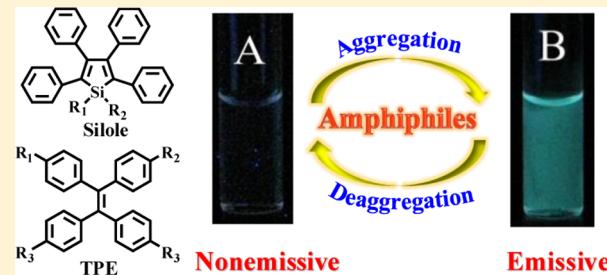


Manipulation of the Aggregation and Deaggregation of Tetraphenylethylene and Silole Fluorophores by Amphiphiles: Emission Modulation and Sensing Applications

Guanxin Zhang, Fang Hu, and Deqing Zhang*

Beijing National Laboratory for Molecular Sciences, Organic Solids Laboratory, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, China

ABSTRACT: In this Feature Article, we have summarized the recent advances in the fluorescence modulation of tetraphenylethylene and silole fluorophores by manipulating the respective aggregation/deaggregation with amphiphiles. These include (i) the assembly of neutral tetraphenylethylene analogues with the aid of an ionic amphiphile, (ii) the aggregation of ionic tetraphenylethylene and silole induced by amphiphiles, and (iii) bio/chemosensors based on the aggregation/deaggregation of AIE fluorophores tuned by ionic amphiphiles.



INTRODUCTION

Organic fluorophores have been intensively investigated and extensively utilized in chemo/biosensing and imaging.^{1–3} They have been also intensively explored for the development of optoelectronic materials with promise in various device applications including organic light-emitting diodes⁴ and organic solid-state lasers.⁵ In general, most of these organic fluorophores are strongly emissive in dilute solutions, but they become weakly fluorescent after aggregation and in the solid states. This is termed aggregation-caused quenching (ACQ) owing to the formation of excimers, exciplexes, and H-type aggregates.^{6–8} Such an ACQ effect not only affects the development of highly emissive materials in the solid states but also limit the application of organic fluorophores in biosensing and imaging because they are generally hydrophobic and tend to aggregate in aqueous solutions. A number of approaches have been devised to prevent this aggregation. For instance, bulky groups were attached to the fluorophores to weaken the intermolecular interactions; accordingly, the aggregation of fluorophores was inhibited.^{9–12}

Notably, there are a few organic fluorophores that exhibit abnormal emissive behaviors; they exhibit almost no emission in solutions, but they emit strongly after aggregation. Such an unusual fluorescent feature is referred to as aggregation-induced emission (AIE), as proposed by Tang and coworkers in 2001.¹³ These AIE fluorophores include tetraphenylethylene (TPE) and 1-methyl-1,2,3,4,5-pentaphenylsilole (Silole), which are nonplanar albeit composed of conjugated fragments. The AIE feature is generally ascribed to the inhibition of internal rotations after aggregation,¹⁴ but aggregation-induced planarization and formation of J-type aggregates are believed to be responsible in some cases.^{15,16}

In recent years, AIE fluorophores have received increasing attention. A number of light-emitting molecules with high fluorescent quantum yields in the solid states were yielded from AIE fluorophores, and some of them were used to fabricate

OLEDs.^{17,18} In particular, AIE fluorophores were successfully utilized for chemo-/biosensing by manipulating the aggregation and deaggregation of AIE fluorophores upon interactions with analytes.^{19,20} The sensing with AIE fluorophores was mainly based on the manipulation of their aggregation and deaggregation. It should be noted that a number of highly selective and sensitive chemo/biosensors have been developed on the basis of FRET (fluorescence resonance energy transfer), PET (photo-induced electron transfer), or ICT (intramolecular charge transfer) mechanisms.^{1–3,21,22} However, compared to the AIE-based sensors, careful molecular design and tedious synthesis were needed for most fluorophore probes in order to tune the FRET, PET, or ICT processes effectively after binding analytes. In comparison, the chemo/biosensors with AIE fluorophores can be both sensitive and selective by proper chemical modification of AIE fluorophores and the combination of specific chemical and enzymatic reactions.^{19,20,23–36} For example, a number of label-free biosensors were established with easily accessible molecules.^{23–36} Also, AIE fluorophores were also utilized for bioimaging by taking advantage of the fact that these fluorophores remain nonemissive before binding the targets, and their emissions are switched on only after binding the targets.^{37–40} Thus, the multiple washing step can be eliminated for bioimaging with AIE fluorophores because the unbound fluorophores exhibit rather weak background fluorescence signals.^{39,40}

The aggregation of AIE fluorophores can be induced by intermolecular interactions, including hydrophobic and electrostatic interactions. Amphiphiles normally can self-assemble to form micelles, vesicles, and other kinds of aggregates.^{41–44} Therefore amphiphiles, in particular, ionic amphiphiles, can be

Received: July 24, 2014

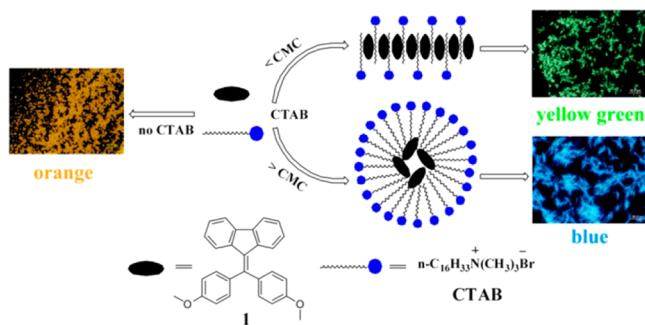
Revised: October 15, 2014

Published: October 20, 2014

utilized to modulate the aggregation of AIE fluorophores in aqueous solutions and thus tune their fluorescence intensities. First, hydrophobic cores of conventional micelles may function as templates for the assembly of AIE fluorophores. Second, the synergic hydrophobic and electrostatic interactions will facilitate the aggregations of AIE fluorophores with appropriate ionic groups. In this Feature Article, we will give an account of the recent advances in the fluorescence modulation of tetraphenylethylene and silole fluorophores by ionic amphiphiles and their applications in bio/chemosensors.

Assembly of Neutral Tetraphenylethylene Analogues with the Aid of Ionic Amphiphile. Some of us reported the polymorphism-dependent emission for di(*p*-methoxyphenyl)-dibenzofulvene (**1**, Scheme 1).⁴⁵ Three solid-state emission

Scheme 1. Illustration of the Self-Assembly of **1 into Three Solid-State Emission Forms in the Absence and Presence of CTAB^a**



^aReproduced with permission from ref 46. Copyright Wiley-VCH.

forms with different emission colors were found for **1**; two crystalline forms are strongly emissive, whereas the amorphous solid is weakly fluorescent. Interestingly, the formation of three emission forms can be controlled with the aid of CTAB (cetyltrimethylammonium bromide).⁴⁶ As depicted in Figure 1,

the addition of **1** to water led to amorphous solids with weak orange emission in the absence of CTAB. However, in the presence of CTAB with a concentration lower than its CMC, yellow-green emissive microrods were formed. Apart from the yellow-green emissive microrods, blue emissive microrods were also observed when the concentration of CTAB used for the assembly of **1** reached 0.80 mM. More blue-emissive rods were formed by further increasing the concentration of CTAB, and only the blue-emissive microrods were generated when the CTAB concentration was higher than 1.20 mM. The controllable formation of three emission forms of **1** is interpreted as follows (Scheme 1): (i) Micelles of CTAB are formed at high concentration, and the alkyl chains are densely arranged. As a result, the space within the hydrophobic core is limited for molecules of **1**. Thus, molecules of **1** may take more twisting conformations because of the compact environment, and accordingly the π conjugation is weakened, leading to blue emission. (ii) In comparison, the alkyl chains of CTAB are less densely packed within the premicelles that are formed when the concentration of CTAB is low; as a result, the hydrophobic space that is accessible for molecules of **1** are relatively larger than those of the respective micelles. Accordingly, it is expected that molecules of **1** can adopt a less-twisted conformation, which is in agreement with the formation of yellow-green emissive microrods. (iii) In the absence of CTAB, molecules of **1** precipitate quickly, leading to the amorphous form. Within the amorphous state, molecules of **1** may become more planar with a higher degree of conjugation, and accordingly the emission spectrum is more red-shifted.

Alternatively, the aggregates of 1,2-diphenyl-1,2-di(*p*-tolyl)-ethene (**2**, Scheme 2), a neutral AIE fluorophore formed in water, can be disassembled in the presence of CTAB when the concentration of **2** is low.⁴⁷ Initially, the fluorescence of **2** was switched on, and its intensity decreased gradually by increasing the concentration of CTAB. Because the concentration of **2** was low, molecules might be well dispersed in the hydrophobic cores of micelles and thus internal rotations within **2** might not be

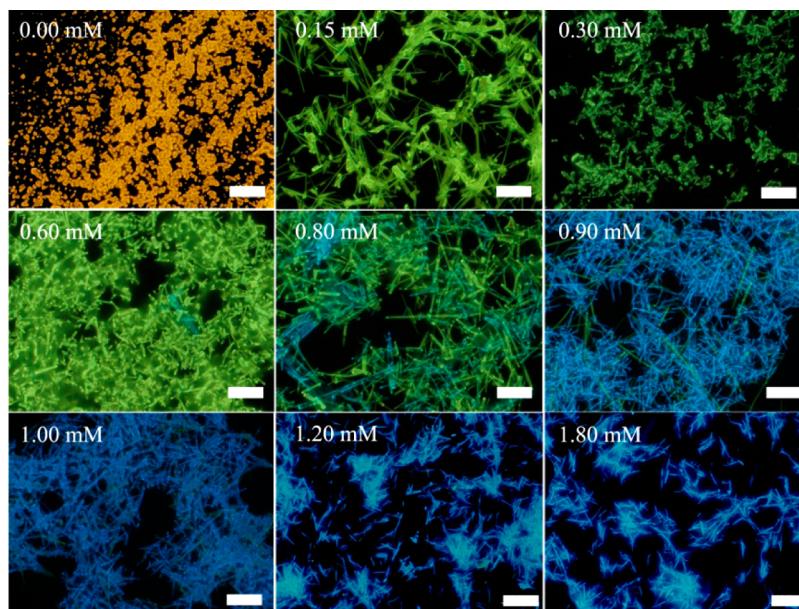
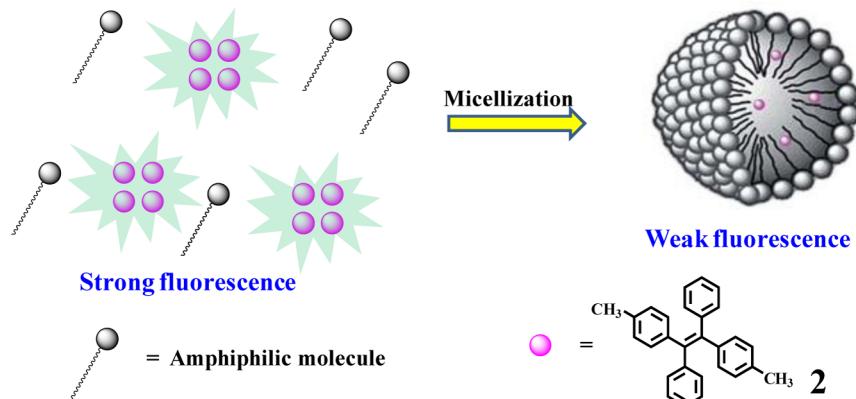


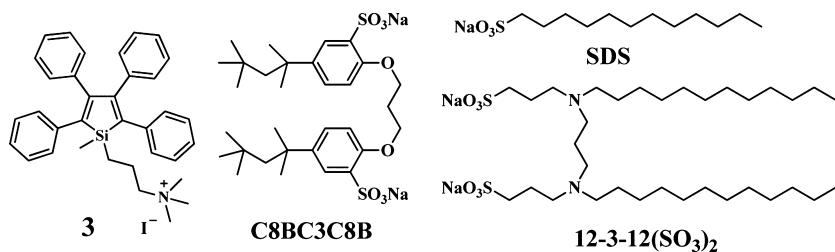
Figure 1. CLSM (confocal laser scanning microscopy) images of the self-assembled structures of **1** (2.0×10^{-4} M) in the presence of different concentrations of CTAB (0.00, 0.15, 0.30, 0.60, 0.80, 0.90, 1.00, 1.20, and 1.80 mM). The scale bar is 10 μ m. Reproduced with permission from ref 46. Copyright Wiley-VCH.

Scheme 2. Mechanism for the Detection of the CMCs Based on the Aggregation-Induced Emission (AIE) and the Chemical Structure of Compound 2^a

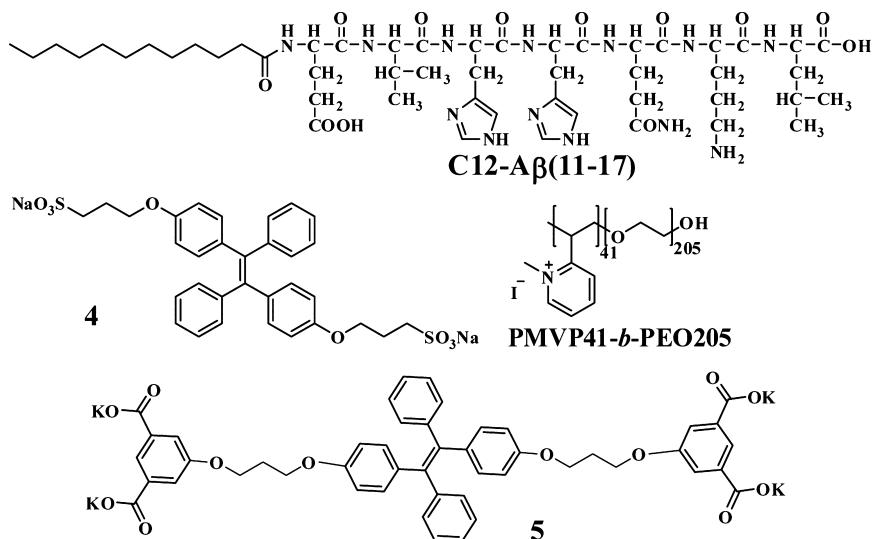


^aReproduced with permission from ref 47. Copyright Royal Society of Chemistry.

Scheme 3. Chemical Structures of Compound 3 and Related Amphiphiles



Scheme 4. Chemical Structures of Compounds 4, 5, C12–A β (11–17), and PMVP41-*b*-PEO205S

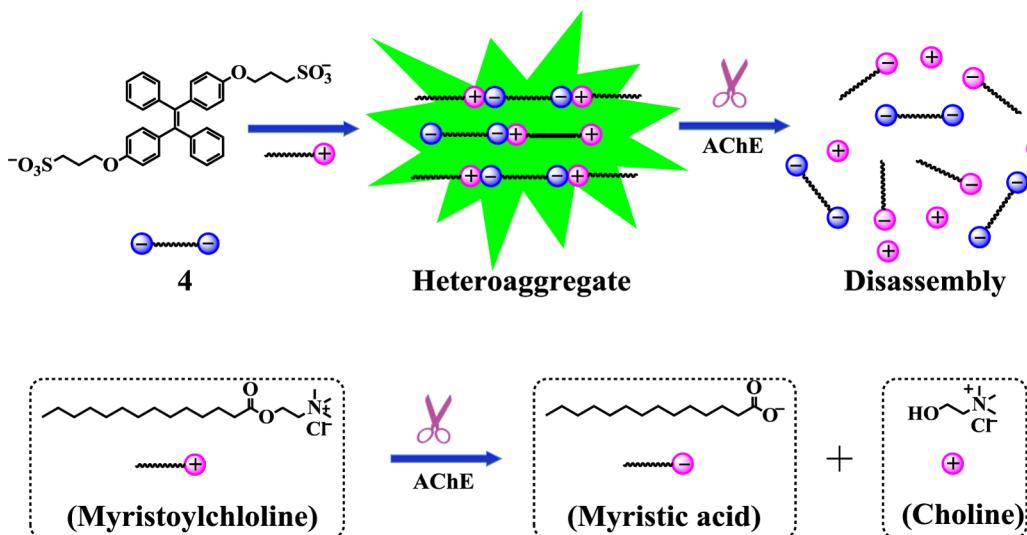


inhibited as illustrated in Scheme 2.⁴⁷ Consequently, the fluorescence of **2** became weak again after further addition of CTAB. Tang and coworkers successfully utilized **2** as a fluorescent probe to determine the CMCs of amphiphiles such as CTAB and even colored ones by taking advantage of the fluorescence variation of **2** after the addition of amphiphiles. In fact, the CMCs measured with **2** as the fluorescent probe agree well with those determined with other methods.

Aggregation of Ionic Tetraphenylethylenes and Silole Induced by Amphiphiles. Some of us reported the aggregation and fluorescence enhancement for ionic tetraphenylethylene and silole in the presence of amphiphiles with

oppositely charged units. Wang and coworkers studied the influences of concentration and the chemical structure of amphiphiles on the aggregations and fluorescence enhancements.⁴⁸ Compound 3 with an ammonium headgroup was found to be soluble in water, and as expected, it was rather weakly emissive in water. However, its fluorescence intensity started to increase after the addition of amphiphiles such as SDS shown in Scheme 3. This is owing to the formation of aggregates of 3 induced by the amphiphiles, which is supported by the DLS (dynamic light scattering) data analysis. Interestingly, the fluorescence intensity decreased by further increasing the concentrations of amphiphiles. More amphiphiles may lead to

Scheme 5. Molecular Design Rationale for AChE Activity Assay and Inhibitor Screening Based on Aggregation-Induced-Emission of Compound 4^a



^aReproduced with permission from ref 52.

the formation of more micelles or other assembled structures. As a result, molecules of 3 may be well dispersed into these micelles or assembly structures, and accordingly, internal rotations become effective again and the fluorescence of 3 is largely quenched.

It is interesting that the degree of fluorescence enhancement is affected by the chemical structures of amphiphiles. The fluorescence intensity of 3 was more significantly enhanced in the presence of the gemini amphiphile C8BC3C8B. This may be relevant to the structural feature of gemini amphiphiles that contain two charged headgroups and two hydrophobic alkyl chains. However, the fluorescence enhancement observed for 3 was relatively small in the presence of gemini amphiphile 12-3-12(SO₃)₂. Thus, more in-depth studies are required to understand the aggregation of charged AIE fluorophores in the presence of amphiphiles.

Co-aggregation of charged AIE fluorophore 4 (Scheme 4) with amphiphile-containing peptide headgroup C12-Aβ(11–17) was investigated.⁴⁹ It is known that the assemblies of peptide amphiphiles with fluorophores have been emerging as scaffolds that are very promising for nano/microscale biomaterials in tissue engineering, and they are potentially useful in regenerative medicine and controlled drug release. However, the emissions would often be weakened largely if normal fluorophore was adopted because of the ACQ effect. C12-Aβ(11–17) was yielded by coupling dodecanoic acid with a fragment of amyloid β-peptide through an amide bond. C12-Aβ(11–17) was self-assembled into rodlike or tapelike fibrils and twisted ribbons at pH 3.0 and 10.0, respectively. The effects of pH and the concentration of C12-Aβ(11–17) on the coassembly structure and fluorescence modulation were studied. At a low concentration of C12-Aβ(11–17), the coassembly of C12-Aβ(11–17) and 4 yielded shorter fluorescent nanofibrils with lengths of less than 5 μm when the pH of the solution was in the range of 4.0–7.0. No nanofibrils were detected without the addition of C12-Aβ(11–17) under the same conditions. In comparison, long fluorescent nanofibrils were formed by the aggregation of C12-Aβ(11–17) and 4 by increasing the concentration of C12-Aβ(11–17) to 1.0 mM. The studies also reveal that the

assembled structures and fluorescence enhancements were influenced by the pH values of the solutions. Twisted nanotapes that were strongly fluorescent were observed at low pH, whereas nanoribbons that were weakly emissive were formed at high pH. This is probably due to the fact that the peptide group in C12-Aβ(11–17) becomes less negatively charged at high pH and as a result the electrostatic interactions between C12-Aβ(11–17) and 4 are weakened.

Huang and coworkers have recently reported the multiple-component assembly of the TPE derivative (5, Scheme 4), metal ions, and the polyelectrolyte.⁵⁰ The coordination of 5 with transition-metal ions (e.g., Ni²⁺ and Zn²⁺) yielded the respective coordination polymers that slowly self-assembled into polydisperse flat cocoonlike sheets. On the basis of the observation that these cocoonlike sheets were weakly emissive, it can be inferred that molecules of 5 were loosely packed within these cocoonlike sheets. However, as soon as the polyelectrolyte (PMVP41-*b*-PEO205) was added at charge stoichiometry, a significant fluorescence enhancement was detected. TEM studies indicated that the polydisperse cocoons immediately transformed into ribbonlike structures with a length greater than 1 μm.

Bio/Chemosensors Based on the Aggregation/Deaggregation of AIE Fluorophores Tuned by Ionic Amphiphiles. As discussed above, ionic amphiphiles can interact with oppositely charged AIE molecules through electrostatic and hydrophobic interactions, leading to the aggregation of AIE fluorophores and thus a fluorescence enhancement. Thus, by properly choosing the amphiphilic molecules, which can be either good substrates of certain analytes (enzymes or chemicals) or can be formed *in situ* in the presence of the analytes (enzymes or chemicals), to manipulate the respective aggregation and deaggregation of AIE fluorophores, new bio/chemosensors were established.

Label-Free Assay for Acetylcholinesterase (AChE). Acetylcholinesterase (AChE) catalyzes the hydrolysis of acetylcholine, which is a central neurotransmitter, and thus AChE plays an important role in the regulation of the neural response system. In fact, Alzheimer's disease (AD), which is a common type of

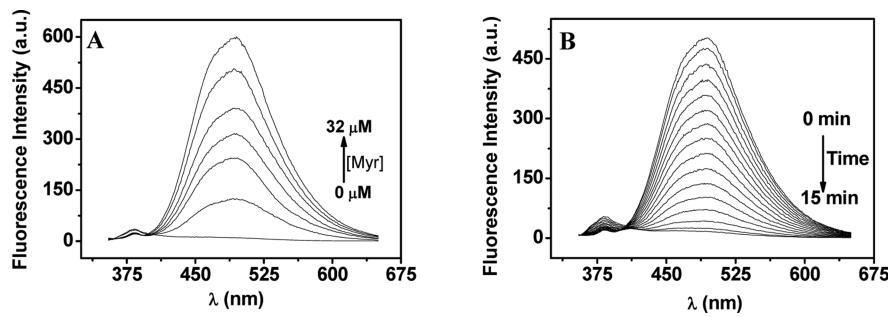
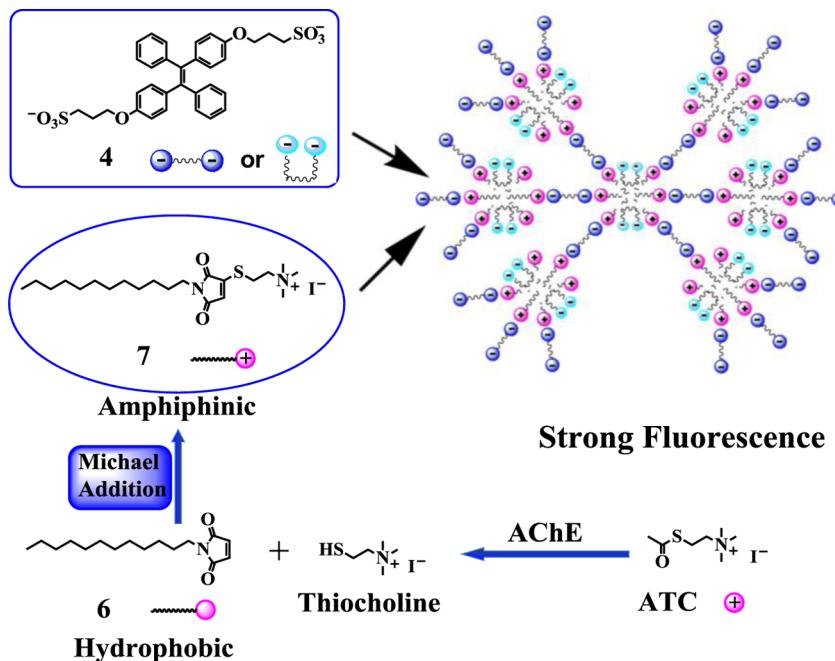


Figure 2. (A) Fluorescence spectra of **4** (20 μM in PBS [10 mM buffer solution, pH 8.0]) upon addition of different amounts of myristoylcholine (from 0 to 32 μM). (B) Fluorescence spectra of the ensemble of **4** (20 μM in PBS [10 mM buffer solution, pH 8.0]) and myristoylcholine (25 μM) after incubation with AChE (0.5 U/mL) at 25 $^{\circ}\text{C}$ for different periods. Reproduced with permission from ref 52.

Scheme 6. Molecular Design Rationale for AChE Activity Assay and Inhibitor Screening on the Basis of the Aggregation-Induced Emission Property of **4^a**



^aReproduced with permission from ref 55.

dementia in elderly people, is relevant to a low level of acetylcholine in the brain. Current clinical treatment of AD is mainly based on the inhibitors of AChE.⁵¹ Therefore, sensitive and selective assay methods for AChE activity and its inhibitor screening are highly desirable.

Various spectroscopic methods were invented for AChE assay. However, drawbacks are found for these assay methods, and convenient, fast, and continuous analytical assays are still demanding. Some of us developed fluorescent assays by manipulating the aggregation and deaggregation of TPE with negatively charged groups in the presence of amphiphiles with positively charged headgroups.⁵² As anticipated, myristoylcholine can induce the aggregation of **4** (Scheme 5) and thus turn on the fluorescence of **4** as depicted in Figure 2A, where the fluorescence spectra of **4** in the presence of different amounts of myristoylcholine are displayed. Obviously, the fluorescence of **4** was switched on upon addition of myristoylcholine, and the fluorescence intensity increased gradually after the addition of more myristoylcholine. As discussed above, this is owing to the aggregation of **4** induced by myristoylcholine.

However, the fluorescence of the ensemble of myristoylcholine and **4** decreased gradually after acetylcholinesterase (AChE) was added to the ensemble (Figure 2B). This is owing to the hydrolysis of myristoylcholine to myristic acid and choline after incubation with AChE; consequently, the fluorescent aggregates were disassembled (Scheme 5). Therefore, a label-free fluorometric assay for AChE was established by using the ensemble of myristoylcholine and **4**. Moreover, this ensemble was also successfully utilized to screen the inhibitors of AChE. 9-Amino-1,2,3,4-tetrahydroacridine (tacrine) as a typical inhibitor for AChE⁵³ was chosen as an example to demonstrate the usefulness of **4** in AChE inhibitor screening. As anticipated, the extent of the fluorescence decrease for the ensemble of **4** and myristoylcholine becomes small after incubation with AChE in the presence of tacrine because it can inhibit the AChE activity. The effectiveness of the inhibitor could be evaluated by measuring the half-maximal inhibitory concentration (IC_{50}).⁵⁴ Using the ensemble of **4** and myristoylcholine, it was estimated that the IC_{50} of tacrine toward AChE was 159 nM, being close to that obtained with commonly used Ellman's reagent ($\text{IC}_{50} = 108$

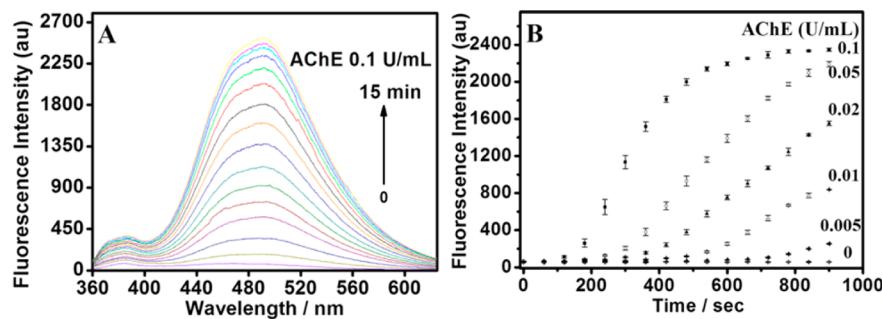
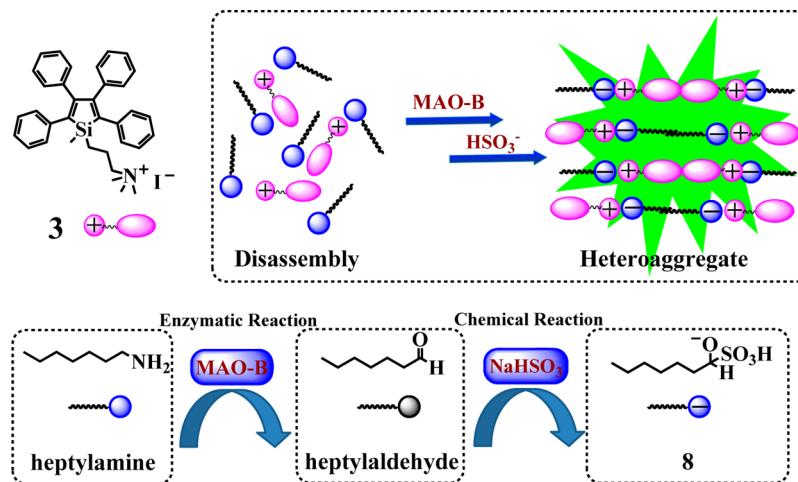


Figure 3. (A) Fluorescence spectra of **4** ($20 \mu\text{M}$ in HEPES (10 mM) buffer solution, pH 7.35) containing compound **6** ($30 \mu\text{M}$) and ATC ($30 \mu\text{M}$) after incubation with AChE (0.1 U/mL) for different periods at room temperature. (B) Variation of the fluorescence intensity at 490 nm vs the reaction time for the ensemble of compounds **4** ($20 \mu\text{M}$ in HEPES (10 mM) buffer solution, pH 7.35), **6** ($30 \mu\text{M}$), and ATC ($30 \mu\text{M}$) after incubation with different concentrations of AChE ($0, 0.005, 0.01, 0.02, 0.05, 0.1 \text{ U/mL}$). Reproduced with permission from ref 55.

Scheme 7. Molecular Design Rationale for Monoamine Oxidase Activity Assay and Inhibitor Screening by Manipulating the Aggregation and Deaggregation of Silole **3^a**



^aReproduced with permission from ref 58. Copyright Royal Society of Chemistry.

nM).⁵³ Thus, a new fluorescent assay for AChE and the inhibitor screening was established with commercially available myristoylcholine and the easily accessible TPE compound (**4**).

Alternatively, the ensemble of acetylthiocholine (ATC) and maleimide **6** as well as **4** as a fluorescence reporter was utilized to establish a fluorescence “turn-on” assay for AChE.⁵⁵ As shown in Scheme 6, ATC, which is a good substrate for AChE, can be hydrolyzed into thiocholine upon addition of AChE. The Michael addition reaction of thiocholine with the maleimide group in **6** yields an amphiphilic **7**, which is expected to be able to induce the aggregation of **4** and thus turn on the fluorescence. Figure 3A shows the fluorescence spectra of the ensemble after incubation with AChE. Obviously, the fluorescence increased more significantly by enhancing the concentration of AChE in the ensemble. The fluorescence spectra of the ensemble were also measured after incubation with different concentrations of AChE for different times. As shown in Figure 3B, the fluorescence intensity of the ensemble was largely enhanced after the ensemble was incubated with a high concentration of AChE. This is understandable because the presence of more AChE can induce the formation of more of amphiphile **7**, which will yield the aggregation of compound **4** and thus lead to a large fluorescence enhancement. Notably, AChE with a concentration as low as 0.005 U/mL can be analyzed with the ensemble of acetylthiocholine (ATC), maleimide **6**, and **4**.

The ensemble was also successfully employed for screening the inhibitors of AChE. For this purpose, the fluorescence spectra of the ensemble were recorded by incubating with both AChE and its inhibitors. In this way, the corresponding IC_{50} values were determined. For instance, IC_{50} of neostigmine, a typical inhibitor of AChE, was estimated to be 50.3 nM , being close to that obtained with other AChE assay methods. Therefore, the ensemble of compounds **4**, **6**, and ATC can be used not only for the AChE activity assay but also for the inhibitor screening by taking advantage of the AIE feature of TPE compounds.

Fluorometric Turn-On Assay for Monoamine Oxidase B. Monoamine oxidase B (MAO-B) is the predominant isoform of MAOs, which catalyze the aerobic oxidative deamination of various amine substrates to generate aldehydes, amines, and H_2O_2 . MAO-B is relevant to age-related neurodegenerative sickness including Parkinson’s and Alzheimer’s diseases.⁵⁶ MAO-B and its analogues become promising therapeutic targets for a variety of brain disorders. Moreover, inhibitors of MAO-B are currently being investigated as potential drugs for the clinical treatment of Parkinson’s and Alzheimer’s diseases and cerebral ischemia during strokes.⁵⁷ A number of sensitive and selective sensors were developed to monitor the activity of MAO-B and for inhibitor screening. Some of us reported a new direct continuous fluorometric turn-on assay for MAO-B with silole

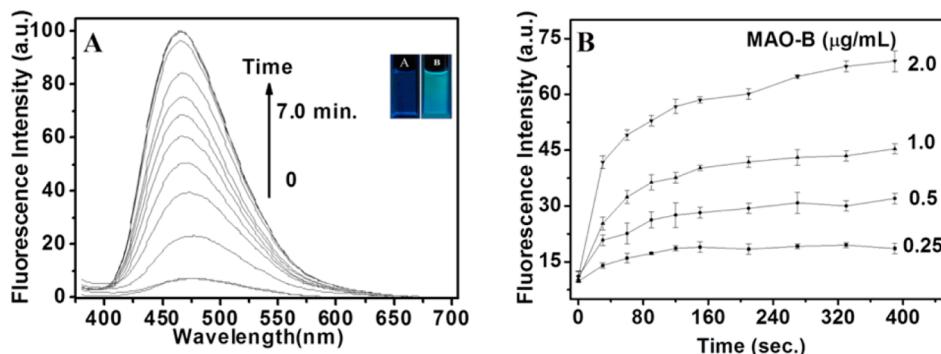


Figure 4. (A) Fluorescence spectra of **3** (7.5×10^{-5} M) containing heptylamine (2.0×10^{-4} M) and NaHSO₃ (1.0×10^{-4} M) in a mixture of HEPES buffer (10 mM, pH 7.4) and THF (200:1, v/v) after incubation with MAO-B (2.2 µg/mL) for different times at room temperature; the inset displays photographs of the corresponding solutions of silole **3** (7.5×10^{-5} M), heptylamine (2.0×10^{-4} M), and NaHSO₃ (1.0×10^{-4} M) in the mixture of HEPES buffer (10 mM, pH 7.4) and THF (200:1, v/v) in the absence (A) and presence of (B) MAO-B (2.2 µg/mL) after incubation for 7.0 min under UV light (365 nm) illumination. (B) Variation of the fluorescence intensity at 467 nm vs the reaction time for the ensemble of **3** (7.5×10^{-5} M), heptylamine (2.0×10^{-4} M), and NaHSO₃ (1.0×10^{-4} M) in a mixture of HEPES buffer (10 mM, pH 7.4) and THF (200:1, v/v) after incubation with different concentrations of MAO-B (0.25, 0.5, 1, 2.0 µg/mL); the excitation wavelength was 370 nm. Reproduced with permission from ref 58. Copyright Royal Society of Chemistry.

compounds that exhibit aggregation-induced emission (AIE) behavior.⁵⁸

This fluorometric assay for MAO-B was based on the ensemble of heptylamine, NaHSO₃, and silole derivative **3**. As shown in Scheme 7, heptylamine can be oxidized to the corresponding heptylaldehyde by MAO-B, and heptylaldehyde can be easily converted to amphiphile **8** after further reaction with HSO₃⁻. This in situ generated amphiphile is able to induce the aggregation of silole **3** and turn on the fluorescence. In this way, a fluorometric assay for MAO-B can be constructed with the ensemble of heptylamine, NaHSO₃, and silole derivative **3**.

As depicted in Figure 4A, the ensemble of heptylamine, NaHSO₃, and silole derivative **3** in buffer solution exhibited rather weak fluorescence. However, the fluorescence intensity of the ensemble was gradually enhanced after incubation with MAO-B for different times (Figure 4A). In fact, such fluorescence enhancement for the ensemble solution after the addition of MAO-B was detectable by the naked eye when illuminating the buffer solution with UV light (365 nm) as shown in the inset of Figure 4A. The DLS data confirmed the formation of large aggregates within the ensemble solution.

The fluorescence spectra of the ensemble were recorded after incubating with different concentrations of MAO-B for different times. As depicted in Figure 4B, a large degree of fluorescence enhancement was observed for the ensemble containing a high concentration of MAO-B. This can be explained by considering the fact that the presence of more MAO-B would lead to the generation of more heptylaldehyde, which would react with HSO₃⁻ to yield amphiphile **8** that would induce the aggregation of silole **3** and the fluorescence enhancement. Therefore, the ensemble of silole **3**, heptylamine, and HSO₃⁻ can be employed for the MAO-B assay, and MAO-B with a concentration as low as 0.25 µg/mL can be analyzed with this new assay.

Similarly, the ensemble of silole **3**, heptylamine, and NaHSO₃ can be utilized to screen the inhibitors of MAO-B. Pargyline-HCl as a typical inhibitor of MAO-B was chosen to demonstrate the application of the ensemble to screen the MAO-B inhibitors. The fluorescence spectra of the ensemble containing different concentrations of pargyline-HCl were recorded after incubation with MAO-B for different times. On the basis of the variation of the fluorescence intensity of the ensemble versus the

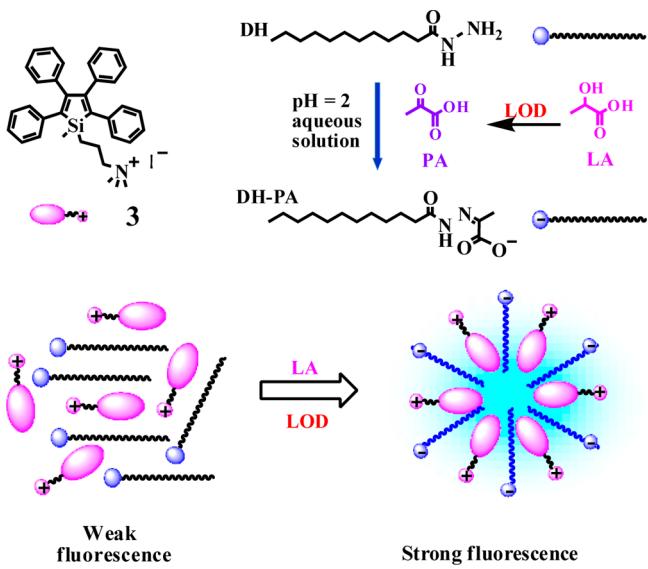
concentration of the inhibitor, the IC₅₀ value of pargyline-HCl toward MAO-B was estimated to be 24.3 mM.

Fluorometric Detection of Small Molecules and Hazardous Analytes. Apart from the enzymatic activity assay, AIE fluorophores were also utilized for the detection of small molecules, ions, and hazardous analytes on the basis of the aggregation and deaggregation mechanism.^{24–28,59,60} For instance, some of us devised a fluorometric turn-on detection of L-lactic acid by using the cascade enzymatic and chemical reactions as well as the usual fluorescence behavior of silole.⁶¹ Note that L-lactic acid can serve as an aid in diagnosing heart disease, in exercise physiology, and in neonatology studies. The level of L-lactic acid is regarded as an indicator of the mentative process in the food industry and is relevant to the freshness, stability, and storage quality of food products such as wine, cider, beer, and milk.⁶²

As shown in Scheme 8, L-lactic acid (LA) can be oxidized to pyruvic acid by lactate oxidase (LOD). Pyruvic acid is able to react with dodecanoic hydrazine (DH) to form the respective Schiff base, an amphiphilic compound with a carboxylic acid group (DH-PA). This amphiphilic compound is expected to form coaggregates with silole **3** via electrostatic and hydrophobic interactions in aqueous solution; accordingly, the emission of silole **3** is tuned on. Therefore, the ensemble of LOD, dodecanoic hydrazine, and silole **3** can be utilized for the fluorescence detection of L-lactic acid.

As shown in Figure 5A, the fluorescence intensity of silole **3** was enhanced after the incubation of LOD and dodecanoic hydrazine with different amounts of L-lactic acid. Moreover, the fluorescence intensity increased gradually by increasing the amounts of L-lactic acid. Indeed, such a fluorescence enhancement detectable with the naked eye as ensemble solutions without and with the addition of L-lactic acid was almost nonemissive and blue-emissive, respectively, under UV (365 nm) light illumination (inset of Figure 5A). Figure 5B displays a plot of the relative fluorescence intensity (I/I_0) of silole **3** versus the concentration of L-lactic acid. To our delight, the fluorescence intensity at 480 nm for silole **3** increased almost linearly with the concentration of L-lactic acid in the range of 0–40 µM as shown in the inset of Figure 5B. Consequently, the detection limit of L-lactic acid was estimated to be 9.2 µM ($n = 11$ and $S/N = 3$). Furthermore, interference from saccharides, amino acids, and

Scheme 8. Schematic Illustration of the Design Rationale for the Fluorescence Turn-On Detection of L-Lactic Acid on the Basis of the AIE Feature of Silole 3^a



^aReproduced with permission from ref 61.

ascorbic acid can be neglected in the detection of L-lactic acid on the basis of the aggregation and deaggregation of silole 3.

A fluorescence turn-on detection of cyanide in aqueous solution was also reported by manipulating the aggregation and deaggregation of silole 3.⁶³ Cyanide is one of the most toxic anions and is harmful to human health and the environment.⁶⁴ Thus, fast, convenient detection of cyanide is highly desirable. The reported sensors for cyanide need to be improved further with respect to selectivity, particularly in the presence of fluoride or acetate. Some sensors for cyanide could not work well in aqueous solution.

Scheme 9 shows the molecular design rationale for sensing cyanide with silole 3. The reaction of cyanide with the trifluoroacetylaminogroup in compound 9 yields an amphiphilic compound with a negative headgroup, which is expected to be able to induce the aggregation of silole 3 leading to fluorescence enhancement. In this way, a fluorescence turn-on detection of

cyanide in aqueous solution can be realized with the ensemble of silole 3 and compound 9.

The mixed solution of silole 3 and compound 9 exhibits rather weak emission as shown in Figure 6A. However, the fluorescence intensity of the solution increased gradually upon addition of different amounts of NaCN (Figure 6A). This is clearly owing to the formation of aggregates of silole 3 induced by the generated amphiphile. Figure 6B displays the variation of the relative fluorescence intensity versus the concentration of cyanide. The detection limit for cyanide with the ensemble of silole 3 and compound 9 under this condition was estimated to be 7.74 μM , being lower than concentrations of cyanide in the blood of fire victims. Possible interference from other anions (OAc^- , Br^- , Cl^- , F^- , H_2PO_4^- , HSO_4^- , N_3^- , and NO_3^-) was examined, and the results revealed that these anions hardly affected the detection of cyanide with the ensemble. This may be interpretable by considering the fact that cyanide is more nucleophilically reactive than other anions such as fluoride and acetate in aqueous solution.

CONCLUSIONS AND OUTLOOK

The past decades have witnessed increasing interest in studying AIE fluorophores and exploring new applications in different areas. In this Feature Article, we have summarized the recent advances in the fluorescence modulation of tetraphenylethylene and silole fluorophores by manipulating the respective aggregation/deaggregation with amphiphiles. These include (i) the assembly of neutral tetraphenylethylene analogues with the aid of an ionic amphiphile, (ii) the aggregation of ionic tetraphenylethylene and silole induced by amphiphiles, and (iii) bio/chemosensors based on aggregation/deaggregation, which is relevant to the inhibition of internal rotations of AIE fluorophores, as tuned by ionic amphiphiles. These reveal that amphiphiles can aid the aggregation and assembly of tetraphenylethylene and silole fluorophores to form strongly emissive self-assembled structures. By manipulating the transformation of polar headgroups of the respective amphiphiles, the aggregation and deaggregation of tetraphenylethylene and silole fluorophores can be tuned and thus the fluorescence of the ensembles can be modulated. By making use of these ensembles, bio/chemosensors are constructed by taking advantage of the AIE feature of tetraphenylethylene and silole fluorophores. In comparison to conventional sensors, these bio/chemosensors have the

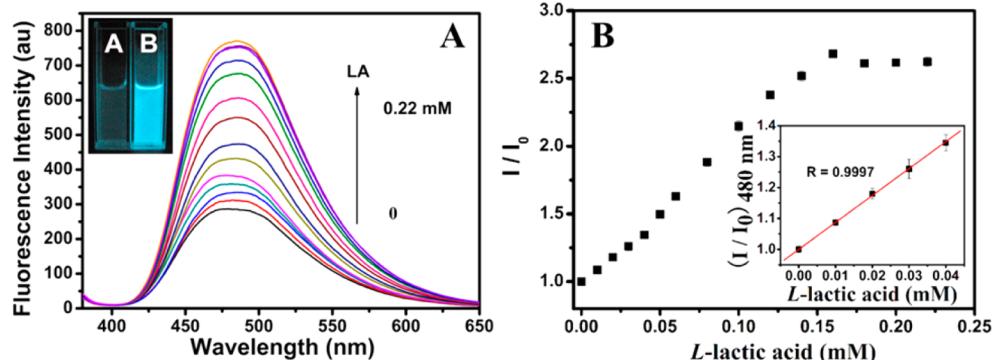
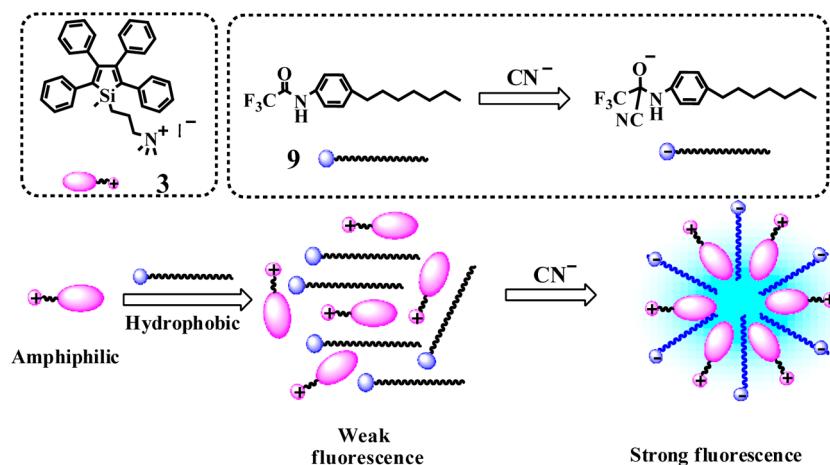


Figure 5. (A) Fluorescence spectra of silole 3 (50 μM) containing DH (0.3 mM) and LOD (0.25 U/mL) in the presence of different amounts of L-lactic acid (0–0.22 mM); the inset displays photographs of the corresponding ensemble solutions without (A) and with (B) the addition of L-lactic acid (0.22 mM) under UV light (365 nm) illumination. **(B)** Plot of the fluorescence intensity ratio (I/I_0 at 480 nm) vs the concentration of L-lactic acid; I_0 represents the fluorescence intensity of silole 3 (50 μM) in the presence of DH (0.3 mM) and LOD (0.25 U/mL). Reproduced with permission from ref 61.

Scheme 9. Schematic Illustration of the Molecular Design Rationale for the Fluorescence Turn-On Detection of Cyanide on the Basis of the AIE Feature of Silole 3^a



^aReproduced with permission from ref 63.

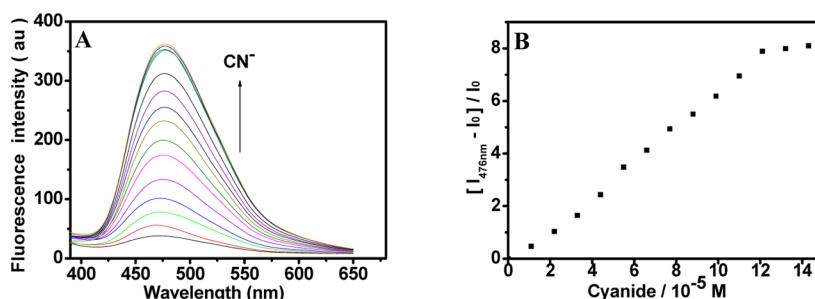


Figure 6. (A) Fluorescence spectra ($\lambda_{\text{ex}} = 370 \text{ nm}$) of silole 3 ($7.5 \times 10^{-5} \text{ M}$) in the presence of compound 9 ($4.0 \times 10^{-4} \text{ M}$) in DMSO/H₂O (1/75, v/v) after the addition of different amounts of sodium cyanide (from 0 to $1.4 \times 10^{-4} \text{ M}$) at room temperature. (B) Plot of $([I_{476} - I_0]/I_0)$, where I_{476} and I_0 refer to the fluorescence intensity of silole 3 at 476 nm in the presence and absence of cyanide, respectively, vs the concentration of cyanide. Reproduced with permission from ref 63.

following features: (i) they are constructed by manipulating the aggregation/deaggregation of tetraphenylethylene and silole fluorophores to modulate their emissions, which are different from those based on PET (photoinduced electron transfer) or ICT (intramolecular charge transfer) mechanisms; (ii) they are mostly operated in aqueous solutions in fluorescence turn-on mode; (iii) no labeling is necessary; and (iv) tetraphenylethylene and silole fluorophores can be modified easily and other components of the sensing ensembles are also easily accessible. These bio/chemosensors based on the AIE fluorophores may be comparable to those based on the aggregation and deaggregation of gold nanoparticles, which can induce the variation of plasmon absorption.^{65–69}

The following aspects deserve further investigations for this emerging area: (i) because the emissions of tetraphenylethylene/silole and their analogues are highly sensitive to aggregation/deaggregation, it is interesting to employ these AIE fluorophores as reporters to study the respective aggregation/deaggregation processes in the presence of amphiphiles; (ii) it is interesting to assemble tetraphenylethylene/silole fluorophores with amphiphiles into nanoparticles, which can be postfunctionalized by choosing the appropriate amphiphiles to form stable fluorescent particles that are promising for biological applications; and (iii) the assembly of tetraphenylethylene/silole fluorophores with amphiphiles that entail either peptides or nucleic acids or oligosaccharides as polar headgroups is expected to generate emissive assembled structures that can be specifically responsive

to either certain biomolecules or enzymes. This may enable us to construct new assays for the selective and sensitive detection of certain biomolecules and new agents for targeted bioimaging.

AUTHOR INFORMATION

Corresponding Author

*E-mail: dqzhang@iccas.ac.cn. Tel: +861062639355. Fax: +8610 62569349.

Notes

The authors declare no competing financial interest.

Biographies



Guanxin Zhang received his M.Sc. in chemistry from Beijing Normal University in 2002 and Ph.D. in organic chemistry from ICCAS in 2005 under the supervision of Prof. Deqing Zhang and Prof. Daoben Zhu. He is now an associate professor at the Institute. His research interests include the design and synthesis of organic functional molecules towards chemo/biosensors and optomaterials.



Fang Hu received his B.S. degree from the College of Chemistry and Molecular Sciences of Wuhan University in 2010. He is currently a Ph.D. candidate at ICCAS under the supervision of Prof. Deqing Zhang. His research interests are the design and synthesis of organic luminescent materials.



Deqing Zhang received his Ph.D. from Ruprecht-Karls University Heidelberg in 1996 under the supervision of Prof. Dr. H. A. Staab. He is currently a research professor at the Institute of Chemistry, Chinese Academy of Sciences in Beijing, China. His research interests include the development of external stimuli-responsive molecular systems for molecular switches, logic gates, and chemo/biosensors. He is also interested in the design and synthesis of organic conjugated molecules toward functional assemblies and materials. He has published more than 240 papers in international peer-reviewed journals, which have been cited more than 6400 times. He serves as an editorial advisory board member for several scientific journals, including *ACS Applied Materials & Interfaces*, *Advanced Functional Materials*, and *Advanced Materials*. He is one of three cochairmen of the editorial board of *Asian Journal of Organic Chemistry*.

■ ACKNOWLEDGMENTS

The present research was financially supported by the Strategic Priority Research Program of the Chinese Academy of Sciences (grant no. XDB12010100), NSFC, and the State Key Basic Research Program.

■ REFERENCES

- (1) Thomas, S. W.; Joly, G. D.; Swager, T. M. Chemical sensors based on amplifying fluorescent conjugated polymers. *Chem. Rev.* **2007**, *107*, 1339–1386.
- (2) Wu, J.; Liu, W.; Ge, J.; Zhang, H.; Wang, P. New sensing mechanisms for design of fluorescent chemosensors emerging in recent years. *Chem. Soc. Rev.* **2011**, *40*, 3483–3495.
- (3) Vendrell, M.; Zhai, D.; Er, J.; Chang, Y. Combinatorial strategies in fluorescent probe development. *Chem. Rev.* **2012**, *112*, 4391–4420.
- (4) Buckley, A., Ed. *Organic Light-Emitting Diodes (OLEDs): Materials, Devices and Applications*; Woodhead Publishing: Oxford, 2013.
- (5) Forget, S.; Chenais, S., Eds. *Organic Solid-State Lasers*; Springer: New York, 2013.
- (6) Friend, R.; Gymer, R.; Holmes, A.; Burroughes, J.; Marks, R.; Taliani, C.; Bradley, D.; Dos Santos, D.; Brédas, J.; Lögdlund, M.; Salaneck, W. Electroluminescence in Conjugated Polymers. *Nature* **1999**, *397*, 121–128.
- (7) Jenekhe, S.; Osaheni, J. Excimers and exciplexes of conjugated polymers. *Science* **1994**, *265*, 765–768.
- (8) Spano, F. The spectral signatures of frenkel polarons in *H*- and *J*-aggregates. *Acc. Chem. Res.* **2010**, *43*, 429–439.
- (9) Hecht, S.; Fréchet, J. Dendritic encapsulation of function: Application nature's site isolation principle from biomimetic to materials science. *Angew. Chem., Int. Ed.* **2001**, *40*, 74–91.
- (10) Nguyen, B.; Gautrot, J.; Ji, C.; Brunner, P.; Nguyen, M.; Zhu, X. Enhancing the photoluminescence intensity of conjugated polycationic polymers by using quantum dots as antiaggregation reagents. *Langmuir* **2006**, *22*, 4799–4803.
- (11) Wurthner, F.; Stepanenko, V.; Sautter, A. Rigid-rod metallocsupramolecular polymers of dendronized diazadibenzoperylene dyes. *Angew. Chem., Int. Ed.* **2006**, *45*, 1939–1942.
- (12) Babu, S.; Praveen, V.; Kartha, K.; Mahesh, S.; Ajayaghosh, A. Effect of the bulkiness of the end functional amide groups on the optical, gelation, and morphological properties of oligo(*p*-phenylenevinylene) π -gelators. *Chem.—Asian J.* **2014**, *9*, 1830–1840.
- (13) Luo, J.; Xie, Z.; Lam, J.; Cheng, L.; Chen, H.; Qiu, C.; Kwok, H.; Zhan, X.; Liu, Y.; Zhu, D.; Tang, B. Aggregation-induced emission of 1-methyl-1,2,3,4,5-pentaphenylsilole. *Chem. Commun.* **2001**, 1740–1741.
- (14) Qin, A.; Tang, B., Eds. *Aggregation-Induced Emission: Fundamentals*; John Wiley and Sons: Chichester, West Sussex, U.K., 2014.
- (15) An, B.; Gierschner, J.; Park, S. π -Conjugated cyanostilbenederivatives: a unique self-assembly motif for molecular nanostructures with enhanced emission and transport. *Acc. Chem. Res.* **2012**, *45*, 544–554.
- (16) An, B.; Lee, D.; Lee, J.; Park, Y.; Song, H.; Park, S. Strongly fluorescent organogel system comprising fibrillar self-assembly of a trifluoromethyl-based cyanostilbene derivative. *J. Am. Chem. Soc.* **2004**, *126*, 10232–10233.
- (17) Yu, G.; Yin, S.; Liu, Y.; Chen, J.; Xu, X.; Sun, X.; Ma, D.; Zhan, X.; Peng, Q.; Shuai, Z.; Tang, B.; Zhu, D.; Fang, W.; Luo, Y. Structures, electronic states, photoluminescence, and carrier transport properties of 1,1-disubstituted 2,3,4,5-tetraphenylsiloles. *J. Am. Chem. Soc.* **2005**, *127*, 6336–6346.
- (18) Zhao, Z.; Lam, J.; Tang, B. Tetraphenylethene: A versatile AIE building block for the construction of efficient luminescent materials for organic light-emitting diodes. *J. Mater. Chem.* **2012**, *22*, 23726–23740.
- (19) Wang, M.; Zhang, G.; Zhang, D.; Zhu, D.; Tang, B. Fluorescent bio/chemosensors based on silole and tetraphenylethene luminogens with aggregation-induced emission feature. *J. Mater. Chem.* **2010**, *20*, 1858–1867.
- (20) Hong, Y.; Lam, J.; Tang, B. Aggregation-induced emission. *Chem. Soc. Rev.* **2011**, *40*, 5361–5388.
- (21) De Silva, A.; Gunaratne, H.; Gunnlaugsson, T.; Huxley, A.; McCoy, C.; Rademacher, J.; Rice, T. Signaling recognition events with fluorescent sensors and switches. *Chem. Rev.* **1997**, *97*, 1515–1566.
- (22) Martínez-Máñez, R.; Sancenón, F. Fluorogenic and chromogenic chemosensors and reagents for anions. *Chem. Rev.* **2003**, *103*, 4419–4476.

- (23) Ding, D.; Li, K.; Liu, B.; Tang, B. Bioprobe based on AIE fluorogens. *Acc. Chem. Res.* **2013**, *46*, 2441–2453.
- (24) Toal, S. J.; Jones, K. A.; Magde, D.; Troglar, W. C. Luminescent silole nanoparticles as chemoselective sensors for Cr(VI). *J. Am. Chem. Soc.* **2005**, *127*, 11661–11665.
- (25) Liu, Y.; Deng, C.; Tang, L.; Qin, A.; Hu, R.; Sun, J.; Tang, B. Specific detection of D-glucose by a tetraphenylethylene-based fluorescent sensor. *J. Am. Chem. Soc.* **2011**, *133*, 660–663.
- (26) Ning, Z.; Chen, Z.; Zhang, Q.; Yan, Y.; Qian, S.; Cao, Y.; Tian, H. Aggregation-induced emission (AIE)-active starburst triarylamine fluorophores as potential non-doped red emitters for organic light-emitting diodes and Cl₂ gas chemodosimeter. *Adv. Mater.* **2007**, *17*, 3799–3807.
- (27) Li, D.; Liu, J.; Kwok, R.; Liang, Z.; Tang, B.; Yu, J. Supersensitive detection of explosives by recyclable AIE luminogen-functionalized mesoporous materials. *Chem. Commun.* **2012**, *48*, 7167–7169.
- (28) Liu, Z.; Xue, W.; Cai, Z.; Zhang, G.; Zhang, D. A facile and convenient fluorescence detection of gamma-ray radiation based on the aggregation-induced emission. *J. Mater. Chem.* **2011**, *21*, 14487–14491.
- (29) Song, P.; Chen, X.; Xiang, Y.; Huang, L.; Zhou, Z.; Wei, R.; Tong, A. A ratiometric fluorescent pH probe based on aggregation-induced emission enhancement and its application in live-cell imaging. *J. Mater. Chem.* **2011**, *21*, 13470–13475.
- (30) Wang, M.; Zhang, D.; Zhang, G.; Zhu, D. The convenient fluorescence turn-on detection of heparin with a silole derivative featuring an ammonium group. *Chem. Commun.* **2008**, 4469–4471.
- (31) Hong, Y.; Feng, C.; Yu, Y.; Liu, J.; Lam, J.; Luo, K.; Tang, B. Quantitation, visualization, and monitoring of conformational transitions of human serum albumin by a tetraphenylethylene derivative with aggregation-induced emission characteristics. *Anal. Chem.* **2010**, *82*, 7035–7043.
- (32) Wang, M.; Zhang, D.; Zhang, G.; Tang, Y.; Wang, S.; Zhu, D. Fluorescence turn-on detection of DNA and label-free fluorescence nuclelease assay based on the aggregation-induced emission of silole. *Anal. Chem.* **2008**, *80*, 6443–6448.
- (33) Hong, Y.; Meng, L.; Chen, S.; Leung, C.; Da, L.; Faisal, M.; Silva, D.; Liu, J.; Lam, J.; Huang, X.; Tang, B. Monitoring and inhibition of insulin fibrillation by a small organic fluorogen with aggregation-induced emission characteristics. *J. Am. Chem. Soc.* **2011**, *134*, 1680–1689.
- (34) Nakamura, M.; Sanji, T.; Tanaka, M. Fluorometric sensing of biogenic amines with aggregation-induced emission-active tetraphenylethenes. *Chem.—Eur. J.* **2011**, *17*, 5344–5349.
- (35) Huang, J.; Wang, M.; Zhou, Y.; Weng, X.; Shuai, L.; Zhou, X.; Zhang, D. Visual Observation of G-quadruplex DNA with the label-free fluorescent probe silole with aggregation-induced emission. *Bioorg. Med. Chem.* **2009**, *17*, 7743–7748.
- (36) Wang, X.; Hu, J.; Zhang, G.; Liu, S. Highly selective fluorogenic multianalyte biosensors constructed via enzyme-catalyzed coupling and aggregation-induced emssion. *J. Am. Chem. Soc.* **2014**, *136*, 9890–9893.
- (37) Shi, H.; Liu, J.; Geng, J.; Tang, B.; Liu, B. Specific detection of integrin $\alpha_3\beta_3$ by light-up bioprobe with aggregation-induced emission characteristics. *J. Am. Chem. Soc.* **2012**, *134*, 9569–9572.
- (38) Shi, H.; Kwok, R.; Liu, J.; Xing, B.; Tang, B.; Liu, B. Real-time monitoring of cell apoptosis and drug screening using fluorescent light-up probe with aggregation-induced emission characteristic. *J. Am. Chem. Soc.* **2012**, *134*, 17972–17981.
- (39) Huang, Y.; Hu, F.; Zhao, R.; Zhang, G.; Yang, H.; Zhang, D. Tetraphenylethylene conjugated with a specific peptide as a fluorescence turn-on bioprobe for the highly specific detection and tracing of tumor markers in live cancer cells. *Chem.—Eur. J.* **2014**, *20*, 158–164.
- (40) Hu, F.; Huang, Y.; Zhang, G.; Zhao, R.; Yang, H.; Zhang, D. Targeted bioimaging and photodynamic therapy of cancer cells with an activatable red fluorescent bioprobe. *Anal. Chem.* **2014**, *86*, 7987–7995.
- (41) Rosoff, M., Ed. *Vesicles*; Marcel Dekker: New York, 1996.
- (42) He, C.; Han, Y.; Fan, Y.; Deng, M.; Wang, Y. Self-assembly of $\text{A}\beta$ -based peptide amphiphiles with double hydrophobic chains. *Langmuir* **2012**, *28*, 3391–3396.
- (43) Liu, X.; Wang, T.; Liu, M. Interfacial assembly of a series of cinnamoyl-containing bolaamphiphiles: spacer-controlled packing, photochemistry, and odd-even effect. *Langmuir* **2012**, *28*, 3474–3482.
- (44) Wang, R.; Tang, Y.; Wang, Y. Effects of cationic ammonium gemini surfactant on micellization of PEO-PPO-PEO triblock copolymers in aqueous solution. *Langmuir* **2014**, *30*, 1957–1968.
- (45) Gu, X.; Yao, J.; Zhang, G.; Yan, Y.; Zhang, C.; Peng, Q.; Liao, Q.; Wu, Y.; Xu, Z.; Zhao, Y.; Fu, H.; Zhang, D. Polymorphism-dependent emission for di(p-methoxyphenyl) dibenzofulvene and analogues: Optical waveguide/amplified spontaneous emission behaviors. *Adv. Funct. Mater.* **2012**, *22*, 4862–4872.
- (46) Gu, X.; Yao, J.; Zhang, G.; Zhang, D. Controllable self-assembly of di(p-methoxyphenyl)dibenzofulvene into three different emission forms. *Small* **2012**, *8*, 3406–3411.
- (47) Zhu, C.; Pang, S.; Xu, J.; Jia, L.; Xu, F.; Mei, J.; Qin, A.; Sun, J.; Ji, J.; Tang, B. Aggregation-induced emission of tetraphenylethene derivative as a fluorescence method for probing the assembling/disassembling of amphiphilic molecules. *Analyst* **2011**, *136*, 3343–3348.
- (48) Yu, D.; Zhang, Q.; Wu, C.; Wang, Y.; Peng, L.; Zhang, D.; Li, Z.; Wang, Y. Highly fluorescent aggregates modulated by surfactant structure and concentration. *J. Phys. Chem. B* **2010**, *114*, 8934–8940.
- (49) Yu, D.; Deng, M.; He, C.; Fan, Y.; Wang, Y. Fluorescent nanofibrils constructed by self-assembly of a peptide amphiphile with an anionic dye. *Soft Matter* **2011**, *7*, 10773–10779.
- (50) Xu, L.; Jiang, L.; Drechsler, M.; Sun, Y.; Liu, Z.; Huang, J.; Tang, B.; Li, Z.; Cohen Stuart, M.; Yan, Y. Self-assembly of ultralong polyion nanoladders facilitated by ionic recognition and molecular stiffness. *J. Am. Chem. Soc.* **2014**, *136*, 1942–1947.
- (51) Selkoe, D. J. Alzheimer's disease: genes, proteins, and therapy. *Physiol. Rev.* **2001**, *81*, 741–766.
- (52) Wang, M.; Gu, X.; Zhang, G.; Zhang, D.; Zhu, D. Convenient and continuous fluorometricassay method for acetylcholinesterase and inhibitor screening based on the aggregation-induced emission. *Anal. Chem.* **2009**, *81*, 4444–4449.
- (53) Harel, M.; Schalk, I.; Ehret-Sabatier, L.; Bouet, F.; Goeldner, M.; Hirth, C.; Axelsen, P. H.; Silman, I.; Sussman, J. Quaternary ligand binding to aromatic residues in the active-site gorge of acetylcholinesterase. *Proc. Natl. Acad. Sci. U.S.A.* **1993**, *90*, 9031–9035.
- (54) Yung-Chi, C.; Prusoff, W. Relationship between the inhibition constant (K_i) and the concentration of inhibitor which causes 50% inhibition (I_{50}) of an enzymatic reaction. *Biochem. Pharmacol.* **1973**, *22*, 3099–3108.
- (55) Peng, L.; Zhang, G.; Zhang, D.; Xiang, J.; Zhao, R.; Wang, Y.; Zhu, D. A fluorescence “turn-on” ensemble for acetylcholinesterase activity assay and inhibitor screening. *Org. Lett.* **2009**, *11*, 4014–4017.
- (56) Tipton, K.; Boyce, S.; O'Sullivan, J.; Davey, G.; Healy, J. Monoamine oxidases: Certainties and uncertainties. *Curr. Med. Chem.* **2004**, *11*, 1965–1982.
- (57) Binda, C.; Newton-Vinson, P.; Hubalek, F.; Edmondson, D.; Mattevi, A. Structure of human monoamine oxidase B, a drug target for the treatment of neurological disorders. *Nat. Struct. Biol.* **2002**, *9*, 22–26.
- (58) Peng, L.; Zhang, G.; Zhang, D.; Wang, Y.; Zhu, D. A direct continuous fluorometric turn-on assay for monoamine oxidase B and its inhibitor-screening based on the abnormal fluorescent behavior of silole. *Analyst* **2010**, *135*, 1779–1784.
- (59) Hu, F.; Huang, Y.; Zhang, G.; Zhao, R.; Zhang, D. A highly selective fluorescence turn-on detection of hydrogen peroxide and D-glucose based on the aggregation/deaggregation of a modified tetraphenylethylene. *Tetrahedron Lett.* **2014**, *55*, 1471–1474.
- (60) Huang, X.; Zhang, G.; Zhang, D. A highly selective fluorescence turn-on detection of cyanide based on the aggregation of tetraphenylethylene molecules induced by chemical reaction. *Chem. Commun.* **2012**, *48*, 12195–12197.
- (61) Shen, X.; Zhang, G.; Zhang, D. A New fluorometricturn-on detection of L-lactic acid based on the cascade enzymatic and chemical reactions and the abnormal fluorescent behavior of silole. *Org. Lett.* **2012**, *14*, 1744–1747.

- (62) Villamil, M.; Ordieres, A.; Blanco, P. T. Immobilized enzyme electrode for the determination of L-lactate in food samples. *Anal. Chim. Acta* **1997**, *345*, 37–43.
- (63) Peng, L.; Wang, M.; Zhang, G.; Zhang, D.; Zhu, D. A fluorescence turn-on detection of cyanide in aqueous solution based on the aggregation-induced emission. *Org. Lett.* **2009**, *11*, 1943–1946.
- (64) Vennesland, B.; Comm, E. E.; Knownles, C. J.; Westly, J.; Wissing, F. *Cyanide in Biology*; Academic Press: London, 1981.
- (65) Nam, J.; Thaxton, C.; Mirkin, C. Nanoparticle-based bio-bar codes for the ultrasensitive detection of proteins. *Science* **2003**, *301*, 1884–1886.
- (66) Rosi, N.; Mirkin, C. Nanostructures in biodiagnostics. *Chem. Rev.* **2005**, *105*, 1547–1562.
- (67) Saha, K.; Agasti, S.; Kim, C.; Li, X.; Rotello, V. Gold nanoparticles in chemical and biological sensing. *Chem. Rev.* **2012**, *112*, 2739–2779.
- (68) Schofield, C.; Haines, A.; Field, R.; Russell, D. Silver and gold glyconanoparticles for colorimetric bioassays. *Langmuir* **2006**, *22*, 6707–6711.
- (69) Wang, M.; Gu, X.; Zhang, G.; Zhang, D.; Zhu, D. Continuous colorimetric assay for acetylcholinesterase and inhibitor screening with gold nanoparticles. *Langmuir* **2009**, *25*, 2504–2507.