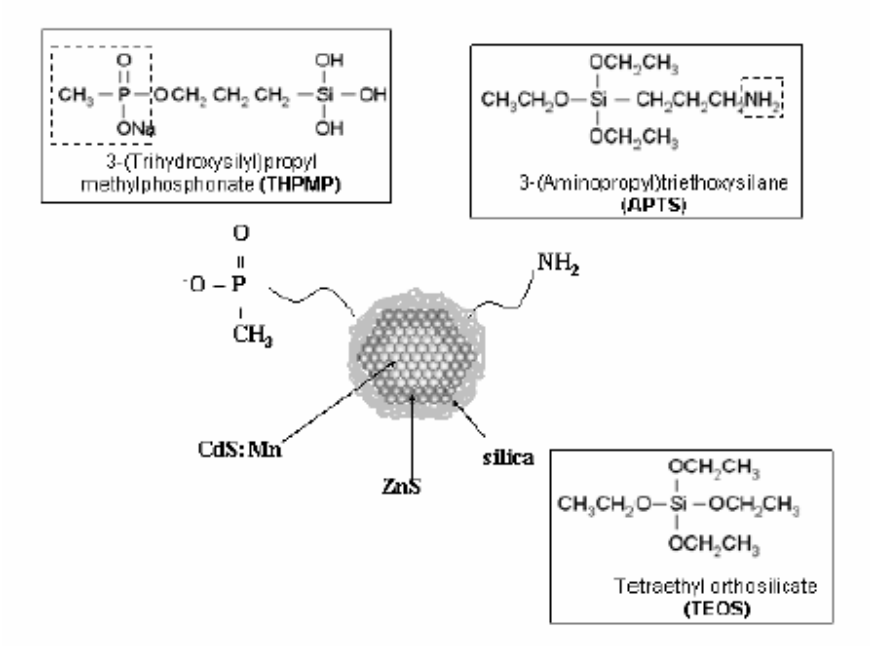
Supplementary Material for Chemical Communications

Supporting information

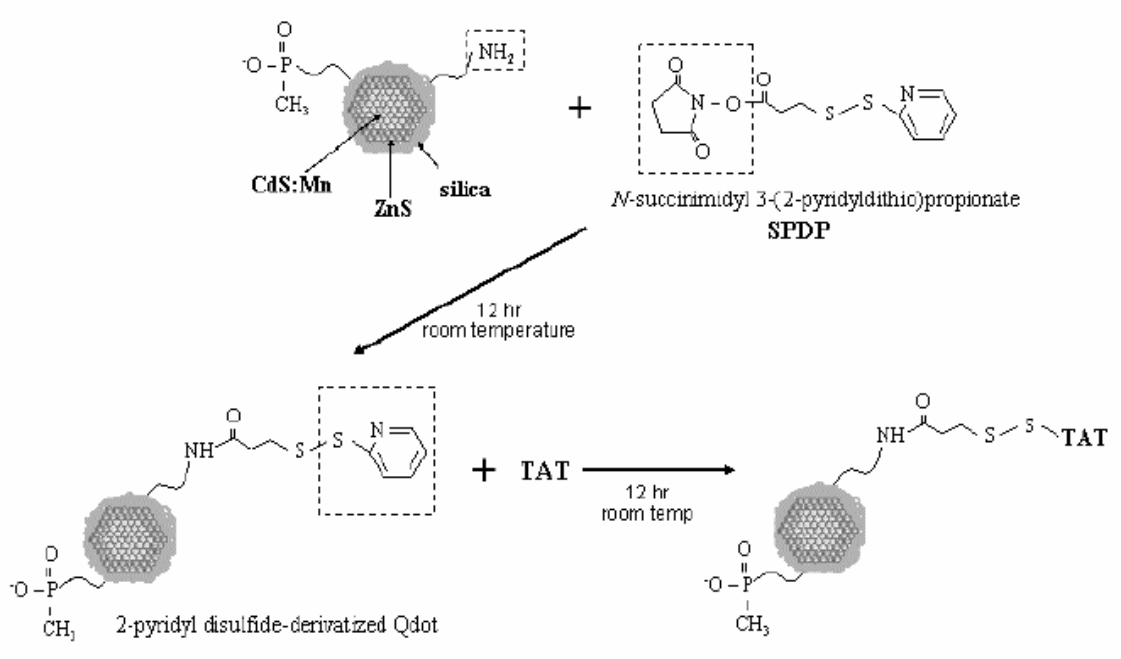
Synthesis of Qdots: In a typical synthesis, water-in-oil (W/O) microemulsion was used by mixing dioctyl sulfosuccinate, sodium salt (AOT, a surfactant), heptane (oil) and an aqueous salt solution. Aqueous solutions of (Cd^{2+} + Mn^{2+}), S^{2-}, and Zn^{2+} were prepared from their precursor salts, $Cd(CH_3COO)_2{\cdot}2H_2O$ + $Mn(CH_3COO)_2$, Na_2S, and $Zn(CH_3COO)_2$, respectively. Mn-doped CdS core Qdots were formed by mixing (Cd^{2+} + Mn^{2+}) and S^{2-}containing microemulsions rapidly for 10–15 min. Then, Zn^{2+}-containing microemulsion was added at a very slow rate (1.5–2 ml/min) into the CdS:Mn Qdot containing microemulsion. To support ZnS shell growth onto CdS:Mn core Qdots, a surplus of sulfur ions was used. The concentrations of Cd^{2+} and Zn^{2+} ions in water are 0.1 and 0.26 M, respectively. The concentrations of water and AOT in heptane are 1 and 0.1 M, respectively, and the ratio of the solution concentrations of ZnS to CdS is 8. The molar ratio of water-to-surfactant (*W*), which determines the size of Qdots, is 10 for all of the (Cd^{2+} + Mn^{2+})-, S^{2-}-, and Zn^{2+}-containing microemulsions. The actual Mn concentration in CdS was determined to be 1.8 mol % using inductively coupled plasma (ICP) analysis. The size of Qdots with a CdS:Mn/ZnS core/shell structure was found to be 3.1 nm with 6-8 % variation in diameter.

Water-dispersible amine functionalization: Highly water-dispersible silica (about 2.5 nm in thickness) coated Qdots were prepared by substantially modifying Schroedter's method. The hydrolysis and co-condensation reaction of tetraethyl orthosilicate (TEOS), 3-(aminopropyl) triethoxysilane (APTS) and 3-(rihydroxysilyl) propyl methylphosphonate (THPMP) led to a highly water-dispersible silica layer around each Qdot. Typically, after addition of the Zn^{2+}-containing microemulsion, 3.7 ml of TEOS is injected into CdS:Mn/ZnS Qdot microemulsion and mixed for 15 min at room temperature. The hydrolysis and condensation reactions are initiated by adding NH_4OH in the form of microemulsion, which is prepared by mixing 2.22 ml of NH_4OH (30 wt %) with AOT (5.5 g)/heptane (75 ml) stock solution. After condensation for 24 hr at room temperature, 1.85 ml of TEOS and 0.37 ml of APTS are injected into the above solution and mixed for 15 min. Subsequently another NH_4OH microemulsion (prepared by mixing 1.32 ml of NH_4OH with AOT (3.27 g)/heptane (30 ml) stock solution) and THPMP (prepared by mixing 1.11 ml of THPMP and 5.33 ml of water with AOT (6.55 g)/heptane (25 ml) stock solution) are injected and reacted for 24 hr. Silica surface-functionalized Qdots are precipitated by addition of a small amount of methanol. After a thorough washing with methanol, these Qdots are dispersed and stable in a phosphate buffer saline solution (PBS, pH 7.4). The picture of surface-functionalized Qdot is shown in Scheme 1.

TAT peptide-conjugation: Typically, a 7 ml Qdot solution (with approximate particle concentration of 10^{16}/ml, 23 mg/ml) was added to 25 mg of *N*-succinimidyl 3-(2-pyridyldithio)propionate (SPDP) in 0.5 ml of dimethyl sulfoxide (DMSO). The mixture was allowed to react for 12 hr at room temperature. The 2-pyridyl disulfide derivatized quantum dots were precipitated with acetone/aqueous NaOH mixture, centrifuged and dispersed in PBS (pH 7.4). Starting with 7 ml of 2-pyridyl disulfide derivatized quantum dots, 4 mg of TAT peptide in 0.2 ml of DMSO was added. The mixture was allowed to react for 12 hr at room temperature. The TAT-conjugated Qdots were precipitated with ethanol, centrifuged and dispersed in a phosphate buffer solution. Typical TAT-conjugation procedures using SPDP chemistry are schematically shown in Scheme. 2.

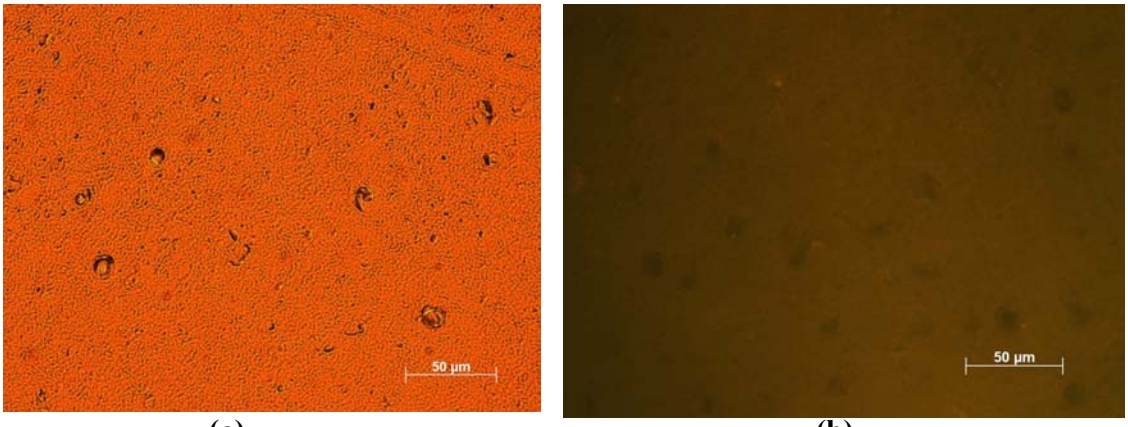


Scheme 1. A cartoon of surface-functionalized Qdot.



Scheme 2. A Schematic of TAT-conjugation procedures using SPDP coupling chemistry.

Autofluorescence study of brain tissue: In order to determine whether or not there is any autofluorescence from rat brain tissue, histological analysis of the tissue sample was performed. Scheme 3 showed the transmission (a) and fluorescence (b) images of the brain sample with the same filter setup as described in Figure 3. From the fluorescence image (Scheme 3 (b)) it was clearly seen that autofluorescence from the native brain tissue was negligible.



(a) **(b)**

Scheme 3. Transmission (**a**) and fluorescence (**b**) microscope images (magnification was 40 X) of a cross-section of a fixed brain tissue without any labeling. Fluorescence images were taken using excitation bandpass 360/40, 400 dichroic longpass and emission bandpass 600/50 filters (obtained from Chroma Technology Corporation, Rockingham, VT). Image (**b**) clearly showed that there was minimal autofluorescence from the brain tissue.