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Formation of Nickelacycles and Reaction with Carbon Monoxide

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1.1 Introduction

Oxidative cyclization is one of the most efficient methods to form carbon–carbon bonds in one step. For example, the trimerization of alkynes to afford arenes catalyzed by a variety of transition metals has been well known as a part of Reppe chemistry, in which the oxidative cyclization of two alkynes with a transition metal to generate a metalacyclopentadiene has been believed to be a key step and might be the most common oxidative cyclization reaction. The reaction of metalacyclopentadiene with carbon monoxide is one of the logical extensions of trimerization of alkynes. The first Pauson–Kahnd-type reaction was reported in 1960 – the reaction of $Fe(CO)_5$ with acetylene to afford the corresponding (η^4-cyclopentadienone)iron complex (Figure 1.1) [1]. In general, the reaction of metal carbonyls with alkynes gives η^4-cyclopentadienone metal complexes. However, the coordination of η^4-cyclopentadienone is too strong to dissociate spontaneously, which makes the expansion of a stoichiometric reaction to a catalytic reaction difficult. On the other hand, both stoichiometric and catalytic Pauson–Kahnd reactions have been reported in 1973 at the same time (Figure 1.2) [2]. This reaction has been developed as a step economy method for the construction of cyclopentenones in one step, including optically active complicated compounds [3]. The minimum requirement for transition metals to promote the Pauson–Kahnd-type reactions is the formation of metalacycles and the following insertion of carbon monoxide and reductive elimination to give the corresponding carbonyl compounds. Thus, the synthesis of a variety of cyclic carbonyl compounds such as lactams and lactone by the catalytic hetero-Pauson–Kahnd reactions seems a logical extension.

1.2 Formation of Hetero-nickelacycles from Nickel(0)

As mentioned above, the first catalytic Pauson–Kahnd reaction had been reported at the same time as the first stoichiometric Pauson–Kahnd reaction. In contrast, to date, a very limited number of examples of the catalytic

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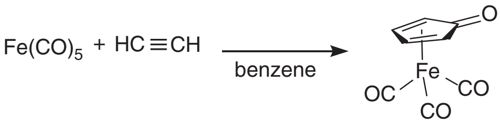

Figure 1.1 Formation of (η^4-cyclopentadienone)iron complex.

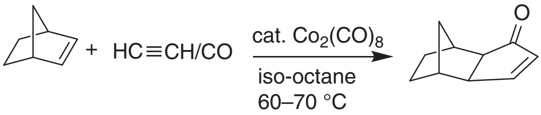

Figure 1.2 Cobalt-catalyzed Pauson–Kahnd reaction.

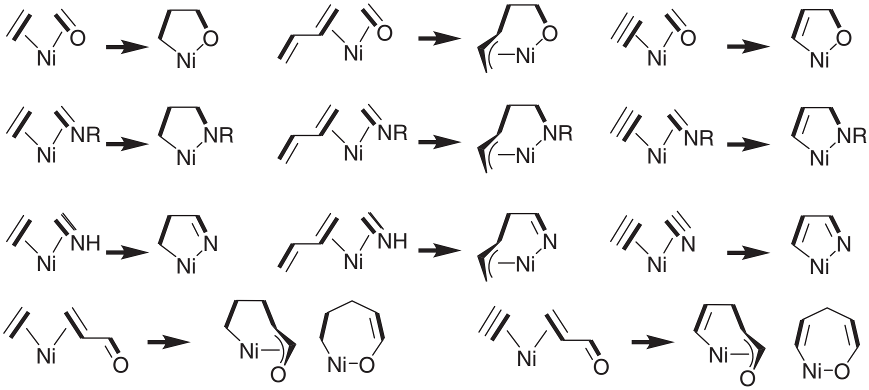

Figure 1.3 Formation of nickelacycles by oxidative cyclization.

Figure 1.4 Formation of nickelacycles by oxidative addition.

hetero-Pauson–Kahnd reactions to afford lactones and lactams have been reported, due to the less transition metals that can form hetero-metalacycles by oxidative cyclization with carbonyl compounds or imines (Figure 1.3) [4–8]. In that sense, nickel is one of the most promising transition metals as a catalyst for the hetero-Pauson–Kahnd reaction. In fact, the formation of a variety of hetero-nickelacycles has been reported. In addition, oxidative addition of strained small ring compounds also affords nickelacycles (Figure 1.4) [9–11].

1.3 Stoichiometric Reaction of Hetero-nickelacycles with Carbon Monoxide

In general, nickel tetra-carbonyl complex, $Ni(CO)_4$, might be the most famous metal carbonyl complex owing to the very high toxicity and its usage for the purification of nickel metal. In addition, Tolman's electronic parameter (TEP) has been evaluated by using a variety of nickel carbonyl complexes, $Ni(CO)_3L$ or $Ni(CO)_2L_2$. These facts indicate that organonickel complexes can react with carbon monoxide to give $Ni(CO)_3L$ or $Ni(CO)_2L_2$ easily. In fact, the reaction of hetero-nickelacycles with carbon monoxide affords a variety of expected cyclic carbonyl compounds quantitatively (Figures 1.5–1.7) [12–15]. However, the oxidative cyclization is a reversible process; thus, there are some exceptions in that the coordination of carbon monoxide promotes carbon–carbon bond cleavage to regenerate the starting unsaturated compounds in the reaction with carbon monoxide. In fact, η^3-allyl-nickelacycle, which is prepared by the reaction of 2,3-dimethylbutadiene and benzaldehyde with $Ni(cod)_2$ and PCy_3, underwent a reductive ring-opening reaction to regenerate 2,3-dimethylbutadiene and benzaldehyde quantitatively, concomitant with the quantitative formation of $Ni(CO)_3(PCy_3)$ (Figure 1.8).

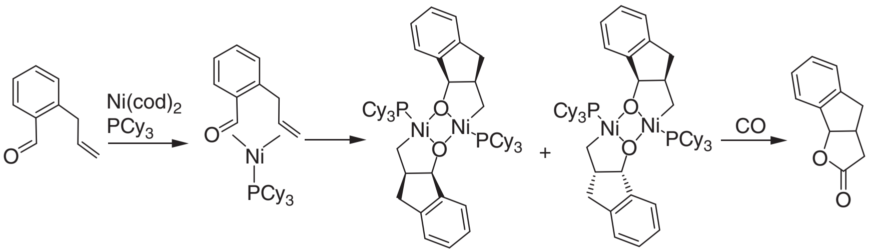

Figure 1.5 Formation of gamma lactone.

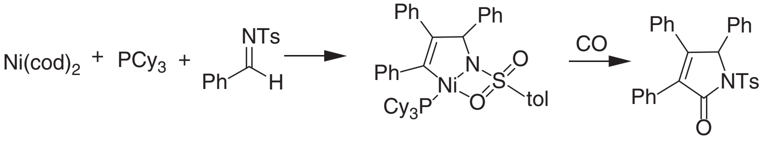

Figure 1.6 Formation of gamma lactam.

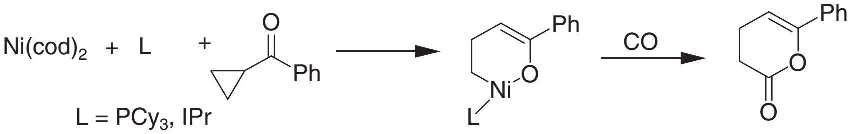

Figure 1.7 Formation of delta lactone.

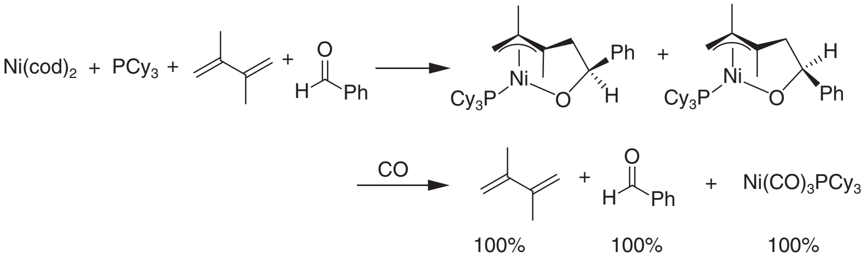

Figure 1.8 Carbon–carbon bond dissociation under carbon monoxide atmosphere.

These reports suggest that nickel is one of the most ideal transition metals to synthesize cyclic carbonyl compounds by using carbon monoxide, if the carbonylation step is irreversible. Nevertheless, neither nickel-catalyzed Pauson–Kahnd reaction nor hetero-Pauson–Kahnd reaction had been reported until 2014. It might be due to the formation of nickel-carbonyl complexes that are too stable to undergo oxidative cyclization to give hetero-nickelacycles. In fact, most of catalytic Pauson–Kahnd reactions have been carried out under relatively low carbon monoxide pressure and high reaction temperature due to the strong coordination of carbon monoxide to the metal center, which inhibits the coordination of either alkynes or alkenes. Thus, chemists have developed methods to control the concentration of carbon monoxide *in situ* or ex situ [16, 17].

The first nickel-catalyzed hetero-Pauson–Kahnd reaction has been achieved [18] by using *in situ* slow generation of carbon monoxide from phenyl formate and triethyl amine (Figure 1.9) [19, 20]. A variety of lactams have been prepared via aza-nickelacyles. The reaction intermediate complex was isolated and the molecular structure confirmed by X-ray crystallography. The reaction of (**X**) with carbon monoxide afforded the corresponding lactam quantitatively. This reaction can be applied to the reaction of norbornene and imine with carbon monoxide. The key to success is the control of the concentration level of carbon monoxide high enough to promote insertion of carbon monoxide and low enough to suppress the formation of $Ni(CO)_3(PCy_3)$, which is too stable to undergo oxidative cyclization. In fact, $Ni(CO)_3(PCy_3)$ is generated at the end of the reaction, which reacts with neither imines nor alkynes under mild conditions.

The most economical carbonylation reaction has to use carbon monoxide gas itself as the carbon monoxide source, in which the formation of nickel carbonyl complexes is inevitable. Thus, the reaction substrates have to be able to react with nickel carbonyl complexes to afford the corresponding carbonyl compound in high yield. Thus, bidentate substrates are appropriate for the carbonylation reaction, since the coordination of the bidentate substrate is an entropically favorable step. In fact, ene-imines can react with $Ni(CO)_3(PCy_3)$ to afford the desired lactam quantitatively (Figure 1.10). The reaction might proceed via an aza-nickelacycle, which has been confirmed by the stoichiometric reaction of isolated aza-nickelacycle with carbon monoxide.

The optimization of the reaction conditions has been conducted in an autoclave with regular equipment. However, only a catalytic amount of lactam X was obtained. To confirm the chemical species in the reaction mixture, the reaction was monitored by NMR. The reaction in the NMR tube afforded the

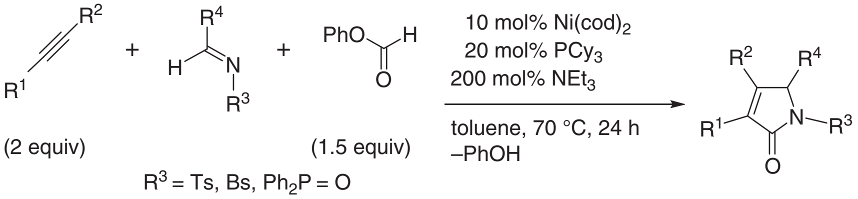

Figure 1.9 Nickel-catalyzed reaction of alkynes and imines with carbon monoxide.

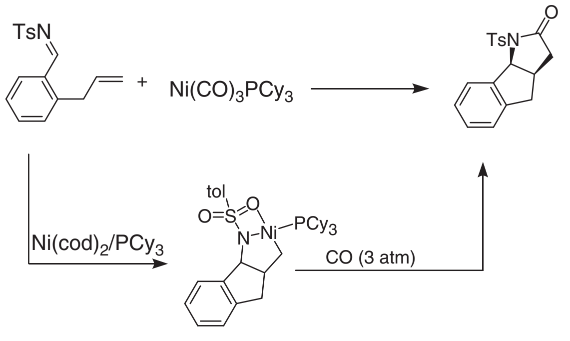

Figure 1.10 Stoichiometric reaction of en-imines with $Ni(CO)_3PCy_3$.

carbonylation product, which was generated quantitatively. This result indicates that stirring the reaction mixture suppresses the formation of nickelacycle. In fact, the reaction in an autoclave without stirring afforded the corresponding lactam quantitatively. The stoichiometric reaction of isolated nickelacycle with carbon monoxide proceeded smoothly to give the lactam quantitatively. A proposed reaction path is depicted in Figure 1.11. Not stirring the reaction mixture keeps the concentration of carbon monoxide in solution low enough to promote the coordination of the ene-imine to $Ni(CO)_3(PCy_3)$. With stirring, the coordination of the substrate to the nickel center is completely inhibited by rapid re-coordination of carbon monoxide to regenerate $Ni(CO)_3(PCy_3)$ under higher concentration of carbon monoxide. As a transition metal catalyzed the Pauson–Kahnd type reaction, the reaction temperature is exceptionally low. Thus, the reaction has been expanded to an asymmetric reaction.

The reaction product is the key synthetic intermediate [21] of strigolactam that is expected as a modified plant hormone. Thus, the nickel-catalyzed

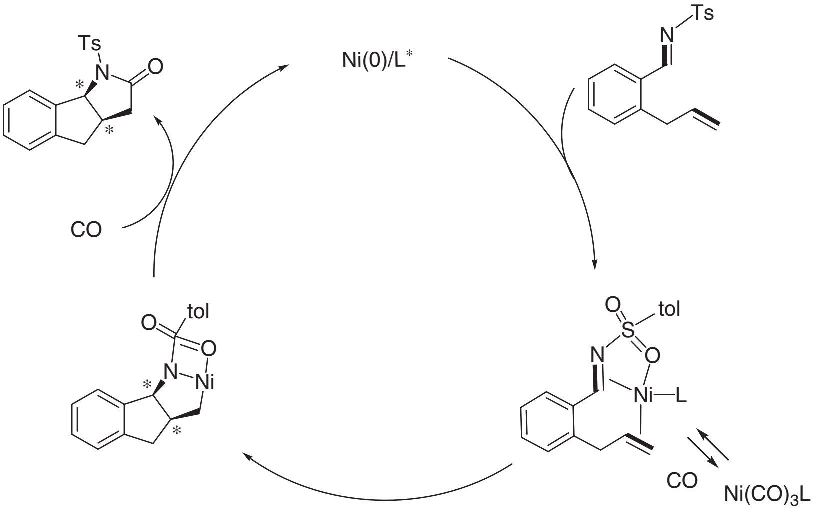

Figure 1.11 Nickel-catalyzed reaction of alkynes and imines with carbon monoxide.

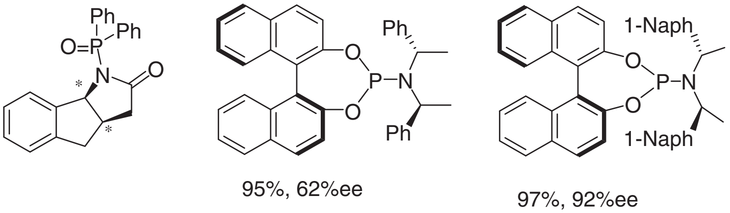

Figure 1.12 Application to asymmetric reaction.

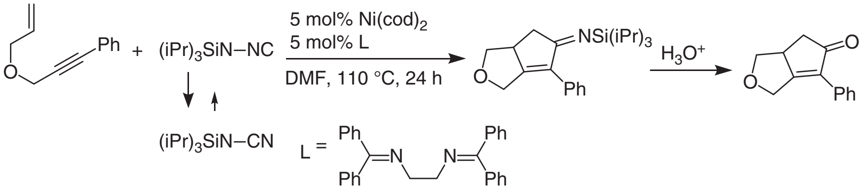

Figure 1.13 The formal nickel-catalyzed Pauson–Khand reaction.

aza-Pauson–Kahnd reaction has expanded asymmetric reaction. For the asymmetric reaction, phosphoramidite was an effective ligand. The ligand screening of phosphoramidite for the reaction was carried out (Figure 1.12) [22].

The formal nickel-catalyzed Pauson–Khand reaction has been reported in 1996 in which triisopropylsilylnitrile was employed instead of carbon monoxide by following hydration to afford the Pauson–Khand reaction product (Figure 1.13) [23].

The first nickel-catalyzed Pauson–Khand reaction has been reported in 2019 (Figure 1.14). In the presence of a catalytic amount of $Ni(CO)_3(IPr)$ in toluene at 175 °C, intramolecular Pauson–Khand reaction proceeded to give the cyclic

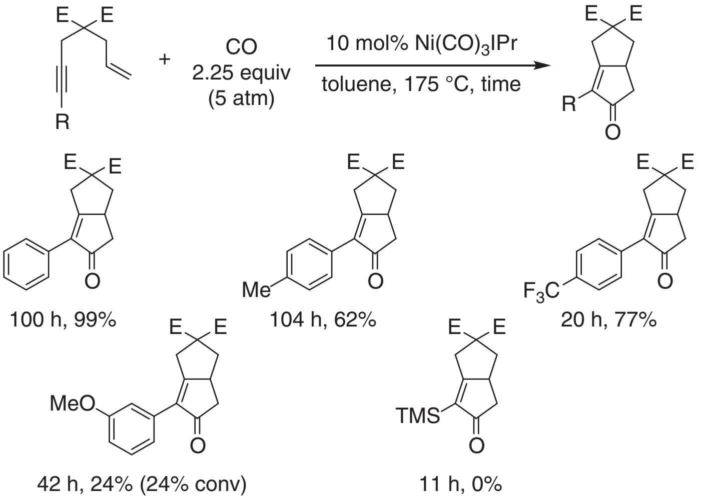

Figure 1.14 Nickel-catalyzed Pauson–Khand reaction.

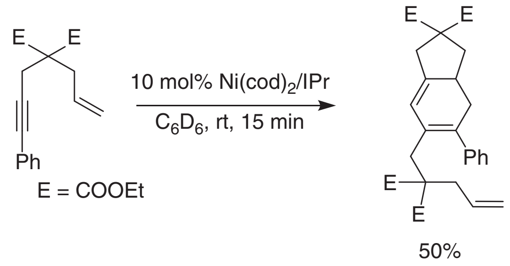

Figure 1.15 Nickel-catalyzed dimerization.

enones quantitatively. In this reaction, $Ni(CO)_3(IPr)$ is the most efficient catalyst. The higher reaction temperature is required for the dissociation of carbon monoxide to promote oxidative cyclization; however, in the presence of $Ni(cod)_2$ and IPr as a catalyst, no carbonylation product was observed. In fact, the reaction of enyne with $Ni(cod)_2$ and IPr gives the dimer compound of the enyne at room temperature in 15 minutes (Figure 1.15). Thus, in this reaction, the strong coordination of carbon monoxide to nickel is required to suppress the occurrence of dimerization of the enyne compound.

In contrast, in the presence of a catalytic amount of $Ni(cod)_2$ and either PCy_3 or IPr, the expected carbonylation product was not observed at all but only dimer of **1a**. This might be the reason why metal carbonyl complexes have been used as the catalyst for the Pauson–Khand reaction.

In this chapter, the formation of nickelacycles by the oxidative cyclization of unsaturated compounds with nickel(0) species and the reaction with carbon monoxide have been introduced. The key to the success of the construction of nickel-catalyzed cyclic carbonylation reaction is the control of the two key steps. One is the oxidative cyclization of unsaturated compounds with nickel(0) complex and the other is the control of the concentration of carbon monoxide in the solution.

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