Supplementary Material (ESI) for Chemical Communications

Driving Oxygen Coordinated Ligand Exchange at Nanocrystal Surfaces Using Trialkylsilylated Chalcogenides

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Supplementary Information

Materials and Methods

All reactions were carried out in dried reaction glassware under a dry nitrogen atmosphere. All chemicals were purchased from Sigma-Aldrich (St. Louis, MO) and were used as received. ^{1}H NMR spectra were collected in $CDCl_3$ or toluene-d_8 at 25 °C using a Bruker Biospin Avance II 500 MHz High Performance Spectrometer. All chemical shifts are reported in the standard δ notation of parts per million. Gas chromatography electron ionization mass spectral (GC-EIMS) analyses were performed on an Agilent Technologies Series 6890 Network Gas Chromatography System equipped with a Series 7683B Injector and Series 5973 Quadrupole Inert Mass Selective Detector. Absorbance spectra were collected on a Cary Varian 5000 UV-VIS-NIR Spectrophotometer or Shimadzu UV-3600 UV-VIS-NIR Spectrophotometer. Fluorescence spectra were collected on a Horiba Jobin Yvon FluoroMax-4 Spectrofluorometer. Quantum yield measurements were performed on a Horiba Jobin Yvon FluoroLog-3 Spectrofluorometer equipped with a Quantum Yield Integrating Sphere. Dynamic light scattering and zeta potential measurements were performed on a Zetasizer Nano Series ZS instrument (Malvern Instruments). All analyses were carried

out at the The Molecular Foundry, Lawrence Berkeley National Laboratory, Berkeley, CA.

General Procedure for Ligand Exchange with TMS-S-TEG for ^{1}H NMR Characterization. Purified nanocrystals and TMS-S-TEG (6.0 μL) were added to chloroform (1 mL). The reaction was stirred at 25 °C for 12 hours, with the resulting nanocrystals purified 3 x by precipitation into hexanes. The nanocrystals were dried and resuspended in $CDCl_3$ or toluene-d_8 for analysis.

6,8-Dimercaptooctanoic acid, Dihydrolipoic acid, DHLA (2). 5-(1,2-dithiolan-3-yl)pentanoic acid (2.440 g, 11.83 mmol) was added to a solution of sodium bicarbonate (0.25 M, 50 mL) at 25 °C in a 100 mL round bottom flask and stirred for 15 min, giving a clear, pale yellow solution. The solution was cooled to 0 °C in an ice bath and sodium borohydride (1.879 g, 49.68 mmol) was added in small portions over 5 min, resulting in vigorous bubbling and a color change from pale yellow to colorless over time. The reaction was stirred at 0 °C for 2 hrs, acidified with dropwise addition of HCl (6 M) to pH 1, extracted with 5 × 25 mL toluene, and the combined organic fractions dried over Na_2SO_4 at 25 °C for 4 hrs. The reaction was filtered and the solvent removed under reduced pressure, giving **2** as clear, viscous, colorless oil that was stored under a nitrogen atmosphere in a glove box at 4 °C (2.025 g, 83% yield). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.93 (1H, m), 2.72 (2H, m), 2.39 (2H, t, *J* = 7.5 Hz), 1.90 (1H, m), 1.76 (1H, m), 1.60 (6H, m), 1.36 (1H, t, *J* = 8.0 Hz), 1.31 (1H, d, *J* = 2.0 Hz). GC-EIMS: calculated for [M^+] 208, found 208.

Trimethylsilyl 6-mercapto-8-(trimethylsilylthio)octanoate, bisTMS-DHLA (3). Imidazole (193.61 mg, 2.84 mmol) was added to a 25 mL round bottom flask equipped

with a reflux condenser. Hexamethyldisilazane (8.715 g, 11.26 mL, 54.00 mmol) was added by syringe and the mixture stirred at 25 °C for 5 min. 6,8-dimercaptooctanoic acid (1.875 g, 1.61 mL, 9.00 mmol) was then added slowly, dropwise by syringe, producing a cloudy solution. The reaction was heated to 100 °C for 24 hrs and the solvent removed under reduced pressure, giving a pale, yellow oil. The oil was dissolved in dichloromethane (100 mL) and cooled to 4 °C. The organic layer was washed briefly with 4 °C H_2O (Millipore, 100 mL) and dried immediately over Na_2SO_4 at 25 °C for 4 hrs. The reaction was filtered and the solvent removed under reduced pressure, giving **3** as a clear, colorless oil that was stored under a nitrogen atmosphere in a glove box at 4 °C (2.857 g, 90% yield). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.93 (1H, m), 2.66 (2H, m), 2.31 (2H, t, *J* = 7.0 Hz), 1.88 (1H, m), 1.80 (1H, m), 1.60 (6H, m), 1.32 (1H, d, *J* = 3.8 Hz), 0.32 (9H, s), 0.28 (9H, s). GC-EIMS: calculated for [M^+] 352, found 352.

Trimethylsilyl 3-(trimethylsilylthio)propanoate, bisTMS-MPA (5). 3-Mercaptopropanoic acid (2.122 g, 1.742 mL, 19.99 mmol) **4** was added to a 100 mL round bottom flask equipped with a reflux condenser. Anhydrous dichloromethane (20 mL) was added subsequently, giving a clear, colorless solution which was stirred at 25 °C for 5 min. 1-(Trimethylsilyl)imidazole (6.39 g, 6.68 mL, 45.53 mmol) was then added and the reaction was heated to 60 °C for 18 hrs. The reaction was cooled to 25 °C and the solvent removed under reduced pressure, giving a clear, viscous oil. Pentane (25 mL) was added and the mixture sonicated for 1 min, resulting in precipitation of imidazole. The pentane soluble fraction was collected by vacuum filtration and the remaining precipitate washed with 3 × 25 mL pentane. The pentane fractions were combined and the solvent removed under reduced pressure, affording a viscous oil that

was purified by vacuum distillation (oil bath temperature 68 °C, vapor temperature 45-48 °C, 0.18 mbar), providing **5** as a clear, colorless oil that was stored under a nitrogen atmosphere in a glove box at 4 °C (3.00 g, 60% yield). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.61 (2H, m), 2.57 (2H, m), 0.33 (9H, s), 0.32 (9H, s). GC-EIMS: calculated for [M^+] 250, found 250.

Trimethylsilyl 11-(trimethylsilylthio)undecanoate, bisTMS-MUA (7). 11-Mercaptoundecanoic acid (3.36 g, 15.39 mmol) **6** was added to a 100 mL round bottom flask equipped with a reflux condenser. Anhydrous dichloromethane (16 mL) was added subsequently, giving a clear, colorless solution which was stirred at 25 °C for 5 min. 1-(Trimethylsilyl)imidazole (4.91 g, 5.14 mL, 35.1 mmol) was then added and the reaction was heated to 60 °C for 18 hrs. The reaction was cooled to 25 °C and the solvent removed under reduced pressure, giving a clear, viscous oil. Pentane (25 mL) was added and the mixture sonicated for 1 min, resulting in precipitation of imidazole. The pentane soluble fraction was collected by vacuum filtration and the remaining precipitate washed with 3 × 25 mL pentane. The pentane fractions were combined and the solvent removed under reduced pressure, affording a viscous oil that was purified by vacuum distillation (oil bath temperature 155-160 °C, vapor temperature 105-115 °C, 0.14-0.16 mbar), providing **7** as a clear, colorless oil that was stored under a nitrogen atmosphere in a glove box at 4 °C (3.35 g, 60% yield). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.54 (1H, m), 2.50 (1H, m), 2.31 (2H, m), 1.61 (4H, m), 1.3 (12H, m), 0.33 (9H, s), 0.32 (9H, s). GC-EIMS: calculated for [M^+] 362, found 362.

General Procedure for Ligand Exchange with Trimethylsilylated Reagents to Afford Water Dispersible Nanocrystals. Invitrogen Qdot 545 ITK or Qdot 605 ITK

organic quantum dots (1 μM in decane, 200 μL, 0.2 nmol) were added to chloroform (800 μL), giving an organic solution that was bright green or orange fluorescent under uv excitation, respectively. The desired trimethylsilylated compound (0.2 mmol) was then added, and the reaction stirred at 25 °C for 12 hrs. Sodium tetraborate buffer, 50 mM, pH 10 (1 mL) was then added, the solution vortexed, and the biphasic solution left to stand for 1 hr at 25 °C. Subsequent addition of NaOH (1 M) was required to adjust the pH to 10. A white film was observed at the interface between the organic and aqueous phases, with the aqueous portion exhibiting bright green or orange fluorescence. The chloroform portion was essentially nonfluorescent, indicating complete transfer of quantum dots to the aqueous phase. The vial was centrifuged at 3.0×10^3 rpm at 25 °C for 3 min and the organic phase removed. The aqueous phase was further extracted with 2 × 1 mL chloroform, with the organic phase removed after centrifugation as explained previously. The resulting QDs were buffer exchanged with 3 × 15 mL sodium tetraborate buffer, 10 mM, pH 10, with 1 mM free ligand using an Amicon Ultra-15 10K MWCO centrifugation device (Millipore Corporation). The concentrated solutions thus afforded were filtered through a PTFE Acrodisc CR Syringe Filter (13 mm, 0.22 μm pore size, Pall Corporation) and stored in the dark at 25 °C. QD concentrations were determined according to previously published literature procedures, and diluted accordingly for analyses.[1]

Direct Comparison Between Conventional Ligand Exchange and Reactive Ligand Exchange. All preparations were performed in a glove box. A stock solution of bis(tetramethylammonium)-MUA (0.575 M) was prepared from MUA (1.255 g, 5.75 mmol), tetramethylammonium hydroxide pentahydrate (1.00 g, 11 mmol) and chloroform (10 mL). The solution was vortexed extensively and allowed to phase separate overnight. After centrifugation, the chloroform layer was transferred to a separate scintillation vial for storage.

Conventional ligand exchange. A dispersion of either Qdot 545 ITK or Qdot 605 ITK (200 µL, 1 µM solution in decane, 0.2 nmol, Invitrogen) was added to a solution of bis(tetramethylammonium)-MUA (0.575 M, 174 µL, 100 *µ*mol, 5 x 10^5 equivalents) in $CHCl_3$ (626 µL). The mixture was vortexed and allowed to stand at room temperature for 16 h (Figure S1, A). Half of the sample (500 µL) was diverted towards aqueous transfer: after diluting the sample with an additional portion of chloroform (500 µL), an equivolume of 50 mM borate buffer pH 10.0 was introduced to the vial and the nanocrystals partitioned between phases via vortexing (Figure S1, B & C). The chloroform layer was removed and excess ligand removed by washing with additional portions of chloroform (2 x 1 mL) before filtration to remove aggregates (0.2 µm, PTFE, Pall Life Sciences). We noted that the chloroform layer during the transfer process contained significant amounts of residual luminescence from nanocrystals (Figure 1, C), indicative of an incomplete exchange of the hydrophobic native ligands. Samples were buffer exchanged to 50 mM borate buffer at pH 10.0 containing 1 mM MUA by spin dialysis (30 kDa MWCO, Millipore) prior to analysis (Figure S1, D). In contrast to

samples prepared from reactive ligand exchange, samples prepared via conventional ligand exchange were not stable, with aggregation present after a few days following the transfer sequence (Figure S1, E & F). Dynamic light scattering indicated the presence of nanocrystal aggregates immediately following aqueous transfer (Figure S2). The remaining samples of exchanged nanocrystals in chloroform were flocculated with an equivolume of acetone and centrifuged to a pellet before resuspension in chloroform (3x). In the final preparation, the Qdots were re-dispersed in 500 μL $CDCl_3$ for ^1H NMR (Figure S3, A & C).

Reactive ligand exchange. For comparison, samples from a reactive ligand exchange process using bisTMS-MUA were also prepared. A dispersion of either Qdot 545 ITK or Qdot 605 ITK (100 μL, 1 μM solution in decane, 0.1 nmol, Invitrogen) was added to a solution of bisTMS-MUA (18 mg, 50 *μ*mol, 5 x 10^5 equivalents) in $CHCl_3$ (400 μL). The mixture was vortexed and allowed to stand at rt for 16 h. MUA-exchanged nanocrystals in chloroform were flocculated with an equivolume of acetone and centrifuged to a pellet before resuspension in chloroform (3x). In the final preparation, Qdots were re-dispersed in 500 μL $CDCl_3$ for ^1H NMR (Figure 3, B & D).

Quantum Yield of CdTe and CdSe cores. Quantum yields of purified phosphonate-capped CdSe (1.5%) and oleate-capped CdTe (2.1%) were collected in $CHCl_3$ as previously described. A solution of bisTMS-MUA (18μL in 100μL of $CHCl_3$) was added to each solution of NCs (100μL) and allowed to stand for 2 hours. The resulting QYs decreased to 0.2% and 0.1%, respectively. Nevertheless, the exchanged cores

demonstrated excellent dispersion in basic aqueous buffers after QY collection (Fig. S6).

References

1. Yu, W. W.; Qu, L.; Guo, W.; Peng, X. *Chem. Mater.* **2003**, *15*, 2854-2860.

Surface Atom Calculation

From E. E. Foos, J. Wilkinson, A. J. Makinen, N. J. Watkins, Z. H Kafafi, J. P. Long. *Chem. Mater.* 2006, **18**, 2886. and C.A. Leatherdale, W.-K. Woo, F.V. Mikulee, and M.G. Bawendi. *J. Phys. Chem. B,* 2002, **106,** 7619.

$$S = \frac{\{4/3\pi r^3 - [4/3\pi(r-d)^3]\}N}{V}$$

Where:

S = # of surface Cd^{2+} atoms

r = particle radius

d = Cd – Se bond length

N = number of Cd-Se units per unit cell

V = Volume of unit cell

Using this formula, we can calculate the % of surface atoms of the system:

$$\%SurfaceAtoms = \frac{r^3 - (r-d)^3}{r^3}$$

We can calculate the concentration and size of CdSe nanocrystals from the absorbance spectrum. For a typical sample add 6.0uL (~5mg) of TEG-S-TMS = 1.77×10^{-2} mmoles to 0.5mL nc solution.

[CdSe nc] = 9.96×10^{-7}M; average nc diameter = 5.44nm; [Cd^{2+}] = 8.26×10^{-6}M

%Surface Atoms = 26.5% = 2.19×10^{-6} moles

For a typical ligand exchange, add 6.0uL (~5mg) of TEG-S-TMS = 1.77×10^{-2} mmoles to 0.5mL nc solution.

Ratio of TEG-S-TMS:CdSe nc = ~3230 equivalents

Ratio of TEG-S-TMS:Cd^{2+} surface atoms = ~8 equivalents

Supplementary Figures

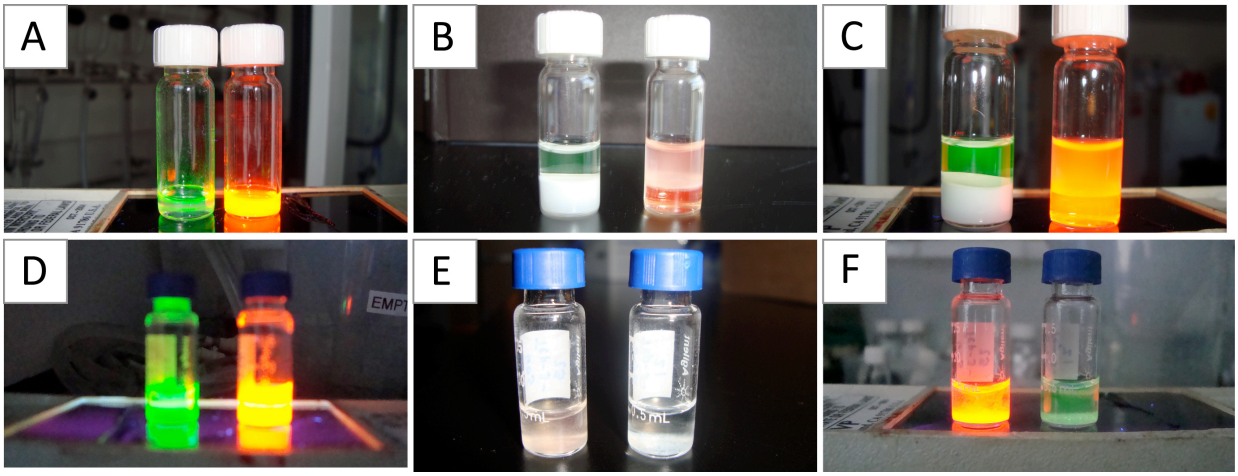

Figure S1. Conventional ligand exchange steps with bis(tetramethylammonium)-MUA ligands and Qdot-545 and Qdot-605 CdSe/ZnS nanocrystals. (A) Solutions of nanocrystals in chloroform during the ligand exchange. (B) Aqueous transfer under biphasic conditions: aqueous layer (top) & chloroform layer (bottom). (C) Same as in (B) except under UV illumination. (D) Purified samples of MUA-exchanged nanocrystals in 50 mM borate buffer containing 1 mM MUA as a stabilizer under UV illumination. (E) Same sample as in (D) under ambient light after 3 days. (F) Same as in (E) under UV illumination.

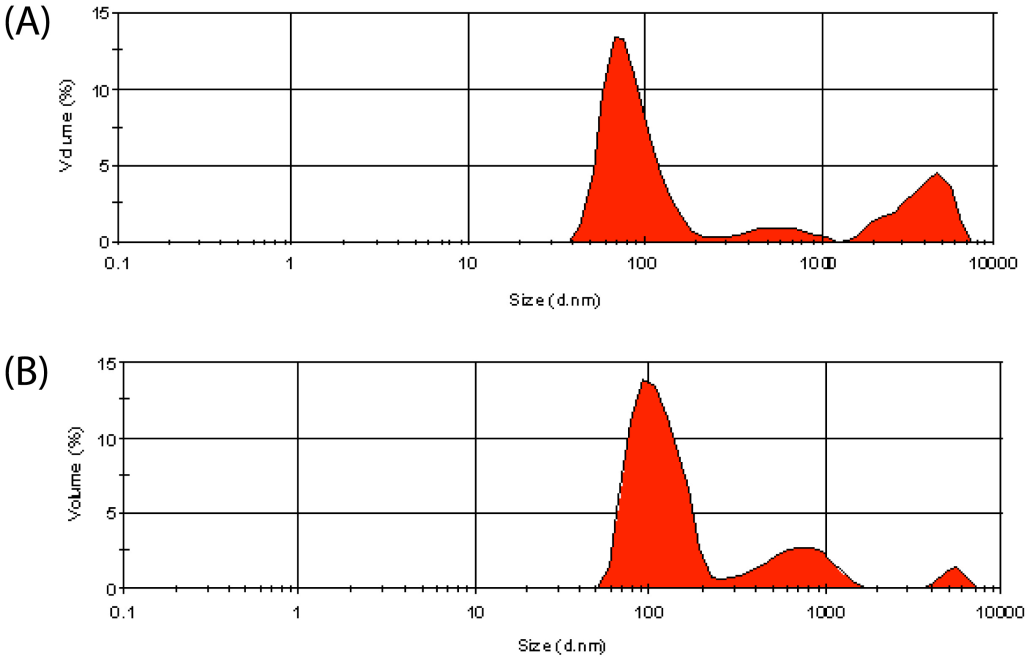

Figure S2. DLS results from aqueous dispersions of Qdot-545 (A) and Qdot-605 (B) samples that have undergone conventional ligand exchange with MUA.

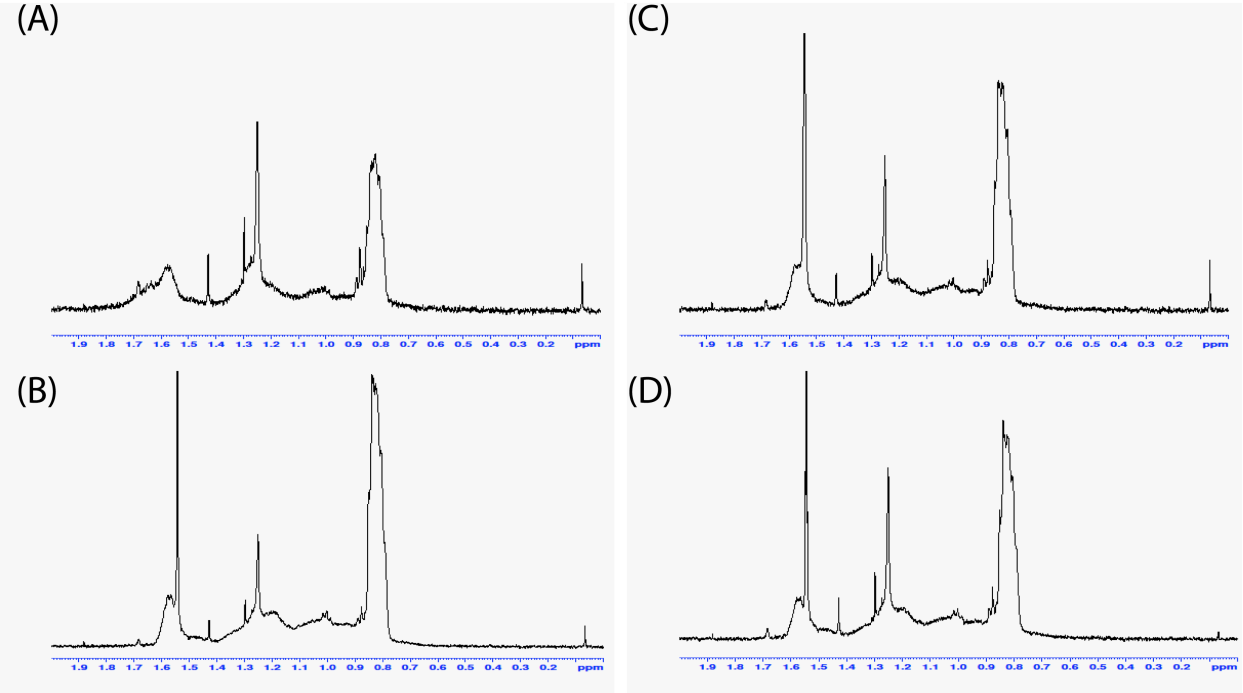

Figure S3. ^{1}H NMR spectra for Qdot-545 samples which have undergone conventional ligand exchange with bis(tetramethylammonium)-MUA ligands (A) or reactive ligand exchange with bisTMS-MUA ligands (B). Similarly, ^{1}H NMR spectra for Qdot-605 samples which have undergone conventional ligand exchange with bis(tetramethylammonium)-MUA ligands (C) or reactive ligand exchange with bisTMS-MUA ligands (D). Broad peaks corresponding to MUA ligands bound to a nanocrystal are clearly present in all spectra. Residual ligand content appears to be minimal. Due to overlapping resonances, it is difficult to quantify the extent of exchange via either protocol.

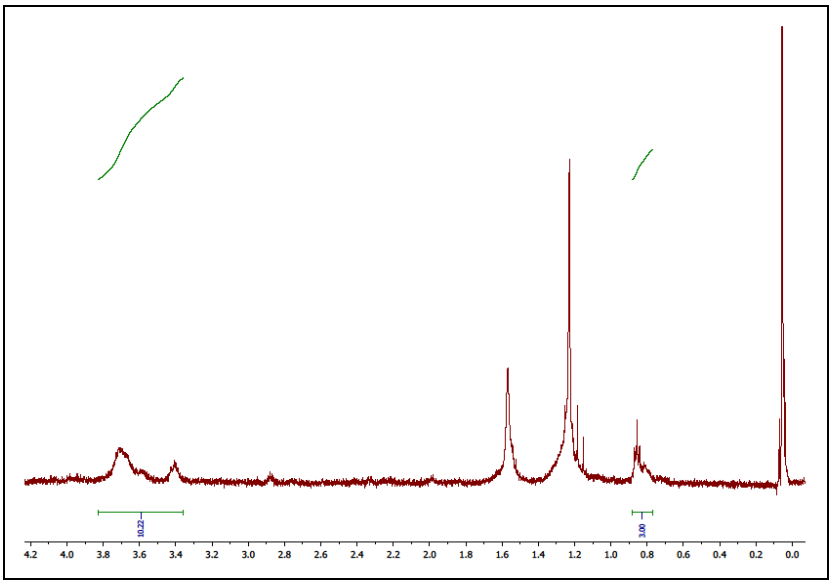

Figure S4. ^{1}H NMR of stearate capped ZnO nanocrystals after exchange with TMS-S-TEG with integrals used to calculate exchange efficiency.

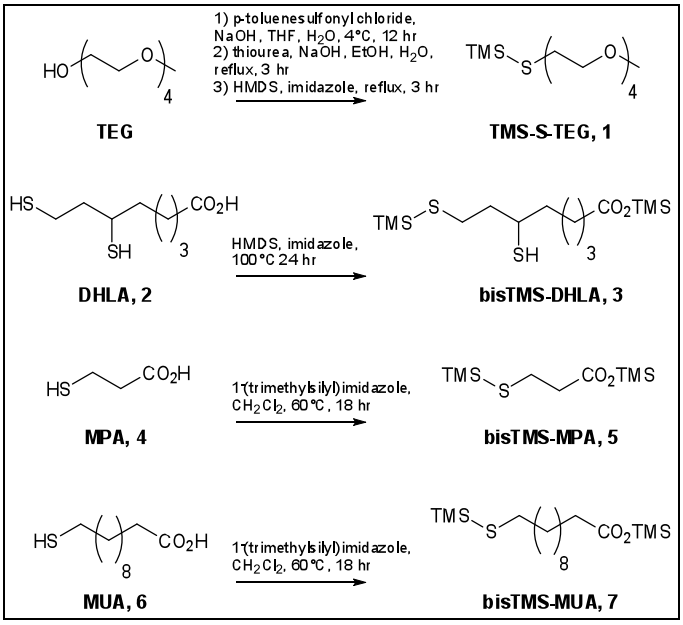

Figure S5. Synthetic scheme for ligand syntheses.

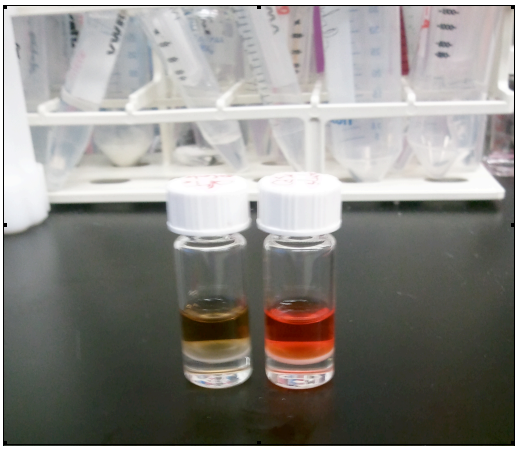

Figure S6. MUA-CdTe (left) and MUA-CdSe (right) NCs after collection of quantum yields and subsequent transfer into a basic aqueous buffer solution (top layer) from $CHCl_3$ (bottom layer).