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Photorelease of Carboxylic Acids Mediated by Visible-Light-Absorbing Gold-Nanoparticles

J. Brian Borak, Susana López-Sola, and Daniel E. Falvey*

Department of Chemistry and Biochemistry, University of Maryland, College Park, Maryland 20742

falvey@umd.edu

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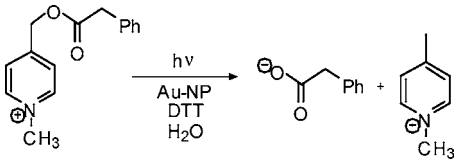
ABSTRACT



Visible-light-absorbing citrate-stabilized gold nanoparticles and tryptophan–dithiane-conjugate-stabilized gold nanoparticles have been used to mediate electron transfer between dithiothreitol (DTT), a good electron donor, and an *N*-methylpicolinium ester in aqueous solution. Quantitative yield of the free carboxylate has been obtained with quantum yields of release, Φ_{rel}, ranging from 0.5 to 4.5.

The use of photoremovable protecting groups (PRPGs) has become an established technique for modulating the reactivity of a variety of functional groups. A large majority of PRPG strategies have been designed to take advantage of a rearrangement and/or radical mechanism that occurs within the chromophore upon light absorption. Nitrobenzyl alcohol,[1] benzoin,[2] phenacyl ester,[3] and coumarinyl[4] derivatives are examples of some of the more highly studied systems in this category. One significant limitation of the aforementioned groups is that ultraviolet (UV) light is required to initiate deprotection which can initiate other unwanted photochemical reactions within the system. As such, many studies have focused on using new chromophores that absorb at higher wavelengths[5] or modifying existing PRPG chromophores to red-shift their absorption profiles.[6,7] Unfortunately, while modification of existing chromophore moieties can lead to a favorable change in the absorption properties, this often comes at the cost of the diminishment in other desirable qualities in the PRPG (i.e., high quantum yield, solubility, background stability, etc.)

In attempts to sidestep this delicate balance, our group has focused on a more recent class of PRPG that relies on sensitized photoinduced electron transfer (PET).[8] In these systems, an excited-state sensitizer initiates an electron-

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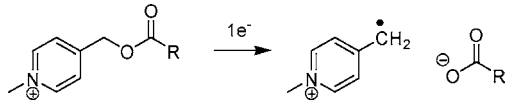
transfer reaction that reduces a protecting group which subsequently initiates release of the attached compound. The light absorption step is, in essence, uncoupled from the deprotection step since reduction of the protecting group, from any source, causes deprotection. This allows for the individual optimization of each step in the deprotection process with relatively little consequence to other steps. However, the introduction of another component into the system does complicate the deprotection scheme to a certain extent. Our group has developed the *N*-alkylpicolinium (NAP) group for use as a PET-PRPG in order to take advantage of the benefits of PET-based deprotection to protect carboxylates and carbamates.[9] Simple one-electron reduction by thermal or photochemical means ($E_{red} = -1.1$ V) using a photoexcited donor results in release of the protected compound. (Scheme 1).

Scheme 1. Reduction of the *N*-Methyl-picolinium Group



The chromophore or sensitizer often represents a significant expense in the deprotection scheme as a stoichiometric amount or greater (relative to the amount of protected compound) is needed to fully deprotect a particular system. However, if a sensitizer is in the presence of a "sacrificial" electron donor with the appropriate oxidation/reduction potentials, the sensitizer can act as a mediator or electron shuttle between the donor and the PRPG. The net effect is to preserve the original state of the chromophore so that it can be recycled in multiple deprotection events. Initial experiments with this system were performed using UV-light-absorbing sensitizers;[10] however, it would be convenient to use visible light instead. It should even be possible to use a substoichiometric amount of sensitizer in these systems, greatly reducing the cost and waste associated with a deprotection photolysis experiment. This is the focus of the current work being discussed.

Given the success of the mediated systems previously studied, we are interested in finding new robust high-wavelength absorbing sensitizers to incorporate into this design. Gold nanoparticles (AuNPs) have recently attracted a great amount of attention due to their unique optoelectronic properties that are dissimilar from those of bulk metal materials or molecular compounds.[11] Additionally, they have proven to be robust under illumination in many cases and would offer an improvement over delicate organic chromophores that decompose over time. AuNPs can be synthesized in a variety of sizes, from one to several hundred nanometers in diameter, and with various organic stabilizing ligand shells surrounding them. AuNPs with core diameters greater than 5 nm exhibit a characteristic strong visible absorption band centered at approximately 520 nm (for 15 nm AuNPs), respresentative of the suface plasmon band (SPB) electron cloud.[12] The position of the λ_{max} of the plasmon resonance band (PRB) is largely dependent on the size of the AuNPs, their shape, and the nature of the stabilizing ligands surrounding them.[11,13,14] In addition to the favorable absorption characteristics, several AuNP systems appear to have favorable reduction potentials as evidenced by electrochemical experiments performed by Murray et al. on smaller AuNP systems (1.1 nm diameter). For those systems, Murray suggests the nanoparticles have one-electron reduction potentials at ca. −1.5 to −1.7 V, potentials sufficiently negative to reduce our NAP-esters in a mediated-PET mechanism.[15] Given the aforementioned qualities, AuNPs seemed to be an interesting candidate for mediated deprotection experimentation.

The scheme designed for these experiments incorporates the nanoparticles in the presence of a large excess of a good electron donor and a NAP-protected ester. Upon absorption of incident radiation, the AuNPs are expected to act as net electron shuttles, transferring an electron between the electron donor (D) and the NAP ester. (Scheme 2)[16]

Although a staggering variety of AuNPs can be prepared, our studies began with citrate-stabilized AuNPs (cit-AuNP) due to their ease of preparation, narrow size distribution, and aqueous solubility. Synthesis of 16 nm citrate-stabilized AuNPs (cit-AuNP) was easily achieved using the modified citrate reduction method by Frens.[17] The nanoparticles were prepared in D_2O to facilitate analysis by proton NMR. Size was confirmed by comparison to reference UV−vis absorption spectra and by transmission electron microscopy (TEM) analysis. Although oxidation/reduction potentials of the cit-AuNPs could not be determined, several aqueous-soluble donor molecules were surveyed, and dithiothreitol (DTT) was chosen since irreversible aggregation of the cit-AuNPs was not observed immediately after addition as it was with other donors (e.g., ascorbic acid and EDTA). *N*-Methyl-picoliniumphenylacetate (mPPA) was chosen as a representative NAP-ester to include in these experiments. A major limitation of the cit-AuNPs is their susceptibility to irreversible aggregation by a variety of sources. This aggregation is accompanied by a red-shifting and reduction in intensity of the PRB, effectively limiting photochemical processes.

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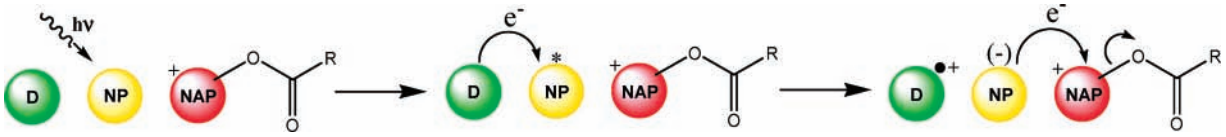
Scheme 2. Proposed Mechanism for Nanoparticle-Based Deprotection



(Figure 1). Careful adjustment of the concentrations of the three components in our experiments identified an optimal ratio in which the solutions were stable. In general, higher concentrations of DTT and lower concentrations of mPPA lead to more stable solutions. Photolysis solutions containing mPPA, DTT, and cit-AuNP were prepared in D_2O with a minimal amount of acetonitrile as cosolvent for mPPA. The

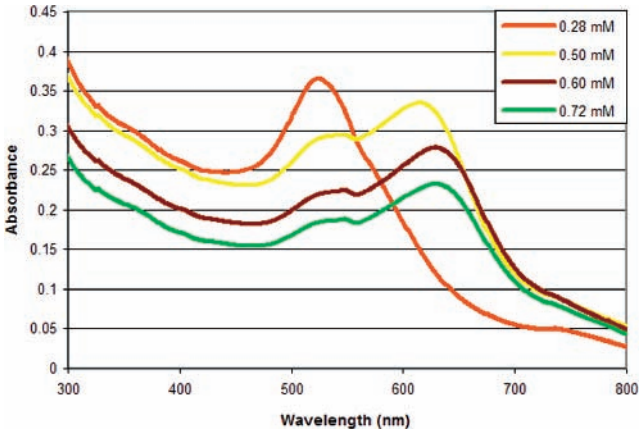


Figure 1. UV−vis spectra of cit-AuNPs with varying concentration of mPPA.

solutions were purged with N_2 for 10 min and irradiated with a 300 W broad-band tungsten-filament lamp for a predetermined amount of time. Free carboxylic acid yields were determined by integration of the aromatic protons of the free picolinium group in the proton NMR spectrum. Yields of phenylacetic acid (PAA) were confirmed by HPLC analysis of the final mixtures. A representative sampling of the data is found in Table 1.

Table 1. Selected Data for the Cit-AuNP Deprotection Experiment

entry	[mPPA] (mM)	[DTT] (mM)	[cit-AuNP] (nM)[a]	irradiation time (min)	% yield of PAA[b]
1	1.24	12.5	1.9	60	64
2	1.24	62.2	0.95	60	80
3	1.24	62.2	1.9	60	95

[a] Theoretical concentrations assuming perfectly spherical 16 nm nanoparticles generated in 100% yield in the synthesis reaction [b] Determined by HPLC, relative to [mPPA] in dark control, error ± 10%

Quantitative yield of PAA was observed after 1 h of irradiation (within the error of integration, ∼10%). Control photolysis experiments that lacked either cit-AuNP or DTT or both resulted in an insignificant amount of deprotected ester (within experimental error). It should be noted that the effective concentration of cit-AuNPs in the photolysis mixture was actually lower than reported due to a particularly peculiar source of aggregation. It appears that the nitrogen purging can trigger partial aggregation through a mechanism that is not clear. Absorbance at the PRB λ_{max} was reduced by an average of 29% after the 10-min nitrogen purge. Solutions containing only cit-AuNPs of identical concentration were unaffected by purging. Purging with argon using identical conditions resulted in a similar reduction in absorbance. Quantum yields of release, Φ_{rel}, of the free carboxylate on the aforementioned system were determined to be $\Phi_{rel} = 0.4$ using monochromatic irradiation at 525 nm ± 10 nm compared to a dark control solution.

Due to the high instability of the cit-AuNP system, a different NP system was explored. DeShong et al. have prepared 4 nm AuNPs stabilized by a L-tryptophan−dithiane derivative[18] (TRP-AuNP). (Figure 2) These NPs are signifi-

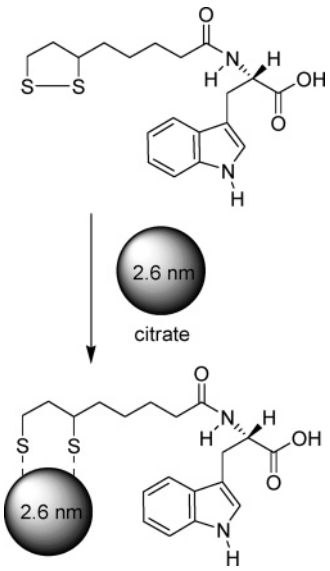


Figure 2. Tryptophan−dithiane ligand used for TRP-AuNP system.

cantly more robust to different environments including a wide range of solution pH values (∼6−14). Additionally, the formation of aggregates or the restoration of free nanopar-

(18) Unpublished work: Park, J.-H.; DeShong, P. University of Maryland, College Park, MD.

ticles can be cycled a limited number of times (~2−4) through protonation or deprotonation of the carboxylate group. While deprotection reactions can be carried out in unbuffered solution, the experiments reported here were performed in 50 mM phosphate buffer at pH 7. Yields were determined by HPLC analysis. Quantitative yield of PAA was observed after 1 h of broad-band visible-light irradiation (Table 2, entry 1). Increasing concentrations of DTT (Table 2, entries 2−8) or TRP-AuNP (Table 2, entries 9−13) subsequently increase the deprotection yield of PAA for a given photolysis period. However, the data seem to indicate a maximum in deprotection yield at about 1:25 mPPA/DTT molar ratio. Control photolysis experiments lacking TRP-AuNP, DTT, light, or any combination of the three resulted in an insignificant yield of PAA (within experimental error). Surprisingly, quantum yields of release, Φ_{rel}, of PAA range from 1.4 to 4.5 for this system. This may be indicative of a radical chain mechanism since these processes typically have quantum yields greater than unity.[19]

Table 2. Selected Data for the TRP-AuNP Deprotection Experiment

entry	[mPPA] (mM)	[DTT] (mM)	[TRP-AuNP] (nM)[a]	irradiation time (min)	% yield of PAA[b]
1	1.25	31.3	15	60	100
2	1.25	1.25	15	30	4.2
3	1.25	2.5	15	30	14.4
4	1.25	5	15	30	15.7
5	1.25	10	15	30	20.2
6	1.25	20	15	30	24.3
7	1.25	40	15	30	24.9
8	1.25	80	15	30	14.2
9	1.25	31.3	0.75	20	30.2
10	1.25	31.3	15	20	40.3
11	1.25	31.3	30	20	44.4
12	1.25	31.3	37.5	20	49.4
13	1.25	31.3	75	20	56.2

[a] Theoretical concentrations assuming perfectly spherical 2.6 nm nanoparticles generated in 100% yield in the synthesis reaction [b] Determined by HPLC, relative to [mPPA] in dark control, error ± 10%

In conclusion, these experiments demonstrate the successful deprotection of a photoinduced electron transfer-based PRPG using gold nanoparticles. To the best of our knowledge, this is the first account of the application of AuNPs for a photodeprotection strategy. The most attractive aspects of both of the explored systems used to initiate deprotection include: (1) the use of visible light, (2) the use of very substoichiometric amounts of the chromophore, and (3) compatibility with aqueous media. Limitations do exist in using cit-AuNPs since irreversible aggregation is triggered by a variety of environmental factors, many of which have yet to be fully described. TRP-AuNPs seem to offer a more stable and easier to control system. It may be possible to identify a larger set of NP ligands that are even more stable to different environments and/or better suited for these reactions. Future work will focus on ellucidating the mechanism of deprotection, kinetics, and identifying other nanoparticle systems for use in this application.

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Supporting Information Available: Experimental procedures, syntheses, and spectral data. This material is available free of charge via the Internet at http://pubs.acs.org

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(19) Although speculative, it is conceivable that the methylpicolinium radical generated in the reaction can oxidze the tryptophan moiety to trigger a radical decarboxylation resulting in the production of a tryptophan radical species. (see Mehta, L. K.; Porssa, M.; Parrick, J.; Candeias, L. P.; Wardman, P. *J. Chem. Soc., Perkin Trans. 2.* **1997**, *8*, 1487−1491.) This radical could potentially promote further deprotection events by reducing the nanoparticle. Since there are a large number of tryptophan moieties on the surface of the nanoparticles, this would effectively amplify the number of deprotection events per absorbed photon, resulting in a larger than unity Φ_{rel}.