Electronic Supplementary Information

Facile In-Situ Fabrication of Orgaic-Inorganic Vesicular Hybrids

Driven by Assembly of Dendritic Amphiphiles: Site-Selective Encapsulation of Nanoparticles

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Materials and Measurements. All commercially available reagents were reagent grade and used without further purification. 1H and 13C NMR spectra were recorded from CDCl3 solution on Varian 200, JEOL JNM-AL400 and Bruker AM500 spectrometers. The purity of the products was checked by thin layer chromatography (TLC; Merck, silica gel 60). Gel permeation chromatography (GPC) measurements were conducted in THF and N,N’-dimethylacetamide (99.9 %) (98 : 2 volume ratio) using a Waters 401 instrument equipped with KF-802, KF-803, AT-G and AT-804S Shodex columns at a flow rate of 1.0 mL·min⁻¹. Microanalyses were performed with a Perkin Elmer 240 elemental analyzer at the Organic Chemistry Research Center, Sogang University, Korea. The compounds were purified by column chromatography (silica gel) and prep-HPLC (Japan Analytical Instrument). Matrix-assisted laser desorption/ ionization time-of-flight mass (MALDI-TOF MS) spectra were obtained on a Perceptive Biosystems Voyager-DE STR system, Korea. UV-Vis absorption spectra were obtained by using a Shimadzu UV-1800 spectrometer. The steady-state
fluorescence spectra were measured in a Perkin Elmer LS-55 fluorescence spectrophotometer. Dynamic light scattering (DLS) measurements were performed using a zeta-potential and particle-size analyzer ELSZ-2 (PhototOtsuka Electronics). Attenuated total reflection Fourier transform infrared (ATR-FTIR) spectra were obtained using a FTS-175C (Bio-Rad Laboratories, Inc). Thermogravimetric analysis (TGA) was performed using a Mettler-Toledo TGA/DSC 1. Fluorescence microscopy was performed using a Nikon Eclipse Ti-E microscope. The transmission electron microscopy (TEM) was performed at 200 kV using JEM-3011.

**Transmission electron microscopy (TEM).** The samples for TEM were prepared by drop-casting 5 μL aliquot of the solution onto a carbon coated copper grid which was placed on a piece of paper to get rid of excess solvent. The thin film of 1 and 2 was dried for at least 6 h. The images were obtained on JEM-3010 operating at 200 or 300 kV accelerating voltage, using the images acquired with a ORIUS-SC 600 CCD camera (Gatan, Inc. Warrendale, PA).

**Cryogenic transmission electron microscopy (cryo-TEM).** The cryo-TEM experiments were performed with a thin film of solution (5 μL) transferred to a lacey supported grid. The thin solution films were prepared under controlled temperature and humidity conditions within a custom-built environmental chamber in order to prevent evaporation of solvent from sample solution. The excess liquid was blotted with filter paper for 1-2 seconds, and the thin aqueous films were rapidly vitrified by plunging them into liquid ethane. The grid was transferred, on a Gatan 626 cryo-holder, using a cryo-transfer device. After that they were transferred to a JEM-3010. Direct imaging was carried out at a temperature of approximately -175 °C and with a 200 kV accelerating voltage, using the images acquired with a SC 1000 CCD camera (Gatan, Inc.; Warrendale, PA).

**Preparation of vesicles.** Self-organized samples were prepared by dissolving codendrimers 1 and 2 in a solvent, respectively. The samples were left in a 15 mL glass vial and sealed with parafilm at room temperature for a day to allow aging.

**Incorporation of inorganic NPs.** All solubilization procedures were performed in the dark. The surfactant-capped nanoparticles (CdSe-TOPO or CdSe/ZnS MUA NPs) were encapsulated during the formation of self-assembled aggregates. For example, 100 μL of a solution of the codendrimer in chloroform (10 mg/mL) was mixed with 50 μL of a solution of the inorganic nanoparticles in chloroform (5 mg/mL) under vigorous stirring, and then chloroform was evaporated by gentle shaking. The addition of 1 mL deionized water or n-hexane leads to swelling and the formation of vesicle. The resulting solution was annealed at room temperature for at least a day. Unencapsulated QD particles were removed through centrifugation and
subsequent dialysis for successful imaging of QDs-loaded vesicles. The unencapsulated QDs were removed by centrifuging the samples at 3200 rpm for 10 min. Since the free QDs were not stable in aqueous solution or n-hexane, they tend to aggregates and can be easily separated at low centrifuge speed. After following the centrifugation, unencapsulated QDs were further removed by dialysis using high molecular weight cutoff (50 kDa) tubing.\textsuperscript{S1}

**Synthesis.** The synthesis of block codendrimers 1 and 2 was performed according to the procedures described previously.\textsuperscript{S2}

![Scheme S1. Synthesis of block codendrimers 1 and 2 via stepwise click reactions.](image)

**Synthesis of compound 5.** Compounds were synthesized using the same procedure. A representative example is described for 5a. 1-Bromo-3,5-diethynylbenzene 3 (0.38 g, 1.85 mmol), 3,4,5-tridodecyloxybenzyl azide 4a (2.8 g, 4.08 mmol), CuSO\textsubscript{4}·5H\textsubscript{2}O (0.1 g, 0.4 mmol) and sodium ascorbate (0.1 g, 0.5 mmol) were dissolved in 30 mL of acetonitrile, 30 mL of THF and 2 mL of deionized water. The reaction mixture was stirred for 24 h at room temperature. After terminating the reaction, the solvent was removed by a rotary evaporator. The resulting mixture was extracted with deionized water and dichloromethane. The dichloromethane layer was washed with deionized water, and dried over MgSO\textsubscript{4}. After removing dichloromethane by a rotary evaporator, the resulting compound was purified by sequential silica gel column chromatographies from dichloromethane to hexane:ethyl acetate = 4:1 mixture as the eluent, to yield 1.8 g (60 %) of a dark brown solid.
5a; ¹H NMR (CDCl₃, δ, ppm): 8.17 (s, Ar-H), 7.93 (s, Ar-H), 7.75 (s, H-triazole), 6.51 (s, benzyl-H), 5.46 (s, CHCH₂N), 3.93-3.97 (m, CH₂OAr), 1.75-1.81 (m, CH₂CH₂OAr), 1.43-1.49 (m, CH₂(CH₂)₃CH₃), 1.27-1.43 (m, CH₂ (CH₂)₃CH₃), 0.89 (t, J = 7.0 Hz, (CH₂)₈CH₃). Anal. Calcd for C₉₆H₁₆₃BrN₆O₆: C, 73.10; H, 10.42; N, 5.33, Found: C, 73.14; H, 10.37; N, 5.29 %. Mₘ_/ₘₙ = 1.04 (GPC).

5b; ¹H NMR (CDCl₃, δ, ppm): 8.20 (s, Ar-H), 8.12 (s, Ar-H), 7.73 (s, H-triazole), 6.49 (s, benzyl-H), 5.45 (s, CHCH₂N), 3.90-3.95 (m, CH₂OAr), 1.75-1.82 (m, CH₂(CH₂)₃CH₃), 1.27-1.49 (m, CH₂(CH₂)₅CH₃), 0.87 (t, J = 6.4 Hz, (CH₂)₇CH₃). Anal. Calcd for C₇₂H₁₁₅BrN₆O₆: C, 69.70; H, 9.34; N, 6.77, Found: C, 70.17; H, 9.44; N, 6.28 %. Mₘ_/ₘₙ = 1.01 (GPC).

Synthesis of compound 6. Compound 5a (1.8 g, 1.18 mmol), trimethylsilyl acetylene (0.76 mL, 5.54 mmol), copper(I) iodide (0.0067 g, 0.035 mmol), and PdCl₂(PPh₃)₂ (0.012 g, 0.017 mmol) were dissolved in 20 mL of dry triethylamine. The mixture was heated at 120 °C for 60 h. After cooling to room temperature, the solvent was removed by a rotary evaporator. Then the mixture was extracted with deionized water and dichloromethane. The dichloromethane layer was washed with deionized water several times, and dried over MgSO₄. The solvent was removed by a rotary evaporator, and the crude product was then purified by sequential silica gel column chromatographies from dichloromethane to ethyl acetate:hexane = 1:4 mixture as the eluent, to yield 1.6 g (91 %) of a dark brown solid.

6a; ¹H NMR (CDCl₃, δ, ppm): 8.22 (s, Ar-H), 7.86 (s, Ar-H), 7.73 (s, H-triazole), 6.49 (s, benzyl-H), 5.44 (s, CHCH₂N), 3.93-3.97 (m, CH₂OAr), 1.23-1.78 (m, ArOCH₂(CH₂)₁₀CH₃), 0.89 (t, J = 7.0 Hz, (CH₂)₁₀CH₃), 0.24 (s, Si(CH₃)₃). Mₘ_/ₘₙ = 1.01 (GPC).

6b; ¹H NMR (CDCl₃, δ, ppm): 8.22 (s, Ar-H), 7.87 (s, Ar-H), 7.74 (s, H-triazole), 6.49 (s, benzyl-H), 5.45 (s, CHCH₂N), 3.93-4.00 (m, CH₂OAr), 1.20-1.90 (m, ArOCH₂(CH₂)₁₀CH₃), 0.87 (t, J = 6.4 Hz, (CH₂)₁₀CH₃), 0.24 (s, Si(CH₃)₃). Mₘ_/ₘₙ = 1.03 (GPC).

Synthesis of compound 7. Compound 6a (1.6 g, 1.00 mmol) and K₂CO₃ (1.38 g, 10.0 mmol) were dissolved in 20 mL of dry THF and methanol. The reaction mixture was stirred for 4 h at room temperature under N₂ atmosphere. Then the mixture was extracted with deionized water and dichloromethane, and dried over MgSO₄. The solvent was removed by a rotary evaporator, and the crude product was then purified by sequential silica gel column chromatographies from dichloromethane to ethyl acetate:hexane = 1:4 solvent mixture as the eluent, to yield 1.5 g (98 %) of a yellowish solid.
7a; $^1$H NMR (CDCl$_3$, $\delta$, ppm): 8.24 (s, Ar-H), 7.88 (s, Ar-H), 7.74 (s, H-triazole), 6.49 (s, benzyl-H), 5.44 (s, CHCH$_2$N), 3.93-3.97 (m, CH$_2$OAr), 3.10 (s, Ar-C≡CH), 1.23-1.78 (m, ArOCH$_2$(CH$_2$)$_{10}$CH$_3$), 0.89 (t, $J = 7.0$ Hz, (CH$_2$)$_{10}$CH$_3$).

7b; $^1$H NMR (CDCl$_3$, $\delta$, ppm): 8.24 (s, Ar-H), 7.88 (s, Ar-H), 7.74 (s, H-triazole), 6.49 (s, benzyl-H), 5.44 (s, CHCH$_2$N), 3.93-4.00 (m, CH$_2$OAr), 3.11 (s, Ar-C≡CH), 1.20-1.90 (m, ArOCH$_2$(CH$_2$)$_6$CH$_3$), 0.87 (t, $J = 6.2$ Hz, (CH$_2$)$_7$CH$_3$).

**Synthesis of compounds 1 and 2.** Compounds were synthesized using the same procedure. A representative example is described for 1. Compound 7a (0.5 g, 0.33 mmol), tetrabranched hydrophilic dendron (0.35 g, 0.39 mmol), CuSO$_4$·5H$_2$O (0.1 g, 0.4 mmol) and sodium ascorbate (0.1 g, 0.5 mmol) were dissolved in 20 mL of acetonitrile, 20 mL of THF and 2 mL deionized water. The reaction mixture was stirred for 13 h at room temperature. After terminating the reaction, the solvent was removed by a rotary evaporator. The resulting mixture was extracted with deionized water and dichloromethane. The dichloromethane layer was washed with deionized water several times, and dried over MgSO$_4$. The solvent was removed by a rotary evaporator, and the remaining hydrophilic dendrons were removed by an HPLC (Japan Analytical Industry), and the crude product was then purified by a silica gel column chromatography using dichloromethane:methanol = 12:1 mixture as the eluent, to yield 0.6 g (80 %) of a yellowish liquid.

1; $^1$H NMR (CDCl$_3$, $\delta$, ppm): 8.28 (s, Ar-H), 8.26 (s, Ar-H), 8.06 (s, H-triazole), 7.89 (s, H-triazole), 6.53 (s, benzyl-H), 5.47 (s, ArCHCH$_2$N), 4.52 (d, $J = 6.5$ Hz, (CH$_2$)$_2$CHCH$_2$N), 3.94-3.98 (m, CH$_2$OAr), 3.50-3.64 (br, CH$_2$OCH$_2$), 3.37 (s, OCH$_3$), 2.49-2.53 (m, (CH$_2$)$_2$CHCH$_2$N), 2.18-2.23 (m, (CH$_2$)$_2$CHCH$_2$O), 1.26-1.83 (br, ArOCH$_2$(CH$_2$)$_{10}$CH$_3$), 0.88 (t, $J = 7.0$ Hz, (CH$_2$)$_{10}$CH$_3$). $^{13}$C NMR (125 MHz, CDCl$_3$, d, ppm): 153.7, 147.4, 146.8, 138.5, 131.9, 129.1, 122.2, 121.6, 120.2, 106.6, 73.5-69.1 (carbon atoms next to oxygen except 69.19), 59.03 (terminal methoxy), 54.77, 40.81, 40.09, 31.95, 31.93, 30.38, 29.76-29.39, 26.15, 26.12, 22.70, 14.15. Anal. Calcd for C$_{138}$H$_{245}$N$_9$O$_{24}$: C, 68.65; H, 10.23; N, 5.22, Found: C, 68.62; H, 10.33; N, 5.13 %. $M_w$/M$_n = 1.01$ (GPC). MALDI-TOF MS: 2413.9 [1 + H]$^+$, 2435.7 [1 + Na]$^+$, 2451.9 [1 + K]$^+$.

2; $^1$H NMR (CDCl$_3$, $\delta$, ppm): 8.28 (s, Ar-H), 8.26 (s, Ar-H), 8.12 (s, H-triazole), 7.95 (s, H-triazole), 6.53 (s, benzyl-H), 5.46 (s, ArCHCH$_2$N), 4.52 (d, $J = 6.5$ Hz, (CH$_2$)$_2$CHCH$_2$N), 3.94-3.98 (m, CH$_2$OAr), 3.50-3.64 (br, CH$_2$OCH$_2$), 3.36 (s, OCH$_3$), 2.49-2.52 (m, (CH$_2$)$_2$CHCH$_2$N), 2.17-2.21 (m, (CH$_2$)$_2$CHCH$_2$O), 1.27-1.83 (br, ArOCH$_2$(CH$_2$)$_{10}$CH$_3$), 0.88 (t, $J = 7.0$ Hz, (CH$_2$)$_{10}$CH$_3$). $^{13}$C NMR (100 MHz, CDCl$_3$, d, ppm): 153.0, 138.8, 129.3, 106.9, 77.5–69.4

Synthesis of surface-modified inorganic nanoparticles (NPs).

**Synthesis of TOPO capped CdSe quantum dots (QDs).** Tri-$n$-octylphosphine oxide (TOPO) capped CdSe quantum dots were synthesized according to the literature procedure.$^{3}$ Briefly, 100 mg of CdO, 440 mg of tetradecylphosphonic acid (TDPA) and 7.56 g of TOPO were loaded in a 3-neck flask. The flask was equipped with thermocouple, stirring bar, and condenser, and sealed with rubber septa. The mixture was heated up to 300 °C under N$_2$ flow until reddish CdO powder was dissolved. The solution was cooled down to 270 °C and Se-TOP stock solution (130 mg selenium powder dissolved in 4 g of TOP) was swiftly injected to the flask. The nanocrystals were let to grow at 250 °C to reach a target size. Quantum dot size can also be adjusted by increasing the heating time of the precursor solution prior to Se injection.

**Preparation of water-soluble CdSe/ZnS QDs.** The hydrophobic surface ligands such as TOPO, TDPA, oleic acid (OA) could be replaced by some water-soluble bifunctional molecules in which one end connects to quantum dot surface atoms and the other end is hydrophilic and may also be reactive to oligoether dendron of codendritic amphiphiles.$^{4,5}$ A 51 mg of CdO, 733 mg of zinc acetate, 5 mL of OA, and 20 mL of 1-octadecene were placed in a 100 mL flask. The mixture was heated to 150 °C under 100 mTorr pressure for 20 min filled with N$_2$ gas, and further heated to 310 °C. At this temperature, 32 mg of Se powder 128 mg of S powder both dissolved in 3 mL of TOP were quickly injected into the reaction flask. The solution was cooled down to 300 °C and it was further cooled down to room temperature. The QDs were purified by adding 20 mL of chloroform and excess amount of acetone, and then redispersed in chloroform. To prepare water-soluble QDs, 20 mg of 3-mercaptopoundecanoic acid (MUA) was dissolved in 15 mL of methanol and the pH increased up to ~10 using tetramethylammonium hydroxide pentahydrate. QDs were dispersed in MUA solution (Cd:MUA molar ratio of 1:4, based on original moles of Cd employed in the synthesis) and the mixture was heated to 60 °C for 1h and cooled down to room temperature. The MUA-coated QDs were extracted by centrifugation at 6000 rpm and purified with ethyl acetate to remove excess MUA ligands. The precipitate was redispersed in methanol and precipitated with ethyl acetate once more.
Fig. S1 MALDI-TOF MS spectra of 1 and 2.

Fig. S2 (a) Absorption spectra of 1 (0.005 wt%) in chloroform (black) and water (blue). (b) Size distribution graphs at a scattering angle 90° from CONTIN analysis of the autocorrelation function from the laser light scattering of 1 and 2 in water (0.01 wt%). (c) Absorption and (d) emission spectra ($\lambda_{ex} = 248$ nm) of 2 (0.005 wt%) in chloroform (black) and water (blue).
Fig. S3 Attenuated total reflection infrared (ATR-IR) spectra of an aqueous solution of 1. The bilayer feature was convinced by ATR-IR spectroscopic data. The solutions of 1 showed two bands at 2954 cm⁻¹ (ν_{anti}) and 2842 cm⁻¹ (ν_{sym}), which correspond to CH₂ stretching vibrations in the crystalline packing of alkyl chains.⁶

Fig. S4 (a) Negatively stained TEM and (b) cryo-TEM images of an aqueous solution of 2 (0.005 wt%).
**Fig. S5** (a) TEM image, (b) UV-Vis absorption and fluorescence spectra of trioctylphosphine oxide (TOPO) capped CdSe nanoparticles (NPs). The emission peak of the CdSe-TOPO NPs showed a sufficiently narrow Gaussian-shaped emission peak with the full width at half-maximum (FWHM) less than 30 nm, indicating that the synthesized quantum dots (QDs) were uniform in size, shape, and chemical composition. (c) UV-Vis and (d) fluorescence spectra ($\lambda_{ex} = 450$ nm) of aqueous solutions (0.005 wt%) of 1 and 1 with CdSe-TOPO NPs. In the UV spectra, the weight ratios of the QDs to the block codendrimer in the aqueous solution were set at 0.02:1, 0.1:1, and 0.2:1.
**Fig. S6** Size distribution graphs at a scattering angle 90° from CONTIN analysis of the autocorrelation function from the laser light scattering of an aqueous solution of 1 (0.01 wt%) and a solution (0.01 wt%) of 1 and CdSe-TOPO NPs (a weight ratio of 1:0.2).

**Fig. S7** (a) Micrographs and (b) a fluorescence photograph of 1 wt% aqueous solutions of 1 (left) and 1 with CdSe-TOPO NPs (right), respectively. (c) Fluorescence spectra ($\lambda_{ex} = 450$ nm) of aqueous solutions (0.005 wt%) of 2 and 2 with CdSe-TOPO NPs. (d) Cryo-TEM image of the hollow capsules of 2 after encapsulating the CdSe-TOPO NPs in an aqueous medium (0.005 wt%). (e) TEM image showing the incorporated nanoparticles within the vesicles of 2 and their single crystalline domains.
**Fig. S8** Cryo-TEM image of CdSe-TOPO-loaded vesicles after purification of unencapsulated QDs by centrifugation and subsequent dialysis. Typically 94-97% of vesicles were loaded with QDs (Of 109 vesicles in this image, 105 vesicles contain QDs in the membrane).

**Fig. S9** (a) TEM image of 3-mercaptopundecanoic acid (MUA) capped CdSe/ZnS NPs (b) with single crystalline domains. (c) UV-Vis absorption and fluorescence spectra of CdSe/ZnS-MUA QDs. The emission peak is narrow with a full width at half-maximum (FWHM) of about 13 nm.
Fig. S10 (a) Fluorescence and (b,c) fluorescence and bright-field overlay image of encapsulated water-soluble CdSe/ZnS NPs inside the vesicles of 1 in the aqueous medium.

Fig. S11 Emission spectra ($\lambda_{ex} = 248$ nm) of both (a) 1 and (b) 2 (0.005 wt%) in chloroform (red) and hexane (black), respectively. The intensity of the fluorescence maxima was enhanced compared to that observed in chloroform, indicating the aggregation of aromatic segments.
Fig. S12 (a) Negatively stained TEM and (b) cryo-TEM images of the spherical micelles of 1 after encapsulating the CdSe/ZnS-MUA NPs in n-hexane (0.005 wt%).

References for Supporting Information