Imine and imine-derived linkages in two-dimensional covalent organic frameworks

Cheng Qian,[1,2] Lili Feng,[1] Wei Liang Teo,[1] Jiawei Liu,[1] Weiqaing Zhou,[1] Dongdong Wang,[1] and Yanli Zhao[1]*

[1]School of Chemistry, Chemical Engineering and Biotechnology, Nanyang Technological University, 21 Nanyang Link, Singapore 637371, Singapore.

[2]State Key Laboratory for Modification of Chemical Fibers and Polymer Materials, College of Materials Science and Engineering, Donghua University, Shanghai 201620, China.

*Email: zhaoyanli@ntu.edu.sg

Covalent organic frameworks (COFs) are porous crystalline polymers that result from the formation of covalent bonds between precisely assembled organic units. The linkage chemistry is a crucial factor in the controllable synthesis and in the resulting physicochemical properties of COFs. A variety of linkages have been employed in the fabrication of COFs, but for polyfunctional two dimensional (2D) COFs in particular the imine bond is popular because it is formed reversibly under thermodynamic control. Recently, there has been increasing interest in expanding beyond imine-linked 2D COFs to those with imine-derived linkages. This review highlights some of the key advances in the development of chemistry to modify and prepare derivatives of imines within 2D COFs and introduce the fascinating properties and potential applications of the materials that result. It begins with a brief introduction to various chemical linkages in COFs. Next, the strategies applied to the derivation of imine bonds via covalent and noncovalent bonding to produce 2D COFs with novel structures and functions are comprehensively reviewed, providing a better understanding of the relationship between covalent linkages and overall performance for 2D COFs. Finally, this review concludes by discussing the major challenges and prediction of the future trends in the development of COFs.

[H1] Introduction

Covalent organic frameworks (COFs) are a class of porous crystalline polymers assembled by stitching together organic units, through the formation of covalent bonds, to form an extended framework[1-3]. In comparison with amorphous porous organic polymers (POPs), such as porous aromatic frameworks (PAFs)[4,5], conjugated microporous polymers (CMPs)[6-8], polymers of intrinsic microporosity (PIMs)[9,10], and hypercross-linked polymers (HCPs)[11], one of the most attractive features of COFs is that they possess predictable structures, in which the organic units are positioned in a specific spatial orientation and extended in three-dimensional (3D) space by covalent bonds. Furthermore, unlike other crystalline materials such as zeolites[12,13], hexagonal boron nitride[14], perovskites[15], metal-organic frameworks (MOFs)[16,17], COFs have the merits of adjustable pore size/shape, high surface area, and low mass density. The robust covalent bonds also endow COFs with unique traits such as high thermal stability and good chemical stability. These advantages mean that COFs are promising systems for a wide variety of applications, including gas sorption and storage[18,19], optoelectronics[20], catalysis[21,22], biomedicine[23], energy storage[24,25], and environmental remediation[26].

A framework linked by covalent bonds consists of two distinct components: linkers (organic subunits) and linkages (covalent bonds formed between precursors upon reticulation)[3]. Organic chemistry provides a powerful tool for the exploration of diverse building blocks and synthetic reactions to prepare COFs with specific functions. As noted by Yaghi and co-workers[27] "All COFs are 3D materials, but their covalent connectivity can be 3D, 2D, or even 1D. In COFs whose connectivity extends in three dimensions, the crystallinity of the system is almost exclusively a result of the order imposed by the linkage. In layered materials where covalent connectivity extends only in 2D, however, noncovalent interactions play a key role.". Thus, the crystallinity of 2D COFs, is governed not only by the covalent linkages in the in-plane direction, but also influenced greatly by out-of-plane noncovalent interactions. Unlike the woven and interpenetrated structures that are found in 1D and 3D COFs respectively, most 2D COFs exhibit eclipsed stacked structures, endowing them with periodic columnar π-arrays and independent 1D channels. To obtain highly ordered 2D COF structures, it is important to precisely control the lateral growth of organic monolayers through covalent bonds and vertical stacking of extended multilayers through noncovalent forces. Chemists must therefore carefully

consider three important aspects prior to embarking upon the synthesis of 2D COFs: selection of suitable organic units, covalent linkages, and stacking modes. The linkage chemistry, in particular, is extremely important for controllable synthesis and physicochemical properties of COFs.

Most 2D COFs are obtained using dynamic covalent chemistry (DCC) in which molecular units are linked into extended structures through the reversible formation of covalent bonds[28,29]. DCC has played an important role in the design and synthesis of functional materials such as discrete molecular architectures and conjugated organic polymers[30-33]. The DCC principle provides ample opportunities for proof-reading and error correction and the guarantee of forming well-defined structures has led to its use for the syntheses of the majority of 2D COFs reported thus far[34]. Boron-based linkages, i.e., boronate esters and boroxines, have been exploited to generate well-ordered crystalline structures in the early stages of COF development. This is because they possess reasonable dynamic reversibility under solvothermal conditions. Although boroxine and boronate ester-based COFs are thermally stable, they are highly susceptible to nucleophilic attack by water, thus limiting their potential applications[35]. Fortunately, there has been great progress in the exploration of other linkages for the construction of crystalline COFs particularly since the report of an imine linkage by Yaghi and colleagues in 2009[36].

Imine-linked COFs have been widely synthesized and employed in diverse applications on account of their reversible formation and broad functional group compatibility under solvothermal conditions. Synthetic strategies towards them, their physiochemical properties, and various applications have been systematically reviewed[37-39]. Recently, there has been increased interest in expanding beyond imine-linking to imine-derived linking. The primary reason for this change is that in addition to their easily reversible formation, imine bonds are moderately chemically stable, offering great potential for further derivation. More than a dozen types of novel linkages, whose formation begins with imine bonds, have been developed to prepare functional 2D COFs for diverse applications. Moreover, noncovalent interactions have proven to be a robust tool to improve the crystallinity and stability of imine-based 2D COFs. These studies belong to the realm of imine-derived linkage chemistry, and have not yet been systematically summarized. The vast majority of representative examples of imine modification

are performed using 2D COFs and these are the focus of this review; it is noted, however, that 3D COFs could likely be modified in a similar fashion.

In this review, we first introduce various types of chemical linkages reported in the construction of COFs. Next we discuss, in detail, the approaches used for the derivation of imine bond in 2D COFs , along with their physicochemical properties of the resulting COFs and their representative applications. Finally, we offer our view on the existing challenges and future directions for linkage chemistry in 2D COFs.

[H1] Imine and imine-derived linkages

A huge variety of reactive linkage groups have been employed in forming COFs, including, but not necessarily limited to: boronic acid, catechol, amine, aldehyde, hydrazine, and nitrile. These groups appended to the ends of COF precursors react selectively with one another, resulting in covalent linkages. The reactions used in the synthesis of COFs can be subdivided into seven general categories on the basis of the type of covalent linkages they form. These are (1) B-O (e.g., boronate ester[1], boroxine[1], borosilicate[40], and spiroborate[41]); (2) C=N (e.g., imine[36], hydrazone[42], azine[43], and iminium[44]); (3) $C=N_{aromatic}$ (e.g., triazine[45], phenazine[46], oxazole[47], quinoline[48], imidazole[49], pyrimidazole[50], boranil[51], and thieno[3,2-c]pyridine[52], aza-bridged bis(phenanthroline) macrocycle[53], chromenoquinoline[54], imidazopyridinium[55], and 4-carboxyl-quinoline[56]); (4) C-N (e.g., *β*-ketoenamine[57], squaraine[58], imide[59], amide[60], viologen[61], urea[62], amine[63], aminal[64], *α*-aminonitrile[65], tetrahydroquinoline[66], propargylamine[67], arylamine[68], quinoxaline[69], α-aminophosphonate[70], and hydrazide[71]); (5) C=C (e.g., cyanovinylene[72], olefin[73], and benzofuran[74]); (6) C-O (e.g., dioxane[75], carbamate[76], thiocarbamate[76], and ester[77]); (7) other (e.g., borazine[78], *trans*-azodioxy[79], silicate[80], C-C[81], B-O-P[82], and azo[83]). The rich chemistry of nitrogen containing compounds results in a greater diversity of nitrogen-based COFs versus than boron-based COFs. From the above list more than a dozen nitrogen-based linkages, whose formation relies in whole or in part on the formation of imine bonds.

An imine-linked COF with dia-c5 topology featuring 5-fold interpenetrated diamond nets, now commonly known as COF-300, was first described by Yaghi et al. in 2009[36]. Since then, a large number of imine-linked 2D COFs have been developed for a wide range of applications. The imine linkage offers good stability though its formation is easily reversed, combined with easy access to precursors, it is perhaps easy to see why there has been such increased interest. Chemists have also been explored further derivation of the imine bond, providing enormous opportunities for the synthesis of 2D COFs with new structures and functions. COF linkages derived from imines can be divided into those formed by covalent and noncovalent modifications. Covalent modifications of imine linkages can be further subdivided into *de novo* synthesis and post-synthetic modification (PSM). The former refers to those COFs that are produced as part of a one pot reaction — imine formation is immediately followed by conversion into another functionality as the COF network is formed. The latter refers to those COFs formed with an imine linkage and then PSM changes the network in some fashion. In the following sections we discuss each of these approaches, including synthetic methods as well as the physicochemical properties and applications of the resulting COFs. A timeline of the significant advancements made in the development of imine and imine-derived linkage chemistry for 2D COFs is presented in FIG. 1.

[H1] *De novo* synthesis

In designing COFs with a particular property three key aspects must be considered: crystallinity, stability and functionality. Stability can be improved by increasing the strength of interactions – either covalent or noncovalent – between framework components. New covalent interactions can be forged between building blocks with preinstalled redox active groups. Noncovalent stability enhancement might for example involve the introduction of additional functional groups that extend π conjugation over the 2D sheets. A typical feature of *de novo* synthesis is that the 2D imine-derived COFs can be directly obtained in one-pot reaction by combining reversible imine formation and effectively irreversible tautomerization/oxidative cyclization under solvothermal conditions. By using this approach, a large number of 2D COFs with novel linkages, such as *β*-ketoenamine, triazine, urea, oxazole, and thiazole, can be directly prepared in one step.

In 2012, Banerjee and colleagues pioneered the use of cascade organic reactions to synthesize crystalline and porous 2D COFs[57]. A reversible Schiff base formation between aromatic diamines and 1,3,5-triformylphloroglucinol (Tp) gave rise to a crystalline enol–imine COF intermediate and this was followed by an effectively irreversible enol–keto tautomerization to generate β-ketoenamine-linked COF. This tautomerization does not influence the crystallinity of the COF, but enhances the chemical stability of the framework. The obtained COFs (TpPa-1 and TpPa-2) exhibited strong resistance to acid (9 M HCl) and boiling water. In TpPa-2, the addition of steric bulk, in the form of two methyl groups, near the base-labile secondary nitrogen centre conferred high stability in a basic medium (9 M NaOH) (FIG. 2a). Yan and co-workers applied a similar effectively irreversible cascade reaction to prepare a chemically stable β-ketoenamine-based 3D COF[84]. By using this methodology, several *β*-ketoenamine-based 2D COFs were developed for various applications such as sensing[85], heterogeneous catalysis[86], photocatalysis[87,88], and electrocatalysis[89]. In general, *β*-ketoenamine-linked COFs built from Tp with three −OH groups exhibited effectively irreversible proton tautomerism, which is attributed to the strong intralayer hydrogen-bonding interactions. Loh and co-workers proposed that the introduction of 2,4,6-triformyl phenol unit with only one hydroxy group into COFs to form less rigid β-ketoenamine intermediate. A reversible proton tautomerism between *cis*-keto and *trans*-keto forms in COFs was observed upon the adsorption and desorption of H_2O (FIG. 2b). This tautomeric structural transformation also enables a dynamic response in the ionic and chemical properties of the pore surface[90].

Iminol-to-ketoenamine tautomerism can also be used to tune the properties of COFs. For example, Vaidhyanathan et al. have shown that reported an anthracene-resorcinol derived COF that emits white light. The keto−enol tautomers present in the COF exhibit dual emission, which can be further regulated with a careful choice of the O-donor and N-donor solvents. The results showed that the blue emission originates from the π-stacked columns of anthracene, and the mixture of red and green stems from the keto−enol tautomerized resorcinol units. The team prepared a flexible white light emitting film by dispersing a small amount of the COF into processable non-photoluminescent poly(methyl methacrylate) (PMMA), highlighting the great potential of COFs for white light emitting applications (FIG. 2c)[91]. A second example are the humidity-sensing 2D COFs reported by Dichtel and co-workers that rely on reversible water-

induced iminol-to-ketoenamine tautomerism. The key design is the integration of 2,5-di(imine)-substituted 1,4-dihydroxybenzene (diiminol) moiety into well-defined frameworks. As the diiminol has the ability to rapidly tautomerize to an iminol/*cis*-ketoenamine instead of a diketoenamine, the TAPB-PDA-OH could be used as reversible humidity sensor. An oriented COF thin film with a long-term stability was constructed for colorimetric humidity sensing, which displayed rapid and reversible optical response toward water (FIG. 2d)[92].

In 2017, Jin and colleagues reported an important step towards crystalline covalent triazine frameworks (CTFs) under mild conditions through tandem Schiff base formation followed by an effectively irreversible Michael addition. The reaction of amidine dihydrochloride with aromatic aldehydes thus led to the production of four CTFs that were shown to be efficient photocatalysts for visible-light-driven hydrogen generation from water with a maximum rate of 2647 μmol h^{-1} g^{-1}. An important feature of this synthetic strategy is the relatively mild reaction conditions by comparison with the reported ionothermal synthesis, thus enabling the design and synthesis of stable CTFs from a broad array of building blocks (Supplementary FIG. 1)[93]. In 2020, the same group reported a modified route that used benzylamine as monomer in place of benzaldehyde/benzyl alcohol to react with amidine dihydrochloride for forming CTFs in the presence of base reagents (FIG. 3a). This route offers significant advantages over the former methods, including higher yield, lower costs, and improved crystallinity. The results showed that the strength of base reagent used has a great influence on the performance for visible-light-driven hydrogen generation from water. The stronger the base reagent, the higher H_2 evolution activity of the CTF-HUST-A1 series (FIG. 3b). Overall photocatalytic water splitting was realized by depositing 4.5 wt% NiP_x and 3.0 wt% Pt as dual co-catalysts in CTF-HUST-A1-^{t}BuOK, giving the H_2 evolution and O_2 evolution rates of 25.4 mmol g^{-1} h^{-1} and 12.9 mmol g^{-1} h^{-1}, respectively. This work enriches the synthetic toolbox for the construction of crystalline CTFs[94].

The combination of a reversible Schiff base reaction with an effectively irreversible tautomerism can also be used to increase the types of linkages found in 2D COFs. In a pioneering example, Yaghi et al. reported a 2D urea-linked COF which exhibited reversible structural changes upon guest inclusion and removal. COF-117 and COF-118 exhibited different dynamic behaviors in response to the presence of guest molecules, such as methanol.

The crystalline COF-117 became amorphous upon desolvation, whereas COF-118 remained crystalline upon removal of methanol, an effect that can be ascribed to the subtle structural differences from their urea C−N bond rotation and interlayer hydrogen bonding. Furthermore, COF-118 showed excellent chemical stability toward acid (12 M HCl), boiling water, and saturated $NaHCO_3$ solution (FIG. 3c)[62].

McGrier et al. reported the preparation of 2D benzobisoxazole (BBO)-linked COFs using a cyanide-catalysed cascade reaction. The aminophenol and formyl precursors initially undergo reversible Schiff base formation to produce crystalline enol-imine COF intermediate, followed by oxidative dehydrogenation and cyclization to form the BBO linkage. Cyanide anions are nucleophiles, that catalyse the formation of the BBO linkage for the growth of ordered 2D COFs. The resultant BBO-COFs exhibited high water stability and good uptakecapacities for CO_2 molecule. The CO_2 uptake values were 150.6 mg g^{-1} and 112.3 mg g^{-1} at 273 K for BBO-COF 1 and BBO-COF 2, respectively[47]. Wang and co-workers also prepared benzoxazole-linked COFs. Once again reversible imine formation is coupled with an effectively-irreversible reaction — in this case oxazole formation. Importantly, the addition of benzimidazole serves two roles in the reaction — facilitating aromatization but also templating the COF formation and enhancing crystallinity. The robust benzoxazole linkages in these COFs exhibited high stability under strongly basic (9 M NaOH) and strongly acidic (9 M HCl) conditions as well as stability when exposed to sunlight. These benzoxazole-linked COFs can be used as photocatalysts for oxidative hydroxylation of arylboronic acids (producing phenols) under visible-light irradiation (FIG. 3d). This work not only demonstrated that benzoxazole-linked COF could be used for photocatalysis, but also revealed the extra advantages offered by extending frameworks[95].

Wang and co-workers reported a distinct strategy to prepare stable COFs through multicomponent reactions. Distinct from the previous approaches in concept for the construction of multivariate COFs using mixed linkers or orthogonal reactions, multicomponent reactions were employed to realize the *in situ* formation of five covalent bonds in each imidazole via reversible/irreversible covalent assemblies[49]. Four imidazole-linked COFs were successfully prepared by a three-component Debus−Radziszewski reaction between tertbutylpyrene tetraone, aromatic aldehydes, and ammonium acetate in one pot. The robust

imidazole linkage confers high chemical stability with the COFs shown to be stable under strongly basic (9 M NaOH) and strong acidic (9 M HCl) conditions for 3 days (FIG. 3e). The imidazole linkage also offers the possibility of modification after COF formation. The team prepared a series modified COFs via a one-step N-alkylation reaction of the imidazole links and showed that the resulting COFs maintained their ordered structures after post-modification. Babu and co-workers also demonstrated that an imidazole-linked COF prepared by a polyphosphoric acid assisted synthetic route can be employed for ultrahigh proton conductivity[96].

Recently, Cooper and co-workers reported a new approach for preparing thiazole-linked COFs through a one-pot multicomponent reaction involving reversible Schiff base formation followed by effectively irreversible C−H functionalization and oxidative annulation[97]. A mechanistic investigation revealed that the imine-linked COF acted as an intermediate before the final crystalline framework formed by one-pot cascade reactions. The results showed that one-pot process leads to a more crystalline COF – versus formation of an imine-linked COF and then treatment with sulfur. The resulting COF has improved performance as a water-splitting catalyst. In addition, they found that the thiazole-linked COFs were good candidate systems for photocatalytic hydrogen evolution on account of their good light absorption capabilities and suitable band gaps. One of the obtained COFs exhibited high performance with a maximum rate of 4296 μmol h^{-1} g^{-1}, which was better than amorphous analogues (676 μmol h^{-1} g^{-1}) or imine-linked ones (1644 μmol h^{-1} g^{-1}) (FIG. 3f).

Yang et al. reported an approach for the fabrication of tetrahydroquinoline-linked COFs through cascade imine condensation and cycloaddition reaction with $Sc(OTf)_3$/$Yb(OTf)_3$ as the catalyst[66]. Both COFs (QH-COF-1 and QH-COF-2) presented high tolerance to the strong acid, strong base and light irradiation, suggesting the improved stability of tetrahydroquinoline-linked COFs over their corresponding imine-linked frameworks (Supplementary FIG. 2). Benefiting from robust tetrahydroquinoline linkage formation, these COFs could be used as photocatalysts in the asymmetric alkylation of aldehydes with the aid of a chiral secondary amine, giving high activity, enantioselectivity, and recyclability for a large substrate scope. This

work not only presents an efficient approach for the synthesis of robust COFs, but also provides new inspirations for the design of new photocatalysts.

Wang and co-workers targeted to overcome this bottleneck by introducing isocyanide chemistry. They successfully synthesized several pyrimidazole-based COFs in one pot by the Groebke−Blackburn−Bienaymé reaction using aminopyridine, isocyanide, and aldehyde precusors[50]. Multicomponent reactions were successfully employed to form pyrimidazole moieties throughout the frameworks via tandem reactions involving reversible imine formation followed by effectively irreversible cyclization with isocyanides under solvothermal conditions. On account of the ubiquitous existence of cyclic pyrimidazole linkages, the as-synthesized COF (LZU-563) exhibited high chemical stability toward various harsh conditions over 3 days. In addition, the properties of pyrimidazole-linked COFs can also be modulated by changing 2-aminopyridine monomers. For example, a COF LZU-562 exhibited a narrower optical band gap (1.88 eV) than those of LZU-564 (2.68 eV), LZU-563 (2.64 eV), and LZU-561 (2.06 eV). This work inspires new endeavors based on isocyanide chemistry for the fabrication of robust functional COFs.

In 2021, Lotsch and co-workers reported a strategy for constructing amine-linked COFs by a one-pot crystallization-reduction approach. By using formic acid and ammonium formate as catalysts, they successfully fabricated fully amine-linked or intermediate amine- / imine-linked COFs from imine-linked starting materials or directly from the corresponding precursors. Three kinds of amine-linked COFs (i.e., rPy1P-COF, rTTI-COF, and rPI-3-COF) were prepared with high surface area and good crystallinity. In addition, the secondary amine linkages endowed these frameworks with the possibilities for further functionalization. The derivatization has been fulfilled by reacting with strong and effective electrophiles such as chlorides or isocyanates. This synthetic method offers an efficient approach to the production of amine-linked COFs from readily accessible monomers[98]. Recently, Ma et. al. also synthesized flexible amine-linked COFs by one-step catalysis and reduction of formic acid[99].

[H2] Advantages and disadvantages

At least eighteen types of 2D COFs with new linkages, including β-ketoenamine, triazine, and so on, were successfully obtained via de novo synthesis. This approach exploits the

reversibility of imine formation to enhance error-correction and thus leads to more crystallinity but then combines that with an essentially-irreversible reaction – cycloaddition, reduction, etc. – to confer greater stability on the resulting COFs. Their porosity and chemical stability are summarized in Supplementary Table 1. It is worth noting that 2D COFs synthesized by a *de novo* approach require well-designed precursors before they are subjected to cascade reactions.

[H1] Post-synthetic modification

PSM is one of the most widely used methods to modify the structure of crystalline porous materials, potentially enabling the properties of functional COFs to be optimized without the need to re-examine porosity and crystallinity. 2D COFs frequently stack to produce ordered 1D channels with large internal surfaces, enabling exposed functional groups to participate in reactions like their solution counterparts. Remarkably, imines generally participate in two types of thermodynamically controlled reactions: imine exchange and metathesis[100]. Imine exchange can be used to prepare COFs that are typically inaccessible by *de novo* synthesis. As the resultant COFs are comprised of new imine bonds, imine exchange can thus be regarded as a special case of imine bond derivation. The synthesis of COFs obeys the principle of DCC, which provides many opportunities to make new types of COFs through imine exchange under thermodynamically controlled conditions. Therefore, the PSM strategies that enable optimization of COF properties can be subdivided into three types: linkage modification, structural doping, and linker exchange, depending on the modification sites. A large number of 2D COFs with novel linkages, such as amide, amine, oxazole, thiazole, quinoline, cyclic carbamate and thiocarbamate, can be obtained by using PSM.

[H2] Derivation by covalent modification

[H3] Linkage modification

Linkage transformation through PSM provides a facile approach to prepare COFs that are difficult to be obtained via *de novo* synthesis. For example, Yaghi and co-workers developed a strategy synthesize 2D amide-based COFs through direct oxidation of the imine linkage using a mild Pinnick-type oxidation reaction[60]. Two amide COFs were thus produced and shown

toretain their crystalline structure and permanent porosity. By contrast with their imine progenitors, the amide-linked COFs exhibited enhanced chemical stability in acidic (12 M HCl) and basic (1 M NaOH) aqueous solutions for 24 hours (FIG. 4a). This post-synthetic linkage oxidation strategy was recently extended to 3D COFs by Cui and co-workers[101]. The 3D chiral COFs thus prepared were found to have improved chemical stability and can be used as chiral stationary phases for chromatographic enantioseparation. Yan and colleagues demonstrated that amide-linked COFs can be directly obtained from imine-linked COF precursors using a building block exchange strategy[102]. The resultant amide-linked COF (JNU-1) exhibited improved chemical stability compared to its precursorand can be employed as a stable adsorbent for selective gold recovery from harsh conditions with ultrafast adsorption kinetics (0.17 min) and outstanding capacity (1127 mg g^{-1}) (Supplementary FIG. 3). The robust amide bond works not only as an inherent linkage to strengthen the framework, but also as active sites to adsorb Au^{III} in the structure of JNU-1. Recently, Zhao and co-workers reported an easy-operational method for the gram-scale synthesis of amide-linked COFs using $KHSO_5$ as an oxidant[103].

New linkages for COFs have been consistently pursued by researchers as they lay the foundation for a further understanding of the structure-property relationships of materials. Deng et al. demonstrated the direct reduction of imine to amine linkages within both 2D and 3D COFs using sodium borohydride[63]. The resultant COFs (COF-366-M-AR and COF-300-AR) preserved their highly ordered structure throughout the reduction process due to the formation of stable amine linkages. The newly formed amine linkages endowed these frameworks with a good stability in strong acid (6 M HCl) and base (6 M NaOH) far beyond their corresponding imine-linked COFs. In addition, the amine linkages in COF-300-AR backbone offer abundant chemisorptive sites for selective capture of CO_2 from aqueous solutions, facilitating the formation of carbamate intermediates to generate CO (Supplementary FIG. 4). In comparison with the PSM approach for the preparation of amine-linked COFs reported by Deng and co-workers, the aforementioned one-pot crystallization-reduction approach reported by Lotsch and colleagues has the merit of controllable synthesis of hybrid COFs with mixed linkages[98]. This could be ascribed to the fact that sodium borohydride has higher reductive activity toward imine bonds than formic acid and ammonium formate. Recently, Beyzavi and colleagues reported the synthesis of amine-linked COFs from readily available amine and aldehydes precursors in one-

pot reaction. The key to the success is the use of H_3PO_3 as a bifunctional catalyst. It not only acted as the catalyst to promote the formation of the imine framework but also functioned as reductant to produce the amine COF. The result showed that the amine-linked COF outperforms its imine analogue in catalyzing Knoevenagel condensation due to the more basic sites and higher stability[104]. Dai and co-workers developed a PSM strategy to transform imine-linked COFs into *α*-aminophosphonate-linked ones through the asymmetric hydrophosphonylation reaction. Benefiting from the phosphorous acid groups generated by acidic hydrolysis, the resultant TFPPY-BT-COF-H_2PO_3 exhibited high intrinsic proton conductivity as high as 1.12 $\times 10^{-3}$ S cm^{-1} under the conditions of 333 K and 98% relative humidity[70].

Zhao and co-workers used 2D imine-linked COF as a chemosensor for the detection of gaseous HCl. This is the first instance where the basicity of imine linkage was utilized to form iminium salt, which broadens the scope for the use of covalent modification of imine bonds[44]. Interestingly, Auras and colleagues reported the synthesis of perylene-based 2D COFs for acid vapor sensing in the same year. The imine-nitrogen lone pair is reversibly protonated when the COF powders or thin films are exposed to acidic solutions or vapors, generating iminium salts, while preserving the COF crystallinity and porosity. The protonation of the imine linkage proceeded via a two-step process in which the second protonation required stronger acids due to the monoprotonation of the neighboring imine (Supplementary FIG. 5)[105]. This stepwise protonation was supported by their corresponding assignments in the spectra. This work improves current understanding to obtain functional COFs for a wide range of applications by utilizing imine bonds as a function-determining moiety.

[H3] Structural doping

In another case, Yaghi and colleagues reported a consecutive PSM strategy to produce oxazole-linked 2D COFs, featuring a combination of linker substitution and oxidative cyclization. The resultant oxazole-linked COF exhibited increased chemical stability toward strong basic (10 M NaOH) and strong acidic solutions for 24 hours as compared to the pristine imine-linked COFs[106]. Unlike the *de novo* synthesis of benzoxazole-linked COFs reported by McGrier and co-workers[47], the PSM approach developed by Yaghi and colleagues offers a new opportunity for the access to oxazole-based COFs. Baek et al. reported the conversion of an

unstable imine-linked COF into a stable benzoxazole-linked one through post-oxidative cyclization approach. The key for successful linkage conversion lies on the type of the oxidant used. 2,3-dichloro-5,6-dicyano-1,4-benzoquinone was found to be the best oxidant in promoting the transformation of imine-linked COF into benzoxazole-linked COF. Due to the formation of robust benzoxazole linkages throughout the skeleton, the obtained benzoxazole-linked COF showed an improved chemical stability in acidic and basic media as compared with the imine-linked COF (FIG. 4b)[107].

Lotsch et al. reported that treatment of an imine-linked 2D COF with elemental sulfur resulted in conversion to a thiazole-linked COF in what they term a post-synthetic locking approach[108]. The sulfur plays two roles in the reaction: as oxidant, converting the imine to a thioamide, but also as a nucleophile to form thiazole rings through oxidative cyclization. The resulting thiazole-linked COFs preserved their crystallinity and porosity during the transformation, showing significantly enhanced chemical stability in harsh conditions. In addition, thiazole-linked COFs also revealed increased electron contrast and improved electron beam stability in comparison with their imine-linked counterparts.

Yaghi and co-workers developed a strategy involving multistep PSM, to transform an imine-linked COF into cyclic carbamate and thiocarbamate-linked COFs without alteration of the underlying topology[76]. COF-170 undergone a structural rearrangement by demethylation to form a favorable orientation stabilized by intralayer hydrogen bonding, followed by the reduction of imine and then reaction with 1,1′-thiocarbonyldiimidazole or 1,1′-carbonyldiimidazole to produce crystalline COFs with cyclic thiocarbamate or carbamate linkages that are inaccessible through *de novo* synthesis. Sequential PSM of COF linkage represents a significant step in the development of solid-state organic synthesis (FIG. 4c).

Liu and colleagues reported a facile and general strategy to transform imine-linked COFs into a series of quinoline-linked COFs by means of a Povarov reaction, reacting with various arylalkynes (MF-1a-e, around 20–30% conversion)[48]. The quinoline-linked COFs thus formed not only preserved their porosity and crystallinity, but also exhibited significantly improved chemical stability over their imine-linked counterparts, which could tolerate harsh conditions such as strong basic, acidic, and redox environments. In addition, the surface wettability of the quinoline-linked COFs could be systematically engineered due to the chemical diversity of the

substrates used for the cycloaddition. MF-1 series displayed controllable hydrophobic/hydrophilic properties of the interface with contact angle ranging from 35º to 155º. The resultant quinoline-linked MF-1 series showed enhanced hydrophobicity compared with the pristine imine-linked COF-1(FIG. 5a). Similarly, Dong et al. reported a synthetic method for the preparation of quinoline-based COFs with high crystallinity via one-pot Povarov reaction, which can complement the existing PSM approach[65]. In 2021, Baek and colleagues reported a new strategy for the synthesis of aza-bridged bis(phenanthroline) macrocycle-linked COFs without need of catalyst or solvent. Distinct from the previous approaches for the preparation of COFs using solvothermal reactions, thermally induced polymerization was first employed to synthesize the target COF[53]. Subsequently, Wang and co-workers developed a PSM strategy to transform imine-linked COFs into chromenoquinoline-linked ones via an intramolecular Povarov reaction. The key design is to use the rigid scaffold 2,5-bis(propargyloxy)-terephthalaldehyde for attaching alkyne moieties[54]. In another work, a series of bicyclic pyrano[4,3-b]pyridine-linked COFs were prepared via a cascade reaction involving imine formation, intramolecular [4 + 2] cycloaddition, and dehydroaromatization[109]. Interestingly, Cai and colleagues demonstrated that 4-carboxyl-quinoline-linked COFs could be obtained by using Doebner reaction in both one-pot and PSM methods[56]. In essence, all of these so-called new linkages belong to quinoline-derived chemistry. Benefiting from the plentiful quinoline units, these COFs showed excellent chemical stability toward strong acid and base.

Then, Zhao and co-workers reported an approach for the construction of thieno[3,2-c]pyridine-linked COFs, featuring a combination of imine formation and a postoxidative cyclization[52]. The obtained COFs (B-COF-2 and T-COF-2) exhibited improved chemical stability compared to their imine counterparts. The fused aromatic linkages increase the extent of π-electron delocalization; two of the thieno[3,2-c]pyridine-linked COFs exhibited semiconducting properties and were employed for photocatalytic regeneration of NAD^+ to NADH. The fully π-conjugated T-COF-2 displayed a high NADH regeneration yield of 74% in 10 min, which was ascribed to the presence of nitrogen-rich triazine units (Supplementary

FIG. 6). This PSM strategy affords a convenient approach for the construction of conjugated COFs with semiconducting properties.

Dong and colleagues reported a strategy for the preparation of α-aminonitrile-linked COFs with high crystallinity using multicomponent one-pot Strecker reactions[65]. The α-aminonitrile-linked COF thus obtained exhibited improved stability over the imine-linked precursor. The generated COFs featured the same structures but better crystallinity than those obtained from the PSM approach (Supplementary FIG. 7). Mechanistic studies showed that the imine-linked COFs acted as an intermediate before the final materials were produced, whereas stepwise PSM strategy proceeded via a solid-state transformation process. This one-pot multicomponent assembly strategy provides a synthetic methodology for the construction of COFs that are inaccessible under PSM conditions. Recently, they reported the preparation of propargylamine-linked chiral COFs decorated with quaternary ammonium bromide through a one-pot multicomponent reaction. The resultant (*R*)-DTP-COF-QA could be used as a catalyst for photocatalytic asymmetric oxidation of sulfides.

Boranils are a class of compounds formed by the complexation of boron(III) precursors with a large variety of anils (aniline–imines)[110]. Zhang and co-workers reported the formation of a boranil-linked COF from an imine-linked COF using a PSM strategy[51]. First, two highly crystalline 2D imine-linked COFs — TPE-COF-OH and TPE-COF-OMe — were prepared. Intralayer hydrogen bonding leads TPE-COF-OH to adopt a different (multiporous) structure. Reaction with $BF_3{\cdot}OEt_2$ leads to formation of the boranil-linked COF which effectively locks this structure in place. Notably, the fluorescence intensity of TPE-COF-BF_2 was 8 times higher than that of TPE-COF-OH under the same conditions and could be further enhanced by the addition of water (ca. 30 vol %) because water might cause the COF particles to aggregate, which suggested that the TPE-COF-BF_2 possessed the typical aggregation induced emission property after the boron complexation (FIG. 5b). The fluorescence turn-on and aggregation-induced emission in TPE-COF-BF_2 could be ascribed to the restricted rotation of imine bonds decorated with BF_2 groups. This method not only improves the structural rigidity but also eliminates the effect of electron transfer from imine bonds to the COF skeletons. Recently, Loh and co-workers demonstrated that imine-linked COFs could be converted into imidazopyridinium-linked ones through a PSM strategy[55]. Remarkably, they mentioned that the

resultant COF prepared by a two-step method exhibited a better crystallinity compared with the imine counterpart obtained by a one-pot synthesis.

[H3] Linker exchange

Linker exchange is a useful strategy for the synthesis of imine and imine-derived COFs. For example, Zhao et al. reported the COF-to-COF transformation via *in situ* linker exchange, generating an isostructural framework with reduced pore metrics while maintaining its crystallinity[111]. The team transformed TP-COF-BZ into TP-COF-DAB — replacing the benzidine moiety in TP-COF-BZ with 1,4-diaminobenzene (DAB). The addition of excess DAB (10 equiv.) shifts the equilibrium toward TP-COF-DAB under solvothermal conditions (Supplementary FIG. 8). Thus far, –N=N– has not yet been demonstrated to serve as a linkage for the synthesis of COFs. The group demonstrated that azo-linked COFs could be directly obtained from imine-linked COF precursors using linker exchange strategy[83]. This work enriches the synthetic toolbox for the preparation of crystalline COFs with azo linkage.

It should be noted that the research community has focused their attention on making single-crystalline COFs. Single-crystalline COFs are appealing as they have well-defined structures, which enable us to obtain their detailed structural information and investigate their unique physicochemical properties. Since the formation and breakage of covalent bonding are less reversible than that of coordinative bonding and hydrogen bonding, it is more challenging to make single-crystalline COFs than other porous crystals such as MOFs and HOFs. So far, there are a few reports on the preparation of single-crystalline COFs. In 2018, Wang and colleagues proposed an imine exchange strategy for the growth of single-crystalline COFs[112]. It was found that aniline played critical roles in the growth of single-crystalline COFs, acting not only as a nucleation inhibitor but also as a competitive modulator (FIG. 5c). Thus, the addition of mono-functional aniline increases the reversibility of imine bond formation and dissociation, leading to the successful preparation of single-crystalline COFs. By adding excess aniline, they successfully prepared a series of 3D imine-linked single crystal COFs in micrometer-size suitable for X-ray diffraction characterization (FIG. 5d). Recently, the group used their imine-exchange strategy to prepare a non-interpenetrated single-crystal COF (LZU-306), which was employed as a matrix-isolation platform to study the intrinsic rotation dynamics of

tetraphenylethylene (TPE) moiety[113]. Not only can the post-synthetic exchange strategy based on dynamic imine linkages be used as a method to synthesize COFs that are inaccessible using *de novo* synthesis, but it also allows for the modification of COFs by structural doping. Some representative examples have been demonstrated by different research teams[114-119].

At least eighteen types of 2D COFs with novel linkages have been successfully prepared using PSM. Imine-linked 2D COFs with novel architectures were also prepared by linker exchange. Their porosity and chemical stability are summarized in Supplementary Table 2. Most of the resultant imine-derived 2D COFs exhibit better chemical stability compared to their precursors under the same conditions, owing to the formation of robust linkages throughout the frameworks. Moreover, PSM provides great flexibility in regulating the properties of resultant materials, as pre-established COFs can be subjected to further modification for a variety of applications without altering their underlying topology. It is worth noting, however, that COFs prepared by the PSM strategies often exhibit decreased crystallinity, reduced porosity, and irreversible conversion.

[H2] Derivation by noncovalent modification

[H3] Metal coordination

Imines can act as ligands to bind transitional metal ions through the nitrogen lone pair. For example, Wang and colleagues synthesized Pd/COF-LZU1 through the post-synthetic metalation of imine-based COF-LZU1[120]. Pd(II) species were successfully intercalated between layers and could be coordinated by imines in neighbouring layers because of the ordered, eclipsed structure of COF-LZU1. The obtained Pd/COF-LZU1 proved to be a useful heterogeneous catalyst, with good catalytic performance, stability, and recyclability in the Suzki-Miyaura coupling reaction (FIG. 6a). Following this pioneering work, many metal-functionalized COFs were constructed[121-124]. Chen et al. reported two imine-linked COFs with imine linkages and hydroxyl groups as chelating sites for $Cu(OAc)_2$. The obtained Cu-COF_{HX} exhibited high catalytic performance and recyclability for selective oxidation of styrene to benzaldehyde[125]. Wang et al. demonstrated that a combination of an N-heterocyclic carbene (NHC) unit appended to a COF building blocks and an imine nitrogen from the linkage could

combine to fix active metal (Pd) into the skeleton of COF-NHC. The as-prepared Pd@COF-NHC displayed high catalytic activity for the Suzuki–Miyaura coupling reaction in aqueous media at room temperature[126]. Gao and colleagues reported the synthesis of an amine-linked COF for heterogeneous catalysis via PSM. The generated ionic COF with coupled Co^{2+} exhibited high catalytic activity and good recyclability for the cycloaddition of epoxides and CO_2[127].

[H3] Hydrogen bonding

Banerjee and colleagues reported the preparation of imine-linked COFs with enhanced chemical stability and crystallinity resulting from intralayer hydrogen bonding[128]. They developed a strategy to protect the COF interior by introducing hydroxy group (-OH) adjacent to the imine bond (N=C) in COFs, thus forming an intralayer O−H···N=C hydrogen bonding. It is worth noting that such an apparently minor difference in the structure of building blocks leads to markedly different properties in the resultant COF materials (DhaTph). DhaTph exhibited better porosity, crystallinity, and chemical stability than the precursor (DmaTph), which could be ascribed to the presence of strong intralayer O−H···N=C hydrogen bonding in DhaTph (FIG. 6b). This intralayer hydrogen bonding ensures that all phenyl moieties lie in a single plane and fixes all imine linkages in the *trans* conformation, thus reducing structural defects and enhancing the crystallinity and porosity of DhaTph versus DmaTph. In addition, the hydrogen-bonding played a crucial role in preventing basic imine nitrogen from hydrolysis in the presence of water and acid... Some other examples have been also demonstrated for the preparation of COFs with high crystallinity via intralayer hydrogen bonding.

Banerjee et al. synthesized several imine-based COFs with high chemical stability stemming from interlayer hydrogen bonding[129]. Six new imine-based COFs were prepared by the polycondensation reaction between 2,4,6-trimethoxy-1,3,5-benzenecarbaldehyde (TpOMe) and six different aromatic amines using a solid-state mixing approach. All the imine-based COFs presented high chemical stability under harsh conditions except TpOMe-BD$(NO_2)_2$. Calculations revealed that the methoxy groups present in TpOMe play a critical role in stabilizing these structures and were almost perpendicularly oriented to the adjacent layers in all the structures except TpOMe-BD$(NO_2)_2$. The C–H bonds in these methoxy groups act as

hydrogen bond donors to the imine nitrogen in an adjacent layer (FIG. 6c and 6d) with between six and twelve interlayer hydrogen bonds being formed per two stacked hexagonal pores within the COFs. Strong interlayer C−H···N hydrogen bonding sterically hinders the imine and increases hydrophobicity, making the frameworks stable in harsh conditions. One COF was transformed into a self-standing and defect-free COF membrane with high chemical stability. The prepared materials exhibited good performance toward waste solvent treatment, such as sulfuric acid recovery and the removal of toxic dyes from drinking water. Smaldone and colleagues demonstrated that the amide units present in COFs could promote the formation of interlayer hydrogen bonding between adjacent layers, resulting in higher stability and crystallinity in comparison to the counterparts without the amide functional groups[130,131].

[H3] π-π stacking

2D COF stability can be attributed to two important factors: the bonding strength between monomers within a sheet and the stacking force between adjacent sheets. The interlayer interactions have a strong influence on the crystallinity and stability of the resulting COFs. Jiang and co-workers demonstrated that resonance effects could reinforce interlayer interactions and lead to extremely stable imine-linked COFs[132]. COF (TPB-DMTP-COF) was able to endure ultraharsh conditions such as strong basic (14 M NaOH), strong acidic (12 M HCl) and boiling water for one week. By contrast, another COF (TPB-DHTP-COF) with intralayer O–H···N hydrogen bonding deteriorated after the same treatment, as observed from the crystallinity and porosity measurements (FIG. 7a, left). Given that oxygen and sulfur atoms have similar electron-donating effects, another imine-linked COF (TAPB-BMTTPA-COF) with high crystallinity was designed by integrating resonance effects at the phenyl edges. The resonance effect provided by methyl sulfide units on the phenyl edges relieves charge repulsions, induced by the polarization of C=N bond between layers, to enhance the stability of the framework skeleton[133]. Benefiting from its large mesopores, high surface area, and dense sulfide groups on the pore wall, TAPB-BMTTPA-COF exhibited high mercury removal capacity of 734 mg g^{-1} and fast adsorption equilibrium within 5 min of exposure (Supplementary FIG. 9).

Jiang and collaborators demonstrated the utilization of hyperconjugation and inductive effects to fabricate stable COFs[134]. The as-synthesized TPB-DMeTP-COF preserved its porosity and crystallinity over 7 days under harsh conditions, whereas the similar structure without hyperconjugative effects, TPB-TP-COF, exhibited a low chemical stability after the same treatment[132]. The exceptionally stable structure of TPB-DMeTP-COF could be attributed to the existence of the methyl groups on the linkers, which weakened the polarization of C=N moieties and softened the interlayer charge repulsion through hyperconjugation and inductive effects. In addition, the nitrogen sites resulted from imine linkage are beneficial for confining and stabilizing the H_3PO_4 network encapsulated in the 1D channels via hydrogen-bonding interactions. The obtained H_3PO_4@TPB-DMeTP-COF exhibited 2–8 orders of magnitude improvement in the rates of proton super flow in comparison with other analogues (FIG. 7a, right). This work represents a new direction for the preparation of stable 2D COFs by the introduction of hyperconjugation and inductive effects.

Cui and co-workers reported the use of hydrophobic effects to synthesize 2D chiral COFs-with improved stability for heterogeneous asymmetric catalysis[135]. They reported the directed-metal synthesis of chiral COF 3 and COF 4 by imine condensations of enantiopure 1,2-diaminocyclohexane with C_3-symmetric trisalicylaldehydes featuring zero or one 3-*tert*-butyl group. The resulting chiral COF 4 exhibited better chemical stability than chiral COF 3 in acidic (1 M HCl) and alkaline solutions (9 M NaOH) due to the difference in the internal structures. For chiral COF 4, hydrophobic effects provided by the bulky tert-butyl groups prevent labile Zn(salen) cores from undergoing hydrolysis in the presence of water, leading to the improved chemical stability of the structure. In contrast, chiral COF 3 without tert-butyl groups on the pore walls was more susceptible to be attacked by nucleophiles, such as water, resulting in the hydrolysis of the skeleton after the same treatment. By using post-synthetic metal exchange, several new chiral COFs were obtained with a retention of crystallinity, which were further employed as efficient heterogeneous catalysts for a plenty of asymmetric reactions, such as cyanation of aldehydes, alkene epoxidation, and Diels–Alder reaction. The team were also able to control on both chemical stability and layer stacking of 2D COFs by manipulating interlayer steric hindrance through a multivariate approach[136]. The chemical stability of imine-linked 2D COFs was affected by the density and types of incorporated alkyl groups, which protected

hydrolytically susceptible backbones and imine linkage via kinetic blocking (FIG. 7b). Benefiting from the increased chemical stability and porosity, the obtained COF showed much higher catalytic activity for the C−H borylation of arenes.

Thus, noncovalent forces, including metal-coordination, intra-/interlayer hydrogen bonding, resonance effect, hydrophobic interactions, and the combination of hyperconjugation and inductive effects, could be employed for the engineering of imine linkage. The chemical stability and porosity of these imine-linked 2D COFs are summarized in Supplementary Table 3. By using metal-coordination, the metal species could be introduced into the networks to produce metalated COFs for heterogeneous catalysis. The chemical stability of imine-linked 2D COFs could be enhanced by taking advantage of other types of noncovalent forces. In particular, the crystallinity and porosity of 2D COFs can be improved by the introduction of intramolecular hydrogen bonding.

[H2] Advantages and disadvantages

We have introduced and discussed many examples of imine and imine-derived linkages formed by covalent and noncovalent modifications. For the case of covalent modification, their advantages and disadvantages clearly depend on the precise research problem. To identify a new COF with a particular property, the PSM seems a quicker route to make many variations. However, for identifying a particular COF with desirable properties, a *de novo* synthesis might result in a more pristine/crystalline material and be optimal. For the case of noncovalent modification, their apparent advantages lie in their great flexibility in tuning the physicochemical properties of the COF. Moreover, compared with covalent modification, the progress for the development of linkage engineering using noncovalent modification to modulate the properties of COF materials lags far behind, which is ascribed to the limited choices of noncovalent forces. Therefore, other noncovalent forces such as van der Waals, aromatic stacking, dipole−dipole interaction, electrostatic interaction, and/or their combinations are expected to be introduced for linkage engineering to exert a positive influence on the properties of the prepared 2D COFs. Noncovalent modification holds a great promise for modulating physicochemical properties of 2D COFs.

[H1] Conclusions and outlook

In this article, we have highlighted the research progress regarding the development of imine and imine-derived linkage chemistry in 2D COFs. Thus far, more than forty kinds of covalent linkages ranging from reversible boroxine, imine, or azine to less reversible triazine, phenazine, olefin or dioxin have been demonstrated suitable for the construction of COFs. The formation of novel linkage involving the participation of imine bond opens a new direction for the development of COF chemistry. Generally, imine-derived COFs produced by covalent interactions exhibit better chemical stability compared to their imine-linked analogues under the same conditions, due to the formation of robust linkages throughout the frameworks. However, this approach has the disadvantage of requiring well-designed monomers or precursors. Noncovalent interactions offer a greater number of possibilities for the modulation of physicochemical properties of COFs, including crystallinity, functionality, and stability. In particular, the influences on physicochemical stability of 2D COFs exerted by covalent linkages were found to heavily depend on the types of noncovalent interactions used. The types of noncovalent interactions used to modify imine bonds rather limited, despite their importance in the field of imine-based 2D COFs. Both covalent and noncovalent interactions are important tools for manipulating the structures or properties of COFs at the molecular level. Although remarkable progress has been made in the field of COFs over the past decade, the exploration of linkage chemistry of 2D COFs is still in its infancy and several key issues remain to be addressed.

(1) COFs with novel linkages could bring new opportunities in many other fields including separation, sensing, catalysis, energy, etc. The lack of suitable chemical reactions for the construction of covalent linkage has become a bottleneck that restricts the development of COF chemistry. Although some dynamic reactions have been developed to fabricate crystalline frameworks, most of them are specific to particular molecular precursors. In other words, only some of the building blocks with suitable functional groups are able to react with each other to form crystalline networks. Consequently, considerable effort should be directed toward the exploration of novel chemical reactions involving the use of dynamic covalent bonds. Recently, effectively irreversible cascade reactions and nucleophilic aromatic substitution reactions have been used to construct extremely stable COFs. These studies also constitute a new direction for

the synthesis of COFs with enhanced performance. It is worth noting that effectively irreversible tautomerization or oxidative cyclization is usually not suitable to be directly used for preparation of highly crystalline COFs. It will always require the step in which a network is formed reversibly to allow for error correction and funneling through to afford the thermodynamic products.

(2) It is highly desirable to develop new synthetic methodologies for the derivation of established linkages in order to explore more appealing functions and innovative applications of COFs materials. Among the established linkages used in the preparation of COFs, more than a dozen types of novel linkages whose formation imines as intermediates have been developed by using covalent modification strategies. Importantly, the derivation of the established COF linkages need not be limited to imines but could be extended to other ones, such as cyanovinylene, olefin, and imidazole. Therefore, more studies should be carried out, using reported linkages as a foundation for the exploration of linkage conversion, to give rise to COFs with adjustable properties.

(3) Although the study of linkage chemistry has greatly enriched the structural diversity of 2D COFs, it is difficult to obtain detailed information about the intrinsic connection between the covalent linkage used and the properties of the resultant materials. In most cases, covalent linkage only acts as a bridge to reticulate organic units into well-defined networks rather than a functional motif in its own right . While some recent studies have shown that the conformation and types of linkages have an important influence on the magnetic, electronic, and optical properties of 2D COFs, the precise impact of covalent linkage on the overall performance of resultant materials remains ambiguous. The interplay between organic units and covalent linkage as well as the interactions between adjacent layers are difficult to investigate and assess using single crystal studies of 2D COFs remains challenging. A general method for preparing single crystal 2D COFs is highly desirable, aiming to provide more information regarding the role of linkage within 2D COFs. Moreover, there are many analytical methods to collectively characterize COF structures prepared by different approaches. For microcrystals, powder X-ray diffraction is employed to determine the crystalline structure of COF samples in combination with computational structural simulations. For single crystals, X-ray crystallography is used to solve the structures with atomic resolution accuracy. For films, grazing incidence X-ray

diffraction is often utilized to analyze the orientation and structures. As most COFs are obtained as microcrystals, it is essential to establish techniques to calculate or estimate the degree of conversion/functionalization in PSM.

(4) The use of computational chemistry is indispensable to the field of reticular chemistry in exploring their structures, interactions, and applications. While computational chemistry has been shown to be an extremely powerful tool to model and simulate the structures of COFs, there have been relatively few studies on the real roles of covalent linkages within the whole frameworks. In order to achieve a better understanding of the fascinating properties, it is anticipated that an integrated computational approach will be needed to evaluate the important functions of linkages present in COFs. The integration of computational studies with experimental data will definitely enable us to control the design and preparation of well-defined COFs.

It is generally recognized that our understanding of how covalent linkages affect the physicochemical properties of COFs is far from sufficient.

In summary, by highlighting recent significant research progress for the derivation of imine bond, we hope that this review will provide the guidance for linkage engineering of 2D COFs. We also expect that it will spark the interest of chemists, physicists, engineers, and materials scientists to further advance the growing field of COFs.

References

1 Cote, A. P. et al. Porous, crystalline, covalent organic frameworks. *Science* **310**, 1166-1170 (2005).

2 Waller, P. J., Gandara, F. & Yaghi, O. M. Chemistry of covalent organic frameworks. *Acc. Chem. Res.* **48**, 3053-3063 (2015).

3 Diercks, C. S. & Yaghi, O. M. The atom, the molecule, and the covalent organic framework. *Science* **355**, eaal1585 (2017).

4 Ben, T. & Qiu, S. Porous aromatic frameworks: synthesis, structure and functions. *CrystEngComm* **15**, 17-26 (2013).

5 Tian, Y. & Zhu, G. Porous aromatic frameworks (PAFs). *Chem. Rev.* **120**, 8934-8986 (2020).

6 Xu, Y., Jin, S., Xu, H., Nagai, A. & Jiang, D. Conjugated microporous polymers: design, synthesis and application. *Chem. Soc. Rev.* **42**, 8012-8031 (2013).

7 Taylor, D., Dalgarno, S. J., Xu, Z. & Vilela, F. Conjugated porous polymers: incredibly versatile materials with far-reaching applications. *Chem. Soc. Rev.* **49**, 3981-4042 (2020).

8 Lee, J. M. & Cooper, A. I. Advances in conjugated microporous polymers. *Chem. Rev.* **120**, 2171-2214 (2020).

9 Ramimoghadam, D., Gray, E. M. & Webb, C. J. Review of polymers of intrinsic microporosity for hydrogen storage applications. *Int. J. Hydrogen Energy* **41**, 16944-16965 (2016).

10 Low, Z. X., Budd, P. M., McKeown, N. B. & Patterson, D. A. Gas permeation properties, physical aging, and its mitigation in high free volume glassy polymers. *Chem. Rev.* **118**, 5871-5911 (2018).

11 Tan, L. & Tan, B. Hypercrosslinked porous polymer materials: design, synthesis, and applications. *Chem. Soc. Rev.* **46**, 3322-3356 (2017).

12 Weckhuysen, B. M. & Yu, J. Recent advances in zeolite chemistry and catalysis. *Chem. Soc. Rev.* **44**, 7022-7024 (2015).

13 Dusselier, M. & Davis, M. E. Small-pore zeolites: synthesis and catalysis. *Chem. Rev.* **118**, 5265-5329 (2018).

14 Weng, Q., Wang, X., Wang, X., Bando, Y. & Golberg, D. Functionalized hexagonal boron nitride nanomaterials: emerging properties and applications. *Chem. Soc. Rev.* **45**, 3989-4012 (2016).

15 Shi, E. et al. Two-dimensional halide perovskite nanomaterials and heterostructures. *Chem. Soc. Rev.* **47**, 6046-6072 (2018).

16 O'Keeffe, M. Design of MOFs and intellectual content in reticular chemistry: a personal view. *Chem. Soc. Rev.* **38**, 1215-1217 (2009).

17 Zhou, H. C., Long, J. R. & Yaghi, O. M. Introduction to metal-organic frameworks. *Chem. Rev.* **112**, 673-674 (2012).

18 Liu, R. et al. Covalent organic frameworks: an ideal platform for designing ordered materials and advanced applications. *Chem. Soc. Rev.* **50**, 120-242 (2021).

19 Liang, R.-R., Jiang, S.-Y., A, R.-H. & Zhao, X. Two-dimensional covalent organic frameworks with hierarchical porosity. *Chem. Soc. Rev.* **49**, 3920-3951 (2020).

20 Zhang, L., Yi, L., Sun, Z. J. & Deng, H. Covalent organic frameworks for optical applications. *Aggregate* **2**, e24 (2021).

21 Banerjee, T., Podjaski, F., Kröger, J., Biswal, B. P. & Lotsch, B. V. Polymer photocatalysts for solar-to-chemical energy conversion. *Nat. Rev. Mater.* **6**, 168-190 (2021).

22 Zhao, X., Pachfule, P. & Thomas, A. Covalent organic frameworks (COFs) for electrochemical applications. *Chem. Soc. Rev.* **50**, 6871-6913 (2021).

23 Feng, L., Qian, C. & Zhao, Y. Recent advances in covalent organic framework-based nanosystems for bioimaging and therapeutic applications. *ACS Mater. Lett.* **2**, 1074-1092 (2020).

24 Zhou, T., Zhao, Y., Choi, J. W. & Coskun, A. Lithium-salt mediated synthesis of a covalent triazine framework for highly stable lithium metal batteries. *Angew. Chem. Int. Ed.* **58**, 16795-16799 (2019).

25 Wang, D.-G. *et al.* Covalent organic framework-based materials for energy applications. *Energy Environ. Sci.* **14**, 688-728 (2021).

26 Geng, K. *et al.* Covalent organic frameworks: design, synthesis, and functions. *Chem. Rev.* **120**, 8814-8933 (2020).

27 Lyle, S. J., Waller, P. J. & Yaghi, O. M. Covalent organic frameworks: organic chemistry extended into two and three dimensions. *Trends Chem.* **1**, 172-184 (2019).

28 Jiang, J., Zhao, Y. & Yaghi, O. M. Covalent chemistry beyond molecules. *J. Am. Chem. Soc.* **138**, 3255-3265 (2016).

29 Yaghi, O. M. Reticular chemistry-construction, properties, and precision reactions of frameworks. *J. Am. Chem. Soc.* **138**, 15507-15509, (2016).

30 Rowan, S. J., Cantrill S. J., Cousins G. R. L., Sanders, J. K. M. & Stoddart, J. F. Dynamic covalent chemistry. *Angew. Chem. Int. Ed.* **41**, 898-952 (2002).

31 Jin, Y., Yu, C., Denman, R. J. & Zhang, W. Recent advances in dynamic covalent chemistry. *Chem. Soc. Rev.* **42**, 6634-6654 (2013).

32 Jin, Y., Wang, Q., Taynton, P. & Zhang, W. Dynamic covalent chemistry approaches toward macrocycles, molecular cages, and polymers. *Acc. Chem. Res.* **47**, 1575-1586 (2014).

33 Beuerle, F. & Gole, B. Covalent organic frameworks and cage compounds: design and applications of polymeric and discrete organic scaffolds. *Angew. Chem. Int. Ed.* **57**, 4850-4878 (2018).

34 Medina, D. D., Sick, T. & Bein, T. Photoactive and conducting covalent organic frameworks. *Adv. Energy Mater.* **7**, 1700387 (2017).

35 Guan, X., Chen, F., Fang, Q. & Qiu, S. Design and applications of three dimensional covalent organic frameworks. *Chem. Soc. Rev.* **49**, 1357-1384 (2020).

36 Uribe-Romo, F. J. et al. A crystalline imine-linked 3-D porous covalent organic framework. *J. Am. Chem. Soc.* **131**, 4570-4571 (2009).

37 Segura, J. L., Mancheno, M. J. & Zamora, F. Covalent organic frameworks based on Schiff-base chemistry: synthesis, properties and potential applications. *Chem. Soc. Rev.* **45**, 5635-5671 (2016).

38 Yusran, Y., Li, H., Guan, X., Fang, Q. & Qiu, S. Covalent organic frameworks for catalysis. *EnergyChem* **2**, 100035 (2020).

39 Hu, J., Gupta, S. K., Ozdemir, J. & Beyzavi, M. H. Applications of dynamic covalent chemistry concept towards tailored covalent organic framework nanomaterials: a review. *ACS Appl. Nano Mater.* **3**, 6239-6269 (2020).

40 Hunt, J. R. Doonan, C. J., LeVangie, J. D., Côté, A. P. & Yaghi, O. M. Reticular synthesis of covalent organic borosilicate frameworks. *J. Am. Chem. Soc.* **130**, 11872-11873 (2018).

41 Du, Y. et al. Ionic covalent organic frameworks with spiroborate linkage. *Angew. Chem. Int. Ed.* **55**, 1737-1741 (2016).

42 Uribe-Romo, F. J., Doonan, C. J., Furukawa, H., Oisaki, K. & Yaghi, O. M. Crystalline covalent organic frameworks with hydrazone linkages. *J. Am. Chem. Soc.* **133**, 11478-11481 (2011).

43 Dalapati, S. *et al.* An azine-linked covalent organic framework. *J. Am. Chem. Soc.* **135**, 17310-17313 (2013).

44 Cui, F.-Z. et al. A gaseous hydrogen chloride chemosensor based on a 2D covalent organic framework. *Chem. Commun.* **55**, 4550-4553 (2019).

45 Kuhn, P., Antonietti, M. & Thomas, A. Porous, covalent triazine-based frameworks prepared by ionothermal synthesis. *Angew. Chem. Int. Ed.* **47**, 3450-3453 (2008).

46 Guo, J. et al. Conjugated organic framework with three-dimensionally ordered stable structure and delocalized π clouds. *Nat. Commun.* **4**, 2736 (2013).

47 Pyles, D. A., Crowe, J. W., Baldwin, L. A. & McGrier, P. L. Synthesis of benzobisoxazole-linked two-dimensional covalent organic frameworks and their carbon dioxide capture properties. *ACS Macro Lett.* **5**, 1055-1058 (2016).

48 Li, X. et al. Facile transformation of imine covalent organic frameworks into ultrastable crystalline porous aromatic frameworks. *Nat. Commun.* **9**, 2998 (2018).

49 Wang, P. L., Ding, S. Y., Zhang, Z. C., Wang, Z. P. & Wang, W. Constructing Robust Covalent Organic Frameworks via Multicomponent Reactions. *J. Am. Chem. Soc.* **141**, 18004-18008 (2019).

50 Liu, J. et al. Pyrimidazole-based covalent organic frameworks: integrating functionality and ultrastability via isocyanide chemistry. *J. Am. Chem. Soc.* **142**, 20956-20961 (2020).

51 Peng, Y. et al. Intramolecular hydrogen bonding-based topology regulation of two-dimensional covalent organic frameworks. *J. Am. Chem. Soc.* **142**, 13162-13169 (2020).

52 Wang, Y. et al. Construction of fully conjugated covalent organic frameworks via facile linkage conversion for efficient photoenzymatic catalysis. *J. Am. Chem. Soc.* **142**, 5958-5963 (2020).

53 Jiang, Y. *et al.* Catalyst- and solvent-free synthesis of a chemically stable aza-bridged bis(phenanthroline) macrocycle-linked covalent organic framework. *Angew. Chem. Int. Ed.* **60**, 17191-17197 (2021).

54 Ren, X. R. *et al.* Constructing stable chromenoquinoline-based covalent organic frameworks via intramolecular Povarov reaction. *J. Am. Chem. Soc.* **144**, 2488-2494 (2022).

55 Li, X. *et al.* Constructing ambivalent imidazopyridinium-linked covalent organic frameworks. *Nat. Synth.* **1**, 382-392 (2022).

56 Yang, Y. *et al.* Constructing chemical stable 4-carboxyl-quinoline linked covalent organic frameworks via Doebner reaction for nanofiltration. *Nat. Commun.* **13**, 2615 (2022).

57 Kandambeth, S. et al. Construction of crystalline 2D covalent organic frameworks with remarkable chemical (acid/base) stability via a combined reversible and irreversible route. *J. Am. Chem. Soc.* **134**, 19524-19527 (2012).

58 Nagai, A. et al. A Squaraine-linked mesoporous covalent organic framework. *Angew. Chem. Int. Ed.* **52**, 3770-3774 (2013).

59 Fang, Q. et al. Designed synthesis of large-pore crystalline polyimide covalent organic frameworks. *Nat. Commun.* **5**, 4503 (2014).

60 Waller, P. J. et al. Chemical conversion of linkages in covalent organic frameworks. *J. Am. Chem. Soc.* **138**, 15519-15522 (2016).

61 Das, G. et al. Viologen-based conjugated covalent organic networks via Zincke reaction. *J. Am. Chem. Soc.* **139**, 9558-9565 (2017).

62 Zhao, C. et al. Urea-linked covalent organic frameworks. *J. Am. Chem. Soc.* **140**, 16438-16441 (2018).

63 Liu, H. et al. Covalent organic frameworks linked by amine bonding for concerted electrochemical reduction of CO_2. *Chem* **4**, 1696-1709 (2018).

64 Jiang, S.-Y. et al. Aminal-linked covalent organic frameworks through condensation of secondary amine with aldehyde. *J. Am. Chem. Soc.* **141**, 14981-14986 (2019).

65 Li, X. T. et al. Construction of covalent organic frameworks via three-component one-pot Strecker and Povarov reactions. *J. Am. Chem. Soc.* **142**, 6521-6526 (2020).

66 Li, C. et al. Asymmetric photocatalysis over robust covalent organic frameworks with tetrahydroquinoline linkage. *Chin. J. Catal.* **41**, 1288-1297 (2020).

67 Wang, J. C., Kan, X., Shang, J. Y., Qiao, H. & Dong, Y. B. Catalytic asymmetric synthesis of chiral covalent organic frameworks from prochiral monomers for heterogeneous asymmetric catalysis. *J. Am. Chem. Soc.* **142**, 16915-16920 (2020).

68 Yang, Z. et al. Arylamine-linked 2D covalent organic frameworks for efficient pseudocapacitive energy storage. *Angew. Chem. Int. Ed.* **60**, 20754-20759 (2021).

69 Kuehl, V. A. et al. Synthesis, postsynthetic modifications, and applications of the first quinoxaline-based covalent organic framework. *ACS Appl. Mater. Interfaces* **13**, 37494-37499 (2021).

70 Lu, Z. *et al.* Asymmetric hydrophosphonylation of imines to construct highly stable covalent organic frameworks with efficient intrinsic proton conductivity. *J. Am. Chem. Soc.* **144**, 9624-9633 (2022).

71 Nguyen, H. L. *et al.* Hydrazine-hydrazide-linked covalent organic frameworks for water harvesting. *ACS Cent. Sci.* doi: 10.1021/acscentsci.2c00398 (2022).

72 Zhuang, X. et al. A two-dimensional conjugated polymer framework with fully sp^2-bonded carbon skeleton. *Polym. Chem.* **7**, 4176-4181 (2016).

73 Lyu, H., Diercks, C. S., Zhu, C. & Yaghi, O. M. Porous crystalline olefin-linked covalent organic frameworks. *J. Am. Chem. Soc.* **141**, 6848-6852 (2019).

74 Su, Y. et al. Crystalline and stable benzofuran-linked covalent organic frameworks from irreversible cascade reactions. *J. Am. Chem. Soc.* **142**, 13316-13321 (2020).

75 Zhang, B. et al. Crystalline dioxin-linked covalent organic frameworks from irreversible reactions. *J. Am. Chem. Soc.* **140**, 12715-12719 (2018).

76 Lyle, S. J. et al. Multistep solid-state organic synthesis of carbamate-linked covalent organic frameworks. *J. Am. Chem. Soc.* **141**, 11253-11258 (2019).

77 Zhao, C., Lyu, H., Ji, Z., Zhu, C. & Yaghi, O. M. Ester-linked crystalline covalent organic frameworks. *J. Am. Chem. Soc.* **142**, 14450-14454 (2020).

78 Jackson, K. T., Reich, T. E. & El-Kaderi, H. M. Targeted synthesis of a porous borazine-linked covalent organic framework. *Chem. Commun.* **48**, 8823-8825 (2012).

79 Beaudoin, D., Maris, T. & Wuest, J. D. Constructing monocrystalline covalent organic networks by polymerization. *Nat. Chem.* **5**, 830-834 (2013).

80 Yahiaoui, O. *et al.* 3D anionic silicate covalent organic framework with srs topology. *J. Am. Chem. Soc.* **140**, 5330-5333 (2018).

81 Zhou, D., Tan, X., Wu, H., Tian, L. & Li, M. Synthesis of C-C bonded two-dimensional conjugated covalent organic framework films by Suzuki polymerization on a liquid-liquid interface. *Angew. Chem. Int. Ed.* **58**, 1376-1381 (2019).

82 Gropp, C., Ma, T., Hanikel, N. & Yaghi, O. M. Design of higher valency in covalent organic frameworks. *Science* **370**, eabd6406 (2020).

83 Zhou, Z. B. *et al.* Toward azo-linked covalent organic frameworks by developing linkage chemistry via linker exchange. *Nat. Commun.* **13**, 2180 (2022).

84 Fang, Q. *et al.* 3D microporous base-functionalized covalent organic frameworks for size-selective catalysis. *Angew. Chem. Int. Ed.* **53**, 2878-2882 (2014).

85 Das, G. et al. Chemical sensing in two dimensional porous covalent organic nanosheets. *Chem. Sci.* **6**, 3931-3939 (2015).

86 Sun, Q., Aguila, B., Perman, J., Nguyen, N. & Ma, S. Q. Flexibility matters: cooperative active sites in covalent organic framework and threaded ionic polymer. *J. Am. Chem. Soc.* **138**, 15790-15796 (2016).

87 Wang, X. et al. Sulfone-containing covalent organic frameworks for photocatalytic hydrogen evolution from water. *Nat. Chem.* **10**, 1180-1189 (2018).

88 Wang, H. et al. Integrating suitable linkage of covalent organic frameworks into covalently bridged inorganic/organic hybrids toward efficient photocatalysis. *J. Am. Chem. Soc.* **142**, 4862-4871 (2020).

89 Zhao, X. et al. Macro/microporous covalent organic frameworks for efficient electrocatalysis. *J. Am. Chem. Soc.* **141**, 6623-6630 (2019).

90 Ning, G. H. et al. Salicylideneanilines-based covalent organic frameworks as chemoselective molecular sieves. *J. Am. Chem. Soc.* **139**, 8897-8904 (2017).

91 Haldar, S. et al. Anthracene-resorcinol derived covalent organic framework as flexible white light emitter. *J. Am. Chem. Soc.* **140**, 13367-13374 (2018).

92 Jhulki, S. et al. Humidity sensing through reversible isomerization of a covalent organic framework. *J. Am. Chem. Soc.* **142**, 783-791 (2020).

93 Wang et al. Covalent triazine frameworks via a low-temperature polycondensation approach. *Angew. Chem. Int. Ed.* **56**, 14149-14153 (2017).

94 Zhang, S. et al. Strong-base-assisted synthesis of a crystalline covalent triazine framework with high hydrophilicity via benzylamine monomer for photocatalytic water splitting. *Angew. Chem. Int. Ed.* **59**, 6007-6014 (2020).

95 Wei, P. F. et al. Benzoxazole-linked ultrastable covalent organic frameworks for photocatalysis. *J. Am. Chem. Soc.* **140**, 4623-4631 (2018).

96 Ranjeesh, K. C. *et al.* Imidazole-linked crystalline two-dimensional polymer with ultrahigh proton-conductivity. *J. Am. Chem. Soc.* **141**, 14950-14954 (2019).

97 Wang, K. et al. Synthesis of stable thiazole-linked covalent organic frameworks via a multicomponent reaction. *J. Am. Chem. Soc.* **142**, 11131-11138 (2020).

98 Grunenberg, L. et al. Amine-linked covalent organic frameworks as a platform for postsynthetic structure interconversion and pore-wall modification. *J. Am. Chem. Soc.* **143**, 3430-3438 (2021).

99 Zhang, M. et al. Construction of flexible amine-linked covalent organic frameworks by catalysis and reduction of formic acid via the Eschweiler-Clarke reaction. *Angew. Chem. Int. Ed.* **60**, 12396-12405 (2021).

100 Meyer, C. D., Joiner, C. S. & Stoddart, J. F. Template-directed synthesis employing reversible imine bond formation. *Chem. Soc. Rev.* **36**, 1705-1723 (2007).

101 Han, X., Huang, J., Yuan, C., Liu, Y. & Cui, Y. Chiral 3D covalent organic frameworks for high performance liquid chromatographic enantioseparation. *J. Am. Chem. Soc.* **140**, 892-895 (2018).

102 Qian, H. L., Meng, F. L., Yang, C. X. & Yan, X. P. Irreversible amide-linked covalent organic framework for selective and ultrafast gold recovery. *Angew. Chem. Int. Ed.* **59**, 17607-17613 (2020).

103 Zhou, Z. B. *et al.* A facile, efficient, and general synthetic method to amide-linked covalent organic frameworks. *J. Am. Chem. Soc.* **144**, 1138-1143 (2022).

104 Hu, J. *et al.* Catalyst-enabled in situ linkage reduction in imine covalent organic frameworks. *ACS Appl. Mater. Interfaces* **13**, 21740-21747 (2021).

105 Kulkarni, R. *et al.* Real-time optical and electronic sensing with a β-amino enone linked, triazine-containing 2D covalent organic framework. *Nat. Commun.* **10**, 3228 (2019).

106 Waller, P. J., AlFaraj, Y. S., Diercks, C. S., Jarenwattananon, N. N. & Yaghi, O. M. Conversion of imine to oxazole and thiazole linkages in covalent organic frameworks. *J. Am. Chem. Soc.* **140**, 9099-9103 (2018).

107 Seo, J. M., Noh, H. J., Jeong, H. Y. & Baek, J. B. Converting unstable imine-linked network into stable aromatic benzoxazole-linked one via post-oxidative cyclization. *J. Am. Chem. Soc.* **141**, 11786-11790 (2019).

108 Haase, F. et al. Topochemical conversion of an imine- into a thiazole-linked covalent organic framework enabling real structure analysis. *Nat. Commun.* **9**, 2600 (2018).

109 Feng, J. *et al.* Fused-ring-linked covalent organic frameworks. *J. Am. Chem. Soc.* **144**, 6594-6603 (2022).

110 Frath, D., Azizi, S., Ulrich, G., Retailleau, P. & Ziessel, R. Facile synthesis of highly fluorescent boranil complexes. *Org. Lett.* **13**, 13, 3414-3417 (2011).

111 Qian, C. et al. Toward covalent organic frameworks bearing three different kinds of pores: the strategy for construction and COF-to-COF transformation via heterogeneous linker exchange. *J. Am. Chem. Soc.* **139**, 6736-6743 (2017).

112 Ma, T. et al. Single-crystal X-ray diffraction structures of covalent organic frameworks. *Science* **361**, 48-52 (2018).

113 Liang, L. et al. Non-interpenetrated single-crystal covalent organic frameworks. *Angew. Chem. Int. Ed.* **59**, 17991-17995 (2020).

114 Zhang, G. et al. Construction of a hierarchical architecture of covalent organic frameworks via a postsynthetic approach. *J. Am. Chem. Soc.* **140**, 2602-2609 (2018).

115 Qian, H.-L., Li, Y. & Yan, X.-P. A building block exchange strategy for the rational fabrication of *de novo* unreachable amino-functionalized imine-linked covalent organic frameworks. *J. Mater. Chem. A* **6**, 17307-17311 (2018).

116 Daugherty, M. C. et al. Improved synthesis of β-ketoenamine-linked covalent organic frameworks via monomer exchange reactions. *Chem. Commun.* **55**, 2680-2683 (2019).

117 Li, Z., Ding, X., Feng, Y., Feng, W. & Han, B.-H. Structural and dimensional transformations between covalent organic frameworks via linker exchange. *Macromolecules* **52**, 1257-1265 (2019).

118 Miao, Z. et al. A novel strategy for the construction of covalent organic frameworks from nonporous covalent organic polymers. *Angew. Chem. Int. Ed.* **58**, 4906-4910 (2019).

119 Zhai, Y. et al. Construction of covalent-organic frameworks (COFs) from amorphous covalent organic polymers via linkage replacement. *Angew. Chem. Int. Ed.* **58**, 17679-17683 (2019).

120 Ding, S. Y. et al. Construction of covalent organic framework for catalysis: pd/cof-lzu1 in Suzuki-Miyaura coupling reaction. *J. Am. Chem. Soc.* **133**, 19816-19822 (2011).

121 Leng, W. G. et al. Sophisticated design of covalent organic frameworks with controllable bimetallic docking for a cascade reaction. *Chem. Eur. J.* **22**, 9087-9091 (2016).

122 Li, H. et al. Synthesis of covalent organic frameworks via in situ salen skeleton formation for catalytic applications. *J. Mater. Chem. A* **7**, 5482-5492 (2019).

123 Qian, C. et al. Linkage engineering by harnessing supramolecular interactions to fabricate 2d hydrazone-linked covalent organic framework platforms toward advanced catalysis. *J. Am. Chem. Soc.* **142**, 18138-18149 (2020).

124 Chen, H. et al. A visible-light-harvesting covalent organic framework bearing single nickel sites as a highly efficient sulfur-carbon cross-coupling dual catalyst. *Angew. Chem. Int. Ed.* **60**, 10820-10827 (2021).

125 Mu, M. et al. Two-dimensional imine-linked covalent organic frameworks as a platform for selective oxidation of olefins. *ACS Appl. Mater. Interfaces* **9***,* 22856-22863 (2017).

126 Yang, J. et al. An N-heterocyclic carbene-functionalised covalent organic framework with atomically dispersed palladium for coupling reactions under mild conditions. *Green Chem.* **21**, 5267-5273 (2019).

127 Yan, Q. *et al.* Post-synthetic modification of imine linkages of a covalent organic framework for its catalysis application. *RSC Adv.* **10**, 17396-17403, doi:10.1039/d0ra02142c (2020).

128 Kandambeth, S. et al. Enhancement of chemical stability and crystallinity in porphyrin-containing covalent organic frameworks by intramolecular hydrogen bonds. *Angew. Chem. Int. Ed.* **52**, 13052-13056 (2013).

129 Halder, A. *et al.* Ultrastable imine-based covalent organic frameworks for sulfuric acid recovery: an effect of interlayer hydrogen bonding. *Angew. Chem. Int. Ed.* **57**, 5797-5802 (2018).

130 Alahakoon, S. B. *et al.* 2D-covalent organic frameworks with interlayer hydrogen bonding oriented through designed nonplanarity. *J. Am. Chem. Soc.* **142**, 12987-12994 (2020).

131 Diwakara, S. D. *et al.* Supramolecular reinforcement of a large-pore 2D covalent organic framework. *J. Am. Chem. Soc.* **144**, 2468-2473 (2022).

132 Xu, H., Gao, J. & Jiang, D. L. Stable, crystalline, porous, covalent organic frameworks as a platform for chiral organocatalysts. *Nat. Chem.* **7**, 905-912 (2015).

133 Huang, N., Zhai, L. P., Xu, H. & Jiang, D. L. Stable covalent organic frameworks for exceptional mercury removal from aqueous solutions. *J. Am. Chem. Soc.* **139**, 2428-2434 (2017).

134 Tao, S. *et al.* Confining H_3PO_4 network in covalent organic frameworks enables proton super flow. *Nat. Commun.* **11**, 1981 (2020).

135 Han, X. et al. Chiral covalent organic frameworks with high chemical stability for heterogeneous asymmetric catalysis. *J. Am. Chem. Soc.* **139**, 8693-8697 (2017).

136 Wu, X., Han, X., Liu, Y., Liu, Y. & Cui, Y. Control interlayer stacking and chemical stability of two-dimensional covalent organic frameworks via steric tuning. *J. Am. Chem. Soc.* **140**, 16124-16133 (2018).

Acknowledgements

This research is supported by the Singapore Academic Research Funds (RG3/21 and MOET2EP10120-0003), the Singapore Agency for Science, Technology and Research (A*STAR) under the Manufacturing, Trade and Connectivity Individual Research Grant (M21K2c0105), the Shanghai Pujiang Program (21PJ1400300) and the Fundamental Research Funds for the Central Universities (2232022D-06). We thank Prof. Hongwei Wu for helpful discussions.

Author contributions

C. Q. researched data for the article and contributed to writing, preparation of figures, and reviewing and editing the manuscript. L. F. and W. L. T. revised the manuscript. J. L., W. Z. and

D. W. contributed to the discussion of content. Y. Z. revised the manuscript, designed figures and conceived the overall direction of the manuscript. All authors have given approval to the final version of the manuscript.

Competing interest statement

The authors declare no competing interests.

Peer review information

Nature Reviews Chemistry thanks A. Coskun, W. Zhang and the other, anonymous, reviewer(s) for their contribution to the peer review of this work.

Fig. 1 | **A timeline of advancements made in the development of linkage chemistry for the derivation of imine bond**

Fig. 2 | **Representative examples of imine-derived COFs obtained by *de novo* synthesis**. **a** | Schematic representation for the synthesis of TpPa-1 and TpPa-2 via cascade reactions. **b** | Synthesis of solvatochromic SA-COF featuring *trans*-keto and *cis*-keto form with the aid of H_2O. **c** | Chemical structure of the IISERP-COF7. The inset image shows dispersion of the COF suspended in NMP pictured under a UV lamp. **d** | Schematic representation of iminol-to-ketoenamine tautomerism and the structure of TAPB-PDA-OH.

Fig. 3 | **Representative examples of imine-derived COFs obtained by *de novo* synthesis**. **a** | Schematic representation for the fabrication of CTF-HUST-A1 from amidine dihydrochloride and benzylamine precursors. **b** | Comparison of hydrogen evolution rates of CTF-HUST-A1. **c** | Schematic representation for the syntheses of urea-linked COF-117 and COF-118. **d** | One-pot preparation of benzoxazole-linked LZU-190 via cascade reactions. **e** | One-pot construction of pyrimidazole-linked COFs from isocyanides, 2-aminopyridines, and aldehydes. **f** | Synthesis and structure of thiazole-linked TZ-COF-4 by a multicomponent reaction.

Fig. 4 | **Typical examples of imine-derived COFs prepared by post-synthetic modification approaches**. **a** | Transformation of imine-linked COF (1) into amide-linked COF (1') via direct oxidation of linkages. **b** | Transformation of the imine-linked COF into benzoxazole-linked COF by oxidative cyclization. **c** | Schematic representation for the synthesis of COFs with cyclic carbamate and thiocarbamate linkages via a three-step solid-state synthesis.

Fig. 5 | **Typical examples of imine-derived COFs prepared by post-synthetic modification**. **a** | Transformation of imine-linked COF-1 into quinoline-linked MF-1a-e series using the Povarov reaction. **b** | Transformation of imine-linked TPE-COF-OH into boranil-linked TPE-COF-BF_2 via complexation with the boron trifluoride etherate. **c** | Proposed mechanism for the growth of single-crystalline COFs via imine exchange. **b** | Chemical structure and scanning electron microscopy (SEM) images of the COF-300. Part **d** is adapted from REF.[112] Springer Nature Limited.

Fig. 6 | **Typical examples for the preparation of imine-linked COFs based on various noncovalent interactions**. **a** | Schematic representation for the construction of Pd/COF-LZU1 by direct metalation of COF-LZU1. **b** | Syntheses and structures of DhaTph and DmaTph by the condensation of square Tph precursor and linear Dma/Dha monomer. **c** | General synthetic routes to imine-based COFs via a PTSA-mediated solid-state mixing approach. **d** | Intra-/intralayer hydrogen bonding presented in the layered structures of TpOMe-BD$(NO_2)_2$ and TpOMe-Pa1. Parts **d** is adapted from REF.[129] Wiley-VCH.

Fig. 7 | **Typical examples for the synthesis of imine-linked COFs based on various noncovalent interactions**. **a** | Schematic representation for the preparation of TPB-DMTP-COF (left) and TPB-DMeTP-COF (right). **b** | Schematic representation for the synthesis of chiral COF 3 and COF 4.

TOC Graphic

Linkage chemistry is crucial for controllable synthesis and physicochemical properties of covalent organic frameworks (COFs). This review describes linkage chemistry for the derivation of imine bond by covalent and noncovalent bonding in two-dimensional COFs.