Advances in Selectivity and Reactivity in Transition Metal Catalysis: Carbon–Silicon Bond Formation, Wacker Oxidation, and Olefin Metathesis

Thesis by

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ABSTRACT

The development of reaction methodology and catalysts that promote challenging transformations with high yields and selectivities is presented in Chapters 2–4 of this thesis. The three projects discussed address challenges in cross-coupling, olefin oxidation, and olefin metathesis.

Chapter 2 describes a nickel-catalyzed cross-coupling strategy for the formation of C–Si bonds using unactivated alkyl halides as substrates. Reaction optimization, exploration of the substrate scope, and mechanistic studies are described. This method is unique in its compatibility with not only secondary alkyl bromides, but tertiary alkyl bromides as well. Low loadings of the nickel catalyst, the absence of an added ligand, and relative tolerance of air and moisture contribute to the efficiency and robustness of this reaction. Mechanistic studies suggest that oxidative addition proceeds through a radical intermediate, consistent with previous studies of C–C bond formation.

Chapter 3 describes the application of an aldehyde-selective Wacker oxidation to allylic fluoride substrates to produce β-fluorinated aldehydes with remarkably high regioselectivities. Efficient anti-Markovnikov oxidation of allylic fluorides bearing a variety of functional groups was possible with reduced loadings of palladium, copper, and nitrite catalysts. In order to highlight the utility of this methodology, further derivatization of the aldehyde products to diverse fluorinated products is described. Mechanistic studies demonstrate the role of inductive effects in enhancing the regioselectivity of oxidation.

Chapter 4 investigates the synthesis, characterization, and reactivity studies of a new class of second-generation ruthenium olefin metathesis catalysts bearing aminophosphine ligands. The incorporation of P–N bonds into the dissociating phosphine ligand results in trends in catalyst initiation rates and catalyst activity that reveal important considerations for ligand design. The results from kinetics experiments correlate well with computational studies, which indicate that there are significant effects derived from sterics, electronic induction, orbital overlap from the nitrogen (aminophosphine) lone pair, and ligand distortion energies that contribute to trends in phosphine dissociation.

PUBLISHED CONTENT AND CONTRIBUTIONS

Crystal K. Chu, Yufan Liang, and Gregory C. Fu. Silicon–Carbon Bond Formation via Nickel-Catalyzed Cross-Coupling of Silicon Nucleophiles with Unactivated Secondary and Tertiary Alkyl Electrophiles. *Journal of the American Chemical Society* **2016**, *138* (20), 6404–6407. DOI: 10.1021/jacs.6b03465.

C.K.C. participated in project design, developed the standard reaction conditions, evaluated the reaction scope, and participated in writing of the manuscript.

Crystal K. Chu, Daniel T. Ziegler, Brian Carr, Zachary K. Wickens, and Robert H. Grubbs. Direct Access to β-Fluorinated Aldehydes by Nitrite-Modified Wacker Oxidation. *Angewandte Chemie International Edition* **2016**, *55* (29), 8435–8439. DOI: 10.1002/anie.201603424.

C.K.C. participated in project design, evaluated the reaction scope and derivatizations of products, and participated in writing of the manuscript.

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