Overview of cobalt-mediated radical polymerization: Roots, state of the art and future prospects

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ABSTRACT

Controlled radical polymerization (CRP) techniques offer the opportunity to properly design polymer chains and adjust their chemical and physical properties. Among these techniques, cobalt-mediated radical polymerization (CMRP) distinguished itself by the high level of control imparted to the polymerization of acrylic and vinyl ester monomers, even for high molar masses. This article summarizes for the first time the advances in understanding and synthetic scope of CMRP since its discovery. Notably, the cobalt-carbon bond formation by dual contribution of reversible termination and degenerative chain transfer is discussed, as well as the impact of additives able to coordinate the metal. The potential of computational chemistry in the field of CMRP as a rationalization and predicting tool is also presented. These mechanistic considerations and achievements in macromolecular engineering will be discussed along with challenges and future prospects in order to assess the CMRP system as a whole.

Keywords: Controlled radical polymerization; Cobalt-mediated radical polymerization; Copolymers; Macromolecular engineering

Contents

1. INTRODUCTION

Polymers are essential in modern life. In order to meet the increasing demand for polymers with specific functionalities and applications, a range of synthetic methods has been developed. In this respect, controlled radical polymerization (CRP) offers the opportunity for macromolecular engineering under mild experimental conditions. CRP has developed uninterruptedly [1] since its discovery in the mid-nineties [2]. Three methods rapidly established themselves initially: nitroxide-mediated radical polymerization (NMP) [3-6], atom transfer radical polymerization (ATRP) [7-10], and radical addition-fragmentation chain transfer (RAFT) [11 -14]. Subsequently, most efforts were devoted to the improvement of these systems and to their exploitation in macromolecular engineering. The choice of technique is mainly based on the adaptability of the controlling agents to an as wide as possible range of monomers, which is crucial for the design of complex polymeric architectures.

In the early nineties, at the very beginning of the CRP saga, the first controlled radical polymerizations using cobalt complexes as controlling species were reported by Wayland et al. [15] and Harwood and co-workers [16]. Despite the very high level of control of the acrylic monomers provided by this so-called cobalt-mediated radical polymerization (CMRP) system, the methodology long remained anecdotic because it appeared to be restricted to acrylic monomers. Ten years later, the first example of CMRP of a non-acrylic monomer was reported by Jérôme et al.: bis(acetylacetonato)cobalt(II) proved high efficiency in controlling the radical polymerization of vinyl acetate (VAc) [17]. This breakthrough was all the more significant since VAc had long been a challenge for CRP because of the high reactivity of the propagating radical, resulting from the lack of stabilizing groups. For example, NMP is not suited for this monomer because the covalent bond between the nitroxide and the polymer chains is not sufficiently labile whatever the structure of the controlling agent [18]. ATRP in the presence of iron catalysts [19] and degenerative chain transfer polymerization based on alkyl iodides [20] offered poor and moderate control for VAc, respectively. Today, effective control of the VAc polymerization can also be achieved by reversible addition-fragmentation chain transfer (RAFT) using dithiocarbamates [21], macromolecular design via interchange of xanthates (MADIX) [21-30], organotellurium- and organostibine-mediated living radical polymerizations (TERP [31] and SBRP [32]).

The propensity of the cobalt-mediated radical polymerization to deal with such a challenging monomer for CRP was a strong incentive to pursue the development of organometallic-mediated radical polymerization (OMRP) [33], and particularly the one based on cobalt complexes. This review gives an overview of cobalt-mediated radical polymerization from its discovery to the most recent advances. Both mechanistic and macromolecular engineering aspects will be discussed in order to assess the system as a whole. Future prospects in CMRP, emphasized by this general presentation, will be discussed.

## 2. ROOTS OF COBALT-MEDIATED RADICAL POLYMERIZATION

In this part, we do not aspire to exhaustively review the state of the art of cobalt chemistry prior to the discovery of CMRP. We rather aim at pointing out important achievements in both organic and polymer chemistry involving cobalt, in order to deeply understand the CMRP principles as well as its possible side reactions.

2.1. Organocobalt complexes in carbon-carbon bond formation

Organocobalt(III) compounds have long attracted attention because of the facile homolytic cleavage of the cobalt-carbon bond under thermal or photolytic conditions [34-40]. Since the Co-C bond cleavage can be achieved under mild conditions, organocobalt complexes have been used as sources of carbon-centered radicals for organic synthesis and in polymer chemistry.

First, it is essential to realize that the chemistry of cobalt complexes is closely related to the "Persistent Radical Effect" (PRE). This general concept, identified by Fischer [41] in 1986, rationalizes the highly specific formation of the cross-coupling product (R_1-R_2) between a persistent radical ($R_1^\bullet$) and a transient one ($R_2^\bullet$) at the expense of the self-termination of the transient radicals (R_2-R_2) [42]. At the early stage of the reaction, a tiny amount of the transient radical ($R_2^\bullet$) disappears by self-termination, while the persistent radical ($R_1^\bullet$) accumulates in the medium, favoring the formation of the cross-coupling product (R_1-R_2). This concept notably explains the unusual stability of methylcobalamine 1 under photolytic treatment, the cobalt complex 2 and the methyl radical 3 being the persistent and the transient radicals, respectively (Fig. 1) [43]. In spite of the high propensity of methyl radicals 3 for cross-coupling reactions, ethane was not the major product. However, addition of carbon monoxide in the medium mainly resulted in the formation of acetylcobalamin 5 [43]. This experiment confirmed the "persistent radical" character of the Co^{II} complex and illustrated the potential of alkyl-cobalt(III) as clean sources of radicals for radical addition reactions.

Fig. 1. *Photolytic transformation of methylcobalamine into acetylcobalamin.*

1 R = -CH₃ (methyl-cobalamine)

5 R = -C(=O)CH₃ (acetyl-cobalamine)
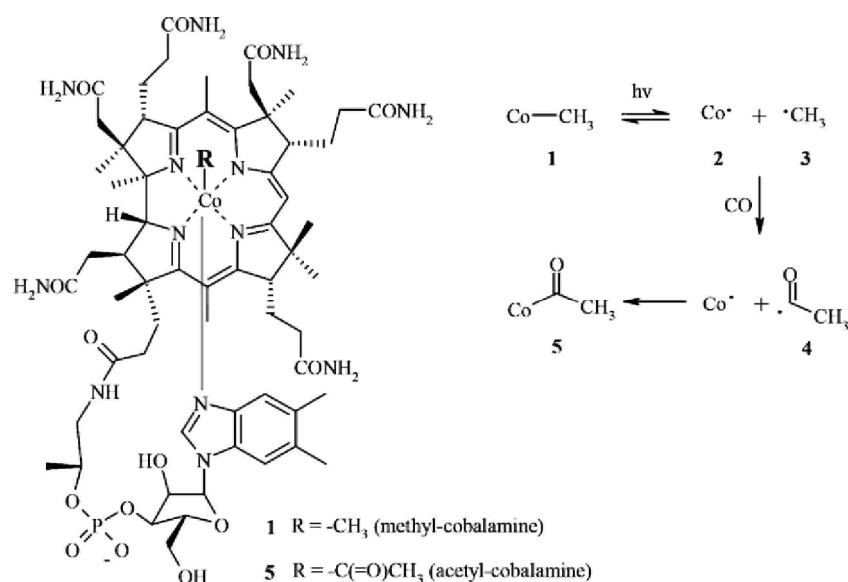
The thermal isomerization of the coenzyme B12 model is another perfect illustration of the PRE involving cobalt complexes, as reported by Finke and Daikh [44]. In this case, thermolysis of the benzyl-cobalt bond in the coenzyme B12 6 leads to an equilibrium between 6 and the benzyl migration product 7, with low formation of bibenzyl (<0.001%), the radical-recombination product (Fig. 2).

The propensity of organocobalt complexes to display the persistent radical effect has largely been exploited in organic synthesis and more particularly for carbon-carbon bond formation, as assessed by an abundant scientific literature [45-47]. A typical example is the cobalt-mediated vinylation, described by Giese and co-workers [48] and illustrated in Fig. 3a. Upon photolysis, the glycosyl-cobalt complex 6 releases glycosyl radicals that add styrene. The coupling product of this radical adduct with the Co^{II} complex was not isolated, but rather formed the alkene 7 by rapid dehydrocobaltation. This type of process was also studied by Branchaud et al. [49,50] and Pattenden and coworkers [51] using alkyl- and acyl-cobalt complexes 8 and 10, as illustrated in Fig. 3b and c.

All these reactions follow the general mechanism shown in Fig. 4. Exposition of the alkyl- or acyl-cobalt(III) complex 14 to light or heat triggers reversible homolytic Co-C bond cleavage and generates a carbon-centered radical 15 and the persistent Co^{II} complex. Subsequent addition of this carbon-centered radical to alkenyl compounds and reversible trapping of the newly formed radical 16 by the persistent Co^{II} species to form 17 are followed by dehydrocobaltation with formation of the final unsaturated product 18.

This mechanism contains the basic reactions typical of cobalt complexes in a free radical polymerization medium. Indeed, as with small organic radicals, growing polymer radicals can react with cobalt complexes according to two pathways: reversible cobalt-carbon bond formation and dehydrocobaltation.

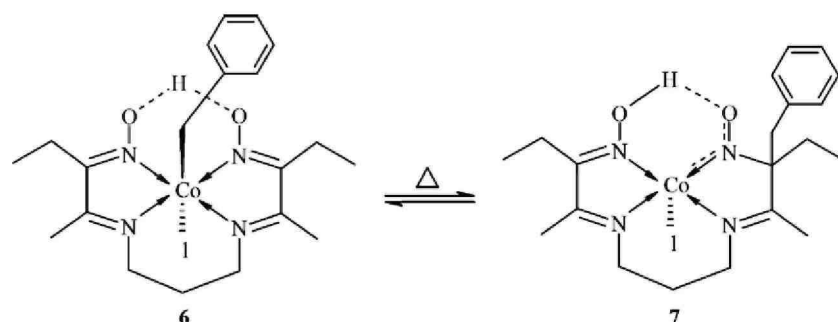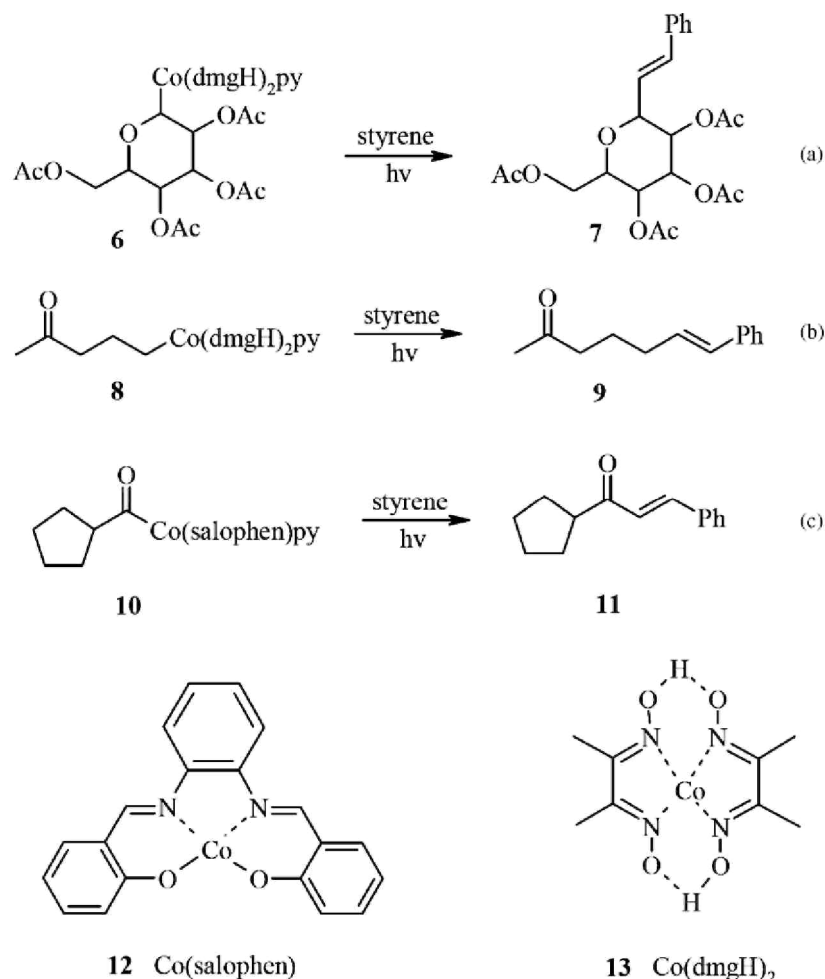**Fig. 2.** *Thermal isomerization of coenzyme B12 model.*

Fig. 3. *Cobalt-mediated vinylation involving alkylcobaloximes or acylcobalt salophen reagents.*

2.2. Catalytic chain transfer polymerization (CCTP)

The dehydrocobaltation observed in the cobalt-mediated vinylation is a key step in the catalytic chain transfer polymerization process (CCTP). As reported and discussed in detail in several reviews [52-54], some cobalt(II) complexes, *e.g.* cobaloximes (*e.g.* complexes 13 and 19, in Fig. 5) and cobalt porphyrins (20) are effective chain transfer catalysts, responsible for moderating the molar mass of polymers prepared by radical polymerization, particularly poly(alkyl methacrylate)s (PMMAs).

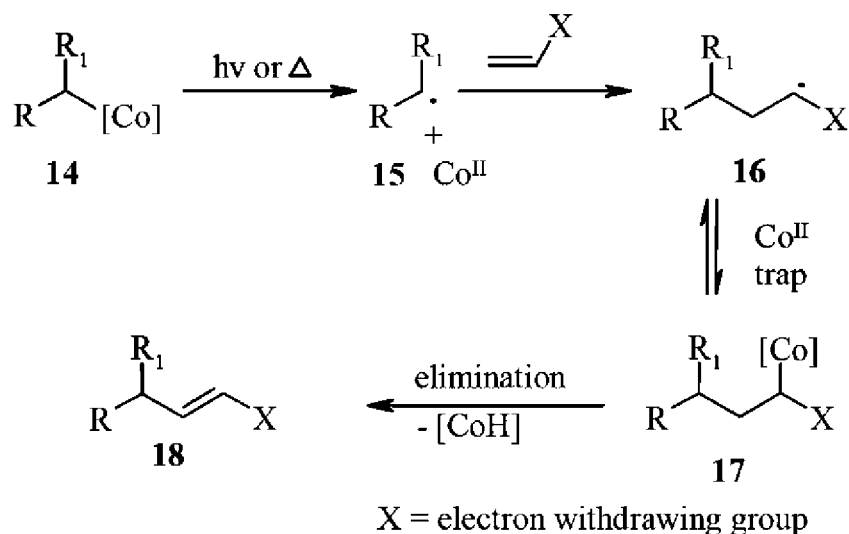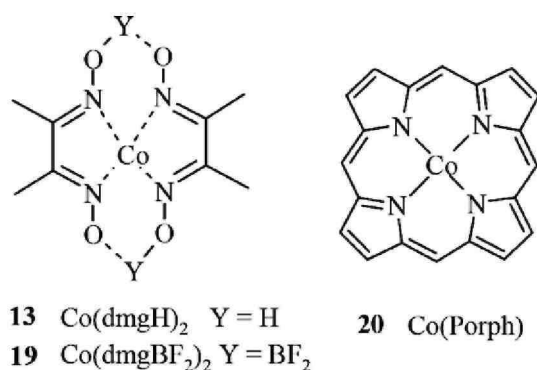**Fig. 4.** *General mechanism of carbon-carbon bond formation by reaction of organocobalt complexes with olefins.*

X = electron withdrawing group

Fig. 5. *Examples of cobalt complexes active in catalytic chain transfer polymerization (CCTP).*

13 Co(dmgH)$_2$ Y = H   **20** Co(Porph)
19 Co(dmgBF$_2$)$_2$ Y = BF$_2$

According to the commonly accepted mechanism [52], a cobalt(II) complex reacts with a polymeric radical 21 forming an alkyl-cobalt(III) complex 22 or can undergo hydrogen atom abstraction by the cobalt with release of a polymer chain with an unsaturated end-group 23 and formation of a cobalt hydride 24 (Fig. 6). The catalytic cycle is closed by generation of a primary radical 25 by hydrogen transfer from 24 to a methyl methacrylate (MMA) monomer unit, followed by propagation. Noteworthy, all growing radicals, including the primary radical 25, can be reversibly trapped by the cobalt(II) complex.

In this mechanism, the persistent radical effect is responsible for the reaction selectivity, *i.e.* the rapid cross-coupling reactions of the polymer radicals with the persistent Co^{II} complex vs. very limited self-termination of the polymer radicals. Moreover, all the polymer chains formed by CCTP bear an unsaturation at the ω-chain end, which makes them potential macromonomers [55-60] and thus precursors of graft copolymers [61,62]. For further information regarding the CCTP process, the reader is invited to read the review by Gridnev [53,54].

Vinylic monomers can be divided into two groups on the basis of their propensity to undergo catalytic chain transfer. Monomers having α-methyl group with hydrogen atoms prone to abstraction, such as methacrylates, α-methylstyrene and methacrylonitrile, are CCT-active monomers [52-54]. The second group includes monomers less prone to CCT reactions, such as acrylates, vinyl acetate, acrylonitrile, etc. In the total absence of hydrogen abstraction, the polymerization carried out in the presence of a cobalt complex is ruled in principle by the reversible Co-C bond cleavage and monomer addition, opening the way to cobalt-mediated controlled radical polymerization. In summary, depending on the propensity of the polymer to undergo hydrogen elimination and the ability of cobalt complex to promote H-abstraction, either "catalytic chain transfer polymerization" (CCTP) or "cobalt mediated radical polymerization" (CMRP) is favored, as emphasized in Fig. 6.

3. COBALT-MEDIATED RADICAL POLYMERIZATION

3.1. General principles and preliminary considerations

A radical polymerization is considered to be under control when the termination reactions are negligible in comparison with propagation. This requires a controlling agent able to temporary deactivate the growing chains and minimize their instantaneous concentration. In the CMRP system, the deactivating species which caps the chains is the cobalt complex. Moreover, in order to limit the chain breaking reactions and obtain well-defined polymers, chain transfer reactions must also be negligible. An ideal CMRP process could thus be schematized according to Fig. 7.

Fig. 6. *Interplay of hydrogen transfer reactions and persistent radical effect (PRE) for polymerizations conducted in the presence of cobalt complexes.*
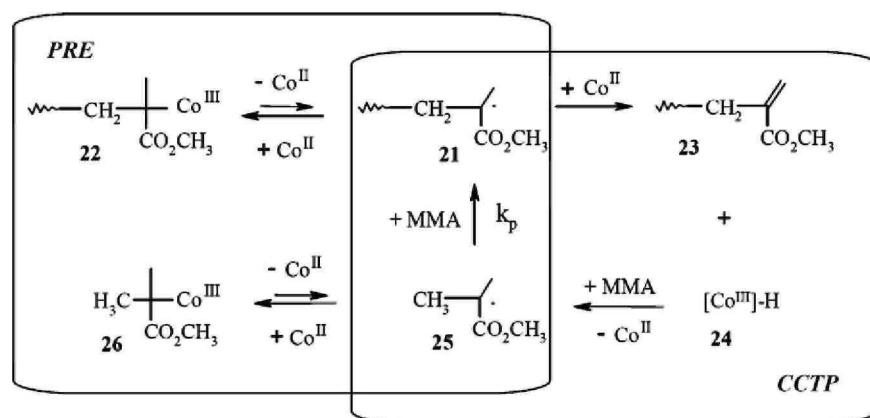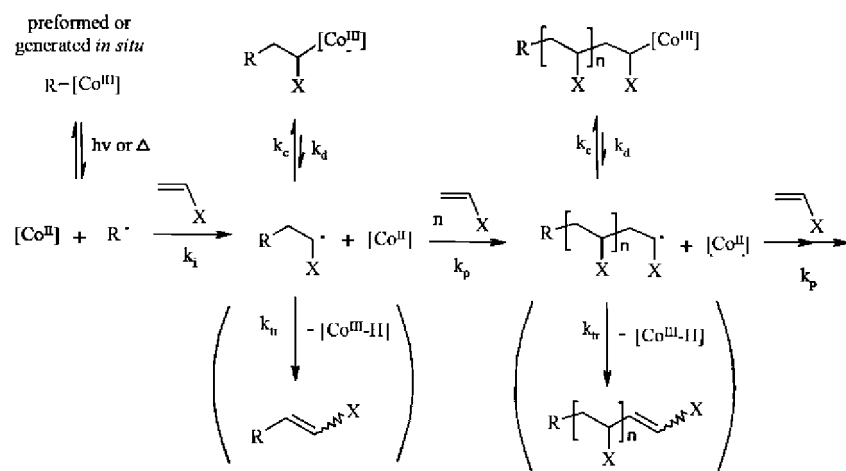

Fig. 7. *General mechanism of cobalt-mediated radical polymerization.*

Upon photolytic or thermal treatment, a preformed organocobalt(III) species undergoes Co-C homolytic cleavage with release of a persistent cobalt "radical" and a transient alkyl radical. In fact, the cobalt(II) product is not necessarily a simple radical, because its electronic configuration may involve in some cases three unpaired electrons (high spin configuration with a quartet ground state, *vide infra),* but always plays the role of a reversible radical trap just as a classical persistent radical. The reactive organic radical adds a first monomer unit and initiates the polymerization. In the absence of hydrogen atoms sensitive to abstraction on the growing polymer chains, and depending on the choice of the cobalt(II) species, the dehydrocobal-tation pathway (k_{tr}) could be disregarded at the expense of the temporary deactivation of the radical chains by the cobalt (k_c). At this stage, the chains are considered as "dormant" and the radical species can be regenerated because of the low Co-C bond strength ‰). The polymer chains can thus further propagate (k_p) until the next reversible deactivation. In other words, the CMRP process can be seen as a series of subsequent carbometallations of vinyl monomers. The instantaneous radical concentration must always be sufficiently low to avoid cross coupling reactions between the chains but sufficiently high to sustain polymerization. The Co-C strength, dictated by the choice of the cobalt

complex structure for a given monomer, is thus a key parameter. Among vinyl monomers, those deprived of α-methyl groups, and particularly acrylic and vinyl ester monomers, are less prone to H-abstraction by cobalt complexes. Consequently, these monomer families have been the first ones to be investigated by CMRP. In the subsequent sections of this review, the reactions are classified on the basis of the monomer. Within each section, the cobalt complexes are sorted by family, *i.e.* cobalt porhyrins and cobaloximes on one side and bis(β-diketonato)cobalt(II) derivatives on the other side.

3.2. Homopolymerization

3.2.1. Acrylic esters

In the early nineties, the groups of Harwood and co-workers [16] and Wayland et al. [15] discovered cobalt-mediated radical polymerization almost simultaneously. Both were focused on the control of acrylate polymerization using cobaloxime and cobalt porphyrin complexes, respectively (see Tables 1 and 2).

As reported by Harwood and co-workers [16,63-65] and patented a few years later [66,67], (isopropy-lpyridinato)cobaloxime 27 (in Table 1), also known as organocobaloxime, is an efficient initiator and controlling agent for the radical polymerization of acrylates upon irradiation, as a result of the photolability of the cobalt-carbon bond. In a typical example, compound 27 photolytically initiated the polymerization of a 66% solution of ethyl acrylate in chloroform [65]. Under these conditions, the molar mass increased with the monomer conversion. However, a discrepancy between observed and expected molar masses appeared above a monomer conversion of 40% and the molar mass distribution was relatively high ($M_w/M_n > 1.5$). Interestingly, it was mentioned that the polydispersity tends to increase in the presence of a larger amount of chloroform (*e.g.* 50 vol%) [65]. However, better results were obtained when the cobaloxime-mediated radical polymerization of acrylate was conducted in the presence of chloroform rather than in bulk or in other solvents (*e.g.* dimethylsulfoxide, benzene, dichloromethane). In these latter cases, it was suggested that chain transfer or termination competes with propagation because the polymer molar masses remained low and did not increase with conversion [65,68]. It was proposed that the unique behavior of chloroform is due to its reaction with cobaloxime leading to chlorocobaloxime [65,69,70] (Eq. (1)), which is inert under the polymerization conditions. Indeed, this would reduce the excess of cobaloxime in the polymerization medium and generate new radicals that can compensate radicals lost during the polymerization, allowing the polymerization to pursue in a pseudo-living manner. Although not perfect, a certain degree of control does exist and allows to synthesize poly(ethyl acrylate) with different molar masses by using various [monomer]/[organocobaloxime 27] molar ratios [65]. The possibility to control the acrylate polymerization in the presence of $Co(dmgH_2)_2$, 13 suggests a low contribution of the transfer reactions, contrary to the polymerization of methacrylates using the same complex [71].

$$CHCl_3 + Co(dmgH_2)_2Py \rightarrow {}^\bullet CHCl_2 + ClCo(dmgH_2)_2Py \quad (1)$$
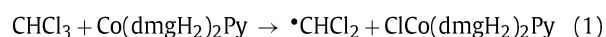
Interestingly, early work by Enikolopyan et al. reports the polymerization of acrylates in bulk at 60 °C using azo-bis-isobutyronitrile (AIBN), as free radical initiator in the presence of hematoporphyrin tetramethyl ether cobalt complex (Co(HPTME), 38 in Table 2) [72]. After an induction period, formation of cobalt bonded polymers was observed. Later, other cobalt porphyrins were successfully used as mediators for efficient CMRP [15]. Tetra(mesitylporphyrin organocobalt(III) complexes (($TMP)Co^{III}$-$CH_2C(CH_3)_3$ 31 and $(TMP)Co^{III}$-$CH(CO_2CH_3)$ CH_3 32, see Table 2) were used as thermal-initiators for the methyl acrylate (MA) polymerization at 60 °C in benzene solution ([MA] = 2.5 M) [15]. In this case, the alkyl radical ($R^\bullet$) and the Co(TMP) complex 30, released by thermal homolysis of the Co-R bond, play the role of initiator and controlling agent, respectively. The linear molar mass increase with the monomer conversion and the relatively low polydispersity (1.1-1.3) indicated an effective controlled radical polymerization process. Interestingly, control was maintained above 70% monomer conversion even when molar masses beyond 200,000 g/mol were targeted. Moreover, the efficiency factor ($f = M_{n,th}/M_{n,exp}$) based on the ratio between the expected and the experimental molar masses was remarkably close to unity, which assessed the growth of one PMA chain per cobalt complex. The establishment of an equilibrium between the dormant organocobalt(III) species on one side and the growing radical and persistent $Co^{II}(TMP)$ complex on the other side was the key step of this control. Self-termination of the growing radicals is effectively reduced according to the PRE. On the other hand, the methylene hydrogen abstraction by the metallic complex, leading to an unsaturated polyacrylate (CCTP), was minimized.

Table 1 : *Cobaloximes derivatives.*

Structure	X	Y	R	Name	No.
(structure)	-H	/	/	$Co^{II}(dmgH)_2$	13
	-H	Py	$-CH(CH_3)_2$	$R-Co^{III}(dmgH)_2Py$	27

Table 2 : *Cobalt porphyrin derivatives.*

Structure	X	Y	R	Name	No.
(porphyrin structure)	-H	-H	/	$Co^{II}(Porph)$	20
	-H	-Ph	/	$Co^{II}(TPP)$	28
	-H	-Ph	$-CH_2C(CH_3)_3$	$R-Co^{III}(TPP)$	29
	-H	(mesityl)	/	$Co^{II}(TMP)$	30
	-H	(mesityl)	$-CH_2C(CH_3)_3$	$R-Co^{III}(TMP)$	31
	-H	(mesityl)	$-CH(CO_2CH_3)CH_3$	$R-Co^{III}(TMP)$	32
	-Br	(mesityl)	/	$Co^{II}(Br_8TMP)$	33
	-Br	(mesityl)	$-CH(CH_3)(OCOCH_3)$	$R-Co^{ra}(Br_8TMP)$	34
	-H	(aryl-OMe)	/	Co"(TAP)	35
	-H	(SO$_3$Na/SO$_3$Na)	/	$Co^{II}(TMPS)$	36
	-H	(phenyl-SO$_3$Na)	/	$Co^{II}(TSPP)$	37
(porphyrin structure)	X = -CH(CH$_3$)OMe	Y = $-(CH_2)_2CO_2Me$		$Co^{II}(HPTME)$	38

It was also demonstrated that the delicate balance between CCTP and CMRP for the polymerization of acrylate in the presence of cobalt complexes largely depends on the structure of the metallic complex, mainly on the steric demand of the ligands [73]. Typically, polymerizations initiated by organocobalt porphyrin complex 29 (in Table 2), parent of (tetraphenylporphyrinato)cobalt (Co(TTP), 28 in Table 2), yield an increased polydispersity (from 1.1 to 1.9) and stagnant molar masses as a function of monomer conversion, which is the clear signature of catalytic chain transfer (CCT) [73]. However, when Co(TTP) 28 was substituted for Co(TMP) 30, the steric

hindrance of the tetramesitylporphyrin ligand prohibits the H-abstraction and allows the process to follow a controlled radical polymerization pathway [15]. Subsequently, Co(TTP) 28 definitely demonstrated its efficiency as catalytic chain transfer agent and its ability to provide macromonomers of PMMA by CCTP [74].
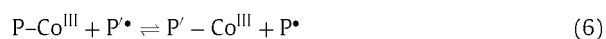
Fig. 8: *Initiation mechanism of the cobalt porphyrin-mediated radical polymerization.*

$$(R(CH_3)(CN)C)_2N_2 \xrightarrow{\Delta} 2\ R(CH_3)(CN)C^{\bullet} + N_2 \qquad (2)$$

$$\text{with } R = -CH_2-C(OCH_3)(CH_3)_2$$

$$R(CN)(CH_3)C^{\bullet} + (TMP)Co^{II} \longrightarrow (TMP)Co^{III}-H + R(CN)C=CH_2 \quad (3)$$

$$(TMP)Co^{III}-H + CH_2=CH(CO_2R) \longrightarrow (TMP)Co^{III}-CH(CO_2R)CH_3 \qquad (4)$$
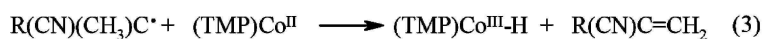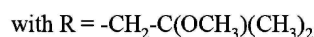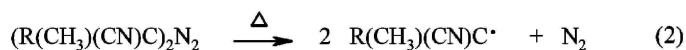
The (octabromotetramesityl)porphyrinato cobalt(II) complex ((Br$_8$TMP)Co, 33 in Table 2) was also reported as efficient mediator for the acrylate polymerization at 60 °C in benzene solution [75]. The control over the molecular parameters was comparable to that obtained with Co(TMP) 30, although the rate of polymerization was substantially higher. Indeed, the apparent first-order rate constant at 60°C (k_{app}) for the MA polymerization initiated by a preformed PMA-Co(Br$_8$TMP) was 30 times larger than for PMA-Co(TMP). Substitution of bromine for hydrogen on the porphyrin core stabilizes cobalt in the oxidation state II and reduces the Co-C homolytic enthalpy, thereby shifting the equilibrium towards the active species and speeding up the polymerization. Since the organocobalt complex R-Co(Br$_8$TMP) has a weaker Co-C bond than R-Co(TMP), it was possible to reduce the polymerization temperature. Indeed, (Br$_8$TMP)Co-CH(CH$_3$)OC(O)CH$_3$ (34 in Table 2) successfully initiated the controlled polymerization of methyl acrylate at room temperature [76].

In a more convenient approach, efficient initiators for CMRP were generated *in situ* by heating methyl acrylate at 60 °C in benzene in the presence of a conventional free radical initiator (2,2'-azo-bis-(4-methoxy-2,4-dimethyl valeronitrile), V-70) and the cobalt(II) complex 30 [77]. The *in situ* formation of the alkyl-cobalt(III) initiator is described as follows (Fig. 8). The tertiary carbon-centered radical formed by the thermal dissociation of the azo-initiator (Eq. (2)) is subjected to hydrogen abstraction by complex 30 leading to an unsaturated olefin and a cobalt hydride complex (Eq. (3)). This complex finally adds the monomer to form (TMP)Co^{III}-CH(CO$_2$R)CH$_3$, *i.e.* the actual initiator of methyl acrylate CMRP (Eq. (4)). The alkenes hydrocobaltation reaction was actually inspired from the reaction between the cobalt(II) porphyrin complex and AIBN, previously described by Wayland and co-workers [78,79]. Importantly, when the concentration of cobalt complex exceeded that of the radicals generated in the medium, the polymerization was extremely slow. However, production of a slight excess of radicals compared to cobalt ([R$^{\bullet}$]/[(TMP)Co^{II}] = 1.2) led to a much faster polymerization. In this case, an induction period was observed prior to polymerization, corresponding to the time needed to inject an amount of radicals in the medium sufficient to convert all the Co^{II} species into organocobalt(III) derivatives. The excess of radicals accelerates the polymerization without depriving the control of the polymerization. Moreover, the molar masses were close to the theoretical values corresponding to one polymer chain per cobalt porphyrin [77]. At that time, the CMRP was still described as a simple metallo-radical "stable free radical polymerization" (SFRP) governed by a combination-dissociation process, but this work announced a drastic change in the mechanistic interpretation of the CMRP system [77].

Indeed, in line with this work, it was notably demonstrated that the organocobalt porphyrin-mediated polymerization of acrylates can follow a reversible termination (RT) process but also a degenerative transfer (DT) pathway [80]. Such dual behavior was previously demonstrated by mechanistic studies for organotellurium [31,81] and organotitanium complexes [82,83]. Unlike systems governed by RT, where the active growing polymer radicals are exclusively produced by homolytic dissociation of the bond between the polymer (P) and the controlling agent (X), a DT process requires a continuous influx of radicals, *i.e.* from a conventional radical initiator, that initiates tiny amounts of propagating chains during the whole polymerization process [84]. In a DT process, the active growing polymer chains (P$^{\bullet}$) are temporarily deactivated by reaction with the dormant species (P-X) with release of a new radical (P$^{\bullet}$). Based on kinetics studies, it was demonstrated that the continuous injection of radicals in the CMRP polymerization medium turned the mechanism from a RT process (Eq. (5)), into a degenerative transfer process (Eq. (6)) [80,85].

$$P-Co^{III} \rightleftharpoons P^{\bullet} + Co^{II} \qquad (5)$$

$$P-Co^{III} + P'^{\bullet} \rightleftharpoons P'-Co^{III} + P^{\bullet} \qquad (6)$$

Such a phenomenon was first illustrated for the methyl acrylate polymerization conducted with (TMP)Co" 30 in the presence and absence of an excess of V-70 relative to the metal [80]. When a default of initiating radicals was used relative to (TMP)Co^{II}, the polymerization was very slow because of the low concentration of radicals involved in the equilibrium (K = [Co^{II}][R$^{\bullet}$]/[Co-R]). In this case, the controlled character was ascribed to the PRE. However, when the total moles of radicals that enter the polymerization medium from V-70 exceeded the initial moles of (TMP)Co^{II}, a fast and controlled polymerization according to the DT mechanism was observed after the induction period. When a conventional V-70 initiator (5.2×10^{-4} M) was added to a preformed CMRP initiator 32 [(TMP)Co-CH(CO$_2$CH$_3$)CH$_3$)] (1.0×10^{-3} M), the rate of the polymerization was close to the rate of an uncontrolled polymerization initiated by the same amount of V-70 without the cobalt complex, as expected for a DT process. Importantly, working under DT conditions allows reducing the concentration of the cobalt(II) complex in the medium and thus the probability for H-abstraction. Consequently, even the sterically less demanding tetra(*p*-methoxyphenyl)porphyrin cobalt(II) complex ((TAP)Co, 35), that normally promotes chain transfer reactions when used under RT conditions, successfully promotes the controlled radical polymerization of acrylates under DT conditions [80]. This change of mechanism is thus of prime importance for changing at demand the activity of the cobalt complex, and consequently, forincreasing the selectivity ofthe desired reaction pathway.

3.2.2. Acrylic acid

Poly(acrylic acid) with low polydispersity and predetermined molar mass was prepared in water at 60 °C by CMRP initiated by V-70 in the presence of hydrosoluble tetra(3,5-disulfonatomesityl)porphinato cobalt complex (Co(TMPS), 36 in Table 2) [86,87]. Similarly to acrylates, the radical polymerization of acrylic acid is mediated by both RT and DT pathways, depending on the amount of free radical initiator used relative to the cobalt complex. Typically, relatively well-defined ($M_w/M_n \sim 1.2$-1.4) polyacrylic acid was obtained up to relatively high molar masses ($M_n \sim 300{,}000$ g/mol), using a slight excess of V-70 compare to the Co(TMPS) in water at 60 °C.
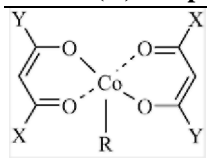
In parallel, polymerizations of methacrylic acid (MAA) initiated at 70°C by 4,4'-azobis(4-cyanopenanoic acid) (V-501) in the presence of the less hindered tetra(*p*-sulfonatophenyl)porphyrinato cobalt complex (Co(TSPP), 37 in Table 2) successfully led to macromonomers of poly(methacrylic acid) by CCTP [88].

3.2.3. Vinyl esters

3.2.3.1. Early results.

In contrast to many vinyl monomers, such as styrenes and (meth)acrylates, vinyl esters, particularly vinyl acetate, remained challenging monomers for controlled radical polymerization until recently. The main difficulty was the high reactivity of the propagating radicals due to the lack of stabilizing groups. However, many efforts have been devoted to the search for CRP systems able to deal with this monomer in order to exploit it in macromolecular engineering, since this monomer only polymerizes radically. Before the first example of CMRP of vinyl acetate was reported in 2005 [17], very few systems proved able to mediate the radical polymerization of this monomer. Degenerative chain transfer using alkyl-iodides [20], RAFT using dithiocarbamates [21] and MADIX using xanthates [21-28] were the first reported methods that promoted a reasonable level of control for VAc. At that time, Jérôme's group developed the so-called "Quinone Transfer Radical Polymerization" (QTRP) [89-92], which proved efficient for controlling the radical polymerization of styrene when conducted in the presence of quinone derivatives associated with a metal catalyst. Acetylacetonato derivatives of nickel(II), manganese(II), aluminum(III) and particularly cobalt(II), were successfully used for QTRP of styrene [89-92]. With the hope of extending this method to other monomers, the QTRP of VAc was tested using phenanthrene quinone in the presence of bis(acetylacetonato)cobalt(II). In this case, a moderate control of the VAc polymerization was observed when the cobalt complex was used in stoichiometric amount compared to the quinone [93]. This result was rapidly and drastically improved when omitting the quinone in the same experiment. Indeed, it appeared that the bulk radical polymerization of VAc initiated at 30 °C by V-70 in the presence of Co(acac)2 (39 in Table 3) alone provided the best level of control achieved for this monomer until then [17]. This experiment encouraged us to cross the bridge between QTRP and CMRP and to further investigate the latter system.

Table 3: *Bis(β-diketonato)cobalt(II) derivatives and bis(β-diketonato)cobalt(III) compounds used in CMRP.*

Cobalt(II) complex	X	Y	R	Name	No.
	$-CH_3$	$-CH_3$	/	$Co(acac)_2$	39
	$-C(CH_3)_3$	$-C(CH_3)_3$	/	$Co(TMHD)_2$	40
	$-CF_3$	$-CH_3$	/	$Co(F_3\text{-}acac)_2$	41
	$-CF_3$	$-CF_3$	/	$Co(F_6\text{-}acac)_2$	42
	$-CH_3$	$-CH_3$	$-CH(OAc)CH_3$	$R\text{-}Co(acac)_2$	43
	$-CH_3$	$-CH_3$	$-(CH(OAc)CH_2)_{<4}\text{-}R_0$ [a]	$R\text{-}Co(acac)_2$	44

[a] Ro being an V-70 initiating fragment: $-C(CH_3)(CN)\text{-}CH_2\text{-}C(OCH_3)(CH_3)_2$.

3.2.3.2. Optimization.

In the initial procedure, the VAc polymerization was initiated in bulk at 30°C in the presence of $Co(acac)2$ 39 using at least a threefold molar excess of initiator (V-70) relative to the controlling agent [17]. Under these conditions, an induction period of several hours was observed, which corresponds to the time required to consume all the Co" in the medium. As expected, this period was shorter when a higher [V-70]/[Co] ratio was used, while preserving the control of the polymerization. It was subsequently demonstrated that one equivalent of V-70 was sufficient, although the induction period was longer [94]. The ensuing VAc polymerization fulfilled all criteria of a controlled process, *i.e.* linear increase of the molar mass with the monomer conversion, molar mass distribution as low as 1.1-1.2, linear dependence of $\ln([M]_0/[M])$ vs. time. Moreover, there was very good agreement between experimental and expected molar masses considering one cobalt complex per chain. Furthermore, in contrast to the cobalt porphyrin used for the acrylate polymerization, $Co(acac)_2$ is commercially available and inexpensive. By analogy to the CMRP based on cobalt porphyrin [15,75,77] and cobaloxime [65], the mechanism proposed for the $Co(acac)_2$-mediated polymerization of VAc carried out in bulk was initially attributed to the reversible deactivation of the chains with the metal (Fig. 9). The equilibrium between the active growing PVAc chains and the dormant PVAc species end-capped by the Co complex could be possible by thermal homolytic cleavage of the metal-carbon bond [17]. However, the fact that the control of the CMRP process was not drastically affected by the large excess of initiator put the simple reversible termination model in question, as discussed hereafter.

Besides the temperature adjustment, which was optimum at 30 °C, the nature and amount of azo-initiator as well as the nature of the cobalt complex were investigated [95]. The reversible chain deactivation key step must be sensitive to the stereoelectronic properties of the cobalt complex. In addition to $Co(acac)_2$, a series of commercially available cobalt derivatives were tested for the VAc polymerization initiated in bulk by V-70, such as sterically hindered bis(2,2',6,6'-tetramethylheptandionato)cobalt(II) ($Co(TMHD)_2$, 40 in Table 3), but also the complexes bis(trifluoro-2,4-pentanedionato)cobalt(II) ($Co(F_3\text{-}acac)_2$, 41 in Table 3) and bis(hexafluoro-2,4-pentanedionato) cobalt(II) ($Co(F_6\text{-}acac)_2$, 42 in Table 3) containing electron-withdrawing CF3 substituents. $Co(F3\text{-}acac)_2$) 41 behaved similarly to $Co(acac)_2$ 39 [95], yielding low polydispersity and good agreement between theoretical and experimental molar masses, whereas $Co(TMHD)_2$ 40 [93] and $Co(F6\text{-}acac)_2$ 42 [95] offered moderate and very poor control of the VAc polymerization, respectively. In the latter case, PVAc with high molar masses and broad polydispersity were formed without induction period, suggesting the inefficiency of this complex as trapping agent.

3.2.3.3. Mechanistic studies.

Although the $Co(acac)_2$ and cobalt porphyrin systems may appear similar, each has its own specificities. While the cobalt atom in the porphyrin system is constrained in a square planar conformation by the macrocyclic ligand and adopts a low spin ($S= 1/2$) configuration [96], the acetylacetonato system adopts a tetrahedral geometry and a high spin ($S = 3/2$) configuration [97]. Both form mono and bis(ligand) adducts, which maintain the same spin state as the corresponding parent compound. The initiation mechanism also reflects the difference between these two systems. It was clearly established that the initiation of the VAc CMRP in the presence of $Co(acac)_2$ does not consist in the *in situ* formation of cobalt hydride followed by hydrocobaltation of a first monomer unit, as was the case for cobalt porphyrin-mediated acrylate polymerization represented in Fig. 8 [77]. Indeed, NMR analyses emphasized the presence of V-70 fragments at the α-chain end of PVAc which confirmed that the VAc polymerization was actually initiated by radicals released by the thermolysis of V-70 (Fig. 10) [98]. This difference is most probably due to the lower propensity of $Co(acac)_2$ for H-atom abstraction compared to Co porphyrins.

Fig. 9. *Equilibrium between dormant and active species in the CMRP of vinyl acetate using bis(acetylacetonato)cobalt(II) 39 as controlling agent.*
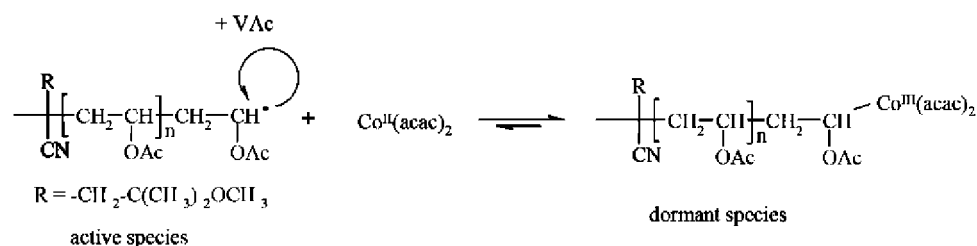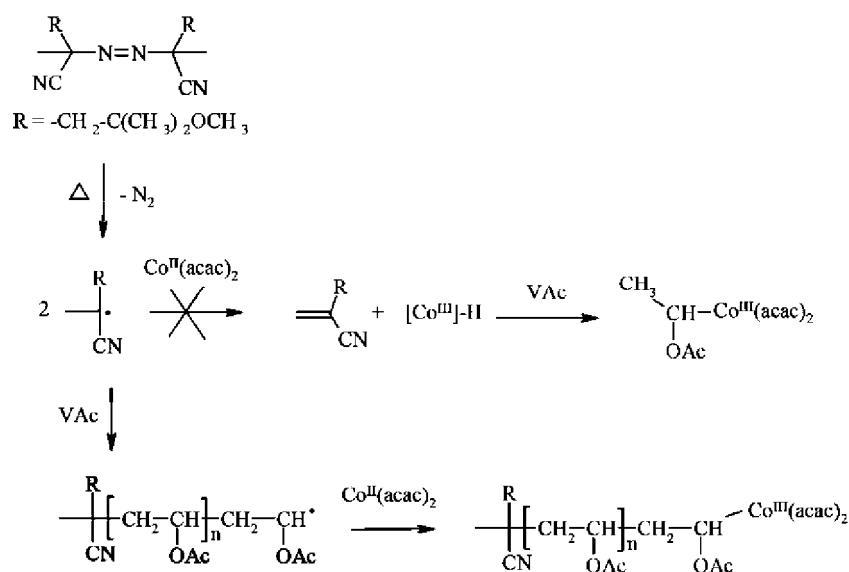

Fig. 10. *Initiation mechanism of the Co(acac)$_2$-mediated radical polymerization of vinyl acetate.*


Since the contribution of a degenerative chain transfer mechanism was clearly evidenced for the cobalt porphyrin-mediated radical polymerization of acrylate [80,85], this possibility could not be ignored in the case of the Co(acac)2-mediated polymerization of VAc, especially when using excess V-70. As already mentioned above, the persistence of control in spite of the large excess of V-70 discredits the pure reversible-termination mechanism hypothesis [17,98]. On the other hand, the observed successful resumption of VAc polymerization from a purified PVAc macroinitiator in the absence of additional V-70 is not compatible with a degenerative chain transfer mechanism [17]. This ambiguity was dispelled by Poli and co-workers [94]. On one hand, when isolated under strictly oxygen and moisture-free conditions, PVAc-Co(acac)2 failed to re-initiate the VAc polymerization, ruling out an RT process under these conditions. On the other hand, it was also demonstrated that addition of water to the purified macroinitiator made the chain extension possible. This clearly suggests that addition of water molecules favors the homolytic cleavage of the Co-C bond and activates the RT process. Water would exert this action by coordinating to the sixth coordinating site of cobalt, as will be analyzed more in detail below. This study emphasized for the first time the key role of Lewis base additives, such as pyridine and water on the course of the VAc CMRP [94]. In summary, the CMRP mechanism of VAc in bulk in the presence of Co(acac)$_2$ changes from degenerative chain transfer (DT) to reversible termination (RT) upon addition of water or pyridine, as supported by kinetic data [94].

The role of coordinating molecules on the CMRP was further investigated. Interestingly, when the VAc polymerization was initiated at 30°C with V-70 in the presence of Co(acac)2 and 30 equivalents of pyridine, no induction period precedes the polymerization of VAc, contrary to the same experiment conducted without additive. In spite of the increase of the molar mass with the monomer conversion that assessed the controlled character of the polymerization, the experimental molar masses were more than twice higher than expected. The first observations is rationalized by the involvement of the cobalt complex in a ligand addition equilibrium, yielding the trans-octahedral Co(acac)$_2$Py$_2$ complex, as evidenced by NMR [94]. This equilibrium energetically stabilizes the Co^{II} species, thereby shifting the Co^{III}-PVAc bond dissociation equilibrium towards the formation of the active radical chain and opening access to the RT mechanism from the very beginning of the process.

The second observation is a natural consequence of the slow production of the active Co^{III}-PVAc chains by the V-70 decomposition. The polymer M_n becomes closer to the theoretical limit as more and more Co^{II} is transformed into Co^{III}. The accordingly revised CMRP mechanism of the VAc is presented in Fig. 11.

In order to conduct an in-depth study of the CMRP mechanism, the synthesis of an alkyl-cobalt(III) model compound, able to initiate and mediate the polymerization, complex, was considered. Due to the high lability of the Co-C bond and sensitivity to oxygen, preparation and isolation of an alkyl-cobalt(III) complex supported by hard-donor ligands. such as acetylacetonate (acac) was expected to be difficult. In fact, all envisioned strategies failed to provide the single Co adduct (Co(acac)2-CH(OAc)CH3, 43 in Table 3) that mimics the PVAc dormant chains end-capped by Co(acac)2 [99,100]. However, reaction of V-70 with an excess of Co(acac)2 in the presence of VAc at 30 °C gives access to low molecular weight cobalt(III) adducts (Co(acac)$_2$-(CH(OAc)CH$_2$)<4-Ro; Ro =V-70 fragment, 44 in Table 3), which consists of about three VAc units [99]. After isolation of 44 by chromatography, kinetic experiments were conducted using the alkyl-cobalt(III) adduct, free of V-70, as CMRP initiator for VAc in bulk at 30°C. By using the Co(acac)2-(CH(OAc)CH2)<4-Ro 44 alone as initiator, a very slow polymerization was observed at 30 °C, which suggests that the PVAc-Co(acac)2 bond is relatively strong at this temperature. DFT calculations notably predicted that chelation by the carbonyl group of the last VAc unit provides an extra stabilization to the Co-C bond (see upper left structure of 44 in Fig. 12 and the DFT section below). Then, addition of 1 equivalent of V-70 to the compound 44 in solution in VAc allows the polymerization to proceed mainly according to a DT process while maintaining a reasonable level of control (Route A in Fig. 12). However, in the presence of a small amount of water or pyridine (1-10 equivalents compare to the cobalt complex), the carbonyl group was replaced from the coordination sphere of 44 by the added Lewis base. In this case, the homolytic cleavage of the Co-C bond is facilitated, triggering the reversible termination mechanism (Route B in Fig. 12). Under these conditions, by adjusting the ratio between the monomer and 44, well-defined PVAc with molar masses as high as 150,000 g/mol and polydispersity as low as 1.1 were obtained, which is the best level of control ever observed for the radical polymerization of VAc by CMRP [99]. The role of coordinating molecules, which could also be the reaction solvent or the monomer itself, was crucial when the polymerization of other monomers and macromolecular engineering were envisioned by the CMRP technique *(vide infra).*

Fig. 11. *Mechanism of the CMRP of VAc in the presence of Lewis bases (e.g. pyridine).*
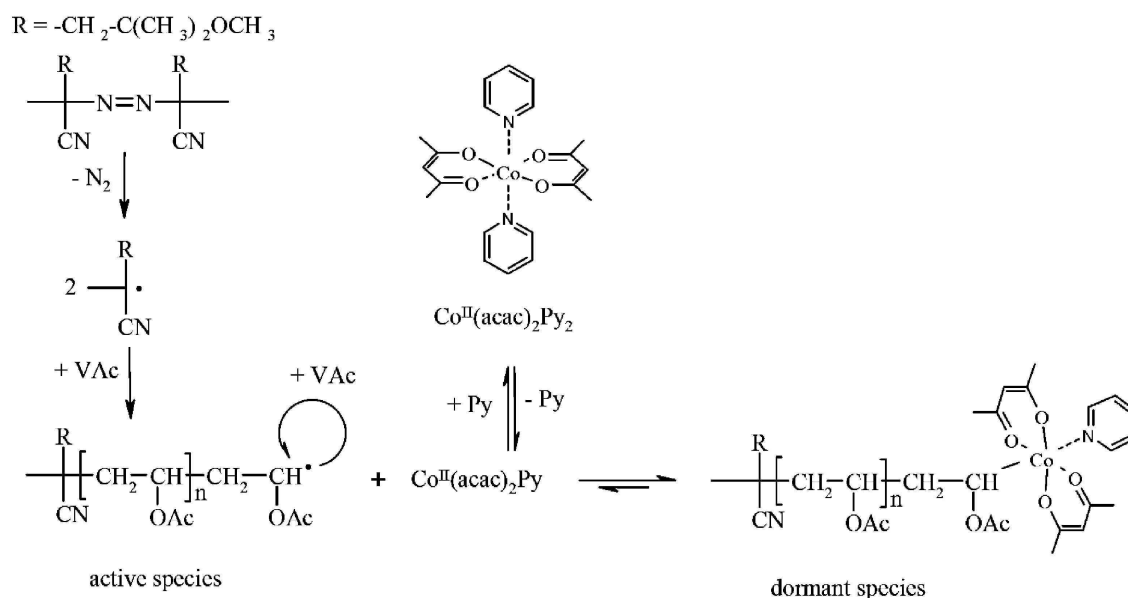
Very recently, the vinyl acetate polymerization was initiated by AIBN and/or V-70 at 60°C in the presence of (TMP)Co (30 in Table 2) [101-103], which had previously been restricted to the control of the acrylic monomers. These experiments were carried out in deuterated benzene solutions in order to monitor the polymer yield by proton NMR. In spite of deviations from ideal CRP due to irreversible radical termination and transfer reactions, homopolymers with narrow molar mass distributions (1.1 -1.3) were prepared at least at low monomer conversion (below 20%). A kinetic study demonstrated the occurrence of a DT mechanism under these conditions [103].

Fig. 12. *Interplay of degenerative chain transfer (A) and reversible termination (B) mechanisms in the CMRP of VAc.*
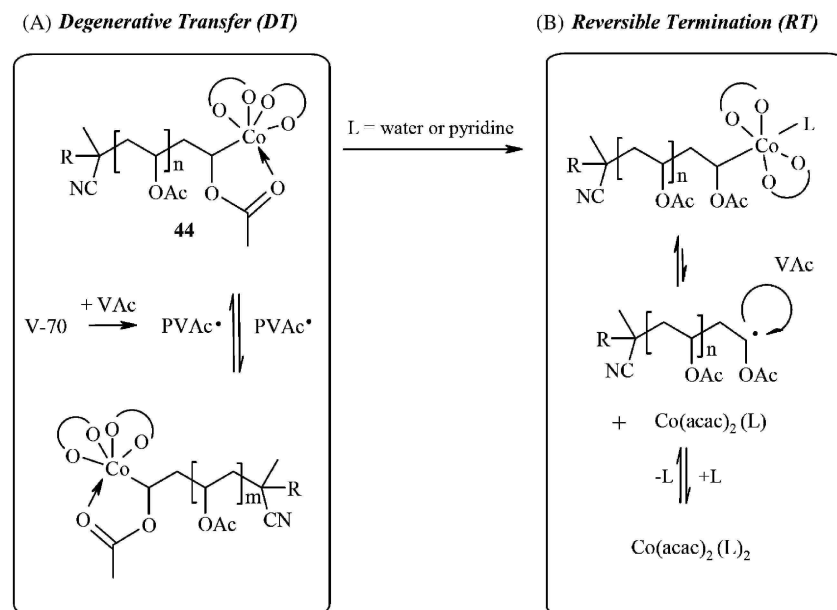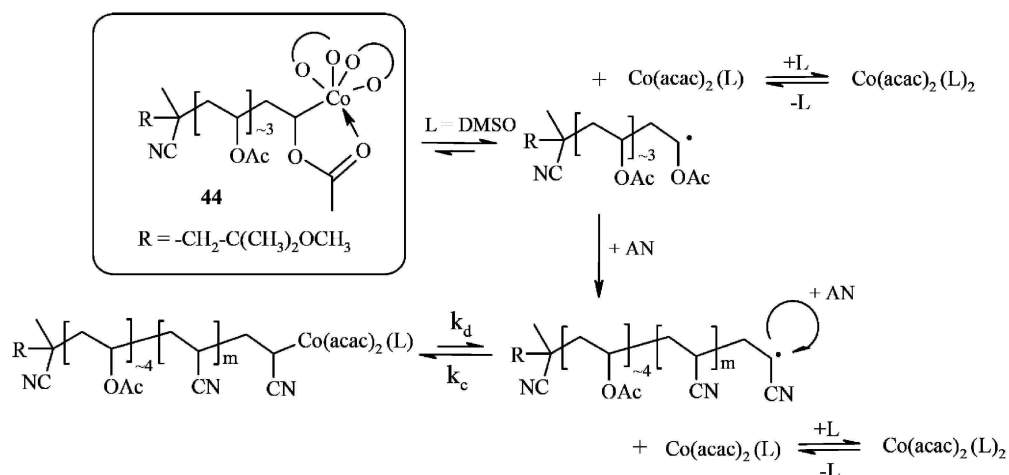

(A) *Degenerative Transfer (DT)*   (B) *Reversible Termination (RT)*

Fig. 13. *CMRP of acrylonitrile initiated by a preformed alkyl-cobalt(III) adduct (44) in dimethylsulfoxide.*

3.2.4. Acrylonitrile

Well-defined poly(acrylonitrile) (PAN) containing materials have great potential, but the controlled polymerization of AN is challenging because of the high monomer reactivity and the low polymer solubility. Very recently, an in-depth study of the AN homopolymerization by CMRP was investigated using Co(acac)2 as controlling agent. The first attempts were carried out in dimethylformamide (DMF) solution at 30 °C using V-70 as initiator. However, the poor solubility of PAN in DMF at 30 °C hampered the process [104]. In the better solvent dimethylsulfoxide (DMSO), a reasonable polymerization rate was observed (50% conversion after 6h). Although the molar mass did not increase perfectly linearly with conversion, especially at the early stage of the experiment, some control was observed [104]. Indeed, PAN with relatively narrow molar mass distributions were obtained ($M_w/M_n \sim 1.4$) and, for a given conversion, the molar mass increased when the [AN]/[Co(acac)2] ratio increased. However, the efficiency factor (f) was much lower than unity (at 50% monomer conversion $f = M_{n,th}/M_{n,exp} = 0.3$).

On the other hand, when the AN polymerization was initiated at 0 °C in DMSO with the alkyl-cobalt(III) compound 44 (Fig. 13), the AN polymerization fulfilled all criteria of a very well-controlled polymerization, *i.e.* the molar masses were close to the expected values (calculated considering the [AN]/[44] ratio), the

polydispersity was close to 1.1 and the chain length increased linearly with the monomer conversion [104].

Since compound 44 is free of azo-initiator residues, the polymerization of acrylonitrile in the presence of DMSO must follow a reversible termination RT mechanism. Coordination of the cobalt(II) complex by DMSO was confirmed by X-ray analysis and supported by DFT calculations [104]. The latter technique also predicted the influence of such coordination on the Co-C bond dissociation enthalpy, as discussed in the DFT section below. This successful control of the acrylonitrile polymerization goes well beyond the extension of the CMRP system to another vinylic monomer. It also illustrates the extreme sensitivity of the CMRP system to the experimental conditions (solvent, temperature, initiating species, additives), opening many possibilities for the application to other monomers.

3.2.5. Conclusions

In general, the CMRP process has been successfully applied to four monomer families: acrylic esters, acrylic acid, vinyl esters and acrylonitrile. One characteristic of this process is that it can be conducted at low temperatures ranging from 0 to 60 °C depending on the Co-C bond strength. Moreover, it proved its efficiency on several occasions when high molar masses were targeted ($M_n > 200,000$ g/mol). However, although CMRP can manage different classes of monomers, it is striking that each of them is specifically controlled by one family of cobalt complexes. Indeed, cobalt porphyrin and cobaloximes are efficient to control the polymerization of acrylic monomers whereas bis(β-diketonato)cobalt(II) derivatives mainly deal with vinyl esters and acrylonitrile. For example, when conducted in the presence of Co(acac)2 the acrylate polymerization is fast and uncontrolled [95] due to a Co-C bond that is too labile as confirmed by DFT calculations [99]. As mentioned previously, one exception to this strict classification is the recent report on the CMRP of VAc at low monomer conversion using the tetra(mesityl porphyri-nato)cobalt complex (30 in Table 2) [101-103].

A challenge in CMRP is to modulate the cobalt complex reactivity in order to deal with a large range of vinylic monomers with the same cobalt complex, which is of utmost importance when block copolymers and other macromolecular architectures are envisioned. In view of the recent results, this goal appears achievable by introduction of coordinating molecules in the polymerization medium. In this respect, computational calculations could be useful to predict the Co-C bond strength taking into account the structure of the monomer and the cobalt complex as well as the polymerization conditions (solvents, additives, etc.).

Fig. 14. *Qualitative diagram relating the enthalpy of the Co^{III} and Co^{II} complexes implicated in CMRP.*
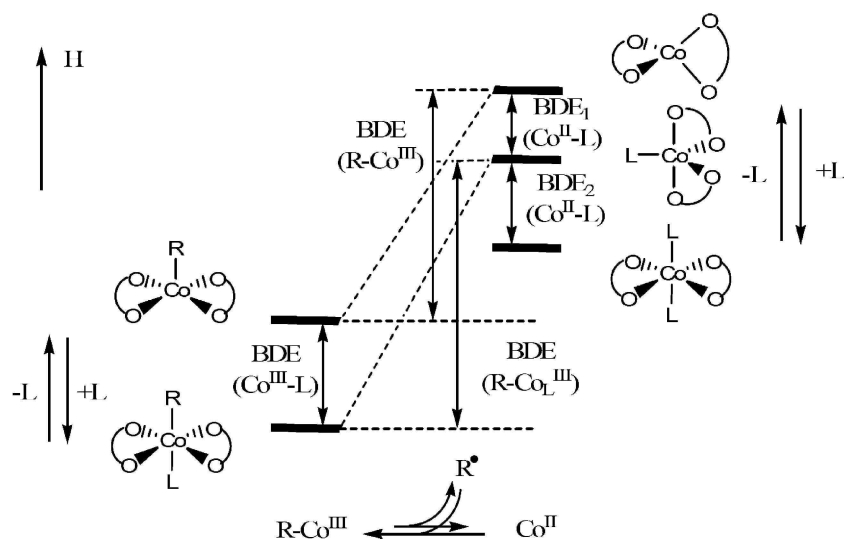
3.3. DFT calculations as rationalizing and predicting tools

The accuracy of theoretical calculations in terms of molecular structure, energetics and physical properties has made enormous progress in the last couple of decades. The application of computational tools, especially Density Functional Theory (DFT) methods, in view of their relatively good performance at comparatively low computational cost, is becoming routine in a variety of different areas of chemistry and controlled radical polymerization is no exception.

Calculations addressing CMRP have so far been limited to the Co(acac)$_2$ system and to thermodynamic issues related to this polymerization technique. According to the accepted mechanism (*e.g.* see Fig. 7), the effective (pseudo-first-order) polymerization rate constant is given by the expression of Eq. (7). The (k_d/k_c) term is the equilibrium constant of the dormant species dissociation equilibrium. The precise nature of the Co^{III} and Co^{II} species involved depends on the presence in solution of donor ligands (L) that are capable of forming coordinative bonds with the two species and on the strength of these bonds, as shown in Fig. 14.

$$k_{eff} = \left(\frac{k_d}{k_c}\right)\left(\frac{[R-Co^{III}]}{[Co^{II}]}\right)k_p \qquad (7)$$

Co^{II}(acac)2 is known to adopt a tetrahedral geometry in dilute solution and the addition of neutral ligands may lead, if the Co^{II}-L bond is strong enough, to the formation of mono or (more frequently) bis-adducts, with, respectively, trigonal bipyramidal and trans-octahedral coordination geometries, as shown in Fig. 14. All these systems adopt a high spin electronic configuration (three unpaired electrons) because of the weak field of the acetylacetonato ligand. The Co^{II}-L bonds have a relatively low strength [small BDE$_1$(Co^{II}-L) and BDE$_2$(Co^{II}-L)] and are labile. The dormant complex R-Co^{III}(acac)2 may also bind L, but no more than one molecule. Although simple alkyl-cobalt(III) complexes having these stoichiometries have not yet been isolated [100], other alkyl-cobalt(III) compounds, mostly with porphyrin and corrin models (*e.g.* Schiff bases), are well known [105-108]. They can either adopt a square pyramidal configuration with an axial alkyl ligand, or a pseudo-octahedral geometry with *trans* R and L. Both systems are diamagnetic because of the strong ligand field of the alkyl ligand. The DFT calculations indicate that these geometries and the diamagnetic ground state are also adopted by the acac systems of Co^{III}.

The chain activation equilibrium will be more displaced towards the free radical and Co^{II} (thereby speeding up the polymerization process) for weaker R-Co^{III} bonds and for ligands L that form stronger bonds with the resulting unsaturated Co^{II} complex. Therefore, calculations have been focused on the evaluation of the strength of these bonds, namely the R-Co^{III} bond [BDE(R-Co^{III}) and BDE(R-Co$_L$^{III})], the Co^{III}-L bond [BDE(Co^{III}-L)], and the Co^{II}-L bonds [BDE$_1$(Co^{II}-L) and BDE$_2$(Co^{II}-L)]. The influence on these bonds by the presence/absence and chemical nature of L is of particular interest.

Fig. 15. *Qualitative energy diagram for the Co^{III}-R homolytic bond rupture: (a) porphyrin and corrin systems, giving low spin (S = 1/2) Co^{II} complexes; (b) bis(acetylacetonato) system, giving high spin (S = 3/2) complexes.*
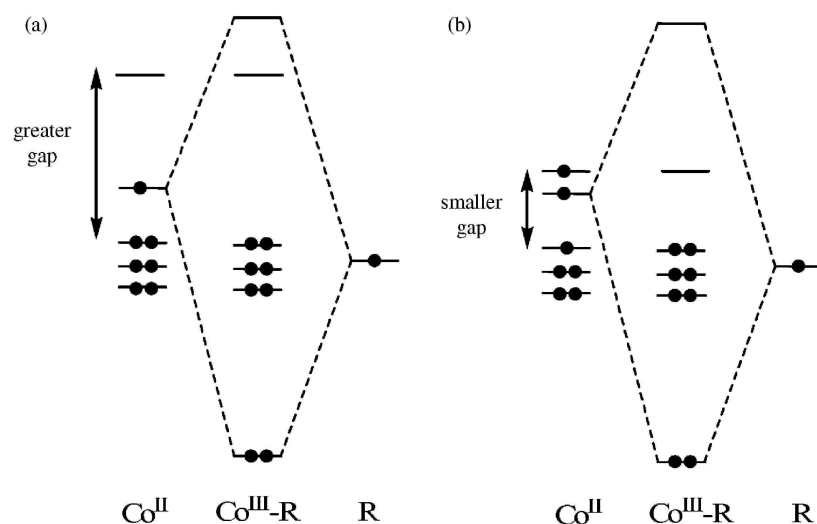
3.3.1 Calculations of R-Co^{III} BDE

Previous calculations of Co^{II}-alkyl bond strengths had mostly been confined to the vitamin B12 system [109-113]. There is a major difference between the porphyrin and corrin model systems and Co(acac)$_2$: the stronger field of the porphyrin and Schiff base ligands forces Co^{II} in the low spin configuration (*S* = 1/2). Therefore, the R-Co^{III} homolytic bond rupture leaves a single unpaired electron on both the radical and the cobalt atom when the latter is coordinated by the stronger porphyrin or Schiff base ligands, whereas the same process is accompanied by the unpairing of two additional electron from a metal *d* orbital for the Co(acac)$_2$ system, see Fig.

15. This is because the energetic separation between filled and empty orbitals is smaller in the presence of the low-field acetylacetonato ligands.

When addressing the specific question of the Co-C bond strength in $(acac)_2Co^{III}$-R systems, a major computational problem concerns the change of spin state associated to the homolytic rupture (from spin singlet ($S = 0$) for Co^{III}-R to a global spin triplet ($S = 1$) resulting from the combination of the quartet ($S = 3/2$) of the Co^{II} complexes and the doublet ($S = 1/2$) of the free organyl radical). For processes where a change of spin is involved, DFT methods provide results that are wildly different, depending on the type of functional used. Accurate bond enthalpies are accessible in principle through high level computational methods, but this is quite impractical for molecules the size of those of interest here. A detailed discussion of this phenomenon is available in other specialized articles [114-117]. In this review, we limit ourselves to mentioning that the most typical and frequently used "hybrid" functionals, such as B3LYP are known to overestimate the relative stability of higher spin states, whereas "pure" functionals, such as BP86 often do the reverse. Unfortunately, no "rule of thumb" is available for the selection of the best functional for a specific problem. An appropriate choice would be made possible by comparing calculated and experimentally available parameters, or by comparison with much higher level *ab initio* calculations, believed to provide a closer approximation of the experimental value. Modified hybrid functionals with a reduced admixture of the exact exchange have been developed using these approaches on simple and well investigated systems, for instance the CO dissociation from $Fe(CO)_5$ (going from singlet to triplet) [115]. For the typical systems used in CMRP, the first approach is impossible because Co-R BDEs are not experimentally available, while the second one is prohibitive given the relative complexity of the systems. Thus, it is wise to compare the results obtained with different functionals and to focus the analysis on trends rather than on absolute values.

Calculations of BDE(R-Co^{III}) and BDE(R-Co_L^{III}) values (see Fig. 14), carried out with the B3LYP functional, were initially restricted to a model system where R = CH_3 [94] and later extended to R = $CH(OCH_3)CH_3$ (as a model of poly(vinyl ether) (PVE)), $CH(OOCCH_3)CH_3$ (as a model of PVAc), $CH(CN)CH_3$ (as a model of PAN), $CH(CO_2CH_3)CH_3$ (as a model of PMA), and $CH(CH_3)_2CN$ (primary radical generated from AIBN) [99,104]. These results (see Table 4) confirm the expected dependence of the bond strength on radical stabilization.

Table 4: *DFT-calculated bond dissociation enthalpies (BDE) at 298 K for R-$Co^{III}(acac)_2(L)$ complexes[a].*

R	L	BDE (kcal mol^{-1})[b]		Ref.
		B3LYP	B3PW91*	
CH_3	-	14.6		[94]
CH_3	py	17.9		[94]
CH_3	NMe_3	17.2		[94]
CH_3	NH_3	17.8		[94]
CH_3	H_2O	18.8		[94]
$CH(OCH_3)CH_3$	-	8.4		[99]
$CH(OOCCH_3)CH_3$	-	5.7	10.0	[99,104]
$CH(OOCCH_3)CH_3$	AN	10.1	16.2	[104]
$CH(OOCCH_3)CH_3$	DMF	8.2	14.1	[104]
$CH(OOCCH_3)CH_3$	DMSO	4.5	9.9	[104]
$CH(OOCCH_3)CH_3$-(κ^2:C,O)	-	11.9	13.0	[99,104]
$CH(CN)CH_3$	-	1.3	6.7	[104]
$CH(CN)CH_3$	AN	7.7	14.2	[104]
$CH(CN)CH_3$	DMF	6.0	12.5	[104]
$CH(CN)CH_3$	DMSO	2.9	9.4	[104]
$CH(COOCH_3)CH_3$	-	-1.5		[99]
$CH(CH_3)_2CN$	-	-5.5		[99]

[a] Only bond energies were given for the bonds reported in ref. [94]. The values reported here are the standard enthalpies, obtained by corrections with the PV term at 298 K.
[b] With both functional, the calculations were carried out using the 6-31G** basis set for the light atoms (C, N, O, H) and the LANL2DZ basis set with an added f polarization function for Co.

The calculations on the model CH_3-$Co(acac)2(L)$ system with L = py, NMe_3, NH_3 and H_2O show that the L coordination strengthens the Co-CH_3 bond by 3-4 kcal mol^{-1}, with apparently little influence of the nature of L [94]. This strengthening phenomenon can be associated to an energetically more favorable relaxation of $Co(acac)2$ from square planar to tetrahedral than $Co(acac)2(L)$ from square pyramidal to trigonal bipyramidal. The practical result is a negative effect on the radical activation process, portrayed qualitatively in Fig. 14 [BDE(R-Co_L^{III})>BDE(R-Co^{III})]. However, it is outweighed by the positive effect of further L coordination to

yield 6-coordinate $Co(acac)_2(L)_2$, which energetically stabilizes the Co^{II} complex, thereby shifting the radical activation equilibrium, *vide infra.* Analogous calculations on R-Co(acac)$_2$(L) with R = $CH(OOCH_3)CH_3$ and $CH(CN)CH_3$ and with L = AN, DMF and DMSO also show an effect of ligand coordination, but this is now modulated by the steric effects: the smaller AN ligand shows a strengthening effect, the slightly more encumbering DMF ligand has a smaller strengthening effect, and the bulkier DMSO ligand has essentially no effect (strengthening by only 1.6 kcal mol^{-1} for $CH(CN)CH_3$; *weakening* by 1.2 kcal mol^{-1} for $CH(OOCCH_3)CH_3$) [104]. These findings are very much in line with previous work on the vitamin B12 models, where the steric bulk of the axial ligand was shown to have an important effect on the Co^{III}-R labilization [37,118].

The PVAc model system, $CH(OOCCH_3)CH_3$, deserves special consideration, because the acetate function of the Co-capped monomer unit is suitably placed to saturate the coordination sphere of Co^{III} by chelation. Thus, the dormant form of the Co-capped PVAc growing chain, PVAc-Co(acac)2, is not 5-coordinated but rather 6-coordinated, as already illustrated above in Fig. 12, even in the absence of external donor ligands. This chelation provides an extra 6 kcal mol^{-1} of stability to the alkyl-cobalt(III) system, at the B3LYP level, and competes effectively with the coordination of the less strongly bonded L ligands, see below [99].

As stated above, the nature of the functional used in the calculation has an important effect on processes where a change of spin state occurs. Use of the B3PW91* functional [115], where the contribution of exact exchange is reduced relative to B3LYP, has the effect of increasing the calculated R-Co^{III} BDE by ca. 6 kcal mol^{-1} on average (see Table 4), but the relative trend of bond strengths as a function of R remains unaltered.

Table 5: *DFT-calculated Co-L bond dissociation enthalpies (BDE) at 298 K for RCo^{III}(acac)$_2$(L), Co^{II}(acac)$_2$(L) and Co^{II}(acac)$_2$(L)$_2$ complexes^a.*

R	L	BDE (kcal mol-^{1})^b		Réf.
		B3LYP	B3PW91*	
RCo^{III}(acac)$_2$(L) complexes				
CH_3	H_2O	9.9		[94]
CH_3	NH_3	11.7		[94]
CH_3	NMe_3	6.2		[94]
CH_3	Py	7.7		[94]
$CH(OOCCH_3)CH_3$	AN	-0.23	0.7	[104]
$CH(OOCCH_3)CH_3$	DMF	6.8	7.0	[104]
$CH(OOCCH_3)CH_3$	DMSO	4.4	3.8	[104]
$CH(CN)CH_3$	AN	1.8	1.9	[104]
$CH(CN)CH_3$	DMF	9.1	8.7	[104]
$CH(CN)CH_3$	DMSO	7.5	6.6	[104]
Co^{II}(acac)$_2$(L) complexes: L=				
AN		-4.6	-5.6	[104]
CH_3COOCH_3		-0.3		[94]
NMe_3		3.5		[94]
py		4.3		[94]
DMF		4.3	2.9	[104]
DMSO		5.9	3.9	[104]
H_2O		5.8		[94]
NH_3		8.4		[94]
Co^{II}(acac)$_2$(L)$_2$ complexes: L=				
AN		1.2	2.4	[104]
NMe_3		3.9		[94]
py		4.4		[94]
DMF		4.7	3.3	[104]
DMSO		4.6	2.8	[104]
NH_3		12.0		[94]

^{a} Only bond energies were given forthe bonds reported in ref. [94]. The values reported here are the standard enthalpies, obtained by corrections with the PV term at 298 K.
^{b} With both functional, the calculations were carried out using the 6-31G** basis set for the light atoms (C, N, O, H) and the LANL2DZ basis set with an added f polarization function for Co.

3.3.2. Calculations of Co^{II}-L and Co^{III}-L BDEs

The Co-L bond strengths studied so far are listed in Table 5. One point worthy of note is that for those bonds that have been investigated at both B3LYP and B3PW91* levels, the values obtained do not differ too much (2 kcal mol^{-1} at the most) between the two functionals. This is because the ligand binding does not result in a change of spin state (S = 0 for the Co^{III} systems, 3/2 for the Co^{II} systems).

The calculations of $BDE_1(Co^{II}$-L) and $BDE_2(Co^{II}$-L) confirms the experimentally established weakness of these bonds. The BDE(Co^{III}-L) values are slightly greater (for instance, *cf.* the values of BDE(Co^{III}-L) and $BDE_1(Co^{II}$-L) for L = NMe$_3$ and H$_2$O(R=CH$_3$) and for L = AN (R = CH(OOCCH$_3$)CH$_3$ or CH(CN)CH$_3$). As shown in Fig. 14, the values of BDE(Co^{III}-L), $BDE_1(Co^{II}$-L), BDE(R-Co^{III}) and BDE(R-Co$_L$^{III}) are tied together in a Hess cycle. Thus, the stronger bond of L with Co^{III} than with Co^{II} (BDE_1 (Co^{II}-L)) is related to the fact that the R-Co^{III} bond is stronger in the 6-coordinate R-Co(acac)$_2$(L) than in the 5-coordinate R-Co(acac)$_2$, at least for sterically unencumbering L molecules.

The calculations show that BDE_1 (Co^{II}-L) is smaller than $BDE_2(Co^{II}$-L) for the unencumbering and poorly coordinating AN ligand, about the same for ligands of intermediate size (NMe$_3$, py, DMF) and greater for the bulkier and more strongly binding DMSO ligand. Two trends emerge from these calculations: electronic factors favor ligand binding in the order Co(acac)$_2$(L) > Co(acac)$_2$, whereas steric factors show the opposite trend.

Fig. 16. *Energy diagram obtained with the B3PW91* functional for the Co-C homolytic bond cleavage and subsequent L addition in (acac)$_2$(L)Co-CH(CN)CH$_3$ (L= nothing, AN, DMSO). The values shown are relative enthalpies in kcal mol^{-1}.*
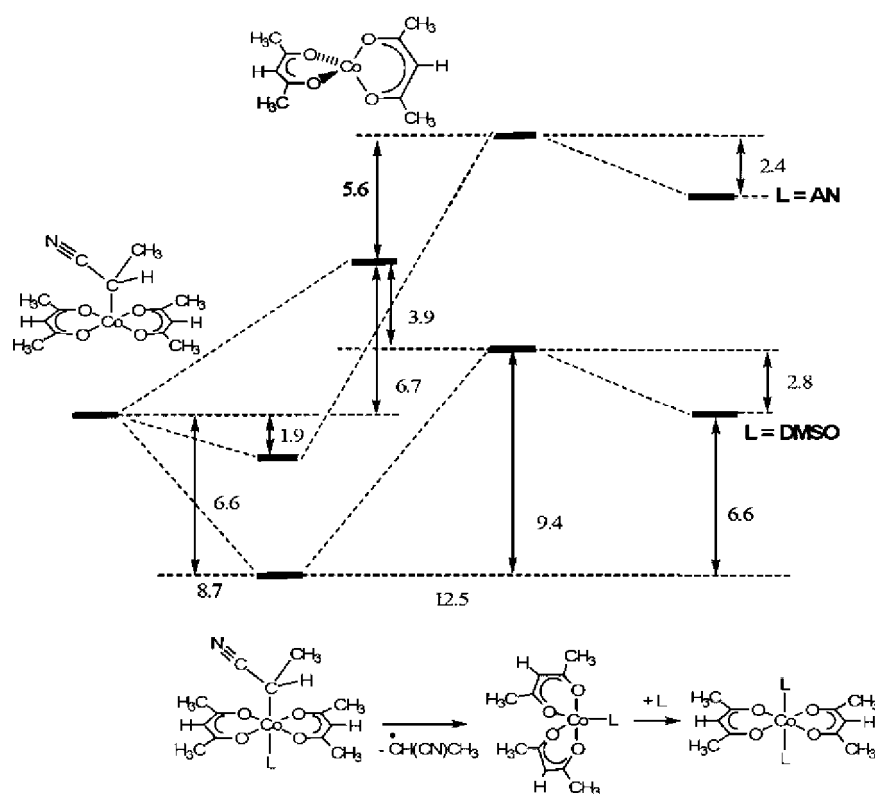
The specific use of the calculated R-Co^{III} and Co$^{II/III}$-L bond strength rationalizes rather well the better ability of Co(acac)$_2$ to control the polymerization of AN in the coordinating solvent DMSO, relative to non-coordinating solvents (toluene or anisole). As shown in Fig. 16, the dormant chain in a non-coordinating solvent is likely to be the 5-coordinated (acac)$_2$Co-PAN (modeled in the calculation by (acac)$_2$Co-CH(CN)CH$_3$), since coordination of AN to this species provides only very small stabilization, probably insufficient to counter the negative effect of the entropy term. Radical dissociation yields Co(acac)$_2$, which also does not enjoy stabilization by AN coordination (both 5-coordinate Co(acac)$_2$(AN) and 6-coordinate Co(acac)$_2$(AN)$_2$ have higher enthalpy and therefore even higher free energy). The radical trapping process provides 6.7 kcal mol^{-1} of enthalpic stabilization but is disfavored entropically. In the presence of DMSO, both the Co^{III} and Co" complexes become

coordinatively saturated, to yield PAN-Co^{III}(acac)$_2$(DMSO) and Co^{II}(acac)$_2$(DMSO)2, respectively. In fact, the latter complex was isolated in crystalline form and characterized by X-ray diffraction. Thus, the trapping process involves loss of DMSO from Co^{II}(acac)$_2$(DMSO)2 followed by radical addition. The enthalpic stabilization is 6.6 kcal mol^{-1}, very similar to that obtained in the absence of DMSO, but the process is now essentially isoentropic. The rationalization of the solvent effect on the initiation of AN polymerization starting from a PVAc-Co(acac)2 macroinitiator will be addressed below within the block copolymer section.

3.3.3. Perspectives for future work

The kinetic aspects of CMRP have not yet been addressed. Although the rate of polymerization (Eq. (7)) depends only on the thermodynamics (equilibrium position) of the organocobalt complex formation process, the trapping rate is of paramount importance for insuring low polydispersities. A trapping process having higher activation barriers will result in a lower trapping efficiency and thus in a greater accumulation of the active radical concentration, with negative effects on terminations and polydispersity. Understanding how the nature of the ligand and the spin state change affect this trapping barrier would be particularly useful for the optimization of the reversible deactivation process. For instance, as shown schematically in Fig. 17, path (a) yields a lower equilibrium concentration of active radical and a faster trapping rate, whereas path (b) would yield a greater concentration of radicals and a less efficient trapping process. Both paths (a) and (b) refer to adiabatic processes without a change of total spin *(e.g.* when the Co complex has S= 1/2). Path (c) illustrates the case of a change of spin, as in the case of the Co(acac)2 system. In such case, the explicit calculation of the Minimum Energy Crossing Point (MECP) [119,120] would be necessary to evaluate the activation barrier. Calculations on associative exchange pathways, as shown in Fig. 18, would also be necessary in order to evaluate the efficiency of systems where the degenerative transfer mechanism predominates. For instance, a system yielding pathway (d) would undergo a slower exchange, and therefore poorer control, than a system yielding pathway (e).

Fig. 17. *Qualitative reaction coordinates for the reversible activation of an organometallic dormant chain. Solid curves correspond to S = O and the dashed curve to S = 1.*
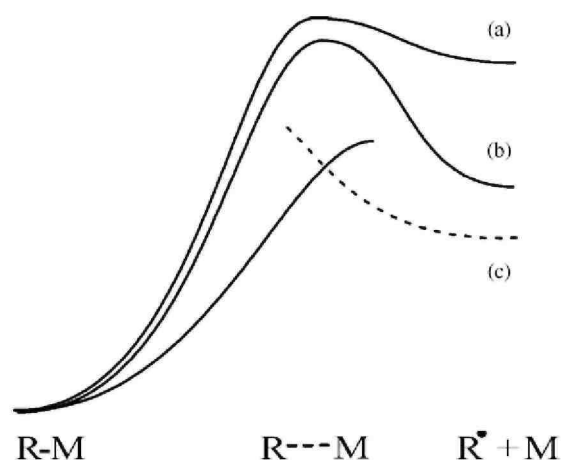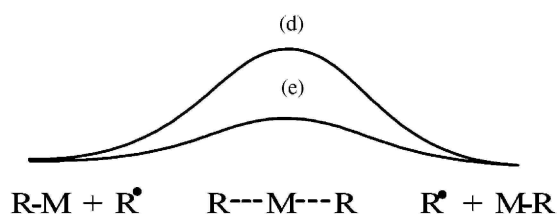

Fig. 18. *Qualitative reaction coordinate for the associative radical exchange on an organometallic dormant chain with low (e) and high (d) energy barrier.*

Finally, a point which is still totally obscure is the role of the metal coordination sphere in determining the aptitude of the complex to yield catalytic chain transfer vs. reversible deactivation. This is again a kinetic issue, determined by the relative height of two activation barriers: that for radical trapping to form an organometallic dormant chain vs. that for H atom transfer to form the hydride complex and a dead chain with an unsaturated chain end. A greater degree of understanding of which parameters regulate these two barriers will give guidance

for the development of tailored complexes with specific roles. In our opinion, the computational tool can also help in this direction.

3.4. Improvement of the technology

In order to bring the CMRP process closer to industrial standards, several questions need to be addressed, *i.e.* compatibility of the technique with aqueous dispersed media, use of widespread initiators, recovery and recycling of the cobalt complex. The Co(acac)2 39 mediated radical polymerization of VAc was used as model to address these challenges.

Most of the radical polymerization processes are carried out in aqueous dispersed media because of the easy control of heat transfer, absence of organic solvent and higher monomer conversion. Therefore, the CMRP of VAc was tentatively carried out in aqueous dispersed media, such as suspension [98,121] and miniemulsion [98,122], rather than in bulk. In this approach, several questions appeared obvious, such as the much higher affinity of the controlling agent (Co(acac)$_2$) for the water phase compared to the monomer and the effect of a large amount of water available to coordinate the cobalt complex. The first problem was tackled by using a preformed PVAc macroinitiator end-capped by cobalt, which is sufficiently hydrophobic to locate the cobalt in the monomer phase. Typically, the PVAc-Co(acac)$_2$ macroinitiator was dissolved in VAc prior to dispersion in water. Polyvinyl alcohol) (PVOH, 0.16 wt% in water) and sodium dodecyl sulfate (SDS, 0.9 wt% in water) were used as surfactant for the suspension and the miniemulsion procedures, respectively. In the latter case, ultrasonication was necessary to obtain the nanometric droplets, precursors of the latex particles. The polymerizations, carried out at 30 °C, always followed a controlled pathway even at high monomer conversion (above 75%) and relatively high molar masses (-100,000 g/mol). However, the molar masses were higher than predicted. Interestingly, compared to the bulk, the polymerization rate was high to extremely high for the suspension (75% conversion in 70min) and the miniemulsion (90% conversion in 30 min), respectively. Although the water content in the monomer droplet might coordinate cobalt and participate to speeding up the reaction [94,99], such a kinetic effect was demonstrated to be mainly due to a partitioning effect, *i.e.* the continuous departure of the deactivating species (Co(acac)2) into the water phase (Fig. 19) [99,121]. At the end, micrometric beads and latexes of well-defined PVAc were obtained in suspension and miniemulsion, respectively.

Throughout our work, V-70 has been chosen as initiator for CMRP because of its low decomposition temperature ($t_{1/2}$ = 12 h at 30°C), which is compatible with the optimum temperature (30°C) dictated by the thermal lability of the Co-C bond. Within the search for a substitute for V-70, redox initiating systems appeared as an interesting alternative because they are effective at room temperature and largely used at the industrial scale [123]. Therefore, the CMRP of VAc was initiated at 30°C from a mixture of peroxide (lauroyl peroxide or benzoyl peroxide) as oxidant, ascorbic acid as reducing agent and Co(acac)2 39 with the dual role of reducing and controlling agent. Under these conditions, the polymerization was fast and remained controlled. However, the initiator efficiency ($f = M_{n,th}/M_{n,exp}$) was low ($0.1 \leq f \leq 0.25$), suggesting that Co(acac)$_2$ also participated to the redox initiation. When ascorbic acid was replaced by citric acid, the polymerization was much faster, while maintaining good control. Substitution of redox systems for V-70 underlined the sensitivity of the Co complex towards oxidizing agents but also emphasized the potential for a reaction scale-up [123].

Fig. 19. *Schematic representation of the VAc CMRP in aqueous dispersed media (suspension and miniemulsion); acceleration of the polymerization in the monomer phase by diffusion of the cobalt(II) deactivating species into the water phase.*
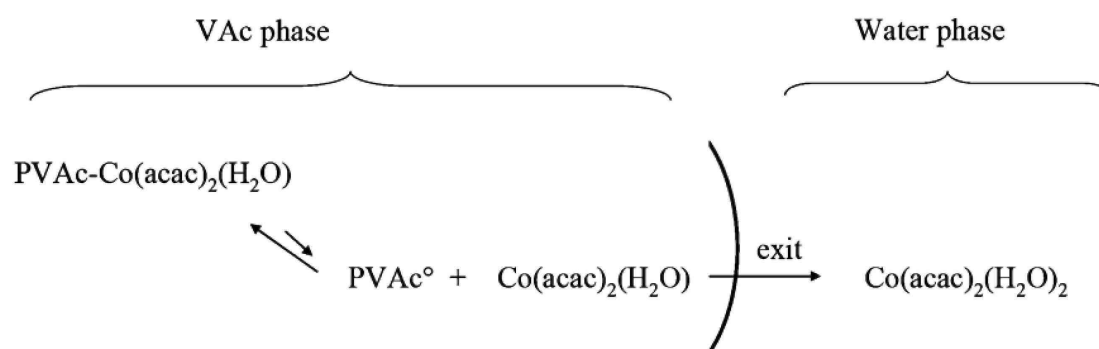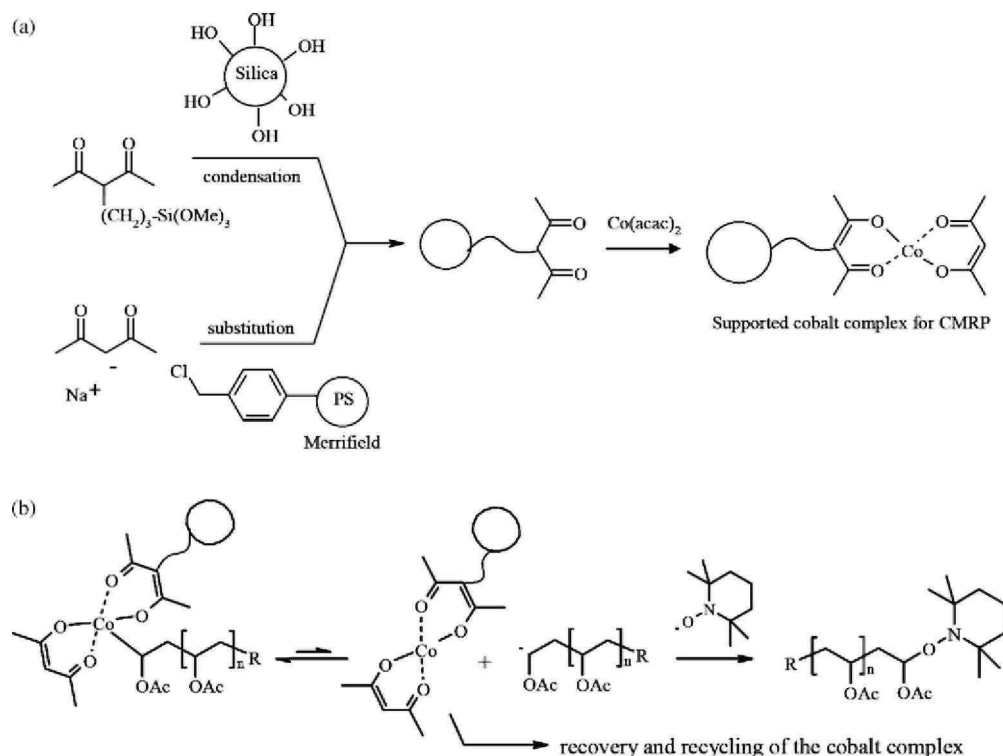
Fig. 20. *General strategy for supported cobalt-mediated radical polymerization (SCMRP): (a) Co(acac)₂ immobilization onto silica or Merrifleld resin; (b) polymerization involving the supported cobalt(II) complex followed by metal recovery and polymer purification.*

Except when the metal content in the polymer falls to the ppm range, it becomes essential to address the question relative to its elimination and recovery. Since a stoichiometric amount of cobalt compared to the polymer chains is intrinsic to the CMRP mechanism, it was of utmost importance to develop an efficient method for polymer purification and for metal complex recycling. In this respect, thermal treatment of the PVAc-Co(acac)2 chains with a nitroxide or a thiol at the end of the polymerization was shown to drastically reduce the cobalt content in the polymer matrix [124]. After homolytic Co-C bond cleavage, the released PVAc radical was scavenged by the nitroxide or abstracted the thiol H atom, respectively. However, although a simple filtration through a silica column allows the removal of the metal from the polymer matrix, these approaches are not compatible with the recovery and recycling of the cobalt complex. In order to solve this problem, the cobalt complex was supported on the surface of inert materials [125]. Acetylacetone groups were first grafted onto silica or Merrifield resin, followed by a ligand exchange reaction involving Co(acac)₂ in order to immobilize the metal on the support surface (Fig. 20). Acetylacetone substituted by a trimethoxysi-lyl group, 3-[3-(trimethoxysilyl)propyl]-2,4-pentanedione (MS-acac-H), was prepared and condensed on the surface of a non-porous silica, whereas nucleophilic substitution of chloride in chloromethyl groups by sodium acetylaceto-nate was carried out for the Merrifield resin (Fig. 20a). The supported complexes were then used to control the bulk polymerization of vinyl acetate initiated by V-70 at 30°C (Fig. 20b). The Supported Cobalt Mediated Radical Polymerization (SCMRP) of VAc was effective and produced PVAc with relatively narrow molar mass distribution [125]. At the end of the reaction, removal of the PVAc chains from the surface-grafted cobalt complex was successfully achieved by addition of a nitroxide (2,2,6,6-tetramethylpiperidinoxy, TEMPO), followed by centrifugation and recovery of the support (Fig. 20b). The successful re-use of the supported cobalt complex was quite encouraging, although partial metal passivation after each cycle was observed.

Although CMRP is still far from industrial development, all these contributions emphasize the difficulties and futures challenges for this system and pave the way in that direction.

3.5. Macromolecular design

Nowadays, the design of novel polymer materials with well-defined structures and specific properties, aiming at the development of a large range of applications, is becoming an essential aspect of polymer science. In this respect, the contribution of controlled radical polymerization is remarkable. A large range of polymers with well-defined molecular characteristics (i.e. length, chain-end, architecture, composition, functionality, etc.) have been

made available by CRP under mild conditions [126-129]. In that context, the ability of CMRP to control the polymerization of difficult monomers constitutes a new opportunity in macromolecular engineering. The approaches that have so far been explored for producing functionalized polymers, copolymers and more complex architectures by CMRP are mentioned below.

Fig. 21. *End-functionalization of the polymer chains in CMRP.*
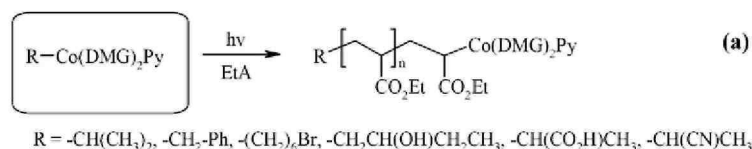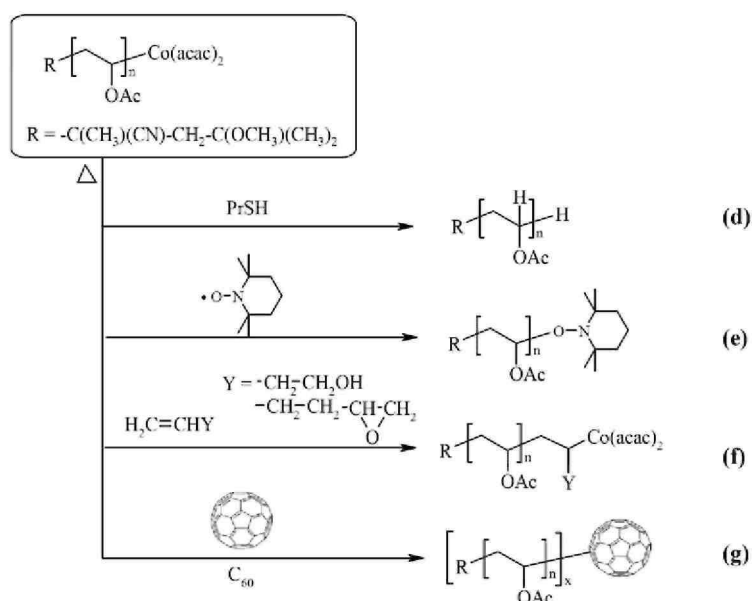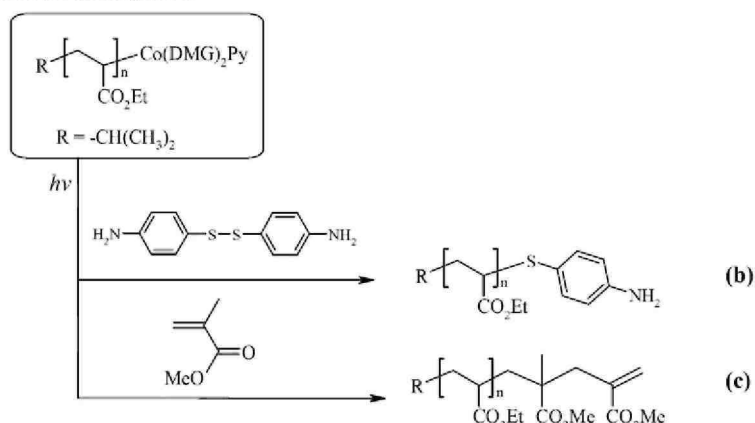
3.5.1. End-functionalization

One major advantage of CRP relative to living ionic polymerizations is its tolerance towards many functional groups allowing the preparation of a large range of telechelic polymers without using protecting groups. Typical examples of end-functionality control for polymers prepared by CMRP are depicted in Fig. 21.

The α-end group is controlled by the initiator structure. Organocobaloximes containing various functional groups, such as phenyl, bromide, hydroxyl, carboxyl and nitrile groups, were prepared and used as photoinitiators to produce α-functionalized poly(acrylates) (Fig. 21a) [65]. For the EA polymerization initiated

by 6-bromohexyl (pyridi-nato)cobaloxime, NMR analyses indicated that about 90% of the PEA chains contained a bromine atom at the α chain end. At the end of the CMRP process, most of the chains are end-capped by the cobalt complex used as controlling agent. Therefore, the well known reactivity of alkyl-cobalt(III) complexes [130-132] can be used to convert and functionalize the polymer ω chain end. A few methods have already been successfully applied. For example, photolytic treatment of PEA-Co(DMG)$_2$(Py) in the presence of bis(p-aminophenyl) disulfide yielded a poly-acrylate having a terminal aminophenylthioether function (Fig. 21b) [65]. Well-defined polyacrylate macromonomers were obtained upon addition of methyl methacrylate on the same PEA-Co(DMG)$_2$(Py) by subsequent radical addition and catalytic chain transfer reaction (Fig. 21c) [65]. PVAc-Co(acac)$_2$ has also been quenched by various scavengers. Addition of alkanethiol to the polymerization medium terminates the chains by a proton and allowed the removal of the cobalt complex (Fig. 21d) [124]. Similarly, TEMPO but also functionalized nitroxides (with epoxy [124], α-bromo ketone and α-bromo ester [133] groups) scavenged the PVAc radicals released by the thermal Co-C bond cleavage (Fig. 21 e). Since the covalent bond between PVAc and nitroxide is strong [18], this approach is valid for the func-tionalization of the PVAc chains [124]. Indeed, it is reported that N-alkoxyamines with a heteroelement in the *a* position (0 in the case of PVAc) present markedly stronger C-TEMPO bond [134]. After treatment with TEMPO or thiols followed by elution through a silica column, the cobalt content in the polymer, prepared by CMRP, was drastically reduced. Finally, addition of functionalized, non-activated olefins, such as 1,2-epoxy-5-hexene and 3-butene-1-ol inhibited the CMRP of VAc leading to the chain end capping by an epoxy and hydroxyl group, respectively (Fig. 21 f) [124]. Following the same principle, fullerenes were successfully grafted with poly(vinyl acetate) and poly(N-vinyl pyrrolidone) (PNVP) chains by radical addition to the double bond of the C$_{60}$ (Fig. 21g) [135,136]. An average number of four chains were detected when a large excess of PVAc-Co(acac)$_2$ was reacted with C$_{60}$ whereas mixtures of nanohybrids with different grafting level (from 1 to 4 polymer chains) were collected when the [PVAc-Co]/[C6o] molar ratio was decreased. The well-defined hydrosoluble and potentially biocompatible PNVP-C60 and poly(vinyl alcohol)-C$_{60}$ (PVOH-C$_{60}$), obtained by hydrolysis of the PVAc ester functions) proved able to generate singlet oxygen upon photolytic treatment, making them promising agents for photodynamic cancer therapy [135,136]. Interestingly, compounds containing several cobalt moieties were synthesized and used as multifunctional CMRP initiator. For example, l,6-bis[(dipyridinato)cobaloxime]hexane (Py(dmgH$_2$)$_2$Co-(CH$_2$)$_6$-Co(dmgH$_2$)$_2$Py, 45 in Fig. 22) was used as difunctional photoinitiator for the ethyl acrylate polymerization in chloroform [16,65]. The resulting PEA (M_n = 19,000g/mol, M_w/M_n = 2.4) presented a Co-C bond at each chain end, opening the way to the formation of triblocks copolymers. Under similar experimental conditions, photoinitiators containing three (CH$_3$CH$_2$C[CH$_2$OCOCH(CH$_3$)Co(DMG)$_2$Py]$_3$, 46 in Fig. 22) and four (C[CH$_2$OCOCH(CH$_3$)Co(DMG)$_2$Py]$_4$, 47 in Fig. 22) cobaloxime moieties were used to promote the synthesis of star-shaped polyacrylates with three and four arms, respectively [65]. In these cases, M_n increased linearly with the monomer conversion but were lower than the expected values ($f = M_{n,th}/M_{n,exp}$ = 1.25), possibly due to transfer reactions. Although it is reasonable to assume that all the arms grew uniformly, additional experiments are necessary to confirm this conclusion.

Fig. 22. *CMRP photoinitiators containing several cobaloximes moieties.*
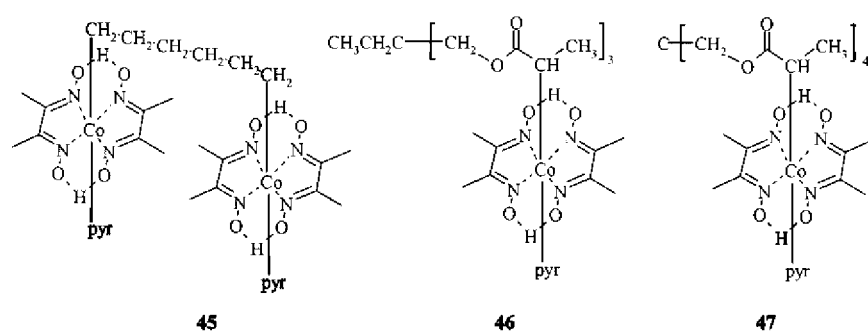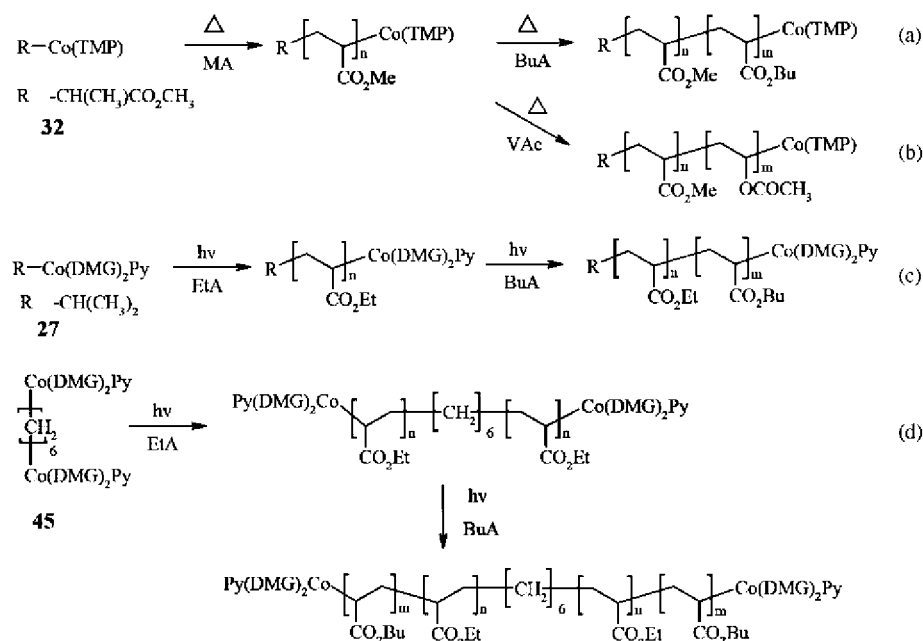

3.5.2. *Copolymerization*

In the era of nanotechnology, the design of well-defined block copolymers able to self-assemble in bulk or in solution into nanodomains is becoming an important aspect of polymer synthesis. In that respect, CMRP has already contributed to the preparation of valuable copolymers.

Wayland et al. was first to demonstrate the ability of CMRP to provide block copolymers [15,73,75,77]. Well-defined PMA chains (M_n = 40,600 g/mol, M_w/M_n = 1.22) end-capped by (TMP)Co (30 in Table 2) and purified from the unreacted monomer were treated with *n*BuA and benzene. Upon thermal activation at 60°C, a PMA-*b*-

PnBuA block copolymer (M_n = 131,400 g/mol, M_w/M_n = 1.29) was formed (Fig. 23a).[15] Although the controlled character of the CMRP was indisputably established, the range of accessible copolymers has long remained limited to acrylic monomers. In a similar approach, a PEA-*b*-PnBuA block copolymer (25,800 g/mol) was prepared by cobaloxime-mediated radical polymerization by sequential polymerization of EA and *n*BuA upon photolytic treatment (Fig. 23c). The block sequencing occurred relatively efficiently provided that growth of the first PEA block (7400 g/mol, M_w/M_n = 1.6) was stopped before reaching high conversions (<60%) [65]. Finally, a PnBuA-b-PEA-b-PnBuA triblock copolymer (M_n =33.500 g/mol, M_w/M_n =2.7) was obtained by nBuA polymerization initiated by a difunctional PEA macroinitiator (M_n = 19,000 g/mol, M_w/M_n = 2.4) obtained from l,6-hexyl[(dipyridinato)cobaloxime] 45 (Fig. 23d) [65].

**Fig. 23.** *Synthesis of block copolymers by CMRP.*

As the controlling ability of cobalt porphyrin and cobaloximes has long remained limited to acrylic monomers, the range of accessible block copolymers was restricted as well. An exception is the VAc polymerization initiated by a Co(TMP)-capped PMA (M_n = 30,000 g/mol, M_w/M_n = 1.11), which led to well-defined PMA-b-PVAc (M_n= 85,000 g/mol, M_w/M_n = 1.21) at low monomer conversion (VAc conversion = 9%) (Fig. 23b) [101,102]. On the other hand, the use of bis(acetylacetonato)cobalt(II) and derivatives significantly enlarged the range of copolymers made available by CMRP. The first efforts were directed to the statistical copolymerization of VAc with various monomers, such as acrylate [95], NVP [137], and chlorovinyl acetate [137,138]. Although acrylates polymerized in a completely uncontrolled fashion in the presence of Co(acac)2, random copolymerization of nBuA with VAc followed a controlled pathway (Fig. 24a) [95]. According to the ^{1}H NMR study, nBuA was incorporated preferentially in the early stages of the copolymerization leading to a gradient sequence distribution in the P⎴BuA-co-PVAc copolymer. Typically, polydispersities as low as 1.2-1.3 could be obtained provided that the initial feed had a high VAc content (above 50%), indicating that deactivation of the VAc-terminated radical chain by the cobalt complex was the critical step to control the copolymerization.

A similar behavior was observed when the statistical copolymerization of NVP with VAc was initiated by V-70 in the presence of Co(acac)2 39 (Fig. 24b) [137]. The synthesis of PNVP-co-PVAc with low polydispersities was achieved in spite of the moderate control observed for the polymerization of NVP alone with the same complex [137]. VAc was also successfully copolymerized with vinyl chloroacetate (VClAc) by CMRP using Co(F$_3$acac)$_2$ 41 as controlling agent, leading to well-defined PVAc-*co*-PVClAc copolymers (Fig. 24c) [137,138]. The pendant α-chloro ester functions of this statistical copolymer were then used as initiators for the styrene atom transfer radical polymerization (ATRP) catalyzed by copper chloride and bis(2-pyridylmethyl)octadecylamine (BPMODA) providing the corresponding PVAc-*graft*-PS (Fig. 24c) [138]. Hydrolysis of the PVAc-*graft*-PS copolymer ester functions allowed releasing the PS side chains for size exclusion chromatography (SEC) analyses. The latter confirmed the monomodal molar mass distribution of the PS segments in spite of a slight tailing towards the low molar mass region.

Since the CMRP method based on Co(acac)$_2$ was not able to impart control to monomers, such as styrene, acrylates and methacrylates, the straightforward synthesis of well-defined PVAc-containing block copolymers by CMRP alone appeared difficult. Therefore, CMRP was combined with ATRP to tackle this problem (Fig. 25). Typically, PVAc-Co(acac)2 chains preformed by CMRP were end-functionalized by nitroxides containing α-bromo ketone or α-bromo ester [133]. The activated halogen was then used to initiate the ATRP of styrene, methyl methacrylate and ethyl acrylate to provide the corresponding well-defined block copolymers [133]. This appeared as a valuable approach to yield thermally robust copolymers, because the nitroxide-PVAc bond is known to be strong [18]. Indeed, SEC analysis of the PVAc-*b*-PMMA copolymer before and after thermal treatment at 180°C remained unchanged [133].

Although efficient, this three-step approach towards block copolymers is time consuming and the real challenge remained to carry out block copolymerization by CMRP only. Therefore, in spite of the poor control reported for the CMRP of styrene, the initiation of this monomer was realized from a PVAc-Co(acac)2 macroinitiator upon thermal treatment (Fig. 26a). As expected, a PVAc-b-PS copolymer with a well-defined PVAc block and an ill-defined PS segment was obtained. Methanolysis of the PVAc block led to an amphiphilic PVOH-b-PS copolymer that was shown to self-assemble into nanocups (bowl-shaped vesicles) in water [139].

Fig. 24. *Synthesis of linear and graft copolymers by CMRP.*
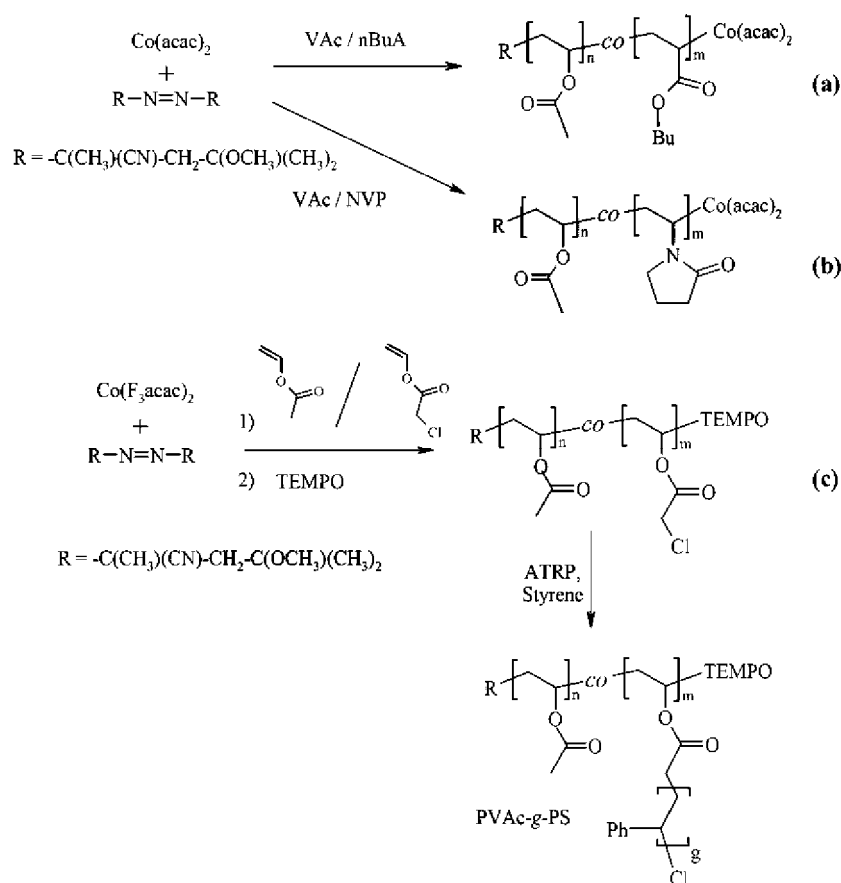
Similarly, the synthesis of PVAc-*b*-polyalkene copolymers was attempted by initiation of ethylene and 1-octene at 30 °C from a well-defined PVAc-Co(acac)2 macroinitiator. However, although the initiation of the polyalkene segment occurred, the monomer conversion was limited to about 15% and the length of this second block was also quite limited (DP~4) due to the low reactivity of these non-activated monomers (Fig. 26b) [140]. Increasing the polymerization temperature to 60 °C did not allow circumventing this problem. Methanolysis of the PVAc block of these products yielded amphiphilic polyvinyl alcohol)-*b*-poly(1-octene). When the copolymerization of vinyl acetate with 1 -octene was initiated by V-70 in the presence of Co(acac)2 or by a poly(vinyl acetate) chain end-capped by Co(acac)2, vinyl acetate was preferentially incorporated, such that a copolymer with a gradient structure was formed.

Fig. 25. *Synthesis of PVAc containing block copolymers by combination of CMRP and ATRP.*
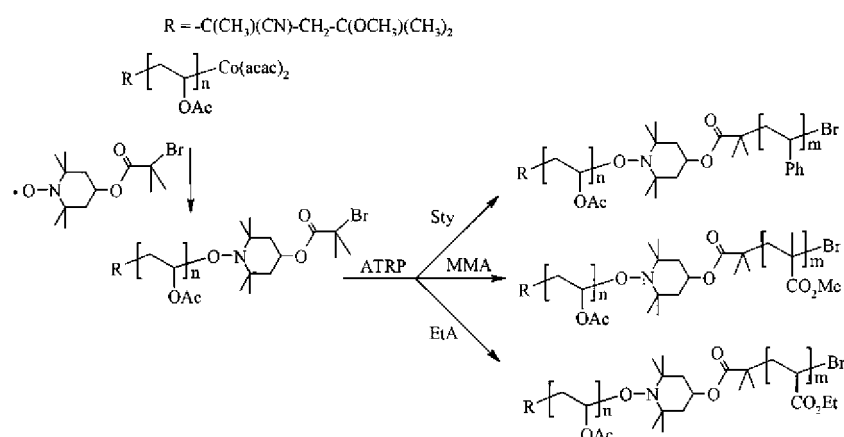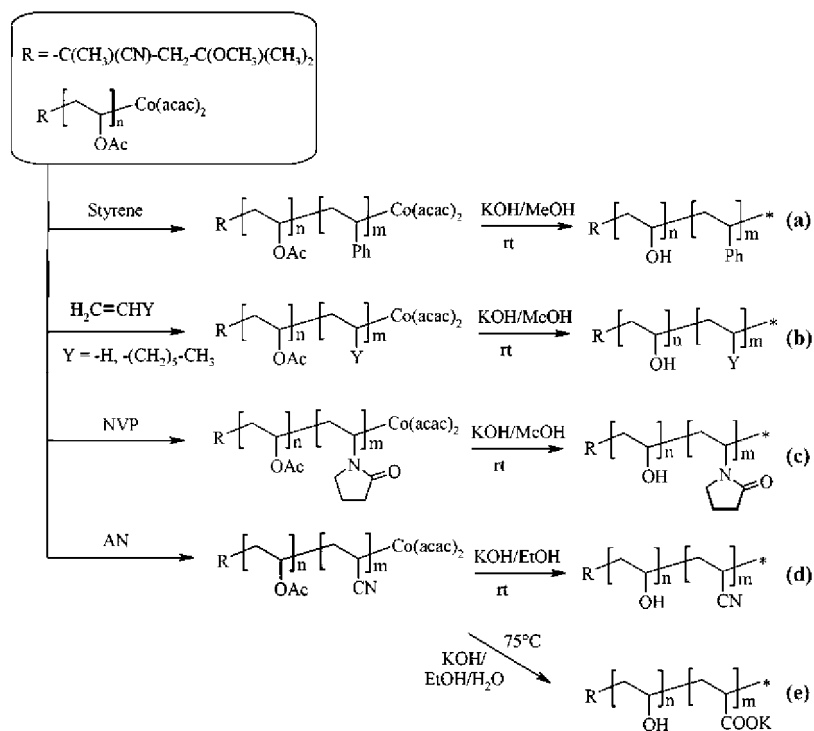

Fig. 26. *Synthesis of PVAc and PVOH containing block copolymers by CMRP.*

The same strategy was also applied to synthesize well-defined PVAc-*b*-PNVP by CMRP (Fig. 26c) [141]. The optimal conditions established for the polymerization of NVP from the Co(acac)$_2$-terminated PVAc were 30 °C in anisole. Under these conditions, all criteria of a CRP process were met and copolymers with a polydispersity around 1.3 were formed. The amphiphilic PVAc-*b*-PNVP copolymers were then easily transformed into the hydrosoluble and potentially biocompatible PVOH-*b*-PNVP block copolymers [141].

Finally, the same approach was applied to the synthesis of PVAc-*b*-PAN block copolymers and the solvent choice turned out to be crucial [142]. Indeed, when carried out at 0°C in anisole, a slow and incomplete initiation of acrylonitrile from the PVAc-Co(acac)$_2$ chains was observed leading to block copolymer contaminated by unreacted PVAc. However, at the same temperature, all the PVAc-Co(acac)2 chains initiated simultaneously the acrylonitrile polymerization when using dimethylformamide as solvent, allowing the formation of well-defined PVAc-b-PAN (M_w/M_n~1.1)(Fig.26d)[142].

The DFT analysis provides a rationalization of this phenomenon. As shown in Fig. 27, the dormant species for the (acac)$_2$Co^{III}-PVAc contains a 6-coordinate complex with a chelated (κ^2:*O,C*) ester function as chain end in a non-coordinating solvent. AN coordination does not provide sufficient stabilization to open this chelate, contrary

to DMF, whereas DMSO provides only weak stabilization. In the absence of solvent, the (acac)2Co-PVAc dormant chain must dissociate to tetrahedral Co(acac)2, which costs 13.1 kcal mol^{-1} in enthalpy, because AN is not a sufficiently strong ligand to coordinate. After conversion of the PVAc radical to a PAN radical by AN addition, subsequent trapping yields the (acac)2Co^{III}-PAN dormant chain, regaining 6.7 kcal mol^{-1}. This dormant chain is not strongly coordinated by AN, since this process is entropically disfavoured as discussed in a previous section. The comparison of the enthalpies involved (13.1 kcal mol^{-1} for the activation of (acac)$_2$Co-PVAc vs. 6.7 kcal mol^{-1} for the reactivation of (acac)$_2$Co-PAN) shows that crossing over from a PVAc block to a PAN block yields slow initiation in a non-coordinating solvent, in agreement with the experimental observation. In DMSO or in DMF, on the other hand, the activation of the (L)(acac)$_2$Co-PVAc dormant chain (yielding in these cases Co(acac)$_2$(L)$_2$) requires an enthalpy only marginally greater than the reactivation of the subsequent (L)(acac)$_2$Co-PAN dormant chain. In DMF, the radical activation equilibrium has an enthalpy of 10.8 kcal mol^{-1} for the Co-capped PVAc vs. 9.2 kcal mol^{-1} for the Co-capped PAN, whereas in DMSO these values are 7.1 and 6.6 kcal mol^{-1}, respectively. Thus, crossing over from a PVAc block to a PAN block is more efficient in the coordinating solvents, particularly DMSO where these two enthalpies are more similar. The main reason for this difference is that coordinating solvents are able to compete with the internal stabilization provided by the chelating ester function for the PVAc dormant species, whereas the PAN dormant chain has no mechanism available for internal stabilization. It can also be observed that the activation is energetically less costly in DMSO, leading to faster polymerization, which agrees with the experimental evidence.

It was also demonstrated that these PVAc-*b*-PAN copolymers are interesting precursors for novel PVOH-containing copolymers, such as hydrosoluble PVOH-*b*-PAA [142] and amphiphilic PVOH-*b*-PAN [143]. The former resulted from hydrolysis of both the ester and the nitrile functions with potassium hydroxide in ethanol/water at 75 °C (Fig. 26e) whereas the latter was obtained by selective hydrolysis of the ester function of the parent PVAc containing copolymer (Fig. 26d). The pH responsiveness of the PVOH-*b*-PAA copolymer was demonstrated by Dynamic Light Scattering pH titration [142]. Finally, controlled pyrolysis of polymeric micelles, made from the self-assembly of PVOH-*b*-PAN block copolymer in water and deposited onto a silicon wafer, led to carbon nanoparticles [143].

Fig. 27. *Energy diagram obtained with the B3PW91* functional for the Co-C homolytic bond cleavage in (acac)$_2$Co-CH(CH3)(OCOCH$_3$) and subsequent trapping of the CH(CN)CH$_3$ radical in the presence of different neutral donors (L=AN, DMF, DMSO). The values shown are relative enthalpies in kcal mol^{-1}.*
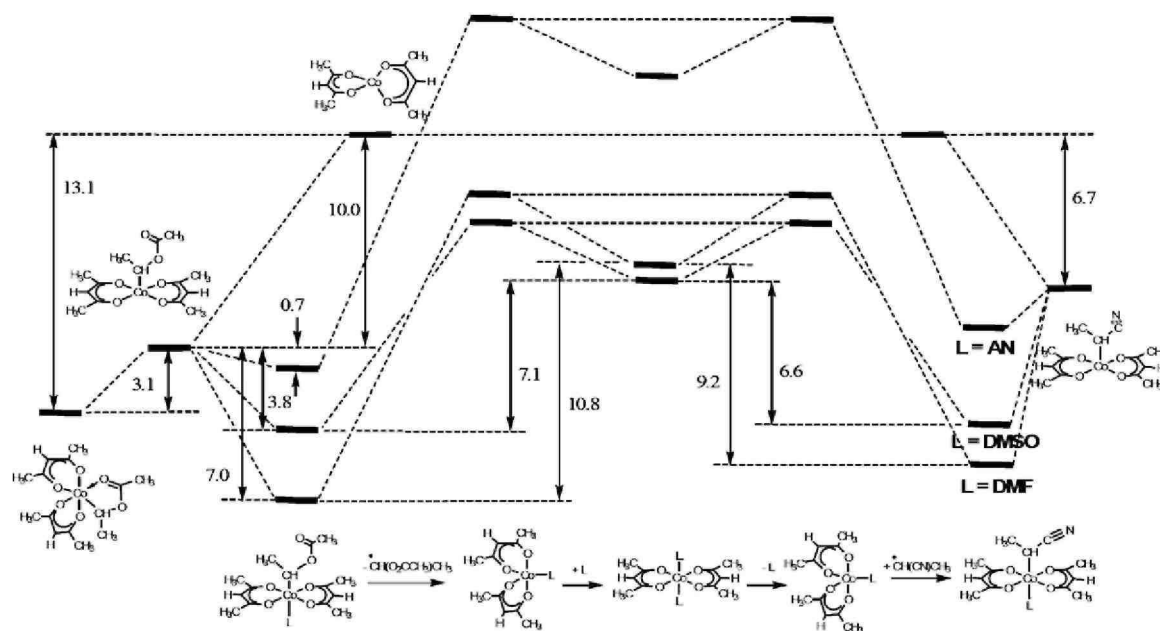
4. CONCLUDING REMARKS AND PERSPECTIVES

Considerable progress has been made in the last decade in the field of controlled radical polymerization (CRP) and the design of well-defined polymer architectures. Among several CRP techniques, cobalt-mediated radical polymerization (CMRP) distinguished itself by its ability to mediate the polymerization of monomers of very different reactivity, such as vinyl acetate and acrylates. This specificity justifies efforts currently devoted to the

improvement of this CRP method and those based on metallic species in general.

This review condenses and comments all the work done in CMRP since its discovery 16 years ago. In summary, it allows a controlled radical polymerization of acrylic esters, acrylic acid, vinyl esters, acrylonitrile and vinylpyrrolidone, leading to the corresponding well-defined polymers with predictable molar masses. One interesting characteristic is the possibility to target high molecular weights (above 200,000 g/mol in some cases) with good control at high conversions. Another striking specificity is the low polymerization temperature, ranging from 60 °C in the case of acrylates mediated by cobalt porphyrins, to 0°C for acrylonitrile in the presence of Co(acac)2.

From the mechanistic point of view, CMRP process has long been considered to occur only by reversible deactivation of the growing chains by the metal, whatever the nature of the cobalt complex and the experimental conditions. More recently, the contribution of the degenerative chain transfer mechanism has been emphasized. Mechanistic studies have also highlighted the crucial role of additives, especially in the case of Co(acac)2. Indeed, addition of Lewis bases, such as water, pyridine, dimethyl-sulfoxide and dimethylformamide, capable of coordinating the cobalt center, deeply modifies the chain activation equilibrium and drives the process towards the reversible termination mechanism.

To date, the main classes of cobalt complexes that have shown activity in CMRP are cobaloximes, cobalt porphyrins and β-diketonato derivatives of cobalt(II). The first two families are particularly efficient mediators for the acrylic esters and acrylic acid polymerizations whereas the last category has so far been found to control the polymerization of vinyl esters, acrylonitrile and vinylpyrrolidone. These observations emphasize that the success of CMRP largely depends on the choice of the monomer/cobalt complex couple.

As it stands today, the field still faces many challenges. First, it is crucial to enlarge the synthetic possibilities of the CMRP and to fine tune both the experimental conditions and the cobalt complex structure in order to control more monomers, such as styrenic derivatives, isoprene, etc. Computational chemistry might be used as a predicting tool in the quest for the adequate cobalt complex/monomer couple or for a controlling agent as universal as possible. This is all the more realistic since DFT calculations have already proved the ability to rationalize experimental observations based on the evaluation of the Co-C bond dissociation enthalpy (BDE) and the relative stabilization ability of several neutral donor molecules for the cobalt(II) "persistent radical". In future endeavours, the kinetic parameters, especially those related to the radical trapping and H-transfer processes, must be investigated and combined to the already available thermodynamic data in order to approach the system as a whole. The future implementation of CMRP to other monomers should considerably enlarge the macromolecular engineering possibilities. The potential to synthesize novel block copolymers and more complex architectures has been highlighted in this review. The main difficulty consists in finding a cobalt complex able to control different co-monomers in order to obtain copolymers with well-defined sequences. A valuable approach, already proven successful for the synthesis of well-defined PVAc-*b*-PAN copolymers, consists of tuning the cobalt reactivity on going from one block to the next one upon introduction of additives with coordinating power. This innovative approach clearly highlights the versatility of CMRP and evidences its potential for accessing new copolymers.

The second challenge consists of bringing the technique closer to industrial standards. As described in this review, a few approaches have already been envisioned. For example, the CMRP has been successfully applied in aqueous dispersed media, such as suspensions and miniemulsions. However, questions relative to the recovery and the recycling of the cobalt complex, used in large amounts in the polymerization, remain pending and need to be addressed. Immobilization of the cobalt complex on an inert support has already been tested with encouraging results. Such an approach certainly deserves further efforts to improve the process efficiency and to preserve the complex activity through multiple recycles.

References

[1] Braunecker WA, Matyjaszewski K. Controlled/living radical polymerization: features, developments, and perspectives. Prog Polym Sci 2007;32:93-146.

[2] Georges MK, Veregin RPN, Kazmaier PM, Hamer GK. Narrow molecular weight resins by a free-radical polymerization process. Macromolecules 1993;26:2987-8.

[3] Hawker CJ, Bosman AW, Harth E. New polymer synthesis by nitroxide mediated living radical polymerizations. Chem Rev 2001;101:3661-88.

[4] Solomon DH. Genesis of the csiro polymer group and the discovery and significance of nitroxide-mediated living radical polymerization. J Polym Sci Part A: Polym Chem 2005:43:5748-64.

[5] Charleux B, Nicolas J. Water-soluble sg1-based alkoxyamines: a breakthrough in controlled/living free-radical polymerization in aqueous dispersed media. Polymer 2007;48:5813-33.

[6] Sciannamea V. Jerome R, Detrembleur C. In-situ nitroxide-mediated radical polymerization (nmp) processes: their understanding and optimization. Chem Rev 2008;108:1104-26.

[7] Matyjaszewski K, Xia J. Atom transfer radical polymerization. Chem Rev 2001;101:2921-90.

[8] Kamigaito M, Ando T, Sawamoto M. Metal-catalyzed living radical polymerization. Chem Rev 2001 ; 101:3689-746.

[9] Tsarevsky NV, Matyjaszewski K. Environmentally benign atom transfer radical polymerization: towards "green" processes and materials. J Polym Sci Part A: Polym Chem 2006;44:5098-112.

[10] Tsarevsky NV, Matyjaszewski K. "Green" atom transfer radical polymerization: from process design to preparation of well-defined environmentally friendly polymeric materials. Chem Rev 2007;107:2270-99.

[11] Lowe AB, McCormick CL. Reversible addition-fragmentation chain transfer (raft) radical polymerization and the synthesis of water-soluble (co)polymers under homogeneous conditions in organic and aqueous media. Prog Polym Sci 2007;32:283-351.

[12] Perrier S, Takolpuckdee P. Macromolecular design via reversible addition-fragmentation chain transfer (raft)/xanthates (madix) polymerization. J Polym Sci Part A: Polym Chem 2005;43:5347-93.

[13] Favier A, Charreyre M-T. Experimental requirements for an efficient control of free-radical polymerizations via the reversible addition-fragmentation chain transfer (raft) process. Macromol Rapid Commun 2006;27:653-92.

[14] Barner-Kowollik C, editor. Handbook of RAFT polymerization. Wiley VCH; 2008.

[15] Wayland BB, Poszmik G, Mukerjee SL, Fryd M. Living radical polymerization of acrylates by organocobalt porphyrin complexes. J Am ChemSoc 1994;116:7943-4.

[16] Arvanitopoulos LD, Greuel MP, Harwood HJ. "Living" free radical polymerization using alkyl cobaloximes as photoinitiators. Polym Prep (Am Chem Soc Div Polym Chem) 1994;35(2):549-50.

[17] Debuigne A, Caille J-R, Jerome R. Highly efficient cobalt-mediated radical polymerization of vinyl acetate. Angew Chem Int Ed 2005;44:1101-4.

[18] LutzJ-F, Lacroix-Desmazes P, Boutevin B, Le Mercier C, Gigmes D, Bertin D, et al. Comparative study of a series of nitroxides and alkoxyamines in controlled/"living" radical polymerization. Polym Prepr (Am Chem Soc Div Polym Chem) 2002;43(2):287-8.

[19] Wakioka M, Baek K-Y, AndoT, Kamigaito M,Sawamoto M. Possibility of living radical polymerization of vinyl acetate catalyzed by iron(I) complex. Macromolecules 2002;35:330-3.

[20] Iovu MC, Matyjaszewski K. Controlled/living radical polymerization of vinyl acetate by degenerative transfer with alkyl iodides. Macromolecules 2003;36:9346-54.

[21] Rizzardo E, Chiefari J, Mayadunne RTA, Moad G, Thang SH. Synthesis of defined polymers by reversible addition-fragmentation chain transfer: the raft process. In: Matyjaszewski K, editor. Controlled/living radical polymerization. ACS Symp Ser, vol. 768. Washington, DC: Am Chem Soc; 2000. p. 278-96.

[22] Charmot D, Corpart P, Adam H, Zard SZ, Biadatti T, Bouhadir G. Controlled radical polymerization in dispersed media. Macromol Symp 2000;150:23-32.

[23] Stenzel MH, Cummins L, Roberts GE, Davis TP, Vana P, Barner-Kowollik C. Xanthate mediated living polymerization of vinyl acetate: a systematic variation in madix/raft agent structure. Macromol Chem Phys 2003;204:1160-8.

[24] Stenzel MH, Davis TP, Barner-Kowollik C. Poly(vinyl alcohol) star polymers prepared via madix/raft polymerization. Chem Commun 2004:1546-7.

[25] Favier A, Barner-Kowollik C, Davis TP, Stenzel MH. A detailed on-line ft/nir and 1H nmr spectroscopic investigation into factors causing inhibition in xanthate-mediated vinyl acetate polymerization. Macromol Chem Phys 2004;205:925-36.

[26] Theis A, Davis TP, Stenzel MH, Barner-Kowollik C. Probing the reaction kinetics of vinyl acetate free radical polymerization via living free radical polymerization (madix). Polymer 2006;47:999-1010.

[27] Simms RW, Davis TP, Cunningham MF. Xanthate-mediated living radical polymerization of vinyl acetate in miniemulsion. Macromol Rapid Commun 2005;26:592-6.

[28] Bernard J, Favier A, Zhang L, Nilasaroya A, Davis TP, Barner-Kowollik C, et al. Poly(vinyl ester) star polymers viaxanthate-mediated living radical polymerization: from poly(vinyl alcohol) to glycopolymer stars. Macromolecules 2005;38:5475-84.

[29] Destarac M, Charmot D, Zard S, Gauthier-Gilaizeau I. Synthesis method for polymers by controlled radical polymerisation with

xanthates. WO 0142312, assigned to Rhone Poulenc chimie Fr; 2001.

[30] Rizzardo E, Chiefari J, Mayadunne R, Moad G, Thang S. Tailored polymer architectures by reversible addition-fragmentation chain transfer. Macromol Symp 2001;174:209-12.

[31] Kwak Y, Goto A, Fukuda T, Kobayashi Y, Yamago S. A systematic study on activation processes in organotellurium-mediated living radical polymerizations of styrene, methyl methacrylate, methyl acrylate, and vinyl acetate. Macromolecules 2006;39:4671-9.

[32] Yamago S, Ray B, Iida K, Yoshida J, Tada T, Yoshizawa K, et al. Highly versatile organostibine mediators for living radical polymerization. J Am Chem Soc 2004; 126:13908-9.

[33] Poli R. Relationship between one-electron transition-metal reactivity and radical polymerization processes. Angew Chem Int Ed 2006;45:5058-70.

[34] Schrauzer GN, Sibert JW, Windgassen RJ. Photochemical and thermal cobalt-carbon bond cleavage in alkylcobalamins and related organometallic compounds. Comparative study. J Am Chem Soc 1968;90:6681-8.

[35] Halpern J, Ng FIT, Rempel GL. Metal-alkyl bond dissociation energies in organocobalt compounds related to vitamin bl2 coenzymes. J Am Chem Soc 1979;101:7124-6.

[36] Halpern J. Determination and significance of transition metal-alkyl bond dissociation energies. Ace Chem Res 1982;15:238-44.

[37] Tsou TT, Loots M, Halpern J. Kinetic determination of transition metal-alkyl bond dissociation energies: application to organocobalt compounds related to Bl2 coenzymes. J Am Chem Soc 1982;104:623-4.

[38] Flora TTN, Rempel GL. Ligand effects on transition metal-alkyl bond dissociation energies. J Am Chem Soc 1982;104:621-3.

[39] Halpern J. Mechanisms of coenzyme bl2-dependent rearrangements. Science 1985;227:869-75.

[40] Hay BP, Finke RG. Thermolysis of the cobalt-carbon bond of adenosylcobalamin. 2. Products, kinetics, and cobalt-carbon bond dissociation energy in aqueous solution. J Am Chem Soc 1986;108:4820-9.

[41] Fischer H. Unusual selectivities of radical reactions by internal suppression of fast modes. J Am Chem Soc 1986;108:3925-7.

[42] Fischer H. The persistent radical effect: a principle for selective radical reactions and living radical polymerizations. Chem Rev 2001;101:3581-610.

[43] Kräutler B. Acetylcobalamin from photoinduced carbonylation of methylcobalamin. Helv Chim Acta 1984;67:1053-9.

[44] Daikh BE, Finke RG. 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;114:2938-43.

[45] Studer A. The persistent radical effect in organic synthesis. Chem Eur J 2001;7:1159-64.

[46] Pattenden G. Cobalt-mediated radical reactions in organic synthesis. Chem Soc Rev 1988;17:361-82.

[47] Iqbal J, Bhatia B, Nayyar NK. Transition metal-promoted free-radical reactions in organic synthesis: the formation of carbon-carbon bonds. Chem Rev 1994;94:519-64.

[48] Ghosez A, Goebel T, Giese B. Syntheses and reactions of glycosyl-cobaloximes. Chem Ber 1988;121:1807-11.

[49] Branchaud BP, Meier MS, 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;29:167-70.

[50] Branchaud BP, Choi YL. Effect of a remote ligand substituent on premature b-hydrogen elimination in a cobaloxime-mediated radical alkyl-alkenyl cross coupling. Tetrahedron Lett 1988;29:6037-8.

[51] Coveney DJ, Patel VF, Pattenden G. Acylcobalt salophen reagents. Precursors to acyl radical intermediates for inter- and intramolecular oxidative Michael addition reactions. Tetrahedron Lett 1987;28:5949-52.

[52[Davis TP, Kukulj D, Haddleton DM, Maloney DR. Cobalt-mediated free-radical polymerization of acrylic monomers. Trends Polym Sci 1995;3:365-73.

[53] Gridnev A. The 25th anniversary of catalytic chain transfer. J Polym Sci Part A: Polym Chem 2000;38:1753-66.

[54] Gridnev AA, Ittel SD. Catalytic chain transfer in free-radical polymerizations. Chem Rev 2001; 101:3611-59.

[55] Melby LR, Janowicz AH, Ittel SD. Cobalt(II) chelates as chain transfer agents in free radical polymerizations. USA: EP196783, assigned to Du Pont de Nemours, E. I., and Co.; 1986.

[56] Moad G, Rizzardo E, Moad CL, Ittel SD, Wilczek L, Gridnev AA. Catalytic polymerization process and the resulting polymers with terminal unsaturation. USA: WO 9731030, assigned to E. I. Du Pont de Nemours & Co.; Commonwealth Scientific & Industrial Research Organization; 1997.

[57] Suddaby KG, Sanayei RA, Rudin A, O'driscoll KF. Catalytic chain transfer in polymerization of methyl methacrylate. Continuous synthesis and purification of macromer. J Appl Polym Sci 1991 ;43: 1565-75.

[58] Chiefari J, Jeffery J, Mayadunne RTA, Moad G, Rizzardo E, Thang SH. Chain transfer to polymer: a convenient route to macromonomers. Macromolecules 1999;32:7700-2.

[59] Chiu TYJ, Heuts JPA, Davis TP, Stenzel MH, Barner-Kowollik C. Synthesis of macromonomers via catalytic chain transfer (cet) polymerization and their characterization via nmr spectroscopy and electrospray ionization mass spectrometry (ESI-MS). Macromol Chem Phys 2004;205:752-61.

[60] Boutevin B, David G, Boyer C. Telechelic oligomers and macromonomers by radical techniques. Adv Polym Sci 2007;206: 31-135.

[61] Cacioli P, Hawthorne DG, Laslett RL, Rizzardo E, Solomon DH. Copolymerization of w-unsaturated oligo(methyl methacrylate): new macromonomers. J Macromol Sci Part A: Pure Appl Chem 1986;23:839-52.

[62] Muratore LM, Steinhoff K, Davis TP. Self-reinforcing hydrogels comprised of hydrophobic methyl methacrylate macromers copoly-merized with either n-vinyl-2-pyrrolidone or 2-hydroxyethyl acrylate. J Mater Chem 1999;9:1687-91.

[63] Greuel MP. Free radical polymerizations modified by cobalt compounds. Ph.D. dissertation. University of Akron; 1992.

[64] Arvanitopoulos LD, King BM, Huang C-Y, Harwood HJ. Radical polymerizations and copolymerizations mediated by organocobalt compounds. Polym Prepr (Am Chem Soc Div Polym Chem) 1997;38(l):752-3.

[65[Arvanitopoulos LD, Greuel MP, King BM, Shim AK, Harwood HJ. Photochemical polymerizations initiated and mediated by soluble organocobalt compounds. In: Matyjaszewski K, editor. Controlled radical polymerization. ACS Symp Ser, vol. 685. Washington, DC: Am Chem Soc; 1998. p. 316-31.

[66] Greuel MP, Arvanitopoulos LD, Harwood HJ. Cobaloxime photoini-tiators for free radical polymerization. USA: US 5468785, assigned to University of Akron; 1995.

[67] Harwood HJ, Shim AK Polymers and copolymers prepared or modified by using cobalt complexes. USA: WO 0050467, assigned to University of Akron; 2000.

[68] Shim AK, Harwood HJ. The effect of solvent on the course of acrylate polymerizations mediated by cobaloxime and the development of novel initiating systems and novel multifunctional macromonomers. Polym Prepr (Am Chem Soc Div Polym Chem) 1999;40(2): 132-3.

[69] Espenson JH, Mcdowell MS. Reactions of bis(dimethylgly-oximato)cobalt(II) complexes with polyhalomethane. Organo-metallics 1982;1:1514-8.

[70] Kijima M, Yamashita H, Sato T. Reactions of alkylcobaloximes with oxygen under irradiation. Oxygenative conversions of the alkyl ligand. J Organomet Chem 1994;474:177-82.

[71] Greuel MP, Harwood HJ. Copolymerization with catalytic chain transfer. Polym Prepr(Am Chem Soc Div Polym Chem) 1991;32(1): 545-6.

[72] Enikolopyan NS, Smirnov BR, Ponomarev GV, Belgovskii IM. Catalyzed chain transfer to monomer in free radical polymerization. J

Polym Sci Polym Chem 1981;19:879-89.

[73[Wayland BB, Mukerjee S, Poszmik G, Woska DC, Basickes L, Gridnev aA, et al. Control of radical polymerizations by metalloradicals. In: Matyjaszewski K, editor. Controlled radical polymerization. ACS Symp Ser, vol. 685. Washington, DC: Am Chem Soc; 1998. p. 305-15.

[74] Li Y, Wayland BB. Macromonomer chain growth in the radical polymerization of MMA by cobalt(II) catalyzed chain transfer. Macromol Rapid Commun 2003;24:307-10.

[75] Wayland BB, Basickes L, Mukerjee S, Wei M, Fryd M. Living radical polymerization of acrylates initiated and controlled by organocobalt porphyrin complexes. Macromolecules 1997;30: 8109-12.

[76] Wei M, Wayland BB, Fryd M. Quasi-living radical polymerization of acrylates by an organocobalt porphyrin complex at room temperature. Polym Prepr (Am Chem Soc Div Polym Chem) 1997;38(1): 681-2.

[77] Lu Z, Fryd M, Wayland BB. New life for living radical polymerization mediated by cobalt(II) metalloradicals. Macromolecules 2004;37: 2686-7.

[78] Gridnev AA, Ittel SD, Fryd M, Wayland BB. Formation of organocobalt porphyrin complexes by reactions of cobalt(ii) porphyrins with azoisobutyronitrile and organic substrates. J Chem Soc Chem Commun 1993:1010-1.

[79] Gridnev AA, Ittel SD, Fryd M, Wayland BB. 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;12:4871-80.

[80] Wayland BB, 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;39:8219-22.

[81] Goto A, Kwak Y, Fukuda T, Yamago S, Iida K, Nakajima M, et al. Mechanism-based invention of high-speed living radical polymerization using organotellurium compounds and azo-initiators. J Am Chem Soc 2003:125:8720-1.

[82] Asandei AD, Moran IW. TiCp2Cl-catalyzed living radical polymerization of styrene initiated by oxirane radical ring opening. J Am Chem Soc 2004:126:15932-3.

[83] Asandei AD, Moran IW, Saha G, Chen Y. Titanium-mediated living radical styrene polymerizations. V. Cp2TiCl-catalyzed initiation by epoxide radical ring opening: effect of solvents and additives. J Polym Sci Part A: Polym Chem 2006:44:2015-26.

[84] Mueller AHE, Yan D, Litvinenko G, Zhuang R, Dong H. Kinetic analysis of "living" polymerization processes exhibiting slow equilibria. 2. Molecular weight distribution for degenerative transfer (direct activity exchange between active and "dormant" species) at constant monomer concentration. Macromolecules 1995:28: 7335-8.

[85] Fu X, Wayland BB, Fryd M. Controlled/living radical polymerization mediated by organocobalt complexes through a degenerative transfer/radical interchange polymerization (rip) process. Polym Prepr (Am Chem Soc Div Polym Chem) 2005:46(2):190.

[86] Lu Z, Li Y, Wayland BB. Cobalt porphyrin controlled living radical polymerization of acrylic acid in water. Polym Prepr (Am Chem Soc Div Polym Chem) 2004:45(1):1053.

[87] Peng C-H, Fryd M, Wayland BB. Organocobalt mediated radical polymerization of acrylic acid in water. Macromolecules 2007:40:6814-9.

[88] Li Y, Wayland BB. Macromonomer living character in the cobalt(II) porphyrin chain transfer catalysis for radical polymerization of methacrylic acid in water. Chem Commun 2003:1594-5.

[89] Caille J-R, Debuigne A, Jerome R. Quinone transfer radical polymerization (qtrp) of styrene: catalysis by different metal complexes. J Polym Sci Part A: Polym Chem 2005:43:2723-33.

[90] Debuigne A, Caille J-R, Jerome R. Quinone transfer radical polymerization of styrene catalyzed by metal complexes in the presence of various o-quinones. Macromolecules 2005:38:6310-5.

[91] Debuigne A, Caille J-R, Jerome R. Quinone transfer radical polymerization of styrene: synthesis of the actual initiator. J Polym Sci Part A: Polym Chem 2006:44:1233-44.

[92] Caille J-R, Debuigne A, Jerome R. Controlled radical polymerization of styrene by quinone transfer radical polymerization (QTRP). Macromolecules 2005:38:27-32.

[93] Debuigne A. From quinone transfer radical polymerization (QTRP) of styrene to cobalt-mediated radical polymerization (CMRP) of vinyl acetate. Ph.D. thesis dissertation. University of Liège: 2004.

[94] 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 2007:13:2480-92.

[95] Kaneyoshi H, Matyjaszewski It Effect of ligand and n-butyl acrylate on cobalt-mediated radical polymerization of vinyl acetate. Macromolecules 2005:38:8163-9.

[96] Walker FA. Electron spin resonance study of coordination to the fifth and sixth positions of alpha, beta, gamma, delta-tetra(p-methoxyphenyl)porphinatocobalt(II). J Am Chem Soc 1970:92:4235-44.

[97] Cotton FA, Soderberg RH. A spectroscopic study of the polymeric nature of bis(acetyl-acetonato)cobalt(II). Inorg Chem 1964:3:1-5.

[98] Debuigne A, Detrembleur C, Bryaskova R, Caille J-R, Jerome R. Cobalt-mediated radical polymerization of vinyl acetate: a new tool for macromolecular engineering. In: Matyjaszewski K, editor. Controlled/living radical polymerization. ACS Symp Ser, vol. 944. Washington, DC: Am Chem Soc: 2006. p. 372-86.

[99] Debuigne A, Champouret Y, 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 2008:14:4046-59.

[100] Baisch U, Poli R. Copper (I/II) and cobalt (II) coordination chemistry of relevance to controlled radical polymerization processes. Polyhedron 2008:27:2175-85.

[101] Wayland BB, Fu X, Peng C-H, Lu Z, Fryd M. Living radical polymerizations mediated by metallo-radical and organo-transition metal complexes. In: Matyjaszewski K, editor. Controlled/living radical polymerization. ACS Symp Ser, vol. 944. Washington, DC: Am Chem Soc: 2006. p. 358-71.

[102] Peng C-H, Scricco J, Li S, Fryd M, Wayland BB. Organocobalt mediated living radical polymerization of vinyl acetate. Macromolecules 2008:41:2368-73.

[103] Li S, De Bruin B, Peng C-H, Fryd M, Wayland BB. Exchange of organic radicals with organocobalt complexes formed in the living radical polymerization of vinyl acetate. J Am Chem Soc 2008:130:13373-81.

[104] 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 2008:14:7623-37.

[105] Bernhauer K, Mueller O, Wagner F. New chemical and biochemical developments. The vitamin bl2 held. Angew Chem Int Ed 1964:3:200-11.

[106] Schrauzer GN, Windgassen RJ. Alkylcobaloximes and their relation to alkylcobalamins. J Am Chem Soc 1966:88:3738-43.

[107] Dolphin D, Halko DJ, Jonhson E. Reversible cobalt-nitrogen alkyl and acyl group migration in cobalt porphyrins. Inorg Chem 1981:20:4348-51.

[108] Marzilli LG, Summers MF, Bresciani-Pahor N, Zangrando E, Charland JP, Randaccio L. Rare examples of structurally characterized five-coordinate organocobalt complexes. Novel dynamic nmr evidence for synergistic enhancement of cis and trans effects in bl2 models. J Am Chem Soc 1985:107:6880-8.

[109] Dölker N, Maseras F, Lledos A. A density functional study on the effect of the trans axial ligand of cobalamin on the homolytic cleavage of the Co-C bond. J Phys Chem B 2001:105:7564-71.

[110] Jensen KP, Ryde U. The axial n-base has minor influence on Co-C bond cleavage in cobalamins. J Mol Struct Theochem 2002:585:239-55.

[111] Jensen KP, Ryde U. Theoretical prediction of the Co-C bond strength in cobalamins. J Phys Chem A 2003:107:7539-45.

[112] Dölker N, Morreale A, Maseras F. Computational study on the difference between the Co-C bond dissociation energy in methylcobalamin and adenosylcobalamin. J Biol Inorg Chem 2005:10:509-17.

[113] Jensen KP, Ryde U How the Co-C bond is cleaved in coenzyme bl2 enzymes: a theoretical study. J Am Chem Soc 2005:127:9117-28.

[114] Salomon O, Reiher M, Hess BA. Assertion and validation of the performance of the b31yp* functional for the first transition metal row and the g2 test set. J Chem Phys 2002:117:4729-37.

[115] Harvey JN, Aschi M. Modelling spin-forbidden reactions: recombination of carbon monoxide with irontetracarbonyl. Faraday Discuss 2003:124:129-43.

[116] Conradie J, Ghosh A. Electronic structure of trigonal-planar transition-metal-imido complexes: spin-state energetics, spin-density profiles, and the remarkable performance of the olyp functional. J Chem Theory Comput 2007:3:689-702.

[117] Wasbotten IH, Ghosh A. Spin-state energetics and spin-crossover behavior of pseudotetrahedral cobalt(III)-imido complexes. The role of the tripodal supporting ligand. Inorg Chem 2007:46:7890-8.

[118] Ng FTT, Rempel GL, Halpern J. Steric influences on cobalt-alkyl bond dissociation energies. Inorg Chim Acta 1983:77:L165-6.

[119] Harvey JN, Aschi M.Schwarz H, Koch W.The singlet and triplet states of phenyl cation. A hybrid approach for locating minimum energy crossing points between non-interacting potential energy surfaces. TheorChem Acc 1998:99:95-9.

[120] Harvey JN, Poli R, Smith KM. Understanding the reactivity of transition metal complexes involving multiple spin states. Coord Chem Rev 2003:238-239:347-61.

[121] Debuigne A, Caille J-R, Detrembleur C, Jerome R. Effective cobalt mediation of the radical polymerization of vinyl acetate in suspension. Angew Chem Int Ed 2005:44:3439-42.

[122] Detrembleur C, Debuigne A, Bryaskova R, Charleux B, Jerome 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.

[123] 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;39:8263-8.

[124] Debuigne A, Caille J-R, Jerome R. Synthesis of end-functional poly(vinyl acetate) by cobalt-mediated radical polymerization. Macromolecules 2005;38:5452-8.

[125] Sciannamea V, Debuigne A, Piette Y, Jerome R, Detrembleur C. Supported cobalt mediated radical polymerization (SCMRP) of vinyl acetate and recycling of the cobalt complex. Chem Commun 2006:4180-2.

[126] Matyjaszewski K, editor. Controlled radical polymerization. ACS Symp Ser, vol. 685. Washington, DC: Am Chem Soc; 1998.

[127] Matyjaszewski K, editor. Controlled/living radical polymerization. ACS Symp Ser, vol. 768. Washington, DC: Am Chem Soc; 2000.

[128] Matyjaszewski K, editor. Advances in controlled/living radical polymerization. ACS Symp Ser, vol. 854. Washington, DC: Am Chem Soc; 2002.

[129] Matyjaszewski K, editor. Controlled/living radical polymerization. ACS Symp Ser, vol. 944. Washington, DC: Am Chem Soc; 2006.

[130] McAllister RM, Weber JH. Preparation and reactions of alkyl-cobalt complexes containing schiff base ligands. J Organomet Chem 1974;77:91-105.

[131] Dodd D, Johnson MD. Organic compounds of cobalt(III). J Organomet Chem 1973;52:1-232.

[132] Kemmitt RDW, Russell DR. In: Wilkinson G, Stone FGA, Abel EW, editors. Comprehensive organometallic chemistry, vol. 5. Oxford: Pergamon Press; 1982. p. 1-276.

[133] Debuigne A, Caille J-R, Willet N, Jerome R. Synthesis of poly(vinyl acetate) and poly(vinyl alcohol) containing block copolymers by combination of cobalt-mediated radical polymerization and ATRP. Macromolecules 2005;38:9488-96.

[134] Ciriano MV, Korth H-G, Van Scheppingen WB, Mulder P. Thermal stability of 2,2,6,6-tetramethylpiperidine-l-oxyl (tempo) and related n-alkoxyamines. J Am Chem Soc 1999;121:6375-81.

[135] Detrembleur C, Stoilova O, Bryaskova R, Debuigne A, Mouithys-Mickalad A, Jerome R. Preparation of well-defined pvoh/c60 nanohybrids by cobalt-mediated radical polymerization of vinyl acetate. Macromol Rapid Commun 2006;27:498-504.

[136] Hurtgen M. Synthesis of poly(vinyl alcohol) and poly(n-vinyl pyrrolidone) containing nanohybrids c60 as photodynamic cancer therapy agents. Masters dissertation. University of Liège; 2007.

[137] Kaneyoshi H, Matyjaszewski K. Radical (co)polymerization of vinyl chloroacetate and n-vinylpyrrolidone mediated by bis(acetylacetonate)cobalt derivatives. Macromolecules 2006;39: 2757-63.

[138] Kaneyoshi H, Matyjaszewski It Synthesis of poly(vinyl acetate)-graft-polystyrene by a combination of cobalt-mediated radical polymerization and atom transfer radical polymerization. J Polym Sci Part A: Polym Chem 2007;45:447-59.

[139] Bryaskova R, Willet N, Debuigne A, Jerome 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 2007;45: 81-9.

[140] Bryaskova R, Willet N, Degee P, Dubois P, Jerome 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;45:2532-42.

[141] 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;40:7111-8.

[142] Debuigne A, Warnant J, Jerome R, Voets I, De Keizer A, Cohen Stuart MA, et al. Synthesis of novel well-defined poly(vinyl acetate)-b-poly(acrylonitrile) and derivatized water-soluble poly(vinyl alcohol)-b-poly(acrylic acid) block copolymers by cobalt-mediated radical polymerization. Macromolecules 2008;41:2353-60.

[143] Warnant J. Preparation of poly(vinyl acetate)-b-poly(acrylonitrile) block copolymers by controlled radical polymerization. Master dissertation. University of Liège; 2007.