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CHIRAL, SYNTHETIC BILAYER MEMBRANES[1)]

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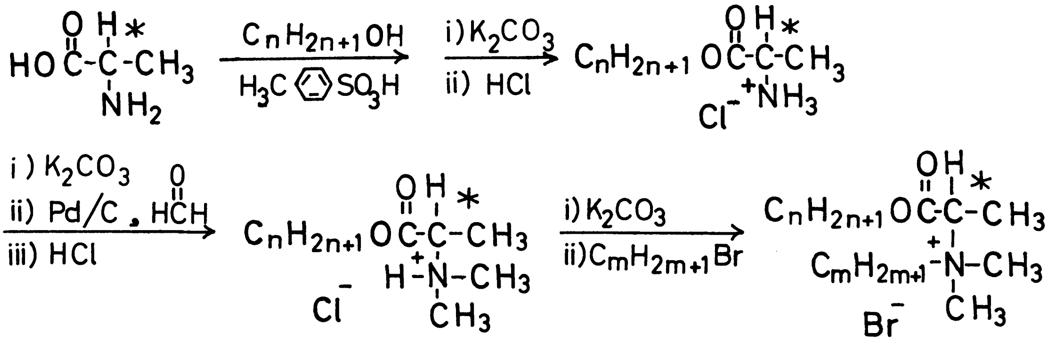
Chiral dialkylammonium surfactants as synthesized from alanine and glutamic acid formed well-developed bilayer membranes when dispersed in water. The phase transition temperature did not differ between the chiral and racemic membranes, and induced circular dichroism was observed with chiral membranes when a hydrophobic azo dye was added.

We have shown quite recently that a variety of ammonium amphiphiles which possess two, long alkyl chains can form the bilayer membrane spontaneously upon dispersion in water.[2-4)] These synthetic membranes show the liquid crystalline behavior as probed by line broadening in NMR spectroscopy,[5)] differential scanning calorimetry,[6)] fluorescence polarization[5,7)] and positron annihilation.[7)]

The synthetic membrane would provide unique microenvironments for reaction when compared with conventional micelles. It was already reported that a cholesteryl nucleophile was specifically activated by an ammonium bilayer[8)] and that the rate of acyl transfer was influenced by the phase transition of the bilayer membrane.[9)] On the other hand, the liquid crystalline nature of the bilayer would be effective for strengthening the chiral influence in order to attain highly stereospecific reactions. As the first step to test this hypothesis, we prepared chiral dialkylammonium amphiphiles and investigated whether they form the bilayer membrane.

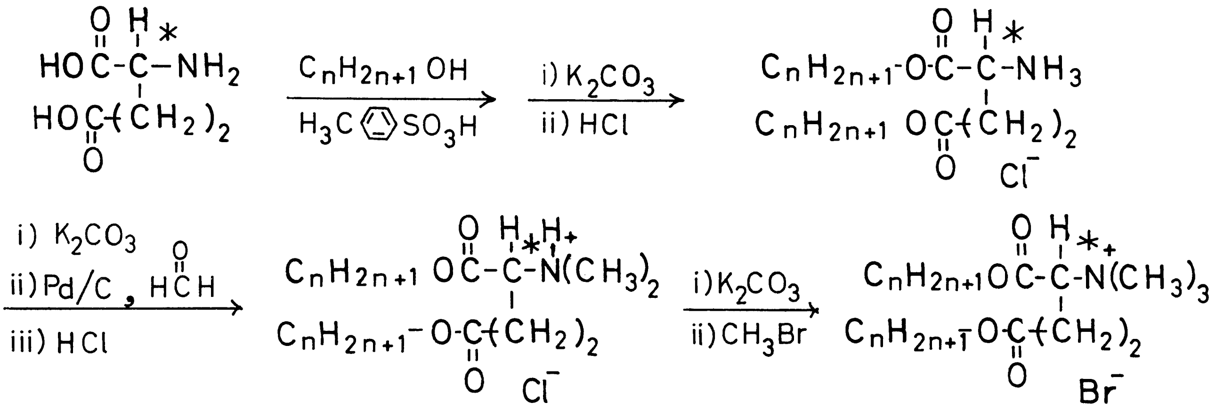
Chiral dialkyl amphiphiles were prepared by the following procedures from alanine (scheme 1) and from glutamic acid(scheme 2). The purities of the intermediates and the final products were confirmed by IR and NMR spectroscopies, by thin layer chromatography, and by elemental analysis. A chiral single-chain surfactant C_{12}-L-AlaN$^+$3C_1(n = 12 and m = 1 in C_nC_m-L-AlaN$^+$2C_1) was also prepared for the comparison purpose.

SCHEME 1



C_nC_mAlaN$^+$2C_1

SCHEME 2



$2C_nGluN^+3C_1$

Table 1 gives melting points and values of specific rotation for the final dialkyl ammonium amphiphiles. The optical purity of these final compounds could not be determined absolutely. However, the reactions employed in the synthetic schemes are relatively safe ones in terms of racemization, and, in addition, the absolute values of optical rotation show a satisfactory agreement between the L- and D-isomers of $2C_{12}GluN^+3C_1$ (+6.6° vs. -7.1°). Therefore, we believe that the ammonium compounds of Table 1 are essentially optically pure.

Table 1. Chiral Ammonium Amphiphiles and their Aggregates

No.	Amphiphile			Aggregate	
	Abbreviation	mp/°C	$[\alpha]_D^{20}$ a)	T_c b)/°C	Electron micrograph (10 mM)
1	$C_{12}C_{16}$-L-AlaN$^+$2C_1	109 - 110	-5.6°	34.5	lamella
2	$C_{12}C_{16}$-DL-AlaN$^+$2C_1	109 - 110	0	34.5	lamella
3	2C_{18}-L-AlaN$^+$2C_1	112.5-115	-5.2°	53.5	lamella
4	2C_{18}-DL-AlaN$^+$2C_1	112 - 115	0	53.2	lamella
5	2C_{12}-L-GluN$^+$3C_1	128 - 130	+6.6°	27.3	vesicle & lamella
6	2C_{12}-D-GluN$^+$3C_1	127 - 129	-7.1°	27.5	vesicle & lamella
7	2C_{12}-DL-GluN$^+$3C_1	112 - 115	0	26.9	vesicle & lamella
8	2C_{18}-L-GluN$^+$3C_1	130 - 132	+5.3°	55.3	lamella
9	2C_{18}-DL-GluN$^+$3C_1	112 - 114	0	55.2	lamella
10	C_{12}-L-AlaN$^+$3C_1	173 - 176	-15.8°	—	no structure

a) 1.2 - 2.5 % ethanol solution(Nos. 1 - 4 and 10). 2.35 % chloroform solution(Nos. 5 - 9).

b) Sample, 1 wt% in water. Temperature was raised from -50°C at the rate of 2°C/min. Instrument, Daini-seikosha SSC/560.

These amphiphiles suspended in water were sonicated by a Bransonic Sonifier for 5 - 15 min to give clear solutions(10 mM). These solutions were stained negatively by uranyl acetate and subjected to electron microscopic examination.[2] As shown in

Fig. 1a, the vesicle structure with diameter of 300 - 500 Å was observed for aqueous $2C_{12}$-L-GluN$^{+}3C_{1}$. The lamellar structure can also be produced, depending on the extent of dispersion. The observed layer width(∿ 40 Å) corresponds approximately to two times the molecular length, supporting the formation of the bilayer structure. Figure 1b is a typical lamellar structure observed for the aggregate of $C_{12}C_{16}$-L-AlaN$^{+}2C_{1}$.

In general, the bilayer structure of these amino acid-derived amphiphiles is better developed than that of simple dialkylammonium counterparts. This suggests that development of the bilayer is appreciably affected by the chemical structure which connects the alkyl chain and the ammonium group.

The aqueous solutions show endothermic peaks in differential scanning calorimetry due to the phase transition between the crystal and liquid crystal phases. The transition temperatures T_c thus determined are also listed in Table 1. The T_c values of the chiral membranes are the same as those of the corresponding racemic membranes within the experimental error in all of the four combinations. For instance, the T_c values of $2C_{12}$-L-GluN$^{+}3C_{1}$ and its racemate are 27.3 and 26.9°C, respectively, although their melting points differ by 15°.

The chiral microenvironment has been often studied by means of induced circular dichroism(ICD). When Methyl Orange was used as a probe, the circular dichroic absorption was not induced with any chiral membrane(Table 1, Nos. 1, 3, 5, 6 and 8) in the 300 - 500 nm region where Methyl Orange possesses an absorption band. In contrast, its alkyl derivative 1 gave marked ICD spectra in the presence of chiral membranes of $2C_{12}$-GluN$^{+}3C_{1}$(D and L isomers), as shown in Fig. 2. No ICD spectra were observed when $2C_{12}$-GluN$^{+}3C_{1}$ was replaced by chiral, micelle-forming C_{12}-L-AlaN$^{+}3C_{1}$(single-chain surfactant). Micelle-induced CD spectra have been reported only in special cases such as aliphatic ketones in a deoxycholate micelle($[\theta]_{max}$ = 10)[10] and Sudan III in a D-12-hydroxystearate micelle ($[\theta]_{max} \cong 10^{4}$).[11] The present data suggest that ICD spectrum can be used as a general means for studying the chiral microenvironment of the bilayer membrane.

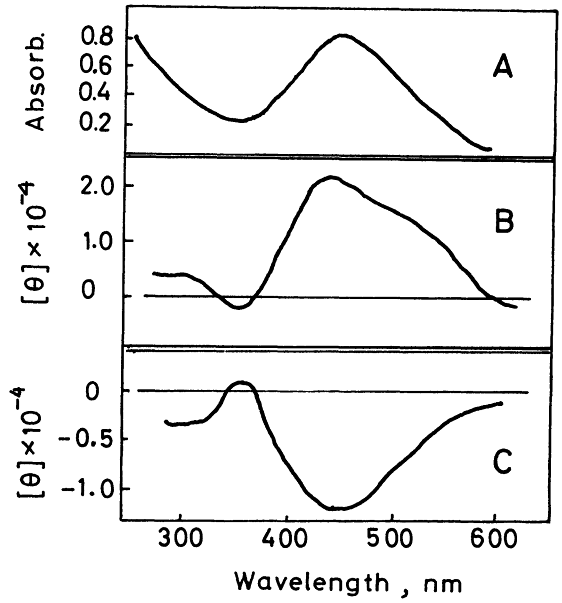
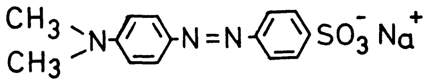


Fig. 2

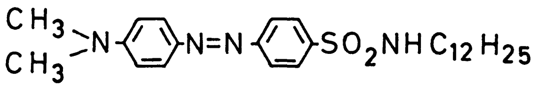
Absorption and ICD spectra of 1(5.0 × 10^{-5} M) in aqueous bilayers of $2C_{12}$-GluN$^{+}3C_{1}$ (6.0 × 10^{-3} M).

A: Absorption spectrum.

B and C: ICD spectra in the presence of D- and L-bilayer membranes, respectively.



Methyl Orange



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In conclusion, it is established that chiral bilayer membranes are formed by spontaneous aggregation of chiral dialkyl surfactants. These chiral membranes are highly organized and would provide unique microenvironments for a variety of reactions.

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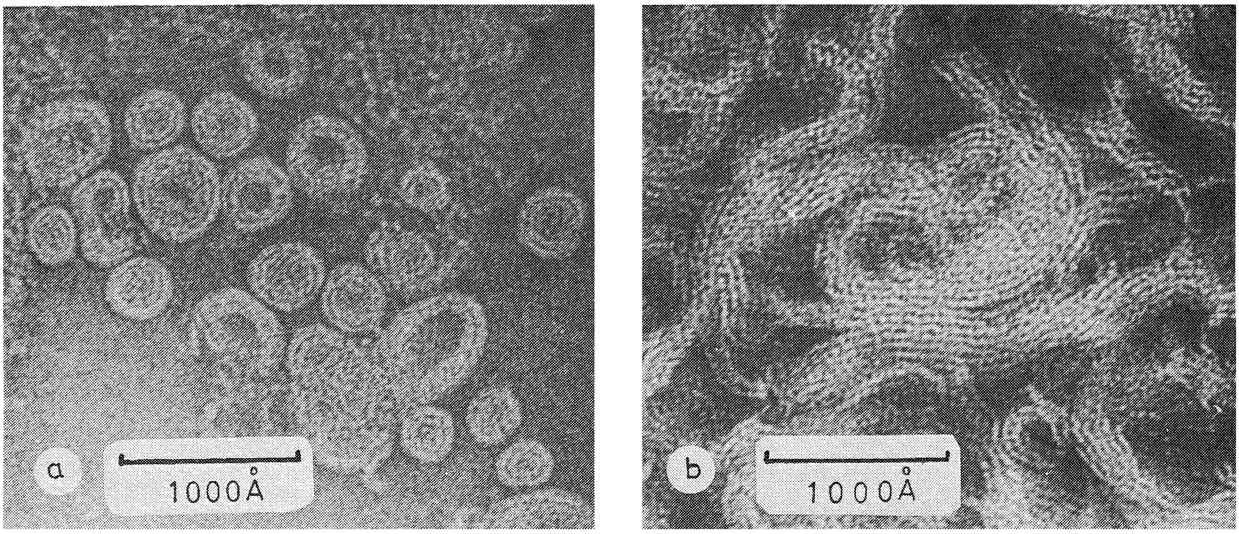

Fig. 1 Electron micrograph

a. $2C_{12}$-L-Glu-$N^{+}3C_{1}$, magnification × 300,000.

b. $C_{12}C_{16}$-L-Ala$N^{+}2C_{1}$, magnification × 300,000.

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