ACCOUNTS
of chemical research

GUEST EDITIORIAL

C−H Functionalization

The conversion of a C−H bond to a C−Z bond where Z is an atom other than hydrogen is the most encompassing transformation in organic chemistry. Yet it has also proven to be one of the most challenging for synthetic chemists to accomplish selectively in the laboratory. In nature, this transformation is essential for metabolism, and individual enzymes have evolved to carry out very specific conversions. In industry, the C−H to C−Z conversion is a core component in energy, fine chemical, and pharmaceutical production, but often the methods used to carry out these conversions involve multiple steps, generate significant byproducts, and/or are energy intensive. Direct transformations of C−H bonds have long been known from reactions in organic chemistry as unselective oxidation processes. However, more recent efforts by investigators around the world have produced refinements that offer high selectivity, and it is for these processes that the term "C−H functionalization" is currently used.

The C−H bond has been called the "unfunctional" group. It is highly stable and generally resistant to reactions with acids and bases or electrophiles and nucleophiles. Early efforts in the area of C−H functionalization have been successful in using functional groups that are attached to carbon to change the reactivity of the nearby C−H bond and contribute to its cleavage. In contrast, more recent efforts have sought to perform transformations on C−H bonds that are not activated by adjacent functional groups: selective C−H functionalization of unactivated C−H bonds. Selective transformations of C−H bonds are even more challenging in complex molecules that have multiple C−H bonds that are electronically similar. Thus, selectivity includes not only chemoselectivity but also regioselectivity and stereoselectivity.

The pathway to activation and cleavage of the C−H bond is central to understanding how selectivity can be achieved. In its early incarnation, the C−H to C−Z bond conversion was focused on free radical oxidative processes or carbene insertion reactions that, for the most part, were unselective. Advances in organometallic chemistry have informed us on how reactivity and selectivity in reactions with C−H bonds could be modified to achieve high selectivity, and the outcome of these advances is revealed in the Accounts that are included in this Special Issue. However, the C−H bond cleavage is only one aspect of functionalization. To achieve high selectivity, understanding of both the path for formation of the new C−Z bond, and of how the catalyst can be recycled, is also needed.

This Special Issue of Accounts covers the breadth of C−H functionalizations that extends from the transformation of alkanes to the synthesis of complex molecules. New advances in method development are revealed. Strategies and successes in selective C−H bond activation and cleavage are presented along with functionalization by dehydrogenation, insertions, or oxidations. Metal carbene chemistry is the basis for recent developments in highly regio- and stereoselective carbenoid insertion reactions. Oxidative transformations that offer directed C−H functionalization and utilization of dioxygen extend the dimensions of C−H functionalization. We are grateful to our esteemed colleagues who have contributed to this issue. They have filled the pages that follow with their unique stories describing their remarkable strategies and achievements in catalysis, mechanistic investigations, synthetic methodologies, and applications, all directed to realizing selective functionalization of the "unfunctional" C−H bond.

Michael P. Doyle
University of Maryland

Karen I. Goldberg
University of Washington
Guest Editors

www.pubs.acs.org/accounts
10.1021/ar300096z