Photo-Controlled Nano-Supramolecular Size and Reversible Luminescent Behaviors Based on Cucurbit[7]uril Cascaded Assembly

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ABSTRACT: Supramolecular luminescent material with switchable behavior and photo-induced aggregation with emission enhancement is a current research hot spot. Herein, a size-tunable nano-supramolecular assembly with reversible photoluminescent behavior was constructed by noncovalent polymerization of diarylethene-bridged bis(coumarin) derivative (DAE-CO), cucurbit[7]uril (CB[7]), and β -cyclodextrin-grafted hyaluronic acid (HACD). Benefiting from the macrocyclic confinement effect, the guest molecule DAE-CO was included into the cavity of CB[7] to give enhanced fluorescence emission of the resulting DAE-CO \subset CB[7]₂ with longer lifetime at 432 nm to 1.43 ns, thereby further enhancing fluorescence output and lifetime (1.46 ns) when further assembled with HACD, compared with the free DAE-CO (0.95 ns). In addition, DAE-CO, DAE-CO \subset CB[7]₂, and DAE-CO \subset CB[7]₂&HACD all possessed characteristics of aggregation-induced emission and reversible photo-switched structural interconversion, exhibiting an obvious photophysical activation phenomenon of self-aggregation into larger nanoparticles with increase in fluorescence emission intensity, lifetime, and size after irradiation, which could be increased step by step with the alternating irradiation of 254 nm (5 min) or >600 nm (30 s) repeated 7 times. These supramolecular assemblies were successfully used in the tumor cells' targeted imaging and anti-counterfeiting because of the capability of HACD for recognizing specific receptors overexpressed on the surface of tumor cells and the excellent photo-regulated switch ability of DAE-CO, providing an approach of constructing photo-induced emission-enhanced luminescent materials.

KEYWORDS: cucurbit[7]uril, supramolecular assembly, anti-counterfeiting, diarylethene (DAE) derivatives, photo-induced aggregation with emission enhancement (PIAEE)

INTRODUCTION

Organic luminescent materials^{1,2} with color tuning and fluorescence switching properties controlled by physical or chemical stimuli are fascinating and vital in fundamental research due to their widespread applications in data storage devices,³ biological labeling,⁴ sensing,⁵ optical memories,⁶ light emitting diodes,⁷ and so on. However, many of organic luminescent scaffolds designed with large π -conjugated frameworks and planar structures often exhibit weak fluorescence in concentrated solution and the solid state suffering aggregationcaused quenching.^{8,9} Therefore, the talented aggregationinduced emission (AIE) platforms have been burgeoned as important photophysical behavior since 2001 by Tang's group.¹⁰ The working mechanism of high luminescence of AIE materials^{11–14} is the restriction of intramolecular motions (RIMs), including restriction of intramolecular vibrations (RIVs) and restriction of intramolecular rotations (RIRs). Up to date, several stimuli-responsive AIE materials have been fabricated.^{15,16} Light, as a powerful non-touch stimulus with no waste generation, high accuracy, and remotely controlled characteristic, is an ideal candidate among the various external stimuli.^{17–20} Therefore, construction of powerful light-controlled platforms based on AIEgens to modulate physicochemical behavior has attracted great interest recently.

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Scheme 1. (a) Schematic Illustration and Chemical Structures of the Highly Reversible Supramolecular Light Switch with Photo-Induced Emission Enhancement Mediated in Two Stages by DAE-CO, CB[7], and HACD and (b) Illustration of the Photoexcitation Process of DAE-CO, DAE-CO \subset CB[7]₂, and DAE-CO \subset CB[7]₂&HACD



Various categories have been employed for realizing AIE-featured photoactivatable fluorophores including (i) reversible photochromic reactions,²¹ (ii) irreversible photochemical reactions,²² (iii) reactive oxygen species-mediated photo-activation,²³ and (iv) light-induced crystallization.²⁴ For example, Wang and Tang et al. developed a new AIE molecule under a new photoactivatable mechanism of photo-induced crystallization with emission enhancement, with emission enhancement by self-assembling into a regular arrangement under UV light irradiation.²⁴

Inspired by the luminescence mechanism of AIEgens, many other methods aiming to prevent intramolecular motions have been developed, such as fabricating 2D metal nanoparticle platforms²⁵ and supramolecular assemblies.^{26–32} From a structural viewpoint, cucurbit[n]urils (CB[n]s), which possess high binding affinity toward a variety of cationic or neutral guests through hydrophobic and electrostatic interaction,^{33–37} can be expected to effectively prevent aggregation-caused quenching by providing macrocyclic fence, suppressing the quenching of the triplet, suppressing the vibrational deactivation of the excited state through host–guest interactions, restricting molecular motions of the encapsulated luminescence silent dyes to undergo various luminescent emissions.³⁸ For instance, we constructed a supramolecular luminescent nanosystem by anthracene-conjugated bromophe-

nylpyridinium salt and CB[8], capable of phototunable transformation from fluorescence to phosphorescence in different organelles.³⁹ Ni et al. reported a CB[8] cavityconfined rigid J-type supramolecular polymer with sensitive photochromic response under UV light and sunlight in the fabrication of smart windows and erasable printing.⁴⁰ Xiao and Liu et al. realized a cold white fluorescence emission under UV light with a E/Z isomerization light-responsive molecular switch.⁴¹ These results indicate that CB[n]-mediated lightresponsive supramolecular assemblies could be utilized as a new type of light-emitting materials endowing light controllable property. Hence, developing novel light-controllable CB[n]-mediated supramolecular assemblies with photoinduced aggregation with emission enhancement (PIAEE) ability is of great significance for practical applications but is rarely reported so far, to the best of our knowledge.

Among the various types of photosensitive building blocks for constructing supramolecular systems, diarylethene derivatives (DAEs)^{42–44} possessing high photoisomerization quantum yield, outstanding fatigue resistance, and easy synthesis with different functional groups have been successfully applied to data storage,⁴⁵ molecular machines,⁴⁶ optical switches,⁴⁷ and helical transfer controllers.⁴⁸ Meanwhile, coumarin and its derivatives are a popular class of supramolecular guests to be captured by macrocyclic hosts such as cyclodextrins and



Figure 1. (a) ¹H NMR spectra changes observed for OF-DAE-CO (1.0 mM, bottom) upon irradiation with UV light (254 nm, middle) and subsequent irradiation with NIR light (>600 nm, top) in d_6 -DMSO at 298 K. Inset: changes of the chemical structure of DAE-CO. (b) UV–vis spectra changes of OF-DAE-CO (1.0×10^{-5} M) in water upon irradiation with 254 nm UV light. Inset: changes of the photographic images upon UV light irradiation. (c) Fluorescence emission spectra of OF-DAE-CO (0.5×10^{-5} M) in H₂O/THF ($\lambda_{ex} = 380$ nm). Inset: photographs of OF-DAE-CO in solution of $R_{THF} = 90\%$ (left) and $R_{THF} = 0\%$ (right) under 365 nm. (d) Fluorescence spectra changes of OF-DAE-CO (1.0×10^{-5} M) in water upon irradiation with 254 nm (5 min) and >600 nm light (30 s) ($\lambda_{ex} = 380$ nm). Inset: modulated emission intensity changes at 540 nm in 12 alternating irradiation cycles.

CB[n]s, with the promising advantages of undergoing [2 + 2]cycloaddition under UV irradiation above 300 nm and photoscission at 254 nm.^{49,50} Herein, we constructed a photo-responsive AIE supramolecular assembly DAE- $CO \subset CB[7]_2$ composed of diarylethene-bridged bis(coumarin) derivative DAE-CO and CB[7], which underwent the firststage emission enhancement and longer fluorescence lifetime to 1.43 ns than DAE-CO (0.95 ns) based on assemblyactivated emission enhancement. Such supramolecular assemblies further bound with β -cyclodextrin-grafted hyaluronic acid (HACD) to form ternary supramolecular nanoparticles DAE- $CO \subset CB[7]_2$ & HACD realizing the second-stage enhancement of emission and lifetime. Interestingly, benefiting from the reversible photoisomerization of the DAE unit, DAE-CO, DAE-COCCB[7]₂ and DAE-COCCB[7]₂&HACD were luminous on/off switchable by alternating the wavelengths of light between 254 and >600 nm, accompanying self-aggregation into larger nanoparticles with step by step increase in fluorescence emission intensity, lifetime, and size after irradiation in several times, via the potential photoactivation mechanism of PIAEE (Scheme 1). Ultimately, these switchable systems have been successfully used in targeted cell imaging and information encryption.

RESULTS AND DISCUSSION

Water-soluble DAE-CO was successfully synthesized as an AIEgen in 98% yield from 1,2-bis(2-methyl-5-(pyridin-4-yl)thiophen-3-yl)cyclopent-1-ene **1** and 6-(bromomethyl)-1H-isochromen-1-one **2** vis a SN₂ substitution as summarized in Scheme S1. Furthermore, DAE-CO was fully characterized by ¹H NMR, ¹³C NMR, 2D ¹H-¹H COSY, and high-resolution mass spectrometry (HRMS) (Figures S1-S3). As

shown in Figures S1 and S3, the same protons in the ringopened form of DAE-CO (OF-DAE-CO) exhibited obviously different chemical shifts in d₆-DMSO and D₂O. Given the introduction of the DAE core, the photochromic and PIAEE properties of OF-DAE-CO were investigated by ¹H NMR, UV-vis absorption spectra, fluorescence emission spectra, dynamic light scattering (DLS), and transmission electron microscopy (TEM). When irradiated at 254 nm, the proton signals of OF-DAE-CO at 5.83 and 9.04 ppm moved downfield to 5.88 and 9.10 ppm, respectively. With the gradual addition of irradiation time to 60 min, above 99% of OF-DAE-CO converted to the ring-closed form (CF-DAE-CO) (Figures S4 and S23). More interestingly, a complete recovery of the original ¹H NMR spectrum was achieved upon irradiation at >600 nm, suggesting the excellent photochromic ability of DAE core and stability of coumarin component under the exposed light (Figure 1a). The UV-vis spectrum of OF-DAE-CO showed three maximum absorption bands at 273, 329, and 386 nm, respectively. When the solution of OF-DAE-CO was irradiated at 254 nm, the peak at 273 nm gradually increased, and those at 329 and 386 nm declined. Meanwhile, a new peak at 690 nm emerged and increased, which could be assigned to CF-DAE-CO, accompanied by the appearance of two isosbestic points at 316 and 431 nm during the transformation process (Figure 1b). Simultaneously, the color of the solution changed from colorless to light green (Figure 1b, inset). Although a complete recovery of the original ¹H NMR spectrum of OF-DAE-CO was achieved upon irradiation of CF-DAE-CO at >600 nm (Figure 1a), the UV-vis spectra could not return to its original shape. The nearly unchanged UV-vis absorption position and the decreased absorption intensities in Figure S5 indicate that the effective concentration



Figure 2. ¹H NMR spectra (500 MHz, D₂O, 298 K) of DAE-CO ([DAE-CO] = 1.0×10^{-3} M) with 0 (I), 2.5 (II) equivalents of CB[7], and CB[7] without DAE-CO (III).

in the solution was lower, which might be caused by the precipitation of big aggregates induced by light. Surprisingly, the more times we exposed DAE-CO to 254 nm/>600 nm, the lower intensity of UV-vis absorption exhibited (Figure S5, inset), presenting a phenomenon of photo-induced aggregation, which was also confirmed by the obvious Tyndall effect of DAE-CO solution after irradiation at 254 nm for 5 min (Figure S6). To further verify the unusual photophysical performance, the emission spectra were recorded in different proportions of H_2O -THF mixed solution. As shown in Figure 1c, when gradually increasing the ratio of THF (R_{THF}) , the emission bands suffered an obvious hypochromic shift accompanying an increase in intensity. Meanwhile, when $R_{\text{THF}} = 0\%$ a weak saffron emission was observed (Figure 1c inset right), but when $R_{\text{THF}} = 90\%$ a strong saffron emission appeared (Figure 1c inset left), suggesting the AIE characteristic of DAE-CO. The switching and aggregation behaviors of DAE-CO induced by light were further investigated by its fluorescence spectra. As illustrated in Figure 1d, when OF-DAE-CO was excited at 380 nm, the fluorescence spectrum of OF-DAE-CO revealed two emission peaks centered at 540 and 425 nm. Upon irradiation with 254 nm, the fluorescence intensity of OF-DAE-CO at 540 nm decreased, accompanying an increase at 425 nm. When the aqueous solution was irradiated with >600 nm light, the fluorescence was recovered with an increase in intensity. It was noteworthy that the fluorescence intensity of DAE-CO gradually increased after alternating illumination with different wavelengths of light (254 nm/>600 nm, Figure 1d inset, Figure S7), thereby the formation of tighter molecular packing mediated by light might be the key for the fluorescence enhancement. To further confirm the photo-induced aggregation, DLS and TEM were employed. Before 254 nm illumination, DLS experiment gave an average hydrodynamic diameter (Dh) of OF-DAE-CO as ca. 61 nm with a narrow distribution (Figure S8a). Meanwhile, the particle sizes of CF-DAE-CO had a dramatic increase as ca. 1174 nm, which was

smaller than the diameter measured by TEM, with 254 nm light irradiation for 5 min (Figure S8b). In addition, the TEM images of OF-DAE-CO showed numbers of dispersed nanoparticles while CF-DAE-CO presented spherical nanoparticles with larger diameter (Figure S9a,b). Consequently, light can efficiently induce the formation of DAE-CO nanoaggregates under a mechanism of PIAEE and regulate the conversion between its ring-opened and ring-closed forms.

It has been well-established that CB[7] can bind positively charged guests. The supramolecular assembly consisting of CB[7] and DAE-CO was investigated by UV-vis, NMR, and fluorescence spectra. Job's plot confirmed a maximum peak at a molar fraction of 0.66, indicating a 2:1 host-guest complex stoichiometry (Figure S10). With the stepwise addition of CB[7] to an aqueous solution of DAE-CO, the absorption peaks of DAE-CO decreased dramatically in the range of 250-450 nm (Figure S11). Therefore, by using a nonlinear leastsquares curve-fitting method, the association constant (K_{a}) was calculated to be 3.49×10^9 M⁻² (Figure S12) by analyzing the sequential changes in the absorption intensity of DAE-CO at 383 nm in the presence of varying concentrations of CB[7], which was comparable to the reported K_a value between CB[7] and coumarin salt.⁵¹ Furthermore, in ¹H NMR spectra of DAE-CO with varying concentrations of CB[7] (Figure S13), peaks of free DAE-CO totally disappeared when 2.0 equiv of CB[7] was added, further implying an ideal host-guest binding ratio. As shown in Figure 2, the chemical shifts of protons (H1, H3, H4, and H5) residing on the coumarin groups, methylene (H6), and those (H7) on the pyridine groups presented upfield shifts ($\Delta \delta = 0.64$, 1.02, 1.07, 0.76, 0.53, and 0.44 ppm for H1, H3, H4, H5, H6, and H7, respectively). The resonances of other protons (H8) residing on the pyridinium rings, thiophene rings (H9), cyclopentene groups (H10 and H11), and those on methyl groups (H12) shifted downfield ($\Delta \delta$ = 0.04–0.40 ppm). In addition, 2D rotating frame Overhauser effect spectroscopy (ROESY) of



Figure 3. (a) Fluorescence spectra of DAE-CO upon the addition of 0, 0.5, 1.0, 1.5, and 2.0 equiv of CB[7] in water at 25 °C ([DAE-CO] = 1.0×10^{-5} M, $\lambda_{ex} = 380$ nm). (b) Fluorescence spectra of DAE-COCCB[7]₂ upon the addition of 0, 0.5, 1.0, 2.0, 3.0, 4.0, 5.0, 6.0, 7.0, 8.0, 9.0, and 10.0 equiv (calculated by β -CD) of HACD in water at 25 °C ([DAE-CO] = 1.0×10^{-5} M, [CB[7]] = 2.0×10^{-5} M, $\lambda_{ex} = 380$ nm). (c) Fluorescence lifetime at 540 nm ([DAE-CO] = 1.0×10^{-5} M) and that at (d) 432 nm.



Figure 4. UV–vis spectra changes of (a) OF-DAE-CO \subset CB[7]₂ and (b) OF-DAE-CO \subset CB[7]₂&HACD ([OF-DAE-CO] = 1.0×10^{-5} M) in water upon alternating irradiation with 254 nm light (5 min) and >600 nm light (30 s). Inset: modulated absorbance intensity changes at 680 nm in 10 alternating irradiation cycles.

DAE-CO \subset CB[7]₂ showed clear NOE cross-peaks between the protons of DAE-CO and CB[7] (Figure S14). Combining the 1D and 2D NMR spectra, it was clear that the positively charged coumarin pyridinium groups were included in the cavity of CB[7]. The more favorable evidence was an intense peak at m/z 1528.94 assigned to [DAE-CO \subset CB[7]₂ – 2Br-]²⁺ in the HRMS spectrum of DAE-CO \subset CB[7]₂ solution (Figure S15), which was in accordance with the calculated result of 1528.95.

Benefiting from the conformational restriction caused by host-guest complexation, the fluorescence intensities of DAE-CO at 432 and 540 nm drastically increased by a factor of 2.3

and 4.6, respectively, with the gradual addition of CB[7] (Figure 3a). Visually, the fluorescence color of DAE-CO turned strong saffron after addition of 2 equiv of CB[7] under 365 nm, which could be observed by the naked eye (Figure 3a, inset). Furthermore, HACD was introduced to further co-assemble with DAE-CO \subset CB[7]₂ by virtue of its excellent water solubility, biocompatibility, and biodegradability. Upon complexation with HACD (obtained from our previous work⁵² with substitution degree of β -CD to be as 19.14%) to 5.0 equiv, the fluorescence intensity of DAE-CO \subset CB[7]₂&HACD increased (Figure 3b) 1.5-fold as compared with that of DAE-CO \subset CB[7]₂ because the construction of ternary assembly



Figure 5. Fluorescence spectra changes of (a) OF-DAE-CO \subset CB[7]₂ and (b) OF-DAE-CO \subset CB[7]₂&HACD ([OF-DAE-CO] = 1.0 × 10⁻⁵ M) in water upon alternating irradiation with 254 nm (5 min) and >600 nm light (30 s) (λ_{ex} = 380 nm). Inset: modulated emission intensity changes at 425 nm in 14 times alternating irradiation.



Figure 6. Encryption information constructed by DAE-CO, DAE-COCCB[7]₂, and DAE-COCCB[7]₂&HACD under daylight and 365 nm UV light.

further inhibited the conformational restriction, and this increase could also be seen by the naked eye (Figure 3b inset). Unfortunately, further increasing the amount of HACD weakened the fluorescence emission intensity (Figure S24). Moreover, the fluorescence lifetime of DAE-CO⊂CB[7]₂&HACD at 540 nm was measured to be 1.45 ns, which was higher than that (1.27, 1.06 ns) of DAE- $CO \subset CB[7]_2$ and free DAE-CO, respectively (Figure 3c, Table S1). In addition, the fluorescence lifetime at 432 nm (Figure 3d, Table S2) was consistent with that at 540 nm. Then, the noncovalent interaction between DAE-CO \subset CB[7]₂ and HACD was investigated by NMR. First, β -CD was selected as reference owing to the complicated structure of HACD. In Figure S16, all proton chemical shifts belonging to coumarin and pyridine groups remained basically unchanged, concurrently accompanied by significant upfield shifts of the rest protons (H9–H12), revealing that β -CD combined with the cyclopentane moiety that was not occupied by CB[7] in DAE- $CO \subset CB[7]_2$. The 2D ROESY spectrum also showed significant NOE cross-peaks between DAE-CO \subset CB[7]₂ and β -CD (Figure S17), providing reliable evidence for the binding mode. The host-guest complexation behavior between DAE-CO and β -CD was also studied by HRMS, wherein an intense peak centered on m/z: 933.28 ([DAE-CO and β -CD – 2Br-]²⁺, Figure S18) was clearly detected for DAE-CO and β -CD, which corresponded with the calculated values of 933.29, thereby confirming the formation of the ternary assembly from the side.

To our excitement, when OF-DAE-CO⊂CB[7]₂ and OF-DAE-COCCB[7]2&HACD were irradiated with UV light of 254 nm, peaks at 331 and 380 nm decreased but that at 273 nm increased. Meanwhile, a new absorption at 680 nm emerged, accompanied by the appearance of two isosbestic points (317 and 427 nm) (Figure 4), indicating the production of supramolecular assemblies in the closed form (CF-DAE- $CO \subset CB[7]_2$ and CF-DAE-CO $\subset CB[7]_2$ &HACD). When the assemblies were subsequently irradiated with >600 nm light, the UV-vis absorption spectra of CF-DAE-CO \subset CB[7]₂ and CF-DAE-CO \subset CB[7]₂&HACD could not recover to their original levels with the position of the absorption peaks unchanged but the absorption intensity decreased. With the increase in the times of alternating irradiation, the absorption intensities in the same form at 680 nm became weaker and weaker in both CF-DAE-CO \subset CB[7]₂ and CF-DAE- $CO \subset CB[7]_2$ & HACD resulting from photo-induced aggregation (Figure 4 inset). In TEM images, we could see several nanoparticles of OF-DAE-COCCB[7]₂ (Figure S9c) and OF-DAE-CO \subset CB[7]₂&HACD (Figure S9e). When it came to CF-DAE-CO⊂CB[7]₂ (Figure S9d) and CF-DAE- $CO \subset CB[7]_2$ & HACD (Figure S9f), the sizes of the discrete nanoparticles became larger, which were further demonstrated by DLS. The average hydrodynamic diameters of nanoparticles formed by OF-DAE-COCCB[7]₂, CF-DAE-COCCB[7]₂, OF- $DAE - CO \subset CB[7]_2 \& HACD$, and CF - DAE- $CO \subset CB[7]_2$ & HACD were 69, 79, 43, and 235 nm (Figure S8c-f), respectively. The fluorescence lifetime of CF-DAE-COCCB[7]₂&HACD at $\lambda = 432$ nm ($\tau = 1.60$ ns) was longer



Figure 7. Cellular imaging of A549 cells after co-staining with the OF-DAE-CO \subset CB[7]₂&HACD assembly, MitoTracker, and DAPI, before (up) and after (down) 254 nm light irradiation.

than that of OF-DAE-CO \subset CB[7]₂&HACD ($\tau = 1.46$ ns) (Figure 3d, Table S2). It was consistent with our assumption that the fluorescence lifetime of OF-DAE-CO \subset CB[7]₂&HACD at $\lambda = 540$ nm became shorter after exposure to 254 nm (1.27 ns) but longer after >600 nm illumination (1.58 ns) than the initial value (1.45 ns) (Figure 3c, Table S1). In addition, CF-DAE-CO \subset CB[7]₂ and CF-DAE-CO \subset CB[7]₂&HACD exhibited an obvious Tyndall effect (Figure S6), indicating the formation of larger aggregates. Accordingly, the aforementioned phenomena altogether indicated that light could cause the aggregation of our assemblies.

The fluorescence emission also exhibited corresponding changes upon light irradiation, wherein the peaks of OF-DAE- $CO\subset CB[7]_2$ and OF-DAE- $CO\subset CB[7]_2$ &HACD at 540 nm gradually decreased upon irradiation with 254 nm UV light, with the quenching efficiency calculated to be 67 and 70%, respectively (Figure 5). Subsequently, the quenched fluorescence emission recovered and became stronger than their initial states (Figures 5, S19, S20) after irradiation with >600 nm light, which could be explained by the combination of their AIE features and light-induced aggregation. Upon alternating between 254 and >600 nm irradiation, this process could be repeated several times. As for the emission at 425 nm, the intensity of the same formed assemblies experienced a continuous increase after irradiation (Figure 5, inset).

Finally, taking advantages of the good photo-switchable luminescence behaviors and their PIAEE features, DAE-CO, DAE-CO \subset CB[7]₂ and DAE-CO \subset CB[7]₂&HACD were successfully used in aspects of information encryption. As depicted in Figure 6, we drew three digits "5", "0", "3" with DAE-CO, DAE-CO \subset CB[7]₂, and DAE-CO \subset CB[7]₂&HACD in 96-well plates, respectively. The digits were hidden in daylight as the solutions were colorless. We further placed the plate under a 365 nm portable UV lamp, saffron yellow fluorescence of digits "503" emerged and the luminescence intensity gradually increased from "5" to "0" to "3". After exposing the plate to 254 nm UV light, the hidden information could be seen by naked eyes in daylight but showed no appreciable fluorescence under 365 nm as the open-formed guest (DAE-CO) changed to closed one. Interestingly, the UV light irradiated digits (seen at daylight and hidden at 365 nm) could completely recover upon irradiation with >600 nm and these cycles could be repeated several times.

The targeted imaging of tumor cells was attempted to illustrate their potential biological applicability as HACD was able to recognize specific receptors overexpressed on the surface of tumor cells. Human lung adenocarcinoma cells (A549 cells) were selected to be co-stained with DAE-CO, DAE-COCCB[7]₂, DAE-COCCB[7]₂&HACD, mitochondria staining dye MitoTracker, and cell nucleus staining dye DAPI followed by the investigation of their intracellular distribution utilizing confocal laser scanning microscopy. As shown in Figure 7, the merged image of red OF-DAE- $CO \subset CB[7]_2$ & HACD and blue DAPI revealed that the ternary supramolecular assembly achieved accurate cell nucleustargeted imaging. Upon irradiation with 254 nm UV light, the assembly OF-DAE-CO⊂CB[7]₂&HACD was converted into its closed-form isomer, which led to the quenching of the red fluorescence in cells, thereby indicating that efficient photo-controlled cell nucleus-targeted cell imaging could be carried out using our system. Similarly, both DAE-CO and DAE-CO \subset CB[7]₂ could realize this cell imaging but with less fluorescence emission intensity (Figures S21, S22).

CONCLUSIONS

In conclusion, photo-switched supramolecular self-assemblies with a photoactivatable mechanism of PIAEE and assemblyactivated emission enhancement were developed by employing the host–guest complex OF-DAE-CO \subset CB[7]₂ and further assembled with HACD. On account of the reversible photoisomerization property of the DAE unit and the efficient AIE feature, the luminescence of DAE-CO could be reversibly switched on/off, despite exhibiting relatively weak emission in aqueous solution. Interestingly, under the stimulation of light, DAE-CO tended to self-assemble into larger aggregates with enhancement in size, lifetime, and fluorescence intensity, and this enhancement could be increased step by step by alternating 254 nm (5 min)/>600 nm (3 s) irradiation in several cycles. Compared with DAE-CO, DAE-CO \subset CB[7]₂ achieved the first stage enhancement of fluorescence emission, and such emission was enhanced at the second stage by assembly with HACD, accompanied by the increased fluorescence lifetime. Significantly, like DAE-CO, both DAE-CO \subset CB[7]₂ and DAE-CO \subset CB[7]₂&HACD had the characteristics of adjustable luminescence and PIAEE. In addition, these smart supramolecular luminescent materials have been successfully applied to information encryption and targeted, photo-controlled tumor cell imaging.

EXPERIMENTAL SECTION

Materials. All manipulations were carried out under a N_2 atmosphere by using standard Schlenk techniques, unless otherwise stated. THF and DMF were distilled under an argon atmosphere from sodium benzophenone. Compounds 1^{53} and 2^{54} were prepared by literature methods or modified literature methods. All other starting materials were obtained commercially as analytical grade and used without further purification.

Characterization. NMR spectra were recorded on a BrukerAV500 spectrometer at 25 °C. High resolution mass (HRMS) spectra were measured in the ESI mode. UV/vis spectra were recorded in a quartz cell (light path of 10 mm) on a Shimadzu UV-3600 spectrophotometer equipped with a PTC-348WI temperature controller. Fluorescence spectra were determined on a fluorescence spectrometer (Edinburgh, FLS 1000). TEM images were acquired using a Tecnai 20 transmission electron microscope operating at an accelerating voltage of 200 kV. The sample for TEM measurements was prepared by dropping a sample solution $(1.0 \times 10^{-5} \text{ M in})$ water) onto a copper grid and was then air-dried. The hydrodynamic diameter (D_h) was determined by DLS experiments at 25 °C, and solution samples (1.0 \times 10⁻⁵ M in water) were examined on a Malvern Zetasizer Nano ZS90. Irradiation experiments ($\lambda = 254$ and >600 nm) were carried out using a hand ultraviolet lamp and a CEL-HXF300 20 V 300 W xenon lamp (Beijing China Education Au-light Co. Ltd., China), respectively. A Hamamatsu Quantaurus-Tau spectrometer was used to measure fluorescence lifetimes. A549 cells were seeded in 35 mm dishes for 24 h and then incubated with complexes (0.1 mM) at 37 °C for 24 h. Cells were washed three times with PBS and visualized by a confocal microscope (LSM 710, Carl Zeiss, Gottingen, Germany) immediately. The photophysical properties of different compounds are summarized in Table S3.

Synthesis of DAE-CO. Compounds 1 (41.5 mg, 0.1 mmol) and 2 (72 mg, 0.3 mmol) were added to DMF (4 mL) and the mixture was stirred for another 24 h at 100 °C. Then, the reaction mixture was cooled, and an excess amount of acetone (200 mL) was added to the solution. The precipitate was filtered and washed with petroleum ether and acetone to yield the desired compound DAE-CO (87 mg, 98% yield). ¹H NMR (500 MHz, DMSO-*d*₆): δ 9.07 (d, *J* = 6.7 Hz, 4H), 8.28 (d, *J* = 6.8 Hz, 4H), 8.21 (s, 2H), 8.09 (d, *J* = 9.6 Hz, 2H), 7.91 (s, 2H), 7.82 (d, *J* = 8.5 Hz, 2H), 7.54 (d, *J* = 8.5 Hz, 2H), 6.59 (d, *J* = 9.6 Hz, 2H), 5.85 (s, 4H), 3.35 (s, 6H), 2.93 (t, *J* = 7.3 Hz, 4H), 2.18–2.08 (m, 2H). ¹³C NMR (126 MHz, DMSO-*d*₆): δ 160.5, 154.7, 148.9, 145.6, 144.7, 139.5, 135.5, 134.4, 134.0, 133.2, 131.7, 129.7, 122.9, 119.9, 118.1, 117.9, 62.0,

23.1, 15.6. HRMS (ESI) m/z: $[M-2Br-]^{2+}$ calcd for $C_{45}H_{36}Br_2N_2O_4S_2$, 366.1053; found, 366.1035.

ASSOCIATED CONTENT

Data Availability Statement

The data that support the findings of this study are available in the Supporting Information of this article.

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsami.3c12242.

Experimental procedures, synthetic pathways, UV-vis spectra, DLS results, TEM results, Job's plot, ¹H NMR spectra, 2D ROESY spectrum, cellular imaging, fluorescence lifetimes, and photophysical data of compounds, (PDF)

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Author Contributions

Y.L., Y.C., and H.-G.F conceived and designed the experiments. H.-G.F synthesized and performed the chemical characterization. X.-X.S., M.L., H.-J.W., and F.Z. were involved in the discussion and contributed to the manuscript preparation. H.-G.F wrote the main manuscript. Y.C. and Y.L. supervised the work and edited the manuscript. All authors analyzed and discussed the results and reviewed the manuscript.

Notes

The authors declare no competing financial interest.

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