ACS Catalysis

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Recent Advances in the Catalytic Preparation of Cyclic Organic Carbonates

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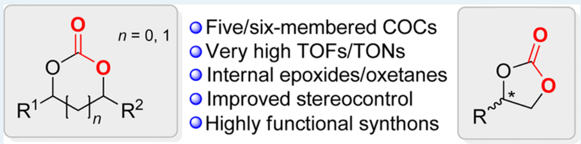


ABSTRACT: The catalytic formation of cyclic organic carbonates (COCs) using carbon dioxide (CO_2) as a renewable carbon feed stock is a highly vibrant area of research with an increasing amount of researchers focusing on this thematic investigation. These organic carbonates are highly useful building blocks and nontoxic reagents and are most commonly derived from CO_2 coupling reactions with oxirane and dialcohol precursors using homogeneous catalysis methodologies. The activation of suitable reaction partners using catalysis as a key technology is a requisite for efficient CO_2 conversion as its high kinetic stability poses a barrier to access functional organic molecules with added value in both academic and industrial laboratories. Although this area of science has been flourishing for at least a decade, in the past 2−3 years, significant advancements have been made to address the general reactivity and selectivity issues that are associated with the formation of COCs. Here, we present a concise overview of these activities with a primary focus to highlight the most important progress made and the opportunities that catalysis can bring about when the synthesis of these intermediates is optimized to a higher level of sophistication. The attention will be limited to those cases in which homogeneous metal-containing systems have been employed because they possess the highest potential for directed organic synthesis using CO_2 as molecular building block. This review discusses examples of exceptional reactivity and selectivity, taking into account the challenging nature of the substrates that were involved, and mechanistic understanding guiding the optimization of these protocols is also highlighted.

KEYWORDS: *carbon dioxide, homogeneous catalysis, organic carbonates, reactivity, selectivity*

1. INTRODUCTION

The use of carbon dioxide (CO_2) as a renewable carbon feed stock in organic synthesis has become an important goal for academic and industrial scientists.[1−9] Of particular interest is the development of chemical methodologies that can convert CO_2 to useful products. For example, it can be used in combination with water (or hydrogen) as a building block to produce chemicals and fuels.[10] Moreover, direct coupling with more complex chemicals (i.e., oxiranes and oxetanes) provides methodology toward value-added plastics and other products.[1,2,6] Despite the disadvantage of CO_2 having sluggish reactivity, recent work has unambiguously demonstrated that new opportunities may become available when proper catalytic methods are designed that help to improve the reactivity, selectivity or sustainability profiles of such processes. Among the most widely studied reactions in CO_2 catalysis is the formation of cyclic organic carbonates (COCs)[11−18] apart from their analogous and related linear carbonates[19] and poly(carbonates).[20−22] These COCs have been frequently associated with numerous applications involving them as nonprotic solvents, precursors for poly(carbonate) synthesis, electrolyte solvents, and more recently as useful intermediates in organic synthesis.[23−25] It is for these reasons, among others, that the interest in COC synthesis has slowly but surely shifted attention toward the preparation of more sophisticated synthetic intermediates, providing new catalytic processes that show increased reactivity behavior, improved enantio- and chemo-selectivity, and amplified substrate scope with excellent functional group tolerance. These endeavors can ultimately lead to the creation of secondary products derived from COC intermediates with applications in (bio)polymer synthesis[26] and pharmaceuticals.[27]

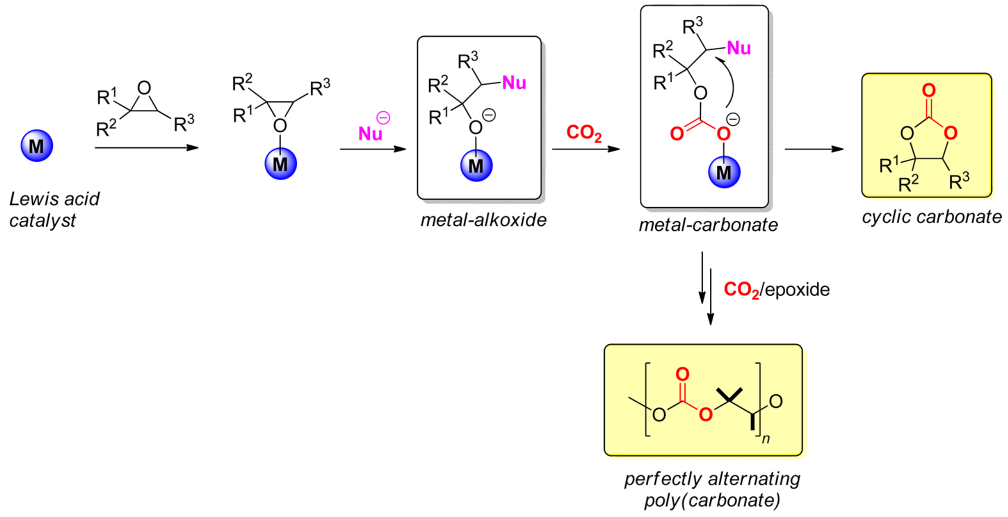
Direct coupling between CO_2 and oxiranes or oxetanes has become one of the focal points in CO_2 catalysis representing an atom-efficient transformation to selectively access COC and polycarbonates from inexpensive and readily available starting materials. An appropriate catalytic system is required to perform these reactions because the metal-free direct coupling of CO_2 and oxiranes is kinetically highly unfavorable as a result of extremely high barriers that are associated with this transformation. For example, the free energy barriers for the uncatalyzed reaction between propylene oxide (PO) and CO_2 in the gas phase was calculated by DFT and found to be 53 and 58 kcal·mol^{-1} for the two possible isomeric transition states, respectively.[28,29]

The most widely employed catalysts are homogeneous metal-based complexes. Different activation mechanisms relying on the activation of the oxirane/oxetane moiety or CO_2 have been proposed. Oxiranes/oxetanes are typically activated by interaction with a Lewis acid through M−O coordination

Received: November 28, 2014
Revised: January 14, 2015
Published: January 15, 2015

DOI: 10.1021/cs5018997
ACS Catal. 2015, 5, 1353−1370

Scheme 1. Key Steps for the Coupling of CO_2 and Oxiranes To Yield Polycarbonates (below) or COCs (top)[a]



[a]Abbreviations: M = metal complex, Nu = nucleophile.

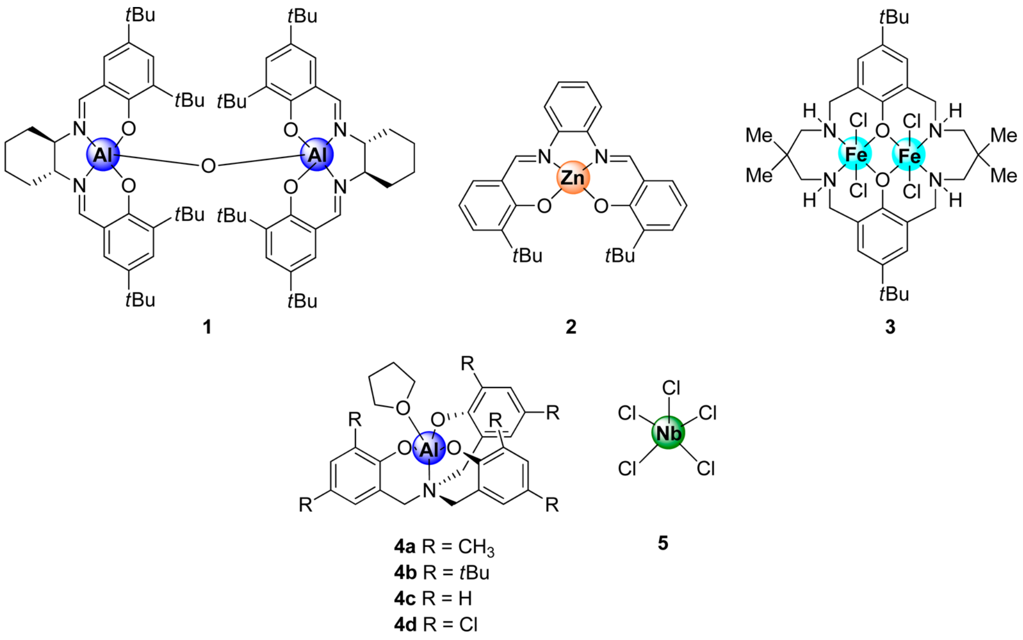


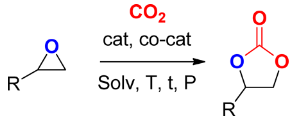
Figure 1. Homogeneous metal catalysts **1**−**5** active toward CO_2 coupling with terminal epoxides under mild reaction conditions.

patterns, followed by a nucleophilic attack and subsequent ring-opening, whereas CO_2 activation can occur both through nucleophilic and electrophilic attack. Regardless the catalytic system employed, in all cases, oxirane or oxetane activation requires a nucleophile. Although the nucleophile itself can be employed as catalyst, generally, (sub)stoichiometric amounts are required and elevated operating temperatures. Binary/bifunctional catalytic systems usually combine a Lewis acid and a suitable nucleophile (most often a halide), making the ring-opening procedure energetically less demanding and the subsequent CO_2 insertion easier (i.e., attack of the metal alkoxide intermediate on the carbon center of the CO_2 molecule). COC formation by metal-catalyzed coupling of CO_2 and oxiranes progresses according to a generally accepted sequence of steps as depicted in Scheme 1.[11−13,17,18]

Selectivity toward the formation of COCs arises from a specific balance between the components of the catalytic mixture, including the choice of substrate, metal catalyst, cocatalyst (nucleophilic additive), type of solvent, and temperature. In particular, the nature of the cocatalyst and its ratio with respect to the metal catalyst affect may dramatically influence the outcome of these coupling reactions. As will be highlighted throughout the text, homogeneous metal catalysts for efficient oxirane/CO_2 coupling reactions include mono- and bimetallic species as well as bifunctional systems that embed both the Lewis acid and the nucleophile within a single molecular entity.[13,17]

In this review article, we highlight the most recent developments in the field of catalytic cyclic organic carbonate (COC) synthesis, with a primary focus on those contributions that have helped to amplify the field of COCs having potential toward organic synthetic applications. Attention will therefore be given to the catalytic processes that have disclosed new reactivity patterns, improved activity profiles, and unusual

Table 1. Metal Catalyzed CO_2 Coupling with Terminal Epoxides[a]



entry[b]	R	cat. (mol %)	co-cat. (mol %)	solv.	T (°C)	t (h)	P (MPa)	conv (%)	selectivity (%)
1[35]	C_6H_5	**1** (2.5)	TBAB (2.5)	neat	25	24	0.1	98	n.d.
2[37]	nC_4H_9	**1** (2.5)	TBAB (2.5)	neat	25	24	0.1	87	n.d.
3[37]	CH_3	**1** (2.5)	TBAB (2.5)	neat	0	3	0.1	77	n.d.
4[38]	C_6H_5	**2** (2.5)	TBAI (2.5)	CH_2Cl_2	45	18	1	80	n.d.
5[38]	nC_4H_9	**2** (2.5)	TBAI (2.5)	CH_2Cl_2	45	18	1	66	n.d.
6[39]	CH_3	**2** (2.5)	TBAI (2.5)	CH_2Cl_2	45	18	1	90	n.d.
7[39]	nC_4H_9	**2** (2.5)	TBAI (2.5)	MEK	45	18	1	>99	n.d.
8[39]	nC_4H_9	**2** (2.5)	TBAI (2.5)	MEK	45	18	0.5	87	n.d.
9[39]	C_6H_5	**2** (2.5)	TBAI (2.5)	MEK	25	18	0.2	89	n.d.
10[39]	nC_4H_9	**2** (2.5)	TBAI (2.5)	MEK	25	18	0.2	86	n.d.
11[39]	CH_3	**2** (2.5)	TBAI (2.5)	MEK	25	18	0.2	73	n.d.
12[41]	C_6H_5	**3** (0.5)	PPN-Cl (1)	neat	25	25	0.1	17	n.d.
13[41]	CH_3	**3** (0.5)	PPN-Cl (1)	neat	25	48	0.1	91	n.d.
14[43]	nC_4H_9	**4a** (0.5)	TBAI (2.5)	neat	30	2	1	74	>99
15[43]	nC_4H_9	**4d** (0.5)	TBAI (2.5)	neat	30	2	1	91	>99
16[43]	nC_4H_9	**2** (0.5)	TBAI (2.5)	neat	30	2	1	46	>99
17[43]	nC_4H_9	**1** (0.5)	TBAB (2.5)	neat	30	2	1	50	>99
18[44]	C_6H_5	**5** (0.005)	TBAB (0.01)	neat	45	12	0.1[c]	91	n.d.
19[44]	CH_3	**5** (0.005)	TBAB (0.01)	neat	25	14	0.05[c]	99	n.d.

[a] Abbreviations used: TBAB = tetrabutylammonium bromide, TBAI = tetrabutylammonium iodide, PPN-Cl = bis(triphenylphosphine)iminium chloride, MEK = methyl ethyl ketone; n.d. = not determined/reported. [b] References given. [c] Partial pressure of CO_2 measured in the CO_2/Ar mixture.

selectivity. Homogeneous catalyst systems have proven to be superior in terms of their synthetic prospective, and therefore, this review will be limited only to catalytic technologies based on this class of systems. Further to this, a major focus will go to those reactions that are based on effective CO_2/epoxide couplings; epoxides and their precursors (alkenes) are abundant and their structural variety and accessibility allow in principle the preparation of a large collection of functional COC scaffolds.[30] The use of computation tools will also be emphasized where appropriate to highlight the use of theoretical analysis of metal-mediated conversion of CO_2 as to support the experimental efforts and to help to design improved and more active/selective catalyst systems for COC synthesis.[31] Finally, future directions are identified in which the formation of COCs (possibly derived from natural sources)[32,33] may help to advance the further valorization of a waste, carbon feedstock such as CO_2 and converting it into value-added organic matter of academic and industrial interest.

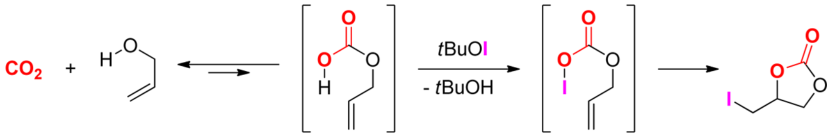
2. DEVELOPMENT OF IMPROVED REACTIVITY IN COC SYNTHESIS

2.1. COC Synthesis under Mild Reaction Conditions. In an effort to develop efficient chemical processes based on the exploitation of CO_2 as a renewable and inexpensive C_1 building block, its use has grown tremendously in recent years and currently includes both coupling reactions (for example, to prepare COCs and oxazolidinones) and reductive processes, leading to products including methanol, formic acid, and methane. Limiting our discussion to COC synthesis, a truly sustainable process for the preparation of cyclic carbonates should preferably employ a catalyst that shows high activity under mild reaction conditions (i.e., at low temperatures and CO_2 pressures) and potentially in waste gases such as flue gas.[34] However, to date, only a handful of the reported homogeneous catalysts show useful activity at low CO_2 pressures ($p(CO_2)$ below 1.0 MPa) and temperatures below 100 °C; these limitations therefore have spurred catalysis research toward the development of more energy efficient procedures and new catalyst structures for COC synthesis (Figure 1; **1**−**5**).

Among the different homogeneous catalytic systems active for cyclic carbonate formation under mild conditions, salen and salphen metal complexes have been extensively studied as active catalysts for direct CO_2 coupling with epoxides to form cyclic or polycarbonates. Salen and salphen ligands provide complexes with a rather planar geometry exerting a tetradentate coordination around the metal center and easy modulation of electronic and steric effects. Depending on the nature of the metal center, these complexes can also accommodate two labile ligands in two axial positions. Therefore, the nucleophile can be embedded or weakly coordinated to the catalyst, resulting in a dual effect: it can act as a nucleophile in the ring-opening of the epoxide or favor the coordination of the oxirane to the metal center by a trans ligand effect.[13]

Salen and salphen catalysts are characterized by an easy preparation, allowing for large-scale synthesis and potential commercial applications. They can also be fine-tuned from a reactivity point of view, by ad hoc structure modifications; the possibility of direct inclusion of a nucleophilic cocatalyst, variation in the type of active metal center, and formation of mono- and multinuclear catalysts. Among the reported salen and salphen catalysts active toward CO_2 coupling with (terminal) epoxides, North's group communicated a dinuclear μ-oxo-bridged Al(salen) complex (Figure 1; **1**) catalytically active at room temperature and atmospheric pressure of CO_2 for the formation of cyclic carbonates from terminal aliphatic and aromatic epoxides (entries 1 and 2, Table 1). The

Scheme 2. A CO_2 Conversion Strategy Developed by Minakata et al. To Trap an Elusive Carbonic Acid Intermediate with *t*BuOI



improved catalytic activity observed when compared with monometallic salen complexes has been ascribed to the presence of two neighboring metal centers capable of simultaneous activation of both oxirane and CO_2 by promoting an intramolecular nucleophilic attack of the alkoxide to the carbon atom of the activated CO_2 molecule.[35−37]

Shortly thereafter, Kleij's group reported on a mononuclear Zn(salphen) complex (Figure 1; **2**) active toward CO_2 coupling with terminal epoxides under moderate CO_2 pressures [$p(CO_2)$ = 0.2−1 MPa] and mild operating temperatures (T = 25−45 °C).[38,39] The high activity of the Zn(salphen) complex was ascribed to its constrained geometry imposed by the ligand scaffold, which imparts increased Lewis acid character to the catalytically active Zn ion. Moreover, the presence of bulky substituents (R = *t*Bu) in the ortho positions of the two iminiphenol donors prevents undesired dimerization and, thus, inactivation of the Zn(salphen) catalyst.[40] Although efficient, these Zn(salphen) systems suffer some limitations, requiring relatively high catalyst loadings (2.5 mol %) and a scope limited to terminal epoxides (entries 4−11, Table 1).

In a search for new catalytic systems capable of operating under mild reaction conditions, Williams and co-workers developed a novel dinuclear, macrocyclic Fe(III) complex (Figure 1; **3**) active for the selective formation of cyclic and polycarbonates, depending on the addition of a nucleophilic additive.[41] This system was active toward the formation of cyclohexene carbonate (CHC), propylene carbonate (PC), and styrene carbonate (SC) under mild conditions (T = 25 °C, $p(CO_2)$ = 0.1 MPa, t = 24−48 h, entries 12 and 13, Table 1); different from the dinuclear Al(III)salen system developed by North and co-workers, this Fe catalyst required only 1 equiv of nucleophilic cocatalyst to achieve quantitative cyclic carbonate formation under these conditions.

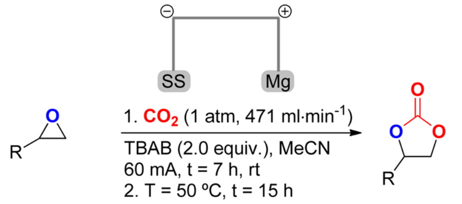
The Kleij's group developed novel homogeneous catalytic systems based on Lewis acidic and abundant metals, reporting on a new class of accessible Al(III)amino(triphenolate) catalysts (Figure 1, **4a−d**) characterized by high activity (vide infra) combined with a wide substrate scope and functional group tolerance.[42] Different from the salen/salphen based systems, the aminotriphenolate ligands impose a trigonal bipyrimidal coordination geometry around the Al(III) center and likely allows for more sterically congested substrates (cf., internal epoxides) to be coordinated/activated and converted into their respective COCs. Particularly, in the case of a binary catalyst, the presence of fewer donor atoms in the plane of the metal would be beneficial for sterically more congested substrates and more easily accommodate an incoming nucleophile approaching the substrate and entering the coordination sphere of the metal. The catalytic potential of catalysts **4a** and **4d** was evaluated by comparison with reported catalysts **1** and **2** using 1,2-epoxyhexane as a benchmark substrate under mild conditions (T = 30 °C, $p(CO_2)$ = 1.0 MPa, t = 2 h). When compared with Al(III)(aminotrisphenolate) catalysts **4a** and **4b**, both the bimetallic Al(III)salen **1** and the Zn(salphen) complex **2** proved to be less effective, observing roughly half of the activity of the Al complex **4d** when employed under similar experimental conditions (entries 14−17, Table 1).[43] This example actually reports one of the very few benchmarking experiments done under similar reaction conditions and application of an identical reactor set up, allowing for a direct comparison among the catalytic efficiencies of various catalyst structures in the formation of COCs.

Apart from changing the catalyst coordination mode, some research groups have explored the reactivity of other metals of the periodic table. For example, Kühn and Cokoja reported on the high catalytic activity of a commercially available Nb(V) salt (Figure 1; $NbCl_5$ **5**) in the coupling of CO_2 with terminal and internal epoxides.[44] When employed with an appropriate cocatalyst such as tetrabutylammonium bromide (TBAB) or dimethylaminopyridine (DMAP), this Nb(V) catalyst showed high catalytic activity under mild conditions (T = 25 °C) and at low concentrations of CO_2, thereby mimicking the waste gas stream of production plants by working with Ar/CO_2 mixtures (entries 18 and 19, Table 1).

Minakata and co-workers reported on an original approach to form COCs starting from unsaturated alcohols and *tert*-butyl hypoiodite (*t*BuOI). This methodology takes advantage of the acidic character of the alkylcarbonic acid generated from CO_2 and an unsaturated alcohol, in which iodination of the carbonic acid with *t*BuOI is the key reaction, which shifts the equilibrium to the cyclization product (Scheme 2) . Thus, the desired CO_2 conversion reaction does not require the use of strong bases, environmentally unfriendly metal reagents, or pressurized conditions. Both homoallylic and propargylic alcohols were successfully converted to their corresponding 5-membered COCs (18 examples, yields 64−94%) under extremely mild reaction conditions [$p(CO_2)$ = 0.1 MPa, T = −20 °C].[45] Although this is not a metal-catalyzed methodology, it readily gives access to functional COCs containing an iodomethyl group representing synthetically valuable building blocks as they can be readily converted into epoxy alcohols and triols.

Recently, Buckley and co-workers have studied the effect of several transition metal catalysts and electrode materials on the conversion of epoxides into COCs under a CO_2 flow using applied potential at atmospheric pressure and ambient temperature.[46] Initially, these studies involved the use of 1 equiv of Ni(II) catalyst [$Ni(BF_4)_2$], which in the presence of excess TBAB (which acts as both the nucleophile and the supporting electrolyte) gave, in most cases, quantitative yields of the corresponding COC starting from terminal epoxides (7 examples, yields 49−93%, Scheme 3). Then a less expensive and less toxic Cu(I) catalyst, $Cu(CH_3CN)_4(BF_4)$, was employed in the same experimental condition and found to be active in catalytic quantities for the conversion of terminal epoxides to the corresponding cyclic carbonates (cat. = 10 mol %, 7 examples, yields 70−97%). Quite surprisingly, electrocarboxylation of epoxides without added metal catalyst also led to the formation of the target COCs in poor to excellent conversion (7 examples, conversions: 33−91% using conditions

Scheme 3. Electrocarboxylation of Terminal Epoxides[a]



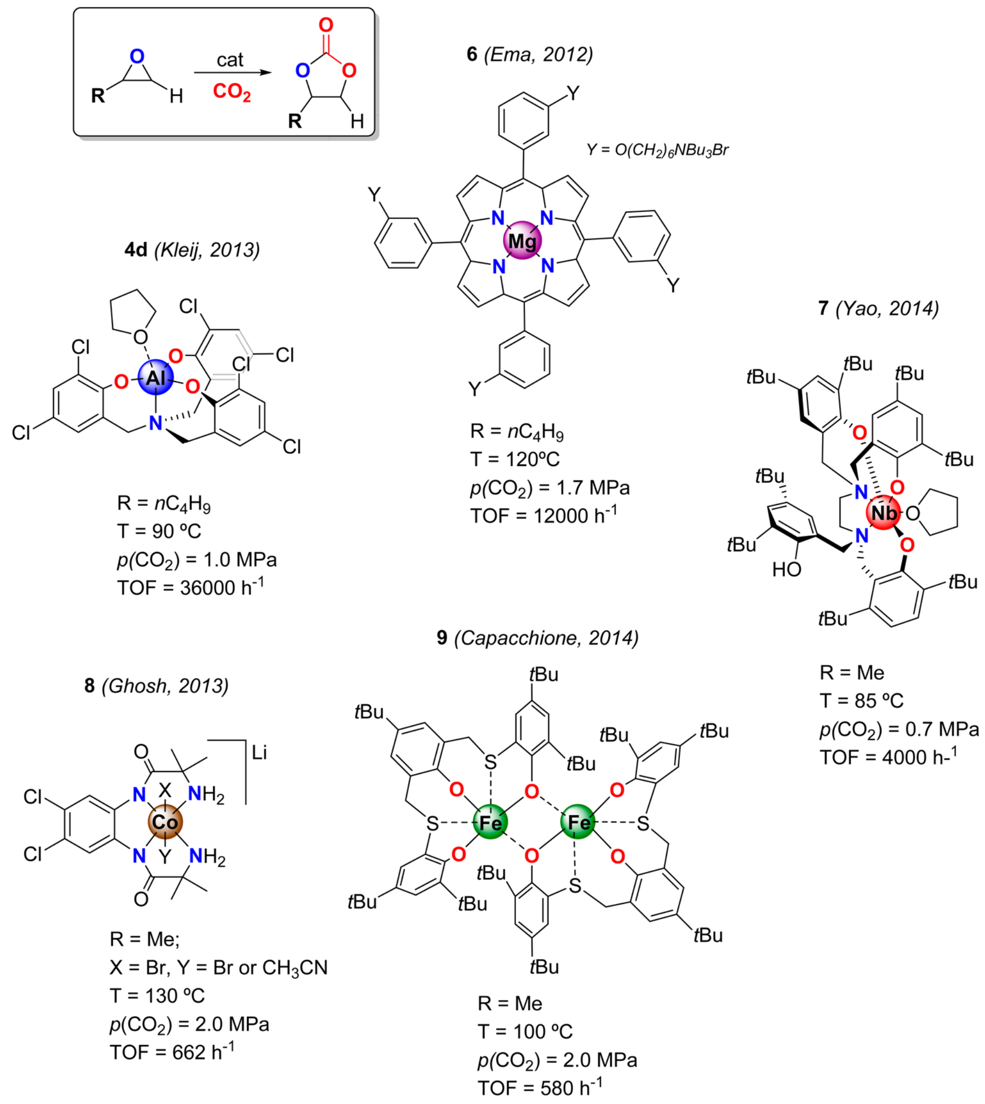
[a] SS = stainless steel cathode, Mg = magnesium anode.

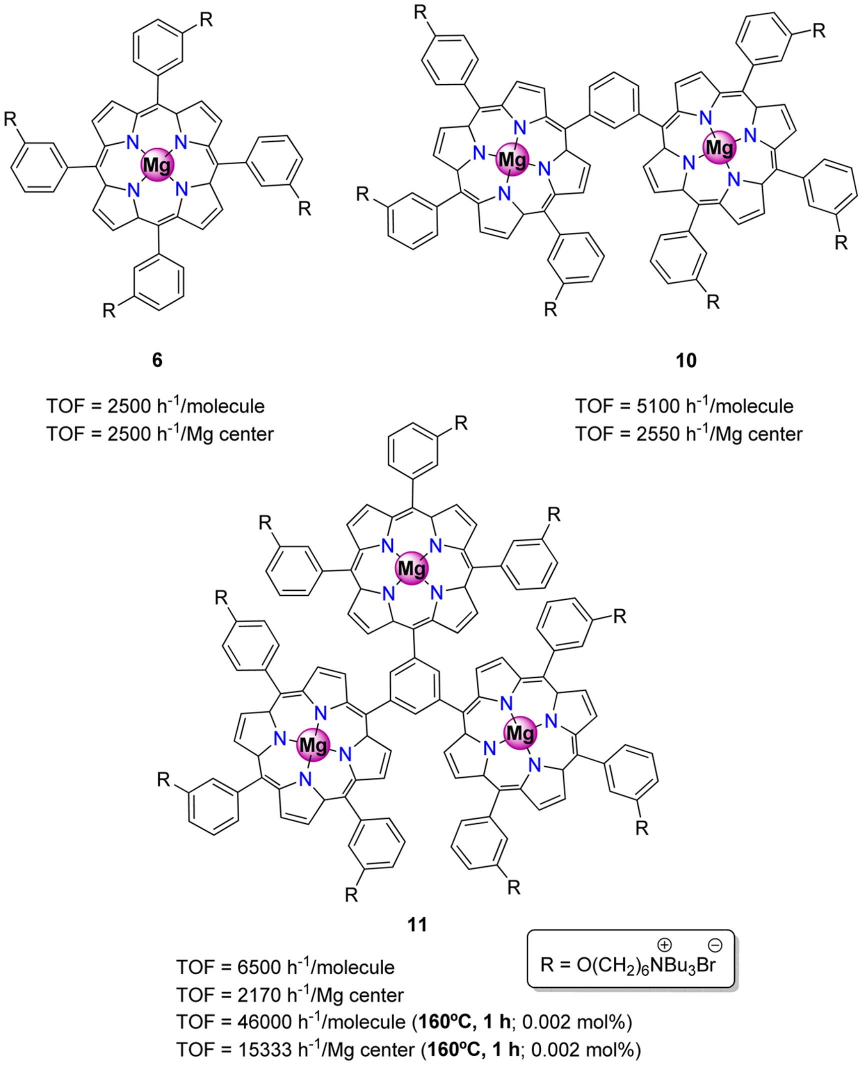
under (2) in Scheme 3), developing a system that obviates the use of a potentially toxic or expensive metal complex. Although the reaction times are rather long and the reaction set-up is quite laborious, the equipment required to perform this CO_2 incorporation reaction is fairly inexpensive and should be readily available.

2.2. High Reactivity; Catalysts with High TONs or Initial TOFs. As stated before, a variety of different metal-based catalyst systems (including binary and bifunctional ones) have been described in the literature for COC formation. Nonetheless, most of them require high catalyst loadings and only a limited amount of examples exhibit very high activities and a broad substrate scope. In this context, the development of highly efficient catalytic systems has been recently reported in the literature, obtained by careful design of new ligand scaffolds/structures to improve the CO_2 coupling to epoxides with high turnover numbers (TONs) and (initial) turnover frequencies (TOFs).

For example, Ghosh et al.[47] discovered a highly active, easily accessible Co(III) catalyst based on bisamido-bisamine ligands (**8**; Scheme 4). In an attempt to enhance the catalytic activity of this system, electron-withdrawing groups were installed in the ligand framework, increasing thereby the Lewis acidity of the metal center. These air and thermally stable Co(III) complexes display good activity and selectivity toward COC formation, displaying linear proportionality between the experimentally derived TOF and the electron-withdrawing nature of the ligands. Specifically, the most active (Lewis acid) catalyst was the one based on the dichlorinated ligand (Scheme 4), employed in conjunction with DMAP as cocatalyst in 1:2 molar ratio. With this binary catalyst, propylene oxide was converted to the corresponding COC in 3 h, measuring an average TOF of 662 h^{-1} (conditions: cat = 0.05 mol %, DMAP

Scheme 4. Structures of Successful Metal Complexes Exhibiting High Catalytic Activity for COC Synthesis





6

TOF = 2500 h^{-1}/molecule
TOF = 2500 h^{-1}/Mg center

10

TOF = 5100 h^{-1}/molecule
TOF = 2550 h^{-1}/Mg center

11

TOF = 6500 h^{-1}/molecule
TOF = 2170 h^{-1}/Mg center
TOF = 46000 h^{-1}/molecule (**160ºC, 1 h**; 0.002 mol%)
TOF = 15333 h^{-1}/Mg center (**160ºC, 1 h**; 0.002 mol%)

R = $O(CH_2)_6\overset{\oplus}{N}Bu_3\overset{\ominus}{Br}$

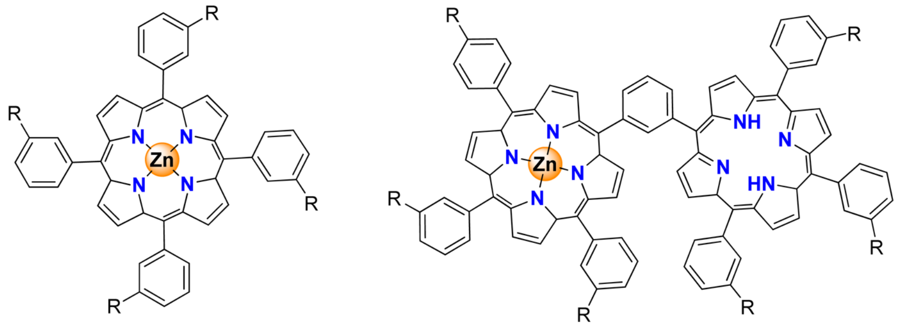
Figure 2. Mononuclear, binuclear and trinuclear Mg(porphyrin)-based catalysts used for CO_2/epoxide coupling reaction. Conditions: 1,2-epoxyhexane as substrate, 120 °C, 1.7 MPa of CO_2, 24 h, cat = 0.0003 mol %.

= 0.1 mol %, $p(CO_2)$ = 2.0 MPa, T = 130 °C). Moreover, this catalytic system exhibits a broad substrate scope, including aromatic an aliphatic terminal epoxides as well as some internal epoxides (vide infra), although the latter were converted at a relatively high reaction temperature of 150 °C.

Another interesting example was described by Capacchione and co-workers,[48] who developed a catalytic system based on an abundant and nontoxic metal (Fe). A dinuclear Fe(III) complex coordinated by dithioether-triphenolate-based ligands (**9**; Scheme 4) was devised, relying on the soft donor properties of the sulfur ligands to increase the Lewis acidity of the metal centers in comparison with catalysts based on N and O ligands, which have been extensively described in the literature. These labile Fe−S bonds facilitate the coordination of the epoxide to the hard Fe (III) metal centers, promoting the formation of COC by a subsequent ring-opening step of the coordinated substrate by the nucleophilic cocatalyst; thus, by combining this binuclear Fe(III) complex with TBAB as a nucleophilic additive, an active catalytic system for the conversion of propylene oxide to the corresponding COC could be developed with observed TON and TOF values of 3480 and 580 h^{-1}, respectively (conditions: **9** = 0.025 mol %, TBAB = 0.1 mol %, $p(CO_2)$ = 2.0 MPa, t = 24 h, T = 100 °C). So far, this is the highest reported TOF reported for an iron-based catalyst.

The use of amino phenolate ligands can be considered of prominent importance in the field of CO_2 coupling catalyst development as a result of their flexible coordination behavior. The coordination geometry around the metal center is different from the observed salphen planar geometry,[13] notably changing the number of donor atoms in the plane of the metal and the ability to activate more sterically congested substrates.[25,43] To date, several amino(triphenolate) complexes have been reported and employed as catalysts for the CO_2 coupling to epoxides. For instance, recent work carried out by Yao and co-workers describes the synthesis and catalytic application of ethylenediamino-bridged lanthanide phenolate complexes (M = Yb, Y, Sm, Nb (**7**); Scheme 4).[49] Propylene oxide was selected as a benchmark substrate to optimize the catalytic activity of **7**, choosing TBAI as the nucleophilic cocatalyst, affording a maximum TOF of 4000 h^{-1} (conditions: **7** = 0.01 mol %, TBAI = 0.04 mol %, T = 85 °C, $p(CO_2)$ = 0.7 MPa, t = 1 h).

The contributions from Kleij et al.[42,43] are prominent examples of amino(triphenolate)-based catalysts, in particular the results obtained for Al-based catalysts. This earth-abundant, nontoxic Lewis acidic metal allowed the preparation of several



12 13

Figure 3. Zn(porphyrin) **12**- and Zn-bis(porphyrin) **13**-based complexes used for comparative reasons. R = $-O(CH_2)_6NBu_3Br$.

robust amino(triphenolate) catalysts (Figure 1, **4a–d**). When tested as catalysts for CO_2 coupling to terminal epoxides in the presence of an appropriate cocatalyst, complex **4d**, having a double chloro substitution on each phenolate unit, turned out to be the most active species. Notably, for CO_2 coupling reactions carried out with 1,2-epoxyhexane, the synergic effect between **4d** and PPN-Br gave quantitative conversion to the corresponding cyclic carbonate (conditions: **4d** = 0.0005 mol %, PPN-Br = 0.05 mol %, $p(CO_2)$ = 1.0 MPa, T = 90 °C, t = 2 h), measuring an initial TOF of 36 000 h^{-1} (TON >100 000 after t = 18 h), which is the highest reported to date for a single-site Al(III)-based catalyst. Interestingly, when tested under the same conditions, Al(III) amino(triphenolate) complex **4d** (0.0005 mol %; cocatalyst 0.05 mol %) exhibited higher activity (TOF = 24 000 h^{-1}) than the bimetallic Al(III) complex **1** published by North (TOF = 15 000 h^{-1}), employed here using TBAI as the nucleophilic cocatalyst.[42]

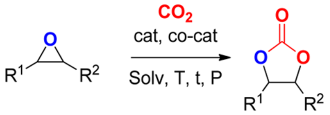
Porphyrin-based catalysts are another class of powerful catalytic systems toward CO_2 coupling with oxiranes. These catalysts are characterized by a planar geometry, which is beneficial for the coordination of terminal epoxides. Moreover, they can be used for the development of bifunctional molecular catalyst to evaluate the effect of the type of central metal atom and of the embedded cocatalyst. The most noticeable example is the work of Ema and co-workers.[50−52] Initially, utilizing bifunctional metalloporphyrins complexes containing both a Lewis acid (LA) center and nucleophilic peripherical pendants (1:4 LA/cocat site ratio) within the same molecular structure (**6**; Scheme 4), they have measured one of the highest TONs for homogeneous metal-based catalysts.[50] In particular, a TON of 103 000 (after t = 24 h) and initial TOF of 12 000 h^{-1} (measured after t = 1 h; conditions: **6** = 0.0008 mol %, T = 120 °C and $p(CO_2)$ = 1.7 MPa) were observed for a Mg(II)-based bifunctional catalyst **6**, obtained after careful optimization of the porphyrin structure in terms of the type of the Lewis acidic metal center and nucleophilic cocatalyst. To further enhance the catalytic activity of these bifunctional Mg(II) porphyrin systems, a Mg(II) porphyrin complex ligated to eight tetraalkylammonium bromide groups (i.e., a 1:8 LA/cocat site ratio) was prepared.[51] Consequently, owing to the increased number of anionic nucleophilic centers tightly coordinated to the cationic catalyst molecule, higher TONs were achieved after t = 24 h (TON = 138 000) and an increased initial TOF of 19 000 h^{-1} (conditions: cat =0.0005 mol %, $p(CO_2)$ = 1.7 MPa, T = 120 °C). For these bifunctional Mg(porphyrin)-based catalysts, the authors suggested a cooperative effect of embedding the nucleophilic moiety (Br) and the Lewis acidic metal center in a tight coordination sphere, leading to a simultaneous epoxide activation/nucleophile attack. It was indeed observed that by increasing the number of nucleophilic centers associated through ionic interactions to the same porphyrin framework, the measured TONs and TOFs were higher.

To further address the activity profiles of bifunctional metalloporphyrin catalysts, the same authors initiated the development of binuclear and trinuclear versions of these bifunctional catalytic systems with the aim of further increasing the observed TONs and TOFs.[52] The overall catalytic activity of the trinuclear porphyrin **11** (TOF = 6500 h^{-1}) is indeed higher than observed for dinuclear Mg(porphyrin) **10** (Figure 2; TOF = 5100 h^{-1}) and the corresponding mononuclear species **6** (TOF = 2500 h^{-1}) when employed in the same experimental conditions (cat = 0.0003 mol %, T = 120 °C, $p(CO_2)$ = 1.7 MPa, t = 24 h) for the conversion of 1,2-epoxyhexane to the corresponding COC. The activity on a per active site basis (i.e., per Mg center) shows that the metal sites in the dinuclear and trinuclear complexes **10** and **11** act virtually independently, with slightly lower TOF/Mg center values and no observable cooperativity between the individual metal sites (Figure 2). The lower TOF value per active center observed for trinuclear complex **11** may be ascribed to the reduced LA/cocat ratio (1:3 for **11** compared with 1:4 for **6**). In addition, the observed solubility of complex **11** in neat epoxide was lower than for **10** and **6**, possibly affecting the overall system activity.

The maximum TOF observed for the trinuclear Mg(porphyrin) **11** complex was 46 000 h^{-1} (Figure 2), and the maximum TON was 220 000 (0.0003 mol % **11**, 72 h, 120 °C) with a normalized TOF/Mg center of 15 333 h^{-1}. Unfortunately, the separate influence of the metal center on the catalytic turnover was not reported (i.e., the activity of the nonmetalated porphyrin scaffold) although Caló and co-workers previously demonstrated that bromide and iodide nucleophiles are also efficient catalysts, in particular at high reaction temperatures (T > 100 °C).[53]

The same study was extended to less Lewis acidic Zn(II)porphyrin-based catalysts.[52] Although the bifunctional Zn(II) catalysts demonstrate somewhat lower initial activity than the corresponding Mg(II)porphyrin, they have been shown to be more robust at higher temperature. The trinuclear Zn(II)-based catalytic system was active for 5 days, displaying a TON of 310 000 and an average TOF of 2580 h^{-1} (conditions: cat = 0.0003 mol %, $p(CO_2)$ = 1.7 MPa, T = 120 °C). Its robustness was further proved by employing this catalyst for t = 5 days at T = 160 °C, observing no appreciable catalyst decomposition, whereas under the same experimental con-

Table 2. Metal-Catalyzed Conversion of Internal Epoxides to the Corresponding Cyclic Carbonates via CO_2 Coupling[a]



entry[b]	R^1	R^2	cat. (mol %)	cocat. (mol %)	solv	T (°C)	t (h)	$p(CO_2)$ (MPa)	conv (%)
1[56]	C_6H_5	C_6H_5	**1** (2.5)	TBAB (2.5)	neat	85	72	1	>99
2[56]	CH_3	CH_3	**1** (2.5)	TBAB (2.5)	neat	85	24	1	49
3[57]	CH_3	CH_3 (trans)	**15** (0.5)	TBAB (5)	MEK	85	18	1	83
4[57]	CH_3	CH_3 (trans)	**14c** (0.5)	TBAB (5)	MEK	85	18	1	82
5[58]	CH_3	CH_3	**14a** (0.5)	TBAB (5)	MEK	85	18	0.2	53
6[58]	CH_3	CH_3 (cis)	**14a** (0.5)	TBAB (5)	MEK	85	18	0.2	39
7[58]	CH_3	CH_3 (trans)	**14a** (0.5)	TBAI (5)	MEK	85	18	0.2	69
8[42]	C_6H_5	C_6H_5	**4d** (0.5)	TBAB (5)	MEK	90	42	1	84 (82)[c]
9[42]	CH_3	CH_3 (trans)	**4d** (0.5)	TBAB (5)	MEK	90	42	1	99 (98)[c]
10[59]	CH_3	CH_3 (cis)	**16a** (2.5)	TBAB (5.0)	neat	25	24	0.1	42[d]
11[59]	CH_3	CH_3 (cis)	**16b** (2.5)	TBAB (5.0)	neat	25	24	0.1	36[d]
12[49]	CH_3	CH_3 (78% trans)	**7** (0.2)	TBAB (0.8)	neat	84	45	1	66[e]
13[47]	$-(CH_2)_7-$		**17** (10^{-3})	DMAP (2×10^{-3})	neat	150	5	2	83[f]

[a] Abbreviations used: TBAB = tetrabutylammonium bromide, DMAP = dimethylaminopyridine, MEK = methyl ethyl ketone; n.d. = not determined/reported. [b] References given. [c] Isolated yields in parentheses. [d] Selectivity cis/trans = 95:5. [e] Selectivity cis/trans = 19:81. [f] Selectivity cis/trans = 90:10.

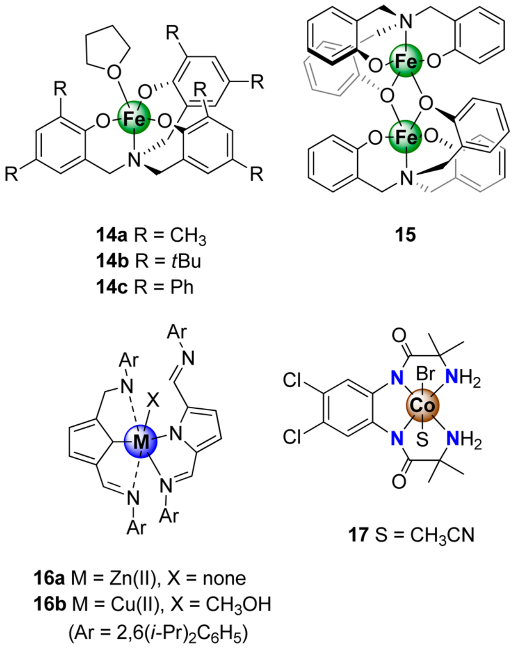
ditions, the trinuclear Mg-based catalyst **11** decomposed. Further investigations focused on mononuclear species **13** comprising two covalently bonded porphyrin rings (cf. **12** and **13**, Figure 3). Complex **13** displays an expected higher activity than the corresponding mononuclear monoporphyrin species **12**, indicating the importance of a higher local concentration of bromide nucleophile supported by the observed TOFs (8500 h^{-1} for **13** vs 5700 h^{-1} for **12**; conditions: cat = 0.0003 mol %, $p(CO_2)$ = 1.7 MPa, T = 120 °C, t = 3 h).

3. CONVERSION OF INTERNAL EPOXIDES AND OXETANES

Although formation of COCs starting from activated and unactivated terminal epoxides has been extensively covered in the literature over the past 10 years, synthetically challenging di- and trisubstituted epoxides have been seldom addressed as CO_2 coupling partners. Nevertheless, the preparation of COCs from internal epoxides represents an ambitious target for the development of CO_2-based protocols starting from synthetically accessible epoxides that are easily prepared using standard epoxidation methodology from (renewable) olefinic compounds, for example, unsaturated fatty acids[54] and terpenes.[26] Not only can these naturally occurring compounds be used with or without minimal prior purification, other promising substrates can also be obtained as byproducts of the biorefinery industry. For example, 1,4-cyclohexadiene is a common byproduct of unsaturated fatty acid metathesis derived from the oleochemical supply chain. This simple bis-alkene can be readily converted to the corresponding mono- and diepoxide or partially reduced to give CHO in a sustainable fashion. The unsaturated epoxides have been employed with some success for the preparation of unsaturated polycarbonates, which can easily undergo postpolymerization functionalization.[32,33] Moreover, the corresponding cyclic carbonate product, cis-cyclohexadiene carbonate is the simplest organic carbonate obtained from methabolism of microbes and fungi. Interestingly, a recent review from Yue et al.[27] has nicely covered the occurrence of many natural COCs, of which the larger part involves di- and trisubstituted carbonate patterns, providing further motivation for the development of catalytic procedures for internal epoxide/CO_2 couplings.

These internal epoxides have so far proven to be mostly unreactive when employing salen- and salphen-based metal catalyst (with the notable exception of CHO, vide infra). In particular, the Zn(salphen) system **2** (Figure 1) reported by Kleij and co-workers showed a limited catalytic activity toward the conversion of internal epoxides,[38,39] observing some degree of success when working with a CO_2-rich or supercritical CO_2 reaction medium.[55] The bimetallic μ-oxo Al(salen) complex **1** (Figure 1) reported by North et al. also exhibited some success when employed as CO_2 coupling catalyst with internal epoxides, observing quantitative formation of the corresponding cyclic carbonates starting from 1,2-diphenyloxirane and 1,2-dimethyloxirane. Although carried out under rather mild reaction conditions (**1** = 2.5 mol %, TBAB = 2.5 mol %, T = 60 °C, $p(CO_2)$ = 1.0 MPa, t = 72 h, entries 1 and 2 of Table 2), these reactions require relative long reaction times.[56]

Homogenous metal catalysts characterized by a more flexible structure have also been tested in the context of CO_2 fixation on internal epoxides. Amino(trisphenolate)-based catalytic systems, in particular, have shown to be more active toward internal epoxides conversion than salen- and salphen-based catalysts. Kleij and co-workers have shown that differently substituted Fe(III)amino(trisphenolate) catalysts (Figure 4) were active catalysts for the conversion of 2,3-epoxybutane (2,3-dimethyloxirane) to the corresponding COC (**14c** or **15** = TBAB = 0.5 mol %, T = 85 °C, $p(CO_2)$ = 1.0 MPa, t = 18 h, entries 3 and 4, Table 2).[57] In an attempt to broaden the scope of these Fe(III)amino(trisphenolate) catalysts, the same group reported on the conversion of different internal epoxides to the corresponding COCs using **14a** as catalyst:[58] Despite the relatively low applied CO_2 pressure, in all cases, moderate to good yields were observed (yield: 39–69%, **14a** = TBAB = 0.5 mol %, T = 85 °C, $p(CO_2)$ = 0.2 MPa, t = 18 h, entries 5–7, Table 2). Different from what previously was reported for terminal epoxides, TBAB is the preferred cocatalyst for these internal epoxides as a probable result of its reduced size of bromide compared with iodide. The use of an iodide-based



14a R = CH_3
14b R = *t*Bu
14c R = Ph

15

16a M = Zn(II), X = none
16b M = Cu(II), X = CH_3OH
(Ar = 2,6(*i*-Pr)$_2$$C_6H_5$)

17 S = CH_3CN

Figure 4. Homogeneous metal-based catalysts active toward formation of cyclic carbonates from internal epoxides.

nucleophile significantly reduced the observed yields of the COC products.

As mentioned previously, the use of Al(III)amino(triphenolate) catalysts improved the overall catalytic system activity while broadening the substrate scope including internal epoxides (entries 8 and 9, Table 2). Most internal epoxides were quantitatively converted to the corresponding COCs at low catalyst loadings, although higher reaction temperatures were required to achieve quantitative conversions (4 examples, yields 55−98%, **4d** = TBAB = 0.5 mol %, T = 90 °C, $p(CO_2)$ = 1.0 MPa, t = 42 h).[42] Nevertheless, this catalytic system is not only one of the most active reported to date, but also one of the most versatile in terms of substrate scope.

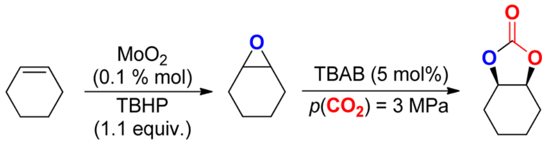
Recently, Muralidharan and co-workers reported on the synthesis of Zn(II) (**16a**) and Cu(II) (**16b**, Figure 4) complexes based on 2,5-bis{*N*-(2,6-diisopropylphenyl)-iminomethyl}-pyrrole ligands among others.[59] These complexes have shown activity toward conversion of internal epoxides to their corresponding COCs under mild conditions (2 examples, yields 36−42%, cat. = 2.5 mol %, TBAB = 5 mol %, T = 25 °C, $p(CO_2)$ = 0.1 MPa, t = 24 h, entries 10 and 11, Table 2). Although the reported yields are not quantitative, the attractive feature of these catalysts is that they are active at room temperature and at low CO_2 pressure.

More flexible lanthanide bridged (polyphenolate) catalysts such as **7** have been employed with limited success as catalyst for CO_2 fixation on internal epoxides. In particular, 2,3-epoxybutane (mixture of isomers, 22:78 cis/trans) was converted in 66% yield to the corresponding COC with overall retention of configuration (19:81 cis/trans; **7** = 0.2 mol %, TBAB = 0.8 mol %, T = 85 °C, $p(CO_2)$ = 1.0 MPa, t = 45 h, entry 12, Table 2).[49]

The bisamino-bisamide Co(III) complex **17** (Figure 4) was also active toward the formation of COCs from internal epoxides. Although the reported scope is limited to a few cyclic scaffolds and the operating temperature is rather high (150 °C), they were able to obtain cyclooctene carbonate in quantitative yield (entry 13, Table 2).[47] This can be considered as the first example cyclooctene carbonate synthesis via direct CO_2 coupling, as this compound is generally obtained in only moderate yields via Pd(II) catalyzed oxidative coupling of CO with diols.[60]

One-pot olefin-to-COC conversion was also applied to the conversion of internal olefins, although only for the case of cyclohexene oxide (CHO). Remarkably, *cis*-cyclohexene carbonate (CHC) was selectively formed in 84% yield, which is one of the highest reported yields for this type of reaction. The reaction conditions included the use of a nearly stoichiometric amount TBHP and low loading of the epoxidation catalyst ($MoO_2(acac)_2$ = 0.1 mol %) operated at 100 °C for 1 h, whereas in the second step, TBAB (5 mol %) was used as catalyst at 140 °C for 6 h at a CO_2 pressure of 3.0 MPa for the epoxide/CO_2 coupling reaction (Scheme 5).[61]

Scheme 5. One-Pot Conversion of Cyclohexene Oxide (CHO) to the Corresponding Cyclohexene Carbonate (CHC)[a]

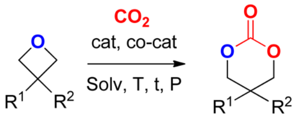


[a]TBHP = *tert*-butyl hydroperoxide.

Compared with epoxides, oxetanes are more challenging substrates for direct coupling reactions involving CO_2 because of their lower reactivity, although this is not due to difference in ring strain energy released upon ring-opening because these values are rather comparable to epoxides.[62] There are other kinetic barriers associated with their conversion, features that are not yet fully understood. The resulting six-membered COC products from oxetane/CO_2 coupling reactions have lower thermal stabilities. Five-membered COCs are thermodynamically more stable than the corresponding six-membered COCs: the latter, in particular, undergo easy ring-opening polymerization (ROP) processes, leading to polycarbonates, whereas this process is thermodynamically disfavored for five-membered COCs.[63,64] This reactivity behavior has been studied in detail by computational methods.[65] For example, coupling of trimethylene oxide with CO_2 occurs, at least in part, through the formation of a 6-membered cyclic carbonate intermediate. Ring-opening of trimethylene carbonate has an enthalpy of -11.3 kcal·mol^{-1} in the gas phase, which is more exothermic than the values calculated for the ring-opening of five-membered cyclic carbonates (-1 to -8 kcal·mol^{-1}) under similar conditions, and explains why ring-opening polymerization of six-membered cyclic carbonates is feasible (vide infra). Ring-opening of five-membered cyclic carbonates, however, requires loss of a CO_2 molecule as an entropy gain to compensate the unfavorable free energy barrier of the process. Thus, six-membered COCs can be considered as highly valuable intermediates/monomers for (functionalized) polycarbonate applications if selectively prepared.

Selective six-membered COC preparation from direct coupling to oxetanes has been seldom addressed in the literature, the main examples including the M-(aminotriphenolate) catalysts (M = Al, Fe) developed by Kleij and co-workers and the selective depolymerization strategies reported by the group of Darensbourg. Kleij's

Table 3. Catalytic Conversion of Oxetanes and CO_2 into Six-Membered COCs[a]

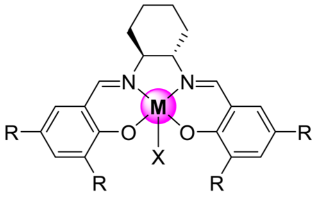


entry[b]	R^1	R^2	cat. (mol %)	cocat (mol %)	solv.	T (°C)	t (h)	$p(CO_2)$ (MPa)	conv. (%)	selectivity (%)
1[42]	H	H	**4d** (0.5)	TBAB (2.5)	MEK	70	4	1	95	>99
2[42]	CH_3	CH_3	**4d** (2.5)	TBAB (2.5)	MEK	70	66	1	26	54
3[66]	H	H	**18a** (0.3)	TBAB (0.6)	neat	110	24	3.5	46.7	79.1
4[70]	H	H	**18b** (0.3)	TBAB	Tol	70	24	3.5	73.7	37.4
5[70]	H	H	**18b** (0.3)	TBAB (0.6)	Tol	60	24	3.5	33.9	86.7
6[70]	H	H	**18b** (0.3%)	TBAB (0.6)	Tol	60	24	1	46.6	53.5
7[72]	Me	OMe	**18b** (1.2×10^{-2})	$TBAN_3$ (2.4×10^{-2})	neat	110	24	3.5	22.4	n.d.
8[64]	H	H	$VO(acac)_2$ (2.5)	TBAB (2.5)	neat	60	4	3.5	57	98.2
9[64]	H	H	$VO(acac)_2$ (5.0)	TBAB (5.0)	neat	50	4	3.5	56	>99
10[64]	H	H	$VO(acac)_2$ (5.0)	TBAB (5.0)	Tol	60	4	3.5	84	>99
11[58]	CH_3	CH_3	**14a** (0.5)	TBAI (5.0)	MEK	85	66	0.2	28	n.d.
12[58]	CH_3	CH_2OH	**14a** (2.5)	TBAB (2.5)	MEK	85	66	0.2	38	n.d.

[a] Abbreviations used: TBAB = tetrabutylammonium bromide, TBAI = tetrabutylammonium iodide, $TBAN_3$ = tetrabutylammonium azide, MEK = methyl ethyl ketone, Tol = toluene; n.d. = not determined/reported. [b] References given.

group tested both Fe(III)- and Al(III)-based amino(triphenolate) catalytic systems for the conversion of oxetanes to the corresponding 6-membered cyclic carbonates.[42,58] Al(III)-based catalyst **4d** was employed as catalyst for the conversion of unsubstituted trimethylene oxide, and quantitative conversion to the corresponding trimethylene carbonate was observed in 4 h (entry 1, Table 3)[42] with nonobservable formation of the polycarbonate side product.

The group of Darensbourg reported on Co(III) and Cr(III) salen complexes (**18a–b**; Figure 5) active toward the selective formation of six-membered cyclic carbonates and polycarbonates starting from substituted and unsubstituted oxetanes.[66] Co(III) salen complex **18a** was active toward the formation of trimethylene carbonate by coupling of CO_2 with trimethylene oxide in the presence of TBAB as cocatalyst (entry 3, Table 3), however, with limited selectivity toward the cyclic carbonate product. This behavior is ascribed to the spontaneous ring-opening polymerization of six- and seven-membered COCs, which occurs at all temperatures (ΔH_p is negative and ΔS_p is positive), as depicted in Scheme 6.[67−69]

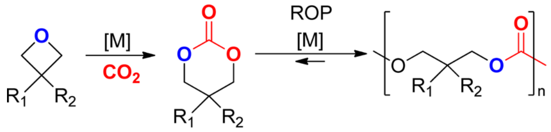


18a: R = *t*Bu; M = Co(II), X = none
18b: R = *t*Bu; M = Cr(III), X = Cl

Figure 5. Salen complexes employed for the synthesis of six-membered COCs from oxetanes.

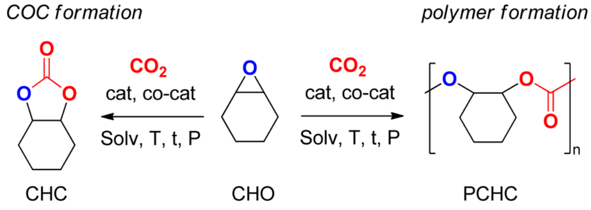
Similar results were obtained for the catalytic activation of trimethylene oxide with Cr(III) salen catalysts: although in this case, lowering the operating temperature from 70 to 60 °C resulted in much lower conversion levels, the selectivity toward the formation of the corresponding trimethylene carbonate increased dramatically (cf. entries 4 and 5, Table 3).[70] In addition, the applied CO_2 pressure plays an important role in the overall process selectivity, since it has also been shown computationally that CO_2 insertion in the salen-based M-alkoxide is the rate-limiting step (cf., entries 5 and 6, Table 3).[31,71] Darensbourg and co-workers also reported on a binary systems composed of a simple metal complex, $V(acac)_2$, and an onium salt (TBAB) active toward the selective preparation of trimethylene carbonate starting from trimethylene oxide.[64] In particular, when adding a noncoordinating cosolvent (toluene), trimethylene carbonate was formed in 4 h (entries 8–10, Table 3) in high chemoselectivity and conversions of up to 84%.

Scheme 6. Spontaneous ROP of Six-Membered Cyclic Carbonates Facilitated by a Metal Catalyst



Coupling reactions of CO_2 with more demanding 3,3′-disubstituted oxetanes have shown, so far, lower degrees of success (entries 2, 7, 11, 12; Table 3) giving lower conversions and significantly poorer selectivities toward the COC as a result of competitive ROP of the product. This challenge still remains to be solved as to capitalize on the use of six-membered COC in organic synthesis. The 3,3′-dimethyl-substituted oxetane was converted into its COC using Al(aminotriphenolate) complex **4d**/TBAB as binary catalyst, affording the targeted product with moderate selectivity (54%) and low yield (26%; entry 2, Table 3).[42] Alternatively, the use of 3-benzyloxymethyl-3-methyloxetane catalyzed by Cr(salen) complex **18b** and $TBAN_3$ resulted in the preferred formation of the polycarbonate species (entry 7, Table 3). This behavior has been ascribed to an increased steric hindrance of the substituents at 3-position.[72] Similar reactivity behavior was also noted by Kleij and co-workers for the substrates 3,3-dimethyloxetane and 3-methyl-3-methoxymethyloxirane using Al(III) or Fe(III) aminotriphenolate-based catalysts (entries 2, 11, 12, Table 3).[42,58] In general, more sterically hindered substrates such as the 3,3-disubstituted oxetanes require increased reaction times and give modest results in terms of conversion and selectivity toward the corresponding COCs. Thus, the selective, high yield synthesis

Table 4. Metal-Catalyzed Conversion of CHO to CHC and PCHC[a]



entry	cat (mol %)	cocat (mol %)	T (°C)	t (h)	$p(CO_2)$ (MPa)	conv. (%)	CHC (%)	PCHC (%)
1[41]	**3** (0.1)		80	24	1.0	70	<1[b]	>99
2[41]	**3** (1.0)	PPN-Cl (2.0)	80	24	0.1	90	>99[c]	0
3[86]	**14a** (0.5)	PPN-Cl (0.5)	85	3	8.0	98		>99
4[86]	**14a** (0.5)	PPN-Cl (5.0)	85	3	8.0	85	>96[c]	0

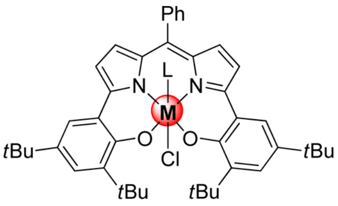
[a] All reactions were performed without solvent. [b] *trans*-CHC. [c] *cis*-CHC.

of substituted six-membered COCs through direct CO_2/oxetane coupling still remains an open challenge.

4. CONTROL OVER SELECTIVITY FEATURES IN COC PREPARATION

4.1. Chemoselectivity: The Case of Cyclohexene Oxide (CHO). Cyclohexene oxide (CHO) can be regarded as a typical benchmark substrate to test simultaneously the activity and chemoselectivity of a given CO_2 coupling catalyst. Most of the catalytic systems reported to date couple CHO with CO_2 unselectively to give the corresponding bicyclic carbonate (CHC) along with substantial amounts of the corresponding polycarbonate PCHC (Table 4). Unlike polycarbonates derived from linear (acyclic) epoxides, the resulting polymerization product poly(cyclohexene)carbonate (PCHC) is not prone to undergo (spontaneous) depolymerization via a backbiting mechanism (vide infra).[65,73] The formation of the cyclic carbonate is generally prevented because of the ring strain placed on the five-membered carbonate ring to accommodate the conformational requirements of the cyclohexyl ring and, as such, the activation barrier for CHC formation is >80 kJ·mol^{-1} higher in energy than that of PCHC.[74,75] Therefore, the development of catalytic systems that can selectively convert CHO into the corresponding polycarbonate PCHC has reached a high level of sophistication, with seminal contributions reported by the groups of Darensbourg,[22,76] Coates,[77,78] Nozaki,[79,80] and Lu.[81,82]

In search of catalytic systems for the synthesis of PCHC providing alternatives to the well-known Co(III) and Cr(III) salen complexes,[5] Nozaki and co-workers reported on the use of tetravalent Ti(IV) and Ge(IV) complexes coordinated by a trianionic $[N_2O_2]$-tetradentate (BOXDIPY) ligand and a monoanionic ancillary ligand to mimic (salen)MX complexes. Different tetravalent metal complexes such as **19a** (Figure 6, M = Ti) and **19b** (Figure 6, M = Ge) that are active toward the selective formation of PCHC (**19a** = **19b** = PPN−Cl = 0.005 mol %, $p(CO_2)$ = 2.0 MPa, T = 60 °C, t = 12 h) were designed. Although under these conditions the yields of PCHC were quite low (46% for **19a** and 36% for **19b**, respectively), the resulting PCHC is highly regular (>99% carbonate links), with respectable M_n values of 13 000−14 000 and polydispersities in the range 1.12−1.27.[83] This recent work further demonstrates that the formation of PCHC is fairly easy with a proper catalyst design, whereas the *selective* formation of the corresponding COC (CHC) is more challenging.[11]



19a M = Ti(IV), L = THF
19b M = Ge(IV)

Figure 6. (BOXDIPY)MCl complexes **19a** and **19b** used for CHO/CO_2 coupling reactions.

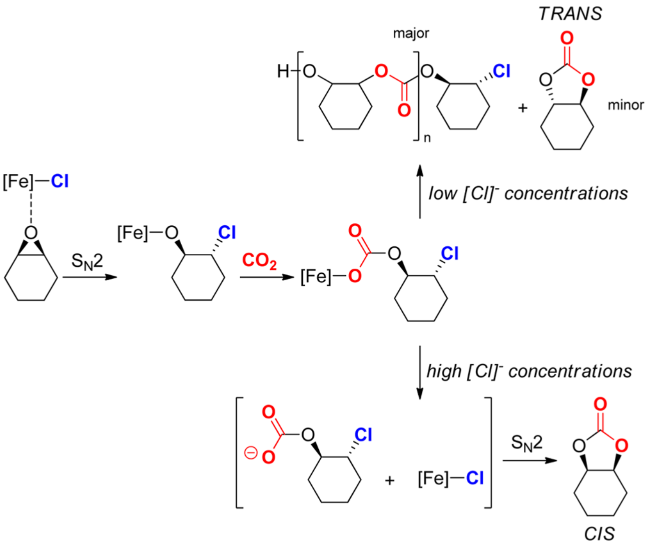
Examples of selective *and* high yield preparation of CHC via CO_2 coupling reactions using CHO as substrate are still limited, although some promising results have been achieved in recent years.[44,56,61,84,85] Pescarmona and co-workers reported on a binary Zn(II)(salphen) **2**/TBAI catalytic system (for the structure of **2**, see Figure 1) operated under $scCO_2$ to boost the selectivity and yield toward the COC product. Interestingly, in a conventional reactor setup (autoclave reactor), up to reaction temperature of 105 °C, no observable formation of carbonate product from CHO was noted.[38,39] The use of $scCO_2$ turned out to be crucial because it allowed for all reactants to (partially) coexist in one phase, giving a moderate yield of the corresponding CHC (yield = 38%; reaction conditions: **2** = 0.05 mol %, TBAI = 0.25 mol %, no cosolvent, $p(CO_2)$ = 8.0 MPa, T = 80 °C, t = 5 h).[55]

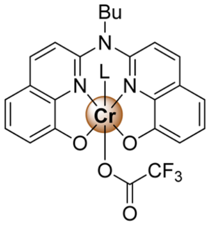
The groups of Kleij and Williams developed catalytic systems which can *selectively* produce CHC or PCHC by slight changes in the experimental conditions. For instance, the previously mentioned dinuclear Fe(III) complex **3**[41] reported by Williams and co-workers (Figure 1) proved to be also active in the context of CO_2 coupling reactions involving internal epoxides. Particularly, in the case of CHO, this catalyst could selectively produce *cis*-CHC or PCHC by changing the operating pressure and cat/cocat ratio (entries 1 and 2, Table 4). At high CO_2 pressure ($p(CO_2)$ = 1.0 MPa) and in the presence of catalytic quantities of the bimetallic catalyst **3** (i.e., no nucleophilic cocatalyst added), exclusive copolymerization took place (CHO conversion up to 70%), thereby selectively obtaining the PCHC copolymer with good TONs of 694 (entry 1, Table 4). The polycarbonate was of excellent quality: the resulting atactic copolymer contained >99% carbonate linkages and the M_n was 11 700 with a narrow molecular weight distribution of 1.13. ^1H NMR peak assignment and MALDI-ToF mass spectral analysis of the PCHC obtained at low CHO conversions showed isotopic distributions corresponding to PCHC chains with chloride end groups resulting from the incorporation of a chloride originating from the catalyst structure **3**. Only traces (<1%) of the backbiting byproduct, *trans*-CHC carbonate, were detected. Under milder reaction conditions (entry 2, Table 4) and in the presence of higher loadings of catalyst **3** and a nucleophilic cocatalyst (PPN-Cl), exclusive formation of *cis*-CHC was observed. This is the first example of a switchable catalyst for organic carbonate formation.

In their initial report on the use of Fe(III) amino-(triphenolate) catalysts,[58] Kleij and co-workers noted that the coupling reaction of CHO with CO_2 generally led to moderate conversions and gave a complex mixture of cyclic and polycarbonates species containing both carbonate and ether linkages. The use of a Fe(III)amino(trisphenolate) catalyst (**14a**; Figure 4) resulted in the selective formation of CHC or PCHC from CHO in CO_2-rich/scCO_2 reaction media.[86] The presence of an equimolar amount of a nucleophilic organic salt containing a poor leaving group (PPN-Cl), when compared with TBAB and TBAI, suppressed the ring-closure reaction, and selective and quantitative formation of PCHC was observed (cat/cocat ratio 1:1; entry 3, Table 4) under supercritical conditions. Because the catalysts employed were not chiral, an atactic polymer with M_n = 6000 was obtained, which is lower compared with those obtained with other catalytic systems (vide supra); moreover, ^{1}H NMR/MALDI analysis of the polymeric product indicated that the polycarbonate chains were end-capped predominantly with hydroxyl groups, suggesting that water was the main cause of the termination of the polymer growth (i.e., being a chain-transfer agent). As a further proof, performing the reaction under more strictly anhydrous conditions in a Fischer−Porter reactor provided much higher M_n values of nearly 19 000. When using sufficiently large excess of the cocatalyst PPN-Cl (cat/cocat ratio 1:10, entry 4, Table 4), the displacement of the metal-bound carbonate intermediate occurred efficiently, and *cis*-CHC became the only carbonate-based product formed.

Generally, the formation of the *cis*-CHC is thermodynamically disfavored and requires a mechanism involving a double-inversion of the original CHO configuration, as shown in Scheme 7. It has been proposed that an excess of PPN-Cl can compete for coordination to the Fe metal center, thereby displacing the intermediate hemicarbonate, giving an outer-sphere type mechanism. Performing the reaction in the presence of substoichiometric quantities of PPN-Cl allows for clean copolymerization to occur through insertion of additional molecules of CHO and CO_2 in the growing polymer chain.[41] The formation of *trans*-CHC is a result of carbonate backbiting and generally believed to proceed with formal inversion of configuration.

Scheme 7. Proposed Formation Routes for the Formation of *trans*-CHC (top) and *cis*-CHC (below) Using Fe -Catalysis





20

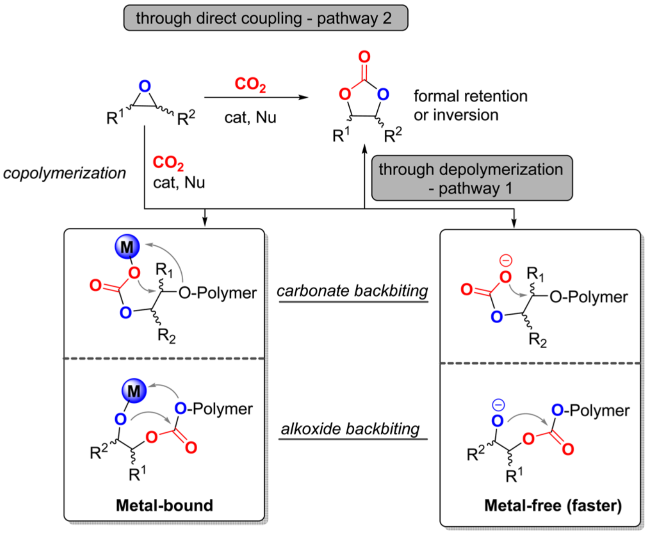
Figure 7. A metal catalyst selective toward CHO conversion to CHC or PCHC.

Recent work from Müller and co-workers using a Cr(III)-based catalyst (**20**; Figure 7) led to different conclusions.[87] This catalyst selectively produced PCHC in high selectivity (yield = 76%; conditions: **20** = 1 mol %, PPN-Cl = 2.5 mol %, $p(CO_2)$ = 2.0 MPa, T = 100 °C, t =3 h) and with high carbonate linkage content (97%), although the observed M_n was quite low (3831). When the reaction was performed in the presence of an appropriate chain transfer agent (1,8-octanediol) and tetrabutylammonium chloride (TBAC), a longer reaction time was needed to achieve a similar yield (6 h, 69%). However, in this case, the chemoselectivity dropped significantly, and a mixture of polycyclohexene/ether carbonate (77%) and CHC (23%) was obtained. Interestingly, the CHC formed consisted of both trans and cis isomers, indicating different mechanistic manifolds occurring simultaneously. The restricted geometry of the cyclohexene ring was suggested to disfavor an inner-sphere CHC formation step, promoting its formation via an alternative backbiting pathway triggered by dissociation of the polymer chain from the coordination sphere of the Cr(III) complex. Anti-attack of a free carbonate end group on the cyclohexene ring in a chair conformation according to a S_N2 mechanism provides *cis*-CHC, whereas *trans*-CHC is obtained by the same carbonate nucleophilic attack on the cyclohexene ring, although in a boat conformation (less favored due to the high ring strain), resulting in a mixture of both isomers, with *cis*-CHC being the major one.

4.2. Diastereoselective Conversions. Although the vast majority of the developed synthetic approaches to exploit CO_2 as a molecular synthon have focused on relatively simple synthetic transformations, the preparation of organic molecules of higher complexity by means of stereochemical methodology has received much less attention. For example, optically active cyclic carbonates can be regarded as precursors of diastereopure *cis*-diols, which are important constituents of natural compounds with pharmaceutical interest.[88] Various routes have been reported over recent years[5] to obtain these heterocyclic derivatives with high degrees of stereocontrol, including CO_2 conversion reactions using unsaturated alcohols.[45,89] Several contributions have demonstrated that stereoselective coupling reactions between CO_2 and 2,3-disubstituted oxiranes epoxides may be possible by a judicious choice of a suitable metal catalyst that is able to control formal inversion or retention of the original configuration of the epoxide reaction partner.

Two main pathways have been identified (Scheme 8): (1) prior formation of a polymer intermediate via CO_2/epoxide coupling followed by depolymerization (backbiting mechanism), thus obtaining the corresponding product with inversion of configuration or, alternatively, (2) direct COC formation preserving the configuration of the starting material in the resulting product. The overall retention of configuration observed for route 2 is the result of two consecutive S_N2 reactions: an initial epoxide ring-opening by nucleophilic attack of the cocatalytic additive followed by CO_2 insertion, and a final carbonate ring-closure reaction. The first route was extensively investigated by Darensbourg and co-workers through experimental and theoretical studies, developing diastereo- and enantioselective processes in which effective catalytic systems based on Co(III) or Cr(III) salen complexes (Figure 5) were used in the presence of quaternary ammonium or phosphonium salts as cocatalysts.[21,31,90−92] Such polymer degradation leading to a cyclic carbonate unit and a shorter polymer chain may occur through distinct pathways based on metal-bound or metal-free backbiting reactions (Scheme 8, route 1). Although the mechanism depends on the substrate and the catalytic system chosen, generally, backbiting processes are slower when the polymer is bound to the metal center, preventing polymer degradation, while the metal-free anionic polymer backbites faster, having a much lower free energy barrier than the metal-bound one.[31,92]

Scheme 8. Different Routes for the Stereo-Selective Formation of COCs from CO_2 and 2,3-Disubstituted Oxiranes[a]



[a] M = metal catalyst, Nu = nucleophile.

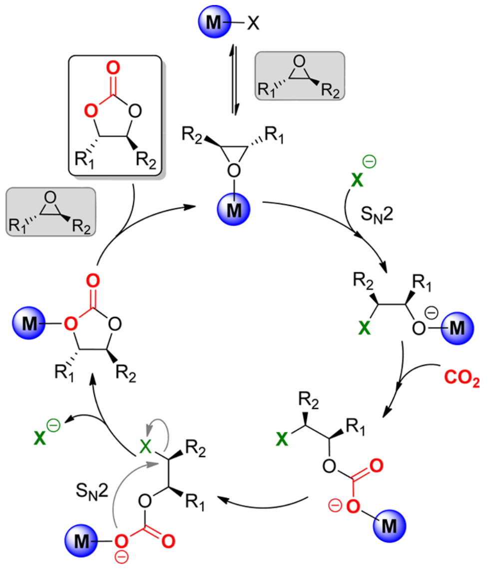
Both types of depolymerization may occur with carbonate or alkoxide backbiting. For example, when working at low CO_2 concentration, the operating mechanism is based on the metal-free alkoxide attack on the growing polymer chain carbonate moiety with inversion of stereochemistry as a result of a lower activation barrier in comparison with the metal-free carbonate backbiting process (10 kcal·mol^{-1}).[31] A remarkable exception is represented by the above-mentioned coupling between CHO and CO_2, which is generally highly selective toward copolymer formation.[75] Although difficult, depolymerization of PCHC occurs exclusively in the absence of CO_2 and the presence of catalytic quantities of **18b** (2 mol %) and an appropriate cocatalyst ($TBAN_3$, 4 mol %). Quantitative (>99%) depolymerization of PCHC occurs in t = 170 h heating at T = 110 °C, producing selectively *trans*-CHC. This accounts for a preferential backbiting process involving a metal-bound alkoxide, with consequent retention of configuration and formal inversion of configuration for the overall CO_2 coupling/depolymerization process.[73] In general, when working under polymerization conditions (i.e., high CO_2 and epoxide concentrations in the presence of a metal catalyst), the calculated alkoxide backbiting metal-free reactions have approximately half the free energy barrier of the metal-bound systems, thus suggesting that under these conditions, indeed, the metal-free alkoxide backbiting is the principal polymer degradation mechanism.[92]

In some cases, both (or at least two different) mechanisms may take place. For example, Kruper and co-worker reported on a Cr(III)porphyrin/DMAP binary system active toward the formation of cyclic carbonates from epoxides.[30] When starting from *trans*-2,3-epoxybutane, a quantitative conversion to the corresponding cyclic carbonate was achieved (conversion = 84%, cat. = 0.013−0.07 mol %, Cr(porphyrin)/DMAP = 1:4−1:10; $p(CO_2)$ = 5.0−5.4 MPa, T = 100 °C, t = 20 h), observing, however, a roughly 1:1 ratio of *cis*- and *trans*-isomeric COC products. This finding has been ascribed to the concomitant formation of both the COC and the corresponding (low molecular weight) polycarbonates. At the operating temperatures, the poly-/oligocarbonates readily undergo depolymerization with formation of the inversion product, i.e. *cis*-4,5-dimethyl-1,3-dioxolan-2-one. In contrast, when Nguyen and co-workers performed similar reactions using a Co(III)TPP/DMAP catalytic system (TPP = tetraphenylporphyrin), 4,5-dimethyl-1,3-dioxolan-2-one was obtained in high yields (93−99%, cat. = 0.04 mol %, Co(porphyrin)/DMAP ratio = 1:2; $p(CO_2)$ = 2.0 MPa, T = 120 °C, t = 9−20 h) and with a high degree of stereoselectivity.[93] The use of both *cis*- and *trans*-2,3-epoxybutane as coupling partners gave the corresponding COCs with exclusive *retention* of configuration, supporting the proposed double inversion mechanism. This is in line with an initial coordination of the epoxide to the metal center (Lewis acid), followed by a Lewis base-catalyzed ring-opening step (Scheme 9).

As mentioned previously, internal epoxide conversion was reported by North and co-workers using their well-known bimetallic Al(salen) catalyst **1** (Figure 1).[56] In this case, starting from diastereo-pure internal epoxide isomers (cis or trans), the corresponding COCs were obtained with overall retention of the configuration ([**1**] = [TBAB] = 2.5 mol %, T = 60 °C, t = 24−72 h, $p(CO_2)$ = 1.0 MPa, yield = 26−99%). Under these conditions, *trans*-stilbene epoxide, *cis*-2,3-epoxybutane, *cis*-cyclohexene epoxide, and *cis*-cyclopentene epoxide were initially converted to the corresponding cyclic carbonates, followed by basic hydrolysis to the corresponding *cis*-diols in 45−90% yield.

Because the overall configuration is retained in the hydrolysis step, CO_2 can be exploited as a temporary protecting group to afford *cis*-diols.[25] A wide-scope method for the formation of such *cis*-diols obtained from cyclic COCs having different ring sizes (5−8) was only recently communicated: more than 18 different (multi)cyclic and hetero(multi)cyclic oxiranes were converted to their corresponding COCs using **4d** (Scheme 4) as catalyst for these CO_2/epoxide coupling reactions (MEK as

Scheme 9. Proposed Mechanism for the Formal Stereochemical Retention of Configuration in the COC Product Arising from a Coupling Reaction between a 2,3-Disubstituted Oxirane and CO_2[a]



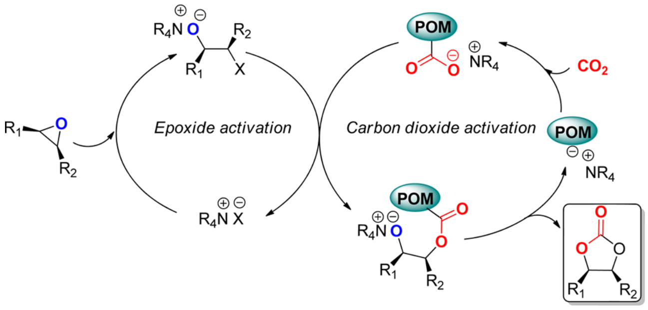
[a]M = metal catalyst, and X = nucleophilic species.

solvent, [**4d**] = 0.1−1 mol %, TBAB = 0.5−5 mol %, T = 70 °C, $p(CO_2)$ = 1.0 MPa, t = 18−66 h, yield =15−98%, COC selectivity >99% in all cases). The cis isomer of the COC was the major product (>95% in most cases), affording selectively the corresponding *cis*-diols after hydrolysis with a suitable base (15 examples; yield = 40−96%).

Significant advances were also made in the work performed by Leitner et al.,[54] who described a different homogeneous catalytic system for the stereoselective CO_2 coupling with internal epoxides derived from the oleochemical industry. The use of metal tetraheptylammonium silicotungstates (THA-M-Si-POM; POM = polyoxometalate) as catalysts gave rise to interesting results from the viewpoint of yield and selectivity while developing a mechanistic proposal. In particular, the combination of the THA-M-Si-POM based on Cr and using TBAB as cocatalyst showed high conversions (95%) and selectivities (98% vs 70% for TBAB used individually) under supercritical CO_2 conditions (T = 100 °C, $p(CO_2)$ = 12.5 MPa, t = 12 h, THA−Cr−Si-POM = TBAB = 2 mol %) because the POM catalyst is readily soluble in the mixture of epoxide substrate, COC product and $scCO_2$. A cooperative effect between both the POM structure and cocatalyst was suggested for this catalytic system: the nucleophile opens the epoxide while at the same time the POM structure, carrying negative charge, is able to coordinate/activate CO_2 (Scheme 10). As a result of this CO_2 activation mode, the reaction involving a double S_N2 pathway (preserving the original configuration) becomes much faster.

The same issue was addressed by Ema and co-workers[51] using Mg(II) and Zn(II) porphyrin-based bifunctional complexes (Figure 1, complex **6**) as active catalyst for the synthesis of COCs. Although activation of true internal oxiranes was formally not achieved, kinetic studies to elucidate the reaction mechanism were performed using *trans*-deuterated-1,2-epoxyhexane as substrate. Complex **6** was able to catalyze the conversion of the epoxide to the corresponding product with retention of configuration, observing a 99:1 trans/cis ratio of the resulting isomeric cyclic carbonates. Such a result accounts for a very selective process in which the bromide ion of the cocatalyst attacks the epoxide, not the CO_2, affording the *trans*-cyclic carbonate through a double inversion mechanism, as depicted in Scheme 9.

Scheme 10. Synergistic Pathway for the Combined POM/Quaternary Salt Catalyst System[a]

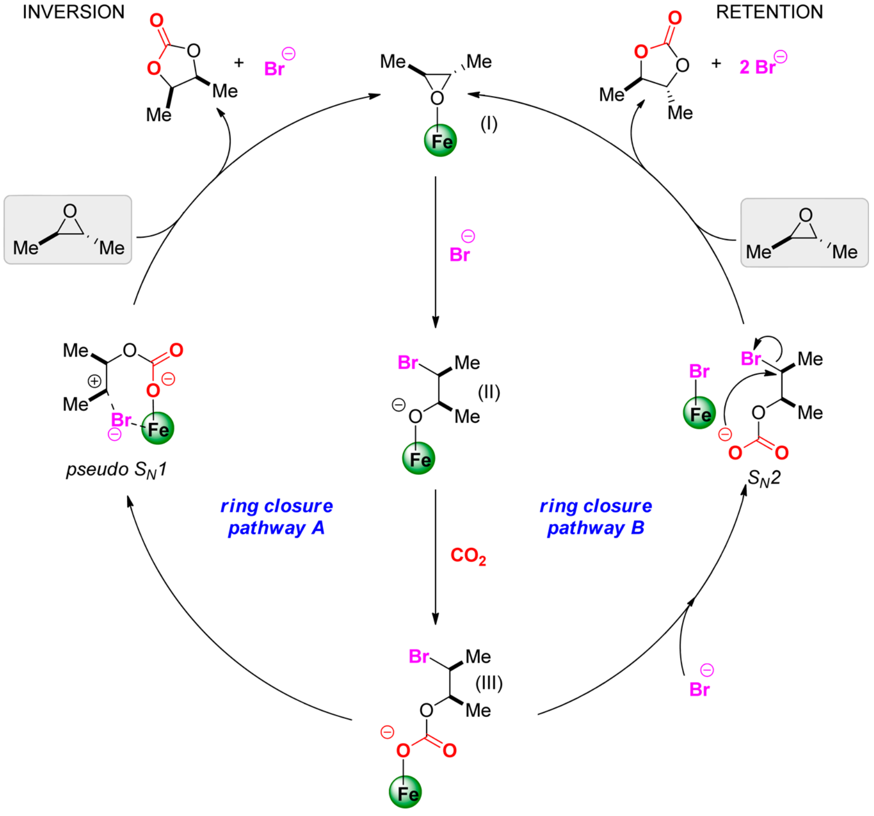


[a]As depicted in reference 54; note that for clarity, only one negative charge of the POM cluster is shown.

A noteworthy control over the diastereoselectivity in the coupling between pure *trans*- or *cis*-2,3-epoxybutane and CO_2 using the previously mentioned Fe(III)amino(triphenolate)/TBAX (X = halide) binary catalyst systems (Figure 4) was published by Kleij and co-workers.[94] Starting from *cis*-2,3-epoxybutane and using the catalyst systems **14a** and **14b,** they were able to correlate the relationship between the cocatalyst loading and the configuration of the COC product. Thus, for example, in the presence of high TBAB loading (2.5−4 mol %; **14**:TBAB ratio = 1:10 to 1:16), *cis*-4,5-dimethyl-1,3-dioxolan-2-one was formed with overall retention (up to >99%) of the configuration, indicating that this reaction follows the classical double inversion pathway (Scheme 11, pathway B). Conversely, at low TBAB concentration (<1.25−0.125 mol %; **14**/TBAB ratio = 3.2:1−32:1) the corresponding *trans*-4,5-dimethyl-1,3-dioxolan-2-one was formed as the major product (up to >99%). This unusual control pointed toward the presence of a complementary mechanism, preferred at relatively low TBAB loadings. In a manner similar to pathway B, the first step of this alternative mechanism (pathway A) involves oxirane coordination to the metal center, followed by epoxide ring-opening, resulting in an inversion of configuration at this carbon center. Then, different from pathway B, after insertion of CO_2 in the metal-alkoxide (Scheme 11, Intermediate III), the bromide dissociates from the hemicarbonate, forming a hexa-coordinated Fe complex by coordination on the vacant cis site of the metal center. Finally, a pseudo-S_N1 type ring-closing reaction occurs, giving the corresponding *trans*-COC product with formal inversion of the configuration. The use of the trans substrate (*trans*-2,3-epoxybutane) gave similar results, and both the cis (85%) and the trans (>99%) COCs could be obtained in high diastereo selectivity.

Alternative strategies to prepare diastereopure COCs have also been reported, including the Pd(II)-catalyzed coupling of CO with diols, as described by Dibenedetto and co-workers.[60] Although modest success was observed in terms of substrate scope and yields, this oxidative carbonylation of 1,2- and 1,3-diols catalyzed by palladium iodide in conjunction with KI gave access to diastereopure COCs starting from diastereoisomeric

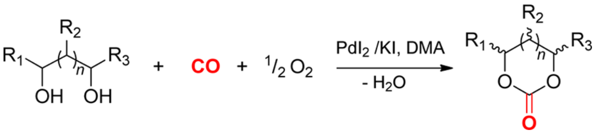
Scheme 11. Proposed Mechanism for CO_2 Coupling with *trans*-2,3-Epoxybutane To Obtain the Corresponding COCs with Formal Inversion of the Configuration (pathway A) or Retention of Configuration (pathway B)[a]



[a] See also ref 94.

mixtures of the substrates (Scheme 12; T = 100 °C, DMA, PdI_2 = KI = 10 mol %, $p(CO_2)$ = 2.0 MPa of a 1:4 CO/air mixture).

Scheme 12. Pd(II)/KI-Catalyzed Carbonylation of 1,2- and 1,3-Diols Carried Out in Dimethylacetamide (DMA)



4.3. Enantioselective Control.

The formation of enantiomerically pure COCs via CO_2 coupling with epoxides is still an open challenge. Enantiopure COCs are key synthetic intermediates in the pharmaceutical industry and are present in numerous relevant biological compounds.[27,95] Given the overall process atom-economy and the numerous reported examples of effective catalysts, CO_2 coupling with epoxides can be regarded as one of the most efficient and, potentially, selective processes for the preparation of such chiral derivatives.

The simplest way to obtain enantiopure cyclic carbonates is by coupling of enantiopure epoxides with CO_2, developing catalytic procedures that favor a high level of retention of configuration at the asymmetric carbon center of the oxirane. Evidently, such procedures have lower synthetic impact but offer useful probes for mechanistic understanding in COC synthesis. Typically, for alkyl-substituted terminal epoxides, ring-opening occurs preferably at the nonsubstituted carbon center (C_α), observing an overall retention of configuration (Figure 8, top). However, when using terminal epoxides containing electron-withdrawing groups (e.g., epichlorohydrin and styrene oxide), an increased preference for ring-opening at the C_β center occurs (Figure 8, bottom), resulting in (partial loss) of the original stereochemical information.[96]

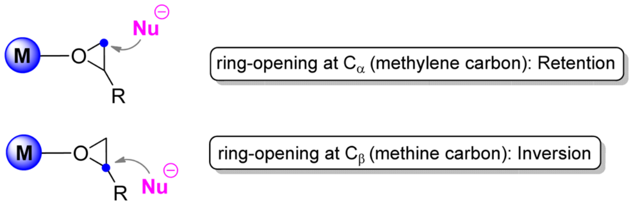
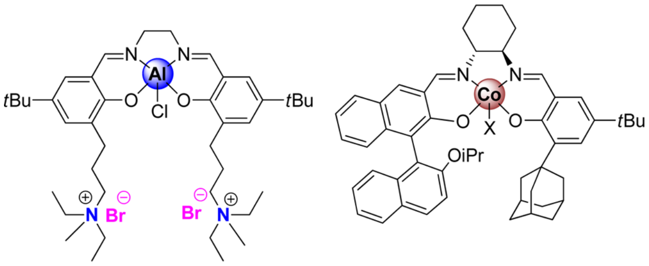


Figure 8. Stereochemistry involved in the ring-opening of a terminal epoxide by a nucleophile (Nu) at the involved carbon centers.

Several different systems active toward activation of enantiomerically enriched epoxides have been reported. Recently, Capacchione and co-workers used Fe(III) complex **9** (Scheme 4) combined with TBAB as a catalytic system.[48] Although the catalytic system is not chiral, it provides reasonable stereoretention in the nucleophilic ring-opening step of the epoxide. For example, with enantio-enriched (R)-styrene oxide (94% ee), (R)-styrene carbonate was obtained in 72% ee (85% yield, conditions: [**9**] = 0.025 mol %, [TBAB] = 0.1 mol %, t = 6 h, T = 100 °C, $p(CO_2)$ = 2.0 MPa), showing that the main ring-opening pathway is through C_α.

Another recent example was described by Lu's group,[97] who developed a novel, active, and stereoselective bifunctional Al(III)salen complex **21** (Figure 9) active toward COC synthesis. Starting from enantiomerically pure epoxides, quantitative conversion to the corresponding enantiomerically



21

22a: X = 2,4-dinitro-phenoxy
22b: X= BF_4

Figure 9. Salen-based complexes **21** and **22** used as catalysts for the enantioselective CO_2 insertion reaction into an epoxide: bifunctional aluminum catalyst and asymmetric cobalt catalyst.

pure cyclic carbonates (>99% ee) was obtained with full retention of configuration (conditions: **21** = 0.01 mol %, t = 3−24 h, T = 60−120 °C, $p(CO_2)$ = 2.5 MPa). When performing the reaction at T = 120 °C using epoxides with electron-withdrawing substituents on the β-carbon, partial loss of the stereochemical information was observed (67% ee for (S)-epichlorohydrin, 83% ee for (S)-styrene oxide), and lowering the reaction temperature to T = 60 °C (for (S)-epichlorohydrin) or T = 80 °C (for (S)-styrene oxide) resulted in complete retention of the stereochemical information, indicating preferred ring-opening at the nonsubstituted carbon center.

Jamison and co-workers reported on a continuous flow method for the formation of COCs from epoxides and CO_2 using inexpensive sources of bromide radical (Br_2 or N-bromosuccinimide, NBS) and using the radical initiator benzoyl peroxide (BPO) as catalyst.[98] Notably, with enantiopure (R)-styrene oxide and (S)-phenyl glycidyl ether epoxide, the corresponding COC products were obtained with full retention of configuration (conditions: $[Br_2]$ or [NBS] = [BPO] = 5 mol %, DMF (2M), t = 0.5 h, T = 120 °C, $p(CO_2)$ = 0.7 MPa). Although this is not a metal-catalyzed approach, it shows that careful design of the experimental flow setup can be beneficial to achieve excellent retention of the stereochemical properties.

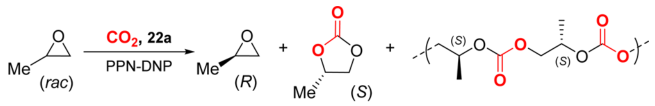
As opposed to the use of chiral starting materials being more costly, various research groups have investigated the use of kinetic resolution to produce chiral COCs. A number of important results have been published in the past decade, mainly focusing on Co(II)/Co(III)salen-based catalysts.[5] For example, Lu and co-workers reported the first example of enantioselective synthesis of propylene carbonate by catalytic kinetic resolution of racemic epoxides with CO_2, developing a process that involves the simple use of chiral Co(III)salen(X)/quaternary ammonium halide binary catalyst systems under extremely mild and solvent-free conditions.[99] Unfortunately the kinetic resolution coefficients measured (k_{rel} < 10) were still far from being optimal compared with well-known hydrolytic kinetic resolution methods.[100]

More recently, the same group reported a multichiral Co(III) complex, **22** (Figure 9), which was used in conjuction with the 2,4-dinitrophenolate salt of PPN (PPN-DNP) as the nucleophilic cocatalyst.[101] From the data reported in Table 5, it can be noted that the addition of a quaternary ammonium salt is essential to perform this coupling reaction smoothly, and this has a significant effect on the catalytic performance of Co(III)salen(X) as well as on the chemoselectivity (entries 3−4, Table 5). The operating temperature has to be chosen carefully to optimize overall conversion and optical purity of the COC product (entries 1−3, Table 5). Higher k_{rel}'s were measured when increasing the cocatalyst loading (entries 1−3, Table 5). This methodology was applied to a discrete family of terminal epoxides (4 examples) with both electron-donating and electron-withdrawing substituents, observing conversions between 12 and 43% producing ee values for the COC products between 68−89%. The results demonstrate a clear potential for these Co(III)salen-based catalysts in the kinetic resolution of (rac)-epoxides in the presence of CO_2 to afford chiral COCs.

5. SUMMARY AND OUTLOOK

In the past 5 years, the area of synthesis and development of more-sophisticated COC scaffolds has developed tremendously, as testified by the contents of this review article. Whereas initially terminal epoxides were successfully coupled to CO_2, affording their corresponding COCs, lately, attention has shifted toward more challenging coupling partners, including internal oxiranes and oxetanes. In addition, efforts have been made to increase the reactivity of the applied catalytic systems, providing very high (initial) TOFs and impressively high TONs. Obviously, catalytic systems that are able to combine robustness, recyclability, cost-effectiveness, and very high reactivity/selectivity features would serve as privileged systems within the area of COC fabrication. Despite the vivid character of this area of CO_2 catalysis, there remain important challenges to be resolved. Among these are the development of a wide-scope, asymmetric synthesis of chiral COCs and related heterocycles starting from racemic precursors, new catalytic strategies for the selective conversion of highly substituted oxetanes into their six-membered carbonates, and effective methodology for the conversion of tri- and tetra-substituted oxiranes. Inspiration from naturally occurring COCs[27] may serve as a useful starting point to approach such synthetic challenges. Another interesting development is the preparation

Table 5. Kinetic Resolution of Terminal (rac)-Propylene Oxide via CO_2 Coupling To Form COCs[a]



PC PPC

entry	cat (mol %)	cocat (mol %)	T (°C)	t (h)	conv. (%)	PC/PPC (%)	PC (% ee)	k_{rel}
1	0.01	2	25	12	46	93:7	86.0	29.1
2	0.05	10	0	12	35	100:0	91.8	40.6
3	0.05	10	−25	12	10	100:0	97.1	75.8
4	0.1	0.1	−25	24	42	0:100	85.2[b]	23.7

[a] Using 0.5−0−6 equiv of CO_2. [b] Enantioselectivity of the COC obtained after depolymerization in the presence of Li(tBuO).

and use of (functional) COCs that are used as intermediates for the synthesis of other, (chiral) organic molecules,[23−25] amplifying the importance of these scaffolds in organic synthesis. Such potential should be able to fuel new developments in the area of COCs and beyond, giving a bright perspective for the use of CO_2 as a molecular C_1 synthon.

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

C.M. gratefully thanks the Marie Curie COFUND Action from the European Commission for cofinancing a postdoctoral fellowship. G.F. kindly acknowledges financial support from the European Community through a Marie Curie Intra-European Fellowship (FP7-PEOPLE-2013-IEF, project RENOVACARB, Grant Agreement no. 622587). Further acknowledgements go to ICIQ, ICREA, and the Spanish Ministerio de Economiá y Competitividad (MINECO) through project CTQ-2011-27385, and support through Severo Ochoa Excellence Accreditation 2014-2018 (SEV-2013-0319).

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