Molecular Golf Balls: Vesicles from Bowl-Shaped Host Molecules**

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Synthetic molecules containing a hydrophilic head group and one or two hydrophobic tails are known to form a great variety of supramolecular structures such as micelles, multilayers, rods, and vesicles.1 It has been proposed that the type of aggregate structure depends on the shape of the amphiphile, as characterized by the so-called "packing parameter".2 Recent studies, however, indicate that other factors are important. For example, single-tail surfactants with a large rigid segment3 or surfactants with a hyperextended chain4 form vesicles instead of micelles, as predicted by the shape—structure concept. Vesicular structures are also formed by two-headed single-chain surfactants, for instance the lariat ether bolaamphiphile.5 We report here that bowl-shaped host 2, which has two tails, two head groups, and a rigid cleft, forms vesicles upon dispersal in water.

Amphiphile 1 was synthesized in two steps (Scheme 1): first 1a6 was treated with hexadecylamine in acetoniitrile under Finkelstein conditions7 (60 %) and subsequently the product was methylated with methyl tosylate in toluene (80 %).

When 2 (10 mmol) was dissolved in methanol (50 µL) and injected in water (3 mL) vesicles were formed, as could be deduced from electron microscopy.

As can be seen in Figure 1, the application of both the freeze-fracture and the negative staining technique show the presence of spherical vesicles with a diameter of approximately 4000 Å. These aggregates have a closed structure, as deduced from subsequent encapsulation experiments8 with the fluorescent dye ethidium bromide.10 Conductivity measurements revealed that the critical aggregation concentration (CAC) of 2 is 2 x 10⁻³ M. A vesicle dispersion of the amphiphile was dried on a glass plate in vacuo to give a cast film which was examined by X-ray diffraction. The diffraction patterns displayed a clear periodicity of 25 Å up to the 10th order reflection.

Fig. 1. Electron micrographs of a 0.02 % dispersion of 2. Freeze-fracture (magnification 28000 x) (a) and negative staining technique (magnification 9000 x) (b).

Scheme 1.

Abbreviations used: biPhMe: 2,2'-bis(j-methylimidazolyl)phenylmethoxy-, Hbpg, N,N'-bis(2-pyridylmethyl)glycine; Mcterm: 1,4,7-tri(methyl-1,4,7-triazacyclononane; tmen: N,N',N'-tetramethylethylene diamine; tsp: tris(2-pyridylmethyl)amine.


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Based on these data, we propose that the vesicles have a structure similar to that of a golf ball (Fig. 2). The thickness of the bilayer is 53 Å, which corresponds to two fully extended hexadeclaylene chains. The host amphiphiles are aligned with their concave binding moieties facing the aqueous phases.

We previously showed[11] that molecular clips such as 1b can bind aromatic substrates in chloroform, for example resorcinol and its derivative 3. Binding occurs by π-stacking interactions with the two aromatic "walls" of 1b and by hydrogen bonding with the urea carbonyl groups, as determined by IR and 'H NMR spectroscopy.

The binding properties of 2 were determined in chloroform and water by NMR and UV/Vis titration experiments.[12] In chloroform, resorcinol and resorcinol derivative 3 form 1:1 inclusion complexes with 2; the corresponding association constants are K ∼ 3400 and 500 M⁻¹, respectively. These values are similar to those measured for these guests 1b with 1b (K ∼ 2600 and 700 M⁻¹, respectively). In water, under the CAC of 2, compound 3 is bound in a 1:1 host–guest ratio with an association constant of K ∼ 3 × 10⁵ M⁻¹. This value is very high when compared to that in chloroform, but is of the same order of magnitude as that found for amphiphilic cyclophanes[13] with nonionic guests. Titration experiments with 2 in concentrations (0 - 5 × 10⁻⁵ M), with a constant host concentration of 2.5 × 10⁻⁴ M. At a concentration above the CAC of 2, the absorbance of 3 was monitored at 534 nm as a function of the guest concentration (0 - 1.5 × 10⁻⁴ M) with a constant host concentration of 2.5 × 10⁻⁴ M. In water, NMR measurements could not be applied for this purpose because of the occurrence of broad lines due to aggregation of 2. Under the CAC of 2 the absorbance of 3 was monitored at 450 nm as a function of the guest concentration (0 - 1.5 × 10⁻⁴ M) with a constant host concentration of 2.5 × 10⁻⁴ M. In water, NMR measurements could not be applied for this purpose because of the occurrence of broad lines due to aggregation of 2. Under the CAC of 2 the absorbance of 3 was monitored at 534 nm as a function of the guest concentration (0 - 5 × 10⁻⁴ M) with a constant host concentration of 2.5 × 10⁻⁴ M. The errors in the binding constants are approximately 10% and 50% for the experiments in chloroform and water, respectively.


[7] T. M. p. 210 C; [8] NMR (CDCl₃, 25 °C, TMS): δ = 0.86 (t, 6H, CH₃(C₃H₇)), 1.24 (s, 5H, CH₂(C₄H₉)), 2.30 (s, 6H, CH₃ tosylate), 4.6 – 5.2 (m, 4H, CH₂CH₃, CH₂CH₃, CH₂O, NCH₂Ar), 5.61 (d, 4H, NCH₂Ar), 6.58 (s, 4H, ArH), 7.13 (m, 14H, ArH, ArH tosylate), 7.81 (d, 4H, ArH tosylate); IR (KBr): 934 nm, 1507 (C=C), 1661 cm⁻¹ (C–O–C), 3150 cm⁻¹ (C–H, mid CH₂), 1540, 1590 cm⁻¹ (CH, mid CM,). 1350 cm⁻¹ (CH₂, mid CM). 1540, 1590 cm⁻¹ (CH₂, mid CM), 1540, 1590 cm⁻¹ (CH₂, mid CM).
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