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A Novel Dendrimer Design for Phase Transfer Catalysis in the Fluorophase

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6. AUTHOR(S)
Sankaran Thayumanavan

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
University of Massachusetts,
Amherst, MA 01003

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Approved for public release; distribution unlimited.

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13. ABSTRACT (Maximum 200 words)

The objective of the proposed work is to achieve efficient phase transfer catalysis in fluorophase. For this purpose, we had developed a new dendrimer design that can potentially be used as the amphiphilic nanocontainer. Since dendrimers are too expensive to synthesize, we are approaching novel polymers as the target nanocontainers to achieve the required properties. The dendrimer design however provides an avenue for the fundamental studies. In this report, we outline the design and synthesis of a new class of fluorocarbon based polymer micelles. The properties of these polymers are being investigated currently in our laboratories.

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Key Features of the Report:

- (i) We have synthesized a polymer that could form both unimolecular micelles and inverse micelles, depending on the solvent.
- (ii) Evidences from dye studies suggest that these polymers retain micellar and inverse micellar properties even at 10^{-8} M concentration. The limitation in the lowest concentration seems to be the analytical technique, not the capability of the polymer.
- (iii) Evidences have been obtained that clearly show the placement of functionalities within the micelle and inverse micelle.
- (iv) The structural features that have been identified here should find use in applications such as the ones outlined in the 'motivations' section below.

Motivations:

Phase transfer catalysis is of interest in several aspects of organic reactions, since the reagents and substrates often have very different solubility properties. The U.S. Army has an interest in this area, since the chemical warfare agents are often hydrophobic and the corresponding anti-warfare agents are often hydrophilic. While the standard phase transfer catalyst such as tetraalkylammonium halides seem like an obvious choice, the process is more challenging due to the following reason. The current optimized procedure for removing warfare agents from surfaces of tanks, clothes, etc. involves fluorinated solvents. Although this treatment cleans the surface, the chemical warfare agent itself is not destroyed in the process. The chemical warfare agent is separately treated by passing the wash-solution through a filter bed. An attractive alternative is to be able to combine the wash and the destruction processes in one step. Thus, the challenge in such an approach is the following: the chemicals for the destruction process themselves involve two incompatible components, *viz.* the lipophilic warfare agent and the hydrophilic neutralizing reagent. The wash solution is fluorocarbon based, which is incompatible with both lipophilic and hydrophilic solvents. Therefore, there is a need for the ability to carry out a phase-transfer catalysis type reaction between a lipophilic substrate and a hydrophilic reagent in fluorinated solvents. Note that this phase-transfer catalysis is not typical, compared to what is commonly encountered in the literature. In the present case, the strategy should involve three immiscible phases. The classical phase-transfer catalysis reactions involve only two immiscible phases.

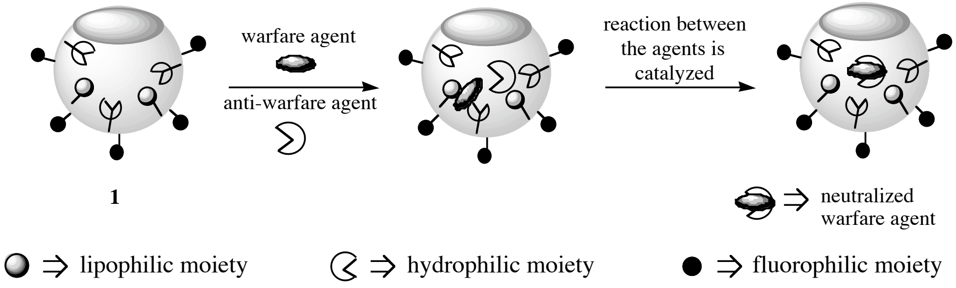


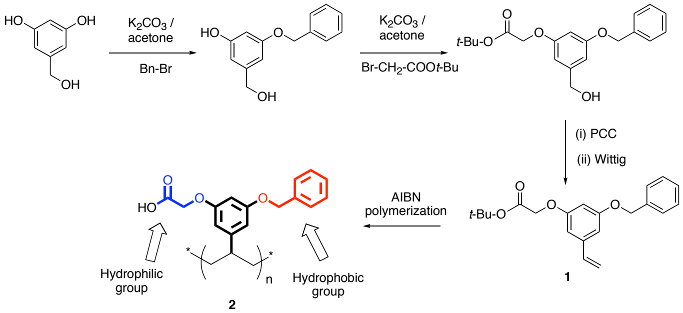
Figure 1. Representation of the Proposed Dendrimers for Phase Transfer Catalysis in HFE-3100

We proposed that facially amphiphilic macromolecules provide a unique opportunity to carry out such catalysis. In this case, the outer face of our macromolecules will contain fluorocarbon substituents, which will render the macromolecules soluble in solvents such as HFE-3100. The interior will be decorated with both hydrophilic and lipophilic substituents. This type of a supramolecular arrangement of substituents in the nanocontainers should render them capable of sequestering both hydrophilic and lipophilic substrates. A schematic representation of our approach is shown in Figure 1. Here, we described a new styrene based polymer that is capable of providing the supramolecular functional group placement described above. This report briefly describes the synthesis of such polymers followed by the more detailed description of our studies that outlines the functional group placements within these polymer micelles.

Synthesis:

The design of our monomer is illustrated by the styrenic molecule **1**. A hydrophilic moiety and a hydrophobic moiety are placed at the *meta*- positions relative to the polymerizable moiety in a benzene ring. Our hypothesis is that upon polymerization, the resulting polystyrene should be capable of acting both as a unimolecular micelle and as a unimolecular inverse micelle depending on the solvent. We hypothesized that the globular conformation of these polymers should place the benzyl side chain in the interior and the carboxylate moieties in the exterior in a micelle and vice versa in the inverted micelle. The proposed conformation is schematically represented in Figure 2. Evidence supporting the presence of such conformation is presented in the following paragraphs.

Scheme 1



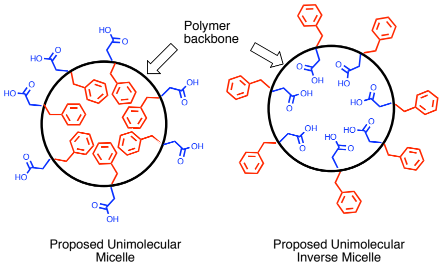


Figure 2. Schematic representation of unimolecular micelles derived from **1**

Studies to Support the Unimolecular Micelle and Unimolecular Inverse Micelle:

The polymer shown above is soluble in water at a pH>7. It is also soluble in water with the addition of just one equivalent of potassium hydroxide relative to the number of carboxylic acid units present in the polymer. The polymer was also soluble in toluene and dicholoromethane in the presence of one equivalent of potassium hydroxide and two to ten equivalents of water. We attribute the later observation to the fact that the carboxylic acid units of the polymer are intermolecularly hydrogen bonded in apolar solvents such as dichloromethane and toluene. These hydrogen bonds are obviously absent when the carboxylic acids are deprotonated with an equivalent of base. This allows the solubility of the polymer in apolar solvents. In order

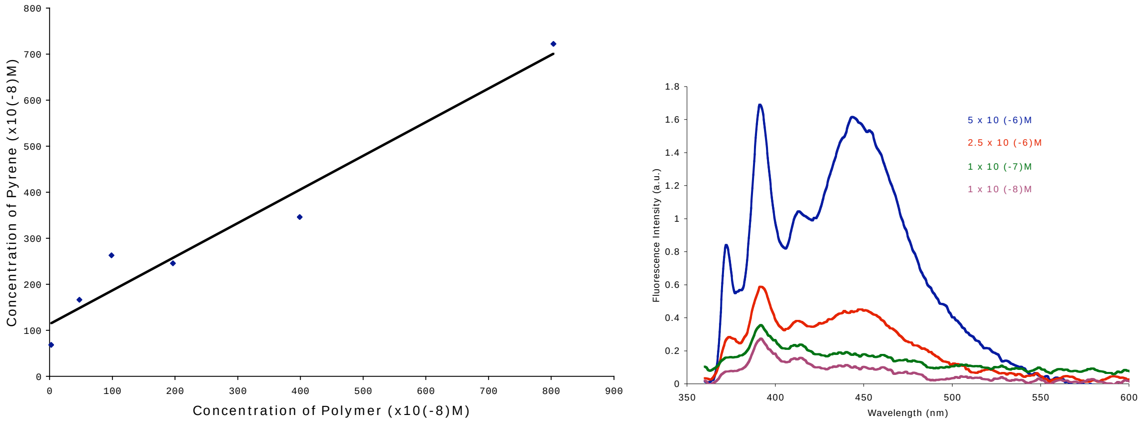


Figure 3. A plot of concentration of pyrene vs. concentration of the polymer (left). A plot of the fluorescence spectra of the pyrene incorporated polymer at difference concentrations.

to identify whether a unimolecular micelle is being formed in water and unimolecular inverse micelle is being formed in dichloromethane and toluene, we performed some dye experiments.

Pyrene was added in solid form to an aqueous solution of the polymer under basic pH. Using UV-visible absorption spectra and fluorescence spectra studies, we noted that pyrene is incorporated in the micelles. As a control, no pyrene could be identified in the aqueous solution in the absence of the polymer. The polarity of the micellar interior was probed using the I1/I3 ratio of the fluorescence peaks in pyrene. The polarity of the interior was comparable to methanol or ethanol. This is comparable to the classical, commercially available small molecule micelles. We also noted that more than one pyrene unit was trapped within the micelles due to the fact that the pyrene exhibited excimer emission. This excimer emission was present even at concentrations as low as 10^{-8} M solution of polymer. Therefore, we suggest that the polymer exists as a unimolecular micelle. The fluorescence spectra and a plot of concentration of polymer vs. concentration of pyrene incorporated are shown in Figure 3.

Similarly, we have also shown that these polymers are capable of forming inverse micelles in toluene by incorporating Rhodamine-6G in toluene. To prove that the dye molecule is indeed trapped inside an inverse micelle, fluorescence spectra of a solution of Rhodamine 6G in water containing KOAc was compared with that of the one in the inverse micelle. The dye molecule trapped inside an inverse micelle exhibited much lower fluorescence, which is known to result with Rhodamine 6G due to self-quenching. This comparison is shown in Figure 4. This experiment was also carried out at low concentrations to show that the dye molecule is still incorporated in the micelle at very low concentrations.

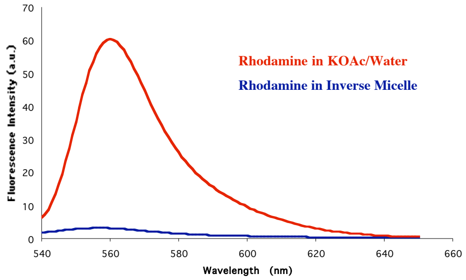
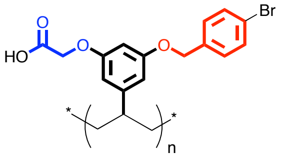


Figure 4. Comparison of Rhodamine 6G fluorescence in inverse micelle and in water.

Study to show the placement of functional groups:

The above studies demonstrate that these facially amphiphilic polymers could behave as both unimolecular micelles and unimolecular reverse micelles. For these polymers to be useful in the applications mentioned in the 'motivations' section of this proposal, it is also important to identify the placement of the functionalities in the micellar structure. For this purpose, we synthesized polymer **3**, which is similar to the polymer **2** above. The difference is the presence of a *p*-bromo functionality in the hydrophobic benzyl substituent. The TEM images of **2** and **3** were compared both in micelles and reverse micelles. We hypothesized that since bromine is a high atomic weight functionality, it should provide a high contrast in TEM images. Thus if the hydrophobic benzyl moiety is to be directed towards the micellar interior in an aqueous solution, the TEM picture should have a dark spot in the interior. On the other hand, if the hydrophobic benzyl moiety is directed towards the exterior in the reverse micelles, the TEM image should have a dark ring. This feature was indeed observed in the TEM images.



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Similarly, in order to identify the placement of the hydrophilic moiety, we deprotonated the carboxylic acid moiety with CsOH. The resulting Cs counterion for the carboxylate is a high atomic weight species and therefore should serve as a useful contrast agent to identify the placement of the hydrophilic functionality within polymer **2**. The TEM images indeed exhibited the dark ring image for the normal micelle and a dark spot in the middle for the reverse micelle, as shown in Figure 5 (actual pictures not shown due to the size of the file that could be e-mailed to ARO)..

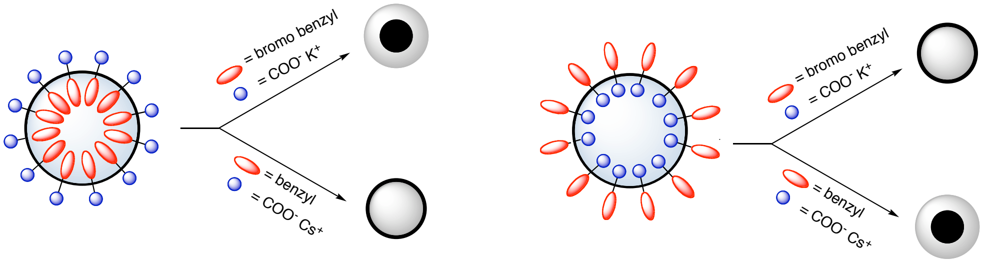

Figure 5. Illustration of expected contrasts in TEM images for micelles upon substitution with heavy atoms.

Summary:

We have designed and synthesized a new class of amphiphilic polymers that are capable of exhibiting both unimolecular micellar and reverse micellar properties. The fact that these polymers exhibit micellar properties even in very dilute solutions render them promising candidates for use in applications such as phase transfer catalysis in chemical warfare destruction, where the concentration of the polymer can be dilute in the wash process. In order to strategically place the functional groups in such a design, it is necessary that we know the supramolecular placement of the functional groups in micelles and reverse micelles. We have utilized TEM images to identify the placement of these functional groups. Utilizing these molecular designs to develop useful nanoscale materials for phase transfer catalysis is now under investigation in our laboratory.

Publications and Presentations: Some of the synthetic results outlined here were reported in the American Chemical Society meeting in New York in Fall 2003 and in Philadelphia in Fall 2004. This presentation was done in the polymer division of the ACS. A manuscript detailing some of the findings outlined here has been submitted.

Scientific Personnel: Currently the funding supports a postdoctoral associate and partially funds another postdoctoral associate.