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Size Reduction of CdSe/ZnS Quantum Dots by a Peptidic Amyloid Supergelator

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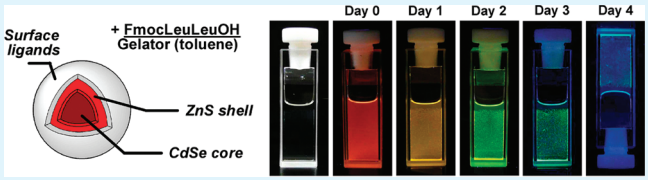
Supporting Information

ABSTRACT: Anchoring of a self-assembling dipeptide on the surface of core/shell CdSe/ZnS quantum dots resulted in a competition between coordination of the surface atoms of the QDs and the strong tendency for the dipeptide to self-assemble in toluene. This resulted in a mild QD etching and in a corresponding increase in the band gap of the nanocrystals whose photoluminescent emission gradually turns blue with time. The FmocLeuLeuOH dipeptide supergelator self-assembles in fibrils in which the Fmoc groups are surrounded by the pendant isobutyl side chains of the leucine residues with vibrational circular dichroism (VCD) and liquid- and solid-state NMR attributes of twist anti-parallel β-sheets.



KEYWORDS: *nanoparticles, etching, peptide, gelator, self-assembly, quantum dots*

Self-assembly of peptides and proteins into fibril structures is of tremendous importance in the formation of aggregates involved in diseases as diverse as Alzheimer's, Huntington's, and Parkinson's.[1,2] Technologically relevant approaches have been attempted to use this strategy for the construction of advanced materials.[3,4] For example, the incorporation of photoluminescent (PL) semiconductor nanocrystals like quantum dots (QDs) in self-assembling peptidic compounds afforded materials with unprecedented architectures and properties.[5−7] However, peptides playing a double role, namely, (i) surface stabilization of QDs and (ii) self-assembly, have not been explored in a competitive context to the best of our knowledge. The competition between stabilization of the QDs surface by means of the carboxylic acid groups of the peptides and the self-assembly power of the anchored aminoacids is likely to enhance the surface reactivity of the QDs if the balance favors self-assembly at the expense of surface binding (successive decoordination and recoordination of the ligand). Here we report the surface functionalization of QDs by a self-assembling dipeptide gelator, subsequent QD etching and preliminary results of the peptide tendency to self-assemble in twisted β-sheets. Dipeptide **1**, structural analogue of a known gelator,[8] was prepared with a functional group (carboxylic acid) enabling to anchor it on the QD surface (Figure 1).

It was easily synthesized from the corresponding diprotected dipeptide[8] (benzylic protective group at the C-terminal extremity) by a simple hydrogenation reaction (see the Supporting Information).

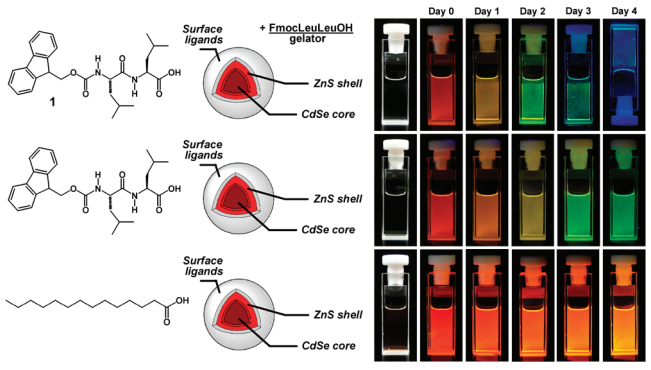


Figure 1. Structure of the QD ligand **1** used to induce etching, which is also a good gelator of toluene as can be seen on the picture day 4 of the top line (inverted vial). The top line refers to the time evolution of the peptide covered QDs with enough additional gelator **1** to induce gelation ([**1**] = 26 mM in toluene). The middle line shows the evolution of the peptide covered QDs with time and the bottom line that of tetradecanoic acid covered QDs as a control.

Ligand exchange of DIPCOOH (**1**) with trioctylphosphine oxide/trioctylphosphine (TOPO/TOP) on the surface of CdSe/ZnS core/shell QDs afforded the targeted DIPCOOH-QDs (see ESI). Careful monitoring of the PL properties over a

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few days showed a blue shift phenomenon of the QDs emission as can easily be seen in Figure 1 (middle line). This was assigned to mild QD etching[9−11] (monitored by UV and PL, Figure 2a) and is most probably related to the strong tendency

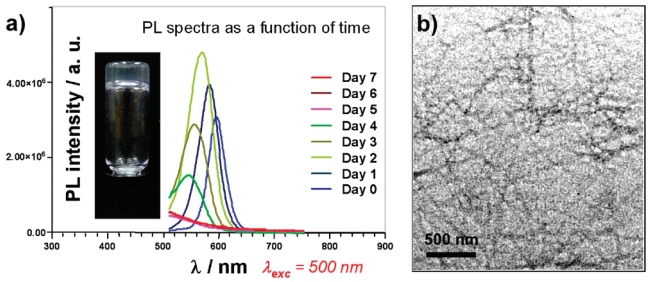

Figure 2. (a) Time evolution of the PL spectrum of a DIPCOOH-QD doped toluene gel of **1** and (b) TEM micrograph of a dried solution of dipeptide **1** and DIPCOOH-QDs in toluene ([**1**] = 36 mM) showing entangled fibers with QDs inside (aging time: three days).

of dipeptide **1** to self-assemble in toluene as observed by NMR, IR, VCD and TEM. The dried xerogel showed the presence of fibers of diameter ∼20−50 nm with darker areas inside the fibers due to the presence of the quantum dots (Figure 2b). When an additional amount of dipeptide **1** was added at the beginning of the etching process, gelation was observed after a few days (Figure 1, top line) with an increased rate of QD etching, likely due to the enhanced concentration of the self-assembling peptide. The fact that the PL emission of the QDs and the peptide aggregation are changing on a similar time scale of several days suggests that these two phenomena are linked. This prompted us to turn our attention on the self-assembling properties of **1**.

Gelation occurred for toluene only (see the Supporting Information) after successive heating and cooling of a suspension of dipeptide **1** (Figure 2a).[12] The kinetics of the liquid harnessing is concentration dependent but is of approximately four days which is reminiscent of the lag time observed for small peptides forming amyloid fibrils.[2] A concentration of 0.3 wt % was sufficient to gel toluene which makes this peptide a member of the supergelator family.[13,14] The ^{1}H NMR spectrum of a toluene-d_8 gel of dipeptide **1** at 25°C showed clear evidence of hydrogen bonding involving the amide N−H protons (δ_{Hc} = 7.30 and δ_{Ha} = 6.09 ppm). Two significant upfield shifts of ∼1.0 ppm occur as the temperature is raised to 100°C (δ_{Hc} = 6.32 ppm and δ_{Ha} = 5.06 ppm), which is a sign of hydrogen bonding disassembly.[15,16] The ^{1}H NMR spectrum after cooling back to room temperature and waiting for 24 h is virtually identical to that of the gel state but no gelation was observed visually. This shows that the dipeptide self-associates even though this may not be detectable visually. The 2D NOESY spectrum (Figure 3b, recorded 1 week after the VT series) shows the cross-correlations to have the same sign as that of the diagonal in line with peptide aggregation.

Chemical exchange cross peaks (amide protons, red area of Figure 3b) indicate that multiple conformations are present even though a major one dominates. NOE cross-peaks are in line with an anti conformation for which the carbamate and the amide functions (and also the isobutyl side chains) are positioned in opposite directions (green area of Figure 3b, Hb−Hc interactions) which is favorable for its assembly in β-sheet structures (such peptides are usually too short to assemble into α-helices).[17] Some additional cross peaks (blue

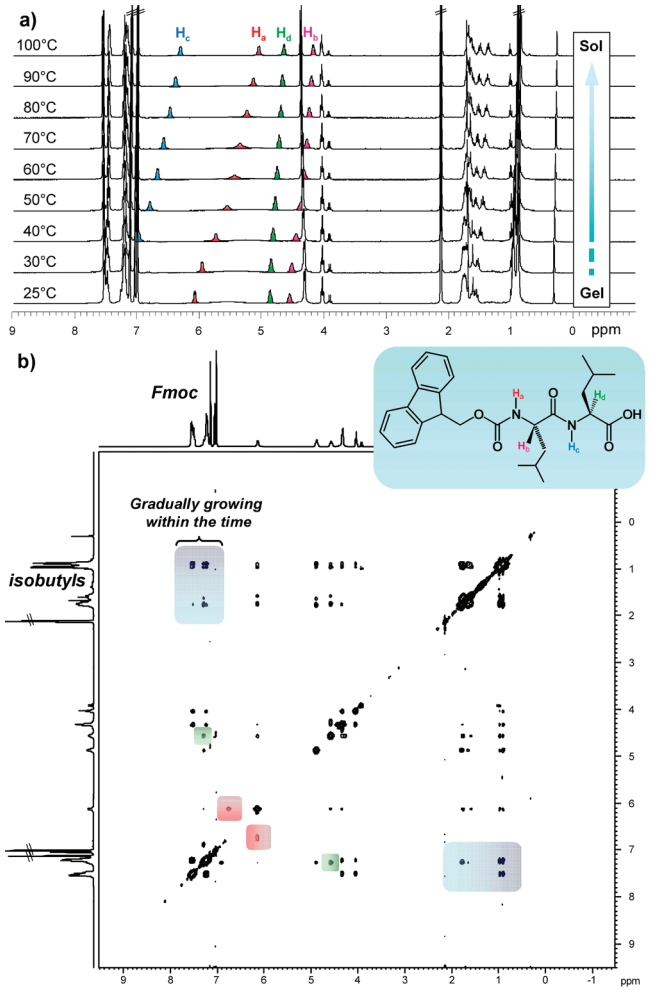

Figure 3. (a) Variable-temperature ^{1}H NMR spectra of dipeptide **1** in toluene-d_8 and (b) 2D NOESY spectrum showing intermolecular interactions between the Fmoc groups and the isobutyl side chains (highlighted in blue, [**1**] = 36 mM, mixing time =300 ms).

area of Figure 3b) that are not present in the liquid-phase spectrum gradually appear within time and provide evidence that in the gel state, the Fmoc groups are held in close proximity to the isobutyl side chains. Solid-state cross-polarization magic angle spinning ^{13}C NMR spectra of the dipeptide **1** xerogel showed the appearance of two narrow signals near 172 and 180 ppm (see the Supporting Information), taken as indicative of β-sheet and helical arrangements respectively present in the same structure.[8,18−20]

Recently, infrared (IR) and vibrational circular dichroism (VCD) spectroscopies have demonstrated their sensitivity to fibril formation and growth.[21,22]

The formation of fibrils in toluene is characterized by intensity decreases and increases of IR and VCD bands in amide I and II regions (Figure 4a). After ∼49 h incubation, the VCD intensities with a − − − + + pattern became enormous reflecting the chiral structuring of the supramolecular assemblies.[21,22] The band that appeared at 1690 cm^{-1} on the IR spectrum after ∼16 h, associated with the bands at 1634 and 1525 cm^{-1}, suggests an antiparallel β-sheet secondary structure[23] as generally observed for similar Fmoc dipeptides.[8,24,25] However, the relative intensity of this peak is unusually strong as is the associated negative VCD band suggesting either distortions of the antiparallel β-sheets (twist

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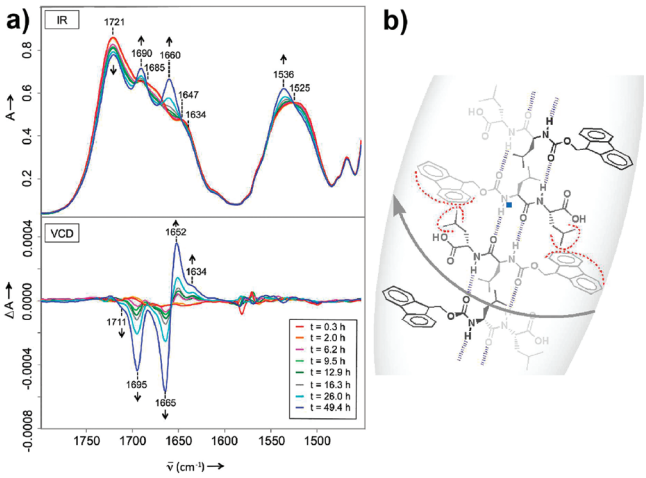

Figure 4. (a) Time evolution of the IR and VCD spectra of **1** in toluene measured at room temperature and (b) proposed twisted anti-parallel β-sheet assembly of **1** in toluene.

β-sheets) or another secondary structure like parallel β-sheets or β-turns.[7,26] In addition, the high symmetric positive couplet at (1652; 1665) cm^{-1} is indicative of left-handed helical twist of anti-parallel β-sheets (in line with SSNMR).

Because of the labile nature of the carboxylic group regarding surface atom coordination of QDs, the peptidic ligands may be significantly mobile, and prone to decoordinate from the QD surface as they self-assemble to twisted antiparallel β-sheets. Yet, the quantum dots continue to emit light but at wavelengths that blue shift with time, suggesting that the dipeptide still tend to passivate the QD surface. The QDs are presumably inside the fibers (TEM) as a result of the surface ligands that are structurally identical to the gelator, thus enhancing the likelyhood of QD surface passivation. Clearly, these results need more investigation, particularly to understand what exactly happens on the QDs surface and address the etching mechanism. Nevertheless, we showed that a suitably designed dipeptide can modulate the emitting properties of quantum dots if the two properties of the dipeptide (QD surface stabilization and self-assembly) are balanced to meet the two requirements simultaneously.

■ ASSOCIATED CONTENT

Supporting Information

Dipeptide synthesis, full characterization, and solid-state NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) Knowles, T. P.; Fitzpatrick, A. W.; Meehan, S.; Mott, H. R.; Vendruscolo, M.; Dobson, C. M.; Welland, M. E. *Science* **2007**, *318*, 1900−1903.

(2) Hamley, I. W. *Angew. Chem., Int. Ed.* **2007**, *46*, 8128−8147.

(3) Chen, C.-L.; Rosi, N. L. *Angew. Chem., Int. Ed.* **2010**, *49*, 1924−1942.

(4) Cherny, I.; Gazit, E. *Angew. Chem., Int. Ed.* **2008**, *47*, 4062−4069.

(5) Kim, J. H.; Lim, S. Y.; Nam, D. H.; Ryu, J.; Ku, S. H.; Park, C. B. *Biosens. Bioelectron.* **2011**, *26*, 1860−1865.

(6) Bardelang, D.; Zaman, Md. B.; Moudrakovski, I. L.; Pawsey, S.; Margeson, J. C.; Wang, D.; Wu, X.; Ripmeester, J. A.; Ratcliffe, C. I.; Yu, K. *Adv. Mater.* **2008**, *20*, 4517−4520.

(7) Yan, X.; Cui, Y.; He, Q.; Wang, K.; Li, J. *Chem. Mater.* **2008**, *20*, 1522−1526.

(8) Bardelang, D.; Camerel, F.; Margeson, J. C.; Leek, D. M.; Schmutz, M.; Zaman, Md. B.; Yu, K.; Soldatov, D. V.; Ziessel, R.; Ratcliffe, C. I.; Ripmeester, J. A. *J. Am. Chem. Soc.* **2008**, *130*, 3313−3315.

(9) Galian, R. E.; de la Guardia, M.; Pérez-Prieto, J. *J. Am. Chem. Soc.* **2009**, *131*, 892−893.

(10) Liu, J.; Yang, X.; Wang, K.; Wang, D.; Zhang, P. *Chem. Commun.* **2009**, 6080−6082.

(11) Palui, G.; Nanda, J.; Ray, S.; Banerjee, A. *Chem.—Eur. J.* **2009**, *15*, 6902−6909.

(12) There are also signs of aggregation in polar solvents as shown by the detection of supramolecular oligomers up to the tetramer by ESI-MS, see the Supporting Information.

(13) Bouas-Laurent, H.; Desvergne, J.-P. *Molecular Gels: Materials with Self-Assembled Fibrillar Networks*; Weiss, R. G.; Terech, P., Eds.; Springer: Dordrecht, The Netherlands, 2006; chapter 12.

(14) Luboradzki, R.; Gronwald, O.; Ikeda, A.; Shinkai, S. *Chem. Lett.* **2000**, 1148−1149.

(15) Seo, M.; Kim, J. H.; Kim, J.; Park, N.; Park, J.; Kim, S. Y. *Chem.—Eur. J.* **2010**, *16*, 2427−2441.

(16) Chowa, H.-F.; Wang, G.-X. *Tetrahedron* **2007**, *63*, 7404−7418.

(17) Cheng, G.; Castelletto, V.; Moulton, C. M.; Newby, G. E.; Hamley, I. W. *Langmuir* **2010**, *26*, 4990−4998.

(18) Baxa, U.; Wickner, R. B.; Steven, A. C.; Anderson, D. E.; Marekov, L. N.; Yau, W.-M.; Tycko, R. *Biochemistry* **2007**, *46*, 13149−13162.

(19) Lim, K. H.; Nguyen, T. N.; Damo, S. M.; Mazur, T.; Ball, H. L.; Prusiner, S. B.; Pines, A.; Wemmer, D. E. *Solid State NMR* **2006**, *29*, 183−190.

(20) Tycko, R. *Quat. Rev. Biophys.* **2006**, *39*, 1−55.

(21) (a) Measey, T. J.; Schweitzer-Stenner, R. *J. Am. Chem. Soc.* **2011**, *133*, 1066−1076. (b) Ma, S.; Cao, X.; Mak, M.; Sadik, A.; Walkner, C.; Freedman, T. B.; Lednev, I. K.; Dukor, R. K.; Nafie, L. A. *J. Am. Chem. Soc.* **2007**, *129*, 12364−12365.

(22) Measey, T. J.; Smith, K. B.; Decatur, S. M.; Zhao, L.; Yang, G.; Schweitzer-Stenner, R. *J. Am. Chem. Soc.* **2009**, *131*, 18218−18219.

(23) (a) Azuma, E.; Kuramochi, K.; Tsubaki, K. *Chem Pharm. Bull.* **2010**, *58*, 680−684. (b) Tang, C.; Smith, A. M.; Collins, R. F.; Ulijn, R. V.; Saiani, A. *Langmuir* **2009**, *25*, 9447−9453. (c) Yamada, N.; Ariga, K.; Naito, M.; Matsubara, K.; Ishida, S. *J. Am. Chem. Soc.* **1998**, *120*, 12192−12199.

(24) Smith, A. M.; Williams, R. J.; Tang, C.; Coppo, P.; Collins, R. F.; Turner, M. L.; Saiani, A.; Ulijn, R. V. *Adv. Mater.* **2008**, *20*, 37−41.

(25) Smith, A. M.; Collins, R. F.; Ulijn, R. V.; Blanch, E. *J. Raman Spectrosc.* **2009**, *40*, 1093−1095.

(26) (a) Kim, J.; Kapitan, J.; Lakhani, A.; Bour, P.; Keiderling, T. A. *Theor. Chem. Acc.* **2008**, *119*, 81−97. (b) Kubelka, J.; Keiderling, T. A. *J. Am. Chem. Soc.* **2001**, *123*, 12048−12058.