Tessellated multiporous two-dimensional covalent organic frameworks

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Abstract | In the past decade, covalent organic frameworks (COFs) have emerged as a new class of highly ordered crystalline organic porous polymers. They have attracted tremendous research interest because of their unique structures and potential applications in gas storage and separation, energy storage, catalysis and optoelectronic materials development. Although the skeletons and pore structures of COFs are customizable through judicious selection of chemical building blocks, COF materials have been mainly limited to uniform pore structures with homogeneous pore environments. Two-dimensional COFs with complex multipore structures are largely unexplored, perhaps owing to the challenges that are inherent in designing selective syntheses. Simple tessellation has been remarkably successful in the preparation of regular 2D COFs, but building multiporous systems requires the aid of mathematical design. In this Perspective, we discuss four different approaches to tessellated 2D COFS with a focus on the mathematical rules for their application. A comparison of these strategies should provide guidance to those designing new applications of COF materials.

Regular arrangement of closed shapes to completely cover a plane, without overlaps and with no gaps, is called tessellation. Such patterns are frequently observed in our everyday surroundings, from animal skins to modern architecture. The Dutch artist M. C. Escher frequently used tessellation — among other mathematical principles — in his art and has often been a source of inspiration for those interested in geometry, including many mathematicians, scientists and crystallographers. Chemists have also practised simple tessellations in their unique way by building beautifully designed 2D frameworks composed of repeating patterns of molecular building units. These 2D polymers extend in the *z* dimension to form bulk materials, which have shown intriguing applications, such as gas storage and separation[1–3], heterogeneous catalysis[4–6], optoelectronic materials[7–9] and ion-conducting materials[10–12].

The capability of producing highly ordered open-framework materials with precise molecular-level control of structures has been one of the most important and exciting recent advances in chemistry and materials science. In 2005, Yaghi and co-workers reported the first example of crystalline covalent organic frameworks (COFs) composed of repeating benzene rings linked by boroxine[13]. Since then, many COFs with regular uniporous tessellations have been described[14–18]. Crystalline polymer networks of predetermined ordered structures with high stability, diverse chemical functionalities, tunable metrics and porosity can be obtained starting from predesigned rigid molecular building blocks through dynamic covalent bond formation. Although the skeletons and pore structures can be customized by selecting the chemical building blocks, these COF materials have largely been limited to uniform pore structures. Two-dimensional COFs with complex multipore structures remain largely unexplored, and this lack of diversity has impeded the continued development of COFs.

In contrast to unipore COFs with regular tessellation arrangements, multipore COFs with structural and functional heterogeneity would have an extraordinary range of potential applications, such as control of semiconductor electron-transport properties by judicious electron–hole doping, or simultaneous uptake and transportation of different guests that otherwise cannot coexist (for example, acid and base, or oxidant and reductant pairs)[19]. It has been demonstrated that introduction of structural heterogeneity can tailor the characteristics of hierarchical porous polymers[20–22]. Each component of a nanostructured material with heterogeneity can deliver specific functions, which can synergistically contribute to their unique physical properties, distinct from those of unifunctional materials. Recently, defect-engineered metal–organic frameworks (MOFs) have attracted great attention: in these materials, various defect sites (for example, linker and/or metal vacancies) can be intentionally introduced by using combinations of distinct types of organic linkers or metal ions[23–29]. Although such defect sites are in most cases randomly distributed within ordered frameworks, they can affect mass-transport pathways through the pores, alter electronic or optical properties by creating electronic coupling states through metal vacancies, or generate complex active sites for catalysis. So far, the development of COFs with intentionally designed structural heterogeneity has lagged well behind that of hierarchical porous polymers and MOFs. Uniporous 2D COFs have been constructed without any overt application of mathematical design principles. Here, we propose that such mathematical design is the key to extending the scope towards more complex tessellations. We present forward-looking discussions on the design and synthesis of 2D COFs with multipore structures and heterogeneous pore environments from a mathematical point of view. Different tessellation topologies and various building-block design strategies including desymmetrized-vertex, angle-specific-vertex, shape-persistent-patch, and mixed-linker or mixed-vertex design strategies are discussed.

Tessellations by polygons

From a mathematical point of view, the formation of 2D COFs by connection of judiciously selected building blocks as vertices and edges into an extended plane is a tessellation process. If a planar framework with periodicity is to be created by using only one type of monomer as vertices, the design of this monomer must satisfy the critical mathematical requirement of tessellation. An infinite number of distinct tessellations are possible when patterns that have different angles at each vertex are combined. However, if we use regular polygons (all sides and angles of the polygon equal) to explore tessellations, the number of possible tessellations is vastly reduced. If we apply a further restriction that the same polygons appear at each vertex in the same order when numbered either clockwise or anticlockwise, there are only three regular and eight semi-regular tessellations, known as the Archimedean tilings (FIG. 1). These regular and semi-regular tessellations are made of identical vertices and regular polygons, with adjacent polygons sharing one full edge. To achieve a viable tessellation, an angle sum of 360° around each vertex of the polygons involved is required. Once these basic tessellation concepts are understood, we can easily derive more complex tessellations consisting of irregular polygons by transforming polygons used in regular or semi-regular tessellations.

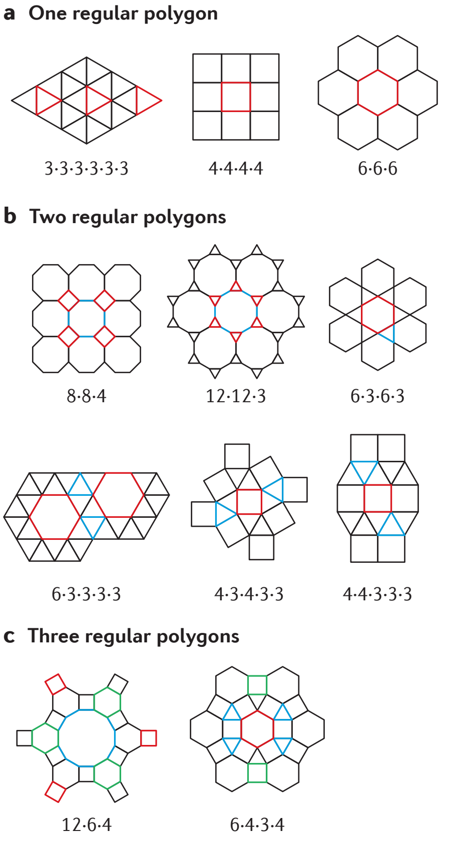

Figure 1 | **Regular and semi-regular tessellations. a** | Regular tessellations made of one type of polygon. **b, c** |Semi-regular tessellations made of two or more polygons, also called Archimedean tessellations. A tessellation is named by looking at the vertex and counting the sides of all the shapes that meet at the vertex. For example, a regular tessellation of triangles is named 3·3·3·3·3·3, as there are six polygons around the vertex and each has three sides.

For 2D COFs consisting of more than one type of polygonal pore, their possible monomer structures can be designed based on a mathematical understanding of these tessellation rules. Monomers that serve as vertices must satisfy the critical geometry requirement in order to be tessellated in a plane and form relatively strain-free COFs. Monomers with mismatching geometry with the targeted tessellation patterns would be unable to produce ordered 2D COFs. Therefore, beside the optimum reaction conditions (for example, solvent and temperature), it is critical to design monomers with favourable geometry to form COFs with periodicity. Because the bond angles and compound geometries that are available to chemists are relatively limited, tessellation patterns that can be realized by chemists are also rather limited. Relatively simple regular or semi-regular tessellations and their variations would be a good starting point, which can be easily realized using available vertex and edge components.

Desymmetrized-vertex design

In the past decade, striking advances have been made in the assembly of 2D COFs with the regular tessellations denoted 3·3·3·3·3·3, 4·4·4·4 and 6·6·6 (FIG. 1a), by using highly symmetrical multitopic molecules with connection-site angles of 60°, 90° or 120° as vertices[14–18]. From these familiar systems, can we develop COFs with more complex tessellation patterns made of two or more different polygons? What will happen if we reduce the symmetry of highly symmetrical equilateral and equiangular vertices of regular tessellations? Desymmetrization of a highly symmetric vertex has significant but so far largely unexplored effects on the tessellation patterns of 2D COFs. Simply elongating one or multiple arms of an originally symmetrical vertex will result in tessellations consisting of two or more similar but non-equilateral polygons. For example, tessellation 6·6·6′, in which two different hexagons are around a vertex, can be obtained when the highly symmetric (D_{3h} symmetry) vertex is transformed to one with lower C_{2v} symmetry (FIG. 2a). Similarly, the symmetry of the vertices can be further reduced to the completely asymmetric vertex **4**. In this case, triple-pore 2D COFs consisting of three different hexagons could be obtained (FIG. 2a). Such a desymmetrized-vertex design strategy could provide opportunities for the development of previously inaccessible multipore COFs. One such example has been successfully demonstrated[30]: in this approach, C_{2v} symmetric 5-(4-formylphenyl)isophthalaldehyde (**2**) or 5-((4-formylphenyl)ethylene)isophthalaldehyde (**3**) were used as tritopic vertices instead of the commonly used highly symmetric trialdehyde **1**. As the vertex building block **2** or **3** is equiangular (120°) but not equilateral, their condensation with hydrazine forms 6·6·6′ tessellated 2D COFs (for example, HP-COF-1) with two different hexagonal pores (FIG. 2b). Powder X-ray diffraction (PXRD) characterization, a computational modelling study of energy-minimized structures and pore-size distribution analysis suggest that the dual-pore structure of the resulting COFs are in an eclipsed AA stacking mode.

A potential problem with such a desymmetrized-vertex design strategy is the possibility of polymorphism owing to the multiple available connecting sequences of unsymmetrical arms. For example, as shown in FIG. 2a, there exist two possible 6·6·6′ isomers, 6·6·6′-A and 6·6·6′-B, depending on the connection patterns of long arms and short arms of **2** or **3**. When long arms connect with short arms, 6·6·6′-A forms. If long arms connect with long arms, 6·6·6′-B forms. Often, these isomers have very similar cell parameters, simulated diffraction patterns and thermodynamic stabilities, which makes unambiguous structure assignment difficult. Assignment of the structure of COFs that were obtained from **2** or **3** was made on the basis of the pore-size distribution analysis. However, the possibility of slightly slipped packing of layers rather than the perfectly eclipsed AA stacking pattern that was simulated, the deviation in pore-size distribution analysis and small pore-size difference between two isomers (<5 Å) create some uncertainty in this assignment. An even larger number of isomers (more than four) would arise if asymmetric compound **4** was used to form the vertices.

Polymorphism might be prevented by introducing sequence directionality into the monomer design. Each monomer or monomer segment can be functionalized with orthogonal functional groups[31,32] to provide control over the specific connection sequence. For example, orthogonal boronic ester formation and imine bond formation can be used simultaneously in one system to form sequence-specific multicomponent 2D COFs. In 2015, two groups individually developed such an approach to prepare COFs consisting of heterogeneous vertex structures[33,34]. As shown in FIG. 3a, two monomers serving as vertices are functionalized with orthogonal functional groups: monomer **5** is functionalized with amines, whereas monomer **6** (2,3,6,7,10,11-hexahydroxytriphenylene, HHTP) is functionalized with diols. Condensation of a 1:1 mixture of **5** and **6** with a bifunctional linear linker, 4-formylphenylboronic acid (FPBA, **7**), provided sequence-specific (with alternating monomers, −A−B−A−B−) multicomponent NTU-COF-2 or HHTP-FPBA-TATTA COF. In such an orthogonal reaction strategy, the monomer connection sequence is encoded in the monomer design, such that monomer A can only be connected to monomer B, with self-connection prohibited. Very recently, there has been a report of the orthogonal use of imine condensation with metal−ligand coordination to form an ordered titanium−organic hybrid framework (MOF-901). Bifunctional 4-aminobenzoic acid (**8**) forms secondary building units that further react with dialdehyde **9** to form framework MOF-901 consisting of two types of organic linkers[35] (FIG. 3b). These examples highlight the power of orthogonal dynamic chemistry in the assembly of hetero-sequenced polymer networks. It is therefore conceivable that the connection sequence of monomers or monomer segments can be programmed through elegant use of orthogonal functional groups to form 2D COFs with a specific topology.

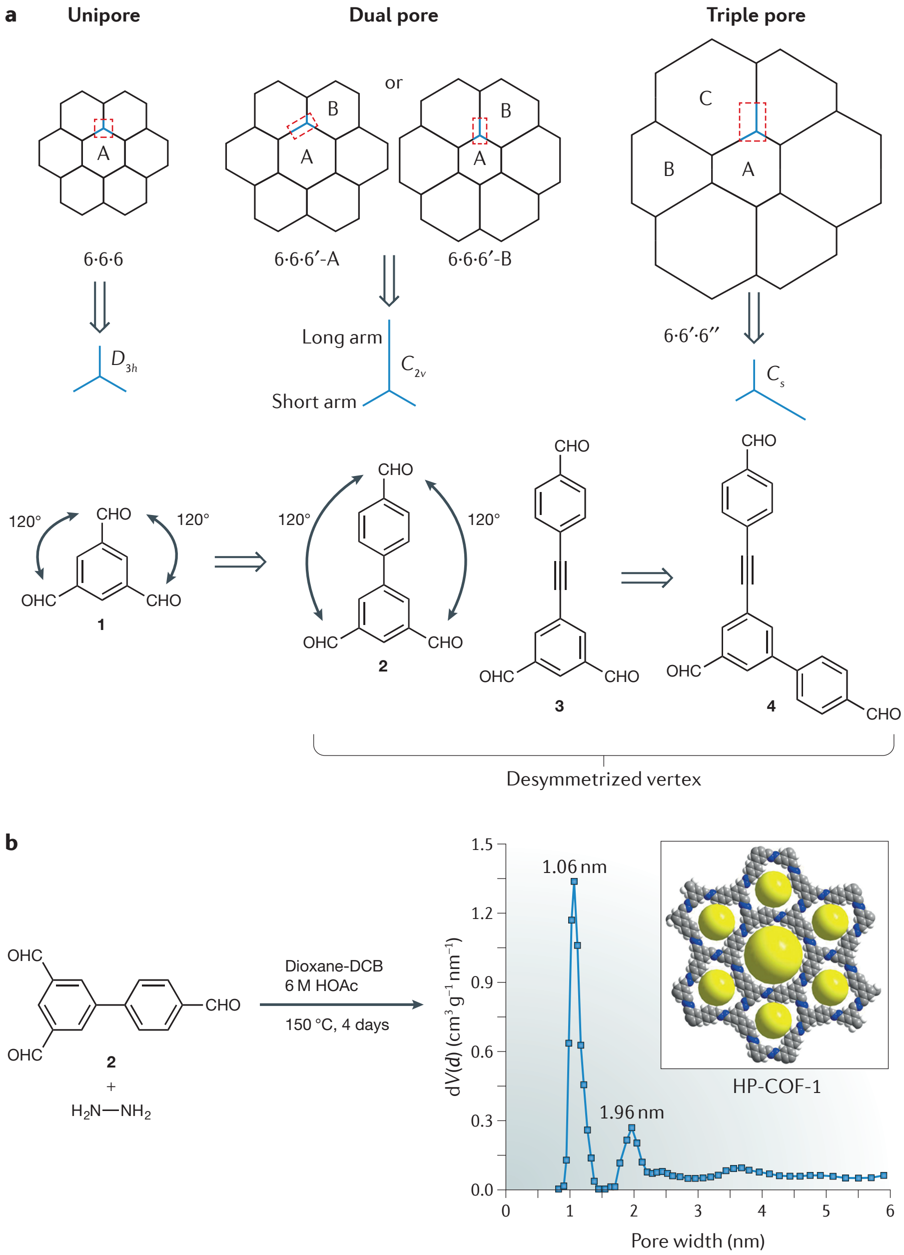

Figure 2 | **The desymmetrized-vertex design strategy. a** | Desymmetrization of a D_{3h} symmetric vertex to one with either C_{2v} or C_s symmetry would allow the formation of hexagonal dual-pore or triple-pore covalent organic framework (COF) structures. **b** | Synthesis of HP-COF-1 with dual hexagonal pores, and its pore-size distribution (where d$V(d)$ is the differential pore volume distribution). DCB, dichlorobenzene. Part **b** is adapted with permission from REF. 30, American Chemical Society.

Angle-specific vertex design

We have discussed how to generate multipore 2D COFs that are composed of the same type of polygons but in different shapes and sizes using equiangular but non-equilateral vertices. Next, we consider more complex semi-regular Archimedean tilings composed of a combination of two or more different polygons. In semi-regular tessellations, each vertex is surrounded by more than one type of regular polygon, so the vertices have to be angle-specific multitopic building blocks. For example, trihexagonal tiling (6·3·6·3), in which each vertex is surrounded by alternating regular hexagons (internal angle 120°) and triangles (internal angle 60°), requires a tetratopic vertex with 60° and 120° angles between two adjacent arms. Similarly, truncated square tiling (8·8·4), in which each vertex is surrounded by one square (internal angle 90°) and two regular octagons (internal angle 135°), requires a tritopic vertex with 90° and 135° angles between two adjacent arms (FIG. 4a). In each case, the angle sum of polygons around a vertex is 360° (120° + 60° + 120° + 60° in 6·3·6·3 and 90° + 135° + 135° in 8·8·4), which satisfies the critical requirement of tessellation. More complex snub hexagonal tiling (6·3·3·3·3), elongated triangular tiling (4·4·3·3·3) or snub square tiling (4·3·4·3·3) would need five-arm

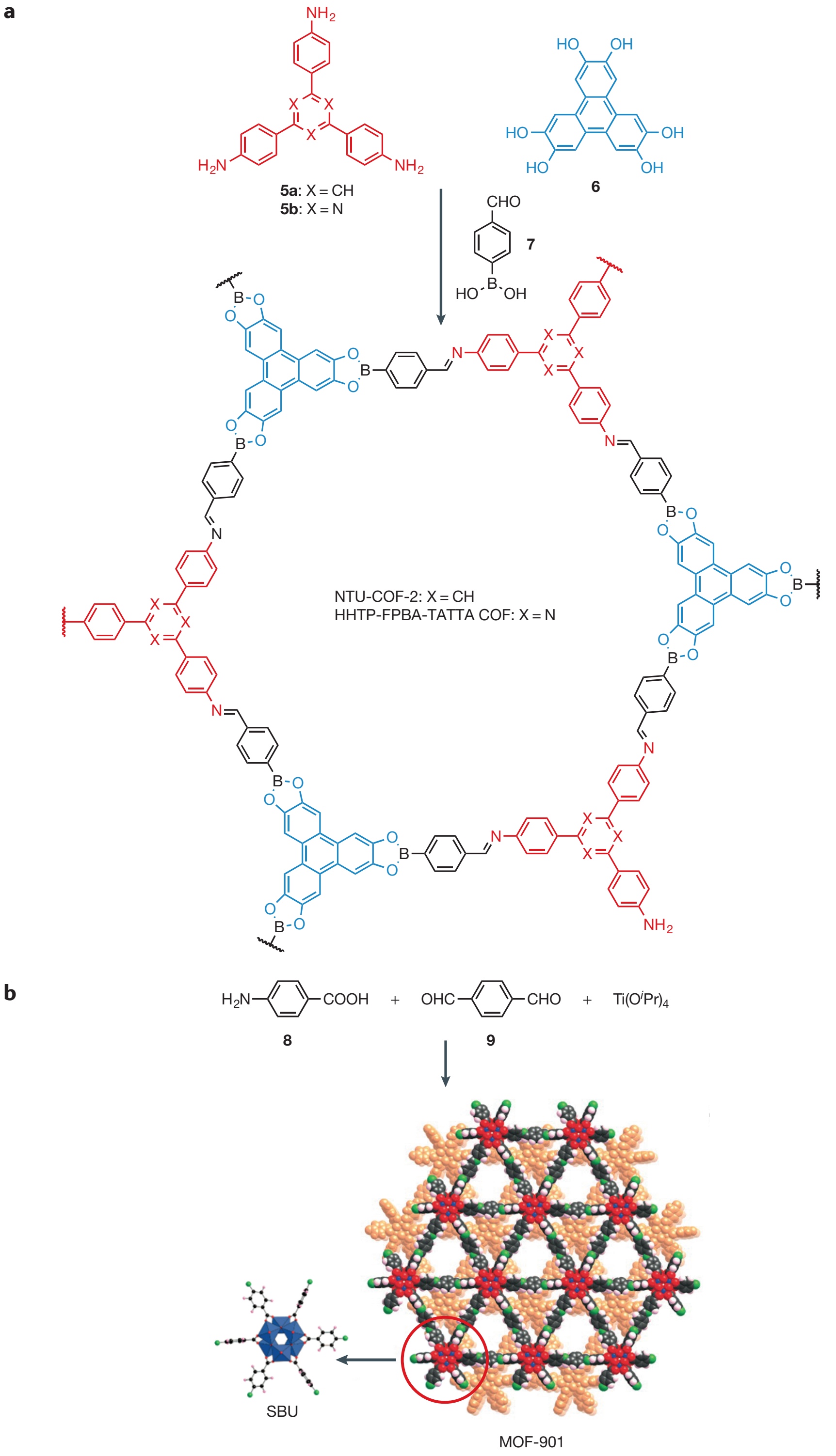

Figure 3 | **The orthogonal reaction strategy. a** | Synthesis of NTU-COF-2 and HHTP-FPBA-TATTA COF. Orthogonal imine condensation and boronic acid condensation of triamine **5**, 2,3,6,7,10,11-hexahydroxytriphenylene (HHTP, **6**), and linear linker 4-formylphenylboronic acid (FPBA, **7**) provided multicomponent covalent organic frameworks (COFs) consisting of two types of vertices. **b** | One-pot synthesis of titanium–organic framework MOF-901 using an orthogonal reaction strategy. Metal–ligand coordination of 4-aminobenzoic acid (**8**) with Ti(IV) forms hexameric amine-functionalized Ti(IV) oxo clusters, which serve as vertices and react with 1,4-phthalaldehyde (**9**) to form MOF-901 in a staggered packing mode. The orthogonality of metal–ligand coordination and imine condensation provides an interesting opportunity to introduce metal clusters into COFs. SBU, secondary building unit. Part **b** is adapted with permission from REF. 35, American Chemical Society.

vertices with specific angles between two arms. This angle-specific vertex design strategy provides an interesting way of disassembling the well-known tessellations into monomers, which would foster the monomer diversity in 2D COF synthesis. A proof of concept for such a design strategy was successfully demonstrated in 2014 (REF. 36). A D_{2h} symmetric monomer, 4,4′,4′′,4′′′-(ethene-1,1,2,2-tetrayl)-tetraaniline (**10a**), with two distinct angles (60° and 120°) between two adjacent arms was selected as the vertex (FIG. 4b). Condensation of **10a** with the C_2 symmetric linear monomer, terephthalaldehyde (**9**), in dioxane–acetic acid (1:0.1, by volume) at 120 °C for 4 days yielded a crystalline solid. Several methods, such as PXRD (FIG. 4c) or nitrogen adsorption–desorption, along with molecular mechanics calculations, were used to characterize the dual-pore structure (a 6·3·6·3 tessellation). The observed PXRD patterns closely match the simulated diffraction patterns of 6·3·6·3 tessellated SIOC-COF in an eclipsed AA stacking mode. Pore-size distribution analysis (FIG. 4d) shows two narrow peaks with sizes that agree well with the calculated values from an energy-minimized model of SIOC-COF with eclipsed AA stacking, further confirming the dual-pore structure of SIOC-COF.

A similar approach was used to synthesize another dual-pore 2D COF with 6·3·6·3 tessellation[37]. In this case, a D_{2h} symmetric monomer **10b** ($R = B(OH)_2$) with equilateral and unequal angular arms (60° and 120° angles) was chosen as the vertex. Instead of polymerizing through imine condensation, the authors used boronic ester formation with 1,2,4,5-tetrahydroxybenzene as the linear linker. A dual-pore 2D COF similar to SIOC-COF was obtained, suggesting the general applicability of angle-specific vertex design strategy in formation of COFs with heterogeneous pore structures.

It has been proposed that the propeller shape of monomers **10a** and **10b** is crucial for the formation of a highly crystalline framework with long-range order[38]. The arrangement of the four phenylene groups of these monomers is proposed to direct perfectly eclipsed interlayer stacking by enabling one monomer to lock into another at a single, well-defined lateral position. Thus, monomers **10a** and **10b** probably act as self-repeating lock-and-key units, providing periodic docking sites and promoting the formation of fully eclipsed layered structures. As a proof of demonstration, a series of 2D COFs consisting of monomer **10a** and linear linkers of varying molecular symmetry and flexibility has been synthesized and studied. PXRD analyses and computational calculations of energy-minimized structure models support the dual-pore 6·3·6·3 tessellation pattern. It was also possible to observe the highly ordered hexagonal arrangement of the mesopores and hexagonal facets in transmission electron microscopy images of such COFs[38], further supporting a structure consisting of hexagonal pores.

Although the angle-specific vertex approach has been successful in preparing multipore COFs, the possibility of forming other topologies with different tessellation patterns cannot be precluded. From a purely geometrical point of view, co-condensation of monomers **9** and **10** might result in two types of tessellation: an orthorhombic framework with repeating rhombuses (4·4·4·4 tessellation), and trihexagonal 6·3·6·3 tiling consisting of regular triangles and hexagons. However, it is possible that the thermodynamic stabilities of the two frameworks would lead to discrimination and selective formation of one. For example, it has been reported that the topology of frameworks can be

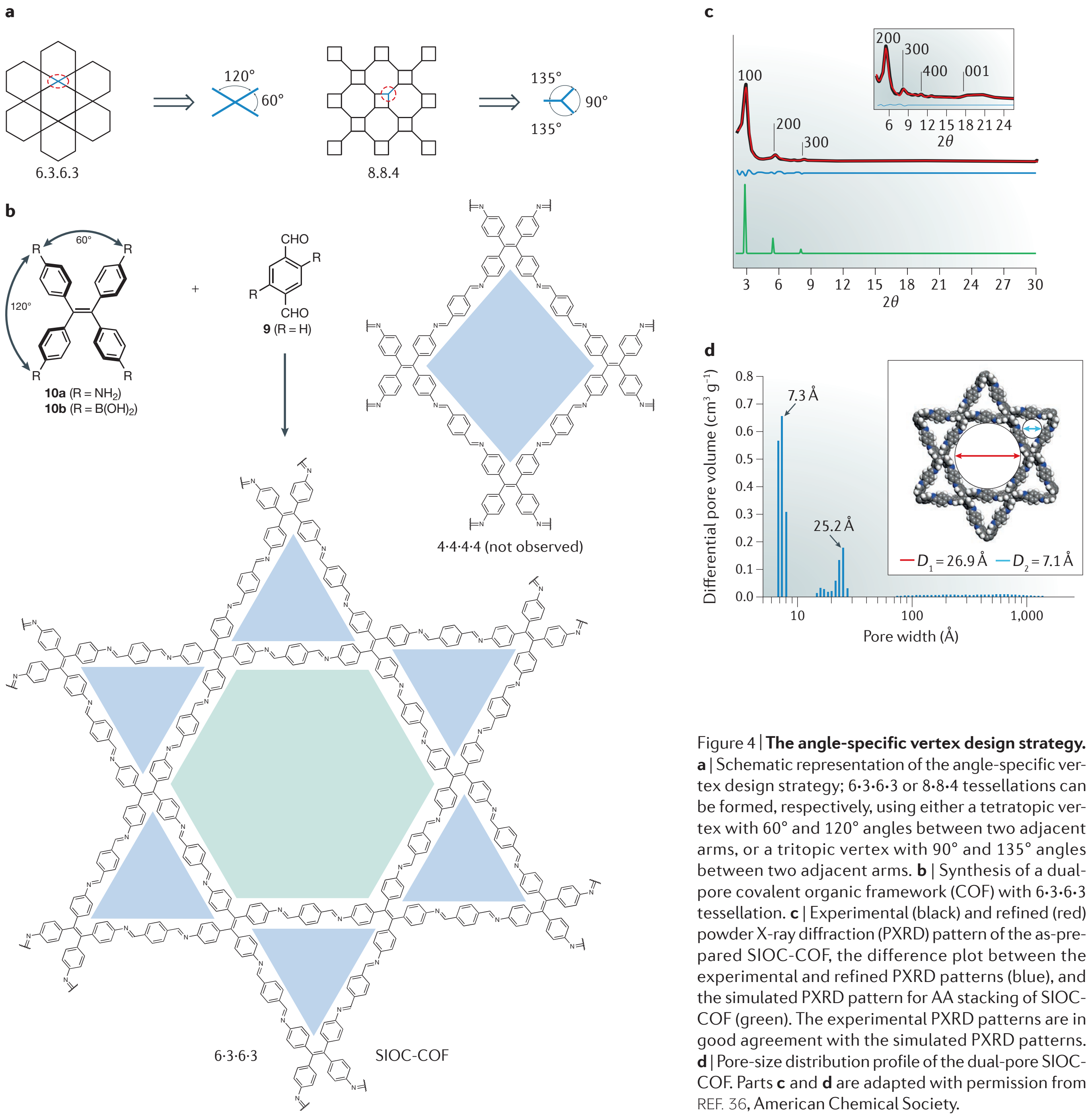

Figure 4 | **The angle-specific vertex design strategy.** **a** | Schematic representation of the angle-specific vertex design strategy; 6·3·6·3 or 8·8·4 tessellations can be formed, respectively, using either a tetratopic vertex with 60° and 120° angles between two adjacent arms, or a tritopic vertex with 90° and 135° angles between two adjacent arms. **b** | Synthesis of a dual-pore covalent organic framework (COF) with 6·3·6·3 tessellation. **c** | Experimental (black) and refined (red) powder X-ray diffraction (PXRD) pattern of the as-prepared SIOC-COF, the difference plot between the experimental and refined PXRD patterns (blue), and the simulated PXRD pattern for AA stacking of SIOC-COF (green). The experimental PXRD patterns are in good agreement with the simulated PXRD patterns. **d** | Pore-size distribution profile of the dual-pore SIOC-COF. Parts **c** and **d** are adapted with permission from REF. 36, American Chemical Society.

manipulated by introducing steric factors that favour one topology over another. Although trihexagonal 6·3·6·3 tiling (for example, SIOC-COF) is favoured when monomer **9** is substituted with R = H or OH, increased steric bulkiness of the substituents (R = OEt or O^{n}Bu) led to the favourable formation of the COF with 4·4·4·4 rhombus tessellation, presumably to minimize repulsion between substituents[39].

It is as yet largely unknown how selectivity is controlled in solvothermal synthesis, which features complex kinetics and thermodynamics involving reversible formation and cleavage of covalent bonds combined with irreversible precipitation or crystallization steps[40–42]. The covalent reactions between soluble species are reversible, enabling error-correction. However, once the products precipitate out from the solution in either crystalline or amorphous form, they are unable to exchange their compositions, and thus error correction becomes impossible. The process of COF formation most probably involves the initial nucleation of large 2D polymers followed by their growth through stacking of smaller soluble oligomers and subsequent repeated monomer addition[40–42]. It is less likely that large ordered 2D polymers form as thermodynamic products in solution and then aggregate or crystallize to form COFs. Therefore, the final COF structures with periodicity must satisfy the mathematical requirements of tessellation, but are not necessarily the most thermodynamically stable species. Researchers should thus be wary of making structure assignments on the basis of thermodynamic stability alone. PXRD analysis and pore-size distribution have been general proofs to support one tessellation over the other. Nevertheless, development of more direct evidence (for example, imaging techniques or single-crystal analysis) is highly desired to unambiguously determine the structures of these COFs. As noted previously, introduction of orthogonal functional groups to the monomer design could provide additional control over the monomer connectivity.

Shape-persistent-patch design

In the previously discussed design strategies (desymmetrized-vertex and angle-specific vertex), polygonal species are formed during the tessellation process. These strategies therefore involve two levels of assembly: subassembly of polygons and further tessellation. Is there a way to control these two assembly processes independently to solve the polymorphism problem? In other words, is it possible to construct polygons with internal cavities first and then use these pre-assembled polygons as building blocks? The difficulty in simultaneously controlling the formation of multiple pores can be minimized by using highly symmetric nano-sized polygonal macrocycles with pre-assembled internal pores as building blocks and controlling the complexity of their connection in two separate processes (FIG. 5a). Recently, such shape-persistent-patch design — also occasionally called a macrocycle-to-framework strategy — has been successfully developed to construct dual-pore 2D COFs with semi-regular tessellation patterns. An early example of such a strategy was reported in which phenanthrene cyclotrimer **11** was used to form 12·12·3 tessellated Star-COF-1 and Star-COF-2. By varying the lengths of linear linkers, such as pyrene-2,7-diboronic acid (PDBA, **15**) or 1,4-benzene diboronic acid (BDBA, **16**), the size of the 12-membered ring could be varied correspondingly[43] (FIG. 5b).

This approach can be viewed as a variation of Yaghi's first synthesis of a 2D COF of 6·6·6 tessellation[13]. In their approach, they used HHTP (**6** in FIG. 3) as vertices and condensed it with linear linker **16**. When this triangular-shaped HHTP vertex unit is expanded into shape-persistent macrocycles with internal cavities, the semi-regular tessellation 12·12·3 is obtained. Various other triangular-shaped macrocycles (**12–14**) have been used as vertices by different groups to form 2D COFs with dual-pore structures[44,45]. Condensation of highly symmetrical macrocycles with linear linkers, such as PDBA (**15**) or BDBA (**16**), provided 2D COFs with AA stacking modes. Variation in macrocycle size or in the length of the linear linker can be used to modulate the pore sizes of the resulting COFs. In each case, the resulting 2D COF exhibits a typical type IV nitrogen adsorption isotherm, showing a sharp gas uptake at low relative pressure ($P/P_0 < 0.01$) followed by a second-stage pore filling in the P/P_0 range of ~0.05–0.4, which is characteristic of mesoporous materials. Analysis of the pore-size distribution showed targeted mesopores of 3–4 nm. So far, however, micropores of ~0.5 nm, which would be predicted to arise from the internal cavity of macrocycles, have not been detected, possibly owing to slight offsets in interlayer stacking.

In addition to the above-mentioned 12·12·3 semi-tessellation, the Zhang group also attempted to synthesize 2D COFs with 8·8·4 tessellation starting from the square-shaped macrocycle **17** (REF. 46) (FIG. 5c). The D_4-symmetric macrocycle **17** is equipped with four diol units that can react with trimethyl borate to form spiroborate linkages. Although multiple peaks in the 2θ range of 2–35° were observed in the PXRD pattern, the authors were unable to deduce the crystal packing of this ionic–covalent organic framework (ICOF) and only proposed a 2D model. Nevertheless, this study suggests that macrocyclic building blocks other than common triangular shaped ones can also be used to form multipore COFs with different tessellation patterns.

Recently, Hisaki *et al.*[47] reported an interesting triple-pore hydrogen-bonded network known as H-HexNet, which was prepared from hexatopic triangular macrocycle **18** (FIG. 6a). In this approach, crystallization of macrocycle **18** in *N*,*N*-dimethylformamide and methyl benzoate formed a crystalline supramolecular network with three types of void (A–C) through the hydrogen bonding between two carboxylic acid groups. X-Ray crystal structure analysis of H-HexNet clearly shows two triangular voids (A and B) of different sizes and one irregular hexagonal void (C) (FIG. 6b). However, the packing diagram shows that the layer stacking is not eclipsed as is commonly observed in 2D COFs. Rather, each layer is inverted and significantly slipped from the adjacent layers (FIG. 6c), and this forms smaller 1D pores compared with the eclipsed stacking structure. Zhao and co-workers reported the preparation of a dual-pore COF with a similar structural motif[48]. Starting from hexatopic building unit **19** (REF. 49), which has a structure that closely resembles macrocycle **18**, dual-pore HAT-COF was obtained through imine condensation with 1,4-phthalaldehyde[48] (FIG. 6d). Based on PXRD analysis and pore-size distribution analysis, the structure and stacking of HAT-COF was assigned as eclipsed AA stacking with dual triangular pores (the calculated mean average pore diameters were $D_1 = 11.64$ and $D_2 = 14.01$ Å, and the observed diameters were $D_1 = 11.3$ and $D_2 = 15.2$ Å). (This is not, strictly speaking, an example of a shape-persistent-patch approach to form a multipore COF. To be classed as such, a patch should be a rigid macrocyclic compound with an accessible internal cavity. Thus, commonly used porphyrin and phthalocyanine derivatives with no accessible internal pores are not included.)

As the macrocyclic building blocks are highly symmetrical and all reactive functional groups are equivalent, a predetermined 2D COF structure with unique tessellation would be formed. The shape-persistent-patch approach therefore represents an interesting method that inherently prevents polymorphism. The obvious drawback is that the synthesis of macrocyclic building blocks might be relatively difficult compared with the other approaches. One possible resolution could be the formation of macrocycles under thermodynamically controlled conditions from simple precursors, for example, a one-step cyclo-oligomerization approach to form arylene–ethynylene macrocycles[50–54] through dynamic alkyne metathesis.

Mixed-vertex or mixed-linker strategy

The final strategy that we consider for the introduction of structural diversity into 2D COFs is a mixed-component (mixed-vertex or mixed-linker) approach in which two different types of multitopic vertices or linear linkers are incorporated into the same COFs. Related strategies have been widely explored for the preparation of MOFs[55–57], but only a few examples have been reported for COF synthesis[58,59]. The Jiang group reported various multicomponent COFs using a mixed-linker strategy, but these were uniporous (either 6·6·6 or 4·4·4·4 tessellation) structures[60]. Zhao and co-workers[59] demonstrated the preparation of triple-pore SIOC-COF-1 by blending a D_{2h}-symmetric tetraamine vertex **10a** with a 1:1 molar ratio of two different C_2-symmetric dialdehydes of different length (**9** and **20**) (FIG. 7a). The triple-pore structure of SIOC-COF-1 was supported by PXRD data and pore-size distribution analysis, which revealed three pore sizes

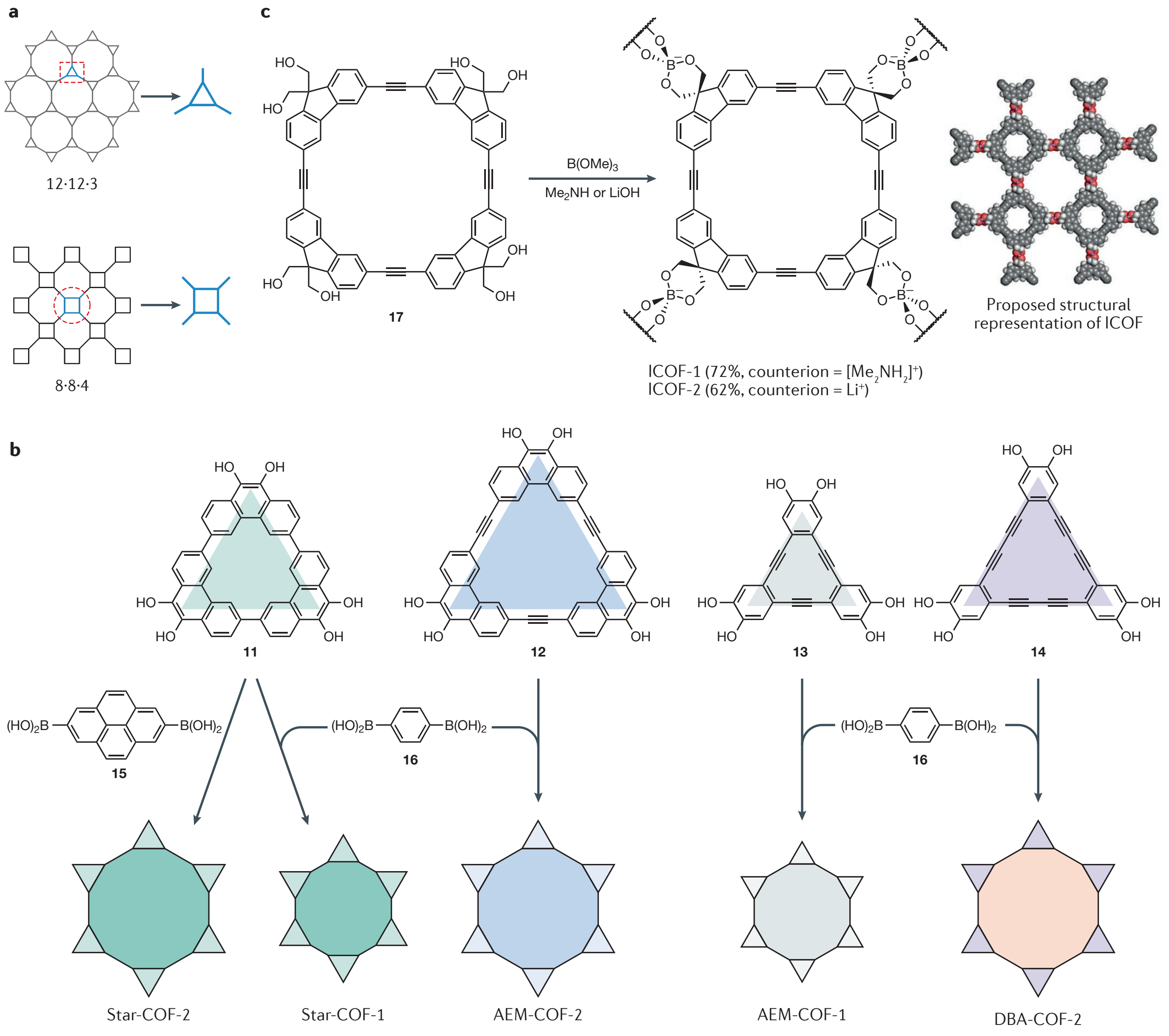

Figure 5 | **Shape-persistent-patch design. a** | Schematic representation of shape-persistent-patch design. **b** | Various macrocycle-containing covalent organic frameworks (COFs) prepared through the shape-persistent-patch strategy. **c** | The synthesis of an ionic–covalent organic framework (ICOF) from square-shaped macrocycle **17**. Part **c** (proposed strutcure of ICOF) is reproduced with permission from REF. 46, Wiley-VCH.

of 7.3, 11.8 and 30.6 Å in diameter that match well with the theoretical pore sizes that were estimated by semi-empirical (PM3) calculations (8.5, 11.3 and 31.3 Å). McGrier and co-workers reported a similar mixed-component strategy in which two macrocycles (**13** and **14**) of different sizes were mixed with linear linker **15** to form Py-MV-DBA-COF with a triple-pore structure[58] (FIG. 7b). These strategies, which use more than one type of linear linker or vertex, provide interesting alternative ways to generate porous materials with heterogeneous pore structures. Although the presence of multiporous structures was supported by PXRD analysis, there has as yet been no direct evidence to prove the periodicity of such multiple pores. The distribution of these mixed linkers or vertices might instead be random, as is observed in many MOFs with mixed organic linkers or inorganic secondary building units. The coexistence of domains of dual-pore COFs and triple-pore COFs could not be completely ruled out either.

Very recently, the Zhao group demonstrated a mixed-vertex strategy in which they used pre-linked vertices[61–63] (FIG. 8). For example, condensation of vertex **10a** with pre-linked vertex pair **21** produced SIOC-COF-6, which has a unique tessellation pattern that consists of two types of pores of different size and shape: irregular hexagons and rhombuses[61]. Owing to the unique combination of vertex angles that are pre-linked together, only one tessellation is formed and possible polymorphism is prevented. A similar strategy was used to combine pre-linked vertices (**22**) with a linear *p*-phenylenediamine linker[62]; imine condensation led to the formation of SIOC-COF-7, with a heterogeneous pore structure consisting of two types of pore with different size and shape.

Summary and outlook

The introduction of structural heterogeneity into ordered frameworks is desirable to tailor material characteristics, such as their electronic, magnetic, mechanical and sorption properties. Efforts to exploit the diverse nature of COFs have thus led to new questions about whether such structural and functional heterogeneity can be included in these ordered frameworks. Development of 2D COFs with controlled hierarchical geometry and functional complexity at the molecular level will open up exciting opportunities for new materials design. A potentially exciting application would be multidrug delivery using a 2D COF with well-separated parallel channels of hydrophilic and hydrophobic pores, which might simultaneously take up hydrophobic and hydrophilic guests. There is growing evidence to show that combination

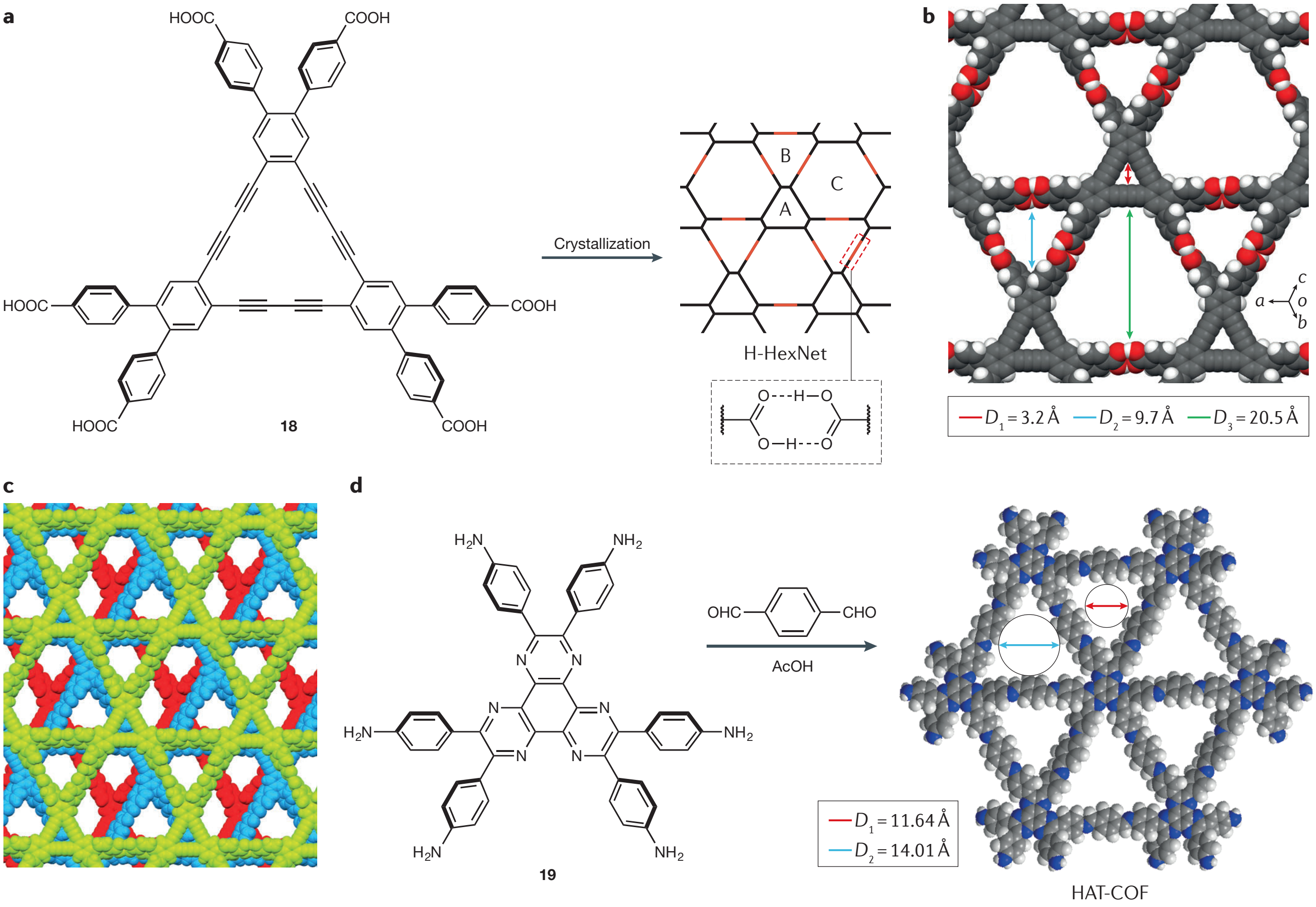

Figure 6 | **Framework construction using hexatopic building blocks. a** | Crystallization of **18** in a mixture of *N*,*N*-dimethylformamide and methyl benzoate at 50 °C yielded H-HexNet crystals. **b** | Crystal structure showing a single layer of H-HexNet with three types of pore. **c** | Packing diagram of three layers in H-HexNet, coloured green, blue and red. **d** | Synthesis of dual-pore HAT-COF; a simulated structure of HAT-COF is shown. *D*, pore diameter. Parts **b** and **c** are adapted with permission from REF. 47, Wiley-VCH. Part **d** (simulated structure) is adapted with permission from REF. 48 , American Chemical Society.

therapies can be more effective (because of synergistic actions) than the sum of individual drug effects[64]. However, if different drugs are simply injected together into the bloodstream, their differing pharmacokinetic properties make it almost impossible to control the molar ratio of these drugs that will be taken up by the same diseased cells. Two-dimensional COFs with hydrophilic and hydrophobic dual-pore channels could hold potential as drug carrier systems for the synchronous delivery of such drugs.

In the past decade, precise control over molecular structures has been achieved for the construction of highly regular 2D COFs, but only a limited number of simple tessellations have been realized from the frameworks that are mathematically plausible. The design of multitopic building units with reduced symmetry and proper geometry to create 2D COFs with complex tessellation patterns and multipore structures is crucial. The strategies discussed herein are rooted in mathematical tessellation rules and would enable the successful construction of 2D COFs with Archimedean tilings, as well as intricate patterns beyond the complexity that is observed in such tilings.

The grand challenge in the preparation of multiporous COFs lies in the control of simultaneous selective formation of multiple desired pores. Even when the symmetry of vertices is reduced to form semi-regular or non-regular tessellations, there frequently remains more than one theoretically possible structure owing to the uncontrolled connection sequence of the building units. Outside the use of pre-assembled polygons with its inherent challenges in building-block synthesis (shape-persistent-patch design), an alternative approach to prevent polymorphism might be the introduction of directionality into the building-block design to further programme their connectivity. For example, multiple arms of vertices can be functionalized with orthogonal functionalities, such as boronic acid and amine groups, so that each vertex connects through the programmed sequence by finding its specific reaction partners. It has been demonstrated that 2D grids with four or more rings are kinetically trapped and cannot undergo self-correction in solution phase[65]. The self-correction mechanism that is in operation during the formation of ordered COFs under solvothermal conditions, which involves complicated reversible (dynamic covalent reactions) and irreversible (precipitation) steps, is not well understood. Thus, attempts to study and ultimately predict the thermodynamics and kinetics of the processes that occur in dynamic covalent chemistry would be of great use[40,42].

The unambiguous structural assignment of COFs remains a challenge in the development of multipore COFs. This is the foremost disadvantage of COFs over MOFs, which have structures that are frequently determined unambiguously by single-crystal X-ray analysis. The possible occurrence of polymorphism creates extra difficulty in determining their structures. In all the cases reported so far, the structures of multipore COFs have been assigned based on PXRD simulations, pore-size distribution analysis and comparisons of thermodynamic stabilities. Each assigned structure is generally accompanied by an initial estimation of possible structures, optimization of structures through energy calculations, computer simulation of their PXRD patterns and matching to the observed experimental data. Although this evidence can be supportive, the exact connectivity of monomers is often hard to determine from simulated PXRD patterns and pore-size distribution analysis alone. In addition, as noted previously, although COFs that are prepared under solvothermal conditions must have mathematically possible tessellation patterns, they are not necessarily the thermodynamically most stable products. Therefore, structure assignment of one topology among multiple possible candidate topologies based on the calculated energy profile should be approached with caution. More direct and unambiguous evidence

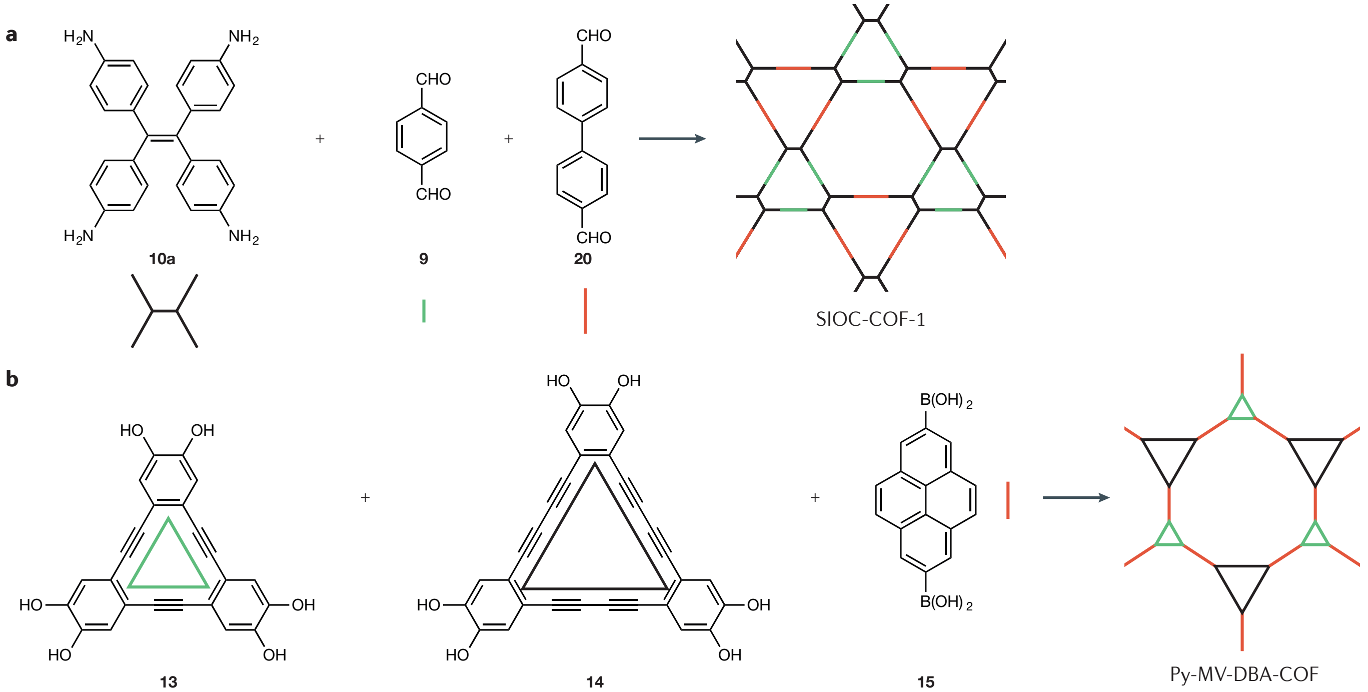

Figure 7 | **The mixed-component design strategy. a** | Mixed linkers of different lengths (that is, **9** and **20**) were used to produce triple-pore SIOC-COF-1. **b** | Macrocycles of different sizes were used as vertices to form Py-MV-DBA-COF with a triple-pore structure.

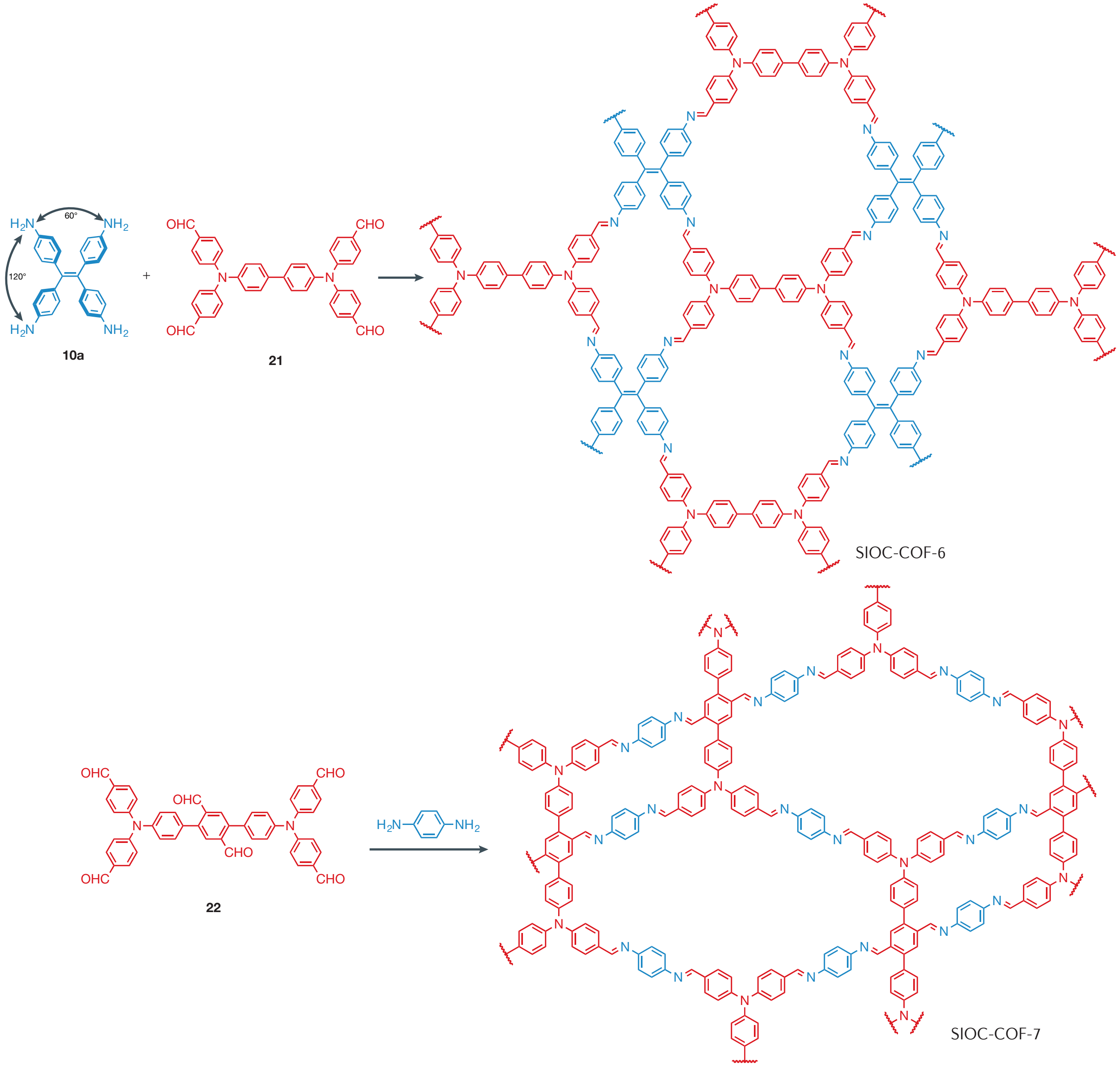

Figure 8 | **Mixed-component design using pre-linked vertices.** Two vertices were pre-linked to form vertex pair **21**, which was used as the linker to connect another type of vertex, **10a** ,to form dual-pore SIOC-COF-6 with mixed vertices. In the synthesis of SIOC-COF-7, four vertices were pre-linked as compound **22**, which further reacted with the *p*-phenylenediamine linker to form a dual-pore structure with two types of vertices.

for determining the monomer connectivity and topology, sharpened characterization and advanced computational algorithms are highly desired.

We hope that this overview of the necessary (yet incomplete) set of bottom-up design strategies, synthetic approaches and difficulties with unambiguous structural characterization of 2D COFs with heterogeneous pore structures offers an overall picture of current feasibility and guidance to transformative and productive research in this exciting area.

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