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Reverse-Vesicle Formation of Organic–Inorganic Polyoxometalate-Containing Hybrid Surfactants with Tunable Sizes

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Abstract: The formation of reverse-vesicular structures of the polyoxometalate-containing hybrid surfactants $[nBu_4N]_3[MnMo_6O_{18}\{(OCH_2)_3-CNHCO(CH_2)_{n-2}CH_3\}_2]$ (Mn-Anderson-C_n, $n=6$, 16) in nonpolar medium was achieved by titrating toluene into Mn-Anderson-C_n/acetonitrile (MeCN) solution. Stepwise change of the solvent polarity induces self-association of the hydrophilic Mn-Anderson cluster on the hybrid amphiphiles. The reverse-vesicle formation was characterized by laser light scattering and further confirmed by transmission electron microscopy techniques, and the vesicle sizes increase with increasing toluene contents. The assembly process was accelerated at an elevated temperature. The length of the alkyl tails on the hybrid surfactants has a minor effect on the vesicle sizes, because the strong attraction between the polyoxometalate clusters is more dominant in the reverse-vesicle formation.

Keywords: amphiphiles • hybrid surfactants • light scattering • polyoxometalates • vesicles

Introduction

Amphiphilic surfactants are known to form self-assembled micellar or vesicular structures in polar solvents. Surfactant vesicles are usually composed of a closely-packed bilayer shell of amphiphiles with their hydrophobic domains staying inside and the hydrophilic domains exposed to the solvent. These mostly spherical and conservative supramolecular structures are technologically significant as mimetic systems for biological cells and as systems with numerous applications, for example, drug delivery and biosensing.[1] The vesicles formed in nonpolar, organic solvents are referred to as "reverse vesicles", which also have bilayer, shell-like structures but with the hydrophobic domains of the amphiphiles exposed to the oily medium.[2] The reverse vesicles could find applications as carriers for controlled release of hydrophobic solutes.[3] However, in comparison to the extensive studies on normal vesicles, the exploration of reverse vesicles, especially related to the rational tuning of the vesicle morphology, is still very limited.[2–5] Furthermore, the use of exotic head groups such as inorganic units and clusters has been almost unexplored.

Polyoxometalates (POMs), a large group of giant transition-metal–oxide clusters with well-defined molecular architectures, are promising functional building blocks with redox, catalytic, photochemical, electronic, and magnetic properties.[6] By covalently grafting hydrophobic tails onto the surface of hydrophilic POMs, new types of amphiphiles can be created as POM-containing hybrid surfactants.[7–8] Compared to conventional surfactants, the "hybrid surfactants" have much larger (in many cases also relatively less hydrophilic) inorganic polar head groups, which may play dominant roles in determining self-assembly processes. Additionally, the properties of such POM head groups can be adjusted by choosing the POM clusters with different charge density, shape, and size, and the type of counterions.

Our recent discovery confirms that POM-containing hybrid surfactants Mn-Anderson-C_n ($[nBu_4N]_3[MnMo_6O_{18}\{(OCH_2)_3-CNHCO(CH_2)_{n-2}CH_3\}_2]$, $n=6$, 16) (Figure 1, left) can demonstrate amphiphilic behavior by forming vesicular structures in polar solvents.[8a] The amphiphilic Mn-Anderson-C_n molecules have a hydrophilic plate-like $\{MnMo_6O_{24}\}$ cluster with dimensions of $\approx 0.9\times0.9\times0.3\ nm^3$, and one hydrophobic alkyl chain (C_5H_{11} or $C_{15}H_{31}$) covalently grafted onto each side of $\{MnMo_6O_{24}\}$ by amide linkages. They have a structure similar to the double-tailed surfactant with a giant polar head group in the middle. Each hybrid molecule carries three negative charges at the Mn-Anderson cluster,

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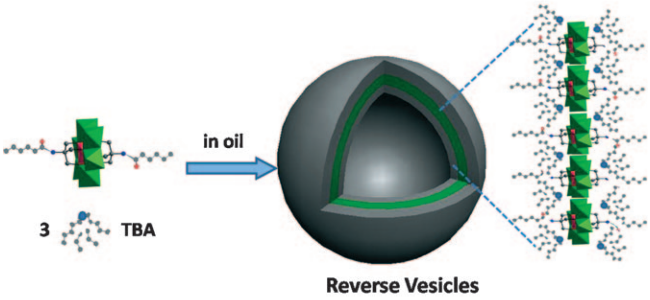

Figure 1. Molecular structures and the reverse-vesicle formation of the POM-containing hybrid surfactants Mn-Anderson-C_n ($n=6$, 16) (Mn = pink, Mo−O polyhedral = green, C = gray, N = blue, and O = red; TBA = $n\mathrm{Bu}_4\mathrm{N}$).

which are balanced by three bulky $n\mathrm{Bu}_4\mathrm{N}$ (TBA) counterions, and the TBAs can be treated as active short-tailed surfactants. Therefore, the whole hybrid molecules can be described as the ion-paired complex of cationic and anionic surfactants. Similar to the vesicle formation by double-tailed surfactants (lipids) or by the mixtures of cationic and anionic single-tailed surfactants,[9] these hybrid molecules self-assemble into bilayer vesicles in polar solvents (MeCN/water mixtures), with the hydrophilic, polar POM head staying at the external layer of the vesicle shell and the hydrophobic tails bending into the core (additional energy is needed for this; as a result, the vesicle formation of the hybrids becomes more difficult than that of conventional surfactants).[8a] The hydrophobic interaction is believed to be responsible for the vesicle formation in Mn-Anderson-C_n/MeCN/water systems. Consequently, the vesicular structures formed by these hybrids are completely different from the vesicle-like blackberry-type structures formed by fully hydrophilic POM macroions.[10]

In this paper, we demonstrate the first example of assembling stable reverse vesicles of POM-containing hybrid surfactants Mn-Anderson-C_n in organic medium (mixed solvents of MeCN and toluene). Formation of reverse vesicles further proves the amphiphilic nature (i.e., surfactant feature) of the Mn-Anderson-C_n hybrids. The relative volume ratio of the two solvent components determines the solvent quality, and, consequently, the formation of reverse vesicles and the vesicle size. We are also interested in understanding the effects of the alkyl tail length and the temperature on the assembly structure.

Results and Discussion

The amphiphilic hybrid surfactants Mn-Anderson-C_n stay as single molecules in the relatively polar solvent MeCN because MeCN is a good solvent for both the Mn-Anderson clusters and the alkyl chains. Continuous addition (titration) of toluene into the Mn-Anderson-C_n/MeCN solution significantly decreases the solvent polarity, which is unfavorable for the solubility of the hydrophilic Mn-Anderson clusters. This change induces stepwise self-association of the hybrid molecules.

The whole toluene titration process was monitored by light scattering techniques. Figure 2 shows the change of the scattered intensity (from static light scattering (SLS)) and the average size of large assemblies (in the average hydrodynamic radius (R_h), from dynamic light scattering (DLS)) with increasing toluene content. The initial scattered intensity of the 0.1 mg mL^{-1} hybrid surfactant Mn-Anderson-C_6 in MeCN is ≈53 Kcps, a very low level, denoting the existence of discrete hybrids in solution (for comparison, the scattered intensity for pure MeCN is ≈20 Kcps). The intensity increases slightly when several drops of toluene are introduced into the solution. When the toluene content reaches 7 vol% in solution, the scattered intensity grows to ≈133 Kcps, indicating the formaiton of a small amount of large structures. CONTIN analysis of the DLS studies shows that the average hydrodynamic radius, R_h, of the assemblies is ≈39 nm. As more toluene is added, the scattered intensity from the solution grows much faster, together with the faster increment of the assembly size, suggesting that a much larger fraction of hybrids forms larger assemblies.

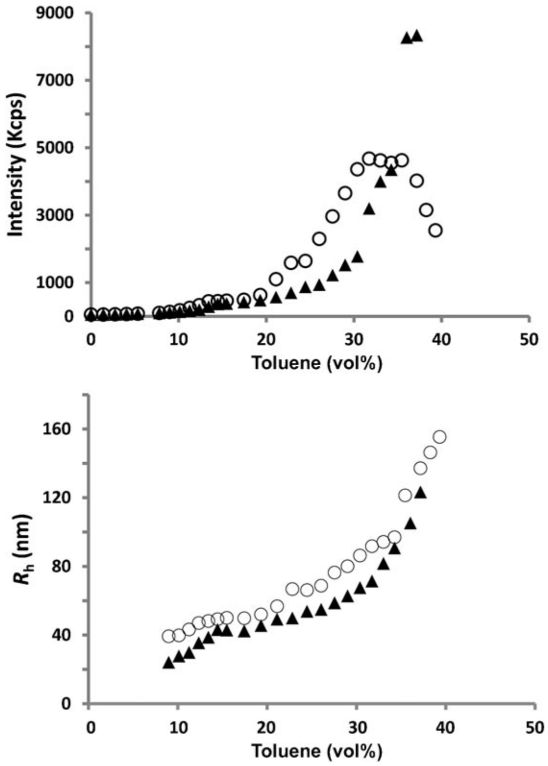

Figure 2. Change of scattered intensities (top) and R_h (bottom) of Mn-Anderson-C_{16} (▲) and Mn-Anderson-C_6 (○) in MeCN solution with a concentration of 0.1 mg mL^{-1} as a function of titrated toluene contents.

The combination of SLS and DLS can be applied to determine the morphology of the assemblies. For example, in the solvent with a toluene content of 21 vol%, the R_h value of the assemblies does not show obvious angular dependence, with R_h at zero angle ($R_{h,0}$) being $\approx 68 \pm 3$ nm. The radius of gyration of the assemblies, R_g, obtained from the SLS measurement is $\approx 66 \pm 3$ nm. Therefore, the ratio of $R_g/R_{h,0}$ is ≈ 1.0, which suggests that the assemblies likely have a hollow, vesicular structure. As shown in Figure 3, vesicles at different steps have a relatively low size distribution with the polydispersity—based on μ_2/Γ^2 values from Constrained Regularization (CONTIN) analysis—in the range of 1.18–1.32. As we observed by SLS studies, such vesicles are quite stable and no obvious change in size and in the amount occurs within one week. When the toluene content reaches 33 vol% in the mixed solvent, the scattered intensity starts to decrease. The solutions become unstable and precipitates appear. Compared to the vesicle formation process of Mn-Anderson-C_6 in the polar solvents, such as MeCN/water, there is no obvious lag period before the vesicle formation in the initial stage of the current process; moreover, the vesicle size is quite sensitive to the solvent quality and changes spontaneously after the addition of more toluene.

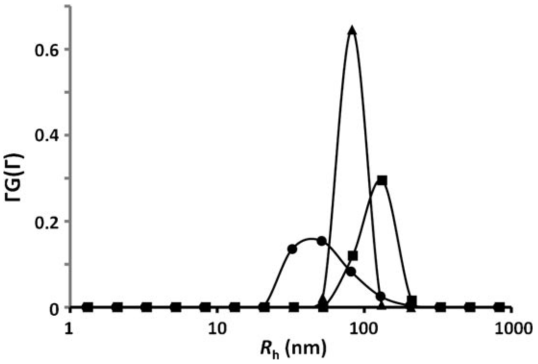

Figure 3. CONTIN analysis of the R_h distribution of vesicles in mixed MeCN/toluene solvents at toluene contents of 15.4 (●), 29 (▲), and 35.5% (■).

TEM characterization confirms the vesicle formation of Mn-Anderson-C_6. As shown in Figure 4, large, collapesd vesicles with average radii of ≈ 200 nm were observed at the final stage of toluene titration (≈ 39 vol%), which is consistent with the DLS result.

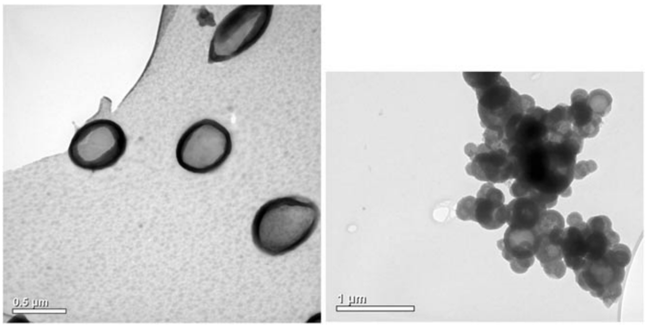

Figure 4. Typical TEM images of reverse-vesicular structure of Mn-Anderson-C_6 in MeCN/toluene solution at a toluene content of 39 vol% (left, scale bar = 0.5 µm) and Mn-Anderson-C_{16} at a toluene content of 37 vol% (right, scale bar = 1 µm).

The possible interior structure of the reverse vesicles of Mn-Anderson-C_6 is shown in Figure 1: a single-layer shell with a layer of solvophobic POM clusters staying in the core and alkyl tails exposed to the nonpolar solvents in the corona, with the whole hybrid molecules extending along the radius axis of vesicles. In this model, we expect that the TBA cations distribute around the POM clusters in order to separate them from the poor solvent. The counterions play a very important role in the self-assembly of the hybrid surfactants, by shielding the repulsive electrostatic interaction between the POMs and by providing additional affinity between hybrid surfactants through their $-C_4H_9$ chains. As an amphiphilic cation, TBA is also sensitive to the solvent polarity. In contrast to the immobile tails, $-C_5H_{11}$ or $-C_{15}H_{31}$, grafted on the Mn-Anderson clusters, the alkyl chains on TBA could be mobile around the POM clusters. Therefore, when the local environment changed, the rearrangement of the TBA surfactant cations might promote the change of vesicle curvatures and allow the unassembled molecules to incorporate into the existing vesicles, resulting in the formation of larger vesicles.

It is known that the morphologies of self-assembled structures formed by amphiphiles are strongly related to the geometries of the amphiphilies. An example is the surfactant-encapsulated POM complex (SEC), where cationic surfactants are strongly interacting with the POM cluster through electrostatic interactions.[11–12] SECs can assemble into various supramolecular structures, such as disks, multilayer cones, multilayer vesicles, and tubes in oily medium.[12–13] Such assemblies often possess similar closely-packed POM layers in which the POMs pack into cystalline-like structures. However, the rearrangement of the oppositely-charged surfactants around the POM clusters under different solvent conditions leads to the formation of different assembled morphologies. In the present work, covalently-grafted alkyl tails (C_5H_{11}) are less flexible and might restrict the crystallization of the Mn-Anderson clusters, but with the aid of the amphiphilic TBA cations the vesicle sizes still can be easily tuned by varying the solvent quality. Additionally, compared to the conventional surfactant molecules,[5] the bulky, rigid, polar head groups are dominant and favor the small curvature for the assemblies, that is, large assembly sizes; and therefore, the reverse micelles or cylindrical micelles, which are too small to accommodate enough amphiphile molecules to lower down the free energy, are not observed in the present system.

The driving force for the formation of reverse vesicles is the solvophobic interaction between the POM clusters, and the sovlophilicity of alkyl tails also plays an important role in balancing the attractive force and furthermore, tuning the morphology of assemblies. Herein, we have also studied the Mn-Anderson-C_{16} (with longer alkyl chains than Mn-Anderson-C_6) in MeCN/toluene mixed solvents by the same titration method. The change of the scattered intensity for the

Mn-Anderson-C_{16} solutions with increasing toluene content shows similar trends to that found for Mn-Anderson-C_6, as shown in Figure 2. After the toluene content reaches 9 vol% in the solvent, the formation of large vesicles is observed. This critical toluene content for the vesicle formation is slightly higher than that of Mn-Anderson-C_6 surfactant (7 vol%). As more toluene is added, the scattered intensity and the R_h value of the assemblies increase stepwise ($R_h \approx 30$–125 nm in the range of 9–37 vol% toluene content). As shown in Figure 2 (bottom), at the same toluene content, the R_h values of vesicles of Mn-Anderson-C_{16} are slightly smaller than that of Mn-Anderson-C_6, indicating that the alkyl chains play certain roles in tuning the vesicle size through balancing the attractive electrostatic interaction. However, the size difference between the vesicles formed by two types of hybrids is relatively small and we believe that the two types of hybrid surfactants undergo similar self-assembly mechanisms in these mixed solvents. The solvophobic portions are still more dominant in the vesicle formation because of the strong attraction between the POM clusters.

Our postulation on the mechanism of the reverse-vesicle formation can be further examined by changing external conditions. Similar results to those described above at 25 °C are observed in Mn-Anderson-C_{16} solutions at higher temperatures. When the Mn-Anderson-C_{16} solution is kept at 35 °C, the vesicle formation process is accelerated. As shown in Figure 5, after 7 vol% of toluene are added, the scattered intensity of the solution starts to grow significantly. With more toluene being added, the scattered intensity and the R_h value grow much faster than those at 25 °C with the same solvent content. The scattered intensity reaches ≈8000 Kcps with $R_h \approx 120$ nm in the solvent containing 20 vol% toluene. It is known that for conventional vesicles formed by surfactants or lipids, the phase transitions of the alkyl chains from gel to liquid–crystalline take place in certain solvent polarity and at certain temperature.[14] In the present work, in the initial MeCN solution, the alkyl chains of hybrid surfactants are relatively rigid due to the polar environment. With the addition of more toluene, their solubility improves and thus, the chains become more flexible (coil-like). On the other hand, with the same solvent content, the alkyl chains become more flexible and tend to be disordered at higher temperature, which favors smaller curvature, that is, larger vesicles. Moreover, the elevated temperature raises the mobility of TBA counterions around the Mn-Anderson clusters, which might also result in stronger solvophobic interaction of the POM clusters.

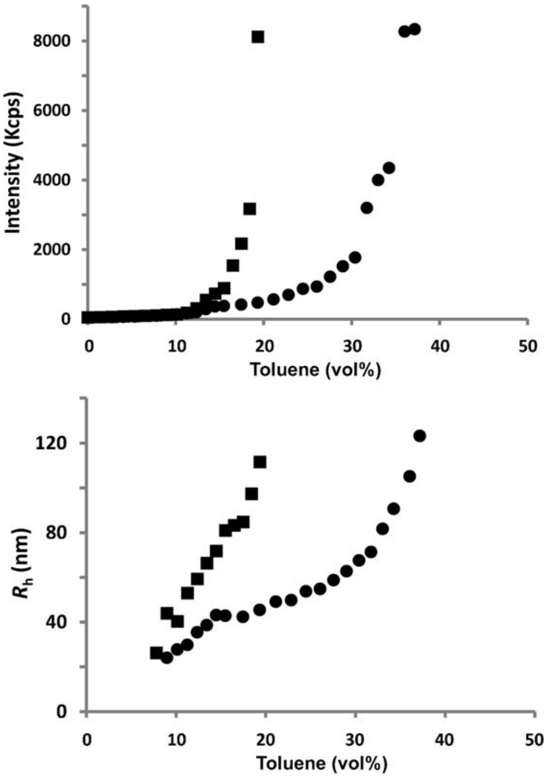

Figure 5. Change of the scattered intensities (top) and R_h (bottom) of 0.1 mg mL^{-1} Mn-Anderson-C_{16} in MeCN solution as a function of titrated toluene contents at different temperatures (● = 25 and ■ = 35 °C).

Only vesicular structures have been identified in the current study. Theoretically other assembled structures, such as micelles, cylindrical and lamellar structures might also appear. In a recent study, Polarz et al. reported that micelles and cylindrical assemblies were found in solutions of another type of hybrid materials, which have polar, polyoxotungstate-type R-$[PW_{11}O_{39}]^{3-}$ head groups and two alkyl chains on the same side of the clusters.[15] In our present work, we did not observe micelles or cylinders probably due to: 1) The lengths of alkyl tails are still relatively short, even for the Mn-Anderson-C_{16} case. We refer to the parameter $p = a_{tail}/a_{hg}$, to make the connection between the geometry and the assembly structure, where a_{tail} and a_{hg} are the cross-sectional areas of the tail(s) of the amphiphile and the head group, respectively. The transition from vesicle to cylinder or micelles would happen if p further increases,[5] that is, with longer alkyl chains. 2) The two tails located at the opposite sides of the Mn-Anderson plate have different conformation from classical surfactants and the possible bending of tails may give rise to geometrical packing constraints into micelles or cylinders. 3) The current study is limited to low solute concentrations due to the limited amount of available samples and the solubility of the materials. 4) The TBA counterions as small "surfactants" are not negligible and closely associated around hybrid surfactants, which makes it more difficult to predict the self-assembled structure by geometry factors.

Conclusion

The amphiphilic hybrid surfactants of Mn-Anderson-C_n with giant Mn-Anderson polyoxometalate clusters being their polar head groups can assemble into reverse vesicles in acetonitrile/toluene mixed solvents due to solvophobic/solvophilic interactions. Elevating temperature can accelerate the assembly process, and the length of the alkyl tails on the hybrid surfactants has a minor effect on the vesicle sizes. The reverse-vesicle size can be tuned by changing the solvent polarity, whereas the solvophobicity and bulk volume of the polar POM head group is the dominant factor in the self-assembly process and electrostatic interactions may also be important in reverse-vesicle formation and stabilization. Finally, the amphiphilic TBA counterions not only shield the repulsive electrostatic interaction but also provide additional affinity between hybrid surfactants. In future work we will attempt to exploit the reverse-vesicle formation by the incorporation of more redox-active POM head groups, thereby allowing the reverse vesicles to be used to compartmentalize, sense, and react to redox reactions encapsulated within the membrane boundary.

Experimental Section

Sample preparation: The hybrid surfactants were synthesized according to the literature.[7a] Dilute solutions in acetonitrile with concentrations of 0.1 $\mathrm{mg\,mL^{-1}}$ were prepared. After all solutions were filtered into dust-free light scattering sample cells through Millipore filters with 0.20 μm pore size, toluene was added dropwise into the solution until reaching the desired amount. A drop of toluene leads to an increment of 1–2 vol% of toluene in the mixed solvent. After the addition of toluene, the solutions were slightly shaken and allowed to stay at 25 °C to reach equilibrium, which was monitored by the time dependence of the total scattered intensity from the solution. The slow self-assembly process in solutions was then monitored by using static and dynamic light scattering techniques at every step.

SLS and DLS measurements: The BIZPM laser-light-scattering spectrometer (Brookhaven Instruments Inc.) equipped with a coherent radiation 200 mW diode-pumped solid-state (DPSS 532) laser with a wavelength of 532 nm and a BI-9000 correlator was used for both SLS and DLS measurements. DLS measured the intensity–intensity time correlation functions at scattering angles of 30–90° at 25 °C. The correlation functions from DLS were analyzed by the Constrained Regularization (CONTIN) method.[16] SLS measurements were performed over a scattering angle range of 30–140°. The data analysis of SLS is based on the Rayleigh–Gans–Debye equation.[17]

Transmission electron microscopy (TEM): Transmission electron microscopy was performed on a JEOL-2000FX TEM operating at an acceleration voltage of 200 kV. A drop of Mn-Anderson-C_n solution containing large assemblies was deposited onto a carbon-coated copper EM grid and dried in air.

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