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Spotlights on Recent *JACS* Publications

STABLE IONIC VESICLES FORM SPONTANEOUSLY IN IONIC LIQUID

Amphiphilic molecules, containing a polar head and a nonpolar tail, spontaneously assemble into vesicles under certain conditions and hold promise for research applications including drug delivery and biological membrane modeling. However, vesicular structure formation often requires mechanical or chemical perturbation and can be difficult to reproduce. Furthermore, vesicles created by traditional methods are often unstable or metastable and prone to aggregation, limiting their usefulness.

To overcome these challenges and to create vesicles with superior performance, Carlos López-Barrón, Norman J. Wagner, and co-workers looked to a cationic double tail surfactant, known as didodecyldimethylammonium bromide (DDAB) (DOI: 10.1021/ja308975e). To help drive the self-assembly process, the team dissolved DDAB into a protic ionic liquid consisting of ethylammonium nitrate, a "green solvent" with properties similar to those of water. The researchers demonstrated, for the first time, the spontaneous formation of thermodynamically stable, non-aggregating vesicles in protic ionic liquids.

This work represents a significant step toward potential applications of this class of vesicles as microreactors, drug carriers, and templates for the synthesis of mesoporous materials. **Christine Herman, Ph.D.**

MOLYBDENUM ENZYMES: LIGANDS WORTH A LOOK

Molybdenum enzymes, enzymes that require the transition metal molybdenum for their activity, are found in nearly all life forms and play crucial roles in the biogeochemical cycles of the key elements nitrogen, sulfur, and carbon. To achieve their versatile enzymatic capabilities, some molybdenum enzymes use an unusual ligand called a pyranopterin dithiolene ligand, which is composed of a heterocyclic pterin group, a pyran ring, and two sulfur atoms that hold the molybdenum in place. To gain insight into the molecular basis for how this unique ligand contributes to molybdenum enzyme function, Sharon Burgmayer and co-workers synthesized chemical models of the enzymatic system (DOI: 10.1021/ja310018e).

The authors used the structural characterization methods X-ray crystallography and nuclear magnetic resonance to explore their molybdenum enzyme model systems. They found that the pyranopterin system may be a dynamic one in which the pyran ring cyclization is reversible. These results suggest that the ligand structure may be an integral part of the versatility of these resourceful enzymes and provide clues about how the enzymes are capable of transforming such diverse inorganic and organic compounds. **Eva J. Gordon, Ph.D.**

NEW MRI CONTRAST AGENTS CAN RELAX IN STRONG MAGNETIC FIELDS

Magnetic resonance imaging (MRI) has revolutionized medicine, allowing doctors to probe tissues for signs of disease with harmless magnets. The intensity of the MRI signal from water varies in different parts of the body, painting a picture of a patient's insides. To see finer detail, doctors can administer a contrast agent that visibly alters the MRI signals of water molecules in close contact with the agent. Unfortunately, commercial contrast agents lose this capacity, called relaxivity, at high magnetic fields, which can independently improve MRI images.

Now, Peter Caravan and colleagues have developed a new type of contrast agent that performs well at high magnetic fields, offering the opportunity to snap better MRI pictures (DOI: 10.1021/ja309187m). The relaxivity of a contrast agent is related to how quickly it rotates in liquid, which in turn depends on the molecule's size and shape. The researchers set out to maintain a contrast agent's relaxivity at high fields by tuning its structure and thus its rotational properties. They started with a rigid core consisting of a gadolinium moiety and then attached a series of linear and cyclic peptides to this core, ending up with six novel contrast agents. The agents' relaxivity was good at low and high magnetic fields, outperforming commercial agents. **Erika Gebel, Ph.D.**

TOWARD A BETTER HIV ANTIVIRAL

The HIV-1 reverse transcriptase is an attractive target for antiviral therapies, and several such compounds have entered the market. These include both nucleotide analogues and non-nucleoside inhibitors. Recently, William Jorgensen, Karen S. Anderson, and colleagues described a pair of highly potent non-nucleoside (catechol diether) inhibitors of HIV-1 reverse transcriptase. One of these compounds has a substantially lower EC_{50} value than either of the two FDA-approved non-nucleoside inhibitors, nevirapine and rilpivirine.

Now, the researchers report the crystal structure of the resulting enzyme–inhibitor complexes (DOI: 10.1021/ja3092642). The crystal structures of the two catechol diether inhibitors with HIV-1 RT show that the molecules form extensive contacts with the enzyme's "non-nucleoside binding pocket", including two "immutable" residues (proline-95 and tryptophan-229) required for enzyme activity. The authors also investigate the interaction between one of the compounds' two halogen atoms and P95, finding that the electrostatic bond angle formed between that atom and the proline oxygen is "significantly bent from the ideal linear geometry."

The analysis suggests the possibility of even more potent inhibitors, the authors write. "From this analysis, a design strategy emerges to improve interactions with P95 and maintain interactions with W229, both residues important for the assembly and activity of HIV-RT and thus not prone to mutation." **Jeffrey M. Perkel**

PICKING APART PAENICIDIN A

Many bacteria produce compounds that are toxic to other bacteria. For example, a compound produced by the bacterium

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Paenibacillus polymyxa inhibits the growth of the bacterium *Campylobacter jejuni*, a common cause of food poisoning, and this activity was traced to a peptide called tridecaptin A. John Vederas and co-workers also identified a new member of the lantibiotic family of cross-linked peptides called paenicidin A (DOI: 10.1021/ja3089229). Lantibiotics have therapeutic potential and are also used as food preservatives, and there is great interest in how their structures influence their activities.

When traditional methods to determine paenicidin A's structure proved unsuccessful, the authors developed a strategy that involved removing some of the sulfur atoms from the compound and using mass spectrometry to help determine how the compound is linked together. They found that paenicidin A is made up of six rings, three of which are interlocking.

This strategy will facilitate investigation of the structures of lantibiotics and other cross-linked peptides, with potential implications for the development of new antibiotics. **Eva J. Gordon, Ph.D.**