Supporting information

A versatile and modular approach to functionalization of deep-cavity cavitand via "click" chemistry

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Materials and instrumentation. All compounds were used without further purification. Solvents were purchased from Pharmaco Aaper, Aldrich, and Fisher Scientific. Triethylamine and *N,N*-dimethylformamide was dried by distillation prior to use. All other solvents were used without further purification. Pentynoic acid, poly(ethylene) glycol monomethyl ether, sodium azide, and methanesulfonyl anhydride were all purchased from Aldrich. The monodisperse poly(ethylene) glycol monomethyl ether 20-mer was purchased from Polypure AS, Norway. All poly(ethylene) glycol was dried prior to use *in vacuo*. Purification of cavitand-polymer conjugates was carried via column chromatography using Bio-Beads as the stationary phase. Bio-Beads® S-X beads are porous cross-linked polystyrene polymers used for gel permeation separations of hydrophobic polymers in the presence of organic solvents. The mechanism of separation of polymers is the same as gel permeation chromatography, which is based on the hydrodynamic volume of the polymers. All ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) were obtained using a Varian Mercury spectrometer (Palo Alto, CA), using TMS = 0.00 ppm for ^{1}H calibration. Mass spectral data was acquired using a Bruker Autoflex III matrix-assisted laser desorption time-of-flight mass spectrometer (MALDI-TOF MS) with delayed extraction using both positive ion and reflector detection modes. Sodium trifluoroacetate or silver trifluoroacetate were used as counterions, and galvinoxyl radical as the matrix. Size exclusion chromatography (SEC) was carried out on a Waters model 1515 series pump (Milford, MA) with threecolumn series from Polymer Laboratories, Inc. consisting of PLgel 5 μm Mixed D (300 mm × 7.5 mm, molecular weight range 200-400 000), PLgel 5 μm 500 Å (300 mm × 7.5 mm, molecular weight range 500-30,000), and

PLgel 5 μm 50 Å (300 mm × 7.5 mm, molecular weight range up to 2000) columns. The system was fitted with a Model 2487 differential refractometer detector and anhydrous tetrahydrofuran was used as the mobile phase (1 mL min^{-1} flow rate). The resulting molecular weight was based on calibration using linear polystyrene standards, and these apparent molecular weights were converted to absolute molecular weights. Data were collected and processed using Precision Acquire software.

Alkyne-Functionalized Cavitand, (2)

Octa-ol cavitand (0.120 g, 0.053 mmol) was dissolved in 6 mL pyridine with dicyclohexylcarbodiimide, DCC, (0.552 g, 2.67 mmol) and N,N-dimethylaminopyridine, DMAP, (0.1089 g, 0.8 mmol). Pentynoic acid (0.262 g, 2.67 mmol) and 4 mL CH_2Cl_2 was added to the reaction mixture. The reaction was stirred vigorously for 6 hours while being monitored by MALDI-TOF MS. Upon completion, the solvent was evaporated and the crude product was precipitated in methanol and chilled for 12 hours. After filtering, the precipitate was purified on a short silica column using 50% acetone/CH_2Cl_2 eluent system. The solvent was evaporated to yield 0.142 grams of pure octa-pentynoate cavitand product; 84.8% yield. ^{1}H ^{1}H-NMR (400 MHz, $CDCl_3$,δ, ppm): 1.66 (p, 8H, J= 6.8 Hz), 1.90 (dd, 8H, J= 2.4 Hz), 2.29 (q, 8H, J= 6.8 Hz), 2.36-2.41 (m, 8 H), 2.43-2.48 (m, 8H), 2.50-2.55 (m, 16H), 4.17 (t, 8H, J= 6.4 Hz), 4.47 (s, 4H), 4.78 (t, 4H, J= 8 Hz), 5.19 (s, 8H), 5.93 (s, 4H), 6.45 (d, 8H, J= 1.6 Hz), 6.52 (t, 4H, J= 2.4 Hz), 6.93 (t, 4H, J= 2.4 Hz), 7.12 (s, 4H), 7.19 (d, 8H, J= 2Hz). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 14.42, 14.59, 26.97, 27.11, 33.43, 35.51, 36.28, 64.35, 65.41, 69.39, 69.49, 82.51, 82.79, 105.89, 107.98, 109.78, 115.26, 115.64, 119.93, 122.08, 136.75, 139.29, 140.40. MALDI-TOF MS: exact *m/z* calculated for $[C_{136}H_{112}O_{32} + Na]^+$: 2279.70; observed: 2279.723. GPC: M_n=2122; polydispersity index (PDI)=1.04.

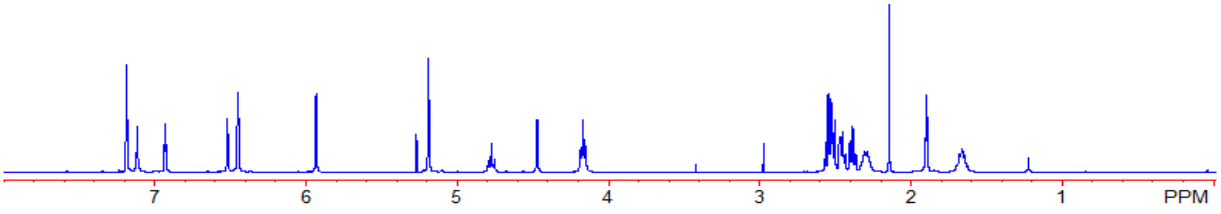


Figure SI-1. ^{1}H NMR of alkyne functionalized cavitand, **2**, in $CDCl_3$.

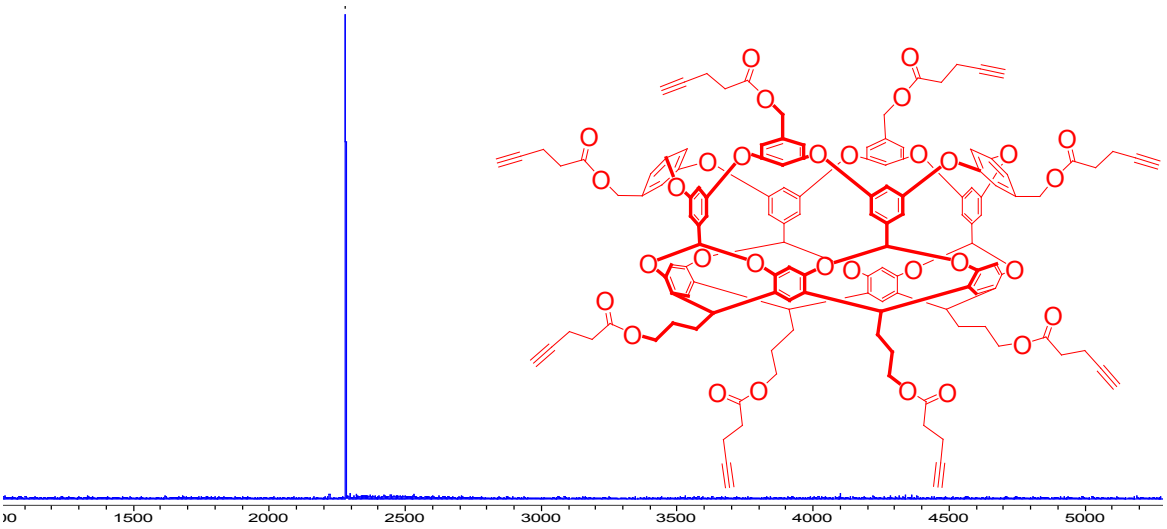
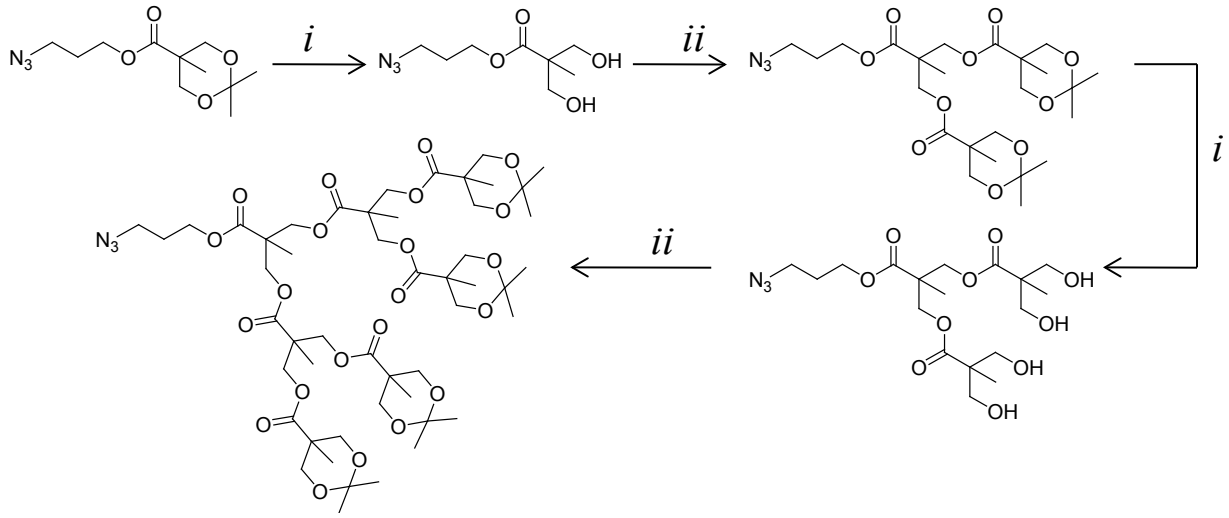


Figure SI-2. MALDI TOF-MS spectrum of alkyne functionalized cavitand, **2**,: Matrix (9-nitroanthracene) and counter ion (sodium trifluoroacetate).

General Procedure for synthesis of azide-functionalized dendrons. The dendrons were synthesized according to a previously reported divergent dendronization procedure.[1] The synthesis utilized the acetonide-protected 2,2-bis(hydroxymethyl)propanoic acid anhydride monomer to couple to the growing hydroxylated dendron during the dendritic growth step, and utilized Dowex acidic resin to remove the acetonide protecting group during the deprotection step. Dendritic growth was initiated by esterification of 3-azidopropanol with the anhydride monomer, and continued via repetition of deprotection and dendritic growth steps to produce the second generation (**3b**) and third generation (**3a**) dendrons.



Scheme S1. Synthesis of azide functionalized dendrons, **3a**, and **3b** using: i) Dowex +H exchange resin, and ii) isopropylidene-2,2-bis(methoxy)propionic acid anhydride.

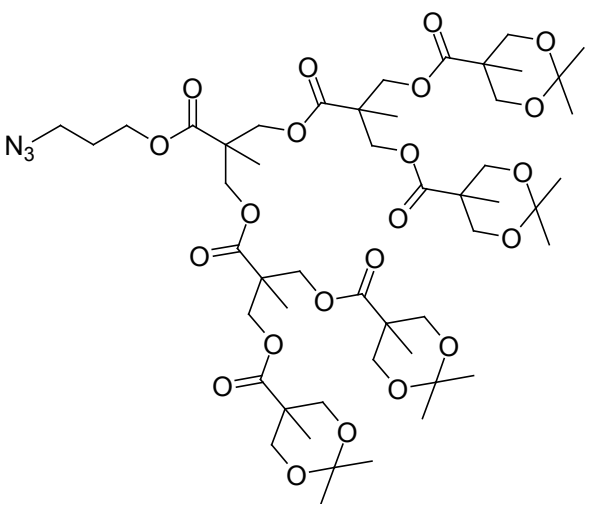


Figure SI-3. [G-3] azide-functionalized dendron, **3a.**

N_3-[G3]-$(Ac)_4$, (3a)

Synthesized according to the ***General Procedure for synthesis of azide-functionalized dendrons.*** Recovered 89% yield. ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 1.10 (s, 12H), 1.25 (s, 9H), 1.32 (s, 12H), 1.39 (s, 12H), 1.92 (p, 2H, J= 6.4Hz), 3.38 (t, 2H, J= 6.4 Hz), 3.59 (d, 8H, 12.8 Hz), 4.12 (d, 8H, J= 12 Hz), 4.12 (t, 2H, J= 6.4 Hz), 4.22-4.30 (m, 12H). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 17.61, 17.70, 18.49, 21.92, 25.36, 28.00, 42.06, 46.67, 46.87, 48.08, 62.59, 64.91, 65.94, 65.99, 98.11, 171.87, 172.00, 173.53. IR (KBr, ν, cm-1): 1745, 2100, 2800-3000. MALDI-TOF MS: exact *m/z* calculated for $[C_{50}H_{79}O_{22}N_3 + Na]^+$: 1096.505; observed: 1096.469. Analysis calculated for $C_{50}H_{79}O_{22}N_3$: C, 55.91; H, 7.41; N, 3.91; O, 32.77; observed: C, 56.19; H, 7.49; N, 3.87. GPC: M_n=1100; PDI=1.02.

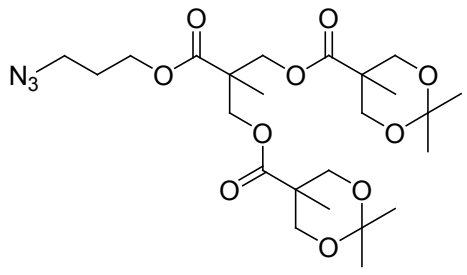


Figure SI-4. [G-2] azide-functionalized dendron, **3b.**

N_3-[G2]-$(Ac)_2$, (3b)

Synthesized according to the ***General Procedure for synthesis of azide-functionalized dendrons.*** Recovered 94.0% yield. ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 1.12 (s, 6H), 1.28 (s, 3H), 1.34 (s, 6H), 1.40 (s, 6H), 1.91 (p, 2H, J= 6.4 Hz), 3.38 (t, 2H, J= 6.8 Hz), 3.61 (d, 4H, J=12.4 Hz), 4.14 (d, 4H, J= 12 Hz), 4.20 (t, 2H, J= 6.4 Hz), 4.32 (s, 4H). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm):17.81, 18.59, 21.92, 25.48, 28.13, 42.18, 46.92, 48.11, 62.31, 65.36, 66.06, 66.10, 98.21, 172.56, 173.66. IR (KBr, ν, cm^{-1}):

810, 1075, 1110-1175, 1200-1275, 1740, 2100, 2810-3000. IR (KBr, ν, cm^{-1}): 1740, 2100, 2800-3000. MALDI-TOF MS: exact *m/z* calculated for $[C_{24}H_{39}O_{10}N_3 + Na]^+$: 552.253; observed: 552.298. Analysis calculated for $C_{24}H_{39}O_{10}N_3$: C, 54.43; H, 7.42; O, 30.21; N, 7.93. Observed: C, 54.42; H, 7.46; N, 7.78. GPC: M_n=550; PDI=1.03.

General Procedure of Cu(I) catalyzed "click" functionalization of cavitand. Alkyne functionalized cavitand, **2**, azide functionalized macromolecule, **3a-g**, and PMDETA (1:8.08:16) were added to a round bottom flask with dichloromethane. After 2 freeze-pump-thaw cycles, Cu(I)Br (1:1 with PMDETA) was added, and the third freeze-pump-thaw cycle was carried out. The reaction was stirred for 16 hours at room temperature, then was washed with de-ionized water and brine, and finally was dried with Na_2SO_4. Following concentration *in vacuo*, the products were run through a short silica gel column to remove residual copper.

[G3]- grafted Cavitand, (4a) The octa-pentynoate cavitand (5.9 mg, 0.003 mmol) was added to a 25 mL round bottom flask with G3-dendron (22.9 mg, 0.021 mmol), and PMDETA (2.50 mg, 132 mmol). Also added was 6 mg CuBr and 1 mg Cu (see ***General procedure of Cu(I) catalyzed "click" functionalization of cavitand***). 29 mg G-3-dendron-grafted-cavitand crude product was isolated and after Bio-bead column, 11 mg product was recovered; 38% yield. ^{1}H-NMR (400 MHz $CDCl_3$, δ, ppm): 1.12 (s, 96H), 1.27 (s, 72H), 1.33 (s, 96H), 1.40 (s, 96H), 1.60 – 1.70 (br, 24H), 2.23 – 2.31 (m, 16H), 2.73 (t, 8H, J= 8 Hz), 2.82 (t, 8H, J= 8Hz), 2.98-3.06 (m, 16H), 3.60 (s, 32H), 3.63 (s, 32H), 4.12 (s, 40H), 4.15 (s, 40H), 4.27-4.37 (m, 104H), 4.42 (t, 8H, J= 6.8 Hz), 4.52 (s, 4H), 5.19 (s, 8H), 5.99 (s, 4H), 6.49 (d, 8H), 6.52 (m, 4), 6.96 (m, 4H), 6.98 (s, 4H), 7.17 (d, 8H), 7.44 (s, 4H), 7.46 (s, 4H). MALDI-TOF MS: average *m/z* calculated for $[C_{534}H_{740}N_{24}O_{210} + Ag]^+$: 10959.55; observed: 10959.11. GPC: M_n=8000; PDI= 1.02.

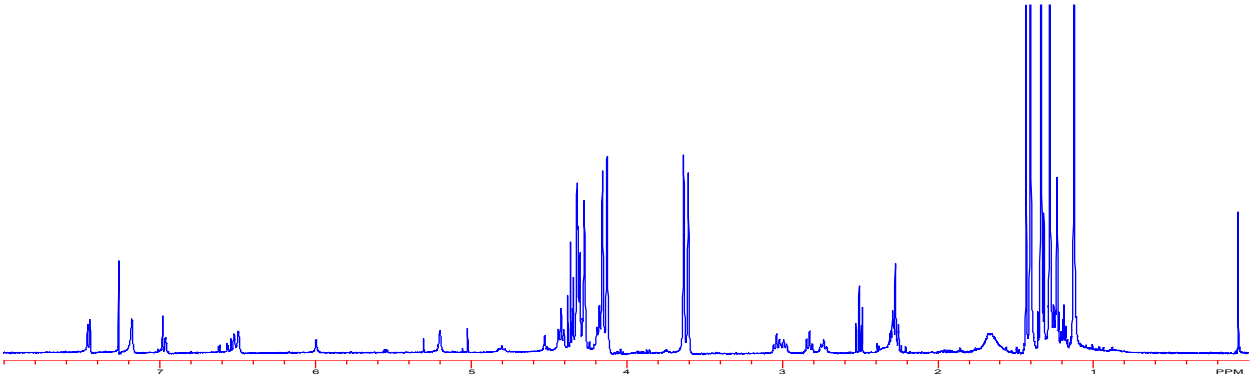


Figure SI-5. ^{1}H NMR of [G-3]-grafted Cavitand, 4a.

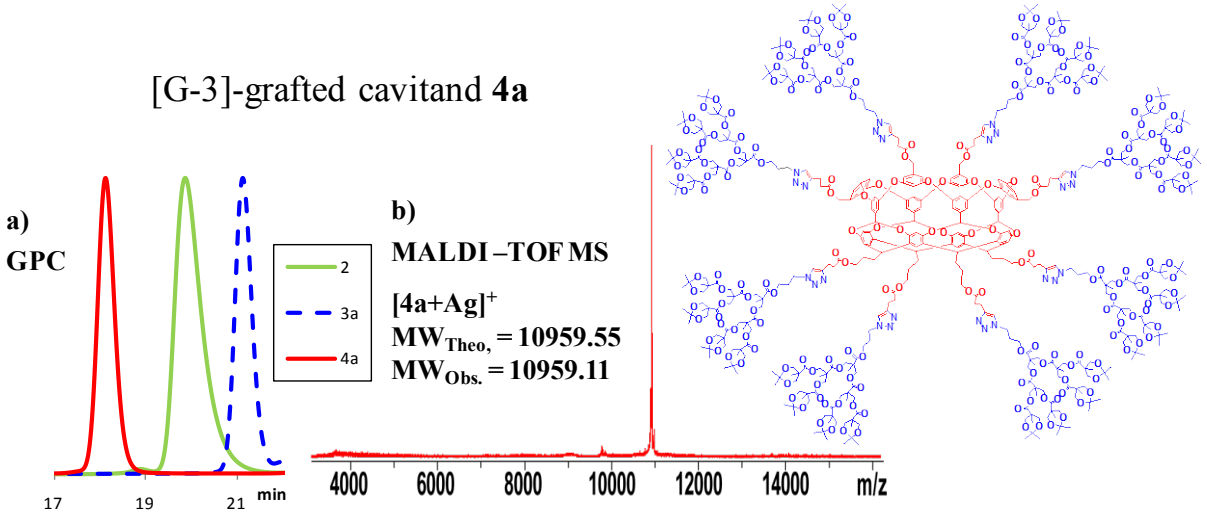


Figure SI-6. GPC trace **(a)** and MALDI-TOF MS spectrum **(b)** of [G-3]-grafted cavitand, **4a**.

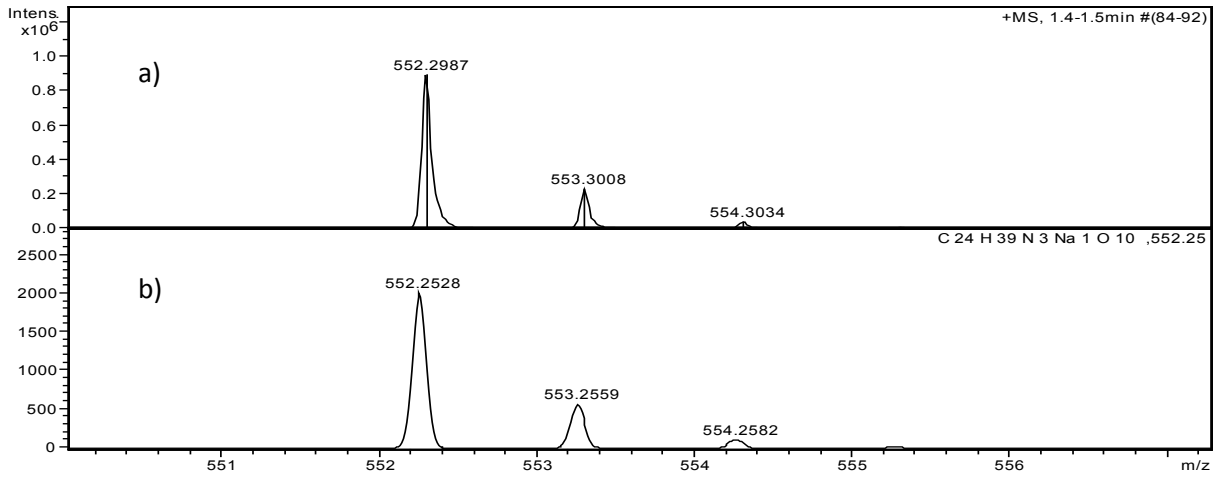


Figure SI-7. Theoretical **(a)** and Observed **(b)** MW analysis of G-2 dendron, **3b**, using electrospray ionization mass spectrometer.

[G2]-grafted Cavitand, (4b). The octa-pentynoate cavitand (5.60 mg, 2.48 mmol) was added to a 25 mL round bottom flask with G2-dendron (10.7 mg, 0.020 mmol), and PMDETA (6.90 mg, 39.8 mmol). Also added was 5.70 mg (0.039 mmol) CuBr, and 0.001 g (0.015 mmol) Cu. *See* ***General procedure of Cu(I) catalyzed "click" functionalization of cavitand***. G-2-dendron-grafted-cavitand, 10.5 mg crude product was recovered; 61.70% yield. ^{1}H NMR (400 MHz, $CDCl_3$ ppm): 1.12 (s, 48H), 1.31 (s, 24H), 1.34 (s, 48H), 1.41 (s, 48H), 1.67 (br, 24H), 2.26 (m, 16H), 2.34 (br, 8H), 2.73 (t, 8H, J= 7.2 Hz), 2.81 (t, 8,H, J= 6.8 Hz), 3.02 (m, 16H), 3.61 (s, 16H), 3.64 (s, 24H), 4.14 (s, 24H), 4.17 (s, 16H), 4.30-4.37 (m, 32H), 4.37-4.44 (m, 8H), 4.52 (s, 4H), 4.80 (t, 4H, J= 8 Hz), 5.20 (s, 8H), 5.98 (s, 4H), 6.50-6.53 (m, 12H), 6.96 (t, 4H, J= 2.4 Hz), 7.18 (d, 8H, J= 2 Hz), 7.21 (s, 4H), 7.41 (s, 4H), 7.45 (s, 4H). MALDI-TOF MS: exact *m/z* calculated for $[C_{328}H_{424}N_{24}O_{112} + Ag]^+$: 6597.73; observed: 6597.24. GPC: M_n=5700; PDI=1.03.

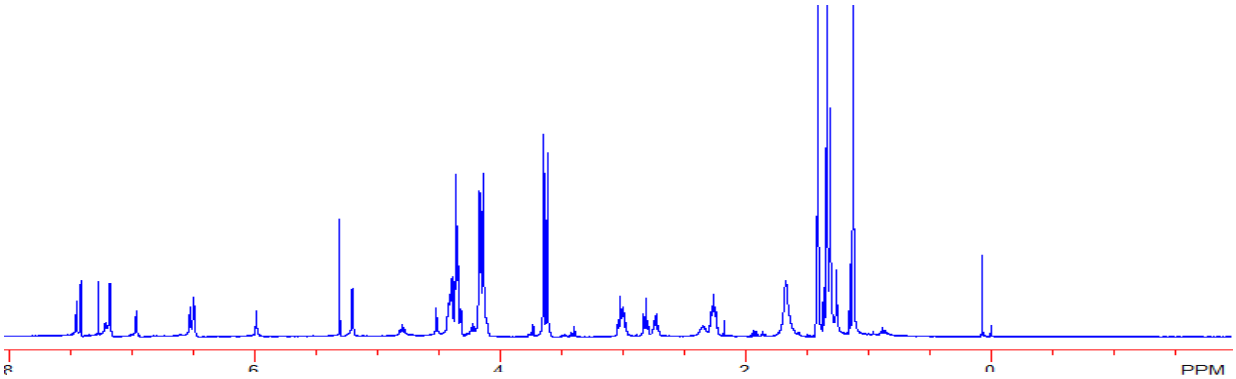


Figure SI-8. ^{1}H NMR of [G2]-grafted Cavitand, **4b**.

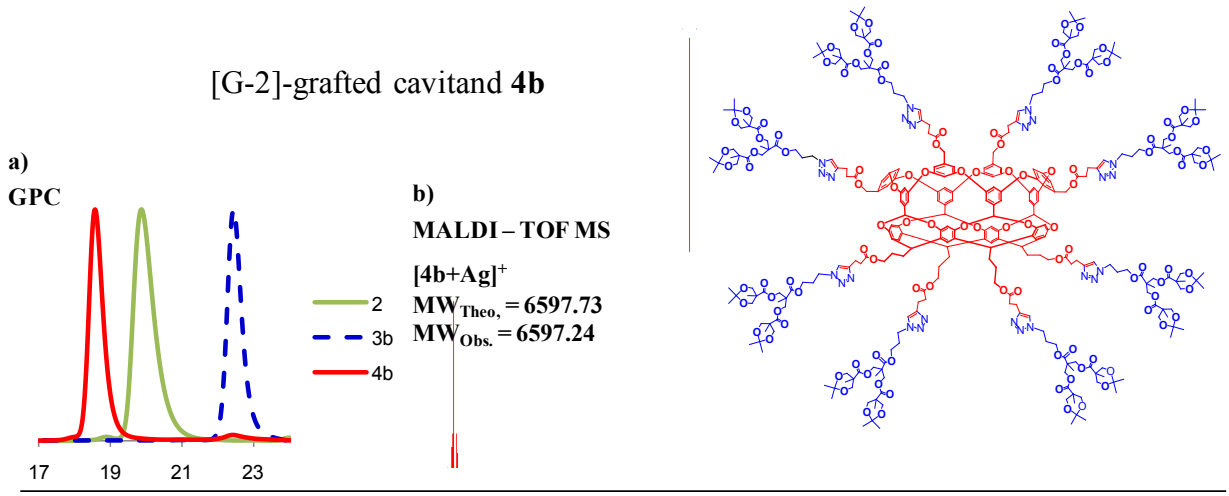
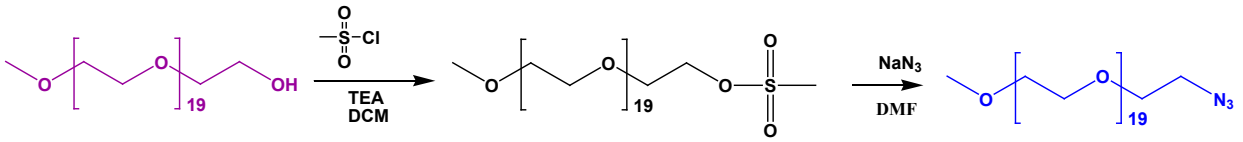


Figure SI-9. GPC trace **(a)** and MALDI-TOF MS spectrum **(b)** of [G-2]-grafted cavitand, **4b**.



Scheme S2. Synthesis of mPEG20mer-OMs, **S1**, and mPEG20mer-N_3, **3c**.

S1 **3c**

Synthesis of Monodisperse mPEG20mer-OMs, (S1). A typical procedure of synthesis of mPEG20mer-Ms was previously reported.[2] PEG-OH (M_n=913.1, 0.3g, 0.33mmol) was heated to 50°C in oil bath and dried *in vacuo* for 12 h. It was cooled to room temperature before dissolved in 50ml mL of dry dichloromethane. The solution was cooled to 0°C in an ice-water bath, and distilled triethylamine (0.5ml, 3.6mmol) and methanesulfonyl chloride (0.38g, 3.3mmol) were sequentially slowly added. After stirring for 12 hours at room temperature under nitrogen, the mixture was filtered and sequentially washed three times with 50 mL of 1M $NaHSO_4$ solution, 50 mL of 1M $NaHCO_3$ solution and 25 mL of brine. The organic layer was dried over anhydrous Na_2SO_4. The product was isolated via filtration and dried *in vacuo*, recovered 0.27g; 84.0% yield. ^{1}H-MR (400 MHz, $CDCl_3$, δ, ppm): 3.04 (br, 3H), 3.32 (br, 3H), 3.48-3.51 (m, 2H), 3.58-3.60 (br, 90H), 3.70-3.73 (br, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 37.90, 59.23, 69.19, 69.55, 70.59, 72.07. MALDI-TOF MS: exact *m/z* calculated for $[C_{42}H_{86}SO_{23} + Na]^+$: 1013.52; observed: 1013.54. GPC: M_n=1500; PDI=1.01.

Synthesis of Monodisperse mPEG20mer-N_3, (3c). A typical procedure of synthesis of mPEG20mer-N_3 was previously reported.[3] mPEG20mer-OMs, **S1**, (0.2 g, 0.20 mmol) and sodium azide (0.13 g, 2.00 mmol) were separately heated to 50°C under vacuum for 12 h, then cooled to room temperature. The mPEG20mer-Ms was dissolved in 3 mL of dried DMF, followed by the addition of sodium azide. The reaction was heated to 50°C and stirred under nitrogen for 12 hours. The reaction was dissolved in 10mL of DCM, then washed with 10 mL of de-ionized H_2O and brine three times. The organic layer was dried over anhydrous Na_2SO_4. The product was isolated via filtration and dried *in vacuo*, recovered 0.14g, 73.0% yield. ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 2.29 (s, 2H), 3.34 (s, 3H), 3.34-3.36 (m, 4H), 3.60-3.68 (br, 90H). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 50.84, 59.24, 70.72, 70.83, 72.09. MALDI-TOF

MS: exact *m/z* calculated for $[C_{41}H_{83}N_3O_{20} + Na]^+$: 960.55; observed: 960.54. GPC: M_n=1400; PDI=1.01.

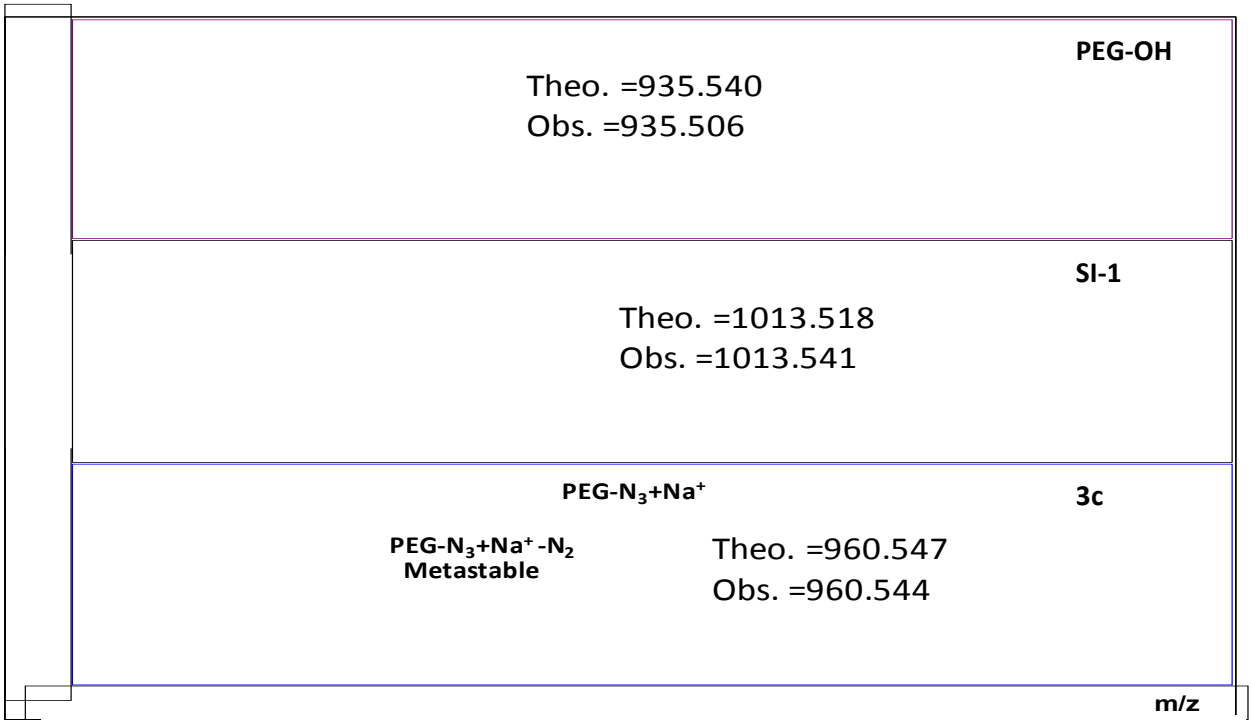


Figure SI-10. ^{13}C NMR of the monodisperse mPEG20mer-OH; mPEG20mer-OMs, **S1**, and mPEG-20mer-N_3, **3c**.

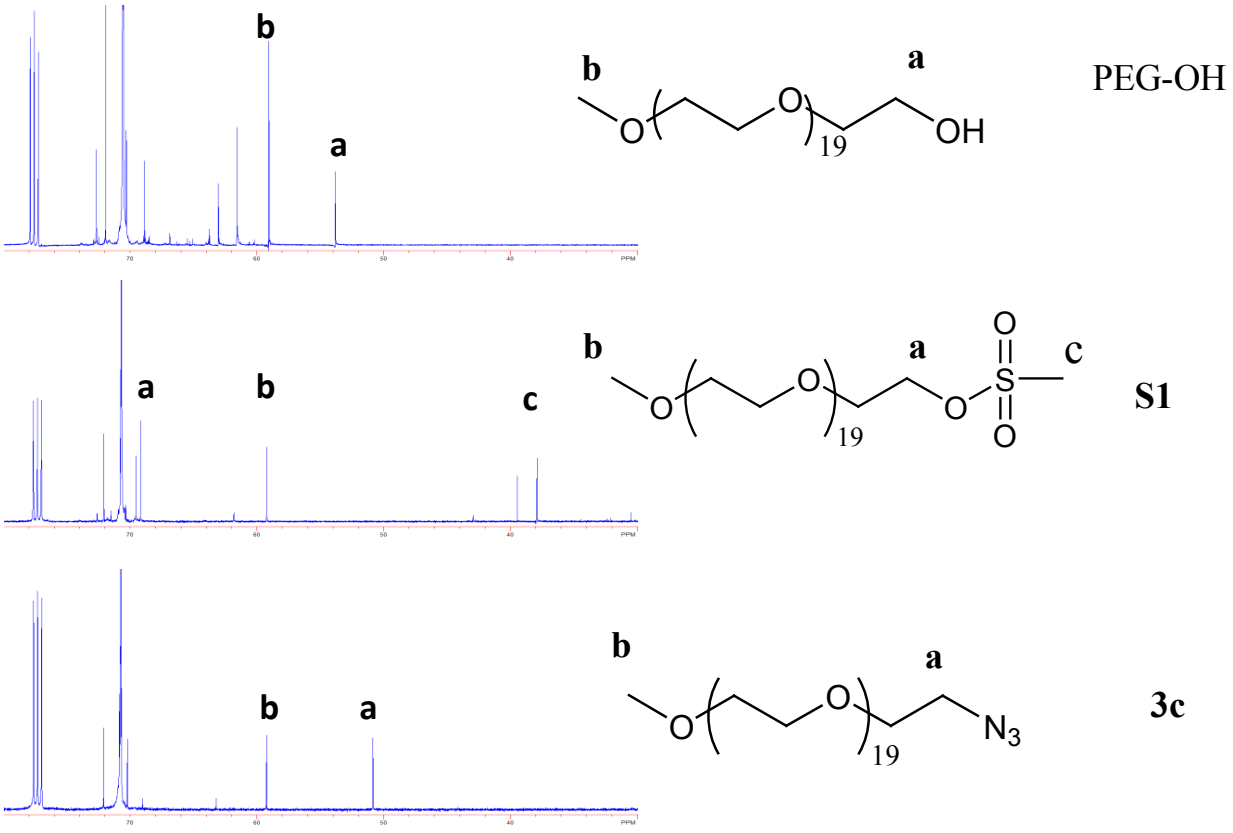


Figure SI-11. ^{13}C-NMR of the monodisperse mPEG20mer, MsO-mPEG20mer, **S1**, and mPEG-20mer-N_3, **3c.** Because the ^{1}H NMR resonances of the end groups are overlaid by the polymer backbone, the ^{13}C NMR was used to characterize the end group transformation.[3]

Monodisperse PEGylated Cavitand, (4c). The octa-pentynoate cavitand (0.025 g, 10.8 mmol) was added to a 25 mL round bottom flask with 0.0839 g mPEG-20mer-N_3, and 0.031 g PMDETA. Also added was 0. 025 g CuBr. See ***General procedure of Cu(I) catalyzed "click" functionalization of cavitand***. 81.3 mg Mono-disperse PEGylated cavitand crude product was recovered; 90.90% yield. After Bio-bead column, the purified fraction is 16mg; 18.11% yield. ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 1.57 (br, 8H), 2.33 (br, 8H), 2.69 (br, 8H), 2.72 (t, 8H, J= 7.2 Hz), 2.96-3.00 (m, 16H), 3.34 (s, 24H), 3.50-3.52 (m, 16H), 3.56 (br, 40H), 3.60-3.67 (m, 540H), 3.80 (t, 24H, J= 5.2 Hz), 4.04 (br, 8H), 4.50-4.47 (m, 20H), 4.70-4.74 (m, 4H), 5.15 (br, 8H), 5.93 (br, 4H), 6.45-6.48 (d, 12H), 6.92-6.94 (d, 8H),

7.13-7.23 (m, 12H), 7.47-7.49 (br, 8H). MALDI-TOF MS: average *m/z* calculated for $[C_{464}H_{776}N_{24}O_{192}$ + Na$]^+$: 9786.16; observed: 9786.3. GPC: M_n=6400; PDI=1.05.

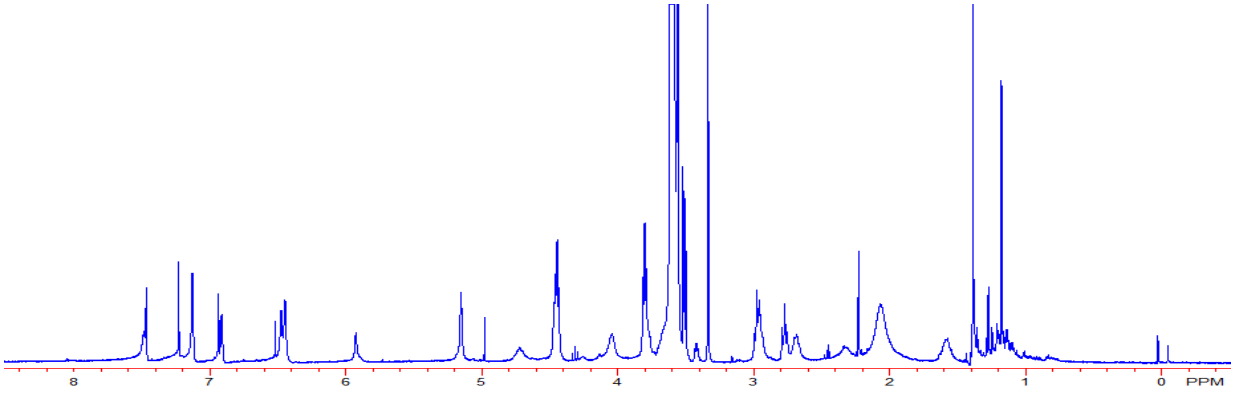


Figure SI-12. ^{1}H of monodisperse mPEG20mer grafted cavitand, **4c**.

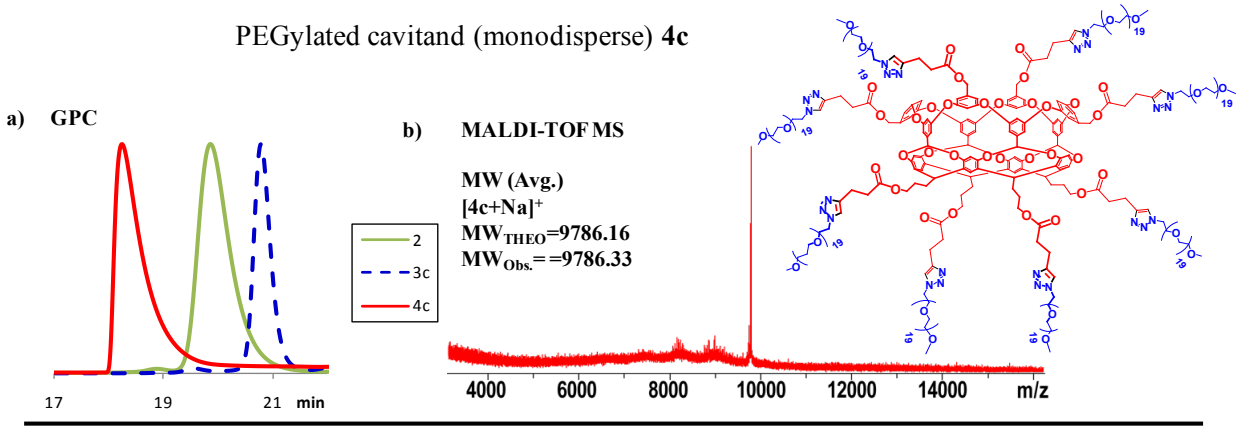
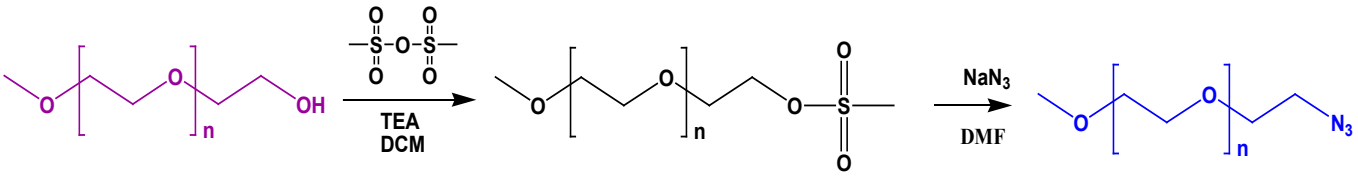


Figure SI-13. GPC trace **(a)** and MALDI-TOF MS spectrum **(b)** of monodisperse mPEG20mer grafted cavitand, **4c**.

PEG-OMs, (S2). A typical procedure of synthesis of PEG-Ms was previously reported.[4] PEG-OH (M_n=2000, 4g, 2mmol) was heated to 50^{o}C in oil bath and dried *in vacuo* for 12 h. It was cooled to room temperature before dissolved in 100 mL of dried dichloromethane. The solution was cooled to 0^{o}C in ice-water bath, and distilled triethylamine (1.53 ml, 11.0 mmol) and methanesulfonyl anhydride (1.74 g, 10 mmol) were sequentially slowly added. After stirring for 12 hours in room temperature under nitrogen, the mixture was filtered and sequentially washed three times with 100 mL of 1M $NaHSO_4$ solution, 100 mL of 1M $NaHCO_3$ solution and 50 mL of brine. The organic layer was dried over anhydrous $MgSO_4$,

filtered, and concentrated prior to precipitation from dichloromethane into 40 mL of cold ethyl ether. The product was isolated via filtration and dried *in vacuo*; 72% yield. ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 3.06 (s, 3H), 3.35 (s, 3H), 3.51-3.53 (m, 2H), 3.61-3.63 (br, 189H), 4.36-4.37 (m, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 37.91, 59.23, 61.80, 69.20, 69.52, 70.47, 72.08, 72.84. MALDI-TOF MS: average *m/z* observed: 2257.91; PDI: 1.01. GPC: M_n=2800; PDI= 1.01.

PEG-N_3, (3d). A typical procedure of synthesis of PEG-N_3 was previously reported.[5] PEG-Ms, **S2**, (2.00 g, 1.00 mmol) and sodium azide (0.33 g, 5.00 mmol) were separately heated to 50°C under vacuum for 12 h, and then cooled to room temperature. The PEG-Ms was dissolved in 25 mL of dried DMF, followed by the addition of sodium azide. The reaction was heated to 50°C and stirred under nitrogen for 12 hours. The reaction was dissolved in 50mL of DCM, and then washed three times with 100 mL of DI H_2O, and three times with 100 mL of brine. The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated prior to precipitation from dichloromethane into 20 mL of cold ethyl ether. The product was isolated via filtration and dried *in vacuo*; 78% yield: ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 1.99 (s, 2H), 3.35 (s, 3H), 3.35-3.37 (m, 4H), 3.62-3.64 (br, 189H). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 50.87, 59.27, 70.25, 70.78, 72.13. MALDI-TOF MS: average *m/z* for observed: 2104.91. GPC: M_n=2700; PDI=1.01.



S2 **3d**

Scheme S3. Synthesis of PEG-OMs, **S2**, and mPEG20mer-N_3, **3d**.

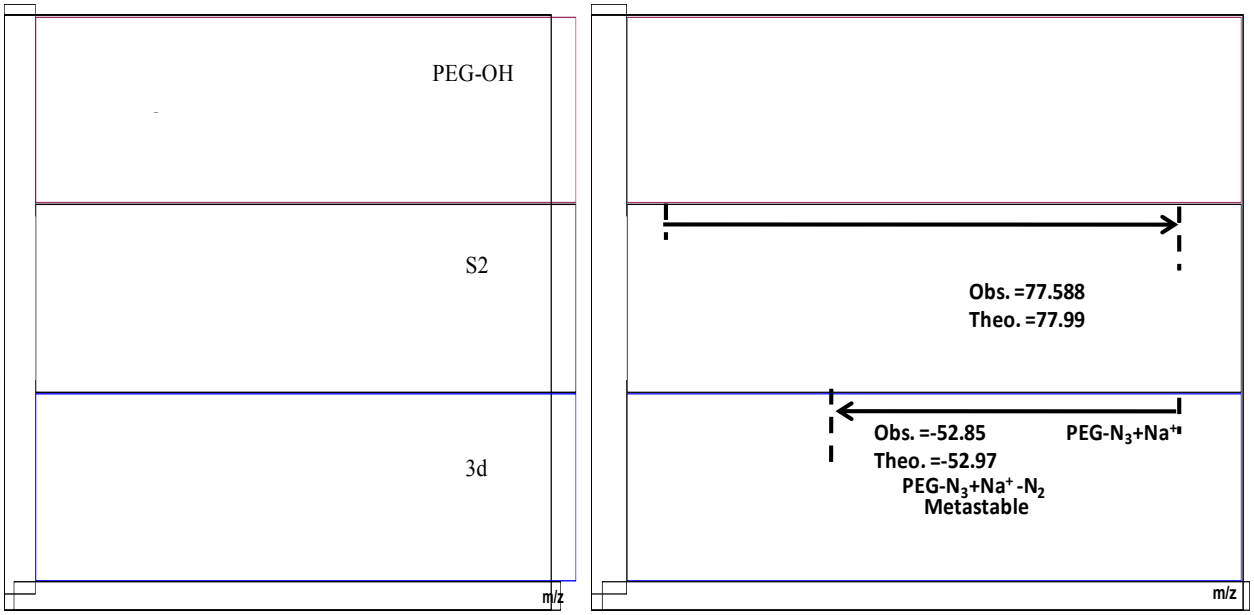


Figure SI-14. MALDI-TOF MS of the PEG methyl ether 2000, PEG-OMs, **S2**, and PEG-N_3,**3d**.

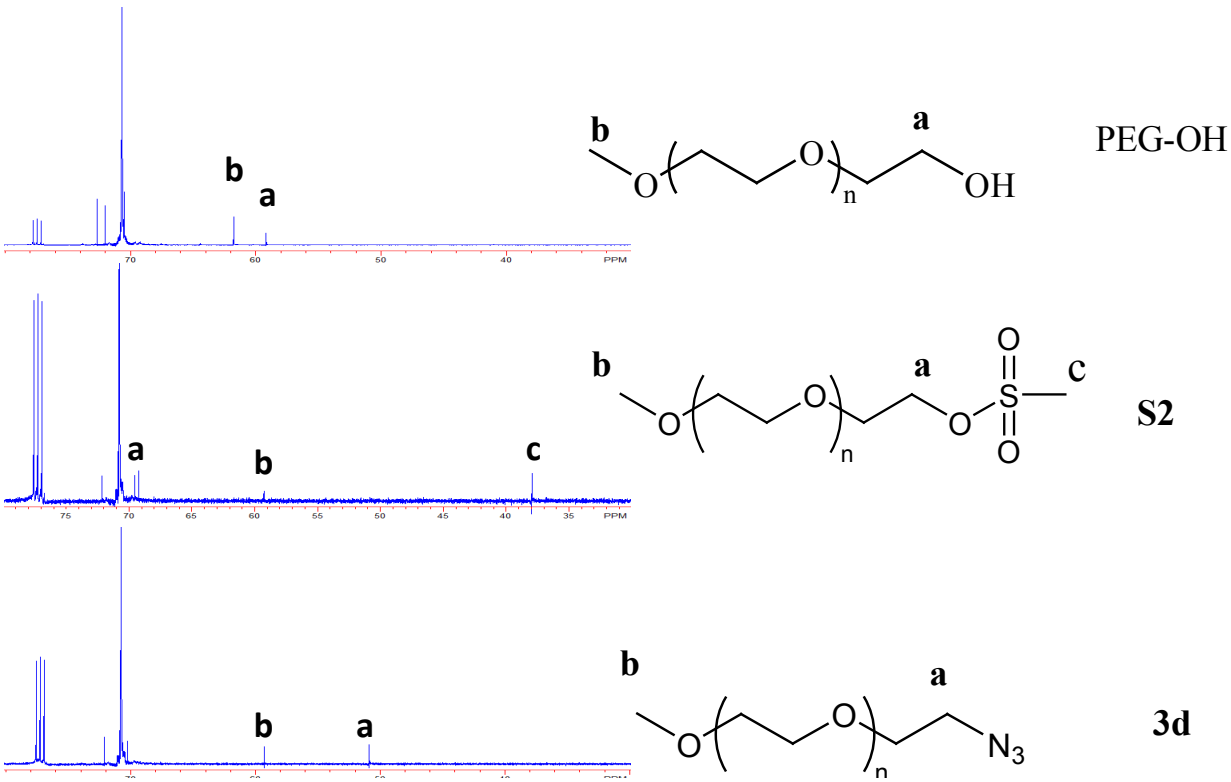


Figure SI-15. ^{13}C-NMR overlay of functionalized PEG methyl ether 2000.

PEGylated Cavitand, (4d). The octa-pentynoate cavitand (17 mg, 7.53 mmol) was added to a 50 mL round bottom flask with 120 mg PEG-N_3, and 20 mg PMDETA. Also added was 20 mg CuBr. See ***General procedure of Cu(I) catalyzed "click" functionalization of cavitand***. 110 mg PEGylated cavitand was recovered; 85.9% yield. With further purification by Bio-bead column, 20 mg of purified product was collected from 60 mg of crude product. ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 1.64 (b, 8H), 2.36 (b, 8H), 2.72 (t, 4H, J= 7.6 Hz), 2.82 (t, 4H, J= 7.6 Hz), 2.99-3.02 (m, 16H), 3.38 (s, 24H), 3.53-3.56 (m, 16H), 3.61 (s, 40H), 3.65-3.66 (m, 1600H), 3.81-3.82 (m, 32H), 3.85 (t, 24H, J= 5.2 Hz), 4.09 (b, 8H), 4.47-4.52 (m, 20H), 4.78 (b, 4H), 5.20 (s, 8H), 5.98 (s, 4H), 6.51 (s, 12H), 6.96 (s, 4H), 7.17 (s, 8H), 7.27 (s, 4H), 7.50 (s, 4H), 4.52 (s, 4H). MALDI-TOF MS: average *m/z* calculated for $[C_{912}H_{1664}N_{24}O_{430} + Ag]^+$: 19,900; observed: 19000. GPC: M_n=16,000; PDI=1.14.

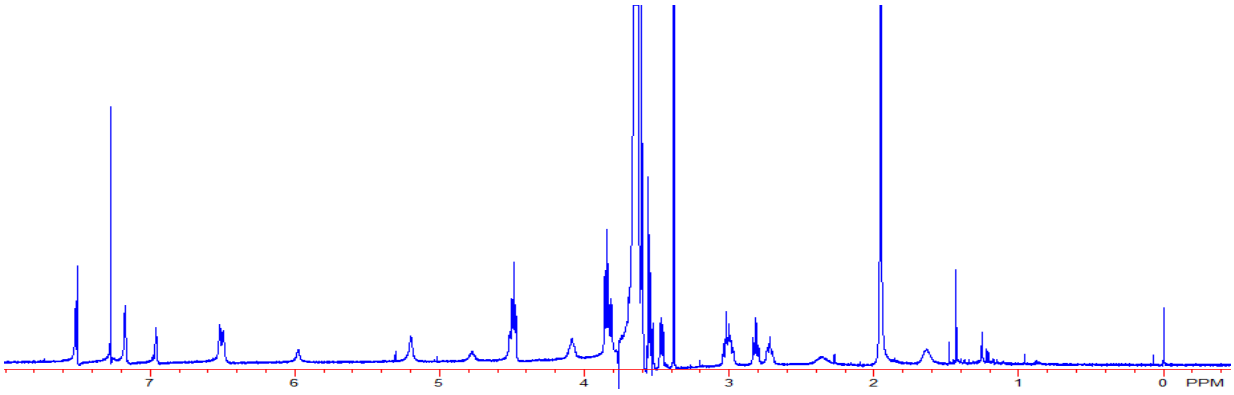


Figure S-I6. ^{1}H NMR of PEGylated cavitand, **4d**.

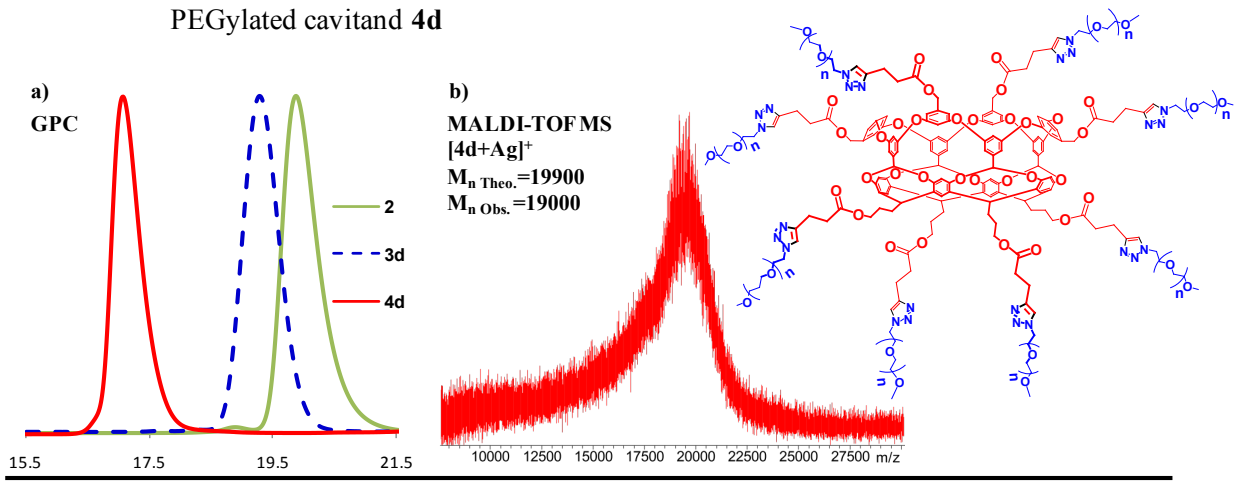


Figure SI-17. GPC trace (a) and MALDI-TOF MS spectrum (b) of PEGylated Cavitand, **4d**.

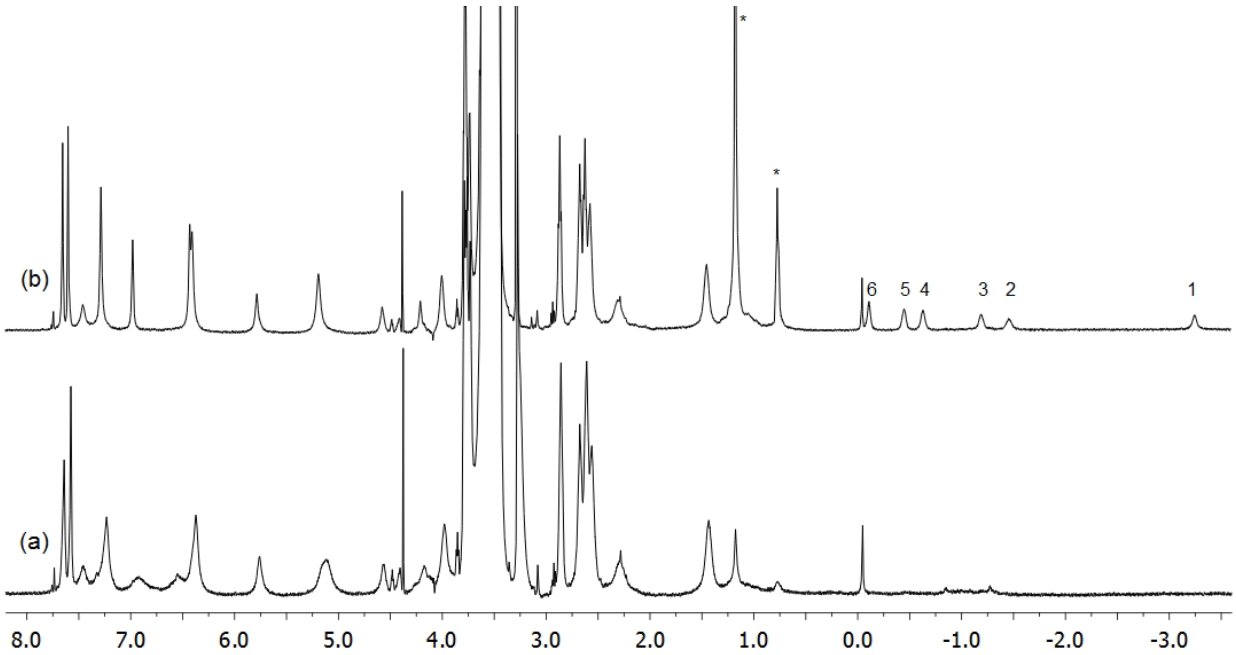


Figure SI-18. ^{1}H NMR of PEGylated cavitand, **4d**, in D_2O (a) and dodecane encapsulation in cavitand (b).

Poly(caprolactone)-grafted Cavitand, (4e). The octa-pentynoate cavitand, 6.50 mg (2.88 mmol), was added to a 100 mL round bottom flask with 51 mg (poly(caprolactone), and 12 mg PMDETA. Also added was 10 mg CuBr and 1.5 mg Cu. See ***General procedure of Cu(I) catalyzed "click" functionalization of cavitand***. Following precipitating and drying, 48 mg caprolactone-grafted cavitand

was recovered; 91% yield. ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 1.26-1.36 (m, 320H), 1.52-1.61 (m, 648H), 2.19-2.27 (m, 320H), 2.65-2.72 (b, 16H), 2.92 (b, 16H), 3.54-3.58 (t, 16H, J= 8 Hz), 3.99 (t, 320H, J= 8 Hz), 4.16 (t, 16H, J= 8 Hz), 4.29 (b, 16H), 4.42 (b, 16H), 4.95 (s, 8H), 5.11 (b, 8H), 5.69 (s, 4H), 6.43 (m, 12H), 6.90 (s, 4H), 7.09 (m, 12H), 7.28 (b, 4H), 7.34 (b, 4H). MALDI-TOF MS: average *m/z* calculated for $[C_{1120}H_{1760}N_{24}O_{369} + Na]^+$: 9786.3: 21,300; observed: 20,600. GPC: M_n=21,000; PDI=1.14.

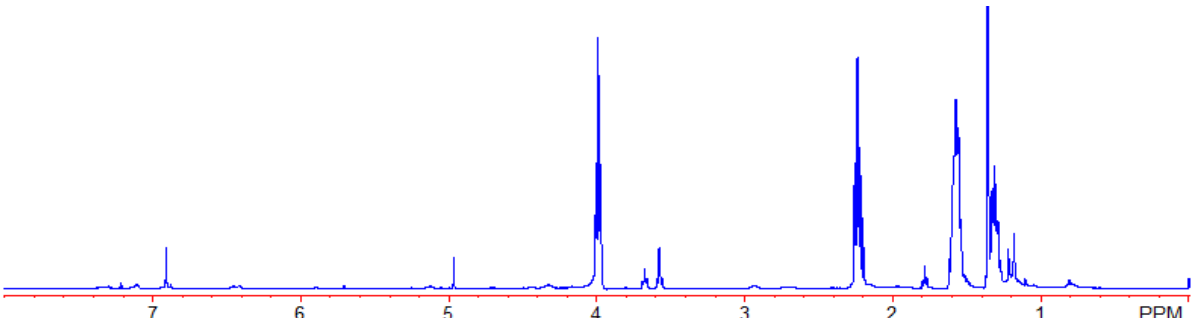


Figure SI-19. ^{1}H NMR of poly(caprolactone)-grafted cavitand, **4e**.

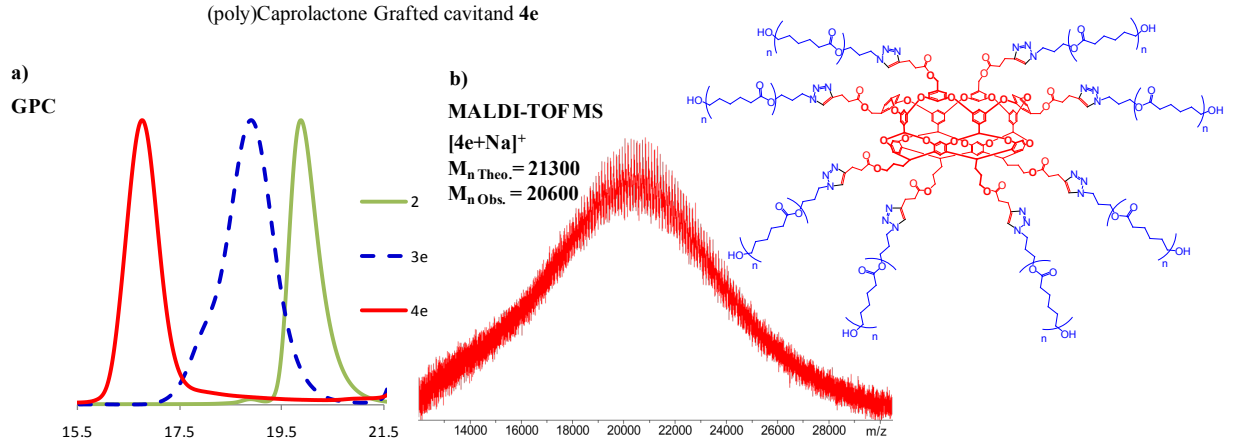


Figure SI-20. GPC trace (a) and MALDI-TOF MS spectrum (b) of (poly)Caprolactone grafted Cavitand, **4e**.

Poly(*N*-Acylethylenimine) (PNAI)-grafted Cavitand, (4f). The octa-pentynoate cavitand (4.6 mg, 2.04 mmol) was added to a 25 mL round bottom flask with 20 mg PNAI, and 10 mg PMDETA. Also added was 4.70 mg CuBr and 0.50 mg Cu. ***See General procedure of Cu(I) catalyzed "click" functionalization***

of cavitand. Following precipitating and drying, 14 mg crude product was recovered; 45% yield. GPC: M_n=5363; PDI=1.03.

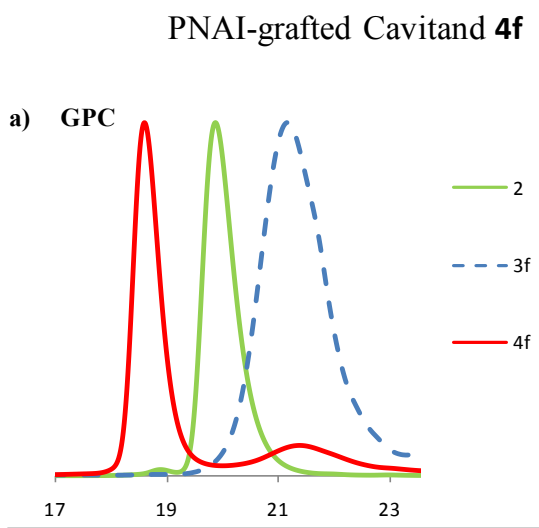


Figure SI-21. GPC trace of PNAI-grafted Cavitand, **4f**.

Polystyrene (PS)-grafted Cavitand, (4g). The octa-pentynoate cavitand (4.6 mg) was added to a 25 mL round bottom flask with 34 mg PS, and 5.70 g PMDETA. Also added was 4.7 mg CuBr and 0.50 mg Cu. ***See General procedure of Cu(I) catalyzed "click" functionalization of cavitand.*** Following precipitating and drying, 14 mg crude product was recovered; 41% yield. GPC: M_n=9151; PDI= 1.34.

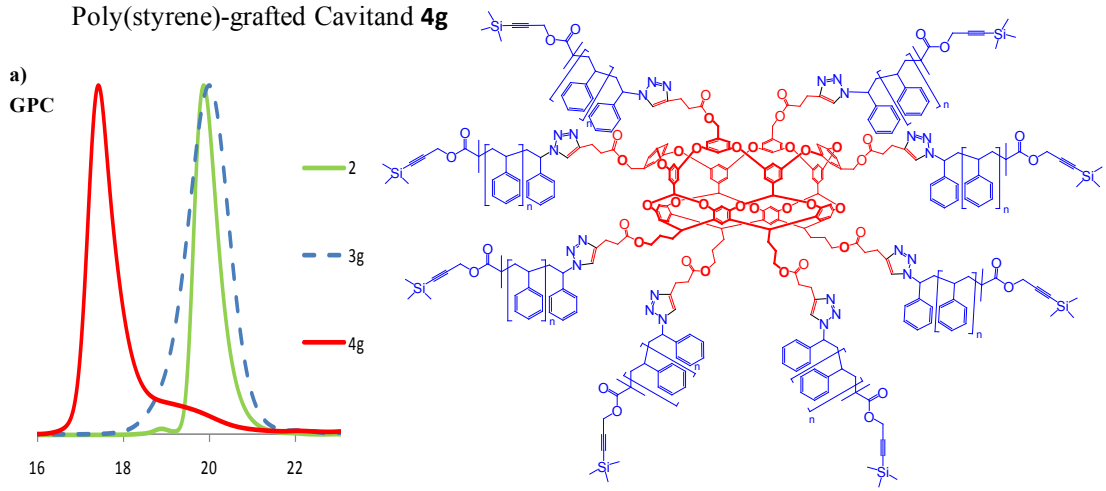


Figure SI-22. GPC trace (a) and MALDI-TOF MS spectrum (b) of poly(styrene)-grafted Cavitand, **4g**.

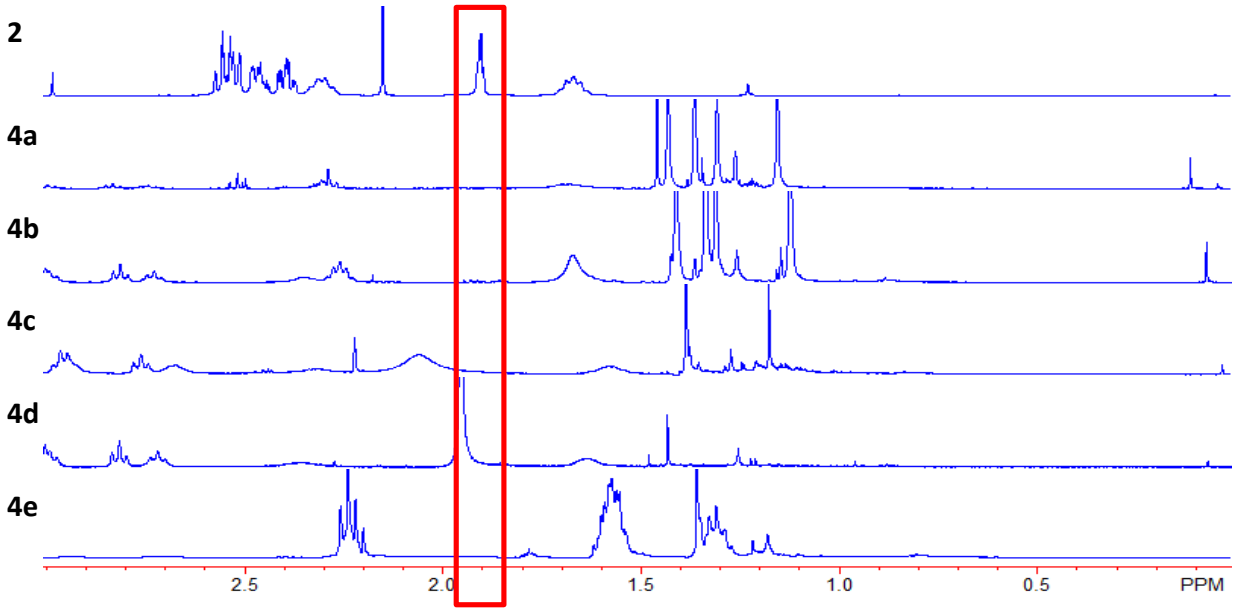


Figure SI-23. ^{1}H NMR of cavitand, **2**, and the grafted side-chains, **4a-e**, identifying the disappearance of acetylene proton. The disappearance of the terminal acetylene proton could be used to confirm the near quantitative grafting of the chain to the cavitand surface using the "click" approach.

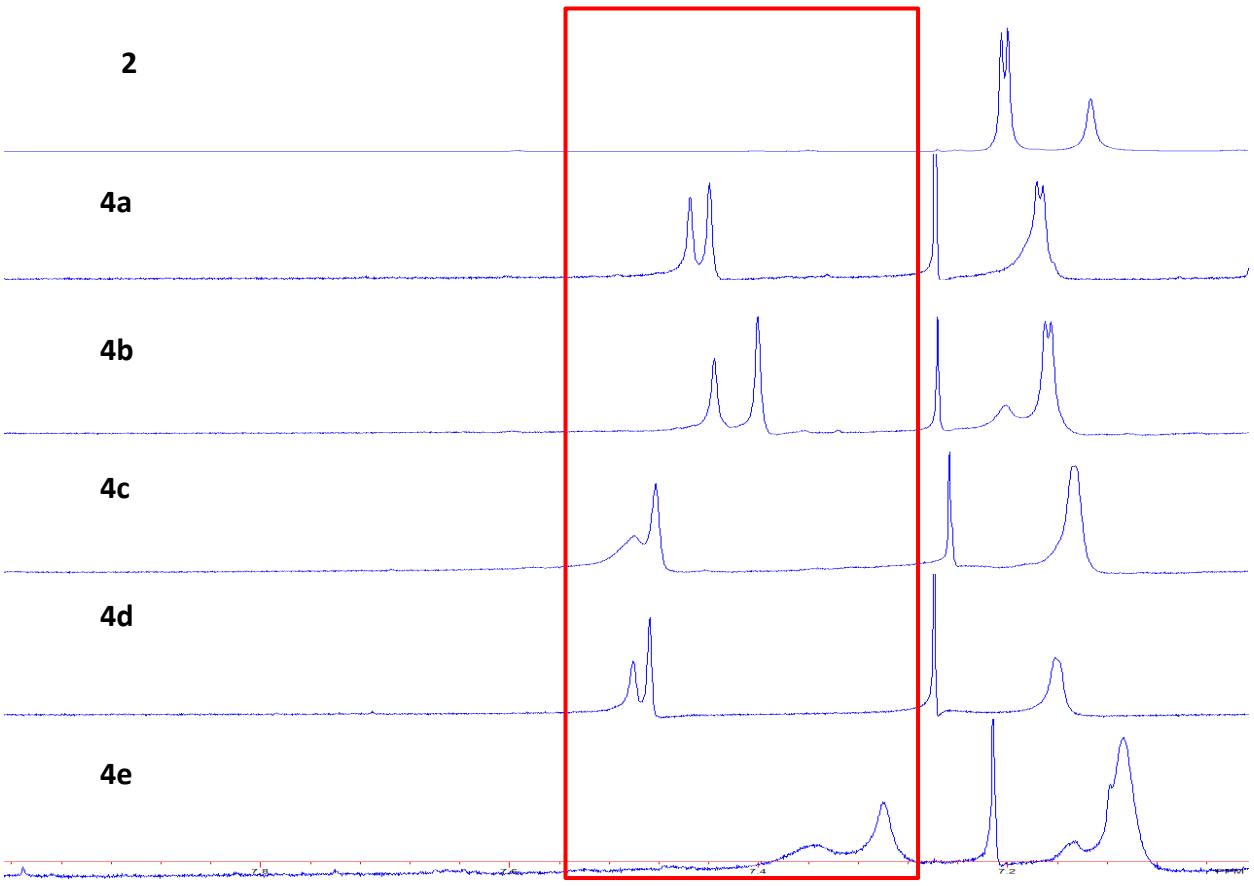


Figure SI-24. [1]H-NMR of cavitand, **2**, and the grafted side-chains, **4a-e**, identifying the appearance of triazole proton. The appearance of the triazole proton was used to further confirm the near quantitative grafting of the polymeric chains onto the cavitand surface using the "click" approach.

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[2] Heyes, J.; Hall, K.; Tailor, V.; Lenz, R.; MacLachlan, I. *J. Controlled Release* **2006**, *112*, 280-290.
[3] Gao, H.; Matyjaszewski, K. *J. Am. Chem. Soc.*, **2007,** *129,* 6633-6639.
[4] Heyes, J.; Hall, K.; Tailor, V.; Lenz, R.; MacLachlan, I. *J. Controlled Release* **2006**, *112*, 280-290.
[5] Gao, H.; Matyjaszewski, K. *J. Am. Chem. Soc.*, **2007,** *129,* 6633-6639.