CHAPTER-1

Cobalt(II)-Catalyzed Organic Transformations
1.1. Introduction

Elements in the d-block of the periodic table (except Zn, Cd and Hg) are generally called transition elements, and share some common characteristic properties, which are listed below. They contain an incomplete $d$ subshell.

They are often paramagnetic.

They have many different oxidation states.

They form complexes.

They are often good catalysts.

The last point concerning catalysis is very important and closely related to the two points above it and the main reason why transition metals are so useful in synthetic organic chemistry.\(^1\) The metals at the end of the transition series are more disposed to exist in coordinatively unsaturated states, and thus, more prone to be active in catalytic transformations. Late transition metals have a higher “catalytic power.”\(^2\) As early as in 1835, Jöns Jakob Berzelius defined his idea of “catalytic power” as the ability of substances “…to awaken affinities, which are asleep at a particular temperature, by their mere presence and not by their own affinity…”\(^3\). Almost every functional group will coordinate to some transition metals and thus altering the reactivity of the group to provide functionalization that is impossible with conventional methods. The reactions are site specific; leaving highly reactive functional groups untouched and, thus, avoids time-consuming protection and subsequent de-protection steps. This specificity can also be seen as a disadvantage, as a small modification of the reaction conditions might disturb the system so much that the catalytic turnover will cease. We can also regard it from another angle; it might be difficult to find optimal reaction conditions because the range
is so narrow. In other words, general conditions for transition metal-catalyzed reactions are rare.\textsuperscript{1}

Transition metal catalysis can roughly be divided into two groups, heterogeneous and homogeneous catalysis. In heterogeneous catalysis, the catalyst is in a solid state or is attached to a solid-phase, which facilitates catalyst recovery, but elevated temperatures are often required, the specificity is low and it is more difficult to elucidate the mechanism behind the transformation. The selectivity and the activity of homogeneous catalysts under mild conditions is unbeaten by their heterogeneous counterparts. \textit{The cobalt-catalyzed organic transformations described in this thesis, all take place in solution using soluble cobalt-salts or complexes, and therefore belong to homogeneous catalysis.}\textsuperscript{4,5}

\section*{1.2. Transition metal catalysts}

The application of the first-row transition metals, such as iron, cobalt and nickel, in synthetic organic transformations has attracted increasing interest for reasons other than simply their lower costs when compared to their higher homologues. A steadily growing number of contributions have appeared in the literature where benchmark transformations such as palladium-catalyzed coupling reactions were conducted with these first-row transition metals. It became obvious that problems in palladium chemistry, such as the $\beta$-hydride elimination, are of reduced importance in the chemistry of iron, cobalt and nickel coupling reactions, probably because of lower rates for the $\beta$-hydride elimination pathway. Therefore, reactions with the first-row transition metals can provide an interesting alternative in established transformations and it is emphasized that cobalt, in
particular, can open up. In this chapter, some of the recent developments in the cobalt(II) catalyzed organic transformations are described.

1.3. Cobalt-catalyzed cross coupling reactions

Over the past thirty years, the development of transition metal-catalyzed cross-coupling reactions have revolutionized techniques for the formation of carbon-carbon bonds, especially C (sp$^2$) centers where typical SN$^2$ substitution can not operate.$^6$ The development of efficient new carbon–carbon bond forming reactions by metal-catalyzed cross-coupling is still progressing impressively and significant advances have been achieved. Among the different catalysts, the most commonly employed and reliable metal is palladium, especially when appropriate ligands are present. Although nickel complexes have less general scope, they also have found applications in highly efficient cross-couplings of organometallics with aryl halides. However, these catalyst systems have disadvantages—the high cost of palladium and the high toxicity of nickel catalysts are two of the more obvious ones—and their use in industrial applications is coming under increasing scrutiny. Fortunately, inexpensive alternative catalysts are available in the form of simple, effective iron and cobalt salts. These green reactions offer new means for carrying out cross-coupling reactions both economically and ecologically. All these catalysts have wide scope and excellent tolerance of various functional groups. There has been much elegant work in iron-based catalysis,$^7$ however cobalt catalysts can sometimes present a higher reactivity for various C–C bond forming reactions. Moreover, the low cost of cobalt complexes and their interesting mode of action make them an attractive alternative for use in cross-coupling reactions.
1.3.1. Cross-coupling reactions via organometallic compounds

The reactivity of Grignard reagents alone is quite extensive but their range of applications can be extended significantly if they are used in conjunction with a catalyst. Kharasch and Fields\(^8\) investigated the effect of transition metals such as cobalt in reactions between organic halides and Grignard reagents as early as in 1941. Few advances have been made in cobalt-catalyzed cross-coupling reactions until 1998 when Cahiez and Avedissian\(^9\) reported the stereo and chemoselective reaction of vinyl halide with an organomagnesium reagent catalyzed by Co(acac)\(_2\) (Scheme 1).

More recently, Oshima and co-workers\(^{10-12}\) have demonstrated the cobalt catalyzed cross coupling reaction (Scheme 2) between alkyl halides and allylic Grignard reagents. Generally, palladium, nickel, and copper catalyzed coupling reactions are difficult for two reasons: the reluctance of alkyl halides to undergo the oxidative addition step, and \(\beta\)-hydride elimination from alkyl palladium and alkyl nickel. However, Oshima and co-workers have overcome with the use of CoCl\(_2\)(dppp) as catalyst.\(^{13}\) Oshima et al., also reported the cross coupling of alkyl and benzyl halides or alkenyl triflates with benzyl, aryl, heteroaryl, vinyl, and propargyl Grignard reagents (Scheme 2).\(^{14-19}\) Knochel and co-workers\(^{20}\) reported the cross coupling of aryl Grignard reagents with a variety of...
heterocyclic chlorides in the presence of 5 mol % CoCl$_2$ or Co(acac)$_2$. The best yields are obtained using CoCl$_2$ in diethyl ether. Homosilanes can also be prepared from trimethylsilylmethylmagnesium chloride, 1,3-dienes and alkyl halides under cobalt catalysis. The combination of CoCl$_2$ and 1,6-bis(diphenylphosphino)hexane catalyzes this in good to excellent yields, through a mechanism, which involves an alkyl halide derived radicals (Scheme 3).

Scheme 2: Cobalt-catalyzed cross-coupling between Grignard reagents and alkyl halides
Scheme 3: Co(II)-catalyzed cross coupling between heterocyclic chlorides and aryl or heteroarylmagnesium compounds

1.3.2. Cross-coupling with organozinc compounds

In general, like in the case of organomagnesium reagents, direct reaction of organozinc reagent with electrophiles is low yielding and inefficient because of the moderate intrinsic reactivity of zinc reagents. The reactivity of organozinc reagents can be vastly enhanced by the use of transition metal catalysts. Gosmini and co-workers have exploited the catalytic prowess of cobalt species by using them in a variety of cross coupling reactions. The group has developed a cobalt catalyzed two component cross-coupling reaction between alkylzinc compounds and acyl chlorides (Scheme 4) in acetonitrile.\(^{21}\)

Scheme 4: Synthesis of functionalized arylzinc reagents and their reaction with acyl chloride
They also have shown that highly functionalized aryl bromides react with allylic acetates in the presence of zinc dust in acetonitrile. In this reaction, catalyzed by CoBr$_2$, the allylic acetate present in the medium directly reacts with the arylzinc compound. In 1996, Knochel and co-workers had reported a CoBr$_2$ catalyzed coupling of ally chlorides or phosphates with alkylzinc halides or dialkylzincs. These reactions lead to the simple SN$^2$ cross-coupling product with the complete stereochemical retention across double bonds. Dunet and Knochel have recently, extended this method to highly functionalized diarylzinc reagents obtained by reacting aryl iodides with zinc.

1.3.3. Synthesis of biaryl compounds

Unsymmetrical biaryl compounds are of considerable interest in organic chemistry. Among the innumerable methods for the construction of aryl–aryl bonds, transition-metal-mediated reactions constitute one of the main strategies used. Generally such reactions involve the coupling of an organometallic reagent of boron, Sn, Si, Zn, Mg, Mn with an aryl halide or pseudohalide. They all require the use of a stoichiometric organometallic reagent, and typically the presence of a Ni or Pd complex as a catalyst. Recently, it was shown that iron and cobalt catalysts could be employed as alternatives to expensive precious metals, such as palladium, or toxic metals, such as nickel in coupling reactions with organometallic reagents. Studies within the realms of metal catalysis have provided several direct aryl–aryl bond-forming transformations for organic synthesis. Catalytic direct arene C-H cross-coupling and the decarboxylative coupling of aromatic carboxylates with aryl halides can be very efficient; however, these methods often require the use of a base, high temperatures, and expensive catalysts. Other
reaction pathways include the palladium-catalyzed reductive coupling of two aryl halides in combination with a reducing agent.

Very recently, Gosmini and co-workers have devised expedient route to the functionalized biaryls including 2-(4-tolyl)benzonitrile, a key intermediate in the synthesis of sartan derivatives and heteroaryl compounds. The reaction is catalyzed by cobalt(II) bromide in combination with manganese dust (Scheme 7). In the proposed mechanism (Scheme 8), cobalt shuttles between +1 and +3 oxidation states. The mechanism is comparable with that of nickel-catalyzed formation of biaryls.

**Scheme 7: Synthesis of unsymmetrical biaryls**
Scheme 8: Proposed mechanism for the Co-catalyzed coupling reaction

1.3.4. Synthesis of diarylmethanes

Diarylmethanes have been shown to possess interesting biological and medicinal properties and are ubiquitous structural constituents in pharmacologically important molecules such as papaverine and beclobrate. These compounds also frequently appear as subunits in supramolecular structures such as macrocycles, catenanes, and rotaxanes. The most general procedures for diarylmethane synthesis are the transition metal-catalyzed cross-coupling between aryl halides and benzylic metals (usually prepared from benzylic halides). The main difficulty with these methods remains the preliminary preparation of the organometallic reagent, especially when the aromatic ring bears
reactive functional substituents. These preformed organometallic reagents often consist of a magnesium, borane, manganese, stannane or zinc derivative and the cross-coupling generally requires an expensive rhodium or palladium catalyst, or a toxic nickel catalyst and typically sophisticated ligands. Some interesting copper-catalyzed reactions have also been shown to form the methylene-linked biphenyl species.\textsuperscript{33, 34} Alternatively, Gosmini and co-workers have developed a cobalt-catalyzed practical procedure\textsuperscript{35} for the synthesis of diarylmethanes containing functional groups. In this reaction (Scheme 9), CoBr\textsubscript{2} catalyzes the reductive cross-coupling between benzyl halide and a variety of electron rich and electron deficient aryl halides to furnish diarylmethanes \textbf{16} in good yields. The homocoupled products were formed in small amounts.

\begin{center}
\textbf{Scheme 9}: CoBr\textsubscript{2} catalyzed synthesis of diarylmethane
\end{center}

1.3.5. Mizoroki-Heck type reaction

Mizoroki-Heck reaction mostly employs aryl and vinyl halides as substrates. However, with the use of a combination of cobalt(II) complex and trimethylmagnesium reagent, the coupling of alkyl halides with vinyl halides (alkyl version of Mizoroki-Heck reaction) can be accomplished. It is worth noting that alkyl chlorides, which are usually less reactive in other transition metal catalyzed reactions, are alkyl sources in cobalt-
catalyzed reactions. The reaction allows various functionalities, including ester and amide
groups, to survive during the reaction (Scheme 10).  

\[ \text{Me}_3\text{SiCH}_2\text{MgCl (2.5 mmol)} + \[\text{CoCl}_2(\text{dpph}) (2.5 \text{ mmol}) \]

\text{ether, reflux, 3 h} \]

\[ \text{R-X= } ^{6}\text{C}_6\text{H}_{14}\text{Br, } ^{9}\text{C}_{12}\text{H}_{25}\text{Cl,}
^{1}\text{C}_4\text{H}_9\text{Br, 1-chloroadamantane}
\]

\text{Yields= 67-91%}

Scheme 10: Cobalt-catalyzed Mizoroki-Heck reaction

1.3.6. Coupling reaction between alkenes and alkynes

Metal-catalyzed functionalization of carbon-carbon triple bond is another important
transformation in organic chemistry and cobalt catalysts in such transformations have
been explored. Oshima and co-workers revealed that cobalt(II) chloride catalyzes allylzincation of 1-aryl-1-alkyne with regio- and stereo-selectivity (Scheme 11).  
The alkenylzinc intermediate 20 was trapped with several electrophiles to furnish
tetrasubstituted alkenes.

Scheme 11: Cobalt(II) chloride catalyzed allylzincation of alkynes
Cheng and co-workers reported a broadly applicable method for reductive intermolecular coupling of alkynes with activated alkenes (*Scheme 12*).\(^{38,39}\) The reaction afforded \(\gamma, \delta\)-unsaturated carbonyls, acids, sulfones or nitriles such as 22. In the intermolecular version of this reaction, a wide variety of nitrogen, oxygen, silicon or sulfur-containing functional groups were tolerated. Cobalt-catalyzed method also has advantages being highly chemo-, regio-, and stereoselective, and it can be used in the intramolecular reaction to generate six or seven membered lactones. Cobalt-catalyzed intramolecular and intermolecular coupling between alkenes and alkynes were also reported by Macria and co-workers\(^{40-42}\) and Hilt and co-workers respectively.\(^{43}\)

\[
\begin{align*}
R_1 & \equiv \equiv R_2 + \overset{\text{Co(PPh}_3)_2\text{I}_2, \text{PPh}_3, \text{Zn}}{\searrow} \overset{\text{CH}_3\text{CN, H}_2\text{O, 80 °C, 12 h}}{\text{R}^1 \equiv \equiv \text{R}^2 \rightarrow \text{R}^1 \equiv \equiv \text{R}^2} \\
\text{R}^1 &= \text{aryl, alkyl, COOR; R}^2 &= \text{aryl, alkyl, SiMe}_3; \text{R}^3 = \text{COOR, CN, SO}_2\text{Ph}
\end{align*}
\]

*Scheme 12:* Coupling of alkyne with an alkene

### 1.4. Synthesis of multiply silylated ethenes

Multiply silylated ethenes such as 1, 2-disilylethenes and 1, 1, 2-silylethenes are intermediates for structurally interesting highly substituted alkenes. However, only a limited number of stereo- and regio-selective procedures are available. An ate-type trimethylsilylmethylcobalt reagent was found to react with dibromosilylmethane or dibromosilylmethane to provide a concise synthesis of 1,2-disilylalkenes or 1,2,3-trisilylethenes in highly stereoselective and regioselective manner (*Scheme 13*).\(^{44}\) The proposed mechanism (*Scheme 14*) includes halogen-cobalt exchange, 1,2-silylmethyl
**Scheme 13**: Cobalt mediated concise synthesis of 1, 2-disilylethenes

\[
\begin{array}{c}
\text{Ph}_2\text{MeSi} \quad \text{SiMe}_3 \\
\text{Br} \quad \text{Br} \quad 23 \\
[\left(\text{PrO}\right)\text{Me}_2\text{SiCH}_2]_4\text{Co}(\text{MgCl})_2 \\
\text{THF, -20 °C} \\
\rightarrow \\
\text{Ph}_2\text{MeSi} \quad \text{SiMe}_3 \\
\text{H} \\
\text{24} \\
54-94 \% \text{ stereoselectivity}
\end{array}
\]

**Scheme 14**: Proposed mechanism for the regio- and stereoselective silylation of alkenes

migration followed by β-hydride elimination. The β-hydride elimination favors a sterically less demanding transition state, which leads to high regio- and stereoselectivity.
1.5. Carbonylative ring opening and ring expansion

A cobalt-catalyzed ring opening reaction of cyclic ethers was reported by Murai and co-workers.\textsuperscript{45} Later, Watanabe demonstrated that cyclic ethers such as oxetanes and oxiranes could undergo ring opening reaction (Scheme 15) with trimethylsilylamines under insertion of carbon monoxide at atmospheric pressure.\textsuperscript{46}

![Scheme 15: Ring opening of oxetane](image)

Alper first reported the formation of \(\beta\)-lactones from epoxides and \(\beta\)-lactames from aziridines and co-workers.\textsuperscript{47} Alper used bis(triphenylphosphine)iminium cobalt tetracarbonyl complex in combination with a Lewis acid, trifluoroborane etherate (BF\(_3\) OEt\(_2\)) as catalyst. Coates and co-workers have later achieved the synthesis of \(\beta\)-lactones from epoxides and \(\beta\)-lactams in good to excellent yields with use of biscyclopentadienyl titanium cobalt tetracarbonyl or aluminium(salophen)cobalt tetracarbonyl complexes.\textsuperscript{48} Coates and co-workers have also succeeded in the double carbonylation of epoxides to furnish succinic anhydrides with inversion of configuration by using bimetallic aluminium porphyrine cobalt tetracarbonyl catalyst.\textsuperscript{49} A wide range of substituted epoxides were used in this reaction and the catalyst loadings are very low which allows for easier purification of the products.\textsuperscript{50}
Scheme 16: Synthesis of β-Lactam from oxirane by CO insertion

Scheme 17: Double carbonylation of oxirane

1.6. Activation of sp\(^3\) C-H bonds

The functionalization of hydrocarbons, the main natural oil and gas constituents, has been identified as a key research strategy for the development of economical and sustainable global carbon management. Undoubtedly one of the most important functionalization is selective oxidation; in particular the selective aerobic oxidation of methane to methanol would be of great industrial interest.\(^{51-54}\) The first cobalt catalyzed activation of sp\(^3\) C-H bond of alkanes was reported by Iqbal and co-workers. Depending on ligand choice, these cobalt catalysts were effective in either the chlorination or sulfochlorination of alkane substrates in good yields.\(^{55}\) The reaction is simply performed by combining the alkane, sulfuryl chloride and the catalyst and heating to 85 °C. Sulfochlorination of polyethylene would lead to polymers with reactive sulfonyl chlorides that could be used for reactive compatibilization and/or polymer grafting reactions.
R = C₄H₇, C₆H₁₁, C₈H₁₅, etc.

Scheme 18:

Recently, Brookhart et.al. have developed catalytic dehydrogenation of alkyl amines with a Co(I) catalyst. Amine substrates are protected with vinyl silanes, followed by catalytic transfer hydrogenation, to yield a broad range of stable protected enamines and 1,2-diheteroatom-substituted alkenes, including several unprecedented heterocycles. (Cp*)Co(VTMS)₂ catalyzes transfer of hydrogenation under surprisingly mild conditions with high chemo-, regio-, and diastereoselectivity (Scheme 19).⁵⁶

Scheme 19: Cobalt(I) catalyzed dehydrogenation

1.7. Oxidation of alcohols to carbonyl compounds

The oxidation of an alcohol to the corresponding carbonyl product is a vital and common transformation in synthetic organic chemistry. Consequently, there are a number of diverse procedures are available in the literature. Chun Cai et.al., reported the
cobalt(II) perfluorooctane sulfonate (Co(OPf)₂) catalyzed oxidation of various types of alcohols to carbonyl compounds under atmospheric pressure of molecular oxygen in fluorous biphasic systems.⁵⁷ By simple separation of the fluorous phase, which contains only pre-catalyst, the reaction can be repeated several times. An efficient method for the oxidation of a variety of activated and non-activated secondary alcohols to the ketones was developed by Bir Sain and co-workers.⁵⁸ In this reaction, Co(acac)₂ in combination with NBS catalyzes the oxidation in acetonitrile (Scheme 20). Recently, method for the oxidation of alcohols (aliphatic, aromatic and cyclic alcohols) to ketones was established by Pedro et al. This reaction is carried out using a square-planar cobalt(III) tetraamine complex as catalyst in the presence of dioxygen and pivaldehyde.⁵⁹

**Scheme 20**: Co(acac) catalyzed oxidation of secondary alcohols to ketones

Very recently, Buxing Han and co-workers have demonstrated the aerobic oxidation of secondary alcohols to ketones using alumina or Zinc oxide supported cobalt(II) chloride or even unsupported cobalt(II) chloride as catalyst.⁶⁰ The aerobic oxidation of benzhydrol, 1-phenylethanol and cyclohexanol to corresponding ketones was carried out in poly(ethylene glycol) (PEG-600)/supercritical CO₂ (SCCO₂) biphasic system. It was shown that CoCl₂·6H₂O, Co(II)/Al₂O₃, and Co(II)/ZnO were all active and selective for the reactions. The reactivity of the substrates followed the order benzhydrol > 1-phenylethanol > cyclohexanol. Co(II)/ZnO was most stable and could be reused four times without considerable reduction of activity.
1.8. Oxidation of Alkenes

The selective oxidation of alkenes to epoxides is one of the most important and fundamental reaction in organic chemistry both at the laboratory and industrial scale. Numerous catalysts have been developed using a variety of reagents to achieve this purpose. However, most of these reagents are required in stoichiometric quantities. Moreover these reagents are expensive and toxic. From an environmental as well as economic point of view, catalytic oxidation processes, especially those, in which molecular oxygen is used as primary oxidant, are particularly attractive. With these view points, Pielichowski and co-workers\textsuperscript{61} made attempts and succeeded in developing an efficient and selective catalytic system consisting of polyaniline supported cobalt(II) chloride. Cobalt(II) chloride supported on polyaniline turned out to be particularly effective in oxidation of alkenes with terminal carbon-carbon double-bond and cycloalkenes.

![Scheme 21: Cobalt(II)-catalyzed oxidation of alkenes to oxiranes](image)

**Scheme 21:** Cobalt(II)-catalyzed oxidation of alkenes to oxiranes
Chavasiri and co-workers\textsuperscript{62} have recently disclosed that the epoxidation of alkenes can be achieved using cobalt(II) calix[4]pyrrole as catalyst and aldehyde/oxygen as an oxidant. Co(II) meso-tetrakis (4-methoxyphenyl)-tetramethyl calix[4]pyrrole was found to show the best catalytic performance to provide the corresponding epoxide in high yields with excellent selectivity stereo- and regioselectivity under mild conditions.

1.9. Cyclopropanation

Metal-catalyzed cyclopropanation of double bonds with carbenoids obtained from diazo compounds is a well known reaction in organic synthesis. The control of both the diastereoselectivity and the enantioselectivity has drawn much attention over the past years. There are various catalysts, such as copper, cobalt, ruthenium and rhodium complexes, that are employed for this purpose and that exhibit excellent stereoselectivity and, in general, result in the formation of the trans products. Recently Katsuki studied metallosalen complexes, which are known to be efficient catalysts for oxene and nitrene transfer reactions. He reported the use of chiral cobalt(salen)\textsuperscript{63} complexes for the analogous carbenoid transfer reaction (Scheme 22). Various styrene derivatives reacted with simple a-diazo esters with diverse salen derived cobalt complexes to produce the cyclopropanation product 41 in excellent yield, diastereoselectivity and enantioselectivity. The cis/trans relationship is influenced by the nature of the ligand and the cobalt centre. Cobalt(III) complexes seem to favor the generation of the trans isomer, and cobalt( II) complexes, the cis isomer (Scheme 22).
Scheme 22: Cobalt(salen) catalyzed Cyclopropanation

Gao et al., reported\textsuperscript{64} the use of dinuclear Robsen-type coupled chiral salen complexes for the same reaction. Zhang and co-workers reported the use of cobalt porphyrin\textsuperscript{65} complexes for the asymmetric cyclopropanation of styrene derivatives with ethyl diazoacetate under mild conditions (Scheme 23). A great number of structurally diverse porphyrin ligands tested and a general preference for the trans isomer was shown.

Scheme 23: Co (porphyrin) catalyzed cyclopropanation

Rose and co-workers very recently reported a chiral cobalt(II)-binaphthyl porphyrins catalyzed asymmetric cyclopropanation of olefins. Cyclopropanation of a variety of substituted styrenes with diazoacetate was achieved in good yields and enantioselectivity unto 90 \% were obtained.\textsuperscript{66} The positive catalytic effect of nitrogen promoter, N-methylimidazole, on reaction rate and enantioselectivity was demonstrated.
1.10. 2+2 Cycloaddition reactions

The supra-supra facial [2+2] Cycloaddition of alkenes or alkynes is thermally forbidden by Hoffmann-Woodward rules. Nevertheless, these reactions are allowed photochemically, by free radical mechanism, by Lewis acid catalysis. Krische reported the first example of an intramolecular, diastereoselective [2+2] cycloaddition of bis-enones to cyclobutanes. The reaction was catalyzed by cobalt species (Scheme 24).\(^{67}\) The reaction was restricted to aryl substituted ketones and the formation of bicyclo[3.2.0] backbones. Cheng and co-workers reported the reaction (Scheme 25) of terminal as well as internal alkynes with bicyclic alkenes \(^{47}\) such as benzooxanorbornadiene to highly functionalized cyclobutenes with the inexpensive and versatile \(\text{CoI}_2(\text{PPh}_3)_2\), triphenylphosphine and zinc catalyst system.\(^{68}\) Hilt very recently reported an extension of this methodology using a cobalt catalyst system, \([\text{CoBr}_2(\text{dppp}), \text{Zn}, \text{ZnI}_2]\). This method is applicable not only for norbornyl derivatives as starting materials but also for acenaphthylene and even cyclobutene derivatives such as \(\text{50 (Scheme 25)}.\(^{69}\)
Scheme 25: Cobalt-catalyzed [2+2] cycloaddition of alkene with an alkyne

1.11. Five member ring formation

Pauson-Khand reaction undoubtedly is one of the most valuable in the construction of five membered rings. It is a [2+2+1]-cycloaddition of an alkyne, an alkene and carbon monoxide. Chung and co-workers combined a cobalt-catalyzed Pauson-khand type reaction in tandem with other cobalt-catalyzed cycloaddition reactions (Scheme 27). After a [2+2+1] cycloaddition, a cyclopentadienone intermediate formed and reacted with either 1,3-dienes in a Diels-alder reaction or with two other alkynes in a [2+2+2]-cycloaddition reaction. Alternatively, a dimerization by Diels-Alder reaction of [2+2+1]-cycloaddition product led to the formation 51, which undergoes rearrangement with the extrusion of CO yielded 52.
1.12. Dipolar Cycloaddition reactions with nitrenes

The 1,3-dipolar cycloaddition of nitrones to alkenes is a very useful reaction in the construction of isoxazolines and can be catalyzed by various Lewis acids. Recently, Desimoni, Kanemsa and Suga carried out studies on these reactions using a diverse Lewis acids including cobalt salts. Yamada and co-workers have reported the use of 3-oxobutyldenimniatocobalt(III) complexes for the enantioselective 1,3-dipolar cycloaddition of nitrones with $\alpha,\beta$-unsaturated aldehydes to furnish 55 (Scheme 28).

Scheme 28:
1.13. Formation of rings containing six to ten members

Cobalt catalysts are also used in the formation of rings containing six to ten members. Most Diels-Alder reactions between neutral substrates require drastic conditions. Hilt and co-workers developed a catalyst system consisting of Co(dppe), zinc iodide and zinc or tertiary butylammonium borohydride to overcome this problem (Scheme 25).\cite{73,74}

\[
\text{Scheme 29: Cobalt-catalyzed Diels-Alder reaction}
\]

Cobalt complexes also catalyze the construction of six membered rings by homo Diels-Alder reaction, [2+2+2] cyclotrimerisation of alkynes, [2+2+2] cyclotrimerization between two alkynes and one alkene, cyclotrimerization of alkynes with nitriles.

Due to their abundance in natural products, the synthesis of seven membered rings is one of major goals of organic chemists. Seven membered rings are constructed by [3+2+2] cycloaddition, [5+2] cycloaddition, [4+3] cycloaddition reactions. Nicholas type reaction, [5+2] cycloaddition reaction of silylenol ethers was catalyzed by cobalt complex and was highly stereoselective. The construction of eight membered rings are achieved by [6+2] cycloaddition, [4+2+2] cycloaddition reactions. Buono and co-workers recently reported a new cobalt catalyzed [6+2] cycloaddition of cyclohepta-1,3,5-triene with terminal alkynes for the construction of bicyclic systems. The [4+2+2] cycloaddition is a powerful method for the construction of eight membered rings. Snyder reported an efficient cobalt system consisting of a mixture of cobalt(II) iodide with 1,2-bis(diphenylphosphino)ethane, zinc and ZnI$_2$. Snyder also demonstrated the application of this methodology in natural
product synthesis. Cobaloxime dienyl complexes were found to catalyze Diels-Alder reactions with tropone derivatives (Scheme 30). Welker observed the [6+4] cycloaddition product. Tropone was conveniently synthesized in excellent yield by cobalt-catalyzed [6+4] cycloaddition.

Scheme 30: 6+4 Cycloaddition reaction

1.14. Cobalt(II)-catalyzed Friedel-Crafts cyclization

Stereoselective construction of medium-sized poly-functional rings is an important subject because these structures are found in a number of natural products. Nagumo and co-workers developed a novel cyclization of eight- and nine-membered iminium ions using a Co₂(CO)₆ complexed acetylene unit. The cyclization was achieved due to the bent conformation of the complex, which facilitates access of the aromatic ring to the iminium ion generated from 63.
Nagumo very recently developed a method for constructing poly-functional eight-membered carbocycles based on the endoselective Friedel–Crafts reaction of vinyloxiranes with Co$_2$(CO)$_6$-complexed benzeneacetylene. The cyclization showed high stereoselectivity and regioselectivity for the opening of the epoxide. Furthermore, decomplexation of the cyclization product proceeded smoothly. This reaction is expected to provide a useful method for the synthesis of natural products with eight-membered carbocycles.

![Scheme 32](image)

**Scheme 32**

Decomplexation was performed under either oxidizing or reducing conditions. Treatment of cyclic molecule 67 with ceric ammonium nitrate afforded 68 in 72% yield. On the other hand, 67 was transformed into poly-functional cyclooctene 69 in high yields upon treatment with tributyl tin hydride in toluene at 70 ºC (Scheme 33).
1.15. Miscellaneous reactions

Kanemasa and co-workers introduced an enantioselective Michael addition reaction catalyzed by cobalt(II) perchlorate hexahydrate and (R,R)-4,6-dibenzofurandiyil-2,2’-bis(4-phenyloxazoline) in a 1:1 mixture of ter-butyl alcohol and tetrahydrofuran to generate chiral polyfunctionalized ketones (Scheme 34). Brookhardt et al recently described an interesting hydrogen shift reaction catalyzed by a CpCo(vinylsilane)$_2$ complex wherein, an enamine was generated by the abstraction of hydrogen and transferring it to vinylsilane group (Scheme 35).

Scheme 33

Scheme 34: Cobalt(II)-catalyzed enantioselective Michael addition
Scheme 35: Cobalt-catalyzed hydrogen shift

A recent study by Forbes and co-workers showed that Jacobsen’s Co(II)salen complex could be used in hydrolytic kinetic resolution of chiral oxiranes.80

Scheme 36

1.16. Conclusion

It is well known fact that cobalt has high potential for catalyzing various reactions. A small change in the catalyst system or parameters such as solvent, ligand or concentrations of the reaction lead to new unexpected results. Even simple salts like cobalt(II) chloride can be tuned to yield wonderful results by choosing proper solvent, ligand and other parameters. The growing interest in cobalt-catalysis among chemists, and the increasing number of interesting and astonishing reactivities and new reaction pathways inspired us to venture into the investigation of cobalt in some of the organic transformations. Indeed, we could succeed in developing new highly efficient synthetic methodology for Friedel-Crafts acylation of some of the electron rich aromatics such as
anisole, thioanisole, and toluene and also a highly efficient procedure for the synthesis of nitriles from dehydration aldoximes.

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