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Organic Nanocrystals of the Resorcinarene Hexamer *via* Sonochemistry: Evidence of Reversed Crystal Growth Involving Hollow Morphologies

John R. G. Sander[†], Dejan-Krešimir Bučar[†], Jonas Baltrusaitis^{†,‡}, and Leonard R. MacGillivray^{†,*}

[†]Department of Chemistry, University of Iowa, Iowa City, IA 52242-1294, United States

[‡]Central Microscopy Research Facility, University of Iowa, Iowa City Iowa 52242-1294, United States

Abstract

Nano- and micrometer scale crystals of a self-assembled hexamer have been synthesized *via* sonochemistry. The application of ultrasonic irradiation afforded hollow rhombic dodecahedron crystals of the *C*-methylcalix[4]resorcinarene hexamer. The formation of the hollow crystals is attributed to a reversed crystal growth mechanism heretofore only described in the synthesis of inorganic-based materials.

Crystals of nano- and micrometer scale dimensions are important materials in fields that range from materials science to medicine.^{1,2} An appreciable number of crystals with sizes reduced to nanodimensions exhibit cubic symmetries and shapes at both the molecular and bulk scales. However, in purely organic systems a cubic lattice is rare.³ A search of the Cambridge Structural Database reveals that less than 0.1% of all reported purely organic crystals are cubic.^{4,5} The lack of organic systems can be attributed to the anisotropy of molecules that largely prohibits packing from meeting cubic symmetry requirements.⁶ *C*-methylcalix[4]resorcinarene (CMCR) is an organic system that crystallizes in a cubic space group (Fig. 1). The bowl-shaped molecule self-assembles to form a chiral sphere composed of six resorcinarenes and eight water molecules in the rare space group *I* 432.⁷ The field of supramolecular chemistry has shown immense interest in hexameric assemblies of resorcin[4]arenes, as well as related calix[4]pyrroles and pyrogallol[4]arenes, owing to an ability to encapsulate guests with potential applications in fields such as drug delivery.^{8–13} Resorcinarenes have also been identified as excellent surfactants for the dispersion, and self-assembly, of metal nanoparticles into well-defined structures.¹⁴ However, the development of resorcinarenes, and more generally, host-guest systems as nanocrystals remains largely unexplored.^{15–17}

With this in mind, we report the fabrication of crystals of nano- and micrometer scale dimensions that comprise the CMCR hexamer. The crystals are achieved *via* a sonochemical approach with crystals as small as 157 nm. The application of ultrasound offers a versatile means to form nanostructured materials inaccessible by conventional methodologies.^{18–21}

Corresponding Author, len-macgillivray@uiowa.edu.

ASSOCIATED CONTENT

Supporting Information. Experimental details, sample characterization, powder X-ray diffraction, and scanning electron microscopy micrographs. Supplementary crystallographic data can be obtained free of charge from the Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/conts/retrieving.html (CCDC reference code LIWQIR). This material is available free of charge *via* the Internet at <http://pubs.acs.org>.

Here, we show that not only is sonochemistry critical to form CMCR nanocrystals but ultrasonic irradiation affords hollow crystals. Solids with hollow interiors of interest include dendrimers, graphite, silica, metals, and inorganic materials with applications in a number of fields (*e.g.* devices).^{18,22–26} The CMCR crystals described here are the first reported hollow, polyhedral crystals composed of purely organic components.²⁷ The formation of the hollow crystals is attributed to a reversed crystal growth mechanism recently elucidated by Zhou *et al.* to account for the formation of hollow zeolite and perovskite crystals.^{28–31} The stages of reversed crystal growth include oriented aggregation of nanoparticles, surface recrystallization, and growth from the surface-to-core.

In the original report,⁷ the CMCR hexamer was prepared by crystallization from boiling nitrobenzene (NO₂Ph) over the course of two weeks. The result was light yellow crystals of cubic morphology suitable for single crystal X-ray diffraction. When the procedure was repeated, we obtained a yellow precipitate comprised of both crystals and a powder, which powder X-ray diffraction (PXRD) confirmed as the CMCR hexamer. A close examination of scanning electron microscopy (SEM) micrographs revealed a mixture of crystalline morphologies comprised of large flakes and rhombic dodecahedra. The rhombic dodecahedron crystals ranged from 4 μ m to 40 μ m in diameter while the size of the flakes was not uniform and varied on the order of hundreds of microns (Figs. 2a,b).

To synthesize CMCR hexamer crystals reduced to nanometer dimensions, we turned to sonochemistry.¹⁸ The coupling of rapid precipitation and sonochemistry has been shown to afford multi-component nanocrystals, or cocrystals, of purely organic components.^{20,21} A typical preparation consisted of dissolving CMCR (0.003 g, 5.5 mmol) in boiling NO₂Ph (1 mL) and rapidly injecting the solution into water (10 mL). During the injection, the water was simultaneously stirred and exposed to ultrasonic irradiation. After two minutes, an aliquot was removed for analysis by PXRD, SEM, and transmission electron microscopy (TEM).

A close examination of SEM and TEM micrographs revealed crystals of rhombic dodecahedron morphology (Fig. 2c). The crystal sizes were reduced relative to the original recrystallization, which were fit to a Gaussian distribution characterized by an average diameter of 630 nm (s.d. 315 nm) with well-defined morphologies as small as 157 nm (Fig. 2d). PXRD analysis confirmed the solid from the sonochemical approach as the CMCR hexamer (Fig. S1). Additional peaks in the powder pattern were assigned to a hydrate of the resorcinarene. Indeed, a solid with a PXRD that matches additional peaks was obtained directly from a water suspension after equilibration for three days.³² A propensity of CMCR to form hydrates, and solvates in general, is well documented.³³

When the nanocrystallization of the CMCR hexamer was repeated with vigorous stirring in water alone, the resulting solid was composed of smooth spherical particles that ranged from 40 nm to 900 nm in diameter (SEM, Fig. S2). When the suspension was allowed to age for two months, no change in size or morphology was observed (SEM, Fig S3). The smooth spheres could be converted, however, to the rhombic dodecahedra upon exposure to ultrasound radiation. SEM analysis clearly demonstrated the presence of well-defined crystals, albeit, of micron dimensions (SEM, Fig S4). From these observations, we concluded that the combined application of the ultrasonic irradiation^{18,19} and rapid precipitation was required to obtain the well-defined nanosized crystals of CMCR.

During the sonochemical preparation of CMCR nanocrystals, we observed rhombic dodecahedra that exhibit a hollow morphology (Fig. 3). SEM micrographs displayed dodecahedra that were likely fragmented (Fig. 3a–c) into two pieces¹⁹ or, remarkably, formed with a hole to reveal a hollow interior (Fig. 3d). The fragmented polyhedra exhibit a

spherical interior and provide approximate shell thicknesses ranging from 70 nm to 230 nm. The occurrence of the hollow crystals was not size dependent, as crystals from 500 nm to 4 μm in diameter exhibited hollow morphologies. Crystals with hollow polyhedral topologies have been observed for inorganic materials,^{28–31} with zeolite analcime and zeolite A being examples based on a porous structure. The zeolites formed according to a reversed crystal growth mechanism that initiated with oriented aggregation of nanoparticles, was followed by surface recrystallization, and concluded with growth from surface-to-core *via* Ostwald ripening.^{29,34}

To gain insight into the formation of the hollow CMCR crystals, crystallization studies were performed in NO_2Ph at 20-fold dilution. A dilution was employed to slow the rate and observe stages of crystallization, however, crystal growth remained rapid compared to zeolites.^{34,35} A SEM analysis revealed plate-like crystals upon only 45 s of sonication, which included sizes as small as 70 nm (Fig 4a). Exposure to ultrasonic irradiation for 2 min converted the plates to the rhombic dodecahedron morphology. Building units, in the form of nanoplatelets were visible with clear boundaries on the surface of the polyhedra (Fig. 4b).²⁹ The presence of platelets was consistent with an oriented aggregation process in which nanocrystallites organize to share identical orientations, whereupon fusion occurs at the interface to form a single crystal.^{36–39} Indeed, SEM micrographs taken in our original attempts to form nanocrystals of CMCR, *without dilution* and as in the case of preparing zeolites,²⁸ revealed disordered aggregates with crystalline "*islands*" of approximate triangular shape (Fig. 4c,d). The islands likely correspond to partially formed polygons and coincide with partial surface crystallization that continues to grow over the surface and self-adjust until the entire surface corresponds to the faces of a rhombic dodecahedron (*e.g.* Fig. 3d). To our knowledge, the reversed growth mechanism displayed by a purely organic in the form of CMCR is a unique occurrence. These observations are particularly important given that surface-adsorbed organics are typically used to only enhance interparticle interactions of inorganic components that are known to exhibit such a mechanism.²⁹

In this report, we have presented a sonochemical preparation of CMCR host-guest crystals of nano- and micrometer dimensions achieved with rapid nucleation of a crystalline phase. The crystals undergo oriented aggregation to yield rhombic dodecahedra and hollow dodecahedron crystals. The mechanism is attributed to a reversed crystal growth process heretofore observed in inorganic-based materials. Efforts are underway to identify additional organics, as well as metal-organics,^{40,41} that exhibit such non-classical crystal growth to afford nanocrystalline solids. Nano- and micrometer-scale crystals of additional and controlled morphologies based on the self-assembled hexamer are also under investigation.⁴²

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
C-methylcalix[4]resorcinarene and cubic solid-state packing of hexamer (disordered molecules omitted).

Figure 2. (a,b) Rhombic dodecahedron CMCR crystals *via* slow solvent evaporation, (c) TEM micrograph of nanocrystals, and (d) particle size distribution of solid prepared *via* sonochemistry.

Figure 3.
SEM micrographs of (a–c) fragmented hollow rhombic dodecahedra and (d) a rhombic dodecahedron formed with a hole.

Figure 4. Comparison of SEM micrographs of organic nanocrystals of CMCR after sonication for (a) 45 s and (b) 2 min at 20-fold dilution of NO₂Ph. (c,d) SEM micrographs showing partial surface crystallization of islands of triangular shape.