A Unique Ionic Liquid with Amphiphilic Properties That Can Form Reverse Micelles and Spontaneous Unilamellar Vesicles

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Reversed micelles (RMs) are spatially ordered macromolecular assembly of surfactants formed in a nonpolar solvent, in which the polar head groups of the surfactants point inward and the hydrocarbon chains point toward the nonpolar medium.[1–3] Vesicles and liposomes are spherical aggregates formed by some amphiphilic compounds, in which the lipid bilayer surrounds an aqueous void volume that can be "loaded" with almost any variety of water-soluble marker molecules.[4,5] To prepare large unilamellar vesicles (LUVs), application of different techniques (such as ultrasonication or extrusion) to convert multilamellar vesicles (formed spontaneously) into LUVs are mandatory.[6,7] There are a wide range of surfactants that form RMs,[1–3, 8–21] and probably the most frequently used surfactant is the anionic sodium 1,4-bis-2-ethylhexylsulfosuccinate (AOT).[8,9,11,12,17,18] AOT RMs have the remarkable ability to solubilize a large amount of water with values of W_0 ($W_0 = $ [Water]/[Surfactant]) as large as 40 to 60 depending on the surrounding nonpolar medium, the solute, and the temperature.[2] Another surfactant is the cationic benzyl-n-hexadecyldimethylammonium chloride (BHDC) that forms RMs without addition of a co-surfactant, but only in aromatic solvents.[9,10,17,18,20,21]

It is known that the mixtures of surfactants (catanionic) can exhibit considerable synergistic advantages in their properties and application.[22] Catanionic surfactants can be classified into two categories: 1) when the surfactants counterions are present in the final system, and the majority of the studies are performed in water. Although these surfactants are out of the scope of this contribution, we want to highlight that Kaler et al.[23] reported the first vesicles (known as catanionic vesicles) formed by mixing sodium dodecylbenzenesulfonate and cetyltrimethylammonium tosylate. 2) The second category corresponds to true catanionic systems, that is, when surfactants are mixed and the counterions are removed.[24,25] This category can also be divided into two groups: a) the most studied systems are those built with surfactants mixed from their acid or hydroxide forms, and no salt from the initial counterions is present. This includes the typical mixtures of alkyltrimethylammonium hydroxide and fatty acids, in which the counterions of the surfactants recombine to form water. These kind of salt-free catanionic surfactants were investigated generating them in situ, and no attempts to isolate the resulting surfactants were done (see the Supporting Information for more details and related references). b) The other group of true catanionic surfactants emerge when ionic surfactants (not the one included in group (a)) are mixed in a 1:1 ratio, and the inorganic salt is totally removed. Although these systems show very different properties than the original surfactants,[26] studies about the properties of the self-assembled aggregates in aqueous solutions formed with this kind of true catanionic surfactants are scarce.[26]

Another interesting topic is the emerging field, in which ionic liquids (ILs) with amphiphilic properties are synthesized. Thus, long-chain imidazolium ILs including a charged hydrophilic head group and one or more hydrophobic tails have been used as surfactants similar to the conventional catanionic surfactant.[27,28]
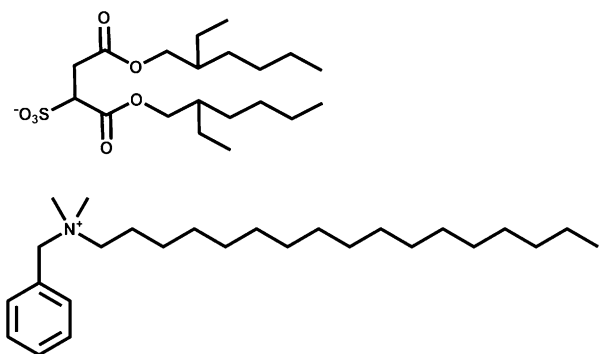
Because our group has been interested for a long time in the study of aqueous[2,8,9,17,20,21,29] and nonaqueous RMs,[12,19,30] vesicles,[5,6] and ILs in confinement,[31] we were interested if it is possible to create a surfactant that can join all the above characteristics, namely, to be an ionic liquid with surfactant properties that can form RMs in nonpolar solvents and spontaneous LUVs systems without forming multilamellar one, in water. Herein, we report for the first time the discovery of a new ionic liquid that fulfill all the above-mentioned requirements. Thus, the aim of this work is to synthesize a new IL with amphiphilic properties made by the combination of two known ionic surfactants, AOT and BHDC, in which the counterions Cl⁻ and Na⁺ are removed giving genesis to the new molecule AOT–BHD

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(Scheme 1). This IL surfactant was isolated from the original surfactant mixture and showed properties absolutely different from AOT and BHDC. We have investigated its ability to form RMs in nonpolar solvents and spontaneous LUVs

Scheme 1. Molecular structure of the catanionic surfactant AOT–BHD.

Figure 1. Apparent diameter (d_{app}) values of the benzene/AOT–BHD/water RMs obtained at 35 °C by varying $W_0 = $[Water]/[AOT–BHD]. [AOT–BHD] = 0.02 M. The straight lines were plotted to guide the eye.

in water, and the results demonstrate that this unique surfactant can form both different organized systems depending on the solvent used. We clearly demonstrate the formation of RMs in benzene and LUVs (that form spontaneously without the help of any mechanical or chemical methods) in water by using dynamic light scattering (DLS)[12,19,21] and small-angle X-ray scattering (SAXS) techniques.[28,32]

AOT–BHD RMs: The detailed synthesis and characterization by ^{1}H NMR analysis of this catanionic surfactant is presented in the Supporting Information (Table S1 and Figure S1). AOT–BHD solubility was tested in *n*-heptane, chlorobenzene, and benzene; as in the case of BHDC, AOT–BHD is only soluble in aromatic solvents. It must be noted that BHDC is a surfactant that cannot be dissolved in aliphatic hydrocarbons,[21] but AOT is perfectly soluble in both kind of solvents. Based on these facts, apparently the solubility of this new surfactant is governed by the cationic surfactant moiety.

DLS measurements were carried out for benzene/AOT–BHD/water at different W_0 ($W_0 = $[Water]/[AOT–BHD]) values and at [AOT–BHD] = 0.02 M. The droplets sizes values obtained are shown in Figure 1, in which it is possible to observe an increase in the droplets size values when the water content increases. For example, the apparent diameter (d_{app}) value for the RMs at $W_0 = 0$ is 4.8 nm and this value increases to 10.5 nm at $W_0 = 1.5$. Moreover, the linear tendency observed indicates that RMs are not interacting, and the shapes are probably spherical. Deviation from the linearity could be explained by several factors, of which the most relevant are: droplet–droplet interaction and/or other RMs shapes.[33] These results confirm the presence of RMs, and that water molecules are effectively entrapped in the organized system. If the spherical shape is assumed, the catanionic surfactant distribution at the interface can be represented as shown in Scheme 2. It is important to note that the d_{app} values obtained for AOT–BHD in benzene are
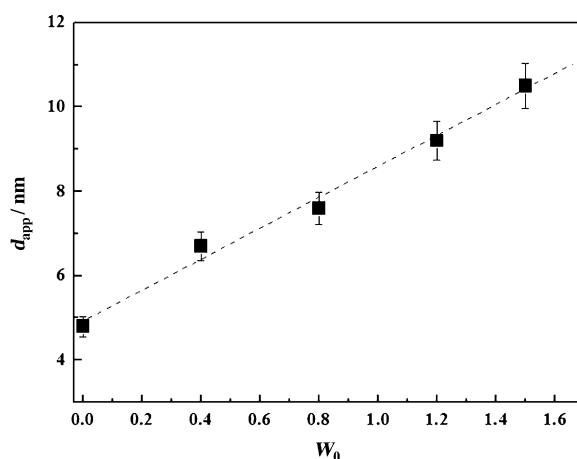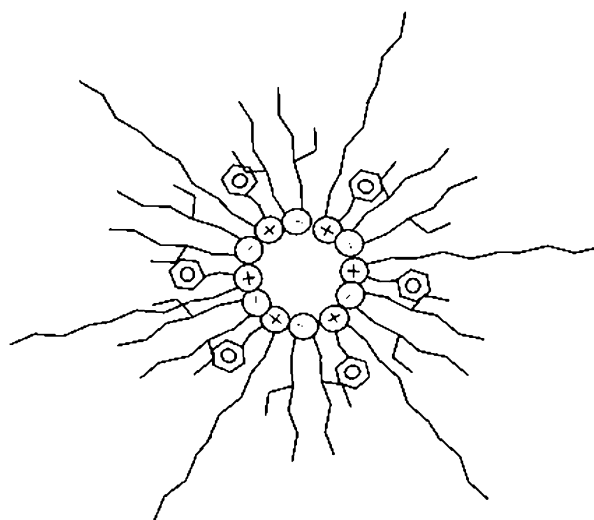
larger than the corresponding values reported for the AOT or BHDC RMs in the same organic solvent (see the Supporting Information).[21,33b] Thus, the intercalated distribution of the surfactants moieties creates a new interface with unexplored physicochemical properties.

Scheme 2. Schematic representation of the AOT–BHD surfactants distribution in the reverse micelle system.

AOT–BHD vesicles: Although neither AOT nor BHDC present the ability to form vesicles in water, when AOT–BHD was dissolved in water, an opalescent solution, which was stable for at least one month, was obtained probably due to vesicles formation. To confirm this, DLS and SAXS measurements were carried out. By DLS analysis, the effect of the [AOT–BHD] on the vesicles sizes was also investigated. The results presented in Table S2 in the Supporting Information show that the d_{app} value is around 80 nm independently of [AOT–BHD] investigated even at high surfactant concentration. Because one characteristic of the vesicles is the lack of critical aggregate concentration (ca. 10^{-10} M),[7]

the d_{app} value of the vesicles at low [AOT–BHD] should not change compared with the values at higher surfactant concentration. The results seems to indicate that the organized media created are vesicles and not normal micelles.[28b]

As can be seen from Table S2 in the Supporting Information, the vesicles obtained at different [AOT–BHD] present low polydispersity index (PDI) values that could suggest another phenomenon: the existence of unilamellar vesicles. It is interesting to denote that the same results were obtained by working with the solutions after they have been passed through an extruder apparatus (see the Supporting Information). Figure 2 shows the SAXS pattern obtained for 5 g L^{-1}
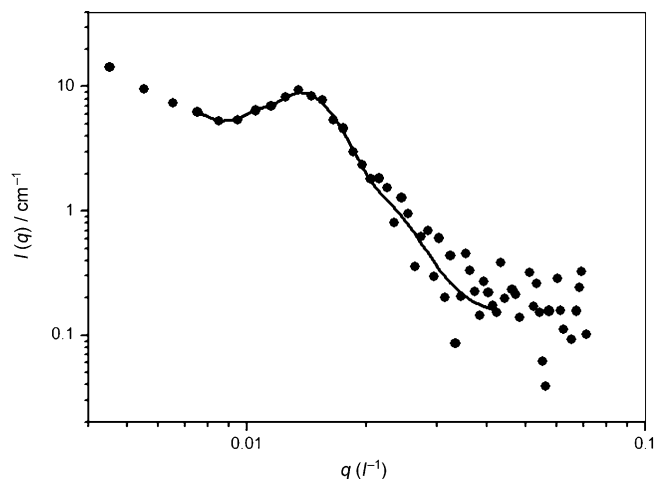

Figure 2. Scattering intensity I of SAXS measurements as a function of scattering vector q for 5 g L^{-1} AOT–BHD vesicles. The solid line is fitted according to Gaussian profile; $T = 24 \,°C$.

AOT–BHD vesicles. Several fit models were attempted to reproduce the experimental data, and the best fit was achieved by using a vesicle model with a single diffuse-lamellar shell. The structure of the shell was simulated assuming a Gaussian profile for the excess electronic density. The relevant vesicle parameters obtained from the nonlinear fit are reported in Table S3 in the Supporting Information. The Gaussian profile for the shell suggests a soft behavior of the vesicle wall probably due to solvent interpenetration. Moreover, the good fitting showed in Figure 2 is consistent with unilamellar vesicles as was proposed by the DLS results.[34] Moreover, the occurrence of a peak in Figure 2 could be associated with intermolecular (in our case, intervesicle) correlation. This interpretation can be ruled out, because experiments performed at lower vesicle concentrations also showed that peak in the same position, indicating that the feature arises more likely from intravesicle scattering. The use of the diffuse shell was justified as a way to avoid introducing much structural details on the excess electronic density of the shell. Fit trials by using a "rigid" shell did not produced the desired fit quality.[34]

It should be noted that other authors have obtained vesicles with catanionic mixtures, but without using equimolar mixture, and in those cases, the generated vesicles were mul-

tilamellar or unilamellar in equilibrium with multilamellar ones.[35, 36] Also, the vesicles phases were obtained at low surfactant concentration. We have obtained unilamellar vesicles of AOT–BHD in water without need to add energy to the system, as was required by traditional methods,[7] and the results were the same, independent from the surfactant concentration used.

In summary, a new catanionic surfactant (AOT–BHD) was synthesized from two traditional ionic surfactants (the anionic AOT and the cationic BHDC). This catanionic surfactant is not only an ionic liquid, but also has amphiphilic properties and can be used to create RMs in nonpolar solvents and spontaneously formed large unilamellar vesicles in water that are not in equilibrium with multilamellar ones. This is very important, because this new system may be used as a drug-delivery agent, which is a field that we are currently investigating. We think that our findings may prove valuable and stimulating to fellow specialists because of the new exciting molecule presented. The unique capacity of the new ionic liquid AOT–BHD to form different stable organized media depending on the surrounding solvents: spherical reverse micelles in benzene and chlorobenzene and spontaneous LUVs in water without forming multilamellar system, may make a significant impact on surfactant and ionic liquid sciences.

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