JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
Communication
pubs.acs.org/JACS

Photocatalytic Carbon Disulfide Production via Charge Transfer Quenching of Quantum Dots

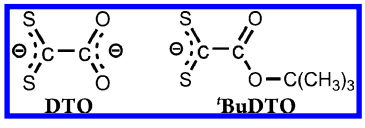
Christopher M. Bernt,[†] Peter T. Burks,[†] Anthony W. DeMartino, Agustin E. Pierri, Elizabeth S. Levy, David F. Zigler, and Peter C. Ford*

Department of Chemistry and Biochemistry, University of California, Santa Barbara, California 93106, United States

Supporting Information

ABSTRACT: Carbon disulfide, a potentially therapeutic small molecule, is generated via oxidative cleavage of 1,1-dithiooxalate (DTO) photosensitized by CdSe quantum dots (QDs). Irradiation of DTO−QD conjugates leads to λ_{irr} independent photooxidation with a quantum yield of ∼4% in aerated pH 9 buffer solution that drops sharply in deaerated solution. Excess DTO is similarly decomposed, indicating labile exchange at the QD surfaces and a photocatalytic cycle. Analogous photoreaction occurs with the *O-tert*-butyl ester ^{t}BuDTO in nonaqueous media. We propose that oxidation is initiated by hole transfer from photoexcited QD to surface DTO and that these substrates are a promising class of photocleavable ligands for modifying QD surface coordination.

Semiconductor quantum dots (QDs) exhibit size and composition dependent optical properties, strong absorption cross sections, high photoluminescence (PL) quantum yields, and customizable solubility through surface ligand exchange.[1] These properties position QDs as attractive sensitizers for photodynamic therapy,[2] photoactivated drug delivery,[3] solar energy conversion,[4] and photocatalysis.[5] Here we describe the photocatalytic cleavage of 1,1-dithiooxalate (DTO) to CS_2 and CO_2 mediated by CdSe QDs. This process serves to "uncage" carbon disulfide (CS_2), a potentially therapeutic agent. Similar reactions are observed with the DTO ester ^{t}BuDTO, and light activated cleavage of such ligands suggests strategies for the controlled modification of quantum dot surfaces.



Fragmentary evidence points toward possible therapeutic roles for carbon disulfide.[6] For example, CS_2 may react with biological amines to form dithiocarbamates, known inhibitors[7] of nuclear factor κB (NF-κB),[8] a crucial mediator in inflammation induced tumor growth and progression.[9] Indeed, dithiocarbamates have been proposed as anticancer agents.[10] Physiological responses to CS_2 or dithiocarbamates include cell growth, apoptosis, and neurotransmission, which are also functions of the small molecule bioregulators NO, CO, and H_2S.[11] Like each of these, CS_2 is considered toxic at higher concentrations, although epidemiological data are contradictory.[12] Thus, the benefit of balancing the therapeutic and toxic effects of CS_2 make the prospect of controlled, targeted delivery an attractive goal.

In these contexts, we are probing DTO−QD conjugates as photochemical CS_2 precursors. These were readily prepared by exchanging DTO dianions for the myristate ligands (n-$C_{13}H_{27}CO_2^-$) originally terminating the QD surface (see Supporting Information (SI) for procedures). Ligand exchange is evidenced by the solubility shift from organic to aqueous media as dianionic DTO replaces the hydrophobic myristate. Purified conjugates show a very strong UV absorption band (∼335 nm) nearly the same as free DTO (λ_{max} ∼335 nm, ε_{max} = 1.5 × 10^4 M^{-1} cm^{-1} in aq. solution) and a QD exciton band red-shifted by as much as 40 nm (Figure 1, SI Table S-1).

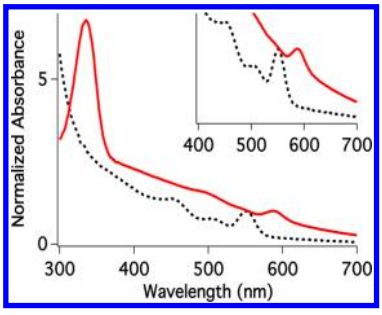


Figure 1. Absorption spectrum of purified DTO−QD_{550} conjugates in pH 9 buffer (50 mM sodium borate) solution (solid line) and that of QD_{550} nanoparticles in toluene prior to ligand exchange (dashed line). *Inset*: Expanded view of the exciton peak shift. (QD subscript refers to exciton λ_{max} before ligand exchange.)[14]

Analogous red shifts in exciton absorptions have been seen when dithiocarbamates were exchanged onto semiconductor QD surfaces,[13] and this effect was attributed to relaxation of exciton confinement in the QD−ligand conjugate owing to alignment of interfacial orbital energies. Lastly, the strong QD PL was completely quenched. Aqueous solutions of the DTO−QD conjugates are stable in the dark for at least 6 h at 37 °C (Figure S-2) and indefinitely stable when stored in a refrigerator.

PL quenching in thiolate terminated QDs has been attributed to hole transfer from the valence band to the surface bound

Received: August 12, 2013
Published: October 23, 2013

   dx.doi.org/10.1021/ja4083599 | *J. Am. Chem. Soc.* 2014, 136, 2192−2195

ligands.[15] Such a mechanism suggested that CdSe QDs could mediate DTO cleavage (eq 1).

$$S_2C{-}CO_2^{2-} \xrightarrow[\text{oxidant}]{\text{hv, QD}} CS_2 + CO_2 \quad (1)$$

In order to test this hypothesis, aerated pH 9 aqueous solutions of the purified DTO−QD_{550} conjugate[14] were irradiated with 365 nm light. This led to a systematic decrease in the 335 nm absorption band indicating that the surface-coordinated DTO was undergoing photodecomposition. The quantum yield for the disappearance of this band (Φ_{dis}) was 0.029 ± 0.008 (see SI, Sec. I and J for details). Notably, this absorbance decrease was accompanied by recovery of the QD PL (Figure 2). At higher photochemical conversion, the QD

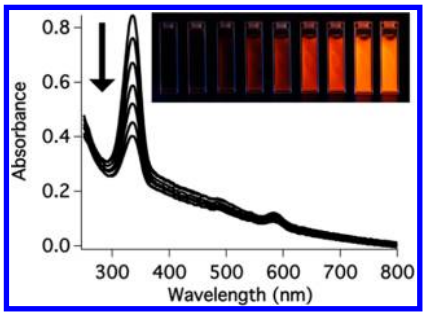


Figure 2. Spectral changes for pH 9 solution of DTO−QD_{550} upon 365 nm excitation over the course of 120 s at 20 s intervals. *Inset*: Photograph showing PL return as photolysis proceeds. (See video in the SI.)

cores precipitated, owing to loss of the water-solvating surface ligands. Photolysis (365 nm) of a comparable solution of DTO alone (~70 μM) showed minimal photoinduced bleaching (Figure S-4) and a much smaller Φ_{dis} (0.004 ± 0.001).

The difference between the DTO−QD conjugates and DTO itself is even more dramatic at longer irradiation wavelengths (λ_{irr}). When buffered solutions of DTO−QD_{550} were excited with light emitting diodes centered at 479, 498, or 530 nm (Figure S-5), bleaching of the 335 nm band occurred with comparable efficiency (Φ_{dis} = 0.045 ± 0.005, 0.032 ± 0.003 and 0.039 ± 0.005 for these respective λ_{irr}) to that seen for λ_{irr} = 365 nm. Again, the PL of the QD cores was restored (Figure S-6). In contrast, solutions of free DTO were unaffected owing to their optical transparency at these longer λ_{irr}, so there is little question that the QDs sensitize the photochemical decomposition of the surface bound DTO.

Similar sensitization of photodecomposition was observed with other DTO−QD conjugates, although there were some differences in the quantum efficiencies. Respective Φ_{dis} values of 0.016 ± 0.003, 0.033 ± 0.003, and 0.035 ± 0.001 were measured for 498 nm irradiation of DTO−QD_{510}, DTO−QD_{550}, and DTO−QD_{580} (Figure 3); however, a larger data set is needed before considering a possible systematic trend.

When the photoreactions were carried out under deaerated conditions, Φ_{dis} values dropped precipitously. For example, 498 nm irradiation of DTO−QD_{550} solutions deaerated by extensive bubbling with argon gave Φ_{dis} = 0.002 ± 0.001. However, an atmosphere of pure O_2 did not increase photoactivity (Φ_{dis} = 0.033 ± 0.001) significantly above that seen in aerobic media. Thus, while the oxidant O_2 appears necessary for efficient net photodecomposition of coordinated

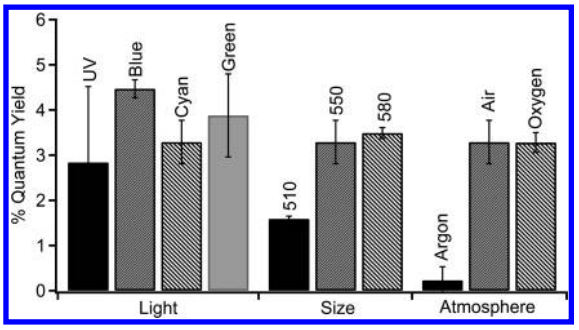


Figure 3. (Left) Φ_{dis} values for the photolysis of DTO−QD_{550} conjugates at different λ_{irr} (UV = 365, blue = 479, cyan = 498, and green = 530 nm). (Center) Φ_{dis} values for λ_{irr} 498 nm of DTO−QD_{510}, DTO−QD_{550}, and DTO−QD_{580}. (Right) Φ_{dis} values for 498 nm photolysis of DTO−QD_{550} under Ar, air, and O_2. All in pH 9 buffer solution.

DTO, this does not appear to be rate-limiting under normal conditions.

If these spectral changes do indeed reflect DTO photodecomposition, then other ligands in solution should coordinate to the resulting open surface sites. Thus, the QDs should be photocatalysts for oxidative decomposition of free DTO in solution.This reactivity was demonstrated using an aerated pH 9 solution of DTO−QD_{550} to which a 2-fold excess of the K^+ salt of DTO (115 μM) had been added. Photolysis at 498 nm led to a rapid decrease in the characteristic DTO absorbance at 335 nm (Figure S-7), and a Φ_{dis} = 0.052 ± 0.006 was measured. Furthermore, the QDs remained in solution and showed little PL until the DTO was nearly consumed according to λ_{max} 335 nm. *Thus, the system is indeed photocatalytic*. Additionally, this confirms that the decomposition of DTO frees the QD surface from dithiolcarboxylate coordination and suggests a strategy for syntheses of new quantum dot conjugates via incorporation of other ligands.

Although it has been speculated[16] that photooxidative decomposition of DTO would occur according to eq 1, CS_2 has not previously been detected as a photoproduct. To address this issue, we exhaustively photolyzed ($\lambda_{irr} \geq$ 479 nm) aerated pH 9 solutions of DTO−QD_{550} in sealed, septa-capped vials. GC-MS analysis of headspace gases by Weck Laboratories (City of Industry, CA) showed that photolyzed samples gave significantly larger amounts of CS_2 than "dark" controls,[17] thereby confirming, qualitatively, formation of CS_2 as a photoproduct.

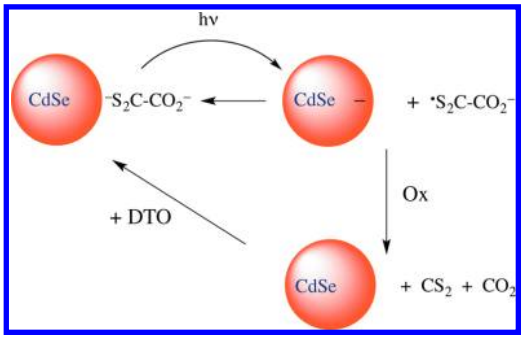
In order to evaluate the CS_2 production quantitatively, we developed a colorimetric assay based on the rapid reaction of CS_2 with amines to form dithiocarbamates.[18] The latter have strong UV absorptions. This procedure clearly confirmed photochemical CS_2 formation, although the amount detected was systematically about 50% that predicted by assuming eq 1 to be the only reaction leading to photobleaching of the DTO peak at 335 nm (SI, Sec. K for details). No CS_2 formation was apparent without photolysis (see Figure S-9).

The other product predicted is CO_2. This was determined by GC analysis of the headspace before and after acidifying the photoproduct solution to ~pH 1, since some of the CO_2 would be trapped as bicarbonate in the pH 9 buffered solutions. Consistent with the colorimetric analysis for CS_2, the CO_2 generated by photolysis of DTO−QD_{550} was about half that predicted by eq 1 for the analysis before acidification and about 70% after acidification (SI, Sec. M).

dx.doi.org/10.1021/ja4083599 | J. Am. Chem. Soc. 2014, 136, 2192−2195

These products and the requirement for O_2 as a coreactant suggest that photolysis of surface coordinated DTO reversibly leads to transient species that are trapped by the external oxidant (Scheme 1). Alternatively, it might be argued that

Scheme 1



photoinduced two-electron transfer from DTO to the QD occurs either simultaneously or sequentially and that "charged" QDs are no longer photoactive until "discharged" by reacting with O_2 (SI, Scheme S-1). The formation of the DTO radicals suggested by Scheme 1 offers a possible explanation for the nonstoichiometric formation of CS_2 and CO_2, given that such species might dimerize to give a disulfide linkage.[19] Regardless of the actual mechanism, the catalytic behavior shows that the QD sensitized photooxidation and cleavage of DTO facilitates removal and replacement of the surface ligands. Ongoing studies will attempt to differentiate the mechanistic possibilities.

While DTO functionalization provides aqueous solubility, QD conjugates of ^{t}BuDTO remain soluble in organic media. Given that CO_2 formation must contribute to the driving force for eq 1, analogous oxidative activation of an O-ester such as ^{t}BuDTO may release a radical, e.g., eq 2.

$$S_2C{-}CO_2R^{-} \xrightarrow[\text{oxidant}]{\text{hv, QD}} CS_2 + CO_2 + R^{\bullet} \qquad (2)$$

Organic soluble conjugates were prepared as described in the SI by exchanging ^{t}BuDTO for the myristate surface ligands of QD_{510}. The spectrum of ^{t}BuDTO−QD_{510} displayed the strong absorption band at 350 nm characteristic of the DTO chromophore and an exciton peak at 523 nm red-shifted from that of the core QD exciton peak (Figure S-8). In addition the ^{t}BuDTO conjugate was not luminescent, as seen for the QD conjugates with DTO. Photolysis of ^{t}BuDTO−QD_{510} with λ_{irr} 498 nm in aerated solution led to bleaching of the 350 nm DTO band, but Φ_{dis} values were small, 0.007 in toluene and 0.0024 in chloroform. Exhaustive photolysis led to PL recovery and a shift of the exciton peak to its original maximum (Figure S-8), while the QDs remained soluble. The colorimetric analytical method described above demonstrated that CS_2 is clearly formed during this photoreaction, but the yields are even lower (∼12%) than with analogous DTO conjugates (SI, Sec. M).

In summary, we have described the preparation of photosensitive conjugates by displacing the native surface ligands on CdSe QDs with 1,1-dithiooxalate and with *O*-*tert*-butyldithiooxalate. The resulting DTO−QD conjugates are water-soluble while the R-DTO conjugates are organic-soluble. For both, the QD exciton bands are shifted to the red and PL is quenched. Photolysis in aerated solutions leads to the photocatalytic oxidative decomposition of these surface ligands with modest quantum yields. By using a colorimetric assay, it was shown in both cases that CS_2 is generated. This represents the first demonstrated photochemical release of this potentially therapeutic small molecule.

We propose that the photooxidation mechanism involves QD excitation-induced hole transfer to surface bound DTO. The efficiency is highly dependent upon the presence of another oxidant, O_2, which serves as the ultimate electron acceptor. The reaction not only decomposes the multiple DTOs bound to the QD surface, but the facile ligand exchange leads to a catalytic cycle for photooxidation of excess free DTO in solution. In addition, this offers a potential pathway for the systematic removal or replacement of QD surface ligands and for the photochemical syntheses of new QD−ligand conjugates.

O-Ester-DTO−QD conjugates undergo analogous photodecomposition. We propose that such a photocleavable ligand may allow the controlled release of organic radicals from QD surfaces. Ongoing studies are directed toward a better quantification of the products as well as expanding the photochemistry to a library of other esters in order to probe the utility of these as photocleavable surface anchors.

■ ASSOCIATED CONTENT

Supporting Information

Experimental details regarding the synthesis and characterization of DTO−QD and ^{t}BuDTO−QD conjugates, photochemical procedures and photoproduct analyses, a video illustrating the photoreaction, and additional data. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

ford@chem.ucsb.edu

Author Contributions

†These authors contributed equally.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was funded by the National Science Foundation (NSF-CHE-1058794). P.T.B. thanks ConvEne-IGERT (NSF-DGE 0801627), C.M.B. thanks the UCSB Graduate Division, A.E.P. and A.W.D. thank PIRE-ECCI (NSF-OISE-0968399), and E.S.L. thanks IRES-ECCI (NSF-OISE-1065581) for fellowships. We thank Weck Laboratories for GC-MS measurements .

■ REFERENCES

(1) (a) Choi, C. L.; Alivisatos, A. P. *Annu. Rev. Phys. Chem.* **2010**, *61*, 369. (b) Medintz, I. L.; Uyeda, H. T.; Goldman, E. R.; Mattoussi, H. *Nat. Mater.* **2005**, *4*, 435.

(2) Samia, A. C. S.; Chen, X.; Burda, C. *J. Am. Chem. Soc.* **2003**, *125*, 15736.

(3) (a) Burks, P. T.; Ford, P. C. *Dalton Trans.* **2012**, *41*, 13030. (b) Sortino, S. *J. Mater. Chem.* **2012**, *22*, 301.

(4) Robel, I. n.; Subramanian, V.; Kuno, M.; Kamat, P. V. *J. Am. Chem. Soc.* **2006**, *128*, 2385.

(5) (a) Ruberu, T. P. A.; Nelson, N. C.; Slowing, I. I.; Vela, J. *J. Phys. Chem. Lett.* **2012**, *3*, 2798. (b) Zhao, J.; Holmes, M. A.; Osterloh, F. E. *ACS Nano* **2013**, *7*, 4316.

(6) (a) Huang, X.; Zhou, Y.; Ma, J.; Wang, N.; Zhang, Z.; Ji, J.; Ding, Q.; Chen, G. *Environ. Toxicol. Pharm.* **2012**, *34*, 679. (b) Munger, S. D.; Leinders-Zufall, T.; McDougall, L. M.; Cockerham, R. E.; Schmid,

A.; Wandernoth, P.; Wennemuth, G.; Biel, M.; Zufall, F.; Kelliher, K. R. *Curr. Biol.* **2010**, *20*, 1438. (c) Tan, X.; Peng, X.; Wang, F.; Joyeux, M.; Hartemann, P. *Int. J. Hyg. Environ. Health* **2002**, *205*, 473. (d) Shreck, R.; Meier, B.; Mannel, D. N.; Droge, W.; Baeuerle, P. A. *J. Exp. Med.* **1992**, *175*, 1181. (e) Valentine, W. M.; Amarnath, V.; Graham, D. G.; Anthony, D. *Chem. Res. Toxicol.* **1992**, *5*, 254.
(7) Cvek, B.; Dvorak, Z. *Curr. Pharma. Des.* **2007**, *13*, 3155.
(8) Gilmore, T. D. *Oncogene* **2006**, *25*, 6680.
(9) Karin, M.; Greten, F. R. *Nat. Rev. Immunol.* **2005**, *5*, 749.
(10) (a) Ali, I.; Wani, W. A.; Saleem, K.; Hseih, M.-F. *Polyhedron* **2013**, *56*, 134. (b) Zhang, X.; Frezza, M.; Milacic, V.; Ronconi, L.; Fan, Y.; Bi, C.; Fregona, D.; Dou, Q. P. *J. Cellular Biochem.* **2010**, *109*, 162.
(11) Fukuto, J. M.; Carrington, S.; Tantillo, D. J.; Harrison, J.; Ignarro, L.; Freeman, B. A.; Chen, A.; Wink, D. A. *Chem. Res. Toxicol.* **2012**, *25*, 769.
(12) Silva, M. *Birth Defects Res. B* **2013**, *98*, 119.
(13) (a) Frederick, M. T.; Weiss, E. A. *ACS Nano* **2010**, *4*, 3195. (b) Frederick, M. T.; Amin, V. A.; Weiss, E. A. *J. Phys. Chem. Lett.* **2013**, *4*, 634.
(14) QD samples were indexed according to the exciton λ_{max} prior to DTO exchange rounded to the nearest 10 nm. Estimated CdSe QD diameters are discussed in the SI, Table S-1.
(15) Wuister, S. F.; de Mello Donego, C.; Meijerink, A. *J. Phys. Chem. B* **2004**, *108*, 17393.
(16) (a) Zigler, D. F.; Tordin, E.; Wu, G.; Iretskii, A. V.; Cariati, E.; Ford, P. C. *Inorg. Chem. Acta* **2011**, *374*, 261. (b) Strauch, P.; Dietzsch, W.; Golic, L. *Z. Anorg. Allg. Chem.* **1997**, *623*, 129.
(17) In the qualitative GCMS measurements, the dark samples showed some CS_2 release, which we attribute to lengthy sample handling under ambient light conditions during analysis by the Weck Laboratories. However, samples deliberately photolyzed prior to transferring to that laboratory for analysis gave GCMS signals about twice those for the dark samples.
(18) Critchfield, F. E.; Johonson, J. *Anal. Chem.* **1956**, *28*, 430.
(19) (a) Aldana, J.; Wang, Y. A.; Peng, X. *J. Am. Chem. Soc.* **2001**, *123*, 8844. (b) Lieder, M. *Electrochim. Acta* **2004**, *49*, 1813.