

Dendritic Growth of a Supramolecular Complex**

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Dendrimers are branched polymers with star- or tree-type structures in which all the segments between branching points are of the same length. They can be used as spacers, building blocks for other structures, and as carriers of drugs, fragrances, cosmetics, herbicides, and other molecules.^[1] Although dendrimers are generally covalent polymers, dendrimerlike structures can also be formed by means of supramolecular polymer chemistry, by self-assembly of complementary monomeric components, by molecular interactions, and by recognition processes.^[2]

Cyclodextrins (CD) and their derivatives form supramolecular structures with a variety of organic molecules in water by means of molecular recognition processes (formation of inclusion complexes).^[3] Recently, we reported that β -cyclodextrin (β -CD) and two mono-amino β -CD derivatives form inclusion complexes in water with the naturally occurring bile salts sodium cholate (NaC) and sodium deoxycholate (NaDC) with 1/1 and 2/1 (CD/bile salt) stoichiometries, respectively.^[4, 5] An interesting supramolecular structure was obtained by the complexation of the head-to-head cyclodextrin dimer *N,N'*-bis(6-deoxy- β -cyclodextrin)pyromellitic acid diamide with NaDC.^[5] This structure resulted from the self-assembly of complementary monomeric units, as proposed by Lehn.^[2]

In view of these results, it seemed feasible to form a new dendrimerlike supramolecular polymer, reminiscent of a Cayley tree (Figure 1), by complexation of ditopic guests with β -CD trimers. To check this possibility the new cyclodextrin trimer **T** (Figure 2a) was synthesized, and its complexation behavior with the ditopic guest NaDC (Figure 2b) was studied.

First, the complexation behavior of **T** with the small molecule 2-naphthalenesulfonate (2NS) was studied by ¹³C NMR spectroscopy. This guest was chosen as a reference model because it forms a 1/1 complex with β -CD ($K \approx 8 \times 10^3 \text{ M}^{-1}$, a value close to that found for the NaC/ β -CD complex)^[5] The continuous variation plot^[6] for the **T**/2NS system (Figure 3) shows the formation of a 1/3 complex.

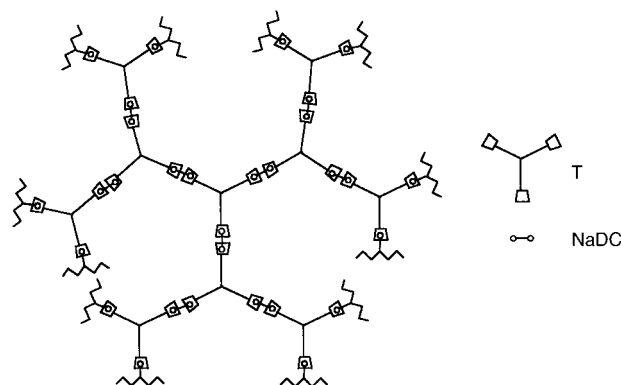


Figure 1. Schematic representation of the Cayley tree dendrimerlike supramolecular structure expected for the cyclodextrin complex **T**/NaDC.

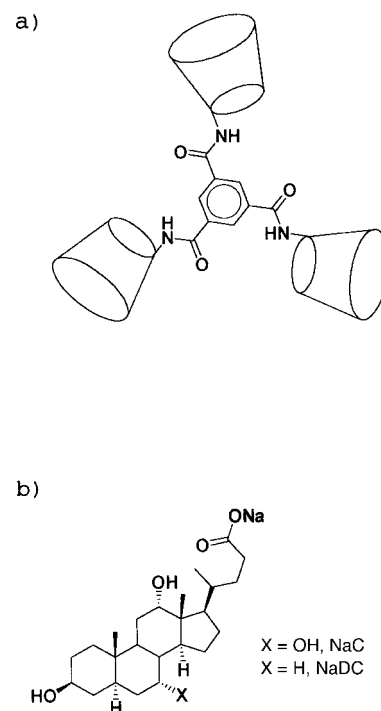


Figure 2. Structures of **T** (a) and the bile salts NaC and NaDC (b).

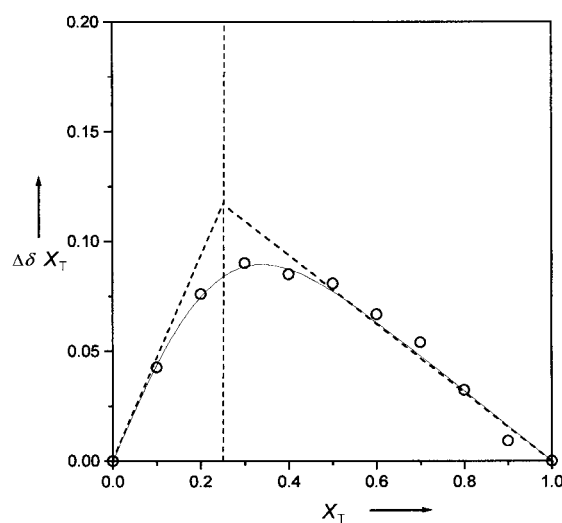


Figure 3. Job plot corresponding to the chemical shift displacement of C-1 of β -CD for the 1/3 **T**/2NS complex. Total concentration $[\mathbf{T}] + [2\text{NS}] = 5 \text{ mM}$.

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A time-dependent stoichiometry was observed by NMR studies with the continuous-variation plot technique^[6] for the complexation of NaC with **T**. Initially (1 h after preparation of the samples) the **T**/NaC system showed a mixture of 1/1 and 1/2 complexes. After one week a mixture of 1/2 and 1/3 complexes was observed, and only after 90 d was the final 1/3 stoichiometry reached. Although no further kinetic studies have been carried out so far, by comparison with former results with 2NS, it seems that steric hindrance plays an important role in the complexation of larger guests.

The complexation of NaDC by **T** was studied by mixing solutions in a 2/1 molar ratio, which corresponds to the stoichiometry of the building brick (two NaDC per **T**) that makes up the Cayley tree in Figure 1. After a few days, a white precipitate appeared on a stage placed at the bottom of the beaker. The mixture was allowed to stand for different periods of time. Figure 4 shows a scanning electron micrograph of the

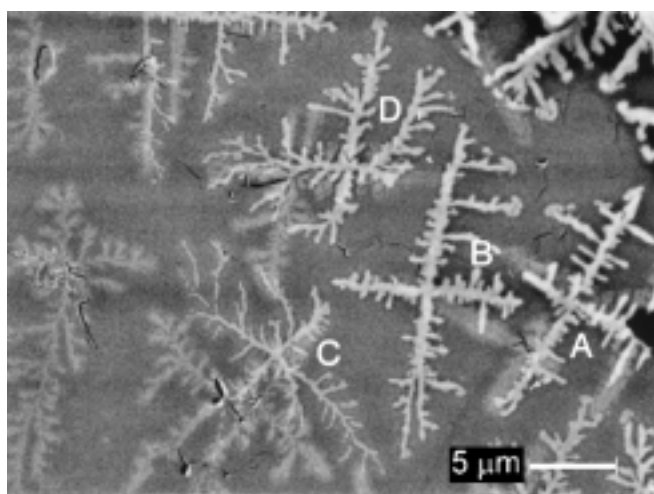


Figure 4. Scanning electron micrograph of the **T**/NaDC system after an aggregation period of 60 d.

surface obtained after two months. Visually, it is possible to distinguish two different types of structures: Structures A and B with a fractal dimension D_f of 1.58, and structure D with a D_f of 1.45. Structure C is a mixture of both. These different structures probably arise from different stoichiometries for each trimer unit. After three months a thin layer covered the stage. Figure 5a shows a general view of this surface obtained by confocal laser scanning microscopy. Structures with an average fractal dimension of 1.63 ± 0.02 can be observed at higher magnification (Figure 5b). This difference between the two groups of structures seems to depend on the aggregation time, which may be a consequence of the steric hindrance, which slows down the supramolecular growth kinetics. Depending on the number of cyclodextrins per trimer unit involved in the complexation process, the obtained fractal structure may present different shapes.

This is the first self-assembled supramolecular structure obtained from cyclodextrin derivatives that has a dendrimer-like structure. The synthesis of ditopic guests with less steric hindrance is in progress.

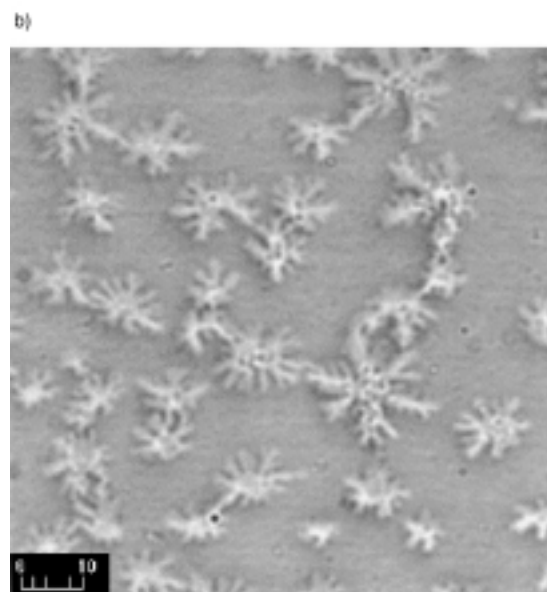
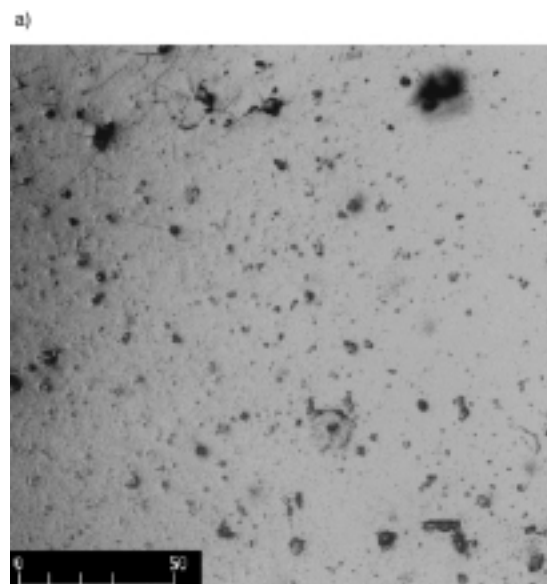


Figure 5. Confocal micrographs of the **T**/NaDC system after an aggregation period of 90 d. a) General view. b) Detail of some isolated dendrimers. The scale bars are in μm .

Experimental Section

Bile salts (Sigma-Aldrich) and β -cyclodextrin were purified as previously reported.^[4] Melting points and L-SIMS mass spectra were determined on a Gallenkamp apparatus and a Micromass Autospec spectrometer, respectively. The ^1H , ^{13}C , and DEPT 135 NMR spectra were recorded on a Bruker AC spectrometer at 300 and 75 MHz at 298.1 ± 0.1 K. All NMR experiments were carried out in D_2O . The stoichiometry of the inclusion complexes formed were determined using the continuous variation technique (Job plot).^[6] Laser scanning confocal micrographs were recorded on a Bio-Rad MRC 1024ES microscope in reflectance mode by using the 488-nm light from a 100-mW argon ion laser. Scanning electron micrographs were recorded on a LEO 435 VT variable-pressure electron microscope. The fractal dimension was determined from the digitized micrographs by using the box-counting method^[7] with a self-written program. This method counts the minimal number of boxes (pixels) that cover the fractal structure for decreasing box size.

T: 6-deoxy-6-amino- β -cyclodextrin^[5] (0.5 g, 0.44 mmol) and triethylamine (60 μ L, 0.44 mmol) were dissolved in dry DMF (10 mL) and cooled to 0 °C. 1,3,5-benzenetricarbonyl trichloride (0.0355 g, 0.134 mmol) was added, and the reaction mixture was kept at 0 °C for 1 h and then at RT for 12 h. The reaction product was precipitated with cold acetone (100 mL). The resulting solid was filtered and washed with cold acetone to remove the DMF. Finally the product was dissolved in water and purified through an Amicon 8050 ultrafiltration cell unit with a YM3 membrane ($M = 3000$) to give a white solid (0.279 g, 0.079 mmol, 59 %). $R_f = 0.12$ (ethyl acetate/isopropyl alcohol/water/concentrated NH_4OH 2/3/4/0.3); m.p. 218–225 °C (decomp); ^1H NMR (D_2O): $\delta = 8.23$ (s, 1H, Ar-H), 4.97–5.05 (brs, 7H, H-1), 3.48–3.96 (m, 42H, H-2, H-3, H-4, H-5, H-6); ^{13}C and DEPT 135: $\delta = 171.5$ (CONH), 137.38 (substituted C_{Ar}), 131.77, (CH_{Ar}), 104.49 (C-1), 85.90 (C-4'), 83.72 (C-4), 75.69 (C-5), 74.68 (C-3), 74.22 (C-2), 62.92 (C-6), 43.57 (C-6'); positive-ion FAB-MS: m/z : 3559.0485 [$M+1$].

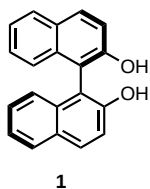
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Lithium Binaphtholates: Chiral Chains and Clusters**

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Binaphthol (H_2binol) is chiral by virtue of restricted rotation about the C–C bond linking the two naphthyl units, and the absolute configuration of (*R*)-binaphthol (**1**) was first established unequivocally by X-ray diffraction in 1968.^[1] The flexibility of the dihedral angle between the two naphthyl rings of this C_2 -symmetric molecule allows coordination to a wide range of metal centers (examples are known from 45° to 110°), and H_2binol



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has been used as a chiral auxiliary in many metal-based enantioselective catalysts and reagents. Examples include the $\text{Yb}(\text{OTf})_3$ -catalyzed asymmetric Diels–Alder reaction,^[2] the TiCl_4 -derived catalyst for the asymmetric ene reaction,^[3] and the chiral modification of LiAlH_4 for use in asymmetric reductions.^[4] Multi-binaphthol species have attracted recent interest; particularly successful examples are Mikami's Ti–binaphtholate catalysts^[5] and the heterometallic alkali metal/lanthanide binaphtholates synthesised by Shibasaki et al.^[6] Examples of catalytically active multi-binaphthol Ti clusters have also been reported.^[7,8] In addition to these applications in asymmetric synthesis, binaphthol has also been of interest as a component of macrocycles for chiral recognition,^[9,10] and as a component of helical polymers with novel properties such as the emission of polarized light.^[11]

In view of this widespread interest in binaphthol-containing species, it is surprising that no structural studies of the lithiated derivatives have been reported (inclusion compounds of *rac*- H_2binol with NaOH and KOH have been structurally characterized^[12]). Lithiated H_2binol has been used in the preparation of many enantioselective catalysts and has also been investigated as a chiral auxiliary in its own right.^[13] Our interest in lithium binaphtholates arose from our use of LiHbinol in the synthesis of anhydrous analogues of Shibasaki's heterometallic catalysts,^[14] and herein we report on investigations of mono- and dilithiated derivatives of optically pure and racemic H_2binol . The previously overlooked structures of these compounds show unexpected diversity.

Lithiated H_2binol compounds [$\text{Li}(\text{rac-Hbinol})$] (**2**), [$\text{Li}(\text{R-Hbinol})$] (**3**), [$\text{Li}_2(\text{rac-binol})$] (**4**), and [$\text{Li}_2(\text{R-binol})$] (**5**) were prepared by reaction of H_2binol with stoichiometric quantities of $n\text{BuLi}$ in THF at 0 °C. All of these lithiated derivatives were precipitated as microcrystalline solids from THF solutions by the addition of petroleum ether, and we were able to grow X-ray-quality single crystals of **2**, **3**, and **4** by the slow diffusion of petroleum ether into the THF solutions at room temperature. Despite numerous attempts and using a range of precipitating solvents, good quality single crystals of **5** could not be obtained from THF solutions.

The monolithiated species **2** and **3** both crystallize as helical polymeric chains with Hbinol^- units linked by [$\text{Li}(\text{thf})_2$]⁺ bridges, as shown for **2** in Figures 1 and 2. The chain structure of **3** is very similar, but less symmetrical, containing two inequivalent Li atoms. Short fragments of the chains of **2** and **3** are shown in Figures 3 and 4, respectively. The structure of **3** is necessarily composed of chains of a single enantiomer whereas that of **2** consists of arrays of *R*-configured polymer and *S*-configured polymer. The remaining O–H group has not been

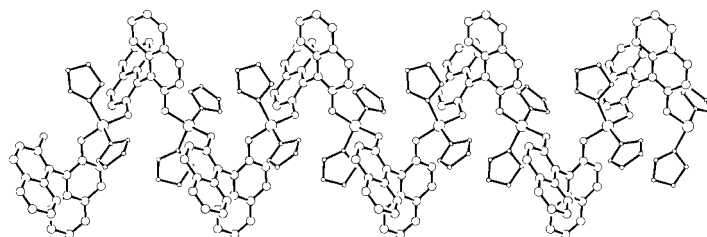


Figure 1. The [$\text{Li}(\text{S-Hbinol})$] chain of [$\text{Li}(\text{rac-Hbinol})$] (**2**).