Controlling the Selectivity of Bioinspired Cu-Mediated O_2 Activation for C–H Oxygenation

Chemo- and regioselective C–H bond activation in hydrocarbons remains a great challenge, in particular if the substrate contains labile C–H bonds. Hence, new catalysts able to promote selective oxygenations of complex substrates are highly sought after. In biological systems, the oxidative functionalization of inert C–H bonds, using O_2 from air as an oxidant, is mostly achieved by metalloenzymes that contain Fe or Cu ions within their active sites. Their catalytic cycles involve a range of different metal/oxygen intermediates, which usually activate the substrate's C–H bond via hydrogen atom abstraction (HAA) that involves concerted $1H^+/1e^-$ transfer (EPT) or related PCET processes leaning towards either ET or PT intermediates. Detailed mechanistic understanding of these reactions offers a guide to rational catalyst design. Of particular current interest is the histidine brace motif found in active sites of some Cu metalloenzymes capable of oxidizing inert C–H bonds with high bond dissociation energies (BDE) exceeding 95 kcal/mol. The goal of this project is the computational support for the development of bioinspired Cu catalysts that are competent of mediating the selective oxidation/oxygenation of specific C–H bonds in a given substrate. To that end, key Cu/O_x intermediates and their e^-/H^+ triggered interconversion will be characterized and their reactivity towards C–H substrates will be studied to elucidate (i) how the thermodynamics and kinetics of the PCET steps are related, (ii) how (a)synchronicity of the PCET process and relative contributions from ET and PT driving forces can be controlled, (iii) to what extent tunneling and nonadiabaticity scenarios play a role and can be exploited for controlling the PCET process, and (iv) how modifications of the scaffold ligands can tune C–H activation rates and mechanisms.