ABSTRACT
PRECISION DEUTERATION AND HYDROFUNCTIONALIZATION OF ARYL ALKYNES AND ALKENES

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The similar nature of the hydrogen atom to its isotope, deuterium, allows for the simple exchange of hydrogen atoms for deuterium atoms in drug molecules to alter the absorption, distribution, metabolism, and excretion properties. Installing the deuterium functionality into a specific site in the molecule is essential. Selective hydrofunctionalization reactions of alkynes and alkenes using the highly reactive catalytic Cu–H species have been well developed, and synthetic organic chemistry methods to selectively incorporate one or two deuterium atoms into the benzylic site of organic compounds, a key metabolic position, are elusive. A Cu–H catalytic approach offers selectivity and reactivity to undergo a transfer hydrodeuteration of alkynes or alkenes. Initiating the reaction development with a transfer hydrogenation protocol demonstrated high chemoselectivity on a diverse array of aryl alkynes. Expanding this method to a transfer deuteration generated aryl alkane products with up to 5 deuterium atoms, 2 of which were located at the benzylic carbon. Preliminary regioselective results were explored, providing 2 deuterium atoms at the benzylic position and 2 hydrogen atoms at the homobenzylic position (*Chapter 1)*. One deuterium atom was installed exclusively into aryl alkanes from aryl alkenes using a transfer hydrodeuteration reaction, and MRR, molecular rotational resonance spectroscopy, was explored as an analytical tool to detect different isotopic species present in the product mixture, confirming the highest selectivity reported to date (*Chapter 2*). Two deuterium atoms were installed selectively into the benzylic site of aryl alkanes from the transfer hydrodeuteration of aryl alkynes, forming α,α-d_2-alkane products, including complex small molecules. This was based on the electronic stability of the DTB-DPPBz ligand, which was explored both experimentally and computationally (*Chapter 3)*. Exchanging the silane source for diphenylsilane and eliminating the alcohol allowed for a regio-, stereo-, and chemoselective hydrosilylation of aryl alkynes to be accomplished on biologically relevant small molecules, as well as 4 drug analogues, to access α-*E*-vinylsilanes. Additionally, this protocol permitted the selective deuterosilylation reaction to access β,β-d_2-alkane products (*Chapter 4)*. Through extensive reaction development, optimization, and mechanistic exploration, highly selective methods of precision deuteration and hydrosilylation were achieved by using a Cu–H catalytic protocol.