Thermodynamic Evidence of Cyclodextrin−Micelle Interactions

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The enthalpy of transfer (ΔH_t) of hydroxypropyl-α-cyclodextrin (HP-α-CD), hydroxypropyl-β-cyclodextrin (HP-β-CD), and β-cyclodextrin (β-CD) from water to the aqueous $C_6F_{13}CO_2Na$ and $C_7F_{15}CO_2Na$ solutions were determined in the pre- and post-micellar regions. The behavior of the macrocycles is system specific. Generally, the magnitude of the enthalpy is influenced by several factors: (1) the alkyl chain length of the surfactant, (2) the cyclodextrin cavity and its alkylation, (3) the interactions between the free cyclodextrin and the free surfactant, (4) the host−guest equilibrium constant, (5) the host/guest stoichiometry, and (6) the micelle-cyclodextrin (free and/or complexed) interactions. As far as the premicellar region is concerned, HP-α-CD does not form the host−guest complexes. β-CD and HP-β-CD in the aqueous $C_7F_{15}CO_2Na$ solutions form host−guest complexes of 1:1 stoichiometry; β-CD shows a larger binding affinity toward the surfactant as a compensative effect between the more negative enthalpy and entropy. Besides 1:1 complexes, HP-β-CD in aqueous $C_6F_{13}CO_2Na$ solutions forms complexes of 1:2 stoichiometry (1 cyclodextrin:2 surfactants). Their presence was evidenced by the minimum in the ΔH_t vs the surfactant concentration ($f_S m_S$) trend. The equation derived to take into account both 1:1 and 1:2 complexes equilibria was successfully applied to the present data and those of HP-α-CD/sodium alkanoate systems previously studied by us. As far as the postmicellar region is concerned, HP-α-CD was treated like an additive, which distributes between the aqueous and the micellar phases. An equation was proposed to rationalize the enthalpy data dealing with the cyclodextrins exhibiting inclusion complex formation. It was based on the following phenomena: (1) formation of 1:1 and 1:2 complexes in the aqueous phase, (2) distribution of free cyclodextrin, 1:1 complex, and 1:2 complex between the aqueous and the micellar phases, and (3) shift of the micellization equilibrium induced by the cyclodextrin. As a general feature, cyclodextrin (free and/or complexed) shows affinity toward the micelles because of the favorable interactions between the carboxylate head in the hydrophilic shell and the hydroxyl groups of the cyclodextrin. $C_6F_{13}CO_2Na$ micelles compared to $C_7F_{15}CO_2Na$ exhibit a slightly larger affinity toward HP-α-CD controlled by more negative enthalpy and entropy changes. A single mechanism governs the interaction between the $C_7F_{15}CO_2Na$ micelles and the 1:1 complexes of HP-β-CD/surfactant and β-CD/surfactant, as the standard free energy, enthalpy, and entropy of transfer of the two complexes from the aqueous to the micellar phases are identical. The 1:2 complex (1 HP-β-CD:2 $C_6F_{13}CO_2Na$) weakly binds to the micelles according to the unfavorable interactions between the micellar surface and the doubly charged complex.

Introduction

It is well documented[1,2] that cyclodextrins form inclusion complexes with a variety of inorganic and organic molecules in aqueous solution. The formation of host−guest complexes occurs through desolvation of both species. Nevertheless, the stability of the complex is related to the amount of water, which may be released by the cyclodextrin upon the encapsulation of the guest molecule.[3,4] Connors[5] reported that amphiphilic compounds form high stability complexes and alkanes do lower stability complexes. Surfactants belong to the former class of guest molecules. Because they undergo the micellization process, the studies are usually confined to the premicellar region. Techniques such as NMR,[6−9] surface tension,[10] potentiometry,[11] sound velocity,[12] etc. were used to determine the host−guest binding constant (K). From the bulk thermodynamic properties (calorimetry,[3,11,13,14] density,[15−19] and heat capacity[15,18]), K and the change in the property for the host−guest complex formation were simultaneously estimated.

Experiments extended to micellar solutions are very few as the cyclodextrin plays only a cosolvent effect on the micellization process. In other words, in our knowledge, micelle−cyclodextrin interactions never were evidenced. Traditionally, it is accepted that the micellization process occurs whenever all of the cyclodextrin is in the complexed form. Therefore, for the 1:1 complexes, the cmc, called *apparent critical micellar concentration*, is expressed[20] as the sum of the stoichiometric cyclodextrin concentration and the cmc in water (cmc_w). Thus, the monomer surfactant concentration is nearly equal to cmc_w. Indeed, this occurs for large K values, but it is not a general rule.[18,21] In fact, even in large excess of free cyclodextrin, the surfactant undergoes the micellization process if its concentration is nearly close to cmc_w.[18] If the host−guest complexes are absent, the cyclodextrin behaves like a hydrophilic cosolvent, which increases the cmc.[18]

Jobe et al.[22] determined the aggregation number of sodium dodecyl sulfate (NaDS) micelles in aqueous solutions of various cyclodextrins. It was inferred that inclusion complexes have a little effect on the size and shape of the micelles toward which

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they do not show affinity. The conclusions drawn from this study are convergent with those of Junquera et al., who showed that the aggregation numbers of dodecylethyldimethylammonium bromide[23] and hexadecyltrimethylammonium bromide[12] micelles are unchanged upon the addition of the cyclodextrin. Kinetic studies did not evidence interactions between cyclodextrin and micelles.[21] As thermodynamic studies are concerned, the apparent molar volumes of sodium perfluoroalkanoates in aqueous solutions of hydroxypropyl-cyclodextrins of various sizes were determined.[18] The obtained partial molar volume of the surfactant in the micellar phase is not affected by the presence of the cyclodextrin. Volume and heat capacity of transfer of dodecyltrimethylammonium bromide (DTAB) and NaDS from water to the aqueous β-cyclodextrin solution exhibit a maximum and a minimum, respectively, at the surfactant concentration around at the cmc_w, thereafter they sharply change reaching a null value at high concentration.[24] As well, the profiles of the apparent molar relative enthalpies and osmotic coefficients as functions of the surfactant concentration are influenced by the presence of the macrocycle.[25] We reported elsewhere[3] that the enthalpy of transfer of hydroxypropyl-β-cyclodextrin from water to the aqueous sodium alkanoate micellar solutions shows a negative dependence on the surfactant concentration. The attempt to ascribe the magnitude of the enthalpy to the presence of inclusion complexes in the aqueous phase and the shift of micellization equilibrium, induced by the cyclodextrin, was unsuccessful. Thus, in contrast to the traditional findings, the presence of interactions between micelle and cyclodextrin was invoked. Unfortunately, the narrow range of the surfactant concentration analyzed (because of the experimental difficulties) did not permit to verify this hypothesis.

To gain further insights into this aspect, we planned to study the calorimetric behavior of hydroxypropyl-α-cyclodextrin (HP-α-CD), hydroxypropyl-β-cyclodextrin (HP-β-CD), and β-cyclodextrin (β-CD) in the aqueous solutions of sodium perfluoroheptanoate and sodium perfluorooctanoate. The hosts were chosen to make a comparison between the effects of the diameter of the macrocycle cavity and the presence of alkyl substituents in the cyclodextrin annulus. The guests are surfactants more hydrophobic than their homologous hydrogenated; accordingly, for $C_6F_{13}CO_2Na$ and $C_7F_{15}CO_2Na$, at 25 °C, the cmc_w values are 0.03 and 0.09 mol kg^{-1} respectively.[18] Thus, it is expected that a wide range of the surfactant concentration in the micellar region may be experimentally investigated. Because HP-β-CD[9,18] and β-CD[7,8,16,17] form inclusion complexes and HP-α-CD[18] does not, we may evidence specific binding affinity of the free cyclodextrin and/or the complex toward the micelles. Finally, the effect of the alkyl substituents in the macrocycle on the complex formation as well as on the cyclodextrin-micelle interactions may be investigated from the enthalpy data dealing with HP-β-CD and β-CD.

Experimental Section

Materials. Perfluoroheptanoic acid (Aldrich) was neutralized with a sodium hydroxide ethanolic solution at 313 K to obtain the corresponding sodium salt ($C_6F_{13}CO_2Na$). The product was precipitated by cooling and was recovered by filtration. Then, it was dried in a vacuum oven at 313 K for at least 4 days. The procedure to synthesize $C_7F_{15}CO_2Na$ from the perfluorooctanoic acid (Fluka) is reported elsewhere.[26] The aqueous surfactant solutions gave pH ≈ 8.5.

The purity of the surfactants was confirmed by their standard partial molar volumes in water, evaluated from density measurements, which agree with those calculated by the additivity rule.[18]

Hydroxypropyl-α-cyclodextrin (HP-α-CD, Sigma), hydroxypropyl-β-cyclodextrin (HP-β-CD, Acros), and β-cyclodextrin (β-CD, Acros) were used as received. The average molar substitution for each glucopyranose residue is 0.6 for HP-α-CD and 0.43 for HP-β-CD. To take into account for the water content in the cyclodextrins, the concentration value of each cyclodextrin aqueous solution was evaluated by using the procedure reported elsewhere.[15]

All solutions were prepared by mass using degassed conductivity water and their concentrations were expressed as molalities.

Equipment. The calorimetric measurements were carried out at 298 ± 0.01 K with a flow LKB 2107 microcalorimeter. The injection of the solutions into the microcalorimeter was made by means of a Gilson peristaltic pump (Minipuls 2).

The experimental enthalpy (ΔH^{exp}) was determined as the difference between the thermal effect due to the mixing process of the cyclodextrin solution with the surfactant solution and that due to the dilution process of the same surfactant solution with water ($\Delta H_{id,S}$). For HP-β-CD, the measurements were carried out at a fixed cyclodextrin concentration (0.0185 mol kg^{-1} at the equilibrium) in a wide interval of the surfactant concentration. Some experiments dealing with HP-β-CD in $C_7F_{15}CO_2Na$ were also done at 0.0075 mol kg^{-1}. The β-cyclodextrin concentration value analyzed is 0.0075 mol kg^{-1} (at the equilibrium) due to its low solubility in water.

The flows of the solutions were determined by weight.

For the mixing of the surfactant and the cyclodextrin solutions, the final concentration of the surfactant ($f_S m_S$) and the cyclodextrin ($f_C m_C$) solutions were calculated by using the dilution factors

$$f_S = \Phi_S/(\Phi_S + \Phi_C) \quad (1)$$

$$f_C = \Phi_C/(\Phi_S + \Phi_C) \quad (2)$$

where Φ_C and Φ_S are the flows of water in the cyclodextrin and surfactant solutions, respectively.

Conductivity. The specific conductivity measurements were performed at 298.0 ± 0.1 K (digital conductimeter Analytical Control 120) in order to evaluate the critical micellar concentration of the surfactant and the degree of ionization of the micelles (β) in water and in the water + cyclodextrin mixture. The former corresponds to the intersection point of the straight lines (in the pre- and postmicellar regions) of the plot of specific conductivity vs surfactant concentration, whereas β is given by the ratio of the slopes of these straight lines.[27] The cmc and β values are collected in Table 1.

Enthalpy of Dilution Calculation. For each cyclodextrin, the enthalpy of dilution with water ($\Delta H_{id,C}$) was calculated by means of the following equations:

$$\Delta H_{id,C} = (L_{\Phi,C})_f - (L_{\Phi,C})_i \quad (3)$$

$$L_{\Phi,C} = B_C m_C + C_C m_C^2 \quad (4)$$

where $L_{\Phi,C}$ is the apparent molar relative enthalpy. The subscripts "i" and "f" indicate the initial and final states, respectively. B_C and C_C are the pair and triplet solute−solute interaction parameters, respectively, the values of which are reported elsewhere.[3] In the case of β-CD, the $\Delta H_{id,C}$ value is 0.1 kJ mol^{-1}.[25]

Enthalpy of Transfer Calculation. The enthalpy of transfer (ΔH_t) of cyclodextrin from water to the aqueous surfactant solution was calculated as difference between ΔH^{exp} and $\Delta H_{id,C}$.

TABLE 1: Physicochemical Properties of Sodium Perfluoroalkanoates in Water and Water + Cyclodextrin Mixtures and Thermodynamic Properties for the Cyclodextrin−Substrate Complex Formation at 298 K[i]

	ΔH_m	V_S	cmc	β	$K_{1:1}$	$\Delta G^0_{1:1}$	$\Delta H_{1:1}$	$T\Delta S^0_{1:1}$	$K_{1:2}$	$\Delta G^0_{1:2}$	$\Delta H_{1:2}$	$T\Delta S^0_{1:2}$
					Water							
$C_6F_{13}CO_2Na$	10[a]	188.22[b]	0.076[c];0.09[b]	0.66[c]								
$C_7F_{15}CO_2Na$	8.9[d]	213.87[e]	0.03[b]	0.56[b]								
					HP-α-CD ($f_Cm_C = 0.0185$ mol kg^{-1})							
$C_6F_{13}CO_2Na$			0.09[c];0.07[f]	0.65[c]								
$C_7F_{15}CO_2Na$			0.035[c];0.034[f]	0.59[c]								
$C_7H_{15}CO_2Na$[g]					731 ± 83	−16.3 ± 0.3	−12.1 ± 0.1	4.2 ± 0.3				
$C_7H_{15}CO_2Na$[h]					800	−16.6	−12.24 ± 0.06	4.4	960	−17.0	−1.6 ± 0.3	15.4
					HP-β-CD ($f_Cm_C = 0.0185$ mol kg^{-1})							
$C_6F_{13}CO_2Na$			0.09[c];0.07[f]	0.67[c]	(1.5 ± 1.5) × 10^3	−18 ± 2	−16 ± 1;	2 ± 1				
$C_6F_{13}CO_2Na$[h]					2 × 10^3	−18.8	−16.8 ± 0.2	2.0	17 × 10^4	−29.8	−13.3 ± 0.2	16.5
$C_7F_{15}CO_2Na$			0.042[c,f]	0.62[c]	(0.7 ± 0.2) × 10^3	−16.2 ± 0.7	−19.5 ± 0.5;	−3.3 ± 0.9				
					β-CD ($f_Cm_C = 0.0075$ mol kg^{-1})							
$C_7F_{15}CO_2Na$			0.032[g]		(6.6 ± 1.8) × 10^3	−21.8 ± 0.7	−28.3 ± 0.3	−6.5 ± 0.8				

[a] From ref 34. [b] From ref 18. [c] From conductivity. [d] From ref 30. [e] From ref 35. [f] From enthalpy. [g] From ref 3. [h] Results of the best fit according to eq 17. [i] Units are as follows: cmc, mol kg^{-1}; $K_{1:1}$, kg mol^{-1}; $K_{1:2}$, kg^2 mol^{-2}; free energy, enthalpy and entropy, kJ mol^{-1}; V_S, cm^3 mol^{-1}.

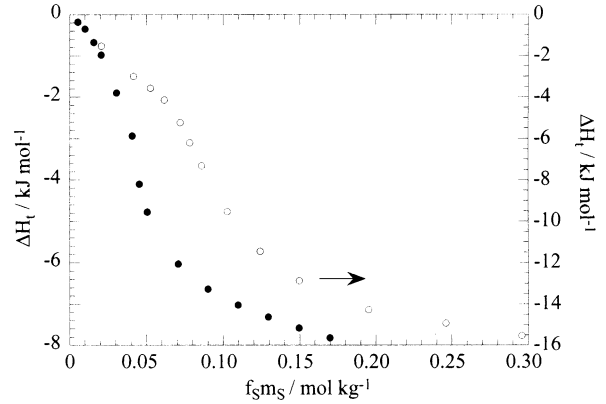

Figure 1. Enthalpy of transfer of HP-α-CD from water to the aqueous solutions of $C_6F_{13}CO_2Na$ (open symbols) and $C_7F_{15}CO_2Na$ (filled symbols) as a function of the surfactant concentration.

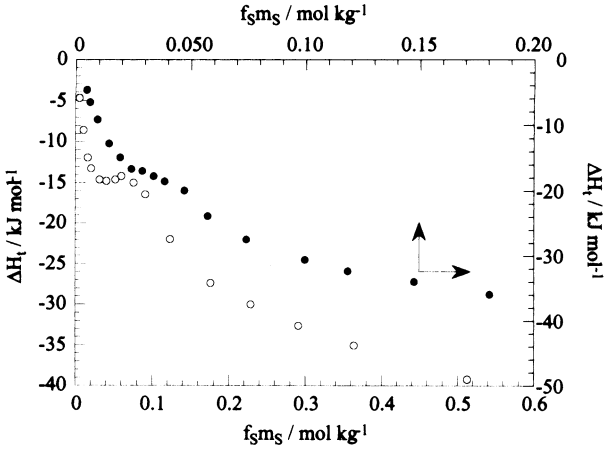

Figure 2. Enthalpy of transfer of HP-β-CD from water to the aqueous solutions of $C_6F_{13}CO_2Na$ (open symbols) and $C_7F_{15}CO_2Na$ (filled symbols) as a function of the surfactant concentration.

Results

Figure 1 illustrates the plots of ΔH_t vs f_Sm_S for the HP-α-CD/$C_6F_{13}CO_2Na$ and the HP-α-CD/$C_7F_{15}CO_2Na$ systems. ΔH_t decreases linearly with f_Sm_S up to ≈0.07 and ≈0.04 mol kg^{-1} for $C_6F_{13}CO_2Na$ and $C_7F_{15}CO_2Na$, respectively; thereafter, it monotonically tends to a constant value at high f_Sm_S. As can be seen in Figure 2, ΔH_t for HP-β-CD/$C_7F_{15}CO_2Na$ decreases in a nonlinear manner with f_Sm_S and exhibits a further decrease around at ca. 0.04 mol kg^{-1}. The ΔH_t vs f_Sm_S trend of HP-β-CD/$C_6F_{13}CO_2Na$ displays a smooth minimum around at ca. 0.04 mol kg^{-1} and a maximum at ca. 0.07 mol kg^{-1} and thereafter decreases. The breaks in the graphs shown in Figures 1 and 2 appear at f_Sm_S values equal to cmc_w for $C_6F_{13}CO_2Na$ and cmc for $C_7F_{15}CO_2Na$ (Table 1). The minimum in Figure 2 is reminiscent of peculiarities detected for other systems.[3] Namely, for the HP-α-CD transfer from water to the aqueous solutions of $C_3H_7CO_2Na$, $C_5H_{11}CO_2Na$ and $C_7H_{15}CO_2Na$, ΔH_t vs f_Sm_S curves display pronounced minima localized at lower concentrations the higher the substrate hydrophobicity is. As well, the ΔH_t vs f_Sm_S curves of HP-β-CD/$C_8H_{17}CO_2Na$ and HP-β-CD/$C_9H_{19}CO_2Na$ exhibited smooth maxima. The data points in the surfactant region below the anomalies were interpreted in terms of the 1:1 inclusion complex formation. The phenomenon responsible for the presence of these peculiarities was not clarified, as the micellization did not explain them. On this aspect, we shall return later.

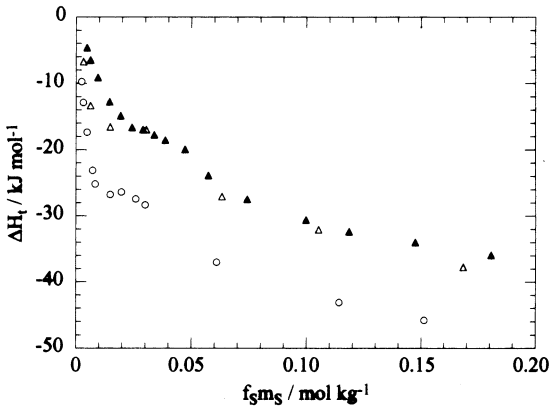

Figure 3. Enthalpy of transfer of HP-β-CD (triangles) and β-CD (circles) from water to the aqueous solutions of $C_7F_{15}CO_2Na$ as a function of the surfactant concentration. Open symbols, $f_Cm_C = 0.0075$ mol kg^{-1}; filled symbols, $f_Cm_C = 0.0185$ mol kg^{-1}.

The features of the enthalpy data for $C_7F_{15}CO_2Na$/β-CD 0.0075 mol kg^{-1} are similar to those for $C_7F_{15}CO_2Na$/HP-β-CD 0.0185 mol kg^{-1} (Figure 3). The large difference in the values may be ascribed to the nature of the cyclodextrin. In fact, the cyclodextrin concentration plays a small effect as the few experimental points dealing with HP-β-CD 0.0075 mol kg^{-1} show (Figure 3). The cmc in the ΔH_t vs f_Sm_S curve is localized at a higher f_Sm_S value upon the increase of the cyclodextrin concentration (Table 1). In particular, the difference in the cmc

corresponds to that in the cyclodextrin concentration values according to the large equilibrium constant for the 1:1 host−guest complex formation.

The cyclodextrin cavity size plays an important role in the premicellar region because the host shows a different affinity toward the guest. The features of enthalpy data for β-CD and HP-β-CD are consistent with the presence of the cyclodextrin-surfactant complexation equilibrium, whereas those for HP-α-CD do not. As well, all of the data in the postmicellar region seem to evidence interactions between micelle and cyclodextrin (free and/or complexed).

Quantitative Analysis of the Experimental Data

The qualitative analysis of the experimental data evidenced the different behavior of HP-α-CD with respect to HP-β-CD and β-CD. For this reason, in the following, two different quantitative approaches shall be proposed.

HP-α-CD in Aqueous Sodium Perfluoroalkanoate Solutions. *Premicellar Region.* The linear dependence of ΔH_t on $f_S m_S$ (Figure 1) excludes the presence of host−guest complexes. This evidence is corroborated by studies showing that α-cyclodextrin[7] and HP-α-CD[18] do not form inclusion complex with fluorinated surfactants because of the small diameter of the macrocycle.

The experimental data may be fitted by means of the McMillan-Mayer approach:[28]

$$\Delta H_t = (2h_{CS} + 3h_{CCS} f_C m_C) f_S m_S + ... \quad (5)$$

where h_{CS} and h_{CCS} represent the pair and triplet cyclodextrin−surfactant interaction parameters, respectively. As observed for the HP-γ-CD/$C_5H_{11}CO_2Na$ system,[3] one may assume that only the h_{CS} interaction term contributes to ΔH_t because the cyclodextrin concentration is low. The h_{CS} values of -34.5 ± 0.6 and -22 ± 1 kJ mol^{-2} kg for HP-α-CD/$C_6F_{13}CO_2Na$ and HP-α-CD/$C_7F_{15}CO_2Na$ were obtained, respectively.

Postmicellar Region. HP-α-CD may be treated like a classical additive, which distributes between the aqueous and the micellar phases according to the following equation:[29]

$$\Delta H_t = \Delta H_{t,C} + \Delta H_t(w \rightarrow aq) - (\Delta H_{t,C} - A_{cdc}\Delta H_m)N_f \quad (6)$$

where $\Delta H_{t,C}$ indicates the standard enthalpy of transfer of the cyclodextrin from the aqueous to the micellar phases and ΔH_t-(w → aq) represents the enthalpy of transfer of the cyclodextrin at the cmc (it may be estimated by means of eq 5 at $f_S m_S$ = cmc). The quantities N_f and $A_{cdc}\Delta H_m N_f$ represent the fraction of the cyclodextrin in the aqueous phase and the shift of micellization equilibrium term, respectively:[29]

$$A_{cdc}\Delta H_m = (\Delta H_m \text{cmc}/2)(2.3K_S + (1+\beta)K_b) \quad (7)$$

$$N_f = 1/[1 + K_b(f_S m_S - \text{cmc})] \quad (8)$$

where K_S and K_b represent the Setchenov constant and the cyclodextrin−micelle binding constant, ΔH_m is the enthalpy of micellization, and β is the degree of ionization of the micelles (Table 1).

The best fits (Figure 4) of the experimental data to eqs 6−8 provided K_b, $\Delta H_{t,C}$, and K_S. Their values are reported in Table 2.

The standard free energy and entropy of transfer of cyclodextrin from the aqueous to the micellar phases were calculated as[29]

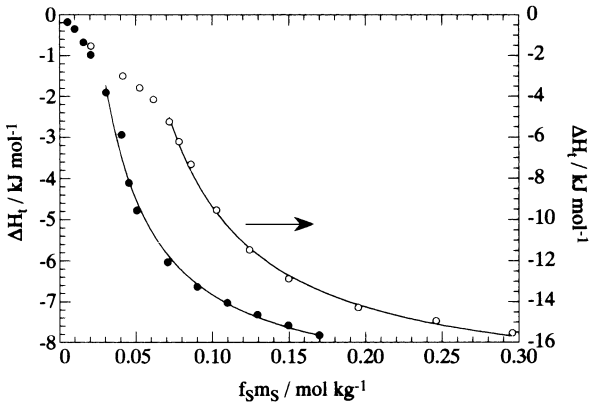

Figure 4. Best fits of the experimental data for HP-α-CD in micellar solutions of $C_6F_{13}CO_2Na$ (open circles) and $C_7F_{15}CO_2Na$ (filled circles) according to eq 6.

$$\Delta G^0_{t,C} = -RT \ln K \quad (9)$$

$$T\Delta S^0_{t,C} = \Delta H_{t,C} - \Delta G^0_{t,C} \quad (10)$$

where K is the partition constant in the molarity scale given by K_b/V_S, with V_S being the partial molar volume of the micellized surfactant (Table 1).

To obtain the thermodynamic properties that evidence the micelle binding affinity toward the macrocycle, the properties of transfer were corrected for the cyclodextrin-surfactant interactions in the aqueous phase according to[30]

$$\Delta G^0_{t,C}(w \rightarrow M) = \Delta G^0_{t,C} + 2.3RTK_S\text{cmc} \quad (11)$$

$$\Delta H_{t,C}(w \rightarrow M) = \Delta H_{t,C} + \Delta H_t(w \rightarrow aq) \quad (12)$$

HP-β-CD in Aqueous Sodium Perfluoroalkanoate Solutions. *Premicellar Region.* The standard enthalpy ($\Delta H_{1:1}$) associated to the formation of 1:1 host−guest complex was obtained from[3]

$$\Delta H_t = \Delta H_t(w \rightarrow w + s) + X_{1:1}\,\Delta H_{1:1} \quad (13)$$

where $X_{1:1}$ is the fraction of the complex correlated to the equilibrium constant ($K_{1:1}$) as

$$K_{1:1} = X_{1:1}/\{f_C m_C(1 - X_{1:1})(R - X_{1:1})\} \quad (14)$$

here $R = f_C m_C / f_S m_S$.

$\Delta H_t(w \rightarrow w + s)$ is the term of interaction between free cyclodextrin and free surfactant, which can be calculated by means of eq 5. It is negligible in the presence of the inclusion complex equilibrium.[3] For this reason, whenever will be the case, we shall neglect it.

According to eq 13, the shape of ΔH_t vs $f_S m_S$ trend reflects the change of $X_{1:1}$ with $f_S m_S$. This occurs for β-CD and HP-β-CD (at both concentrations analyzed) in aqueous $C_7F_{15}CO_2Na$ solutions and for HP-β-CD in aqueous $C_6F_{13}CO_2Na$ solutions up to 0.04 mol kg^{-1}. An example of the best fit is shown in Figure 5, whereas the $K_{1:1}$ and $\Delta H_{1:1}$ values together with the standard free energy ($\Delta G^0_{1:1}$) and entropy ($T\Delta S^0_{1:1}$) for the inclusion complex formation (eqs 9 and 10) are collected in Table 1.

The different dependence of ΔH_t on $f_S m_S$ for HP-β-CD 0.0185 and 0.0075 mol kg^{-1} in the aqueous $C_7F_{15}CO_2Na$ solutions is only due to the difference in the cyclodextrin concentrations (eq 14). In fact, the experimental data at 0.0075 mol kg^{-1} are

TABLE 2: Thermodynamic Properties for the Binding between Cyclodextrins and Sodium Perfluoroalkanoate Micelles at 298 K[a]

	HP-α-CD		HP-β-CD	
	$C_6F_{13}CO_2Na$	$C_7F_{15}CO_2Na$	$C_6F_{13}CO_2Na$	$C_7F_{15}CO_2Na$
K_b	18 ± 2	24 ± 4		
K_S	−18 ± 1	−24 ± 2		11 ± 1
$\Delta G^0_{t,C}$	−11.3 ± 0.3	−11.7 ± 0.4		
$\Delta H_{t,C}$	−18.4 ± 0.4	−9.3 ± 0.4		
$T\Delta S^0_{t,C}$	−7.1 ± 0.5	2.4 ± 0.6		
$\Delta G^0_{t,C}(w \rightarrow M)$	−18.5 ± 0.4	−16.4 ± 0.6		
$\Delta H_{t,C}(w \rightarrow M)$	−23.2 ± 0.4	−11.1 ± 0.4		
$T\Delta S^0_{t,C}(w \rightarrow M)$	−4.7 ± 0.8	5.3 ± 0.7		
$K^M_{1:1}$				21 ± 3
$\Delta G^0_{t,1:1}$			−11.4 ± 0.4[b]	−11.4 ± 0.4
$\Delta H_{t,1:1}$			−18.1 ± 0.4	−13.3 ± 0.9
$T\Delta S^0_{t,1:1}$			−6.7 ± 0.6	−1.90 ± 0.98
$K^M_{1:2}$			3.5 ± 0.2	
$\Delta G^0_{t,1:2}$			−7.2 ± 0.1	
$\Delta H_{t,1:2}$			−16.6 ± 0.5	
$T\Delta S^0_{t,1:2}$			−9.4 ± 0.5	

[a] Units are as follows: free energy, enthalpy, and entropy, kJ mol^{-1}; binding constant and Setchenov constant, kg mol^{-1}. [b] Stated equal to $\Delta G^0_{t,1:1}$ of HP-β-CD/ $C_7F_{15}CO_2Na$ system (see text).

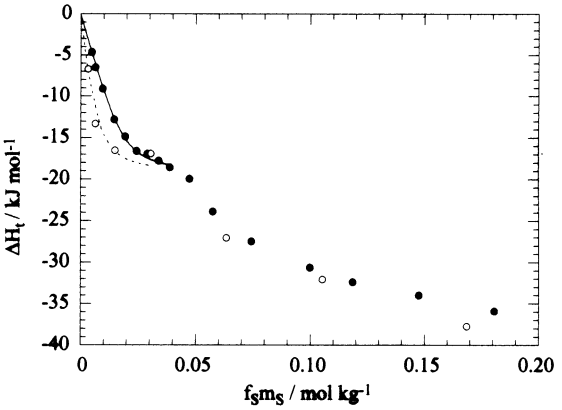

Figure 5. Enthalpy of transfer of HP-β-CD 0.0075*m* (open symbols) and 0.0185*m* (filled symbols) as a function of the surfactant concentration. Solid line, fit according to eq 13. Broken line, simulation of data at $f_C m_C$=0.0075 mol kg^{-1} (see text).

well simulated by the enthalpy estimated by using $K_{1:1}$ and $\Delta H_{1:1}$ obtained from the data at 0.0185 mol kg^{-1} (Figure 5). This evidences that at least up to 0.0185 mol kg^{-1} $\Delta H_{1:1}$ corresponds to the standard property.

The minimum in the enthalpy curve of HP-β-CD in aqueous $C_6F_{13}CO_2Na$ solutions (Figure 2) at $f_S m_S$ = 0.04 mol kg^{-1} is not unusual because, as stated earlier, minima or maxima are exhibited by the ΔH_t vs $f_S m_S$ trends of other systems. We may attempt to ascribe them to nonideal effects arising from the higher surfactant concentrations; in other words, we assume that $K_{1:1}$ and $\Delta H_{1:1}$ are no more constant thereafter the maxima or minima. As far as $K_{1:1}$ is concerned, the nonideal contribution is negligible because the activity coefficient of the free cyclodextrin may be stated unity and those of the free surfactant and the complex largely cancel out even at moderate ionic strength.[13] As concerns the enthalpy, based on the McMillan−Mayer approach,[28] $\Delta H_{1:1}$ was expressed in terms of the standard partial molar property and the contribution for the interactions between like and unlike solute molecules. Despite the fact that the simulation of the experimental data resulted in very good fits for the present and the literature[3] systems, the physical meaning of the fitting parameters provided unreliable information.

Higher order complexation 1 cyclodextrin:2 substrates (1:2) and/or 2 cyclodextrins:1 substrate (2:1) may take into account these peculiarities. A ^{19}F NMR chemical shift study[9] of sodium perfluoroalkanoates in β-CD and its alkylated derivatives showed that the steric effects due to the cyclodextrin alkylation influence the stoichiometry and the host/guest binding affinity. Thus, β-CD forms 1:1 and 2:1 complexes with $C_7F_{15}CO_2Na$ and $C_8F_{17}CO_2Na$, whereas methylated cyclodextrins form 1:1 and 1:2 complexes with $C_8F_{17}CO_2Na$. Complexes of 2:1 stoichiometry may be formed by the guest having long alkyl chain which, in part, is encapsulated into the cyclodextrin cavity and, in part, is protruded to the bulk solution. In the excess of the macrocycle, the capping of a second cyclodextrin molecule onto the 1:1 complex may occur. Besides β-CD/sodium perfluoroalkanoates,[7,9] these complexes were evidenced for 2,6-O-dimethyl-β-cyclodextrin/hexadecyltrimethylammonium bromide,[12] β-CD/sodium alkanoates,[16] etc. On the basis of these literature findings, the anomalies in the enthalpy curves cannot be correlated to the 2:1 complexes because they would be present in the $f_S m_S$ region where the surfactant is in excess relative to cyclodextrin. Furthermore, it is unreliable the onset of 2:1 binding between HP-α-CD and sodium alkanoates featured by short alkyl chains. Notwithstanding, attempts to simulate the enthalpy data by assuming the formation of 1:1 and 2:1 complexes were done. For this purpose, we used the $K_{1:1}$ and $\Delta H_{1:1}$ available values. Moreover, the 2:1 complex equilibrium constant ($K_{2:1}$) and the corresponding enthalpy ($\Delta H_{2:1}$) were arbitrarily changed. The general result is that the simulation successfully fitted the data points in the surfactant region below the anomalies according to the 1:1 complex formation, but it was unable to predict the data above them. Simulations of enthalpy data by using arbitrary $K_{1:1}$ and $\Delta H_{1:1}$ values did not even reproduce the data in the dilute surfactant region. Figure 6 shows an example of simulation for the HP-α-CD/$C_7H_{15}CO_2Na$ system. The $K_{2:1}$ value chosen (7.3 kg^2 mol^{-2}) is 2 orders of magnitude lower than $K_{1:1}$ (Table 1) according to literature findings,[9,16] and $\Delta H_{2:1}$ is −20 kJ mol^{-1}. Note that the calculated ΔH_t values remained practically unchanged even using 20 kJ mol^{-1} for $\Delta H_{2:1}$.

Thus, the hypothesis of the higher order 1:2 complexation for the systems investigated is the most reliable. Accordingly, the maxima or minima in the enthalpy curves occur because of the appearance of the 1:2 complex contribution, which becomes more and more important with increasing the surfactant concentration. Note that in the literature[9] only 1:1 complexes

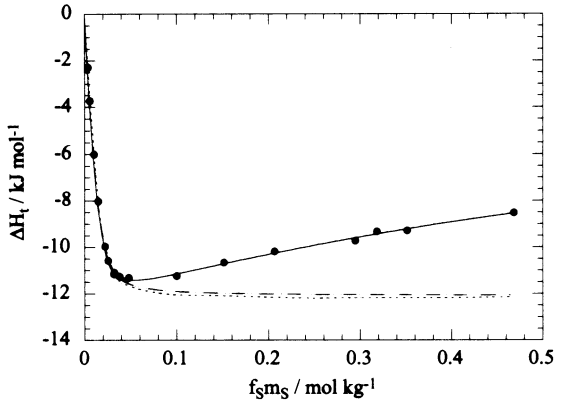

Figure 6. Enthalpy of transfer of HP-α-CD from water to the aqueous $C_7H_{15}CO_2Na$ solutions as a function of the surfactant concentration. − − −, simulation according to the 1:1 complex formation. ···, simulation according to the 1:1 and 2:1 complex formation. Solid line, fit according to eq 17.

were evidenced for the HP-β-CD/$C_6F_{13}CO_2Na$ system, but we remind the reader that methylated cyclodextrins form 1:2 complexes with $C_8F_{17}CO_2Na$.

Therefore, we revised eq 13 to consider the simultaneous 1:1 and 1:2 inclusion complex formation equilibria

$$\mathrm{CD} + \mathrm{S} \rightarrow \mathrm{CD\text{-}S} \tag{15}$$

$$\mathrm{CD} + 2\mathrm{S} \rightarrow \mathrm{CD\text{-}S_2} \tag{16}$$

where CD and S represent the cyclodextrin and the surfactant, respectively.

The following was obtained

$$\Delta H_t = \Delta H_t(\mathrm{w} \rightarrow \mathrm{w} + \mathrm{s}) + X_{1:1}\Delta H_{1:1} + X_{1:2}\Delta H_{1:2} \tag{17}$$

here $X_{1:2}$ represents the fraction of the 1:2 complex, which can be related to the equilibrium constant $K_{1:2}$, whereas $\Delta H_{1:2}$ is the enthalpy change (eq 16). The meaning of the other symbols is the same as above.

To fit the experimental data through eq 17, the Newton−Raphson method was used to calculate the concentration of the species in solution. Then, in the minimization procedure, $K_{1:1}$ and $K_{1:2}$ were changed in order to minimize the standard deviation of $\Delta H_t/X_{1:1}$ vs $X_{1:2}/X_{1:1}$ plot, which provided $\Delta H_{1:1}$ and $\Delta H_{1:2}$ as intercept and slope of the obtained straight line, respectively. The minimization of the experimental data resulted in very good fits for the present as well as the literature[3] systems. For each system, both $K_{1:1}$ and $\Delta H_{1:1}$ values are very close to those obtained by applying eq 13 to the surfactant concentration region below the minima or maxima. These findings confirm that the 1:1 host−guest complex formation is the dominant process in the surfactant dilute region. However, some aspects need to be discussed. Namely, for HP-α-CD in aqueous solutions of $C_3H_7CO_2Na$ and $C_5H_{11}CO_2Na$ and for HP-β-CD in aqueous solutions of $C_8H_{17}CO_2Na$ and $C_9H_{19}CO_2Na$, very low $K_{1:2}$ and very large $\Delta H_{1:2}$ values were obtained. This minimizing procedure provides unreliable estimates of $\Delta H_{1:2}$ when $K_{1:2}$ values are low and the range of the surfactant concentration is narrow. Figure 6 shows an example of the minimization according to eq 17. It is evident that the equilibrium for 1:1 complex formation alone does not take into account the experimental data in all of the range of the surfactant concentration. The same occurs if the simultaneous 1:1 and 2:1 inclusion complex formation equilibria are considered (Figure 6). The results of the best fits for the HP-α-CD/$C_7H_{15}CO_2Na$ and HP-β-CD/$C_6F_{13}CO_2Na$ systems are collected in Table 1 together with the standard free energy and entropy for the 1:1 and 1:2 complex formation (eqs 9 and 10).

Postmicellar Region. A number of phenomena affect the magnitude of ΔH_t in the postmicellar region: the formation of complexes of different stoichiometry in the aqueous phase, the interactions between micelle and cyclodextrin (free and complexed), and the shift of micellization equilibrium induced by the cyclodextrin. By taking into account all of these contributions and by assuming that the properties in the aqueous phase correspond to those in water, the power of the mixing process of a micellar solution and a cyclodextrin solution is written as

$$\begin{aligned}\Delta W/(\Phi_C + \Phi_S) = {} & m^w_{1:1}[H^w_{1:1} - H_{M,f} - H_{C,f}] + \\ & m^w_{1:2}[H^w_{1:2} - 2H_{M,f} - H_{C,f}] + m^M_{1:1}[H^M_{1:1} - H_{M,f} - H_{C,f}] + \\ & m^M_{1:2}[H^M_{1:2} - 2H_{M,f} - H_{C,f}] + f_S m_S(H_{M,f} - H_{M,i}) - \\ & \mathrm{cmc}'(H_{M,f} - H_{m,f}) + f_C m_C(H_{C,f} - H_{C,i}) + \\ & f_S \mathrm{cmc}_w(H_{M,i} - H_{m,i}) + m_{C,M}(H_{C,M} - H_{C,f})\end{aligned} \tag{18}$$

where $H_{1:1}$ and $H_{1:2}$ indicate the partial molar enthalpies of the 1:1 and 1:2 complexes, respectively; H_M and H_m are the partial molar enthalpies of the micellized and unmicellized surfactant, respectively; H_C is the partial molar enthalpy of the free cyclodextrin. cmc′ represents the monomer surfactant concentration in the final state. The symbols "w" and "M" stand for the aqueous and the micellar phases, respectively. The subscripts "i" and "f" indicate the initial and final states, respectively.

On the basis of the pseudo-phase-transition model, the enthalpy of micellization (ΔH_m) corresponds to ($H_M - H_m$) and the quantity $f_S m_S(H_{M,f} - H_{M,i})$ can be written as $f_S m_S \Delta H_{id,S} + \mathrm{cmc}_w(H_{M,f} - H_{m,f}) - f_S \mathrm{cmc}_w(H_{M,i} - H_{m,i})$. Therefore, dividing eq 18 by $f_C m_C$, one obtains

$$\begin{aligned}\Delta H_t = {} & \Delta H_t(\mathrm{w} \rightarrow \mathrm{w} + \mathrm{s}) + X^w_{1:1}(\Delta H_{1:1} - \Delta H'_m) + \\ & X^w_{1:2}(\Delta H_{1:2} - 2\Delta H'_m) + X^M_{1:2}(\Delta H_{t,1:2} - 2\Delta H'_m + \Delta H_{1:2}) + \\ & X^M_{1:1}(\Delta H_{t,1:1} - \Delta H'_m + \Delta H_{1:1}) + X_{C,M}\Delta H_{t,C} + \\ & \Delta H'_m(\mathrm{cmc}_w - \mathrm{cmc}')/f_C m_C\end{aligned} \tag{19}$$

where $\Delta H_{t,1:1}$ and $\Delta H_{t,1:2}$ represent the standard enthalpies of transfer of the 1:1 and 1:2 complexes from the aqueous to the micellar phases, respectively. Note that the last term at the right-hand side of eq 19 is the shift of micellization equilibrium ($A_{cdc}\Delta H_m'$) where $\Delta H_m'$ is the enthalpy of micellization in the presence of cyclodextrin. The meaning of the other symbols is the same as above.

The fractions of the species in the aqueous and the micellar phases may be written as

$$\begin{aligned}X^M_{1:2} &= X^w_C K_{1:2} K^M_{1:2}(\mathrm{cmc}')^2(f_S m_S - \mathrm{cmc}) \\ X^M_{1:1} &= X^w_C K_{1:1} K^M_{1:1}\mathrm{cmc}'(f_S m_S - \mathrm{cmc})\end{aligned} \tag{20}$$

$$X^w_{1:1} = X^w_C K_{1:1}\mathrm{cmc}' \quad X^w_{1:2} = X^w_C K_{1:2}(\mathrm{cmc}')^2 \tag{21}$$

$$X_{C,M} = X^w_C K^M_C(f_S m_S - \mathrm{cmc}) \tag{22}$$

where the fraction of the free cyclodextrin in the aqueous phase (X^w_C) is given by

$$\begin{aligned}X^w_C = {} & \{K_{1:1}\mathrm{cmc}'[1 + K^M_{1:1}(f_S m_S - \mathrm{cmc})] + K_{1:2}(\mathrm{cmc}')^2[1 + \\ & K^M_{1:2}(f_S m_S - \mathrm{cmc})] + K^M_C(f_S m_S - \mathrm{cmc}) + 1\}^{-1}\end{aligned} \tag{23}$$

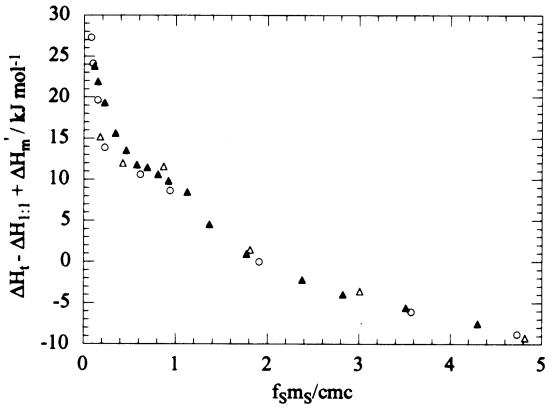

Figure 7. Enthalpy of transfer for HP-β-CD (triangles) and β-CD (circles) in $C_7F_{15}CO_2Na$ solutions, corrected for the enthalpy of 1:1 complex formation and micellization, as a function of the reduced concentration. Open symbols, $f_C m_C = 0.0075$ mol kg^{-1}. Filled symbols, $f_C m_C = 0.0185$ mol kg^{-1}.

Here cmc stands for the *apparent critical micellar concentration.* The binding constants between the micelles and the free cyclodextrin (K_C^M), the 1:1 complex ($K_{1:1}^M$), and 1:2 complex ($K_{1:2}^M$), based on eq 8, are given by

$$m_{1:1}^M/m_{1:1}^w = K_{1:1}^M(f_S m_S - \text{cmc})$$
$$m_{1:2}^M/m_{1:2}^w = K_{1:2}^M(f_S m_S - \text{cmc})$$
$$m_C^M/m_C^w = K_C^M(f_S m_S - \text{cmc}) \quad (24)$$

Equations 20−23 were derived by assuming that the free surfactant concentration is constant and, then, equal to the cmc′, according to the pseudo-phase-transition model.

(i) HP-β-CD and β-CD in Micellar $C_7F_{15}CO_2Na$ Solutions. We have earlier shown that HP-β-CD and β-CD in aqueous $C_7F_{15}CO_2Na$ solutions form only complexes of 1:1 stoichiometry. Therefore, the contributions due to the 1:2 complexes disappear in eq 19. This latter equation predicts that ΔH_t is constant if the cyclodextrin (free and/or complexed) does not interact with the micelles; that is not the case here. Equation 19 may be simplified by reasonably stating that $X_{C,M} \approx 0$ being the cyclodextrin essentially in the complexed form. In addition, remembering that $\Delta H_t(w \rightarrow w + s)$ is negligible in the presence of complexes, from eqs 19−23, one obtains

$$\Delta H_t - \Delta H_{1:1} + \Delta H_m' = \Delta H_{t,1:1} - \frac{\Delta H_{t,1:1} - A_{cdc}\Delta H_m'}{1 + K_{1:1}^M(f_S m_S - \text{cmc})} \quad (25)$$

The $A_{cdc}\,\Delta H_m'$ term can be evaluated by means of eq 7.

For HP-β-CD 0.0185 and 0.0075 mol kg^{-1} and β-CD 0.0075 mol kg^{-1} in aqueous $C_7F_{15}CO_2Na$ solutions, the quantity at the left-hand side of eq 25 as a function of the surfactant concentration was plotted (graph not shown). The large difference in ΔH_t between HP-β-CD and β-CD (Figure 3) is strongly reduced in this ordinate scale evidencing that the alkyl substituents influence essentially the host−guest inclusion complex formation. Because the cmc is a function of the cyclodextrin concentration, we plotted ($\Delta H_t - \Delta H_{1:1} + \Delta H_m'$) vs the reduced surfactant concentration, i.e., $f_S m_S$/cmc (Figure 7). The two distinct trends in the premicellar region, relative to the two different cyclodextrin concentrations, support the previous results that the alkylation of the cyclodextrin influences essentially the enthalpy of complexation. A single line can correlate all of the experimental data in the postmicellar region. This means that (1) the enthalpy of transfer corresponds to the standard property, as observed in the premicellar region, (2) the hypothesis following which $X_{C,M} = 0$ is reliable, and (3) the standard free energy ($\Delta G_{t,1:1}^0$), enthalpy ($\Delta H_{t,1:1}$), and entropy ($T\Delta S_{t,1:1}^0$) of transfer from the aqueous to the micellar phases for the HP-β-CD/$C_7F_{15}CO_2Na$ and β-CD/$C_7F_{15}CO_2Na$ complexes are identical.

To fit enthalpy data of HP-β-CD in $C_7F_{15}CO_2Na$ micellar solutions by means of eq 25, the $\Delta H_m'$, cmc, and β values (obtained from conductivity) reported in Table 1 were used. Table 2 collects the $\Delta H_{t,1:1}$, $K_{1:1}^M$, and K_S obtained from the minimizing procedure together with $\Delta G_{t,1:1}^0$ and $T\Delta S_{t,1:1}^0$ calculated by means of eqs 9 and 10, respectively.

(ii) HP-β-CD in Micellar $C_6F_{13}CO_2Na$ Solutions. The dependence of ΔH_t on the surfactant concentration is an indication of interactions between micelle and cyclodextrin (free and/or complexed). Because HP-β-CD in the dispersed $C_6F_{13}CO_2Na$ solutions exhibits host−guest complexes of 1:1 and 1:2 stoichiometries, the enthalpy data must be fitted by means of eqs 19−23, which contain several unknown parameters. Notwithstanding, some simplifications can be done. First, to estimate the shift of micellization equilibrium term, eq 7 was written as

$$A_{cdc}\Delta H_m' = (\Delta H_m' \text{ cmc}/2)[2.3K_S(X_{1:1}^w + X_{1:2}^w) + (1+\beta)K_{1:2}^M X_{1:2}^w + (1+\beta)K_{1:1}^M X_{1:1}^w] \quad (26)$$

where K_S was assumed being the same for the two kinds of complexes.

In addition, because of the simultaneous presence of 1:1 and 1:2 complexes, the free cyclodextrin concentration is very low; thus, the contribution to ΔH_t for the free cyclodextrin−micelle interactions may be neglected. On the basis of results for HP-α-CD in both surfactants, it is expected a similarity between HP-β-CD/$C_7F_{15}CO_2Na$ and HP-β-CD/$C_6F_{13}CO_2Na$ systems. Therefore, the partition constant and the K_S values of the former system were assumed for HP-β-CD/$C_6F_{13}CO_2Na$. Equation 19, through eqs 20−23 and 26, was reduced to a three-parameter equation ($K_{1:2}^M$, $\Delta H_{t,1:1}$, and $\Delta H_{t,1:2}$). The results of the best fit are collected in Table 2.

Discussion

Interaction between Cyclodextrin and Dispersed Surfactant. The hydrophobicity of $C_6F_{13}CO_2Na$ and $C_7F_{15}CO_2Na$ is sufficient to promote the formation of the inclusion complex with HP-α-CD but steric effects prevent it. The interactions between HP-α-CD and free surfactant minimize the free energy, as the interaction parameter g_{CS} (given[31] by $RTK_S/4$) is negative. Moreover, the small decrease of g_{CS} with the alkyl chain length of the surfactant may reflect the apolar−apolar interactions. Accordingly, as stated in the literature,[7] segments of the fluorinated chain may be located at the opening of the cavity, which shows a decreased polarity because of the presence of the hydroxypropyl groups. The h_{CS} parameter as well as that for the entropy are negative. To the best of our knowledge, interaction parameters for similar systems are available only for the enthalpy.[3] Studies on $C_3H_7CO_2Na$/HP-β-CD and $C_3H_7CO_2Na$/HP-γ-CD systems show that the cyclodextrin cavity does not influence the h_{CS} parameter. As well, for the HP-γ-CD/sodium alkanoate systems, h_{CS} is positive and depends on the surfactant alkyl chain length. The perfluoromethylene group contribution to h_{CS} is 1.5 times that of the methylene group calculated[32] from the HP-γ-CD/sodium alkanoate data. This result agrees[18,33] with the CF_2 group hydrophobicity 1.5 times larger than that of the CH_2 group.

The positive K_S value for 1:1 complex/$C_7F_{15}CO_2Na$ evidences the unfavorable (ion−ion and apolar−polar) interactions between the free surfactant and the inclusion complex.

Let us focus our attention on the cyclodextrin−surfactant interactions leading to the formation of host−guest complexes. Wilson and Verrall[9] reported that alkylated cyclodextrins, with respect to the natural ones, show a decreased binding affinity toward a common surfactant because the alkyl groups inhibit the ion−dipole interactions. The present $K_{1:1}$ values for HP-β-CD/$C_7H_{15}CO_2Na$ and β-CD/$C_7H_{15}CO_2Na$ agree with these findings. The different $\Delta H_{1:1}$ values may be ascribed to the interactions between the carboxylate group and the annulus region. In fact, the decreased $\Delta H_{1:1}$ and $T\Delta S_{1:1}$ for β-CD/$C_7F_{15}CO_2Na$ may reflect a larger extent of hydrogen bounds formation between the carboxylate and the hydroxyl groups. However, they may also reflect the different interactions between the cyclodextrin and water in the initial state.

A comparison between the standard thermodynamic properties for the HP-β-CD/$C_6F_{13}CO_2Na$ and HP-β-CD/$C_7F_{15}CO_2Na$ host−guest complex formation gives information on the effect of the alkyl chain length of the surfactant. The $K_{1:1}$ values, within the errors, are very close as observed in the literature.[9] However, they are smaller than those reported by Wilson and Verrall.[9] The difference may not be ascribed to the different degree of substitution of the cyclodextrin, as $K_{1:1}$ values are larger for the more alkylated cyclodextrin in contrast to literature findings.[9] $\Delta H_{1:1}$ is negative and decreases with the alkyl chain length of the surfactant. As far we know, enthalpies are available for similar systems:[3] for sodium alkanoates/HP-β-CD, $\Delta H_{1:1}$ is positive, whereas for sodium alkanoates/HP-α-CD, $\Delta H_{1:1}$ is negative. The same hydrophobic forces, which control the complex formation of the latter systems may be responsible for the present $\Delta H_{1:1}$ data. In fact, a similarity is expected, as the ratio between the HP-β-CD cavity surface and the van der Waals surface area of the fluorinated chain is practically the same as that between the HP-α-CD cavity surface and the van der Waals surface area of the hydrogenated chain. This hypothesis is supported by the contribution of the methylene group to $\Delta H_{1:1}$ in HP-α-CD (-2.6 ± 0.1 kJ mol^{-1}) which is comparable to that of the perfluoromethylene group in HP-β-CD (-2.1 ± 0.7 kJ mol^{-1}). The difference in the $\Delta H_{1:1}$ magnitude is to be ascribed to the carboxylate group/cyclodextrin interaction. Its contribution, evaluated as the intercept of the $\Delta H_{1:1}$ vs the number of carbon atoms in the alkyl chain (n_c), is 6.1 ± 0.7 kJ mol^{-1} for HP-α-CD/carboxylate group and 2.1 kJ mol^{-1} for HP-β-CD/carboxylate group. Entropy shows a maximum with n_c for the sodium alkanoate/HP-α-CD complexes and decreases for the present systems. This property, compared to the enthalpy, seems to be sensitive to other phenomena. In fact, the contribution of the perfluoromethylene group to $T\Delta S^0_{1:1}$ in HP-β-CD (-5 ± 1 kJ mol^{-1}) is different from that of the methylene group to $T\Delta S^0_{1:1}$ in HP-α-CD (-2.3 ± 0.4 kJ mol^{-1}), which was evaluated from the decreasing trend of $T\Delta S^0_{1:1}$ vs n_c. Thus, it may occur that entropy is sensitive to the different conformational states of the hydrogenated and fluorinated chains in the cyclodextrin cavity as it is reported[7,9] that hydrogenated chain coils to minimize the apolar−polar interactions, whereas the fluorinated chain assumes an all-trans conformation because of steric effects.

The effect of the surfactant hydrophobicity on the 1:2 cyclodextrin/surfactant complex formation cannot be analyzed because this kind of complexation was detected only for $C_6F_{13}CO_2Na$/HP-β-CD. Perhaps, also $C_7F_{15}CO_2Na$ forms 1:2 complexes in the surfactant concentrated region, but the micellization occurring at low concentration prevents the formation of these kind of complexes.

The higher order complexation (1:2 and/or 2:1) is controlled by a single phenomenon, which tends to minimize the contact between the fluorocarbon chain and the aqueous environment Thus, the unusual formation of complexes of 1:2 stoichiometry for $C_6F_{13}CO_2Na$/HP-β-CD can be explained by considering that the hydroxypropyl groups of HP-β-CD decrease the polar character of the annulus regions and may extend the effective length of the torus.[9] Because of electrostatic repulsions and steric effects, the capping of a second $C_6F_{13}CO_2Na$ molecule onto the 1:1 complex may occur by the side of the annulus region opposite to that lodging the first surfactant molecule. For this process, the equilibrium constant ($K' = K_{1:2}/K_{1:1}$) is 87 kg mol^{-1} and the enthalpy change ($\Delta H' = \Delta H_{1:2} - \Delta H_{1:1}$) is 3.5 ± 0.4 kJ mol^{-1}. For HP-α-CD/$C_7H_{15}CO_2Na$, $K' = 1.2$ kg mol^{-1} and $\Delta H' = 10.6 \pm 0.3$ kJ mol^{-1}. The $\Delta H'$ values suggest that hydrophilic interactions are also involved according to the positive contribution to $\Delta H_{1:1}$ for the interactions between cylodextrin and the carboxylate group.

The $K_{1:2}$ for both HP-β-CD/$C_6F_{13}CO_2Na$ and HP-α-CD/$C_7H_{15}CO_2Na$ systems is larger than $K_{1:1}$ (Table 2). These results are reliable because the 1:2 inclusion process minimizes the unfavorable apolar−polar interactions more effectively than the 1:1 inclusion process. However, because of mass balance effect, 1:2 complexes are detectable at high surfactant concentrations.

As stated earlier, to the best of our knowledge, for cyclodextrin−surfactant systems, 1:2 complexes were evidenced for $C_8F_{17}CO_2Na$ and methylated cyclodextrins.[9] In contrast to the present findings, $K_{1:2}$ is smaller than $K_{1:1}$. Any general discussion on this aspect may be hazardous because data are available only for a very few systems.

Interaction between Cyclodextrin and Micellized Surfactant. The $\Delta G^0_{t,C}$ values for HP-α-CD in micelles of both surfactants, within the uncertainties, are the same. In contrast, $\Delta G^0_{t,C}$ (w → M) are slightly different and indicate that $C_6F_{13}CO_2Na$ micelles show a larger binding affinity toward the macrocycle. The free energy data may reflect the favorable interactions between the carboxylate groups on the micellar surface and the hydroxyl groups of HP-α-CD. The solubilization of the alkyl substituents of the cyclodextrin in the palisade layer cannot be excluded although it does not seem to be favored by the increase of the surfactant hydrophobicity. Despite $\Delta H_{t,C}$(w → M) is a tool more useful than $\Delta H_{t,C}$, its understanding is not straightforward. The negative $\Delta H_{t,C}$(w → M) values are due to the hydrophilic interactions. Accordingly, a negative (-2.7 ± 1.7 kJ mol^{-1}) value of the enthalpy of transfer of the hydroxyl group from the aqueous to the $C_7F_{15}CO_2Na$ micellar phases is evaluated from literature data.[30] The strong $\Delta H_{t,C}$(w → M) increase with the surfactant alkyl chain length cannot be justified even invoking a different extent of hydroxypropyl groups solubilization in the micelles which is expected to involve a positive effect based on enthalpy data of hydrogenated alcohols in $C_7F_{15}CO_2Na$ micelles.[30] Alternatively, the cyclodextrin molecule may have different sites of binding on the micellar surface depending on the size and the degree of ionization of the micelles. Thus, the micelles of smaller aggregation number and larger β values are expected to show larger binding affinity toward the macrocycle; that is the case here. To minimize the free energy, this process may occur through conformational changes of HP-α-CD. This explanation takes into account for $T\Delta S^0_{t,C}$ (w → M) that increases with the hydrophobicity of the surfactant. The evidence that the enthalpy and entropy essentially

compensate to each other, as occurs when conformational effects are involved, supports this idea.

The same values of the standard free energy of transfer for the complexed HP-β-CD and β-CD from the aqueous to the $C_7F_{15}CO_2Na$ micellar phases do not indicate that the micelles show same binding affinity toward the two species because the initial state of the two macrocycles is different. However, the identical values of enthalpy and entropy of transfer suggest that the micelles do not distinguish whether the cyclodextrin is natural or alkylated and, then, that the contribution due to the hydroxypropyl groups solubilization in the micellar phase is very small or null. Because of the electrostatic repulsions between the micellar surface and the complex, it may be inferred that the smaller annulus region is involved in the interactions with the micelles.

It was assumed above that $C_6F_{13}CO_2Na$ and $C_7F_{15}CO_2Na$ micelles exhibit the same binding affinity for the 1:1 HP-β-CD/surfactant complex. This process is enthalpy−entropy compensated as $\Delta H_{t,1:1}$ and $T\Delta S_{t,1:1}$ increase with the alkyl chain of the surfactant. These results suggest that the mechanism of interaction between the complex and the micelles is the same as that observed for HP-α-CD and the micelles.

The $C_6F_{13}CO_2Na$ micelle affinity toward the 1:2 complex is small according to the unfavorable interactions between the micellar surface and the doubly charged complex. The different values of $\Delta G^0_{t,1:1}$ and $\Delta G^0_{t,1:2}$ are the result of comparable $\Delta H_{t,1:1}$ and $\Delta H_{t,1:2}$ values and different entropies being $T\Delta S^0_{t,1:2}$ more negative.

Conclusion

The enthalpy of transfer of β-CD, HP-β-CD, and HP-α-CD from water to the aqueous $C_6F_{13}CO_2Na$ and $C_7F_{15}CO_2Na$ solutions were determined in the pre- as well as postmicellar regions. The magnitude of the enthalpy is influenced by several phenomena: (1) the interactions between the free cyclodextrin and free surfactant, (2) the host−guest equilibrium constant, (3) the host/guest stoichiometry, (4) the alkyl chain length of the surfactant, and (5) the micelle-cyclodextrin (free and/or complexed) interactions.

As concerns the premicellar region, HP-α-CD does not form complexes, whereas β-CD and HP-β-CD do. Apart 1:1 complexes, for some systems complexes of 1:2 stoichiometry (1 cyclodextrin:2 surfactants) were evidenced.

As far as the postmicellar region is concerned, for the systems, which exhibited inclusion complex formation, a new equation was proposed on the basis of the following contributions: (1) formation of 1:1 and 1:2 complexes in the aqueous phase, (2) distribution of free cyclodextrin, 1:1 complex and 1:2 complex between the aqueous and the micellar phases, and (3) shift of the micellization equilibrium induced by the cyclodextrin. As a general feature, the cyclodextrin (free and/or complexed) shows affinity toward the micelles because of the favorable interactions between the carboxylate head on the micellar surface and the hydroxyl groups of the macrocycle.

To the best of our knowledge, this is the first experimental evidence of interactions between micelle and cyclodextrin (free or complexed). Consequently, it questions the information provided not only by the structural studies but also by the thermodynamic ones. However, this inconsistency disappears if some points are focused on. It was documented[29] that the best experimental approach to the thermodynamics of solubilization of polar additives in the micellar phase is studying a standard property of the additive as a function of the surfactant concentration. The alternative approach based on studying the property of the surfactant in the water + additive mixture as a function of its concentration is not so sensitive to the micelle−additive interactions specially if the additive approaches the standard state. This argumentation explains why the present enthalpy of transfer of the cyclodextrin evidences the micelle−cyclodextrin interactions, whereas the apparent molar volume of the sodium perfluoroalkanoates in aqueous cyclodextrin solution does not.[18]

Finally, another important factor is the ability of the enthalpy in detecting any kind of solute−solvent and solute−solute interactions.

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Supporting Information Available: Table of the experimental enthalpies of mixing of aqueous cyclodextrin solution with the aqueous surfactant solution. Table of the specific conductivities for $C_6F_{13}CO_2Na$ in water and in aqueous solutions of HP-α-CD and HP-β-CD and for $C_7F_{15}CO_2Na$ in aqueous solutions of HP-α-CD and HP-β-CD. This material is avaliable free of charge via the Internet at http://pubs.acs.org.

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