

Spotlights on Recent JACS Publications

■ LIGAND TUNES SELECTIVITY BETWEEN ALKOXYCARBONYLATION AND AMINOCARBONYLATION

Esters and amides are essential functional groups that play an important role in a number of fields of chemistry, and they can be formed by catalytic carbonylation using carbon monoxide with higher atomic efficiency than conventional methods. However, this transformation is still hindered by the lack of chemoselectivity when hydroxyl and amino groups are both present in the substrate.

In order to determine factors that steer such selectivity, Howard Alper and Tongyu Xu systematically examine various combinations of ligands and bases in Pd-catalyzed carbonylation of aminophenols (DOI: 10.1021/ja508588b). They discover that high selectivity for ester or amide formation can be achieved using specific ligand/base pairs in cases of 3- or 4-aminophenols. They suggest this chemoselectivity is regulated by the ligand with the assistance of the base.

The researchers have made a major contribution toward a long-known challenge in selective functionalization in the presence of competing reactive groups. In addition to aminophenols, this strategy suggests compatibility with amino-alcohols as well, demonstrating a wide scope. The established ligand/additive effect may also be extended to the exploration of other chemoselective catalytic reactions.

Xin Su, Ph.D.

■ MECHANISM MATTERS FOR ENGINE-SCRUBBING ANTIOXIDANTS

Derek Pratt and colleagues have determined the radical-trapping mechanism of powerful antioxidants called diarylamines that are used in motor oils (DOI: 10.1021/ja509391u).

Antioxidants are added to motor oil to prevent buildup of combustion products and corrosion. Diarylamines are an unusually potent class of these antioxidants: at the temperatures of combustion, each amine molecule can trap multiple radicals. Researchers have hypothesized that this property stems from the compounds' ability to regenerate through autoxidation, but so far the details of the mechanism have not been clear.

Now Pratt and co-workers have elucidated this mechanism through computational studies and confirmed it with experiment. They show that the key step in the reaction can proceed by two different mechanisms, depending on the types of both the diarylamine and the substrate.

The more productive pathway for antioxidant regeneration and radical trapping, a concerted retro-carbonyl-ene reaction, proceeds from diphenylamines and unsaturated substrates, or from *N*-phenyl- β -naphthylamine and saturated substrates. In contrast, a mechanism derived from diphenylamines and saturated substrates is much less effective at trapping radicals. The work could advance the design of more potent engine-cleaning additives through the incorporation of suitable diarylamines.

Deirdre Lockwood, Ph.D.

■ SMOOTH AS SILK: HOW SPIDER SILK GETS MADE AT THE MOLECULAR LEVEL

Material scientists envy web-weaving spiders. The animals transform soluble proteins called spidroins into silk fibers of tensile strength and extensibility superior to those of man-made fibers. Researchers want to understand how spidroins come together at the molecular level so they can better design synthetic fibers.

Hannes Neuweiler and colleagues now have analyzed the N-terminal domain of spidroins, which is involved in the polymerization of the proteins in a pH-dependent process (DOI: 10.1021/ja508760a). The investigators modify the domain with a fluorescent label on a tryptophan residue and track motions by a technique called single-molecule photo-induced electron transfer. With this approach, they measure the domain's internal motions at the 1-nm scale and with a time resolution of nanoseconds. Neuweiler and colleagues have discovered that the N-terminal domain folds and changes structure extremely fast within a fraction of a millisecond.

The data suggest that rapid motions change the shape of the N-terminal domain such that it is suitable for polymerization. The speed of motion in this structural switch makes sense in light of how rapidly spiders synthesize silk as they drop down on a dragline.

Rajendrani Mukhopadhyay, Ph.D.

■ POLYPHENYLENES WITH NEAR-PERFECT FOLDING

A class of oligomers known as *ortho*-phenylenes is known for the oligomers' ability to fold into helical conformations thanks to aromatic stacking interactions. Such polyphenylenes would make for great functional units within more complex molecular architectures if only they could be counted on to adopt predictable, well-defined conformations in high yields. Now, researchers led by C. Scott Hartley demonstrate that controlling the strength of the aromatic stacking interactions can enable chemists to create *o*-phenylenes with effectively perfect folding (DOI: 10.1021/ja509902m).

The team has created several new series of *o*-phenylene oligomers by varying both the nature and orientation of the substituents on each repeat unit. The researchers probe the molecules' behavior with NMR spectroscopy, DFT calculations, and X-ray crystallography and find that oligomers with substituents that are more electron-withdrawing have substantially improved folding properties. For example, moderately electron-withdrawing groups, such as acetoxy, yield >90% of the perfectly folded conformer, while stronger electron-withdrawing groups, such as triflate and cyano, result in oligomers that appear perfectly folded when analyzed via NMR. The principles derived through this study may lead to the design of other types of polyphenylenes with predictable and well-defined structures.

Christine Herman, Ph.D.

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■ TRIPLE CATALYTIC SELECTIVITY IN DEAROMATIC HYDROSILYLATION OF QUINOLINES

Synthetic methodologies combining selective reduction and functionalization are highly desired by organic chemists, as in the case of accessing tetrahydroquinoline derivatives, an important class of intermediates of natural products and pharmaceuticals. However, selectivity and controlled reduction are often challenging in existing strategies, such as in the reduction of quinolines by metal hydrides or hydrogen.

By harnessing the Lewis acidic catalytic activity of tris-(pentafluorophenyl)borane, Sehoon Park, Sukbok Chang, and co-workers have developed a new method to prepare silylated tetrahydroquinolines by reducing quinolines with diethylsilane (DOI: 10.1021/ja510674u). While the silyl group is directed to add to the β -position of the nitrogen heteroatom, its stereochemistry is dominated by pre-existing neighboring groups, being *syn* and *anti* to α - and γ -substituents, respectively.

In addition to its excellent chemo-, regio-, and stereo-selectivity, this metal-free transformation is compatible with a broad range of similar substrates, including isoquinolines, benzoquinolines, and phenanthrolines. Also noteworthy is the asymmetric induction when appropriate chiral substrates are used, in which two new stereocenters can be defined. The readily available conversion of C–Si bonds into C–OH moieties makes the products ideal building blocks especially for functionalized alkaloids.

Xin Su, Ph.D.