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## Protic Ionic Liquid when Entrapped in Cationic Reverse Micelles Can Be Used as Suitable Solvent for a Bimolecular Nucleophilic Substitution Reaction

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### ABSTRACT

In this work was explored how the confinement of the protic ionic liquid (IL) ethylammonium nitrate (EAN) inside toluene/benzyl-*n*-hexadecyldimethylammonium chloride (BHDC) reverse micelles (RMs) affects the Cl<sup>-</sup> nucleophilicity on the bimolecular nucleophilic substitution ( $S_N$ 2) reaction between this anion and dimethyl-4-nitrophenylsulfonium trifluoromethanesulfonate. To the best of our knowledge this is the first report where toluene/BHDC RMs uses EAN as polar component and is used as nanoreactor for carrying out kinetic experiments. Dynamic light scattering results reveal the formation of RMs containing the protic IL. The kinetic results show that upon confinement EAN becomes a suitable solvent for the  $S_N$ 2 reaction even that in homogenous media is bad option. Entrapped in BHDC RMs, due to strong hydrogen bond interactions, EAN behave as an aprotic-like IL which cannot deactivate the nucleophilic power of Cl<sup>-</sup> and yet increasing the substrate solubility. These facts show the versatility of this kind of organized system to alter the polar solvent entrapped and its influence on reaction rate when they are used as nanoreactors.

Keywords: protic ionic liquids, reverse micelles, BHDC, ethylammonium nitrate.

### **INTRODUCTION**

Reverse micelles (RMs) are spatially ordered macromolecular assemblies 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.<sup>1-3</sup> RMs are an interesting subject due to their broad applications in chemical reactions, separation science, materials science, and the pharmaceutical industry, among others.<sup>1,4</sup> These nanoscale aggregates are suitable media for processes that involve hydrophobic and hydrophilic reactants in a variety of chemical and biological reactions.<sup>1,4-7</sup> There are a wide range of surfactants that form RMs, including anionic, cationic and nonionic molecules.<sup>1-16</sup> One of them, the cationic surfactant benzyl*-n*-hexadecyldimethylammonium chloride (BHDC, Scheme 1), can make RMs in aromatic solvents without addition of cosurfactant.<sup>1,8,17-23</sup>

Ionic liquids (ILs) have received significant attention as powerful alternatives to conventional molecular organic solvents.<sup>24-26</sup> According to their proton availability, ILs can be classified as protic or aprotic.<sup>27</sup> Particularly, protic ILs have been used in several applications.<sup>24,28</sup> Ethylammonium nitrate (EAN, Scheme 1) is a widely studied protic IL and it is known that it has many similarities to water such as high polarity and the ability to form hydrogen bond.<sup>29,30</sup>



BHDC



Scheme 1. Molecular structures of BHDC and EAN.

The use of protic ILs (predominantly EAN) in organized systems is usually as a replacement for water as the polar phase in direct micelles or vesicles. In this sense, very recently Greaves et al.<sup>31</sup> reported in detail the backgrounds in this field. However, with regard to the formation of RMs containing protic ILs much less information is available. These RMs can provide potential applications owing to the unique features of both ILs and RMs. However, the majority of the studies containing protic ILs employed non-ionic surfactants such alkyl oligoethylene oxide  $(C_n E_m)^{32,33}$  or Brijs<sup>34</sup> and they used normally as non-polar phase n-alkanes or benzene<sup>34</sup> and EAN as polar phase. Only a few works performed by Zech et al.<sup>35-37</sup> have focused on the use of cationic surfactant, particularly 1-hexadecyl-3-methyl imidazolium chloride (C<sub>16</sub>mimCl), with decanol as cosurfactant, EAN as the polar phase, and dodecane as the non-polar continuous phase.<sup>35,36</sup>

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With regard to BHDC RMs, although the traditional solvent used as polar component in this cationic RMs is water,<sup>8,17</sup> different aprotic ILs<sup>18-23</sup> have been entrapped in the polar core but not information about the possibility to use EAN is found. This system is interesting to explore since it is well known that the physicochemical properties of polar solvents (water and aprotic ILs) entrapped inside RMs change dramatically from those of the bulk solvents as a result of specific interactions and confined geometries.<sup>1,9,18-21,23</sup> This can cause, for example, alterations in the reactants and in the course of reactions. Particularly, nucleophilic substitution reactions provide a familiar avenue for examination of solvent effects on chemical reactions.<sup>23,24,38-41</sup> As a chemical probe it is

possible to use the nucleophilic substitution reaction of Cl<sup>-</sup> with dimethyl-4nitrophenylsulfonium (S<sup>+</sup> in Scheme 2).<sup>23,40,41</sup> Previously, we have study the same S<sub>N</sub>2 reaction in toluene/BHDC RMs but with 1-butyl-3-methylimidazolium tetrafluoroborate (bmimBF<sub>4</sub>) as encapsulated aprotic IL.<sup>23</sup> We observed that upon confinement, the ionic interactions between the cationic surfactant polar head groups and the surfactant counterion modifies substantially the performance of the aprotic IL as solvent. Taking into account this background, the aim of the present work is to show that a protic solvent, EAN, can be used as worthy reaction media when it is entrapped in BHDC RMs while is a bad option in homogeneous media. Here, it is important to note that the task of our work is not to try to discover new materials or transformations but to use a chemical reaction as a model reaction to evaluate the solvent effect in a complex system such as RMs.



**Scheme 2**. The  $S_N 2$  reaction of Cl<sup>-</sup> with dimethyl-4-nitrophenylsulfonium (S<sup>+</sup>) to produce methyl-4-nitrophenyl sulfide (P) and Cl-CH<sub>3</sub>.

### **RESULTS AND DISCUSSION**

In order to explore the effect of confinement on EAN in the  $S_N2$  reaction studied, the nucleophilic reactivity of Cl<sup>-</sup> in homogeneous and confined media was evaluated. Thus, the results obtained are presented in two different sections corresponding to the studies performed in *(i)* neat EAN and *(ii)* toluene/BHDC/EAN RMs at different IL contents defined as  $W_s = [EAN]/[BHDC]$ . The  $S_N 2$  reaction was followed by monitoring the absorbance changes at  $\lambda = 340$  nm corresponding to the formation of the demethylated sulfide product (Scheme 2). All the experiments were carried out under pseudo first order conditions, were the sulfonium salt concentration ([S<sup>+</sup>] = 5 x 10<sup>-5</sup> M) was always smaller than the [CI<sup>-</sup>].

### i) Studies in neat EAN

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Absorbance spectra of the mixture of Cl<sup>-</sup> and S<sup>+</sup> in neat EAN at different times are presented in Figure S1. Ammonium chloride (NH<sub>4</sub>Cl) as source of Cl<sup>-</sup> ion was used and the variation of the Cl<sup>-</sup> concentration between 1 x  $10^{-2}$  M and 0.2 M were performed. As it can be observed in Figure S1, no absorbance changes using the protic IL as solvent are detected, even after long time of reaction. Similar results were found by Hallet et. al.<sup>41</sup> for the same reaction performed in water and methanol. The authors explained the absence of reaction as due to the strong hydrogen bond interaction between the solvents with the nucleophile, thus reducing its reactivity. In fact, EAN presents a high Kamlet-Taft's  $\alpha$  parameter value (0.85<sup>25</sup>), which is consistent with the ability of the solvent to interact through hydrogen bond. In consequence, the Cl<sup>-</sup> anions in EAN are not available to act as nucleophile because they are associated to the ethylammonium cation.<sup>41</sup>

### ii) Studies in toluene/BHDC/EAN RMs

Prior to study the  $S_N^2$  reaction in toluene/BHDC/EAN system and because it is not known if EAN is truly encapsulated by BHDC to form RMs, Dynamic light scattering (DLS) experiments were performed. When new RMs are explored, a crucial question has to be answered: is the polar solvent effectively entrapped by the surfactant creating a true RMs or is dissolved only in the organic solvent/surfactant mixture without any

molecular organization (bicontinous structureless microemulsion)?<sup>42</sup> DLS normally is used to assess this matter because if the polar solvent (water for example) is really encapsulated and interacting with the RM interface, the droplets size must increase as the water content ( $W_0 = [water]/[surfactant]$ ) increases with a linear tendency (swelling law of RMs) as it is well established for other RMs.<sup>9,17,43</sup> A deviation from the linearity on the droplets sizes indicates that the RMs droplet – droplet interactions are favored thus changing the shape of the RMs previous to the phase separation.<sup>23,44,45,46,47</sup> On the other hand, if the polar solvent is not encapsulated by the surfactant the droplets sizes could remain constants or even decrease with the polar solvent addition.<sup>42</sup>

In the present work, as the RMs solutions are not at infinite dilution (DLS experiments were performed at a fixed surfactant concentration equal to 0.2 M) it is appropriate to introduce an apparent hydrodynamic diameter ( $d_{app}$ ) in order to describe the results.<sup>48</sup> Figure 1 shows the  $d_{app}$  values for the toluene/BHDC/EAN system at different W<sub>s</sub> values. As can be seen, there is an increase in the droplet size values when the IL content increases, showing that EAN is effectively entrapped by the surfactant layer, yielding RMs. The sizes obtained for toluene/BHDC/EAN RMs are comparable to the values reported previously for aprotic ILs entrapped in BHDC RMs.<sup>18,20,21,23,43</sup> However, the amount of the protic IL that the toluene/BHDC RMs dissolve is quite small, W<sub>s</sub> = 0.3. Similar results by Dai et al.<sup>49</sup> in the ternary system cyclohexane/TX-100/EAN (W<sub>s</sub> = 0.4) and by Zech et al.<sup>36</sup> in dodecane/decanol/C<sub>16</sub>mimCl/EAN (W<sub>s</sub> = 0.18) have been reported.

Additionally from Figure 1, is it interesting to mention that the droplet size values increase slightly (only 0.5 nm) with the  $W_s$  suggesting that the IL is interacting weakly with BHDC at the interface of RMs.<sup>18,20,21</sup>



Figure 1. Apparent diameter ( $d_{app}$ ) values for toluene/BHDC/EAN RMs obtained at 30 °C varying W<sub>s</sub>. [BHDC] = 0.2 M.

As it was mentioned above, we have studied previously<sup>23</sup> the same  $S_N 2$  reaction in BHDC RMs; particularly in that work we performed kinetic experiments also in neat toluene and toluene/BHDC RMs at  $W_s = 0$ . In both cases, the reaction takes place but different behaviors were observed.<sup>23</sup> In neat toluene, always working below the critical micellar concentration, the formation of ion pairs between Cl<sup>-</sup> with its counterion increases with salt concentration, in such a way that the fraction of free Cl<sup>-</sup> available as nucleophile to react with sulfonium ions decreases and consequently the observed rate constant also decreases.<sup>23</sup> In toluene/BHDC RMs at  $W_s = 0$ , the incorporation of S<sup>+</sup> into the RMs is favored (in comparison with toluene) and the presence of Cl<sup>-</sup> at the interface of the RMs allows the observation of reaction.<sup>23</sup>

Taking into account these backgrounds and the ability of RMs to alter the structure of the polar solvent entrapped, in the present contribution we want to explore if the presence of RMs can affect or not the performance of a bad solvent for

nucleophilic substitution reactions such as EAN. In this sense, in toluene/BHDC/EAN RMs the  $S_N2$  reaction was studied varying the [BHDC] keeping constants the [S<sup>+</sup>] and  $W_s$  values. Typical kinetic results in toluene/BHDC/EAN RMs are shown in Figure 2. Also an example of the absorbance changes at  $\lambda = 340$  nm as a function of time at [BHDC] = 0.1 M and  $W_s = 0.05$  are shown in Figure S2. As can be seen in these Figures and opposite to the results obtained in neat EAN (Figure S1), the reaction in toluene/BHDC/EAN is observed.

The reaction of the sulfonium  $S^+$  with chloride ion presented in Scheme 2 is a bimolecular reaction, which kinetics follows the rate law descripted by equation 1:

$$rate = \frac{d[P]}{dt} = k_2[Cl^-][S^+]$$
(1)

If  $[Cl^-] \gg [S^+]$ , a pseudo first order behavior for the kinetics of the reaction is assumed in order to quantify the reaction rate. Thus, the expression for the observable rate constant (k<sub>obs</sub>) can be defined as equation 2:

$$k_{obs} = k_2[Cl^-] \tag{2}$$

where  $k_2$  is the second order rate constant and [Cl<sup>-</sup>] is the total nucleophile concentration.



**Figure 2.** Absorption spectra of the reaction of Cl<sup>-</sup> with S<sup>+</sup> in toluene/BHDC/EAN RMs at  $W_s = 0.05$ . [BHDC] = 0.1 M. [S<sup>+</sup>] = 5 x 10<sup>-5</sup> M. T = 30 °C. The spectra were recorded at 60 second intervals.

As in the RMs, the BHDC surfactant was used as the source of Cl<sup>-</sup> ion (See structure in Scheme 1), the  $k_{obs}$  values obtained in toluene/BHDC/EAN RMs at different total concentration of BHDC ([BHDC]<sub>tot</sub>) and W<sub>s</sub> are shown in Figure 3.



**Figure 3.**  $k_{obs}$  values as a function of total concentration of BHDC ([BHDC]<sub>tot</sub>) in toluene/BHDC/EAN at different W<sub>s</sub>. W<sub>s</sub>: (**n**) 0.02, (**•**) 0.05, (**▲**) 0.11 and (**∨**) 0.17.  $[S^+] = 5 \ge 10^{-5} \text{ M}$ . T = 30 °C.

Two facts emerge from Figure 3: (*i*) the  $k_{obs}$  values increase with the amount of BHDC but not in linear tendency at all the W<sub>s</sub> evaluated as could be expected for a simple S<sub>N</sub>2 reaction; (*ii*) the  $k_{obs}$  values in the RMs are dependent on the EAN content. In Figure 4, are plotted the  $k_{obs}$  values in the toluene/BHDC/EAN RMs as a function of the EAN content at [BHDC]<sub>tot</sub> constant.



**Figure 4.**  $k_{obs}$  values as a function of  $W_s$  in toluene/BHDC/EAN at different [BHDC]<sub>tot</sub>. [BHDC]<sub>tot</sub> (M): ( $\blacktriangle$ ) 0.10, ( $\blacksquare$ ) 0.15 and ( $\bullet$ ) 0.2. [S<sup>+</sup>] = 5 x 10<sup>-5</sup> M. T = 30 °C.

As it can be observed, at low  $W_s$  (0.02 – 0.11),  $k_{obs}$  has similar values in the toluene/BHDC/EAN RMs and they are independent on the EAN content. Only when the  $W_s$  value is large enough ( $W_s = 0.17$ ) there is an impact on the rate constant which decreases dramatically. It should be noted that even at this  $W_s$  value the reaction is still observed. It is evident that the Cl<sup>-</sup> availability is responsible for the changes on rates of

the reaction.

In order to explain the results obtained in the BHDC RMs performed at different [BHDC] and  $W_s$ , is important to consider which kinetic model is appropriated to analyse the data.

In view of the S<sup>+</sup> chemical structure, it is possible that the substrate solubilize (in different magnitude) in two regions of the toluene/BHDC/EAN system: the organic and the RMs pseudophases. Thus, the overall reaction can be descripted as Scheme 3 illustrates.



**Scheme 3.** Schematic representation of the reaction site in toluene/BHDC/EAN RMs.  $S_{o}^+$ ,  $CL_{o}^-$ ,  $CL_{RMs}^-$  and  $S_{RMs}^+$  are the reactants in the organic and in the RMs pseudophases, respectively.

As in the present work we used [BHDC] > critical micellar concentration (cmc) value  $(0.01 \text{ M})^{50}$ , S<sup>+</sup> is incorporated into the RMs (as is expressed by equation 3) favored by its low solubility in the aromatic solvent.

$$S_0^+ + BHDC_{RMs} \longrightarrow S_{RMs}^+$$
 (3)

where  $S_o^+$  and  $S_{RMs}^+$  symbolize the substrate in the toluene and in the RMs pseudophases, respectively. BHDC<sub>RMs</sub> represents the cationic RMs. As it is

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conventional for micellar aggregates, the concentration of micellized<sup>51</sup> surfactant defined as  $[BHDC]_{RMs}$  (where  $[BHDC]_{RMs}$  can be approximated to  $[BHDC]_{tot} - cmc$ ) can be calculated, and if the mass balance for S<sup>+</sup> ( $[S^+]_{tot} = [S^+]_o + [S^+]_{RMs}$ ) is considered, the partition constant of the substrate ( $K_p$ ) is defined as equation 4:

$$K_{p} = \frac{[S^{+}]_{RMs}}{[S^{+}]_{o}[BHDC]_{RMs}}$$

$$\tag{4}$$

Taking into consideration the procedure used previously for the RMs containing other  $ILs^{23}$ , it is possible to obtain the following rate equation (see supporting information section for a complete rate equation deduction):

$$k_{obs} = k_{obs}^{cmc} + \frac{k_2^{RMs} \beta}{\overline{v}_{BHDC}} \frac{K_p[BHDC]_{RMs}}{1 + K_p[BHDC]_{RMs}}$$
(5)

Where  $k_{obs}^{cmc}$  and  $k_2^{RMs}$  are the second order rate constants values in the cmc and [BHDC] > cmc, respectively. [BHDC]<sub>RMs</sub> is the surfactant concentration referred to the total volume,  $\overline{V}_{BHDC}$  is the molar volume of BHDC and  $\beta$  is the fraction of surfactant neutralized charge.<sup>23</sup>

As Figure 4 shows no dependence on the  $k_{obs}$  values at low  $W_s$ , the experimental data obtained for toluene/BHDC/EAN RMs at  $W_s$  between 0.02 – 0.11 were analyzed by equation 5 and for example, in Figure 5 the fitting at  $W_s = 0.02$  is presented.



Figure 5. Plot of  $k_{obs}$  values as a function of  $[BHDC]_{RMs}$  in toluene/BHDC/EAN at  $W_s$ = 0.02 analyzed according equation 5.

From the fitting of the results at W<sub>s</sub> values between 0.02 - 0.11 and using  $\overline{V}_{BHDC} = 0.42$  M<sup>-1</sup>, average values of K<sub>p</sub> = 25.1 ± 0.7 M<sup>-1</sup> and k<sub>2</sub><sup>RMs</sup>  $\beta$  = 4.4 ± 0.2 x 10<sup>-4</sup> M<sup>-1</sup> s<sup>-1</sup> were obtained. To estimate k<sub>2</sub><sup>RMs</sup> it is necessary to know the value of  $\beta$ . Previous studies showed that, independently of the RMs composition,<sup>23</sup>  $\beta$  remains constant around 0.96; thus using this value we have estimated the k<sub>2</sub><sup>RMs</sup>  $\approx$  4.6 ± 0.2 x 10<sup>-4</sup> M<sup>-1</sup>s<sup>-1</sup>. Additionally, the K<sub>p</sub> value confirms that in the toluene/BHDC/EAN RMs S<sup>+</sup> is practically located at the RMs interface. Moreover, the partition constant value is larger than in the absence of polar solvent<sup>23</sup> (K<sub>p</sub> = 22.4 ± 0.6 M<sup>-1</sup> at W<sub>s</sub> = 0). Thus, for example at [BHDC] = 0.2 M the 83% of the substrate is incorporated to the toluene/BHDC/EAN RMs.

If the same analysis is performed to the RMs at the maximum of EAN entrapped ( $W_s = 0.17$ ) where the  $k_{obs}$  values dramatically decrease in comparison with the values obtained at  $W_s$  values between 0.02-0.11 (Figure 4), values of  $k_2^{RMs} = 1.7 \pm 0.2 \times 10^{-4}$  M<sup>-1</sup>s<sup>-1</sup> and  $K_p = 18 \pm 2$  M<sup>-1</sup> are obtained. This drop on the rate constant value (about to 4 times) can be explained considering that in the RMs at the maximum of  $W_s$  reached, the

polar solvent interact much less with the interface than at low  $W_s$ , and thus a reduction in the nucleophilic power of Cl<sup>-</sup> is expected. However, it is important to note that even at  $W_s = 0.17$  the behavior of EAN confined in BHDC RMs is not equal to the neat EAN, where the reaction does not take place.

In comparison with the previous results using aprotic IL bmimBF<sub>4</sub>,<sup>23</sup> the reactivity of Cl<sup>-</sup> ions in toluene/BHDC/EAN RMs is smaller ( $k_2^{bmimBF4} = 2.3 \pm 0.1 \times 10^{-3} M^{-1} s^{-1}$ ).<sup>23</sup> In Table 1, the second order rate constant values obtained in both RMs and homogeneous media are presented. Interestingly, in the EAN case the most notable fact is that the RMs produce strong alterations in the protic solvent when entrapped in BHDC RMs which entirely affects the Cl<sup>-</sup> nucleophilicity in comparison with its behavior in homogeneous media. These alterations are more important than that the changes observed in the systems using bmimBF<sub>4</sub> (Table 1).

 Table 1. Second order rate constant (k<sub>2</sub>) values obtained in neat ILs and entrapped in

 BHDC RMs.

System	$k_2 (M^{-1}s^{-1})$
neat solvent	
EAN	N.D.
$bmimBF_4$	$2.6 \pm 0.1 \text{ x } 10^{-3a}$
RMs	
toluene/BHDC/EAN	$4.6 \pm 0.2 \ge 10^{-4}$
toluene/BHDC/bmimBF <sub>4</sub>	$2.3 \pm 0.1 \ge 10^{-3a}$

N.D.: no reaction detected. <sup>a</sup> Data from reference 23.

Hence, we show evidences that EAN can be consider as a good solvent for the

 $S_N 2$  reaction even that in homogenous media is bad option. In order to explain these results, we propose that the key is the magnitude of the hydrogen bond of EAN when the solvent is in confinement. In this sense, the ability of ILs to form hydrogen bond with a solute or between the ions in neat solvent has been described in terms of two competing equilibria.<sup>24,25</sup> In the EAN case (a protic solvent), the cation first interacts by hydrogen bond with its counterion according to equation 6:

$$Ethyl - NH_3^+ + NO_3^- = Ethyl - NH_3^+ \cdots NO_3^-$$
(6)

Additionally, the cation  $Ethyl - NH_3^+$  can also complex with the Cl<sup>-</sup> present in the reaction media (equation 7):

$$Ethyl - NH_3^+ + Cl^- \iff Ethyl - NH_3^+ \cdots Cl^-$$
(7)

Since in the reaction media both equilibria (equations 6 and 7) can be involved<sup>24,25</sup>, the results in neat EAN (where not reaction is observed) is possible to deduce that the amount of free Cl<sup>-</sup> (equation 7) is clearly very low. In contrast, in BHDC RMs we observe reaction and this is due to the availability of Cl<sup>-</sup> to react because EAN is entrapped in the organized media. This fact suggests that the amount of ethylammonium associated to the Cl<sup>-</sup> ions (Ethyl –  $NH_3^+ \cdots Cl^-$ ) is smaller than the Ethyl –  $NH_3^+ \cdots NO_3^-$  (equation 6). We believe that this phenomenon is enhanced as a consequence of the IL-interface interactions present in the BHDC RMs. In this situation, the interactions between the cationic surfactant and the ions present in the interfacial zone, also have to be considered. It seems that the cationic surfactant moiety (BHD<sup>+</sup>) cannot be solvated by  $NO_3^-$  thus, at the interface the interaction between BHD<sup>+...</sup>Cl<sup>-</sup> is stronger than

BHD<sup>+…</sup>NO<sub>3</sub><sup>-</sup> and ethylammonium only interacts with NO<sub>3</sub><sup>-</sup>. This behavior has been observed before in BHDC RMs containing other ILs such as 1-butyl-3methylimidazolium trifluoroacetate (bmimTfA).<sup>21</sup> In that work, the results suggested that even that the IL-surfactant interaction was weak (as in the present case), the ion pairing effect between bmim<sup>+</sup>-TfA<sup>-</sup> was substantially enhanced upon confinement, altering the structure and properties of the entrapped bmimTfA. Thus, the consequence of the confinement in BHDC RMs, is that EAN is more auto-associated (stronger hydrogen bond interaction between Ethyl – NH<sub>3</sub><sup>+</sup> and NO<sub>3</sub><sup>-</sup>) than in bulk solution. These strongly associated EAN molecules interact weakly with the BHDC interface, generating only small changes in the droplet sizes of the RMs, as DLS show (Figure 1).

### CONCLUSIONS

In the present contribution we have shown how upon confinement EAN can be used as suitable solvent for a  $S_N2$  reaction, situation quite different with the one observed in homogenous media where EAN acts as any protic solvent complexing the nucleophile. Additionally, to the best of our knowledge this is the first report where toluene/BHDC RMs uses EAN as polar component and is used as nanoreactor for carrying out kinetic experiments. Thus, EAN entrapped in BHDC RMs, strongly auto-associates rendering an aprotic-like IL which is not able to deactivate the nucleophilic power of Cl<sup>-</sup>. Finally, our results highlight the importance of RMs as nanoreactor media for classical reactions, where the reactants not only improve their solubilities but increase their reactivities in comparison with homogeneous media. These facts show how everything that happens in homogeneous solution has to be reconsidered because the fascinating effect of the confinement. We hope to stimulate the scientific community to use these attractive and unique nanoreactors to perform different kind of chemical reactions and

nanoparticle synthesis.

**Supplementary Information**. Figure S1: Absorption spectra of the reaction of Cl<sup>-</sup> with  $S^+$  in neat EAN at 30 °C; Figure S2: Absorbance at 340 nm as a function of time in the reaction shown in Figure 2; Table S1:  $k_{obs}$  values obtained in toluene/BHDC/EAN RMs, varying the [BHDC] at different  $W_s$  and, derivation of rate equation are available free of charge.

### **EXPERIMENTAL SECTION**

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Benzyl-n-hexadecyldimethylammonium chloride (BHDC) from Sigma (> 99% purity) was dried at reduced pressure prior use. Toluene from Sigma (HPLC quality) was used without prior purification. The IL ethylammonium nitrate (EAN) was synthesized under anaerobic condition following standard procedures according references 29 and 52. Thus, equimolar concentration of nitric acid (from Sigma, 70% in water) and ethylamine (from Sigma, 70 % in water) was used. Nitric acid was added slowly to ethylamine contained in a round-bottom flask over ice in stirring condition. Excess water was removed by drying under vacuum. Prior to use EAN was discolored with activated charcoal and dried at reduced pressure at 60 °C for 4 hours.

The substrate dimethyl-4-nitrophenylsulfonium  $(S^+)$  trifluoromethanesulfonate was synthesized following the literature procedure.<sup>40</sup>

Preparation of BHDC RMs solutions: stock solutions of BHDC in toluene were prepared by mass and volumetric dilution. Aliquots of these stock solutions were used to make individual reverse micelle solutions with different amount of IL, defined as  $W_s$ = [EAN]/[BHDC]. The incorporation of EAN into each micellar solutions were performed using calibrated microsyringes. The resulting solutions were clear with a single phase and they were used in the kinetic experiments. The  $W_s$  was varied between

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0-0.3 for toluene/BHDC/EAN RMs. It was not possible to obtain higher values of  $W_s$ due to turbidity problems. The lowest value for  $W_s$  ( $W_s = 0$ ), corresponds to a system without the IL addition. It is important to note that, at room temperature EAN is not soluble in toluene and neither in toluene/BHDC solutions at surfactant concentrations lower than the critical micelle concentration (around 0.01 M).<sup>50</sup>

*Kinetic procedure:* Nucleophilic substitution reactions were followed by monitoring the UV-Vis absorbance of the demethylated sulfide product (Scheme 2) using a HP 8452A spectrophotometer with a thermostated cell holder. In all experiments the wavelength used for kinetic studies was 340 nm. All the experiments were carried out under pseudo first order conditions were the sulfonium salt concentration ( $[S^+] = 5 \times 10^{-5} \text{ M}$ ) was always smaller than the [Cl<sup>-</sup>]. All experiments were carried out at  $30.0 \pm 0.1$  °C. Kinetics were studied by following the integrated method where the integrated first order rate equation was fitted to the kinetic data, using a nonlinear regression analysis program to give the observed rate constants,  $k_{obs}$ .<sup>23,40,41</sup> The pooled standard deviation of the kinetic data, using different prepared samples, was less than 5%. Because of solubility problems in the different media used in this study, we were forced to utilize the anion trifluoromethanesulfonate as counterion of the cationic sulfonium. No rate differences were found previously between studies involving the different sulfonium salts in molecular solvents and ILs,<sup>40,41</sup> which is consistent with the view that the cationic center itself acts as the electrophilic site for reaction.

*Kinetic procedure in neat EAN:* stock solutions of  $NH_4Cl$ , as source of Cl, dissolved in neat EAN were prepared by mass and volumetric dilution. Aliquots of these stock solutions containing Cl were added to a 1.0 cm path length UV/Vis quartz cuvette under anaerobic conditions, after which pure EAN was added to a total volume of 2 ml. After thermostatting for 15 min, the reaction was initiated by injection of a stock solution containing the sulfonium electrophile dissolved in EAN. Spectra were recorded at regular time intervals using a spectrophotometer with a thermostated sample holder. <u>*Kinetic procedure in BHDC RMs:*</u> when the reaction was investigated in toluene/BHDC/EAN RMs, the [Cl<sup>-</sup>] was modified varying only the [BHDC] ([BHDC] > cmc) at  $W_s$  = constant. Thus, the appropriate amount of toluene/BHDC/EAN stock

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solution to obtain the desired final [Cl<sup>-</sup>] in the micellar system was transferred into a 1.0 cm path length UV/Vis quartz cuvette to obtain a final volume of 2 ml. After thermostating for 15 min, the reaction was initiated by injection of a stock solution containing the sulfonium electrophile dissolved in toluene ( $[S^+] = 5 \times 10^{-3}$  M). Spectra were recorded at regular time intervals using a spectrophotometer with a thermostated sample holder.

<u>DLS experiments</u>: The apparent diameters of toluene/BHDC/EAN RMs were determined by dynamic light scattering (DLS, Malvern 4700 with goniometer) with an argon-ion laser operating at 488 nm. Cleanliness of the cuvettes used for measurements was of crucial importance for obtaining reliable and reproducible data.<sup>53</sup> Cuvettes were washed with ethanol, and then with doubly distilled water and dried with acetone. Prior to use, the samples were filtered three times using an Acrodisc with 0.2 µm PTFE membrane (Sigma) to avoid dust or particles presents in the original solution. Before introducing each sample to the cuvette, it was rinsed with pure toluene twice, then with the 0.2 M surfactant stock solution, and finally with the sample to be analyzed. Prior to making measurements on a given day, the background signals from air and toluene were collected to confirm cleanliness of the cuvettes. Prior to data acquisition, samples were equilibrated in the DLS instrument for 10 min at 30 °C. To obtain valid results from DLS measurements requires knowledge of the system's refractive index and viscosity in addition to well-defined conditions. Since we worked with dilute solutions, the

refractive indices and viscosities for the RM solutions were assumed to be the same as neat toluene.<sup>54,55</sup> Multiple samples at each size were made, and thirty independent size measurements were made for each individual sample at the scattering angle of 90°. The instrument was calibrated before and during the course of experiments using several different size standards. Thus, we are confident that the magnitudes obtained by DLS measurements can be taken as statistically meaningful for all the systems investigated. The algorithm used was CONTIN and the DLS experiments show that the polidispersity of the toluene/BHDC/EAN RMs size is less than 5 %.

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