

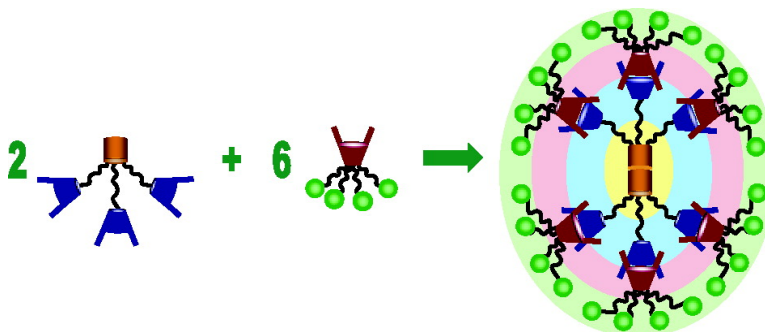
Communication

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## Self-Assembly of Programmed Building Blocks into Structurally Uniform Dendrimers

Yuliya Rudzevich,<sup>†</sup> Valentyn Rudzevich,<sup>†,‡</sup> Chulsoon Moon,<sup>§</sup> Ingo Schnell,<sup>§</sup> Karl Fischer,<sup>||</sup> and Volker Böhmer\*<sup>†</sup>

*Abteilung Lehramt Chemie, Fachbereich Chemie, Pharmazie und Geowissenschaften, Johannes Gutenberg-Universität Mainz, Duesbergweg 10-14, D-55099 Mainz, Germany, Max Planck Institut für Polymerforschung, Postfach 3148, 55021 Mainz, Germany, and Institut für Physikalische Chemie, Johannes Gutenberg-Universität Mainz, Jakob-Welder-Weg 11, D-55128 Mainz, Germany*

Received August 5, 2005; E-mail: vboehmer@mail.uni-mainz.de

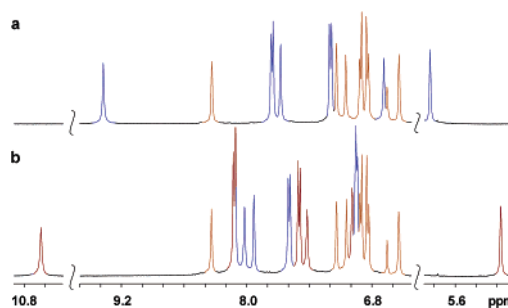
Calix[4]arenes, substituted on their wide rim by four urea residues, form dimeric capsules in aprotic, apolar solvents, which are held together by a seam of hydrogen bonds between the urea functions.<sup>1</sup> This dimerization may be used to build up linear polymers<sup>2</sup> from building blocks, in which two tetraurea units are covalently linked via their narrow rims. The exclusive formation of heterodimers in an equimolar solution of tetraaryl- and tetratosylureas<sup>3</sup> can be used to introduce directionality along the chain or to obtain alternating polymers via self-assembly. We recently could show that triurea derivatives **1** derived from triphenylmethanes form hydrogen-bonded dimers analogously, although without guest inclusion.<sup>4</sup> This dimerization does not intervene with the dimerization of calix[4]arene derived tetraaryl- and tetratosylureas.

Various attempts to obtain dendrimers via self-assembly have been reported among which we concentrate on hydrogen-bonded assemblies. In most examples, two or more covalently linked dendrons are held together by complementary hydrogen-bonding motifs just in the core.<sup>5</sup> Only recently a first approach was published in which the whole dendritic assembly was built up, shell by shell, in a self-assembly process.<sup>6</sup> It was based on a single complementary pair of hydrogen-bonding motifs **A** and **B** forming an **AB**-assembly. Self-assembled dendrimers are formed by mixing a tripodal core **A**<sub>3</sub> with a branched linker **BA**<sub>2</sub> and a capping unit **B** in the required ratio.

However, in such a system, it cannot be guaranteed that the tripodal core **A**<sub>3</sub> combines only with the **B** site of the linker and that the capping **B** combines only with the **A** sites of the linker (in the outer shell). "Wrong" combinations, such as **B** with **A**<sub>3</sub>, are also possible, and the ratio of the three compounds only determines the average size of a mixture which, in principle, may consist of structurally different assemblies.

We demonstrate in the following that the self-sorting process of different tri- and tetraurea derivatives described above can be used to self-assemble dendritic architectures, which are uniform in size and structure.

As demonstrated in Figure 1a, a mixture of **1b** with **2b** contains just the two homodimers **1b·1b** and **2b·2b**. The <sup>1</sup>H NMR spectrum corresponds exactly to the superimposition of the spectra of the single dimers. Addition of a tetratosylurea (e.g. **4c**) in a quantity equal to **2b** leads to the complete disappearance of the signals for **2b·2b**, which are replaced by those of the heterodimer **2b·4c**, while the signals of **1b·1b** remain unchanged (Figure 1b). Monomeric species are not observed under these conditions (*c* ≈ 5 mM), in



**Figure 1.** Sections of the <sup>1</sup>H NMR spectra (*c* = 5 mM, C<sub>2</sub>D<sub>2</sub>Cl<sub>4</sub>, 25 °C, 400 MHz) of stoichiometric mixtures of **1b** and **2b**, containing the dimers **1b·1b** (yellow) and **2b·2b** (blue) (a); **1b**, **2b**, and **4c**, dimers **1b·1b** (yellow) and **2b·4c** (blue/red) (b).

agreement with association constants of ~10<sup>6</sup>–10<sup>8</sup> M<sup>-1</sup> reported for similar dimers,<sup>7</sup> making these systems highly appropriate for the intended construction of dendrimers.<sup>8</sup>

As shown in Scheme 1, we linked, for a central building block **3**, three tetratosylurea units **2a** via sufficiently long and flexible spacers<sup>9</sup> to the triurea **1a**. Tetratosylureas **4** bearing two (**4a**) or four (**4b**) phthalimide residues at the narrow rim were prepared in the usual way, by reaction of the respective wide rim tetraamine<sup>10</sup> with tosylisocyanate.

Under conditions suitable for the dimerization of the three oligoureia motifs (e.g., in CDCl<sub>3</sub> as solvent), **3** has limited solubility. However, it can be solubilized by the addition of **4**. The <sup>1</sup>H NMR spectrum of a mixture of **3** and **4** in the ratio 1:3 in C<sub>2</sub>D<sub>2</sub>Cl<sub>4</sub> contains all spectroscopic elements expected for a **3**<sub>2</sub>·**4**<sub>6</sub> assembly: signals for the homodimer **1·1** and (much stronger of course) signals for the heterodimer **2·4**<sub>3</sub>; see Figure 2. The fact that **3** alone is not soluble results from homodimerization of **1** and **2**, which will lead to larger branched or even cross-linked structures. Only if all units **2** are involved in (or saturated by) heterodimerization with **4**, the dendritic architecture shown in Figure 3 is formed, an assembly with 12 or 24 phthalimide residues in the periphery. Considering the fact that each dimeric capsule **2·4** contains one solvent molecule as guest,<sup>11</sup> these assemblies consist of 14 molecules with a total molecular mass of 21 734 and 25 832 g/mol, respectively. This explains also the broadening of peaks at room temperature.

<sup>1</sup>H DOSY NMR experiments<sup>12</sup> yielded a common (the same) diffusion coefficient of 5.4 × 10<sup>-11</sup> m<sup>2</sup>/s for all <sup>1</sup>H signals of the **3**<sub>2</sub>·**4**<sub>6</sub> assembly, which results in an effective hydrodynamic radius of 2.1 ± 0.2 nm. This proves the existence of a uniform dendritic assembly as well as the absence of both larger aggregates and smaller components. DOSY data were recorded also for the individual components **4b** and **3x** (a precursor of **3** bearing nitro

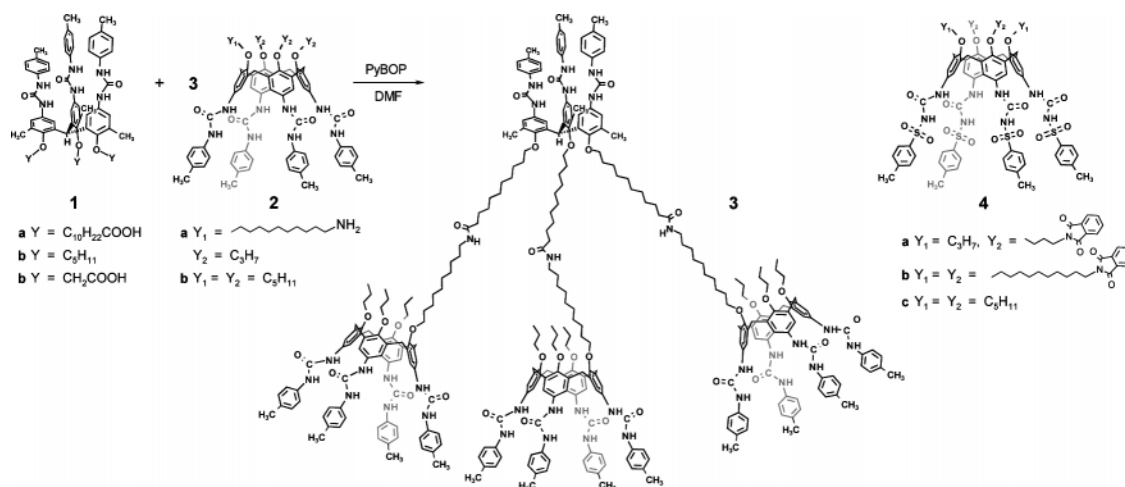
<sup>†</sup> Abteilung Lehramt Chemie, Johannes Gutenberg-Universität Mainz.

<sup>‡</sup> Permanent address: Institute of Organic Chemistry, NAS of Ukraine, Murmanska str. 5, Kyiv-94, 02094 Ukraine.

<sup>§</sup> Max Planck Institut für Polymerforschung.

<sup>||</sup> Institut für Physikalische Chemie, Johannes Gutenberg-Universität Mainz.

Scheme 1



groups instead of the urea functions of the calixarenes). Diffusion coefficients of  $8.6 \times 10^{-11}$  and  $6.2 \times 10^{-11}$  m<sup>2</sup>/s corresponding to hydrodynamic radii of 1.3 and 1.8 nm were found. They reasonably agree with values expected for the homodimers **4b**<sub>2</sub> and **3x**<sub>2</sub> as models for the dimers at the outer sphere and in the core of the dendrimer. The uniform size of the dendritic assembly **3**<sub>2</sub>·**4b**<sub>6</sub> was also confirmed by dynamic light scattering, which led to a hydrodynamic radius of 2.4 nm. Considering the fact that we are not dealing with *rigid* spherical assemblies (and that this radius describes only a sphere moving with the same speed), the values obtained by the two different methods are in reasonable agreement.

Phthalimide groups at the narrow rim of **4a** and **4b** were not only introduced since their signals appear in an “empty” NMR window. Their cleavage by hydrazine leads to aliphatic amino functions, which are potentially useful for the attachment of further molecules, such as dyes. Covalent attachment of other tetraurea

calixarenes in combination with further self-sorting selectivities<sup>13</sup> may enable the construction of dendrimers of higher generation(s).

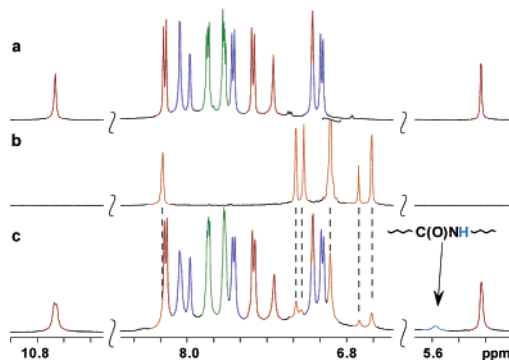
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**Supporting Information Available:** Essential synthetic procedures and selected NMR spectra. This material is available free of charge via the Internet at <http://pubs.acs.org>.

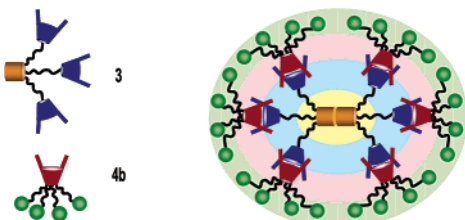
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**Figure 2.** Sections of the <sup>1</sup>H NMR spectra (C<sub>2</sub>D<sub>2</sub>Cl<sub>4</sub>, 75 °C, 400 MHz) of stoichiometric mixture of **2b** and **4b**, the outer shell (a); **1b**, the core (b); **3** and **4b** in the ratio 1:3, the entire dendritic structure. (c) For the color code, see Figure 3.



**Figure 3.** Schematic representation of a dendrimer self-assembled of two molecules of **3** and six molecules of **4b**.