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CHEM-E4315 - Topics in Synthesis

Rh(III) Catalysis for C–H Functionalization

Korhonen Eero

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1 Introduction

Transition metal catalysis have historically been based on ligands. Metal—ligand relationship can greatly alter the results of a reaction. Commonly, it can have an impact in selectivity and physical properties. C–H bond functionalization with transition-metal-catalysis have become foundation for development of new bond forming strategies. Palladium is a popular metal for these kinds of usage. (Piou et al. 2018) Rhodium sitting next to palladium, it is no wonder why rhodium has been investigated for C–H bond functionalization.

The basic scheme of C–H bond functionalization is presented in Figure 1. The functionalization can happen in few different ways, but this is the general scheme. The first step is to activate the C–H bond by transition metal catalyst. This will generate a transition state with C–ML_n bond. Finally, one way or another, C–H bond is cleaved and C–X bond is formed.

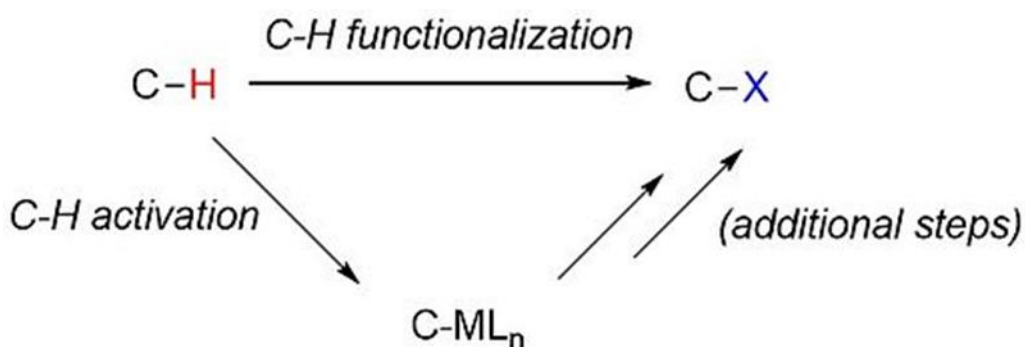


Figure 1. General scheme of C–H functionalization.

C–H bond functionalization is great way to add value to a molecular structure. Oxygen and nitrogen are fundamental part of organic structures, and they can alter behavior of the substance. C–H bonds are very common in organic structures, thus ability to modify C–H bonds to C–O or C–N is significant. (Song et al. 2012)

2 Cp*Rh(III) Complexes

Pentamethylcyclopentadienyl (Cp*) Rh(III) complexes have risen as an effective catalysis for C–H bond functionalization. These complexes enable various ways of reactivity. Some benefits of using these complexes are usually mild reaction conditions, which extends functional group tolerance, and low required catalyst loading. (Song et al. 2015, Piou et al. 2018) Cp*Rh(III) complexes are commercially available making them nearly universally employed as rhodium source (Song et al. 2012). Structure of Cp*Rh(III) complex is shown in figure 2.

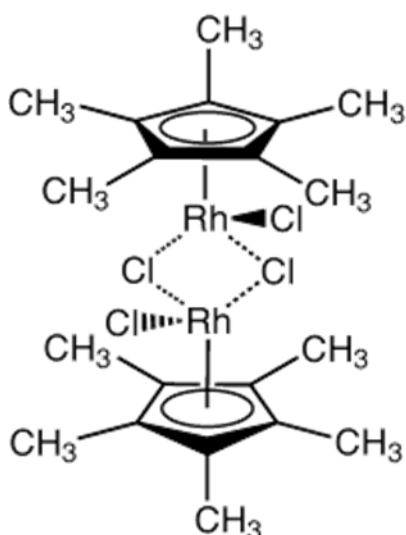


Figure 2. Structure of 2 Cp*Rh(III) complex.

Many properties of Cp*Rh(III) complexes can be improved by modifying the cyclopentadienyl ring. Some possible structures are shown in figure 3. Different cyclopentadienyl ring structures can improve chemoselectivity, regioselectivity, diastereoselectivity, reactivity and reaction yield. For example, chemoselectivity in carboamination can be enhanced with Cp*^{t-Bu}. (Piou et al. 2018)

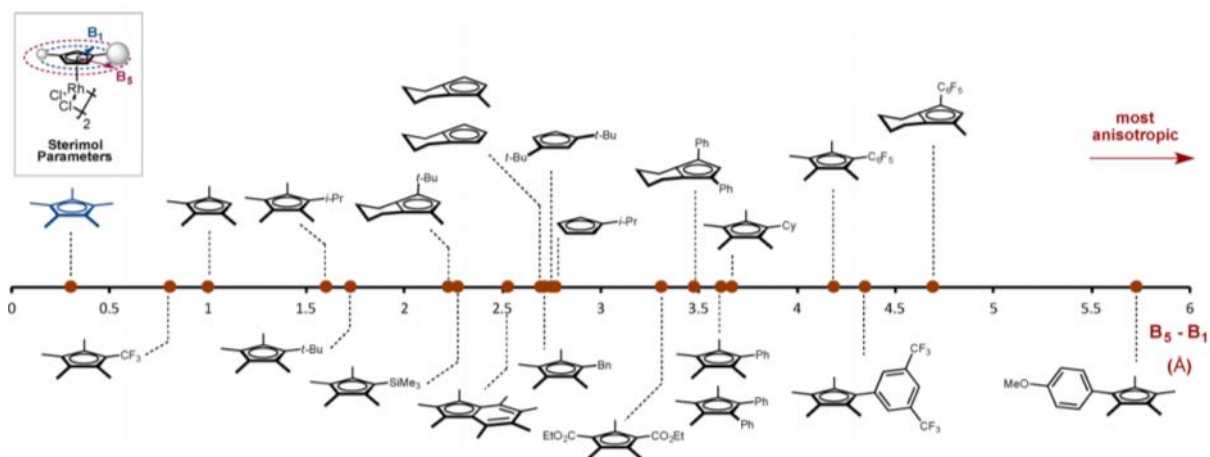


Figure 3. Some possible structures of cyclopentadienyl ring (Piou et al. 2018).

3 Electrophilic and Oxidative Activation

Electrophilic and oxidative activations are two different mechanisms possible with Rh(III) catalysis. Mechanism of electrophilic activation is shown in figure 4. Activation starts with electrophilic deprotonation producing an aryl-Rh intermediate with the help of a directing group (DG) to the ortho position. Insertion of a desired alkene into the newly formed bond generates an alkyl-Rh complex. Heck-type product is generated by β -hydride elimination. Rh(III) is recycled throughout the reaction. With electrophilic activations, it is possible for example to utilize insertion into alkenes and polar π bonds. (Colby et al. 2011)

Oxidative activation mechanism is shown in figure 5. Anionic E atom acts as a DG, giving five or six membered rings because of bond cleavage. Ortho C-H activation happens after coordination of DG. An alkyne inserts into the newly formed metallacycle giving an expanded rhodacycle. Product is generated while Rh(I) is oxidized back to Rh(III). Oxidative activation is mostly limited to C(sp²)-H bonds and unsaturated molecules such as alkenes and alkynes and the reaction is generally limited to chelation assistance. Nitrogen heterocycles formation, cyclopropanations and

carboaminations, as an example, are possible with oxidative activation. (Lewis et al. 2008, Song et al. 2012)

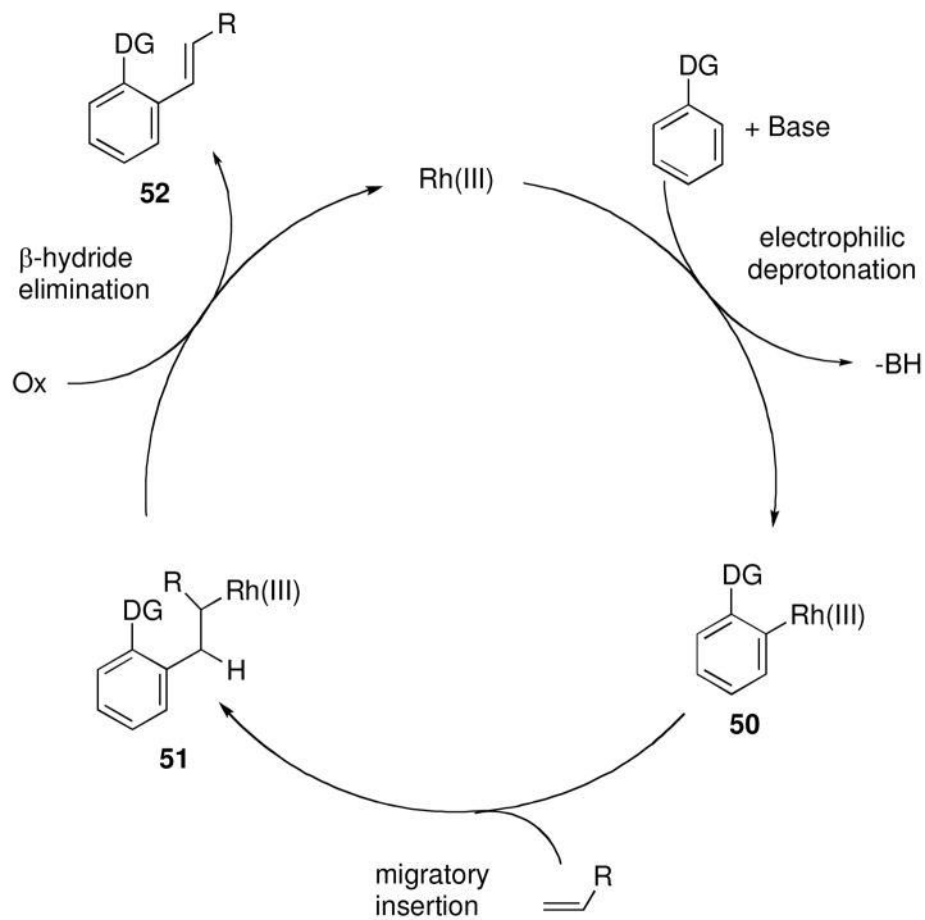


Figure 4. Example mechanism of electrophilic activation (Colby et al. 2011).

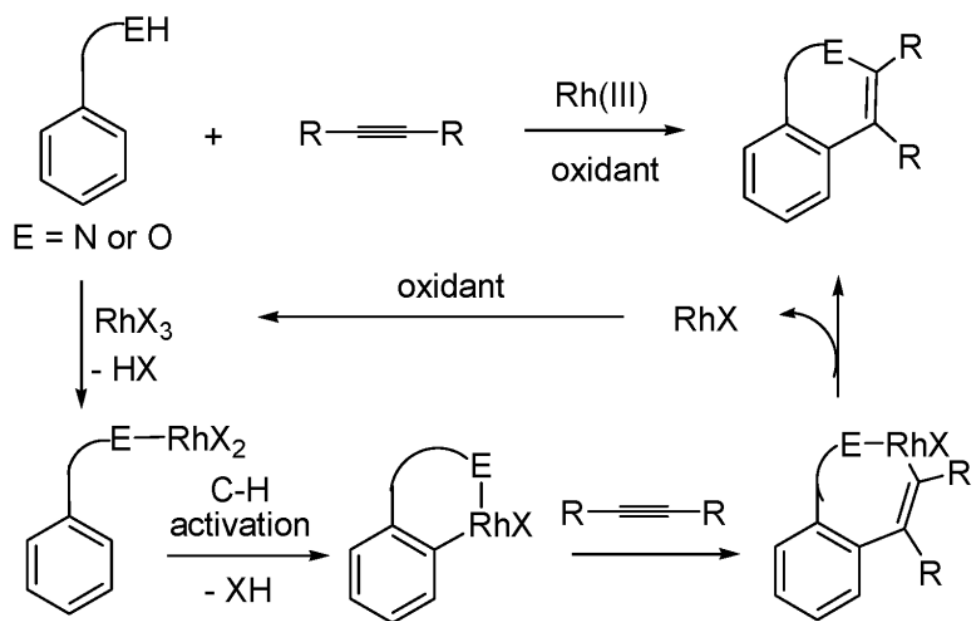


Figure 5. Example mechanism of oxidative activation (Song et al. 2012).

4 Summary and Outlook

Rh(III) catalysis is an attractive methodology to form N-heterocycles. Compared to palladium, Rh(III) can have improved properties. Although Rh(III) still has some limitations compared to Pd. For example catalytic activation of C(sp³)-H bonds are a lot more common with palladium catalysis. Rh needs more development and research in the future. Rh catalysis is still in its infancy. Many additional reactions will be explored and developed soon, and more applications will be found for C-H activation with Rh(III).

References

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