CHEMISTRY LETTERS, pp. 387-390, 1977. Published by the Chemical Society of Japan

FORMATION OF THE BILAYER MEMBRANE FROM A SERIES OF QUATERNARY AMMONIUM SALTS

Toyoki KUNITAKE,*[1] Yoshio OKAHATA,[1] Kiyoshi TAMAKI,[1]
Fumiko KUMAMARU,[2] and Motowo TAKAYANAGI[2]
Department of Organic Synthesis[1] and Applied Chemistry,[2]
Faculty of Engineering, Kyushu University, Fukuoka 812

A series of dimethylammonium salts having two long alkyl groups were shown by electron microscopy to form in water lamellar and vesicle structures which are composed of the bilayer structure similar to that of biomembranes.

The fundamental organization of biomembranes is based on the bilayer structure of lipid molecules. The nature of the bilayer structure has been extensively studied using biomembranes as well as lipsomes and black membranes of bio-lipids.[1)]

The formation of the bilayer structure using totally synthetic systems would be extremely important for establishing the physicochemical basis of the biomembrane structure and for developing membrane-related chemical processes. We have observed that aqueous didodecyldimethylammonium bromide forms vesicles and lamellae whose structures are similar to those of the lecithin bilayer.[2)] In this communication we report the formation of the bilayer structure from series of dialkyldimethylammonium salts.

These ammonium salts are commercial products or were prepared by the stepwise alkylation of dimethylamine. They were recrystallized from ethyl acetate, and their purities were confirmed by elemental analysis and NMR spectroscopy.

Stock solutions for the electron micrographic study were prepared by sonication(Branson cell disrupter) of ammonium salts suspended in deionized water for 3-5 min at temperatures below 35°C. Two ml of the stock solution containing 10 mM of an ammonium salt were mixed with 2 ml of an uranyl acetate solution(2 % in water), sonicated for 15 sec, kept in ice water, and applied to a carbon grid. In several cases, stock solutions were prepared by sonication for 3 hr at 80°C in a water-bath type sonicator(Bransonic 12 type).

Figure 1a is an electron micrograph of a slightly turbid solution of dioctadecyldimethylammonium chloride($2C_{18}N^{+}2C_{1}$). Lamellar structures of ca. 50 Å layer width are observed. Further sonication did not detectably alter this structure: however, addition of hexadecyltrimethylammonium bromide(CTAB) caused fragmentation of the lamellar structure. On the other hand, an electron micrograph of a ditetradecyldimethylammonium chloride($2C_{14}N^{+}2C_{1}$) solution shows the presence of lammellae and vesicles(Figure 1b).

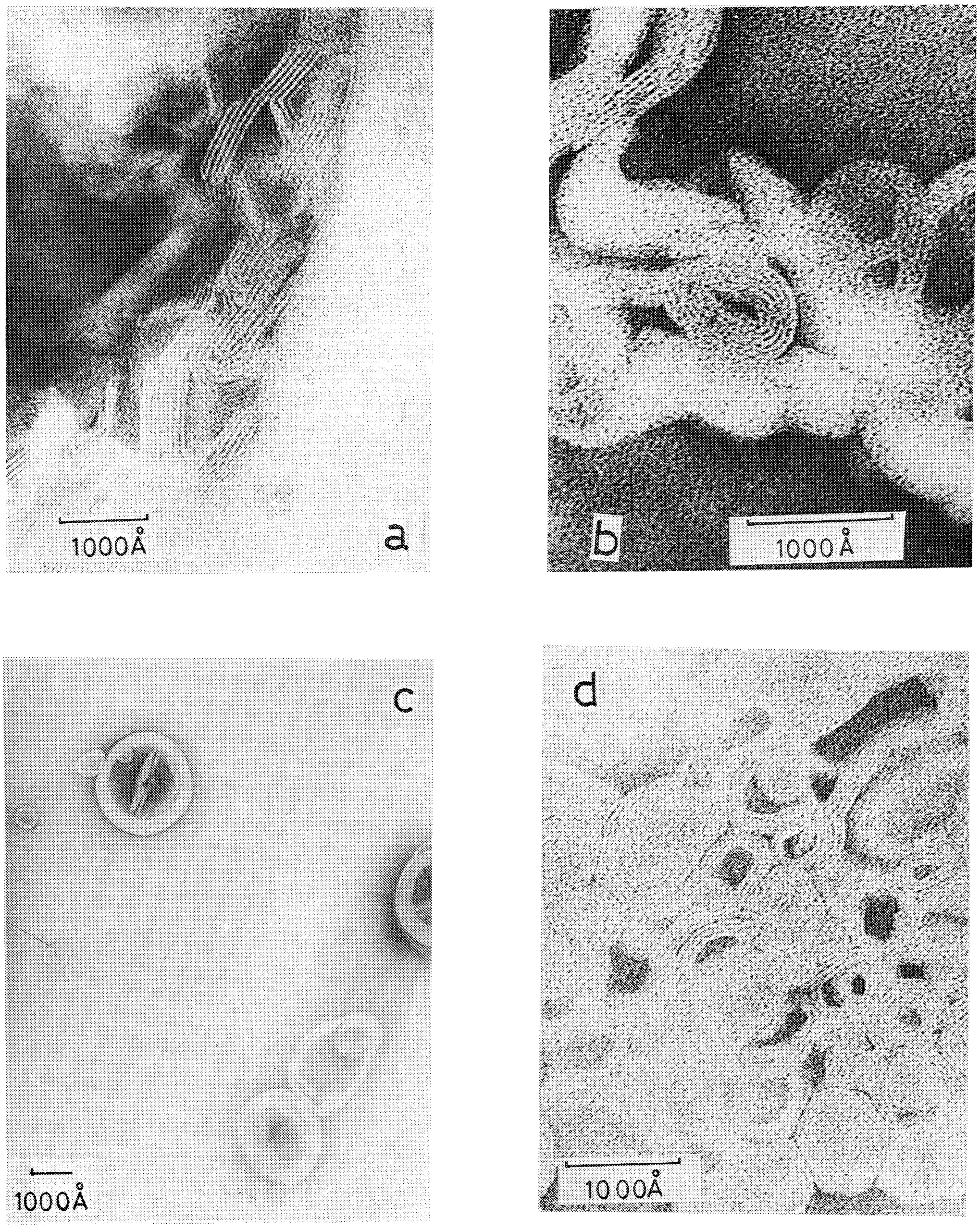

Fig. 1. Electron micrographs(Hitachi model H-500)

a. $2C_{18}N^{+}2C_{1}$, magnification x 150,000.

b. $2C_{14}N^{+}2C_{1}$, magnification x 250,000.

c. $C_{18}C_{12}N^{+}2C_{1}$, magnification x 70,000.

d. $C_{18}C_{12}N^{+}2C_{1}$, magnification x 200,000.

Table I Electron Micrographic Observation

Ammonium salt $R_1R_2N^+(CH_3)_2Br^-$ R_1	R_2	Abbreviation	Melting point °C	Appearance of stock solution	Electron micrographic observation
$C_{22}H_{45}$	$C_{22}H_{45}$	$2C_{22}N^+2C_1$	89-90	insoluble	——
$C_{18}H_{37}$	$C_{18}H_{37}$	$2C_{18}N^+2C_1$[a)]	73-75	slightly turbid	lamella
$C_{14}H_{29}$	$C_{14}H_{29}$	$2C_{14}N^+2C_1$[a)]	50-51	slightly turbid	vesicle and lamella
$C_{12}H_{25}$	$C_{12}H_{25}$	$2C_{12}N^+2C_1$	55-56	clear	vesicle
$C_{18}H_{37}$	$C_{16}H_{33}$	$C_{18}C_{16}N^+2C_1$	74-75	slightly turbid	lamella
$C_{18}H_{37}$	$C_{14}H_{29}$	$C_{18}C_{14}N^+2C_1$	62-63	slightly turbid	vesicle and lamella
$C_{18}H_{37}$	$C_{12}H_{25}$	$C_{18}C_{12}N^+2C_1$	62-63	clear	vesicle
$C_{18}H_{37}$	$C_{10}H_{21}$	$C_{18}C_{10}N^+2C_1$	60-61	clear	vesicle
$C_{18}H_{37}$	C_8H_{17}	$C_{18}C_8N^+2C_1$	57-58	clear	no structure
$C_{16}H_{33}$	CH_3	CTAB	237-239	clear	no structure

a) Ammonium chloride.

Similar studies were carried out for a series of unsymmetrical dimethylammonium salts. Electron micrographs for octadecyldodecyldimethylammonium bromide($C_{18}C_{12}N^+2C_1$) are shown as examples in Figures 1c and 1d. Figure 1c is an electron micrograph for a stock solution of $C_{18}C_{12}N^+2C_1$ which was prepared by sonication at higher temperatures. Although well-defined vesicles of varying sizes are observed, the layer structure is not developed sufficiently. Upon aging of the stock solution in ice water, the layer structure can be seen more clearly(see Figure 1d).

These results are summarized in Table I. Didococyldimethylammonium bromide ($2C_{22}N^+2C_1$) could not be dispersed in water. Other ammonium salts produce clear or slightly turbid solutions which contain well-defined molecular aggregates. Aqueous solutions of octadecyloctyldimethylammonium bromide($C_{18}C_8N^+2C_1$) and hexadecyltrimethylammonium bromide(CTAB) did not provide any indication of the structure formation.

It is now concluded that ammonium salts with two long alkyl groups can aggregate in water to form well-defined organizations such as vesicles and lamellae. The fundamental unit of these organizations appears to be the bilayer structure similar to that of the biomembrane, since the layer thickness is 40-50 Å. The development of the bilayer structure will depend on the structure of the ammonium salt and on the preparative condition.

The authors are grateful to Kao Soap Company, Ltd. for supplying two of the ammonium salts, and to Prof. J. Sunamoto(Nagasaki University) for lively discussions.

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(Received February 22, 1977)