

Tailor-making of Desired Assemblies from Well-designed Monomers: Use of Calix[4]arene Conformers as Building Blocks

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Water-soluble, conformationally-immobilized calix[4]arenes with cone and 1,3-alternate conformations (cone-**1** and 1,3-alternate-**1**, respectively) have been synthesized. In aqueous solution cone-**1**, with a cone-shaped surface, aggregated into micelles with 20–40 Å diameter whereas 1,3-alternate-**1**, with a cylindrical surface, could not form such aggregates for concentrations up to 0.010 mol dm⁻³.

In aqueous solution, amphiphilic compounds tend to aggregate so that they can reduce the surface area in contact with water molecules. The energy gain thus obtained is the origin of a hydrophobic force.¹ The concept suggests that if the hydrophobic surface shape of the monomer is different, the resultant aggregate may have different three-dimensional architecture. Thus a desired architecture may be tailor-made by skillfully designing the hydrophobic surface shape of the building block. In the formation of synthetic bilayer membranes, for example, Kunitake *et al.*² demonstrated that the aggregation morphology can be partly regulated by the shape of the hard segment inserted into the central part of the amphiphile.

For several years, we and others have been accumulating basic knowledge about the syntheses of various calix[4]arene conformers.^{3–5} It has been established that introduction of *O*-substituents bulkier than an ethyl group (*e.g.* propyl group) can inhibit the conformational isomerism which occurs *via* the oxygen-through-the-annulus rotation.^{3,4} We here noticed that the surface shape of each conformer is quite different, so that

they will aggregate into different three-dimensional architectures when they are dispersed into aqueous solution. This idea has already been realized by Regen *et al.*^{6,7} and others^{8,9} in a two-dimensional monolayer system. Among calix[4]arene conformers, the surface shape of the cone and 1,3-alternate forms is particularly different: cone-calix[4]arene has a 'cone'-shaped surface¹⁰ which will aggregate into a globular micelle [Fig. 1(a)] whereas 1,3-alternate-calix(4)arene has a cylindrical surface^{5,10,11} which will aggregate into a two-dimensional lamella [Fig. 1(b)]. To test this hypothesis, we synthesized water-soluble, conformationally-immobilized 5,11,17,23-tetrakis(trimethylammoniomethyl)-25,26,27,28-tetrapropoxycalix[4]arene tetrachloride with a cone conformation or with a 1,3-alternate conformation (cone-**1** or 1,3-alternate-**1**, respectively). Physical characterizations have shown that in aqueous solution cone-**1** forms a micellar structure with a hydrophobic domain inside whereas 1,3-alternate-**1** does not form any detectable aggregate structure.

Preparations of cone- and 1,3-alternate-25,26,27,28-tetra-

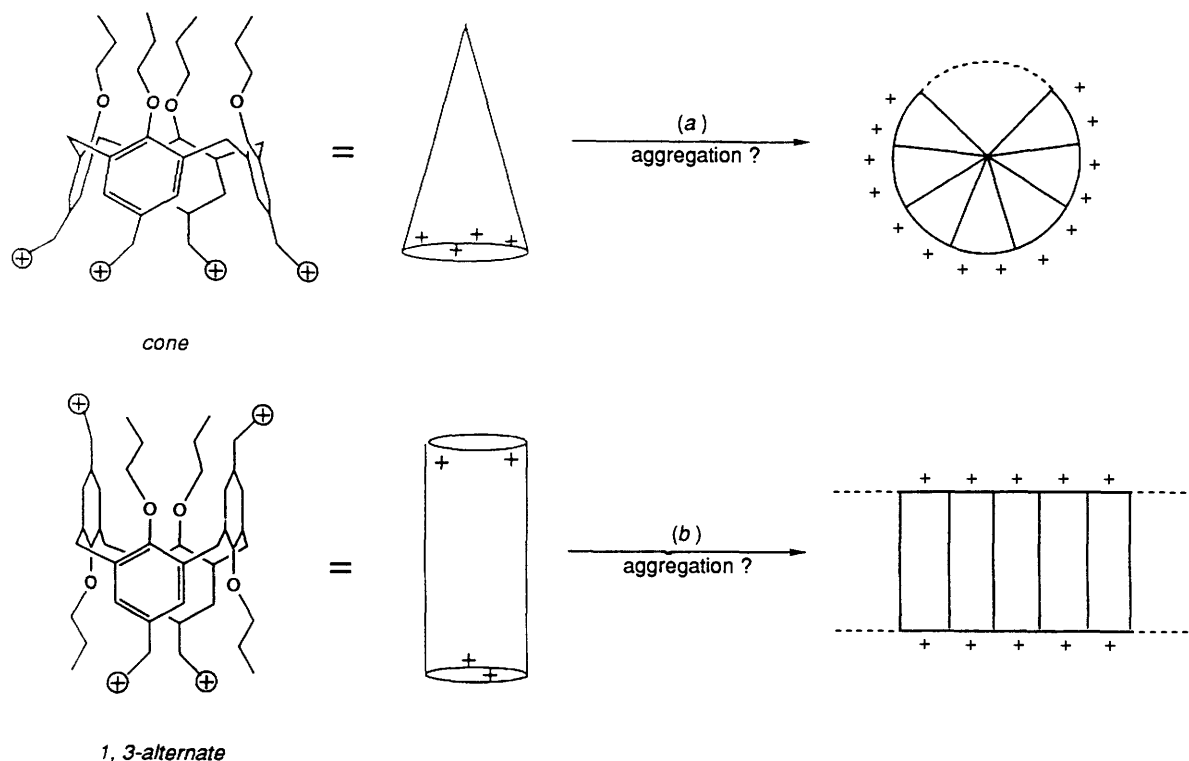


Fig. 1 Expected aggregation modes for cone-shaped cone-**1** (a) and cylindrical 1,3-alternate-**1** (b)

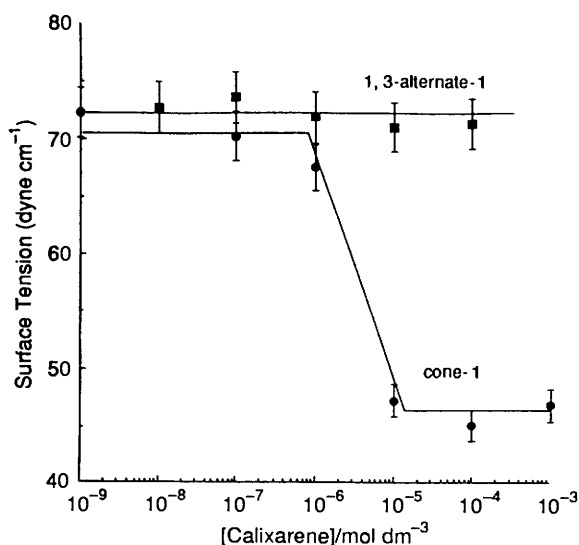
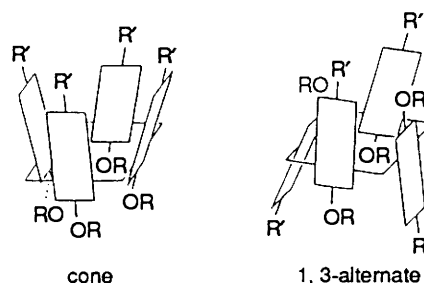
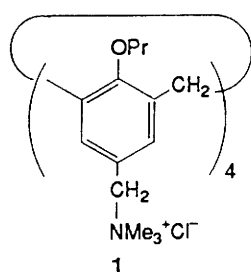


Fig. 2 Surface tension plotted against concentration of **1** at 17 °C

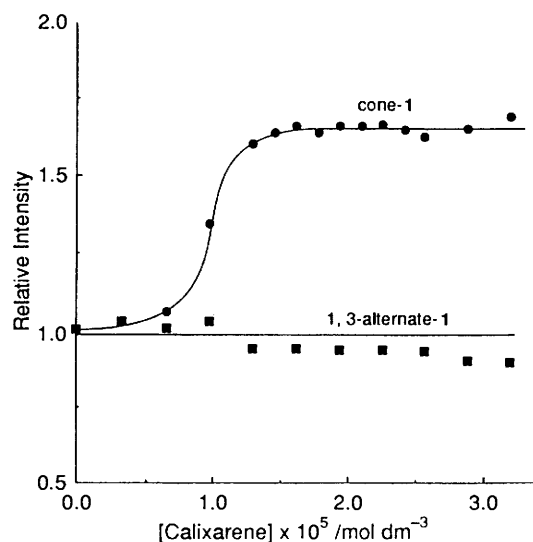


Fig. 3 Fluorescence intensity of 2-anilinonaphthalene (1.00×10^{-6} mol dm⁻³) at 450 nm plotted against concentration of **1**; 30 °C, excitation wavelength 315 nm

proproxycalix[4]arenes have been described previously.^{5,12} Chloromethylation and subsequent quaternization were conducted in a similar manner to those described for 25,26,27,28-tetramethoxycalix[4]arene.¹³ Cone-1 and 1,3-alternate-1 were identified by ¹H NMR spectroscopy and elemental analysis.*

We examined the aggregate formation of cone-1 and 1,3-alternate-1 by three independent methods. Surface tension (Wilhelmy method) of aqueous **1** was measured at 17 °C in 'pure' water.¹⁴ As shown in Fig. 2, the surface tension for cone-1 abruptly decreased at around 10⁻⁵ mol dm⁻³ whereas that for 1,3-alternate-1 was almost constant for up to 10⁻⁴ mol dm⁻³. In Fig. 3 we illustrate the fluorescence intensity of a hydrophobic probe, 2-anilinonaphthalene in the presence of **1**. It is seen from this figure that in the presence of cone-1 the fluorescence intensity abruptly increases at 1.0 × 10⁻⁵ mol dm⁻³ whereas in the presence of 1,3-alternate-1 the fluorescence intensity remains constant. The light-scattering measurement (Otsuka Electronics DLS-700) of aqueous **1** at 30 °C established that cone-1 (0.010 mol dm⁻³) aggregates into particles with 20–40 Å diameter. Examination of CPK molecular models suggests that the length of the long axis of cone-1 is about 15 Å. Thus, each particle should consist of several (probably, less than 10)

molecules. In contrast, we could not find any perceptible particle for 1,3-alternate-1 (0.010 mol dm⁻³) by the light-scattering method. The fact that even a particle with 20 Å diameter cannot be found allows us to conclude that 1,3-alternate-1 exists discretely as a monomer even at 0.010 mol dm⁻³. We consider that the interaction among cylindrical hydrophobic surfaces of 1,3-alternate-1 is not strong enough to maintain the lamellar structure by molecular aggregation. We believe that the formation of the lamellar structure will be realized by introduction of a proper hydrophobic group into 1,3-alternate-1.

The foregoing findings consistently support the view that cone-shaped cone-1 forms micellar aggregates at around 10⁻⁵ mol dm⁻³ whereas cylindrical 1,3-alternate-1 does not form such aggregates for concentrations up to 10⁻² mol dm⁻³. This difference implies that the aggregation mode is well regulated by the surface shape designed on the basis of calix[4]arene conformers. It is known that calix[4]arene conformers can be modified by various substituents^{3,4,15,16} and some of them are useful as a 'core' of starburst dendrimers.^{17,18} We believe, therefore, that the basic skeleton of calix[4]arene conformers is useful for the design of new surface shapes, which will eventually lead to the regulation of the three-dimensional architecture of molecular assemblies.

* Cone-1: m.p. (decomp.) > 235 °C; δ_H(D₂O; DSS standard; 25 °C; 250 MHz) 1.03 (12 H, t, CCH₃), 2.01 (8 H, m, CH₂ in Prⁿ), 2.91 (36 H, s, NCH₃), 3.44 and 4.57 (4 H each, d each, ArCH₂Ar), 4.01 (8 H, t, OCH₂), 4.23 (8 H, s, NCH₂) and 6.97 (8 H, s, ArH) (Found: C, 64.65; H, 8.15; N, 5.35. C₅₆H₈₈Cl₄N₄O·H₂O requires C, 64.59; H, 8.73; N, 5.38%). 1,3-Alternate-1: m.p. (decomp.) > 269 °C; δ_H(D₂O; DSS standard; 25 °C; 250 MHz) 0.89 (12 H, t, CCH₃), 1.56 (8 H, m, CH₂ in Prⁿ), 3.02 (36 H, s, NCH₃), 3.72 (8 H, t, OCH₂), 3.95 (8 H, s, NCH₂), 4.35 (8 H, s, ArCH₂Ar) and 7.36 (8 H, s, ArH) (Found: C, 63.98; H, 8.35; N, 5.2. C₅₆H₈₈Cl₄N₄O₄·2H₂O requires C, 63.49; H, 8.77; N, 5.29%). The water content in these samples has been confirmed by a Karl Fischer titration.

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Paper 3/00899A

Received 15th February 1993

Accepted 1st March 1993