

Spotlights on Recent JACS Publications

■ PROTEIN SIDE CHAIN STRUCTURES BY NMR

When it comes to protein structure determination, NMR can reveal a structurally detailed view of the backbone, but the often dynamic side chains are typically harder to pin down using this technique. Now, Ad Bax and colleagues describe a strategy for determining the rotameric equilibrium of nearly every side chain in a model protein (DOI: [10.1021/jacs.5b10072](https://doi.org/10.1021/jacs.5b10072)).

The researchers sample ^1H and ^{13}C residual dipolar couplings for every amino acid in the 56-residue protein, GB3. They place the protein, with and without targeted surface mutations, in each of three different liquid crystal matrices to yield distinct protein orientations, capturing data at up to 900 MHz. These collected data result in a high-resolution structure that includes an equilibrium distribution of the side chain torsion angles, χ_1 . For about half the residues, the authors find that a single rotameric state dominates, which then agrees tightly with crystallographic data, whereas for the remaining residues, substantial population of alternate states is seen.

Though it will not be simple to extend this strategy to other proteins, the authors note, “our data will provide a new benchmark for evaluating the impact of side chain conformations on chemical shifts, an area that remains underdeveloped but holds strong potential for increasing the level of structural detail that can be extracted from these readily accessible parameters.”

Jeffrey M. Perkel

■ PVC'S NEW GOLD STANDARD

Making vinyl chloride monomer (VCM) is big business. Over 40 million tons of VCM are produced annually, in large part to create PVC (polyvinyl chloride), the third highest selling polymer. In this Perspective, Graham Hutchings and colleagues discuss the traditional production of VCM using mercury-aided catalysis, and why gold is poised to become the new standard (DOI: [10.1021/jacs.5b07752](https://doi.org/10.1021/jacs.5b07752)).

While the Western world no longer produces the majority of VCM from coal, China's current abundance of inexpensive coal has led to a resurgence in coal-driven VCM manufacturing. This reaction requires a certain kind of catalyst, and usually this catalyst contains mercury. But mercury use presents numerous concerns. At reaction temperatures the mercuric chloride sublimates, deactivates, and is ultimately lost into the environment, exacting steep financial, environmental, and health costs.

The researchers discuss the history and chemistry behind gold as an attractive alternative. While once the cost of gold would have been prohibitive, recent experiments have shown that even ultra-low levels of gold work well to facilitate VCM synthesis reactions. In contrast to mercury-based catalysts, gold catalysts deactivate slowly, retain selectivity, and can be reclaimed for use in a new catalyst. Advances in production and a new catalyst manufacturing plant herald the industry's pivot away from mercury, toward a new gold standard.

Jenny Morber, Ph.D.

■ REVEAL OF HYDROGEN SULFIDE SENSING MECHANISM RAISES MORE QUESTIONS

Hydrogen sulfide (H_2S) is a signaling molecule active in the cardiovascular, gastrointestinal, immune, and nervous systems. Detecting H_2S is important in the study of biological processes like inflammation, insulin regulation, and blood vessel growth. Now, Hillary Henthorn and Michael Pluth have revealed the mechanism behind a common method of sulfide detection: reaction with an aryl azide to create a fluorescent aryl amine.

Under physiological conditions, the majority of H_2S is found as hydrosulfide anion, HS^- . Using mechanistic experiments and calculations, the researchers study the reaction of HS^- with 4-methyl-7-azidocoumarin. They identify the rate-limiting step of the reduction, and they find that the reaction requires two equivalents of HS^- (DOI: [10.1021/jacs.5b10675](https://doi.org/10.1021/jacs.5b10675)). In a biological system, that extra equivalent of sulfide might come from a thiol, which could disrupt the delicate redox balance within a cellular environment.

The mechanism of how aryl amines serve as a chemical sensing probe for H_2S raises questions about how the sensing reaction impacts a biological process under investigation. It can also provide design clues for future chemical sensing probes.

Melissae Fellet, Ph.D.

■ CHANGING TRAJECTORIES TO GOVERN SELECTIVITY

Selectivity in organic reactions, be it chemo-, regio-, or stereoselectivity, is a fundamental requirement in the fruitful synthesis of useful molecules and materials. Conventionally, selectivity is achieved by changing the relative energy of competing transition states, favoring formation of the desired product.

While this process has proven to be effective by countless examples, it is no longer the only way of controlling selectivity. Now, Daniel Singleton and Bibaswan Biswas report the surprising finding that the timing of the generation a single transition state can be fine-tuned to influence [1,2] versus [2,3] selectivity in sigmatropic rearrangements of ammonium ylides (DOI: [10.1021/jacs.5b08635](https://doi.org/10.1021/jacs.5b08635)). Combining experimental and computational studies, the researchers show that paths of dynamic trajectories passing through this transition state dictate the reaction outcome.

In this work, mechanistic nuances are exploited to rationally direct the regioselectivity in this synthetically useful reaction. These results offer a completely new strategy to control selectivity, but more importantly, they demonstrate the immense potential of reaction dynamics in regulating general reactivity.

Xin Su, Ph.D.

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