

Spotlights on Recent JACS Publications

■ INNOVATION ON REPETITION: “ASSEMBLY LINES” FOR NATURAL PRODUCTS

Modern assembly-line production, since its initial adoption in building automobiles a century ago, has dramatically revolutionized the manufacturing industry. Likewise, assembly-line organic synthesis holds the promise of delivering complex molecular targets in an efficient and progressive way using interchangeable reagents, but obstacles such as functional-group interconversions and purifications can be problematic in synthetic design.

Having demonstrated the iterative “one-pot” construction of chiral carbon chains, Varinder Aggarwal and co-workers now apply this strategy to the concise syntheses of (+)-kalkitoxin and (+)-hydroxyphthioceranic acid, both of which are biologically active natural products containing long permethylated backbones (DOI: 10.1021/ja512875g). Full stereocontrol in the iterative chiral chain growth is achieved by repetitive addition using two enantiomeric lithiated benzoate esters. The reaction sequence does not require stepwise isolation.

These new synthetic routes to these natural products are much better than those previously reported in terms of both stereo and chemical efficiency, showcasing the power of this assembly-line methodology. Moreover, the reported method enables library synthesis of enantiomers and diastereomers via a divergent strategy simply by controlling the sequence of reagent addition. **Xin Su, Ph.D.**

■ SEMISYNTHETIC STRATEGY ENABLES PARKINSON'S DISEASE STUDIES

One of the distinguishing characteristics of Parkinson's disease and related neurodegenerative conditions is the presence of protein aggregates and fibers in affected brain regions. Parkinson's aggregates are composed of α -synuclein, a protein with four tyrosine residues that can be nitrated. Evidence suggests that α -syn nitration may impact disease pathogenesis, yet to date there has been no efficient method—other than mutagenesis—to specifically modify particular residues and probe their biology. Now, there is.

Hilal Lashuel and colleagues report a “semisynthetic” strategy for incorporating 3-nitrotyrosine into α -syn at either of two positions (DOI: 10.1021/ja5131726). The new method involves both bacterial and solid-phase peptide synthesis, chemical ligation, and desulfurization. The team uses their technique to create milligram quantities of α -syn isoforms nitrated on either tyrosine-39 or tyrosine-125, and employs those proteins, and protein mutants, to study α -syn fibril formation, as well as the fibrils' oligomerization, conformation, and membrane interactions, processes that play important roles in regulating the normal and pathogenic properties of this protein.

“Our semisynthetic strategy for generating site-specifically nitrated proteins opens new opportunities for assessing the role of nitration in regulating protein structure and function in health and disease,” they conclude.

Jeffrey M. Perkel

■ BETTER MODELING OF NANOCATALYSTS

Developing a better understanding of how nanoscale transition metal catalysts accomplish their reaction-accelerating feats could help improve how the nanocatalysts are used in various industrial applications. However, previous efforts to clarify the action of these tiny catalysts have modeled them either as clusters of just a few tens of atoms or as large slabs of the bulk material and have ignored the effects that temperature and the surrounding environment exert on the reaction. Without these missing pieces, the picture of how nanocatalysts behave could be unrealistic.

To overcome these limitations, Xingchen Liu and Dennis Salahub have developed a new way of modeling that could deliver a more accurate description of nanocatalyst performance (DOI: 10.1021/jacs.5b01494). Using the example of hydrogenation catalyzed by molybdenum carbide nanoparticles—an important reaction in the petroleum industry for converting heavy oil sands into lighter hydrocarbons—the researchers account for benzene solvent and high temperature.

Their work reveals that the free energy of this system changes over the course of the reaction. The authors suggest that future modeling efforts for this reaction could be made even more realistic by including the contribution of sands that are often present in addition to the hydrocarbons and nanocatalysts.

Christen Brownlee

■ ORGANOMETALLIC GOLD(III) COMPLEX USED IN ORGANIC MEMORY DEVICE

Organic memory devices made with electrically responsive polymers or organic molecules could be cheaper and easier to prepare than current silicon-based memory. Vivian Wing-Wah Yam and her colleagues have taken a significant step toward making these devices a reality by building the first organic memory device that contains a small-molecule organometallic complex (DOI: 10.1021/jacs.5b02113).

These types of devices encode information in materials that change resistance in response to a particular voltage. To build this new device, the researchers synthesize an alkynylgold(III) complex, then sandwich a film of this complex between an indium–tin oxide electrode and a thin film of aluminum electrode. The researchers apply a voltage to the device and notice that the assembly switches to a low resistance state around 2.5 V. This state is analogous to writing memory. The device stays “on” in this low resistance state through two successive voltage sweeps, and it relaxes to an “off” state when the power is turned off. Other performance characteristics the authors observe are favorable for device stability as well.

Small molecules are attractive candidates for organic memory devices because they can be readily synthesized and modified. These molecules also have a variety of electronic, light-responsive, and light-emitting properties that could provide alternative ways to encode information.

Melissae Fellet, Ph.D.

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