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JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
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NEW TYPE OF NONCLASSICAL HYDROGEN BONDING

Nonclassical hydrogen bonds—where an X−H bond interacts with an aromatic ring—play an important role in biological structures and other demonstrations of supramolecular self-assembly. Several types of nonclassical hydrogen bonds have been documented, including those involving C−H, N−H, and O−H. In each of those cases of X−H bonds, the X atom is more electronegative than hydrogen. On that basis, one would expect that the B−H interaction with aromatic groups would be repulsive rather than attractive, since boron is less electronegative than hydrogen. But in a new study, researchers led by Hong Yan and Dieter Cremer present the first demonstration of an attractive B−H···π interaction (DOI: 10.1021/jacs.6b01249).

To increase the strength of the B−H···π interaction, the team set out to invert the polarity of the B−H bond. They accomplish this by pairing B_2H_6, which contains electron-deficient boron in the form of carborane, with benzene. The researchers describe the interaction in the solid state, in solution, and in the gas phase, using computational models, X-ray diffraction, and ^{1}H NMR spectroscopy, and confirm the B−H···π interaction is electrostatic in nature.

Christine Herman, Ph.D.

CHEMICAL BIOLOGY ON DEMAND AND IN HIGH-DEFINITION

To understand how chemical processes in the cell produce biological responses, researchers must think small—that is, they must clarify molecular interactions that take place over minute scales of space and time. In this Perspective, Yimon Aye and colleagues survey diverse efforts to use small-molecule tools to accomplish this goal in a field known as proximity enhancement (DOI: 10.1021/jacs.5b12608). They also help researchers choose among the many tools at their disposal.

The authors describe two main strategies for proximity enhancement and illustrate them with many examples. In the first, more established approach, called multifunctional scaffolding, chemists devise molecules that are permanently tethered to one another; these probes elicit cellular responses by interacting with proteins of interest. In a more cutting-edge strategy known as on-demand precision targeting, researchers deploy probes containing a moiety that selectively interacts with proteins and a "latent warhead" portion that is activated on demand.

The authors advise using multifunctional scaffolding for controlling or reporting biological functions based on known associations, and on-demand precision targeting for discovering new interactions and specific biological responses. They also describe innovative uses of these tools, for example how proximity targeting has helped determine the function of myriad proteins in nuclear pore complexes.

Deirdre Lockwood, Ph.D.

SUICIDE ENZYME MECHANISM REVEALED

Enzymes are protein catalysts: they accelerate chemical reactions, and they are also generally reusable, driving multiple reaction cycles. But *Saccharomyces cerevisiae* thiazole synthase is different: It is consumed in a one-and-done "suicide" reaction that extracts sulfur from an active-site cysteine to create adenylated thiazole.

Here, a team led by Tadhg Begley and Steven Ealick investigates the mechanism of the bacterial thiazole synthase MjThi4 from *Methanococcus jannaschii*, which derives sulfur from exogenous sodium sulfide (DOI: 10.1021/jacs.6b00445). The researchers find that MjThi4 drives an iron-dependent reaction that appears to proceed via the same intermediates as its yeast ortholog, though with a turnover rate of 0.04/min. Using X-ray crystallography, they trace the active site geometry, suggesting a potential reaction mechanism.

A single cysteine-to-alanine substitution in the yeast Thi4 protein is sufficient to allow the enzyme to use exogenous sulfide instead of cysteine as a reactant, the authors note, begging the question of why a cellular organism would evolve to use a suicide enzyme. Perhaps, they speculate, the "inactive" enzyme performs additional functions, such that "yeast thiamin thiazole biosynthesis represents a sophisticated post-translational modification in which the post-translational modification chemistry is coupled to the production of an essential metabolite."

Jeffrey M. Perkel

CARBONATE SPLITTING: DIIRIDIUM CATALYSTS ENABLE NEW CO_2 MITIGATION

Among the varied approaches to carbon dioxide sequestration and conversion, splitting CO_2 back to carbon monoxide and dioxygen is very appealing but also very challenging due to the high energy demand to break the stable C═O bond. Toward this goal, Tsun-Ren Chen and his team instead target carbonate as a source and develop a pair of iridium-based bimetallic complexes that directly break down carbonate to CO and O_2 (DOI: 10.1021/jacs.6b00715).

The process involves a two-step redox transformation, where the first diiridium complex captures carbonate, followed by the spontaneous release of CO, and the second diiridium complex generates O_2 upon exchange with chlorine. Unlike existing methods for the chemical reduction of carbon dioxide, this catalyst system functions at room temperature and does not require any sacrificial agent, minimizing both energy and materials input.

What makes the discovery especially attractive is that it can be coupled with current CO_2 sequestration techniques to acquire carbonate feedstock. Further integration that allows for in situ chlorine regeneration will lead to a highly efficient and possibly even self-sustaining solution for CO_2 utilization.

Xin Su, Ph.D.

Published: March 29, 2016

DOI: 10.1021/jacs.6b02793
J. Am. Chem. Soc. 2016, 138, 4269−4269