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<https://doi.org/10.3390/sym8010004>

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Review

# Synthesis of Chiral Cyclic Carbonates via Kinetic Resolution of Racemic Epoxides and Carbon Dioxide

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Received: 18 November 2015; Accepted: 11 January 2016; Published: 14 January 2016

Academic Editor: Svetlana Tsogoeva

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**Abstract:** The catalytic synthesis of cyclic carbonates using carbon dioxide as a C1-building block is a highly active area of research. Here, we review the catalytic production of enantiomerically enriched cyclic carbonates via kinetic resolution of racemic epoxides catalysed by metal-containing catalyst systems.

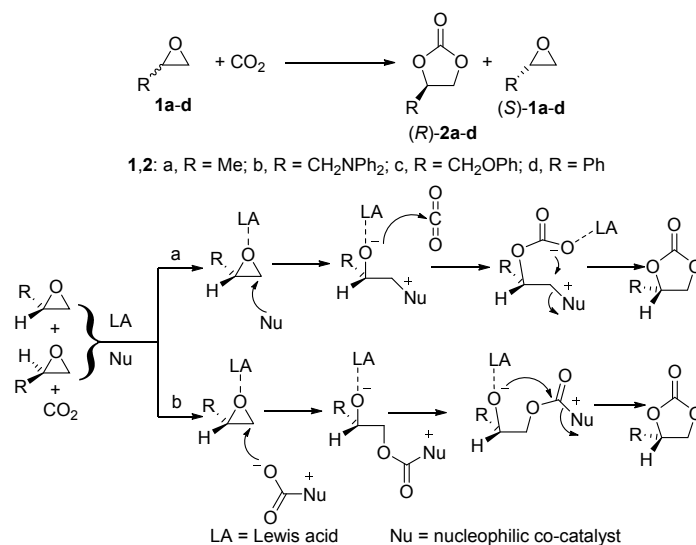
**Keywords:** carbon dioxide; catalysis; metal catalysts; cyclic carbonates; kinetic resolution

## 1. Introduction

Carbon dioxide is considered to be a cheap, non-toxic and versatile carbon source and its direct chemical fixation has received a great deal of attention in recent years [1–5]. The preparation of cyclic carbonates via the coupling reaction of carbon dioxide and epoxides is one of the most effective routes for carbon dioxide fixation. Although a number of catalyst systems have been developed for this process, only a handful have been used for the enantioselective synthesis of cyclic carbonates. Both enantiopure epoxides and cyclic carbonates are important intermediates because of their versatile reactivity. In particular, stereoselective ring-opening reactions of epoxides with nucleophiles can provide a range of bifunctional compounds, and chiral cyclic carbonates are also valuable building blocks for masked 1,2-diols, polymeric materials and in pharmaceutical and fine chemical synthesis [6–8]. This review will focus on the enantioselective synthesis of a variety of cyclic carbonates from epoxides and carbon dioxide via kinetic resolution.

## 2. Enantioselective Synthesis of Cyclic Carbonates via Kinetic Resolution of Epoxides

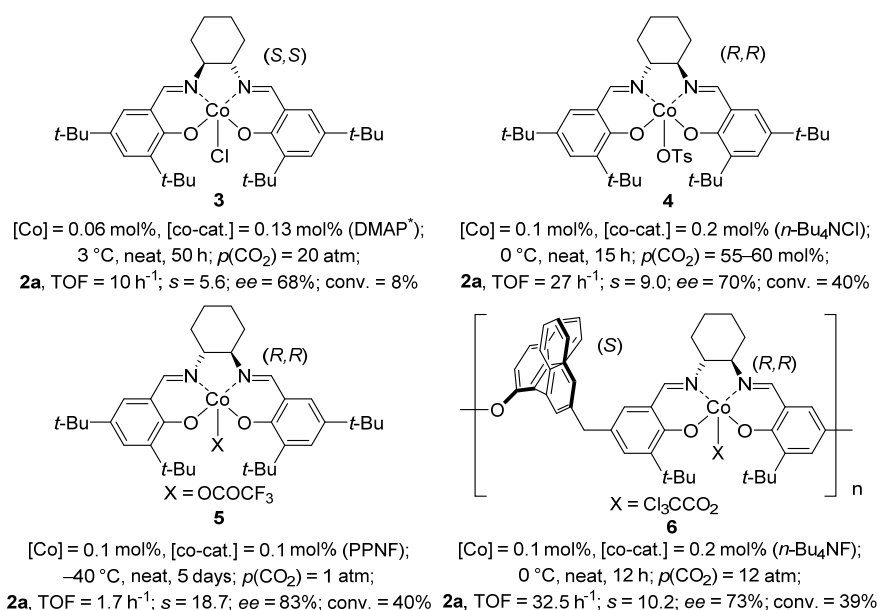
One way to synthesise enantiomerically-enriched cyclic carbonates is via kinetic resolution. In this system, it was proposed that a chiral Lewis acid selectively complexes to one enantiomer of a racemic epoxide. Subsequent attack of a nucleophile or activated carbon dioxide towards the coordinated epoxide then leads to enantioselective ring-opening of the epoxide, with intramolecular elimination providing the enantiomerically-enriched cyclic carbonate. Consequently, the enantiomeric excess of the remaining epoxide would be increased (Figure 1) [9].



**Figure 1.** Possible mechanisms for the coupling reaction of carbon dioxide and epoxides.

### 2.1. Cobalt(III) Salen Complexes

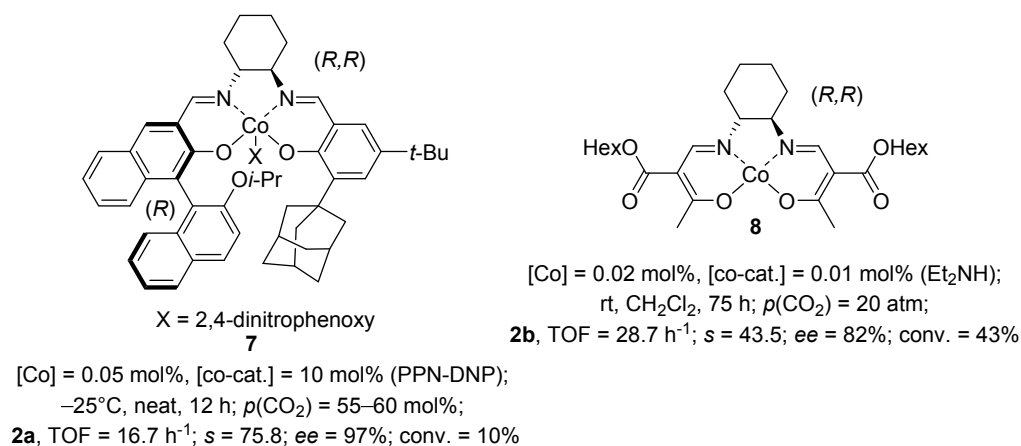
The first example of the preparation of enantiomerically-pure cyclic carbonates via kinetic resolution of epoxides using a cobalt(III) salen complex was reported by Nguyen in 2004 [10]. Propylene carbonate **2a** was produced in up to 68% *ee*, corresponding to a selectivity factor *s* of 5.6, when chiral cobalt(III) complex **3** (Figure 2) and DMAP\* [(*R*)-(+)-4-dimethyl-aminopyridinyl (pentaphenylcyclopentadienyl)iron] were employed. Notably, the chiral Lewis base did not contribute significantly to the enantioselectivity. Later, Lu reported the use of a similar cobalt(III)salen complex **4** in the presence of two equivalents of *n*-NBu<sub>4</sub>Cl (*n*-tetrabutylammonium chloride) for the synthesis of enantioenriched propylene carbonate **2a** [11]. The bulky *p*-toluene-sulfonate counterion was essential to obtain high enantioselectivity. By replacing the counterion with trifluoroacetyl to give the resulting cobalt(III) complex **5** and employing PPNF [(bis-(triphenylphosphoranylidene)ammonium fluoride)] as co-catalyst, propylene carbonate **2a** was obtained in 40% yield and 83% *ee* at atmospheric carbon dioxide pressure and  $-40\text{ }^{\circ}\text{C}$  [12]. This corresponded to a significant increase in selectivity (*s* = 18.7).



**Figure 2.** Cobalt(III) salen based catalyst systems for the synthesis of optically active cyclic carbonates.

Since the initial report, a number of modifications to the cobalt(III) salen catalyst system have been reported, all of which demonstrated some degrees of success [13–22]. Jing and co-workers reported a chiral polymer based on BINOL cobalt(III) salen complex **6** for the asymmetric addition of carbon dioxide to racemic propylene oxide **2a** [23]. A comparable enantioselectivity and selectivity factor to that of similar homogeneous cobalt(III) salen systems were reported. Notably, the catalyst could be easily recovered and reused more than ten times without loss of activity or enantioselectivity.

In 2012, Lu and co-workers [24] reported the most effective catalytic system to date for the kinetic resolution of racemic epoxides into enantioenriched cyclic carbonates. This system consisted of a chiral cobalt(III) salen complex **7** (Figure 3) with an (*R,R*)-configured side group as the catalyst and PPN-DNP [(bis-(triphenylphosphoranylidene)ammonium 2,4-dinitrophenoxide)] as the co-catalyst [24]. Propylene carbonate **2a** was obtained in 97% *ee* and *s* value of 76. The variation of the co-catalyst and its relative loading dramatically changed both the selectivity and enantioselectivity of the reaction. Furthermore, the anion and cation of the ammonium-based co-catalysts also significantly affected the enantioselectivity. The use of both a nucleophilic anion with poor leaving group ability and a bulky cation were beneficial for improving the enantioselectivity. The excess co-catalyst loading also favours selective production of cyclic carbonates via the intramolecular elimination of the resultant linear carbonate over the formation of the corresponding polymer. The utility of the catalyst system containing cobalt(III) complex **7** was demonstrated for the conversion of other epoxides such as butylene oxide into its corresponding chiral cyclic carbonate with a *s* value of 31.5 and 88.5% *ee*.



**Figure 3.** Cobalt(III) and cobalt(II) salen based catalyst systems for the synthesis of optically active cyclic carbonates.

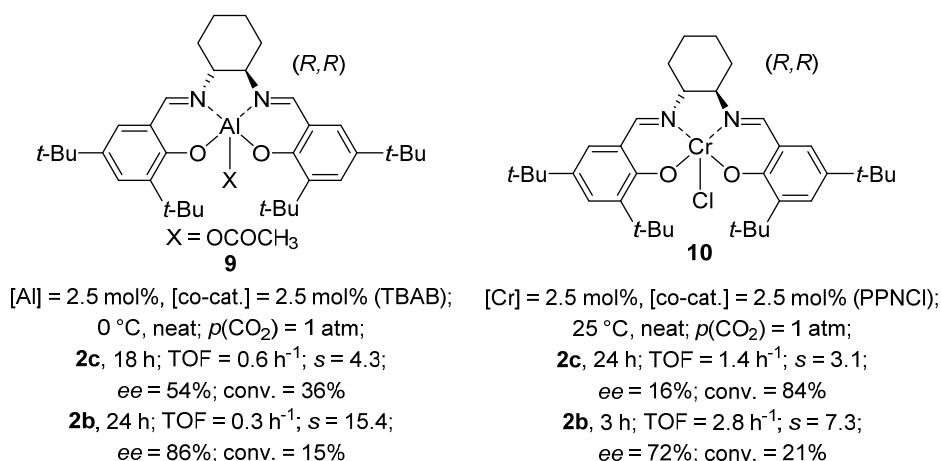
## 2.2. Cobalt(II) Salen Complexes

Yamada and co-workers reported that the chiral ketoiminatocobalt(II) complex **8** catalysed the enantioselective synthesis of cyclic carbonates [25,26]. Although the combination of complex **8** and diethylamine could work with a range of epoxides, it was found that the catalytic system is substrate dependent, giving the highest *s* value of 43.5 with *N*-(2,3-epoxypropyl)diphenylamine **1b** as the epoxide.

## 2.3. Other Metal Salen Complexes

Although a number of metal-based salen complexes have been developed [11,18] only a few catalytic systems gave comparable results to that of cobalt-based complexes. Recently, North *et al.* have reported the use of aluminium(III) and chromium(III) salen complexes for the kinetic resolution of terminal epoxides via carbon dioxide coupling (Figure 4) [27]. It is worth highlighting that they have reported the first aluminium-based catalysts capable of performing the kinetic resolution of epoxides by carbon dioxide coupling for the synthesis of enantiomerically enriched cyclic carbonates.

Moreover, aluminium is one of the six most abundant and sustainable metals [28] and therefore makes these catalysts very attractive in a future green chemicals industry. The authors reported that a combination of aluminium(III)(salen) acetate and *n*-Bu<sub>4</sub>NBr (*n*-tetrabutylammonium bromide) was the most active and selective catalytic system for the synthesis of optically active cyclic carbonates from racemic epoxides. It was observed that kinetic resolution of epoxides via carbon dioxide coupling was substrate dependent. Hence, when phenyl glycidyl ether **1c** was used as a substrate, 36% conversion and 54% *ee* were obtained at one atmosphere carbon dioxide pressure and 0 °C. However, 15% conversion and 86% *ee* were obtained under the same reaction conditions when *N*-(2,3-epoxypropyl)diphenylamine **1b** was used. These results suggested that the reaction mechanisms occur via a different stereodetermining step. Chromium(III) salen complexes were also investigated for the kinetic resolution of phenyl glycidyl ether **1c**. Firstly, the counterion of the catalyst was investigated using *n*-Bu<sub>4</sub>NBr or DMAP as a co-catalyst. This showed that chloride or tosylate counterions on the chromium centre gave enantioselective catalysts though with low *s* values (1.1–2.2). Subsequently, the effect of the co-catalyst was studied and the results showed that a combination of chromium(III)(salen) acetate and PPNCl [(bis-(triphenylphosphoranylidene)ammonium chloride)] was the most efficient catalyst for the kinetic resolution of phenyl glycidyl ether **1c**, achieving 84% conversion and a *s* value of 3.1 at 25 °C and one atmosphere of carbon dioxide pressure for 24 h. Similarly, the use of *N*-(2,3-epoxypropyl)diphenylamine **1b** gave a *s* value of 7.3 when the reaction was carried out at 25 °C and one atmosphere of carbon dioxide pressure for 3 h.



**Figure 4.** Bifunctional aluminium(III) and chromium(III) salen complexes **9** and **10** for the synthesis of optically active cyclic carbonates.

A novel three-dimensional chiral mixed metal-organic framework (MOF) based on an enantiopure nickel(II)(salen) metalloligand and a tetranuclear cadmium cluster was reported by Jiang and co-workers in 2013 [29]. With each cadmium cluster linked by eight nickel complexes and each nickel complex surrounded by two cadmium clusters, a three-dimensional structure which displayed both high porosity and stability was generated. This material was tested as a catalyst for the enantioselective synthesis of propylene carbonate from racemic propylene oxide using *n*-Bu<sub>4</sub>NBr as a co-catalyst at 25 °C and 20 atmospheres of carbon dioxide pressure for 4 h. Under these reaction conditions, propylene carbonate was obtained in 28% conversion and 52% *ee* with a *s* value of 3.8. A recyclability study was performed and showed that no significant loss of activity or selectivity was detected after three cycles. The catalyst was also studied after each cycle via PXRD, with the resulting powder patterns found to be identical to the freshly synthesised MOF. Moreover, analysis of the solution by ICP-AES showed that less than 5% of the nickel and cadmium ions had leached into the reaction mixture. These findings demonstrated that the MOF can act as a very efficient self-supported heterogeneous catalyst for the enantioselective synthesis of propylene carbonate.

#### 2.4. Other Metal Complexes

The first kinetic resolution of epoxides using metal catalysts was reported by Vogt and co-workers in 1993 [30]. The best result was obtained using a combination of (*R*)-(+)-binaphthol in conjunction with zirconium tetrabutoxide as the Lewis acid. 4-(Chloromethyl)-1,3-dioxolan-2-one was obtained from epichlorohydrin in 39% *ee* and with a *s* value of 2.5 at  $-40\text{ }^{\circ}\text{C}$  and 5 atmospheres of carbon dioxide pressure for 65 h using *n*-Bu<sub>4</sub>NI as a co-catalyst. When styrene oxide was used as the substrate, the catalyst system consisting of (*R*)-(+)-binaphthol, titanium isopropoxide and *n*-Bu<sub>4</sub>NI as a co-catalyst displayed the highest selectivity. Thus, styrene carbonate was obtained in 35% *ee* and a *s* value of 2.6 at room temperature and 5 atmospheres of carbon dioxide pressure for 24 h.

Optically active niobium(IV) catalysts have been studied by Dibenedetto *et al.* for the enantioselective synthesis of propylene and styrene carbonate from their corresponding racemic epoxides [31]. (*R*)-styrene carbonate was synthesised in up to 74% yield in 22% *ee* using NbCl<sub>4</sub>(DIOP) [(4*S*,5*S*)-4,5-bis(diphenylphosphino-methyl)-2,2-dimethyl-1,3-dioxolane] as catalyst in dimethylformamide at 135 °C and 50 atmospheres of carbon dioxide pressure for 12 h. The low enantioselectivity is due to the exchange of the enantiopure ligand with the solvent under the reaction conditions.

### 3. Conclusions

In conclusion, chiral cyclic carbonates are useful synthons in organic synthesis. The most important developments for the enantioselective synthesis of cyclic carbonates via kinetic resolution have been summarized. It is evident that significant advances have been made. However, for the synthesis of chiral cyclic carbonates to be industrially viable, more progress needs to be made.

**Acknowledgments:** José A. Castro-Osma acknowledges financial support from UCLM-CYTEMA and the Plan Propio de la Universidad de Castilla-La Mancha.

**Conflicts of Interest:** The authors declare no conflict of interest.

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