Electronic Supplementary Information

Controlled drug delievery from mesoporouse silica using a pH-response release system

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Experimental section

Compound 5

A solution of thionyl chloride (12.5 mL) was added to D-alanine (D-alanine, 4.46 g, 50 mmol) in ethanol (10 mL) at 0 °C. The reaction mixture was maintained at 40 ºC for 4 h. The solvent was removed and crystallization from methanol/ethyl ether yielded 4.65 g (86%). Mp 76-78 ºC.[17] ^{1}H NMR (300 MHz, DMSO-d_6, 25 ºC): δ 8.66 (s, 3H, NH_3), 4.17 (q, 1H, J=7.2 Hz), 4.00 (q, 2H, J=7.2 Hz), 1.40 (d, 3H, J=7 Hz), 1.22 (t, 3H, J=7.2 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, 25 ºC): δ 170, 53, 48, 16; MS(EI) 103.06 $(M+H)^+$; Anal. Calcd for $C_4H_9NO_2$: C, 46.59; H, 8.80; N, 13.58. found : C, 46.59; H, 8.70; N, 13.50.

Compound 4

DCC (105.6 mg, 0.51 mmol) and HOBt (69.2 mg, 0.51 mmol) were added to a solution of **5** (0.1 g, 0.118mmol) and Oleic acid (55 mg, 0.36 mmol) in ethylacetate (4 mL) at 0 ºC. The reaction mixture was stirred at room temperature overnight. The insoluble material was filtered off and the solution was washed successively with saturated $NaHCO_3$, saturated $NaHSO_4$, and saturated $NaHCO_3$. After drying with $MgSO_4$ the solvents were removed under reduced pressure. This crude product was purified by column chromatography (ethyl acetate/hexane, 1/2 v/v) to give the product (70%). Mp 81.3-82.0 ºC. ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC): δ 5.82 (s, 1H, NH), 4.58 (q, 1H, J=6 Hz), 4.17 (q, 2H, J=7.2 Hz), 2.18 (t, 2H, J=6.9 Hz), 2.05 (m, 4H), 1.54-1.30 (m, 22H), 0.91 (t, 3H, J=7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC): δ 176, 174, 71, 65, 60, 45, 32, 31, 29, 21, 17, 15; IR (KBr, cm^{-1}): 3322, 2957, 2917, 2849, 1742, 1648, 1537, 1472, 1421, 1030, 951; MS (EI) m/z 381.32 $(M+H)^+$. Anal. Calcd for $C_{22}H_{41}NO_3$: C, 73.09; H, 9.76; N, 3.87. Found; C, 73.15; H, 9.78; N, 3.85.

Compound 6

Compound **7** (200 mg, 0.89 mmol) was diluted in methanol (5 mL). After 5 min of N_2 purging, Pd on activated carbon (10 wt.-%, 40 mg) was added to compound **7** in solution. Under H_2 (3 atm), the reaction was allowed to proceed for 1 h. After filtration by Celite 545 and concentration, compound **6** was ob tained as a yellow solid (173 mg). ^{1}H NMR (300 MHz, CDCl3, 25 °C): δ = 8.75 (d, 1 H), 8.55 (d, 1 H), 7.73 (d, 1 H), 7.46 (d, 1 H), 7.26 (d, 1 H), 6.80 (d, 1 H), 5.20 (s, 2 H) ppm. ^{13}C NMR (75 MHz, CDC_{l3}, 25 °C): δ = 146, 145, 141, 136, 132, 130, 128, 122, 120, 118, 115 ppm. MS (FAB) (%): m/z = 196 [M + H]+. $C_{12}H_9N_3$ (195.22): calcd. C

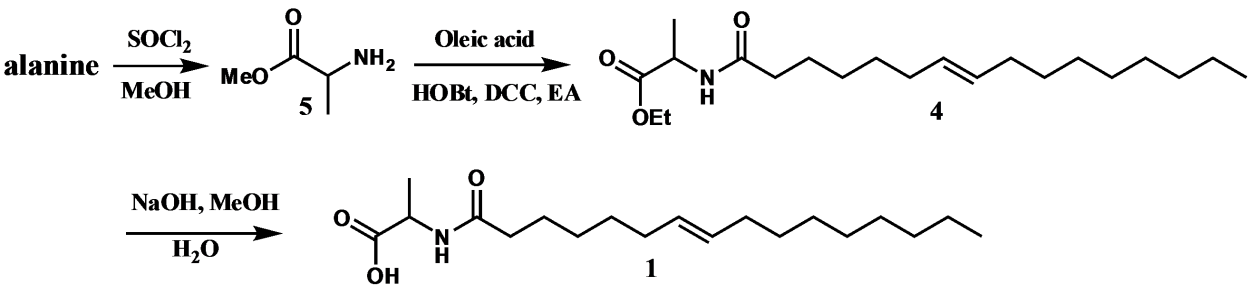
73.83, H 4.65, N 21.52; found C 73.61, H 4.51, N 21.22.

Compound 2

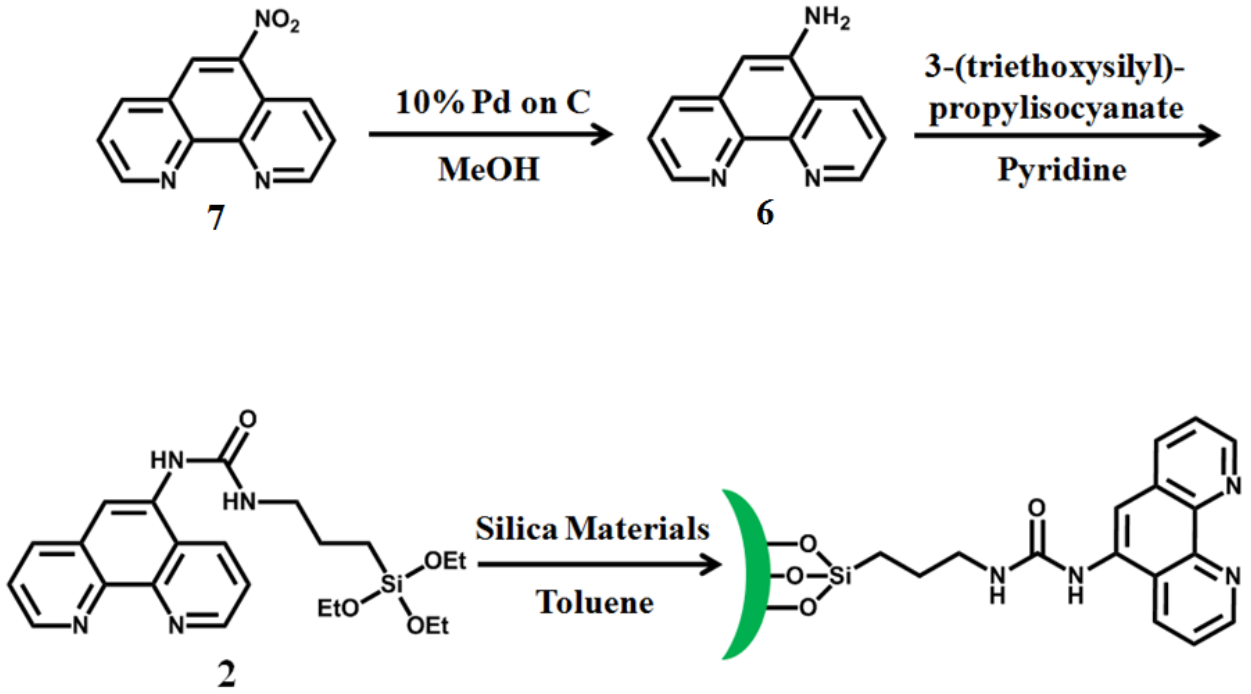
A solution of **6** (175 mg, 0.9 mmol) in pyridine (5 mL) at 80 °C was treated with 3-(triethoxylyl)propylisocyanate (115 mg, 1.17 mmol). The reaction mixture was stirred overnight at 80 °C, and then cooled to room temperature. After removal of solvent, the crude product was purified by flash column chromatography on aluminum oxide, by elution with ethyl acetate to provide the title compound (215 mg, 81%). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.72 (d, 1 H), 8.57 (d, 1 H), 7.74 (d, 1 H), 7.39 (d, 1 H), 7.22 (d, 1 H), 6.75 (d, 1 H), 3.77 (m, 6 H), 3.13 (d, 1 H), 1.45 (m, 2 H), 1.18 (m, 9 H), 0.84 (m, 2 H) ppm. ^{13}C NMR (75 MHz, CDC_{l3}, 25 °C): δ = 146, 145, 141, 136, 132, 130, 128, 122, 120, 118, 115 ppm. MS (FAB) (%): m/z = 443 $[M + H]^+$. $C_{22}H_{30}N_4O_4Si$ (442.58): calcd. C 59.70, H 6.83, N 12.66; found C 60.21, H 6.75, N 12.51.

Compound 1

A solution of **4** (0.12 g, 0.33 mmol) in methanol (5 mL) was added to 1 M NaOH (1 mL, 1 mmol). The reaction mixture was stirred at room temperature for 4 h, and 1 M HCl (2.5 mL, 2.5 mmol) was then added. The solvent was removed under reduced pressure and the solution thus obtained was cooled in an ice bath and acidified with 1 M HCl (3 mL) with vigorous stirring and extracted with ethyl acetate (50 mL). The organic layer was dried over $MgSO_4$. Removal of the organic solvent in vacuo afforded a white solid. This crude product was purified by column chromatography (ethanol/ hexane) to give the product (95%). Mp 92.0-93.1 ºC. ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC): δ 8.01 (s, 1H), 5.32 (t, 2H), 4.45 (q, 1H, J=6 Hz), 2.24 (t, 2H, J=6.9 Hz), 2.10 (m, 4 H), 1.58-1.35 (m, 26H), 0.93 (t, 3H, J=7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC): δ 174.9, 172.3, 130.0, 47.9, 35.4, 34.1, 31.7, 29.5, 29.2, 29.1, 29.0, 27.0, 25.6, 22.5, 17.8, 14.4; IR (KBr, cm^{-1}): 3315, 2915, 2839, 1696, 1633, 1565, 1518, 1449, 1405, 1300, 1231, 1078, 910, 705, 631, 565, 533; MS (EI) m/z 353.29 $(M+H)^+$. Anal. Calcd for $C_{21}H_{39}NO_3$: C, 71.34; H, 11.12; N, 3.96. Found; C, 71.14; H, 11.02; N, 3.93.



Scheme S1. Synthetic route for **1**.



Scheme S2. Synthetic route of **2** and its immobilization on to the mesoporous hollow silica particles.

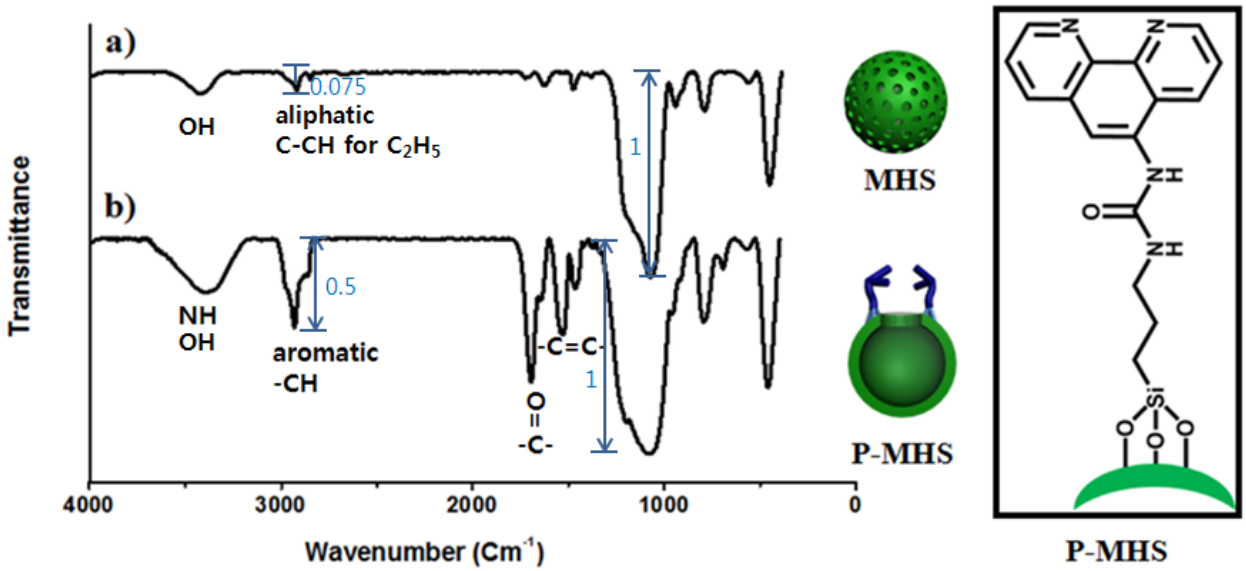


Fig. S1 FT-Infrared spectra of (a) **MHS** and (b) phenanthroline-immobilized mesoporous hollow silica particles (**P-MHS**).

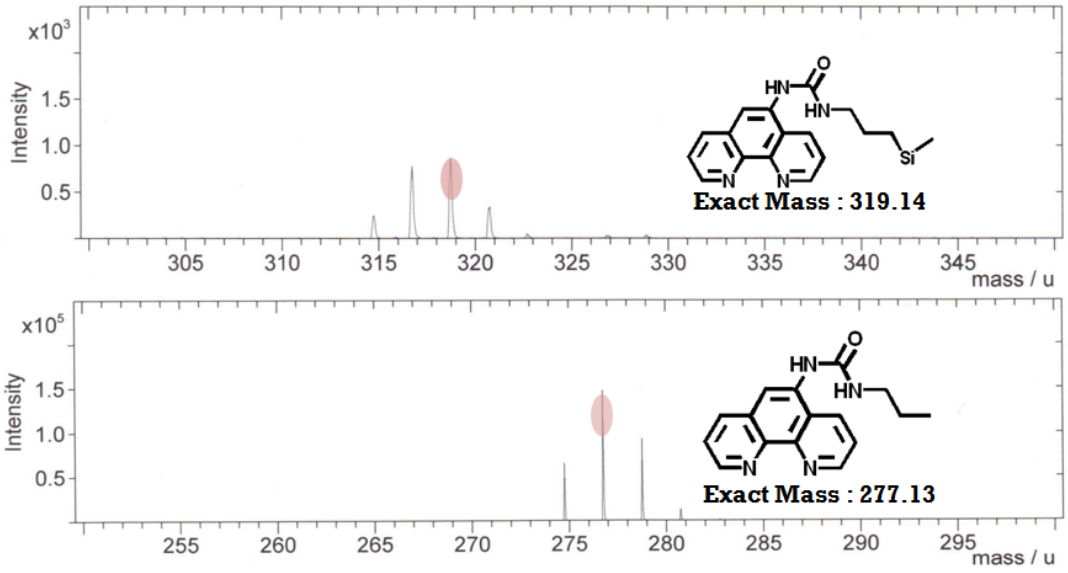


Fig. S2 TOF-SIMS spectra of **P-MHS**.

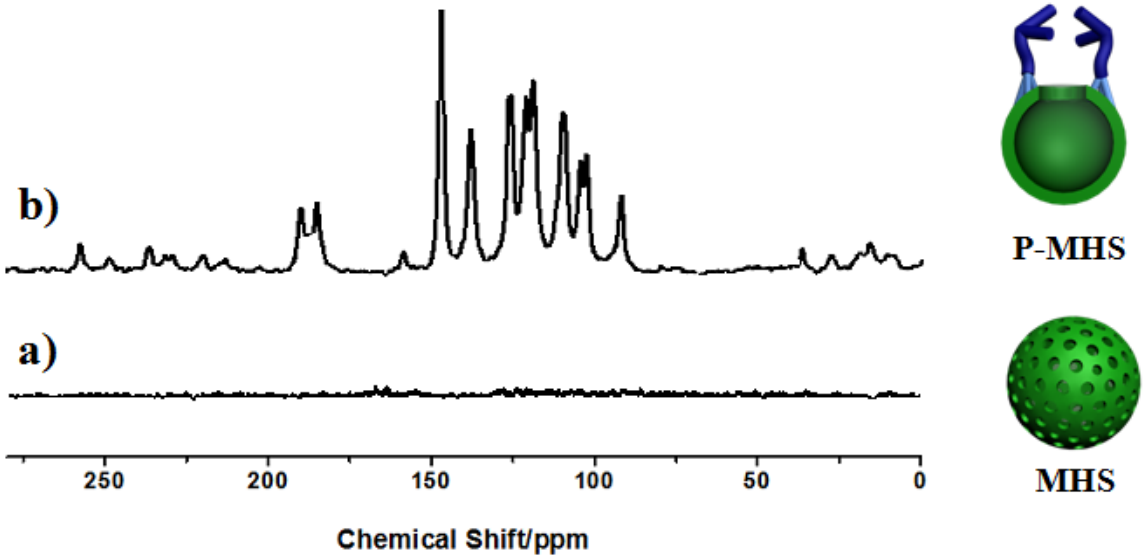


Fig. S3 ^{13}C CP/MAS NMR spectra of (a) **MHS** and (b)**P-MHS**.

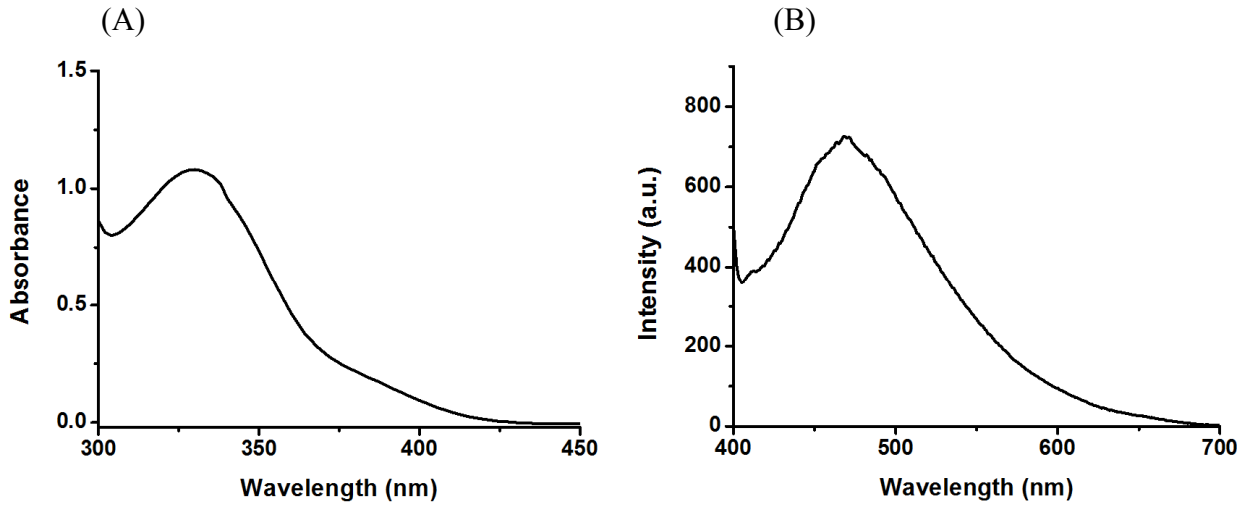


Fig. S4 **(**A) Absorption and (B) fluorescence spectra of the suspension of **P-MHS (**1.0 x 10^{-4} M**)**.

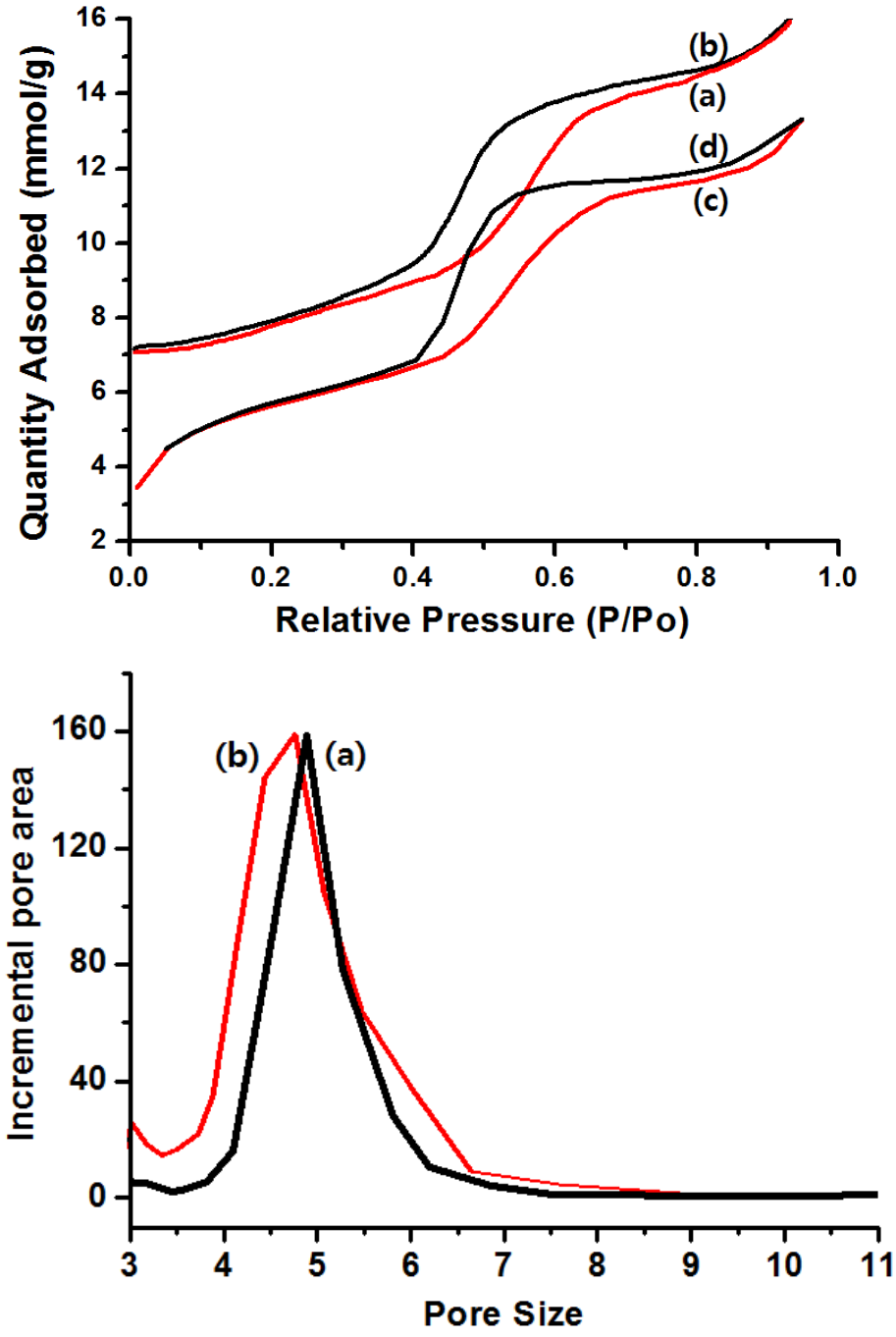


Fig. S5 (A) N_2 adsorption-desorption isotherms (a and b) **MHS** and (c and d) **P-MHS** at 78 K. (B) pore size distribution of (a) **MHS** and (b) **P-MHS** at 78 K.

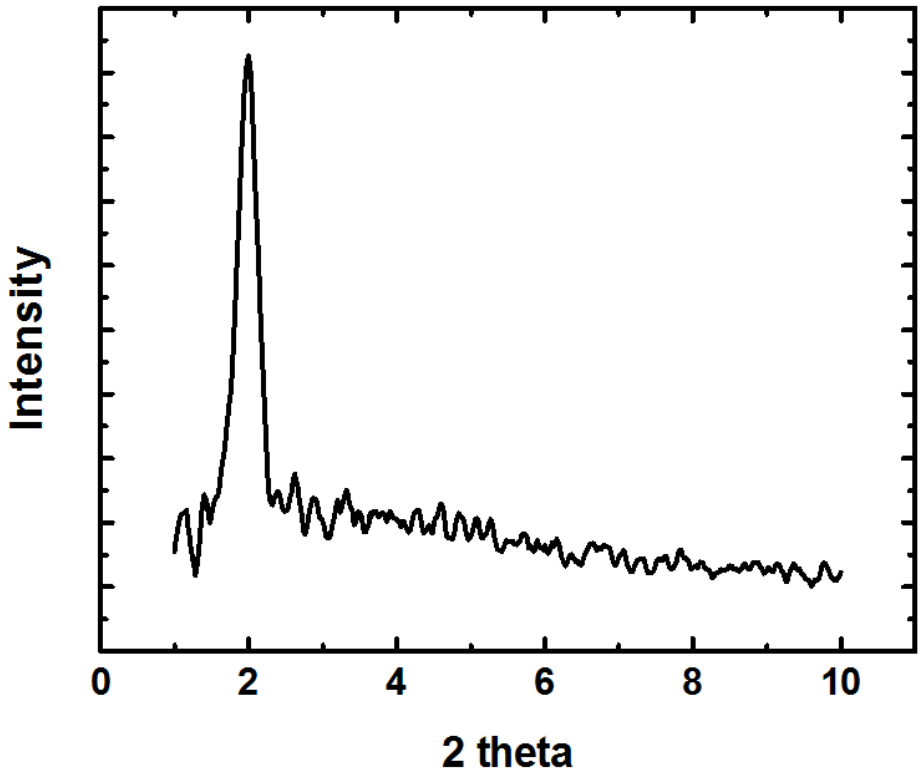


Fig. S6 PXRD pattern of **P-MHS** after remove the self-assembled **1**.

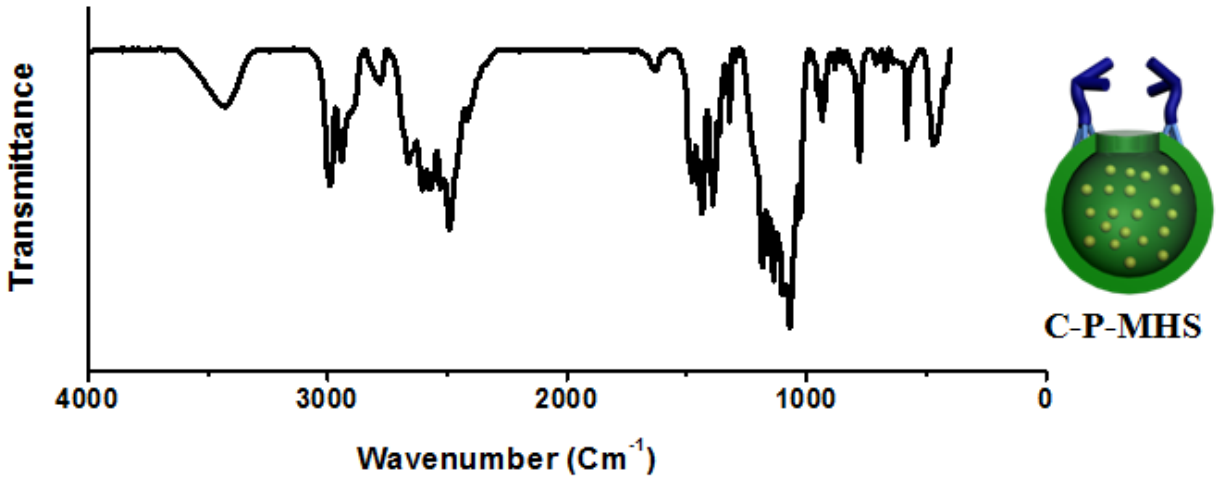


Fig. S7 FT-Infrared spectrum of curcumin-loaded phenanthroline-immobilized mesoporous hollow silica particles (**C-P-MHS**).

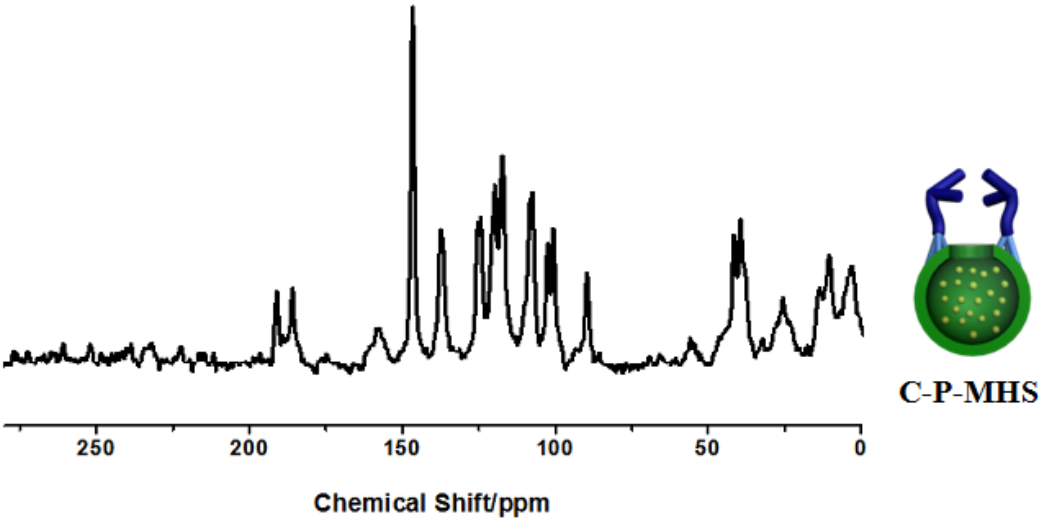


Fig. S8 ^{13}C CP/MAS NMR spectrum of **C-P-MHS**.

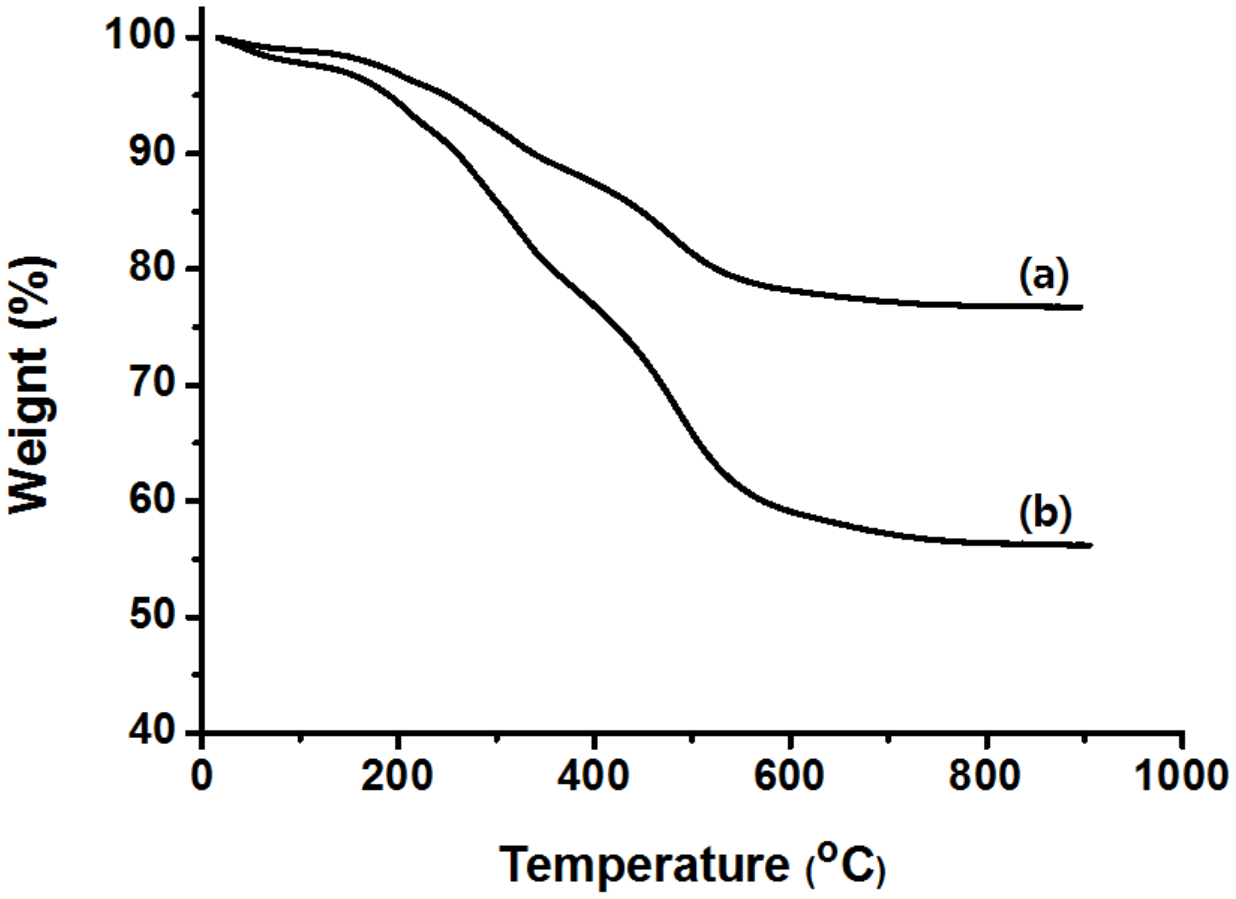


Fig. S9 TGA thermograms of (a) **P-MHS** and (b) **C-P-MHS**.

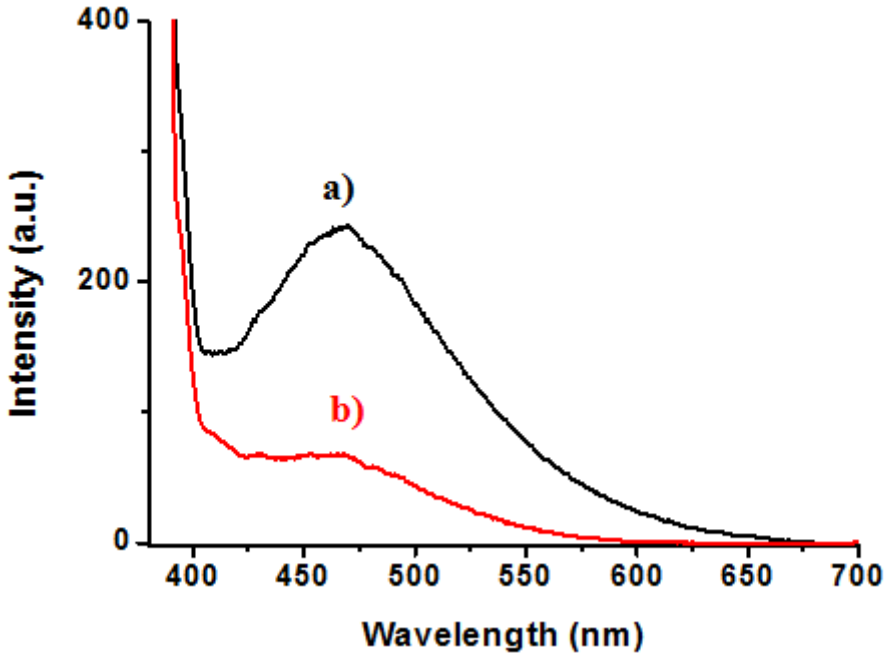


Fig. S10 Fluorescence spectra of **C-P-MHS** (10 mM) in the (a) absence and (b) the presence of Cu^{2+} (5.0 mM)