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Spotlights on Recent *JACS* Publications

ORGANIC MOLECULES FORM HONEYCOMB NANOSTRUCTURES IN WATER

They are the stuff that crystals are made of, except this time they remain in solution. For the first time, researchers led by Zhan-Ting Li demonstrate a single-layer, solution-phase supramolecular organic framework (SOF) in water (DOI: 10.1021/ja4086935).

SOFs are well-ordered structures that result when organic molecules self-assemble on the basis of non-covalent interactions. The building blocks of this particular SOF have three "arms" made of 4,4′-bipyridin-1-ium that interlock with arms on neighboring molecules with the help of the rigid macrocycle cucurbit[8]uril, resulting in stable SOFs that have a porous, honeycomb-like pattern. Challenges in creating single-layer nanostructures in solution include solubility and preventing the molecules from stacking on top of one another. To address these issues, the team installs bulky hydrophilic groups at the core of the tripods, which ensure solubility and confine the framework to a single layer. In addition to being structurally attractive, SOFs hold promise for applications in sensing and separations and may serve as ordered platforms for more advanced architectures.

Christine Herman, Ph.D.

A CYTOCHROME P450 IN THE TERPENE CYCLASE BUSINESS

The alarming emergence of drug-resistant bacteria, such as methicillin-resistant *Staphylococcus aureus* (MRSA), underscores the need for new antibiotics that are active against these menacing strains. Viridicatumtoxin is a natural product made in fungi that is structurally related to the tetracyclic antibiotic tetracycline, but it has an additional unique spirobicyclic ring system. The compound exhibits impressive activity against MRSA by inhibiting an enzyme called undecaprenyl diphosphate synthase, a potential new drug target. Toward gaining a deeper understanding of the biology of viridicatumtoxin, Yi Tang and co-workers decipher its biosynthetic pathway in the fungus *Penicillium aethiopicum* (DOI: 10.1021/ja408966t).

The authors combine genetic studies, enzymatic activity analysis, and computational models to explore the biosynthesis of viridicatumtoxin. They surprisingly find that the enzyme responsible for catalyzing the formation of the spirobicyclic ring system is a member of the cytochrome p450 family of oxidative enzymes. The enzyme, called VrtK, is the first example of a cytochrome p450 capable of executing this type of cyclization reaction.

Understanding the biosynthetic pathway of viridicatumtoxin could contribute to drug development efforts surrounding this compound class. In addition, these findings illuminate novel functions for cytochrome p450 enzymes, which may have implications in the biosynthesis of other interesting natural products.

Eva J. Gordon, Ph.D.

CATALYSTS IN ACTION: A DYNAMIC PICTURE

Darío Stacchiola, Ashleigh Baber, and co-workers challenge the traditional understanding of heterogeneous catalysts as static structures in this study, where the authors show a catalyst undergoing changes in chemical state and morphology during a reaction (DOI: 10.1021/ja408506y).

Heterogeneous catalytic processes—most commonly where the catalyst is a solid while the reaction occurs in the liquid or gas phase—are ubiquitous in a variety of industrial processes. These reactions are typically studied by surface scientists under idealized model conditions such as ultra-high vacuum, which can obscure mechanistic details or the detection of some reaction species. Here, the researchers study copper-based catalysts in a reaction where a copper oxide film is reduced by carbon monoxide under more realistic ambient pressure conditions.

The atomic-scale morphology of the catalyst during this reaction is visualized by high-resolution scanning tunneling microscopy, revealing a structural transformation of the ordered copper oxide film to a ring-like structure and finally to metallic copper. Complementary spectroscopic studies of the catalytic surface show that the reduction proceeds in the presence of adsorbed carbon monoxide molecules and results in a change in the catalyst's oxidation state. Understanding the mechanisms of catalytic reactions under realistic conditions can guide the design of improved catalysts.

Dalia Yablon, Ph.D.

COMPUTATIONAL NMR APPROACH DECIPHERS WHAT OTHER METHODS CANNOT

Molecules can crystallize in different forms, which may have variable stability or solubility properties. For materials and pharmaceutical applications that use microcrystalline powders, manufacturers must be able to reliably produce specific crystal forms and have analytical methods available to ensure that they are doing so.

By combining computational work and solid-state nuclear magnetic resonance spectroscopy (NMR), a team led by Lyndon Emsley and Graeme M. Day has pioneered a technique to solve the crystal structure of a medium-sized organic molecule (DOI: 10.1021/ja4088874). The new approach improves on solid-state NMR techniques for determining three-dimensional structures, in large part by sidestepping the need for isotopic labeling of samples.

Their technique includes three parts. First, they use computational analysis to develop a set of possible crystal structures of a molecule on the basis of its chemical structure. Then, they calculate the ^{1}H NMR chemical shifts each crystal structure would show. Finally, they match the calculated chemical shifts to the experimental spectrum obtained from the powder.

The team reporting the new work has also analyzed an AstraZeneca drug candidate for type 2 diabetes called

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AZD8329. The drug has seven known crystal forms; AstraZeneca chose two for development on the basis of their material properties. One of the two, "form 4", has not previously been structurally characterized. The Emsley–Day team uses their new approach to identify 34 crystal structure candidates computationally—one of the structures exhibits a calculated spectrum that matches that of the form 4 powder.
Jyllian Kemsley, *C&EN*

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