PHOTOPHYSICAL STUDIES IN SUPRAMOLECULAR SYSTEMS

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Abstract

Supramolecular interactions have enormous potential for controlling and modulating molecular properties for numerous applications. Our studies have helped in understanding the photophysical properties of guest molecules encapsulated in supramolecular systems and to use these systems as soft templates for creating different kinds of molecular architectures or aggregation patterns. Apart from modulating photophysical properties, the supramolecular systems have also been found to be responsive toward external stimuli, leading to controlled release/exchange processes for prospective use in drug delivery or therapeutic applications.

Keywords: Organized assembly, macrocyclic host, H-aggregate, fluorescence enhancement, stimulus response

Introduction

Supramolecular systems are formed from molecular building blocks held together by ‘weak’ noncovalent intermolecular forces such as electrostatic interactions, hydrogen bonds, π-stacking or the hydrophobic effect. Although individual noncovalent interactions are weak, the summation of a large number of weak bonds in a ‘supramolecule’ can lead to strong overall bonding and stability. Supramolecules, however, are quite flexible due to the continuous making and breaking of the weak bonds and it is this process that leads to the rich diversity and complexity of supramolecular systems. The flexibility and selectivity of supramolecular complexes is what has made the “chemistry beyond the molecule” a very versatile and much investigated research area with wide ranging applications. For the past couple of years we have been interested in different kinds of supramolecular systems, such as organized assemblies of surfactants or lipids and also rigid cage like molecules, like cyclodextrins and cucurbiturils that are capable of trapping suitable guest species. Our research focuses on two complementary aspects: the use of photophysics to characterize supramolecular systems and the use of supramolecular systems to alter the photophysical properties of molecules. We are also interested in the biological aspects of supramolecular systems and their applications for fluorescence on/off sensing or drug release and uptake. This article describes the interesting changes in the photophysical behavior and aggregation patterns of one such biologically important molecule, thiazole orange (TO), in the presence of surfactants, such as sodium dodecyl sulfate (SDS) and sodium bis(2-ethylhexyl) sulfosuccinate (AOT) and macrocyclic hosts, such as cucurbit[8]uril (CB8).

Fig. 1: Chemical structures of the dye, Thiazole Orange (a), Surfactants, SDS (b) and AOT (c) and the macrocyclic host, Cucurbituril (d).
Surfactant Induced Aggregation Patterns of Thiazole Orange

Thiazole Orange (TO) is a cationic cyanine dye (Fig. 1a) that can exist in the monomeric, dimeric or higher aggregated forms in aqueous solutions, depending on its concentration.\textsuperscript{1} It is widely used as a fluorogenic probe for the detection of DNA since its fluorescence is enhanced upon binding to nucleic acids.\textsuperscript{2} The TO-DNA binding is very much dependent on the aggregation state of the dye as well as on the dye/ nucleic acid ratio. So it is important to have a clear idea about the photophysical characteristics and aggregation behavior of TO in order to understand the DNA binding interactions of this dye. On the other hand, the self-association of organic dyes is in itself a very interesting phenomenon due to its applications in many areas like photography, photodynamic therapy, non-linear optics and photoelectric devices.\textsuperscript{3} Two types of ordered aggregates are typically observed, J-aggregates, formed by the alignment of molecules in an edge to edge configuration and H-aggregates, composed of dye molecules stacked face to face in a sandwich-like configuration.\textsuperscript{3} The tendency and type of aggregation depends on a number of factors like the structure of the dye, temperature and the kind of environment. Researchers have studied the role of different additives in controlling and designing the aggregation patterns of dyes. Considering the inherent property of surfactants to form supramolecular assemblies of different morphologies, we expected a pronounced effect on the aggregation behavior of TO in the presence of surfactants, depending on the dye-detergent interactions.\textsuperscript{4} We investigated the aggregation behavior of TO in two different, well-characterized anionic surfactant systems, namely premicelles/micelles of SDS (sodium dodecyl sulfate) and pre reverse micelles/reverse micelles of AOT (sodium bis(2-ethylhexyl) sulfosuccinate). In the case of SDS/water system, we observed that TO initially exists in the monomer form in aqueous solution. At low concentrations of SDS, the surfactant induces the formation of H-aggregate/dimer forms of TO. Beyond the critical micelle concentration (CMC), de-aggregation of the dyes occurs due to their incorporation within the SDS micelles.\textsuperscript{5} Interestingly, the observed changes in the absorption and emission characteristics of TO due to the surfactant induced formation of H-aggregates/dimers, is found to be useful for estimating the surfactant concentration parameters for premicellar aggregation of SDS.\textsuperscript{5} In the AOT/heptane system, the TO dyes are initially present as H-aggregates due to the clustering of the cationic dyes in the nonpolar solvent.\textsuperscript{4} With increasing AOT concentration, the H-aggregates of TO are disrupted and gradually converted to H-dimers due to the electrostatic interactions between the dye and the AOT head groups, and the association of AOT into pre-reverse micellar aggregates. However, in contradiction to the Poisson distribution statistics, the H-dimer form of TO persists even for AOT concentration much higher than the CMC for reverse micelle formation. The H-dimers are proposed to be facilitated by the combined effect of the strong tendency for self-aggregation of the TO dyes and the favorable electrostatic interactions between TO and the AOT head groups. With increasing water content, the hydration of the dyes favors the disintegration of the H-dimers to the monomer form. Aggregation patterns of TO in SDS/water and AOT/heptane systems gives us information regarding the existence of premicellar and pre-reverse micellar aggregates in these surfactants. Interestingly, these initial aggregates serve as templates for bringing two or more TO dyes in close proximity, thus promoting the dye aggregation.\textsuperscript{5} These studies are therefore relevant for the design of molecular

\begin{figure}
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\includegraphics[width=\textwidth]{figure2.png}
\caption{Schematic of the surfactant induced H-dimer and H-aggregate formation of Thiazole Orange.}
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assemblies and ordered molecular structures with desired aggregation patterns, for various applications.

**Spectacular Fluorescence Enhancement of Thiazole Orange within Macrocyclic Host, Selective Exchange and Release**

Studies on recognition-mediated supramolecular assemblies have captured much attention in recent years because of their direct application in fluorescence sensing, on/off switches, controlled drug uptake/release, enzymatic assays, stimulus-responsive functional devices and so on. Cucurbit[n]urils are a class of fascinating host molecules with excellent binding affinities for cationic guests. Cucurbit[8]uril (CB8) has the special ability to hold two suitably sized guest molecules within its hydrophobic cavity. We observed that CB8 has a strong interaction with TO and forms two types of supramolecular complexes with the dye; a 1:2 complex composed of two TO molecules inside one CB8 moiety (CB8-2TO) and a 2:2 complex composed of two TO molecules capped by two CB8 moieties from either end (CB8-2TO-CB8). The 2:2 complexation lends immense structural rigidity to the TO molecules and prevents their intramolecular twisting. This leads to a spectacular, 1700 fold enhancement in the fluorescence intensity of TO. Excited by this host induced ‘light-up’ of TO, we attempted a stimulus responsive stoichiometric control over the host-guest supramolecular assembly. We selected different chemical additives like metal ions (NaCl), tryptophan (Trp), or adamantylamine (AD) as external stimuli, based on their biological importance and varying binding affinity toward CB8. Interestingly, each of these additives produced a distinct supramolecular response with corresponding photophysical changes. In the presence of NaCl, the CB8-2TO-CB8 complex broke down into the CB8-2TO complex, while in the presence of AD, the CB8-2TO-CB8 complex was totally disrupted leading to the release of free TO. With Trp, the CB8-2TO-CB8 complex was converted to CB8-TO-Trp, i.e. one of the TO molecules was replaced by a Trp molecule within the supramolecular complex. We feel that this controlled exchange and release strategy can be evolved into general protocols for designing functional supramolecular systems for targeted applications.

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**References**