

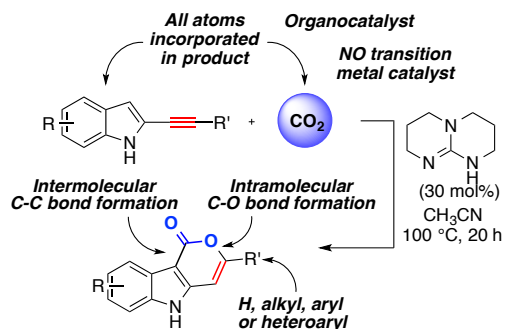
# Carbon Dioxide Activation Center 2015 - HIGHLIGHTS

## About the center

The Carbon Dioxide Activation Center (CADIAC) was established in 2015 by Prof. Troels Skrydstrup and Prof. Kim Daasbjerg at Aarhus University in collaboration with two outstanding international groups headed by Prof. Melanie Sanford at the University of Michigan, USA, and Prof. Matthias Beller at the Leibniz Institute for Catalysis, Germany. Three assistant professors, Dr. Nina Lock, Dr. Anders T. Lindhardt and Dr. Joseph Iruthayaraj are also part of the research activities. The goal of the research center is to explore new methods for the activation of carbon dioxide thereby providing smart sustainable solutions for the exploitation of this molecule as a valuable reagent to high-value chemicals of industrial importance. The highlights of published work from CADIAC for the year 2015 and start of 2016 are described below.

## Organocatalyzed Transformation of CO<sub>2</sub>

CADIAC scientists reported in *Angewandte Chemie International Edition*, the possibility of exploiting specific organobases for the promotion of a formal [4+2] cycloaddition between CO<sub>2</sub> and a 2-alkynyl indole providing access to a library of indole lactones (Figure 1). Remarkably, this reaction allows for the simultaneous formation of a carbon-carbon and a carbon-oxygen bond. The indole skeleton represents an important structural constituent in a number of natural products and pharmaceuticals displaying a wide variety of biological activities. Hence, this simple transformation, which can generate tricyclic indole derivatives in a single and mild chemical step with an inexpensive organocatalyst, will have interest for synthetic chemists working on the chemical functionalization of the indole ring system. A variety of aromatic, heteroaromatic and aliphatic 2-alkynyl indoles proved to be competent substrates for this transformation allowing for the preparation of a library of tricyclic chemical structures.



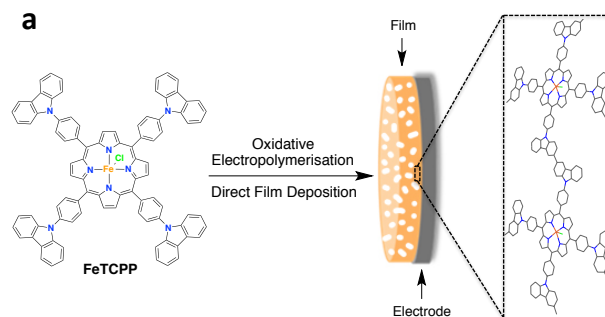
**Figure 1:** The organobase-promoted formal [4+2] cycloaddition between CO<sub>2</sub> and a 2-alkynyl indole.

## Immobilization of CO<sub>2</sub>-Reducing Catalysts

In a recent study reported in *Chemical Communications*, the CADIAC team has presented a straightforward strategy for the immobilization of iron-porphyrin catalysts inside a microporous carbon dioxide absorbing material (Figure 2). This is accomplished by carrying out an oxidative electropolymerization on glassy carbon or indium tin oxide electrodes of pendant carbazole substituents chemically linked to the catalyst itself. The iron-porphyrins have a dual function, serving both as the electrocatalyst and the mediator for the electron-hopping processes occurring across the polymer film. Hence, in general, the procedure outlined reveals great potential for the immobilization of molecular catalysts, in porous materials having a high CO<sub>2</sub> uptake capacity.

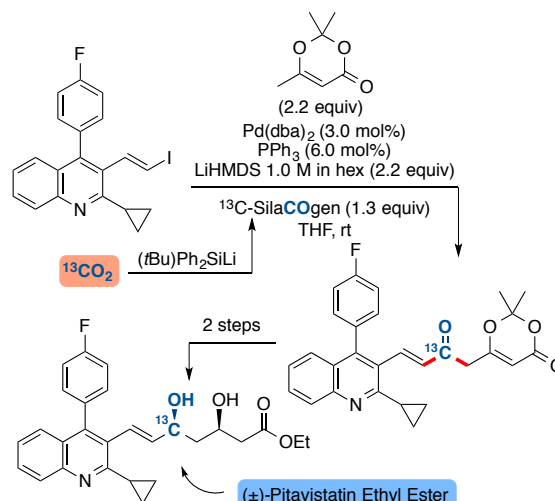
## Conversion of CO<sub>2</sub> to Pharmaceutical Compounds

CADIAC members were able to devise a new approach of taking carbon monoxide prepared from CO<sub>2</sub>, and applying this



**Figure 2:** Illustration of the film formation via oxidative electropolymerisation of the iron porphyrin catalyst, FeTCPP.

gas for the generation of a class of HMG-CoA reductase inhibitor drugs namely the statins. The work, which was published in the *Journal of the American Chemical Society* and demonstrates for the first time a palladium(0)-mediated carbonylation reaction with a new class of nucleophiles represented by vinylogous enolates (Figure 3). Particularly interesting with this synthetic approach is the ability to adapt the protocol for carbon isotope-labeling as illustrated in the synthesis of a carbon-13 labeled version of the commercially available drug, pitavastatin.



**Figure 3:** The use of <sup>13</sup>CO<sub>2</sub> for the synthesis of isotopically labeled pitavastatin.

## References

- [1] Z. Xin, C. Lescot, S. D. Friis, K. Daasbjerg, T. Skrydstrup, "Organocatalyzed CO<sub>2</sub> Trapping Using Alkynyl Indoles" *Angew. Chem. Int. Ed.* **2015**, *54*, 6862.
- [2] X. Hu, Z. Salmi, M. Lillethorp, E. B. Pedersen, M. Robert, S.U. Pedersen, T. Skrydstrup, K. Daasbjerg, "Controlled electropolymerisation of a carbazole-functionalised iron porphyrin electrocatalyst for CO<sub>2</sub> reduction" *Chem. Commun.*, Manuscript accepted for publication.
- [3] I. S. Makarov, T. Kuwahara, X. Jusseau, I. Ryu, A. T. Lindhardt, T. Skrydstrup "Palladium-Catalyzed Carbonylative Couplings of Vinylogous Enolates: Application to Statin Structures" *J. Am. Chem. Soc.* **2015**, *137*, 14043.