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ORGANOCOBALT COMPLEXES AS SOURCES OF CARBON-CENTERED RADICALS FOR ORGANIC AND POLYMER CHEMISTRIES

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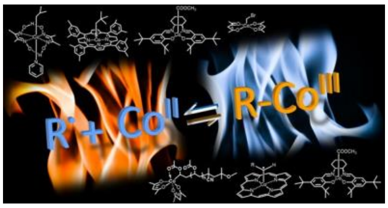
ABSTRACT:



Organocobalt(III) complexes (R-Co^{III}), defined as cobalt complexes featuring a carbon–cobalt bond, are largely used to produce carbon-centered radicals by homolytic cleavage of their C–Co bond under mild conditions. They are key compounds in cutting-edge developments in the fields of organic chemistry, biochemistry, medical research, radical reactions, and organometallic chemistry. This is the first Review of the use of R-Co^{III} in both organic and polymer chemistries. Although pioneering works in organic synthesis have largely contributed to the implementation of R-Co^{III} in polymer design, the two fields have evolved independently, with many breakthroughs on both sides. The main motivation of this Review is to confront both fields to stimulate cross-fertilization. It notably describes the most important synthetic pathways for R-Co^{III}, the influence of the ligand structure and the environment of the complex on the C–Co bond strength, the modes of formation of the radicals, and the most relevant R-Co^{III}-promoted radical reactions, with a focus on the main reaction mechanisms.

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1. INTRODUCTION AND MOTIVATION

Carbon−carbon bond formation involving carbon-centered free radicals is extremely important in both organic and polymer syntheses. Although carbon-centered radicals exhibit a number of attractive features, including tolerance of functional groups and water compatibility, they are often highly reactive species, susceptible to multiple side reactions. Nevertheless, the old notion of free-radical reactions being "notoriously uncontrollable" now belongs to the past, due to the development of a multitude of innovative routes to control both the production of radicals and their subsequent reactions for the synthesis of complex structures.[1−14] Transition-metalpromoted radical reactions have largely contributed to these breakthroughs, with the generation of carbon-centered radicals from organometallic reagents based on titanium, vanadium, manganese, iron, copper, ruthenium, or cobalt, to cite the most relevant ones.[2,10,15] In particular, the contribution of cobalt in radical chemistry is remarkable (Scheme 1).[1,3,8,16−21]

Organocobalt(III) complexes (R-Co^{III}), defined as cobalt complexes featuring a carbon−cobalt bond, have shown the ability to produce radicals in a controlled manner by homolytic cleavage of their C−Co bond upon thermal treatment or irradiation by light.[22,23] The R-Co^{III} derivatives and their radical activation pathway have been studied for more than half a century and are important in cutting edge developments in the fields of biochemistry, medical research, and organic, polymer, and organometallic chemistries (Scheme 1).[7,16,24,25] A key concept to understand the radical chemistry of R-Co^{III} and the applications arising therefrom is the "persistent radical effect" (PRE),[26,27] which extends the lifetime of the generated radicals, allowing their selective reaction with a third substrate rather than self-coupling. Typically, the carbon-centered radical (transient radical 2) released from the R-Co^{III} is reversibly deactivated by the Co^{II} complex 1 acting as a persistent radical and preventing the self-termination of two transient radicals (Scheme 2, 2).[27,28]

The cobalt−carbon bond dissociation energy (BDE) is a key parameter which governs the reactivity of R-Co^{III} species in radical processes. The strength of the C−Co bond can be easily tuned by modifying the ligands and the R group of the complex.[29] In this respect, organocobalt complexes have undergone a long-term development starting with the discovery of vitamin B_{12} (VitB_{12} or simply "B_{12}"), or cyanocobalamin (Scheme 3, CNCbl 1a), which plays a crucial role in the proper functioning of the human body[30] and in the catalysis of a multitude of radical reactions.[1,16,31−35] In the 1950s, Hodgkin et al. elucidated the crystal structure of 5′deoxyadenosylcobalamin (AdoCbl) containing the first isolated stable C−Co bond with a corrin ring as ligand.[36] In the 1960s, Dolphin and Clarke synthesized R-Co^{III} complexes based on planar porphyrin ligands which have simpler structures and reactivities close to those of B_{12} coenzymes (Scheme 3, 2b).[37−39] Recently, cobalt porphyrin complexes were widely developed in metallo-radical catalysis (MRC) by Zhang and de Bruin with the formation of an intermediate carbene radical as the R group (Scheme 3, 2b'),[5,40,41] or for the precision synthesis

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of polymers by Wayland.[4] Oxime-based R-Co complexes emerged and showed properties similar to those of the corrin cores of cobalamin (Scheme 3, 2c).[19,22] Research was then conducted on structural modifications of the ligands of the cobalt center in order to prepare novel RCo^{III} complexes with partially to fully oxygenated ligands such as organocobalt(III) salen[12,42,43] (Scheme 3, 2d) and organocobalt(III) bis(acetylacetonate)[44] (Scheme 3, 2e). As will be discussed later, the incorporation of electron-withdrawing ligands weakened the Co−C bond and allowed the production of more-reactive radicals under milder experimental conditions, which paved the way to novel reaction processes.

This Review covers the field of $R\text{-}Co^{III}$ complexes exploited as sources of radicals in organic and polymer chemistries. Currently, this research area is covered by hundreds of publications from the two communities, which are most often constrained to their respective domain. Here, the use and development of organocobalt complexes in both organic and polymer chemistries are described and confronted in a single work for the first time in the hope that it will stimulate the cross-fertilization of these research fields. For the sake of clarity, the text is organized into sections, corresponding to the ligands of the cobalt complexes, starting from the pioneering works on vitamin B_{12}. Notably, we will discuss (i) the most important synthetic pathways for $R\text{-}Co^{III}$, (ii) the influence of the ligand structure and the environment of the complex on the C−Co bond strength, (iii) the modes of formation of the carbon-centered radicals by the homolytic cleavage of the C− Co bond, and (iv) the most relevant $R\text{-}Co^{III}$-promoted radical reactions for organic and polymer syntheses, with a focus on the main reaction mechanisms. Without aiming to be exhaustive, we present important reactions of the organocobalt complexes, with special care to describe the state-of-the-art achievements in this field, including radical processes offering a high level of stereochemical control.[5] For detailed information about early or complementary references, the reader is directed to some excellent previous reviews on the subject.

2. VITAMIN B_{12}-TYPE ORGANOCOBALT(III)

The first class of $R\text{-}Co^{III}$ complexes that is investigated in this Review concerns the close analogues of vitamin B_{12} ($VitB_{12}$) structures. B_{12} compounds, and particularly AdoCbl, have significantly drawn the attention of biochemists because they represent the most familiar biological source of radicals resulting from thermal homolysis.[45,46] Many researchers have dedicated their work to the discovery and the reactivity of B_{12} analogues. With the advances in computational science, the action of $VitB_{12}$ cofactors, such as MeCbl and AdoCbl, has been recently modeled, and these studies helped scientists to comprehend their mechanism in biological applications.[47,48] Organic synthesis using $VitB_{12}$-type $R\text{-}Co^{III}$ has been largely developed, whereas examples of their exploitation in polymer chemistry are rare.

In biological conditions, stable forms of B_{12} compounds (1b and 1c) bear a cobalt complex in the oxidation state of III (Scheme 3). Cleavage of the C−Co bond can follow three different paths, inducing the interaction of coenzymes and substrate.[49] Heterolytic dissociation follows the catalytic process of $R\text{-}Co^{III}$ as MeCbl and leads to a “supernucleophilic” Co^{I} with a lone electron pair (Scheme

4, Track A).[31] Another type of heterolysis appears in the case of electrophilic attack, such as with a mercury salt (represented as MX_2) that can trap the alkyl group (R^-) and produce an X-Co^{III} complex (Scheme 4, Track B).[50,51] Reactions involving heterolysis of R-Co^{III} have been summarized by Marzilli and co-workers.[52] The last pathway, for example with AdoCbl, involves homolytic cleavage of the C−Co bond, producing a stable paramagnetic Co^{II} complex and a reactive carbon-centered radical, such as 5′-deoxyadenosyl radical ($R^{\bullet}$ in Scheme 4, Track C). In this Review, we focus on the homolysis mechanism of R-Co^{III} (Track C) and its contribution to organic and polymer chemistries.

2.1. SYNTHETIC ROUTES

MeCbl (Scheme 3, 1b) was first isolated in 1964 from bacteria.[53] In 1972, the teams of Eschenmoser and Woodward successfully realized the total synthesis of $VitB_{12}$ starting from cobyric acid.[54] However, the biosynthesis always prevailed over the total synthesis. Indeed, only bacteria and microorganisms were able to produce this vitamin at large scale through enzymatic fermentation.[24] Later on, different strategies were developed for the synthesis of R-Co^{III} of the cobalamin type: (1) the reaction of Co^{III} complexes with nucleophilic reagents such as Grignard reagents (Scheme 5, Track A), (2) the addition of carbon-centered radicals to Co^{II} species (Scheme 5, Track B), (3) the reactions of Co^{I} or cobalt-hydride complexes with alkyl halides (Scheme 5, Track C), (4) the acetylation of methylcobalamin(III) by carbon monoxide (Scheme 5, Track D), and (5) the recent formation of aryl- and alkynocobalamin complexes (Scheme 5, Track E).

In the mid-1960s, Bernhauer et al. developed the first strategy by reacting cobyrinic acid heptaethyl ester as the Co^{III} complex with an excess of CH_3MgI, as Grignard reagent (Scheme 5, Track A), providing the corresponding R-Co^{III} complex, a close structure of methylcobalamin.[55]

The second strategy (Scheme 5, Track B) involved the reaction of the reduced form of cobalamin (B_{12r}) as radical scavenger with carboxylic acid (as acetic acid) in the presence of oxygen and vanadium(III) salts. The carbon-centered radical ($^{\bullet}CH_2COOH$) that was in situ formed by H abstraction from CH_3COOH was trapped by B_{12r} to yield the corresponding carboxyalkyl-cobalamins.[56]

Certainly one of the most widely used pathways for R-Co^{III} is the reaction between Co^{I} or a cobalt-hydride complex and electrophilic reagents such as alkyl halides (Scheme 5, Track C). Johnson and Smith were pioneers in this reductive elimination/oxidative addition route.[24] Its prevalence is due to the large range of alkyl halides that are available, giving access to a large diversity of R-Co^{III} of different reactivity by tuning the nature of the alkyl group. The first step of this process involved reduction of hydroxocobalamin (Scheme 5, 1d) by various reducers, such as sodium borohydride ($NaBH_4$) or zinc dust in acetic acid, producing a Co^{I} nucleotide that reacted with an alkylating agent (most often an alkyl/alkene halide, such as ethyl iodide) to form the corresponding R-Co^{III}. To date, this procedure remains the simplest for the synthesis of B_{12} analogues.

As an alternative to the use of chemical reducers, Scheffold et al. developed an electro-reductive alkylation of hydroxocobalamin (Scheme 5, (OH)Cbl 1d). Indeed, a R-Cbl complex (with R = $-CH_2COOCH_3$) was formed by electro-reduction of (OH)Cbl in the presence of methyl bromoacetate as alkylating agent.[57] This was carried out by using a H-type electrolytic cell by applying a constant potential of −1.1 V (vs SCE) in a $LiClO_4/H_2O/MeOH$ solution. Under these electrochemical conditions, (OH)Cbl was reduced into Co^I that was directly involved in an oxidative addition with methyl bromoacetate.

Krautler et al. investigated the formation of acetylcobalamin via the modification of methylcobalamin (MeCbl) by the addition of carbon monoxide (Scheme 5, Track D).[58] The methyl radical, released by the C−Co bond cleavage of MeCbl, added to carbon monoxide to form the acetyl radical that was rapidly trapped by cross-coupling with Co^{II} (Scheme 6). This experiment illustrates the PRE mechanism with the recovery of the cross-coupled product as the main component instead of ethane (that would form by coupling two methyl radicals).

Recently, aquacobalamin chloride was used to synthesize aryl- and alkynyl-cobalamin complexes following Track E, Scheme 5.[59−61] As shown in Scheme 7, the reduction of aquacobalamin chloride was first promoted by formate ions, providing the corresponding Co^{II} species.[62] This Co^{II} species intercepted an alkynyl radical (generated from alkynyl iodide) or ethyl benzyl radical (released from ethylbenzyldiazonium salt) to furnish the corresponding alkynyl- or arylcobalamin. These modified cobalamins are more resistant to cleavage by enzymes and metabolic transformations and were seen as potential "antivitamins B_{12}".[60,63]

2.2. REACTIVITY

The reactivity of R-Co^{III} complexes is dictated by many parameters, such as the type and the basicity of the donating ligand or the cone angle. In this section, we aim to present the main parameter that encompasses the particular reactivity of the C−Co bond: its BDE. Bond length and strengths are closely related, and the following discussion will mainly focus on the BDE. Several techniques were used for the determination of the C−Co BDEs, such as kinetic radical trapping or pulsed photoacoustic calorimetry.[64,65] The homolytic C−Co splitting can be induced by three different ways: thermal homolysis, also called thermolysis, irradiation by light/UV, namely photolysis, or electrochemical reduction. For many years, thermolysis of R-Co^{III} was preferred over photolysis and electrochemical reduction. However, in the past 15 years, photolysis has found increasing interest for the B_{12} C−Co bond cleavage in photochemistry and photobiology, and for the future use of B_{12} derivatives in biotechnological applications, as in photosynthesis of bacteria or in photosystem gene expression. This topic has been discussed in a recent review by Jones.[66]

The thermolysis of methylcobalamin (CH_3-Cbl) was followed by Finke et al. in ethylene glycol via the use of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) as radical trapping agent. The measured BDE was about 37 $kcal \cdot mol^{-1}$ and was strongly influenced by the ligation of the 5,6dimethylbenzimidazole (DMB) axial ligand (Table 1, ref 67). The axial bonding of DMB with the cobalt center is in equilibrium with the opened form, following the so-called "base-on/base-off equilibrium" (Scheme 8). The influence of this ligand exchange on the BDE value was later investigated by pulsed photoacoustic calorimetry that was preferred over the thermolysis. Indeed, the latter generally requires elevated temperatures (>80 °C), which induces a competition with the heterolytic cleavage of the CH_3-Cbl bond (Table 1, ref 65), and a mixture of both base-on and base-off forms was present under these conditions. Therefore, photolysis constituted the ideal method for the quantification of homolytic methylcobalamin activation. The photolysis of CH_3-Cbl showed a C− Co BDE approaching 39 kcal·mol^{-1} in water for the base-on form. In acidic media, the protonation of the DMB ligand provided the base-off form with a BDE value up to 42 kcal· mol^{-1} (Table 1, ref 65). This shift in the C−Co BDE with the base-on/base-off equilibrium was verified for Ado-Cbl, and the reinforcement of the C−Co bond strength was also noted when the N-donating axial ligand was removed from the cobalt center (base-off form) (Table 1, ref 68).

The kinetics of Ado-Cbl thermolysis has been followed with the use of various spin-trapping agents. Halpern first evaluated the C−Co BDE of Ado-Cbl with the use of bis(dimethylglyoximato)cobalt(II) (abbreviated Co(dmgH)$_2$) as spin-trap, which rapidly intercepted free radicals to form C−Co bonds that were considerably stronger than the Ado-Cbl bond (Table 1, ref 64). Later, Finke et al. measured C−Co BDE values close to 30 kcal·mol^{-1} in water (Table 1, ref 70). This value was further confirmed by pulsed photoacoustic calorimetry (Table 1, ref 65). Recent theoretical studies showed an underestimated BDE (33.6 and 27.2 kcal·mol^{-1} respectively for CH_3Cbl and Ado-Cbl) compared to the experimental studies on both CH_3-Cbl and Ado-Cbl.[47,71]

Concerning the activation of the C−Co bond by electrolysis, Scheffold et al. studied the reduction potential of alkylcobalamine and alkylcobyrinates using single-scan voltammetry by varying the axial ligand (namely the R group of R-Co^{III} complexes).[72] Accordingly, a correlation was established between the reduction potential of R-Co^{III} and the pK_a of RH, which helped in the visualization of intermediates formed during the light-induced insertion of an olefin into the C−Co bond of the R-Co^{III}. However, no BDE value was reported. The single-scan voltammetry also served for the understanding of the mechanism of oxidative addition of alkyl halides to corrinato- and porphyrinatocobalt(I).[73]

2.3. ORGANIC REACTIONS

Vitamin B_{12} is a natural and nontoxic catalyst that has been exploited for many types of reactions. For over half a century, it has been established that VitB_{12} and particularly coenzyme AdoCbl are catalytically involved in many organic reactions via homolysis pathways, such as isomerizations or reductions.[45] The general catalytic mechanism for these reactions is exemplified in Scheme 9. The common first step of all reactions was the reduction of VitB_{12} into Co^{I} (or Co^{II}). These species then reacted with a substrate R to form, in situ, a RCo^{III} intermediate. The final product B was then produced by a radical pathway involving R radicals and A as reagent, and the catalyst (Co^{I} or Co^{II}) was regenerated. As it will be detailed later, the intimate mechanism for the formation of B was strongly dependent on the substrates that were involved. However, the main feature for all VitB_{12}-catalyzed reactions was the C−Co bond homolytic splitting of the in situ-formed R-Co^{III}, leading to a carbon-centered radical.

The mechanism for the AdoCbl-dependent isomerase was first elucidated in 1967 (Scheme 10).[74] Isomerases belong to the largest families of B_{12}-dependent enzymes found in nature. Their mechanism is based on an enzymatic 1,2 rearrangement of amino acid derivatives and rules a plethora of reactions in human body, such as the replication of DNA.[45] The first step involves homolysis of the AdoCbl C−Co bond with the formation of a $^{\bullet}CH_2R$ radical (Scheme 10). After a first hydrogen abstraction on reagent by the radical species, a 1,2 rearrangement of the X group occurs to form the corresponding isomer. The final step is a second H-abstraction followed by the regeneration of the C−Co^{III} complex that enters again the catalytic cycle.

Scheme 11 summarizes 10 selected rearrangement reactions catalyzed by coenzyme B_{12}. The first class of compounds (reactions 1−3) were catalytically produced via B_{12} cofactor followed by a 1,2 rearrangement,[75] according to the reaction mechanism illustrated in Scheme 9. The second category concerns a skeletal rearrangement (reactions 4−6), as represented with the enzymatic conversion of glutamate to β-methylaspartate (reaction 4).[75] The third class of reactions involved an elimination of water or ammonia (reactions 7−9). As an example, diol dehydrase enzymes allowed the conversion of glycerol into first a geminal diol, which was then converted into 3-hydroxypropanal and water via coenzyme B_{12} (reaction 8). The formation of geminal diol (two OH functions on the same carbon) has been recently confirmed by computational chemistry, showing this favored intermediate in the presence of B_{12}, while in the absence of B_{12}, a direct loss of water is favored.[76] The final rearrangement (reaction 10) occurred with class II ribonucleotide reductases, involving the formation of thiyl radicals that catalyzed the reduction of this ribonucleotide.[45] This reaction is essential in the DNA replication process. A theoretical study on these enzymatic reactions was recently published for the different classes of AdoCbldependent enzymes.[77]

Besides these enzymatic rearrangements, many other B_{12}catalyzed radical reactions were reported, such as dehalogenation, halide coupling, alkene coupling, cyclopropanation, reductive coupling of aryl halides and non-activated alkyl tosylates,[78] and 1,4-additions onto activated double bonds.[31] Scheme 12 presents the most relevant reactions and illustrates that all these B_{12}-catalyzed reactions require reducing conditions. The in situ reduction of the cobalamin derivative furnished the supernucleophilic Co^{I} species that then reacted with some of the reagents (alkyl halide, alkene, etc.) to give a novel R_1-Co^{III} adduct. The C−Co bond of this R_1-Co^{III} was then cleaved with appropriate stimuli (UV light or electrolysis) to release a radical ($R^{\bullet}$) that reacted with various radicals or substrates. The Co^{II} species was then reduced in situ into Co^{I} that entered again the catalytic cycle. The in situ formation of R_1-Co^{III}, followed by the controlled release of $R^{\bullet}$ and the concomitant reduction of the cobalt complex into Co^{I}, are thus at the core of all these B_{12}-catalyzed radical reactions. In this work, we will not detail all these reactions that have already been discussed in a recent tutorial review.[31] Table 2 summarizes some selected relevant examples with the reaction conditions that are discussed below.

The dehalogenation of various species has gained huge interest over the past decades due to its utility to treat toxic halogenated contaminants for environmental purposes.[79−82] Mono-, di-, tri-, and tetrachloroethylene were the first compounds studied in this area due to their great utilities as solvents, in paints, etc. (Table 2, entry 1).[79−82] Dechlorination of polychlorinated ethylene led to the formation of ethylene. These studies opened the way to many developments in dehalogenation reactions of toxic chloro, bromo, and fluoro compounds. Research in this field is still ongoing, notably in the comprehension of the mechanism for B_{12}-dependent dehalogenation,[83] in the development of vinylcobalamin for enhancing the process,[84] and in the dehalogenation pathways using CO_2 radical anion as reactant[85] or pH as the driving force.[86]

Non-activated alkenes, such as styrene and derivatives, underwent radical coupling when treated with reduced cobalamin (produced in situ from a mixture of (CN)Cbl 1a and Ti(III) citrate under light irradiation).[87–90] In contrast, a 1,4-addition reaction occurred with activated alkenes (thus bearing an electron-withdrawing group) in aprotic environment in the presence of a radical source such as an alkyl halide. As a representative example, VitB$_{12}$ was recently used to catalyze the atom-transfer radical addition (ATRA) of organic halides (aryl or alkyl halides) to olefins (such as phenyl vinyl sulfone, acrylate, or acrylamide) in the presence of a reducing agent ($NaBH_4$) (Table 2, entry 2).[91] In this process, VitB$_{12}$ was reduced by $NaBH_4$ into Co^I that reacted with the organic halide to yield the corresponding R-Co^{III}. The C−Co bond splitting released R$^\bullet$ that added to the olefins, forming the corresponding radical adduct. The transfer of halogen from the organic halide to the radical adduct furnished the desired product. Also, the VitB$_{12}$-catalyzed electrochemical reduction of acetic anhydride in the presence of activated olefins under visible light involved the formation of acylcobalamin followed by the light-induced C−Co bond splitting and the 1,4-addition of the released acetyl radical to the olefin (Table 2, entry 3).[92] Recently, an acylation mechanism has been applied to 38 different 2-S-pyridyl thioesters, being the acyl radical source, using (CN)Cby(H_2O) as catalyst, Zn as reductant, and LED light as initiating system.[93] Again, acyl-VitB$_{12}$ complex was formed, followed by C−Co bond homolysis, forming acyl radicals that reacted with alkenes, such as acrylonitrile or nbutyl acrylate, to furnish the corresponding acyl product (Table 2, entry 4).

Reduced cobalamin compounds were also involved in the coupling of aryl olefins, as well as aryl halide, leading to dimers (Table 2, entry 5).[87] Mechanistic studies showed a high rate of combination of two radicals thanks to reducing agents such as Ti(III) or Zn, which reduce Co^{II} species and prevent their recombination with alkyl radicals. Another B$_{12}$-catalyzed reaction involving an arylalkene, such as styrene, has been developed by Zhang with the reaction of ethyl diazoacetate (EDA) as co-reagent and (OH)Cbl as catalyst (Table 2, entry 6).[94] This thermally activated reaction led to the formation of cis-dominant cyclopropanes in excellent yields and moderate enantioselectivity. Similarly, Gryko et al. focused on the photolytic reaction of this EDA with the diarylalkene and (CN)CbEster as catalyst.[95] Alkyl esters were obtained with excellent yields (Table 2, entry 7). The deprotection of (allyloxy)arenes represents another reaction promoted by reduced VitB$_{12}$ under photolysis (Table 2, entry 8)[96] that constitutes a sustainable alternative to commonly used noble metal-catalyzed deprotection reactions.

VitB$_{12}$ immobilized onto TiO_2 particles was also developed and exploited for highly selective photolytic reactions.[88,97] As relevant examples, depending on the alkene used as substrate, reduction or dimerization occurred with high yields (Table 2, entry 9).[88] Oxygenation of trichlorinated compounds was also carried out to provide alkene dimer, ester, or amide with excellent yields (Table 2, entry 10).[97] This photocatalyzed reaction made it possible to obtain high-value products via dechlorination of toxic trichlorinated compounds. Recently, the same research group investigated the photocatalytic dechlorination of trichlorinated compounds and bromoethylbenzene by using different polymer-supported B$_{12}$ complexes bearing a ruthenium tris-bipyridine photosensitizer.[98,99]

Scheffold investigated in depth the electrochemical reduction of R-Co^{III} complexes in the presence of various substrates, giving access to reductive eliminations (A), isomerizations (B), the electrosynthesis of bicyclic ketones (C), or nucleophilic acylations (D) (Scheme 13).

Among these B_{12}-based reactions, the reductive removal of haloethyl protecting groups of carboxylic acids was studied.[100] Indeed, hydroxocobalamin (VitB_{12} 1d) was reduced at −1.5 V into Co^{I} that further reacted with the haloethyl carboxylate to create the corresponding carboxylic acid and ethylene (Scheme 13, Track A, and Table 2, entry 11).

The electro-reductive reaction of Co^{III} to Co^{I} also served in the isomerization of various achiral compounds into optically active ring-opened products: (1) epoxides to allylic alcohols,[101−104] (2) cyclopropane into olefins,[105] and (3) aziridine into allylic amines.[106] As exemplified in Scheme 13, Track B, cyclopentene oxide was converted into (R)-2-cyclopenten-1-ol with high yields (up to 78%, Table 2, entry 12).[103] This process was also implemented for a series of transformations involving radical intermediates and leading to prostaglan-dins.[102]

This electrochemical reduction of VitB_{12} was used in cyclization reactions converting bromocyclohexenones into bicyclic ketones.[107] In this process, a 1,4 addition of alkyl derivatives ($-CH_2Br$ group) with an enone olefin was electrochemically catalyzed by B_{12} to create a bicyclic compound with a yield up to 95% in the case of a C_6 ring (Table 2, entry 13). When C_5 and C_7 rings were targeted, the cyclization was less favored, and mainly open-chain products were collected (R = $-CH_2CH_2-$ for C_5 ring and R = $-(CH_2)_4-$ for C_7 ring, Scheme 13, Track C).

Similarly to the acylation of olefins reported in entry 2 of Table 2,[92] nucleophilic acylation of olefins was also investigated by electrochemical reduction B_{12} catalysis.[108] Notably, the formation of an aldehyde using an anhydride and an olefin was driven by the light-assisted electrochemical reduction of (OH)Cbl (1d) (Scheme 13, Track D). An 80% yield of aldehyde was obtained from an n-C_7H_{15} anhydride and propylene, as exemplified in Table 2, entry 14.

2.4. POLYMERIZATIONS

Although the propensity of VitB_{12} and derivatives to produce radicals under UV irradiation has been established for years, these compounds have been rarely used in the field of photopolymerization. Only one report by Lawrence et al. described the exploitation of VitB_{12}-type R-Co^{III} as initiator for radical polymerization.[109] They synthesized various alkylcobalamins bearing an ethyl group and a fluorophore linked to the side chain of the corrin ring (Scheme 14).[109] In contrast to common photoinitiators having a maximal absorbance between 300 and 520 nm, this fluorophore was specifically chosen because of its maximal absorption up to 600 nm. This advantage could furnish greater curing depths than previous systems. Upon irradiation of an aqueous solution containing acrylic and acrylamide monomers and a diacrylate cross-linker (poly(ethylene glycol) diacrylate (PEGDA)) by visible light, the excitation of the fluorophore induced cleavage of the C− Co. The released ethyl radical initiated the radical polymerization to provide a hydrogel.[109] These alkyl-cobalamin-based complexes might find applications in the field of phototherapy of damaged cartilage to glioblastoma via hydrogels using safe visible light.[110−112]

2.5. B_{12}-BASED DRUG DELIVERY SYSTEMS

Lawrence et al. investigated the exploitation of novel cobalamin derivatives as phototherapeutics.[11] In this domain, VitB$_{12}$ appeared to be inefficient as a light absorber beyond 550 nm. To tackle this problem, the researchers notably used commercial fluorophores, such as 5-carboxytetramethylrhodamine (TAMRA group) (Scheme 15a).[113,114] These fluorophores were linked to the cobalt either via the alkyl group or via the axial ligand "queue" serving as antennas to capture long-wavelength light and to allow the cleavage of the C−Co bond at different wavelengths, up to 800 nm (Scheme 15a). R-Co^{III} complexes were synthesized from a reduction− alkylation pathway (Scheme 5, Track C) using 3-chloropropylamine as R-X agent. The amine was then reacted with COOHterminated fluorophore (Scheme 15a).[114] This novel type of R-Co^{III} is highly attractive for the controlled release of bioactive species at long-visible and near-IR light for drug delivery applications. This is made possible when the bioactive species is linked to the R group that is released under appropriate light irradiation. For instance, new drug delivery systems were created from erythrocyte carriers known for their long lifespan to target a desired cell (Scheme 15b).[115] These drugs, covalently attached to the alkyl group of modified cobalamin, were released from the cobalt center to an adjacent cell. The release of the drug was activated by photoirradiation of an external fluorophore (Cy5-modified antenna, in green on Scheme 15b) designed for working at a specific wavelength and for transmitting its energy to the Cbl-drug assembly.[115] Finally, a thiolato-cobalamin complex was synthesized, and the fluorophore antenna facilitated the photolytic cleavage of the S−Co bond to release thiyl radical.[116] The large variety of Rcobalamin(III), R being either alkyl or thiyl chains, as unique photocleavable compounds at long-wavelength light offers many applications, ranging from drug delivery systems to tissue engineering or surgery.[112]

3. ORGANOCOBALT(III) PORPHYRINS

3.1. SYNTHETIC ROUTES

Scheme 16 summarizes the four main synthesis routes toward organocobalt(III) porphyrins (R-Co^{III}(por)). In the late 1960s, Dolphin and Clarke synthesized R-Co^{III}(por) species derived from VitB$_{12}$[37−39] by applying the reductive elimination/ oxidative addition pathway established by Johnson and Smith[117] (Scheme 16, Track A). This procedure gave access to a plethora of R-Co^{III}(por) of various reactivity. Later, RCo^{III}(por) complexes were formed by reaction of Co^{II}(por) derivatives with olefins in the presence of Na or Hg acting as reducing agent of Co^{II}(por) (Scheme 16, Track B).[118]

The first synthesis of R-Co^{III} porphyrins by radical pathways was reported in the 1990s, involving the reaction of Co^{II}(por) with a conventional free-radical initiator, such as azobis(isobutyronitrile) (AIBN), and a vinyl compound (Scheme 16, Track C).[119,120] Under thermal treatment, the initiator decomposed in two carbon-centered radicals (Scheme 17, eq 1) that reacted with Co^{II}(por) (in this example, tetrakis(pmethoxyphenyl)porphyrinato)cobalt(II), Co^{II}(TAP)) with the formation of the transient cobalt hydride (H-Co(TAP); Scheme 17, eq 2). This cobalt complex transferred its hydride radical to the olefin (e.g., styrene), providing the corresponding alkyl radical that was rapidly trapped by Co^{II}(TAP) with the formation of the corresponding R-Co^{III}(por) (Scheme 17, eq 3).[121] The same strategy was implemented for alkynes instead of olefins.[119,120]

Organocobalt(III) tetramesitylporphyrin (R-Co^{III}(TMP)) was prepared from a similar protocol developed by Costa et al. for R-Co^{III}(salen)[42,122] by the reaction of methanol, carbon monoxide, Co^{II}(TMP), and a reducing agent (Scheme 16, Track D).[123] This complex, namely (TMP)Co^{III}-CO_2CH_3, was recently used for the controlled photopolymerization of acrylates, acrylamides, and vinyl ketones, as will be discussed later.[124,125]

3.2. REACTIVITY

Compared to AdoCbl, the porphyrin ligand confers lower flexibility to the global structure, and the corrin ring is only partially conjugated, whereas the porphyrin is delocalized around all four pyrrole rings. The porphyrin ligand provides a strong tetrapyrrole donor group with four nitrogen atoms coordinating the cobalt atom. The structural and electronic environment of the porphyrin ring can therefore deeply influence the BDE of the C−Co bond.

These structural features explain the main differences between the chemistries of cobalamin and cobalt porphyrin.

The planar structure of R-Co^{III}(por) confers to the complex a certain stability in terms of BDE of the C−Co bond. The cleavage of the C−Co bond of $PhCH_2$-Co^{III}(por)L complex was followed via a radical trapping method,[126] and the influence of the electronic and steric properties of the cobalt complex on the BDE was evaluated by tuning the nature of the axial phosphorus ligand (L). The porphyrin ring appeared to act as a "shield" for the C−Co bond toward steric perturbation of the L group. Indeed, the porphyrin ligand is not sufficiently flexible to allow its torsion by bulky axial ligands, such as PPh_3, and the C−Co BDE is therefore not much influenced by these ligands. However, increasing the basicity of the ligand (e.g., PBu_3 vs PPh_3) increased the BDE values (Table 3, entry 1).[126]

More recently, a Density Functional Theory (DFT) investigation of the BDEs of R-Co^{III}(por) containing various substituents on the porphyrin core and R groups was carried out for the living polymerizations of different vinyl monomers.[127] From these studies, different trends were established in terms of electronic effects and steric hindrance on the C−Co^{III} BDE. First, the substitution of H-atoms of the porphyrin ring by strongly electron-withdrawing fluorine atoms slightly decreased the BDE, for instance from 24 to 22 kcal· mol^{-1} for the same R group (−CH(CH_3)CN) (Table 3, entry 2).[127] Second, carbon-centered radicals that are poorly stabilized, such as $^{\bullet}CH(CH_3)OAc$, also led to C−Co bonds with a higher BDE value (24 kcal·mol^{-1}) compared to radicals that are stabilized, such as $^{\bullet}CH(CH_3)C(=O)O$*t*Bu (14 kcal· mol^{-1}) (Table 3, entry 3).[127] The bulkiness of the R group had also a strong influence on the BDE value, with a significant decrease in BDE when decreasing the steric hindrance of R, for instance from a methyl acrylate (MA) radical (18 kcal·mol^{-1}) to a tert-butyl acrylate one (14 kcal·mol^{-1}) (Table 3, entry 3).[127]

As confirmation of the above-mentioned effects, the NMR method revealed to be complementary with the radical trapping experiments for the determination of BDE in RCo^{III}(por).[128] Tested for R-

Co^{III}(por) with a pentyl- or methylstyryl R group, a higher value of BDE was noted for the $C_5H_9{-}Co^{III}$ complex than for the styryl one, in agreement with the higher stability of the secondary radical ($^{\bullet}CH(CH_3)Ph$) compared to the primary one ($^{\bullet}C_5H_9$) (Table 3, entry 4, ref 128).

Stolzenberg et al. studied the complexation of the methylcobalt octaethylporphyrin with an axial ligand, as pyridine, to mimic the "base-on" effect that was found in $VitB_{12}$ with the indole group.[129] By X-ray diffraction experiments, he discovered that the binding of pyridine induced an elongation of the C−Co bond and facilitated its homolysis, which translated the "base-on" effect observed in $VitB_{12}$.

3.3. ORGANIC REACTIONS

R-Co^{III}(por) have been most often produced in situ and used as transient catalysts in different types of reactions,[130] such as in dechlorination of chlorinated olefins,[131] cyclopropanation of olefins,[5] oxidation of vinyl ethers,[132] in the formation of 2Hchromene compounds[133] or *E*-aryl-diene,[134] etc., as discussed below.

Due to structural and chemical similarities between Co^{II}(por) and $VitB_{12}$, tetrakis(N-methy1-4-pyridiniumyl)porphyrin (CoTMPyP) cationandcobalt-(tetrasulfophthalocyanine) (CoPcTs) anion were used as homogeneous catalysts for the dehalogenation of CCl_4.[135] Also, the water-soluble tetrakis(4-carboxyphenyl)porphyrin cobalt(II) ((TCPP)Co), demonstrated a similar dechlorination behavior for perchloroethylene than $VitB_{12}$ but with superior activity.[131] This Co^{II}(por) complex worked according to a similar mechanism as the one of $VitB_{12}$, thus by (i) reduction into Co^{I}(por), (ii) addition of chlorinated alkene with the formation of R-Co^{III}(por), and (iii) reductive elimination to give the dechlorinated olefin and to regenerate the catalyst. This cobalt-catalyzed reaction has the potential to treat the widespread groundwater chlorinated ethylene pollutants, such as perchloroethylene (PCE) and trichloroethylene (TCE).[136,137]

More recently, the easy photolytic cleavage of C−Co bond has been used for the formation of C−C bond from alkyl halides for the production of useful chemical fuels.[138] Meyer et al. integrated single-electron transfers to catalytic multielectron-transfer reactions by combining the semiconductor nanocrystallites of TiO_2 and Co^{I}(TCPP) complex. As represented in Scheme 18, Co^{I} reacted with R-X (as benzyl bromide) to form R-Co^{III}(TCPP). Light then promoted the C−Co bond homolytic splitting and produced two alkyl radicals that underwent radical coupling. The blue portion of the solar spectrum induced band gap excitation of the TiO_2 with the concomitant regeneration of the number of electrons to close the catalytic cycle.

Most of the recent developments and breakthroughs in Co^{II}(por)-catalyzed reactions of great utility for the construction of important novel building blocks deal with the reaction of Co^{II}(por) with carbene precursors, such as diazo compounds or N-tosylhydrazones, to give Co^{III}-carbene radical intermediates (also named α-Co^{III}-alkyl radicals) (Scheme 19, compound 1).[5,40,41,133,139−149] The formation of this transient carbene species has been experimentally proved via NMR (trapping thanks to a TEMPO radical) and X-ray crystallography.[139] These in situ formed Co^{III} species are key intermediates in many useful MRC reactions, including (enantioselective) alkene cyclopropanation,[41,141−144,150,151] C−H functionalization,[145,146] regioselective synthesis of β-lactams,[147] construction of 2H-chromenes[133] and 1H-indenes,[148] and the preparation of 1,2-dihydronaphthalenes and E-aryl-dienes.[134] Indeed, these Co^{III} species can undergo radical additions and H-atom abstractions as well as subsequent radical substitution, leading to a large diversity of novel catalytic systems for various unprecedented radical transformations. Most of these Co^{II}-mediated reactions are appealing because they provide important products, most often from simple and readily available organic building blocks, and in some cases with a perfect stereocontrol of the products when asymmetric Co^{II}(por) was used.

The first example illustrates the utility of Co^{II}(por)-catalyzed reaction for the selective synthesis of diverse heterocycles, 2Hchromenes, that are difficult to prepare otherwise, by a catalytic tandem radical addition-cyclization process (Scheme 19, compound 2).[133,152] This process involves the reaction of various substituted salicyl N-tosylhydrazones with alkynes in the presence of a base (Scheme 20a). Under these conditions, the salicyl N-tosylhydrazones were converted into the corresponding diazo compounds that reacted with Co^{II}(por) to give the Co^{III}-carbene radical. The vinyl radical intermediate was then formed through radical addition of Co^{III}-carbene radical to the alkyne substrate. Subsequent hydrogen atom transfer (HAT) from the ortho-hydroxy group to the vinyl radical moiety then produced the 2H-chromene product. In this study, non-chiral porphyrin ligand appeared to be the most efficient one (Scheme 20a).[133] When salicyl N-tosylhydrazones was substituted for α-diazocarbonyls, still in combination with alkynes, multisubstituted furans (Scheme 19, compound 3) were selectively produced by MRC.[153]

Importantly, substituting salicyl N-tosylhydrazones for ostyryl N-tosylhydrazones afforded substituted 1,2-dihydronaphthalenes by a mechanism proceeding via o-quinodimethane intermediates that again involved the formation of Co^{III}carbene radical in the first step (Scheme 19, compound 4).[134] Substrates with an alkyl substituent at the allylic position reacted to form the kinetically controlled E-aryldiene products rather than the expected thermodynamically controlled 1,2dihydronaphthalenes (Scheme 19, compound 5).

The Co^{III}-carbene radical was also very useful for the cyclopropanation of various alkenes, as exemplified in Scheme 19, compound 6.[5,139,144,154,155] The first study of this cyclopropanation reaction involving Co^{II} complex (a chiral vic-dioximatocobalt(II)), alkene, and diazoacetate was conducted by the team of Otsuka at the end of the 1970s,[156] and this research gained more attention in the 2000s with Co(por) complexes. Mechanistically, the carbene-radical intermediate added to the olefin to form the corresponding transient radical. An intramolecular radical-type C−C bond coupling then occurred, with the simultaneous homolytic splitting of the C− Co bond to give the cyclopropane adduct and release of Co^{II}(por) that entered again in the catalytic cycle (Scheme 20b). Importantly, when the Co^{II} complex contained a chiral porphyrin, such as D_2-symmetric chiral porphyrin ($Co(D_2Por^*)$; Scheme 21a), the ligand provided a confined and chiral nanospace around the active site that enabled catalyzing the asymmetric olefin cyclopropanation.[6,41,154,157] This asymmetric Co^{II}-based catalytic system worked for a broad range of olefins and afforded the desired cyclopropane products in high yields with both high diastereo- and enantioselectivity. More recently, Zhang et al. described another variant for this MRC cyclopropanation of alkenes by reacting α-formyldiazoacetates and N-arylsulfonyl hydrazones with $Co(D_2\text{-}Por^*)$, also with Scheme 21. (a)

Co^{II}(3,5-DitBu-ChenPhyrin) and (b) Co^{II}(HuPhyrin) Complexes, Examples of Co^{II}(D_2-Por*) Chiral Complex Studied in MRC[6,41,154,155,157−159] high diastereo- and enantioselectivity.[155,158] All these Co(D_2Por*)-catalyzed asymmetric reactions have a high potential for stereoselective organic synthesis. Another Co(D_2-Por*) bearing chiral amidoporphyrins with alkyl bridges across two chiral amide units, called Co^{II}(HuPhyrin) (Scheme 21b), was very recently synthesized by the same group.[159] Remarkably, this complex showed a significant improvement in reactivity and stereoselectivity. The length of the alkyl bridge also had a huge influence on the catalytic performances of the complex. For example, the cobalt complex with an alkyl bridge n = 1 showed higher catalytic activity for radical cyclopropanation, whereas the one with n = 2 gave higher yields for aziridination. Very recently, Megiatto et al. elegantly adapted the cyclopropanation of olefins catalyzed by Co^{II}(por) to the synthesis of rotaxanes from diazo compounds and styrene derivatives, by a radical-carbene-transfer reaction.[160] The process involved the design of a novel Co^{II}(por)-macrocycle, with the macrocycle creating an asymmetry on the two axial positions of Co^{II}(por) due to steric hindrance. In the presence of a bulky pyridine, the selective coordination of this ligand occurred only outside the cavity of the macrocycle. The free internal axial site was therefore available for the activation of the non-bulky substrates, affording cyclopropane-linked rotaxanes by an active-metal-template approach (Scheme 22).[160]

Co^{III}(por)-carbene radicals also underwent carbonylation to form ketenes that were in situ trapped with a large scope of amines, alcohols, or imines to give esters, amides, or β-lactams in an elegant one-pot cascade manner (Scheme 19, compounds 7 and 8).[147] Recently, an annulene cobalt complex showed a particularly high trans selectivity for the formation of β-lactams from imines.[161]

Zhang et al. elaborated the MRC enantioselective radical cyclization of saturated C−H substrates (aliphatic diazo compounds) for the efficient construction of various 5membered cyclic compounds. A three-step catalytic mechanism was involved (Scheme 20c): (i) the radical activation of sulfonyl hydrazone, (ii) H-atom abstraction, and (iii) the radical substitution leading to the cyclic compound (Scheme 19, 9).[162] This one-pot cyclization mechanism involving a D_2symmetric chiral porphyrin complex has been also applied for the synthesis of chiral indolines (Scheme 20c).[163] This innovative radical cyclization process is a fundamentally different alternative to the traditional radical cyclization of unsaturated substrates and provides a new strategy for the construction of 5-membered chiral cyclic molecules from readily available starting products.

In MRC, the metalloradical complex can be assimilated to a metal-supported organic radical that constrains the subsequent radical reactions in its close environment. When these complexes are chiral, highly stereoselective radical reactions are thus possible. These MRC reactions clearly highlight that radical reactions can now be exploited for the enantioselective construction of complex organic molecules.

3.4. POLYMERIZATIONS

The first use of R-Co^{III}(por) and Co^{II}(por) complexes in radical polymerizations involved a process called "catalytic chain-transfer polymerization" (CCTP).[3] This technique is employed for the industrial production of methacrylic macromonomers. CCTP products, which find applications in paintings or in adhesives,[3] were discovered in the 1980s by Enikolopyan et al.[164] and investigated in depth in the 1990s by Ittel and Gridnev.[3,165,166] This process involves reacting a methacrylate (e.g., methyl methacrylate, MMA) with an azoinitiator (e.g., AIBN) in the presence of a Co^{II} complex that is prone to hydrogen abstraction (e.g., Co^{II}(por)). The first step is the formation of alkyl radicals by decomposition of AIBN (Scheme 23). A β-H abstraction of the cyanoisopropyl radical by Co^{II}(por) provides cobalt hydride that reacts with MMA by hydrogen transfer to give the corresponding radical ($^{\bullet}CH(CH_3)COOCH_3$). This radical is then trapped by Co^{II}(por) to in situ form the corresponding R-Co^{III}(por). Homolytic splitting of the C−Co bond then releases Co^{II}(por) and $^{\bullet}CH(CH_3)COOCH_3$. The latter initiates the MMA polymerization. β-H abstraction at the growing chain is then promoted by the released Co^{II}(por) and yields the PMMA macromonomer and the cobalt hydride that enters again the catalytic cycle. R-Co^{III}(por) is thus formed in situ in this CCTP process (Table 4, entry 1). Note that the exact nature of the intermediate state in the CCTP mechanism, i.e., the adduct between cobalt and the propagating radical (R-Co^{III}L) or a radical pair (Co^{II}L + $R^{\bullet}$), has been subject to debate. Nevertheless, experiments conducted by Gridnev[167] involving porphyrin cobalt complexes with various steric hindrance support the hypothesis of the radical pair (Co^{II}L + $R^{\bullet}$) as real intermediate of CCT reaction as depicted by Scheme 23. Indeed, when using a more sterically hindered porphyrin complex, no CCT was observed for styrene whereas the CCT activity was maintained for MMA. The opposite trend was expected if the alkyl-cobalt was the intermediate of the CCTP because the more sterically hindered $PMMA^{\bullet}$ radical species should be completely screened from interaction with the cobalt complex. This CCTP process with Co(por) has been reviewed by Gridnev et al.[3] However, Co(por) was revealed to rapidly reach its limits in CCTP, and another class of Co^{II} complexes, cobaloxime complexes, met real success in that field in the mid1980s, as will be detailed in one of the next sections.[3]

So, the apparent propensity of a cobalt complex to induce CCTP and β-H abstraction is related to two main factors: (i) the nature of the propagating radicals and (ii) the type of metal complex.[168] Indeed, certain radicals, such as MMA, have a high ability for β-H abstraction due to the availability of the methacrylic protons and due to its stabilized tertiary form (more stable than secondary radicals, as acrylic ones). Thus, both electronic and steric effects of the cobalt complex play important roles in favor of organometallic dormant species against the CCTP process.[169,170] The number of growing radical chains, and thus the molar mass of the polymers, are determined not by the amount of radical initiator but by the βH abstraction ability of the complex (and thus its transfer constant) and its concentration.

In 1994, Wayland et al. pioneered the field of cobaltmediated radical polymerization (CMRP), initially for acrylates, and then they extended it to other monomers by using R-Co^{III}(por) complexes (Scheme 24).[4,171] This research group opened the door to a novel family of controlled radical polymerization (CRP) techniques, called organometallicmediated radical polymerization (OMRP), which includes other transition metals as titanium, manganese, or chromium.[15,25] Comprehensive reviews have recently been published on all these OMRP processes and will not be detailed here.[15,169] We will mainly focus on the implementation of RCo^{III} for the CMRP process that is the most widely implemented OMRP technique.

Wayland et al. first reported the radical polymerization of acrylates (Scheme 19) with tetramesitylporphyrin (TMP) as ligand of the Co center (Table 4, entry 2).[4] He first described the unimolecular route by the use of neopentyl-Co^{III}(TMP) that plays two important roles (Scheme 25A). First, thermal activation of the C−Co bond yields the initiator of the radical polymerization of methyl acrylate (MA), i.e., the neopentyl radical ($^{\bullet}CH_2C(CH_3)_3$). The released Co^{II}(TMP) then acts as the controlling agent by reversibly trapping the growing chains (the active chains) with the formation of chains end-capped by the cobalt complex (dormant chains). The equilibrium between the active and dormant chains, shifted toward the dormant one, avoids their irreversible termination by conventional bimolecular termination events. The labile C−Co bond at each terminal chain-end of the polymer is the key element toward the control of the macromolecular parameters of the chains. This bond is labile enough to permit the release of the propagating radical that is able to add a few monomer units before being again reversibly trapped by Co^{II}(TMP) to avoid irreversible bimolecular chains terminations. Other R groups were also successfully used for R-Co^{III}(TMP), e.g., $-CH(CO_2CH_3)CH_3$, and conducted to a similar control. Due to the controlled character of the polymerization, a linear increase of the molar mass (M_n) was observed with the monomer conversion, and high molar mass poly(acrylate)s ($M_n = 1.7 \times 10^5$ g·mol^{-1}) were achieved by adjusting the acrylate/RCo^{III}(TMP) molar ratio. The lability of the C−Co bond at the polymer chain-end was then elegantly exploited for the chain extension with other acrylic monomers such as n-butyl acrylate (nBA), giving well-defined PMA-b-PnBA diblock copolymers with a low dispersity (Đ). Furthermore, this study revealed that TMP ligands, contrary to tetraphenylporphyrin (TPP) ones, have sufficient steric hindrance to avoid β-H abstraction at the polymer chain end, thus limiting the occurrence of CCTP and favoring the control of the polymerization. A few years later, they synthesized a brominated version of R-Co^{III}(TMP) (RCo^{III}(Br_8TMP)) and successfully used it for the CMRP of MA.[171]

In 2004, instead of using a pre-formed R-Co^{III}(por) complex for the CMRP of acrylates, the bimolecular system consisting in a mixture of Co^{II}(TMP) and a diazo compound initiator, 2,2′-azobis(4-methoxy-2,4-dimethylvaleronitrile) (V70), was developed.[172,181] During the initial stage of the process, an induction period was observed that corresponded to the in situ formation of the cobalt hydride by H-abstraction with the alkyl radicals generated by thermal decomposition of V70. Cobalt hydride then rapidly reacted with the monomer to provide the corresponding alkyl radical that was rapidly trapped by Co^{II}(TMP) to give R-Co^{III}(TMP). Polymerization could then occur from this CMRP initiator/controlling agent (Scheme 25 B).

Importantly, although the C−Co bond is at the core of the CMRP process, two types of mechanism can occur in CMRP, depending on the polymerization conditions: a reversible deactivation (RT; equation A) or a degenerative transfer (DT; equation B) mechanism.

The first one (RT) implies a reversible termination of the growing chains by the Co^{II} complex. It occurs when R-Co^{III} is the exclusive source of radicals (Scheme 26, Equation A). The efficiency of the process is thus strongly dependent on the C− Co bond strength. In contrast, the DT mechanism requires a continuous flux of tiny amount of external radicals, e.g., from a conventional azo-initiator, in addition to R-Co^{III} (in situ generated or not). The active growing chains ($P'^{\bullet}$) in a DT mechanism are temporarily deactivated by reaction with the dormant chains (P-Co^{III}) ((Scheme 26, Equation B). The cobalt complex is therefore exchanged from a dormant chain to an active one, the first one becoming active and the second one dormant. Some mechanistic studies emphasized the connection between the equilibrium constant (K_{eq}), which depends on the cobalt complex and the nature of the growing radical chains, and the mechanism of control.[182] The authors suggested that the RT mechanism is dominant for equilibrium constant between 10^7 and 10^9, whereas homolytic dissociation of the Co−C bond is disfavored above 10^{10}. In the latter case, the DT mechanism would be the major pathway.

Moreover, in the case of the DT mechanism, the content of external free-radical initiator clearly influences the rate of polymerization. This effect has been noticed by increasing the ratio of V70/Co^{II}(TMP) that speeds up the polymerization.[181] A few years later, the CMRP of MA and VAc with R-Co^{III} complexes and V70 allowed a better understanding of the mechanism (Table 4, entries 2 and 3).[173−175] The choice of the polymerization mechanism, and therefore of the operating conditions, is particularly important for succeeding in controlling some difficult monomers such as vinyl acetate (VAc). Interested readers are invited to read some recent reviews on the topic for detailed mechanistic discussions.[7,8]

Wayland et al. then investigated other monomers in CMRP mediated by Co^{II}(por). By modifying the ligand by sulfonate groups, the cobalt complex was soluble in aqueous media, which enabled control over the radical polymerization of acrylic acid (Table 4, entry 4).[176,177] Excellent control was obtained until high molar mass (M_n < 300 000 g/mol and Đ = 1.2−1.4), and both RT and DT mechanisms were performed according to the amount of external free-radical initiator (4,4′azobis(4-cyanovaleric acid) (V501) or V70) that was added.

Dispersion and emulsion polymerizations of acrylamide (AM) and tert-butyl acrylate (tBA) were recently carried out by using tetramethoxyphenylporphyrin, Co^{II}(TMOP), and 2,20-azobis[2-(2-imidazolin-2-yl)propane] dihydrochloride (VA-044) in a bimolecular pathway (Table 4, entries 5 and 6).[178,179] DMF and ethanol were used in combination with water as the reaction medium, and well-defined PAM and PtBA spherical particles were produced under mild conditions.

A Co(por) complex bearing a long alkyl alcohol chain on the porphyrin ligand, namely Co^{II}(TMP-OH), also allowed the CRP of various monomers (acrylates and acrylamide) under thermal activation in both polar and nonpolar media and was used for the synthesis of various block copolymers (Table 4, entry 7).[180]

More recently, the visible-light-induced activation of the C− Co bond of R-Co^{III}(por) derivatives was successfully implemented by the groups of Fu and Peng to control the radical polymerization of different families of monomers, e.g., acrylates, acrylamides, or vinyl ketones (Table 4, entries 8−10).[123−125] The C−Co bond homolysis of the R-Co^{III}(por) complexes and of the corresponding dormant chains (that are end-capped by the cobalt complex) is promoted by visible light at room temperature. Therefore, the cobalt-terminated polymers prepared by CMRP were easily reactivated to initiate the polymerization of a second monomer, providing the corresponding block copolymers as listed in Table 4, entries 8−10. For instance, photoactivation of PMA- or PDMACo^{III}(TMP-OH) (Table 4, entry 8) in the presence of a new feed of monomers (acrylates or acrylamides) allowed the chain extension with the formation of well-defined block copolymers when the second monomer was different from the one used for the first block (Table 4, entry 8).[123,124] A similar study was conducted with R-Co^{III}(TMP) complex, with R being $-CO_2CH_3$, as the radical source (Table 4, entry 9).[123,124] By switching on/off the light, the polymerizations were accordingly activated or stopped, demonstrating that photoactivation was required for the polymerization to proceed at room temperature. Finally, Fu et al. applied their previous system to ethyl vinyl ketone (EVK) and succeeded to provide new PVEK-based block copolymers by sequential photoactivated copolymerization (Table 4, entry 10).[125]

4. ORGANOCOBALOXIME(III) COMPLEXES

Many contributions have been dedicated to the family of cobaloxime complexes. Due to the close structural analogy of these complexes to VitB$_{12}$, the synthesis and the reactivity of organocobaloximes (R-Co^{III}(ox)) have been studied in depth over the past 50 years.[16,22,23,183,184] Compared to organocobalt porphyrin complexes, R-Co^{III}(ox) complexes have less rigid structure and behave more like the corrin ring of VitB$_{12}$. For these reasons, R-Co^{III}(ox) have been largely investigated as model compounds of VitB$_{12}$, and most of the reactions cited in this section have been applied for R-Co^{III}(ox) as well.

4.1. SYNTHETIC ROUTES

The synthesis of organocobaloximes(III) began in the 1960s with the advances in VitB$_{12}$ chemistry. Since then, the synthesis of R-Co^{III}(ox) has been reviewed in many reports.[185,186] Schrauzer et al. first focused on the formation R-Co^{III}(ox) from Co^{II} complex bearing dimethylglyoximato monoanions (dmgH$^-$) as ligands.[19] Several pathways were followed in the synthesis of R-Co^{III}(ox) with three different types of starting reagents: cobalt(I) or cobalt hydride (Table 5, Series A and B), cobalt(II) (Table 5, Series C), and cobalt(III) complexes (Table 5, Series D).[186]

The reaction of Co^{I} or cobalt hydride, acting as supernucleophile, with electrophilic reagents has been by far the most implemented method for the formation of R-Co^{III}(ox) (Scheme 27).[185] Many alkylating agents, namely R-X, have been employed. R may be alkyl, alkenyl, benzyl, etc., while X$^-$ can be Cl$^-$, Br$^-$, tosylate, etc. (Table 5, Series A). Co^{I} species are generally obtained by three methods: the reduction of Co^{II} or Co^{III} by $NaBH_4$ in alkaline medium, the disproportionation of Co^{II} to Co^{III} and Co^{I} in alkaline medium, and the reduction of Co^{II} by hydrogen in different media.[186] The alkylation of Co^{I} may occur via two mechanisms, either S_N2 or electron transfer, depending on the alkylating agent and the reaction conditions. The addition of alkyne on Co^{I} complex is also possible (Table 5, Series A) and involves a nucleophilic attack on the β-carbon of the alkyne and a transfer of proton from the solvent.[186] Unlike the reaction of Co^{I} with halo-alkyl chains, the addition of hydride species with alkene and alkyne produced α-substituted R-Co^{III}(ox) (Table 5, Series B).

The second type of reactions leading to R-Co^{III}(ox) is based on the reaction of Co^{II} with various alkylating agents, such as alkyl halide, organic hydrazines, or alkyl hydroperoxides (Table 5, Series

C).[186] The mechanism is essentially based on a radical atom transfer of the R-X to the Co^{II} following eqs 1 and 2 (Scheme 28).

Finally, halocobalt complexes (X-Co^{III}) can notably react with Grignard compounds to give R-Co^{III}(ox) (Table 5, Series D). Alkyl-Co^{III}(ox) were preferably formed from Series A (Table 5) while phenylethynyl-Co^{III}(ox) were synthesized with higher yields with the latter method, as exemplified in Scheme 29, eq 1.[186] Likewise, X-Co^{III} can also react with vinyl ethers to produce the corresponding R-Co^{III}(ox) via an intermediate olefin π complex (Scheme 29, eq 2).[75]

4.2. REACTIVITY

Electronic and steric factors act differently on the stability of the C−Co bond of R-Co^{III}(ox).[130] Halpern et al. studied the influence of the basicity of the ligand (L) of R-$Co^{III}(dmgH)_2L$ (with R states for $-CH(CH_3)Ph$ and L for pyridine or parasubstituted pyridine) on the BDE of the C−Co bond.[23] An increase of the BDE value was noticed with L of higher pK_a, as for 4-NH_2-py (21 kcal·mol^{-1}) and for 4-CN-py (18 kcal· mol^{-1}) (Table 6, ref[23,29]). The steric effect of phosphorus axial ligand in $Ph(CH_3)CH$-$Co^{III}(dmgH)_2L$ was also investigated by measuring the BDE for complexes with ligands of different steric hindrance, PMe_2Ph and PPh_3. The BDE decreased with the increase of the θ cone angle of the phosphorus ligand, from 30 kcal·mol^{-1} with L = PMe_2Ph to 26 kcal·mol^{-1} with L = PPh_3 (Table 6, ref 187).[188]

Sonnenberg et al. calculated the strength of the C−Co bond by DFT for R-$Co^{III}(dmgH)_2(py)$ with R = methyl or isopropyl. BDE decreased from 33 for methyl to 21 kcal·mol^{-1} for isopropyl (Table 6, ref 189), in agreement with the higher stability of the isopropyl radical compared to the methyl one.

4.3. ORGANIC REACTIONS

In the organocobaloxime chemistry, one of the main reactions that has been studied over the last decades concerns the insertion of dioxygene into the cobalt−carbon bond.[190] Fixation of O_2 has a huge impact in biological systems[190,191] and also for synthetic products.[186] O_2 insertion reactions have been performed on 27 organocobaloxime complexes under thermal and UV light treatment and reached relatively high yields, as exemplified in Scheme 30, 1.[190] Sato et al. also studied the irradiation of alkylcobaloximes under oxygen in chloroform which led to the formation of carbonyl and alcoholic compounds.[192] Similarly, sulfur dioxide was also incorporated in R-Co^{III}(ox), with the formation of alkylsulfonylcobaloxime following a rearrangement and in some cases leading to a five-member cyclization (as depicted in Scheme 30, 2).[193]

In 1982, Tada et al. studied the catalytic activity of Co^{I}(dmgH)(py) in the reductive cyclization of 2-propargyloxyalkyl bromide, using $NaBH_4$ as reductant (Scheme 30, 3).[17,194] Good yields of cyclic compounds were obtained with primary bromides. Later, Hoffmann and Pattenden applied these conditions for different heterocyclic compounds, such as halogeno propargyl acetal[195] and 2-allyloxyalkyl bromides.[196]

Branchaud et al. developed the alkyl−alkenyl cross-coupling reaction promoted by R-Co^{III}(ox).[1,197] A representative example is shown in Scheme 31 by the coupling of various alkyl halides (R-X) with styrene catalyzed by $Co^{II}(dmgH)_2(py)$ following a two-step process. The first step consisted in the formation of R-$Co^{III}(dmgH)_2(py)$ by reaction of Co^{I} (in situ produced by reduction of $Co^{II}(dmgH)_2(py)$). Then, the photolysis of R-$Co^{III}(dmgH)_2(py)$ occurred in a second step in the presence of styrene. The light-induced splitting of the C−Co bond of R-$Co^{III}(dmgH)_2(py)$ released $R^{\bullet}$ that added to styrene to give the corresponding adduct R-CH_2−$CH(Ph)^{\bullet}$. β-H abstraction induced by $Co^{II}(dmgH)_2(py)$ yielded the alkyl-alkenyl cross-coupled product, R-CH=CHPh. The hydridocobalt(III) complex ($HCo^{III}(dmgH)_2(py)$) subsequently decomposed to H_2 and Co^{II} complexes. As this disproportionation is irreversible, it drove the reaction to completion. Various olefins were easily accessible by this process by varying the nature of the R group of R-Co^{III}. This cross-coupling reaction could also occur from in situ formed R-Co^{III} in the presence of zinc.[198,199] More recently, the in situ regeneration of Co^{I} by deprotonation of H−$Co^{III}(dmgH)_2(py)$ by a tertiary amine (iPr_2NEt) permitted to regenerate R-$Co(dmgH)_2(py)$ by reaction of Co^{I} with alkyl iodide (Scheme 31, dotted line).[32] Under these conditions, catalytic amounts of the cobalt complex were required for the reaction. Based on this mechanism, a radical cyclization was represented in Scheme 30 (compound 4). This cobaltcatalyzed alkyl Heck cyclization has been used for the synthesis of (+)-daphmanidin E* (compound having a vasorelaxant activity).[200]

R-$Co^{III}(dmgH)_2(py)$ compounds were also involved in radical alkyl−heteroaromatic substitutions with positively charged compounds such as pyridinium, quinolinium, or benzothiazolinium p-toluenesulfonate (Scheme 30, 5).[201] Under visible light irradiation, this cross-coupling reaction substituted the C−H in the protonated heteroaromatic compound by a C−R, where R is the alkyl group of R-$Co^{III}(dmgH)_2(py)$.

Similarly to Branchaud experiments, addition reactions were investigated on glycosylcobaloximes under photolytic treatment with a nitroso alkane to provide a nitroxide or with nitrogen monoxide to give the corresponding hydroxylamine or with an alkene such as MA to yield to two different addition products, as represented in Scheme 32.[202]

The synthesis of different organocobaloximes bearing a 1,3butadiene group as alkyl chain was realized for the Diels−Alder reactions with several dienophiles.[203−207] This Diels−Alder reactions using R-Co^{III} not only gave the advantage of mild conditions (for C−Co cleavage) and cobalt recovery after a demetalation reaction but, most importantly, provided an exo diastereoselectivity. This process, which is complementary to traditional endo-selective Diels−Alder reactions, is exemplified in Scheme 30, 6.

As discussed in this section, for many reactions involving $RCo^{III}(ox)$, a hydridocobalt complex (H−$Co^{III}(ox)$) was generated in situ and was involved in additions to olefins through H radical transfer. The resulting carbon-centered adduct was then reacted with various substrates to lead to the final product or was rearranged into another adduct, with the release of H−$Co^{III}(ox)$ that entered again the catalytic cycle. Although the recent reactions by Norton discussed below do not directly involve R-$Co^{III}(ox)$ as the starting material or do not seem to in situ produce R-$Co^{III}(ox)$, they also involve H−$Co^{III}(ox)$ that catalyzes important radical reactions, with the synthesis of important products. For the sake of completeness and to facilitate establishing connections between the synthetic organic field and the polymer one, they are briefly introduced here.

Norton et al. investigated the radical isomerization and cycloisomerization of terminal olefins with $Co^{II}(BF_2\text{-dmg})_2L_2$(L = H_2O, THF) under H_2 pressure.[208,209] The reaction of H_2 with the cobaloxime complex provided the corresponding hydridocobaloxime ($H\text{-}Co^{III}(BF_2\text{-dmg})_2L$; Scheme 33A)[208,210,211] that catalyzed radical isomerizations and cycloisomerizations. In the presence of terminal olefins, $H\text{–}Co^{III}(BF_2\text{-dmg})_2L$ followed a HAT, resulting in the formation of a novel carbon-centered radical and in the release of $Co^{II}(BF_2\text{-dmg})_2L_2$ (Scheme 33B1). This Co^{II} complex was then abstracting a hydrogen to the adjacent carbon atom of the carbon radical to yield the isomerized alkene. The soregenerated $H\text{–}Co^{III}(BF_2\text{-dmg})_2L$ was finally entering again the catalytic isomerization cycle. When an olefin bearing an internal double bond was considered, the transfer of H radical to the olefin initiated a radical intramolecular cyclization, leading to the corresponding carbon-centered radical (Scheme 33B2). The final step was a H radical transfer to Co^{II}, resulting in cycloisomerization and in the release of $H\text{–}Co^{III}$. Importantly, this work demonstrated that the low concentration of the cobalt complex involved in these reactions favored the isomerizations comparatively to hydrogenations when the concentration of the $H^{\bullet}$ donor was high.[209]

When polymerizable olefins prone to β-H abstraction (such as methacrylates) were involved in processes that in situ generated $H\text{–}Co^{III}$, the advent of the reaction is different. Indeed, the carbon-centered radical formed by transfer of H radical from $H\text{–}Co^{III}$ to the olefin might add to other monomers, leading to chain propagation. After few monomers insertion, H transfer at the polymer chain end promoted by Co^{II} provided the polymer terminated by an olefin, thus a macromonomer. This transfer reaction was associated with the release of $H\text{–}Co^{III}$ that entered again into the catalytic cycle. This process is similar to CCTP promoted by Co^{II}(por) derivatives (Scheme 25) and is further discussed in the next section. Here, there is an evident connection between the fields of synthetic organic and polymer chemistry. In the first case, there is only one addition of H radical to the olefin, followed by rearrangement/isomerization, and completed by H abstraction by Co^{II} to furnish the final organic product. In the polymer field, there is an additional propagation step before the final H abstraction by the cobalt complex.

4.4. POLYMERIZATIONS

In comparison to Co(por) complexes, CCTP based on cobaloxime complexes has been much more developed.[3] Many companies and research centers, such as DuPont,[212] ICI/Zeneca,[213] and CSIRO,[214] have dedicated considerable effort to studying the CCTP of different monomers via Co^{II}(ox) complexes, notably for coating applications. Conventional free-radical initiators, as AIBN, were used for the in situ formation of $R\text{-}Co^{III}$(Ox) species, as previously seen in Scheme 25B. Cobaloxime complexes, and especially BF_2-bridged complexes (Scheme 34A) that are less sensitive to oxidation and hydrolysis, showed a much higher activity in CCTP than cobalt porphyrins.[215] This cobalt BF_2-dialkyl glyoxime complex (alkyl being either $-CH_3$ or -Ph) is an efficient catalyst for CCTP of methacrylic monomers, but also for styrene (St), αmethylstyrene (AMS), dimethyl itaconate (DMI), and phenyl allyl alcohol (PAA) (Scheme 34B). Nevertheless, monomers without an α-methyl group, such as vinyl esters or acrylates, showed a much lower activity.[215] More details concerning chain-transfer constants with the corresponding monomers and Co^{II} catalysts can be found in an excellent review by Heuts and Smeets.[215]

Different R-Co^{III}(BF_2-alkylglyoxime)$_2$(L) complexes, with R being an isopropyl, ethyl, or methyl group and L being either pyridine or water, have been designed and compared in emulsion CCTP with their Co^{II} counterparts by Rizzardo et al.[216] They noticed that the activity of the R-Co^{III} is not simply inherent to the reactivity of the complex, but it is also influenced by the monomer phases and the rate of partitioning. This process also served in the one-pot synthesis of hyperbranched methacrylic polymers by direct free-radical polymerization of ethylene glycol dimethacrylate by RCo^{III}(ox) (Scheme 35).[217] This R-Co^{III}(ox) controlled the competition between chain transfer and propagation, enabling the formation of a hyperbranched polymer instead of an insoluble macrogel. A recent review realized by Smeets highlighted the potential of CCTP for the synthesis of hyperbranched polymers via the copolymerization of vinyl and divinyl monomers by Co^{II} complexes.[218]

The combination of recent advances in CCTP by cobaloxime complexes[215] and in sequential CRP, such as in atom-transfer radical polymerization (ATRP)[219,220] or in reversible addition–fragmentation transfer polymerization (RAFT),[221,222] extended the field of possibilities in terms of precise macromolecular engineering of methacrylic copolymers in emulsion polymerization.[223–227] The technique, called sulfur-free RAFT (SF-RAFT), was developed in emulsion of methacrylic monomers using $K_2S_2O_8$ as radical initiator.[223]

First, CCTP of MMA led to the formation a PMMA macromonomer serving as macro-chain-transfer agent (mCTA) with a vinyl ω-end group. In the presence of $K_2S_2O_8$ and other methacrylic monomers, this vinyl ω-end group underwent β-scission (addition/fragmentation) and led to the extension of the macromonomer chains with welldefined molecular weight. This reaction is exemplified in Scheme 36 and shows many advantages, such as a precise design of the block sequence, fast polymerization rates, absence of odorous materials, molecular weights up to 55 $kg \cdot mol^{-1}$, and $Đ \leq 1.25$ with a conversion above 99%.[224] This later study showed the potential role of the organocobalt chemistry in applications requiring a perfect control of the polymer backbone.

Using CoPhBF complex (Scheme 34) as CCT agent, Hutchinson et al. demonstrated the efficiency of this catalyst to produce poly(butyl methacrylate) macromonomers having low dispersity values (1.3).[228]

For monomers that are not prone to hydrogen abstraction, such as acrylates, Harwood et al. pioneered the CMRP promoted by photolysis of R-Co^{III}(ox) with R being an isopropyl group and with pyridine as axial ligand.[229–232] RCo^{III}(ox)-containing R groups with hydroxyl, carboxylic acid, ester, or nitrile groups were also used to provide polymers with these functionalities at the α-chain end.[231]

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5. ORGANOCOBALT(III) COMPLEXES WITH SCHIFF BASE LIGANDS

Vitamin B_{12} inspired other ligand structures related to its planar geometry, and one of the most developed analogues has been classified in the Schiff base ligands. This category of ligand is based on imine functions that coordinate the cobalt center. We will mainly describe two types of partially aminated ligands: N,N′-bis(salicylidene)ethylenediamine, or salen, and N,N′-bis(salicylidene)phenylenediamine, or saloph (Scheme 37). Therefore, this class of complexes will be named Co(sal).

5.1. SYNTHETIC ROUTES

The synthesis of organocobalt(III) bearing Schiff base ligands was initiated by Costa et al. in the mid-1960s.[42,43,233] As for RCo^{III}(ox), the formation of organocobalt(III) bearing salentype ligands (R-Co^{III}(sal)) has been realized from Co^{III}, Co^{II}, and Co^{I} species depending on the nature of the target R-Co^{III} as illustrated in Scheme 38. As typical examples, stable carbon−cobalt bond can be formed by reaction of Grignard reagents on Co^{III} complex.[43] Cobalt(II) (e.g., Co(sal)) and alkyl halide (e.g., bromoethane) were also reacted to yield the corresponding R-Co^{III}(sal) complexes.[234] Co^{II}(sal) followed a carbonylation reaction to yield RO_2C-Co(sal) complexes. Finally, cobalt(I) species were reacted with epoxides, acetylene, or acrylonitrile in acidic media to form the corresponding R-Co^{III}(sal).[43]

Recently, Peng et al. described the synthesis of methoxycarbonyl cobalt(III) salen complexes by reaction of RCo^{III}(sal) with carbon monoxide and methanol for controlled radical polymerization purposes.[12] This carbonylation method was further extended by Martin et al. for the preparation of 33 examples of alkoxycarbonylcobalt(III) compounds by varying the nature of the aliphatic alcohol bearing alkyl chains as ethyl, benzyl, or tert-butyl (Scheme 39).[235] Both Co^{II} and X-Co^{III} complexes bearing salen and saloph ligands have been used for these R-Co^{III}(sal) synthesis with excellent yields, up to 99%. Various R′HN(O)C-Co^{III}(salen) were also recently synthesized from the reaction between MeO_2C-Co^{III}(salen*) complex and aliphatic amines bearing alkynyl, tert-butyl, phenyl, cyclohexyl, fluoride, chloride, furyl, or thienyl functionalities.[236]

5.2. REACTIVITY

The determination of the BDE of the C−Co bond of various R-Co(saloph) has been first studied in pyridine solution below 100 °C.[23,237] The BDE values were dependent on the nature of the R group, ranging from 25 kcal·mol^{-1} for n- propyl to 20 kcal·mol^{-1} for isopropyl (Table 7). This in line with the higher stability of the secondary radical compared to a primary one that is less stabilized and shows a higher C−Co BDE.

Zhang et al. investigated R-Co(salen) by photoacoustic calorimetry for the determination of the C−Co bond strength.[238] This study revealed the influence of electronic and steric factors of the alkyl group and trans base ligand on the BDE value. With H_2O as axial trans ligand, a general trend on C−Co BDE has been noticed with variation of the alkyl group in the order $CH_3 > C_2H_5 > n\text{-}C_4H_9 > i\text{-}C_4H_9 > i\text{-}C_3H_7$. The increasing size of the alkyl group has a large influence on the C−Co bond weakening due to the C−Co bond lengthening and bond angle distortion. In Table 7, we present the largest difference in BDE between methyl (CH_3) and isopropyl ($CH(CH_3)_2$)) groups: ~20 kcal·mol^{-1}. These values of C−Co bond strength have been theoretically verified by using two different methods of DFT calculations with very close values.[29]

5.3. ORGANIC REACTIONS

A large library of R-Co^{III}(sal) complexes with various R groups were made available for organic reactions by Pattenden in the 1980s.[2,16] Oxidative free-radical cyclization has been performed for the formation of heteroaromatics, such as benzofurans, indoles, and benzopyrans.[239] As exemplified in Scheme 40 (compounds 1a and 2a), the photolysis of the C− Co bond in methylbenzofuran-Co^{III}(salen) led to the formation of two different products, depending on the presence or absence of oxygen.

The photolysis of C−Co bond was also exploited for the formation of C−C bond through cobalt mediated radical addition−elimination to ethyl acrylate as exemplified in Scheme 40 (compound 3).[240] This reaction, applied to methyl methacrylate, conducted to various oligomers.[241]

The photolysis of the C−Co bond of acylcobalt salophen produced a carbon-centered radical after in situ decarbonylation that was intercepted with oxygen-, nitrogen-, halogen-, sulfur-, and selenium-containing radical trapping agents, leading to the corresponding adducts (Scheme 40, compound 4).[242] Pattenden et al. also developed strategies to prepare of β-, γ-, and δ-lactams by photolysis of R-Co^{III}(saloph) (Scheme 40, compounds 5 and 6).[243] For example, a mixture of α methylene-γ-lactam (n = 2 in Equation R) and isomeric pyrrolidinone was synthesized after dehydrocobaltation.[243]

Among the organic reactions developed by organoCo^{III}(salen) complexes involving C−Co bond homolysis, radical hydrofunctionalizations represent a very important class of reactions.[10] In this mechanism, Carreira and Hiroya's teams, being two of the main protagonists in the study of reactions involving HAT and Co(salen) complexes, developed a large panel of reactions: hydrohydrazination,[13,34] hydroazidation,[244] hydrocyanation,[245] hydrochlorination,[246] hydrooximation,[247] hydrofluorination,[248] and hydroalkoxylation.[33] Mukaiyama and Isayama are certainly pioneers in this field, but they were mainly focused on Co(acac)$_2$ reactions that will be developed in the next section.[249] All these reactions are represented in Scheme 41 with the most important Co(sal) catalysts. As representative example, the hydroalkylation of an unactivated alkene (as 4-allyl-1,2-dimethoxybenzene) and ethanol led to the product 7 by using a Co(sal) catalyst (Scheme 40).[33] This mechanism, recently discovered by Hiroya et al., shows the importance of $PhSiH_3$ and a source of fluorine for the formation of intermediate organocobalt compounds leading to carbon-centered radicals and subsequently carbocations as reactive species for the hydroalkylation process (Scheme 42).

Complementary to Norton's work,[208,209] Shenvi et al. have recently demonstrated that in certain conditions, isomerization predominates over hydrogenation in a HAT equilibrium.[250] Indeed, the use of $Co^{II}(sal^{tBu,tBu})Cl$ complex and organosilanesin catalytic amounts produces (A) isomerization reaction with terminal alkenes, (B) cycloisomerization in the case of a pendant alkene, and (C) retro-cycloisomerization when the alkene is adjacent to a strained ring (Scheme 43). This study was pursued by the Markovnikov olefin hydroarylation using this Co^{II}(sal) complex and nickel catalyst (Scheme 43D).[251]

5.4. POLYMERIZATIONS

The family of R-Co^{III}(salen) has gained more and more interest in the field of polymerization these past 20 years. Nakano et al. were the first to discover the potential of the chiral structure of (R,R)-N,N′-bis(3,5-di-tert-butylsalicylidene)-1,2-cyclohexanediaminatocobalt(II), called Co(salen*), for polymer synthesis.[252−254] Chiral Co(salen*) served as catalyst for the free-radical polymerization of methacrylic monomer leading to isotactic polymers. A few years later, Peng et al. demonstrated that the polymerizations of methyl acrylate (MA) and vinyl acetate (VAc) initiated by a conventional freeradical initiator (AIBN) were controlled by Co^{II}(salen*) (Table 8, entry 1).[255] An induction period was noticed and corresponded to the time required for the in situ formation of R-Co^{III}(salen*) by reaction of Co^{II}(salen*) with carboncentered radicals. The polymerization then occurred in a controlled fashion, and poly(vinyl acetate)-block-poly(methyl acrylate) (PVAc-b-PMA) was prepared by sequential polymerization of VAc (a less activated monomer (LAM) and a more activated monomer (MAM)).

Subsequently, Fu and Peng investigated the photolytic behavior of this Co(salen*) complex in polymerization[256] and synthesized a novel R-Co^{III}(salen*) with methoxylcarbonyl being the R group, for the polymerization of various monomers (MA, n-BA, t-BA, DMA, DEA, AMO, VAc) (Scheme 44 and Table 8, entry 2).[12] The photolysis of the C−Co bond was driven by visible light and was facilitated by the use of a photoinitiator, namely 2,4,6-trimethylbenzoyl diphenylphosphine oxide (TPO).

In a recent publication, various R′HN(O)C-Co^{III}(salen) compounds were exploited for the controlled polymerization of both MAMs and LAMs (Scheme 44) to achieve α- and ωend chain-functionalized polymers under visible-light photolysis (Table 8, entry 3).[236]

Other advances in CMRP were realized by Debuigne and Detrembleur et al. with the exchange of bidentate (bis(acetylacetonate), or acac ligand) to tetradentate (salen and salen*) for the block copolymerization of VAc with $Co(acac)_2$ and n-BA with Co(salen) complex (Table 8, entry 4).[257] Recently, the block copolymerization of VAc and MA controlled by R-Co^{III}(salen*) was possible, and the hydrolysis of the block copolymers led to the formation of highly stretchable poly(vinyl alcohol)-block-poly(acrylic acid) (PVOH-b-PAA) films.[262]

Substitution of the ligand functions were realized on Co^{II}(salen*) in order to evaluate their effect on the polymerization control of different monomers, such as St, MMA, or VAc (Table 8, entry 5).[258] In all cases, polymerizations revealed high dispersity values (1.65−2.4), indicating that irreversible termination reactions were prevalent. In the case of St, polymerization at 120 °C using Co^{II}(salen*) complexes bearing different substituents (R_1 = tBu and R_2 = tBu, NO_2, OMe, NMe_2) showed a good agreement between theoretical and experimental molar masses for the less electron-rich complexes Co(salen*)^{tBuNO_2} and Co(salen*)^{tButBu}. However, deviations were noticed with the more electron-donating OMe and NMe_2 R_2 substituents in Co(salen*)^{tBuOMe} and Co(salen*)^{tBuNMe_2} complexes. Although a higher level of control was noticed for the Co(salen*)^{tButBu}, reaction kinetics revealed a stagnation of M_n, and NMR analysis showed olefin-terminated polymers, both factors indicating a CCTP mechanism under these conditions.

Aside from Co(salen) complexes, Mc Neil et al. studied the efficiency of various β-ketoiminate cobalt(II) complexes for the VAc polymerization (Table 8, entry 6).[259] The influence of the steric hindrance and the electronic properties of the ligands on the control of the polymerization were investigated. A competition between CMRP and CCTP was noticed, but the latter prevailed at higher temperature. Subsequently, a novel square planar Et-Co^{III}(β-ketiminato) complex was synthesized from triethylborane and Co^{II}(β-ketoiminate), isolated, and tested in polymerization of MA at 50 °C with an efficient control (Table 8, entry 7).[260]

Recently, Peng et al. synthesized a cobalt(II) bipyridine bisphenolate (Co^{II}(BpyBph) for the CMRP of VAc, MA, AN, NVP, N-isopropylacrylamide (NIPAM), and St (Table 8, entry 8) with good control of the polymerizations.[261] The calculation of equilibrium constant of the C−Co cleavage during the polymerization demonstrated a DT mechanism in the case of VAc and RT process for MA.

6. ORGANOCOBALT(III) COMPLEXES BEARING BIS(ACETYLACETONATE)-TYPE LIGANDS

The C−Co bond strength of R-Co^{III} is in close relationship with the ligand environment of the cobalt. Indeed, nitrogenrich ligands, such as porphyrin (N_4) or glyoximes (N_2O_4), provide a higher stability to the R-Co^{III} complexes. On the other hand, bis(acetylacetonate) ligands (O_4) generally confer to R-Co^{III} a lower BDE.[169] This particular reactivity has a crucial influence in radical polymerization mediated by RCo^{III}(acac)$_2$, especially in the case of less-activated monomers (LAMs) such as vinyl esters or ethylene.

6.1. SYNTHETIC ROUTES

Due to their low C−Co bond strength, R-Co^{III}(acac)$_2$ compounds are extremely challenging to prepare and to purify, in contrast to R-Co^{III}(por) and R-Co^{III}(sal), which are more stable. Until now, only two R-Co^{III}(acac)$_2$ compounds have been reported, with different R groups: one is composed of a short poly(vinyl acetate) chain (four VAc units on average) as R group (Scheme 45a),[44] and the other is made of a chloromethyl or bromomethyl moiety (Scheme 45b).[263] Both compounds were prepared by radical pathways as discussed below.

OligoPVAc-$Co^{III}(acac)_2$ was prepared by reacting $Co^{II}(acac)_2$ with V70 in excess of VAc at 40 °C. V70 decomposed into the corresponding radicals that added a few VAc units. The short growing PVAc radicals were then rapidly trapped by $Co(acac)_2$(used in large excess compared to V70) to produce the corresponding R-$Co^{III}(acac)_2$(Scheme 46).[44]

The formation of XCH_2-$Co(acac)_2$ (X = Br or Cl) was conducted through another radical process involving $Co(acac)_2$, a radical source (AIBN or V70), a silane (tris(trimethylsilyl)silane, or TTMSS), and a dihalogenated solvent (CH_2X_2) (Scheme 47).[263] TTMSS was used as a radical reducing agent for its propensity to radical dehalogenation reactions of halogenated compounds. The reaction of tertiary alkyl radicals (generated by thermal decomposition of AIBN or V70) with TTMSS formed tris(trimethylsilyl) radicals ($(Me_3Si)_3Si^\bullet$) by hydrogen abstraction. Halogen abstraction from CH_2X_2 promoted by the silyl radicals provided halomethyl radicals ($XCH_2^\bullet$) that were then rapidly trapped by $Co(acac)_2$ to give XCH_2-$Co(acac)_2$.

6.2. REACTIVITY

Concerning the strength of C−Co bond of R-$Co^{III}(acac)_2$, their enthalpy of formation have been evaluated by DFT calculations.[44,264] Therefore, although these values are qualitative, trends can be identified, such as the effect of the addition of ligands on the C−Co strength. The values listed in Table 9 have been calculated from the difference of enthalpies between the R-$Co^{III}(acac)_2$ square pyramidal structure and the radical $R^\bullet$, with a tetrahedral coordination geometry for $Co(acac)_2$. In this particular case, a change of spin is associated with this bond rupture.[7]

As model of oligoPVAc-$Co^{III}(acac)_2$ (Scheme 45a), $-CH(OOCCH_3)(CH_3)$ was chosen as alkyl group of R-$Co^{III}(acac)_2$ for the calculation of BDEs by DFT.[264] The optimized geometry of this model compound revealed that the carbonyl group of the acetate substituent filled the sixth coordination position at Co^{III}, yielding the octahedral complex (Table 9, entry 1). This five-membered ring stabilized the C−Co bond by over an additional 6 kcal·mol^{-1} (BDE = 17.3 kcal·mol^{-1}) compared to R-Co^{III} without this intramolecular coordination (BDE = 11.1 kcal·mol^{-1}). When a − $CH_2CH_2(OOCCH_3)$ group is linked to $Co(acac)_2$ (resulting from the head-to-head addition of VAc to $Co(acac)_2$), a six-membered ring chelation with the $Co(acac)_2$ complex is formed with a BDE value of 18.3 kcal·mol^{-1}. The C−Co bond of the two isomers were demonstrated to be labile at 30 °C (Table 9, entry 2).

In the presence of coordinating molecules such as DMF or DMSO, DFT calculations, associated with X-ray analyses showed that these molecules broke the intramolecular coordination of the carbonyl group of acetate in the 5membered ring chelate [$(acac)_2Co$-$CH(OOCCH_3)(CH_3)$] with the formation of $(L)(acac)_2Co$-$CH(OOCCH_3)(CH_3)$ species, with L in axial position. This coordination of the cobalt complex changed its reactivity. As a rule, the C−Co bond of $Co(acac)_2$-$CH(OOCCH_3)(CH_3)$ was weaker with DMSO (BDE = 9.9 kcal·mol^{-1}) or DMF (BDE = 14.1 kcal· mol^{-1}) (Table 9, entries 3 and 4).[265] The same observation was made with pyridine or water.[266]

The photolytic cleavage of the C−Co bond of oligoPVAc$Co^{III}(acac)_2$ was demonstrated by electron spin resonance spin-trapping experiments under UV irradiation (λ > 320 nm).[267]

Although no DFT calculation was made on $XCH_2Co(acac)_2$ (X = Br or Cl), their use in polymerization (see section 6.4) has provided evidence that halomethyl radicals were easily produced at 30 °C.

6.3. ORGANIC REACTIONS

Most of the papers involving $Co(acac)_2$ in radical organic reactions concern the catalytic role of the Co(II) center for hydrofunctionalization of olefins. A recent review has been published on the main reactions involving $Co(acac)_2$ complexes.[10] As one of the leading group in the $Co(acac)_2$based HAT reactions, Mukaiyama et al. investigated the hydration of olefins using different types of $Co(acac)_2$ derivatives (Scheme 48A).[249,269,270] During this reaction, molecular oxygen and silane were used as the main reagents. R-Co^{III} species are intermediates created during the addition of the alkene (Scheme 48B). Nojima's group notably demonstrated the validity of this type of mechanism by using either alkyl-Co^{III}(acac) complex and alkylperoxo-Co^{III}(acac) for a similar reaction, namely the triethylsilylperoxidation of alkenes with molecular oxygen and triethylsilane. In both cases, the cobalt catalyst led to the formation of hydroxylated product.[271] Mukaiyama's group developed a series of reactions on alkene (Scheme 48C), notably hydration (1),[35,269] hydroperoxidation (2),[272] formation of ketones from vinylsilanes (3),[273] oxidative cyclization into furan derivatives (4)[274] and the formation of βhydroxy nitriles, esters, and amides by coupling reaction between alkenes and aldehyde (5).[275]

Recent works by Herzon's group have been published on HAT reaction using $Co(acac)_2$, silane, and tert-butyl-hydroperoxide. He developed various selective HAT reactions, such as the hydrogenation of alkenyl halides to alkyl halides,[276] or the reduction[277] or the hydropyridylation of alkenes.[278] As representative example, the hydrogenation of 2-chloroallyl 4methoxybenzoate into 2-chloropropyl 4-methoxybenzoate showed a yield close to 80% (Scheme 48C, compound 6).[276] Recently, Wan et al. constructed β-ester-γ-amino ketones by an innovative tandem process involving $Co(acac)_2$, tert-butyl hydroperoxide, a tertiary amine, and a diazo compound following the simplified mechanism represented in Scheme 49.[279] Briefly, this process started with the in situ formation of a carbene radical by reaction of $Co(acac)_2$ with the diazo compound, and then the addition of α-aminoalkyl radical provided the corresponding organocobalt intermediate. The homolytic C−Co bond splitting of this compound yielded the carbon-centered radical that added to styrene to form the more stabilized benzyl radical that coupled to the tert-butoxy radical. Finally, the so-formed peroxide intermediate underwent a Kornblum−DeLaMare reaction to yield the β-ester-γ-amino ketone in a one-pot process.

6.4. POLYMERIZATIONS

During these past 15 years, controlled radical polymerizations driven by R-$Co^{III}(acac)_2$ were pioneered and largely developed by Debuigne and Detrembleur which found numerous potential applications in nanoelectronics, energy,[280] and biomedicine.[8] Due to the high lability of the C−Co bond of R-$Co^{III}(acac)_2$ complexes, and at the polymer chain-end of the dormant species, LAMs have a high propensity to be controlled by these complexes (Scheme 50). Vinyl esters,[44,281−290] ethylene,[9,291,292]

1-octene,[291,293] perfluorohexylethylene,[294] vinyl chloride,[295] vinylidene fluoride,[296,297] Nvinylimidazolium salts,[298–304] and vinyl amides[305–310] (Scheme 50) were successfully controlled in homopolymerization and/or copolymerization with VAc.[8] The facility to tune the C−Co bond strength of R-Co^{III}(acac)$_2$ complexes or at the polymer chain end by the nature of the solvent, the addition of coordinating molecules, the temperature, or the use of UV light has enabled to further extend the process to the CMRP of MAMs (styrene,[311] acrylates,[267,284,312] acrylonitrile,[265,313–315] and fluorinated methacrylate[316]). Currently, oligoPVAcCo^{III}(acac)$_2$ is the most versatile R-Co^{III}(acac)$_2$ for controlling a large diversity of monomers of different reactivity by CMRP.

The main monomers that can be controlled by R-Co^{III}(acac)$_2$, and the corresponding reaction conditions, are summarized in Table 10.

The Co(acac)$_2$-mediated radical polymerization was first implemented for the polymerization of VAc initiated by a conventional diazo free-radical initiator, V70, in the presence of Co(acac)$_2$ at 30 °C in the bulk (Table 10, entry 1).[283] After an induction period that corresponded to the time required for the in situ formation of oligoPVAc-Co^{III}(acac)$_2$ (Scheme 46), the polymerization started by C−Co bond cleavage followed by propagation. Co(acac)$_2$ imparts control to polymerization. An unprecedented high degree of control over the polymerization of VAc was reached with molar masses close to 100 000 g·mol^{-1} and low dispersity ($Đ = 1.33$). As all polymer chains contained a labile C−Co bond at the ω-chain end, this bond was exploited for the facile functionalization of the chain-end by radical pathways. The addition of spin-traps such as (functional) nitroxides (TEMPO derivatives) or propanethiol (PrSH) provided the corresponding terminated polymers (Scheme 51).[282] According to the same principle, fullerene (C_{60}) or carbon nanotubes were also employed as the radical spin traps, giving the corresponding fullerene or carbon nanotubes grafted by PVAc chains (Scheme 51).[317,318] When nitrones were employed, polymers were coupled with the introduction of an alkoxyamine at the middle of the chain. Functional nitrones were also employed to produce star- and H-shaped (co)polymers by derivatization of the alkoxyaminebearing polymers (Scheme 51).[319]

Under appropriate conditions, oligoPVAc-Co^{III}(acac)$_2$ could also initiate and control the radical polymerization of VAc in aqueous-based media. Indeed, in situ produced oligoPVAcCo^{III}(acac)$_2$ was successfully used for the CMRP of VAc in suspension in water to give PVAc beads with a high monomer conversion and a predictable molecular weight.[281] In miniemulsion conditions, the same R-Co^{III} provided PVAc latexes with a solid content up to 30 wt% in very short reaction time with a good control of the polymerization.[320] The successful copolymerization of ethylene or 1-octene with VAc was also reported using this bimolecular system (V70 and Co(acac)$_2$), although the content of 1-alkene in the copolymer was limited and polymerizations were slow (Table 10, entry 2).[291]

The labile C−Co bond at the polymer chain end was largely exploited for the synthesis of various block copolymers by the addition of a feed of another monomer. Reactivation of the chain end released the macroradical that initiated the controlled polymerization of the second monomer. For instance, the addition of N-vinylpyrrolidone (NVP) to a PVAc-Co(acac)$_2$ prepared by the V70/Co(acac)$_2$ binary system yielded the amphiphilic copolymer PVAc-b-PNVP (Table 10, entry 7).[305] Similarly, CMRP allowed the formation of PVAc-b-PAN and PVAc-b-PS copolymers (Table 10, entries 8 and 9).[311,313] All types of copolymers prepared by CMRP have been reviewed elsewhere.[7]

In contrast to cobalt porphyrins and cobaloximes, $Co(acac)_2$ is not prone to β-H abstraction and is thus not appropriate for the preparation of macromonomers by CCTP of methacrylates. In addition, controlling the polymerization of methacrylates by CMRP is currently still challenging due to the weakness of the C−Co bond of the resulting alkyl-cobalt, even at room temperature. Nevertheless, Ameduri et al. recently demonstrated that the copolymerization of tert-butyl-2trifluoromethacrylate (MAF-TBE) with VAc was possible at 40 °C by the binary system, leading to the controlled alternated fluorinated copolymers (Table 10, entry 6).[316]

In order to bypass 2,2′-azobis(4-methoxy-2,4-dimethylvaleronitrile) (V70) as the initiator in the CMRP of VAc mediated by $Co(acac)_2$, Jerome et al. exemplified the use of redox initiators composed of ascorbic acid or citric acid as the reducer, and lauroyl peroxide (LPO) or benzoyl peroxide (BPO) as the oxidant (Table 10, entry 12).[321] Later on, some of these redox initiators were implemented for the CMRP of other vinyl esters, such as vinyl pivalate (VPv),[287] vinyl benzoate (VBz),[287] vinyl stearate (VS),[288] and vinyl laurate (VL)[288] (Table 10, entries 15 and 16). Another variant was to implement a combination of $Co(acac)_2$ with the peroxide without ascorbic or citric acid for the CMRP of VAc (Table 10, entry 12).[321] In this case, $Co(acac)_2$ had a double role, i.e., (i) as the reducer to activate the peroxide by redox reaction with the formation of the initiating radicals, and (ii) as the controlling agent by reversibly trapping the growing chains. In 2014, this concept was further extended by Detrembleur et al. for the CMRP of N-vinylimidazolium salts (VImX in water by the combination of $Co(acac)_2$ with tert-butyl hydroperoxide in water (Table 10, entry 17).[299] In 2019, Ameduri and Poli exploited this process for the controlled polymerization of VDF in dimethyl carbonate by using bis(tert-butylcyclohexyl) peroxydicarbonate as the oxidant at 60 °C. Chain-extension of PVDF-$Co(acac)_2$ by vinyl acetate was also possible, with the synthesis of PVDF-b-PVAc block copolymers (Table 10, entry 18).[297]

In 2012, Detrembleur et al. exploited the photolysis of the C−Co bond of R-$Co^{III}(acac)_2$ for the CMRP of n-butyl acrylate (nBA). As the C−Co bond at the PnBA chain end was very labile at 30 °C, its polymerization could only be controlled at 0 °C. The use of photoinitiators (e.g., AIBN or 2,2-dimethoxy-2-phenylacetophenone, I651) was here highly attractive to initiate the polymerization at this temperature.[267] For the first time, the nBA polymerization was controlled with a binary system up to very high molar masses ($>4 \times 10^6$ g· mol^{-1}) with low dispersities using $Co(acac)_2$ as controlling agent (Table 10, entry 10). The photoinitiator as well as the irradiation time had to be appropriately chosen to reach acceptable initiator efficiencies while maintaining an optimal control over the polymerization.[267] The same team also exploited the photoactivation of azo-initiators for the precision synthesis of various poly(N-vinyl amides)[308,322] (Table 10, entry 11), providing polymers bearing a hydroxyl group and $Co(acac)_2$ at the α- and ω-chain ends, respectively. Zhu et al. described the photo-CMRP of VAc and MDO using (2,4,6trimethylbenzoyl)diphenylphosphine oxide (TPO) as photoinitiator and $Co(acac)_2$ as control agent, providing degradable copolymers (Table 10, entries 13 and 14).[286,323]

The effect of substituents on the acac ligand of the cobalt complex was investigated by Matyjazewski et al. for the (co)polymerization of VAc and n-BA initiated by V70 at 30 °C (Table 10, entry 3).[284] $Co(acac)_2$ and $Co(F3\text{-}acac)_2$ successfully mediated the radical polymerization of VAc, while complex

$Co(F6\text{-}acac)_2$ did not provide any control to the polymerization. Only the $Co(acac)_2$ was able to control the copolymerization of nBA with VAc (Table 10, entry 3). Homopolymerization of VClAc was difficult to control with these three complexes, but $Co(F3\text{-}acac)_2$ provided the best results.[285] The same improvements with $Co(F3\text{-}acac)_2$ compared to the two other complexes were realized when copolymerizing VClAc with VAc (Table 10, entry 3).[285] Later on, the substitution of the methyl groups of acac ligands by tert-butyl ones was not beneficial to the CMRP of VAc (Table 10, entry 4) due to increased steric hindrance of the cobalt complex.[324]

Aside from the already-developed structure of acac ligands, derivatives have been investigated in CMRP, as noticed in Table 10, entries 18−20.[325−327] Very recently, Poli et al. prepared $Co^{II}(OPN)_2$ (OPN = deprotonated 9-oxyphenalenone) and evaluated its activity in the polymerization of VAc at 30 °C using V70 as the initiator (Table 10, entry 19).[325] For the first time, the authors demonstrated the occurrence of a CCTP mechanism for the VAc polymerization, rather than a CMRP one. PVAc chains terminated by an unsaturated double bond were produced. A complex based on $Co(SAL)_2$ (SAL = 2-formylphenolato or deprotonated salicylaldehyde) was also explored for the formation of well-defined copolymers based on tert-butyl-2-trifluoromethacrylate (MAF-TBE) with VAc (Table 10, entry 20).[326] In contrast to 9-oxyphenalenone (OPN) ligands, this study did not evidence the occurrence of CCTP.

Finally, 1,3-bis(2-pyridylimino)isoindolatocobalt(II) (Co^{II}(Bpi)) complex was used in the CMRP of acrylates (nBA, MA) with an external radical source, namely V70, at 60 °C in benzene (Table 10, entry 21).[327] Different versions of ligands were synthesized and tested in polymerization with close results in term of control (Table 10, entry 21). The in situ formation of the R-Co^{III}(bpi) complex with R = $-C(CH_3)(CH_2C(CH_3)_2OCH_3)CN$ (coming from decomposition of V70) was deduced from MALDI-TOF analysis of the polymer, with no β-H abstraction being observed (Scheme 52).

For all these binary systems, an induction period (up to a few hours) was observed that was the time required to in situ form the R-Co^{III} complex. In order to overcome this limitation, R-$Co^{III}(acac)_2$ complexes were synthesized and purified before being used for initiating and controlling the polymerizations (Scheme 25).[44] OligoPVAc-$Co^{III}(acac)_2$ was demonstrated to be very efficient for controlling a large diversity of LAMs and MAMs, including vinyl esters (VAc,[44] VLev, and VTr[289,290]), AN,[314] acrylates (n-BA and EGA),[312,328] vinyl chloride (VC),[295] vinyl amides (NVP, NVA, NMVA, and NVCL),[306,307,329,330] and N-vinylimidazolium salts (VImX)[298−304] (Table 11, entries 1−9). In 2014, the challenging controlled copolymerization of ethylene (E)[9,292] with LAMs (E, NMVA) and MAMs (AN) was made possible, as well as the copolymerization of 1-octene (Oct) with VAc[293] (Table 11, entries 10 and 11). Perfluorohexylethylene (PFHE)[294] was also successfully copolymerized with VAc (Table 11, entries 12), and the homopolymerization of vinylidene fluoride (VDF)[296] was controlled at a level that could not be achieved by any other controlled radical polymerization technique (Table 11, entry 13). Also, the random copolymerization of CO_2-sourced (DMMDO)[331] or plant oil-derived (AODMC, AODMC, ODM10U, M10U, and AMC)[332] olefins with VAc was recently reported (Scheme 50 and Table 11, entries 14 and 15). The low polymerization temperature (40 °C) enabled us to limit the occurrence of side reactions, such as transfer reactions, that are commonly observed with many plant-oil derived allylic monomers[332] that do not homopolymerize. Well-defined poly(vinyl amineco-vinyl alcohol) copolymers with precise composition were also prepared via at two-step process based on the statistical cobalt-mediated radical copolymerization of NVA and VAc followed by hydrolysis of the pendant amide and ester functions.[330]

The polymerizations mediated by oligoPVAc-$Co^{III}(acac)_2$ were demonstrated to be versatile and robust and could be implemented in the bulk,[44] in solution, in aqueous media,[299,304] or in supercritical carbon dioxide.[333] Coordinating solvents were demonstrated to affect the rate and control of the polymerizations by complexation of the cobalt complex at the polymer chain-end and also $Co(acac)_2$ that was released during an activation cycle.[266] Other important parameters were also identified to influence the CMRP process such as the presence of hydrogen bonding or intramolecular coordination of the last monomer unit with the cobalt at the polymer chainend. All these important factors have been comprehensively reviewed in a recent article.[8]

A novel macromolecular engineering tool, the cobaltmediated radical coupling (CMRC), was also developed to promote the quantitative coupling of two polymers end-capped by $Co(acac)_2$ (Scheme 53) via the addition of conjugated dienes, typically isoprene or butadiene, at room temperature.[314,334,335] In this process, the growing chain released by the C−Co bond cleavage added to the diene to form allyl radicals. As the propagation rate constant of the diene is extremely low at room temperature, the diene did not polymerize. Moreover, the recombination of these allyl radicals with $Co(acac)_2$ was disfavored due to the very low C−Co bond strength ($1\ kcal{\cdot}mol^{-1}$).[335] Therefore, as all chains were rapidly bearing an allyl radical at their ω-end, the coupling of two allyl radicals terminated chains rapidly occurred. As main advantages, CMRC of α-functional polymers yielded telechelic polymers,[322] whereas CMRC of AB diblock copolymers furnished symmetrical ABA triblock copolymers.[9,296,300,303,309,336–338]

In 2015, XCH_2-$Co(acac)_2$ (X = Br or Cl) opened new perspectives for the chain-end functionalization of well-defined polymers based on LAMs, such as VAc and VEtImBr (Table 11, entry 16).[263] For instance, $BrCH_2$-$Co(acac)_2$ allowed the preparation of unprecedented α-functional PVAc and ethylene/vinyl acetate copolymers (EVA) that were coupled by CMRC to provide the corresponding telechelic polymers (Table 11, entry 17). They were then further derivatized to prepare novel cyclic polymers (Scheme 54).[339]

By the precise control of the macromolecular parameters and the functionality of the (co)polymers, the CMRP technique mediated by R-$Co^{III}(acac)_2$ gave access to an impressive diversity of novel polymers with many potential applications. To cite only few of them, (i) PVAc-b-PAN block copolymers were converted into gold-loaded carbon nanoparticles for potential application as catalysts,[315] nanoporous carbon fibers,[340] or micelles loaded with silver nanoparticles for antibacterial purposes;[341] (ii) PVAc-co-PNVP-$Co(acac)_2$ copolymers were used as reactive stabilizers for polymerizations in aqueous media;[310] (iii) PVAc-modified carbon nanotubes were employed for the preparation of polymer nanocomposites with some electrical conductivity;[318] (iv) poly(vinyl imidazolium salts) bearing polyphenols were tested for long-lasting smart coatings but also as redox-active materials for battery purposes[280,303] etc.[8]

Except for $VitB_{12}$, which is a natural nontoxic compound, most other cobalt complexes present some toxicity that depends on several factors, such as the ligand, the oxidation state, etc.[342] Nevertheless, efficient cobalt removal procedures have been implemented even for the purification of polymers synthesized by CMRP[282] allowing their use in biomedical applications. The purification procedure consists in irreversibly deactivating the polymer chains by the addition of a spin-trap, such as TEMPO, a thiol, or fullerene (according to reactions illustrated in Scheme 51), followed by removing the released cobalt complex by filtration onto silica or by dialysis. The polymers did not present any cytotoxicity after removal of the cobalt complex. For example, PVAc/C_{60} nanohybrids were hydrolyzed into water-soluble PVOH/C_{60} and exploited in photodynamic cancer therapy applications.[317,343] Also, welldefined cobalt-free poly(vinyl amine)s resulting from hydrolysis of poly(vinyl amides) formed by CMRP demonstrated excellent cell viability and high potential for gene transfection.[344,345]

7. CONCLUSIONS

Since the structure and the mode of action of vitamin B_{12}, which catalyzes many types of reactions, have been established, the research field involving organocobalt complexes (R-Co^{III}) has rapidly expanded. The controlled formation of a carboncentered radical by the C−Co bond cleavage is at the origin of all R-Co^{III} promoted radical reactions. This species reacts with various substrates such as radicals or carbon electrophiles and gives products in high yield and most often with a high selectivity. The low bond dissociation energy of the C−Co bond renders possible most reactions operating under mild experimental conditions, by gentle thermal treatment or light irradiation. The environment of the cobalt center, and thus the nature of its ligands, dictate the strength of this C−Co bond and the reactivity of R-Co^{III}. Well beyond catalyzing radical processes, R-Co^{III} are now able to achieve excellent stereochemical control and/or enantioselectivity during radical reactions, which constitutes a real breakthrough in the field of the construction of complex organic molecules. This high level of structural control is made possible by metallo-radical catalysis (MRC), developed by de Bruin and Zhang. Importantly, MRC behaves differently to most of the other radical processes promoted by R-Co^{III}. In MRC, the metalloradical, in situ formed by reaction of Co^{II} with a substrate, catalyzes all σ-bond-forming steps. The entire targeted organic molecule is therefore constructed on this metallo-radical, which explains the excellent stereocontrol observed with asymmetric ligands (of the porphyrin-type) that provide a confined and chiral nanospace around the cobalt active site. As Co^{II} is released at the end of the reaction, it is again involved in MRC and is therefore considered as a true catalyst. In contrast, for most of the other R-Co^{III} promoted radical reactions (including polymerizations), the homolytic splitting of the C− Co bond of R-Co^{III} generates a carbon-centered radical that initiates the cycle with the formation of a C−C bond and the corresponding radical adduct. The released Co^{II} then stops the cycle following various elimination pathways discussed in this Review. Therefore, the construction of the organic molecule does not occur at the metal center, which is in sharp contrast to MRC. Whether Co^{II} is a catalyst or not depends on the reaction that is considered.

Importantly, polymer chemists were inspired by the pioneering works in R-Co^{III} radical promoted reactions for the precision synthesis of functional macromolecules. The common feature to all R-

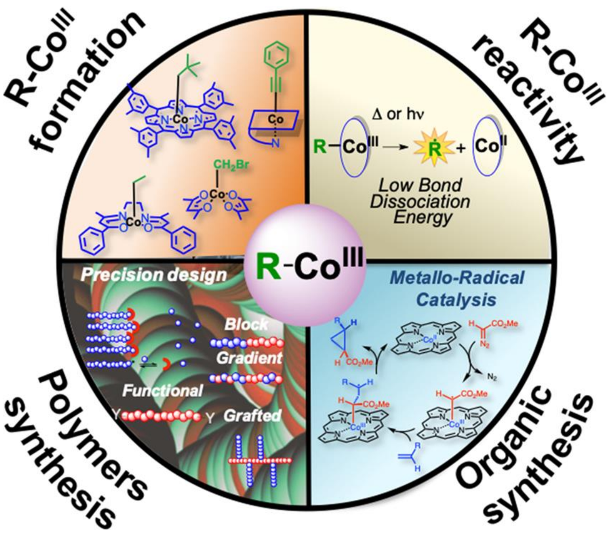
Co^{III}-based polymerizations is the initiation of the process by the carbon-centered radical released by the C−Co homolysis. The advent of the growing chains, and thus of the structure of the final polymer, however, is dictated by the nature of the cobalt ligand and of the monomer. Cobalt complexes with a high propensity to hydrogen abstraction provide macromonomers when the growing chains are prone to β-H abstraction (polymethacrylates for instance). Catalytic amounts of the cobalt complexes are required for the most efficient ones. This process, called catalytic chain-transfer polymerization (CCTP), is industrially implemented for coating applications. For monomers that are not prone to this reaction, the cobalt complex can reversibly trap the growing chains and control their growth. In this cobalt-mediated radical polymerization (CMRP) process, all polymer chains are end-capped by the cobalt complex. The C− Co bond can be cleaved "on demand" in a controlled manner to release the macroradical that can be involved in a multitude of radical reactions. This has been widely exploited to functionalize the chain-end of the polymers or to synthesize unprecedented well-defined (co)polymers of multiple architectures of the block, gradient, star, or cyclic type.

With all these breakthroughs in organic and polymer chemistries, the old notion that radical reactions are notoriously "uncontrollable" is clearly over. Although the pioneering works in synthetic organic chemistry have largely contributed to the implementation of R-Co^{III} in polymer design, both fields have rapidly evolved independently. By confronting them all in one Review, we aimed at stimulating cross-fertilization by suggesting some common challenges.

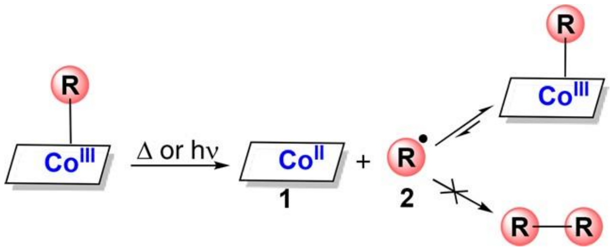
In the field of organic synthesis, the stereocontrolled and enantioselective radical reactions promoted by confining the reactive species in the close environment of asymmetric cobalt complex represent a huge potential to the challenging design of polymers with controlled tacticity. Similarly to reactions on small organic molecules, the cobalt complex might orient the addition of the vinyl monomer at the polymer chain- end, furnishing elusive stereoregular polymers of prime importance. In the field of polymerizations, the developments in CMRP have largely contributed to understand the conditions for the reversible formation of a C−Co bond based on the cobalt environment and on the monomer that is polymerized. Novel R-Co^{III}, either of low molar mass or of macromolecular type, were prepared and isolated, and their ability to initiate and control the polymerizations of a large diversity of monomers was evaluated. However, many of these R-Co^{III} were never tested in synthetic organic chemistry. As selected examples, RCo^{III} based on acetylacetonate (acac) ligands appear to be attractive candidates due to the multitude of R groups (possibly) available. Indeed, all synthetic organic reactions involving $Co(acac)_2$ are based on the in situ generation of RCo^{III}. We clearly foresee here the potential of the novel preformed R-Co^{III} for catalyzing novel organic reactions, where the R group will dictate the solubility and the reactivity of the complex.

The R-Co^{III}-promoted organic syntheses provide "small" molecules, most often produced by the addition of two reagents. In contrast, macromolecules consisting of the repetition of tens to a few thousands monomer units are prepared by R-Co^{III}-promoted polymerizations. These two fields now have to merge to enable the construction of molecules with a perfect control of the "one-by-one" incorporation of the reagents in order to produce sequencedefined molecules, ideally in a stereocontrolled manner. A challenge of this magnitude can only be addressed if both communities are sharing efforts and ideas.

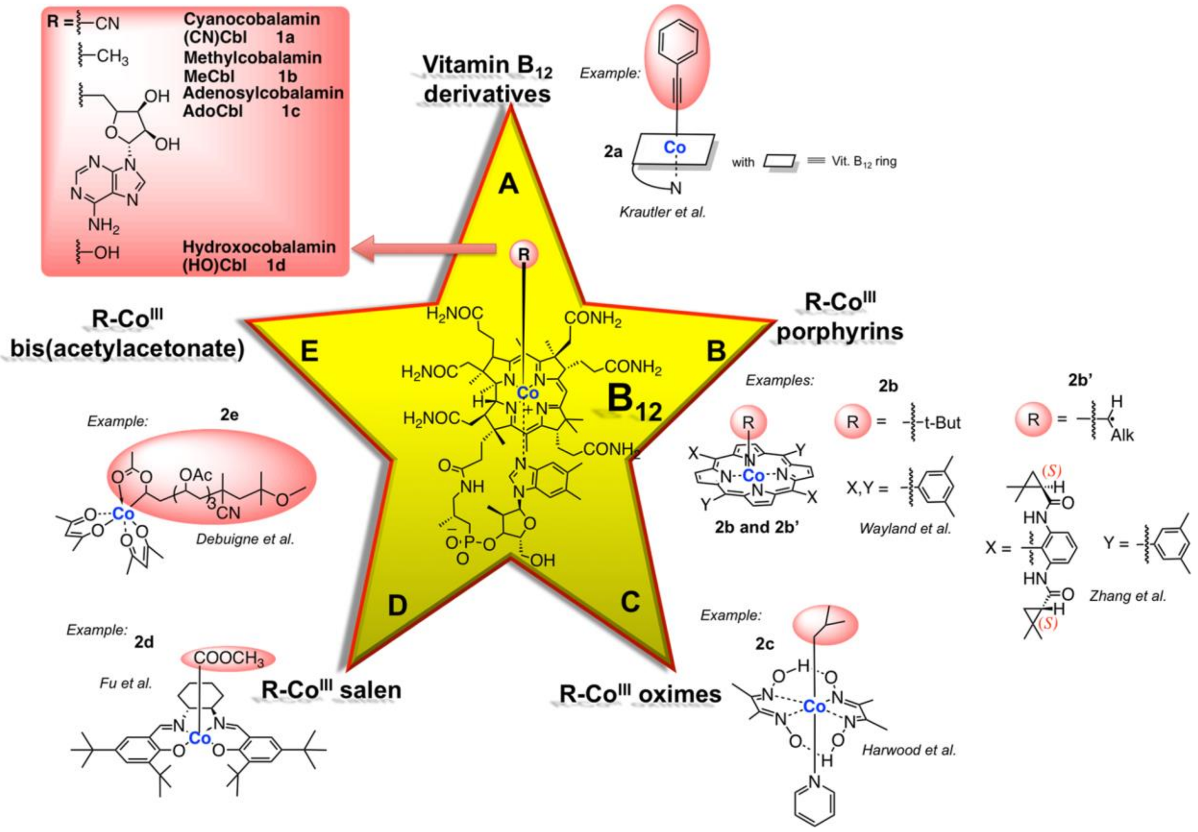
Scheme 1. *Overview of R-Co^{III} Chemistry and Applications*



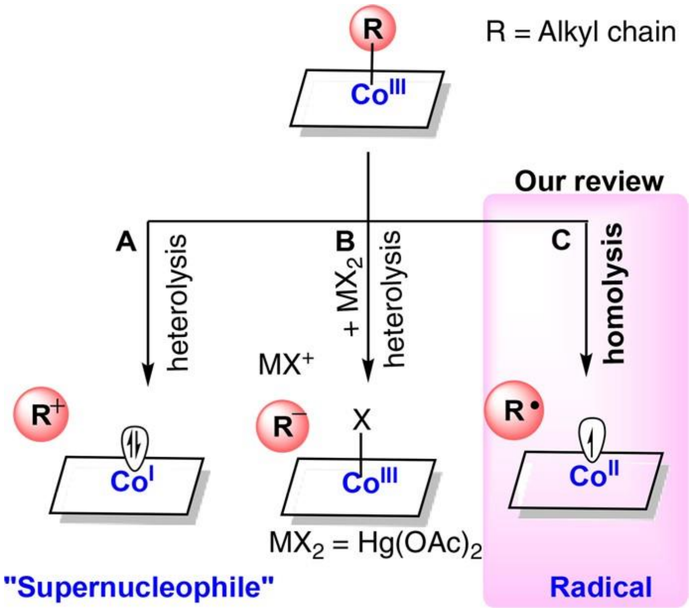
Scheme 2. *Persistent Radical Effect (PRE) with R-Co^{III} Complexes*



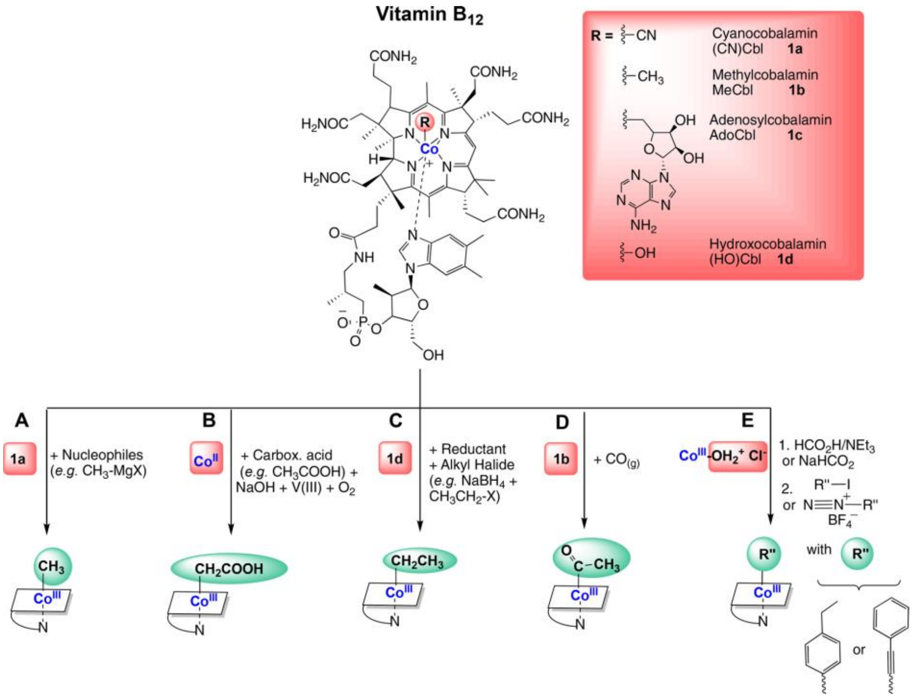
Scheme 3. *Overview of R-Co^{III} Families*



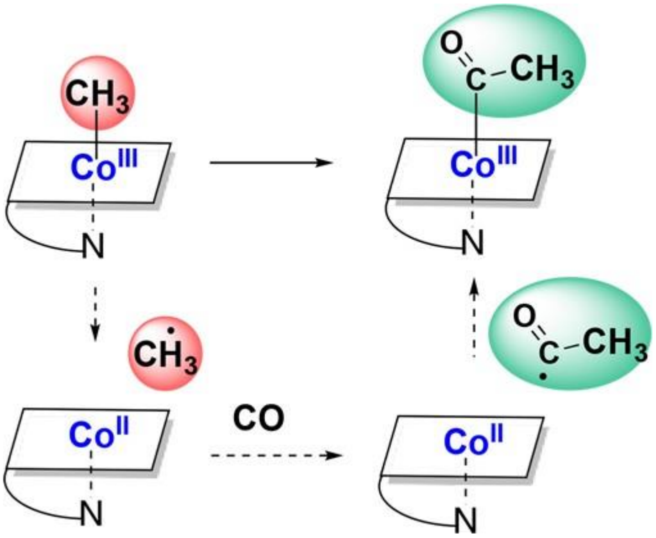
Scheme 4. *Mechanisms of C−Co Bond Dissociation of R-Co^{III}*



Scheme 5. *Main Synthetic Routes for R-Co^{III} from Vitamin B$_{12}$ Compounds*



Scheme 6. *Acetylation Radical Mechanism Pathway of MeCbl*



Scheme 7. *Radical Mechanism for the Synthesis of “Antivitamins B*$_{12}$*” Phenylethynylcobalamin Established by Kräutler*[59]

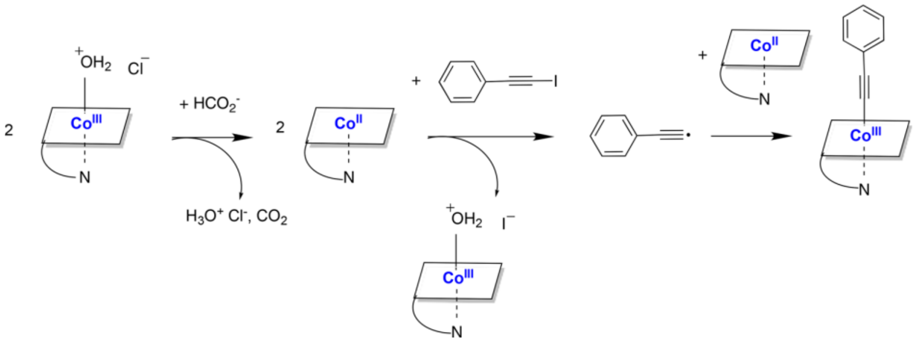
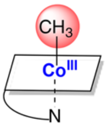
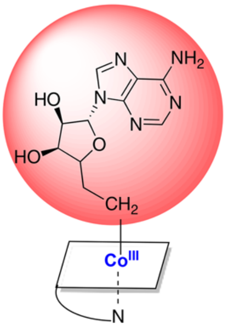
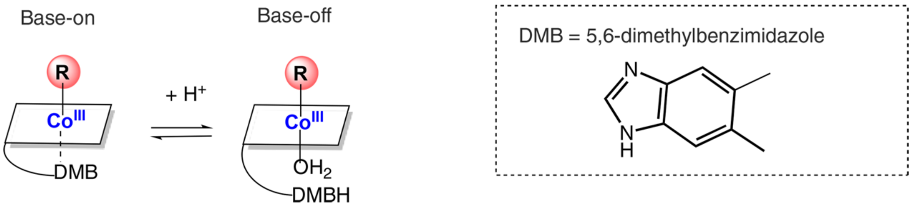


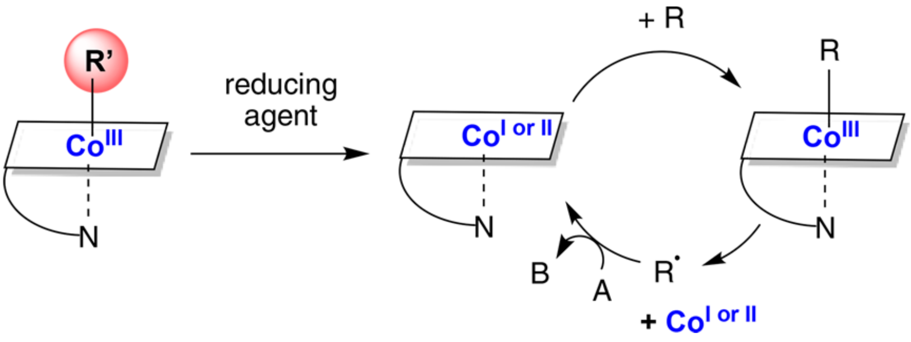
Table 1. *Bond Dissociation Energies of CH_3-Cbl and Ado-Cbl*

R-Co Type	Homolysis pathway	Conditions	Method of BDE determination	BDE (kcal mol^{-1})	Ref.
*CH_3-Cbl (**1b**)*  	Thermolysis	120-140 °C in ethylene glycol	Kinetic of trapping radicals with TEMPO	37 ± 3	67
	Photolysis	10-30 °C in water	Pulsed photoacoustic calorimetry	38.9 ± 5	65
		10-30 °C in water + HCl (0.05M) [base-off]		42.0 ± 5	65
	Photolysis	-2-40 °C in water + phosphate buffer (pH ~7)	Pulsed photoacoustic calorimetry	36 ± 4	69
*Ado-Cbl (**1c**)*  	Thermolysis	84-103 °C in water	Kinetic of trapping radicals with Co(dmgH)$_2$	26 ± 2	64
		85-110 °C in water	Kinetic of trapping radicals with TEMPO	30 ± 2	70
		105-130°C in water + phosphate buffer (pH ~ 7) [base-off]		34.5 ± 1.8	68
	Photolysis	10-30°C in water	Pulsed photoacoustic calorimetry	30.8 ± 4	65

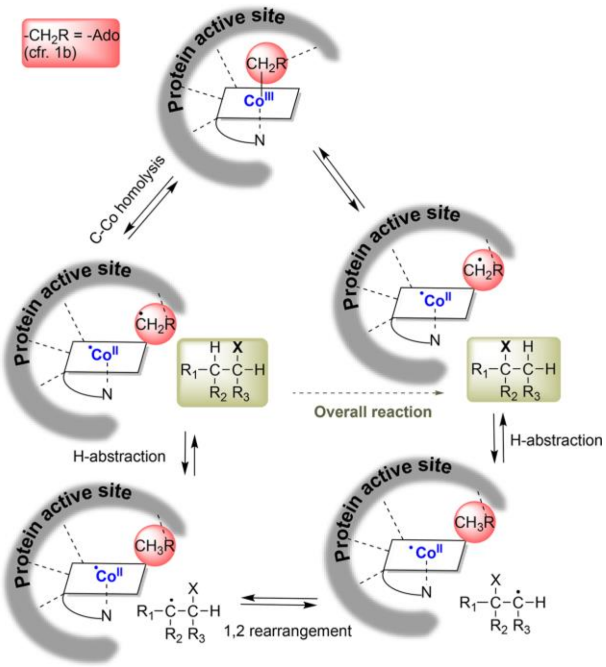
Scheme 8. *Equilibrium between Base-On and Base-Off Forms of Alkyl-cobalamin*



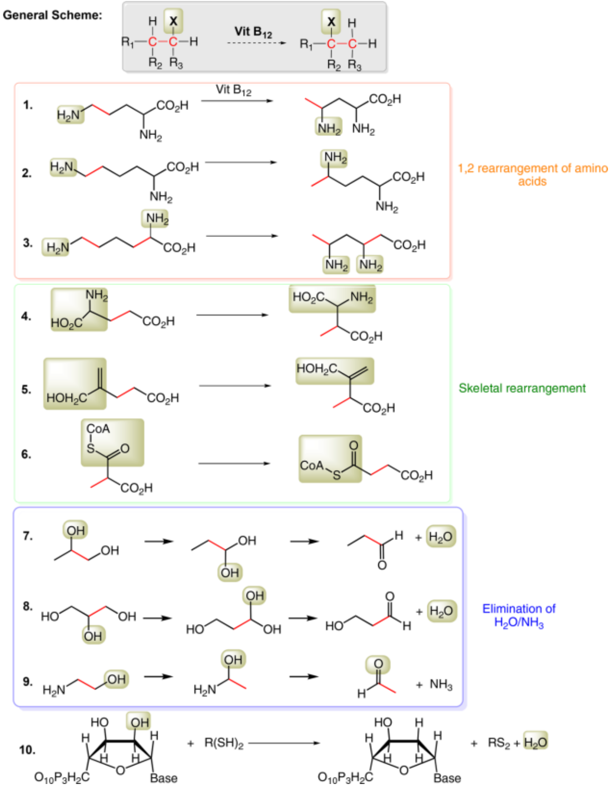
Scheme 9. *General Mechanism Using Reduced VitB$_{12}$ as Catalyst*



Scheme 10. *Role of the Organocobalamin in the Isomerization Mechanism Conducted by AdoCbl-Dependent Isomerase*[74,a]

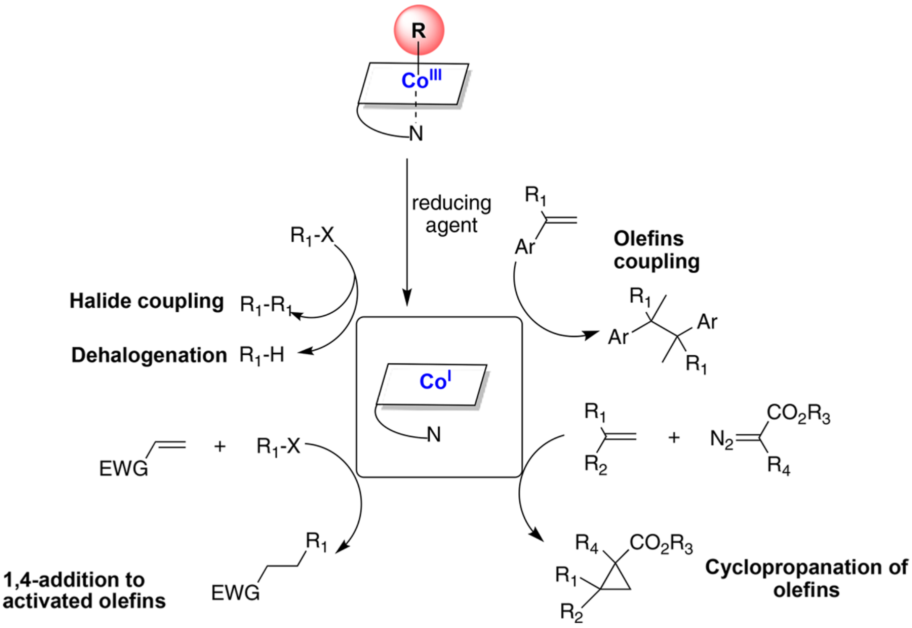


Scheme 11. *Enzymatic Rearrangements Catalyzed by AdoCbl*



[a] X, R_1, R_2, and R_3 substituents are listed in Scheme 11.

Scheme 12. *Main VitB$_{12}$-Catalyzed Radical Reactions*



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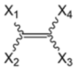
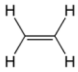
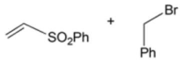
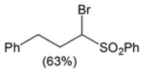
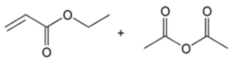
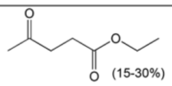
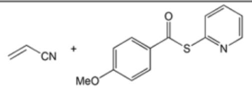
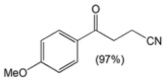
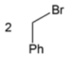
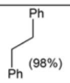
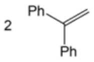
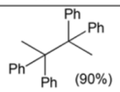
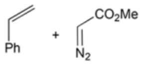
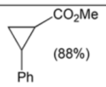
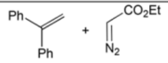
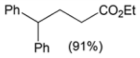
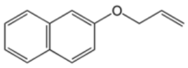
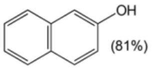
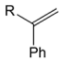
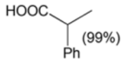
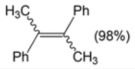
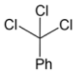
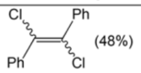
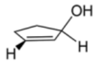
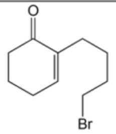
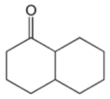
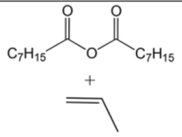
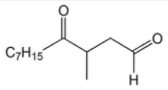
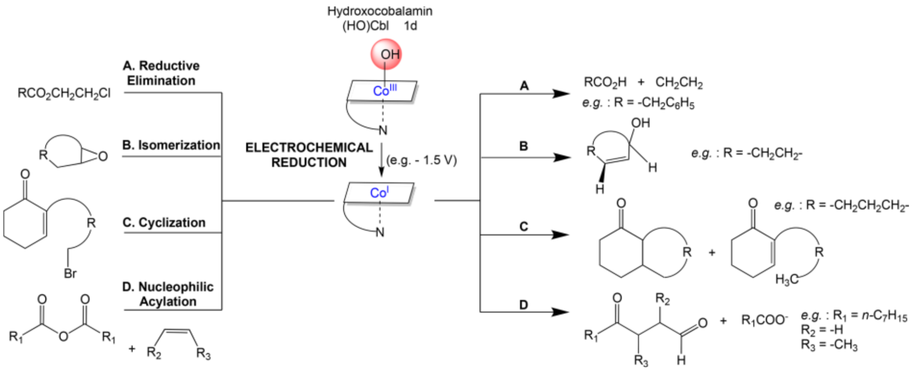
Status : Postprint (Author's version)

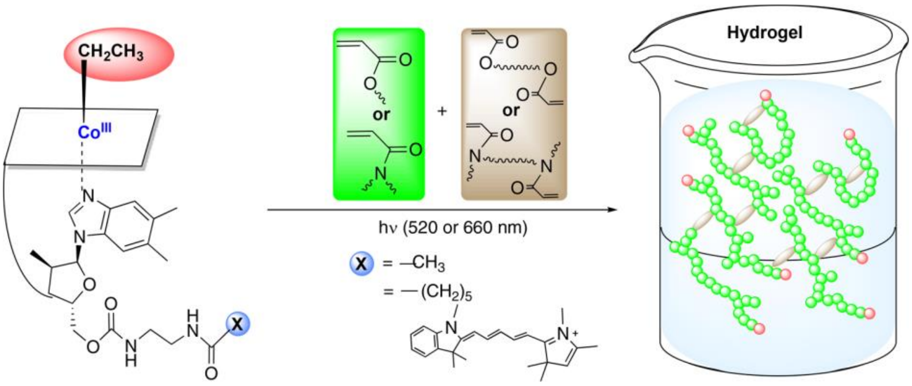
Table 2. *Examples of Organic Reactions Involving a Reduction of the Co^{III} Complex*

Entry	Reaction type	VitB$_{12}$ and Reducing agent	Reactants	Product (yield)	Cond.	Ref.
1	Dehalogenation	(CN)Cbl + Ti(citrate)			rt	79–82
2	Atom Transfer Radical Addition	(CN)Cby(OMe)$_7$ + NaBH$_4$			90 °C (300 MW)	91
3	Acylation of Activated Olefins	(H$_2$O)Cbl			-1V hυ	92
4	Acylation of Activated Olefins	(CN)Cby(H$_2$O) + Zn, NH$_4$Cl			hυ	93
5	Dimerization of Arylhalide	B$_{12}$ + Ti(III)citrate			rt	87
	Olefin Coupling					
6	Cyclopropanation of Olefins	(OH)Cbl			80°C	94
7	Alkylation of Olefins	(CN)CbEster + Zn, NH$_4$Cl			hυ	95
8	Deprotection of (Allyloxy)arenes	(CN)Cbl + TiO$_2$			hυ MeOH	96
9	Reduction of Olefins	B$_{12}$-TiO$_2$		R = H or CH$_3$: dimer (82 and 79%) R= COOH  R = Br 	hυ	88
10	Oxygenation of Trichlorinated compounds	B$_{12}$-TiO$_2$			hυ, N$_2$ MeOH	97
				Ph—CO$_2$Me (99%)	hυ, air MeOH	
				Ph—C(O)N(Et)$_2$ (98%)	hυ, air MeOH + 30 mol NEt$_3$	
11	Reductive Elimination	(OH)Cbl	$C_6H_5CH_2COOCH_2CH_2Cl$	$C_6H_5CH_2COOH$ (98%) + CH_2CH_2	rt -1.5V	100
12	Isomerization	(OH)Cbl		 (78%)	rt + Zn/NH$_4$Cl or -1.1V	101
13	Cyclisation	(OH)Cbl		 (95%)	rt -1.9V	107
14	Nucleophilic acylation	(OH)Cbl		 (80%)	hυ, rt -0.95V	108

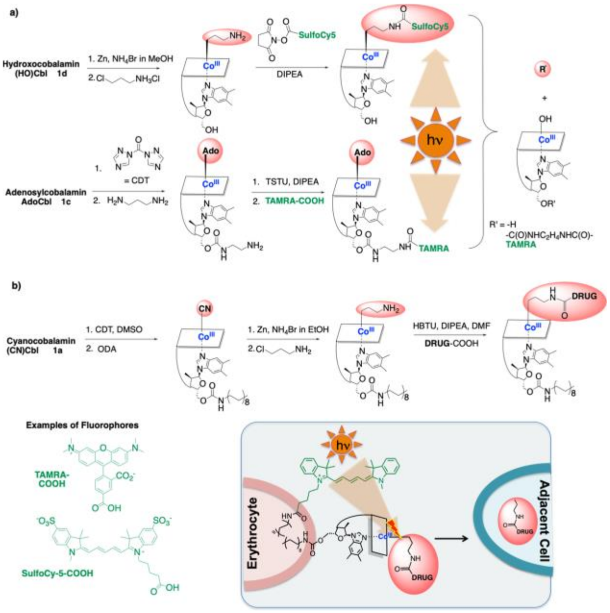
Scheme 13. *Electrochemically Reduced VitB$_{12}$-Catalyzed Radical Reactions*



Scheme 14. *Light-Induced Activation of C−Co Bond of Ethyl-cobalamin Derivatives and Formation of Hydrogel*



Scheme 15. *Reactions of Photocleavable R-Cobalamin(III) for Phototherapy*[a]



[a]Abbreviations: TSTU and HTBU, N,N,N′,N′-tetramethyl-O-(N-succinimidyl)uronium tetrafluoroborate and hexafluorophosphate; DIPEA, N,Ndiisopropylethylamine; CDT, 1,1′-carbonyl-di-(1,2,4-triazole); ODA, octadecylamine.

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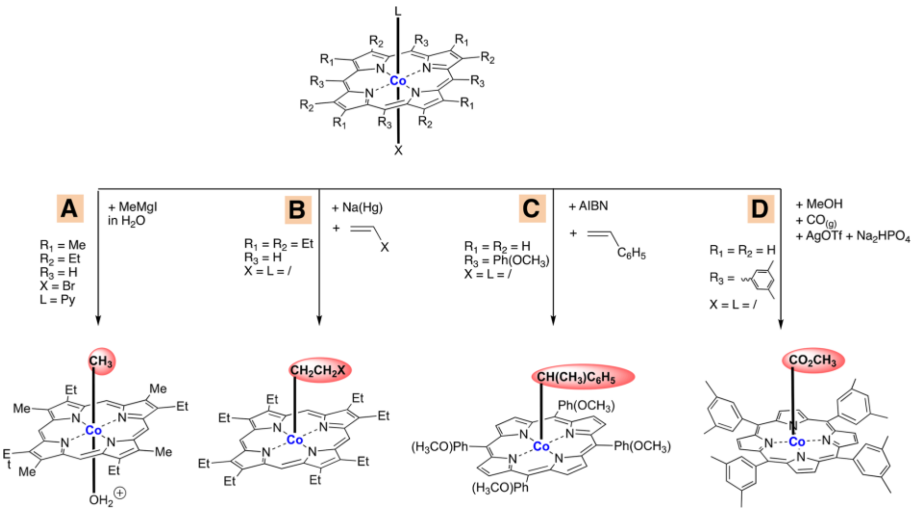
Scheme 16. *Routes to Synthesis of R-Co^{III} Complexes from Cobalt Porphyrin Compounds*



Scheme 17. *Formation of (TAP)Co^{III}-R by Reaction of an Olefin with a Radical Initiator*

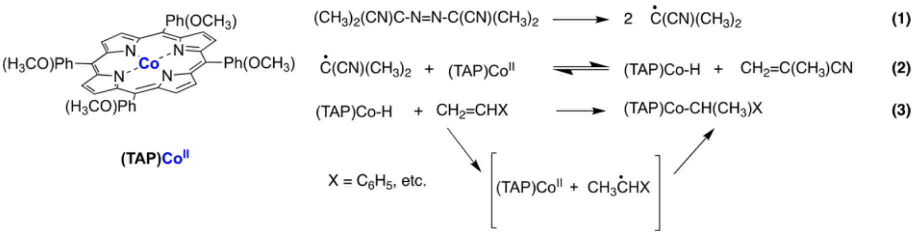
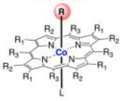
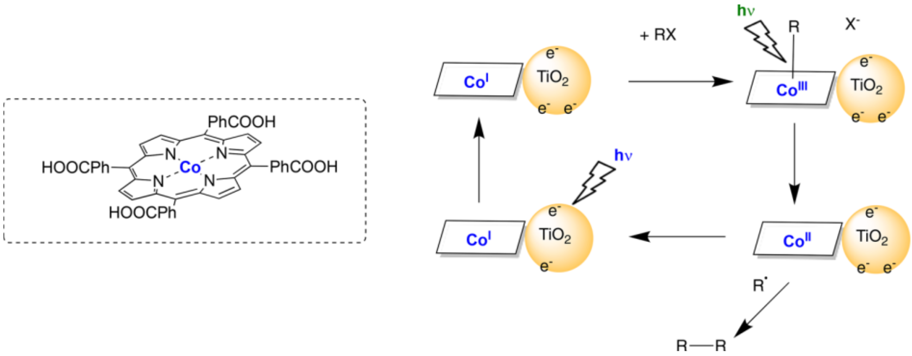


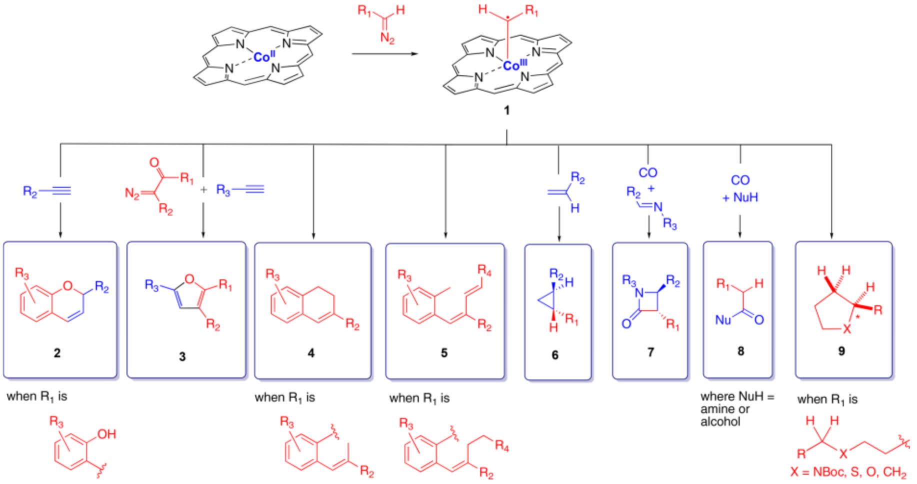
Table 3. *Bond Dissociation Energies of R-Co(por)*

R-Co Type	Entry	Homolysis pathway	Co Substituents (R and L)	Ring Substituents (R_1, R_2, R_3)	Conditions	Method of BDE determination	BDE (kcal mol^{-1})	Ref.
R-Co(por)L 	**1**	Thermolysis	R = -CH_2Ph and **L = -PBu_3** R = -CH_2Ph and **L = -PPh_3**	R_1 = R_2 = Et, R_3 = H	63 °C in pyridine	Kinetic of trapping radicals with TEMPO	29 24	126
	2	DFT	R = **-CH(CH_3)CN** and L = /	R_1 = R_2 = H, R_3 = C_6F_5 R_1 = R_2 = H, R_3 = -Ph(Me)$_3$	/	DFT	22 24	127
	3	DFT	R = **-CH(CH_3)OAc** and L = / R = **-CH(CH_3)C(O)O*t*Bu** and L = / R = **-CH(CH_3)C(O)OMe** and L = /	R_1 = R_2 = H, R_3 = -Ph(Me)$_3$	/	DFT	24 14 18	127
	4	Thermolysis	R = **-CH(CH_3)Ph** and L = / R = **-C_5H_9** and L = /	R_1 = R_2 = H, R_3 = Anisyl	60 °C	^{1}H NMR	20 31	128

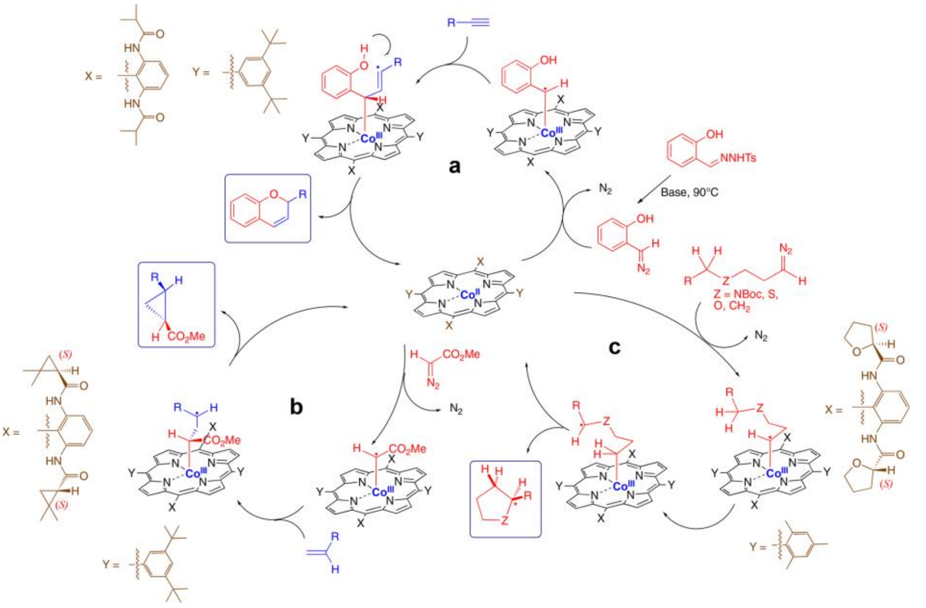
Scheme 18. *Mechanism of Photoactivated Coupling of Alkyl Halides by CoTCPP and TiO_2*



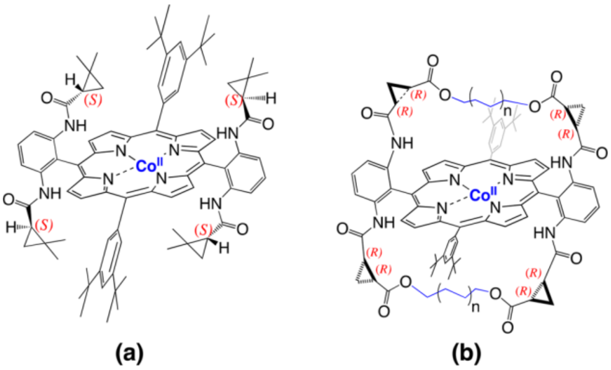
Scheme 19. *Cobalt-Catalyzed Reactions Using Carbene Radicals as Reactive Species*



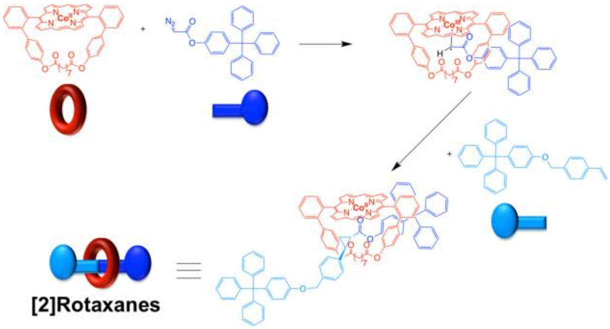
Scheme 20. *Simplified Representations of the Co^{II}(por)-Catalyzed Metallo-radical: (a) Synthesis of 2H Chromenes by Coupling-Cyclization Reaction of Alkynes and Salicyl Tosylhydrazones, (b) Cyclopropanation of Olefins, and (c) Cyclization for α-Substituted Pyrrolidines via C−H Alkylation*



Scheme 21. *(a) Co^{II}(3,5-DitBu-ChenPhyrin) and (b) Co^{II}(HuPhyrin) Complexes, Examples of Co^{II}(D2-Por*) Chiral Complex Studied in MRC*[6,41,154,155,157−159]



Scheme 22. *Synthesis of [2]Rotaxanes Based on Co(por) by Olefin Cyclopropanation by Carbene-Transfer Reactions*



Scheme 23. *Catalytic Chain-Transfer Polymerization (CCTP) of Methyl Methacrylate (MMA) with Co^{II}(por)*

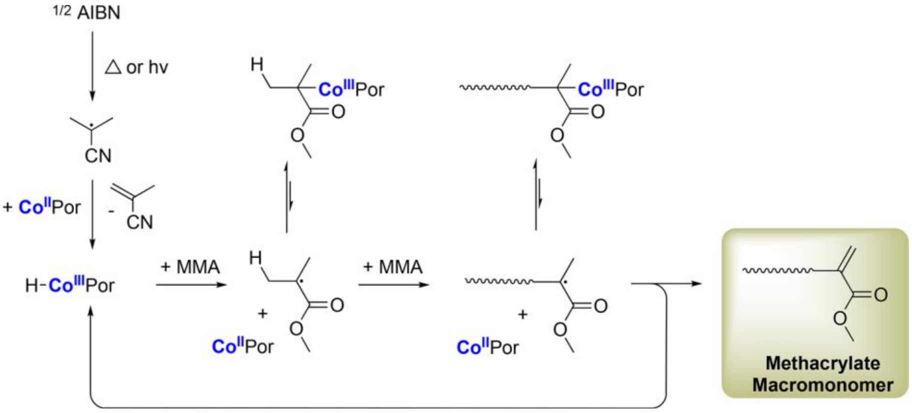
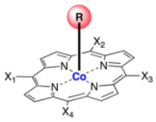
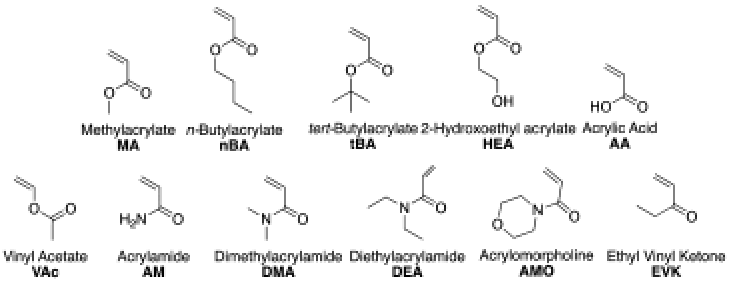


Table 4. *Polymerization Initiated by Organocobalt(III) Porphyrin Complexes through Thermal Treatment or Photoactivation*

	Entry	C-Co activation	Monomer(s)[a]	Ligand Substituent(s) (X_1-X_4)	Synthetic route (**A** or **B**)[b] and possible R group	Process	Ref
	**1**	Δ (60°C)	MMA	-Ph(OCH_3)	**B**, R = none , AIBN	CCTP	[3]
	2		MA, nBA	-Ph(Me)$_3$	**A,** R = -CH(CO_2CH_3)CH_3 and **B**, R = none, V70	CRP	[4,172]
	3		VAc	-Ph(Me)$_3$	**B,** R = none, AIBN or V70	CRP	[173–175]
	4		AA	-Ph(SO_3Na) and -Ph(SO_3Na)$_2$(Me)$_3$	**B**, R = none, V501 or V70	CRP in water	[176,177]
	5	Δ (55°C)	AM	-Ph(OCH_3)	**B**, R = none, VA-044	CRP in DMF/water [c]	[178]
	6	Δ (50°C)	tBA			CRP in EtOH/water [d]	[179]
	7	Δ (50°C)	DMA, DEA AMO, MA, nBA, tBA, HEA	-Ph(Me)$_3$ for X_{1-3} and -Ph(O(CH_2)$_{10}$OH) for X_4	**B**, R = none, AIBN	CRP in MeOH	[180]
	8	hν (rt) and Δ (50°C)	DMA, DEA AMO, MA, nBA, tBA, HEA	-Ph(Me)$_3$ for X_{1-3} and -Ph(O(CH_2)$_{10}$OH) for X_4	**A, R = -PMA and -PDMA**	CRP	[123,124]
	9		MA, nBA, tBA, DMA, DEA, AMO	-Ph(Me)$_3$	**A**, R = -PMA and –CO_2CH_3		
	10	hν	EVK, DMA and MA	-Ph(Me)$_3$	**A**, R = -PEVK and –CO_2CH_3	CRP	[125]

[a] Abbreviations of monomers have been listed in Scheme 24.[b] Route A or B refers to Scheme 24 with the unimolecular (A) and bimolecular (B) pathways. [c]Dispersion polymerization process. [d]Dispersion and free-soap emulsion polymerization process.

Scheme 24. *List of Monomers Controlled by R-Co^{III}(por) Complexes in Radical Polymerization*



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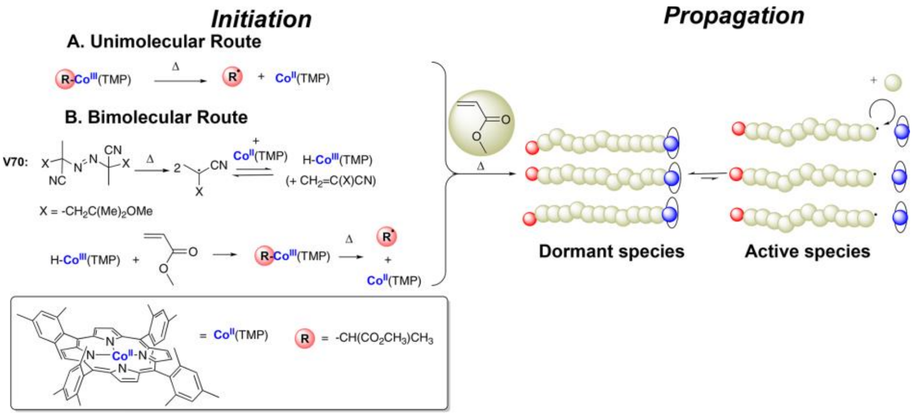
Status : Postprint (Author's version)

Scheme 25. *CMRP of Methylacrylate by the Bi- and Unimolecular Systems*



Scheme 26. *(A) Reversible Deactivation (RT) and (B) Degenerative Transfer (DT) Mechanisms*

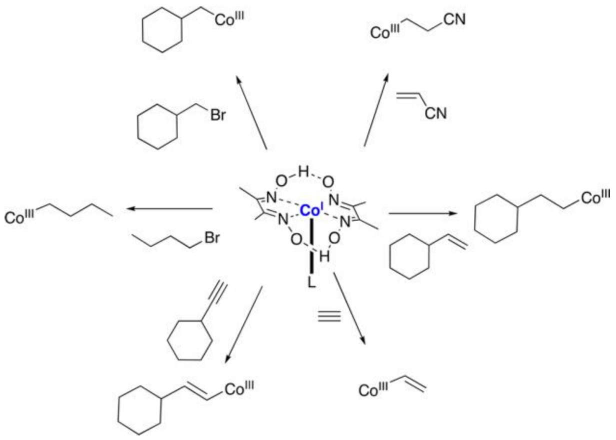
$$\text{P-Co}^{\text{III}} \rightleftharpoons \text{P}^{\bullet} + \text{Co}^{\text{II}} \qquad \text{(A)}$$

$$\text{P-Co}^{\text{III}} + \dot{\text{P}}' \rightleftharpoons \text{P}'\text{-Co}^{\text{III}} + \dot{\text{P}} \qquad \text{(B)}$$

Table 5. *Methods for the Synthesis of Organocobaloxime(III) Complexes*[186]

series	cobalt complex	alkylating agent	products
A	Co^{I}	R-X, X = halide, tosylate, etc.	$\text{R-Co}^{\text{III}} + \text{X}^-$
	Co^{I}	XCH═CHPh, X = Br, Cl	$\text{PhCH═CH-Co}^{\text{III}}$
	Co^{I}	XCH═CH_2, X = CN, etc.	$\text{XCH}_2\text{CH}_2\text{-Co}^{\text{III}}$
	Co^{I}	RC≡CH, R = Ph, etc.	$\text{RCH═CH-Co}^{\text{III}}$
B	H−Co^{III}	RCH═CH_2	$\text{MeCHR-Co}^{\text{III}}$
	H−Co^{III}	RC≡CH	$\text{CH}_2\text{═CR-Co}^{\text{III}}$
	H−Co^{III}	$\text{PhNH}_2\text{/HCHO}$	$\text{PhNHCH}_2\text{-Co}^{\text{III}} + \text{H}_2\text{O}$
C	Co^{II}	RX, X = halide	$\text{R-Co}^{\text{III}} + \text{X-Co}^{\text{III}}$
	Co^{II}	$\text{RNH-NH}_2\text{/O}_2$	$\text{R-Co}^{\text{III}} + \text{N}_2 + \text{H}_2\text{O}$
	Co^{II}	$\text{RC(CH}_3\text{)}_2\text{OOH}$	$\text{R-Co}^{\text{III}} + \text{OH-Co}^{\text{III}} + (\text{CH}_3)_2\text{CO}$
D	X-Co^{III}	R-M_t, M_t = metal	$\text{R-Co}^{\text{III}} + \text{MX}$
	X-Co^{III}	$\text{CH}_2\text{═CHOR/ROH}$	$(\text{RO})_2\text{CHCH}_2\text{−Co}^{\text{III}}$

Scheme 27. *Synthesis of Organocobaloxime Complexes from Co^{I} Species (Table 5, Series A)*



Scheme 28. *Co^{II}(ox)-Based Mechanism for the Formation of Organocobaloximes (R-Co^{III})*

$$\mathrm{Co^{II}} + \mathrm{R\text{-}X} \xrightarrow{\text{slow}} \mathrm{X\text{-}Co^{III}} + \mathrm{R^{\bullet}} \quad (1)$$

$$\mathrm{R^{\bullet}} + \mathrm{Co^{II}} \xrightarrow{\text{fast}} \mathrm{R\text{-}Co^{III}} \quad (2)$$

Scheme 29. *Examples of R-Co^{III}(ox) Complexes Prepared from X-Co^{III}(ox)*

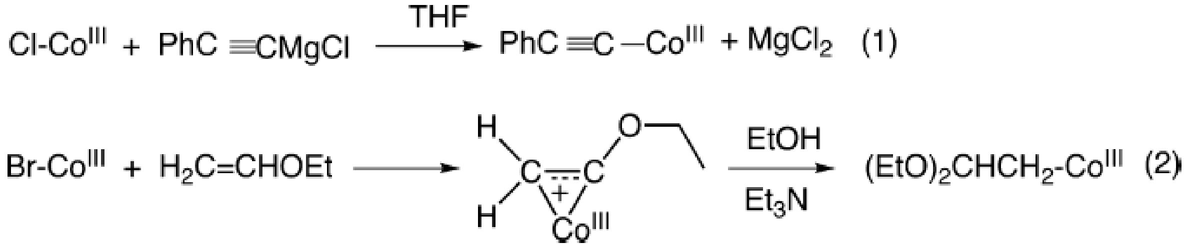


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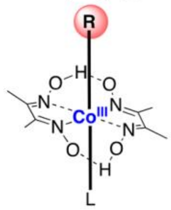
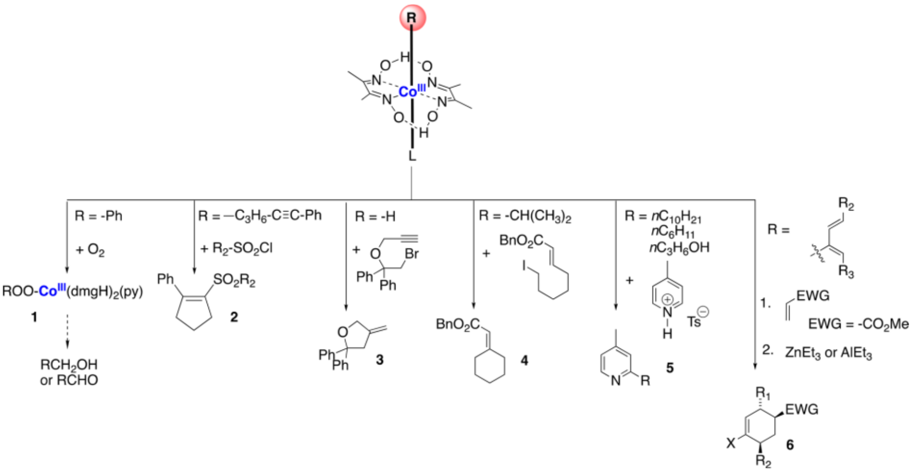
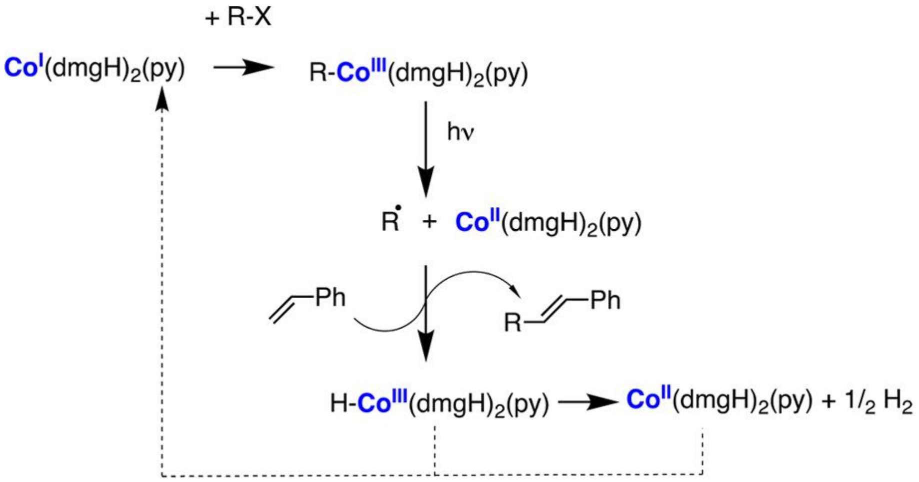
Table 6. *Bond Dissociation Energies of R-Co^{III}(dmgH)$_2$L*

R-Co Type	Homolysis pathway	Co Substituents (R and L)	Conditions	Method of BDE determination	BDE (kcal mol^{-1})	Ref.
R-Co(dmgH)$_2$L 	Thermolysis	R = -CH(CH$_3$)Ph and **L = -4-NH2-py**	63 °C	Kinetic of trapping radicals with R-SH	21	23,29
		R = -CH(CH$_3$)Ph and **L = -4-CN-py**			18	
	Thermolysis	R = -CH$_2$Ph and **L = -P(CH$_3$)$_2$Ph**	63 °C	Kinetic of trapping radicals with TEMPO	30	187
		R = -CH$_2$Ph and **L = -PPh$_3$**			26	
	DFT	R = **-CH$_3$** and L = py	/	DFT	33	189
		R = **-CH(CH$_3$)$_2$** and L = py			21	

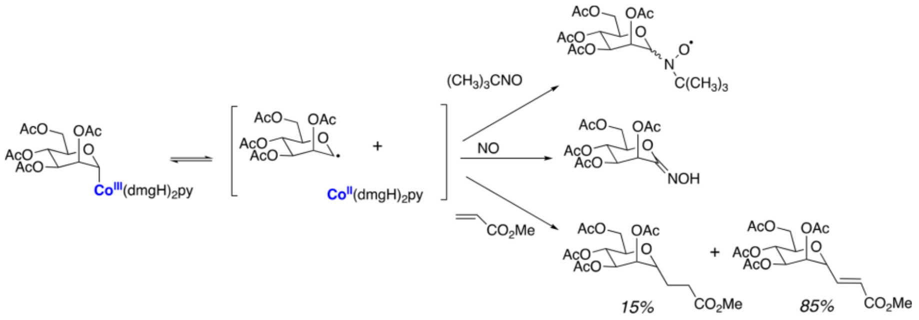
Scheme 30. *R-Co^{III}(ox) Radical Reactions*



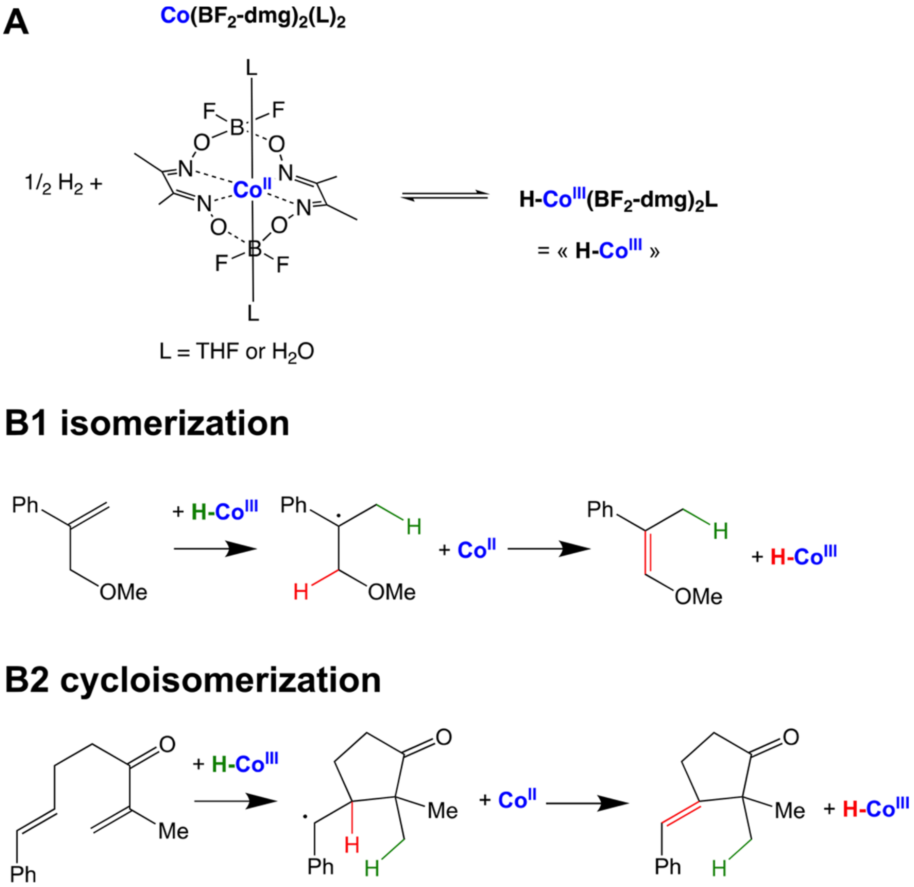
Scheme 31. *Alkyl–Alkenyl Cross-Coupling Mechanism Reaction under Photolytic Treatment*



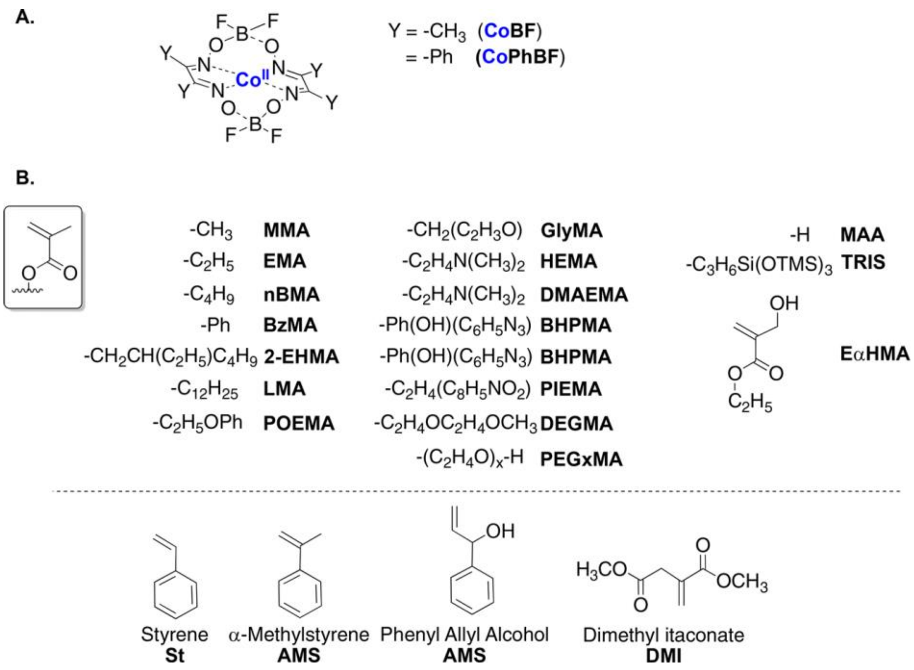
Scheme 32. *Glycosylcobaloxime Photolysis and Addition Reaction of Nitroso Alkane, Nitrogen Monoxide, and Alkene*



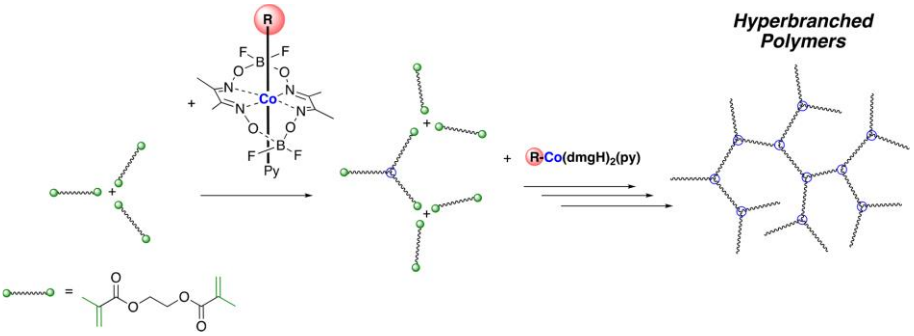
Scheme 33. *Radical Isomerization and Cycloisomerization Mechanism by $Co^{II}(BF_2\text{-}dmg)_2L_2$ Complex*



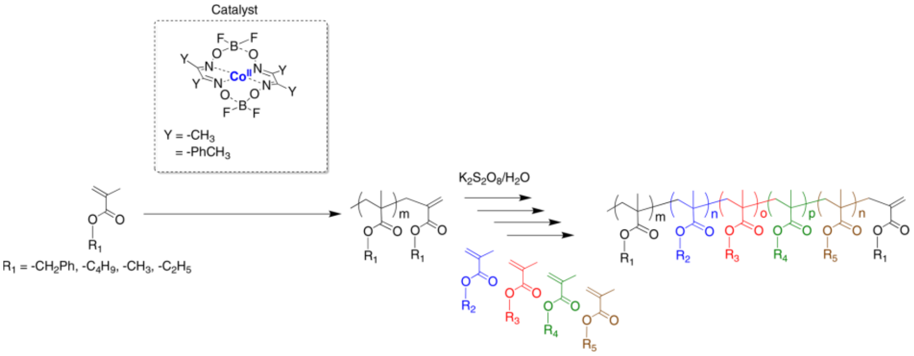
Scheme 34. *(A) $Co^{II}(BF_2\text{-}alkyl\ glyoxime)_2$ Used for CCTP of (B) Monomers Used in CCTP*



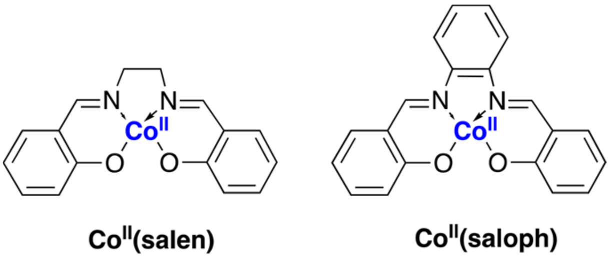
Scheme 35. *Formation of Hyperbranched Polymers from Ethylene Glycol Dimethacrylate and R-Co^{III}(ox) by CCTP*



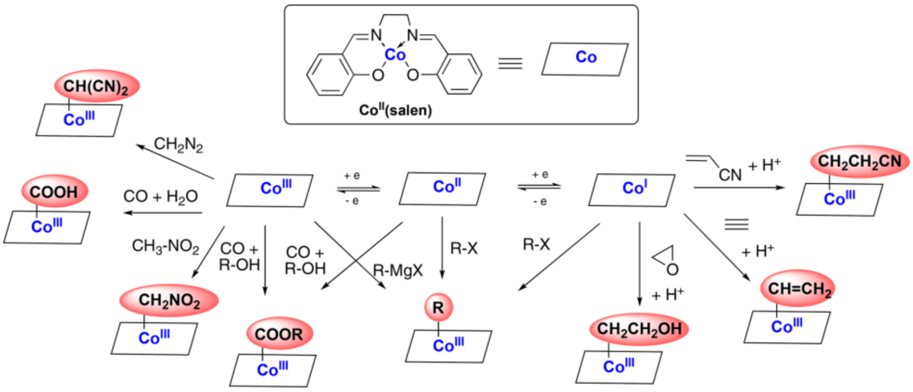
Scheme 36. *Application of CCTP by Cobaloxime Complexes for the Precise Design of Sequenced Copolymers Based on Methacrylic Monomers*



Scheme 37. *Structures of Co^{II}(salen) and Co^{II}(saloph)*



Scheme 38. *Synthesis Routes for R-Co^{III}(sal)*



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Scheme 39. *Synthesis of RO_2C-Co^{III}(sal) via Direct Carbonylation of Co^{II} and X-Co^{III} Salen-Type Complexes*

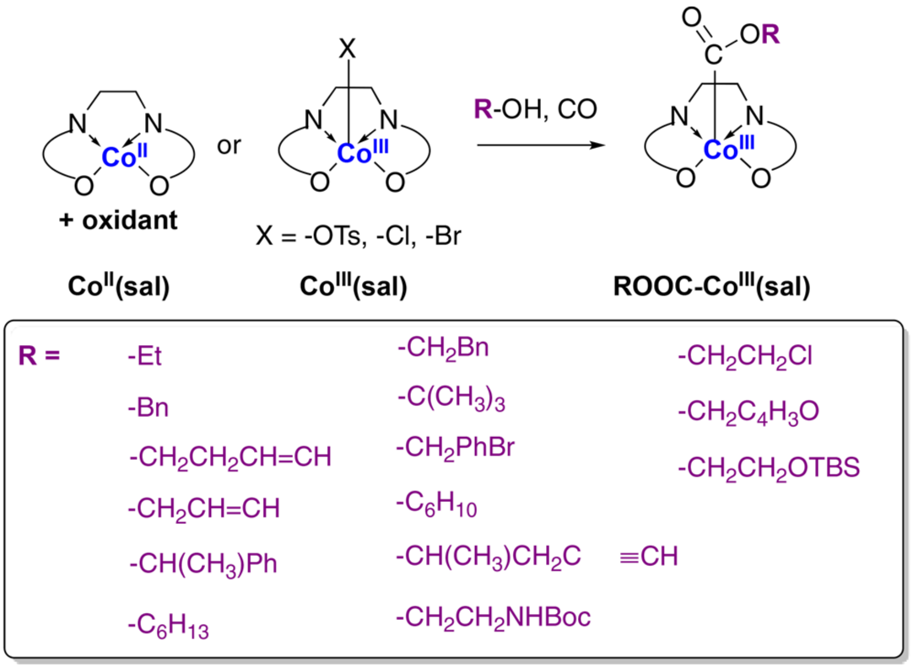
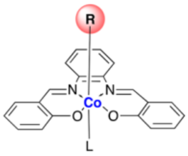
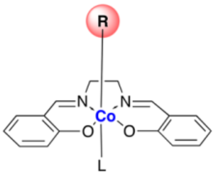
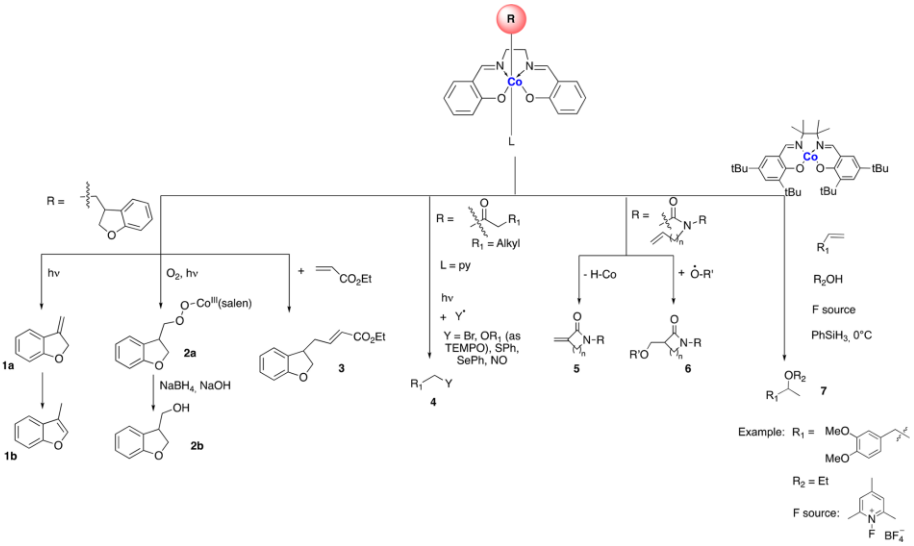


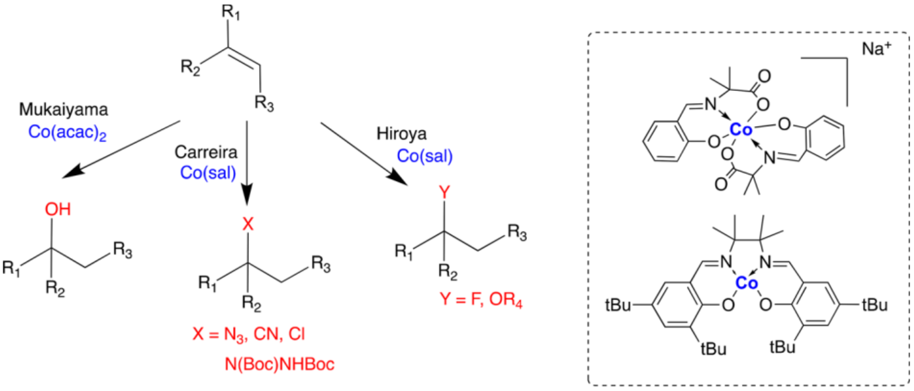
Table 7. *Bond Dissociation Energies of R-Co(sal)$_2$L*

R-Co Type	Homolysis pathway	Co Substituents (R and L)	Conditions	Method of BDE determination	BDE (kcal mol^{-1})	Ref.
R-Co(saloph)L 	Thermolysis	**R = -$CH_2CH_2CH_3$** and L = -py	63 °C in pyridine	Kinetic of trapping radicals with R-SH	25	237
		R = -$CH(CH_3)_2$ and L = -py			20	
R-Co(salen)L 	Photolysis	**R = -CH_3** and L = -H_2O	25 °C	Kinetic of trapping radicals with TEMPO	40	238
		R = -$CH(CH_3)_2$ and L = -H_2O			19	

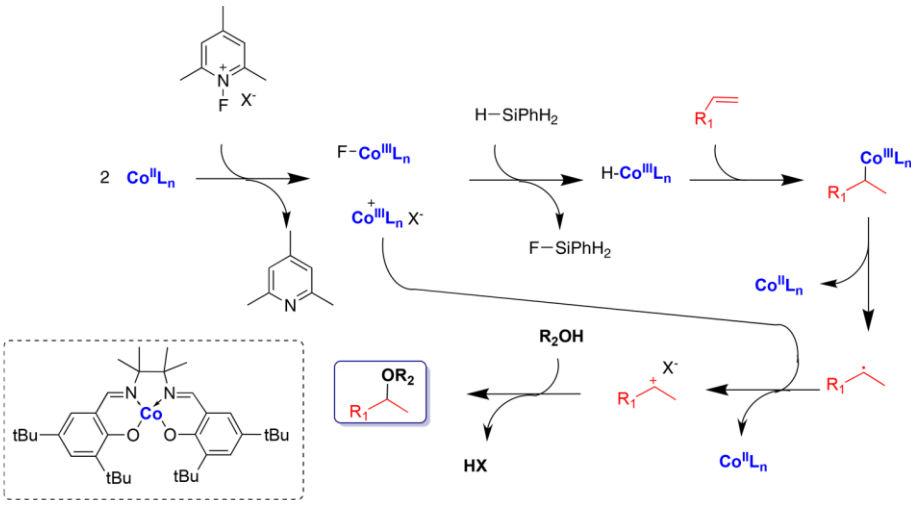
Scheme 40. *R-Co^{III}(salen) Radical Reactions*



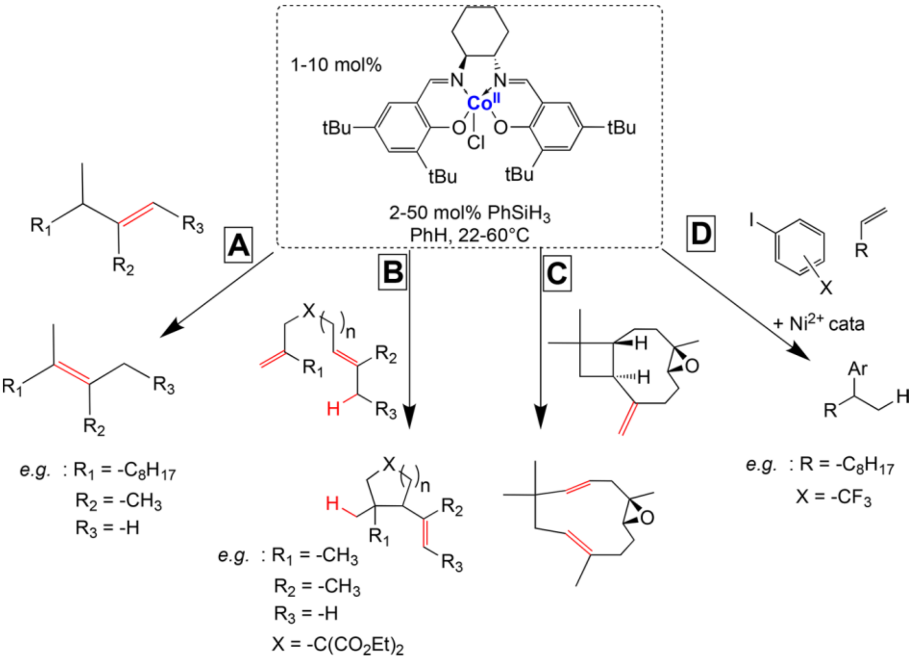
Scheme 41. *Cobalt-Catalyzed Hydrofunctionalization Reactions Using Co(sal) and Co(acac)$_2$ Complexes*



Scheme 42. *Mechanism of the Catalytic Hydroalkylation of Unactivated Alkenes Using Co(sal) as Catalyst*



Scheme 43. *Reactions Involving Co^{II}(sal^{tBu,tBu})Cl-Based HAT Isomerizations (A−C) and Branch-Selective Hydroarylation of Olefins*



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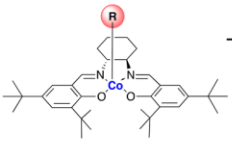
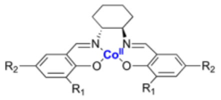
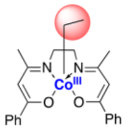
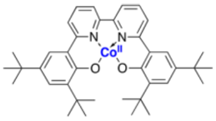
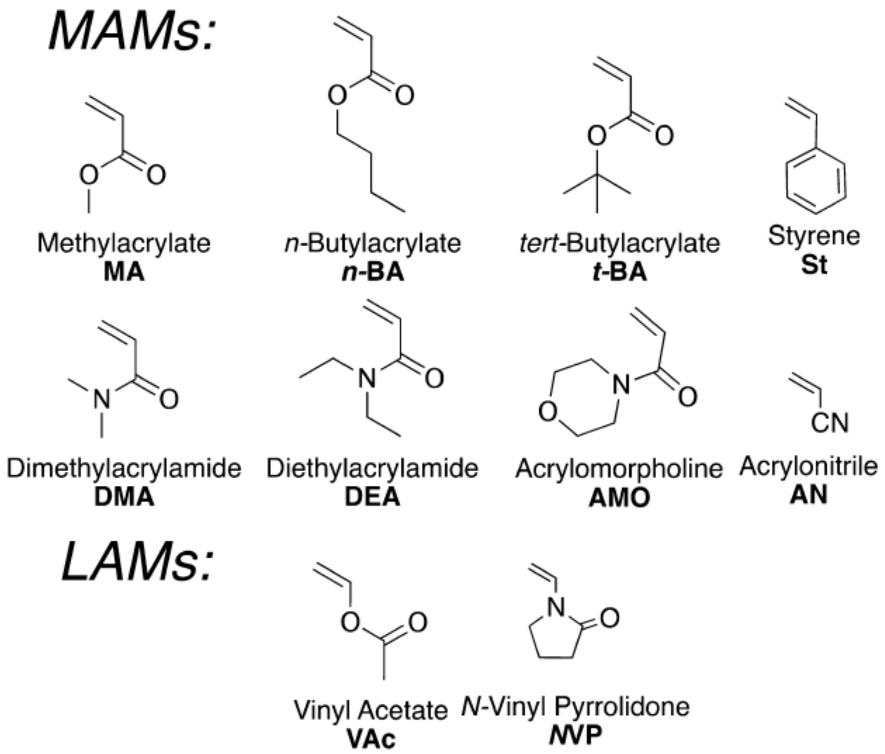
Status : Postprint (Author's version)

Table 8. *Controlled Radical Polymerization Mediated by R-Co^{III}(salen*) and Co(β-Ketoiminate) Complexes*

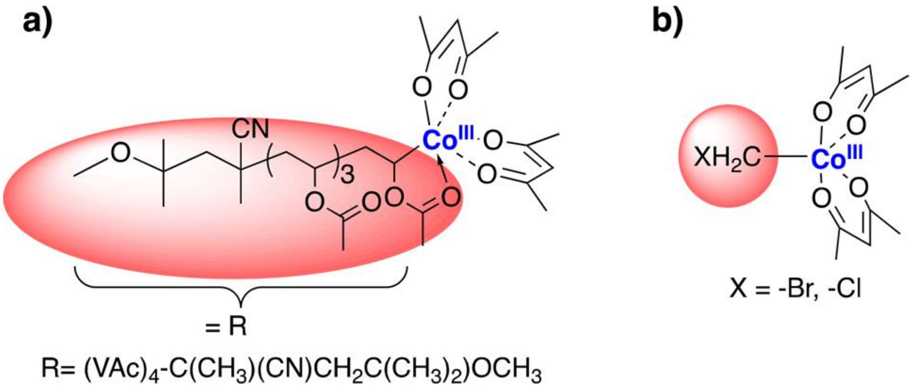
R-Co^{III} Type	Entry	C-Co bond activation	Monomer(s)[a]	R group	Radical initiator	Ref
R-Co^{III}(salen)* 	**1**	Δ (60°C)	MA, VAc	/	AIBN	255
	2	hν (rt)	MA, nBA, tBA, DMA, DEA, AMO, VAc	-COOCH$_3$	/	12
				/	TPO[b]	
	3	hν (rt)	MA, nBA, tBA, DMA, DEA, AMO, VAc	-C(O)NHR' with R' = alkynyl, tert-butyl, phenyl, cyclohexyl, fluoride, chloride, furyl, or thienyl group	/	236
	4	Δ (30°C)	nBA	/	V70	257
				-OligoPVAc	/	
Co^{II}(salen)^{R1,R2}*  R_1 = tBu or H R_2 = NO_2, tBu, OMe or NMe_2	**5**	Δ (120°C)	St, MMA, VAc	/	AIBN	258
Co^{II}(β-ketoiminate)  Ar = -Ph -Xyl -*p*-$C_6H_4CF_3$	**6**	Δ (30-90°C)	VAc	/	AIBN	259
Et-Co^{III}(β-ketoiminate) 	**7**	Δ (50°C)	MA	-C_2H_5	/[c]	260
Co^{II}(BpyBph) 	**8**	Δ (50°C)	VAc, MA, NVP, AN, NIPAM, St	/	AIBN	261

[a]Abbreviations of monomers are listed in Scheme 44. [b]TPO, 2,4,6-trimethylbenzoyl diphenylphosphine oxide. [c]Co^{II}(β-ketiminato) complex was also tested for comparison with V70.

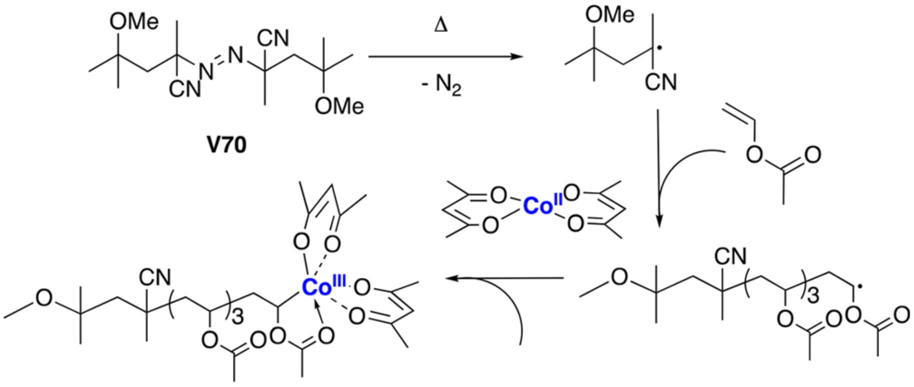
Scheme 44. *Monomers Used in CMRP with R-Co^{III}(sal) Complexes*



Scheme 45. *Structures of the Two Isolated R-Co^{III}(acac)$_2$ Compounds: (a) OligoPVAc-Co^{III}(acac)$_2$ and (b) XCH$_2$Co(acac)$_2$*



Scheme 46. *Synthetic Radical Pathway for OligoPVAc-Co^{III}(acac)$_2$*



Scheme 47. *Synthetic Radical Pathway for XCH_2-Co(acac)$_2$*

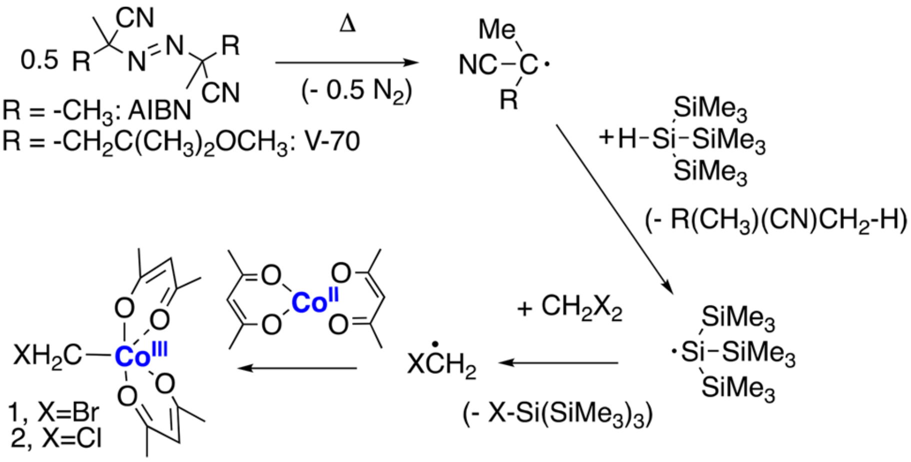
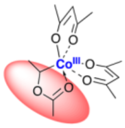
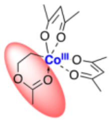
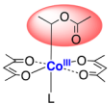
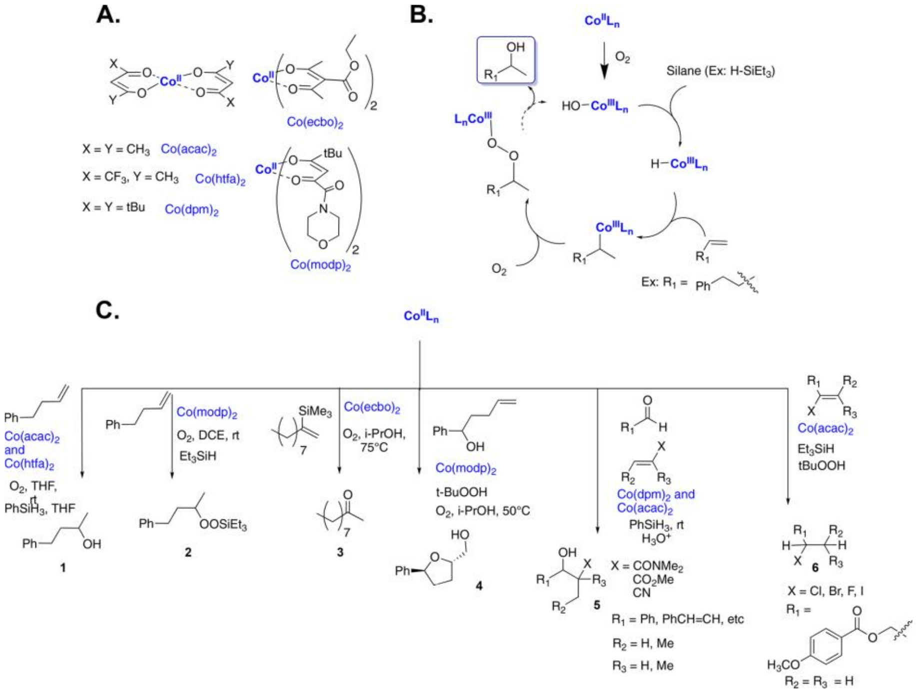


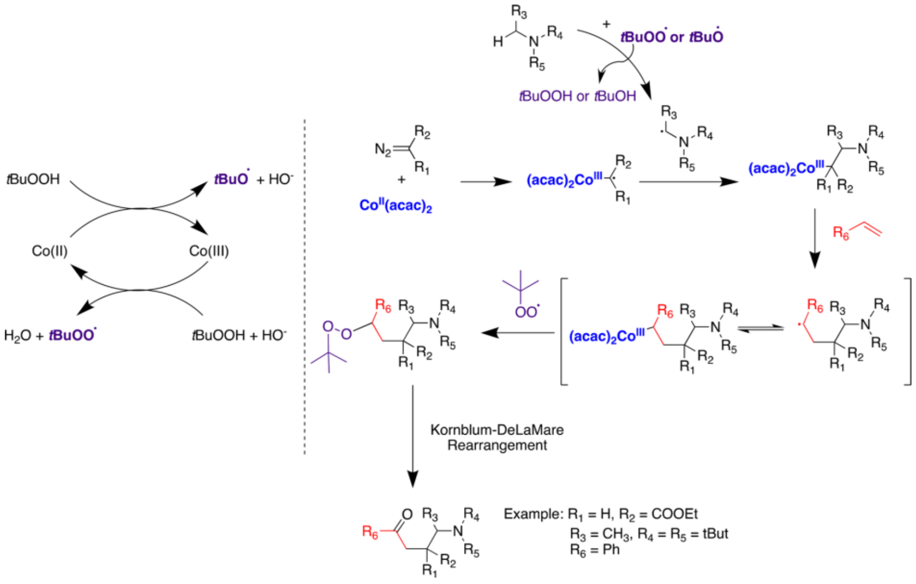
Table 9. *Bond Dissociation Enthalpies of R-Co^{III}(acac)$_2$L Determined by DFT (B3LYP[268] and BPW91* [264] as Hybrid Functional Method)*

R-Co^{III} Type	Entry	Ligand	Bond dissociation enthalphies (kcal.mol^{-1})	Ref.
$(CH_3)(CH_3COO)CH$-Co(acac)$_2$ 	**1**	L = / [5-membered ring chelation]	17.3	264
$CH_3COOCH_2CH_2$-Co(acac)$_2$ 	**2**	L = / [6-membered ring chelation]	18.3	
$(CH_3)(CH_3COO)CH$-Co(acac)$_2$(L) 	**3**	L = DMSO	9.9	265
	4	L = DMF	14.1	

Scheme 48. *(A) Co(acac)$_2$ Complexes Used in HAT Reactions of Alkene, (B) Mechanism of Mukaiyama's Reduction−Hydration Reaction, and (C) Main HAT Reactions Using Co(acac)$_2$ Derivatives*



Scheme 49. *Mechanism of the Reaction of Carbene Radicals with Olefins and α-Aminoalkyl Radicals Catalyzed by Co(acac)$_2$*



Scheme 50. *Monomers Used in CMRP with R-Co^{III}(acac)$_2$*

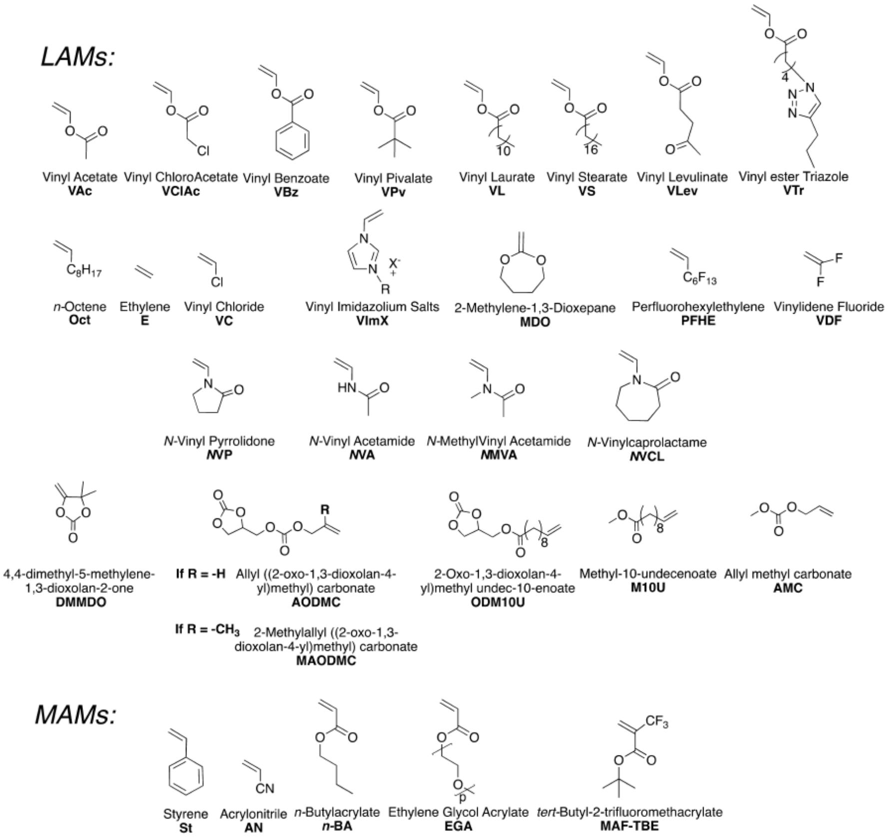


Table 10. *Controlled Radical Polymerization Mediated by* Co^{II} *Complexes Bearing Acetylacetonate Ligand Types and Initiated by an External Radical Source*

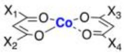
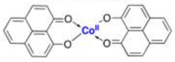
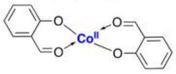
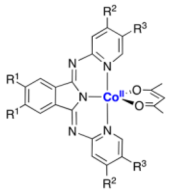
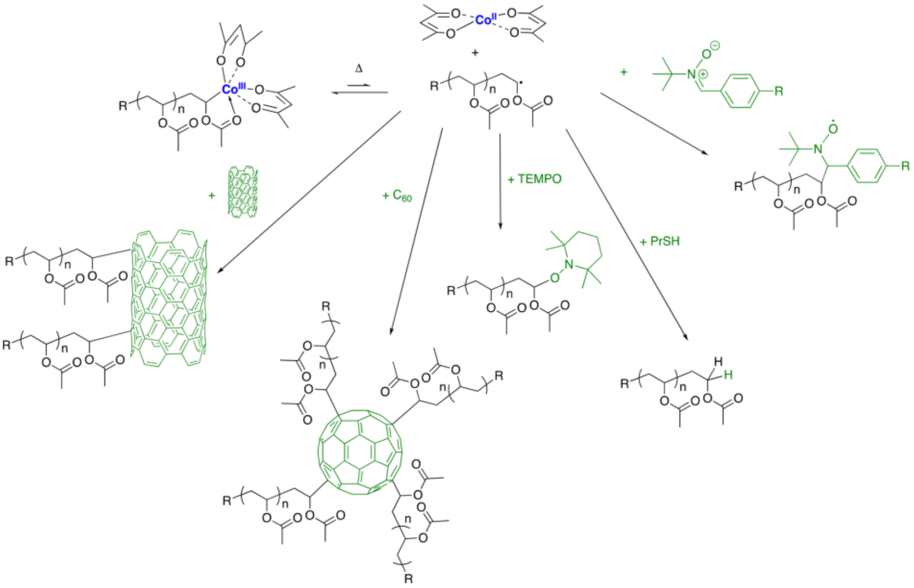
R-Co^{III} Type	Entry	C-Co bond activation	Monomer(s) [a]	Initiator	X substituent	Ligand	Ref.
	**1**	Δ (30°C)	VAc	V70 or PVAc-Co(acac)$_2$ (Macroinitiator)	X_{1-4} = -CH_3	None or H_2O	[281–283]
	2	Δ (30°C)	VAc, Oct and E	V70	X_{1-4} = -CH_3	/	[291]
	3		VAc/*n*-BA and VClAc/VAc		X_{1-4} = -CH_3 ; $X_{1,4}$ = -CH_3 and $X_{2,3}$ = -CF_3 (= **Co(F3-acac)$_2$**); X_{1-4} = -CF_3 (= **Co(F6-acac)$_2$**)		[284,285]
	4		VAc		$X_{1,4}$ = -CH_3 and $X_{2,3}$ = -*tert*-butyl		[324]
	5		VAc and NVP		X_{1-4} = -CH_3		[285]
	6	Δ (40°C)	VAc and MAF-TBE		X_{1-4} = -CH_3		[316]
	7	Δ (6-30°C)	VAc and NVP	PVAc-Co(acac)$_2$ (Macroinitiator)	X_{1-4} = -CH_3	/	[305]
	8	Δ (0°C)	VAc and AN			DMSO/ DMF	[313]
	9	Δ (30°C)	VAc and St			/	[311]
	10	hν (0°C) and Δ (30°C)	*n*-BA and VAc	AIBN and I651	X_{1-4} = -CH_3	/	[267]
	11	hν (0°C to rt)	NVA and NVP	VA-086	X_{1-4} = -CH_3	MeOH	[308,322]
	12	hν (30°C)	VAc	LPO and BPO	X_{1-4} = -CH_3	/	[321]
	13		VAc	TPO			[286]
	14		MDO and VAc				[323]
	15	Δ (30-40°C)	VAc, VPv and VBz	LPO and citric acid	X_{1-4} = -CH_3	/	[287]
	16		VL and VS				[288]
	17	Δ (40°C)	VImX	*t*-BuOOH	X_{1-4} = -CH_3	water	[299]
	18	Δ (60°C)	VDF and VAc	Perkadox 16	X_{1-4} = -CH_3	DMC	[297]
Co^{II}(OPN)$_2$ 	**19**	Δ (30°C)	VAc	V70	/	py	[325]
Co^{II}(SAL)$_2$ 	**20**	Δ (40°C)	VAc and MAF-TBE	V70	/	/	[326]

Table 10. *Continued*

R-Co^{III} Type	Entry	C-Co bond activation	Monomer(s) [a]	Initiator	X substituent	Ligand	Ref.
Co^{II}(Bpi)  R^1 = Me, Hex, H, Cl or NO_2 R^2 = *t*Bu, Cl, H or OMe R^3 = H or Cl	**21**	Δ (60°C)	nBA, MA	V70	/	/	327

[a] Abbreviations of monomers listed in Scheme 50.

Scheme 51. *End-Functionalization of R-PVAc-Co(acac)$_2$ by Different Radical Trapping Agents*



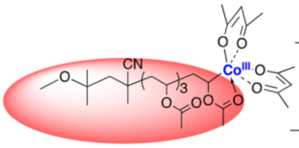
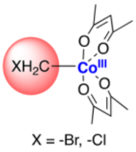
Scheme 52. *Mechanism of Formation of R-Co^{III}(bpi) during the Polymerization of MA*

$$\text{V70} \longrightarrow R^{\bullet} \quad \text{with } R^{\bullet} = \dot{C}(CH_3)RCN$$

$$R^{\bullet} + Co^{II}(Bpi) \longrightarrow R\text{-}Co^{III}(Bpi)$$

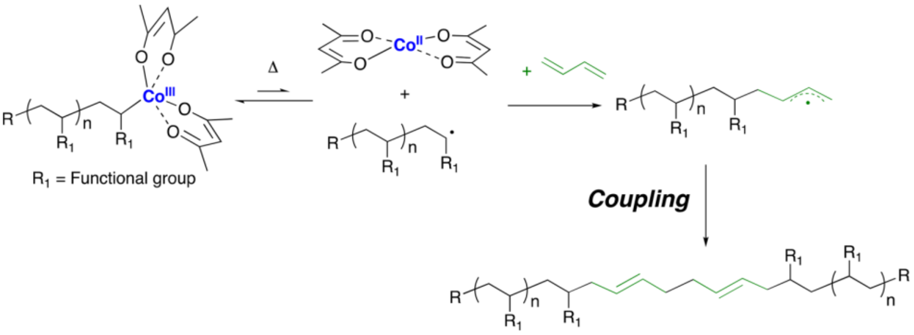
$$R\text{-}Co^{III}(Bpi) + CH_2{=}CH(CO_2CH_3) \longrightarrow R\text{-}CH_2\text{-}CH(CO_2CH_3)\text{-}Co^{III}(Bpi)$$

Table 11. *Controlled Radical Polymerization Mediated by R-Co^{III}(acac)$_2$ Complexes*

R-Co^{III} Type	Entry	C-Co bond activation	Monomer(s)	Ligand	Ref.
	**1**	Δ (30-40°C)	VAc	None, H_2O or Pyridine	44
	2	Δ (30°C)	VLev	DMSO	289
	3	Δ (30°C)	VTr		290
	4	Δ (0°C)	AN		314
	5	Δ (30°C)	*n*-BA	None or DMSO	312
	6	Δ (30°C)	EGA	/	328
	7	Δ (40°C)	VC		295
	8	Δ (40-60°C)	NVA (alone and with VAc), NVP, NVCL, NMVA		306,307,329,330
	9	Δ (0-40°C)	VImX	H_2O + Acetone / EtOAc/ DMF/ MeOH	298–304
	10	Δ (40°C)	VAc and E E and NMVA E and AN	/	9,292
	11	Δ and hν (40-80°C)	VAc and Oct	EtOAc	293
	12	Δ (40°C)	VAc and PFHE	/	294
	13	Δ (40°C)	VDF	DMC	296
	14	Δ (40°C)	DMMDO and VAc	/	331
	15	Δ (40°C)	AODMC, AODMC, ODM10U, M10U, AMC with VAc	/	332
	**16**	Δ (40°C)	VAc	/	263
			VEtImBr	H_2O	
	17	Δ (40°C)	VAc and E	/	339

^{a} Abbreviations of monomers listed in Scheme 50.

Scheme 53. *Cobalt-Mediated Radical Coupling Mechanism*



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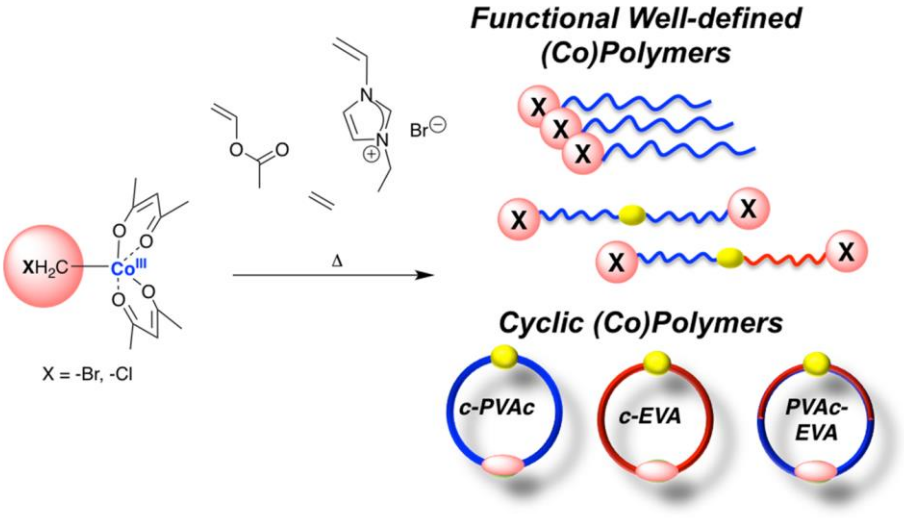
***Scheme 54**. XCH_2-$Co(acac)_2$-Based Macromolecular Engineering in CMRP*



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NOTES

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Jérémy Demarteau received his undergraduate education in chemistrý in Belgium. In 2013, he started his Ph.D. work at the laboratory of CERM (Liège, Belgium). During that time, supervised by Dr. Christophe Detrembleur, he investigated the controlled radical polymerization of less-activated monomers using organocobalt complexes, notably with the synthesis of block copolymers based on vinyl acetate and ethylene. In 2017, he joined the Innovative Polymers Group of POLYMAT (San Sebastian, Spain) as a postdoctoral researcher. Within the team of Dr. Haritz Sardon, he is working on the organocatalytic depolymerization of commodity polymers, such as polyesters, into valuable monomers and their use in a circular economy.

Antoine Debuigne obtained his Ph.D. from the University of Liege in 2004, under the guidance of Prof. Robert Jérôme. His doctoral thesis focused on the development of cobalt-mediated radical polymerization. After graduation, he joined the group of Prof. Michael K. Georges at the University of Toronto as a postdoctoral researcher and developed controlled radical polymerization methods under emulsion conditions. In 2006, he returned to Liege as FNRS Postdoctoral Researcher and was promoted to FNRS Research Associate in 2010, in the Center for Education and Research on Macromolecules (CERM). His research interests deal with macromolecular engineering essentially based on radical chemistry and emulsion polymerization.

Christophe Detrembleur obtained his Ph.D. degree in 2001, under the supervision of Prof. R. Jérôme at the Center for Education and Research on Macromolecules (CERM), University of Liege, Belgium. His doctoral thesis focused on the development of new regulators for the controlled radical polymerization of (meth)acrylic monomers. He then joined Bayer AG in Leverkusen, Germany, in 2001, where he worked on the use of controlled radical polymerization processes for the design of new materials, and on the preparation of new highperformance UV coatings. In October 2003, he left Bayer for a permanent Research Associate position at the University of Liege, funded by the National Fund for Scientific Research (FNRS). He was promoted to Senior Research Associate in 2008, and Research Director in 2012. The main research activities of his group deal with the precision design of novel copolymers by controlled radical polymerization techniques and the development of strategies to convert carbon dioxide onto novel functional polymers.

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REFERENCES

(1) Branchaud, B. P.; Meier, M. S.; Choi, Y. Alkyl-Alkenyl Cross Coupling via Alkyl Cobaloxime Radical chemistry. An Alkyl Equivalent to the Heck Reaction Compatible with Common Organic Functional Groups. Tetrahedron Lett. 1988, 29, 167–170.

(2) Iqbal, J.; Bhatia, B.; Nayyar, N. K. Transition Metal-Promoted Free-Radical Reactions in Organic Synthesis: The Formation of Carbon-Carbon Bonds. Chem. Rev. 1994, 94, 519–564.

(3) Gridnev, A. A.; Ittel, S. D. Catalytic Chain Transfer in FreeRadical Polymerizations. Chem. Rev. 2001, 101, 3611–3660.

(4) Wayland, B. B.; Poszmik, G.; Mukerjee, S. L.; Fryd, M. Living Radical Polymerization of Acrylates by Organocobalt Porphyrin Complexes. J. Am. Chem. Soc. 1994, 116, 7943–7944.

(5) Dzik, W. I.; Xu, X.; Zhang, X. P.; Reek, J. N. H.; de Bruin, B. Carbene Radicals in CoII(por)-Catalyzed Olefin Cyclopropanation. J. Am. Chem. Soc. 2010, 132, 10891–10902.

(6) Chen, Y.; Ruppel, J. V.; Zhang, X. P. Cobalt-Catalyzed Asymmetric Cyclopropanation of Electron-Deficient Olefins. J. Am. Chem. Soc. 2007, 129, 12074–12075.

(7) Debuigne, A.; Poli, R.; Jérôme, C.; Jérôme, R.; Detrembleur, C. Overview of Cobalt-Mediated Radical Polymerization: Roots, State of the Art and Future Prospects. Prog. Polym. Sci. 2009, 34, 211–239.

(8) Debuigne, A.; Jerome, C.; Detrembleur, C. OrganometallicMediated Radical Polymerization of "Less Activated Monomers": Fundamentals, Challenges and Opportunities. Polymer 2017, 115, 285–307.

(9) Kermagoret, A.; Debuigne, A.; Jérôme, C.; Detrembleur, C. Precision Design of Ethylene- and Polar-Monomer-Based Copolymers by Organometallic-Mediated Radical Polymerization. Nat. Chem. 2014, 6, 179–187.

(10) Crossley, S. W. M.; Obradors, C.; Martinez, R. M.; Shenvi, R. A. Mn-, Fe-, and Co-Catalyzed Radical Hydrofunctionalizations of Olefins. Chem. Rev. 2016, 116, 8912–9000.

(11) Shell, T. A.; Lawrence, D. S. Vitamin B12: A Tunable, Long Wavelength, Light-Responsive Platform for Launching Therapeutic Agents. Acc. Chem. Res. 2015, 48, 2866–2874.

(12) Zhao, Y.; Yu, M.; Zhang, S.; Wu, Z.; Liu, Y.; Peng, C.-H.; Fu, X. A Well-Defined, Versatile Photoinitiator (salen)Co-CO2CH3 for Visible Light-Initiated Living/controlled Radical Polymerization. Chem. Sci. 2015, 6, 2979–2988.

(13) Waser, J.; Gaspar, B.; Nambu, H.; Carreira, E. M. Hydrazines and Azides via the Metal-Catalyzed Hydrohydrazination and Hydroazidation of Olefins. J. Am. Chem. Soc. 2006, 128, 11693–11712.

(14) Peng, C.-H.; Yang, T.-Y.; Zhao, Y.; Fu, X. Reversible Deactivation Radical Polymerization Mediated by Cobalt Complexes: Recent Progress and Perspectives. Org. Biomol. Chem. 2014, 12, 8580–8587.

(15) Hurtgen, M.; Detrembleur, C.; Jérôme, C.; Debuigne, A. Insight into Organometallic-Mediated Radical Polymerization. Polym. Rev. 2011, 51, 188–213.

(16) Pattenden, G. Simonsen Lecture. Cobalt-Mediated Radical Reactions in Organic Synthesis. Chem. Soc. Rev. 1988, 17, 361–382.

(17) Okabe, M.; Tada, M. The Reaction of Bis-(dimethylglyoximato)(pyridine)cobalt(I), Cobaloxime(I), with 2(Allyloxy)ethyl Halides and the Photolysis of the Resulting OrganoCobaloximes. Bull. Chem. Soc. Jpn. 1982, 55, 1498–1503.

(18) Bernd, G.; Jens, H.; Jianing, H.; Ottmar, H.; Andreas, K. On the Formation of "Free Radicals" from Alkylcobalt Complexes. Angew. Chem., Int. Ed. 1989, 28, 325–327.

(19) Schrauzer, G. N.; Windgassen, R. J. Alkylcobaloximes and Their Relation to Alkylcobalamins. J. Am. Chem. Soc. 1966, 88, 3738–3743.

(20) Schrauzer, G. N.; Lee, L.-P.; Sibert, J. W. Alkylcobalamins and Alkylcobaloximes. Electronic Structure, Spectra, and Mechanism of Photodealkylation. J. Am. Chem. Soc. 1970, 92, 2997–3005.

(21) Allan, L. E. N.; Perry, M. R.; Shaver, M. P. Organometallic Mediated Radical Polymerization. Prog. Polym. Sci. 2012, 37, 127– 156.

(22) Schrauzer, G. N. Organocobalt Chemistry of Vitamin B12 Model Compounds (Cobaloximes). Acc. Chem. Res. 1968, 1, 97–103.

(23) Halpern, J. Mechanisms of Coenzyme B12-Dependent Rearrangements. Science 1985, 227, 869–875.

(24) Smith, E. L.; Mervin, L.; Johnson, A. W.; Shaw, N. Partial Synthesis of Vitamin B12 Coenzyme and Analogues. Nature 1962, 194, 1175.

(25) Poli, R. Radical Coordination Chemistry and Its Relevance to Metal-Mediated Radical Polymerization. Eur. J. Inorg. Chem. 2011, 2011, 1513–1530.

(26) Daikh, B. E.; Finke, R. G. The Persistent Radical Effect: A Prototype Example of Extreme, 105 to 1, Product Selectivity in a Free-Radical Reaction Involving Persistent. CoII[macrocycle] and Alkyl Free Radicals. J. Am. Chem. Soc. 1992, 114, 2938–2943.

(27) Fischer, H. The Persistent Radical Effect in Controlled Radical Polymerizations. J. Polym. Sci., Part A: Polym. Chem. 1999, 37, 1885– 1901.

(28) Studer, A. The Persistent Radical Effect in Organic Synthesis. Chem. - Eur. J. 2001, 7, 1159–1164.

(29) Qi, X.-J.; Li, Z.; Fu, Y.; Guo, Q.-X.; Liu, L. Anti-SpinDelocalization Effect in Co-C Bond Dissociation Enthalpies. Organometallics 2008, 27, 2688–2698.

(30) Gruber, K.; Puffer, B.; Krautler, B. Vitamin B12-Derivativeš ⍰ enzyme Cofactors and Ligands of Proteins and Nucleic Acids. Chem. Soc. Rev. 2011, 40, 4346–4363.

(31) Giedyk, M.; Goliszewska, K.; Gryko, D. Vitamin B12 Catalysed Reactions. Chem. Soc. Rev. 2015, 44, 3391–3404.

(32) Weiss, M. E.; Kreis, L. M.; Lauber, A.; Carreira, E. M. CobaltCatalyzed Coupling of Alkyl Iodides with Alkenes: Deprotonation of Hydridocobalt Enables Turnover. Angew. Chem., Int. Ed. 2011, 50, 11125–11128.

(33) Shigehisa, H.; Aoki, T.; Yamaguchi, S.; Shimizu, N.; Hiroya, K. Hydroalkoxylation of Unactivated Olefins with Carbon Radicals and Carbocation Species as Key Intermediates. J. Am. Chem. Soc. 2013, 135, 10306–10309.

(34) Waser, J.; Carreira, E. M. Convenient Synthesis of Alkylhydrazides by the Cobalt-Catalyzed Hydrohydrazination Reaction of Olefins and Azodicarboxylates. J. Am. Chem. Soc. 2004, 126, 5676–5677.

(35) Mukaiyama, T.; Isayama, S.; Inoki, S.; Kato, K.; Yamada, T.; Takai, T. Oxidation-Reduction Hydration of Olefins with Molecular Oxygen and 2-Propanol Catalyzed by bis(acetylacetonato)cobalt(II). Chem. Lett. 1989, 3, 449–452.

(36) Hodgkin, D. C.; Kamper, J.; Mackay, M.; Pickworth, J.; Trueblood, K. N.; White, J. G. Structure of Vitamin B12. Nature 1956, 178, 64–66.

(37) Clarke, D. A.; Dolphin, D.; Grigg, R.; Johnson, A. W.; Pinnock, H. A. Alkyl-, Aryl-, and Acyl-metal(III) Complexes of Etioporphyrin I. J. Chem. Soc. C 1968, 0, 881–885.

(38) Clarke, D. A.; Grigg, R.; Johnson, A. Alkyl- and Aryl-metal(III) Complexes of Etioporphyrin I. Chem. Commun. 1966, 0, 208–209.

(39) Dolphin, D.; Johnson, A. W. Alkylcobalt(III) Complexes of Etioporphyrin I. Chem. Commun. 1965, 0, 494–495.

(40) Dzik, W. I.; Zhang, X. P.; de Bruin, B. Redox Noninnocence of Carbene Ligands: Carbene Radicals in (Catalytic) C-C Bond Formation. Inorg. Chem. 2011, 50, 9896–9903.

(41) Zhu, S.; Perman, J. A.; Zhang, X. P. Acceptor/acceptorSubstituted Diazo Reagents for Carbene Transfers: Cobalt-Catalyzed Asymmetric Z-Cyclopropanation of Alkenes with α-Nitrodiazoacetates. Angew. Chem., Int. Ed. 2008, 47, 8460–8463.

(42) Costa, G.; Mestroni, G.; Tauzher, G.; Stefani, L. Organometallic Derivatives of Cobalt Chelates of Bis(acetylacetone)ethylendiamine. J. Organomet. Chem. 1966, 6, 181–187.

(43) Costa, G. Recent Developments in the Field of Organometallic Derivatives of Cobalt Chelates. Coord. Chem. Rev. 1972, 8, 63–75.

(44) Debuigne, A.; Champouret, Y.; Jérôme, R.; Poli, R.; Detrembleur, C.; Jerome, R.; Poli, R.; Detrembleur, C. Mechanistic Insights into the Cobalt-Mediated Radical Polymerization (CMRP) of Vinyl Acetate with cobalt(III) Adducts as Initiators. Chem. - Eur. J. 2008, 14, 4046–4059.

(45) Banerjee, R. Radical Carbon Skeleton Rearrangements: Catalysis by Coenzyme B12-Dependent Mutases. Chem. Rev. 2003, 103, 2083–2094.

(46) Zelder, F. Recent Trends in the Development of Vitamin B12 Derivatives for Medicinal Applications. Chem. Commun. 2015, 51, 14004–14017.

(47) Andruniow, T.; Zgierski, M. Z.; Kozlowski, P. M. Theoretical Determination of the Co-C Bond Energy Dissociation in Cobalamins. J. Am. Chem. Soc. 2001, 123, 2679–2680.

(48) Jensen, K. P.; Ryde, U. How the Co-C Bond Is Cleaved in Coenzyme B12 Enzymes: A Theoretical Study. J. Am. Chem. Soc. 2005, 127, 9117–9128.

(49) Randaccio, L.; Geremia, S.; Demitri, N.; Wuerges, J. Vitamin B12: Unique Metalorganic Compounds and the Most Complex Vitamins. Molecules 2010, 15, 3228–3259.

(50) Schrauzer, G. N.; Weber, J. H.; Beckham, T. M.; Ho, R. K. Y. Alkyl Group Transfer from Cobalt to Mercury: Reaction of Alkylcobalamins, Alkylcobaloximes, and of Related Compounds with Mercuric Acetate. Tetrahedron Lett. 1971, 12, 275–277.

(51) Fritz, H. L.; Espenson, J. H.; Williams, D. A.; Molander, G. A. Inversion at Carbon in the Cleavage of Cobalt-Carbon Bonds by Mercuric Ion. J. Am. Chem. Soc. 1974, 96, 2378–2381.

(52) Toscano, P. J.; Marzilli, L. G. B12 and Related Organocobalt Chemistry: Formation and Cleavage of Cobalt Carbon Bonds. Prog. Inorg. Chem. 2007, 31, 105–204.

(53) Lindstrand, K. Isolation of Methylcobalamin from Natural Source Material. Nature 1964, 204, 188–189.

(54) Eschenmoser, A.; Wintner, C. E. Natural Product Synthesis and Vitamin B12. Science 1977, 196, 1410–1420.

(55) Wagner, F.; Bernhauer, K. New Aspects of the Structure of Corrinoid Coenzymes. Ann. N. Y. Acad. Sci. 1964, 112, 580–589.

(56) Schrauzer, G. N.; Hashimoto, M. Studies on Vitamin B12 and Related Compounds. 49. Direct Synthesis of Alkyl- and of ωCarboxyalkylcobalamins from Vitamin B12 and Aliphatic Carboxylic Acids Under "oxidizing-Reducing" conditions. J. Am. Chem. Soc. 1979, 101, 4593–4601.

(57) Tinembart, O.; Walder, L.; Scheffold, R. Reductive Cleavage of the Cobalt-Carbon Bond of [(Methoxycarbonyl)methyl]cobalamin. Ber. Bunsen-Ges. 1988, 92, 1225–1231.

(58) Kraeutler, B. Acetylcobalamin from Photoinduced Carbonylation of Methylcobalamin. Helv. Chim. Acta 1984, 67, 1053–1059.

(59) Ruetz, M.; Salchner, R.; Wurst, K.; Fedosov, S.; Krautler, B. Phenylethynylcobalamin: A Light-Stable and Thermolysis-Resistant Organometallic Vitamin B(12) Derivative Prepared by Radical Synthesis. Angew. Chem., Int. Ed. 2013, 52, 11406–11409.

(60) Ruetz, M.; Gherasim, C.; Gruber, K.; Fedosov, S.; Banerjee, R.; Krautler, B. Access to Organometallic Arylcobaltcorrins through Radical Synthesis: 4-Ethylphenylcobalamin, a Potential "antivitamin B(12). Angew. Chem., Int. Ed. 2013, 52, 2606–2610.

(61) Miller, N. A.; Wiley, T. E.; Spears, K. G.; Ruetz, M.; Kieninger, C.; Krautler, B.; Sension, R. J. Toward the Design of Photoresponsive Conditional Antivitamins B12: A Transient Absorption Study of an Arylcobalamin and an Alkynylcobalamin. J. Am. Chem. Soc. 2016, 138, 14250–14256.

(62) Linn, D. E., Jr.; Gould, E. S. Electron Transfer. 92. Reductions of Vitamin B12a (Hydroxocobalamin), with Formate and Related Formyl Species. Inorg. Chem. 1988, 27, 1625–1628.

(63) Kraeutler, B. Antivitamins B12 - A Structure- and ReactivityBased Concept. Chem. - Eur. J. 2015, 21, 11280–11287.

(64) Halpern, J.; Kim, S. H.; Leung, T. W. Cobalt-Carbon Bond Dissociation Energy of Coenzyme B12. J. Am. Chem. Soc. 1984, 106, 8317–8319.

(65) Luo, L. B.; Li, G.; Chen, H. L.; Fu, S. W.; Zhang, S. Y. LaserInduced Photoacoustic Calorimetric Determination of Enthalpy and Volume Change in Photolysis of 5′-deoxyadenosylcobalamin and Methylcobalamin. J. Chem. Soc., Dalton Trans. 1998, 12, 2103–2108.

(66) Jones, A. R. The Photochemistry and Photobiology of Vitamin B12. Photochem. Photobiol. Sci. 2017, 16, 820–834.

(67) Martin, B. D.; Finke, R. G. Methylcobalamin's Full- vs. HalfStrength Cobalt-Carbon σ Bonds and Bond Dissociation Enthalpies: A > 1015 Co-CH3 Homolysis Rate Enhancement Following OneAntibonding-Electron Reduction of Methylcobalamin. J. Am. Chem. Soc. 1992, 114, 585–592.

(68) Hay, B. P.; Finke, R. G. Thermolysis of the Cobalt-Carbon Bond in Adenosylcorrins. 3. Quantification of the Axial Base Effect in Adenosylcobalamin by the Synthesis and Thermolysis of Axial BaseFree Adenosylcobinamide. Insights into the Energetics of EnzymeAssisted Cobalt-Car. J. Am. Chem. Soc. 1987, 109, 8012–8018.

(69) Hung, R. R.; Grabowski, J. J. Listening to Reactive Intermediates: Application of Photoacoustic Calorimetry to Vitamin B12 Compounds. J. Am. Chem. Soc. 1999, 121, 1359–1364.

(70) Hay, B. P.; Finke, R. G. Thermolysis of the Cobalt-Carbon Bond of Adenosylcobalamin. 2. Products, Kinetics, and CobaltCarbon Bond Dissociation Energy in Aqueous Solution. J. Am. Chem. Soc. 1986, 108, 4820–4829.

(71) Qu, Z.; Hansen, A.; Grimme, S. Co-C Bond Dissociation Energies in Cobalamin Derivatives and Dispersion Effects: Anomaly or Just Challenging? J. Chem. Theory Comput. 2015, 11, 1037–1045.

(72) Zhou, D. L.; Tinembart, O.; Scheffold, R.; Walder, L. Influence of the Axial Alkyl Ligand on the Reduction Potential of alkylcob(III)alamins and alkylcob(III)yrinates. Helv. Chim. Acta 1990, 73, 2225–2241.

(73) Zhou, D. L.; Walder, P.; Scheffold, R.; Walder, L. SN2 or Electron Transfer? A New Technique Discriminates the Mechanisms of Oxidative Addition of Alkyl Halides to Corrinato- and porphyrinatocobalt(I). Helv. Chim. Acta 1992, 75, 995–1011.

(74) Frey, P. A.; Essenberg, M. K.; Abeles, R. H. Studies on the Mechanism of Hydrogen Transfer in the Cobamide CoenzymeDependent Dioldehydrase Reaction. J. Biol. Chem. 1967, 242, 5369– 5377.

(75) Abeles, R. H.; Dolphin, D. The Vitamin B12 Coenzyme. Acc. Chem. Res. 1976, 9, 114–120.

(76) Kovacevic, B.; Baric, D.; Babic, D.; Bilic, L.; Hanzevacki, M.; Sandala, G. M.; Radom, L.; Smith, D. M. Computational Tale of Two Enzymes: Glycerol Dehydration With or Without B12. J. Am. Chem. Soc. 2018, 140, 8487–8496.

(77) Sandala, G. M.; Smith, D. M.; Radom, L. Modeling the Reactions Catalyzed by Coenzyme B12-Dependent Enzymes. Acc. Chem. Res. 2010, 43, 642–651.

(78) Komeyama, K.; Ohata, R.; Kiguchi, S.; Osaka, I. Highly Nucleophilic Vitamin B12-Assisted Nickel-Catalysed Reductive Coupling of Aryl Halides and Non-Activated Alkyl Tosylates. Chem. Commun. 2017, 53, 6401–6404.

(79) Gantzer, C. J.; Wackett, L. P. Reductive Dechlorination Catalyzed by Bacterial Transition-Metal Coenzymes. Environ. Sci. Technol. 1991, 25, 715–722.

(80) Schanke, C. A.; Wackett, L. P. Environmental Reductive Elimination Reactions of Polychlorinated Ethanes Mimicked by Transition-Metal Coenzymes. Environ. Sci. Technol. 1992, 26, 830– 833.

(81) Assaf-Anid, N.; Hayes, K. F.; Vogel, T. M. Reduction Dechlorination of Carbon Tetrachloride by cobalamin(II) in the Presence of Dithiothreitol: Mechanistic Study, Effect of Redox Potential and pH. Environ. Sci. Technol. 1994, 28, 246–252.

(82) Glod, G.; Brodmann, U.; Angst, W.; Holliger, C.; Schwarzenbach, R. P. Cobalamin-Mediated Reduction of Cis- and Trans-Dichloroethene, 1,1-Dichloroethene, and Vinyl Chloride in Homogeneous Aqueous Solution: Reaction Kinetics and Mechanistic Considerations. Environ. Sci. Technol. 1997, 31, 3154–3160.

(83) Payne, K. A.; Quezada, C. P.; Fisher, K.; Dunstan, M. S.; Collins, F. A.; Sjuts, H.; Levy, C.; Hay, S.; Rigby, S. E.; Leys, D. Reductive Dehalogenase Structure Suggests a Mechanism for B12Dependent Dehalogenation. Nature 2015, 517, 513–516.

(84) McCauley, K. M.; Pratt, D. A.; Wilson, S. R.; Shey, J.; Burkey, T. J.; van der Donk, W. A. Properties and Reactivity of Chlorovinylcobalamin and Vinylcobalamin and Their Implications for Vitamin B12-Catalyzed Reductive Dechlorination of Chlorinated Alkenes. J. Am. Chem. Soc. 2005, 127, 1126–1136.

(85) Heckel, B.; Cretnik, S.; Kliegman, S.; Shouakar-Stash, O.; McNeill, K.; Elsner, M. Reductive Outer-Sphere Single Electron Transfer Is an Exception Rather than the Rule in Natural and Engineered Chlorinated Ethene Dehalogenation. Environ. Sci. Technol. 2017, 51, 9663–9673.

(86) Heckel, B.; McNeill, K.; Elsner, M. Chlorinated Ethene Reactivity with Vitamin B12 Is Governed by Cobalamin Chloroethylcarbanions as Crossroads of Competing Pathways. ACS Catal. 2018, 8, 3054–3066.

(87) Shey, J.; McGinley, C. M.; McCauley, K. M.; Dearth, A. S.; Young, B. T.; van der Donk, W. A. Mechanistic Investigation of a Novel Vitamin B12-Catalyzed Carbon-Carbon Bond Forming Reaction, the Reductive Dimerization of Arylalkenes. J. Org. Chem. 2002, 67, 837–846.

(88) Shimakoshi, H.; Hisaeda, Y. B12-TiO2 Hybrid Catalyst for Light-Driven Hydrogen Production and Hydrogenation of C = C Multiple Bonds. ChemPlusChem 2014, 79, 1250–1253.

(89) McCauley, K. M.; Wilson, S. R.; van der Donk, W. A. Synthesis and Characterization of Chlorinated Alkenylcobaloximes To Probe the Mechanism of Vitamin B12-Catalyzed Dechlorination of Priority Pollutants. Inorg. Chem. 2002, 41, 393–404.

(90) McGinley, C. M.; Relyea, H. A.; van der Donk, W. A. Vitamin B12 Catalyzed Radical Cyclizations of Aryl Alkenes. Synlett 2006, 211–214.

(91) Proinsias, K. o.; Jackowska, A.; Radzewicz, K.; Giedyk, M.; Gryko, D. Vitamin B12 Catalyzed Atom Transfer Radical Addition. Org. Lett. 2018, 20, 296–299.

(92) Walder, L.; Orlinski, R. Mechanism of the Light-Assisted Nucleophilic Acylation of Activated Olefins Catalyzed by Vitamin B12. Organometallics 1987, 6, 1606–1613.

(93) Ociepa, M.; Baka, O.; Narodowiec, J.; Gryko, D. Light-Driven Vitamin B12-Catalysed Generation of Acyl Radicals from 2-S-Pyridyl Thioesters. Adv. Synth. Catal. 2017, 359, 3560–3565.

(94) Chen, Y.; Zhang, X. P. Vitamin B12 Derivatives as Natural Asymmetric Catalysts: Enantioselective Cyclopropanation of Alkenes. J. Org. Chem. 2004, 69, 2431–2435.

(95) Giedyk, M.; Goliszewska, K.; Proinsias, K.; Gryko, D. Cobalt(I)-Catalysed CH-Alkylation of Terminal Olefins, and Beyond. Chem. Commun. 2016, 52, 1389–1392.

(96) Giedyk, M.; Turkowska, J.; Lepak, S.; Marculewicz, M.; Proinsias, K. O.; Gryko, D. Photoinduced Vitamin B12-Catalysis for Deprotection of (Allyloxy)arenes. Org. Lett. 2017, 19, 2670–2673.

(97) Shimakoshi, H.; Hisaeda, Y. Oxygen-Controlled Catalysis by Vitamin B12-TiO2: Formation of Esters and Amides from Trichlorinated Organic Compounds by Photoirradiation. Angew. Chem., Int. Ed. 2015, 54, 15439–15443.

(98) Shimakoshi, H.; Nishi, M.; Tanaka, A.; Chikama, K.; Hisaeda, Y. Photocatalytic Function of a Polymer-Supported B12 Complex with a Ruthenium Trisbipyridine Photosensitizer. Chem. Commun. 2011, 47, 6548–6550.

(99) Zhang, W.; Shimakoshi, H.; Houfuku, N.; Song, X.-M.; Hisaeda, Y. A Polymerized Ionic Liquid-Supported B12 Catalyst with a Ruthenium Trisbipyridine Photosensitizer for Photocatalytic Dechlorination in Ionic Liquids. Dalt. Trans. 2014, 43, 13972–13978.

(100) Scheffold, R.; Amble, E. Synthesis and Reactions of Porphinoid Metal Complexes. 9. Vitamin B12 and a Vitamin B12 Model Compound as Catalysts for the Reductive Cleavage of βHaloethyl Protective Groups of Acids. Angew. Chem. 1980, 92, 643– 644.

(101) Su, H.; Walder, L.; Zhang, Z. Da; Scheffold, R. Asymmetric Catalysis by Vitamin B12. The Isomerization of Achiral Epoxides to Optically Active Allylic Alcohols. Helv. Chim. Acta 1988, 71, 1073– 1078.

(102) Busato, S.; Tinembart, O.; Zhang, Z. Da; Scheffold, R. Vitamin B12, a Catalyst in the Synthesis of Prostaglandins. Tetrahedron 1990, 46, 3155–3166.

(103) Bonhote, P.; Scheffold, R. Asymmetric Catalysis by Vitamin B12. The Mechanism of the cob(I)alamin-Catalyzed Isomerization of 1,2-Epoxycyclopentane to (R)-Cyclopent-2-Enol. Helv. Chim. Acta 1991, 74, 1425–1444.

(104) Essig, S.; Scheffold, R. Asymmetrical Catalysis by Vitamin B12: Isomerization of Achiral 1,4-Epiperoxides to Optically Active 4Hydroxycycloalk-2-En-1-Ones. Chimia (Aarau) 1991, 45, 30–32.

(105) Troxler, T.; Scheffold, R. Asymmetric Catalysis by Vitamin B12: The Isomerization of Achiral Cyclopropanes to Optically Active Olefins. Helv. Chim. Acta 1994, 77, 1193–1202.

(106) Zhang, Z. Da; Scheffold, R. Asymmetric Catalysis by Vitamin B12: The Isomerization of Achiral Aziridines to Optically Active Allylic Amines. Helv. Chim. Acta 1993, 76, 2602–2615.

(107) Scheffold, R.; Dike, M.; Dike, S.; Herold, T.; Walder, L. Synthesis and Reactions of Porphine-Type Metal Complexes. 8. Carbon-Carbon Bond Formation Catalyzed by Vitamin B12 and a Vitamin B12 Model Compound. Electrosynthesis of Bicyclic Ketones by 1,4 Addition. J. Am. Chem. Soc. 1980, 102, 3642–3644.

(108) Scheffold, R.; Orlinski, R. Synthesis and Reactions of Porphine-Type Metal Complexes. 15. Carbon-Carbon Bond Formation by Light Assisted B12-Catalysis. Nucleophilic Acylation of Michael Olefins. J. Am. Chem. Soc. 1983, 105, 7200–7202.

(109) Rodgers, Z. L.; Hughes, R. M.; Doherty, L. M.; Shell, J. R.; Molesky, B. P.; Brugh, A. M.; Forbes, M. D. E.; Moran, A. M.; Lawrence, D. S. B12-Mediated, Long Wavelength Photopolymerization of Hydrogels. J. Am. Chem. Soc. 2015, 137, 3372–3378.

(110) Sharma, B.; Fermanian, S.; Gibson, M.; Unterman, S.; Herzka, D. A.; Cascio, B.; Coburn, J.; Hui, A. Y.; Marcus, N.; Gold, G. E.; et al. Human Cartilage Repair with a Photoreactive Adhesive-Hydrogel Composite. Sci. Transl. Med. 2013, 5, 167ra6.

(111) Shell, T. A.; Shell, J. R.; Rodgers, Z. L.; Lawrence, D. S. Tunable Visible and Near-IR Photoactivation of Light-Responsive Compounds by Using Fluorophores as Light-Capturing Antennas. Angew. Chem., Int. Ed. 2014, 53, 875−878.

(112) Shell, T. A.; Lawrence, D. S. Vitamin B12: A Tunable, Long Wavelength, Light-Responsive Platform for Launching Therapeutic Agents. Acc. Chem. Res. 2015, 48, 2866−2874.

(113) Priestman, M. A.; Shell, T. A.; Sun, L.; Lee, H.-M.; Lawrence, D. S. Merging of Confocal and Caging Technologies: Selective ThreeColor Communication with Profluorescent Reporters. Angew. Chem., Int. Ed. 2012, 51, 7684−7687.

(114) Shell, T. A.; Shell, J. R.; Rodgers, Z. L.; Lawrence, D. S. Tunable Visible and Near-IR Photoactivation of Light-Responsive Compounds by Using Fluorophores as Light-Capturing Antennas. Angew. Chem., Int. Ed. 2014, 53, 875−878.

(115) Smith, W. J.; Oien, N. P.; Hughes, R. M.; Marvin, C. M.; Rodgers, Z. L.; Lee, J.; Lawrence, D. S. Cell-Mediated Assembly of Phototherapeutics. Angew. Chem., Int. Ed. 2014, 53, 10945−10948.

(116) Rodgers, Z. L.; Shell, T. A.; Brugh, A. M.; Nowotarski, H. L.; Forbes, M. D. E.; Lawrence, D. S. Fluorophore Assisted Photolysis of Thiolato-Cob(III)alamins. Inorg. Chem. 2016, 55, 1962−1969.

(117) Johnson, A. W.; Mervyn, L.; Shaw, N.; Smith, E. L. A Partial Synthesis of the Vitamin B12 Coenzyme and Some of Its Analogs. J. Chem. Soc. 1963, 0, 4146−4156.

(118) Ogoshi, H.; Watanabe, E.; Koketsu, N.; Yoshida, Z. Synthesis and Properties of Organocobalt(III)octaethylporphyrins. Bull. Chem. Soc. Jpn. 1976, 49, 2529−2536.

(119) Gridnev, A. A.; Ittel, S. D.; Fryd, M.; Wayland, B. B. Formation of Organocobalt Porphyrin Complexes from Reactions of cobalt(II) Porphyrins and Dialkylcyanomethyl Radicals with Organic Substrates: Chemical Trapping of a Transient Cobalt Porphyrin Hydride. Organometallics 1993, 12, 4871−4880.

(120) Gridnev, A. A.; Ittel, S. D.; Fryd, M.; Wayland, B. B. Formation of Organocobalt Porphyrin Complexes by Reactions of cobalt(II) Porphyrins with Azoisobutyronitrile and Organic Substrates. J. Chem. Soc., Chem. Commun. 1993, 0, 1010−1011.

(121) Morrison, D. A.; Davis, T. P.; Heuts, J. P. A.; Messerle, B.;

(122) Gridnev, A. A. Free Radical Polymerization with Catalytic Chain Transfer: Using NMR to Probe the Strength of the Cobalt-Carbon Bond in Small Molecule Model Reactions. J. Polym. Sci., Part A: Polym. Chem. 2006, 44, 6171−6189.

(123) Costa, G.; Mestroni, G.; Stefani, L. Organometallic Derivatives of cobalt(III) Chelates of Bis(salicylaldehyde) Ethylenediimine. J. Organomet. Chem. 1967, 7, 493−501.

(124) Zhao, Y.; Yu, M.; Zhang, S.; Liu, Y.; Fu, X. Visible Light Induced Living/Controlled Radical Polymerization of Acrylates Catalyzed by Cobalt Porphyrins. Macromolecules 2014, 47, 6238−6245.

(125) Zhao, Y.; Yu, M.; Fu, X. Photo-Cleavage of the Cobalt-Carbon Bond: Visible Light-Induced Living Radical Polymerization Mediated by Organo-Cobalt Porphyrins. Chem. Commun. 2013, 49, 5186−5188. (125) Zhao, Y.; Liu, X.; Liu, Y.; Wu, Z.; Zhao, X.; Fu, X. When CMRP Met Alkyl Vinyl Ketone: Visible Light Induced Living Radical Polymerization (LRP) of Ethyl Vinyl Ketone (EVK). Chem. Commun. 2016, 52, 12092−12095.

(126) Halpern, J. Determination of Transition Metal-Alkyl Bond Dissociation Energies from Kinetic Measurements. Polyhedron 1988, 7, 1483−1490.

(127) Dong, H.; Hou, T.; Zhao, Y.; Fu, X.; Li, Y. DFT Study of Cobalt Porphyrin Complex for Living Radical Polymerization of Olefins. Comput. Theor. Chem. 2012, 1001, 51−59.

(128) Woska, D. C.; Xie, Z. D.; Gridnev, A. A.; Ittel, S. D.; Fryd, M.; Wayland, B. B. Determination of Organo-Cobalt Bond Dissociation Energetics and Thermodynamic Properties of Organic Radicals through Equilibrium Studies. J. Am. Chem. Soc. 1996, 118, 9102− 9109.

(129) Stolzenberg, A. M.; Summers, J. S. Cis-Influence of Hydroporphyrin Macrocycles on Axial Ligation Equilibria and Alkyl Exchange Reactions of Alkylcobalt(III) Porphyrin Complexes. Inorg. Chem. 2000, 39, 1518−1524.

(130) Pfeffer, M.; Grellier, M. Cobalt Organometallics. In Comprehensive Organometallic Chemistry III; Elsevier Ltd., 2007; Vol. 7, pp 1−119.

(131) Fritsch, J. M.; McNeill, K. Aqueous Reductive Dechlorination of Chlorinated Ethylenes with Tetrakis(4-Carboxyphenyl)porphyrin Cobalt. Inorg. Chem. 2005, 44, 4852−4861.

(132) Hayashi, T.; Okazaki, K.; Urakawa, N.; Shimakoshi, H.; Sessler, J. L.; Vogel, E.; Hisaeda, Y. Cobaltporphycenes as Catalysts. The Oxidation of Vinyl Ethers via the Formation and Dissociation of Cobalt-Carbon Bonds. Organometallics 2001, 20, 3074−3078.

(133) Paul, N. D.; Mandal, S.; Otte, M.; Cui, X.; Zhang, X. P.; de Bruin, B. Metalloradical Approach to 2H-Chromenes. J. Am. Chem. Soc. 2014, 136, 1090−1096.

(134) Te Grotenhuis, C.; Das, B. G.; Kuijpers, P. F.; Hageman, W.; Trouwborst, M.; de Bruin, B. Catalytic 1,2-Dihydronaphthalene and E-Aryl-Diene Synthesis via CoIII-Carbene Radical and O-Quinodimethane Intermediates. Chem. Sci. 2017, 8, 8221−8230.

(135) Ukrainczyk, L.; Chibwe, M.; Pinnavaia, T. J.; Boyd, S. A. Reductive Dechlorination of Carbon Tetrachloride In Water Catalyzed by Mineral-Supported Biomimetic Cobalt Macrocycles. Environ. Sci. Technol. 1995, 29, 439−445.

(136) Doherty, R. E. A History of the Production and Use of Carbon Tetrachloride, Tetrachloroethylene, Trichloroethylene and 1,1,1Trichloroethane in the United States: Part 2 - Trichloroethylene and 1,1,1-Trichloroethane. Environ. Forensics 2000, 1, 83−93.

(137) Squillace, P. J.; Moran, M. J.; Lapham, W. W.; Price, C. V.; Clawges, R. M.; Zogorski, J. S. Volatile Organic Compounds in Untreated Ambient Groundwater of the United States, 1985−1995. Environ. Sci. Technol. 1999, 33, 4176−4187.

(138) Ardo, S.; Achey, D.; Morris, A. J.; Abrahamsson, M.; Meyer, G. J. Non-Nernstian Two-Electron Transfer Photocatalysis at Metalloporphyrin-TiO2 Interfaces. J. Am. Chem. Soc. 2011, 133, 16572−16580.

(139) Lu, H.; Dzik, W. I.; Xu, X.; Wojtas, L.; de Bruin, B.; Zhang, X. P. Experimental Evidence for cobalt(III)-Carbene Radicals: Key Intermediates in cobalt(II)-Based Metalloradical Cyclopropanation. J. Am. Chem. Soc. 2011, 133, 8518−8521.

(140) Lyaskovskyy, V.; de Bruin, B. Redox Non-Innocent Ligands: Versatile New Tools to Control Catalytic Reactions. ACS Catal. 2012, 2, 270−279.

(141) Doyle, M. P. Exceptional Selectivity in Cyclopropanation Reactions Catalyzed by Chiral Cobalt (II)-Porphyrin Catalysts. Angew. Chem., Int. Ed. 2009, 48, 850−852.

(142) Zhu, S.; Ruppel, J. V.; Lu, H.; Wojtas, L.; Zhang, X. P. CobaltCatalyzed Asymmetric Cyclopropanation with Diazosulfones: Rigidification and Polarization of Ligand Chiral Environment via Hydrogen Bonding and Cyclization. J. Am. Chem. Soc. 2008, 130, 5042−5043.

(143) Fantauzzi, S.; Gallo, E.; Rose, E.; Raoul, N.; Caselli, A.; Issa, S.; Ragaini, F.; Cenini, S. Asymmetric Cyclopropanation of Olefins Catalyzed by Chiral Cobalt(II)-Binaphthyl Porphyrins. Organometallics 2008, 27, 6143−6151.

(144) Xu, X.; Zhu, S.; Cui, X.; Wojtas, L.; Zhang, X. P. Cobalt(II)Catalyzed Asymmetric Olefin Cyclopropanation with α-Ketodiazoacetates. Angew. Chem., Int. Ed. 2013, 52, 11857−11861.

(145) Ruppel, J. V.; Kamble, R. M.; Zhang, X. P. Cobalt-Catalyzed Intramolecular C-H Amination with Arylsulfonyl Azides. Org. Lett. 2007, 9, 4889−4892.

(146) Lu, H.; Li, C.; Jiang, H.; Lizardi, C. L.; Zhang, X. P. Chemoselective Amination of Propargylic C(sp3)-H Bonds by Cobalt(II)-Based Metallo-Radical Catalysis. Angew. Chem., Int. Ed. 2014, 53, 7028−7032.

(147) Paul, N. D.; Chirila, A.; Lu, H.; Zhang, X. P.; de Bruin, B. Carbene Radicals in Cobalt(II)-Porphyrin-Catalysed Carbene Carbonylation Reactions; A Catalytic Approach to Ketenes. Chem. - Eur. J. 2013, 19, 12953−12958.

(148) Das, B. G.; Chirila, A.; Tromp, M.; Reek, J. N. H.; Bruin, B. de. Co(III)-Carbene Radical Approach to Substituted 1H-Indenes. J. Am. Chem. Soc. 2016, 138, 8968−8975.

(149) Huang, L.; Chen, Y.; Gao, G.-Y.; Zhang, X. P. Diastereoselective and Enantioselective Cyclopropanation of Alkenes Catalyzed by Cobalt Porphyrins. J. Org. Chem. 2003, 68, 8179−8184.

(150) Cui, X.; Xu, X.; Lu, H.; Zhu, S.; Wojtas, L.; Zhang, X. P. Enantioselective Cyclopropenation of Alkynes with Acceptor/Acceptor-Substituted Diazo Reagents via Co(II)-Based Metalloradical Catalysis. J. Am. Chem. Soc. 2011, 133, 3304−3307.

(151) Xu, X.; Lu, H.; Ruppel, J. V.; Cui, X.; Lopez de Mesa, S.; Wojtas, L.; Zhang, X. P. Highly Asymmetric Intramolecular Cyclopropanation of Acceptor-Substituted Diazoacetates by Co(II)Based Metalloradical Catalysis: Iterative Approach for Development of New-Generation Catalysts. J. Am. Chem. Soc. 2011, 133, 15292− 15295.

(152) Majumdar, N.; Paul, N. D.; Mandal, S.; de Bruin, B.; Wulff, W. D. Catalytic Synthesis of 2H-Chromenes. ACS Catal. 2015, 5, 2329− 2366.

(153) Cui, X.; Xu, X.; Wojtas, L.; Kim, M. M.; Zhang, X. P. Regioselective Synthesis of Multisubstituted Furans via Metalloradical Cyclization of Alkynes with α-Diazocarbonyls: Construction of Functionalized α-Oligofurans. J. Am. Chem. Soc. 2012, 134, 19981− 19984.

(154) Zhu, S.; Xu, X.; Perman, J. A.; Zhang, X. P. A General and Efficient Cobalt(II)-Based Catalytic System for Highly Stereoselective Cyclopropanation of Alkenes with α-Cyanodiazoacetates. J. Am. Chem. Soc. 2010, 132, 12796−12799.

(155) Wang, Y.; Wen, X.; Cui, X.; Wojtas, L.; Zhang, X. P. Asymmetric Radical Cyclopropanation of Alkenes with In SituGenerated Donor-Substituted Diazo Reagents via Co(II)-Based Metalloradical Catalysis. J. Am. Chem. Soc. 2017, 139, 1049−1052.

(156) Nakamura, A.; Konishi, A.; Tatsuno, Y.; Otsuka, S. A Highly Enantioselective Synthesis of Cyclopropane Derivatives through Chiral cobalt(II) Complex Catalyzed Carbenoid Reaction. General Scope and Factors Determining the Enantioselectivity. J. Am. Chem. Soc. 1978, 100, 3443–3448.

(157) Ruppel, J. V.; Gauthier, T. J.; Snyder, N. L.; Perman, J. A.; Zhang, X. P. Asymmetric Co(II)-Catalyzed Cyclopropanation with Succinimidyl Diazoacetate: General Synthesis of Chiral Cyclopropyl Carboxamides. Org. Lett. 2009, 11, 2273–2276.

(158) Xu, X.; Wang, Y.; Cui, X.; Wojtas, L.; Zhang, X. P. Metalloradical Activation of α-Formyldiazoacetates for the Catalytic Asymmetric Radical Cyclopropanation of Alkenes. Chem. Sci. 2017, 8, 4347–4351.

(159) Hu, Y.; Lang, K.; Tao, J.; Marshall, M. K.; Cheng, Q.; Cui, X.; Wojtas, L.; Zhang, X. Next-Generation D2-Symmetric Chiral Porphyrins for Cobalt(II)-Based Metalloradical Catalysis: Catalyst Engineering by Distal Bridging. Angew. Chem., Int. Ed. 2019, 58, 2670–2674.

(160) Alcantara, A. F. P.; Fontana, L. A.; Rigolin, V. H.; Andrade, Y. F. S.; Ribeiro, M. A.; Barros, W. P.; Ornelas, C.; Megiatto, J. D. J. Olefin Cyclopropanation by Radical Carbene Transfer Reactions Promoted by Cobalt(II)/Porphyrinates: Active-Metal-Template Synthesis of [2]Rotaxanes. Angew. Chem., Int. Ed. 2018, 57, 8979–8983.

(161) Chirila, A.; van Vliet, K. M.; Paul, N. D.; de Bruin, B. [Co(MeTAA)] Metalloradical Catalytic Route to Ketenes via Carbonylation of Carbene Radicals. Eur. J. Inorg. Chem. 2018, 2018, 2251–2258.

(162) Wang, Y.; Wen, X.; Cui, X.; Zhang, X. P. Enantioselective Radical Cyclization for Construction of 5-Membered Ring Structures by Metalloradical C-H Alkylation. J. Am. Chem. Soc. 2018, 140, 4792–4796.

(163) Wen, X.; Wang, Y.; Zhang, X. P. Enantioselective Radical Process for Synthesis of Chiral Indolines by Metalloradical Alkylation of Diverse C(sp3)-H Bonds. Chem. Sci. 2018, 9, 5082–5086.

(164) Enikolopyan, N. S.; Smirnov, B. R.; Ponomarev, G. V.; Belgovskii, I. M. Catalyzed Chain Transfer to Monomer in Free Radical Polymerization. J. Polym. Sci., Polym. Chem. Ed. 1981, 19, 879–889.

(165) Gridnev, A. A.; Ittel, S. D.; Wayland, B. B.; Fryd, M. Isotopic Investigation of Hydrogen Transfer Related to Cobalt-Catalyzed FreeRadical Chain Transfer. Organometallics 1996, 15, 5116–5126.

(166) Gridnev, A. A.; Ittel, S. D. Dependence of Free-Radical Propagation Rate Constants on the Degree of Polymerization. Macromolecules 1996, 29, 5864–5874.

(167) Gridnev, A. The 25th Anniversary of Catalytic Chain Transfer. J. Polym. Sci., Part A: Polym. Chem. 2000, 38, 1753–1766.

(168) Poli, R. Relationship between One-Electron Transition-Metal Reactivity and Radical Polymerization Processes. Angew. Chem., Int. Ed. 2006, 45, 5058–5070.

(169) Poli, R. New Phenomena in Organometallic-Mediated Radical Polymerization (OMRP) and Perspectives for Control of Less Active Monomers. Chem. - Eur. J. 2015, 21, 6988–7001.

(170) Kukulj, D.; Davis, T. P. Mechanism of Catalytic Chain Transfer in the Free-Radical Polymerization of Methyl Methacrylate and Styrene. Macromol. Chem. Phys. 1998, 199, 1697–1708.

(171) Wayland, B. B.; Basickes, L.; Mukerjee, S.; Wei, M.; Fryd, M. Living Radical Polymerization of Acrylates Initiated and Controlled by Organocobalt Porphyrin Complexes. Macromolecules 1997, 30, 8109–8112.

(172) Lu, Z.; Fryd, M.; Wayland, B. B. New Life for Living Radical Polymerization Mediated by Cobalt(II) Metalloradicals. Macromolecules 2004, 37, 2686–2687.

(173) Peng, C.-H.; Scricco, J.; Li, S.; Fryd, M.; Wayland, B. B. Organo-Cobalt Mediated Living Radical Polymerization of Vinyl Acetate. Macromolecules 2008, 41, 2368–2373.

(174) Li, S.; Bruin, B. de; Peng, C.-H.; Fryd, M.; Wayland, B. B. Exchange of Organic Radicals with Organo-Cobalt Complexes Formed in the Living Radical Polymerization of Vinyl Acetate. J. Am. Chem. Soc. 2008, 130, 13373–13381.

(175) Hsu, C.-S.; Yang, T.-Y.; Peng, C.-H. Vinyl Acetate Living Radical Polymerization Mediated by Cobalt Porphyrins: KineticMechanistic Studies. Polym. Chem. 2014, 5, 3867–3875.

(176) Peng, C.-H.; Fryd, M.; Wayland, B. B. Organocobalt Mediated Radical Polymerization of Acrylic Acid in Water. Macromolecules 2007, 40, 6814–6819.

(177) Li, Y.; Basickes, L.; Wayland, B. B. Applications of WaterSoluble cobalt(II) Porphyrin in Controlled Radical Polymerizations of Acrylates in Aqueous Media. Polym. Prepr. 2001, 42, 200.

(178) Wang, L.; Zhao, H.; Wang, B.; Sun, J.; Zhang, Y.; Ji, L.; Cao, Z. Dispersion Polymerization of Acrylamide with Living Character and Controlled Morphologies Initiated and Mediated by Cobalt Porphyrin. RSC Adv. 2016, 6, 63519–63524.

(179) Zhao, H.; Wang, B.; Li, Q.; Wang, L.; Sun, J.; Zhang, Y.; Ji, L.; Cao, Z. Dispersion and Soap-Free Emulsion Polymerization of TertButyl Acrylate with the Living Character and Controlled Particle Size Mediated by Cobalt Porphyrin. RSC Adv. 2017, 7, 10124–10131.

(180) Zhao, Y.; Dong, H.; Li, Y.; Fu, X. Living Radical Polymerization of Acrylates and Acrylamides Mediated by a Versatile Cobalt Porphyrin Complex. Chem. Commun. 2012, 48, 3506–3508.

(181) Wayland, B. B.; Peng, C.-H.; Fu, X.; Lu, Z.; Fryd, M. Degenerative Transfer and Reversible Termination Mechanisms for Living Radical Polymerizations Mediated by Cobalt Porphyrins. Macromolecules 2006, 39, 8219–8222.

(182) Wang, F.-S.; Yang, T.-Y.; Hsu, C.-C.; Chen, Y.-J.; Li, M.-H.; Hsu, Y.-J.; Chuang, M.-C.; Peng, C.-H. The Mechanism and Thermodynamic Studies of CMRP: Different Control Mechanisms Demonstrated by CoII(TMP), CoII(salen*), and CoII(acac)2 Mediated Polymerization, and the Correlation of Reduction Potential, Equilibrium Constant, and Control Mechanism. Macromol. Chem. Phys. 2016, 217, 422–432.

(183) Marzilli, L. G.; Summers, M. F.; Bresciani-Pahor, N.; Zangrando, E.; Charland, J. P.; Randaccio, L. Rare Examples of Structurally Characterized Five-Coordinate Organocobalt Complexes. Novel Dynamic NMR Evidence for Synergistic Enhancement of Cis and Trans Effects in B12 Models. J. Am. Chem. Soc. 1985, 107, 6880– 6888.

(184) Bresciani-Pahor, N.; Forcolin, M.; Marzilli, L. G.; Randaccio, L.; Summers, M. F.; Toscano, P. J. Organocobalt B12 Models: Axial Ligand Effects on the Structural and Coordination Chemistry of Cobaloximes. Coord. Chem. Rev. 1985, 63, 1–125.

(185) Dodd, D.; Johnson, M. D. Organic Compounds of cobalt(III). J. Organomet. Chem. 1973, 52, 1–232.

(186) Gupta, B. D.; Roy, S. Organocobaloximes: Cobalt-Carbon Bond Stability and Synthesis. Inorg. Chim. Acta 1988, 146, 209–221.

(187) Geno, M. K.; Halpern, J. Why Does Nature Not Use the Porphyrin Ligand in Vitamin B12? J. Am. Chem. Soc. 1987, 109, 1238–1240.

(188) Tolman, C. A. Steric Effects of Phosphorus Ligands in Organometallic Chemistry and Homogeneous Catalysis. Chem. Rev. 1977, 77, 313–348.

(189) Toscano, P. J.; Seligson, A. L.; Curran, M. T.; Skrobutt, A. T.; Sonnenberger, D. C. Cobalt-Carbon Bond Disruption Enthalpies: The First Reliable Measurement of a Co-Methyl BDE via Solution Thermochemical Methods. Inorg. Chem. 1989, 28, 166–168.

(190) Gupta, B. D.; Kanth, V. V.; Singh, V. Organocobaloximes: Synthesis, Oxygen Insertion and Kinetics. J. Organomet. Chem. 1998, 570, 1–7.

(191) White, R. E.; Coon, M. J. Oxygen Activation by Cytochrome P-450. Annu. Rev. Biochem. 1980, 49, 315–356.

(192) Kijima, M.; Yamashita, H.; Sato, T. Reactions of Alkylcobaloximes with Oxygen under Irradiation. Oxygenative Conversions of the Alkyl Ligand. J. Organomet. Chem. 1994, 474, 177–182.

(193) Das, I.; Chowdhury, S.; Ravikumar, K.; Roy, S.; Gupta, B. D. Organocobaloximes in Organic Synthesis. An Unusual RadicalDependent Five-Member Cyclization. J. Organomet. Chem. 1997, 532, 101–107.

(194) Okabe, M.; Tada, M. Reductive Cyclization Caused by Cobaloxime. I. A New Method for the Synthesis of β-Methylene-γButyrolactones. J. Org. Chem. 1982, 47, 5382–5384.

(195) Last, K.; Hoffmann, H. M. R. Vicinal Bromopropargoxylation of Cyclic Olefins and Cobaloxime-Mediated Heteroannulation to Functionalized 3-Methyleneoxacyclopentanes. Synthesis (Stuttg.) 1989, 12, 901–905.

(196) Ladlow, M.; Pattenden, G. Intramolecular Free Radical Cyclizations onto Vinyl Ethers. A Method for the Synthesis of β-Oxyγ-Butyrolactones. Tetrahedron Lett. 1984, 25, 4317–4320.

(197) Branchaud, B. P.; Yu, G. X. An Example of the Persistent Radical Effect in Cobaloxime-Mediated Radical Alkyl-Alkenyl Cross Coupling. Organometallics 1993, 12, 4262–4264.

(198) Branchaud, B. P.; Detlefsen, W. D. Cobaloxime-Catalyzed Radical Alkyl-Styryl Cross Couplings. Tetrahedron Lett. 1991, 32, 6273–6276.

(199) Giese, B.; Erdmann, P.; Gobel, T.; Springer, R. CobaltCatalyzed Carbon-Carbon Bond Formation via Radicals. Tetrahedron Lett. 1992, 33, 4545–4548.

(200) Weiss, M. E.; Carreira, E. M. Total Synthesis of (+)-Daphmanidin E. Angew. Chem., Int. Ed. 2011, 50, 11501–11505.

(201) Branchaud, B. P.; Choi, Y. L. Cobaloxime-Mediated Radical Alkyl-Heteroaromatic Substitution. J. Org. Chem. 1988, 53, 4638– 4641.

(202) Ghosez, A.; Goebel, T.; Giese, B. Syntheses and Reactions of Glycosylcobaloximes. Chem. Ber. 1988, 121, 1807–1811.

(203) Wright, M. W.; Smalley, T. L., Jr.; Welker, M. E.; Rheingold, A. L. Synthesis of Cobalt Substituted 1,3-Diene Complexes with Unusual Structures and Their Exo Selective Diels-Alder Reactions. J. Am. Chem. Soc. 1994, 116, 6777–6791.

(204) Wright, M. W.; Welker, M. E. Transition Metal Mediated Exo Selective Diels-Alder Reactions: Preparation of 2-Cobalt-Substituted 1,3-Dienes Containing C2 Symmetric 2,3-Dibenzobicyclo[2.2.2]octanedione Dioxime Equatorial Ligands and Their Use in Thermal and Lewis Acid Catalyzed 4 + 2 C. J. Org. Chem. 1996, 61, 133–141.

(205) Pickin, K. A.; Kindy, J. M.; Day, C. S.; Welker, M. E. Simple Preparation of Cobaloxime Dienyl Complexes and Their Exo Selective Diels-Alder Cycloadducts. Progress toward Transition Metal-Mediated Diels-Alder Reactions Which Are Catalytic in Metal Dienyl Complex. J. Organomet. Chem. 2003, 681, 120–133.

(206) Tucker, C. J.; Welker, M. E.; Day, C. S.; Wright, M. W. Preparation of an Aquocobaloxime 1,3-Dienyl Complex and Its DielsAlder Reactions in Water and Organic Solvents. Organometallics 2004, 23, 2257–2262.

(207) Pidaparthi, R. R.; Welker, M. E.; Day, C. S. [6 + 4] And [4 + 2] Cycloaddition Reactions of Cobaloxime 1,3-Dienyl Complexes and Tropones. Organometallics 2006, 25, 974–981.

(208) Li, G.; Han, A.; Pulling, M. E.; Estes, D. P.; Norton, J. R. Evidence for Formation of a Co-H Bond from (H2O)2Co(dmgBF2)2 under H2: Application to Radical Cyclizations. J. Am. Chem. Soc. 2012, 134, 14662–14665.

(209) Li, G.; Kuo, J. L.; Han, A.; Abuyuan, J. M.; Young, L. C.; Norton, J. R.; Palmer, J. H. Radical Isomerization and Cycloisomerization Initiated by H.bul. Transfer. J. Am. Chem. Soc. 2016, 138, 7698–7704.

(210) Li, G.; Estes, D. P.; Norton, J. R.; Ruccolo, S.; Sattler, A.; Sattler, W. Dihydrogen Activation by Cobaloximes with Various Axial Ligands. Inorg. Chem. 2014, 53, 10743–10747.

(211) Estes, D. P.; Grills, D. C.; Norton, J. R. The Reaction of Cobaloximes with Hydrogen: Products and Thermodynamics. J. Am. Chem. Soc. 2014, 136, 17362–17365.

(212) Melby, L. R.; Janowicz, A. H.; Ittel, S. D. Cobalt(II) Chelates as Chain-Transfer Agents in Free-Radical Polymerizations. Eur. Pat. Appl. EP199436A1, 1986.

(213) Haddleton, D. M.; Muir, A. V. G.; Leeming, S. W. Free Radical Polymerization Process. PCT Int. Appl. WO9517435A1, 1995.

(214) Hawthorne, D. G. Oligomerization Process. PCT Int. Appl. WO8703605A1, 1987.

(215) Heuts, J. P. A.; Smeets, N. M. B. Catalytic Chain Transfer and Its Derived Macromonomers. Polym. Chem. 2011, 2, 2407–2423.

(216) Krstina, J.; Moad, C. L.; Moad, G.; Rizzardo, E.; Berge, C. T.; Fryd, M. A New Form of Controlled Growth Free Radical Polymerization. Macromol. Symp. 1996, 111, 13–23.

(217) Guan, Z. Control of Polymer Topology through TransitionMetal Catalysis: Synthesis of Hyperbranched Polymers by CobaltMediated Free Radical Polymerization. J. Am. Chem. Soc. 2002, 124, 5616–5617.

(218) Smeets, N. M. B. Amphiphilic Hyperbranched Polymers from the Copolymerization of a Vinyl and Divinyl Monomer: The Potential of Catalytic Chain Transfer Polymerization. Eur. Polym. J. 2013, 49, 2528–2544.

(219) Chuang, Y.-M.; Ethirajan, A.; Junkers, T. Photoinduced Sequence-Controlled Copper-Mediated Polymerization: Synthesis of Decablock Copolymers. ACS Macro Lett. 2014, 3, 732–737.

(220) Anastasaki, A.; Nikolaou, V.; McCaul, N. W.; Simula, A.; Godfrey, J.; Waldron, C.; Wilson, P.; Kempe, K.; Haddleton, D. M. Photoinduced Synthesis of A,ω-Telechelic Sequence-Controlled Multiblock Copolymers. Macromolecules 2015, 48, 1404–1411.

(221) Gody, G.; Maschmeyer, T.; Zetterlund, P. B.; Perrier, S. Rapid and Quantitative One-Pot Synthesis of Sequence-Controlled Polymers by Radical Polymerization. Nat. Commun. 2013, 4, 2505.

(222) Gody, G.; Maschmeyer, T.; Zetterlund, P. B.; Perrier, S. Pushing the Limit of the RAFT Process: Multiblock Copolymers by One-Pot Rapid Multiple Chain Extensions at Full Monomer Conversion. Macromolecules 2014, 47, 3451–3460.

(223) Engelis, N. G.; Anastasaki, A.; Nurumbetov, G.; Truong, N. P.; Nikolaou, V.; Shegiwal, A.; Whittaker, M. R.; Davis, T. P.; Haddleton, D. M. Sequence-Controlled Methacrylic Multiblock Copolymers via Sulfur-Free RAFT Emulsion Polymerization. Nat. Chem. 2017, 9, 171–178.

(224) Engelis, N. G.; Anastasaki, A.; Whitfield, R.; Jones, G. R.; Liarou, E.; Nikolaou, V.; Nurumbetov, G.; Haddleton, D. M. Sequence-Controlled Methacrylic Multiblock Copolymers: Expanding the Scope of Sulfur-Free RAFT. Macromolecules 2018, 51, 336–342.

(225) Lotierzo, A.; Schofield, R. M.; Bon, S. A. F. Toward SulfurFree RAFT Polymerization Induced Self-Assembly. ACS Macro Lett. 2017, 6, 1438–1443.

(226) Schreur-Piet, I.; Heuts, J. P. A. In Situ Stabilizer Formation from Methacrylic Acid Macromonomers in Emulsion Polymerization. Polym. Chem. 2017, 8, 6654–6664.

(227) Nurumbetov, G.; Engelis, N.; Godfrey, J.; Hand, R.; Anastasaki, A.; Simula, A.; Nikolaou, V.; Haddleton, D. M. Methacrylic Block Copolymers by Sulfur Free RAFT (SF RAFT) Free Radical Emulsion Polymerisation. Polym. Chem. 2017, 8, 1084– 1094.

(228) Zhang, M.; Hutchinson, R. A. Synthesis and Utilization of Low Dispersity Acrylic Macromonomer as Dispersant for Nonaqueous Dispersion Polymerization. Macromolecules 2018, 51, 6267– 6275.

(229) Arvanitopoulos, L. D.; Gruel, M. P.; Harwood, H. J. Living free Radical Polymerization Using Alkyl Cobaloximes as Photoinitiators. Polym. Prepr. 1994, 35, 549–550.

(230) Greuel, M. P.; Arvanitopoulos, L. D.; Harwood, H. J. Cobaloxime Photoinitiators for Free Radical Polymerization. U.S. Patent US5468785A, 1995.

(231) Arvanitopoulos, L. D.; Greuel, M. P.; King, B. M.; Shim, A. K.; Harwood, H. J. Photochemical Polymerizations Initiated and Mediated by Soluble Organocobalt Compounds. ACS Symp. Ser. 1998, 685, 316–331.

(232) Harwood, H. J.; Shim, A. K. Polymers and Copolymers Prepared or Modified by Using Cobalt Complexes. PCT Int. Appl. WO2000050467A1, 2000.

(233) Costa, G.; Mestroni, G. Acyl-and carboxyalkylcobalt(III) Chelates. Tetrahedron Lett. 1967, 19, 1783–1784.

(234) McAllister, R. M.; Weber, J. H. Preparation and Reactions of Alkyl-Cobalt Complexes Containing Schiff Base Ligands. J. Organomet. Chem. 1974, 77, 91–105.

(235) Chambers, D. R.; Sullivan, R. E.; Martin, D. B. C. Synthesis and Characterization of Alkoxycarbonyl Cobalt Complexes via Direct Carbonylation Methods. Organometallics 2017, 36, 1630–1639.

(236) Liu, X.; Tian, L.; Wu, Z.; Zhao, X.; Wang, Z.; Yu, D.; Fu, X. Visible-Light-Induced Synthesis of Polymers with Versatile End Groups Mediated by Organocobalt Complexes. Polym. Chem. 2017, 8, 6033–6038.

(237) Tsou, T. T.; Loots, M.; Halpern, J. Kinetic Determination of Transition Metal-Alkyl Bond Dissociation Energies: Application to Organocobalt Compounds Related to B12 Coenzymes. J. Am. Chem. Soc. 1982, 104, 623–624.

(238) Li, G.; Zhang, F. F.; Chen, H.; Yin, H. F.; Chen, H. L.; Zhang, S. Y. Determination of Co-C Bond Dissociation Energies for Organocobalt Complexes Related to Coenzyme B12 Using Photoacoustic Calorimetry. J. Chem. Soc., Dalton Trans. 2002, 0, 105–110.

(239) Patel, V. F.; Pattenden, G.; Russell, J. J. Synthesis of Benzofurans, Indoles and Benzopyrans via Oxidative Free Radical Cyclizations Using Cobalt Salen Complexes. Tetrahedron Lett. 1986, 27, 2303–2306.

(240) Patel, V. F.; Pattenden, G. Cobalt Mediated Radical AdditionElimination Carbon-Carbon Bond Forming Reactions in Synthesis. J. Chem. Soc., Chem. Commun. 1987, 0, 871–872.

(241) Bandaranayake, W. M.; Pattenden, G. Cobalt-Catalyzed Oligomerization of Methyl Methacrylate; Reactivation of Oligomers by Hydrocobaltation. J. Chem. Soc., Chem. Commun. 1988, 1179– 1181.

(242) Patel, V. f.; Pattenden, G. Free Radical Reactions Initiated by Organocobalt Complexes. A New Method for the Degradation of Carboxylic Acids to Functionalized Noralkanes via Acylcobalt Salophen Intermediates. Tetrahedron Lett. 1988, 29, 707–710.

(243) Gill, G. B.; Pattenden, G.; Reynolds, S. J. Cobalt-Mediated Reactions. A New Synthetic Approach to β-, γ- and δ-Lactams. Tetrahedron Lett. 1989, 30, 3229–3232.

(244) Waser, J.; Nambu, H.; Carreira, E. M. Cobalt-Catalyzed Hydroazidation of Olefins: Convenient Access to Alkyl Azides. J. Am. Chem. Soc. 2005, 127, 8294–8295.

(245) Gaspar, B.; Carreira, E. M. Mild Cobalt-Catalyzed Hydrocyanation of Olefins with Tosyl Cyanide. Angew. Chem., Int. Ed. 2007, 46, 4519–4522.

(246) Gaspar, B.; Carreira, E. M. Catalytic Hydrochlorination of Unactivated Olefins with Para-Toluenesulfonyl Chloride. Angew. Chem., Int. Ed. 2008, 47, 5758–5760.

(247) Gaspar, B.; Carreira, E. M. Cobalt Catalyzed Functionalization of Unactivated Alkenes: Regioselective Reductive C-C Bond Forming Reactions. J. Am. Chem. Soc. 2009, 131, 13214–13215.

(248) Shigehisa, H.; Nishi, E.; Fujisawa, M.; Hiroya, K. CobaltCatalyzed Hydrofluorination of Unactivated Olefins: A Radical Approach of Fluorine Transfer. Org. Lett. 2013, 15, 5158–5161.

(249) Isayama, S.; Mukaiyama, T. A New Method for Preparation of Alcohols from Olefins with Molecular Oxygen and Phenylsilane by the Use of bis(acetylacetonato)cobalt(II). Chem. Lett. 1989, 18, 1071–1074.

(250) Crossley, S. W. M.; Barabe, F.; Shenvi, R. A. Simple, Chemoselective, Catalytic Olefin Isomerization. J. Am. Chem. Soc. 2014, 136, 16788–16791.

(251) Green, S. A.; Matos, J. L. M.; Yagi, A.; Shenvi, R. A. BranchSelective Hydroarylation: Iodoarene-Olefin Cross-Coupling. J. Am. Chem. Soc. 2016, 138, 12779–12782.

(252) Nakano, T.; Okamoto, Y. Helix-Sense-Selective Free-Radical Polymerization of 1-Phenyldibenzosuberyl Methacrylate Using a Cobalt(II) Complex. Macromolecules 1999, 32, 2391–2393.

(253) Nakano, T.; Tamada, D.; Miyazaki, J.; Kakiuchi, K.; Okamoto, Y. Asymmetric Radical Polymerization of Maleimides Using a Chiral cobalt(II) Complex. Macromolecules 2000, 33, 1489–1491.

(254) Nakano, T.; Yade, T.; Okamoto, Y. Revised Interpretation for N-Cyclohexylmaleimide Polymerization in the Presence of an Optically Active Cobalt(II) Complex: Polymerization Mediated by Anionic Species Formed through Monomer-Co(II) Complex-O2 Interaction. Macromolecules 2003, 36, 3498–3504.

(255) Liao, C.-M.; Hsu, C.-C.; Wang, F.-S.; Wayland, B. B.; Peng, C.-H. Living Radical Polymerization of Vinyl Acetate and Methyl Acrylate Mediated by Co(Salen*) Complexes. Polym. Chem. 2013, 4, 3098–3104.

(256) Zhao, Y.; Zhang, S.; Wu, Z.; Liu, X.; Zhao, X.; Peng, C.-H.; Fu, X. Visible-Light-Induced Living Radical Polymerization (LRP) Mediated by (salen)Co(II)/TPO at Ambient Temperature. Macromolecules 2015, 48, 5132–5139.

(257) Kermagoret, A.; Jerome, C.; Detrembleur, C.; Debuigne, A. In Situ Bidentate to Tetradentate Ligand Exchange Reaction in CobaltMediated Radical Polymerization. Eur. Polym. J. 2015, 62, 312–321.

(258) Chiang, L.; Allan, L. E. N.; Alcantara, J.; Wang, M. C. P.; Storr, T.; Shaver, M. P. Tuning Ligand Electronics and Peripheral Substitution on Cobalt Salen Complexes: Structure and Polymerisation Activity. Dalton Trans. 2014, 43, 4295–4304.

(259) Santhosh, K. K. S.; Li, Y.; Gnanou, Y.; Baisch, U.; Champouret, Y.; Poli, R.; Robson, K. C.; McNeil, W. S. Electronic and Steric Ligand Effects in the Radical Polymerization of Vinyl Acetate Mediated by Beta-Ketoiminate Complexes of cobalt(II). Chem. Asian J. 2009, 4, 1257–1265.

(260) Sherwood, R. K.; Kent, C. L.; Patrick, B. O.; McNeil, W. S. Controlled Radical Polymerisation of Methyl Acrylate Initiated by a Well-Defined Cobalt Alkyl Complex. Chem. Commun. 2010, 46, 2456–2458.

(261) Lin, Y.-C.; Hsieh, Y.-L.; Lin, Y.-D.; Peng, C.-H. Cobalt Bipyridine Bisphenolate Complex in Controlled/Living Radical Polymerization of Vinyl Monomers. Macromolecules 2014, 47, 7362–7369.

(262) Wang, F.-S.; Wang, T.-F.; Lu, H.-H.; Ao-Ieong, W.-S.; Wang, J.; Chen, H.-L.; Peng, C.-H. Highly Stretchable Free-Standing Poly(acrylic Acid)-Block-Poly(vinyl Alcohol) Films Obtained from Cobalt-Mediated Radical Polymerization. Macromolecules 2017, 50, 6054–6063.

(263) Demarteau, J.; Kermagoret, A.; German, I.; Cordella, D.; Robeyns, K.; De Winter, J.; Gerbaux, P.; Jerome, C.; Debuigne, A.; Detrembleur, C. Halomethyl-Cobalt(bis-Acetylacetonate) for the Controlled Synthesis of Functional Polymers. Chem. Commun. 2015, 51, 14334–14337.

(264) Morin, A. N. A. N.; Detrembleur, C.; Jérôme, C.; De Tullio, P.; Poli, R.; Debuigne, A.; Jerome, C.; De Tullio, P.; Poli, R.; Debuigne, A. Effect of Head-to-Head Addition in Vinyl Acetate Controlled Radical

Polymerization: Why Is Co(acac)2-Mediated Polymerization so Much Better? Macromolecules 2013, 46, 4303– 4312.

(265) Debuigne, A.; Michaux, C.; Jérôme, C.; Jérôme, R.; Poli, R.; Detrembleur, C. Cobalt-Mediated Radical Polymerization of Acrylonitrile: Kinetics Investigations and DFT Calculations. Chem. - Eur. J. 2008, 14, 7623–7637.

(266) Debuigne, A.; Poli, R.; Jerome, R.; Jerome, C.; Detrembleur, C. Key Role of Metal-Coordination in Cobalt-Mediated Radical Polymerization of Vinyl Acetate. ACS Symp. Ser. 2009, 1024, 131– 147.

(267) Detrembleur, C.; Versace, D.-L.; Piette, Y.; Hurtgen, M.; Jeró̂me, C.; Lalevee, J.; Debuigne, A. Synthetic and Mechanistić Inputs of Photochemistry into the Bis-Acetylacetonatocobalt-Mediated Radical Polymerization of N-Butyl Acrylate and Vinyl Acetate. Polym. Chem. 2012, 3, 1856–1866.

(268) Maria, S.; Kaneyoshi, H.; Matyjaszewski, K.; Poli, R. Effect of Electron Donors on the Radical Polymerization of Vinyl Acetate Mediated by [Co(acac)2]: Degenerative Transfer versus Reversible Homolytic Cleavage of an organocobalt(III) Complex. Chem. - Eur. J. 2007, 13, 2480–2492.

(269) Inoki, S.; Kato, K.; Takai, T.; Isayama, S.; Yamada, T.; Mukaiyama, T. Bis[(trifluoroacetyl)acetonato]cobalt(II)-Catalyzed Oxidation-Reduction Hydration of Olefins. Selective Formation of Alcohols from Olefins. Chem. Lett. 1989, 18, 515–518.

(270) Isayama, S.; Mukaiyama, T. Hydration of Olefins with Molecular Oxygen and Triethylsilane Catalyzed by bis-(trifluoroacetylacetonato)cobalt(II). Chem. Lett. 1989, 18, 569–572.

(271) Tokuyasu, T.; Kunikawa, S.; Masuyama, A.; Nojima, M. Co(III)-Alkyl Complex- and Co(III)-Alkylperoxo Complex-Catalyzed Triethylsilylperoxidation of Alkenes with Molecular Oxygen and Triethylsilane. Org. Lett. 2002, 4, 3595–3598.

(272) Isayama, S.; Mukaiyama, T. Novel Method for the Preparation of Triethylsilyl Peroxides from Olefins by the Reaction with Molecular Oxygen and Triethylsilane Catalyzed by bis(1,3diketonato)cobalt(II). Chem. Lett. 1989, 18, 573–576.

(273) Kato, K.; Mukaiyama, T. A Convenient Method for the Direct Preparation of Ketones from Vinylsilanes with Molecular Oxygen Catalyzed by a cobalt(II) Complex. Chem. Lett. 1989, 18, 2233–2236.

(274) Inoki, S.; Mukaiyama, T. A Convenient Method for the Stereoselective Preparation of Trans-(2-Hydroxymethyl)tetrahydrofurans by the Oxidative Cyclization of 5-Hydroxy-1-Alkenes with Molecular Oxygen Catalyzed by cobalt(II) Complex. Chem. Lett. 1990, 19, 67–70.

(275) Isayama, S.; Mukaiyama, T. Cobalt(II)-Catalyzed Coupling Reaction of β-Unsaturated Compounds with Aldehydes with the Use of Phenylsilane. New Method for Preparation of β-Hydroxy Nitriles, Amides, and Esters. Chem. Lett. 1989, 18, 2005–2008.

(276) King, S. M.; Ma, X.; Herzon, S. B. A Method for the Selective Hydrogenation of Alkenyl Halides to Alkyl Halides. J. Am. Chem. Soc. 2014, 136, 6884–6887.

(277) Ma, X.; Herzon, S. B. Non-Classical Selectivities in the Reduction of Alkenes by Cobalt-Mediated Hydrogen Atom Transfer. Chem. Sci. 2015, 6, 6250–6255.

(278) Ma, X.; Herzon, S. B. Intermolecular Hydropyridylation of Unactivated Alkenes. J. Am. Chem. Soc. 2016, 138, 8718–8721.

(279) Zhang, J.; Jiang, J.; Xu, D.; Luo, Q.; Wang, H.; Chen, J.; Li, H.; Wang, Y.; Wan, X. Interception of Cobalt-Based Carbene Radicals with a -Aminoalkyl Radicals: A Tandem Reaction for the Construction of B -Ester- G -Amino. Angew. Chem., Int. Ed. 2015, 54, 1231–1235.

(280) Patil, N.; Aqil, M.; Aqil, A.; Ouhib, F.; Marcilla, R.; Minoia, A.; Lazzaroni, R.; Jerő me, C.; Detrembleur, C. Integration of RedoxActive Catechol Pendants into Poly(ionic Liquid) for the Design of High-Performance Lithium-Ion Battery Cathodes. Chem. Mater. 2018, 30, 5831–5835.

(281) Debuigne, A.; Caille, J. R.; Detrembleur, C.; Jerő me, R. Effective Cobalt Mediation of the Radical Polymerization of Vinyl Acetate in Suspension. Angew. Chem., Int. Ed. Engl. 2005, 44, 3439– 3442.

(282) Debuigne, A.; Caille, J.-R.; Jerő me, R. Synthesis of EndFunctional Poly (Vinyl Acetate) by Cobalt-Mediated Radical Polymerization. Macromolecules 2005, 38, 5452–5458.

(283) Debuigne, A.; Caille, J.-R. R.; Jerő me, R. Highly Efficient Cobalt-Mediated Radical Polymerization of Vinyl Acetate. Angew. Chem., Int. Ed. 2005, 44, 1101–1104.

(284) Kaneyoshi, H.; Matyjaszewski, K. Effect of Ligand and NButyl Acrylate on Cobalt-Mediated Radical Polymerization of Vinyl Acetate. Macromolecules 2005, 38, 8163–8169.

(285) Kaneyoshi, H.; Matyjaszewski, K. Radical (Co)polymerization of Vinyl Chloroacetate and N-Vinylpyrrolidone Mediated by Bis(acetylacetonate)cobalt Derivatives. Macromolecules 2006, 39, 2757–2763.

(286) Miao, X.; Zhu, W.; Zhang, Z.; Zhang, W.; Zhu, X.; Zhu, J. Photo-Induced Cobalt-Mediated Radical Polymerization of Vinyl Acetate. Polym. Chem. 2014, 5, 551–557.

(287) Bunck, D. N.; Sorenson, G. P.; Mahanthappa, M. K. CobaltMediated Radical Polymerization Routes to Poly(vinyl Ester) Block Copolymers. J. Polym. Sci., Part A: Polym. Chem. 2011, 49, 242–249.

(288) Nze, R.-P.; Colombani, O.; Nicol, E. Synthesis of Poly(vinyl Laurate)-B-Poly(vinyl Stearate) Diblock Copolymers by CobaltMediated Radical Polymerization in Solution. J. Polym. Sci., Part A: Polym. Chem. 2012, 50, 4046–4054.

(289) Allaoua, I.; Goi, B. E.; Obadia, M. M.; Debuigne, A.; Detrembleur, C.; Drockenmuller, E. (Co)Polymerization of Vinyl Levulinate by Cobalt-Mediated Radical Polymerization and Functionalization by Ketoxime Click Chemistry. Polym. Chem. 2014, 5, 2973– 2979.

(290) Obadia, M. M.; Colliat-Dangus, G.; Debuigne, A.; Serghei, A.; Detrembleur, C.; Drockenmuller, E. Poly(vinyl Ester 1,2,3Triazolium)s: A New Member of the Poly(ionic Liquid)s Family. Chem. Commun. 2015, 51, 3332–3335.

(291) Bryaskova, R.; Willet, N.; Degee, P.; Dubois, P.; Jérôme, R.; Detrembleur, C. Copolymerization of Vinyl Acetate with 1-Octene and Ethylene by Cobalt-Mediated Radical Polymerization. J. Polym. Sci., Part A: Polym. Chem. 2007, 45, 2532–2542.

(292) Demarteau, J.; Kermagoret, A.; Jerome, C.; Detrembleur, C.; Debuigne, A. Controlled Synthesis of Ethylene-Vinyl Acetate Based Copolymers by Organometallic Mediated Radical Polymerization. ACS Symp. Ser. 2015, 1188, 47–61.

(293) Kermagoret, A.; Wenn, B.; Debuigne, A.; Jerome, C.; Junkers, T.; Detrembleur, C. Improved Photo-Induced Cobalt-Mediated Radical Polymerization in Continuous Flow Photoreactors. Polym. Chem. 2015, 6, 3847–3857.

(294) Demarteau, J.; Ameduri, B.; Ladmiral, V.; Mees, M. A.; Hoogenboom, R.; Debuigne, A.; Detrembleur, C. Controlled Synthesis of Fluorinated Copolymers via Cobalt-Mediated Radical Copolymerization of Perfluorohexylethylene and Vinyl Acetate. Macromolecules 2017, 50, 3750–3760.

(295) Piette, Y.; Debuigne, A.; Jerôme, C.; Bodart, V.; Poli, R.; Detrembleur, C. Cobalt-Mediated Radical (Co)polymerization of Vinyl Chloride and Vinyl Acetate. Polym. Chem. 2012, 3, 2880–2891.

(296) Banerjee, S.; Ladmiral, V.; Debuigne, A.; Detrembleur, C.; Poli, R.; Ameduri, B. Organometallic-Mediated Radical Polymer- ization of Vinylidene Fluoride. Angew. Chem., Int. Ed. 2018, 57, 2934–2937.

(297) Falireas, P. G.; Ladmiral, V.; Debuigne, A.; Detrembleur, C.; Poli, R.; Ameduri, B. Straightforward Synthesis of Well-Defined Poly(vinylidene Fluoride) and Its Block Copolymers by CobaltMediated Radical Polymerization. Macromolecules 2019, 52, 1266– 1276.

(298) Detrembleur, C.; Debuigne, A.; Hurtgen, M.; Jerôme, C.; Pinaud, J.; Fevre, M.; Coupillaud, P.; Vignolle, J.; Taton, D. Synthesis of 1-Vinyl-3-Ethylimidazolium-Based Ionic Liquid (Co)polymers by Cobalt-Mediated Radical Polymerization. Macromolecules 2011, 44, 6397–6404.

(299) Cordella, D.; Kermagoret, A.; Debuigne, A.; Riva, R.; German, I.; Isik, M.; Jerôme, C.; Mecerreyes, D.; Taton, D.; Detrembleur, C. Direct Route to Well-Defined Poly(ionic Liquid)s by Controlled Radical Polymerization in Water. ACS Macro Lett. 2014, 3, 1276– 1280.

(300) Cordella, D.; Kermagoret, A.; Debuigne, A.; Jerome, C.; Mecerreyes, D.; Isik, M.; Taton, D.; Detrembleur, C. All Poly(ionic Liquid)-Based Block Copolymers by Sequential Controlled Radical Copolymerization of Vinylimidazolium Monomers. Macromolecules 2015, 48, 5230–5243.

(301) Weiss-Maurin, M.; Cordella, D.; Jerome, C.; Taton, D.; Detrembleur, C. Direct One-Pot Synthesis of Poly(ionic Liquid) Nanogels by Cobalt-Mediated Radical Cross-Linking Copolymerization in Organic or Aqueous Media. Polym. Chem. 2016, 7, 2521– 2530.

(302) Cordella, D.; Debuigne, A.; Jerome, C.; Kochovski, Z.; Taton, D.; Detrembleur, C. One-Pot Synthesis of Double Poly(Ionic Liquid) Block Copolymers by Cobalt-Mediated Radical PolymerizationInduced Self-Assembly (CMR-PISA) in Water. Macromol. Rapid Commun. 2016, 37, 1181–1187.

(303) Patil, N.; Cordella, D.; Aqil, A.; Debuigne, A.; Admassie, S.; Jerome, C.; Detrembleur, C. Surface- and Redox-Active Multifunctional Polyphenol-Derived Poly(ionic Liquid)s: Controlled Synthesis and Characterization. Macromolecules 2016, 49, 7676–7691.

(304) Cordella, D.; Ouhib, F.; Aqil, A.; Defize, T.; Jerome, C.; Serghei, A.; Drockenmuller, E.; Aissou, K.; Taton, D.; Detrembleur, C. Fluorinated Poly(ionic Liquid) Diblock Copolymers Obtained by Cobalt-Mediated Radical Polymerization-Induced Self-Assembly. ACS Macro Lett. 2017, 6, 121–126.

(305) Debuigne, A.; Willet, N.; Jerome, R.; Detrembleur, C. Amphiphilic Poly(vinyl Acetate)-B-poly(N-Vinylpyrrolidone) and Novel Double Hydrophilic Poly(vinyl Alcohol)-B-poly(N-Vinylpyrrolidone) Block Copolymers Prepared by Cobalt-Mediated Radical Polymerization. Macromolecules 2007, 40, 7111–7118.

(306) Debuigne, A.; Morin, A. N. A. N.; Kermagoret, A.; Piette, Y.; Detrembleur, C.; Jérôme, C.; Poli, R. Key Role of Intramolecular Metal Chelation and Hydrogen Bonding in the Cobalt-Mediated Radical Polymerization of N-Vinyl Amides. Chem. - Eur. J. 2012, 18, 12834–12844.

(307) Kermagoret, A.; Fustin, C.-A.; Bourguignon, M.; Detrembleur, C.; Jerome, C.; Debuigne, A. One-Pot Controlled Synthesis of Double Thermoresponsive N-Vinylcaprolactam-Based Copolymers with Tunable LCSTs. Polym. Chem. 2013, 4, 2575–2583.

(308) Drean, M.; Guegan, P.; Detrembleur, C.; Jerome, C.; Rieger, J.; Debuigne, A. Controlled Synthesis of Poly(vinylamine)-Based Copolymers by Organometallic-Mediated Radical Polymerization. Macromolecules 2016, 49, 4817–4827.

(309) Kermagoret, A.; Mathieu, K.; Thomassin, J.-M.; Fustin, C.-A.; Duchene, R.; Jerome, C.; Detrembleur, C.; Debuigne, A. Double Thermoresponsive Di- and Triblock Copolymers Based on NVinylcaprolactam and N-Vinylpyrrolidone: Synthesis and Comparative Study of Solution Behavior. Polym. Chem. 2014, 5, 6534–6544.

(310) Mumtaz, M.; Labrugère, C.; Cloutet, E.; Cramail, H. Synthesis of Poly(3,4-Ethylenedioxythiophene) Latexes Using poly(N-Vinylpyrrolidone)-Based Copolymers as Reactive Stabilizers. J. Polym. Sci., Part A: Polym. Chem. 2010, 48, 3841–3855.

(311) Bryaskova, R.; Willet, N.; Debuigne, A.; Jérôme, R.; Detrembleur, C. Synthesis of Poly(vinyl Acetate)-B-Polystyrene and Poly(vinyl Alcohol)-B-Polystyrene Copolymers by Cobalt-Mediated Radical Polymerization. J. Polym. Sci., Part A: Polym. Chem. 2006, 45, 81–89.

(312) Hurtgen, M.; Debuigne, A.; Jérôme, C.; Detrembleur, C. Solving the Problem of Bis(acetylacetonato)cobalt(II)-Mediated Radical Polymerization (CMRP) of Acrylic Esters. Macromolecules 2010, 43, 886–894.

(313) Debuigne, A.; Warnant, J.; Jérôme, R.; Voets, I.; De Keizer, A.; Stuart, M. A. C.; Detrembleur, C. Synthesis of Novel Well-Defined Poly (Vinyl Acetate) - B -Poly (Acrylonitrile) and Derivatized WaterSoluble Poly (Vinyl Alcohol) - B -Poly (Acrylic Acid) Block Copolymers by Cobalt-Mediated Radical Polymerization. Macromolecules 2008, 41, 2353–2360.

(314) Debuigne, A.; Jérôme, C.; Detrembleur, C. Isoprene-Assisted Radical Coupling of (Co)polymers Prepared by Cobalt-Mediated Radical Polymerization. Angew. Chem., Int. Ed. 2009, 48, 1422–1424.

(315) Bryaskova, R.; Willet, N.; Duwez, A. S.; Debuigne, A.; Lepot, L.; Gilbert, B.; Jerome, C.; Jerome, R.; Detrembleur, C. Gold-Loaded Carbon Nanoparticles from Poly(vinyl Alcohol)-B-Poly(acrylonitrile) Non-Shell-Cross-Linked Micelles. Chem. - Asian J. 2009, 4, 1338– 1345.

(316) Banerjee, S.; Ladmiral, V.; Ameduri, B.; Debuigne, A.; Detrembleur, C.; Rahaman, S. M. W.; Poli, R. OrganometallicMediated Alternating Radical Copolymerization of Tert-Butyl-2Trifluoromethacrylate with Vinyl Acetate and Synthesis of Block Copolymers Thereof. Macromol. Rapid Commun. 2017, 38, 1700203.

(317) Detrembleur, C.; Stoilova, O.; Bryaskova, R.; Debuigne, A.; Mouithys-Mickalad, A.; Jeró̂me, R. Preparation of Well-Defined PVOH/C60 Nanohybrids by Cobalt-Mediated Radical Polymerization of Vinyl Acetate. Macromol. Rapid Commun. 2006, 27, 498– 504.

(318) Thomassin, J. M.; Molenberg, I.; Huynen, I.; Debuigne, A.; Alexandre, M.; Jerome, C.; Detrembleur, C. Locating Carbon Nanotubes (CNTs) at the Surface of Polymer Microspheres Using Poly(vinyl Alcohol) Grafted CNTs as Dispersion Co-Stabilizers. Chem. Commun. 2010, 46, 3330–3332.

(319) Detrembleur, C.; Debuigne, A.; Altintas, O.; Conradi, M.; Wong, E. H. H.; Jérôme, C.; Barner-Kowollik, C.; Junkers, T. Synthesis of Star and H-Shape Polymers via a Combination of

CobaltMediated Radical Polymerization and Nitrone-Mediated Radical Coupling Reactions. Polym. Chem. 2012, 3, 135−147.

(320) Detrembleur, C.; Debuigne, A.; Bryaskova, R.; Charleux, B.; Jérôme, R. Cobalt-Mediated Radical Polymerization of Vinyl Acetate in Miniemulsion: Very Fast Formation of Stable Poly(vinyl Acetate) Latexes at Low Temperature. Macromol. Rapid Commun. 2006, 27, 37−41.

(321) Bryaskova, R.; Detrembleur, C.; Debuigne, A.; Jerome, R. Cobalt-Mediated Radical Polymerization (CMRP) of Vinyl Acetate Initiated by Redox Systems: Toward the Scale-Up of CMRP. Macromolecules 2006, 39, 8263−8268.

(322) Debuigne, A.; Schoumacher, M.; Willet, N.; Riva, R.; Zhu, X.; Rutten, S.; Jerome, C.; Detrembleur, C. New Functional poly(NVinylpyrrolidone) Based (Co)polymers via Photoinitiated CobaltMediated Radical Polymerization. Chem. Commun. 2011, 47, 12703− 12705.

(323) Ding, D.; Pan, X.; Zhang, Z.; Li, N.; Zhu, J.; Zhu, X. A Degradable Copolymer of 2-Methylene-1,3-Dioxepane and Vinyl Acetate by Photo-Induced Cobalt-Mediated Radical Polymerization. Polym. Chem. 2016, 7, 5258−5264.

(324) Kumar, K. S. S.; Gnanou, Y.; Champouret, Y.; Daran, J. C.; Poli, R. Radical Polymerization of Vinyl Acetate with bis(tetramethylheptadionato)cobalt(II): Coexistence of Three Different Mechanisms. Chem. - Eur. J. 2009, 15, 4874−4885.

(325) Bellan, E. V.; Thevenin, L.; Gayet, F.; Fliedel, C.; Poli, R. Catalyzed Chain Transfer in Vinyl Acetate Polymerization Mediated by 9-Oxyphenalenone Cobalt(II) Complexes. ACS Macro Lett. 2017, 6, 959−962.

(326) Banerjee, S.; Bellan, V. E.; Gayet, F.; Debuigne, A.; Detrembleur, C.; Poli, R.; Améduri, B.; Ladmiral, V. Bis(formylphenolato)cobalt(II)-Mediated Alternating Radical Copolymerization of Tert-Butyl 2-Trifluoromethylacrylate with Vinyl Acetate. Polymers 2017, 9, 702.

(327) Langlotz, B. K.; Lloret Fillol, J.; Gross, J. H.; Wadepohl, H.; Gade, L. H. Living Radical Polymerization of Acrylates Mediated by 1,3-bis(2-pyridylimino)isoindolatocobalt(II) Complexes: Monitoring the Chain Growth at the Metal. Chem. - Eur. J. 2008, 14, 10267− 10279.

(328) Hurtgen, M.; Debuigne, A.; Fustin, C. A.; Jerố me, C.; Detrembleur, C. Organometallic-Mediated Radical Polymerization: Unusual Route toward (Quasi-) Diblock Graft Copolymers Starting from a Mixture of Monomers of Opposed Reactivity. Macromolecules 2011, 44, 4623−4631.

(329) Stiernet, P.; Drean, M.; Jé rố me, C.; Midoux, P.; Guegan, P.́; Rieger, J.; Debuigne, A. Tailor-Made Poly(vinylamine)s via Thermal or Photochemical Organometallic Mediated Radical Polymerization. ACS Symp. Ser. 2018, 1284, 349−363.

(330) Stiernet, P.; Jerome, C.; Debuigne, A. Precision Design of Vinyl Amine and Vinyl Alcohol-Based Copolymers via CobaltMediated Radical Polymerization. Polym. Chem. 2019, DOI: 10.1039/C9PY00020H.

(331) Scholten, P. B. V.; Demarteau, J.; Gennen, S.; De Winter, J.; Grignard, B.; Debuigne, A.; Meier, M. A. R.; Detrembleur, C. Merging CO2-Based Building Blocks with Cobalt-Mediated Radical Polymerization for the Synthesis of Functional Poly(vinyl Alcohol)s. Macromolecules 2018, 51, 3379−3393.

(332) Scholten, P. B. V; Detrembleur, C.; Meier, M. A. R. PlantBased Nonactivated Olefins: A New Class of Renewable Monomers for Controlled Radical Polymerization. ACS Sustainable Chem. Eng. 2019, 7, 2751–2762.

(333) Kermagoret, A.; Chau, N. D. Q.; Grignard, B.; Cordella, D.; Debuigne, A.; Jerome, C.; Detrembleur, C. Cobalt-Mediated Radical Polymerization of Vinyl Acetate and Acrylonitrile in Supercritical Carbon Dioxide. Macromol. Rapid Commun. 2016, 37, 539–544.

(334) Debuigne, A.; Poli, R.; De Winter, J.; Laurent, P.; Gerbaux, P.; Wathelet, J.-P.; Jérôme, C.; Detrembleur, C. Effective CobaltMediated Radical Coupling (CMRC) of Poly(vinyl Acetate) and Poly(N-Vinylpyrrolidone) (Co)polymer Precursors. Macromolecules 2010, 43, 2801–2813.

(335) Debuigne, A.; Poli, R.; De Winter, J.; Laurent, P.; Gerbaux, P.; Dubois, P.; Wathelet, J.-P.; Jerốme, C.; Detrembleur, C. CobaltMediated Radical Coupling (CMRC): An Unusual Route to Midchain-Functionalized Symmetrical Macromolecules. Chem. - Eur. J. 2010, 16, 1799–1811.

(336) Debuigne, A.; Hurtgen, M.; Jerome, C.; Detrembleur, C. Radical Coupling of Polymers Formed by Cobalt-Mediated Radical Polymerization. ACS Symp. Ser. 2012, 1100, 217–230.

(337) Debuigne, A.; Hurtgen, M.; Detrembleur, C.; Jerome, C.; Barner-Kowollik, C.; Junkers, T. Interpolymer Radical Coupling: A Toolbox Complementary to Controlled Radical Polymerization. Prog. Polym. Sci. 2012, 37, 1004–1030.

(338) Debuigne, A.; Detrembleur, C.; Jerome, C.; Junkers, T́. Straightforward Synthesis of Symmetrical Multiblock Copolymers by Simultaneous Block Extension and Radical Coupling Reactions. Macromolecules 2013, 46, 8922–8931.

(339) Demarteau, J.; De Winter, J.; Detrembleur, C.; Debuigne, A. Ethylene/Vinyl Acetate-Based Macrocycles via OrganometallicMediated Radical Polymerization and CuAAC "Click" Reaction. Polym. Chem. 2018, 9, 273–278.

(340) Thomassin, J.-M.; Debuigne, A.; Jérôme, C.; Detrembleur, C. Design of Mesoporous Carbon Fibers from a Poly(acrylonitrile) Based Block Copolymer by a Simple Templating Compression Moulding Process. Polymer 2010, 51, 2965–2971.

(341) Bryaskova, R.; Pencheva, D.; Kyulavska, M.; Bozukova, D.; Debuigne, A.; Detrembleur, C. Antibacterial Activity of Poly(vinyl Alcohol)-B-Poly(acrylonitrile) Based Micelles Loaded with Silver Nanoparticles. J. Colloid Interface Sci. 2010, 344, 424–428.

(342) Egorova, K. S.; Ananikov, V. P. Toxicity of Metal Compounds: Knowledge and Myths. Organometallics 2017, 36, 4071–4090.

(343) Hurtgen, M.; Debuigne, A.; Mouithys-Mickalad, A.; Jerốme, R.; Jérôme, C.; Detrembleur, C. Synthesis of Poly(vinyl alcohol)/C60 and poly(N- vinylpyrrolidone)/C60 Nanohybrids as Potential Photodynamic Cancer Therapy Agents. Chem. - Asian J. 2010, 5, 859–868.

(344) Drean, M.; Debuigne, A.; Goncalves, C.; Jerome, C.; Midoux, P.; Rieger, J.; Guegan, P. Use of Primary and Secondary Polyvinylamines for Efficient Gene Transfection. Biomacromolecules 2017, 18, 440–451.

(345) Dréan, M.; Debuigne, A.; Jérôme, C.; Goncalves, C.; Midoux, P.; Rieger, J.; Guegan, P. Poly(N-Methylvinylamine)-Based Copoly-́mers for Improved Gene Transfection. Macromol. Biosci. 2018, 18, 1700353.

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