JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
Spotlights
pubs.acs.org/JACS

Spotlights on Recent *JACS* Publications

DRUG–DIAGNOSTIC COMBO KNOCKS OUT TUMOR CELL POWERHOUSE

Jong-Hoon Kim, Jong Seung Kim, and colleagues have designed a therapeutic–diagnostic tool for treating cancer that can induce and monitor cell death by targeting the mitochondria of tumor cells (DOI: 10.1021/ja510421q).

In recent years, anticancer strategies have advanced to include theranostics—molecular tools that can deliver drugs to cancer cells while also helping to diagnose and monitor the disease. Now the team introduces a clever theranostic prodrug approach that acts on tumor cells' mitochondria, the organelle that regulates the cell death machinery.

With biotin tags, the theranostic prodrug preferentially targets tumor cells and localizes in the mitochondria. There, it reacts with hydrogen peroxide, which is elevated in the mitochondria, to activate the anticancer drug 5′-deoxy-5-fluorouridine. As the drug induces cell death, or apoptosis, the fluorophore ethidium reports on this process.

The new approach could be developed to diagnose cancer in its early stages and to design more efficient, individualized strategies for its treatment.

Deirdre Lockwood, Ph.D.

SAME TREE, DIFFERENT FRUIT: SWITCHABLE N-HETEROCYCLIC CARBENE CATALYSIS

N-Heterocyclic carbenes (NHCs)—neutral carbon atoms with two unshared electrons, that are stabilized by neighboring nitrogen atoms—are carbene species with increased stability. Their ability to coordinate to carbon electrophiles, such as aldehydes, esters, and Michael acceptors, makes them excellent organocatalysts, especially for heterocyclic annulation reactions. It is, however, still unclear how activation by NHCs is controlled by their steric and electronic properties.

Now, Frank Glorius and co-workers demonstrate that, by only switching NHC catalysts in the cycloaddition between enals and *in situ* generated azoalkenes, the products can be selectively obtained as 1,2-diazepines or pyrazoles through formal [4+3] or [4+1] annulation pathways, respectively (DOI: 10.1021/ja510737n). While an electron-rich chiral NHC favors the homoenolate route, leading to enantioenriched 1,2-diazepines, a less electron-rich analogue leads to the formation of acyl anion intermediates that yield pyrazoles.

During the development of the first NHC-catalyzed asymmetric synthesis for 1,2-diazepines, the authors have identified key electronic and steric factors that regulate the reactivity of NHCs, which may also inform the design of NHC catalysts for other applications. In addition, this study represents an unusual example where the regioselectivity in product formation from same substrates is completely dominated by a structural difference in the catalyst.

Xin Su, Ph.D.

SNUG SPACING HELPS SYNTHETIC PROTEIN MIMIC NATURAL ELECTRON TRANSFER

Giovanna Ghirlanda and colleagues have designed a protein that mimics an important class of natural electron-transfer proteins, the ferredoxins (DOI: 10.1021/ja510621e).

The life-maintaining processes of photosynthesis and respiration rely on metalloproteins called ferredoxins, which transfer electrons using chains of [4Fe-4S] clusters. Researchers would like to insert these clusters into synthetic peptides to create new enzymes that can be manipulated for a variety of applications in redox chemistry. But so far, chemists have struggled to generate a platform in which the clusters are spaced at an optimal distance for electron transfer.

Now Ghirlanda and co-workers have solved this problem: they have made a protein, DSD-Fdm, with two [4Fe-4S] clusters spaced 12 Å apart, which is similar to natural ferredoxins. The protein folds into stable dimers and successfully transfers electrons to cytochrome *c*, an important natural electron-transfer protein. The team also shows that DSD-Fdm accepts energy from a porphyrin photosensitizer, suggesting that it could be applied in designing solar fuel cells. The work could also help generate artificial redox pathways for synthetic biology applications.

Deirdre Lockwood, Ph.D.

NEW SMALL-MOLECULE CANDIDATE FOR OPTICAL MEMORY STORAGE MATERIALS

When it comes to the design of photoswitchable "smart" materials for optical memory storage systems, not just any light-activated molecule will do. The compounds must allow writing and erasure processes to occur efficiently and reliably, which requires the ability to undergo repeated cycles of photocyclization and photocycloreversion with high quantum yields and without photochemical side reactions, even at elevated temperatures. Now, researchers led by Vivian Yam describe a new silole-containing dithienylethene molecule that meets these requirements (DOI: 10.1021/ja5101855).

The study is the first to investigate a dithienylethene molecule that incorporates the promising yet underexplored class of heterocycles known as siloles into its cyclic ethene backbone. The researchers find the molecule has promising photochromic properties, and they perform computational studies that provide insight into the electronic structure of the compound and the nature of its excited states. The results reveal that the molecule has excellent thermal stability and fatigue resistance, making it a strong candidate for applications in optical memory storage systems and other photoswitchable devices.

Christine Herman, Ph.D.

Published: December 24, 2014

dx.doi.org/10.1021/ja512748v | *J. Am. Chem. Soc.* 2014, 136, 17691–17691