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Spotlights on Recent *JACS* Publications

DUAL-MODE MICROBUBBLES ENHANCE ULTRASOUND IMAGING

Ultrasound imaging of organs and tissues is an important noninvasive diagnostic tool in medicine, and its efficacy has been increased by using microbubbles as contrast agents. These bubbles, typically 1−10 μm in size, are fluorinated gases encapsulated in a spherical shell of lipids, albumin, or polymers. They are strong reflectors of ultrasound waves, and when injected into the bloodstream of the patient, improve the visibility of blood vessels. In another imaging technique, called photoacoustic tomography, optical absorbers themselves emit ultrasonic waves when irradiated with short laser pulses. Previously, these two imaging technologies required two different types of contrast agents, one primed as an ultrasound reflector and the other as an ultrasound emitter.

A group of researchers led by Gang Zheng report that the inclusion of porphyrin−lipid in the shell of the microbubbles results in "unexpected physical properties" (DOI: 10.1021/ja305988f). The use of a porphyrin−lipid in the shell makes the shell stiffer, increasing the mechanical stability of these microbubbles and enhancing their response to laser pulses. Another result is that their size distribution peaks sharply at 2.5 μm, making them suitable as a contrasting agent because they respond to the sound frequency used in current ultrasound imaging.

These new microbubbles would, according to the researchers, allow the combination of classical ultrasound imaging with photoacoustic tomography and result in more effective imaging technology. **Alexander Hellemans**

NEUTRON DIFFRACTION PROVIDES SNAPSHOT OF DRUG−TARGET INTERACTION

A clearer understanding of how small-molecule inhibitors bind their targets could equip researchers to design more precisely targeted drugs. With this goal in mind, researchers led by Robert McKenna perform the first neutron diffraction analysis of a drug−enzyme complex composed of the clinically used acetazolamide (AZM) and its primary target, human carbonic anhydrase II, or HCA II (DOI: 10.1021/ja3068098).

Carbonic anhydrases (CAs) are a family of enzymes involved in many physiological processes, including respiration and fluid secretion. Several CA inhibitors are currently used in clinical settings to treat glaucoma, mountain sickness, epilepsy, and osteoporosis and are being tested for certain types of cancer. Due to the sequence similarity of different members of the CA family, however, most small-molecule CA inhibitors bind to more than one CA isoform.

In order to develop isoform-specific drugs, the research team set out to better understand how AZM binds to HCA II. They obtained crystals of the AZM-HCA II complex and analyzed them with neutron diffraction, which allowed them to directly observe hydrogen atoms and identify the hydrophobic interactions that play a key role in the drug−enzyme interaction. The study reveals molecular details that could not be seen with traditional X-ray diffraction techniques. **Christine Herman, Ph.D.**

CATALYST HELPS ACHIEVE MAXIMUM POLYBORYLATION IN AROMATIC COMPOUNDS

The synthesis of polyborylated compounds is often hampered by the formation of mixtures of compounds with varying degrees of C−H activation. Lawrence Scott and Maria Eliseeva have developed a new method for the direct polyborylation of aromatic compounds in high yields (DOI: 10.1021/ja307547j).

When C−H bonds in aromatic compounds are activated via borylation, they can be further converted into C−C bonds with known chemistry, which opens the door to the synthesis of more complex molecules, such as carbon nanotubes, dendrimers, and other potentially useful materials.

The traditional approach to polyborylation of aromatic compounds involves the use of an iridium catalyst and excess borylating reagent, and it often results in low yields of the desired product. The researchers discovered that by using a catalytic amount of base in conjunction with a high loading (20%) of the standard catalyst, they could achieve high yields in the polyborylation of the bowl-shaped molecule corannulene, and highly regioselective polyborylations of several other aromatic compounds. The secret to the success of their approach lies in the successive deborylation and reborylation of undesired compounds until the product with the maximum number of borylation sites is achieved. **Christine Herman, Ph.D.**

MOLECULAR GLUE MUSCLES-OPEN MEMBRANE BARRIER

Cell membranes are like bouncers at an exclusive night club, deciding who should be allowed in. Modifying the permeability of cell membranes may allow scientists to understand how molecules that would normally not be able to cross the membrane could affect cell behavior. In a new study, Kou Okuro, Takuzo Aida, and co-workers develop a "molecular glue" called Azo-^{18}Glue that sticks to membranes and changes shape in UV light, altering the structure and permissiveness of the membrane (DOI: 10.1021/ja3074424).

The Azo-^{18}Glue core is flanked by six chemical arms, each with three molecular fingers ending in a positively charged guanadinium ion. This thick forest of positive charges is the glue that binds Azo-^{18}Glue to the negatively charged surface of membranes. At the very center of the core is a molecular bond that switches to one conformation in UV light and to another in visible light.

The researchers mixed Azo-^{18}Glue with membrane vesicles in a buffer containing hydroxide ions. Normally, the vesicles do not permit the ions to enter. However, exposing the vesicles to UV and visible light increased the pH inside the particles, suggesting that hydroxide ions had indeed penetrated the membrane. The researchers concluded that Azo-^{18}Glue sticks to

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the particles' surface and creates disorder in membranes by a molecular friction as a result of the shift between two conformations, allowing hydroxide ions to slip inside. **Erika Gebel, Ph.D.**

METAL IONS LET SMALL MOLECULES JUMP ON, JUMP OFF

Multivalency—the ability of a molecular system to develop multiple interactions with its target—is an important concept in biotargeting and nanomedicine. However, most synthetic systems are designed and synthesized to express only a fixed number of ligands. Valency that can be altered after synthesis is a desired trait, since it would allow selective capturing of a variety of specific targets. Gold clusters with a surface monolayer are good candidates for such a system, as they are easy to synthesize and modify at the monolayer surface.

Leonard Prins and co-workers synthesized such a gold nanoparticle-based supramolecular system that can "catch and release" small molecules through the addition and removal of zinc and copper metal ions from the surface monolayer (DOI: 10.1021/ja307621d). The ratio of these two different metal ions also determines how fast small molecules are released; valency and the rate of release can also be controlled by pH. In addition to being fully reversible, the system is also water based, making it attractive for biomedical uses. The reaction takes place at low concentrations, suggesting important ramifications for the controlled release of small molecules for biosensor purposes, or small-molecule drug delivery. **Leigh Krietsch Boerner, Ph.D.**

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