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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.** 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”.** Recent studies, however, indicate that other factors are important. For example, single-tail surfactants with a large rigid segment or surfactants with a hyperextended chain 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. 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 was synthesized in two steps (Scheme 1): first 1 was treated with hexadecylamine in acetonitrile under Finkelstein conditions (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 with the fluorescent dye ethidium bromide. Conductivity measurements revealed that the critical aggregation concentration (CAC) of 2 is 2 M.

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<td><img src="image" alt="Electron micrograph of a 0.02 mm thick dispersion of 2, Freeze-fracture (magnification 28000 x)" /> (a) and negative staining technique (magnification 9000 x) (b).</td>
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<td><img src="image" alt="Crystal structure of 1b" /></td>
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**Scheme 1.

**Fig. 1. Electron micrographs of a 0.02 mm thick dispersion of 2, Freeze-fracture (magnification 28000 x) and negative staining technique (magnification 9000 x).
Fig. 2. Schematic representation of a vesicle formed by 2.

We previously showed\(^1\)\(^{-1}\) that molecular clips such as \(1b\) can bind aromatic substrates in chloroform, for example resorcinol and its derivative \(3\). Binding occurs by \(\pi\)-stacking interactions with the two aromatic "walls" of \(1b\) and by hydrogen bonding with the urea carbonyl groups, as determined by IR and \(^1\)H NMR spectroscopy.\(^4\)

The binding properties of \(2\) were determined in chloroform and water by NMR and UV/Vis titration experiments.\(^1\)\(^{-1}\) In chloroform, resorcinol and resorcinol derivative \(3\) form a 1:1 inclusion complexes with \(2\); the corresponding association constants are \(K = 3400\) and 500 \(\text{M}^{-1}\), respectively. These values are similar to those measured for these guests with \(1b\) (\(K = 2600\) 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 \(K = 3 \times 10^5 \text{M}^{-1}\). 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\(^1\)\(^{-1}\) with nonionic guests. Titration experiments with \(2\) in concentrations above the CAC indicated that only 50% of the molecular bowls are capable of binding a guest molecule. In a separate experiment we checked with electron microscopy that the vesicle structure is not destroyed by guest binding. The titration curve could only be fitted by assuming that half of the host molecules are involved in the binding process. In this case, we obtained a good correlation for a 1:1 complex with a binding constant of \(K = 4 \times 10^5 \text{M}^{-1}\). This result suggests that only the dimples on 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 test the end synthesis of chiral derivatives of \(2\) is currently in progress.

Received: February 19, 1994 \[Z 6699 IE\]

German version: Angew. Chem. 1994, 106, 1741


\(^{[9]}\) Z. MP 210 1/111 NMR CDCl3, 25°C; TMS: \(\delta = 0.06 \) (CH3CD3), 1.24 (s, 5H, CH2), 3.48 (4H, CH2CD3), 4.63 (2H, CH2), 7.31 (4H, C6H4) ppm.

\(^{[10]}\) \(K = 4 \times 10^5 \text{M}^{-1}\).

\(^{[11]}\) \(K = 2600\) and 700 \(\text{M}^{-1}\), respectively.

\(^{[12]}\) V(C=C)=1692 cm\(^{-1}\) (C=O); IR (KBr): v [cm\(^{-1}\)] » 3080, 2980 (ArH), 2960–2820 (CH3 and C2H5), 1517 (C=N), 1380 (CH3), 1370 (C=N), 1150–1050 (C=C); IR (D2O, 5 \(\times 10^{-4}\) M): \(v = 1692 \text{cm}^{-1}\) (C=O).


\(^{[15]}\) R. B. Mewes, R. P. Sijbesma. * Accounts in the literature regarding the chemistry of SO2 as a ligand and solvent.*

\(^{[16]}\) E. Loke, J. Petersen, and Rüdiger Mews*.

\(^{[17]}\) The chemistry of SO2 as a ligand and solvent has been studied in great detail. The coordination behavior of SO2 molecules differs. Passmore and Desjardins\(^1\)\(^{-1}\) have suggested that only the dimples on the outer surface of the molecular golf balls are accessible to guest molecules and that the inner part of the aggregates cannot be reached.

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\(^{[**]}\) This work was supported by the Fonds der Chemischen Industrie.