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## Distal functionalization via transition metal catalysis

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The ubiquitous presence of  $sp^3$  C–H bonds in natural feedstock makes them inexpensive, easily accessible, and attractive synthons for the preparation of common and/or complex molecular frameworks in biologically active natural products, pharmaceuticals, agrochemicals, and materials. However, the inertness of these bonds due to the high bond dissociation energies and low polarity difference between the carbon and hydrogen atoms makes them challenging reaction partners. Moreover, the desired site selectivity is often an issue in reactions with multiple analogous  $sp^3$  C–H bonds. To overcome these problems, transition metal-catalyzed C–H functionalization has been developed with the assistance of various well-designed directing groups which can coordinate to a metal center to deliver it on a targeted C–H bond through an appropriate spatial arrangement, enabling C–H activation via the

formation of a cyclometalated species. However, the requirement of often additional steps for the construction of the directing groups and their subsequent removal after the desired operation severely hampers the efficacy and compatibility of the reactions. A promising solution would be the utilization of a transient ligand that can bind to the substrate and coordinate with the metal center in a reversible fashion. In this way, the directing group is installed,  $sp^3$  C–H functionalization occurs, and the directing group is then removed in situ without affecting the substrate function after the catalysis is finished. Overall, the whole process occurs in a single reaction pot. Herein, we are presenting our studies on transition metal-catalyzed transient directing group-enabled C–H functionalization reaction.

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