New supramolecular amphiphiles based on renewable resources†

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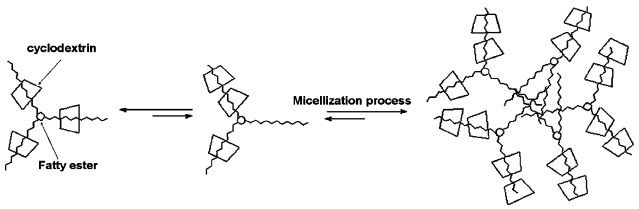
The complexation between esters derived from sorbitol and β-cyclodextrin was studied. Isosorbide dioleate and sorbitan trioleate formed well-defined inclusion complexes with β-cyclodextrin and these inclusion complexes exhibited surfactant behaviour.

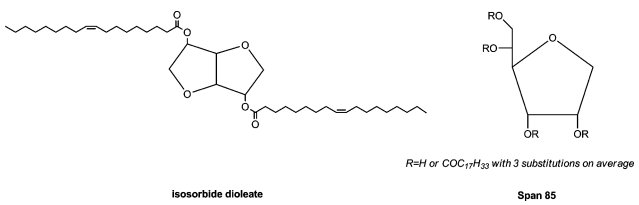
Native cyclodextrins are oligosaccharides composed of six or more D-glucopyranose residues attached by β-1,4-linkages in a cyclic array. The most common cyclodextrins contain six, seven or eight glucose residues and are named α-cyclodextrin (α-CD), β-cyclodextrin (β-CD) and γ-cyclodextrin (γ-CD), respectively. They have the shape of a truncated cone with a hydrophobic inner cavity.[1] This internal cavity can accommodate a wide range of guest molecules, ranging from polar compounds such as alcohols, acids, amines and small inorganic anions to apolar compounds such as aliphatic and aromatic hydrocarbons.[2] Numerous researchers have investigated the interaction between surface active compounds and cyclodextrin.[3] In particular, it has been demonstrated that the formation of inclusion complexes between cyclodextrin and surfactant greatly modifies the surface active properties of the surfactant. In fact, this association generally results in the hydrophilisation of surfactant leading to an increase in CMC (critical micelle concentration).[4] Indeed, the inclusion of the hydrophobic part of the surfactant molecule into the CD cavity postpones the micellization process.[5] However, surface active supramolecular entities can be formed in the presence of cyclodextrin. For instance, it is well known that cyclodextrins can be used as additives to stabilize emulsions. In this case, cyclodextrins form *in situ* surface active agents by interacting with the components of the oil phase at the oil/water interface.[6] The interaction between non-ionic polyethylene oxide-based surfactants and β-cyclodextrin[7] or amphiphilic β-cyclodextrin[8] gives also rise to noncovalent amphiphiles. Interestingly, it has been recently demonstrated that surface active inclusion complexes can be isolated by using a suspension method. So, N. Laugh-de Viguerie *et al.* have reported that inclusion complexes of cyclodextrin with fatty alcohols or fatty acids behave as supramolecular surfactants.[9] The β-CD/alcohol inclusion complexes were found to be much more surface active than the β-CD/acid complexes. Furthermore, the surface properties of the β-CD/alcohol complexes were strongly dependent on the length of hydrocarbon chain and only alcohols having 10–12 carbon atoms exhibited surface activity. In fact, the surface activity of these supramolecular complexes was attributed to hydrophobic chain of the guest protruding outside of the CD cavity.

In this work, we have investigated the possibility of forming supramolecular amphiphiles by noncovalent associations between β-cyclodextrin and highly hydrophobic polyesters containing several alkyl chains. Indeed, contrary to previous studies, it was expected that use of such compounds will make the formation of micelles easier, as schematically represented in Scheme 1 by using a guest containing three alkyl chains



Scheme 1 Formation of micelle from amphiphile inclusion complexes.

In fact, we have postulated that the presence of several long alkyl chains on the guest should permit a redistribution of cyclodextrins, leading to well-defined hydrophilic and hydrophobic parts. In order to validate our concept, two sorbitol derivatives substituted by oleoyl chains were chosen as guest. These compounds were isosorbide dioleate and sorbitan trioleate (Span 85) (Scheme 2).



Scheme 2 Sorbitol-derivatives esters chosen for the elaboration of supramolecular surfactant **1** and **2**.

These compounds are environmentally friendly and produced from renewable resources. So, the dehydration of sorbitol yields a mixture of sorbitan and the further dehydration of sorbitan

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produces isosorbide.[10] Esterification of these compounds gives rise to isosorbide dioleate and sorbitan trioleate (Span 85).[11]

Inclusion complexes between β-CD and sorbitol-derivatives substituted by oleoyl residues were prepared using the suspension method. Briefly, an aqueous equimolar suspension of β-CD and esters was vigorously stirred at room temperature for 24 h. The resulting suspension was filtered to collect a white powder. This experiment was performed with isosorbide dioleate and the Span 85 as guest and β-CD as host and the resulting solids collected are named compounds **1** and **2**, respectively.

The collected precipitates were analyzed by ^{1}H NMR spectroscopy in DMSO-d_6. As an example, the ^{1}H NMR spectrum of compound **2** is displayed in Fig. 1.

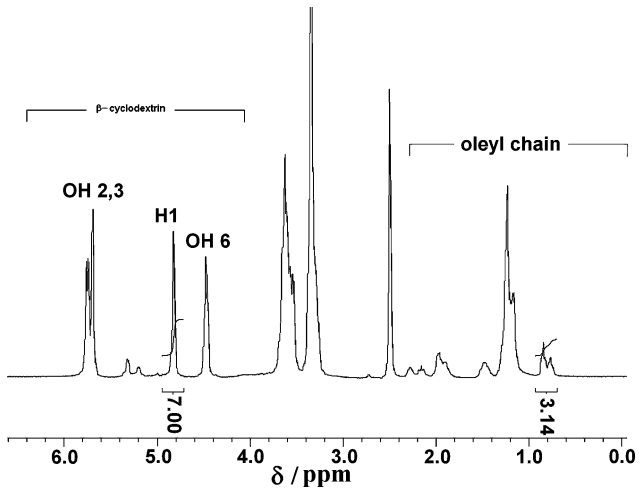

Fig. 1 ^{1}H NMR spectrum of the compound **2** collected after mixing Span 85 and β-CD with suspension method (DMSO-d_6).

For the two samples, characteristic peaks of both β-CD and esters were observed. Furthermore, integration of ^{1}H NMR signals of the methyl protons of esters (δ = 0.84 ppm) and H1 protons of β-CD (δ = 4.85 ppm) allowed determination of the relative amount of cyclodextrin and ester in the sample. Interestingly, the amount of CD was found to be three times more important than that of ester in the solids containing sorbitan trioleate. In contrast, for isosorbide dioleate, β-CD amount was twice as important than that of isosorbide dioleate. It is worth mentioning that these ratios were also confirmed by elemental analysis on the precipitates. Finally, we have determined that the β-CD/ester ratios in the precipitates were independent of the initial amounts of β-CD and ester. Indeed, all preparations conducted with different β-CD/ester ratios (2 : 1; 1 : 1 and 1 : 2) have led to precipitates containing a CD/sorbitan trioleate ratio and a CD/isosorbide dioleate ratio of 3 and 2, respectively.

These above experiments, and the fact that compounds **1** and **2** rapidly precipitate when esters are mixed with cyclodextrin aqueous solution below the solubility limit of the macrocycle alone, suggest that the precipitates are well-defined compounds. In fact, it is reasonable to assume that these compounds are inclusions complexes.

In order to confirm this hypothesis, the samples were analyzed by differential scanning calorimetry (DSC). Indeed, the disappearance or shifting of endothermic peaks in DSC thermograms are generally an indication of the formation of inclusion complexes.[12] For comparison, pure esters, β-CD and β-CD/esters physical mixtures obtained by simple blending were also analyzed by DSC. The experiments were conducted from –40 °C to 220 °C as both esters were liquid at room temperature. The results obtained with the β-CD and Span 85 are represented in Fig. 2.

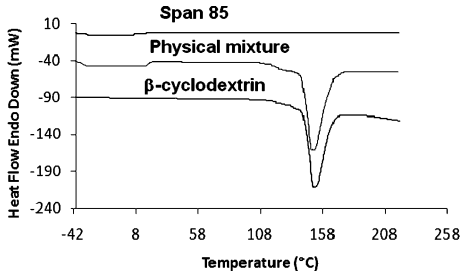

Fig. 2 DSC curves of β-CD, Span 85 and physical mixture of Span 85/β-CD. First cycle of heating from –40 to 220 °C (flow 10 °C min^{-1}).

As expected for β-CD, a large endothermic peak is observed at about 150 °C when β-CD is heated from –40 °C to 220 °C for the first time (Fig. 2). This broad peak disappears during the second cycle of heating and is attributed to the loss of crystal water (see ESI†). In this range of temperature, it should be noticed that no supplementary peaks are observed as the melting and decomposition of the β-CD occur at 265 °C (see ESI†).[13] The thermogram of pure Span 85 shows a broad endothermic peak at about 0 °C, corresponding to the melting of the crystalline forms of this ester mixture (Fig. 2). The DSC thermogram of the physical mixture heated for the first time shows the same broad endothermic peak at around 0 °C and a large endothermic peak at about 155 °C. In fact, it appears clearly that the DSC curve of the physical mixture is a superposition of the DSC curves of pure Span 85 and β-CD, confirming that no inclusion occurs by physical blending.

DSC thermograms of compound **2** show special features compared with the pure β-CD and Span 85, as well as the β-CD/Span 85 physical mixture (Fig. 3).

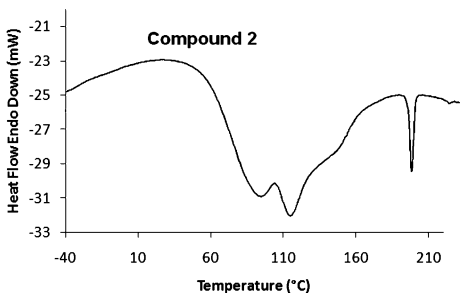

Fig. 3 DSC curve of compound **2**. First cycle of heating from –40 to 220 °C (flow 10 °C min^{-1}).

For the first heating of compound **2**, the peak corresponding to the Span 85 at 0 °C has disappeared. Two new peaks at about 100 °C and at 195 °C are noticed (Fig. 3). Interestingly, the peaks

observed at about 100 °C have disappeared during the second cycle of heating, suggesting a dehydration process.

During the second cycle of heating, it also should be noticed that the small endothermic peak at 195 °C is still observed and that an exothermic peak appears at 175 °C when compound **2** is cooled (Fig. 4). The enthalpies ΔH for transitions at 175 °C and 195 °C are found to be similar, indicating that these peaks are associated with the melting and crystallisation processes of the same compound. In fact, it seems that the peak at 175 °C corresponds to the crystallization of a supercooled liquid phase. Finally, it is worth mentioning that the pure β-CD endothermic peak at 265 °C was no longer present when compound **2** was heated to 300 °C (ESI†). These DSC data undoubtedly indicate that compound **2** is not a simple mixture of β-CD and Span 85. Indeed, the presence of a single peak at 195 °C on the thermogram suggests the participation of both species in the formation of a new crystalline phase such as inclusion complex.[14]

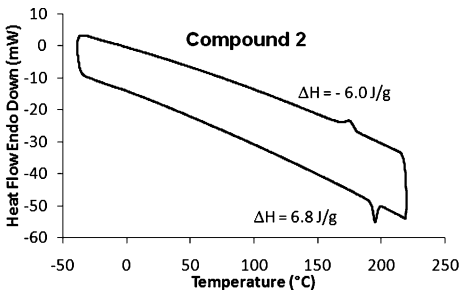

Fig. 4 DSC curve of compound **2**. Second cycle of heating (down) and cooling (up) (flow 10 °C min^{-1}).

Finally, DSC experiments performed on compound **1** also suggest that **1** is an inclusion complex. Indeed, the endothermic peak corresponding to the melting point of isosorbide dioleate ester disappears in the DSC thermogram and a new peak at 190 °C is observed (ESI†).

In order to determine if compounds **1** and **2** are effectively supramolecular amphiphiles, the surfactant properties of Span 85/β-CD and isosorbide dioleate/β-CD were tested by surface tension measurements. As oleate esters are not soluble in water, surface tension effect of Span 85 or isosorbide dioleate alone could not be performed. Fig. 5 shows the variation of surface tension as a function of inclusion complexes concentration.

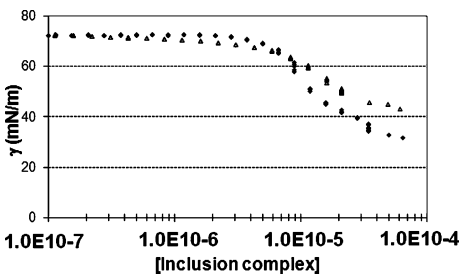

Fig. 5 Variation of the surface tension (γ) in water *versus* the concentration of compound **1** (△) and **2** (♦).

For both inclusion complex solutions, an appreciable decrease in surface tension is observed from a concentration of complex about 8×10^{-6} M until the limit of solubility is achieved. Furthermore, a breakpoint could be noticed at 3×10^{-5} M in each case. This surface activity cannot be attributed to the decomplexation of inclusion complexes. Indeed, the aqueous solution remained clear and the formation of an oil phase composed of sorbitan trioleate or isosorbide dioleate was never observed. In these conditions, it can be considered that sorbitan trioleate/β-CD and isosorbide dioleate/β-CD inclusion complexes exhibit a surfactant behavior with CMC values in the range 3×10^{-5} to 5×10^{-5} M. Furthermore, these inclusion complexes appear as powerful surfactants, since they greatly reduce the surface tension of pure water from 72 mN m^{-1} to values between 32 and 42 mN m^{-1}.

In conclusion, we have demonstrated that new supramolecular amphiphiles can be easily obtained from renewable resources. Indeed, sorbitan trioleate and isosorbide dioleate form well-defined inclusion complexes with the β-CD and these inclusion complexes exhibit high surface activity. Works are currently underway to determine precisely the origin of the surface activity and especially the structure of the surface-active inclusion complexes in aqueous solution.

Acknowledgements

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