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"Access to Multi-substituted 6-Membered Cyclic Carbonates using 3,4-Epoxyalcohols and Carbon Dioxide *via* Payne-type Rearrangement"

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Without you it would not have been possible!

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Introduction

CO_2 Valorization

Carbon dioxide (CO_2) is engraved in our collective memory as a threat. Since the industrial revolution, our ever-increasing demand for energy production has been satisfied by the combustion of fossil fuels, entailing the emission of enormous amounts of the greenhouse gas CO_2. Particularly since the 1950's emissions have increased dramatically, from approximately five billion tons in 1950 to over 36 billion tons in 2017[1]. Consecutively, we are running out of fossil fuels and the predicted demands for those resources, constituting the main feed stock of material in chemical research and industry, will not be met in the near future. Next to the development of new and renewable sources of energy, modern chemists face the challenge of finding more sustainable feed stocks for chemical materials. The threat of CO_2 becomes an opportunity: CO_2 is a cheap, widely available, and non-toxic waste molecule that can be valorized into a renewable carbon feedstock. Inspired by nature, where atmospheric CO_2 is transformed into thousands of valuable compounds, in organic synthesis CO_2 can serve as an alternative C1 building block in the construction of molecules. Figure 1 shows industrial syntheses that utilize CO_2 as a C1 source.

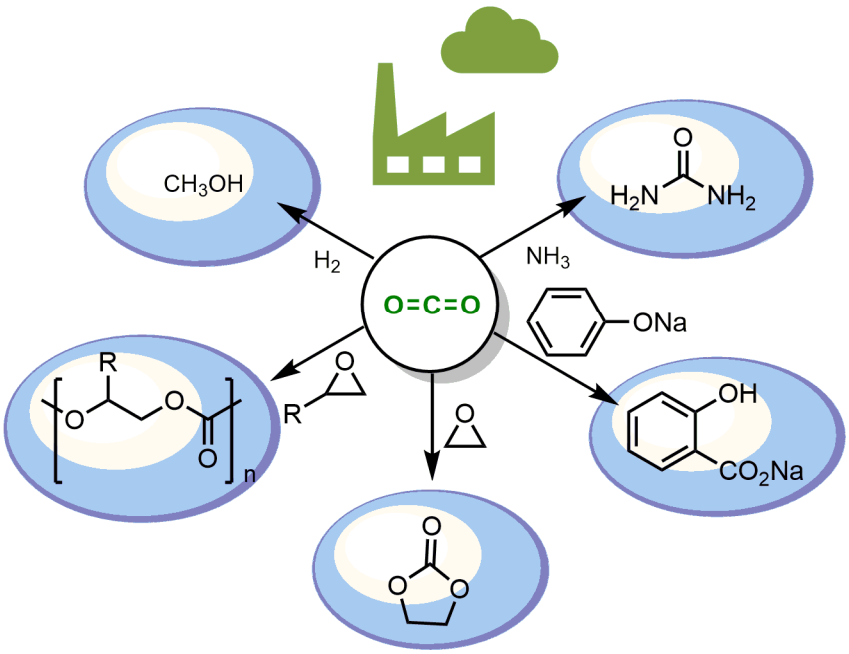


Figure 1 Industrial application of CO_2 valorization

Small molecule activation comprises a field in chemistry seeking to transform simple, inert molecules such as O_2, N_2 or CO_2, or methane and simple alkanes into value-added compounds such as fuels, fine-chemicals, active pharmaceutical ingredients, or polymers. An important subsection in small molecule activation is the valorization of CO_2, which can be structured into three major categories[2]: a) the non-reductive conversion of CO_2, where the oxidation state of +IV of the carbon center is retained upon incorporation into molecular scaffolds, b) the reductive conversion of CO_2, where the oxidation state of the carbon center is reduced, and c) the direct reduction of CO_2 to obtain fuels[3].

A challenge in activating CO_2 is its thermodynamic and kinetic stability. The fully oxidized carbon center is accountable for the low reactivity of the molecule. However, satisfying reactivity can be achieved using high-energy starting materials such as hydrogen, highly nucleophilic species, or strained cyclic ethers or amines (see Figure 2) able to decrease the activation barrier of the specified reaction. To overcome the kinetic stability of CO_2 an appropriate catalyst is necessary.

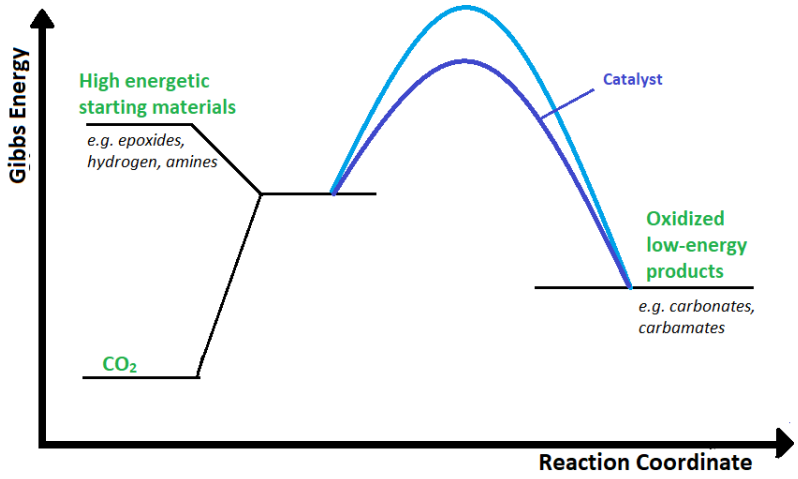


Figure 2 Reactivity profile for CO_2 coupling reactions with high-energy substrates

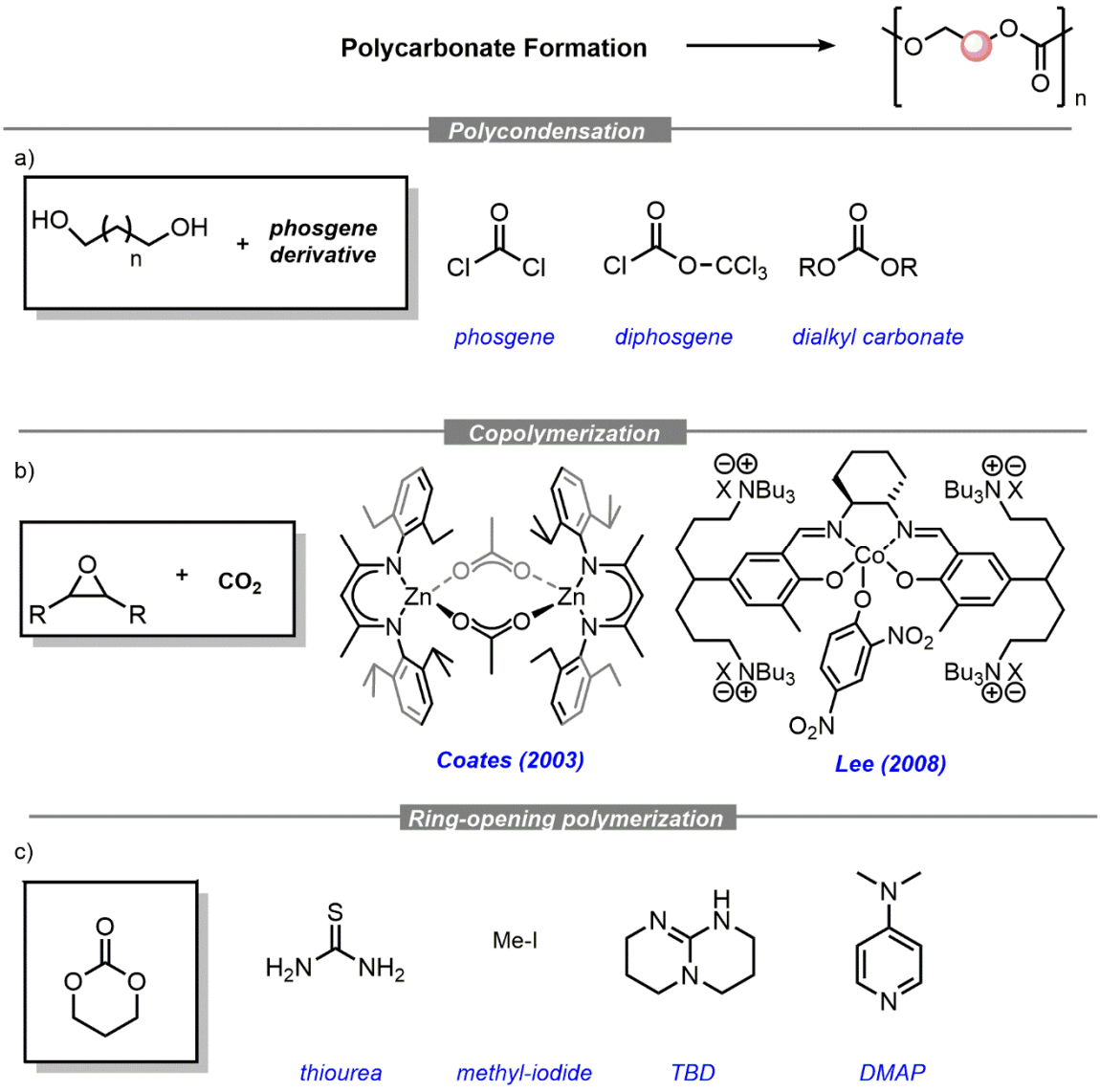
Various organic compounds have been prepared from CO_2: methanol, urea, lactones, various heterocycles, (bio)degradable polymers, carboxylated structures, and more[4]. The reactions in which CO_2 is coupled to strained cyclic ethers, such as epoxides and oxetanes, to form cyclic carbonates are amongst the most studied. Due to their easy access from olefins, epoxides have been studied intensively over the last decade as substrates upon which CO_2 can be incorporated. As such, a wide substrate scope and mild

reaction conditions are available for this cycloaddition reaction[5][6]. The coupling of CO_2 with epoxides represents one of the few industrial processes for the valorization of CO_2 that can be performed under mild conditions (under 100°C, under 10 bar).

Polycarbonates

Polymers are one of the most widely used chemical products, industrially synthesized in millions of tons per year[7]. As those materials are mostly made from fossil resources and are often not recyclable, concerns about their sustainability have grown. The utilization of CO_2 as a renewable carbon source poses a sustainable alternative to petrochemical feedstocks in the construction of polymers. The synthesis of polycarbonates is one of the biggest industrial applications of CO_2 valorization.

Polycarbonates are polymers with the carbonate repeating unit [-O-C(O)-O-] in the backbone. Aliphatic polycarbonates (APCs) contain only aliphatic groups between the carbonate linkers, unlike aromatic polycarbonates which include aromatic groups in the backbone. For a long time, aliphatic polycarbonates have been largely neglected for commercial applications as well as in research. In contrast to their popular aromatic counterparts, APCs show low melting points and poor stability, being susceptible to hydrolysis. Exactly these properties, however, caught interest for biomedical applications, as (bio)degradability is highly desirable in this field. Their combination of biodegradability and biocompatibility (low toxicity) makes polycarbonates ideal candidates for medical applications such as hydrogels, drug delivery systems, and tissue engineering scaffolds. After their use, APCs can be degraded into cyclic carbonate monomers, which importantly are biocompatible as well. The presence of functional groups in the polymer is an important tool to engineer physical properties and degradability. It also enables post-functionalization of the polymer, for example, in drug-delivery applications[8]. In the past 20 years, much progress has been made in the development of APCs[9][10][11][12]. The three main synthetic routes to access polycarbonates include a) polycondensation of diols with dialkyl carbonate or other carbonylation agents, b) copolymerization of epoxides (or other strained cyclic ethers) and CO_2, and c) ring-opening polymerization (ROP) of cyclic organic carbonate monomers (Scheme 1).



Scheme 1 Polycarbonate formation through polycondensation, copolymerization and ring-opening polymerization including selected catalysts/reagents. TBD = 1,5,7-Triazabicyclo[4.4.0]dec-5-en, DMAP = 4-dimethylaminopyridine.

Polycondensation of diols was originally achieved employing phosgene as a carbonylation agent. (Scheme 1a) The use of phosgene derivatives such as dialkyl carbonates[13] is preferable due to easier handling, high molecular weights of the products, and a narrow weight distribution. Polycarbonates with aliphatic linkages of different length can be prepared easily, depending on the length of diol used. However, the toxic nature and poor atom economy of those reagents impose a major drawback.

The copolymerization of epoxides and CO_2 has become one of the most well-studied technologies in the large-scale application of CO_2 as a carbon feedstock, leading to greener and more sustainable products[14][15]. A remarkable number of catalysts working under mild conditions (1 bar CO_2) have been developed over the years. Two of the most

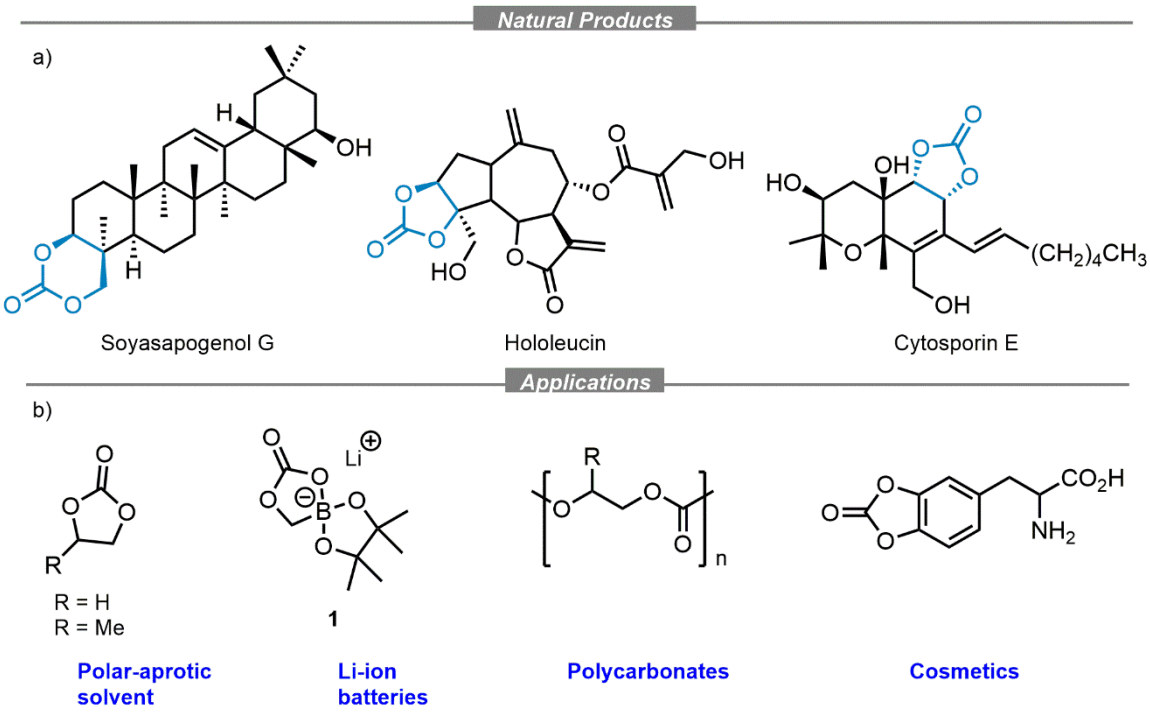
active catalysts can be seen in Scheme 1b. Even though the development of catalytic systems has reached a high level of sophistication, only a handful of different epoxides can be utilized effectively in this reaction. Most studied are the polymerisations with propylene oxide and cyclohexene oxide. Polycarbonates with side-chain functionalization have rarely been synthesized by this method. This is even though substitution on polycarbonates can be an important tool to tune polymer properties.

The synthesis of polycarbonates by ROP of cyclic carbonates is the most effective method to date, producing high quality polymers (high molecular weights, narrow molecular weight distribution) in high reproducibility. Best investigated is the ROP of 6-membered cyclic carbonates. They are thermodynamically more prone to ring-opening than 5-membered cyclic carbonates usually showing high positive polymerization enthalpy[16]. Many different catalytic systems with distinct mechanisms are known, such as cationic, anionic, coordination-insertion, monomer activation, or enzymatic activation mechanisms. Transition metal catalysts, acidic and basic organocatalysts and enzymes can be used to promote the polymerization[9][10]. As residual toxic metals should be avoided in materials used in biomedical applications, the development of organocatalysts has gained importance. Tertiary amines, guanidines, and thiourea, among others, have been employed as basic organocatalysts. Diphenyl phosphate, methanesulfonic acid and triflic acid have been used as acidic organocatalyst. Representative organocatalysts are shown in Scheme 1c.

Polycarbonates are most commonly prepared from simple 6-membered cyclic carbonates such as trimethyl carbonate (TMC) or dimethyl trimethyl carbonate. Several polycarbonates from 2,2-disubstituted TMC have been prepared as well. However, those monomers are mostly synthesized from diols with phosgene derivatives. The development of functional and substituted carbonate monomers is important, as functionalized polymers could bring forth properties not attainable using simpler polycarbonates. However, general methods for the synthesis of functionalized 6-membered cyclic carbonates in a sustainable fashion and without the use of problematic phosgene-derived reagents are still subject to investigation. Therefore, truly sustainable routes to functionalized polycarbonates are not yet available.

Cyclic Organic Carbonates

Cyclic organic carbonates form a compound class characterized by a carbonyl group flanked by two alkoxy groups. When this functional group is incorporated in cyclic scaffolds, the compounds are generally referred to as cyclic (organic) carbonates. While 5- and 6-membered cyclic carbonates are common, only few synthetic routes towards 7-membered cyclic carbonates or larger macrocycles are known. The synthesis of 5-membered cyclic carbonates has been studied intensively over the last decade, while synthetic routes to 6-membered cyclic carbonates are still to advance in terms of reaction conditions and substrate scope.



Scheme 2a) examples of naturally occurring cyclic carbonates. b) Industrial applications of cyclic carbonates

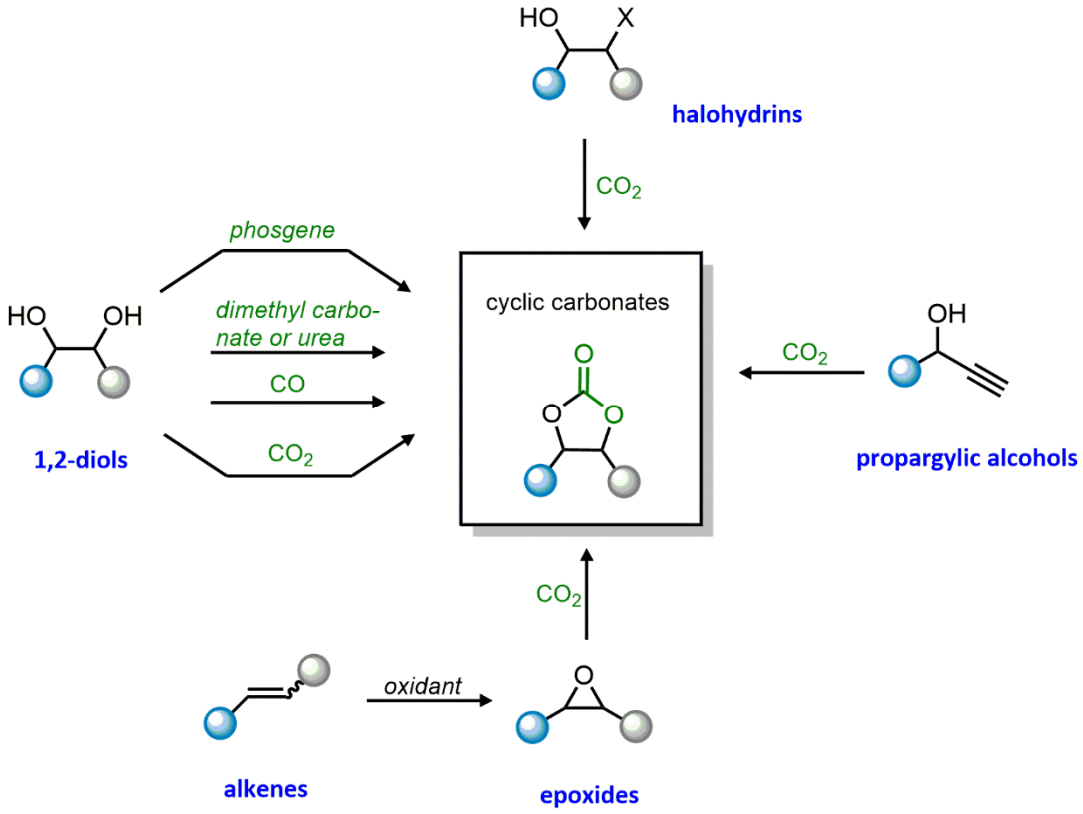
Cyclic organic carbonates play an important role in modern life, industry and academia due to their remarkable properties. Typically, they are liquid and stable compounds. They appear as substructures in various naturally occurring compounds[17]. Due to their highly polar and aprotic nature and wide liquid temperature range, they find application in industry as solvents: most prominently, cyclic carbonates such as **1** are used in Li-batteries as electrolytes. Alternatively, they are used in paint, coatings and as solvents for chemical reactions. Cyclic organic carbonates can also be found in cosmetics or herbicides. The use

of cyclic carbonates as monomers for ROP to access polycarbonates is one of the most influential applications.

In recent years, product scope, functional group tolerance, and enantio- and chemo-selectivity, as well as reactivity of the synthesis of cyclic carbonates have been expanded and improved dramatically. This enables the wider use of cyclic carbonates as synthetic intermediates[2]. Chiral carbonates can be used as surrogates for cis- or trans- diols and the aminolysis of cyclic carbonates leads to linear carbamates. Vinyl cyclic carbonates have proven to be especially interesting precursors for a range of (asymmetric) synthetic routes towards allylic heterocycles and acyclic products.

Synthesis of 5-Membered Cyclic Carbonates

Currently, 5-membered cyclic carbonates are the most investigated group of cyclic carbonates. Their synthesis is relatively straight-forward, owing to their stability. Recently, diverse scaffolds as well as chemo- and enantioselective routes have emerged. Various synthetic routes to 5-membered cyclic carbonates are summarized in Scheme 3.



Scheme 3 Synthetic approaches to 5-membered cyclic carbonates

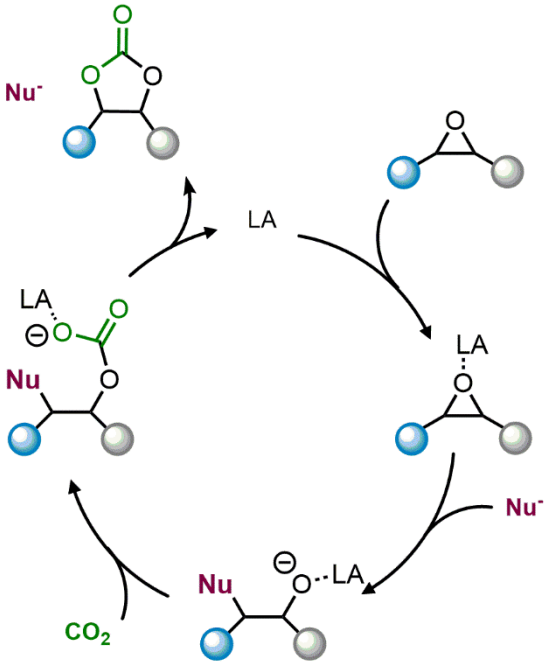
Conventionally, 5-membered cyclic carbonates have been synthesized by condensation of 1,2-diols with phosgene or its derivatives, such as triphosgene[18]. Besides a poor atom economy, the high toxicity of phosgene and its derivatives, and the formation of two equivalents of HCl as side product make this transformation unappealing for modern chemistry. However, this approach is still used in industrial contexts. Less hazardous reagents for the transformation of 1,2-diols to cyclic carbonates include carbonate esters such as dimethyl carbonate[19], ureas[20], or carbon monoxide[21] (CO). The most widespread approach, both in academia and industry, is the use of CO_2 as a C1 reagent in the formation of cyclic organic carbonates. Transformations of 1,2-diols[22], halohydrins[23], propargylic alcohols[24], and epoxides with CO_2 have been explored. One of the few transformations of CO_2 possible at mild, almost ambient, conditions is the

formal [3+2]-cycloaddition of epoxides and CO_2. Due to the elevated free energy of epoxides, the coupling is thermodynamically favored as ring-strain is released (see Figure 2). Epoxides are prepared easily from widely available olefin precursors utilizing standard oxidation conditions. This, along with the cheap, nontoxic, and renewable nature of CO_2, has fueled researcher's interest, particularly over the last decade. Great advances have been made for substrate scope and reaction conditions as well as catalyst development for this transformation[5][25][2][4][26][27][6]. This redox-neutral process displays a 100% atom economic approach.

Metal-Catalyzed Synthesis of 5-Membered Cyclic Carbonates

Both heterogeneous and homogeneous catalysts have been studied for the coupling of epoxides with CO_2. While organocatalysts have superior properties in terms of sustainability and biocompatibility, metal-catalysts show a significantly increased efficiency and an extended substrate scope. Metal-centered catalysts employed in the coupling of CO_2 with epoxides are usually Lewis-acidic species that coordinate to the epoxy-oxygen atom to activate the substrate. For the substrate activation an external nucleophile is required as a cocatalyst. Commonly, halide salts such as tetrabutyl ammoniumbromide (TBAB) are employed. Therefore, binary catalytic systems, consisting of a metal-catalyst and a nucleophile are commonly used. Another possibility is incorporating the nucleophilic species in the skeleton of the metal-complex to form a bifunctional catalyst[28] that activates the epoxide. The mechanistic pathway of the coupling of epoxides with CO_2 employing Lewis-acidic metal complexes is illustrated in Scheme 4[5].

Initially, the epoxide is activated by the Lewis-acidic metal complex, which enables the attack by the nucleophilic species in a S_N2 reaction. After the epoxide is opened, the CO_2 molecule inserts in the M-O bond, to form a stabilized hemiester of a carbonic acid. This species closes the heterocycle in a S_N2 reaction, releasing the nucleophile and the metal-complex for the next catalytic cycle. In chiral molecules this double-inversion pathway retains the stereoconfiguration of the epoxide.



Scheme 4 Mechanism for the metal-catalyzed cycloaddition of CO_2 to epoxides. Nu^- = nucleophile, LA = Lewis acid

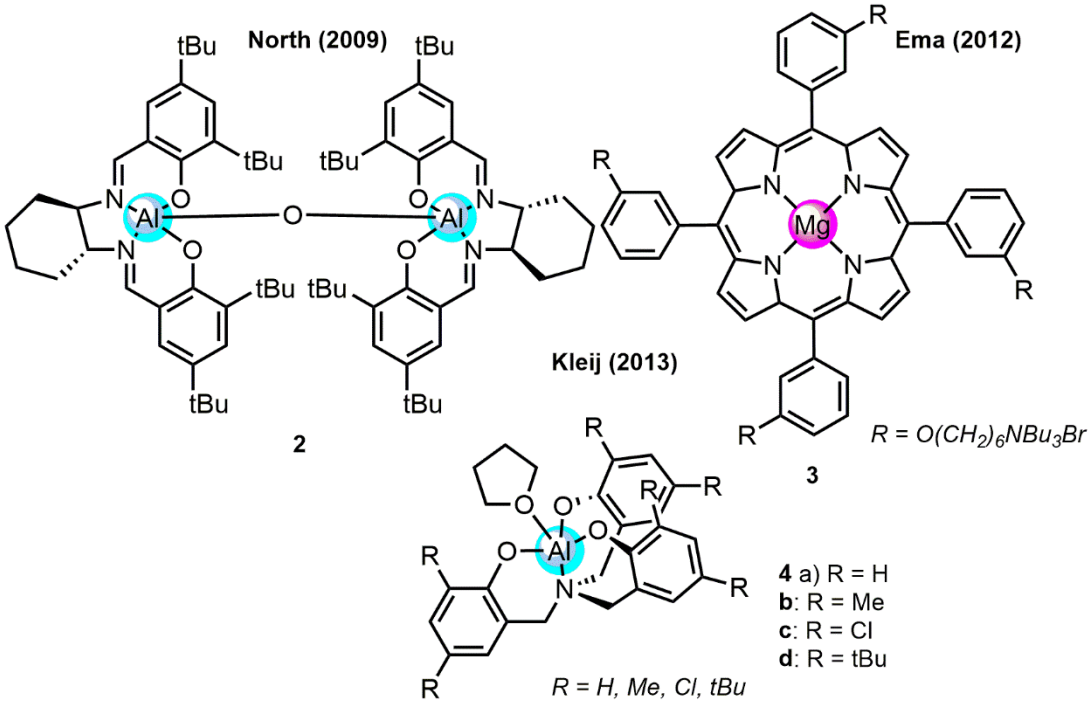


Figure 3 Homogeneous catalysts for the coupling of CO_2 to epoxides

The most active metal catalysts (**2**-**4**) for this transformation are shown in Figure 3. An advantage of these catalysts is the non-toxic and cheap nature of earth-abundant aluminium and magnesium. In 2009 North *et al.* presented a binuclear μ-oxo-bridged Al(salen) complex **2** showing remarkable reactivity in combination with TBAB[29]. Terminal aromatic and aliphatic epoxides, such as propylene oxide, can be transformed to the

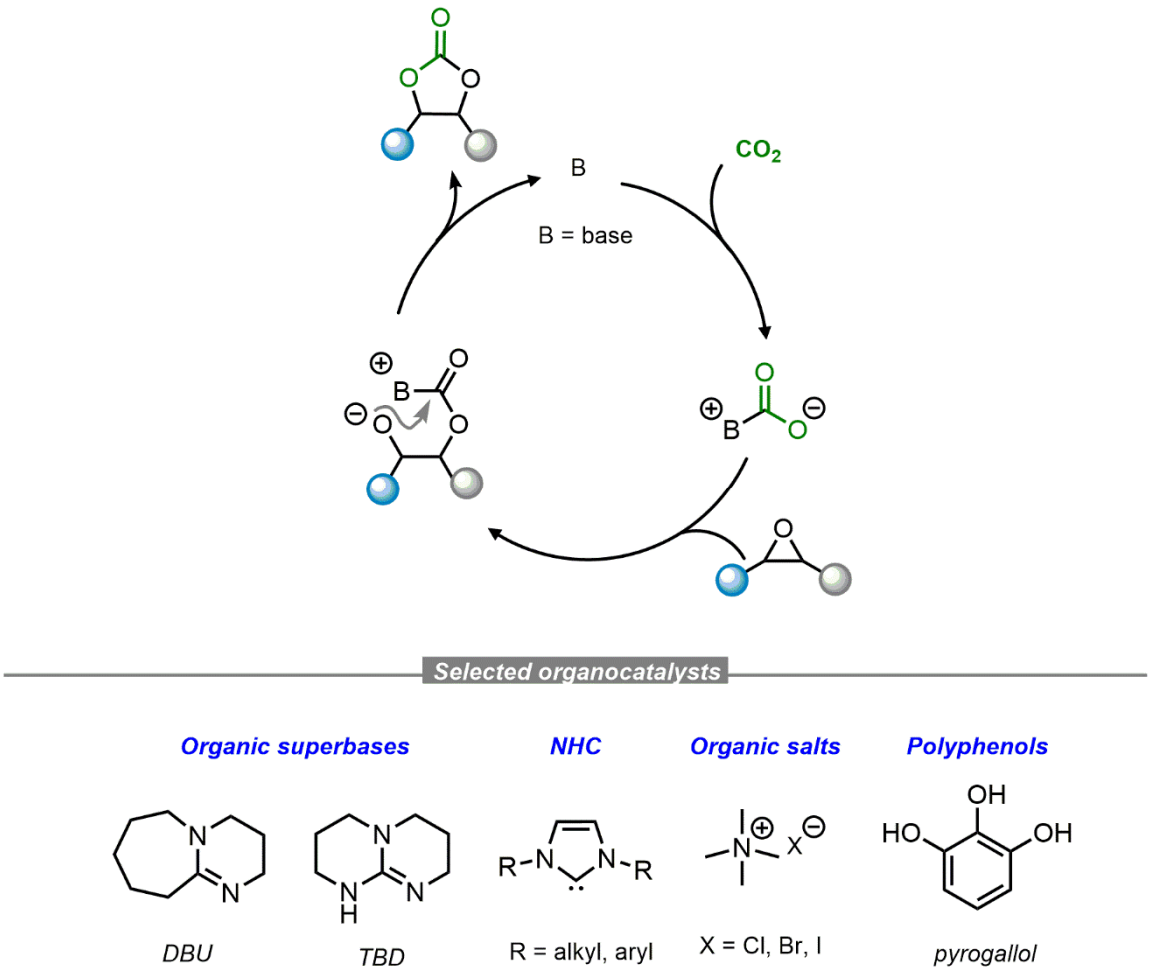
corresponding 5-membered cyclic carbonate at room temperature and atmospheric pressure in high yields.

Ema *et al.* were able to increase the catalytic activity with a bifunctional Mg(porphyrin) complex **3**[30]. An ammonium halide cocatalyst is incorporated in the porphyrin scaffold, improving reactivity by creating a transition state in which both Lewis acid and cocatalytic nucleophile are in close contact. Ema's metalloporphyrins show a broad scope in the conversion of both mono- and disubstituted epoxides to cyclic organic carbonates, despite the complexity of the bifunctional porphyrin skeleton.

In 2013, Kleij *et al.* developed the most versatile novel class of catalytic systems known to date[31]. Next to high reactivity, the easily accessible Al(III)amino(triphenolate) complexes **4a-d** are characterized by a wide substrate scope and functional group tolerance. In comparison to salen and porphyrin compounds, the amino(triphenolate) ligand coordinates in a trigonal bipyramidal fashion around the metal center, giving more sterically demanding substrates access to the catalytic center. The catalytic system shows high reactivity and the widest substrate scope to date. Remarkably, heteroatoms in functional groups of substrates are widely tolerated, despite the strong Lewis-acidic nature of the Al-center.

Organocatalyzed Synthesis of 5-Membered Cyclic Carbonates

Metal-centered homogenous catalysts for converting CO_2 into cyclic carbonates stand out with their excellent catalytic activity, substrate scope, and low catalyst loadings. Organocatalysts for this transformation have yet to reach such a level of sophistication. However, their clear advantages over metal catalysts is the potential for sustainability, biocompatibility, and simplicity of those metal-free compounds. Furthermore, no additional cocatalytic external nucleophile is required in the catalytic cycle. As serious development of organocatalysts for this transformation began relatively recently, there is still room for improvement[25][32][33].



Scheme 5 Above: Catalytic cycle for organocatalyzed CO_2 activation and insertion. Below: selected organocatalysts. TBD = 1,5,7-Triazabicyclo[4.4.0]dec-5-ene, NHC = N-heterocyclic carbene

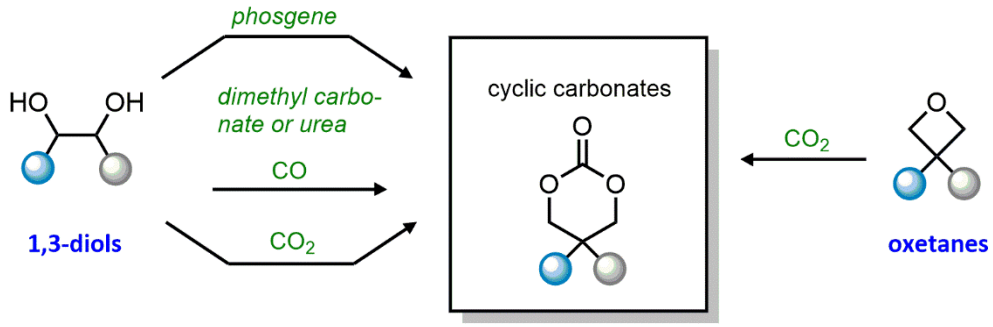
Three commonly employed groups are N-based heterocycles, such as organic bases, superbases, and N-heterocyclic carbenes (NHC), then (poly)phenols and polyalcohols, and finally organic salts used as ionic liquids or molten salts. Scheme 5 shows a selection of representative organocatalysts. Nucleophilic organocatalysts, such as organic bases and NHCs, catalyze the formation of cyclic carbonates by directly activating the CO_2 molecule for the attack of the epoxide. As depicted in Scheme 5, the formed alkoxide species subsequently cyclizes into the 5-membered cyclic carbonate, releasing the organocatalyst for the next cycle. Other organocatalysts, such as organic salts or ionic liquids activate the epoxide substrate, analogous to the cocatalyst shown in the mechanism in Scheme 4.

Multi-Substituted 5-Membered Cyclic Carbonates

Multisubstituted 5-membered cyclic carbonates can be found in various naturally occurring compounds[17], however, the synthesis of those compounds still remains a challenge. Naturally occurring renewable olefinic compounds, such as unsaturated fatty acids or terpenes easily converted into the corresponding epoxides, represent attractive substrates for a truly sustainable synthesis. In 2012, the first synthesis of a trisubstituted 5-membered cyclic carbonate, cyclic limonene dicarbonate, was prepared by Mülhaupt *et al.*[34] from limonene oxide, the epoxidized product of the commonly occurring natural compound limonene. Nevertheless, not until 2016 was a more general synthesis of trisubstituted cyclic carbonates derived from terpene scaffolds reported[35]. Due to the steric impediment around the epoxide, disfavoring both the Lewis acid activation and nucleophilic ring-opening, the catalytic activity of these transformations is reduced. Consequently, longer reaction times, higher pressure, and elevated temperature are necessary to obtain the trisubstituted compounds. With its sterically less restricted and more flexible architecture, the Al-complex **4b** has proven to be a useful catalyst[36].

Synthesis of 6-Membered Cyclic Carbonates

While significant progress has been made in the area of cyclic carbonate synthesis, most of it is owed to advances in the synthesis of 5-membered cyclic carbonates. A much bigger challenge is posed by the formation of 6-membered cyclic carbonates. To date, this has only been achieved through a limited number of synthetic pathways[37], even though 6-membered cyclic carbonates, such as trimethylene carbonate (TMC), are highly valuable monomers for ROP to obtain aliphatic polycarbonates.

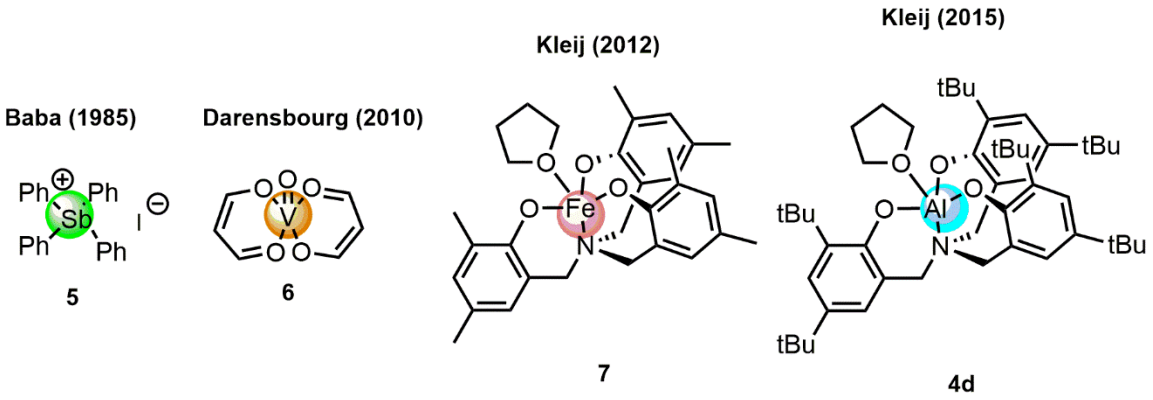


Scheme 6 Synthetic routes to access 6-membered cyclic carbonates

Traditionally, 6-membered cyclic carbonates have been prepared from 1,3-diols utilizing phosgene, or its derivatives (di- and triphosgene, alkyl chloroformate)[38][39], as a carbonylation agent. Unfortunately, these reagents are highly toxic and corrosive. Stochiometric halide waste is produced, and these reagents are prepared industrially through an energy intensive process. Less hazardous carbonylation agents have been employed, such as dimethyl carbonate or carbonyldiimidazole. However, they are industrially also prepared from phosgene and produce stochiometric waste in the formation of 6-membered cyclic carbonates. The carbonylation with CO[40] is considered a greener alternative, as no stochiometric side products are formed. Harsh conditions are required in the reaction with this toxic gas, while the scope of substituted 6-membered cyclic carbonates is limited to only a few examples. The coupling of diols with CO_2 proceeds at ambient reaction conditions, giving rise to a small number of mono- and disubstituted 6-membered cyclic carbonates. However, DBU, NEt_3 and TsCl are used as stochiometric additives, completely slashing atom economy of this approach.

Synthesis from Oxetanes and CO_2

Analogous to the most efficient and versatile formation of 5-membered carbonates, the most promising approach to 6-membered cyclic carbonates lies in the use of CO_2 as a C1 carbonyl source. While 5-membered cyclic carbonates are easily prepared from a coupling reaction between CO_2 and epoxides, the same reaction with their 4-membered strained cyclic ether counterpart, oxetanes, is much less investigated. This can be ascribed to the more challenging formation of 6-membered cyclic carbonates and the poor availability of oxetanes, compared to the easily accessible and cheap epoxides[39]. In comparison to epoxides, oxetanes show a remarkably lower reactivity. Furthermore, 6-membered cyclic carbonates are generally not thermodynamically stable and are prone to ring-opening polymerization. This poses a challenge in terms of chemoselectivity on catalysts: obtaining the kinetically favored 6-membered cyclic carbonates without forming polycarbonates.

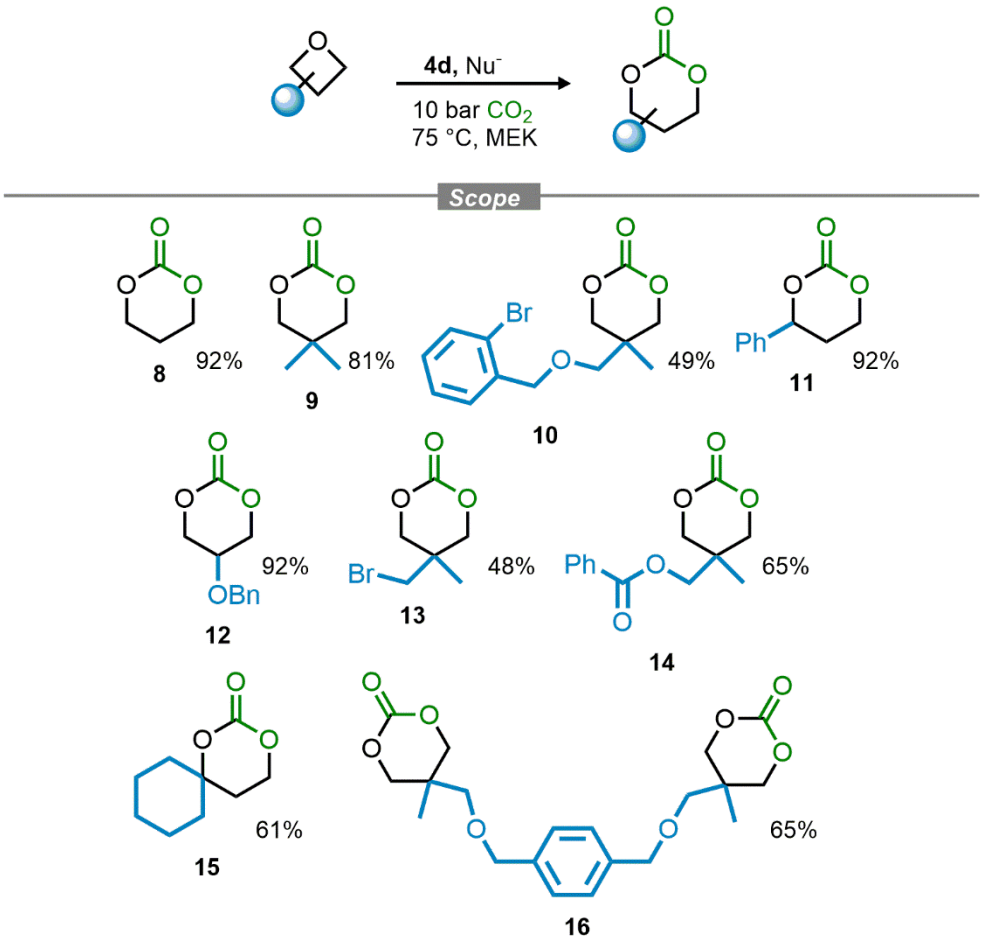


Scheme 7 Catalysts for the coupling of CO_2 with oxetanes

Until today, only few catalysts (Scheme 7) are known for the coupling of oxetanes with CO_2, even less so for the synthesis of a broader scope. The first coupling of CO_2 with oxetane has been reported in 1985[41], in a reaction under harsh conditions catalyzed by Ph_4SbI **5**, yielding TMC. In 2010, Darensbourg *et al*. showed that the same reaction could be achieved using catalytic amounts of the Lewis-acidic $VO(acac)_2$ **6** and TBAB as a nucleophile[42]. This transformation is not applicable to substituted 6-membered cyclic carbonates.

A breakthrough in the synthesis of 6-membered cyclic carbonates from oxetanes was achieved by Kleij *et al*., who discovered a Fe-aminotriphenolate catalyst **7**, which was utilized for the synthesis of 5- and 6-membered cyclic carbonates from strained cyclic

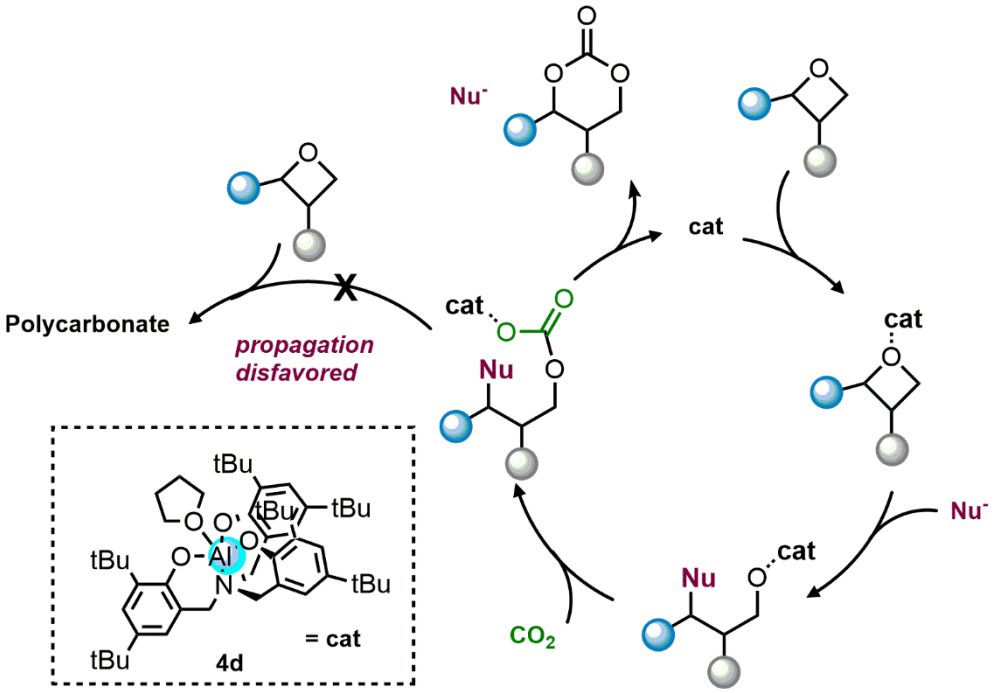
ethers[43]. They were able to advance their catalyst design, and in 2015, reported the first general approach to access a variety of mono- and disubstituted 6-membered cyclic carbonates from oxetanes utilizing Al-centered catalyst **4d**[44]. Representative carbonates **8-16** are shown in Scheme 8.



Scheme 8 Coupling of various substituted oxetanes to obtain 6-membered cyclic carbonates utilizing an Al-aminotriphenolate catalyst. MEK = methyl ethyl ketone

Steric control, induced by peripheral substituents in the ligand framework of the catalyst, has a significant effect on the reactivity of this reaction. Comparing catalysts **4a-d** with varying substituents on the aromatic position demonstrates the best catalytic activity and chemoselectivity can be achieved with complex **4d** bearing bulky *tert*-butyl groups. After oxetane activation and CO_2 insertion, a catalyst must discriminate between a ring-closing, (achieving a 6-membered cyclic carbonate), or an attack of another oxetane molecule, (leading to a polycarbonate), in order to attain chemoselectivity. Polymerization would require the proximity of another oxetane molecule to the activated Al-alkoxide species, which is hindered by a bulky catalyst scaffold. The proposed mechanism for the coupling

of oxetanes/CO_2 is analogous to the coupling of epoxides/CO_2 and is depicted in Scheme 9.



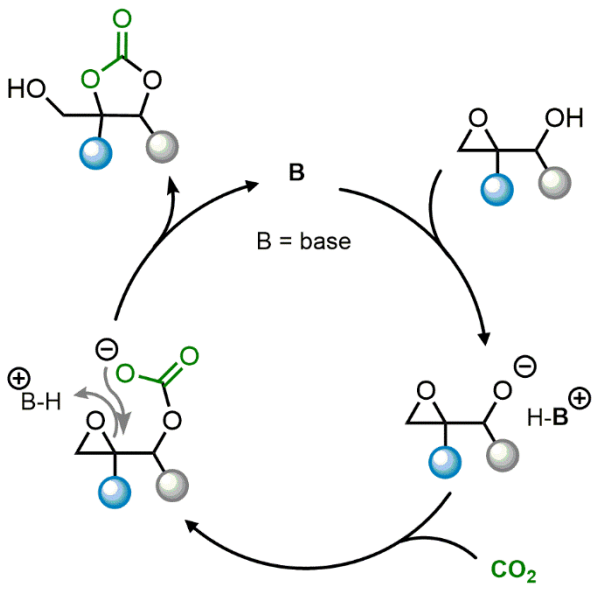
Scheme 9 Mechanistic route to 6-membered cyclic carbonates by oxetane/CO_2 coupling promoted by Al-catalyst

Various substitution patterns could be achieved and synthetically useful functional groups such as esters, bromoaryls and alkyl bromides were well tolerated. The efficiency of this synthetic route depends strongly on the type of nucleophile used (TBAB, TBAC, PPNCl) and the reaction conditions, such as temperature and pressure.

Up to date, this report represents the only general method to access 6-membered cyclic carbonates from oxetanes. Especially in terms of substrate scope, there is still much room for advancement. As 6-membered cyclic carbonates are extremely valuable monomers in the formation of polycarbonates by ROP, an easy, mild, and sustainable synthetic path to those compounds is of high interest. As substitution and post-modification play huge roles in adjusting the properties of a polymer, the synthesis of substituted and functionalized 6-membered cyclic carbonates remains an important task to be tackled.

Substrate-Assisted CO_2 Activation

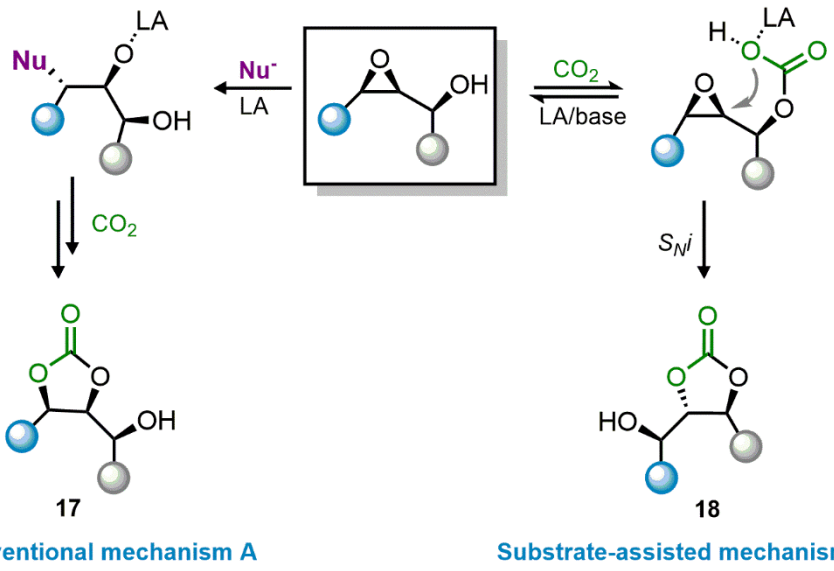
Despite the progress made in the last years, the coupling of CO_2 to multi-substituted epoxides remains a challenge - especially in the formation of tetrasubstituted cyclic carbonates, previously unobtainable through the conventional mechanism. In 2016, Kleij *et al*. elaborated including the substrate in the activation of CO_2 as an alternative and mechanistically distinct pathway to access multi-substituted cyclic carbonates[45]. For this purpose, epoxy alcohols have proven ideal substrates to develop a substrate-assisted catalytic approach. Epoxy alcohols are highly accessible, easy to synthesize, and available in a broad scope. In a new approach, the alcohol unit of the epoxy alcohol plays a crucial role in activating the CO_2 molecule[46] (Scheme 10), leading to the formation of a hemiester of a carbonic acid. This hemiester can serve as an intramolecular nucleophile for the ring-opening of the epoxide, forming a cyclic carbonate incorporating the oxygen atom of the alcohol in the cyclic scaffold. This reaction can be catalyzed by either Lewis-acidic metal catalysts or organic bases (depicted as B in Scheme 10) such as Al-aminotriphenolates **4** or DBU.



Scheme 10 Substrate-assisted activation of CO_2.

Epoxyalcohols can be divergently converted into cyclic carbonates through two distinct mechanisms yielding differently substituted cyclic carbonates (Scheme 11). This is possible, because the substrate-assisted mechanism B in Scheme 11 does not require the

addition of an external nucleophile, while the conventional mechanism A is dependent on such a species for a nucleophilic opening of the epoxide and subsequent CO_2 incorporation. Scheme 11 shows that the use of only a nucleophile (e.g. TBAB) as catalytic system results in full selectivity towards the carbonate **17** stemming from the conventional mechanism. When only a Lewis-acidic catalyst is employed without an additional nucleophile, full selectivity towards the product **18** of the substrate-assisted mechanism is achieved. The addition of substochiometric amounts of base (e.g. N,N-diisopropylethylamine) can improve the catalytic activity. Stereoselective transformations can be achieved employing single diastereomers of epoxyalcohols. The two consecutive S_N2 reactions of the conventional mechanism retain the configuration of the substrate. In the substrate-controlled CO_2 insertion process, only one S_Ni reaction takes place, inverting one stereocenter[47].

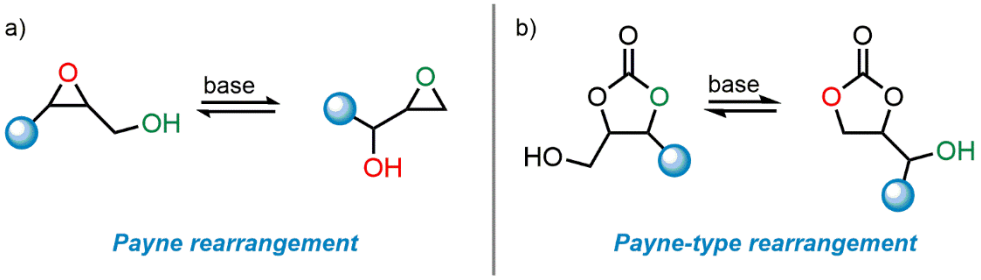


Scheme 11 Product divergence in the coupling of epoxyalcohols and CO_2. Nu- = nucleophile (TBAB), LA = Lewis acidic catalyst

This substrate-assisted mechanism allows for the synthesis of challenging 4,5-disubstituted and 4,4,5-trisubstituted cyclic carbonates. The trisubstituted cyclic carbonates cannot be obtained through a conventional epoxide/CO_2 coupling approach. Furthermore, epoxyamines can also be utilized in this transformation, yielding cyclic carbamates through the same substrate-assisted mechanism[48].

Payne-type Rearrangement

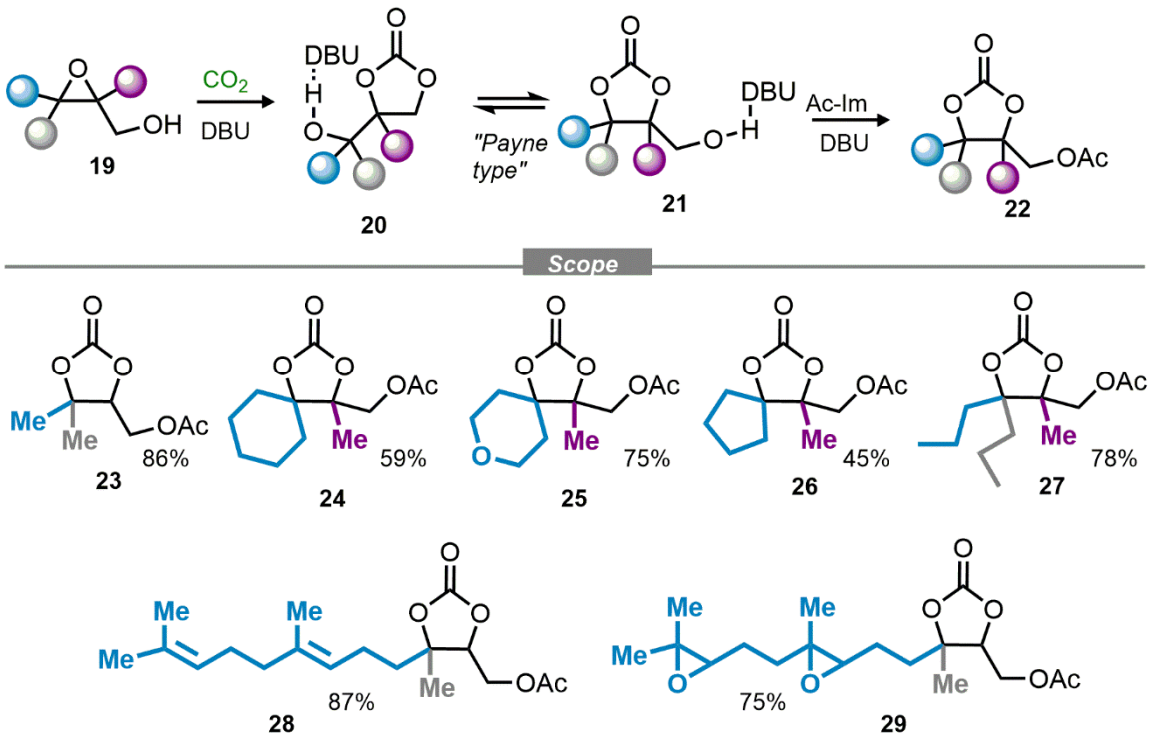
In 2018, Kleij's group found that hydroxymethyl-substituted 5-membered cyclic carbonates can undergo a rearrangement, so-called "Payne-type rearrangement", comparable to the equilibrium reaction of epoxyalcohols called Payne-rearrangement[49].



Scheme 12 Base-promoted a) Payne rearrangement of 1,2-epoxy alcohols and b) Payne-type rearrangement of hydroxymethyl substituted cyclic carbonates.

In the Payne-rearrangement[50], the alcohol function of a 1,2-epoxy alcohol opens the epoxy-group under basic conditions, forming an isomeric epoxyalcohol in equilibrium (Scheme 12a). Similarly, hydroxymethyl-substituted cyclic carbonates undergo a base-assisted isomerization. Thereby, the free hydroxy group is activated by a base and can attack the cyclic carbonate in an intramolecular nucleophilic fashion. An equilibrium between the two isomeric carbonates is established (Scheme 12b).

By selective protection of the more reactive alcohol-group, this equilibrium reaction can be shifted to obtain tri- and tetrasubstituted cyclic carbonates. An appropriate protecting agent like acetyl-imidazole (Ac-Im) can selectively protect the primary alcohol of **21** without interfering with the unreactive tertiary alcohol of **20**, shifting the equilibrium to give the final product **22**. Scheme 13 shows a selection of multi-substituted cyclic carbonates **23-29** that were obtained in a domino cycloaddition/Payne-type rearrangement reaction.



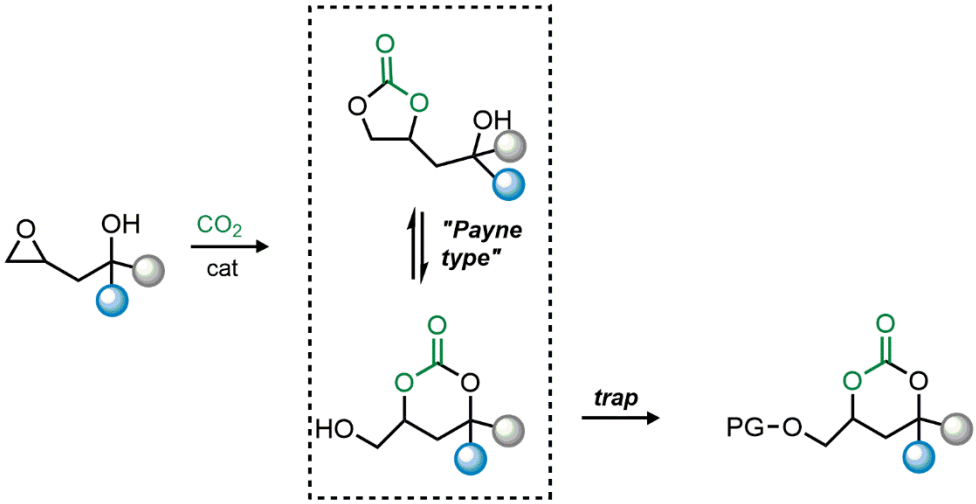
Scheme 13 Synthesis of tri- and tetrasubstituted 5-membered cyclic carbonates through a domino cycloaddition of epoxyalcohol/CO_2 and payne-type rearrangement

Along with complex tetrasubstituted cyclic carbonates, trisubstituted cyclic carbonates derived from terpene scaffolds have been prepared successfully. The synthesis of **29** shows the chemoselectivity of this approach impressively. While the trisubstituted epoxy groups of **29** remain unreactive, only the monosubstituted epoxy group with neighbouring alcohol function reacts in the domino reaction.

DBU currently is the most effective organocatalyst to promote both the cycloaddition of CO_2/epoxyalcohol and the "Payne-type rearrangement", avoiding the addition of metal catalysts or additional nucleophiles. The shown tri- and tetrasubstituted cyclic carbonates cannot be accessed through the conventional epoxide/CO_2 coupling mechanism due to their high steric demand. To date, these are the first and only examples for tetrasubstituted cyclic carbonates.

Aim

A novel access to 6-membered cyclic carbonates, especially with substituents attached, would be an important achievement in the field of cyclic carbonates. 6-membered cyclic carbonates are valuable compounds, specifically as monomers for the ROP to obtain polycarbonates, highly functional materials in the field of biomedicine. To date, only few synthetic routes can access those molecules and only a limited number of functional groups and substitution patterns have been successfully introduced so far. While the condensation reaction of diols with phosgene derivatives is undesirable due to the toxic nature of those reagents, the cycloaddition of oxetanes with CO_2 is highly challenging and limited in terms of substrate scope.



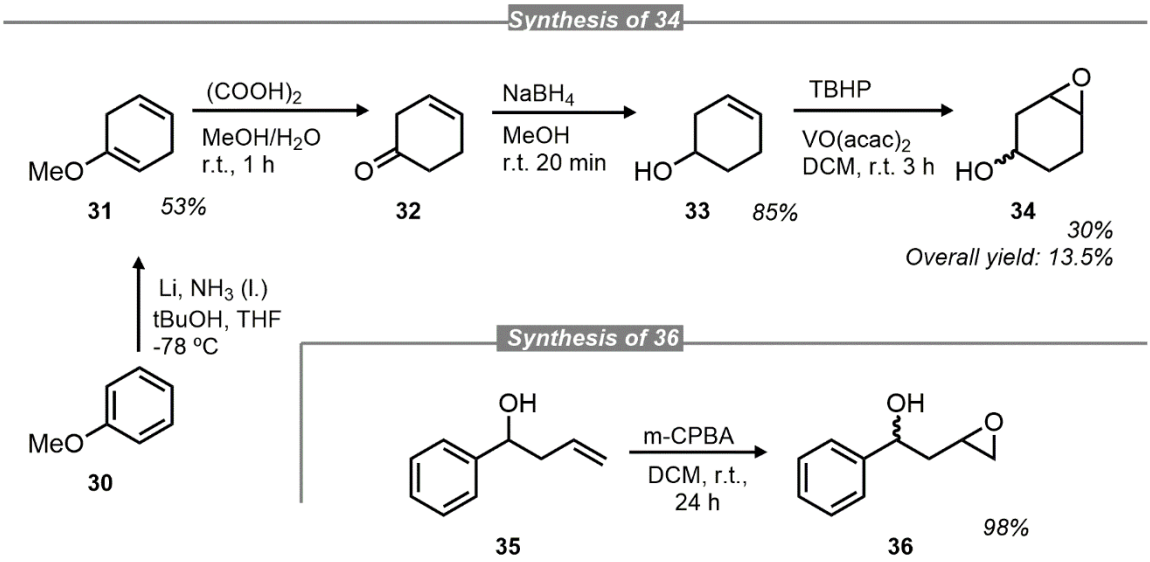
Scheme 14 Envisioned synthetic path to access 6-membered cyclic carbonates from cycloaddition of CO_2 and epoxy alochols. PG = protecting group

We envisioned the "Payne-type rearrangement" would also take place between a hydroxyethyl-substituted 5-membered cyclic carbonate and a hydroxymethyl-substituted 6-membered cyclic carbonate derived from the cycloaddition of 3,4-epoxy alcohols and CO_2. (Scheme 14) As 6-memberd cyclic carbonates are generally thermodynamically disfavored compared to their 5-membered counterparts,[51] it seems unlikely that they would form directly without reacting back in the "Payne-type rearrangement". Our aim was to closely investigate those methylhydroxy substituted 6-membered cyclic carbonates. We wanted to find if these 6-membered molecules exist and can be isolated, or if the equilibrium is too far on the side of the 5-membered cyclic carbonates. We further wanted to explore if transiently formed 6-membered cyclic carbonates can be

trapped by selective protection of the pendent hydroxy group, analogous to the procedure reported by Kleij[49]. In this way, we set out to find a novel synthetic route to multi-substituted 6-membered cyclic carbonates.

Results and Discussion

Synthesis of 3,4-Epoxy Alcohols 34 and 36



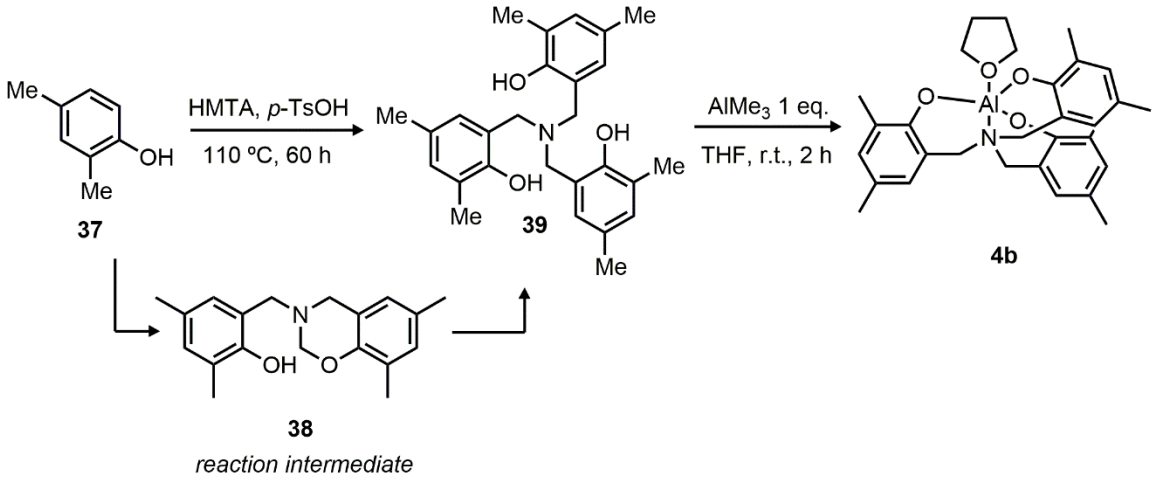
Scheme 15 Synthesis of 3,4-epoxyalcohols 34 and 36

To investigate a direct formation of 6-membered cyclic carbonates from the coupling of 3,4-epoxy alcohols and CO_2, 3,4-epoxy alcohols **34** and **36** were chosen as the first targets (Scheme 15). **36** was synthesized according to literature via epoxidation with *meta*-chloroperoxybenzoic acid (*m*CPBA) yielding 98% in a 1:1 mixture of two diastereomers that could not be separated by column chromatography.

Further, **34** was synthesized in a four-step synthesis from anisole **30**. In a Birch reduction[52], employing Li in liquid ammonia, diene **31** was obtained in 53% yield. Demethylation of **31** was achieved quantitatively. The resulting ketone **32** was employed without further purification in a reduction with sodium borohydride affording the homoallylic alcohol **33**. This compound was subsequently purified by column chromatography, yielding 85% over two steps from diene **31**. Different epoxidation methods were tried in order to obtain **34**: *m*CPBA, TBHP with $Al(OiPr)_3$, TBHP with $Mo(CO)_6$, and magnesium monoperoxyphtalate. They all proved to be unsuccessful. While the reaction of **33** with *m*CPBA and with TBHP/$Al(OiPr)_3$ gave complex reaction mixtures, the reaction with magnesium monoperoxyphtalate did not show any conversion. Ultimately, the desired product **34** was obtained by employing two equivalents of TBHP with catalytic $VO(acac)_2$. Various side products were produced, but epoxy alcohol **34** was

obtained in 30% yield, which corresponds to an overall yield of 13.5% over four steps from anisole.

Synthesis of Al-catalyst **4b**

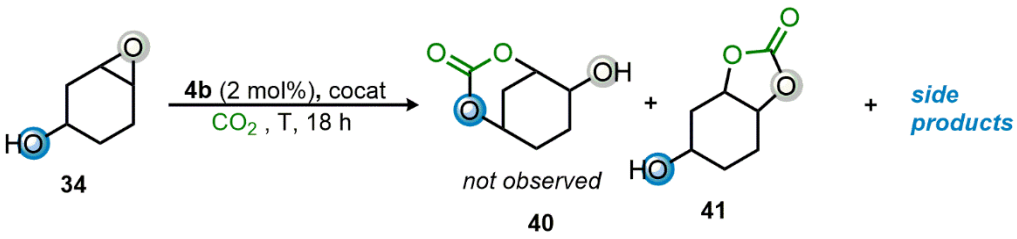


Scheme 16 Synthesis of Al-complex 4b

To investigate the formation of 6-membered cyclic carbonates from the coupling of 3,4-epoxy alcohols and CO_2, an appropriate catalyst is necessary. The Al(III)-aminotriphenolate complex **4b** was chosen as a catalyst as it has been reported to efficiently couple epoxides with CO_2[31][5]. It has been utilized in the substrate-assisted formation of 5-membered cyclic carbonates from 2,3-epoxy alcohols[45][47]. **4b** was prepared according to literature[53][47] from 2,4-dimethylphenole **37** and hexamethylenetetramine (HMTA) catalyzed by *para*-toluene sulfonic acid. After 22 h ^{1}H NMR spectroscopy showed signals corresponding to the reaction intermediate **38**. Instead of one singlet, which should be observed for the three identical CH_2-groups of the desired product **39**, three distinct singlets for non-equivalent CH_2-groups of the intermediate **38** were observed. After 60 h, the desired product **39** was isolated by recrystallization from a mixture of ethanol and acetone, yielding 68%. ^{1}H NMR matched literature[47]. The compound was dried thoroughly under reduced pressure.

For the formation of the Al(III)-centered catalyst **4b**, the obtained ligand **39** was mixed with $AlMe_3$ in THF. It was necessary to work under strictly water free conditions due to the pyrophoric nature of $AlMe_3$. **4b** was isolated by precipitation with hexane as an air-stable white powder. After five months stored under air at 4 °C, no decrease in reactivity was detected. As the signals were broad and hard to identify in $CDCl_3$, a ^{1}H NMR spectrum was taken in d_4-MeOD, in which even the protons of the coordinated THF molecule could be identified.

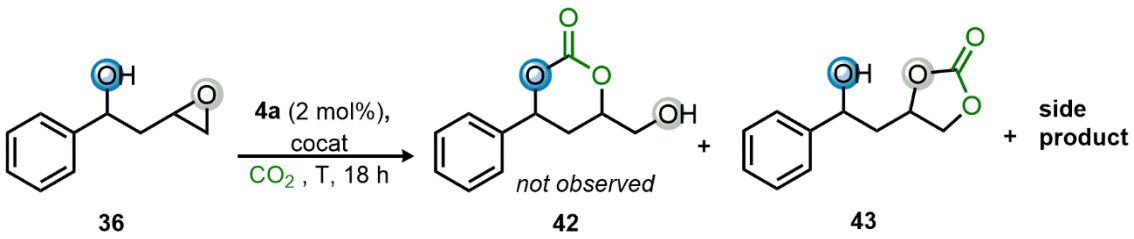
Direct Coupling of 3,4-Epoxy Alcohols with CO_2



Scheme 17 Coupling of **34** with CO_2

Initially, the conversion of epoxy alcohol **34** with CO_2 to achieve 5- and 6-membered cyclic carbonates (Scheme 17) was attempted utilizing previously prepared complex **4b** as catalyst and tetrabutyl ammonium bromide (TBAB) as nucleophilic cocatalyst. The reaction resulted in a slimy, brown, mostly insoluble product - presumably a result of polymerization. The insoluble material was removed by column chromatography. IR spectroscopy of the small amount of remaining product showed a signal at 1796 cm^{-1}.

The frequency of the C=O band is sensitive to the environment of the C=O group, for example, the bond angles, determined by the ring-size of a cyclic carbonate[54]. 6-membered cyclic carbonates, similar to the desired product, show the C=O stretch band between 1745 cm^{-1} and 1720 cm^{-1}[44], while similar 5-membered cyclic carbonates range between 1800 cm^{-1} and 1760 cm^{-1}[49]. The IR spectrum of the product therefore suggested only 5-membered cyclic carbonate, and no 6-membered cyclic carbonate, was formed in the reaction. Replacing the cocatalyst TBAB with the organic base DBU or *N,N*-diisopropylethylamine (DIPEA) gave the same result. Lowering the temperature from 70 °C to 40 °C or employing Al-complex **4b** or DBU alone as catalyst only resulted in low to no conversion. The yield of the product **41** was not determined, as the largest portion of the product mixture was made up of the insoluble polymeric side product.



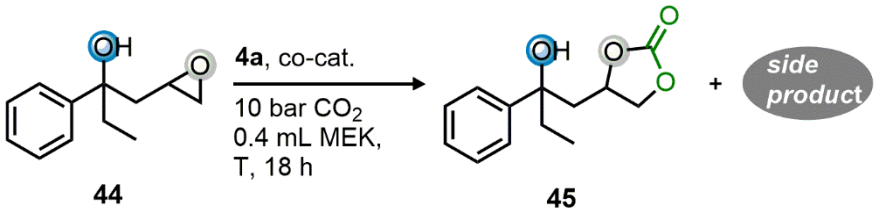
Scheme 18 Coupling of 36 with CO_2

On the other hand, conversion of epoxy alcohol **36** with CO_2 in the presence of catalyst **4b** and TBAB afforded a mixture of two compounds. The IR spectrum showed only one band in the cyclic carbonate C=O-stretch area at 1786 cm^{-1} suggesting the formation of a 5-membered cyclic carbonate, with no indication of 6-membered cyclic carbonate. Replacing TBAB with DBU, decreasing CO_2 pressure, increasing the reaction temperature, as well as prolonging the reaction time, all gave similar results. The two compounds could not be separated due to similar polarities. Any formation of 6-membered cyclic carbonate **42** could not be observed. Even though it is known that 6-membered cyclic carbonates are generally thermodynamically less stable than their 5-membered counterparts[51], we theorized that a small amount of 6-membered cyclic carbonate should be formed in equilibrium.

According to results by Kleij *et al*.[49], the Payne-type equilibrium lies more heavily towards the more-substituted cyclic carbonate. For this reason, we set out to increase the substitution on the alcohol group of the epoxyalcohol to obtain a tertiary alcohol. We hypothesized the use of a tertiary epoxyalcohol could reduce the thermodynamic disfavor of the 6-membered cyclic carbonate by introducing three substituents on the carbonate ring. Precursor **44** was therefor synthesized by Grignard addition of allyl magnesium chloride to propiophenone followed by epoxidation with *m*CPBA, yielding 85% of the epoxyalcohol over both steps.

The epoxyalcohol **44** was then subjected to conditions reported by Kleij *et al.* using **4b** and either DBU or TBAB as cocatalyst[35][45]. Table 1 reports the yields of product **45**. Again, no formation of desired 6-membered cyclic carbonate could be observed.

Table 1 Coupling of **44** with CO_2 to obtain 5-membered cyclic carbonate



44 45

Entry	T [°C]	Cocatalyst	Conversion	Side product	**45**
1	75	DBU (10 mol%)	97%	34% (30% isolated)	59% (50% isolated)
2	75	TBAB (5 mol%)	100%	25% (20% isolated)	68% (65% isolated)
3	50	TBAB (5 mol%)	100%	traces	73% isolated
4	75	---	59%	Multiple side products	---
5*	75	DBU (10 mol%)	52%	9%	43%
6	85	---	31%	Multiple side products	traces
7*	85	DBU (10 mol%)	61%	8%	53%

* p = 30 bar

Employing catalyst **4b**, in combination with either the nucleophile TBAB or the base DBU as cocatalyst, at 75 °C and 10 bar CO_2 pressure resulted in the formation of 5-membered cyclic carbonates and one side product. With DBU as a cocatalyst, substantially more of the side product was formed. After decreasing the reaction temperature from 75 °C to 50 °C, only traces of the side product could be observed in the crude ^{1}H NMR and GC. The isolated yield of 5-membered cyclic carbonate **45** increased from 65% to 73%. The IR spectrum of the crude mixture showed only one band in the C=O stretch region at 1775 cm^{-1} which suggests the presence of only 5-membered cyclic carbonates, and not 6-membered cyclic carbonates in the crude product. The carbonates were separated from the side product by column chromatography and were identified as diastereomers by ^{1}H NMR. The diastereomers themselves were not separable by column chromatography and were analyzed as a mixture. In ^{1}H NMR, signals for the carbonate protons were found between 5 ppm and 3 ppm, the same area reported for similar 5-membered cyclic carbonates[49]. The diastereomeric ratio was found to be dependent on the type of cocatalyst (1:1 for DBU, 10:1 for TBAB at 75 °C) and the temperature. The same reaction with TBAB as cocatalyst at 50 °C afforded the 5-membered cyclic carbonates in a d.r. of

7:3. The most characteristic signal in IR spectrum of the isolated carbonates matched with the 1775 cm^{-1} of the crude mixture.

The isolated side product did not show an IR band indicative for a carbonate, even though it showed ^{1}H NMR signals in the same region as carbonates. By comparing NMR spectra, we could exclude the presence of a triol, the hydrolysis product of the epoxyalcohol. Most likely, the side product is a cyclic ether, either oxolane or oxetane. Employing **4a** without cocatalyst at 75 °C resulted in a complex mixture of undesired products. DBU alone at 75 °C as a catalyst showed acceptable selectivity towards the 5-membered cyclic carbonate, with only moderate conversion of the starting material. Conversions did not improve substantially with the increase of temperature from 75 °C to 85 °C.

In an attempt to explain the absence of any 6-membered cyclic carbonate in the product mixture, we conducted DFT calculations to gain insight in the stabilities of respective 5- and 6-membered cyclic carbonate isomers. We calculated the difference in Gibbs energy (ΔG°) between the model carbonates **46** and **47** in Figure 4 to amount to 6.29 kcal/mol. This corresponds to an equilibrium constant of K_{eq} = 2.39 x 10^{-5} for the equilibrium between 5-membered- and 6-membered cyclic carbonate. This very small number explains the lack of 6-membered carbonate formation. The equilibrium is calculated to lie on the side of the 5-membered carbonate by a factor of 10,000.

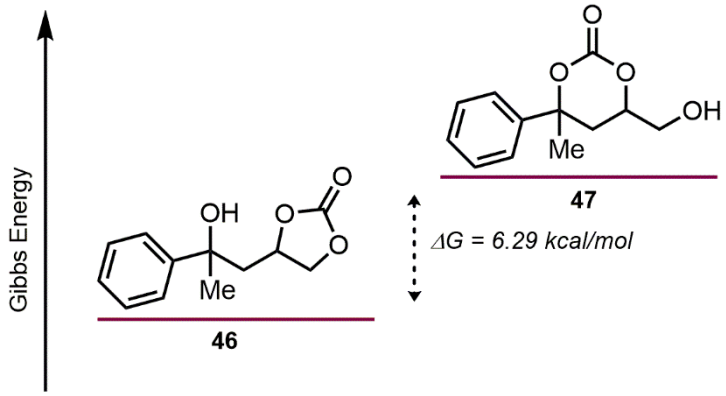
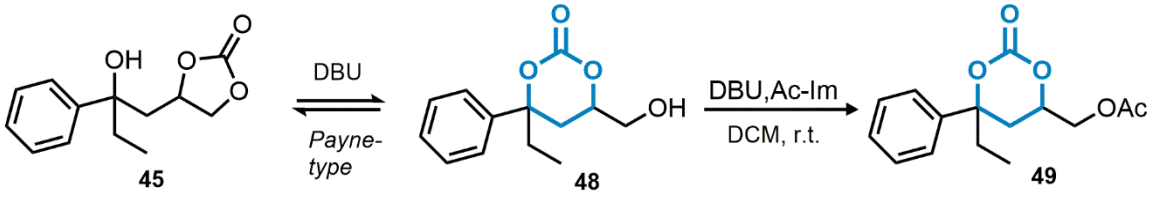


Figure 4 Difference in Gibbs Energy of 5-membered cyclic carbonate and 6-membered cyclic carbonate, calculated by DFT

Synthesis of 6-Membered Cyclic Carbonates by Selective Trapping

Due to their thermodynamic instability, 6-membered cyclic carbonates did not form in appreciable quantities from the coupling of 3,4-epoxy alcohols and CO_2. To overcome this difficulty we decided to trap potentially transiently formed 6-membered cyclic carbonates by the use of a suitable protective group[49]. DBU was employed as a base to promote the "Payne-type rearrangement" of a 5-membered cyclic carbonate to a 6-membered cyclic carbonate. **45** was chosen as a first substrate. The tertiary alcohol group in this compound is expected to have a significantly lower reactivity compared to the primary alcohol in a transiently formed isomeric 6-membered cyclic carbonate **48** (Scheme 19). Acetyl-Imidazole (Ac-Im) was selected as a reagent for trapping, as it selectively acetylates primary alcohols, while not reacting with secondary and tertiary alcohols[55].



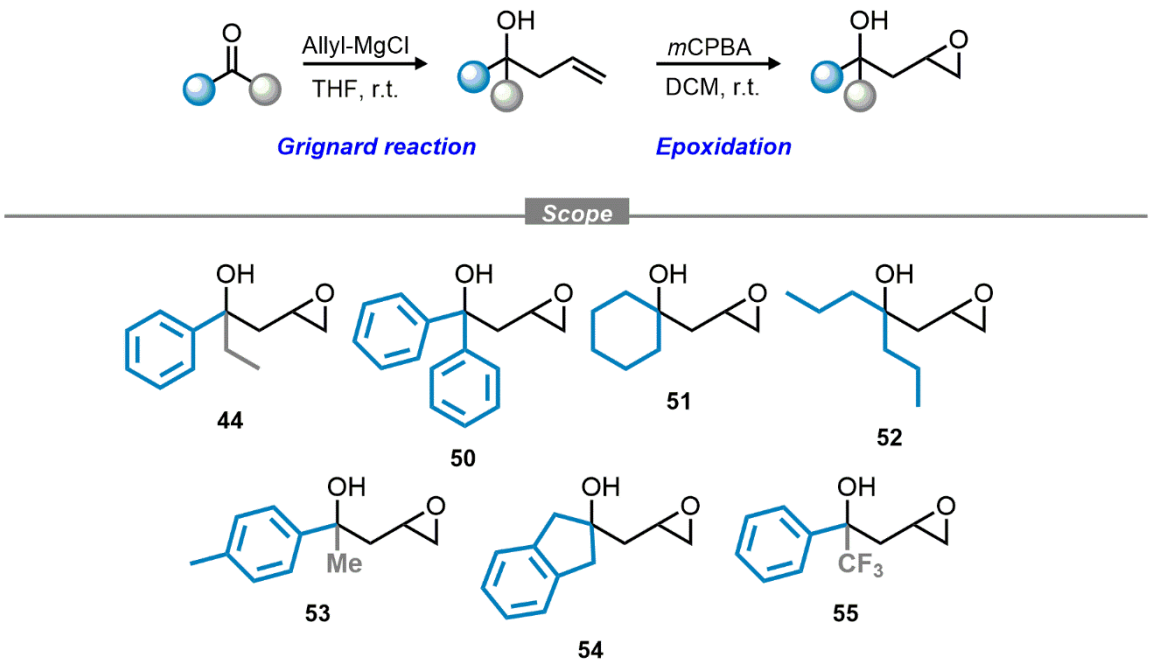
Scheme 19 Synthesis of 6-membered cyclic carbonate by Payne-type rearrangement followed by selective trapping

DBU was added to the **45**, and after five minutes, Ac-Im was added to the mixture. An IR spectrum of the reaction mixture at the beginning of the experiment showed both the C=O stretch of the 5-membered cyclic carbonate **45** (1793 cm^{-1}), and Ac-Im (1739 cm^{-1}), as well as the broad signal of the O-H stretch of the hydroxy group (3300 – 3100 cm^{-1}). The reaction was monitored by TLC, showing the formation of a single product after two hours. An IR spectrum of the crude reaction mixture showed that the band at 1793 cm^{-1} had decreased substantially, while the principal band of the spectrum appeared at 1742 cm^{-1}. After 23 h the reaction was stopped, and the formed product was purified. After column chromatography, the smaller carbonyl signal at 1793 cm^{-1}, and the broad and intense O-H band around 3200 cm^{-1}, were no longer visible, indicating the absence of 5-membered cyclic carbonate and hydroxyl group. Due to overlapping signals (1742 cm^{-1}, 1739 cm^{-1}) we observed a single C=O stretch for both carbonyl groups in the molecule **49** at 1742 cm^{-1}. This goes in line with IR spectra reported in literature for 6-membered cyclic carbonates[44]. The structure of **49** was further confirmed with ^{13}C NMR. Two signals observed at 148.6 ppm and 148.4 ppm were ascribed to the carbonyl carbons of the two diastereomers of **49**. 6-membered cyclic carbonates have characteristic carbonyl signals

between 147.0 and 148.9 ppm[56][44]. ^{1}H NMR of the purified product showed a singlet integrating to 3H for the acetyl group and shifted signals for the carbonate protons compared to the starting material. The mass of the compound was confirmed by HRMS. We were able to obtain the 6-membered cyclic carbonate **49** in a yield of 43%. To our delight, Ac-Im therefore allowed the trapping of the primary alcohol formed through the "Payne-type rearrangement" to yield the corresponding protected 6-membered cyclic carbonate **49**.

Purification of the 5-membered cyclic carbonate prior to the Payne-rearrangement was found to be crucial in this reaction. A one-pot reaction, where Ac-Im was added directly after the formation of the 5-membered cyclic carbonate **45** from the 3,4-epoxy alcohol **44** did not yield any of the desired product. Instead, two side products were observed. We assume the Al-catalyst **4b** was interfering with the reaction.

Synthesis of 3,4-Epoxy alcohol and 5-Membered Cyclic Carbonate Precursors

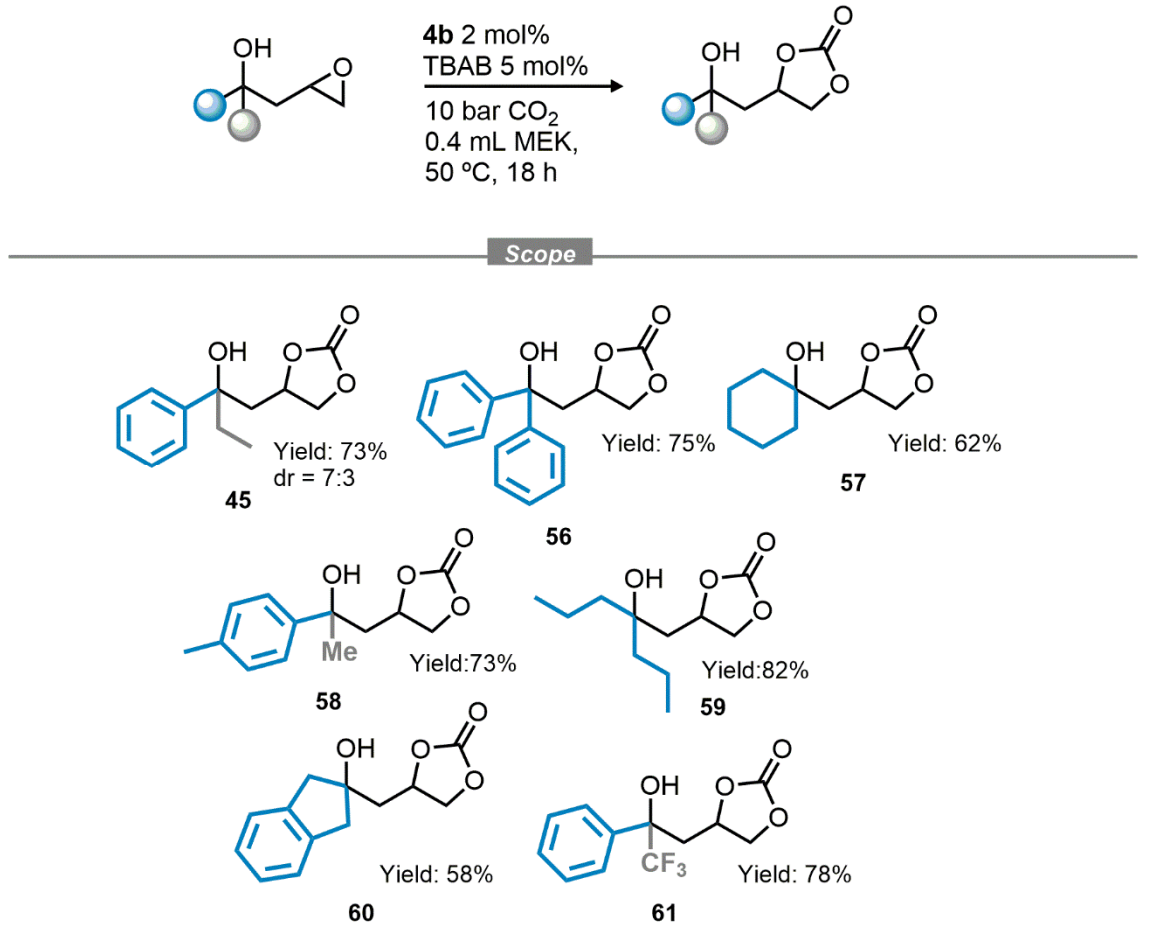


Scheme 20 Scope: 3,4-epoxy alcohols. 50-55 were provided by Chang Qiao

Next, we set out to investigate the generality of our newly found synthetic approach to 6-membered cyclic carbonates, starting from 5-membered cyclic carbonates with pendent α,α-disubstituted hydroxyethyl groups. These carbonates were synthesized from epoxy alcohols, which we prepared starting from ketones. In a Grignard reaction, allylmagnesium chloride was added to the ketone, which was consequently reduced to a tertiary alcohol. Without further purification, the double bond of the resulting homoallylic alcohol was epoxidized utilizing the oxidant *m*CPBA (Scheme 20). The resulting 3,4-epoxy alcohols were purified by column chromatography. Epoxides **50-55** were synthesized and provided to me by Chang Qiao. They were all synthesized from the corresponding homoallylic alcohols by reaction with 1.2 equivalents of *m*CPBA in DCM. The characterization of epoxides **50** and **51** matched literature[57][58]. The compounds **44** and **52 -55** were characterized by ^{1}H NMR, ^{13}C NMR and HRMS and matched with reported similar compounds[57][58].

^{1}H NMR showed **44** was generated as a diastereomeric mixture in a ratio of 7:3. It was possible to separate the diastereomers via column chromatography in a combined yield of 85% over both steps. However, also a mixed fraction of both diastereomers was

collected. The diastereomeric mixtures of **53** and **55** prepared by Chang Qiao were not separated and were used as mixtures.

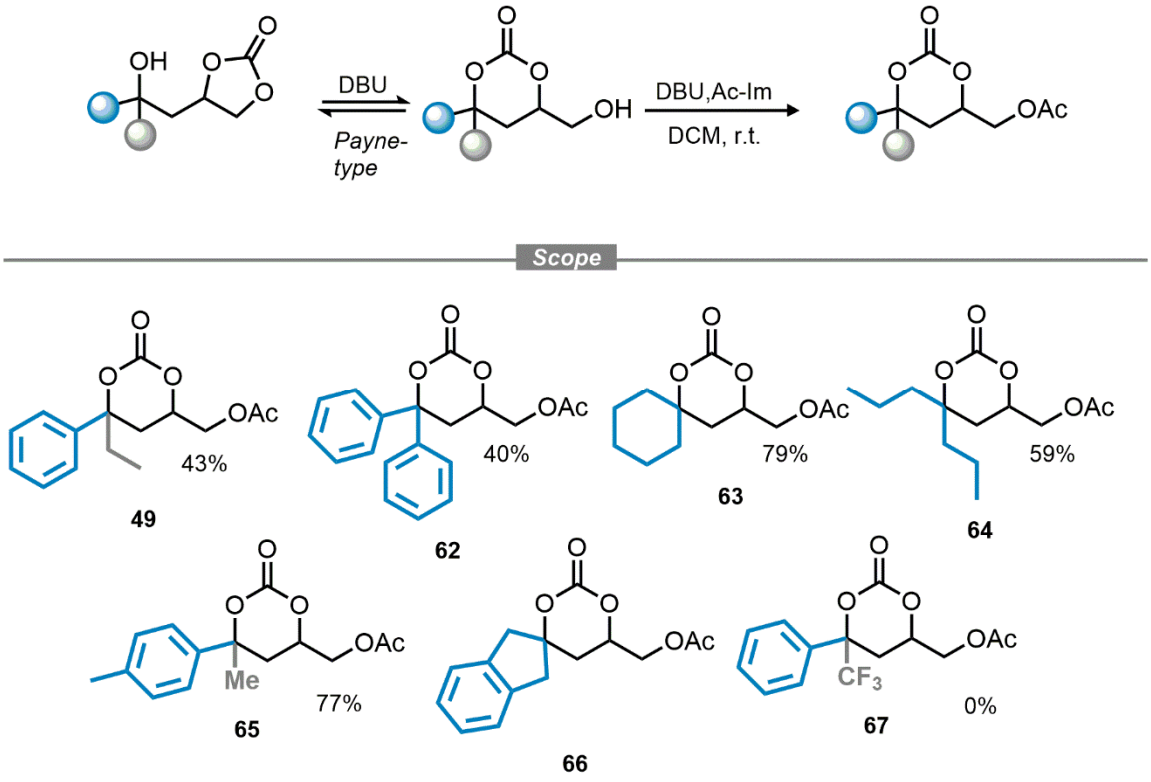


Scheme 21 Synthesized 5-membered cyclic carbonates

The epoxyalcohols were then converted to the corresponding cyclic carbonates as reported in entry 3 of Table 1. 50 °C, 10 bar CO_2, employing **4b** (2 mol%) and TBAB (5 mol%) as catalytic system gave the highest isolated yield for **45**. We synthesized seven different 5-membered cyclic carbonates on a 0.5 mmol scale in appreciable to good yields (Scheme 21). Compounds with different aromatic and aliphatic substituents, as well as one with an electron withdrawing CF_3-group, have been prepared successfully. The yields mostly range between 70% and 80%. Carbonate **57** and **60** show a slightly decreased yield of 62% and 58%. Both compounds have a spirocyclic cycloalkane substituent. The highest yield with 82% was found for carbonate **59** bearing two propyl-groups. **45**, **58** and **61** were prepared from a single diastereomer epoxy alcohol and obtained as different diastereomeric mixtures. Their diastereomeric ratios were determined by ^{1}H NMR. Even the electron-withdrawing CF_3-group in **61** was well tolerated in the reaction. All

compounds showed a band in the C=O stretch region of the IR spectrum typical for 5-membered cyclic carbonates, and were characterized as well by ^{1}H NMR, ^{13}C NMR and HRMS upon purification. Their spectroscopic data matched with the data of similar 5-membered cyclic carbonates known to literature[47][40][45].

Substrate Scope: 6-Membered Cyclic Carbonates



Scheme 22 Scope 6-membered cyclic carbonates

We subjected our newly synthesized 5-membered cyclic carbonates **45** and **56-61** to the same reaction conditions as shown in Scheme 22 to synthesize 6-membered cyclic carbonates. We were pleased to discover that the trapping by protection of the alcohol of 6-membered cyclic carbonates existing in a Payne-type equilibrium can be used as a general approach to synthesize 6-membered cyclic carbonates. Under mild conditions (room temperature, ambient atmosphere) five trisubstituted, otherwise elusive 6-membered cyclic carbonates **49** and **62-65** could be obtained in appreciable to good yields of up to 79%, including different phenyl- and alkyl substituents. This constitutes the first general approach to trisubstituted 6-membered cyclic carbonates utilizing CO_2 as a carbonylation agent.

The best yields were obtained for **65** and **63** with 77% and 79% yield. **64** shows a slightly lower yield, presumably due to the steric bulk close to the carbonate cycle. The reduced yields of **49** and **62** do not stem from low conversion or side product formation but can be explained by a loss of material for analysis during the reaction (TLC, NMR), as

sample-taking from the 300 µL reaction mixture results in measurable differences. Instead of **66**, an unknown product was produced. However, Chang Qiao was able to obtain **66** from the same reaction conditions as in Scheme 22 working under H_2O-free conditions. **67** could not be obtained from the corresponding 5-membered cyclic carbonate. Instead, an unknown product, which is not a 6-membered carbonate, formed. Most likely, the electron-withdrawing nature of the CF_3-substituent interferes with the reaction.

Prolonged reaction times and additional additions of DBU and Ac-Im were employed (denoted in experimental part) to achieve full conversion of the starting material, which facilitated the purification of the 6-membered cyclic carbonate. Careful exclusion of H_2O could improve the overall yield. This hypothesis should be tested in future work. All compounds were analyzed by ^{1}H NMR, ^{13}C NMR, HRMS, and IR and showed spectra similar to the described results of **49**, and in accordance with literature spectra for similar 6-membered cyclic carbonates[44][56]. X-ray crystallography of **62** and **66** of crystals obtained by Chang Qiao further confirmed the structure of the obtained 6-membered cyclic carbonates.

Significance for Polycarbonate Formation

Our newly developed synthetic route gives rise to 6-membered cyclic carbonates interesting for the formation of polycarbonates. Various substituents that can tune polymer properties can now be introduced with ease. Especially appealing is the pendent protected methylhydroxy group immanent to this synthetic approach. Selective deprotection of those hydroxy groups in the polymer could lead to a backbiting of the free alcohol, resulting in the degradation of the polymer to 5-membered cyclic carbonate monomers. This feature could be an interesting tool in the design of recyclable polymers.

We attempted the polymerization of 6-membered cyclic carbonate monomer **62** using TBD as a catalyst, and benzyl alcohol as an initiator under strictly H_2O-free conditions. Unfortunately, low conversion, and no formation of polycarbonate could be observed. Small amounts of 5-membered cyclic carbonate **56** could be identified with ^{1}H NMR, suggesting the base-assisted deprotection of the acetyl-protected alcohol took place instead of ring-opening polymerization. Ac-Im proved to be a useful protecting group the formation of 6-membered cyclic carbonates, however it complicated ROP of the obtained monomers due to the comparable reactivity of carbonates and esters. Therefore, we tested the utilization of other protecting groups with contrasting reactivity for the formation of 6-membered cyclic carbonates. **45** was subjected to DBU and *tert*-butyldimethylsilyl chloride, or trimethylsilyl chloride, to trap the transiently formed 6-membered cyclic carbonate in a silylether. No conversion was observed. The explanation of this result remains open for further investigation. In future work, it will be interesting to explore different trapping agents for the formation of 6-membered cyclic carbonates. Following this, more thorough investigations should be led into the polymerization of those 6-membered cyclic carbonate monomers and the potential recyclability of the resulting polymers.

Thermodynamic Investigations

We have observed that the direct coupling of 3,4-epoxy alcohols with CO_2 results in the formation of 5-membered cyclic carbonates. Corresponding 6-membered cyclic carbonates that could exist in an equilibrium promoted by "Payne-type rearrangement" did not form in appreciable quantities. This was ascribed to a big difference in Gibbs energy of the two isomers, which is responsible for a very small K_{eq} for the equilibrium reaction. However, adding base and Ac-Im as a trapping agent to the 5-membered cyclic carbonates with pendent ethylhydroxy groups resulted in the formation of 6-membered cyclic carbonates. According to Kleij *et al*., the reaction of Ac-Im with primary alcohols occurs at a much higher rate than with tertiary alcohols, so only the protection of primary alcohol takes place. In this case, the small amount of 6-membered cyclic carbonate would be trapped by protection of its pendent primary alcohol, pulling it out of the equilibrium with the 5-membered cyclic carbonate. This would be driving the equilibrium towards the 6-membered cyclic carbonate product. To further explain the outcome of this reaction we calculated the relative stabilities of the two possible products, an acetylated 5-membered cyclic carbonate **68** and an acetylated 6-membered cyclic carbonate **69** (Figure 5).

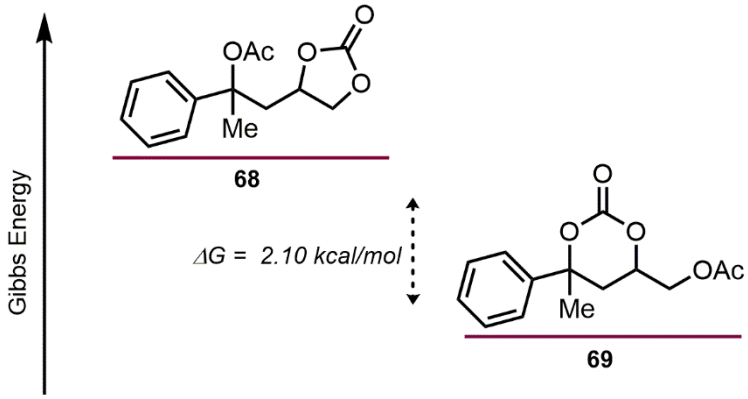


Figure 5 Thermodynamic stabilities of acetylated 5- and 6-membered cyclic carbonate

To our surprise, we calculated a 2.10 kcal/mol Gibbs energy difference with the acetylated 6-membered cyclic carbonate being thermodynamically more stable than the acetylated 5-membered cyclic carbonate. This could imply that the formation of 6-membered cyclic carbonate is not (only) driven kinetically, but also under a thermodynamic influence. More thorough investigations should be led into this truly remarkable finding.

Conclusion and Outlook

6-membered cyclic carbonates are valuable monomers for the synthesis of polycarbonates. Even though different substitution patterns and functional groups are interesting for adjusting polymer properties, and allowing for post-polymerization functionalization, methodologies for the synthesis of such 6-membered cyclic carbonates are scarce. In this work, we have presented a novel approach to obtain multi-substituted 6-membered cyclic carbonates previously considered elusive. This newly developed protocol is based on the base-assisted isomerization between an ethylhydroxy-substituted 5-membered cyclic carbonate and a methylhydroxy-substituted 6-membered cyclic carbonate in a "Payne-type rearrangement". The thermodynamic disfavor of the 6-membered cyclic carbonate species in this equilibrium can be overcome by selective protection of the free primary alcohol unit of the molecule with an acetyl group, trapping the carbonate in its 6-membered form. Our approach is characterized by mild conditions and easy execution. We were able prove the generality of this method with the synthesis of five trisubstituted 6-membered cyclic carbonates, fully characterized and in good yields. The corresponding 5-membered cyclic carbonates for this transformation were prepared by formal [3+2] cycloaddition of CO_2 and 3,4-epoxy alcohols. Therefore, this practical method represents the first synthetic route to trisubstituted 6-membered cyclic carbonates based on CO_2 valorization, and without resorting to the use of hazardous phosgene-derived reagents.

These compounds are most interesting for the formation of polycarbonates. Selective deprotection of the alcohol function in the polymer could lead to recycling of the polymer. In future work, the polymerization of those new compounds should be tested. For this, the introduction of different protective groups in the trapping of the 6-membered cyclic carbonates might be necessary for compatibility with the reaction conditions of the ROP. We believe that optimized reaction conditions and H_2O-free atmosphere can tremendously increase the efficiency of this process in further research.

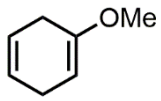
Experimental Part

General Information

All reagents were used as received from commercial suppliers unless otherwise stated. Epoxy alcohols **50-55** were provided by Chang Qiao. ^{1}H NMR and ^{13}C NMR were recorded at room temperature on a Bruker AV-500 spectrometer and referenced to the residual solvent signal of the deuterated solvent. Chemical shifts (δ) are quoted in ppm and coupling constants (J) are quoted in Hz. 1H splitting patterns were designated as singlet (s), doublet (d), triplet (t), quartet (q) or combinations thereof. Splitting patterns that could not be interpreted were designated as multiplet (m). Diastereomeric ratios were obtained by ^{1}H NMR. FTIR spectra were recorded neat on a Bruker Optics FTIR Alpha spectrometer. Wavenumbers (υ) are reported in cm^{-1}. Mass spectrometric analyses were performed by the Research Support Area in ICIQ using electrospray ionization. Reaction progress was monitored by TLC. Visualization was achieved by ultraviolet light, potassium permanganate stain or cerium molybdate stain.

Synthesis of Epoxy Alcohols

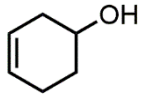
1-Methoxycyclohexa-1,4-diene (31). The compound was prepared according to literature[59] in 53% yield. Characterization matches literature.



31

^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.74 – 5.64 (m, 2H), 4.63 (t, *J* = 3.1 Hz, 1H), 3.55 (s, 3H), 2.85 – 2.76 (m, 2H), 2.75 – 2.68 (m, 2H) ppm.

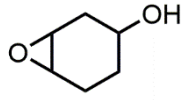
Cyclohex-3-en-1-ol (33). The compound was prepared according to literature[60] and purified by column chromatography with 15% EA in hexane. Yield: 85%. Characterization matches literature[60].



33

^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.71 – 5.62 (m, 1H), 5.62 – 5.53 (m, 1H), 4.01 – 3.91 (m, 1H), 2.42 – 1.58 (m, 6H) ppm.

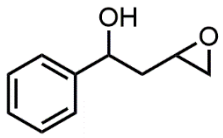
7-Oxabicyclo[4.1.0]heptan-3-ol (34). The compound was prepared according to literature[60] in 30% yield from **33**. Characterization matches literature[61].



34

^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.84 – 3.67 (m, 1H), 3.25 – 3.14 (m, 2H), 2.23 – 1.40 (m, 7H) ppm.

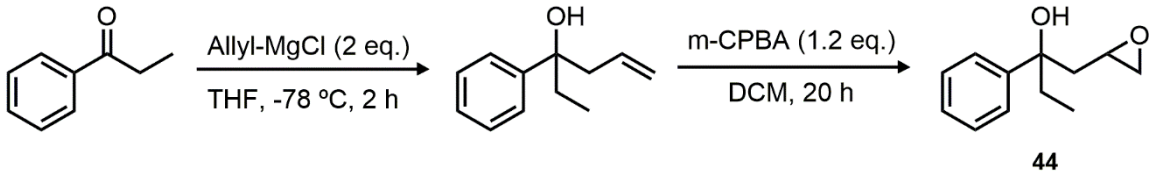
2-(Oxiran-2-yl)-1-phenylethan-1-ol (36). The compound was prepared according to literature[62] in 98% yield and a diastereomeric ratio of 1:1. Characterization matches literature.



36

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.41 – 7.27 (m, 5H), 5.00 – 4.92 (m, 1H), 3.21 – 3.15 (m, 0.5H), 3.07 – 2.99 (m, 0.5H), 2.83 (dd, J = 4.8, 4.1 Hz, 0.5H), 2.76 (dd, J = 4.8, 4.1 Hz, 0.5H), 2.62 (dd, J = 4.8, 2.8 Hz, 0.5H), 2.51 (dd, J = 4.8, 2.8 Hz, 0.5H), 2.15 (ddd, J = 14.5, 9.0, 4.0 Hz, 0.5H), 2.10 – 2.02 (m, 0.5H), 1.96 – 1.86 (m, 0.5H), 1.82 (ddd, J = 14.5, 6.7, 3.5 Hz, 0.5H) ppm.

1-(Oxiran-2-yl)-2-phenylbutan-2-ol (44).



44

3-Phenylhex-5-en-3-ol was prepared from propiophenone (1.00 g, 7.45 mmol) according to literature[63] and used without further purification. The crude homoallylic alcohol was dissolved in DCM (100 mL) at 0 °C and *m*CPBA (2.00 g, 8.94 mmol, 1.2 eq.) was added. The mixture was allowed to warm to room temperature and was stirred for 20 h. The reaction was quenched with sat. Na_2SO_3 solution (30 mL), the organic phase was washed with $NaHCO_3$ (2 x 30 mL) and sat. aq. NaCl (30 mL) and was dried over Na_2SO_4. The solvent was removed *in vacuo* and the crude product was purified by flash chromatography giving **44** over both steps in a diastereomeric ratio of 73:27 in 85% yield.

Diastereomer a: **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.48 – 7.42 (m, 2H), 7.39 – 7.32 (m, 2H), 7.28 – 7.21 (m, 1H), 2.84 – 2.77 (m, 1H), 2.63 (dd, J = 4.8, 4.1 Hz, 1H), 2.39 (dd, J = 4.8, 2.8 Hz, 1H), 2.32 (dd, J = 14.5, 3.4 Hz, 1H), 1.87 (qd, J = 7.4, 2.4 Hz, 2H), 1.75 (dd, J = 14.5, 8.5 Hz, 1H), 0.77 (t, J = 7.4 Hz, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 145.6, 128.3, 126.6, 125.4, 49.7, 46.7, 44.7, 36.2, 7.6 ppm.

Diastereomer b: **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.47 – 7.40 (m, 2H), 7.40 – 7.32 (m, 2H), 7.29 – 7.22 (m, 1H), 3.00 – 2.92 (m, 1H), 2.71 (dd, *J* = 4.9, 4.1 Hz, 1H), 2.45 (dd, *J* = 4.9, 2.8 Hz, 1H), 2.07 (d, *J* = 5.7 Hz, 1H), 1.97 (qd, *J* = 7.4, 0.9 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 1H), 0.78 (t, *J* = 7.4 Hz, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 145.6, 128.3, 126.8, 125.3, 49.3, 47.2, 44.9, 34.9, 7.8 ppm.

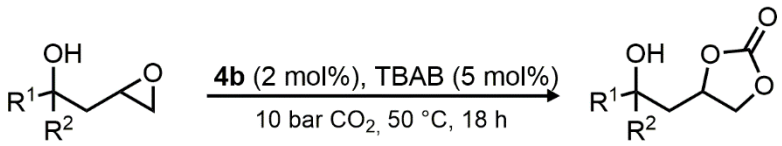
HRMS (ESI+) m/z $[M\text{-}OH]^+$ calculated: 175.1117, found: 175.1115.

CO_2 Coupling Reaction with 7-oxabicyclo[4.1.0]heptan-3-ol 34.

In a HEL-multireactor **xy** (0.08 to 0.52 mmol), catalyst xy (2 mol%) and cocatalyst (5-10 mol% of TBAB, DBU or PPNCl) were dissolved in MEK (200 µL). The reactor was purged twice with CO_2(10 bar), then charged with CO_2 (40 bar). The mixture was stirred for 18 h at a set temperature (50°C – 85°C) after which the vessel was cooled in an ice bath and depressurized. The crude mixture was analyzed by IR and ^{1}H NMR.

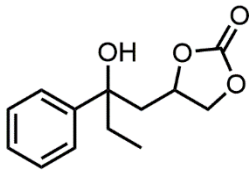
Synthesis of 5-membered cyclic carbonates 45 and 56 - 61

General procedure



In a stainless-steel HEL-multireactor epoxide **44, 50-56** (0.5 mmol) was dissolved in MEK (400 µL) and Al-catalyst **4b** (0.01 mmol 2 mol%, 5.1 mg) and TBAB (0.05 mmol 10 mol%, 8.0 mg) were added. The reactor was purged twice with CO_2 (10 bar) and then charged with CO_2 (10 bar). The mixture was stirred at 50 °C for 18 h, then cooled in an ice bath and carefully depressurized. The solvent was removed *in vacuo* and the resulting product was purified by flash chromatography employing 10 % - 25% EA in hexane as eluent.

4-(2-Hydroxy-2-phenylbutyl)-1,3-dioxolan-2-one (45). The product was isolated as a pale-yellow oil. Yield: 73%, 7:3 d.r.



45

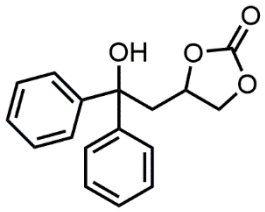
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.41 – 7.23 (m, 5H), 4.86 – 4.76 (m, 0.7H), 4.49 (dd, *J* = 8.4, 7.1 Hz, 0.3H), 4.41 – 4.32 (m, 0.3H), 4.29 (t, *J* = 8.4 Hz, 0.3H), 4.06 (dd, *J* = 8.7, 7.7 Hz, 0.7H), 3.68 (t, *J* = 8.6 Hz, 0.7H), 2.54 – 2.39 (m, 1H), 2.25 – 2.10 (m, 1H), 2.05 – 1.83 (m, 2H), 0.76 (t, *J* = 7.4 Hz, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 144.3, 128.8, 127.4, 125.0, 124.9, 75.8, 75.1, 74.7, 71.3, 70.2, 46.9, 46.0, 36.5, 35.6, 7.5, 7.2 ppm.

HRMS (ESI+) m/z $[M+Na^+]$ calculated: 259.0941, found: 259.0948.

IR (ATR) ν =3492, 3027, 2971, 1776, 1447, 1376, 1174, 1054, 701 cm^{-1}.

4-(2-hydroxy-2,2-diphenylethyl)-1,3-dioxolan-2-one (56). The product was isolated as a white solid. Yield: 75%.



56

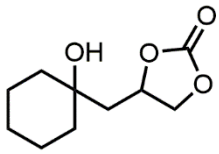
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.48 – 7.33 (m, 8H), 7.33 – 7.27 (m, 2H), 4.73 – 4.63 (m, 1H), 4.30 (dd, *J* = 9.0, 7.6 Hz, 1H), 4.05 (t, *J* = 8.8 Hz, 1H), 2.99 (dd, *J* = 13.7, 3.6 Hz, 1H), 2.73 (dd, *J* = 13.7, 9.3 Hz, 1H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 154.7, 145.7, 144.9, 128.7, 128.6, 127.9, 127.7, 125.6, 75.1, 70.8, 45.5 ppm.

HRMS (ESI+) m/z [M+Na^+] calculated: 307.0941, found: 307.0941.

IR (ATR) ν = 3456, 1777,1448, 1176, 1060, 700 cm^{-1}.

4-((1-Hydroxycyclohexyl)methyl)-1,3-dioxolan-2-one (57). The product was isolated as a white solid. Yield: 62%.



57

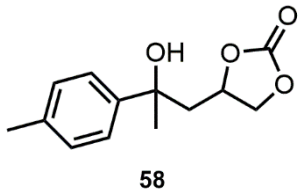
^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.03 – 4.93 (m, 1H), 4.58 (dd, *J* = 8.7, 7.8 Hz, 1H), 4.14 (t, *J* = 8.7 Hz, 1H), 2.10 (dd, *J* = 14.5, 6.3 Hz, 1H), 1.83 – 1.20 (m, 11H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 74.4, 70.9, 45.5, 39.5, 37.0, 25.4, 22.2, 22.1 ppm.

HRMS (ESI+) m/z [M+Na^+] calculated: 223.0941, found: 223.0941.

IR (ATR) ν = 3589, 2932, 2857, 1787, 1177, 1058 cm^{-1}.

4-(2-Hydroxy-2-(p-tolyl)propyl)-1,3-dioxolan-2-one (58). The product was isolated as a pale-yellow oil. Yield: 73%, 7:3 d.r.



58

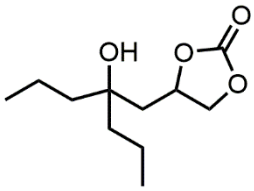
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.35 – 7.23 (m, 2H), 7.21 – 7.14 (m, 2H), 4.92 – 4.82 (m, 0.7H), 4.48 (dd, *J* = 8.5, 7.5 Hz, 0.3H), 4.43 – 4.33 (m, 0.3H), 4.30 – 4.17 (m, 1H), 3.79 (t, *J* = 8.6 Hz, 0.7H), 2.46 (dd, *J* = 13.8, 4.0 Hz, 0.3H), 2.40 – 2.31 (m, 3.7H), 2.24 – 2.10 (m, 1H), 1.72 – 1.53 (m, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 143.7, 142.6, 137.2, 129.4, 124.4, 124.3, 100.1, 75.1, 74.8, 71.1, 70.3, 47.8, 47.3, 32.1, 30.7, 21.0 ppm.

HRMS (ESI+) m/z [M+Na^+] calculated: 259.2562, found: 259.0962.

IR (ATR) ν = 3476, 2975, 2925, 1783, 1372, 1177, 1055, 820, 776 cm^{-1}.

4-(2-Butyl-2-hydroxyhexyl)-1,3-dioxolan-2-one (59). The product was isolated as a pale-yellow oil. Yield: 82%.



59

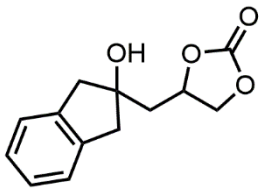
^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.00 – 4.90 (m, 1H), 4.58 (dd, *J* = 8.8, 7.7 Hz, 1H), 4.14 (t, *J* = 8.8 Hz, 1H), 2.12 – 2.01 (m, 1H), 1.79 (dd, *J* = 14.5, 6.7 Hz, 1H), 1.55 – 1.20 (m, 8H), 0.99 – 0.87 (m, 6H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) = δ 155.2, 74.8, 73.5, 71.0, 43.0, 42.9, 41.1, 17.2, 16.6, 14.61, 14.60 ppm.

HRMS (ESI+) m/z [M+Na^+] calculated: 239.1254, found: 239.1252.

IR (ATR) ν = 3493, 2959, 2934, 2873, 1775, 1466, 1379, 1177, 1055, 987, 776 cm^{-1}.

4-((2-Hydroxy-2,3-dihydro-1H-inden-2-yl)methyl)-1,3-dioxolan-2-one (60). The product was isolated as a colorless oil. Yield: 58%.



60

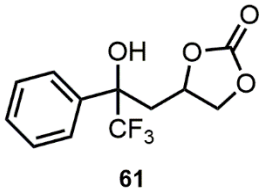
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.34 – 7.21 (m, 4H), 5.19 – 5.09 (m, 1H), 4.69 (dd, *J* = 8.7, 7.8 Hz, 1H), 4.28 (t, *J* = 8.7 Hz, 1H), 3.13 (ddd, *J* = 39.6, 24.1, 16.3 Hz, 4H), 2.31 (qd, *J* = 14.3, 6.4 Hz, 2H) ppm.

^{13}C NMR (126 MHz, $CDCl_3$) δ = 139.77, 127.16, 127.12, 125.43, 125.26, 80.58, 74.85, 70.54, 48.36, 46.72, 43.52 ppm.

HRMS (ESI+) m/z [M+Na^+] calculated: 257.0784, found: 257.0792.

IR (ATR) ν = 3452, 2924, 1792, 1481, 1388, 1174, 1058, 745 cm^{-1}.

4-(3,3,3-Trifluoro-2-hydroxy-2-phenylpropyl)-1,3-dioxolan-2-one (61). The product was isolated as a pale-yellow oil. Yield: 78%, 93:7 d.r. Only the signals of the major diastereomer are reported.



61

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.60 – 7.47 (m, 2H), 7.45 – 7.29 (m, 3H), 4.82 – 4.67 (m, 1H), 4.06 – 3.93 (m, 1H), 3.80 – 3.68 (m, 1H), 2.70 (dd, *J* = 14.2, 4.9 Hz, 1H), 2.42 (dd, *J* = 14.6, 7.3 Hz, 1H) ppm.

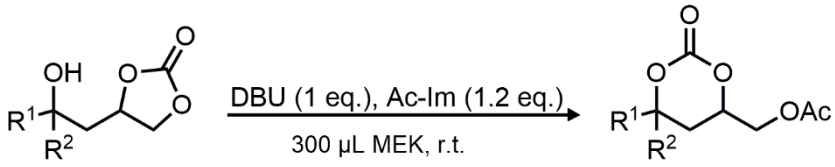
^{13}C NMR (101 MHz, $CDCl_3$) δ = 129.0, 128.7, 125.9, 73.7, 70.0, 39.8 ppm.

HRMS (ESI+) m/z [M+Na^+] calculated: 299.2004, found: 299.0491.

IR (ATR) ν = 3422, 1786, 1270, 1160, 1073, 770, 705 cm^{-1}.

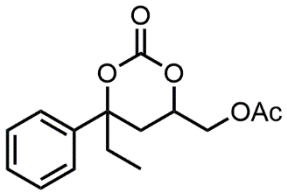
Synthesis of 6-membered cyclic carbonates 49 and 62 - 67

General procedure



Carbonate **75** or **91 - 95** (0.2 mmol) and DBU (0.2 mmol, 30 mg, 1 eq.) were stirred in DCM (300 µL) in a glass vial. After 5 min Ac-Im (0.3 mmol 33 mg, 1.5 eq.) was added and the mixture was stirred at room temperature. The reaction was monitored by TLC and ^{1}H NMR and the reaction times varied on the substrate. The crude product was purified by flash chromatography with 10 -25 % EA in hexane as eluent. Reaction times and possible further additions of DBU and Ac-Im are denoted for each compound.

(6-Ethyl-2-oxo-6-phenyl-1,3-dioxan-4-yl)methyl acetate (49). The compound was prepared according to the describe procedure with a total reaction time of 26 h. After 18 h additional DBU (0.2 mmol, 30 mg, 1 eq.) and Ac-Im (0.2 mmol, 22 mg, 1 eq.) was added. The product was isolated as a pale yellow liquid. Yield: 43%, 38:62 d.r.



49

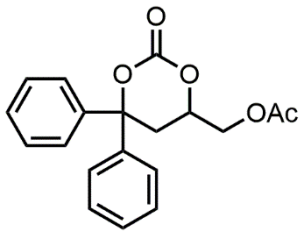
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.47 – 7.24 (m, 5H), 4.89 – 4.80 (m, 0.38H), 4.30 – 4.09 (m, 2.62H), 2.48 – 2.35 (m, 1H), 2.22 – 2.15 (m, 1H), 2.10 – 2.05 (m, 3.38H), 2.03 – 1.94 (m, 0.62H), 0.88 – 0.77 (m, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 148.6, 148.4, 141.8, 140.5, 129.2, 128.8, 128.3, 128.1, 124.7, 124.4, 86.6, 85.8, 73.8, 73.5, 64.8, 64.7, 36.3, 34.5, 33.9, 33.5, 7.8, 7.3 ppm.

HRMS (ESI+) m/z [M+Na^{+}] calculated: 301.1046, found: 301.1045.

IR (ATR) ν = 2975, 2938, 1738, 1448, 1367, 1224, 1135, 1074, 1050, 762, 703 cm^{-1}.

(2-Oxo-6,6-diphenyl-1,3-dioxan-4-yl)methyl acetate (62). The compound was prepared according to the describe procedure with a total reaction time of 19 h. After 18 h additional DBU (0.2 mmol, 30 mg, 1 eq.) was added. The product was isolated as a clear liquid. Yield: 40%.



62

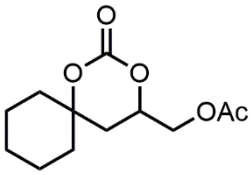
^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.48 – 7.27 (m, 10H), 4.53 – 4.42 (m, 1H), 4.34 – 4.17 (m, 2H), 2.91 (dd, *J* = 14.4, 3.2 Hz, 1H), 2.58 (dd, *J* = 14.4, 12.2 Hz, 1H), 2.10 (s, 3H) ppm.

^{13}C NMR (126 MHz, $CDCl_3$) δ = 170.4, 147.9, 142.3, 140.9, 129.2, 128.6, 128.47, 128.46, 125.2, 125.1, 73.9, 64.6, 34.2, 20.6 ppm.

HRMS (ESI+) m/z [M+Na^+] calculated: 349.1046, found: 349.1039.

IR (ATR) ν = 3063, 2956, 1736, 1450, 1367, 1216, 1129, 1045, 752, 700 cm^{-1}.

(2-Oxo-1,3-dioxaspiro[5.5]undecan-4-yl)methyl acetate (63). The compound was prepared according to the describe procedure with a total reaction time of 35 h. After 15 h additional DBU (0.2 mmol, 30 mg, 1 eq.) and Ac-Im (0.2 mmol, 22 mg, 1 eq.) was added. The product was isolated as a clear oil. Yield: 79%.



63

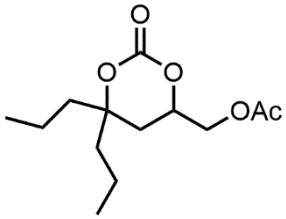
^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.76 – 4.66 (m, 1H), 4.27 (dd, *J* = 12.2, 3.5 Hz, 1H), 4.16 (dd, *J* = 12.2, 5.4 Hz, 1H), 2.10 (s, 3H), 2.04 – 1.91 (m, 2H), 1.89 – 1.30 (m, 10H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.7, 148.8, 82.0, 72.9, 65.0, 38.7, 35.0, 33.7, 25.1, 21.7, 21.4, 20.8 ppm.

HRMS (ESI+) m/z [M+Na^+] calculated: 265.1046, found: 265.1052.

IR (ATR) ν = 2937, 2864, 1736, 1449, 1370, 1221, 1123, 1089, 1050 cm^{-1}.

(2-Oxo-6,6-dipropyl-1,3-dioxan-4-yl)methyl acetate (64). The compound was prepared according to the describe procedure with a total reaction time of 60 h. After 24 h additional DBU (0.2 mmol, 30 mg, 1 eq.) and Ac-Im (0.2 mmol, 22 mg, 1 eq.) was added. The product was isolated as a xy. Yield: 59%.



64

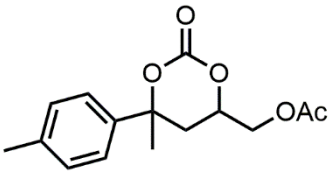
^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.71 – 4.63 (m, 1H), 4.25 (dd, *J* = 12.2, 3.5 Hz, 1H), 4.16 (dd, *J* = 12.2, 5.5 Hz, 1H), 2.10 (s, 3H), 1.94 – 1.83 (m, 2H), 1.69 – 1.55 (m, 4H), 1.49 – 1.26 (m, 4H), 0.94 (td, *J* = 7.3, 4.1 Hz, 6H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.7, 149.1, 85.2, 73.1, 65.0, 41.4, 39.3, 31.6, 20.8, 16.9, 16.3, 14.4, 14.2 ppm.

HRMS (ESI+) m/z [M+Na^+] calculated: 281.1359, found: 281.1362.

IR (ATR) ν = 2962, 2938, 1876, 1737, 1457, 1369, 1322, 1218, 1130, 1105, 1046, 766 cm^{-1}.

(6-methyl-2-oxo-6-phenyl-1,3-dioxan-4-yl)methyl acetate (65). The compound was prepared according to the describe procedure with a total reaction time of 35 h. After 24 h additional DBU (0.2 mmol, 30 mg, 1 eq.) and Ac-Im (0.2 mmol, 22 mg, 1 eq.) was added. The product was isolated as a xy. Yield: 77%, 7:3 d.r.



65

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.35 – 7.15 (m, 4H), 4.90 – 4.81 (m, 0.3H), 4.33 – 4.09 (m, 2.7H), 2.42 (dd, *J* = 14.2, 3.1 Hz, 0.7H), 2.35 (s, 3H), 2.34 – 2.28 (m, 0.3H), 2.23 – 2.13 (m, 1H), 2.10 – 2.06 (m, 3H), 1.79 (s, 0.9H), 1.72 (s, 2.1H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.6, 148.58, 148.52, 140.9, 139.0, 138.2, 138.1, 129.9, 129.5, 124.0, 123.7, 84.0, 83.1, 74.0, 73.7, 64.8, 64.6, 35.7, 35.5, 31.2, 27.6, 21.1, 21.0, 20.8, 20.7 ppm.

HRMS (ESI+) m/z [M+Na^+] calculated: 301.1046, found: 301.1057.

IR (ATR) ν = 2982, 2925, 1743, 1369, 1229, 1046, 1020 cm^{-1}.

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Appendix

Abstract

The synthesis of 6-membered cyclic carbonate remains a challenge, especially concerning multisubstituted and functionalized compounds. This is the case, even though 6-membered cyclic carbonates are popular monomers for the synthesis of polycarbonates by ring-opening polymerization. In this work, we present a novel synthetic route to multisubstituted 6-membered cyclic carbonates. We utilized the base-assisted equilibration between a 5-membered cyclic carbonate with pendent α,α-disubstituted hydroxyethyl group and a methylhydroxy-substituted 6-membered cyclic carbonate, a so-called “Payne-type rearrangement”. The thermodynamic disfavor of the 6-membered cyclic carbonate was overcome by selective protection of the free hydroxy group of the compound, trapping the carbonate in its 6-membered form. Five 6-membered multisubstituted cyclic carbonates have been synthesized and characterized as possible monomers for the synthesis of novel polycarbonates from CO_2 and readily available starting materials.

Zusammenfassung in deutscher Sprache

Noch immer stellt die Synthese sechsgliedriger zyklischer Carbonate eine große Herausforderung dar - besonders hinsichtlich mehrfachsubstituierter und funktionalisierter Verbindungen. Der Zugang zu diesen Verbindungen ist allerdings erstrebenswert, da sechsgliedrige zyklische Carbonate gefragte Monomere für die Synthese von Polycarbonaten durch ringöffnende Polymerisierung darstellen. In dieser Arbeit präsentieren wir einen neuen Syntheseweg zu sechsgliedrigen zyklischen Carbonaten, der auf einer Basen-assistierten Gleichgewichtsreaktion zwischen einem fünfgliedrigen zyklischen Carbonat mit anhängender α,α-disubstituierter Ethylhydroxygruppe und einem Methylhydroxy-substituierten sechsgliedrigen zyklischen Carbonat beruht - dem sogenannten „Payne-type rearrangement“. Der thermodynamische Nachteil des sechsgliedrigen zyklischen Carbonates konnte überwunden werden, indem die freie primäre Alkoholgruppe der Verbindung selektiv geschützt und die Verbindung so in ihrer sechsgliedrigen Form abgefangen wurde. Dadurch konnten fünf verschiedene mehrfachsubstituierte sechsgliedrige zyklische Carbonate synthetisiert und charakterisiert werden. Sie stellen interessante Monomere für die Synthese neuer Polycarbonate aus CO_2 und leicht verfügbaren Startmaterialien dar.