Organic Seminar

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The Prospect of Molecular Prosthetics: Small Molecules with Protein-Like Functions

Human diseases caused by an excess of protein function can often be treated effectively using small molecules that bind to proteins and turn them off. In contrast, many diseases caused by protein deficiencies are refractory to this classic approach. Our group therefore aims to advance the frontiers of medicine towards molecular prosthetics, i.e., small molecules that serve as functional substitutes for missing or dysfunctional proteins that underlie currently incurable human diseases. Toward this end, our research focuses on the synthesis and study of small molecules with the capacity to perform higher-order, protein-like functions in the context of living systems. To enable these studies, we are developing a simple and highly modular strategy for making small molecules which is analogous to peptide synthesis and involves the iterative cross-coupling of haloboronic acids protected as the corresponding N-methyliminodiacetic acid (MIDA)-boronates. We are currently harnessing the power of this new chemistry to systematically dissect the structure/function relationships that underlie the protein-like activities of a variety of prototypical natural products, including the ion-channel-forming polyene macrolide amphotericin B. Collectively, these efforts ultimately seek to build the foundation for the development of molecular prosthetics into a powerful and general strategy for the understanding and betterment of human health.