

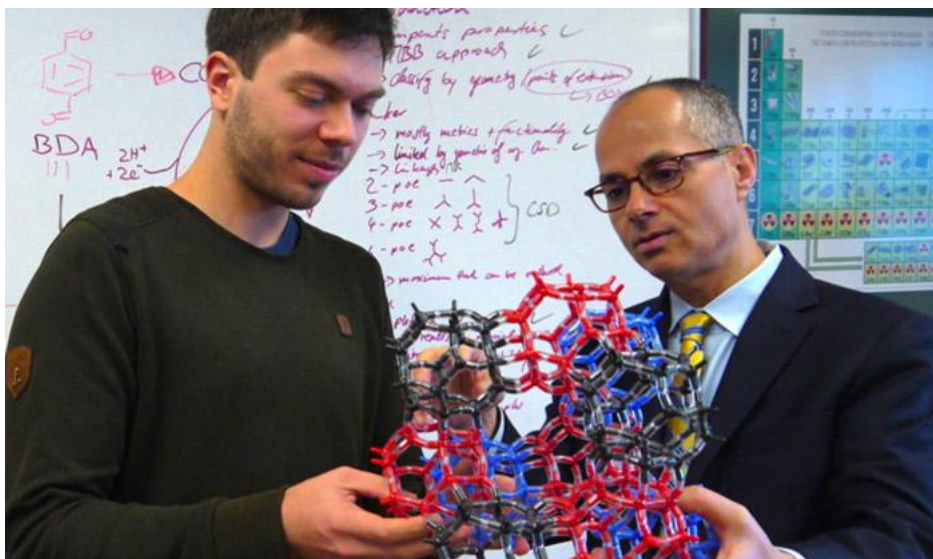
College of Chemistry (/)

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Diercks, Yaghi commemorate seminal 1916 G.N. Lewis paper

by Michael Barnes, College Editor

March 2, 2017



Berkeley chemistry professor Omar Yaghi and grad student Christian Diercks have paid homage to a critical G.N. Lewis paper a century after its publication. Writing in the March 3 issue of *Science* magazine, the authors extend Lewis's 1916 analysis in "The Atom and the Molecule" to covalent-organic frameworks.

Among the first things that all students learn in chemistry is the Lewis dot structure of atoms and molecules. Says Yaghi, "The significance of Lewis's legendary formulation of covalent bonds as dot diagrams continues to have an effect on every student and researcher of chemistry."

Lewis, the first dean of the College of Chemistry, came to UC Berkeley in 1912 and continued to work until his death in his lab in 1946. He initially published his thoughts and approach to interpreting and illustrating bonding between atoms in his landmark 1916 paper. A plaque from the ACS Division of the History of Chemistry, mounted in office of the current dean of the College of Chemistry, commemorates the paper.

Nobel Laureate Roald Hoffman noted in 1993, "Organic chemists are masterful at exercising control in zero dimensions. One subculture of organic chemists has learned to exercise control in one dimension. These are polymer chemists, the chain builders.... But in two or three dimensions, it's a synthetic wasteland."

Yaghi is a pioneer in creating porous three-dimensional molecular structures, including metal-organic frameworks (MOFs) and covalent-organic frameworks (COFs). It was his development of two- and three-dimensional COFs that converted this barren landscape into a fertile realm of discovery and extended Lewis's concepts beyond atoms and molecules to include frameworks.

In their review, Diercks and Yaghi outline the intellectual basis of designing COFs and synthesizing them as crystalline porous materials. They discuss how the ultra-high porosity of these materials can make them useful in organic catalysis, as two-dimensional electronics and as luminescent materials. In addition, these organic frameworks show promise for capturing carbon dioxide from power plants and converting it to fuels and high-value chemicals.



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March 2, 2017

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REVIEW SUMMARY

SYNTHETIC CHEMISTRY

The atom, the molecule, and the covalent organic framework

Christian S. Diercks and Omar M. Yaghi*

BACKGROUND: Just over a century ago, Gilbert N. Lewis published his seminal work “The Atom and the Molecule” on what later became known as the covalent bond. Since then, organic chemists have systematically developed synthetic methodologies for covalent molecular chemistry, and this has led to the art and science of total synthesis. Extending these organic reactions beyond the molecule to making covalently linked two- and three-dimensional (2D and 3D) organic structures has been a long-standing objective. Recently, this has been realized in the reticular synthesis of covalent organic frameworks (COFs)—extended porous structures entirely composed of light elements and held together by strong covalent bonds. COFs have robust architectures endowed by high porosity and thermal and chemical stability, which have allowed organic and inorganic reactions to be carried out on these frameworks without losing their porosity or crystallinity. This has given rise to the “chemistry of the framework,” where Lewis’ concept of the atom and the molecule is extended to the framework in which matter can be further controlled and manipulated.

ADVANCES: The ability to design COFs and to adjust their pore metrics using the principles of reticular synthesis has given rise to frameworks with ultralow densities (0.17 g cm^{-3}), high surface areas ($4210 \text{ m}^2 \text{ g}^{-1}$), large pore sizes (up to 4.7 nm), and high charge-carrier mobility ($8.1 \text{ cm}^2 \text{ V}^{-1} \text{ s}^{-1}$). The combination of adjustable pore metrics with the backbone functionalization of the framework by means of pre- and postsynthetic modification has successfully been used to tailor COFs for a plethora of applications in areas such as gas separation, energy storage, catalysis, and electronics. Recently, the union between the covalent and the mechanical bond in the context of the chemistry of the framework has resulted in the first implementation of the concept of molecular weaving. The added degrees of flexibility in woven COFs have the potential to combine dynamics with resilience in solids. At present, this methodology is being applied to the design of frameworks with different modes of entanglement, such as interpenetration of 2D and 3D networks or formation of extended structures based on the interlocking of discrete (0D) rings to make molecular chain mail.

OUTLOOK: Historically, the field of chemistry has flourished as our ability to control matter on the molecular level has improved. COFs are the first examples of controlling the covalent bond beyond molecules and demonstrate how this control results in expansion of the scope of covalent organic solids and their properties. Organic chemists study the chemistry of new organic molecules, and similarly we expect the study of the basic structure and reactivity of

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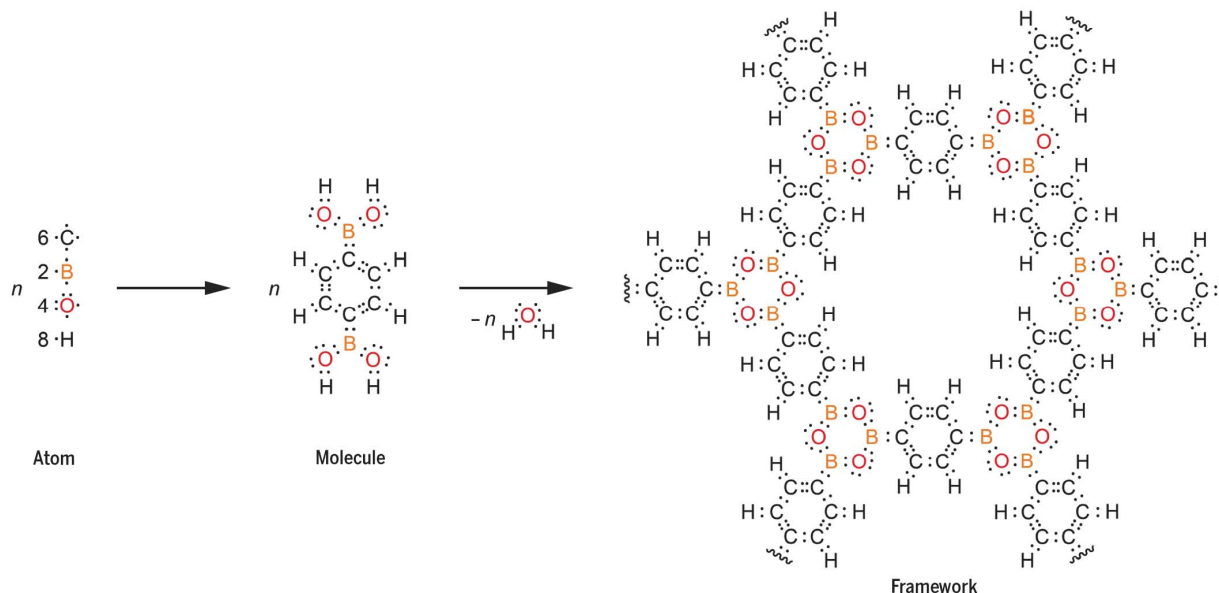
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COFs and the investigation of their properties to continue. However, this emerging chemistry of the framework is already pointing to several new directions, such as the ability

to work with atomically well-defined interfaces. The traditional view that interfaces are 2D is not strictly applicable in the framework, where substrates form boundaries with 2D as well as 3D frameworks, which are atomically and metrically well defined. By virtue of the framework chemistry outlined in this contribution, such 3D interfaces can be chemically functionalized and metrically altered. In this way, heterogeneously arranged functionalities can be arranged within well-defined distances to operate in a manner akin to active sites of enzymes. The extension of Lewis’ original concept from atoms to molecules and now to covalent organic frameworks adds pore space into the realm of synthetic chemists’ ability to control matter. ■

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The atom, the molecule, and the covalent organic framework. Since the discussion of strong chemical interactions between atoms by Gilbert N. Lewis in 1916, covalent organic chemistry has progressed from discrete molecules to porous covalent organic frameworks such as COF-1, the first COF, illustrated here in the traditional Lewis dot structure.



REVIEW

SYNTHETIC CHEMISTRY

The atom, the molecule, and the covalent organic framework

Christian S. Diercks and Omar M. Yaghi*

Just over a century ago, Lewis published his seminal work on what became known as the covalent bond, which has since occupied a central role in the theory of making organic molecules. With the advent of covalent organic frameworks (COFs), the chemistry of the covalent bond was extended to two- and three-dimensional frameworks. Here, organic molecules are linked by covalent bonds to yield crystalline, porous COFs from light elements (boron, carbon, nitrogen, oxygen, and silicon) that are characterized by high architectural and chemical robustness. This discovery paved the way for carrying out chemistry on frameworks without losing their porosity or crystallinity, and in turn achieving designed properties in materials. The recent union of the covalent and the mechanical bond in the COF provides the opportunity for making woven structures that incorporate flexibility and dynamics into frameworks.

Gilbert N. Lewis' seminal work on chemical bonding, "The Atom and the Molecule," introduced the concept of what would become known as the covalent bond (1). He outlined a conceptual approach for addressing the fundamental questions of how atoms can be joined to make molecules, and how to describe the bonding of the atoms within these molecules and its impact on reactivity and molecular properties. Chemists have since exploited these concepts in their efforts to master the craft of synthesizing specific molecules of varying structure and complexity, which has led to the art and science of total synthesis (2, 3). Today, the precision with which organic molecules can be functionalized and their geometry controlled has matured to the point of rational synthesis.

However, such methods are not useful in controlling how molecules link together by covalent bonds to design extended structures. Such a reticulation process must be carried out under synthetic conditions that maintain the integrity of the molecule while allowing for microscopic reversibility in order to afford ordered, crystalline products. The chemistry of such extended organic solids remained largely undeveloped throughout the 20th century, most likely because reticulating molecules formed through covalent bonds were amorphous materials, thus precluding their structural characterization by x-ray crystallography. This was especially true for two-dimensional (2D) and 3D covalent organic solids, as highlighted by an article published in 1993 (4): "Or-

ganic chemists are masterful at exercising control in zero dimensions. One subculture of organic chemists has learned to exercise control in one dimension. These are polymer chemists, the chain builders. ... But in two or three dimensions, it's a synthetic wasteland."

The challenge of making 2D and 3D covalent organic solids was addressed in the discovery and development of covalent organic frameworks (COFs), where extended structures are made by stitching organic molecules together through strong covalent bonds in a process termed reticular synthesis (5–7). The molecular units used in reticulation possess the functionality necessary to form specific linkages in a chemically and geometrically defined fashion to construct the framework. In the synthesis of crystalline COFs and the application of precision organic chemistry to their structures without losing crystallinity, covalent bonds create robustness and directionality (necessary to control the spatial orientation of the building blocks), achieve well-defined crystalline solids, and ultimately introduce variations and complexity. In the context of Lewis' original work, COFs become the natural extension of the molecule. In a manner akin to how molecules are geometric constructs of atoms, COFs are geometric constructs of molecules linked by covalent bonds. Furthermore, just as the molecule positions atoms, COFs position molecules in a specific spatial orientation to encompass space into which the reactivity of the atom and the molecule are revealed and used in ways not possible in discrete molecules. Here, we highlight the theoretical basis for designing the framework and show how the covalent backbone allows for organic chemistry to be exercised beyond the molecule. We also describe the emerging union of the covalent and the mechanical bond in the framework and demonstrate how this leads to frameworks of mechanical entanglements, including interlocking and weaving

of threads, with added degrees of freedom, dynamics, and flexibility.

A chronology of chemistry beyond molecules

Since Lewis' conceptual paper on the covalent bond, the systematic development of synthetic organic methodologies has led to several important advances in chemistry, a few of which are depicted in Fig. 1. The discovery of large macromolecular structures (1D polymers) opened up the field of organic performance materials (8). Another major milestone was the retrosynthesis of complex organic natural products and their use in the pharmaceutical industry (2). Improvements in synthetic methodology resulted in the realization of elaborate molecules, but the problem remained of how to get these molecules to assemble in a regular fashion into more complex, functional systems. One solution was supramolecular chemistry, in which noncovalent interactions guide molecular recognition processes, such as selective binding in the original crown ethers and cryptands (9, 10). Molecular recognition proved useful not only for selective binding of guest molecules, but also as a means of templating the synthesis of molecular macrocycles and cages (11), and led to the templated synthesis of catenanes—molecules held together by mechanical interlocking of molecular rings (12). The manner in which mechanical bonds are introduced into frameworks is discussed below.

The knowledge of specific interactions can furthermore be used for the design of systems that undergo self-organization—that is, well-defined extended supramolecular architectures produced by virtue of having selective weak interactions built into their molecular components (13, 14). However, such supramolecular assemblies are difficult to modify without losing their structure, because (i) modification of the building blocks will alter the interactions between the constituents and thus lead to different assemblies, (ii) performing chemistry on these assemblies is difficult without destroying their structural integrity, and (iii) the thermal and chemical robustness of their structure puts a limit on their applications. Although nature uses self-organization to assemble complex architectures such as those of enzymes or DNA, these assemblies generally have a 1D covalent backbone that plays a crucial role in maintaining their overall structural integrity. Thus, it is essential to develop strategies that align molecular building blocks not by weak interactions, but rather by those based on strong covalent interactions in a geometrically well-defined manner. When this goal is achieved, it becomes possible to introduce functionalities and complexity within the backbone of such covalent frameworks.

Inspired by the underlying dynamic processes that form the basis for supramolecular chemistry, extensive research has been devoted to the formation of covalent bonds under thermodynamic control (15, 16). This area has received widespread attention during the past decade, as such control would facilitate the formation of interlocking

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molecules, shape-persistent organic cage compounds, and other complex molecular architectures (17–20). In 2005, the strategy of forming covalent bonds reversibly, which provides for error correction, was used to reticulate molecular building blocks into extended, crystalline covalent organic frameworks (6). The advantages of reticular synthesis were apparent: The strong bonding allowed for the removal of residual solvent molecules from these organic solids, resulting in highly porous crystalline 2D and 3D frameworks (Fig. 1). The architectural and chemical robustness of these COFs meant that precision organic and inorganic chemistry could be carried out on a COF while maintaining its crystallinity, thus commencing the development of the chemistry of the framework. The same chemistry used to make the COF backbone can be deployed along with metal-ion templates to make metallated COFs, which upon demetallation yield woven framework structures with unusual elasticity (21) (Fig. 1). Because COFs maintain their crystallinity and their structure remains well-defined upon carrying out reactions with the precision of molecular chemistry, they constitute a true extension of the covalent bond beyond the molecule (22). Although we focus on the transition from molecular chemistry to the framework and illustrate the latter by discussion of covalent organic frameworks, the concepts that will be introduced in going from the atom and the molecule to the framework are also applicable to other extended structures, such as metal-organic frameworks.

Conceptual basis of covalent organic frameworks

Organic chemistry offers an extensive library of molecules that can be synthesized to serve as building blocks in the construction of COFs. A framework, whether a COF or any other covalent extended structure, is composed entirely of two distinct components: linkers (building units) and linkages (bonds formed between those units upon reticulation). Thus, the organic synthesis of COFs starts with the synthesis of the building blocks and ends with the reticulation of these building blocks by stitching them together in a designed way into an extended framework. The general approach for the reticular synthesis of COFs is illustrated in Fig. 2. In step 1, a target network topology is identified and deconstructed into its fundamental geometric units (23). In step 2, these constituents are evaluated according to their points of extension (connectivity) and their geometry (e.g., tetrahedral versus square planar for the connectivity of four). In step 3, equivalents of these geometric units are found in molecules and then deployed as linkers. Large rigid polyatomic molecules such as 1,3,5-tris(4-aminophenyl)benzene are often used as linkers because they predispose the linking functionality in a specific geometry; connecting such large molecules yields porous structures with accessible space, low density, and high internal surface area. Furthermore, these properties play a critical role in providing access and space to address the molecules that are now locked in position at precise locations through-

out the framework. Specific parts of these molecules can function as the sites of reactivity in catalytic transformations, binding of gases for applications in storage and separations, and modulation of electronic properties affecting the entire framework.

In terms of the underlying net, the geometry of the molecular building block is represented as a vertex figure to be linked into what is described as the augmented net. From the large number of possible structures that could result, which ones are likely to form? For example, linking of tetrahedra may result in one or more structures from a large number of possible structures (as many as several million). Among this vast structure space, which will form? It has been the thesis of reticular synthesis that the most symmetric structures are the most likely to form when high-symmetry building blocks are used. Indeed, this has been found to be the case for a large majority of reported structures (24–26). The judicious choice of building blocks and the design of angles between the building blocks' points of extension is a way to direct the synthesis to a target structure that may not be the most symmetric possibility.

When constructing a COF based on a desired topology, it is preferable to use rigid and well-defined building blocks that remain unaltered throughout the construction process. In step 4, the COF is produced through the formation of strong covalent bonds between the linkers. Typically, synthetic conditions must first be identified for crystalline products to be obtained. By balancing

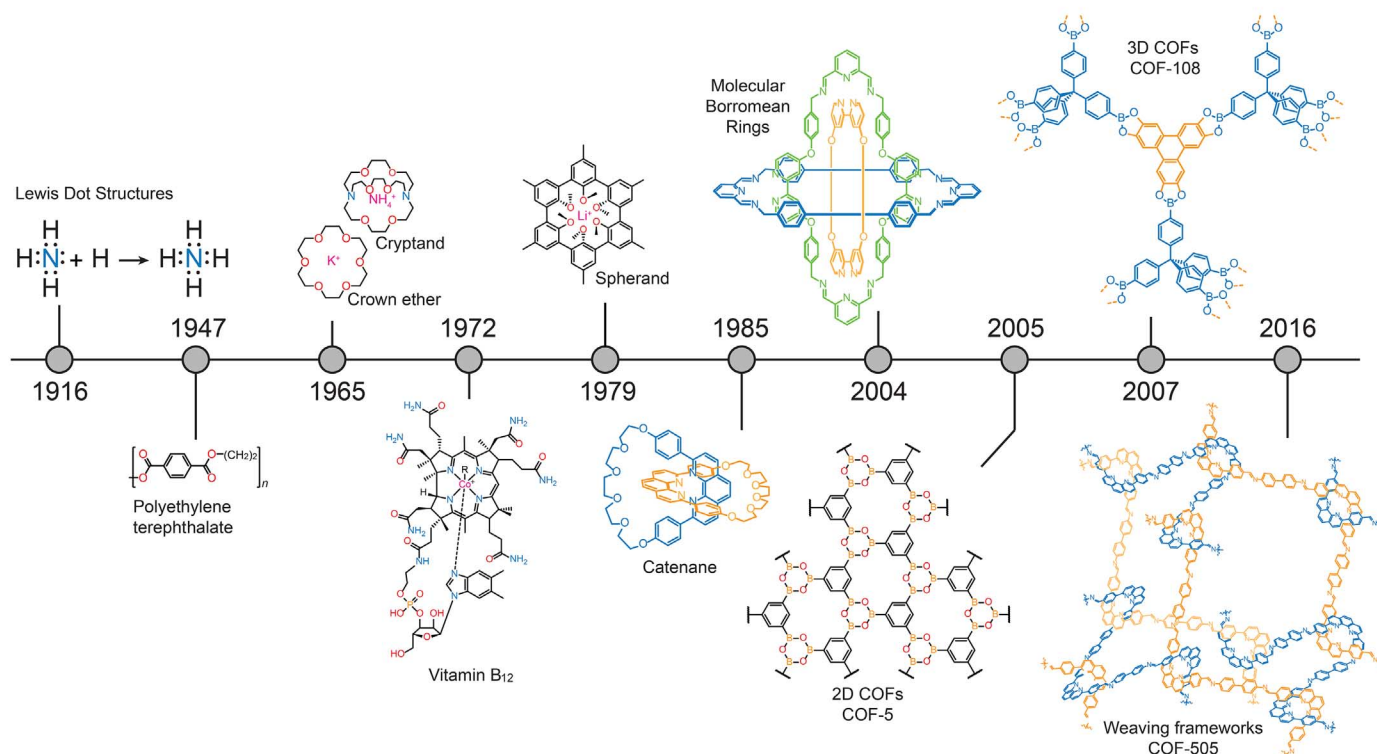


Fig. 1. Chronology of advances from Lewis' original concept of the covalent bond. Shown are important advances in synthetic organic chemistry that have led to the development of 2D and 3D covalent organic frameworks (COFs) and, more recently, weaving frameworks.

the thermodynamics (microscopic reversibility of the linkages between the building units) and the kinetics (appropriate rate of the reaction) of the COF-forming reaction, crystalline 2D and 3D frameworks can be made (6, 7). Finally, in step 5, if the product is single-crystalline in nature, the material is characterized by x-ray or electron diffraction techniques. When suitable single crystals cannot be achieved, powder x-ray diffraction (PXRD) is used to evaluate whether the targeted structure has been successfully obtained.

Indeed, it is often the practice that a PXRD pattern is calculated for the expected structure and compared to the experimentally acquired data. Such comparison, which facilitates the determination of the structure, would not be possible without knowledge of the targeted framework, so COFs are illustrative examples of true design in making solid-state materials.

At present, more than 100 COF structures have been reported, with at least twice that number in derivatives. All of these structures were prepared

following the concepts outlined above and illustrated in Fig. 2. Table 1 summarizes the connectivity, vertex figure, resulting topology, and first reported example of various COFs. Thus far, all known COFs are based on a total of eight common topologies. In the case of 2D COFs, there are five possible topologies for which the vertices are connected by one kind of edge (fig. S1) (23–27). Four of these have already been made as COFs (Table 1 and figs. S2 to S5) (6, 28–30). For 3D topologies, there are many more possibilities, but only four of these have been reported in COFs (Table 1 and figs. S6 to S10) (7, 31, 32).

COFs of varying linker connectivity, linker size, and character of the linkages have been reported (Fig. 3). In general, the reactions that are used in the formation of COFs can be classified in terms of the linkages they form. These are (i) B–O (boroxine, boronate ester, borosilicate, and spiroborate) (6, 33, 34); (ii) C=N (imine, hydrazone, and squaraine) (31, 35, 36); (iii) C=N_(aromatic) (triazine and phenazine) (37, 38); (iv) C=C (alkene) (39); (v) C–N (β-ketoenamine, imide, and amide) (40–42); and (vi) B=N (borazine) (43) or N=N (azodioxy) (44) (fig. S11). The chemical stability of the resulting linkages follows the expected corresponding trends known in molecular organic chemistry; for example, the phenazine- and β-ketoenamine-based COFs maintain their structure and porosity in strong acids and bases, respectively. Molecular reactions for selected linkages are shown in Fig. 3 to highlight the importance of carrying out the reaction under reversible conditions, which is generally achieved by solvothermal synthesis at elevated temperatures, typically up to 200°C with acid or base catalysts. In molecular organic chemistry, most reactions are kinetically controlled and thus prone to errors that require postsynthetic purification. This procedure is not possible in framework chemistry because the products of the reaction are insoluble. In essence, the challenge that was overcome by reticulating building blocks through covalent bonds to make COFs is to achieve, in a single step, the formation of the product as both phase-pure and crystalline.

Framework reactions and properties

To design materials tailored for specific properties (Table 2), specific functionalities need to be present in the COF backbone. Functionalization of COFs can be carried out (i) presynthetically by functionalizing the molecular building blocks (45), or (ii) through postsynthetic modification of the preformed framework itself (46, 47). The question of whether a functionality should be introduced pre- or postsynthetically depends on whether this functional group is compatible with the COF-forming reaction. Not all chemical functionalities can be used in COF formation—for example, the covalent bonds may be too strong to be sufficiently reversible—so some functionalities must be added into existing frameworks. Fortunately, the open and accessible pores of the organic backbone allow for precise functionalization of the structures' interior space.

One example that illustrates the versatility and the scope of the functionalization of COFs is

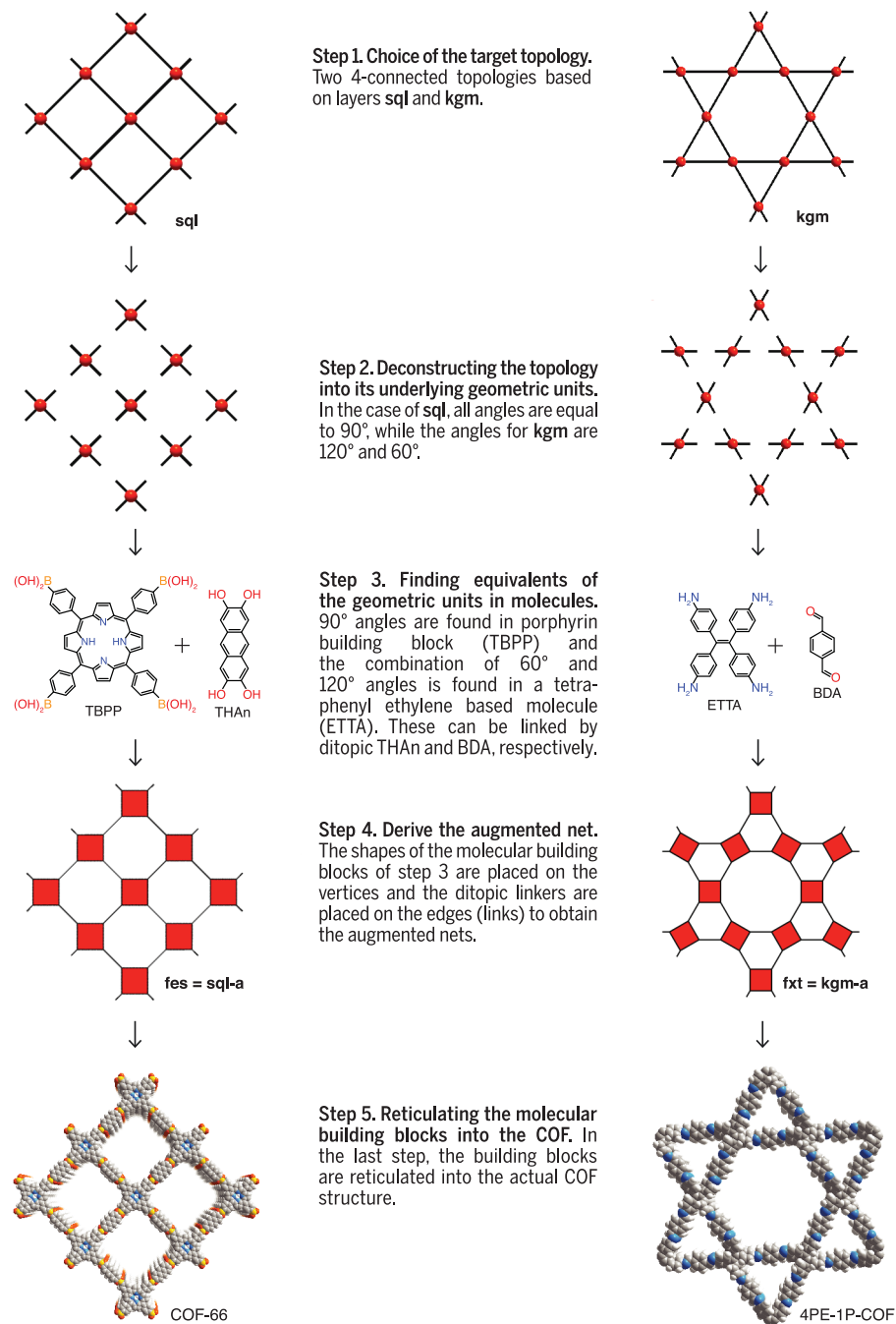


Fig. 2. Topological design and reticular synthesis of COFs. Shown are the steps involved in choosing the topology, deconstructing it into its fundamental geometric units, finding the equivalents of these in molecules, and eventually reticulating them into the desired COF.

COF-366 (Fig. 4) (48). Initially, this layered 2D material received much attention because of its high charge-carrier mobility. Both pre- and post-synthetic modification have been used to tune COF-366 for vastly different applications (Table 2). Pore functionalization of COF-366 was carried out for the optimization of its CO₂ uptake. In this context, the pore was decorated with varying amounts of hydroxyl or carboxyl groups to increase the interactions of the framework with CO₂ (49). Because COF-366 is reticulated by the formation of imine bond linkages, the hydroxyl groups are tolerated during the framework formation and can thus be presynthetically installed on the organic building blocks. However, carboxyl groups were integrated postsynthetically by ring-opening reactions of hydroxyl groups on the linker with maleic anhydride. This synthetic strategy was essential, as presynthetic installation of carboxyl groups would interfere with the reaction conditions used to make the COF. A different strategy for the introduction of functional groups onto the COF-366 backbone is the use of the copper(I)-catalyzed click reaction. Azides were installed on the linker and then postsynthetically reacted with alkynes bearing hydroxyl, carboxyl, or amino functional groups. Both strategies resulted in substantially improved CO₂ uptake capacities (50).

COF-366 has also been used in enantioselective catalysis, where copper(I)-catalyzed click chemistry was applied to covalently incorporate chiral proline moieties within the framework's pores. The resulting material showed high activity in catalytic enantioselective Michael additions (51). Interestingly, immobilizing catalytic units on this well-defined COF made this transformation amenable to continuous flow conditions. Recently, metallation of the porphyrin building block resulted in a cobalt-functionalized derivative, COF-366-Co (52). This framework and other derivatives showed high activity and selectivity for the electrocatalytic reduction of CO₂ to CO in water with improved performance (factor of 26 increase in activity) over the molecular catalyst. This example shows how the intrinsic properties of the structure (high charge-carrier mobility and permanent porosity) in combination with the functionalization of the framework (metallation with cobalt) result in a highly tunable material, leading to higher performance. In sum, modification of COFs with a large number of different functionalities has been used to adjust pore metrics (45), to stabilize the framework itself (53, 54), to improve interactions with gases (49, 50, 55), for applications in energy storage (40), and for a manifold of catalytic transformations as summarized in Table 2 (47, 51, 52, 56, 57). These modifications of COFs can be done without losing crystallinity or porosity, giving credence to the notion of frameworks being used in chemical transformations as molecules (58).

The union of the covalent and mechanical bonds in the framework

An intriguing feature of biological macromolecules such as nucleic acids and proteins is that they have a primary structure formed by strong

Table 1. Important nets in the chemistry of covalent organic frameworks. If there are p kinds of vertex, q kinds of edge (link), r kinds of ring (faces), and s kinds of tile, the transitivity is defined as $pqrs$.

Coordination number	Net symbol	Vertex figure	Transitivity	First report (ref.)
2D topologies				
3	hcb	Triangle	111	2005 (6)
4	sql	Square	111	2011 (28)
4	kgm	Square	112	2014 (29)
6	hxl	Hexagon	111	2015 (30)
3,6	kgd	Triangle, hexagon	211	—
3D topologies				
4	dia	Tetrahedron	1111	2009 (31)
3,4	ctn	Triangle, tetrahedron	2122	2007 (7)
3,4	bor	Triangle, tetrahedron	2122	2007 (7)
4,4	pts	Square, tetrahedron	2122	2016 (32)

Table 2. Selected properties of covalent organic frameworks. Lowest and highest reported values for the indicated property are listed. S_{BET}, Brunauer-Emmett-Teller surface area.

Property	Compound	Achieved value or year of report	Ref.
Lowest reported value			
Density	COF-108	0.17 g cm ⁻³	(7)
Highest reported value			
Pore aperture	HHTP-DPB COF	4.7 nm	(71)
S _{BET} for 3D COFs	COF-103	4210 m ² g ⁻¹	(7)
S _{BET} for 2D COFs	TPB-DMTP-COF	2015 m ² g ⁻¹	(72)
Excess CO ₂ uptake (273 K)	[HO] _{50%} -H ₂ P-COF	174 mg g ⁻¹	(34)
Proton conductivity (373 K)	TPB-DMTP-COF	7.0 × 10 ⁻⁴ S	(73)
Charge mobility	COF-366	8.1 cm ² V ⁻¹ s ⁻¹	(48)
Earliest report			
Capacitance	DAAQ-TFP COF	2013	(40)
Heterogeneous catalysis	Pd/COF-LZU1	2011	(47)
Electrocatalysis	COF-366-Co	2015	(52)
Photocatalysis	TFPT-COF	2014	(57)
Postsynthetic modification	COF-LZU1	2011	(47)
Oriented thin films	COF-5	2011	(74)
Photoluminescence	TP-COF	2008	(75)
Photoconduction	TP-COF	2009	(76)

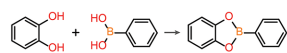
covalent bonds, whereas the secondary and tertiary structure—those parts that are responsible for the spatial orientation of the system—typically arise from noncovalent interactions, such as hydrogen bonding. Large-amplitude structural motions can occur repeatedly and reversibly without loss of structural integrity. It would be desirable to achieve this dynamic resilience in solid-state materials, especially in the chemistry of the framework; practical applications often put materials under cycles of stress and strain that can lead to fatigue and damage. However, to date, there has been no advance in developing a viable conceptual approach to tackle this issue. Supramolecular assemblies suffer from structural degradation upon large motions of their building blocks with respect

to each other. Traditional covalent organic frameworks suffer from a common problem in covalent extended solids: When they are flexible, they ultimately fail. Large-amplitude motions in covalently linked frameworks lead to breaking of bonds, which results in defects and consequently structural collapse. One strategy used to enable motions on the molecular level is mechanical interlocking, in which two molecules are mechanically entangled in such a manner that they cannot part company without the breaking of at least one covalent bond.

To appreciate the power of combining the covalent and the mechanical bonds, it is helpful to consider the evolution of the latter. The first successful synthesis of a molecule held together by

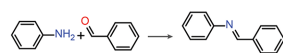
COF linkages

B–O bond formation



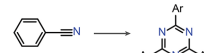
boronate ester, boroxine, borosilicate, spiroborate

C=N bond formation



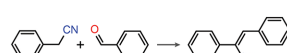
imine, hydrazone, azine, squaraine, oxazole

C=N(Ar) bond formation



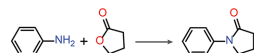
triazine, phenazine

C=C bond formation

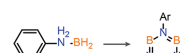


alkene

C–N bond formation

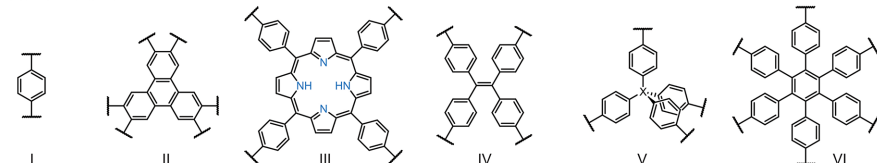
imide, β -ketoenamine, amide

B=N bond formation



borazine

COF linkers



|C=N(Ar) CTF-1 (hcb)

|B–O COF-5 (hcb)

|C=N COF-366 (sql)

|C=N 4PE-1P-COF (kgm)

|C–N PI-COF-5 (dia)

|C=N HPB-COF (hxl)

|B–O COF-108 (bor)

|B–O COF-102 (ctn)

COF structures

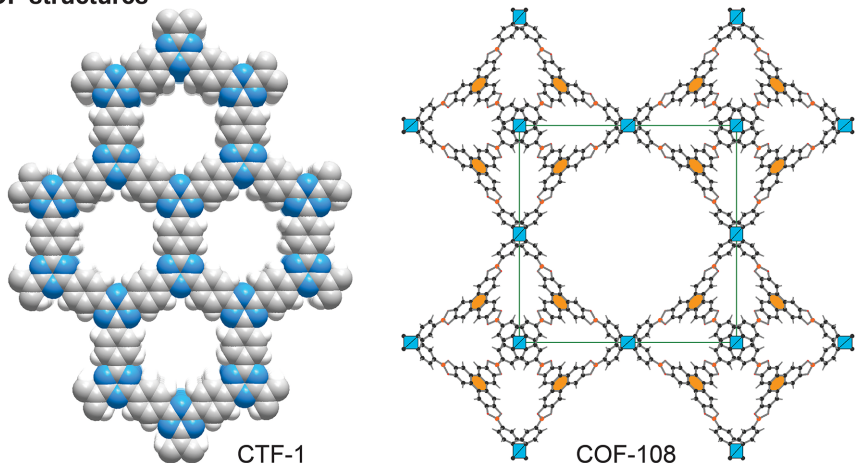


Fig. 3. Linkages, linkers, and framework structures. COFs are composed of two main components: linkages and linkers. Shown are examples of various linkages and linkers that have been used for the synthesis of COFs, along with the combination of building units used to make COF structures.

mechanical bonds was reported in 1960 (59, 60). Statistical interlocking of rings resulted in the formation of the desired product with <1% yield. The directed formation of catenanes was reported in 1964 in a multistep organic synthesis (61). Mechanically interlocked molecules remained elusive species until the field was transformed in 1983 by the introduction of metal-ion templating to direct the crossover points inherent in all molecular links (62). Subsequently, many different

kinds of template were introduced, including donor-acceptor interactions (63), hydrogen bonding (64), single-halogen bonding (65), and radical interactions (66).

The next prominent leap forward was the transition from kinetically controlled reactions for the ring-closing step toward dynamic covalent chemistry. In early examples of catenanes, the yields were generally low and the reactions had to be carried out in dilute solutions over ex-

tended periods of time to favor the formation of the envisioned macrocycles over polymeric byproducts. Dynamic covalent chemistry favors the formation of the thermodynamic product, which allows for the possibility of making catenanes much more effectively through careful design of the starting materials. In combination with specific templates, the formation of much more elaborate interlocking molecules has been reported (17, 20, 67). However, the extension of these techniques for mechanically interlocked frameworks has yet to be achieved.

On the molecular level, ring closing can be used to realize a mechanical bond. In the solid state, infinite chains can be held together by mechanical entanglement, reminiscent of the way that threads are held together in woven fabric. We note that this is only possible in the context of extended structures such as the framework: The mechanical extension of the material is never great enough to pull out a single thread, so despite the lack of true interlocking, the material retains its woven character. We have recently expanded the concept of the mechanical bond with the introduction of what has been termed “molecular weaving.” Here, 1D threads, composed of covalently linked molecules, are designed to intersect at regular intervals by means of metal templates. The copper centers that are used to template the formation of the framework are topologically independent of the weaving within the resulting framework, termed COF-505 (Fig. 1) (21), and can be reversibly removed and subsequently reinserted. In a manner akin to peptide structures, the primary structure of the woven compound arises from strong covalent bonds, but the 3D secondary structure is created by weak interactions, much like how nature designs flexible functional macromolecular architectures. Upon removal of the copper centers, the mechanical properties can be altered, as evidenced by the change in the Young’s modulus of the woven framework by an order of magnitude. The elasticity can be reversed by remetallation with the copper ions while retaining the crystallinity of the framework. We attribute the reversibility and flexibility of the woven framework to the ability of the threads to carry out large motions without unzipping the structure. This weaving approach demonstrates how covalent bonds within the threads and mechanical bonds between the threads can function together to make flexible yet resilient materials.

Entanglements of frameworks of different dimensionality

We expect four distinct modes of entanglements in the chemistry of the framework. The entanglement of 3D structures and 2D structures is referred to as interpenetration [also termed polycatenation (68)]. We define mechanically linked 1D chains as weaving, and mechanical entanglement of discrete (0D) rings as interlocking (Fig. 5). Thus far, only 3D interpenetrating frameworks and 1D weaving structures (COF-505) have been reported in the field of COF chemistry. Controlling the mechanical entanglement in the solid

state is not only of fundamental interest; it also may lead to more flexible, dynamic materials that would be important synthetic targets. We anticipate that the dynamics of entangled materials will directly correlate with the dimensionality of their respective constituents.

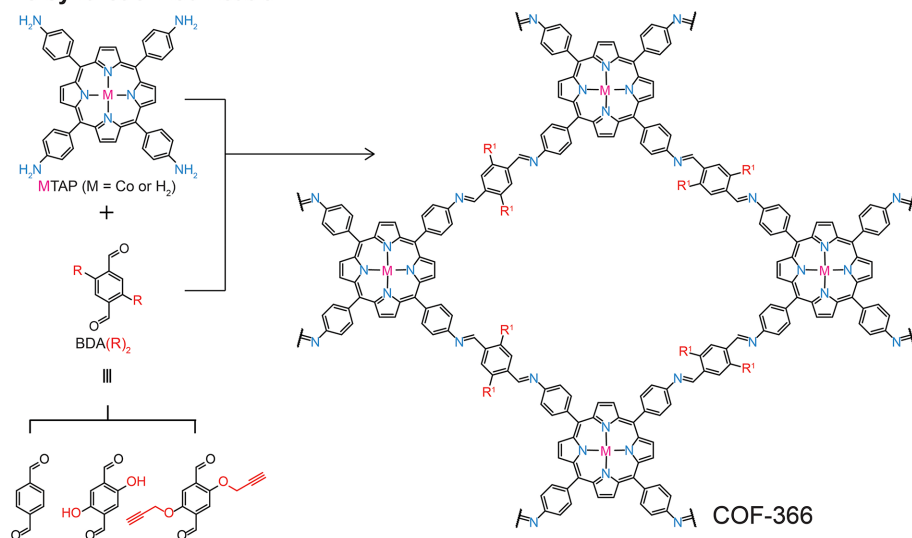
In the case of 3D and 2D interpenetration, the potential for motion of the fragments with respect to each other is limited because the entire extended 3D or 2D frameworks would have to be dislocated. The formation of extended structures based on weaving or interlocking motifs has long been sought, as the many degrees of freedom of their building units allow for enormous spatial deviations to take place without deteriorating the overall structure. Interpenetration of 3D and 2D frameworks is well established in other classes of solid-state materials such as metal-organic frameworks, coordination polymers, or inorganic extended structures (68, 69). In most of these cases, the formation of the interpenetrated structures occurs randomly even though in some examples specific modes of interpenetration can be targeted. The first example of interpenetration in COFs also occurred by chance: Diamond nets are known to interpenetrate, and the first example of a COF with this topology has a five-fold interpenetrating structure (31). The degree of interpenetration can be controlled to a certain extent, depending on the length of the linker (70).

The other three modes of interpenetration are much less likely to form. The 2D sheets of COFs tend to orient coplanar to maximize van der Waals interactions between the layers. Similarly, 1D chains favor parallel arrangements, and there is no thermodynamic driving force for 0D rings to interlock. We anticipate the reticular synthesis of COFs to provide a directed and general approach to access materials with these different modes of entanglement. As illustrated in Fig. 5, this goal can be achieved with a strategy similar to that used for the generation of woven structures. A target compound is chosen and the topology of the framework is determined. The crossover points in the structure can be templated with molecular building blocks that already encode this information. Although interpenetrating structures of 2D layers are already known for other material classes, the synthesis of extended structures composed of 1D chains and 0D rings that are held together exclusively by mechanical bonds had not been reported. As mentioned earlier, the synthesis of a woven COF has recently been realized, but the formation of an extended structure held together by interlocking rings is yet to be achieved. This synthetic target is a long-standing challenge in the field of mechanically interlocking molecules. We believe that the reticular chemistry of COFs and the union of the mechanical and the covalent bond, as illustrated by the woven COF-505, point to how ring interlocking frameworks can be made.

Future prospects

The reticular synthesis of covalent organic frameworks is still at an early stage of its development. Currently, the field is mostly driven by potential

Pre-synthetic modification



Post-synthetic modification

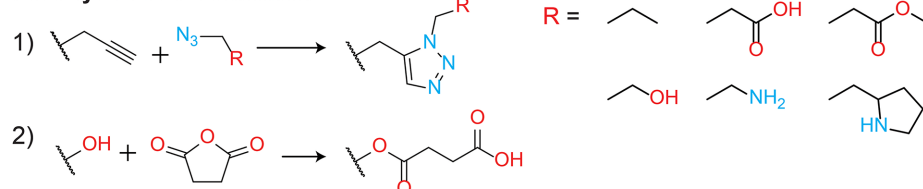


Fig. 4. Precise introduction of functionality onto the COF backbone. Organic and inorganic functionalization of COFs by presynthetic and postsynthetic modification, as exemplified by COF-366, can lead to materials with tailored properties for applications in areas such as CO₂ capture, enantioselective catalysis, and electrocatalysis.

Modes of entanglement

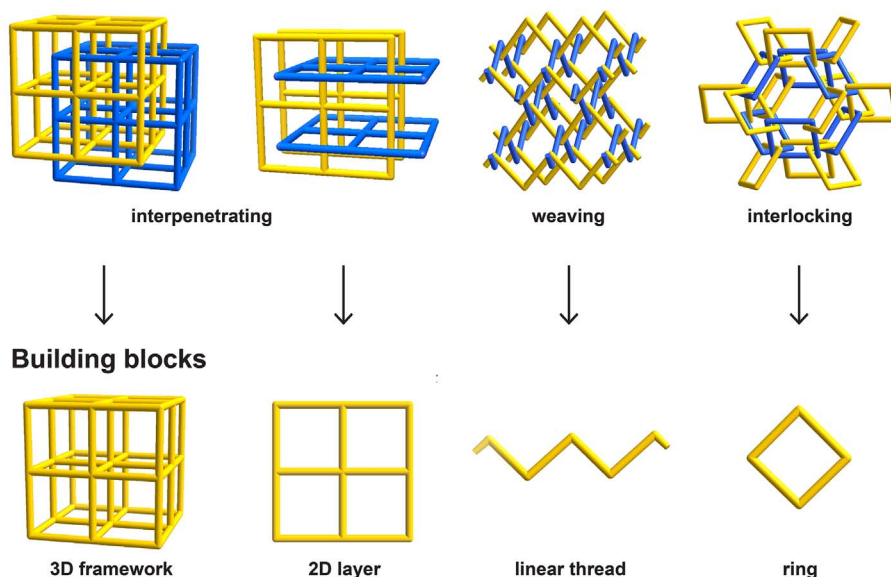


Fig. 5. Four modes of entanglement in frameworks. The entanglement of 3D or 2D structures is referred to as interpenetrating, the formation of mechanical bonds between 1D chains is referred to as weaving, and interlocking structures are obtained by the entanglement of 0D rings.

future applications, often at the expense of developing the basic chemistry of the framework or its design principles. However, there is no doubt that the ability to build frameworks by covalently stitching together organic molecules will continue to be important because of the precision of this process and the control being exercised in placing molecules in specific geometric and spatial arrangements. The power of this practice is already leading to unusual materials and properties with a wide range of applications in catalysis, gas storage and separations, and electronics. We anticipate that this will continue to be important well into the future because historically, the field of chemistry has flourished as our skills to control matter on the atomic and molecular level have advanced. In the present context, the progression from atoms and molecules to assemblies and, more recently, to frameworks is an intellectually engaging and rewarding endeavor. At this juncture, the question is how these exquisite designs combined with our well-honed synthetic skills will bring new understanding of problems in chemistry. It is possible to provide a glimpse into the impact that the chemistry of the framework will make on various challenging topics such as interfaces, molecular complexity, and hierarchical structures, to mention a few. We see at least three features of this chemistry that will make a difference in our understanding of such important topics. We examine interfaces and use this subject as an illustrative example.

First, the chemistry of the framework gives precise definition to the underlying atomic arrangement of the structure. We think of interfaces as boundaries between different phases of matter or materials. In the framework, the interface is the boundary defining the framework-substrate interaction, which, unlike many other interfaces, is well defined and can be altered nearly at will without changing the integrity of the backbone structure. This provides flexibility to craft the boundary between the substrate molecule and the framework to affect a highly specific process. For example, one can envision functionalizing the boundary so that it mimics the active site of an enzyme for chemical transformations to be carried out in a stable framework, thus foregoing the fragility of the enzyme.

Second, the framework intrinsically imparts complexity within order to the geometry of the internal surface. Not only is the composition of the binding sites being controlled, but this is also accomplished in the confines of a well-defined, ordered geometry and with precise metrics describing where the binding sites are located on the internal surface of the framework. Because the backbone remains unchanged when substrates bind, the distance between these binding sites is fixed, and it is possible to dial in and apportion the active sites in the exact amount and distribution necessary. Such structures make it possible for substrates to sample a wide range of binding site coverages on the surface.

Third, the traditional view of the surface as being 2D, which means that it can be approached freely by an incoming substrate to produce an

interface, is no longer true in the framework. Here, the surface can be 2D, but more important, it can also assume various different 3D surface geometries, each of which may have a hierarchical arrangement of pores capable of confining the substrates to interacting with binding sites of a specific size and geometry. The ability to have a network interface within a 3D framework construct that can be chemically modified, its pore shape and size systematically varied, and the electronic and steric character of the designed binding sites crafted to promote a specific binding, constitutes the emergence of shape-selective, size-selective, and electronically selective surfaces and interfaces.

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SUPPLEMENTARY MATERIALS

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Figs. S1 to S11

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The atom, the molecule, and the covalent organic framework
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Editor's Summary

A framework for molecular assembly

Covalent molecular frameworks are crystalline microporous materials assembled from organic molecules through strong covalent bonds in a process termed reticular synthesis. Diercks and Yaghi review developments in this area, noting the parallels between framework assembly and the covalent assembly of atoms into molecules, as described just over a century ago by Lewis. Emerging challenges include functionalization of existing frameworks and the creation of flexible materials through the design of woven structures.

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