Synthesis and Properties of Dialkylmethyl Sulphate Bilayers

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Sodium dialkylmethyl sulphates have been prepared and converted into vesicles which possess main phase transition temperatures comparable with those of the corresponding phospholipids and show an inertia for the two-phase electron transfer of ascorbic acid in the aqueous phase to nitroxide in the inner leaflet of the bilayers.

Synthetic surfactant vesicles of various structures, believed to be the simplest functional bilayer membrane models,[1] have been extensively investigated[2—5] in the past decade. Since the first formation of vesicles from the simple surfactant didodecyldimethylammonium bromide (DDDAB) reported by Kunitake,[2] the surfactants which have been used for preparing vesicles include quaternary ammonium salts,[1—3] benzenesulphonates,[4] and amino phospholipids.[5,6] However, no vesicle has been formed from a synthetic surfactant with a sulphate head group.[7] For comparison with the aggregation and the microenvironmental properties of the molecular organization of single-chain alkyl sodium sulphates, we have prepared a series of sodium dialkylmethyl sulphates to study their aggregation and other properties. The surfactants were prepared from the corresponding ethyl esters *via* Claisen condensation, decarboxylation, reduction, acidification, and esterification (Scheme 1).

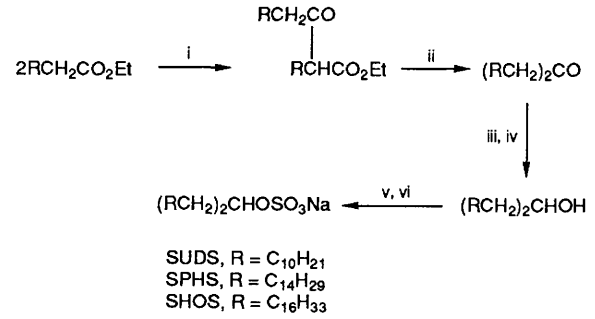
Table 1. Transition temperatures (T/°C) of sodium dialkylmethyl sulphate vesicles.

Compound	Pre-transition[a] Fluorescence	Main transition[a] Fluorescence	Main transition[a] DSC
SUDS		15	15
SPHS	28.4	33.1	32.6
SPHS[b]	30.0	33.4	
SHOS	40.5	42.8	43.0

[a] Average deviation is ± 0.2 for fluorescence, ±0.4 for DSC. [b] Vesicle formed by stirring at room temperature.

The structures of the intermediates and products were established by elemental analysis, IR and NMR spectroscopy. The total yields based on the esters are *ca.* 40% for sodium 1-undecyldodecyl sulphate (SUDS) and sodium 1-pentadecylhexadecyl sulphate (SPHS) and 13% for sodium 1-heptadecyloctadecyl sulphate (SHOS).

Water dispersions of the surfactants were formed by indirect ultrasonication or stirring a lyophilized sample film in deionized water containing 1% of sodium phosphotungstate above the phase transition temperature of the formed bilayer for *ca.* 1 h. The dispersion was kept at this temperature for another 2 h, cooled rapidly to below its transition temperature, and then incubated at the latter temperature for 2 days. Formation of spherical vesicles of three surfactants was confirmed by electron micrographs negatively stained with



Scheme 1. *Reagents and conditions*: i, EtONa, heat, reduced pressure; ii, 95% EtOH, 5% NaOH, heat;[8] iii, Pr^iOH, $Al(OPr^i)_3$; iv, dil. HCl;[9] v, $ClSO_3H$, −15 °C, dry Et_2O; vi, 1 M $NaHCO_3$.[10]

sodium phosphotungstate. The stirred water dispersion of SUDS showed the formation of globular aggregates. The vesicle sizes ranged between 100 and 1300 Å. The electron micrograph of a stirred SPHS dispersion indicated multi-walled vesicles with bilayer bands. However, SHOS formed mainly multi-walled vesicles by stirring but single-compartment vesicles by sonicating.

The transition temperatures of these vesicles were measured by both fluorescence and differential scanning calorimetry (DSC) methods and the results are given in Table 1. The fluorescence method measures both the intensity ratio of the maximum excimer emission (I_e) to the maximum monomer emission (I_m) (I_e/I_m) and the monomer vibrational I_1 to I_3 intensity ratio (I_1/I_3) of bilayer-embedded pyrene as a function of temperature.[7] The temperatures related to the two breaks on the I_e/I_m or I_1/I_3 *vs.* T plot for each vesicle are taken as that of the pre-transition and the main transition, respectively. The transition temperatures obtained from the two measurements coincide well. For the SUDS vesicle, no pre-transition was observed since the change of ratio with temperature was too small to be measured. The main transitions of these vesicles are between those of the amino phospholipid vesicles and that of the quaternary ammonium vesicles with the same length of alkyl chain. Also the fluorescence method is more sensitive than the DSC method for which no pre-transition was observed for any of the vesicles studied.

It has been reported[11] that nitroxide is easily reduced by ascorbic acid (vit. C). The morphological structures of the bilayers were also characterized by tracing the two-phase electron-transfer reaction between the water soluble vit. C and the hydrophobic stable free radical 4-hexadecanoyloxy-2,2,6,6-tetramethylpiperidin-1-yloxyl (4-HD-TEMPO) by EPR spectroscopy. After the addition of an excess of aqueous vit. C solution (>5 equiv.) to a suspension of the bilayer containing 4-HD-TEMPO at a temperature below that of its transition, the EPR signal for 4-HD-TEMPO suddenly decreased to a value which remained constant for several hours at least. However, as the temperature was increased to above that of the transition, the signal of 4-HD-TEMPO diminished in a few minutes. The intensity of the EPR signal for 4-HD-TEMPO in a SUDS bilayer in the presence of excess of vit. C is 40% of that in the absence of vit. C, whereas the intensity of the EPR signal for 4-HD-TEMPO in SHOS and SPHS vesicles in the presence of vit. C is less than 40% of that in the absence of vit. C and the reproducibility of the experimentation is poor. Since the surface density of the probe in the inner bilayer is approximately the same as that in the outer layer,[12] the EPR results again indicate that the vesicles formed from SUDS are mostly single-compartment vesicles, while those from SHOS and SPHS are multilamellar.

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