

Development of Efficient Organic Synthetic Reactions via Novel Activation of Unsaturated Hydrocarbons

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Organic synthesis is one of the most important methods to provide various kind of essential organic compounds in medicinal and material chemistry. Therefore, the efficient processes, containing catalytic, selective, atom economical, and step economical reactions are desired for the construction of the organic molecules.

Unsaturated hydrocarbons (such as alkene and alkyne) are useful carbon sources for modern organic synthesis. It is well known that various kind of addition reactions via carbocation, carbanion and radical species proceed to construct π bonds for the synthesis of unsaturated hydrocarbons. On the contrary, unsaturated hydrocarbons are less reactive as nucleophiles and seldom used as carbanion equivalents. For example, the coupling reaction of carbonyl compounds with alkene (or alkyne) is so extremely difficult to utilize the C-C bond formations.

Nickel can promote oxidative cyclization of unsaturated hydrocarbons and carbonyl compounds to provide oxanickellacycle intermediates. Therefore, it is efficient method to form C-C bond between unsaturated hydrocarbon and carbonyl compound. Furthermore, the oxanickellacycles can react with organometallic reagents (such as organozinc, organoaluminum, and organoborane) via σ -bond metathesis. In general, the organometallic reagents are more reactive nucleophiles than unsaturated hydrocarbons, but the reactivities change dramatically by nickel catalysis. As a result, Ni-catalyzed multicomponent coupling reactions of unsaturated hydrocarbons, carbonyl compounds, and organometallic reagents can be achieved to provide complicated molecules in a single manipulation.

In this thesis, multicomponent coupling reactions of unsaturated hydrocarbons, carbonyl compounds, and organometallic reagents by using of nickel catalysis and specific reactivities of organozinc and organoaluminum were described. The reaction features are shown as follows.

I. The use of unsaturated hydrocarbons as nucleophiles. **II.** The controlling of chemo-, regio-, and stereoselectivities in unsaturated hydrocarbons having multiple π bonds. **III.** The reaction of carbon dioxide as an electrophile with unsaturated hydrocarbons.

Chapter 1: Ni-Catalyzed Three-Component Coupling Reaction of Conjugated Enyne, Aldehyde, and Organozinc Reagent

Remarkably selective formation of allenyl and dienyl alcohols via Ni-catalyzed three-component coupling reaction of conjugated enynes, aldehydes, and organozinc reagents is described. Ligand effects dramatically controlled the chemo- and regioselectivities of the products depending on the stability of oxanickellacycle intermediates. In the absence of a ligand, the three-component coupling reaction proceeded via 1,4-addition of aldehydes and alkyl groups of organozinc reagents to the enynes to give allenyl alcohols with high regio- and stereoselectivities. On the other hand, in the presence of a ligand, a similar coupling reaction of conjugated enynes, aldehydes, and organozinc reagents proceeded via 3,4-addition of aldehydes and alkyl groups of organozinc reagents to the enynes to afford dienyl alcohols.

Chapter 2: Ni-Catalyzed Multicomponent Coupling Reaction of Alkyne, Buta-1,3-diene, and Dimethylzinc under Carbon Dioxide

Ni-Catalyzed multicomponent coupling reaction of alkyne, 1,3-butadiene, and dimethylzinc under carbon dioxide is described. This reaction proceeded via bis(allyl)nickel intermediate, which was generated through oxidative cyclization of two equivalents of dienes to a Ni catalyst. The bis(allyl)nickel species could react with carbon dioxide regioselectively at C3 position to form oxanickellacycle intermediate, followed by alkyne insertion and transmetalation, and then provided trienylcarboxylic acids. On the other hand, in the case of diethylzinc, the reductive coupling proceeded without insertion of alkyne to give dienylcarboxylic acids instead of trienylcarboxylic acids.

Chapter 3: Ni-Catalyzed Reductive Coupling Reaction of Carbon Dioxide with Conjugated Diene Promoted by Diisobutylaluminum Hydride (DIBAL-H)

Ni-Catalyzed reductive coupling reaction of carbon dioxide with conjugated diene promoted by diisobutylaluminum hydride (DIBAL-H) is described. In this case, one equivalent of conjugated diene reacted with carbon dioxide to give the β,γ -unsaturated carboxylic acids without dimerization and oligomerization of conjugated diene under the Ni-catalytic conditions. The Ni-DIBAL-H catalysis showed different reaction feature in contrast to the results of Ni-Et₂Zn catalysis in Chapter 2.

Chapter 4: Ni-Catalyzed Three-Component Coupling Reaction of Alkene, Carbon Dioxide, and Organoaluminum Reagent

Ni-Catalyzed three-component coupling reaction of monosubstituted alkene, carbon dioxide, and organoaluminum reagent is described. The reaction provided the homoallylic alcohol with high regio- and stereoselectivities. The first step in the reaction, carbon dioxide reacted with organoaluminum to form ketone, and then formal carbonyl-ene type reaction of alkene with ketone provided the homoallylic alcohol.