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SYNTHESIS AND PROPERTIES OF MEMBRANOUS SURFACTANTS BEARING AN ANION-CAPPED CROWN RING AS A HEAD GROUP

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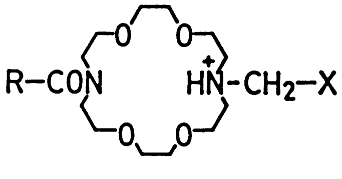
Membrane-forming dialkyl amphiphiles (2a and 2b) bearing an anion-capped crown ether ring as a head group were synthesized. The CMC of 2b, as well as that of a single-chain analogue, was enhanced only on the addition of K^+ (salt-in effect). Electron microscopy established that 2b forms lamellar and rod-like aggregates at pH 6.0. This is the first substantial example for the membrane formation from crown-containing dialkyl amphiphiles.

Since the first report (in 1977) on the formation of stable bilayer membranes from totally synthetic surfactants,1) it was shown in several laboratories that a number of long-chain dialkyl amphiphiles forms stable bilayer membranes in aqueous solution.2-6) It occurred to us that combination of host-guest chemistry with these membranous systems would provide a new field of chemistry which could mimic partly the action of receptor molecules in biological membranes. One potential approach would be the synthesis of dialkyl amphiphiles with host molecules (e.g., crown ethers) as a head group which could serve as recognition sites on the membrane surface. Monserrat et al.7) and Czugler et al.8) have reported on the synthesis of such crown ethers having dialkyl long-chains, but except for the light-scattering data,7) almost nothing is known with certainty as to the solution properties of these crown ethers: the experimental difficulty arose from poor solubility, instability of the aggregates, and complexity in sample preparation for electron microscopy.7,8) In order to resolve these problems, we introduced an anion-cap into crown-containing dialkyl long-chains (2a and 2b). We have found that these amphiphiles (particularly, 2b) can be dispersed in water to form stable aggregates and that the aggregate structure is sensitively affected by pH and added metal cations.



	R–	–X
1a;	$CH_3(CH_2)_{10}$–	$-COO^-$
2a;	$[CH_3(CH_2)_{15}OCH_2]_2CHOCH_2$–	$-COO^-$
1b;	$CH_3(CH_2)_{10}$–	$-CH_2SO_3^-$
2b;	$[CH_3(CH_2)_{15}OCH_2]_2CHOCH_2$–	$-CH_2SO_3^-$

Preparation of **1a** was described previously.[9)] **2a**, **1b**, and **2b** were synthesized by the reaction of $C_{12}H_{25}N_2O_4$-CH_2X with the corresponding acid chlorides. The products were isolated by a TLC method and identified by IR, NMR, and elemental analysis: **2a**, mp 44-46 °C; **1b**, mp 50-52 °C; **2b**, mp 36-37 °C.

1a and **1b** were well soluble in water. When the dialkyl amphiphiles (**2a** and **2b**) were dispersed in water by a Branson cell disruptor 185, an aqueous solution containing **2b** became clear but **2a** gave a slightly turbid solution. From an acid-base titration of these surfactants (2.0×10^{-3} M: 1 M = 1 mol dm^{-3}) at 30 °C, the following pK_a values were determined: $pK_{a1} = 3.45$ and $pK_{a2} = 6.99$ for **1a**; $pK_a = 7.09$ for **1b**; $pK_a = 7.10$ for **2b**. **2a** gave a turbid dispersion in water, so that the pK_a values could not be determined precisely. These pK_a values indicate that the head group of **1a** changes as $>NH^+CH_2COOH \rightleftharpoons >NH^+CH_2COO^- \rightleftharpoons >NCH_2COO^-$ with increasing medium pH, while **1b** and **2b** have a zwitterionic head ($>NH^+CH_2CH_2SO_3^-$) in the acidic pH region and an anionic head ($>NCH_2CH_2SO_3^-$) in the basic pH region. Differential scanning calorimetry (DSC) shows that the solutions containing **2a** and **2b** give pH-dependent DSC peaks at the following temperatures: **2a**, 44 °C (pH 1.3 with HCl), 47 °C (pH 9.0 with 0.001 M borate); **2b**, 41 °C (pH 3.0 with HCl), 40 °C (pH 10.0 with 0.001 M borate). These DSC data support that **2a** and **2b** form oriented aggregates in water.

Kalyanasundaram and Thomas[10)] have established that vibronic band intensities in pyrene monomer fluorescence is a convenient probe to accurately determine critical micelle concentrations (CMC): the ratio (band III/ band I) in water (0.63) increases to 0.90 in micellar sodium dodecylsulfate (SDS) solution. The CMCs determined by this method are summarized in Table 1. The length of the aliphatic chains of SDS and **1b** is similar. It is seen from Table 1, however, that the CMC of **1b** is lower by one order of magnitude than that of SDS. This suggests that the crown ether moiety in **1b** rather facilitates the micelle formation. The CMC for **2b** (membrane-forming dialkyl analogue) was much lower.

In general, the CMCs of ionic surfactants are lowered by the addition of salts (salting-out effect). In fact, the CMC of SDS was lowered on the addition of K^+ and Me_4N^+ (Table 1). The CMCs of **1b** and **2b** were lowered or almost unaffected by the addition of Li^+ and Me_4N^+ but enhanced only on the addition of K^+. The difference should be attributed to the specific binding of K^+ to the diaza-18-crown-6 moiety of **1b** and **2b**. The phenomenon (salting-in effect) has been noticed by Le Moigne and Simon[11)] and Okahara et al.[12)] for crown ethers having single aliphatic chains. Conceivably, the crown ether rings become more hydrophilic through complexation with metal cations.

The aggregate structure of **2b** was evaluated by electron microscopy. When **2b** (3.0 mM) was dispersed in a buffered aqueous solution (pH 6.0) without sonication, the lamellar structure with 40-50 Å wall-width was observed (Fig. 1A). When the solution was sonicated at pH 6.0, **2b** gave the rod-like aggregates (Fig. 1B). Similar rod-like aggregates have been found for some single-chain ammonium amphiphiles.[13)] In the present system, the diameter of rods was 130 ± 15 Å.[14)] When **2b** was dispersed with sonication at pH 9.0, it gave less clear aggregates. The head group structure is zwitterionic and anionic at pH 6.0 and 9.0,

Table 1. Influence of added cations on CMCs of 1b, 2b, and SDS[a)]

Surfactant	CMC /mM			
	water	LiOH[b)]	KOH[b)]	Me_4NOH[b)]
1b	0.75	——	3.0	0.55
2b	0.025	0.025	0.080	0.030
SDS	7.0	——	4.0	3.5

a) 30 °C, [pyrene] = 2.00×10^{-6} M.

b) [MOH] = 0.010 M.

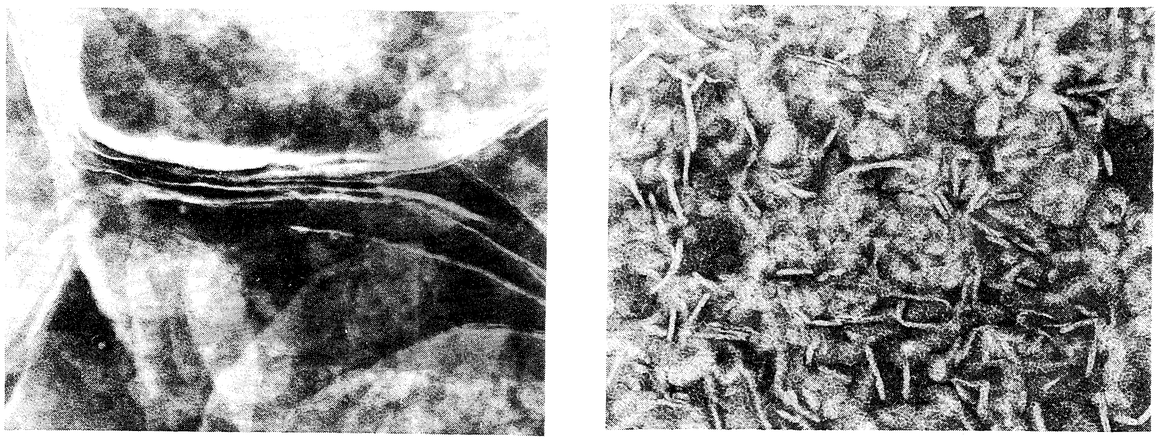

(A) (B)

Fig. 1. Electron micrographs of 2b stained by ammonium molybdate (1.0 wt%): (A) without sonication at pH 6.0 (x30000 as provided); (B) pH 6.0 with sonication (x75000).

respectively, so that the aggregate morphology is strongly affected by the nature of the surface charge. The aggregate morphology was also not clear at pH 8.0-9.0 in the presence of NaCl (1.0 M) or KCl (1.0 M). The fluorescence data mentioned above indicated that the binding of K^+ to the crown ring makes the crown head group more hydrophilic. However, its influence on the morphological change could not be evaluated clearly from electron microscopy.

In conclusion, the present study clearly demonstrated the formation of membranous aggregates from crown-containing dialkyl amphiphiles. Although crown ethers having dialkyl long-chains have been synthesized previously,[7,8)] our result is the first example to support the membrane formation unequivocally. The phenomena observed herein remind us of the role of biological receptor molecules, metal binding to which induces conformational or morphological changes in peptides or membranes. Further characterizations and applications are continued in these laboratories.

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14) The width of a single bilayer wall estimated from CPK models is 40-50 Å. Probably, the present tubular aggregates consist of a dual bilayer wall.

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