

Spotlights on Recent JACS Publications

■ PROTEIN FOLD BOUNCES BACK AFTER THE PRESSURE IS OFF

Martin Gruebele, Klaus Schulten, and colleagues show that a protein domain can refold rapidly after it is denatured by a sudden pressure increase (DOI: 10.1021/ja412639u).

Understanding the kinetics of protein folding is fundamental to biochemistry. Researchers have used molecular dynamics simulations to capture the short time scale on which a protein refolds in response to brief temperature-induced denaturation. But comparatively few studies have used pressure perturbations to examine protein folding dynamics.

In this work, the authors have determined, by experiment and a molecular dynamics simulation, how an 80-residue protein domain responds to a microsecond-scale burst of 5 kbar of pressure. They find that the protein domain almost completely refolds after about 19 μ s, with the exception of one helix formation at the end of the polypeptide chain.

The work provides new insights into how proteins refold after pressure-induced denaturation. It also sheds light on how proteins pass through transition states in the process of folding. **Deirdre Lockwood**, Ph.D.

■ GOLD TRIPODS MAKE BIOIMAGING BETTER

Imagine an army of tiny tumor-finding robots that travel around in the blood, looking for a tumor. When they find one, they gather there and illuminate what they have found. Importantly, the bots cause no harm. This scenario is what biomedical imaging probes are supposed to do. The problem has been that what makes them good at finding tumors and not causing harm tends to make them not as good at signaling. Zhen Cheng and co-workers have found a way around this conundrum with an imaging probe that has a strange shape: a tripod (DOI: 10.1021/ja412001e).

Composed of a platinum cube with gold spheres attached to three faces, the imaging probes are both incredibly small and able to signal from deep within tissues. Studies on mice show that when tumor-seeking molecules are added to the tripods, they find tumors, accumulate there, signal more strongly than other probes, and cause no acute toxicity. The experiments suggest that after a while the probes may be able to leave the body through urine excretion.

Because the probe-making process is predictable and controlled, the researchers note that their strategy should allow others to tailor the optical and physical properties of such nanostructures to specific biomedical uses.

Jenny Morber, Ph.D.

■ ELUCIDATING THE STRUCTURE OF IONIZED MOLECULES: BENZENE²⁺

Using very low temperature infrared spectroscopy, Jana Roithová and co-workers have found that doubly ionized benzene forms a high-energy six-membered-ring structure, which can then undergo rearrangement to a pyramidal structure (DOI: 10.1021/ja412109h).

Benzene is an iconic molecule within the history of chemical structure and bonding, and Kekule's model of a hexagonal arrangement of six carbon bonds with alternating double bonds is well known. But directly probing the structure of the benzene dication is challenging experimentally due to its high reactivity and small cross-section; therefore, such investigations have primarily been theoretical studies.

Here, the authors investigate these ions by infrared predissociation spectroscopy, where the ion of interest forms a complex with an inert helium atom at low temperatures. By comparing the measured spectra with calculated spectra of potential isomers, the researchers are able to determine both the initial structure that is formed as well as the transformation to a more stable isomer. This work represents a promising method to probe the structure and bonding of very reactive ionic species that are difficult to study by other means.

Dalia Yablon, Ph.D.

■ STRIP DOWN, RATHER THAN PUTTING ON

The uncommon C–F bond confers unique biological properties on organofluorine compounds, especially fluorinated aromatics, making them highly desirable targets in pharmaceuticals and agricultural chemistry. While there are a variety of established approaches to monofluorinated arenes, partial aromatic fluorination to install two or more fluorine atoms proves to be problematic, suffering from low efficiency and poor selectivity.

Hydrodefluorination (HDF) of perfluoroarenes—in other words, replacing some fluorines in a molecule with hydrogen atoms—provides an alternative route to partially fluorinated arenes. In an effort to develop a simple and robust HDF method, Jimmie Weaver and colleagues introduce an iridium(III)-based photocatalyst to facilitate selective fluoride elimination, along with an inexpensive amine reductant (DOI: 10.1021/ja500031m). Besides its broad compatibility, the photocatalyst can achieve extremely high turnover numbers.

Given the easy accessibility to perfluorinated aromatic substrates, this novel transformation can lead to a number of polyfluorinated arenes in a convenient and economical way. Capable of being scaled up using continuous flow synthesis, it also holds the promise of replacing existing methods in commercial manufacturing.

Xin Su, Ph.D.

■ RADICALS MAKE FULLERENES ACT DOPED

Fullerenes are soccer-ball-shaped carbon structures. Since the discovery of fullerenes more than three decades ago, researchers continue to probe their fascinating properties. Now, Yataka Matsuo, Eiichi Nakamura, and colleagues have discovered that a solid made up of pairs of bonded fullerenes has an unusual response to high temperature (DOI: 10.1021/ja500340f).

Published: March 10, 2014

With enough thermal energy to break a dimer's fullerene–fullerene bond, each singlet is left with an unpaired electron. As the solid cools, the singlet fullerenes do not recombine but rotate and maintain their dangling bonds. Normally such “free radicals” are highly reactive, but with only bonded fullerene dimers nearby, the radicals instead increase electron mobility of the entire solid. The unbonded fullerenes act like dopants. Interestingly, the effect is long-lasting and remains stable in experiments after repeated heating and cooling cycles, for more than 16 h.

The researchers suggest that this behavior stems in part from the ease with which an unbonded fullerene can rotate within a fullerene crystal. Like a layer of ball-bearings on a smooth floor, a single sphere can move freely and never touch its neighbors.
Jenny Morber, Ph.D.