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Spotlights on Recent *JACS* Publications

SNIFFING OUT THE BIOSYNTHESIS OF L-ALLO-ISOLEUCINE

One form the amino acid isoleucine, called L-*allo*-isoleucine (L-*allo*-Ile), is found in various types of organisms, where the molecule may be incorporated into natural products. In humans, L-*allo*-Ile appears at trace levels in blood plasma. However, in maple syrup urine disease, L-*allo*-Ile is found at high levels in the plasma and urine because patients suffering from this rare genetic disorder cannot properly metabolize isoleucine and some other branched chain amino acids.

Now Jianhua Ju and colleagues have shed light on the molecule's biosynthesis by identifying two sets of enzyme pairs that make L-*allo*-Ile (DOI: 10.1021/jacs.5b11380). Using bacterial strains isolated from the South China Sea and genetic, biochemical, and bioinformatics approaches, the investigators closely study the pathways of two important classes of bacterial compounds that incorporate L-*allo*-Ile. The researchers have discovered an enzyme pair in each compound's pathway; each pair consists of an aminotransferase and an isomerase that convert isoleucine into L-*allo*-Ile and vice versa.

"These findings lay the foundation for further studies into the origins of L-*allo*-Ile in assorted living systems," say the authors. "The well-established elevated L-*allo*-Ile levels in humans suffering from maple syrup urine disease, in particular, gives cause for significant excitement in the biomedical and diagnostics arena."

Rajendrani Mukhopadhyay, Ph.D.

LYSOBACTIN LOCKS UP PATHOGENIC BACTERIA

Ever since their discovery in 1940s, antibiotics have been used with great success to treat infectious diseases. But their widespread global use has prompted infectious organisms to evolve resistance against antibiotics. According to the Centers for Disease Control and Prevention, at least 2 million people in the U.S. become infected with antibiotic-resistant bacteria each year. Of those infected, at least 23,000 die.

Scientists are searching for new drugs to thwart antibiotic-resistant bacteria. In 1987, researchers discovered lysobactin, also known as katanosin B, a potent molecule that can take down the bacteria that cause pneumonia, food poisoning, skin infections, and respiratory illnesses. Although scientists know that lysobactin interferes with the synthesis of the thick, protective cell walls in bacteria, they do not know how lysobactin carries out the inhibition.

Now Suzanne Walker, Daniel Kahne, and their colleagues demonstrate that the potent killing mechanism of lysobactin stems from its ability to directly bind to cell wall precursors (DOI: 10.1021/jacs.5b11807). The investigators show that lysobactin sequesters the precursors by forming complexes with them, thereby inhibiting the enzymes that need those precursors to make the bacterial cell wall. The authors conclude, "In view of its potent activity against a broad spectrum of important pathogens, lysobactin may be a promising candidate for further development."

Rajendrani Mukhopadhyay, Ph.D.

LEAD HALIDE PHOTOVOLTAICS: PROCESSING, PROPERTIES, PERFORMANCE

Alexander Sharenko and Michael Toney discuss the development of lead halide ($CH_3NH_3PbI_3$) perovskite thin films for solar cells in this Perspective (DOI: 10.1021/jacs.5b10723). Currently, photovoltaic devices based on this material exhibit power conversion efficiencies as high as 20%, and unlike many competing materials, lead halide perovskite thin films can be readily solution processed. Each protocol creates a film with unique morphology and properties, variations that researchers have exploited to identify key elements for improving efficiency.

The Perspective focuses on these processing−property−performance relationships and identifies the fabrication of large uniform grains as critical to producing high-quality photovoltaic material. Only a few of the many fabrication techniques can create the morphology necessary for efficient solar cells. Further complicating fabrication, the films are extremely sensitive to environmental and experimental conditions at each step. The authors stress the need for additional work to improve the size and continuity of film grains, and to understand the relationships between material processing, structure, and properties.

Despite rapid gains over the past half-decade, these materials have yet to reach their theoretical performance limit. This Perspective points researchers toward promising areas of focus for continued rapid evolution toward reproducible, large-scale, highly efficient lead halide perovskite solar cells.

Jenny Morber, Ph.D.

CONNECTING THE IMPROBABLE DOTS BETWEEN AROMATICITY AND OPTICAL ACTIVITY

Aromaticity and optical activity, two fundamental concepts introduced in virtually every organic chemistry textbook, are both characterized by electromagnetic moments generated from the circulation of electrons in molecules under external fields. However, they seem to be two parallel subjects that never intersect, because aromaticity is mostly studied in flat molecules while optical activity is almost always associated with chiral structures.

The latter assumption has recently been amended for achiral, conjugated hydrocarbons by Bart Kahr and co-workers, and the researchers continue by clarifying the relationship between aromaticity and optical activity (DOI: 10.1021/jacs.5b11138). Using quantum chemical computations, they find that aromaticity diminishes optical activity as a result of uncoupled electric and magnetic dipoles, while anti-aromaticity has the opposite effect.

For the first time, a qualitative relationship has been established between aromaticity and optical activity, two seemingly unrelated properties. The conclusions enable extensive electronic structure−chiroptical property correlations, making an important and useful contribution to structural organic chemistry.

Xin Su, Ph.D.

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LIGHT-CONVERTING NANOPARTICLES DELIVER ON COMMAND

When taking medicines to treat a specific area of the body, patients often suffer from undesirable side-effects triggered as the drug spreads through the body. Scientists have used nontoxic polymers to carry drugs to targeted regions and release them upon light exposure. But most of these polymers are sensitive only to ultraviolet light, which not only is carcinogenic but also does not adequately penetrate tissues.

Now Marta Cerruti, Fiorenzo Vetrone, and colleagues have a potential solution using near-infrared light that penetrates the body well and is not harmful: the investigators have created nanoparticles that convert light from near-infrared into ultraviolet (DOI: 10.1021/jacs.5b12357). The nanoparticles carry a biomolecule tethered by a light-sensitive polymer. When the nanoparticles are hit with near-infrared light, they convert it to ultraviolet light through a process known as upconversion. As a result, the ultraviolet light cleaves the polymer and releases the biomolecule.

These nanoparticles can be tracked in cell culture and made to release the biomolecule on command in specific locations. Moreover, they function even when the near-infrared light must pass through tissue as thick as 2 cm. The investigators say, "Efficient, noninvasive, on-demand drug release and deep tissue imaging make these nanoparticles an excellent theranostic platform when localized and on-demand drug delivery is required, such as in the treatment of post-surgical wounds, localized infections, and tumors."

Rajendrani Mukhopadhyay, Ph.D.

SIMULATIONS SUPPORT ANION-EXCHANGE MEMBRANES FOR NEXT-GENERATION FUEL CELLS

When it comes to electric energy conversion and storage, proton exchange membranes (PEMs) have received much attention for their ability to conduct protons via their anionic side chains. Widespread applications of PEMs, however, have been hindered by their cost: they require platinum-containing catalysts, owing to the membrane's highly acidic nature. In contrast, anion exchange membranes (AEMs) are anion-conducting polymer electrolytes that contain positively charged side chains bound to a polymer backbone in an alkaline environment, which allows for the use of more affordable, non-noble catalysts. But AEMs have typically suffered from worse overall performance—measured by conductivity, mechanical strength, and chemical stability—compared to PEMs.

Now, researchers led by Gregory Voth have taken a step toward the rational design of improved AEMs (DOI: 10.1021/jacs.5b11951). The team performs computer simulations that shed light on AEM structures and their ion transport mechanisms. Classical molecular dynamics approaches cannot describe the series of O−H bond breaking and formation processes—known as proton hopping—that occur when hydroxide ions are transported in hydrated environments. So the team develops a new algorithm that accounts for these processes. The findings may lead to the design of new materials based on AEMs for next-generation fuel cells.

Christine Herman, Ph.D.

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