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

Spotlights on Recent *JACS* Publications

■ ASYMMETRIC BIARYL COUPLING SIMPLIFIES NATURAL PRODUCT SYNTHESIS

Chiral biaryls are a unique structural motif that exists in many pharmaceutical drugs and natural products. Suzuki−Miyaura coupling—one of the methods for constructing chiral biaryls—has attracted a great deal of attention due to the mild reaction conditions. However, application in natural product syntheses has yet to be fully explored. Wenjun Tang and co-workers have developed an asymmetric Suzuki−Miyaura catalytic system that is successfully applied in the efficient total synthesis of michellamine B, a potent anti-HIV agent that naturally occurs in Cameroon Liana *Ancistrocladus korupensis* (DOI: 10.1021/ja409669r).

The method is able to build the axially chiral biaryl motif in precursors of michellamine B (korupensamines A and B) in only one step, which would otherwise require arduous synthetic efforts, and a wide range of synthetically useful chiral biaryls are prepared in excellent yields with high enantioselectivities. This new strategy greatly expands the scope of Suzuki−Miyaura coupling in the realm of asymmetric synthesis and can be readily employed for the concise syntheses of a variety of natural products with chiral biaryl moieties.

Xin Su, Ph.D.

■ DECIPHER THE CODE OF GOLD

Gold-based oxidative catalysis has contributed greatly to C−C and C−X bond formations over the past decade. Whereas strategies such as gold-catalyzed direct arylation are of broad synthetic interests, detailed mechanisms of these reactions, especially the oxidation states of gold involved in catalytic cycles, still remain elusive.

After successfully developing a regio- and chemoselective approach to biaryls from arenes and aryltrimethylsilanes under gold catalysis, Liam Ball, Guy Lloyd-Jones, and Christopher Russell continue with mechanistic studies of this transformation (DOI: 10.1021/ja408712e). Through studies of the kinetics of catalytic and stoichiometric reactions with an improved precatalyst, the authors establish a Au(I)/Au(III) redox catalytic cycle, where a sequential electrophilic aromatic substitution cascade is responsible for the chemoselectivity toward cross-coupling.

This study thoroughly unravels the role and interconversion of active gold species in a C−C coupling reaction, which is critical to understanding the entire catalytic cycle. More importantly, the mechanistic insights can provide guidelines for developing improved biaryl synthesis by designing novel catalytic cycles with more efficient catalysts and oxidants.

Xin Su, Ph.D.

■ NEW METHOD DETECTS PROTEIN-SPECIFIC GLYCOSYLATION EVENTS

Glycosylation—the attachment of sugars to proteins—regulates many cell communication and signaling processes. Researchers have genetic strategies for labeling specific proteins, but glycan labeling methods are less discriminating. It is therefore difficult to link particular glycoforms to specific proteins, especially in live cells. Now Xing Chen and colleagues report a FRET-based method to do just that (DOI: 10.1021/ja410086d).

The method employs two bioorthogonal labeling events. An alkyne-containing sugar is incorporated into all sialylated glycans via metabolic labeling. Those sugars are then tagged with Alexa Fluor 647 via copper-catalyzed azide−alkyne cycloaddition (CuAAC). The protein of interest is genetically tagged at its N-terminus with a peptide called LAP, which is conjugated to a picolyl azide via an enzymatic process and then (by CuAAC) to Fluor 488-alkyne. Sialylation on the protein of interest is detected by FRET between the two fluorophores.

Using this method, the authors visualize sialylated glycoforms of integrin β2, EGFR and TGF-β receptor I, and they suggest it should also be applicable to other sugars, including *N*-acetylgalactosamine and fucose.

The strategy "thus offer[s] a powerful tool for probing how the functions of a [protein-of-interest] are regulated by its glycoforms on live cells," the authors conclude.

Jeffrey M. Perkel

■ SLOW DOWN, MOVIN' WAY TOO FAST

Adsorption and desorption of macromolecules from surfaces are complex processes involving large energy scales and complicated conformational changes. Roland Netz, Thorsten Hugel, and co-workers have successfully measured and modeled the kinetics of desorption of single protein molecules from a hydrophobic surface, revealing a much slower process than expected (DOI: 10.1021/ja410278r).

Using a microscopic cantilever covalently bonded to the proteins coupled with atomic force microscopy, the researchers pull on individual proteins to desorb them from a hydrophobic surface, modeled by a self-assembled monolayer. By measuring the force exerted onto the cantilever as it pulls the protein away from the surface in a variety of solvents, they determine the adsorption energy and analyze the results with a simple kinetic model to yield a desorption rate constant.

The authors hypothesize that the observed slow kinetics are due to the connectivity or coupling between the various monomers within the peptide. The slower-than-expected rate constant has important consequences for the kinetics of protein folding and other processes involving the reconfiguration of peptide chains in a confined state.

Dalia Yablon, Ph.D.

Published: January 7, 2014

dx.doi.org/10.1021/ja5001483 | *J. Am. Chem. Soc.* 2014, 136, 527−527