

Light-Triggered Charge Reversal of Organic–Silica Hybrid Nanoparticles

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S Supporting Information

ABSTRACT: A functional nanoparticle with light-triggered charge reversal based on a protected amine-bridged polysilsesquioxane was designed. An emulsion- and amine-free sol–gel synthesis was developed to prepare uniform nanospheres. Photolysis of suspensions of these nanoparticles results in a reversal of the ζ potential. This behavior has been used to trigger nanoparticle self-assembly, nanocomposite hydrogel formation, and nanoparticle release, showing the potential of this material in nanoscale manipulation and nanoparticle therapy.

There has been substantial progress in the synthesis and applications of uniform, spherical bridged polysilsesquioxane (BPS) xerogel nanoparticles (NPs). Emulsion,¹ modified Stöber,² templated modified Stöber,³ and self-assembly^{4,5} methods were developed for NP synthesis from monomers spanning a range of water solubilities, shapes, and rigidity. Applications of BPS NPs include their use as photodeformable and photopatternable materials,⁴ cellular-imaging NPs,⁶ and the active component in solid-state electrochromic devices.⁷

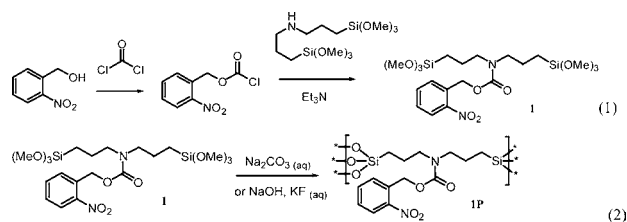
Both inorganic and organic moieties can contribute significantly to the colloidal charge of BPS NPs. While uncondensed silanol groups ($pK_a \approx 4$) generally provide abundant negative charge at pH 5 or higher, recent findings² have shown that functional organic bridging groups (e.g., alkylamines) may contribute positive charge that only partially compensates for the surface negative charge (negative ζ potential) under basic conditions but eventually dominates the surface charge (positive ζ potential) under neutral or acidic conditions. This phenomenon offers the potential to modulate the colloidal charge over a wide range.

The self-assembly of NPs based on charge interactions has been proven to be one of the most effective and reliable strategies for the fabrication of novel nanostructured materials. The methods range from layer-by-layer assembly⁸ for planar or colloidal structures⁹ to NP “complexes”,¹⁰ superlattices or crystals,¹¹ and nanocomposites.¹² Applications include electronic devices,¹³ HPLC stationary phases,¹⁴ solar cells,¹⁵ imaging quantum dots,¹⁶ self-healing hydrogels,¹⁷ and therapeutic NPs.¹⁸

NPs with charge-reversal capability have recently attracted attention in the release of therapeutic agents triggered by pH change^{19,20} or UV irradiation.^{21,22} The strength of the latter strategy lies in its site and time specificity. However, most current research in the field is focused on triggered release of therapeutic small molecules or nucleic acids from NPs. The

release of therapeutic NPs that function by “direct interaction” (such as those that capture toxins²³ or disrupt deleterious cells²⁴) still remains a challenge. In this study, we report a novel type of BPS NP with charge-reversal functionality triggered by a photochemical reaction and model studies suggesting its applications in fields such as nanomaterial self-assembly and nanoparticle therapy. The design of our nanomaterials features a negative colloidal charge that is intrinsic to the as-synthesized BPS NPs. Upon UV irradiation, secondary amine groups emerge in the bridging moieties, reversing the overall colloidal charge from negative to positive. BPS NPs with *o*-nitrobenzyl carbamate-protected amine²⁵ bridging groups were chosen as the photoresponsive material to demonstrate this concept.

To prepare the precursor for the nanomaterials, *o*-nitrobenzyl chloroformate²⁶ was slowly added to a solution of equimolar bis(trimethoxysilylpropyl)amine and excess Et₃N at -12 °C. NMR analysis of the reaction mixture showed full consumption of the chloroformate with ~ 3 mol % decomposed chloroformate and ~ 3 mol % unreacted monomer. A corresponding amount of the chloroformate was added. This procedure yielded *o*-nitrobenzyl-*N,N*-bis(trimethoxysilylpropyl) carbamate (1), the monomer for the photoresponsive BPS materials (eq 1).



Typical sol–gel syntheses of SiO₂ or organic-silica hybrid NPs involve reaction in aqueous ammonia solution. Since the carbamate group is known to be unstable in the presence of NH₃, a protocol for base-catalyzed BPS NP synthesis without highly nucleophilic reagents was needed. The synthesis of uniform, spherical BPS NPs (1P) from monomer 1 was achieved in aqueous solution containing catalysts such as Na₂CO₃, NaOH, and KF and 1-PrOH as a cosolvent (eq 2 and Table 1). Model studies using *o*-nitrobenzyl-*N,N*-diethyl carbamate in the catalyst solutions showed no reaction of the starting material, suggesting that the carbamate bridging moiety would be stable under these polymerization conditions.

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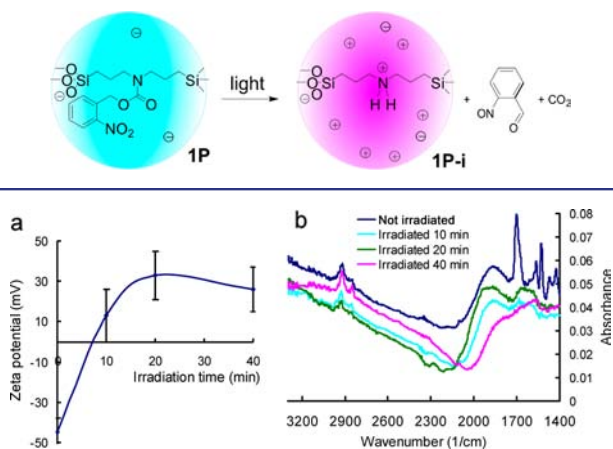
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Table 1. Amine-Free Modified Stöber Synthesis and Size Control of BPS NPs 1P (A Recipe for Finer Size Control Is Included in the Supporting Information)

[Na ₂ CO ₃] (mM)	[NaOH] (mM)	[KF] (mM)	1-PrOH (%)	[1] (mM)	T (°C)	D _n (nm) ^a
20	0	0	0	50	60	400
10	0	0	0	20	25	200
10	0	0	10	20	25	260
2.5	0	0	0	20	25	160
0	5.0	10	0	10	25	83
0	5.0	20	5	10	25	110
0	7.5	0	0	10	25	42
0	7.5	10	0	10	25	63

^aNumber-average diameter determined by DLS. All DLS measurements gave a polydispersity index (PDI) of <0.09, suggesting monodisperse NPs.

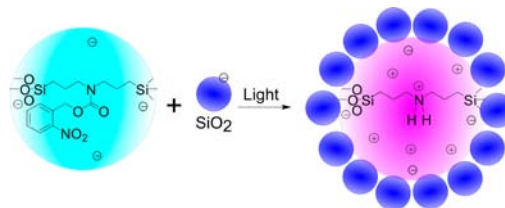
Suspensions of dialyzed carbamate-BPS NPs were irradiated with a hand-held UV lamp (4 mW/cm² of 254 nm UV light). Little change in particle size was observed by dynamic light scattering (DLS), and the ζ potential was reversed from negative to positive upon irradiation (Scheme 1 and Figure 1a).

Scheme 1. Light-Triggered Charge Reversal and Chemistry of 1P NPs**Figure 1.** (a) ζ potential measurements of suspensions of 1P NPs after UV irradiation for various durations. 1P NPs of various sizes generally gave nearly identical results. (b) IR spectra of 1P and 1P-i NPs with various durations of UV irradiation in water suspension.

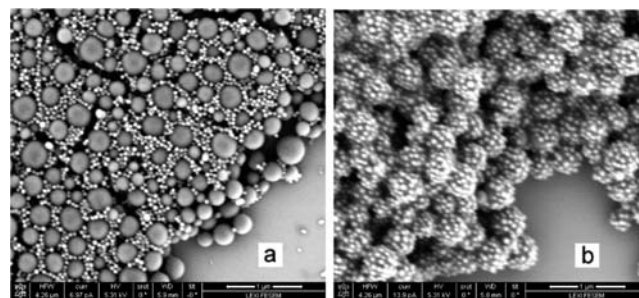
This experiment showed that 10 min of UV irradiation with a hand-held UV lamp was sufficient for reversal of the colloidal charge. This was confirmed by the IR spectra of 1P and 1P-i NPs drop-coated on a CaF₂ plate. Samples prepared from suspensions of 1P exhibited absorptions at 1698 cm⁻¹ (C=O) and 1530 cm⁻¹ (NO₂). After irradiation for 10 min or longer, these absorptions were no longer detectable (Figure 1b).

An application of light-triggered colloidal charge reversal was demonstrated by the triggered self-assembly of nanomaterials. A suspension of 1P (with number- and volume-average diameters D_n = 160 nm and D_v = 200 nm, respectively) and SiO₂ NPs (70 nm, prepared by the published Stöber process) was prepared by mixing deionized water suspensions of the two types of NP. We expected that without UV irradiation, the negatively charged BPS NPs and SiO₂ NPs would show little affinity for each other. However, upon UV irradiation, the BPS

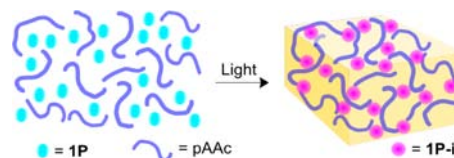
NPs would be transformed into species with a positive ζ potential, providing the potential for self-assembly of a shell of SiO₂ NPs on the surface of the BPS NPs (Scheme 2).

Scheme 2. Light-Triggered “NP Shell” Assembly

The expectation from the preceding experimental design was supported by DLS measurements. The volume average of “large NPs” in the presence of 70 nm SiO₂ particles showed a significant increase in size after irradiation, with D_v increasing to ~260 nm (Figure S4 in the Supporting Information; D_n increased to 230 nm). Since the diameter measured by DLS is an “equivalent spherical” (or “same-size sphere”) diameter,²⁷ such a size increase corresponds to close to a monolayer of 70 nm SiO₂ NPs assembled on the BPS NPs. The volume ratio between “large NPs” and SiO₂ NPs showed an over-representation of the former in both mixtures and thus is less representative of the difference between the irradiated and non-irradiated mixtures. SEM images of a better “visualized” example obtained by using larger 1P NPs is presented in Figure 2.

**Figure 2.** SEM image of centrifuged, resuspended, and dried mixture suspension of 1P (260 nm) and SiO₂ NPs (70 nm) (a) before and (b) after UV irradiation. Scale bar: 1 μ m.

The light-triggered self-assembly phenomenon could also be applied in the formation of a bulk nanocomposite hydrogel (Scheme 3). A mixture containing 1P NPs (D_n = 42 nm) and poly(acrylic acid) (pAAc, MW = 1.0 × 10⁶, pH adjusted to 8.1 by KOH) appeared as a viscous fluid. With UV irradiation, the mixture turned into a nanocomposite hydrogel that was soft but held its own weight and kept its shape even after being stored upside down for more than 2 weeks (Figure 3). This is

Scheme 3. Light-Triggered “Nanocomposite Hydrogel” Assembly

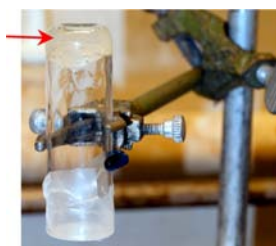


Figure 3. Photograph of a mixture of 1P NPs ($D_n = 42$ nm) and aqueous pAAc (K^+ salt), stored as shown for 14 days after UV irradiation.

attributed to cross-linking of the linear polyanion by the positively charged 1P-i NPs (converted from negatively charged 1P NPs) through charge interactions. It is also noteworthy that the total non-water mass percent in the hydrogel network was $\sim 0.2\%$. An optimized version of the nanocomposite hydrogel may exhibit properties such as high mechanical toughness and self-healing¹⁷ and provide applications in fields such as tissue engineering²⁸ and catalytic hydrogels.²⁹ These applications are currently under investigation.

The triggered release of functional NPs could also be accomplished by the BPS NPs with light-triggered charge-reversal capability. (Scheme 4) "PA+74" NPs (74 nm, ζ

Scheme 4. Light-Triggered Release of "Plastic Antibody" NPs



potential = $+37 \pm 7$ mV) belong to a family of therapeutic polymer hydrogel NPs with antibody-like affinity for peptides.^{30,31} 1P ($D_n = 160$ nm) was slowly added into a suspension of PA+74 NPs. After mixing and sonication, the suspension consisted of 1P NPs loaded with PA+74 NPs in excess. We expected that charge reversal of 1P NPs induced by UV irradiation would trigger release of the PA+74 NPs by charge repulsion.

The expectation from this experimental design was supported by DLS data. The size of 1P NPs loaded with PA+74 ($D_n = 255$ nm, $D_v = 340$ nm; minor aggregation among multiple 1P and PA+74 NPs may have occurred during the loading process) showed a significant decrease after irradiation (Figure S6; $D_n = 201$ nm, $D_v = 238$ nm). The volume contributed by PA+74 NPs, although underrepresented by DLS in both samples, also increased from 31% in the non-irradiated sample to 37% in the irradiated sample. Overall, the size distribution difference between the irradiated and non-irradiated mixtures suggests that the release of PA+74 NPs from the surface of 1P NPs triggered by UV irradiation takes place with significant efficiency. This experiment suggests the possibility of triggered release of therapeutic NPs. Optimization

of materials for cell and tissue experiments is under investigation.

Hydrogel NPs (PA+74) remained suspended in the supernatant under centrifugation while BPS NPs were deposited as a solid. This difference was utilized to visualize the light-triggered release. Without irradiation, the SEM image of the NP complex collected by centrifugation showed organic PA+74 NPs collected along with 1P NPs. Following light-triggered release, the image suggested that PA+74 was no longer associated with 1P-i (Figure 4). An experiment using

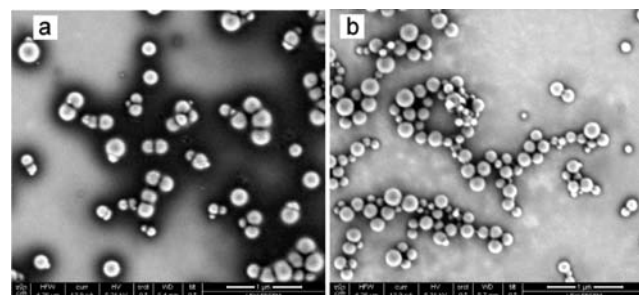


Figure 4. SEM images of centrifuged, resuspended, and dried 1P NPs ($D_n = 160$ nm) assembled with PA+74 NPs (a) without and (b) with UV irradiation in H_2O suspension. The dark region in (a) is dried PA+74 (lightly cross-linked hydrogel) NPs (Figure S6).

fluorescence-labeled PA+74 NPs confirmed this observation. The hydrogel NPs were released into water as a stable suspension after the light-triggered release. With UV irradiation, far more fluorescent hydrogel NPs stayed in the supernatant rather than being removed by centrifugation with 1P NPs, providing the supernatant with higher fluorescence intensity (Figure 5).

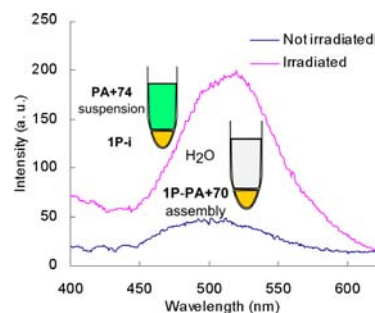


Figure 5. Fluorescence spectrum ($\lambda_{ex} = 330$ nm) of the supernatant after a centrifugation that removed 1P loaded with PA+74 NPs from the suspension (blue). The 1P-PA+74 assembly was isolated from the excess PA+74 prior to the experiment. The same sample was then redispersed, UV-irradiated, and centrifuged, and the fluorescence spectrum of the resulting supernatant was taken (pink).

In this research, we have demonstrated the first amine-free modified Stöber synthesis of uniform bridged polysilsesquioxane NPs (and size control strategies), the design and synthesis of photoresponsive organic-silica hybrid NPs, and their function of light-triggered charge reversal. We have also accomplished light-triggered NP self-assembly, nanocomposite hydrogel formation, and NP release based on the light-triggered charge reversal of the BPS NPs. Our strategy and materials have been shown to be compatible with organic or inorganic, soft or rigid NPs as well as linear polymers. Thus, this research reveals

a novel strategy for nanoscale manipulation with good potential for applications that include controlled formation of nanostructured materials and nanocomposites as well as release of polymer and NP drugs.

■ ASSOCIATED CONTENT

📄 Supporting Information

Detailed synthesis and characterization data as well as experimental procedures and data supporting the statements about the function of materials. 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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