Characterization of the Cyclodextrin−Surfactant Interactions by Volume and Enthalpy

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Volume and enthalpy of transfer of hydroxypropyl-α-cyclodextrin (HP-α-CD) and hydroxypropyl-γ-cyclodextrin (HP-γ-CD) from water to the aqueous solutions of sodium alkanoates (sodium hexanoate, sodium decanoate and sodium dodecanoate) were determined at 298 K. The cyclodextrin concentration was kept constant, and that of the surfactant was varied in order to analyze both the pre- and postmicellar regions. The experimental data in the premicellar region were consistent with the formation of 1:1 and 1:2 (1 cyclodextrin:2 surfactants) inclusion complexes, with the exception of the HP-α-CD/sodium dodecanoate system which presented only the 1:1 complexes. The mechanism of the 1:2 complexes formation of HP-α-CD/surfactant is different from that involving HP-γ-CD. The quantitative analysis of the experimental data in the post-micellar region supplied parameters indicating that the cyclodextrin−micelles forces are ion−dipole (carboxylate head/hydroxylic group) in nature. The present results combined with the literature ones clarify the effect of the cavity size of the cyclodextrin as well as the hydrophobicity of the surfactant on the cyclodextrin-dispersed surfactant and cyclodextrin−micelle interactions.

Introduction

The capability of the cyclodextrin to form inclusion complexes generated great interest in several fields.[1] Recently, cyclodextrins have been considered attractive for removing hydrophobic organic compounds from the subsurface systems.[2−4] Hydropropyl-β-cyclodextrin (HP-β-CD), for example, was effective in remediating an aquifer contaminated with nonaqueous phase liquids during a pilot-scale field test.[4]

There is a restricted number of thermodynamic studies on water−cyclodextrin−surfactant systems based on different techniques. Surface tension,[5] emf,[6] and NMR[7,8] data supplied the host−guest binding constant (K), whereas properties such as enthalpy,[6,9−11] volume,[12−15] heat capacity,[13,15] and compressibility[16] did the property change for the complex formation and, sometimes, K. Surfactants show chemical structures similar to phospholipids and, hence, are considered good models to give insights into the cyclodextrin−cellular membranes binding process. It was shown[5] that the cyclodextrins suppress the surfactant-induced hemolysis because they bind the surfactants more strongly than phospholipid and cholesterol in the erythrocyte membrane.

Chemically modified cyclodextrins have been synthesized to improve their properties. Amphiphilic cyclodextrins,[17] for instance, form micellar aggregates having a core−shell structure with the cyclodextrin units exposed to the aqueous phase. The features of such aggregates did candidate them as molecular carriers, especially for drugs delivery.[18] These structures are unusual because, besides a very few thermodynamic evidences,[10,11,19] surfactant−cyclodextrin mixed micelles have not been detected.

The thermodynamic behavior of HP-β-CD in the presence of sodium alkanoates is well defined,[10−14] whereas it is not so for hydroxypropyl-α-cyclodextrin (HP-α-CD) and hydroxypropyl-γ-cyclodextrin (HP-γ-CD).[10,11] To gain information on the effect of the cavity size of the cyclodextrin as well as the hydrophobicity of the surfactant on the cyclodextrin-surfactant interactions, volume and enthalpy studies of HP-α-CD and HP-γ-CD in aqueous sodium alkanoate solutions were carried out.

Experimental Section

Materials. Sodium hexanoate (NaHex), sodium decanoate (NaDec), and sodium dodecanoate (NaL) (Sigma) were used as received. Their aqueous solutions gave pH ≈ 8.5. The purity of the surfactants was checked by means of the apparent molar volumes, determined in the premicellar region, which were in very good agreement with those reported elsewhere.[13,20] These data provided the standard partial molar volumes which agree with the values calculated through the additivity rule.[21] Sodium chloride (Aldrich, 99.999%) was dried in an oven at 573 K for 2 days. Hydroxypropyl-α-cyclodextrin (HP-α-CD, Aldrich) and hydroxypropyl-γ-cyclodextrin (HP-γ-CD, Aldrich) were used as received. The average molar substitution for each glucopyranose residue is 0.6 for both the cyclodextrins. The water content of the cyclodextrins was determined by using the procedure reported elsewhere.[13]

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

Equipment. *Density.* The solutions densities were measured at 298 K by using a vibrating tube flow densimeter (model 03D, Sodev Inc.) sensitive to 3 ppm. The temperature was maintained constant within 0.001 K by using a closed loop temperature controller (model CT-L, Sodev Inc.). The calibration of the densimeter was made with water ($d = 0.997\ 047$ g cm^{-3})[22] and aqueous sodium chloride solutions of known densities.[23]

The apparent molar volumes ($V_{\Phi,C}$) of the cyclodextrin in the given solvent were calculated by means of the following equation:

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$$V_{\Phi,C} = \frac{M}{d} - \frac{10^3(d - d_0)}{m_C d d_0} \quad (1)$$

where m_C and M are the molality and the molecular weight of the cyclodextrin, d is the density of the solution, and d_0 is the density of the water + surfactant binary mixture. The latter was evaluated from the apparent molar volume of the surfactant in water available at several concentrations.[13,20]

The cyclodextrin concentration value of 0.05 mol kg^{-1} was chosen to both determining $V_{\Phi,C}$ with a small error (±0.1 cm^3 mol^{-1}) and treating $V_{\Phi,C}$ as a standard property.

The volume of transfer of the cyclodextrin from water to the aqueous surfactant solution (ΔV_t) was calculated as difference between $V_{\Phi,C}$ and the apparent molar volume of the cyclodextrin in water, evaluated by using the literature data.[13]

The presence of HP-α-CD and HP-γ-CD 0.05 mol kg^{-1} in the aqueous solutions of NaL at concentrations greater than 0.15 mol kg^{-1} caused the appearance of a solid which prevented from carrying out measurements.

Enthalpy. The enthalpies of mixing were determined at 298.00±0.01 K by means of a flow LKB 2107 microcalorimeter. The injection of the solutions into the equipment was made by means of a Gilson peristaltic pump (Minipuls 2).

The experimental enthalpy (ΔH^{exp}) was determined as 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. The flows of the solutions were determined by weight. The enthalpy of transfer (ΔH_t) of the cyclodextrin from water to the aqueous surfactant solution was calculated as the difference between ΔH^{exp} and the enthalpy of dilution of the cyclodextrin with water ($\Delta H_{id,C}$), which was evaluated by means of the following equations:

$$\Delta H_{id,C} = (L_{\Phi,C})_f - (L_{\Phi,C})_i \quad (2)$$

$$L_{\Phi,C} = B_C m_C + C_C m^2{}_C \quad (3)$$

where $L_{\Phi,C}$ is the apparent molar relative enthalpy. The subscripts "i" and "f" indicate the initial and the final states, respectively. B_C and C_C are the pair and triplet solute−solute interaction parameters,[10] respectively.

The final concentration of the surfactant ($f_S m_S$) and the cyclodextrin ($f_C m_C$) solutions upon the mixing process were calculated by using the following dilution factors

$$f_S = \Phi_S/(\Phi_S + \Phi_C) \quad (4)$$

$$f_C = \Phi_C/(\Phi_S + \Phi_C) \quad (5)$$

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

The experiments were done at $f_C m_C = 0.0185$ mol kg^{-1} to make the data consistent with the others[10] dealing with the surfactant homologues. However, based on previous findings,[11] the measured ΔH_t can be considered a standard property.

Conductivity. To determine the critical micellar concentration (cmc) and the degree of ionization of the micelles (β) of NaDec and NaL in the presence of HP-α-CD and HP-γ-CD 0.0185 and 0.05 mol kg^{-1}, conductivity measurements were carried out at 298.0 ± 0.1 K by using a conductimeter Analytical Control 120. Both cmc and β were determined by using the literature procedure[24] and are collected in Table 1. The study is inapplicable to NaHex due to its large cmc.

Results

Figure 1 illustrates the dependence on the surfactant concentration (m_S) of the volume of transfer (ΔV_t) of HP-γ-CD in NaHex, NaDec, and NaL. To compact the abscissa scale, for each system, m_S was normalized with respect to its value at the maximum (m_S^{max}). ΔV_t strongly increases with m_S to ca.. 0.03, 0.1, and 1.2 mol kg^{-1} for NaL through NaHex; thereafter, it decreases tending to a constant value. For the HP-γ-CD/NaHex, the profile of the ΔV_t vs m_S plot below the maximum is S-shaped like. The ΔH_t vs $f_S m_S/(f_S m_S)^{max}$ curves for HP-γ-CD in NaL and NaDec are shown in Figure 2 where data[10] of HP-γ-CD in sodium octanoate (NaOct) and NaHex (available to ca. 0.6 mol kg^{-1}) are also represented. The properties start to decrease at ca. 0.025, 0.1, and 0.3 mol kg^{-1} for NaL through NaOct, respectively. The curves in Figures 1 and 2 exhibit the same features with maxima localized at surfactant concentration values close to the critical micellar concentration in water (cmc_w).[10,20] According to findings of γ-cyclodextrin/amphiphilic guest systems,[5,25,26] the data in the region below cmc_w may reflect the simultaneous presence of the 1:1 and 1:2 (1 cyclodextrin:2 surfactant molecules) inclusion complexes. The 1:2 complexes do form because the cyclodextrin cavity is large enough to accommodate two alkyl chains.

The nature of the cyclodextrin influences the magnitude of the property of transfer and its dependence on m_S. For the HP-α-CD/NaL system, ΔV_t changes almost linearly with m_S to ca.. 0.03 mol kg^{-1} beyond which it decreases tending to a constant value whereas the dependence of ΔH_t on $f_S m_S$ seems to be monotonic (Figure 3). The volumes of transfer of HP-α-CD in NaDec and NaHex exhibit minima at ca. 0.06 and 0.07 mol kg^{-1} and maxima at ca. 0.1 and 1.3 mol kg^{-1}, respectively (Figures 4 and 5). Similar characteristics are displayed by the enthalpy (Figure 4). As observed for the HP-γ-CD/surfactant systems, the maxima in the plots shown in Figures 4 and 5 are present at surfactant concentrations close to the cmc_w values. The change of the properties of transfer with concentration over the $0 \le m_S \le cmc_w$ region reveals the host−guest complexes formation. For NaL/HP-α-CD, the 1:1 complexes are likely forming because of the monotonic variation of ΔH_t with concentration. The unlikely shape of the volume curve may be due to the different value of the fraction of the bound cyclodextrin which, for a given equilibrium constant, reaches the constant value at larger m_S the higher the cyclodextrin concentration is. According to findings of other homologues,[11] the minima in the graphs of Figures 4 and 5 may be ascribed to the appearance of the 1:2 complexes occurring when the surfactant amount is in excess with respect to that of the cyclodextrin. This takes into account for the localization of the minima which in the ΔH_t vs $f_S m_S$ curves are present at lower concentrations compared to those of the ΔV_t vs m_S curves. The small size of HP-α-CD prevents the accommodation of two alkyl chains into the cavity. Notwithstanding, thermodynamic[11] and NMR studies[8] evidenced the 1:2 complexes for alkylated-β-cyclodextrins and sodium perfluoroalkanoates. These systems and ours present identical host/guest geometric ratios calculated from the cavity volume of the cyclodextrin[27] and the van der Waals volume of the surfactant chain.[27,28] As well, it is reported[8,29−31] that the alkyl or hydroxyalkyl (methyl, propyl, etc.) groups lengthen the cyclodextrin torus enhancing the binding with lipophilic compounds. Hence, the hydrophobic extension of HP-α-CD can interact with the second surfactant

TABLE 1: Critical Micellar Concentrations and Degrees of Ionization for Sodium Alkanoates in the Presence of Hydroxypropyl−Cyclodextrins at 298 K[a]

	HP-α-CD		HP-γ-CD	
	NaDec	NaL	NaDec	NaL
β ($m_C = 0$)	0.52[b]	0.46[c]		
m_S*($m_C = 18.5$)	110	44	150	43
cmc ($m_C = 18.5$)	107 ± 3	40.6 ± 0.6	101 ± 7	55 ± 2
β ($m_C = 18.5$)	0.597 ± 0.006	0.546 ± 0.002	0.64 ± 0.01	0.589 ± 0.005
m_S*($m_C = 50$)	148	64	160	75
cmc ($m_C = 50$)	144 ± 2	61 ± 2	181 ± 9	94 ± 15
β ($m_C = 50$)	0.671 ± 0.002	0.591 ± 0.006	0.699 ± 0.007	0.79 ± 0.01

[a] Units are mmol kg^{-1} for concentrations. [b] From ref 40. [c] From ref 41.

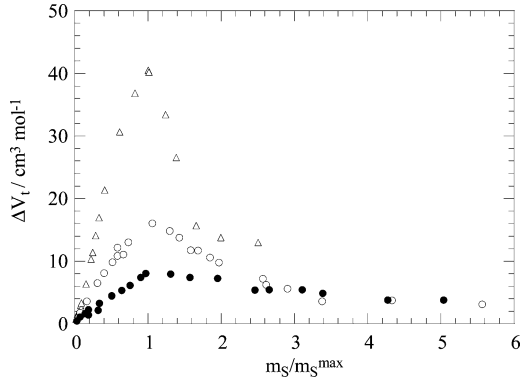

Figure 1. Volume of transfer of hydroxypropyl-γ-cyclodextrin from water to the aqueous solution of NaHex (△), NaDec (○), and NaL (●) as a function of the surfactant concentration normalized with respect to its value at the maximum. $m_S^{max} = 0.03$, 0.10, and 1.2 mol kg^{-1} for NaL, NaDec, and NaHex, respectively.

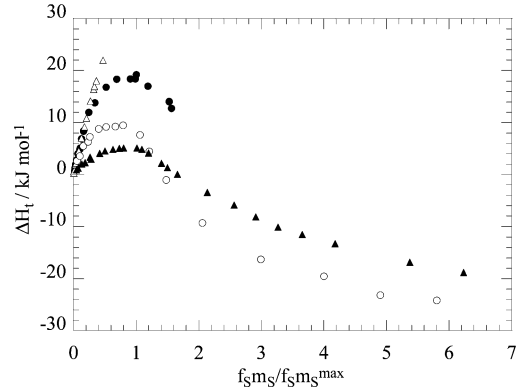

Figure 2. Enthalpy of transfer of hydroxypropyl-γ-cyclodextrin from water to the aqueous solution of NaHex (△), NaOct (●), NaDec (○), and NaL (▲) as a function of the surfactant concentration normalized with respect to its value at the maximum. $f_S m_S^{max} = 0.024$, 0.1, 0.3, and 1.2 mol kg^{-1} for NaL through NaHex. Data dealing with NaHex and NaOct are from ref 10.

molecule allowing complexes with structures different from those of the HP-γ-CD/surfactant systems.

Theoretical Background

We recently proposed[11] an equation to rationalize the enthalpy of transfer of cyclodextrin from water to the aqueous surfactant solutions based on the idea that (1) host−guest complexes do form in the aqueous phase, (2) the cyclodextrin induces the shift of the micellization equilibrium, and (3) micelles and cyclodextrin do interact to each other. The obtained equation is valid for a generic property first derivative of Gibbs energy (Y) and, therefore, also for the volume. By assuming the pseudo-phase transition model for the micellization and a mass action model

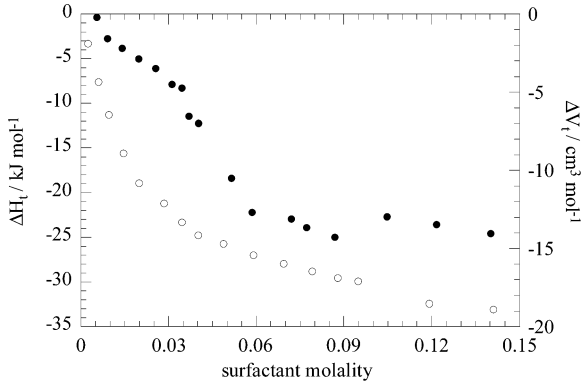

Figure 3. Enthalpy (○) and volume (●) of transfer of hydroxypropyl-α-cyclodextrin from water to the aqueous NaL solution as functions of the surfactant concentration.

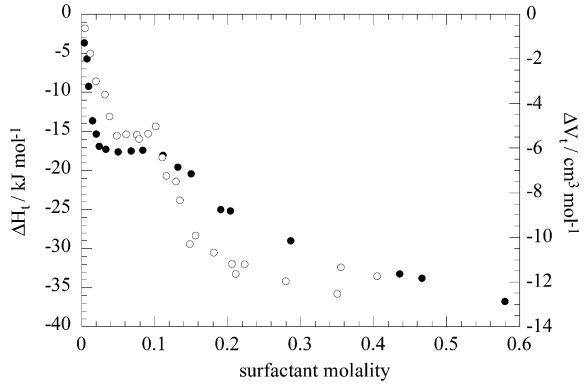

Figure 4. Volume (○) and enthalpy (●) of transfer of hydroxypropyl-α-cyclodextrin from water to the aqueous NaDec solution as functions of the surfactant concentration.

for the cyclodextrin distribution between the aqueous and the micellar phases, if 1:1 and 1:2 complexes are present, the following was reported:

$$\Delta Y_t = X^w_{1:1}\Delta Y_{1:1} + X^w_{1:2}\Delta Y_{1:2} + \Delta Y_m\left\{\frac{cmc_w - cmc'}{m_C} - X^w_{1:1} - 2X^w_{1:2}\right\} + X^M_{1:2}(\Delta Y_{t,1:2} - 2\Delta Y_m + \Delta Y_{1:2}) + X^M_{1:1}(\Delta Y_{t,1:1} - \Delta Y_m + \Delta Y_{1:1}) + X_{C,M}\Delta Y_{t,C} \quad (6)$$

The first two terms on the rhs of eq 6 represent the host−guest binding contributions where $X^w_{1:1}$ and $X^w_{1:2}$ are the fractions of the 1:1 and 1:2 complexes in the aqueous phase and $\Delta Y_{1:1}$ and $\Delta Y_{1:2}$ are the related property changes. The third term stands for the shift of the micellization equilibrium induced by both the complexes and the free cyclodextrin: cmc_w and cmc′ indicate the dispersed surfactant concentration in the binary and

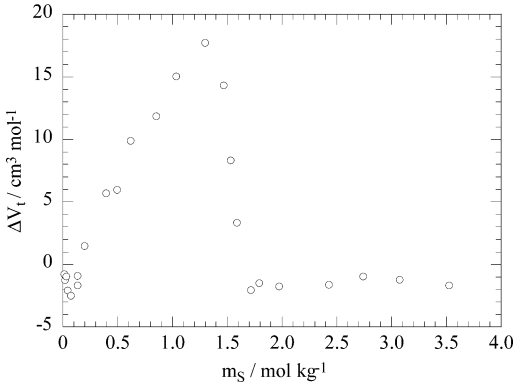

Figure 5. Volume of transfer of hydroxypropyl-α-cyclodextrin from water to the aqueous NaHex solution as a function of the surfactant concentration.

ternary system, respectively, whereas ΔY_m is the property of micellization. The other terms take into account the interactions between the cyclodextrin (free and complexed) and the micelles: $X_{C,M}$, $X^M_{1:1}$, and $X^M_{1:2}$ are the fractions of the free cyclodextrin, 1:1, and 1:2 complexes bound to the micelles whereas the corresponding variations of the property are $\Delta Y_{t,C}$, $\Delta Y_{t,1:1}$, and $\Delta Y_{t,1:2}$, respectively.

The various fractions are expressed as

$$X^M_{1:2} = X^w_C K_{1:2} K^M_{1:2} (\mathrm{cmc}')^2 (m_S - \mathrm{cmc})$$
$$X^M_{1:1} = X^w_C K_{1:1} K^M_{1:1} \mathrm{cmc}' (m_S - \mathrm{cmc}) \quad (7)$$

$$X^w_{1:1} = X^w_C K_{1:1} \mathrm{cmc}' \qquad X^w_{1:2} = X^w_C K_{1:2} (\mathrm{cmc}')^2 \quad (8)$$

$$X_{C,M} = X^w_C K^M_C (m_S - \mathrm{cmc}) \quad (9)$$

where X^w_C is given by

$$X^w_C = \{K_{1:1}\mathrm{cmc}'[1 + K^M_{1:1}(m_S - \mathrm{cmc})] + K_{1:2}(\mathrm{cmc}')^2[1 + K^M_{1:2}(m_S - \mathrm{cmc})] + K^M_C(m_S - \mathrm{cmc}) + 1\}^{-1} \quad (10)$$

here cmc represents the apparent critical micellar concentration at which micelles are forming. $K_{1:1}$ and $K_{1:2}$ are the equilibrium constants for the formation of the 1:1 and 1:2 complexes in water. K^M_C, $K^M_{1:1}$, and $K^M_{1:2}$ indicate the binding constants between the micelles and the free cyclodextrin, the 1:1 complex, and 1:2 complex, respectively. The quantity $\Delta Y_m(\mathrm{cmc}_w - \mathrm{cmc}')/m_C$ may be expressed as

$$\Delta Y_m(\mathrm{cmc}_w - \mathrm{cmc}')/m_C = (\Delta Y_m \mathrm{cmc}'/2)[2.3K_S(X^w_{1:1} + X^w_{1:2} + X^w_C) + (1 + \beta)(K^M_{1:2} X^w_{1:2} + K^M_{1:1} X^w_{1:1} + K^M_C X^w_C)] \quad (11)$$

where K_S is the Setchenov constant assumed being equal for the two kinds of complexes and free cyclodextrin and (β) is the degree of ionization of the micelles.

Premicellar Region: Quantitative Analysis of the Experimental Data. The decrease of both the thermodynamic properties taking place at $m_S \approx \mathrm{cmc}_w$ is due to the shift of the micellization equilibrium induced by the macrocycle. In fact, if the cyclodextrin and the surfactant form complexes, the number of surfactant molecules available to form micelles is less with respect to the water/surfactant binary system. Consequently, micelles are forming at a concentration (cmc) larger than cmc_w which increases with the cyclodextrin amount in agreement with the conductivity results (Table 1) and the literature findings.[13,32] Therefore, in the surfactant concentration region to $m_S = \mathrm{cmc}_w$, eq 6 reduces to the following

$$\Delta Y_t = X^w_{1:1}\Delta Y_{1:1} + X^w_{1:2}\Delta Y_{1:2} \quad (12)$$

To apply eq 12 to the experimental data, the Newton−Raphson method was used to calculate the concentration of the species in solution, and the $K_{1:1}$ and $K_{1:2}$ values, minimizing the standard deviation of $\Delta Y_t/X^w_{1:1}$ vs $X^w_{1:2}/X^w_{1:1}$ plot, were taken. Indeed, the fitting procedure did not converge when the equilibrium constants were small and/or the range of the surfactant concentration was narrow. The failure of such a method occurred, for instance, for the HP-γ-CD/surfactant systems. Thus, to reduce the number of the unknown parameters, $X^w_{1:1}$ and $X^w_{1:2}$ were evaluated through $K_{1:1}$ and $K_{1:2}$ calculated from the additivity rule. Namely, enthalpy data[10] of HP-γ-CD/NaOct available in a wide range of m_S were analyzed according to eq 12 providing $K_{1:1}$ and $K_{1:2}$ (Table 2). The latter were combined with the methylene group contributions, calculated from the standard free energies of γ-CD/ω-phenylalkanoic acids,[25] giving the equilibrium constants of the systems analyzed (Table 2). Good fits were obtained for HP-γ-CD in NaHex and NaDec. The best fit of the experimental points of HP-γ-CD/NaL was obtained by using the equilibrium constants for sodium undecanoate/HP-γ-CD. This seems to indicate that at $n_c = 10$ the saturation of the cyclodextrin cavity occurs. The $\Delta Y_{1:1}$ and $\Delta Y_{1:2}$ values obtained by means of this procedure are collected in Table 2.

According to the literature,[28] the fitting process converges if the fraction of the complexes changes from small to high values over the fitting interval. Such variation is more evident the larger the range of fit is. As stated previously, the premicellar region of the ternary system is wider compared to the binary one. This may allow the data to be analyzed with success in a more extended surfactant region by means of the following equation

$$\Delta Y_t = X^w_{1:1}\Delta Y_{1:1} + X^w_{1:2}\Delta Y_{1:2} + \Delta Y_m\left\{\frac{\mathrm{cmc}_w - \mathrm{cmc}'}{m_C} - X^w_{1:1} - 2X^w_{1:2}\right\} \quad (13)$$

Equation 13 based on the pseudo-phase transition model for micellization may be impracticable because such a model predicts a break at cmc_w contrarily to the experimental evidences. Consequently, a mass action model was chosen.[34] For the former model, the dispersed surfactant concentrations in the absence (cmc_w) and the presence (cmc′) of the cyclodextrin are constant quantities, whereas for the second one, they are functions of m_S and, hereinafter, will be represented as $[m_o]$ and $[m]$, respectively. The $[m_o]$ values were calculated by means of the Newton−Raphson method using the equilibrium constant for micellization[19] and the aggregation number.[19] The latter quantities together with the values of $K_{1:1}$ and $K_{1:2}$ gave the concentrations of the 1:1 and 1:2 complexes and $[m]$. Provided that ΔY_m was evaluated with the available parameters,[19,20,34−36] the term of the micellization shift was obtained. Then, the fit of the experimental data was performed using a nonlinear least-squares fitting program based on a Marquardt−Levenberg algorithm. The errors on the obtained parameters (collected in Tables 2 and 3) were calculated from the diagonal of the variance−covariance matrix.

The good fits for HP-γ-CD in NaHex and NaDec provided $K_{1:1}$ and $K_{1:2}$ values which were in a satisfactory agreement with those calculated on the basis of the additivity rule (Table 2). As well, for NaHex, the shift of the micellization equilibrium is important influencing the volumes for the complex formation.

TABLE 2: Thermodynamic Properties for the Inclusion Complex Formation between Hydroxypropyl-γ-Cyclodextrin and Sodium Alkanoates at 298 K[a]

	obtained through eq 12				obtained through eq 13		
	NaHex	NaOct	NaDec	NaL	NaHex	NaDec	NaL
$K_{1:1}$	0.82[b]	7.2 ± 0.7	55[b]	155[b]	1.2 ± 0.2[c]	44 ± 3[c];52 ± 2[d]	155[b]
$\Delta G^0_{1:1}$					−0.5 ± 0.4	−9.37 ± 0.17[c]; −10.06 ± 0.09[d]	−12.5[b]
$\Delta H_{1:1}$		35 ± 1	17.4 ± 0.6	17.4 ± 0.8		17 ± 2	15 ± 2
$T\Delta S_{1:1}$						26 ± 3[c];27 ± 3[d]	28 ± 2
$\Delta V_{1:1}$	34 ± 2		16.2 ± 0.9	23 ± 2	22 ± 2	17 ± 2	18 ± 2
$K_{1:2}$	1.9[b]	47 ± 13	1.3 × 10³ [b]	6.4 × 10³ [b]	1.53 ± 0.07[c]	1494 ± 2[c]; 1110 ± 1[d]	6.4 × 10³ [b]
$\Delta G^0_{1:2}$					−1.1 ± 0.1	−18.109 ± 0.003[c]; −17.587 ± 0.003[d]	−21.7[b]
$\Delta H_{1:2}$		14 ± 1	5 ± 1	−21 ± 4		5 ± 3	−15 ± 5
$T\Delta S_{1:2}$						23 ± 4[c,d]	9 ± 6
$\Delta V_{1:2}$	61 ± 2		22 ± 2	−20 ± 20	84 ± 3	23 ± 2	16 ± 6

[a] Units are $K_{1:1}$, kg mol^{-1}; $K_{1:2}$, kg^2 mol^{-2}; kJ mol^{-1} for free energy, enthalpy, and entropy; cm^3 mol^{-1} for volume. $\Delta G^0 = -RT \ln K$; $T\Delta S = \Delta H - \Delta G°$. [b] Calculated by means of the additivity rule (see text). [c] From the volume data. [d] From the enthalpy data.

TABLE 3: Thermodynamic Properties for the Inclusion Complex Formation between Hydroxypropyl-α-Cyclodextrin and Sodium Alkanoates at 298 K[a]

	NaHex	NaDec	NaL
$K_{1:1}$	445 ± 3[b]	700 ± 280[c]; 940 ± 390[d]	700 ± 400[d]
$\Delta G^0_{1:1}$	−15.1±0.2[b]	−16.2 ± 1.0[c]; −17.0 ± 1.0[d]	−16.2 ± 1.4
$\Delta H_{1:1}$	−6.44 ± 0.06[b]	−19.9 ± 0.6	−24.3 ± 1.8
$T\Delta S_{1:1}$	8.7 ± 0.2[b]	−3.7 ± 1.1[c]; −2.9 ± 1.1[d]	−8 ± 2
$\Delta V_{1:1}$	−2.7 ± 0.4	−7.3 ± 0.2	−7.4 ± 0.1
$K_{1:2}$		(21 ± 14) × 10³[c]; (33 ± 19) × 10³[d]	
$\Delta G^0_{1:2}$		−24.7 ± 1.7[c]; −25.8 ± 1.4[d]	
$\Delta H_{1:2}$		−16.1±0.9	
$T\Delta S_{1:2}$		9.6 ± 1.7[d]	
$\Delta V_{1:2}$		−2.7 ± 0.5	

[a] For units, see Table 2. [b] From ref 11. [c] From the volume data. [d] From the enthalpy data.

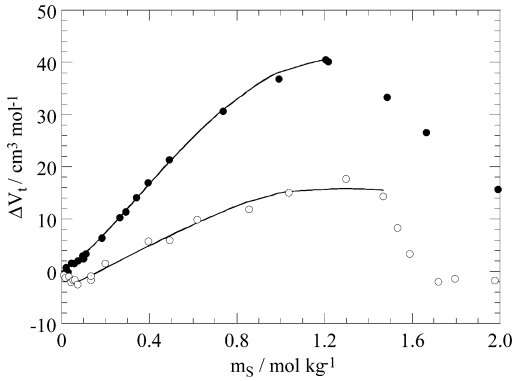

Figure 6. Volumes of transfer of HP-α-CD (○) and HP-γ-CD (●) from water to the aqueous NaHex solution as functions of the surfactant concentration. Lines, fit according to eq 13.

The fit did not still converge for HP-γ-CD in NaL, and hence, the property changes for the complexes formation were derived by using the calculated equilibrium constants. The best fits are shown in Figures 6−8. In the case of HP-α-CD/surfactant systems, the 1:1 model was consistent for NaL, whereas the formation of the 1:1 and 1:2 complexes was invoked for the other homologues. The independent fits of the volume and the enthalpy for HP-α-CD/NaDec (Figure 9) supplied $K_{1:1}$ and $K_{1:2}$ which, within the errors, agree to each other. The ΔV_t analysis of HP-α-CD/NaL allowed a quite uncertain $K_{1:1}$ due to the narrow range of m_S. Then, $K_{1:1}$, evaluated from the enthalpy, was employed to calculate $\Delta V_{1:1}$. The best fits of both the

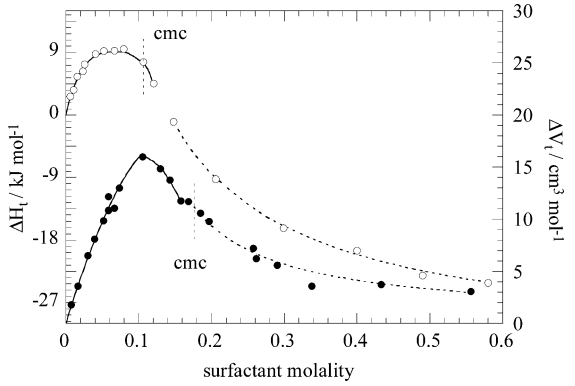

Figure 7. Enthalpy (○) and volume (●) of transfer of hydroxypropyl-γ-cyclodextrin from water to the aqueous NaDec solution as functions of the surfactant concentration. Lines, best fits according to eq 13 (solid) and eq 6 (broken), respectively.

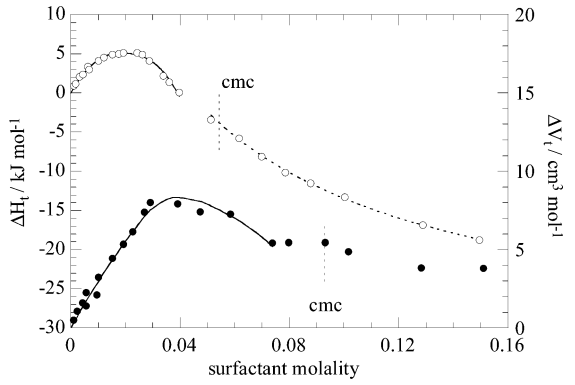

Figure 8. Enthalpy (○) and volume (●) of transfer of hydroxypropyl-γ-cyclodextrin from water to the aqueous NaL solution as functions of the surfactant concentration. Lines, best fits according to eqs 13 (solid) and eq 6 (broken), respectively.

properties are represented in Figure 10. It is to be noticed that, despite the larger hydrophobicity of NaL, the 1:2 complexes were not detected because of a mass balance effect. In fact, calculations based on $K_{1:2}$ for NaDec predict the detection of such complexes just below the cmc. On the other hand, larger $K_{1:2}$ values do not reproduce even qualitatively the experimental data. The ΔV_t fit for HP-α-CD/NaHex was unsuccessful. With $K_{1:1}$ being known,[10] $\Delta V_{1:1}$ was determined from the data below the minimum. By using these quantities, the minimizing process through eq 13 was done (Figure 6) providing very uncertain parameters ($K_{1:2}$ = 60 ± 50 kg mol^{-1} and $\Delta V_{1:2}$ = 180 ± 140

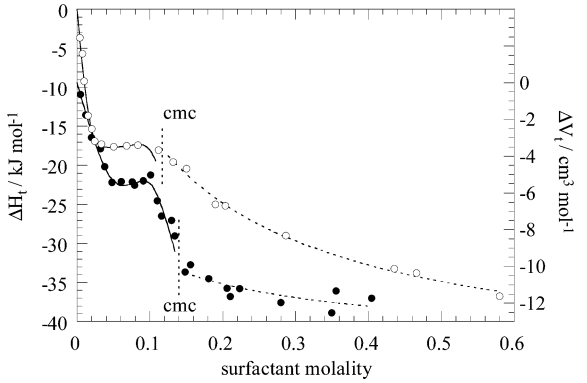

Figure 9. Enthalpy (○) and volume (●) of transfer of hydroxypropyl-α-cyclodextrin from water to the aqueous NaDec solution as functions of the surfactant concentration. Lines, best fits according to eqs 13 (solid) and eq 6 (broken), respectively.

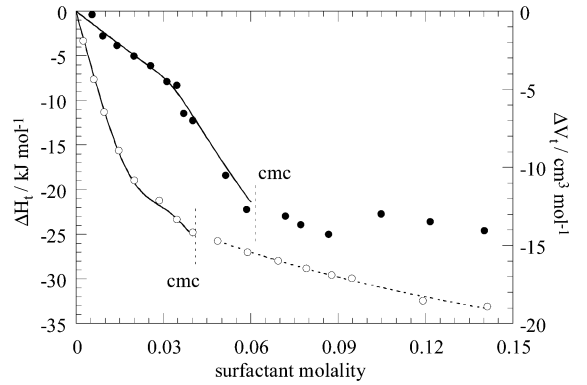

Figure 10. Enthalpy (○) and volume (●) of transfer of hydroxypropyl-α-cyclodextrin from water to the aqueous NaL solution as functions of the surfactant concentration. Lines, best fits according to eqs 13 (solid) and eq 6 (broken), respectively.

cm^3 mol^{-1}). However, it is to be noticed that the order of magnitude of $K_{1:2}$ is consistent with that of the other homologues.

Finally, it is to be noted that for each system, eq 13 was able to fit quantitatively the experimental data over an interval of concentration to a m_S* value close to the experimental cmc (Table 1). This result corroborates the validity of the assumed models and stoichiometries if one reminds that the cmc[33] is usually represented as the sum of the concentrations of both the dispersed and the complexed surfactant; in our case, cmc is given by $([m] + m^w_{1:1} + 2m^w_{1:2})$.

Micellar Region: Quantitative Analysis of the Experimental Data. From the previous results, one can infer that, above m_S*, micelles are present and interact with the cyclodextrin. The utilization of the mass action model for the micellization makes impractical the use of eq 6, and then, the pseudo-phase transition model was assumed; that is valid for NaDec and NaL. As well, according to previous findings,[11] the 1:2 complexes were stated to be in the aqueous phase because unfavorable interactions between the doubly charged complex and the micellar surface are expected. The ΔH_t points of HP-α-CD and HP-γ-CD in NaL and NaDec were analyzed by assuming that the micelles-free cyclodextrin interaction term is negligible because $X^w_C \approx 0$ at the cmc. The best fits provided $K^M_{1:1}$, K_S, and $\Delta H_{t,1:1}$. The narrow fitting interval of the NaL micellar region and the small variation of the volume of transfer prevented the application of eq 6 for both of the cyclodextrins. Although the range of the micellar concentration for HP-α-CD/NaDec was large, in applying eq 6 to the volume of transfer, $K^M_{1:1}$ (derived from the enthalpy) was used due to the small change of the property. The minimizing method was successful for ΔV_t of HP-γ-CD/NaDec. The β values were taken from Table 1. The fitting parameters were collected in Table 4, whereas the best fits are illustrated in Figures 7−10.

Discussion

The standard free energies ($\Delta G^0_{1:1}$) for the 1:1 HP-α-CD/sodium alkanoate complex formation, including those previously published,[11] decrease with the number of carbon atoms in the alkyl chain (n_c) to $n_c = 6$ beyond which they are constant. An identical trend is defined by $\Delta G^0_{1:1}$ of α-CD/alkanoate ions complexes,[9] with the exclusion of α-CD/octanoate, indicating that the alkylation of the cyclodextrin does not reduce the stability of the complexes. From the linear $\Delta H_{1:1}$ vs n_c trend, the contribution of the $-CH_2$ group of -2.9 ± 0.1 and -2.6 ± 0.3 kJ mol^{-1} and that of the hydrophilic group of 7.5 ± 0.8 kJ mol^{-1} and -2 ± 1 kJ mol^{-1}, for the HP-α-CD/substrate and α-CD/substrate[9] complexes, respectively, were evaluated. Therefore, the alkyl groups of the macrocycle influence the interaction between the surfactant head and the shell of the cyclodextrin, whereas they do not influence the forces exerting between the alkyl chain and the cyclodextrin cavity. From these results and literature data, dealing with the inclusion of sodium alkanoates[9,10] and sodium perfluorooctanoate[11] in β-CD and HP-β-CD, one may infer that, regardless of the macrocycle cavity size, the alkylation of the cyclodextrin causes a $\Delta H_{1:1}$ increase of ca. 7−9 kJ mol^{-1} which can be ascribed to both the reduction of the ion−dipole interactions and the loss of hydrophobic hydration of the cyclodextrin alkyl groups.

In agreement with previous findings,[13] the $\Delta V_{1:1}$ values for HP-α-CD/sodium alkanoate are negative and decrease to $n_c = 7$ beyond which they are constant (Figure 11) reflecting the saturation of the cyclodextrin cavity. As far we know, similar systems were studied by Wilson and Verrall,[12] who determined the standard partial molar volumes of transfer (ΔV^0_S) of α,ω-alkyl dicarboxylate anions (C_x^{2-}) from water to the aqueous α-CD solution. By comparing them with the present data, volumetric information on the alkylation effect of the cyclodextrin on the surfactant alkyl chain solubilization into the cyclodextrin cavity can be drawn. The ΔV^0_S points fall on the $\Delta V_{1:1}$ vs n_c trend defined by our data (Figure 11). This does not mean that the volumetric property is sensitive to only the hydrophobic interactions because ΔV^0_S may be dissimilar from $\Delta V_{1:1}$. Therefore, whenever possible, we calculated $\Delta V_{1:1}$ for the literature systems and plotted them in Figure 11. As can be seen, they are shifted in a parallel mode toward more negative values and basically evidence the independence of the methylene group contribution on both the cyclodextrin alkylation and the surfactant polar moiety which, in turn, influences the hydrophilic contribution.

From the present and literature data,[10] a representation of the cavity size effect of the modified cyclodextrin on the thermodynamics of inclusion complex formation can be done. For a fixed n_c, $\Delta G^0_{1:1}$ follows the order HP-α-CD < HP-β-CD < HP-γ-CD which is the same as that of the natural cyclodextrins. This stability scale is controlled by the hydrophilic interactions for HP-α-CD and HP-β-CD because the $-CH_2$ group contribution to $\Delta G^0_{1:1}$ is -4.0 ± 0.2, -4.17 ± 0.05 and -2.3 ± 0.1 kJ mol^{-1} for HP-α-CD through HP-γ-CD, respectively. For a given substrate, $\Delta H_{1:1}$ follows the order HP-γ-CD > HP-β-CD > HP-α-CD. Both the enthalpy and the entropy govern the HP-α-CD/sodium alkanoate complex formation for $n_c < 8$, whereas

TABLE 4: Thermodynamic Properties for the Interaction between Hydroxypropyl−Cyclodextrins and Micelles of Sodium Alkanoates at 298 K[a]

	HP-α-CD		HP-γ-CD	
	NaDec	NaL	NaDec	NaL
K_S	10.3 ± 0.5^b; 2.9 ± 0.3^c	17 ± 1	2.3 ± 0.5^b; 1 ± 1^c	6.6 ± 0.7^b
$K^M_{1:1}$	15 ± 4^b	5 ± 2	20 ± 3^b; 33 ± 6^c	24 ± 4^b
$\Delta G^0_{t,1:1}$	-11.0 ± 0.7	-8 ± 1	-11.7 ± 0.4^b	-11.8 ± 0.4
$\Delta H_{t,1:1}$	-18 ± 3	-19 ± 8	-43 ± 2	-43 ± 2
$T\Delta S_{t,1:1}$	-7 ± 2	-11 ± 9	-31 ± 2	-31 ± 2
$\Delta V_{t,1:1}$	3.6 ± 0.8		-6.2 ± 0.7	

[a] Units are $K^M_{1:1}$ and K_S, kg mol^{-1}; $\Delta G^0_{t,1:1}$, $\Delta H_{t,1:1}$, and $T\Delta S_{t,1:1}$, kJ mol^{-1}; $\Delta V_{t,1:1}$, cm^3 mol^{-1}. [b] From the enthalpy data. [c] From the volume data. The standard free energy of transfer of the 1:1 complex from the aqueous phase to the micellar phase (molarity scale) was calculated[42] as $\Delta G^0_{t,1:1} = -RT \ln(K^M_{1:1}/V_S)$ where V_S is the partial molar volume of the micellized surfactant.[20,43]

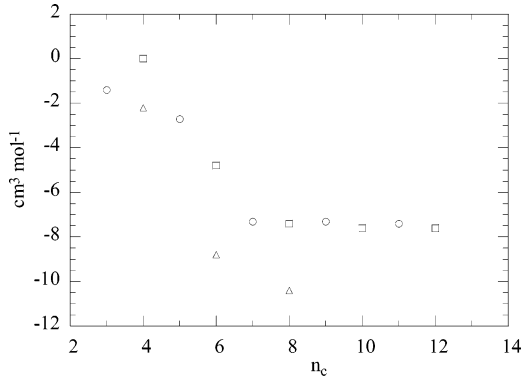

Figure 11. Dependence on the number of carbon atoms in the surfactant alkyl chain of the standard volumes of transfer of α,ω-alkyl dicarboxylate anions from water to the aqueous α-CD solution (□) and volumes for the 1:1 complex formation for α-CD/α,ω-alkyl dicarboxylate anions (△) and HP-α-CD/sodium alkanoates (○). Circles, data at $n_c = 3$ and 7 are from ref 13; squares, data are from ref 12; triangles, calculated by us from data in ref 12.

the process is enthalpy driven for larger n_c. The entropy controls the substrate inclusion into the cavities of HP-β-CD and HP-γ-CD. The $\Delta V_{1:1}$ values for the HP-γ-CD/sodium alkanoate are positive and slightly decrease with n_c; those for HP-β-CD/sodium alkanoates[13] are positive and increase to $n_c = 7$, and thereafter, they are constant. The value of 1.1 cm^3 mol^{-1}, calculated as difference between the partial molar volume of the $-CH_2$ group in apolar solvents (17 cm^3 mol^{-1})[37] and in water (15.9 cm^3 mol^{-1}),[21] is expected for the solubilization of a solvated methylene group into the no hydrated hydrophobic cyclodextrin cavity. The difference between this calculated value and the experimental one, negative for HP-α-CD and HP-γ-CD and positive for HP-β-CD, reflects not only the release of water molecules from the cyclodextrin cavity but also possible conformational changes of the cyclodextrin[38] and the methylene group. It must be remembered that the gauche conformations of hydrocarbons involve negative volumes.[37]

Based on the properties of 1:1 and 1:2 complexes formation, one can elucidate the mechanism of interaction between each guest molecule and the cyclodextrin by analyzing the thermodynamics of 1:1 complexation and that for the interaction between the second guest molecule and the 1:1 complex ($\Delta Y' = \Delta Y_{1:2} - \Delta Y_{1:1}$). For HP-γ-CD/sodium alkanoates, the following is obtained: $\Delta G^0_{1:1} < \Delta G'$, $\Delta H' < \Delta H_{1:1}$, $T\Delta S' < T\Delta S_{1:1}$ and $\Delta V' < \Delta V_{1:1}$. The smaller $\Delta V'$, the negative $\Delta H'$ and the unfavorable $T\Delta S'$ are consistent with the tight association of the surfactant molecule to the HP-γ-CD cavity half-occupied by one guest molecule. In the case of HP-α-CD/surfactant (NaDec and NaOct[11]), one obtains $\Delta G^0_{1:1} < \Delta G'$, $\Delta H' > \Delta H_{1:1}$, $T\Delta S' > T\Delta S_{1:1}$ and $\Delta V' > \Delta V_{1:1}$. These results agree with the interactions between the second surfactant molecule and the torus extended by the hydroxypropyl groups.

Finally, the different mechanisms of interaction for the formation of 1:2 complexes proposed for HP-γ-CD and HP-α-CD are corroborated by the CH_2 group contribution to $\Delta G^0_{1:2}$ which for the former (-2.09 ± 0.04 kJ mol^{-1}) is equal to that of $\Delta G^0_{1:1}$, whereas for the second, it is one-half (-2.1 ± 0.2 kJ mol^{-1}).

As concerns the interactions between cyclodextrin and micelles, the standard free energies of transfer of the 1:1 complex from the aqueous to the micellar phases are essentially independent of the hydrophobicity of the surfactant and the cyclodextrin cavity (Table 4). These data together with the $\Delta H_{t,1:1}$ and $T\Delta S_{t,1:1}$ are consistent with the cyclodextrin−micelles affinity due to the ion−dipole interactions. These results are supported by the increase of the degree of dissociation of the micelles in the presence of cyclodextrin. These results agree with other findings, dealing with natural and modified cyclodextrins in sodium perfluoroalkanoates,[11] evidencing that the cyclodextrin may interact with the hydrophilic shell of the micelles regardless of the nature of both the macrocycle and the surfactant.

Conclusions

Thermodynamic experiments on some water/surfactant/cyclodextrin ternary systems were carried out in both the pre- and postmicellar regions. The experimental data were analyzed by means of a model, reported elsewhere,[11] based on (1) the formation of host−guest complexes of 1:1 and 1:2 (1 cyclodextrin:2 surfactants) stoichiometries in the aqueous phase, (2) the displacement of the micellization equilibrium, and (3) the binding of the cyclodextrin to the micelles. The model was validated by the insights on the binding processes provided when the parameters generated by the model for the various systems were compared among themselves and to the literature ones.

The failure of the minimizing procedure which occurred for some systems does not question the physical validity of the model. The fitting process to be successful must be applied over an interval where not only the variation of the concentration of the bound cyclodextrin defines the curvature related to the equilibrium constant but also the corresponding property change is large. Representative is the NaHex/HP-α-CD mixture. The quantitative analysis did not provide either $K_{1:1}$ with accuracy (despite its large value) because $\Delta V_{1:1}$ is small or precise $K_{1:2}$ and $\Delta V_{1:2}$ values because of the smooth variation of $X^w_{1:2}$ in the fitting interval. Derenleau[39] applied the information theory to the formation constants of 1:1 weak molecular complexes. He concluded that the equation of the model truly represents the experimental data via the fitting process if the saturation curve is defined by ca. 75%. This case is not valid for the present

systems. However, we observed that the minimizing procedure failed when the $X^{w}_{1:2}$ saturation curve was ca. 60%, whereas it was successful when this value increased to 80%.

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Supporting Information Available: Table of the enthalpies of transfer of cyclodextrins from water to the aqueous surfactant solution. Table of the apparent molar volume for HP-α-CD and HP-γ-CD in aqueous surfactant solutions. Table of conductance of sodium decanoate and sodium dodecanoate in aqueous solutions of HP-α-CD and HP-γ-CD. This material is available free of charge via the Internet at http://pubs.acs.org.

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