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The Syntheses of Amphiphilic Camouflaged Carboranes as Modules for Supramolecular Construction

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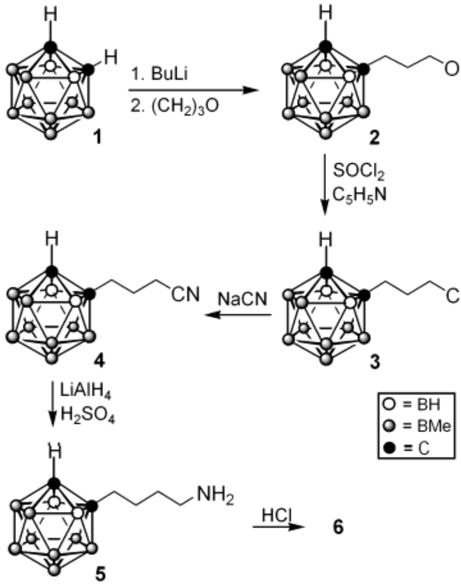
Over time, enormous interest has developed in the design, preparation, and physiochemical properties of self-organized supramolecular structures and synthetic biomembranes which promise numerous functional applications.[1] It was recognized that totally synthetic amphiphiles may spontaneously assemble to form bilayer structures in the presence of water and that bilayer formation is a general phenomenon not restricted to structures composed of biolipid molecules. Recently, amphiphilic C_{60} derivatives have been prepared and employed as molecular building blocks in self-organized aggregates and superstructures. Hirsch et al. synthesized C_{60} derivatives containing up to six amphiphilic dendritic substituents and used these compounds to form artificial membranes and vesicles.[2,3] It was demonstrated that simple C_{60} amphiphiles containing one or two protonated aminoalkyl substituents readily form supramolecular aggregates having a variety of shapes and sizes if dispersions or cast films are ultrasonicated in the presence of water.[4,5] Interestingly, the ability to form aggregates seems to be independent of the length of the alkyl chain carrying the polar ammonium headgroup. Tour et al. recently reported the formation of supramolecular nanorods from C_{60}−*N*,*N*-dimethylpyrrolidinium iodide dissolved in dimethyl sulfoxide by first adding water, and then benzene.[6] They also reported the formation of vesicles with diameters of 10−70 nm if aqueous solutions of the same compound are ultrasonicated and filtered using a 0.45 μm filter.

As a part of our research regarding camouflaged boron clusters we described the exhaustive methylation of the three isomeric dicarba-*closo*-dodecaboranes (1,2-*o*-, 1,7-*m*-, and 1,12-*p*-)[7] with CH_3I leading to the corresponding polymethylated cluster species.[8] Only the para derivative allowed complete methylation of all available BH-vertexes, whereas the ortho and meta carborane products contain two unreacted BH functions adjacent to the CH-vertexes. In all three isomers the boron clusters, shielded by methyl groups, possess remarkably increased chemical stability, compared to their nonmethylated counterparts, as well as excellent solubility in common organic solvents.

Of special importance is the fact that the size of the polymethylated carboranes resembles that of C_{60} and thus can be regarded as C_{60} surrogates with respect to size and shape.[9]

Scheme 1. Synthesis of the Amino Amphiphile **5** Based on Octa-*B*-methyl-*o*-carborane



One aim of our studies is to prepare amphiphilic polymethylated carboranes containing polar headgroups and to explore their ability to form self-organized structures in aqueous solutions leading to novel carborane-containing nanomaterials. Previously, we described functionalized derivatives of decamethyl-1,12-dicarba-*closo*-dodecaborane which were obtained after deprotonation of the cluster CH functions with *n*-butyl- or methyllithium followed by reaction with trimethylene oxide or paraformaldehyde.[9] Here we report the synthesis of the first camouflaged carborane amphiphiles composed of the octamethylated 1,2- and 1,7-dicarba-*closo*-dodecaborane(12) icosahedra and terminal aminoalkyl groups. The 1,2-*o*- and the 1,7-*m*-carborane isomers exhibit dipole moments of 4.5 and 2.8 D, respectively.[10]

The synthesis of the aminobutyl derivative **5,** starting from the octamethyl-ortho isomer **1,** is shown in Scheme 1. Deprotonation of one of the two CH functions present in **1** with *n*-butyllithium followed by addition of trimethylene oxide gave **2** in 46% yield. Reaction of **2** with thionyl chloride in the presence of pyridine afforded **3** in 86% yield. Species **3** was characterized by NMR and mass spectrometry as well as X-ray structure analysis.

Treatment of **3** with sodium cyanide in hot DMSO afforded the carboranyl nitrile **4** in 92% yield. Due to the shielding methyl groups no cyanide ion-mediated deboronation[11] was observed during the reaction.

The NMR and mass spectrometry data display signals expected for **4**. Figure 1 shows the results of an X-ray structure analysis performed with single crystals of **4**. In **4** the B−B bond lengths vary between 1.759(7) and 1.798(6) Å, the B−B distances from apex to apex range from 3.374(7) to 3.404(7) Å, the B−CH_3 bond lengths range from 1.569(7) to 1.596(6) Å, and the distances between the methyl carbon atoms across the icosahedron range from 6.530(7) to 6.548(7) Å.

The reduction of the nitrile function in **4** to the amine **5** could be achieved in 61% yield by employing aluminum hydride generated in situ by reaction of lithium tetrahydroalanate and concentrated sulfuric acid (Scheme 1).

The synthesis of the aminopropyl compound **11**, derived from the octamethyl-meta isomer **7**, is depicted in Scheme 2. Depro-

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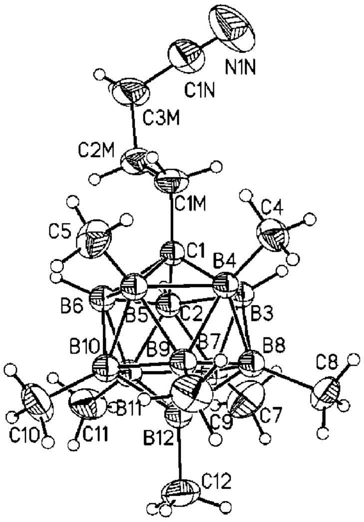


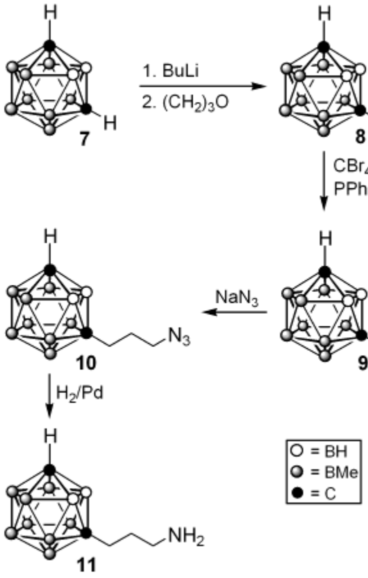
Figure 1. Results of an X-ray structure analysis performed with **4**. The ellipsoids represent a 30% probability level. Selected bond lengths [Å]: C1−B12, 3.275(6); B3−B10, 3.374(7); B6−B8, 3.378(7), C1M−C12, 6.355(7); C4−C11, 6.548(7); C5−C7, 6.530(7).

tonation of one CH function in **7** with *n*-BuLi followed by the reaction with trimethylene oxide gave the alcohol **8** in 65% yield. Conversion of **8** to the bromide **9** was accomplished in 92% yield by reaction with tetrabromomethane in the presence of triphenylphosphine. The subsequent treatment of **9** with sodium azide afforded the azide derivative **10** in 85% yield. Palladium-catalyzed hydrogenation of **10** led to the amine **11** in 75% yield.

We have presented two synthetic strategies to convert octamethylated carboranyl alcohols to the corresponding amines in good overall yields. By employing sodium cyanide (Scheme 1) followed by nitrile reduction the carbon chain length increases by one methylene group, whereas by using the azide reduction (Scheme 2) the carbon chain length remains constant.

The amphiphilic amine hydrochloride **6** was formed by passing hydrogen chloride through a solution of **5** in diethyl ether (Scheme 1). Species **6** was characterized by NMR and mass spectrometry. Remarkably, despite the great hydrophobicity of the polymethylated carborane cage, **6** is sparingly soluble in water, and aqueous solutions were prepared by dissolving **6** in distilled water followed by filtration through a 0.45 μm filter. The clear filtrate did not form self-organized aggregates upon standing at room temperature for a period of 2 days, as determined by light-scattering analysis. However, ultrasonication of the same solution almost immediately produced a dispersion which contained aggregates ranging in size from 50 to 160 nm. Upon prolonged ultrasonication the size of the aggregates increased up to 1 μm. After the ultrasonication had ceased, the aggregates were observed to be stable for at least 5 days at room temperature.

Scheme 2. Synthesis of the Amino Amphiphile **11** Based on Octa-*B*-methyl-*m*-carborane



These preliminary results demonstrate the potential of the newly prepared polymethylated carborane amphiphiles to form self-organized supramolecular aggregates. Detailed studies including transmission electron microscopy of these aggregates are planned and will be reported elsewhere. Important aspects to be elucidated include possible structure−activity relationships of the carborane ammonium-alkyl amphiphiles with respect to their polar chain lengths, and the size, shape, and stability of the resulting superstructures. Of special significance is the fact that a variety of structurally different amphiphilic cluster modules can be designed, since the polymethylated carboranes exist as three isomers (ortho, meta, and para) and their two CH vertexes are available for functionalization with polar headgroups.

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Supporting Information Available: Full experimental and spectroscopic details for all compounds reported (PDF). X-ray crystallographic data for compounds **3** and **4** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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