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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.[13] 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 segment[13,4] or surfactants with a hyperextended chain [2] 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 bolaamphiphiles. [50] 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 2[17] was synthesized in two steps (Scheme 1): first 1a[51] was treated with hexadecylamine in acetonitrile under Finkelstein conditions[10] (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 experiments[15] with the fluorescent dye ethidium bromide. [11] Conductivity measurements revealed that the critical aggregation concentration (CAC) of 2 is 2 × 10⁻⁵ M. A vesicle dispersion of the amphiphile was dried on a glass plate for subsequent encapsulation experiments.[11] A vesicle dispersion of 2 was methylated with methyl tosylate in toluene (80%).

Fig. 1. Electron micrographs of a 0.025% dispersion of 2. Freeze-fracture (magnification 3000 ×) (a) and the negative staining technique (magnification 9000 ×) (b).
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 hexadecylamine 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-π stacking interactions with the two aromatic "walls" of 1b and by hydrogen bonding with the aminocarboxyl groups, as determined by IR and 1H 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 $K_a = 3400$ and $500 \text{M}^{-1}$, respectively. These values are similar to those measured for guest 1b ($K_a = 2600$ and 700 $\text{M}^{-1}$, respectively). In water, under the CAC of 2, compound 3 is bound in a 1:1 host–guest ratio with an association constant of $K_a = 3 \times 10^5 \text{M}^{-1}$. 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 above the CAC indicated that only 50% of the molecular bowls are accessible to the outer surface of the molecular golf balls are accessible to guest molecules and that the inner part of the aggregates cannot be reached.

In summary, we have shown that molecular objects with high binding affinities can be formed from rigid host molecules that have two tails and two ammonium groups. Further studies are aimed at stabilizing the aggregates by polymerization. Application of the polymerized structures can be conceived in the field of chromatographic separation of organic molecules. To store the end of this synthesis of chiral derivatives of 2 is currently in progress.

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