

A cautionary tale from the past

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Publication Date: March 11, 1992

The following essay was written some time ago, but continues to pop up on laboratory doors around MIT, most recently at the Ceramics Processing Research Laboratory where it was read by a Tech Talk reporter. It is reprinted here with Dr. Sharpless' permission in an effort to reach everyone in the MIT community. Dr. Sharpless was a long-time member of the MIT faculty, last holding the Arthur C. Cope Professorship in Chemistry. He is now at the Scripps Research Institute in California.

Many of you may know that I was blinded in one eye during a lab accident in 1970, shortly after I arrived at MIT as an assistant professor. I always wore glasses whenever I was at my bench, and while I felt I conscientiously observed safety measures, my experience proves one can't be too cautious about wearing safety glasses.

As I prepared to go home from the lab during the early hours of the morning of the accident, I looked in the bays to see what my co-workers were doing, and then returned to my own bench, removed my safety glasses, and put on my parka. As I was walking to the door, I passed the bench where a first-year graduate student was flame-sealing an NMR tube. I asked how it was going, and he replied, "Good, I've got it sealed."

He was sealing off the tube at atmospheric pressure under a flow of nitrogen gas while cooling the tube in a liquid nitrogen bath, a technique neither of us had performed before. Nor, I regret to say, had we looked up the procedure, which we subsequently discovered to be incorrect.

I stopped by his bench, picked up the tube from the bath, and held it to the light. The tube immediately frosted over, and, as I wiped it to better see the contents, I noticed that the solvent level was exceedingly high. Suddenly the solvent level dropped several inches. Though I instantly realized condensed oxygen had been sealed in the NMR tube, I was quite literally unable to move a muscle before it exploded. Glass fragments shredded my cornea, penetrated the iris, and cause the partial collapse of one eye. My only other injuries were superficial face cuts.

My first two weeks at Mass Eye & Ear were spent totally immobilized and with both eyes bandaged. The pain was terrific, but my fear was even greater: I had been warned that when my eyes were uncovered there was a small chance I might blind in both eyes due to "sympathetic ophthalmia." Because eyes are walled off from the rest of the body in utero, eye protein driven into the blood stream can raise an immune response that leads to the "killing" of the uninjured eye. My disappointment at having no functional vision in my injured eye was, needless to say, surpassed by my joy at retaining full vision in my good eye.

The lesson to be learned from my experience is straightforward: there's simply never an adequate excuse for not wearing safety glasses in the laboratory at all times.

A version of this article appeared in the March 11, 1992 issue of MIT Tech Talk (Volume 36, Number 23).

The dynamic art of growing COF crystals

Growth modulation leads to large, high-quality covalent organic framework crystals

By Jorge A. R. Navarro

Diamonds consist of an ordered array of tetrahedral carbon atoms, held together by strong covalent bonds. Despite this simple structure, making diamond crystals is difficult, requiring extremely high pressures and temperatures that can only be achieved deep in Earth's crust or through sophisticated experiments. Building covalent organic frameworks (COFs) similarly involves the ordered spatial arrangement, in a two- or three-dimensional crystalline network, of organic units linked together by strong covalent bonds. Growing single crystals of robust COFs is challenging because it requires the dynamic formation and cleavage of strong covalent bonds. On page 48 of this issue, Ma *et al.* (1) report a simple method for growing large, high-quality single crystals of COF networks held together by strong imine covalent bonds.

COFs are a class of synthetic porous organic materials that provide well-structured, confined spaces for selective molecular recognition processes and enhance the reactivity of the hosted molecules. These properties are attractive for a wide variety of potential applications, including gas adsorption and separation, catalysis, sensing, and energy storage and generation (2).

The properties of the imine bond make it particularly suitable for building robust crystalline COF networks. First, the strength of this bond leads to highly chemically and thermally robust materials that can withstand the harsh conditions required for environmental and industrial applications (3). Second, the imine bond can form and dissociate dynamically, providing one of the few examples of dynamic covalent chemistry (4).

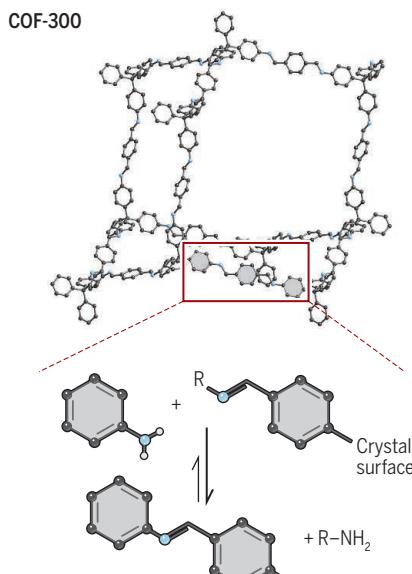
The difficulties encountered in trying to grow high-quality single crystals has hampered the use of single-crystal x-ray diffraction to obtain accurate structural data on COF materials; these data are necessary for a full understanding of their properties. Previous reports have shown the formation of robust two-dimensional (2D) and 3D COF networks based on imine bonds, but the crystalline order was limited to the nanoscale, which is unsuitable for single-crystal x-ray diffraction (5). Structural determinations of

these porous materials therefore relied on x-ray powder and electron diffraction methods, which revealed the basic structural features but could not resolve the molecular conformation, the degree of framework interpenetration, or the nature of interactions with guest molecules.

Ma *et al.* now show that the use of a large excess of aniline during COF synthesis gives rise to the competitive formation of terminal benzene imine moieties at the COF crystal surface (see the figure). This approach provides an error-correction mechanism during crystal growth, ultimately leading to the formation of crystals with sufficiently high quality and size to obtain high-resolution single-crystal x-ray diffraction data in standard laboratory equipment. The authors illustrate the power of this approach by retrieving accurate structural features for single crystals of several imine-based 3D COFs, including COF-300 and COF-303. The results show that this approach is general for imine-based COFs and might eventually inspire related approaches to COF crystals based on additional types of dynamic covalent bonds (6).

Editing COF crystals with aniline

A competitive reaction with an excess of aniline provides an error-correction mechanism during COF crystal growth.



Growth modulation

The aniline excess promotes imine bond reversibility.

The accuracy of the retrieved structural features allows the authors to establish the degree of interpenetration and structural distortions in the diamond network of the COF-300 system without ambiguity. Moreover, they show that the single-crystal features are preserved in the hydrated form of COF-300. The authors could thus visualize the interactions of water molecules with the imine groups of the host framework via O-H...N hydrogen bonds, as well as resolve infinite water chains hosted in the pore channels. They could also accurately establish the subtle conformational differences between the imine and reversed imine isomeric networks COF-300 and COF-303.

Metal organic framework (MOF) chemistry, which is based on more labile coordination bonds, enabling high-quality single-crystal x-ray diffraction analysis that makes it possible to obtain single-crystal x-ray diffraction data. These data can reveal structural features of guest molecules (7), elucidate the stepwise formation and visualization of ultrasmall metal nanoparticles (8), and resolve catalytic steps (9). It is therefore envisaged that the possibility of obtaining good-quality single crystals will facilitate the synthesis, characterization, and applications of COFs and related materials of increased complexity, as already realized in MOFs. It remains to be seen whether this approach can be extended to highly anisotropic 2D (10, 11) and/or entangled COF structures (12), in which the strengths of intra- and interlayer (polymer) interactions differ by several orders of magnitude. ■

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ACKNOWLEDGMENTS

The author gratefully acknowledges the financial support from Spanish MINECO (CTQ2017-84692-R) and EU FEDER funding.

The green pigment of life

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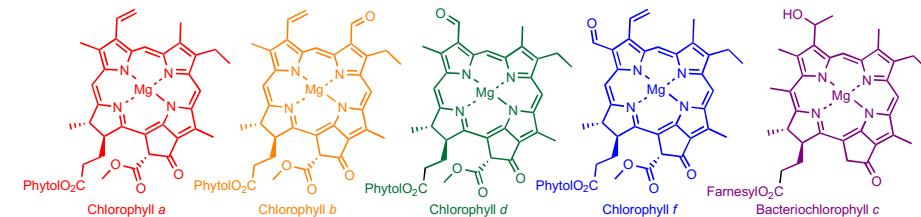
Madison Knapp and Jennifer Bridwell-Rabb explore the functions of chlorophyll and explain how our understanding of this green pigment has changed over time.

Green is the prototypical colour of nature. This stems from chlorophyll – a pigment that allows plants to absorb energy from light – which tints the leaves of plants and trees, and therefore also the landscapes of forests, parks and gardens. This molecule, along with other tetrapyrrole systems such as haeme and vitamin B₁₂, are referred to as the pigments of life¹. These compounds arise from a common biosynthetic pathway that uses a series of chemical steps to build and tailor a template scaffold to perform critical functions in biology.

With 10¹² tons produced annually by plants, algae and bacteria, chlorophyll is one of the most abundant of the pigments. Characterized by a central magnesium ion, five-ring-containing scaffold, hydrophobic tail, and the ability to absorb light, chlorophyll and its structural analogues are found wherever photosynthesis is happening². These locations include the most unexpected parts of the Earth and environments that experience different temperatures, wavelengths of light, and concentrations of oxygen. For example, both *Fischerella thermalis* strain PCC 7521 and *Chlorobium phaeobacteroides*, which are native to the hot springs of Yellowstone and the Black Sea, respectively, produce chlorophyll pigments for photosynthesis.

Typically, the biochemical function of chlorophyll in photosynthetic organisms is two-fold. First, chlorophyll molecules serve as antenna pigments and photoreceptors to harness light energy from the Sun. Second, they are used to facilitate the production of oxygen and the eventual conversion of CO₂ into chemical energy. These functions unite biology, chemistry, and physics, making chlorophyll an appealing subject to study in all disciplines.

Chlorophyll was named based on the Greek words *chloros* (green) and *phyllon* (leaf) after it was first isolated from plants in 1817 by Joseph Bienaimé Caventou and Pierre-Joseph Pelletier. It was initially described as an alcohol-soluble



pigment from leaves, and remained a structural enigma until the mid-twentieth century when a series of papers from the laboratories of Hans Fischer and James Conant culminated in a molecular description of the most abundant chlorophyll pigments, chlorophyll *a* and chlorophyll *b*. Following the release of these structural details, a 49-step total synthesis of chlorophyll, known as the Woodward synthesis, was completed in 1960³. This synthesis has yet to be rivalled at the bench and helped earn Robert Woodward the Nobel Prize in Chemistry in 1965. Today, additional synthetic protocols to access various chlorophyll derivatives that contain Cd²⁺, Cu²⁺, Zn²⁺ or Fe²⁺ in place of the Mg²⁺ ion, or alternative functional groups on the scaffold, also exist⁴.

As a compound, chlorophyll is relatively difficult to work with due to its insoluble, light-sensitive, and oxygen-sensitive nature, needing organic solvents such as acetone or acetonitrile, complete darkness, and oxygen-free environments to prevent its degradation. As such, chlorophyll has traditionally been difficult to study, probably accounting for the missing molecular details regarding how this pigment is biologically produced, degraded and modified to produce the different varieties found in nature.

Nearly 100 years after the initial elucidation of the structure of chlorophyll, new derivatives are still being identified. The most recently discovered derivatives are chlorophyll *d* and chlorophyll *f*^{5,6}. These pigments, like the other naturally occurring chlorophyll derivatives, arise from a common chlorophyll *a* precursor scaffold. They contain formyl groups at C3 and C2, respectively, and have received attention for their ability to absorb light in the infrared, rather than the visible region of the absorption spectrum. Similar absorption properties are noted in the bacteriochlorophyll class of pigments, which are found in photosynthetic organisms that grow in O₂-depleted, or anaerobic environments.

Bacteriochlorophyll pigments can showcase a reduced bacteriochlorin scaffold, a 12-carbon farnesyl chain at C17, and differences in the identity and combination of functional groups that decorate the scaffold.

Collectively, modified chlorophyll and bacteriochlorophyll pigments have received interest due to their potential to increase photosynthetic efficiency², their ongoing applications as colourful dyes in the fashion, cosmetic and food industries⁴, and their promise for use as photodynamic therapy agents in medical applications⁷. Along these lines, a fictional chlorophyll-enriched drink found fame after its cinematic use by the Marvel Series superhero Iron Man to counteract the harmful side effects of free palladium in his body. Finally, the amazing ability of chlorophyll pigments to harness the inexhaustible resource of sunlight and mediate its conversion into clean, usable energy has inspired research into strategies of sustainably supporting life on earth, or as the saying goes, ways of 'going green'.

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Published online: 27 September 2022

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Competing interests

The authors declare no competing interests.