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Influence of self-assembly of amphiphilic imidazolium ionic liquids on their host–guest complexes with cucurbit[*n*]urils

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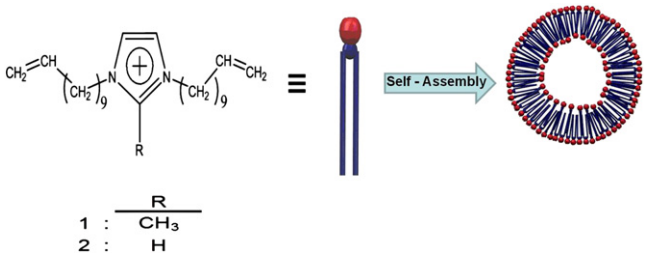
ABSTRACT

Two symmetric amphiphilic imidazolium ionic liquids having ω-undecenyl chains form supramolecular complexes with CB[7] and CB[8] in water as revealed by ^{1}H NMR spectroscopy and MALDI-MS. Binding constants in the range 10^4 to 10^5 M^{-1} were estimated from the conductivity measurements for the 1:1 complexes of these imidazolium ionic liquids with CB[7] and CB[8]. Radical initiated polymerization of these host–guest complexes at concentrations above the critical self-assembly concentration of imidazolium ionic liquids to form liposomes, destroys completely (CB[7]) or partially (CB[8]) the host–guest ionic liquid@CB[*n*] complex; this behaviour was proved by titration with acridine orange tricyclic dye, of CB[*n*]s in the colloidal solutions of the liposomes before and after performing dialysis to remove free CB[*n*]s. Thus, the increase in the fluorescence emission of acridine orange by CB[7] is not observed if the polymerized ionic liquid@CB[7] complex is submitted to dialysis to remove uncomplexed CB[7]. Analogous study by titration of absorbance change of acridine orange solutions caused by CB[8], reveals only a partial destruction of the host–guest complex by self-assembly of amphiphilic ionic liquid above the critical self-assembly concentration. The results obtained have been rationalized considering that the driving force for the formation of supramolecular ionic liquid@CB[*n*] complexes is a hydrophobic interaction between the apolar alkenyl chain and the cucurbituril interior cavity and that these hydrophobic interactions are disturbed when self-assembly leading to liposomes occurs.

1. Introduction

Amphiphilic ionic liquids with imidazolium units substituted by long ω-alkenyl chains undergo, in aqueous solutions, self-assembly giving rise to spherical liposomes from 400 to 500 nm in diameter.[1] Scheme 1 shows the structure of two symmetric amphiphilic imidazolium ionic liquids (compounds **1** and **2**) and their spontaneous assembly to form spherical agglomerates.[1] The presence of a methyl group at the 2-position of the imidazolium ring can serve to determine the influence of substitution on the association constants of the host–guest complexes. Furthermore, imidazolium ionic liquids having short chain alkyl groups such as 1-butyl-3-methyl imidazolium have been reported to form host–guest complexes with cucurbiturils.[2–9]

Cucurbiturils, CB[*n*] are pumpkin-shaped organic molecules constituted by cyclic oligomers of glycoluril units bridged by methylene groups, having an empty internal cavity.[10–14] Depending on the number of glycoluril units the size and internal cavity dimension of CB varies.[10,12,14] It has also been recently reported that



Scheme 1. Structure of two symmetric amphiphilic imidazolium ionic liquids and the resulting liposomes formed by spontaneous self-assembly.

for imidazolium ions the strength of the interaction with CBs, determined by calorimetry, depends on the CB cavity size and the alkyl chain length of ionic liquid, reaching a maximum interaction enthalpy when the length of the alkyl chain allows this hydrophobic moiety to fit completely into the CB cavity.[9] This study has concluded that CB[6] can accommodate an alkyl chain of four carbon atoms, for monocationic alkylammonium guests, and six carbon atoms for dicationic alkylammonium guests, and the strength of interaction decreases as the number of carbon atoms is lower or larger than this value.[9] Complexation of 1-alkyl-3-methyl

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imidazolium ionic liquids inside CB[6] has also been reported and the corresponding ^{1}H NMR spectra changes interpreted assuming the polarization of the imidazolium aromatic ring upon complexation.[6]

Herein we present the results showing that CB[7] and CB[8] form host–guest complexes with the amphiphilic imidazoliums **1** and **2**, that are larger molecules than others reported. However, when the critical self-assembly concentration of these compounds in water is overcome and then the liposomes are formed and maintained by cross-linking radical polymerization of the terminal C=C bond, these host–guest complexes are completely destroyed in the case of CB[7] or partially dissociated in the case of CB[8]. Accordingly, CB[7] and in part CB[8] become dissociated from imidazoliums **1** and **2** when the liposomes are formed, and freely available into the aqueous phase. The results presented are relevant to understand how self-assembly of amphiphilic compounds with long alkyl chains, influences the equilibrium of the host–guest complexes due to the variations in the hydrophobic environment when going from individual imidazolium molecules to the corresponding liposomes. Our study based on CBs complements related precedents reporting the formation of micelles and liposomes in the presence of cyclodextrins[15–18] and CBs[19,20] and provides additional evidence showing that self-aggregation of included guests alters the binding with organic capsules.

2. Results and discussion

2.1. Formation of the host–guest complexes of ionic liquids with CB[7] and CB[8]

In the first part of our study we determine the formation of unassembled host–guest complexes between CB[7] and CB[8] and imidazolium ionic liquids **1** and **2** based on ^{1}H NMR spectroscopy and MALDI-MS. Figs. 1 and 2 show the ^{1}H NMR spectra recorded in diluted aqueous solutions of imidazoliums **1** and **2** in the presence of an excess of CB[7] and CB[8], respectively. The aim for using this CB[*n*] excess is to ensure the complete complexation of imidazoliums **1** and **2** by CB. This series of ^{1}H NMR spectra were recorded by adding 20 mg of the appropriate CB to a 1 ml solution of the corresponding imidazolium (1 mg) and sonicating for 5 min. Under these conditions no complete dissolution of CB occurs, but the presence of an excess of CB does not affect the quality of the ^{1}H NMR spectra.

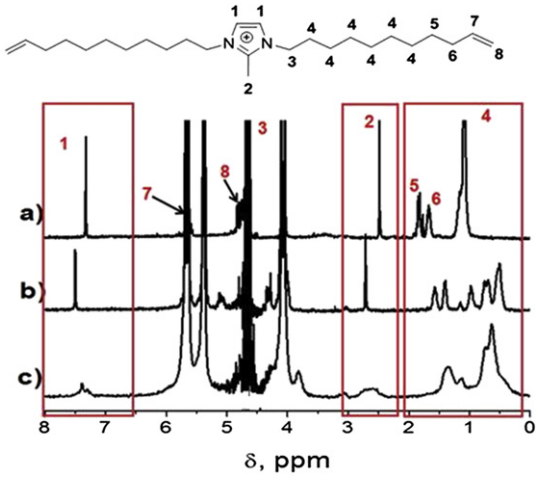


Fig. 1. ^{1}H NMR spectra recorded immediately after mixing at room temperature in deuterated aqueous solution for imidazolium **1**, 2.5×10^{-3} M (a), in the presence of 20 mg CB[7] (b) and CB[8] (c).

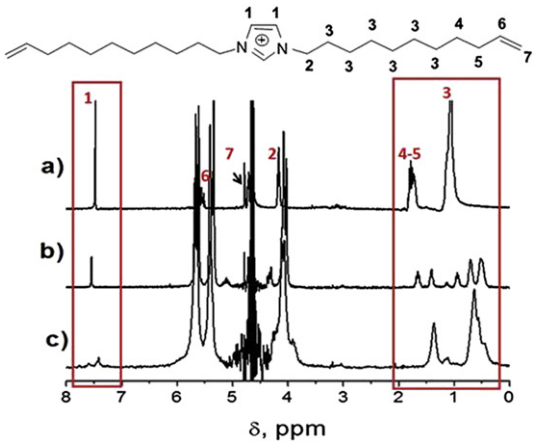


Fig. 2. . ^{1}H NMR spectra recorded immediately after mixing at room temperature in deuterated aqueous solution for imidazolium **2**, 2.7×10^{-3} M (a) in the presence of 20 mg CB[7] (b) and CB[8] (c).

For the four possible combinations (imidazoliums **1** and **2** with CB[7] and CB[8]) the corresponding ^{1}H NMR spectra show changes compatible with the formation of the host–guest complexes (see highlighted regions in Figs. 1 and 2). Moreover, in the four cases the signals of the alkyl chain (protons 4, 5 and 6 for imidazolium **1** and 3, 4 and 5 for imidazolium **2**) shifted upfield indicating the inclusion of the alkyl chain inside the organic capsule (the hydrophobic, shielded region of CBs). In addition, for the spectra containing CB[7] (Figs. 1b and 2b) the signals of the alkyl chains are doubled into two groups indicating the accommodation of a single alkyl chain inside CB[7] cavity and a slow kinetics of threading/dethreading in the NMR time scale.

In the case of CB[8], both imidazolium ionic liquids undergo broadening of the signals for all the protons, due to a fast complexation/decomplexation in the NMR time scale. The signals of the alkyl chains also shift slightly upfield indicating their inclusion inside CB[8]. In contrast, the protons of the methyl group of imidazolium ionic liquid **1** shifted downfield (up to 0.24 ppm) being this compatible with the interaction with the carbonyls at the portals (see Figs. 1c and 2c). As commented earlier, a recent precedent appeared in the literature studying the influence of the alkyl chain length on the binding constant has proposed that the hydrophobic alkyl chains of the polar imidazolium cycle 'hidden' inside CB[*n*] minimizing the hydrophobic interaction with water.

Besides the changes in the δ values of the alkenyl chain, the imidazolium ring, also shifts downfield for the complexes of ionic liquids **1** (0.19 ppm) and **2** (<0.1 ppm) with CB[7], indicating that this polar heterocycle is located near the carbonyl portals. In the case of CB[8], due to the fast to intermediate exchange rate, two aromatic signals appear as a broad band; one of them is slightly shifted downfield, being this compatible with the different interaction mode of the protons with the deshielding region of CB[8].

For a better understanding of the changes recorded in ^{1}H NMR spectroscopy, molecular models for ionic liquids **1** and **2** with CB[8] were performed (see Fig. 3a and b). In the molecular models, it can be seen that the two imidazolium protons 1 lose their symmetry because one becomes closer the carbonyl portals than the other, this explaining the presence of two ^{1}H NMR signals for them (see left highlighted region in Figs. 1c and 2c).

Association of imidazolium and CB[*n*] complexes was also supported by MALDI-MS, where an intense peak corresponding to the mass of compound **1** or **2** plus the organic capsules CB[7] or CB[8] was observed for the four possible combinations. In addition, the possibility of formation of aggregates, particularly in the case of CB [8] with or without ionic liquids as recently described[21] can be

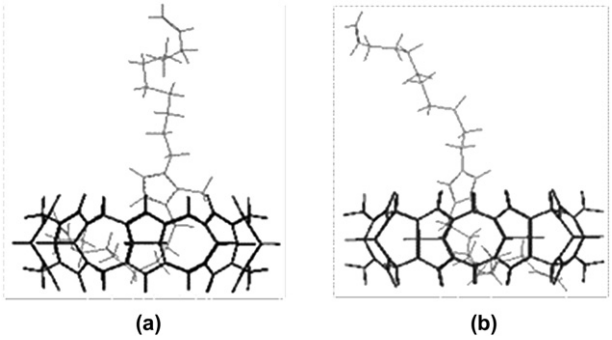


Fig. 3. Molecular models of the ionic liquid **1**@CB[8] (a) and ionic liquid **2**@CB[8] (b) calculated by MM2 molecular dynamics. Note that according to the models the symmetry of the ionic liquids is lost upon complexation.

firmly disregarded based on the lack of detection of the corresponding *n*CB[*n*] peaks or the corresponding adducts with ionic liquid (see Supplementary data). Table 1 summarizes the peaks recorded and their relative intensity. Besides the peaks corresponding to the 1:1 stoichiometry, MALDI-MS also show much less intense peaks whose value corresponds to the mass of imidazoliums **1** and **2** associated with two CB[7] or CB[8] (see Table 1). Although observation of these imidazolium@CB[*n*] complexes having 1:2 stoichiometry is interesting, the fact that their intensity is negligible with respect to the intensity of the major imidazolium@CB[*n*] 1:1 complex (100% relative intensity), indicates that the concentration of the 1:2 stoichiometry complex is low compared to the 1:1. This observation is compatible with our previous rationalization of the ^{1}H NMR spectra based on the formation of an asymmetric imidazolium@CB[*n*] 1:1 complex.

Table 1
MALDI-MS peaks and their relative intensity observed for each combination of imidazolium ionic liquid and CB

m/z	Mass	CB[7] relative intensity (%)	Mass	CB[8] relative intensity (%)
1@CB[*n*]	1549	100	1715	100
1@2CB[*n*]	2711	7.5	3043	1.8
2@CB[*n*]	1536	100	1702	100
2@2CB[*n*]	2698	2	3030	1.8

The binding constants for the 1:1 host–guest unassembled complexes **1**@CB[*n*] and **2**@CB[*n*] (*n*: 7 and 8) at a concentration of ionic liquids **1** and **2** below the critical self-assembly concentration was determined by conductimetry as described in the Experimental section. The results obtained were $(5.18\pm0.03)\times10^4$ M^{-1} and $(4.59\pm0.04)\times10^4$ M^{-1} for complexes of ionic liquid **1** with CB[7] and CB[8], respectively. For ionic liquid **2**, the corresponding binding constants were $(5.05\pm0.02)\times10^5$ M^{-1} and $(4.81\pm0.04)\times10^5$ M^{-1} for CB[7] and CB[8], respectively. The binding constants for ionic liquid **2**@CB[*n*] complex presented higher values, as we expected due to the absence of the methyl group in the 2-position of the imidazolium ring.

2.2. Self-assembly of the imidazolium@CB host–guest complexes

After having proved the formation of the individual host–guest complexes between monomeric ionic liquids **1** and **2** and CB[7] and CB[8] using diluting solutions of **1** and **2**, we were interested in determining what is the influence of liposome formation in the host–guest system. Considering that the hydrophobic interactions between the interior of CBs and the long alkenyl chain is the driving force for host–guest complexation,[9] the leading hypothesis is that this driving force should necessarily be disturbed during the self-assembly of the ionic liquid. This self-assembly leads to liposomes whose structure can be frozen by polymerization of the terminal C=C bonds.

In order to prove this hypothesis, we performed the polymerization of host–guest complexes of ionic liquids **1** and **2** with CB[7] and CB[8] at concentrations higher than the critical self-assembly concentration (4×10^{-3} M), using potassium persulfate (30 mg, 0.11 mmol) as radical initiator at 80 °C. Under the conditions in which the polymerization was performed ionic liquids **1** and **2** were in excess with respect to CB[7] and CB[8] and, therefore only a fraction of ionic liquids (about 0.25) will be forming the host–guest complex. These experimental conditions are different from those used for recording the ^{1}H NMR spectra. In addition, the presence of a small percentage of CBs does not change the critical self-assembly concentration with respect to pure imidazolium ionic liquid. Although the binding constants with CBs of ionic liquids **2** are higher than for ionic liquid **1**, this apparently does not influence the polymerization process, since the formation of the liposomes is observed in both cases.

In fact, the success of the polymerization of liposomes using these host–guest amphiphilic ionic liquid–CB[*n*] complex solutions was assessed by electron microscopy imaging. As an example of the four samples prepared, Fig. 4 shows representative TEM micrographs of the liposomes obtained in the present study that are somewhat larger than those obtained in the absence of CB[*n*], particularly in the case of CB[8].[1] The important point is that for the four combinations of ionic liquids **1** and **2** and CB[7] and CB[8], liposomes of quasi-spherical shape and average particle size ranging from 400 to 1000 nm were obtained. This increase in the average particle size of the liposomes may reflect an increase in the molecular size of the monomers undergoing self-assembly and polymerization due to the presence of CB[*n*].

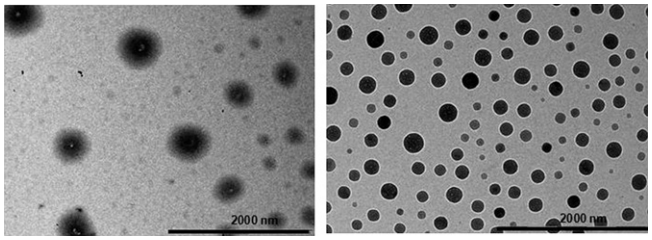
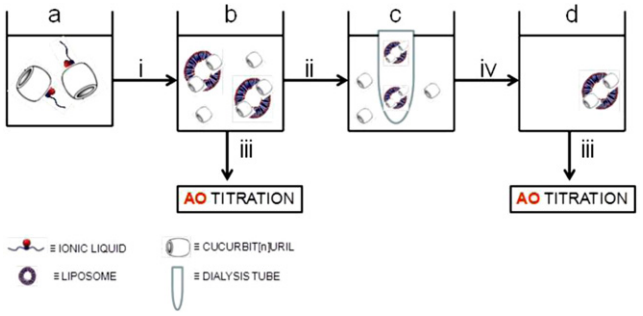


Fig. 4. TEM images of the liposomes prepared by polymerization above the critical self-assembly concentration of solutions of ionic liquid **2** containing CB[7] (right image) and CB[8] (left image).

One main point of the present work is to assess if the host–guest ionic liquid@CB[*n*] complex, characteristic of the monomeric ionic liquid, is retained when the liposome is formed. To address this point we proceeded to titrate a basic tricyclic dye, namely acridine orange (AO), with each of the four liposomes samples. Those liposomes containing available CB[7] should increase the AO fluorescence, while samples containing CB[8] are titrated based on the changes of the absorption spectrum of AO dye. In a recent publication a similar strategy using AO was employed to determine the percentage of free CB[*n*] not complexed with adamantyl amine covalently attached to a non-porous microsphere.[22] In our case to determine the availability of CBs, we compared the titration behaviour before and after dialysis of the colloidal solutions of the liposomes. Dialysis should remove from the liposome solutions most of the free, uncomplexed CBs. Our assumption was that no detection of CBs in the non-dialyzed samples is an indication that these CBs were forming a host–guest complex with the liposomes

and the difference in the AO titration before and after dialysis is due to the free, unbound CBs that are removed in the separation process.

The experimental conditions for fluorescence measurements were similar to those previously reported in the study describing the formation of AO@CB[7] complexes[23,24] and due to the high sensitivity these measurements are performed at sufficiently diluted concentrations in which AO does not form dimers (10^{-6} M) in solution. Scheme 2 illustrates the procedure used to determine the presence of CB[7] and CB[8] in the liposomes after polymerization. In a first step (a), the host–guest complexes of imidazolium ionic liquids and CBs that will act as monomers were prepared. After the polymerization of the C=C bond (b), an aliquot of the colloidal solutions of liposomes were used to titrate a 10^{-6} M solution of AO; a second aliquot was reserved and submitted to dialysis (c) in order to remove free CBs. The dialyzed solutions were titrated also with 10^{-6} M solution of AO in order to compare the fluorescence and absorption spectral changes before and after the dialysis. For the sake of comparison, we also made controls by submitting to the same protocol two analogous samples of liposomes derived from ionic liquids **1** and **2** in the absence of CBs.



Scheme 2. Procedure to determine the presence of free CB[7] and CB[8] in the liposomes resulting from the polymerization of complexes of ionic liquids **1** and **2** with CBs.

To illustrate the changes observed in the fluorescence (for those titrations of samples containing CB[7]) or optical absorption (for those samples containing CB[8]), Fig. 5 shows the set of spectra recorded for AO titration of liposomes obtained from the polymerization of ionic liquid **1** with CBs. On the other hand, Table 2 lists the relative increments of fluorescence and absorption for AO titration of liposomes obtained by polymerization of ionic liquids in the presence of CBs.

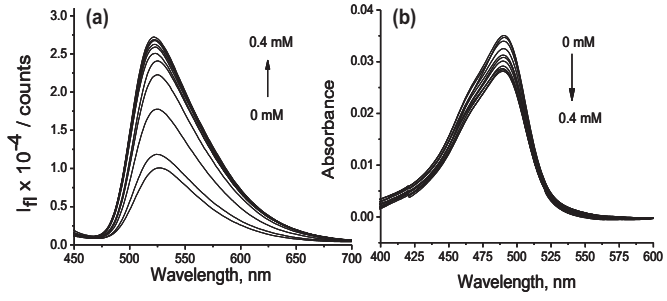


Fig. 5. Fluorescence (λ_{ex}=427 nm) (a) and absorption (b) spectra recorded for AO titrated with liposomes obtained from the polymerization of ionic liquid **1**@CB[7] complex (a) and ionic liquid **1**@CB[8] complex (b). The concentration range of ionic liquid **1** is indicated in the plot and the arrow marks the increase or decrease of the spectral signals.

It was reasoned that if the ionic liquid–CB complex is destroyed after polymerization and formation of the liposomes, purification by dialysis of the colloidal solutions of liposomes will give a sample that will show a contrasting behaviour with respect to that of the same solution not submitted to dialysis. Moreover, after polymerization and dialysis, the behaviour of the liposome if the complex is destroyed should be the same as that of the liposome obtained without CB.

Table 2
Relative increments of fluorescence intensity (CB[7]) and absorbance (CB[8]) recorded for AO when 1 μM solutions of this dye are titrated by liposomes (5 mM concentration of **1** or **2**) obtained by polymerization of **1** or **2** complexes with CBs before or after being dialyzed. Control data obtained for liposomes that have not been exposed to CBs are also included (the letter P as a prefix in the sample column indicates 'polymerized')

Sample	$\Delta I_{fl}/I_{fl}$ (%)[a]	ΔAbs/Abs[b] (%)
Before dialysis[c]		
P(**1**@CB[7])	162.0 ± 8.1	—
P(**2**@CB[7])	64.9 ± 3.24	—
P(**1**@CB[8])	—	−17.8 ± 0.9
P(**2**@CB[8])	—	−33.4 ± 1.7
After dialysis[d]		
P(**1**@CB[7])	−26.9 ± 1.4	—
P(**2**@CB[7])	−36.9 ± 1.9	—
P(**1**@CB[8])	—	−20.6 ± 1.0
P(**2**@CB[8])	—	−32.1 ± 1.6
Titrations without CB[n][e]		
P**1**	−20.4 ± 1.0	− 47.2± 2.4
P**2**	−31.9 ± 1.6	−19.4 ± 1.0

[a] $\Delta I_{fl}/I_{fl}$: relative increase of fluorescence intensity (in percentage) measured at 540 nm.
[b] ΔAbs/Abs: relative decrease of absorbance intensity (in percentage) of AO measured at 490 nm.
[c] Titration using liposomes directly after polymerization.
[d] Titration using liposomes that after polymerization have been submitted to dialysis.
[e] Titration using liposomes prepared as those indicated in footnote c, but without containing CBs.

As it can be seen in Table 2, the experimental values always indicate that dialysis reduces significantly the intensity of fluorescence for ionic liquid@CB[7] complexes, indicating that CB[7] is free after self-assembly and polymerization, and can be removed by dialysis. In agreement with this observation, the behaviour of the dialyzed liposomes containing CB[7] is very similar to that of the liposomes prepared from ionic liquids that have not been complexed with CBs and in both cases a decrease in fluorescence intensity is observed. In contrast, the titrations before dialysis reveal the presence of free CB[7] that leads to an increase in AO fluorescence.

Table 2 also shows the data corresponding to liposome formation and polymerization of CB[8] complexes. In this case titration was carried out by monitoring the changes of absorption band corresponding to AO monomer.[23] Negligible differences between the polymerized liposome before and after dialysis were observed indicating the absence of free CB[8]. In addition, these P(**1**@CB[8]) and P(**2**@CB[8]) behave differently with respect to the sample in which CB[8] was absent, i.e., P1 and P2 in Table 2. Thus, it can be concluded that the association of ionic liquids **1** and **2** with CB[8] remains after self-assembly and polymerization. Moreover, AO forms dimers inside CB[8] that exhibit characteristic absorption spectrum,[25] not observed in the present case. It is remarkable that the supramolecular complexes between ionic liquids **1** and **2** even though they are stronger for CB[7] and the kinetics of the threading/dethreading is slower, are those that are destroyed in the polymerization process at 80 °C.

In conclusion, the present data establish that amphiphilic ionic liquids characterized by a polar imidazolium head and long ω-undecenyl hydrophobic chains form in water host–guest complexes with CB[7] and CB[8] of moderate binding constants. In the

case of CB[7] the host–guest complexes with monomeric ionic liquids are apparently destroyed upon self-assembly of the amphiphilic ionic liquid at values above the critical self-assembly concentration and polymerization of the carbon–carbon double bond in the liposomes. This decomplexation was demonstrated by comparing samples of the liposomes that have been submitted or not to dialysis with the behaviour of liposomes that have never been exposed to CB[7]. In contrast, due to its larger cavity size, the host–guest complexes of ionic liquids **1** and **2** with CB[8] survive self-assembly and polymerization, since no changes in the behaviour of the liposomes before and after dialysis with respect to AO titration are observed and these samples behave differently than the control liposome without CB[8]. The present results have been rationalized considering that the driving force for host–guest complexation is the hydrophobic interaction between long alkenyl chains and the interior of the cucurbiturils. Self-assembly and liposome formation is also a phenomena arising from hydrophobic forces and in this way competes with and disturbs the formation of the supramolecular inclusion complexes, causing their destabilization in the case of CB[7]. For CB[8] the larger size allows apparently self-assembly without destruction of the host–guest complex.

3. Experimental section

3.1. General

All the materials used in the present work were commercially available and used as received. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker AV-300 spectrometer at 300 and 75 MHz, respectively. MALDI-TOF analyses were performed on a RÈFLEX IV (Bruker Daltonics) mass spectrometer. The TEM pictures were taken using a Philips CM300 FEG system with an operating voltage of 100 kV.

3.2. Synthesis of the ionic liquids 1 and 2

Ionic liquid **1** was prepared starting from 2-methylimidazole and 11-bromo-1-undecene in toluene as previously reported in the literature.[1] Ionic liquid **2** was prepared analogously, but using imidazole instead of 2-methylimidazole, by performing the reaction at reflux temperature for 48 h adding triethylamine as a base. After this time the reaction mixture was cooled and filtered to remove the ammonium salt and the clear solution was concentrated under vacuum. The oily residue was exhaustively washed with hexanes. Compound **2** was obtained as viscous oil. The overall yield was 63%. ^{1}H NMR (300 MHz, D_2O): δ=7.54 (s, 3H), 5.71–5.57 (m, 2H), 4.84–4.79 (dd, J_1=6.0 Hz, J_2=6.3 Hz, 4H), 4.23–4.03 (t, J_1=10.2 Hz, J_2=10.5 Hz, 4H), 1.88–1.77 (m, 8H), 1.13 (m, 24H); ^{13}C NMR (75 MHz, D_2O): δ=138.58, 122.69, 114.37, 72.05, 62.48, 49.25, 33.76, 29.71, 29.69, 29.67, 29.65, 29.62, 29.61, 29.01, 6.37 ppm.

3.3. Polymerization of the host–guest complexes

Prior to polymerization, liposomes of complexes of ionic liquids and CBs were prepared using 77.5 mg (0.2 mmol) and 74.8 mg (0.2 mmol) of ionic liquids **1** and **2**, respectively, dissolved in 50 ml of milliQ water and adding 0.025 mmol of CBs. The solution was stirred at 40 °C for 92 h under inert atmosphere. After this time, a catalytic amount of potassium persulfate (30 mg) was added to the solution. The solution was stirred for 24 h at 80 °C. Formation of the corresponding liposomes was monitored by TEM and the particle size distribution determined by counting a statistically relevant number of liposomes.

3.4. Conductimetry titrations

Binding constants for ionic liquids **1** and **2** below the critical self-assembly concentration were determined by conductimetry using a Crison conductivity-meter 524 previously calibrated using aqueous KCl solutions. In brief, to an aqueous solution (10^{-4} M and 10^{-5} M for titration of ionic liquids **1** and **2**, respectively) of CB[7] and CB[8] in milliQ water, aliquots of 50 μl of ionic liquid **1** (10^{-2} M) and ionic liquid **2** (10^{-3} M) were added under magnetic stirring and the conductivity value measured immediately after equilibration.

$$\Lambda_m = \frac{\Lambda \cdot 1000}{[IL]} \quad (1)$$

$$\theta = \frac{\Lambda_m - \Lambda_{m0}}{\Lambda_{m\infty} - \Lambda_{m0}} \quad (2)$$

$$\frac{1}{K_B} = \frac{dy}{dx} \quad (3)$$

From these conductivity values (Λ), the molar conductivity (Λ_m) was estimated by applying Eq. 1, and the molar conductivity at 0 (Λ_{m0}) and ∞ ($\Lambda_{m\infty}$) concentration were determined from the plots of Λ_m versus concentration of ionic liquids **1** and **2** ([IL1] and [IL2], respectively). With these values (Λm, Λm_0 and Λm_∞) the dissociation level (θ) was determined by applying Eq. 2. The binding constant (K_B) was calculated from the slope of the linear relationship between $1/\theta$ versus 1/[IL] by applying Eq. 3 (see Supplementary data for more details).

3.5. Dialysis

Dialysis was performed by placing the solution containing the liposomes obtained by polymerization of the host–guest ionic liquid@CB[n] complex (5 ml of a 10^{-4} M solution in CB[n]) in a tubular dialysis membrane (Sigma–Aldrich benzoylated dialysis tubing, average flat width of 32 mm, normalized molecular weight cut off 2000). The dialysis membrane was previously washed by putting it into milliQ water for 24 h. This tube containing the liposomes solution to be dialyzed was placed in a 500 ml beaker containing milliQ water. The solution was magnetically stirred and the content of the beaker replaced four times each 24 h.

3.6. Measurements of the concentration of CB[7] and CB[8] by titration with acridine orange (AO)

The presence of free CB[7] and CB[8] was established by titration of AO solutions either by fluorescence (CB[7]) or absorption spectroscopy (CB[8]). These measurements were carried out by diluting 10 times the titrating solutions and adding increasing volumes (30 μl each) of these solutions (up to 300 μl) in a cuvette containing 3 ml of a 10^{-6} M solution of AO. No significant changes in the absorbance of the band of AO monitored at 427 nm (corresponding to the excitation wavelength) were observed, making the correction of the emission due to AO dilution unnecessary. Fluorescence measurements were carried out after purging the cuvette and the titrating solution with a N_2 flow (1 ml/min) for at least 15 min before the measurements. Fluorescence spectra were recorded with a PTI LPS-220B and absorption spectra with a JASCO-1650 spectrophotometer. Three different solutions were titrated. Two of them were those corresponding to the liposomes obtained by polymerizing the host–guest ionic liquid@CB[n] before and after dialysis. The third solution was a control of a liposome solution obtained by polymerization of ionic liquids **1** and **2** in the absence of CB[n] (see Supplementary data for more details).

3.7. UV–visible titrations

Titration of uncomplexed CB[8] present after polymerization of the **1**@CB[8] and **2**@CB[8] complexes were carried out by adding increasing volumes (30 μl each) of the solutions containing the polymerized complexes in the range from 0 to 300 μl to a 10^{-6} M aqueous solution of AO monitoring the UV–visible absorption spectrum of the solution after each addition (see Supplementary data for more details).

3.8. ^{1}H NMR titrations

^{1}H NMR spectra were recorded in a Bruker AV-300 at 300 MHz spectrometer using D_2O as solvent (1 ml) and 1 mg of the ionic liquid. This results in a concentration of 2.6 and 2.7 mM for ionic liquids **1** and **2**, respectively. The spectra of the host–guest complexes were recorded under these conditions but after saturating the D_2O with 20 mg of CB[7] or CB[8]. This situation corresponds to an excess of CBs (1.7×10^{-2} M) with respect to ionic liquids, whose concentration was constant (2.6×10^{-3} M and 2.7×10^{-3} M for **1** and **2**, respectively). These conditions using over stoichiometric amounts of host ensure the possibility the complete complexation of ionic liquids.

3.9. MALDI-TOF mass spectrometry

MALDI-TOF measurements of solutions containing ionic liquids and CBs were performed with a RÈFLEX IV (Bruker Daltonics) mass spectrometer. The relative intensity of the ions appearing in Table 1 was determined by the instrument (see Supplementary data for more details).

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Supplementary data

Supplementary data related to this article can be found in the online version, at doi:10.1016/j.tet.2012.03.044.

References and notes

1. Buaki, M.; Aprile, C.; Dhakshinamoorthy, A.; Alvaro, M.; Garcia, H. *Chem.—Eur. J.* **2009**, *15*, 13082–13089.
2. Montes-Navajas, P.; Corma, A.; Garcia, H. *J. Mol. Catal. A: Chem.* **2008**, *279*, 165–169.
3. Jiao, D. Z.; Biedermann, F.; Scherman, O. A. *Org. Lett.* **2011**, *13*, 3044–3047.
4. Noujeim, N.; Leclercq, L.; Schmitzer, A. R. *J. Org. Chem.* **2008**, *73*, 3784–3790.
5. Wang, R. B.; Yuan, L. N.; Macartney, D. H. *Chem. Commun.* **2006**, 2908–2910.
6. Zhao, N.; Liu, L.; Biedermann, F.; Scherman, O. A. *Chem. Asian J.* **2011**, *5*, 530–537.
7. Liu, L.; Zhao, N.; Scherman, O. A. *Chem. Commun.* **2008**, 1070–1072.
8. Biczok, L.; Wintgens, V.; Miskolczy, Z.; Megyesi, M. *Isr. J. Chem.* **2011**, *51*, 625–633.
9. Wintgens, V.; Biczok, L.; Miskolczy, Z. *Supramol. Chem.* **2010**, *22*, 612–618.
10. Cintas, P. *J. Inclusion Phenom. Mol. Recognit. Chem.* **1994**, *17*, 205–220.
11. Das, D.; Scherman, O. A. *Isr. J. Chem.* **2011**, *51*, 537–550.
12. Lagona, J.; Mukhopadhyay, P.; Chakrabarti, S.; Isaacs, L. *Angew. Chem., Int. Ed.* **2005**, *44*, 4844–4870.
13. Lee, J. W.; Samal, S.; Selvapalam, N.; Kim, H. J.; Kim, K. *Acc. Chem. Res.* **2003**, *36*, 621–630.
14. Mock, W. L. *Cucurbiturils, Supramolecular Chemistry* **1995**, *175*, 1–24 Taylor and Francis.
15. Kolman, V.; Marek, R.; Strelcova, Z.; Kulhanek, P.; Necas, M.; Svec, J.; Sindelar, V. *Chem.—Eur. J.* **2009**, *15*, 6926–6931.
16. Leclercq, L.; Lacour, M.; Sanon, S. H.; Schmitzer, A. R. *Chem.—Eur. J.* **2009**, *15*, 6327–6331.
17. Topchieva, I.; Karezin, K. *J. Colloid Interface Sci.* **1999**, *213*, 29–35.
18. Ondo, D.; Tkadlecov, M.; Dohnal, V.; Rak, J.; Cala, J.; Lehmann, L. K.; Heintz, A. A.; Ignatiev, N. *J. Phys. Chem. C* **2011**, *115*, 10285–10297.
19. Pessego, M.; Basilio, N.; Moreira, J. A.; Garcia-Rio, L. *ChemPhysChem* **2011**, *12*, 1342–1350.
20. Zhou, Q.; Wang, H.; Gao, T.; Yu, Y.; Ling, B.; Mao, L.; Zhang, H.; Meng, X.; Zhou, X. *Chem. Commun.* **2011**, 11315–11317.
21. Da Silva, J. P.; Jayaraj, N.; Jockusch, S.; Turro, N. J.; Ramamurthy, V. *Org. Lett.* **2011**, *13*, 2410–2413.
22. Hennig, A.; Hoffmann, S.; Borcherding, H.; Thiele, T.; Schedlerb, U.; Resch-Gengerahem, U. *Chem. Commun.* **2011**, 7842–7844.
23. Montes-Navajas, P.; Garcia, H. *J. Photochem. Photobiol., A* **2009**, *204*, 97–101.
24. Montes-Navajas, P.; Gonzalez-Bejar, M.; Scaiano, J. C.; Garcia, H. *Photochem. Photobiol. Sci.* **2009**, *8*, 1743–1747.
25. Montes-Navajas, P.; Corma, A.; Garcia, H. *ChemPhysChem* **2008**, *9*, 713–720.