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Interactions of β-Cyclodextrin with 4-Alkylmorpholine *N*-Oxide Surfactants

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Interactions of β-cyclodextrin (CD) with nonionic surfactants of the 4-alkylmorpholine *N*-oxide type (alkyl = C_9—C_{16}) in aqueous solutions were investigated using the spectrophotometric method with methyl orange and the solubilization method, respectively. Results from both the methods confirmed that the process of surfactant association in aqueous solutions is affected by the formation of water-soluble CD surfactant inclusion complexes. In the presence of CD each phase of this process (*i.e.* monomers, fractional micelle formation range, micellar zone) is shifted towards higher surfactant concentrations. The ratio ΔCMC/*c*(CD) expressing the measure of the CD surfactant interaction decreases with prolongation of the alkyl chain. It seems that the CD interacts with the alkyl chain of the surfactant molecule and not with its polar head group.

Several studies on inclusion complexes of organic molecules with cyclodextrin (CD) indicate that the cavity of CD forms in aqueous medium a hydrophobic environment [1—6]. β-Cyclodextrin interacts with both ionic as well as nonionic surfactants containing an alkyl chain in their molecule, which is demonstrated *e.g.* by a shift in critical micellar concentration (CMC) of the surfactant to higher values [7—11]. The goal of our work was the study of interactions between β-cyclodextrin and a series of nonionic 4-alkylmorpholine *N*-oxide surfactants in aqueous solutions. The spectrophotometric method using methyl orange as well as the solubilization method were adopted for this study. The spectrophotometric method utilized the characteristic changes of the methyl orange absorbance values by interaction with the surfactants in molecular and associate state, respectively.

EXPERIMENTAL

The homologous series of 4-alkylmorpholine *N*-oxides (alkyl = nonyl (*I*), decyl (*II*), undecyl (*III*), dodecyl (*IV*), tridecyl (*V*), tetradecyl (*VI*), pentadecyl (*VII*), and hexadecyl (*VIII*)) was synthesized according to [12].

β-Cyclodextrin (CD) (Chinoin, Budapest), methyl orange (MO), and pyrene (Lachema, Brno) were used. Pyrene was purified by multiple crystallization from benzene.

For determination of the CMC of 4-alkylmorpholine *N*-oxides in aqueous solutions (pH approxi-

mately 6.5) and in the presence of CD (θ = (20 ± 0.2) °C) the spectrophotometry with MO and pyrene solubilization method were used. Detailed description of these methods is in Refs. [7, 8].

RESULTS AND DISCUSSION

In aqueous solutions of 4-alkylmorpholine *N*-oxide surfactants the absorption spectrum of methyl orange (c(MO) = const.) in the visible wavelengths region showed intense changes depending upon the surfactant concentration (*i.e.* on the association degree of the surfactants molecules) which were similar to those observed with *e.g.* ionic surfactants of the type of *N*,*N*′-bis(alkyldimethyl)-1,6-hexanediammonium dibromide [8].

Three phases could be found in the dependence of MO absorbance in aqueous solutions upon concentration of surfactants. At extremely low concentrations which correspond to solutions containing almost exclusively monomers, the absorbance of MO has shown virtually no change with increasing surfactant concentration (observed, however, only with surfactants having shorter (C_9, C_{10}) alkyl chain in their molecule) (Fig. 1). In the case of surfactants possessing longer alkyl chains (C_{11} to C_{16}) a steeply descending dependence was found with a simultaneous shift of the maximum of MO absorption band towards lower wavelength (Fig. 2). This shift due to the interaction between molecules of the surfactant and MO is generally smaller in the case of nonionic surfactants ($\Delta\lambda_{max}$ = 40 nm) as compared to ionic ones ($\Delta\lambda_{max}$ = 85—90 nm) as reported previously [8]. The dependence studied in the concentration interval of the surfactants where fractional micelles are formed (c_1 to CMC region) has shown an increasing trend with all

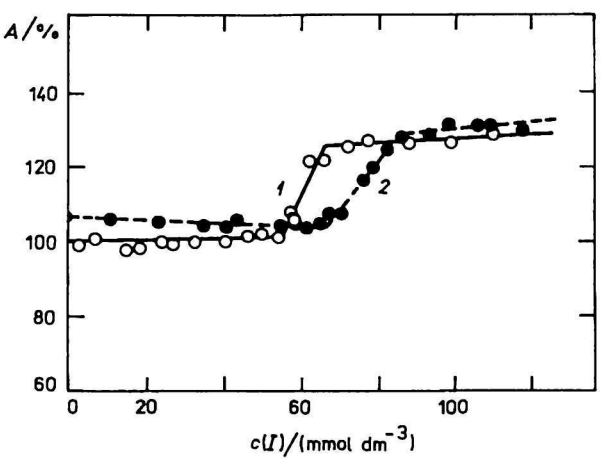

Fig. 1. Absorbance changes of methyl orange due to its interaction with 4-nonylmorpholine *N*-oxide (*I*) in aqueous solution (*1*) and in the presence of CD (*2*).

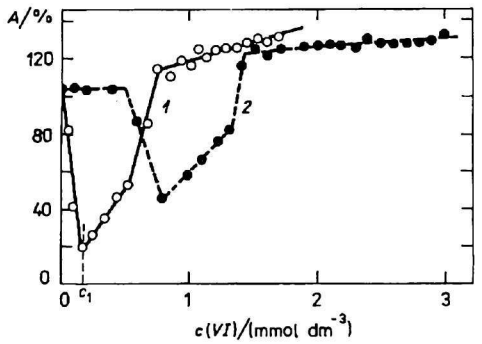

Fig. 2. Absorbance changes of methyl orange due to its interaction with 4-tetradecylmorpholine *N*-oxide (*VI*) in aqueous solution (*1*) and in the presence of CD (*2*).

surfactants used with a simultaneous shift of the MO absorption band maximum back towards higher wavelengths. After having reached the CMC virtually no further changes in the absorption band position can be observed.

The dependence of absorbance of MO *vs.* surfactant concentration can be used for characterization of its association processes in aqueous system (*e.g.* c_1 — the concentration from which premicellar surfactant associates, *i.e.* fractional micelles are formed, and the CMC, respectively (Figs. 1 and 2; curve *1*)).

In aqueous surfactant solutions containing CD (c(CD) = const.) the values of c_1 and CMC are shifted towards higher surfactant concentrations (Figs. 1 and 2; curve *2*). In these systems the concentration of the surfactant monomers is lowered by the CD surfactants inclusion complex formation and thus the association of surfactants mol-

Table 1. Parameters Characterizing the Association Process of Aqueous Solutions of 4-Alkylmorpholine *N*-Oxides (Alkyl = C_9—C_{16}) *I*—*VIII* and those in the Presence of β-Cyclodextrin (CD) Determined by Spectrophotometry Using Methyl Orange (θ = (20 ± 0.2) °C)

N-Oxide	*N*-Oxide with c(CD)	c_1	CMC	ΔCMC
	mmol dm^{-3}	mmol dm^{-3}	mmol dm^{-3}	c(CD)
I		54.73	67.40	
	9.15	66.89	85.20	1.95
II		11.59	19.69	
	9.22	24.32	32.85	1.43
III		2.85	5.56	
	5.00	6.46	11.84	1.20
IV		1.42	2.59	
	2.34	3.23	4.76	0.91
V		0.36	1.20	
	1.24	1.66	2.22	0.81
VI		0.16	0.75	
	0.77	0.79	1.43	0.90
VII		0.08	0.64	
	0.79	0.75	1.22	0.74
VIII		0.08	0.36	
	0.43	0.15	0.64	0.65

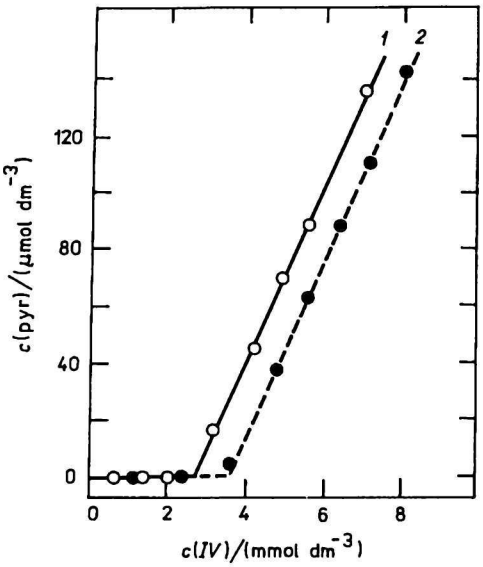

Fig. 3. Solubilization of pyrene in aqueous solutions of 4-dodecylmorpholine *N*-oxide (*1*) and in the presence of CD (*2*).

ecules to premicellar fractional micelles and to micelles above the CMC can occur only at higher surfactant concentrations than in their aqueous solutions (without added CD). The corresponding values of c_1 and CMC for the systems investigated as well as the values of ΔCMC/*c*(CD) are summarized in Table 1. The value of the ΔCMC/*c*(CD) ratio (ΔCMC — the shift of the CMC of the surfactant observed in the presence of CD concentration) seems to be a suitable parameter for expressing the measure of the CD—surfactant interaction.

Solubilization studies carried out with five of 4-alkylmorpholine *N*-oxides (dodecyl to hexadecyl) have also confirmed that CD affects the association process of aqueous surfactant solutions, and the CMC shift towards higher surfactant concentrations was observed (Fig. 3). The values of the slopes of the premicellar (s_1) and micellar (s_2) solubilization lines as well as the values of corresponding ΔCMC/*c*(CD) parameters are presented in Table 2. In the presence of CD the values of s_1 were generally lower than in aqueous surfactant solutions. However, for s_2 slopes close values were obtained. The decrease of the ΔCMC/*c*(CD) parameter with the lengthening of the alkyl chain of the nonionic 4-alkylmorpholine *N*-oxides was confirmed by both experimental methods used (Tables 1 and 2). From the values obtained with *N*-oxides having relatively short alkyl chains (Table 1; ΔCMC/*c*(CD) > 1) it can be assumed that more than one surfactant molecule interact with one CD molecule.

Table 2. Slopes of the Premicellar (s_1) and Micellar (s_2) Parts of Solubilization Lines, Values of CMC and of the Parameter ΔCMC/*c*(CD) of Aqueous Solutions of 4-Alkylmorpholine *N*-Oxides and those in the Presence of β-Cyclodextrin (CD) Determined by Solubilization of Pyrene (θ = (20 ± 0.2) °C)

N-Oxide	*N*-Oxide with *c*(CD) / mmol dm^{-3}	$s_1 \cdot 10^3$	$s_2 \cdot 10^3$	CMC / mmol dm^{-3}	ΔCMC / *c*(CD)
IV		0.42	30.80	2.76	
	0.99	0.04	31.54	3.64	0.891
V		0.66	43.18	1.54	
	1.00	0.09	39.72	2.38	0.832
VI		1.96	52.16	0.768	
	1.17	0.15	52.03	1.67	0.766
VII		0.26	66.75	0.428	
	0.64	0.53	58.35	0.847	0.658
VIII		21.54	47.50	0.654	
	0.57	8.69	46.49	0.968	0.551

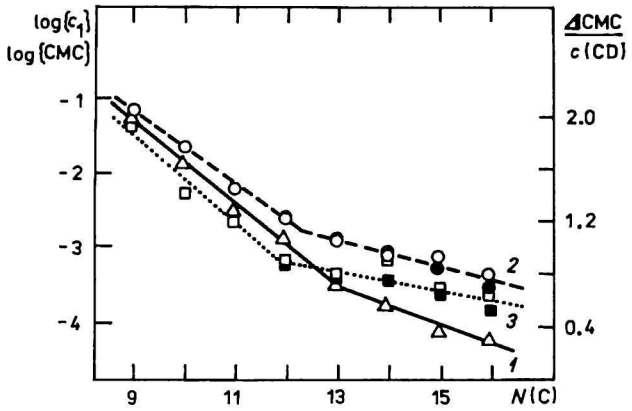

Fig. 4. Dependences of log (c_1/(mmol dm^{-3})) (*1*), log CMC (*2*), and ΔCMC/*c*(CD) (*3*) values upon the number of carbons of alkyl chain of 4-alkylmorpholine *N*-oxides (Δ, ○, □ – values obtained by spectrophotometry; ●, ■ – values obtained by solubilization).

The dependences of log c_1 and of log CMC upon the number of carbons of alkyl chain of the surfactant show a break in the linearity between the dodecyl (C_{12}) and tridecyl (C_{13}) derivatives (Fig. 4). Similar results were obtained by *Mlynarčík et al.* [12] and *Devínsky et al.* [13] in the investigation of antimicrobial properties of *N*-oxides of *N*-alkyl derivatives of saturated heterocyclic amines. According to *Devínsky et al.* [13—16] such a break in the linearity of certain physicochemical and biological properties of amine oxides depending on their alkyl chain length is due also to the change in the sterical arrangement of the surfactant molecule, above all its alkyl chain. After reaching a certain length (usually 10—12 carbon atoms in the chain) its partial twisting as well as its possible interaction with the polar head group of the surfactant molecule can be assumed. The break in the linearity of dependences log c_1, log CMC, and ΔCMC/*c*(CD) *vs.* *N*(C) (Fig. 4) seems to confirm the importance of the stereochemistry of the alkyl chain of the surfactant not only for association processes but also for their interaction with CD.

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