

## Spotlights on Recent JACS Publications

### ■ MOLECULAR MODELING CLARIFIES PHOSPHORYL TRANSFER REACTION MECHANISMS

Phosphate ester hydrolysis is a critical component of cellular energy metabolism, nucleotide biochemistry, and enzymology. Naturally, researchers are interested in working out the particulars of phosphate (and sulfate) transfer chemistry, and both computational and experimental approaches have been applied to the problem. Yet the precise reaction mechanisms and molecular geometries have remained unclear, in part because different studies have reached different conclusions.

Lynn Kamerlin, Nicholas Williams, and colleagues computationally model the hydrolysis energetics and bond lengths of three model compounds, *p*-nitrophenyl phosphate, methyl phosphate, and *p*-nitrophenyl sulfate, in water and use those data to differentiate between solvent- and substrate-assisted reaction mechanisms (DOI: 10.1021/ja5082712). They also explore the impact of the leaving group on the reaction mechanism, as well as kinetic isotope effects. To make the problem computationally tractable, the team spike their models with varying numbers of discrete solvent molecules and studies their impact.

“Overall, our results provide a unifying mechanistic framework that is consistent with the experimentally measured kinetic isotope effects and reconciles the discrepancies between theoretical and experimental models for these biochemically ubiquitous classes of reaction,” the authors conclude.

Jeffrey M. Perkel

### ■ UNUSUAL, STABLE GOLD NANOCUSTER REVEALED

Tiny clusters of gold atoms are emerging as powerful tools for fundamental science and exciting applications. Ranging from less than 20 to more than 100 atoms, they have been explored for cell staining and tracking, anticancer agents, pollutant detection, molecular electronics, catalysis, and much more. For more fundamental pursuits, their precise compositions and sizes help researchers unveil connections between properties and molecular arrangement.

Quan-Ming Wang, De-en Jiang, and colleagues create a new cluster of 19 gold atoms ( $\text{Au}_{19}$ ) and report its synthesis, structure, optical properties, and electronic structure (DOI: 10.1021/ja512133a). According to the researchers, this work presents the first structural determination of a ligand-protected  $\text{Au}_{19}$  nanocluster. Experiments show that the  $\text{Au}_{19}$  cluster is stable, with optical properties that hold promise for light-harvesting and as a photosensitive agent.

Perhaps more importantly, this cluster contains unusual alkynyl–gold bonds, suggesting the possibility that many more of these kinds of clusters are waiting to be discovered, and perhaps stimulating more work in this emerging field. This report provides a rare atomic-level view of a new class of gold nanoparticle and its surface ligand layer.

Jenny Morber, Ph.D.

### ■ BUILDING QUATERNARY CHIRAL CARBONS FROM TERTIARY NUCLEOPHILES

Quaternary chiral centers are common molecular motifs in targets of organic synthesis, such as natural products and pharmaceuticals. Their construction can be envisioned as a straightforward stereoselective coupling between tertiary nucleophiles and appropriate electrophiles. In practice, however, it remains a challenge to generate viable tertiary nucleophilic species, especially for complex precursors.

Now, Larry E. Overman and co-workers, by employing chiral tertiary organocuprates and radicals as coupling intermediates, are able to construct C9-quaternary chiral carbons in the bicyclic system of *trans*-clerodanes, a class of plant diterpenoids with well-recognized insect antifeedant activity (DOI: 10.1021/ja512527s). The key transformation involves 1,6-addition of the tertiary nucleophiles to  $\beta$ -vinylbutenolide, a stereoselective reaction in which coupling occurs exclusively from the less-hindered equatorial face.

Overall, this study is not limited to being a more concise synthetic strategy to the *trans*-clerodane backbone; it also introduces a general method to access quaternary stereogenic carbons, particularly in a complex structural environment.

Xin Su, Ph.D.

### ■ FLUORESCENT PROBES “FLIP OUT” IN CELL MEMBRANES

In many respects, biological membranes remain mysterious to scientists. For example, how do lipids within the bilayer maintain their order? And how do cells control membrane potential, as well as the tough-to-detect yet biologically important characteristic known as membrane tension? To answer questions like these, scientists need probes that allow them to visualize membrane processes they otherwise could not see. Now, researchers led by Stefan Matile and Marta Dal Molin report a new class of mechanosensitive probes, dubbed “fluorescent flippers”, that emit light in response to physical changes in their environment (DOI: 10.1021/ja5107018).

In order for a fluorescent probe to be useful in biology, the molecule must be sensitive enough to respond to small changes in the environment, and it must have a high quantum yield so that it is bright enough to be seen with current imaging technologies. The team creates a probe based on dithienothiophenes and their *S,S*-dioxides, which have twisted “push-pull” scaffolds that undergo shifts in excitation wavelength upon mechanical stimulation, detectable also in emission. The probes are the first mechanophores to report on the lateral organization of lipid bilayers with quantum yields above 80% and lifetimes above 4 ns, representing a significant step toward uncovering the secrets of biological membranes.

Christine Herman, Ph.D.

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