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Supramolecular Chemistry in Solid State Materials such as Metal-Organic Frameworks

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Dedicated to Professor Omar M. Yaghi, in occasion of being awarded with the Wolf Prize in Chemistry 2018, and in acknowledgement for his global mentoring.

Abstract: Supramolecular chemistry has enriched the scientific research for more than fifty years reaching one of its summits in 2016, when the *Chemistry Nobel Prize* was awarded for the *design and synthesis of molecular machines*, in which host-guest chemistry plays a fundamental role. Recently, the groups of Omar Yaghi and Fraser Stoddart, among others, have demonstrated that this chemistry can be extended to the pores of metal-organic frameworks (MOFs). This heterogenization of supramolecular chemistry can be achieved through the incorporation of macrocycles to the organic struts of these highly porous and crystalline materials. Throughout this short review we summarize interesting examples of selective recognition by naturally occurring and synthetic macrocycles in solution and solid state; and later we survey important milestones to achieve specific recognition sites and develop host-guest chemistry at the pores of MOFs.

This summary contains examples of different synthetic strategies to incorporate macrocycles to solid state materials, and in particular, to prepare *supramolecular MOFs* with particular properties and related applications. Specifically, the revised research includes the incorporation of both naturally occurring and synthetic macrocycles to solid state materials such as polymers, metal nanoparticles, etc., as prelude of the solid phase recognition studied in MOFs. An important number of the contributions presented here feature porous solids with smooth access to the host's cavity incorporated in the pores, allowing specific recognition of guest molecules. This smooth access to those active recognition sites in materials with extremely high surface area such as MOFs, open the possibility to develop the next generation of frontier materials with application in fields such as selective capture of water toxins and heterogeneous catalysis, among others.

Keywords: Metal-Organic Frameworks (MOFs) · Supramolecular Chemistry · Macrocycles · Solid phase recognition process

1. Introduction

Since the discovery of crown ethers by Pedersen fifty years ago,^[1] host/guest supramolecular chemistry has undoubtedly attracted a major attention among researchers from all over the world. The ability of synthetic and naturally occurring macrocycles to *recognize* guest molecules with specific properties and geometries, resemble the formation of highly selective molecular complexes in enzymatic catalysis (Figure 1). Be-

sides the crown ethers reported by Pedersen in 1967, and natural macrocycles such as cyclodextrins,^[2] an important number of synthetic macrocyclic compounds were explored in the precedent decades: calixarenes,^[3] cucurbiturils,^[4] pillar- enes,^[5] torands,^[6] cyclophanes,^[7] resorcinarenes,^[8] and recently, multifarenes.^[9] The variety in the prepared macrocycles and their functionalizations, expanded the opportunities of exploring molecular recognition and constrained-environment's chemistry.

The concept of host-guest chemistry was first coined by Cram in 1974,^[10] who described the complexation of a guest molecule as a *recognition process* based on the complementary arrangement of binding sites and steric features. This *recognition process* determines the selectivity and efficiency of the chemistry that takes place within the cavity. Our group,^[11] and others,^[12] have demonstrated that the reactivity

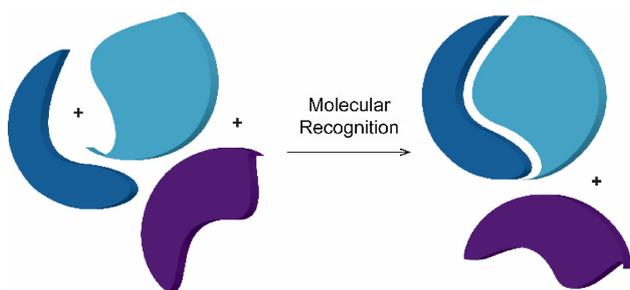


Figure 1. Schematic representation for the concept of molecular recognition taking place in a host-guest complex.

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and properties of included guest molecules can be drastically changed upon host-guest complexation with a macrocycle. Therefore, and as suggested by Cram's recognition idea, structural differences in the hosts have profound impact in the obtained supramolecular complexes. During the last decades, the supramolecular chemistry was enriched with the discovery of new 2D, 3D, rigid and flexible synthetic macrocycles,^[13] which impacted deeply in new research frontiers such as the design of molecular machines.^[14]

Recently, this rich host-guest chemistry in solution briefly described above, has been expanded through the incorporation of macrocycles to solid materials. This *heterogenization* of the studied supramolecular chemistry add additional advantages to the resultant materials such as recyclability (specially useful when "synthetically expensive" macrocycles are used). In addition, and particularly attractive for applications such as selective capture/filtration of contaminants, solid materials incorporating macrocycles present enhanced processability, and lower heat capacity (thus decreasing the energy intensive recovery process), compared to analogous compounds in aqueous solution.^[15]

Polymeric materials incorporating macrocycles have been known for the past two decades, being the most popular among them, those in which the host-guest chemistry is used to join the building units that comprise the material. This is the case of many reported supramolecular polymers^[16] that take advantage of the reversibility and responsiveness of these supramolecular interactions to design functional polymeric structures.

Another rich class of solid and functional materials, are the recently developed metal-organic frameworks (MOFs). MOFs are a promising class of crystalline and highly porous materials built by strong bonds between organic struts and inorganic clusters, also known as secondary building units (SBUs).^[17] Their construction flexibility, based on the availability of building units, allow to access great structural diversity in terms of pore structure, pore environment and

functionality. This synthetic variety caused an exponential grow in the number of reported MOF's publications (Figure 2, compared to supramolecular polymers) and MOFs structures, which can be currently estimated as more than ca. 70,000 in the Cambridge Structural Database (CSD).^[18]

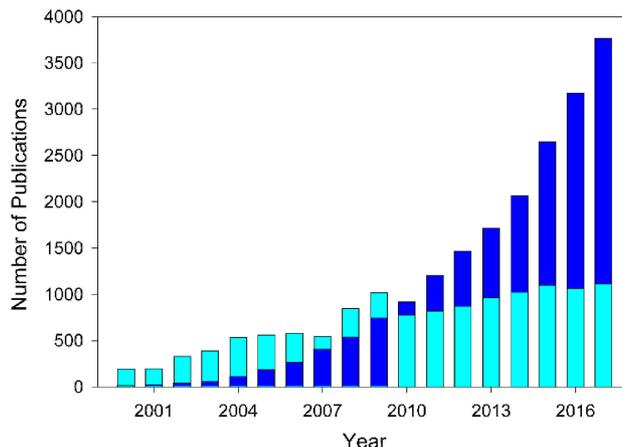


Figure 2. Scientific publications identified with the keyword *MOFs* (blue bars) and *Supramolecular Polymers* (cyan bars), in the last 17 years. Source: Scopus

To understand the dimension of this structural versatility and rationalize the outcome obtained in the material's design, their network topology has to be considered.^[19]

For instance, a single type of SBU such as $\text{Cu}_2(\text{CO}_2)_4$ (also known as Cu-paddlewheel) can originate diverse structures with different pore properties depending on the selected organic strut and its *topicity* (Figure 3). Considering the variety of SBUs available, as well as the number of potential organic struts with different *topicity* and geometry, it is not difficult to understand the material's variety.



Alejandro M. Fracaroli received his PhD in Chemistry in 2009 from Universidad Nacional de Córdoba (UNC), Argentina, under the supervision of Prof. Rita H. de Rossi. Soon after, he joined the group of Dr. Kentaro Tashiro at the International Center for Materials Nanoarchitectonics (MANA-NIMS), in Tsukuba Japan, where he stayed until January 2013. Between February 2013 and April 2016, he was appointed post-doctoral fellow in the Lab of Prof. Omar Yaghi at the University of California, Berkeley in the U.S.A. Since May 2016, he is Assistant Professor and Researcher (INFIQC-CONICET), at the Department of Organic Chemistry, in the College of Chemical Sciences of Universidad Nacional de Córdoba, where he has started his research program on reticular materials such as MOFs and COFs (<http://rhr.investigacion.unc.edu.ar/>).



Rita H. de Rossi completed PhD in Chemistry at the Universidad Nacional de Córdoba (UNC), Argentina, working under the supervision of Prof. Héctor E. Bertorello. After her thesis, she was appointed as a Research Fellow in Chemistry at the University of California at Santa Cruz, U.S.A. (1970–1972), at the beginning under the supervision of Prof. Joseph Bunnett and later in Prof. Claude Bernasconi's Lab. She was appointed as Professor at the Organic Chemistry Department in the College of Chemical Sciences, Universidad Nacional de Córdoba in 1974, and from 2009 she is Emeritus Professor in the same Department. Prof. H. de Rossi has published more than 150 scientific articles, advised more than 15 PhD students, and she is still actively advising several researchers in their early careers.

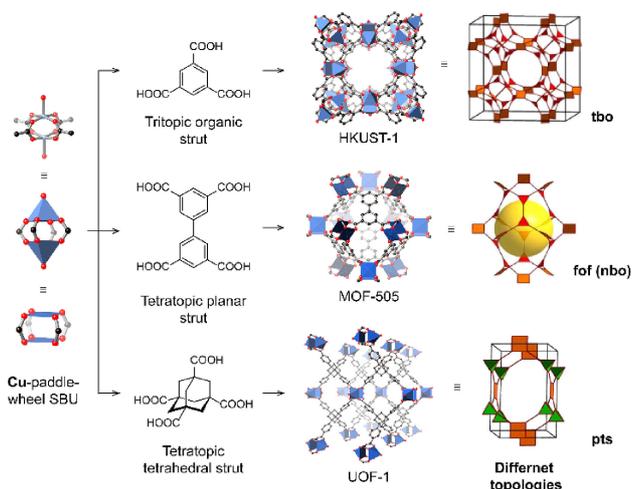


Figure 3. Schematic representation of the structural versatility produced by a single SBU upon changing the geometry and topology of the organic strut. Topological graphs reprinted with permission ref. 19c. Copyright 2014 American Chemical Society.

Throughout this short review we will revise important recent contributions on the incorporation of macrocycles, and their supramolecular chemistry, to solid materials that feature designed recognition properties useful for different applications.

2. Recognition Process using Macrocycles

2.1 Molecular Systems

The recognition process for the different types of macrocycles was recently reviewed.^[20] Among the reported examples, our group has had some seminal contributions worth highlighting at this point, which led to some insights on the supramolecular chemistry of cyclodextrins and cucurbiturils.

Naturally occurring cyclodextrins (CD) are cyclic oligomers of D-(+)-glucopyranosyl units linked by α -1,4-glycosidic bonds. One of the appealing point of this macrocycle is that they are readily available, harmless, and capable to form elaborated supramolecular structures in aqueous solutions. There are three readily available cyclodextrins named: α -, β -, and γ -CDs containing six, seven, or eight glucose units, respectively. Due the arrangement of the glucopyranose units, CDs have a truncated cone-shape with a hydrophobic cavity featuring diameters of 0.49, 0.62, and 0.80 nm, for α -, β -, and γ -CD correspondingly.

It has been reported that small differences in the macrocycle cavity's dimension can affect drastically its host-guest chemistry. A clear example is the inclusion of the organophosphorus insecticide *fenitrothion* [*O,O*-dimethyl *O*-(3-methyl-4-nitrophenyl) phosphorothioate],^[21] which forms a 1:2 inclusion complex with the small cavity permethylated α -cyclodextrin (TRIMEA) as observed by X-ray crystallogra-

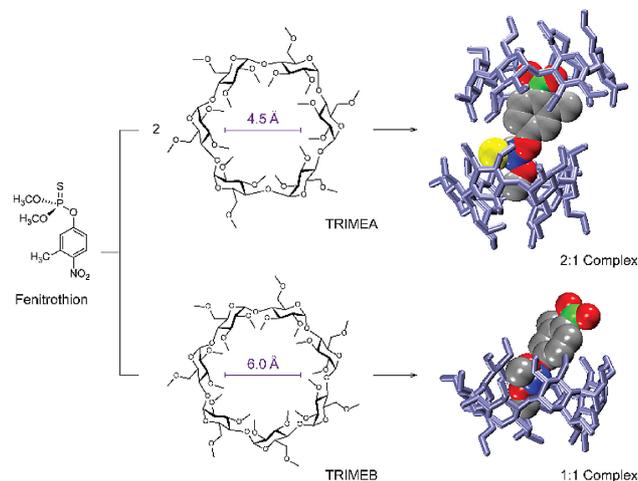


Figure 4. Schematic representation for the formation of the 2:1 and 1:1 inclusion complexes between fenitrothion and TRIMEA or TRIMEB, respectively. Hydrogen atoms were removed for clarity purposes.

phy.^[22] However the same guest molecule forms a 1:1 inclusion complex when the cavity is expanded, as in the case of permethylated β -cyclodextrin (TRIMEB, Figure 4).

As it can be noted above, a difference of *c.a.* 1.5 Å in the macrocycle's cavity diameter (volume difference of *c.a.* 88 Å³),^[23] causes important changes in the architecture of the inclusion complexes, thus leading to a drastic modification in the guest reactivity as well. The X-ray structure of the fenitrothion/TRIMEB 1:1 inclusion complex (Figure 4, bottom), shows that the thiophosphate ester group is deeply included in the cavity of the permethylated β -cyclodextrin causing a 6-fold reduction in the observed rate constant for the hydrolysis in the presence of base ($k_{\text{obs}} = 1.26$ and 0.22×10^{-3} , respectively).^[24]

It is important to highlight here that fenitrothion is an oil at room temperature, and thus, its X-ray structure was never reported before this example of inclusion complex. This fact suggest that the host-guest chemistry that takes place in the presence of TRIMEB, offers the possibility of obtaining structural information in molecules that otherwise cannot be crystallized. In addition, the discovery of this insecticide recognition process by both, native and functionalized cyclodextrins, motivated research projects targeting important applications in different areas, such as medicinal chemistry and agrochemical industry formulation of biologically active compounds, among others.

Other widely used synthetic macrocycles, with remarkable aqueous host-guest chemistry, are the cyclic oligomers of glycoluril units bridged by $2n$ methylene units, known as Cucurbit[*n*]urils (CB[*n*], with $n = 5-8$). The cyclic structure of these guests molecules, first reported by Behend in 1905,^[25] defines a hydrophobic cavity with two identical openings.^[26] CB[*n*] interesting properties were extensively explored by Kim,^[27] Day^[28] since 2000s, and reviewed recently.^[29] It was

demonstrated that the hydrophobic cavity of CB[6] is able to selectively recognize saturated and unsaturated hydrocarbons^[30] and short polypeptides of different sequence.^[31] Also their known affinity for diammonium salts allowed to find the highest binding constant ever reported for a synthetic host (CB[7]/diadamantane diammonium ion, $K_a = 7.2 \times 10^{17} \text{ M}^{-1}$, in water).^[32] This attractive nature of the CB[*n*] family motivated a large number of studies on inclusion complexes with guest molecules of diverse nature,^[33] and catalysis.^[34]

The host-guest chemistry that takes place at the macrocycle's cavities can also affect photophysical properties of emissive guest molecules. A relatively new class of synthetic macrocycles named pillar[*n*]arenes are pillar-shaped hosts first reported by Nakamoto and coworkers in 2008.^[35] Pillar[*n*]arenes are composed of repeating phenolic moieties that can be efficiently functionalized for a specific application. For instance, it has been recently reported that a ditopic pillarene can behave as a multi-responsive photochemical sensor upon solvent/thermal/pH induction of its supramolecular dimer formation.

Although the host-guest chemistry of natural and synthetic macrocycles was extensively explored during the last fifty years, the idea of incorporating them to extended structures is rather new. Covalent incorporation of these macrocycles to 2D and 3D networks offers the advantage of translating this rich and selective supramolecular chemistry to solid supports able to be mounted into different devices, and to be recycled after the recognition processes with no loss of material. Recently, and as a consequence of the above stated, an increasing interest is observed for the study of different heterogeneization strategies, and the unique chemistry that these macrocycle-containing solids, would present as opposed to the well-established solution phase behaviour.

2.2 Solid Phase Recognition

The solid phase recognition properties of various supramolecular systems is of paramount importance for industrial applications in areas such as water purification, catalysis, drug delivery, etc. For instance, in order to ensure the slow release or a homogeneous distribution of the complexed substances such as fragrances, antimicrobial agents, dyes, insecticides, the natural occurring macrocycle cyclodextrin (CD) has been incorporated to polymers and materials.^[36]

When applied in food industry, the incorporation of antimicrobial agents into food packaging has been realized through their inclusion complexes with CD bound to the polymers, and then used to fabricate these containers preserving the quality of the food and ensuring longer shelf-lives for the packaged items.^[37] In this way, the propagation of microorganisms on surface of enwrapped products is prevented. In a similar approach, CD containing polymers have been used to slowly release fragrances, protected against UV-light-induced deterioration, oxidation, etc.

An insoluble β -cyclodextrin bead polymer (BBP) was prepared and used as a mycotoxin-binder. It was demonstrated that even relatively small amounts of BBP can strongly decrease the mycotoxin content of aqueous solutions. After the first application, the polymer could be completely reactivated after elimination of the toxins from the cyclodextrin cavities by washing with a 50 v/v% ethanol-water mixture. The authors suggest that the insoluble cyclodextrin polymers prepared may be suitable tools to deplete mycotoxins from contaminated water.^[38]

Recently, copper-free Sonogashira and Heck coupling reactions in aqueous media, and mild reaction conditions, were carried out using a novel solid catalyst prepared hybridizing carbon nanotubes, cyclodextrin (CD) nanosponges (CDNS) and Pd nanoparticles (Pd-NPs). Cyclodextrin nanosponges are hyper-cross linked polymers incorporating CD, in which crystallinity and morphology can be varied by changing the ratio of CDs to cross-linking agents. CDNS have been employed as solid supports with selective recognition particular reagents which are later approached to the vicinity of encapsulated Pd-NPs.^[39] It has been demonstrated that the presence of both, CDs cavities and the 3D polymeric network cavities makes CDNS a proper candidate to arrange different molecules with diverse size, shape and polarity.^[40] In the case of this Pd-heterogeneous catalyst, aryl iodide, bromide and chloride were used as substrates for the coupling reactions and in short reaction times afforded the corresponding products in high yields. Moreover, the catalyst had negligible Pd leaching after six recycling rounds.

In addition, the host-guest interactions of native and modified CDs have been widely used to decorate the surface of inorganic nanoparticles (NPs).^[41] This decoration allowed to drastically change the properties of the NPs such as solubility, affinity for targeted substrates, aggregation behavior, etc. A clear example of the effect of this capping procedure, is the stabilization Ru NPs as hydrogenation catalyst in which a water soluble β -CD polymer allow the catalyst to remain practically unaffected upon pH change and recycling for several runs.^[42]

Clays have also been used as heterogeneous support for catalyst's immobilization, being this a well-established methodology for developing heterogeneous catalysts with simple recovery and improved reusability. In particular, halloysite nanotubes, known as Hal, are a class of natural clay minerals with the general formula of $(\text{Al}_2(\text{OH})_4\text{Si}_2\text{O}_5 \cdot 2\text{H}_2\text{O})$ and Al:Si ratio of 1:1.^[43] In Hal, the layers are arranged in a way that tetrahedral siloxane units place on the external surface and aluminol units form the inner surface with the multiple rolled layers separated by a monolayer of water. Hal are of interest due to their porosity, bio and eco-compatibility, inert nature, chemical and mechanical stability. The utility of Hal has been already demonstrated in fields such as heterogeneous catalysis, energy storage, separation, electrical and optical applications, waste water treatment, among others. The Hal surface functionalization has the potential to widen its applications and can be achieved by using cyclodextrins.^[44] Based on

known CD properties, Hal-CD hybrids are used as phase transfer agents, template or capping agents, and, in the specific case of ternary hybrid system containing Hal, CD and polyacrylamide (Hal-P-CD), as solid supports for catalytically active species such as Pd-NPs.^[45] The catalytic activity of Pd@Hal-P-CD was evaluated in Sonogashira C–C coupling reactions and Heck reactions, demonstrating synergistic effects between polyacrylamide and CD and negligible Pd-NPs leaching by ICP-AES analysis.

Similar results were obtained immobilizing Pd-NPs with another ternary hybrid system combining halloysite nanotubes (HNTs), cyclodextrin nanospheres (CDNS), and graphitic carbon nitride (gC_3N_4) to form Pd@HNTs-CDNS- gC_3N_4 . Since gC_3N_4 is a metal-free polymeric semiconductor, its incorporation to the composite allowed to perform ligand and copper-free Sonogashira and Heck couplings in aqueous media (Figure 5).^[46] It was postulated that in this hybrid system the presence of CDNS, form inclusion complexes with substrates and bring them close to the catalytic active sites accelerating the reaction rate, while gC_3N_4 could also suppress the Pd leaching.

Another example of solid phase recognition is provided by a type of broken symmetry objects named *Janus Particles* (JPs). These structured nano-/microobjects, in which molecular interactions are superimposed on particle surfaces or aggregates of particles (e.g., colloidal molecules) through shape anisotropy or localized attractive spots. JPs are unique because they provide asymmetry, and therefore, two or more different recognition sites coalesce in the same discrete particle.^[47] Currently, JPs attract a lot of attention due to the potential applications derived from the tunability of their properties which can be modulated by system design thus imparting drastical differences and directionality within a single particle.

Many examples of JPs have been reported during the last five years, among them, some made use of the macrocycle's recognition properties to produce the particles. For instance,

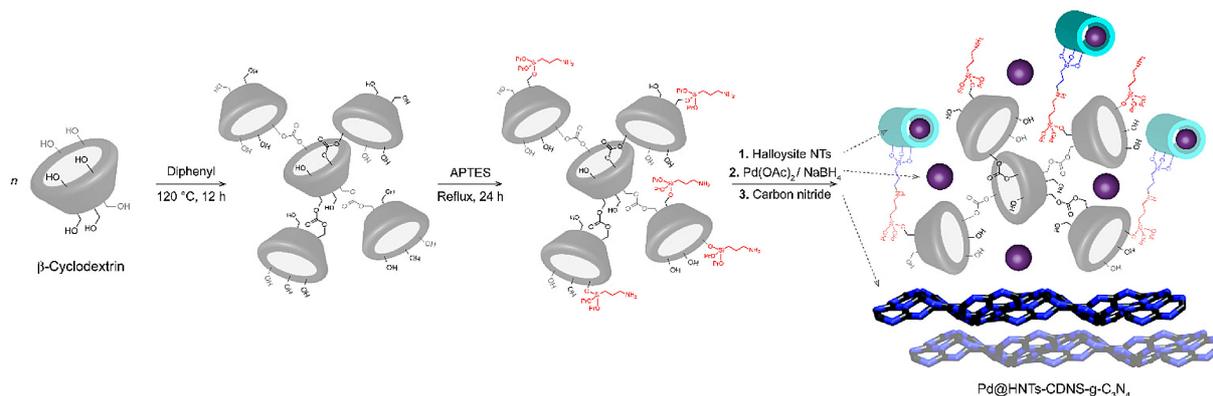


Figure 5. Stepwise synthesis and schematic representation of the product, in cyan: Hal nanotubes, in blue and black: graphitic carbon nitride, in purple: Pd nanoparticles, in grey: modified CD. Adapted from Figure S1, in ref. 46. Synthetic strategy for the Pd@HNTs-CDNS- gC_3N_4 composite.

Ravoo *et al.* recently reported the synthesis of light-responsive colloidal JPs that can be controlled by an external magnetic field. In this case, the particles were prepared by post-modification using sandwich micro-contact printing.^[48] Along this work, the authors could demonstrate that host-guest interaction of CDs are a versatile binding motif for constructing mesoscopic self-assemblies. In this particular example, ca. 10 nm magnetite nanoparticles, functionalized with per-6-deoxy-per(carboxylpropyl)thio- β -cyclodextrin (CD-MNPs), were used as supramolecular magnetic glue to connect the alternating JPs in aqueous solution. Indeed, the multivalent host-guest interaction between arylazopyrazole located on the caps of the microparticles, and the CDs on the magnetite nanoparticles, resulted in the spontaneous formation of chains consisting mostly of two to four *Janus* microparticles (Figure 6).

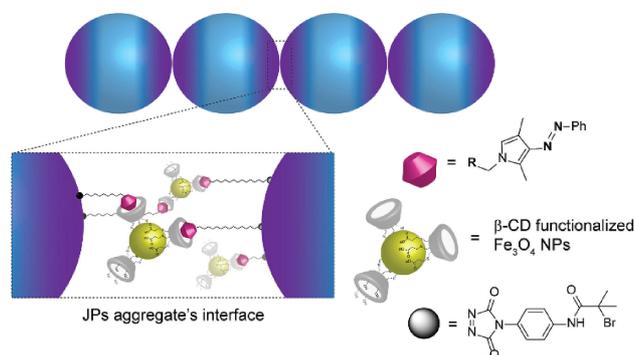


Figure 6. Schematic representation *Janus Particle's* (JPs) aggregates, driven by an interfacial arrangement of supramolecular interactions (adaptation from Figure 1, ref. 48). The figure inset shows a magnification of this interface and the key components for this arrangement.

As summarized above, the use of modified cyclodextrin led to the formation of a self-assembled and highly stable linear particle oligomers, which can be manipulated through an external magnetic field to be assembled or disassembled due to the influence of light.

In the examples so far revised, CD macrocycles have been incorporated to solid supports in order to take advantage of their host-guest chemistry. This strategy led to interesting materials such as biocide packaging, complex heterogeneous catalysts, and self-assembled microparticles, among others. Nevertheless, the heterogeneization of the recognition properties can be achieved not only by CDs, but also by other type of hosts. For example, it was demonstrated that cucurbit[7]uril (CB[7]), can be used to decorate poly(lactic acid) (PLA) and poly(lactic-*co*-glycolactic) acid (PLGA) nanoparticles.^[49] This CB[7] addition provides to the particles with specific recognition sites for the loading of secondary drugs such as oxaliplatin, turning this nanoparticles into a biocompatible and versatile drug delivery platform.

One of the challenges of integrating macrocycles to solid materials, is to obtain materials in which the macrocycle's cavities remain available after assembling the structure. In many of the revised examples, the host-guest chemistry provided by the presence of macrocycles is employed to prepare the structures, and therefore the cavities are no longer available for further solid phase recognition. This is the case in supramolecular polymers,^[50] or the JPs described above, in which the cavities of the macrocycles already interacting with guest molecules to maintain the solid structure. In addition, solid materials incorporating macrocycles in which the host-guest chemistry of the cavity is not employed for the aggregation process, very often present limited access to those free cavities (*i.e.* non porous polymers in which the diffusion of guest molecules can only happen in the surface of the particles^[51]). Recently, it was demonstrated that an efficient strategy to enhance the access to the incorporated macrocycles is to increase the rigidity of the structure, thus creating pores through which the guest molecules can easily diffuse to reach those cavities.

Dichtel and co-workers,^[52] have shown that the copolymerization of β -cyclodextrin (β -CD) and 2,3,5,6-tetrafluoroterephthalonitrile in the presence of K_2CO_3 lead to mesoporous polymers (*ca.* Brunauer–Emmett–Teller (BET) = 35 to 260 $m^2 g^{-1}$), with β -CD covalently incorporated in their structure (Figure 7). The importance of achieving porosity, and concomitantly access to the macrocycle's cavity, is clear when comparing the rate of water-pollutant sequestration. These porous CD polymers (P-CD-Ps) have adsorption rate constants between 15 to 200 times larger for different organic micropollutants compared to activated carbons or non-porous CD containing polymers.

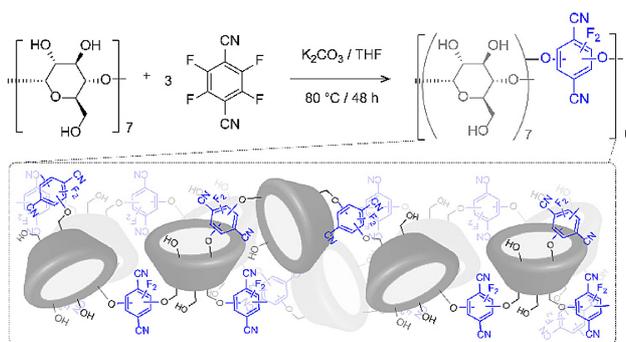


Figure 7. Representation for the β -CD and 2,3,5,6-tetrafluoroterephthalonitrile copolymerization reaction and the mesoporous polymer obtained, which covalently incorporates the macrocycles with available cavities for further host-guest chemistry realization. Adapted from Figure 1, ref. 52.

2.3 Incorporation of Macrocycles to MOF Extended Structures

As mentioned in the introduction of this review, MOFs pore environments can be carefully customized by chemical functionalization in order to specifically recognize a particular guest molecule.^[53] For instance, chiral pore environments of MOF-520 were used to anchor and solve the absolute configuration of stereocenters present in different guest molecules.^[54] In addition, chiral induction of dopants has been employed to prepare Eu-MOFs with two different pore recognition properties. In this example the authors demonstrated that the chiral enriched pore's environments incorporated to mixed-matrix membranes (MMMs), can be used to achieve enantioselective permeation.^[55]

Besides intrinsic pore design to achieve selective recognition of guests, a second level of hierarchy is achieved in MOFs by incorporating macrocycles. Examples of this strategy have been reviewed recently,^[56] where the authors highlight the access to two levels of porosity: the intrinsic pores of the material, and the macrocycle cavity. Based on our previous comments, this second level of porosity also provides a way of heterogenizing the rich host-guest chemistry of useful hosts such as CD, CB, rotaxanes, etc. In the majority of reported cases, MOF crystallinity and high porosity ensure that most of macrocycle's cavities are accessible to targeted guest molecules. However, there are some examples of macrocycles at MOFs in which the cavities participate in the MOF formation and, as in the general case of supramolecular polymers, they are no longer available for further recognition interactions.^[57]

So far, there has been mainly two different strategies to incorporate macrocycles into MOF extended structures: *i*) *covalent incorporation of macrocycles to MOF organic struts* (pre-synthetic), and *ii*) *the use macrocycles as organic struts* (Figure 8). Both strategies are applied depending on the macrocycle behaviour under the MOF synthetic conditions. Often, due to the coordination capabilities of macrocycles (or

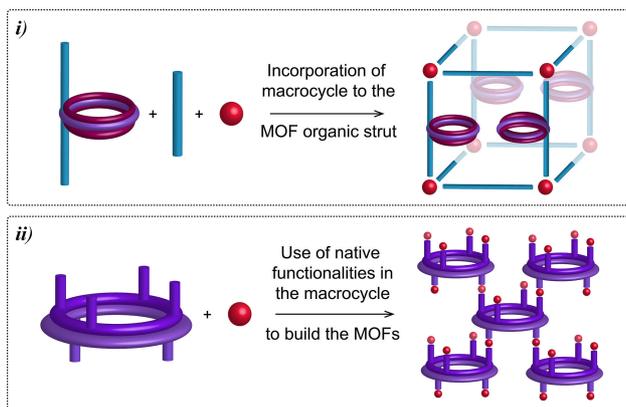


Figure 8. Schematic representation of strategies employed to achieve covalent incorporation of macrocycles to MOFs. *i)* Organic strut modification to incorporate the macrocycles pre-synthetically, and *ii)* use of macrocycles as organic struts.

other present functionalities in the struts), they cannot be incorporated pre-synthetically as they will prevent the MOF crystallization to happen.^[58]

It has been shown that simple self-assembly of synthetic macrocycles can form porous structures.^[59] The synthesis of cucurbit[6]uril (CB[6]) in the presence of HCl led to a crystalline structure for this macrocycle. The crystallographic analysis of the structure in this case, revealed a self-assembled 3D network joined by a strong C–H...O bonds between the carbonyl groups at the opening of the macrocycle and their CH or CH₂ groups. This assembly crystallizes forming 1D channels/pores having an aperture of *ca.* 6 Å in diameter,

filled with water molecules in the as-prepared material. Although this is a 3D supramolecular framework, it presents permanent porosity, featuring a BET = 210 m² g⁻¹ upon activation (water molecules removal).

Besides its permanent porosity this does not formally represent an example of macrocycle containing MOF, as their building units are not connected by strong bonds but rather supramolecular interactions. Even this aggregate showed permanent porosity, conditions affecting the H-bond network will affect the framework structure, and therefore, their permanent porosity.

Traditionally, carboxylate-metal clusters have been the most widely used secondary building units (SBUs) in MOF construction. In 2009, Yaghi, Stoddart and coworkers, reported one of the early examples of a MOF covalently incorporating macrocyclics and their use as recognition modules.^[60] The construction of the so called MOF-1001 was achieved by the covalent binding of crown ether receptors to the traditional linear ditopic organic struts to build an archetypical MOF-5 cubic structure (Figure 9).^[61] This approach, depicted as *i)* in Figure 8, allowed to prepare a MOF capable of host-guest recognition process demonstrated by the color change of the crystalline solid upon adsorption of paraquat dication (PQT²⁺) on the available crown ether rings, which correspond to the charge transfer interactions between host and guest molecules.

Another example of strategy *i)* is the synthesis of mechanically interlocked organic struts (MIMs) and their use as building units for the preparation of MOFs. An example of this approach was reported by Yaghi, Sauvage and Stoddart in 2012 (see Figure 9), with the goal of obtaining switchable components included in a MOF pore, allowing for independent dynamics without compromising the fidelity of the whole

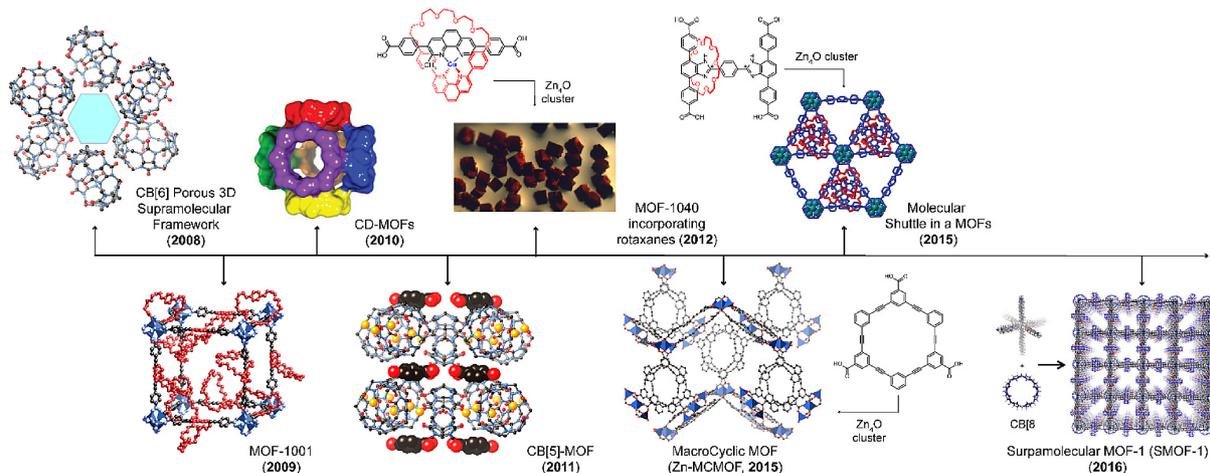


Figure 9. Time-line for the seminal contributions to the field. The figure shows different approaches to incorporate supramolecular chemistry to the pores of MOFs. From *left to right*: CB^[6] self-assembled porous structures (ref. 59), Zn.MOF incorporating crown ethers (ref. 60), MOFs made from β-cyclodextrin, reprinted with permission ref. 65a (copyright 2011, American Chemical Society) (refs. 64, 65), construction of CB^[5]-MOFs using *p*-hydroxy-benzoic acid as template (ref. 66), MOF-1040 which features mechanically interlocked molecules (MIMs, ref. 62), MCMOF constructed from shape-persistent organic struts (ref. 67), MOF including molecular shuttles in their pores (ref. 68a), and threading of CB^[8] on the supramolecular organic struts (ref. 68b).

system.^[62] Thus, copper coordinated pseudorotaxanates incorporated into linear ditopic organic struts containing phenanthroline, were reacted with $\text{Zn}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$ to obtain the three-fold interpenetrated structure of MOF-1040. The oxidation of Cu(I) to Cu(II) was monitored by EPR demonstrating the possibility to freely change the Cu oxidation state, and therefore, the geometry of the Cu complex in the pore interiors without affecting the underlying topology of the MOF. Also the possibility of demetallating this structure was confirmed by ICP-MS.

An additional example for MIMs pre-synthetically incorporated to organic struts is the synthesis of a Cu paddlewheel-MOF denoted University of Windsor Dynamic Material (UWDM-1).^[63] In this case, tetratopic organic struts featuring^[2]rotaxanes with varying sizes of crown ethers were prepared and linked to Cu-SBUs to obtain blue color MOF crystals, in which the mobility of the crown ethers in the pore of the MOF was demonstrated by ^2H solid-state NMR.

As a clear example of the approach depicted as *ii*) in Figure 8, the hydroxyl functional groups present in the cyclodextrin apertures were utilized to obtain CD-MOFs. In 2010, the groups of Yaghi and Stoddart reported the preparation of a body-centered cubic structure termed CD-MOF-1, composed of γ -CD linked by potassium ions and with the empirical formula $[(\text{C}_{48}\text{H}_{80}\text{O}_{40})(\text{KOH})_2]_n$ (see Figure 9).^[64] Later on, this methodology was extended for the preparation of CD-MOF-2 made by the coordination of γ -CD and Rb^+ cations, which was employed for the selective uptake of carbon dioxide and different solution phase extractions, taking advantage of the available CD cavities and their recognition process.^[65]

After these seminal contributions important examples of macrocycle incorporation to MOFs were reported, such as the construction of MOF using CB[5] IK and *p*-hydroxybenzoic acid featuring accessible channels.^[66] It was also demonstrated that shape-persistent macrocycles can also be used as organic struts for the construction of MOFs.^[67] In this example, a tritopic *m*-phenylene ethynylene macrocyclic ligand, with a transannular distance of 8.62 Å (Figure 9), was crystallized with Zn_4O clusters to form the so called MacroCyclic Metal Organic Framework (Zn-MCMOF) with $\text{BET} = 520 \text{ m}^2 \text{ g}^{-1}$.

Complexity and dynamics can be built in the pores of MOFs through the inclusion of molecular shuttles in the structure. This was exquisitely demonstrated by the threading of crown ethers and CB[8] in a tetratopic and hexatopic organic struts, respectively.^[68]

The revised examples to this point demonstrate that selective recognition processes typically achieved by macrocycles in solution, can be also achieved in solid state, and in particular, at the pores of MOFs. This opens the possibility for applying these MOFs in different applications such as chromatographic separations and selective capture of toxins, among others.

3. Summary

The chemistry of metal-organic frameworks (MOFs) has had an exponential growth in the last 20 years, becoming one of the trend topics and highly cited fields in Chemistry. This relatively new class of crystalline porous materials had directly impacted different areas of application such as heterogeneous catalysis, selective gas capture and storage, sensing and purification, and drug delivery among others.

The incorporation of macrocycles to solid state materials, including MOFs, extended the application of supramolecular recognition traditionally studied in solution. This host incorporation together with the MOF's high surface area and ease of functionalization, provides with a powerful design tool to challenge the preparation of the new generation of functional materials.

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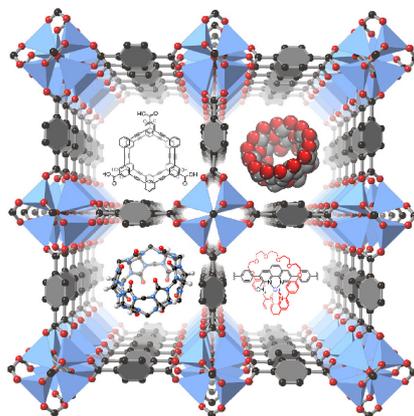
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Supramolecular Chemistry in Solid State Materials such as Metal-Organic Frameworks
