Supplementary Information

Supramolecular Nanocatalyst in Water: Successive Click-Driven Assembly of Click-Derived Rod Amphiphiles

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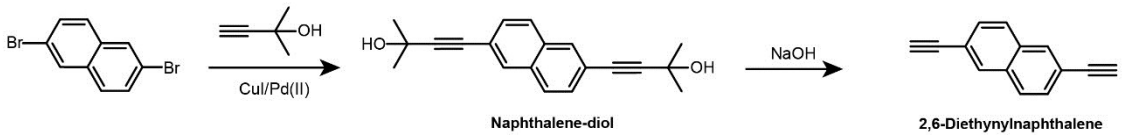
Materials and Instruments All commercially available reagents were reagent grade and used without further purification. L-Ascorbic acid sodium salt (NaAsc, 98+%) and pyridine (99.5+%) were obtained from Junsei Chemical Co., Ltd. (Tokyo, Japan). Benzyl azide (94%), *N*-acetylglycine (99%), and phenylacetylene (98+%) were purchased from Thermo Fisher Scientific (Seoul, Republic of Korea) and trimethylsilylacetylene (98+%), 2,4-dihydroxy benzaldehyde (98+%), anhydrous sodium acetate (98.5+%), sodium nitrite ($NaNO_2$, 98.5+%), coumarin (99.0+%), and bis(triphenylphosphine)palladium(II) dichloride ($PdCl_2(PPh_3)_2$) were obtained from Tokyo Chemical Industry Co., Ltd. (Tokyo, Japan). 2,6-Dibromonaphthalene, 2-methyl-3-butyn-2-ol, triethylamine, copper(I) iodide (CuI, 98%), hydrogen chloride (HCl), propyl gallate, tetrahydrofuran (THF), thionyl chloride ($SOCl_2$), potassium iodide (KI, 99+%), fluorescein 5(6)-isothiocyanate (FITC, 90+%), 4-toluenesulfonyl chloride, triethylene glycol monomethyl ether, and acetic anhydride (99+%) were purchased from Merck (Seoul, Republic of Korea). Copper(II) sulfate (97.5+%), dichloromethane (DCM, 99.5+%), sodium azide (NaN_3, 99.0+%), sodium hydroxide (NaOH, 97+%), and 4 Å molecular sieve were obtained from Daejung Chemicals (Siheung, Republic of Korea). Anhydrous magnesium sulfate ($MgSO_4$, 99%) and anhydrous potassium carbonate (K_2CO_3, 99%) were purchased from Duksan Pure Chemicals Co., Ltd. (Ansan, Republic of Korea). Silica gel was purchased Samchun Chemicals (Pyeongtaek, Republic of Korea). Nile red (99+%) was purchased from Acros Organics (Fischer Scientific, Morris Plains, NJ, USA). Dialysis tubing (1 kDa molecular weight cut-off, MWCO) was purchased from Spectrum Laboratories Inc. (Rancho Dominguez, CA, USA). *N,N'*-Dimethylformamide (DMF) was distilled under vacuum, and stored over a type 4 Å molecular sieve. THF was dried by distillation from sodium metal and stored over a type 4 Å molecular sieve. Triethylamine and pyridine were distilled from calcium hydride and stored over a type 4 Å molecular sieve. 3-Azido-7-hydroxycoumarin was synthesized according to the literature.[1] ^{1}H nuclear magnetic resonance (NMR) spectra were recorded from $CDCl_3$ and D_2O solution on Bruker AVANCE DRX 300 NMR spectrometer. Ultraviolet-visible (UV-Vis) absorption spectra were obtained by using a NEOSYS-2000 spectrometer (Scinco, Seoul, Republic of Korea). The fluorescence spectra were obtained from FS-2 fluorescence spectrometer (Scinco, Seoul, Republic of Korea). Dynamic light scattering (DLS) measurements were performed using ELS-Z (Otsuka Electronics, Osaka, Japan). Transmission electron microscopy (TEM) and cryogenic (cryo-) TEM images were taken from 120 kV TEM (JEM-1400, JEOL Ltd., Tokyo, Japan). Fluorescence microscopy was performed using a Nikon Eclipse Ti-E microscope (Nikon, Kobe, Japan).



1. Synthesis of vesicular nanocatalyst (VC)[2]

Figure S1. Synthesis of 2,6-diethynylnaphthalene.

Synthesis of naphthalene-diol 2,6-Dibromonaphthalene (1.0 g, 3.5 mmol) and 2-methyl-3-butyn-2-ol (5.0 mL, 14.0 mmol) were dissolved in 30 mL of triethylamine. Then, catalytic amounts of CuI and $PdCl_2(PPh_3)_2$ were added to the solution. The mixture was heated at reflux for 3 d with stirring under N_2 atmosphere. After cooled to room temperature, triethylamine was removed by extraction with a diluted HCl solution and DCM. The DCM layer was washed with deionized water several times, and then dried over $MgSO_4$. After removing DCM by a rotary evaporator, the resulting mixture was purified by the several recrystallizations using *n*-hexane, to yield 0.55 g (55%). ^{1}H-NMR ($CDCl_3$, δ, ppm): 7.99 (s, Ar-*H*, 2H), 7.75 (d, *J* = 8.4 Hz, Ar-*H*, 2H), 7.54 (d, *J* = 8.4 Hz, Ar-*H*, 2H), 1.65 (s, $C(CH_3)_2OH$, 12H).

Synthesis of 2,6-diethynylnaphthalene Naphthalene-diol (0.55 g, 1.88 mmol) and NaOH (0.75 g, 18.8 mmol) were dissolved in 30 mL of toluene. The reaction mixture was heated to reflux for 4 h under N_2 atmosphere. After cooling to room temperature, the solvent was removed by a rotary evaporator. The resulting mixture was extracted with deionized water and DCM. The DCM layer was washed with deionized water two times, and dried over $MgSO_4$. After removing DCM by a rotary evaporator, the resulting compound was purified by a silica gel column chromatography using hexane as the eluent, to yield 0.20 g (60%). ^{1}H-NMR ($CDCl_3$, δ, ppm): 7.99 (s, Ar-*H*, 2H), 7.75 (d, *J* = 8.4 Hz, Ar-*H*, 2H), 7.54 (d, *J* = 8.4 Hz, Ar-*H*, 2H), 3.18 (s, Ar-C≡C*H*, 2H).

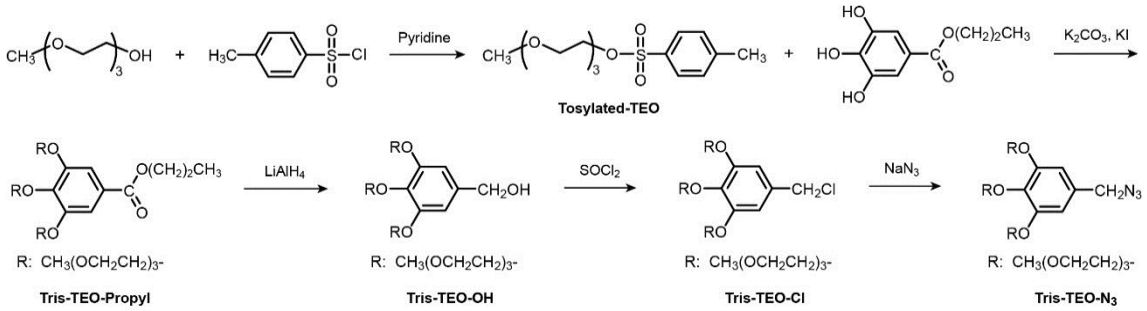


Figure S2. Synthesis of azide-terminated hydrophilic dendron (tris-TEO-N_3).

Synthesis of tosylated-TEO Triethylene glycol monomethyl ether (100 g, 609 mmol), 4-toluenesulfonyl chloride (9.31 g, 48.8 mmol), and pyridine (98.1 mL, 1218 mmol) were dissolved in 500 mL of dry DCM. The reaction mixture was stirred for 2 d at room temperature under N_2 atmosphere. The pyridine was removed by extraction with a diluted HCl solution. The DCM layer was washed with deionized water several times, and then dried over $MgSO_4$. After removing DCM by a rotary evaporator, the resulting compound was purified by sequential silica gel column chromatography frosm DCM to DCM:methanol (MeOH) = 8:1 solvent mixture as the eluents, to yield 150 g (77.0%). ^{1}H-NMR ($CDCl_3$, δ, ppm): 7.78 (d, *J* = 8.0 Hz, Ar-*H*, 2H), 7.35 (d, *J* = 8.0 Hz, Ar-*H*, 2H), 4.16 (t, *J* = 5.2 Hz, CH_2CH_2OTs, 2H), 3.42–3.68 (m, CH_2CH_2O and CH_2CH_2OTs, 10H), 3.37 (s, CH_3O, 3H), 2.45 (s, Ar-CH_3, 3H).

Synthesis of tris-TEO-propyl Propyl gallate (3.7 g, 17.5 mmol), tosylated-TEO (22.3 g, 70 mmol), K_2CO_3 (12.1 g, 87.5 mmol), and KI (2.91 g, 17.5 mmol) were dissolved in 65 mL of methyl ethyl ketone. The reaction mixture

was heated at reflux for 26 h under N_2 atmosphere. The reaction mixture was extracted with ethyl acetate (EA) and deionized water three times, and then dried over $MgSO_4$. After removing organic solvents using a rotary evaporator, the resulting mixture was purified by sequential silica gel column chromatography from DCM:EA = 4:1 solvent mixture to EA:MeOH = 30:1 solvent mixture as the eluents, to yield 7.49 g (65.8%). ^{1}H-NMR ($CDCl_3$, δ, ppm): 7.23 (s, Ar-*H*, 2H), 4.10–4.25 (m, C*H*$_2$OAr and ArCOOC*H*$_2$, 8H), 3.42–3.90 (m, C*H*$_2$C*H*$_2$O and C*H*$_2$CH$_2$OAr, 30H), 3.37 (s, C*H*$_3$O, 9H), 1.67–1.80 (m, COOCH$_2$C*H*$_2$, 2H), 0.98 (t, *J* = 7.4 Hz, COOCH$_2$CH$_2$C*H*$_3$, 3H).

Synthesis of tris-TEO-OH Tris-TEO-propyl (4.38 g, 6.73 mmol) was dissolved in 15 mL of THF, and $LiAlH_4$ (0.38 g, 10.1 mmol) was slowly added to the solution. The reaction mixture was stirred for 24 h, and quenched by adding water dropwise. The precipitate was filtered off, and the transparent solution was dried over $MgSO_4$. After removing organic solvents using a rotary evaporator, 4.45 g (84.6%) of a colorless oil was obtained as the product. ^{1}H-NMR ($CDCl_3$, δ, ppm): 6.63 (s, Ar-*H*, 2H), 4.57 (d, *J* = 6.0 Hz, ArC*H*$_2$OH, 2H), 4.12–4.17 (m, C*H*$_2$OAr, 6H), 3.42–3.90 (m, C*H*$_2$C*H*$_2$O and C*H*$_2$CH$_2$OAr, 30H), 3.37 (s, C*H*$_3$O, 9H), 2.03 (t, *J* = 6.0 Hz, ArCH$_2$O*H*, 1H).

Synthesis of tris-TEO-Cl Tris-TEO-OH (4.11 g, 6.91 mmol) and catalytic amount of DMF were dissolved in 41 mL of DCM. To the solution, 0.70 mL (9.68 mmol) of $SOCl_2$ was added carefully. The reaction mixture was stirred for 30 min, and then volatile compounds were removed using a rotary evaporator. The residual mixture was extracted with DCM and deionized water three times. After removing DCM using a rotary evaporator, 4.14 g (97.9%) of a colorless oil was obtained as the product. ^{1}H-NMR ($CDCl_3$, δ, ppm): 6.62 (s, Ar-*H*, 2H), 4.57 (s, ArC*H*$_2$Cl, 2H), 4.12–4.17 (m, C*H*$_2$OAr, 6H), 3.42–3.90 (m, C*H*$_2$C*H*$_2$O and C*H*$_2$CH$_2$OAr, 30H), 3.37 (s, C*H*$_3$O, 9H).

Synthesis of tris-TEO-N$_3$ Tris-TEO-Cl (4.14 g, 6.76 mmol) and NaN_3 (4.40 g, 67.6 mmol) were dissolved in 15 mL of DMF. The reaction mixture was heated at 100 °C for 3 d under N_2 atmosphere. The reaction mixture was extracted with DCM and deionized water three times, and then dried over $MgSO_4$. After removing DCM using a rotary evaporator, the resulting mixture was purified by a silica gel column chromatography to DCM:MeOH = 50:1 as the eluent, to yield 2.61 g (62.3%). ^{1}H-NMR ($CDCl_3$, δ, ppm): 6.54 (s, Ar-*H*, 2H), 2.67 (s, ArC*H*$_2$N$_3$, 2H), 4.12–4.17 (m, C*H*$_2$OAr, 6H), 3.42–3.90 (m, C*H*$_2$C*H*$_2$O and C*H*$_2$CH$_2$OAr, 30H), 3.37 (s, C*H*$_3$O, 9H).

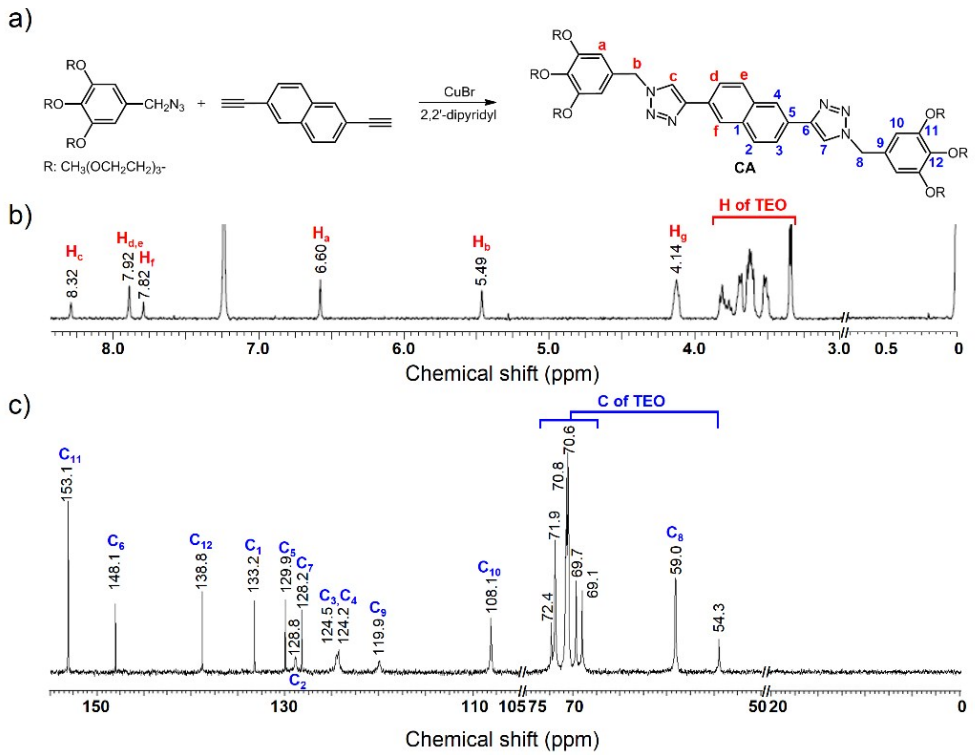


Figure S3. a) Synthesis of click-derived rod amphiphile **CA**. b) ^{1}H- and c) ^{13}C NMR spectra of **CA** measured in $CDCl_3$.

Synthesis of rod amphiphile CA[2] In a glove box, 2,6-diethynylnaphthalene (0.2 g, 1.58 mmol), tris-TEO-N_3 (2.16 g, 3.16 mmol), CuBr (1.13 g, 7.9 mmol), and 2,2'-dipyridyl (1.23 g, 7.90 mmol) were dissolved in deoxygenated anhydrous THF. The reaction mixture was degassed by performing freeze-pump-thaw cycle three times, and allowing the reaction mixture to equilibrate to room temperature. The reaction mixture was allowed to stir for 12 h at room temperature. The solvent was removed using a rotary evaporator, and the residue was purified by a silica gel column chromatography using EA:MeOH = 20:1 as the eluent. Yield: 44%. ^{1}H-NMR (500 MHz, $CDCl_3$, δ, ppm): 8.32 (s, triazole-*H*, 2H), 7.92 (s, Ar-*H*, 4H), 7.82 (s, Ar-*H*, 2H), 6.60 (s, trialkoxybenzyl protons, 4H), 5.49 (s, -NCH_2(phenyl), 4H), 4.11–4.17 (m, CH_2OAr, 12H), 3.50–3.90 (m, CH_2CH_2O and CH_2CH$_2$OAr, 60H), 3.36 (s, CH_3O, 18H). ^{13}C-NMR (400 MHz, $CDCl_3$, δ, ppm): 153.1, 148.1, 138.8, 133.2, 129.9, 128.8, 128.2, 124.5, 124.2, 119.9, 108.1, 72.4, 71.9, 70.8, 70.6, 69.7, 69.1 (carbons of TEO chains), 59.0 (*C*H$_3$O), 54.3 (benzylic carbon). M_w/M_n (GPC) = 1.02.

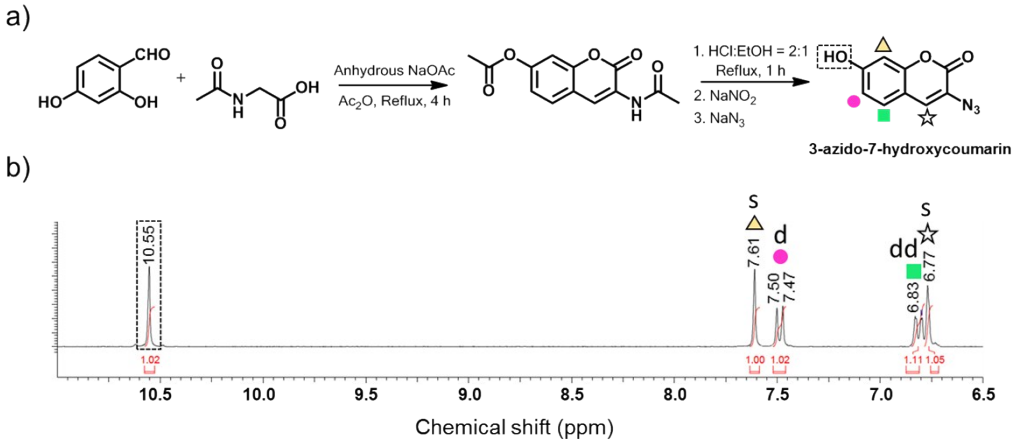


Figure S4. a) Synthetic procedure of 3-azido-7-hydroxycoumarin and b) the ^{1}H NMR analysis.

Synthesis of 3-azido-7-hydroxycoumarin 3-Azido-7-hydroxycoumarin was prepared according to the literature.[1] A mixture of 2,4-dihydroxy benzaldehyde (0.552 g, 4 mmol), *N*-acetylglycine (0.468 g, 4 mmol), and anhydrous sodium acetate (0.984 g, 12 mmol) in acetic anhydride (20 mL) was refluxed at 140 °C under stirring for 4 h. The reaction mixture was cooled in ice bath to give a yellow precipitate. After filtration, the yellow solid was washed by ice water and then refluxed in a solution of concentrated HCl and ethanol (2:1, 30 mL) for 1 h. Then, ice water (40 mL) was added to dilute the solution. The solution was then cooled in ice bath and $NaNO_2$ (0.551 g, 8 mmol) was added. The mixture was stirred for 5–10 minutes and NaN_3 (0.976, 15 mmol) was added dropwise. After stirring for another 15 min, the resulting precipitate was filtered off, washed with distilled water, and dried under reduced pressure to afford a brown solid; 0.05 g (30% overall yield). The product was pure enough for further reactions (Figure S4). ^{1}H-NMR (300 MHz, DMSO-d_6, δ, ppm): 10.55 (s, 1H), 7.61 (s, 1H), 7.47 (d, J = 8.5 Hz, 1H), 6.83 (dd, J = 8.4, 2.2 Hz, 1H), 6.77 (s, 1H).

2. Preparation of Cu(I)-chelated vesicular nanocatalyst (Cu^{I}-VC)

Aqueous Cu^{I}-VC solution Pre-nanocatalyst **Cu^{II}-VC** was prepared by dissolving **CA** in water, followed by addition of 0.5 equiv. $CuSO_4$ with stirring under Ar atmosphere. Cu^{II} was reduced to Cu^{I} by addition of reducing agent, NaAsc (3.0 equiv. mol to $CuSO_4$), to the **Cu^{II}-VC** solution. The resultant solution of **Cu^{I}-VC** was left in a 4 mL glass vial and sealed with parafilm at room temperature for a day to allow aging.

3. Cu^{I}-catalyzed azide-alkyne cycloaddition (CuAAC) click reaction by Cu^{I}-VC

To optimize the amount of **Cu^{I}-VC** for efficient click reactions, click reactions with various concentration of **Cu^{I}-VC** (1, 2.5, 5, and 10 mM) were performed with same reaction conditions. As increasing the concentration of **Cu^{I}-VC** from 1 to 2.5 to 5 mM, the conversion efficiency was accordingly increased. However, at 10 mM, the ^{1}H NMR signals were mainly observed for **CA** which indicates that the amount of product was considerably low. This result could be explained by the steric and diffusion limitation of reagents at very high concentration of nanocatalyst. Therefore, 5 mM **Cu^{I}-VC** was used for conducting CuAAC reaction.

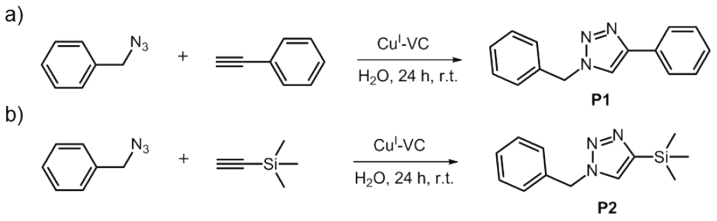


Figure S5. Synthesis of a) **P1** and b) **P2**.

Synthesis of P1 The aqueous solution of **Cu^{I}-VC** (5 mM) was added to 4 mL vial containing benzyl azide (5 equiv., 12.5 μmol) and phenylacetylene (5 equiv., 12.5 μmol) with stirring under Ar atmosphere. The CuAAC reaction was carried out in the dark at room temperature for 24 h between benzyl azide and phenylacetylene catalyzed by Cu^{I} chelated within the vesicular membrane. The quantitative e analysis of formed **P1** was conducted using ^{1}H NMR spectroscopy. The excess of **P1** precipitated as white solid was removed by filtration. The loading efficiency of **P1** within **Cu^{I}-VC** was determined to be 77% by relative integration of benzylic protons of **CA** and **P1** in ^{1}H NMR spectrum. ^{1}H-NMR (300 MHz, $CDCl_3$, δ, ppm): 7.78–7.81 (d, J = 9.0 Hz, 2H), 7.65 (s, 1H), 7.31–7.44 (m, 8H), 5.58 (s, 2H).

Synthesis of P2 The aqueous solution of **Cu^{I}-VC** (5 mM) was added to 4 mL vial containing benzyl azide (5 equiv., 12.5 μmol) and trimethylsilylacetylene (5 equiv., 12.5 μmol) with stirring under Ar atmosphere. The CuAAC reaction was carried out in the dark at room temperature for 24 h between benzyl azide and trimethylsilylacetylene catalyzed by Cu^{I} chelated within the vesicular structure. The quantitative analysis of formed **P2** was conducted using ^{1}H NMR spectroscopy. The excess **P2** of yellow liquid was removed using a dialysis membrane (MWCO, 1 kDa). The loading efficiency of **P2** within **Cu^{I}-VC** was calculated to be 20% by relative integration of the benzylic protons of **CA** and **P2** in ^{1}H NMR spectrum. ^{1}H-NMR (300 MHz, $CDCl_3$, δ, ppm): 7.41 (s, 1H), 7.34–7.37 (m, 3H), 7.26–7.28 (d, J = 4.0 Hz, 2H), 5.55 (s, 2H), 0.29 (s, 9H).

P1 synthesis by Click I-to-Click II reaction of P2-loaded Cu^{I}-VC **P2**-loaded **Cu^{I}-VC** (5 mM) was prepared by the procedure described above. The CuAAC reaction of **P2**-loaded **Cu^{I}-VC** to synthesize **P1** was proceeded with benzyl azide (5 equiv., 12.5 μmol) and phenylacetylene (5 equiv., 12.5 μmol) stirring under Ar atmosphere at room temperature for 24 h in the dark. The quantitative analysis of **P1** product was performed using ^{1}H NMR spectrometry.

P2 synthesis by Click I-to-Click II reaction of P1-loaded Cu^{I}-VC **P1**-loaded **Cu^{I}-VC** (5 mM) was prepared by the procedure described above. The CuAAC reaction of **P1**-loaded **Cu^{I}-VC** to synthesize **P2** was proceeded with benzyl azide (5 equiv., 12.5 μmol) and phenylacetylene (5 equiv., 12.5 μmol) stirring under Ar atmosphere at room temperature for 24 h in the dark. The quantitative analysis of **P2** product was performed using ^{1}H NMR spectrometry.

Synthesis of coumarin-derived CP1 or CP2 The **Cu^{I}-VC** solution (5 mM) was added to 4 mL vial containing 3-azido-7-hydroxycoumarin (5 equiv., 12.5 μmol) and phenylacetylene (5 equiv., 12.5 μmol) with stirring under Ar atmosphere. The CuAAC reaction was carried out in the dark at room temperature for 24 h between 3-azido-7-

hydroxycoumarin and phenylacetylene catalyzed by Cu^{I} chelated within the vesicular structure. For the synthesis of CP2, trimethylsilylacetylene was used instead of phenylacetylene.

4. Characterization of Cu^{I}-VC

DLS DLS experiments were performed with the aqueous solution of **Cu^{I}-VC** (20 μM) prepared before and after proceeding click reaction, forming **P1** or **P2** at a scattering angle of 90° at 25 °C, using a He-Ne laser operating at 632.8 nm. The hydrodynamic diameters were determined from the DLS autocorrelation functions by the cumulants and the CONTIN methods using the software provided by the manufacturer.

TEM A drop of each sample in aqueous solution was placed on a formvar/carbon-coated copper grid and allowed to evaporate under ambient conditions. When sample was stained, a drop of aqueous uranyl acetate solution (2 wt%) placed onto the surface of the sample-loaded grid. The staining agent deposited about 3 min at least, and excess solution was wicked off by filter paper. The specimen was observed with a JEM-1400 operating at 120 kV. The data were analyzed with Simple Measure program (JEOL Ltd., Tokyo, Japan).

Cryo-TEM Cryo-TEM experiments were performed with a thin film of aqueous solution of sample (3 μL) transferred to a lacey supported grid by plunge-dipping method. The thin aqueous films were prepared at ambient temperature and with humidity of 97–99% within a custom-built environmental chamber in order to prevent evaporation of water from sample solution. The excess liquid was blotted with filter paper for 2–3 sec, and the thin aqueous films were rapidly vitrified by plunging them into liquid ethane (cooled by liquid nitrogen) at its freezing point. The specimen was observed with a JEM-1400 operating at 120 kV. The data were analyzed with Simple Measure Program (JEOL Ltd., Tokyo, Japan).

5. Incorporation of fluorescent dyes

Both hydrophilic and hydrophobic dyes were incorporated into the nanostructure during the formation of self-assembled aggregates in water. Unencapsulated dyes were removed by dialysis using low molecular weight cutoff (1 kDa) tubing.

Loading of FITC FITC was used to demonstrate the formation of vesicular structure of **P2**-loaded **Cu^{I}-VC** after click-to-click reaction to synthesize **P1** in water. After **P1**-forming CuAAC reaction of **P2**-loaded **Cu^{I}-VC** (0.5 mM), water was removed by rotary evaporation. 1 equiv. of FITC in deionized water was added and mixed under vigorous stirring. The resulting solution was annealed at room temperature for at least a day leading to swelling and the formation of vesicle. Unencapsulated FITC was removed through dialysis using low molecular weight cutoff (1 kDa) tubing for 48 h.

Release of FITC Encapsulated FITC was released from **P1**-loaded **Cu^{I}-VC** after click reaction to synthesize **P2**. **P2**-forming CuAAC reaction was conducted using **P1**-loaded **Cu^{I}-VC** in dialysis membrane (1 kDa), which was suspended in 20 mL of deionized water at room temperature with constant shaking at 170 rpm. After 1 h, the released FITC was detected by fluorescence spectroscopy (λ_{ex} = 490 nm).

Loading of coumarin Coumarin was tested as a hydrophobic probe before synthesizing nonfluorescent coumarin-derivative, which emits fluorescence after CuAAC reaction to form click product. After evaporation of water in **Cu^{I}-VC** solution, 5 equiv. of coumarin in chloroform was added and mixed under vigorous stirring, followed by evaporation of chloroform. 1 mL deionized water was added and the resulting solution was annealed at room temperature for at least a day. Unencapsulated coumarin was removed through centrifugation and subsequent dialysis using low molecular weight cutoff (1 kDa) tubing for 48 h.

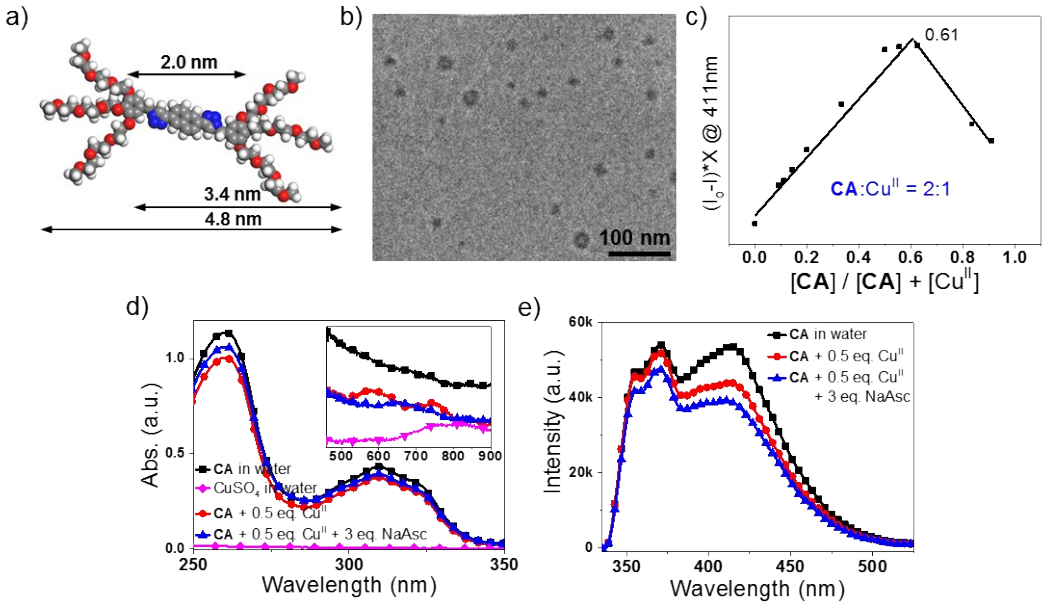


Figure S6. a) Molecular length of **CA** calculated by CPK modeling. The extended molecular length is ~4.8 nm. b) Cryo-TEM image of **CA** in water, showing the vesicular structures. c) Job's plot suggesting the 2:1 stoichiometric ratio of **CA**:Cu^{II}. d) UV-Vis and e) fluorescence spectroscopies of **CA** after addition of Cu^{II} ($CuSO_4$) and NaAsc to generate **Cu^{I}-VC** in water (λ_{ex} = 260 nm).

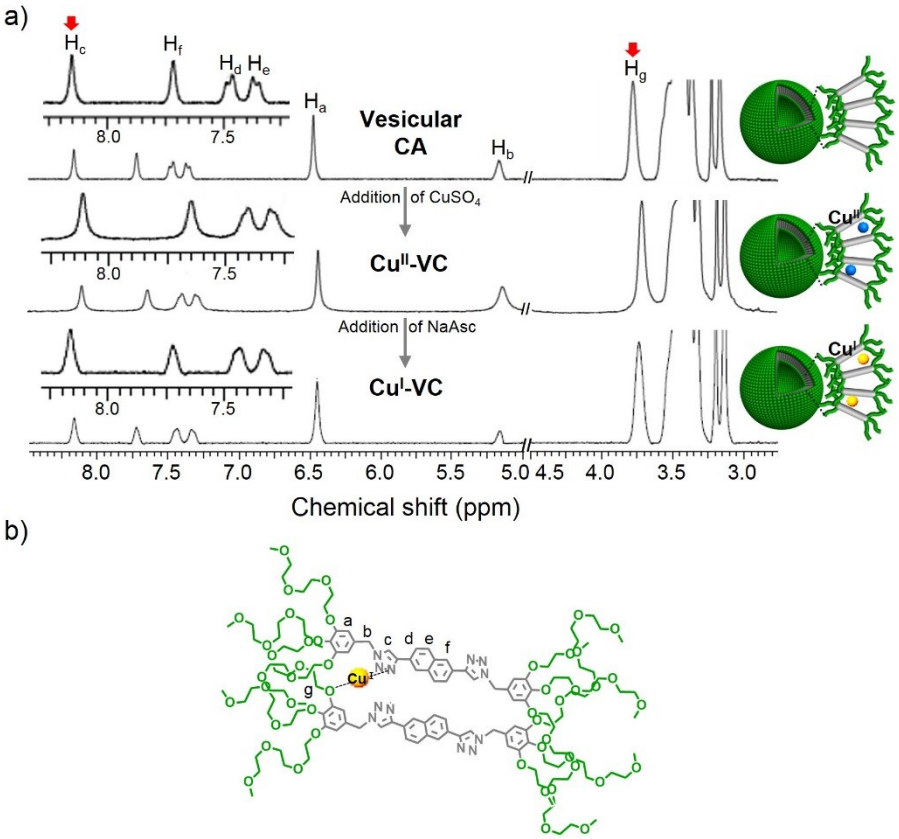


Figure S7. a) Comparison of the ^{1}H NMR signals of the self-assembled vesicle of **CA** in D_2O (5 mM) and after addition of 0.5 equiv. Cu^{II}, followed by reduction to Cu^{I} by further addition of 3.0 equiv. NaAsc. b) The possible Cu^{I}-binding mode of **CA**.

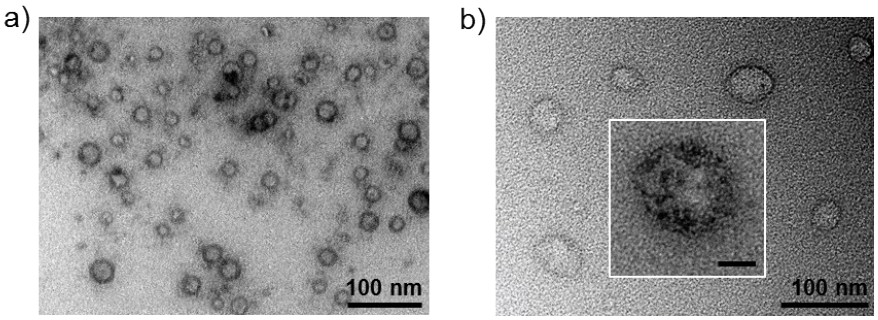


Figure S8. Unstained TEM images of self-assembled vesicular **CA** after a) addition of 0.5 equiv. Cu^{II} and b) reduction of Cu^{II} to Cu^{I} by further addition of 3.0 equiv. NaAsc (inset scale bar: 20 nm).

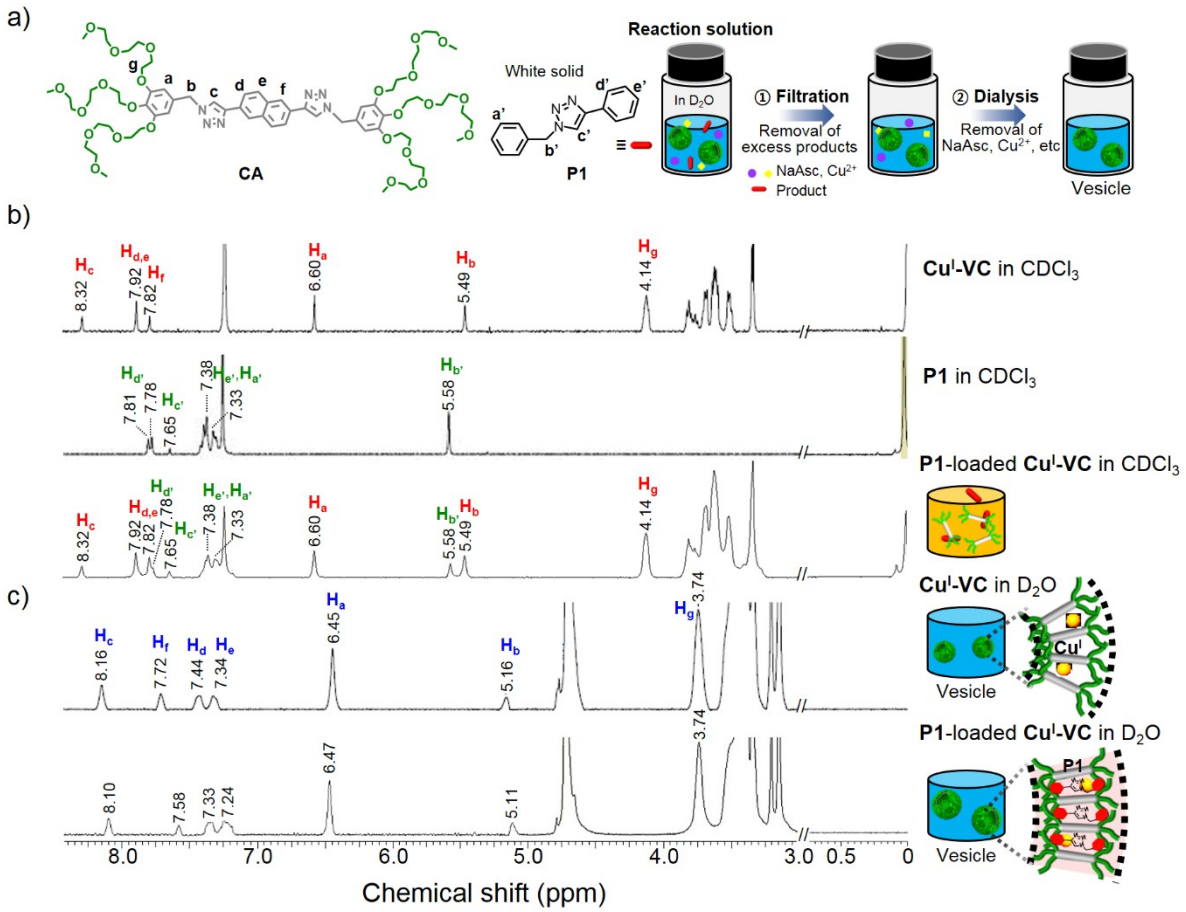


Figure S9. a) Chemical structure of **CA** and **P1**. Schematic illustration preparing the **P1**-loaded **Cu^{I}-VC**. ^{1}H NMR spectra of b) **Cu^{I}-VC**, **P1**, and **P1**-loaded **Cu^{I}-VC** measured in $CDCl_3$ and c) **Cu^{I}-VC**, **P1**-loaded **Cu^{I}-VC** measured in D_2O (at 300 MHz, 25 °C).

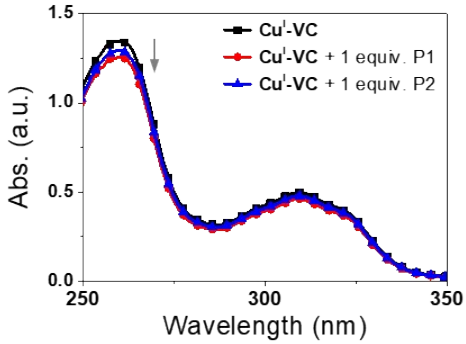


Figure S10. a) UV-Vis absorption spectra of 0.02 mM **Cu^{I}-VC** in water before and after click reaction to form **P1** or **P2**, respectively.

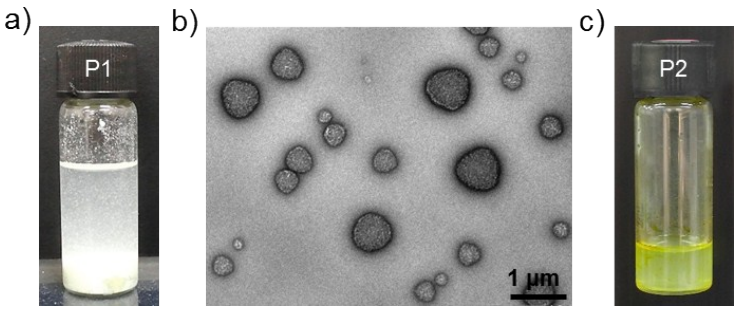


Figure S11. a) A photograph of **Cu^{I}-VC** solution with excess **P1** precipitated as white solid and b) the negatively stained TEM image of **P1**-loaded **Cu^{I}-VC** obtained from solution after filtration of excess **P1**. c) A photograph of **Cu^{I}-VC** solution with excess **P2** of yellow liquid. The CuAAC reaction was carried out with 1.05 mmol phenylacetylene, trimethylsilylacetylene, and 1.00 mmol benzyl azide at room temperature for 24 h in water.

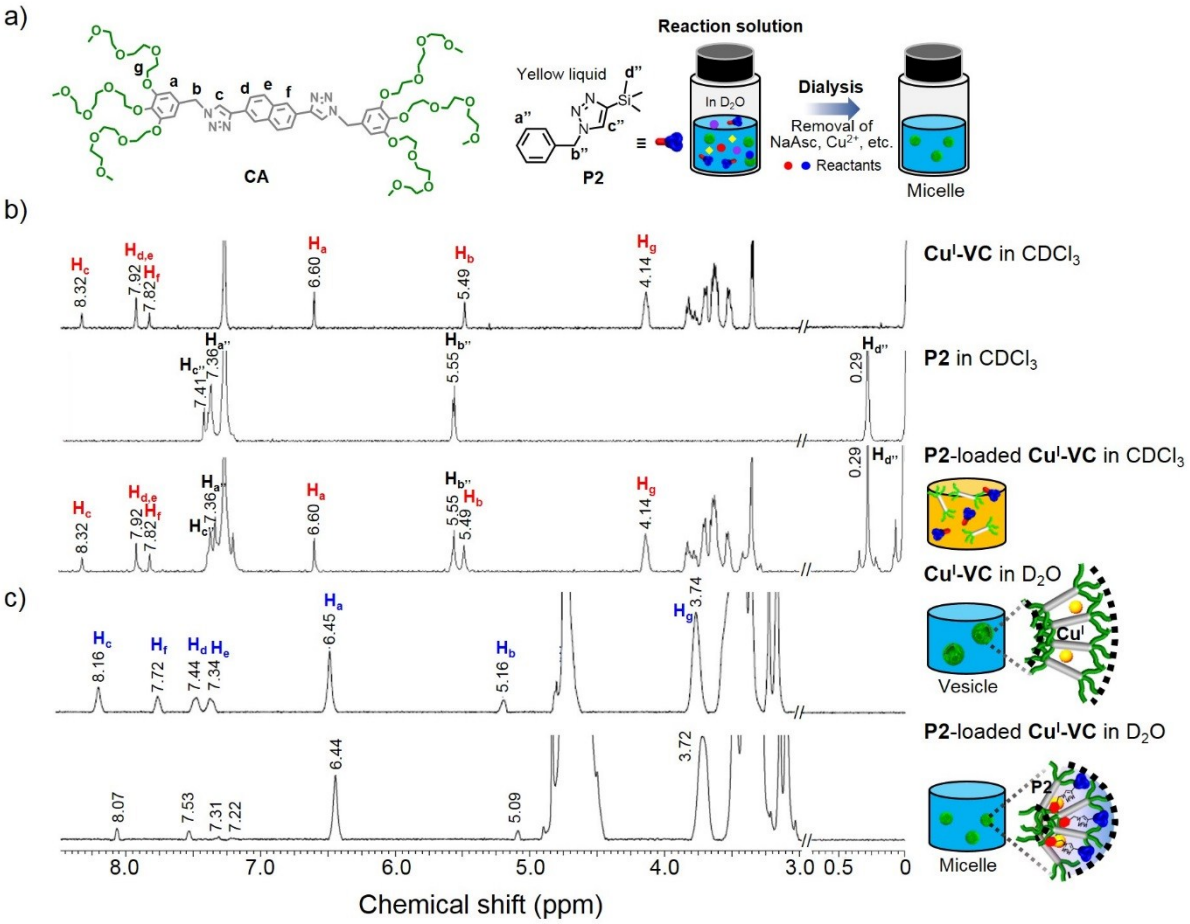


Figure S12. a) Chemical structures of **CA** and **P2**. Schematic illustration preparing the **P2**-loaded **Cu^{I}-VC**. ^{1}H NMR spectra of b) **Cu^{I}-VC**, **P2**, and **P2**-loaded **Cu^{I}-VC** measured in $CDCl_3$ and c) **Cu^{I}-VC**, **P2**-loaded **Cu^{I}-VC** measured in D_2O (at 300 MHz, 25 °C).

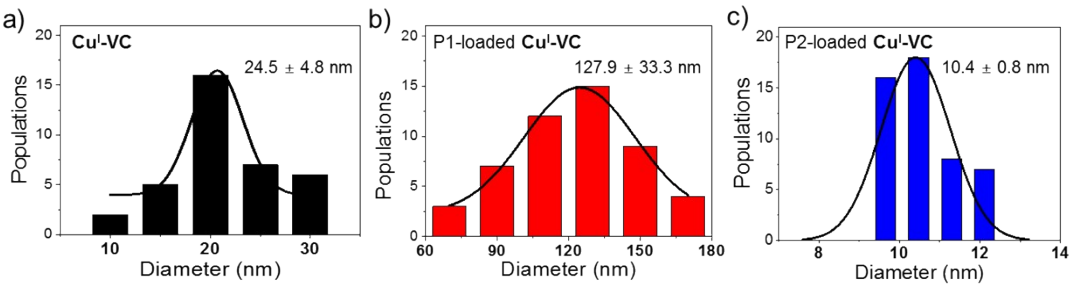


Figure S13. Diameter of a) **Cu^{I}-VC**, b) **P1**- and c) **P2**-loaded **Cu^{I}-VC** obtained from TEM measurements.

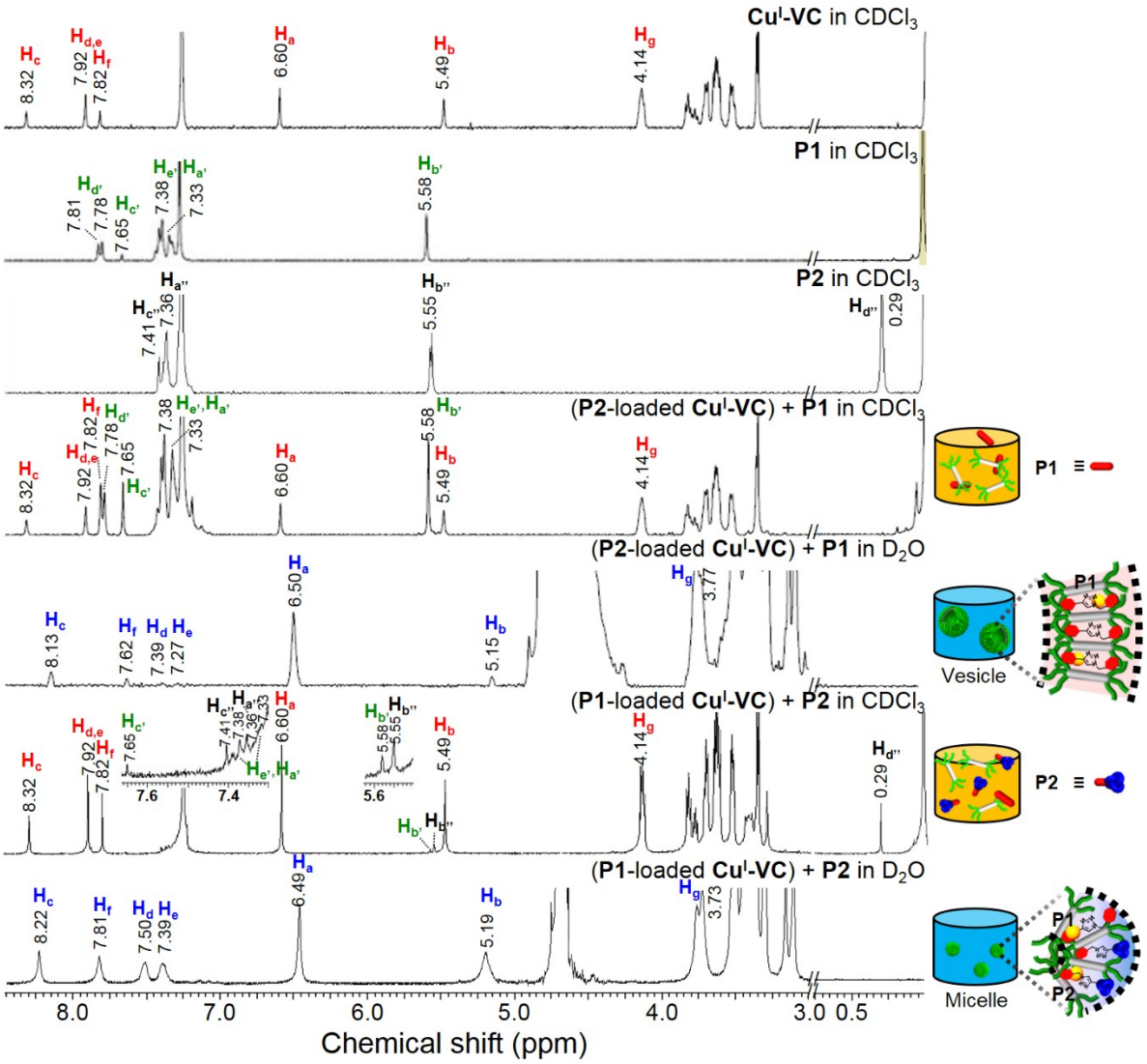


Figure S14. ^{1}H NMR spectra of **Cu^{I}-VC**, **P1**, and **P2** measured in $CDCl_3$ and **P2**-loaded **Cu^{I}-VC** and **P1**-loaded **Cu^{I}-VC** after click-to-click reaction to generate **P1** and **P2**, respectively, measured in $CDCl_3$ and D_2O (at 300 MHz, 25 °C). See Figures S9,12 for assignment.

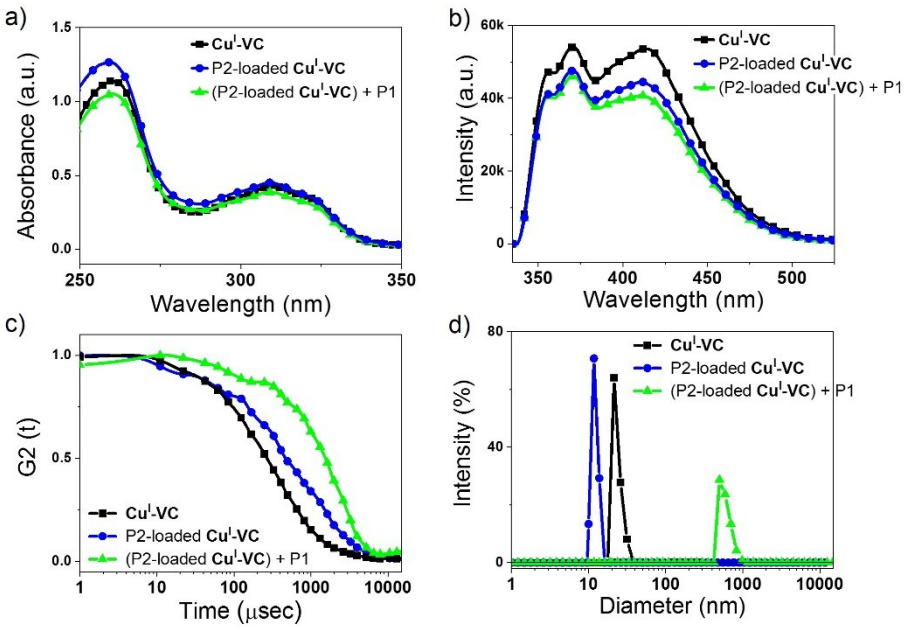


Figure S15. a) The absorption and b) emission spectra (λ_{ex} = 260 nm) of **Cu^{I}-VC** (0.02 mM) after successive click reactions to form **P1**. c) Autocorrelation functions of **Cu^{I}-VC** (0.02 mM) after successive click reactions to form **P1** and d) their corresponding hydrodynamic diameter, indicating the morphological change from vesicle (black) to micelle (blue) to vesicle (green).

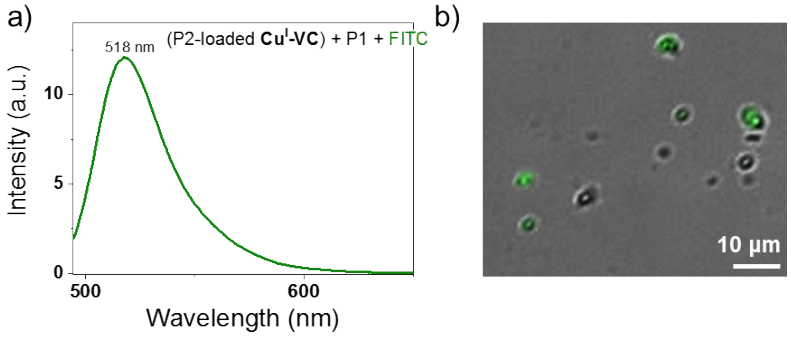


Figure S16. a) Emission spectrum (λ_{ex} = 490 nm) and b) fluorescence and bright-field overlay micrograph of **P2**-loaded **Cu^{I}-VC** (0.02 mM) in water after conducting **P1**-forming CuAAC reaction, followed by addition of FITC. Unencapsulated FITC was removed through dialysis using dialysis tubing (MWCO, 1 kDa) for 48 h

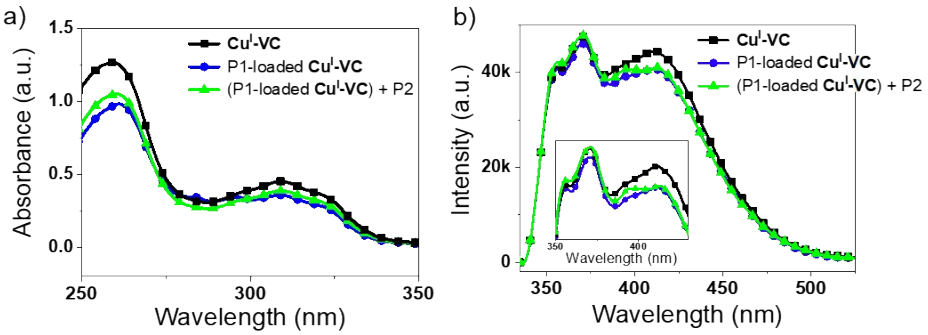


Figure S17. a) The absorption and b) emission spectra (λ_{ex} = 260 nm) of **Cu^{I}-VC** (0.02 mM) after successive click reactions to form **P2**.

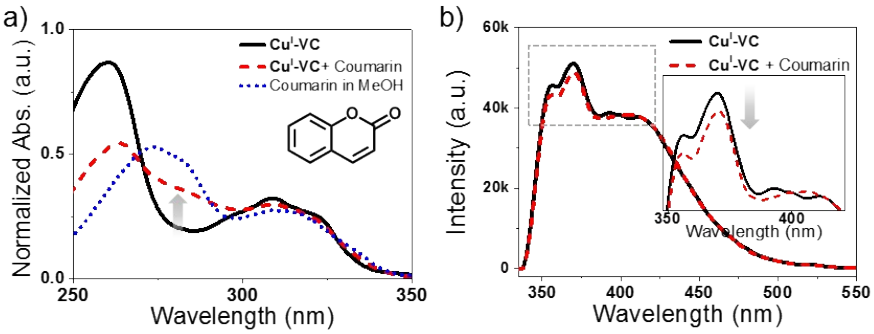


Figure S18. a) UV-Vis absorption and b) fluorescence spectra of **Cu^{I}-VC** before and after addition of hydrophobic coumarin (λ_{ex} = 260 nm). The inset of a) is the molecular structure of coumarin.

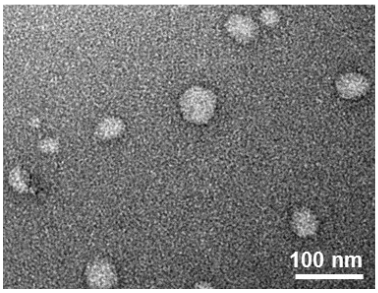


Figure S19. Negatively stained TEM image of the **CP1**-incorporated **Cu^{I}-VC** with 2 wt% uranyl acetate. Considering the molecular length of fully extended **CA** (~4.8 nm), the observed nanostructures can be identified as vesicles.

References

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(2) I. Kim, N.-E. Lee, Y.-J. Jeong, Y.-H. Chung, B.-K. Cho and E. Lee, *Chem. Commun.*, 2014, **50**, 14006–14009.