Self- or directing group-aided remote C(sp^3)-H functionalization of bifuntional compounds

Bifunctional compounds, such as diols, diamines or amino alcohols, are ubiquitous structural motifs found in naturally occurring bioactive compounds. They are also key structural units of vast number of approved therapeutic agents, and pharmaceutical candidates, as well as agrochemicals. High importance of listed classes of compounds in organic and medicinal chemistry makes that the development of methods that enable rapid synthesis and late-stage diversification of these molecules is appealing from the standpoint of drug discovery. Nowadays, special emphasis is placed on a development of methods of C-functionalization of native heterocyclic rings.

The conventional organic reactions require a pre-functionalization or biasness in the system to functionalize the C-H bonds due to their high enthalpic stability. In past few decades implementation of transition metal catalyzed reactions as well as radical reactions at both room temperature and photolytic conditions are exploited. The transition metals, such as Cu, Rh, Pd, Ni, Ir, Ru catalyzed C-H bond functionalization has been recognized as one of the most attractive and dependable approaches to achieve new C-C bond formation, but they usually need good coordinating site (N, O atom) to bind with the substrate, which makes the α-C-H bond more facile to get functionalized. In contrast, radical-mediated C-H functionalization, while discovered earlier, has played a much less significant role in advancing the frontiers of selective C-H functionalization. This is somewhat surprising given that intramolecular hydrogen atom transfer (HAT) of a C-H to a remote radical site is typically quite selective and exergonic and may be promoted under milder reaction conditions than their metal-mediated counterparts.

Current research assumes to use benefits of modern, particularly photochemically and electrochemically driven, radical based transformations, to provide efficient method for a divergent functionalization of various bifunctional systems under mild reaction conditions and high functional group tolerance. We propose the direct C(sp^3)-H functionalization of diols, diamines and amino alcohols based on radical promoted remote C-H bond cleavage *via* 1,5-hydrogen atom transfer (1,5-HAT) and an attendant C-C bond formation by an interception of the radical intermediate by a radical trap agent. The 1,5-HAT process will be executed by *N*-, *C*- or *O*-centered radical species located at the auxiliary HAT-directing group (HDG) attached to either nitrogen atom or hydroxyl group of the starting material. In other approach OH or NH functionality will serve as an internal HAT reagent. The proposed investigation will involve search for suitable directing group to initiate HAT process, optimization of C-H functionalization sequence, and scope and limitations studies. We intend to focus on a development of photochemical driven process to facilitate radical-mediated C(sp^3)-H functionalization under "green" and mild reaction conditions. Special attention will be provide on asymmetric version of the investigated remote C-H functionalization, particularly enantioselective fashion. Moreover, proposed strategy will be tested for a formation of various C-C (sp^3-sp, sp^3-sp^2, and sp^3-sp^3) and C-heteroatom bond by varying radical trap agent, that will enable diversification of native bifunctional structures.