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Spotlights on Recent *JACS* Publications

HUMBLE DNA ORIGAMI FOR EXTRAORDINARY APPLICATIONS

To make DNA origami, researchers bind long strands of DNA with short "staple" strands at precisely determined locations. In the past decade, DNA origami has moved beyond an art form into a promising scientific tool, but progress has been slowed by practical problems: complex design, limited scaffolds, and the need for hundreds of staple strands drive up time and financial costs.

Yossi Weizmann and colleagues focus on a one-pot "cooking" method, which creates ribbon-like bunches of DNA from only a few staple strands (DOI: 10.1021/ja512665z). The technique's simplicity promises higher yields at lower cost.

The geometry and rigidity of these DNA nanoribbons (DNRs) also make them attractive to cells, which, when incubated together, pull the DNRs into their cytoplasm-filled cavities. In exciting proof-of-concept experiments, the researchers have decorated the DNRs with fluorescein (a tracer dye), biotin (a common binding molecule), and even small interfering RNA (siRNA, which interferes with gene expression) without affecting the ribbons' structure or cellular uptake. In experiments, siRNA delivered into human ovarian cancer cells with DNRs silences a common cancer-promoting gene within the cells. This work illustrates the DNRs' potential for cellular drug and molecule delivery, pH sensing, and selective gene silencing with a scalable, cost-effective technique.

Jenny Morber, Ph.D.

AN ENZYME THAT GETS AROUND

To synthesize new compounds, chemists increasingly look to biological tools, including enzymes that often have the power to work far beyond their expected capabilities. Here, David Berkowitz and co-workers illustrate this potential by using a bacterial enzyme to rearrange a family of substrates with chirality opposite to substrates previously used with this enzyme; the researchers produce a range of compounds that could form the basis for new pharmaceuticals (DOI: 10.1021/jacs.5b00022).

The researchers study an alcohol dehydrogenase derived from *Clostridium acetobutylicum*, a soil-dwelling bacterium that has been used extensively in commercial applications for a century. Though the authors had already found this enzyme to be useful in asymmetrically reducing a family of compounds known as ω-ketoesters, the authors now test the biological catalyst on a different family of compounds, known as α-fluorinated, β-ketophosphonates, and find that the enzyme reduces these too, very selectively, but to give the opposite chirality in the products.

By combining the enzymatic chemistry with a new and very facile sigmatropic rearrangement, a process made significantly faster when the precursor molecule is fluorinated, the β-phosphonates are chemo-enzymatically transformed into highly value-added compounds. The resulting products could be used as inhibitors for Zn-aminopeptidase A, an enzyme that is an emerging target for hypertension.

Christen Brownlee

AMMONIA SYNTHESIS UNDER AMBIENT CONDITIONS

Ammonia is an attractive fuel for alternative energy because its combustion byproducts lack carbon. Researchers want to develop catalysts to synthesize ammonia from nitrogen and hydrogen gas under mild conditions. They find inspiration in the way that enzymes form N−H bonds using a process called proton-coupled electron transfer (PCET). Using this pathway, transfer of a proton and an electron helps lower the energy barrier to product formation.

Iraklis Pappas and Paul Chirik at Princeton University have applied a PCET reaction to induce an organometallic catalyst to release ammonia (DOI: 10.1021/jacs.5b01047). The researchers first measure and calculate the relative free energy for the dissociation of N−H bonds in several ammonia-containing titanocene and zirconocene complexes. Because the dissociation energy reflects the relationship between bond strength and the redox potential of the complex, they then pair the complexes with the strongest N−H bonds with hydride catalysts for PCET.

To demonstrate the utility of this method, they mix a chlorotitanocene amide complex with hydrogen gas and 5 mol% of a rhodium hydride complex. This reaction generates ammonia in 92% yield after 5 days at room temperature. PCET is an attractive approach for ammonia synthesis because it could enable ammonia production under lower pressures and temperatures than currently used in industrial processes.

Melissae Fellet, Ph.D.

ONE-STEP ACCESS TO CHIRAL BROMOCHLOROALCOHOLS WITH TRIPLE SELECTIVITY

Nature has produced a vast array of biologically active compounds with multiple chlorinated and/or brominated stereocenters, most likely through enzymatic dihalogenation of carbon−carbon double bonds. Although dihalogenation is a classic transformation covered by almost all organic chemistry textbooks, stereo- and regioselective versions of this type of reaction are few and far between, especially for interhalogenation, which involves two different halogens.

Now, researchers led by Noah Burns report a general catalytic bromochlorination strategy for allylic alcohols with full control over chemo-, regio-, and enantioselectivity (DOI: 10.1021/jacs.5b01384). Using a simple chiral Schiff base as the catalyst, the authors are able to prepare a variety of bromochloroalcohols with constitutionally and stereochemically well-defined halogen substituents from readily available chlorine and bromine sources.

The utility of this methodology is exemplified by the concise three-step enantioselective synthesis of bromochloromyrcene, a cytotoxic marine natural product. More importantly, its scope can be expanded to include enantioselective dibromination and dichlorination, both of which will enable facile access to chiral polyhalogenated frameworks.

Xin Su, Ph.D.

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