

Spotlights on Recent JACS Publications

■ CONJUGATED PORPHYRIN DIMERS: INSIGHT INTO NEW RECEPTORS FOR C₆₀

The development of photovoltaic devices depends in part on the availability of materials that can enable efficient transfer of both charge and energy. Although a primary focus has been on developing covalent hybrids with this goal in mind, there is growing interest in exploring whether supramolecular approaches may be able to perform just as well. Now, researchers led by Enrique Ortí, Nazario Martín, and Jean-François Nierengarten describe the synthesis of two new porphyrin-based supramolecular receptors for C₆₀ in a study that provides new insights into the design of porphyrin-based supramolecular assemblies for the recognition of fullerene (DOI: [10.1021/jacs.6b07250](https://doi.org/10.1021/jacs.6b07250)).

The supramolecular complexes are composed of conjugated porphyrin dimers endowed with ammonium-crown ether rings that enable them to bind to fullerene-ammonium salt derivatives. The team performs theoretical calculation to understand the nature of the interactions controlling the binding processes and teases out both the cooperative effects and electronic communication that take place within the supramolecular ensembles. The authors say the insights gleaned from this new study may lead to the development of more efficient charge- and energy-transfer architectures potentially useful in artificial photosynthesis and organic photovoltaics.

Christine Herman, Ph.D.

■ MIGHTY “PEN” FOR BIOMEDICAL APPLICATIONS

Plasmonic nanoparticles, which confine and amplify light in an ultrasmall volume by localizing and combining collective oscillations of free electrons with electromagnetic waves, have already proven useful for a variety of applications, including certain spectroscopies, photovoltaics, and plasmonic catalysis. In a new Perspective, Jwa-Min Nam and co-workers describe a rapidly expanding new arena for these materials: as plasmonically engineered nanoproboscopes (PENs) for biomedical applications (DOI: [10.1021/jacs.6b09451](https://doi.org/10.1021/jacs.6b09451)).

The authors detail the importance of precisely designing and synthesizing PENs for specific applications by combining selected nanostructures with structural and functional modulators, such as small organic molecules or polymers, and non-plasmonic nano-building blocks, such as DNA nanostructures or magnetic particles. The resulting probes have been widely investigated in biosensing, bioimaging and theranostics. For example, PENs have been successfully developed for biomolecular sensors based on localized surface plasmon resonance or Rayleigh scattering, as well as chiroplasmonic sensors to enhance circular dichroism spectroscopy. Others PENs have detected and imaged single molecules with surface-enhanced Raman scattering or shed light on basic cell biology by serving as photoluminescent probes or through nanometal surface energy transfer. Still other PENs have potential for diagnostics as well as treating various diseases through photothermal therapy or as drug carriers. Although a thorough evaluation of the biological risks and practical benefits of these

materials will be required before their widespread use, the authors foresee a bright future for PENs in biomedical applications.

Christen Brownlee

■ HEAVY HEART ENZYME REVEALS PROTEIN-PROMOTING VIBRATIONS

Chemists have proposed, on the basis of computational simulations, that small motions of proteins on the time scale of femtoseconds to picoseconds—called protein-promoting vibrations—help reactants cross the chemical barrier in the transition state. Now Vern Schramm and colleagues test this hypothesis experimentally for a biochemically important and well-studied enzyme, human heart lactate dehydrogenase (LDH). It catalyzes the last step of anaerobic glycolysis, the reduction of pyruvate to L-lactate (DOI: [10.1021/jacs.6b09049](https://doi.org/10.1021/jacs.6b09049)).

The researchers create a “heavy” lactate dehydrogenase by labeling the amino acids in the protein with ¹³C, ¹⁵N, and deuterium to perturb potential vibrations. They then examine the turnover rates of the labeled enzyme and its light counterpart. Evidence suggests that protein-promoting vibrations are coupled with barrier crossing. They also elucidate the mechanism of the reaction, showing that hydride and proton transfer involved in the reduction of pyruvate are concerted rather than stepwise. The work provides experimental evidence for protein-promoting vibrations and also helps uncover the mechanistic details of human heart LDH.

Deirdre Lockwood, Ph.D.

■ TRANSIENT AND FAINT, YET POTENT

Directing groups are commonly used in site-selective C–H activation reactions. In particular, transient directing groups that can reversibly attach to the substrates often lead to high step- and atom-economy, because they avoid covalent installation and removal processes.

Using catalytic quantities of 2-hydroxynicotinaldehyde as a transient directing group, Jin-Quan Yu and colleagues have for the first time developed a palladium(II)-catalyzed γ -C(sp³)-H arylation reaction of free primary amines with broad substrate scope (DOI: [10.1021/jacs.6b09653](https://doi.org/10.1021/jacs.6b09653)). The labile imine and anionic hydroxyl groups coordinate to palladium in a six-membered ring, forming catalytically active bis-chelated species that are responsible for the regioselectivity, high efficiency, and wide substrate compatibility.

The reported transformation enables convenient one-step access to a diverse range of aryl-functionalized aliphatic amines, as demonstrated by the one-pot synthesis of the biologically active 3-ethyl-1,2,3,4-tetrahydronaphthyridine. In addition, it has elegantly solved the long-standing problem of the formation of unreactive complexes in palladium-catalyzed C–H functionalization of free amines.

Xin Su, Ph.D.

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■ FLEXIBLE METAL–ORGANIC FRAMEWORKS AND PROGRESS TOWARD PHASE-CHANGE MATERIALS

Materials that bind to gas molecules and respond with a structural change would be extremely valuable for applications in gas storage and separations. One of the central problems in designing such materials is maintaining control over the pressure at which the structural changes occur. To this end, researchers led by Jeffrey Long design and synthesize a new family of metal–organic frameworks (MOFs) with similar structural topologies and tunable adsorption-induced phase changes (DOI: [10.1021/jacs.6b09155](https://doi.org/10.1021/jacs.6b09155)).

The so-called isorecticular MOFs are derived from the flexible framework known as Co(bdp). The team experiments with the addition of different substituents onto the central ring of the ligand and finds that certain moieties—methyl and fluoro groups, for example—shift the methane adsorption isotherm of the parent compound to higher or lower pressures, respectively. This property allows researchers to tune the adsorption-induced phase change in the flexible framework. The synthetic control achieved in Co(bdp) may lead to the development of other flexible MOFs and provide materials science researchers with a generalizable strategy and powerful new tool for optimizing phase-change adsorbents for gas storage and other industrial applications.

Christine Herman, Ph.D.

■ PEERING DEEP INTO ENZYMES WITH NMR CRYSTALLOGRAPHY

Pyridoxal-5'-phosphate (PLP) is a cofactor workhorse. A number of enzymes make use of this cofactor to catalyze a wide variety of transformations, including racemization, transamination, α/β -decarboxylation, and $\alpha/\beta/\gamma$ -elimination and substitution. To determine how PLP can help catalyze so many different types of reactions, Leonard Mueller and colleagues study PLP in one particular enzyme—tryptophan synthase—in unprecedented detail (DOI: [10.1021/jacs.6b08937](https://doi.org/10.1021/jacs.6b08937)). The findings reveal that the fate of the reaction depends on a small, but critical detail: the protonation state of PLP and the reaction substrates.

To come to this insight, the researchers investigate the tryptophan synthase reaction using “NMR crystallography”, an integrated approach that combines computational modeling, solid-state nuclear magnetic resonance spectroscopy, and X-ray crystallography. The NMR experiments provide chemical shift information for substrates, cofactor, and amino acids near the active site. By comparing experimental and predicted chemical shifts in the context of the enzyme’s crystal structure, the researchers tease out the structure of the intermediate species. The evidence rules against a canonical quinonoid intermediate in favor of a carbanionic species that provides reaction specificity. These results underscore the potential for NMR crystallography to garner insight into transient chemical structures within the active sites of enzymes.

Erika Gebel Berg, Ph.D.