

## Kleij Research Group



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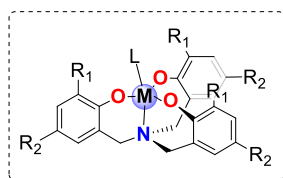
### Abstract

Our research activities focus on the valorization of carbon dioxide and renewable feed stocks into value-added organic matter using organocatalytic and metal-mediated catalytic approaches. We have and continue to be active in the preparation of highly functional organic carbonates, focusing on sustainable solutions and improving activity and stereo-selectivity profiles. We have recently expanded our portfolio of activities to other classes of relevant compounds such as oxazolidinones, CO<sub>2</sub>-based (bio)polymers and more complex organic matter derived from stereo-selective, multi-component

coupling approaches. An important part of our work puts attention to new catalyst design and efforts to get a higher degree of understanding concerning the observed reactivity/selectivity features by means of mechanistic and computational studies. Collaborations with the industrial sector form part of our work in order to be able to potentially transfer technological advancements from bench to pilot scale and beyond. More recently we have begun to use functional organic carbonates as a starting point for unprecedented stereo-selective and enantioselective syntheses of various fine chemicals including allylic amines and sulfones.

### Carbon Dioxide Conversion

Our ongoing efforts in the area of carbon dioxide valorization (representing a waste compound from all combustion processes) has resulted in a series of new catalytic processes based on organocatalytic or metal-mediated CO<sub>2</sub> conversions to value-added organic compounds including organic carbonates, polymers and other heterocyclic compounds of academic and industrial interest. Some highlights of our work are provided below. In many of the research activities that focus on the catalytic conversion of CO<sub>2</sub> we make use of highly modular complexes based on aminotriphenolate scaffolds as shown in Figure 1.



- M = Al(III), Fe(III), Co(II), Co(III), Mn(III), Cr(III)
- Modular ligands - tunable properties
- Among the best catalysts for carbonate formation
- Excellent polymerization potential (Fe, Al)

Fig. 1 – Al(III) based aminotriphenolate complexes are privileged catalysts in CO<sub>2</sub> conversion to various products.

### OXETANE CONVERSION:

Oxetanes are cyclic ethers and compared to epoxides generally less reactive in terms of ring-opening by nucleophilic reagents. The origin of this more sluggish reactivity is not a significant difference in the ring strain found in these cyclic ethers but the kinetic barriers associated to intermediate steps which are controlled by aromatic (epoxide case) or anti-aromatic transition states (oxetanes) with the latter thus leading to slower reactions. The use of Al(III) complexes in combination with suitable halide nucleophiles under optimized conditions turned out to provide unique reactivity towards the chemo-selective formation of six-membered cyclic carbonates (6MCCs; Figure 2) which are useful precursors for ring-opening polymerization (ROP) to form polycarbonates. However, since the polycarbonates derived from oxetanes are the thermodynamic products, a kinetically controlled process is required and typically should operate at low(er) reaction temperatures. This combined with the sluggish reactivity of oxetanes poses a challenge towards the selective formation of the cyclic over the poly-carbonate species. The combination of a

sterically hindered Al(III) complex (Figure 1, R<sup>1</sup>/R<sup>2</sup> = **tBu**) and a bromide based nucleophile (TBAB) proved to be beneficial towards 6MCC formation and the first general route to these ROP precursors was thus devised.

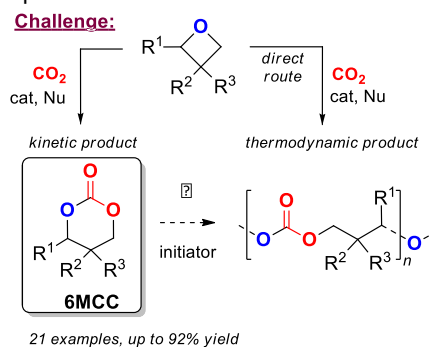


Fig. 2 – 6MCC formation using an Al(III) based aminotriphenolate/Br binary catalyst system (75°C, 10 bar).

### POLYCARBONATES :

A second major achievement has been the development of a new copolymerization process that involved the use of a bio-renewable synthon, *viz.* limonene (Figure 3). The monoxide of this terpene, limonene oxide (LO), was conveniently polymerized by a binary catalyst comprising a methyl-substituted Al(III) complex (Figure 1, R<sup>1</sup>/R<sup>2</sup> = **Me**) and a chloride based nucleophile (PPNCl). Since commercial limonene comes as a mixture of two stereoisomers, first attempts were done with this mixture to find the appropriate process parameters as to optimize molecular weight (*M<sub>n</sub>*), polydispersity (*Đ*) and stereo-regularity. Interestingly, we found that the *cis*-LO isomer reacts significantly faster than its *trans*-LO analogue, and therefore further optimization focused on the pure *cis*-LO substrate. Under strictly anhydrous conditions (to prevent chain transfer by adventitious water) the polymer properties could be optimized (*M<sub>n</sub>* = 11 kg/mol, *Đ* = 1.4, 96% *trans* units in the polymer) and almost fully stereo-regular polymers were obtained with high *T<sub>g</sub>* values of up to 112°C. The catalysis process was shown to behave as a living system, and reports on the copolymerization of these challenging and bulky oxiranes with CO<sub>2</sub> are scarce. Currently this work is expanded to new LO terpolymerization processes that focus on the control over the amount and location of the olefin groups in the terpolymer, and subsequently over the glass transition behavior and thermal stability of the « cured » polymers obtained through thiol-ene

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chemistry. Preliminary results demonstrate that such cured polymers show enhanced glass transitions ( $T_g$  up to 150°C) and improved thermal stability properties ( $T_d^{10}$  roughly 20-30°C higher).

In a separate approach, we have used Yb(III)-centered salen catalysts (Figure 4) for the copolymerization of CO<sub>2</sub> and cyclohexene oxide (CHO): lanthanide based catalysts are interesting targets as they typically possess the required Lewis acidic features for epoxide activation, and the salen ligand framework can fine-tune the reactivity of the metal center in a modular fashion. As such we started to investigate the use of various new lanthanide based binary catalysts for CO<sub>2</sub>/CHO copolymerization and found that the ytterbium based systems shown in Figure 4 showed the highest activity while maintaining excellent selectivity towards the fully alternating copolymer.

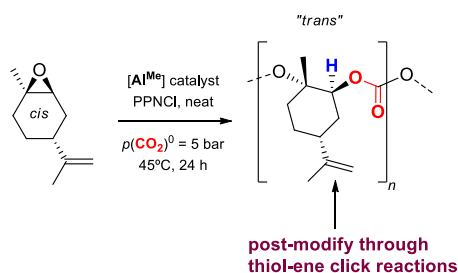


Fig. 3 – Al(III) catalyzed stereo-regular copolymerization of cis-LO and CO<sub>2</sub> giving access to a “bio-based” polycarbonate.

In order to assess better the results obtained with this catalytic process, benchmarking against highly active and attractive Cr(III) and Co(III) salen based catalysts was carried out and illustrated, although being less effective, that the Yb-based catalytic system exhibits similar order-of-magnitude reactivity (expressed in the TOF/h) and polymer properties ( $M_n$  and  $\bar{D}$ ).

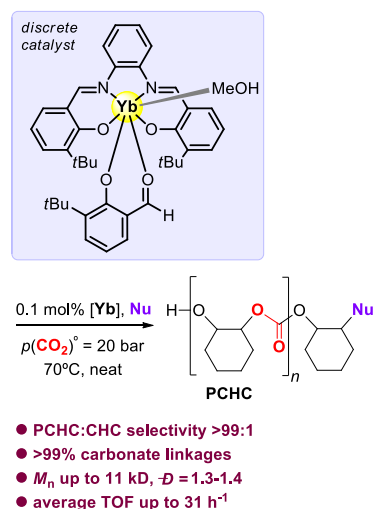


Fig. 4 – Yb(III) catalyzed copolymerization of CHO and CO<sub>2</sub>.

### FINE CHEMICALS :

The potential of CO<sub>2</sub> (and CO<sub>2</sub>-derived cyclic carbonates or alike structures) is large and several different products have been prepared through newly developed catalytic processes using Al(III) based complexes (see Figure 1) or simple (commercially available) organocatalysts. Cyclic carbonates are generally considered as interesting targets because of their application as non-protic solvents and fine-chemical precursor potential. We therefore considered the development of environmentally more benign catalytic processes as a useful target. Whereas the vast majority of the catalysts used in the area of carbonate formation are based on metal systems, organocatalysis has recently begun to provide reasonable catalytic alternatives. However, the need to improve on the overall catalytic efficiency and particularly the reactivity remains a challenge. As a possible solution towards the creation of more active organocatalysts to convert CO<sub>2</sub> into cyclic carbonates we considered the (commercially available) polyphenol “tannic acid” (Figure 5) as an interesting and cheap system to promote CO<sub>2</sub> conversion. The presence of a high local concentration of reactive groups (cf., the various oligophenol fragments) showed higher thermal resistance at elevated temperatures and therefore improved the longevity compared to the simpler pyrogallol based catalyst. These features are important for long-term applications, and the creation of higher TON values was hence realized while maintaining good TOF and TON characteristics.

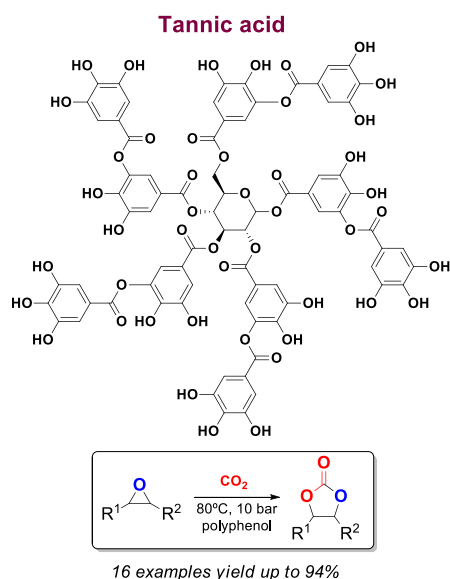


Fig. 5 – Tannic acid catalyzed formation of organic carbonates.

The cyclic carbonates themselves (and alike carbamates), if appropriately functionalized, have large synthetic potential in the preparation of various relevant chemicals. With this important objective in mind we envisioned the coupling of epoxides and phenyl carbamate (readily available and cheap precursors) towards the preparation of a series of oxazolidinones with wide substitution diversity (Figure 6). The oxazolidinones (or: cyclic carbamates) were indeed easily prepared from the aforementioned reagents by applying an Al(III)-catalyzed approach (Figure 1;  $R^1/R^2 = \text{Cl}$ ). Subsequently the oxazolidinones could be conveniently converted into non-symmetric ureas by aminolysis of the cyclic carbamates producing highly functionalized synthons; their potential use in further derivatization was demonstrated by converting an alkyne-based urea through “click chemistry” showing that such ureas can be used to produce supported versions thereof.

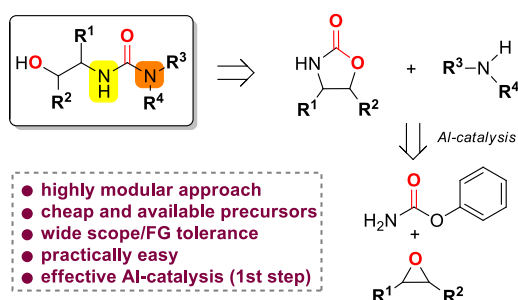


Fig. 6 – The general scheme for the formation of oxazolidinones from epoxides and phenyl carbamate

catalyzed by Al(III) complexes, and their conversion into highly functional non-symmetrical ureas.

Whereas cyclic carbamates are useful synthons towards highly functional non-symmetrical ureas, alternatively cyclic carbonates can represent a general starting point for linear *N*-aryl carbamates (NCAs) by a nucleophilic aminolysis in the presence of aromatic amines. However, this approach is rather challenging as aromatic amines are very weak nucleophiles, and for any reaction to occur, very high temperatures are needed ( $\geq 120^\circ\text{C}$ ). However, at such high reaction temperatures the chemo-selectivity towards the NCA target is minimal and a plethora of other products (those based on alkylated amines and diols among others) are formed: no (significant amount of) NCA can be detected under these high temperature conditions in the non-catalyzed *N*-aryl carbamate formation. We anticipated the use of TBD (= 1,5,7-triazabicyclo[4.4.0]dec-5-ene) as a catalytic mediator, and this proved to be crucial as it allows the coupling between various mono- and di-substituted cyclic carbonates to be carried out under ambient and neat reaction conditions. The chemo-selectivity towards the NCA product can, consequently, be controlled to a large extent (Figure 7).

These NCA scaffolds are important intermediates “*en route*” to pharma-relevant compounds, and may offer a new way towards the formation of important *N*-aryl isocyanates upon heating the NCA precursor and releasing an alcohol unit: such aryl-isocyanates are one of the most important compounds used in industry for the curing of epoxy-based resins and/or polymers.

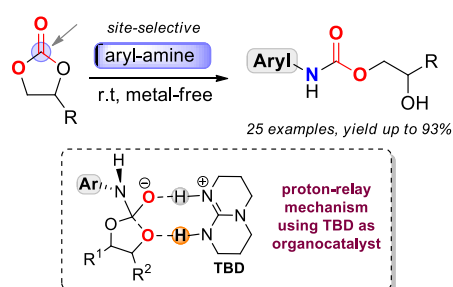


Fig. 7 – NCA formation by reacting cyclic carbonates with aromatic amines under TBD catalysis under mild reaction conditions.

Extensive computational investigations on the TBD-mediated aminolysis of cyclic carbonates by alkyl/aryl amines has revealed two major disclosures: (1) first, the aminolysis of a cyclic



carbonate by a more nucleophilic alkyl amine is assisted by two water molecules; their presence is vital as it brings down the implied transition state (ring-opening of the carbonate by the amine) by 12 kcal/mol to around 24 kcal/mol, thus enabling ambient conversion in these cases. However, the use of aromatic amines requires a more powerful proton-relay catalyst and TBD provides the necessary proton-shuttling potential to enable (after activating the amine and carbonate substrates through a ternary intermediate) ambient formation of the NCA compounds.

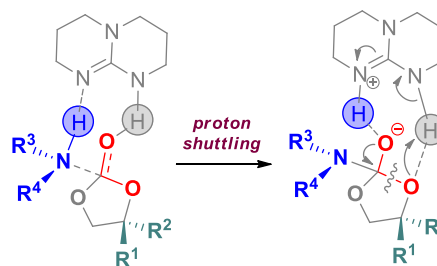


Fig. 8 – Formation of a ternary intermediate computed by DFT.

Summarizing, the use of powerful organocatalysts and Al(III) based aminotriphenolate complexes allows for the valorization of carbon dioxide into a range of organic products including (biobased) polycarbonates, cyclic carbonates, oxazolidinones, non-symmetrical ureas and linear carbamates.

## Articles

“Meet Our Editorial Board Member”

*Curr. Org. Chem.* (2015) 19 - 2321-2321

A. W. Kleij\*

“Copolymerization of CO<sub>2</sub> and Cyclohexene Oxide Mediated by Yb(salen)-Based Complexes”

*Macromolecules* (2015) 48 - 8197-8207.

A. Decortes, R. M. Haak, C. Martín, M. Martínez Belmonte, E. Martín, J. Benet-Buchholz, A. W. Kleij\*

“Highly Efficient Organocatalyzed Conversion of Oxiranes and CO<sub>2</sub> into Organic Carbonates”

*ChemSusChem* (2015) 8 - 3248-3254

S. Sopeña, G. Fiorani, C. Martín, A. W. Kleij\*

“Aluminium-Catalysed Oxazolidinone Synthesis and their Conversion into Functional Non-Symmetrical Ureas”

*Adv. Synth. Catal.* (2015) 357 - 2849-2854

V. Laserna, W. Guo, A. W. Kleij\*

“A Metal-free Synthesis of N-Aryl Carbamates under Ambient Conditions”

*Angew. Chem. Int. Ed.* (2015) 54 - 11686-11690

W. Guo, J. González-Fabra, N. A. G. Bandeira, C. Bo, A. W. Kleij\*

“Highly Chemo-Selective Catalytic Coupling of Substituted Oxetanes and Carbon Dioxide”

*Chem. Eur. J.* (2015) 21 - 10754-10762

J. Rintjema, W. Guo, E. Martín, E. C. Escudero-Adán, A. W. Kleij\*

“Highly Efficient Chirality Transfer from Diamines Encapsulated within a Self-Assembled Calixarene-Salen Host”

*Chem. Eur. J.* (2015) 21 - 7144-7150

L. Martínez-Rodríguez, N. A. G. Bandeira, C. Bo, A. W. Kleij\*

“Al(III)-Catalysed Formation of Poly(limonene)carbonate: DFT Analysis of the Origin of Stereoregularity”

*Chem. Eur. J.* (2015) 21 - 6115-6122

L. Peña Carrodegua, J. González-Fabra, F. Castro-Gómez, C. Bo, A. W. Kleij\*

“New Iron Pyridylamino-Bis(Phenolate) Catalyst for Converting CO<sub>2</sub> into Cyclic Carbonates and Cross-Linked Polycarbonates”

*ChemSusChem* (2015) 8 - 1034-1042

M. Taherimehr, J. P. Cardoso Costa Serta, A. W. Kleij, C. J. Whiteoak, P. P. Pescarmona

“Sustainable conversion of carbon dioxide: the advent of organocatalysis”

*Green Chem.* (2015) 17 - 1375-1389

G. Fiorani, W. Guo, A. W. Kleij\*

“Recent Advances in the Catalytic Preparation of Cyclic Organic Carbonates”

*ACS Catal.* (2015) 5 - 1353-1370

C. Martín, G. Fiorani, A. W. Kleij\*

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“Diastereo- and Enantioselective Valorization of  
Cyclic Organic Carbonates”

*ChemCatChem* (2015) 7 - 51-53

A. W. Kleij, C. J. Whiteoak