Infinite coordination polymer (ICP) particles and metal-organic frameworks (MOFs) are attractive materials for a diverse array of applications, namely, catalysis, gas storage, chemical separations, photonics, and detections systems. Although promising, these micro- and nano-materials possess certain shortcomings that require further examination through fundamental studies. Towards overcoming these shortcomings, we proposed to investigate and drastically improve upon a series of key properties, specifically size and shape control, surface functionalization, volumetric surface area, and chemically specific gas sorption. Through these efforts, we have made significant progress.
Final Report: Infinite Coordination Polymer Nano- and Micro- Particles

ABSTRACT

Infinite coordination polymer (ICP) particles and metal-organic frameworks (MOFs) are attractive materials for a diverse array of applications, namely, catalysis, gas storage, chemical separations, photonics, and detections systems. Although promising, these micro- and nano-materials possess certain shortcomings that require further examination through fundamental studies. Towards overcoming these shortcomings, we proposed to investigate and drastically improve upon a series of key properties, specifically size and shape control, surface functionalization, volumetric surface area, and chemically specific gas sorption. Through these efforts, we have made significant discoveries, leading to the realization of biomolecule-functionalized nano-ICPs, unprecedentedly robust MOF topologies, and unique MOF structures with significant hydrogen and methane adsorption properties. Specifically, the novel DNA-ICP conjugates realized herein have demonstrated their utility as an in vitro gene regulatory tool, lending this construct to potential applications in therapeutics and diagnostics. Additionally, the carborane-MOF and MOP constructs described herein possess unique structural properties, making them key candidates for applications in selective gas sorption and boron neutron capture therapy (BNCT).
Enter List of papers submitted or published that acknowledge ARO support from the start of the project to the date of this printing. List the papers, including journal references, in the following categories:

(a) Papers published in peer-reviewed journals (N/A for none)

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C. Michael McGuirk, Charlotte L. Stern, Chad A. Mirkin. Small Molecule Regulation of Self-Association and Catalytic Activity in a Supramolecular Coordination Complex, Journal of the American Chemical Society, (03 2014): 0. doi: 10.1021/ja500214r


Chad A. Mirkin, Daniel J. Clingerman, Robert D. Kennedy, Joseph E. Mondloch, Amy A. Sarjeant, Joseph T. Hupp, Omar K. Farha. An exceptionally high boron content supramolecular cuboctahedron, Chemical Communications, (08 2013): 0. doi: 10.1039/c3cc44173c

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TOTAL: 29

Number of Papers published in peer-reviewed journals:

(b) Papers published in non-peer-reviewed journals (N/A for none)

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Patents Submitted


Patents Awarded

Awards

• 2015 Royal Society of Chemistry (RSC) Centenary Prize
• 2014 Friends of the National Library of Medicine Distinguished Medical Science Award
• 2014 Honorary Degree, Universidade Federal do Rio Grande do Sul

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### Student Metrics

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- The number of undergraduates funded by your agreement who graduated during this period and will continue to pursue a graduate or Ph.D. degree in science, mathematics, engineering, or technology fields: 0.00
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**Sub Contractors (DD882)**
Biocompatible Infinite Coordination Polymer Nanoparticle-Nucleic Acid Conjugates for Antisense Gene Regulation

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The Role of Modulators on the Colloidal Stability and Polydisperity of a Nanoscale Metal-Organic Framework

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William Morris
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Scientific Progress

Technology Transfer

See patent activity.
Abstract

Infinite coordination polymer (ICP) particles and metal-organic frameworks (MOFs) are attractive materials for a diverse array of applications, namely, catalysis, gas storage, chemical separations, photonics, and detections systems. Although promising, these micro- and nano-materials possess certain shortcomings that require further examination through fundamental studies. Towards overcoming these shortcomings, we proposed to investigate and drastically improve upon a series of key properties, specifically size and shape control, surface functionalization, volumetric surface area, and chemically specific gas sorption. Through these efforts, we have made significant discoveries, leading to the realization of biomolecule-functionalized nano-ICPs, unprecedentedly robust MOF topologies, and unique MOF structures with significant hydrogen and methane adsorption properties. Specifically, the novel DNA-ICP conjugates realized herein have demonstrated their utility as an \textit{in vitro} gene regulatory tool, lending this construct to potential applications in therapeutics and diagnostics. Additionally, the carborane-MOF and MOP constructs described herein possess unique structural properties, making them key candidates for applications in selective gas sorption and boron neutron capture therapy (BNCT).

Subject Terms
Nanoparticles, infinite coordination polymer (ICP), microparticles, metal-organic frameworks (MOF)

Number of Pages: 15
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DNA-ICP Particles for *in vitro* Gene Regulation

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Stabilization of a Highly Porous MOF Using a Carborane-Based Linker Strut

Metallocarborane-Based MOF with a Complex Topology

Carborane-Based Metal-Organic Polyhedron

References
Statement of Problem Studied

We have recently described a new class of inorganic nanoparticles made by judiciously halting the polymerization of metal ions and polydentate ligands at early stages in the chemical process. These materials, known as infinite coordination polymer (ICP) particles, can be synthesized with a wide array of metal ions and ligand building blocks, spanning the micro- and nanoscale dimensions. The community’s interest in ICP particles is growing rapidly, as an ever growing list of potential applications is being realized. This vast array of potential applications is in part due to the fact that these structures, consisting of repeating ligands interconnected by metallic nodes, can be made from readily available and highly tailorable metal and ligand precursors. This modularity allows ICP particles to have chemically adjustable porosities and relatively high internal surface areas, giving researchers access to a network structure that can be logically modified for many applications, such as catalysis, gas storage, separations, photonics, and detection systems.

Considering that much of the groundwork for ICPs has only been laid in the past decade, significant advances have already been made. Yet, for ICPs to fulfill their technological potential, considerable further fundamental insights and discoveries are required. One such critical and fundamental parameter is the shape and size of ICP particles. The realization of a logical pathway towards accurate and precise particle design is desirable. With the ever-emerging field of nanomaterials and nanomedicine, the ready and repeatable realization of ICP particles on the nano-scale may have huge implications in future applications, such as therapeutics and diagnostics. Another significant current shortcoming in ICP technology is the limited ability to functionalize and characterize their surfaces. The functionality of micro- and nano-materials is directly dependent on the chemistry of their surfaces. Whereas there are a wide variety of techniques for attaching ligands to the surfaces of inorganic nanoparticles, similar approaches for ICPs are limited. Thus, for the advancement and application of ICP particles on these dimensions, developing a thorough understanding of the possible routes to surface functionalization is crucial. Therefore, a major goal of the proposed research was to develop an unprecedented tailorable and modular understanding of both particle size/shape and particle surface functionalization. In particular, we aimed to utilize this fundamental understanding for the realization of nano-scale ICP-biomolecule hybrids for in vitro gene regulation.

In addition to elucidating novel physical and chemical parameters for ICPs, we have made significant advances in expanding the chemical catalogue of a closely related material, metal-organic frameworks (MOFs), and in the process realized a series of novel and technologically relevant architectures. Previously, our group has shown that MOFs and ICPs containing inorganic carborane units can be effectively employed for the separation of gas mixtures. In order to expand upon these promising early efforts, we proposed to examine the ability of these unique inorganic moieties to significantly affect key parameters and functionalities of known MOF structures. Namely, we planned to study how the inclusion of carborane, and the related bis(dicarbollide), moieties into the linkers of these structures
manipulates volumetric surface area, selective gas sorption, and structural robustness. In addition, these studies have led to realization of novel polyhedron-type structures with record-setting levels of boron. Such structures lend themselves to applications such as boron neutron capture therapy (BNCT). Through our concerted efforts, we have made significant advancements in: 1) the control of ICP particle size on the nano-scale, 2) the controlled functionalization of ICP particles with biomolecules, and 3) the improvement of the structural integrity and selective gas sorption properties of carborane-functionalized MOFs.

Summary of Results
DNA-ICP Particles for \textit{in vitro} Gene Regulation$^{13}$

In the Mirkin lab, we have previously developed a gold nanoparticle-based construct for the delivery of genetic material to cells, termed spherical nucleic acids (SNAs).$^{14}$ These constructs are composed of gold nanoparticle cores (typically, 10-30 nm) with oligonucleotides (e.g., DNA) densely decorated on the surface of the particle in a highly oriented fashion.$^{15}$ Importantly, SNAs have the ability to enter cells via endocytotic pathways and effect designed changes in the biochemical processes of the cell. Unfortunately, concerns have been raised about the potential long-term toxicity of gold nanoparticles and their metabolic fate. Thus, our lab is extremely interested in new forms of SNAs with alternative cores that are biocompatible and readily synthesized. In particular, we have targeted ICP-based constructs, as these materials can be synthesized from the combination of chemical building blocks approved by the FDA and well-understood and biologically abundant metals. In order to realize ICP particles for the delivery of oligonucleotides to cells, some fundamental hurdles had to be overcome, namely the repeatable synthesis of relatively mono-disperse particles (i.e., size control) and the high-yielding covalent attachment of oligonucleotides to the surface (i.e., surface functionalization). Towards these goals, we have developed a novel ligand motif for the realization of post-synthetic surface functionalization as well as a promising methodology for the generalizable synthesis of monodisperse nano-scale ICPs.

It is known that synthetically modular ditopic 3-hydroxy-4-pyridinone (HOPO) ligands can form coordination polymers with Fe(III), the most abundant transition metal in the body.$^{16}$ Derivatives of this ligand motif also have been approved by the FDA for the treatment of iron-overload in humans. Therefore, using this HOPO-Fe(III) tandem, we saw an opportunity to design biocompatible ICP particles that could be post-synthetically modified on their surface with DNA. Thus, we synthesized the HOPO derivative DABA-bis-HP-N$_3$, which contains two potentially coordinating moieties as well as an azide group for oligonucleotide attachment (Figure 1). Particles were synthesized by combining DABA-bis-HP-N$_3$ and ferric nitrate in dilute NaOH. The crude particles were purified by centrifugal filtration using a 100 kDa molecular-weight cutoff filter. The desired particles were collected and their size was measured using dynamic light scattering (DLS), which gave a mean diameter of 10-20 nm. The particles also were characterized by TEM and AFM imaging, which corroborated the DLS results. After synthesis and characterization of the mono-disperse particles, which contained pendant azide
moieties, oligonucleotides were covalently appended via azide-strained alkyne “click-chemistry”. DNA functionalized with the strained alkyne dibenzocyclooctyne (DBCO) were conjugated to the azide-functionalized ICP particles by simply mixing the two reactants in aqueous NaCl, followed by repeated filtration to removed unreacted DNA. The resulting colloid proved to be stable in Tris-HCl buffer over a wide range of temperatures. The resulting structures were characterized by AFM, DLS, zeta potential, UV/Vis, and inductively couple plasma mass spectrometry (ICPMS). All of these techniques corroborated the nano-scale ICP-DNA hybrid architecture. Importantly, the layer of DNA on the surface of the particles imparts properties similar to their gold-nanoparticle predecessors, namely, increases in size, surface charge, and colloidal stability. Significantly, we have shown that through judicious organic ligand design and reaction conditions one can simply and repeatedly synthesize size-controlled ICP nanoparticles. Additionally, by appending desired functional moieties to the organic ligand, the ICP particle surface can be functionalized post-synthetically using chemistry that is orthogonal to the coordination events within the particle itself.

Having demonstrated that we can overcome the synthetic hurdles for the realization of nano-scale ICPs and their selective surface functionalization, we examined if indeed these ICP-DNA hybrid structures could enter cells and deliver genetic information for the regulation of endogenous biochemical

Figure 1: Synthesis and assembly of ICP particles and their cellular uptake. (a) Synthetic route to DABA-bis-HP-N₄: a) maltol, n-propanol, reflux, 16 h; b) maltol, ethoxyethanol, 64 h, reflux; c) 4-azidobutan-1-amine, HATU, diisopropylethylamine, DMSO, RT, 4h. (b) Assembly of ICP particles from Fe(NO₃)₃ and 4, followed by DNA conjugation.

Figure 2: Cellular uptake. (a, b) Confocal microscopy images of HeLa cells treated with Cy5-ssDNA (a) and ICP-DNA particles (b; 100 nm DNA in each case). Hoechst stain denotes the nucleus in blue, whereas the Cy5 dye attached to DNA is red.
processes. To test our hypothesis, cellular uptake was examined in HeLa cervical cancer cells using dye-labeled DNA (Figure 2). The ICP-DNA particles were found to cross cell membranes with efficiency very similar to the analogous gold nanoparticle-based SNA. Knowing that the particles were able to readily enter cells, we tested whether or not they could efficiently deliver their genetic cargo to the cell and effect expression of a known cancer-related mRNA transcript \textit{in vitro}. SKOV-3 ovarian cancer cells were chosen for this purpose since they over express the HER2 gene, which is known to contribute to malignant cell growth and differentiation. Cells were treated with non-targeting ICP-DNA particles, HER2-targeting ICP-DNA particles, or HER2-targeting free DNA complexed with the commercial transfection agent Lipofectamine\textsuperscript{TM} (Figure 3). Treatment with anti-HER2 ICP-DNA particles reduced HER2 expression by up to 81\% in a dose-dependent fashion. Importantly, in contrast to Lipofectamine\textsuperscript{TM}, no toxic effects or cell death resulted from treatment with the ICP-DNA particles.

In summary, we have elucidated a facile method for the synthesis of biocompatible, DNA-functionalized ICP nanoparticles that are able to readily traverse the cellular membrane and deliver genetic material for the regulation of protein translation. The core of the ICP particle is composed of benign building blocks that are not expected to pose significant health hazards. This study represents a major step towards clinically viable gene regulation and demonstrates the utility and modularity of ICP technology.

Our ongoing efforts are focused on the systematic synthetic modification of HOPO derivatives to include various orthogonal organic functionalities that promote DNA conjugation. By creating a library of HOPO derivatives with different organic moieties capable of orthogonal “click-type” reactions, we can deliver ICP-DNA nanoparticles with multiple different DNA sequences on a single particle. The construction of these architectures will allow for the simultaneous regulation of multiple intracellular processes using a single chemical entity.

\textbf{Figure 3:} Expression of HER2 protein in SKOV-3 cells treated with nontargeting (NT) ICP-DNA particles, HER2-targeting ssDNA + Lipofectamine\textsuperscript{TM} (25 nm DNA basis), and HER2-targeting ICP-DNA in increasing doses.
Nanoporous materials such as MOFs form an important class of materials that can potentially be used for the separation and storage of energy and environmentally relevant gases, such as methane and hydrogen. In particular, MOFs have been pegged as potential sorption materials for onboard storage of methane and/or hydrogen in the next generation of vehicles, which could be useful to the ARO. Importantly, the ability of MOFs to adsorb gases, especially in a chemically specific manner, is a function of the pore geometry, volume, surface area, and density. These properties in turn are highly dependent on the structure and chemical make-up of the linker struts used to build the MOF. Previously, we have shown that the inclusion of carborane moieties into the linker struts of MOFs can impart exciting properties on the construct, such as high thermal stability and selective adsorption. However, these previously reported structures had low surface area and small pore volumes, making them relatively poor performers overall. Thus, using this concept of carborane-functionalization, we continued to explore if we could realize novel architectures with appreciably larger surface area and volume parameters. We hoped to elucidate any properties of the MOF that were a direct consequence of the inclusion of the chemically unique carborane

**Figure 4:** Synthesis of carborane-bis(isophthalic acid) ligand (LH$_4$) used to construct NU-135. Reaction conditions: i) $n$-BuLi, THF; CuCl, THF -40 to 70 °C; diethyl 5-iodoisophthalate, Pd(PPh$_3$)$_4$, NMP, 100 °C, 16 h (42 %). ii) LiOH (1 M), THF/H$_2$O 2:1, RT, 36 h; H$_3$O$^+$ (84 %).

**Figure 5:** Representations of the crystal structure of NU-135. (a) Detail of pores, viewed along the $ab$ plane. Lilac spheres indicate the largest sphere-shaped voids that can be found within the evacuated MOF as defined by the internal van der Waals surface of the material. Hydrogen atoms removed for clarity. (b) Simplified nbo network viewed along the $ab$ plane. Blue squares = Cu$_2$ paddlewheels; pink rectangles = carborane bis(isophthalic acid) ligands. (c) Space-filling representation, viewed along the $c$ axis, illustrating the carborane-lined pores. Atom code; C = grey; H = white; O = red; B = pink; Cu = blue.
moiety by directly comparing our new MOF to a reported isoreticular predecessor containing purely organic (phenylene-based) linker struts.

To realize a new carborane-based MOF with a large pore volume and surface area, the long para-carborane-containing strut LH$_4$ was synthesized (Figure 4). By combing this strut with copper nitrate under common solvothermal conditions, blue crystals were realized, which upon single-crystal X-ray diffraction analysis proved to be a new MOF architecture (NU-135, Figure 5). Importantly, this structure is isoreticular with the MOF built from the purely organic (terphenylene) analog strut (NOTT-101). Therefore, we could directly compare these structures to determine how the presence of the carborane affects structural and functional parameters.

Upon activation of the structure by supercritical CO$_2$, the volumetric surface area of NU-135 was determined to be ca. 30% greater than that of the NOTT-101 analog. This significant change in surface area is a direct function of the globular nature of the carborane, thus acting as an effective sphere with a diameter approximately that of a single benzene ring. This is highly interesting as increasing volumetric surface area is a well-known method for increasing gas adsorption. Therefore, in collaboration with the National Institute of Standards and Technology (NIST), the gas uptake properties of NU-135 were measured (Figure 6). NU-135 shows significantly high overall uptake compared to previous carborane-functionalized ICPs and MOFs, owing to the increased surface area and pore volume. Importantly, we observed very high capacity of methane uptake, specifically an absolute methane storage capacity of 10.3 mmol/cm$^3$ at 65 bar. This represents is an important advance as it demonstrates the ability of a material to absorb natural gas to the extent where it may become commercially attractive. Sample degradation was not observed over multiple cycles. The ability of NU-135 to adsorb hydrogen, another potential fuel of the future, was also examined. NU-135 was measured to have a maximum absolute volumetric hydrogen uptake value of ca. 49 g/L above ca. 55 bar at 77 K. This value places NU-135 amongst the highest for all MOFs for volumetric hydrogen storage.

From the empirically determined volumetric surface area and the combined results of methane and hydrogen adsorption studies we can conclude that the unique quasi-spherical geometry of carboranes allows for the synthesis of MOFs that are

![Figure 6: Experimental (blue) and simulated (red) high-pressure absolute gas adsorption isotherms for NU-135 at several temperatures.](image-url)
isoreticular to their organic analogs, yet exhibited enhanced structural and functional parameters. The incorporation of carborane polyhedrals into other high-performance MOFs is an exciting prospect, and it will hopefully lead to novel materials with record-breaking gas sorption properties. This novel strategy, in which a carborane moiety is employed to greatly increase volumetric surface area, will allow us and others to expand the current capability of porous materials for gas storage applications.

Stabilization of a Highly Porous MOF Using a Carborane-Based Linker Strut

Having demonstrated that the inclusion of carborane motifs into MOFs can impart structural parameters that are unachievable with their organic analogs, we sought to examine if we could use the steric bulk and rigidity of carboranes to stabilize highly porous MOF topologies that are known to be unstable with the analogous purely organic linker. As previously stated, structures with high surface areas and porosity are desirable for applications in gas storage of interest to the ARO.

**Figure 7:** Reaction conditions: i) n-BuLi, THF; CuCl, THF - 40 to 70 °C; 1,3,5-tribromobenzene, PdCl₂(PPh₃)₂, 70 °C, 12 h (79 %). ii) n-BuLi, THF; ethyl chloroformate -78 °C to RT, 12 h (68 %); iii) LiOH, THF/EtOH/H₂O 3:2:1 rt, 12 h; H₃O⁺ (90 %).

**Figure 8:** Detail of pores, viewed along the 111 plane of (a) HKUST-1; (b) MOF-143; (c) NU-700. Lilac spheres indicate the largest sphere-shaped voids that can be found within the evacuated MOF as defined by the internal van der Waals surface of the material. Hydrogen atoms removed for clarity.
One method for accessing such MOF architectures is through using linker struts that impart significant spacing between the metal nodes. This symmetric tritopic linker struts, but somewhat unexpectedly, when many of these structures are activated (e.g., vacuum, heat, supercritical CO₂) their crystallinity is destroyed and their porosity is lost. Thus, we hypothesized that by modifying these tritopic organic linkers to contain rigid and sterically bulky polyhedral carboranes we could rigidify and stabilize these highly porous structures and realize new and promising architectures for efficient gas storage.

Having synthesized the three-fold symmetric tritopic carborane-containing linker H₃BCA (Figure 7), the linker was added to copper nitrate under solvothermal conditions, which yielded single crystals suitable for an X-ray diffraction study. The crystallographically determined structure (NU-700) proved to be isoreticular with the unstable organic analog MOF-143 (Figure 8). Critically, we were able to demonstrate that, in contrast to MOF-143, NU-700 could be activated via supercritical CO₂ and vacuum/heating. Upon activation, the porosity of the framework was measured using nitrogen adsorption at 77 K, which gave a Brunauer-Emmett-Teller surface area of 1,870 m²/g. The improved stability of NU-700 over MOF-143 is attributed to the unique properties of the constituent carboranyl moieties. In addition to rigidity and steric bulk, we hypothesize that the radially oriented, hydridic B-H units of carborane exhibits a highly symmetric and uniform charge density that precludes strong interactions with the solvent molecules, which is known to destroy MOF crystals through capillary forces. Importantly, this work demonstrates a potentially general platform for the stabilization of difficult-to-activate MOFs, whereby simple replacement of phenyl spacers with carboranes does not affect the

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Figure 9: (a) Synthesis of linker [PPh₄][5].³ (b) ORTEP-type representation of the crystallographically determined molecular structure of the [5]⁻ anion in its cesium salt.⁴

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1. Reagents and conditions: (i) (trimethylsilyl)ethynylmagnesium bromide (3 equiv), PdCl₂(PPh₃)₂ (5 mol%), THF/Et₂O, 65°C, 16 h, 92%. (ii) KOH (2 equiv), H₂O/MeOH (1:4), rt, 2 h, 96%. (iii) diethyl 5-iodoisophthalate, Pd(PPh₃)₄ (3 mol%), CuI (10 mol%), i-Pr₂NEt/THF (1:1), 65°C, 24 h, 85%. (iv) CsF, EtOH, reflux, 6h, 95%. (v) CoCl₂, NaOH (40% aq), 105°C, 1 h, Et₂O, HCl (aq); [PPh₄]Br, H₂O. b) Thermal ellipsoids are drawn at 50% probability. Atom color code: Co = purple; C = grey; H = white; B = pink; O = red. Cesium cations are omitted for clarity.
underlying structure.

Metallocarborane-Based MOF with a Complex Topology

In our efforts to realize novel MOF structures with unique structural and functional properties through the inclusion of carborane-based linker struts, we examined the realization of MOFs based on axially functionalized bis(dicarbollide) metal complexes as linkers. We originally became interested in these chemical motifs as they present an intriguing combination of rich redox chemistry and a linear geometry, making these complexes perfectly suited for the construction of redox-active MOF materials. In particular, we imagined the realization of metallacarborane-based constructs for stimuli responsive porous materials, selective gas separation and storage, sensing, and waste remediation. Towards these goals, we targeted an analog of the highly porous and phase-pure MOF NOTT-104, which is based on a linear terphenylene-derived linker. Therefore, we synthesized the symmetric and linear cobalt bis(dicarbollide)-based linker \( \text{PPh}_4[5] \) (Figure 9). This linker design was chosen specifically because of the above-mentioned propensity of the organic analogs to form, reliably and in high purity, highly porous MOFs with a singular topology (fof). In stark contrast to the organic analogs, the solvothermal reaction between \( \text{PPh}_4[5] \) and copper nitrate yielded an array of topologies, included one never-before-seen architecture.

The mixing of \( \text{PPh}_4[5] \) and copper nitrate under solvothermal conditions resulted in the growth of small, green crystals, which upon closer inspection consisted of three different crystal habits: plates, prisms, and cubes. Through single-crystal X-ray diffraction studies it was determined that the plate-like crystals were the predicted archetypical fof topology (NU-150) (Figure 10). Of particular interest in this structure is the apparent bend at each alkyne region in the struts, giving an overall linear structure and allowing for the fof topology. In contrast, studies of the prismatic crystals elucidated the alternative and rare, but
known, sty topology (NU-151, Figure 10). Although the overall topology is fairly similar between these two architectures, in NU-151 the bending of the alkyne regions of the strut area aligned in concert, giving each strut a pronounced bend in the crystal structure. Finally, a single crystal X-ray diffraction study of the cubic crystal revealed a novel hbk topology (NU-152, Figure 11), which is uniquely composed of interconnected metal-organic polyhedral (MOPs). These coordination polyhedral, are composed of 12 biscopper paddlewheels, making up the vertices of a cuboctahedron. In this structure, the cobalt bis(dicarbollide)-based linkers exhibit not only bending in the alkyne regions, but also twisting at the cobalt metal center. These structural considerations behave in concert to allow this unprecedented topology. Importantly, this novel arrangement of linkers in three-dimensions produces a void space in NU-152 (79 %) that is significantly greater than that observed in NU-150 and NU-151 (70 %). Importantly, this work illustrates that the expected topology is not always obtained, even when a particularly robust system is used. In this case, it seems that the length and flexibility of the linker play an important role in the formation of the unprecedented framework and deviation from the predicted one. This work exemplifies how new topologies may be accessed by using structural units that possess properties that are not usually associated with MOFs, such as flexibility and curvature.

**Figure 11:** Representations of the crystal structure of NU-152. (a,b,d,e) The bis(dicarbollide) linkers are represented by two red triangles connected by grey conjoined icosahedra, and the biscopper(II) paddlewheels are represented by blue squares (as shown in Figure 5.1). (c) A single cuboctahedral supercluster (grey) with crystallographically independent linkers shown in blue and pink. (f) Purple spheres represent the centroids of the 10-coordinate cuboctahedra, and black lines represent the connectivities between the cuboctahedra via sets of four ‘pink’ linkers or sets of two ‘blue’ linkers.
Carborane-Based Metal-Organic Polyhedron

Inspired by the presence of the unique metal-organic polyhedra (MOPs) in the three-dimensional \textbf{hbkt} topology of NU-152, we sought to realize an analogous free-standing polyhedron containing carborane moieties, as boron-rich nanomaterials have recently proven to be potentially applicable for the neutron capture therapy of tumors. By synthesizing boron-rich nanomaterials in this way (i.e., through the combination of organic ligands and metals), we could realize well-defined constructs that could be structurally characterized through single-crystal X-ray diffraction studies, a uncommon feature in this field. Towards this goal, we synthesized the carborane-based ligand \( \text{LH}_2 \) (Figure 12), which unlike the previous carborane-containing motifs does not possess the necessary symmetry to form three-dimensional infinite networks. To realize the targeted MOP, \( \text{LH}_2 \) was mixed with copper acetate under solvothermal conditions, yielding blue, block-like crystals. Upon isolation, visual inspection showed crystals of a single crystal habit that were shown to possess bulk purity.

![Figure 12](image_url)

**Figure 12:** The synthesis of compound 3. Reaction conditions: i) \( n\text{-BuLi, THF; CuCl, THF, -40 to 70 \degree C; diethyl 5-iodoisophthalate, PdCl}_2\text{(PPh}_3\text{)}_2, \text{NMP, 100 \degree C, 48 h (48 \%).} \) ii) \( \text{LiOH (1 M), THF/H}_2\text{O 2:1, rt, 36 h; H}_3\text{O}^+ \) (100 \%). iii) \( \text{Cu}_2\text{(OAc)}_4\cdot2\text{H}_2\text{O, DMF, RT, 4 days (42 \%).} \) The representation of the compound 3 is simplified: pink icosahedra = carborane cages; blue squares = biscopper paddlewheel nodes; grey hexagons = benzene rings.

![Figure 13](image_url)

**Figure 13:** Representation of the crystallographically derived molecular structure of 3. (a) View along the crystallographic c axis. This axis corresponds to a molecular \( C_3 \) symmetry axis. (b) View along the molecular \( C_4 \) symmetry axis. Color key for (a) and (b): pink icosahedra = carborane cages; blue squares = biscopper paddlewheel nodes; grey hexagons = benzene rings. (c) Space-filling representation of 3. Color key: pink = B; red = O; blue = Cu; grey = carbon; white = hydrogen. (Coordinated solvent removed for clarity).
via powder X-ray diffraction (PXRD). Importantly, the crystallinity of the complex allows for a single crystal X-ray diffraction study, allowing for the elucidation of the structure of the realized supramolecular cage (CB-MOP, 3) (Figure 13). The determined structure has a diameter of 3.6 nm and an internal cavity with a diameter of 1.6 nm. The structure could be activated, giving a surface area of 625 m$^2$/g, is consistent with the porous nature of the material and demonstrative of its stability. Each molecular polyhedron contains 240 boron atoms, corresponding to a gravimetric boron content of 29 %, which is currently the largest amount of boron atoms reported in a molecular species. Owing to its high and dense boron content, a carborane-base MOP, such as CB-MOP (3), is a prime candidate for exploration of boron neutron capture therapy.

References:


