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Eco-Friendly Approach to Craft High-Demand Cyclic Carbonates for the Pharmaceutical Industry

Chaired by Dr. Alfredo Berzal-Herranz and Prof. Dr. Maria Emília Sousa

pharmaceuticals MDPI

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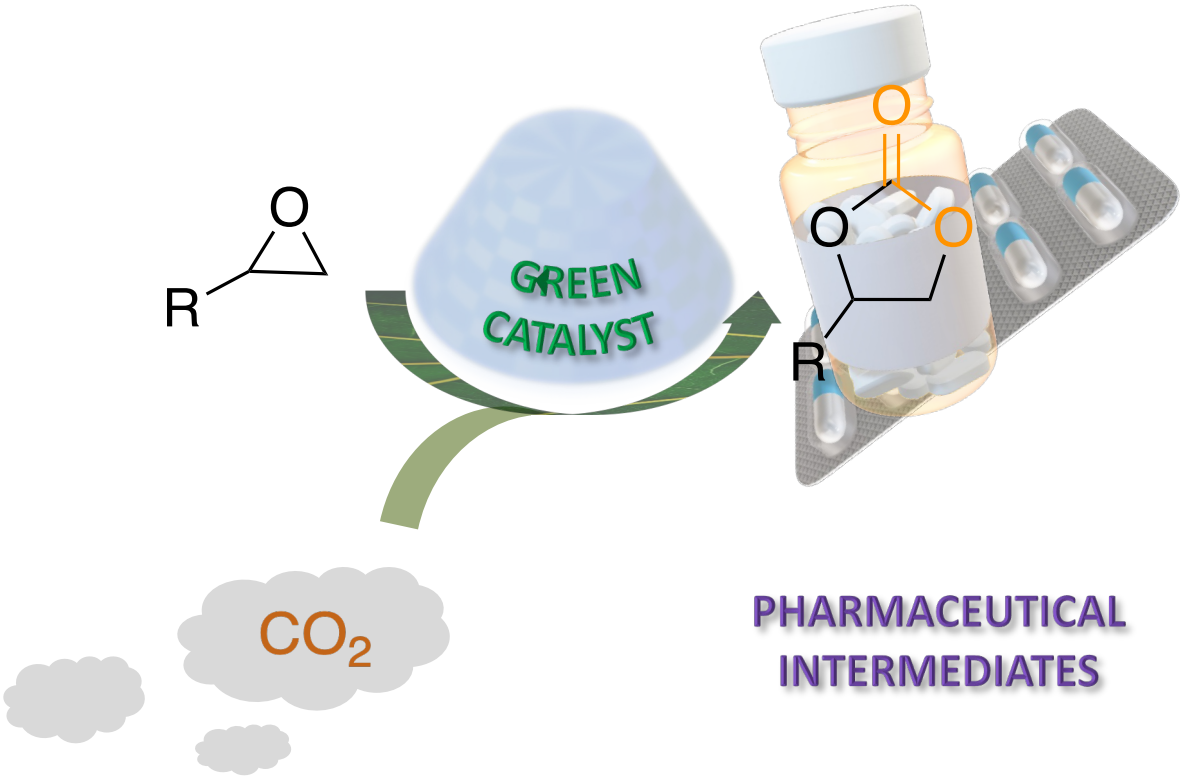
Eco-Friendly Approach to Craft High-Demand Cyclic Carbonates for the Pharmaceutical Industry



Abstract:

Cyclic carbonates play a crucial and multifaceted role in the pharmaceutical industry due to their versatile properties and applications. They are essential intermediates in synthesizing various pharmaceutical compounds, making them indispensable in drug development. With an increasing focus on sustainable and environmentally friendly practices in the pharmaceutical sector, cyclic carbonates offer a greener alternative. They can be produced using more cycloaddition reactions of carbon dioxide to substitute epoxides, which represents an eco-friendly and economically viable procedure to form cyclic carbonates compared to traditional chemical processes, aligning with the industry's sustainability goals.

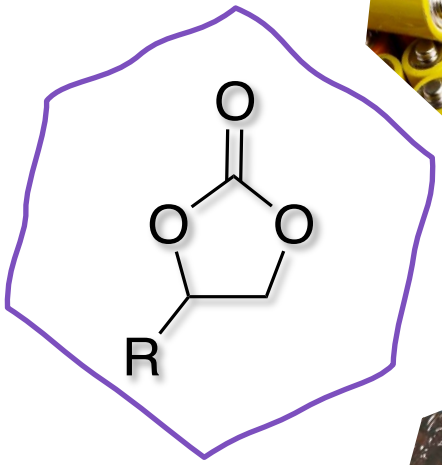
This study investigates the development of a green and efficient catalytic process for synthesizing carbonates as pharmaceutical intermediates using carbon dioxide as a reagent. The heterogeneous catalyst employed in this research was designed and synthesized based on its environmentally benign characteristics, cost-effectiveness, and catalytic efficiency. This catalyst's utilization minimizes the reaction's environmental impact and enhances the selectivity and yield of the interested products. The reaction mechanism and kinetics are elucidated to gain insight into the catalytic process. Furthermore, the production of cyclic carbonates as pharmaceutical precursors underscores its significance in synthesizing various drugs, providing a sustainable alternative to conventional methods.

This study highlights the importance of green chemistry principles in synthesizing valuable compounds like carbonates. Combining a heterogeneous catalyst with carbon dioxide as a renewable and abundant resource demonstrates the potential for sustainable chemical processes in the pharmaceutical industry.

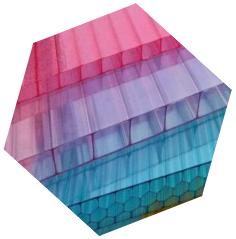
Keywords: carbon dioxide fixation; cyclic carbonate; environment-friendliness; functionalized β-cyclodextrins; solvent and metal-free catalysis; sustainability

Introduction

Versatile properties and applications of cyclic carbonates



electrolytes in lithium batteries



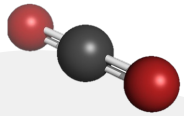
precursors for polycarbonate materials

green polar aprotic solvents

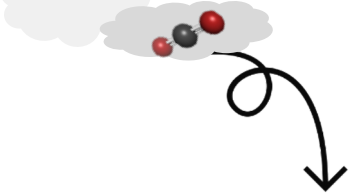
pharmaceuticals and raw materials

Synthetic methods for cyclic carbonate

- TRADITIONAL PHOSGENATION
- TRANSESTERIFICATION
- DIRECT COUPLING OF CO_2 WITH EPOXIDES
- CYCLOADDITION OF CO_2 TO EPOXIDE



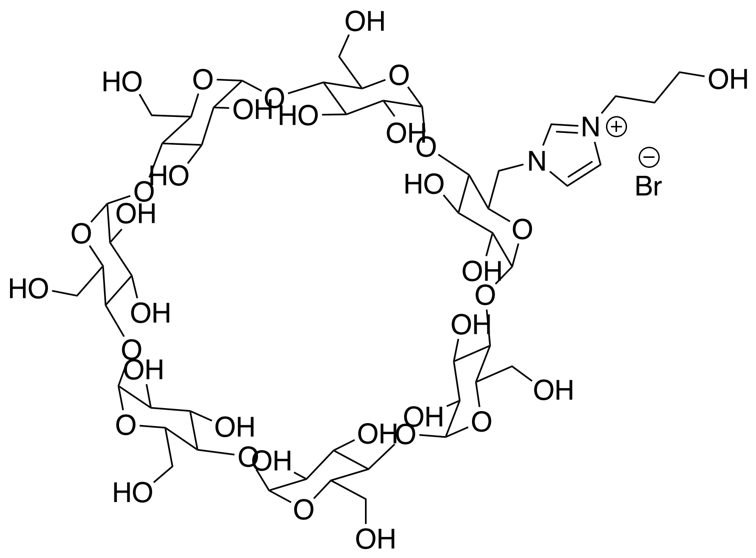
CO_2 capture is a key part of managing carbon resources and reducing carbon emissions



Due to the thermodynamic and kinetic stability of CO_2, catalysts and solvents are required to accelerate its chemical conversion.
Among them **Ionic liquids** are the most commonly employed catalysts.

Results and discussion

We designed a **new one-component eco-friendly catalyst** that utilizes the OH groups of *β*-CD as hydrogen bond donors for epoxide activation and the halide ion of imidazolium bromide to promote the ring opening.

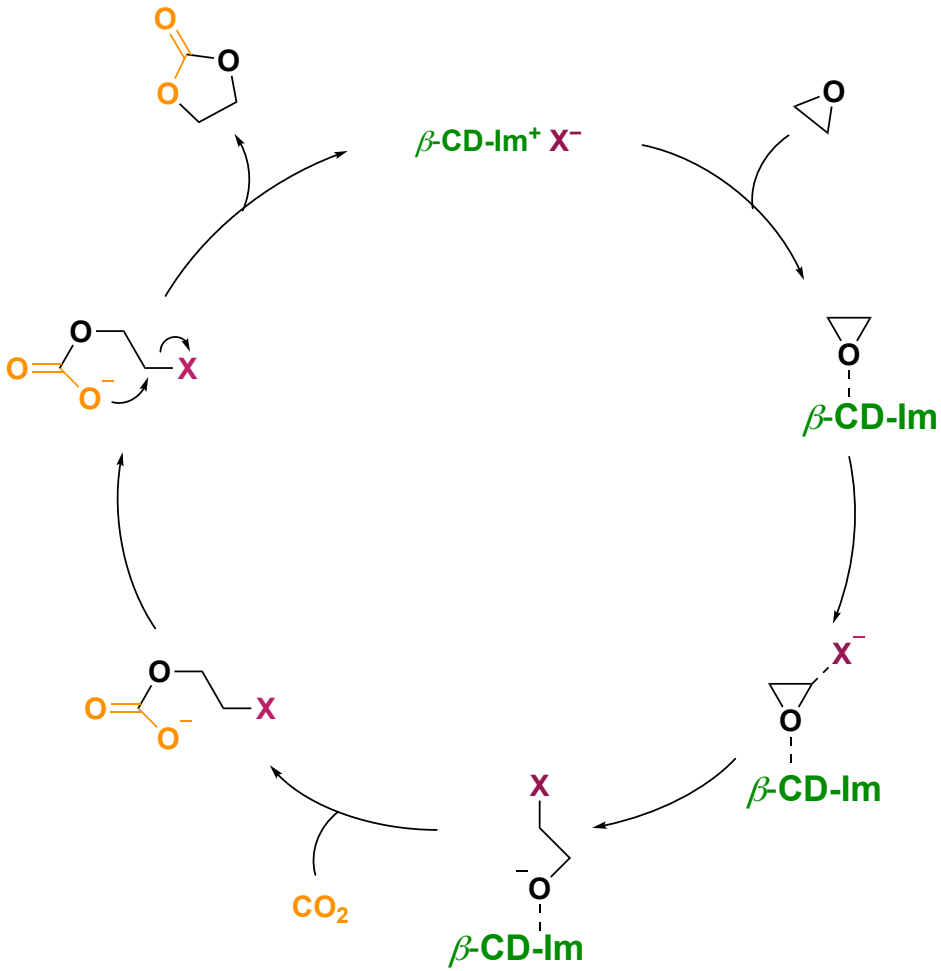


β-CD-Im$^+$Br$^-$

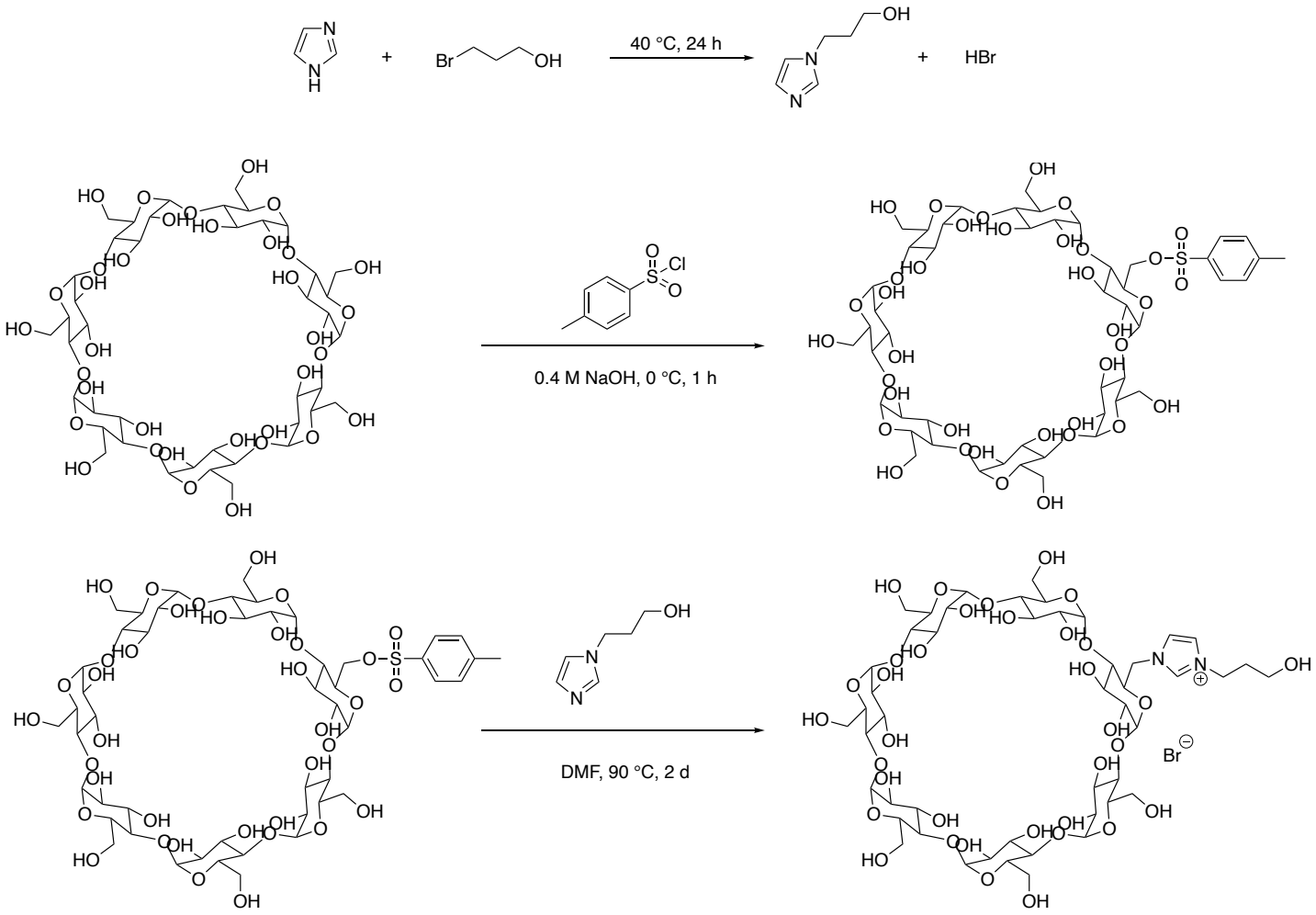
The advatages of the catalyst are:

- recoverable
- low cost
- easily prepared
- high catalytic efficiency

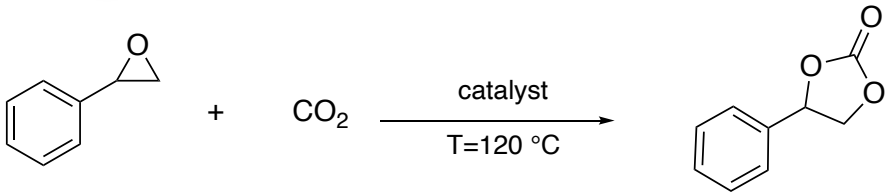
Proposed mechanism of β-CD-Im⁺Br⁻ catalytic cycle



Synthesis of β-CD-Im$^+$Br$^-$ catalyst

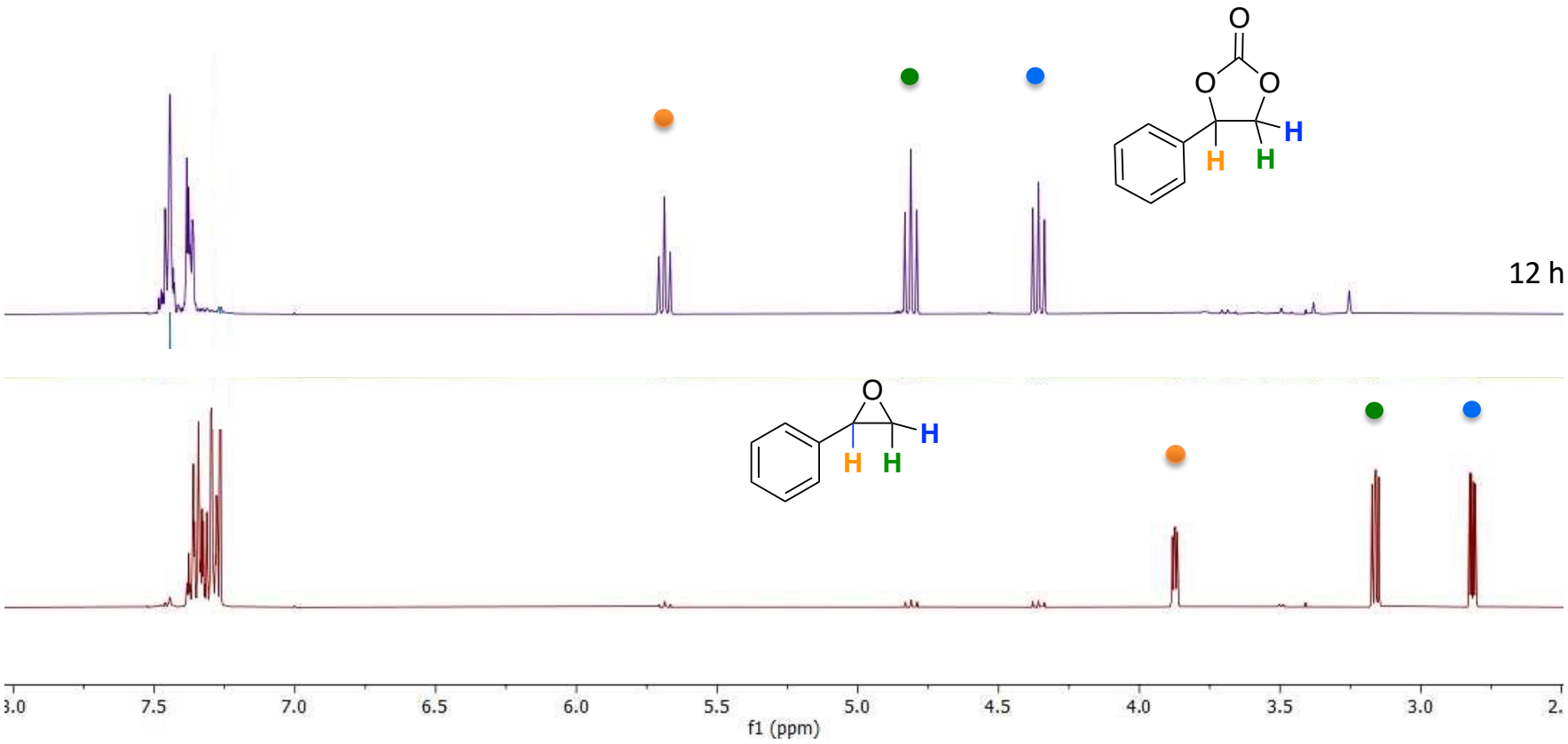


Catalyst screening for the cycloaddition of styrene oxide with CO_2

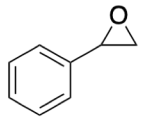
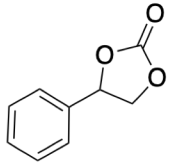
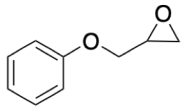
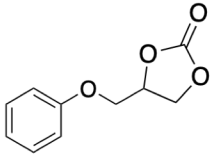
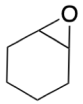
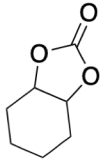
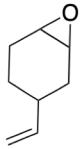
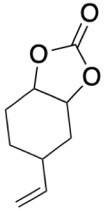


β-CD-Im⁺	
Temperature (°C)	**Conversion (%)**
40	0
60	15
80	44
100	68
120	99

β-CD-Im⁺	
Time (h)	**Conversion (%)**
1	45
3	45
6	73
12	96


12 h
f1 (ppm)

Synthesis of carbonates from CO_2 and various epoxides

Epoxide	Carbonate	Yield (%)
		99
		95
		71
		38

Conclusions

- A new eco-friendly cyclodextrin-based catalyst (β-CD-Im^{+}Br^{-}) was successfully synthesized and used to catalyze the fixation of CO_2 into epoxides to produce cyclic carbonates.
- All synthetic steps were performed with non-toxic, environmentally safe, and low-cost reagents.
- The catalytic reaction in a solvent-free environment significantly diminished its ecological footprint while demonstrating outstanding conversion rates into the desired carbonates.

Future perspective

Directly incorporate the obtained carbonates into a synthesis of intermediates and pharmaceuticals.