

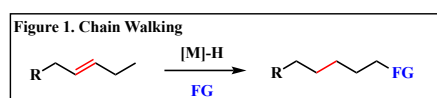
# FIRST ROW TRANSITION METAL CATALYZED REMOTE FUNCTIONALIZATION VIA CHAIN-WALKING

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10/30/18

## Introduction

Remote functionalization was described by Martin as “indirect activation of a site distant from the initial functional group.”<sup>1</sup> Many strategies have been developed to afford remote functionalization, but many of these methods require a form of directing group or some other preinstalled functionality to determine the site of reactivity. In contrast, chain-walking allows control of the site selectivity via choice of metal, ligand, and terminating functional group. This proceeds via consecutive 1,2- or 1,3- hydride eliminations followed by metal-hydride migratory insertion and functionalization (Figure 1).

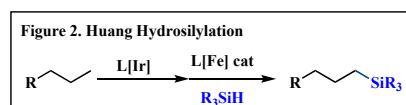


Chain-walking is a thriving field that has seen development of a broad range of metals. Much of the field has been focused on developing catalytic systems utilizing second and third row transition metals. Important contributions from Sigman using a palladium system, Grotjahn using a ruthenium based catalyst, and Beller using a rhodium catalyst have contributed to the development of the field.<sup>1</sup>

First-row transition metal catalyzed chain-walking has seen much development in recent years. These metals demonstrate differing reactivity from later transition metals and show high activity for desirable functionalization.

## Iron Chain-Walking

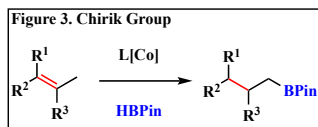
The first report of iron catalyzed olefin isomerization was in the early 1960's.<sup>2</sup> Research groups were attempting to form iron-olefin complexes from skipped dienes; they observed that skipped dienes were isomerizing to conjugated 1,4 dienes.<sup>2</sup> This phenomenon was underutilized in organic synthesis until 2016. The Huang group found that they could isomerize mixtures of internal olefins, derived from their iridium catalyzed transfer dehydrogenation, to the terminal position, and selectively perform a hydrosilylation (Figure 3). Notably, considering this remarkable demonstration, the field of iron catalyzed chain walking remains relatively



underdeveloped.

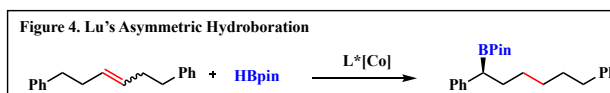
## Cobalt Chain-Walking

Cobalt chain-walking has been pioneered largely by the Chirik group. They observed that



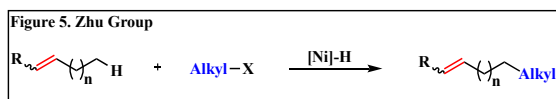
an in-situ generated cobalt hydride species can perform a migratory insertion, followed by chain-walking the metal to the terminal position, where it reductively eliminates to form a boronic ester (Figure 3).<sup>3</sup>

Recently, an intriguing cobalt catalyzed asymmetric alkene isomerization-hydroboration was reported by the Lu group (Figure 4).<sup>4</sup> This was one of the first examples of a cobalt catalyzed asymmetric chain walk. This impressive result suggests new possibilities for discovering other first row catalyzed asymmetric chain-walking processes.

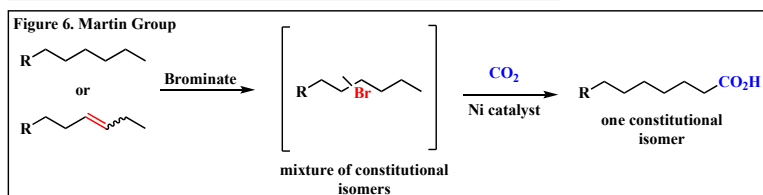


## Nickel Chain-Walking

Recently the Zhu and Martin groups have reported on novel methods for generating nickel hydride and achieving selective olefin isomerization and functionalizing. The Zhu group reported



a benzylic coupling of aryl halides with olefins and also a formal  $sp^3$ - $sp^3$  coupling of olefins with alkyl



halides (Figure 5).<sup>6,7</sup> The Martin group discovered a system which transforms a regioisomeric mixture of bromoalkanes or alkenes to a

single carboxylic acid stereoisomer (Figure 6).<sup>1,8</sup> This method demonstrated the power of chain-walking by transforming a mixture of olefin isomers to a higher value carboxylate in a one pot procedure.

## References

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