Multiple Deuterium Atom Transfer Perdeuteration of Unactivated Alkenes under Base-Assisted Cobalt/Photoredox Dual Catalysis

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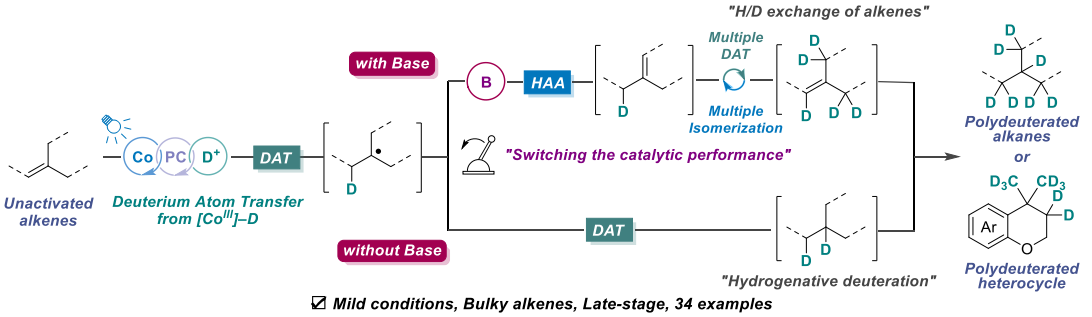
Recently, deuterium-labeled compounds have garnered increasing attention in drug discovery for their strategic potential to modify ADME properties.[1] Given this background, the development of new deuterium-labeling methodologies has witnessed significant advances in modern synthetic organic chemistry, but it remains difficult to construct polydeuterated aliphatic moieties at a late-stage.[2] To address this challenge, we propose leveraging our previously reported deuterium atom transfer (DAT) deuteration method[3] to synthesize inert polydeuterated alkanes from diverse alkenes.

In this study, we have newly developed the stepwise or one-pot perdeuteration of unactivated alkenes via multiple hydrogen atom abstraction (HAA) and multiple deuterium atom transfer (DAT) under base-assisted cobalt/photoredox dual catalysis.[4] The addition of a suitable base plays a key role in controlling two competing pathways—"H/D exchange" and "hydrogenative deuteration" of alkenes—by switching the catalytic performance of the cobalt/photoredox dual catalyst system. This radical mechanism-based approach enables the synthesis of various polydeuterated tertiary alkanes with high functional group tolerance, providing a complementary method to the pioneering hydrogenative perdeuteration reported by Milstein and co-workers[5]. Additionally, this method provides access to complex deuterium-labeled compounds, including polydeuterated amino acid and dipeptide derivatives, as well as pharmaceutical analogs. The presentation will also cover reaction mechanism analysis, details of the one-pot procedure, and several practical applications.



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