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Sustainable Conversion of Carbon Dioxide: The Advent of Organocatalysis

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1. Introduction

Our current chemical needs depend highly on the availability of fossil fuels as feed stock. Predictions have been made that somewhere in the near future we will be running out of these reserves and/or their immediate availability can no longer fulfill the increasing global demand for these raw materials. As such, contemporary chemists are facing a huge challenge to develop more sustainable alternatives for chemical production. Carbon dioxide is a waste product from all combustion processes and represents a potential and alternative carbon feed stock for the preparation of a variety of useful chemicals including MeOH, urea, lactones, various heterocycles, biodegradable polymers, and carboxylated structures among others.

In particular, direct CO2 utilisation for the preparation of polycarbonates, poly(ether)carbonates and polyurethanes is a viable technology to access novel tailor-made CO2-based materials. The development of cost- and energy-efficient synthetic methodologies to exploit CO2 as a C1 synthon could eventually loosen the grip on our fossil fuel dependence, contributing to a reduction of the overall CO2 emissions and offering tangible alternatives to physical sequestration methods.

In nature, CO2 is captured, converted and/or reduced to carbohydrates by a series of cascade reactions carried out by specific metalloenzymes present in photosynthetic organisms. Similarly, the field of CO2 conversion catalysis is dominated by the use of transition metal-based catalysts being either heterogeneous or homogeneous in nature. While the use of a catalytic system generally implies a sustainability improvement, some marked differences can be foreseen between choosing metal-based or organo-catalysts. It has been shown that activation and/or stabilization of substrates/intermediates through metal complexes or immobilized metal species via coordination motifs is far more efficient compared with organo-based catalytic mediators. Organocatalysts, on the other hand, are generally low cost, non-toxic molecules, characterized by a good stability and inertness towards moisture and air. As such, from a reaction design point of view, they can be regarded as safer reaction components. Moreover, in some cases, they can be readily derived from renewable feed stocks, devising technically and economically practicable ad hoc procedures starting from biomass and CO2, thus eventually developing “carbon-neutral” processes to produce sustainable chemicals, fuels, and materials.

It is known that organocatalysis can sometimes lead to additional energy expenditure during reaction and work-up time, requiring higher catalyst loadings, higher operating temperatures and prolonged reaction times. Nevertheless, in some cases, (e.g., when using ionic liquids as reaction solvents and/or catalysts) the reagents/products can be recovered by simple distillation. Devising more safe and atom-economical processes while avoiding commonly employed waste generating work-up procedures. Catalyst heterogenisation has been extensively exploited to increase the lifetime of organo-catalyst simplifying reaction monitoring and work-up procedures, while providing a possible route towards the development of continuous flow reactions. Organocatalysis is especially advantageous to develop metal-free products or processes, since the incorporation of chemicals into consumer products require that the amount of metal residues to be present as low as possible to avoid any toxicity issues. Since these requirements are becoming more stringent by the year, alternative processes that can circumvent the use of metal catalysts would provide a means to produce targeted chemicals in a safer and potentially greener way. In this respect, organo-based catalysts (i.e., organocatalysts) are of growing interest and importance in the area of CO2 catalysis and conversion. Recently, the pace with which organocatalytic procedures are being utilized in organic preparations that involve CO2 as a key reagent is unquestionably increasing. There are a number of structurally different organocatalyst systems that are considered as catalytic mediator including those based on ionic...
liquids (ILs),33-35 N-heterocyclic carbenes (NHCs),36 phenolic compounds,37 and sophisticated azaphosphatranes.38 This is a true testimony of the increasing prominence of organocatalysis in the area of CO₂ fixation to create value-added organic matter from a waste material.

This review intends to showcase the most recent developments in CO₂ catalysis where organocatalytic systems have helped to increase the overall sustainability of the process in terms of more efficient energy usage, raw material conversion, avoiding solvent and/or metals and improvement of selectivity/reactivity features. A complete overview of all the literature is not feasible and therefore avoided; instead, the key contributions in specific areas of CO₂ research are highlighted. Also, a critical evaluation of the reported organocatalytic methodologies is a requisite for comparison with metal-based systems. This may help to identify, where possible, improvements that lead to a more widespread use of organocatalysts in CO₂ conversion. Other excellent reviews focusing on the use of hetero- and/or homogenous catalyst systems have recently appeared,5,7-10,18,19,39-42 and may serve as a reference point.

In the first section, attention is given to the various activation modes that are the basis for the organocatalytic transformations. Hereafter, the main types of organocatalysed CO₂ coupling reactions are discussed followed by a section on the latest developments concerning new types of reactivity.

2. Activation modes of organocatalysts

Organocatalysis has become an essential tool for synthetic organic chemists as testified by the variety of organocatalysed organic transformations that can be performed with high chemoselectivity, regio- and enantio-selectivities.43-45 Although the currently available CO₂ conversion reactions are relatively simple from a chemical reactivity point of view, the continuous development of new and more efficient metal- and/or organo-catalysis is essential due to the kinetic inertness of CO₂. Although the array of available organocatalysed CO₂ valorisation reactions is expanding constantly, currently the field is dominated by reductive and non-reductive coupling processes (see Figure 1).

Up to now, the reported organocatalysts active in CO₂ conversion catalysis can be roughly divided into three distinct categories: (1) nitrogen-based heterocycles (including organic bases and N-heterocyclic carbenes, NHCs); (2) organic salts, molten salts and ionic liquids (ILs); and (3) (poly)phenolic and poly-alcohol compounds. Most of these catalysts are active in a small series of CO₂ based synthetic processes which are illustrated in Figure 1. Beside the established heterocyclic synthesis based on CO₂ coupling to epoxides and aziridines (Figure 1, top), organocatalysis has also proved to be particularly attractive for CO₂ reduction (Figure 1, bottom). However, depending on the type of reaction (non-reductive vs. reductive coupling), the mechanistic hypothesis and the role of the catalyst can be quite different.

Similarly to what has been reported for metal-based catalysts, insights into the operative mechanism of organocatalysed CO₂/epoxide coupling reactions to afford cyclic carbonates have shown that the role of the catalytic species can be either (a) direct CO₂ activation; (b) activation of high energy co-reactants (e.g., epoxides, aziridines, oxetanes and azetidines); or (c) dual activation of both CO₂ and the associated high-energy reactant as summarised in Scheme 1. Evidence of a dual activation mechanism has been seldom reported for CO₂ conversion catalysts; notable examples include polyoxometalate based systems developed by Mizuno46 and Leitner,47 respectively. While a general reactivity pattern may be readily derived for organocatalysed non-reductive CO₂ coupling reactions, a general mechanism for reductive CO₂ couplings has not yet been defined given the different reducing agents employed.
2.1. Organic \(N\)-heterocyclic bases

Organic bases are probably the simplest organocatalysts studied in the context of \(CO_2\) conversion as a result of their availability and structural diversity including alkyl/aryl mono- and polyamines, \(N\)-heterocyclic derivatives and amide- and guanidine-like structures. So far, these compounds have proven to be useful in the epoxide/\(CO_2\) couplings and reduction of \(CO_2\) to methanol. Concerning the scope of this review, the most important class of organic bases reported to date are based on \(N\)-heterocyclic scaffolds, particularly the structures depicted in Figure 2.

The most commonly employed and effective organic catalysts for \(CO_2\) valorisation are 4-dimethylamino-pyridine (DMAP) and amidine- and guanidine-derived superbases. Given the differences in Lewis basicity strength, the catalytic role of these two classes of compounds is quite different. DMAP has proven to be an efficient homogeneous and heterogeneous catalyst for the synthesis of cyclic carbonates from epoxides, even though high operating temperatures (120 °C) and relatively high \(CO_2\) pressures (17–40 bar) were required; however, in presence of Lewis acid co-catalysts such as phenols, this dual catalytic system showed a good catalytic activity for the preparation of cyclic carbonates from epoxides. A definitive mechanism for the activation by DMAP has not been elucidated yet. One mechanistic hypothesis relies on the sole activation of the epoxide as depicted in Scheme 1. An alternative mechanism based on a dual activation mode that involves both the epoxide and the \(CO_2\) molecule has also been postulated.

![Scheme 1 General organocatalytic activation modes for the synthesis of cyclic carbonates from epoxides and \(CO_2\).](image_url)

On the other hand, organic superbases such as DBU, TBD and \(N\)-methyl TBD (MTBD) (Figure 2) have been extensively employed as catalysts for \(CO_2\) coupling reactions. As a typical example, Sartori et al. reported the use of MTBD as the sole catalyst for the synthesis of cyclic carbonates from \(CO_2\) and epoxides. When using both homogeneous and heterogeneous silica-supported MTBD catalysts, different terminal and internal
epoxides were converted to the corresponding cyclic carbonate with good to excellent yield (60-98%) and high chemoselectivities (90-98%) although the reaction conditions were quite harsh (T = 140 °C, p(CO₂) = 50 bar). Catalyst heterogenisation has been exploited as a straightforward, feasible way to address recyclability issues and to work under milder conditions (T = 50 °C), while the addition of a co-catalyst has been generally shown to improve reaction rates, yields and selectivities. Recently, renewable based molecules such as cellulose, were successfully employed as co-catalytic mediators for the synthesis of cyclic carbonates.\(^\text{54}\)

The catalytic role of guanidine-derived organic superbases is not limited to non-reductive CO₂ coupling reactions; these compounds are currently conquering a prominent role as CO₂ catalysts for the synthesis of methanol by reductive coupling of CO₂ with organosilanes\(^\text{55}\) and organoboranes.\(^\text{56}\) Regardless of the hydride donor employed, formation of a superbase-CO₂ salt is crucial to start the catalytic cycle forming a catalytically active CO₂ complex (Scheme 2).

![Scheme 2 CO₂ reduction catalysed by TBD.](image)

Whether involved in catalytic CO₂ coupling or CO₂ reduction processes, the catalytic cycle involving superbases generally starts with an initial “coordination” of the CO₂ molecule. Stable organic superbase-CO₂ adducts have been isolated and fully characterized,\(^\text{57,58}\) thus providing experimental proof that this class of compounds is capable of direct interaction with CO₂.

### 2.2. N-heterocyclic carbenes (NHCs)

Since their first isolation by Arduengo in 1991, NHCs have proved to be versatile ligands for homogeneous metal catalysis and organocatalysis.\(^\text{59}\) Being highly nucleophilic in nature, NHCs need to bind suitable electrophiles to form air- and moisture-stable adducts; a classic example is the formation of a zwitterionic NHC–CO₂ adduct (Scheme 3).\(^\text{60}\) These adducts are labile in solution, making them suitable for catalytic turnover.

NHC-promoted CO₂ activation allows for CO₂ coupling reactions with high-energy reaction partners, including the preparation of cyclic carbonates and oxazolidinones from epoxides and aziridines,\(^\text{61,62}\) respectively, and the synthesis of \(\alpha\)-methylene-carbonates and \(\alpha\)-methylene-oxazolidinones from propargylic alcohols.\(^\text{62,63}\)

To further improve catalyst lifetime and recyclability, NHC-based catalysts have been heterogenised. When NHC scaffolds (Scheme 3; \(R¹ = \text{i-Pr}, R² = \text{H}\)) were grafted onto a silica MCM-41 support, the resultant catalyst was active towards cyclic carbonate formation at 0.5 mol% catalyst loading under relatively mild conditions (T = 120 °C, p(CO₂) = 20 bar, t = 24–48 h), whereas this supported catalyst was also used for the synthesis of oxazolidinones under even milder conditions (T = 80–100 °C) affording \(N\)-substituted oxazolidinones in excellent yields.\(^\text{64}\) A different NHC (\(R¹ = 2,6(\text{i-Pr})_2\text{C}_6\text{H}_3; R² = \text{H}\)) was covalently embedded within a tubular, micro-porous organic network. When using this heterogeneous catalytic system, propylene oxide (PO) was quantitatively converted to propylene carbonate in 10 h with a catalyst load of only 0.065 mol% (Yield = 92%; TOF = 142 s\(^{-1}\), T = 160 °C, p(CO₂) = 30 bar).\(^\text{65}\)

Since their catalytic activity is based on direct CO₂ activation, NHCs were also the first class of organocatalysts to show catalytic activity towards CO₂ reduction with different reduction partners, including mild reducing agents such as silanes. Cascade reactions have been reported in the presence of both a silane reductant (including polymethylhydrosiloxane (PHMS, an industrial by-product) and appropriate nucleophiles (amines, anilines, imines, hydrazines, hydrazones, \(N\)-heterocycles), thus employing CO₂ as a versatile \(C\)₁ synthon for the preparation of, inter alia, formamidine derivatives (Scheme 4).\(^\text{23,66}\)
2.3. Catalysis by organic salts and ionic liquids

As highlighted in detail in a recent review by Kerton et al.,32 the use of organic salts/ionic liquids as organocatalysts for CO\textsubscript{2} conversion has come a long way since the seminal work of Caló et al. published in 2002.67 These catalysts have almost exclusively been employed for the coupling of CO\textsubscript{2} with strained heterocycles such as epoxides and aziridines. Their nucleophilic character mediates the ring-opening of the heterocycles while stabilizing the ring-opened alkoxide intermediate by ion-pairing interactions with the cationic part of the salt/IL.68 Beside commercially available quaternary ammonium salts and phosphonium halide salts,69,71-73 a number of phosphonium,74 imidazolium,75,77 pyridinium,76 pyrrolidinium78 and superbases10,79 derived ILs (including those based on DABCO, DBU and TBD; Figure 4) have also been prepared and employed as CO\textsubscript{2} coupling catalysts obtaining with, in some cases, excellent results in terms of conversion and selectivity. It is generally assumed that catalysis occurs through an epoxide/aziridine activation pathway (Scheme 1, right), however, depending on the chosen anion/cation combination some peculiar behaviour has been observed.

In most reported cases, the heterocycle/CO\textsubscript{2} coupling product can be recovered quantitatively from the reaction mixture by simple distillation. To address catalyst stability/recyclability issues, efforts have been made to develop heterogeneous IL-based catalysts including silica-supported,72,80,81 co-polymerized,73,82-84 PEGylated85 and dendrimeric ILs.86,87 Moreover, task-specific hydroxy-88,89 and carboxy-functionalized ILs90,91 have been designed, synthesized and tested as catalysts. These ILs have shown improved activity, mainly due to more efficient epoxide activation through H-bonding interactions (Scheme 5), and subsequently have been developed in their heterogeneous form.81,92-94

2.4. Phenolic and polyhydroxy compounds

This broad class of organocatalysts is quite attractive since most of them are naturally occurring or readily available from renewable resources. The term “polyhydroxy” compounds refers to several structurally different compounds (Figure 5) including pyrogallol,100 linear non-conjugated polyols101 and...
Due to their potential to form an (extended) hydrogen-bond network upon activation of the substrate, these catalysts have been employed almost exclusively for epoxide/CO₂ coupling reactions. This activation mechanism (vide infra) can be applied to all hydroxyl and polyhydroxy compounds, including the polysaccharide-based catalytic systems (cellulose, CMC and chitosan). In general, their catalytic behaviour is based on epoxide activation through the formation an H-bonding intermediate or network as for hydroxyl-functionalised ILs (Scheme 5).

![Image of Pyrogallol, Pentaerythrol, Chitosan, Cellulose, and Carboxymethylcellulose](image)

**Fig. 5** Phenolic, polyhydroxy- and polysaccharide-based organocatalysts for CO₂ coupling reactions.

The extent of the H-bonding network depends on the type of polyhydroxy catalyst chosen. Generally, halide salts or organic bases are required as co-catalytic additives to ensure efficient catalysis. In the case of polysaccharides, however, the co-catalyst moiety can be embedded within the polysaccharide backbone by direct quaternization of the biopolymer, thus resulting in a bifunctional catalyst system. Polysaccharides (cellulose, carboxymethylcellulose (CMC) and chitosan) are particularly interesting for practical applications: they are easily obtained from renewable resources and they can be further functionalized by physical and chemical methods to improve the overall catalytic activity. These functionalization methods are based on the impregnation of ILs, electrostatic interactions with ILs, organic superbases or covalent incorporation of nucleophilic moieties. The possibility of multiple interactions between the catalyst and the substrates is exemplified in Scheme 7 for a heterogeneous chitosan catalyst functionalized with imidazolium moieties.

3. Heterocyclic structures based on CO₂

Heterocyclic structures that incorporate a “carbonate” or “carbamate” fragment as highlighted in Scheme 8, can serve as valuable monomers of polyurethanes and polycarbonates, drugs, electrolytes or reagents in a wide range of chemical transformations and therefore have attracted a great deal of interest in industrial and academic research. The most elegant way of producing these heterocyclic scaffolds involves coupling reactions of CO₂ with readily available epoxides or aziridines in the presence of a suitable catalyst. One should keep in mind that non-exclusive selectivity in the ring-opening step of a mono-substituted aziridine may result in two regio-isomeric structures. However, virtually one isomeric form (generally the 5-substituted oxazolidinone) may be obtained when suitable reaction parameters and catalysts are used.

**Scheme 7** Proposed mechanism for CS-EMIm-Br catalysed CO₂ coupling reactions. CS stands for cellulose and EMIm-Br for an imidazolium bromide unit.

**Scheme 8** Preparation of heterocyclic structures from the reactions of CO₂ and epoxides or aziridines.

Undoubtedly, ILs are the most widely studied organocatalysts for the formation of heterocyclic structures from CO₂ which has been reviewed in detail by Kerton and co-workers recently. In this review, most of the ionic organocatalysts reported in the last eight years were listed and discussed, ranging from simple “onium” species to supported IL catalysts. In order to avoid unnecessary duplication, only some selected examples of IL catalysts are discussed here in the context of heterocyclic synthesis using CO₂.
For instance, He’s group reported on the use of polyethylene-glycol (PEG) bridged basic ionic liquids: the most important structural feature is an ethylene glycol that ties two quaternary 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) units (Figure 2, Scheme 9). These TBD units are known to interact with CO₂ to form an activated carbamate intermediate that may activate an epoxide substrate through H-bonding. Nucleophilic ring-opening of the activated epoxide may then easily occur using a bromide nucleophile providing a complementary activation pathway. The attack of the carbamate unit on the ring-opened epoxide (i.e., an alkoxide) produces a hemi-carbonate that after ring-closure leads to a cyclic carbonate. This work is exemplary for the majority of the organocatalytic promoters reported to date: compared to metal based catalysts, the substrate activation potential is lower, generally requiring higher reaction temperatures for efficient catalytic turnover. However, despite this kinetic drawback, most organocatalysts are readily available and accessible from cheap and relatively non-toxic scaffolds.

A large improvement on the kinetic limitation in the organocatalytic conversion of epoxides and CO₂ was provided by a pyrogallol (1,2,3-trihydroxybenzene) based binary catalyst comprising Bu₄NI. Pyrogallol is a commercially available polyphenol and its excellent catalytic performance is a result of the adjacent nature of the phenolic groups. As with many other systems, the mode of activation of the epoxide substrate is through hydrogen-bonding. The three phenol units are all being involved in the stabilization of key intermediates (Scheme 10). Interestingly, the synthesis of the cyclic carbonate products could be done under highly mild conditions (T = 25–45 °C, p(CO₂) = 10 bar), providing a low net CO₂ emission reaction setup. When compared to a previously reported metal based catalytic system, comprising of a Lewis acidic Zn(salphen) catalyst and using Bu₄NI as co-catalyst employed under similar conditions (i.e., MEK as solvent, T = 45 °C, p(CO₂) = 10 bar, t = 18 h), both the metal based and organocatalytic systems showed similar activities: when using 2 mmol of 1,2-epoxyhexane as substrate in 5 mL of MEK, quantitative conversion to the corresponding cyclic carbonate (conversion > 99%) was observed with Zn(salphen)/Bu₄NI (both 2.5 mol%) as well as with pyrogallol/Bu₄NI (both 5.0 mol%). This simple comparison is further evidence of the exceptional potential of pyrogallol as a CO₂ coupling catalyst, exhibiting activities comparable to metal-based systems.

At a later stage, a bifunctional, polystyrene-supported version of this pyrogallol catalyt was also successfully applied under comparable mild conditions with the advantage that the catalyst could be efficient recycled producing a more stable system and producing thus higher turnovers. Additionally, this organocatalysis protocol allowed for a multi-substrate campaign with minimal cross-contamination upon recycling the supported catalyst. These pyrogallol based catalysts are probably among the most active reported to date considering the low operating temperatures that are required. Other examples of phenol/catechol-mediated synthesis of cyclic carbonates have also appeared in recent literature, though being generally less efficient compared to the aforementioned pyrogallol systems.

Dufaud et al. recently developed a green method using azaphosphatrane as catalysts. This method allows for the efficient coupling of epoxides and CO₂ at 80°C and atmospheric pressure of CO₂ using a 0.1 mol % of catalyst loading. Azaphosphatrane can be considered structurally tunable catalysts, and as such their catalytic activity can be optimised by changing the substituents attached to the peripheral N-atoms (R, Scheme 11). Whereas the presence of methyl substituents (R = Me) results in catalyst degradation during the reaction, bulkier R substituents such as p-methoxybenzyl and neo-pentyl result in azaphosphatrane with increased stability, thus developing longer-lived systems. Detailed optimization of the reaction conditions showed that the azaphosphatrane bearing p-methoxybenzyl groups exhibits the highest catalytic activity.

Insights into the reaction mechanism were provided on the basis of a series of detailed kinetic studies with the reaction between styrene oxide (SO) and CO₂ serving as a benchmark model. From the kinetic data it was deduced that SO first forms an adduct through a hydrogen-bond to the cationic P center. This first step is then followed by insertion of the CO₂ into the P–N bond, resulting in an unusual tricyclic phosphoryl- carbamate intermediate which is highly reactive and sensitive toward hydrolysis (Scheme 11). This intermediate can be stabilized more efficiently by bulkier R groups and the reaction then
proceeds to the product via a nucleophilic attack of the chloride anion, and subsequent attack of the resultant alkoxide species on the activated CO$_2$.

Given the low kinetic stability of the tricyclic phosphorylcarbamate intermediate in the absence of any steric protection, the same authors have come up with an alternative, successful strategy to stabilize this intermediate and to avoid degradation of the catalyst through encapsulation by means of self-assembly giving a nano-cage.$^{38}$ Thus, several hemicryptophane-caged azaphosphatranes were designed and tested in the coupling reaction of CO$_2$ and epoxide under reasonably mild conditions (T = 100 °C; p(CO$_2$) = 1 bar; 0.1 mol % of catalyst loading) taking the corresponding non-caged catalysts as references. Indeed, the encapsulated azaphosphatane systems showed much better catalytic activity and higher stability when compared to the corresponding non-caged catalysts. This study on supramolecular catalysis also provided new evidence concerning the previously proposed mechanism involving the simultaneous dual activation of the epoxide and CO$_2$.$^{116}$ The hemicryptophane was carefully chosen as a building block to construct the cages. This aspect deserves to be highlighted as it allowed the use of only 0.1 mol % of catalyst, although most of the known supramolecular catalysts suffer from product inhibition and have to be used in stoichiometric amounts. This strong structure-activity correlation sheds light on the design of new advanced, supramolecular catalysts for the synthesis of heterocyclic carbonates from CO$_2$.

Alternative organocatalytic methodologies make use of NHCs and their derivatives as catalysts in the reaction of CO$_2$ and epoxides. Ikariya et al.$^{62}$ reported on imidazolidium-2-carboxylates (NHC-CO$_2$ adducts) that can be employed as NHC surrogates to catalyze the cycloaddition of CO$_2$ and epoxides. The proposed mechanism involves the nucleophilic addition of the NHC–CO$_2$ adduct to the epoxide, followed by an intramolecular cyclization of the alkoxide intermediate (Scheme 12). The nucleophilic attack of the CO$_2$ moiety bound to the NHC on the substrates is thought to be the rate-limiting step: this hypothesis seems to be supported by a significant positive effect of electron-donating alkyl substituents on the NHC heteroatoms. Previously, Lu and coworkers$^{60}$ reported on the use of 1,3-diarylimidazolium-2-carboxylates as catalysts in similar transformations. At a later stage, the same group has shown that a NHC-CO$_2$ adduct could also be immobilized on a MCM-41 support and the catalytic activity of this hybrid material in the coupling between CO$_2$ and epoxides was investigated.$^{64}$ Although applicable, these protocols based on NHC catalysts and their corresponding derivatives require high CO$_2$ pressures (> 20 bar) and temperatures (> 100 °C). The hybrid silica material is indeed recyclable; however, its multi-step synthesis and isolation may result in extra energy and cost consumption, compromising to some extend the overall process sustainability.

It is worth mentioning that cyclic α-alkylidene carbonates, can also be prepared from the reaction of propargylic alcohols with CO$_2$ (p(CO$_2$) = 45 bar) under NHC or NHC–CO$_2$ catalysis at 60 °C.$^{56}$ Promisingly, Lu’s group$^{117}$ found that N-Heterocyclic Qlefin-CO$_2$ adducts (NHO–CO$_2$) work more efficiently as catalysts in this transformation (Scheme 13) under basically ambient reaction conditions. X-ray analysis of the NHO-CO$_2$ adduct revealed that the length of the C$_x$(carboxylate)-C$_x$(NHO) bond is significantly longer than that of the corresponding C$_y$(carboxylate)-C$_y$(NHO) bond. Therefore, the higher activity of the NHO–CO$_2$ adduct was tentatively ascribed to its lower stability compared to NHC-CO$_2$ adducts, thus facilitating the release of the CO$_2$ and/or the coupling product which may possible be rate-limiting in the catalytic cycle.
A creative approach towards cyclic carbonate synthesis using organic molecules as mediators was described by Jamison and his group.118 Combination of N-bromosuccinimide (NBS) with a radical initiator (benzoyl peroxide, BPO) in the presence of dimethylformamide (DMF) as solvent in a continuous flow set up allows for the efficient coupling reaction between epoxides and CO₂. Under optimized conditions, high conversion levels and yields can be attained for various epoxide substrates. A series of (kinetic) experiments suggested epoxide activation by electrophilic attack from the bromine formed in situ. A slight drawback from this approach may be presented by the use of DMF as solvent/reactant requiring higher reaction temperatures (120 °C) as opposed to reactions carried out under milder, neat conditions. However, this method could pave the way towards continuous flow methodology for larger scale syntheses.

In contrast to epoxide/CO₂ couplings, aziridine/CO₂ couplings have been much less investigated, probably as a result of the easier access to epoxide reagents. As further detailed in the review by Kerton and coworkers,32 a number of ILs and their polymer-supported derivatives has been used as catalysts in these aziridine/CO₂ coupling reactions. However, most of the reported catalytic systems either require high reaction temperatures (> 120 °C) and CO₂ pressures (> 50 bar) or deliver the heterocyclic products in low yields/conversions and with poor regio-selectivities.10,119-121

Gao’s group recently reported122,123 an alternative strategy for the selective preparation of 3-substituted cyclic carbamates from the reaction between a cyclic carbonate (made using CO₂) and aromatic amines using 1-butyl-3-methylimidazolium acetate (BmimOAc) as catalyst (Scheme 14). DFT calculations revealed that both the cationic and the anionic moieties of the catalyst activate in a cooperative fashion the substrates (i.e., cyclic carbonates and aromatic amines) by means of hydrogen-bonding. Despite the fact that this procedure is CO₂-free and requires relatively high reaction temperatures (140 °C), the use of metals and high-pressure reaction conditions can be avoided, thus developing a novel green method for the preparation of cyclic carbamates. Moreover, cyclic carbonates, which can be easily produced via direct CO₂ coupling reactions with epoxides and/or oxetanes, are conveniently used as substrates for this type of reaction. Organocatalysts other than ILs including phenolic compounds50 and NHCs64 also have found applicability in this transformation but similar selectivity issues, as aforementioned, have been encountered.

The synthesis of five-membered cyclic carbonates and carbamates has been a highly active research area over the last five years. However, the formation of six-membered cyclic heterocycles based on direct coupling between suitable precursors (oxetanes or azetidines) and CO₂ is generally more difficult. It is further complicated by the lower accessibility and reactivity of oxetanes/azetidines compared with oxiranes/aziridines. Thus, this subfield of organic carbonate/carbamate formation is still in its infancy, though very recently several research teams have been able to design transition metal based catalytic protocols that allow for (substituted) oxetane-into-carbonate conversions.29,124-125

4. Organocatalysed CO₂ reduction

Organocatalysis has also proven to be a powerful tool for CO₂ reduction. Various CO₂ reduction products have already been obtained including carbon monoxide (CO), formic acid, formamide derivatives, methoxysilanes and methoxyboranes, of which the latter two can be easily converted to methanol and methane. Both MeOH and methane are energy vectors and the formation of these higher free energy molecules starting from CO₂ represents a possible alternative to fossil fuel based energy supply.

N-heterocyclic carbenes (NHCs) have been extensively applied as catalysts for the nucleophilic activation and subsequent reduction of CO₂. For example, NHC catalysts have been employed for the CO₂ reduction to CO in presence of inexpensive aldehyde reaction partners as (sacrificial) reductants. Although this reaction does not fall into the “reductive CO₂ coupling” category, it does show the potential of organocatalytic systems to access other type of transformations with formal reduction of the oxidation state of the CO₂ reactant. Initially, Zhang and Gu achieved the NHC-mediated catalytic reduction of CO₂ with aromatic aldehydes as oxygen acceptors.126 The authors proposed that the NHC catalyst reacts with CO₂, resulting in an imidazolium carboxylate intermediate (Scheme 15, below left; cf. Scheme 12); this species attacks the 2-position of cinnamaldehyde realising through a [1,5] H–shift, the corresponding oxidation product as a potassium salt. The catalyst is regenerated by a quick decay of the NHC–CO adduct intermediate, with concomitant release of CO.
In 2010 Nair et al. reported a similar NHC–mediated oxidation of aromatic aldehydes with CO₂ leading to carboxylic acids. The expected aryl glyoxylic acid product, resulting from trapping of the Breslow intermediate (Scheme 15, centre) with CO₂, was not observed. Different from what was previously reported, the postulated reaction mechanism relies on an initial addition of the catalyst to the aldehyde to form a nucleophilic Breslow intermediate which then reacts with CO₂. However, in 2011, both suggested mechanisms and experimental results were questioned by Bode and co-workers. After detecting non-neglectable traces of air (and therefore oxygen) in both reported procedures, they suggested that exogenous molecular oxygen was likely the actual stoichiometric oxidant in the above-discussed reactions. In presence of oxygen, the NHC catalyst triggers the formation of NHC-acyl intermediates (Scheme 15, right), which are capable of transferring their acyl group to a nucleophile (traces of water) to produce the corresponding carboxylic acids. In the mechanistic hypothesis of Bode et al. CO₂ only accounts for the reduction of aldehyde dimerization or oligomerisation side products. This particular chemistry therefore represents an interesting subject of debate likely to induce further detailed investigations into the role of the CO₂ reagent as oxidant.

Although organocatalyzed CO₂ reduction to MeOH is still not as powerful as transition metal based methodologies, organocatalysis offers tangible and diverse approaches to reduced forms of carbon. For example, NHC catalysts have been employed for the reduction of CO₂ to methanol. Ying et al. reported on the reduction of imidazolium carboxylates by silanes yielding methanol. The reaction is particularly interesting because the mesitylimidazolylidene carboxylate NHC catalyst (IMes–CO₂) employed is air stable, can be used in low concentration (0.05 mol %) while maintaining high TONs and TOFs (1840/25.5 h⁻¹, respectively). All these features help to overcome the typical drawbacks (catalyst deactivation, requirement of an air- and oxygen-free atmosphere) of metal-catalysed CO₂ reduction protocols. The proposed reaction mechanism, based on experimental and spectroscopic evidence, is based on the initial formation of a NHC-CO₂ adduct. Computational and experimental studies performed independently by different research groups led to distinct conclusions: Wang and co-workers postulated that the catalytic cycle starts with an initial attack of the NHC on the silane generating a pentavalent silicon species able to deliver a highly nucleophilic hydride to CO₂, while a computational study by Zhang et al. supports an initial formation of an IMes–CO₂ adduct followed by a rate-determining [1,5] H-shift to give the corresponding formylsilane by hydrosilylation, in agreement with the mechanism proposed initially.

Another class of organocatalysts active for the reduction of CO₂ to methoxysilanes and methoxyboranes (and thus, to methanol) are guanidine-based organic superbases (TBD and MTBD; see Figure 2). In an effort to broaden the range of compounds available from CO₂ reduction, Cantat et al. combined both reduction of CO₂ and formation of C–C, C–N, and C–O bonds reporting on the organocatalysed synthesis of formamidine derivatives starting from CO₂, trialkylsilane as reducing agents and N-based nucleophiles: with this approach they were able to synthesize different formamidine derivatives of amines, anilines, imines, hydrazines, hydrazones and N-heterocycles (Scheme 2 for an example). This process is particularly appealing from a practical point of view because of its sustainable nature; in particular, it has been optimized to reuse two common industrial wastes: CO₂ being a by-product from all combustion processes involving organic matter and polymethylhydrosilane (PMHS).

It has been recently demonstrated that rather mild (ambient) conditions can be used for organocatalytic CO₂ conversions. TBD or TMBD catalysts (0.025 mol%) have shown to be active towards CO₂ reduction using 9–BBN (9-borabicyclo[3.3.1]nonane) as reducing agent giving the corresponding dialkylmethoxyborane in >90% yield with TONs and TOFs up to 548 and 33 h⁻¹, respectively. Although for both guanidine based catalysts the reduction of CO₂ with R₂BH and thus the first C–H bond formation is rate determining, with experimental and computational investigations revealing that TBD and MTBD follow different mechanisms. MTBD was proposed to promote the reduction of CO₂ through direct activation of the hydroborane reagent and formation of ion pairs, while TBD is converted into an FLP that first activates CO₂ and facilitates the hydride transfer from the boron to the carbon center (see Scheme 17).
In both cases formate type (HCOOBR₂) and acetal-like H₂C(OBR₂)₂ derivatives were identified as reaction intermediates. In addition, stoichiometric and catalytic reductions of CO₂ have been reported which utilise frustrated Lewis pairs (FLPs) for CO₂ activation and dihydrogen, silanes, or boranes as the hydrogen source. The first evidence of FLPs catalysing CO₂ reduction was reported by O’Hare et al. in 2009: when heated at 110 °C at 1–2 bar of H₂ pressure, B(Ph₃)₃ and TMP (TMP = 2,2,6,6-tetramethylpiperidine) were shown to bind CO₂ stoichiometrically and generate a formate-borate product. Extended heating at 160 °C for several days yielded, after isolation by distillation, methanol as the sole C₁ product (Scheme 18, left). Piers et al. reinvestigated the system using hydrosilanes as reductants in the presence of additional equivalents of the Lewis acid, and under those conditions the system effectively catalysed the reduction of CO₂ to methane (Scheme 18, right). The reaction could be monitored spectroscopically (NMR), allowing the authors to propose a stepwise hydrosilylation process that was later supported computationally. Unfortunately, the calculated turnover numbers are still far from those reached with transition metal-based systems based on, for instance, iridium.

This transformation was proposed to occur through simultaneous nucleophilic activation of the borane and electrophilic “fixation” of CO₂. It was postulated that the reduction process occurs through a stepwise process: initial CO₂ coordination forming a formato-borate intermediate which, upon rearrangement, loses the formaldehyde fragment necessary to generate the final methoxide derivative. More recently, the same authors reported a novel in situ generated FPL catalyst active towards reductive hydroboration of CO₂ based on a relatively non-nucleophilic proton sponge [= 1,8-bis(dimethylamino)naphthalene]. In the presence of stoichiometric quantities of a BH₃·SMe₂ reductant, at 80 °C and 1 bar of CO₂ this system reached a TOF value of 64 h⁻¹. Here the postulated mechanism relies on the activation of BH₃·SMe₂ and converting it into a boronium–borohydride ion pair which, in the presence of CO₂, can evolve into a formate derivative. Final BH₃⁺ abstraction from another FLP borane-proton sponge complex leads to elimination of the methoxyborane product.

The organocatalyzed N-methylation of amines using CO₂ and suitable reducing agents (hydroboranes) has recently emerged as another attractive catalysis route towards CO₂ valorisation. Contributions from Cantat et al. and Dyson and co-workers have set the stage for new conversions mediated by proazaphosphatrane superbases and NHC based organocatalysts. The results highlight the versatile catalytic use of NHCs towards the conversion of CO₂ into a variety of organic molecules such as alkylated amines, MeOH, formamidines and organic carbonates. As such they represent privileged catalyst systems with high potential in other types of CO₂ transformations.

5. Other reactions

The use of organocatalysis for other types of CO₂ conversion reactions is briefly discussed. Beside the formation of organic carbonates and products derived from reductive couplings, the formation of quinazoline–2,4(1H,3H)–diones (see Figure 1, Scheme 20) has also drawn considerable attention. Similar to organic carbonate formation, the formal oxidation state of the C(CO₂) carbon centre does not change, however, mechanistic proposals seem to indicate that water may play a role in the
formation mechanism involving H$_2$CO$_3$ or bicarbonate. Though suggested by DFT analysis of the mechanism, it remains an open question whether the CO$_2$ is fully incorporated into the substrate.

Whereas metal based systems are known to catalyse the efficient formation of these heterocyclic structures from CO$_2$ generally using 2-amino-benzonitriles as reaction partners, organocatalytic methods have been investigated successfully providing green alternatives. Quinazoline-2,4(1H,3H)-diones are considered as biologically and pharmacologically relevant and thus represent interesting synthetic targets. To date various organocatalysts for the reaction between 2-amino-benzonitriles and CO$_2$ have been reported including IL based systems, amine-based heterocycles and carbonates/base impregnated clay minerals. The use of water as a medium has been proposed for the non-catalytic formation of quinazoline-2,4(1H,3H)-diones. In this latter case, the crucial role of the formation of H$_2$CO$_3$ acting as an intermediate was proposed, though higher reaction temperatures/pressures were required and relative longer reaction times were needed for high substrate conversion.

6. Summary and outlook

In the last five to ten years, the field of CO$_2$ chemistry and conversion catalysis has expanded enormously. Whereas homogeneous and heterogeneous metal catalysis still fulfil a prominent position within this vivid area of research, organocatalysis is emerging as a potential and useful alternative tool in specific CO$_2$ conversion reactions.

The current review shows that some organocatalyst structures such as NHCs and ILs can be regarded as “privileged” systems, as these are widely applicable systems for different organic transformations that are not limited to CO$_2$ couplings. However, the chemistry of other organocatalyst structures (including azaphosphatrane derivatives) seems highly promising, and the quest for a more diverse set of organocatalysts able to compete with metal catalysis is an ongoing challenge. In order to meet the challenges of sustainable though highly effective catalysis, new and conceptually different approaches may be warranted making clever use of cooperative, confinement and/or site—isolation effects. Without a doubt, there is a bright future for organocatalysis as a green alternative in CO$_2$ conversion catalysis, and this review will hopefully spur the catalysis community to develop new methodology of common interest to academic and industrial experts.

Acknowledgements

GF kindly acknowledges financial support from the European Community through FP7-PEOPLE-2013-IEF project RENOVACARB (grant agreement Nº622587). WG thanks the CELLEX foundation for financial support. ICIQ, ICREA and the Spanish Ministerio de Economía y Competitividad (MINECO; through the Severo Ochoa Excellence Accreditation 2014-2018 (SEV-2013-0319) and project CTQ2011-27385 are also acknowledged for support.

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Notes and references

5 One of the industrial processes leading to urea starting from ammonia and CO2 is known as the Bosch-Meiseur urea process. See for more information: http://boschmeiserprocess.wikispaces.com/.
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