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# Redox-sensitive dendrimersome assembled from amphiphilic Janus dendrimer for siRNA delivery

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## 1. Synthesis of dendron P2

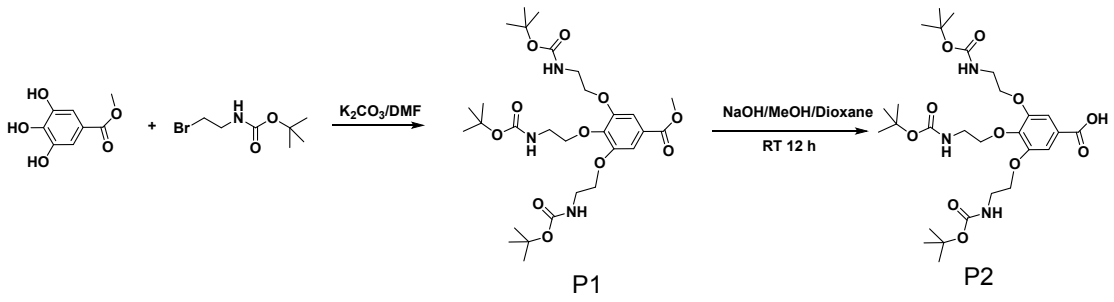


Figure S1. Synthesis procedure of the dendron P2.

### 1) Synthesis of 3,4,5-tris-(2-*t*-butoxycarbonylaminoethoxy)benzoic acid methyl ester (P1)

Methyl 3,4,5-trihydroxybenzoate (1.000g, 5.43 mmol), tert-butyl (2-bromoethyl)carbamate (3.640g, 16.30 mmol), and $K_2CO_3$ (7.500g, 54.30mmol) were added into a dried round-bottom flask. The reaction was conducted in 20 mL anhydrous DMF at 80°C for 24 h. Then, DMF was removed under reduced pressure, and DCM was added to dissolve the mixture. After filtration, the filtrate was collected and washed with $NaHCO_3$ and NaCl solution consecutively. The organic layer was collected and dried with $MgSO_4$. After filtration, the solution was concentrated and subject to column chromatography using ethyl acetate/hexane (1/9 to 1/1, v/v) as the eluent. The product was yellow solid with yield of 60%.

### 2) Preparation of 3,4,5-tris(2-((tert-butoxycarbonyl)amino)ethoxy)benzoic acid (P2)

3,4,5-tris-(2-*t*-butoxycarbonylaminoethoxy)benzoic acid methyl ester (0.500g) was dissolved in 4M NaOH:MeOH:Dioxane (1:1:14) solution, and stirred at room temperature for 12 h. $KHSO_4$ solution (1M) was added to adjust the pH of the solution to 2. Massive white solid precipitated out, collected and dried. Yield: 90%.

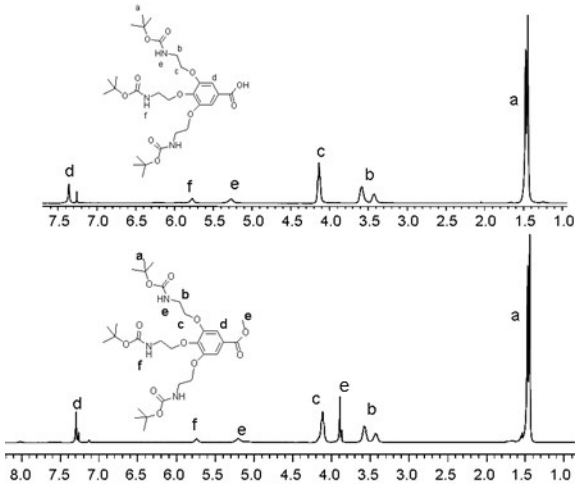


Figure S2. $^{1}$H NMR of dendron P2.

## 2. Preparation of hydrophobic dendron A2

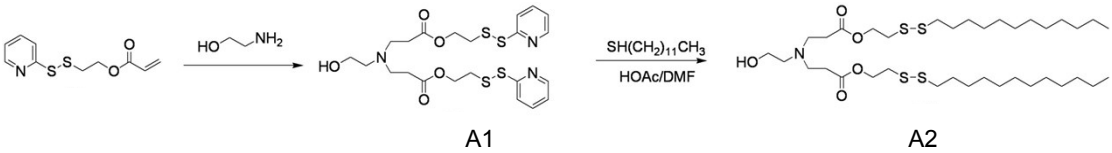


Figure S3. Synthesis procedure of the dendron A2.

The hydrophobic dendron (A2) was prepared. 2-(2-pyridyldithio)-ethyl acrylate (1.98 g, 8.22 mmol) and ethanolamine (0.20 g, 3.28 mmol) were mixed and reacted at room temperature overnight, then the temperature was increased to 50 °C, and further reacted for 48 h. After dissolving in an aliquot of methylene chloride (DCM), the mixture was precipitated into cold hexane/ethyl ether (1/1, v/v). The procedure was repeated three times to get A1. ESI-MS: (*m/z* = 544.17 $[M+H]^+$ and 565.17 $[M+Na]^+$).

Then, A1 was reacted with 1-dodecanethiol to obtain the hydrophobic dendron A2. A1 (1.00 g, 1.84 mmol) and 1-dodecanethiol (0.93 g, 4.60 mmol) were dissolved in 5 mL of anhydride *N,N*-Dimethylformamide (DMF). The reaction was conducted at room temperature for 5 h under the catalysis of glacial acetic acid (80 μL). After removal of DMF, the mixture was precipitated into DMF three times to obtain the raw product. The final purified product A2 was obtained by column chromatography using ethyl acetate/hexane (1/1, v/v) as the eluent. Yield: 41%. $^{1}$H NMR (400 MHz, $CDCl_3$), δ (ppm): 0.88 (t, 6H), 1.26 (s, 32H), 1.37 (m, 4H), 1.67 (m, 4H), 2.49 (t, 4H), 2.60 (t, 2H), 2.70 (t, 4H), 2.81 (t, 4H), 2.90 (t, 4H), 3.58 (t, 2H), 4.34 (t, 4H). ESI-MS: *m/z* = 726.26 $[M + H]^+$.

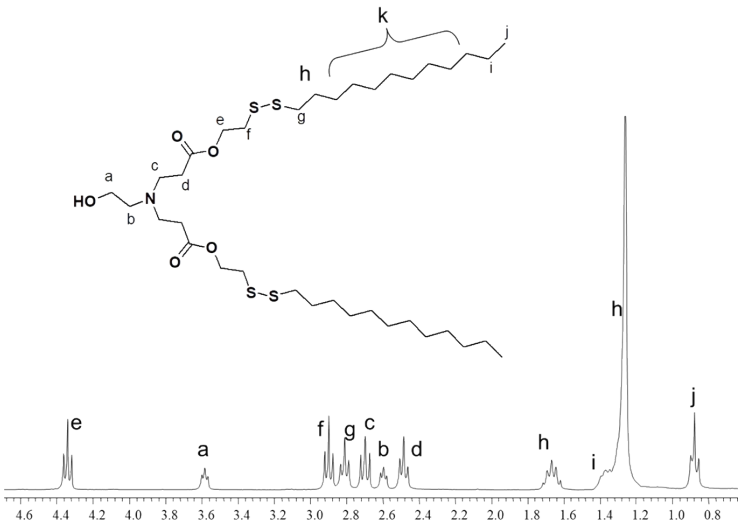


Figure S4. $^{1}$H NMR of dendron A2.

## 3. Synthesis of control Janus dendrimer (JD) without disulfide linker

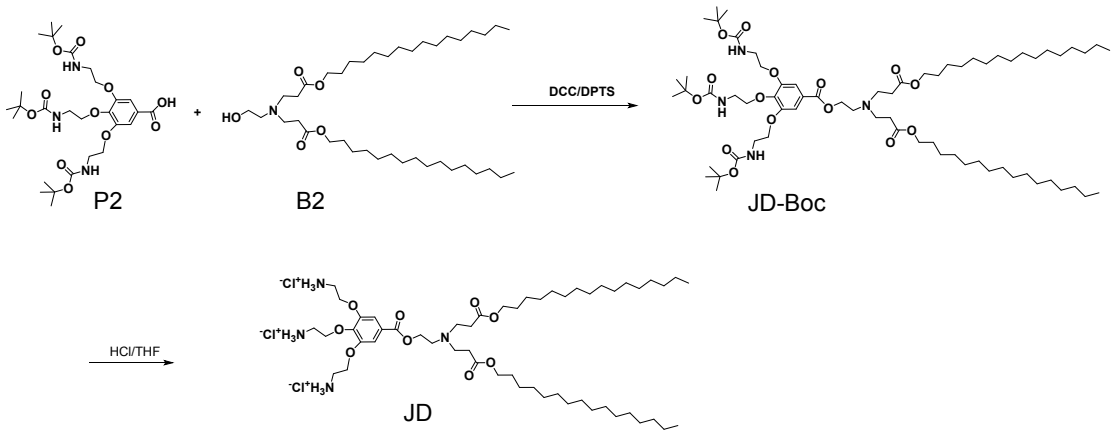


Figure S5. Synthesis procedure of JD.

The control Janus dendrimer (JD) without disulfide linker was synthesized similarly with ssJD except that replacing A2 with B2, in which B2 was synthesized by reacting ethanolamine with hexadecyl acrylate. All the reaction and purified procedures were the same with ssJD. The $^{1}$H NMR and ESI-MS results were shown below.

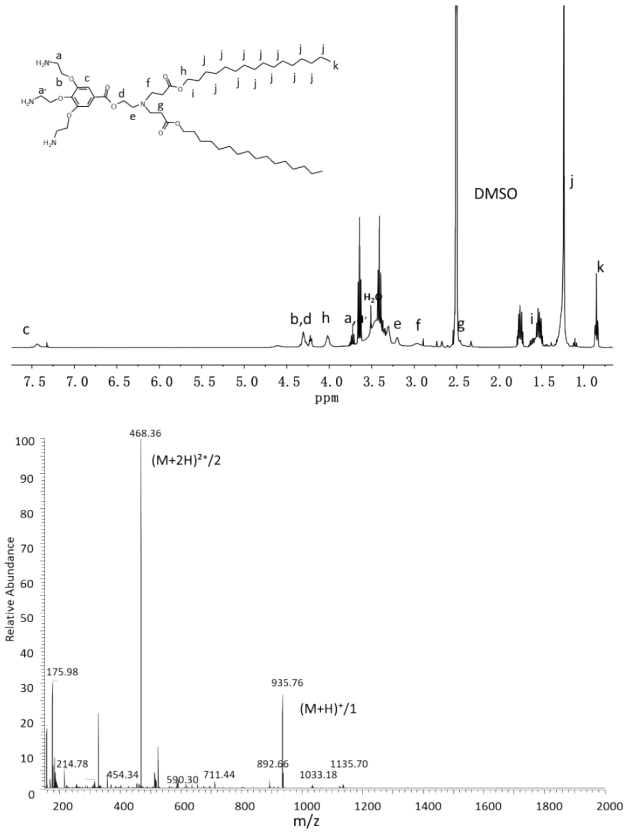


Figure S6. $^{1}$H NMR (top) and ESI-MS (bottom) of JD.