

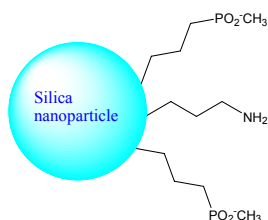
Supporting Information

Molecule-Scale Controlled-Release System Based on Light-Responsive Silica Nanoparticles

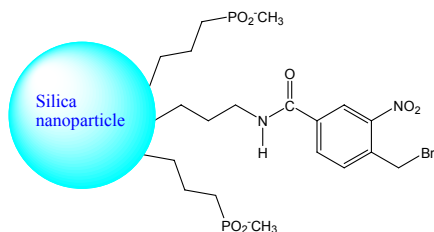
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Experimental section

Synthesis of silica nanoparticles: Silica nanoparticles were synthesized in the w/o microemulsion system. The microemulsion consisted of a mixture of 10.6 mL of Triton X-100, 10.8 mL of n-hexanol, 45.0 mL of cyclohexane, 3.0 mL of deionized water, and 1.0 mL of ammonium hydroxide that was stirred for 30 min, and then 0.30 mL of TEOS was added. After 24 h of stirring, 0.60 mL of TEOS was added to the above solution and stirred for 30 min. Then adding 0.6 mL of negatively charged 3-(trihydroxysilyl)propyl methylphosphonate (42 wt. % in aqueous solution), stirring for 5 min, and finally adding 0.06 mL 3-aminopropyltriethoxysilane followed by 24 h stirring. After the reaction was complete, silica nanoparticles were isolated from the microemulsion using acetone, centrifuged and further washed with ethanol, deionized water and N, N'-dimethyl formamide (DMF) several times to remove surfactant and superfluous dye molecules. The obtained nanoparticles were finally redispersed in 20 mL DMF for further use.

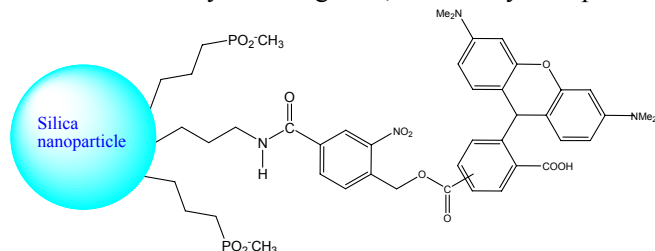


Covalent conjugation of *o*-nitrobenzyl bromide molecules with silica nanoparticles: 13.0 mg 4-bromomethyl-3-nitrobenzoic acid and 10.3 mg N, N'-dicyclohexylcarbodiimide (DCC) were added to a plastic tube containing 3.0 mL of the above silica nanoparticles. The reaction was complete after approximately 6 h. Then the prepared silica nanoparticles were collected and washed with DMF by centrifugation, and finally redispersed in 3 mL DMF.



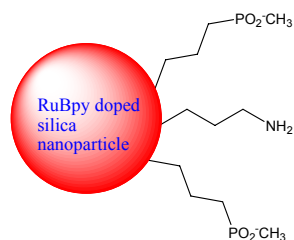
Esterification of 5(6)-carboxytetramethylrhodamine (CTMR) with *o*-nitrobenzyl bromide groups on the surface of silica nanoparticles: 10 mg of CTMR was added to a plastic tube containing 3.0 mL of the above *o*-nitrobenzyl bromide bound silica nanoparticles, and then 1.0 mL triethylamine was added. After approximately 10 h, the nanoparticles were collected and

washed with DMF and deionized water by centrifugation, and finally redispersed in 4 mL deionized water. **Control experiment:** 10 mg of CTMR was added to a plastic tube containing 3.0 mL of silica nanoparticles without *o*-nitrobenzyl bromide, and then 1.0 mL triethylamine was added. After approximately 10 h, the nanoparticles were collected and washed with DMF and deionized water by centrifugation, and finally redispersed in 4 mL deionized water.



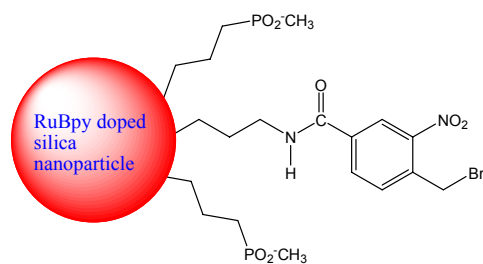
Synthesis of tris(2, 2'-bipyridyl)dichlororuthenium (II) (RuBpy) doped silica nanoparticles:

RuBpy doped Silica nanoparticles were synthesized in the w/o microemulsion system. The microemulsion consisted of a mixture of 10.6 mL of Triton X-100, 10.8 mL of n-hexanol, 45.0 mL of cyclohexane, 3.0 mL of deionized water, 18.0 mg RuBpy, and 1.0 mL of ammonium hydroxide that was stirred for 30 min, and then 0.60 mL of TEOS was added. After 24 h of stirring, 0.30 mL of TEOS was added to the above solution and stirred for 30 min. Then adding 0.6 mL of negatively charged 3-(trihydroxysilyl)propyl methylphosphonate (42 wt. % in aqueous solution), stirring for 5 min, and finally adding 0.06 mL 3-aminopropyltriethoxysilane followed by 24 h stirring. After the reaction was complete, silica nanoparticles were isolated from the microemulsion using acetone, centrifuged and further washed with ethanol, deionized water and N, N'-dimethyl formamide (DMF) several times to remove surfactant and superfluous dye molecules. The obtained nanoparticles were finally redispersed in 20 mL DMF for further use.

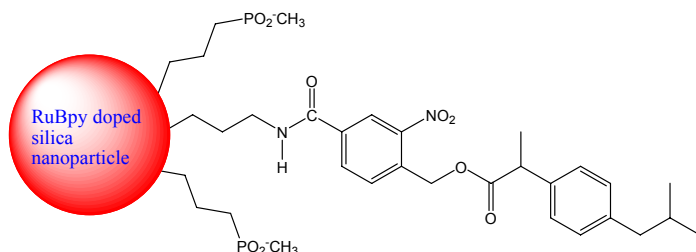


Covalent conjugation of *o*-nitrobenzyl bromide molecules with RuBpy doped silica nanoparticles:

13.0 mg 4-bromomethyl-3-nitrobenzoic acid and 10.3 mg N, N'-dicyclohexylcarbodiimide (DCC) were added to a plastic tube containing 3.0 mL of the above silica nanoparticles. The reaction was complete after approximately 6 h. Then the prepared silica nanoparticles were collected and washed with DMF by centrifugation, and finally redispersed in 3 mL DMF.



Conjugation of ibuprofen with RuBpy doped silica nanoparticles: 10 mg of ibuprofen was added to a plastic tube containing 3.0 mL of the above *o*-nitrobenzyl bromide binded RuBpy doped silica nanoparticles, and then 1.0 mL triethylamine was added. After approximately 10 h, the nanoparticles were collected and washed with DMF and deionized water by centrifugation, and finally redispersed in 4 mL deionized water.



Characterization of particles: A UV-VIS spectrophotometer was used for recording the absorption spectra. A Shimadzu RF-5301pc spectrofluorometer was used for recording the fluorescence spectra. All fluorescence spectra were performed at room temperature by using a Xenon lamp as the source of excitation and a 3 mL standard quartz cuvette (10 mm × 10 mm). Particle characterizations were performed on a Tecnai F30 electron microscope. For the high resolved transmission electron microscopy (HRTEM), sample preparation was done by placing a drop of the freshly prepared colloidal solution on a carbon coated copper grid and the excess solution then removed. The average particle size was determined from TEM images of at least 100 particles.

Photolysis of CTMR carried silica nanoparticles: An aqueous solution of CTMR carried silica nanoparticles (2.5 mg mL⁻¹) was irradiated using a home-made UV-illumination system with wavelengths longer than 310 nm in a 1 cm path length quartz cuvette. After irradiation of the aqueous solution with appropriate time, 0.3 mL of the irradiated solution was taken out with a pipette. Then the irradiated solutions were centrifuged. After that, 0.20 mL of the supernate which contains the photoproduct, CTMR, was taken out and diluted with deionized water for fluorescence measurements.

Fluorescence images: Raw 2647 cells in Dulbecco's Modified Eagle Medium (DMEM) were incubated with drug carried silica nanoparticles (5 μg) for 24 h on culture plates followed by washing with PBS buffer. Confocal fluorescence images were obtained with a Leica MRC1024 microscope with excitation at 488 nm and emission at 590 nm for red channel.

Supplementary data

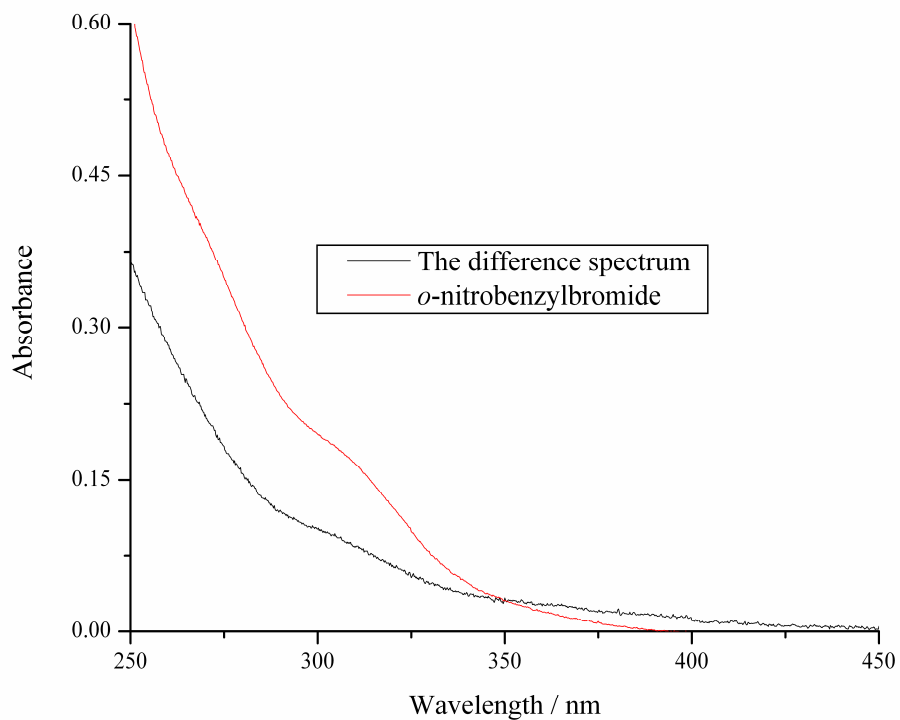


Figure S1. Absorption spectrum of an aqueous solution of *o*-nitrobenzyl bromide (red line) and the difference spectrum (black line) computed from line 2 and 3 in Figure 2b of the paper.

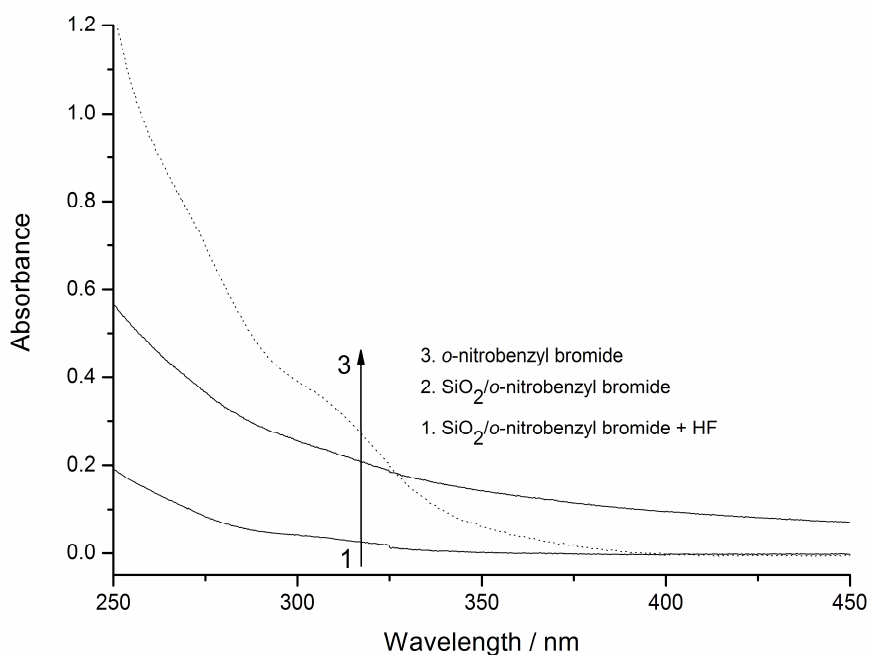


Figure S2. Absorption spectra of an aqueous solution of *o*-nitrobenzyl bromide (line 3), silica nanoparticles conjugated with *o*-nitrobenzyl bromide (line 2), and *o*-nitrobenzyl bromide carried silica nanoparticles (line 1) treated with 2% HF in aqueous solution to dissolve silica nanoparticles.

Figure S2 further confirms the successful conjugation of *o*-nitrobenzyl bromide molecules on the particle surface.

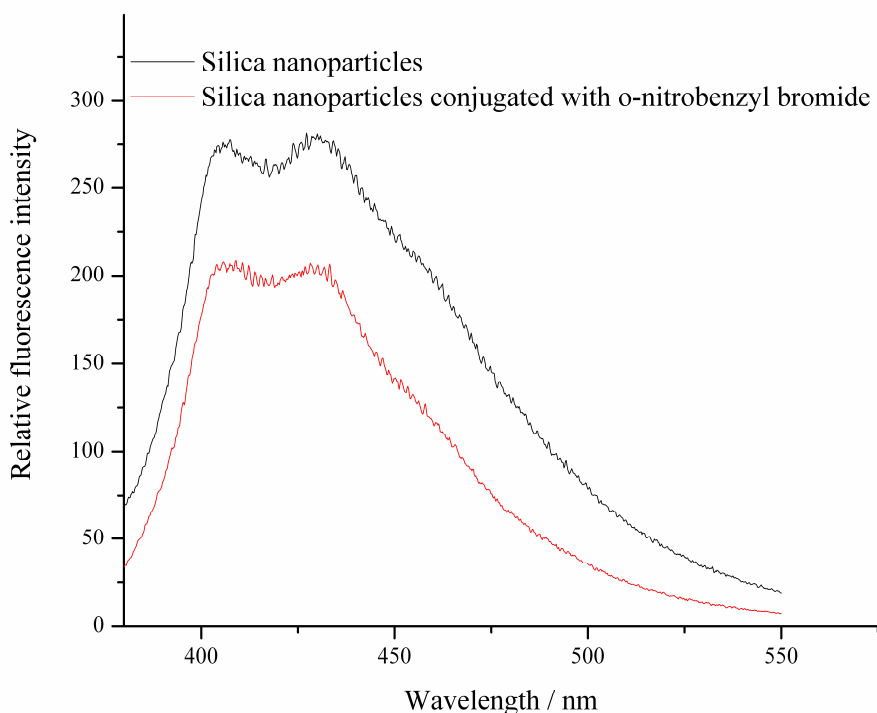


Figure S3. Fluorescence spectra of fluorescamine solutions after reacting with silica nanoparticles (black line) and *o*-nitrobenzyl bromide conjugated silica nanoparticles (red line).

Fluorescence measurements were conducted to verify the attachment of amine groups on the surface of the original silica nanoparticles. The amine groups on the surface of the original silica nanoparticles and the unreacted amine groups on the surface of *o*-nitrobenzyl bromide conjugated silica nanoparticles were quantitatively monitored by the fluorescence intensity of fluorescamine. The fluorescence of fluorescamine solutions, indicative of surface amine groups, was measured using an excitation wavelength of 356 nm. Figure S3 shows the fluorescence spectra of fluorescamine solutions after reacted with the original silica nanoparticles and *o*-nitrobenzyl bromide conjugated silica nanoparticles, respectively. It can be estimated that there are about 30 percents of amines groups on the surface of silica nanoparticles are capable to bind with *o*-nitrobenzyl bromide.

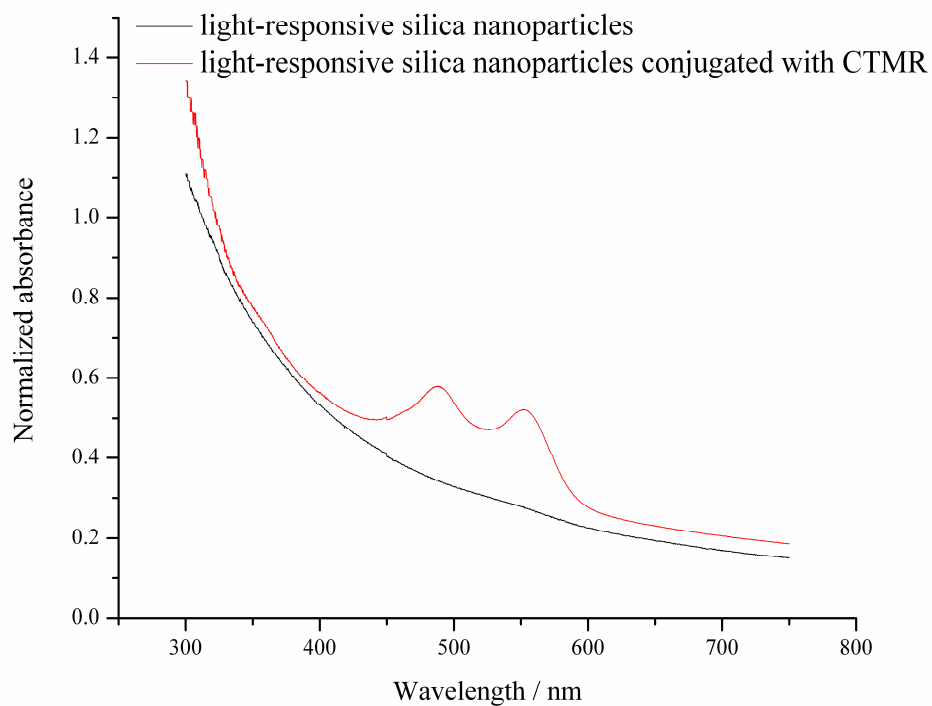


Figure S4. Absorption spectra of CTMR on the surface of silica nanoparticles with (red line) and without (black line) *o*-nitrobenzyl bromide groups

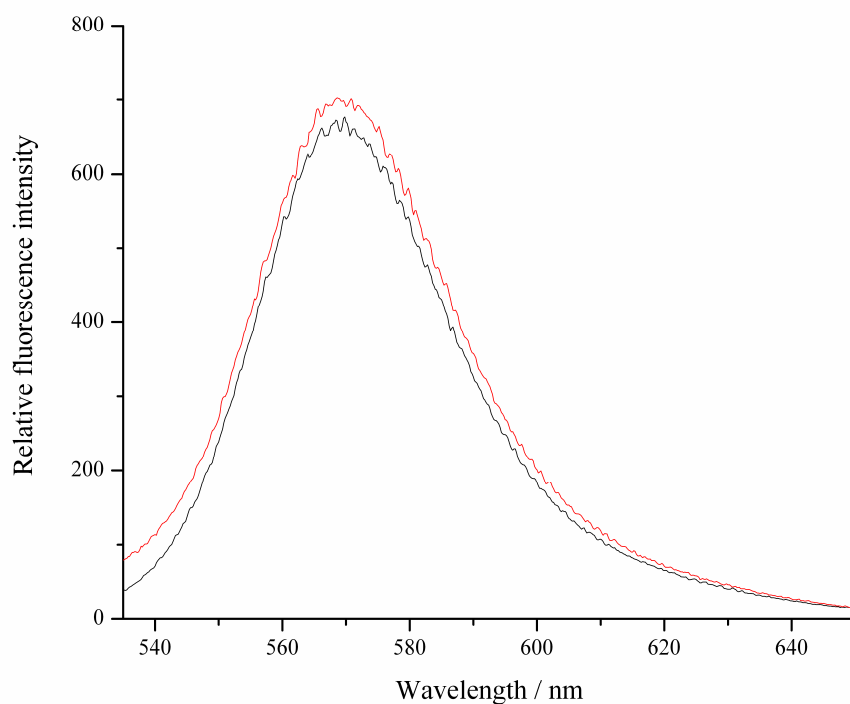


Figure S5. Fluorescence spectra of CTMR conjugated silica nanoparticles (0.41 mg/mL, red line) and CTMR solution (4.65×10^{-7} mol/L, black line).

Assuming that the density of the nanoparticles is equal to pure silica (1.96 g/cm^3), the weight of one nanoparticles of 70 nm can be calculated ($1.96 \times 4/3 \cdot \pi r^3$) to be 3.52×10^{-16} g; thus, the concentration of nanoparticles's solution used for Figure S5 (0.41 mg/mL) corresponds to about 1.94×10^{-9} mol/L. The concentration of CTMR solution used for Figure S5 is 4.65×10^{-7} mol/L. Thus, we could estimate that about 240 CTMR molecules were capable to bind to each silica nanoparticle.

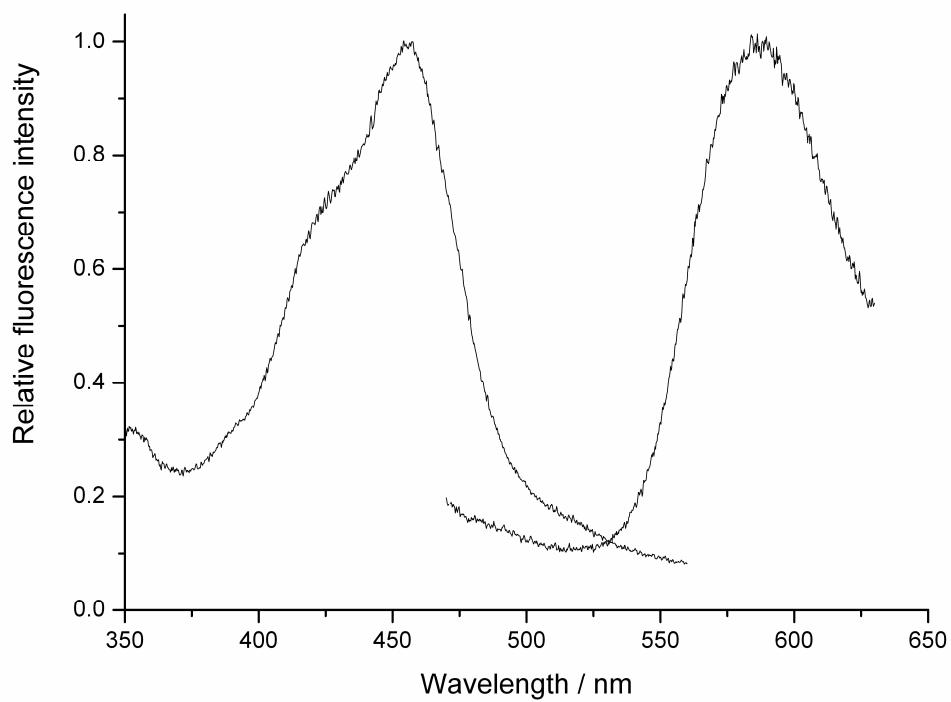


Figure S6. The fluorometric excitation and emission spectra of RuBpy doped silica nanoparticles.