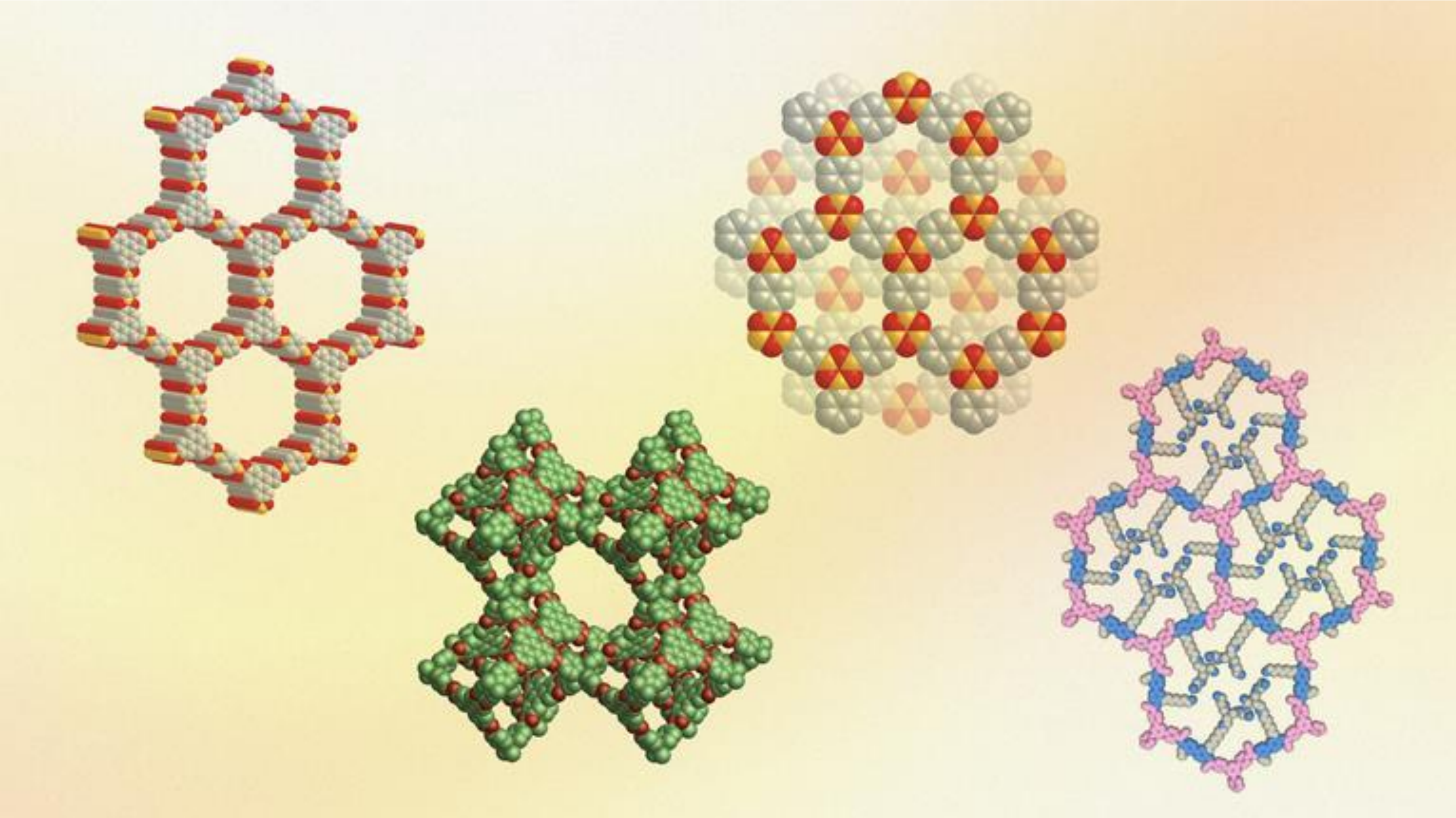

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COFs head for the big time

BY  NINA NOTMAN | 10 MARCH 2025

Two decades on from the first reported covalent organic frameworks, Nina Notman investigates what their future holds

In Nobel laureate Roald Hoffmann's 1993 essay in *Scientific American* he pondered the future of organic chemistry, noting that the field's tools at that time predominantly only worked in zero dimensions. 'One subculture of organic chemists has learned to exercise control in one dimension. These are polymer chemists, the chain builders,' he wrote. 'But in two or three dimensions, it's a synthetic wasteland. The methodology for exercising control so that one can make … extended structures on demand is nearly absent.'

'When I started as assistant professor that was the state of affairs,' says Omar Yaghi of the University of California, Berkeley, US. 'We were interested in using the power of organic chemistry to make [2D and 3D] structures that ultimately could be functionalisable.' Metal–organic frameworks (MOFs) came first. Yaghi published one of the first of these highly-ordered extended open frameworks in *Nature* in 1995; it contained repetitive networks of building blocks composed of metal nodes joined together by charged organic linkers to form strong bonds.

Ten years later, Yaghi's group succeeded in crystallising the first fully organic structures of this type – constructions that he coined covalent organic frameworks (COFs), due to them being held together by covalent bonds. COFs are composed of light elements such as hydrogen, carbon, boron, nitrogen and oxygen. Yaghi's group published the first 2D COFs in 2005 and the first 3D versions in 2007. Both contained highly reversible boron–oxygen linkages. Microscopic reversibility is key to enabling crystallisation, as it enables the crystals to be dissolved back to their original building blocks and recrystallised repeatedly until a uniform structure forms.

COFs can be made from almost all common organic linkages

Prior to this, Yaghi's team had spent years trying to create boron–oxygen containing COFs, always ending up with amorphous structures instead. The initial breakthrough came when an undergraduate student, Annabelle Benin, observed a small sharp peak within the background hump of an x-ray diffraction pattern in one of the experiments. 'That told us that there is some organisation of large molecules… I was really excited,' Yaghi says. His postdoc, Adrien Côté, then optimised the reaction conditions to perfect the crystallisation process and make the aptly named COF-1.

Since 2005, thousands of novel COFs have been made in the lab, some with linkages that are progressively less reversible (but still able to be crystallised) and tools have been developed to transform COF appendages after they have been built. 'With these developments, COFs can be made from almost all common organic linkages, thus vastly expanding the scope of organic chemistry,' says Yaghi.

Putting holes to work

As with MOFs, it is the multitude of permanent pores (voids) within the framework of COFs, and the resulting huge internal surface areas, that scientists hope to exploit commercially. 'COFs have immense potential across diverse applications,' says Rahul Banerjee, an expert in porous polymers at the Indian Institute of Science Education and Research Kolkata.

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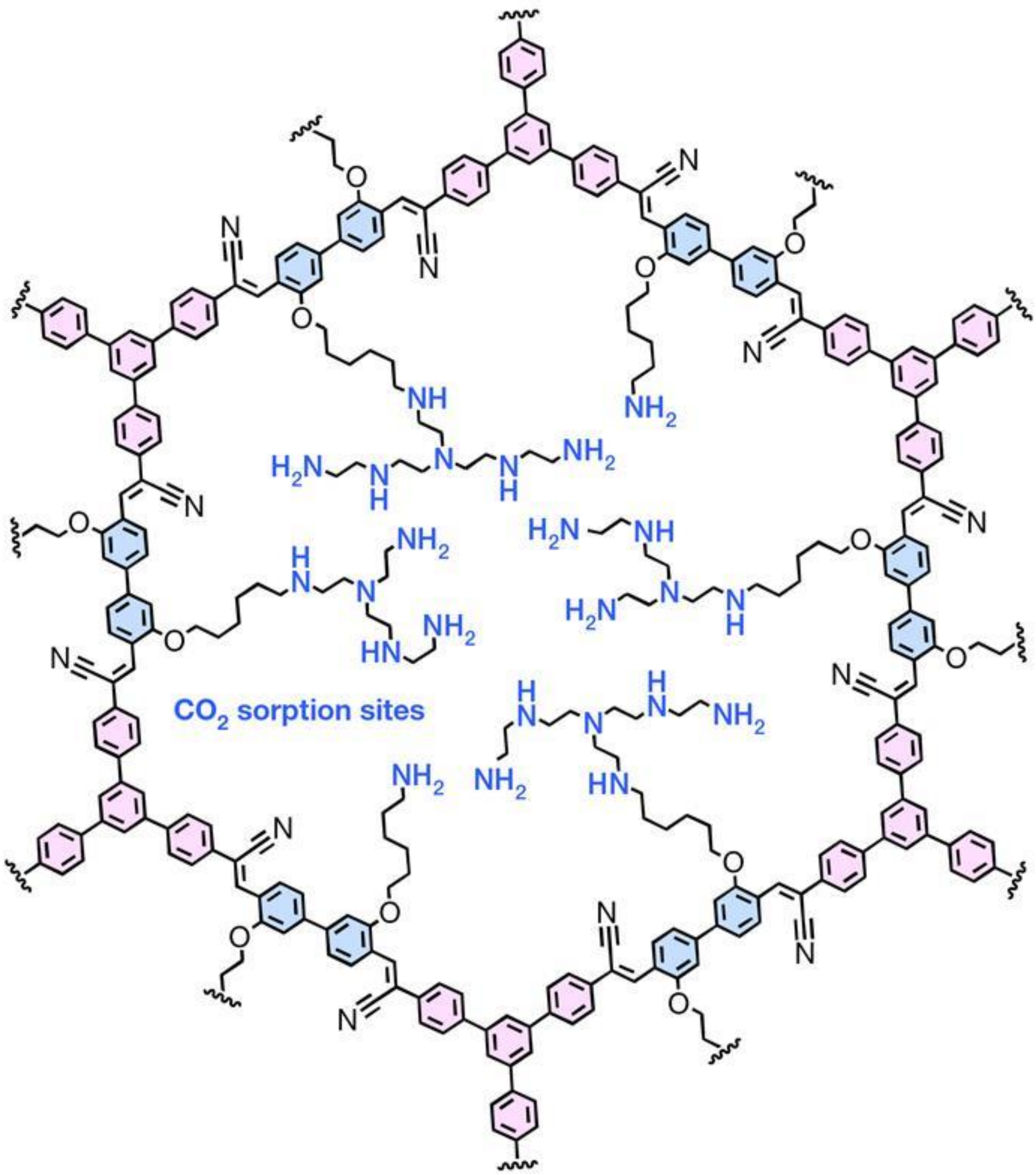
COFs can store large volumes of gas in very compact spaces, making them an appealing prospect for gas storage. Fuel tanks for hydrogen- or methane-powered vehicles could store a lot more gas than standard tanks if they contained COFs, allowing them to travel further between fuelling.

Another potential application for COFs is selectively plucking desired molecules out of mixtures. In 2020, for example, Yaghi reported an imine-linked COF able to extract water from air. He has already launched a spin-off company to commercialise water harvesting MOF devices able to provide drinking water in water-scarce regions. 'COFs could store a lot more per unit weight water compared to MOFs,' says Yaghi, 'because you can functionalise [their pores] with hydrogen bond donors and hydrogen bond acceptors easily.'



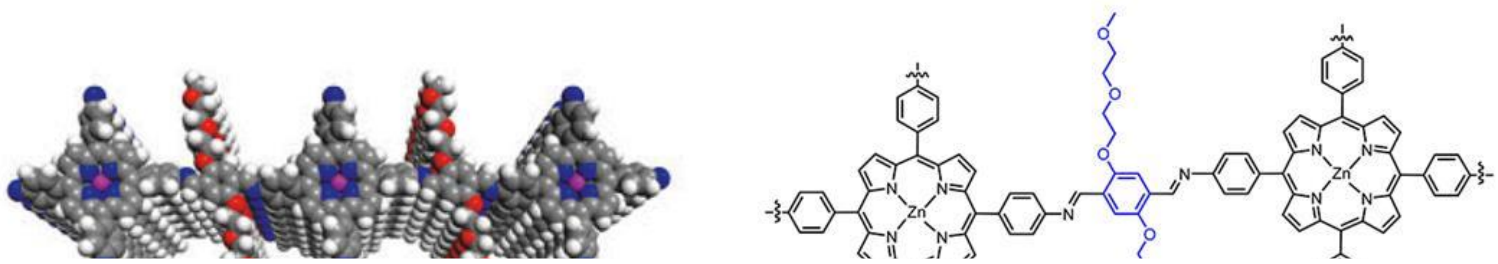
COF-999
$[(TCPB)_2(BPDA\text{-}NH_2)_3(C_2H_5N)_n]_{olefin}$

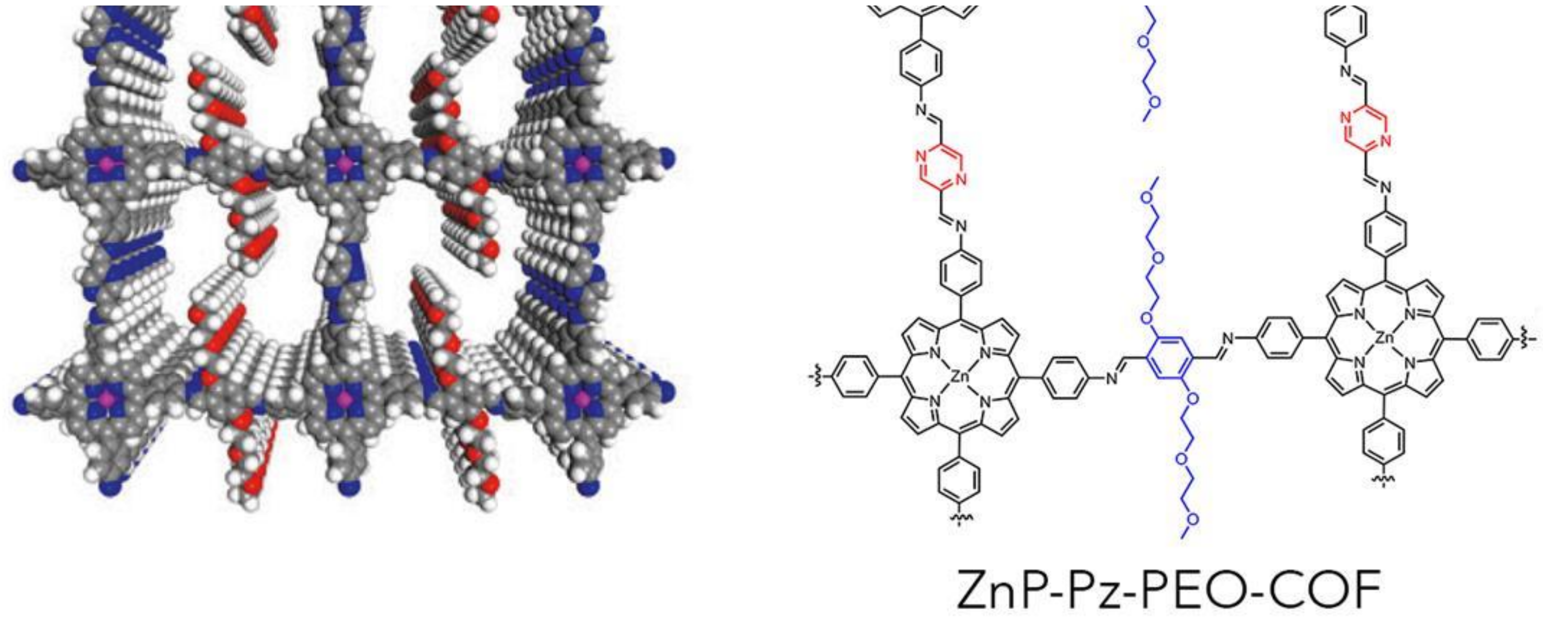
COF-999, with its amine groups dangling in to the pores, can absorb carbon dioxide from the air

And in 2024, Yaghi reported a COF (COF-999) with olefin linkages able to capture excess carbon dioxide from the air. COF-999 was modified after construction to transform the azide groups dangling into its pores into amines and then polyamines. It is these polyamines that act as the sorption sites for carbon dioxide. 'Carbon dioxide capture from air is an emerging application [for COFs that] looks very promising,' Yaghi says.

COFs are also ideal platforms for heterogeneous catalysis due to their high surface areas and the ease with which active sites can be designed into their pores. Their structures also provide channels to facilitate the movement of reactants and products. 'The pores of COFs serve as highways to enable the delivery of reactants to the catalytic sites. They can [also] deliver the products outside of the pores,' explains Donglin Jiang, an expert in COFs and 2D polymers at the National University of Singapore.

The photocatalytic properties of COFs are an area of considerable interest. This application exploits the extended p-conjugation present in many COF structures, something that was first reported Jiang in 2008. By contrast the metals in MOFs prevent extended conjugation. In 2023, Jiang reported COF photocatalysts able to efficiently generate hydrogen gas from water. Water splitting has already been extensively explored as a means to generate green hydrogen fuel in the future, but current systems are not efficient enough. Jiang's COF photocatalysts contain porphyrins as the photon-harvesting units with the structures' p-conjugation enhancing this property. '[For COF] photocatalysts you need to have the light harvesting by unit to ensure you can harvest the photons [and] you need to integrate a lot of p structures to enhance light-harvesting capability,' says Jiang. With the COFs designed in his lab, 'you don't need to add any additional co-catalysts or any sacrificial agents to promote reactions', he adds. In 2024, Jiang reported COF photocatalysts able to produce hydrogen peroxide through a photosynthesis process using water or seawater, sunlight and air as sole inputs.





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ZnP-Pz-PEO-COF is able to catalytically generate hydrogen gas from water

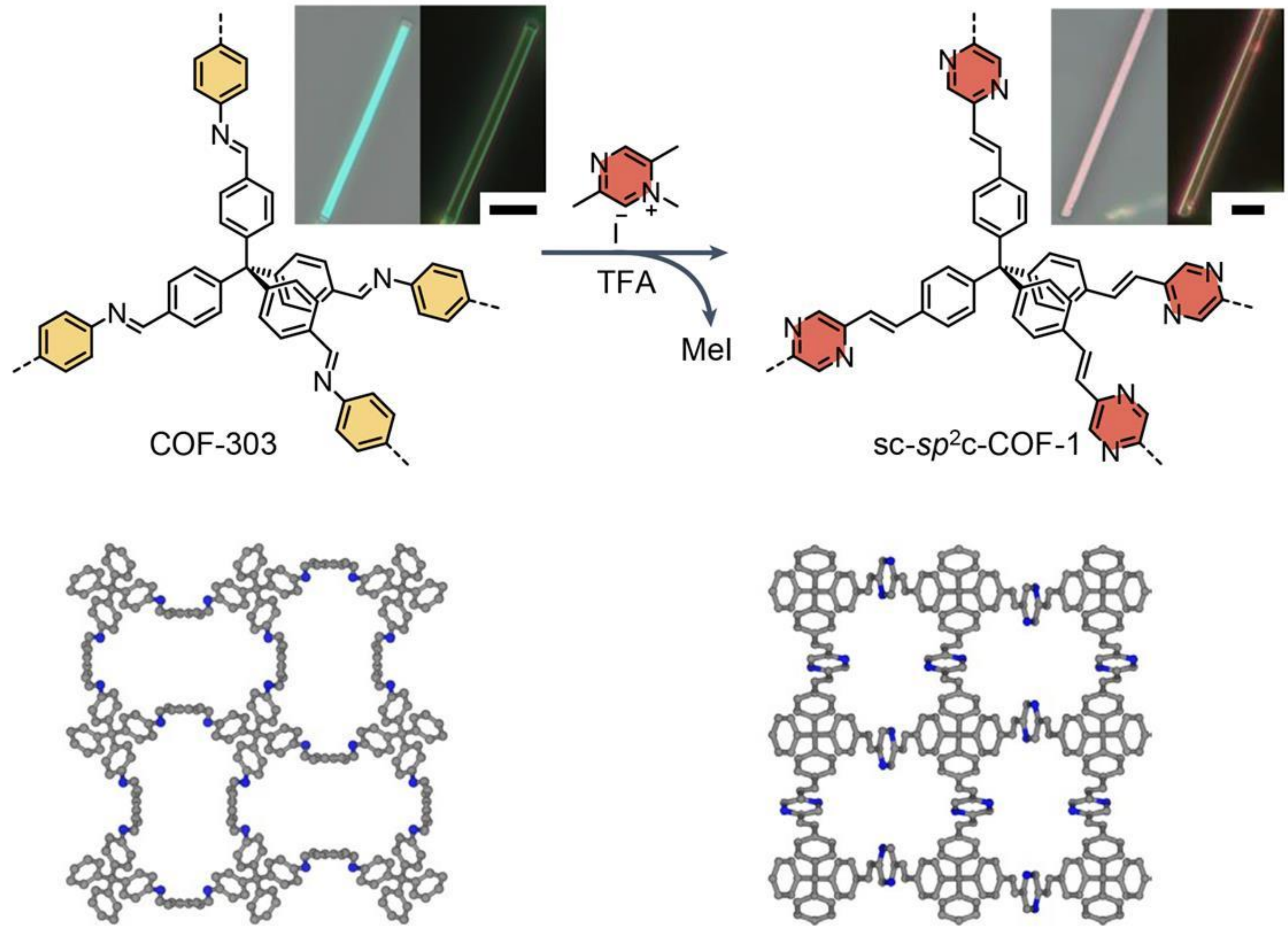
Photocatalytic COFs are also being extensively explored for the reduction of carbon dioxide into useful chemical building blocks. Chemists are also starting to use them for catalysing organic reactions. In 2023, for example, Banerjee reported the use of photocatalytic enamine-linked COFs to catalyse the C–H borylation of azines using visible light.

COFs' combination of high thermal conductivity and electrical insulation makes them attractive for semiconductor applications. 'It's generally very hard to design materials with both of those properties,' says William Dichtel, a porous polymer expert at Northwestern University in Illinois, US. For microprocessors to keep shrinking, better performing materials with these dual properties are needed. 'We have a big heat dissipation problem in chips, yet we also need low dielectric constant materials, as we don't want the electric field of one wire to have too much influence on the electronics of an adjacent wire,' he adds. In 2021, Dichtel and colleagues reported a boronate ester-linked COF thin film with a combination of high thermal conductivity and a low dielectric-constant suitable for using in next generation integrated circuit components. Among other applications being explored for COFs are targeted drug delivery and as fluorescence-based sensors able to detect a broad range of analytes.

Synthesis secrets

This search for viable future uses for COFs is taking place alongside extensive and broad efforts to explore what is possible in their synthesis. The development of tools to tweak COF structures after construction – an idea known as post-synthetic modifications – has been ongoing for more than a decade. This concept includes changing the groups dangling into pores, as Yaghi did to create the carbon dioxide-loving polyamine groups in COF-999. The idea is to have a single COF material that can then be modified for different purposes, explains Dichtel. 'People have used all kinds of chemistry to do that,' he says, adding that 'very reliable reactions like click reactions' are favoured due to guaranteed results.

Another type of post synthetic conversion being developed for COFs is changing the linkages, a concept first reported in 2016. Typically, these conversions turn imine linkages into more stable bonds. Imine-linked COFs tend to be the easiest COFs to crystallise, due to the reversible nature of imine bonds. But this reversibility can impact the stability of the material. 'If you want more chemical stability, or other properties, it's nice to be able to transform imine linkages into things that are much more stable,' says Dichtel.



Imine to olefin transformation

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Transforming the functional groups on the linkages makes it easier to obtain COFs that are otherwise hard to synthesise

'Imine to amide is a classic conversion,' Dichtel adds. Other common examples include using an aza-Diels–Alder cycloaddition to turn the imine linkages into more robust quinoline-linked COFs. Tools for imine to olefin post-synthetic transformation first started to appear in 2019. In 2024, Tao Zhang from the Chinese Academy of Sciences in Ningbo and colleagues reported an interesting new approach to transform imine-linked COFs into sp^2 -carbon-linked COFs. Synthesing an olefin-linked COF without using a transformation is challenging, as the robust olefin bonds hindered the self-correction of the polymerisation process needed to obtain high quality crystals. They used trifluoroacetic acid to catalyse the transformation of imines to olefins.

Another way to improve the stability of imine-linked COFs is to transform them into their enamine form. In 2022, Andy Cooper, an expert in advanced functional materials at University of Liverpool, UK, reported an indirect route to enamine-linked COFs by first building highly-crystalline COFs with urea linkages and then transforming them into enamine-linked analogues. 'The way that works is we make [a urea-linked] COF where the bonding in the framework is very reversible, and hence crystalline and quite unstable. Then we do a dehydration reaction that turns it into a different type of COF, which has very well good stability and, surprisingly, didn't lose its crystallinity,' says Cooper.

COF synthesis methods are expected to continue to mature to enable an ever wider variety of COFs to be made. And as with many areas of chemistry, a better understanding of the fundamental chemistry coupled with artificial intelligence approaches is expected to make the synthesis of novel COFs easier. 'We are looking at the way COF synthesis is done and trying to… understand exactly how these networks simultaneously polymerise and form crystalline structures,' explains Dichtel.

Scaling up

For COFs to reach their commercial potential, a means to manufacture them at scale is needed, something that has only just begun to be attempted. 'Cost-effective and high-yield methods are crucial for large-scale production,' says Banerjee. By contrast, MOFs – which are a decade further into their development – can now be made at scale. 'There's nothing about COF synthesis per se that looks like it wouldn't be scalable,' Dichtel reassures.

In the lab, COF synthesis is dominated by solvothermal methods. This method, originally devised in Yaghi's lab 20 years ago, involves dissolving building blocks in solvent and then heating them under pressure. Solvothermal synthesis can provide a very high crystallinity and is applicable to various types of linkages and reactions, says Jiang. A number of solvent-free methods with green chemistry credentials have also been developed over the years. While none of these methods have yet been attempted at scale, the assumption is that their scale-up should be viable.

Continuous flow synthesis is another approach with industrial-scale potential. In 2024, Dichtel reported a two-step continuous flow route to synthesise an imine-linked COF and then remove methyl protecting groups to make a hydroxylfunctionalised COF. In that work, 'we were doing throughputs of a few grams an hour', Dichtel says. 'Continuous flow synthesis offers a significant advancement by combining efficiency with reproducibility, ensuring scalability without compromising quality,' adds Banerjee, who is also championing a continuous flow synthesis approach for COF manufacture.

Olefin COFs are among the most stable porous materials, even in strong acid and base or boiling water

Yaghi may be the first to achieve the large-scale synthesis of a COF. His start-up Atoco has licensed COF-999 to develop for direct carbon capture, and is already developing MOFs for the same purpose. The synthetic route the company plans to use to make COF-999 at scale hasn't been announced. 'Our short-term aim is to show that they can be made in kilogram scale. But then our long-term goal is to achieve the very large quantities like we do with MOFs,' says Yaghi.

Cooper predicts that the first commercially successful applications of COFs will be niche applications where these porous materials offer specific advantages over cheaper alternatives, such as activated carbon. Their crystallinity or p-conjugation are two such COF properties with high potential.

As well as finding a killer application and perfecting synthesis at scale, more testing is needed to ensure the chosen COFs are stable and robust enough to meet their commercial aspirations, says Jiang. Some COFs are more robust than others, explains Yaghi. 'Olefin COFs are among the most stable porous materials, and are very stable in strong acid and base and boiling water,' he says. 'Testing under the operational conditions [is necessary] to understand their long-term performance,' adds Jiang. Strong partnerships between academic and industry are needed to build pilot projects to 'showcase the feasibility of COF-based technology for various applications'. But his hopes are high: 'In terms of commercialisation, I think the next 5–10 years might be very promising.'

Nina Notman is a science writer based in Salisbury, UK

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