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Article

Host-Assisted Aggregation-Induced Emission of a Tetraphenylethylene Derivative and Its Responses toward External Stimuli

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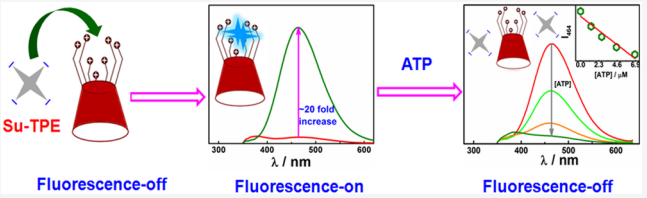
ABSTRACT: Aggregation-induced emission (AIE) of fluorogenic dyes offers many opportunities as smart materials, fluorescence sensing of analytes, bioimaging, molecular electronics, and many others. AIE dyes (called AIEgens) produce emission through aggregation, which are more advantageous than conventional emission of monomeric fluorophores, as the latter is unduly susceptible toward various quenching processes. Here, we report AIE enhancement of a polyanionic sulfonato-tetraphenylethylene (SuTPE) derivative, achieved through supramolecularly assisted dye aggregation, as SuTPE interacts with a multicationic amino-β-cyclodextrin (AβCD) host. Aggregation of the dye is induced mainly because of strong electrostatic interaction of SuTPE with AβCD, causing a significant extent of charge neutralization for the polyanionic dyes, helping their assemblage at the multicationic host portal. Job's plot studies suggest preferential formation of 2:1 dye-to-host stoichiometric complexes in the present system. Ionic-strength-dependent studies nicely support the involvement of electrostatic interaction in the present system through salt-induced disintegration of the SuTPE−AβCD complexes. The AIE enhancement for the SuTPE−AβCD system is very sensitive to the external stimuli, such as pH and temperature, suggesting its prospects in various stimuli-responsive applications. Furthermore, the SuTPE−AβCD system can suitably quantify an important bioanalyte, ATP, following a competitive binding strategy, suggesting its potential application as a supramolecular biosensor.



1. INTRODUCTION

The discovery of aggregation-induced emission (AIE) by Tang and co-workers in 2001 has introduced a completely new domain in the fluorescence spectroscopy and its applications.[1−5] AIE is a unique phenomenon where very flexible fluorogenic dyes containing free rotor groups can display largely improved emission yield in their aggregated state, compared to their very weakly emissive monomeric state. The AIE dyes, which are commonly referred as AIEgens, can overcome many limitations involving conventional fluorophores with monomeric emission, especially regarding their uses in biological sciences.[1−5] Conventional fluorophores with monomeric emission usually suffer a large reduction in emission intensity at the higher fluorophore concentrations, because of nonemissive molecular aggregate formations, generally referred as the aggregation caused quenching (ACQ).[1−3,6] The ACQ is very detrimental in the uses of conventional fluorophores in various applications where significantly higher dye concentrations are needed, especially in biological studies. As the AIEgens are highly flexible molecules, aggregation of these dyes drastically reduces their degrees of freedoms for molecular motions and accordingly reduces the nonradiative deactivation pathways of these molecules very significantly.[1,2,4,5] Accordingly, the AIEgens can display huge increases in their emission yield and fluorescence lifetime, because of their aggregation, which is just opposite to that observed with conventional fluorophores, and thus can render improved uses of these probes in different applications. Furthermore, for some AIEgens, their emission can also be tuned very effectively by changing either the solvents or the use of suitable chemical agents, widening their prospects very significantly. Many AIEgen systems have been explored in the literature focusing their uses in various areas like turn-on fluorescent probes for protein sensing, DNA

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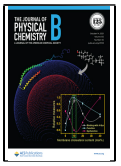

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labeling, metal ion sensing, heparin sensing, protamine sensing, bioimaging, molecular electronics, and so on.[2,7−15]

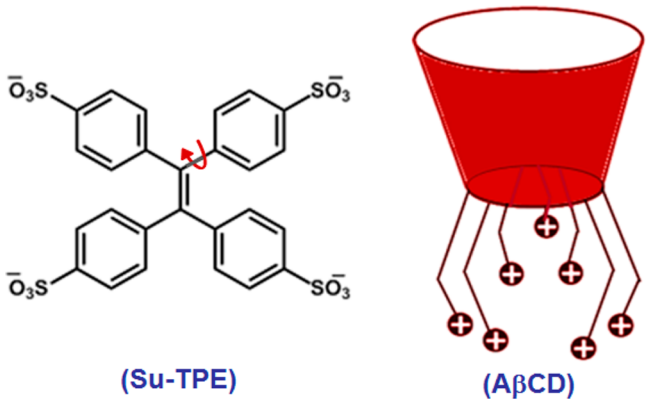
The dyes containing tetraphenylethylene (TPE) moieties are the most celebrated molecules among AIEgen systems. These dyes are very weakly emissive in their monomeric state but are highly emissive in their aggregated state, because of the AIE process. Tetrakis(4-sulfophenyl)ethylene (SuTPE) is an important TPE derivative in which all the *para*-hydrogens of the four phenyl arms are substituted by the sulfonate groups.[16] The presence of the four negatively charged sulfonate groups makes the SuTPE molecule a polyanionic dye, making it highly soluble in water, which is an advantage for various biological applications of the dye using water or aqueous buffer as the solvent. Being polyanionic dye, SuTPE displays very large AIE enhancement in the presence of cationic polymers, which is found to be useful in the detection and quantification of biological species such as enzymes, ATP, pesticides, etc.[17,18]

Supramolecular host-induced aggregations of AIEgens can offer large AIE enhancements even in substantially dilute solutions, which can be beneficial in various applications. Furthermore, the dynamic nature of the supramolecular dye−host complex formations involving the weaker noncovalent interactions can make these assemblies quite responsive to external stimuli such as pH, temperature, light, pertinent analytes, and so on, which are very useful in developing many supramolecular-based applications. Although some studies have been reported in the literature on the TPE derivatives,[16−18] the supramolecular interactions of these AIEgen molecules with different macrocyclic hosts have very rarely been reported.

In supramolecular studies, the cyclic oligosaccharides such as α-, β-, and γ-cyclodextrins (αCD, βCD, and γCD), which are comprised of 6, 7, and 8 D-(+)-glucopyranose units joined by α-1,4-glycosidic linkages, are the most extensively used macrocyclic host molecules.[19−22] The hydroxyl groups present at the portals of these CD hosts assist their water solubility, while their lipophilic cavities provide the required hydrophobic environment for the inclusion of organic guest dyes to form dye−host complexes, stabilized through hydrophobic and hydrogen bonding interactions.[19−22] Among cyclodextrins, βCD is the most popular host, mainly because of its easy availability, low cost, and substantial binding affinity for organic dyes and drugs.[22−25] In recent years, various βCD derivatives have been developed, improving the properties of these hosts for their diverse applications.[26,27] The heptakis-(6-deoxy-6-amino)-βCD (AβCD) is one such derivative, that exists as a polycation in aqueous solution, because of protonation of all its seven amino groups at its lower rim, showing its high solubility and preferential binding for anionic guests, especially involving strong electrostatic interaction.[28−30]

Although AβCD host has been explored as a template for applications such as detection of various ionic species, catalyzing regioselective reactions, and so on,[29−32] the use of this host in supramoleculer studies to modulate properties of organic dyes are very limited. Furthermore, studies on the modulations in the emission properties of AIEgens, induced by macrocyclic hosts, are in fact very limited, although such studies are envisaged to contribute immensely in the ever-growing research area of AIEgen photochemistry. In the present study, we report the interaction of polyanionic SuTPE dye with the multicationic AβCD host, investigated using ground-state absorption, steady-state (SS) emission, fluorescence lifetime, and fluorescence anisotropy decay measurements. Results indicate substantial aggregation of SuTPE, assisted by the interaction of AβCD host, causing a large AIE enhancement for the dye, which is further substantiated by molecular docking studies. Host-assisted SuTPE aggregation appears to be highly sensitive to external stimuli such as pH, ionic strength, and temperature. Additionally, the SuTPE−AβCD system also responds effectively in detecting and quantifying ATP, which is an important bioanalyte. The details of these findings are discussed systematically in the present paper. Chemical structure of the SuTPE dye and the schematic of the macrocyclic AβCD host are shown in Scheme 1 for their quick visualizations.

Scheme 1. Chemical Structure of the SuTPE Dye and Schematic Presentation of the AβCD Host[a]



[a]In the schematic, the groups with plus signs (+) represent the seven $-NH_3^+$ units at the lower AβCD rim.

2. EXPERIMENTAL SECTION

The dye SuTPE was synthesized following the reported procedure.[16] Heptahydrochloride salt of AβCD (purity >95%) was purchased from Cyclolab, Hungary, and used as received. SuTPE concentration in the solution was determined from its absorbance at 315 nm using molar absorption coefficient as $\varepsilon_{315} \approx 16000\ M^{-1}\ cm^{-1}$.[33] Unless otherwise stated, most experimental studies were performed at pH ∼4.5, where SuTPE showed maximum AIE enhancement induced by AβCD (vide infra). Excluding the temperature-dependent studies, all other measurements were performed under ambient temperature, i.e., at 25 ± 1 °C.

Ground-state absorption and SS emission studies were perofrmed using a UV-2700 spectrophotometer (Shimadzu) and a Fluoromax-4 spectrofluorimeter (Horiba), respectively. For temperature-dependent SS emission studies, solution temperature was increased stepwise at 5 °C intervals, with an accuracy of ±0.5 °C, using a Newport Model 350B temperature controller, allowing the solution to equilibrate at each temperature for ∼10 min before measurement. Fluorescence lifetime measurements were performed employing a time-correlated single photon counting (TCSPC) spectrometer (Horiba Jobin Yvon IBH),[34,35] using a 374-nm pulsed diode laser (1 MHz) as the excitation source and a PMT-based detector module to record the fluorescence decays. Instrument response function (IRF) for this set up was ∼160 ps at fwhm, estimated by recording the time profile of excitation light scattered by an aqueous TiO_2 suspension. In

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this setup, the sample holder is attached to a Peltier-based controller, whereby solution temperature was controlled within ±0.5 °C. The software version DAS-6 from IBH was used to fit the observed fluorescence decays that generally followed as a multiexponential function (eq 1) and the quality of these analyses was judged from the observed χ_r^2 values.[36]

$$I(t) = I(0) \sum \alpha_i \exp\left(-\frac{t}{\tau_i}\right) \quad (1)$$

where $I(0)$ is the total initial intensity, while α_i and τ_i are the relative amplitude and fluorescence lifetime, respectively, for the ith decay component. For the multiexponential decays, average fluorescence lifetimes were estimated using the following relationships:[36]

$$\tau_{avg} = \sum A_i \tau_i \quad (2)$$

where A_i is the lifetime weighted emission contribution of the i^{th} component, representing its relative contribution to the integrated intensity under the observed fluorescence decay ($A_i = \alpha_i \tau_i / \sum \alpha_i \tau_i$).

Fluorescence anisotropy decay measurements were also performed using the same TCSPC setup, where sample was excited with the vertically polarized 374-nm pulsed diode laser light and two decays, $I_{\parallel}(t)$ and $I_{\perp}(t)$, for parallel and perpendicular emission polarizations were recorded, respectively, for subsequent construction of anisotropy decay, $r(t)$, as[36]

$$r(t) = \frac{I_{\parallel}(t) - GI_{\perp}(t)}{I_{\parallel}(t) + 2GI_{\perp}(t)} \quad (3)$$

where polarization bias of the detection setup is corrected by using the factor G, which was estimated independently by measuring two perpendicularly polarized fluorescence decays, keeping the polarization of the excitation light at horizontal position.

In the present study, ^{1}H NMR spectra were recorded in D_2O solution using a 400 MHz NMR spectrometer (Varian). In these measurements, the ^{1}H NMR peak observed at 4.69 ppm for the residual HDO present in the used D_2O solvent was taken as the internal reference to correlate the ^{1}H NMR signals appeared for the studied samples.

Molecular docking calculations were performed using the software, AutoDock Vina.[37] In these calculations, input files were created by using the optimized SuTPE and AβCD structures obtained at the PM3 level following Gaussian 03 software.[38] During optimization of SuTPE structure, while three phenyl rings were kept free to take any orientation, the fourth phenyl ring was made to remain fixed in the plane of the ethylene double bond, with the presumption that an extended π-conjugation is essential for the dye to emit at the longer wavelength region, as observed experimentally. With a completely twisted structure, the SuTPE dye cannot give the longer wavelength emission band.[39] After optimization, one SuTPE molecule was first docked into the structure of the AβCD receptor. The energetically best conformation for 1:1 stoichiometric SuTPE−AβCD complex thus obtained was subsequently used for the docking calculation of the 2:1 (dye-to-host) stoichiometric $(SuTPE)_2$−AβCD complex, where the second SuTPE molecule was docked into the former 1:1 SuTPE−AβCD complex. A three-dimensional volume of 40 Å × 40 Å × 40 Å with a grid spacing of 1 Å was explored in the present calculations. The exhaustiveness parameter for the docking calculations, which represents the level of the conducted search, was set to 1000, to ensure that the search is reasonably extensive to obtain the energetically best docked conformations. The docked structures were visualized using the Discovery Studio Visualizer 16.1 software available from Accelrys Software, Inc.

3. RESULTS AND DISCUSSION

3.1. Steady-State Fluorescence and Ground-State Absorption Studies. Effect of host−guest interaction on the photophysical properties of SuTPE dye (20 μM) were studied conveniently using steady-state (SS) fluorescence measurements in the presence of varying concentration of AβCD host.[34,40−42] Present measurements were performed in aqueous solution at pH 4.5 and the observed results are shown in Figure 1. The reason for selecting pH 4.5 is already

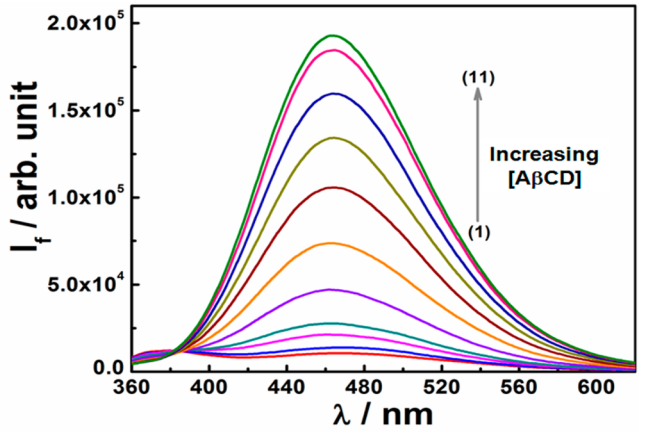

Figure 1. Changes in the emission spectra for SuTPE dye (20 μM) in aqueous solution at pH 4.5 with the increasing concentration of AβCD host. For spectra 1 to 11, [AβCD]/μM are 0, 1.9, 3.6, 4.6, 5.5, 6.6, 7.6, 8.5, 9.5, 10.6, and 11.6, respectively. Excitation wavelength was 320 nm.

mentioned earlier in Section 2, which will be further justified in Section 3.3. It is seen from Figure 1 that, in the absence of AβCD, the SuTPE dye shows a very weak emission spectrum consisting of a relatively narrow, shorter wavelength band (360−410 nm region; peak at ∼378 nm) and a reasonably broad longer wavelength band (410−620 nm region; peak at ∼470 nm). Following Zhang et al.,[39] we infer that the shorter wavelength band is due to localized emission from the completely twisted conformers of the SuTPE dye, and the longer wavelength band is due to SuTPE conformers having extended π-conjugation, owing to one or more phenyl rings residing in the plane of the ethylene double bond. Extremely weak emission of SuTPE in the absence of AβCD is attributed to the very flexible structure of the dye (cf. Scheme 1), causing the excited state of the dye to undergo an efficient nonradiative deactivation process.[10,17,33] With gradual additions of AβCD, however, the emission intensity for the longer wavelength band increases very largely, with a concomitant decease in intensity for the shorter wavelength band (cf. Figure 1). In this context, we have also plotted the changes in the emission intensity for the longer and shorter wavelength bands, as a function of the AβCD concentration, representing the concerned binding isotherms, as shown in Figure S1 in the Supporting

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Information (SI). It is indicated that the changes in the two emission bands correlate quite nicely with each other, suggesting a considerably strong interaction of SuTPE dye with the AβCD host. It is suggested that the π-conjugated conformers of the dye undergo complexation with the AβCD host and thereby the population of the twisted conformers gradually decreases in the solution. Interestingly, however, for the present system, the binding isotherms obtained from both shorter and longer wavelength emission bands do not follow the usual asymptotic nature,[34,40] but display a kind of sigmoidal behavior (cf. Figure S1). Accordingly, we could not apply any suitable model to fit the observed binding isotherms for the studied dye−host system.

Since SuTPE is a polyanionic dye and AβCD is a polycationic host (cf. Scheme 1), it is expected that a strong electrostatic interaction would exist between them in the solution. Furthermore, it is anticipated that, because of such strong electrostatic interaction, the polyanionic dyes at the multipositive host portals would experience substantial extent of charge neutralization, which can thus lead to some extent of dye aggregation or stacking on the host surface, resulting an AIE enhancement for the studied dye. As expected, the AβCD-assisted aggregation or stacking of the SuTPE dyes would be stabilized by the combined effects of electrostatic, van der Waals, and $\pi-\pi$ interactions.[42,43] In these dye−host complexes, since the structural flexibility of SuTPE dye is reduced very significantly,[11,42] there is a large decrease in the nonradiative deactivation processes for the excited dye, resulting an enormous increase in the fluorescence intensity. Figure 1 shows that, while fluorescence intensity of SuTPE undergoes a huge enhancement on its interaction with AβCD, there is no appreciable shift in the emission spectra of the dye, although a critical inspection indicates a very small blue shift for the emission band of the SuTPE−AβCD complex (peak at ~464 nm), compared to that of the free SuTPE dye (peak at ~470 nm). Since the SuTPE conformers having π-conjugated structures are only expected to undergo aggregation or stacking at the cationic AβCD surface, and because the SuTPE molecules in these dye−host complexes would be quite largely exposed to bulk water phase, a very small spectral shift can only be expected for the present system.

To get further details of the SuTPE−AβCD system, we also performed ground-state absorption measurements for 20 μM dye solution at pH 4.5 in the presence of varying host concentration, and the results are shown in Figure 2. In the absence of the host, the dye shows somewhat structured absorption bands, with the strongest peak at ~245 nm and two relatively weaker peaks at ~289 nm and ~315 nm, respectively. Upon the addition of AβCD host, the strongest peak (~245 nm) undergoes a small decrease in absorbance and the two weaker peaks (~289 and ~315 nm) undergo some increase, along with the development of the longer wavelength absorption tail, whose absorbance increases gradually with the increasing host concentration. These changes largely corroborate with the changes observed in the SS fluorescence studies, supporting quite a strong interaction of SuTPE dye with the AβCD host.

Development of the longer wavelength tail in the absorption spectra certainly indicates the appearance of mild turbidity in the solution due to dye−host supramolecular interactions. Therefore, it is likely that, in the SuTPE−AβCD system, there can be some scattering in the solution, because of the appearance of turbidity, which can affect the measured

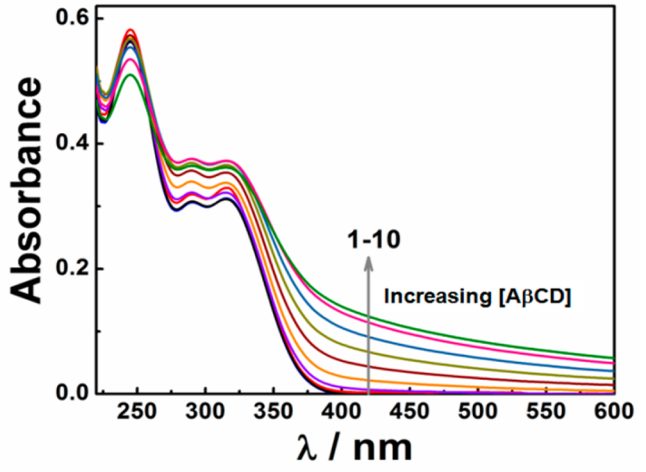

Figure 2. Changes in the absorption spectra of SuTPE dye (20 μM) in aqueous solution at pH 4.5 with the increasing concentration of AβCD host. For spectra 1 to 10, the AβCD concentrations in μM are 0, 1.9, 3.6, 5.6, 6.6, 7.6, 8.5, 9.5, 10.6, and 11.6, respectively.

fluorescence data. To check the severity of this effect, we performed ground-state absorption and SS fluorescence measurements for 20 μM SuTPE solution in the absence and presence of a known light scatterer, namely, the TiO_2 suspension, keeping tail absorption in the latter case quite comparable to that of our actual SuTPE−AβCD system (O.D. $\approx$ 0.1 at 600 nm). Obtained results from these measurements are shown in Figure S2 in the SI. In the absorption results, unlike the SuTPE−AβCD system, where absorbance for 245 nm peak, relative to 289 or 315 nm peak, shows a distinct change, for the SuTPE−TiO_2 system, the scattering effect is just added as an offset to the overall absorption spectra of the dye. In the emission results, it is indicated that the scattered light intensity in the presence of TiO_2 is much less, compared to that in the presence of AβCD host. Therefore, it is inferred that, despite the appearance of mild turbidity in the solution, there is no significant alteration in the measured fluorescence intensity for the SuTPE−AβCD system.

3.2. Effect of pH on the SuTPE−AβCD Complexes. In the cases where either dye or the host molecules possess prototropic functional groups, the host-guest complexation can show strong pH-dependent changes.[35,44] In this study, changes in the AIE behavior for the SuTPE−AβCD complexes were investigated as a function of the changing pH of the solution; the results are shown in Figure 3. In these experiments, the SuTPE−AβCD complexes were first prepared in nanopure water using 20 μM dye and 11.6 μM host. For a part of this solution, the pH was then decreased slowly by adding small quantities of adequately diluted HCl solutions, keeping in mind that the total volume of the solution does not change any appreciably. Similarly, for the other part of the solution, the pH was increased slowly by adding small quantities of adequately diluted NaOH solutions. Note that, in the present pH-dependent study, no buffer was added in the experimental solution and the same was also true for all the other photophysical studies performed in the present work.

It is seen from Figure 3 that the AIE intensity for the SuTPE−AβCD complexes becomes the highest at pH ~4.5, and it decreases very sharply both at the lower and the higher sides of this pH, indicating the maximum stability of these complexes is observed at pH ~4.5. The reasons for these pH-

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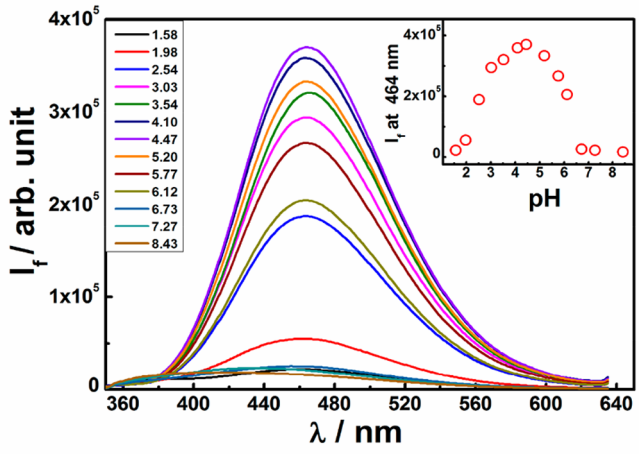

Figure 3. Changes in the emission spectra for SuTPE(20 μM)−AβCD (11.6 μM) system with the changing pH of the solution. Excitation wavelength = 320 nm.

dependent changes in the dye−host complexation can be related to either the possible prototropic processes of the dye or host molecules involved or the changes in the ionic strength of the solution, with the changing pH values. For the studied pH region below ∼4.5, the decrease in AIE intensity cannot be attributed to any protonation/deprotonation process for the dye or the host, because the pK_a values for the sulfonic acid groups of the SuTPE dye are largely negative,[45,46] and those of the $-NH_3^+$ groups of the AβCD host are comparatively higher, in the range of 6.9−8.5.[47,48] Therefore, we feel that, at this lower pH region, the changing ionic strength of the solution is mainly responsible for the changing AIE intensity for the Su-TPE−AβCD complexes. This is expected because the increasing ionic strength would cause a screening effect for the electrostatic interaction of the polyanionic SuTPE dye with the polycationic AβCD host, resulting the disintegration of the SuTPE-AβCD complexes present in the solution. To support this proposition, we have also performed ionic strength dependence studies for the Su-TPE−AβCD system and the results are discussed later in Section 3.6.

For the pH values above ∼4.5 and up to ∼8.5, as used in the present study (cf. Figure 3 inset), the changes in the ionic strength values are not expected to be large enough to cause a substantial decrease in the SuTPE−AβCD complex formation, and hence on the AIE intensity for the system. Since the pK_a values of the $-NH_3^+$ groups of the AβCD host are in the range of 6.9−8.5,[47,48] it is anticipated that, for the pH region of 4.5−8.5, these $-NH_3^+$ groups will gradually undergo deprotonation with increasing pH, causing a decrease in the positive charge density on the host molecule, leading to a decrease in the SuTPE−AβCD complex formation, and consequently a decrease in the AIE intensity. This is expected because the binding affinity of the AβCD host for the polyanionic SuTPE dye will decrease gradually upon deprotonation of the $-NH_3^+$ groups, as there will be a decrease in the electrostatic interaction between the dye and the host. Note that the pH-dependent AIE behavior for SuTPE-AβCD system is also substantiated by ground-state absorption studies as are shown in Figure S3 in the SI. It is seen that, for the SuTPE-AβCD system, the longer wavelength absorption tail is the strongest at pH ∼4.5 but the intensity of this tail decreases very sharply as the solution pH is made either lower or higher from the pH value of ∼4.5.

3.3. Interaction of SuTPE Dye with Parent βCD Host.

To substantiate that a positive charge on the multicationic AβCD host is responsible to induce aggregation of the polyanionic SuTPE dye, SS fluorescence measurements for the dye were also performed at pH 4.5 in the presence of the parent βCD host, which is a neutral molecule. Figure 4

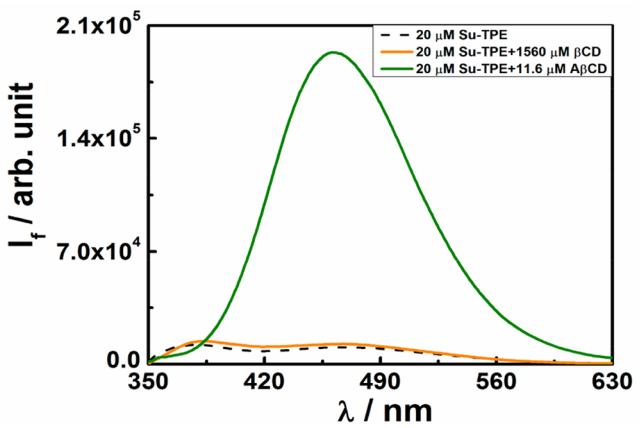

Figure 4. Comparative emission spectra of 20 μM SuTPE in water (black dotted spectrum), in the presence of 1560 μM βCD (orange spectrum) and 11.6 μM AβCD host (green spectrum).

compares the fluorescence spectra of SuTPE dye in the absence and presence of both βCD and AβCD hosts. While the fluorescence intensity of the dye (20 μM) increases very largely, by ∼20-fold, just on using a much lower AβCD concentration (11.6 μM), the intensity is not increased that appreciably even on using a much higher βCD concentration (1560 μM). Absolute changes observed in the absorption and fluorescence spectra for the dye with the increasing βCD concentration are shown in Figure S4 in the SI, for their visualizations. Present results clearly indicate that a strong electrostatic interaction is, indeed, responsible mainly for the AβCD-assisted aggregation of SuTPE dye.

3.4. Job's Plot Analysis for SuTPE−AβCD System.

Changes in the physicochemical property of the dyes in the presence of the hosts can help in estimating the stoichiometry of the dye−host complexes following Job's plot analysis.[34,35,44,49] For SuTPE−AβCD system, since the fluorescence intensity undergoes large changes, we measured the relative intensity changes (ΔI_f) of the system at pH ∼4.5, keeping the sum of the dye and host concentrations constant at 20 μM. Therefore, the Job's plot was constructed by plotting ΔI_f values against mole fraction ($X_{A\beta CD}$) of the host, as shown in Figure 5. The observed plot shows its maximum at $X_{A\beta CD} \approx 0.35$, suggesting the predominant formation of the 2:1 dye-to-host stoichiometric complexes in the solution.

3.5. Fluorescence Lifetime Measurements.

Fluorescence lifetime measurements are useful to understand the role of changing microenvironment on the decay dynamics of the excited dyes. Since microenvironment for the dyes changes largely on host−guest complex formation, it can cause significant changes in the fluorescence lifetime of the studied dyes.[34,44] In the present study, thus, fluorescence decays of SuTPE dye were recorded in aqueous solution at pH 4.5 in the presence of varying AβCD concentration, as shown in Figure 6. In the absence of AβCD, fluorescence decay of SuTPE is very fast and can be fitted to a triexponential function, giving an average fluorescence lifetime (τ_{avg}) as ∼0.78 ns. For

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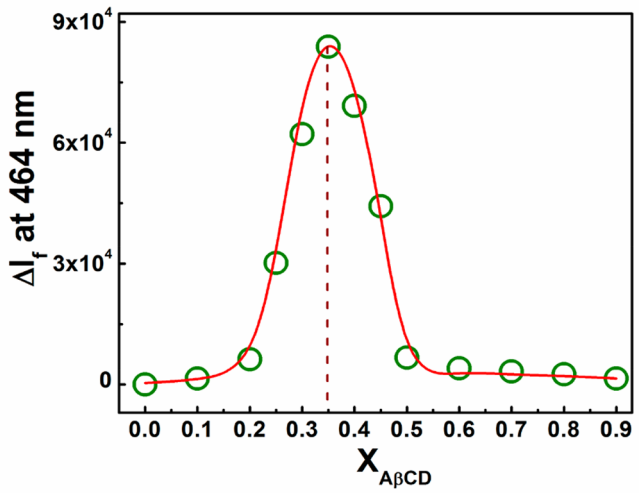

Figure 5. Job's plot for the SuTPE−AβCD system at pH ∼4.5, constructed by plotting the relative emission intensity changes (ΔI_{464} = $I_{\text{SuTPE-A}\beta\text{CD}} - I_{\text{SuTPE-water}}$) at 464 nm against the mole fraction of the AβCD host. Circles denote the experimental data, and the continuous curve is drawn through data points just as a visual guide. Sum of SuTPE and AβCD concentrations was 20 μM, and λ_{ex} = 320 nm.

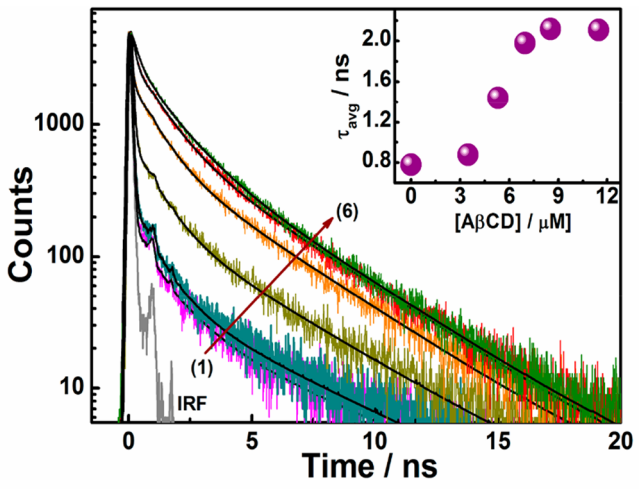

Figure 6. Changes in the fluorescence decay traces for 20 μM Su-TPE dye at pH 4.5 with the increasing concentration of AβCD host. [AβCD]/μM for traces 1−6 are 0, 3.5, 5.3, 7.0, 8.5 and 11.6, respectively. λ_{ex} = 374 nm, λ_{em} = 464 nm. Instrument response function (IRF) is shown by the gray line. Inset shows changes in the τ_{avg} values for Su-TPE dye with the increasing concentration of AβCD host.

structurally flexible molecular rotor dyes, it is generally observed that their fluorescence decays are very fast and multiexponential in nature, as we find for the SuTPE dye.[14,50,51] In the present case, as the AβCD concentration is systematically increased in the dye solution, the fluorescence decay gradually becomes retarded quite largely. In these cases also, the decays can be fitted to a triexponential function and the decay parameters thus estimated are listed in Table 1. Note that as the AβCD concentration increases, the relative contribution A_1 for the τ_1 component shows a systematic decrease and the relative contributions A_2 and A_3 for the τ_2 and τ_3 components show a concomitant increase, suggesting the steadily increased formation of the SuTPE−AβCD complexes in the solution. In the present cases, however, as no systematic

Table 1. Excited-State Lifetime of SuTPE Dye (20 μM) with the Increasing Concentration of AβCD Host[a]

[AβCD] (μM)	τ_1[b] (ns)	A_1 (%)	τ_2 (ns)	A_2 (%)	τ_3 (ns)	A_3 (%)	τ_{avg} (ns)
0	0.03	78.1	1.26	9.6	5.19	12.3	0.78
0.7	0.03	74.7	1.17	10.8	4.94	14.5	0.86
3.5	0.03	74.3	1.20	12.1	5.26	13.6	0.88
5.3	0.03	48.1	1.06	22.5	4.04	29.4	1.44
7.0	0.03	20.0	0.86	31.3	3.51	48.7	1.98
8.5	0.03	10.9	0.81	34.3	3.37	54.8	2.12
11.6	0.03	5.1	0.71	35.2	3.12	59.7	2.11

[a] λ_{ex}= 374 nm, λ_{em}= 464 nm and pH ∼ 4.5. [b] To obtain satisfactory fits for the decays, this τ_1 component is required to be fixed as 0.03 ns, similar to the time resolution of our TSCPC setup.

trends could be found for the τ_2 and τ_3 components, especially, we effectively relied on the changes in the τ_{avg} values to correlate them with the changing host concentration. A very large change for τ_{avg} is observed, from ∼0.78 ns for free dye to ∼2.11 ns with the highest AβCD concentration (11.6 μM), witnessing a huge increase in the decay time for the excited dyes in the dye−host complexes.[43] We infer that formation of the SuTPE aggregates assisted by AβCD host causes a large reduction in structural flexibility of the molecular rotor dye SuTPE, causing the nonradiative deactivation process for the excited dye to decrease substantially and thus increasing the fluorescence intensity and lifetime very largely.

3.6. Time-Dependent Fluorescence Anisotropy Studies. Fluorescence anisotropy decays for the free SuTPE (20 μM) and SuTPE(20 μM)−AβCD(11.6 μM) system were measured at pH 4.5 and are shown in Figure 7. For the free

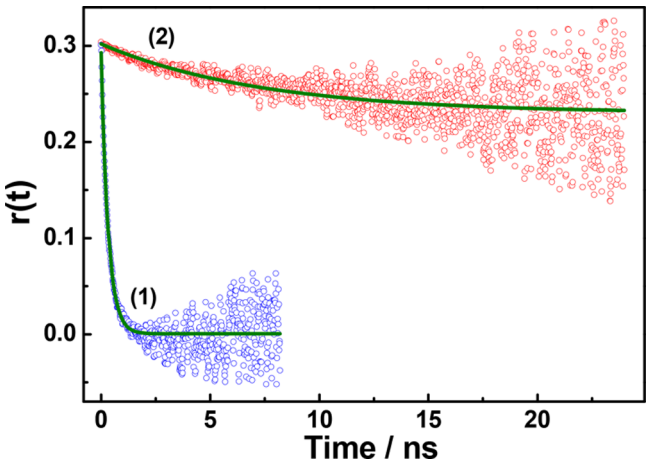

Figure 7. Fluorescence anisotropy decay traces for (1) free SuTPE dye (20 μM) and (2) SuTPE(20 μM)−AβCD(11.6 μM) system in aqueous solution at pH 4.5. λ_{ex} = 374 nm and λ_{em} = 464 nm.

dye, the decay fits with a single-exponential function, providing a rotational correlation time (τ_r) of ∼0.32 ns. Since Su-TPE is a very bulky molecule and its four sulfonate groups are highly hydrated in aqueous solution, a somewhat higher τ_r value of ∼0.32 ns for this dye seems quite reasonable.[34,44] For the SuTPE−AβCD system also, the anisotropy decay fits reasonably well with a single-exponential function, giving a substantially long τ_r value as ∼7.4 ns, although, in this case, there also exists an unusually large residual anisotropy, as ∼0.23. We anticipate that the decay component with $\tau_r \approx$ 7.4

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ns arises because of isolated SuTPE−AβCD complexes formed in the system, preferentially with 2:1 dye-to-host stroichiometric composition, as indicated previously from the Job's plot study, whereas the large residual anisotropy can be attributed to the agglomerated SuTPE−AβCD complexes, whose presence is clearly indicated by the appearance of the long wavelength absorption tail in the presence of the added AβCD host (cf. Figure 2). For these agglomerates, it is apparent that their rotational correlation time is so long, compared to the time window of the present measurement (~25 ns), that we cannot observe any decay for the anisotropy arising from the agglomerated SuTPE−AβCD complexes. Since the amplitudes of the anisotropy decay components are not directly related to the compositions of the respective emissive species present in the solution,[36] it is not possible to comment on the exact degree of agglomeration of the complexes taking place in the present case. However, the large residual anisotropy definitely indicates that a substantial extent of the dye−host complexes undergo clustering in the solution.

3.7. Effect of Ionic Strength on the SuTPE−AβCD System. For host−guest complexes that are stabilized by electrostatic interaction, the changing ionic strength of the solution largely influence such complexation process.[34,35,43,52] Therefore, in the present study, we performed SS emission studies for the SuTPE(20 μM)−AβCD(11.6 μM) system in the presence of gradually increasing concentration of NaCl, and the results are shown in Figure 8. It is indicated that, with

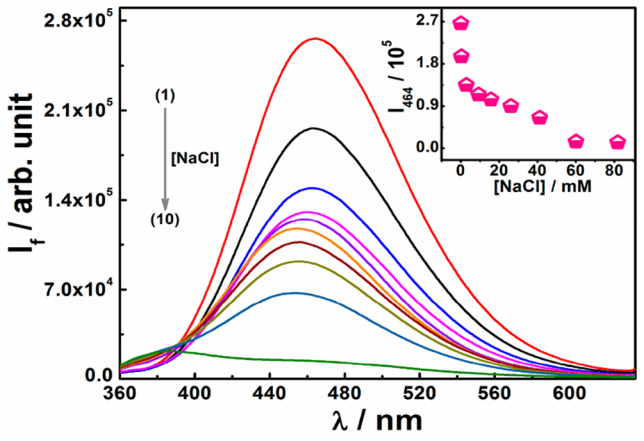

Figure 8. Emission spectra of SuTPE (20 μM)-AβCD (11.6 μM) system at pH 4.5 with increasing NaCl concentration. For spectra 1−10, [NaCl]/mM are 0, 0.3, 0.6, 1.0, 5.1, 9.2, 15.7, 26.1, 41.2, and 60, respectively. Inset shows fluorescence intensity changes at 464 nm with increasing NaCl concentration.

increasing salt concentration, the fluorescence intensity of the initially formed SuTPE−AβCD complexes decreases very sharply, suggesting the salt induced disintegration of the SuTPE aggregates from the AβCD surface. This happens because, with the increasing ionic strength, the electrostatic interaction between oppositely charged dye and host is screened quite largely, reducing the binding strength of the dye−host complexes. Furthermore, the large quantities of the Cl^- ions that are introduced in the solution during addition of NaCl would also bring out a competitive interaction for the multicationic AβCD host, forcing the initially formed SuTPE-AβCD complexes to undergo some disintegration and causing an additional decrease in the binding strength for the dye−host complexes.

To substantiate the above SS emission results, we also performed ground-state absorption studies for the SuTPE(20 μM)−AβCD(11.6 μM) system in the presence of increasing NaCl concentration; the results are shown in Figure S5 in the SI. It is seen that the intensity of the longer wavelength absorption tail, as was achieved initially in the absence of any salt, decreases quite sharply as the NaCl concentration increases. In fact, upon the addition of ~60 mM NaCl, the absorption spectrum for the SuTPE(20 μM)−AβCD(11.6 μM) system eventually becomes quite similar to that of the free dye in the solution (cf. Figure 2), indicating almost quantitative disintegration of the initially formed SuTPE−AβCD complexes.

The effect of added salt on the SuTPE(20 μM)−AβCD(11.6 μM) system was further investigated, following NaCl-concentration-dependent changes in the fluorescence decays and decay parameters (cf. Figure 9, as well as Table S1 in the

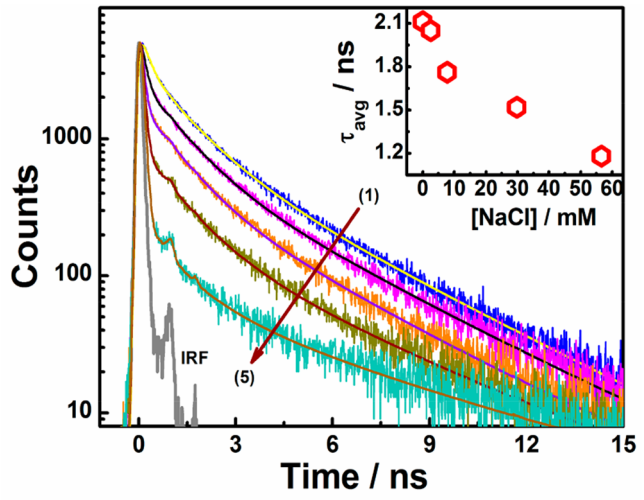

Figure 9. Fluorescence decay traces for the SuTPE(20 μM)−AβCD (11.6 μM) system with the increasing concentration of NaCl salt. For traces 1−5, the NaCl concentrations (in mM) are 0, 2.6, 7.8, 29.9, and 56.6, respectively. Inset shows changes in the average fluorescence lifetime for the SuTPE-AβCD system with increasing NaCl concentration. λ_{ex} = 374 nm, λ_{em} = 464 nm, and pH ~4.5.

SI). As the salt concentration increases, the decay gradually becomes faster and the τ_{avg} decreases quite systematically, from ~2.11 ns initially to ~1.18 ns in the presence 56 mM NaCl. These results also indicate the ionic strength induced disintegration of the SuTPE−AβCD complexes because of the reduced electrostatic interaction.

To determine whether Cl^- ions have any quenching effect on the fluorescence intensity of the SuTPE dye, we also performed an SS fluorescence study using 20 μM dye solution in the presence of varying Cl^- ion concentration, and the results are presented in Figure S6 in the SI. Observed results clearly indicate that there is no Cl^--ion-mediated quenching for the SuTPE fluorescence. Accordingly, the observed decrease in the fluorescence intensity for the SuTPE−AβCD system that is attributable to the presence of added NaCl is certainly due to the effect of increased ionic strength of the solution.

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To investigate the ionic strength effect further, we also performed fluorescence titration studies for the SuTPE−AβCD system under the conditions of two largely different ionic strengths, namely, in the presence of NaCl in concentrations of 0.62 and 3.2 mM, and the observed titration results are shown in Figure S7 in the SI, along with the corresponding results obtained in the absence of any salt. It is seen that, with the increasing AβCD concentration, the fluorescence intensity of the dye increases with a faster rate and larger magnitude in the absence of any salt than those observed in the presence of NaCl in concentrations of 0.62 mM and 3.2 mM, respectively. These results clearly indicate that the extent of formation of the SuTPE−AβCD complexes is gradually decreased upon increasing the NaCl concentration, because the increased ionic strength of the solution reduces the electrostatic interaction between the polyanionic dye and the multicationic host. In all cases, however, the observed binding isotherms are found to be quite sigmoidal in nature (cf. Figure S7) than the usually observed asymptotic behavior of the isotherms found for most of the dye−host systems.[34,40,44] Accordingly, we were not able to adopt any suitable model to fit these binding isotherms.

3.8. Effect of Temperature on SuTPE−AβCD Complexes. In modulating the stability of the host−guest complexes, temperature plays a very important role.[34,35,43,52] Thus, temperature-dependent SS fluorescence studies were performed for the SuTPE(20 μM)−AβCD(11.6 μM) system, and the results are shown in Figure 10. As the temperature

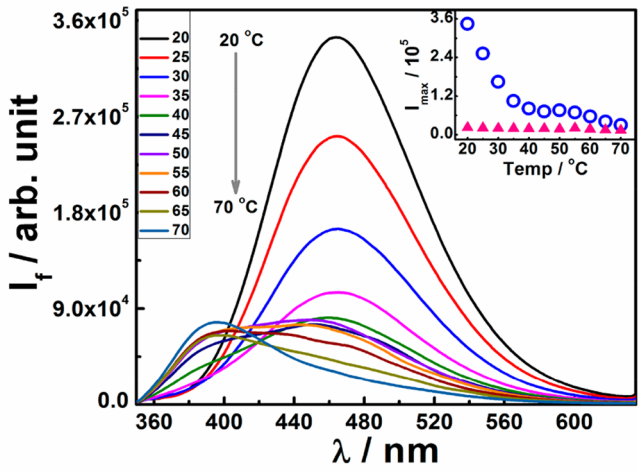

Figure 10. Changes in the emission spectra for SuTPE (20 μM)−AβCD (11.6 μM) system at pH 4.5 with the temperature of the solution. Inset shows a comparison of emission intensity changes at 464 nm for the SuTPE−AβCD system (open circles) and free dye (solid triangles) with increasing temperature.

increases, the fluorescence intensity of the system decreases very sharply, implying a substantial disintegration of the dye−host complexes. It is apparent that the increased thermal agitation at elevated temperatures causes the dye−host complexes formed through the weaker noncovalent interactions to undergo disintegration, resulting in a decrease in AIE intensity for the studied system. Note here that, with increasing temperature, there can also be an increase in the nonradiative deactivation process for the excited fluorophores, which can also add to reduced AIE intensity for the studied dye−host system. However, considering that the fluorescence intensity for the free dye does not undergo any appreciable temperature-dependent changes (cf. inset of Figure 10), we infer that the decrease in fluorescence intensity for the SuTPE−AβCD system is mainly due to disintegration of the dye−host complexes at elevated temperatures. Note here that the temperature effect is apparently quite drastic for the present dye−host system, which is possibly due to largely increased flexibility and twisting of the molecular rotor dyes at elevated temperatures, making their stacking on AβCD surface quite difficult, thereby causing the SuTPE−AβCD complexes to disintegrate very easily.

Thermally induced disintegration of the SuTPE−AβCD complexes was further substantiated from temperature-dependent fluorescence decay measurements, as shown in Figure S8 in the SI. For the SuTPE (20 μM)−AβCD (11.6 μM) system, the fluorescence decays gradually become faster with increasing temperature, indicating the dissociation of the complexes at elevated temperature. This is also substantiated from the analysis of these decay traces (cf. Table S2 in the SI), whereby the estimated τ_{avg} values show a progressive decrease with the increasing temperature of the solution (cf. inset of Figure S8).

3.9. ^{1}H NMR Measurements. The ^{1}H NMR is a very useful tool to understand the changing electronic environments of different guest and host protons, because of dye−host complex formations. Accordingly, ^{1}H NMR study can provide useful information related to binding motifs of the dye−host complexes formed.[53−56] Therefore, in the present study, we have performed the ^{1}H NMR measurements for the SuTPE−AβCD system in D_2O solution, and the results thus obtained are shown in Figure 11. It is indicated that, in the SuTPE−

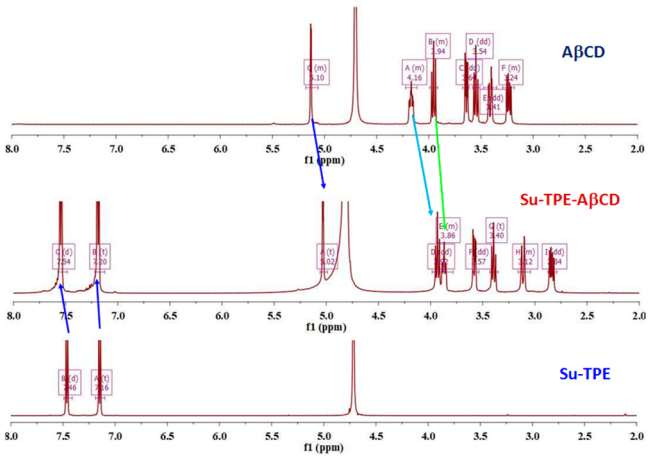

Figure 11. ^{1}H NMR spectra obtained for free SuTPE dye, SuTPE-AβCD complex, and free AβCD host in D_2O solution.

AβCD system, the chemical shifts for the protons of both the guest and the host molecules undergo very substantial changes, compared to their corresponding signals in their free states in the absence of each other.

In the SuTPE−AβCD system, the proton signals for the host molecule are seen to undergo significant upfield shifts, which can be attributed to the decreased cationic character of the host as the negatively charged dye molecules bind with them, introducing considerable shielding effects for the host protons. The protons signals of the dye molecule, on the other hand, undergo significant downfield shifts in the SuTPE−AβCD system, indicating significant deshielding effects for these protons on dye−host complex formations. As the polyanionic SuTPE molecules aggregate in the vicinity of the multicationic

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AβCD portals, there is a significant extent of charge neutralization for the anionic dyes. Accordingly, the protons of the dye molecules experience quite substantial decrease in the electron density around them as they undergo complexation with the polycationic host molecules, resulting in considerable deshielding effects for the dye protons in the NMR study. Thus, observed ^{1}H NMR results for the SuTPE−AβCD system nicely corroborate with our inference that polyanionic SuTPE dyes undergo aggregation at the multicationic portals of the AβCD hosts.

3.10. Molecular Docking Studies on the SuTPE−AβCD System. To understand the possible binding motifs in the SuTPE−AβCD complexes, we also performed molecular docking studies using AutoDock Vina software,[37] following the methodology given in Section 2. Energetically best stabilized structure obtained for a 2:1 dye-to-host stoichiometric complex is shown in Figure 12. It is indicated that, while

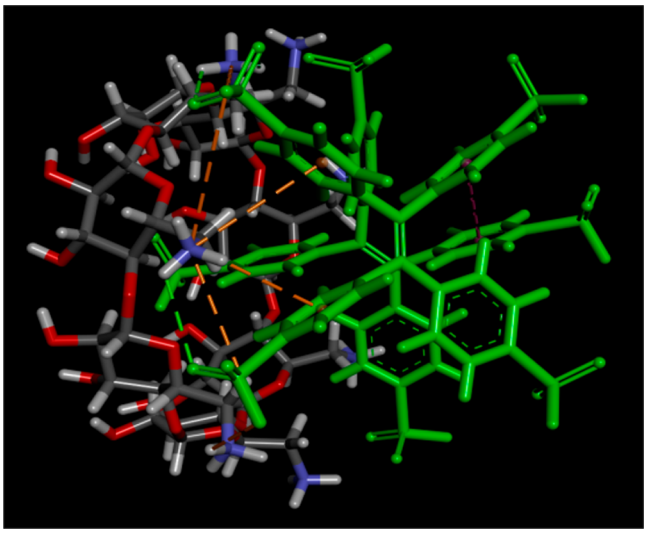

Figure 12. Energy-minimized structure of the 2:1 dye-to-host stoichiometric SuTPE-AβCD complex obtained from molecular docking studies. The different noncovalent interactions involving host and guest groups are shown by the dotted lines.

two SuTPE molecules bind suitably at the polycationic portal of the AβCD host involving strong electrostatic interaction, the other noncovalent interactions, such as π−π stacking (between two dye molecules), π-cation interaction (between π-clouds of the dye and positive charge centers of the host), and the π−H interaction (between π-clouds of the dye and H atoms of protonated amino groups of the host) also contribute quite significantly in stabilizing the dye dimers at the host portals. The docking structure also suggests extensive electrostatic and hydrogen-bonding interactions between negatively charged O atoms of the sulfonate groups of SuTPE dye and positively charged N atoms of the amino groups of AβCD host, providing additional stability for the dye−host complexes formed. The binding energy for the best docked 2:1 dye-to-host stoichiometric complex is found to be approximately −6.8 kcal/mol, suggesting a substantial stability of the complex formed. In brief, molecular docking results largely corroborate with the results obtained from fluorescence and absorption studies, as discussed in the previous sections.

3.11. Response of the SuTPE-AβCD System toward Adenosine Triphosphate. To check the applicability of the present dye−host system, we also investigated the optical response of the SuTPE (20 μM)−AβCD (11.6 μM) system toward the presence of an important anionic bioanalyte, namely, adenosine triphosphate (ATP). In biology, ATP works as the available energy capsules and provides energy to cells through their participation in the metabolic processes. ATP also plays a crucial role in controlling biological activities such as nerve impulses propagations, muscle contractions, food metabolisms, etc.[57−61] Changes in ATP concentration can cause several physiological problems in the body. Thus, development of an efficient ATP sensor for periodic monitoring in the body is highly warranted. Since ATP is a polyanionic molecule and the studied SuTPE−AβCD complexes involve electrostatic interaction predominantly in their formation, it is expected that the presence of polyanionic ATP would lead to the disintegration of the SuTPE−AβCD complexes, because of competitive binding of ATP with the AβCD host. Therefore, with this consideration, we conducted SS fluorescence measurements for SuTPE (20 μM)−AβCD (11.6 μM) system in the presence of the varying ATP concentration, and the observed results are shown in Figure 13.

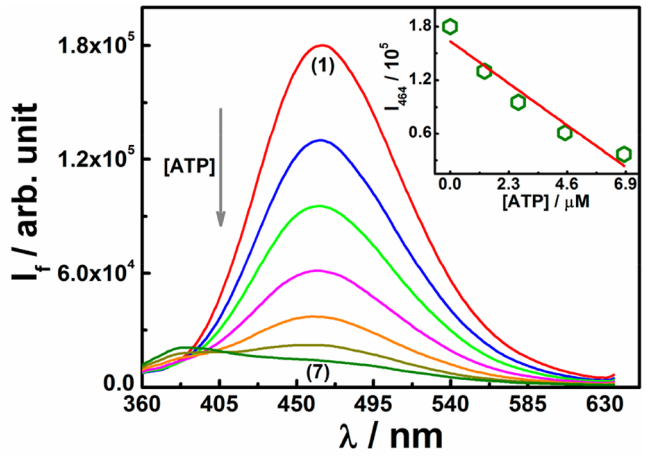

Figure 13. Fluorescence spectra of SuTPE (20 μM)−AβCD (11.6 μM) system at pH ∼4.5 with increasing ATP concentration (in μM): (spectrum 1) 0, (spectrum 2) 1.3, (spectrum 3) 2.7, (spectrum 4) 4.5, (spectrum 5) 6.8, (spectrum 6) 9.8, and (spectrum 7) 13.5. Inset shows the variation of emission intensity of the SuTPE−AβCD complex with increasing concentration of ATP from 0 to 6.8 μM.

It is indicated that the fluorescence intensity for the SuTPE(20 μM)−AβCD(11.6 μM) system decreases very drastically upon increasing the ATP concentration, suggesting the dissociation of the SuTPE−AβCD complexes due to the competitive binding of ATP with the AβCD hosts. For the ATP concentration range of ∼0−6.8 μM, the decrease in the fluorescence intensity is determined to be quite linear in nature, providing a regression analysis, such as $I_{464} = 2.05 \times 10^4 x + 163610.7$, where $x = [\text{ATP}]/\mu\text{M}$, $R^2 = 0.921$; this leads to a limit of detection (LOD) value for ATP in solution of ∼0.79 μM. In the present context, a list of the LOD values, as reported in the literature for ATP detection using different probes, is given in Table S3 in the SI, for a comparison with the result obtained with the SuTPE−AβCD system. It is seen that the LOD value obtained in the present study is relatively better than most of the results reported previously for ATP detection.

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The ATP-induced disintegration of the SuTPE−AβCD complexes was further established from ground-state absorption studies, showing the gradual decrease in the strength for the longer wavelength absorption tail that was initially developed in the SuTPE (20 μM)−AβCD (11.6 μM) system, as shown in Figure S9 in the SI. Experimental findings clearly suggest that the SuTPE-AβCD system might find its usefulness in sensing and estimation of ATP and similar other polyanionic analytes, following their competitive binding in the dye displacement strategy.

4. CONCLUSION

With an effort to construct a host-assisted supramolecular AIE system, in the present study, we have investigated the interaction of a polyanionic AIEgen dye, namely, the TPE derivative (SuTPE) with a multicationic host (i.e., the βCD derivative, AβCD), using various spectroscopic measurements. A strong electrostatic interaction operates between the polyanionic dye and the multicationic host, inducing aggregation/stacking of SuTPE molecules at the positive portals of the AβCD hosts, leading to a large enhancement in the AIE property of the dye. Since SuTPE is a molecular rotor dye, enhancement in its AIE intensity is attributed to the large reduction in the nonradiative deactivation process for the excited dye as it undergoes host-assisted aggregation in the solution. Upon binding to the AβCD hosts, the polyanionic dye molecules experience charge neutralization to a significant extent, which supports the stacking of the dyes at the multicationic portals of the hosts. Job's plot analysis indicates predominant formation of 2:1 dye-to-host stoichiometric complexes, which is also supported by the results obtained from molecular docking calculations. Studied SuTPE−AβCD complexes are found to be extremely sensitive toward pH, ionic strength, and temperature of the solution, suggesting the potential of the dye−host system for various stimuli responsive applications. The SuTPE−AβCD system is also found to be highly responsive in sensing the important bioanalyte, ATP, suggesting the usefulness of such AIEgen−host systems in sensing and estimating the concentration of ATP and similar other polyanionic analytes through competitive binding mechanisms.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.jpcb.1c04653.

Additional results on scatter and pH-dependent changes, results on SuTPE−βCD system, fffect of NaCl on absorption spectra and fluorescence isotherms, ATP-dependent results, tabulation of NaCl and temperature-dependent fluorescence decay parameters, and listing of LOD values reported for ATP detection using different probes (PDF)

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Notes

The authors declare no competing financial interest.

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