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Spotlights on Recent *JACS* Publications

SILICA COATS PROVIDE SOLUTION TO NANODIAMOND PRECIPITATES

Fluorescent nanodiamonds *should* make ideal biological markers: they do not bleach away or blink in light like fluorescent dyes, and they do not have toxicity concerns like quantum dots. They fluoresce in the near-infrared range, which means that their light can shine through tissues several centimeters deep. But fluorescent nanodiamonds are difficult to work with. Rather than dispersing nicely in solution they clump up, and adding chemical linkers to their surface is a challenge.

Keir Neuman and his team report a solution that addresses these problems without losing fluorescent nanodiamonds' positive attributes (DOI: 10.1021/ja4016815). The researchers use a liposome-based process to encapsulate single nanodiamonds in silica—a material commonly known as sand. The covering renders nanodiamonds dispersible in a variety of solutions, microbe-resistant, biocompatible, and easily modified by chemical linkers. In a proof-of-concept experiment, the team attaches a DNA molecule to a nanodiamond and tracks its movements in three dimensions. This method allows the study of nucleic acids and how they interact with proteins.

With prior frustrations removed, researchers are now free to use silica-coated nanodiamonds as MRI contrast agents for targeted drug delivery, biomolecule labels, and versatile markers for ultra-high-resolution microscopy and imaging. **Jenny Morber, Ph.D.**

CYCLOADDITION MECHANISM VARIES BY CATALYST

Xin Hong, Barry M. Trost, and Ken Houk clarify the mechanistic details of a ruthenium-catalyzed cycloaddition and ene reaction using density functional theory (DOI: 10.1021/ja4012657). As seven-membered rings are found in many natural products and drugs, such as the popular antihistamine desloratadine, chemists have sought to develop efficient ways to synthesize them. Though this task still presents a challenge, great strides have been made by using transition metals to catalyze cycloaddition reactions.

Here, the researchers have found that the mechanism of one such reaction—the intramolecular cycloaddition and ene reaction of vinylcyclopropanes and alkynes—depends on the metal chosen as catalyst. The ruthenium-catalyzed reaction involves formation of a metallacyclopentene intermediate, in contrast with the metallacyclohexene intermediate favored when rhodium is used as a catalyst. Additionally, they find that acetone solvent facilitates the reaction by lowering the reaction barrier through destabilizing the resting state of the catalyst.

The authors suggest that using different transition metal catalysts in cycloaddition reactions could allow researchers to fine-tune selectivity and reactivity for different substrates. **Deirdre Lockwood**

RESEARCHERS SPY CHEMICAL BOND FORMATION WITH SPECIAL AGENT

Magnetic resonance imaging (MRI) is a window into the body, and since people are mostly water, the dominant MRI signal comes from the hydrogen atoms in water molecules. The strength of the signal is very sensitive to the water molecules' environment, allowing doctors to visualize structures in the body. To get more detailed information, such as the location of disease-linked proteins, scientists have developed contrast agents that tweak water's MRI signal in areas where enzymes break chemical bonds. In an extension of this method, Dina Hingorani, Edward Randtke, and Mark Pagel describe the first such agent that detects the formation of a chemical bond (DOI: 10.1021/ja400254e).

The researchers focus their efforts on transglutaminase, an enzyme that is abundant in tumors. The enzyme connects proteins by forming a bond between amine groups in the side chains of certain amino acids. Pagel and his team synthesize Tm-DO3A-cadaverine, which has an amine group that tricks transgluatminase into creating a bond between itself and a protein. In the process, the amine group is converted into an amide group, tuning Tm-DO3A-cadaverine into a contrast agent, and thereby allowing researchers to detect water molecules near transglutaminase. The hope is that Tm-DO3A-cadaverine could help doctors find tumors by pinpointing transglutaminase activity in the body. **Erika Gebel, Ph.D.**

BETA CARBONS UPSTAGE ALPHAS IN OLEFIN INSERTION REACTIONS

Organometallic catalysts allow chemists to control regioselectivity in reactions of organic molecules. This control is important in industrial settings, where specific compounds need to be made as efficiently as possible. Now William Jones and co-workers have found evidence that the strength of β-carbon–hydrogen bonds dictates the formation of linear versus branched olefin insertion products (DOI: 10.1021/ja400966y).

Conventional wisdom states that, in olefin insertion reactions, alkenes with an electron-withdrawing group tend to give branched insertion products, while their parent hydrocarbons tend to give linear products. Chemists have long thought this selectivity was controlled by the strength of the metal–carbon bond, a direct result of electronic effects at the α-carbon. Reports that this selectivity can be reversed suggest that additional variables must affect the outcome.

Here, the researchers synthesize a series of substituted methyl derivatives of a rhodium complex and measure the kinetics of the reductive elimination of the substituted methanes. They then examine the correlation between the metal–carbon and the carbon–hydrogen bond energies. The researchers find that α-halogen substituents in $Rh-CH_2X$ have a stabilizing effect, but that most electron-withdrawing groups actually weaken the $Rh-CH_2X$ bond in substituted com-

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pounds. This finding challenges the idea that α-carbon substitution strengthens the metal–carbon bond, and may lead to more efficient control of specific hydrocarbon isomerizations in the future. **Leigh Krietsch Boerner, Ph.D.**