

Final Report

„Large scale application of P based organocatalysts in batch and flow for the synthesis of fatty acid derived cyclic carbonates“

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* z.B. Conference contributions, publications (with status), funding applications (with status)

1. Summary

In this project new catalyst systems for the conversion of CO₂ with epoxides to the corresponding cyclic carbonates were developed. In this context bifunctional phosphonium salts were initially used as one-component catalysts as well as the new catalyst systems based on earth abundant metals. In this regard, bifunctional one-component catalysts combine a nucleophilic and an electrophilic function for an effective activation of the epoxides. Two different homogeneous bifunctional phosphonium salt catalysts were developed, which were used on one hand for the conversion of fossil resources derived epoxides and on the other hand for the conversion of internal bio-based epoxides. Moreover a heterogeneous bifunctional phosphoniumsalt catalyst was synthesized and evaluated, which showed high activities under relatively mild conditions. Additionally, this catalyst was reused up to 15 times and the deactivation of the catalyst was thoroughly investigated. In addition, a binary catalyst system based on a monofunctional nucleophilic phosphoniumsalt and an electrophilic iron salt co-catalyst for the conversion of biobased epoxides was developed. Furthermore, three different catalyst systems based on CaI₂ in combination with different halides and/or co-catalysts were reported. These catalysts were used for the synthesis of terminal as well as internal carbonates under very mild reaction conditions and investigations regarding the reaction

mechanisms were conducted. All in all in this thesis seven different catalyst systems were extensively evaluated and described. For all the described catalyst systems the reaction conditions for the synthesis of cyclic carbonates have been systematically optimized and a broad variety of cyclic carbonates were synthesized and isolated in excellent yields. This work was accompanied by detailed mechanistic investigations. Furthermore a flow system was assembled and initial test reactions using the developed immobilized catalyst were performed. However, the conversion of (bio-based)epoxides with CO₂ under the chosen flow conditions proved to be difficult.

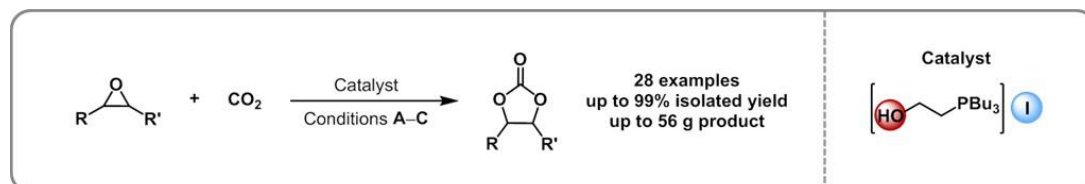
2. Introduction and aim of the project

Large scale application of phosphorous based organocatalysts in batch and flow for the synthesis of fatty acid derived cyclic carbonates. Aim of this project was the preparation of novel supported phosphorous based catalysts and their application for the scalable synthesis of cyclic carbonates based on epoxidized fatty acids (methyl oleate derivatives). In this context different recycling concepts respectively separation techniques were supposed to be evaluated. Special analytical methods (in situ IR and NMR experiments in a pressure tube) should be utilized to gain insights in the catalytic cycle and to optimize the activity of the supported P-based catalyst. It was planned to optimize the system apply it to the conversion of methyl oleate derivatives with carbon dioxide in a batch reactor on preparative scale. Furthermore a suitable test set up for a flow reactor system should be assembled and the best recycling concept determined from the batch experiments was supposed to be implemented. Finally as a proof of principle, initial experiments will be performed in the flow system.

3. Results and discussion

Cyclic carbonates can be prepared by the addition of CO₂ to epoxides.¹ Initially we extended our work on bifunctional one-component phosphorus-based organocatalysts.² In this respect, numerous bifunctional organocatalysts were synthesized and tested for the atom-efficient addition of carbon dioxide and epoxides to produce cyclic carbonates. These catalysts are based on phosphonium salts containing an alcohol moiety in the side chain for substrate activation through hydrogen bonding. In the model reaction, converting 1,2-

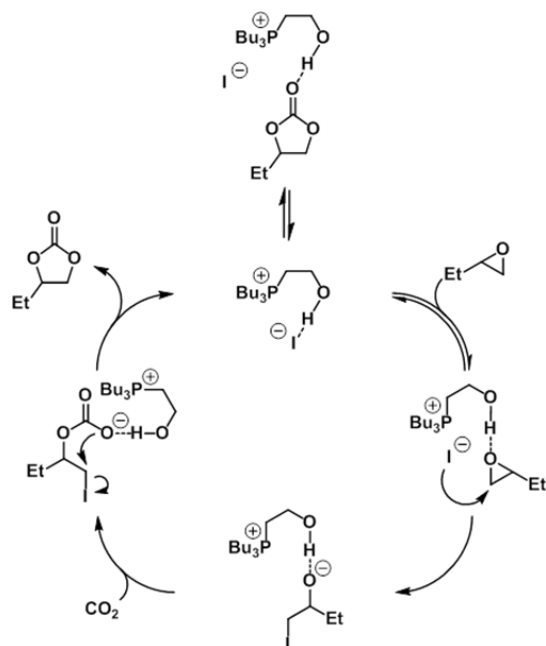
butylene oxide with CO₂, 19 catalysts were tested to determine structure–activity relationships. In total, 28 epoxides were converted with CO₂ to give the respective cyclic carbonates in yields of up to 99 % (Scheme 1). Even at 45 °C, the most active catalyst was able to produce cyclic carbonates selectively in high yields.



Scheme 1. Synthesis of cyclic carbonates from epoxides and the most active aliphatic bifunctional catalyst.

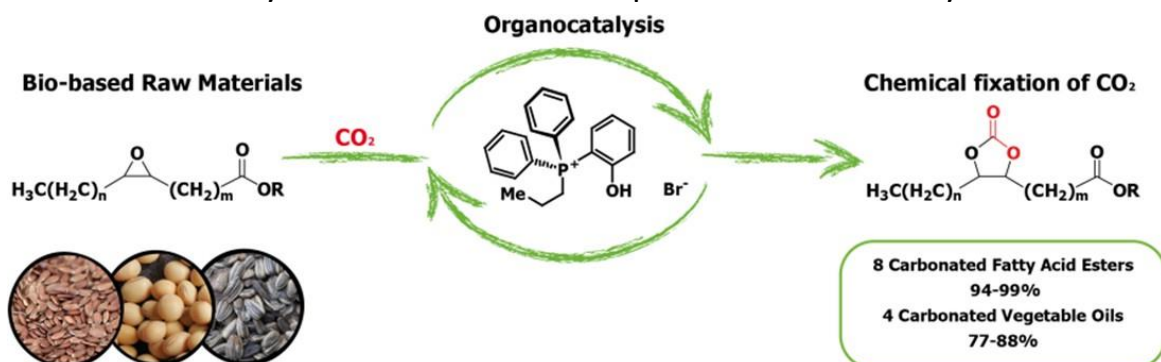
The carbonates were generally obtained as analytically pure products after simple filtration over silica gel. This single-component catalyst system works under neat and mild reaction conditions and tolerates several useful moieties. Subsequently we evaluated frequently employed tetrabutyl ammonium and phosphonium halides as well as their bifunctional analogues as catalysts in cyclic carbonate synthesis under benchmarked conditions.³ The kinetic data of all catalysts were evaluated and the rate constants determined. Moreover, a systematic infrared spectroscopic study of the interactions between cation and anion of the catalysts as well as the interactions between the catalysts and the substrate were conducted to support our proposed catalytic cycle (Scheme 2). These experimental results were additionally supported by DFT calculations. The conversion of butylene oxide with CO₂ in the presence of monofunctional ammonium and phosphonium salts under standard reaction conditions (2 mol% catalyst, p(CO₂)= 1.0 MPa, 90 °C, 6 h) followed a 1st order kinetics. The rate constants were determined for the monofunctional salts 3 and 4 which proved that [nBu₄P]Cl was the most active catalyst ($k^{obs}= 0.291 \text{ h}^{-1}$). IR spectroscopic investigations showed that the interaction between the cations and the anions depended on the nature of the anion and correlated with the observed wavenumber in the order Cl[−] > Br[−] > I[−] while the order of activity showed the same trend. Similar activity was observed for the phosphonium bromide and chloride. The infrared spectroscopic investigations indicate that the epoxide is activated by the onium cation. The observed superior activity of the chlorides in the monofunctional onium salt series might be addressed to the fact that Cl[−] is the best nucleophile in polar aprotic solvents such as reactant butylene oxide and the product (butylene carbonate) respectively

(under solvent-free conditions the substrate and product may be considered as solvent). Additionally, the weaker interaction between the chloride and the cation might allow a stronger activation of the epoxide by the cation. The kinetic studies on the bifunctional catalysts showed the opposite trend in activity for the respective anion ($I^- > Br^- > Cl^-$) compared to the monofunctional salts. This can be explained by the inversed nucleophilicity of the anions in a polar protic environment which is provided by the hydroxyl moiety in the bifunctional catalyst. The infrared spectroscopic investigations revealed the strongest interaction between the chloride and the OH group leading to low catalytic activity. In contrast the iodides showed the highest activity and lowest interaction between the OH group and the anion. Notably, the calculated infrared spectra of the catalyst showed the same trend in the interactions. The actual activation of the epoxide by hydrogen bonding was also observed when the reaction was monitored by in situ infrared measurements of the reaction mixture. Interestingly, a new species was observed which was identified as adduct between the catalyst and the product. Additionally, the initially assumed 1st order kinetics did not fit for these catalysts. Thus a Michaelis-Menten model including a reversible product inhibition which is valid for the case of a 1st order with respect to the substrate was assumed. A simultaneous integration-regression procedure led to a much better description of the experimental results. The observed trends in the interaction between the onium cation and the anion are correlated to their catalytic activity. Moreover, these investigations revealed the mode of the substrate activation for the monofunctional and the bifunctional catalysts. Furthermore, the kinetic studies and in situ infrared experiments revealed a product inhibition of the bifunctional catalysts via the unexpected formation of catalyst-carbonate adducts. The interaction between the catalysts and the product was further studied by infrared spectroscopy. Finally, the rate and the equilibrium constants for the bifunctional catalysts were determined by a Michaelis-Menten model considering a reversible product inhibition.



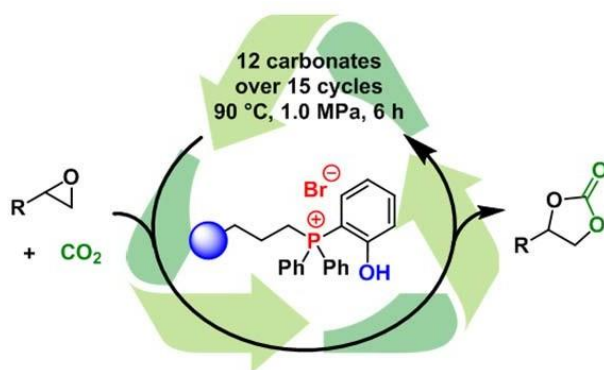
Scheme 2. Proposed catalytic cycle.

Based on these findings we developed a new catalyst with an phenol scaffold for the synthesis of oleochemical carbonates (Scheme 3).⁴ These catalysts proved to be highly efficient for the atom-economic reaction of CO₂ and epoxidized oleochemicals. Notably, those products are obtained from CO₂ and renewable feedstocks only. Structure-activity relationships have been deduced from a screening of 22 organocatalysts in a test reaction. Bifunctional catalysts based on a phosphonium salt bearing a simple phenolic moiety proved to be extraordinarily active under comparatively mild and solvent-free reaction conditions. In the presence of the most active organocatalyst 12 oleochemical carbonates were isolated in excellent yields up to 99 %. This organocatalyzed reaction represents an excellent example for the realization of the 12 Principles of Green Chemistry as well as the 12 Principles of CO₂ Chemistry.



Scheme 3. Novel phenol-based phosphonium salt and conversion of epoxidized fatty acids to oleochemical carbonates.

Several of these bifunctional phosphonium salt catalysts were prepared and immobilized on silica and polystyrene supports.⁵ The immobilized systems were compared with their homogeneous analogs in cyclic carbonate synthesis. Interestingly, in some cases, higher activities were observed for the immobilized catalysts. The most active system was the phenol-functionalized phosphonium salt supported on a silica surface. The covalent linkage of the phosphonium unit to the silica was verified by solid-state NMR and FT-IR. SEM and EDX measurements revealed a homogeneous distribution of the phosphonium salt on the particle surface. This catalyst facilitated the addition of CO₂ to epoxides under mild conditions. The evaluation of the substrate scope and the catalyst recycling were combined in one set of experiments. In 15 consecutive runs, the synthesis of 12 cyclic carbonates in yields of up to 98% was achieved. The investigation of the catalyst after the recycling experiments revealed the loss of the original anion (bromide) as well as a decrease in the number of phosphonium units, which explained the observed deactivation of the catalyst during the recycling experiments. These type of immobilized catalysts were also studied in a flow reactor but so far gave only unsatisfying results.

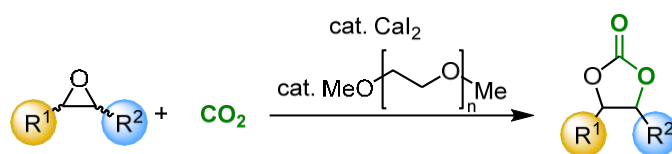


Scheme 4. Most active immobilized phosphonium salt and general representation of the conversion of epoxides to cyclic carbonates.

Since we were generally interested in the synthesis of fatty acid derived cyclic carbonates we also studied binary catalytic systems which contained simple phosphonium salts in combination with sustainable metals such as Iron-salts.⁶ In this study organic phosphorus salts proved to be selective catalysts for this reaction. In a widespread screening 11 inexpensive and nontoxic iron salts were evaluated as cocatalysts to enhance the reaction rate. In the presence of 0.25 mol% iron chloride the selectivity and conversion were significantly

improved. The reaction parameters were optimized under solvent-free conditions, and the scope and limitation were evaluated for 9 epoxidized fatty acid esters and 4 epoxidized vegetable oils. The biobased carbonates were isolated in excellent yields up to 95% and can be considered to be based on 100% CO₂ in respect to carbon. This binary catalyst system features high efficiency and plain simplicity while valorizing CO₂ into cyclic carbonates based on renewable feedstocks.

Subsequently we studied other sustainable metal and were able to develop two catalytic systems based on CaI₂. In the first one we used CaI₂ in combination with poly(ethylene glycol) dimethyl ether (PEG DME 500) as an efficient catalyst system for the addition of CO₂ to epoxides (Scheme 5).⁷ Fifteen terminal epoxides were converted at room temperature to give the desired products in yields up to 99 %. Notably, this system was also effective for the synthesis of twelve challenging internal carbonates in yields up to 98 %.

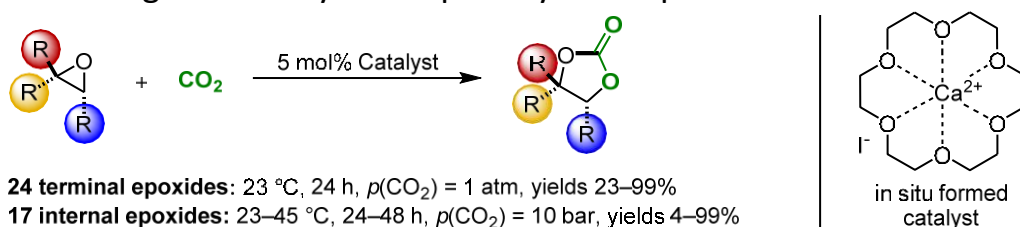


15 terminal epoxides: 25 °C, 24 h, $p(\text{CO}_2) = 10$ bar, yields 75–99%

12 internal epoxides: 70–90 °C, 24–48 h, $p(\text{CO}_2) = 20$ –50 bar, yields 29–98%

Scheme 5. Catalytic system based on CaI₂ and PEG DME 500 for the synthesis of cyclic carbonate.

The second protocol is based on the use of calcium iodide in combination with 18-crown-6 ether (Scheme 6).⁸ ¹H NMR experiments revealed the selective in situ formation of a crown ether complex. This catalyst allows the conversion of various terminal epoxides under 1 atm CO₂ pressure even at room temperature. Remarkably, a broad range of internal epoxides with various substitution patterns and substituents were smoothly converted which confirms the high efficiency and capability of the protocol.



24 terminal epoxides: 23 °C, 24 h, $p(\text{CO}_2) = 1$ atm, yields 23–99%

17 internal epoxides: 23–45 °C, 24–48 h, $p(\text{CO}_2) = 10$ bar, yields 4–99%

Scheme 5. Catalytic system based on CaI₂ and PEG DME 500 for the synthesis of cyclic carbonate.

We turned our attention to the conversion of challenging internal and trisubstituted cyclic carbonates from bio-derived epoxides such as epoxidized fatty acid derivatives and CO₂ under mild reaction conditions.⁹ Several crown ethers were tested as ligands in combination with various co-catalysts for the possible activation of CO₂. The most active system consists of a dicyclohexyl functionalized 18-crown-6 ether and triphenyl phosphane in addition to calcium iodide. The in situ complexation of Ca²⁺ by the crown ether was detected by ¹H NMR spectroscopy. Interestingly, the addition of triphenyl phosphane as a co-catalyst leads to a significant increase in activity, which is similar or even higher to organic superbases like DBU and TBD. The catalytic system was employed in the conversion of 16 different bio-derived epoxides, including fatty acid esters, oils and terpenes with CO₂ and is able to facilitate the reaction under mild conditions. Various internal epoxides were converted at only 45 °C, 0.5 MPa CO₂ pressure, a catalyst loading of 5 mol% and a reaction time of 24 h with isolated yields up to 98% of the respective carbonate. The challenging terpene-based carbonates were isolated in yields up to 81%, although harsher reaction conditions were necessary.

4. References

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9. Longwitz, L.; Steinbauer, J.; Spannenberg, A.; Werner, T., Calcium-Based Catalytic System for the Synthesis of Bio-Derived Cyclic Carbonates under Mild Conditions. *ACS Catal.* **2018**, *8*, 665–672.

5. Further achievements/ benefit from the project

The outcomes of this project have been communicated in the following publications:

- 9 „Mechanistic Study on the Addition of CO₂ to Epoxides Catalyzed by Ammonium and Phosphonium Salts: A Combined Spectroscopic and Kinetic Approach”, J. Steinbauer, C. Kubis, R. Ludwig, T. Werner, *ACS Sustainable Chem. Eng.*, **2018**, *6* 10778–10788.
- 8 „Calcium-Based Catalytic System for the Synthesis of Bio-Derived Cyclic Carbonates under Mild Conditions”, L. Longwitz, J. Steinbauer, A. Spannenberg, T. Werner, *ACS Catal.* **2018**, *8*, 665–672.
- 7 „Immobilized bifunctional phosphonium salts as recyclable organocatalysts in the cycloaddition of CO₂ and epoxides”, J. Steinbauer, L. Longwitz, M. Frank, J. Epping, U. Kragl, T. Werner, *Green Chem.* **2017**, *19*, 4435–4445. (Highlighted in Synfacts 2017)
- 6 „Poly(ethylene glycol)s as Ligands in Calcium-Catalyzed Cyclic Carbonate Synthesis”, J. Steinbauer, T. Werner, *ChemSusChem* **2017**, *10*, 3025–3029.
- 5 „An in situ formed Ca²⁺-crown ether complex and its use in CO₂-fixation reactions with terminal and internal epoxides”, J. Steinbauer, A. Spannenberg, T. Werner, *Green Chem.* **2017**, *19*, 3769–3779. (Part of

the Themed Collection: 2017 Green Chemistry Hot Articles)

- 4 „Recent developments in the synthesis of cyclic carbonates from epoxides and CO₂”, H. Büttner, L. Longwitz, J. Steinbauer, C. Wulf, T. Werner, *Top Curr. Chem.* **2017**, 375, 50–106.
- 3 „Organocatalyzed synthesis of oleochemical carbonates from CO₂ and renewables”, H. Büttner, J. Steinbauer, C. Wulf, M. Dindaroglu, H.-G. Schmalz, T. Werner, *ChemSusChem*, **2017**, 10, 1076–1079.
- 2 „Iron-based binary catalytic system for the valorization of CO₂ into bio-based cyclic carbonates”, H. Büttner, C. Grimmer, J. Steinbauer, T. Werner, *ACS Sustainable Chem. Eng.* **2016**, 4, 4805–4814. (*ACS Editors' Choice*)
- 1 „Synthesis of cyclic carbonates from epoxides and CO₂ using bifunctional one-component phosphorus-based organocatalysts”, H. Büttner, J. Steinbauer, T. Werner, *ChemSusChem* **2015**, 8, 2655–2669.

The results were presented as oral presentations as well as posters at different conferences:

Oral presentations:

- 4 „Synthesis of immobilized phosphonium salts and their application in the synthesis of cyclic carbonates”, L. Longwitz, J. Steinbauer, M. Frank, J. Epping, T. Werner, *22nd International Conference of Phosphorus Chemistry (ICPC)*, Budapest, 08.–13. Juli **2018**, Budapest, Hungary.
- 3 „Oleochemical carbonates from CO₂ and renewables”, T. Werner, H. Büttner, J. Steinbauer, C. Wulf, 9th Workshop on Fats and Oils as Renewable Feedstock for the Chemical Industry, 19.–21. März 2017, Karlsruhe Institute of Technology (KIT), Karlsruhe, Deutschland. (INVITED)
- 2 „Organocatalyzed conversion of CO₂ with epoxides”, H. Büttner, J. Steinbauer, T. Werner, Chemiedozententagung 2017, 13.–15. März 2017, Philipps Universität Marburg, Marburg, Deutschland.

- 1 „CO₂ valorization utilizing new P-based catalysts“, J. Steinbauer, H. Büttner, T. Werner, 8th International Phosphorus Workshop (IPW8), 12.–16. September 2016, Universität Rostock, Rostock, Deutschland.

Posterpresentations:

- 8 „Synthesis of immobilized phosphonium salts and their application in the synthesis of cyclic carbonates“, L. Longwitz, J. Steinbauer, M. Frank, J. Epping, T. Werner, Summer School "Advanced Organocatalysis" ADVOCAT, Köln, 26.–30. August **2018**, Universität Rostock, Deutschland.
- 7 „Synthesis of immobilized phosphonium salts and their application in the synthesis of cyclic carbonates“, L. Longwitz, J. Steinbauer, M. Frank, J. Epping, T. Werner, 2. JCF-Posterparty, 11. April 2018, Universität Rostock, Deutschland.
- 6 „Synthesis of immobilized phosphonium salts and their application in the synthesis of cyclic carbonates“, L. Longwitz, J. Steinbauer, M. Frank, J. Epping, T. Werner, 51. Jahrestreffen Deutscher Katalytiker, 14.–16. März 2018, Weimar, Deutschland.
- 5 „Synthesis of immobilized phosphonium salts and their application in the synthesis of cyclic carbonates“, J. Steinbauer, L. Longwitz, M. Frank, J. Epping, T. Werner, 3. Internes P-Campus Symposium, 08.–09. November 2017, Rostock, Deutschland.
- 4 „Calcium catalyzed synthesis of cyclic carbonates from epoxides and CO₂“, J. Steinbauer, T. Werner, 1. JCF-Rostock Posterparty, 19. April 2017, Rostock, Deutschland.
- 3 „Alkali- and earth alkali metal salts as catalysts for the cycloaddition of CO₂ to epoxides“, J. Steinbauer, W. Li, T. Werner, ORCHEM 2016, 05.–07. September 2016, Weimar, Deutschland.
- 2 „Bifunctional phosphonium salts for the conversion of CO₂ with terminal and internal oxiranes“, J. Steinbauer, H. Büttner, T. Werner, 49. Jahrestreffen Deutscher Katalytiker, 16.–18. März 2016, Weimar,

Deutschland.

- 1 „One-component catalytic system for the conversion of CO₂ with oxiranes“, J. Steinbauer, H. Büttner, W. Desens, T. Werner, 5. Statuskonferenz der BMBF Fördermaßnahme "Technologien für Nachhaltigkeit und Klimaschutz - Chemische Prozesse und stoffliche Nutzung von CO₂", 21.–22. April 2015, Berlin, Deutschland.

The research was supported by two master students in their thesis:

- 2 „Synthesis of immobilized phosphonium salts and their application in catalysis“
Herr B. Sc. Lars Longwitz
Kolloquium: 30. Mai 2017
- 1 „Entwicklung von Katalysatorsystemen für die Synthese cyclischer Carbonate“
Herr B. Sc. Christoph Grimmer
Kolloquium: 07. September 2015