Metal Complexes Catalyzed Cyclization with CO_2

Jeroen Rintjema, Leticia Peña Carrodeguas, Victor Laserna, Sergio Sopeña, and Arjan W. Kleij

Abstract This chapter describes in general terms the catalytic methodology that has been made available for the use of carbon dioxide (CO_2) in cyclization reactions that incorporate an intact CO_2 fragment without changing the formal oxidation state of the carbon center. The major focus of this chapter will be on the most successful organometallic/inorganic complexes that have been used as catalyst systems throughout the last decade and the preferred ligand frameworks leading to elevated reactivity and/or selectivity behavior in CO_2 coupling reactions. Attention will be especially given to homogeneous catalyst systems as they have proven to be more versatile in CO_2 conversion catalysis and often have modular characteristics that allow for optimization of structure–activity relationships. The most important reactions that have been studied in the current context are designated CO_2 "addition" reactions to small molecule heterocycles such as epoxides and aziridines, though more recently other coupling partners such as diamines, dialcohols, and amino nitriles have further advanced the use of CO_2 in organic synthesis providing access to a wider range of structures. This chapter will serve to demonstrate the utility of CO_2 as a carbon reagent in the catalytic formation of the most prominent organic structures using cyclization strategies specifically.

Keywords Addition reactions · Carbon dioxide · Coupling reactions · Homogeneous catalysis · Organic synthesis

Contents

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1   Introduction

Carbon dioxide (CO$_2$) has recently emerged as an attractive carbon reagent that may partially substitute fossil fuels in synthetic strategies toward a wide range of organic structures [1–3]. It represents a cheap and abundant carbon building block, but its kinetic stability is a challenge that can only be addressed by devising efficient catalytic processes and ditto catalyst systems [4, 5]. Therefore, a lot of focus in the scientific communities has been on the design of suitable catalyst systems than can potentially combine modular features, high reactivity and selectivity, and amplified substrate scope that would serve to increase the synthetic application of CO$_2$ as a building block [6, 7]. The most widely studied reactions include the formation of polycarbonate polymers [8], the formation of carboxylated scaffolds [9], and the coupling between epoxides/oxetanes/aziridines [10–12] leading to various heterocyclic structures with synthetic, pharmaceutical, or solvent-derived application potential.

The latter category of organic molecules is particularly interesting for a number of reasons. Cyclic carbonates, derived from epoxide/CO$_2$ couplings, are organic compounds that possess very interesting properties such as low evaporation rates, low toxicity, and biodegradability [13]. These properties make them useful for industrial or scientific applications such as aprotic high-boiling polar solvents, electrolytes for lithium-ion batteries, precursors for polymeric materials, fine chemical intermediates, fuel additives, plastic materials, and agricultural chemicals [14, 15]. One of the most important examples in this respect is propylene carbonate which is produced at an industrial level. Apart from their industrial applications, cyclic carbonate structures also appear in various natural compounds present in fungi, bacteria, and/or plants. Some examples of such cyclic carbonate-containing natural products include Hololeucin and Cytosporin E [16] which are shown in Fig. 1.

In industry, cyclic carbonates are mostly obtained by environmentally hazardous methodologies which involve the use of phosgene. Although phosgene is a versatile reagent widely used in the production of plastics and pesticides, it is also a toxic, corrosive, and difficult to handle gas. Exposure to phosgene may have adverse consequences to health, and therefore its use is not desirable. For these reasons, its application in industrial large-scale synthesis should be avoided, and a lot of effort has been put into finding suitable alternatives. In the last decades, greener routes for the synthesis of cyclic carbonates such as those based on the use of carbon dioxide have generated great interest. This chemistry has also been amplified to similar
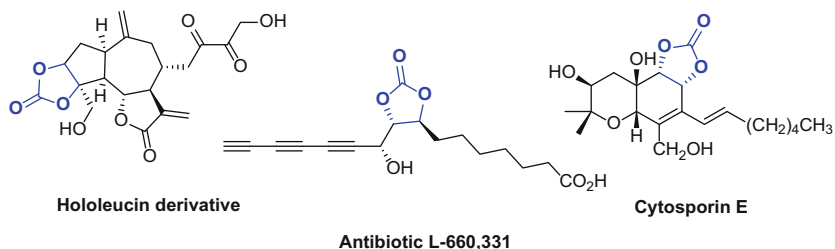
Fig. 1 Some examples of cyclic carbonate-containing natural compounds found in plants, fungi, and bacteria. Note that the carbonate unit is highlighted in *blue*

types of coupling reactions that involve aziridines and oxetanes. In general, the development of low-toxic, cost-effective, and highly active catalytic systems has been a major milestone providing attractive solutions for the chemical fixation of CO_2 producing organic matter with an increased value.

With the rise of green chemistry, the number of environmentally more friendly processes toward CO_2-based heterocyclic structures and alike has been increasing at a rapid pace. Some of these new greener processes involve the use of ionic liquids [17], organocatalysts [18–23], supercritical CO_2 [24, 25], or metal-based photocatalysts [26, 27] although the most commonly used catalysis methodology for the synthesis of these compounds is the metal-catalyzed "cycloaddition" of carbon dioxide to small heterocyclic substrates better referred to as CO_2/substrate couplings. The use of ring-strained substrates thermodynamically favors the formation of the heterocyclic compounds. When using oxiranes (epoxides) as substrates, five-membered cyclic carbonates are obtained, and in a similar way six-membered cyclic carbonates are derived from oxetanes (Scheme 1). The conversion of oxetanes into six-membered carbonates has been much less studied probably due to their lower intrinsic reactivity and more limited accessibility compared to oxiranes. In the conversion of epoxides, the cyclic carbonates are the thermodynamic products with possible competitive formation of polycarbonates, which are the kinetic products. The selectivity toward polycarbonates or cyclic carbonates generally depends on the catalyst, additives, temperature, pressure, and epoxide concentration [28].

During the last 30 years, the homogeneously catalyzed formation of cyclic carbonates through CO_2 addition chemistry has been a thoroughly investigated topic, and many catalytic systems have appeared that address different process features such as chemo-selectivity, enantioselectivity, sustainability, reactivity, and substrate scope. In the next sections, a detailed description of these classes of catalyst systems will be given together with their specifics. As such, a comprehensive overview of the literature is avoided, as the intention is to showcase the most important developments in this area of CO_2 catalysis.
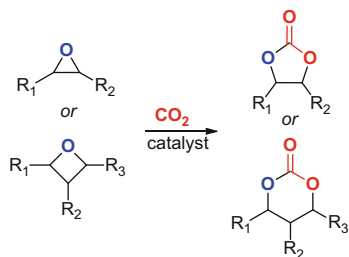
Scheme 1 Cyclic carbonate synthesis from oxiranes and oxetanes

2 Binary Type Catalysts

Undoubtedly, the most popular catalyst type in the context of CO_2 addition catalysis is the binary catalyst system. These systems usually consist of a metal complex acting as an (Lewis acid) activator in the presence of amines or ammonium/phosphonium halides as nucleophilic cocatalysts. It is known that metal complex catalysts combining both a Lewis acidic and basic function effectively couple carbon dioxide and epoxides to afford cyclic carbonates [29]. In 2002, Caló and coworkers [30] reported on the cyclic carbonate synthesis from carbon dioxide and oxiranes using tetrabutylammonium halides as solvents and/or catalysts under atmospheric pressure of CO_2. Alternatively, Lau and coworkers [23] reported on the coupling of carbon dioxide and oxiranes catalyzed by bis(triphenylphosphine) iminium (PPN) salts to yield cyclic carbonates. These two contributions can be considered as milestones in the field, as these PPN and tetrabutylammonium salts are the most employed salts as cocatalysts. However, the use of metal complexes as substrate activators has resulted in far better catalyst systems enabling significantly higher reactivities and selectivities.

Important advances in this area have been obtained by using complexes based on transition/main group metals such as aluminum, cobalt, or iron with ligand frameworks such as porphyrins [26], phthalocyanines [31–33], triphenolates [34], and salens (Fig. 2) [35–40]. Metalloporphyrinates and metallophthalocyanines are compounds that have been typically used as dyes, functional materials, and oxidation catalysts. These metal complexes possess high activity towards the coupling reaction between carbon dioxide and oxiranes allowing the formation of linear or cyclic carbonates and polycarbonates in high yields. However, typically high reaction temperatures are required for efficient catalytic turnover making the systems of lesser value from a sustainability point of view (Scheme 2).

Metal–salen complexes are the most versatile and popular catalysts applied in the reactions between carbon dioxide and oxiranes [6]. One of the reasons for their popularity is the ease of synthesis in comparison with porphyrins and the fact that the condensation of the diamine and the aldehyde precursors allows for a straightforward modulation of the steric and electronic properties of the metal catalyst [41]. The large number of possible structural combinations has enabled the development of a extensive number of catalysts based on salphens, binaphthyl-derived salens, and bimetallic salen complexes (Fig. 3), among others. These metal complexes require,
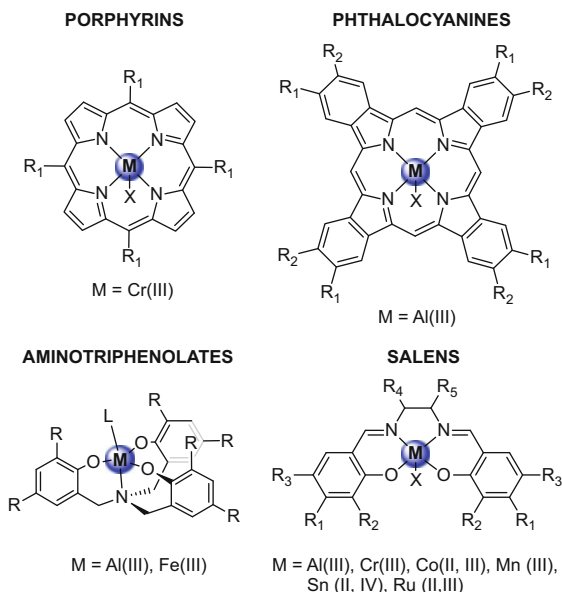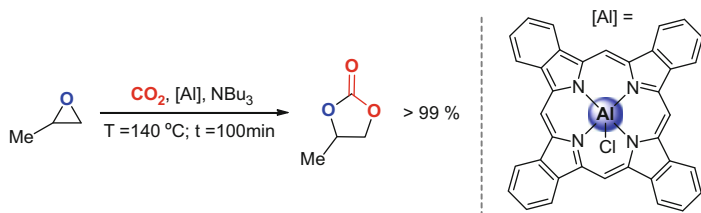
PORPHYRINS

PHTHALOCYANINES

M = Cr(III)

M = Al(III)

AMINOTRIPHENOLATES

SALENS

M = Al(III), Fe(III)

M = Al(III), Cr(III), Co(II, III), Mn (III),
Sn (II, IV), Ru (II,III)

Fig. 2 Typically used metal complexes derived from porphyrins, phthalocyanines, amino-triphenolates, and salens used as catalysts for the synthesis of cyclic carbonates from oxiranes and oxetanes. The X usually refers to a halide

CO_2, [Al], NBu$_3$

T =140 ºC; t =100min

> 99 %

[Al] =

Scheme 2 Example of a binary catalyst system formed by an Al(phthalocyanine) complex and tributylamine as nucleophilic cocatalyst in the coupling reaction between propylene oxide and carbon dioxide

as is the case for porphyrin and phthalocyanine metal-based catalysts, an additional nucleophilic cocatalyst to attain high activity (i.e., binary-type catalyst).

Jacobsen and coworkers discovered that Co(III)salens are highly efficient catalysts for the hydrolytic kinetic resolution of (*rac*)-epoxides using water as the nucleophile [42]. The formation of cyclic carbonates shows large resemblance with this seminal work of Jacobsen as the ring opening of an oxirane by a nucleophile/Lewis base is requisite to react it with CO_2. In the absence of any cocatalytic nucleophile, high activity cannot be obtained, and only trace amounts of the cyclic carbonate are formed. Generally, the activity of a binary catalytic system can be increased with increasing basicity of the Lewis base. In the case of halide
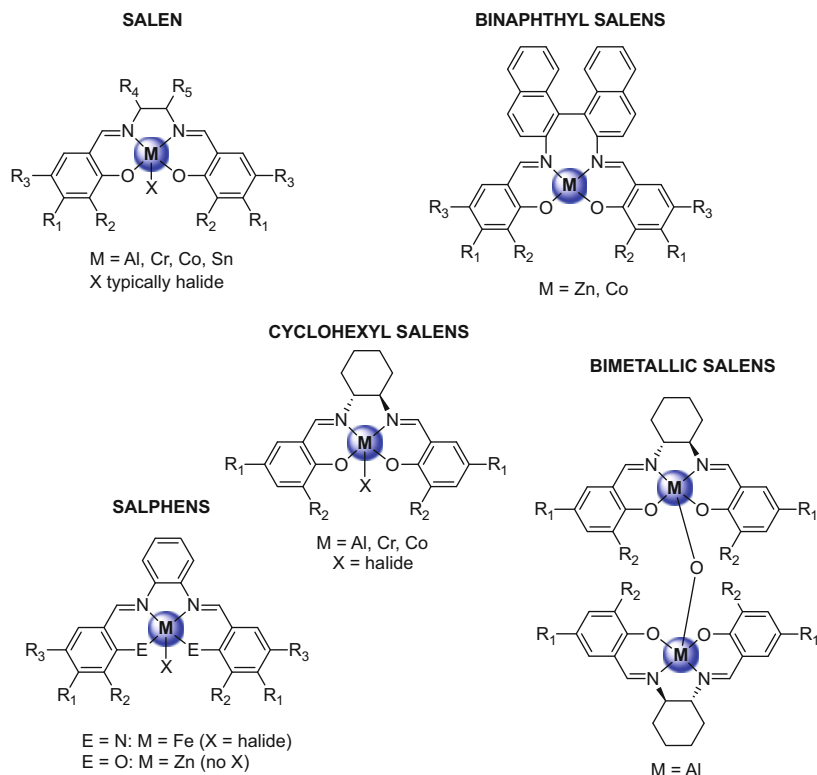
Fig. 3 Most commonly used metal–salen structures derived from salen, salphen, and binaphthyl-based ligand scaffolds

nucleophiles, also the leaving group ability and size features are important parameters controlling the reactivity.

A clear example that illustrates the easy fine-tuning of salen complexes with respect to chemo-selectivity was provided by the work from Darensbourg and coworkers [8]. The presence of electron-donating or electron-withdrawing groups on the backbone of the metal–salen complex can be used to favor the preferred formation of the cyclic or polycarbonate product [43–46].

Although there are various contributions that focus on the conversion of terminal epoxides into their respective carbonates in high yields and under relatively mild reaction conditions [47–49], further improvement of the substrate scope is still warranted. Both chemo-selectivity and higher reactivity are required to achieve high catalytic efficiency with less reactive substrates such as internal epoxides and oxetanes. As a potential solution for these challenges, other types of catalysts have to be considered. Kleij et al. [34] developed a binary catalytic system (Scheme 3) that consists of a triphenolate complex acting as Lewis acid and tetrabutylammonium bromide (TBAB) as cocatalyst. In this case, the choice of cocatalyst and also the ratio between the iron catalyst and the nucleophilic cocatalyst are of high importance as this controls the activity and selectivity [50] of the reaction,
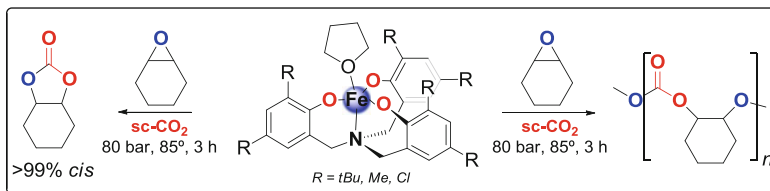
Scheme 3 Reaction of cyclohexene oxide with carbon dioxide under supercritical conditions in the presence of a binary catalyst system comprising of a Fe(III) aminotriphenolate complex

allowing, for instance, the selective conversion of cyclohexene oxide into either the cyclic carbonate or the polycarbonate depending on the catalyst/nucleophile ratio.

The stereo-controlled preparation of value-added commodities from CO_2 has recently emerged as one of the future challenges [51]. Optically active substances, in particular the ones which contribute to biological activity, are key substances in different areas such as the pharmaceutical industry and agriculture. Traditional extraction from natural sources cannot always satisfy the current demand for these types of compounds. This situation has resulted in the development of new alternative synthetic drugs that are obtained through asymmetric synthesis from racemic precursors. Taking advantage of the ease of modulation of salen ligands in general, groundbreaking approaches toward chiral epoxidation [52, 53] and hydrolytic kinetic resolution of (*rac*)-epoxides [54] have been developed by Jacobsen and Katsuki. These previous developments have been and still are of significant importance to the field of (poly)carbonate formation.

The simplest way to produce enantiopure cyclic carbonates is from enantiopure epoxides and carbon dioxide using catalytic procedures that favor a high level of retention of configuration at the chiral carbon center of the oxirane unit. DiBenedetto and Aresta [55] used Nb (IV) and Nb (V) complexes based on chelating diphosphine, pyrrolidine, or oxazoline ligands to convert (*R*)- or (*S*)-configured terminal epoxides, hereby achieving retentions higher than 98%. Kinetic resolution of racemic oxiranes is more attractive in this respect as it creates new chiral centers from cheaper precursors. The most widely studied substrate has been propylene oxide, and chiral catalysts have been used that are able to convert one of the epoxide enantiomers with a significantly higher rate providing thus a basis for epoxide resolution. Lu and coworkers reported on an elegant and efficient chiral Co (III)salen/quaternary ammonium halide binary-type catalyst (Scheme 4) that allows the direct synthesis of optically active cyclic carbonates from racemic epoxides under mild and solvent-free conditions. This study demonstrated clearly the influence of the anion of the quaternary ammonium salt in the binary catalyst systems, as it directs the enantiomeric purity and reaction rate [56].

Other studies concerning the asymmetric coupling reaction between CO_2 and oxiranes were carried out by Jing and coworkers, who developed chiral binaphthyl-based Co(III)salen complexes. In this case, the use of the binaphthyl-based salen ligands (see Fig. 4) provided access to two different types of catalysts being either mono- or dinuclear. In both cases, the catalysts retained the chiral information in the bridging cyclohexyl fragment [57]. The structural variety and success in catalytic
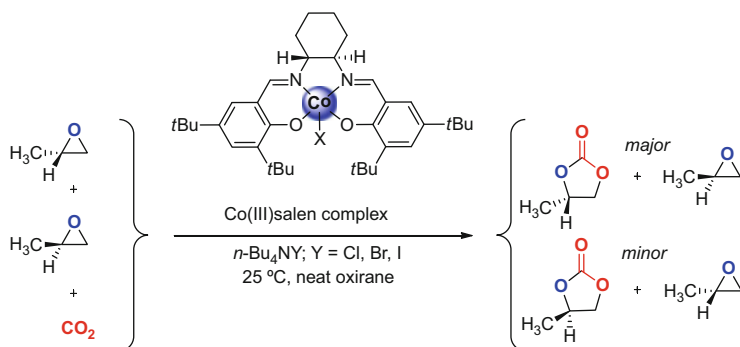
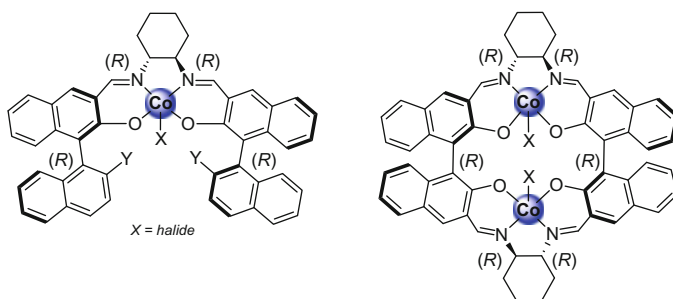**Scheme 4** Kinetic resolution of a racemic epoxide mixture using a Co(III)salen type (spatial) catalyst

Fig. 4 Example of BINAP-based Co(III)salen structures used as chiral catalysts in CO_2/epoxide couplings

operations are obviously an attractive feature, and for this reason it is not surprising that the vast majority of the catalysts developed for CO_2/epoxide couplings are based on Co(salen) structures.

Due to the ease of synthesis of these chiral M(salen) catalysts, other systems have also been studied including their Al(III) derivatives. The first studies reporting on this type of Al catalyst focused on the polymerization of epoxides [58], but in 2002, He et al. developed a binary catalyst system that mediated the formation of cyclic carbonate from propylene oxide in supercritical carbon dioxide in the presence of quaternary ammonium or phosphonium salts [36, 59]. A complementary study developed by Lu and coworkers showed how the coupling of CO_2 and oxiranes is altered by changing the substitution on the aromatic rings of the salen ligands and by using various crown ethers as cocatalysts [60]. North and coworkers demonstrated that bimetallic Al(salen) complexes display a much higher catalytic conversion than their monometallic analogues. In this case, the reaction, which gave no conversion in the absence of either the catalyst or cocatalyst, took place under very mild conditions (25°C, 1 atm), aspects that may be of interest for commercial applications [61].
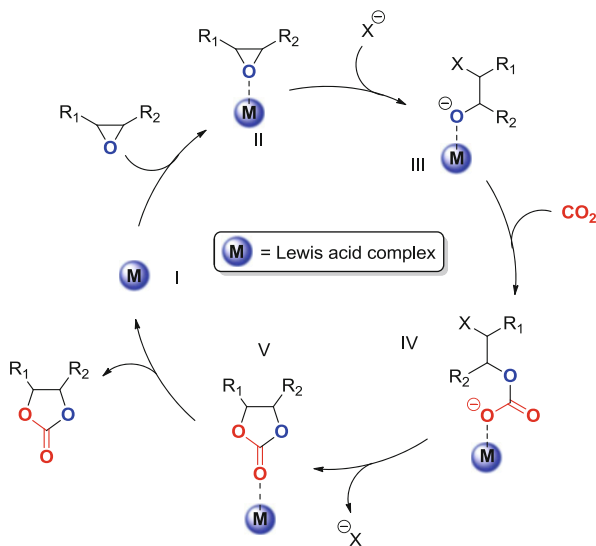
Scheme 5 Generally proposed mechanism for the coupling of CO_2 to oxiranes catalyzed by a Lewis acid (M) in combination with a suitable nucleophile X

Other coordination/organometallic compounds such as $[M(PR_3)X_2]$ (M = Ni [62], M = Zn), $[(dppp)Mn(CO)_3X]$ [38], various copper complexes embedded in macrocyclic ligands [63], $[(OC)CpRu(\mu\text{-dppm})Mn(CO)_4]$ [64], and $[VO(acac)_2]$ [65] are also active in the synthesis of cyclic carbonates from CO_2 and epoxides. However, when compared to the previously mentioned Co(salen) complexes, the scope, reactivity, and/or selectivity features are generally less appealing.

The widely accepted mechanistic proposal that involves binary systems in the synthesis of organic carbonates is explained in Scheme 5. First, the oxirane/epoxide coordinates to the metal center through a coordinative M–O bond (stage II) resulting in the activation of the epoxide. The anion X here acts as a nucleophile, usually attacking the less hindered side of the oxirane furnishing a metal alkoxide intermediate species (III). Then, insertion of CO_2 into the metal alkoxide occurs to form a linear hemi-carbonate (IV) that undergoes a ring closure leading to the formation of the cyclic carbonate (V) that is released by the metal complex to allow for further turnover. Some of these elementary steps have been supported by X-ray crystallographic analysis (in the case of the resting state of some of the catalysts reported) [66] and computational studies [67].

3 Bifunctional Catalysts

In the last decades, the concept of green chemistry has turned out to be an important aspect in designing new catalytic systems. Using less toxic or nontoxic metals, increasing energy efficiency, and minimizing the amount of waste are key issues to be dealt with in synthetic chemistry. To address this problem, bifunctional catalysts
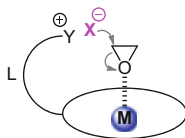
Scheme 6 Conceptual approach toward cooperative activation of an epoxide by a bifunctional type catalyst [70]

have gained increased attention as they may offer more efficient strategies towards the conversion of organic substrates by means of cooperative and/or synergistic effects [68]. Bifunctional catalysis in the context of CO_2 conversion has also conquered a prominent position, and the catalysts that are generally used differ from binary type catalysts having complementary built-in functions (i.e., basic sites or nucleophiles) that entropically favor catalytic turnover. Also, these bifunctional systems often allow for catalyst immobilization and do not require the presence of additional (external) cocatalytic additives thereby increasing the overall efficiency. Most known bifunctional catalysts have a counteranion (= nucleophile) implemented in the catalytic structure in the form of an ammonium/phosphonium halide unit. The metal ion, counteranion, and substrate are all arranged in close proximity, which enhances the reaction rate and/or selectivity. Usually the cocatalyst unit used for ring opening of the substrate (in the case of cyclic carbonate formation) is attached to the catalyst via a linker unit (L), and the rigidity and linker length are crucial for optimal catalyst performance [69].

The proposed reaction mechanism for cyclic carbonate formation from CO_2/ epoxide couplings mediated by bifunctional catalyst systems is rather similar to that reported for the binary systems (Scheme 5). Initial coordination of the epoxide to a metal complex is followed by ring opening by intramolecular, nucleophilic attack from the anion. The anion is ion paired to a (flexible) cationic linker group of the catalyst structure and therefore already in close proximity to facilitate the ring-opening step (Scheme 6). Subsequent steps proceed in a similar way as for the binary system, which finally leads to the formation of the cyclic carbonate and regeneration of the catalyst.

An example of an effective bifunctional catalytic system was reported in 2009 by North et al. [71]. They reported on a bimetallic Al(salen) complex where the cocatalyst is implemented in the catalytic system by modifying the salen units with ammonium salts having bromide counteranions. In terms of catalyst reactivity and stability, the bifunctional catalyst gives similar or even better results than the binary system [72], leading to high yields under very mild conditions (atmospheric CO_2 pressure, room temperature). The main advantage in comparison to the binary system is that this bifunctional catalyst can be immobilized on a solid support which opens the possibilities for use in flow reactors, and the same authors demonstrated at a later stage that this is indeed feasible [73]. Although this bifunctional catalyst can be reused for multiple runs, the catalytic activity gradually decreases over the consecutive cycles probably due to *retro*-Menshutkin or Hofmann elimination like chemistry. Similar strategies to create a bifunctional Al catalyst having built-in
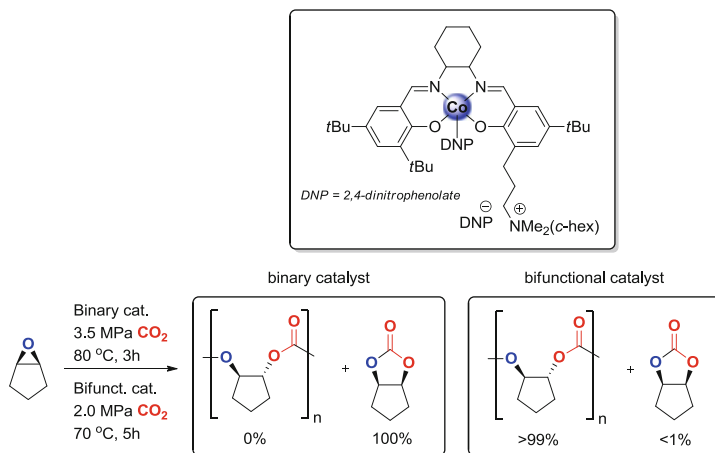
Scheme 7 Improved selectivity toward polycarbonate formation from CPO/CO_2 using a bifunctional Co(salen) catalyst

quaternary ammonium salts led to a variety of one-component catalytic systems for cyclic carbonate formation. Whereas the first catalytic systems showed a considerable decrease in catalytic activity in subsequent cycles, the Al(salen) catalyst reported by Darensbourg in 2012 showed higher stability towards moisture and heat; it tolerates process impurities and shows only a minor loss in activity over five catalytic cycles [74].

Facilitating the immobilization of catalysts for flow reactors is not the only potential advantage of using a bifunctional catalyst. The selectivity for cyclic carbonate formation toward exclusive polymer formation in the coupling between an epoxide and CO_2 can be achieved by replacing the binary system for a bifunctional analogue. This feature was demonstrated by Lu and coworkers using Co(salen) derived catalyst, and its binary and bifunctional derivative were evaluated in terms of chemo-selectivity behavior in the asymmetric copolymerization of CO_2 and epoxides [75].

A similar comparison was done by Darensbourg et al. employing bifunctional (*R,R*)–(salen)M(III) catalysts with M being Cr or Co [76]. In the latter case, the performance of a binary and a bifunctional catalyst was compared in the copolymerization of CO_2 with either cyclopentene (CPO) or cyclohexene oxide (CHO). The binary catalyst system gives an excellent selectivity for polycarbonate formation when CHO is used as substrate, while in the case of CPO, only cyclic carbonate is observed. The bifunctional catalyst (see Scheme 7), however, is able to form selectively the polycarbonate product from CPO with virtual perfect selectivity. The specific conformation of the bifunctional catalyst system promotes polymer chain growth instead of ring closure that leads to cyclic carbonate formation.

Another interesting catalytic system was developed by Sakai and Ema, a bifunctional porphyrin-based catalyst modified with peripheral quaternary ammonium bromide groups (Scheme 8) [70]. This system exhibited an extremely high activity
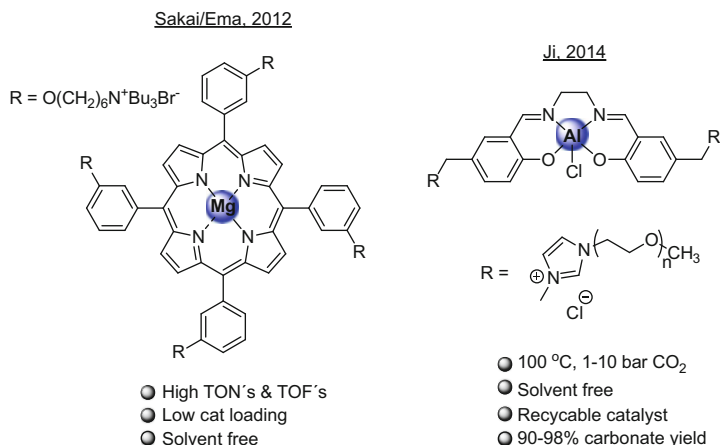
Scheme 8 Examples of successful bifunctional catalyst designs in cyclic carbonate formation
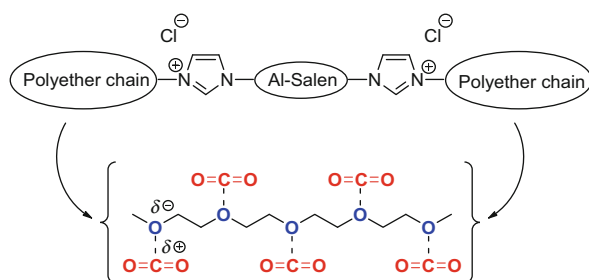
Scheme 9 Proposed "CO_2 capture effect" by polyether chains

in the reaction of CO_2 with epoxides, leading to one of the highest reported turnover numbers (TONs, 103,000) and turnover frequencies (TOFs, 12,000 h^{-1}). The cooperative effect of the catalyst and cocatalyst induced by the bifunctional catalyst turned out to be highly important, as a binary-type system comprising of a Mg (porphyrin) and tetrabutylammonium bromide (TBAB) gave only 4% yield (TON, 5,000) under similar conditions. Differently substituted epoxides could be converted with high yield (81–99%) with no observable by-product formation.

Ji and coworkers recently reported on an Al(III)–salen complex functionalized by imidazolium groups (Scheme 8) [77]. These bifunctional Al(salen) complexes do catalyze the formation of cyclic carbonates from epoxides although in moderate yield. A significant enhancement in the yield of the carbonate product was obtained upon employing a *trifunctional* catalyst system having additional polyether chains incorporated. These polyether chains are proposed to increase the local density of CO_2 by assumed weak interactions between the oxygen atoms of the ether fragments and CO_2 as depicted in Scheme 9. As such, the reaction shows a significantly reduced diffusion-dependent kinetic behavior and thus increased reactivity and product yields.

Various epoxides were converted in excellent yields (94–99%) by the trifunctional catalyst. In comparison, the catalyst without polyether groups only provides moderate conversion or no reaction at all under similar conditions. Comparable effects of increasing the local concentration of CO_2 by a judicious choice of the solvent medium have also been reported [48]. Another advantage of these modified Al(salen) complexes is the facile catalyst separation and recyclability. The catalyst can be separated from the reaction mixture by addition of ether which causes the Al-complex to precipitate. The catalyst can be used in subsequent catalytic cycles with virtually no loss in reaction rate and only a minor decrease in selectivity to 98% after six consecutive runs. Since the advent of bifunctional catalysis as an alternative to binary catalysis, various research groups have reported bifunctional catalysts of which the noteworthy ones include a bimetallic macrocyclic Fe(III) complex [78], a trinuclear bis-salphen metalloligand [79], and other chiral Co(salen)-based systems [80].

4 Addition of Carbon Dioxide to Double and Triple Bonds

Chemical fixation processes with CO_2 should preferably rely on low-energy processes to minimize the net output of CO_2 during the reaction. Ideally, cyclic carbonates could be obtained from a reaction between CO_2 and an unsaturated alcohol, leading to the formation of an elusive carbonic acid mono-alkyl ester, though these compounds are too unstable to be observed and isolated [81]. An interesting strategy to overcome this problem was reported by Minakata et al. in 2010 [82]. They reported on the formation of carbonic acid intermediates from unsaturated alcohols and CO_2. Despite the unfavorable thermodynamic equilibrium, the carbonic acid derivative can be conveniently trapped by *tert*-butyl hypoiodite (*t*-BuOI) to form a carbonic acid iodide intermediate (Scheme 10). In the presence of an alkene/alkyne group in the substrate, fast ring closure toward a cyclic carbonate product is observed that drives the equilibrium toward the targeted product through an intramolecular addition onto the double bond. A variety of unsaturated alcohols with either alkene- or alkyne-accepting groups can be easily converted by this innovative reaction with good to excellent yields under very mild conditions using only 1 bar of CO_2 at temperatures as low as $-20\,^\circ$C.

Another recent example of CO_2 addition to unsaturated carbon–carbon bonds is the conversion of CO_2 and olefins to form cyclic carbonates, a process reported by Hatton and Jamison in 2014 [83]. They used a flow system containing a
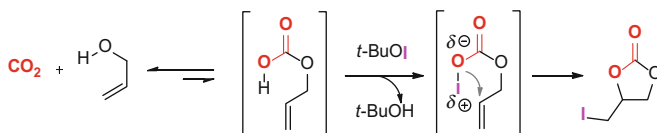
Scheme 10 Trapping of a carbonic acid intermediate with *tert*-butyl hypoiodite
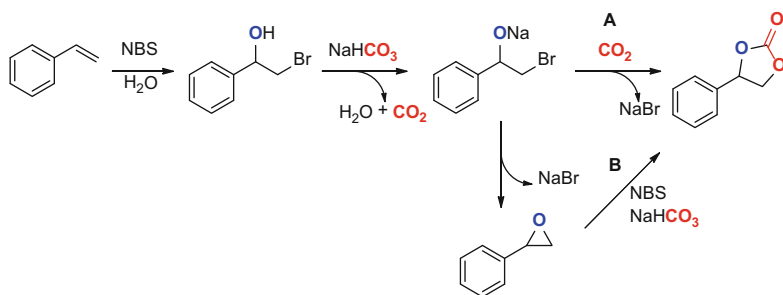
Scheme 11 Proposed mechanism for the formation of cyclic carbonates from olefins using a NBS/NaHCO$_3$/water medium

combination of *N*-bromo-succinimide (NBS), 1,8-diazabicycloundec-7-ene (DBU) as a base, water, and CO$_2$. The optimal temperature for this reaction turned out to be 100 °C, as at lower temperatures the main product is the epoxide and at higher reaction temperatures, the formation of the diol (through carbonate hydrolysis) is favored. Under these optimized reaction conditions, styrene could be fully converted into styrene carbonate in up to 85% isolated yield without the formation of by-products.

The proposed mechanism [84] of this reaction most likely follows one of the two pathways described in Scheme 11 using sodium bicarbonate as the CO$_2$ source. The first step is the reaction of the olefin with NBS and water to form a reactive bromohydrin, which can be deprotonated by sodium bicarbonate to release CO$_2$ and water. The anionic intermediate of the halohydrin can then react directly with CO$_2$ to produce the cyclic carbonate (path A) or via the epoxide (path B). As the reaction that forms the epoxide proceeds faster than the coupling with CO$_2$, a substantial amount of cyclic carbonate is supposed to form through the latter pathway. Although the approaches from Minakata et al. and Jamison/Hatton do not make use of metal catalysis, they serve as inspiring examples of efficient CO$_2$ conversion catalysis examples.

Compared to carbon–carbon double bonds, the carbon–carbon triple bond is more reactive and thus generally does not require elevated temperatures for its reaction with carbon dioxide. The addition of a strong base or in some cases an organocatalyst is sufficient to convert propargylic alcohols [85] and propargylic amines [86] to cyclic carbonates and oxazolidinones [87, 88], respectively. Although there are various reported examples that concern the use of bases, this work will focus on metal-catalyzed addition reactions that involve CO$_2$ as a reagent. Significant contribution to this field was made by Yamada and coworkers; they reported on the Ag-catalyzed CO$_2$ incorporation into propargylic alcohols [85]. The CO$_2$ reacts with the alcohol group of the substrate, after which ring closure occurs through activation of the alkyne group by the Ag complex to give a cyclic carbonate with an exo-cyclic double bond. In subsequent work, the same authors showed that cyclic carbonates can be formed from bis-propargylic alcohols at low temperatures allowing for practical enantioselective reactions (Scheme 12) [89]. The combination of AgOAc and a chiral Schiff base ligand gave access to a
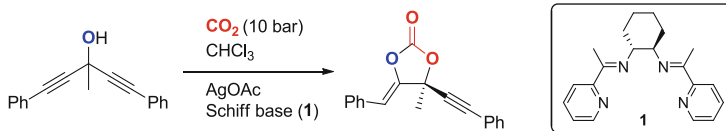
Scheme 12 Addition of CO_2 to a bis-propargylic alcohol catalyzed by a chiral silver complex based on Schiff base (1)

variety of cyclic carbonates in high yields (90–98%) and with *ee*'s of up to 93%. These reactions can be performed under mild conditions using 10 bars of CO_2 at 5 °C. At this temperature, there is excellent enantio-control though at the expense of the reaction rate: under low-temperature conditions, the reactions require 2–7 days to reach complete conversion of the substrates.

An interesting contribution to this field was made by the group of Jiang that reported on *N*-heterocyclic carbene–Ag complexes immobilized on a polystyrene support [90]. Various terminal secondary and tertiary propargylic alcohols were conveniently converted to their cyclic carbonate products by this supported catalyst with excellent selectivity and yield. These reactions could be performed under relatively mild conditions at 40 °C using 50 bars of CO_2 pressure. For some of the more sterically hindered substrates, a slightly higher temperature was required to give high yields. An additional benefit of this system is its recyclability; after 15 catalytic cycles, no significant change in the activity was observed.

5 Synthesis of Oxazolidinones Using CO_2 and Metal Catalysts

Oxazolidinones (also known as five-membered cyclic carbamates) are an important class of heterocyclic compounds widely present in pharmaceutically relevant organic structures. Particularly, 5-substituted oxazolidin-2-ones have shown extensive antibacterial and antimicrobial activity, and these structures are represented in several (commercially available) synthetic drugs (Fig. 5) [91–94]. Furthermore, these cyclic carbamates are frequently used in synthetic organic chemistry [51, 95] since Evans [96] reported in 1981 on the use of enantiomerically pure 4-substituted oxazolidinones as chiral auxiliaries in asymmetric synthesis (i.e., the use of a polymer-supported chiral Evans' auxiliary in diastereoselective *syn*-aldol reactions) [97]. Finally, the commercialization of linezolid, an oxazolidinone-based antibacterial drug, raised the interest of the scientific community toward developing new synthetic routes for oxazolidinones especially those that are based on the use of CO_2 as a reagent [98].

The conventional preparation of oxazolidinones includes the use of environmentally harmful/toxic reagents such as phosgene, isocyanates, or carbon monoxide. Most popular routes which lead to oxazolidinones include the carboxylation of
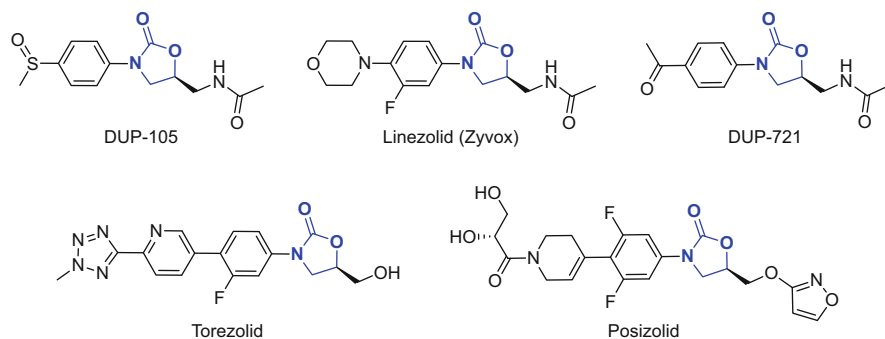
Fig. 5 Schematic structures of some oxazolidinone-based biologically relevant compounds. All are industrially produced as antibiotic against Gram-positive bacteria

1,2-amino alcohols using phosgene [99] as a carbonyl source, coupling between epoxides and isocyanates [100], or a two-step process involving the carboxylation of β-amino alcohols with CO followed by an oxidative cyclization with molecular oxygen [101]. As the oxazolidinone building block has gained extensive synthetic and medical applications over the last years, the development of greener chemical methodologies has attracted considerable attention. In order to avoid the use of phosgene or isocyanates, great effort has been devoted to incorporate CO_2 as an alternative C1 carbon source [102]. There are three main synthetic strategies using CO_2 as C1 building block depending on the starting material employed: (1) insertion/addition of CO_2 (in)to an aziridine moiety, (2) reaction of 1,2-amino alcohols with CO_2, and (3) reaction of propargylic amines with CO_2. These methods will be discussed in more detail in the sections below.

5.1 Insertion of CO_2 into an Aziridine Moiety

Aziridines are important three-membered, small-sized heterocyclic compounds. Structurally, they are analogous to epoxides with the nitrogen group replacing the oxygen. The chemistry of aziridines has been studied extensively over the last few decades, and their applications have been greatly expanded. Since aziridines are highly ring-strained compounds, they are promising candidates to react with relatively inert CO_2 without the need for extreme reaction conditions. The direct coupling reaction between CO_2 and aziridines represents obviously an attractive route to oxazolidinones compared to the processes based on phosgene or CO. An efficient aziridine/CO_2 coupling reaction is 100% atom efficient, which is an important factor for sustainable development. As a result, different research groups have developed relatively green approaches toward the synthesis of oxazolidinones through catalytic and non-catalytic routes. The reaction of aziridines with CO_2 usually affords two regio-isomeric structures: the 4- and 5-substituted isomer
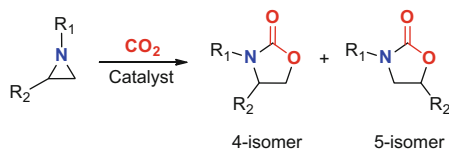
Scheme 13 Reaction scheme of the insertion of carbon dioxide into an aziridine group

Table 1 Influence of the aziridine substituents on the oxazolidinone isomer ratio using different catalytic systems

R_1 aziridine	R_2 aziridine	Preferred oxazolidinone		
		MX_n (Pinhas)	Co(salen)/DMAP (Nguyen)	$ZrOCl_2 \cdot 8H_2O$ (Wu)
Alkyl	Alkyl	67% (4)	5-Isomer	4-Isomer
Alkyl	Phenyl	5-Isomer	5-Isomer	5-Isomer
Phenyl	Phenyl	No reaction	5-Isomer	No reaction

(Scheme 13). The ratio between these two isomers is mostly dependent on the aziridine substituents (R^1 and R^2, Table 1).

The main drawback in the synthesis of oxazolidinones from CO_2 is the relative inertness of the latter combined with the lower reactivity of aziridines compared to epoxides. These limitations can be (partially) overcome by using a high CO_2 pressure and/or electrolysis methods [103]. Good results for the insertion of CO_2 into the C–N bond of aziridines have been obtained by electrosynthesis using stable and readily available complexes of Ni(II) incorporating a cyclam ligand (1,4,8,11-tetra-azacyclo-tetradecane) or using a bipyridine ligand. The reaction takes place under extremely mild reaction conditions (ambient pressure and temperature) which provides a green chemical approach compared with existing methodologies. Both types of Ni(II) complexes led to the corresponding oxazolidinones in good yields (50–99%) depending on the substituents present in the starting aziridine and displayed moderate to good regioselectivities for the 4-isomer product (50–84%).

Endo et al. reported in 2003 on the first selective synthesis of 2-oxazolidinones by coupling of CO_2 with an aziridine [104]. The conversion of 2-methylaziridine and 2-phenylaziridine into their corresponding oxazolidinones was studied using simple and cheap metal halides as catalysts such as LiBr and NaBr. In both cases, the reaction shows an excellent regioselectivity and provides exclusively the 4-substituted oxazolidinone (Scheme 13). Whereas ambient conditions ($pCO_2 = 1$ bar and room temperature) were used for the coupling of 2-methylaziridine with CO_2, an increase in the reaction temperature (up to 100 °C) was required for the conversion of 2-phenylaziridine probably as a result of an increasing steric effect at the ring-opening stage of the reaction.

Simultaneously, Pinhas and coworkers reported on the use of an identical metal halide catalyst for the conversion of *N*-substituted aziridines under similar conditions as those reported by Endo (i.e., ambient conditions) [105]. A dramatic effect of the aziridine substitution on the regio-isomer distribution was observed. When the R^1 and R^2 groups (Table 1) are both alkyl groups, a 2:1 mixture of 4- and 5-isomer is obtained. On the other hand, if R^2 is a phenyl group, the mixture product is almost quantitatively enriched in the 5-isomer. However, if R^1 is a phenyl group (Table 1) or any electron-withdrawing group, no reaction is observed at all.

This problem was solved by Nguyen in 2004, who reported on a highly active and selective catalyst [106] based on a binary complex comprising of a Cr(III)–salen complex and 4-dimethylaminopyridine (DMAP) for the coupling reaction between CO_2 and *N*-substituted aziridines under mild reaction conditions. The Nguyen method proved to be successful with *N*-phenyl-substituted aziridines (Table 1, Scheme 14) which is highly important as all oxazolidinone-based biologically relevant compounds have *N*-aryl substitutions. In addition, for the first time this catalytic system showed a general and clear preference for the formation of the 5-isomer. The excellent regioselectivity is of high importance as only the 5-substituted oxazolidinones have shown to exhibit biological activity. Furthermore, this binary complex shows high catalytic activity for a wide range of substrates, and the oxazolidinone products were generally obtained in excellent yields and regioselectivities.

The proposed mechanism is shown in Scheme 14. The aziridine is first activated by coordination to the metal center replacing the labile chloride atom. As a result of
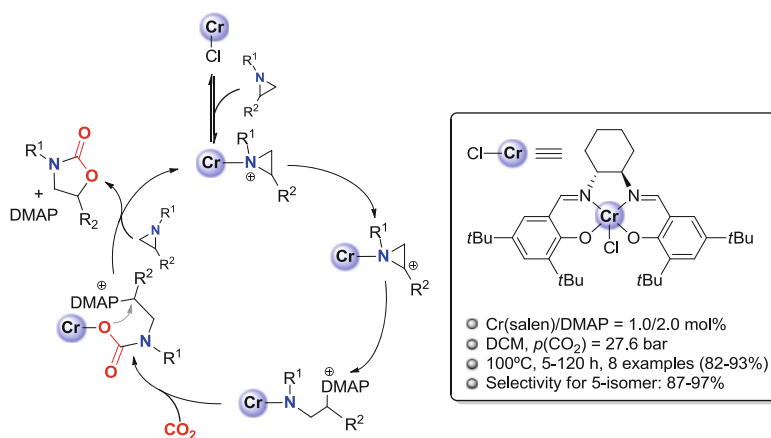

Scheme 14 Proposed mechanism for the coupling of CO_2 and aziridines by a Cr(III)–salen/DMAP binary catalyst system

this coordinative interaction, a partially positive charge is delocalized over the aziridine ring allowing nucleophilic attack by the Lewis base cocatalyst DMAP at the most substituted carbon. The regioselectivity of the reaction is controlled by this step affording predominantly the 5-isomer.

A different method to obtain 5-substituted oxazolidinones in excellent yields and regioselectivities was reported by Wu and coworkers [107]. Zirconyl chloride (ZrOCl$_2$·8H$_2$O) was used as an effective solid catalyst for the coupling between CO$_2$ and aziridines under mild conditions without the need of any additives or solvent. This methodology was successfully applied to the synthesis of a variety of *N*-alkyl-2-phenyl aziridines to obtain *N*-alkyl-5-phenyl-based oxazolidinones. The 4-substituted product is the predominant one when CO$_2$ is coupled to 2-alkyl aziridines (Table 1). The activity of the ZrOCl$_2$·8H$_2$O catalyst, which is regarded to be an ionic cluster of [Zr$_4$(OH)$_8$(H$_2$O)$_{16}$]Cl$_8$, can be explained by the coexistence of Lewis acidic zirconium (IV) and Lewis basic chloride. The bifunctional catalyst can be easily recovered from the reaction mixture by filtration and reused for at least five times without significant loss in catalytic activity, rendering the process economically and potentially viable for commercial applications.

In addition to these methods, other catalytic systems have been developed to get 4,5-disubstituted oxazolidinones. Pinhas [105] studied the formation and stereochemistry of oxazolidinones starting with 2,3-disubstituted aziridines. Using LiI as catalyst, high yields (85–90%) were obtained for dialkyl-substituted aziridines with retention of the starting *cis/trans* stereochemistry. At a later stage, a binary catalytic system composed of palladium-dibenzylideneacetone [Pd$_2$(dba)$_3$] and tetrabutyl-ammonium difluorotriphenylsilicate (TBAT) was reported by Aggarwal and coworkers [108] to effectively convert 2-allyl-3-substituted aziridines to the corresponding oxazolidinones in mild conditions (0 °C and 1 bar of CO$_2$); see Scheme 15. This Pd-mediated reaction proceeds with overall retention of configuration although the palladium intermediate can possibly isomerize to yield the product with opposite configuration. The effect of this isomerization process could almost be fully suppressed under the reaction conditions (0 °C) but becomes a significant competitive pathway at room temperature or in the absence of a halide
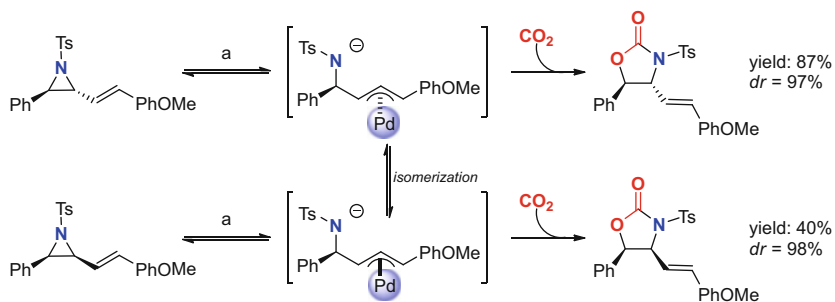
Scheme 15 Stereoselective palladium-catalyzed oxazolidinone synthesis from aziridines and CO$_2$. (a) Reaction conditions: Pd$_2$(dba)$_3$, CHCl$_3$, PPh$_3$, TBAT, p(CO$_2$) = 1 bar, toluene

salt. A Pd(0) complex acts as catalyst for the ring-opening "cyclization" reaction forming a π-allyl palladium intermediate. Trapping of this intermediate by CO_2 gives the vinyl oxazolidinone after ring closure by attack of the carbamate group onto the activated Pd–allyl fragment.

Other methods for the coupling reaction between CO_2 and aziridines comprise the use of I_2 [109, 110], organocatalysts such as N-heterocyclic carbenes [111], or recyclable systems based on a polyethylene glycol support containing quaternary NBu_3Br groups [112] and polymer-supported amino acids [21]. Interestingly, Pinhas et al. demonstrated that the coupling of aziridines and CO_2 could also be performed without catalyst using 2-aryl- and 2-alkylaziridines as substrates affording selectively the 5-oxazolidinones in good yields making use of high-speed ball milling as a mechanical stimulus [113]. However, this section focuses on metal-mediated processes; thus, these latter examples fall out of the primary scope of this chapter.

5.2 CO_2 Coupling Reactions with Amino Alcohols and Propargylic Reagents

Alternative ways to obtain oxazolidinones include the coupling of CO_2 with 2-amino alcohols or propargylic amines (Scheme 16). However, these processes are not (always) atom efficient; considerably harsh conditions may be required for efficient turnover and produce significant amounts of waste. Therefore, they are considered less sustainable than those based on aziridines and CO_2 couplings, and these methods will therefore only be briefly discussed in this chapter.

Since 2-amino alcohols are readily available derivatives of amino acids, they have been frequently used in the synthesis of oxazolidinones using CO_2 as the carbonyl source. The main drawback of the reaction is finding a suitable dehydrating pathway after the insertion of CO_2 in the 2-amino alcohol moiety as the reaction is thermodynamically not favored. Nomura and coworkers reported the first organometallic catalyst for this reaction (Ph_3SbO) [114], which was able to
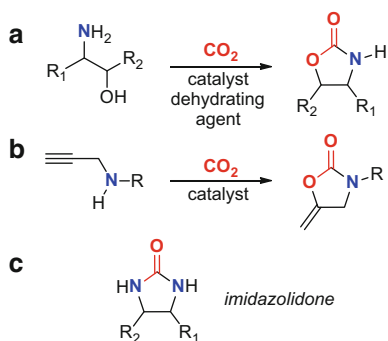
Scheme 16 Synthesis of oxazolidinones from 1,2-amino alcohols (**a**) and N-substituted propargylamines (**b**). Under (**c**) an example of an imidazolidone product observed by Shi et al.

perform the conversion to 2-oxazolidinones in good yield (over 94%) but under harsh temperature conditions (160°C, 24 h) using molecular sieves (3 Å) as dehydrating additive. After this initial report, other catalysts were used in this transformation such as chlorostannoxanes reported by Ghosh [115]. In the presence of 1,3-dichloro-1,1,3,3-tetraalkyldistannoxanes, retention of chirality (up to 99%) of the starting amino alcohols and high turnover numbers (up to 138) were observed under the reaction conditions. Other catalytic systems that were studied for this reaction are based on the use of carbodiimides and phosphines [116, 117].

The reaction between propargylamines and carbon dioxide is one of the most common approaches toward the formation of unsaturated oxazolidinones. An important example of a binary catalyst system for the formation of these types of oxazolidinones was reported by Mitsudo [118] in 1987 using a Ru catalyst [i.e., (4-1,5-cyclooctadiene) (6-1,3, 5-cyclooctatriene)ruthenium] and a tertiary phosphine to give the 5-methylene-2-oxazolidinone products from *N*-substituted propargylamines and CO_2 in high yield and good regio- and stereoselectivity. In this context, Costa reported some interesting examples of unsaturated oxazolidinone formation in 1996 and 1999. First, the use of strong organic bases as catalysts for the synthesis of 5-substituted oxazolidinones was probed using propargylamines [87], and hereafter oxazolidinone synthesis was investigated using PdI_2 as catalyst [119]. With this methodology, 3-substituted oxazolidinones were obtained in good yields and with a 1:3 *E/Z* ratio after optimization of the reaction conditions. Shi and coworkers also studied various palladium-based catalysts such as $Pd(OAc)_2$ and $Pd(PPh_3)_4$ for the reaction between propargylamines and CO_2 under mild reaction (20 °C) conditions [120]. The latter example demonstrates that the chemo-selectivity can be an issue when propargylic amines are used as substrates. The combination of a suitable Pd salt with an appropriate counteranion can drive the selectivity toward the desired oxazolidinone or alternatively toward the imidazolidinone product (Scheme 16c). The use of a basic phosphine [P(*t*Bu)$_3$] fully suppressed the formation of the imidazolidinone and gave the highest yield of the desired oxazolidinone (90%).

6 Synthesis of Ureas and Quinazolines

Ureas and their derivatives are an important type of organic compounds where two amine groups are connected by a carbonyl group. They are important end products or intermediates for pharmaceuticals, agricultural pesticides, antioxidants in gasoline, dyes, and resin precursors [121]. Many cyclic derivatives can be synthesized using CO_2 as a reactant. Substituted 2,4-dihydroxyquinazolines have been interesting for their biological activities. For example, 7-chloro-1-carboxymethyl-3-(4-bromo-20-fluorophenylmethyl)-2,4(1*H*,3*H*)quinazolinone was developed as an aldol reductase inhibitor as a remedy for complications of diabetes mellitus.
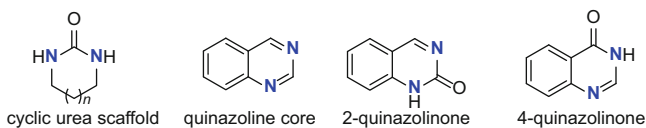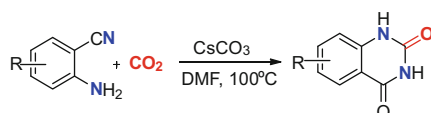
Fig. 6 Structures of some urea/urea-like scaffolds

Scheme 17 Bhanage's quinazoline-2,4(1H,3H)-dione synthesis from 2-aminobenzonitriles

Quinazolinones are also a class of drugs which function as hypnotic/sedative drugs that contain a 4-quinazoline core (Fig. 6).

Generally, their synthesis is carried out by treatment of anthranilic acid with urea, anthranilamide with phosgene, carbon monoxide with sulfur, or anthranilic acid with potassium cyanate. Obviously, these methods are considerably limited because of the high toxicity of the reagents employed and/or the drastic reaction conditions applied. Mizuno et al. [122] reported in 2000 the first synthesis of these types of compounds using CO_2 as a reactant. 2,4-Dihydroxyquinazolines were prepared in high yield starting from 2-aminobenzonitriles and CO_2 under mild conditions (1 atm, 20 °C) in the presence of DBU. The use of DBU is disadvantageous due to problems associated with its handling including its hygroscopic nature, high viscosity, and tedious rework procedures. Following the need for simpler and more practical methods for the synthesis of these compounds, Bhanage et al. proposed [123] an alternative method using cesium salts for the synthesis of quinazoline-2,4(1H,3H)-diones using CO_2 and 2-aminobenzonitriles (Scheme 17).

The proposed mechanism starts with deprotonation of the Ar-NH₂ that reacts with CO_2 to afford a Cs-amide intermediate. This amide then attacks the nitrile group in an intramolecular process giving rise to a cyclized species that rearranges into an isocyanate intermediate followed by another intramolecular process where a hydroxyl-imine group attacks the carbon center of the isocyanate yielding a new cyclized compound that finally stabilizes/rearranges into the desired dihydroxyquinazoline. Improvements of the method are still required as the process needs high pressures (≥13 bar) and temperatures (100 °C).

Other basic catalysts which have proved to be very efficient in CO_2 fixation (TON up to 938) into urea derivatives are polyoxometalates such as the mononuclear and simplest tungstate $[WO_4]^{-2}$. $TBA_2[WO_4]$ (TBA = $[(n\text{-}C_4H_9)_4N]^+$) can act as a highly efficient homogeneous catalyst for the conversion of CO_2 with amines, 2-aminobenzonitriles, and propargylic alcohols to give urea derivatives, quinazoline-2,4(1H,3H)-diones, and unsaturated cyclic carbonates, respectively [124, 125]. Interestingly, the tungstate used in this latter work seems to be able to activate both types of substrates, and NMR investigations have supported that the

(bifunctional) catalyst species is involved in binding of a CO_2 molecule thus activating it for catalytic turnover. Mechanistic investigation [125] showed unambiguously that the formation of a carbamic acid intermediate and its subsequent conversion by $TBA_2[WO_4]$ plays a key role in the synthesis of the heterocyclic products. Other methods towards quinazoline derivatives using CO_2 as reagent have also recently been disclosed but will not be discussed in detail here [126].
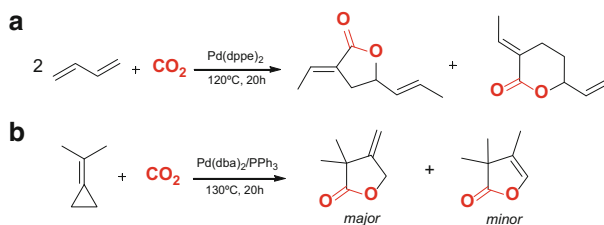
7   Formation of Lactones

A lactone is defined as a cyclic ester, and it may be regarded as the condensation product of an alcohol and an acid group within the same molecule. It consists of a cycle of at least 2 carbon atoms and a single *endo*-cyclic oxygen atom with an adjacent carbonyl group. In this section, we will focus on the importance of this type of molecules and the different synthetic routes that have been reported utilizing CO_2 as a key reagent. The kinetic stability of CO_2 towards its conversion represents a huge challenge, and therefore the development of catalytic methods for its activation is crucial. Cyclic structures containing ester functions require complex synthetic routes, and their formation can be formally achieved through the insertion of CO_2 into C–H, C–C, E–C, or C–O–C bonds (E represents other elements than H, C, or O). These reactions are expected to have favorable thermodynamics associated to adverse kinetics. The main CO_2 activation strategy has been the direct interaction of the CO_2 molecule with a metal center. The first structurally characterized metal complex capable of binding CO_2 was reported in 1975 by Aresta and coworkers [127], and since then, the insertion of CO_2 into M–E bonds has been intensively investigated with the aim of discovering new catalysts for (direct) CO_2 conversion.

In essence, there are two principal routes considering CO_2 insertion into organic molecules leading to lactone-based structures: (1) reactions of CO_2 with olefins or alkynes and (2) the insertion of CO_2 into metal–element bonds, which, depending on the co-reactants, leads to different transformation products such as carboxylates, esters, or carbonates. First, the focus will be on the first route which leads to the production of lactones and metallo-lactones. In nearly all reported cases, late transition metals have been used including Fe(0), Rh(I), Ni(0), Pd(0), and Pd (II) as they are highly basic and capable of binding weak σ-donor ligands such as olefins through π-back bonding. Many recent reports are still based on the initial research from the 1970s and 1980s, published by the groups of Inoue, Musco, Hoberg, Walther, and Behr, who focused their research in the field of catalytic CO_2 activation. The pioneering examples of lactone formation using CO_2 were provided by Inoue et al. and Musco et al. in the late 1970s [128–132]. Using $Pd(dppe)_2$ as a catalyst [131], 1,3-dienes could be activated towards coupling with CO_2 to afford five- and six-membered lactones (Scheme 15a) although resulting in a (complex) mixture of products. Another interesting contribution in the field of lactone formation describes the coupling between CO_2 and (substituted) methylenecyclopropanes
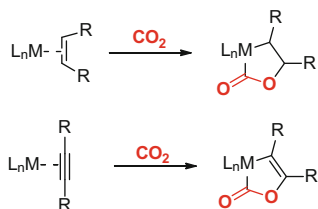
**Scheme 18** Reaction of CO_2 with olefins and alkynes giving metallo-lactones

Scheme 19 Inoue's contributions in the field of lactone formation using CO_2: (**a**) dppe = Ph_2P $(CH_2)_2PPh_2$ and (**b**) dba = dibenzylideneacetone

[130] using a Pd(0) complex based on Pd(dba)$_2$ and PPh$_3$ (ratio 1:4) as catalyst (Scheme 19b). The main issues of these reactions were the high CO_2 pressures needed (40 bar) combined with low chemo-selectivity. Two types of lactones were observed, one with an *exo*-cyclic and one with an *endo*-cyclic double bond, and a challenge is the combination of high conversion and high selectivity for either lactone while maintaining high isolated yields (Scheme 18).

The reaction involving the telomerization of butadiene with CO_2 (Scheme 19a) to form a functional lactone has been a topic of intensive research after the first contributions from Inoue and coworkers as these lactones potentially have multiple applications as an organic intermediate. Over the years, the yields and selectivity have been successfully increased (up to 48% and 95%, respectively), and the process was optimized to mini-plant scale [133–135]. Several investigations were conducted to explain in more detail the reaction/mechanistic pathway (Scheme 20).

The proposed reaction mechanism involves the formation of a Pd(0)–phosphine complex (PdL$_n$) from a palladium(II) precursor and a tertiary phosphine. The second step is the coordination of two butadiene molecules forming a bis-η^3-allyl–Pd complex **A**. This species is in equilibrium and can either react to form 1,3,7-octatriene **B** or give rise to an allylic carbonate **D** by insertion of CO_2 in one of the allyl–Pd bonds in **C**. Through ring closure of this intermediate **D,** various cyclic lactones can be obtained, although there are side reactions which can produce other aliphatic cyclic esters **F** and **G**. Another important side reaction that has to be taken into account is that the Pd catalyst can also promote the coupling of a different number of molecules of butadiene before the carboxylation step, which leads to linear open-chain ester products of different lengths/sizes (cf., formation of **H** and
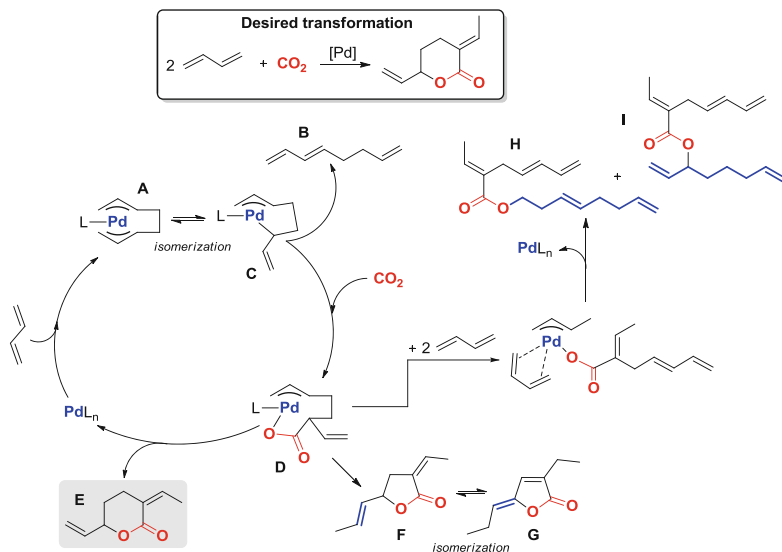
Scheme 20 The reaction mechanism for the telomerization of CO$_2$ and butadiene proposed by Behr et al.

I). This detailed mechanism therefore explains the low yield and poor selectivity of the reaction in the first seminal reports, but clearly optimization based on by-product recycling drastically increased the selectivity towards the δ-lactone **E**.

The resulting lactone is highly functional allowing for various post-synthetic manipulations. Through further conversion with different bulk reagents, several relevant industrial products may be prepared, and the lactone could be regarded as an ideal chemical platform molecule amenable toward hydrogenation, hydro-formylation, hydroamination, oxidation, and polymerization among other valuable conversions (Scheme 21).

In 2014, Nozaki [136] and coworkers were able to develop a strategy to create a polymer from dienes and CO$_2$ in which CO$_2$ represented 29% of the weight of the product. The key feature to make this process feasible was to employ the *meta-stable* δ-lactone **E** to overcome the thermodynamic barrier. Copolymerization of CO$_2$ and dienes to form polylactones has always been an appealing research topic as it would allow for the preparation of new materials from inexpensive feed stocks such as CO$_2$ and dienes. This has generally not been possible due to the inertness of CO$_2$ combined with the high kinetic barrier associated with the alternating co-polymerization of ethylene/polyene and CO$_2$.

Nozaki et al. made clever use of the optimized synthetic methodology developed by Behr for δ-lactone **E** which could easily undergo thermally initiated radical polymerization under aerobic conditions in the presence of an appropriate thermally activated radical initiator [i.e., ABCN = 1,1′-azo-bis(cyclohexane-1-carbonitrile)]. The system was optimized to obtain high molecular weights (62–85 kDa) with narrow molecular weight distributions (PDIs around 1.3) and polymer yields around 48%. As depicted in Scheme 22, the copolymerization results in the
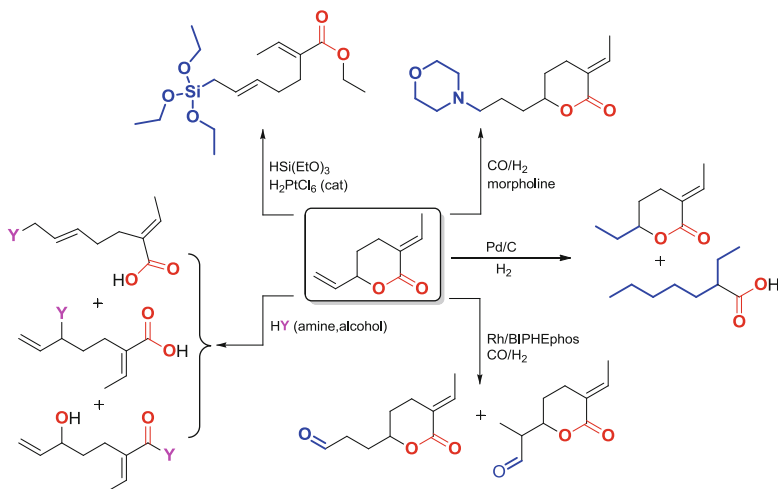
Scheme 21 Functionalization reactions of the δ-lactone E from Scheme 20 towards several products with potential industrial applications
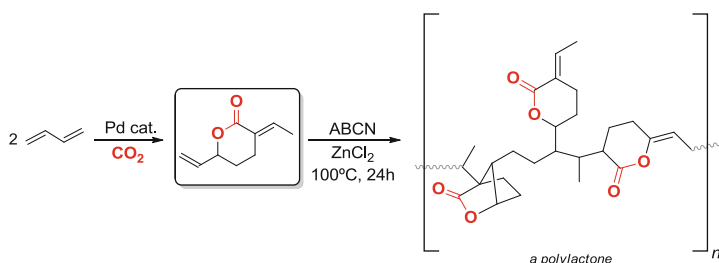
Scheme 22 Nozaki's strategy to create a novel lactone copolymer based on CO_2

formation of several isomeric subunits in the polymer. The scope of polymerization reactions was extended to the incorporation of more complex diene structures (e.g., 1,3-pentadiene and isoprene) within the polymeric chain.

Revisiting Inoue's work in the 1970s, the same group also discovered that by using Ni(COD)$_2$–dppb as a catalyst (COD = 1,5-cyclooctadiene), it is possible to combine two alkyne molecules with CO_2 affording six-membered lactones [128]; using internal alkynes they were able to obtain more reasonable yields of the lactone products. First, CO_2 coordinates to electron-rich metal centers in a η^2-form (see Fig. 7). Alkenes or alkynes in the presence of stoichiometric amounts of the metal–CO_2 complex form metallocycles, which are important intermediates in the lactone synthesis. The most widely studied metallocycles are the ones formed with Ni(0) precursors, the so-called oxa-nickelacycles.

Hoberg et al. [137] published in the 1980s a series of air-stable complexes where CO_2, a suitable Ni precursor and an unsaturated substrate, forms a series of metallocyclic complexes incorporating a carboxylate (O=C–O) moiety. As

Fig. 7 A η^2-(C,O) chelating CO_2 complex reported by Aresta et al.
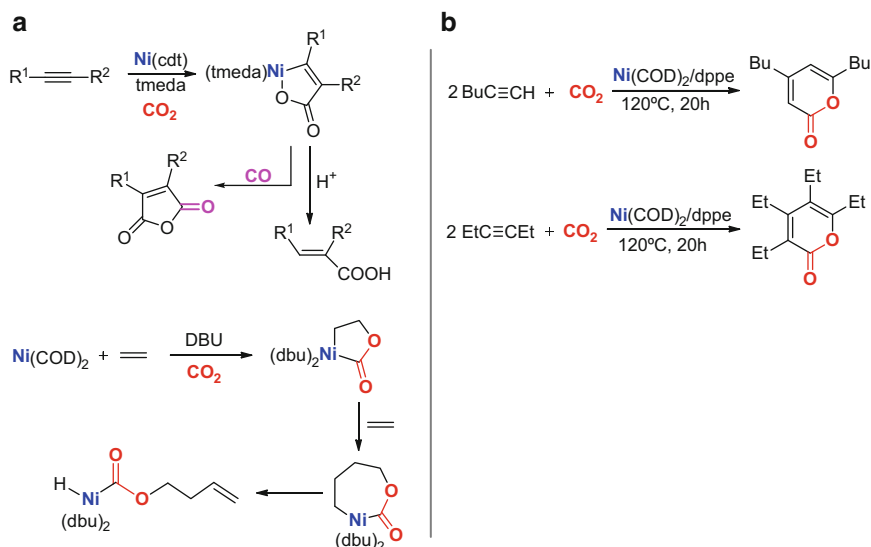
Scheme 23 (**a**) Hoberg's work on oxa-nickelacycles (cdt = cyclododeca-1,5,9-triene; COD = 1,5-cyclooctadiene; tmeda = tetramethylethylenediamine; dbu = 1,8-diazabicyclo[5.4.0] undec-7-ene) and (**b**) Inoue's work on quinone synthesis from alkynes

illustrated in Scheme 23a, these metallocycles can be useful precursors for other compounds by expanding the ring through incorporation of more ethene molecules or through ring opening to form unsaturated carboxylic structures. A clear disadvantage is the lack of true catalytic turnover, an aspect that has recently regained the attention of the scientific communities focusing on the direct coupling of alkenes and CO_2 [138–140]. An oxa-nickelacycle is also an important intermediate in the quinone synthesis from alkynes and CO_2 described by Inoue (Scheme 23b) [128].

Strained rings can be easily carboxylated [141], and the final product can vary in structural nature, but all reactions are formally CO_2 insertion reactions into C–C bonds. A major drawback, however, is that generally the reaction intermediate is a highly stable metallocycle. The lactone formation reaction is promoted by transition metals such as Ni or Rh, but the chemistry has little practical use as it requires stoichiometric amounts of metal with TONs rarely exceeding 1 making these processes far from economically acceptable. Recent work [138–140] has indicated that a delicate catalyst design may help to overcome these limitations in the (near) future.

The ability of Ni(0) to bind both unsaturated species (i.e., alkenes and alkynes) and CO_2 was further demonstrated by Tsuda et al. who prepared bicyclic α-pyrones

by treating α-,ω-diynes under high CO_2 pressure (~50 bar) and in the presence of a Ni(COD)-bis-trialkylphosphine pre-catalyst (10 mol%) [142]. Tailoring the ligand further, i.e., by using a N-heterocyclic carbene ligand (IPr) [143], led to significant improvement in catalyst efficiency and yields (>80%) of the α-pyrone products and allowed lowering of the metal loading (typically 5 mol%) needed for fast enough turnover and the pressure of CO_2 to 1 bar. This process can be considered a formal [2 + 2 + 2] cycloaddition reaction between diynes and CO_2. In Scheme 24a, the proposed mechanism for this reaction shows both a Ni(0)-bis-alkyne-CO_2 adduct and an oxa-nickelacycle intermediate.

Coupling between two alkynes has found useful applications in synthetic chemistry; it has been applied to the preparation of arylnaphthalene lignan lactones which are valuable natural products (Scheme 24b) with promising anticancer and antiviral properties. In this case, the alkynes were present in different precursor molecules, and the catalyst used was based on AgI. Anastas et al. [144] envisioned that the cross-coupling reaction between phenylacetylene, CO_2, and 3-bromo-1-
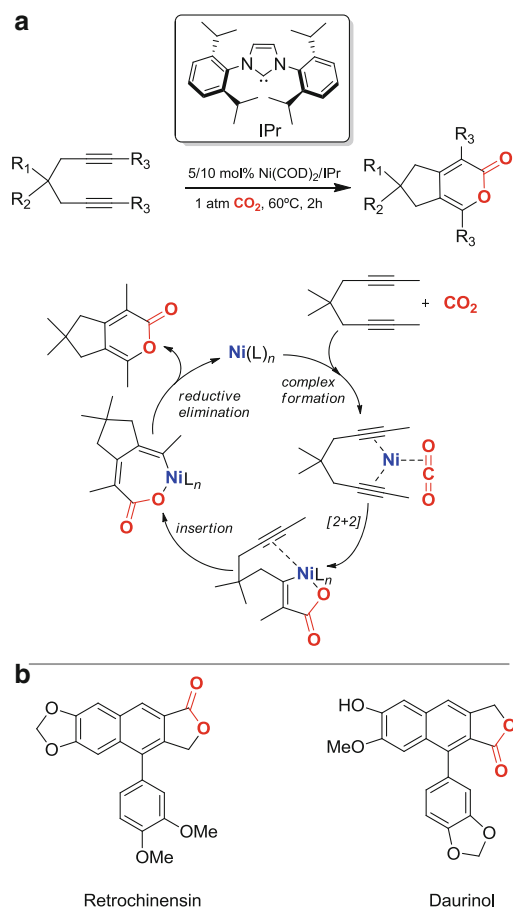
Scheme 24 (**a**) Reaction mechanism proposed by Tekavec et al. for the formation of bicyclic α-pyrones from diynes and CO_2. (**b**) Examples of natural products based on the α-pyrone core
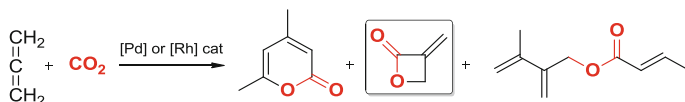
Scheme 25 Possible products derived from the reaction of allenes and CO_2

phenyl-1-propyne would generate the corresponding 1,6-diyne which could then subsequently cyclize to the naphthalene core through a formal $[2+2+2]$ cycloaddition.

Allenes can also be transformed into pyrones (Scheme 25) [145] albeit in lower yields to 4-membered lactones, which is the result of a formal $[2+2]$ addition of both cumulenes, CO_2 and the allene. In both cases, the catalysts employed were based on noble metals such as Pd and Rh. This $[2+2]$ addition represents the first example of this type of coupling reaction obtained by using CO_2 as a reagent. Allenes and CO_2 are *iso*electronic, but the energy gap between the HOMO (highest occupied molecular orbital) and LUMO (lowest occupied molecular orbital) is large; therefore, *homo*-coupling is energetically favored. In order to make the hetero-coupling reaction possible, optimization of the reaction conditions is essential to control the chemo-selectivity of the reaction. In order to stir the chemo-selectivity toward the 4-membered lactone product, high CO_2 pressures combined with low H_2 pressures and room temperature conditions are necessary. Despite all the efforts made, only limited yields of the lactone products were obtained, and therefore more sophisticated catalysts are required to make this process more attractive.

8 Outlook

This book chapter intends to give an overview of the most recent developments of the catalytic coupling of CO_2 with various reaction partners to give cyclized products while maintaining the formal oxidation state of the carbon center. Thus, these reactions are regarded as non-reductive couplings. Rather than giving a comprehensive overview of all the literature that has appeared over the years, typical examples of each class of coupling reaction involving CO_2 as a key reagent have been discussed emphasizing the synthetic merits and challenges that (still) need to be overcome. These coupling reactions involve the formation of saturated and unsaturated cyclic carbonates, oxazolidinones, imidazolidinones, cyclic ureas, quinazoline derivatives, and various lactone-based molecules. Despite this wealth of distinct and useful methodology yet developed, there still exists a need to expand the use of CO_2 as a coupling partner to get access to other types of (functional) molecules where the formal oxidation state of the CO_2 coupling partner may change through the catalytic event making the process a formal reductive coupling step [146]. It is not likely that the efforts to develop new and improved catalytic processes will lead to a net reduction of the global CO_2 emissions that we are currently facing, but its use as a carbon feedstock that is cheap, renewable, basically

nontoxic, and readily available in large quantities may help to present a viable carbon feedstock alternative for our fossil fuel-based economies. In this respect, research devoted to the design and implementation of modular, selective, and highly active catalysts can be regarded as a key strategy toward the increase of sustainable chemical processing. In the near future, this may help to preserve our standard of living and improving (where necessary) problems associated with raw material usage, energy consumption, and waste management. Undoubtedly, organometallic chemistry will continue to be an important discipline that can contribute both from a fundamental and application point of view providing the knowledge to create our future catalysts required in fine chemical and bulk chemical synthesis.

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