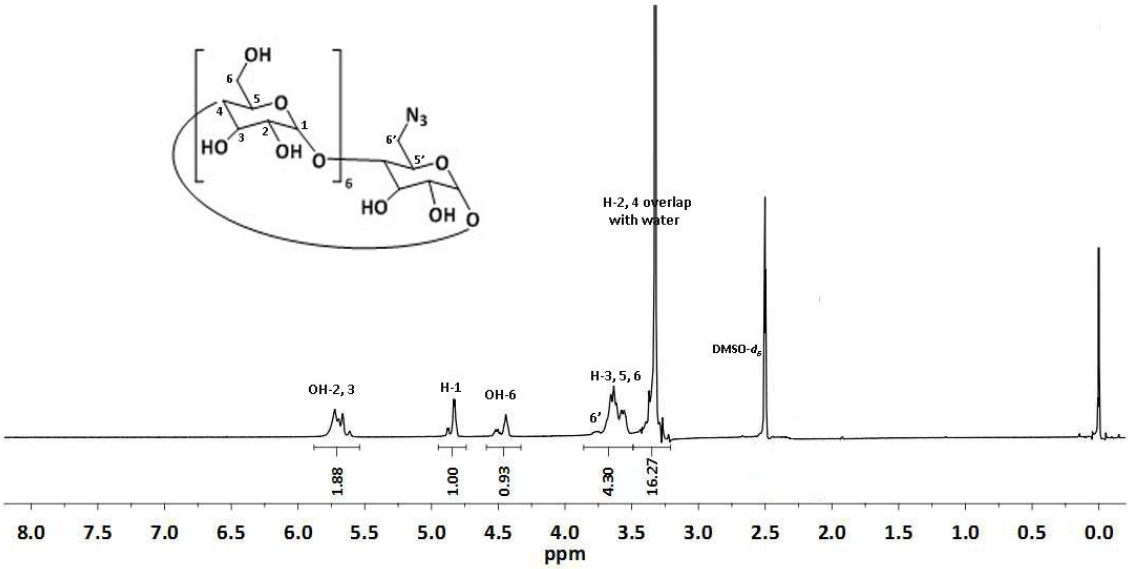


Figure S2. ^{1}H NMR spectrum of β-CD-N_3 in DMSO-d_6 at room temperature.

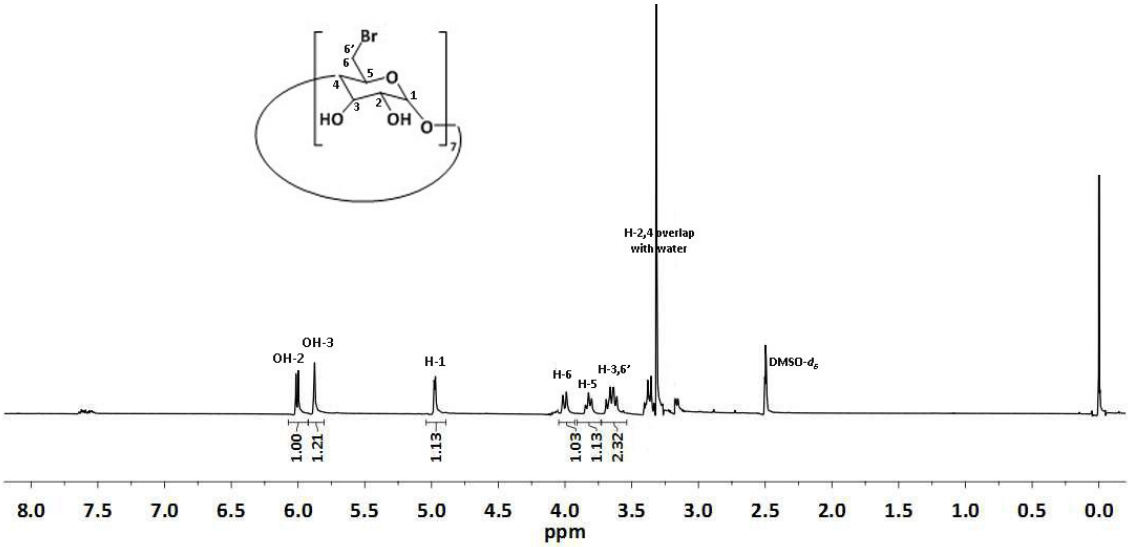


Figure S3. ^{1}H NMR spectrum of β-CD-(Br)$_7$ in DMSO-d_6 at room temperature.

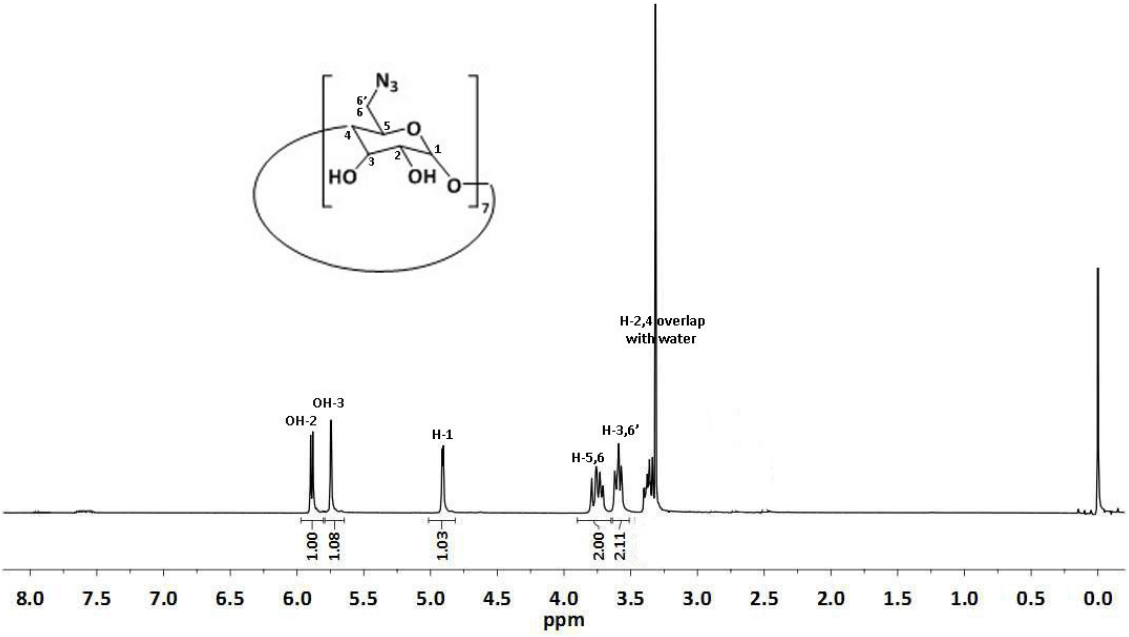


Figure S4. ^{1}H NMR spectrum of β-CD-(N$_3$)$_7$ in DMSO-d_6 at room temperature.

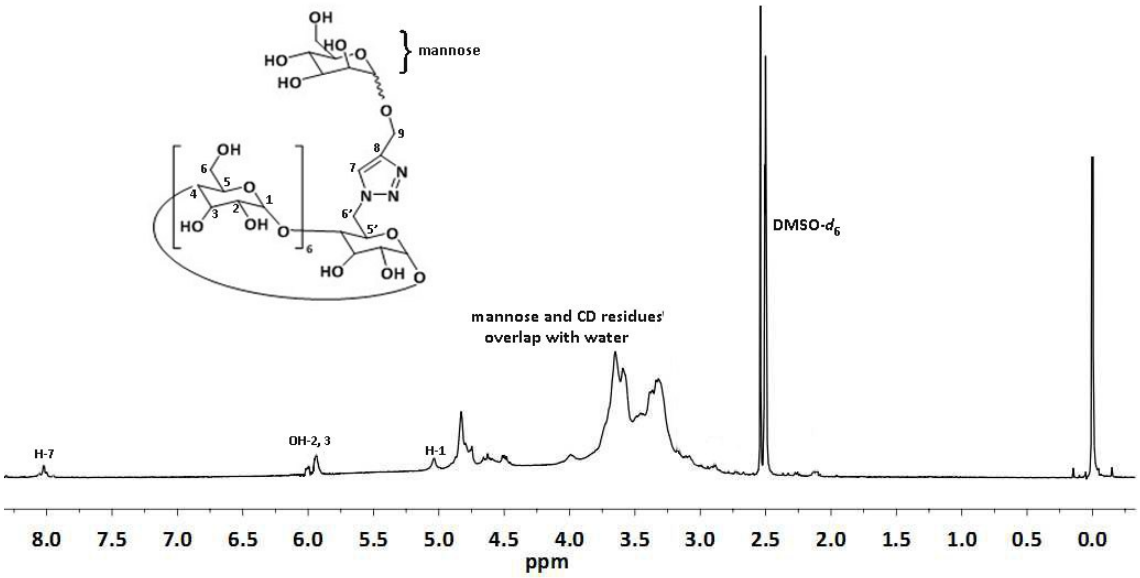


Figure S5. ^{1}H NMR spectrum of β-CD-Mannose (**CD$_1$**) in DMSO-d_6 at room temperature.

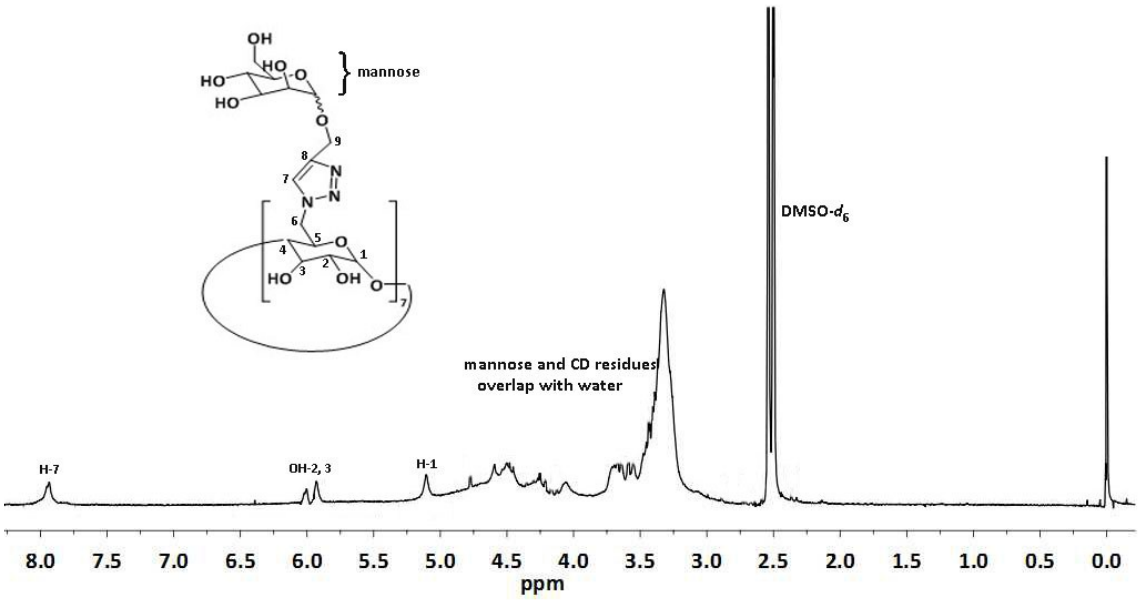


Figure S6. ^{1}H NMR spectrum of β-CD-(Mannose)$_7$ (**CD$_7$**) in DMSO-d_6 at room temperature.

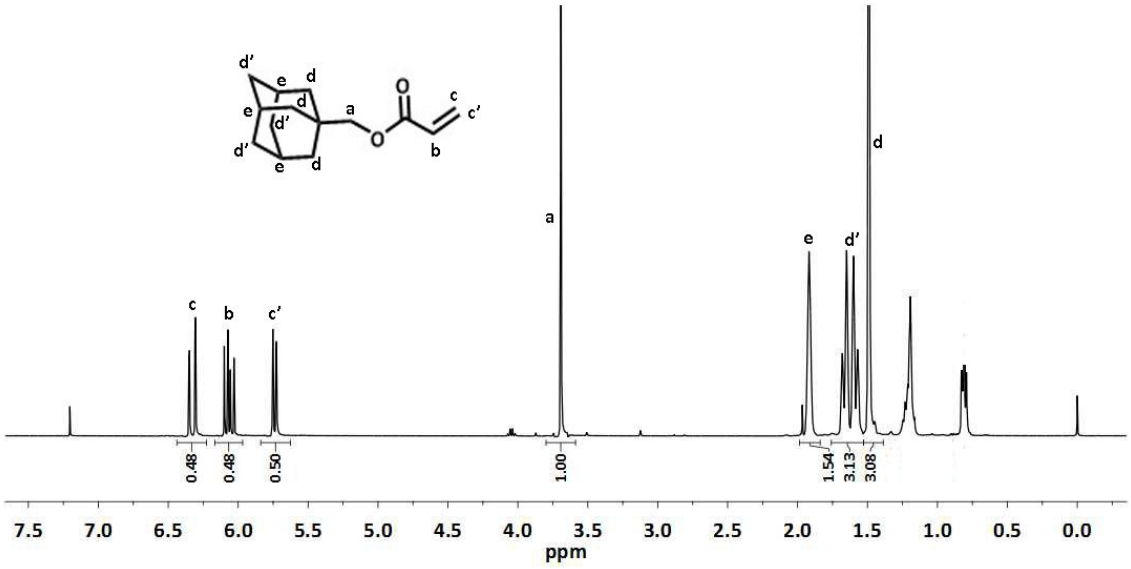


Figure S7. ^{1}H NMR spectrum of adamantane acrylate monomer in $CDCl_3$ at room temperature.

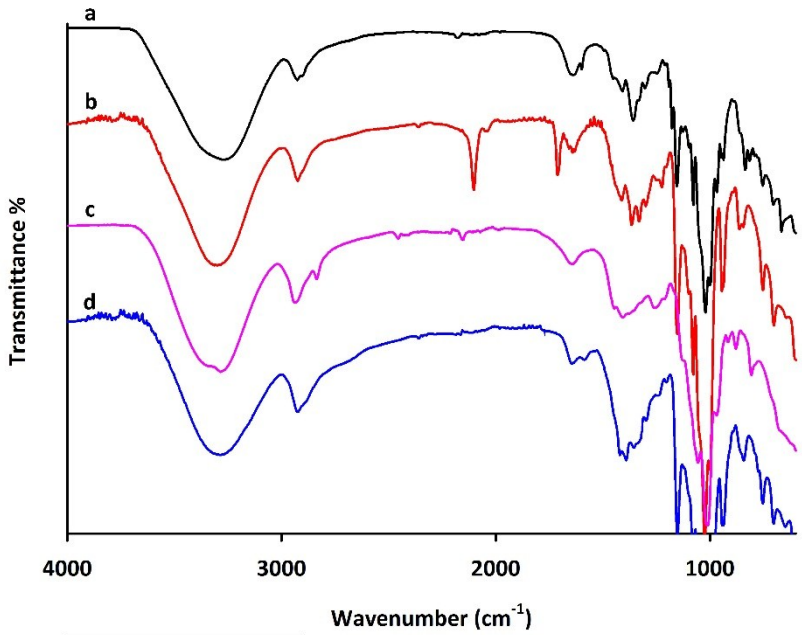


Figure S8. FTIR spectra of (a) *β*-CD-OTs (b) *β*-CD-N_3 (c) 1-(2′-Propargyl) D-Mannose and (d) *β*-CD-Mannose (**CD_1**).

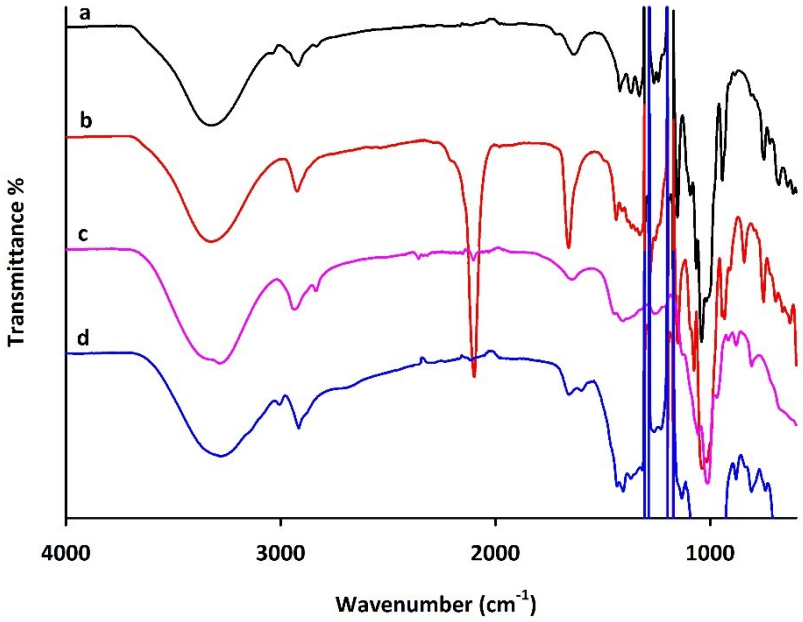


Figure S9. FTIR spectra of (a) β-CD-$(Br)_7$ (b) β-CD-$(N_3)_7$ (c) 1-(2′-Propargyl) D-Mannose and (d) β-CD-$(Mannose)_7$ (**CD_7**).

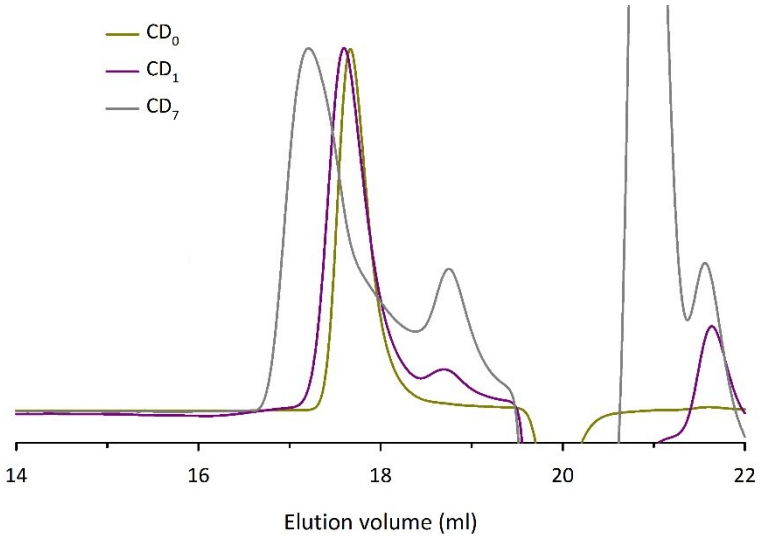


Figure S10. SEC traces of β-CD (**CD_0**), β-CD-mannose (**CD_1**), and β-CD-$(mannose)_7$ (**CD_7**) using RI detector in DMF at 50 ^oC.

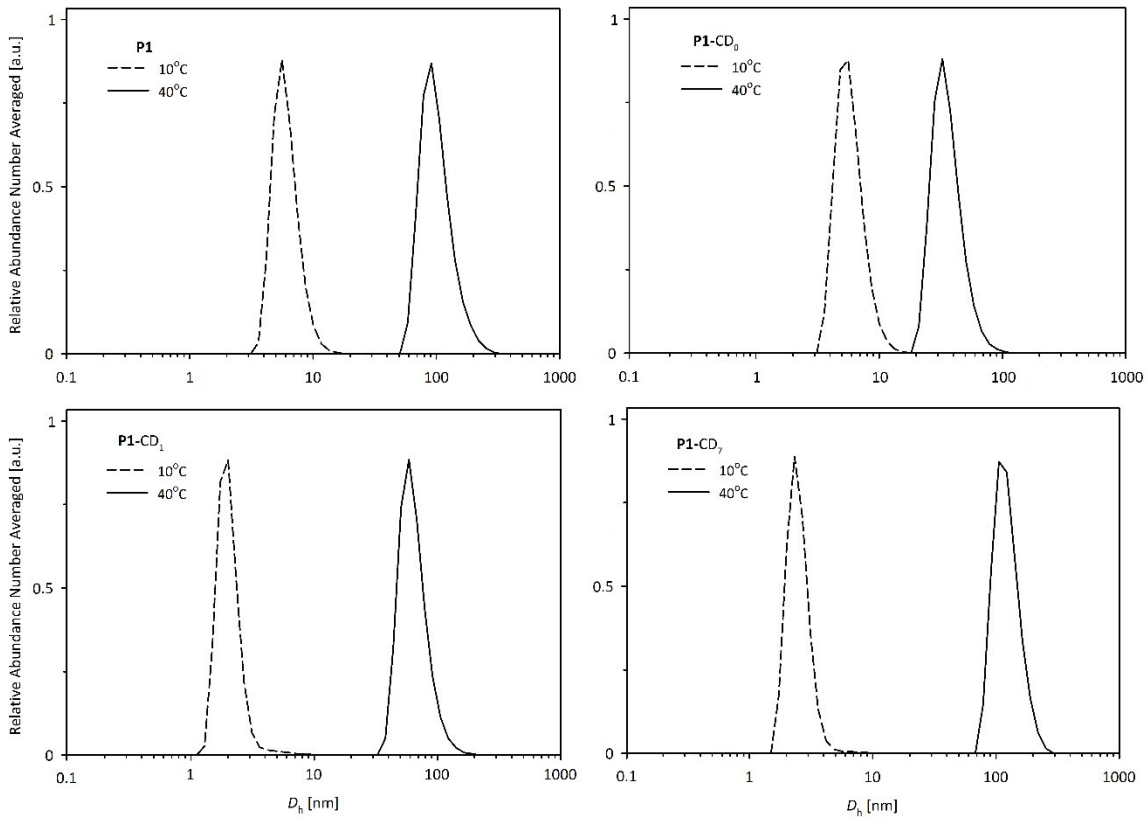


Figure S11. Comparison of the number average particle size distributions obtained from DLS measurements at 1 mg.mL^{-1}. The control samples of adamantyl functionalized building block **P1** and its complexes with β-CD derivatives at 10 °C and 40 °C,respectively.

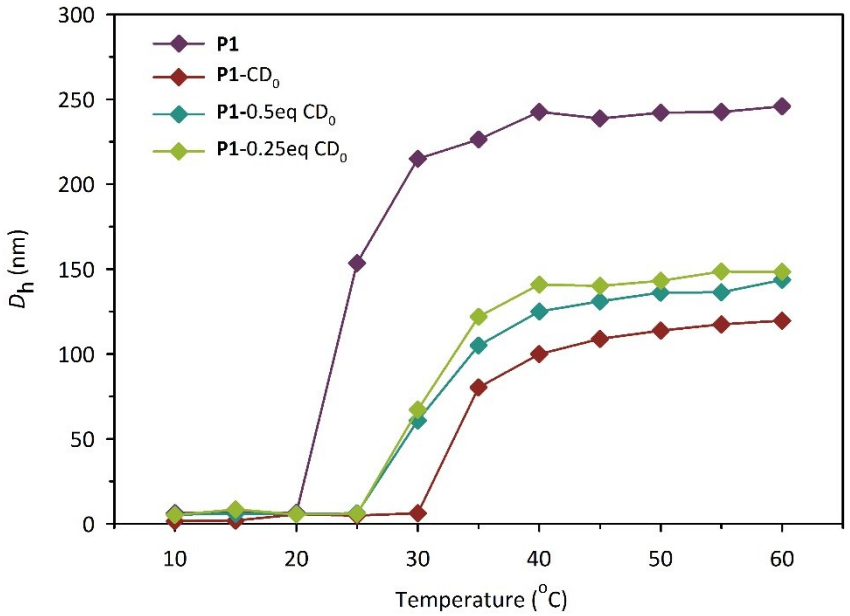


Figure S12. Temperature responsive behavior of adamantyl functional building block (**P1**) and its complexes with different amount of β-CD (**CD$_0$**) at 1 mg.mL^{-1} in H_2O.

Table S1. Experimental conditions used for the preparation of the triblock copolymers in 1,4-dioxane at 65˚C with AIBN as initiator.

run	**P1**				
cycles	**1**		**2**	**3**	
monomer	DMA	Adac	NIPAM	DMA	Adac
$DP_{targeted}$	8	2	20	8	2
$m_{mononer\ added}$ (g)	0.481	0.267	1.370	0.481	0.267
$m_{CTA\ added}$ (mg)	255.0		-	-	
$m_{AIBN\ added}$ (mg)	0.765		0.619	0.619	
$V_{dioxane\ added}$ (mL)	5.560		5.940	2.734	
V_{total} [a] (mL)	6.060		12.000	15.150	
$m_{AIBN\ total}$ [b] (mg)	0.765		0.765	0.765	
$[AIBN]_0$ (x10^3) (mmol.L^{-1})	7.69		3.88	3.08	
$[M]_0$ (mol.L^{-1})	1.00		1.00	0.4	
$[CTA]_0/[AIBN]_0$	130		130	130	

[a] represent the sum of the volume of the solvent added + volume of the monomer added + V_{total} previous block [b] represent the total weight of AIBN at time t_0 considering the weight of AIBN added ($m_{AIBN\ added}$) + the weight of AIBN remaining ($m_{AIBN\ remaining}$) from the previous block after precised time ($m_{AIBN\ remaining} = m_{AIBN\ total} \times 2fe^{-kdt} \times (1-f_c/2)$ with f=0.5, f_c=0, $k_d = 1.92\ 10^{-5} s^{-1}$)

Run	Structure	Cycle	Reac. time (h)	Conversion[a] (%) DMA	Adac	NIPAM	$M_{n,th}$[b] (g mol^{-1})	$M_{n,SEC}$[c] (g mol^{-1})	PDI
P1	($PDMA_8$-$PAdac_2$)-*b*-$PNIPAM_{20}$-*b*-($PDMA_8$-$PAdac_2$)	1	6	95	93	-	1580	774	1.19
		2	5	-	-	93	3680	2600	1.27
		3	9	95	92	-	4840	3130	1.30

[a]Determined by gas chromatography; [b]$M_{n,th} = [M]_0 \times p \times M_M / [CTA]_0 + M_{CTA}$; [c]Determined by the refractive index detector in size exclusion chromatography running in DMF with PMMA used as molecular weight standards.

Table S2. Characterisation of the triblock copolymers.

Table S3. Molecular weight results of adamantyl functionalized building block **P1** and its complexes with CD derivatives after waiting enough time for inclusion complexation.

run	$M_{p,SEC}$[a] (g mol^{-1})	$M_{n,SEC}$ (g mol^{-1})	$M_{w,SEC}$ (g mol^{-1})
P1	5180	3785	4980

P1-CD$_0$	3620	3160	3950
P1-CD$_1$	3975	2800	4110
P1-CD$_7$	5450	2770	4450

[a] Determined by SEC/RI in DMF with PMMA used as molecular weight standards.

References.

1. Roy, B., Mukhopadhyay, B., *Tetrahedron Lett.* **48**, 3783–3787 (2007).
2. Amajjahe, S., Choi, S., Munteanu, M., Ritter, H., *Angew. Chem., Int. Ed.* **47**, 3435−3437 (2008).
3. Zhang, Q., Su, L., Collins, J., Chen, G., Wallis, R., Mitchell, D. A., Haddleton, D. M., Becer, C. R., *J. Am. Chem. Soc.* **136**, 4325−4332 (2014).
4. Zhang, Q., Slavin, S., Jones, M. W., Haddleton A. J., Haddleton, D. M., *Polym. Chem.* **3**, 1016–1023 (2012).