# Photoswitchable Nanocarrier with Reversible Encapsulation Properties

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S *Supporting Information*

ABSTRACT: An amphiphilic dendritic polymer with polyethylenimine (PEI) as the hydrophilic core, steric ester (STA) as the hydrophobic shell, and azobenzene (AZO) groups as the photoswitchable moieties was synthesized via amidation reaction. The synthesized dendritic macromolecule was characterized by ^{1}H nuclear magnetic resonance (NMR), FT-IR spectroscopy, and dynamic light scattering (DLS). With alternating UV and visible-light irradiation, azobenzene moieties of polyethylenimine-steric ester-azobenzene (PEI-STA-AZO) undergo a reversible isomerization between the *cis* and *trans* state. The encapsulation tests demonstrated that PEI-STA-AZO with *trans*-isomer is not capable of encapsulating anionic guests, whereas the one with *cis*-isomers is able to encapsulate the anionic guests from the aqueous solution to the organic layer. Molecular modeling by Spartan was utilized to explain the special encapsulation property of PEI-STA-AZO. Azobenzene groups functioned as a reversible "photo-switch" in the dendritic guest–host system, and the reversibility of encapsulation capability of PEI-STA-AZO was also demonstrated.
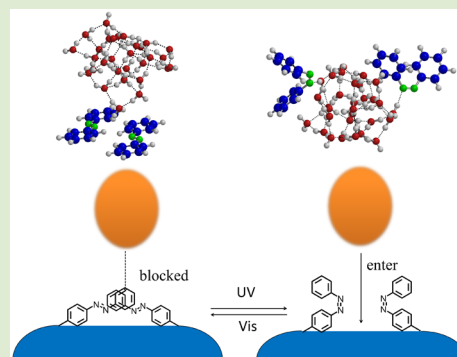
I n the realm of polymer materials, the control of architectures, properties, and functions triggered by a specific external stimulus has always been a challenging subject.[1−5] Among the numerous stimuli, such as temperature,[6,7] electrical potential,[8,9] pH,[10] and magnetic field,[11] light is particularly advantageous due to its remote activation with the spatial and temporal precision.[12−15] Over the years, light-responsive polymeric micelle/nanoparticle/complex/films were successfully employed to the controlled release of encapsulated cargo,[16−18] heterogeneous separation of homogeneous catalyst,[14,19] and the reversible transition of surface wettability.[20,21]

Compared with supramolecularly assembled micelles, covalently bonded dendritic polymers with a core–shell structure are intrinsically stable nanocarriers, which cannot easily be affected by shear force, temperature, concentration, or pressure.[22] Thus, amphiphilic dendritic polymers are excellent guest hosts for different applications, such as drug/biomolecule delivery, mixture separation, and nanocatalysis.[5,23−29] Haag et al. fabricated a series of pH-sensitive dendritic polymers as the smart host for dye, anticancer agent, DNA, or Cu^{2+} ions.[23,30−32] Some other groups also demonstrated some interesting examples of pH-sensitive dendritic polymer hosts.[26,33] More recently, utilization of photosensitive dendritic polymers as the hosts was reported, while most of the research groups were focused on the supramolecular assembly of dendritic polymers.[34,35] Light-sensitive dendritic polymers employed as the single molecular hosts were reported by a few groups.[36,37] Smith and co-workers synthesized a series of photodegradable dendrons with high affinity to DNA molecules, and the multivalent interactions could be "switched off" by photo-

degradation.[37−39] However, the utilization of the *o*-nitrobenzyl groups as the photolabile groups is irreversible.

The azobenzene (AZO) group is a well-known photosensitive functional group, whose isomerization process is completely reversible.[40] Moreover, the process is accompanied by a major configuration change, and the configuration change provides the AZO-containing molecules a feature to control both the spatial alignment and polarity.[14] Therefore, incorporation of AZO groups in the dendritic polymer host could probably control the guest encapsulation property in a reversible manner.

To demonstrate the concept, an AZO-based dendritic polymer host was synthesized, and its capability to encapsulate anionic guests upon alternating UV and visible-light irradiation was also tested.

A light-responsive dendritic polymer host was prepared via a two-step reaction as shown in Scheme 1. Commercially available polyethylenimine (PEI) was utilized as the core of the dendritic polymer host. Stearic acid chloride (STA) was added to the chloroform solution of PEI to form the amphiphilic dendritic polymer PEI-STA. Then 4-(phenylazo)-benzoyl chloride in chloroform was added dropwise to the anhydrous chloroform solution of PEI-STA. The resulting polymer, PEI-STA-AZO for short, was further purified by dialysis against dichloromethane (DCM). It is worth noting that one-pot synthesis is also possible for the synthesis of PEI-
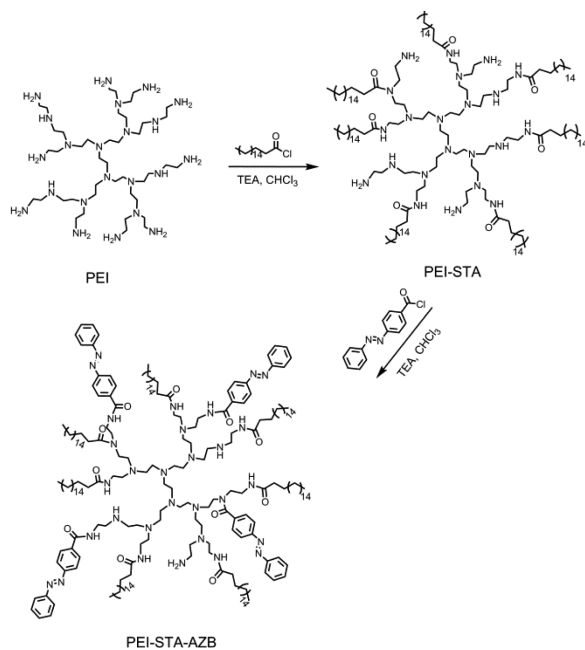
Scheme 1. Preparation of the Dendritic Polymer Host

STA-AZO. However, dendritic polymer PEI-STA is an excellent control sample to the light-responsive PEI-STA-AZO on the characterization and encapsulation property studies later on.[28] Therefore, two-step synthesis was performed here.

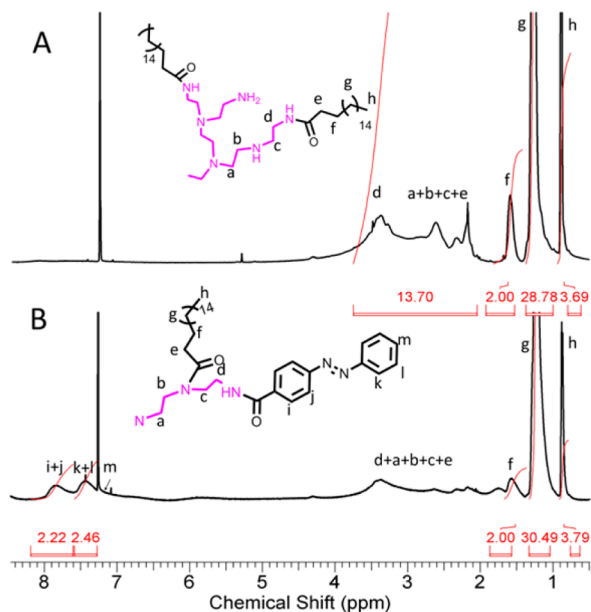The ^{1}H NMR spectrum of PEI-STA and PEI-STA-AZO is shown in Figure 1. From the integrations of relative protons, it

Figure 1. ^{1}H NMR spectrum of (A) PEI-STA and (B) PEI-STA-AZO.

was calculated that around 35% of the amines (230 amines in one PEI MW = 10K molecule with 33% primary amines, 40% secondary amines, and 27% tertiary amines) were functionalized by stearic acid with an initial feeding ratio of 37%.[28,41] Afterward, around 46 amines per molecule on average were successfully functionalized by azobenzene units to form the light-responsive dendritic polymer. The chemical structures of

synthetic nanocarriers were also confirmed by infrared (IR) spectroscopy (Figure S2 in the Supporting Information). The broad peak lying from 3367 to 3083 cm^{-1} in the IR spectrum of PEI revealed the presence of a large number of primary amines and secondary amines. With the increased transformation of the amines to amides (from PEI to PEI-STA and then to PEI-STA-AZB), the intensity of the corresponding peaks decreased. At the same time, the intensity of the peak at 1645 cm^{-1}, which is commonly observed for the C=O stretching vibrations of amide, increased. Moreover, some other peaks lying at 3060, 1424, and 686 cm^{-1} are direct evidence of the presence of azobenzene groups.

Unfortunately, the limited solubility of dendritic polymers in tetrahydrofuran (THF) prevents the molecular weight (MW) measurement by size exclusion chromatography (SEC). To measure the size and molecular weight of dendritic polymers in solution, dynamic light scattering (DLS) and static light scattering (SLS) were performed in chloroform solution (Supporting Information Figure S3 and Table S1). The MW determined by SLS is consistent with the one calculated from the integrations of the ^{1}H NMR spectrum. The hydrodynamic diameter increase from PEI ($D_{(mean)}$ = 9.2 nm) to PEI-STA ($D_{(mean)}$ = 23.2 nm) confirmed the formation of a core−shell structured dendritic host. However, there is no obvious diameter increase from PEI-STA to PEI-STA-AZO ($D_{(mean)}$ = 26.1 nm) despite the obvious molecular weight increase derived from the ^{1}H NMR spectrum integrations. The reason is the azobenzene groups are solely attached to the core of the core−shell nanohost, whereas the peripheries of the polymers are still the same.

As one of the well-studied photochromic molecules, the isomerization process of the AZO moiety is accompanied by a dramatic optical property change.[40] Upon UV irradiation, the absorption intensity of PEI-STA-AZO solution at 322 nm corresponding to the $\pi-\pi^*$ transition decreases, and the peak at 447 nm corresponding to the $n-\pi^*$ transition increases, which evidences the trans-to-cis isomerization.[42] The cis-azobenzene moieties go back to the trans state after visible-light illumination. The isomerization process of PEI-STA-AZO by light irradiation is quite quick, where 40 and 20 s are enough for a trans-to-cis and cis-to-trans transformation, respectively (Supporting Information Figure S4). Five cycles of alternating UV and visible-light irradiations were applied to the THF solution of PEI-STA-AZO, and the isomerization process is completely reversible (Supporting Information Figure S5).

Amphiphilic dendritic polymers based on the PEI core and hydrophobic shell are well reported for their excellent guest encapsulation properties.[28,29] Adopting a similar method,[25,28] a core−shell structured dendritic polymer was employed to capture the anionic guests. Herein, methyl orange (MO) and direct red (DR) were employed as the anionic guests. As expected, the amphiphilic polymer PEI-STA is able to transfer anionic guests (MO or DR) to the organic layer by electrostatic affinity between cationic PEI and anionic guests (Supporting Information Figure S6). To our surprise, the chloroform solution containing trans-PEI-STA-AZO is not able to capture anionic guests from the aqueous solutions. After UV irradiation, the cis-PEI-STA-AZO is able to transfer the DR or MO to the organic layer (Figure 2 and Supporting Information Figure S7). The amount of MO or DR cis-PEI-STA-AZO can encapsulate is less than that captured by PEI-STA (Supporting Information Table S2). UV−vis analysis of the organic layer after mixing with aqueous solution of MO or DR also confirmed this
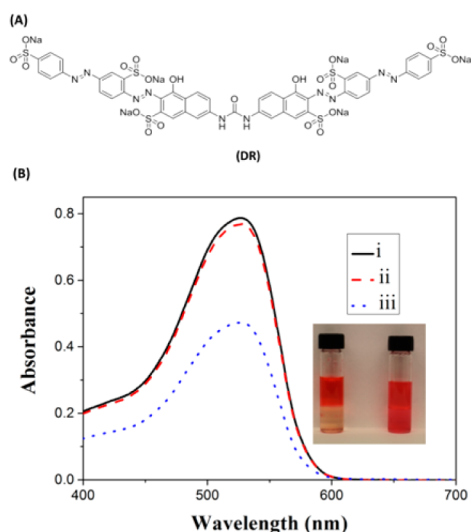
Figure 2. (A) Chemical structure of DR and (B) UV–vis spectrum of the aqueous solution of DR (i) before mixing, (ii) after mixing with *trans*-PEI-STA-AZO, and (iii) after mixing with *cis*-PEI-STA-AZO. Inset is the photograph of DR in aqueous solution mixed with *trans*-PEI-STA-AZO (left) and *cis*-PEI-STA-AZO (right) in chloroform solution.

phenomenon (Supporting Information Figure S8). As a control study, the encapsulation capabilities of the amphiphilic polymer PEI-STA before and after UV irradiation were also tested. As expected, the two PEI-STA solutions exhibited near the same encapsulation capability to both MO and DR (Supporting Information Figure S9). Results show that the azobenzene groups can act as the "photoswitch" for the encapsulation of anionic guests to the dendritic host as shown in Figure 3.
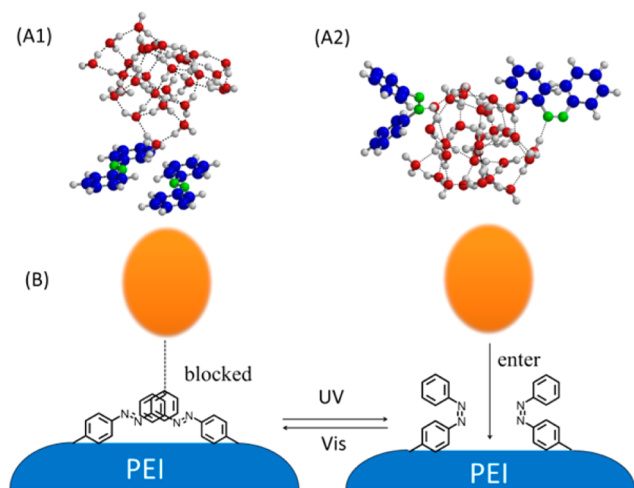

Figure 3. Molecular modeling of the two (A1) *trans*-azobenzene groups or (A2) *cis*-azobenzene groups and 30 water molecules. (B) Illustration of the photoswitch upon alternative UV and vis light irradiation.

The question is how does the azobenzene group play as the photoswitch of the dendritic host. One explanation is that the *cis* isomer is bulkier than the *trans* one and hence has lower periphery density of the inner core. Moreover, the isomerization process of the azobenzene is accompanied by a strong polarity change (0 D for the *trans*-isomer and 3 D for *cis*-isomer).[40] Therefore, the *trans*-azobenzene groups at the

periphery of the PEI will act as a barrier and block the entrance due to the hydrophobic interactions or/and π−π stacking. After the UV irradiation, the *cis*-isomers become smaller in size, and the hydrophobic interaction turns weaker and even vanished, which results in the "open" form of the entrance to the PEI core.

Molecular modeling was utilized to confirm the hypothesis. The structures as shown in Figure 3(A) and (B) are the lowest-energy conformations calculated with ΔE equal to −1787.63 and −2091.89 kJ/mol, respectively (see Supporting Information Table S3 for details). During the liquid−liquid extraction protocol, water played an important role in bringing the nonorganic soluble molecules to the hydrophilic cores of the dendritic host.[25] As shown in Figure 3(A1), the optimized structure implies that the π−π stacking of *trans*-AZO groups will prevent the entrance of polar molecules. Actually, the π−π interaction of *trans*-AZO moieties was observed in the AZO-containing dendrimers, which renders the self-assembly of polymers to giant vesicles.[43] On the other hand, the *cis*-AZO moieties can inteact with water molecules brought about by the increase of the polarity. Water channels can easily be formed between the *cis*-AZO groups and thus allow the polar molecules to pass through.[44]

To further understand the role of periphery azobenzene groups on the encapsulation capabilities of the dendritic polymer, the polymer solutions exposed to UV irradiation at different time durations were also employed for encapsulation tests (see Supporting Information Figure S10). A specific volume of PEI-STA-AZO solution was sequentially taken out after 5 s, 10 s, 15 s, 20 s, 30 s, and 40 s of UV irradiation, and their encapsulation capabilities were tested separately. It was noticed that after 5 s of UV irradiation (the intensity of peak at 322 nm decreased from 1.4 to 1.1) the encapsulation capability to both MO and DR increased significantly. With longer irradiation time, the encapsulated guest number per polymer host stayed similar. The result is consistent with our previous discussion, and it can be explained as this. The transformation of some *trans*-AZO moieties to *cis*-AZO moieties will allow the formation of some water channels. As long as the water channel can be formed, the anionic guests will enter and saturate the cationic PEI core. The increased amount of *cis*-AZO moieties will render the formation of more or larger water channels, but the number of guests per PEI core that can be encapsulated stays the same.

Moreover, the reversibility of the photoswitch in dendritic polymer was also tested. Due to the possible photodegradation of chloroform (CHCl₃) under UV light irradiation, THF was always selected as the solvent for UV or visible-light irradiation. An equal amount of PEI-STA-AZO solution was sequentially taken out from the polymer solution which was exposed to alternating UV and visible-light irradiation. The THF solution of PEI-STA-ZO was evaporated and redissolved in chloroform for an encapsulation test. As shown in Figure 4, the dendritic host showed excellent photoreversibility regarding the encapsulation of MO. There is no obvious change even after fives cycles of alternating UV and visible-light irradiations. A similar result was also observed for the encapsulation of DR (Supporting Information Figure S11).

In summary, an amphiphilic dendritic polymer was synthesized, and its encapsulation property to anionic guests can be well controlled by an AZO-based "photoswitch". A polymer host with PEI as the hydrophilic core, steric ester as the hydrophobic shell, and azobenzene groups as the
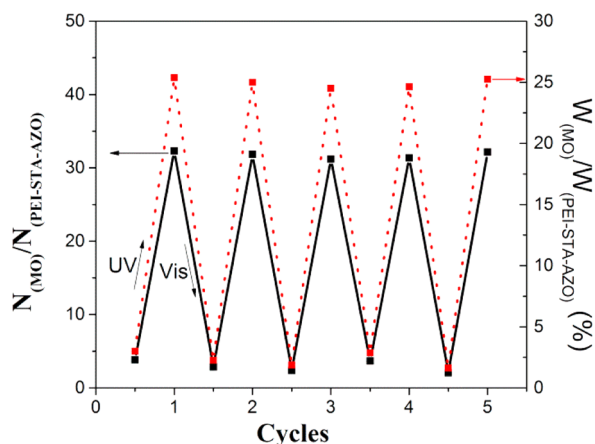
Figure 4. Switch the encapsulation capability of the dendritic polymer by alternating photoirradiation (black line is the number ratio, red line is the weight ratio).

"photoswitch" was synthesized via a two-step reaction. DLS analysis showed a dramatic diameter increase from PEI to PEI-STA, while a similar dynamic radius was observed for PEI-STA and PEI-STA-AZO. PEI-STA is capable of transferring anionic guests to the organic layer, whereas the *trans*-PEI-STA-AZO is not able to due to the hydrophobic interactions of *trans*-AZO moieties. After UV irradiation, the *cis*-PEI-STA-AZO can capture the anionic guests, but less than the PEI-STA. Molecular modeling demonstrated that the $\pi-\pi$ stacking of *trans*-AZO moieties can block the entrance of polar molecules, whereas the *cis*-AZO units will allow polar molecules passing through. Utilization of the azobenzene groups as the "photoswitch" for the encapsulation of MO or DR is completely reversible.

PEI-STA-AZO was demonstrated as the smart covalently bonded dendritic host whose encapsulation property was well controlled by the light. Thus, it is promising to be applied in the field of biotechnology as "smart" materials, and the strategy demonstrated here can be further developed for other applications, such as controlled release, switchable permeability of the membrane, nanosensor, and nanocatalysis.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental details, the data of UV−vis analysis, DLS curves, the typical FTIR and ^{1}H NMR spectra, and the typical photoluminescent 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.

■ ACKNOWLEDGMENTS

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