

## Spotlights on Recent JACS Publications

### ■ CAGE-LIKE MATERIAL EXHIBITS RARE PROPERTY IDEAL FOR SENSING

Most materials shrink in all directions under hydrostatic pressure. A Styrofoam cup sent deep underwater surfaces as a mini version of itself. Much more unusual are the materials that expand in one or two directions when hydrostatically compressed.

Leonard Barbour, Andrzej Katrusiak, and colleagues create a porous metal–organic framework (MOF)—a material composed of metal atom joints and organic linkers—that expands in two dimensions under hydrostatic pressure (DOI: [10.1021/jacs.5b03280](https://doi.org/10.1021/jacs.5b03280)). This rare property is called negative area compressibility, or NAC. The soft porous MOF reported here exhibits the strongest NAC ever observed, so strong, in fact, that the effect can be observed visually. The unique behavior arises from a flattening and lengthening of puckered quadrangular rings. The extent of the material's compression and expansion can be tuned with careful choice of solvent molecules that move into or out of the spaces between the MOF's open scaffold.

This material also demonstrates electric charge fluctuations as it compresses, a property called piezo-electricity, which is sought for applications that include pressure sensors, actuators, and composites. The observation of such exceptional NAC in a MOF suggests a new route for the design of ultrasensitive sensing components.

Jenny Morber, Ph.D.

### ■ FUSED HETEROCYCLES FROM “CUTTING-AND-SEWING” $\beta$ -LACTAMS

The “cut-and-sew” strategy in organic synthesis, which involves activation of inert carbon–carbon bonds followed by inserting unsaturated species, is especially ideal for intramolecular ring expansion reactions. It has been successfully applied to assemble fused carbocyclic frameworks by “cutting open” cyclobutane and then “sewing up” with olefins.

Masahiro Murakami and his team have now extended the scope of this convenient strategy, in which they can cleave carbon–nitrogen bonds in  $\beta$ -lactams and intramolecularly insert terminal alkenes to form benzoindolizinedione derivatives (DOI: [10.1021/jacs.5b05308](https://doi.org/10.1021/jacs.5b05308)). This transformation is catalyzed by palladium(0) and may undergo palladacyclization, alkene insertion, and finally elimination of Pd(0), where the ligand assumes a crucial role in mediating effective bond activation.

The new C–N version of the “cut-and-sew” approach is compatible with a range of functional groups in substrates and shows excellent diastereoselectivity. The authors demonstrate its utility in the two-step preparation of a benzoindolizone-based non-nucleoside HIV-1 reverse transcriptase inhibitor. Needless to say, one-step access to the fused N-heterocyclic unit will also simplify the synthesis of bioactive natural products such as valmerins and nuevamines.

Xin Su, Ph.D.

### ■ WATER CONTROLS FOLDING OF ALKYL DIAMMONIUM CATIONS

The number of water molecules surrounding the ammonium ion in an amino acid can influence a protein's structure as well as the local structure of the protein's aqueous surroundings. To better understand how water influences molecular structure, David Russell and his colleagues have used cryo-ion mobility-mass spectrometry to measure structural changes that occur upon stepwise removal of water molecules from alkyl diammonium cations (DOI: [10.1021/jacs.5b05448](https://doi.org/10.1021/jacs.5b05448)).

The researchers show clear evidence that dehydration induces a distinct unfolding transition for 1,7-diaminoheptane, 1,8-diaminooctane, and 1,10-diaminodecane over a different, specific, narrow range of water molecules. For larger hydrated clusters, the alkyl chains adopt folded conformations in which both ammonium ions are solvated by a single droplet of water, whereas smaller, less hydrated clusters exist as elongated chains with individually solvated ammonium ions.

This information provides insight into the effects of hydration on intramolecular interactions and structural transitions expected in larger solvated biomolecules, the researchers write.

Melissae Fellet, Ph.D.

### ■ MERGED REDOX BOND FORMATION EXPEDITES POLYKETIDE SYNTHESIS

Polyketides are products of bacterial metabolism that often exhibit useful biological activity, and hence, are widely used in human medicine—directly as found in nature or after some man-made modifications. From a synthetic perspective, the uniquely complex skeletons of polyketides often require repetitive redox and protection–deprotection transformations, rendering their chemical synthesis arduous and lengthy.

To address this obstacle, Michael J. Krische and co-workers have developed an iridium catalyst that directly upgrades simple 1,3-diols into triketide motifs in a bidirectional manner. This key reaction furnishes a triketide stereopolyad with five chiral centers in just one step, dramatically simplifying the total synthesis of (+)-zincophorin methyl ester, a potent ionophore antibiotic (DOI: [10.1021/jacs.5b05296](https://doi.org/10.1021/jacs.5b05296)). The key reaction is the two-directional double *anti*-crotylation of 2-methyl-1,3-propane that furnishes the C4–C12 triketide stereopolyad with five chiral centers in just one step.

This new method enhances efficiency by combining transfer hydrogenation and carbonyl addition, reducing by almost half the steps previously required to produce (+)-zincophorin methyl ester. Best of all, the triketide motif made by this reaction is found in other polyketides, such as 6-deoxy-erythronolide B, where again the number of required steps is nearly cut in half.

Xin Su, Ph.D.

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