Supporting Information

Dendritic Star Polymers for Efficient DNA Binding and Stimulus-Dependent DNA Release

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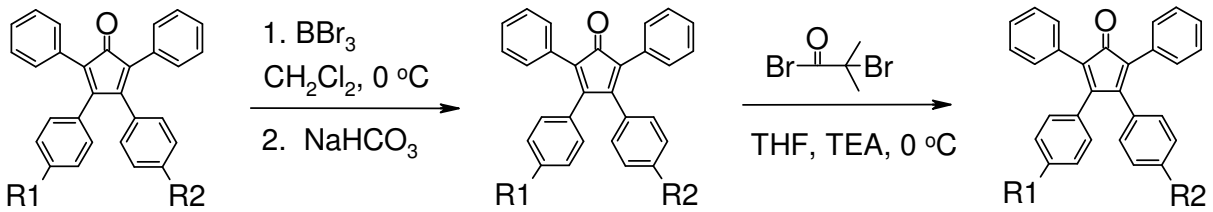
Materials and Methods

1. Synthesis of asymmetrical cyclopentadienone CP-OCOC$(CH_3)_2$Br (1a)



CP-OMe, R_1=H, R_2=OMe
CP-(OMe)$_2$, R_1= R_2=OMe

CP-OH, R_1=H, R_2=OH
CP-(OH)$_2$, R_1=R_2=OH

1a. R_1=H, R_2=OCOC$(CH_3)_2$Br
1b. R_1= R_2=OCOC$(CH_3)_2$Br

Scheme S1. Functionalization of asymmetrical cyclopentadienone CP-OCOC$(CH_3)_2$Br (**1a**) and symmetrical cyclopentadienone CP-(OCOC$(CH_3)_2$Br)$_2$ (**1b**).

Boron tribromide (1M in CH_2Cl_2, 3 mL) was dropped slowly into the solution of **CP-OMe** (1.8 g, 4.3 mmol) in CH_2Cl_2 (20 mL) under argon at 0 °C. After stirring for 5 h, the reaction was quenched with ice-water at 0 °C. The reaction mixture was diluted in ethyl acetate (80 mL) and washed by concentrated sodium hydrocarbonate and brine for two times (80 mL). The organic phase was collected and dried over magnesium sulfate. The solvents were removed in vacuum, and the crude product was purified by column chromatography (silica gel, CH_2Cl_2) to yield pure product 3-(4-hydroxyphenyl)-2,4,5-triphenylcyclopenta-2,4-dienone (**CP-OH**, 1.2 g, 69%) as a dark powder.

^{1}H-NMR: (250 MHz, d_6-DMSO, 303K): δ (ppm) = 9.78 (s, 1H, OH), 7.30-7.13 (m, 13H, aromatic H), 7.00 (d, J=7.5 Hz, 2H, aromatic H), 6.71 (d, J=8.5 Hz, 2H, aromatic H), 6.60 (d, J=8.5 Hz, 2H, aromatic H); ^{13}C-NMR (75 MHz, d_6-DMSO, 303K): δ (ppm) = 199.7, 157.9, 155.1, 154.3, 132.9, 131.0, 130.6, 129.8, 129.7, 128.9, 128.5, 127.9, 127.4, 127.2, 125.1, 123.3, 122.8, 114.9. FD-Mass spectra (8 kV): m/z [%]: 401 (100%) Calcd. for $C_{29}H_{20}O_2$ (400.5).

2-Bromo-2-methylpropionyl bromide (1.2 g, 5.28 mmol) was added dropwise into the solution of compound (**CP-OH,** 1.1 g, 2.75 mmol) in dry tetrahydrofuran (50 mL) and triethylamine (5 mL) at 0 °C. After stirring for 6 hours, the reaction was quenched with methanol in ice bath. After removing the solvent, the crude product was purified by flash chromatography (silica gel, CH_2Cl_2/petroleum ether (1:1)) to afford desired product **CP-OCOC(CH$_3$)$_2$Br** (**1a**, 1.35 g, 89%) as a dark red powder.

^{1}H-NMR: (250 MHz, CD_2Cl_2, 303K): δ (ppm) = 7.22-7.10 (m, 13H, aromatic H), 6.92-6.80 (m, 6H, aromatic H), 1.94 (s, 6H; CH_3); ^{13}C-NMR (75 MHz, CD_2Cl_2, 303K): δ (ppm) = 200.5, 170.3, 154.9, 153.6, 151.2, 133.5, 131.4; 131.1, 131.0, 130.5, 129.7, 128.9, 128.5, 128.0, 127.9, 126.3, 126.0, 121.1, 56.0, 30.8. FD-Mass spectra (8 kV): m/z [%]: 550 (100%) Calcd. for $C_{33}H_{25}BrO_3$ (549.5).

2. Synthesis of functional symmetrical cyclopentadienone CP-(OCOC(CH$_3$)$_2$Br)$_2$ (1b)

Boron tribromide (1 M in CH_2Cl_2, 5 mL) was dropped slowly into the solution of **CP-(OMe)$_2$** (4.44 g, 10.0 mmol) in CH_2Cl_2 (20 mL) under argon at 0 °C. After stirring for 5 h, the reaction was quenched with ice-water at 0 °C. The reaction mixture was diluted in ethyl acetate (80 mL) and washed by concentrated sodium hydrocarbonate and brine for two times (80 mL). The organic phase was collected and dried over magnesium sulfate. The solvents were removed in vacuum, and the crude product was purified by column chromatography (silica gel, CH_2Cl_2/acetone (2:1)) to yield pure product 3-(4-hydroxyphenyl)-2,4,5-triphenylcyclopenta-2,4-dienone **CP-(OH)$_2$** (2.57 g, 62%) as a dark powder.

^{1}H-NMR (250 MHz, d_6-DMSO, 303K): δ (ppm) = 9.78 (s, 2H, OH), 7.30-7.10 (m, 10H, aromatic H), 6.73 (d, J=8.5 Hz, 4H, aromatic H), 6.63 (d, J=8.5 Hz, 4H, aromatic H).

^{13}C-NMR (300 MHz, d_6-DMSO, 303K): δ (ppm) = 199.7, 157.9, 154.7, 131.1, 131.7, 130.0, 129.6, 127.6, 127.1, 123.7, 123.0, 114.9. FD-Mass spectra (8 kV): m/z [%]: 417 (100%), Calcd. for $C_{29}H_{20}O_3$, m/z = 416.5.

2-Bromoisobutyryl bromide (366 mg, 16 mmol) was added dropwise into the solution of compound **CP-(OH)$_2$** (1.66 g, 4.0 mmol) in dry tetrahydrofuran (100 mL) and triethylamine (15 mL) at ice bath. After stirring for 6 hours, the reaction was quenched with methanol at 0 °C. The solvent was evaporated under reduced pressure and the residue was further purified by flash chromatography (silica gel, CH_2Cl_2/petroleum ether (1:1)) to give the desired product **CP-(OCOC(CH$_3$)$_2$Br)$_2$** (**1b**, 2.57 g, 90%) as a red powder.

^{1}H-NMR (250 MHz, CD_2Cl_2, 303K): δ (ppm) = 7.20-7.30 (m, 10H, aromatic H), 7.01 (s, 8H, aromatic H), 2.04 (s, 12H, CH_3); ^{13}C-NMR (75 MHz, CD_2Cl_2, 303K): δ (ppm) = 200.2, 170.2, 153.6, 151.3, 131.2, 131.0, 130.5, 128.4, 128.0, 121.6, 126.8, 56.0, 30.8. FD-Mass spectra (8 kV): m/z [%]: 715 (100%), Calcd. for $C_{37}H_{30}Br_2O_5$ (714.5).

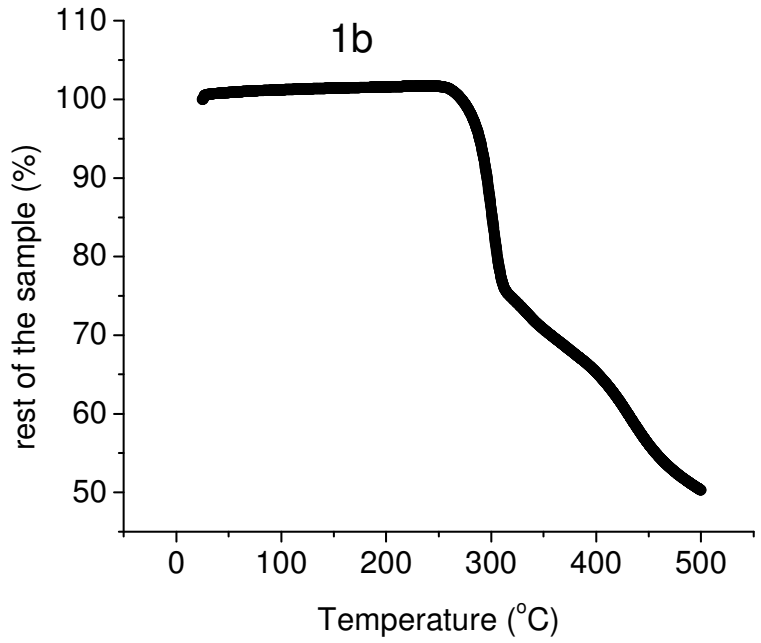
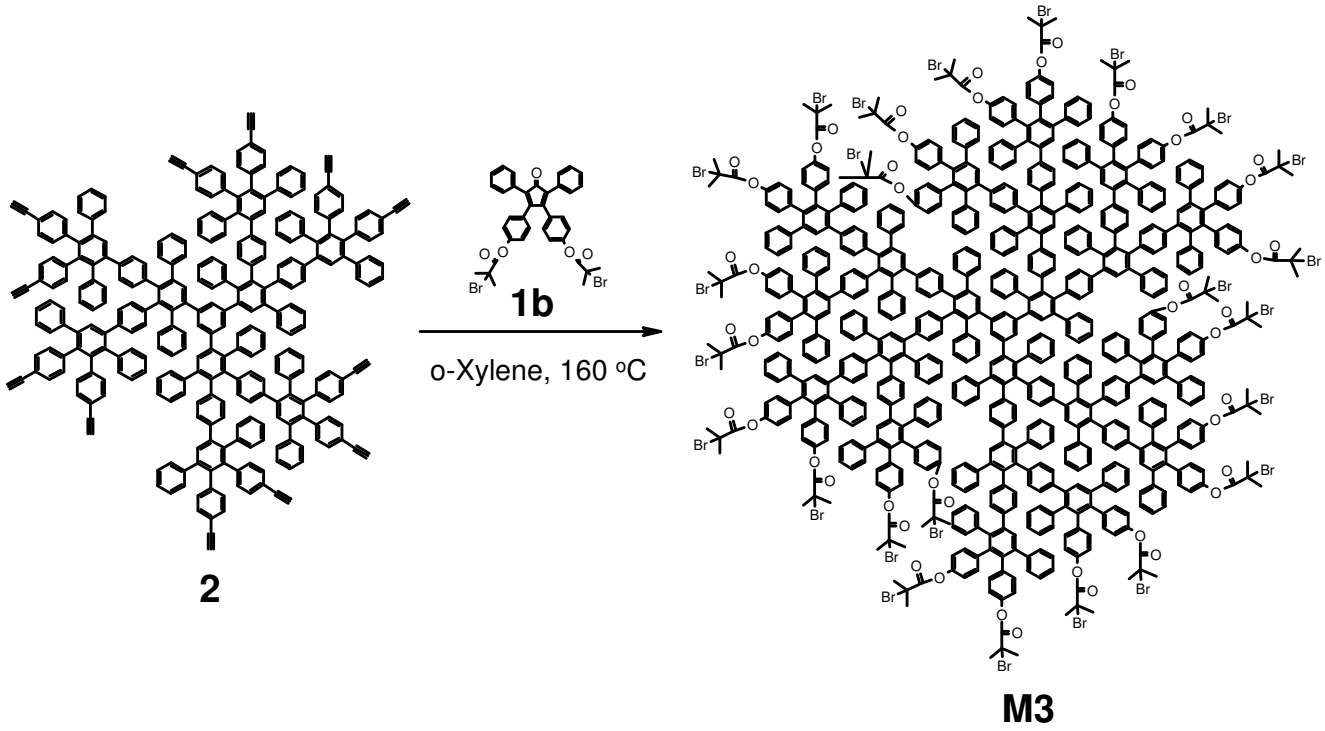


Figure S1. TGA curve of the modified cyclopentadienone (**1b**, CP-$(OCOC(CH_3)_2Br)_2$). Note: An exemplified thermogravimetric analysis (TGA) of **1b** showed decomposition above 250 °C thus indicating that these building blocks survive reaction conditions required for the *Diels-Alder* cycloaddition reaction (160 °C).

3. Synthesis of third-generation dendrimer core bearing twenty four 2-bromo-2-methylpropionic ester groups Tri-G_3-$(OCOC(CH_3)_2Br)_{24}$ (M3)



Scheme S2. Synthesis of third-generation macroinitiator (**M3**). Note: The functionaized symmetrical cyclopentadienone (**1b**) was used in approximate two-fold excess per ethynyl group and the excess of **1b** was recycled during the purification of desired product. *Via* this optimized procedure, the macroinitiator **M3** was produced in higher yield, shorter reaction times (2-3 hours), and with smaller amounts of reagents compared to previous experiments regarding the synthesis of the first and the second generation macroinitiators **M1** and **M2**.[1]

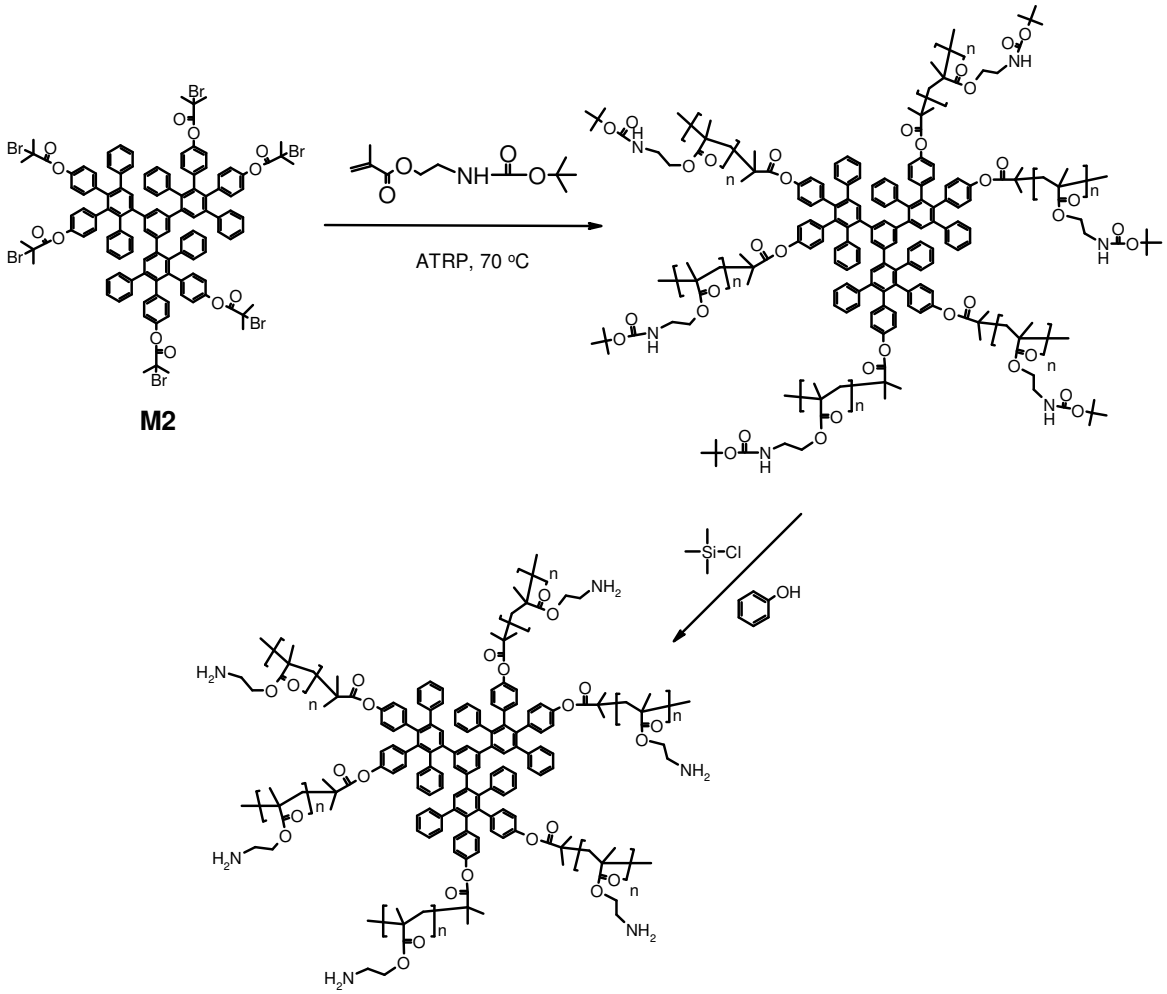
The Diels-Alder cycloaddition of second generation of dendrimer containing 12 ethynyl groups **2** (120 mg, 0.032 mmol) and functional symmetrical cyclopentadienone **1b** (548.7 mg, 0.768 mmol) was operated in 5 ml *o*-xylene in a microwave reactor at 160 °C (max. power 300 W, max. pressure 11 bar). The process was monitored by mass spectrometry. Column chromatography (silica gel, CH_2Cl_2) afforded the pure product **M3** (338 mg, yield 88.0%) as a colorless powder.

MS (MALDI-TOF): m/z (%) = 12029 (broad, $[M+H]^+$); (calcd for $C_{732}H_{546}Br_{24}O_{48}$: 12028). ^{1}H-NMR (300 MHz, CD_2Cl_2): δ ppm; 7.42-6.50 (m, 402H, aromatic H); 1.96, 1.95 (d, 144 H, CH_3); ^{13}C-NMR (75 MHz, CD_2Cl_2): δ ppm; 170.3, 170.2, 149.2, 149.0, 141.9, 141.3, 141.2, 141.1, 140.5, 140.1, 139.7, 139.0, 138.8, 138.6, 138.5, 138.4, 132.9, 132.8, 131.8, 131.2, 130.1, 128.0, 127.4, 126.8, 126.6, 120.0,

119.7, 56.1, 30.8. Elemental analysis (%) calcd for $C_{732}H_{546}Br_{24}O_{48}$: C 73.10, H 4.58; found: C 73.22, H 4.60.

4. ATRP polymerization

The general synthetic strategy of core-shell structures is depicted using the first-generation macroinitiator (**M1**) as an example (Scheme S3).



Scheme S3. Synthesis of first-generation water-soluble star polymer (M:Br(in macroinitiator):CuBr:DTB-bipy =200:1:1:1, 70 °C).

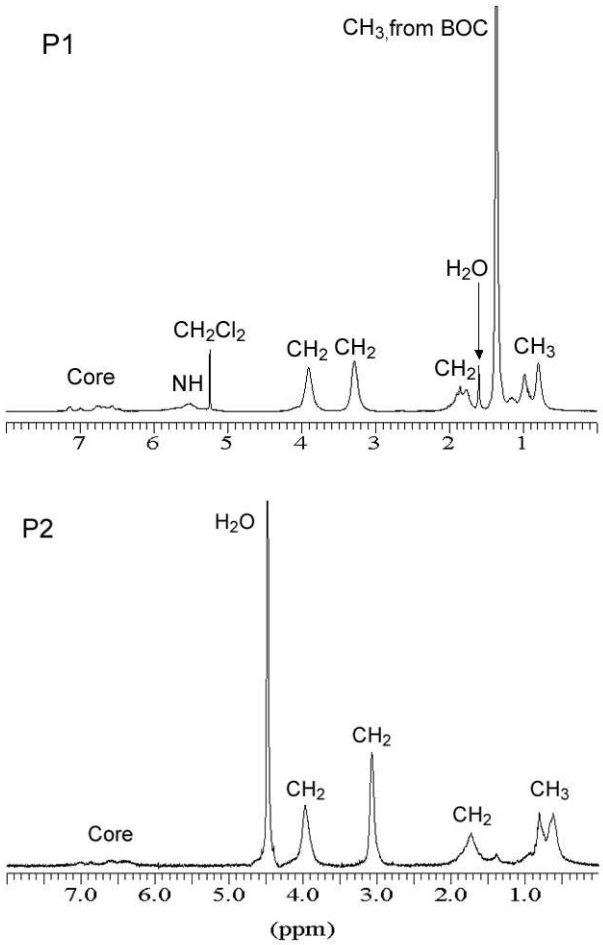


Figure S2. ^{1}H-NMR spectra of product **P1** (in CD_2Cl_2, 250 MHz, 298 K) and **P2** (in D_2O 250 MHz, 298 K); Note: By comparing ^{1}H-NMR spectrum of **P1** to that of **P2**, one can clearly observe that the methyl groups from BOC protective groups have been completely removed.

5. Equation Used for Fitting the ITC Data

The binding constant K_B for the complexation of a macromolecule M by the injected ligand L

$$M + X \rightleftharpoons MX$$

is described by the formula

$$K_B = \frac{\Theta}{(1-\Theta)\cdot[X]} \qquad (1)$$

where Θ represents the fraction of sites from macromolecule M occupied by ligand X, while [*X*] is the concentration of the free ligand.

The total concentration of the ligand $[X]_t$ can be expressed as function of the free and bound ligand molecules

$$[X]_t = [X] + n\Theta[M]_t \qquad (2)$$

where *n* stands for the stoichiometry, and $[M]_t$ is the bulk concentration of the macromolecule.

Combining the equations (1) and (2) gives

$$\Theta^2 - \Theta\left[1 + \frac{[X]_t}{n\cdot[M]_t} + \frac{1}{n\cdot K_B\cdot[M]_t}\right] + \frac{[X]_t}{n\cdot[M]_t} = 0 \qquad (3)$$

The heat absorbed or released Q of the solution in V_0 (cell volume) at fraction saturation Θ is

$$Q = n\cdot\Theta\cdot[M]_t\cdot\Delta H\cdot V_0 \qquad (4)$$

where ΔH is the enthalpy of ligand binding. Solving the quadratic equation (3) and then substituting this into equation (4) gives

$$Q = \frac{n\cdot[M]_t\cdot\Delta H\cdot V_0}{2}\left[1 + \frac{[X]_t}{n\cdot[M]_t} + \frac{1}{n\cdot K_B\cdot[M]_t} - \sqrt{\left(1 + \frac{[X]_t}{n\cdot[M]_t} + \frac{1}{n\cdot K_B\cdot[M]_t}\right)^2 - \frac{4[X]_t}{n\cdot[M]_t}}\right] \qquad (5)$$

The value of *Q* can be calculated (for any designated values of *n*, K_B, and ΔH) at the end of the i^{th} injection (called Q_i). The expression for *Q* in equation (5) only applies to the liquid contained in the cell volume V_0. Therefore, a correction was made for displaced volume during each injection (ΔV_i), that the displaced liquid contributes about 50% as much heat effect as an equivalent volume remaining in V_0.

The corrected expression for the heat released ΔQ_i during the ith injection is

$$\Delta Qi = Qi + \frac{dV_i}{V_0} \cdot \left[\frac{Qi + Q(i-1)}{2} \right] - Q(i-1) \qquad (6)$$

The process of fitting experimental data involves:

- initial guess of the n, K, and ΔH;
- calculation of ΔQi for each injection and comparison of these values with the measured heat for the corresponding experimental injection;
- improvement of the *n*, K_B, and ΔH values;
- iteration of the above procedure until no further improvement in fit occurs.

Reference:

1. Yin, M.; Bauer, R.; Klapper, M.; Müllen K. *Macromol. Chem. Phys.*, **2007**, *208*, 1646-1656.