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Introduction to Cobalt Chemistry and Catalysis

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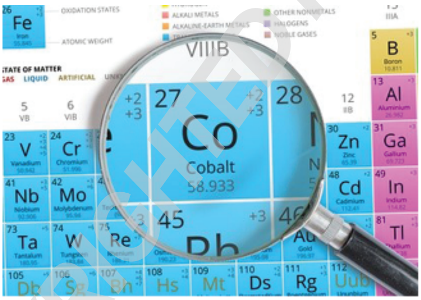
1.1 Introduction



Cobalt (Co) is the first and lightest element among the group 9 transition metals, further members being rhodium (Rh), iridium (Ir), and meitnerium (Mt). In contrast to their significance in organic synthesis and catalysis, cobalt is by far the most abundant element of the group in the geosphere, compared with rhodium and iridium as its heavier congeners (Co:Rh:Ir = c. $10^4 : 5 : 1$) [1]. While rhodium and iridium complexes have been at the forefront of organotransition metal chemistry with relation to organic syntheses, steadily enabling novel and often unprecedented transformations of simple starting materials to complex products or opening the gate to novel fields of catalysis as has happened with C–H functionalisation reactions, cobalt stood back for a long time. Expression for the different significance of the three transition metals is also found in the literature, as monographs for either rhodium and iridium as catalyst metals for organic

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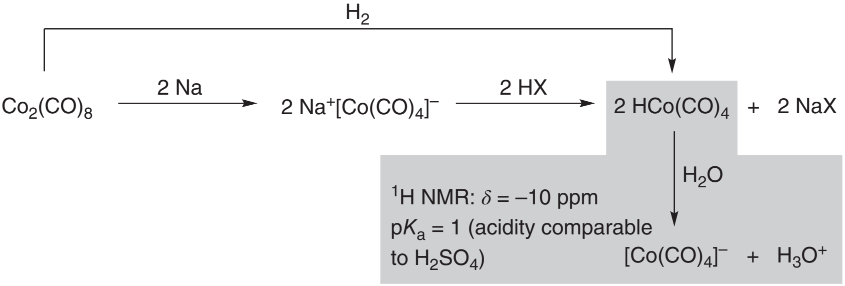
synthesis have already been published [2, 3]. However, some direct comparisons of the application of group 9 metals for organic synthesis and catalysis can be found in the literature [4]. Next to its membership in the first row of the transition metals, relative abundance, and biorelevance, it is also considered a sustainable metal, among other elements in this nowadays particularly important field [5].

Cobalt (the name is derived from the German word "Kobold" meaning goblin, due to the behaviour and confusion with silver–copper ores in medieval mining) has been isolated for the first time in 1735 by the Swedish chemist *Georg Brand*, who also recognised its elemental character. It is an essential trace element for humans and animals, and its main purpose is the constitution of vitamin B_{12} (cobalamin), which has an important role for the regeneration of erythrocytes. Cobalamines are organometallic compounds with cobalt–carbon bonds, possessing cobalt in the oxidation states +1 to +3, and provide the only known cobalt-containing natural products.

Beside the importance for the human physiology, cobalt has evolved from an unwanted and downright abhorred element during silver and copper mining to a metal of strategic industrial importance and in recent years also a rising young star in homogeneous catalysis. How does this chemical version of "rags to riches" come into play? One modern reason is the importance of cobalt as metal used in high-performance alloys (e.g. stellite), permanent magnets, rechargeable batteries, cell phones, and many more technical applications [6]. Requirements of our modern society with respect to the production of chemicals and materials also heavily rely on the late, rare, and rather expensive platinum group metals (PGM). The implementation of sustainability and efficiency thus leading the way to explore the earth-abundant metals for both homogeneous and heterogeneous catalytic purposes [7, 8].

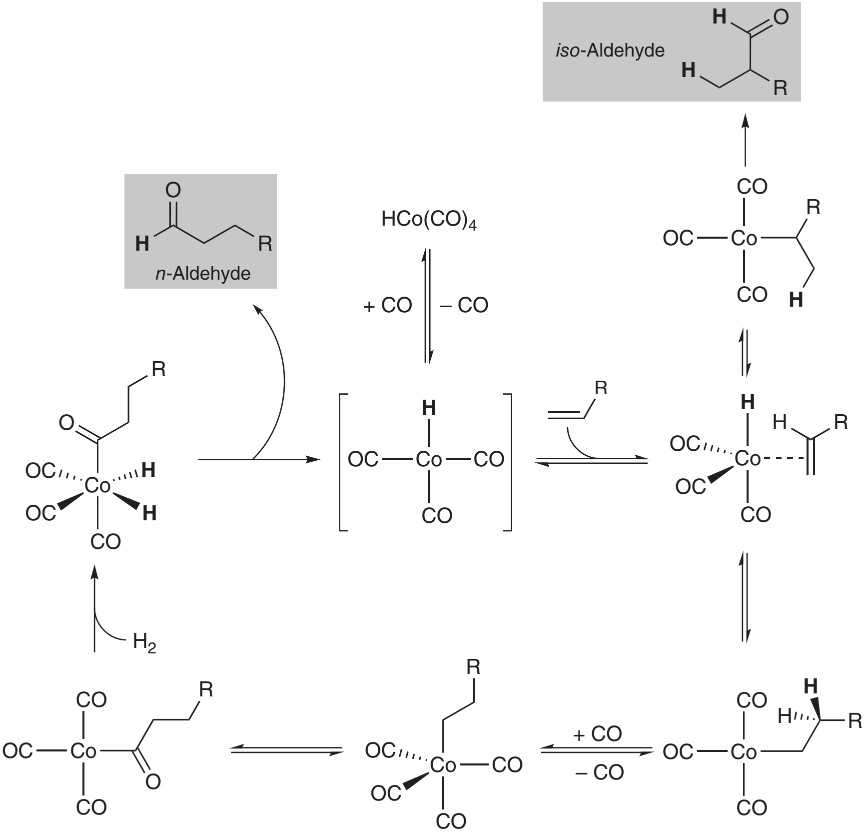
From a chemical and catalytical point of view, cobalt already inherits the role of a major player in the awakening of homogeneous organometallic catalysis in the first half of the twentieth century [9]. *Otto Roelen* at Ruhrchemie (now Oxea) in Oberhausen discovered the "oxo synthesis" in 1938, today named hydroformylation reaction, and introduced $HCo(CO)_4$ as catalyst for this reaction. Still today beside rhodium as metal with higher reactivity cobalt complexes are used as catalysts. Basis for this reaction was work from *Walter Hieber* on the synthesis of carbonyl metallates via the so-called "*Hieber* base reaction", affording $H_2Fe(CO)_4$ by the reaction of $Fe(CO)_5$ with NaOH. Because for cobalt no mononuclear binary carbonyl compound is known, therefore the related compound $HCo(CO)_4$ was generated from the prominent carbonyl complex $Co_2(CO)_8$ by reductive splitting with sodium metal and protonation or even directly by oxidative splitting by molecular hydrogen itself (Scheme 1.1). The resulting cobalt carbonyl hydride is a proton donor, able to protonate water with an acidity comparable to sulfuric acid.

The mechanism of the hydroformylation process using $HCo(CO)_4$ and related compounds $HCo(CO)_3L$ (L = phosphine) has been studied in great detail, first proposed by *Breslow* and *Heck* [10]. Scheme 1.2 displays the now generally accepted mechanistic pathway for the cobalt-catalysed process [11]. Starting from the hydridic $HCo(CO)_4$, reversible dissociation of a CO ligand followed by reversible olefin coordination led to migratory insertion, which would pave the way to either the *n*-aldehyde or *iso*-aldehyde, depending on the course of the



Scheme 1.1 Synthesis of cobalt carbonyl hydride (the reaction with H_2 can be reversible).

insertion. Following the reaction cycle, alkyl migration led to formation of an acylcobalt species, which after oxidative addition of hydrogen was reductively eliminated as the *n*-aldehyde. This catalytic cycle combines all the significant elementary steps of homogeneous catalysis with metal complexes and provides a taste on the complexity for studying such reaction mechanisms in detail. Interest



Scheme 1.2 Mechanism of the classical cobalt-catalysed hydroformylation reaction of terminal olefins.

and detailed studies in these first molecularly defined catalysts for the purpose of synthesising structurally advanced organic molecules has since filled the knowledge of organometallic chemistry.

1.2 Organometallic Cobalt Chemistry, Reactions, and Connections to Catalysis

Cobalt is a d^9-metal and the by far mostly frequently occurring oxidation states in its compounds are −1, 0, +1, +2, and +3. The latter oxidation states also play the major role in stoichiometric/catalytic reactions, while complexes with the oxidation states −1 and 0 are found in some prominent complexes and starting materials. The preference of formal +1/+3 oxidation states in many catalytic transformations is in close relation to the catalytic behaviour of the heavier congeners, rhodium and iridium. In general, the largest number of contemporary catalytic processes include a catalyst generation step, in which, e.g. Co(II) salts are introduced, together with an appropriate ligand and a reducing agent or other additives to lower the oxidation state to +1, from which the species enters the catalytic cycle. On the other hand, a large number of organometallic compounds based on the unsubstituted cyclopentadienyl (Cp), related substituted cyclopentadienyl (Cp′), or pentamethylcyclopentadienyl (Cp*) ligands are reported and well known, beside numerous isolated complexes with P- and N-donor atom-containing ligands. However, the coordination and organometallic chemistry of cobalt is a wide and multifaceted field and has been involved in ground-breaking research in either area [12].

Cobalt is also a widely used catalyst metal for heterogeneously catalysed processes. Especially the famous *Fischer–Tropsch* process is still relying on cobalt as the principal catalyst metal, as it was already from the initial reports on this large-scale industrial process [13]. Further modern applications in heterogeneous catalysis are often related to the conversion of small molecules in steam-reforming or partial oxidation processes (ethanol, methane) towards the formation of syngas, together with other applications for the allocation of clean energy. A highly current topic is therefore, e.g. the use of cobalt in heterogeneously catalysed electrochemical water splitting [14] or the reduction of CO_2 on cobalt-containing surfaces [15]. Analysis of the chemistry and catalytic performance of cobalt on surfaces is still a topic of ongoing investigations [16].

1.2.1 Cobalt Compounds and Complexes of Oxidation States +3 to −1

Cobalt is an electron-rich transition metal, like its latter group congeners; however, it is a first-row transition metal, which inherits also significant differences. Due to its electron richness, it belongs to the so-called “base metals”, including the neighbouring first-row transition metals manganese, iron, nickel, and copper. The abundance of low oxidation states (0, −1) is, however, quite unique for cobalt and also rather known for the compounds of neighboring iron than for the heavier metals of group 9. Comparable especially to rhodium catalysis is the oxidation state +3 as usually highest occuring state during catalytic reactions.

1.2.1.1 Co(III) Compounds

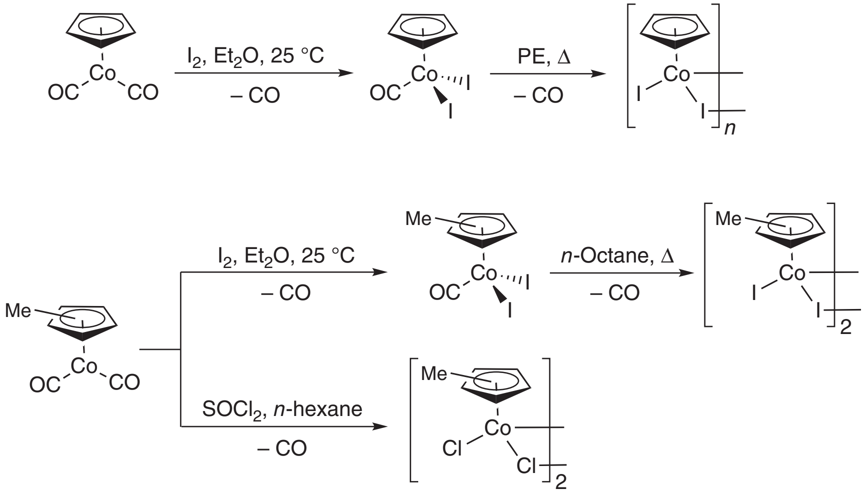
Isolated cobalt complexes in the oxidation state +3 are most often found in coordination compounds, because the d^6 configuration is highly stable with ligands possessing a strong ligand field. There is only a limited number of Co(III) compounds commercially available and from the halides, only the binary CoF_3 is known, which is an oxidant and can be used as fluorinating agent. This is in stark contrast to rhodium and iridium, where the oxidation state +3 is well known in compounds and all binary halides MX_3 (X = F, Cl, Br, I) are available for these metals. $RhCl_3$ and $IrCl_3$ and their hydrated versions are usually the starting materials for synthesising numerous precursor compounds and precatalysts for catalytic purposes, while $CoCl_3$ is an unstable compound [17].

Cobalt(III) complexes played an important role in the development of the theory of coordination compounds by *Alfred Werner*, concerning the complexes of $CoCl_3$ with different equivalents of ammonia, NH_3. The complexes $[Co(NH_3)_4Cl_2]Cl$ exist in the form of two stereoisomers (*cis*- and *trans*-isomers of the octahedral polyhedron), allowing to address the stereochemistry of coordination compounds. The Co(III) complexes are kinetically inert, octahedral complexes with the configuration t_{sg}^6. Due to the inertness, indirect methods of synthesis are common, meaning to use Co(II) salts as starting compounds, coordination with desired ligands, and subsequent oxidation by, e.g. oxygen, to furnish the desired Co(III) complexes.

There are more organometallic Co(III) compounds known, owing to the strong ligand field of many groups used as organometallic ligands. As an example, cobaltocene, Cp_2Co is a rather unstable, 19-electron Co(II) complex, which can act as efficient one-electron reducing agent, yielding the stable cobaltocenium Co(III) cation (Cp_2Co^+), being isoelectronic with ferrocene. While for ferrocene an extremely rich and diverse chemistry has been developed, e.g. as ligand backbone for phosphine ligands, such application of the cobaltocenium cation is lacking and started to develop only recently [18]. In addition, the synthesis of half-sandwich CpCo(III) complexes is well known and shares common features with Cp*Co complexes. This is best exemplified by the reaction of the $CpCo(CO)_2$ and $Cp^*Co(CO)_2$ with elemental halides, furnishing the corresponding Co(III) complexes, which has been reported already during the time when the Cp–metal chemistry was still in its infancy (Scheme 1.3) [19, 20]. Especially $Cp^*CoI_2(CO)$ has become a precursor for a wide range of precatalyst compounds. The chemistry and catalytic applications of CpCo(III) and Cp*Co(III) complexes as well as some structurally related Cp′Co(III) complexes has been compiled very recently [21].

1.2.1.2 Co(II) Compounds

Compared with its higher homologs, rhodium and iridium, the oxidation state +2 is one out of the two most important, while for the other two elements, it has only minor importance. All halides of this oxidation state are known and commercially available, stable compounds, being the starting material for a



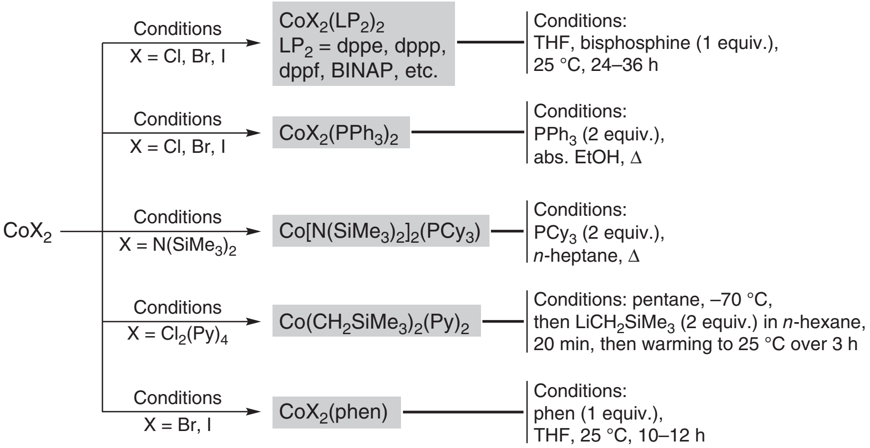
Scheme 1.3 Synthesis of CpCo- and Cp*Co-halides as synthetically useful precursors and precatalysts.

large number of complexes, e.g. as the hydrate $CoCl_2{\cdot}6H_2O$. The configuration of Co(II) ions as being d^7 does not favour a particular ligand arrangement for such paramagnetic complexes. Examples of coordination geometries comprise linear (e.g. $[Co\{N(SiMe_3)_2\}_2]$), tetrahedral (e.g. $[CoCl_4]^{2-}$, $[Co(N_3)_4]^{2-}$, $[CoCl_3(NCMe)]^-$), square-based pyramidal (e.g. $[Co(CN)_5]^{3-}$), and dodecahedral (e.g. $[Co(NO_3)_4]^{2-}$) forms, among many others, depending on the ligand properties [17].

Co(II) salts used as precatalysts in catalytic reactions are usually reduced by less noble metals, such as zinc or manganese to Co(I), which upon complexation to an appropriate ligand acts as catalytically active species. The salts can be introduced separately as halide salts and free ligand or as the isolated complex. The synthesis conditions of some typical Co(II) complexes are compiled in Scheme 1.4 [22]. A useful and very recently reported alternative to complexes of the type $[Co(R)_2(Py)_2]$ is the compound $[Co(R)_2(TMEDA)_2]$ ($R = CH_2SiMe_3$, CH_2CMe_3, CH_2CMe_2Ph), allowed facile substitution of the “dummy” ligand for *N*-heterocyclic carbene (NHC) ligands or bidentate phosphines [23].

The reduction depends on conditions like the applied Co(II) salt, solvents, reductants involved, and even additives like *Lewis* acids, being able to remove a remaining halide from the metal centre [24]. In cross-coupling reactions utilising cobalt(II) precatalysts, the reduction to Co(I) or even Co(0) can also be achieved by an excess of the organometallic coupling reagent, often *Grignard* reagents [25].

Recently, novel Co(II) precursor compounds for catalytic applications came to the forefront and opened the door also for the synthesis of complexes being comparable to known precursor molecules with the latter homologs, e.g. $[M(COD)Cl]_2$ (M = Rh, Ir) or $[Rh(COD)_2](BF_4)$. *Chirik* introduced $(Py)_2Co(CH_2SiMe_3)_2$ as precursor for the coordination to bisphosphines and subsequent asymmetric hydrogenation reactions, providing evidence for the



Scheme 1.4 Synthesis of Co(II) complexes from simple Co(II) salts.

superiority of the cobalt precursor $(Py)_2Co(CH_2SiMe_3)_2$ compared with simple Co(II) salts [26].

1.2.1.3 Co(I) Compounds

There are significantly less Co(I) complexes known and commercially available compared with the Co(+2) and Co(+3) oxidation state. Most complexes are generated *in situ* or require strict handling under inert conditions. A common source is the *Wilkinson* complex, $RhCl(PPh_3)_3$ and analogue of cobalt, $CoCl(PPh_3)_3$, which is used as synthetic precursor for the assembly of Co(I) complexes as well as precatalyst itself. Comparing the synthesis of these complexes nicely points out the differences between the metals (Scheme 1.5) [27, 28]. Synthesis of the bromide and iodide complexes, $CoX(PPh_3)_3$ (M = Br, I), can be obtained on an identical route compared with $CoCl(PPh_3)_3$ [29]. The iridium analogue $IrCl(PPh_3)_3$ is even more difficult to obtain and is not a suitable hydrogenation catalyst due to strong bonding of hydrogen [30]. In addition, it very readily undergoes *ortho*-metallation of a phosphine phenyl ring.

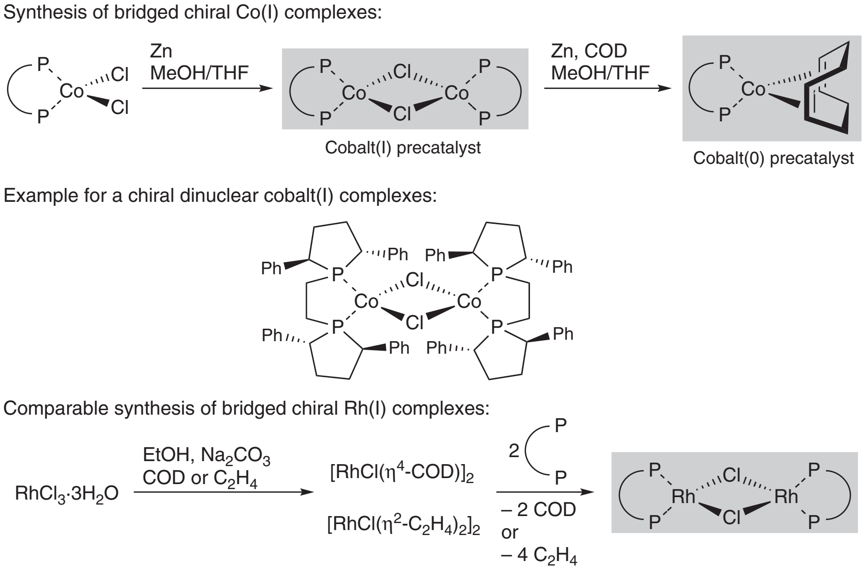
$$CoCl_2 \cdot 6H_2O \xrightarrow[\text{Reductand: Zn, NaBH}_4]{3\ PPh_3,\ THF,\ 25\,^\circ C} CoCl(PPh_3)_3$$

$$RhCl_3 \cdot 3H_2O \xrightarrow[-\ OPPh_3]{4\ PPh_3,\ EtOH,\ reflux} RhCl(PPh_3)_3$$

Scheme 1.5 Synthesis of complexes of type $MCl(PPh_3)_3$ (M = Co, Rh).

While the *Wilkinson* complex is the classical catalyst for hydrogenation of multiple bonds, the cobalt analogue has been used much less in general and reported reactions comprise more cyclisations and only few examples of hydrogenation [31].

As Rh(I) and Ir(I) complexes, suitable as metal sources for catalytic purposes, a number of either dinuclear, often halide-bridged olefin complexes, or mononuclear cationic complexes are readily available. This is in stark contrast to the lightest group member, which did not possess such a range of precursors. Only recently several examples for comparable complexes were reported. *Chirik* investigated the synthesis and reduction of $CoCl_2$(bisphosphine) by zinc and independently synthesised chlorido-bridged dinuclear Co(I) complexes, which can then also further be reduced to Co(0) complexes (Scheme 1.6) [32]. The analogue process for dinuclear Rh(I) complexes was systematically investigated by *Heller*, demonstrating the so far operationally more simple procedure for rhodium, which is possible by simply mixing the stable precursors $[RhCl(COD)]_2$ or $[RhCl(C_2H_4)_2]_2$ with 2 equiv. of the diphosphine (Scheme 1.6) [33]. This methodology is very variably applicable to broad range of chiral ligands.



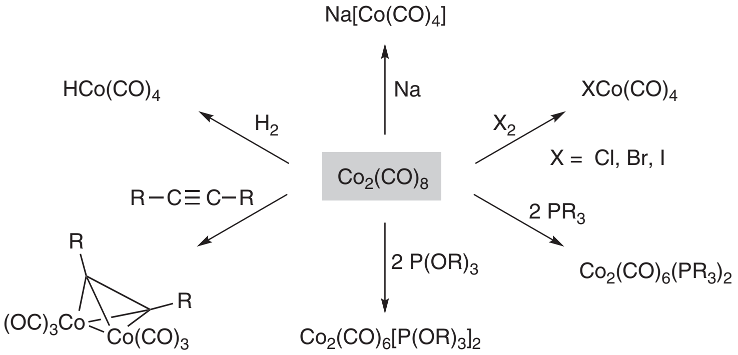
Scheme 1.6 Synthesis of dinuclear halide-bridged Co(I)(diphosphine) complexes and the synthesis of related Rh(I) complexes for comparison.

Another rather large class of compounds are CpCo(I) complexes with different neutral ligands, often simply derived from $CpCo(CO)_2$ by ligand exchange or reaction of the metallated Cp either with Co(II) halides under reductive conditions or from Co(I) halide complexes and subsequent ligand exchange [34]. The generation from cobaltocene by reductive removal of one Cp ligand in the presence of the corresponding ligand is also a possibility, *vide infra*.

1.2.1.4 Co(0) Compounds

The most important Co(0) compound for synthetic and catalytic purposes is certainly the binary carbon monoxide-containing compound $Co_2(CO)_8$, an

18-electron metal complex. $Co_2(CO)_8$ is not only synthesised by reaction of $Co(OAc)_2$ with hydrogen and CO at 150–200 °C and high pressure but can also be obtained from elemental cobalt and CO and is commercially available. It decomposes at increasing temperature to yield higher cobalt clusters compounds while releasing CO. The CO ligands can easily be exchanged for other donor ligands, and reactions with halides, hydrogen, or alkali metals can lead to either formal cationic or anionic $[Co(CO)_4]$ fragments, in both cases stabilised by the electronic moderation of the CO ligands (Scheme 1.7). These fragments are useful reagents for further synthetic transformations. Monodentate and bidentate phosphines as well as phosphite ligands can easily be introduced by ligand exchange, just to name the most prominent examples. The complexation of alkynes plays a significant role in the mechanism of the *Pauson–Khand* reaction, the *Nicholas* reaction or [2+2+2] cycloaddition reactions as well as one of the few protection groups for alkynes (see the corresponding chapters 6, 8 and 9 in this book).

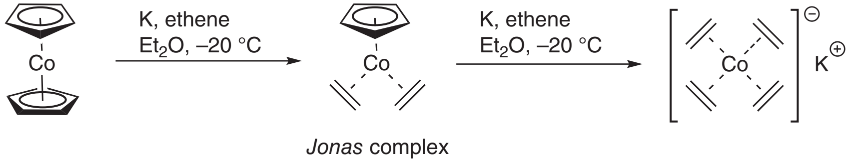


Scheme 1.7 $Co_2(CO)_8$ as precursor for cobalt-carbonyl compounds.

Another 17-electron Co(0) compound, which has been used in catalytic applications like C–H activation and reductive C–C coupling [35], is the complex $Co(PMe_3)_4$, which can be prepared from Co(II) halides in the presence of PMe_3 by reduction with sodium amalgam [36]. The electron richness of this complex makes application in C–H functionalisation reactions a self-evident possibility.

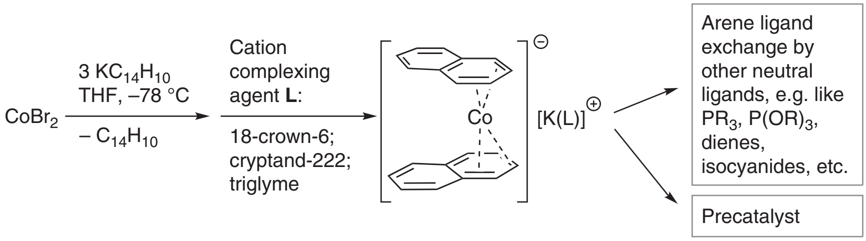
1.2.1.5 Co(−I) Compounds

As mentioned earlier, a formal anionic carbonyl cobaltate $[Co(CO)_4]^-$ can be simply generated by reaction of $Co_2(CO)_8$ with an alkali metal. The compounds are rather strong nucleophiles and therefore alkylation reactions are possible. An elegant reaction pathway was described by *Jonas*, who reduced cobaltocene in the presence of olefins (ethene, COD) with alkali metals by reductive removal of the Cp ligands (Scheme 1.8) [37]. Driving force of the reaction is the formation of the 18-electron complex from the 19-electron cobaltocene. The procedure is quite general and can be applied also to other olefins as general entry to CpCo(I)-olefin and -diene complexes [38, 4b]. The olefin ligands act as π-acceptor ligands, thus reasonably stabilising the metallate.



Scheme 1.8 Synthesis of the *Jonas* complex and subsequently the binary olefin cobaltate complex.

Other anionic cobaltates have been prepared by the inclusion of arene ligands by reduction in the presence of alkali metals (Scheme 1.9) [39]. The synthesis using naphthalene or anthracene yielded the bis(naphthalene)cobaltate (−I) or bis(anthracene)cobaltate (−I) as potassium salt, which can easily be transformed into metallates containing other neutral ligands, like dienes, phosphanes, phosphites, isocyanides beside the arenes, or exclusively containing the other ligands [40]. Such complexes are promising for the use in hydrogenation reactions, as was demonstrated recently by *Wolf* and *Jacobi von Wangelin* [41].

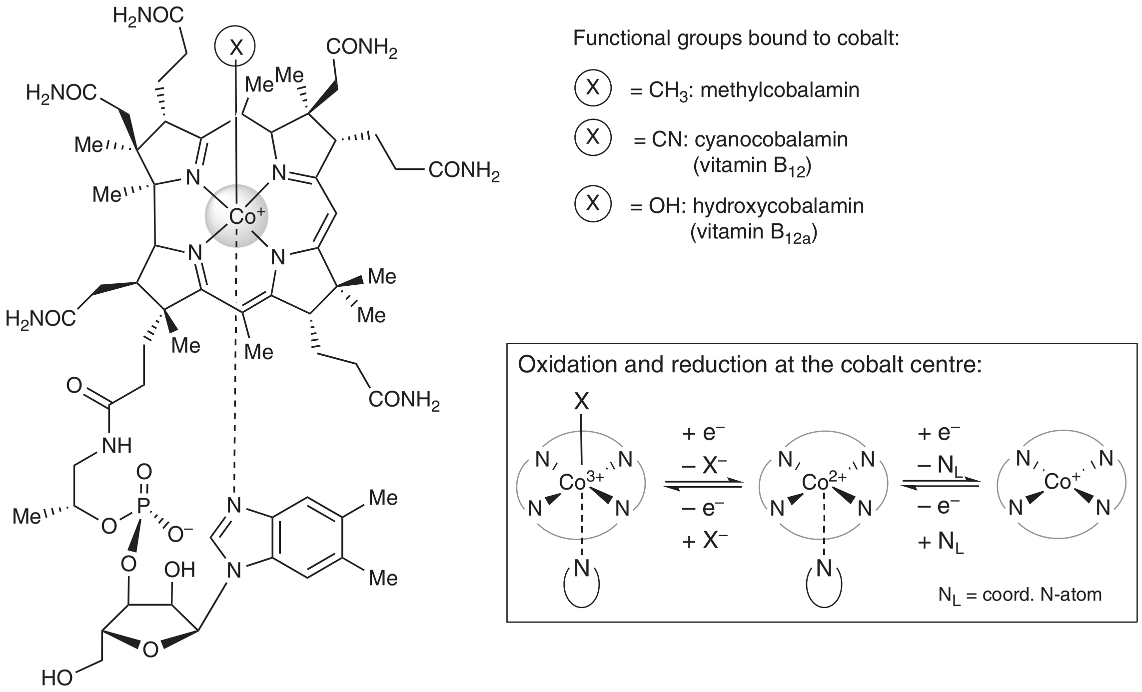


Scheme 1.9 Preparation of anionic bis(naphthalene) Co(−I) complexes and subsequent reaction possibilities.

1.2.2 Bioorganometallic Cobalt Compounds

Cobalt is one of the few transition metals with a biorelevant organometallic chemistry. This is quite surprising, because it is the least abundant of the first-row (3d) transition metals in the Earth's upper crust and in sea water [42]. The coenzyme B_{12}, part of the cobalamins, which feature corrin as the organic framework, and the studies of derivatives including vitamin B_{12} have earned a lot of reputation for contributing significant knowledge not only to the organometallic chemistry of cobalt but moreover to bioorganometallic chemistry in general, natural product synthesis, and structure analytics [43]. The last aspect was spectacularly illustrated by awarding the Nobel Prize for chemistry to *Dorothy Crowfoot Hogdkin* for her X-ray crystallographic investigation of vitamin B_{12}, beside other structurally complex molecules. Scheme 1.10 represents a structural overview on the cobalamins and the coordination environment of the cobalt centre during redox events.

The Co—CH_3 bond in methylcobalamin is unusually stable against hydrolysis in aqueous media; however, it can be homolytically split by formation of a methyl radical under enzymatic control. Electron donation and therefore reduction



Scheme 1.10 Cobalamins, vitamin B_{12}, and the role of cobalt as metal centre.

of the cobalt from Co(III) to Co(I) is accompanied by removal of the axial ligands, thus resulting in a square planar Co(I) complex. A natural process is the methylation step in the synthesis of the amino acid methionine, where a generated methyl cation is transferred to the homocysteine moiety of the substrate, thus leaving the Co(I) as an electron-rich supernucleophilic d^8-configurated metal centre. Two electrons occupy and fill up the antibonding d_{z^2} orbital, thus leading to an orbital with high affinity towards electrophiles, allowing for such electronically configurated metals typical reactions like the oxidative addition of organic compounds R–X. This property allows the abstraction of a methyl cation from methyltetrahydrofolate, closing the catalytic cycle of the methylation process. Cobalamines are subject to a number of studies on their modification and application in catalytic organic transformations [44].

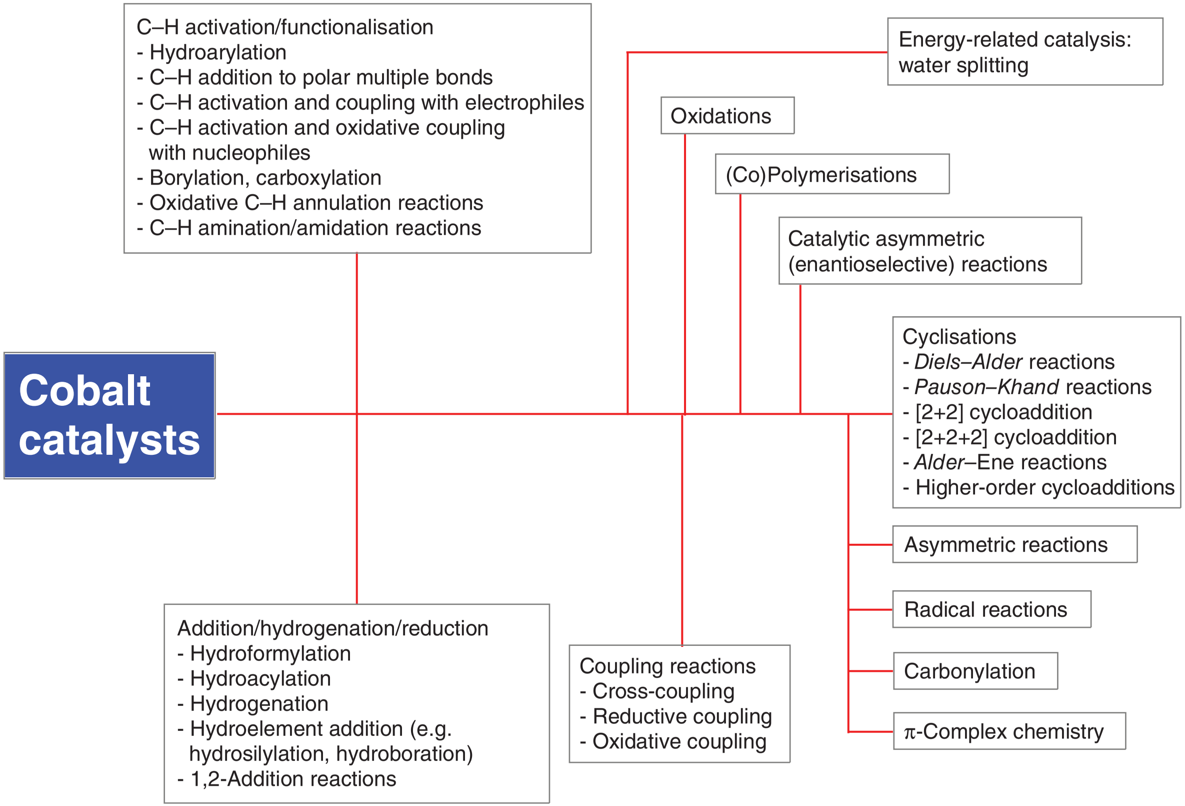
1.3 Applications in Organic Synthesis and Catalytic Transformations

Cobalt has become one of the rising stars in base metal catalysis for synthetic purposes, which have emerged over the recent decade. Interestingly, even when reviewed in 2011, no large-scale applications in the synthesis of pharmaceuticals were mentioned so far [45]. It can be foreseen that this situation might change in the future, following the recent developments in the area of cobalt-mediated reactions. As comparison with the other base metals provides, cobalt together with iron and nickel clearly dominate among the other 3d metals, when it comes to versatility of the reactions being mediated or catalysed [5]. In many cases even stereo- and enantioselective variants of achiral reactions have already been developed and implemented, although there is certainly room for improvement for future inquiries [46].

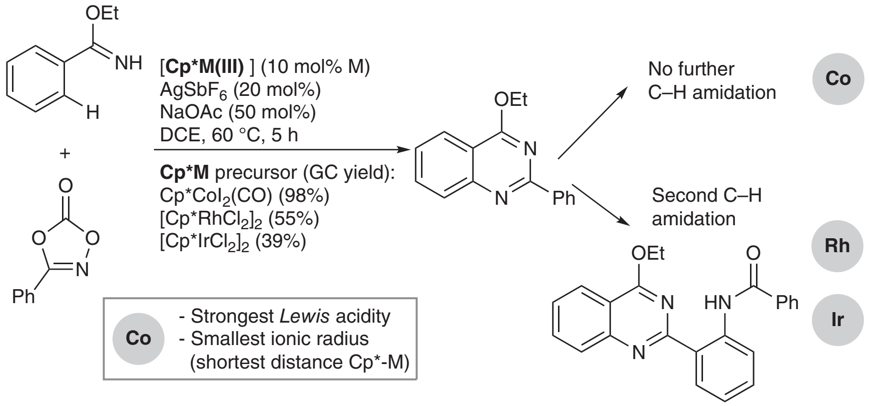
Scheme 1.11 illustrates an overview on different reactions that are either mediated by non-catalytic amounts of cobalt complexes or that are catalysed by cobalt complexes.

In the following just few aspects of the behaviour of cobalt catalysts in organic synthesis will be exemplarily discussed, as much more details can be found in the following chapters of this book.

The field of C–H activation/functionalisation reactions of cobalt complexes has flourished tremendously in recent years and although only relatively few complexes are applied, the substrate scope has extended very rapidly. This particular class of reactions can also serve as an example for the possibilities of the first-row transition metals to offer different oxidation states for catalysis compared with the heavier congeners [47]. Such comparative investigations have corroborated the differences between the group 9 transition metals, exemplified by catalytic C–H functionalisation of aryl imines and aryl amides with dioxazolones catalysed by Cp*M derivatives as reported by *Chang* and *Glorius* independently (Scheme 1.12) [48, 49]. The latter investigation provided the insight that the strong *Lewis* acidity and smallest ionic radius of the Co(III) centre played a pivotal role in the reactivity of the Cp*M fragment for accomplishing



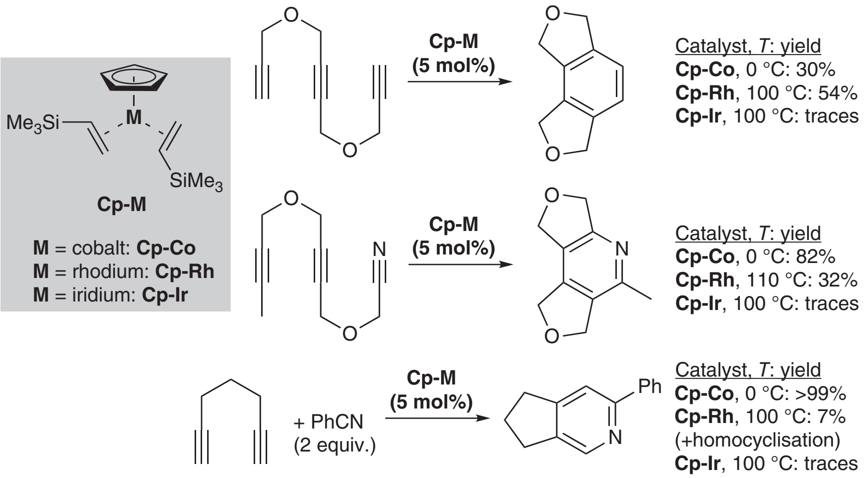
Scheme 1.11 Cobalt-mediated and cobalt-catalysed reactions for synthetic purposes.



Scheme 1.12 C–H functionalisation with group 9 metal complexes.

a complete and smooth reaction without changes in the formal oxidation state of the cobalt atom. While the *Lewis* acidity promoted the intramolecular cyclisation of the primary amidation product to yield the desired quinazoline derivative, the small ionic radius and shorter distance to the sterically cantilevered Cp* group preventing the second undesired amidation step due to steric hindrance, thus yielding a single product. The results are comparable when $[Cp^*CoCl_2]_2$ is used instead of $Cp^*CoI_2(CO)$, as the investigation by *Chang* showed [48]. A detailed overview on shifts in selectivity and reactivity for the group 9 metal catalysts revealed the significant differences, especially between cobalt and rhodium complexes [50]. Unusual activation of other inert bonds (C—H, C—O) with 3d neighbour metal complexes and cobalt have also seen startling results in recent years, potentially allowing to rethink conventional approaches for C—C and other bond formations [51].

Reactions with substrates containing π bonds is a “home game” for cobalt complexes, which is illustrated throughout the literature [52]. Reactivity differences between the group 9 metals were exemplarily also illustrated for different reactions [4a], in particular for cyclotrimerisation reactions, where all three group 9 metals have found large applications [4b]. Especially for the cyclisation of diynes/nitriles, cyanodiynes, and triynes, when structurally identical complexes except for the central metal atom were applied, significant differences were accounted for (Scheme 1.13) [53]. The synthesis of the complexes **Cp-M** already demonstrated the different approaches to obtain the respective complexes with **Cp-Co** on one hand and **Cp-Rh** and **Cp-Ir** following identical protocols with the introduction of the Cp-ligand on the final stage on the other hand. In addition, the latter two complexes were rather stable and could in contrast to **Cp-Co** be handled in air, at least for short periods of time. The reactivity screening corroborated also the differences; in all investigated cases the precatalyst **Cp-Ir** was virtually inactive. Cyclisation of a terminally unsubstituted triyne gave 30% yield for **Cp-Co** even at 0 °C (higher temperatures led to increased decomposition), while **Cp-Rh** required 100 °C to promote the reaction, although with higher yields (Scheme 1.13, top). This changed when reacting cyanodiynes, again

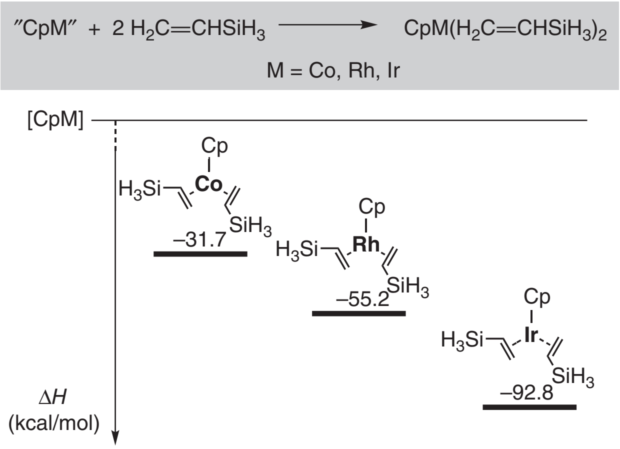


Scheme 1.13 Cyclotrimerisation with structurally identical group 9 metal-cyclopentadienyl complexes and different substrates.

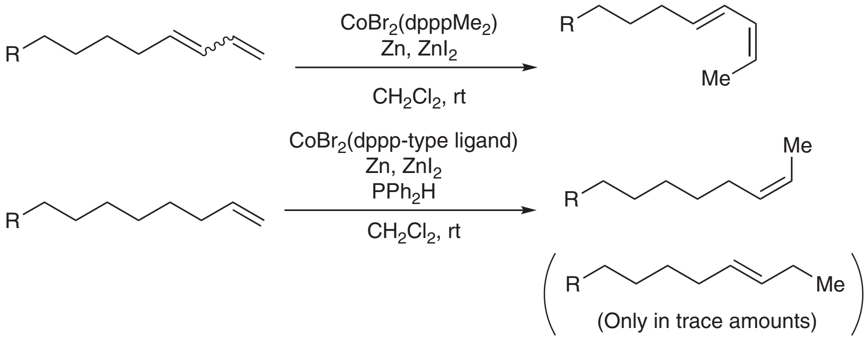
a reaction in completely intramolecular fashion. Here, **Cp-Co** gave excellent 82% pyridine, while **Cp-Rh** only furnished 32% (Scheme 1.13, middle). This even changed more dramatically in the case of the reaction of 1,6-heptadiyne with benzonitrile, yielding quantitative amounts of the pyridine product with **Cp-Co** and only 7% with **Cp-Rh** (Scheme 1.13, bottom). Here, however, larger quantities of aromatic homocyclisation product from the diyne were observed with **Cp-Rh**, providing evidence for the preference for carbocyclisation for the rhodium catalyst.

Further reactivity differences for **Cp-M** were encountered in hydrogenation and hydroformylation reactions, with the inclination of the cobalt complex for isomerisation of the double and not exclusively hydrogenation. Assessment of the reactivity of the complexes of the type **Cp-M** from computational calculations indicated the increasing stability of the olefin complexes when going to the heavier congeners (Scheme 1.14).

The previously mentioned isomerisation of double bonds has found increasing attention during the last decade due to the growing importance of selectively shifting this synthetically highly important functionality within a molecule. Cobalt complexes have also been utilised for the migrational transposition of double bonds along a carbon chain. Besides the isomerisation of a terminal 1,3-diene subunit towards a stereodefined 2*Z*,4*E*-product also a transposition of a terminal alkene towards a 2*Z*-alkene could be realised by *Hilt* (Scheme 1.15) [54]. Crucial for the latter reaction was the application of diphenylphosphine (PPh_2H) as ligand, and it is worth to mention that the chain walking of the double bond, e.g. towards the corresponding 3-alkenes and so on was only observed in trace amounts. Nevertheless, later on *Hilt* could show that the corresponding nickel-catalysed reactions were associated with a significantly higher reactivity and a broader substrate scope [54d–f].



Scheme 1.14 Energetics of olefin coordination to CpM (M = Co, Rh, Ir) fragments. Source: Weding et al. 2011 [53]. Reproduced with permission of John Wiley and Sons.

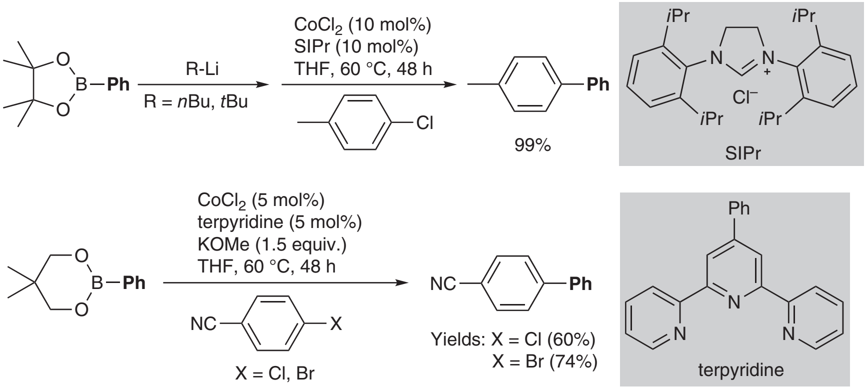


Scheme 1.15 Cobalt-catalysed migrational transposition of double bonds.

To exemplarily delineate a forth field of catalytic applications, which interestingly has only seen cobalt to flourish in contrast to its heavier group congeners, is through cross-coupling reactions. This is certainly a big difference to the neighbouring group 10, where the heavier congener to nickel, palladium, is the archetype metal in cross-coupling catalysts [55]. On the other hand, neighbouring 3d element iron has seen a significant amount of application in cross-coupling reactions, including puzzling of the available reaction mechanisms [56]. Due to its very low toxicity and abundance, iron-catalysed cross-coupling reactions are of remarkable interest for manufacturing pharmaceuticals [57].

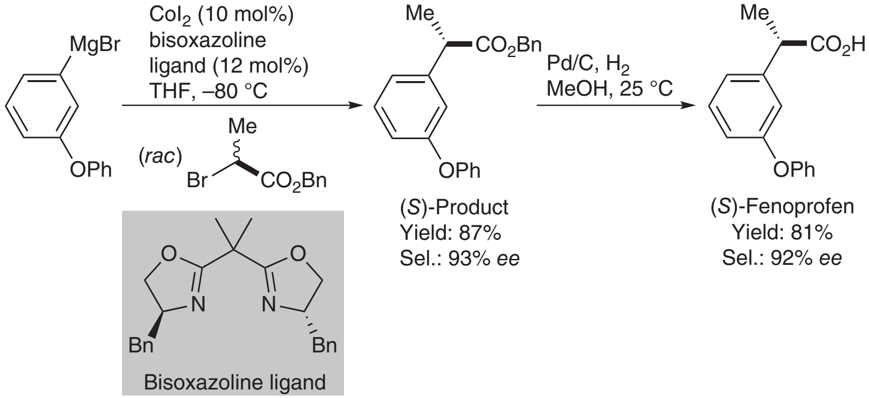
Cobalt-catalysed cross-coupling reactions have in principle a long history; however, mostly single reports on successful coupling reactions were recorded for a long time [25]. Especially during the last two decades, many useful protocols for introducing cobalt salts as catalysts for most cross-coupling reactions have been published. While for palladium-catalysed reactions the whole range of phosphorus-based ligands are usually applied, the picture is more differentiated for cobalt complexes. The most versatile methodology with a very diverse array of nucleophiles has been established by the *Suzuki–Miyaura* reaction. Especially the direct application of the rather stable boronic acids, available with a huge structural diversity, is advantageous for this coupling protocol.

Initial experimental insight into the transmetallation in cobalt-catalysed *Suzuki–Miyaura* coupling through investigations by *Chirik*, utilising a Co(I)-PNP (bis(diisopropylphosphinomethyl)pyridine) pincer complex and aryl triflate and heteroarylboronic acid esters, showed that a cross-coupling with neutral boron nucleophiles is possible, when the cobalt centre carried a alkoxide anion [58]. However, so far no reliable successful *Suzuki–Miyaura* coupling with the free boronic acids has been established. Exemplary coupling reactions demonstrating the usefulness of cobalt catalysis in the coupling of aryl groups are shown in Scheme 1.15. *Bedford* applied NHC ligands like SIPr together with $CoCl_2$ in a 1 : 1 ratio and a preformed anionic boron nucleophile for the successful coupling with halides, especially aryl chlorides, in good to excellent yields (Scheme 1.16) [59]. Possibly, the cobalt atom is reduced to Co(0) during the reaction. The cross-coupling with neopentyl glycolatophenyl boronates in the presence of a Co-terpyridine complex and a base allowed the coupling of arylchlorides and arylbromides as well as heteroarylhalides with often good to very good yields (Scheme 1.16) [60]. Regarding the importance of the *Suzuki–Miyaura* for pharmaceutical ingredients and fine chemicals synthesis and production [61], the cobalt-catalysed version is still in its infancy.



Scheme 1.16 Cobalt-catalysed *Suzuki–Miyaura* coupling reactions for the preparation of biaryls.

The field of (asymmetric) cross-coupling reactions is dominated by nickel catalysis, especially with reaction partners possessing a sp^3-hybridised carbon atom, where the coupling is taking place [62]. Particularly interesting is the possibility to use ethers and esters as electrophiles for such reactions. Therefore, nickel complexes adopt an outstanding role as catalysts in this particular field of research [63]. However, quite recently the first asymmetric *Kumada* coupling catalysed by a cobalt complex has been published by *Zhong*

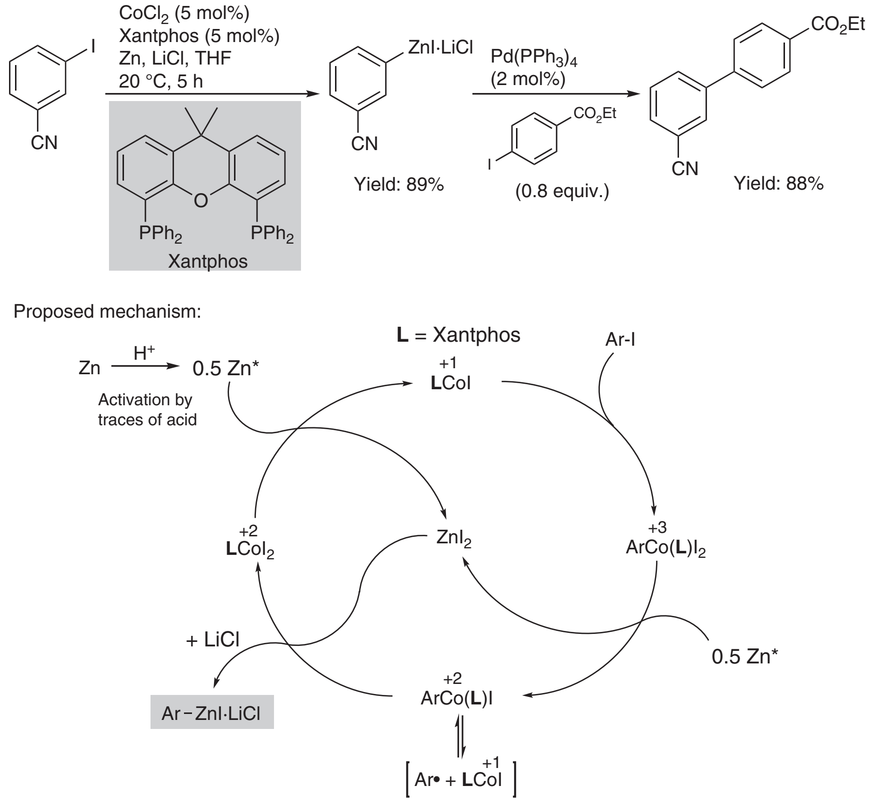


Scheme 1.17 Asymmetric cobalt-catalysed *Kumada* cross-coupling reaction with alkyl bromides.

and *Bian* (Scheme 1.17) [64]. Again nitrogen-based chiral C_2-symmetrical bisoxazoline ligands were most successful for the formation of an efficient catalytic system. The investigation towards different cobalt sources showed the strong dependence from the counterion, with CoI_2 being the preferable metal source. The observation of a strong influence of the cobalt source on *in situ*-generated catalysts is frequently observed, and screening of cobalt salts is therefore routine during the development of catalytic systems. The investigated reactions were performed at temperatures as low as −80 °C, providing evidence for the extraordinary reactivity of the cobalt catalyst and accessing a rather unusual parameter space for cross-coupling reactions. In addition, at such low temperatures, *Grignard* reagents are quite tolerant for the presence of functional groups in the molecule, significantly broadening the scope of application of the methodology.

Finally, to demonstrate the unusual properties and catalytic possibilities of cobalt complexes, the metalation of an aryl iodide catalysed by a Co(I)-Xantphos complex is presented (Scheme 1.18). The metalation is followed by a cross-coupling reaction, e.g. with another aryl halide mediated by $Pd(PPh_3)_4$ in a one-pot reaction without interference of the cobalt catalyst [65]. The reaction allows the preparation of arylzinc compounds from aryl iodides, bromides, and chlorides, and the added LiCl facilitates the reaction and later on complexes the organozinc reagent. The involved species presumably comprise Co(I) and Co(III) oxidation states, starting from Co(II) by one-electron reduction using the elemental zinc. The proposed reaction mechanism is illustrated in Scheme 1.18. Identical conditions were developed to prepare aryl- and heteroarylindium compounds from indium metal [66]. Interestingly, however, the applied most efficient cobalt catalyst was a Co(I)-bathophenanthroline complex, although the likely mechanism followed the one proposed in Scheme 1.18.

The broad scope and exciting reactions catalysed by cobalt are illustrated significantly in more depth in the following chapters of this book.



Scheme 1.18 Application of a catalysed zincation of an aryl iodide and subsequent palladium-catalysed *Negishi* coupling reactions, including the illustrated assumed mechanism of the cobalt–Xantphos-catalysed metalation reaction.

1.4 Conclusion and Outlook

Over recent years, cobalt complexes have seen a significant increase in application for modern and challenging reactions, which have so far often been the domain of its heavier, and more expensive group homologs, rhodium and iridium. This is interesting as the catalytic application of cobalt complexes in homogeneous catalysis has been long known, evidenced by the discovery of the so-called oxo-process (hydroformylation of alkenes) in the 1930s. Cobalt complexes are available in a large range of oxidation states, ranging from −1 to +3, allowing rather simple change of oxidation states in catalytic reactions as well as the possibility to prepare compounds in the respective oxidation states. Current efforts are directed often to prepare novel cobalt complexes with diverse ligand structures and properties and to screen their potential towards the mediation of reactions, so far not or not typically catalysed or mediated by cobalt.

Abbreviations

Ac	acetyl
Ar	aryl
BINAP	2,2′-bis(diphenylphosphino)-1,1′-binaphthyl
COD	1,5-cyclooctadiene
Cp	cyclopentadienyl
Cp′	substituted cyclopentadienyl
Cp*	pentamethylcyclopentadienyl
DCE	1,2-dichloroethane
dppb	1,4-bis(diphenylphosphino)butane
dppe	1,2-bis(diphenylphosphino)ethane
dppf	1,1′-bis(diphenylphosphino)ferrocene
dppp	1,3-bis(diphenylphosphino)propane
ee	enantiomeric excess
equiv.	equivalent
Et	ethyl
GC	gas chromatography
Me	methyl
NHC	*N*-heterocyclic carbene
NMR	nuclear magnetic resonance
phen	1,10-phenanthroline
PE	petrol ether
Ph	phenyl
PGM	platinum group metals
*i*Pr	isopropyl
Py	pyridine
rac	racemic
sel.	selectivity
T	temperature
Tf	triflate
THF	tetrahydrofuran
TMEDA	*N*,*N*,*N*′,*N*′-tetramethylethylenediamine
triglyme	1,2-bis(2-methoxyethoxy)ethane

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