

Visible Light Excitation of CdSe Nanocrystals Triggers the Release of Coumarin from Cinnamate Surface Ligands

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Abstract: The photochemical properties of organic ligands on the surface of nanocrystalline CdSe particles were examined. A number of thiols carrying a substituted cinnamate tail was synthesized. In solution, these cinnamate compounds undergo light-induced (374 nm) *E*–*Z* isomerization, followed by a nonphotolytic lactonization to give highly fluorescent coumarin. The cinnamate-thiols were successfully exchanged onto the CdSe nanocrystal, and the photochemical behavior of these conjugates was studied. Upon aerobic photolysis at 374 nm, the surface cinnamates released coumarin accompanied by rapid nanocrystal degradation. This degradation was not observed under similar anaerobic conditions or when the organic ligands did not contain the cinnamate group. Surprisingly, very similar results were obtained upon irradiation at visible wavelengths at which the cinnamate has no absorption. With the aid of UV–visible absorption spectroscopy, fluorescence spectroscopy, and electrochemistry, a unified theory for both the increased photoinstability of the nanocrystal as well as the coumarin release was proposed. It involves cinnamate radical anions on the CdSe surface, formed upon electron transfer from the excited nanocrystal to the surface cinnamate, undergoing *E*–*Z* isomerization. Practically, this results in the remarkable ability to release coumarin from nanocrystal ligands simply by exciting the nanocrystal with visible light. This new photorelease protocol not only aids in the understanding of fundamental nanocrystal–ligand interactions but may also offer new opportunities in the areas of drug delivery and imaging.

Introduction

Semiconductor nanocrystals (NCs) have received extensive interest in the past decades.^{1,2} The existence of the quantum confinement effect gives rise to spectacular size-dependence of the nanocrystals properties,³ such as their optical⁴ and electronic properties.⁵ CdSe nanocrystals have been popular objects of study as well-defined syntheses for these species exist,^{4,6,7} and a variety of exciting applications has been disclosed.⁸ CdSe NCs have to be stabilized with surface ligands to prevent them from

aggregating into larger insoluble agglomerates. In the classical CdSe syntheses, the trioctyl-phosphine oxide (TOPO) ligand serves this purpose, providing steric protection of the nanocrystal surface. Furthermore, it enhances the solubility of the NCs in organic solvents. However, with the increasingly specialized applications of NCs, the need for tailor-made and functionalized surface ligands becomes more and more evident. The original TOPO ligands offer an excellent starting point toward this further functionalization. Methodology has been developed to replace TOPO ligands with compounds such as alkylamines,⁹ pyrimidines,¹⁰ and thiols. The latter have been popular ligands owing to the strong binding of the SH group to the surface Cd atoms. For example, many groups have prepared NCs that are covered with biomolecules through thiol linkers.¹¹ A rapidly expanding area is the binding of small organic ligands, which are prepared through multistep synthesis. The attachment of small organic ligands provides a unique means to direct the

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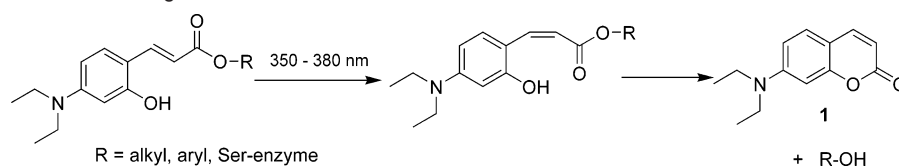
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Scheme 1. Mechanism of Photocleavage of Cinnamate Esters

properties of the NC without altering its overall size significantly. Several examples using thiols, amines, and phosphine oxides have been reported over the last years, with applications ranging from the fields of medicinal to polymer chemistry.¹² However, in most cases the focus has been on the interaction of the organic surface ligand with the exterior environment rather than with the NC itself. Systematic studies on the mutual dynamic interaction of CdSe NCs with small but functionalized organic surface ligands have mostly been lacking. Yet, these interactions will prove relevant in the chemistry of NCs covered with larger surface (bio)molecules. Moreover, it affords the chance to probe the intrinsic properties of the NC from a different point of view, i.e., from its surface layer. Triggered by these opportunities, we set out to investigate the chemistry of functionalized organic thiols on the CdSe surface, with a clear focus on the interaction between the ligand and the NC.

We decided to focus on photoactive organic surface ligands, as this combines well with the interesting photonic properties of CdSe NC. The design of the ligands was based on photoactive serine protease inhibitors, in which our group has had an interest over the past decades.^{13,14} The chromophore in these inhibitors is an *o*-hydroxy *E*-cinnamate ester unit ($\lambda_{\text{max}} = 374$ nm) that upon photolysis yields the *Z*-isomer, which subsequently lactonizes to release a coumarin unit and an alcohol or phenol¹⁴ (Scheme 1). The *p*-diethylamino substituted cinnamate proved to be most efficient as serine protease inhibitors, giving 7-diethylaminocoumarin (**1**, hereafter denoted as “coumarin”) as product.¹⁵ Conveniently, coumarin is highly fluorescent ($\lambda_{\text{ex}} = 374$ nm, $\lambda_{\text{em}} = 438$ nm) whereas the cinnamate precursors are not, providing excellent means to follow this chemistry in situ by fluorescence spectroscopy. Inspired by this, we selected the cinnamate unit depicted in Scheme 1 as the key feature of a synthetic thiol that was attached to the surface of CdSe NC. In this paper, we report on the synthesis and photochemical studies of the NC covered with this photoactive thiol, confirm the existence of photointeraction between the cinnamate unit and the NC and propose a mechanism for this interaction. Remarkably, we demonstrate that isomerization and subsequent

Table 1. Different Types of Nanocrystals Prepared

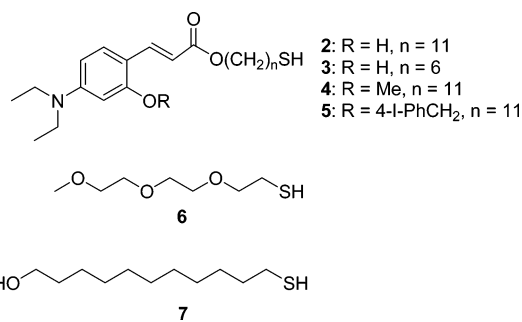
NC type	size NC (Å)	ligand(s)
I	31	2,6
II	31	3,6
III	31	4,6
IV	31	5,6
V	31	6
VI	31	7

lactonization of the surface ligand to release coumarin can be initiated simply by exciting the nanocrystal.

Results and Discussion

Synthesis and Characterization of NC–Thiol Conjugates.

The ideal ligand consists of a thiol group that attaches to the CdSe surface, a spacer to provide steric flexibility and the photoactive cinnamate unit. Thiol **2** satisfies these demands. It was prepared from a functionalized Wittig reagent and a substituted salicylaldehyde in 5 steps (see Supporting Information). For purposes discussed later, derivatives **3–5** were prepared analogously. All cinnamates thus made had UV–visible absorption maxima at 374–376 nm. The ligands were attached to the NC by stirring pyridine-coated CdSe nanocrystals (py-NC)¹⁶ in deoxygenated HCl-free chloroform with ligands **2–5** and 3 equiv of **6**.¹⁷ Inert coligand **6** was applied to induce better solubility and to ensure high dilution of the cinnamates on the surface, so that direct interaction between two cinnamates, once on the surface, could be minimized. The exchange was followed by precipitation, removal of any free ligand by extensive washing, and drying (see Table 1). NCs coated with just **6** or mercapto-undecanol (**7**) were prepared for reference purposes.



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All NCs show continuous absorption far into the visible region (Figure 1A), a property typical for CdSe NC,⁴ with the first excitation peak at 560 nm. A key feature from these UV–visible absorption spectra is the increased absorption around 374 nm of Type I NC as compared to Type V. The differential absorption peak centered at 374 nm (see inset of Figure 1A)

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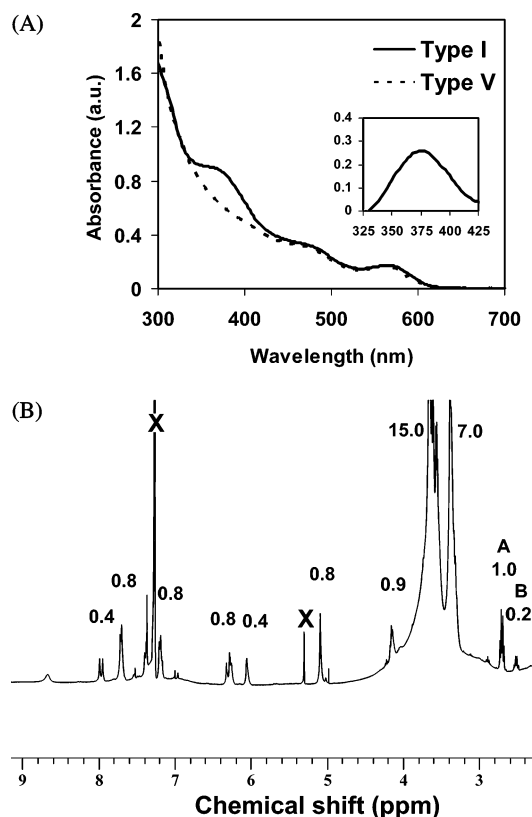


Figure 1. (A) Representative UV–visible absorption spectra for Types I and V CdSe NC in DMF. (Inset) 325–425 nm spectrum obtained after subtraction of spectrum of Type V from spectrum of Type I. (B) ^1H NMR of Type IV NC in CDCl_3 with integration of key-peaks. Peaks marked with X are residual solvent peaks (CHCl_3 and a trace of CH_2Cl_2).

stems from cinnamate ligands, either surface bound or released to the solvent (vide infra). Using the ratio of this differential absorption peak versus the NC absorption at 560 nm in conjunction with the ϵ -values for CdSe NC¹⁸ and for cinnamates 2–5 at 374 nm (see Supporting Information), it was determined that 5–8 cinnamates were on the surface of Types I–IV NC before dissolution.¹⁹ NCs covered with iodinated ligand 5 (Type IV) were prepared for detailed analysis with ^1H NMR spectroscopy and Rutherford Back Scattering (RBS).²⁰ The ^1H NMR spectrum of Type IV NC in CDCl_3 (Figure 1B) showed proton resonances for the cinnamate downfield protons (vinylic and aromatic, 6.0–8.0 ppm) and the alkyl protons (ca. 3.5 ppm) of the glycol coligand (6). None of the protons of the cinnamate π -system (6.0–8.0 ppm) broadened extensively, which indicated that the NC surface monolayers were reasonably homogeneous. A signal for the unbound cinnamate thiol (5), a sharp quartet B for CH_2SH group, is visible and it contributed only 25% to the “total” amount of 5 as established by comparison to the integration of the aromatic protons and the benzylic group at 5.1 ppm. The same observation was made for coligand (6, quartet A). The shifted CH_2S signals for the corresponding bound thiols were buried under the multitude of peaks starting

at 2.8 ppm, analogously to shifts reported in the literature.^{21,24} Evidently, upon dissolving the NC some 25% of surface thiols were released and migrated into solution. This was confirmed by subjecting freshly dissolved Type IV NC to centrifugation through a size-exclusion membrane, which resulted in recovery of $\sim 40\%$ of the cinnamate ligands in the filtrate. These findings indicate that upon NC dissolution, an equilibrium between free and bound thiol ligand was established, which is in agreement with a recent report describing reversible ligand detachment of a variety of ligands on CdSe NCs.²²

Combining the RBS spectrum (see Supporting Information) and the ^1H NMR spectrum, we were able to roughly estimate the stoichiometry on the surface of Type IV NC. It followed that, on average, the surface of 1 nanocrystal before dissolution was covered with ~ 160 molecules of TOPO, ~ 60 of PEG-thiol 6, and ~ 15 of cinnamate 5, affording almost 100% total coverage based on available surface Cd atoms.²⁰ Clearly, the single py-exchange was only moderately effective in replacing TOPO, as observed before.¹⁶ The coverage numbers for Type IV NC obtained from RBS/NMR and UV–visible absorption spectroscopy (15 and 5 cinnamates per NC, respectively) both confirm the important notion that there is low coverage of the dry nanocrystals by the cinnamates of interest. The quantitative discrepancy between the two can be attributed to the relatively large errors in the RBS/NMR estimation, and as such coverage numbers obtained from UV–visible absorption spectroscopy were used throughout the rest of the work. The low coverage likely holds true for all types of NC, because the same exchange procedure was used for all NC and incorporation of an iodobenzyl-group, located on the outer spheres of the surface monolayer, would have only little effect on the stacking efficiency.

Photolysis Studies: Photostability. Photolysis studies were performed on all types of NC in DMF solution at similar concentrations (optical density at the first excitation peak ~ 0.15). It is well-known that aerobic photolysis of CdSe NC results in decomposition.^{23,24} Peng et al performed an extensive study on this process using thiol-coated CdSe NC and irradiation at 254 nm.²⁴ Figure 2A shows the evolution of the UV–visible absorption spectrum of Type I NC upon aerobic irradiation at 374 nm. After an incubation period (ca. 1 h), the first excitation peak shifts from 560 to 542 nm over 6 h accompanied by general washing out of absorption pattern and precipitation of NC, indicating NC decomposition through oxidation of surface Cd and Se atoms.^{23,25,26} Surprisingly, Type I NC decomposed dramatically faster than Type V NC (Figure 2B) under identical conditions; the latter only started to decompose after > 15 h of irradiation. We think that Type V NC shows the moderate photoinstability reported for NC coated with long-chain thiols²⁴ and that Type I NC actually undergoes unusually rapid photodegradation. Superoxide (O_2^-) was found to be a reactive oxygen species involved in this photodegradation.²⁷ This was

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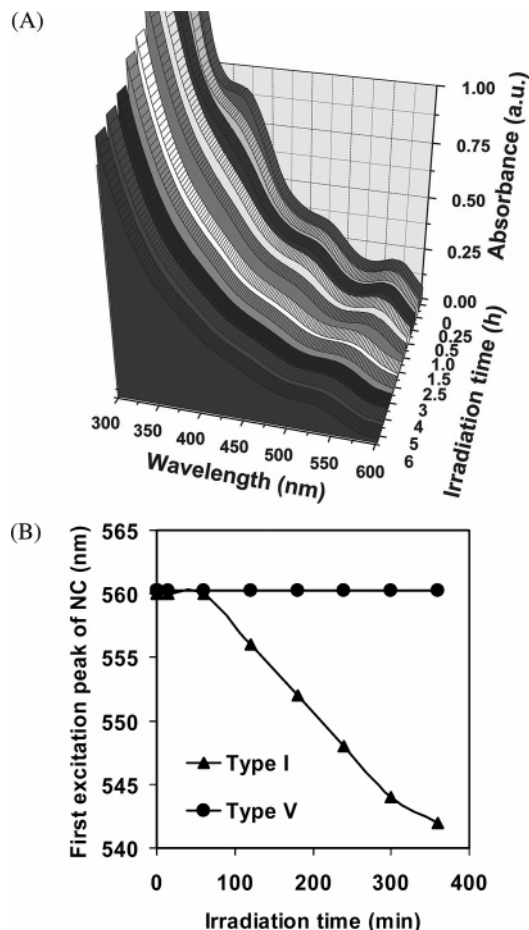


Figure 2. Evolution of absorption spectra during aerobic irradiation of Type I NC and Type V NC in DMF at 374 nm. (A) Three-dimensional representation of full-scale UV-visible absorption spectra for Type I. (B) Time-evolved first excitation peaks for Types I and V.

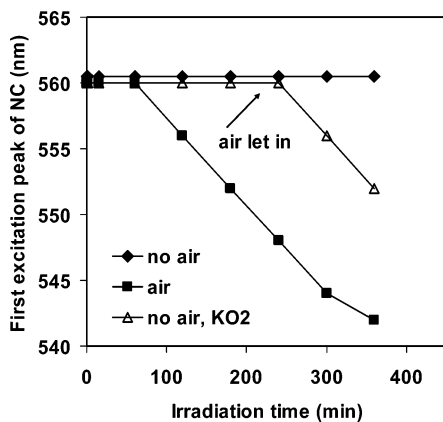


Figure 3. Irradiation of Type I NC at 374 nm in the presence or absence of 2.2 mM KO_2 -crownether complex and/or air. For the curve with open triangles (no air, KO_2), air was let in the system after 4 h.

deduced from the increased oxidation of epinephrine²⁸ to adrenochrome by formed O_2^- (see Supporting Information). However, O_2^- itself did not induce NC photodegradation. Rather, molecular oxygen (O_2) was necessary to initiate the photodecomposition (Figure 3). Furthermore, singlet oxygen ($^1\text{O}_2$) was found not to be actively involved as its quencher NaN_3 did not inhibit photodegradation (results not shown).²⁹ All this

points toward electron transfer from excited NC (NC^*) to O_2 as the key-step.^{27,30} A striking finding was that the accelerated photodegradation of Type I NC occurred at wavelengths all the way to 560 nm and only then when O_2 was present (see Supporting Information).³¹ The cinnamate ligands having no absorption >440 nm, this excluded excited surface cinnamates as triggers in the NC decomposition.

NC covered with various cinnamates related to **2** showed the same behavior. Thus, replacement of the phenolic $-\text{OH}$ in Type I NC by a $-\text{OMe}$ (Type III NC) or reduction of the spacer length to 6 carbons (Type II NC) afforded NC that also photodegraded easily at 374 or 560 nm, albeit with a longer incubation time for Type III NC (see Supporting Information). In sharp contrast to Types I–III, cinnamate-lacking Type V and VI NC did not show significant photodecomposition under the employed conditions. Importantly, no degradation occurred either upon irradiation of Type V NC in the presence of free cinnamate **8** (see Supporting Information), emphasizing that the enhancement in photodegradation for Types I–III is solely a result of bound cinnamates and that cinnamates released to the solvent (vide supra) do not contribute appreciably. Conceivably, cinnamate surface ligands enhanced the key step in the degradation, i.e., electron transfer to O_2 .³² Proof for this was achieved by adding the external electron donor *N,N,N',N'*-tetramethylphenylenediamine (TMPD) or acceptors tetranitromethane (TNM) and CBr_4 , the latter both being better acceptors than O_2 .³³ In the presence of TNM, Type I NC photodegraded dramatically faster than with just air (Figure 4A). Similar results were observed for Type II NC when CBr_4 (1.0 mM) was used (not shown). On the other hand, 1 mM of TMPD completely inhibited photodegradation of Type I, even after 24 h of irradiation.³⁴ Interestingly, Type V NC photodegraded very fast in the presence of 100 μM TNM, in sharp contrast to their insignificant degradation with just air (Figure 4B). An experiment in which light, then air, were introduced stepwise showed that only light and not air were necessary for Type V NC to rapidly degrade in the presence of TNM, i.e., NC^* reacted directly with TNM. Thus, the instability of the NC is strictly regulated by the ease with which an electron from NC^* can be transferred to any electron acceptor in solution.

Photolysis Studies: (Photo)Chemistry of Surface Ligands.

Having established a dramatic effect of the cinnamate ligands on the photostability of the NC, we turned to an investigation of the chemistry of the cinnamate ligands to probe if this photoeffect also revealed itself in the organic coating. Toward this end, we analyzed for coumarin **1** by in situ fluorescence spectroscopy during all photolyses described previously.³⁵ Upon

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 (35) The fluorescence counts for coumarin could only be used qualitatively since we found that part of the coumarin emission was quenched by the NC (not shown).

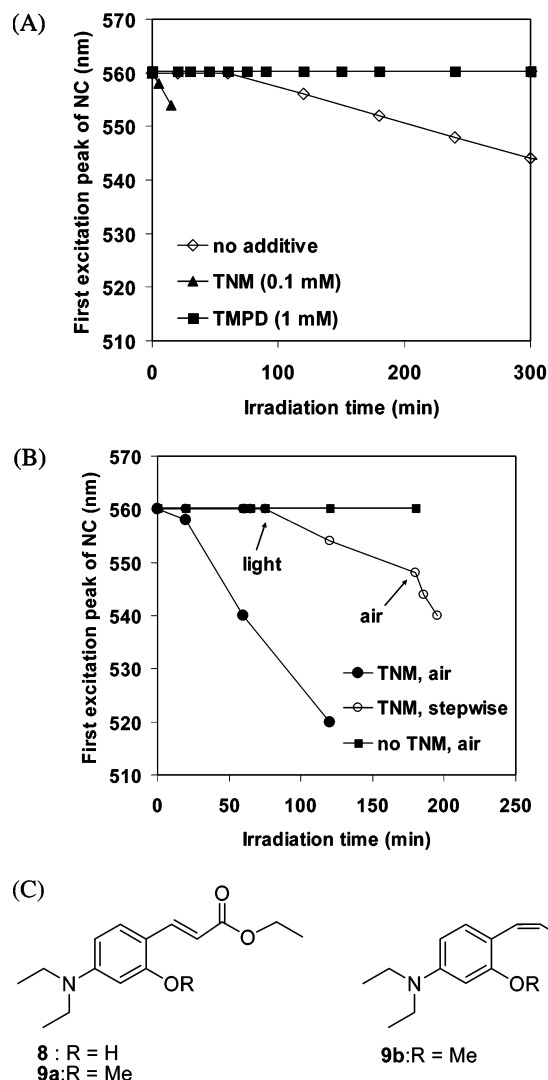


Figure 4. (A) Aerobic 560 nm irradiation of Type I NC in the absence or presence of additives TNM or TMPD. Beyond 20 min of photolysis time for the TNM experiment, decomposition was too extensive for accurate analysis. (B) 374 nm irradiation of Type V NC in the presence and absence of 0.1 mM TNM. In the stepwise experiment, light was turned on after 80 min, followed by the introduction of air after 180 min. (C) Structures of model cinnamate compounds.

photolysis of Type I NC, the following observations were made: (1) Coumarin was formed at 374 nm and at a faster rate aerobically than anaerobically (Figure 5A). (2) Epinephrine, a superoxide quencher, reduced the rate of coumarin formation at 374 nm (not shown). (3) Coumarin was formed upon irradiation with a variety of wavelengths, i.e., from 374 to 560 nm (Figure 6). The first two observations can simply be explained by assuming that the rate-determining dark lactonization step (see Supporting Information) is accelerated by the strongly basic superoxide anion. Indeed, adding KO_2 dramatically increased coumarin formation at 374 nm (Figure 5B).³⁶ The third observation, however, is of a considerably more intriguing nature. This coumarin formation at visible light was reproducible for Type II NC, whereas Type III, lacking the

(36) It has been known that the superoxide anion has reasonable stability in DMF (Boon, P. J.; Olm, M. T.; Symons, M. C. R. *J. Chem. Soc., Faraday Trans.* **1988**, *84*, 3341) The authors do mention that part of the superoxide anion adds to the carbonyl group of DMF, but this species is presumably also strongly basic.

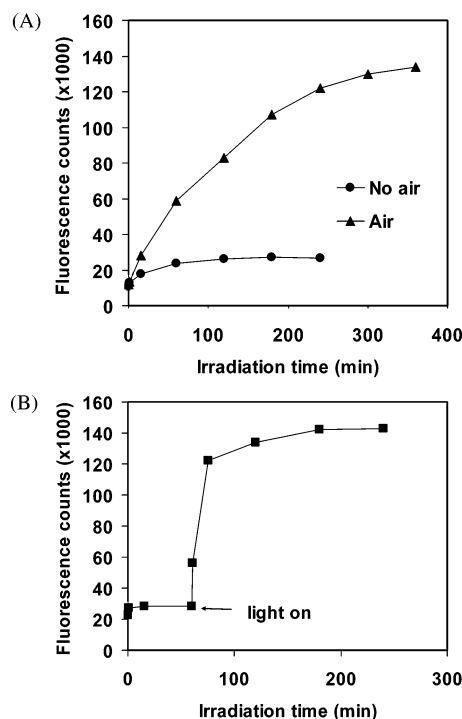


Figure 5. (A) Formation of coumarin from Type I NC upon (an)aerobic irradiation at 374 nm. (B) Formation of coumarin from Type I NC upon anaerobic irradiation at 374 nm in the presence of 2.2 mM KO_2 /crownether complex. Light source was turned on after 1 h in Graph B. Coumarin fluorescence was measured with $\lambda_{\text{ex}} = 374$ nm and $\lambda_{\text{em}} = 438$ nm.

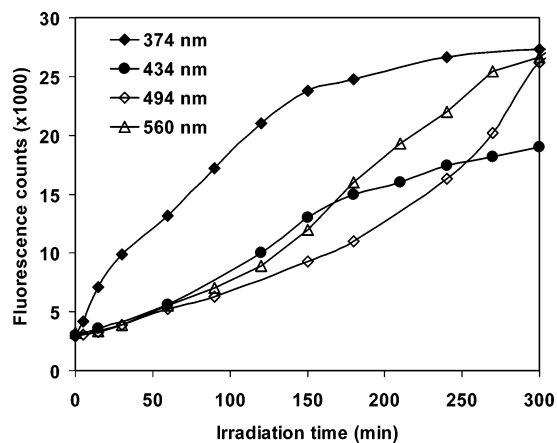


Figure 6. Coumarin formation during aerobic irradiation of Type I NC at various wavelengths. Coumarin fluorescence was measured with $\lambda_{\text{ex}} = 374$ nm and $\lambda_{\text{em}} = 438$ nm.

phenol group, failed to give any increase in fluorescence at 438 nm. The cinnamate unit has no absorption >440 nm, and hence, these findings necessarily imply that the isomerization of the surface cinnamates >440 nm proceeds by a mechanism different from the photochemical isomerization depicted in Scheme 1.

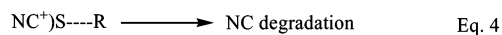
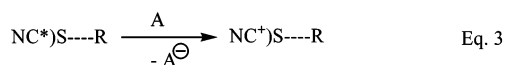
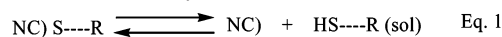
Air-free photolyses of Types I and II at 560 nm followed by separation and subsequent quantitative analysis of NC and filtrate were carried out to estimate the efficiency of the coumarin formation (see Supporting Information). The NC cores were still perfectly intact as the first excitation peak had not shifted. The 374 nm absorption highlighted in Figure 1A, however, is no longer found in the NC but can be fully recovered in the filtrate. Amounts of coumarin in the filtrates were quantified using both fluorescence spectroscopy and GC analysis, which matched acceptably. In all cases, GC analysis also

revealed substantial amounts of free coligand **6** in both dark and irradiated samples, usually in 20–30% range. This is in full agreement with the previously discussed equilibrium between bound and free ligand. The “photolysis efficiency” was approximated by dividing the amount of coumarin in the filtrate by the coverage numbers deduced from the UV–visible absorption spectra (Figure 1A), i.e., the percentage of cinnamate ligands that were converted to coumarin. Types I and II gave high photolysis efficiencies of $93 \pm 5\%$ and $83 \pm 3\%$ ($n = 2$), respectively, upon 24 h anaerobic irradiation at 560 nm.³⁷

Mechanism of Double Bond Isomerization. Intuitively, the mechanisms for cinnamate-accelerated NC decomposition and coumarin formation at >440 nm seem intimately related. The observation that coumarin formation at 560 nm was inhibited almost completely by adding the electron donor TMPD (see Supporting Information) solidly indicates that electron transfer also plays a key role in the rotation of the double bond. Electron transfer from NC* to nearby (organic) acceptors has been reported for CO₂,³⁸ nitroxides,³⁹ Au NC connected by small organic spacers,⁴⁰ and a series of quinones.⁴¹ In our case, electron transfer leads to a surface cinnamate radical anion. Gratifyingly, we were able to prove by electrochemistry that such cinnamate radical anions can rotate around the double bond without decomposition (see Supporting Information). Some electrochemical isomerizations of *Z*-isomers of dimethylmaleate and 1,2-diarylsulfonyl ethenes via radical anions are known.⁴² Cyclic voltammograms (CVs) of model cinnamates **8** and **9a,b** recorded in DMF⁴³ showed an oxidation peak around 0.8–0.9 V and a reduction peak around -1.3 to -1.5 V. We performed dark bulk electrolyses in DMF in conjunction with HPLC analysis.⁴³ Electrolysis of **8** at -1.5 V gave little formation of coumarin in 3 h, meaning that either the *E*–*Z* isomerization or lactonization is not favored under these particular conditions. Importantly, no decomposition of the radical anion of **8** was observed.⁴⁴ A clearer picture was obtained from the electrolysis of *Z*-MeO-model **9b** at -1.5 V, in which no lactonization step is involved. After 3 h, 4% *E*-isomer (**9a**) had formed whereas there was no decomposition of either **9a** or **9b**. Prolonged electrolysis led to ca. 10% isomerization after 20 h.

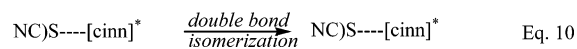
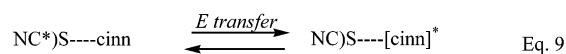
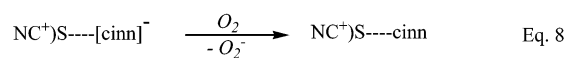
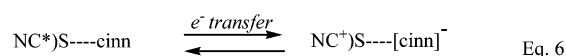
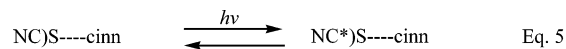
General Mechanism for Enhanced Photodegradation and Coumarin Release. We propose the following general mechanism to explain both the enhanced photodecomposition of the NC upon attachment of cinnamate ligands as well as the

Scheme 2. Photodegradation of All Types of NC in the Presence of Excellent Electron Acceptors^a



^a R = ligand. A = electron acceptor.

Scheme 3. Decomposition of NC Covered with Cinnamate Ligands and Possible Mechanisms for NC-Induced Isomerization of the Cinnamate Ligands^a



^a “Cinn” represents both *Z*- and *E*-isomers.

chemistry of the surface ligands at wavelengths > 440 nm.⁴⁵ Despite the fact that the bound ligands are in equilibrium with solution ligands (eq 1), we believe all relevant steps take place with bound ligands, i.e., at the NC surface.

Upon irradiation of a nanocrystal (Scheme 2), an electron and hole are formed in the excited state of the NC (eq 2). Part of the time, these two will recombine to emit fluorescence light. If an excellent electron acceptor A is in solution (TNM or CBr₄, to a much lesser extent O₂), an electron can be transferred from the NC* to A leaving an unpaired hole in the NC (eq 3). This NC cation (NC⁺) induces ligand oxidation and cleavage and subsequent surface oxidation leading to decomposition (eq 4).²⁵ If cinnamate ligands cover the NC surface, an additional triggering mechanism can take place even without excellent electron acceptors in solution (Scheme 3).

After absorption of light (eq 5), the excited NC transfers an electron to the nearby cinnamates π -system (eq 6) at a rate much higher than transfer to O₂ in solution. The resulting cinnamate radical anion ([cinn]^{•-}) has several pathways available to it. Most importantly, it can rotate around its double bond during its lifetime (eq 7). Furthermore, it can transfer its electron, either back to the NC (eq 6) or into solution provided a reasonable electron acceptor such as O₂ is present (eq 8). In the first scenario, the NC hole and electron will recombine and no net electrons or atoms are lost. However, in the second case, a NC hole is left unpaired, and this will eventually lead to degradation (eq 4). Most evidence presented by us points toward this

(37) We found similar results with 72 Å NC covered with ligand **2**. Thus, coumarin was efficiently formed from these NC using 620 nm light. However, the tendency for the thiol ligands to detach upon dissolution was dramatically higher for these NC than for the 31 Å NC. Therefore, 72 Å NC are of limited use and are not explicitly discussed in this paper.

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(43) Platinum electrodes as working and counter electrode; silver electrode as reference electrode; ^tBu₄N⁺PF₆⁻ as supporting electrolyte. Platinum itself was shown not to induce isomerization of the cinnamate by coordination chemistry.

(44) Interestingly, electrolysis of **8** at +0.9 V was accompanied by vast decomposition of the radical cation, thereby excluding any mechanisms that involve the radical cation in explaining the coumarin formation from the NC.

(45) At wavelengths < 440 nm, the same proposed mechanisms will hold true but now isomerization can also occur by direct absorption of the light by the surface cinnamates. The latter pathway was predictable and not of high interest.

involvement of electron transfer in the cinnamate isomerization step. However, as of yet, it cannot be fully excluded that transfer of excited energy between NC and ligand (eq 9) was occurring in some form. This leaves the cinnamate ligand in the excited state, at which point it can isomerize as well (eq 10). A strong argument against energy transfer from the NC* to the ligand is the fact that this involves an energetically uphill pathway, although nonvertical energy transfer directly to the triplet cinnamate state may significantly reduce the energetic requirements for such a transfer.⁴⁶ We also considered a 2-photon mechanism, but this was deemed unlikely due to insufficient power of the light source to achieve 2-photon excitation.⁴⁷ Irrespective of the exact isomerization mechanism, nonphotolytic lactonization of any *Z*-cinnamate can take place at any time. The latter step will produce coumarin **1** which migrates into solution, and hydroxyundecyl ligands are left on the NC (as in Type VI NC).

Conclusion & Outlook

We have synthesized and characterized 31 Å CdSe nanocrystals with *E*-cinnamate ligands bound to the NC surface by thiol groups. Upon dissolution of these NC in organic solvents, some surface thiols are released into solution. The NCs have dramatically increased aerobic photoinstability as compared to NC without cinnamate ligands. We propose this is because the surface cinnamate facilitates electron transfer from excited NC* to O₂ in solution by acting as an electron carrier. Even in the absence of air, this reversible electron transfer between NC* and cinnamate occurs. While carrying the electron in its radical anion form, the double bond of the cinnamate unit partially rotates, giving small amounts of the *Z*-isomer. This *Z*-isomer undergoes lactonization and releases coumarin into solution. Thus, using visible light and anaerobic conditions, we efficiently

released coumarin from ligands on a CdSe nanocrystal carrier without decomposition of the NC core. That is, the organic-chemical cascade is initiated simply by exciting the NC.

The presented findings further progress the fundamental understanding of nanocrystal–ligand composites by revealing dynamic core–ligand interactions that may be invisible on many occasions. Moreover, the photorelease concept itself could prove useful in a variety of areas, such as drug delivery and bio-imaging. However, some critical issues need to be addressed first: most importantly, the inherent (in)stability of the NC. First, the photostability of the cinnamate-covered NC in the presence of O₂, a given parameter in biological media, has to be enhanced, which will likely be a significant challenge. Major advances in this area have been made recently.¹² Second, the equilibrium between bound and unbound ligands upon dissolution will be unacceptable for biological applications. Ligand headgroups that bind tighter could overcome this hurdle. Last, the rate of lactonization has to be improved substantially. This problem might solve itself when biological aqueous systems are used.⁴⁸

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Supporting Information Available: General materials and methods; procedures for ligand exchange, photolyses, and electrochemistry; synthetic scheme and procedures; GC- and HPLC-retention times; selected NMR spectra; RBS spectrum of Type V NC; UV–visible absorption spectrum of filtrate and NC after Type II NC 560 nm photolysis; plots for CV and bulk electrolysis; additional time-evolved photolysis graphs. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(48) The rate of coumarin formation from cinnamates in solution can be increased as much as 1000–10 000-fold by simply switching from DMF to water or ethanol instead. This is a result of acid-catalysis of the lactonization step.