Self-assembled Microstructures from a Polymerizable Ammonium Surfactant: Di(Hexacosa-12,14-diynyl)dimethylammonium Bromide

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Micron-size cylindrical and quasi-spherical assemblies have been obtained from aqueous dispersions of di(hexacosa-12,14-diynyl)dimethylammonium bromide.

We have observed the formation of some unusual microstructures produced from di(hexacosa-12,14-diynyl)dimethylammonium bromide (DHDAB) (**1**). Our earlier studies demonstrated that diacetylenic phospholipids produced tubular microstructures as well as vesicles from aqueous dispersion.[1—3] The formation of tubules, both from diacetylene-containing phosphatidylcholine[4] (PC) and a non-diacetylenic glutamate[5]-based amphiphile, has been thought to proceed *via* precipitation from solvent solution as helices,[5] which grow into continuous cylinders. The chiral centre of these molecules can be correlated with the handedness of the overall molecular assembly.[4—6] It is clear that the diacetylenic moiety has an important role in the formation of these microstructures[2] since only those PCs which contain the diacetylene moiety in the alkyl chains form tubules and helices. Diacetylenic racemates have also been observed to form tubules and helices with both right- and left-handed structures.[7] The presence of the diacetylenic moiety also has been shown for other materials including phosphatidylcholines to allow a 1,4-polymerization to occur upon irradiation by 254 nm light.[8]

We report a study of the microstructures produced from an achiral, non-phospholipidic amphiphile. Both normal vesicles and cylinders (similar, but not identical with previously reported tubular structures[1]) were observed. These results suggest that chirality is not an absolute requirement for the formation of hollow cylindrical microstructures.

Preliminary differential scanning calorimetry studies on the aqueous dispersion (concentration 200 mg ml^{-1}) of the DHDAB showed two broad endotherms of almost equal size at 22.4 and 33.8 °C on heating, and a sharp, major exotherm at 31 °C and a small broad exotherm at 15 °C upon cooling (scan rate 2 °C min^{-1}). The values of cooling enthalpy are smaller than the values measured for the heating cycle.

$$\mathrm{Me_2\overset{+}{N}([CH_2]_{11}\text{–}C{\equiv}C\text{–}C{\equiv}C\text{–}[CH_2]_{10}Me)_2\ Br^-}$$

(**1**)

$$\underset{(2)}{\mathrm{HO[CH_2]_{11}\text{–}C{\equiv}CH}} + \underset{(3)}{\mathrm{IC{\equiv}C\text{–}[CH_2]_{10}Me}} \xrightarrow{\mathrm{CuCl,\ EtNH_2}}$$

$$\underset{(4)}{\mathrm{HO[CH_2]_{11}\text{–}C{\equiv}C\text{–}C{\equiv}C\text{–}[CH_2]_{10}Me}} \xrightarrow{\mathrm{PBr_3/Et_2O}}$$

$$\underset{(5)}{\mathrm{Br[CH_2]_{11}C{\equiv}C\text{–}C{\equiv}C\text{–}[CH_2]_{10}Me}} \xrightarrow{\mathrm{Me_2NH/toluene}}$$

$$\underset{(6)}{\mathrm{Me_2N[CH_2]_{11}\text{–}C{\equiv}C\text{–}C{\equiv}C\text{–}[CH_2]_{10}Me}} \xrightarrow{(5),\ 60\,°\mathrm{C},\ 72\ \mathrm{h}} (1)$$

Scheme 1

An aqueous dispersion of the amphiphile DHDAB (2 mg ml^{-1}) made by vortexing the sample at 45 °C produced polydispersed vesicular structures (observed under the optical microscope). The dispersions were also examined by transmission electron microscopy after staining with uranyl acetate. After more than 2 h at 28 °C the vesicles began to show evidence of a change in morphology [Figure 1(a)]. After 24—36 h this change is manifested as distinct cylinders [Figure 1(b) and (c)]. By increasing the initial concentration above 6 mg ml^{-1} the time for vesicles to be transformed into cylinders was reduced considerably. As the lower phase transition temperature was approached, the cylinders become unstable and bilayer sheet structures began to dominate, as observed by optical microscopy. For any of the morphologies, irradiation by u.v. (254 nm) light produced a strongly coloured product: only a trace of the monomeric amphiphile was detected by t.l.c. after less than 10 s irradiation. Exposure to u.v. radiation produced a robust morphology which was able to withstand freeze-drying and rehydration procedures.[9]

The synthesis of DHDAB (**1**),† was performed as shown in Scheme 1. Syntheses of tridec-12-yn-1-ol (**2**) and 1-iodotridecyne (**3**) and their coupling to produce hexacosa-12,14-diyn-1-ol (**4**) were performed by published procedures.[11,12] Compound (**4**) upon reaction with phosphorus tribromide in dry ether at 2 °C produced 1-bromohexacosa-12,14-diyne (**5**) in 70% yield. Dimethyl(hexacosa-12,14-diynyl)amine (**6**) was prepared by reaction of (**5**) with dimethylamine in dry toluene at room temperature {^{1}H n.m.r. (CDCl$_3$) δ 0.9 (t, 3H, CH$_3$), 1.2 (s, 36H, –[CH$_2$]–), 2.1—2.39 (m, 4H, –CH$_2$–C$\equiv$C–), and 2.45—2.7 (m, 8H, CH$_3$–N and CH$_2$–N)}. Synthesis of di(hexacosa-12,14-diynyl)dimethylammonium bromide (**1**) was completed by the reaction of compounds (**5**) and (**6**) at 60 °C for 72 h under an inert atmosphere. The product, isolated by column chromatography on silica gel, eluted with chloroform, and further purified by crystallization (acetone), was collected in 52% yield. The ^{1}H n.m.r. spectrum showed δ 0.85 (t, 6H, CH$_3$), 1.2 (s, 72H, –[CH$_2$]–), 2.1—2.3, (m, 8H, –CH$_2$–C$\equiv$C–), and 2.6—3.0 (m with emerging sharp singlet at 2.7, 10H, CH$_3$–N and CH$_2$–N).

Our observations of microstructure morphologies in aqueous dispersions of this achiral compound, coupled with

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† In this amphiphile the alkyl chains bearing the diacetylene units are directly attached to the nitrogen atom. A diacetylene-containing ammonium surfactant has been reported where the alkyl chains containing the diacetylenic moiety are attached through an ester bond.[10] We synthesized (**7**) in our laboratory. This surfactant produced only vesicles in aqueous dispersion and was not transformed into any other morphology below its chain-melting transition (T_m), which is 19.7 °C.

$$\mathrm{Me_2\overset{+}{N}\{CH_2CH_2OC(O)[CH_2]_8\text{–}C{\equiv}C\text{–}C{\equiv}C\text{–}[CH_2]_9Me\}_2\ Br^-}$$

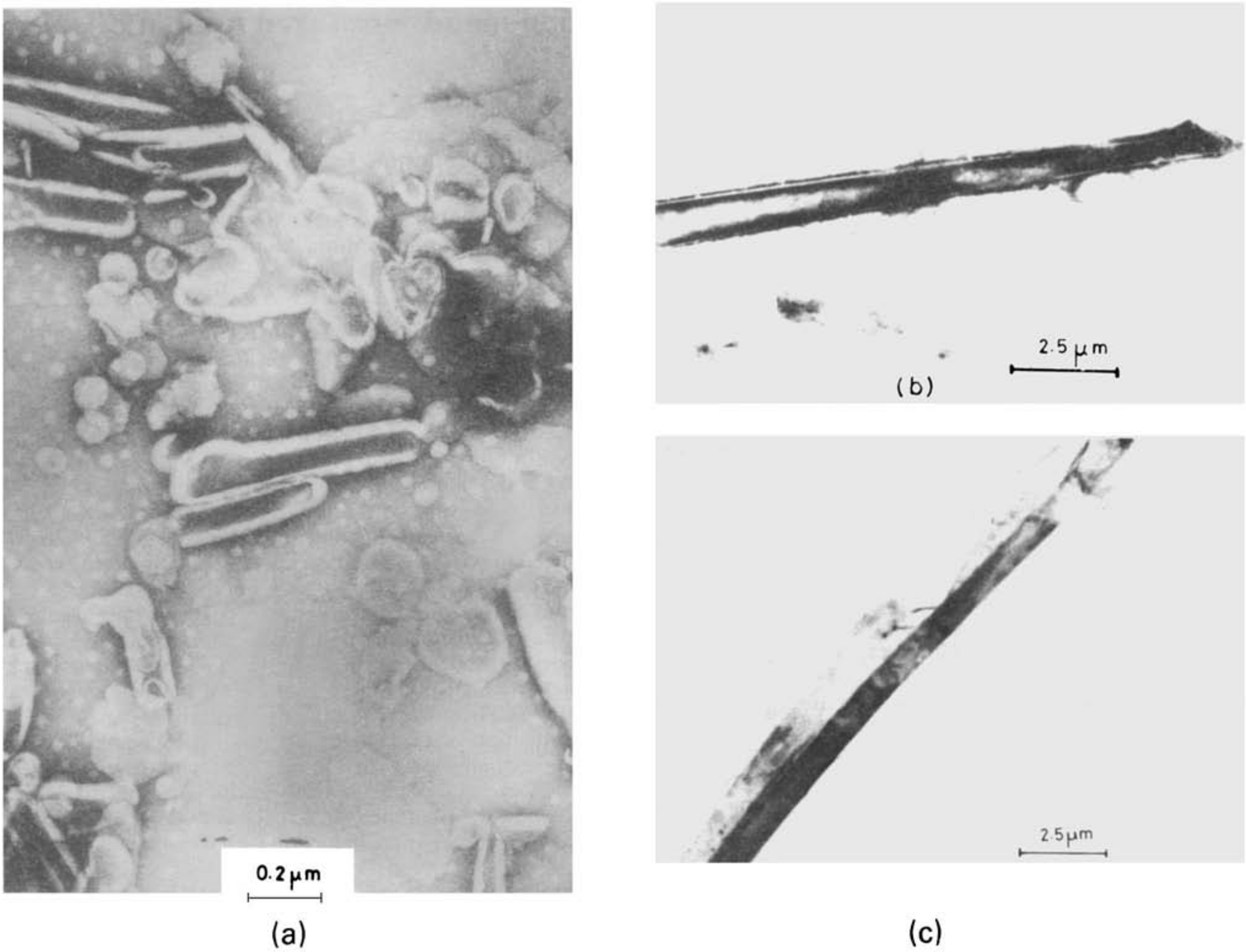

Figure 1. Changes in morphology of the DHDAB vesicles after (a) 2 h, (b) and (c) 24—36 h, as shown by transmission electron microscopy.

earlier observations, clearly demonstrate that the molecular factors involved in the process of self-assembly are complex. Recently, de Gennes[6] has proposed a model for the formation of cylindrical microstructures based on the chirality of the phosphatidylcholine from which they have been observed to be formed. On the other hand our results suggest the possibility of more than one mechanism for the formation of tubules, since the present example demonstrates that chirality is not an essential requirement for cylindrical microstructures.

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References

1 P. E. Schoen and P. Yager, *Mol. Cryst. Liq. Cryst.*, 1984, **106**, 371.
2 J. M. Schnur, R. Price, P. Schoen, P. Yager, J. Calvert, J. Georger, and A. Singh, *Thin Solid Films*, 1987, **152**, 181.
3 P. Yager, P. E. Schoen, C. A. Davies, R. Price, and A. Singh, *Biophys. J.*, 1985, **48**, 899.
4 J. H. Georger, A. Singh, R. R. Price, J. M. Schnur, P. Yager, and P. Schoen, *J. Am. Chem. Soc.*, 1987, **109**, 6169.
5 N. Nakashima, S. Asakuma, and T. Kunitake, *J. Am. Chem. Soc.*, 1985, **107**, 509; T. Kunitake, *Ann. N.Y. Acad. Sci.*, 1986, **471**, 70.
6 P. G. de Gennes, *C. R. Seances Acad. Sci.*, 1987, **304**, 259.
7 A. Singh, T. G. Burke, J. M. Calvert, J. H. Georger, B. Herendeen, R. R. Price, P. E. Schoen, and P. Yager, *Chem. Phys. Lipids*, 1988, **47**, 135.
8 H. Bader, B. Hupfer, and H. Ringsdorf, *Adv. Polym. Sci.*, 1985, **64**, 1.
9 R. L. Juliano, S. L. Regen, M. Singh, M. J Hsu, and A. Singh, *Biotechnology*, 1984, **1**, 882.
10 L. Gros, H. Ringsdorf, and H. Schupp, *Angew. Chem., Int. Ed. Engl.*, 1981, **20**, 305.
11 A. Singh and J. M. Schnur, *Synth. Commun.*, 1986, **16**, 847.
12 T. H. Vaughen and J. A. Nieuwland, *J. Org. Chem.*, 1933, **55**, 2150.