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Reductive and Non-Reductive CO₂ Valorization strategies: development of integrated processes in Sustainable Chemistry.

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strategies: development of integrated processes in
Sustainable Chemistry.**

List of Abbreviations

AE	Atom Economy
AFM	Atomic Force Microscopy
APIs	Active Pharmaceutical Ingredients
AsTC	Assisted-Tandem Catalysis
ATRP	Atom Transfer Radical Polymerizations
AuTC	Auto-Tandem Catalysis
BET	Back Electron Transfer
BHMF	bis(hydroxymethyl)furan
BHTHF	2,5-bis(hydroxymethyl)tetrahydrofuran
BPR	Back Pressure Regulator
CAT	Catecholate
CCU	Carbon Capture and Utilization
CDs	Carbon Dots
CF	Continuous Flow
CHC	Cyclohexene Carbonate
CHO	Cyclohexene Oxide
COCs	Cyclic Organic Carbonates
CU	CO ₂ utilization
CV	Check-Valve
DBU	1,5-Diazabicyclo[5.4.0]undec-7-ene
DMC	Dimethylcarbonate
DMF	2,5-dimethylfuran
DOC	Direct Oxidative Carbonation
EC	Ethylene Carbonate
ET	Electron Transfer
EY	Eosin Y
FDCA	2,5-furandicarboxylic acid

FFC	Furan-2,5-dicarbaldehyde
FT-IR	Fourier Transform Infrared Spectroscopy
GC	Green Chemistry
GC-FID	Gas Chromatography – Flame Ionization Detector
GC-MS	Gas Chromatography – Mass Spectroscopy
GPC	Gel Permeation Chromatography
GSK	GlaxoSmithKline
GUI	Graphical User Interface
HAT	Hydrogen-Atom Transfer
HBD	Hydrogen Bond Donor
HC	Hexane Carbonate
HE	1,2-epoxyhexane
HEBIB	2-hydroxyethyl-2-bromo-2-methylpropanoate
HMC	Hydrogen methylcarbonate
HMF	5-hydroxymethylfurfural
HOMO	Highest Occupied Molecular Orbital
HPLC	High Pressure Liquid Chromatography
HYD	Hydroquinolate
ICP	Inductively Coupled Plasma
ICP-AES	Inductively Coupled Plasma–Atomic Emission Spectroscopy
ILs	Ionic Liquids
ISC	Intersystem Crossing
LCA	Life Cycle Assessment
LED	Light Emitting Diode
LUMO	Lowest Unoccupied Molecular Orbital
MEK	Methyl Ethyl Ketone
MES	Mesitylene
METAC	[2-(methacryloyloxy)ethyl]trimethylammonium chloride

MFCs	Mass Flow Controllers
MLCT	Metal-to-Ligand Charge Transfer
MOFs	Metal Organic Framework
Mo-ILs	Molybdate Ionic Liquids
MW	Molecular weight
NHC	<i>N</i> -Heterocyclic Carbene
NMR	Nuclear Magnetic Resonance
OBMF	5,5'-oxy(bismethylene)-2-furaldehyde
OBMF-H	5,5'-oxybis(methylene)bis(furan-5,2-diyl)dimethanol
OTC	Orthogonal-Tandem Catalysis
PC	Photocatalyst
PCHC	Poly(cyclohexenecarbonate)
PET	Photoinduced Electron Transfer
PID	Proportional–Integral–Derivative
PMDTA	<i>N, N, N', N'', N''</i> -pentamethyldiethylenetriamine
PO	Propylene oxide
POMs	Polyoxometalates
PTC	Phase Transfer Catalyst
QPS	Quaternary Phosphonium Salts
RES	Resorcinolate
RWGS	Reverse Water Gas Shift
S ₁	Singlet Excited State
SC	Styrene carbonate
scCO ₂	Supercritical CO ₂
SDGs	Sustainable Development Goals
SEM	Scanning Electron Microscopy
SET	Single Electron Transfer
SO	Styrene oxide

SV	Switch valve
T ₁	Triplet Excited State
TA	Tannic acid
TBAB	Tetrabutylammonium bromide
TBAI	Tetrabutylammonium iodide
TBHP	<i>Tert</i> -butyl hydroperoxide
TEA	Triethylamine
TEAB	Tetraethylammonium bromide
TEM	Transmission Electron Microscopy
TEMPO	(2,2,6,6-Tetramethylpiperidin-1-yl)oxyl
TGA	Thermogravimetric analysis
TOA	Trioctylamine
TON	Turnover number
UN	United Nations
UV	Ultraviolet
XPS	X-ray Photoelectron Spectroscopy

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1. General Introduction

1.1 Green Chemistry

“Green chemistry is the design of chemical products and processes that reduce or eliminate the use or generation of hazardous substances. Green chemistry applies across the life cycle of a chemical product, including its design, manufacture, use, and ultimate disposal. Green chemistry is also known as sustainable chemistry.”¹

The innovative idea of developing alternative synthetic pathways to mitigate environmental hazards and pollution commonly associated to traditional chemical processes, was first introduced by Paul Anastas and Roger Garrett in 1991. Joe Breen later coined the term “green chemistry” (**GC**) to define this innovative approach.² The idea of **GC** became more effective with the definition of the “12 principles” (**Figure 1.1**), which were designed by Paul Anastas and John Warner to guide chemists aiming at increasing the sustainability of synthetic and/or purification processes.¹ Since then, **GC** has emerged as a critical discipline aimed at reducing the environmental and human health impacts of chemical processes and products. Focusing on the design of chemical products and processes that minimize the use and generation of hazardous substances, **GC** is transforming industries such as pharmaceuticals, agriculture, and energy.^{3,4}



Figure 1.1: 12 principles of green chemistry.

The principles of **GC** applied to green synthesis should lead to processes characterized by:⁴

- a) Efficient use of raw materials, especially 100% recycled solvents, optimizing the synthetic process by reducing unnecessary waste.^{5,6}
- b) Utilization of self-degrading biobased building blocks.⁷
- c) Design of new synthetic procedures where all the process input materials are incorporated into the final product; this means a theoretical 100% atom economy for the process.^{8,9}
- d) Use of greener, safer raw materials as solvents, such as water,^{10,11} and enzymes as biocatalysts,^{12,13} to produce low-toxicity substances with minimal impact on human health and on the environment.^{14,15}
- e) Development of multicomponent reactions,^{16–18} and one-pot cascade synthesis,^{19–21} lowering the number of reaction steps, simplifying active pharmaceutical ingredients (**APIs**) purification, and ultimately reducing waste while enhancing atom economy and efficiency.
- f) Adoption of continuous processing/engineering is crucial for rapid reaction screening and optimization in green synthesis.^{22–24} In-line reaction analysis, coupled with improved automation and modernized hybrid equipment, enhance reactor productivity and produce purer products.^{25,26} Continuous processing techniques reduce raw material and energy consumption while enabling real-time analysis, control, and improved safety. Additionally, flow chemistry can be used to efficiently explore multidimensional reaction spaces, enhancing reaction design and process efficiency.²⁴ Flow-screening platforms are also vital for scaling up processes with time and material efficiency, making flow chemistry a key area for future exploration in green synthesis.^{24,27}
- g) If waste is produced, it should undergo appropriate treatment and disposal to mitigate and eliminate its major toxic effects before final handling.^{28,29}

Additionally, Campos *et al.* reported that machine-learning techniques can be applied to the optimization of complex, pharmaceutically relevant catalytic approach. For example, prediction of the performance of Buchwald–Hartwig amination reaction was performed with a multivariable approach, combining reaction pathway prediction, catalyst preparation to control cycloisomerization reaction, optimization of ligands with enhanced selectivity and rate over the existing ligand and forward reaction prediction.³⁰ Therefore, extending *in silico* approaches to biobased transformations and materials represents the future of green synthesis through **GC**, accelerating the design of next generation green catalysts, and improving both molecular editing and molecular design for reduced hazard.³¹

A recent report projected significant growth in the global **GC** market, which reached \$98.5 billion by the end of 2020 and continues its rapid expansion.³² Sustainability has increasingly become a key pillar of policymaking and is constantly gaining importance in the development of industrial strategies, becoming deeply integrated into the frameworks that guide social interventions and influence behavior. One of the most well-known initiatives is the 2030 Agenda for Sustainable Development, adopted by all United Nations (**UN**) Member States in 2015. This plan offers a common vision for achieving peace and prosperity for both people and planet Earth. The core of the 2030 Agenda relies on the definition of 17 Sustainable Development Goals (**SDGs**), summarized in **Figure 1.2**, which represent a global call to action for all nations to collaborate. The central idea of **SDGs** is to propose accessible, practical societal and economical solutions, *e.g.* improving health and education, reducing inequalities, spurring economic growth while tackling global environmental challenges, such as climate change and preservation of oceans and forests. **SDGs** overarching goal is the development of a 'sustainable well-being', which must be equitably shared both within and among nations, and is interdependent with the well-being of the rest of nature.³³



*Figure 1.2: Sustainable Development Goals (SDGs) of the 2030 Agenda for Sustainable Development from the United Nations.*³³

Increasing the sustainability of chemical processes from lab scale to complete industrialization, crosses many of the **SDGs**. Notably, implementation of **GC** practices is a key factor in reducing the amount of chemical waste released into the environment, contributing to its increasing market value. For example, the production of raw materials, intermediates, and **APIs** in the pharmaceutical industry generates significant waste, including hazardous byproducts such as contaminated solvents, reagents, and toxic gases.^{34,35} Compared to oil refining and bulk or fine chemical industries, pharmaceutical manufacturing produces considerably more waste per unit of product. However, pharmaceutical products are far more complex, often orders of magnitude more intricate, than the

outputs of the chemical or petroleum sectors, adding to the challenge of minimizing waste and improving sustainability.^{34,35}

In this context, green metrics provide essential tools to evaluate and enhance the sustainability of chemical processes. Key metrics include the **E-Factor**, introduced by Roger Sheldon in 1992, providing an easy estimation of resource efficiency in chemical manufacture by measuring the mass of waste per unit of product (calculated as described in Equation 1, **Figure 1.3**), while the **Atom Economy (AE)**, Equation 2, **Figure 1.3**, quantifies the proportion of atoms from the reagents that contribute to the product's molecular structure.^{8,35} **Reaction Mass Efficiency (RME)**, Equation 3, **Figure 1.3** combines atom economy and yield, emphasizing how effectively reagents are converted into the final product, while **Process Mass Intensity (PMI)**, Equation 4 of **Figure 1.3** evaluates the total material input relative to the product output. It is important to emphasize that these metrics provide an overall perspective on the sustainability of a process, focusing primarily on material consumption. However, they do not take into account other critical parameters, such as energy consumption, toxicity of materials (including solvents and reagents), or associated costs.

$$E\ Factor = \frac{\text{mass of total waste}}{\text{mass of product}} \quad (\text{Eq. 1})$$

$$AE = \frac{\text{molecular weight of product}}{\text{total molecular weight of reactants}} \quad (\text{Eq. 2})$$

$$RME = \frac{\text{mass of isolated product}}{\text{total mass of reactants}} \quad (\text{Eq. 3})$$

$$PMI = \frac{\text{total mass used in a process or process step}}{\text{mass of product}} \quad (\text{Eq. 4})$$

Figure 1.3: Mass-Based Metrics for measuring greenness.

GlaxoSmithKline (GSK) reported a life cycle analysis of APIs, revealing that 80% of their production process waste is represented by solvents.³⁶ Therefore, for the pharmaceutical industry significant improvements of processes sustainability could stem from solvent selection, recovery, recycling, and regulated disposal: these combined strategies could significantly reduce environmental hazards and toxicity in the environment.¹⁰ In practice, this increasing awareness could be combined with **GC** tools, contributing in developing multiple emerging areas of research, including the development of green solvents,^{37–39} water,^{11,40,41} and solventless or no-media-involved reactions,^{42,43} as well as reaction media in the form of aqueous biphasic catalysis.⁴⁴ As a result, traditional drug synthesis routes are evolving through the adoption of green solvents.⁴⁵ Additionally, bio-based building blocks from renewable resources are emerging as sustainable alternatives to petrochemical-derived solvents.^{12,13} Moreover, to align with **GC** principles, scientists are also developing novel synthetic strategies with an improved sustainability profile, exploring advanced reaction mechanisms,

including C–H activation, metal-catalyzed cross-coupling, alcohol activation for nucleophilic displacement, use of biocatalysis and organocatalysis, *etc. etc.*^{46–50}

1.2 CO₂ Utilization

The emissions of CO₂ from anthropic activities amounted to ca. 36.8 GtCO₂ in 2023, 85% of which was generated from burning fossil fuels such as coal, oil, and natural gas for energy, electricity production, transportation, and industrial activities (**Figure 1.4**).⁵¹

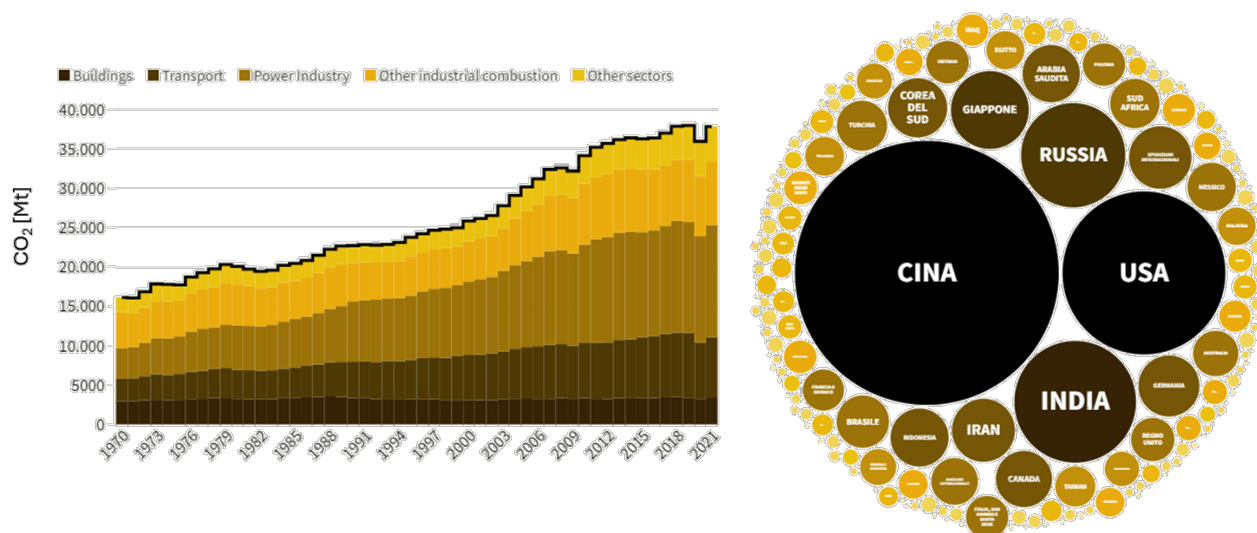


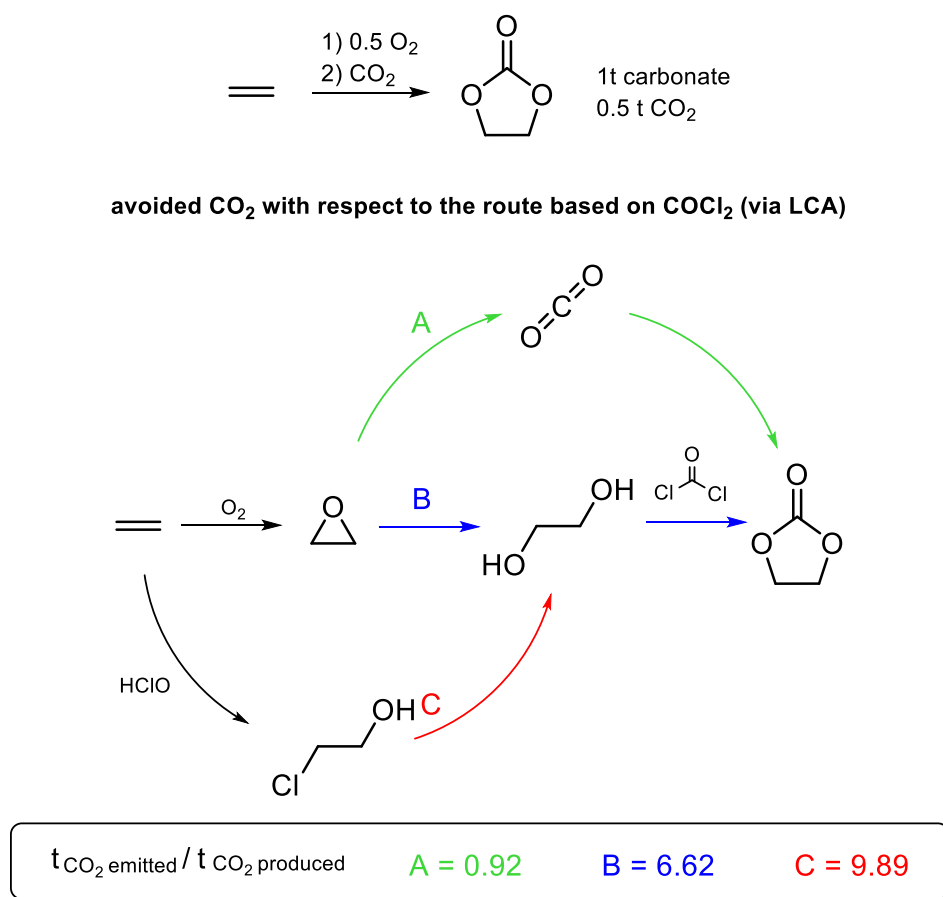
Figure 1.4: Trend over time of CO₂ emissions by sector (left); CO₂ emissions by country (right).⁵²

CO₂ utilization (**CU**) is gaining increasing attention because it can either contribute to carbon cycling (similarly to how Nature creates molecular complexity from atmospheric CO₂) or help reduce the impact of climate change by replacing more harmful chemicals (such as: COCl₂, HCN etc.). **CU** can be classified into four main categories: **i)** chemical production (*e.g.* urea, salicylic acid, HCOOH, organic carbonates, etc. etc.); **ii)** fuel production (CH₃OH or CH₄); **iii)** enhanced biological processes (CO₂ reduction with enzymes); **iv)** technological uses that may not require CO₂ conversion (oil recovery with scCO₂).⁵³

The natural carbon cycle handles yearly over 750 Gt of CO but cannot absorb the additional 36.8 Gt/y generated from anthropogenic activity, even though it represents only 5% of the total employed in the carbon cycle. The resulting accumulation of CO₂ in the atmosphere, amplifies the greenhouse effect and probably contributes to the global temperature rise. Although direct evidence of this relationship is still debated, the concurrent increase of global population, energy consumption, CO₂ emissions, and atmospheric CO₂ levels strongly suggest a connection.⁵³ Therefore, reducing CO₂ emissions is critical to avoid reaching irreversible climate "no-return points". The target should be "avoiding CO₂" emissions rather than merely "using CO₂", meaning that new CO₂-based synthetic processes must emit less CO₂ than current fossil-based methods.⁵³

Currently, life cycle assessment (**LCA**) methodology is the only tool that can effectively quantify the environmental benefits of CO₂-based synthetic processes, including both "used" and "avoided" CO₂,

and quantitatively measure the overall environmental impact reduction. A useful example is the production of ethylene or ethene carbonate (**EC**), which can be obtained through various industrially relevant synthetic methods, summarized in **Scheme 1.1**. Traditional synthetic routes (routes **B** and **C**, **Scheme 1.1**) use phosgene (COCl_2), a highly reactive and extremely toxic compound, generating over stoichiometric quantities of harmful by-products, *e.g.* chlorinated salts. Due to these drawbacks, phosgene is banned from industrial use in many countries and can only be used in research contexts under strict operational protocols. By contrast, alternative processes based on CO_2 were developed, consuming only 0.5 t of CO_2 (t_{CO_2}) per t of **EC** (t_{EC}) produced (route **A**, **Scheme 1.1**).⁵³ LCA calculations show that route **A** emits only 0.92 $t_{\text{CO}_2}/t_{\text{EC}}$, significantly less than routes **B** and **C**, emitting 6.62 and 9.89 $t_{\text{CO}_2}/t_{\text{EC}}$, respectively. Thus, for every ton of **EC** produced via route **A**, 0.5 tons of CO_2 are released, while with phosgene-based methods, 5.70 or 8.94 tons of CO_2 are released for route **B** and route **C**, respectively. This highlights the importance of reducing both direct and indirect CO_2 emissions in new synthetic technologies. Moreover, using CO_2 should also lower the E-factor, meaning less waste is generated compared to the product, by promoting more efficient, less carbon- and energy-intensive processes.⁵³



*Scheme 1.1: Used and avoided CO_2 in the synthesis of ethene carbonate, **EC**. Per each t of **EC** 0.5 t_{CO_2} are used following route **A**, which avoids the combined release of 5.5 and 8.97 t_{CO_2} measure for phosgene based **EC** synthetic routes (route **B** + route **C**).*

From a sustainability point of view, CO₂ release is minimized by developing synthetic processes that:

- utilize simple catalytic systems that are easily recovered and reused for multiple cycles;
- exhibit high substrate conversion rates, high turnover number (**TON**), with excellent selectivity and minimal waste generation (both by-products and solvents);
- avoid the use of toxic reagents;
- operate under mild conditions, such as low temperatures and pressures.

In essence, CO₂ valorization processes should aim at minimizing the associated carbon footprint, material consumption, and energy intensity, aligning with various goals of **UN Agenda 2030**. These include Goal 7 (advancing renewable energy and efficiency), Goal 9 (adopting green technologies in industry), Goal 11 (developing sustainable cities with low-emission transport), Goal 12 (promoting responsible production and consumption), Goal 13 (taking climate action to mitigate global warming) and Goal 15 (enhancing reforestation to absorb CO₂).³³

CO₂ is a well-known stable molecule ($\Delta G_f^\circ = -396\text{ kJ/mol}$, see **Figure 1.5**) and its reactivity could be divided into two main categories. The first involves low-energy, non-reductive transformations where the carbon atom retains its + 4 oxidation state. Examples of such reactivity include the synthesis of carbamates, linear and cyclic organic carbonates (linear and cyclic), ureas, and polymers like polycarbonates and polyurethanes, along with inorganic carbonates and hydrogen carbonates.

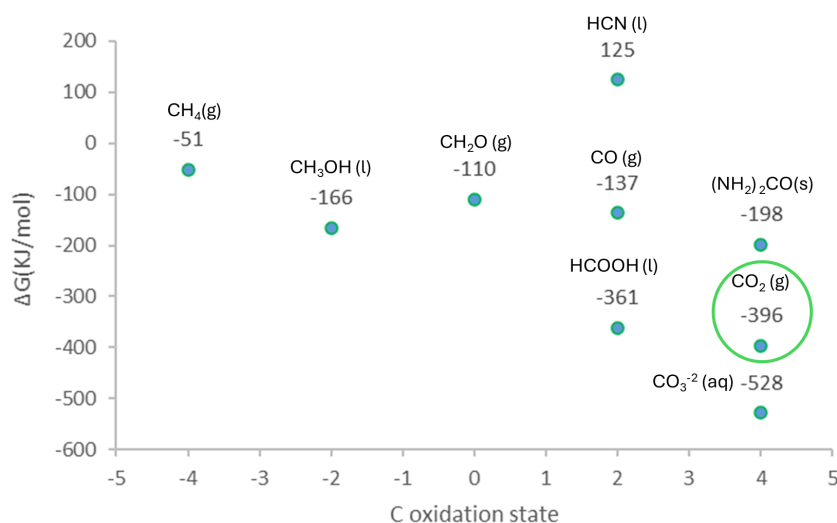


Figure 1.5: Free energy of formation of C¹ species versus the oxidation state of carbon.

The second category involves high-energy, reductive transformations, where the CO₂ carbon oxidation state drops to + 2 or lower, synthesizing different CO₂ reduction products, such as formic acid (HCOOH), carbon monoxide (CO), formaldehyde (H₂CO), methanol (CH₃OH), methane (CH₄), and hydrocarbons. This latter class of reactions requires an external energy source, which can come in the form of electrons (electrochemical reduction), hydrogen, metals, radiation, or heat.

These two categories correspond roughly to the synthesis of a) chemicals, occurring for non-reductive CO₂ transformations and b) fuels, obtained upon reductive CO₂ valorization, with the fuel

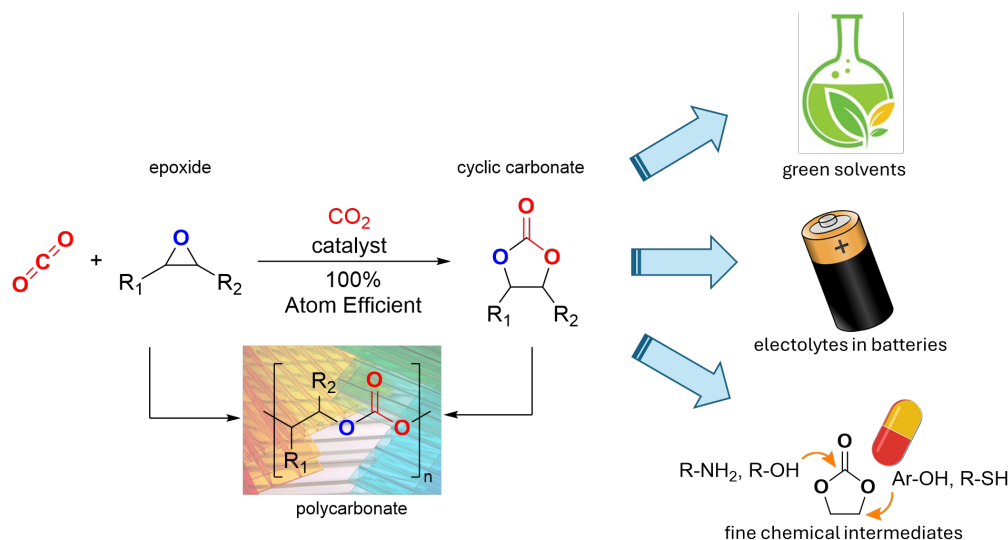
1.3 Cyclic Organic Carbonates (COCs)

[illegible]

One of the most extensively studied reactions in chemical valorization of CO₂ is the formation of cyclic organic carbonates (**COCs**),^{55–61} alongside related processes, like the production of linear carbonates and poly(carbonates).^{62–64} Traditional processes, developed before 1980, which relied on stoichiometric phosgenation of methanol, have been progressively phased out globally due to the severe toxicity and safety reasons.⁶⁵

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synthesis, with an increasing focus on development of more advanced synthetic intermediates. This has led to the creation of novel catalytic processes characterized by enhanced reactivity, improved enantio- and regioselectivity, and broader substrate compatibility, with excellent tolerance for functional groups.^{72,73} Ultimately, these advancements pave the way for secondary products derived from **COCs** intermediates, which hold promise for applications in (bio)polymer synthesis,⁶⁸ and pharmaceuticals.⁶⁷



*Scheme 1.2: **COCs** synthesis starting from CO₂ and epoxides (left), and selected applications of **COCs** (right).*

The main CO₂ based synthetic route to produce **COCs** is represented by CO₂ insertion into strained heterocycles, such as oxiranes and oxetanes. Oxiranes, or epoxides, are three-membered cyclic ethers widely utilized in organic synthesis, especially in polymer production and as intermediates in chemical manufacturing. The primary industrial process for epoxides preparation is epoxidation of alkenes, traditionally accomplished through non-catalytic chlorination processes, co-epoxidation, or catalytic methods employing peroxides and peracids.⁶⁹ The reactivity of epoxides in CO₂ insertion reactions to form **COCs** is influenced by several structural and electronic factors, including the type of substituents on the epoxide ring, ring strain, and steric effects.⁷⁰ Typically, less-substituted and more strained epoxides exhibit greater reactivity in CO₂ insertion reactions due to reduced steric hindrance and increased ring strain, while epoxides with bulky or electron-donating groups tend to react more slowly. In comparison, oxetanes present greater challenges as substrates for direct CO₂ coupling reactions due to their inherently lower reactivity. This difference does not stem from variations in ring strain energy released upon ring-opening, as these values are fairly similar between oxetanes and epoxides.⁷¹ Furthermore, six-membered COC products are characterized by lower thermal stabilities compared to five-membered COCs.⁷⁰

Effective catalytic systems are essential for the direct coupling of CO₂ with oxiranes or oxetanes, as catalyst-free reactions are kinetically unfavorable due to the high energy barriers involved. For example, DFT calculations revealed that the free energy barriers for the uncatalyzed reaction between propylene oxide and CO₂ in gas phase is up to 58 kcal·mol⁻¹.⁷⁰

Numerous catalytic metal-based and/or organocatalytic systems have been applied to CO₂ insertion reaction to date,^{70,72–76} with homogeneous metal-based complexes catalysis remaining the most efficient. Examples of the most commonly employed metal- and organo-based homogenous catalysts employed in CO₂ insertion reactions are summarized in **Figure 1.7**.

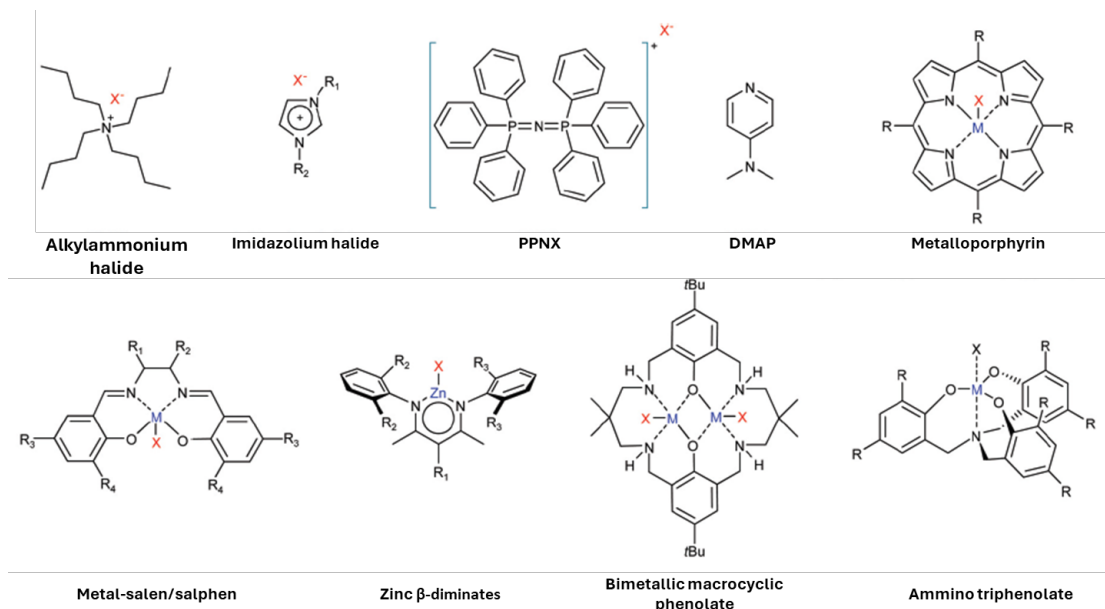
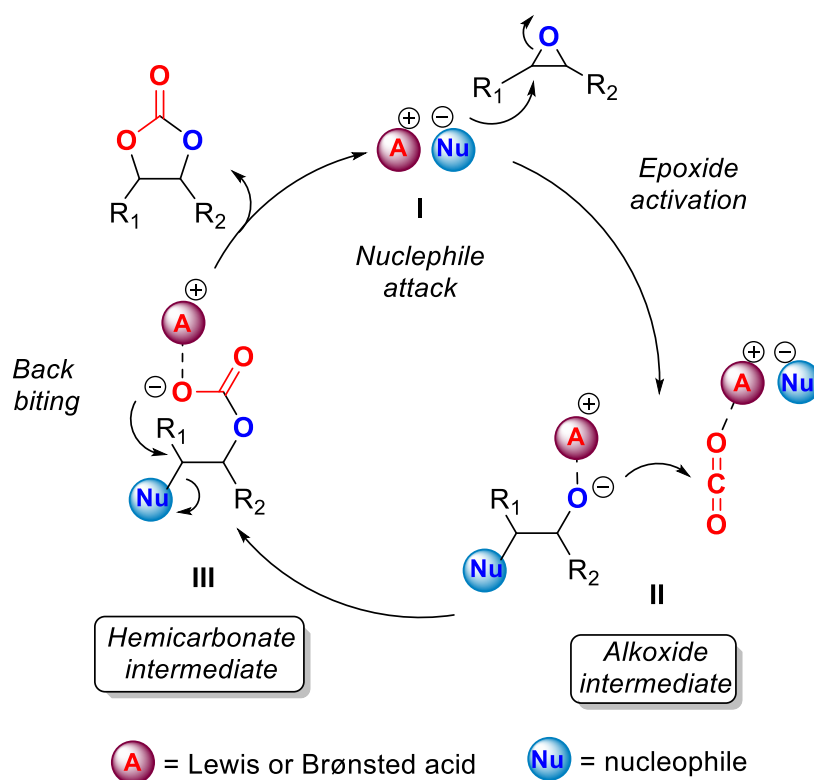


Figure 1.7: homogeneous metal- and organocatalysts for the CO₂ insertion reaction on epoxides.⁷⁵

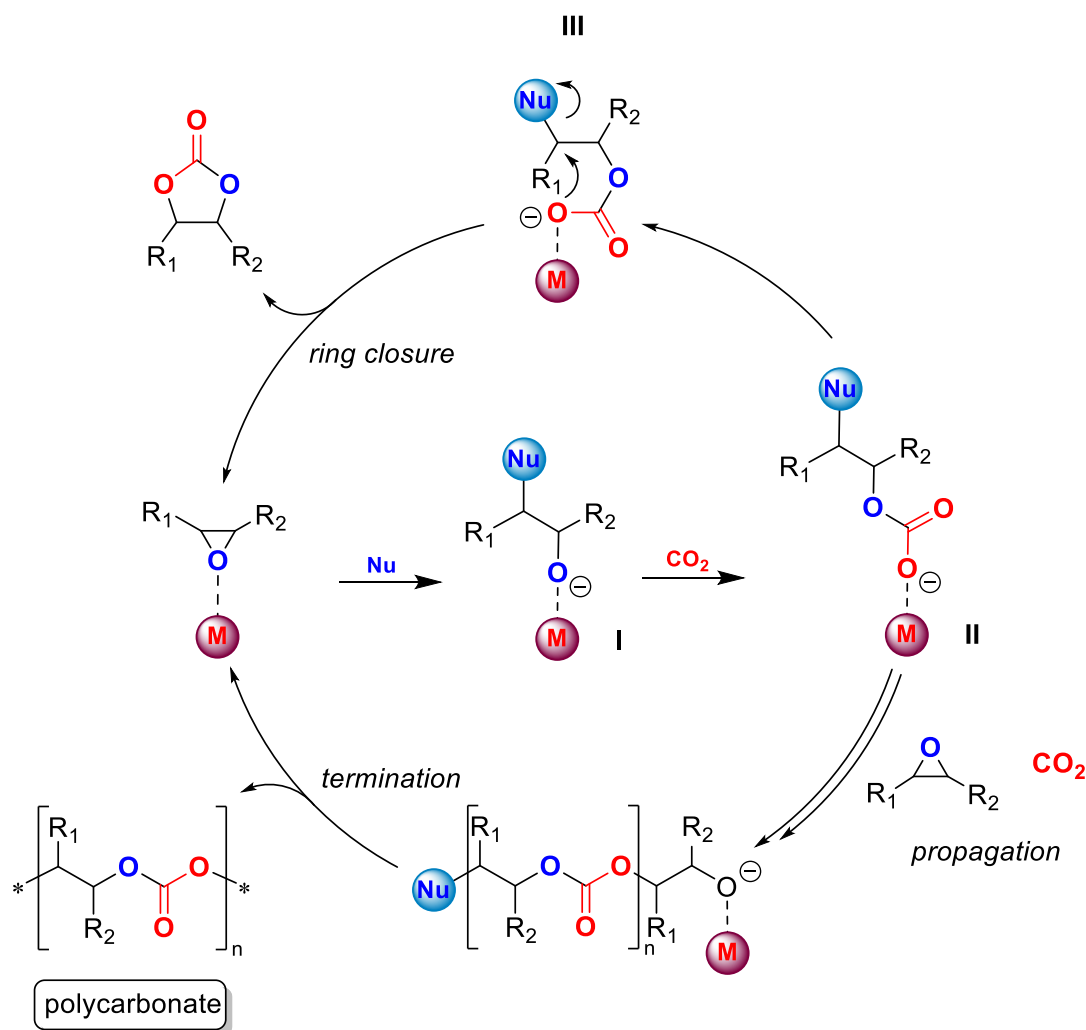
Several mechanisms have been proposed to explain this reactivity as detailed in the following paragraphs. As depicted in **Scheme 1.3**, the generally accepted mechanism for **COCs** synthesis upon CO₂ insertion reactions includes two catalytically active moieties: an electrophile, typically a Lewis or Brønsted acid (A⁺), which activates the epoxide (**I**, **Scheme 1.3**), and a nucleophile (Nu[−]), which plays a dual role by initially promoting epoxide ring opening and stabilizing the formation of both alkoxide (**II**, **Scheme 1.3**) and hemicarbonat (**III**, **Scheme 1.3**) intermediates, while acting as a good leaving group in the final ring closing step. Usually A⁺ is an onium cation, a metal-based Lewis acid (*e.g.* Fe, Cr, Co, Al, and Sn),⁷⁷ or a species with H-bonding ability (*e.g.* −OH, −COOH, and −NH groups),⁷⁸ while Nu[−] is a halide salt, typically a bromide or iodide salt with organic counteranions.⁶⁰



Scheme 1.3: General mechanism for CO₂ insertion into an epoxide.

Recently, the development of halide-free CO₂ insertion protocols and the use of bio-based materials for CO₂ valorization have become active and exciting areas of research and will be discussed in more detail in **Chapter 3**.^{76,79–86}

The selectivity of this reaction is highly influenced by the characteristics of the catalytic system, as well as other factors, including substrate type and reaction conditions, in particular temperature and CO₂ pressure.^{55,62,87,88} The chemoselectivity of the catalytic system depends on a fine balance between the nucleophile's leaving group ability and its molar ratio to the Lewis acid site. Nucleophiles characterized by a good leaving ability, *e.g.* halides, promote selective **COCs** formation, while poor ones (*e.g.* Cl⁻, 2,4-dinitrophenoxide anion) promote multiple CO₂/epoxide insertion and formation of the polycarbonate product.⁵⁵ A/Nu ratio ≥ 1 typically leads to **COCs** formation, whereas for A/Nu < 1 polycarbonate production is favored, as depicted in **Scheme 1.4**.⁸⁹



Scheme 1.4: Mechanism for the catalytic coupling reaction of CO₂ and epoxide, involving a common initial epoxide activation step, followed by nucleophilic attack and ring opening: formation of the **COC** product occurs via intramolecular cyclization of the hemicarbonate intermediate (top), while consecutive multiple CO₂/epoxide insertions lead to the formation of the corresponding polycarbonate via propagation.

The type of epoxide also directly influences whether cyclic or polymeric carbonates are formed (**Figure 1.8**). For example, cyclohexene oxide (**CHO**), an alicyclic disubstituted epoxide, tends to favor polycarbonate formation due to the geometric strain caused by the two connected rings in cyclohexene carbonate, while terminal aliphatic monosubstituted epoxides, *e.g.* propylene oxide, **PO**, lead to the preferential formation of **COCs**.^{64,90} Interestingly, formation of the **COC** product is favored with monosubstituted styrene oxide (**SO**) because the electron-withdrawing effect of the phenyl group, promoting intramolecular ring closure.⁵⁵

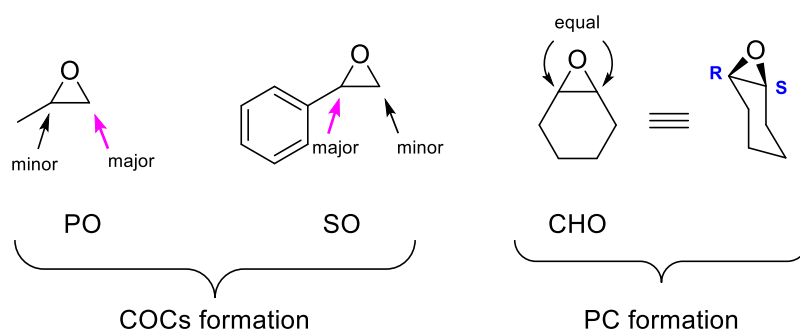
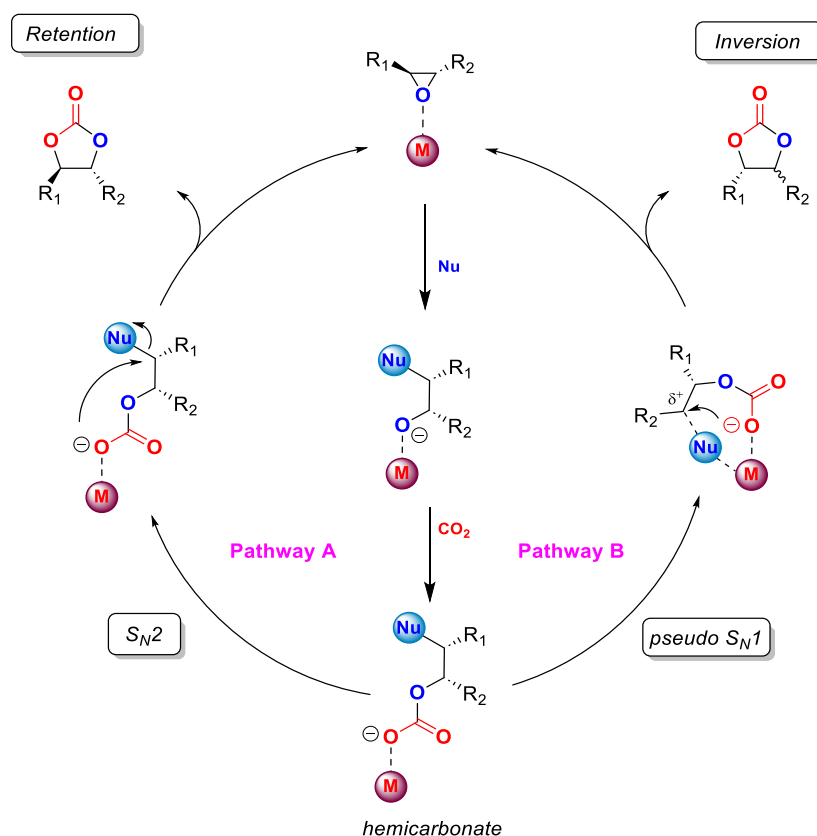


Figure 1.8: Most probable positions for the nucleophilic attack on different epoxides.

Variation of reaction conditions, in particular reaction temperature and CO₂ pressure, affect product yield and chemoselectivity between polycarbonates and **COCs**. Higher temperatures ($T > 100\text{ }^{\circ}\text{C}$) generally increase epoxide conversion and formation of the **COC** thermodynamic product. Conversely, polycarbonate formation is favored at $T < 100\text{ }^{\circ}\text{C}$: while $T \approx 80\text{ }^{\circ}\text{C}$ is required to observe chemoselective copolymerization of CO₂ and **CHO**, polycarbonates synthesized from terminal epoxides and CO₂ can only be obtained at $T \approx 0^{\circ}\text{C}$.⁹¹ Operating under liquid or supercritical CO₂ conditions enhances epoxide conversion by improving contact between reactants. However, excessive CO₂ pressure can dilute or isolate the catalyst in a phase segregation reducing the activity.⁵⁵ Higher pressure can also boost polycarbonate selectivity by promoting chain growth and minimizing COC or ether linkage formation.^{89,92}

The stereoselective synthesis of COCs via CO₂/epoxide coupling reactions was largely investigated in the last decade.^{93,94} Two main reaction pathways were devised: (I) a direct **COC** formation (**Scheme 1.5**) and *backbiting mechanism* (polymerization-depolymerization pathway) (**Figure 1.9**). The direct **COC** formation (pathway I, **Scheme 1.5**), in which the **COC** product formally retains the configuration of the epoxide reagent: this pathway occurs through a double inversion process and does not involve oligo- or polycarbonate intermediates.^{99–102} The stereochemical configuration of the starting epoxide is formally retained through the occurrence of two consecutive S_N2 reactions. Initially, the nucleophilic co-catalyst attacks the epoxide in an S_N2 fashion, resulting in formation of the alkoxide intermediate with inversion of configuration. Then, CO₂ insertion and formation of the hemicarbonate intermediate occurs: the COC product is formed via intramolecular cyclization of the hemicarbonate, also occurring in an S_N2 fashion leading to a second inversion of configuration (pathway A, **Scheme 1.5**).

In some cases, an S_N1 mechanism was observed, due to the presence of either strong Lewis acids stabilizing the carbocation intermediate, or high temperatures, facilitating the spontaneous detachment of the leaving group. The resulting planar carbocation intermediate can be attacked by an incoming nucleophile from either side, leading to both *cis* and *trans* cyclic carbonates (pathway B, **Scheme 1.5**).¹⁰³



Scheme 1.5: Proposed mechanism for direct CO₂ coupling with trans-2,3-Epoxybutane to obtain the corresponding COCs with formal inversion of the configuration (pathway A) or retention of configuration (pathway B).

The second pathway (II) is a *backbiting mechanism* (polymerization-depolymerization pathway),^{63,95–98} resulting in formal inversion of configuration when starting from enantiopure epoxides (**Figure 1.9**). The polymer chain "backbites," meaning that a part of the growing polymer chain reacts with itself to break down into smaller **COC** units. Because the nucleophile is the intramolecular hemicarbonate, this process leads to an inversion of stereochemistry. The rate of depolymerization depends on whether the polymer is bound to a metal catalyst or free in solution:^{95,98} metal-bound backbiting is generally slower due to a higher energy barrier, as the growing polymer chain is still attached to the active metal center, while metal-free backbiting is faster and has a lower energy barrier, leading to a quicker **COC** formation.⁹⁵

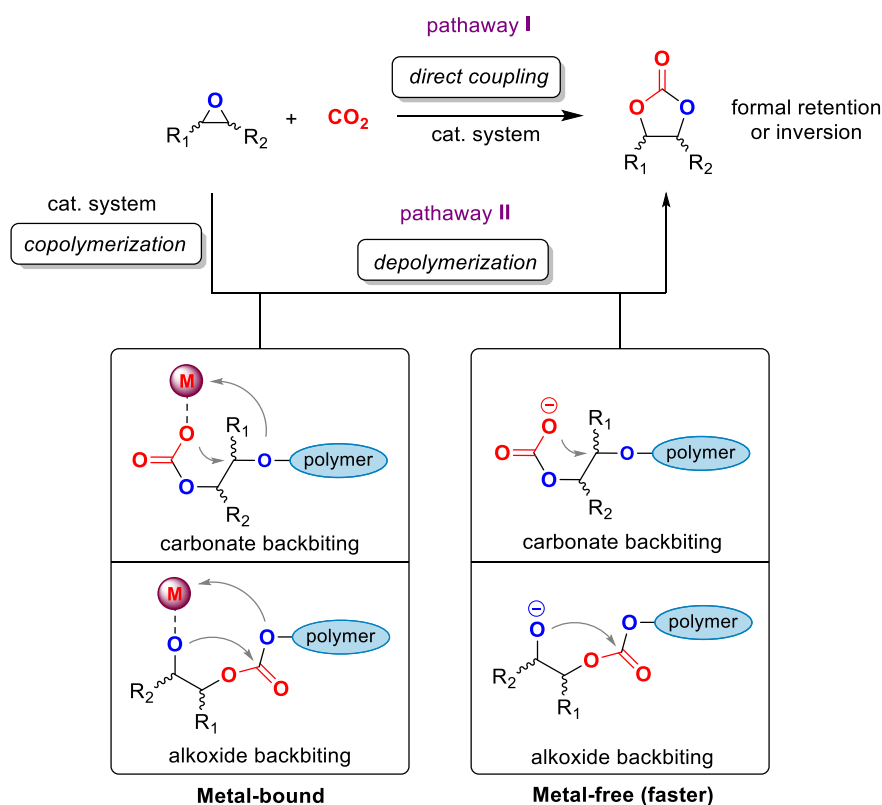


Figure 1.9: Different reported catalytic routes for the stereo-selective Formation of COCs from CO_2 and disubstituted oxiranes by backbiting mechanism (polymerization-depolymerization pathway).

The preparation of COCs through CO_2 insertion reactions aligns tightly with several **GC** principles: it involves CO_2 , a renewable and abundant feedstock, reducing waste and developing atom economical processes by fully incorporating CO_2 into the final product. Moreover, CO_2 insertion processes combine the discovery of new active catalytic systems with the development of efficient and environmentally friendly processes, by utilizing non-toxic catalysts, operating under mild experimental conditions, minimizing both energy consumption and use of hazardous reagents and/or solvents. By converting a greenhouse gas into valuable chemicals, these processes support environmental sustainability and foster a circular economy approach. Furthermore, the resulting COCs can serve as intermediates for biodegradable materials, contributing to sustainable lifecycle design.

1.4 Organic-Photoredox catalysis and flow technology

Sunlight irradiates our planet every day ($4.2 \cdot 10^6$ TWh/day) with more energy than we consume in a whole year ($1.6 \cdot 10^5$ TWh/year). This abundant and widely available resource has inspired many scientists to research how light can be exploited efficiently to promote organic chemistry reactivity.^{105–107} Using light to activate molecules provides access to reaction pathways which are otherwise impossible to reach with traditional thermochemical activation, as shown in **Figure 1.10**.^{108–111}

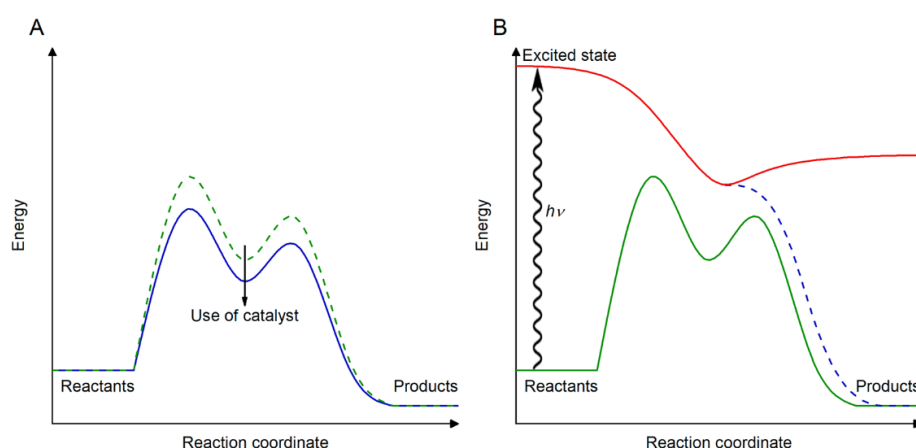
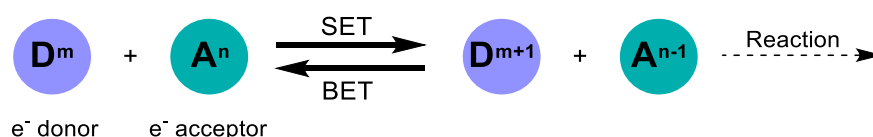


Figure 1.10: Thermochemical (A) versus photochemical activation (B). *§. Reproduced with permission from ref¹¹²*

One of the most intriguing aspects of photochemistry is the use of photons as “traceless and green reagents”, enhancing, formally, the sustainability of the processes. Over the last decade, visible light photoredox catalysis emerged, in particular, as an innovative and powerful mode to activate small molecules.^{113–116}

Photoredox catalytic reactions generally follow two distinct mechanistic pathways, single electron transfer (SET) and back electron transfer (BET), each defined by the direction of electron transfer (ET) relative to the excited photocatalyst (PC*). Photoinduced Electron Transfer (PET) cycles are generally based on SET, occurring between an electron donor ($D^m \rightarrow D^{m+1}$) and an electron acceptor ($A^n \rightarrow A^{n-1}$), as illustrated in **Scheme 1.6**. The reverse process, is known as BET and restores the ground state donor (D^m) and acceptor (A^n).¹¹⁴



Scheme 1.6: Single Electron Transfer (SET)

While ground-state chemical oxidants or reductants can drive certain SET pathways, PET offers unique advantages, such as enhanced oxidant/reductant strength or the ability to simultaneously use both. PET begins when one redox partner, typically the photocatalyst (PC), is excited by visible light (PC^*). This light absorption promotes the PC to a singlet excited state (S_1), represented in the simplified Jablonski diagram in **Figure 1.11**. From this point, various outcomes are possible: radiative relaxation through fluorescence or non-radiative processes like spin-forbidden intersystem crossing (ISC) to the triplet excited state (T_1). Additionally, the triplet state may relax radiatively via phosphorescence, though this process is spin-forbidden.^{114,117,118}

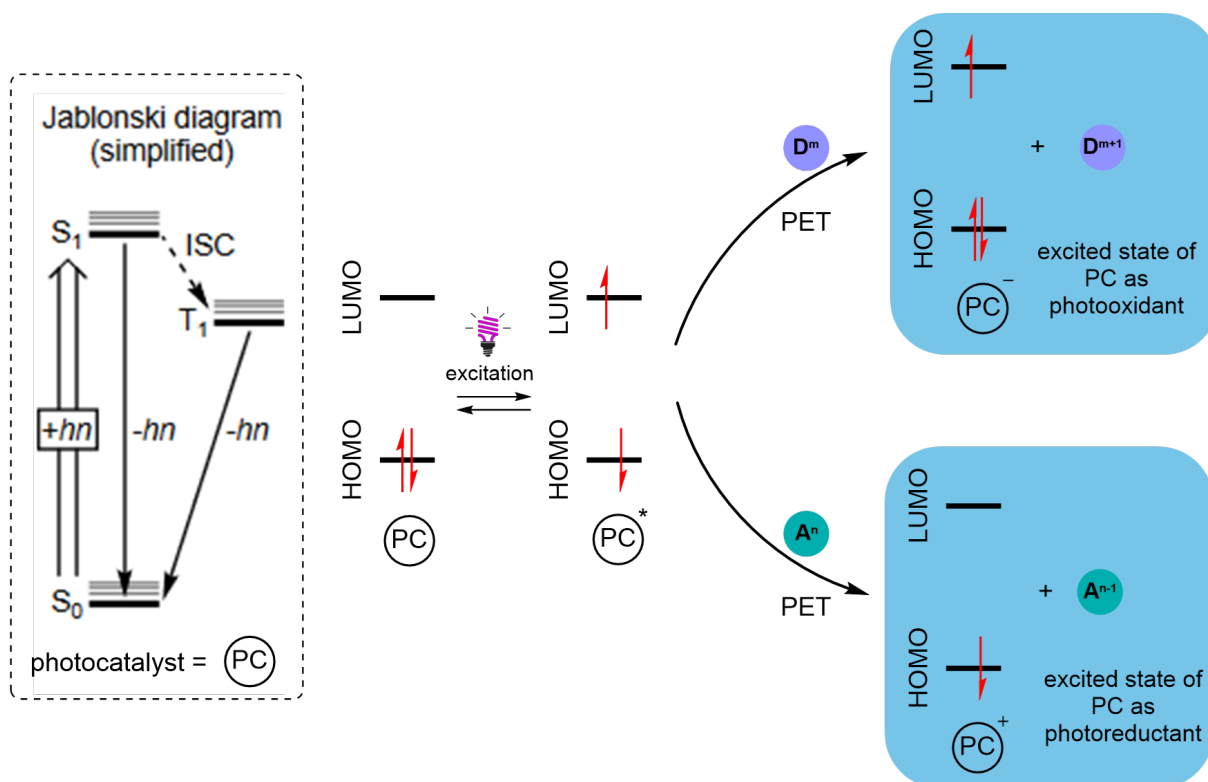


Figure 1.11: Photoinduced Electron Transfer (PET).

In the ground state, ET with the PC are endergonic; however, photoexcitation of PC to PC^* promotes an electron to the LUMO and creates a vacancy in the HOMO, as depicted in **Figure 1.11**. The reactivity of PC^* depends on the presence of electron-rich donor (D^m) substrates, characterized by a high energy orbital with one or more electrons, or electron-accepting acceptors (A^n) characterized by a low energy orbital with one or more vacancies. Quenching occurs through ET: in presence of a suitable donor D^m , PC^* can act as an excited state photo-oxidant, accepting an electron with formation of the reduced photocatalyst (PC^-) and oxidized donor (D^{m+1}). Conversely, PC^* behaves as a photo-reductant, with an appropriate acceptor with LUMO at lower energy, donating a spare electron to produce the oxidized photocatalyst (PC^+) and a reduced acceptor (A^{n-1}).^{114,117,118}

PET may involve singlet or triplet excited state catalyst, or species formed via charge transfer, such as metal-to-ligand charge transfer (MLCT). The dominant mechanism depends on the catalyst, as

the nature of the excited state affects factors like its lifetime and redox potential.^{114,117,118} Combining effectively D and A species can lead to photocatalytic cycles, which can be oxidative or reductive. In an oxidative quenching cycle (**Figure 1.12**, left), an acceptor (A^n) initially quenches the excited photocatalyst (PC^*), forming the oxidized photocatalyst PC^+ and the reduced acceptor, A^{n-1} . PC^+ undergoes a second redox reaction with an electron donor (D^m) then regenerates the ground PC oxidizing the donor to D^{m+1} , completing the cycle. In this model, the substrate (A^n) directly engages with the excited PC, accepting an electron and becoming activated. Alternatively, redox-active mediators like methyl viologen or co-catalysts can quench the PC^* . The reduced reagent or cocatalyst may activate a substrate, or the more strongly oxidizing intermediate PC^+ may activate a donor substrate (D^m) during the catalyst turnover step, a process known as secondary quenching.^{114,117,118}

A reductive quenching cycle (**Figure 1.12 right**) takes place when the photogenerated PC^* interacts initially with an electron donor (D^m), leading to the reduction of the photocatalyst to PC^- and donor oxidation to D^{m+1} . The cycle is completed by a subsequent redox reaction between PC^- and an electron acceptor (A^n), which restores the ground-state PC forming the reduced form of the acceptor, A^{n-1} . In this process, direct activation of the substrate occurs when an electron donor substrate transfers an electron to the excited catalyst, *e.g.* generating a cation radical intermediate from an olefin.^{114,117,118} In cases where the substrate is not directly activated by PET, a redox-active donor reagent, like an amine, or a co-catalyst can quench the excited catalyst. The oxidized form of this reagent can then activate the substrate, for example through hydrogen atom abstraction. Alternatively, secondary quenching may occur when an acceptor substrate is activated by the strongly reducing intermediate PC^- during the catalyst turnover step. These complementary quenching cycles highlight photocatalysts ability to act as both an oxidant and a reductant in a concerted fashion.^{114,117,118}

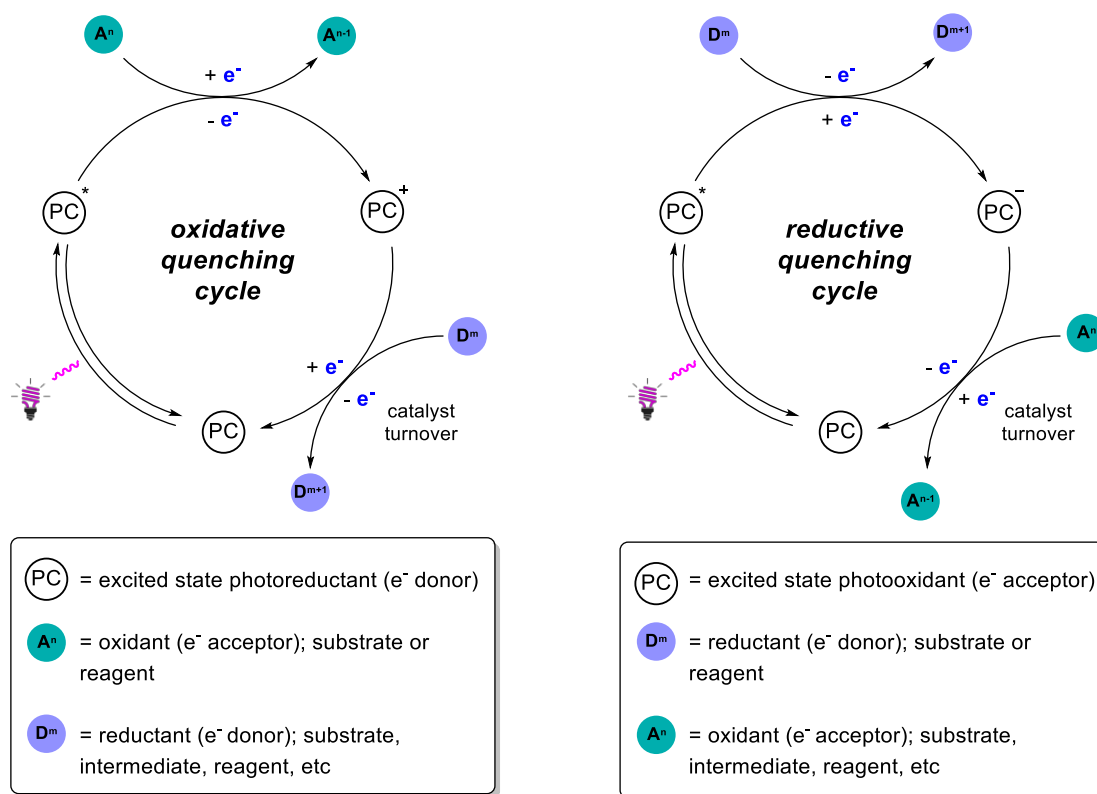


Figure 1.12: Oxidative quenching cycle (left); reductive quenching cycle (right).

The recent rediscovery of photochemistry has also contributed to detangling several unresolved challenges related to the scalability of photoassisted processes, which is largely prevented by the inherent complexity of photochemical reactions. One major limitation in scaling up such processes is the reduction of photon transport increasing the size of the photoreactor, as described by the Bouguer–Lambert–Beer law (Equation 1, **Figure 1.13**). In larger reactors, prolonged reaction times can lead to over irradiation of the reaction mixture, resulting in unwanted by-products formation and complicated purification procedures. Continuous flow systems applied to photochemical approaches have gained significant attention as a practical solution to the above mentioned scalability issues, offering a way to by-pass the limitations typically encountered in batch photoreactors.^{119–122}

One essential advantage of flow photochemistry is the enhanced irradiation of the reaction mixture, which ensures more uniform light exposure and thus higher photoefficiency. In the case of strong light absorbers, *i.e.* commonly employed photosensitizers and organic dyes, light intensity diminishes quickly approaching the center of the reactor. Microreactor flow technologies, in particular, represent an effective solution to keep a steady radiation distribution and improve the photochemical process efficiency, as depicted in **Figure 1.13**.²⁷

$$(1) \quad A = \log_{10} T = \log_{10} \frac{I_0}{I} = \epsilon c l$$

$$(2) \quad \Phi = \frac{\text{N}^\circ \text{ molecules of product}}{\text{N}^\circ \text{ of photons absorbed}}$$

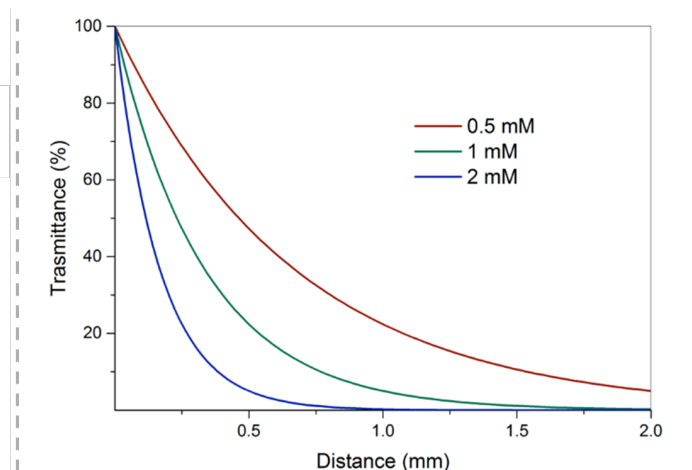


Figure 1.13: **left:** equation (1) is the definition of Bouguer–Lambert–Beer law, where A = absorbance, T = transmittance, I_0 = light intensity received by the light-absorbing medium [$\text{W}\cdot\text{m}^{-2}$], I = light intensity after passing through the light absorbing medium [$\text{W}\cdot\text{m}^{-2}$], ϵ = molar attenuation coefficient [$\text{L}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$], c = concentration [$\text{mol}\cdot\text{L}^{-1}$], l = optical path length [cm]; equation (2) is the definition of quantum yield (Φ) ; **right:** Transmission of light as a function of distance in a photocatalytic reaction using $\text{Ru(bpy)}_3\text{Cl}_2$ ($c = 0.5, 1$ and 2 mM , $\epsilon = 13000\text{ cm}^{-1}\text{M}^{-1}$) utilizing the Bouguer-Lambert-Beer correlation.²⁷

The absorption of photons is essential to observe photochemical reactions. However, not every photon leads to the conversion of one molecule of starting material, as excited states may return to their ground state through radiative or non-radiative processes, such as heat dissipation. The efficiency of a photochemical reaction is described by its quantum yield (Φ , Equation 2, **Figure 1.13**). For non-chain mechanisms, Φ typically ranges between 0 and 1. When the Φ exceeds 1, it indicates a chain reaction is taking place, typically occurring in photoredox catalysis or photopolymerization reactions.^{123–125}

In addition, flow setups offer reliable scalability by maintaining consistent reaction conditions, ultimately improving the selectivity and reproducibility of the photo assisted process. Light-assisted processes scale-up with photomicroreactors is generally carried out following two main approaches, summarized in **Figure 1.14**: (1) extending operation times and increasing output by raising flow rates, or (2) employing a numbering-up strategy.^{27,112}

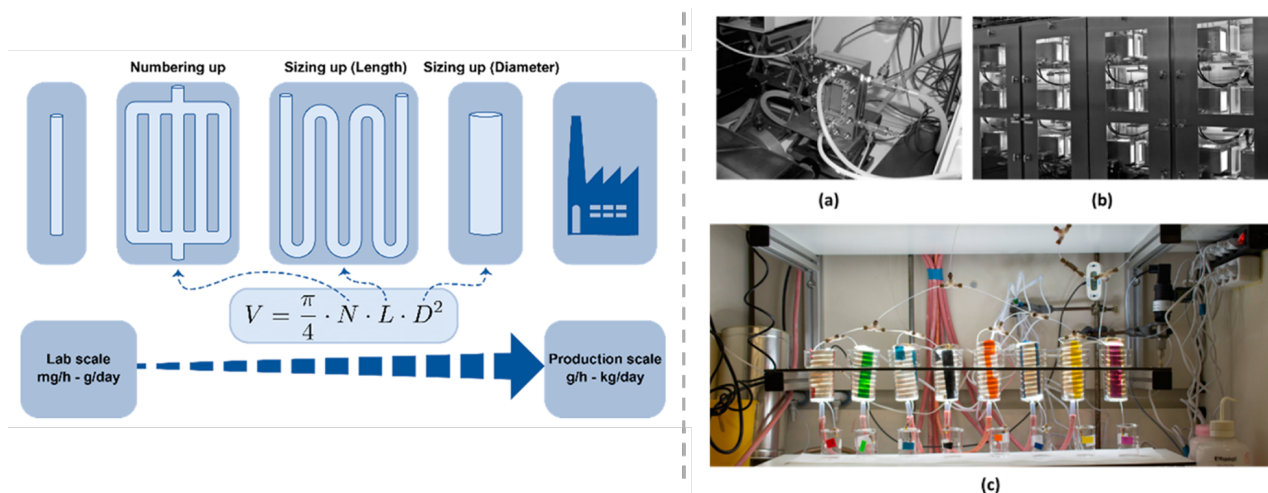
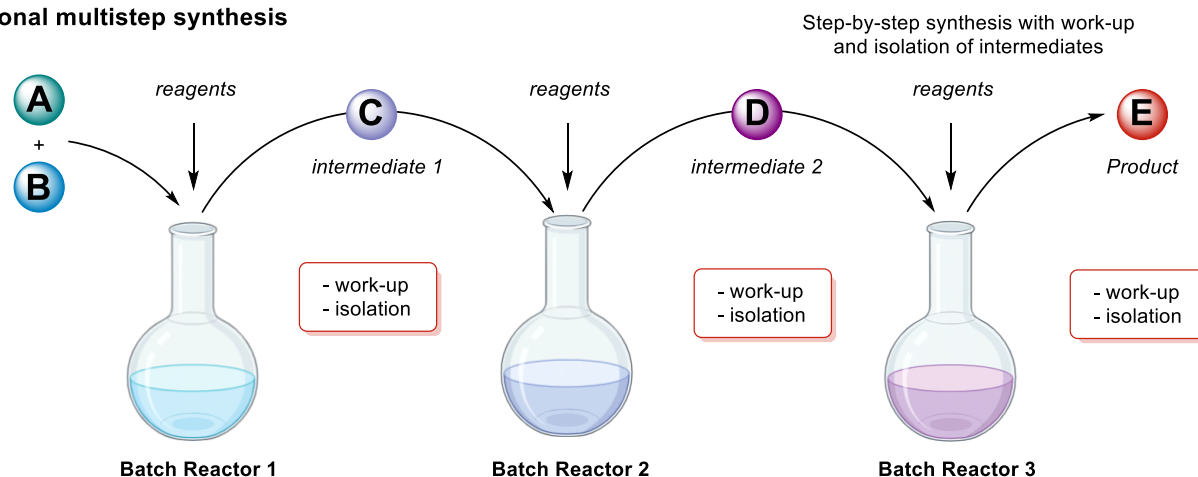


Figure 1.14: **Left:** Scale-up strategies for tubular flow reactors: numbering up, sizing up by increasing channel length, and sizing up by increasing the channel diameter. A tubular reactor volume can be calculated using the given equation. **Right:** Examples of numbering-up for the scale-up of photochemical transformations: (a) Internal numbering-up in a falling film microreactor. (b) External numbering-up of a photochemical production unit by Heraeus Noblelight GmbH. (c) Internal numbering-up of photomicroreactor for gas–liquid visible light photocatalysis. Reproduced with permission from ref. ^{27,112}

Photochemical transformations are significantly accelerated in microreactors. Reaction times reduced from hours in batch processes to just minutes or even seconds in continuous flow.^{27,112} This dramatic improvement leads to a notable increase in productivity over traditional batch methods. Continuous flow systems also improve rapid mixing and efficient heat exchange, which are both critical parameters for controlling reaction rates, particularly in complex, multistep reactions. Furthermore, flow technologies allow for a quick integration of multiple reaction and purification steps into a single, streamlined process, reducing manual intervention and delivering considerable time and cost savings (**Figure 1.15**).^{126,127} The utilization of inline spectroscopic tools, self-optimization protocols, and automation further minimizes the need for human oversight, enhancing both efficiency and precision in relation with the **GC** principles.^{128–130}

Traditional multistep synthesis



Multistep synthesis in flow

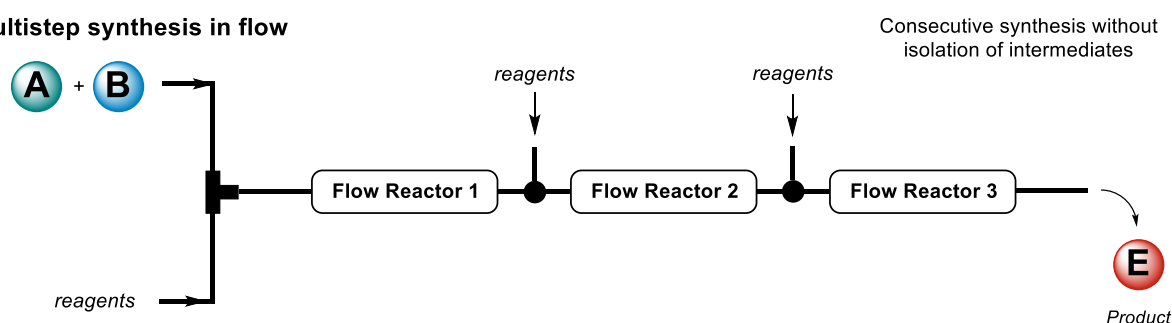


Figure 1.15: Multistep reaction sequence in batch and flow experimental conditions.^{27,112}

Flow microreactors can also dramatically improve the performance of multiphase reactions, *e.g.* oxidations, hydrogenations, halogenations, and phase-transfer catalysis, which are widely used in the chemical industry. These reactions occur in two or more immiscible phases, such as liquid-liquid or gas-liquid systems. When mass transfer between phases becomes the rate-limiting step, maximizing the interfacial area is pivotal. In batch processes, the interfacial area is often small and poorly defined, leading to prolonged reaction times. Microreactors, with their large interfacial areas (up to $9000 \text{ m}^2 \cdot \text{m}^{-3}$), improve mass transfer efficiency, with volumetric mass transfer coefficients ($k_L a$) 1-2 orders of magnitude higher than in traditional reactors.^{27,112}

As summarized in **Figure 1.16**, several different microreactor designs have been developed to carry out multiphase reaction conditions.^{131,132} Single channel microreactor systems (*e.g.* transparent capillaries) are generally employed with flow regimes such as segmented (Taylor) flow and annular flow. In segmented flow, slugs and bubbles create toroidal vortices that enhance mixing and mass transfer. In annular flow, a high-velocity phase flows in the center of the microreactor, while the other forms a thin film along the walls, maximizing photon exposure in photochemical reactions. Other designs include falling film reactors, where gravity drives liquid over channels, and membrane reactors, where phases are separated by a permeable membrane for controlled diffusion. Segmented flow also minimizes particle size distribution, ensuring more uniform reaction conditions and lower polydispersity.^{27,112}

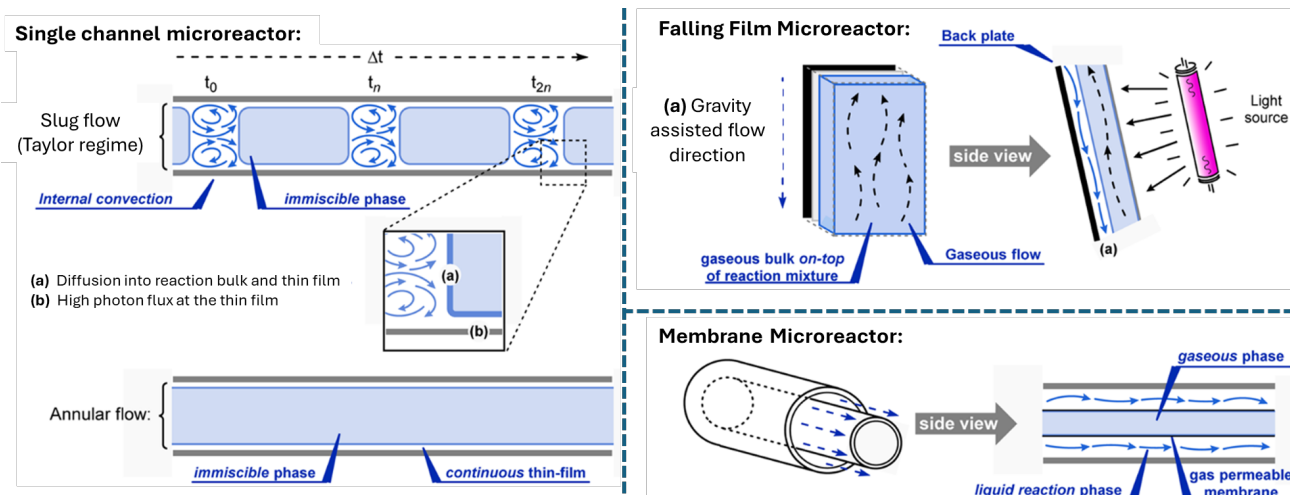


Figure 1.16: Overview of the most common microreactor types used for multiphase flow Reproduced with permission from ref. ^{27,112}

In conclusion, photoredox catalysis exploits light as a renewable energy source to develop efficient and selective reaction protocols under mild operating conditions, significantly reducing energy consumption and generation of hazardous waste. Combining light assisted synthetic protocols and microflow technologies represents a significant advance in sustainable reaction design, enabling precise control of reaction parameters, accelerating multiphase reaction scalability and minimizing waste. Intriguingly, modular flow setups, advanced (micro)reactor designs, and/or offline analysis can be effectively implemented with sustainable reaction conditions to further increase the overall process efficiency. Together, these innovations comply with several different **GC** principles including energy efficiency, waste prevention, and catalysis and directly contribute to specific **SDGs**, such as Goal 7 (advancing renewable energy and efficiency), Goal 12 (promoting responsible production and consumption), and Goal 13 (climate action to combat global warming).³³

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2. Aim and structure of the Thesis

The overarching goal of this thesis is the development of innovative and more sustainable synthetic procedures, focusing on CO₂ valorization strategies. For this latter topic, the results have been summarized and discussed in three distinct chapters, *e.g.* **Chapter 3: Non-Reductive CO₂ Valorization strategies**, **Chapter 4: Reductive CO₂ Valorization strategies** and **Chapter 5: Photochemistry**.

Chapter 3 showcases four key studies for the development of novel catalytic systems for the synthesis of cyclic organic carbonates (COCs) through CO₂ insertion into epoxides. **Section 3.1** explores dihydroxybenzene-derived ILs as halide-free single component organocatalysts. **Section 3.2** describes the application of 5-HMF derivatives as active complexing agents to promote CO₂ insertion into epoxides. **Section 3.3** and **3.4** focus on one-pot tandem oxidative carbonation process using molybdenum-based ILs. More precisely, in **Section 3.3**, a variety of Mo-containing ILs were evaluated as halide-free catalysts for CO₂ fixation into epoxides. While, in **Section 3.4**, the oxidative properties of Mo-containing ILs are exploited in biphasic systems to initially generate the epoxide from the corresponding alkene and then react it with CO₂ to achieve COC production a one pot-reaction.

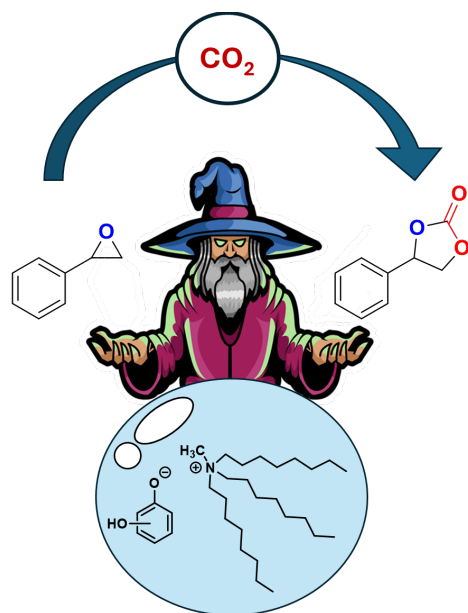
Chapter 4 describes the photothermal reduction of CO₂ to CO. **Section 4.1** describes a standardized reactor system equipped with automated control over temperature, light intensity, pressure, residence time, and reagent stoichiometry, enabling the execution of gas-phase chemistry in a robust and reproducible manner. Furthermore, the generated CO was exploited in a diverse array of palladium catalyzed carbonylative cross-coupling reactions.

Chapter 5 focuses on the use of photochemistry and reports two different examples of photo-assisted processes. **Section 5.1** describes the application of photoactive carbon dots (CDs) in photoinduced atom transfer radical polymerizations (ATRP) as green, metal-free sensitizers. **Section 5.2** summarizes the preliminary results on the development of a new methodology for aryl radical carbonylations using photo-redox catalysis in continuous flow.

This thesis was developed in the Green Organic Synthesis Team (GOST) of the Università Ca' Foscari di Venezia, led by Prof. Dr. Giulia Fiorani, Prof. Maurizio Selva and Prof. Alvis Perosa. The experimental work presented in Chapter 3 and Section 5.1 was carried out in the GOST laboratories, with the experimental facilities available through the Molecular Sciences and Nanosystems Department of Ca' Foscari University of Venice. Part of the research activities of this PhD program was carried out during a 9-month stay at the Vant'Hoff Institute of the University of Amsterdam (Netherlands) in the laboratories of Noël Research Group (NRG) led by Prof. Dr. Ing. Timothy Noël. In particular, the experimental work carried out at NRG is focused on the flow technologies described in **Section 4.1** and **5.2**.

3. Non-Reductive CO₂ Valorization strategies

3.1 Dihydroxybenzene-derived ILs as Halide-Free, Single component Organocatalysts for CO₂ Insertion Reactions



This Work:

- IL single component catalyst
- Simple halide-free & sustainable preparation
- Active on terminal & internal epoxides

3.1.1 Abstract

The investigation of CO₂ insertion reactions into terminal epoxides for the preparation of cyclic organic carbonates (COCs) performed during this thesis work started with the development of a series of dihydroxybenzene-derived ILs as organocatalyst. These ILs were synthesized through a halide-free, eco-friendly methodology and fully characterized by NMR spectroscopy and gravimetric techniques. Their activity as single component catalyst was evaluated, observing that methyltriocetylammmonium hydroquinolate, [N_{8,8,8,1}][HYD], was the most active catalyst in the proposed optimized conditions ([N_{8,8,8,1}][HYD] 10 % mol, T = 120 °C, t = 6h, p⁰(CO₂) = 20 bar, 12 examples, conversion > 99 %, yield up to 98 %). Interestingly, [N_{8,8,8,1}][HYD] was also an active catalyst for CO₂ insertion reactions with cyclohexene oxide (CHO), observing formation of both the COC and polycarbonate product. It is proposed that for p⁰(CO₂) ≥ 10 bar, the catalytically active species is the hemicarbonate derivative of the hydroquinolate anion, active towards epoxide ring opening via an unusual hemicarbonatealkoxide pathway. The results reported in this chapter have been published in "Bragato, N.; Perosa, A.; Selva, M. and Fiorani, G. Dihydroxybenzene-Derived ILs as Halide-Free, Single-Component Organocatalysts for CO₂ Insertion Reactions, *ChemCatChem* **2023**, 15, e202201373."¹

3.1.2 Introduction

Phenolic derivatives are molecules containing a benzene ring and one or more hydroxyl substituents and represent the largest group of plant secondary metabolites. These compounds are mainly found in lignocellulosic biomass and are biosynthesized through the shikimate metabolic pathway that produces simple molecular phenol-derived structures as well as more complex polycyclic (tannins, coumarins, flavonoids, chromenes, xanthenes) and polymeric structures (*e.g.* lignanes). Common to the different classes of phenolic compounds, is the presence of antioxidant, cytotoxic and antimicrobial activities.^{2,3} The importance of phenolics is not limited to biological worlds as they are extensively employed in synthetic and materials chemistry applications thanks to their versatile chemical reactivity.⁴ These compounds exhibit a versatile amphoteric reactivity, ascribed to the acidity of the hydroxyl group conjugated to the benzene ring which, in turn, improves the strength of the phenolate conjugated base ($pK_a = 10$ in H_2O).⁵ Phenolate-based organocatalysts are active towards CO_2 capture, storage and chemical conversion. In particular, ionic liquids (**ILs**) containing phenolate moieties are highly active in CO_2 chemisorption due to their low volatility, thermal stability, high CO_2 capacity, selectivity, and rapid capture kinetics, facilitating a direct and reversible interaction with CO_2 .^{6–10} Additionally, simple polyhydroxybenzene derivatives have been employed as organocatalysts for CO_2 insertion into epoxides, a well-established method for the chemical valorization of CO_2 (*vide infra*).

Metal-free catalytic systems for CO_2 insertion and activation have now achieved a high level of sophistication, exhibiting catalytic activities and selectivities comparable to those of traditional metal or halide-based systems in the synthesis of **COCs**.¹¹ Various polyhydroxybenzene containing catalysts have demonstrated catalytic activity for the synthesis of **COCs** via CO_2 insertion.^{12–14} Polyhydroxybenzene derivatives mainly act works as Brønsted acidic co-catalysts coordinating the epoxide co-reactant.^{15,16}

Pyrogallol (1,2,3-trihydroxybenzene) was initially reported by Kleij and co-workers, who developed an homogeneous catalytic systems composed by pyrogallol and tetrabutylammonium iodide (TBAI) as the nucleophilic co-catalyst, active under mild conditions ($T = 25–45\text{ }^\circ\text{C}$, $p(CO_2) = 10\text{ bar}$, 5 mol % catalyst, 5 mol % TBAI and 5mL of MEK) towards CO_2 insertion into terminal and internal epoxides (14 examples, 52–94 % isolated yield).¹⁷ The same group also developed an heterogeneous bifunctional catalysts anchoring pyrogallol on a polystyrene scaffold which promoted the formation of mono- and disubstituted COCs at $T = 45\text{ }^\circ\text{C}$: interestingly this heterogeneous catalyst could be reused up to ten times, though requiring methyl iodide for effective regeneration due to halohydrin by-product formation.¹⁸ Kleij and co-workers also reported tannic acid (TA)-based catalytic systems active for CO_2 insertion into epoxides in combination with TBAI; TA-based catalytic systems showed an improved longevity compared to pyrogallol ascribed to the complex structure of TA and its limited solubility in neat epoxide mixtures.¹⁹ Effective catalysis was also observed when performing CO_2 insertion reactions in presence of supramolecular, organized cavitand structures based on resorcin[4]arenes as hydrogen bond donors: at $T = 50\text{ }^\circ\text{C}$, and in combination with excess TBAI, catalytic activity was observed for CO_2 insertion reaction with epoxides performed in MEK, achieving the corresponding COCs in high yields and conversions. Notably, more challenging internal epoxides

were also selectively transformed into the corresponding COCs at $T = 80\text{ }^{\circ}\text{C}$ and in solventless conditions.²⁰ Shirakawa,²¹ Suga,²² and Werner^{23,24} independently reported phenol-functionalized quaternary phosphonium salts derived from 2'-(phosphinomethyl)-[1,1'-biphenyl]-2-ol and 2-(phosphinomethyl)phenol. These systems exploit the hydrogen bond donor (HBD) functionality within the phosphonium cation to promote epoxide ring-opening and facilitate CO_2 insertion.²⁵ Despite their effectiveness under mild conditions, all these systems required a halide counter anion for catalysis. Dai and co-workers prepared a series of pincer-type single component organocatalysts incorporating an *N*-heterocyclic carbene (NHC) precursor and a carboxylic group as HBD. These catalysts were effective for CO_2 insertion into both internal and terminal epoxides, in very mild conditions, *e.g.* $p(\text{CO}_2) = 1\text{ bar}$ and *rt* for terminal epoxides. However, also this catalytic system required a halide counteranion for *in situ* NHC formation.²⁶ More recently, Milani and co-workers prepared a library of hydroxy-functionalized triazolium halide ILs active towards CO_2 insertion into epoxides. These catalysts worked with both terminal and internal epoxides and could be used at catalyst loadings as low as 0.075 mol %.²⁷

Conversely, halide-free single component organocatalysts active towards CO_2 insertion into epoxides were far less studied, and the examples communicated so far are depicted in **Figure 3.1**.

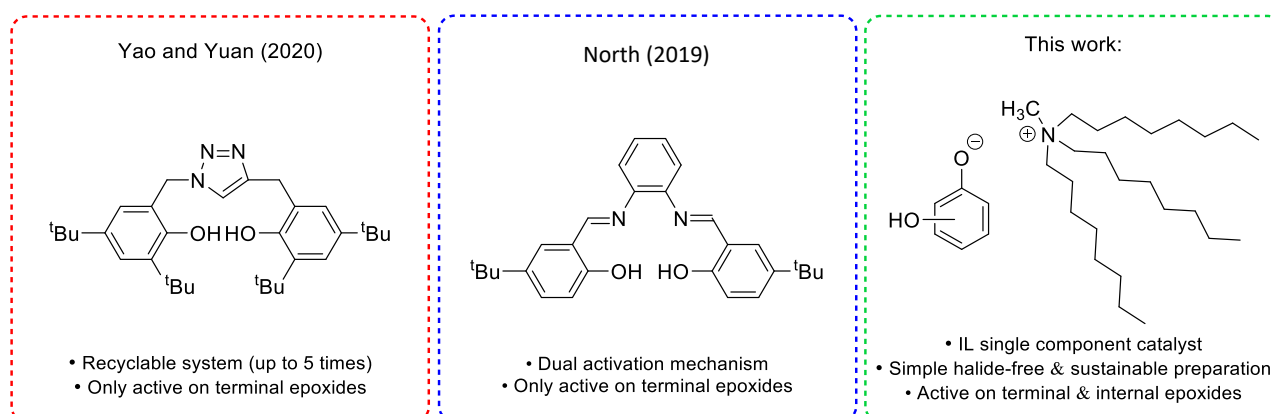


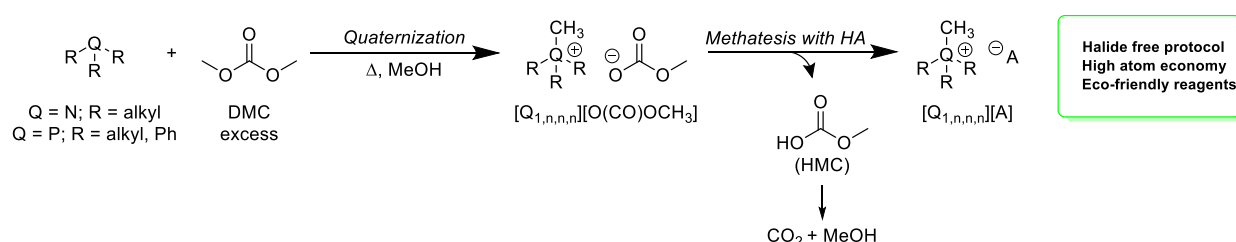
Figure 3.1: Single component, halide-free, bifunctional organocatalysts active towards CO_2 insertion into epoxides.

Yao, Yuan, and Hao initially reported the catalytic activity of a 1,2,3-triazole-bridged bisphenol as a halide-free single-component organocatalyst for CO_2 fixation onto terminal epoxides at $T = 120\text{ }^{\circ}\text{C}$ and $p(\text{CO}_2) = 10\text{ bar}$. However, enhanced reactivity as a HBD under milder conditions ($T = 40\text{ }^{\circ}\text{C}$, $p(\text{CO}_2) = 1\text{ bar}$) was observed only with (over)stoichiometric amounts of a nucleophilic co-catalyst such as TBAI (**Figure 3.1**, left).²⁸ North and co-workers reported an halide-free CO_2 fixation catalysis based on *N,N'*-phenylenebis(5-*tert*-butylsalicylideneimine) as a single-component catalyst (**Figure 3.1**, center): at $T = 120\text{ }^{\circ}\text{C}$ and $p(\text{CO}_2) = 10\text{ bar}$, it displayed catalytic activity with eight different terminal epoxides, transformed into the corresponding COCs with 62-99 % conversion and 57-89 % yield, in solventless conditions or using renewable-based 2-MeTHF as solvent.²⁹ In 2023 we reported the preparation of a series of single component catalysts based on tetraalkylammonium, phosphonium and alkylmethylimidazolium ILs containing phenolate or dihydroxybenzene based

counter anions (**Figure 3.1**, right). The resulting ILs were fully characterized and tested in CO₂ insertion reactions on different epoxides.

3.1.3 Ionic Liquids (ILs) synthesis

Hydroxybenzene containing ILs were synthesized following a halide-free, sustainable protocol developed by our research group. The process involves two main steps: i) preparation of the methylcarbonate IL precursor, [Q_{1,n,n,n}][H₃CO(CO)O], through selective methylation of trialkylamine or trialkylphosphine with dimethyl carbonate (DMC), and ii) metathesis of [Q_{1,n,n,n}][H₃CO(CO)O] in presence of equimolar amounts of a Brønsted acids (HA), which are precursors of the target anion, yielding pure [Q_{1,n,n,n}][A].³⁰ As illustrated in **Scheme 3.1**, the second step produces the corresponding anion (A) and hydrogen methylcarbonate (HMC).



Scheme 3.1 Synthesis of [Q_{n,n,n,1}][A] via metathesis between [Q_{n,n,n,1}][H₃CO(CO)O] and a Brønsted acid (HA).

HMC is unstable at temperatures above - 36 °C, therefore at room temperature it rapidly decomposes into methanol and CO₂.³¹ These by-products can be easily and quantitatively removed under vacuum, yielding the desired [R₃CH₃Q][A] as a pure product. Due to the moderate Brønsted acidity of dihydroxybenzenes, the metathesis process is relatively slow, requiring more than 12 h to reach completion. However, the equilibrium is shifted towards product formation by the decomposition of HMC and subsequent removal of methanol and CO₂ from the system. Several different ILs containing isomeric dihydroxybenzene (*e.g. ortho, meta* and *para*) were synthesized following this methodology starting from methyltriocetylammmonium methylcarbonate, [N_{8,8,8,1}][H₃CO(CO)O], as summarised in **Figure 3.2**.

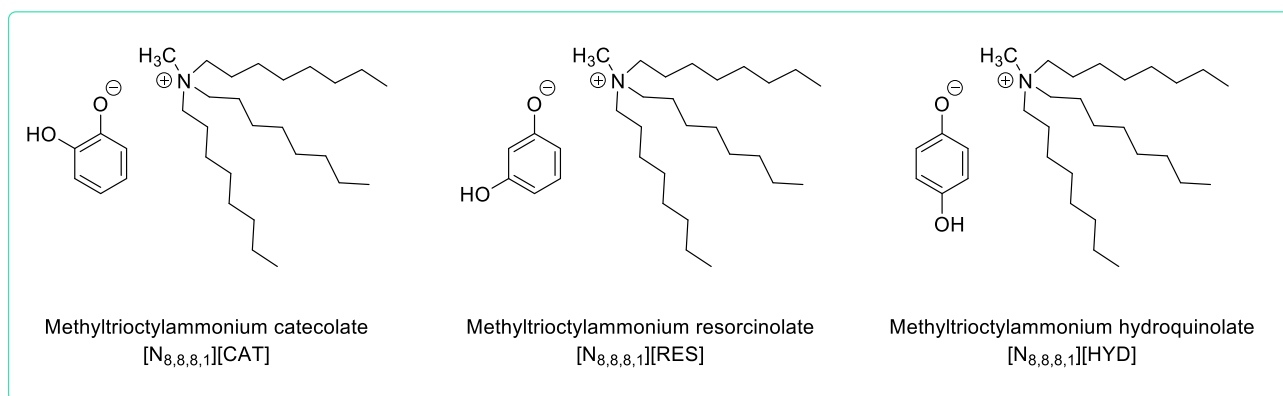


Figure 3.2: Dihydroxybenzene ILs with [N_{8,8,8,1}]⁺ counter cations.

With the notable exception of the halide-free phosphorus-ylide CO₂ adducts reported by Lu and co-workers, the nature of the heteroatom embedded within the counteranion influences the chemoselectivity of the CO₂ insertion process.³² This is especially true for phosphonium ILs: as illustrated in **Figure 3.3** for the synthesis of various trialkylmethylphosphonium *para*-dihydroxybenzene (hydroquinolate: HYD) derived ILs, the formation of an undesired phosphine oxide by-product was observed in all cases.

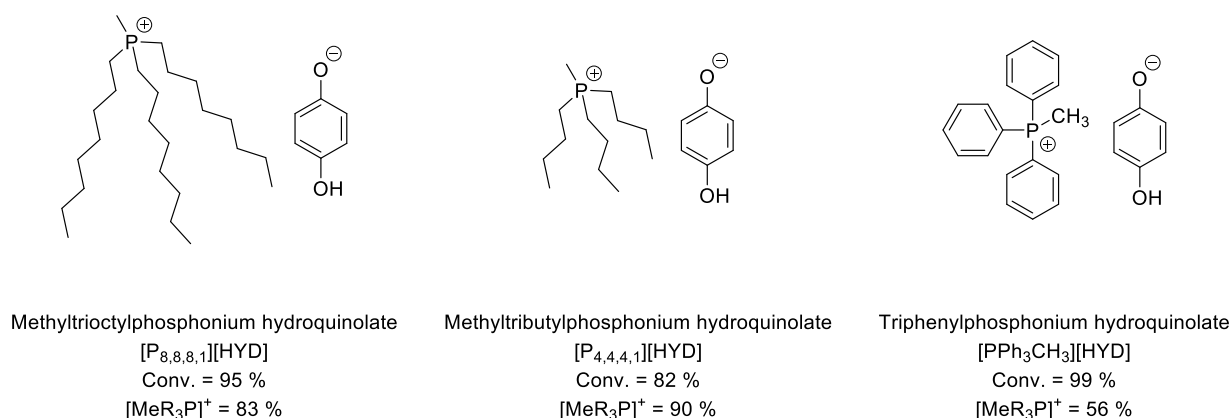
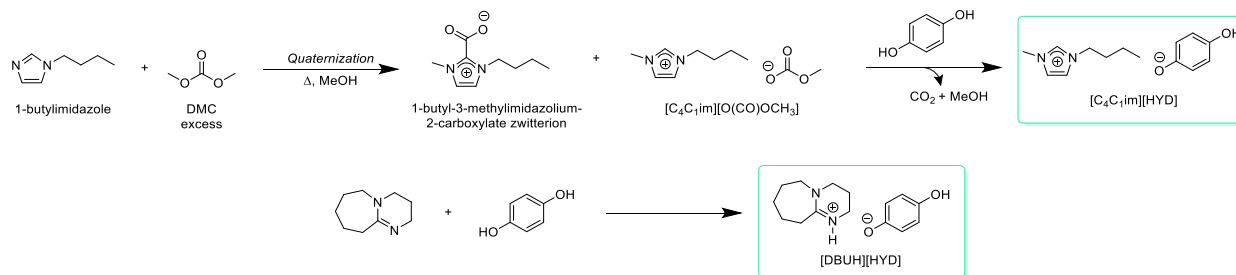


Figure 3.3: [P_{1,n,n,n}][HYD] ILs. QPS quantification was performed by ³¹P NMR.

The observed experimental behavior is consistent with the reduced stability of quaternary phosphonium salts (QPS) in presence of oxygenated anions, in agreement with previous independent reports by Selva and co-workers and Brennecke *et al.*^{9,33} Moreover, recent findings by Nikitin and co-workers revealed that phenolates basicity can promote irreversible QPS hydrolysis to the corresponding phosphine oxide in presence of adventitious water.³⁴ Consequently, the thermal stability of [N_{8,8,8,1}][HYD] was experimentally evaluated by thermogravimetric analysis (TGA), determining a T_{onset} = 174 °C (see **Figure A1** and **A2** in **Appendix Chapter 3** section). Additionally, as depicted in **Scheme 3.2**, two other hydroquinone derived ILs were synthesized: 1-butyl-3-methylimidazolium hydroquinolate, [C₄C₁im][HYD] and [DBUH][HYD].



Scheme 3.2: Top: synthesis of [C₄C₁im][HYD]; bottom: synthesis of [DBUH][HYD].

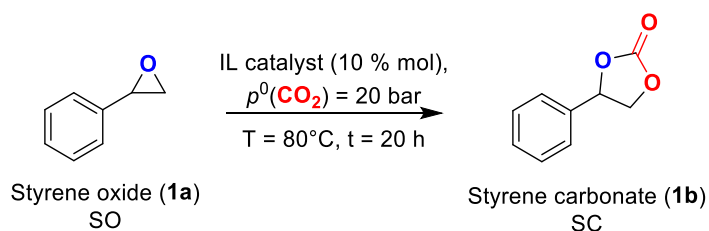
In the former case, two different products were produced by quaternization of 1-butylimidazole with DMC: the expected salt, 1-butyl-3-methylimidazolium methyl carbonate, [C₄C₁im][H₃CO(CO)O], and zwitterionic 1-butyl-3-methylimidazolium-2-carboxylate.^{35,36} For the metathesis step, the resulting mixture was reacted as such with stoichiometric amounts of hydroquinone, obtaining [C₄C₁im][HYD] in quantitative yield. [DBUH][HYD] was obtained in a single step process, upon

neutralization of stoichiometric amounts of hydroquinone with DBU (1,5-diazabicyclo[5.4.0]-5-undecene) superbase.³⁷ Catalytic activity towards CO₂ insertion reactions with epoxides was evaluated only with *N*-based dihydroxybenzene ILs containing [N_{8,8,8,1}]⁺, [C₄C₁im]⁺ and [DBUH]⁺ cations.

3.1.4 CO₂ insertion reactions

The synthesized dihydroxybenzene derived ILs were all tested as single component catalysts for CO₂ insertion reactions in terminal epoxides. Styrene oxide (SO, **1a**) was chosen as model terminal epoxide, due to its limited volatility and easy analytical detection. Mesitylene was added as internal standard at the end of the reaction time. As summarized in **Table 3.1**, all single component ILs catalysts were active in the chosen experimental conditions (*T* = 80 °C, *p*⁰(CO₂) = 20 bar, *t* = 20 h) with comparable activity (*cfr.* SO conversion for entries 1–3, **Table 3.1**).

Table 3.1: Initial comparison of the catalytic activity of different hydroxybenzene ILs towards CO₂ insertion reactions on SO.^a



Entry	IL catalyst	SO Conversion (%) ^b	SC selectivity (%) ^b	SC yield (%) ^b
1	[N _{8,8,8,1}][CAT]	48	96	46
2	[N _{8,8,8,1}][RES]	49	86	42
3	[N _{8,8,8,1}][HYD]	49	99	49
4	[C ₄ C ₁ Im][HYD]	55	72	32
5	[DBUH][HYD]	35	58	20

^aReaction conditions: SO (4.00 mmol), cat. (10% mol; 0.4mmol), mesitylene (20% mol; 0.80 mmol), *T* = 80 °C, *p*⁰(CO₂) = 20 bar, *t* = 20 h, solventless conditions.

^bDetermined by quantitative ¹H NMR analysis with an internal standard (mesitylene).

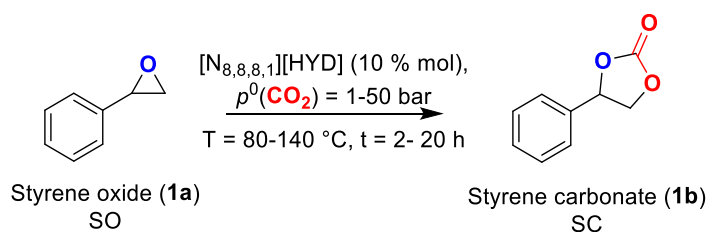
Interestingly, the most selective catalyst was [N_{8,8,8,1}][HYD] (Entry 3, **Table 3.1**). The improved selectivity towards styrene carbonate (SC, **1b**) formation observed with [N_{8,8,8,1}][CAT] and [N_{8,8,8,1}][HYD] as catalysts (*cfr.* Entries 1 and 3, **Table 3.1**), was attributed to the additional electronic-donating inductive effects of the -OH substituents, increasing the nucleophilicity of the counter anion moiety of the catalyst. Conversely, [N_{8,8,8,1}][RES] lacks this additional electron-donating effect, resulting in lower selectivity towards SC formation (Entry 2, **Table 3.1**). Next, ILs bearing [HYD] anions and different counter cations (*e.g.* imidazolium and DBUH) were also evaluated as catalysts.

However, both catalysts exhibited lower selectivity compared to [N_{8,8,8,1}][HYD] (Entries 4 and 5 vs. Entry 3, **Table 3.1**). A thorough inspection of the ¹H NMR spectra of the crude reaction mixtures indicated the formation of the corresponding diol as a by-product (13% diol by-product for [C₄C₁Im][HYD] and 15 % with [DBUH][HYD]). Poor selectivity and extensive diol formation were observed with [DBUH][HYD], highlighting the non-innocent and detrimental role of basic counter cations when combined with dihydroxybenzene-derived anions.

The limited selectivity towards COC formation observed with [C₄C₁im][HYD] (Entry 4, **Table 3.1**) was attributed to the strong electrostatic cation- π interaction for this cation-anion combination, preventing CO₂ activation and thus limiting COC formation. The distinct catalytic activity observed varying the cation-anion combinations reflects the nature of the specific anion-cation interactions. This interaction varies when using cations bearing acidic protons, such as alkylmethylimidazolium or [DBUH]⁺, compared to tetraalkylammonium counter cations. In the former case, H-bonding interactions between the cation and substrate are possible, which are mostly counterbalanced by a decrease in nucleophilicity of the anion. With non-acidic cations like tetraalkylammonium, which cannot establish strong Coulombic interactions, the nucleophilicity of the counteranion is higher due to weaker cation-anion pairing interactions.³⁸

Once determined that the most active and selective catalyst was [N_{8,8,8,1}][HYD], the reaction conditions were further optimized. SO (**1a**) remained the model epoxide substrate, while catalyst loading, reaction temperature, and CO₂ pressure were varied as reported in **Table 3.2**.

Table 3.2: Influence of reaction parameters on the activity of $[N_{8,8,1}][HYD]$ towards CO_2 insertion on SO.^a



Entry	p^0CO_2 (bar)	T (°C)	t (h)	SO Conversion (%) ^b	SC selectivity (%) ^b	SC yield (%) ^b
1	20	80	20	49	99	49
2	20	100	20	89	87	77
3	20	120	20	100	80	80
4	20	140	20	100	65	65
5	20	120	14	100	79	79
6	20	120	10	100	83	83
7	20	120	6	97	85	82
8	20	120	2	80	84	67
9	1	120	6	93	39	36
10	10	120	6	95	80	76
11	20	120	6	97	85	82
12	30	120	6	95	85	81
13	50	120	6	95	92	87

^aReaction conditions: SO (4.00 mmol), cat. (10 % mol; 0.40 mmol), mesitylene (20 % mol; 0.80 mmol), solventless conditions. ^bDetermined by quantitative ¹H NMR analysis with an internal standard (mesitylene, 20 % mol).

Increasing the reaction temperature improved the conversion of SO. However, performing CO_2 insertion reactions at temperatures > 120 °C for extended reaction times was detrimental to the selectivity towards SC (see Entries 1–4, **Table 3.2**). However, setting the reaction temperature at $T = 120$ °C allowed for a significant reduction in reaction time (Entries 5–8, **Table 3.2**): quantitative SO conversion was achieved in $t = 10$ h (Entry 6, **Table 3.2**), and SO conversions > 80 % were observed even with reaction times as short as $t = 2$ h (Entry 8, **Table 3.2**). A reaction time of $t = 6$ h (Entry 7, **Table 3.2**) was found to be the best compromise, balancing SO conversion with SC selectivity, and was therefore selected for further optimization studies. Although varying the CO_2 pressure did not impact SO conversion, its effect on the reaction outcome was significant, observing relevant selectivity towards SC only for $p^0(CO_2) \geq 10$ bar (Entries 9–13, **Table 3.2**). Subsequently, the scope of our optimized protocol for COCs synthesis was evaluated also for other terminal and internal epoxides, as summarized in **Figure 3.4**.

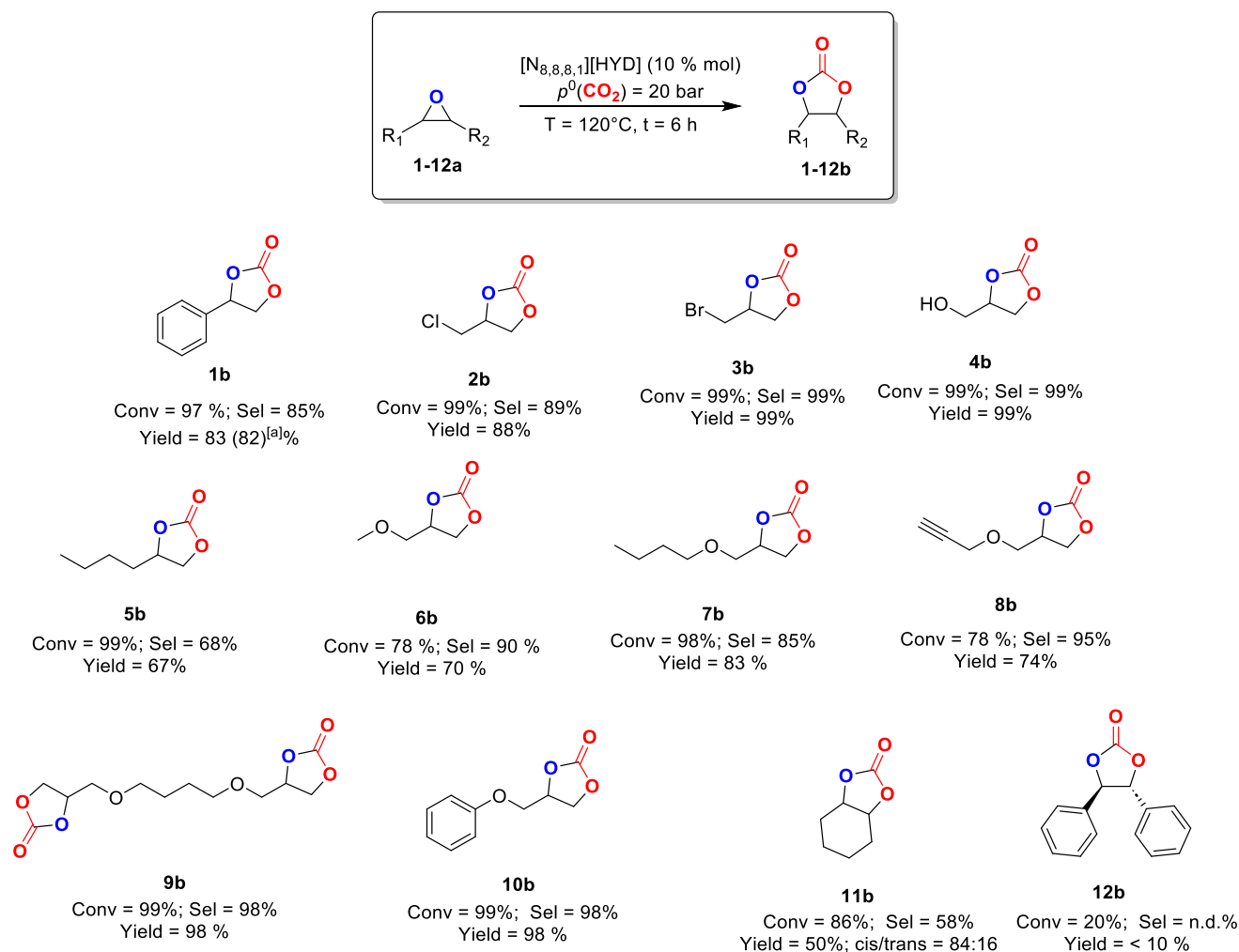
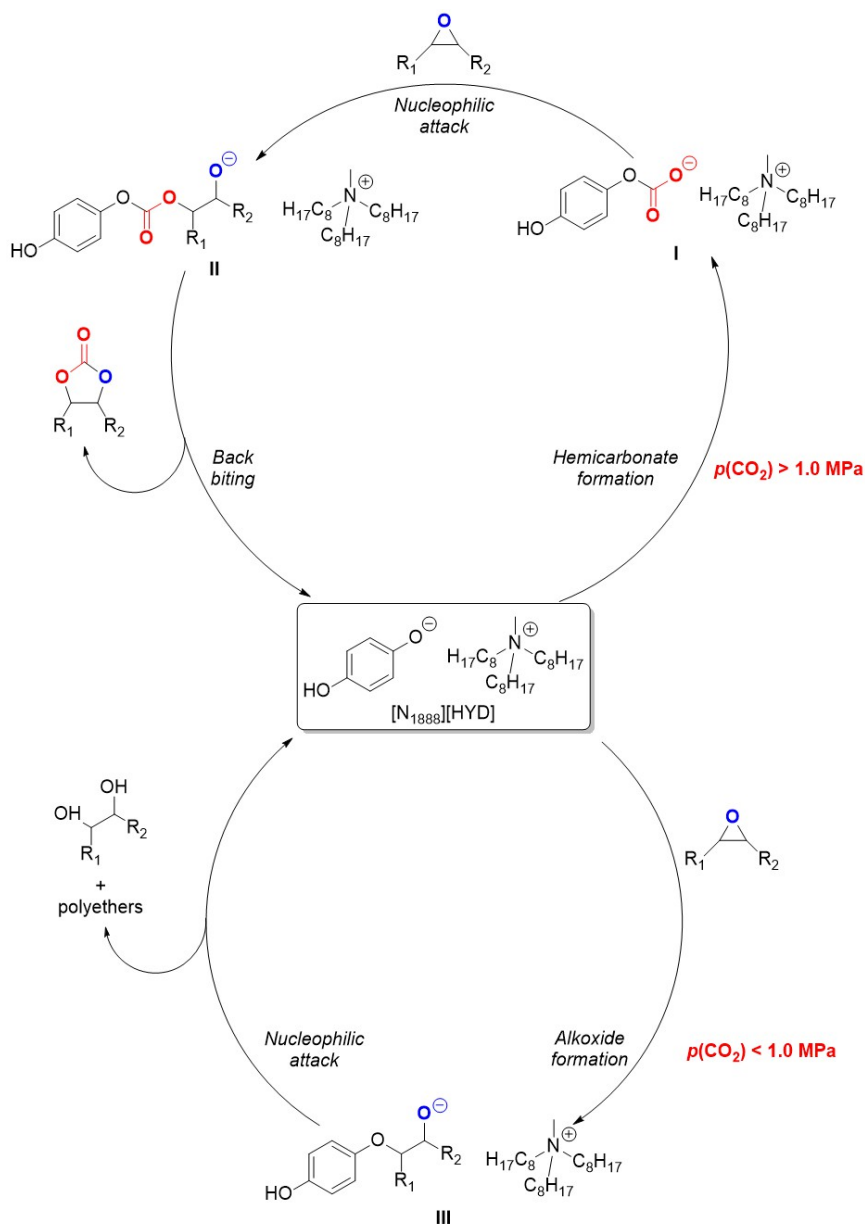


Figure 3.4: Substrate scope for COCs synthesis via CO₂ insertion on terminal and internal epoxides. Reaction conditions: **1a–12a** (4.0 mmol), [N_{8,8,8,1}][HYD] (10% mol), T = 120 °C, p⁰(CO₂) = 20 bar, t = 6 h, solventless conditions. Conversions, yields and selectivities were determined by quantitative ¹H NMR analysis with an internal standard (mesitylene, 0.2 equiv.). ^[a]Isolated yield starting from SO (8.00 mmol).

Surprisingly, high conversions (86 %) were also observed with cyclohexene oxide (CHO, **11a**), an alicyclic epoxide, in contrast with the behavior of previously reported single-component catalysts that exhibited significant catalytic activity only with terminal epoxides. The low selectivity value reported for cyclohexene carbonate (CHC, **11b**) is attributed to the competing formation of poly(cyclohexenecarbonate) (PCHC) and *cis*-1,2-cyclohexanediol, both clearly detectable by ¹H NMR (Figure A4, Appendix Chapter 3 section). The formation of PCHC is further supported by the presence of *trans*-cyclohexene carbonate (*trans*-CHC, 9 % yield) among the reaction products. Interestingly, CHO-derived polyethers, formed upon thermal decomposition of this epoxide, were not detected by ¹H NMR. In contrast, with *trans*-stilbene oxide (**12a**) a sluggish reactivity was observed, with formation of the corresponding COC product **12b** only in trace quantities (Figure A5, Appendix Chapter 3 section). Further optimization studies, beyond the scope of this paper, are required to rationalize the reactivity of [N_{8,8,8,1}][HYD] with internal linear and alicyclic epoxides. Based on the above-mentioned preliminary reactivity data, the proposed mechanism for CO₂ insertion reaction catalyzed by hydroquinolate ILs is reported in Scheme 3.3.



Scheme 3.3: Top: proposed mechanism for COC formation catalysed by $[N_{8,8,8,1}][HYD]$ at CO_2 overpressures ($p^0(CO_2) \geq 10 \text{ bar}$). Bottom: activity of $[N_{8,8,8,1}][HYD]$ at low CO_2 overpressures ($p^0(CO_2) < 10 \text{ bar}$), leading to the formation of epoxides ring opening products.

Two different mechanistic manifolds occur depending on CO_2 overpressure. At high CO_2 overpressures ($p^0(CO_2) > 10 \text{ bar}$, **Scheme 3.3**, top), CO_2 activation occurs initially via nucleophilic attack of the hydroquinolate anion, producing a hemicarbonate intermediate (I), that performs nucleophilic ring opening of the epoxide, itself activated by electrostatic interaction with the tetralkylammonium counteranion. The resulting alkoxide intermediate (II) then undergoes intramolecular cyclization releasing the COC product, regenerating the $[N_{8,8,8,1}][HYD]$ catalyst. This mechanism differs significantly from the commonly accepted double insertion mechanism, where the hydroquinolate anion attacks the epoxide producing an alkoxide intermediate, which then

evolves in a hemicarboxylate intermediate upon insertion of CO₂, yielding the COC product via irreversible intramolecular cyclization.

Moreover, ¹³C NMR analysis of [N_{8,8,8,1}][HYD] homogeneous mixtures recorded in the polar aprotic solvent DMSO-d₆ in the presence of CO₂ overpressure ($p^0(\text{CO}_2) = 0.5$ bar) showed a novel peak at 162 ppm, attributed to the formation of the hemicarboxylate intermediate (**I**) (see **Figures A5 and A6, Appendix Chapter 3** section for further details). Interestingly, performing the reaction in the absence of CO₂ led to the formation of epoxide ring-opening products, such as diol and polyethers, as depicted in **Figure A7, Appendix Chapter 3** section, confirming that, at low CO₂ overpressures ($p^0(\text{CO}_2) < 10$ bar) epoxide ring opening products are mainly formed via a double nucleophilic attack mechanism through the alkoxide intermediate (**III**) (**Scheme 3.3**, bottom). The proposed mechanism is in agreement with the CO₂ chemisorption ability observed for phenolate based ILs,⁹ which are currently employed for post-combustion CO₂ capture.³⁹ Further experimental and computational studies are required to fully understand the role of polyhydroxybenzene anions in CO₂ interaction/activation. In particular when employing ILs as catalysts, it is difficult to assess independently the role of the anion, requiring alternative liquid sorbents composed of phenolate and alkali metal cations coordinated by crown ethers.¹⁰

3.1.5 Conclusions

A series of dihydroxybenzene derived ILs organocatalysts were prepared following an effective, eco-friendly, halide-free synthetic methodology. These ILs displayed catalytic activity as single component catalysts for the preparation of monosubstituted COCs via CO₂ insertion into terminal epoxides: in all cases catalytic activity was observed without requiring an external nucleophile (*e.g.* halide salt). Hydroquinone derived methyltrioctylammonium hydroquinolate, [N_{8,8,8,1}][HYD], was the most active catalyst of the series. Preliminary activity data on a simple, internal cyclic epoxide, cyclohexene oxide (CHO) showed catalytic activity, which is unprecedented for single component organocatalysts, although with limited selectivity, due to the tendency of CHO of evolving into both the COC and polycarbonate product. In all cases, $p^0(\text{CO}_2) \geq 10$ bar is required to observe appreciable selectivity towards the desired COC product: this is ascribed to the *in situ* formation of the catalytically competent hemicarboxylate derivative, which promotes CO₂ insertion into epoxides via an unusual hemicarboxylate-alkoxide pathway.

3.1.6 Experimental

Materials and Methods

All reagents and solvents employed [ethyl acetate (EtOAc), diethyl ether (Et₂O), petroleum ether, toluene, methanol (MeOH), mesitylene (MES), dimethylcarbonate (DMC), trioctylamine (TOA), catechol (CAT), resorcinol (RES), hydroquinone (HYD), styrene oxide (SO), epichlorohydrin, 1,2-epoxyhexane, butyl glycidyl ether, phenyl glycidyl ether, silica gel (70–230 mesh), chloroform-d (CDCl₃), MeOH-d₄ and dimethyl sulfoxide-d₆ (DMSO-d₆)] were purchased from Sigma Aldrich (now Merck)

with > 98 % purity, and, unless otherwise specified, used without further purification. Catechol was purified prior its use, by recrystallization from toluene. CO₂ 99.999 % was supplied by SIAD. Qualitative and quantitative analysis and characterization of reaction mixtures and pure products were performed with: a) GC-MS system consisting of an Agilent 6890N GC equipped with an HP-5 capillary column (30 length, 0.32mm internal diameter, 0.25mm film thickness), coupled with Agilent Technologies 5975 mass detector operating at 70eV; b) Bruker Ascend 400(AV400) NMR spectrometer, operating at 400MHz for ¹H nuclei, 100MHz for ¹³C nuclei and 75Hz for ³¹P nuclei; c) Perkin-Elmer Spectrum One FT-IR spectrometer, operating at wavenumbers ranging from 400 to 4000 cm⁻¹. Thermogravimetric (TGA) analysis were performed with a Perkin Elmer TGA4000 instrument. Thermal stabilities were evaluated in ramp mode (T ramp: 10 °C·min⁻¹ to 600 °C, N₂: flow 40 mL·min⁻¹, ceramic pans). GC-MS analyses were performed in EtOAc or Et₂O, while ¹H NMR and ¹³C NMR samples were prepared using deuterated solvents (CDCl₃, MeOH-d₄ or DMSO-d₆, deuteration grade > 99.9% D in all cases). For ¹H NMR spectra, the deuterated solvent residual signal was selected as the spectrum reference.

Quaternization reactions

Methyltrioctylammonium methylcarbonate [N_{8,8,8,1}][MC] was synthesized according to a previously reported literature procedure.³⁰ 15 mL (178 mmol) of DMC, 10 mL (23 mmol) of trioctylamine (TOA) and 15 mL of methanol were introduced in a 100 mL stainless steel autoclave. The autoclave was sealed and the mixture degassed executing three vacuum-nitrogen cycles and finally backfilled with nitrogen. The autoclave was heated at T = 140 °C for t = 20 h under vigorous stirring. Then, the autoclave was cooled to room temperature, vented and opened. Methanol and residual DMC were quantitatively removed from the mixture by evaporation under reduced pressure at T = 40 °C, to give [N_{8,8,8,1}][MC] (10 g, 28 mmol) as a viscous clear pale-yellow liquid synthesized in > 99 % yield. A small amount (< 1.0 equiv, determined by ¹H NMR) of methanol remained incorporated in the sample even after extensive drying under high vacuum. The same procedure was used to synthesize 1-butyl-3-methylimidazolium methylcarbonate [C₄C₁Im][MC], employing 23 mmol of 1-butylimidazole instead of TOA.^{38,39} [C₄C₁Im][MC] was obtained as a mixture of the desired ILs and zwitterionic 1-butyl-3-methyl-imidazolium-2-carboxylate (for further details, see **Figures S3** and **S4**, **Characterization Chapter 3** section) and used in the subsequent metathesis step without further purification.⁴⁰

General procedure for ILs metathesis

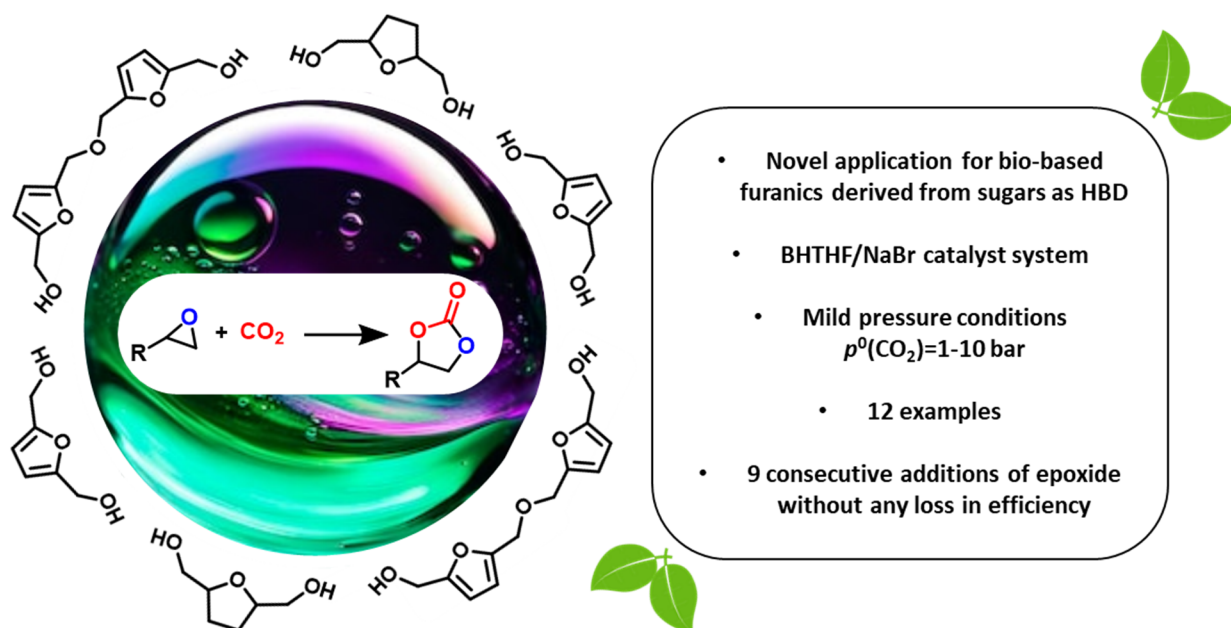
Metathesis reactions were carried out according to a previously reported literature procedure.³⁰ A methanol solution of the corresponding dihydroxybenzene derivative (4.5 mmol, 0.49 g in 5 mL of MeOH) was slowly added dropwise under stirring, to a methanol solution of [N_{8,8,8,1}][MC] (4.5 mmol, 2.00 g in 10 mL of MeOH). The round bottom flask was equipped with a condenser and heated at T = 60 °C. The solution was stirred for t = 18 h (overnight): during this time the initial clear yellow solution turned dark red/brown. The solution was cooled, and methanol was quantitatively removed from the mixture by evaporation under reduced pressure at T = 45 °C, to give the corresponding ionic liquid in quantitative yield. [N_{8,8,8,1}][CAT], [N_{8,8,8,1}][RES] and [N_{8,8,8,1}][HYD] were

synthesized following this methodology and characterized by ^1H NMR and ^{13}C NMR. The same procedure was used to synthesize $[\text{C}_4\text{C}_1\text{im}][\text{HYD}]$ and $[\text{DBUH}][\text{HYD}]$ starting from 4.5 mmol of $[\text{C}_4\text{C}_1\text{im}][\text{MC}]$ or 1,8-diazabicyclo[5.4.0]undec-7-ene, respectively.

General procedure for CO_2 insertion reactions on styrene oxide (1a**)**

A 3 mL glass inlet for autoclave reactors, equipped with a pierced glass stopper and a stirring bar, was charged with 4.00 mmol of styrene oxide (SO, **1a**, 0.50 g), 0.4 mmol (0.1 equiv.) of the ILs catalyst to be tested and mesitylene (0.8 mmol, 114 μL , 0.2 equiv.) as internal standard. The glass reactor was introduced into a 10 mL stainless steel autoclave and charged with CO_2 [$p^0(\text{CO}_2) = 10\text{--}50$ bar]. CO_2 insertion reactions were performed at $T = 80\text{--}140$ $^\circ\text{C}$ for $t = 2\text{--}18$ h. At the end of the reaction time the autoclave was cooled in a water bath, vented and the crude reaction mixtures were analysed by ^1H NMR spectroscopy. Catalytic tests at $p^0(\text{CO}_2) = 1$ bar were carried out in a similar fashion using a round bottom flask equipped with a stirring bar, reflux condenser, and an adaptor connected to a CO_2 balloon. The substrate scope was conducted using the same procedure with different epoxides (4.00 mmol) instead of **1a**. Isolated Yields. Isolated yields were obtained purifying the products via column chromatography using SiO_2 (230–400 mesh) as stationary phase. The eluent was a gradient mixture of petroleum ether/ethyl acetate (7:3, 6:4 and 1:1 V/V). For the ^{13}C NMR tests under CO_2 overpressure, 0.1 g of $[\text{N}_{8,8,1}][\text{HYD}]$ were introduced in a 3 mL glass inlet for autoclave reactor and dissolved in 0.5 mL of DMSO-d_6 . The glass reactor was equipped with a pierced glass stopper and a stirring bar and introduced into a 10 mL stainless steel autoclave and charged with CO_2 [$p^0(\text{CO}_2) = 30$ bar]. The system was heated at $T = 80$ $^\circ\text{C}$ for $t = 1$ h before transferring the mixture into a high-pressure NMR tube which was then filled with CO_2 [$p^0(\text{CO}_2) = 5$ bar]. ^{13}C NMR experiments were recorded for 5120 scans.

3.2 5-HMF derivatives as active complexing agent for CO₂ insertion reaction

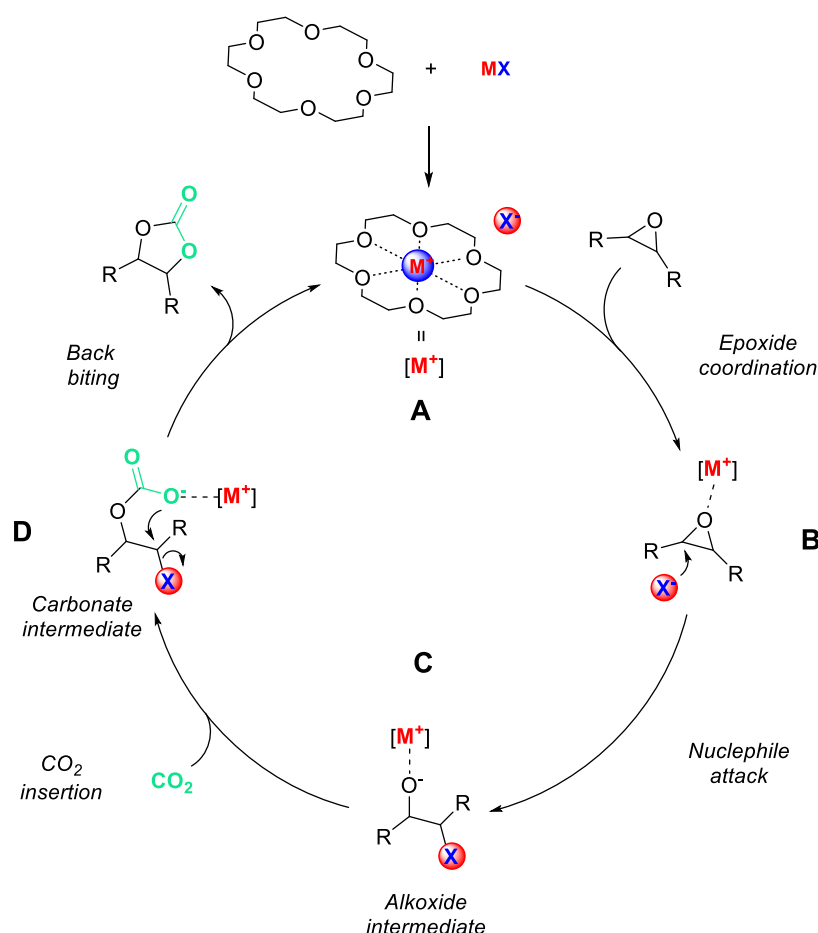


3.2.1 Abstract

This section describes a novel application of renewable-based, furanic derivatives which were successfully employed in CO₂ insertion reaction into epoxides. Temperature, reaction time, reagents' ratio and pressures were optimized prior to testing various bio-based complexing agents in combination with different halide salts. 2,5-bis(hydroxymethyl)tetrahydrofuran (BHTHF), in particular, exhibited superior activity as complexing agent in combination with NaBr, promoting the synthesis of industrially relevant cyclic carbonates in high yields (12 examples, 94-99 % yield) under mild pressure conditions ($p^0(\text{CO}_2) = 1\text{-}10\text{ bar}$, $t = 6\text{ h}$ and $T = 120\text{ }^\circ\text{C}$). Moreover, the robustness of the BHTHF/NaBr catalytic system was demonstrated through nine consecutive additions of epoxide (8 mmol each) without any loss of catalytic efficiency. The results reported in this chapter have been submitted for publication.

3.2.2 Introduction

As explained in **Paragraph 1.2** and **1.3**, CO₂ is the main greenhouse gas present in the atmosphere, but in terms of sustainable organic synthesis it could be considered as a cheap, abundant, non-toxic C¹ building block. A key non-reductive valorization strategy is represented by CO₂ conversion into COCs by reactions with epoxides. This requires overcoming CO₂ low reactivity by combining it with high-energy co-reactants, e.g. epoxides, and specialized catalytic systems incorporating both Lewis/Brønsted acidic and nucleophilic functionalities, high temperature and CO₂ overpressures. The design of active catalytic systems containing both Brønsted or Lewis acid functionalities, is necessary to activate both epoxide and CO₂ as we showed in **Scheme 1.3** in **Section 1.3**. A typical CO₂ insertion catalytic process, requires initial epoxide activation via coordination to an acidic moiety, followed by ring opening of the activated epoxide in presence of a nucleophile, typically as an halide salt.¹ Given the low solubility of cheap and abundant alkali metal halide salts in organic solvents, they are often used in the presence of complexing agents (*e.g.* crown ethers, polyethers and glycols) to improve their solubility in non-aqueous media.⁴¹ As shown in **Scheme 3.4**, crown ether 18-crown-6 is able to coordinate selectively K⁺ and, to a lower extent, Na⁺, the forming a coordination complex (**A**) which allows both epoxide activation as well as increasing the availability of the nucleophilic halide anion. The resulting activated epoxide undergoes by nucleophilic attack by the halide anion (**B**), resulting in the formation of an alkoxide intermediate (**C**). Subsequently, nucleophilic attack of C on CO₂ forms a hem碳酸 intermediate (**D**) which undergoes intramolecular ring closure via a back-biting reaction, releasing the COC product and restoring the catalytic system.



Scheme 3.4: General mechanism for CO₂ insertion into epoxides in presence of a halide salt and a cation complexing agent, 18-crown-6 as hydrogen bond donor (HBD).

After the seminal report by Kuran *et al.* in 1984, on the use of KI in combination with 18-crown-6 ether and other ligands,⁴¹ a plethora of catalytic system based on complexing agent and halide-metal salts active have been reported so far; interestingly, some catalytic systems display catalytic activity for terminal, internal and trisubstituted epoxides.⁴² For example, Werner *et al.* developed a reusable catalyst system based on KI and polydibenzo-18-crown-6, which was used as a polymeric support.⁴³ Additionally, amines such as 4-dimethylaminopyridine,⁴⁴ cucurbit[6]uril,⁴⁵ polydopamine,⁴⁶ and triethanolamine,⁴⁷ as well as hydrogen bond donors like ethylene glycols,⁴⁸ propylene glycol,⁴⁹ pentaerythritol,⁵⁰ and formic acid⁵¹ were investigated as catalysts for CO₂ insertion reactions into epoxides. KI was employed between 0.1 and 10 mol % in combination with ligands or co-catalysts in a wide range of concentrations, up to 50 - 66 % wt. , performing the reaction at temperatures between 40-130 °C.^{42,43,48} More recently, our research group reported a binary homogeneous mixture comprising NaBr and diethylene glycol, optimizing a CO₂ insertion protocol both in batch and continuous flow (CF) conditions. In particular, the continuous flow reaction took place at T = 220 °C and p = 120 bar improving COC productivity up to 27.6 mmol·h⁻¹, and allowing catalyst recycle for 4 subsequent CF-tests through a semi-continuous extraction procedure.⁵²

By contrast, divalent alkaline earth metals have been less investigated: in 2019 Werner and co-workers developed a COC synthetic methodology involving CaI_2 in combination with poly(ethyleneglycol) dimethyl ether (PEG DME 500) as catalysts. This system proved effective towards CO_2 insertion into both terminal and internal epoxides: at $T = 25\text{--}90\text{ }^\circ\text{C}$ and $p^0(\text{CO}_2) = 10\text{--}50$ bar, the corresponding COCs (27 examples) were obtained in yields ranging from 51 to 99%. The catalytic system was then further optimized using PEG400 dimethyl ether as a complexing agent, allowing to scaling up the CO_2 insertion reaction starting from 10 g of epoxide.⁵³

To improve the overall sustainability profile and reduce the toxicity of some of the above-mentioned catalytic systems, numerous bio-based products derived have been utilized as catalysts or in combination with catalytic materials for the conversion of CO_2 into cyclic carbonates. These include amino acid-based systems, cellulose, saccharides, lignin and lignocellulosic materials, choline-derived species, guanidine and guanidinium salts, among other less explored compounds as detailed in this recent review.⁵⁴ Notably, bio-based system for the insertion of CO_2 into epoxides based on furan derivatives were not reported so far, therefore this work reports the first example of furan-based catalytic systems applied to CO_2 insertion reactions.

5-hydroxymethylfurfural (HMF) is the most chemically versatile sugar-derived furan.^{55,56} HMF can be transformed through oxidation,^{57,58} hydrogenation,^{57,59} hydrolysis,⁶⁰ esterification,⁶¹ etc. etc. into various chemicals such as furan-2,5-dicarbaldehyde (FFC),⁵⁵ 2,5-furandicarboxylic acid (FDCA)⁶² and its esters,⁶³ bis(hydroxymethyl)furan (BHMF)⁶⁴ and its derivatives, 5,5'-oxy(bismethylene)-2-furaldehyde (OBMF),⁶⁵ 2,5-dimethylfuran (DMF),⁵⁹ and levulinic acid.⁶⁶ These compounds find applications as reaction intermediates, monomers for biopolymers, or fuel additives. Although HMF has been identified as a key platform chemical for sustainable chemistry, current technological limitations and high production costs limit its industrial competitiveness. Despite the synthetic limitations, new applications for furanic bio-based molecules represent a relevant and timely research topic. In this project, we focused mainly on the use of BHMF, 2,5-bis(hydroxymethyl)tetrahydrofuran (BHTHF), and 5,5'-oxybis(methylene)bis(furan-5,2-diyl)dimethanol (OBMF-H) as co-catalysts for the insertion of CO_2 into epoxide substrates, with the ultimate goal of obtaining COCs.

We observed that CO_2 insertion in model epoxides is possible employing a catalytic system based on 2,5-bis(hydroxymethyl)tetrahydrofuran (BHTHF) and NaBr. BHTHF was selected as a model hydrogen bond donor (HBD) due to its effective coordination of Na^+ cations. After an initial screening of reaction parameters under batch conditions in pressurized containers, the reaction was also conducted under atmospheric CO_2 pressure. The optimized conditions were applied to several different terminal and internal epoxides (12 examples), observing excellent conversions for terminal ones (from 94 to > 99 %) and obtaining the corresponding COCs with selectivity from 70 to 99 %. Moreover, the robustness of the BHTHF/NaBr catalytic system was demonstrated through nine repeated additions of epoxide (8 mmol each) without any loss in catalytic efficiency.

3.2.3 Preparation of Furanic derivatives

To obtain large amounts of HMF derivatives (*ca.* 20 g), we exploited a synthetic procedure recently reported by Aricò and co-workers, suitable for the synthesis of HMF and HMF-derived BHMF, OBMF and OBMF-H on a multigram scale, as shown in **Figure 3.5**.⁶⁷ Initially, HMF was directly synthesized for D-fructose (*ca.* 40 g) in presence of an heterogeneous Brønsted acid catalyst, tetraethylammonium bromide (TEAB) in presence of DMC as solvent. Part of the HMF was reduced quantitatively to BHMF using NaBH₄ as reducing agent, while the remaining HMF underwent an auto-etherification reaction, obtaining OBMF (Yield = 97 %), which was subsequently reduced quantitatively to OBMF-H, again using NaBH₄ as reductant.⁶⁸ Finally, BHMF (3.00 g, 23.4 mmol,) was further reduced to BHTHF (2.98 g, Yield = 98 %,) using Ru/C (5% w/w) with $p^0(\text{H}_2) = 30$ bar in THF. The Ru/C catalyst was recovered and recycled up to four times for the preparation of a new batch of BHTHF (*vide infra*).

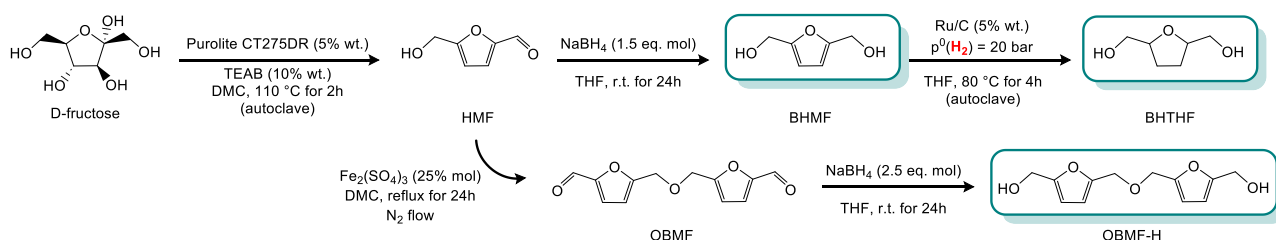


Figure 3.5: Synthesis of HMF derivatives starting from D-fructose.

3.2.4 CO₂ insertion reactions

Styrene oxide (SO, **1a**) was chosen as model terminal epoxide, due to its limited volatility and easy analytical detection, while mesitylene (20 % mol) was added as internal standard. All CO₂ insertion reactions were carried out in solventless conditions (see Experimental Section for further details). BHMF was initially chosen as a model complexing agent, thanks to its simple, high yielding and straightforward preparation (*vide supra*, **Figure 3.5**). The influence of temperature was initially investigated in the range between T = 80 and 140 °C as reported in **Figure 3.6**. CO₂ insertion reaction on **1a** were monitored for t = 18 h, in the following experimental conditions $p^0(\text{CO}_2) = 40$ bar, 1.20 mmol of BHMF, 0.40 mmol of NaBr (NaBr/BHMF = 1:3 mol/mol).

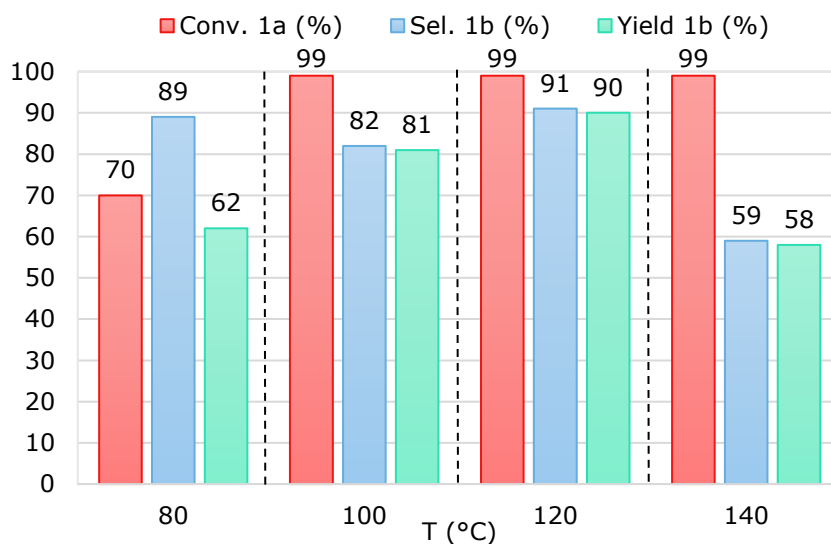
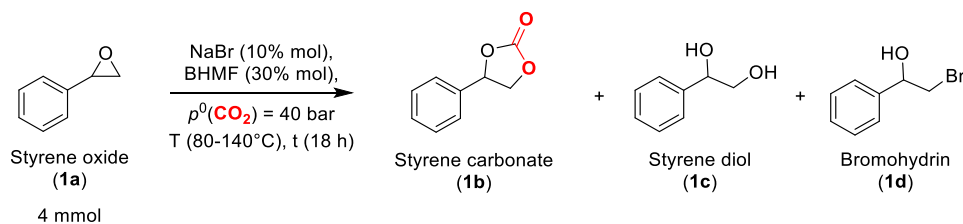


Figure 3.6: Influence of reaction temperature on CO_2 insertion into styrene oxide (**1a**) catalyzed by NaBr/BHMF. Conditions: **1a** (4.0 mmol), NaBr/BHMF = 1:3 mol/mol (0.4 mmol of NaBr and 1.2 mmol of BHMF) $t = 18 \text{ h}$, $T = 80-140^\circ\text{C}$, $p^0(\text{CO}_2) = 40 \text{ bar}$. Conversion of **1a**, selectivity and **1b** yield were calculated by ^1H NMR in presence of an internal standard (mesitylene).

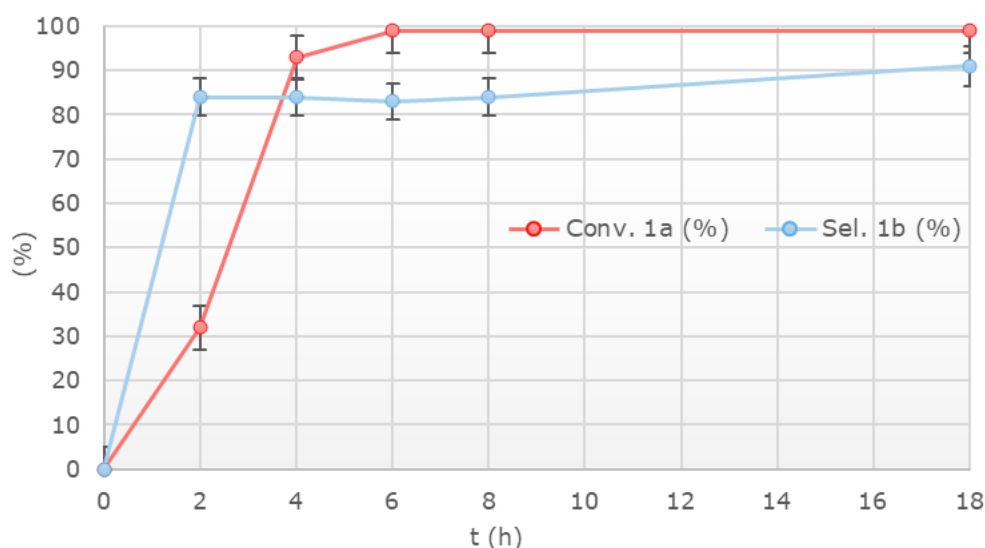
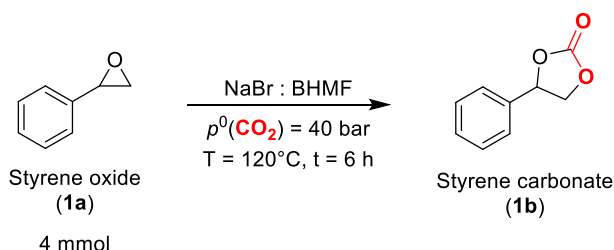


Figure 3.7: Influence of reaction time on CO_2 insertion into styrene oxide (**1a**) catalyzed by NaBr/BHMF. Conditions: **1a** (4.0 mmol), NaBr/BHMF = 1:3 mol/mol, $[\text{NaBr}] = 0.4 \text{ mmol}$, $[\text{BHMF}] = 1.2 \text{ mmol}$, $t = 0-18 \text{ h}$, $T = 120^\circ\text{C}$, $p^0(\text{CO}_2) = 40 \text{ bar}$. Conversion of **1a** and selectivity towards **1b** calculated by ^1H NMR in presence of an internal standard (mesitylene).

Then the influence of reaction time was evaluated as shown in **Figure 3.7**. Quantitative conversion of **1a** was already after $t = 6$ h, observing a selectivity towards **1b** always $> 83\%$. Finally, as shown in **Table 3.3**, a series of experiments was carried out at $T = 120$ °C, $t = 6$ h and $p^0(\text{CO}_2) = 40$ bar, to study the effect of the relative ratio of NaBr and BHMF.

Table 3.3: Effect of the ratio of NaBr and BHMF on CO_2 insertion into **1a**.



Entry	NaBr (mmol)	BHMF (mmol)	Conv. ^a 1a (%)	Sel. ^a 1b (%)	Yield ^a 1b (%)
1	0.40	none	n.d.	0	0
2	none	1.20	n.d.	0	0
3	0.40	1.20	99	79	78
4	0.20	1.20	99	80	79
5	0.10	1.20	99	76	75
6	0.40	2.40	99	66	65

Conditions: **1a** (4.0 mmol), $t = 6$ h, $T = 120$ °C, $p^0(\text{CO}_2) = 40$ bar. ^aConversion of **1a**, selectivity and yield towards **1b** calculated by ^1H NMR in presence of an internal standard (mesitylene, 0.2 equiv.).

Initially, some blank tests were performed with only one of the components of the catalytic system (Entries 1 and 2, **Table 3.3**) to demonstrate that their simultaneous presence is essential to carry out the reaction. When employing the NaBr/BHMF catalytic system, we observed that increasing the amount of BHMF, the selectivity towards **1b** decreased (*cfr.* Entries 3 and 6, **Table 3.3**). The observed behavior was ascribed to the increased viscosity of the reaction mixture, preventing an ideal mixing of the solution during the reaction. Conversely, decreasing the amount of NaBr from 0.40 mmol to 0.10 mmol (*cfr.* Entries 3-5, **Table 3.3**), had a mild effect on the selectivity towards **1b**. For this reason, we chose to continue the study using an NaBr/BHMF ratio of 1:6 mol/mol ($[\text{NaBr}] = 0.2$ mmol, $[\text{BHMF}] = 1.2$ mmol). As reported in **Figure 3.8**, the influence of CO_2 pressure was explored between 5 and 60 bar, performing the reaction at $T = 120$ °C for $t = 6$ h using a catalytic system consisting of NaBr/BHMF 1:6 mol/mol.

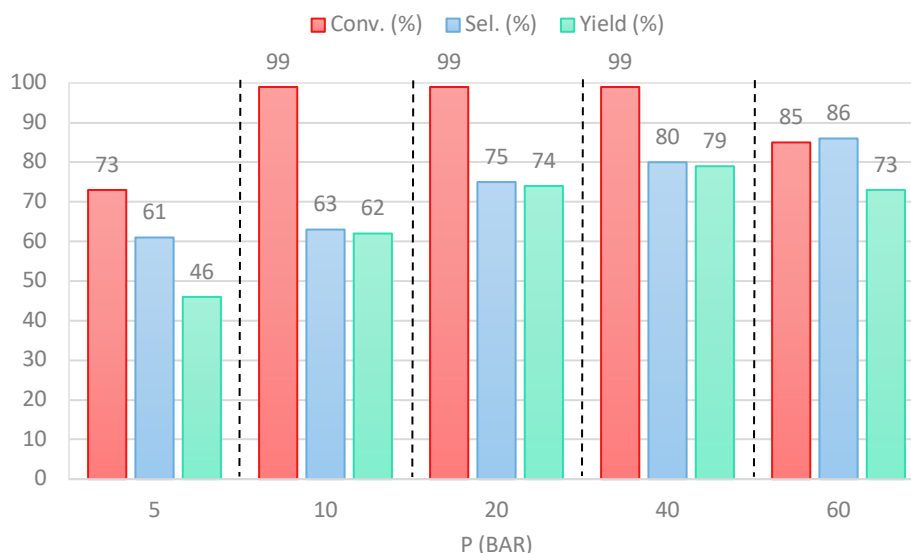
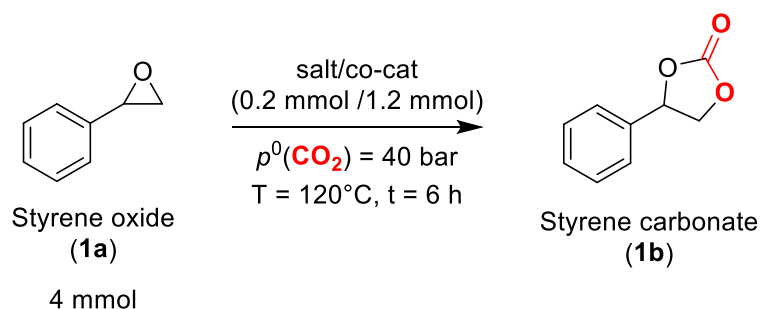


Figure 3.8: Influence of CO₂ pressure on the synthesis of **1b** via CO₂ insertion into **1a** catalyzed by NaBr/BHMF. Conditions: **1a** (4.0 mmol), NaBr/BHMF = 1:6 mol/mol, [NaBr] = 0.2 mmol, [BHMF] = 1.2 mmol, t = 6 h, T = 120 °C, $p^0(\text{CO}_2)$ = 40 bar. Conversion of **1a**, selectivity and yield towards **1b** were calculated by ¹H NMR in presence of an internal standard (mesitylene, 0.2 equiv.).

Although **1a** conversion was always quantitative, the highest selectivity towards **1b** (80 %) was observed performing the reaction at $p^0(\text{CO}_2)$ = 40 bar, while poorer results were obtained with $p^0(\text{CO}_2)$ = 5-20 bar. Increasing the CO₂ pressure to 60 bar led to a lower selectivity towards **1b**. This behavior was rationalized observing the endogenous pressure value in the autoclave (75 bar), typical of super-critical conditions and likely causing a lower interaction between CO₂ and the epoxide, decreasing the overall activity of the catalytic system.⁶⁹

With optimized conditions established, we proceeded to investigate the effects of various alkali salts and furan-based complexing agents, as detailed in **Table 3.4**.

Table 3.4: Effects of the different alkali metal salts and furan-derived Brønsted acidic co-catalyst on CO₂ insertion into **1a**.



Entry	co-cat	salt	Conv. 1a (%) ^a	Sel. 1b (%) ^a	Yield 1b (%) ^a
1	BHMF	NaCl	16	44	7
2	BHMF	KCl	25	44	11
3	BHMF	NaBr	99	80	79
4	BHMF	NaI	99	76	75
5	BHMF	KBr	99	75	75
6	BHMF	KI	74	77	57
7	OBMF-H	NaBr	49	83	40
8	BHTHF	NaBr	99	90	90
9 ^b	BHTHF	NaBr	99	85	85
10 ^c	BHTHF	NaBr	94	84	80

Reaction conditions: **1a** (4.0 mmol), NaBr/BHMF = 1:6 mol/mol, $p^0(\text{CO}_2) = 40 \text{ bar}$, $T = 120^\circ\text{C}$ and $t = 6 \text{ h}$. Conversion of **1a**, selectivity and yield towards **1b** were calculated by ¹H NMR in presence of an internal standard (mesitylene, 0.2 equiv.). ^bPerformed at $p^0(\text{CO}_2) = 10 \text{ bar}$. ^cPerformed at $p^0(\text{CO}_2) = 1 \text{ bar}$

The alkali metal salts served as direct nucleophile sources, showing a typical halide nucleophilicity trend ($\text{I} \approx \text{Br} > \text{Cl} > \text{F}$) for the CO₂ insertion reactivity in the presence of H-bond donors (see Entries 1, 3 and 4, **Table 3.4**). The use of chloride salts, however, resulted in lower reactivity (Entries 1 and 2, **Table 3.4**), likely due to their diminished efficiency as nucleophile and decreased selectivity owing to their poorer leaving group ability. Conversely, bromide and iodide salts were more active, achieving in all cases a quantitative **1a** conversion with excellent selectivity towards the desired **1b** product (75-80 %, Entries 3-6, **Table 3.4**). Considering the ionic radii of the alkali metal cations used ($\text{K}^+ = 138 \text{ pm}$, $\text{Na}^+ = 102 \text{ pm}$) it is plausible to assume that this characteristic could affect the complexing activity of furanic derivatives. However, our experimental comparison did not reveal any significant difference in reactivity between sodium and potassium salts, indicating that BHMF exhibits robust complexing capacity regardless of the cation size. Subsequently, different furanic derivatives, such as OBMF-H and BHTHF were tested as complexing agents using NaBr as the halide source. OBMF-H led to a poor conversion (Entry 7, **Table 3.4**). The observed poorer catalytic performance was ascribed to the partial solubility of OBMF-H in neat epoxide solutions, preventing its complete solubilization in the reaction mixture. On the other hand, BHTHF outperformed BHMF under optimized reaction conditions (*cfr.* Entries 3 and 8, **Table 3.4**). Interestingly, when the

NaBr/BHTHF catalytic system was tested at lower CO₂ pressures, it retained a good catalytic performance even at atmospheric CO₂ pressure, achieving 94% of conversion of **1a** and 84% selectivity towards **1b** (Entries 8-10, **Table 3.4**). Performing CO₂ insertion reactions at atmospheric CO₂ pressure allowed for the use of standard laboratory glassware, avoiding specialized equipment to handle overpressure conditions. This experimental setup simplification is particularly useful for scaling up the reaction.

The scope of the optimized protocol for COCs synthesis was also evaluated on a library of terminal and internal epoxides, as summarized in **Figure 3.9**.

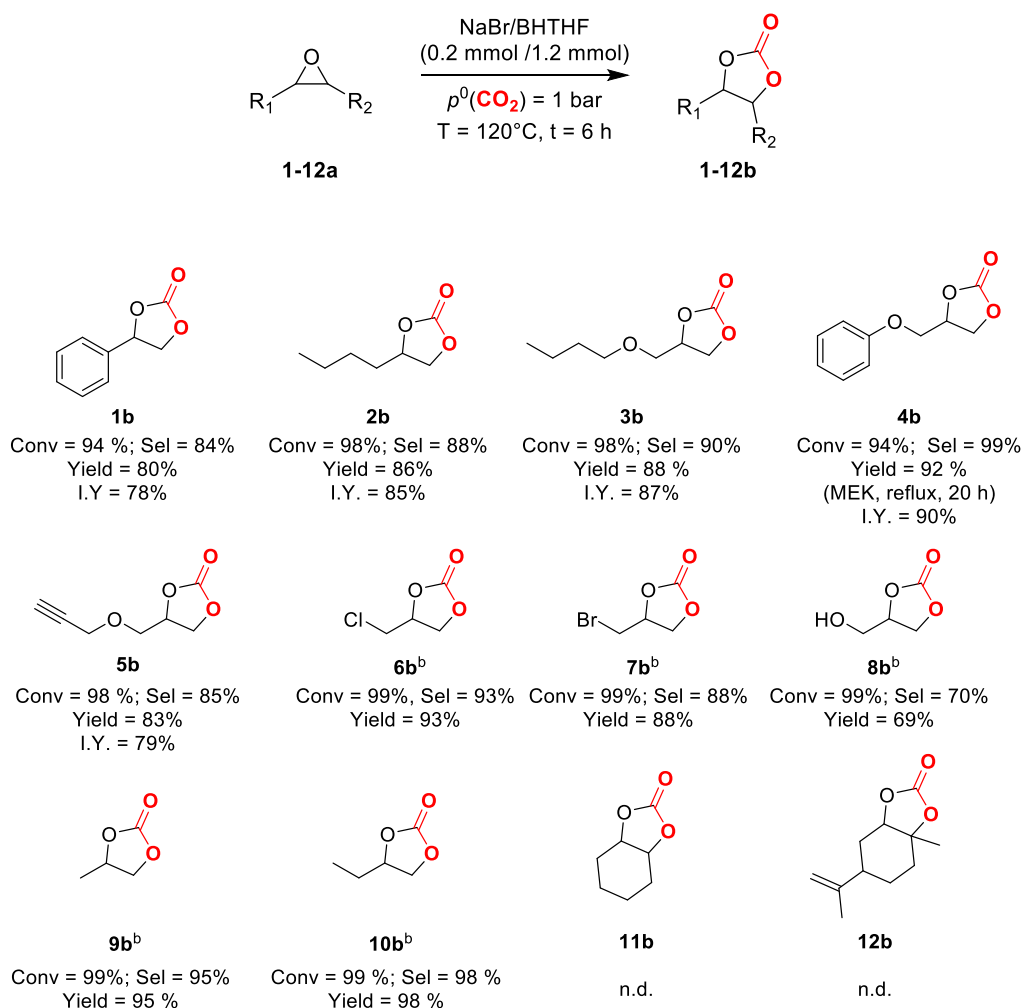


Figure 3.9: Substrate scope of BHTHF/NaBr catalyzed CO₂ insertion reactions. Experimental conditions: **1a-12 a** (4.0 mmol); *t* = 6 h, *T* = 120 °C, *p*⁰(CO₂) = 1 bar, epoxide (4.0 mmol), NaBr/BHTHF = 1:6 mol/mol, [NaBr] = 0.2 mmol, [BHTHF] = 1.2 mmol. Conversion, yield and selectivity were determined by quantitative ¹H NMR analysis with an internal standard (mesitylene, 0.2 equiv.). ^bPerformed at *p*⁰(CO₂) = 10 bar.

Terminal epoxides **2a-5a** were quantitatively converted in the corresponding COCs with excellent selectivity and were subsequently isolated by column chromatography (see Experimental Section for further details). Industrially relevant substrates such as epichlorohydrin (**6a**), epibromohydrin (**7a**) and glycidol (**8a**) were tested at atmospheric CO₂ pressure, yielding the corresponding COC

products in moderate yield (Yield = 51-59 %, see Table S1). For these substrates a change in the reaction mixture appearance was observed, shifting from transparent and homogeneous to a cloudy white heterogeneous mixture at increasing epoxide conversions. This physical change was attributed to the progressive formation of COC product, leading to a change in the overall polarity of the reaction mixture from apolar to polar aprotic, reducing the solvation of the halide salt and lowering the activity of the catalytic system. More promising results were observed by performing these reactions at $p^0(\text{CO}_2) = 10$ bar (**Figure 3.9**). Moreover, for substrates **9b** and **10b**, ^1H NMR analysis of the crude reaction mixture obtained at $p^0(\text{CO}_2) = 1$ bar indicated a loss of material, due to the high volatility of the epoxide reagents in the chosen experimental conditions. Increasing CO_2 pressure to 10 bar yielded to improved results (Yield ≥ 95 %). Internal disubstituted (**11b**) and trisubstituted (**12b**) epoxides were also tested, but, unfortunately, formation of the corresponding COC products was not observed in both cases, confirming the lower reactivity of these substrates, ascribed to the presence of bulky and rigid substituents on the reactive cyclooxapropene moiety. A mechanistic hypothesis for catalytic activation by BHTHF is shown in **Figure 3.10**: BHTHF plausibly plays a dual role, acting as both chelating agent for Na^+ and as HBD promoting epoxide ring opening. This system is similar to diethylene glycol based one previously reported by our group, which is a well-documented example of HBD complexing activity.^{48,53,70–72}

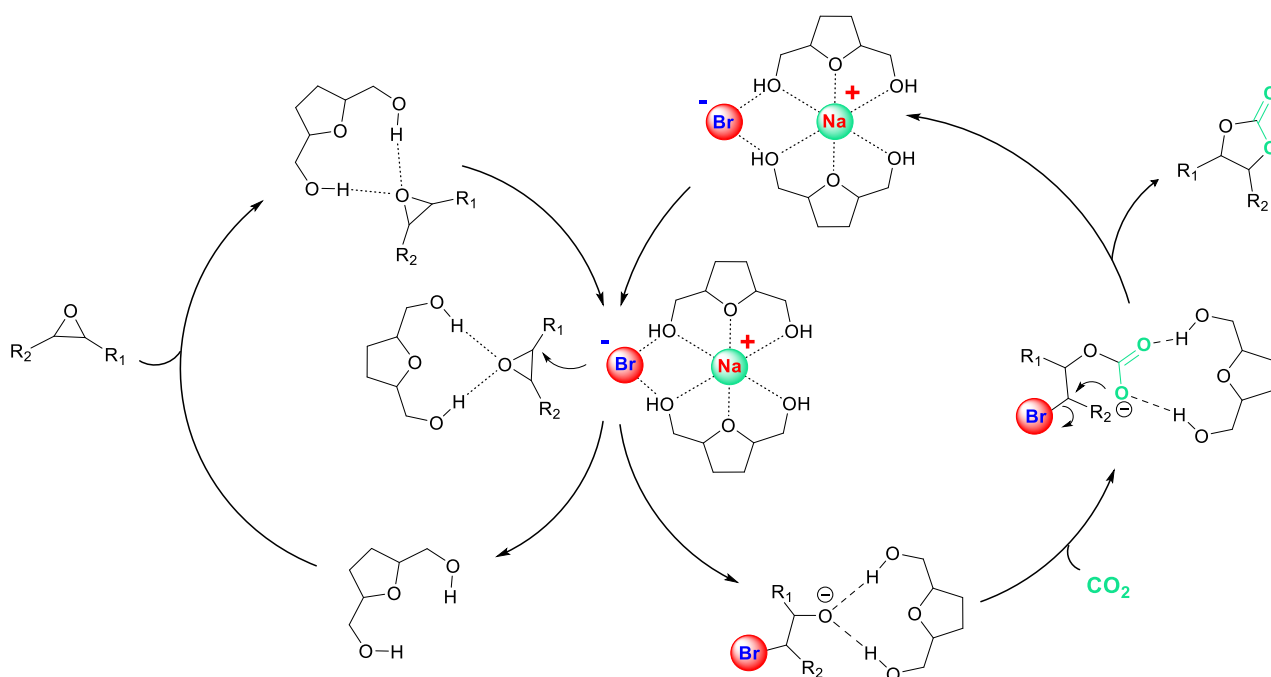
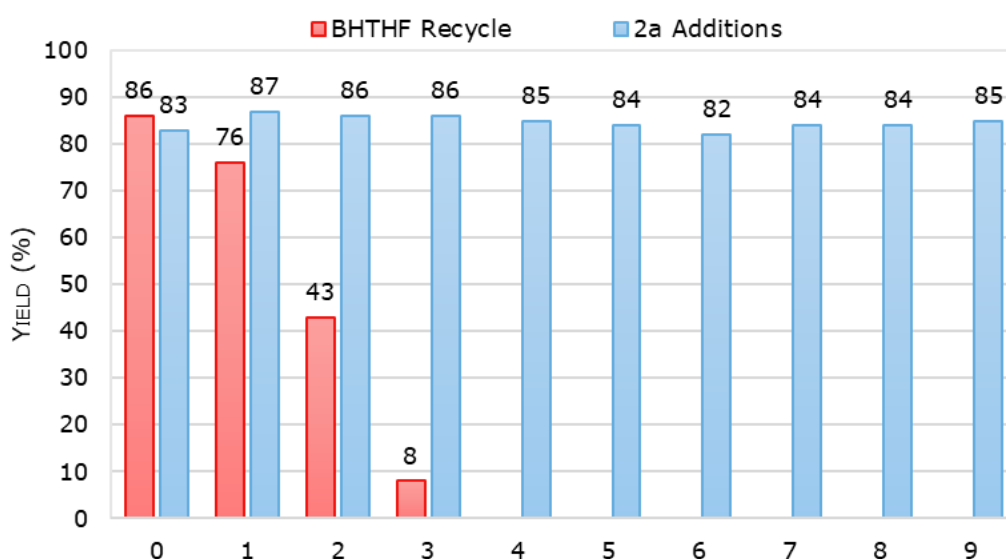


Figure 3.10: Proposed mechanism for the co-catalytic effect of BHTHF, active towards both Na^+ complexation, HBD epoxide activation and stabilization of the reaction intermediates.

Finally, we tried to design an optimized procedure to recycle the catalytic systems. We exploited the low solubility of BHTHF in Et_2O to extract it selectively from the reaction mixture containing also the COC product. Moreover, we selected **2a** as a model epoxide substrate for recycling studies thanks to the presence of the linear C_4 alkyl chain (see **Figure A9**, **Appendix Chapter 3** section), necessary to ensure a good solubility in Et_2O . The insertion reaction was conducted using 0.826 g (1.0 mL, 8.0 mmol) of **2a** in the optimized reaction conditions ($t = 6$ h, $T = 120$ °C, $p^0(\text{CO}_2) = 1$ bar).

Unfortunately, the catalytic system could not be recovered multiple times through extraction, as indicated by the red bars in **Figure 3.11**. This issue arises from the poor solubility of BHTHF in Et₂O, which progressively reduces the concentration of the complexing agent, leading to a quick loss of catalytic efficiency. However, as shown in **Figure A10** (**Appendix Chapter 3** section), the selectivity remained high across the four attempted recycles. To demonstrate the robustness of the BHTHF/NaBr catalytic system, repeated additions of epoxide **2a** were performed. As indicated by the blue bars in **Figure 3.11**, this approach allowed us to perform CO₂ insertion reaction for nine additional runs without any loss in catalytic efficiency in terms of selectivity and yield. In each consecutive run quantitative conversion of the starting epoxide was observed, as shown in **Figure A11** (**Appendix Chapter 3** section).



*Figure 3.11: Comparison of catalytic recycles by extraction with Et₂O (red bars) with repeated additions of **2a** (blue bars). Conditions: **2a** (8.0 mmol), *t* = 6 h, *T* = 120 °C, *p*⁰(CO₂) = 1 bar, NaBr/BHTHF = 1:6 mol/mol, [NaBr] = 0.4 mmol, [BHTHF] = 2.4 mmol. Conversion of **2a**, yield and selectivity towards **2b** were determined by quantitative ¹H NMR analysis with an external standard.*

3.2.5 Conclusion

In summary, we successfully demonstrated a novel application of bio-based furanics derived from sugars, *e.g.* BHTHF, and OBMF-H. These bio-based compounds were tested for the first time as catalysts for CO₂ fixation into epoxides in combination with cheap and abundant alkali metal salts. Initially, key reaction parameters, such as *e.g.* temperature, reaction time, catalyst/co-catalyst ratio, CO₂ overpressure, choice of alkali metal halide salt co-catalyst, were screened and optimized. BHTHF was an effective complexing agent in combination with NaBr, promoting the synthesis of industrially relevant COCs, obtained in high yields under mild reaction conditions (*p*⁰(CO₂) = 1-10 bar, 6 h at *T* = 120 °C). Furthermore, the robustness of the BHTHF/NaBr catalytic system was demonstrated

performing nine consecutive additions of epoxide (8.0 mmol each) without any loss in catalytic efficiency. This reaction system represents a significant advancement in the use of 5-HMF derivatives (especially bio-based polymers) for COCs synthesis under mild reaction conditions, potentially offering a sustainable and efficient pathway for industrial applications.

3.2.6 Experimental

Materials and Methods

All reagents and solvents employed, ethyl acetate (EtOAc), diethyl ether (Et₂O), petroleum ether, mesitylene (MES), dimethyl carbonate (DMC), tetrahydrofuran (THF), D-fructose, Purolite CT275DR, tetraethylammonium bromide (TEAB), sodium borohydride (NaBH₄), iron(III) sulfate [Fe₂(SO₄)₃], sodium chloride (NaCl), sodium bromide (NaBr), sodium iodine (NaI), potassium chloride (KCl), potassium bromide (KBr), potassium iodine (KI), styrene oxide (SO), epichlorohydrin, epibromohydrin, glycidol, propylene oxide, butylene oxide, 1,2-epoxyhexane, butyl glycidyl ether, phenyl glycidyl ether, 2-((prop-2-yn-1-yloxy)methyl)oxirane, cyclohexane oxide, limonene oxide, sodium sulfate (Na₂SO₄), silica gel (70–230 mesh), chloroform-d (CDCl₃), MeOH-d₄ and dimethyl sulfoxide-d₆ (DMSO-d₆), were purchased from Sigma Aldrich (now Merck) with > 98% purity, and, unless otherwise specified, used without further purification. CO₂ 99.999 % was supplied by SIAD. Qualitative and quantitative analysis and characterization of reaction mixtures and pure products were performed with:

- GC-MS system consisting of an Agilent 6890N GC equipped with an HP-5 capillary column (30 m length, 0.32mm internal diameter, 0.25mm film thickness), coupled with Agilent Technologies 5975 mass detector operating at 70eV;
- Bruker Ascend 400 (AV400) NMR spectrometer, operating at 400MHz for ¹H nuclei and 100 MHz for ¹³C nuclei;

GC-MS analyses were performed in EtOAc or Et₂O, while ¹H NMR and ¹³C NMR samples were prepared using deuterated solvents (CDCl₃, MeOH-d₄ or DMSO-d₆, deuteration grade > 99.9%D in all cases). For ¹H NMR spectra, the solvent residual signal was selected as the spectrum reference.

Conversions, yields, and selectivities were calculated by GC with mesitylene as internal standard. Tests were repeated at least twice to ensure reproducibility: conversion and products distribution differed by less than 3% from one experiment to another.

General procedure for CO₂ insertion reactions on styrene oxide (1a)

A 3 mL glass inlet for autoclave reactors, equipped with a pierced glass stopper and a stirring bar, was charged with 4.00 mmol of styrene oxide (SO, **1a**, 0.50 g), NaBr (0.40 mmol, 41 mg), BHMF (1.20 mmol, 154 mg) and mesitylene (0.80 mmol, 114 μL, 0.20 equiv.) added as internal standard. The glass reactor was introduced into a 10 mL stainless steel autoclave and charged with CO₂ [*p*⁰(CO₂) = 40 bar]. CO₂ insertion reactions were performed at T = 80–140 °C for t = 2–18 h. At the end of the reaction time the autoclave was cooled in an ice-water bath, vented (cautiously) and the crude

reaction mixtures were analyzed by ^1H -NMR spectroscopy using CDCl_3 as deuterated solvent. Catalytic tests at $p^0(\text{CO}_2) = 1$ bar were carried out in a similar fashion using a round bottom flask equipped with a stirring bar, reflux condenser, and an adaptor connected to a CO_2 balloon. The substrate scope was carried out according to the same procedure with different epoxides (4.00 mmol) instead of **1a**. Isolated yields were determined purifying the products via column chromatography using SiO_2 (230-400 mesh) as stationary phase. The eluent was a gradient mixture of petroleum ether/ethyl acetate (7:3; 6:4 and 1:1 V/V).

Catalyst recycling and repeated additions

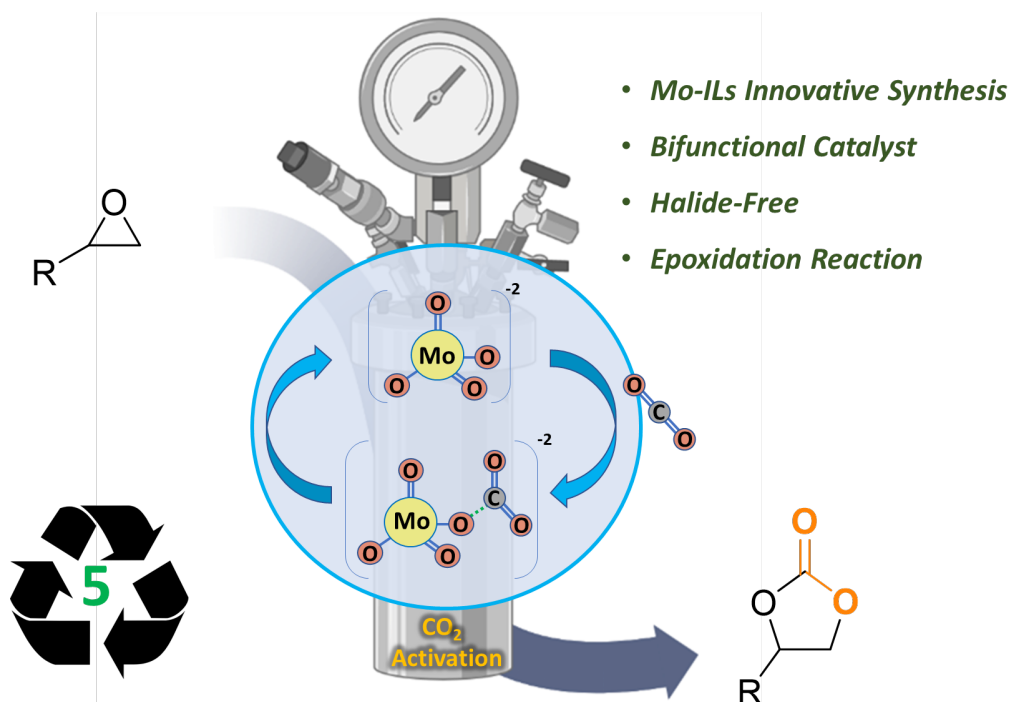
Catalytic system recycling was performed in a 5 mL round bottom flask equipped with a stirring bar, reflux condenser, and an adaptor connected to a CO_2 balloon. The reactor was charged with **2a** (8.00 mmol, 0.83 g, 1.00 mL), NaBr (0.40 mmol, 41 mg), and BHTHF (2.40 mmol, 358 mg). The reactions were carried out under a CO_2 pressure of 1 bar at 120 °C for 6 hours. After each reaction, the product was quantitatively extracted with 3 x 3 mL of Et_2O . The reactor, still containing the catalyst system BHTHF/NaBr, was put under vacuum to remove all residual Et_2O . Subsequently, the reactor was recharged with **2a** (8.00 mmol) for the next recycling cycle. The extracted product mixture was also treated with rotary evaporation to remove excess Et_2O . Mesitylene (228 μL , 1.60 mmol) was then added as an internal standard. The crude reaction mixtures were analyzed by ^1H -NMR spectroscopy using CDCl_3 as deuterated solvent.

For repeated additions, reactions were conducted in a 10 mL round bottom flask. After each run, a 5 μL aliquot of the reaction mixture was withdrawn and diluted with 0.5 mL of a 70 mM solution of mesitylene in CDCl_3 . This solution was then analyzed by ^1H NMR spectroscopy. The reactor, still containing the crude reaction mixture, was recharged with additional 8.00 mmol of **2a** and put under to a CO_2 pressure of 1 bar before proceeding with the subsequent reaction cycle.

Preparation of 2,5-bis(hydroxymethyl)tetrahydrofuran (BHTHF)

3.00 g (23.4 mmol) of BHMF, 5% mol of Ru/C (5% w/w) and 30 mL of THF were charged in a 100 mL stainless steel autoclave. The autoclave was sealed and the mixture degassed by executing three vacuum-nitrogen cycles and left under vacuum before backfilling with 30 bar of hydrogen. The autoclave was heated at $T = 80$ °C for $t = 5$ h under vigorous stirring. Then, the autoclave was cooled to room temperature, vented and opened. The reaction mixture was filtered to recover the catalyst and THF was quantitatively removed by evaporation under reduced pressure to give BHTHF (2.98 g, 98 % yield) as a viscous transparent liquid.

3.3 One-pot processes: Molybdate Ionic Liquids as Halide-Free Catalysts for CO₂ Fixation into Epoxides



3.3.1 Abstract

This section describes the syntheses of a series of molybdate and polyoxomolybdate ionic liquids (ILs), their full spectroscopic characterization (FT-IR, ¹H-, ¹³C-, ³¹P-, and ⁹⁵Mo-NMR and ICP-MS), a comparison of their properties, and their applications as bifunctional catalysts for CO₂ insertion into epoxides. The synthetic procedures to obtain ILs rely on anion exchange and acid–base reactions, including an innovative route for the synthesis of molybdate ionic liquids (Mo-ILs) using a halide-free organic IL precursor. The use of Mo-ILs as catalysts for CO₂ fixation was investigated using 1,2-epoxyhexane as a model substrate. In the presence of 2.5 % mol of tetrabutylammonium molybdate, 4-butyl-1,3-dioxolan-2-one was obtained in up to 86 % yield at T = 120 °C, p⁰(CO₂) = 30 bar in t = 9 h, under solventless conditions and without any added halide co-catalysts. The substrate scope was broadened to other 12 terminal and internal epoxides; moreover, the reaction was scaled up to 2 g of the substrate and catalyst recyclability was demonstrated up to 5 recycles. The results reported in this chapter have been published in “Bragato, N.; Perosa, A.; Selva, M.; Fiorani, G. and Calmanti, R. Molybdate ionic liquids as halide-free catalysts for CO₂ fixation into epoxides, *Green Chem*, **2023**, 25, 4849-4860”.

3.3.2 Introduction

As introduced in **Chapter 1.2**, the rise in anthropogenic CO₂ emissions (approximately 36.8 Gt per year) has raised global concerns due to its link to climate change.⁷³ Chemical valorization of CO₂ has gained attention as it offers a renewable, abundant and low-cost carbon source, which can be exploited for the preparation of functional molecules, energy vectors and materials developing processes that can potentially mitigate fossil fuels depletion.⁷⁴

Although CO₂ chemical fixation currently finds limited practical applications, largely ascribed to the inefficiencies in storage, it represents a promising approach for the production of renewable-based fine chemicals and energy vectors including, among others, ureas,⁷⁵ carbamates,⁷⁶ organic carbonates,⁷⁷ polycarbonates,⁷⁸ carboxylic acids,⁷⁹ heterocycles,⁸⁰ and methanol.⁸¹ Among the different catalytic approaches reported, bifunctional catalysts activating simultaneously both CO₂ and co-reactants have been applied, in particular, to CO₂ insertion reactions into epoxides to synthesize cyclic organic carbonates (**COCs**). As already discussed in **Section 1.3** and **3.1**, bifunctional metal- and organo-catalysts typically require an halide salt co-catalyst to act as nucleophile for epoxide ring-opening.^{42,82} As detailed in the previous **Section 3.1** development of halide-free CO₂ insertion protocols, represents a significant advancement in the field of CO₂ valorization.^{83–89}

Polyoxoanions or polyoxometalates have gained importance in organic synthesis and material chemistry due to their unique acidity, photothermal, and redox features with a constantly increasing number of applications in catalysis, energy storage, biomedicine, and other research fields. The term polyoxometalates (**POMs**) refers to a class of compounds based on early transition metal (groups 5 and 6) oxide building blocks with a general formula of (MO_x)_n, where M = Mo, W, V, Nb, Ta etc.^{90,91} In the past decades, several different POM-based compounds have been reported as efficient catalysts or promoters for CO₂ fixation processes.^{92,93} Interestingly, only limited examples of molybdenum-based active catalytic systems have been reported for CO₂ fixation into epoxides. In 2011, Hu and co-workers developed a one-pot two-step epoxidation/CO₂ insertion protocol for the synthesis of COCs starting from olefins, *tert*-butyl hydroperoxide as the oxidant and CO₂ as the C¹ source in the presence of a catalytic system composed of MoO₂(acac)₂ and TBAB.⁹⁴ The authors demonstrated the conversion of terminal and internal olefins into the corresponding COCs, stating that the presence of MoO₂(acac)₂ was fundamental in the first epoxidation step while its presence practically did not affect the insertion step, which was promoted by the halide salt co-catalyst. In 2016, Werner and co-workers developed a MoO₃/tetrabutylphosphonium bromide catalytic system active towards the synthesis of bio-derived COCs starting from CO₂ and epoxidized fatty acid esters.⁹⁵ In 2018, Cheng and co-workers synthesized a novel binuclear molybdenum alkoxide catalyst, (Mo₂(O^{*t*}Bu)₆), which was employed in combination with TBAB for COC synthesis under mild conditions (rt and *p*⁰(CO₂) = 1 bar).⁹⁶ More recently, Dai *et al.* optimized the preparation of three *N*-heterocyclic carbene–nitrogen molybdenum complexes, active for the preparation of 1,2-butylene carbonate from 2-ethyloxirane when used in combination with TBAI (cat: 0.5 mol%, TBAI: 2 mol%, T = 80 °C, t = 20h, *p*⁰(CO₂) = 5 bar).⁹⁷ In these studies, molybdenum species were mainly exploited as Lewis acid co-catalysts for the activation of the epoxide in combination with a tetraalkylammonium and/or phosphonium halide salt acting as a nucleophilic ring-opening promoters. In this section, we

report the preparation and characterization of different molybdate and polyoxomolybdate ILs (Mo-ILs), demonstrating the effective interaction between CO₂ and Mo-ILs, which were evaluated as bifunctional catalysts for halide-free CO₂ activation to synthesize **COCs** under solventless conditions.

3.3.3 Synthesis and characterization of Mo-ILs

A library of different molybdenum salts (compounds **(1)–(8)**, shown in **Figure 3.12**) were synthesized to explore the correlation between their catalytic activity and the type of organic cation (ammonium, phosphonium, imidazolium and diazobicycloundecenium cations, characterized by distinctive lipophilic properties), as well as the structure of molybdenum-based anions, which represent the active site of the catalysts.

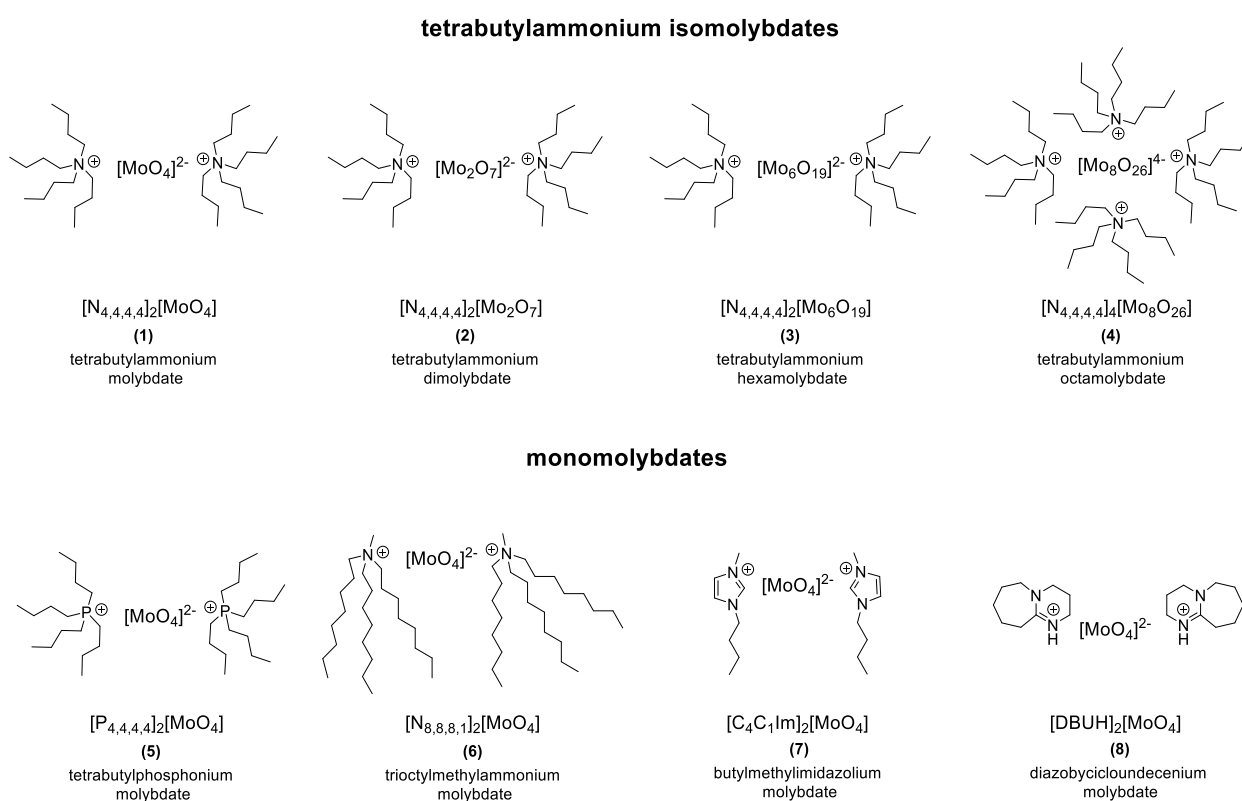
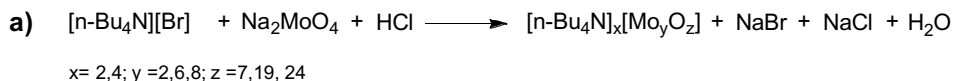


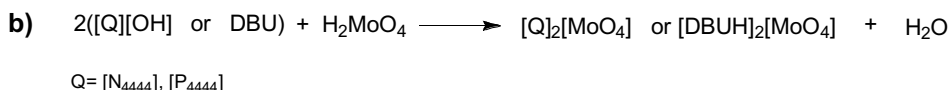
Figure 3.12: Mo-ILs synthesized and used in this work. It is worth noting that the respective monomolybdates, compounds (1) and (5)–(8), meet the IUPAC definition of ionic liquids as bulk salts with melting points below 100°C.

Compounds **(1)–(8)** were obtained through three different methodologies depicted in **Figure 3.13**.

Conventional



Acid-Base Exchange



Methylcarbonate-ILs

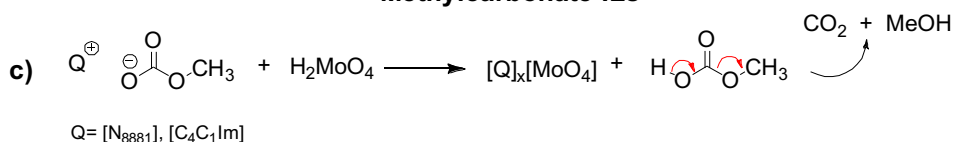
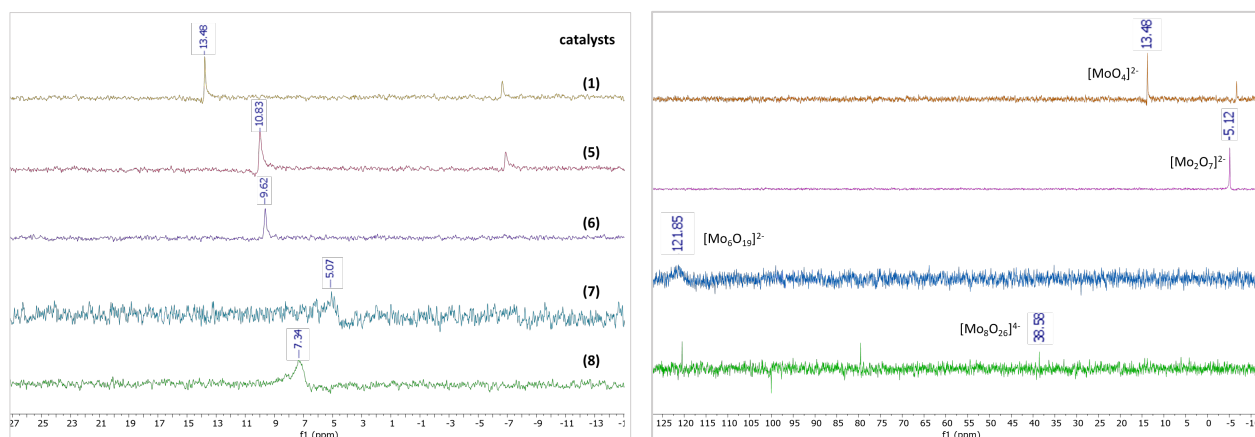


Figure 3.13: Synthetic routes for the preparation of Mo-ILs.

Tetrabutylammonium isopolyoxomolybdates (**2**), (**3**) and (**4**) were synthesized according to a reported procedure based on the reaction between sodium molybdate dihydrate ($\text{Na}_2\text{MoO}_4 \cdot 2\text{H}_2\text{O}$) and $[\text{N}_{4,4,4,4}][\text{Br}]$ in an acidic environment (Figure 3.13a).⁹⁸ ILs (**1**), (**5**) and (**8**) were prepared by acid–base neutralization between tetraalkylammonium, phosphonium or 1,8-diazabicyclo[5.4.0]undec-7-enium hydroxide, $[\text{Q}][\text{OH}]$ and molybdic acid (H_2MoO_4) (Figure 3.13b).⁹⁹ Catalysts (**6**) and (**7**) were synthesized upon metathesis of methylcarbonate ILs with H_2MoO_4 , extending the applicability of a sustainable methodology previously developed by our group for the preparation of tungstate-based ILs to molybdenum-based ILs.¹⁰⁰ As depicted in Figure 3.13c, the latter methodology allowed the preparation of different Mo-ILs via a simple, halide-free and clean protocol avoiding work-up steps. As discussed in the previous section, the formation of methylcarbonic acid (*i.e.* the half ester of carbonic acid), which spontaneously decomposed to methanol and CO_2 above -36°C , is the driving force of the reaction.³³ The structures of Mo-ILs were confirmed by FT-IR, ^1H -, ^{13}C -, ^{31}P - and ^{95}Mo -NMR spectroscopy (see Characterization Chapter 3 section for further details). In particular, the presence of molybdate species for compounds (**1**) and (**5**)-(**8**) was confirmed by FT-IR, by the presence of large absorption band associated to Mo–O stretching vibration observed between 831 and 826 cm^{-1} (see Figure S28, S44, S49, S53 and S57), while the dimolybdate (**2**) was characterized by a strong and broad absorption band at 883 cm^{-1} (see Figure S32). Tetrabutylammonium isopolyoxomolybdates **3** and **4** showed a different kind of absorption due to the more complex polyoxoanion structure: more precisely, catalyst **3** was characterized by two strong absorption bands at 799 and 954 cm^{-1} (Figure S36), while for catalyst **4** three characteristic absorption bands at 661 , 807 and 922 cm^{-1} were observed (Figure S40), in agreement with previously published results.⁹⁸ ^{95}Mo -NMR spectroscopy provides further confirmation of different oxomolybdenum species: for example, the monomolybdate counteranions present in catalysts (**1**), (**5**), (**6**), (**7**) and (**8**)

were characterized by ^{95}Mo NMR chemical shifts ranging from 5 to 13 ppm. (see **Figure 3.14** and **Figure S27, S43, S48, S52 and S56**).^{101–103}



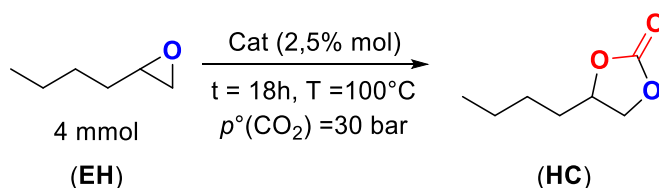
*Figure 3.14: left) ^{95}Mo -NMR spectra of $[\text{MoO}_4]^-$ ILs. (cfr. **Characterization Chapter 3** section for the full spectra, **Figures S27, S43, S48, S52 and S56**). right) ^{95}Mo -NMR spectra of tetrabutylammonium isopolyoxomolybdate. (cfr. **Characterization Chapter 3** section, **Figures S27, S31, S35 and S39**).*

The observed differences in chemical shifts were ascribed to the interaction of the monomolybdate species with the counteranions, which influences the electronic environment. In some cases (see **Figure 3.14**, left for cat (1) and (5) and **Figure S27 and S43** in the **Characterization Chapter 3** section), the contemporary presence of dimolybdate species (–5 ppm) caused by water promoted counteranion degradation processes is evident.¹⁰¹ ^{95}Mo -NMR spectra of tetrabutylammonium isopolyoxomolybdates showed single peaks between –5 ppm and 125 ppm, in agreement with previously reported characterization data,¹⁰⁴ and confirmed the assumptions derived from FT-IR spectroscopy characterizations (**Figure 3.14**). As reported in **Table A1 (Appendix of Chapter 3** section), ICP characterization further confirmed the structures and molecular weights of compounds (1), (2), (3) and (4). It should be noted that compound (1) has a lower correspondence due to its hygroscopicity. ^1H , ^{13}C , and ^{31}P NMR spectroscopy experimentally confirmed the structure of organic counteranions. For Mo-ILs (6) and (7), the disappearance of the peaks of the methyl carbonate anion of the precursor, observed in the ^1H NMR spectra, allowed us to verify the quantitative formation of the desired ILs obtained through path c, **Figure 3.13**. Finally, ^{31}P NMR spectra confirmed the presence of a phosphonium cation in the case of catalyst (5) (see **Figure S47**).

3.3.4 Mo-IL-catalyzed insertion of CO_2 into epoxides

Initially, the activity of different molybdate anions was determined by performing CO_2 insertion reaction with 1,2-epoxyhexane (EH) as a model substrate, to yield 4-butyl-1,3-dioxolan-2-one (hexane carbonate, HC) under solventless conditions. **Table 3.5** reports the results obtained by using the various Mo-ILs as catalysts, at 2.5 % mol of Mo with respect to the substrate, regardless of the Mo salt used.

Table 3.5: Insertion of CO₂ into 1,2-epoxyhexane catalysed by different polyoxomolybdates



Entry	Catalysts	Conversion (%) ^a	Selectivity (%) ^a	Yield (%) ^a
1	[N _{4,4,4,4}] ₂ [MoO ₄]	93	68	63
2	[N _{4,4,4,4}] ₂ [Mo ₂ O ₇]	79	64	51
3	[N _{4,4,4,4}] ₂ [Mo ₆ O ₁₉]	0	-	-
4	[N _{4,4,4,4}] ₂ [Mo ₈ O ₂₆]	0	-	-
5	[NH ₄] ₂ [MoO ₄]	0	-	-
6	[Na] ₂ [MoO ₄]	0	-	-

Reaction conditions: 1,2-epoxyhexane (4.0 mmol), catalyst (2.5 % mol), $p^{\circ}(CO_2) = 30$ bar, $T = 100$ °C, $t = 18$ h, solventless reaction. ^aConversion, selectivity and yield calculated by ¹H NMR.

[N_{4,4,4,4}]₂[MoO₄] (Entry 1, **Table 3.5**) gave almost quantitative EH conversion forming HC in good selectivity (68 %), while [N_{4,4,4,4}]₂[Mo₂O₇] (Entry 2, **Table 3.5**) showed a poorer performance in terms of conversion of the substrate and selectivity towards HC. Tetrabutylammonium *iso*-polyoxomolybdates (**3**) and (**4**) (hexa- and octamolybdate) (Entries 3 and 4, **Table 3.5**) did not exhibit significant conversion of the substrate: the molybdate atoms were likely poorly accessible and thus unable to coordinate CO₂ and promote the reaction, indicative of the importance of small anionic species like [MoO₄]²⁻. We postulated that the greater catalytic activity of ILs containing [MoO₄]²⁻ and/or [Mo₂O₇]²⁻ can be ascribed to two main reasons: (i) interaction between CO₂ and monomeric/dimeric Mo species demonstrated by ¹³C and ⁹⁵Mo NMR spectra (see **Figure 3.19**); this interaction was not observed with *iso*-polyoxometalates (**3**) and (**4**), in particular when recording ⁹⁵Mo NMR spectra under a CO₂ atmosphere (*vide infra*); (ii) greater solubility of Mo-ILs (**1**) and (**2**) in the neat epoxide reaction mixture, while *iso*-polyoxomolybdates (**3**) and (**4**) are not soluble. Ammonium and sodium molybdates were also tested (Entries 5 and 6, **Table 3.5**), displaying negligible conversion, suggesting that the organic counter cation is necessary to ensure quantitative solubilization of the catalyst. The inactivity of ammonium and sodium molybdates is probably due to their insolubility in the substrate and the lack of interaction of these salts with CO₂ (see **Figure A 12** in the Appendix). Catalyst (**1**) was therefore chosen as a model catalyst to optimize the reaction conditions for the CO₂ insertion reaction into 1,2-epoxyhexane. The influence of temperature ($T = 50$ - 160 °C) for the reaction of EH in the presence of $p^{\circ}(CO_2) = 30$ bar of CO₂ and 2.5 % mol of catalyst for $t = 18$ h is reported in **Figure 3.15**.

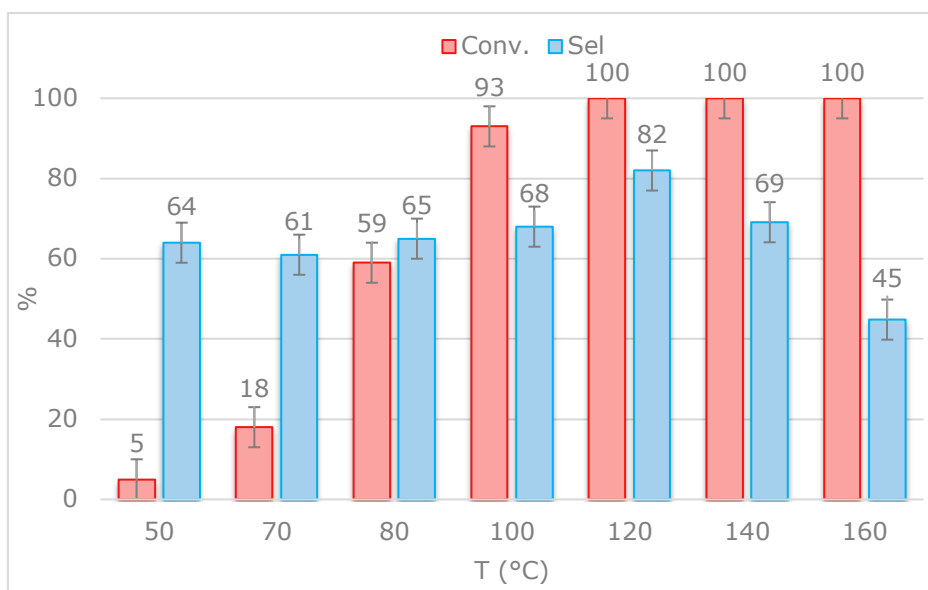


Figure 3.15: Effect of the temperature on CO₂ insertion into 1,2-epoxyhexane (EH) to obtain hexane carbonate (HC). Reaction conditions: EH (4.0 mmol), **1** (2.5 % mol), $p^0(\text{CO}_2)$ = 30 bar, t = 18 h, T = 50–160 °C, solventless reaction. Conversion, selectivity and yield were calculated by ¹H NMR.

Conducting the reaction at $T \geq 120$ °C was crucial to observe quantitative conversion of EH, while lower temperatures did not allow adequate CO₂ activation towards the formation of HC. However, at reaction temperatures >120 °C a decrease in selectivity was observed due to the formation of polyethers as secondary products, as observable by the appearance of broad peaks at 3.90–3.30 ppm in the ¹H NMR spectra. The main by-product at $T \leq 120$ °C was 1,2-hexanediol (according to ¹H NMR, ¹³C NMR and GC-MS analysis, see **Figure S67–S69, Characterization Chapter 3** section) while 1-(2-hydroxyhexoxy)hexan-2-ol was also formed as by-product in traces (see **Figure S70–S72, Characterization Chapter 3** section). The formation of these compounds was ascribed to the presence of adventitious water which, combined with catalytically active molybdate anions, led to ring-opening hydration of the epoxide substrate. Crystallization of water is always observed in molybdate-based ILs since they are very hygroscopic (see **Figure S28**). Having identified the optimal operating temperature as $T = 120$ °C, the kinetic of the reaction was monitored for $t = 18$ h and the resulting product distribution is shown in **Figure 3.16**.

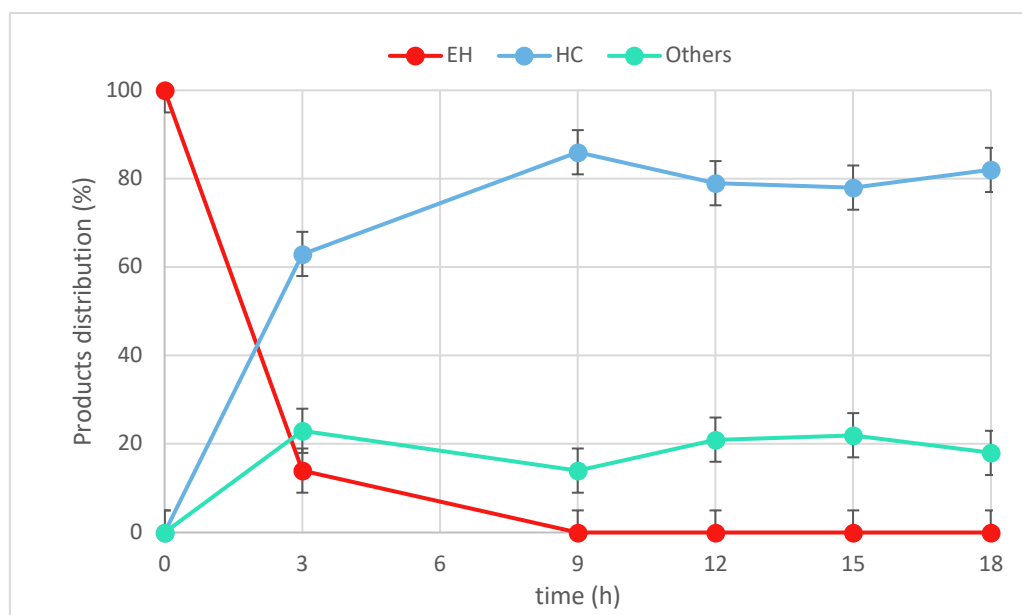


Figure 3.16: Effect of the reaction time on CO_2 insertion into 1,2-epoxyhexane (EH) to obtain hexane carbonate (HC). Reaction conditions: EH (4.0 mmol), Mo-IL **1** (2.5 % mol), $p^0(\text{CO}_2) = 30$ bar, $T = 120$ °C, $t = 3$ –18 h, solventless conditions. Yield^d and conversion determined by GC-FID.

The conversion of EH was quantitative after $t = 9$ h, intriguingly a slight degradation or side reaction of the COC product formed, was also observed at $t = 9$ h, as highlighted by the increase of by-products (*i.e.* others, aqua green line, Figure 3.6).

The influence of $p^0(\text{CO}_2) = 1$ –50 bar was explored by performing the reaction at $T = 120$ °C for $t = 9$ h (Figure 3.17).

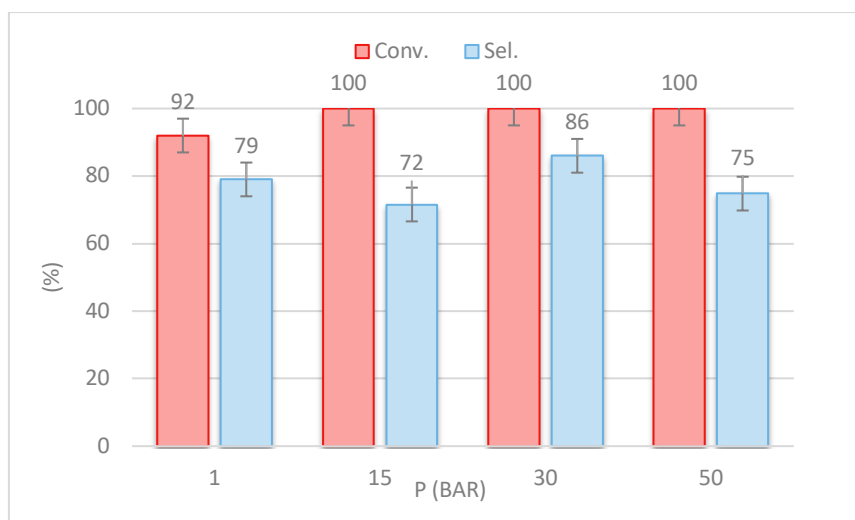


Figure 3.17: Pressure screening for CO_2 insertion into 1,2-epoxyhexane (EH) to obtain hexane carbonate (HC). Reaction conditions: EH (4.0 mmol), Mo-IL **(1)** (2.5 % mol), $T = 120$ °C, $t = 9$ h, $p^0(\text{CO}_2) = 1$ –50 bar, solventless conditions. Conversion and selectivity were calculated by ^1H NMR.

Although EH conversion was always quantitative, 30 bar of CO_2 were necessary to achieve the best selectivity (86%) while poorer results were obtained with $p^0(\text{CO}_2) \leq 15$ bar. Increasing CO_2 pressure to 50 bar led to a lower selectivity towards HC. This behavior could be explained by observing the

endogenous pressure value in the autoclave, 65 bar, typical of quasi-critical conditions and likely causing a lower interaction between CO₂ and the epoxide, hence promoting the formation of polyethers.

Once proved that the monomolybdate species is the most active for CO₂ fixation into the epoxide, the effect of the organic -onium cation was investigated. The catalytic activity of four different Mo-ILs (**5**), (**6**), (**7**), and (**8**) was tested in a model CO₂ fixation reaction under the optimized operative conditions (T = 120 °C, p⁰(CO₂) = 30 bar CO₂, t = 9 h). The results are summarized in **Table 3.6**.

Table 3.6: CO₂ insertion into 1,2-epoxyhexane (EH) catalyzed by different Mo-ILs.^a

Entry	Catalysts	Conversion (%) ^b	Selectivity (%) ^b	Yield (%) ^b
1	[N _{4,4,4,4}] ₂ [MoO ₄]	>99	86	86 (83) ^c
2	[P _{4,4,4,4}] ₂ [MoO ₄]	>99	79	79
3	[N _{8,8,8,1}] ₂ [MoO ₄]	96	75	72
4	[C ₄ C ₁ Im] ₂ [MoO ₄]	88	75	67
5	[DBUH] ₂ [MoO ₄]	68	34	23

^aReaction conditions: 1,2-epoxyhexane (4.0 mmol), p⁰(CO₂) = 30 bar, T = 120 °C, t = 9 h, solventless conditions. ^b Conversion, selectivity and yield calculated by ¹HNMR. ^cIsolated yield

The reaction conversion showed a fluctuating trend consistent with the type of counter cation present on the Mo-IL: the use of [N_{4,4,4,4}]₂[MoO₄] and [P_{4,4,4,4}]₂[MoO₄] allowed for achieving comparable conversion of EH, while [N_{8,8,8,1}]₂[MoO₄] and [C₄C₁Im]₂[MoO₄] showed slightly poorer performance. It is worth noting that the conversion of EH and selectivity towards HC collapsed with DBUH₂[MoO₄] (68 % and 34 %, respectively, Entry 5, **Table 3.6**). Probably the lipophilic character of catalysts (**1**) and (**5**)–(**7**) is crucial to ensure a good performance, as already remarked for [NH₄]₂[MoO₄] and [Na]₂[MoO₄] (Entries 5 and 6, **Table 3.5**). Additional control tests were performed with the catalyst precursors (*e.g.* [N_{4,4,4,4}][OH], [P_{4,4,4,4}][OH], [N_{8,8,8,1}][CH₃OCOO] and [C₁C₄im][CH₃OCOO]), further confirming the improved performance of our Mo-ILs (see **Table A 3**). Catalyst loading tests performed on the catalytically active Mo-ILs (see **Table A 4**) confirmed 2.5 % mol as the optimal loading for Mo-IL (**1**). Hence, we decided to continue our investigation by using (**1**) as the catalyst since it allowed us to reach an excellent selectivity for the COC product (Entry 1, **Table 3.6**), also leading to the maximum yield of HC. With the optimized conditions in hand, the scope of the coupling reaction was broadened by testing CO₂ fixation into various linear and cyclic aliphatic epoxides with [N_{4,4,4,4}]₂[MoO₄] (**Figure 3.18**).

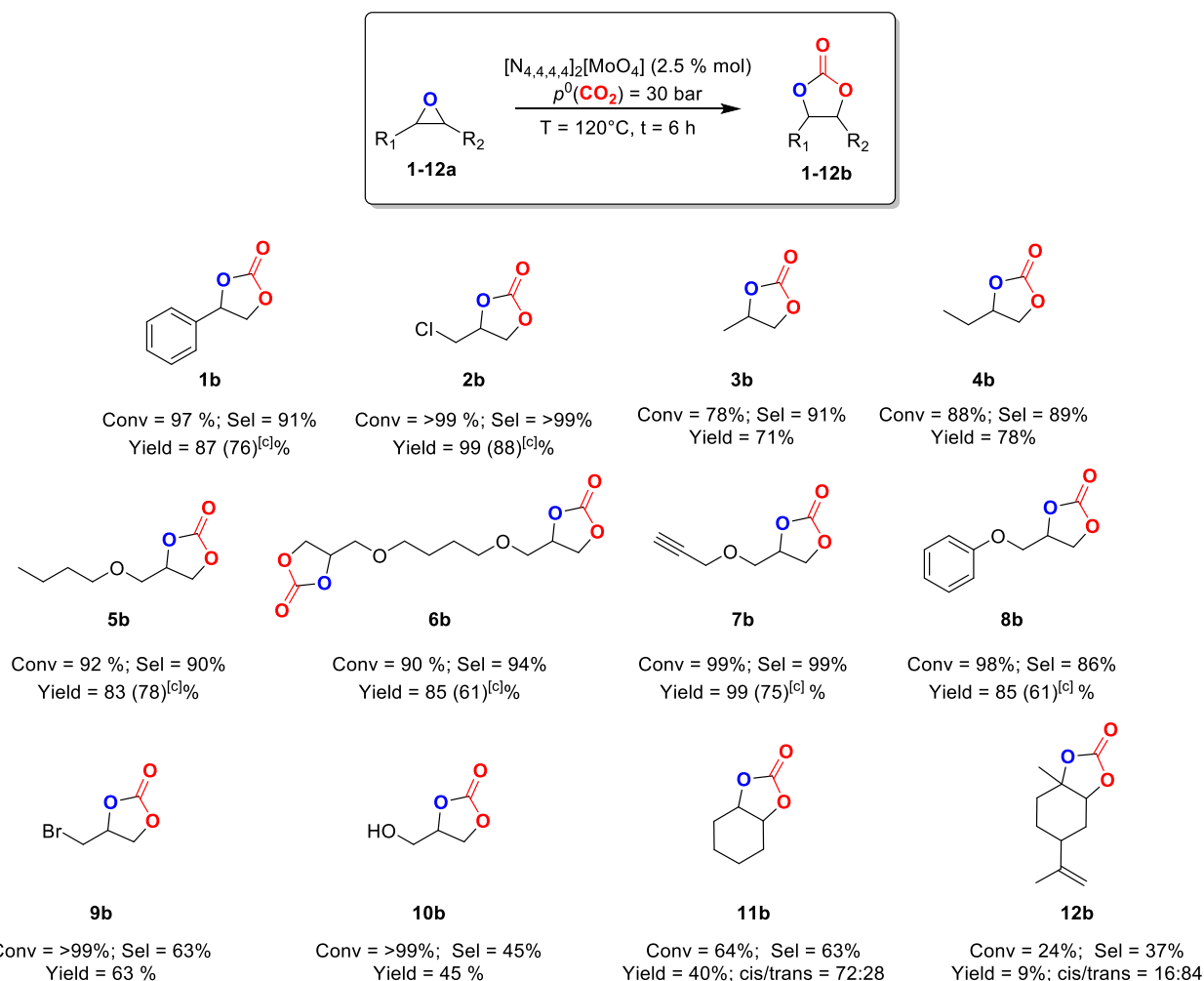


Figure 3.18: ^aReaction conditions: epoxide (4.0 mmol), $p^0(CO_2) = 30 \text{ bar}$, $T = 120^\circ C$, $t = 9 \text{ h}$, solventless. ^bConversion, selectivity and yield calculated by ¹H NMR. ^cIsolated yield.

The results demonstrated Mo-IL (**1**) catalytic activity for CO₂ fixation into terminal epoxides **1a–8a** (Figure 3.18): these compounds were converted into the corresponding COC products with conversion and selectivity similar or higher than the one reported for 1,2-epoxyhexane. In particular, we have observed an excellent catalytic performance with industrially relevant epoxides such as epichlorohydrin (**2a**) and propylene oxide (**3a**). 1,2-epoxybutane (**4a**) shows a slightly higher conversion than **3a** probably as a consequence of its lower volatility that improves the interaction between Mo-ILs and their adducts with CO₂. Terminal epoxides **9a** and **10a** were quantitatively converted but the selectivity towards the corresponding COCs decreased due to the formation of polyethers. The different behavior of **9a** compared to **2a** is probably due to the better leaving group ability of bromide compared to chloride, which allows the formation of polyethers. Nonetheless, Mo-ILs demonstrated significant tolerance to different functional groups such as in the cases of **1a**, **2a**, **5a**, **6a**, **7a** and **8a**, also observing higher conversions compared to **3a**, probably due to the greater volatility of propylene oxide in the investigated reaction conditions. Internal alicyclic epoxides, such as **11a** and **12a**, were less reactive, presumably because of the steric factors. In particular for **11a** the selectivity towards the carbonates decreased in favour of polyethers and polycarbonates detected by ¹H NMR, with the appearance of diagnostic signals at 3.40 and 4.40 ppm in CDCl₃,

respectively (see **Figure A13** in the Appendix section).^{105,106} Formation of cyclohexanone was not detected by ^1H NMR analysis, hence excluding the occurrence of side products obtained via Meinwald rearrangement.¹⁰⁷ Presence of both *cis* and *trans* isomers (see **Figure A13**) of disubstituted epoxide **11a** is due to the possible ring closure of the five-membered ring and can occur by both $\text{S}_{\text{N}}1$ and $\text{S}_{\text{N}}2$ mechanisms, but with a marked preference for the formation of the *cis* product. This behavior was already reported in the literature and by us in previous papers regarding the use of transition metal-based catalysts for CO_2 fixation into internal epoxides.^{36,95} The presence of Mo-ILs evidently promotes an $\text{S}_{\text{N}}2$ pathway and formation of the *cis* cyclic carbonate product, while the formation of the *trans* cyclic carbonate product is favored by an $\text{S}_{\text{N}}1$ pathway and the possible depolymerization of the polycarbonate by-product. In the case of limonene oxide (**12a**, **Figure 3.18**), the high degree of substitution of the oxirane prevents its coordination to the active molybdenum species, leading to a low yield (9 %) and selectivity towards the corresponding COC. $[\text{MoO}_4]^{2-}$ anions are hence able to activate CO_2 and catalyze its insertion into epoxides without the addition of a halide to promote ring-opening. We then conducted further NMR experiments to better understand the interaction of molybdate with CO_2 and derive a self-consistent reaction mechanism (**Figure 3.19**).

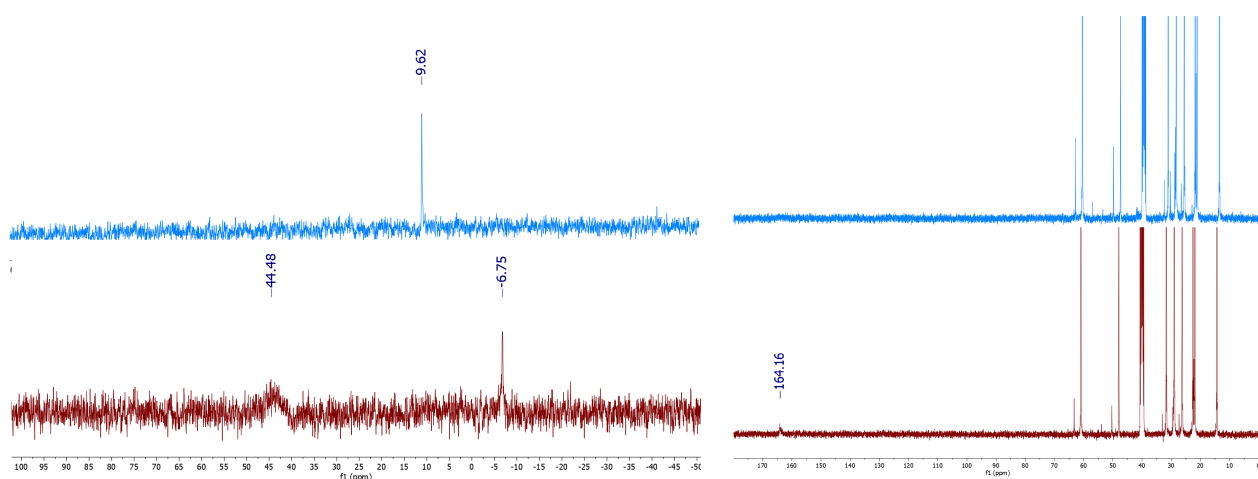


Figure 3.19: ^{95}Mo NMR (left) and ^{13}C NMR (right) analyses of $[\text{N}_{8,8,8,1}]_2[\text{MoO}_4]$ before (blue) and after (red) treatment with CO_2 . Operative conditions: $[\text{N}_{8,8,8,1}]_2[\text{MoO}_4]$ 0.4 M in DMSO-d_6 , $T = 25^\circ\text{C}$, $p^0(\text{CO}_2) = 5$ bar

Upon addition of 5 bar of CO_2 to a 0.4 M DMSO-d_6 solution of catalysts **1** or **6** at room temperature, in a pressure-resistant NMR tube, the formation of new species became quickly evident. As reported in **Figure 3.19**, left, the ^{13}C NMR spectra showed the appearance of a peak at 164.16 ppm typical of a carbonyl group. ^{95}Mo NMR analysis (**Figure 3.19**, right) highlighted the substantial disappearance of the initial molybdate species (9.62 ppm) and the formation of a new broad peak at 44.48 ppm distinctive of a molybdenum– CO_2 adduct. These observations are in agreement with previous reports on the reversible binding of $[\text{MoO}_4]^{2-}$ with CO_2 through ^{95}Mo NMR and single crystal X-ray diffraction analyses, demonstrating the formation of $[\text{MoO}_3(\text{CO}_3)]^{2-}$ carbonate complexes (^{95}Mo NMR = + 46.7 ppm and ^{13}C NMR = 165.7 ppm).¹⁰⁴ In our case, ^{95}Mo NMR analysis also clearly indicates the presence of $[\text{Mo}_2\text{O}_7]^{2-}$, identified by a signal at - 6.75 ppm.¹⁰¹ These observations led

us to propose the mechanism described in **Figure 3.20** for CO₂ insertion into epoxides catalyzed by Mo-ILs.

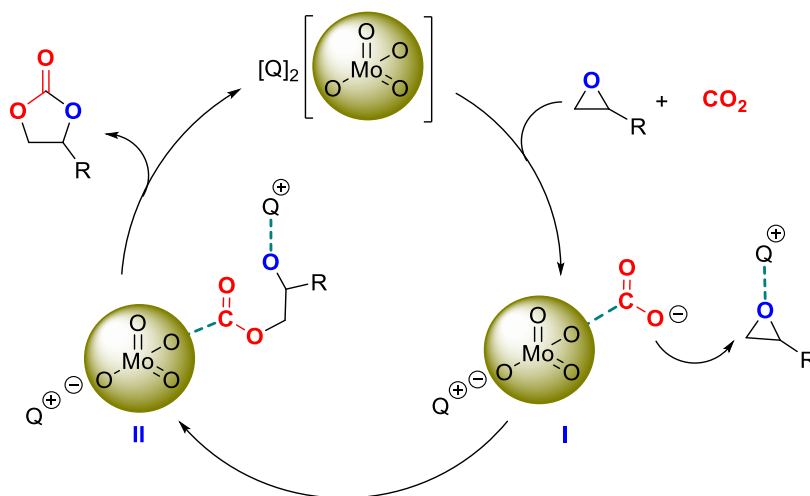


Figure 3.20: Mechanistic hypothesis for CO₂ fixation into epoxides catalyzed by Mo-ILs.

The molybdate–CO₂ carbonate complex **I** formed *in situ* could itself act directly as the nucleophile and attack the cation-activated epoxide, yielding the hemicarbonate intermediate **II**, which can ring-close with the formation of a COC product and the release of the molybdate IL. This mechanism was coherent with the fact that CO₂ insertion did not take place at $T < 50\text{ }^{\circ}\text{C}$ but only at $T > 70\text{ }^{\circ}\text{C}$, where complex **I** was able to release activated CO₂, as already observed for $[\text{MoO}_3(\text{CO}_3)]^{2-}$.¹⁰³ While most of the metal-based catalytic systems active towards CO₂ fixation into epoxides require the presence of a halide (Cl^- , Br^- , I^-) and/or a nucleophile co-catalyst to achieve any conversion,^{94–97} molybdate anions were active in the absence of a halide source or other external nucleophiles. The mechanism proposed is supported by the evidence of CO₂–Mo complex formation described above, as well as by a comparison with other mechanisms reported for the synthesis of polycarbonates mediated by metal complexes containing an alkoxide or aryloxy group ($-\text{OR}$) that are able to undergo CO₂ insertion into epoxides without requiring an external nucleophile.¹⁰⁸ Finally, we evaluated the recyclability of our catalytic system and tested the scaling-up of our protocol. The results obtained from the first five recycles are reported in **Figure 3.21** while more details are reported in **Figure A14–A18** (see **Appendix, Chapter 3** section). The reactions were carried out using 2.0 g of 1,2-epoxyhexane (EH, 20.0 mmol) and 2.5 % mol% of (**1**) under a CO₂ pressure of $p^0(\text{CO}_2) = 30\text{ bar}$. The experiments were conducted in a glass liner placed inside an autoclave at $T = 120\text{ }^{\circ}\text{C}$ for $t = 9\text{ h}$. At the end of each cycle, the products were separated through short path distillation apparatus (see **Figure A14**, left) while the catalyst was totally recovered and reused without further processing. The product mixture was recovered as a clear transparent liquid by distilling the vapors between $T = 65$ and $75\text{ }^{\circ}\text{C}$ at $p = 0.9\text{ mbar}$ (see **Figure A14**, right).

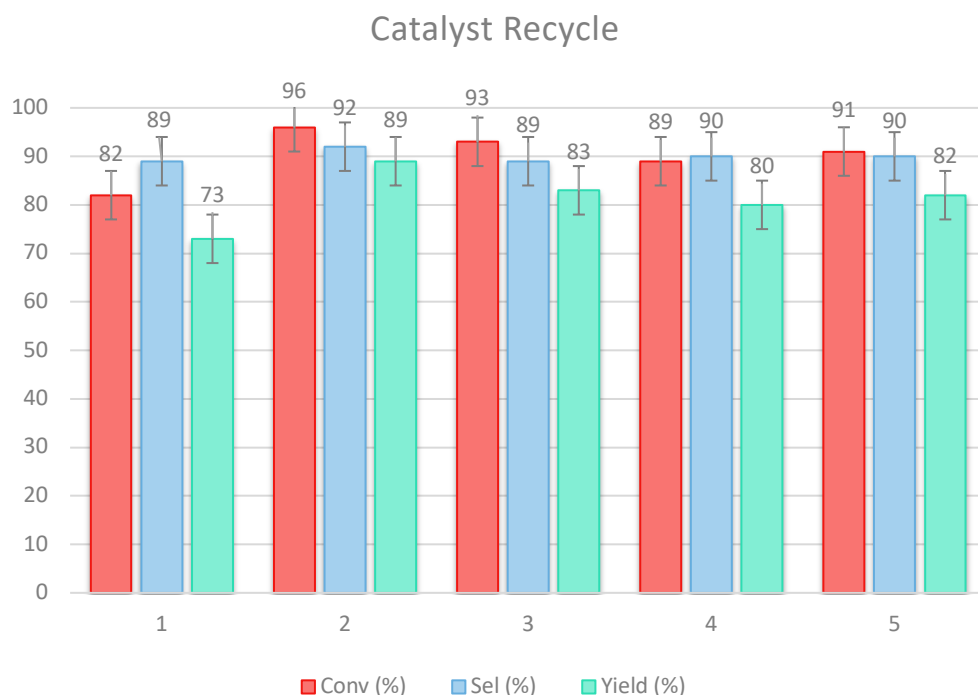


Figure 3.21: Catalyst recycling tests for CO₂ insertion into 1,2-epoxyhexane (EH) to obtain hexane carbonate (HC). Reaction conditions: EH (20.0 mmol), Mo-IL (**1**) (2.5 % mol%), T = 120 °C, t = 9 h, p⁰(CO₂) = 30 bar, solventless conditions. Conversion, selectivity and yield were calculated by ¹H NMR.

The distilled fraction was characterized by ¹H NMR analysis, observing that it was mainly composed of the COC product, with traces of diol and dimerized ether 1-(2-hydroxyhexoxy)hexan-2-ol as the main detectable by-products (see **Figure A15** for further details). Since our original objective was to demonstrate catalyst recyclability, we did not optimize the fractional distillation of each recycle run, nevertheless this system appeared suitable for both separation and recycling of the homogeneous catalyst. From **Figure 3.11**, we can see how Mo-IL (**1**) could be used and recovered effectively for 5 consecutive cycles without any loss of activity. Except for recycle 1, in which a conversion and a lower selectivity were achieved due to the loss of the product inside the distillation system, the other steps maintained a conversion between 96 and 89% and a selectivity between 92 and 89%. Our catalytic system remains efficient when compared to other halide-free (and solvent-free) protocols. **Table 3.7** summarizes and compares our results with some recently reported systems for CO₂ fixation into epichlorohydrin as an industrial key model epoxide. ECH was chosen as a model substrate for comparison since many studies did not explore the use of EH. Mo-ILs showed a catalytic activity comparable to other homogeneous metal catalysts (Entries 2–4, **Table 3.7**), heterogeneous metal catalysts, such as ZIFs, MOFs, and amorphous polymers (Entries 5–9, **Table 3.7**), organic ILs (Entries 10–13, **Table 3.7**), homogeneous organocatalysts (Entries 14–17, **Table 3.7**), and heterogeneous organocatalysts (Entries 18 and 19, **Table 3.7**). Interestingly, most catalysts are active under similar operative conditions (*e.g.* T = 60–150 °C, t = 3–24 h, p⁰(CO₂) = 10–30 bar) and yields are usually > 90%. Compared to other homogeneous catalysts (see Entries 2–5 and 10–17, **Table 3.7**), Mo-ILs showed enhanced recyclability and were reused up to 5 times without significant

loss of catalytic activity. All the reported studies are relevant for the use of (renewable) CO₂ but several other factors should be considered with a view to achieving sustainable organic transformations, such as synthesis routes, safety of the reactants, complexity, greenness and atom economy for the synthesis of catalysts, recyclability, the presence of co-catalysts, the presence of solvent, etc. Mo-ILs are excellent catalysts since they are synthesized through a green, halide-free route starting from simple and cheap precursors compared to other catalysts reported in **Table 3.7**. They are easily recyclable and reusable. This is the first example in the literature of Mo-based catalysts effective for CO₂ activation through a halide-free pathway. The downside of Mo-ILs is the presence of a metal since many recent studies focused on organocatalysts (*cfr.* entries 10–19, **Table 3.7**) which may have a greener connotation. However, although the catalytic systems surveyed in **Table 3.7** are useful for CO₂ fixation, none are conceived to act in different consecutive catalytic transformations in a divergent approach.^{36,109} Here we established that Mo-ILs are active for both CO₂ fixation into epoxides and the epoxidation of olefins that will be discussed thoroughly in the following **Chapter 4**.

Table 3.7: Literature survey of the CO₂ insertion reaction on ECH under solvent-free conditions with halide-free catalysts

No.	Catalyst	T (°C)	t (h)	CO ₂ (bar)	Yield (%)	Number of recycles	Ref.
1^{a,c}	[N₄₄₄₄][MoO₄] – our work	120	9	30	99	5	
2^{a,c}	(DBUH) ₃ NbO ₅	130	5	30	90	8	89
3^a	[(C ₄ H ₉) ₄ N] ₃ H ₇ GeW ₉ Mn ₃ (H ₂ O) ₃ O ₃₇	150	3	30	93	No	110
4^a	Cr(0) complex	100	4	10	99	No	111
5^b	HE-ZIF-PM	100	8	10	97	No	112
6^b	ZIF-67	120	6	10	95	3	113
7^b	Zn/Co-ZIF-H2Ar-1000	140	8	8	93	11	114
8^b	(Me ₂ NH ₂) ₂ [Zn ₈ (Ad) ₄ (DABA) ₆ O] ₇ (MOF)	100	24	10	99	5	115
9^b	Aluminium-based polymeric (Al-PDC)	100	20	1	93	11	116
10^c	[P ₄₄₄₄][bzim]	100	3,5	10	88	no	117
11^c	Pyridinium saccharinate (PPy-Sac)	60	24	1	90	no	118
12^c	Butyl methyl imidazolium acetate	80	2	10	78	no	119
13^c	[APBIm][Glu]	105	3	5	98	5	120
14^d	Salophen ligand	120	24	10	76	no	28
15^d	Acen-H catalyst	110	4	10	99	no	121
16^d	Carbodicarbene	100	12	20	92	no	122
17^d	2-aminopyridine	60	16	10	90	no	123
18^e	Chitosan biochar	100	12	20	90	no	124
19^e	N-doped shrimp shell carbon	150	4	30	93	6	125

^aMetal homogeneous catalysts. ^b Metal heterogeneous catalysts. ^c Ionic liquids. ^d Homogeneous organocatalysts. ^e Heterogeneous organocatalysts.

3.3.5 Conclusions

A set of novel molybdate ILs (Mo-ILs) was synthesized through a novel halide-free synthetic route and fully characterized with different spectroscopic techniques. These new compounds proved to be viable catalysts for CO₂ fixation into epoxides; in particular, catalyst **(1)** ([N_{4,4,4,4}]₂[MoO₄]) promoted the conversion of 1,2-epoxyhexane to the corresponding cyclic carbonate in 86 % yield at $p^0(\text{CO}_2) = 30$ bar and $T = 120$ °C. To explain these results, a reaction mechanism based on the formation of a molybdate–carbonate intermediate as the active nucleophile was proposed in light of an evident interaction between CO₂ and Mo established through ⁹⁵Mo NMR analysis. Although the investigated Mo-ILs were less efficient than other metal-based catalysts coupled with nucleophile sources, Mo-ILs exhibit a surprisingly higher catalytic activity with respect to other metals when used alone. To the best of our knowledge, this study describes the first example in which simple Mo-ILs are successfully used for the cycloaddition of CO₂ to epoxides without the use of any halide co-catalysts.

3.3.6 Experimental section

Materials and methods

All chemicals were purchased from Sigma Aldrich (now Merck) and used as received. Trioctylmethylammonium methylcarbonate ([N_{8,8,8,1}][CH₃OCOO]) and 1-butyl-3-methylimidazolium methylcarbonate ([C₄C₁im][CH₃OCOO]) were synthesized following a procedure previously reported by our group.³⁰ Qualitative and quantitative analyses and characterization of reaction mixtures and pure products were performed with: (a) a GC-MS system consisting of an Agilent 6890N GC equipped with an HP-5 capillary column (30 m length, 0.32 mm internal diameter, and 0.25 mm film thickness) coupled with an Agilent Technologies 5975 mass detector operating at 70 eV, (b) a Bruker Ascend 400 (AV400) NMR spectrometer operating at 400 MHz for ¹H nuclei, 100 MHz for ¹³C nuclei, 75 Hz for ³¹P nuclei and 26 MHz for ⁹⁵Mo nuclei, and (c) a PerkinElmer Spectrum One FT-IR spectrometer operating at wavenumbers ranging from 400 to 4000 cm⁻¹. GC-MS analyses were performed in EtOAc or Et₂O, while ¹H NMR and ¹³C NMR samples were prepared using deuterated solvents (CDCl₃, MeOH-d₄ or DMSO-d₆, deuteration grade >99.9% D in all cases). In the ¹H NMR spectra, the deuterated solvent residual signal was selected as the spectrum reference. ICP-MS analysis was conducted with a Nexion 350XX coupled with a seaFAST autosampler optimized in KED mode (4.4 ml of He) using Pt 195 as an internal standard.

General synthesis of [N_{4,4,4,4}]₂[MoO₄], [P_{4,4,4,4}]₂[MoO₄] and [DBUH]₂[MoO₄]¹⁰⁰

In a 50 mL round bottom flask, 1.85 mmol of H₂MoO₄ were slowly added in portions to a solution of [N_{4,4,4,4}][OH] (3.7 mmol, 2.0 equiv.) in 10 mL of H₂O. The solution was then stirred for $t = 3$ h at room temperature. During this time the initial white suspension slowly dissolved, obtaining a clear, homogeneous solution accompanied by a pH variation from 13 to 9. Water was quantitatively

removed from the mixture by evaporation *in vacuo* at $T = 100\text{ }^{\circ}\text{C}$, yielding the corresponding $[\text{N}_{4,4,4,4}]_2[\text{MoO}_4]$ as a white powder in quantitative yield. A similar procedure was followed to synthesize $[\text{P}_{4,4,4,4}]_2[\text{MoO}_4]$ and $[\text{DBUH}]_2[\text{MoO}_4]$ starting from 3.7 mmol of $[\text{P}_{4,4,4,4}][\text{OH}]$ or 1,8-diazabicyclo[5.4.0]undec-7-ene, respectively. The IL products were characterized by FT-IR, ^1H NMR, ^{13}C NMR, ^{31}P NMR (if suitable) and ^{95}Mo NMR spectroscopy.

Synthesis of trioctylmethylammonium molybdate, $[\text{N}_{8,8,8,1}]_2[\text{MoO}_4]$.

H_2MoO_4 (0.51 g, 3.16 mmol) was slowly added to an aqueous solution of $[\text{N}_{8,8,8,1}][\text{CH}_3\text{OCOO}]$ (2.80 g, 6.32 mmol, 2.0 equiv.). The solution was stirred for $t = 3\text{ h}$ at $T = 50\text{ }^{\circ}\text{C}$, and it was observed that the initially opalescent solution turned yellow. The solution was cooled to rt, and the product, $[\text{N}_{8,8,8,1}]_2[\text{MoO}_4]$, was extracted with ethyl acetate. 2.49 g (2.78 mmol) of the IL were obtained (88% yield). The product was characterized by FT-IR, ^1H NMR, ^{13}C NMR and ^{95}Mo NMR spectroscopy.

Synthesis of 1-butyl-3-methylimidazolium molybdate, $[\text{C}_4\text{C}_1\text{im}]_2[\text{MoO}_4]$

$[\text{C}_4\text{C}_1\text{im}]_2[\text{MoO}_4]$ was prepared following the same procedure as $[\text{N}_{8,8,8,1}]_2[\text{MoO}_4]$, starting from 1-butyl-3-methylimidazolium methylcarbonate $[\text{C}_4\text{C}_1\text{im}][\text{CH}_3\text{OCOO}]$. The IL product was characterized by FT-IR, ^1H NMR, ^{13}C NMR and ^{95}Mo NMR spectroscopy.

Typical procedure for CO_2 insertion reactions

The selected epoxide (4.0 mmol, 1.0 equiv.), molybdate catalyst (2.5 % mol) and mesitylene as an internal standard (20 % mol) were charged in a 5 mL glass reactor equipped with a stirring bar and a pierced glass cap. The glass reactor was placed inside a 10 mL stainless steel autoclave. The autoclave was sealed, degassed via two vacuum/ CO_2 cycles and pressurized with CO_2 (1–50 bar). The autoclave was then electrically heated at the desired temperature (50–160 $^{\circ}\text{C}$) and the reaction mixture was magnetically stirred for the desired time (3–18 h). At the end of each run, the autoclave was rapidly cooled in an ice bath and vented. The final mixture was analysed by ^1H -NMR (CDCl_3) to calculate the conversion, yield and selectivity.

Scaled-up procedure and recycling of the catalyst

2 g of 1,2-epoxyhexane (20.0 mmol, 1.0 equiv.) and catalyst **1** (0.05 mmol, 0.025 equiv.) were charged in a 5 mL glass reactor equipped with a stirring bar and a pierced glass cap. The glass reactor was placed inside a 100 mL stainless steel autoclave. The autoclave was sealed, degassed via two vacuum/ CO_2 cycles and pressurized with 30 bar of CO_2 . The autoclave was then heated at $T = 120\text{ }^{\circ}\text{C}$ under stirring for $t = 9\text{ h}$. At the end of each run, the autoclave was rapidly cooled in an ice bath and vented. The glass reactor was removed from the autoclave and equipped with short distillation apparatus to separate the catalyst from the reaction mixture. 0.8 mmol of mesitylene as an external standard were added to the distilled fraction which was then analyzed by ^1H -NMR (CDCl_3) to calculate the conversion, selectivity and yield. The glass liner containing the catalyst was recharged with 2 g (20 mmol) of 1,2-epoxyhexane for another catalytic run. The procedure was repeated 4 times (5 runs).

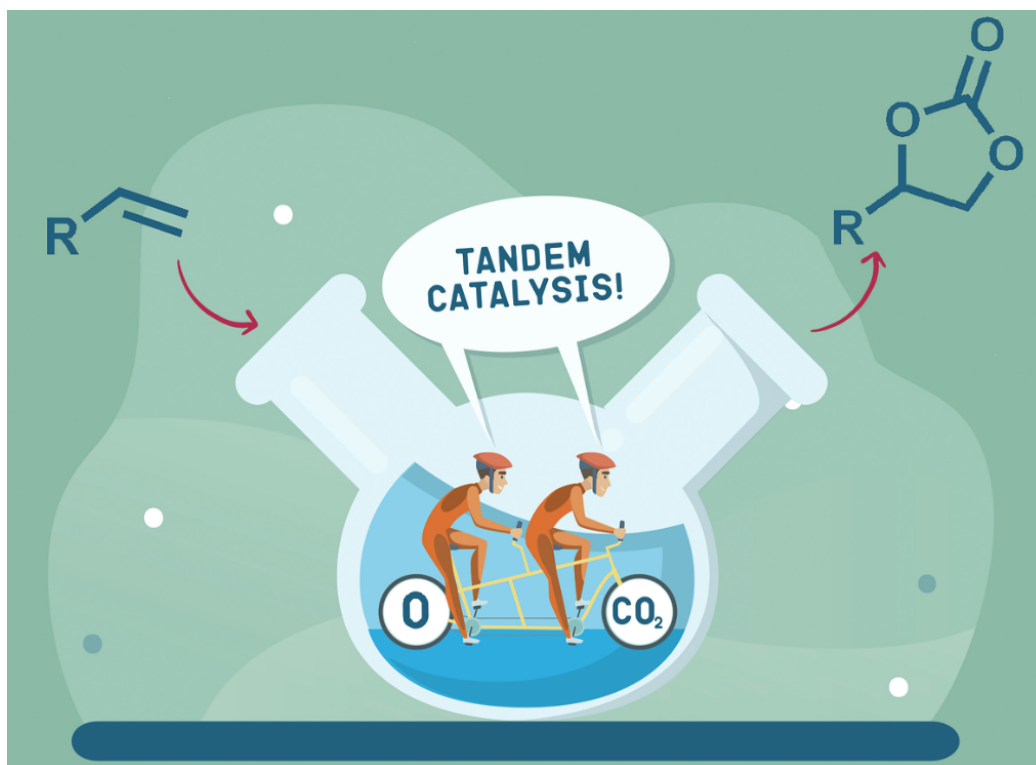
Procedure for ^{13}C -NMR and ^{95}Mo -NMR tests under CO_2 overpressure

A 0.4 M DMSO- d_6 solution of $[\text{N}_{4,4,4,4}]_2[\text{MoO}_4]$ or $[\text{N}_{8,8,8,1}]_2[\text{MoO}_4]$ was introduced into a 3 mL glass inlet of an autoclave reactor. A glass reactor equipped with a pierced glass stopper and a stirring bar was introduced into a 10 mL stainless steel autoclave and charged with CO_2 [$p^0(\text{CO}_2) = 0.5 \text{ MPa}$]. The system was kept at room temperature for $t = 4 \text{ h}$ before transferring the mixture into a pressure-resistant tube which was then filled with CO_2 [$p^0(\text{CO}_2) = 5 \text{ bar}$]. The ^{13}C NMR and ^{95}Mo NMR spectra were recorded for 5120 scans.

Sample preparation for ICP analysis

Around 10 mg of each compound were weighed into separate Teflon vessels and 6 ml of aqua regia were added. The vessels were then sealed and microwave-heated in a Milestone Ethos Up. Samples were then diluted to 50 mL in MilliQ water and analyzed by ICP-MS. The instrument Nexion 350XX coupled with seaFAST autosampler was optimized in KED mode (4.4 ml of He) using Pt 195 as internal standards. For the quantification of Mo, the mass 95 was selected, and a 5-points calibration curve was used for the mass estimation.

3.4 One-pot processes: Molybdate Ionic Liquid in a Divergent Approach for a Tandem Oxidative Carbonation Process



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3.4.1 Abstract

Building on previous studies of Mo-ILs in CO₂ insertion reactions, this chapter focuses on combining CO₂ insertion and alkene epoxidation in tandem processes. Alkene epoxidation reactions were catalyzed by [N_{8,8,8,1}]₂[MoO₄], synthesized applying a sustainable, halide-free methodology discussed in detailed in previous section. Epoxidation reactions were conducted in a biphasic system H₂O/alkene in presence of a catalytic system composed of [N_{8,8,8,1}]₂[MoO₄] (5 % mol) and H₃PO₄ (5 % mol) at T = 80 °C, with variable amounts of excess H₂O₂, depending on the nature and the degree of substitution of the alkene employed. The catalytically active species is a peroxophosphomolybdate formed in situ, detected by FT-IR and NMR spectroscopy. Upon epoxidation, the corresponding COC derivatives were synthesized applying different approaches. COCs derived from terminal alkenes (e.g. 1-decene) were selectively obtained following a one-pot, three-step assisted tandem catalysis (AsTC) process involving a transcarbonation reaction with dimethylcarbonate, obtaining 4-octyl-1,3-dioxolan-2-one in 66 % yield. COCs derived from disubstituted acyclic alkenes like methyl oleate were selectively prepared by a one-pot, two-step AsTC process with a direct CO₂ insertion step on epoxidized methyl oleate, producing methyl oleate carbonate in 54 %. The results reported in this chapter have been submitted for publication.

3.4.2 Introduction

Catalysis plays a prominent role in sustainable organic chemistry, however to achieve truly eco-friendly, energy-efficient, and cost-effective processes it needs to be integrated with other parameter optimization approaches.¹²⁷ One promising approach for the synthesis of complex molecules from simple precursors is the development of one-pot tandem catalytic reactions, where a single catalyst performs multiple chemical transformations. Tandem catalytic reactions involve the sequential formation of substrates through multiple distinct processes.¹²⁸ In contrast, one-pot tandem procedures provide a greener and more efficient alternative to traditional stepwise methods. By eliminating the need for intermediate isolation and workup steps, these approaches reduce material use and simplify the overall process, aligning with the principles of green chemistry. However, the widespread adoption of tandem processes is limited by the challenging design of suitable reaction conditions combining compatible catalysts, reagents, and solvents functioning together throughout the entire reaction sequence and with a broad substrate scope. Tandem catalysis can be categorized into three types: i) *Auto-tandem catalysis (AuTC)*, where a single catalyst promotes distinct reactions without any additional input; ii) *Assisted-tandem catalysis (AsTC)*, where a single catalyst requires a change in reaction conditions, such as temperature or the addition of a co-catalyst, to switch between catalytic mechanisms; iii) *Orthogonal-tandem catalysis (OTC)*, where two or more catalysts with distinct mechanisms operate simultaneously.¹²⁹

Direct oxidative carbonation (DOC) of olefins to produce cyclic organic carbonates (COCs) is a promising tandem reaction that proceeds through two consecutive epoxidation-carbonation steps, as depicted in **Figure 3.23**.

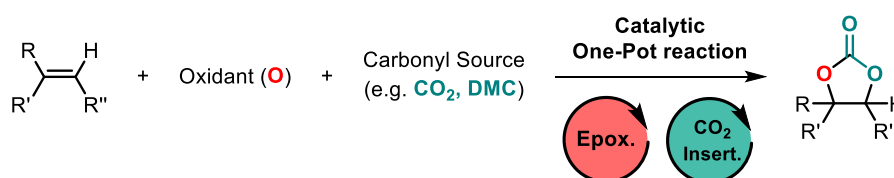


Figure 3.22 : General reaction scheme for the direct oxidative carboxylation of olefins through epoxidation and CO₂ insertion reactions.

As detailed in the previous section, the most employed synthetic methodology to produce COCs involves CO₂ fixation into epoxides. While CO₂ can be considered as a renewable-based feedstock, the use of epoxides as starting materials is neither sustainable, nor safe, nor green.¹³¹ Tandem DOC avoids the use of toxic and potentially explosive epoxides by directly employing olefins, their unsaturated precursors. Despite its practical potential, integrating epoxidation and CO₂ insertion steps into a single process is challenging.¹²⁶

Choosing the right oxidant for the epoxidation step is difficult. While organic peroxides like *tert*-butyl hydroperoxide (TBHP) are commonly used for laboratory scale epoxidations, they are undesirable from a sustainable chemistry point of view, mainly because of the formation of (over)stoichiometric quantities of acid waste. Molecular oxygen (O₂) represent the greenest option in terms of atom economy, but requires catalytic design for its selective chemical activation and can cause undesired radical side reactions.¹³² Hydrogen peroxide (H₂O₂) is a widely employed alternative

and sustainable oxidant, thanks to its wide applicability, scalability, and minimal environmental impact.¹⁰⁹ Its high atom economy, minimal hazard at concentrations < 30 % wt., and cost-effectiveness, have boosted H₂O₂ applications as sustainable oxidant, even if its current production processes cannot be considered sustainable.¹³³ Combining olefin epoxidation using H₂O₂ with CO₂ fixation without added solvents is an appealing and ambitious synthetic challenge. However, several issues including reactant miscibility in multiphasic mixtures, overoxidation, and COC hydrolysis make this approach only seldomly explored.^{134–137}

As mentioned in **Section 3.3**, POMs refer to a class of compounds composed of oxide building blocks based on early transition metals from groups V and VI. Specifically, the term heteropolymetalates describes POMs that incorporate non-metal heteroatoms (X = P, Si, As, Ge), following the general formula (X_aM_bO_c)ⁿ⁻. More specifically, molybdenum-based polyoxometalates have demonstrated remarkable versatility and efficiency in catalyzing a wide array of oxidation processes, including olefin epoxidation and oxidation of alcohols, glycols, and phenols.^{138,139} Mo-POMs are active catalysts in Venturello-Ishii phase transfer catalyst (PTC) conditions, which are widely employed in epoxidation reactions.^{140–145} PTC systems typically consists of a peroxopolymetalate anion (with M = W or Mo) and a quaternary ammonium counter cation (R₄N⁺). As depicted in **Figure 3.24**, the POM anion reacts selectively with H₂O₂ and Brønsted acids, typically in presence of H₃PO₄, generating a peroxo-POM anion. This latter complex is highly reactive towards epoxidation, transferring oxygen selectively from H₂O₂ to the alkene co-reactant. The quaternary ammonium counter cation is necessary to facilitate peroxo-POM anion phase transfer from the aqueous phase, where it is generated, to the organic phase containing the alkene.^{141,142}

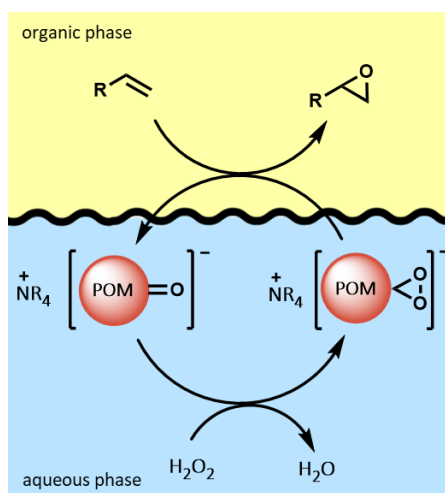


Figure 3.23: Selective epoxidation with Venturello-Ishii phase PTC: formation of the active catalytic specie by PTC.

Ishii *et al.* performed the oxidation of various organic substrates using commercially available 35 % H₂O₂ in homogeneous phase or, more commonly, in a biphasic system.^{143,145,146} This process employs a catalyst composed of heteropolyacids ([PW₁₂O₄₀]³⁻ or [PMo₁₂O₄₀]³⁻) and cetylpyridinium chloride as PTC. This catalyst promoted alkenes epoxidation,¹⁴³ and allylic alcohols epoxidation in a biphasic system with CHCl₃ as co-solvent.¹⁴⁶ Subsequently, Csányi and Jaky found that in biphasic system, heteropolyacids H₃[PW₁₂O₄₀] and H₃[PMo₁₂O₄₀], in presence of excess H₂O₂ and a phase

transfer agent, decomposed forming various peroxo complexes, such as $\{\text{PO}_4[\text{WO}(\text{O}_2)_2]_4\}^{3-}$ and $\{\text{PO}_4[\text{MoO}(\text{O}_2)_2]_4\}^{3-}$, which then migrated into the organic phase.¹⁴⁷ They proposed that these peroxo-POM anions, derived from $[\text{PW}_{12}\text{O}_{40}]^{3-}$ and $[\text{PMo}_{12}\text{O}_{40}]^{3-}$, are the catalytically active species for biphasic epoxidation of olefins. In particular, $[\text{PMo}_{12}\text{O}_{40}]^{3-}$ showed lower activity compared to $[\text{PW}_{12}\text{O}_{40}]^{3-}$, which achieved a high yield of 1-epoxyoctane (Yield = 79 %) when performing the epoxidation reaction on neat 1-octene, without PTC in presence of aqueous H_2O_2 as the oxidant. No catalytic activity was observed when all reagents were mixed simultaneously. Unfortunately, the main drawbacks of the Venturello-Ishii process include fast catalyst deactivation and the use of halogenated solvents (**Figure 3.25**, left).¹⁴⁸

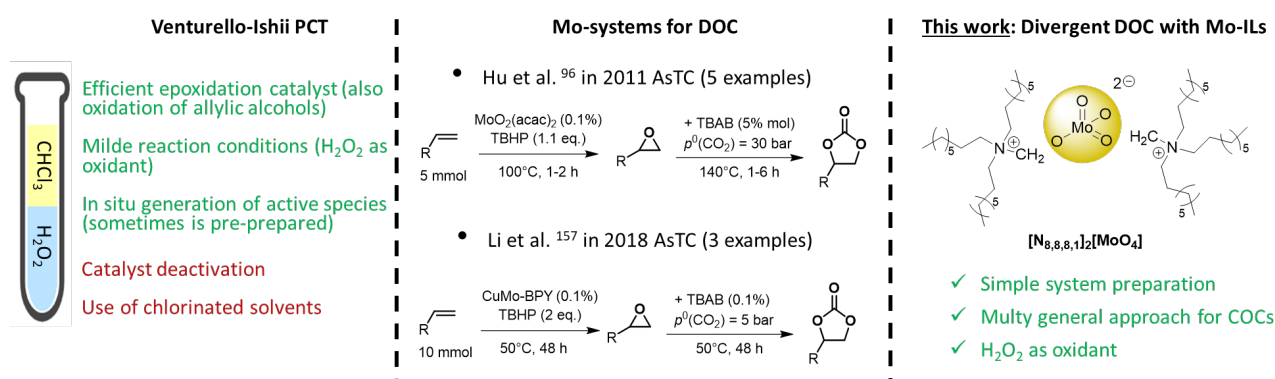


Figure 3.24: State of the art on Mo-based POMs suitable for tandem processes (left and center) and scope of this work (right).

While many literature studies focused on tungsten-based phase transfer system, molybdenum based ones were much less studied as epoxidation catalysts, due to their lower reactivity compared with W-based catalysts.^{138,147,148} The use of molybdenum-based POMs in H_2O_2 -based oxidations marks a notable advancement in the field of oxidation catalysis. However, the current applications of these systems are limited. Expanding their synthetic use would significantly contribute to the broadening of the range of possible applications of Mo-POM in green chemistry. Among the examples reported, Aubry *et al.* explored the reactivity of $\text{H}_2\text{O}_2/[\text{MoO}_4]^{2-}$ oxidation system for epoxidation or peroxidation of tiglic acid, observing selective epoxidation *via* tetraperoxodimolybdate $[\text{Mo}_2\text{O}_3(\text{O}_2)_4]^{2-}$ formation.¹⁵⁰ In another interesting study reported by Kiefer and co-workers the epoxidation activity of peroxomolybdenum complexes $[\text{MoO}(\text{O}_2)_2(\text{OXR}_3)]$ (X = N, P, As; R = *n*-dodecyl) was evaluated in a biphasic chloroform-1-octene/ H_2O_2 system, and rationalized combining density functional calculations and Raman spectroscopy.¹⁵¹

More recently, different works reported the combined use of ILs with *in situ* generation of polyoxomolybdate species for effective epoxidation reactions. Kühn *et al.* studied the catalytic epoxidation of cyclooctene using *in situ* prepared polyoxomolybdates, obtained from 1-carboxymethyl-3-methylimidazolium chloride and Na_2MoO_4 with H_2O_2 as oxidant.¹⁵² Zhang reported the *in situ* preparation of $[\text{C}_4\text{C}_1\text{im}]_3[\text{PMo}_{12}\text{O}_{40}]$ from $[\text{C}_4\text{C}_1\text{im}][\text{Br}]$ and $\text{H}_3\text{PMo}_{12}\text{O}_{40}$; the resulting catalytically active specie was employed in the epoxidation of cyclododecene with H_2O_2 as the oxidant.¹⁵³ Silva *et al.* explored the catalytic activity of $\text{H}_3\text{PMo}_{12}\text{O}_{40}$ as Brønsted acid towards

epoxidation reactions of terpene alcohols with aqueous H_2O_2 as oxidant, observing a comparable reactivity with traditional Brønsted acids ($\text{H}_3\text{PW}_{12}\text{O}_{40}$, $\text{H}_3\text{PMo}_{12}\text{O}_{40}$ and $\text{H}_4\text{SiW}_{12}\text{O}_{40}$): in particular, nerol was selectively epoxidized to nerol epoxide with a 99 % conversion and 97 % selectivity.¹⁵⁴

As noted in **Section 3.3**, various molybdenum-based systems are capable of directly interacting with CO_2 . However, only a few of these systems have been reported to effectively perform tandem DOC reactions. Hu *et al.* reported an efficient protocol for the preparation of COCs from olefins and CO_2 through an assisted tandem process using molybdenyl acetylacetonate ($\text{MoO}_2(\text{acac})_2$) combined with TBHP and TBAB (**Figure 3.25**, center).⁹⁴ In particular, the epoxidation step was carried out by charging the reactor with the alkene (5.0 mmol), $\text{MoO}_2(\text{acac})_2$ (0.1 % mol), and TBHP (5.5 mmol) and heating at $T = 100\text{ }^\circ\text{C}$ for $t = 1\text{--}2\text{ h}$. After completion of the epoxidation step, the autoclave was charged with the appropriate amount of TBAB co-catalyst (5.0 % mol), filled with $p^0(\text{CO}_2) = 30\text{ bar}$, and reacted at $T = 140\text{ }^\circ\text{C}$ for $t = 1\text{--}6\text{ h}$. This methodology was applied to five different alkenes (both terminal and cyclic), obtaining the corresponding COC in 31 - 83 % yield. In 2018, Li *et al.* reported a bifunctional catalyst, $\text{Cu}_3(\mu_3\text{-OH})_2(4,4'\text{-bpy})(\text{MoO}_4)_2$ (CuMo-BPY), for the assisted tandem catalytic conversion of alkenes into COCs (**Figure 3.25**, center).¹⁵⁵ The epoxidation reaction was performed using 10.0 mmol of alkene, 0.1 % mol of CuMo-BPY, and 2.0 equiv. of TBHP at $T = 50\text{ }^\circ\text{C}$ for $t = 48\text{ h}$. The CO_2 insertion step was carried out by adding 0.1 mmol of TBAB and $p^0(\text{CO}_2) = 5\text{ bar}$, performing the reaction at $T = 50\text{ }^\circ\text{C}$ for $t = 48\text{ h}$. While epoxidation was achieved with six different alkenes, the tandem reaction could only be completed for three examples, due to the structural and reactivity differences of epoxides, yielding the corresponding COCs in 85 - 91 % yield.

In this study, we optimized the catalytic activity of $[\text{N}_{8,8,8,1}]_2[\text{MoO}_4]$ in tandem oxidation-carboxylation process. $[\text{N}_{8,8,8,1}]_2[\text{MoO}_4]$ was synthesized through a sustainable procedure, and in presence of H_3PO_4 as co-catalyst and H_2O_2 as oxidant, it is possible to generate catalytically active peroxo-POM *in situ* is active towards epoxidation reactions in a H_2O /alkene biphasic system without requiring additional solvents (**Figure 3.25**, right). The peroxo-POM species was characterized by FT-IR and ^{31}P NMR spectroscopy. Moreover, following epoxidation, we applied multiple divergent methodologies for the preparation of the corresponding COC derivatives. Depending on the structural features of the starting olefin, this was achieved either via an AsTC one-pot three-step methodology involving a transcarbonation reaction with DMC or through a AsTC one-pot two-step process involving a CO_2 insertion reaction.

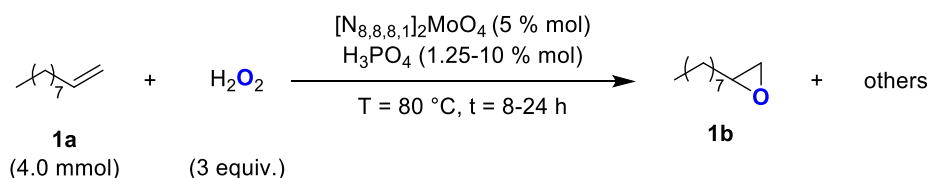
3.4.3 Mo-IL preparation

Trioctylmethylammonium molybdate, $[N_{8,8,8,1}]_2[MoO_4]$, (Catalyst **(6)** of **Figure 3.13**) was prepared following a previously published green, halide-free procedure starting from trioctylamine, dimethylcarbonate (**DMC**) and molybdic acid, depicted in **Scheme 3.5** and described in **Section 3.1.3**.⁶⁹ Catalyst **(6)** was selected due to the presence of a lipophilic tetraalkylammonium counteranion, which can act as a phase transfer agent, in combination with a molybdate anion, whose activity towards CO_2 insertion reactions was recently reported by our group, as described in **Paragraph 3.3**.⁶⁹ Furthermore, we aimed at discovering if **(6)** specie was also active in alkene epoxidation reactions to design a tandem **DOC** approach for the preparation of COCs.

3.4.4 Epoxidation

1-Decene (**1a**) was chosen as the model substrate to optimize the catalytic activity of **6** catalyzed epoxidation. **1a** is an aliphatic terminal olefin, which is typically poorly reactive towards epoxidation due to the presence of a deactivated double bond.¹⁵⁶ We aimed at pursuing a sustainable, solvent-free procedure because our Mo-IL could act simultaneously as oxidation catalyst as well as PTC facilitating the biphasic reaction. Given our previous experience with these catalytic systems (see **Paragraph 3.3**),¹⁰⁹ we initially tested different amounts of **6** catalyst and H_3PO_4 co-catalyst, using 1-decene (**1a**, 4.0 mmol) as a model olefin in presence of H_2O_2 (30% w/w), as summarized in **Table 3.9**.

Table 3.8: Variation of the amount of **6** catalyst and H_3PO_4 co-catalyst on the epoxidation of 1-decene (**1a**) to 1-decene oxide (**1b**)^a



Entry	$[N_{8,8,8,1}]_2[MoO_4]$ (% mol)	H_3PO_4 (% mol)	H_2O_2 (equiv.)	t (h)	Conv (%) ^b	Sel (%) ^b
1	5	None	2.0	8	-	-
2	none	5.00	2.0	8	-	-
3	5	1.25	3.0	8	-	-
4	5	2.50	3.0	8	5	100
5	5	5.00	3.0	8	35	96
6	5	10.00	3.0	8	45	71
7 ^c	5	5.00	9.0	24	71	95

Reaction conditions: **1a** (4.0 mmol), H_2O_2 30 % V/V (1-4 equiv.), in presence of $[N_{8,8,8,1}]_2[MoO_4]$ (5 % mol) and, where indicated, H_3PO_4 . ^bConversion, selectivity and yield calculated by GC-MS analysis using mesitylene as internal standard. ^c H_2O_2 (aq) added using syringe pump

Initially, two blank tests without catalyst- or co-catalyst were performed, observing in both cases no conversion of **1a** (Entries 1 and 2, **Table 3.9**). It is worth noting that using H_3PO_4 in the absence of **(6)** demonstrated that the latter is required to activate H_2O_2 , confirming that phosphoric acid acts only as a co-catalyst. The use of a phosphorous-based promoter (in our case H_3PO_4) improves the epoxidation step through *in situ* formation of peroxophosphomolybdate species, known to be catalytically active in biphasic mixtures.^{138,157} Lowering the quantity of H_3PO_4 co-catalyst (*cfr.* Entries 3 and 4, **Table 3.9**) to sub-stoichiometric concentrations, with respect to the quantity of **(6)**, lead to a sluggish catalytic activity. On the other hand, overstoichiometric quantities of co-catalyst (up to 10 % mol H_3PO_4 , Entry 6, **Table 3.9**) led to a good catalytic activity (Conv. **1a** = 45 %) albeit with a lower selectivity towards the desired epoxidation product **1b** (Sel. **1b** = 75 %). These results indicate that there is an optimal 1:1 catalyst/co-catalyst molar ratio for $\text{H}_3\text{PO}_4/[\text{N}_{8,8,8,1}]_2[\text{MoO}_4]$ which is not related to the stoichiometry of the active species of the catalyst. The $\text{H}_3\text{PO}_4/[\text{N}_{8,8,8,1}]_2[\text{MoO}_4]$ molar ratio affects the pH of the solution and is turn crucial for the formation of the most catalytically active peroxo-phosphomolybdate species for the epoxidation reaction.

Subsequently a temperature screening was performed as depicted in **Figure 3.25**. We observed that $T = 80\text{ }^\circ\text{C}$ (green line, **Figure 3.25**) was the optimal operating temperature, achieving a 32 % conversion of 1-decene with 87 % selectivity toward 1-decene oxide (**1b**) after $t = 8\text{ h}$. Prolonging the reaction time resulted in complete loss of selectivity and formation of over-oxidation products such as 1,2-decanediol, decan-2-one, and decanoic acid in traces (see **Figure A 19** in the appendix section). Increasing the reaction temperature to $T = 100\text{ }^\circ\text{C}$ (red line, **Figure 3.25**), no conversion of **1a** was observed, likely due to the fast decomposition of H_2O_2 . While when decreasing the operating temperature to $T = 60\text{ }^\circ\text{C}$ (blue line, **Figure 3.25**), some conversion of **1a** was observed only after $t = 24\text{ h}$ (Conv. **1a** = 23 %, Sel. **1b** = 99 %), indicating that the epoxidation rate is very slow at this temperature.

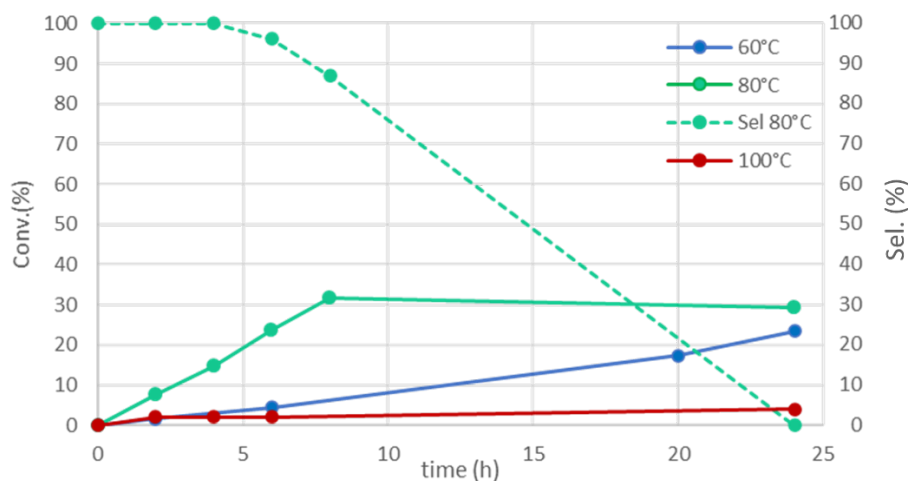
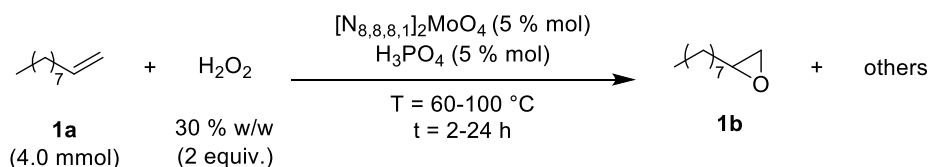


Figure 3.25: Reaction temperature optimization for the epoxidation of 1-decene (**1a**) to decene oxide (**1b**). ^aReaction conditions: **1a** (4.0 mmol), H₂O₂ 30 % V/V (2.0 equiv.), [N_{8,8,8,1}]₂[MoO₄] (5.0 % mol) and H₃PO₄ (5.0 % mol). ^bConversion, selectivity and yield were calculated by GC-MS analysis using mesitylene (20 % mol) as internal standard.

The quantity of oxidant (H₂O₂ 30 % w/w) was then optimized at T = 80 °C. Epoxidation reactions were carried out varying the amount of H₂O₂ (between 1.0 and 4.0 equiv. respect to the substrate), heating at T = 80 °C for t = 8 h, as depicted in **Figure 3.26**. Using only 1.0 equiv. of H₂O₂ resulted in no significant conversion of **1a** after t = 8 h (Conv. **1a** < 5 %). By contrast, using 3.0 equiv. of H₂O₂ a maximum 35 % conversion of **1a** was achieved after t = 8 h with 96% selectivity for **1b**. Increasing the amount of H₂O₂ to 4 equiv. led to a loss of selectivity and formation of over oxidation products. A slight excess of hydrogen peroxide is required to balance its consumption in both formation of the catalytically active species and thermal degradation.

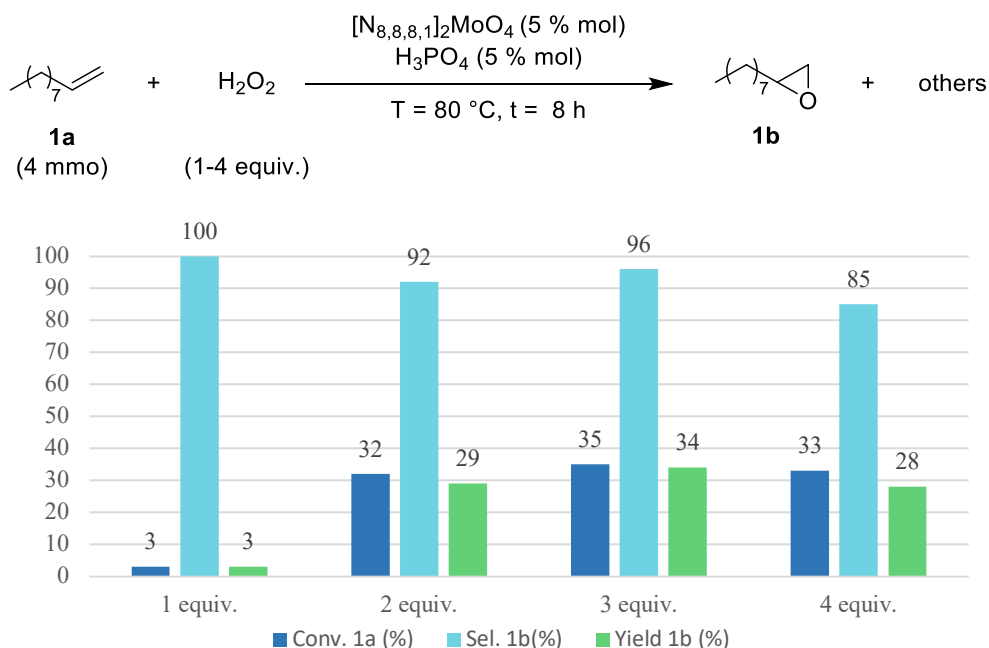


Figure 3.26: Variation of the amount of H₂O₂ for the epoxidation of 1-decene (**1a**) to decene oxide (**1b**). ^aReaction conditions: 1-decene (4.0 mmol), H₂O₂ 30 % w/w (1.0 – 4.0 equiv.), [N_{8,8,8,1}]₂[MoO₄] (5 % mol) and H₃PO₄ (5 % mol). Conversion, selectivity and yield calculated by GC-MS analysis using mesitylene (20 % mol) as internal standard

3.4.5 Characterization of catalyst system

To understand better the structural and electronic features and rationalize the activity of the catalytic system, the different species formed during the epoxidation reaction were characterized using various spectroscopic techniques. **Figure 3.27** shows the FT-IR spectra of different molybdate species formed during epoxidation. The spectra of [N_{8,8,8,1}]₂[MoO₄] is displayed in **Figure 3.27**, top left: presence of molybdate species is confirmed by the broad absorption band at 824 cm⁻¹, assigned to Mo–O stretching (*vide supra*, **Section 3.3**).⁶⁹

When 2 equiv. of H₂O₂ were directly added to the initial catalyst, the reaction mixture quickly turned from pale yellow (attributed to the presence of (**6**)) to red (see **Figure A20**, Appendix section): the observed color change was accompanied by formation of oxygen bubbles, ascribed to the catalytic decomposition of hydrogen peroxide.¹⁵⁸ Given the slight basicity of [N_{8,8,8,1}]₂[MoO₄] (pH ≈ 8-9, measured by pH test strip), formation of the corresponding tetraperoxomolybdate species [Mo(O₂)₄]²⁻ was hypothesized. This was further confirmed by FT-IR spectra (**Figure 3.27**, top right) with the appearance of the typical absorption bands of tetraperoxomolybdate $\nu(\text{Mo}=\text{O})$ at 958 cm⁻¹, $\nu(\text{O}-\text{O})$ at 855 cm⁻¹ and $\nu_{\text{asym}}(\text{Mo}-\text{O}_2)$ at 618 cm⁻¹.^{159,160} Unfortunately, this complex is inactive for the epoxidation reaction, due to the fast catalytic degradation of H₂O₂.

Conversely, when adding H₃PO₄ before the oxidant, H₂O₂, the reaction mixture became green-yellow, and this color was attributed to the formation of new molybdate species active towards epoxidation. In particular, the observed green-yellow color was ascribed to the formation of various peroxo-phosphomolybdate species, *e.g.* {PO₄[MoO(O₂)₂]₄}³⁻ and {HPO₄[MoO(O₂)₂]₂}²⁻, which were

previously reported as catalytically active species in the biphasic epoxidation of olefins.^{138,157} This hypothesis is supported by the FT-IR spectra (**Figure 3.27**, bottom left), showing the appearance of a more intense band at 1113 cm^{-1} assigned to $\nu(\text{P-O})$, and of an intense absorption around $950\text{--}920\text{ cm}^{-1}$ due to (Mo=O) and $\nu(\text{O-O})$ at 857 cm^{-1} .

When following the epoxidation of 1-decene for prolonged reaction times ($t = 8\text{--}24\text{ h}$, **Figure 3.25**), after $t = 8\text{ h}$ we observed a loss of selectivity attributed to the formation of catalytically inactive phosphomolybdic species $[\text{PMo}_{12}\text{O}_{40}]^{3-}$, indicated by the appearance of a blue colored solution. This was further confirmed by FT-IR, observing the typical absorption of $\nu(\text{P-O})$ at 1062 cm^{-1} , $\nu(\text{Mo-O})$ at 959 cm^{-1} and $\nu(\text{Mo-O-Mo})$ at 808 cm^{-1} (**Figure 3.27**, bottom right).¹⁵⁴ Interestingly, adding additional H_2O_2 to the blue solution of $[\text{PMo}_{12}\text{O}_{40}]^{3-}$ allowed the regeneration of peroxophosphomolybdic species, visualized by a change in of the solution from blue to green-yellow (see **Figure A20**, Appendix section).¹⁵⁴

H_2O_2 was also added constantly to the reaction mixture with a syringe pump: with this setup the concentration of H_2O_2 was maintained constant during the whole reaction, avoiding the loss of selectivity due to the formation of phosphomolybdate species. In these latter conditions, **1a** conversion increased to 71%, observing the highest selectivity for **1b** (Sel. **1b** = 95 %, Entry 7, **Table 3.9**). It should be noted that phosphomolybdic acid is an excellent oxidant, commonly used in organic chemistry laboratories in ethanol solution for the development of TLC.

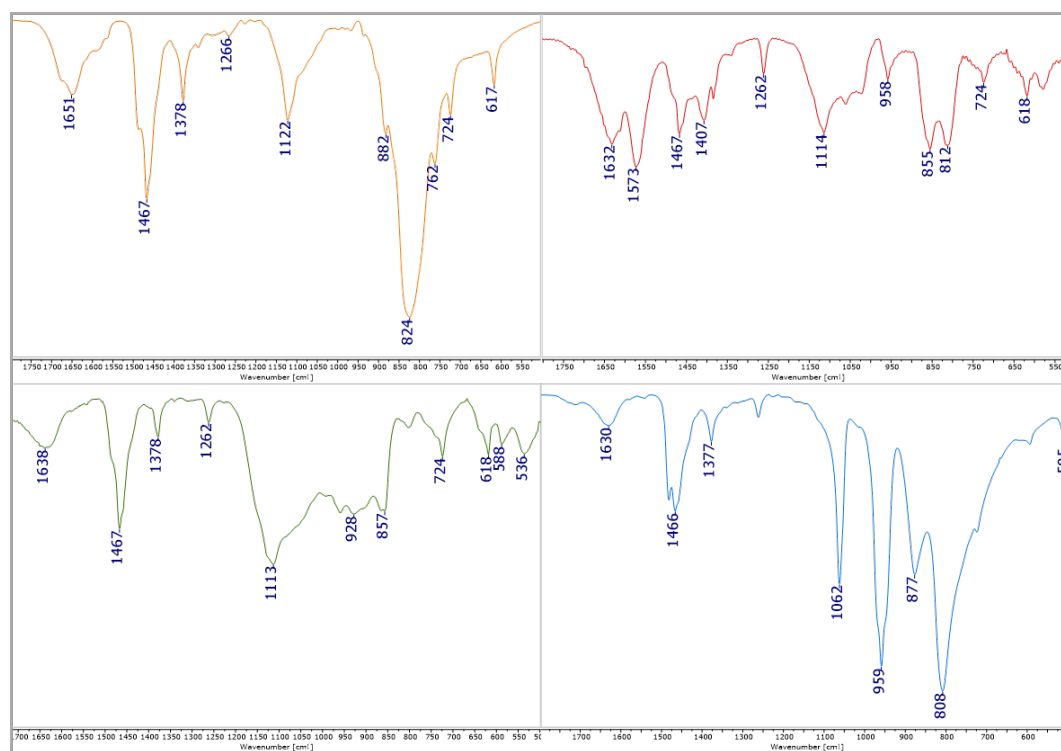


Figure 3.27: FT-IR spectra of the different molybdates species formed during the epoxidation process. Top left: $[\text{N}_{8,8,8,1}]_2[\text{MoO}_4]$; top right: $[\text{Mo}(\text{O}_2)_4]^{2-}$; bottom left: $\{\text{PO}_4[\text{MoO}(\text{O}_2)_2]_4\}^{3-}$ and $\{\text{HPO}_4[\text{MoO}(\text{O}_2)_2]_2\}^{2-}$; bottom right: $[\text{PMo}_{12}\text{O}_{40}]^{3-}$.

Epoxidation reaction mixtures were also further characterized by ^{31}P NMR analysis, as shown in **Figure 3.28**. When 0.2 mmol of H_3PO_4 were added to $[\text{N}_{8,8,8,1}]_2[\text{MoO}_4]$ (0.2 mmol) in CDCl_3 solution, a variation of chemical shift from 0.00 to 0.92 ppm, indicating an interaction between the two species (**Figure 3.28**, blue trace). When excess H_2O_2 30 % wt. (0.5 mL, 5.0 mmol) was added to this solution, formation of three species with chemical shifts at 6.75, 3.18 and 1.59 ppm, respectively, was observed (**Figure 3.28**, green trace). As an additional test to verify the reversibility of our catalytic system, we synthesized separately $[\text{N}_{8,8,8,1}]_3[\text{PMo}_{12}\text{O}_{40}]$ starting from $[\text{N}_{8,8,8,1}][\text{OCOOCH}_3]$ and $\text{H}_3\text{PMo}_{12}\text{O}_{40}$ and characterized it via ^{31}P NMR in CDCl_3 , observing a single peak at -3.86 ppm (**Figure 3.28**, light green trace). When H_2O_2 was added to this solution, a new signal at 6.75 ppm was observed (**Figure 3.28**, red trace): this latter signal was attributed to the *in situ* formation of peroxophosphomolybdate species active in the epoxidation reaction. These combined analyses confirm the equilibrium relationship between molybdate and phosphomolybdates species while demonstrating the *in situ* generation of active peroxophosphomolybdate species from simple components. Maintaining a constant concentration of hydrogen peroxide avoids the formation of $[\text{PMo}_{12}\text{O}_{40}]^{3-}$, limiting the loss of selectivity during the epoxidation reaction.

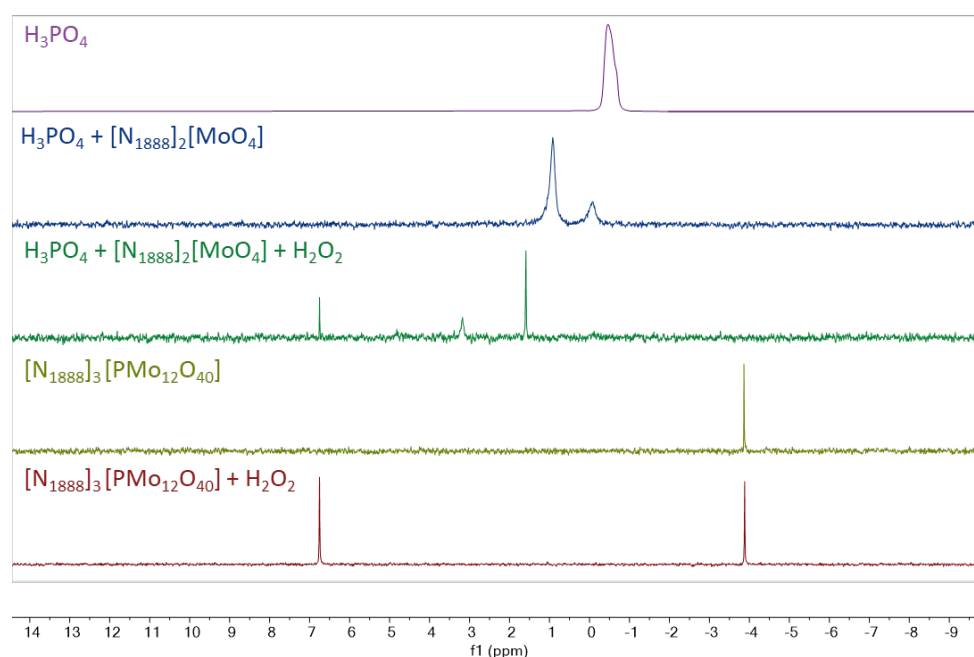


Figure 3.28: ^{31}P NMR spectra of H_3PO_4 (purple), H_3PO_4 and $[\text{N}_{8,8,8,1}]_2[\text{MoO}_4]$ (blue), H_3PO_4 with $[\text{N}_{8,8,8,1}]_2[\text{MoO}_4]$ and H_2O_2 (green), $[\text{N}_{8,8,8,1}]_3[\text{PMo}_{12}\text{O}_{40}]$ (light green) and $[\text{N}_{8,8,8,1}]_3[\text{PMo}_{12}\text{O}_{40}]$ (red). All spectra were acquired after adding H_2O_2 .

3.4.6 Epoxidation Substrate Scope

The catalyst system $[\text{N}_{8,8,8,1}]_2[\text{MoO}_4]/\text{H}_3\text{PO}_4$ was subsequently tested with other alkenes showing a similar reactivity trend for epoxidation reactions. In fact, more activated di- and trisubstituted alkenes reacted faster and required lower excess of H_2O_2 to perform the epoxidation reaction in good conversion and selectivity (reaction times and H_2O_2 equiv. are indicated in **Figure 3.29** for each

substrate). In particular, excellent results were obtained with disubstituted alkenes, *e.g.* methyl oleate (**3a**) and cyclooctene (**4a**) after $t = 8$ h and $t = 2$ h, respectively. On the other hand, no reactivity was observed with electron poor alkenes, such as methyl crotonate (**6a**) and dimethyl maleate (**7a**). Tertiary alkenes also showed a good reactivity, but for these substrates selectivity was somewhat critical, as observed for citronellyl acetate (**8a**). Some exceptions were observed: for example, styrene (**2a**), an electron poor cycloalkene, displayed a high conversion with low selectivity towards the epoxidation product **2b**, generating selectively the overoxidation product benzaldehyde, while cyclohexene (**5a**) was oxidized quantitatively, but the epoxidation product **5b** was rapidly hydrolyzed to the corresponding 1,2-*trans*-cyclohexandiol (**5c**). When epoxidation was tested on limonene (**9a**), chemoselectivity problems were observed due to the presence of two non-chemically equivalent double bonds, which were both overoxidized generating a multitude of different oxidation products.

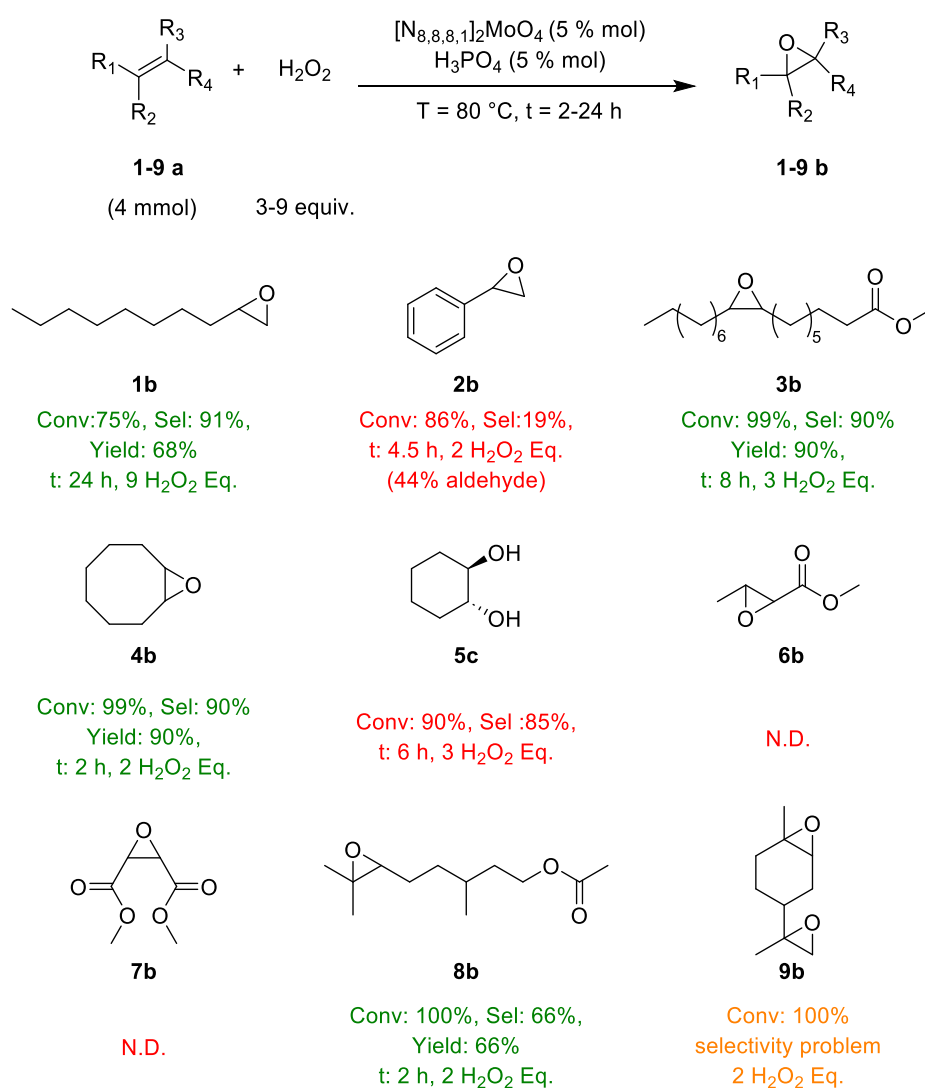


Figure 3.29: Epoxidation reaction with various unsaturated substrates catalyzed by $[\text{N}_{8,8,8,1}]_2[\text{MoO}_4]/\text{H}_3\text{PO}_4$ system. Reaction conditions: olefin (4.0 mmol), H_2O_2 (1-9 equiv.), in presence of $[\text{N}_{1888}]_2[\text{MoO}_4]$ (5 mol %) and H_3PO_4 (5 mol %). Conversion, selectivity and yield calculated by GC-MS and ^1H NMR analysis using mesitylene (20 % mol) as internal standard.

3.4.7 AsTC one-pot three-step methodology for decene carbonate formation

1-Decene is a terminal aliphatic olefin poorly reactive towards epoxidation. Conversely, the insertion of CO₂ into monosubstituted epoxides is easier compared to internal and more sterically congested ones.¹⁶¹ Some preliminary attempts to perform CO₂ insertion tests with 1-epoxydecene were carried out using our Mo-IL/H₃PO₄ catalyst system. Unfortunately, the main product observed was not the corresponding COC, but rather the hydrolysis product 1,2-decanediol. Therefore, we decided to investigate a new strategy involving an initial hydrolysis of the terminal epoxide followed by COC synthesis through a transcarbonation reaction with dimethyl carbonate (DMC).

1,2-epoxyhexane was initially chosen as a model substrate to perform hydrolysis tests under both acidic and basic conditions (**Table A5** in Appendix Section) before verifying the efficacy of this approach with epoxydecene. We observed that in presence of the catalytic system [N_{8,8,8,1}][MoO₄]/H₃PO₄ 1:1 mol/mol led to sluggish results (epoxyhexane conv. = 7 %), mainly ascribed to the residual Brønsted acidity of the reaction mixture. Increasing the concentration of H₃PO₄ from 5.0 to 15.0 mol % (Entries 6 and 7, **Table A5** in Appendix Section), resulted in quantitative formation of the hydrolysis product. However, coupling this high concentration of H₃PO₄ with the previous epoxidation reaction led to a loss of chemoselectivity towards the epoxide product with formation of overoxidation by-products (*vide supra*). Therefore, we replaced H₃PO₄ with H₂SO₄, which did not display over-oxidation issues (Entry 6, **Table A5** in Appendix Section).

The transcarbonation step was initially studied separately under various reaction conditions (**Table A6** in Appendix Section), verifying that both [N_{8,8,8,1}]₂[MoO₄] and [N_{8,8,8,1}][OCOOCH₃] pre-catalyst are active catalysts for the transcarbonation reaction, achieving quantitative conversion and total selectivity for the COC product at t = 3.5 h and t = 2 h, respectively (Entries 1 and 2, **Table A6** in Appendix Section). It was also observed that the presence of water is not tolerated by both these catalytic systems. Therefore, it was necessary to remove water traces before proceeding with the transcarbonation step, which was easily accomplished drying the crude reactant mixture *in vacuo*. With the optimized conditions in hand, a three-step, one-pot process for the assisted tandem synthesis of 1-decene carbonate from 1-decene was developed, as depicted in **Figure 3.30**. After the initial epoxidation reaction (performed in the conditions of Entry 7, **Table 3.8**), 5 mol % of H₂SO₄ were added to the reaction mixture. The hydrolysis was completed in t = 12 h at T = 95 °C, yielding 1,2-decanediol in 68 % yield (**Figure 3.30**, step 2). After the epoxidation reaction, complete H₂O₂ consumption was qualitatively verified by peroxide test (starch iodide paper). Subsequently, water traces were removed *in vacuo*, and excess DMC (3.5 mL, 20.0 equiv.) and [N_{8,8,8,1}][OCOOCH₃] (10 % mol) were introduced for the transcarbonation step, obtaining 1-decene carbonate in 66 % yield after t = 16 h at T = 90 °C (**Figure 3.30**, step 3).

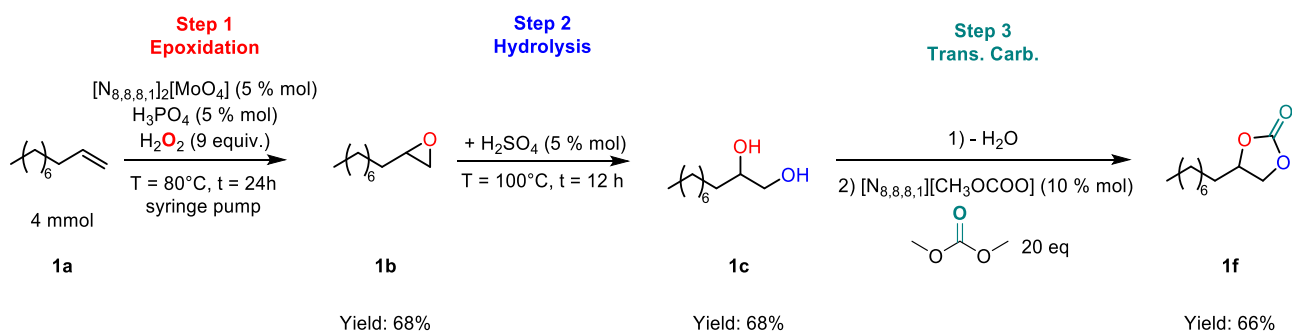


Figure 3.30: Three-step one-pot process for the assisted tandem synthesis of 1-decene carbonate from 1-decene.

3.4.8 AsTC one-pot two-step process for methyl oleate carbonate formation:

Methyl oleate, a fatty acid methyl ester derived from biodiesel manufacture was chosen as the secondary alkene model for studying the direct oxidative carbonation (DOC).¹⁶⁵ The corresponding methyl oleate epoxide (**2c**) was synthesized using a biphasic system with $[N_{8,8,8,1}]_2[MoO_4]$ (5 mol%), H_3PO_4 (5 mol%), and 3 equiv. of H_2O_2 over $t = 8$ h at $T = 80^\circ C$ (Figure 3.31, step one). Differently from 1-epoxydecene (*vide supra*), **2c** is not hydrolyzed during the CO_2 insertion step, which allowed for further investigation of direct CO_2 insertion. The results of these investigations are summarized in Table A7 in the Appendix Section.

Initially, the CO_2 insertion step was performed without adding a co-catalyst at $p^0(CO_2) = 40$ bar, $T = 100^\circ C$ and $t = 10$ h, resulting in trace conversion of **2c** (Entry 1, Table A7 in Appendix Section). Differently from the previous results reported in Section 3.3,⁶⁹ in presence of H_3PO_4 and residual water from the epoxidation step, Mo-IL catalyst displayed a sluggish reactivity. It is also important to highlight that compound **2c** is a sterically hindered internal epoxide, which is inherently less active towards CO_2 insertion reactions compared to terminal epoxides. To improve the conversion, the introduction of a co-catalyst was necessary. The best results were achieved in the presence of TBAB (5 % mol) as the nucleophilic co-catalyst (Entry 2, Table A7 in Appendix Section). Subsequently, various parameters such as temperature, pressure, and reaction time were optimized. The most favorable conditions were: TBAB (5 % mol), $T = 100^\circ C$, $p^0(CO_2) = 40$ bar $t = 24$ h. Under these optimized conditions, the direct synthesis of methyl oleate carbonate (**3c**) via AsTC one-pot two-step procedure was achieved with an overall 54 % yield.

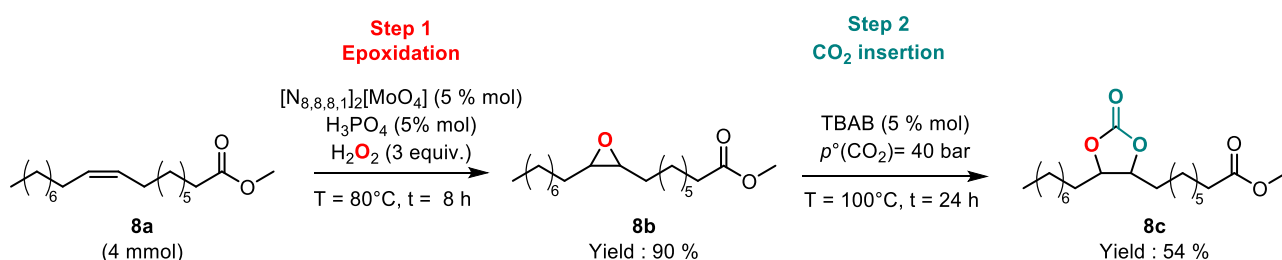


Figure 3.31: Two-step one-pot process for the assisted tandem synthesis of methyl oleate carbonate (8c) from methyl oleate (8a).

3.4.9 Conclusion

In this chapter, we demonstrated the ability of $[N_{8,8,8,1}]_2[MoO_4]$ to generate catalytically active peroxo-phosphomolybdate species in presence of H_2O_2 as oxidant. The resulting catalyst was employed in epoxidation reactions within a biphasic H_2O /alkene system without the need for additional solvents. The formation of peroxo-phosphomolybdate species was confirmed by FT-IR and ^{31}P NMR spectroscopy. After the epoxidation step, we explored multiple methodologies to prepare the corresponding COCs derivatives. This included a one-pot, three-step AsTC methodology involving a transcarbonation reaction with DMC for 1-decene, and a one-pot, two-step AsTC process involving CO_2 insertion for methyl oleate. We are currently developing a similar one-pot, three-step AsTC process using cyclooctene as substrate. Achieving the synthesis of the corresponding COC is a challenging yet promising objective that would advance current synthetic methods.

3.4.10 Experimental Section

Materials and methods

All reagents and solvents employed [ethyl acetate (EtOAc), diethyl ether (Et_2O), petroleum ether, methanol (MeOH), mesitylene (MES), dimethylcarbonate (DMC), trioctylamine (TOA), 1-decene, H_2O_2 (30% w/w), phosphoric acid (>99%), sulfuric acid, molybdic acid, phosphomolybdic acid, styrene, oleic acid, cyclooctene, cyclohexene, crotonic acid, dimethyl maleate, citronellyl acetate, citronellol, limonene, triethylamine (TEA), sodium hydroxide, tetrabutylammonium bromide (TBAB), tetrabutylammonium iodide (TBAI), potassium bromide, silica gel (70-230 mesh), chloroform-*d* ($CDCl_3$), methanol-*d*4 (CD_3OD-d_4), deuterium oxide (D_2O-d_2) and dimethyl sulfoxide-*d*₆ ($DMSO-d_6$)] were purchased from Sigma Aldrich (now Merck) with $\geq 98\%$ purity, and used without further purification, unless otherwise specified. CO_2 (99.999 %) was supplied by SIAD.

Qualitative and quantitative analysis and characterization of reaction mixtures and pure products were performed with a GC-MS system consisting of an Agilent 6890N GC equipped with an HP-5 capillary column (length: 30 m, i.d.: 0.32mm, film thickness: 0.25mm), coupled with Agilent Technologies 5975 mass detector operating at 70 eV. Bruker Ascend 400 (AV400) NMR spectrometer, operating at 400 MHz for 1H , 100 MHz for ^{13}C , 75 Hz for ^{31}P and 26 Hz for ^{95}Mo nuclei. Perkin-Elmer Spectrum One FT-IR spectrometer (PerkinElmer Italia, Milano, Italy) recording at wavenumbers ranging from 400 to 4000 cm^{-1} . GC-MS analyses were performed in EtOAc or Et_2O , while 1H NMR and ^{13}C NMR samples were prepared using deuterated solvents ($CDCl_3$, CD_3OD-d_4 , D_2O or $DMSO-d_6$, > 99.9 % D in all cases). Conversions, yields, and selectivity were calculated by GC-FID and GC-MS with mesitylene as internal standard. Tests were repeated at least twice to ensure reproducibility: conversion and products distribution differed by less than 3% from one experiment to another. For 1H and ^{13}C NMR spectra, the deuterated solvent residual signal was selected as the spectrum reference. ^{95}Mo NMR spectra were referenced to a 2 M Na_2MoO_4 in D_2O external standard ($\delta = 0$ ppm). The spectra were acquired on saturated $DMSO-d_6$ or CD_3CN-d_3 samples using a sweep

width of 1000 ppm, an acquisition time of 2 s per scan, and, depending on the sample, acquiring 2000 to 5000 scans.

Peroxide titration tests were performed according to literature procedure or by peroxides test paper (starch iodide paper purchased from Vetrotecnica Padova).¹⁶³

Typical procedure for the epoxidation reaction.

1-decene (**1a**, 4.0 mmol, 1.0 equiv.), $[\text{N}_{8,8,8,1}]_2[\text{MoO}_4]$ (5 % mol, respect to the substrate **1a**), mesitylene (20 % mol) as internal standard and, where applicable, H_3PO_4 (0–10 mol%) were charged into a 30 mL single neck round bottom flask equipped with a magnetic stirrer and reflux condenser. The mixture was stirred for 1 minute, then hydrogen peroxide (30% w/w in H_2O , 1.0–9.0 equiv.) was added under vigorous stirring. The reactor was heated at the desired temperature ($T = 60\text{--}95\text{ }^\circ\text{C}$) and the mixture stirred at 800 rpm. At chosen intervals, an aliquot of the reaction mixture was sampled and eluted with EtOAc or Et_2O through a Pasteur pipette filled with a plug of 2–3 cm of silica gel to remove the ionic catalyst and Na_2SO_4 to dry the sample. Each aliquot was analysed by GC-MS and ^1H -NMR to calculate conversion, selectivity, and yield. The same procedure was also used for the other alkenes.

Epoxidations were also carried out for $t = 24\text{ h}$: 4 mmol of **1a**, $[\text{N}_{8,8,8,1}]_2[\text{MoO}_4]$ (5 % mol), H_3PO_4 (5 % mol) mesitylene (20 % mol) as internal standard were charged into a 30 mL two-neck round bottom flask equipped with a magnetic stirrer and reflux condenser. The mixture was stirred for 1 minute and hydrogen peroxide (30% w/w H_2O , 3 equiv.) was added. The reactor was heated at $T = 80\text{ }^\circ\text{C}$ and stirred at 800 rpm. After $t = 8\text{ h}$, 6 equiv. of H_2O_2 (30% w/w in H_2O) were added at constant flow with a syringe pump set at a flow rate of 0.15 mL/h. The syringe was further loaded with additional 0.2 mL of H_2O_2 30 % w/w in H_2O to ensure the exact addition of 6 equiv. of oxidant.

Typical procedure for hydrolysis reaction

1,2-Epoxyhexane (4.0 mmol, 1.0 equiv.), 3 mL of H_2O milliQ and the other components indicated in **Table A5** (Appendix Section) were charged in a 30 mL single neck round bottom flask equipped with a magnetic stirrer and reflux condenser. The reactor was heated at $T = 95\text{ }^\circ\text{C}$ and stirred at 800 rpm for $t = 4\text{--}12\text{ h}$. The final mixture was analyzed using ^1H -NMR to calculate conversion, selectivity, and yield using mesitylene (20 % mol) as internal standard.

Typical procedure for transcarbonation reaction with DMC.

1,2-Decandiol (4.0 mmol, 1.0 equiv.), 3.5 mL of DMC (40.0 mmol, 10.0 equiv.) and the other components indicated in **Table A6** (Appendix Section) were charged in 30 mL single neck round bottom flask equipped with a magnetic stirrer and reflux condenser. The reactor was heated at reflux T and stirred at 800 rpm for $t = 2\text{--}16\text{ h}$. The final mixture was analyzed using ^1H -NMR and GC-MS to calculate conversion, selectivity, and yield using mesitylene (20 % mol) as internal standard.

Typical procedure for the AsTC one pot two step DOC reaction

Methyl oleate (**8a**, 4.0 mmol, 1.0 equiv.), $[\text{N}_{8,8,8,1}]_2[\text{MoO}_4]$ (5 % mol with respect to the substrate **8a**), and H_3PO_4 (5 % mol) were charged into a 30 mL single neck round bottom flask equipped with a magnetic stirrer and a reflux condenser. The mixture was stirred for 1 minute before adding H_2O_2 (30% w/w in H_2O , 6 equiv). The reaction mixture was heated at $T = 80\text{ }^\circ\text{C}$ and stirred at 800 rpm for $t = 8\text{ h}$. At the end of the reaction time, the reaction mixture was cooled to room temperature, and the selected halide co-catalyst (5 % mol) was added. The glass reactor was then placed inside a 100 mL stainless steel autoclave, which was sealed, degassed via two vacuum- CO_2 cycles, and pressurized with 20–50 bar of CO_2 . The autoclave was heated to the selected temperature ($T = 80\text{--}120\text{ }^\circ\text{C}$) and the reaction was kept under vigorous stirring for $t = 10\text{--}48\text{ h}$. At the end of each run, the autoclave was rapidly cooled in an ice bath and vented. The final mixture was analyzed by ^1H -NMR to determine conversion, yield, and selectivity.

Synthesis of trioctylmethylammonium phosphomolybdate, $[\text{N}_{8,8,8,1}]_3[\text{PMo}_{12}\text{O}_{40}]$

$\text{H}_3\text{PMo}_{12}\text{O}_{40}$ (2.01 g, 1.0 mmol) was slowly added to an aqueous solution of $[\text{N}_{8,8,8,1}][\text{CH}_3\text{OCOO}]$ (1.33 g, 3.0 mmol). The solution was stirred for $t = 3\text{ h}$ at $T = 70\text{ }^\circ\text{C}$, observing the formation of a green precipitate. The mixture was cooled to rt, and 20 mL of EtOAc were added to solubilize the product, $[\text{N}_{8,8,8,1}]_3[\text{PMo}_{12}\text{O}_{40}]$. The organic phase was washed with 3 x 10 mL of water in order to remove $\text{H}_3\text{PMo}_{12}\text{O}_{40}$ in excess. The organic phase was dried over Na_2SO_4 , filtered and the solvent removed *in vacuo* obtaining 2.69 g of $[\text{N}_{8,8,8,1}]_3[\text{PMo}_{12}\text{O}_{40}]$ (0.92 mmol, 92% yield).

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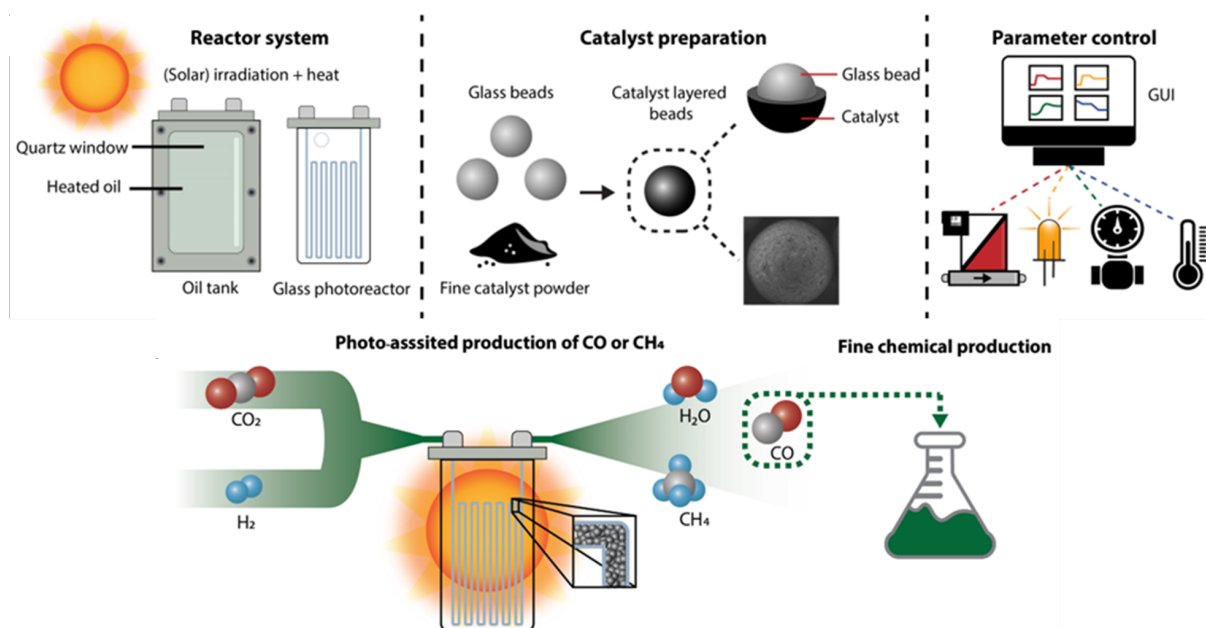
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4. Reductive CO₂ Valorization strategies

4.1 Photothermal reduction of CO₂ to CO



This study has been conducted in the laboratories of Prof. Timothy Noël at the Vant' Hoff Institute, University of Amsterdam, Netherlands. The results reported in this chapter were published in Schuurmans, J. H. A.; Masson, T. M.; Zondag, S. D. A.; Pilon, S.; Bragato, N.; Claros, M.; Den Hartog, T.; Sastre, F.; Van Den Ham, J.; Buskens, P.; Fiorani, G.; Noël, T. Light-Assisted Carbon Dioxide Reduction in an Automated Photoreactor System Coupled to Carbonylation Chemistry. *Chem. Sci.* **2024**, 15 (47), 19842–19850. In this work Nicola performed the experimental investigations on carbonylation reactions.

4.1.1 Abstract

Continuous-flow (CF) methodologies currently represent a strong leverage towards sustainable processing thanks to the precise process control, facile scale-up and excellent heat-and mass transfer. The small dimensions of CF reactors make them highly suitable for light-assisted reactions, as showcase for light-assisted carbon dioxide hydrogenations. Although CF is contributing to mitigating greenhouse gas emissions thanks to the milder reaction conditions required and the possibility of performing scalable light assisted reactions, there are still no commercial standardized reactor systems. The reactor system developed for this work is characterized by improved reproducibility, modularity and automation, facilitating the determination of optimized experimental conditions and catalysts screening. Control over temperature, light intensity, pressure,

residence time, and reagent stoichiometry was established for selective CO₂ reduction to CO over different heterogeneous catalysts. Direct utilization of the produced CO was demonstrated on various carbonylation reactions protocols optimizing an on-demand protocol for the synthesis of functionalized fine chemicals and/or fine chemicals precursors.

4.1.2 Introduction

The ever-rising concentrations of greenhouse gases in our atmosphere, with CO₂ as a notorious example, have propelled sustainable processing and carbon capture and utilization (CCU), which are at the forefront of both academic and industrial research efforts.^{1–5} Tackling the carbon footprint challenge necessitates a collaborative endeavor across various disciplines. As previously discussed in Chapter 1, chemistry and chemical engineering, guided by the principles of green chemistry, have a pivotal role in achieving this overarching goal.^{6,7} This ambitious objective entails a fundamental shift from conventional fossil fuel-based methodologies towards sustainable alternatives, exemplified by the emergence of photochemical processes and circular chemistry practices.^{8,9} These approaches require milder conditions and, where feasible, harness solar energy as a green and renewable driving force for reactions.^{10–13} Integrating solar-powered or light-assisted techniques with continuous-flow (CF) technologies offers enhanced control, scalability, selectivity, as well as superior mass and heat transfer process capabilities.^{14–17} Although CO₂ represents an ideal C¹ building block, its inert nature has limited widespread application in synthetic organic chemistry. Arguably, a more promising approach involves converting CO₂ into diverse C¹ building blocks like methane or carbon monoxide.¹⁸

Carbon monoxide (CO), in particular, has an established role in synthetic chemistry as an activated C¹ building block. CO can be obtained upon reduction of CO₂ achieved through different hydrogenation reactions, such as the Sabatier reaction and reverse water gas shift (**RWGS**) reaction. These reactions have also been investigated as light-assisted processes in photochemical or photothermal systems,^{19–21} thereby lowering energy consumption and enhancing sustainability.^{22–24} To date, significant advances have been made in the development and evaluation of catalysts and reactor systems for CO₂ hydrogenation.^{25–33} However, direct comparison of the performance and efficacy of these catalysts remains challenging due to the absence of standardized operational procedures. In this endeavor, we aim to tackle these challenges by introducing an automated, integrated, and modular reactor system. The automation is facilitated by a custom-built, open-source code, accessible for use in any facility worldwide. While standardization methodologies have been effectively employed in batch processes for high-throughput screening and CF liquid systems, their application to light-assisted gas-phase reactions over heterogeneous catalysts remains relatively unexplored in this context.^{34–39} To bridge this gap, we present a standardized reactor system equipped with automated control over crucial parameters such as temperature, light intensity, pressure, residence time, and reagent stoichiometry, enabling the execution of gas-phase chemistry in a robust and reproducible manner. The precise control and modularity of this system facilitate the continuous light-assisted production of CO₂ hydrogenation products, which can be

seamlessly integrated into downstream units. In this study, we employed CO generated on demand as a reagent in a diverse array of palladium catalyzed carbonylative cross-coupling reactions, demonstrating the versatility and synthetic utility of our approach.

4.1.3 Design of the automated, modular CF photoreactor setup

We began our research by developing a reactor assembly tailored to evaluating catalysts for high temperature light-driven processes, particularly relevant for light-assisted CO₂ reduction, which is depicted in **Figure 4.1**.^{19,40,41} This assembly features a heated stainless steel tank with a quartz window for irradiation which can house glass microchannel photoreactors. Transparent silicon oil was employed as heating fluid to ensure efficient and uniform heat transfer between the tank and the reactor. The reflective properties of stainless steel, combined with the high refractive index of the oil and quartz, maximize photon utilization and confinement within the reactor unit. Moreover, the oil-filled tank offers versatility, accommodating various reactors, resulting in a highly modular system with broad applicability (**Figure 4.1 left**). Our investigation primarily focused on commercially available microchannel photoreactors, well-suited for CF reactions within our experimental framework (**Figure 4.1 right**).^{42,43}

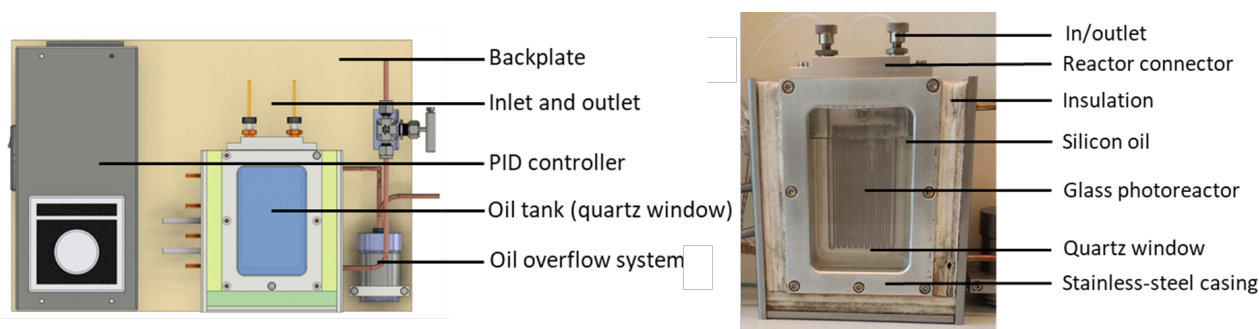


Figure 4.1: left) Front view of the 3D model of the reactor system; right) image of the oil tank with the immersed photoreactor filled with catalyst-coated beads.

These reactors were filled with an immobilized catalyst, uniformly coated onto glass beads (**Figure 4.2b** and **4.3b**), creating a packed-bed system.^{44,45} This configuration facilitated a large irradiation area and ensured reproducible packing, enhancing the reliability of our experimental setup.

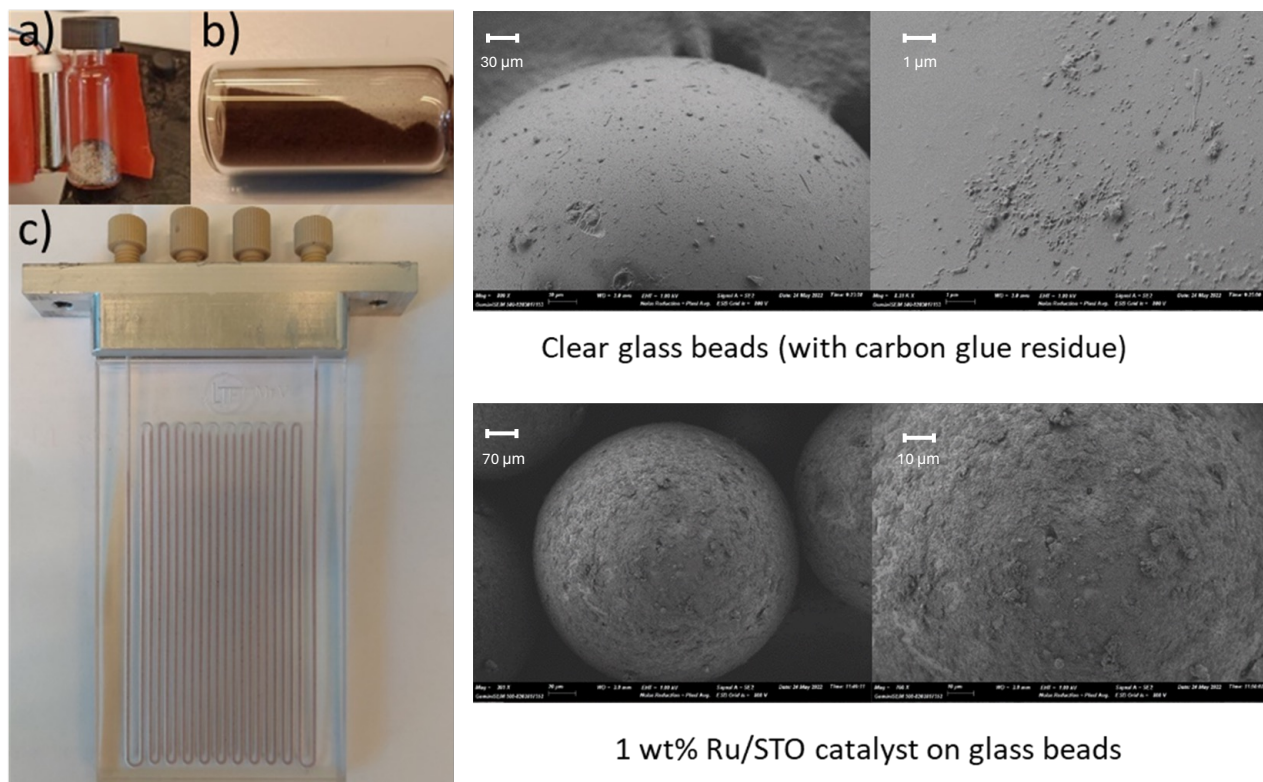


Figure 4.2: a) vibrating mixer taped to the glass vial with the catalyst and glass beads; b) evenly dispersed catalyst on the glass beads; c) catalyst-coated beads loaded in the glass photoreactor; top right: non-coated glass beads scanning electron microscopy (SEM) images at different scales; bottom right: Ru/STO (1 % wt) coated glass beads scanning electron microscopy image at different scales (see **Characterization** Section of **Chapter 4** for further details).

Utilizing automation to precisely regulate and adjust reaction parameters aligns with the modularity and CF nature of our system. The labor-intensive process of screening various conditions and benchmarking catalysts can be streamlined into a reproducible and automated procedure. All monitored reaction parameters are under electronic control, coordinated by a computer interface that enables users to modify and monitor each parameter as needed. The flow rate of individual reagents is precisely controlled by mass flow controllers (MFCs), while the temperature of the silicon oil is maintained by a proportional–integral–derivative (PID) controller connected to a heating element and thermocouple within the oil tank. Reaction pressure is monitored and regulated by a sensor at the reactor outlet, with adjustment facilitated by a mechanical back pressure regulator (BPR). To enable electronic pressure control, a closed-loop system was established between the pressure sensor and a motor controlling the BPR. Furthermore, the intensity of the light emitting diode (LED) light source was adjusted through an electronically controlled LED power supply. Both pressure and light control devices were custom-designed and manufactured using cost-effective electronic components and sensors and were operated by Arduino microcontrollers (UNO boards). A centralized control over reagent stoichiometry, residence time, oil temperature, pressure, and light intensity was managed by a Python script running on a dedicated computer as depicted in **Figure 4.3**.

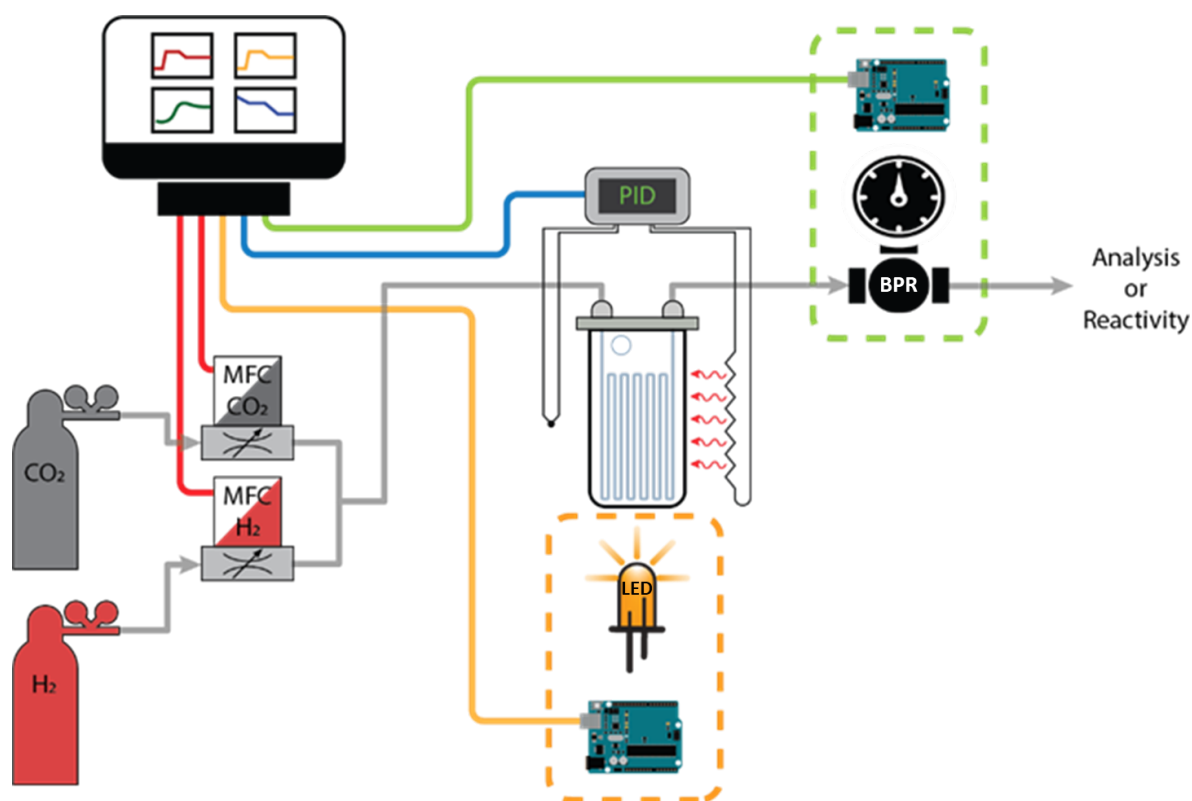


Figure 4.3: Overview of the devices connected and controlled by the automation system.

An intuitive graphical user interface (GUI) has been developed to facilitate automation of reaction conditions, as well as real-time adjustment and monitoring of all parameters without requiring advanced scripting knowledge, as depicted in the screenshot of **Figure 4.4**. This control code, along with detailed construction specifications and firmware for the in-house developed devices, is provided as open-source software, facilitating systematic experiment reproducibility and adaptation for similar automation setups.

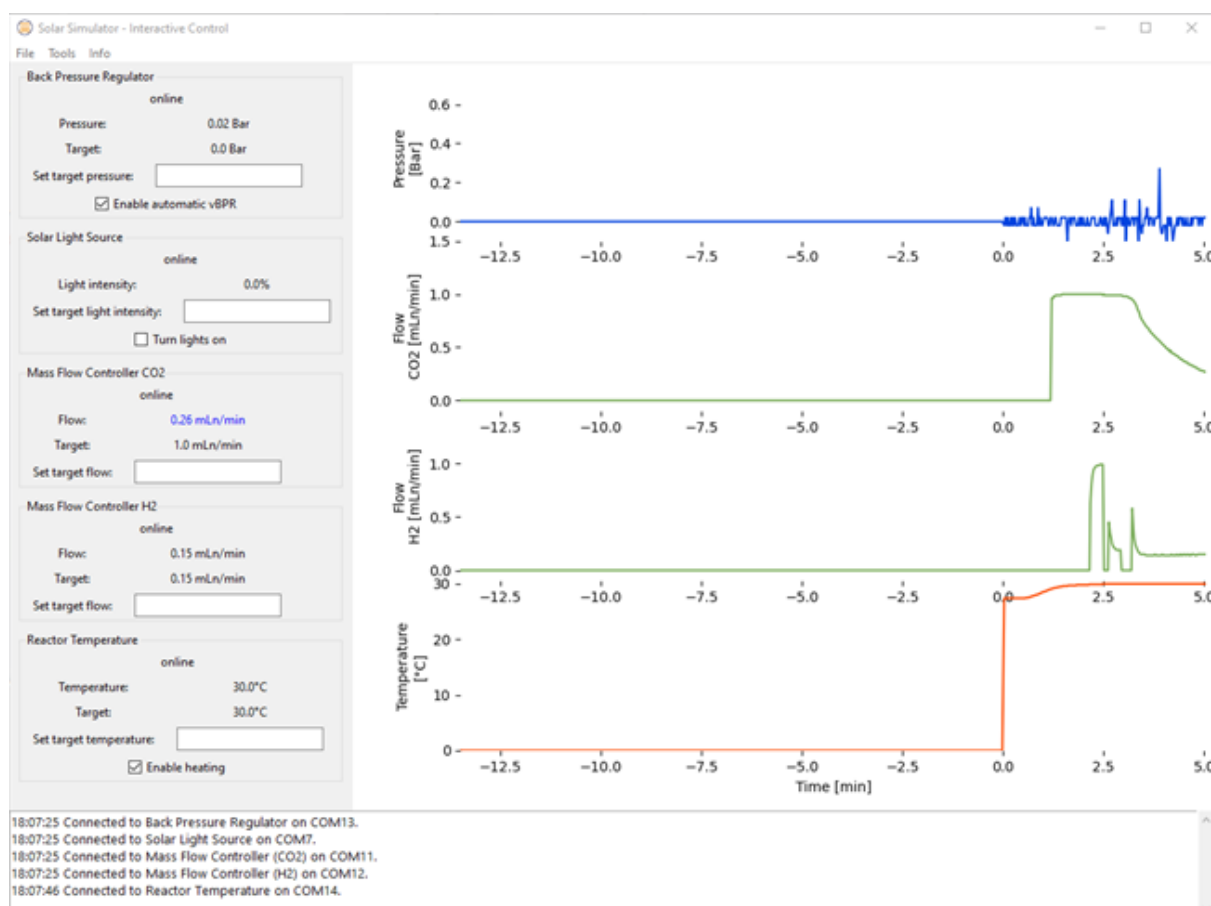


Figure 4.4: Main window of the system automation monitor controlling the reaction setup.

To assess the efficacy of each catalyst across diverse reaction conditions, the gas mixture exiting the reactor was analyzed using an online gas chromatograph equipped with both a thermal conductivity detector and a flame ionization detector (see **Experimental Section 4.1.7** for further details). The automated system was utilized to optimize CO₂ hydrogenation, targeting a range of hydrogenation products, including CO. This compound can be generated *ex situ* and directly utilized as a feedstock in carbonylative cross-coupling reactions, relevant for the synthesis of various fine chemicals, pharmaceuticals and agrochemicals.^{46,47} The benefits of this automated flow system include parametric screening, fast catalyst selection and quick operation optimization for subsequent reactions.

4.1.4 Light-assisted CO₂ hydrogenation

The platform's versatility was demonstrated for light-assisted CO₂ hydrogenation, wherein this stable compound was transformed into the corresponding reduction products, such as CH₄ and CO, through the application of heat and light. To comprehensively assess the impact of key variables such as light intensity, temperature, pressure, and flow rate, we conducted systematic experiments across a range of heterogeneous catalysts (see **Tables A8-A13, Appendix Section** for further details).

Among the screened commercially available, heterogeneous catalysts, commercially available cobalt(II,III) oxide (Co_3O_4) was selected as a benchmark, providing a well-established reference for comparative analysis with other catalysts.⁴⁸ **Figure 4.5** illustrates the selectivity, conversion, and productivity of light-assisted CO_2 hydrogenation in presence of various metal-based heterogeneous catalysts. Notably, commercial Co_3O_4 exhibited remarkable selectivity towards methane production, which improved increasing the reaction temperatures (see **Table A9** for further details). However, performing CO_2 hydrogenation in presence of ruthenium nanoparticles on titanium dioxide (Ru/TiO_2), allowed to achieve nearly complete conversion with 100 % selectivity towards methane. This novel catalyst was synthesized by introducing RuCl_3 into an aqueous dispersion of TiO_2 P90, a commercially available blend of rutile and anatase (see **Experimental Section 4.1.7** for further details). This process led to the formation and deposition of ruthenium(III) oxide and/or hydroxide species over the TiO_2 surface, which were subsequently reduced to ruthenium nanoparticles. Analysis by inductively coupled plasma–atomic emission spectroscopy (ICP-AES) revealed a ruthenium content of 5.5 % w/w, corresponding to a ruthenium incorporation yield of 96 %. Transmission electron microscopy examination (TEM) images displayed a uniform distribution of spherical Ru nanoparticles on the TiO_2 surface, with an average particle size of 1.79 ± 0.51 nm (lognormal distribution, see **Figures S104-S108, Characterization Section**).

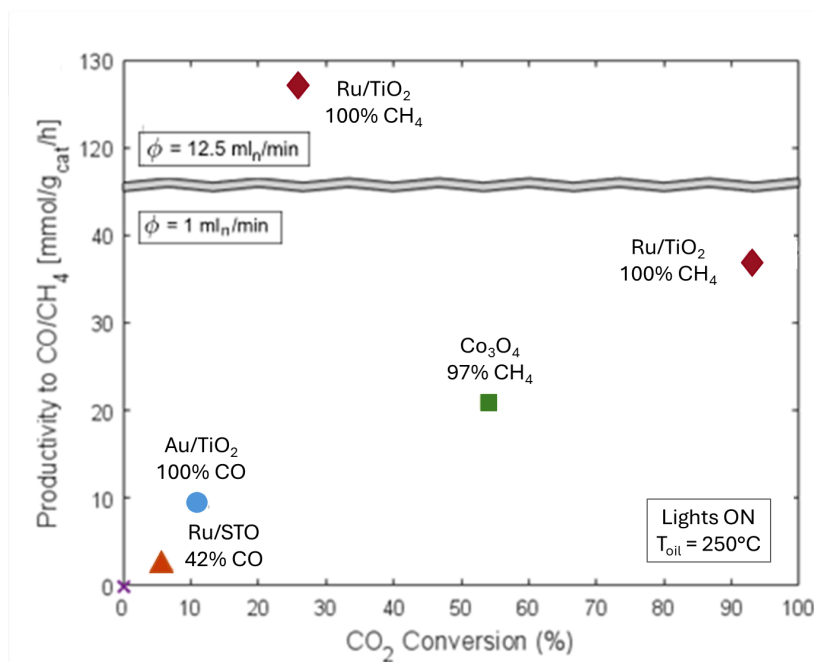


Figure 4.5: An overview of the catalysts evaluated in CO_2 hydrogenation, presenting the total CO_2 conversion against the productivity towards the desired reduction product. The overall selectivity is given in the data labels. The point at the origin represents the control experiment in which no hydrogenation products were observed. CO_2/H_2 feed ratio is equal to 1:4 V/V for reactions targeting methane and 1:1 V/V for reactions targeting CO.

Notably, the productivity of this catalyst could be further enhanced to $127 \text{ mmol g}_{\text{cat}}^{-1} \text{ h}^{-1}$ by increasing the flow rate (Entry 10, **Table A10**). Control experiments confirmed that the targeted compounds were exclusively generated from the catalyst-mediated transformation of the feedstock (Entry 1, **Table A8**). Furthermore, the versatility and adaptability of this screening platform were

highlighted by seamlessly transitioning to alternative catalyst systems. For instance, a catalyst comprising ruthenium (oxide) nanoparticles supported on strontium titanate (STO, Ru/STO) exhibited varying selectivity in carbon monoxide production (approximately ranging between 40 % and 70 %, see **Table A11**), depending on the specific reaction conditions and duration of operation. Previous studies had reported high methane selectivity for a similar catalyst, suggesting that the observed variance could be attributed to the catalyst's exposure to distinct reaction environments.⁴⁹ Conversely, another catalyst consisting of gold nanoparticles dispersed on titanium dioxide (Au/TiO₂ 3.1% w/w gold on anatase), characterized by spheroidal gold particles averaging 1.70 nm in diameter with a lognormal distribution (see **Figures S110-S113 Characterization Section**), consistently yielded CO as the primary product across all investigated conditions. With this catalyst CO was obtained with productivity up to 9.5 mmol g_{cat}⁻¹ h⁻¹ (Entry 8, **Table A12**), showcasing its robust performance under diverse reaction conditions. Precise automated control over oil temperature, light intensity, and individual flow rates facilitated systematic condition screening, with selected results depicted in **Figure 4.6**.

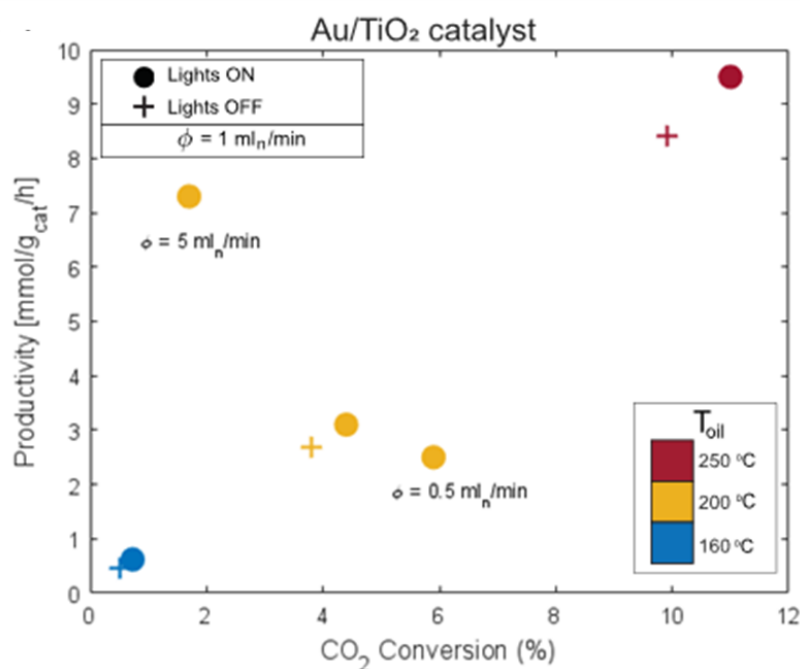


Figure 4.6: Results of the parametric screening of the gold nanoparticles on titanium dioxide (Au/TiO₂) heterogeneous catalyst for the selective formation of carbon monoxide (see **Table A12** for further details).

Irradiation of the reactor system notably enhanced CO production in presence of the Au/TiO₂ catalyst. Interestingly, flow rate variation exhibited a dual influence, with productivity and conversion showing a trade-off relationship, likely attributable to decreased residence time at higher throughputs. Furthermore, reaction temperature emerged as a critical parameter to ensure high conversion and productivity. In particular, significant CO production only occurred at $T > 160$ °C, highlighting the importance of thermal heating or robust light sources to supply the requisite thermal energy for catalyst-driven reactions. Overall, the parametric screening process offered invaluable insights into optimizing reaction conditions to meet predefined criteria, thereby enabling selective on-demand production of CO or CH₄ from CO₂. A further comparison about the

performance of various catalysts under specific conditions for the production of both CH₄ and CO are summarized in **Table A13** in the **Appendix Chapter 4** section.

4.1.5 On-demand supply of carbon monoxide in carbonylation reactions

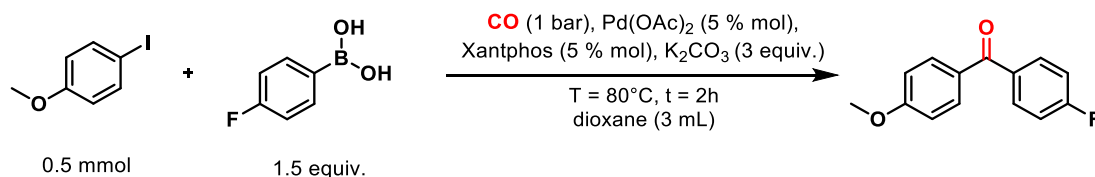
Carbonylation reactions are among the most extensively studied processes in synthetic chemistry, largely due to the remarkable versatility imparted by the carbonyl functional group (C=O). This functional group not only serves as a key intermediate in numerous organic transformations but also plays a critical role in the structure and function of biologically active molecules and pharmaceuticals. The significance of carbonylation in both organic synthesis and drug development has led to extensive research focused on carbonylative coupling reactions involving various substrates, often facilitated by transition metals such as Pd, Rh, Ni, Fe.^{50,51}

Despite the broad applicability of carbonylation reactions, they often require harsh conditions, such as high pressures and elevated temperatures, to achieve selectivity and yield. These requirements are in sharp contrast to non-carbonylative coupling reactions, which typically proceed under milder conditions.⁵² However, advancements in reaction methodologies have enabled the development of more efficient carbonylation processes.

This experimental work demonstrates that carbonylative Suzuki coupling, alkoxycarbonylation, and aminocarbonylation reactions can be successfully conducted using on-demand generated CO from an automated photoreactor system. These reactions were carried out in mild experimental conditions, *e.g.* low pressures and moderate temperatures, marking a substantial improvement in the practicality and safety of carbonylation protocols.^{53,54} This application highlights the synthetic potential of this new CO₂ upgrading approach, providing efficient and sustainable synthesis routes for diverse carbonylation reactions.

The optimization of reaction conditions was carried out on Pd-catalyzed Suzuki coupling of 4-iodoanisole with 4-fluorophenylboronic acid as model reaction as reported in **Table 4.1**.

Table 4.1: The effect of the controlled addition of boronic acid, solvent system (volume ratio), flow rate and CO/H₂ volume ratio on the Suzuki carbonylation reaction.



Entry	Reactor	Differing conditions	Flow rate (ml/min)	Time (h)	Conv. (%)	Sel. (%)	Yield (%)
1	Batch	-	-	2	76	47	36
2	Batch	Pd(Br) ₂ (5 % mol), tpp (10% mol)	-	2	50	82	43
3	Fed-batch	-	0.05	2	65	96	62
4	Fed-batch	Dioxane:THF* 98:2	0.05	2	54	98	53
5	Fed-batch	Dioxane:THF 98:2	0.025	2	57	93	53
6	Fed-batch	Dioxane:THF 98:2	0.0125	3	94	99	93 (82) ^a
7	Fed-batch	Dioxane:THF 98:2 CO:H ₂ 1:9	0.0125	3	63	8	5
8 ^b	Fed-batch	Dioxane:THF 98:2 CO:H ₂ 1:9	0.005	4	56	43	24
9 ^b	Fed-batch	Dioxane:THF 98:2 CO:H ₂ 1:9	0.004	5	54	53	29
10 ^b	Fed-batch Connected to modular photoreactor	Dioxane:THF 98:2 Gas mixture 7.5 mol% Pd catalyst, Xantphos	0.0028	6 + 1 ^c	97	95	92 (79) ^a

Reaction conditions: 4-iodoanisole (0.50 mmol), 4-fluorophenylboronic acid (1.5 equiv.), Pd(OAc)₂ (5 % mol), Xantphos (5 % mol), K₂CO₃ (3 equiv.), dioxane (3 mL) at T = 80 °C. Conversion, selectivity and yield were calculated by GC-MS (qualitative, area based). The theoretical yields were checked by ¹⁹F-qNMR using fluorobenzene as standard.^a Isolated yield. ^b Performed using 0.10 mmol of 4-iodoanisole (all other reagents scaled accordingly). ^c Addition over t = 6 h, t = 7 h total reaction time. *Ratio after addition, THF was added to increase the boronic acid solubility.

Initial batch reactions were conducted under controlled atmospheric conditions using a CO balloon (**Figure 4.7a**), revealing that a catalytic system comprising PdBr₂, triphenylphosphine (TPP), and K₂CO₃ in dioxane achieved a moderate conversion of 50 %, with 82 % selectivity towards the desired carbonylated product (Entry 2, **Table 4.1**). However, when hydrogen (H₂) was introduced into the system, essential for CO₂ reduction, both conversion and selectivity decreased (see **Figure A21** in

Appendix Section). This behavior was attributed to the decreased availability of CO in presence of gaseous H₂, which also promoted the undesired reduction of the Pd^(II) pre-catalyst to the catalytically inactive Pd⁽⁰⁾ precipitate.^{55,56} To overcome these challenges, we conducted a comprehensive screening of catalysts, solvents, and ligands. Among the tested combinations, Pd(OAc)₂ (5 % mol) paired with Xantphos (5 % mol) proved to be the most effective catalytic system, achieving a 76 % conversion after within = 2 h at T = 80 °C, yielding the target product with 47 % selectivity. The optimization study was continued with Pd(OAc)₂ as the Pd source, chosen for its higher activity compared to PdBr₂, despite the latter displayed a better selectivity towards the desired carbonylation product. To mitigate the selectivity loss observed for the more active catalytic system, we implemented continuous addition of boronic acid via a syringe pump (**Figure 4.7b**). This approach allowed us to regulate boronic acid concentration, aligning it with the rate of the transmetalation step in the palladium catalytic cycle. Further optimizations, including the addition of tetrahydrofuran (THF) as a co-solvent, significantly improved the results, leading to a 94 % conversion with 99 % selectivity (Entry 6, **Table 4.1**). When the reaction was coupled with the modular photoreactor, the conversion of the starting material decreased to 58 %, but a high selectivity towards the desired product was maintained. Under the optimal conditions for CO₂ reduction, 0.7 mmol (1.4 equiv.) of CO were introduced into the system. Extending the reaction time to t = 7 h and increasing the catalyst loading to 7.5 mol% resulted in a 92 % yield of the desired carbonylated product (Entry 10, **Table 4.1**).

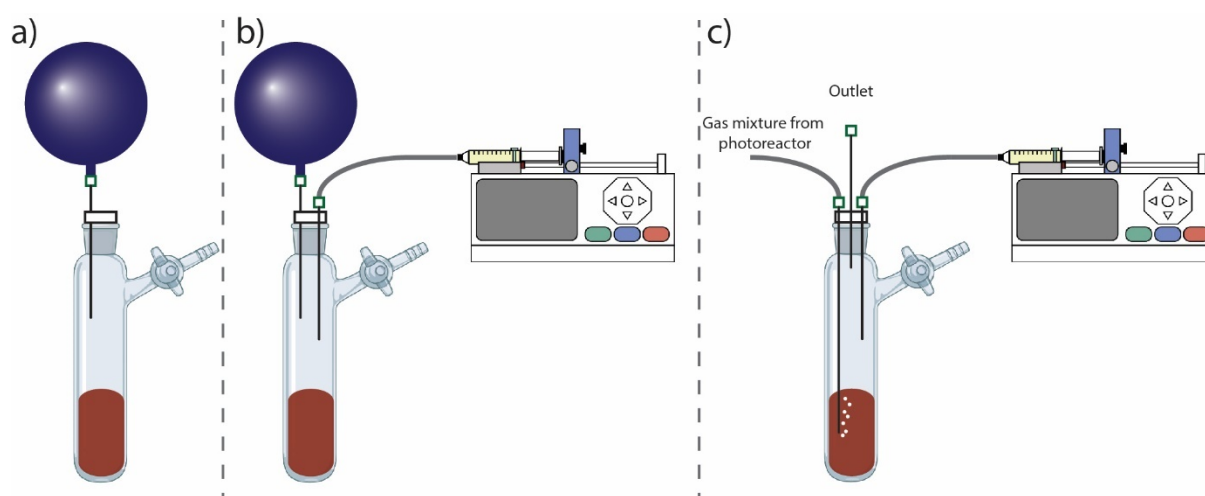
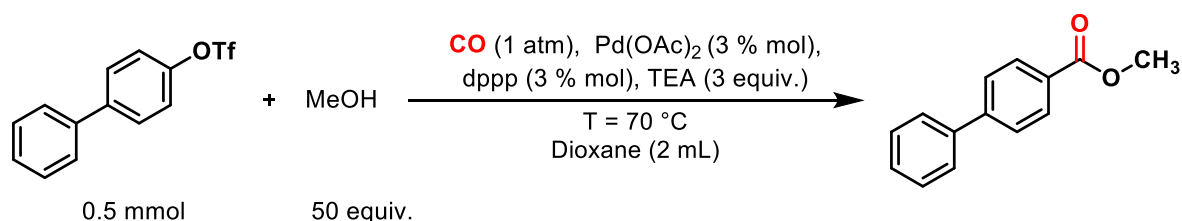


Figure 4.7: Overview of the batch (a), fed-batch (b), and coupled (c) system to carry out different carbonylation reactions.

Similarly, in alkoxycarbonylation and aminocarbonylation protocols, the limiting reagents ([1,1'-biphenyl]-4-yl trifluoromethanesulfonate and (*E*)-1-iodooct-1-ene, respectively), were continuously added to the reaction mixture to ensure a constant concentration throughout the whole reaction length (see **Table 4.2** and **Table 4.3** for alkoxycarbonylations and aminocarbonylations, respectively).

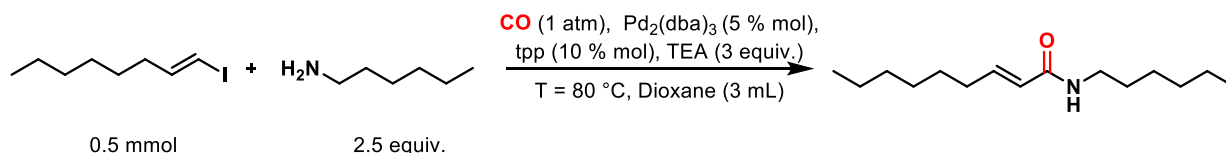
Table 4.2: Alkoxycarbonylation reaction performed with different CO/H₂ volume ratios employing the modular photoreactor system as CO source.



Entry	Reactor	Differing conditions	Flow rate (ml/min)	Time (h)	Conversion (%)	Selectivity (%)	Yield (%)
1	Batch	-	-	3	82	100	82 (68) ^a
2	Batch	CO/H ₂ 1:9 V/V	-	3	19	21	4
3 ^b	Fed-batch Connected to modular photoreactor	5 % mol Pd catalyst, dppp (5 % mol)	0.0028	6 + 0.5 ^c	98	69	68 (61) ^a

Reaction conditions: [1,1'-biphenyl]-4-yl trifluoromethanesulfonate (0.5 mmol), methanol (50 equiv.), Pd(OAc)₂ (3 % mol), dppp (3 % mol), TEA (3 equiv.), dioxane (3 mL) at T = 70 °C. Conversion, selectivity and yield were calculated by GC-MS (qualitative, area based). ^aIsolated yield. ^bPerformed with 0.1 mmol of [1,1'-biphenyl]-4-yl trifluoromethanesulfonate. ^cAddition over t = 6 h, t = 6.5 h total reaction time.

Table 4.3: Aminocarbonylation reaction performed with different CO/H₂ volume ratios employing the modular photoreactor system as CO source.



Entry	Reactor	Differing conditions	Flow rate (ml/min)	Time (h)	Conversion (%)	Selectivity (%)	Yield (%)
1	Batch	-	-	3	>99	90	90 (78) ^a
2 ^b	Fed-batch Connected to modular photoreactor	10 mol% Pd catalyst, tpp	0.0035	5 + 0.5 ^c	>99	82	82 (72) ^a

Reaction conditions: (E)-1-iodooct-1-ene (0.5 mmol), 1-hexylamine (2.5 equiv.), Pd₂(dba)₃ (5 % mol), tpp (5 % mol), TEA (3 equiv.), dioxane (3 mL) at T = 80 °C. Conversion, selectivity and yield were calculated by GC-MS (qualitative, area based). ^aIsolated yield. ^bPerformed with 0.1 mmol of (E)-1-iodooct-1-ene. ^cAddition over t = 5 h, t = 5.5 h total reaction time.

This strategy resulted in excellent selectivity towards the desired carbonylated products, facilitated by the low relative concentration of the added reagent and the continuous replenishment of CO. The targeted products of carbonylative Suzuki coupling, alkoxycarbonylation, and aminocarbonylation reactions were isolated in good yields (79 %, 61 %, and 72 % isolated yield, respectively, **Figure 4.8**). These findings highlight the adaptability of fine chemical production to

specific CO₂ sources, with potential for scalability through a numbering-up or sizing-up strategy to adjust the carbon monoxide production accordingly.^{57,58}

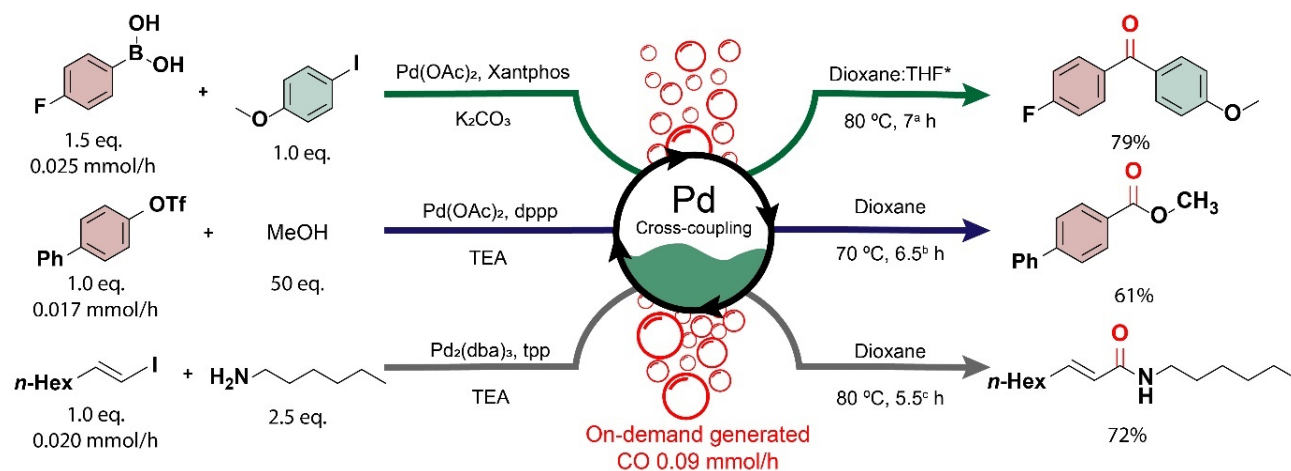


Figure 4.8: Carbon monoxide generated by the photoreactor is subsequently used as a reagent in the (i) carbonylative Suzuki coupling: Pd(OAc)₂ (7.5 mol %) and Xantphos (7.5 % mol), K₂CO₃ (3.0 equiv.), in dioxane/THF = 98:2 V/V, addition over *t* = 6 h, total reaction time *t* = 7 h, *T* = 80 °C; (ii) alkoxy carbonylation: Pd(OAc)₂ (5 % mol), dppp (5 % mol), TEA (3.0 equiv.), dioxane, addition over *t* = 6 h, total reaction time *t* = 6.5 h, *T* = 70 °C; (iii) aminocarbonylation: Pd₂(dba)₃ (10 % mol), tpp (10 % mol), K₂CO₃ (3.0 equiv.), dioxane, addition over *t* = 5 h, total reaction time *t* = 5.5 h, *T* = 80 °C

4.1.6 Conclusions

We have developed a novel modular and automated photoreactor system designed to facilitate light-assisted CO₂ hydrogenation. Effective integration of automation and modularity allowed us to perform standardized screening of diverse catalysts and reaction conditions. Employing a packed-bed approach, where the metal catalyst is deposited on glass beads, offered several advantages, including providing extensive irradiation areas, ensuring reproducible loading and optimizing catalyst utilization. The platform's versatility enabled evaluation of novel catalysts under tightly controlled reaction parameters, effectively addressing a critical need in the scientific community for a standardized system assessing and comparing heterogeneous catalysts in both thermal and light-assisted gas conversion processes. Moreover, the developed automated system enabled temperature-controlled, light-assisted reactions, facilitating swift mechanistic studies on photothermal reaction pathways.⁵⁹ The synthetic versatility was combined with commercially available components, open-source code and a user-friendly interface, establishing a framework for future advancements in automation within the field.

Furthermore, the integrated flow system allowed for seamless integration of downstream units, enabling immediate utilization of generated products. This is exemplified by the on-demand, selective CO production employed for various carbonylative cross-coupling reactions. Tailoring the catalyst and operation conditions enabled stable carbon monoxide production required for these purposes.

In conclusion, the reported modular and automated photoreactor system not only advances the understanding and exploration of light-assisted gas conversion processes but also lays the groundwork for future developments in automation within the field, offering a promising avenue for sustainable chemical synthesis.

4.1.7 Experimental:

Materials and Methods

All reagents and solvents used: ethyl acetate (EtOAc), dioxane, dichloromethane, pentane, tetrahydrofuran (THF), methanol, fluorobenzene, 4-iodoanisole, 4-fluorophenylboronic acid, *trans*-1-iodo-1-octene, 1-hexylamine, 4-phenylphenol, pyridine, trifluoromethanesulfonic anhydride, palladium(II)bromide (PdBr₂), palladium(II)acetate [Pd(OAc)₂], tris(dibenzylideneacetone)palladium(0) [Pd₂(dba)₃], triphenylphosphine (tpp), 1,3-bis(diphenylphosphino)propane (dppp), 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (Xantphos), triethylamine (TEA), K₂CO₃, Na₂SO₄, chloroform-d (CDCl₃), were purchased from Sigma Aldrich (now Merck) with ≥ 98 % purity, and, unless otherwise specified, used without further purification. Gaseous carbon monoxide (4.8 purity) was purchased from Nippon gases. (1,1'-biphenyl)-4-yl trifluoromethanesulfonate was prepared according to reported procedures.⁶² Product isolation was performed by a Biotage® Isolera Four, with Biotage® SNAP KP-Sil 4 or 10 g flash chromatography cartridge, or manually, using silica (P60, SILICYCLE). TLC analysis was performed using Silica on aluminum foils TLC plates (F254, SILICYCLE) with visualization under ultraviolet light (254 nm and 365 nm) or appropriate TLC staining (potassium permanganate). Qualitative and quantitative analysis and characterization of reaction mixtures and pure products were performed with GC-MS and NMR. The GC-MS system used was an Agilent 8890 GC equipped with an HP-5MS UI capillary column (length: 30 m, i.d.: 0.25 mm, film thickness: 0.25 μm), coupled with Agilent Technologies 5977C mass detector operating at 70 eV. Helium was used as carrier gas and an injection temperature of 300 °C was employed, using a temperature program of 60 °C (3.5 min) – 300 °C (3 min) at 30 °C/min. For NMR analysis, an AV 300-I NMR spectrometer was used, operating at 300 MHz for ¹H nuclei, 75 MHz for ¹³C nuclei and 282 MHz for ¹⁹F nuclei. ¹H NMR spectra are reported in parts per million (ppm) downfield relative to CDCl₃ (7.26 ppm) and all ¹³C NMR spectra are reported in ppm relative to CDCl₃ (77.16 ppm) unless stated otherwise. The multiplicities of signals are designated by the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), sext (sextet), m (multiplet), dd (doublet of doublets), dt (doublet of triplets), td (triplet of doublets), ddd (doublet of doublet of doublets). Coupling constants (J) are reported in hertz (Hz). NMR data was processed using the MestReNova 14 software package. Known products were characterized by comparing the ¹H NMR, ¹³C NMR and ¹⁹F NMR spectra with those available in the literature.

Modular reactor system

A glass photoreactor (LTF MR-LAB-V) was immersed into a heated oil reactor case with a quartz window. The backplate of the casing contained ceramic heating rods to heat the oil (CAS 68083-14-7) to a set temperature using a PID controller. The pressure was regulated with an automated back pressure regulator developed in-house. An overflow tube and vessel are present to prevent pressure buildup in the tank. Irradiation was provided by an array of four white chip-on-board LEDs (CXB3590, cool white, 86 W electrical input power per chip) placed at 2 cm from the window. Gases were supplied through mass flow controllers (MFC, Bronkhorst max. 10 ml/min, volume at normal conditions; 0 °C and 1 atm), connected to a supply at 5 bars, and could be co-fed into the reactor. Stainless-steel Swagelok and IDEX fittings in combination with FEP tubing (OD 1.6 mm) were used to connect the distinct parts. The analysis was conducted with a gas chromatograph (Shimadzu Nexis GC-2030) equipped with both a flame ionization detector (FID) and a thermal conductivity detector (TCD) and two column system (SH-Q-BOND and SH-MSieve 5A), a by-pass was employed to analyze all relevant gaseous compounds.

Ruthenium on titanium dioxide catalyst

The Ru/TiO₂ catalyst was synthesized by a direct chemical reduction method, RuCl₃ (ruthenium (III) chloride hydrate, 99.9% (PGM basis), Alfa Aesar) was used as the ruthenium precursor. A 6 mM RuCl₃ solution was prepared with 100 ml ultra-filtered water (Milli-Q Millipore, 18.2 MΩ cm) in vigorous stirring for 5-10 minutes in a three necked round bottom flask. The support TiO₂ (1.00 g, AEROXIDE TiO₂ P90 Evonik) was added to the mixture. The dispersion was left in vigorous stirring for at least 1 hour at 100 °C. A 0.18 M NaBH₄ solution was prepared using demineralized water. 10 ml of this solution was added to the previous mixture using a pump with a flow rate of 3 ml/min and the mixture was left stirring for an extra 30 minutes. The solid was recuperated by filtration and extensively washed with ultra-filtered water. Further characterization details can be found in the **Characterization Chapter 4** section.

CO₂ hydrogenation

The catalyst was deposited on glass beads (150-212 μm) following a previously published procedure,⁶⁰ prior to placement in the glass reactor. A layer of the catalyst was obtained on the glass beads by first grinding the catalyst, followed by mixing with the glass beads. Approximately 1.5 g of coated beads were deposited in the glass reactor (1.0 % wt. of catalyst). The catalysts were supplied by partners and prepared following previously published literature procedures,^{29,61} apart from commercially available Co₃O₄ (sold by Sigma Aldrich, now Merck). The desired reaction parameters were set in the graphical user interface. Samples were taken after steady-state was reached, whereafter the transient behavior could be investigated.

CO₂ hydrogenation catalyst preparation and loading

Glass beads (150-212 μm) were weighed and transferred to a glass sample vial. The catalyst was weighed and grinded with a mortar until obtaining a fine and homogeneous powder. This powder was added to a vial containing glass beads. A vibrating mixer was taped on the sample vial and

turned on, resulting in mixing of the glass beads and catalyst (**Figure 4.2a**). The mixer was removed after 5 minutes, observing an even distribution of the catalyst on the beads, as can be seen in **Figure 4.2b**. The prepared catalyst-coated beads were loaded into the photoreactor through a funnel, followed by overpressure generation using pressurized gas to move it through the channels. The outlet was blocked with a particle filter to prevent loss of the material. The bed remained fixed during reactor operation, as the overpressure within the experimental operating window proved insufficient to result in bed movement (maximum of 4 bar overpressure). Additionally, no leaching of the coated catalyst was observed for the gas phase reactions. For replacement of the catalyst after deactivation or possible reactor contamination, the glass beads are easily flushed out of the reactor using a flow of liquid under sonication. After drying the reactor, a new batch of coated glass beads was loaded, and the reactor was subsequently re-inserted into the reactor holder and casing (**Figure 4.2c**).

Carbonylation reactions in batch

Pre-determined amounts of the reagents, catalyst and additives were charged in a Schlenk flask (put under nitrogen). Before heating, the headspace of the flask was filled with a specific ratio of gases (using a balloon and autoclave, see **Appendix Chapter 4**). Hereafter, the Schlenk flask was immersed in an oil bath and heated to the desired operating temperature. Reactions were performed under continuous stirring. Qualitative and quantitative analysis and characterization of reaction mixtures and pure products were performed with: GC-MS and NMR.

Carbonylation reactions with on-demand produced carbon monoxide

Pre-determined amounts of the reagents, catalysts and additives were charged in a Schlenk tube kept under a nitrogen inert atmosphere. Before heating, gas from the automated system was purged through the solution, to fill the headspace with the gas mixture. Hereafter, the Schlenk tube was immersed in an oil bath and heated to the desired operating temperature. One of the co-reagents was supplied as a THF solution by a syringe pump at a specific flow rate. Reactions were performed under continuous stirring. Qualitative and quantitative analysis and characterization of reaction mixtures and pure products were performed with: GC-MS and NMR.

Carbonylative Suzuki in batch conditions

105 mg of 4-fluorophenyl boronic acid (0.75 mmol, 1.5 equiv.), 5.6 mg of Pd(OAc)₂ ($2.5 \cdot 10^{-2}$ mmol, 5 % mol), 14.5 mg of 4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene (Xantphos, $2.5 \cdot 10^{-2}$ mmol, 5 % mol%) and 205 mg of anhydrous K₂CO₃ (1.5 mmol, 3.0 equiv.) were introduced in a 10 ml Schlenk tube equipped with a stirring bar. The system was capped with a septum and flushed under nitrogen through 3 vacuum/N₂ cycles before adding 3 ml of dry dioxane and 117 mg of 4-Iodoanisole (0.50 mmol, 1.0 equiv.). The Schlenk flask was purged with a balloon containing CO or the gas mixture (CO/H₂ = 1:9 V/V) for 5 minutes before introducing it into an oil bath pre-heated at T = 80 °C. The reaction was allowed to stir continuously under these conditions for t = 2 h. Then, the Schlenk tube was cooled down to room temperature and purged with N₂, before introducing 47 µl (0.50 mmol,

1.0 equiv.) of fluorobenzene as analytical standard. The system, used for these and other reactions in batch, is illustrated in **Figure 4.7a**.

Carbonylative Suzuki in batch-fed conditions

5.6 mg of $\text{Pd}(\text{OAc})_2$ ($2.5 \cdot 10^{-2}$ mmol, 5 % mol), 14.5 mg of Xantphos ($2.5 \cdot 10^{-2}$ mmol, 5 % mol) and 205 mg of K_2CO_3 (1.5 mmol, 3.0 equiv.) were introduced in a 10 ml Schlenk tube equipped with a stirring bar. The system was capped with a septum and flushed with nitrogen through 3 vacuum/ N_2 cycles before the addition of dry dioxane (2 mL) and 117 mg of 4-iodoanisole (0.50 mmol, 1.0 equiv.). Separately, in a 5 ml vial equipped with a septum cap, 105 mg of 4-fluorophenyl boronic acid (0.75 mmol, 1.5 equiv.), were dissolved in 1 ml of dry dioxane/THF mixture 95:5 V/V and kept under inert atmosphere (N_2). The Schlenk tube was purged with a balloon containing CO or a CO-based gas mixture ($\text{CO}/\text{H}_2 = 1:9$ V/V) for 1 minute before introducing it into an oil bath preheated at $T = 80^\circ\text{C}$. The reaction was allowed to stir continuously under these conditions during the addition of the 4-fluorophenyl boronic solution with the help of a syringe pump (Chemyx Fusion 200, corresponding flow rate detailed in **Table 4.1**) and then left under vigorous stirring for the desired reaction time. At the end of the reaction time, the Schlenk flask was cooled down to room temperature and purged with N_2 before introducing 47 μl (0.50 mmol, 1.0 equiv.) of fluorobenzene as analytical standard. The batch-fed system is shown in **Figure 4.7b**.

Alkoxy carbonylation in batch conditions

151 mg of [1,1'-biphenyl]-4-yl trifluoromethanesulfonate (0.50 mmol, 1.0 equiv.), 3.4 mg of $\text{Pd}(\text{OAc})_2$ ($1.5 \cdot 10^{-2}$ mmol, 3 % mol) and 6.2 mg of 1,3-bis(diphenylphosphino)propane (dppp, $1.5 \cdot 10^{-2}$ mmol, 3 % mol) were introduced in a 10 ml Schlenk tube equipped with a stirring bar. The system was capped with a septum and flushed with nitrogen through 3 vacuum/ N_2 cycles before adding dry dioxane (2 mL), 1 ml of methanol (25.0 mmol, 50.0 equiv.) and 209 μl of triethylamine (TEA, 1.50 mmol, 3.0 equiv.) under nitrogen flow. The Schlenk tube was purged with a balloon containing CO or a CO-based gas mixture ($\text{CO}/\text{H}_2 = 1:9$ V/V) for 1 minute before introducing it into an oil bath preheated at $T = 70^\circ\text{C}$. The reaction was allowed to stir continuously under these conditions for 3 hours. At the end of the reaction time, the Schlenk tube was cooled down to room temperature and purged with N_2 before the analysis.

Aminocarbonylation in batch conditions

22.9 mg of $\text{Pd}_2(\text{dba})_3$ ($2.5 \cdot 10^{-2}$ mmol, 5 % mol), 13.1 mg of triphenylphosphine (tpp, 0.05 mmol, 10 % mol) were introduced in a 10 ml Schlenk tube equipped with a stirring bar. The system was capped with a septum and flushed with 3 vacuum/ N_2 cycles before adding dry dioxane (3 mL) followed by 119 mg of (*E*)-1-iodooct-1-ene (0.50 mmol, 1.0 equiv.), 165 μl of 1-hexylamine (1.25 mmol, 2.50 equiv.) and 209 μl of triethylamine (TEA, 1.50 mmol, 3.0 equiv.) under nitrogen flow. The Schlenk tube was then purged with a balloon containing CO for 1 minute before introducing it into an oil bath pre-heated at $T = 80^\circ\text{C}$. The reaction was allowed to stir continuously under these conditions for $t = 3$ h. Afterwards, the Schlenk tube was cooled down to room temperature and purged with N_2 before the analysis.

Gas mixture preparation

For the preparation of CO and H₂ gas mixtures, a stainless-steel autoclave equipped with an electronic manometer with a capacity of V = 952 ml was used. The autoclave was first degassed through 3 vacuum/N₂ cycles and left under vacuum. Then, the autoclave was charged with H₂ followed by CO reaching a total pressure of 5 bar. The gaseous mixture was collected in a balloon which was subsequently used to carry out the carbonylation reaction.

Carbonylative Suzuki coupling with on-demand produced CO

23.4 mg of 4-iodoanisole (0.10 mmol, 1.0 equiv.), 1.7 mg of Pd(OAc)₂ ($7.5 \cdot 10^{-2}$ mmol, 7.5 % mol), 4.3 mg of 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (Xantphos, $7.5 \cdot 10^{-2}$ mmol, 7.5 % mol) and 41.4 mg of anhydrous K₂CO₃ (0.15 mmol, 3.0 equiv.) were introduced in a 10 ml Schlenk tube equipped with an X-shape stirring bar. The system was capped with a septum and flushed with N₂ through 3 vacuum/N₂ cycles. Separately, in a 5 ml vial with a septum cap, 32.2 mg of 4-fluorophenylboronic acid (0.23 mmol) were dissolved in 1.5 ml of a mixture of dry dioxane/THF 95:5 V/V. The solution was sonicated and purged with N₂ to ensure complete solubilization of the boronic acid and deoxygenation of the mixture. Then, 0.5 ml of dry dioxane were added to the 10 ml Schlenk tube under continuous nitrogen flow. The system was then purged with the photoreactor output for 30 minutes under continuous stirring at room temperature. In the meanwhile, a 3 ml syringe ($\varnothing$ = 9.5 mm) was charged with the boronic acid solution. The syringe was mounted on the syringe pump and a flow rate of 0.0028 ml/min was set to add continuously 1 ml (0.15 mmol, 1.5 equiv.) of the boronic acid solution. Once all preparations were completed, the Schlenk tube was immersed in an oil bath pre-heated at T = 80°C, while beginning of the addition of the boronic acid solution via the syringe pump (see **Figure 4.7c**). At the end of the t = 6 h of addition, the mixture was left to react for an additional hour, after which the mixture was cooled down to room temperature and then flushed with nitrogen to remove any CO still present inside the reactor. 9.4 μ l (0.10 mmol, 1 equiv.) of fluorobenzene were added as analytical standard. The reaction mixture was extracted with EtOAc/water, and the organic layer was dried over Na₂SO₄. After removing the solvent under vacuum, the residue was loaded onto silica gel and purified via flash chromatography, using pentane/EtOAc mixtures as the eluent (starting from 100 % pentane to 100 % EtOAc), to isolate the product.

Based on the well-established mechanism for the Pd-catalyzed carbonylative Suzuki coupling, an oxidative addition step followed by CO insertion precedes the transmetallation event between the palladium intermediate and the boronic acid.⁶³ By controlling the presence of both CO and the transmetallating agent, it is possible to manage the selectivity of the process. Conversely, when dripping the aryl halide under low concentrations of CO, there are more opportunities for transmetallation between the oxidative addition palladium intermediate to occur before the CO insertion, leading to a loss of selectivity.

Alkoxycarbonylation with on-demand produced CO

mg of Pd(OAc)₂ ($5.0 \cdot 10^{-2}$ mmol, 5 % mol) and 2.1 mg of 1,3-bis(diphenylphosphino)propane (dppp, $5.0 \cdot 10^{-2}$ mmol, 5 % mol) were introduced in a 10 ml Schlenk tube equipped with stirring bar. The system was capped with a septum and put under inert environment through 3 vacuum/N₂ cycles. Separately, in a 5 ml vial with a septum cup, 45.3 mg of [1,1'-biphenyl]-4-yl trifluoromethanesulfonate (0.15 mmol) were dissolved in 1.5 ml of dry dioxane. The solution was sonicated and purged with N₂ to ensure complete solubilization of the substrate and deoxygenation of the mixture. Then, 0.2 ml of dry methanol and 0.3 ml of dry dioxane were added to the 10 ml Schlenk tube followed by 42 µl of triethylamine (TEA, 0.30 mmol, 3.0 equiv.) under nitrogen flow. The system was then purged with the photoreactor output for 30 minutes under continuous stirring at room temperature. In the meanwhile, a 3 ml syringe (ø = 9.5 mm) was charged with the [1,1'-biphenyl]-4-yl trifluoromethanesulfonate solution. The syringe was mounted on the syringe pump and a flow rate of 0.0028 ml/min was set to add continuously 1 ml (0.1 mmol, 1.0 equiv.) of the substrate solution. Once all preparations are complete, the Schlenk tube was immersed into the oil bath preheated at T = 70 °C, while beginning the addition of the limiting reagent solution via the syringe pump. At the end of the t = 6 h of addition, the mixture was left to react for an additional 30 minutes after which the reaction mixture was cooled down to room temperature and then flushed with nitrogen to remove any CO still present inside the reactor. The reaction mixture was extracted with EtOAc/water, and the organic layer was dried over Na₂SO₄. After removing the solvent under vacuum, the residue was loaded onto silica gel and purified via flash chromatography, using pentane/EtOAc mixtures as the eluent (from 100 % pentane to 20 % EtOAc in pentane), to obtain the product.

Aminocarbonylation with on-demand produced CO

9.2 mg of Pd₂(dba)₃ (0.01 mmol, 10 % mol) and 5.2 mg of triphenylphosphine (tpp, 0.02 mmol, 20 % mol) were introduced in a 10 ml Schlenk tube equipped with stirring bar. The system was capped with a septum and put under inert environment through 3 vacuum/N₂ cycles. Separately, in a 5 ml vial with a septum cup, 35.7 mg of (*E*)-1-iodooct-1-ene (0.15 mmol) were dissolved in 1.5 ml of dry dioxane. The solution was sonicated and purged with N₂ to ensure complete solubilization of the substrate and deoxygenation of the mixture. Then, 0.5 ml of dry dioxane were added to the 10 ml Schlenk flask followed by 42 µL of triethylamine (TEA, 0.30 mmol, 3 equiv.) and 33 µL of 1-hexylamine (0.25 mmol, 2.5 equiv.) under nitrogen flow. The system was then purged with the photoreactor output for 30 minutes under continuous stirring at room temperature. In the meanwhile, a 3 ml syringe (ø = 9.5 mm) was charged with the (*E*)-1-iodooct-1-ene solution. The syringe was mounted on the syringe pump and a flow rate of 0.0035 ml/min was set to add continuously 1 ml (0.1 mmol, 1.0 equiv.) of the substrate solution. Once all preparations were complete, the Schlenk tube was immersed inside to the oil bath preheated at T = 80°C, while beginning the addition of the limiting reagent solution via syringe pump. At the end of t = 5 h of addition, the mixture was left to react for additional 30 minutes after which the mixture was cooled down to room temperature and then flushed with nitrogen to remove any CO still present inside the reactor. The reaction mixture was extracted with EtOAc/water, and the organic layer was dried

over Na_2SO_4 . After removing the solvent under vacuum, the residue was loaded onto silica gel and purified via flash chromatography, using pentane/EtOAc mixtures as the eluent (from 100 % pentane to 50 % of EtOAc in pentane), to obtain the product.

4.2 Bibliography Chapter 4

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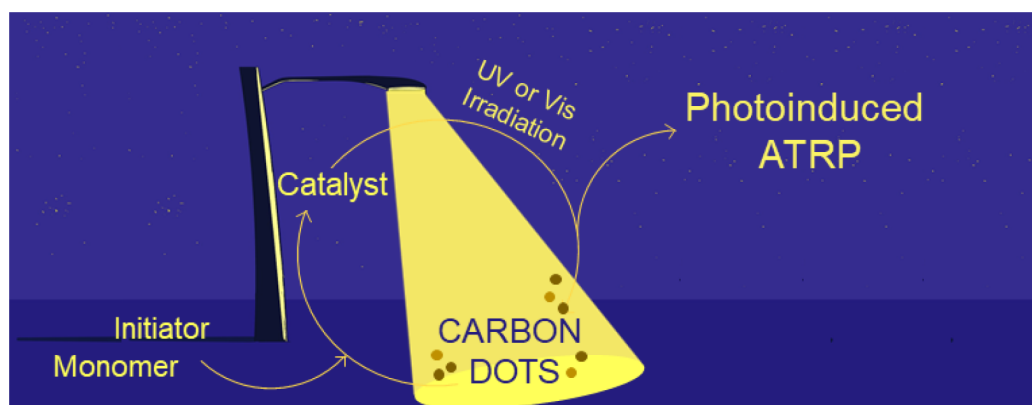
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5. Photochemistry

5.1 Carbon Dots as Green Photocatalyst for Atom Transfer Radical Polymerization of Methacrylates



5.1.1 Abstract

*This chapter discusses the application of carbon dots (CDs) as green metal-free sensitizers in photoinduced atom transfer radical polymerizations (ATRP). More specifically, it explores polymethacrylate photopolymerization using inexpensive and readily available CDs made from citric acid and diethylenetriamine, as photocatalysts under both ultraviolet (UV, $\lambda = 365$ nm) and visible light. Various solvent systems were evaluated and a Cu(II) complex was used as co-catalyst. Under the optimized conditions, the resulting methacrylate polymer was obtained in 89 % conversion and with a narrow polydispersity ($\bar{M}_w/\bar{M}_n = 1.4$). Additional kinetics and "on-off" experiments confirmed the stable radical concentration and the controlled nature of the polymerization process. The results reported in this chapter have been published in Campalani, C.; Bragato, N.; Morandini, A.; Selva, M.; Fiorani, G. and Perosa A. Carbon dots as green photocatalysts for atom transfer radical polymerization of methacrylates, *Catal. Today*, 2023, **418**, 114039. In this work, Nicola actively contributed in conducting the experimental work on ATRP photopolymerization.*

5.1.2 Introduction

Since the first reports of atom transfer radical polymerizations (ATRP) in 1995, significant progresses have been made in synthetic polymer chemistry.¹⁻³ Moreover, radical polymerization processes, being more tolerant of functional groups and impurities, have become the preferred method in industrial polymer production.⁵ Contrarily from ionic or radical polymerizations, ATRP processes are relatively unsensitive to the reaction conditions and thus can be applied to a plethora of different monomers, employing different active and versatile metal-based catalytic systems and/or initiators, ultimately leading to well-defined polymers and controlled architectures.⁴

ATRP is a redox process mediated by the reversible interaction between a low oxidation state metal complex (the catalyst, Mt^n/L) and an alkyl halide initiator (P_n-X). As depicted in **Figure 5.1**, during activation, the metal catalyst is oxidized ($Mt^n \rightarrow Mt^{n+1}$) with the formation of an active radical species ($P_n^\bullet$), which initiates polymerization.

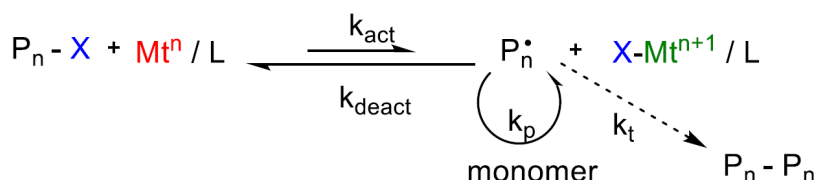


Figure 5.1 : General mechanism of the equilibrium in ATRP processes.

The subsequent deactivation pathway comprises the addition of the monomer with formation of the initial dormant species (P_n-X) and reduction of the catalyst to its former low oxidation state with a specific rate constant of deactivation, k_{deact} . Polymer chains grow by the addition of the intermediate radicals to monomers in a manner similar to conventional radical polymerization, with a rate constant of propagation k_p . Generation of the oxidized metal complex (Mt^{n+1}) reduces the stationary concentration of growing radicals and minimizes their contribution to termination reactions.⁶ Termination reactions (k_t) also occur in ATRP, mainly through radical coupling and disproportionation: however, in a well-controlled ATRP process, no more than a few percent of the polymer chains undergo termination. In order to have a successful ATRP together with a small contribution of terminated chains, a uniform growth of all the chains is required. This last is accomplished through fast initiation and rapid reversible deactivation.

The rate of ATRP depends on the rate constant of propagation (k_p) and on the concentrations of monomer and growing radicals.⁷ The latter is defined by the ATRP equilibrium constant ($K_{ATRP} = k_{act}/k_{deact}$), the concentration of dormant species (P_n-X) and the ratio of the concentrations of activator (Mt^n/L) and deactivator (XMt^{n+1}/L), as detailed in **Equation 5.1**.

$$R_p = \ln \frac{[M]_0}{[M]_t} = k_p K_{ATRP} \left(\frac{[P_n X][Mt^n/L]}{[XMt^{n+1}/L]} \right)$$

Equation 5.1: ATR Polymerization rate.

Reaction conditions such as temperature, solvent, and pressure, along with the nature of the monomer, dormant species and ligand, can significantly influence the activation (k_{act}) and deactivation (k_{deact}) rate constants.^{8,9} Quantifying K_{ATRP} provides valuable insights on the catalyst's activity during ATRP.¹⁰ The catalytically active complexes, however, are formed dynamically and their formation is governed by certain stability constants that regulate also the concentration of catalytic species in specific reaction media. In conclusion, the rate of ATRP is generally proportional to the catalyst activity K_{ATRP} , however, under some conditions it can diminish due to competing radical termination and significant reduction of $(M_t^n/L)/(M_t^{n+1}/L)$ ratio, because of the persistent radical effect.⁶ Considering an ideal ATRP polymerization processes, occurring in absence of chain termination and transfer reactions, it can be stated that the uniformity of polymers chain (namely the dispersity of molecular weights $\mathcal{D} = M_w/M_n$ where M_w is the weight-average molar mass and M_n is the number-average molar mass) is related to the concentration of dormant species ($P_n\text{-X}$) and deactivator (M_t^{n+1}/L), to the rate constant of propagation (k_p) and deactivation (k_{deact}) and to the conversion of monomer (x), according to **Equation 5.2**.⁷

$$\mathcal{D} = \frac{M_w}{M_n} = 1 + \left(\frac{k_p [P_n\text{X}]}{k_{\text{deact}} [X M_t^{n+1}/L]} \right) \left(\frac{2}{x} - 1 \right)$$

Equation 5.2: Dispersity for polymers prepared via ATRP

Hence, using the same monomers, a catalyst with a fast growing chains deactivation rate will lead to a smaller ratio k_p/k_{deact} and produce polymers with a narrower dispersity. Dispersity can be decreased also by increasing the concentration of deactivator and reducing the concentration of the dormant species. As already stated, ATRP are multicomponent systems composed of a monomer, an initiator and a catalyst. A wide range of monomers, including styrenes, methacrylates, methacrylamides, and acrylonitrile, were effectively polymerized via ATRP.¹¹ Even under identical conditions, each monomer has a unique equilibrium constant for its active and dormant species, along with its own radical propagation rate. To maintain control over polymerization, the concentration of propagating radicals and the rate of radical deactivation must be fine-tuned for each specific monomer.

The initiator defines the number of growing polymer chains. If initiation is fast and termination or transfer reactions are minimal, the number of growing chains remains constant and corresponds to the initial initiator concentration. Common initiators are alkyl halides (RX), where the halide (X) must rapidly and selectively migrate between the growing chain and catalyst to produce well-defined polymers with narrow molecular weight distributions. Chloride and bromide typically offer the best control over molecular weight. In general, any RX species with activating substituents on the α carbon can serve as an ATRP initiator.

Transition metal complexes are typically employed as ATRP catalysts; the catalyst is the key component in ATRP processes as it controls the atom transfer equilibrium and regulates the exchange between dormant and active species. In order to be efficient, the catalysts must meet several criteria: the metal center must have at least two oxidation states separated by a single electron, exhibit a high affinity for halogens, and possess an expandable coordination sphere to

selectively bind a halide. Additionally, the ligand should form a strong complex with the metal to ensure efficient catalysis.

Key parameters in ATRP include solvent choice, temperature, and reaction time. Concerning the solvent, ATRP can be performed in bulk, in solution or in heterogeneous systems and many different solvent have been used such as benzene, toluene, acetone, ethyl acetate, water.⁵ A solvent is especially useful when the polymer product is insoluble in its monomer, though care must be taken to minimize chain transfer to the solvent and potential interactions with the catalyst. Polymerization rates increase with the reaction temperature due to the higher radical propagation rate constant and the atom transfer equilibrium constant. However, high temperatures can also promote chain transfer, side reactions,¹² and catalyst decomposition.^{13,14} Moreover, high temperatures can also promote chain transfer, side reactions, and catalyst decomposition. Longer reaction times can lead to near-complete monomer conversion without significantly affecting polymer dispersity but may result in the loss of end groups.⁵

A major drawback of ATRP is the need for large amounts of catalyst to maintain control over polymerization. To address environmental and practical concerns, recent approaches have focused on generating the metal catalyst *in situ* through various initiation techniques. These methods involve different reduction pathways to form the activator species (M_{tn}) and have employed reducing agents,¹⁵ electrochemical processes,¹⁶ copper-containing nanoparticles,¹⁷ and photochemical redox processes.^{18–23} The use of light in photochemical ATRP is particularly promising, as it is environmentally friendly, widely available, non-invasive, and enables precise spatial and temporal control over the polymerization process.²⁴

Various photoactive molecules, such as dyes and commercial photoinitiators, can act as effective reducing agents, facilitating photoinitiated ATRP. Under light irradiation, these molecules enable the *in situ* generation of the reduced metal complex (typically Cu^I from Cu^{II}), allowing polymerization to proceed with lower catalyst concentrations, as depicted in **Figure 5.2**.²⁵ Notably, the polymerization can be easily paused and resumed by switching off the light source. Photoinduced ATRP has been successfully carried out using a range of light sources, including UV,^{19,21} visible,²⁶ or near-infrared light.²⁷

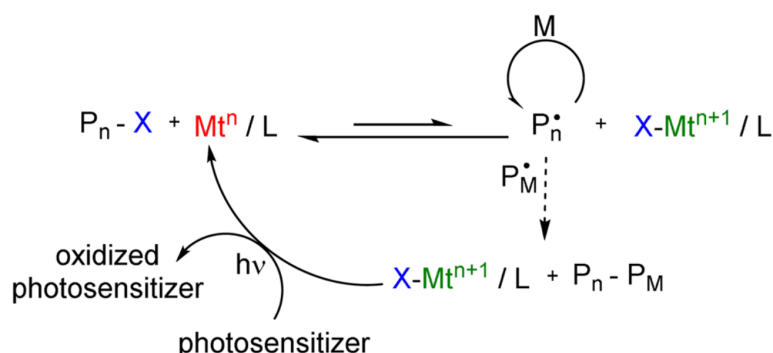


Figure 5.2: General mechanism of the equilibrium in ATRP processes with regeneration of the activator via electron transfer induced by light.

Despite its potential, photo-ATRP still faces some practical challenges, particularly regarding the sustainability and environmental impact of most of the reported photosensitizers, which often involve harmful reagents in the respective synthetic pathways. In response, carbon dots (CDs) derived from natural feedstocks have emerged as a promising alternative. Recently, CDs have gained attention for their use in photoinduced reversible addition-fragmentation chain-transfer polymerization,²⁸ marking their first application in photo-controlled radical polymerization. In 2020, CDs synthesized from sodium alginate and ethylenediamine were successfully used in the photo-ATRP of methyl methacrylate in dimethyl sulfoxide, achieving narrow polymer dispersity albeit with a relatively low conversion rate (Conv. = 30% in $t = 2.5$ h).²⁵

Under light irradiation carbon dots (CDs) can be excited and act as reducing agents, converting Cu^{II} to Cu^{I} *in situ*. The thus formed Cu^{I} complex then reacts with a bromide initiator to form free radicals that initiate polymerization. CDs have shown promise as photocatalysts in various applications, including photooxidation, photodegradation, and photoreduction,^{29–31} and can be easily synthesized from inexpensive and abundant carbon precursors. Additionally, doping CDs with specific agents can enhance their photoactivity, allowing for the customization of their optical, electrical, and chemical properties to meet specific needs.^{32,33}

This chapter describes the use of CDs derived from citric acid and diethylenetriamine as photosensitizers for the photoinduced ATRP of methacrylate. Photopolymerizations were conducted in different media, using non harmful solvent systems and irradiating with both UV ($\lambda = 365$ nm) and visible light.

5.1.3 CDs synthesis and characterization

As a novel type of photosensitizer for activating ATRP, two types of carbon dots (CDs) were tested: nitrogen-doped (N-cit-CDs) and non-doped (cit-CDs), both synthesized from citric acid via a bottom-up technique (see Experimental section for further details). The synthesis of these two families of CDs and their photocatalytic performances were previously reported elsewhere.^{34,35} Detailed analyses including HR-TEM, FT-IR, UV-Vis, XPS, PL/PLE, ESI-MS, $^1\text{H}/^{13}\text{C}\{^1\text{H}\}$ and DOSY NMR indicated the amorphous nature of both nanoparticles.^{34,35} Cit-CDs exhibited poorly defined shapes with diameters between 9 and 12 nm,³⁴ while N-cit-CDs were characterized by a more uniform diameter of around 13 nm, confirmed by atomic force microscopy (AFM).³⁰ As can be seen in **Figure 5.3**, both CDs are able to absorb in the UV region, but only N-cit-CDs presented some absorption also in the visible range: this evidence prompted us to test this class of nanoparticles also for visible light photoinduced ATRP. In addition, nitrogen doping has shown to improve the activation of these types of polymerizations: in the N-doped electron-rich carbon nanostructure, the π electrons were activated by their conjugation with the lone pair electron of nitrogen, resulting in excellent electrochemical and catalytic performances.^{32,36}

The amount of nitrogen doping in N-Cit-CDs was evaluated via elemental analysis showing a carbon/nitrogen ratio equal to 3.2.

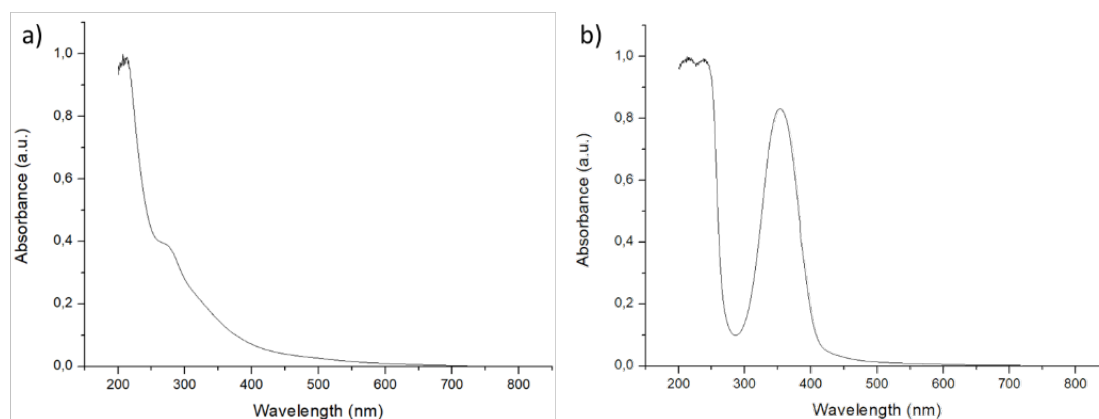
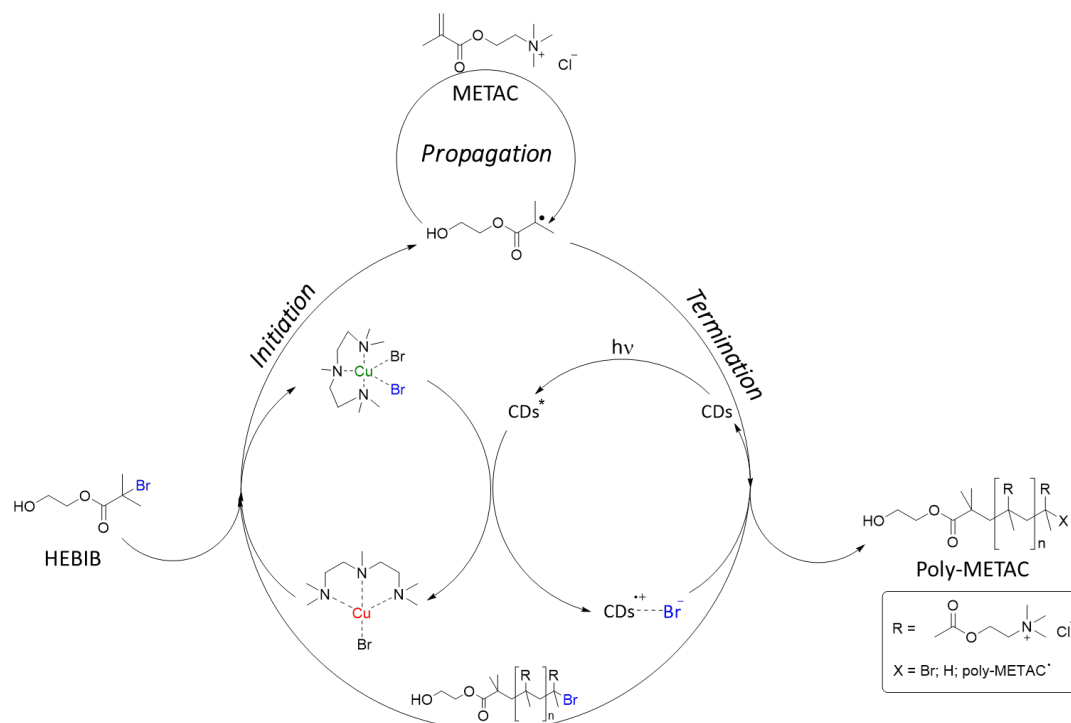


Figure 5.3: UV-Vis spectra of the synthesized CDs. a) non doped cit-CDs; b) doped N-Cit-CDs.

5.1.4 ATRP experiments

The ability of CDs to mediate photoinduced ATRP was evaluated by irradiating solutions of CDs with UV light ($\lambda = 365$ nm LEDs) and visible light (5600 K LEDs) in various solvent systems (H_2O , $\text{H}_2\text{O}/\text{CH}_3\text{OH}$, and $\text{H}_2\text{O}/\text{CH}_3\text{CN}$). ATRP photopolymerization were carried out using 2-hydroxyethyl-2-bromo-2-methylpropanoate (HEBIB) as the initiator and $\text{CuBr}_2/\text{N,N,N',N'',N'''}\text{-pentamethyldiethylenetriamine}$ (PMDTA) complex as catalyst, targeting the polymerization of [2-(methacroyloxy)ethyl]trimethylammonium chloride (METAC) under inert atmosphere. The proposed mechanism outlining the role of CDs in this process is shown in **Scheme 5.1**.



Scheme 5.1: Proposed mechanism for photoinduced ATRP of METAC using CDs.

After irradiation, the photoexcitation of CDs results in the population of the excited state (CDs*) that can perform an electron transfer to $[\text{Cu}^{\text{II}} \text{PMDTA}]\text{Br}_2$. This leads to the reduction of the Cu^{II} complex to the respective Cu^{I} form that can initiate the radical polymerization of the alkyl bromide (HEBIB).

The feasibility of CDs to reduce the Cu^{II} complex is supported also by the analysis of the redox potentials of the species. As reported in our previous study, N-cit-CDs possess $E_{\text{red}} = 1.94 \text{ V}$ and $E_{\text{ox}} = +1.12 \text{ V}$, and cit-CDs $E_{\text{red}} = 1.83 \text{ V}$ and $E_{\text{ox}} = +0.52 \text{ V}$,³⁵ while the redox potentials of the Cu complex are reported to be $E_{\text{red}} = 0.155 \text{ V}$ and $E_{\text{ox}} = 0.045 \text{ V}$.¹⁷ These data prompted us to test both the synthesized CDs for the activation of the metal catalyst. The regeneration of CDs takes place in the photocatalytic cycle, when the oxidized CDs (CDs^{*+}) react with bromide.²⁵

Scheme 5.1 reports different possible polymer termination pathways such as radical disproportionation, combination of two active chain ends or halogen termination. In the latter case, the polymer itself can become an initiator restarting the cycle. All experiments were conducted at room temperature under different light sources and in different solvents, with a constant ratio between the reagents $[\text{METAC}]/[\text{HEBIB}]/[\text{CDs}]/[\text{CuBr}_2]/[\text{PMDTA}] = 100:1:1:1:3 \text{ mol/mol}$ and constant exposure time ($t = 1 \text{ h}$). Lower ratios of catalyst ($[\text{METAC}]/[\text{CuBr}_2]/[\text{PMDTA}] = 100:0.1:0.3 \text{ mol/mol}$, $100:0.25:0.75 \text{ mol/mol}$ and $100:0.5:1.5 \text{ mol/mol}$) have also been tested but production of the desired polymer was not observed in all cases.

The investigation started by testing the CDs under UV irradiation at 365 nm in different solvent mixture, namely water, water/methanol (1:1 V/V) and water/acetonitrile (1:1 V/V), as summarized in **Table 5.1**.

Table 5.1: UV light ($\lambda = 365 \text{ nm}$) induced ATRP of METAC using different CDs and in different solvents.^[a]

Entry	CDs	Solvent	Conv. (%) ^b	$M_n (\text{g}\cdot\text{mol}^{-1})^c$	$M_m (\text{g}\cdot\text{mol}^{-1})^c$	$\bar{D}^c$
1	N-cit-CDs	H ₂ O	88	1600	2500	1.5
2	N-cit-CDs	H ₂ O/CH ₃ OH 1:1 V/V	89	1896	2655	1.4
3	N-cit-CDs	H ₂ O/CH ₃ CN 1:1 V/V	85	1430	2610	1.8
4	Cit-CDs	H ₂ O/CH ₃ OH 1:1 V/V	-	-	-	-
5	-	H ₂ O/CH ₃ OH 1:1 V/V	-	-	-	-

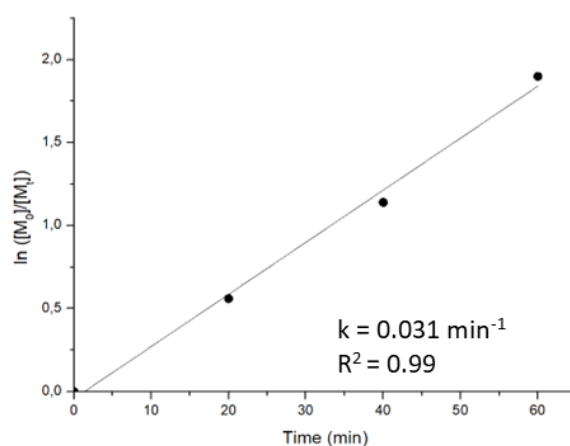
^a Experiments were conducted at ambient temperature for $t = 1 \text{ h}$ using a ratio $[\text{METAC}]/[\text{HEBIB}]/[\text{CDs}]/[\text{CuBr}_2]/[\text{PMDTA}] = 100:1:1:1:3 \text{ mol/mol}$; ^bDetermined gravimetrically; ^cDetermined by gel permeation chromatography using PEG standards.

High monomer conversions, between 85 and 89 %, were obtained after only $t = 1 \text{ h}$ of light exposure using the doped N-cit-CDs in all the three solvents (Entries 1-3, **Table 5.1**). The resulting polymers

showed dispersity ($\bar{D}$) always < 2 , demonstrating a good control over the polymerization reaction. Changing the reaction solvents, some minor differences concerning the weight-average molar mass, number-average molar mass and dispersity were observed. The 1:1 mixture of water and methanol was selected as the best performing solvent mixture, leading to 89 % METAC conversions (Entry 2, **Table 5.1**) and narrower dispersity (1.4). The presence of methanol probably leads to a longer lifetime of the Cu^{I} catalytic species in the solution modifying the kinetic constants leading to a more favorable pathway.

To gain more insights on the polymerization mechanism, an experiment using the same conditions but in absence of CDs was performed (Entry 5, **Table 5.1**). In this case no polymer was obtained demonstrating the necessity to photoactivate the copper catalyst. The absence of polymer was confirmed via GPC analysis where only molecular weights lower than $200 \text{ g}\cdot\text{mol}^{-1}$ were observed. Other blank tests, namely in absence of light, catalyst and without CDs/irradiation, were performed to confirm the importance of all the components for photoinduced ATRP of METAC. All the blank tests were carried out using a 1:1 V/V mixture of water and methanol as the designed solvent and in all tested conditions no formation of polymer was observed (see **Table A14, Appendix Chapter 5**).

Once chosen the best reaction conditions, a kinetic study was performed to confirm the linear increase of the conversion during the irradiation time. As shown in **Figure 5.4**, a linear correlation between the logarithm of monomer concentration ($\ln [M_0]/[M_t]$) and time (t , starting at $t = 0$), highlighted a first order kinetic. This evidence indicates that the concentration of active free radicals can be seen as constant during the reaction.^{25,37}



*Figure 5.4: Kinetic plot of the polymerization system using N-cit-CDs under UV irradiation and relative rate constant. Experimental conditions reported in Entry 2, **Table 5.1**.*

To better understand the influence of the nitrogen doping on the photosensitizer, non-doped CDs (Cit-CDs) were tested in the best conditions found for N-cit-CDs (Entry 4, **Table 5.1**). However, the non-doped nanoparticles did not show consistent photocatalytic activity and polymer formation was not detected after $t = 1 \text{ h}$ of irradiation. This result was further evidence of the importance of nitrogen doping in CDs in order to obtain active photosensitizers. Nitrogen doping on CDs, indeed,

allowed the presence of more defect states on the surface of the dots together with molecular like fluorophores that are able to effectively promote a more effective excitation of the electron.³⁸ Concerning visible light, the non-doped CDs were not used since they have negligible absorbance in the visible region (see UV spectrum in **Figure 5.3**). As for UV exposed experiments, three different solvents were examined but only using H₂O/CH₃OH 1:1 V/V it was possible to observe the presence of the polymer (Entry 2, **Table 5.2**). After t = 1 h of irradiation, poly-METAC was obtained in 70 % conversion and a narrow dispersity (1.5) highlighting the possibility to activate this reaction using visible light as a green, cheap and safe reagent.

Table 5.2: Visible light (5600 K) induced ATRP of METAC using N-cit-CDs in different solvents.^a

Entry	CDs	Solvent	Conv. (%) ^b	M _n (g·mol ⁻¹) ^c	M _m (g·mol ⁻¹) ^c	Đ ^c
1	N-cit-CDs	H ₂ O	-	-	-	-
2	N-cit-CDs	H ₂ O/CH ₃ OH 1:1 V/V	70	1460	2170	1.5
3	N-cit-CDs	H ₂ O/CH ₃ CN 1:1 V/V	-	-	-	-
4	-	H ₂ O/CH ₃ OH 1:1 V/V	-	-	-	-

^a Experiments were conducted at ambient temperature for 1 h using a ratio [METAC]/[HEBIB]/[CDs]/[CuBr₂]/[PMDTA] = 100/1/1/1/3; ^b Determined gravimetrically; ^c Determined by gel permeation chromatography using PEG standards

An experiment under the same conditions but without the addition of CDs has been performed (Entry 4, **Table 5.2**) but no polymer was detected, underlying once again the essential presence of photoactive carbon nanoparticles in order to activate the reaction. Another blank test in absence of the copper catalyst was performed and, also in this case, no poly-METAC was observed (see **Table A14, Appendix Chapter 5**). The absence of polymer was confirmed via GPC analysis where only molecular weights lower than 200 g·mol⁻¹ were detected.

To further confirm the linearity of the relationship between the monomer concentration and the irradiation time, a kinetic study was conducted also under visible light. As can be seen in **Figure 5.5**, a first order kinetic was observed indicating once again an almost constant concentration of free radicals during polymerization. The difference in the rate constant of the ATRP under UV irradiation ($k = 0.031 \text{ min}^{-1}$) and visible light ($k = 0.023 \text{ min}^{-1}$) underlined the higher speed of the polymerization at 365 nm, confirming an improved photoreduction activity of the carbon nanoparticles at that wavelength.

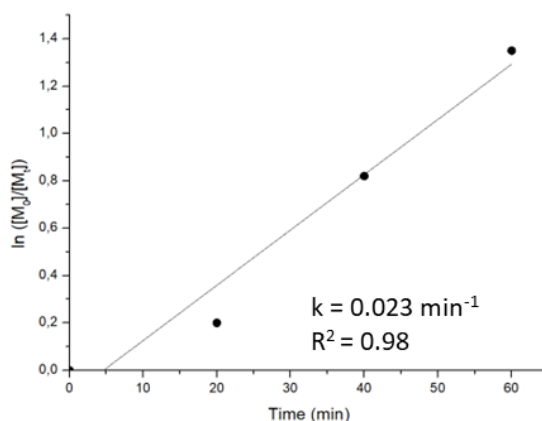


Figure 5.5: Kinetic plot of the polymerization system using N-cit-CDs Under Vis irradiation and relative rate constant. Conditions reported in Entry 2, Table 5.2.

5.1.5 Polymer characterization

Characterization of the obtained polymer was performed using gel permeation chromatography (Table 5.1 and 5.2), thermogravimetric analysis, differential scanning calorimetry and NMR (see Figures S129-S132, Characterization section). The polymeric product is a thermoplastic, amorphous and transparent polymer with a glass transition temperature (T_g) of 100 °C (see Figure S131, Characterization section), similar to polymethylmethacrylate (T_g = 110 °C). The thermogravimetric analysis of the polymer (see Figure S132, Characterization section) showed a first small weight loss (circa 2.5 %) at T = 100 °C due to polymer dehydration upon removal of the residual humidity.³⁹ The second stage, between 280-300 °C, corresponded to the thermal decomposition of the groups that protruded from the polymer chain,⁴⁰ while the third weight loss at T = 390-400 °C, was ascribed to exothermic reactions due to the decomposition of the ammonium salts.⁴¹ The obtained poly-METAC retained the luminescence properties of the CDs revealing the presence of part of the photo-initiator trapped in the polymeric mass (see Figure A22 in the Appendix Chapter 5 section). In order to understand if the presence of the CDs affects the characteristics of the polymer, a classical ATRP of METAC has been conducted and the obtained material was characterized and compared with the poly-METAC obtained with CDs. The two polymers had the same aspect and consistency being transparent and amorphous and no substantial differences were highlighted from TGA and DSC analyses (Figures S133 and S134 in the Characterization Chapter 5 section). The only difference is luminescence. For these reasons, the presence of CDs in the polymer matrix was not considered detrimental but added luminescence properties to the material, which could be useful for further applications.

5.1.6 “On-off” experiments

Light “on-off” experiments were performed both under UV (conditions of Entry 2, Table 5.1) and visible light (conditions of Entry 2, Table 5.2). The polymerization mixtures were subjected to

repeated light exposure by irradiating the sample for 20 min and then keeping the same sample in dark for 10 min. The obtained results (**Figure 5.6**) highlighted the dependence of polymerization on the irradiation: no polymerization occurred when the solutions were kept in a dark environment. During the light exposure time, light induced ATRP occurred showing also the different polymerization rates under UV and visible light.

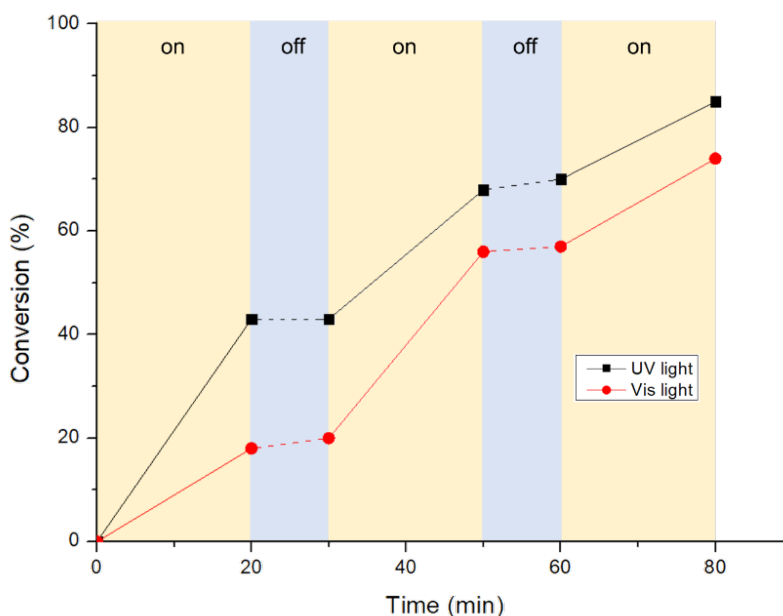


Figure 5.6: Monomer conversion (%) versus time using CDs to determine the dependency on irradiation (UV = black line, Vis = red line). Yellow regions refer to light on, blue regions to light off. The UV irradiated experiment was performed following the conditions reported in **Table 5.1**, Entry 2; the Vis irradiated following the conditions in **Table 5.2**, Entry 2.

5.1.7 Conclusions

We herein report an efficient photoinduced atom transfer radical polymerization (ATRP) protocol activated by citric acid-derived CDs (N-cit-CDs). In particular, nitrogen doped carbon nanoparticles were synthesized and used as photosensitizer for the preparation of poly-METAC (2-(methacryloyloxy)ethyl]trimethylammonium chloride) following a greener and sustainable synthetic procedure. The reaction was found to be efficient in water-based solvent, in particular in water/methanol 1:1 V/V solutions, and the presence of a photosensitizer allowed to use small amounts of metal catalyst (1:100 mol/mol with respect to the monomer). It was highlighted that N-cit-CDs are able to photoactivate polymerization under both UV and visible light paving the way towards an eco-friendly, cheap and affordable synthetic procedure for polymethacrylates. After only $t = 1$ h of irradiation it was possible to obtain the polymer with 89 % conversion and $\bar{D} = 1.4$ under UV light, while under visible light poly_METAC was obtained in 70% conversion and $\bar{D} = 1.5$. A first order kinetic was observed in both cases, confirming an almost constant concentration of radicals, typical of ATRP mechanisms. “On-off” experiments and blank tests confirmed the necessity of all the reagents (light, CDs, initiator and catalyst) in order to obtain the polymer. In comparison

with the only other example in the literature,²⁵ the present procedure was more effective in terms of polymer conversion (70-89 % in $t = 1$ h versus 30% in $t = 2.5$ h); moreover, it allowed to perform ATRP avoiding to use dimethyl sulfoxide. In conclusion, a new, cheap and effective photosensitizer for ATR polymerization has been herein studied demonstrating the possibility to achieve greener and efficient processes in polymer preparation.

5.1.8 Experimental

Materials and Methods

All the reagents were purchased from Merck Life Science S.r.l. (Milano, Italy), were of analytical grade and used without further purification. MilliQ water, used as a solvent throughout the experiment, was obtained with a Merck Millipore C79625 system. CHNS analysis was performed on an Elemental Unicube (Elementar Italia Srl, Lomazzo, Italy). For the optical characterization of CDs, an UV-Vis spectrophotometer Agilent 8456 (Agilent Technologies Italia, Milano, Italy) has been used. ^1H and $^{13}\text{C}\{^1\text{H}\}$ NMR spectra were recorded on a Bruker AV 400 spectrometer (^1H : 400 MHz; ^{13}C : 100 MHz; Bruker GmbH, Mannheim, Germany). The chemical shifts (δ) were reported in parts per million (ppm) relative to the residual solvent signal, used as an internal reference. Gel permeation chromatography (GPC) was performed on an Agilent Infinity 1260 system equipped with refractive index detector and using an injection volume of 20 μL and a flow rate of 1 mL/min. A Phenomenex PolySep linear was used as size exclusion chromatography (SEC) column maintaining a constant temperature of $T = 40$ °C during the analysis. An aqueous solution of LiCl 0.1 M was used as eluent and polyethylene glycol mixtures were used as standard. DSC analyses were performed on a DSC 3 analyzer (Mettler Toledo, USA). The temperature of the instrument was calibrated using indium as standard. Poly-METAC (about 10.0 mg) was weighed into aluminium oxidized melting pots, sealed, and heated from room temperature to 300 °C at 10 °C/min. An empty sealed melting pot was used as reference. Thermogravimetric analyses were performed using a Perkin Elmer TGA 4000 instrument. The analyses were carried out weighting 10 mg of poly-METAC in a ceramic crucible, in a temperature range from 30 °C to 600 °C with a heating rate of 10 °C/min and under a nitrogen flow of 20 mL/min.

Synthesis of Cit-CDs

The non-doped nanoparticles were synthesized hydrothermally as already reported.³⁴ In detail, 2.0 g of citric acid were dissolved in 20 mL of MilliQ; the solution was heated in a sealed stainless steel autoclave for $t = 24$ h at $T = 180$ °C. The mixture was then neutralized to neutral pH with an aqueous NaOH solution, filtered on paper and evaporated to dryness leading to a dark yellow luminescent oil (25 % wt. yield) which was used without any further purifications. The obtained nanoparticles have been characterized via NMR, UV-Vis and CHNS elemental analysis.

Synthesis of N-cit-CDs

The nitrogen doped CDs were hydrothermally synthesized by heating an aqueous solution of citric acid (2.0 g in 20 mL of MilliQ water) and diethylenetriamine (0.67 g) in a sealed stainless steel autoclave for $t = 6$ h at $T = 180$ °C.³⁵ The mixture was then filtered and evaporated to dryness leading to a brown solid (72 % wt. yield) which was used without any further purifications. The obtained nanoparticles have been characterized via NMR, UV-Vis and CHNS elemental analysis.

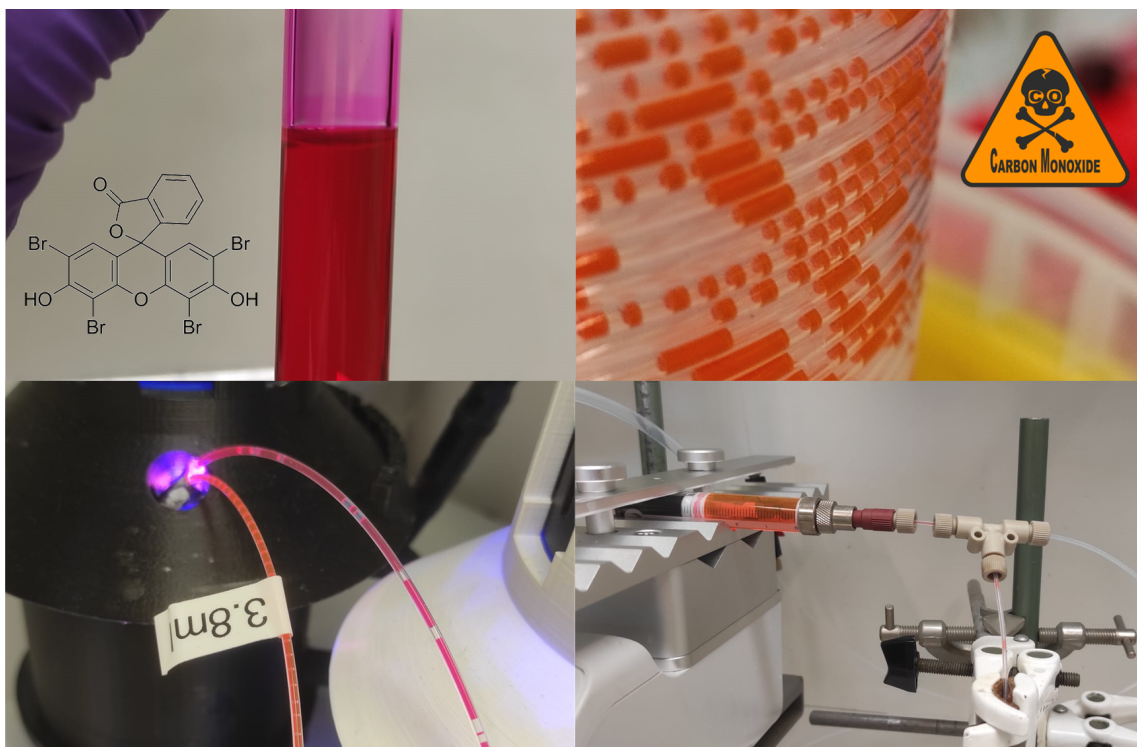
Synthesis of 2-hydroxyethyl-2-brom-2-methylpropanoate (HEBIB)

For the synthesis of the initiator, 1.5 mol of ethylene glycol and 60 mmol of triethylamine were dissolved in 30 mL of anhydrous tetrahydrofuran and placed in a round bottom flask. The reaction flask was put under inert atmosphere and kept under stirring in an ice bath while adding dropwise (in 30 min) 30 mmol of α -bromoisobutyryl bromide. After stirring at room temperature for $t = 16$ h, 200 mL of deionized water were added to the flask and the product was extracted with dichloromethane (3 x 30 mL). The organic fraction was washed with 30 mL of an aqueous solution of HCl 1 M. The solvent was removed *in vacuo* leading to HEBIB as a yellow oil in 94.5 % yield. ¹H NMR (400 MHz, CDCl₃): 1.96(s, 6H), 3.87 (t, 2H), 4.31 (t, 2H). ¹³C NMR (100 MHz, CDCl₃): 30.7, 55.8, 60.7, 63.3, 67.4, 171.8

ATRP experiments

10 mmol of [2-(methacryloyloxy)ethyl]trimethylammoniumchloride (METAC), 0.1 mmol of 2-hydroxyethyl-2-brom-2-methylpropanoate (HEBIB), 6.3 mg of CDs (N-cit-CDs or Cit-CDs) and 1 mL of an aqueous solution of CuBr₂ and *N,N',N'',N'''*-pentamethyldiethylenetriamine (PMDTA) ([CuBr₂] = 0.1 M, [PMDTA] = 0.3 M) were added to a Schlenk tube. The chosen solvent was added in quantity equal to the volume of monomer and CuBr₂/PMDTA solution. After 5 vacuum/nitrogen cycles the reactor was kept under continuous stirring and irradiation (UV = 365 nm or Vis = 5400 K LEDs) for $t = 1$ h. The polymer was precipitated using acetone as antisolvent. After removal of the solvent *in vacuo*, the product was dissolved in methanol subsequently removed by rotary evaporation. The polymer was kept in vacuum oven at $T = 70$ °C ($p = 80$ mbar) overnight. The product was obtained as a glassy, transparent solid and characterized via NMR, DSC and TGA.

5.2 Aryl Radical Carbonylation



This study has been conducted in the laboratories of Prof. Timothy Noël at the Van't Hoff Institute of the University of Amsterdam, Netherlands. This line of research is still active.

5.2.1 Abstract

In this study, we report the preliminary results on the development of a new methodology for aryl radical carbonylations using photo-redox catalysis in continuous flow (CF). CF technologies enable a more efficient handling of gaseous reagents, which are often challenging to manage in batch processes, by facilitating their interaction with liquid-phase reaction partners. We report two radical aryl carbonylation reactions involving distinct electron-poor alkenes and employing CO as the carbonylation co-reagent. The reactions were conducted under optimal conditions identified thus far, employing various Michael acceptors and thianthrenium salts. Additionally, we propose a possible reaction mechanism based on these findings.

5.2.2 Introduction

Carbonyl compounds are among the most ubiquitous functional groups and the basis of many traditional polar transformations.^{42–44} Therefore, carbonylation, or the incorporation of carbon monoxide into an organic substrate to give a carbonyl compound, is one of the most developed transformations in organic synthesis.^{45,46} Traditionally, carbonylations are mediated by transition metals, exploiting the beneficial interaction of σ -bonding and π -back bonding between the metal and carbon monoxide ligand to get in close proximity with the activated reaction partner in the metal's inner-shell environment.⁴⁷ This has led to developing industrially relevant bulk chemical processes, such as hydroformylation of alkenes ($10.4 \times 10^6 \text{ t}\cdot\text{y}^{-1}$)⁴⁸ and the synthesis of acetic acid from methanol ($7 \times 10^6 \text{ t}\cdot\text{y}^{-1}$),⁴⁹ but also to widespread applications in the fine-chemical industry, such as carbonylative cross-coupling reactions.^{50,51}

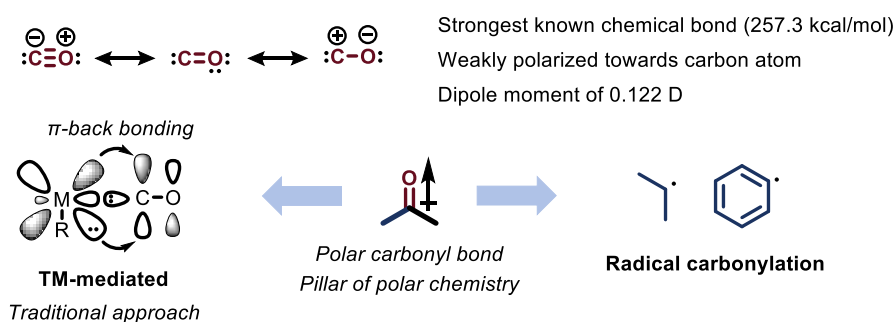


Figure 5.7: Carbon monoxide: C^1 building block of choice and formation of carbonyl compounds.

With the advent of photo-redox catalysis, alternative activation methods were developed to achieve established or newly developed transformations under mild conditions, which were previously impossible using traditional thermal or metal-mediated activation.⁵² Under irradiation with an appropriate light source, a photocatalyst is excited to a higher energy state, becoming a better oxidant and/or reductant than in its ground state. The excited photocatalyst can then selectively activate organic substrates, through a number of processes, such as energy transfer (ET), single-electron transfer (SET) or hydrogen-atom transfer (HAT).⁵³ In this manner, open-shell reactive intermediates that engage in various radical transformations can be formed. Noël's group has recently reported on the carbonylation of carbon-centered alkyl radical species originating from $C(sp^3)$ -H bonds in various hydrocarbons, including light alkanes, to form a variety of unsymmetrical ketones.⁵⁴ Reactions were performed in CF reactors to bring the gaseous reagents in contact with both the photocatalyst as well as with the reaction partners dissolved in the liquid phase, resulting in an extremely efficient process under mild conditions. Given these premises, we were wondering if we could achieve the more challenging aryl radical carbonylation of sp^2 -hybridized carbon atoms and engage in a similar transformation.^{55,56} The less favorable polarity for carbonylation of the electrophilic aryl radical, compared to the nucleophilic alkyl radical, and the extremely high reactivity of the aryl radical intermediate, suggests that in this case the use of flow technologies would be even more crucial to minimize and ultimately avoid undesired side-reactions.^{57,58} Additionally, photochemical reactions with gas- and liquid reaction partners are notoriously difficult

to scale in batch and often require extended reaction times.^{59–61} Indeed, only a number of aryl radical carbonylation reactions are reported, all of which use a highly efficient trap of the acyl intermediate along with extreme reaction conditions, and suffer from a limited scope, as well as limited reaction scale.^{62–69}

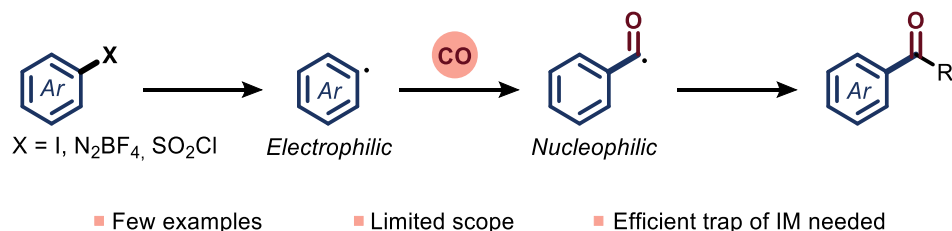


Figure 5.8: Aryl radical carbonylation previous examples

For the source of aryl radicals, aryl thianthrenium salts were chosen as bench-stable reagents which are generated in one-step, with impressive and predictable selectivity, are easily activated with photoredox catalysts, including organic dyes, and allow the functionalization of highly complex arenes, with broad structural diversity.^{70–72} Organothianthrenium- and related salts have recently been used in C–C, C–N, C–F, C–S, C–O, C–B, C–Si and C–P bond formation, including for the late-stage functionalization of drug-like molecules and peptides. Compared to other aryl radical sources they offer higher stability, facile incorporation and higher selectivity due to combined electronic and steric effects.⁷³ However, to date, radical carbonylation reactions that make use of aryl thianthrenium salts have not been reported. Herein, we developed a novel CF methodology to obtain said carbonylation of aryl radicals, generated from aryl thianthrenium salts as a formal late-stage C(sp²)–H functionalization, and conjugative coupling of the acyl radical intermediate with Michael acceptors (**Figure 5.9**).

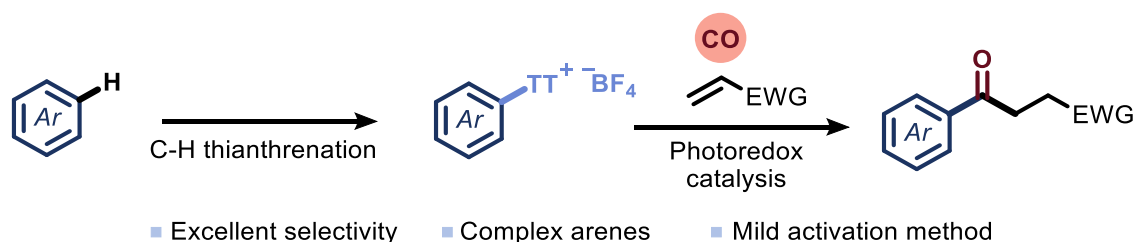


Figure 5.9: This work: formal C(sp²)-H radical carbonylation of aryl thianthrenium salts.

5.2.3 Reactor set up

As anticipated in the introduction, the reactions were performed in a CF reactor to optimize contact of the gaseous reagents with the other reaction partners in the liquid phase, improving the overall process efficiency. The most cost-effective strategy for carbonyl installation would utilize readily available, inexpensive carbon monoxide from the hydrocarbon reforming industry.⁴⁵ However, while safety hazards associated with carbon monoxide would pose substantial risks in conventional

batch reactors, safe processing can be ensured in flow due to the limited amount of chemicals in the microreactor.^{74,75} Additionally, the short length scales in micro flow reactors result in a uniform irradiation of the reaction mixture, reducing reaction times and providing opportunities for scaling up (**Figure 5.10**).⁷⁶

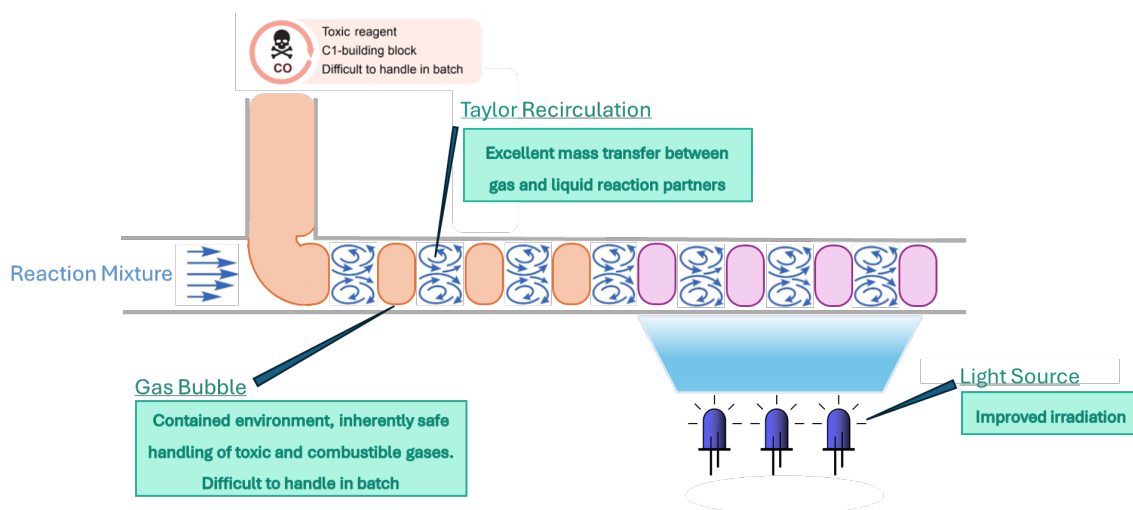


Figure 5.10: gas-liquid reactions using flow technology.

An important factor for achieving reproducible results in gas-liquid reactions is a stable gas-liquid flow with a constant distribution of gas-liquid segments. Additionally, small gas and liquid segments correspond to a high contact area between the gas and liquid phase and thus a higher chance of reaction between the gaseous and liquid reagents.

A schematic representation of gas-liquid reactions performed in flow is reported in **Figure 5.11**. Reactions can only be performed in continuous mode when the pressure of all input streams is higher than the pressure at the outlet of the reactor. This means that all equipment which is used for injecting a gas stream (gas cylinder, reducer of gas cylinder and MFC) and for injecting a liquid stream (syringe pump with gastight/disposable syringe, HPLC pump) should be at a higher pressure or should be able to operate at a higher pressure than the design pressure of the BPR and additional pressure drop of the reactor system. Given that the reducer of the CO cylinder in Noël's lab is set to 10 bar, reactions in continuous mode cannot exceed this pressure. Additionally, an HPLC pump should be used at pressures > 10 bar, rather than a syringe pump and gas-tight syringe. Importantly, a check-valve (CV) should be placed after the inlet of gas and liquid stream,s to ensure that flow can only move in one direction.

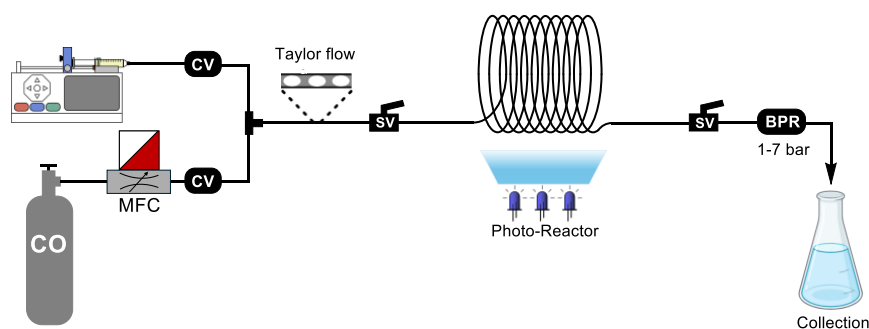


Figure 5.11: Schematic representation of gas-liquid reactions performed in continuous-mode. MFC: Mass Flow Controller; CV: Check Valve, SV: Switch Valve, BPR: Back-Pressure.

For reactions above the maximum pressure of the liquid stream (syringe pump or syringe with 10-15 bar limit pressure both) or above the maximum pressure of the gas stream (10 bar limit pressure of the gas cylinder or reducer), a different procedure needs to be applied. In these cases, the gas and liquid stream are first combined in a filling loop (Figure 5.12), then pressurized with a HPLC pump and finally injected into the reactor coil under the desired flow rate with the HPLC pump (Figure 5.13).

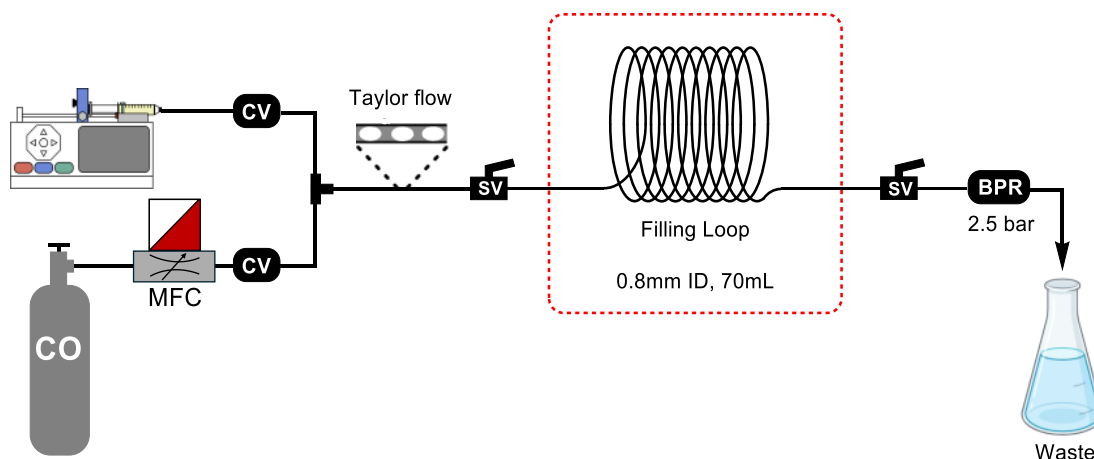


Figure 5.12: Schematic representation of gas-liquid reactions performed with a loop filling method. Step 1: Loop filling of gas-liquid mixture. MFC: Mass Flow Controller, CV: Check-Valve, BPR: Back-Pressure Regulator, SV: Switch Valve.

Combination of the gas and liquid stream in the filling loop occurs in the same fashion as the reactions at low pressure. However, after the T-mixer, the gas-liquid stream is injected in a filling loop instead of the photochemical reactor. The filling loop has switch valves connected at either sides, allowing the user to contain the gas-liquid mixture inside the loop after injecting the complete reaction mixture. A large gas slug is usually injected before and after the reaction mixture, to avoid dilution of the reaction mixture with solvent. Once the gas-liquid mixture is contained in the filling loop, the outlet switch valve is connected to the solvent-filled photoreactor with the desired BPR (17-69 bar) at the outlet, while the inlet switch valve is connected with a HPLC pump. The outlet

valve towards the photoreactor can then slowly be opened, with the purpose of preserving the gas-liquid separation in separate slugs as much as possible. Sudden depressurization of the filling loop can cause by-passing of liquid slugs by gas slugs, resulting in lower gas-liquid contact area during the reaction. While flowing solvent towards the filling loop and photoreactor, the capillary tubing between the HPLC pump and BPR are pressurized, the gas segments are compacted, and the gas is partially solubilized. However, flow over the BPR only starts when the system has reached the design pressure of the BPR. Once this pressure is reached, the flow rate of the HPLC pump is adjusted to achieve the desired residence time. Reaction is then performed through irradiation of the solution inside the reactor and the reaction mixture is collected at the outlet.

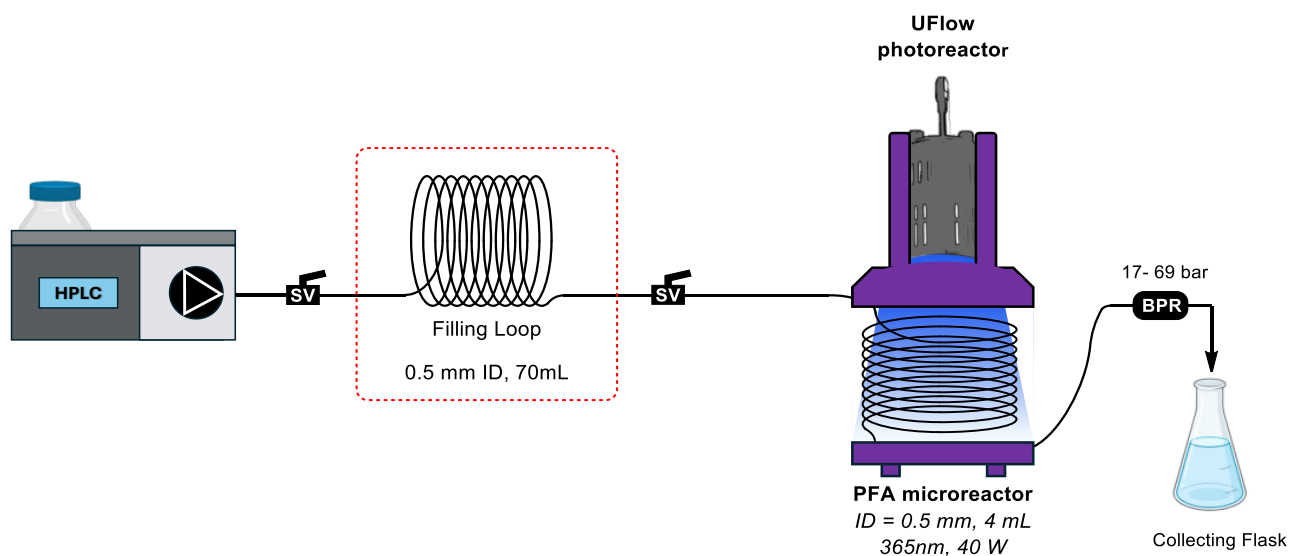
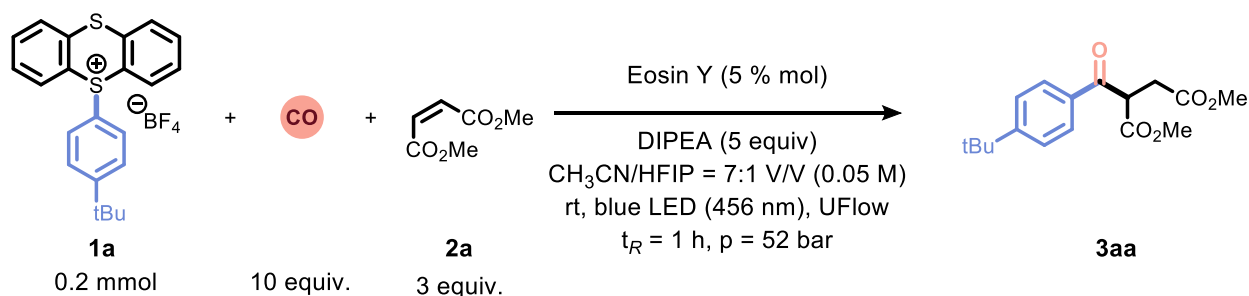


Figure 5.13: Schematic representation of gas-liquid reactions performed with a loop filling method. Step 2: Pressurizing system and reaction under correct flow rate, SV: Switch Valve, BPR: Back-Pressure Regulator.

5.2.4 Results and discussion

Our investigation started activating arylthianthrenium salt **1** with 5 % mol eosin Y (EY) as photocatalyst and couple it with CO (10 equiv.) and dimethyl maleate **2** (3 equiv.), in a solvent mixture CH_3CN /hexafluoroisopropanol (HFIP) in a ratio of 7:1 V/V and in presence of diisopropylethylamine (DIPEA, 5 equiv.) as stoichiometric reductant.⁷⁷ The reaction mixture was irradiated with a blue LED Kessil lamp (456 nm, 40 W input power) in a 3D-printed photochemical flow reactor (**UFlow**, 0.8 mm I.D., 4.5 mL).^{77,78} The results are summarized in **Table 5.3**.

Table 5.3: Selected optimization experiments for the carbonylative conjugate addition of aryl thianthrenium 1 and dimethyl maleate.



Entry ^a	t _R [min] ^b	PC (mol %)	Molar Ratio Aryl/Alkene	Solvent	Conv. 1 ^b (%)	Yield 4 ^b (%)
1	5	Eosin Y (5%)	1:3	CH ₃ CN/HFIP (7:1)	44	8
2	60	Eosin Y (5%)	1:3	CH ₃ CN/HFIP (7:1)	72	16
3	120	Eosin Y (5%)	1:3	CH ₃ CN/HFIP (7:1)	84	24
4	60	Eosin Y (5%)	3:1	CH ₃ CN/HFIP (7:1)	59	24
5	60	Rhodamine B (5%)	3:1	CH ₃ CN/HFIP (7:1)	43	20
6	60	Ru(bpy) ₃ (1%)	3:1	CH ₃ CN/HFIP (7:1)	91	28
7	60	Eosin Y (10%)	3:1	CH ₃ CN/HFIP (7:1)	84	31
8	60	Eosin Y (5%)	3:1	CH ₃ CN	72	14
9	60	Eosin Y (5%)	3:1	CH ₃ CN/H ₂ O (7:1)	89	13
10	60	Eosin Y (5%)	3:1	CH ₃ CN/CH ₃ OH (7:1)	80	21
11	60	Eosin Y (5%)	3:1	CH ₃ CN/DMSO (7:1)	85	11
12	60	Eosin Y (5%)	3:1	CH ₃ CN/HFIP (3:1)	49	29
13	60	Eosin Y (5%)	3:1	CH ₃ CN/HFIP (15:1)	81	21

^aReaction conditions: A stock solution was prepared with 0.2 mmol of **1a**, 0.6 mmol of **2a** (or vice versa), 5 % mol of eosin Y and 1 mmol of DIPEA dissolved in 4 mL of CH₃CN/HFIP 7:1 V/V. The solution was loop filled with CO gas (10 equiv.), pressurized and the gas-liquid slugs were pumped into the reactor. ^bYields were calculated by ¹H NMR in presence of an external standard (trichloroethylene, TCE).

After 5 minutes residence time, only 8 % qNMR yield was obtained, with a 44 % conversion of the arylthianthrenium starting material (Entry 1, **Table 5.3**). Extending the residence time to t = 1 h and t = 2 h gave an appreciable increase in yield, with formation of the desired product in 16 % and 24 % yield, respectively (Entries 2 and 3, **Table 5.3**). However, generally a low mass balance was observed. Reversing the reaction stoichiometry, with the alkene as the limiting reagent resulted in a slight increase in yield (30 %, Entry 4, **Table 5.3**). Next the ability of other photocatalysts to promote this transformation was tested (Entries 5-7, **Table 5.3**), with similar results obtained for Rhodamine B and for Ru(bpy)₃(PF₆)₂ as for Eosin Y and a slight increase in yield by increasing the amount of eosin Y to 10 % mol. Then, the solvent system was varied: removing HFIP as co-solvent, or replacing it by H₂O, CH₃OH or DMSO, did not improve the reaction outcome, and a moderate difference in yield was observed when changing the ratio of solvent/co-solvent from 7:1 to 3:1 or 15:1 (Entries 8-13, **Table 5.3**).

After an initial screening with dimethyl maleate as alkene coupling partner, we tested the radical carbonylative coupling of arylthianthrenium salts with vinyl ketones, to form 1,4-diketone products,

as this would ultimately allow us to prepare structurally diverse heterocycles through Paal-Knorr synthesis (**Figure 5.14**).^{79–81}

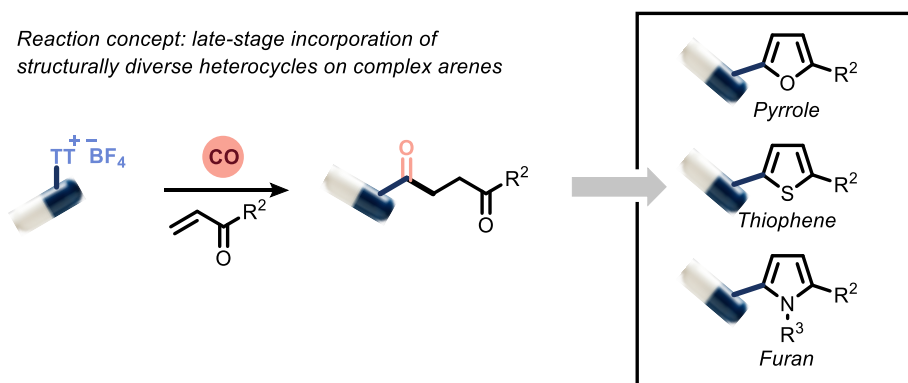


Figure 5.14: Direct access to complex heterocycles through carbonylation of drug-like arenes and conjugate addition with vinyl ketones.

The efficacy of our reaction conditions was evaluated with methyl vinyl ketone (**2b**), achieving a 50 % yield of the desired product based on ¹H NMR, along with 13 % of the conjugate addition product (Entry 1, **Table A15**, Appendix). Encouraged by these results, we sought to improve the yield, selectivity, and mass balance of this model reaction through a more elaborate screening process (details provided in **Table A15**, Appendix).

The majority of the screening experiments were conducted using Ru(bpy)₃(PF₆)₂ (1 % mol) as the photocatalyst, chosen for its comparable activity to eosin Y but superior reproducibility. Our strategy was to switch back to EY once optimal conditions were identified.

Despite the adjustments, only modest improvements were observed. Specifically, base concentration (3.5 equiv.), CO amount (30 equiv.) and reaction pressure (69 bar) were varied without significantly affecting conversions and yields. Additionally, substrate concentrations were varied between 0.025 and 0.1 M. The most significant improvement was observed when employing deuterated solvent (CD₃CN), resulting in a 58 % yield based on ¹H NMR (46 % isolated yield), as illustrated in **Figure 5.15**.

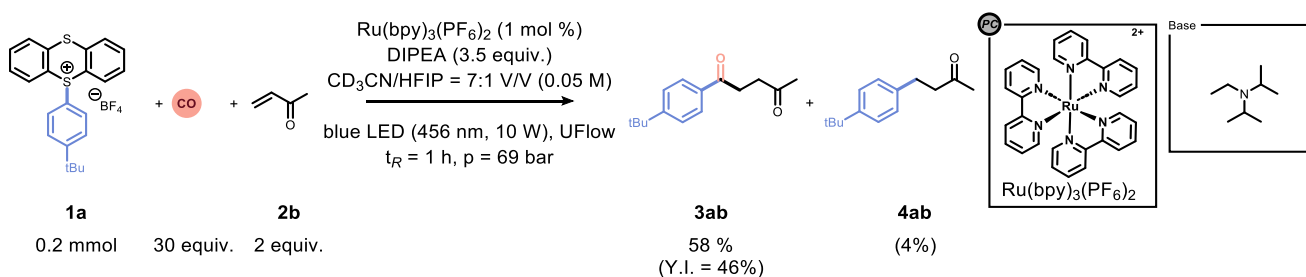


Figure 5.15: Best conditions for the aryl radical carbonylation of aryl thianthrenium **1** and methyl vinyl ketone **2b**.

Given the unsustainability cost of CD_3CN as a solvent, we explored the influence of other parameters, such as green light ($\lambda = 525 \text{ nm}$) instead of blue light ($\lambda = 456 \text{ nm}$), since EY exhibits two absorption peaks in the visible spectrum.⁸² Additionally, light intensity was varied between 10 and 40 W. Our findings indicated that switching to green light led to a decrease in conversion but an increase in selectivity (*cfr.* Entries 18-22, **Table A15**). Simultaneously, a preliminary substrate scope study was conducted under the reaction conditions shown in **Figure 5.16**.

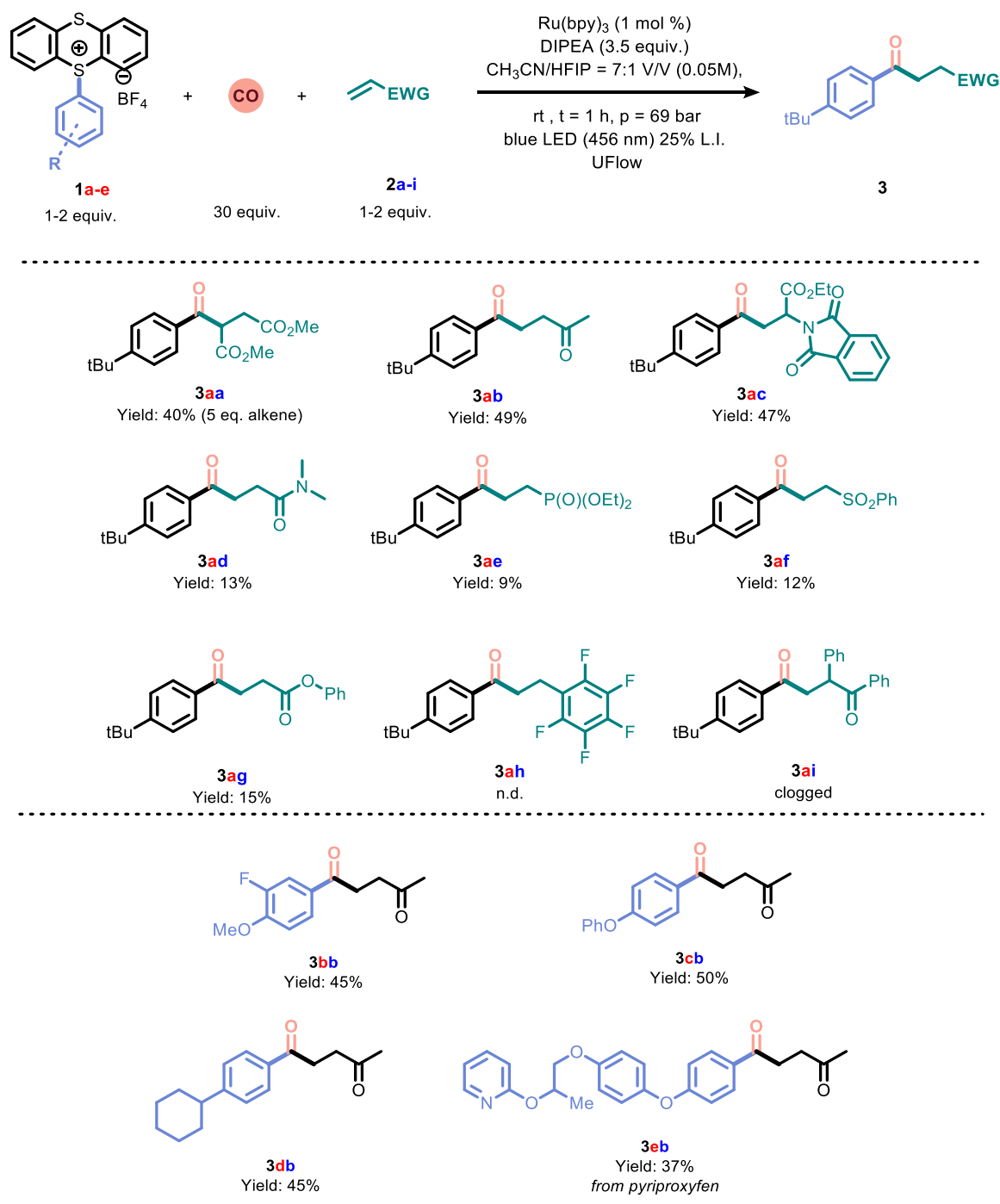


Figure 5.16: Reaction scope for the aryl radical carbonylation of aryl thianthrenium salts and conjugate addition with structurally diverse alkenes.

This study included testing various Michael acceptors (**2a-i**) and different types of arylthianthrenium salts (**1a-e**). Our observations suggest that the electrophilic character of the Michael acceptors significantly impacts the reaction's progress. Reaction with more electrophilic alkenes results in poor mass balance (such as **2a**, requiring overstoichiometric quantities to improve the yields), while reaction with less electrophilic alkenes (*e.g.* **2b**) led to selectivity issues due to partial direct coupling with the aryl radical. Conversely, the type of arylthianthrenium salt had a less pronounced effect on the reaction yield, with observed yields ranging from 37 to 50 %.

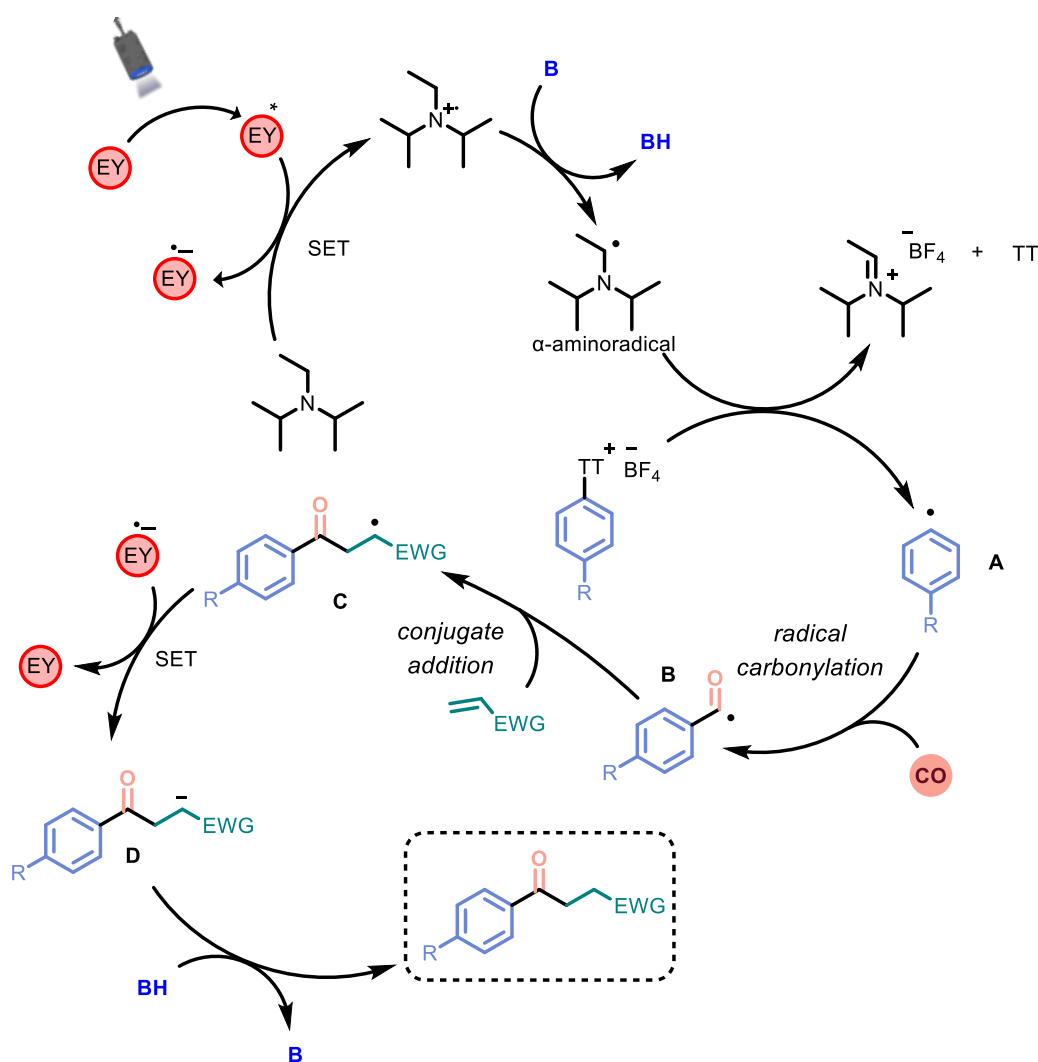


Figure 5.17: Proposed mechanism for the photocatalytic aryl radical carbonylation with thianthrenium salts.

Under visible light irradiation EY was promoted to its excited state (EY^*), which underwent reductive quenching in presence of the sacrificial reductant DIPEA, generating a DIPEA radical cation ($\text{DIPEA}^{\bullet+}$). $\text{DIPEA}^{\bullet+}$ subsequently underwent deprotonation at its secondary α -carbon (mediated by another DIPEA molecule), resulting in the formation of an α -amino radical.⁸³ This latter specie was then capable of activating arylthianthrenium salts, leading to the formation of the corresponding aryl radical (A). The aryl radical (A) rapidly reacted with carbon monoxide (CO) generating a benzoyl radical (B), which subsequently attacked an electron-deficient alkene to form a coupled radical intermediate

(C). The intermediate (C) reacted, through a second single-electron transfer (SET), with the reduced form of $EY^{\bullet-}$, yielding a secondary carbanion (D). The carbanion (D) was rapidly protonated to produce the desired carbonyl product, completing the catalytic cycle. To confirm the proposed reaction mechanism, radical trapping experiments were conducted using **TEMPO** as a radical trap. However, these experiments did not provide additional information about the reaction intermediates, leaving certain mechanistic aspects unverified.

5.2.5 Conclusion

We have reported some preliminary results on a novel methodology for the radical carbonylation of aryl thianthrenium salts through photocatalytic activation in flow. At the time of writing, the procedure is under development, giving appreciable yields of up to 58 % qNMR yield for a model reaction with methyl vinyl ketone as electrophilic trap. We are particularly excited about the prospect of a direct method to generate 1,4-diketones from highly complex arenes and vinyl ketones, to subsequently form structurally diverse furans, pyrroles and thiophenes through Paal-Knorr synthesis.

5.2.6 Experimental

Materials.

All reagents and solvents were used as received without further purification. Reagents and solvents were bought from Sigma Aldrich, TCI and Fluorochem. Technical solvents were bought from VWR International and used as received. Carbon monoxide gas (4.8purity) was purchased from Nippon gases, ^{13}C gas (99.3% purity) was purchased from Eurisotop. Disposable syringes were purchased from Laboratory Glass Specialist. Syringe pumps were purchased from Chemix Inc. model Fusion 200 Touch. All capillary tubing, microfluidic fittings and Back Pressure Regulator (BPR) were purchased from IDEX Health & Science. Product isolation was performed automatically, by a Biotage® Isolation Four, with Biotage® SNAP KP-Sil 4 or 10 g flash chromatography cartridges, or manually, using silica (P60, SILICYCLE). TLC analysis was performed using Silica on aluminum foils TLC plates (F254, SILICYCLE) with visualization under ultraviolet light (254 nm and 365 nm) or appropriate TLC staining (potassium permanganate). Organic solutions were concentrated under reduced pressure with a Büchi rotary evaporator (in vacuo at $T = 40\text{ }^{\circ}\text{C}$, $p = 5\text{ mbar}$).

NMR spectroscopy.

^1H (400 and 300 MHz), ^{13}C (101 and 128 MHz), ^{19}F (282 and 376 MHz) and ^{31}P (121 and 162 MHz) spectra were recorded at ambient temperature using Bruker AV 300-I, AV 400 and AV 500-NEO. ^1H NMR spectra are reported in parts per million (ppm) downfield relative to CDCl_3 (7.26 ppm) and all ^{13}C NMR spectra are reported in ppm relative to CDCl_3 (77.16 ppm) unless stated otherwise. The multiplicities of signals are designated by the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), sext (sextet), m (multiplet), dd (doublet of doublets), dt (doublet of triplets), td (triplet of doublets), ddd (doublet of doublet of doublets). Coupling constants (J) are reported in hertz (Hz). NMR data was processed using the MestReNova 14 software package. Known products were characterized by comparing to the corresponding ^1H NMR, ^{13}C NMR, ^{19}F NMR and ^{31}P NMR with those available in the literature.

Mass spectrometry. High resolution mass spectra (HRMS) were collected on an AccuTOF GC v 4g, JMS-T100GCV Mass spectrometer (JEOL, Japan).

General procedure for aryl radical carbonylation:

0.2 mmol of the selected thiantrenium salt is placed in a screw-cap 10 mL vial, which is equipped with a rubber septum. Alongside this, 1-3 equivalents of the alkene substrate (0.2 - 0.6 mmol) and 5 % mol of Eosin Y (or another chosen catalyst) are added. The vial is then sealed and purged with nitrogen to create an inert atmosphere. Next, 5 equiv. of DIPEA and 4 mL of a dry solution of CH_3CN and HFIP in a 7:1 volume ratio are introduced into the vial. The stock solution (0.05 M) is prepared and loaded into a gastight syringe, which is then positioned in a syringe pump. This setup allows for the controlled addition of the stock solution while introducing CO gas in quantities ranging from 10 to 30 equivalents through a T-mixer. The first filling loop is then filled under a back pressure regulator (BPR) set at 5.2 bar. Subsequently, this filling loop is connected between an HPLC pump and the reactor system (UFlow), and the system is pressurized to a range of 30 to 70 bar to prepare

for the reaction. The reaction mixture is then pumped through a UFlow reactor, which operates at 465 nm with an output power of 40 W. The reactor features a FEP capillary with an inner diameter between 0.5 and 0.1 mm, and a volume of *ca.* 4 mL. The flow rate is adjusted to ensure that the residence time within the reactor is approximately 1 h. Once the reaction is complete, the solvent from the resulting mixture is removed under reduced pressure. To facilitate analysis, an internal standard (20% mol of trichloroethylene, TCE) is added. The final product is then analyzed using ^1H NMR, or alternatively, purified by flash column chromatography on silica gel to yield the desired products in the specified yields.

5.3 Bibliography Chapter 5

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6. Summary and General Conclusions

This PhD thesis showcases some examples of both (I) chemical valorization of renewable-based starting materials and (II) sustainable synthetic approaches, relying on energy efficient and environmentally benign processes. These two main topics were developed aiming at combining green technologies for the development of sustainable protocols for chemical upgrading of CO₂ and process intensification through photochemistry and/or continuous flow techniques. In particular, **Chapter 3** and **Chapter 4** focused on the chemical valorization of carbon dioxide (CO₂), while **Chapter 4** and **Chapter 5** describe light-assisted synthetic approaches for the preparation of functional (bio)active molecules and materials.

More in detail, **Chapter 3** describes different organo- and metal-base catalytic systems employed for non-reductive CO₂ valorization. In **Section 3.1** a series of dihydroxybenzene derived ILs organocatalysts were prepared following an effective, eco-friendly, halide-free synthetic methodology. In addition to displaying as single component catalysts for monosubstituted COCs. Preliminary data displays unusual catalytic activity on internal cyclic epoxide as cyclohexene oxide (CHO), although with limited selectivity, due to the tendency of CHO of evolving into both the COC and polycarbonate product. For these systems, $p^0(\text{CO}_2) \geq 10$ bar is required to observe appreciable selectivity towards the desired COC product ascribed to the *in-situ* formation of the catalytically competent hemicarbonate derivative. In **Section 3.2** a series of bio-based furanics derived from sugars (*e.g.* BDMF, BHTHF, and OBMF-H) were tested for the first time as active HBD component for CO₂ fixation into epoxides in combination with cheap and abundant alkali metal salts. BHTHF/NaBr system promoting the synthesis of industrially relevant COCs under mild pressure conditions ($p^0(\text{CO}_2) = 1\text{-}10$ bar). **Section 3.3** and **Section 3.4** focus on the development of tandem oxidative carbonation one-pot processes. A set of novel molybdate ILs (Mo-ILs) were synthesized through a halide-free synthetic route. Firstly, these new compounds proved to be viable catalysts for CO₂ fixation into epoxides; in particular, [N_{4,4,4,4}]₂[MoO₄] showed excellent activity at $p^0(\text{CO}_2) = 30$ bar and T = 120 °C, providing the first example of Mo-ILs active towards cycloaddition of CO₂ to epoxides without the use of an halide co-catalysts. Furthermore, in **Section 3.4**, [N_{8,8,8,1}]₂[MoO₄] was selected as phase transfer catalyst (PTC) in combination with H₂O₂ as green oxidant, to carry out the epoxidation reactions within a biphasic H₂O/alkene system without the need for additional solvents. Thanks to the previous knowledge acquired on **Section 3.3**, two different methodologies to synthesize the corresponding COCs derivatives have been designed. This included a one-pot, three-step AsTC methodology involving a transcarnation reaction with DMC for 1-decene, and a one-pot, two-step AsTC process involving CO₂ insertion for methyl oleate.

Photothermal reduction of CO₂ is described in **Chapter 4** and includes applications of photogenerated CO to synthetically relevant and more sustainable carbonylation reactions. The novel platform's versatility enables the evaluation of catalysts under tightly controlled reaction parameters for a standardized system to measure and compare catalysts in both thermal and light-assisted heterogeneous-catalyzed gas conversion processes. Direct utilization of the produced CO

was demonstrated on various carbonylation reactions protocols to produce functionalized fine chemicals and/or fine chemicals precursors using CO generated on-demand.

Finally, **Chapter 5** describes two novel light-mediated processes: Atom Transfer Radical Polymerization (ATRP) of methacrylates, employing renewable based CDs as photocatalysts and the preliminary findings on the development of a new methodology for aryl radical carbonylations using photo-redox catalysis in continuous flow. In particular, **Section 5.1** describes a greener approach towards light-mediated polymerization using inexpensive and readily available CDs as photocatalysts under both ultraviolet ($\lambda = 365$ nm) and visible light. Various solvent systems were evaluated and a Cu(II) complex was used as co-catalyst. Under the optimized conditions, the resulting methacrylate polymer was obtained in 89% conversion and with a narrow polydispersity of $\bar{D} = 1.4$. **Section 5.2** describes the preliminary results obtained for the development of a new methodology for aryl radical carbonylations using photo-redox catalysis in continuous flow is reported. The use of a CF methodology allows us to carry out two-phase liquid-gas reactions using milder reaction conditions and safer compared to traditional batch methodologies for this reactivity.

This PhD thesis aims to provide valuable insights and actionable steps for valorizing CO₂ and biobased materials through a range of green and sustainable methodologies. Even though the green protocols described in this work are characterized by promising features, their sustainability must be further and quantitatively evaluated considering the production costs, availability of renewable-based materials, scalability and safety and toxicology issues. Nevertheless, this work provides significant insights on novel catalytic approaches applied to CO₂ valorization, potentially leading to more sustainable processes from both economic and environmental perspectives. We hope that combining these green solutions with the principles of the circular economy will ultimately replace current hazardous, energy-intensive, and environmentally harmful practices.

7. Appendix

Appendix Chapter 3

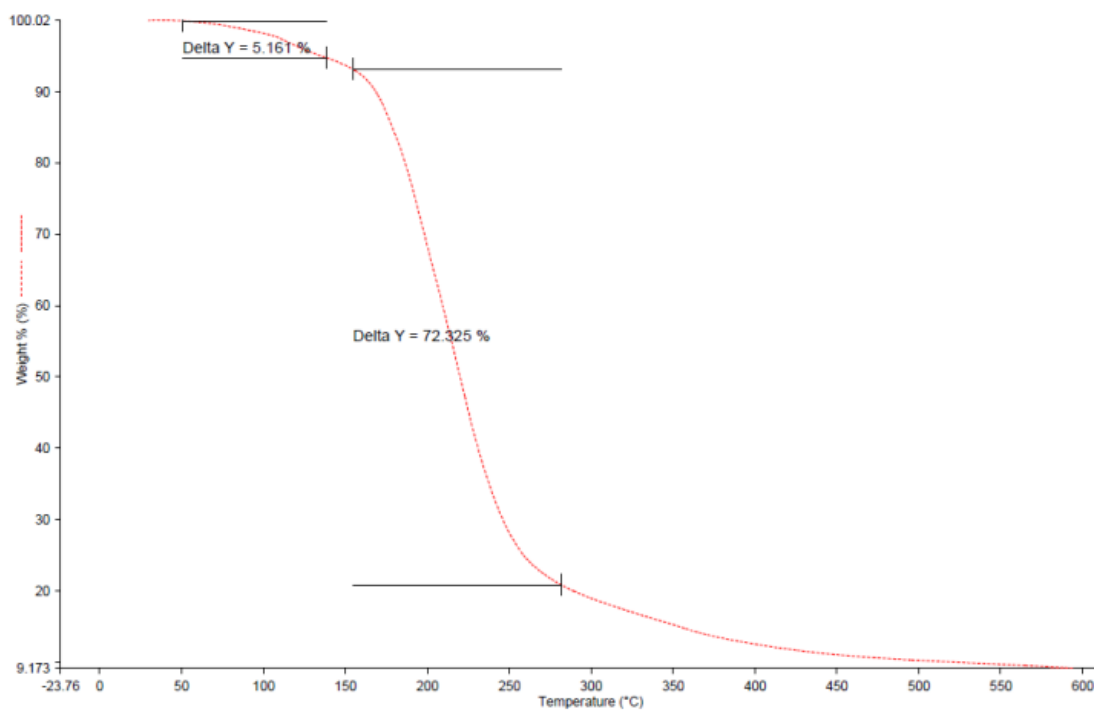


Figure A 1: TGA analysis of $[N_{8,8,8,1}][HYD]$.

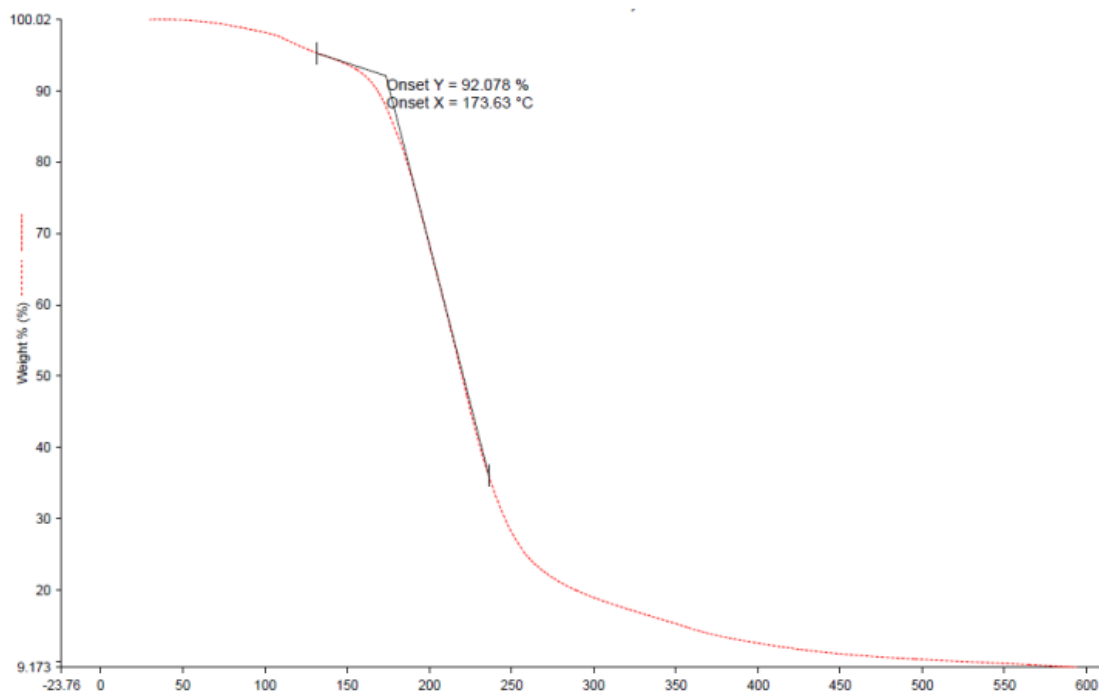


Figure A 2: T_{onset} determination for $[N_{8,8,8,1}][HYD]$.

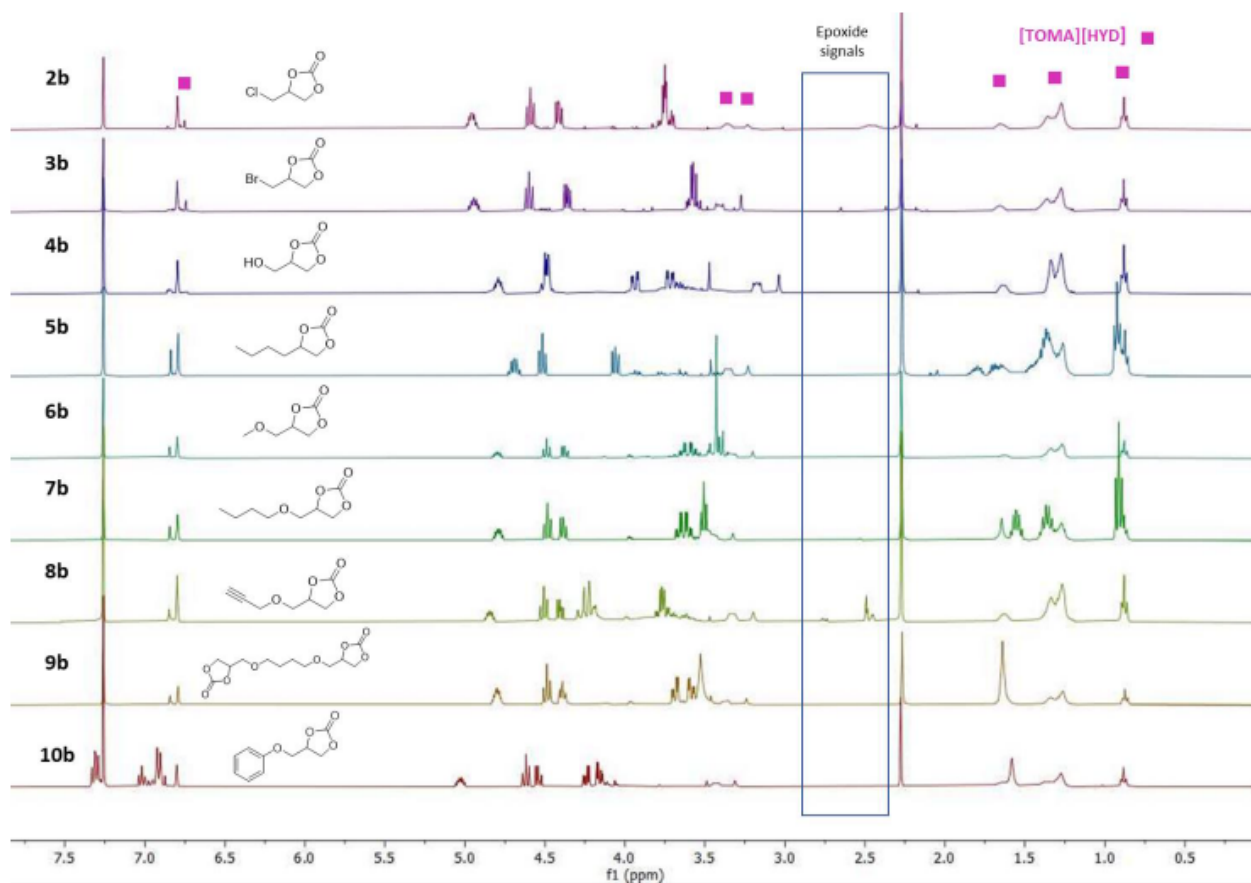


Figure A 3: ^1H NMR (400 MHz, CDCl_3) of the crude CO_2 insertion reaction mixtures with the corresponding COC products: a) 4-chloromethyl-1,3-dioxolan-2-one (**2b**);¹ b) 4-bromomethyl-1,3-dioxolan-2-one (**3b**);² c) 4-hydroxymethyl-1,3-dioxolan-2-one (**4b**);³ d) 4-butyl-1,3-dioxolan-2-one (**5b**);⁴ e) 4-methoxymethyl-1,3-dioxolan-2-one (**6b**); f) 4-(butoxymethyl)-1,3-dioxolan-2-one (**7b**);⁴ g) 4-((prop-2-yn-1-yloxy)methyl)-1,3-dioxolan-2-one (**8b**);⁵ h) 4,4'-[(butane-1,4-diylbis(oxy))bis(methylene)bis(1,3-dioxolan-2-one) (**9b**);³ i) 4-(phenoxy)methyl-1,3-dioxolane-2-one (**10b**).¹

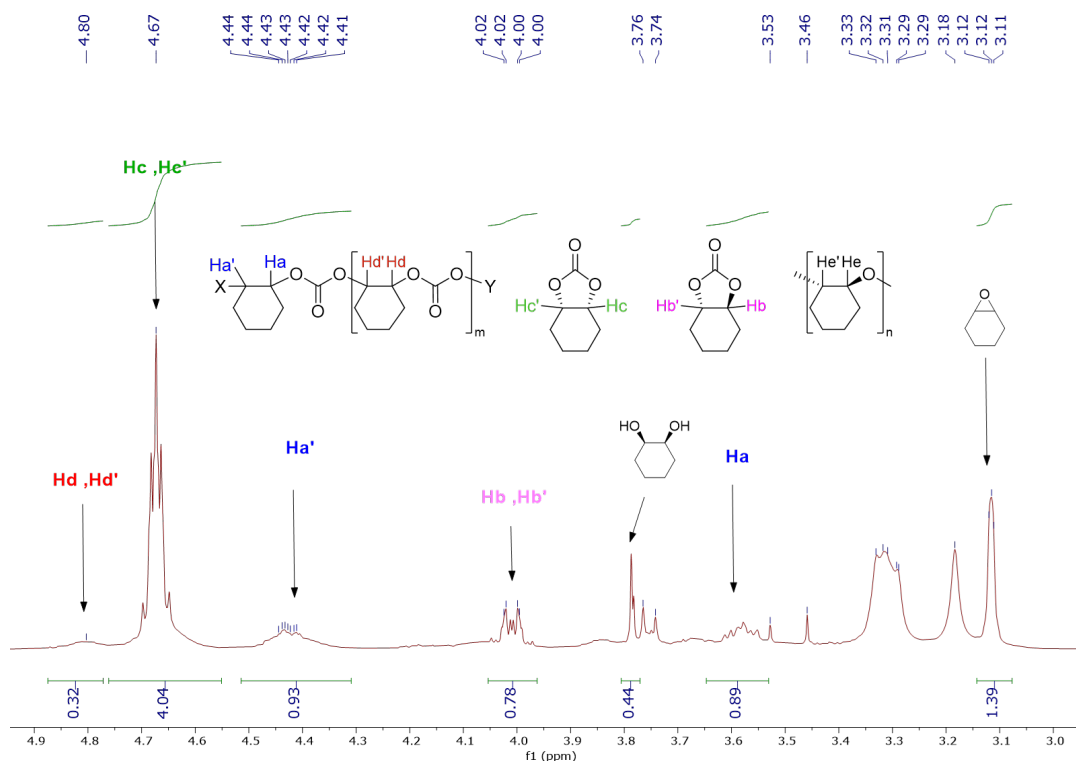


Figure A 4: ^1H NMR (400 MHz, CDCl_3) analysis of the crude reaction mixture obtained upon CO_2 insertion with cyclohexene oxide (CHO, **11a**). Reaction conditions: CHO (4.00 mmol), $[\text{N}_{8,8,8,1}][\text{HYD}]$ (10 % mol; 0.4 mmol), mesitylene (20 % mol; 0.80 mmol), $T = 120^\circ\text{C}$, $p^0(\text{CO}_2) = 20$ bar, $t = 6$ h, solventless conditions.⁷ Presence of polyethers between 3.35–3.25 ppm.

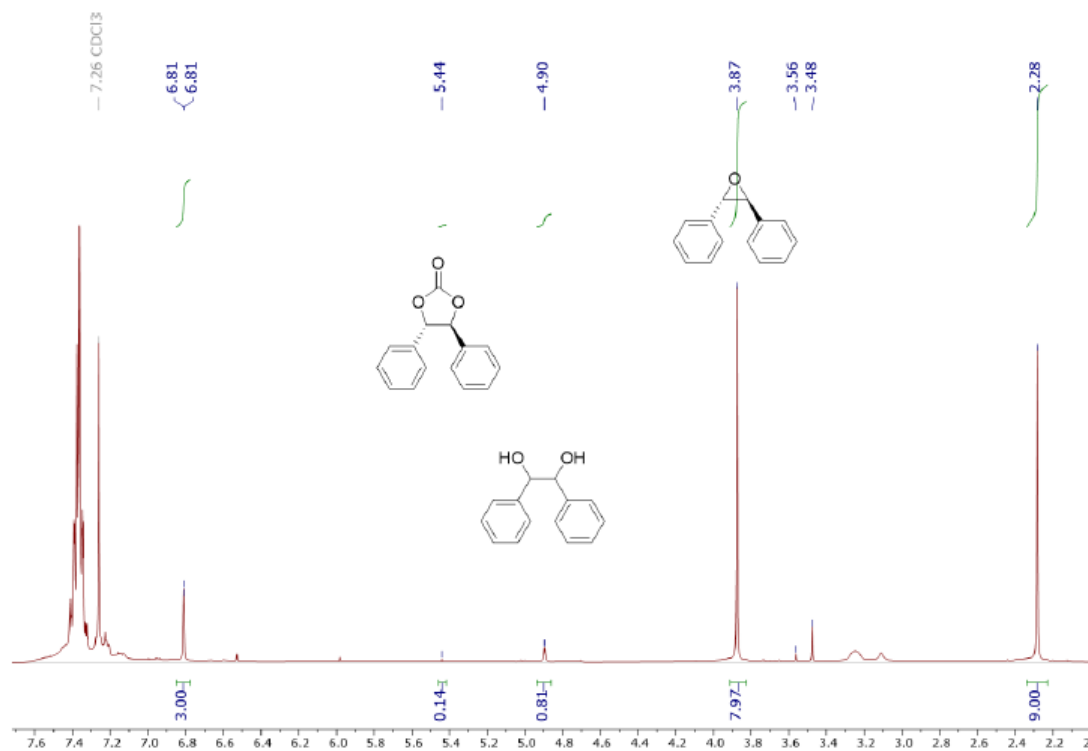


Figure A 5: ^1H NMR (400 MHz, CDCl_3) analysis of the crude reaction mixture obtained upon CO_2 insertion with trans-stilbene (**12a**). Reaction conditions: trans-stilbene (4.00 mmol), $[\text{N}_{8,8,8,1}][\text{HYD}]$ (10 % mol, 0.4 mmol), mesitylene (20 % mol, 0.80 mmol), $T = 120^\circ\text{C}$, $p^0(\text{CO}_2) = 2.0$ MPa, $t = 6$ h, solventless conditions.

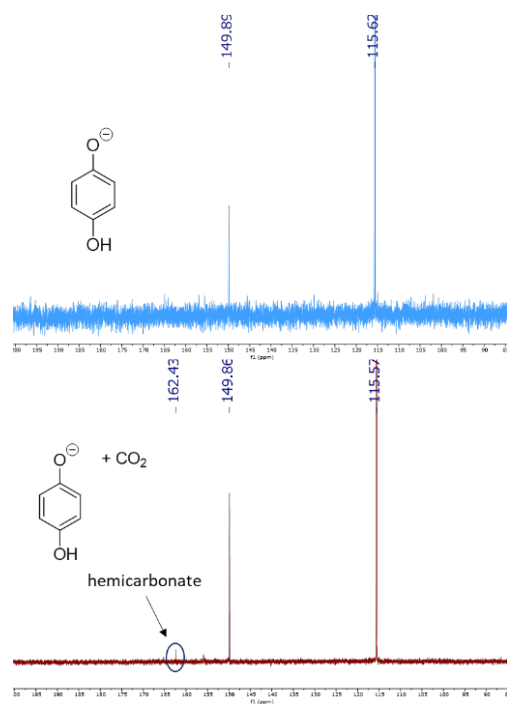


Figure A 6: ^{13}C NMR of $[\text{N}_{8,8,8,1}][\text{HYD}]$ before CO_2 (blue) and after CO_2 treatment (red) which shows a new peak around 162 ppm after CO_2 absorption at 1 bar and room temperature.

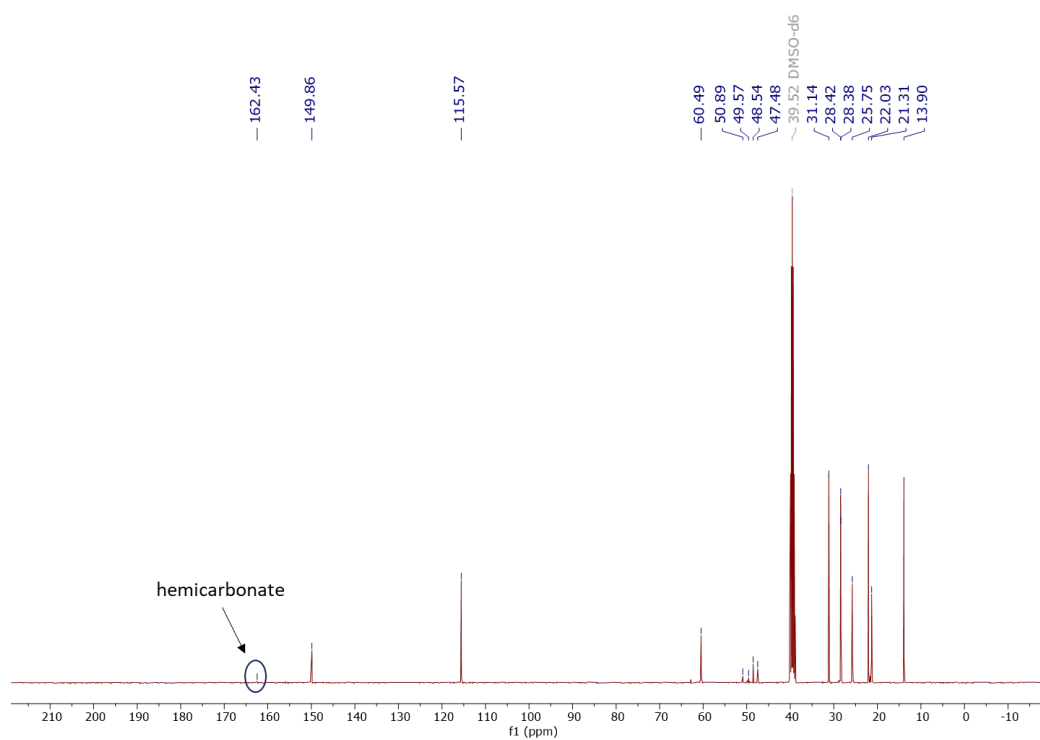


Figure A 7: ^{13}C NMR of $[\text{N}_{8,8,8,1}][\text{HYD}]$ after CO_2 treatment.

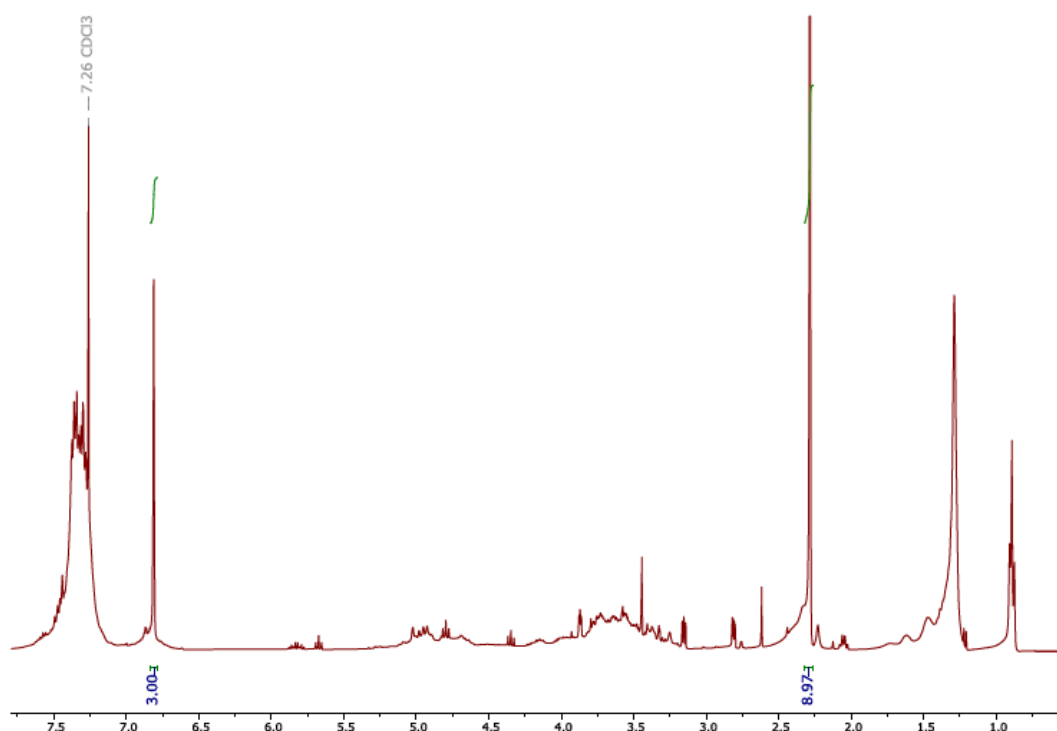


Figure A 8: ^1H NMR (400 MHz, CDCl_3) analysis of the crude reaction mixture obtained upon reacting **1a** with $[\text{N}_{8,8,8,1}][\text{HYD}]$ (10 % mol; 0.4 mmol), mesitylene (20 % mol; 0.80 mmol), $T = 120^\circ\text{C}$, $t = 6$ h, solventless conditions in absence of CO_2 , evidencing quantitative **1a** conversion and formation of polyethers and diol ring opening product.⁷

Table A 1: Substrate scope using **6a**, **7a** and **8a** at $p^0(\text{CO}_2) = 1$ bar.

$ \begin{array}{ccc} \text{R}_1 \text{---} \text{C}_2\text{H}_4 \text{---} \text{C}_1\text{H}_2 \text{---} \text{O} & \xrightarrow[\text{T} = 120^\circ\text{C}, \text{t} = 6 \text{ h}]{\text{NaBr/BHTHF (0.2 mmol / 1.2 mmol), } p^0(\text{CO}_2) = 1 \text{ bar}} & \text{R}_1 \text{---} \text{C}_2\text{H}_4 \text{---} \text{C}_1\text{H}_2 \text{---} \text{O} \text{---} \text{C}(=\text{O}) \text{---} \text{O} \text{---} \text{C}_1\text{H}_2 \text{---} \text{C}_2\text{H}_4 \text{---} \text{O} \\ \text{1-12a} & & \text{1-12b} \end{array} $				
Entry	Epoxide	Conv. (%) ^a	Sel. (%) ^a	Yield (%) ^a
1	 6a	76	77	59
2	 7a	68	75	51
3	 8a	78	67	52

Reaction conditions: **6a–8a** (4.00 mmol), $t = 6$ h, $T = 120$ °C, $p^0(\text{CO}_2) = 1$ bar, epoxide, NaBr/BHTHF = 1: 6 mol/mol, [NaBr] = 0.05 mmol, [BHTHF] = 0.30 mmol. Conversions, yields and selectivity were determined by quantitative ^1H -NMR analysis with an internal standard (mesitylene, 0.2 equiv.).

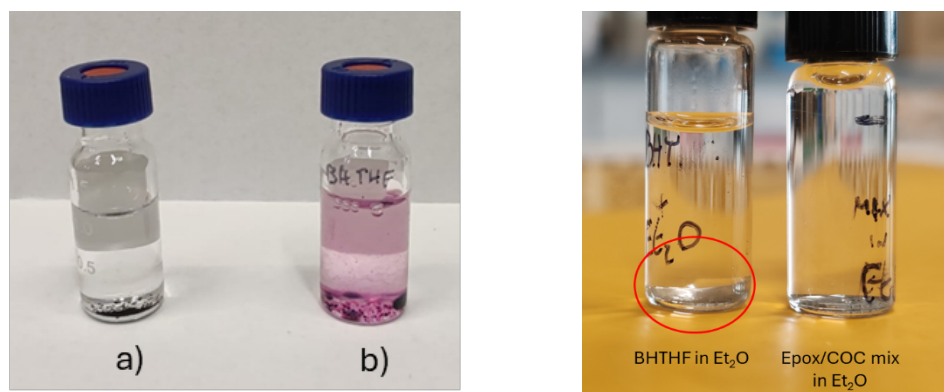


Figure A 9: Left: a) KMnO_4 in toluene, b) KMnO_4 in toluene and BHTHF; right: phase separation between BHTHF and Et_2O (left, red circle) compared to an homogeneous solution of 1,2-epoxyhexane and 4-butyl-1,3-dioxolan-2-one in Et_2O .

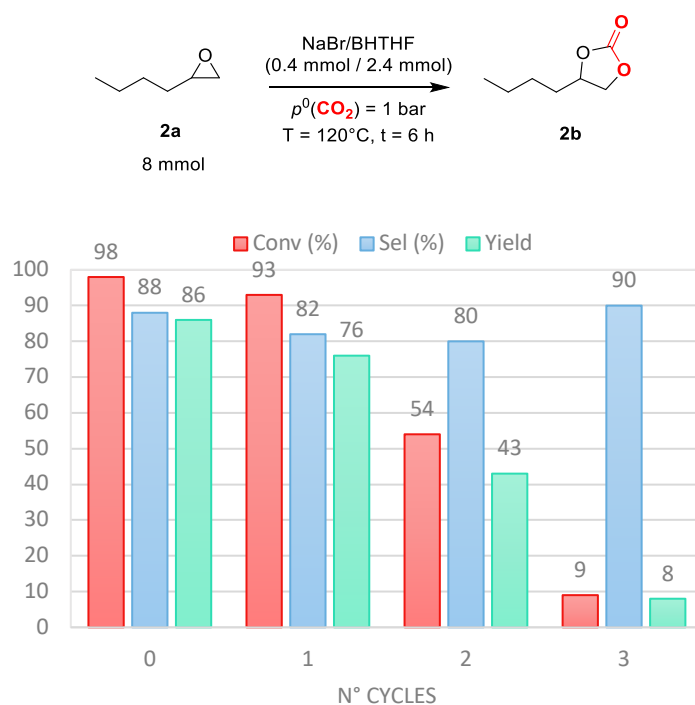


Figure A 10: Catalytic system recycles by extraction with Et_2O . Conditions: **2a** (8.00 mmol), NaBr/BHTHF = 1:6 mol/mol, [NaBr] = 0.40 mmol, [BHTHF] = 2.40 mmol, $t = 6$ h, $T = 120$ °C and $p^0(\text{CO}_2) = 1$ bar. Conversion, yield and selectivity were determined by quantitative ^1H NMR in presence of mesitylene as internal standard.

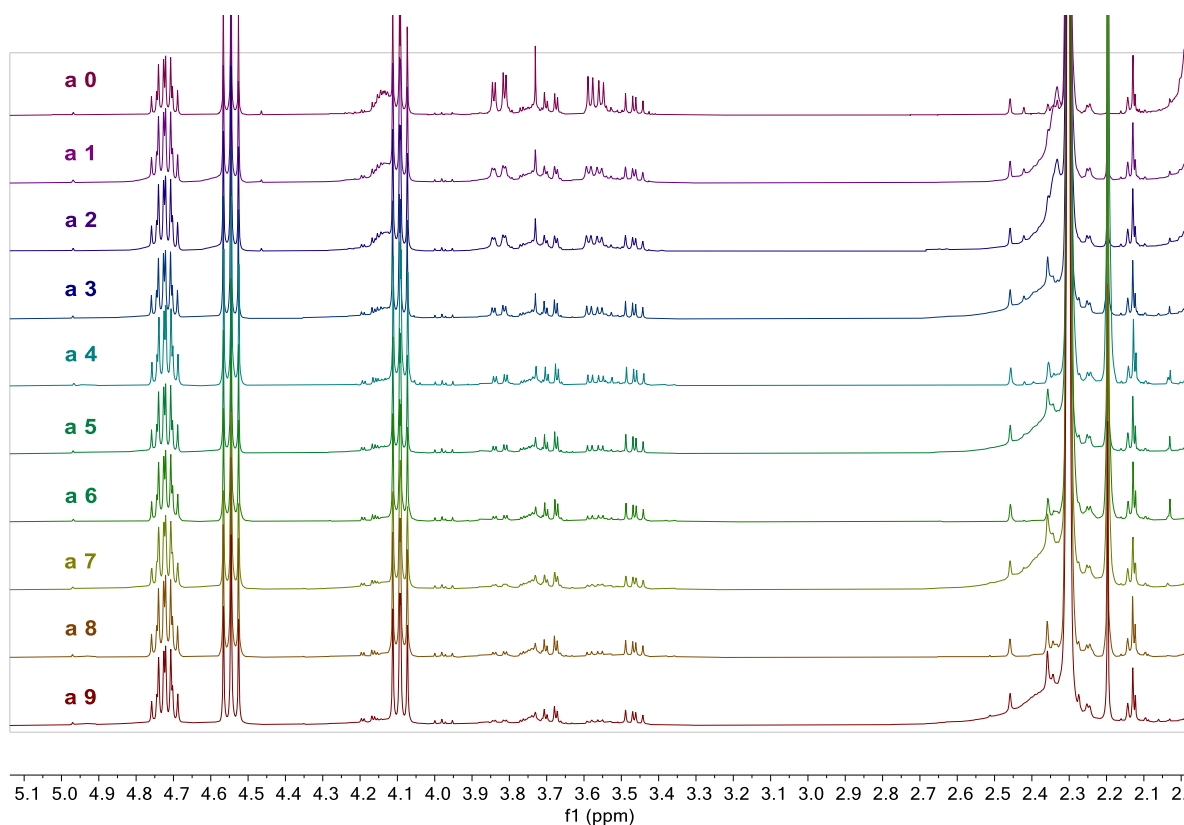


Figure A 11: ^1H NMR (400 MHz, CDCl_3) of the CO_2 insertion reaction mixtures with **2a** after all the repeated additions. Interestingly, in the region between 2.6-3.3ppm there are no resonance signals, indicating complete conversion of epoxide **2a** in each consecutive run.

Table A 2: ICP data analysis collection.

Compound	MW (g/mol)	(mg) weighed	Mo theoretical contribution (mg/g)	Mo detected (mg/g)	recovery (%)	RSD (%)
$[\text{N}_{4444}]_2[\text{MoO}_4]$	644	6.90	206	158	77	1.7
$[\text{N}_{4444}]_2[\text{Mo}_2\text{O}_7]$	788	10.35	252	246	97	1.0
$[\text{N}_{4444}]_2[\text{Mo}_6\text{O}_{19}]$	1364	10.36	437	417	95	0.1
$[\text{N}_{4444}]_4[\text{Mo}_8\text{O}_{26}]$	2153	10.71	382	352	92	0.9

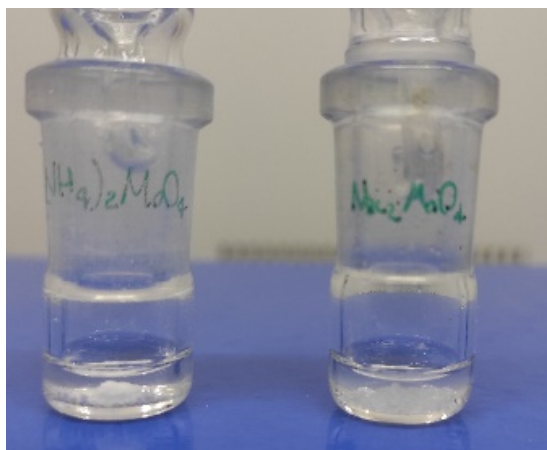


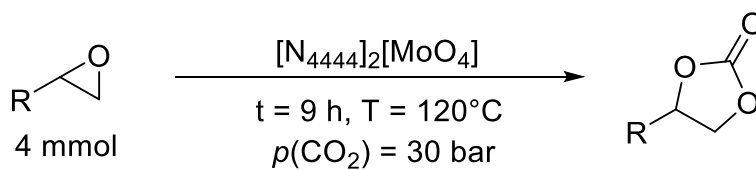
Figure A 12: Pictures of crude reaction mixtures with insoluble catalysts: left, catalyst: $(\text{NH}_4)_2\text{MoO}_4$ (Entry 5, Table 3.1); right: Na_2MoO_4 (Entry 6, Table 3.1).

Table A 3: Control experiments of the catalyst precursors.

Entry	Catalytic System	Conversion (%) ^a	Selectivity (%) ^a	Yield (%) ^a
1	H_2MoO_4	0	n.d.	n.d.
2	$[\text{N}_{4444}][\text{OH}]$	84	75	63
3	$[\text{P}_{4444}][\text{OH}]$	24	39	9
4	$[\text{N}_{1888}][\text{CH}_3\text{OCOO}]$	78	80	62
5	$[\text{C}_4\text{C}_{1\text{im}}][\text{CH}_3\text{OCOO}]$	67	68	46
6	DBU	10	14	1

Reaction conditions: 1,2-epoxyhexane (4.0 mmol), $p^0(\text{CO}_2) = 30$ bar, $T = 120$ °C, $t = 9$ h, solventless.^aConversion, selectivity and yield determined by ^1H NMR.

Table A 4: Catalyst loading experiments



Entry	Loading (mol %)	Conversion (%) ^a	Selectivity (%) ^a	Yield (%) ^a
1	0.25	53	73	39
2	1.25	92	89	82
3	2.50	100	86	86
4	5.00	100	84	84

Reaction conditions: 1,2-epoxyhexane (4 mmol), $p^0(\text{CO}_2) = 30 \text{ bar}$, $T = 120^\circ\text{C}$, $t = 9 \text{ h}$, solventless.

^aConversion, selectivity and yield determined by ^1H NMR.

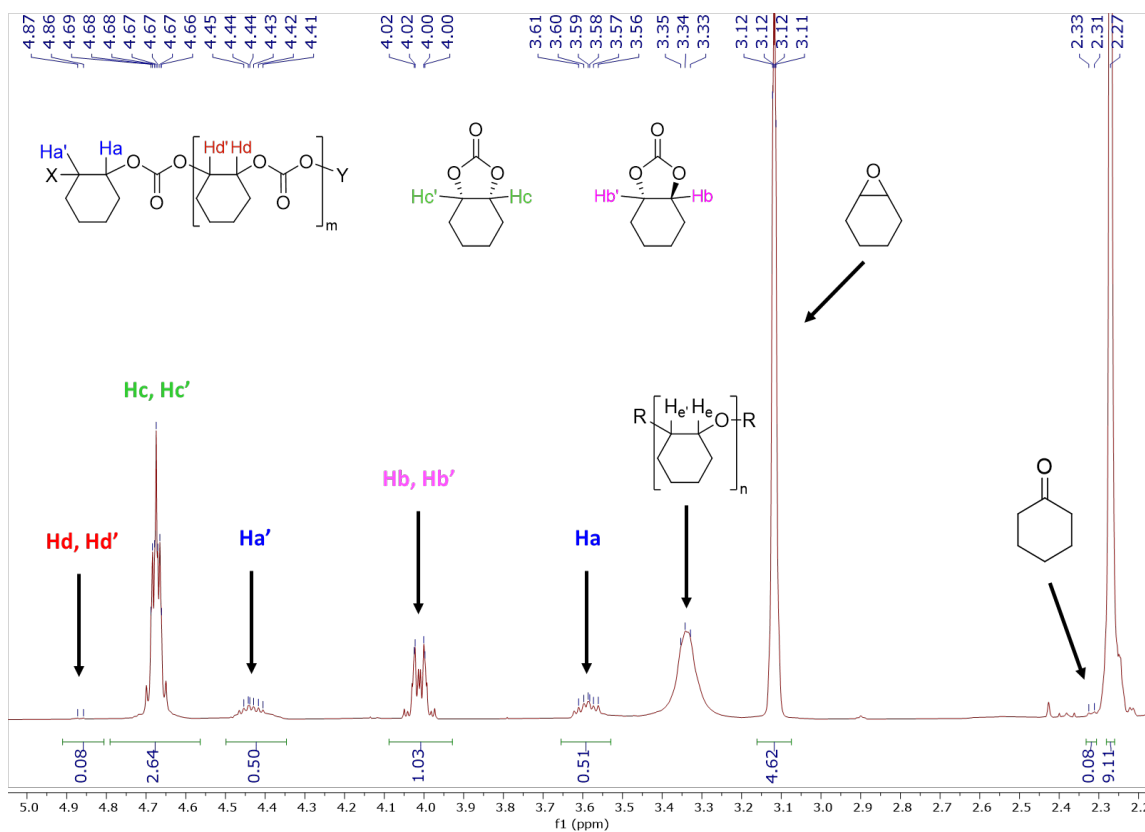


Figure A 13: ^1H NMR spectrum of the crude reaction mixture of CO_2 fixation into cyclohexene oxide (Figure 3.8).

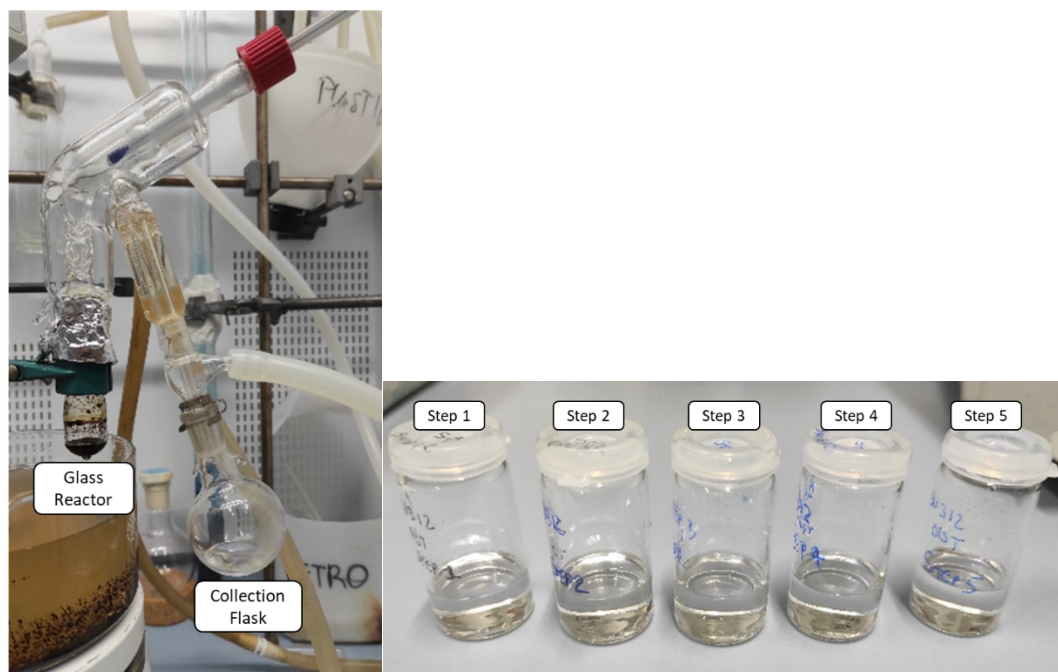


Figure A 14: Catalyst recycle: short path distillation setup for catalytic recycles (left); product mixtures obtained after each recycle (right).

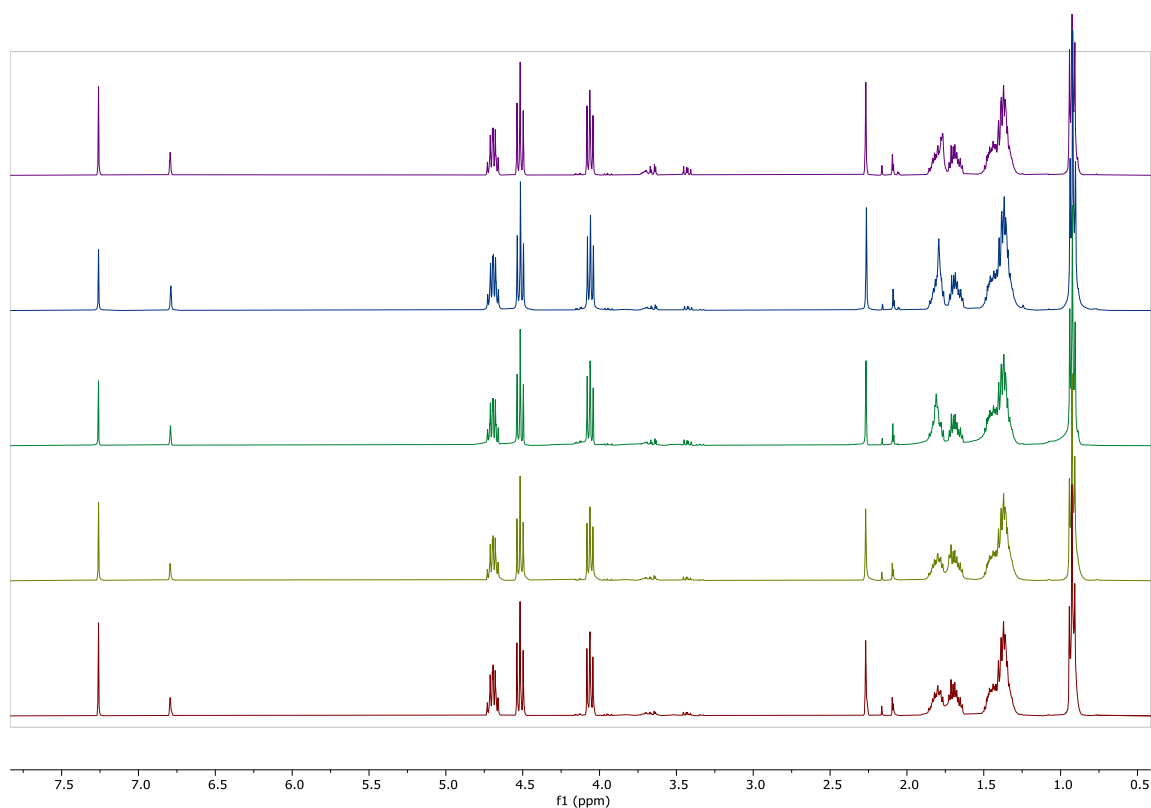


Figure A 15: ^1H NMR spectra of the COC products obtained from the recycle runs from the first (top) to the fifth (bottom) recycle.

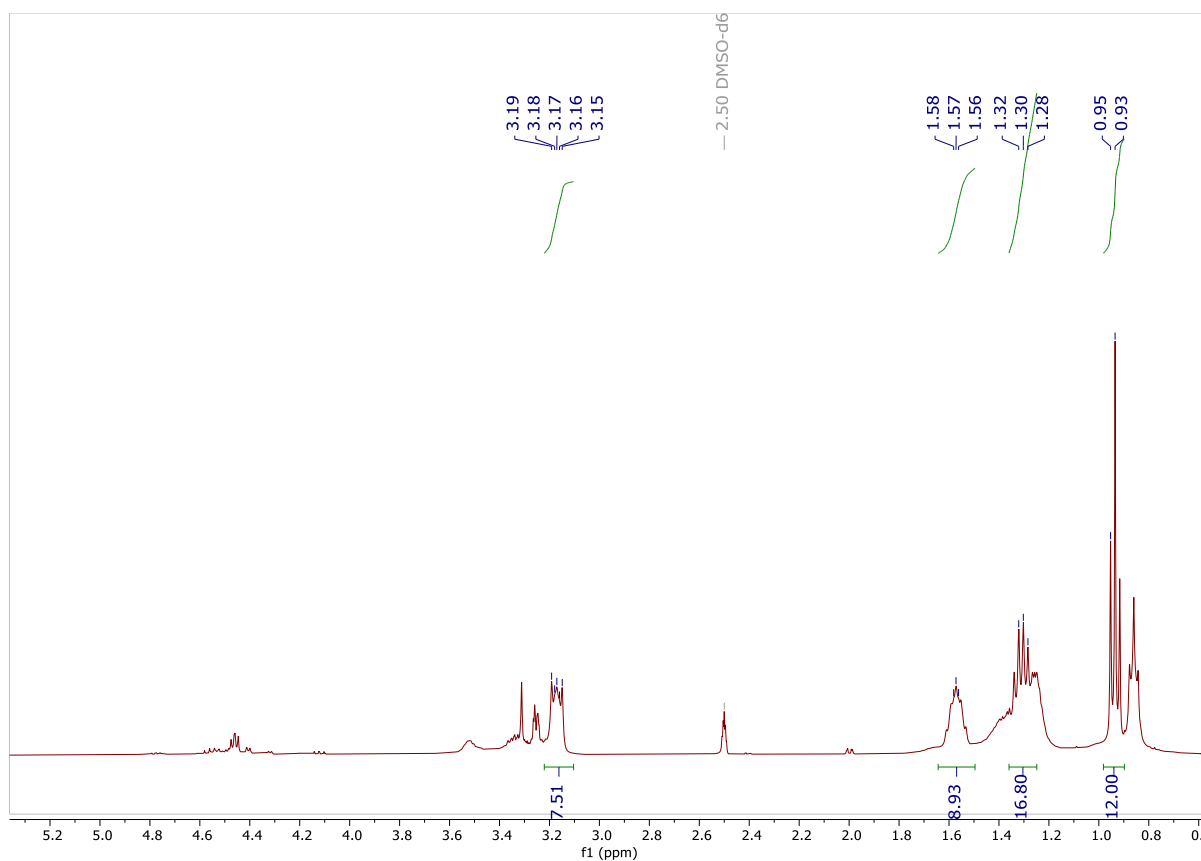


Figure A 16: ¹H NMR (400 MHz, DMSO-d₆) of the catalyst after the fifth recycle run.

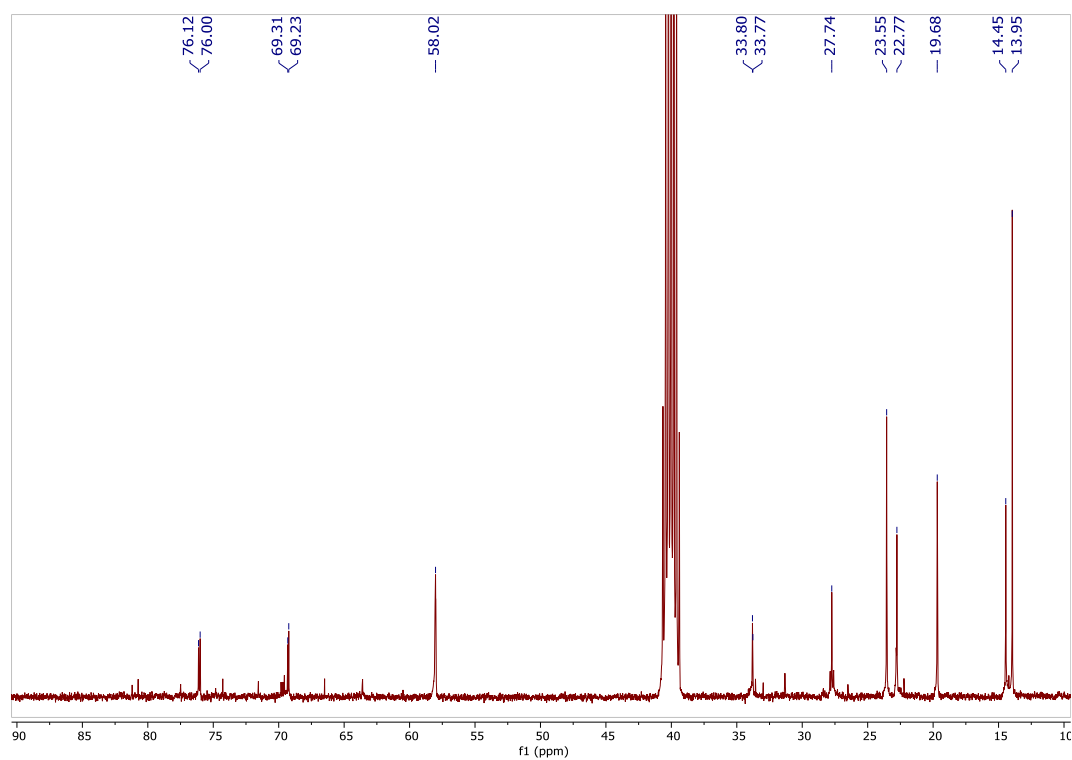


Figure A 17: ¹³C NMR (101 MHz, DMSO-d₆) of the catalyst after the fifth recycle run.

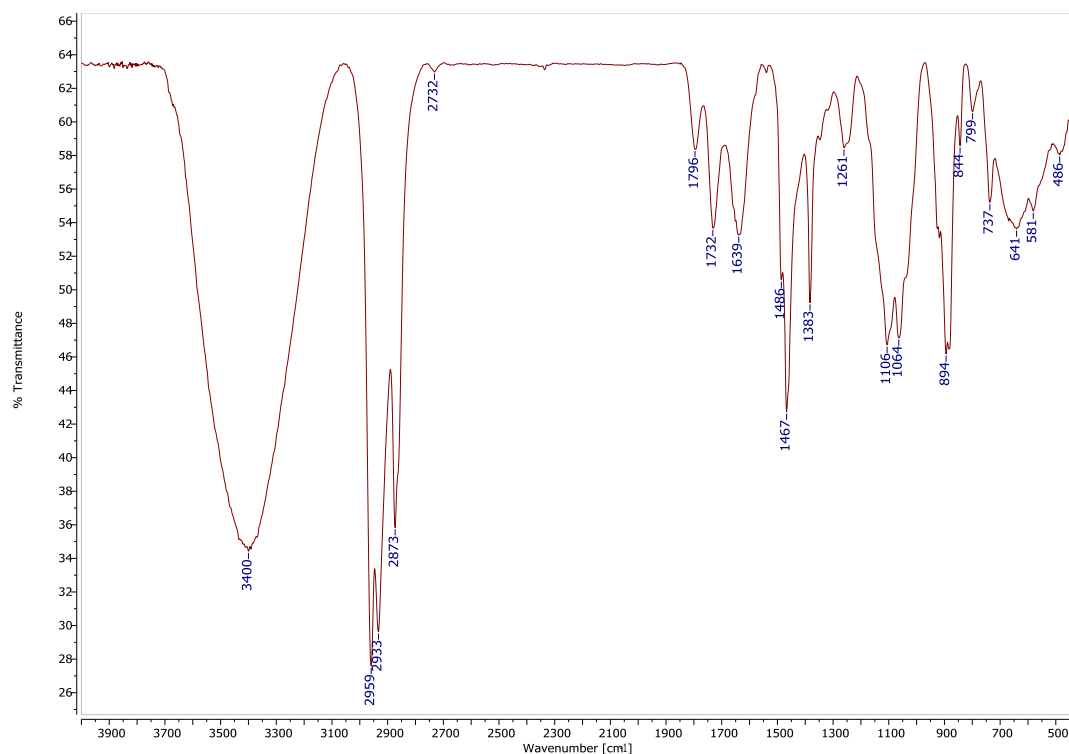


Figure A 18 FT-IR spectrum of the catalyst after the fifth recycle run.

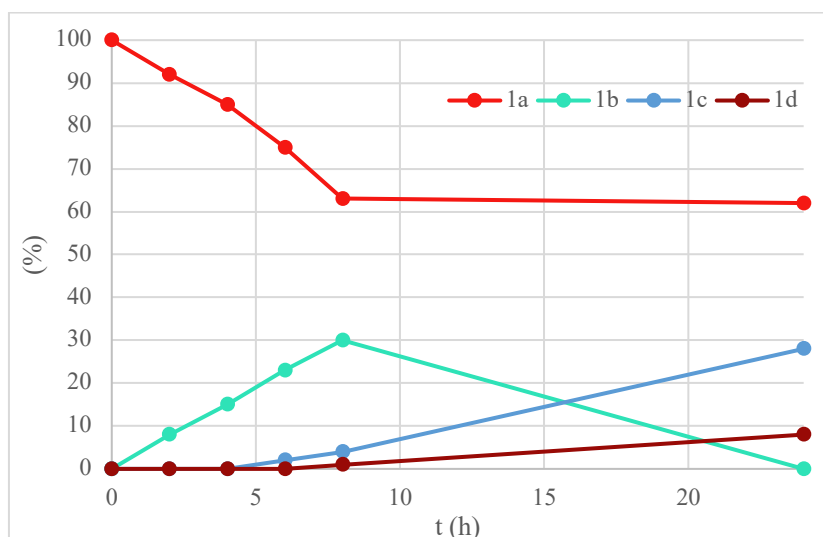
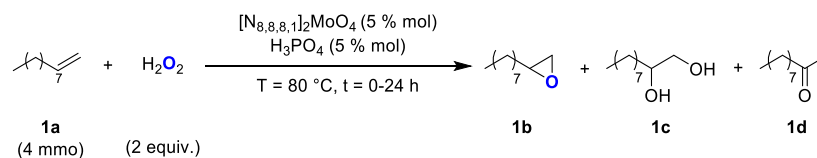


Figure A 19: Epoxidation of 1-decene (**1a**) to decene oxide (**1b**). ^aReaction conditions: **1a** (4.0 mmol), H₂O₂ 30 % V/V (2.0 equiv.), [N_{8,8,8,1}]₂[MoO₄] (5.0 mol %) and H₃PO₄ (5.0 mol %). ^bConversion, selectivity and yield were calculated by GC-MS analysis using mesitylene (20 % mol) as internal standard.

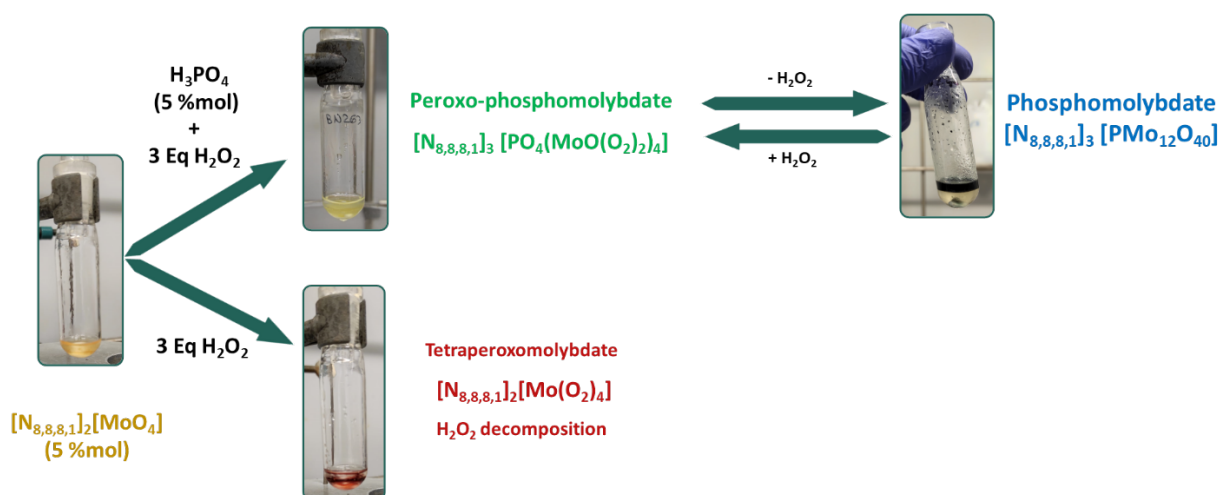
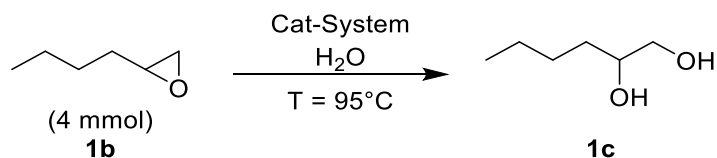


Figure A 20: Different molybdates species formed in the epoxidation process in different conditions.

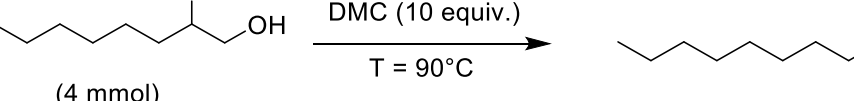
Table A 5: hydrolysis reaction of 1,2-epoxyhexane with different catalytic system.



Entry	Cat-System	Time (h)	Conv (%) ^a	Sel (%) ^a
1	$[\text{N}_{1888}]_2[\text{MoO}_4]$ (5 %), H_3PO_4 (5 %)	4	7	>99
2	$[\text{N}_{1888}][\text{OCOOCH}_3]$ (5 %)	4	46	99
3	NaOH (5 %)	4	35	>99
4	H_3PO_4 (5 %)	4	>99	>99
5	H_2SO_4 (5 %)	4	>99	>99
6	$[\text{N}_{1888}]_2[\text{MoO}_4]$ (5 %), H_3PO_4 (10 %)	4	93	>99
7	$[\text{N}_{1888}]_2[\text{MoO}_4]$ (5 %), H_3PO_4 (15%)	4	>99	95
8 ^c	H_2SO_4 (5%)	12	>99	>99

Reaction conditions: 1,2-epoxyhexane (4.0 mmol) and H_2O (V = 3 mL). Conversion, selectivity and yield calculated by GC-MS and ^1H NMR analysis using mesitylene as internal standard. ^cAfter epoxidation step using 1-decene.

Table A 6: Transcarbocation reaction of 1,2-epoxihexane with different catalytic system



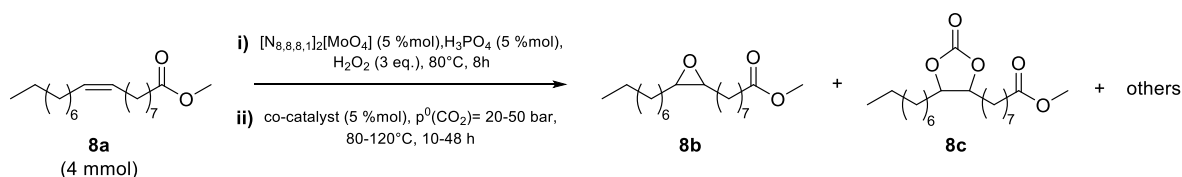
CCCCCCCCC(O)CO (4 mmol) **1c**
 $\xrightarrow[\text{T} = 90^\circ\text{C}]{\text{Cat-System DMC (10 equiv.)}}$
CCCCCCCCC1OCC(=O)O1 **1f**

Entry	Cat System (% mol)	t (h)	Yield (%) ^a
1	[N ₁₈₈₈][OCOOCH ₃] (5 %)	2	>99
2	[N ₁₈₈₈] ₂ [MoO ₄] (5 %)	3.5	>99
3	[N ₁₈₈₈] ₂ [MoO ₄] (5 %), H ₃ PO ₄ (5 %)	10	32
4	[N ₁₈₈₈] ₂ [MoO ₄] (5 %), H ₃ PO ₄ (5 %), [N ₁₈₈₈][OCOOCH ₃] (5 %)	10	>99
5^b	[N ₁₈₈₈] ₂ [MoO ₄] (5 %), H ₃ PO ₄ (5 %), [N ₁₈₈₈][OCOOCH ₃] (5 %),	10	nd
6^c	[N ₁₈₈₈][OCOOCH ₃] (10 %)	16	66 ^d

Reaction conditions: ^a1,2-decanediol (4.0 mmol) determined with ¹H NMR using mesitylene as internal standard.

^bPerformed in presence of 2mL of water. ^cPerformed after hydrolysis step removing the water by rotavapor. ^dYield of decane carbonate at the end of the tandem reaction.

Table A 7: Effect of the co-catalysts and parameter conditions (pressure, temperature and time) on the direct oxidative carbonation reaction for the synthesis of methyl oleate carbonate (**3c**) from methyl oleate (**1c**).^a



Entry	Co-cat (5%mol)	$p^o(CO_2)$ bar	T (°C)	t (h)	Conv. of 2c (%) ^c	Sel. of 3c (%) ^c	Yield (%) ^c	Ratio (cis:trans) ^c
1	-	40	100	10	10	70	7	92 : 8
2	TBAB	40	100	10	56	60	37	86 : 14
3	TBAI	40	100	10	85	44	37	42 : 58
4	KBr	40	100	10	21	100	21	73 : 27
5	TBAB	20	100	10	50	16	8	67 : 32
6	TBAB	50	100	10	91	41	37	79 : 21
7	TBAB	40	80	10	24	83	20	84 : 16
8	TBAB	40	120	10	75	49	37	70 : 30
9	TBAB	40	100	24	90	59	54	85 : 15

Reaction conditions: ^aMethyl oleate (**8a**, 4.00 mmol), H_2O_2 (3 equiv.), $[N_{1,8,8,8}]_2MoO_4$ (5 % mol) and H_3PO_4 (5 % mol) performed at $T = 80$ °C for $t = 8$ h followed by the raw addition of a selected co-catalyst (5 % mol), $p^o(CO_2)$ = 20-50 bar without any intermediate work-up. The reaction was further performed for 10-48 h at $T = 80$ -120°C. ^b Conversion of **8a** is always >98%. ^cConversion, selectivity and cis:trans ratio are calculated by NMR spectroscopy using mesitylene as internal standard; ^dthe main by-products are dihydroxy methyl oleate and the corresponding ketones due to Meinwald rearrangement.

Bibliography Appendix Chapter 3

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Appendix Chapter 4

Additional results CO and CH₄ production

Table A 8: Control experiment, results obtained for the reduction of carbon dioxide without any catalyst (only glass beads).

Entry	T (°C)	flow rate (ml/min)	ratio CO ₂ :H ₂	Power lights (%)	CO ₂ Conv. (%)	Sel. to CH ₄ (%)	CH ₄ product. (mmol/g _{cat} /h)
1	250	1	1:4	100	0	-	-

All catalysts have been tested with a feed of pure hydrogen under typical reaction conditions (200 °C, 1 ml_n/min), where for none of the catalysts carbon containing products were detected in the analysis, supporting that the carbon dioxide fed in the reactor is reduced.

Table A 9: reduction of carbon dioxide with cobalt(II,III) oxide catalyst.

Entry	T (°C)	flow rate (ml/min)	ratio CO ₂ :H ₂	Power lights (%)	CO ₂ Conv. (%)	Sel. to CH ₄ (%)	CH ₄ product. (mmol/g _{cat} /h)
1	200	0.5	1:4	100	32	98	6.1
2	200	1	1:4	100	23	98	8.9
3	200	5	1:4	100	6.9	93	13
4	200	1	1:1	100	6.1	92	5.5
5	160	1	1:4	100	1.8	96	0.66
6	160	1	1:4	0	1.2	96	0.45
7	250	1	1:4	100	54	97	21
8	250	1	1:4	0	44	95	17

Table A 10: reduction of carbon dioxide with ruthenium nanoparticles on titanium dioxide (Ru/TiO₂) catalyst.

Entry	T (°C)	flow rate (ml/min)	ratio CO ₂ :H ₂	Power lights (%)	CO ₂ Conv. (%)	Sel. to CH ₄ (%)	CH ₄ product. (mmol/g _{cat} /h)
1	200	0.5	1:4	100	70	100	14
2	200	1	1:4	100	48	100	19
3	200	1	1:4	0	35	100	14
4	200	5	1:4	100	11	100	22
5	200	1	1:1	100	14	100	14
6	160	1	1:4	100	8.9	100	3.5
7	160	1	1:4	0	5.7	100	2.3
8	250	1	1:4	100	93	100	37
9	250	1	1:4	0	87	100	35
10	250	12.5	1:4	100	26	100	127

Table A 11: reduction of carbon dioxide with ruthenium nanoparticles on strontium titanate(Ru/STO) catalyst.

Entry	T (°C)	flow rate (ml/min)	ratio CO ₂ :H ₂	Power lights (%)	CO ₂ Conv. (%)	Sel. to CO (%)	CH ₄ product. (mmol/g _{cat} /h)
1	200	0.5	1:1	100	1.9	38	0.37
2	200	1	1:1	100	1.3	54	0.81
3	200	1	1:1	0	1.0	57	0.69
4	200	5	1:1	100	0.64	71	2.3
5	200	1	1:4	100	0.47	66	0.78
6	160	1	1:1	100	0.26	67	0.18
7	160	1	1:1	0	0.15	60	0.10
8	250	1	1:1	100	5.7	42	2.4
9	250	1	1:1	0	3.9	51	2.0

Table A 12: reduction of carbon dioxide with gold nanoparticles on titanium dioxide (Au/TiO₂) catalyst.

Entry	T (°C)	flow rate (ml/min)	ratio CO ₂ :H ₂	Power lights (%)	CO ₂ Conv. (%)	Sel. to CO (%)	CH ₄ product. (mmol/g _{cat} /h)
1	200	0.5	1:1	100	5.9	100	2.5
2	200	1	1:1	100	4.4	100	3.1
3	200	1	1:1	50	4.1	100	2.9
4	200	1	1:1	0	3.8	100	2.7
5	200	5	1:1	100	1.7	100	7.3
6	160	1	1:1	100	0.73	100	0.62
7	160	1	1:1	0	0.52	100	0.45
8	250	1	1:1	100	11	100	9.5
9	250	1	1:1	0	9.9	100	8.4
1.0 bar overpressure							
10	200	1	1:1	100	6.2	100	4.4
2.0 bar overpressure							
11	200	1	1:1	100	7.5	100	5.3

Table A 13: performance of a variety of catalysts under specified conditions in literature.

Entry	Catalyst	Temperature (°C)	Total flow rate (ml/min)	Volumetric ratio CO ₂ :H ₂	Light source	Productivity (mmol/g _{cat} /h)	Ref.
1	Iridium on MOF	250	20	1:4	300W Xe 2.4 W/cm ²	CH ₄ 20	1
2	Nickel on silica/aluminum oxide	225	5	1:4	LED max. 2200 mW/m ²	CH ₄ 54	2
3	Ruthenium on aluminum oxide	218	11	1:4.5	1440 mW/cm ²	CH ₄ 79	3
4	Ruthenium on strontium titanate	150	25	1:4	300 W Xe 0.1 W/cm ²	CH ₄ 15	4
5	Platinum/ Molybdenum on silica	200	15	1:1	Dolan-Jenner visible light source	CO 1.6 (Conversion rate)	5
6	Rhodium on titanium dioxide	250	20	1:4	300 W Xe 2.7 W/cm ²	CO 21	6
7	Gold on titanium dioxide	200	135	4:1	1440 mW/cm ²	CO 33	7

Catalyst deactivation

Deactivation under continuous-flow conditions can be tested by running the same conditions over elongated times. During the parameter screening deactivation could be observed over the full-time frame (typically more than 10 hours), depending on the catalyst (always below 20 % for the targeted compound), showing a qualitative screening where promising conditions are pinpointed for further investigations. During the operation of the gold nanoparticles on titanium dioxide, it was found to be crucial not to cool down the system under reaction conditions (especially with hydrogen) as this led to severe deactivation of the catalyst, hypothesized to be caused by the formation of liquid water at lower temperatures. Ruthenium nanoparticles on strontium titanite showed a decreasing productivity of methane with elongated operation times, causing a varying selectivity towards carbon monoxide.

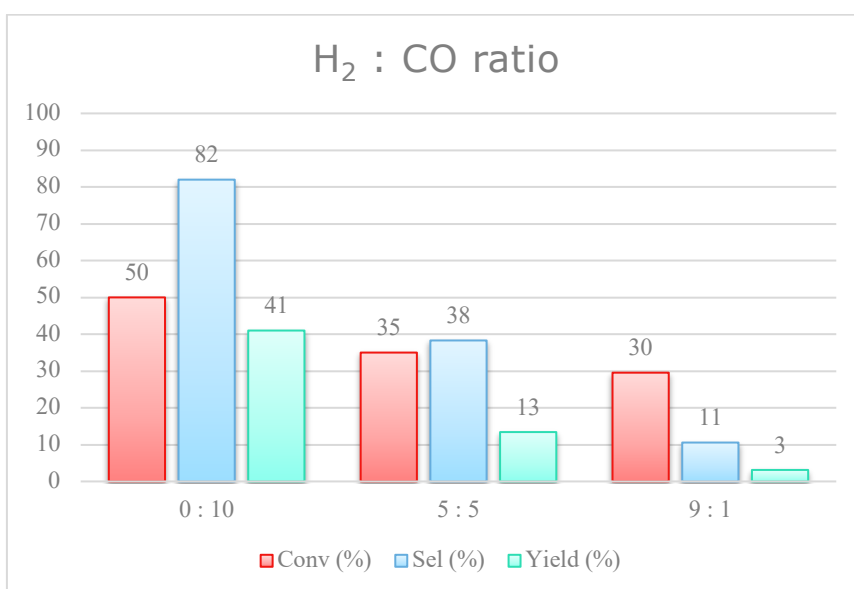


Figure A 21: Study of the Suzuki reaction conducted with different gaseous mixtures of H₂ and CO (0:10; 5:5 and 9:1). Reaction conditions: 4-iodoanisole (0.5 mmol), 4-fluorophenylboronic acid (1.5 equiv.), PdBr₂ (5 % mol), tpp (10 % mol), K₂CO₃ (3 equiv.), dioxane (3 mL) at T = 80 °C. Conversion, selectivity and yield were calculated by GC-MS. The theoretical yields were double check through ¹⁹F-qNMR using 1 equiv. of fluorobenzene as internal standard.

Bibliography Appendix Chapter 4

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Appendix Chapter 5

Table A 14: Blank tests for induced ATRP of METAC.

Entry	CDs	Catalyst	Irradiation	Conversion (%) ^[b]
1	-	Yes	-	0
2	a-N-CDs	Yes	-	0
3	a-N-CDs	No	UV	0
4	a-N-CDs	No	Vis	0
5	-	Yes	UV	0
6	-	Yes	Vis	0

^a Experiments were conducted at ambient temperature for 1h using a ratio [METAC]/[HEBIB]/[CDs]/[CuBr₂]/[PMDTA] = 100/1/1/1/3 and a 1:1 mixture of water and methanol as the solvent; ^b determined gravimetrically.

Table A 15: Copper catalyst concentration tests for induced ATRP of METAC. [a]

Entry	Reagent molar ratios respect the monomer		Solvent	Conversion (%) ^[b]
	CuBr ₂	PMDTA		
1	1	3	Water	88
2	1	3	H ₂ O/MeOH 1:1 V/V	89
3	1	3	H ₂ O/CH ₃ CN 1:1 V/V	85
4	0.5	1.5	Water	0
5	0.5	1.5	H ₂ O/MeOH 1:1 V/V	0
6	0.5	1.5	H ₂ O/CH ₃ CN 1:1 V/V	0
7	0.25	0.75	Water	0
8	0.25	0.75	H ₂ O/MeOH 1:1 V/V	0
9	0.25	0.75	H ₂ O/CH ₃ CN 1:1 V/V	0
10	0.1	0.3	Water	0
11	0.1	0.3	H ₂ O/MeOH 1:1 V/V	0
12	0.1	0.3	H ₂ O/CH ₃ CN 1:1 V/V	0

^[a] Experiments were conducted at r.t. for 1 h, under UV irradiation (λ = 365 nm) using a constant ratio [METAC]/[HEBIB]/[CDs] = 100/1/1 mol/mol (typically 10 mmol of METAC were used) and varying the [CuBr₂]/[PMDTA] ratio; ^[b] determined gravimetrically.

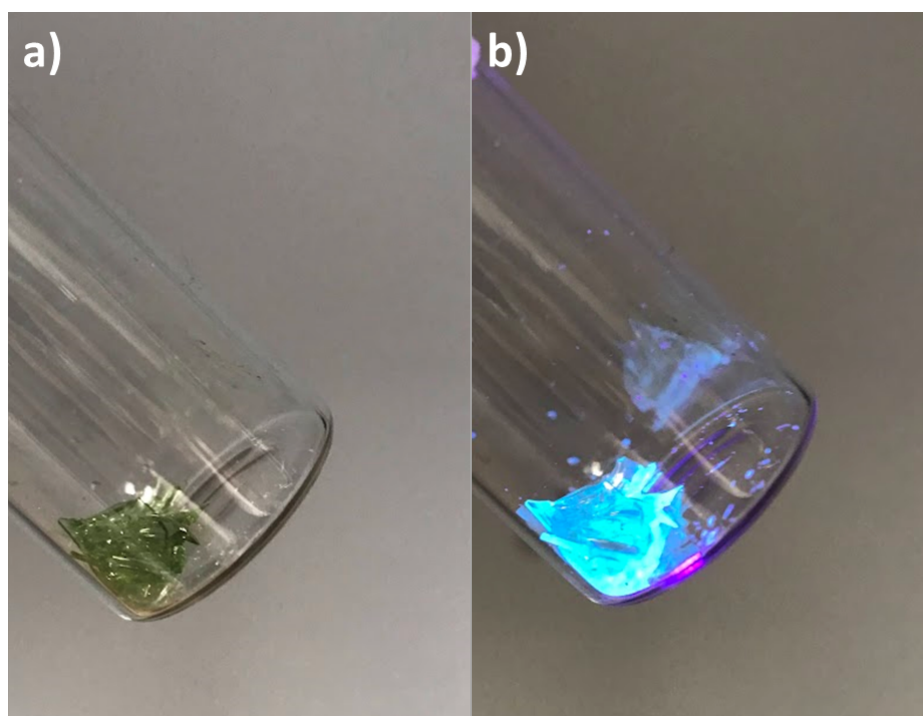
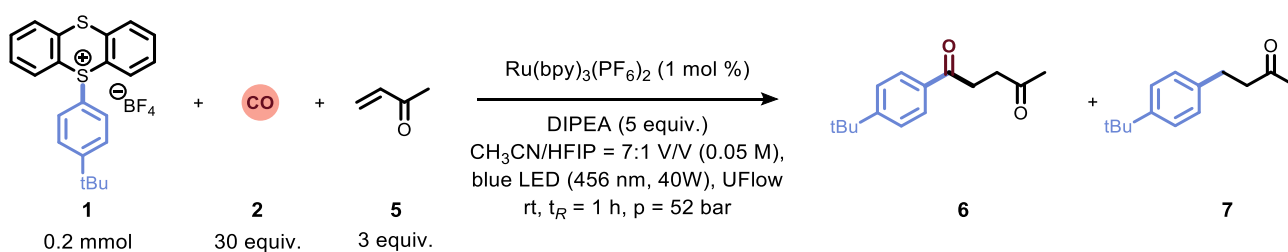


Figure A 22. Picture of the obtained poly-METAC under daylight (a) and under UV irradiation (b).

Table A 16: Selected optimization experiments for the carbonylative conjugate addition of aryl thianthrenium 1 and methyl vinyl ketone 5.



Entry ^a	Deviation from scheme	Conv 1. ^b (%)	6 ^b (%)	7 ^b (%)
1	EY 10% - 3:1 Aryl/Alkene, CO 10 eq	81	50	13
2	EY 10% - 1:3 Aryl/Alkene, CO 10 eq	96	44	26
3	-	>99	41	10
4	1:1 Ratio Aryl/Alkene	>99	29	3
5	No. DIPEA	-	n.d.	n.d.
6	2 eq. DIPEA	65	20	18
7	3.5 eq. DIPEA	96	49	23
Deviation from entry 7				
8	3.5 eq. 1-ethyl-2,2,6,6-tetramethyl piperidine	34	10	n.d.
9	3.5 eq. triethylamine	29	5	n.d.
10	0.05 M – 1:2 Aryl/Alkene	94	41	5
Deviation from entry 10				
11	0.025 M	81	50	5

12	0.1 M	>99	27	5
13	69 bar, 30 eq. CO	>99	41	12
14	69 bar, 30 eq. CO , 10 W	>99	49	4
15	CD ₃ CN, 69 bar, 30 eq. CO , 10 W	>99	58	4
16	0.5% Ru, 69 bar, 30 eq. CO , 10 W	93	48	6
17	0.25% Ru, 69 bar, 30 eq. CO, 10 W	80	40	4
18	EY 10% , 69 bar, 30 eq. CO, 10 W	42	15	2
19	EY 10 %,green LED 525 nm, 10 W, 69 bar, 30 eq. CO	53	17	3
20	EY 10%,green LED 525 nm, 20 W, 69 bar, 30 eq. CO	65	31	4
21	EY 10%, green LED 525 nm, 30 W, 69 bar, 30 eq. CO	78	40	4
22	EY 10%, green LED 525 nm, 40 W, 69 bar, 30 eq. CO	78	43	14

^a Reaction conditions: A stock solution was prepared with 0.2 mmol of **1**, 0.6 mmol of **3** (or vice versa), 5 % mol of eosin Y and 1 mmol of DIPEA dissolved in 4 mL of CH₃CN/HFIP (7:1). The solution was loop filled with CO gas (2, 10 equiv.), pressurized and the gas-liquid slugs were pumped into the reactor. ^b ¹H NMR yields are calculated with an external standard (trichloroethylene)



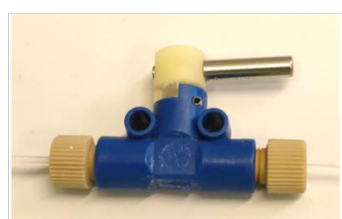
Syringe pump (Chemyx Fusion 200) and Gastight syringe (SGE Luer Lock 5 mL)



HPLC pump (Shimadzu LC-20AD)



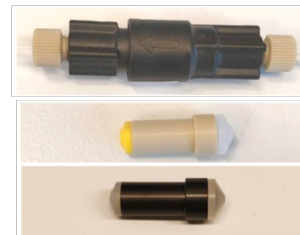
Mass Flow Controller (Bronkhorst EL-FLOW)



Switch Valve (IDEX P-783)



T-mixer (IDEX P-712)



BPR holder (IDEX P-789 BPR Cartridge (IDEX P-789) and Check valve cartridge (IDEX CV-3000)

Figure A 23: Details of flow equipment used for photocatalytic carbonylation reactions.

UFLOW reactor

For all flow experiments a homemade, 3D-printed reactor was adopted (**Figure A23**, left). The reactor consists of a lid to host the Kessil lamp and a support around which a PFA tubing (0.8-0.5 mm inner diameter) is coiled (**Figure A23**, middle); a fan (SUNON DC Lüfter 24 V; 50x50x15 Vapo RoHS) is mounted on the bottom of the reactor for cooling. The coil is inserted in a S7 cylindrical plastic body (**Figure A23**, right) with holes to allow the air flow to escape the reactor and keep the temperature stable around 30–33 °C. Additional details on the reactor could be find here.⁷⁸



Figure A 24: Overview of the 3D-printed flow reactor. Left: overall reactor; middle: inside of the reactor (flow loop) and holder for the Kessil lamp in the center; right: main body, internally coated with reflective tape. A fan is mounted on the bottom to keep the temperature stable around 30–33 °C.

8. Characterization

Characterization Chapter 3

$[\text{N}_{8,8,1}][\text{CH}_3\text{OCOO}]^1$

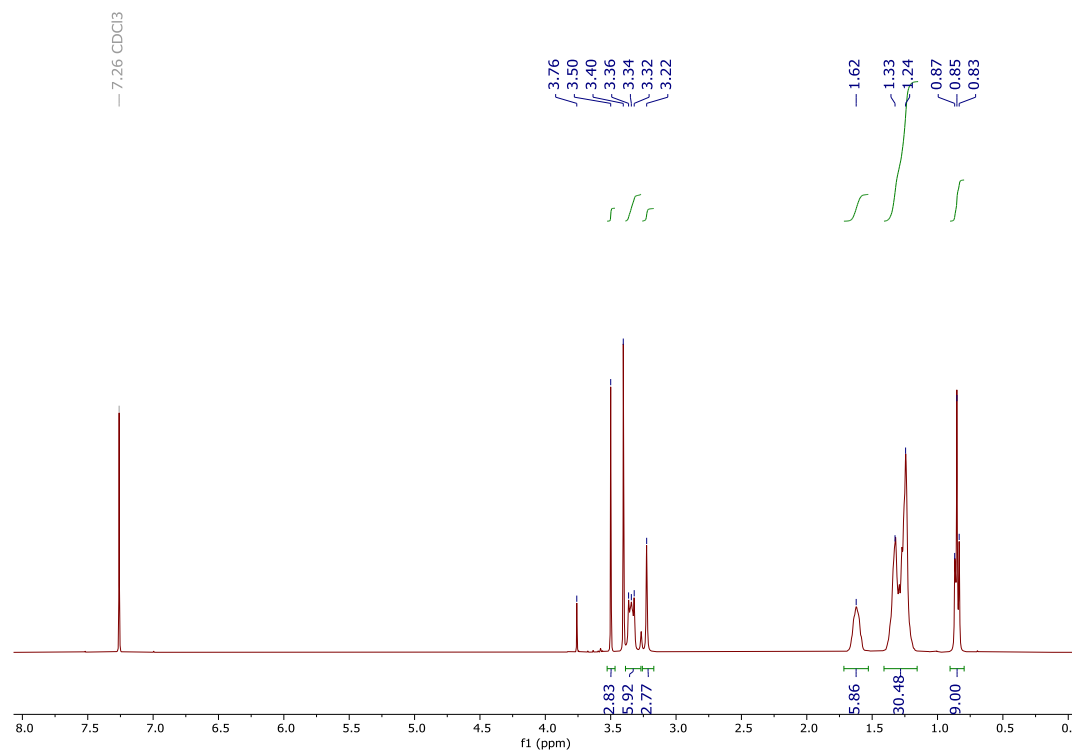


Figure S 1: ^1H NMR (400 MHz, CDCl_3) $\delta(\text{ppm})$: 3.50 (s, 3H), 3.39 – 3.27 (m, 6H), 3.22 (s, 3H), 1.72 – 1.53 (m, 6H), 1.41 – 1.16 (m, 30H), 0.84 (t, $J = 6.5$ Hz, 9H).

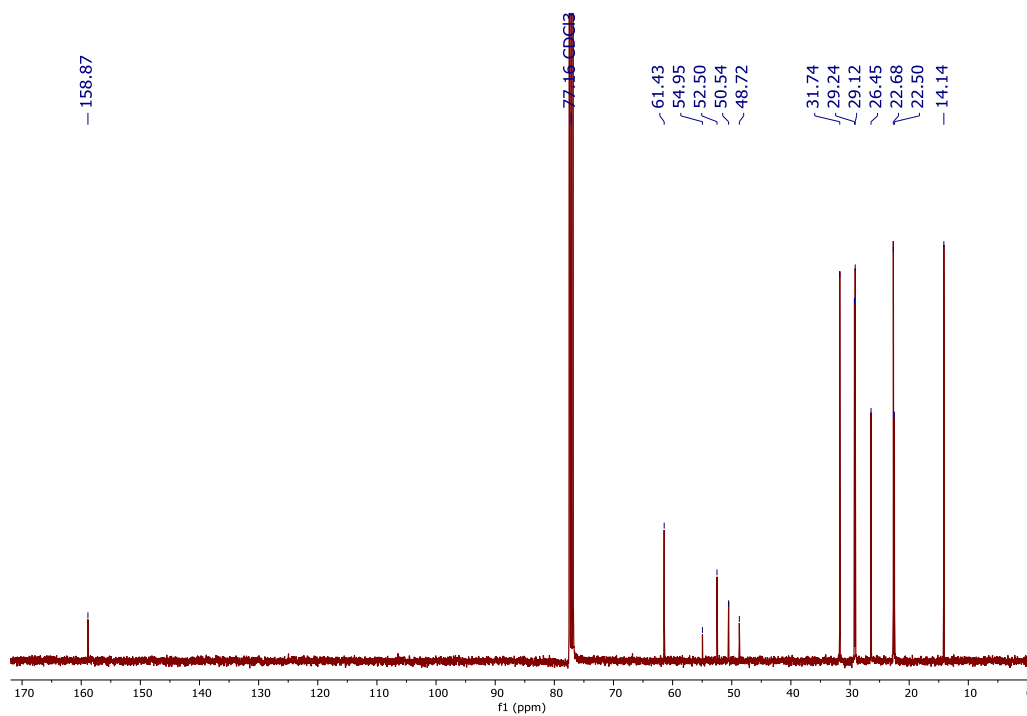


Figure S 2: ^{13}C NMR (101 MHz, CDCl_3) $\delta(\text{ppm})$: 158.87; 61.43; 54.95; 52.50; 48.72; 31.74; 29.24; 29.12; 26.45; 22.68; 22.50; 14.14.

1-butyl-3-methylimidazolium methylcarbonate/1-butyl-3-methylimidazolium-2-carboxylate²

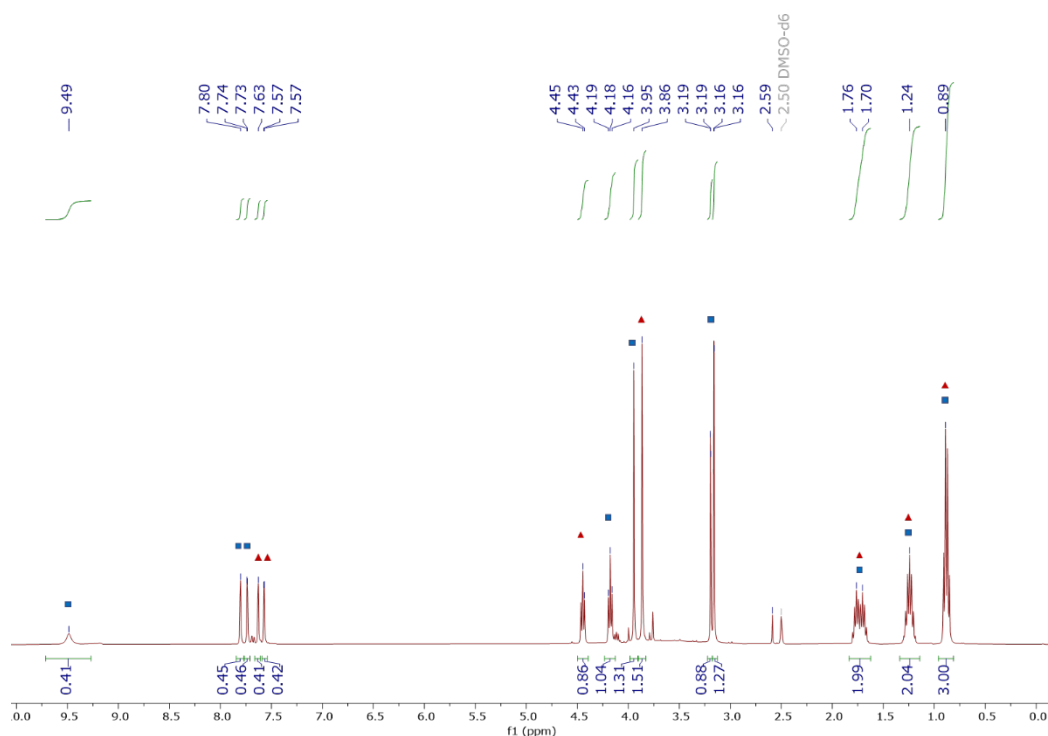


Figure S 3: ¹H NMR (400 MHz, DMSO-d₆) δ (ppm): **(1-butyl-3-methyl-2-carboxyimidazolium)** 7.63 (d, J = 2.0 Hz, 1H), 7.57 (d, J = 1.9 Hz, 1H), 4.45 (t, J = 7.3 Hz, 2H), 3.95 (s, 3H), 1.83-1.62 (m, 2H), 1.24 (m, 2H), 0.88 (q, J = 7.7 Hz, 3H). **[C₄C₁im][CH₃OCOO]** 9.49 (s, 1H), 7.80 (d, J = 1.9 Hz, 1H), 7.74 (d, J = 1.9 Hz, 1H), 4.18 (t, J = 7.2 Hz, 2H), 3.86 (s, 3H), 3.19 (s, 3H), 1.83-1.62 (m, 2H), 1.24 (m, 2H), 0.88 (q, J = 7.7 Hz, 3H).

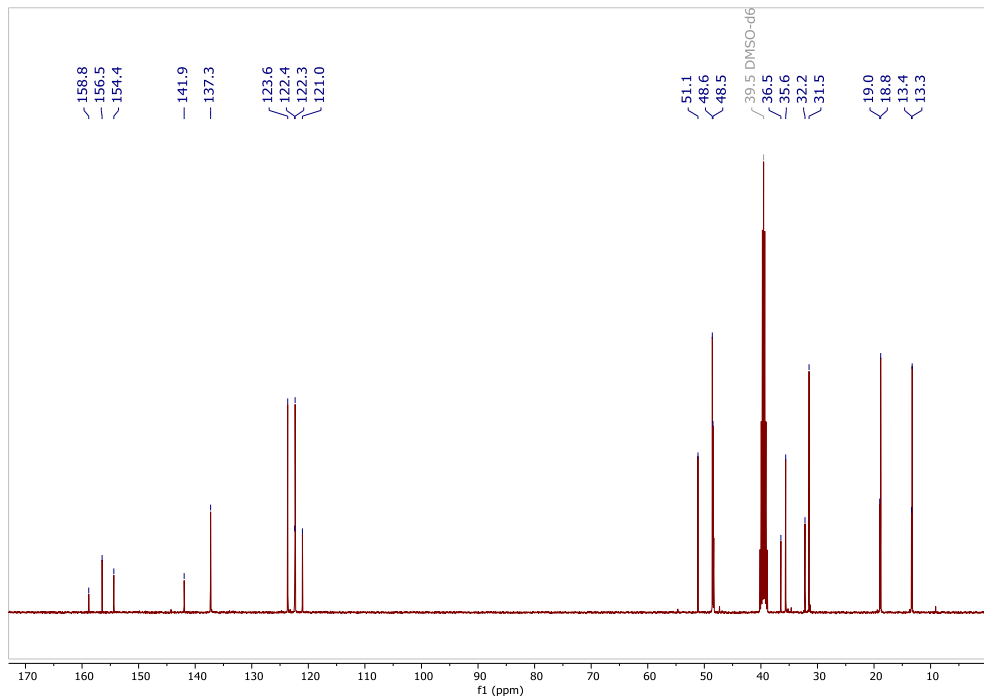


Figure S 4: ¹³C NMR (101 MHz, DMSO-d₆) δ(ppm): **(1-butyl-3-methyl-2-carboxyimidazolium)** 158.8;141.9; 122.4; 121.0; 48.6; 36.5; 32.2; 19.0; 13.4.; **[C₄C₁im][CH₃OCOO]** 156.5; 137.3; 123.6; 122.3; 51.1; 48.5; 35.6; 31.5; 18.8; 13.3.

Trioctylmethylammonium catecolate, [N_{8,8,1}][CAT]

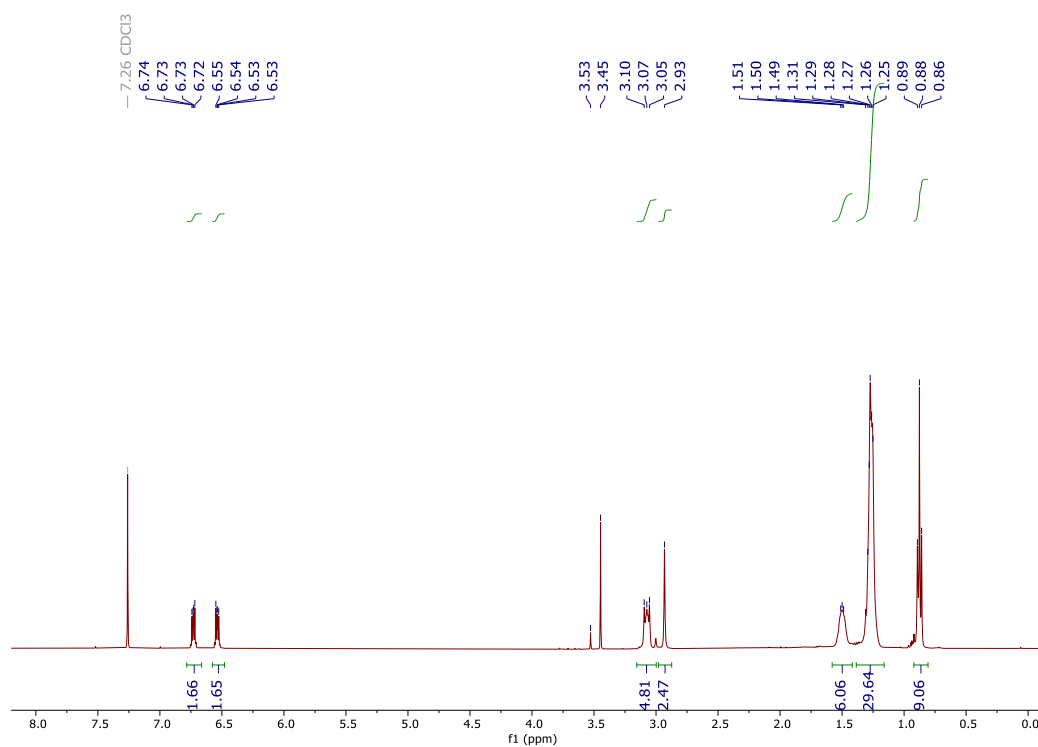


Figure S 5: ¹H NMR (400 MHz, CDCl₃) δ (ppm): 6.73 (dd, J = 5.8, 3.6 Hz, 2H), 6.54 (dd, J = 5.8, 3.6 Hz, 2H), 3.16-3.00 (m, 6H), 2.93 (s, 3H), 1.58-1.42 (m, 6H), 1.27 (m, 30H), 0.88 (t, J = 6.8 Hz, 9H).

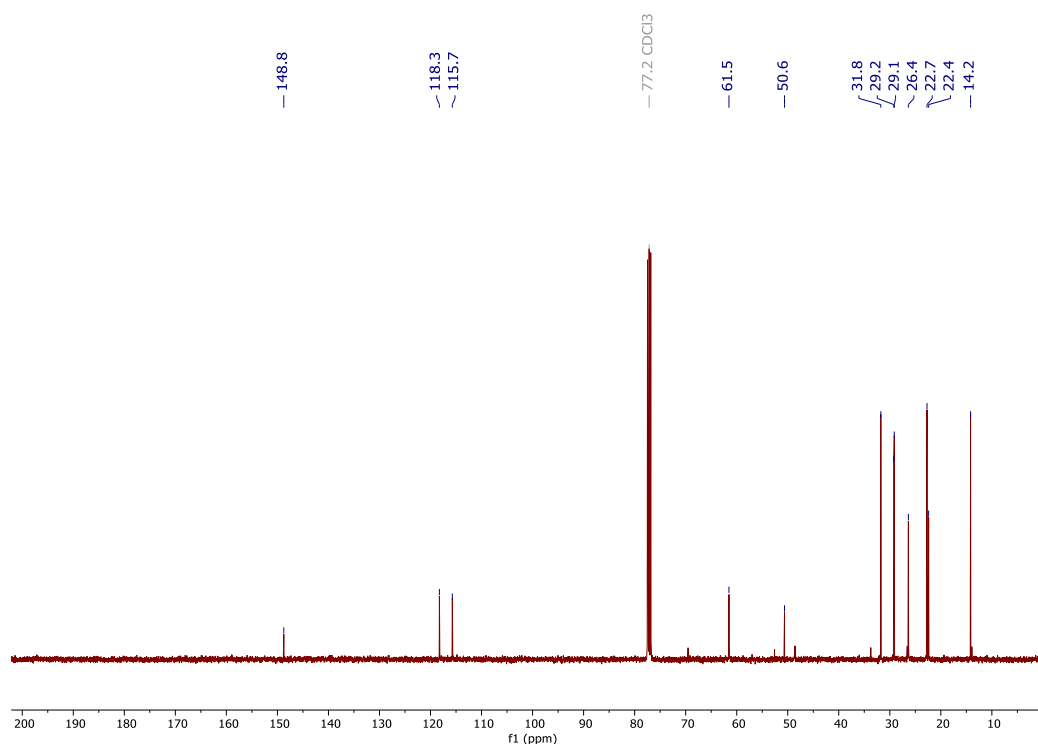


Figure S 6: ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 14.2, 22.4, 22.7, 26.4, 29.1, 29.2, 31.8, 61.5, 115.7, 118.3, 148.

Trioctylmethylammonium resorcinolate, [N_{8,8,8,1}][RES]

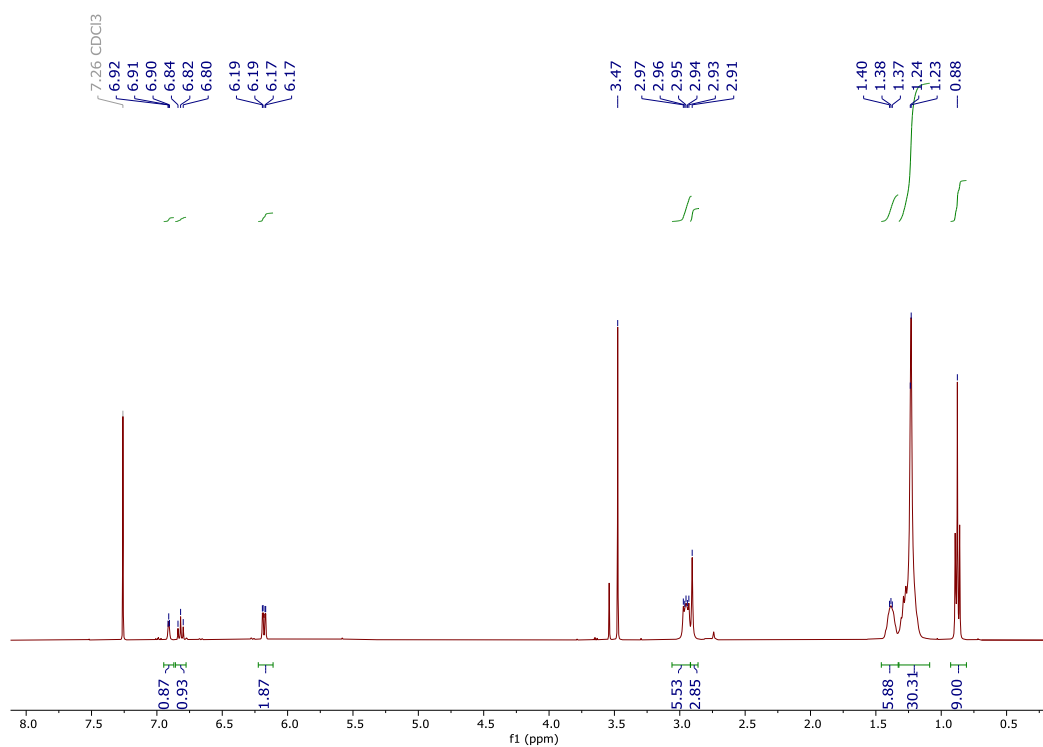


Figure S 7: ¹H NMR (400 MHz, CDCl₃) δ (ppm): 6.91 (t, J = 2.3 Hz, 1H), 6.82 (t, J = 8.0 Hz, 1H), 6.18 (dd, J = 8.0, 2.1 Hz, 2H), 3.06-2.92 (m, 6H), 2.91 (s, 3H), 1.46-1.33 (m, 6H), 1.23 (m, 30H), 0.88 (t, J = 6.8 Hz, 9H).

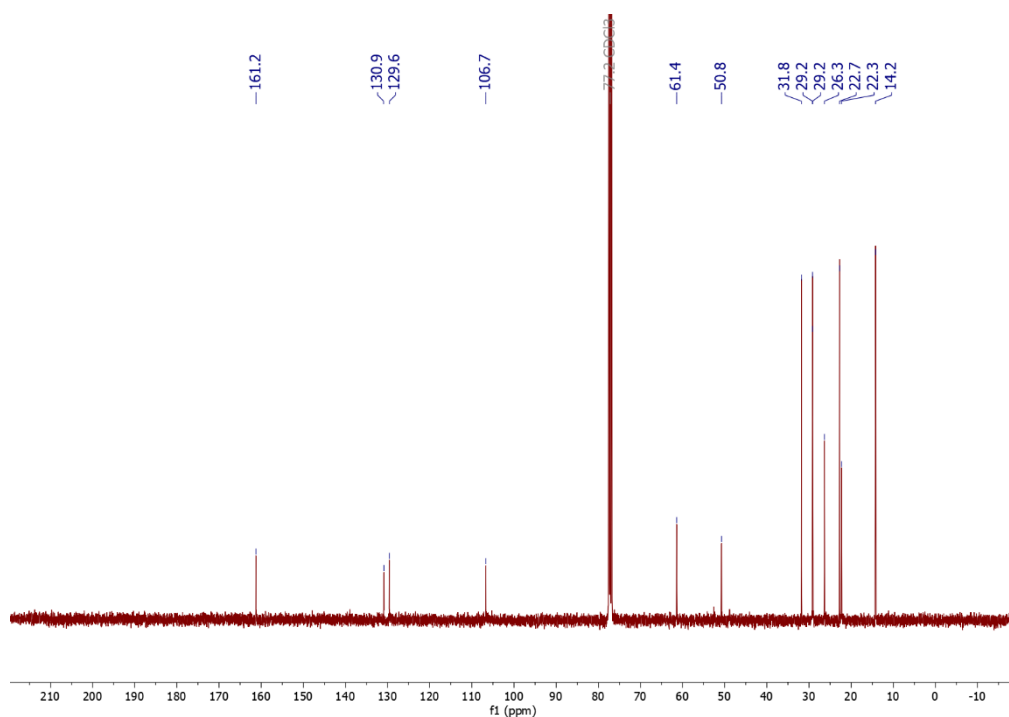


Figure S 8: ¹³C NMR (101 MHz, CDCl₃) δ (ppm): 14.2, 22.3, 22.7, 26.3, 29.2, 29.2, 31.8, 61.4, 106.7, 129.6, 130.9, 161.2.

Trioctylmethylammonium hydroquinolate, [N_{8,8,8,1}][HYD]

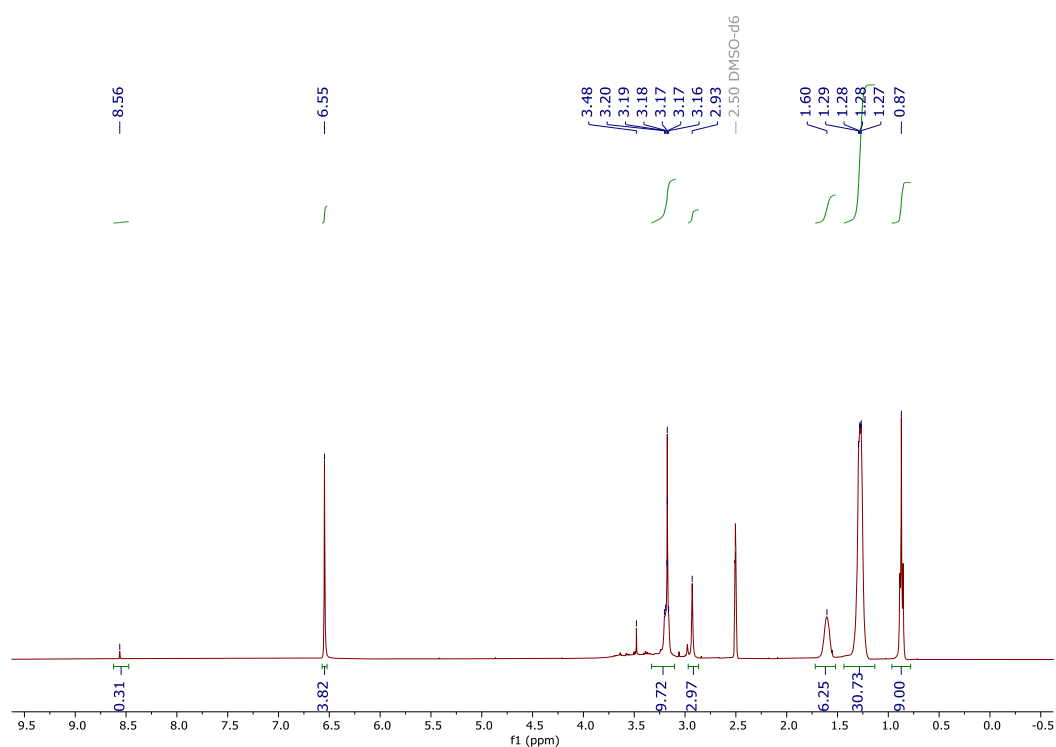


Figure S 9: ¹H NMR (400 MHz, DMSO-d₆, 298 K) δ (ppm): 8.56 (OH), 6.55 (s, 4H), 3.19-3.16 (m, 6H), 2.93 (s, 3H), 1.60 (m, 6H), 1.29-1.27 (m, 30H), 0.87 (t, J = 6.9 Hz, 9H).

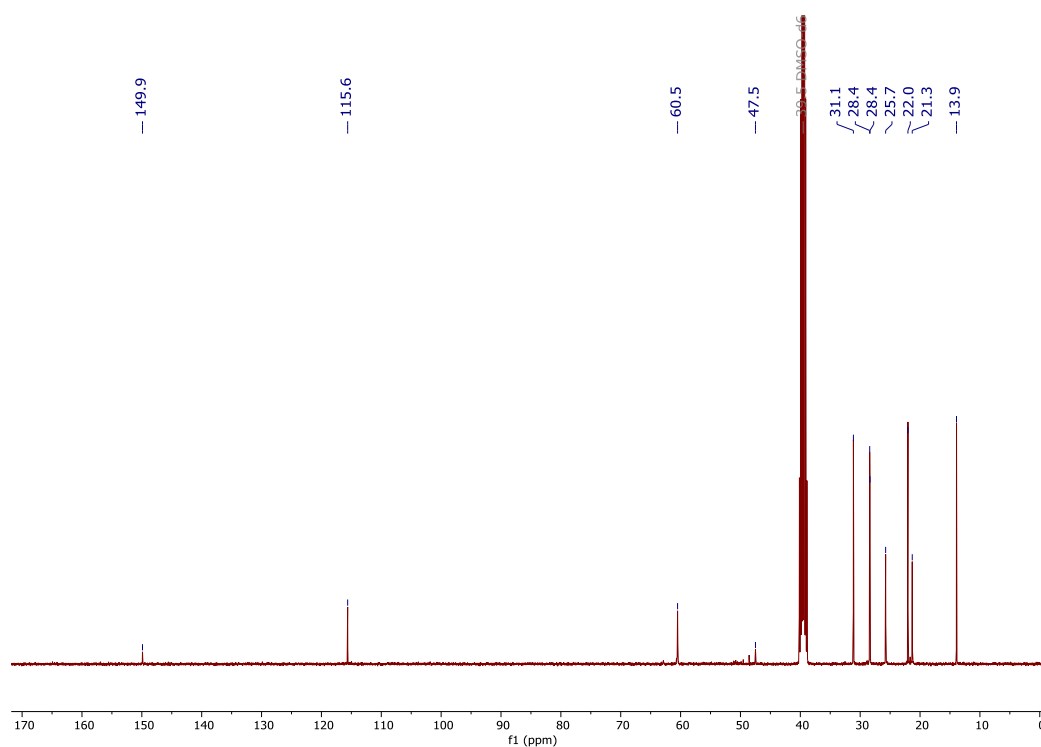


Figure S 10: ¹³C NMR (100 MHz, DMSO-d₆) δ (ppm): 13.9, 21.3, 22.0, 25.7, 28.4, 28.4, 31.1, 47.5, 60.5, 115.6, 149.9.

1-butyl-3-methylimidazolium hydroquinolate, [C₄C₁im][HYD]

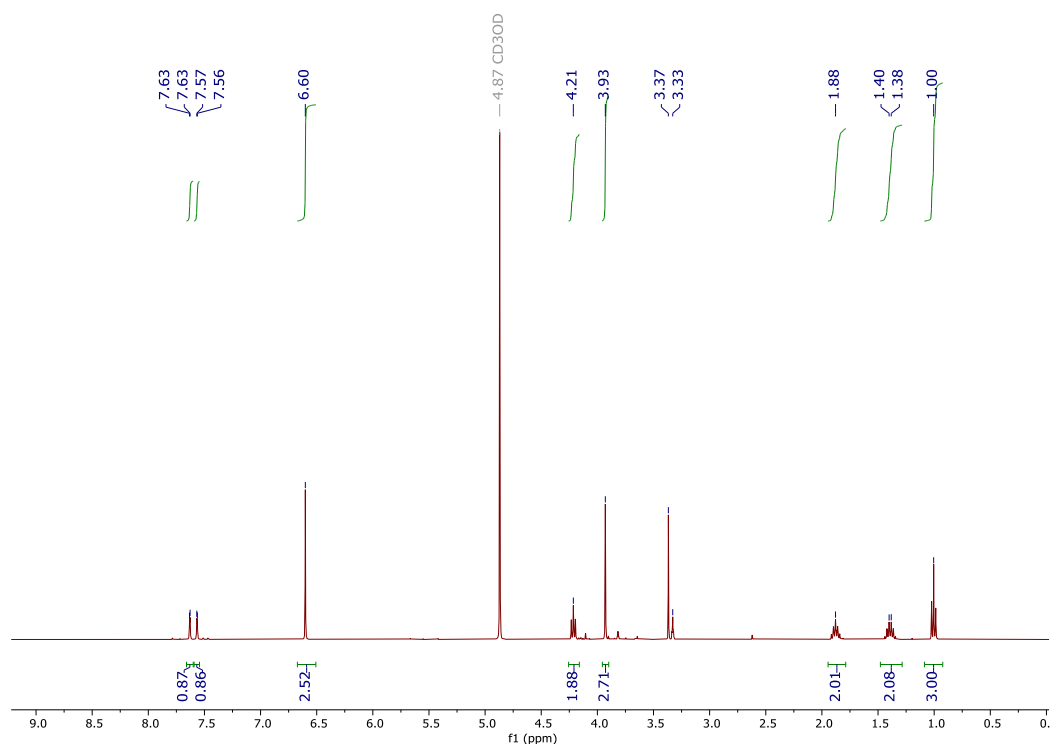


Figure S 11: ¹H NMR (400 MHz, MeOD) δ (ppm): 7.63 (d, J = 2.0 Hz, 1H), 7.57 (d, J = 2.0 Hz, 1H), 6.60 (s, 4H), 4.21 (t, J = 7.3 Hz, 2H), 3.93 (s, 3H), 1.88 (p, J = 7.6 Hz, 2H), 1.39 (h, J = 7.4 Hz, 2H), 1.00 (t, J = 7.4 Hz, 3H).

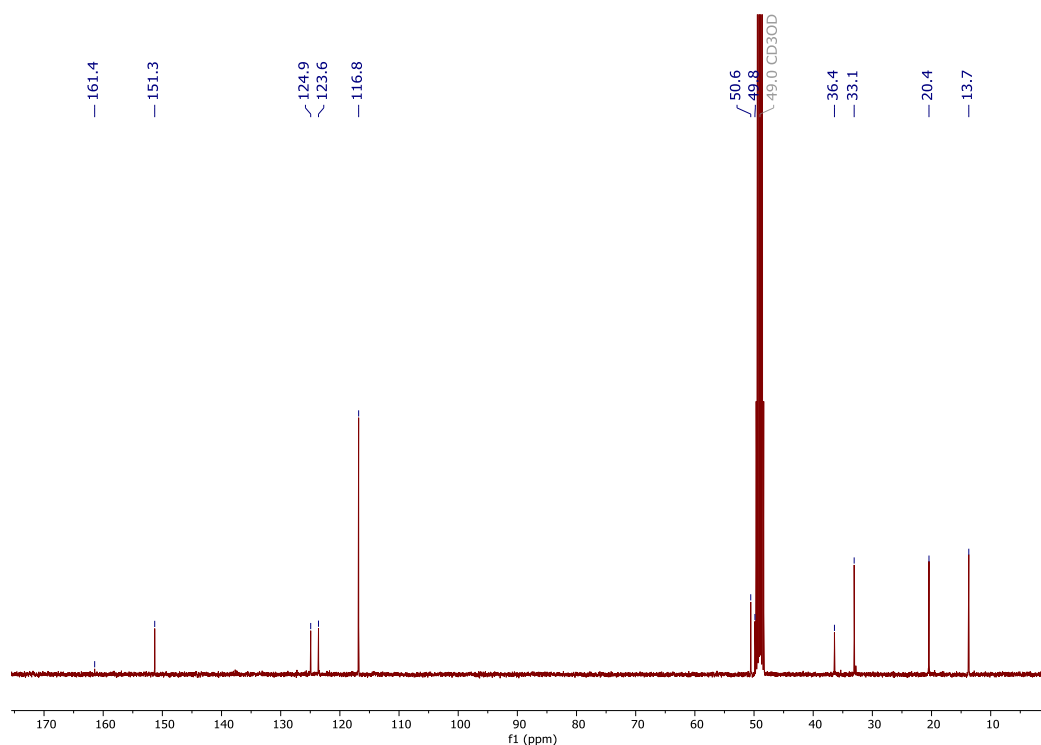


Figure S 12: ¹³C NMR (100 MHz, CD₃OD, 298 K) δ (ppm): 13.7, 20.4, 33.1, 36.4, 50.6, 116.8, 123.6, 124.9, 151.3, 161.4.

1,8-Diazabicyclo[5.4.0]undec-7-enium hydroquinolate [DBUH][HYD]

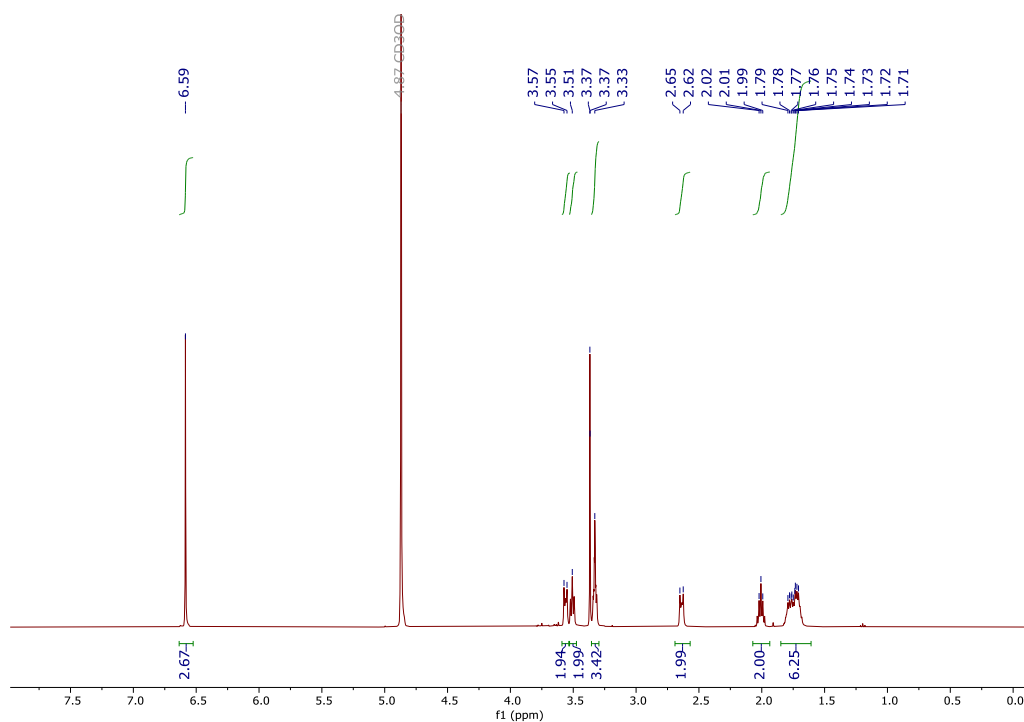


Figure S 13: ¹H NMR (400 MHz, CD₃OD) δ (ppm): 1.75 (m, 6H), 2.01 (m, 2H), 2.62 (m, 2H), 3.33 (m, 2H), 3.51 (m, 2H), 3.57 (m, 2H), 6.59 (s, 4H).

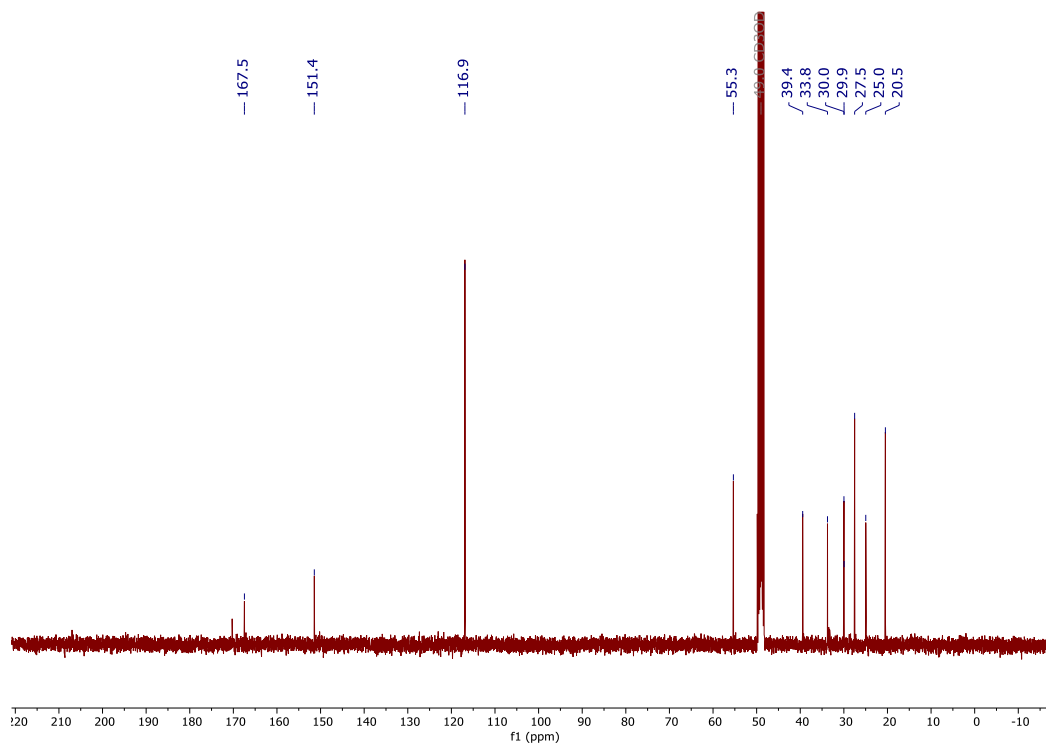


Figure S 14: ¹³C NMR (100 MHz, CD₃OD) δ (ppm): 20.5, 25.0, 27.5, 29.9, 30.0, 33.8, 39.4, 55.3, 116.9, 151.4, 167.

5-Hydroxymethylfurfural (HMF)³

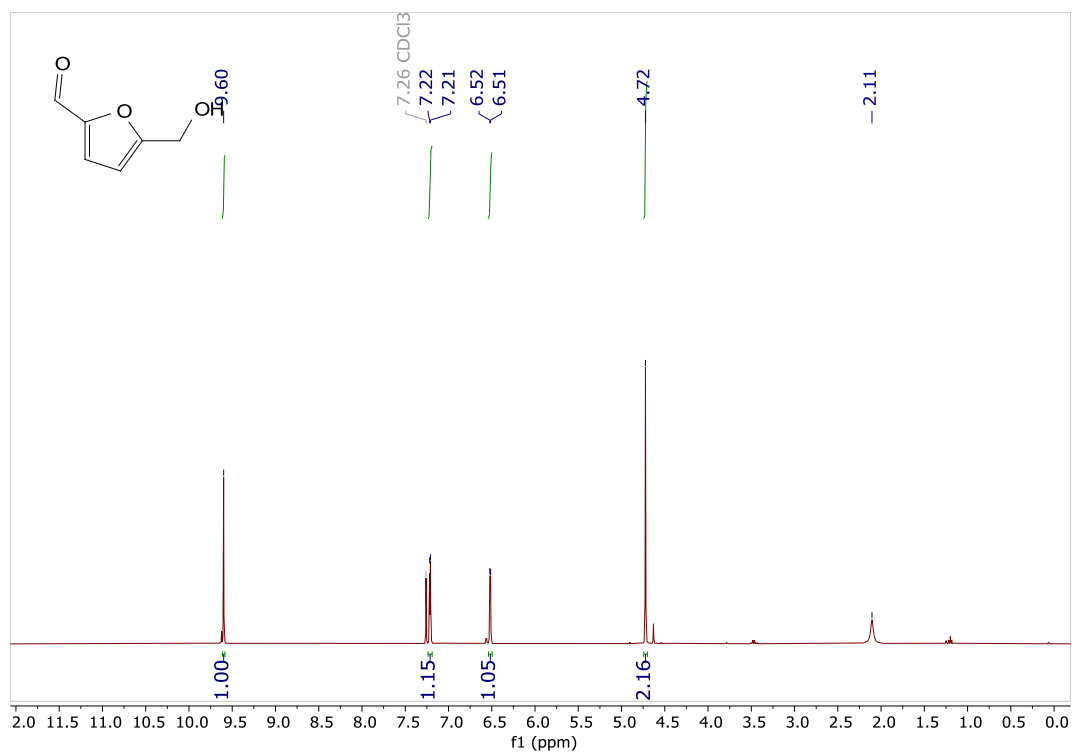


Figure S 15: ¹H NMR (400 MHz, CDCl₃) δ (ppm): 9.60 (s, 1H), 7.21 (d, J = 3.6 Hz, 1H), 6.52 (d, J = 3.5 Hz, 1H), 4.72 (s, 2H), 2.11 (br, OH).

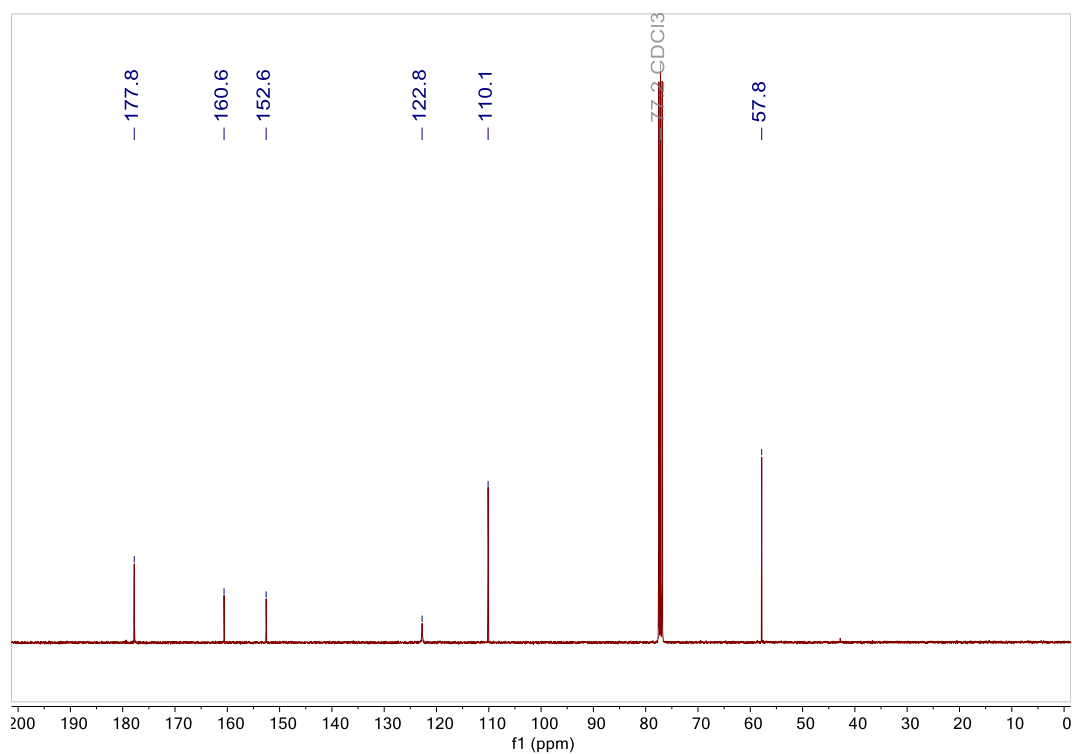


Figure S 16: ¹³C NMR (101 MHz, CDCl₃) δ (ppm): 177.8, 160.6, 152.6, 122.8, 110.1, 57.8.

5,5'-oxy(bis-methylene)-2-furaldehyde (OBMF)⁴

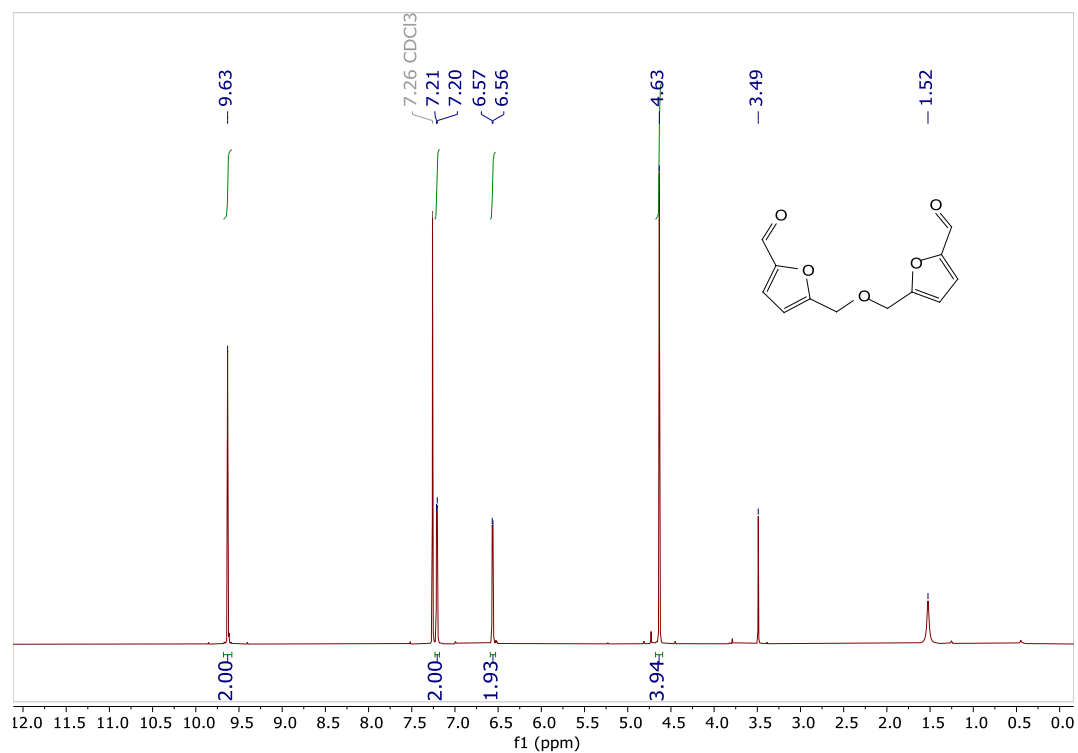


Figure S 17: ¹H NMR (400 MHz, CDCl₃) δ (ppm): 9.63 (s, 2H), 7.21 (d, J = 3.6 Hz, 2H), 6.56 (d, J = 3.5 Hz, 2H), 4.63 (s, 4H).

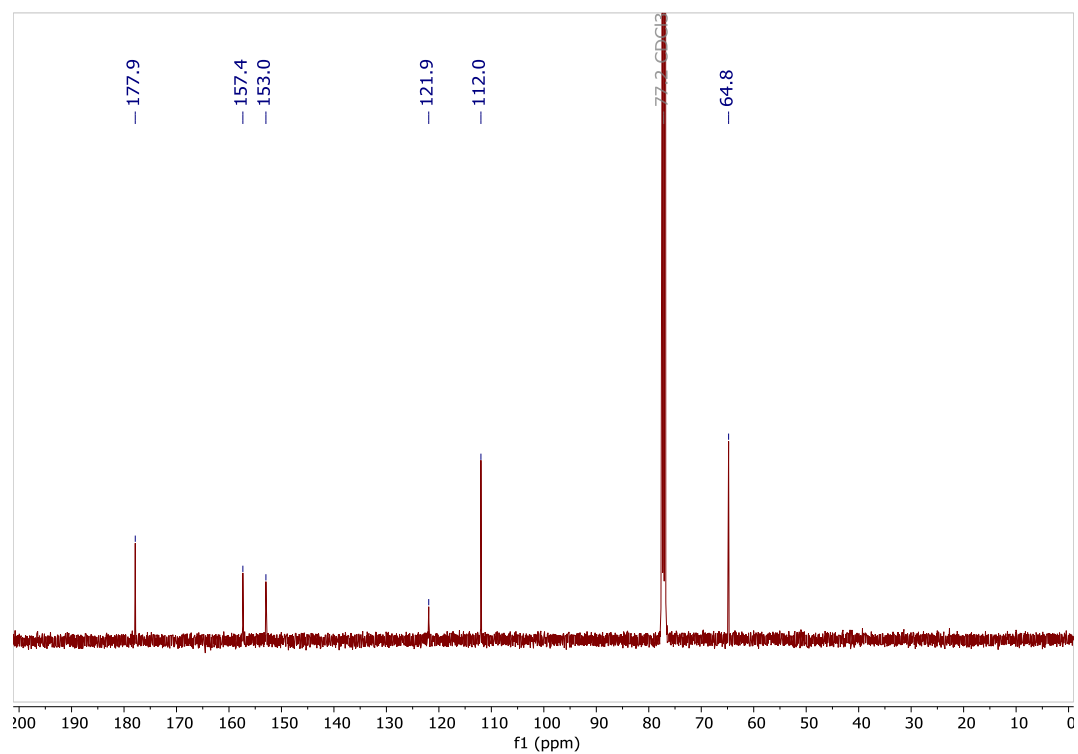


Figure S 18: ¹³C NMR (101 MHz, CDCl₃) δ (ppm): 177.9, 157.4, 153.0, 121.9, 112.0, 64.8.

Bis(hydroxymethyl)furan (BHMF)³

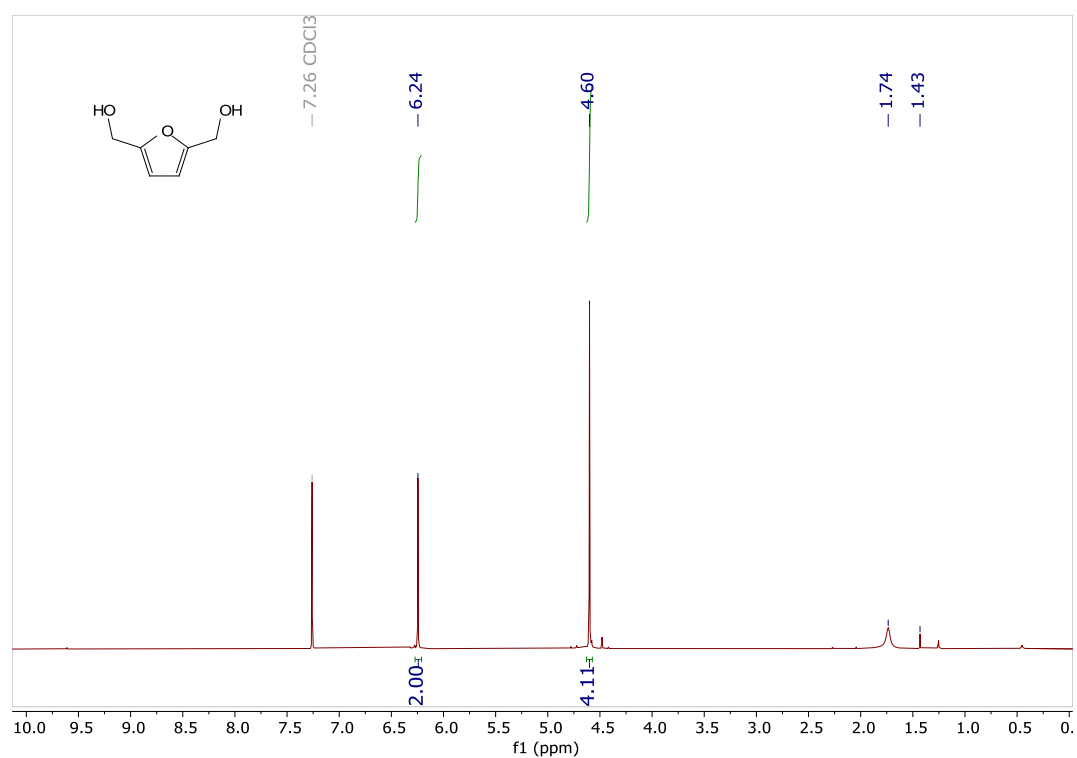


Figure S 19: ¹H NMR (400 MHz, CDCl₃) δ (ppm): 6.24 (s, 2H), 4.60 (s, 4H).

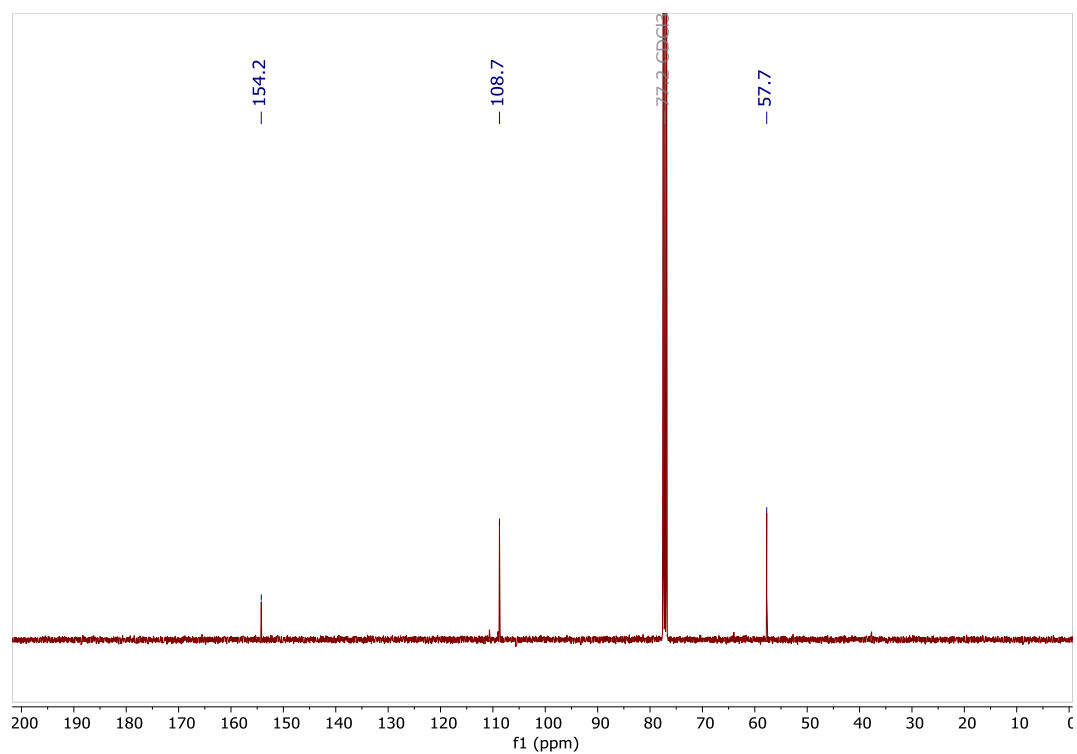


Figure S 20: ¹³C NMR (101 MHz, CDCl₃) δ (ppm): 154.2, 108.8, 57.7.

5,5'-oxybis(methylene)bis(furan-5,2-diyl)dimethanol (OBMF-H)⁴

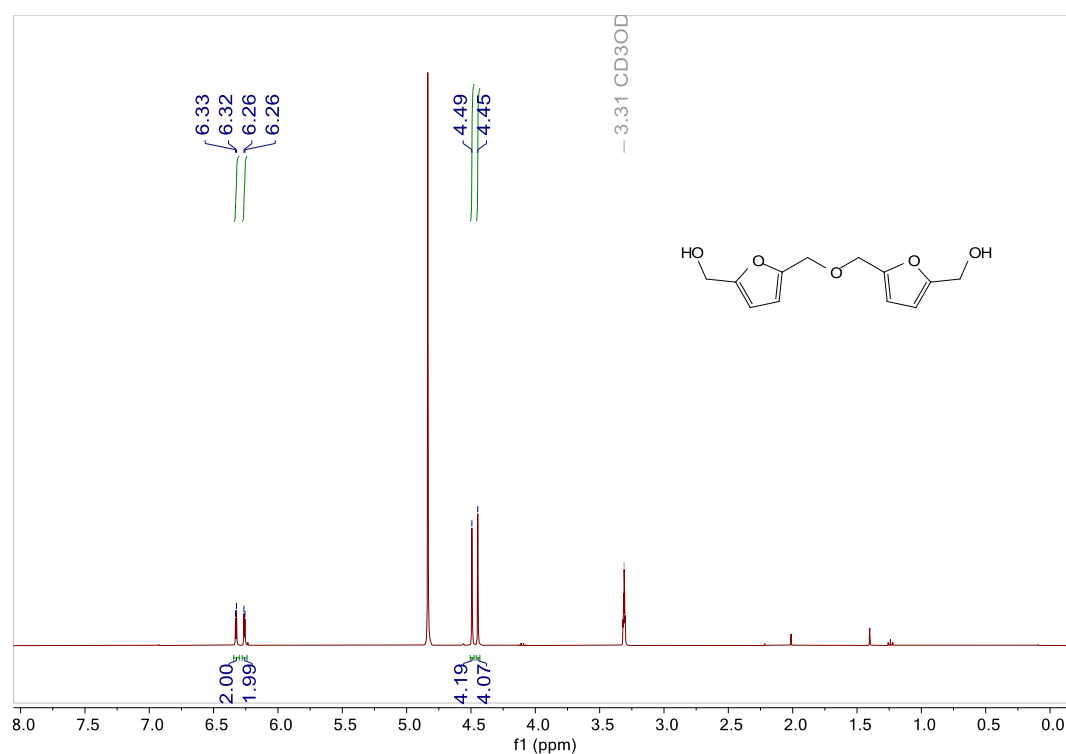


Figure S 21: ¹H NMR (400 MHz, MeOD-d₄) δ (ppm): 6.33 (d, J = 3.1 Hz, 2H), 6.26 (d, J = 3.1 Hz, 2H), 4.49 (s, 4H), 4.45 (s, 4H).

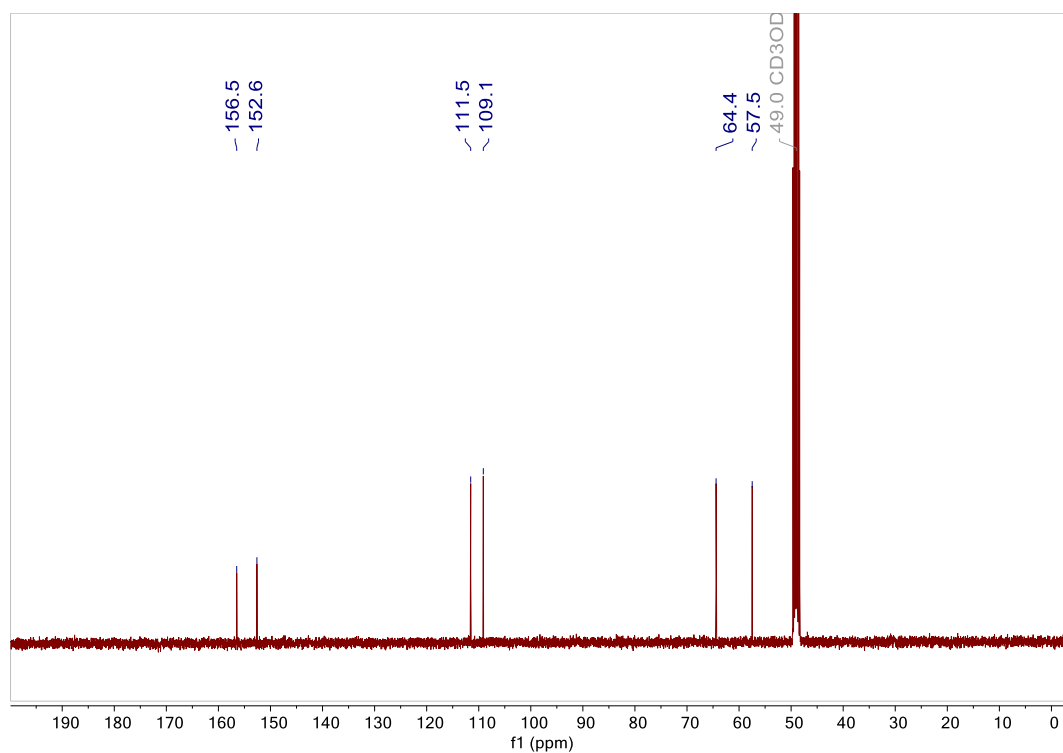


Figure S 22: ¹³C NMR (101 MHz, MeOD-d₄) δ (ppm): 156.5, 152.6, 111.5, 109.1, 64.4, 57.5.

2,5-bis(hydroxymethyl)tetrahydrofuran (BHTHF)⁵

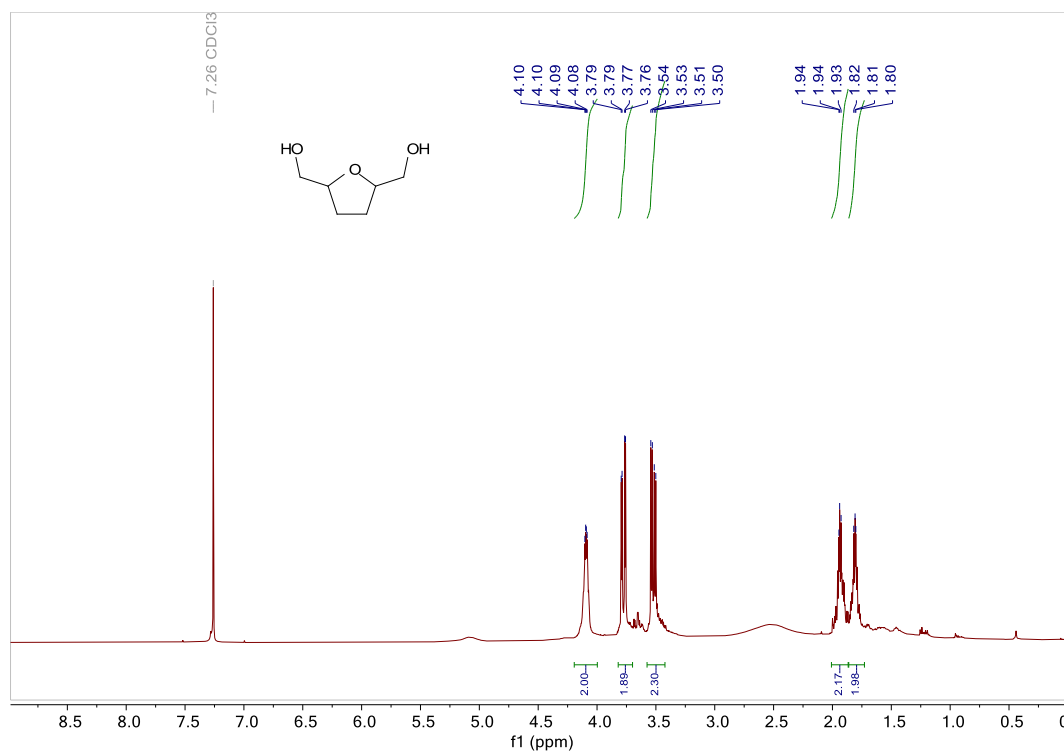


Figure S 23: ¹H NMR (400 MHz, CDCl₃) δ (ppm): 4.19 – 4.00 (m, 2H), 3.78 (dd, J = 11.7, 2.9 Hz, 2H), 3.52 (dd, J = 11.7, 5.2 Hz, 2H), 2.01 – 1.87 (m, 2H), 1.86 – 1.73 (m, 2H).

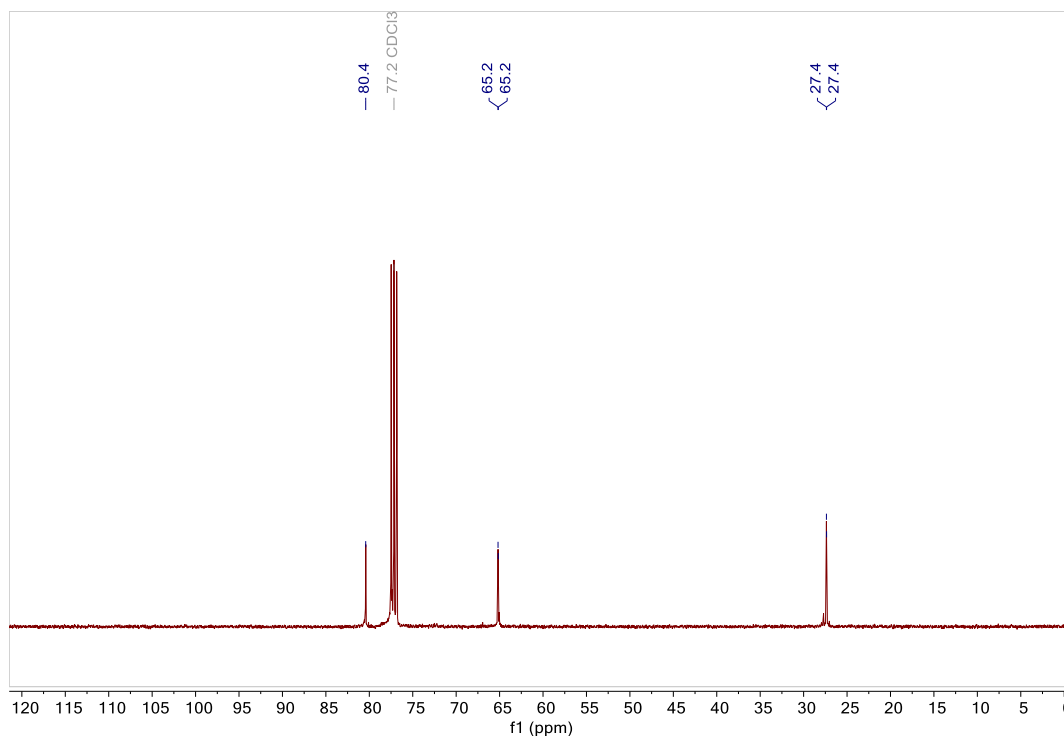


Figure S 24: ¹³C NMR (101 MHz, CDCl₃) δ (ppm): 80.4, 65.2, 65.2, 27.4, 27.4.

Tetrabutylammonium molybdate(VI) [N_{4,4,4,4}]₂[MoO₄]

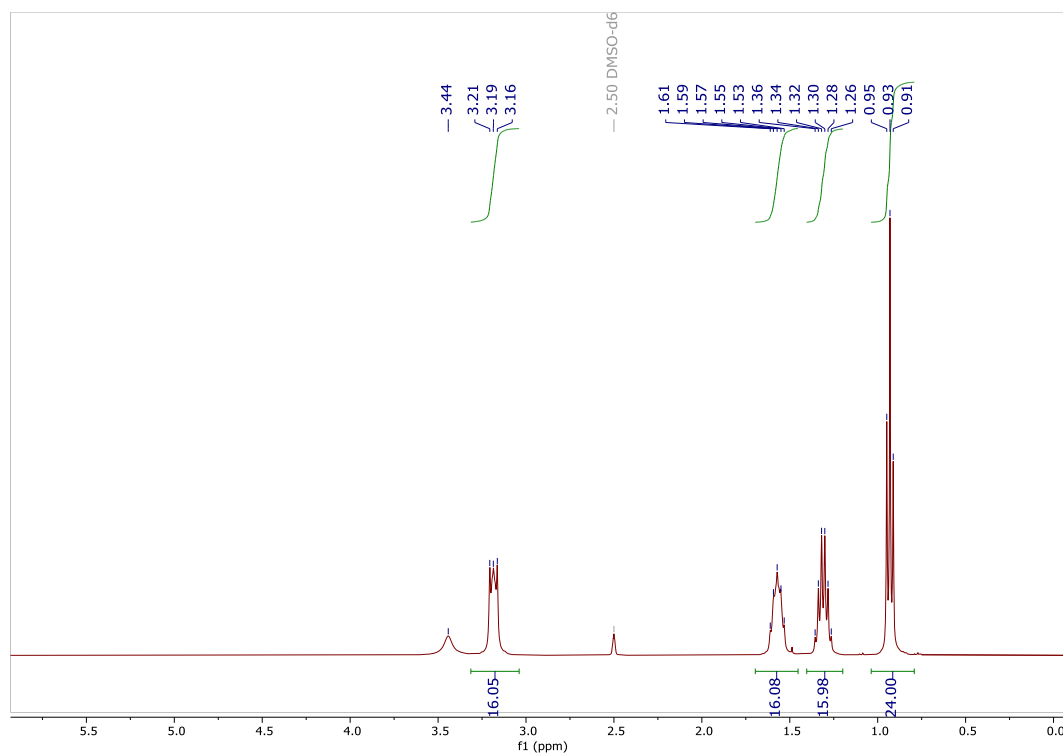


Figure S 25: ¹H NMR (400 MHz, DMSO-d₆) δ (ppm): 3.31 – 3.04 (m, 16H), 1.57 (m, 16H), 1.31 (m, 16H), 0.93(t, J = 7.4 Hz, 24H).

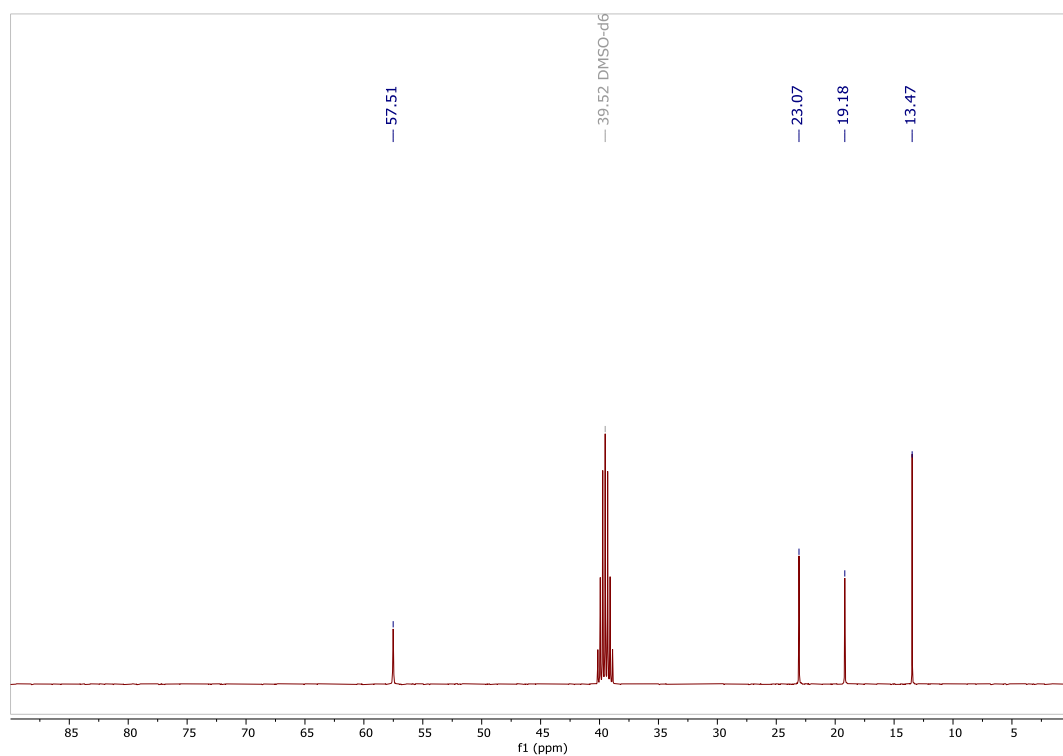


Figure S 26: ¹³C NMR (101 MHz, DMSO-d₆) δ (ppm): 57.51; 23.07; 19.18; 13.47.

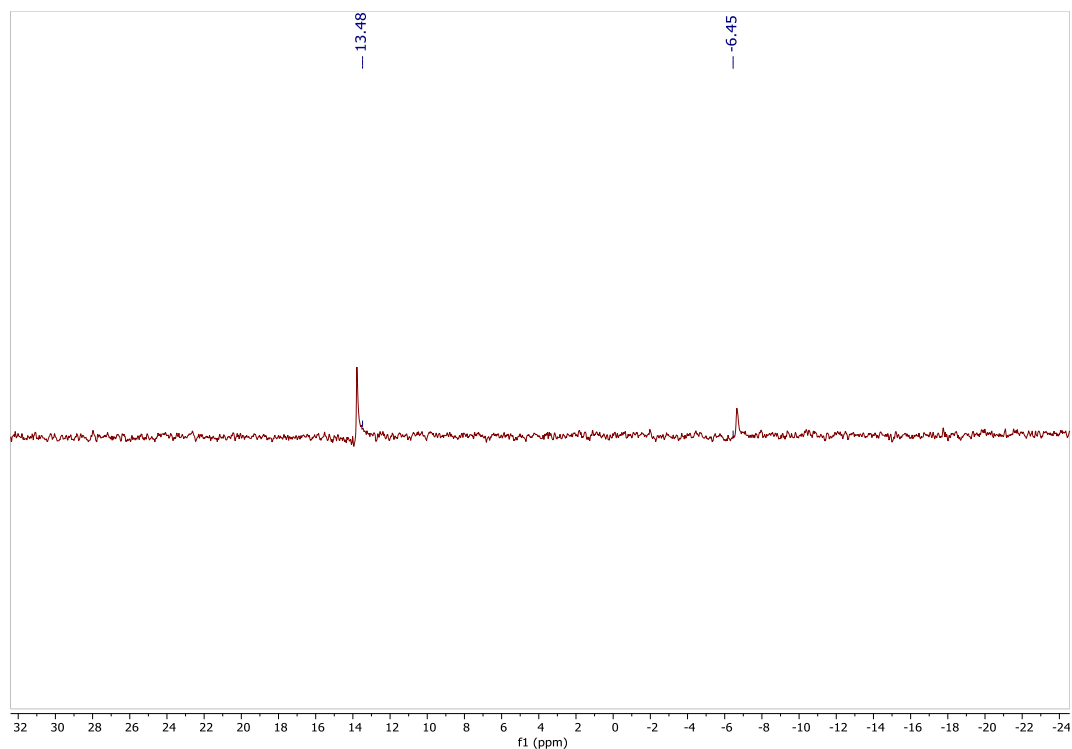


Figure S 27: ^{95}Mo NMR (26 MHz, DMSO-d_6) δ (ppm): 13.48.

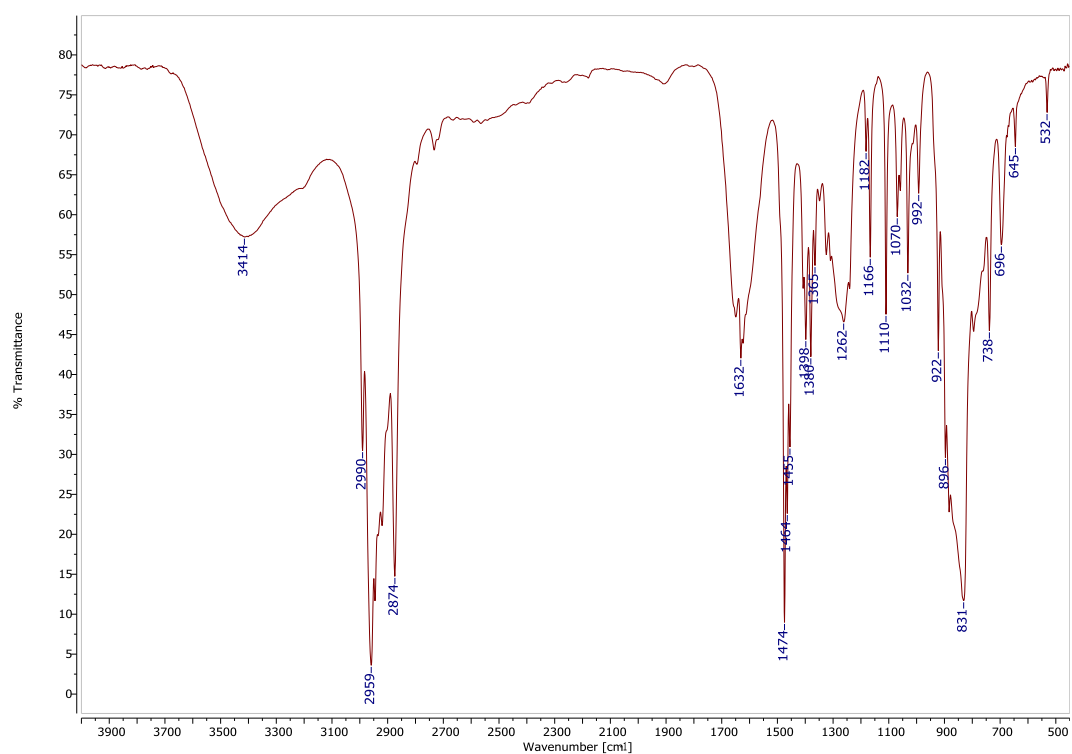


Figure S 28: FT-IR spectrum of $[\text{N}_{4444}]_2[\text{MoO}_4]$ (KBr).

Tetrabutylammonium dimolybdate(VI) [N_{4,4,4,4}]₂[Mo₂O₇]

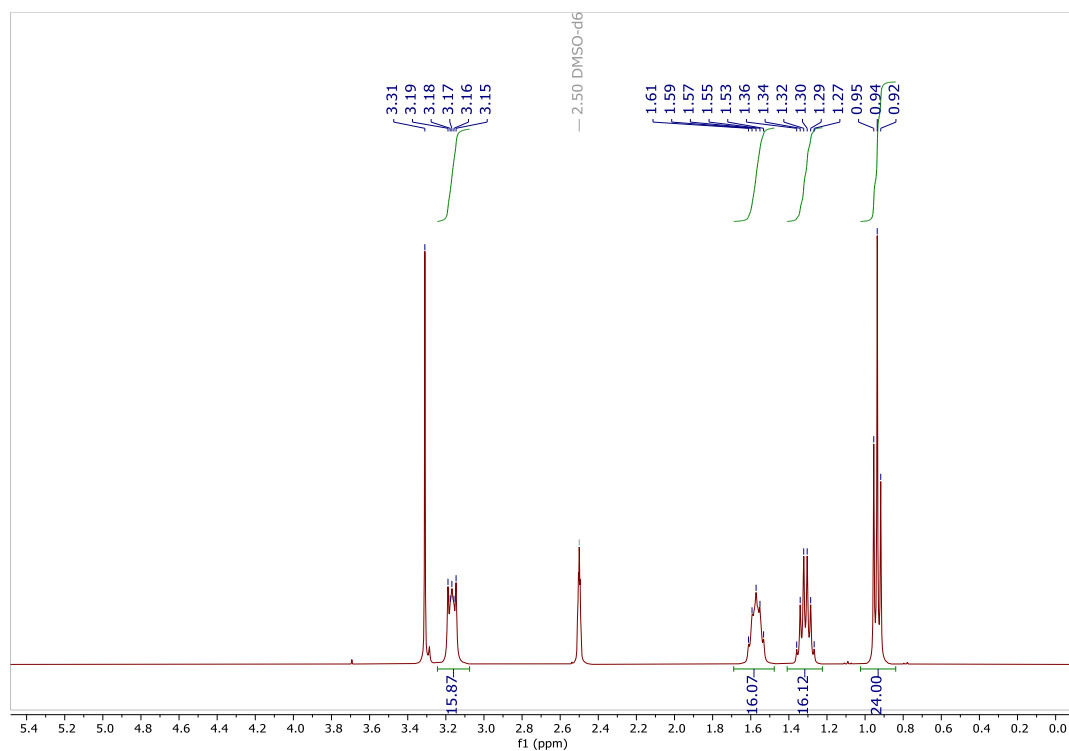


Figure S 29: ¹H NMR (400 MHz, DMSO-d₆) δ (ppm): 3.24 – 3.08 (m, 16H), 1.57 (m, 16H), 1.31 (m, 16H), 0.94 (t, J = 7.3 Hz, 24H).

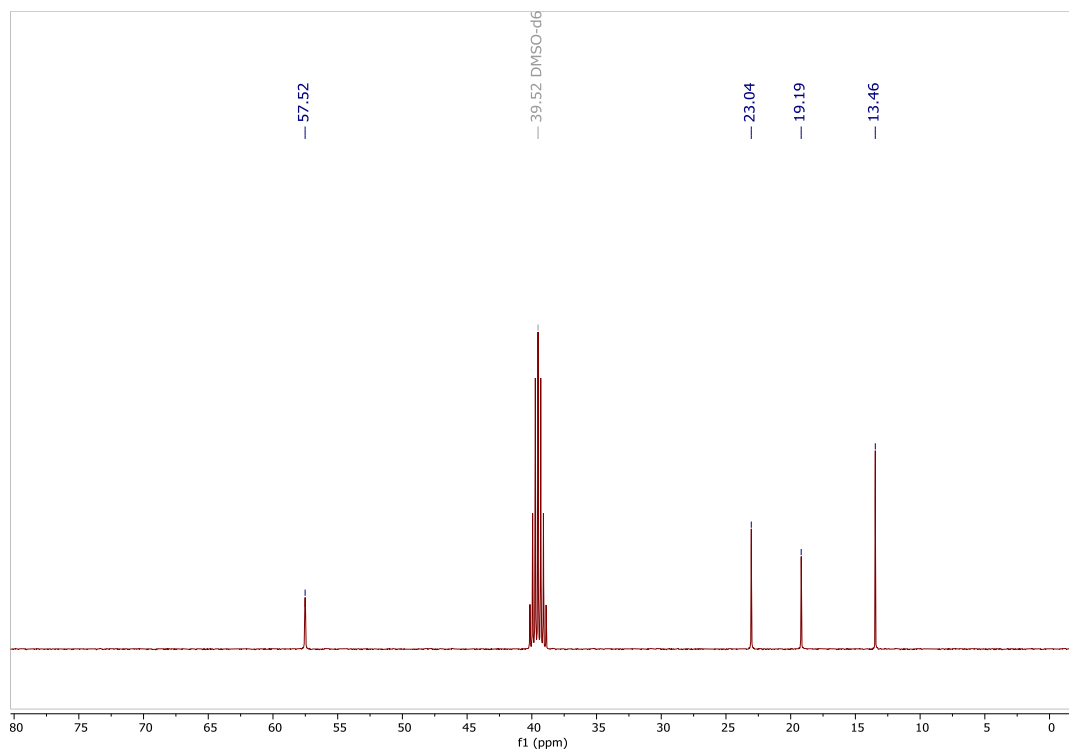


Figure S 30: ¹³C NMR (101 MHz, DMSO-d₆) δ (ppm): 57.51; 23.04; 19.19; 13.46.

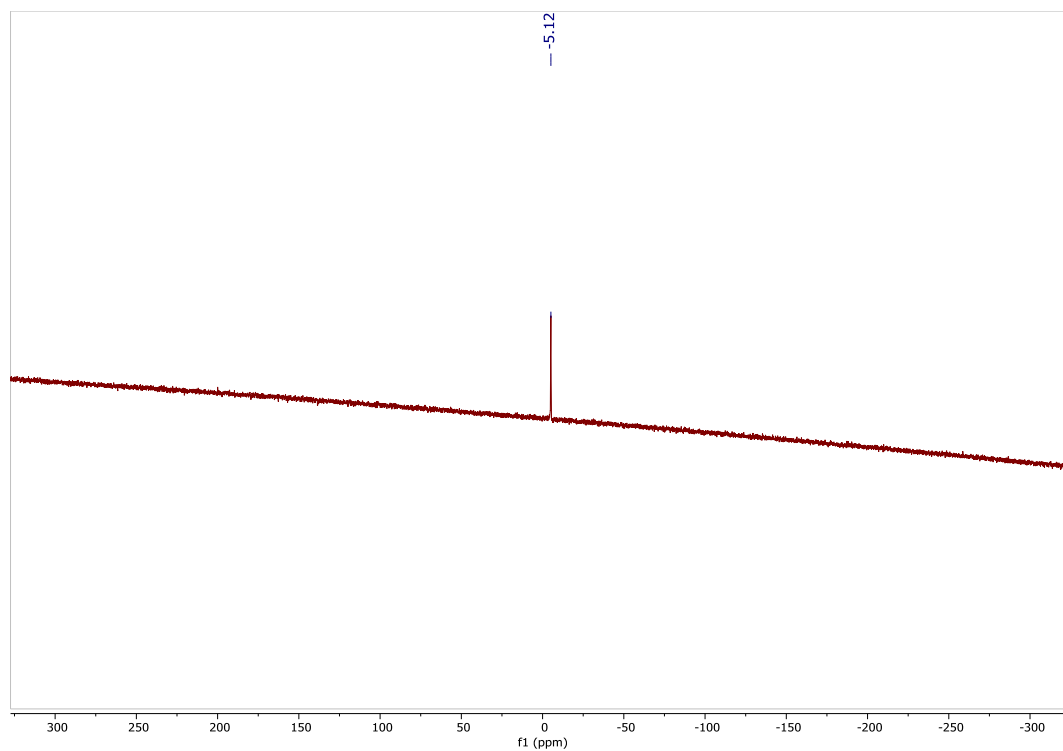


Figure S 31: ^{95}Mo NMR (26 MHz, DMSO-d_6) δ (ppm): -5.12.

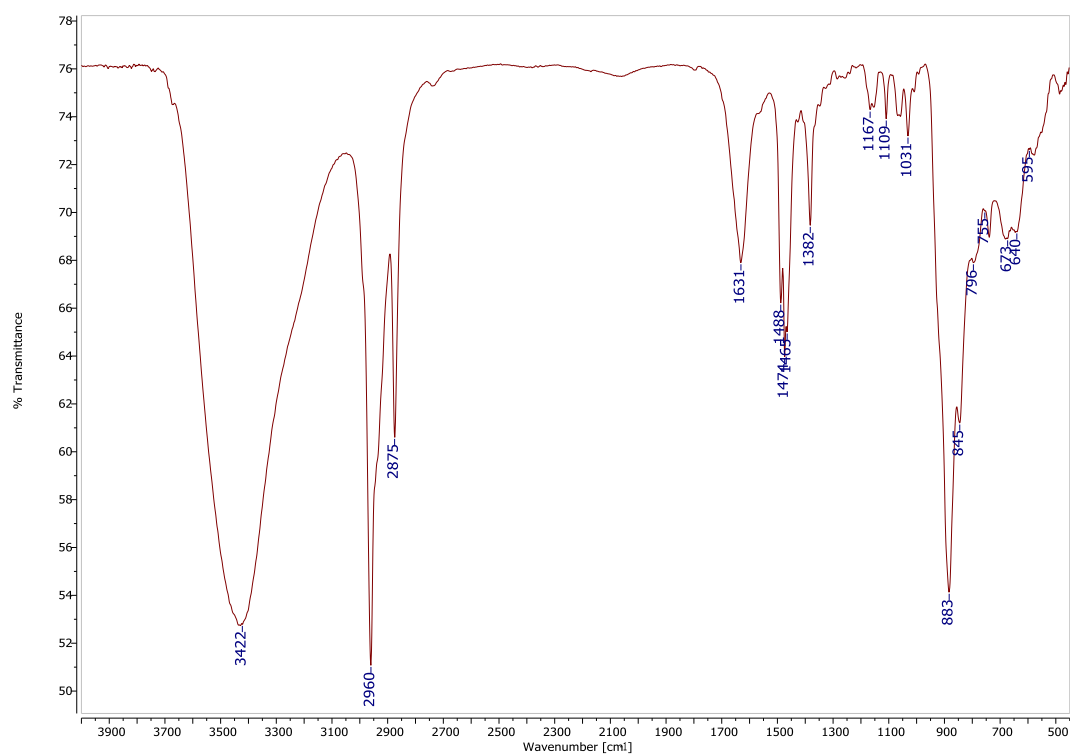


Figure S 32: FT-IR spectrum of $[\text{N}_{4444}]_2[\text{Mo}_2\text{O}_7]$ (KBr).

Tetrabutylammonium hexamolybdate(VI) [N_{4,4,4,4}]₂[Mo₆O₁₉]

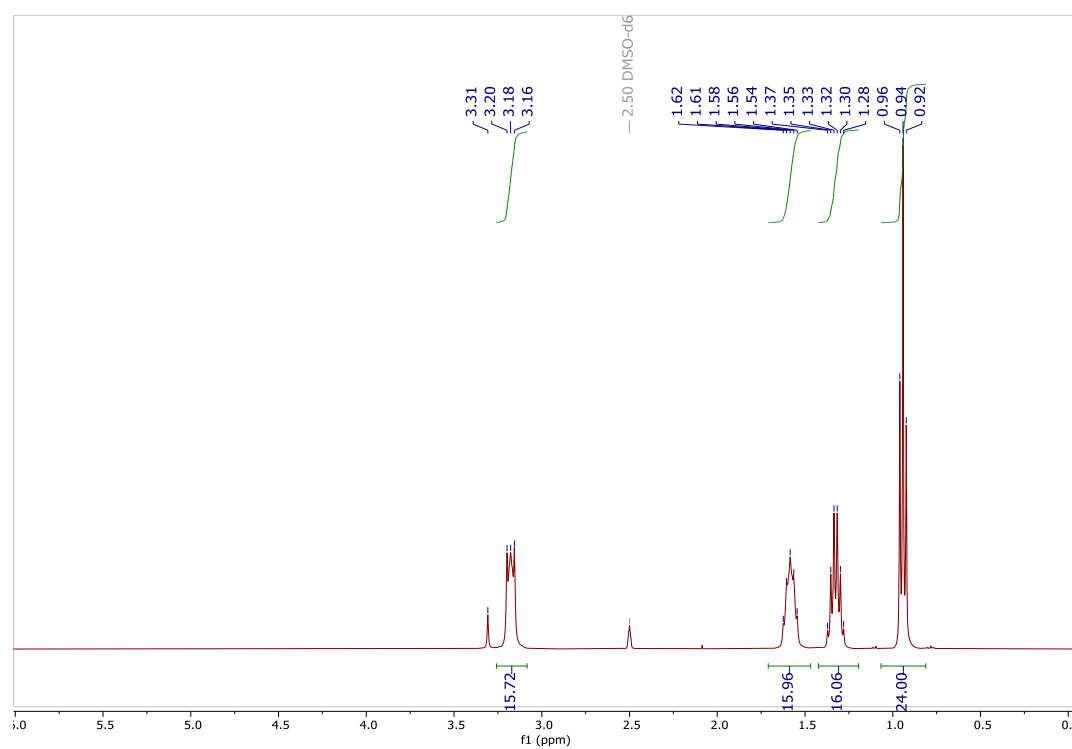


Figure S 33: ¹H NMR (400 MHz, DMSO-d₆) δ (ppm): 3.26 – 3.08 (m, 16H), 1.58 (m, 16H), 1.33 (m, 16H), 0.94 (t, J = 7.3 Hz, 24H).

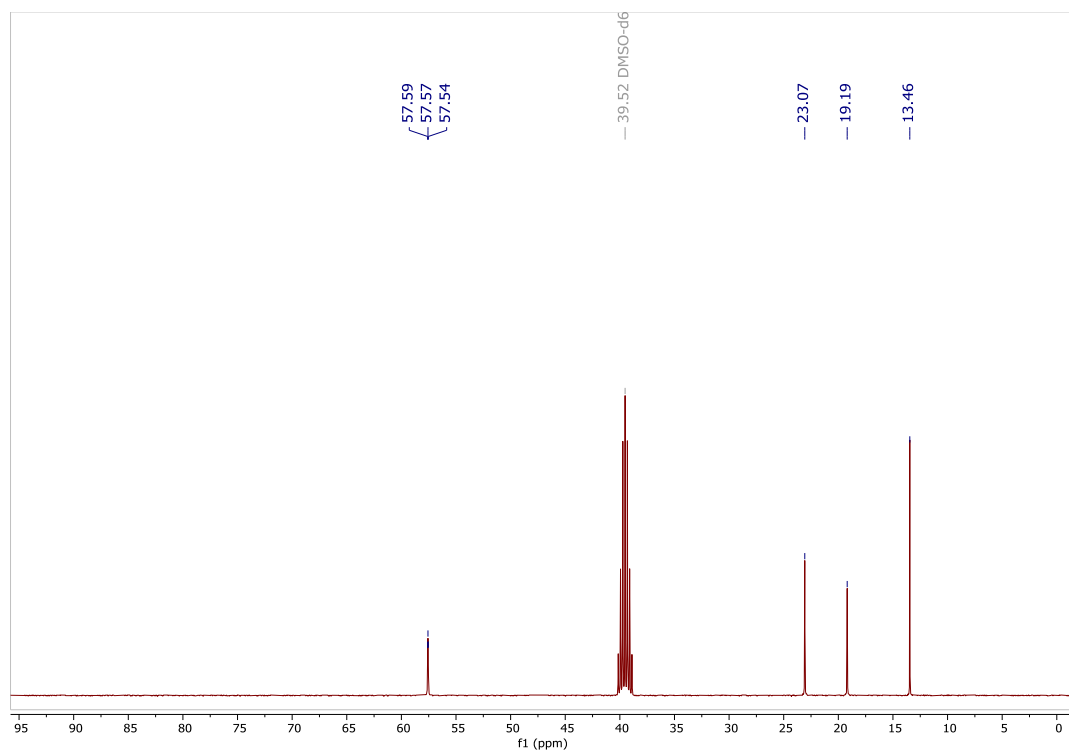


Figure S 34: ¹³C NMR (101 MHz, DMSO-d₆) δ (ppm): 57.57; 23.07; 19.19; 13.46.

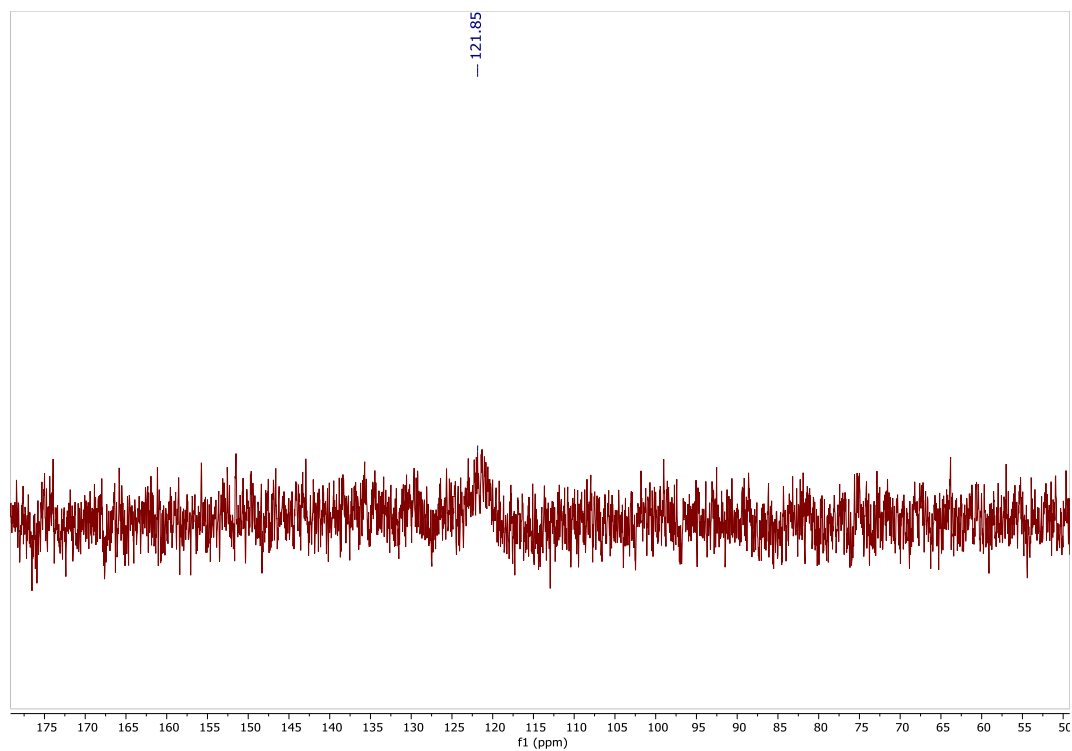


Figure S 35: ^{95}Mo NMR (26 MHz, CD_3CN) δ (ppm): 121.85.

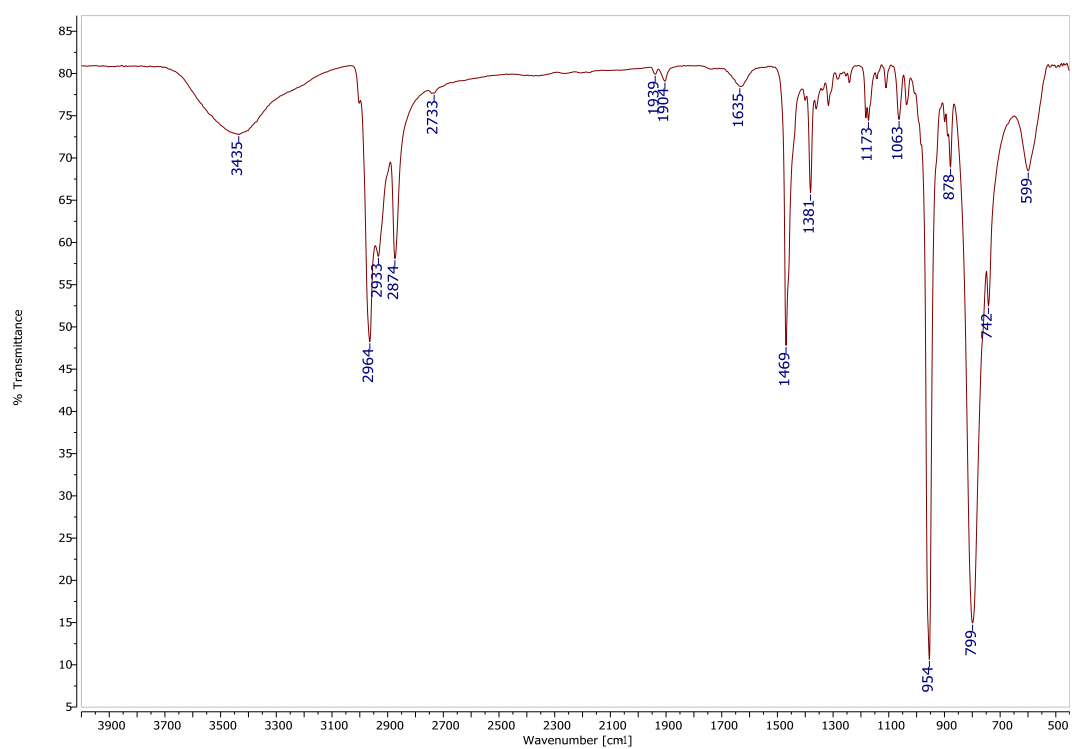


Figure S 36: FT-IR spectrum of $[\text{N}_{444}]_2[\text{Mo}_6\text{O}_{19}]$ (KBr).

Tetrabutylammonium octamolybdate(VI) [N_{4,4,4,4}]₄[Mo₈O₂₆]

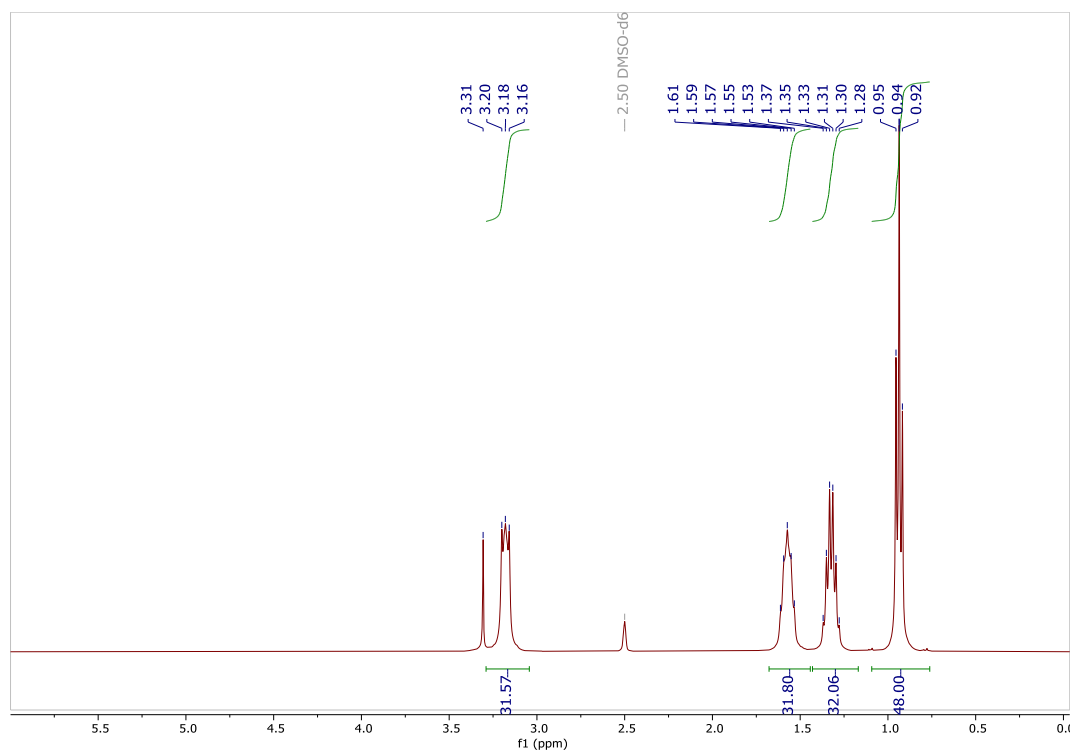


Figure S 37: ¹H NMR (400 MHz, DMSO-d₆) δ (ppm): 3.29 – 3.04 (m, 32H), 1.57 (m, 32H), 1.32 (m, 32H), 0.94 (t, J = 7.3 Hz, 48H).

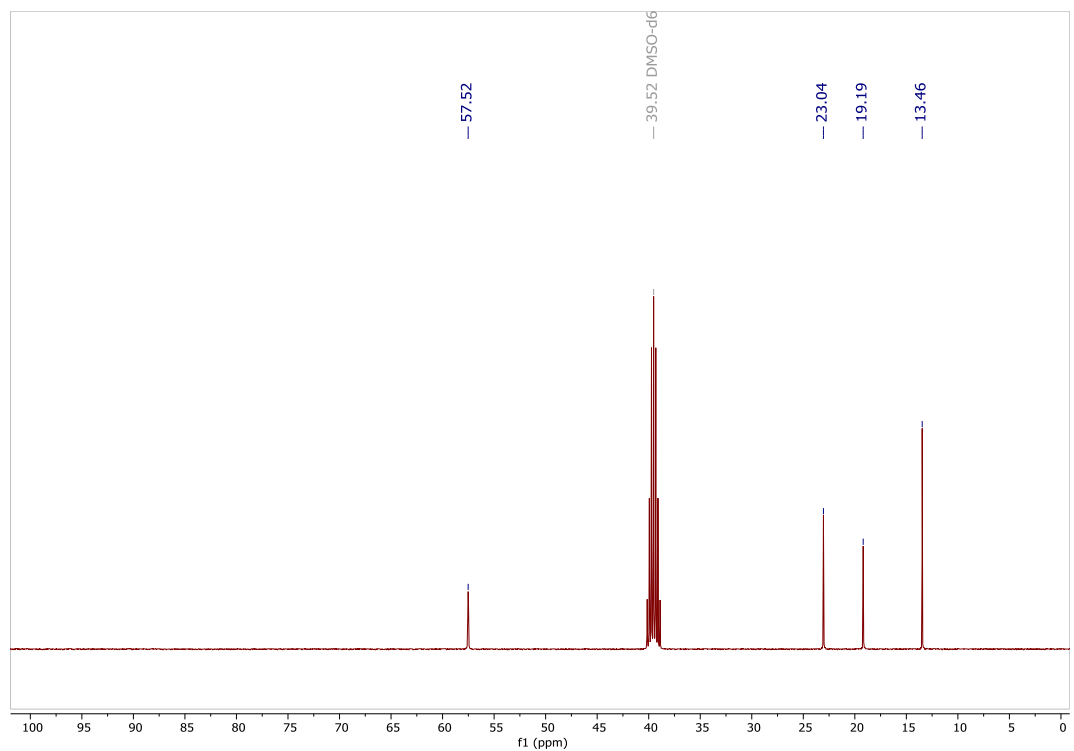


Figure S 38: ¹³C NMR (101 MHz, DMSO-d₆) δ (ppm): 57.52; 23.04; 19.19; 13.46.

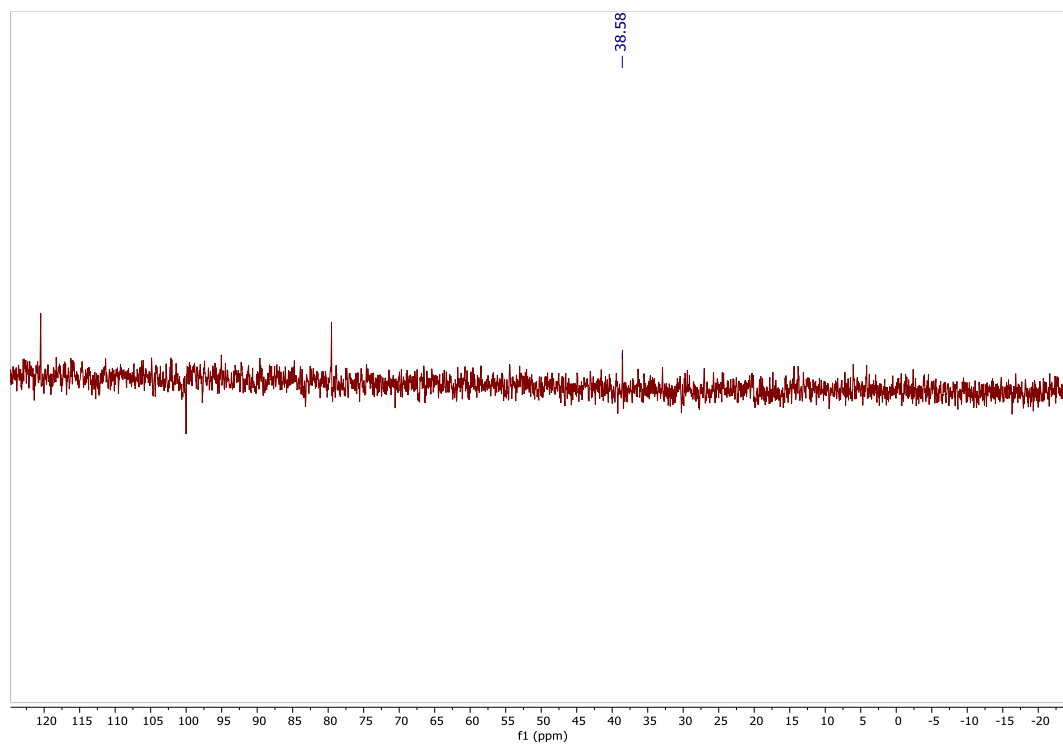


Figure S 39: ^{95}Mo NMR (26 MHz, DMSO- d_6) δ (ppm): 38.58; spike signals are present at 120, 100 and 80 ppm.

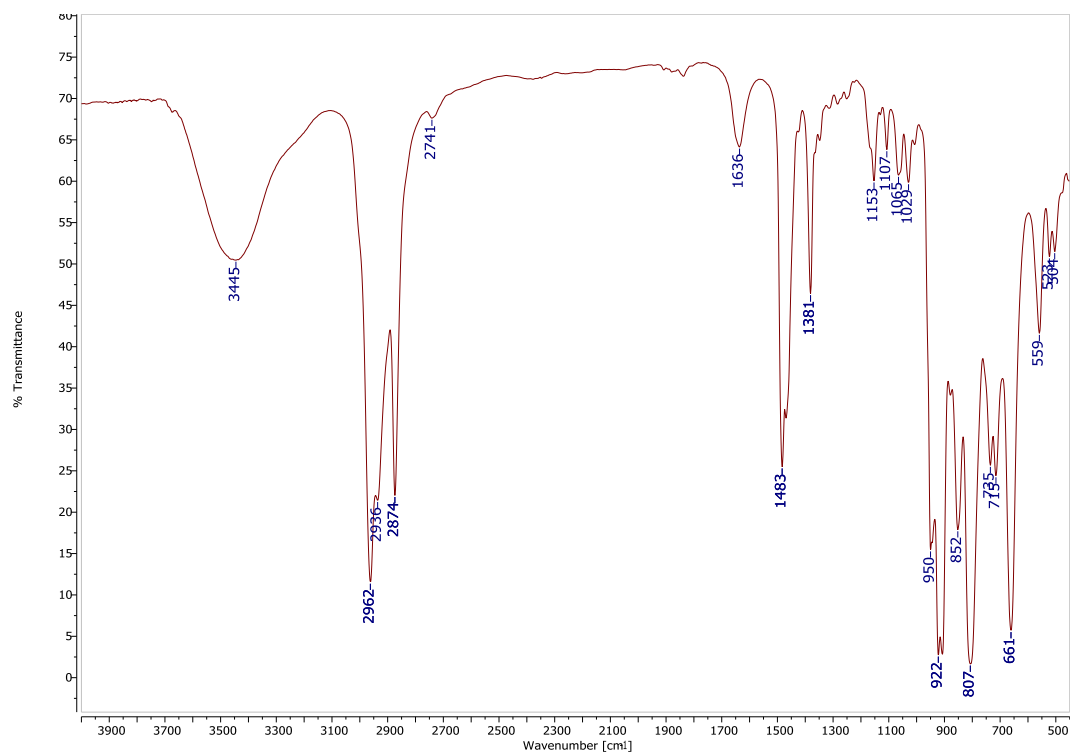


Figure S 40: FT-IR spectrum of $[\text{N}_{4444}]_4[\text{Mo}_8\text{O}_{26}]$ (KBr).

Trioctylmethylammonium molybdate(VI) [N_{8,8,8,1}]₂[MoO₄]

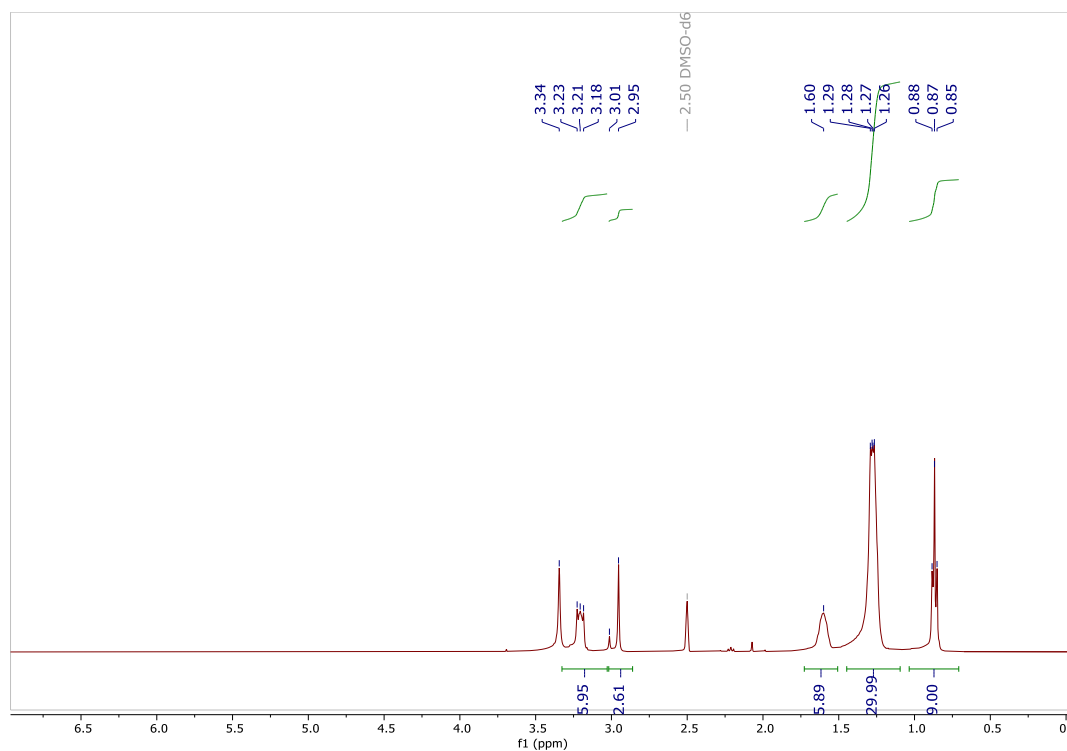


Figure S 41: ¹H NMR (400 MHz, DMSO-d₆, 298 K) δ (ppm): 3.33 – 3.03 (m, 6H), 2.95 (s, 3H), 1.73-1.51 (m, 6H), 1.45 – 1.09 (m, 30H), 0.87 (t, J = 6.6 Hz, 9H).

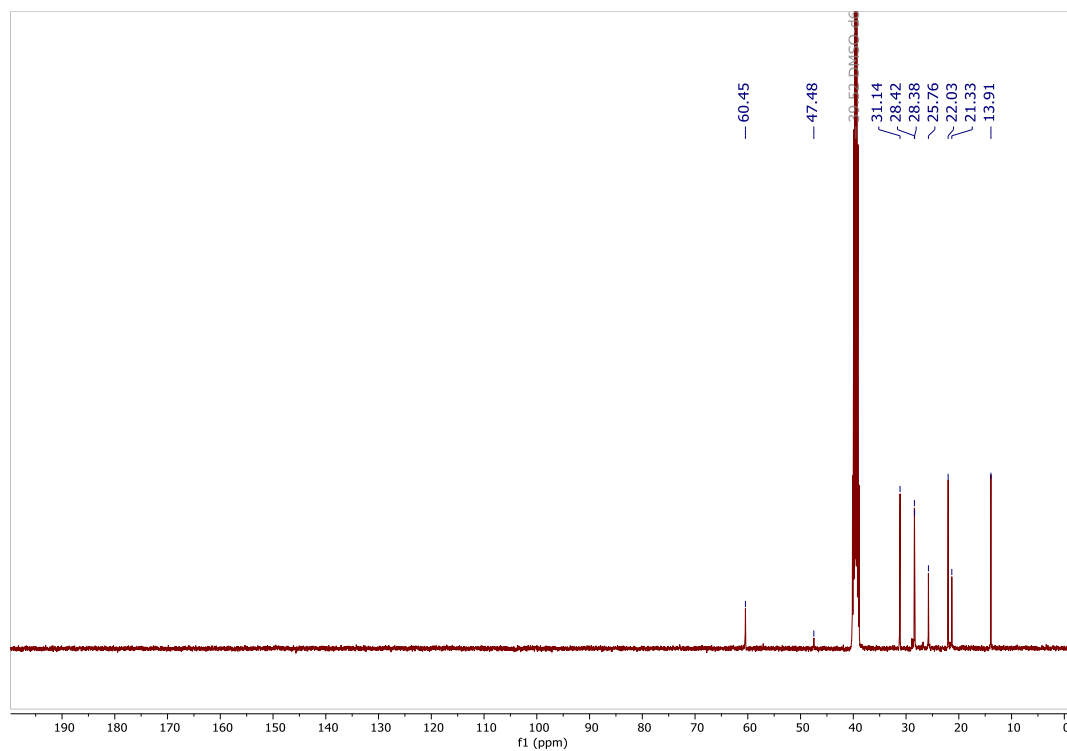


Figure S 42: ¹³C NMR (101 MHz, DMSO-d₆, 298 K) δ (ppm): 60.45; 47.48; 31.14; 28.42; 28.38; 25.76; 22.03; 21.33; 13.91.

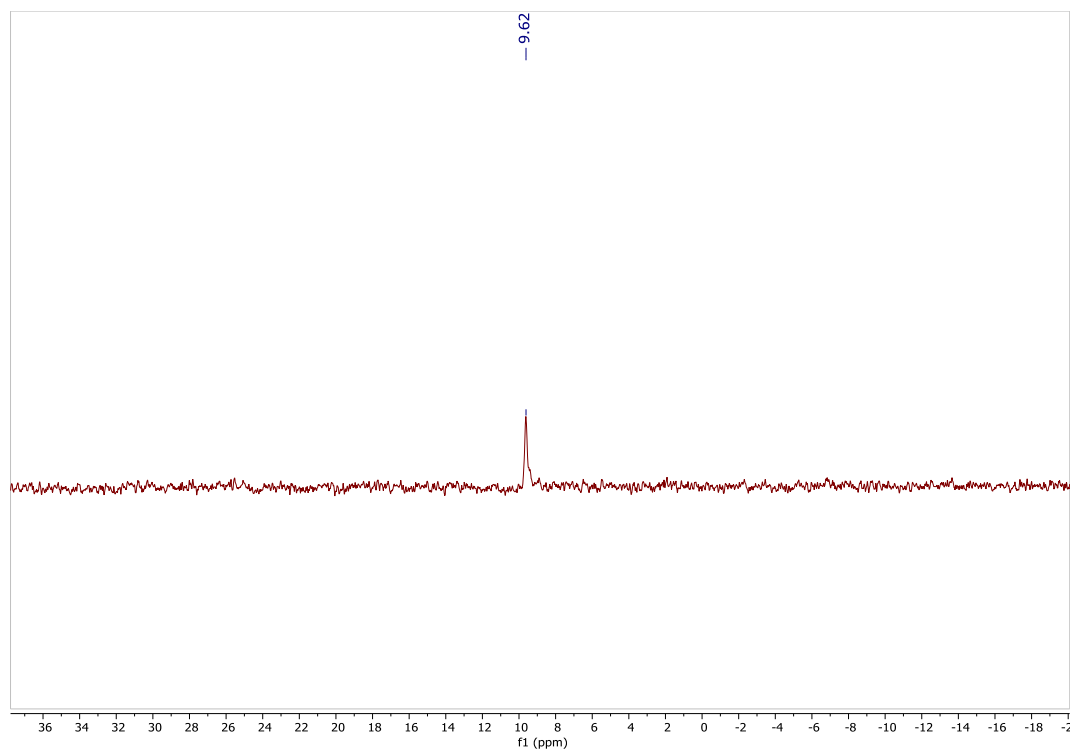


Figure S 43: ^{95}Mo NMR (26 MHz, DMSO-d_6) δ (ppm): 9.62.

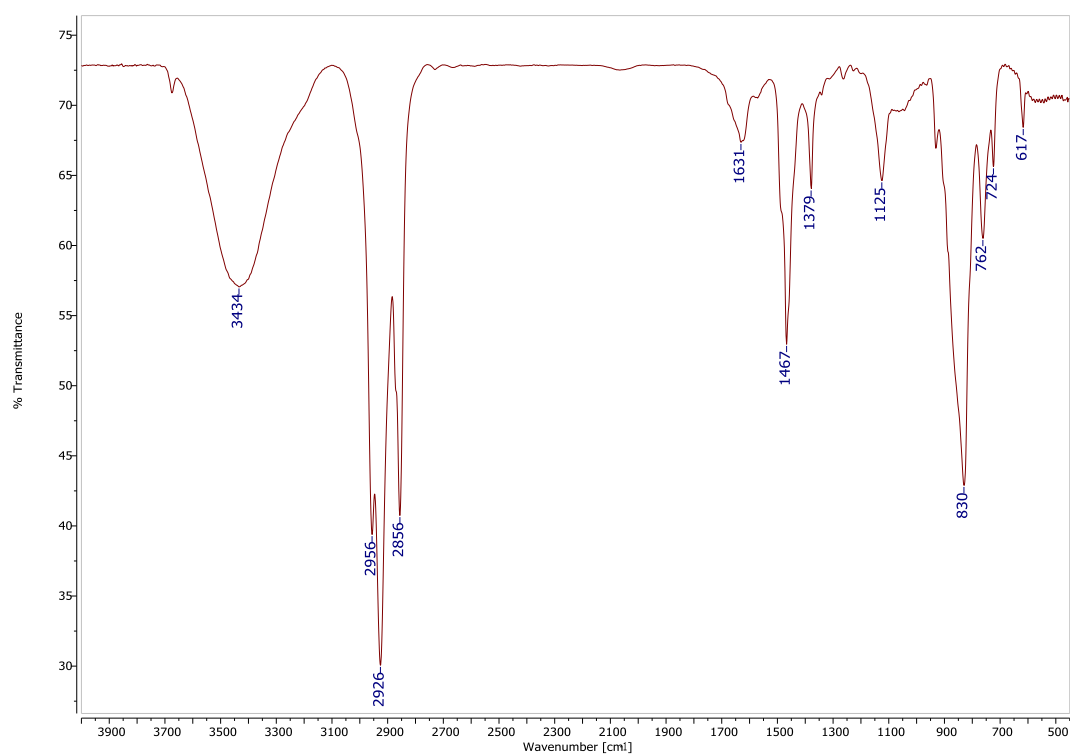


Figure S 44: FT-IR spectrum of $[\text{N}_{1888}]_2[\text{MoO}_4]$ (KBr).

Tetrabutylphosphonium molybdate(VI) [P_{4,4,4,4}]₂[MoO₄]

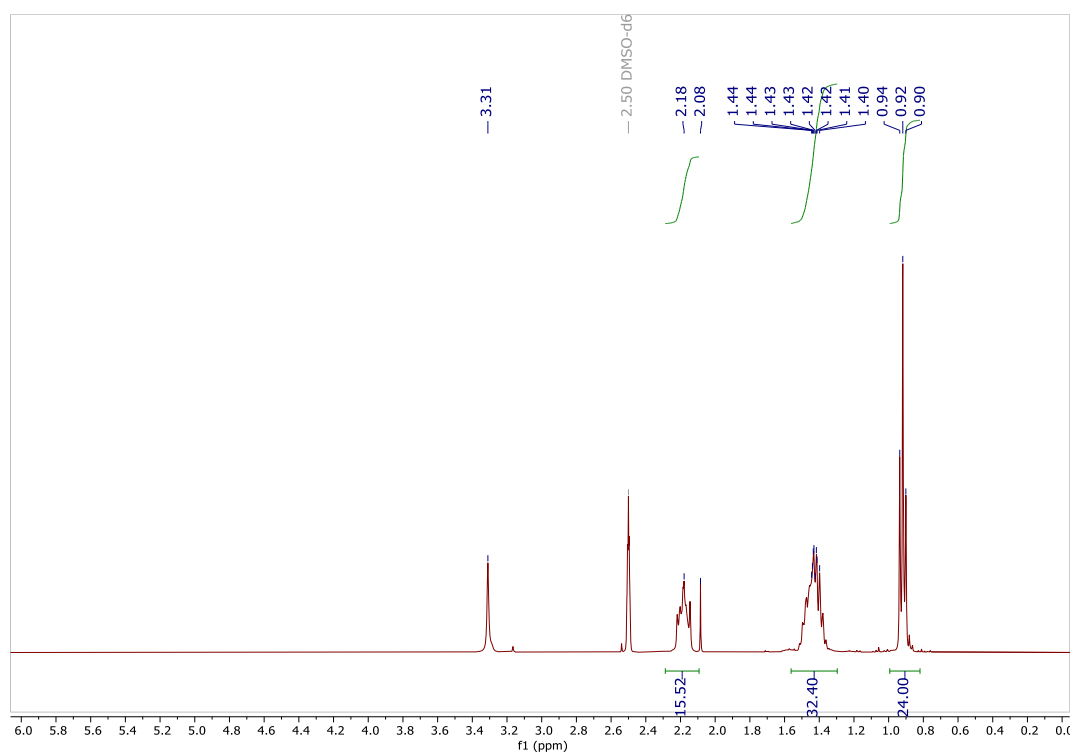


Figure S 45: ¹H NMR (400 MHz, DMSO-d₆) δ (ppm): 2.18 (m, 16H), 1.56 – 1.30 (m, 32H), 0.92 (t, J = 7.0 Hz, 24H).

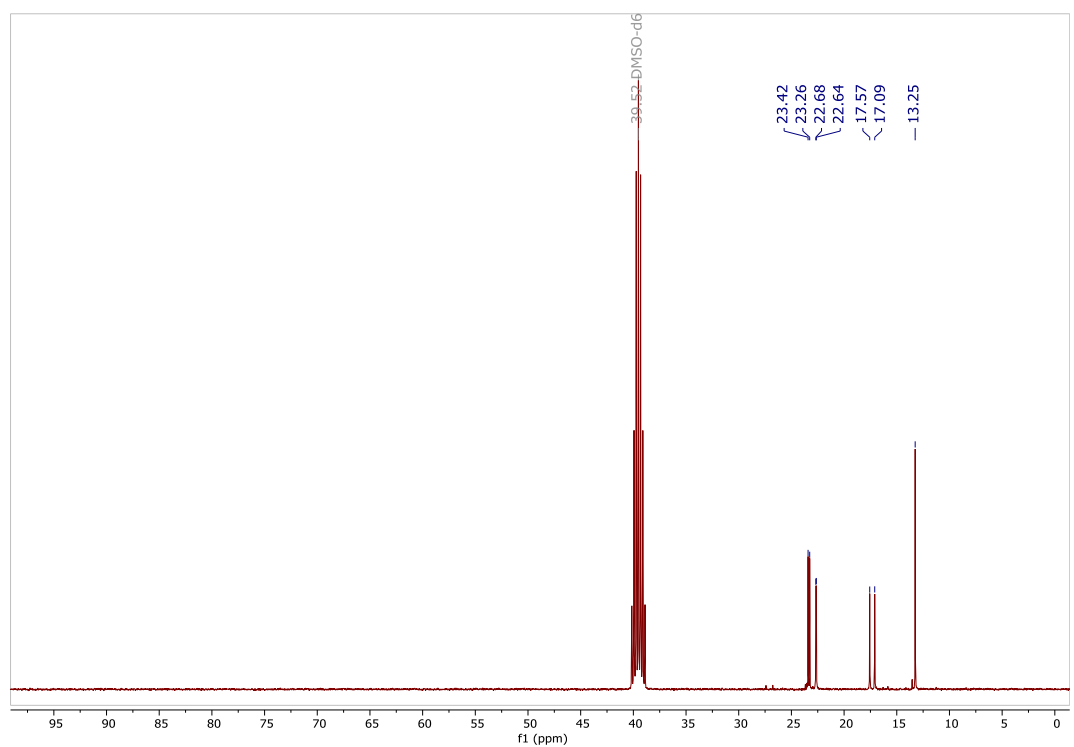
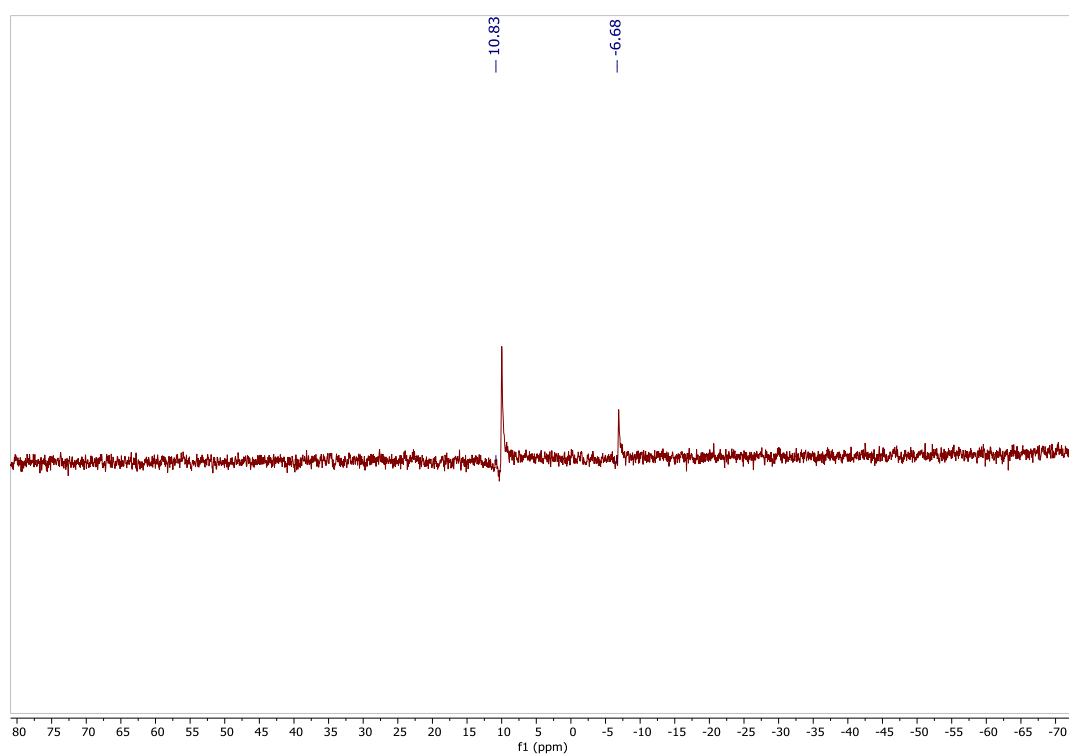
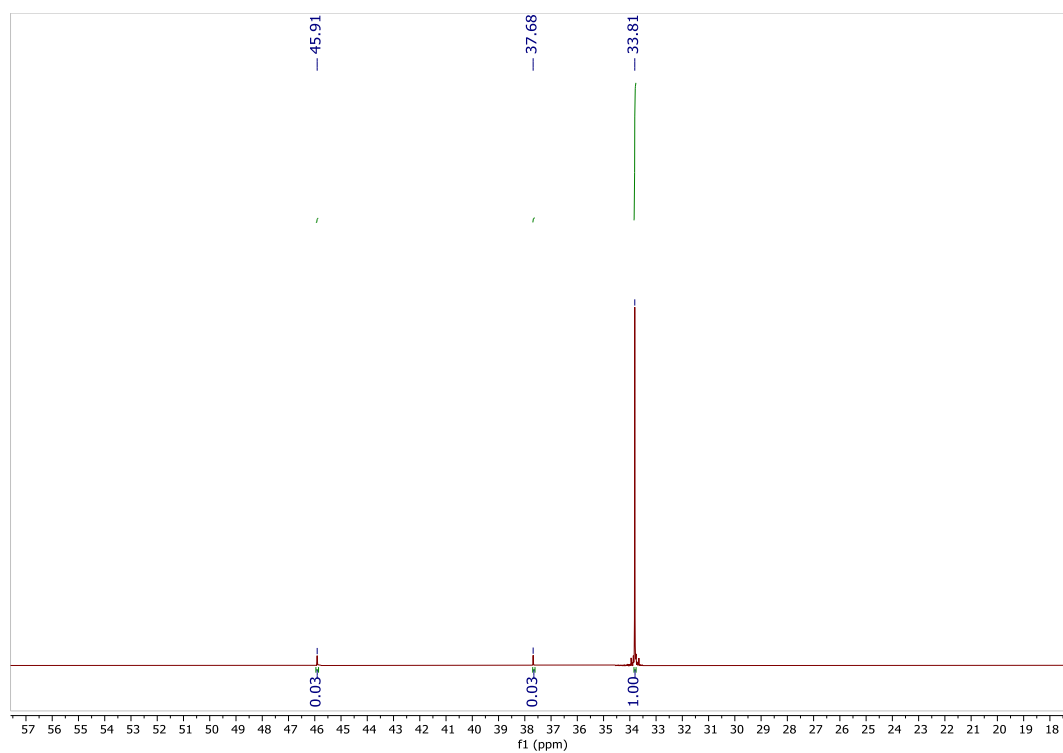


Figure S 46: ¹³C NMR (101 MHz, DMSO) δ 23.42, 23.26, 22.68, 22.64, 17.57, 17.09, 13.25.



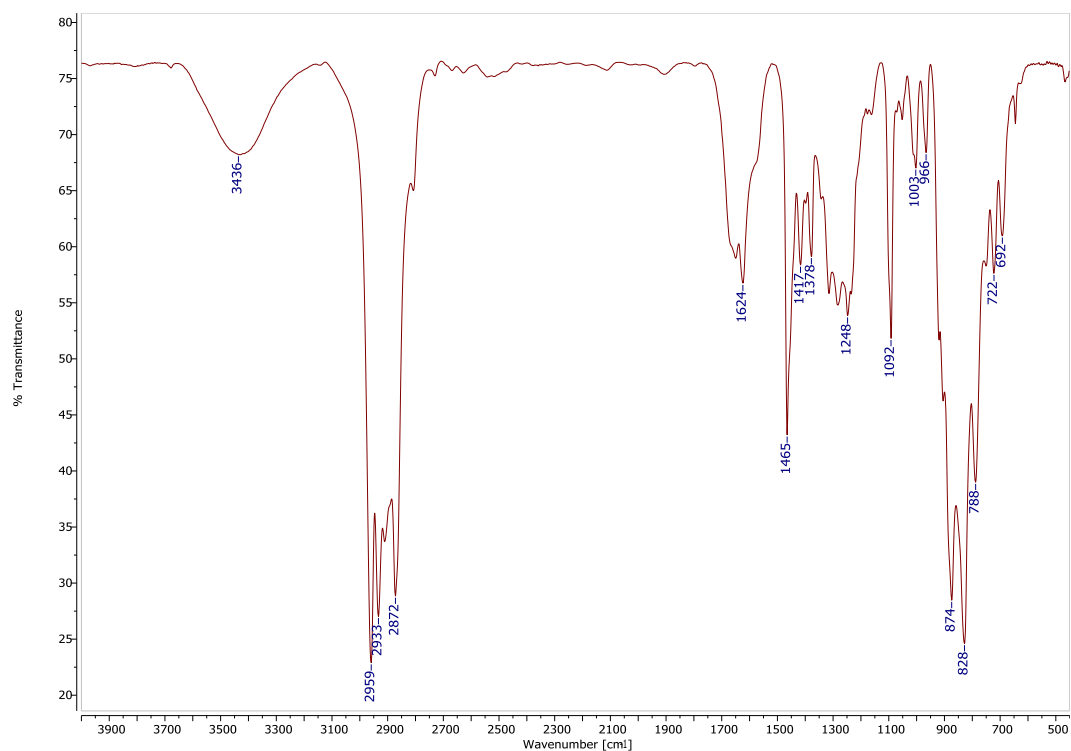


Figure S 49: FT-IR spectrum of $[P_{4444}]_2[MoO_4]$ (KBr).

1-butyl-3-methylimidazolium molybdate(VI) $[C_4C_1im]_2[MoO_4]$

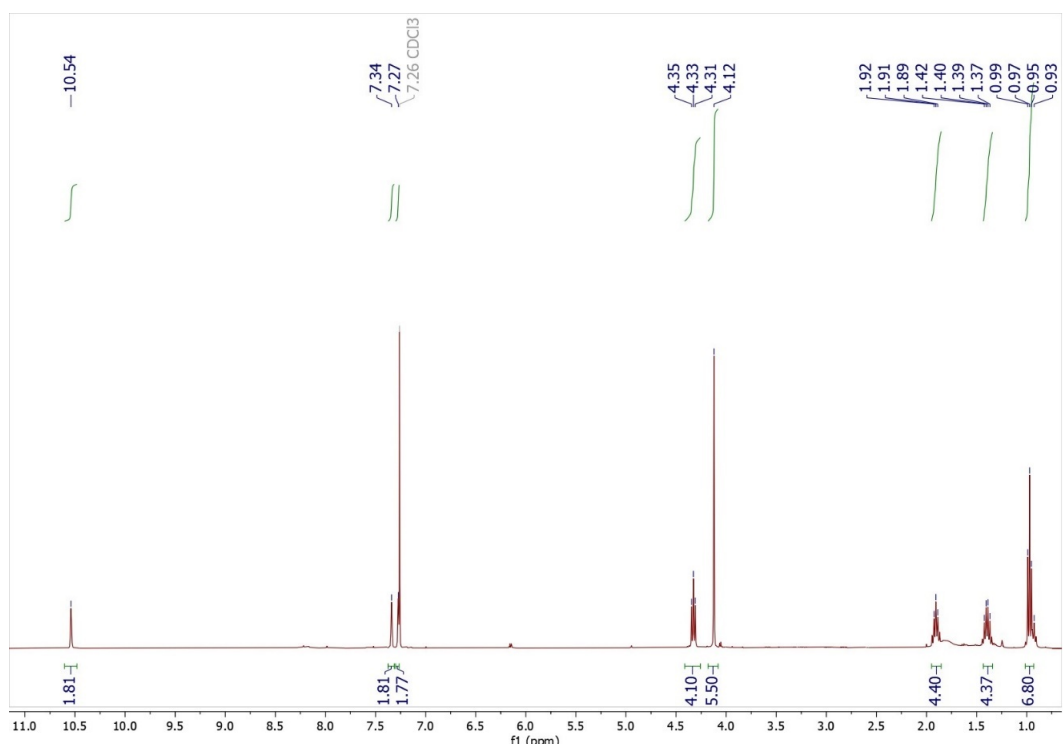


Figure S 50: 1H NMR (400 MHz, $DMSO-d_6$) δ (ppm): 10.54 (s, 2H), 7.34, (d, 2H), 7.27 (d, 2H), 4.33 (m, 4H), 4.12 (s, 6H), 1.91 (m, 4H), 1.39 (m, 4H), 0.95 (t, $J = 7.1$ Hz, 6H).

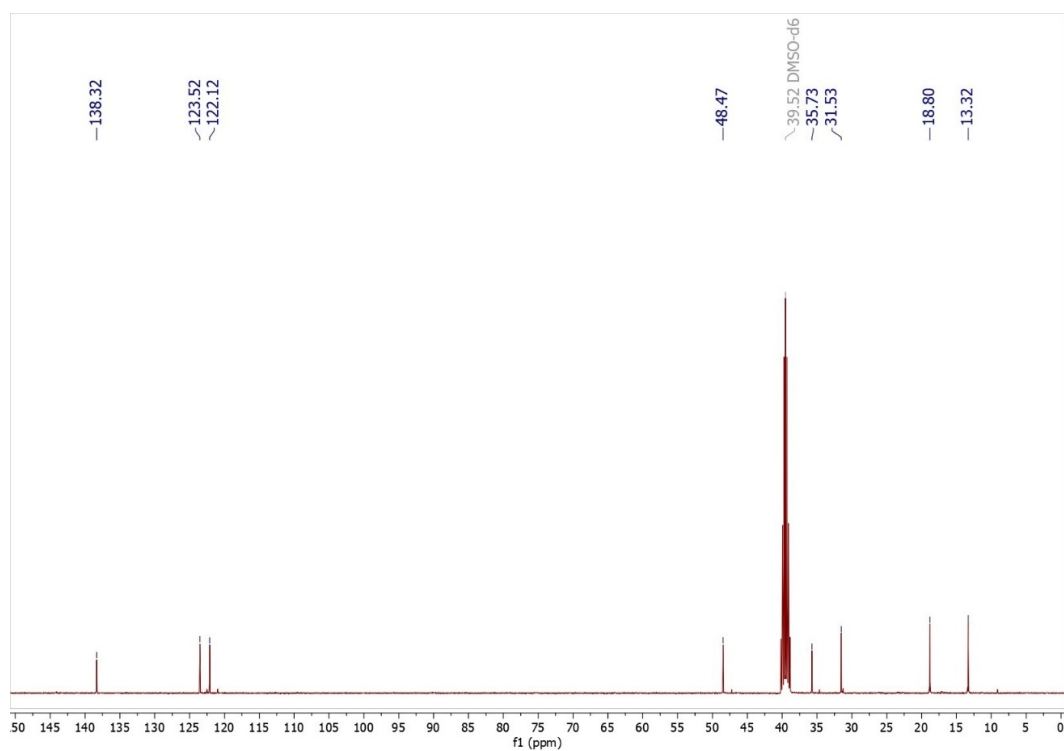


Figure S 51: ^{13}C NMR (101 MHz, DMSO- d_6) $\delta(\text{ppm})$: 138.32; 123.53; 122.12; 48.47; 35.73; 31.53; 18.80; 13.32.

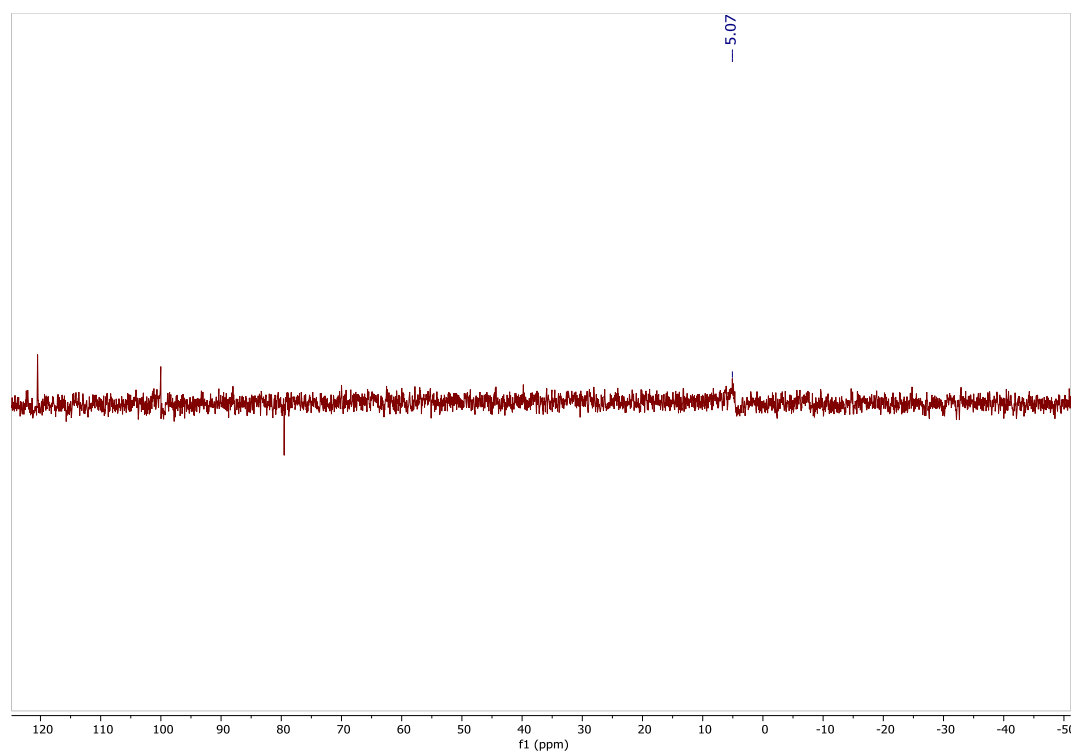


Figure S 52: ^{95}Mo NMR (26 MHz, DMSO- d_6) $\delta(\text{ppm})$: 5.07; spike signals at 120, 100 and 80 ppm.

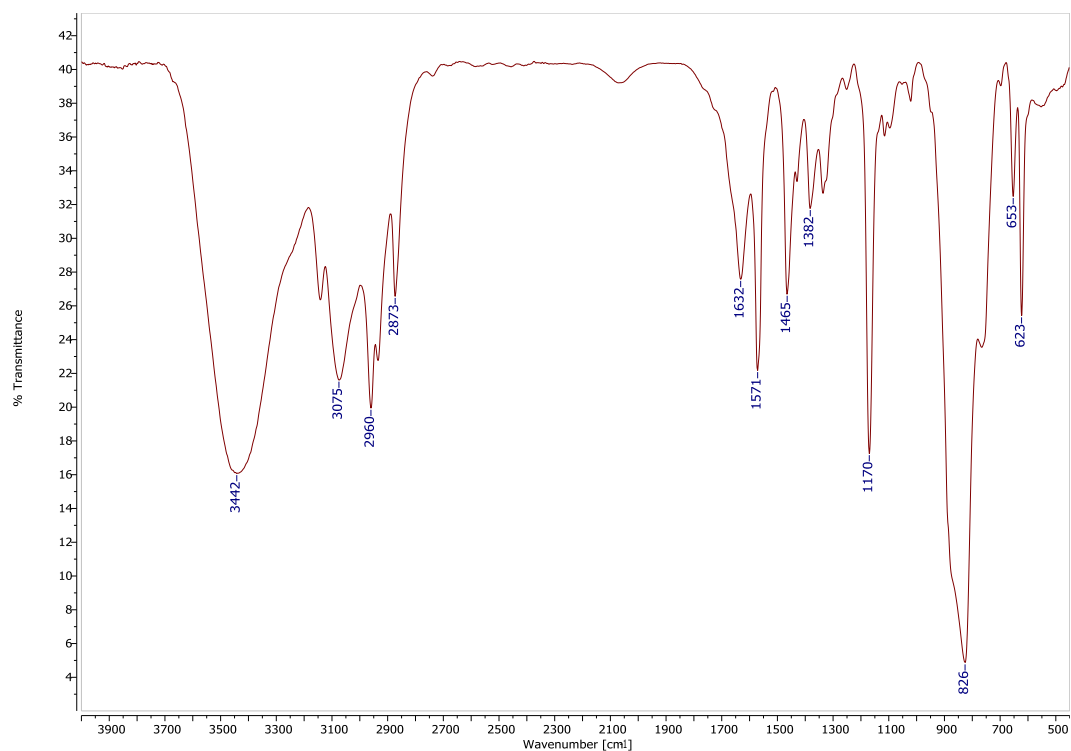


Figure S 53: FT-IR spectrum of $[C_4C_{1im}]_2[MoO_4]$ (KBr)

Diazabicycloundecene molybdate(VI) $[DBUH]_2[MoO_4]$

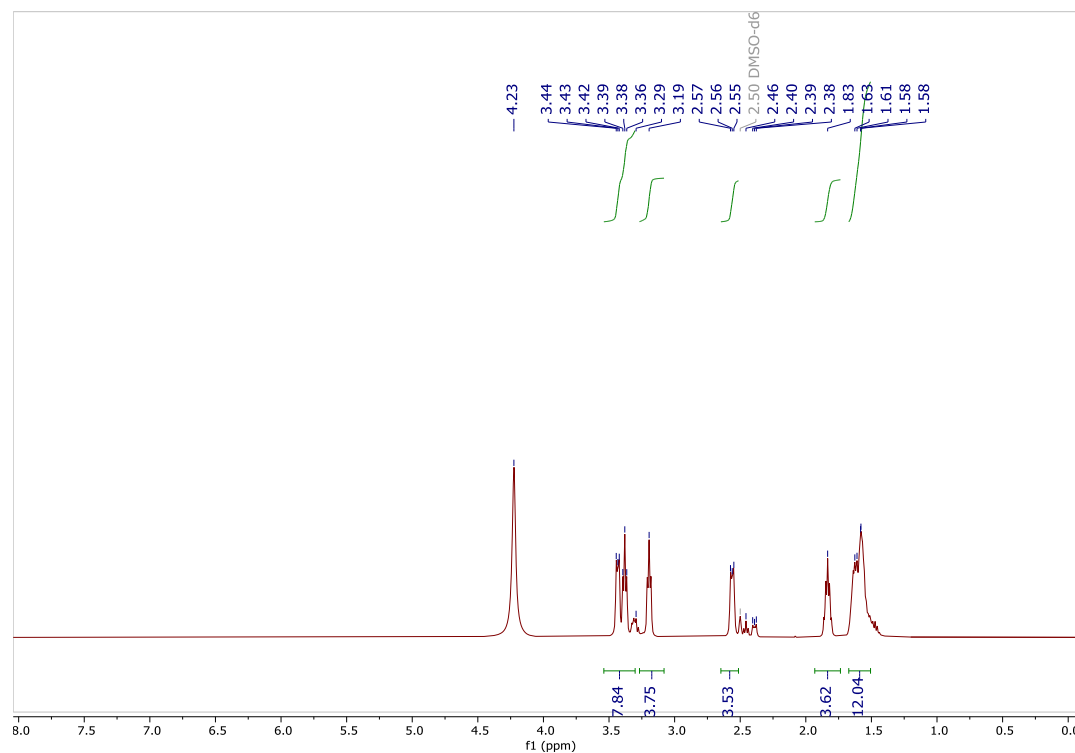


Figure S 54: 1H NMR (400 MHz, $DMSO-d_6$) δ (ppm): 3.59 – 3.39 (m, 4H), 3.27 (t, 2H), 2.65 – 2.54 (m, 2H), 2.00 – 1.88 (m, 2H), 1.63 (m, 6H).

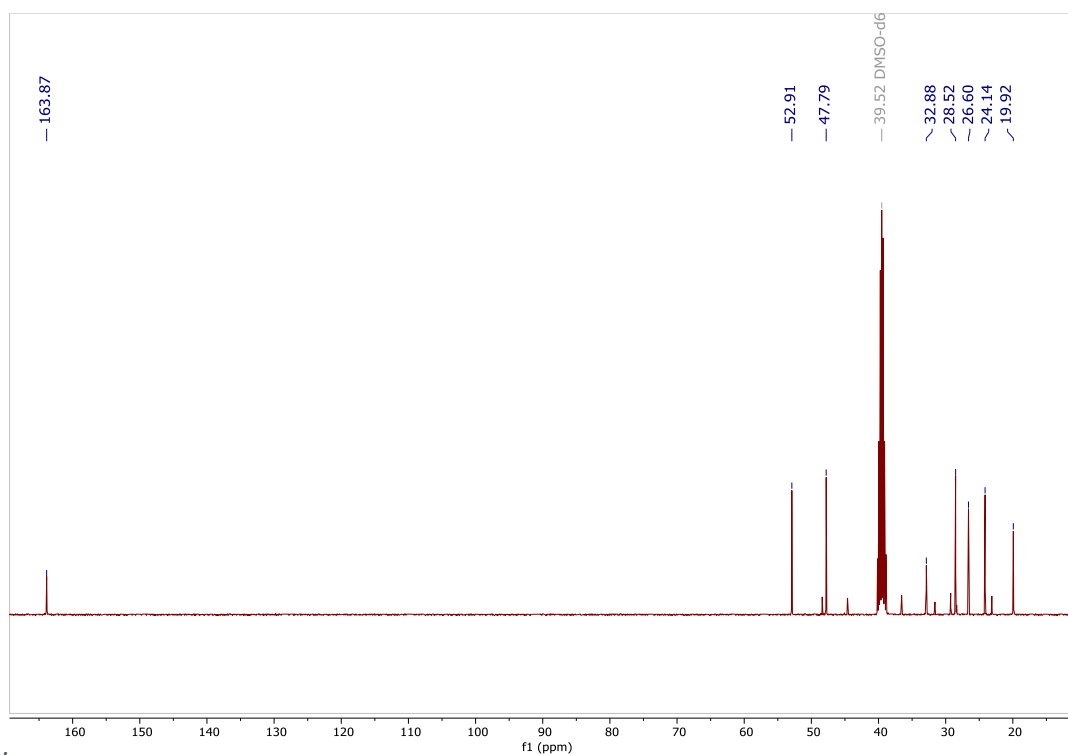


Figure S 55: ^{13}C NMR (101 MHz, DMSO- d_6) δ (ppm): 163.87; 52.91; 47.79; 32.88; 28.52; 26.60; 24.14; 19.92.

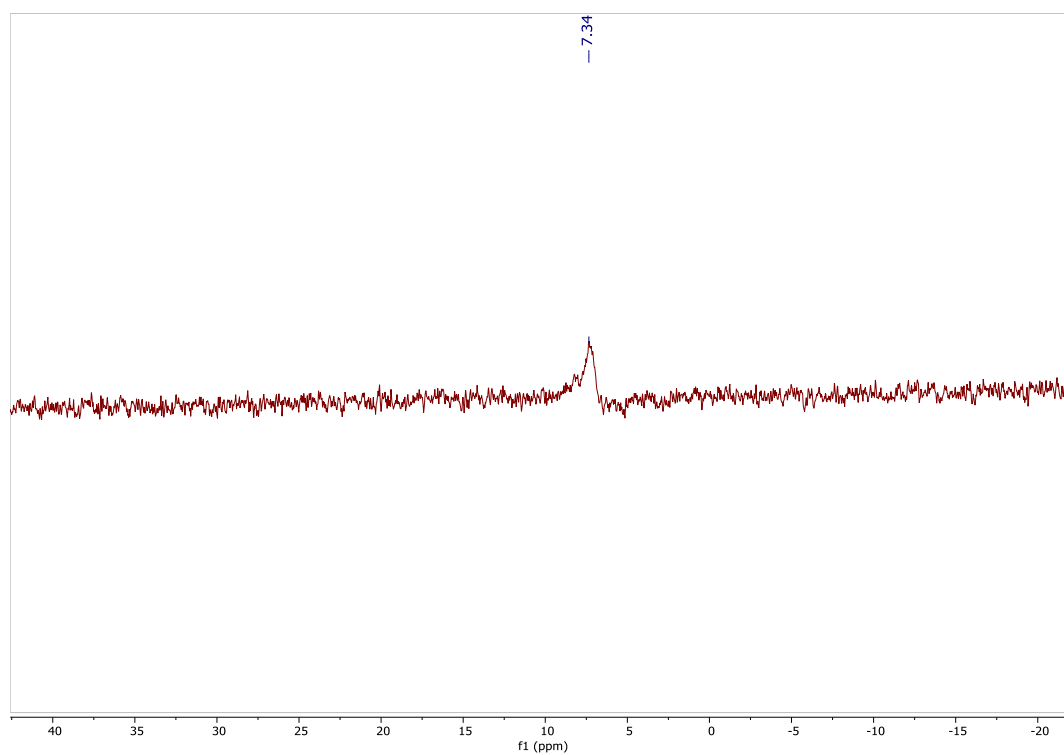


Figure S 56: ^{95}Mo NMR (26 MHz, DMSO- d_6) δ (ppm): 7.54.

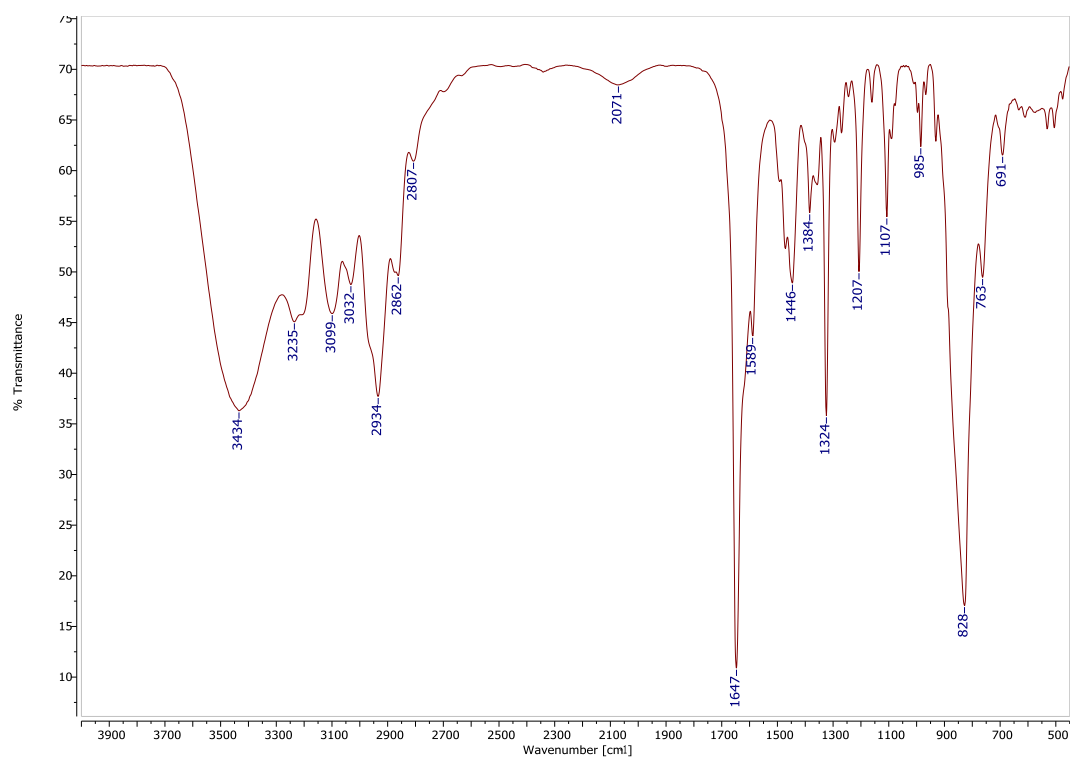


Figure S 57: FT-IR spectrum of $[\text{DBUH}]_2[\text{MoO}_4]$ (KBr).

Trioctylmethylammonium phosphomolybdate $[\text{N}_{8,8,8,1}]_3[\text{PMo}_{12}\text{O}_{40}]^6$

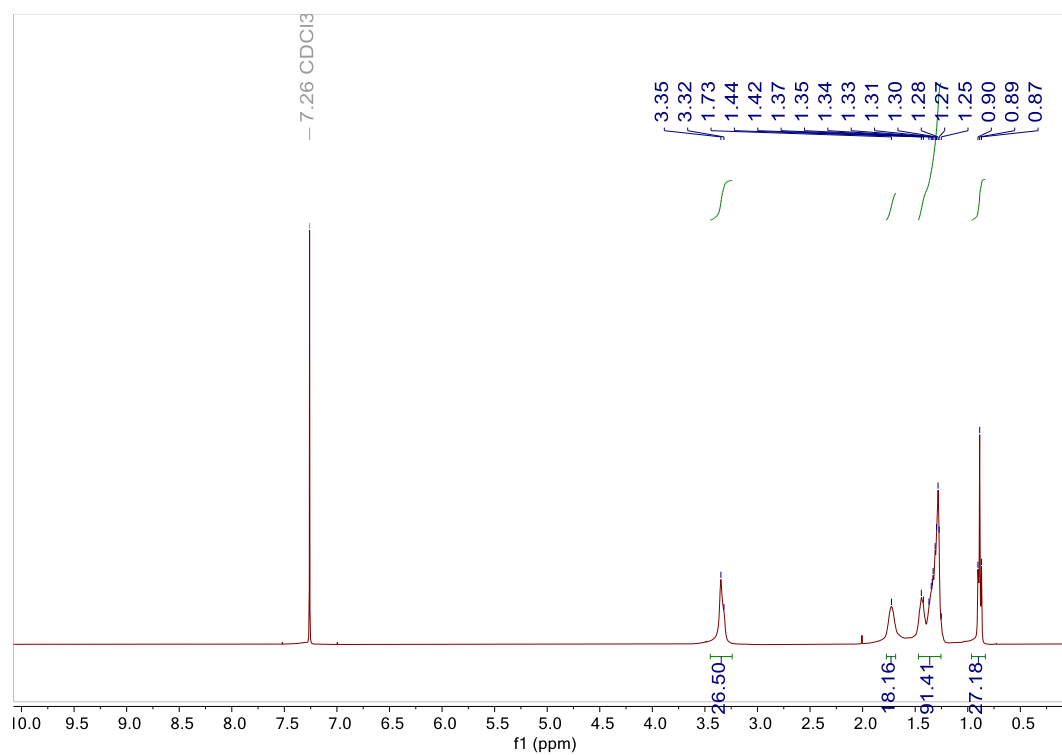


Figure S 58: ^1H NMR (400 MHz, CDCl_3) $\delta(\text{ppm})$: 3.33 (d, $J = 11.6$ Hz, 27H), 1.73 (s, 18H), 1.47 – 1.26 (m, 90H), 0.96 – 0.83 (m, 27H).

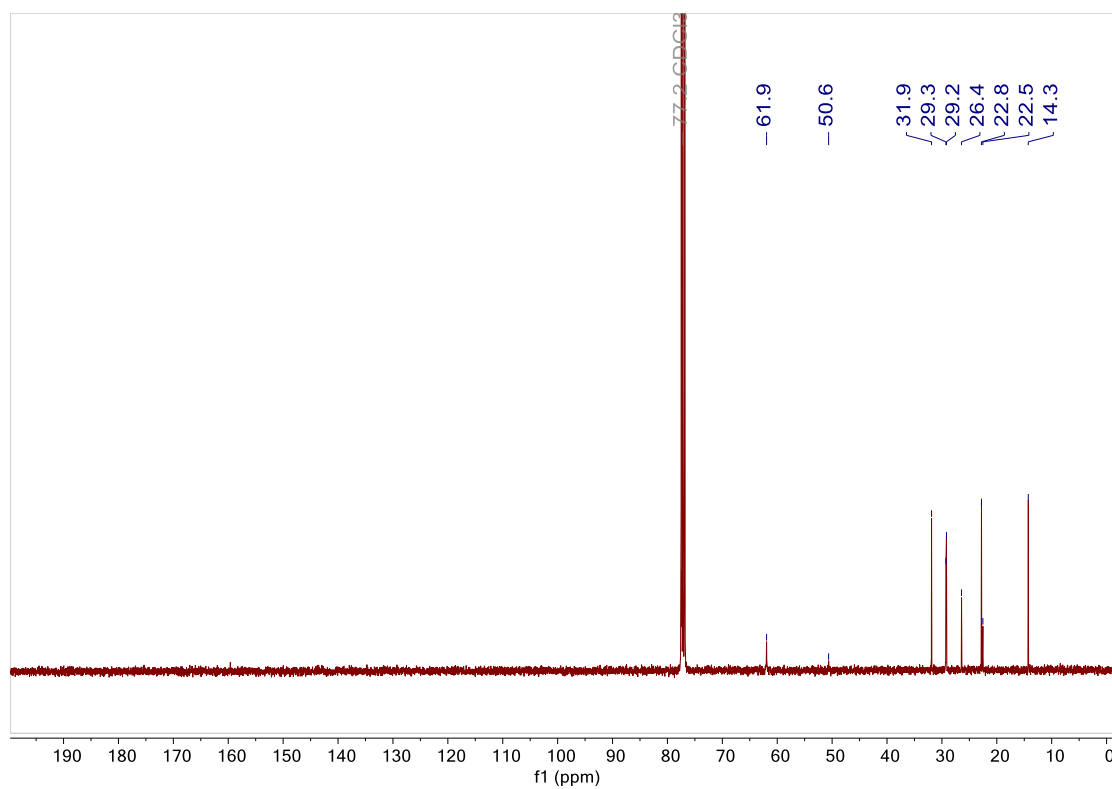


Figure S 59: ^{13}C NMR (101 MHz, CDCl_3) $\delta(\text{ppm})$: 61.9, 50.6, 31.9, 29.3, 29.2, 26.4, 22.8, 22.5, 14.3.

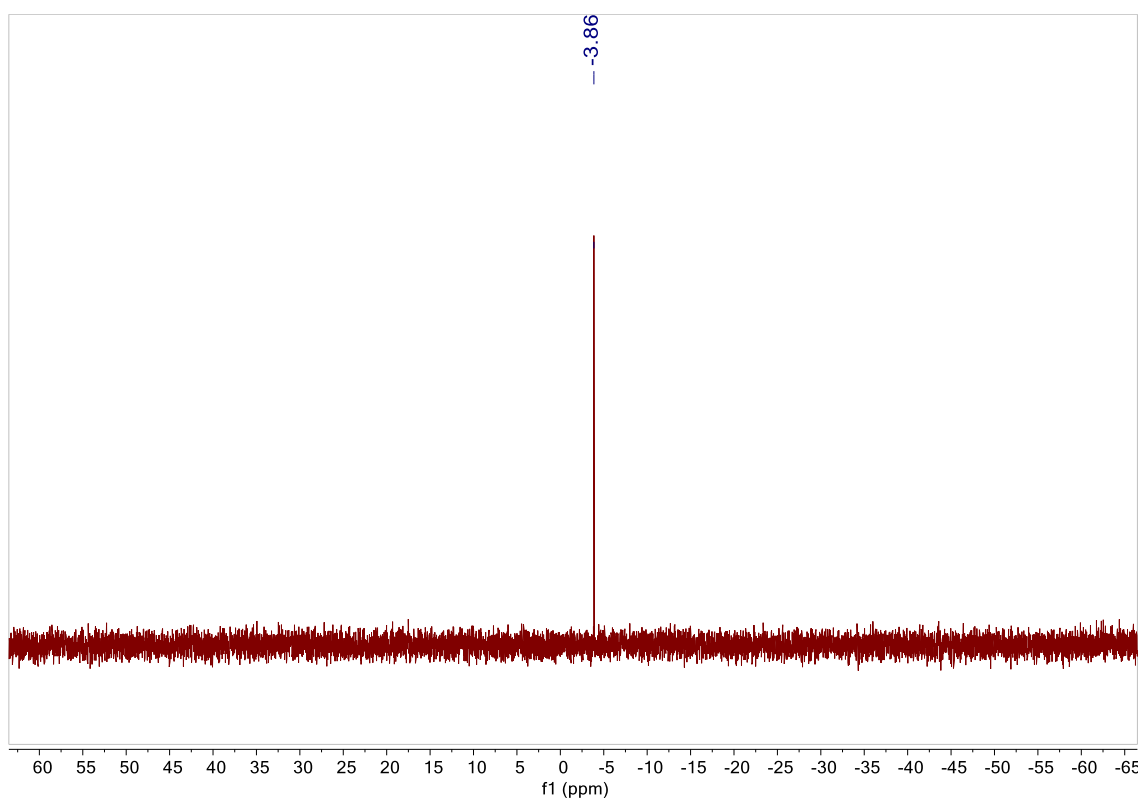


Figure S 60: ^{31}P NMR (162 MHz, D_2O) $\delta(\text{ppm})$: -3.86.

4-Phenyl-1,3-dioxolan-2-one⁷

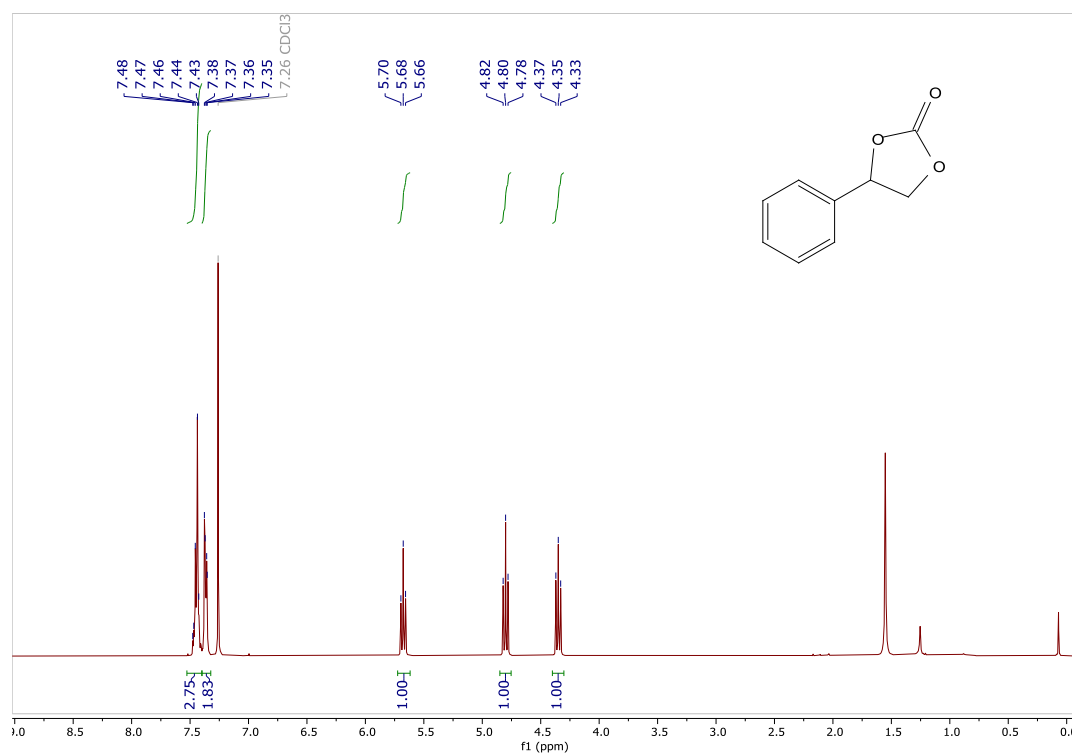


Figure S 61: ¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.45 (d, J = 7.5 Hz, 3H), 7.36 (dd, J = 7.5, 2.2 Hz, 2H), 5.68 (t, J = 8.0 Hz, 1H), 4.80 (t, J = 8.4 Hz, 1H), 4.35 (t, J = 8.2 Hz, 1H).

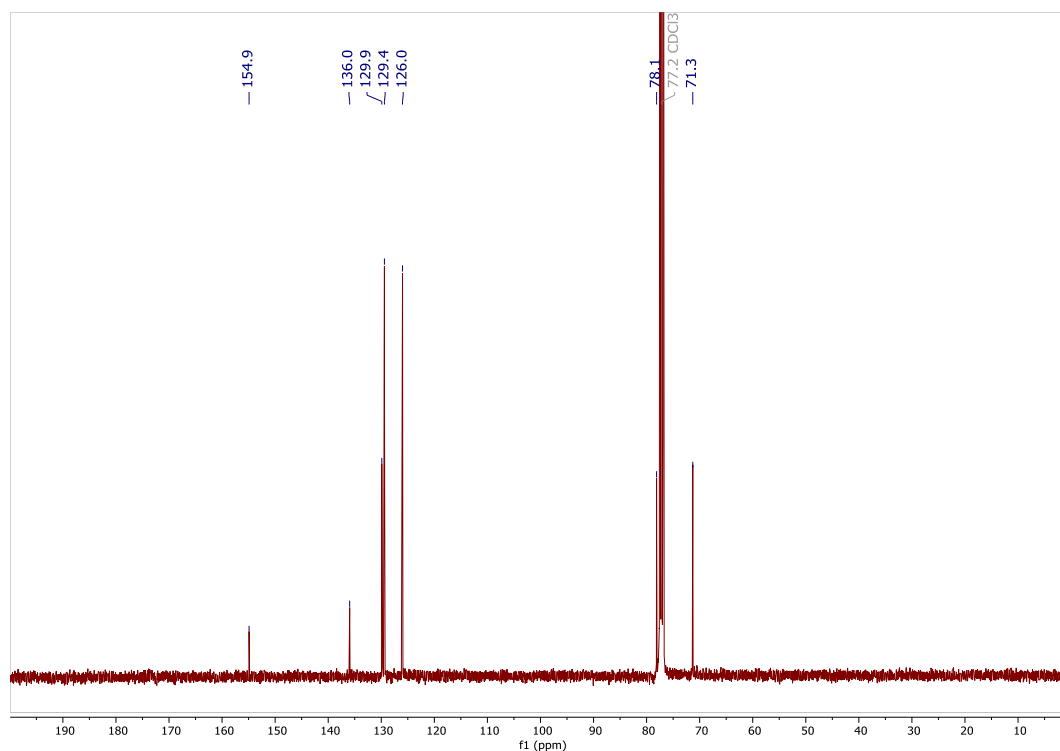


Figure S 62: ¹³C NMR (101 MHz, CDCl₃) δ (ppm): 154.9, 136.0, 129.9, 129.4, 126.0, 78.1, 71.3.

4-chloromethyl-(1,3)dioxolan-2-one

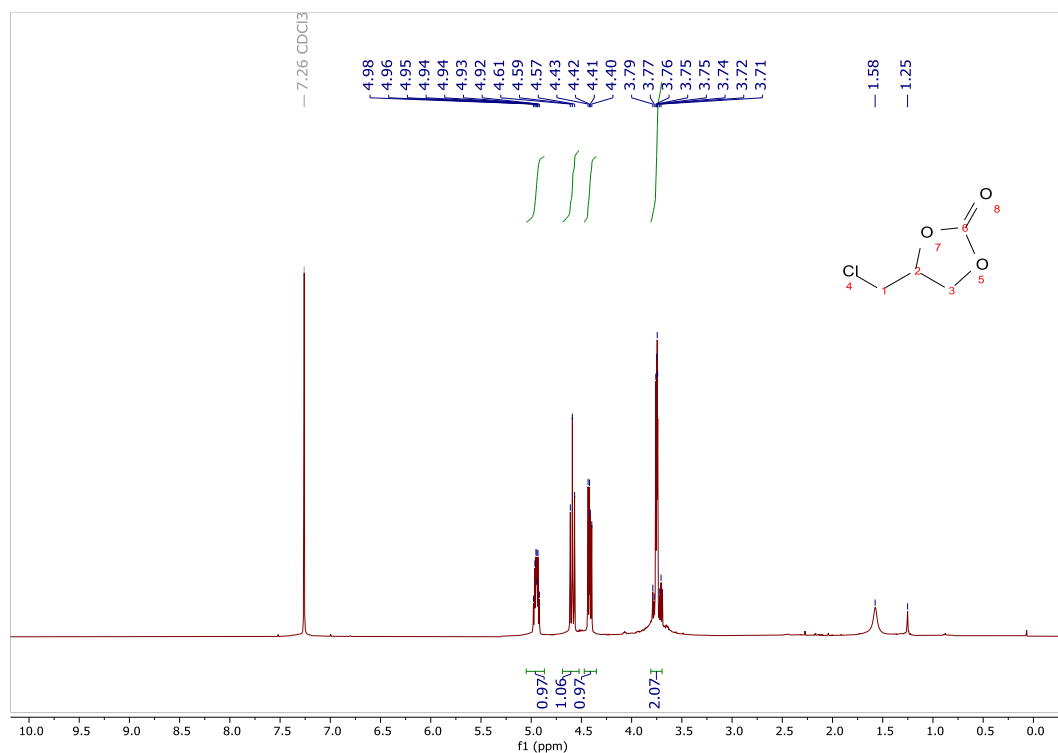


Figure S 63: ¹H NMR (400 MHz, CDCl₃) δ (ppm): 5.05 – 4.87 (m, 1H), 4.69 – 4.52 (m, 1H), 4.42 (dd, J = 8.9, 5.7 Hz, 1H), 3.81 – 3.70 (m, 2H).

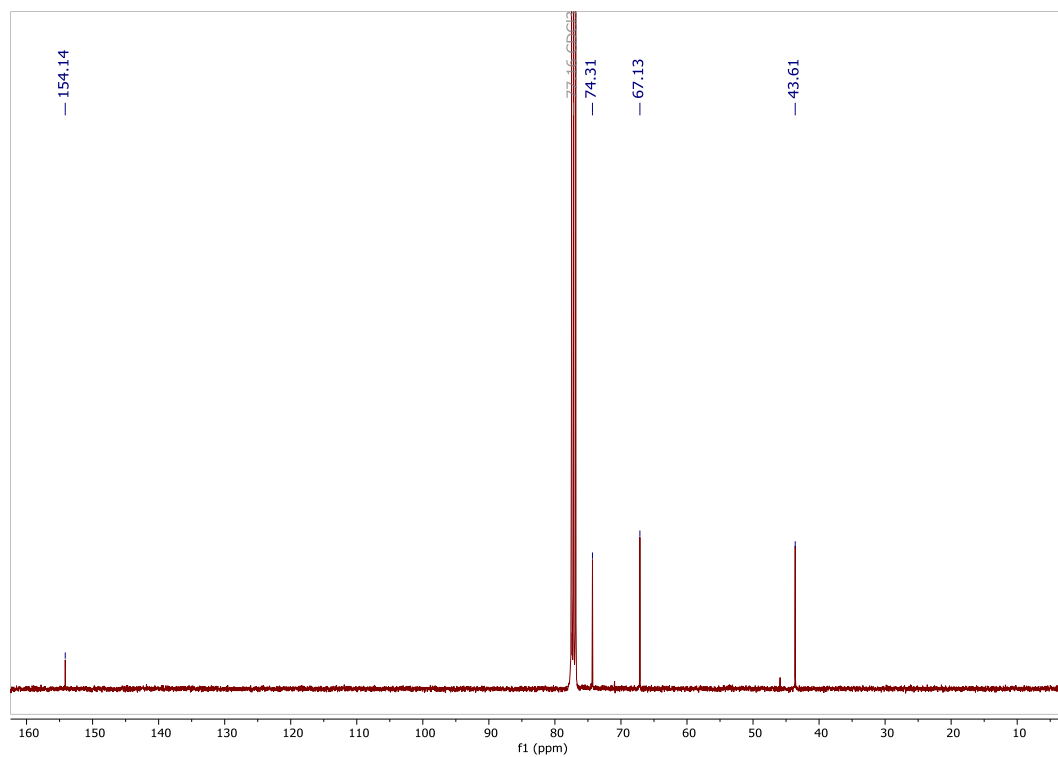


Figure S 64: ¹³C NMR (101 MHz, CDCl₃) δ(ppm): 154.14; 74.31; 67.13; 43.61.

4-butyl-1,3-dioxolan-2-one⁷

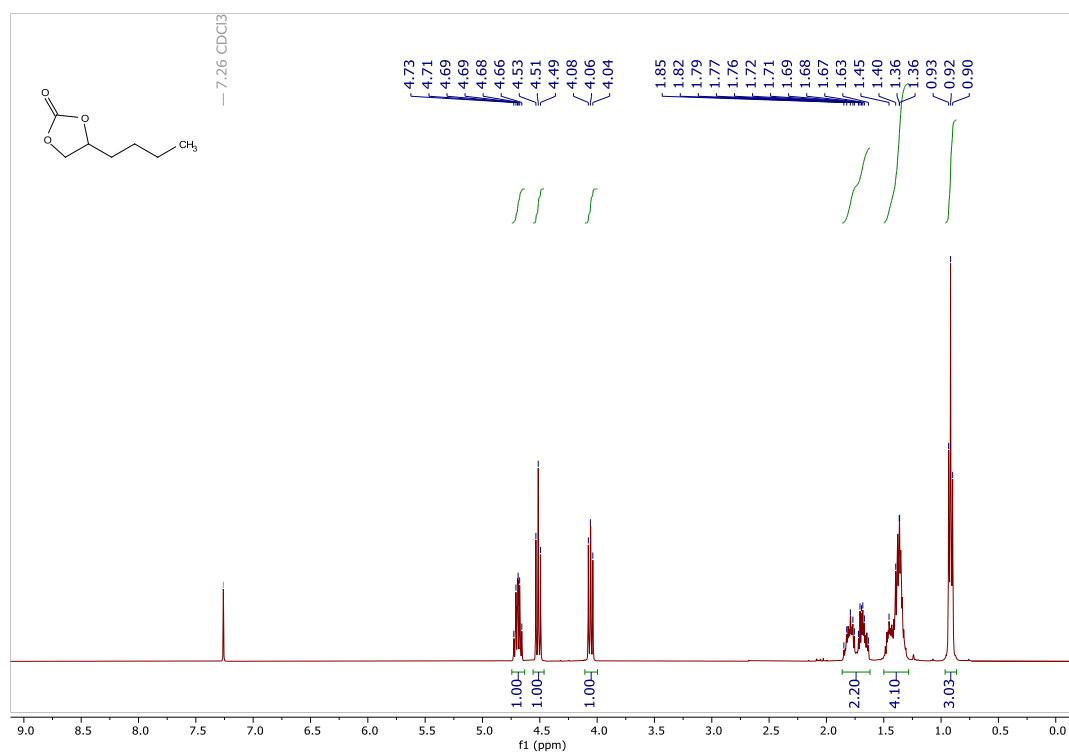


Figure S 65: ¹H NMR (400 MHz, CDCl₃) δ (ppm): 4.74 – 4.63 (m, 1H), 4.51 (t, J = 8.1 Hz, 1H), 4.11 – 4.00 (m, 1H), 1.86 – 1.62 (m, 2H), 1.50 – 1.28 (m, 4H), 0.92 (t, J = 7.0 Hz, 3H).

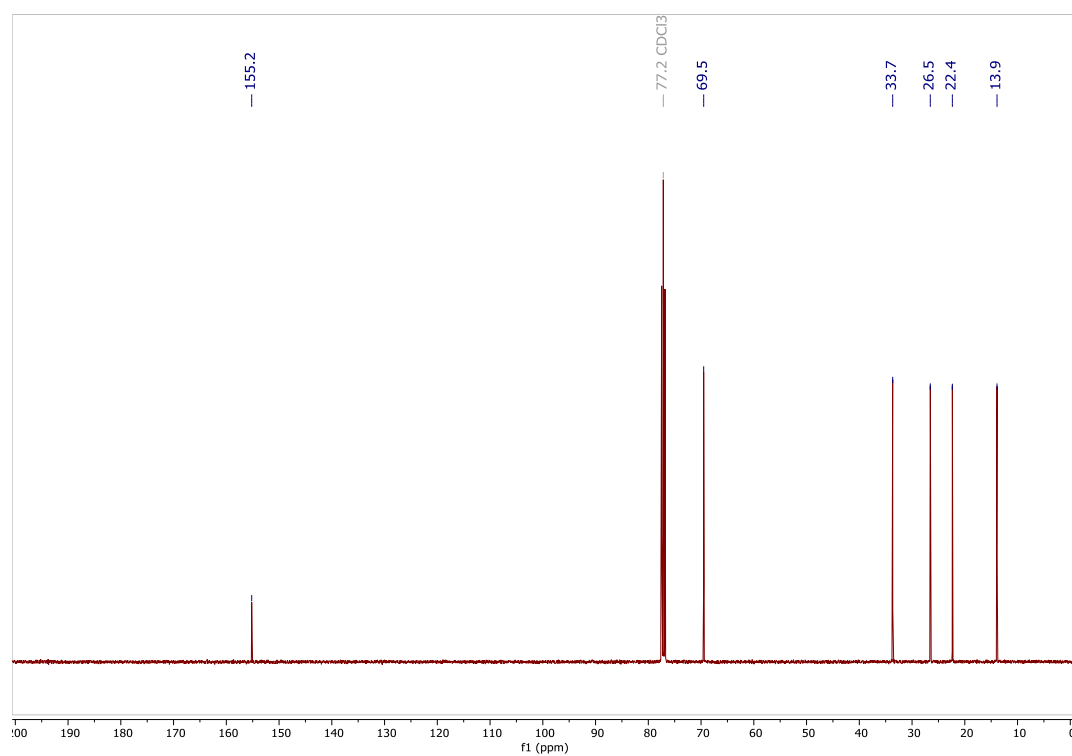


Figure S 66: ¹³C NMR (101 MHz, CDCl₃) δ (ppm): 155.2, 69.5, 33.7, 26.5, 22.4, 13.9.

Hexane-1,2-diol

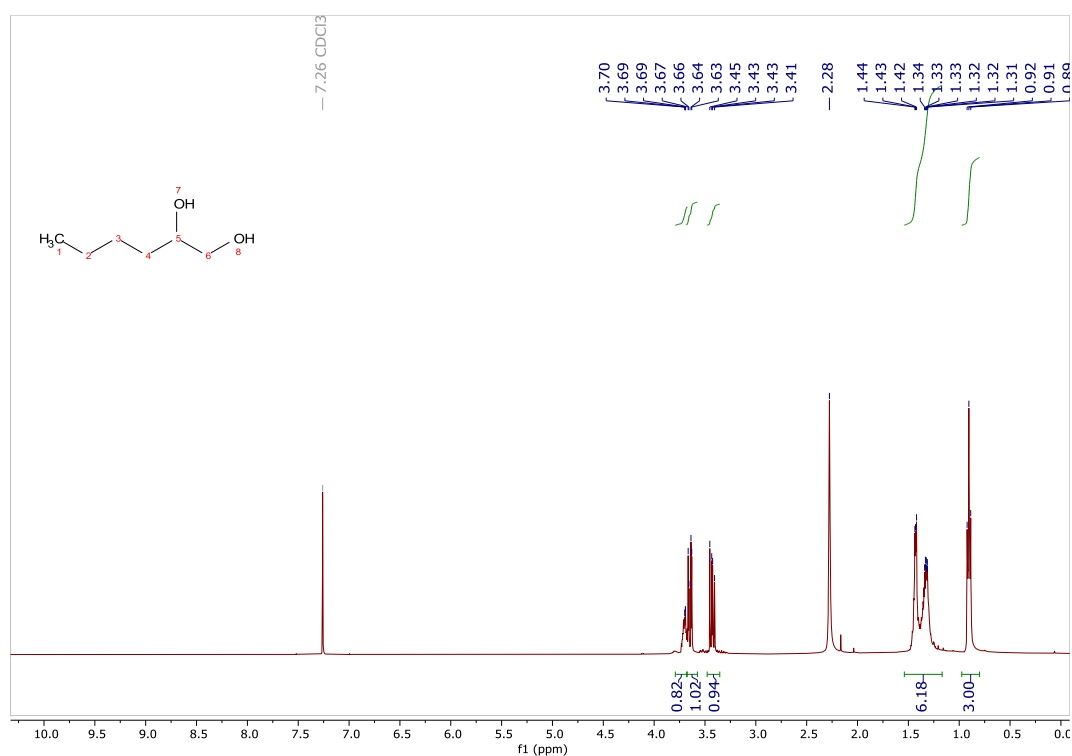


Figure S 67: ¹H NMR (400 MHz, CDCl₃) δ (ppm): 3.79 – 3.68 (m, 1H), 3.65 (dd, J = 11.1, 3.0 Hz, 1H), 3.43 (dd, J = 11.0, 7.6 Hz, 1H), 2.28 (s, OH), 1.54 – 1.17 (m, 6H), 0.90 (t, J = 7.1 Hz, 3H).

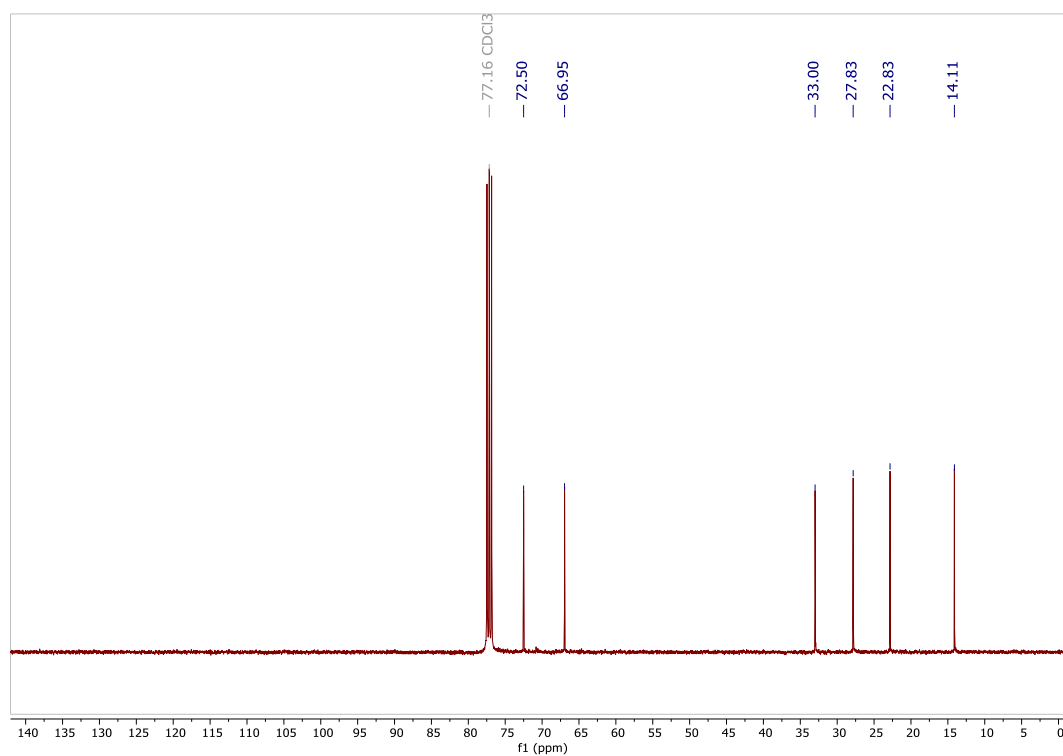


Figure S 68: ¹³C NMR (101 MHz, CDCl₃) δ (ppm): 72.50; 66.95; 33.00; 27.83; 22.83; 14.11.

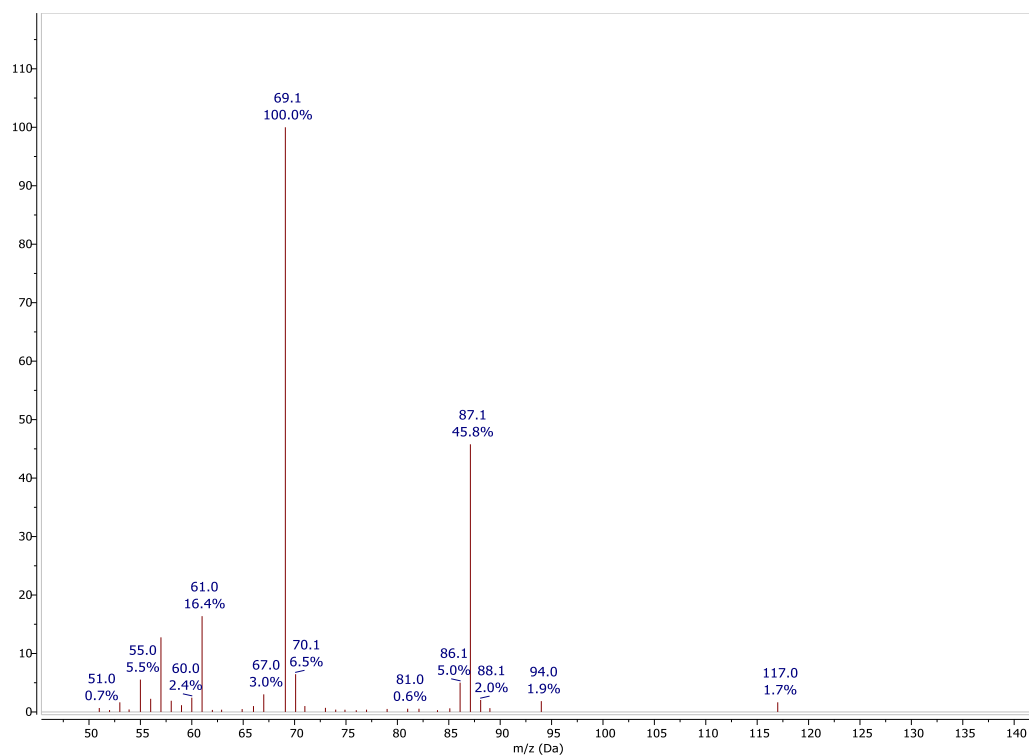


Figure S 69: EI-MS (70 eV) spectrum of hexane-1,2-diol.

1-(2-hydroxyhexoxy)hexan-2-ol

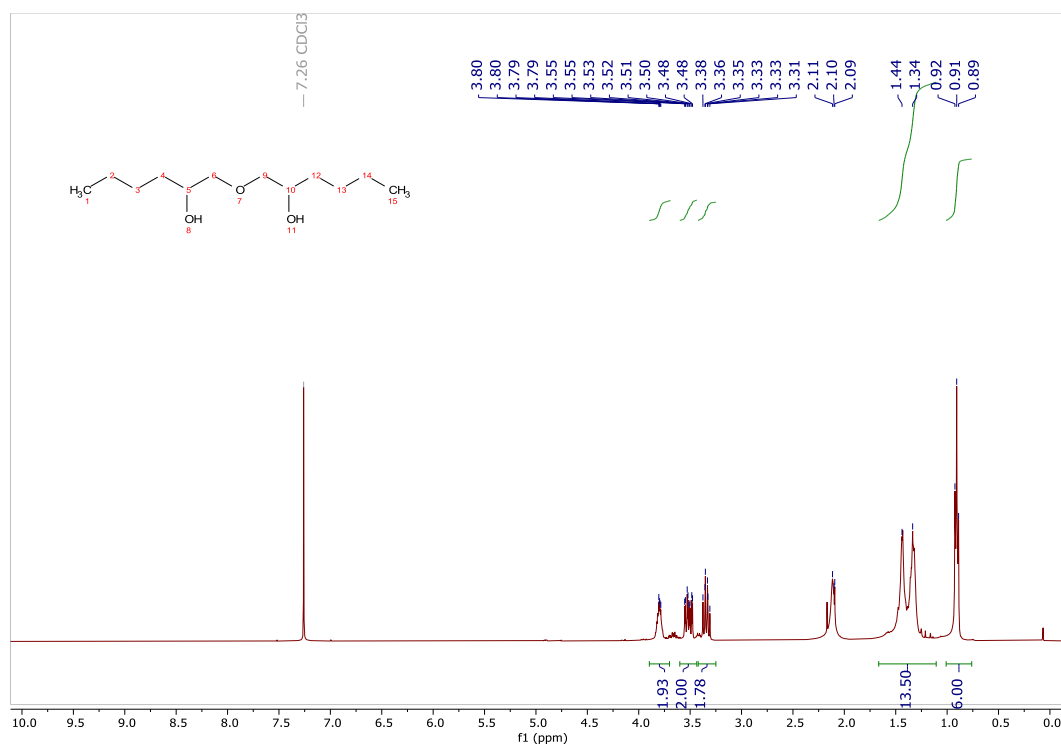


Figure S 70: ^1H NMR (400 MHz, CDCl_3) $\delta(\text{ppm})$: 3.79 (m, 2H), 3.51 (m, 2H), 3.34 (m, 2H), 2.10 (OH, 2H), 1.67 – 1.13 (m, 14H), 0.91 (t, $J = 7.2$ Hz, 6H).

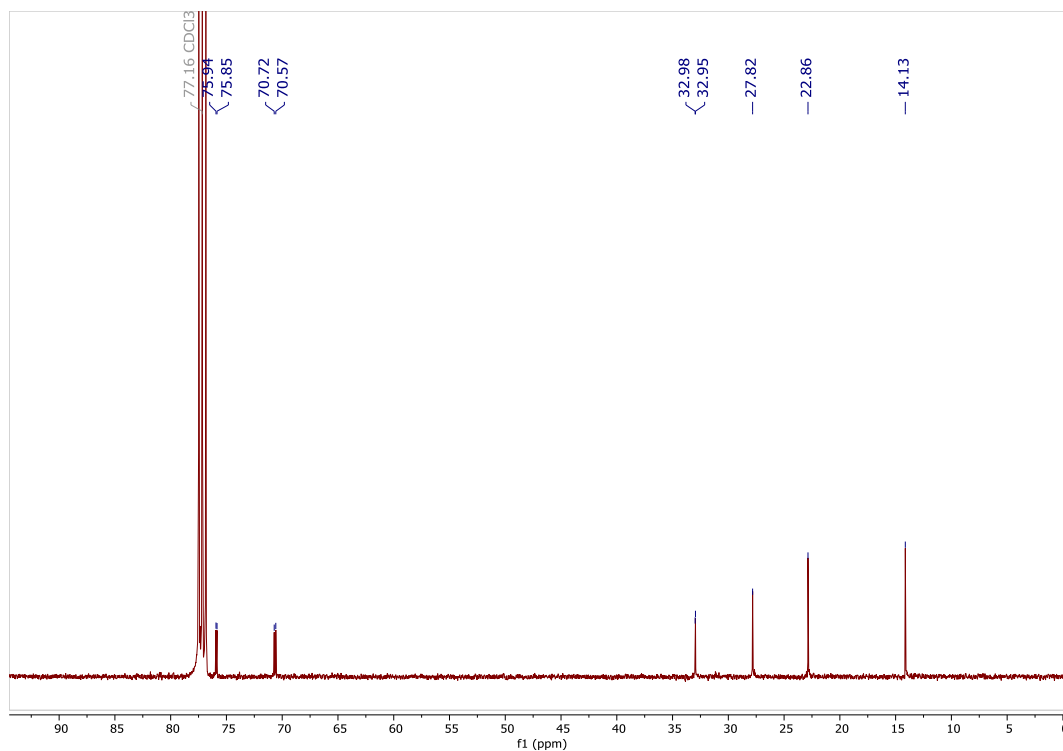


Figure S 71: ^{13}C NMR (101 MHz, CDCl_3) δ (ppm): 75.94; 75.85; 70.72; 70.57; 32.98; 32.95; 27.82; 22.86; 14.13.

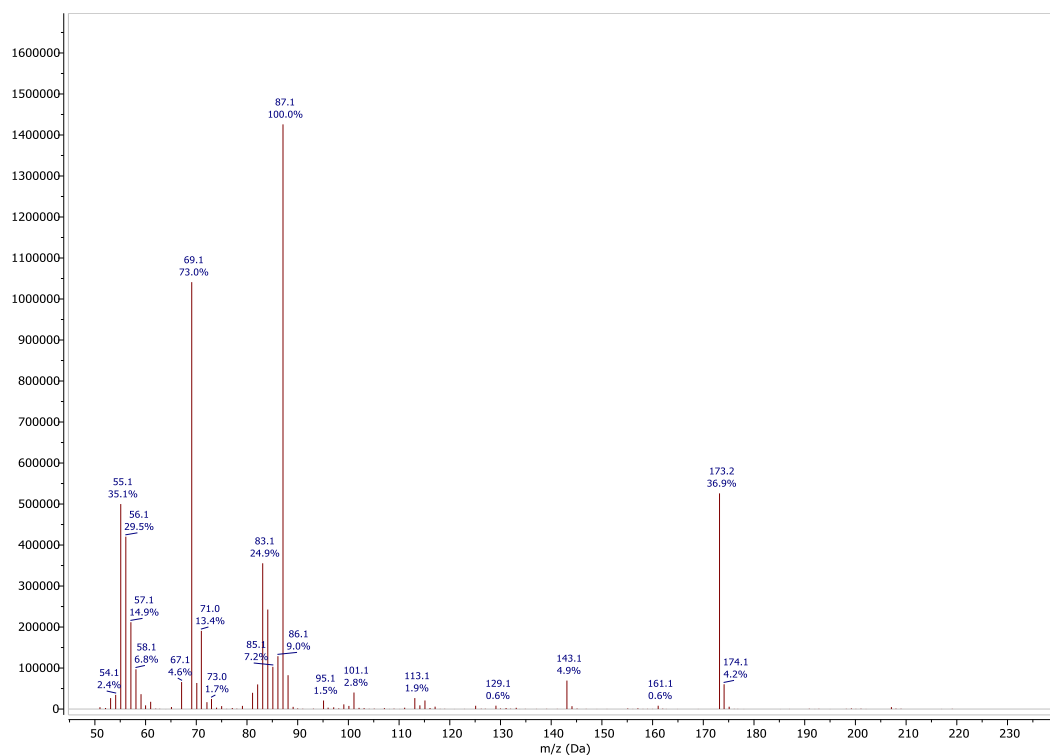


Figure S 72: EI-MS (70 eV) spectrum of 1-(2-hydroxyhexoxy)hexan-2-ol.

1,2-epoxydecene⁸

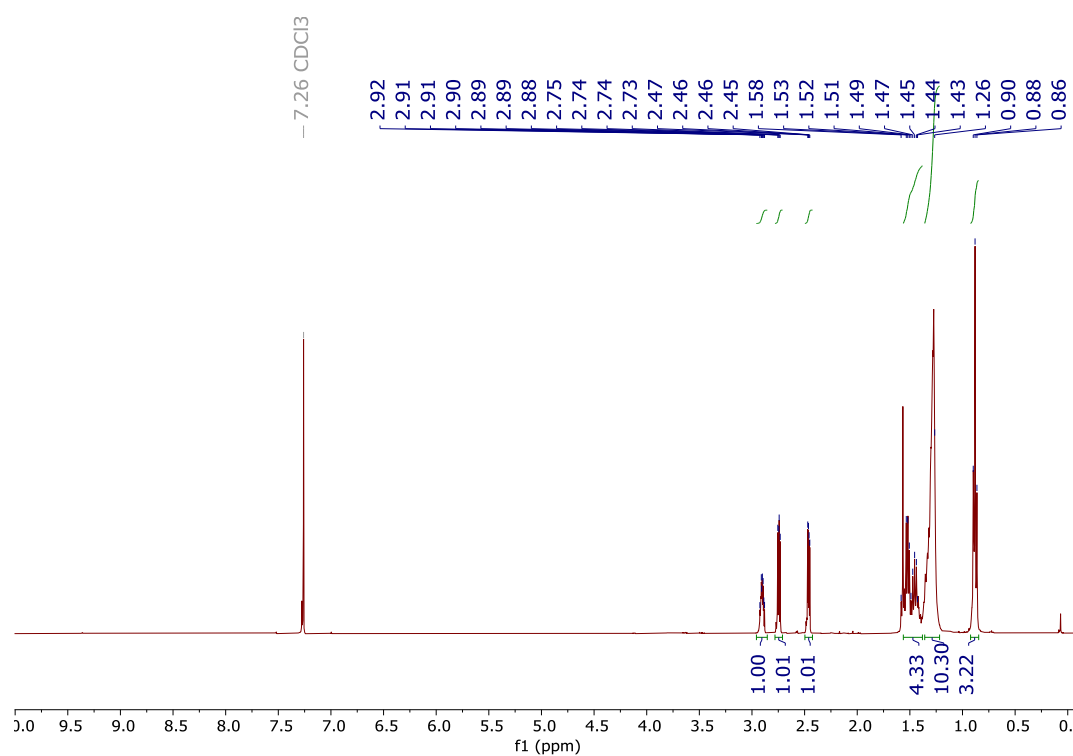


Figure S 73: ¹H NMR (400 MHz, CDCl₃) δ(ppm): 2.96 – 2.85 (m, 1H), 2.74 (dd, J = 5.1, 3.9 Hz, 1H), 2.46 (dd, J = 5.0, 2.7 Hz, 1H), 1.56 – 1.38 (m, 4H), 1.26 (s, 10H), 0.88 (t, 3H).

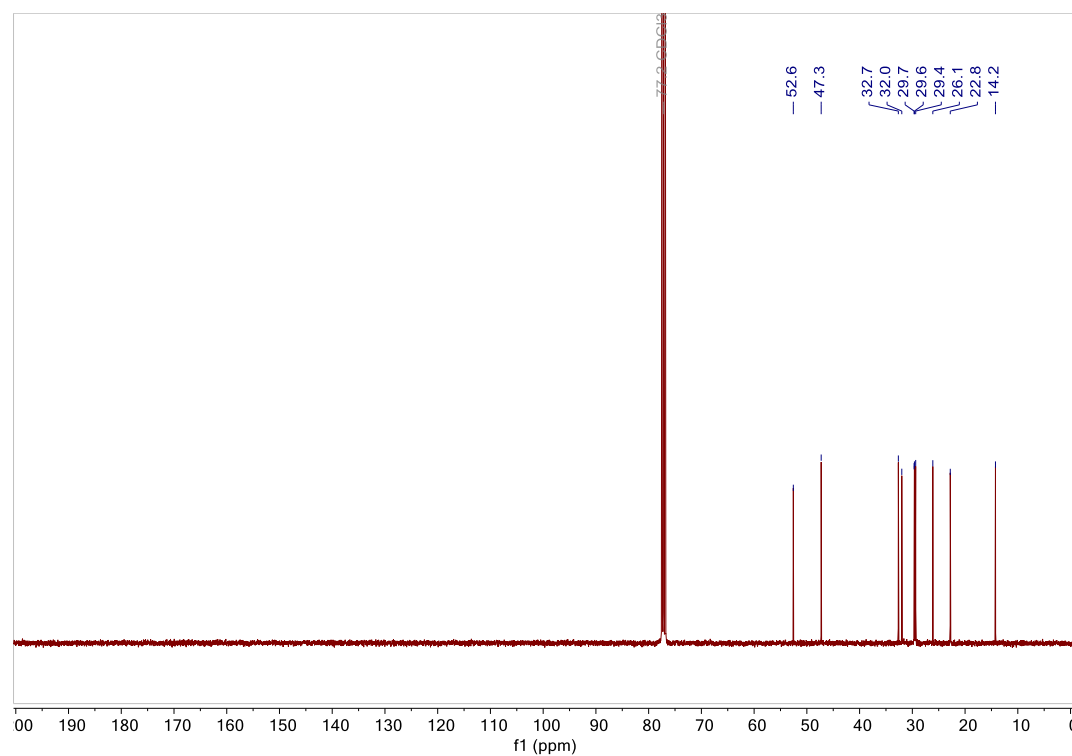


Figure S 74: ¹³C NMR (101 MHz, CDCl₃) δ(ppm): 52.6, 47.3, 32.7, 32.0, 29.7, 29.6, 29.4, 26.1, 22.8, 14.2.

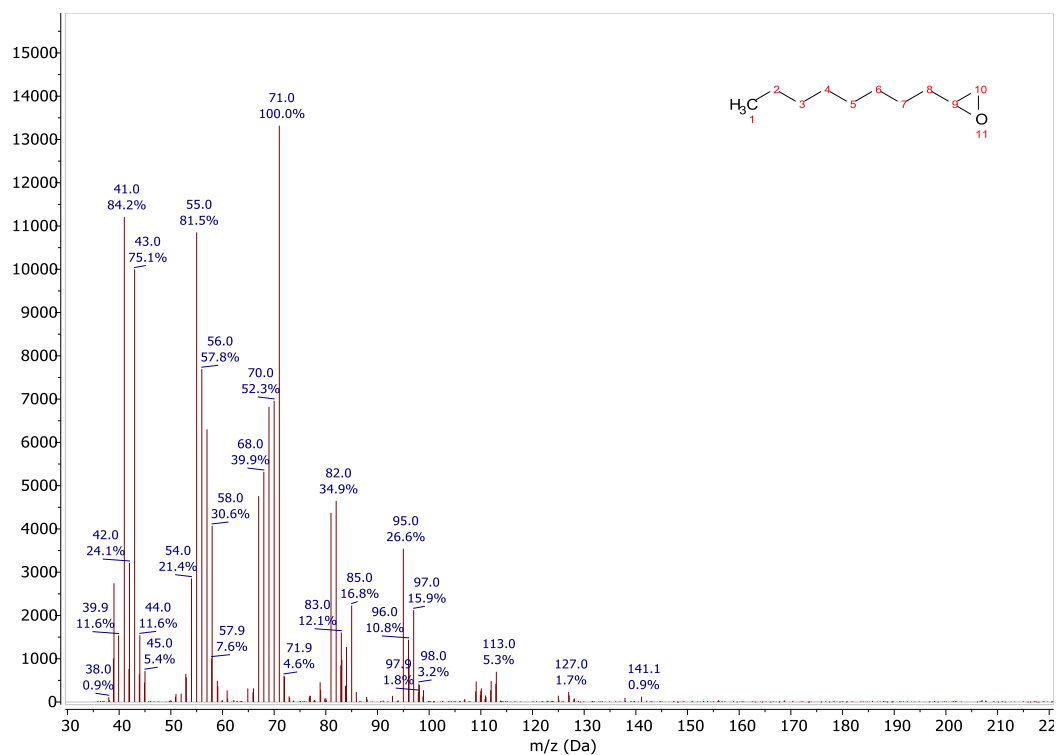


Figure S 75: EI-MS (70 eV) spectrum of 1,2-epoxydecene.

4-octyl-1,3-dioxolan-2-one (or decan carbonate)⁸

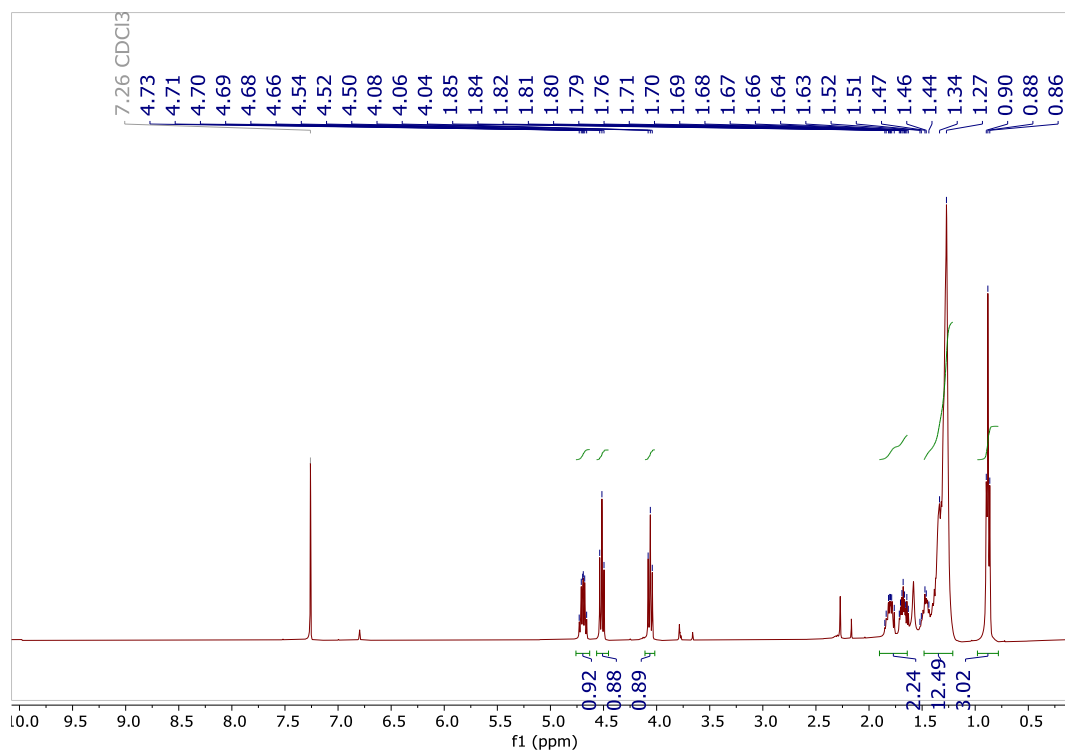


Figure S 76: ^1H NMR (400 MHz, CDCl_3) δ (ppm): 4.76 – 4.63 (m, 1H), 4.52 (t, J = 8.1 Hz, 1H), 4.06 (t, J = 7.8 Hz, 1H), 1.90 – 1.64 (m, 2H), 1.48 – 1.21 (m, 12H), 0.88 (t, 3H).

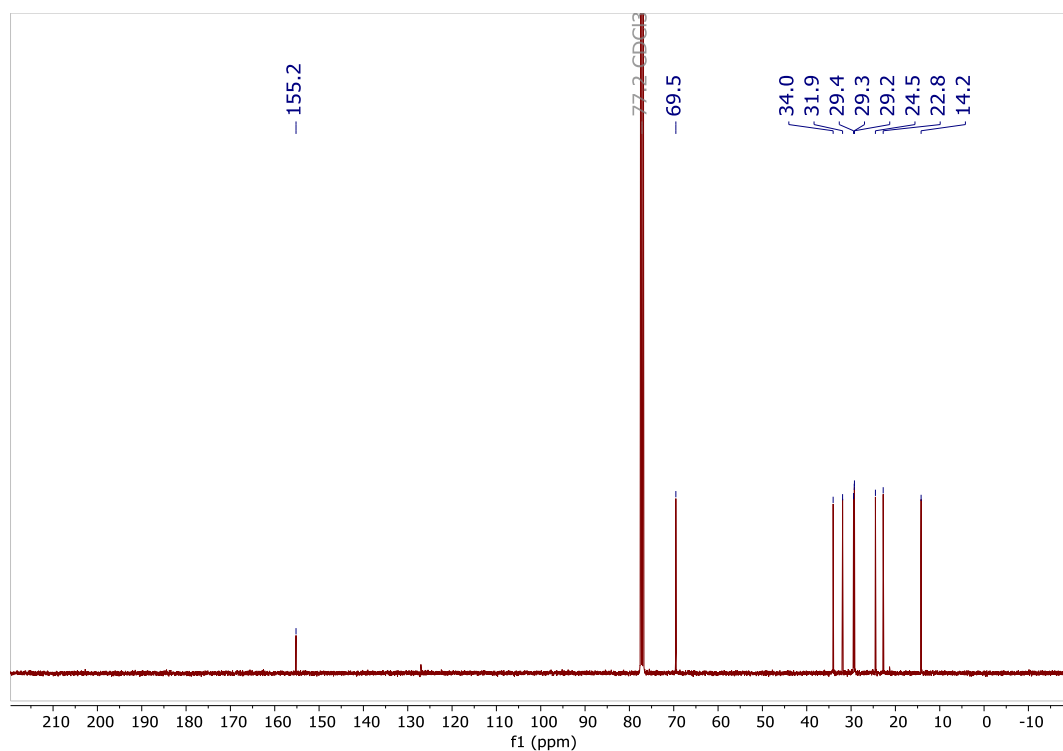


Figure S 77: ^{13}C NMR (101 MHz, CDCl_3) $\delta(\text{ppm})$: 155.2, 69.5, 34.0, 31.9, 29.4, 29.3, 29.2, 24.5, 22.8, 14.2.

1,2-decanediol⁸

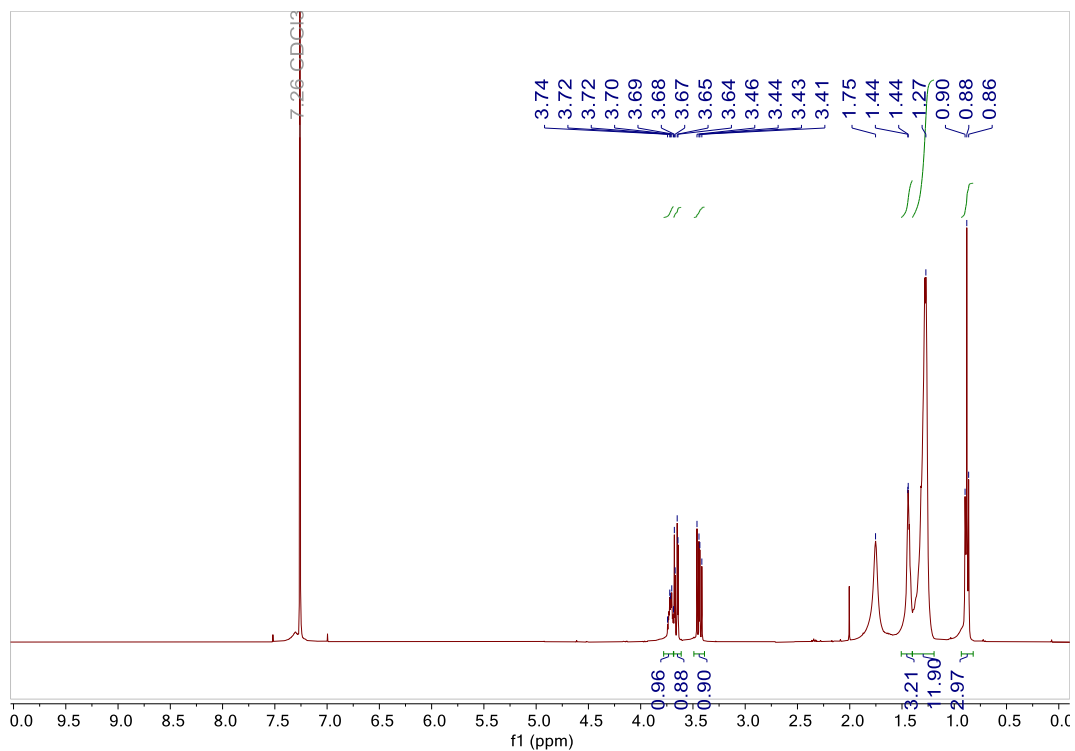


Figure S 78: ^1H NMR (400 MHz, CDCl_3) $\delta(\text{ppm})$: 3.78 – 3.69 (m, 1H), 3.66 (dd, $J = 10.9, 3.1$ Hz, 1H), 3.44 (dd, $J = 11.0, 7.6$ Hz, 1H), 1.75 (br, -OH), 1.44 (s, 3H), 1.27 (s, 12H), 0.88 (m, 3H).

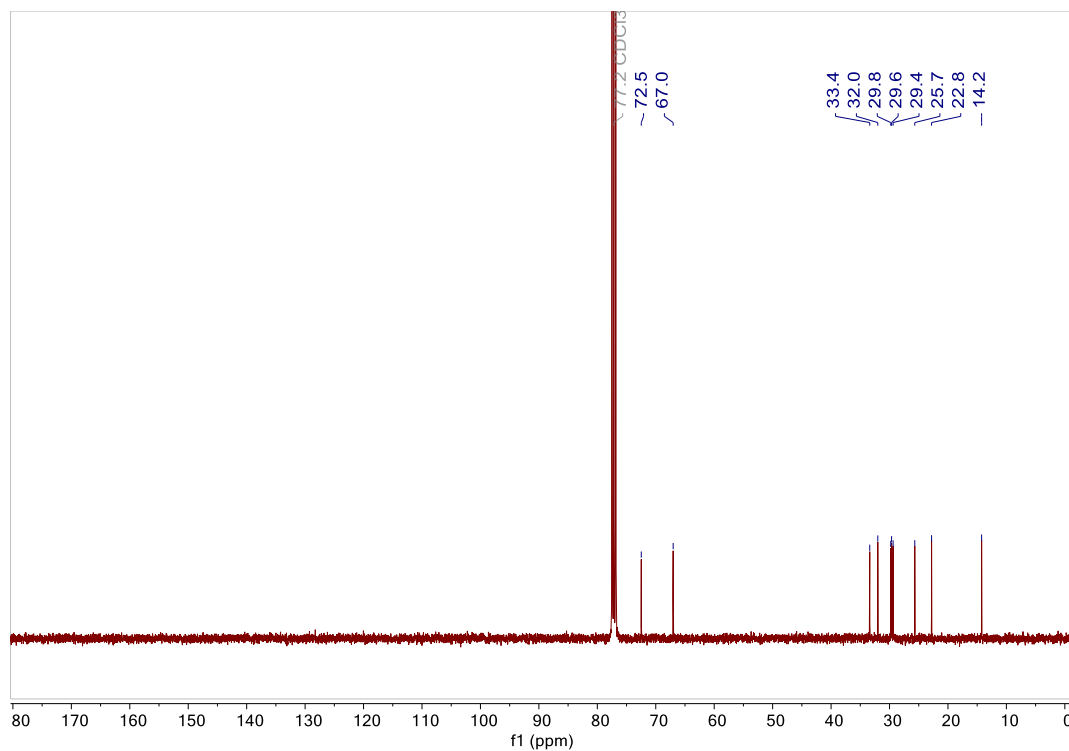


Figure S 79: ^{13}C NMR (101 MHz, CDCl_3) δ (ppm): 72.5, 67.0, 33.4, 32.0, 29.8, 29.7, 29.4, 25.7, 22.8, 14.2.

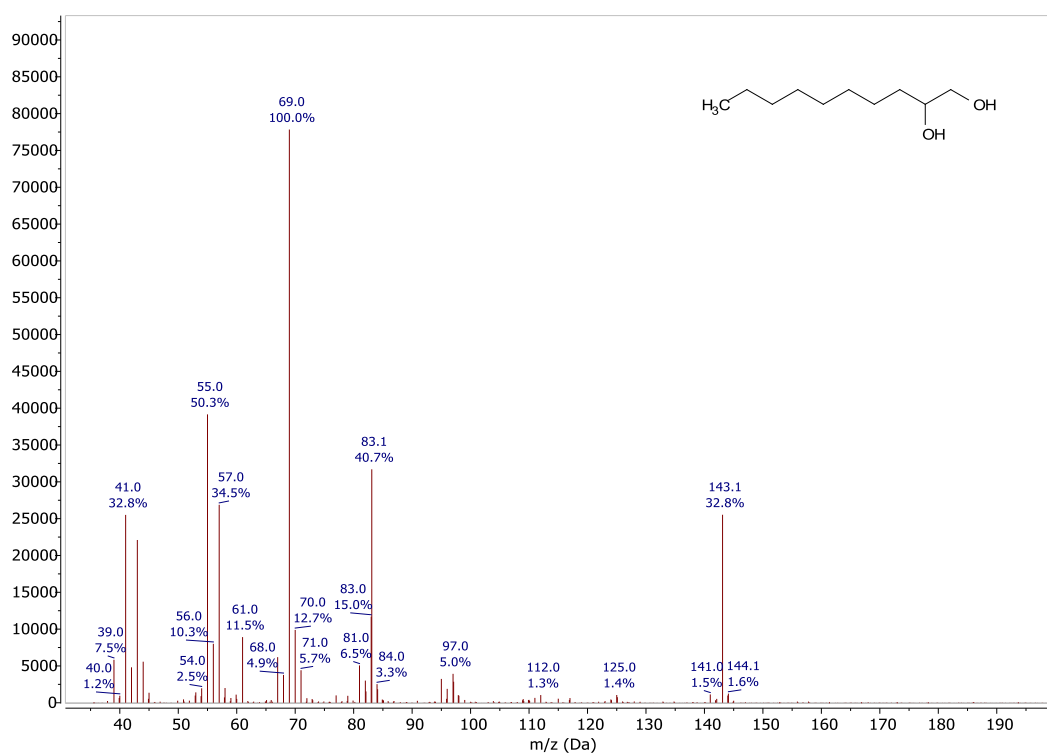


Figure S 80: EI-MS (70 eV) spectrum of 1,2-decanediol.

4-[(prop-2-yn-1-yloxy)methyl]-1,3-dioxolan-2-one⁷

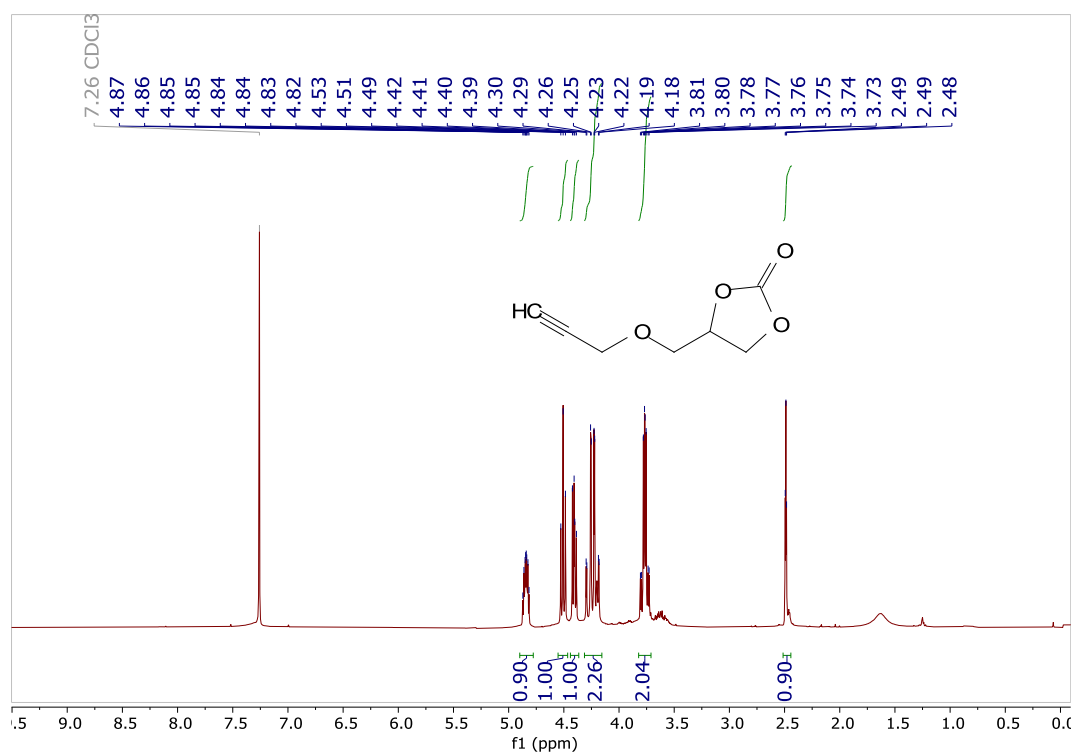


Figure S 81: ¹H NMR (400 MHz, CDCl₃) δ (ppm): 4.90 – 4.78 (m, 1H), 4.51 (t, J = 8.4 Hz, 1H), 4.40 (dd, J = 8.4, 6.0 Hz, 1H), 4.31 – 4.16 (m, 2H), 3.82 – 3.71 (m, 2H), 2.49 (t, J = 2.4 Hz, 1H).

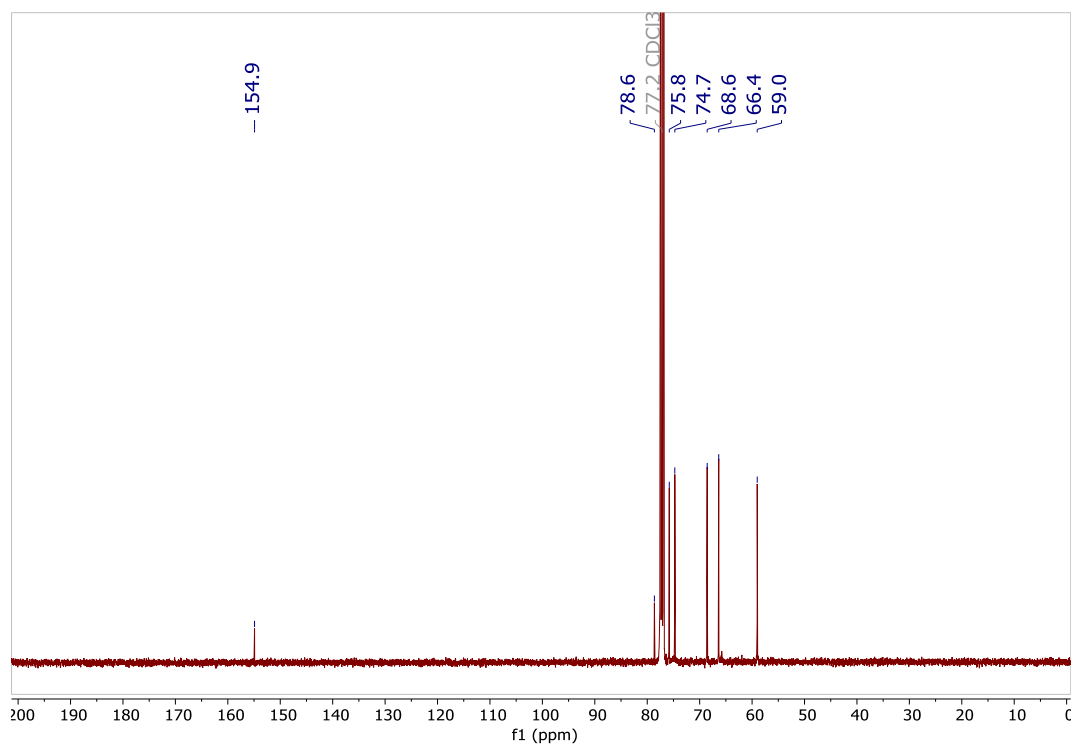


Figure S 82: ¹³C NMR (101 MHz, CDCl₃) δ (ppm): 154.9, 78.6, 75.8, 74.7, 68.6, 66.4, 59.0.

4,4'-[[butane-1,4-diylbis(oxy)]bis(methylene)]bis(1,3-dioxolan-2-one)

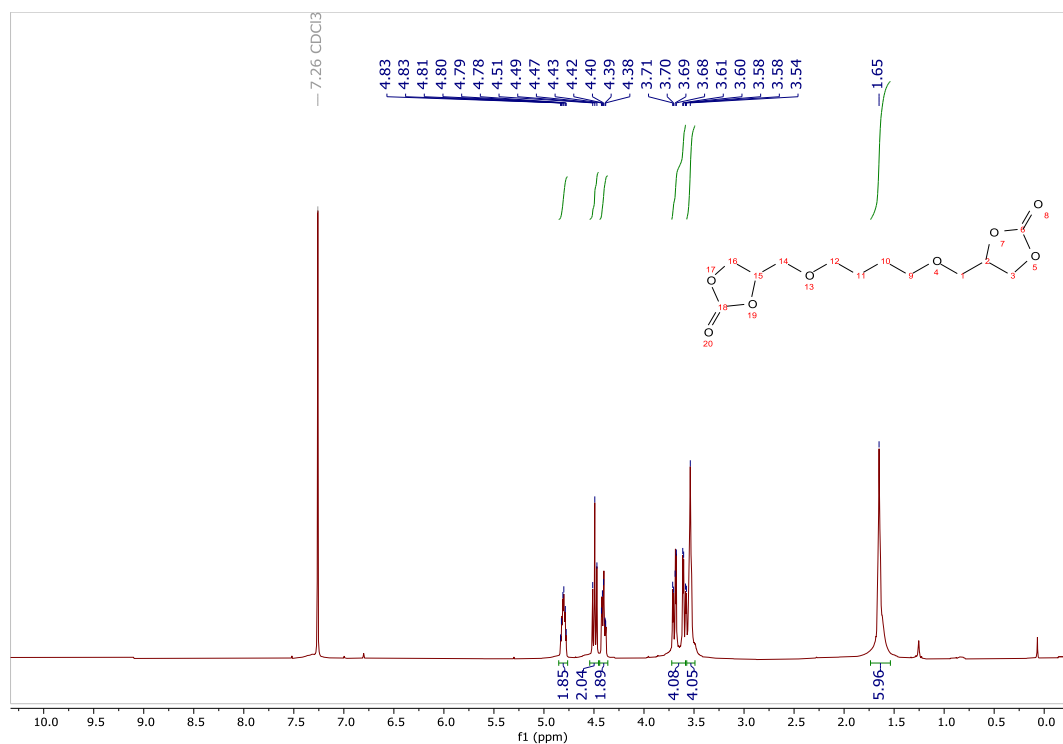


Figure S 83: ^1H NMR (400 MHz, CDCl_3) $\delta(\text{ppm})$: 4.85 – 4.76 (m, 2H), 4.49 (t, $J = 8.4$ Hz, 2H), 4.44 – 4.36 (m, 2H), 3.72 – 3.59 (m, 4H), 3.57 – 3.49 (m, 4H), 1.74 – 1.54 (m, 6H).

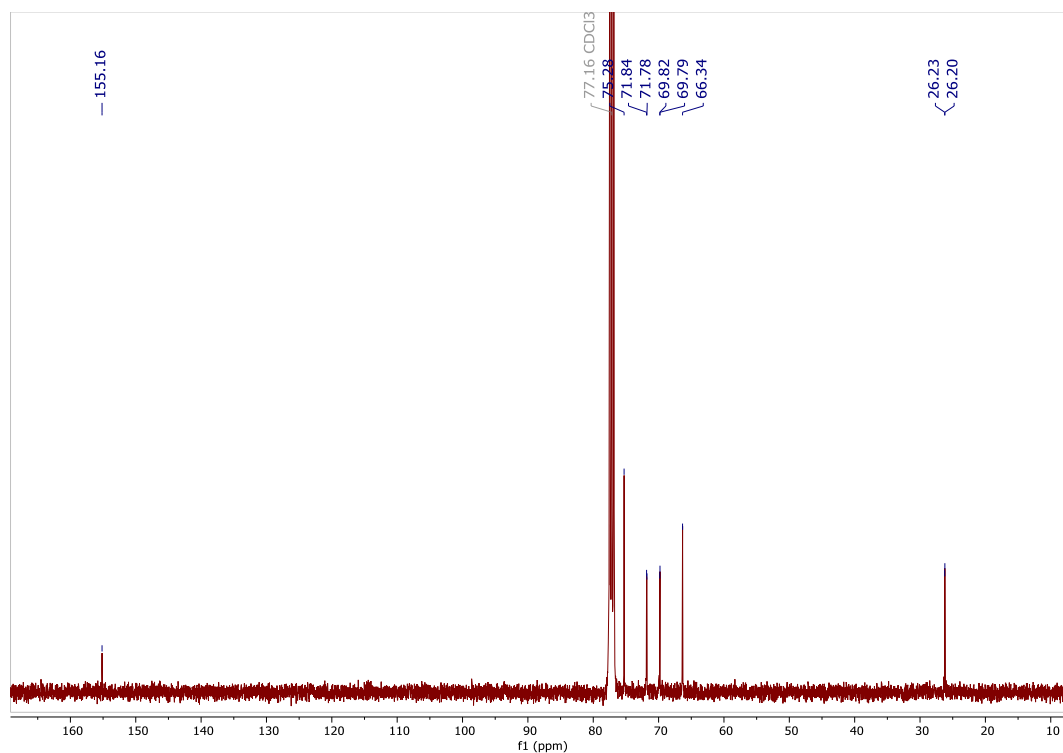


Figure S 84: ^{13}C NMR (101 MHz, CDCl_3) $\delta(\text{ppm})$: 155.16; 75.28; 71.84; 71.78; 69.82; 69.79; 66.34; 26.23; 26.20.

4-(phenoxy)methyl-1,3-dioxolane-2-one⁹

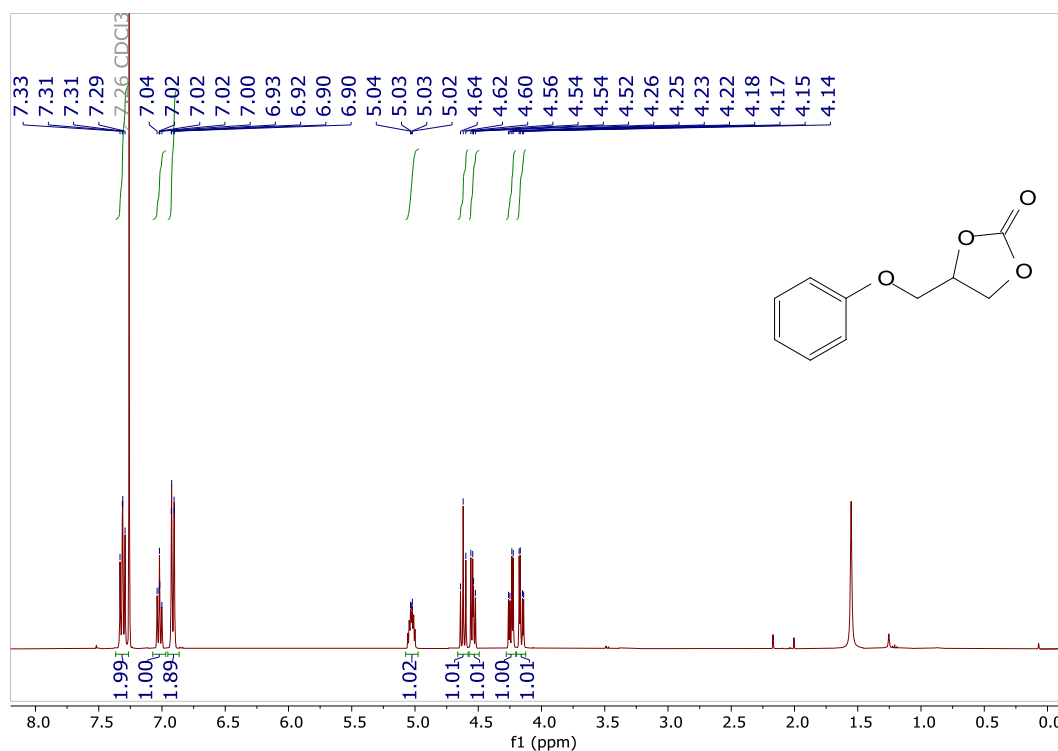


Figure S 85: ¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.31 (dd, *J* = 8.7, 7.3 Hz, 2H), 7.07 – 6.97 (m, 1H), 6.91 (dd, *J* = 8.7, 1.0 Hz, 2H), 5.03 (dd, *J* = 4.2, 1.8 Hz, 1H), 4.62 (t, *J* = 8.4 Hz, 1H), 4.54 (dd, *J* = 8.5, 6.0 Hz, 1H), 4.24 (dd, *J* = 10.5, 4.4 Hz, 1H), 4.16 (dd, *J* = 10.5, 3.6 Hz, 1H).

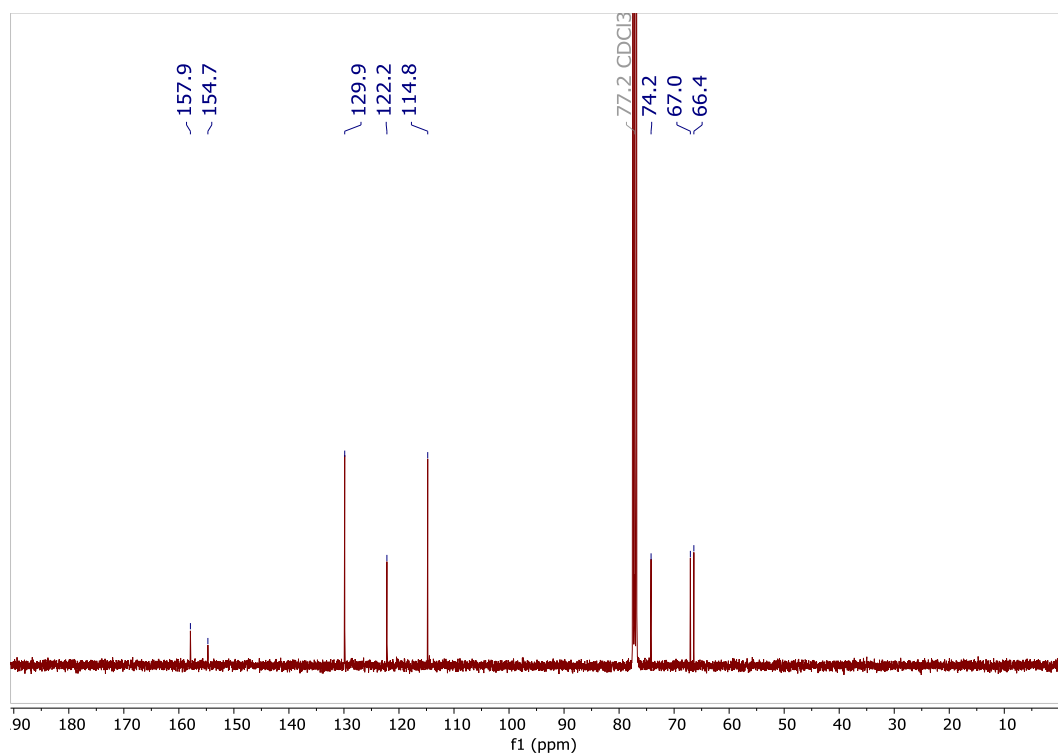


Figure S 86: ¹³C NMR (101 MHz, CDCl₃) δ (ppm): 157.9; 154.7; 129.9; 122.2; 114.8; 74.2; 67.0; 66.4.

4-(butoxymethyl)-1,3-dioxolan-2-one⁹

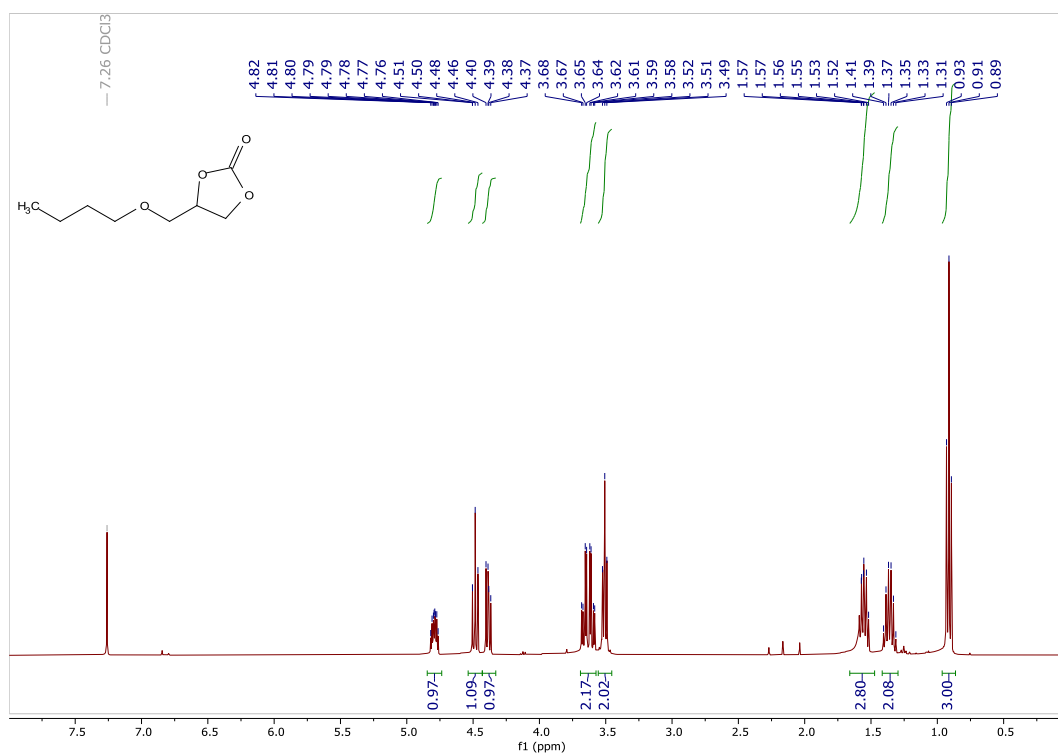


Figure S 87: ¹H NMR (400 MHz, CDCl₃) δ (ppm): 4.82-4.76 (m, 1H), 4.48 (t, J = 8.3 Hz, 1H), 4.38 (dd, J = 8.3, 6.1 Hz, 1H), 3.69–3.57 (m, 2H), 3.56–3.45 (m, 2H), 1.66–1.47 (m, 3H), 1.36 (dq, J = 14.5, 7.3 Hz, 2H), 0.91 (t, J = 7.4 Hz, 3H).

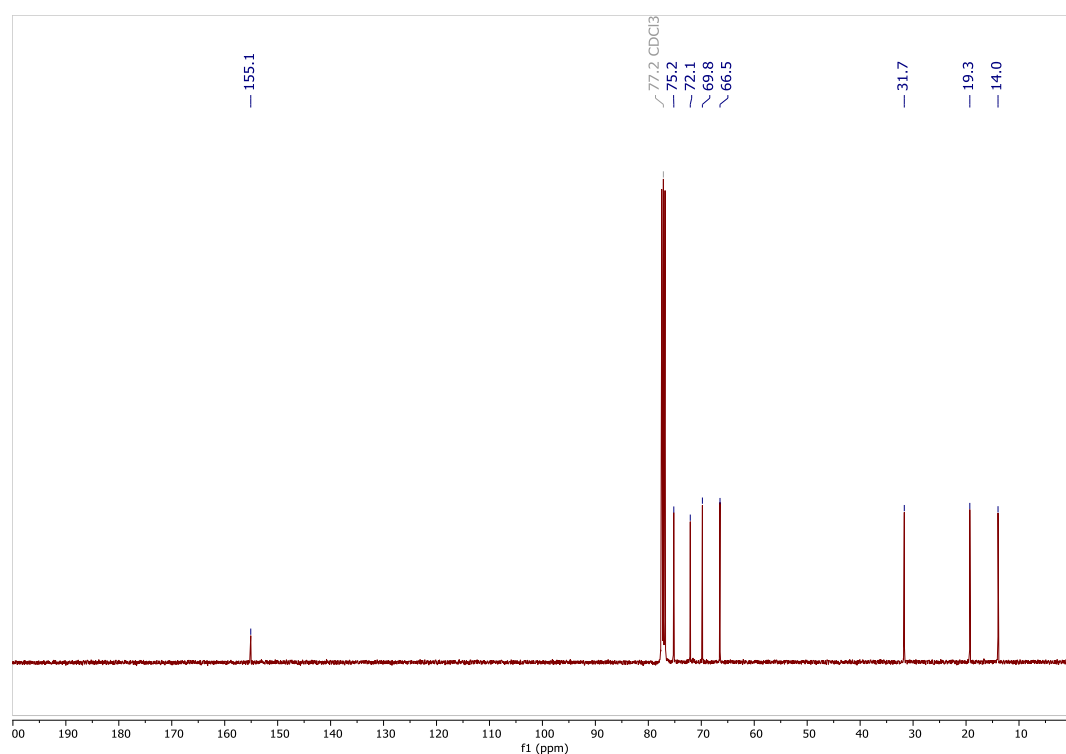


Figure S 88: ¹³C NMR (101 MHz, CDCl₃) δ (ppm): 155.1, 75.2, 72.1, 69.8, 66.5, 31.7, 19.3, 14.0

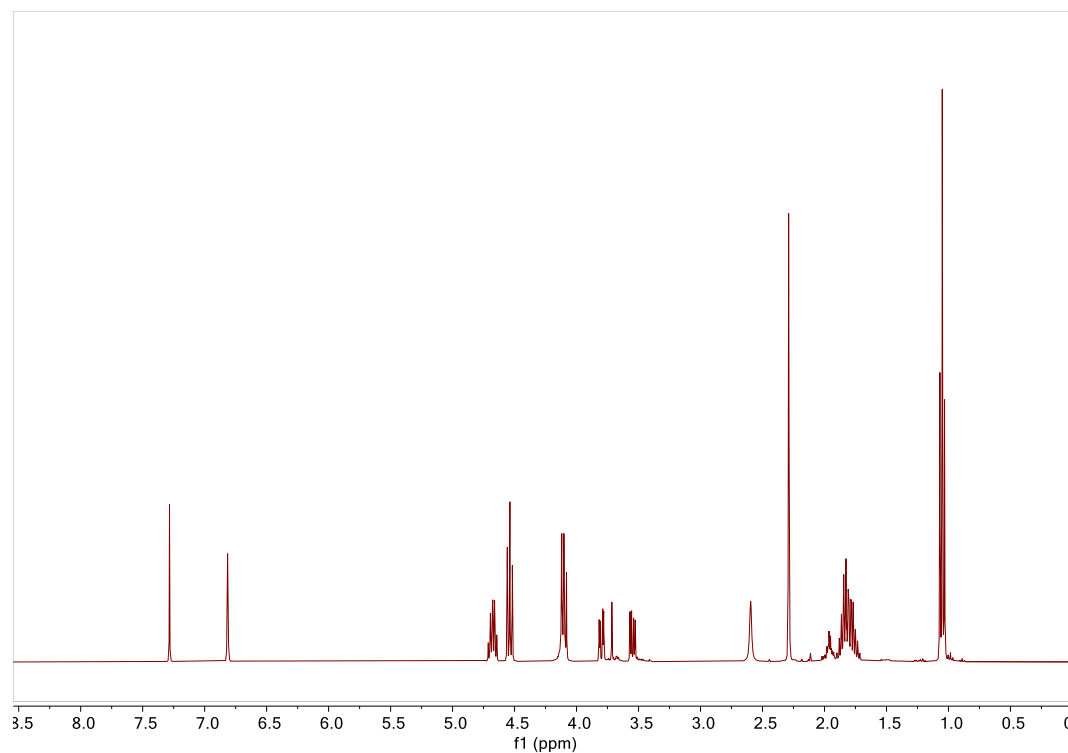


Figure S 89: ^1H NMR spectrum (400 MHz, CDCl_3) of the crude reaction mixture for CO_2 insertion into 1,2-epoxybutane at $p^0(\text{CO}_2) = 10$ bar.

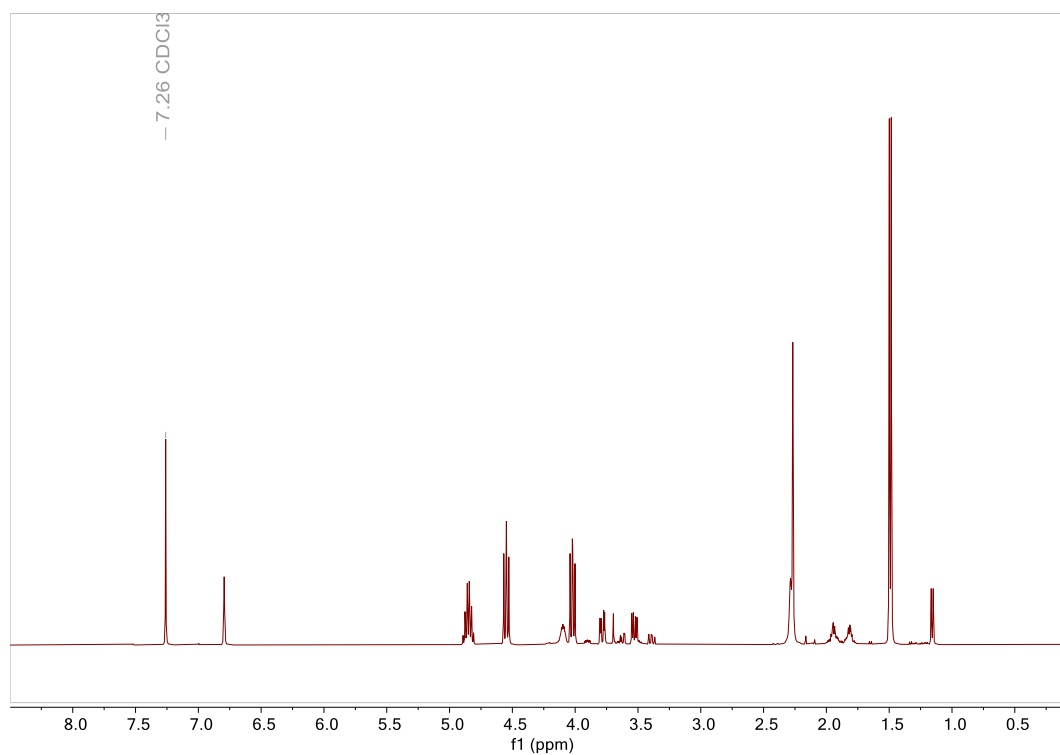


Figure S 90: ^1H NMR spectrum (400 MHz, CDCl_3) of the crude reaction mixture for CO_2 insertion into 1,2-epoxypropane at $p^0(\text{CO}_2) = 10$ bar.

4-methyl-1,3-dioxolan-2-one

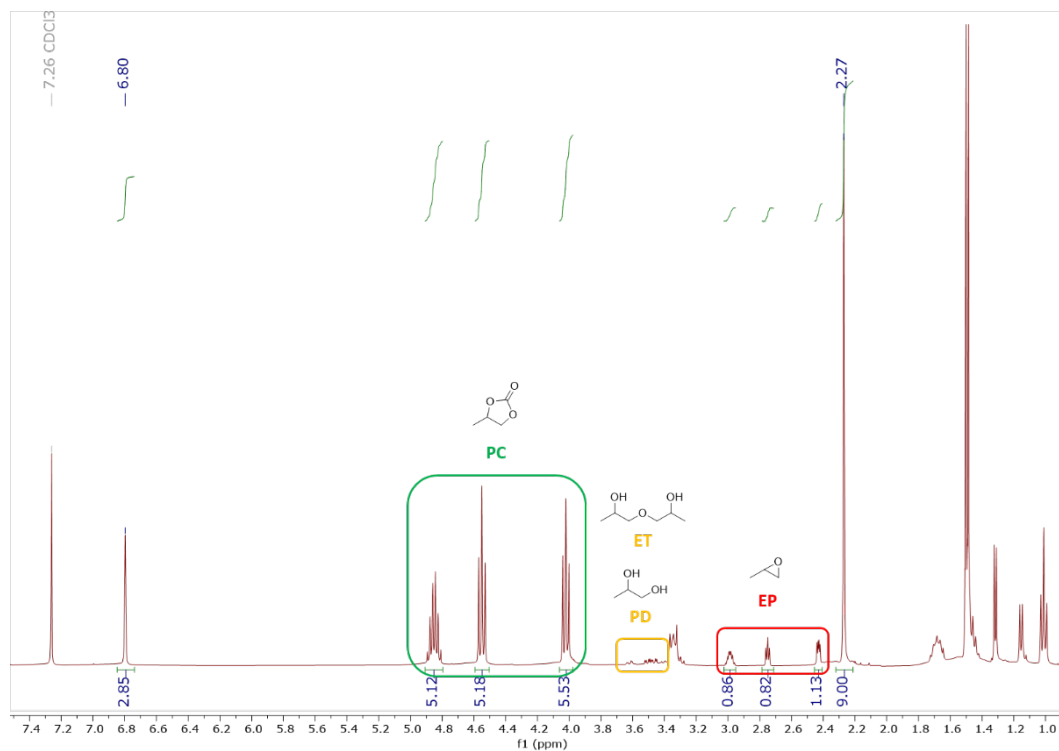


Figure S 91: ¹H NMR spectrum (400 MHz, CDCl₃) of the crude reaction mixture for CO₂ fixation into 1,2-epoxypropane.

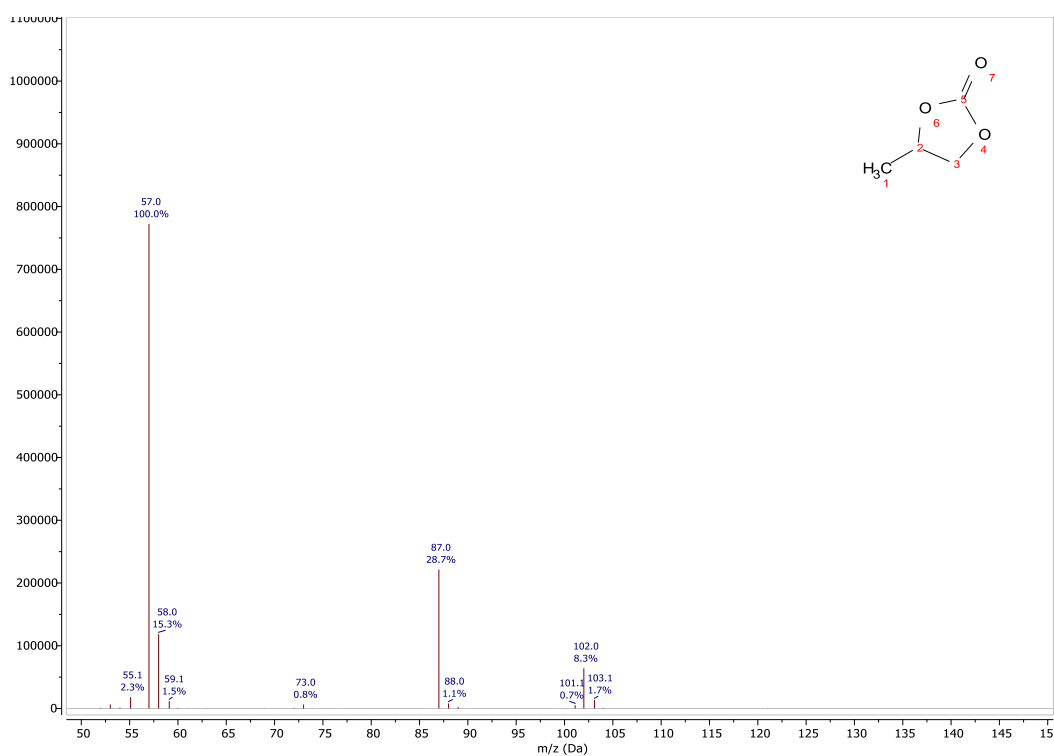


Figure S 92: EI-MS (70 eV) spectrum of 4-methyl-1,3-dioxolan-2-one.

Methyl 8-[3-(octan-3-yl)oxiran-2-yl]octanoate (methyl oleate)²

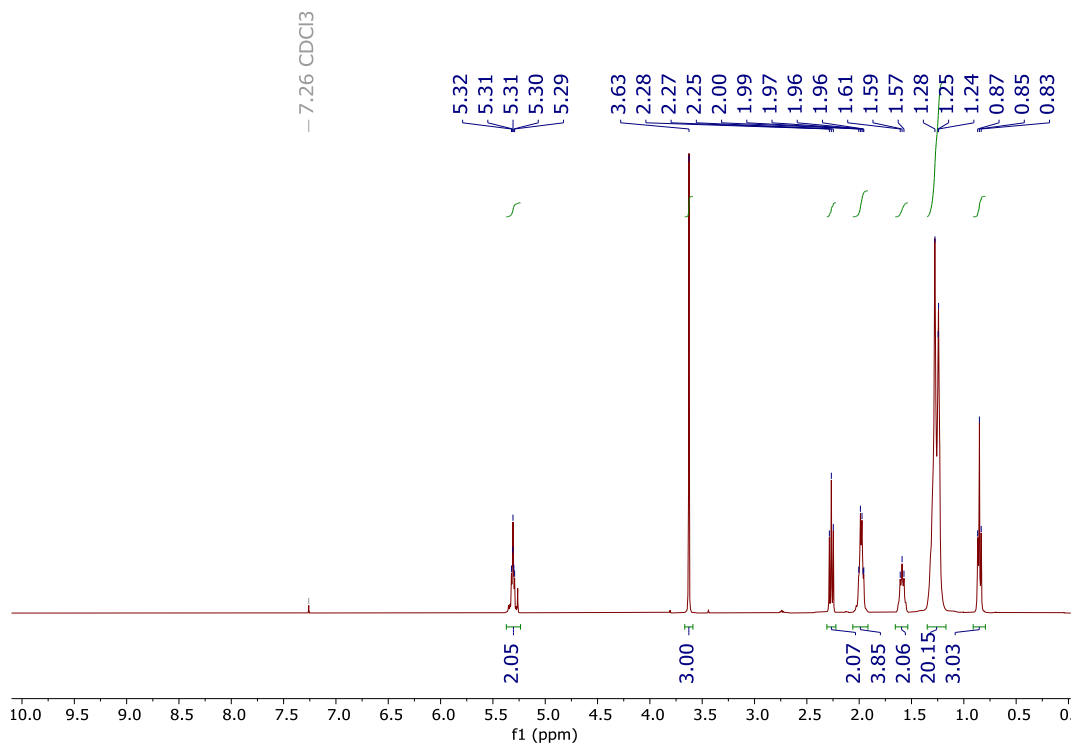


Figure S 93: ^1H NMR (400 MHz, CDCl_3) δ 5.4 – 5.2 (m, 2H), 3.6 (s, 3H), 2.3 (t, $J = 7.5$ Hz, 2H), 2.0 (q, $J = 6.6$ Hz, 4H), 1.6 (t, $J = 7.2$ Hz, 2H), 1.3 – 1.2 (m, 20H), 0.9 (t, $J = 6.8$ Hz, 3H).

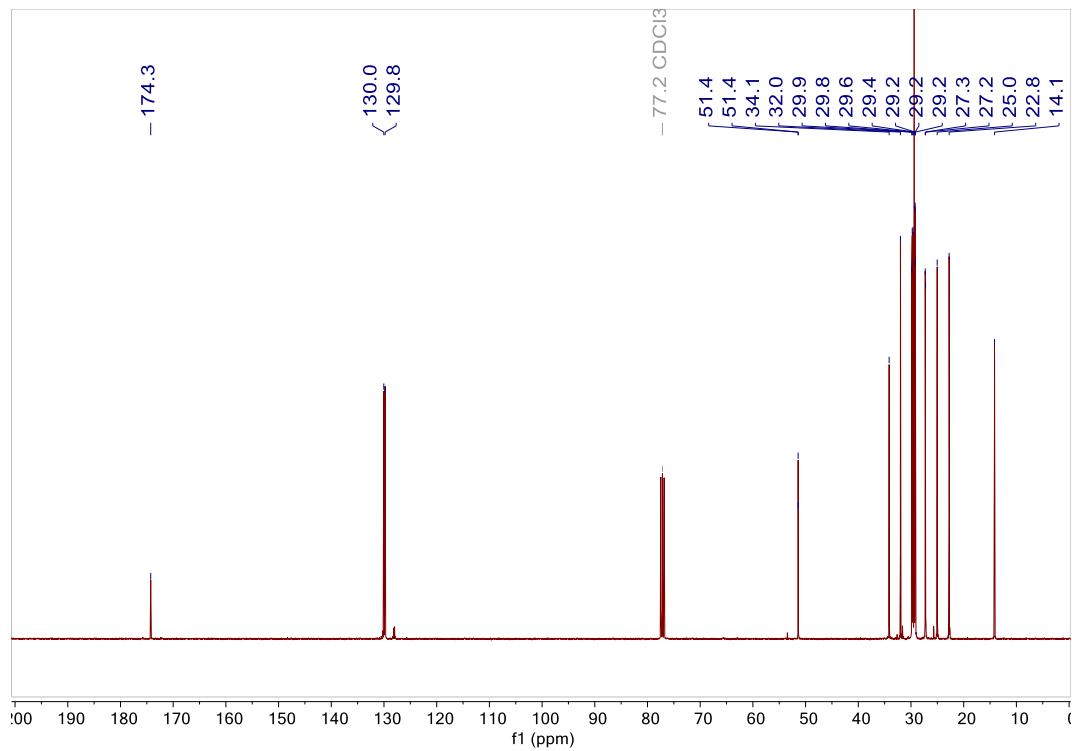


Figure S 94: ^{13}C NMR (101 MHz, CDCl_3) δ 174.3, 130.0, 129.8, 51.4, 51.4, 34.1, 32.0, 29.9, 29.8, 29.6, 29.4, 29.2, 29.2, 29.2, 27.3, 27.2, 25.0, 22.8, 14.1.

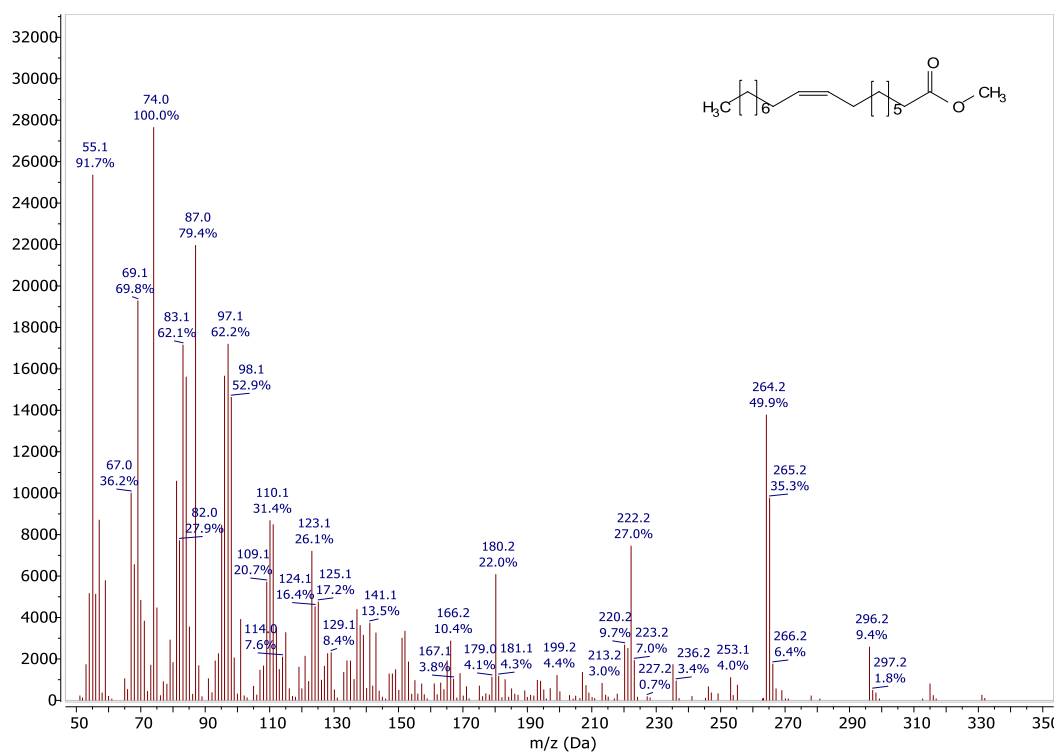


Figure S 95: EI-MS (70 eV) spectrum of methyl oleate.

Methyl oleate epoxide {methyl 8-[(2R,3S)-3-octyloxiran-2-yl]octanoate}²

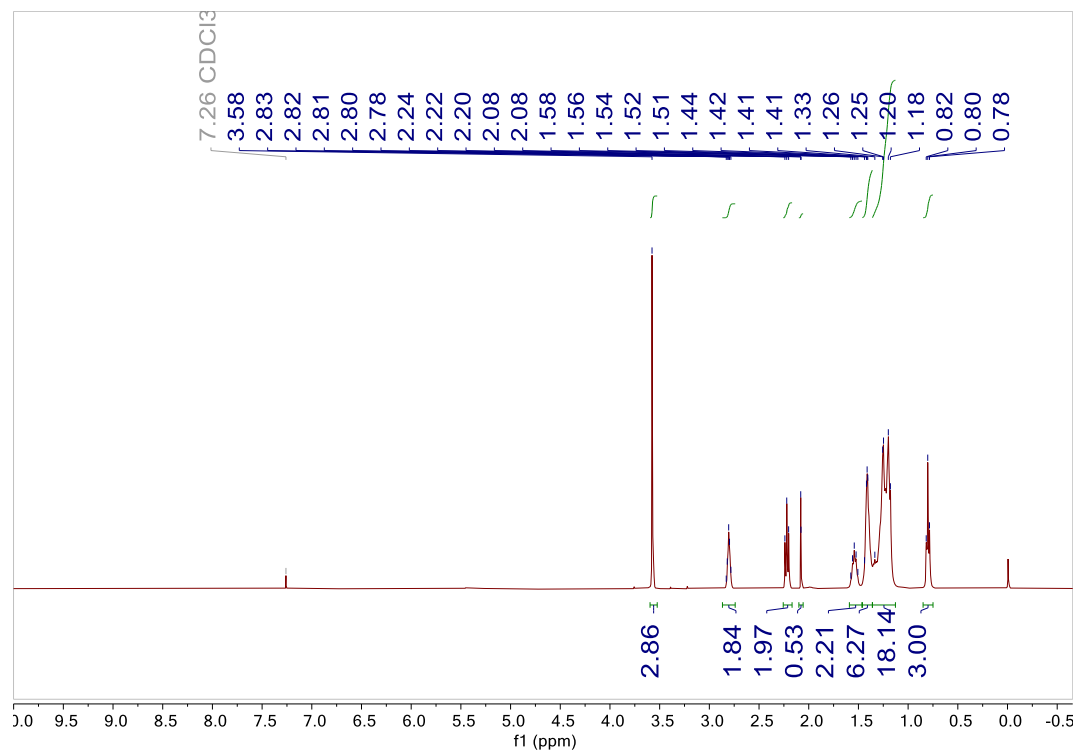


Figure S 96: ^1H NMR (400 MHz, CDCl_3) δ 3.58 (s, 3H), 2.87 – 2.74 (m, 2H), 2.22 (t, $J = 7.5$ Hz, 2H), 2.08 (d, $J = 1.0$ Hz, 1H), 1.54 (t, $J = 7.1$ Hz, 2H), 1.46 – 1.36 (m, 6H), 1.36 – 1.13 (m, 18H), 0.80 (d, $J = 7.0$ Hz, 3H).

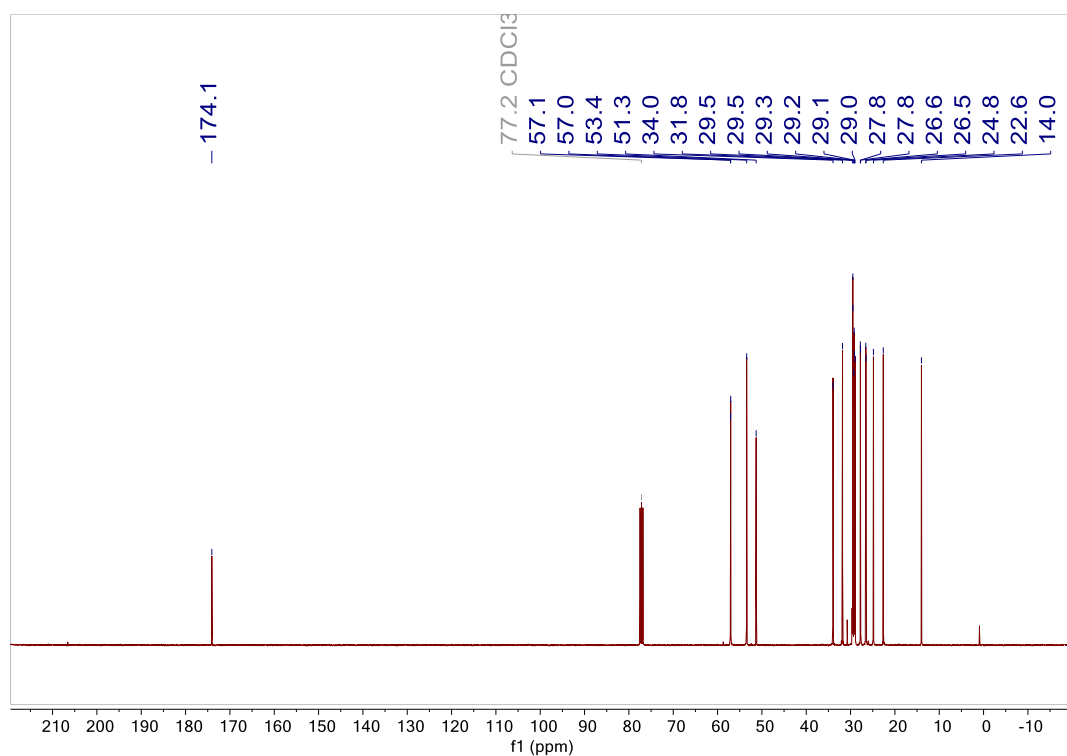


Figure S 97: ^{13}C NMR (101 MHz, CDCl_3) δ 174.1, 57.1, 57.0, 53.4, 51.3, 34.0, 31.8, 29.5, 29.5, 29.3, 29.2, 29.1, 29.0, 27.8, 27.8, 26.6, 26.5, 24.8, 22.6, 14.0.

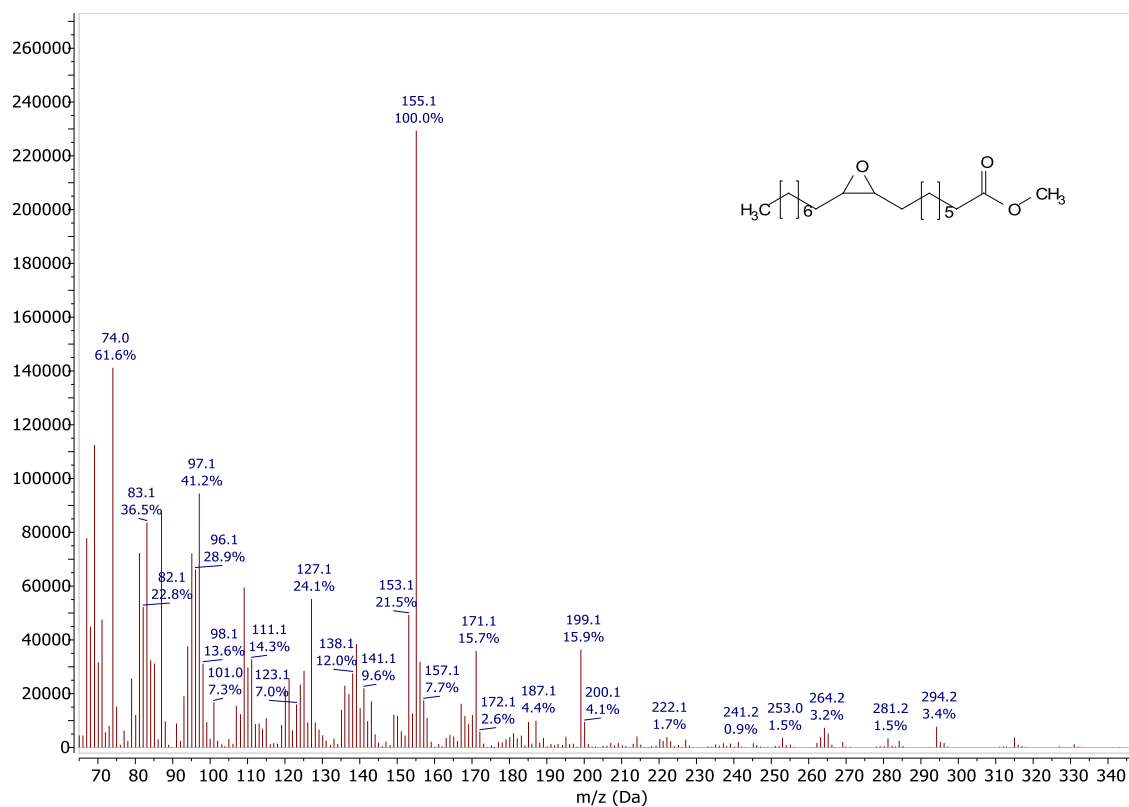


Figure S 98: EI-MS (70 eV) spectrum of methyl oleate epoxide {methyl 8-[(2R,3S)-3-octyloxiran-2-yl]octanoate}.

***cis/trans* mixture of methyl 8-[5-octyl-2-oxo-1,3-dioxolan-4-yl] octanoate²**

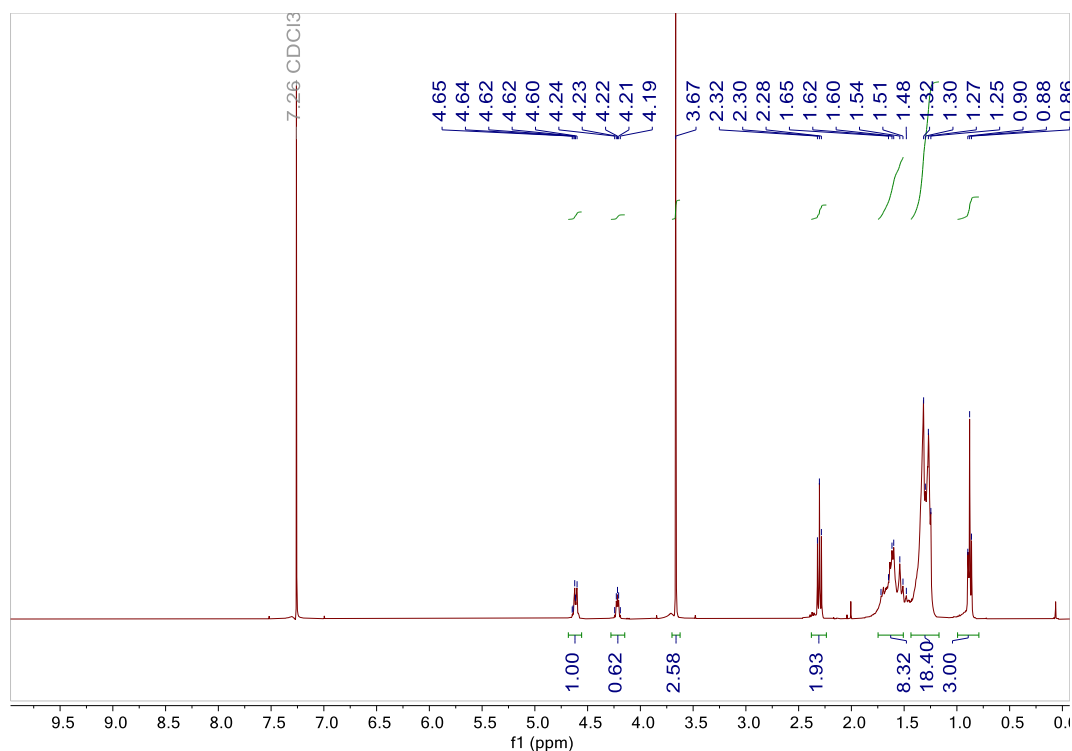


Figure S 99: ^1H NMR (400 MHz, CDCl_3) δ 4.68 – 4.56 (m, 2H, *-cis*), 4.28 – 4.15 (m, 2H, *-trans*), 3.67 (s, 3H), 2.30 (t, J = 7.5 Hz, 2H), 1.83 – 1.48 (m, 8H), 1.48 – 1.17 (m, 18H), 0.88 (t, J = 7.0 Hz, 3H).

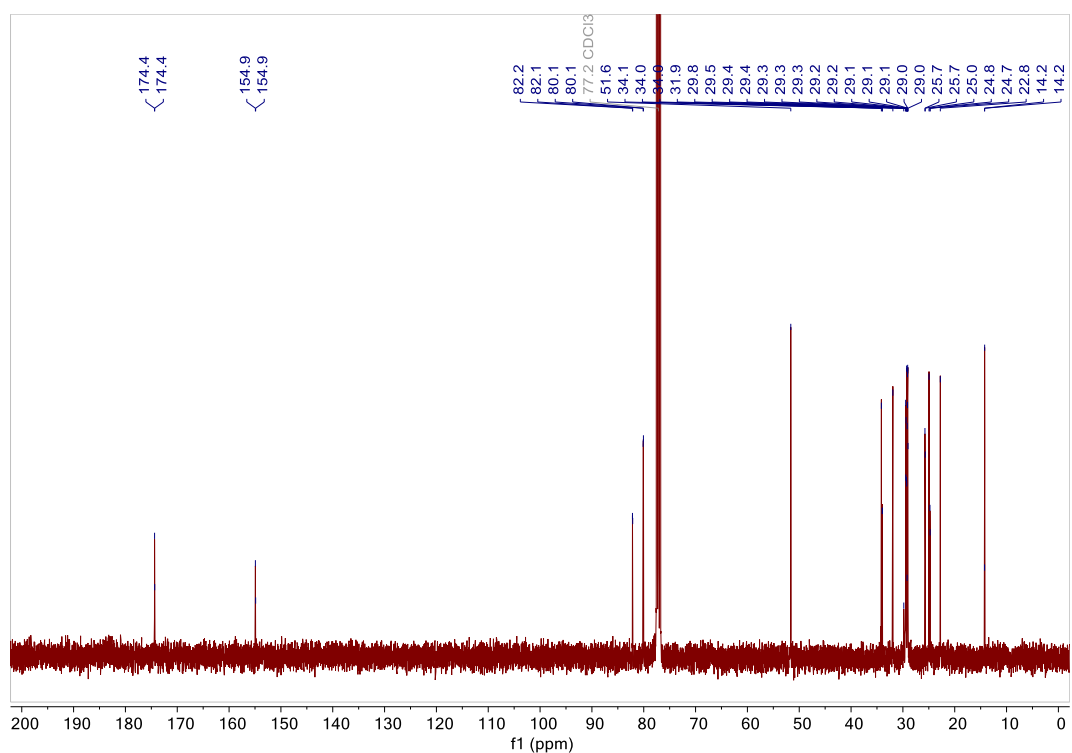


Figure S 100: ^{13}C NMR (101 MHz, CDCl_3) δ 174.37, 174.36, 154.92, 154.88, 82.17, 82.13, 80.11, 80.06, 51.63, 34.15, 33.97, 33.96, 31.93, 29.83, 29.47, 29.45, 29.39, 29.31, 29.29, 29.26, 29.19, 29.17, 29.13, 29.11, 29.08, 29.05, 29.02, 25.75, 25.69, 24.96, 24.78, 24.74, 22.78, 14.25, 14.23.

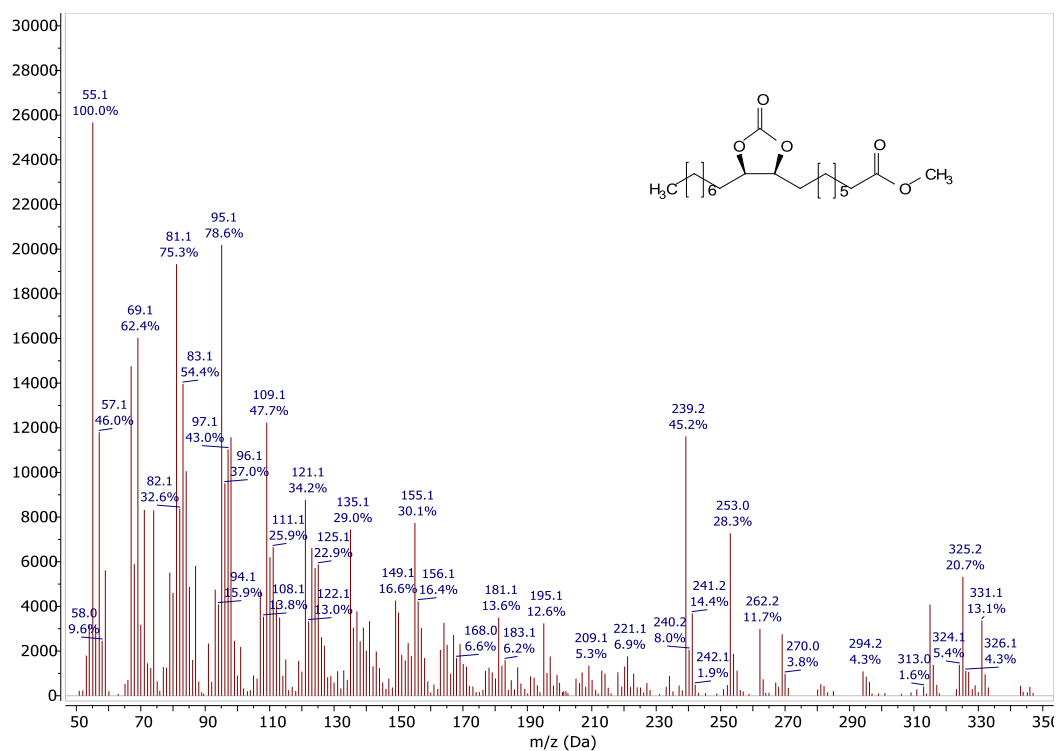


Figure S 101: EI-MS (70 eV) spectrum of cis-methyl oleate carbonate.

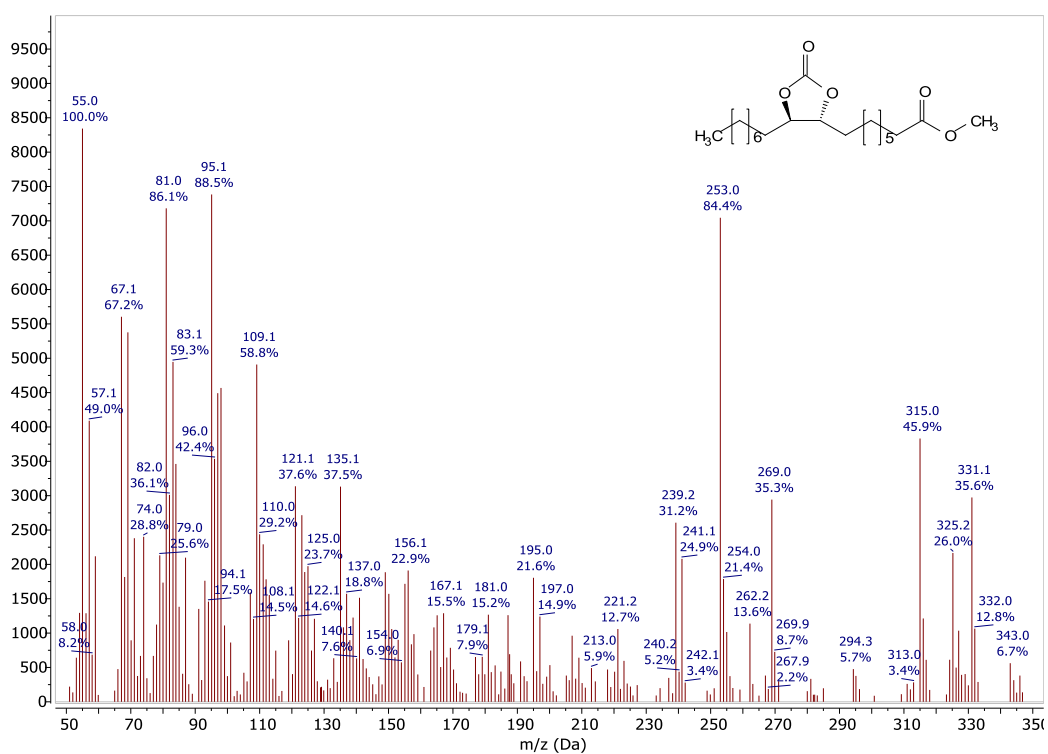


Figure S 102: EI-MS (70 eV) spectrum of trans-methyl oleate carbonate.

Bibliography Characterization Chapter 3

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- (9) Ma, H.; Liu, S.; Wang, H.; Li, G.; Zhao, K.; Cui, X.; Shi, F. *In Situ* CO₂ Capture and Transformation into Cyclic Carbonates Using Flue Gas. *Green Chem.* **2023**, *25*, 2293–2298. <https://doi.org/10.1039/D2GC04757H>.

Characterization Chapter 4

Catalyst Characterization Paragraph 4.1

The disposition of the catalyst of all the examined catalyst (1 % wt.) coated glass beads was analyzed using a field emission scanning electron microscope (FESEM, model Auriga Compact from ZEISS company, equipped with X-Ray detector (EDS) and electron backscatter diffraction (EBSD)). Samples were prepared according to CO₂ hydrogenation catalyst preparation and loading, and a fraction of the beads was deposited on carbon tape. Subsequently, a thin layer of carbon was sputtered (sputter EM MED020 from LEICA) to provide conductivity to the samples. A reference is provided by non-coated glass beads, shown in **Figure S103**, displaying the particle size distribution of the beads. **Figure S104**, **Figure S108**, **Figure S109** and **Figure S114** indicate that the beads are comparably coated with the catalyst powder.

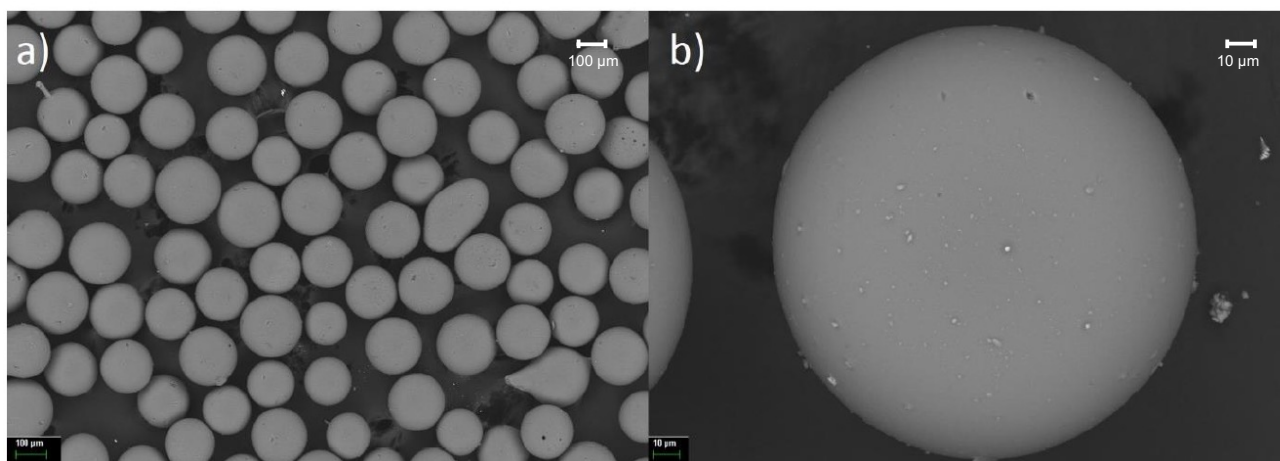


Figure S 103: Non-coated glass beads scanning electron microscopy image at different scales (a and b).

Cobalt(II,III) oxide

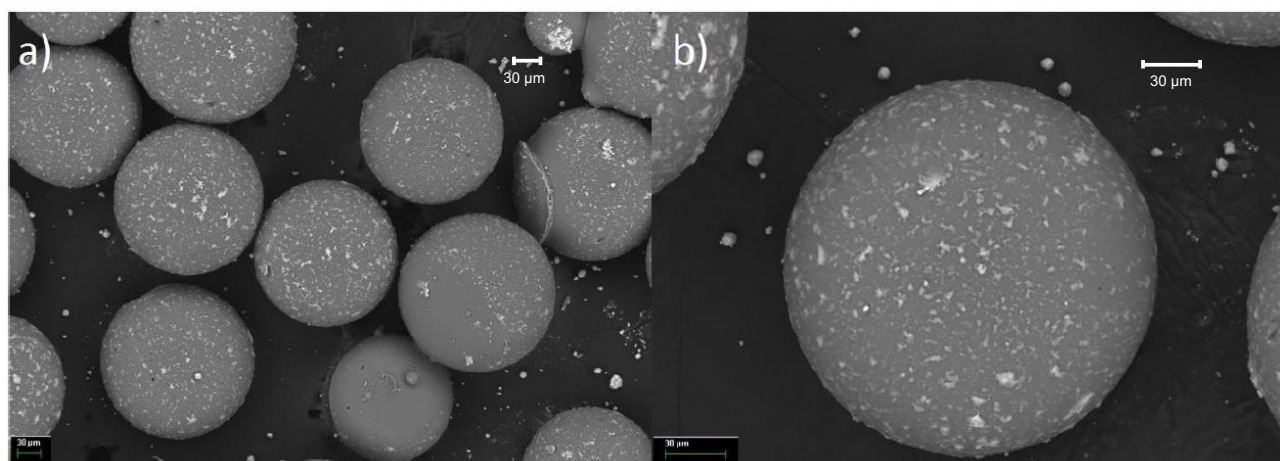


Figure S 104: Cobalt(II,III) oxide (1 % wt.) coated glass beads scanning electron microscopy image at different scales (a and b).

Ruthenium nanoparticles (5.76 wt%, 1.79 ± 0.51 nm) on titanium dioxide (Evonik Aeroxide P90, < 45 μm)

The ruthenium content in the catalyst was analyzed via inductively coupled plasma atomic emission spectroscopy (ICP-AES) in axial detection mode. Hereto, the sample was digested using a 10 ml mixture of mineral acids (HCl/HNO₃/HF in a 3:1:1 volumetric ratio) in a Milestone microwave setup, whereupon dilution in a 50 ml polypropylene flask was carried out. The digestion procedure is executed *in duplo* and average values are reported. An external calibration curve is used for quantification starting from a 1000 ppm Merck Ru standard in 7% HCl. 5 ppm QC measurements are regularly checked to ensure the instrument's constant performance. High-resolution transmission electron microscopy (HRTEM, **Figure S105a**) studies were performed using a JEOL ARM 200F Transmission Electron Microscope, probe corrected, equipped with a 100 mm² Centurio SDD EDX detector, operated at 200 kV. Imaging was performed in High Angle Annular Dark Field (HAADF) Scanning TEM mode. The HAADF detector uses the electrons scattered over large angles for imaging. The HAADF detector is therefore mass sensitive, which means that higher brightness in the image corresponds to the presence of (a larger concentration of) heavier atoms. This allows for a fast and accurate inventory of the ruthenium particle size on the TiO₂ support. Samples were prepared by preparing a suspension of the material in ethanol and by depositing a drop of this suspension onto a carbon-coated copper TEM grid and drying at room temperature. In order to determine the average size of the ruthenium nanoparticles and the particle size distribution (shown in **Figure S105b**), we measured the dimensions of 250 nanoparticles from the corresponding HRTEM micrograph, using the image analysis software ImageJ.

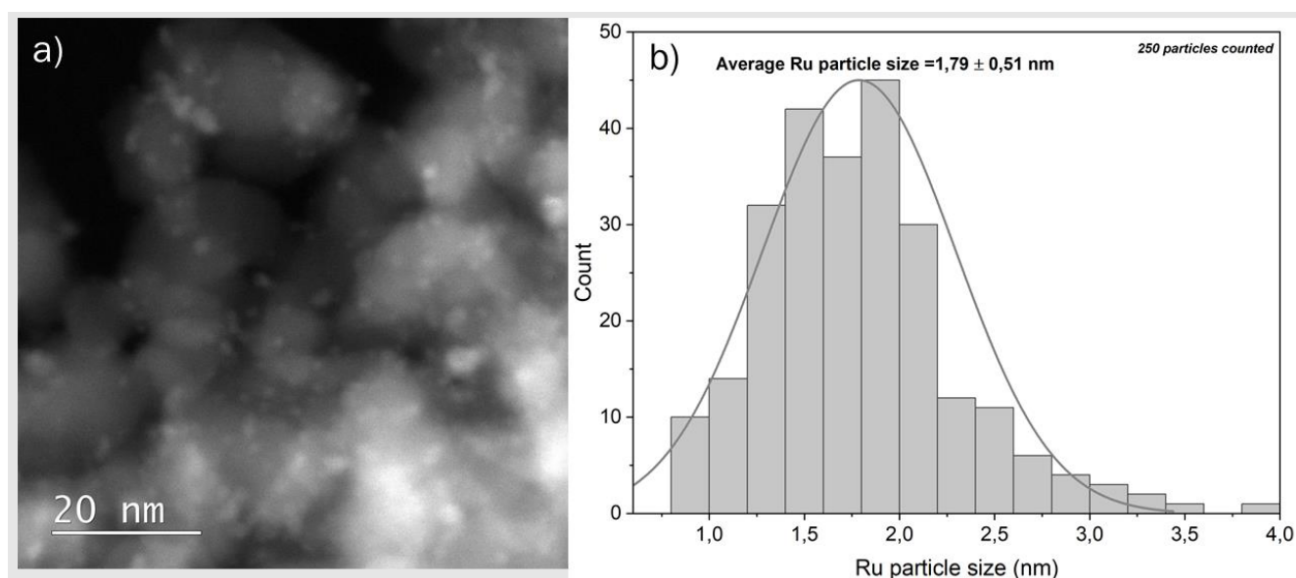


Figure S 105: Ruthenium nanoparticles (on TiO₂ support) high-resolution transmission electron microscopy micrographs (a) and associated size distribution histogram (b).

X-ray diffraction (XRD) data sets in **Figure S106** were collected using a powder diffractometer (Panalytical) equipped with a Prefix Bragg BrentanoHD mirror and a copper radiation source with a fixed slit of $\frac{1}{4}$ inch. A Pixcel 1d detector and an anti-scatter slit of 1 inch were used. The incident beam path is 4.41° , radius 240 mm. The used wavelength is K-Alpha1 ($1.5405980 \text{ \AA}$). Powder samples were prepared in a ceramic sample holder.

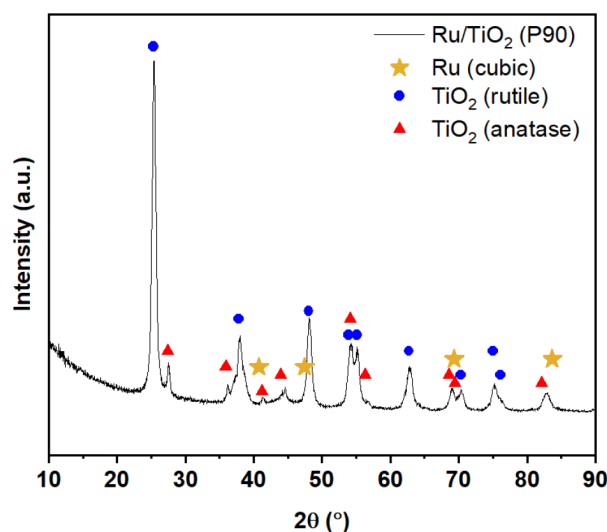


Figure S 106: XRD pattern of the Ru/TiO₂ (P90) nanocatalyst showing TiO₂ anatase, TiO₂ rutile and Ru cubic peak positions.

The UV-Visible diffuse reflectance spectrum (**Figure S107**) was obtained using a Shimadzu UV-3600 spectrophotometer. The powder samples were pressed on a support, and their reflectance was measured in the range between 300 nm and 1200 nm through an integrating sphere. The baseline for the measurements was done with BaSO₄.

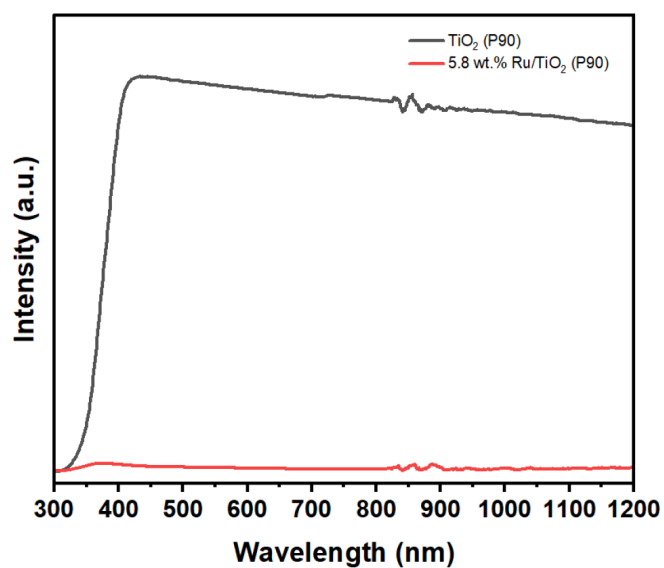


Figure S 107: Diffuse reflectance UV-Vis NIR spectra for the $\text{TiO}_2(\text{P90})$ (black curve) and Ru/TiO_2 (red curve).

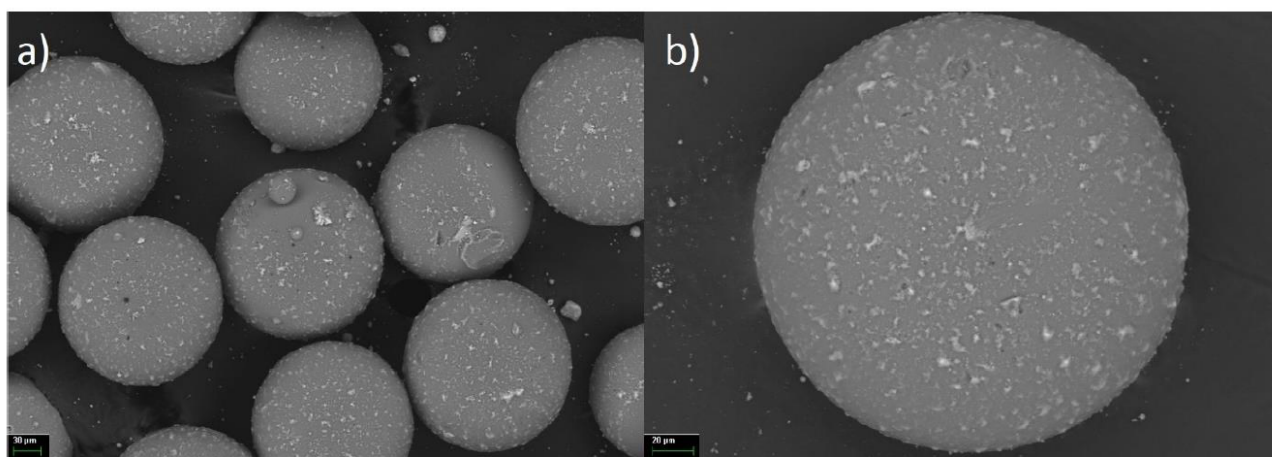


Figure S108: Ru/TiO_2 (1 % wt.) coated glass beads scanning electron microscopy image at different scales (a and b).

Ruthenium nanoparticles (2.5 wt%, 1.4 ± 0.4 nm) on strontium titanate (80 nm)

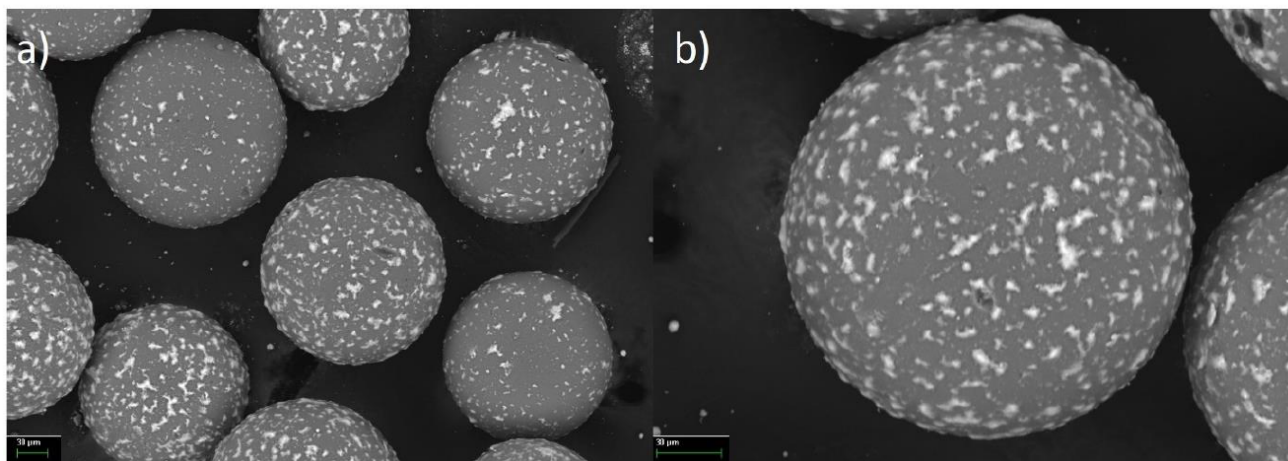


Figure S109: Ru/STO (1 % wt.) coated glass beads scanning electron microscopy image at different scales (a and b).

Gold nanoparticles (2.5 wt%, 2.44 ± 0.61 nm) on titanium dioxide (Evonik Aeroxide P90, < 45 µm)

The gold content in the catalyst was analyzed via ICP-AES in axial detection mode. Hereto, the sample was digested using a 10 ml mixture of mineral acids (HCl/HNO₃/HF in a 3:1:1 ratio) in a Milestone microwave setup, where upon dilution in a 50 ml polypropylene flask was carried out. The digestion procedure is executed *in duplo* and average values are reported. An external calibration curve is used for quantification starting from a 1000 ppm Perkin Elmer Au standard in 10% HCl. 5 ppm QC measurements are regularly checked to assure the instrument's constant performance. HRTEM (**Figure S110**) studies were performed using a JEOL ARM 200F Transmission Electron Microscope, probe corrected, equipped with a 100 mm² Centurio SDD EDX detector, operated at 200 kV. Imaging was performed in HAADF Scanning TEM mode. An inventory of the gold particle size on the TiO₂ support is shown in **Figure S111**. Samples were prepared by preparing a suspension of the material in ethanol and by depositing a drop of this suspension onto a carbon-coated copper TEM grid and drying at room temperature.

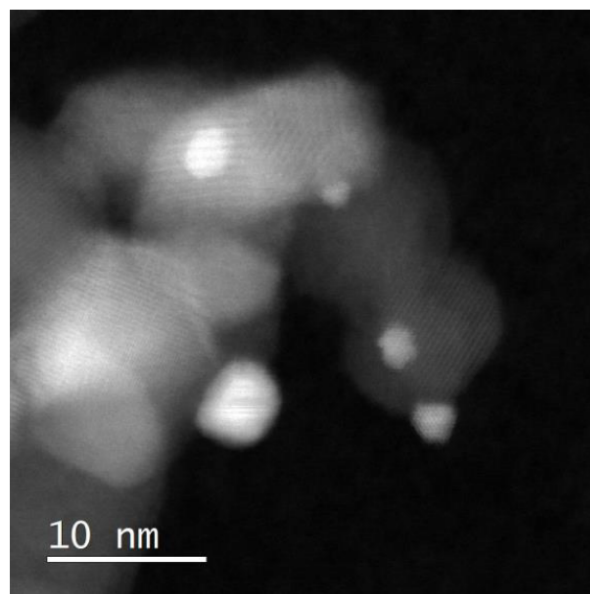
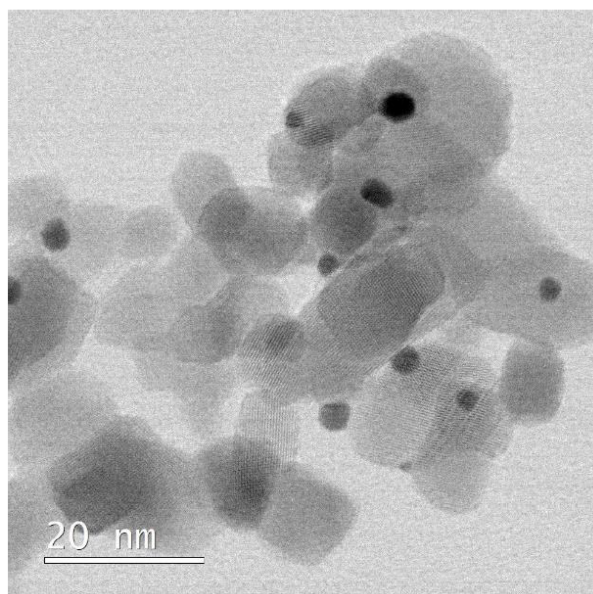


Figure S110: Representative high-resolution transmission electron microscopy images of the gold supported on TiO₂.

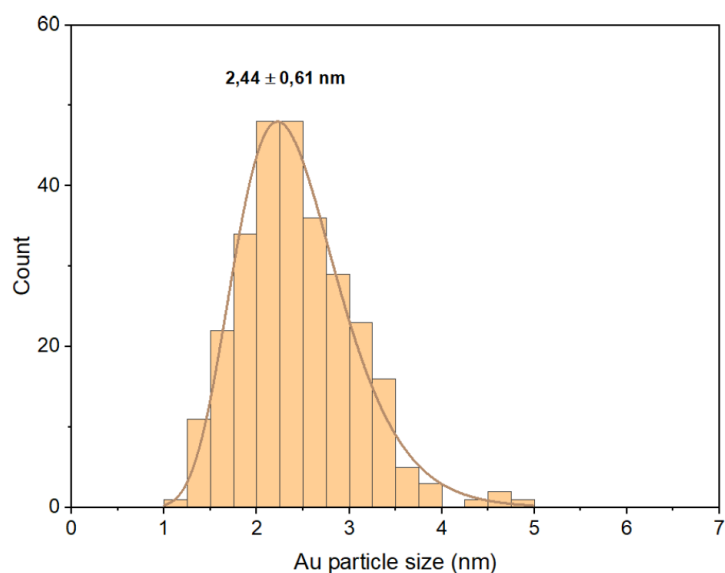


Figure S111: Gold nanoparticle size distribution histogram.

XRD data sets in **Figure S112** were collected using a powder diffractometer (Panalytical) equipped with a Prefix Bragg BrentanoHD mirror and a copper radiation source with a fixed slit of ¼ inch. A Pixcel 1d detector and an anti-scatter slit of 1 inch were used. The incident beam path is 4.41°, radius

240 mm. The used wavelength is K-Alpha1 (1.5405980 Å). Powder samples were prepared in a ceramic sample holder.

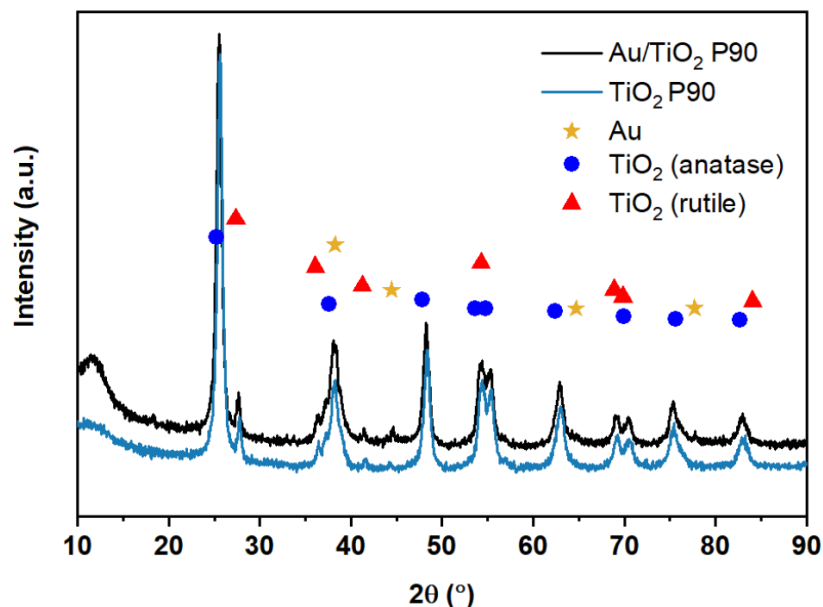


Figure S112: XRD pattern of the Au/TiO₂ nanocatalyst.

The UV-Visible diffuse reflectance spectrum (**Figure S113**) was obtained using a Shimadzu UV-3600 spectrophotometer. The powder samples were pressed on a support, and their reflectance was measured in the range between 300 nm and 1200 nm through an integrating sphere. The baseline for the measurements was recorded with BaSO₄.

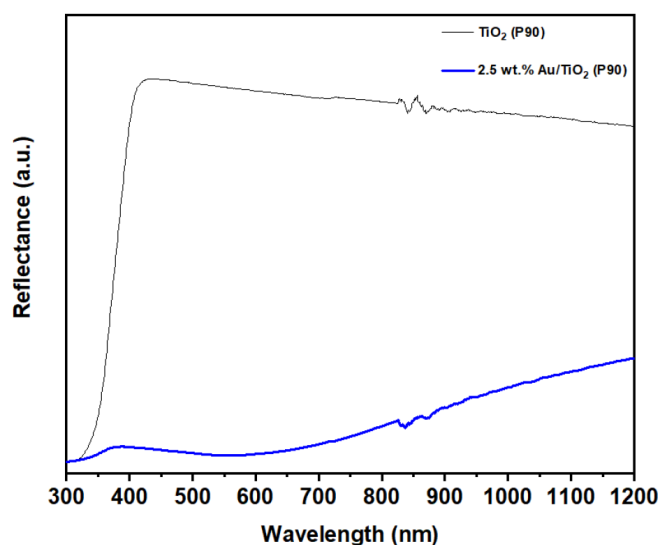


Figure S 113: Diffuse reflectance UV–Vis NIR spectra for TiO₂ (P90) (black curve) and Au/TiO₂ (blue curve).

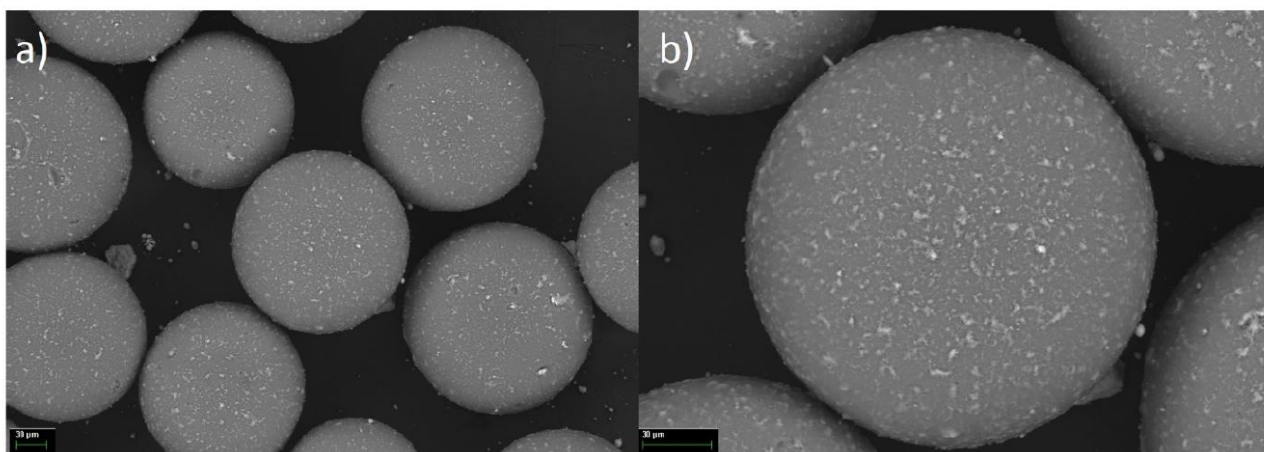


Figure S 114: Au/TiO₂ (1 % wt.) coated glass beads scanning electron microscopy image at different scales (a and b).

(4-fluorophenyl)(4-methoxyphenyl)methanone

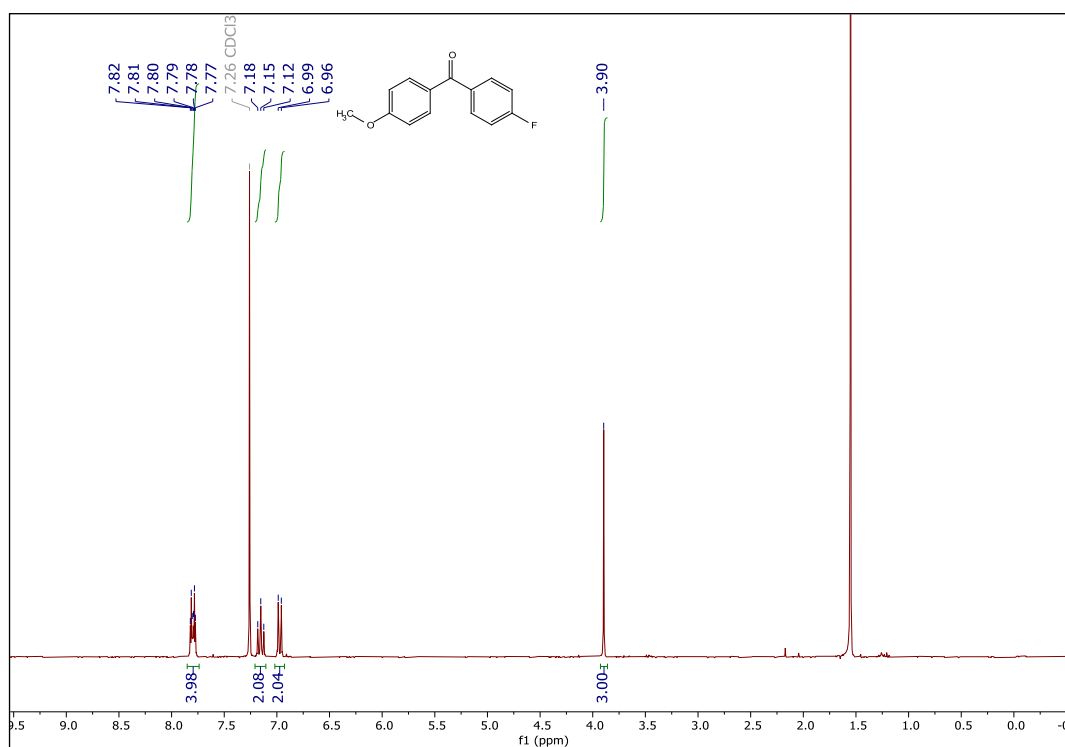


Figure S 115: ¹H NMR (300 MHz, CDCl₃): δ 7.85 – 7.74 (m, 4H), 7.15 (t, J = 8.6 Hz, 2H), 6.97 (d, J = 8.9 Hz, 2H), 3.90 (s, 3H).

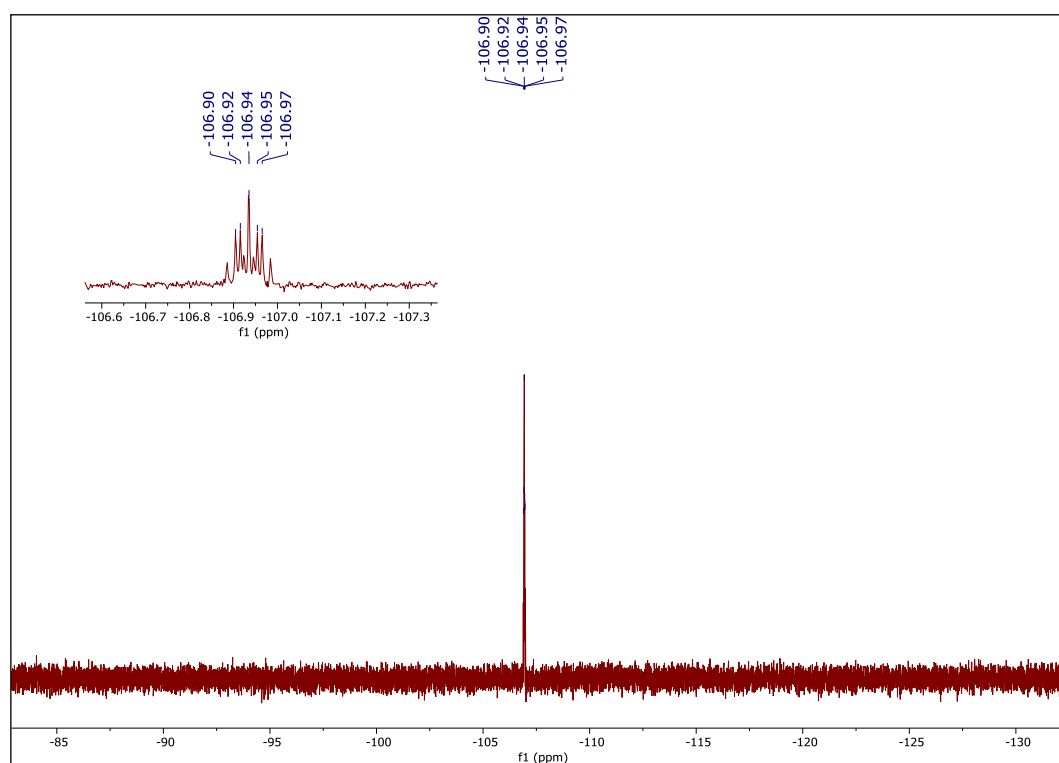


Figure S 116: ¹⁹F NMR (282 MHz, CDCl₃): δ -106.94 (m).

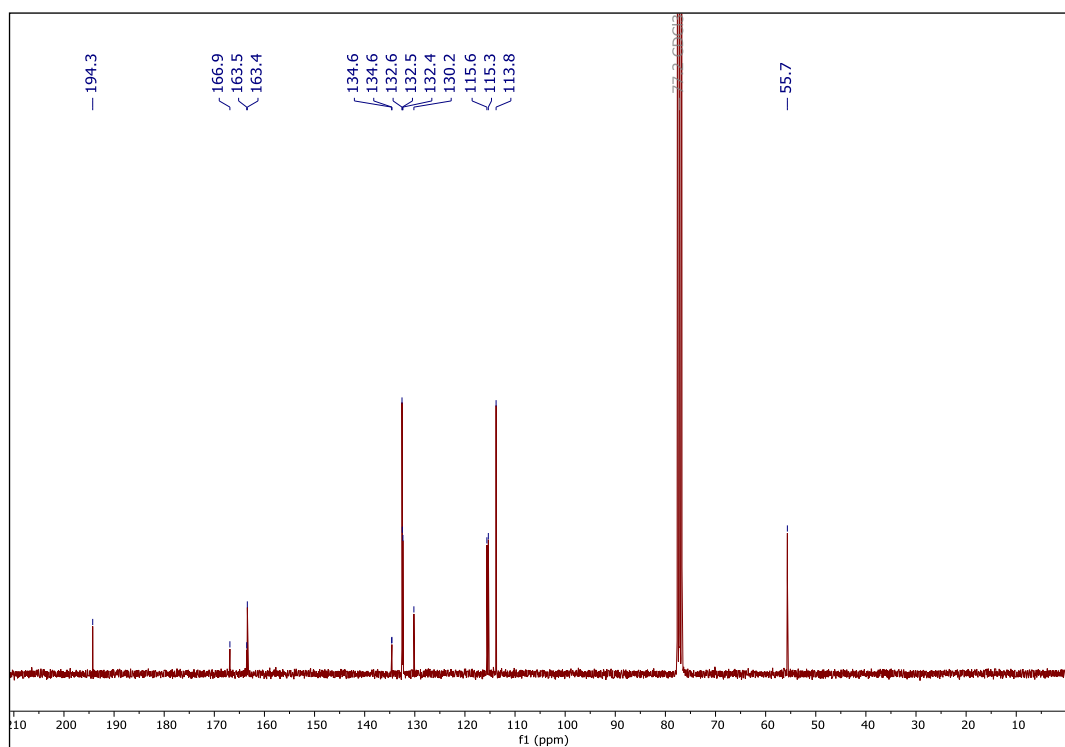


Figure S 117: ^{13}C NMR (75 MHz, CDCl_3): δ 194.3, 166.9, 163.5, 163.4, 134.6, 134.6, 132.6, 132.5, 132.4, 130.2, 115.6, 115.3, 113.8, 55.7.

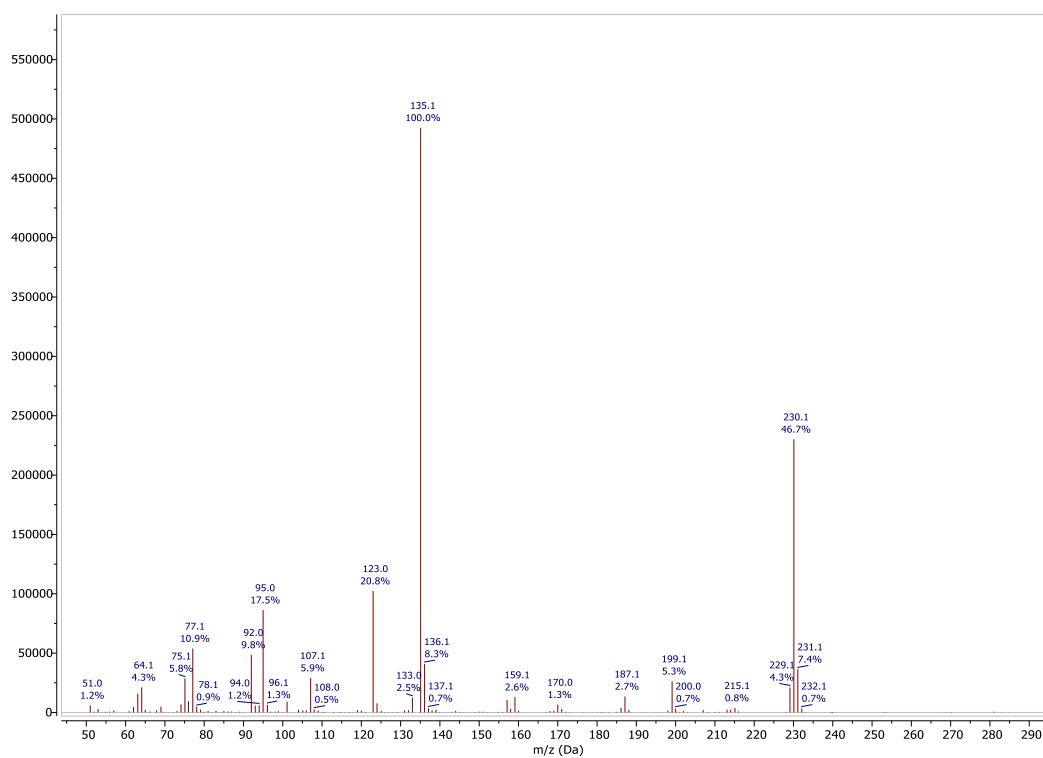


Figure S 118: EI-MS, m/z calcd. for (4-fluorophenyl)(4-methoxyphenyl)methanone $[M]^+$: 230.1, found 230.1.

[1,1'-Biphenyl]-4-yl trifluoromethanesulfonate

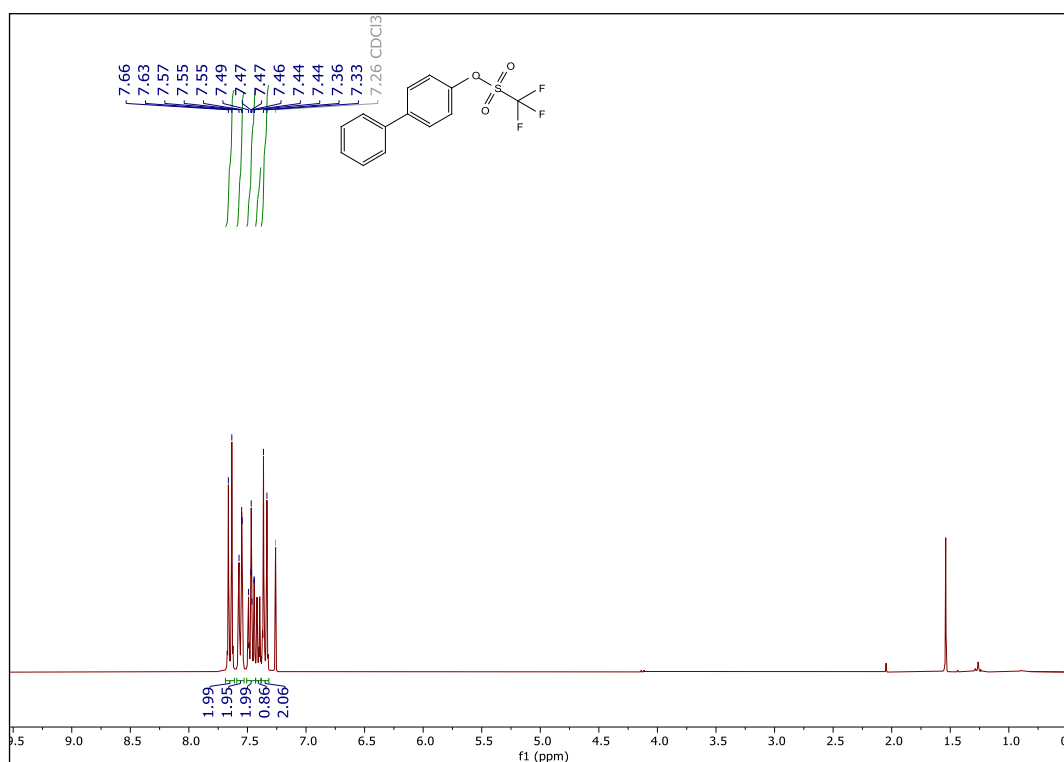


Figure S 119: ¹H NMR (300 MHz, CDCl₃): δ 7.66–7.63 (m, 2H), 7.59–7.53 (m, 2H), 7.51–7.43 (m, 2H), 7.43–7.38 (m, 1H), 7.36–7.34 (m, 2H).

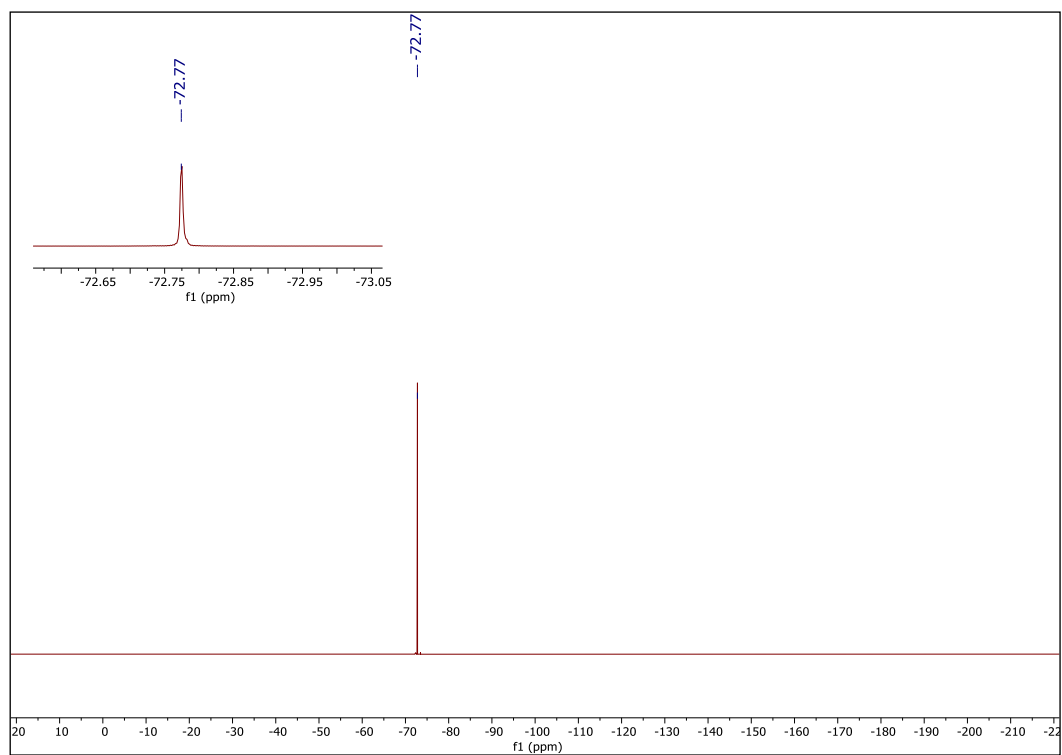


Figure S 120: ^{19}F NMR (282 MHz, CDCl_3) δ -72.77.

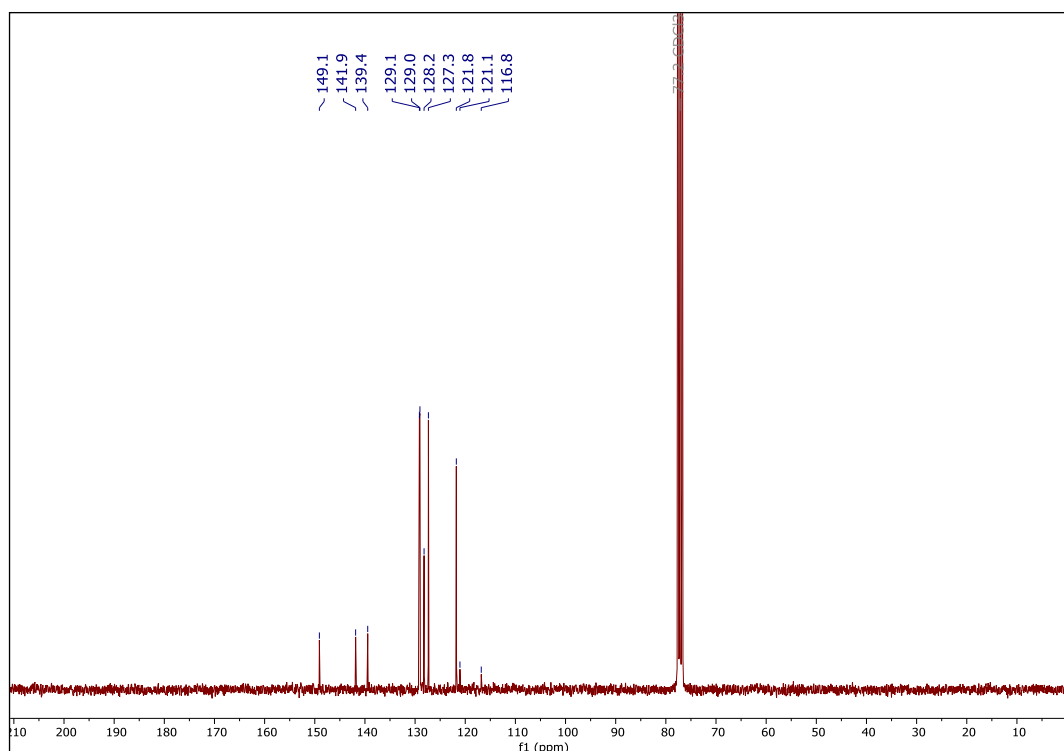


Figure S 121: ^{13}C NMR (75 MHz, CDCl_3) δ 149.1, 141.9, 139.5, 129.1 (2C), 129.0 (2C), 128.2, 127.3 (2C), 121.8 (2C), 118.9(q, $J = 320.7\text{Hz}$)

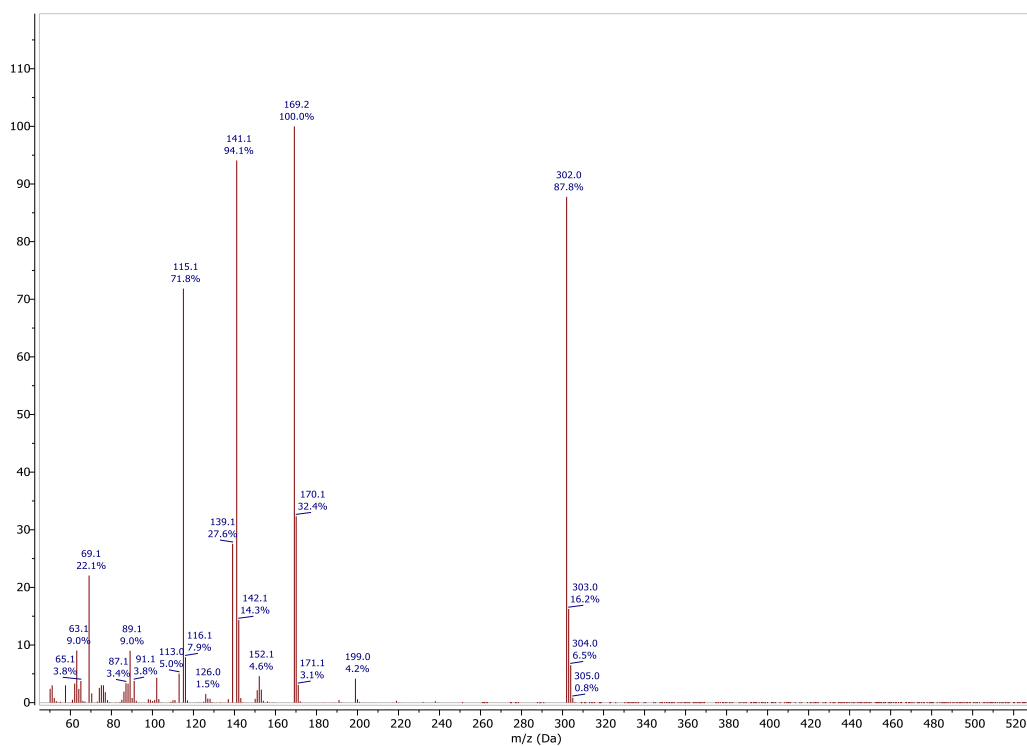


Figure S 122: EI-MS, m/z calcd. for [1,1'-Biphenyl]-4-yl trifluoromethanesulfonate $[M]^+$: 302.0, found 302.0.

Methyl [1,1'-biphenyl]-4-carboxylate

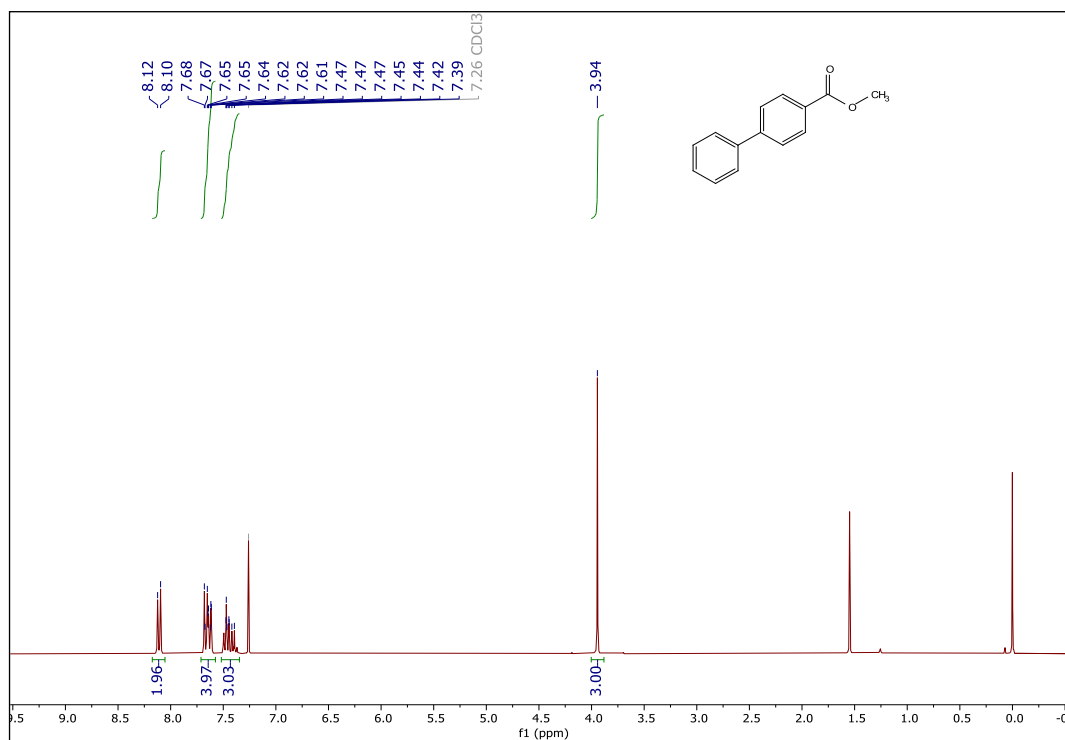


Figure S 123: ¹H NMR (300 MHz, CDCl₃) δ 8.17 – 8.05 (m, 2H), 7.71 – 7.57 (m, 4H), 7.52 – 7.35 (m, 3H), 3.94 (s, 3H).

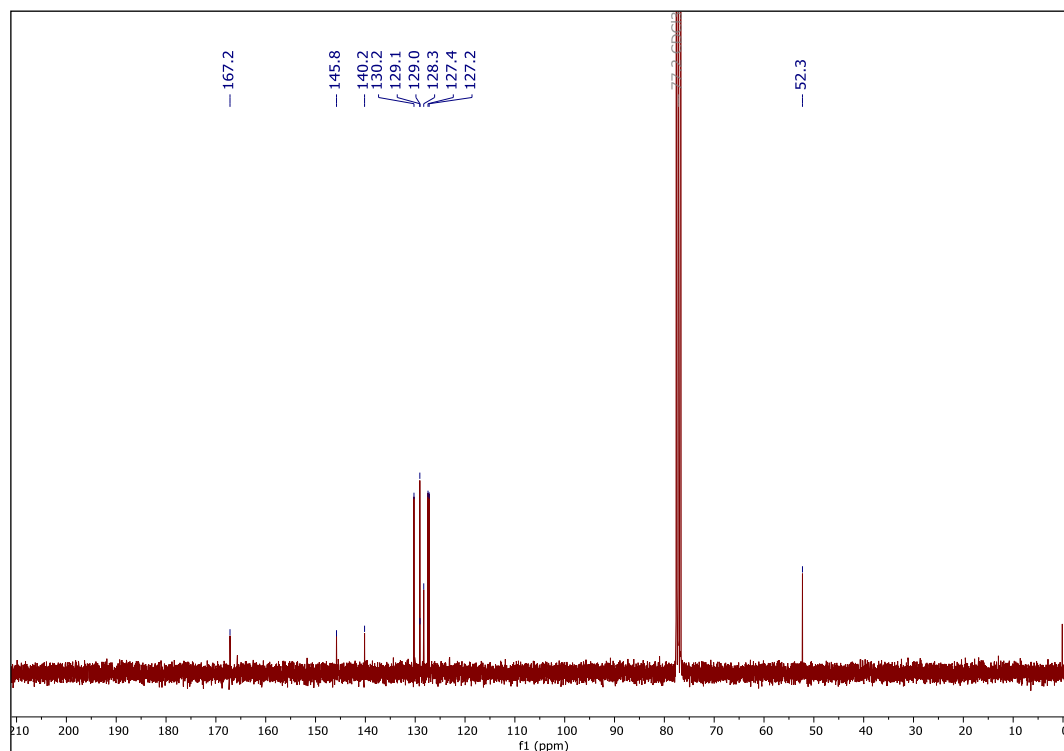


Figure S 124: ¹³C NMR (75 MHz, CDCl₃) δ 167.2, 145.8, 140.2, 130.2 (2C), 129.1 (2C), 129.0, 128.3, 127.4 (2C), 127.2 (2C), 52.3.

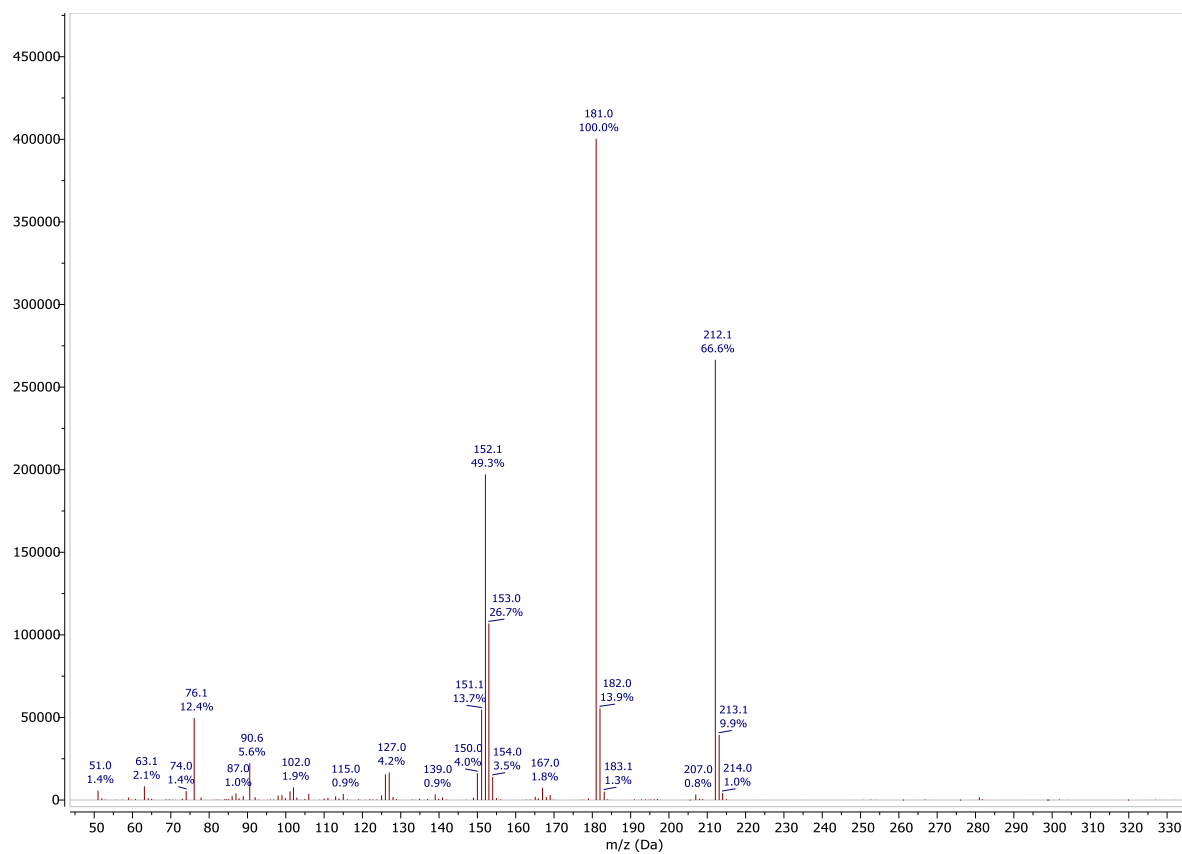


Figure S 125: EI-MS, m/z calcd. for methyl [1,1'-biphenyl]-4-carboxylate $[M]^+$: 212.1, found 212.1.

(E)-N-hexylnon-2-enamide

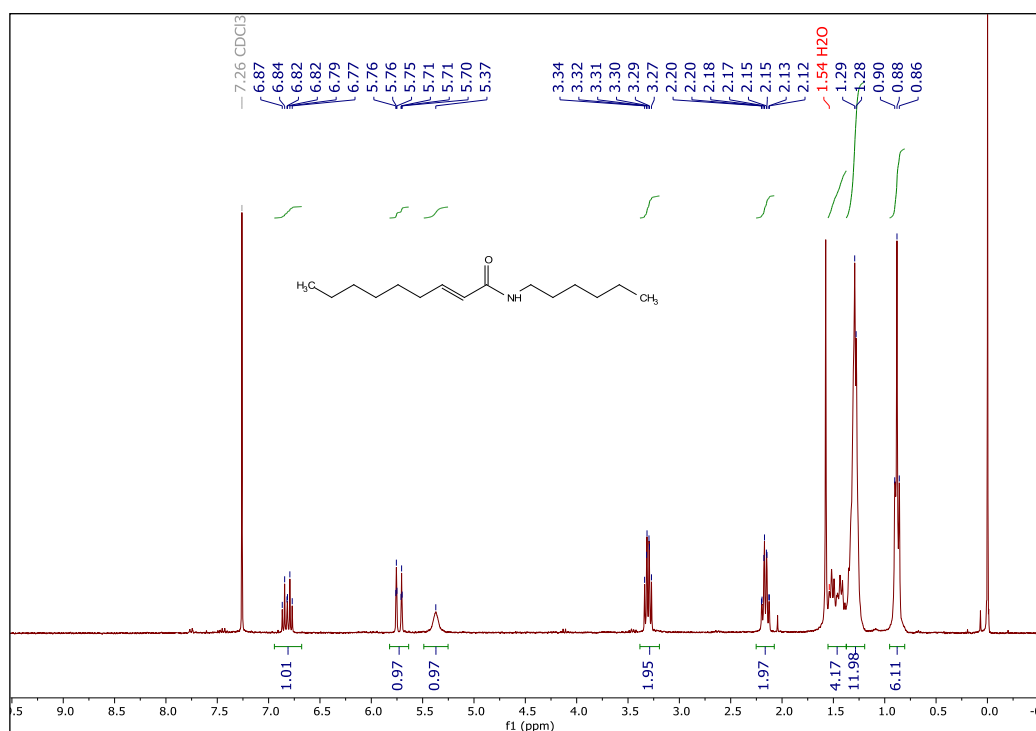


Figure S 126: ¹H NMR (300 MHz, CDCl₃) δ 6.82 (dt, *J* = 15.3, 6.9 Hz, 1H), 5.73 (dt, *J* = 15.3, 1.6 Hz, 1H), 5.37 (bs, 1H), 3.31 (td, *J* = 7.2, 5.8 Hz, 2H), 2.16 (qd, *J* = 7.1, 1.6 Hz, 2H), 1.55-1.38 (m, 4H), 1.37-1.23 (m, 12 H), 0.95 – 0.81 (m, 6H).

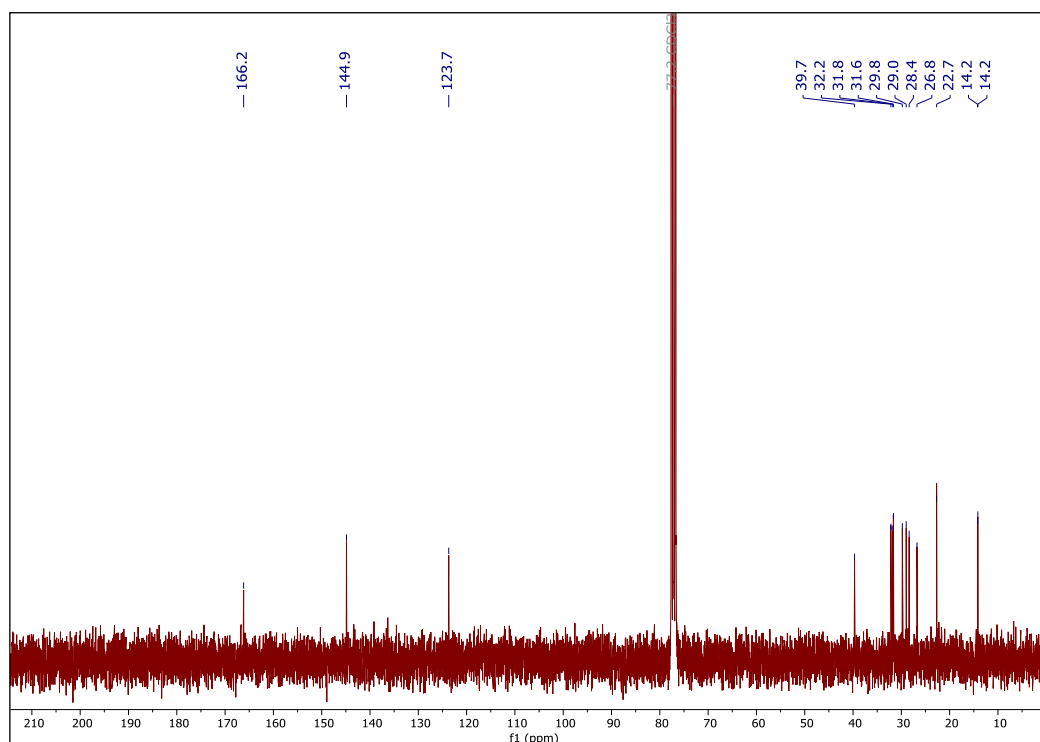


Figure S 127: ¹³C NMR (75 MHz, CDCl₃) δ 166.2, 144.9, 123.7, 39.7, 32.2, 31.8, 31.6, 29.8, 29.0, 28.4, 26.8, 22.7 (2C), 14.2 (2C).

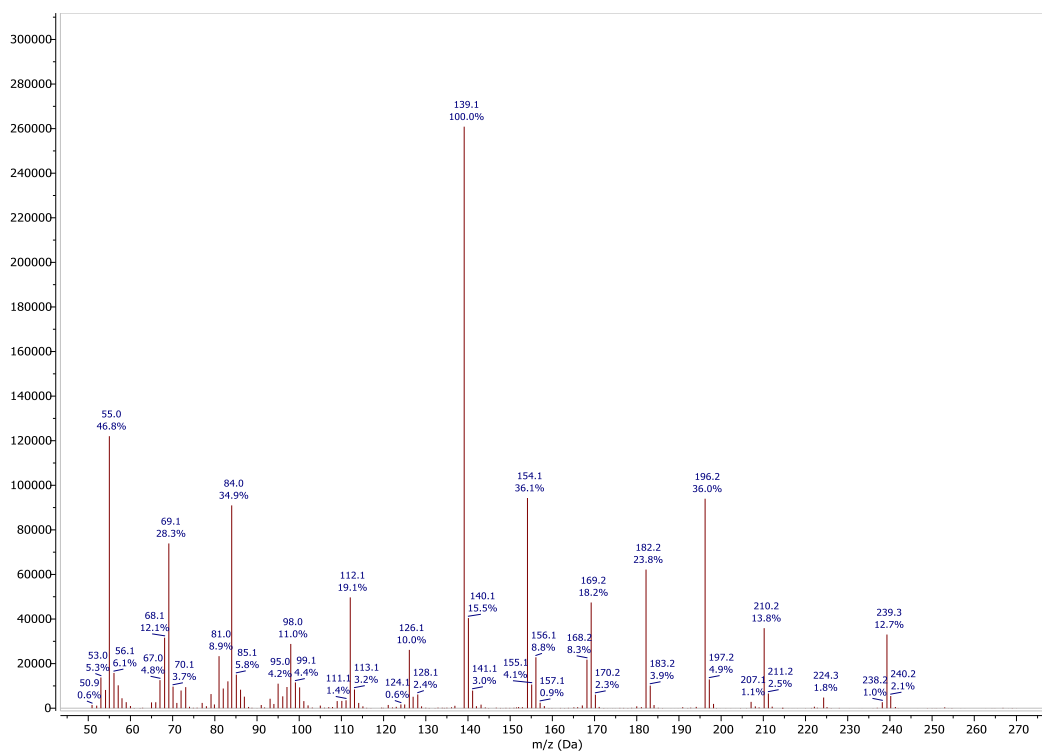


Figure S 128: EI-MS, m/z calcd. for (E)-N-hexylnon-2-enamide $[M]^+$: 239.2, found 239.3

Characterization Chapter 5

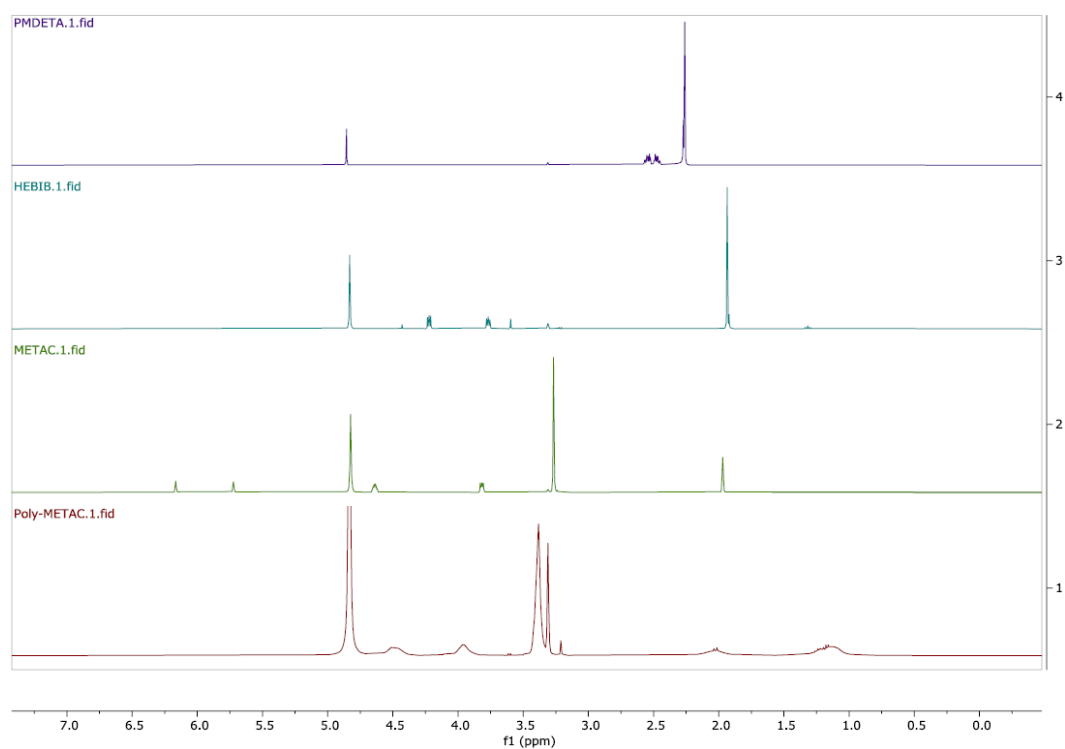


Figure S 129: ^1H NMR of the ligand (PMDETA, purple line), the initiator (HEBIB, blue line), the monomer (METAC, green line) and the product (poly-METAC, red line) in methanol- d_4 .

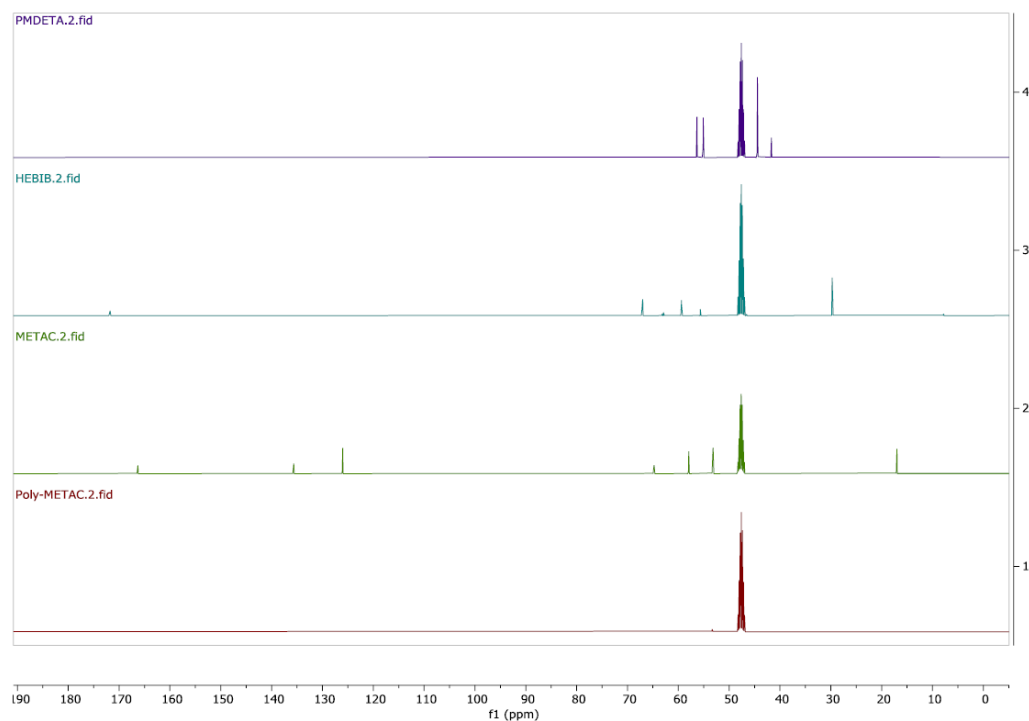


Figure S 130: ^{13}C NMR of the ligand (PMDETA, purple line), the initiator (HEBIB, blue line), the monomer (METAC, green line) and the product (poly-METAC, red line) in methanol- d_4 .

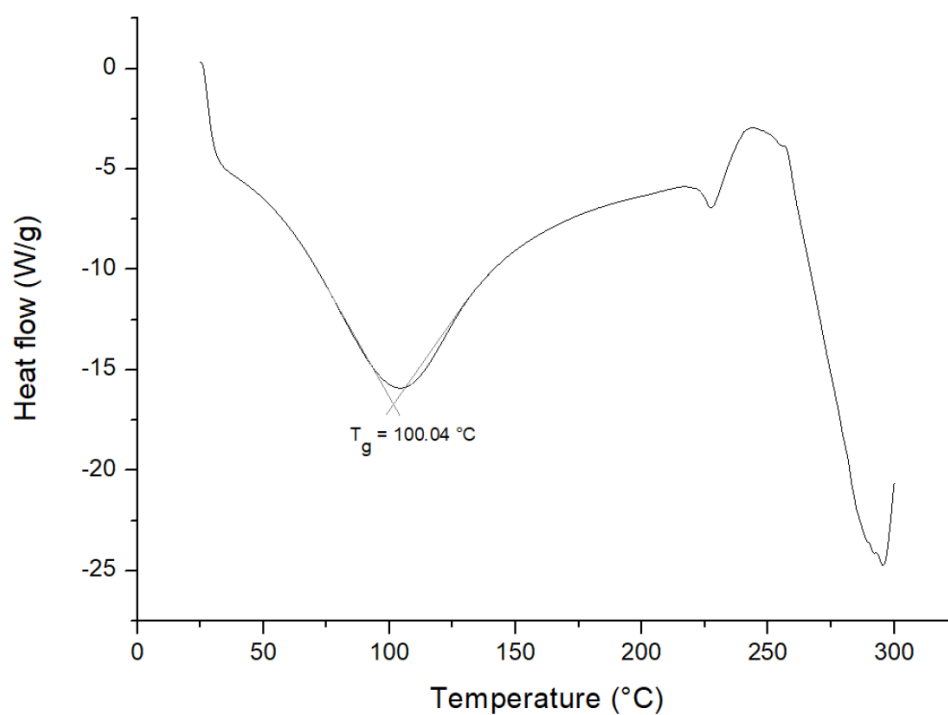


Figure S 131: DSC curve for the obtained poly-METAC.

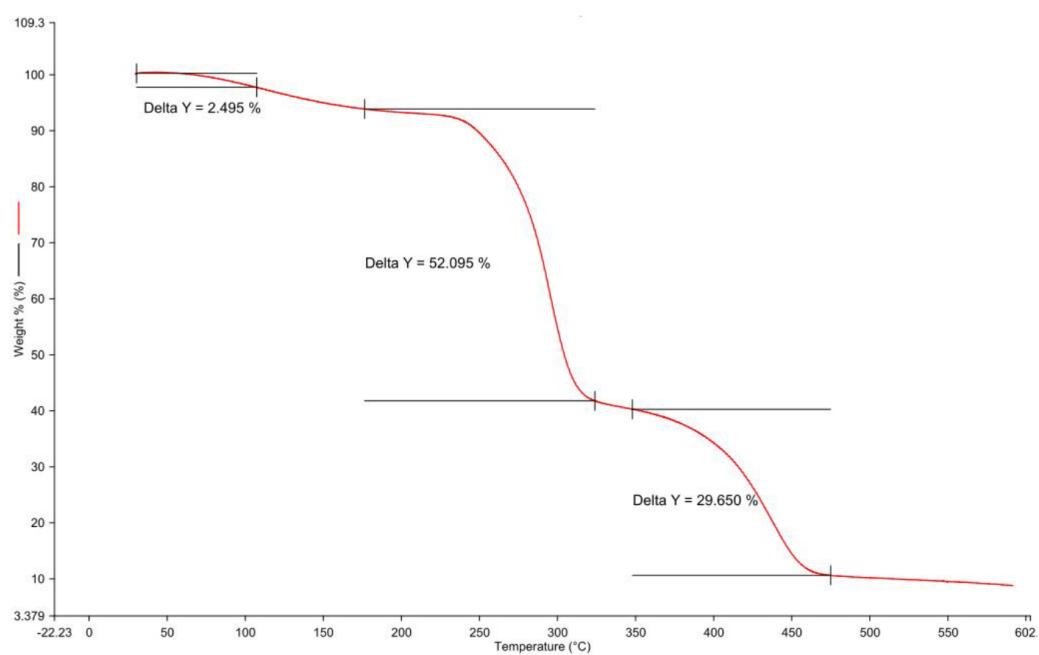


Figure S 132: Thermogravimetric analysis of the obtained poly-METAC.

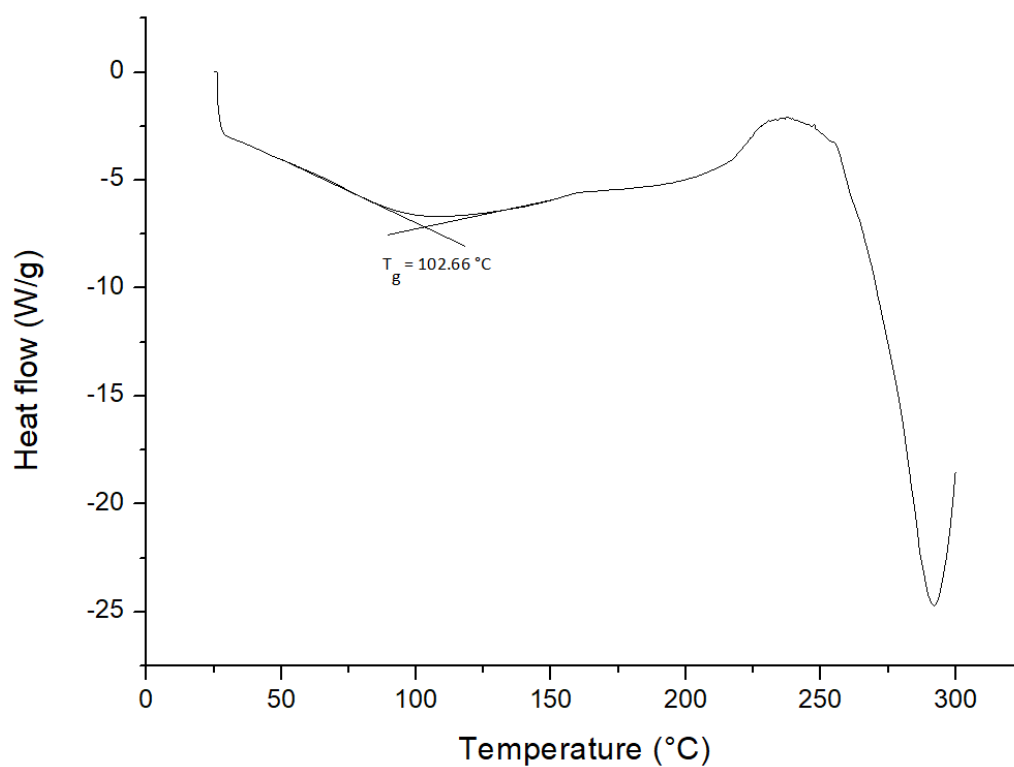


Figure S 133: DSC curve for the poly-METAC obtained with classical ATRP without CDs.

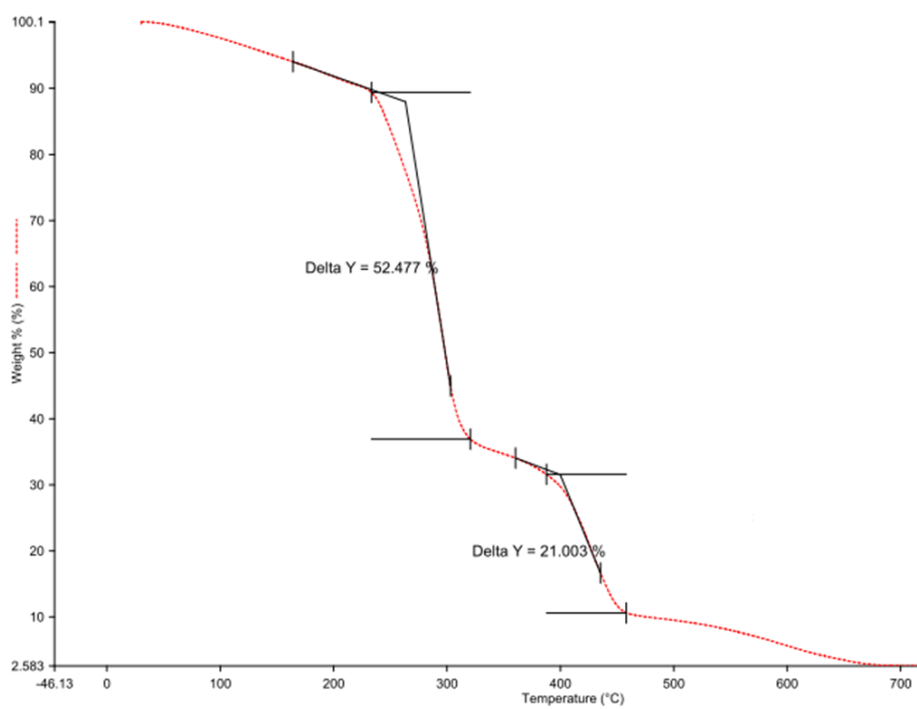


Figure S 134: Thermogravimetric analysis of the poly-METAC obtained with classical ATRP without CDs.

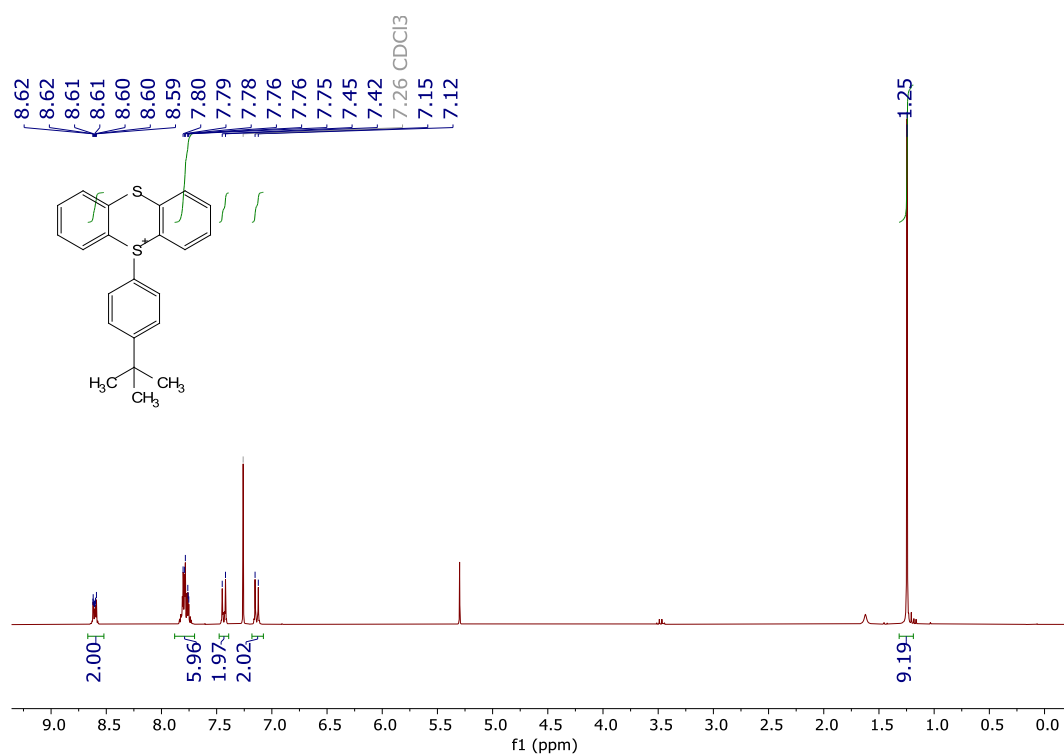


Figure S 135: ¹H NMR (300 MHz, CDCl₃) δ 8.67 – 8.52 (m, 2H), 7.88 – 7.70 (m, 6H), 7.43 (d, J = 8.9 Hz, 2H), 7.14 (d, J = 8.8 Hz, 2H), 1.25 (s, 9H)

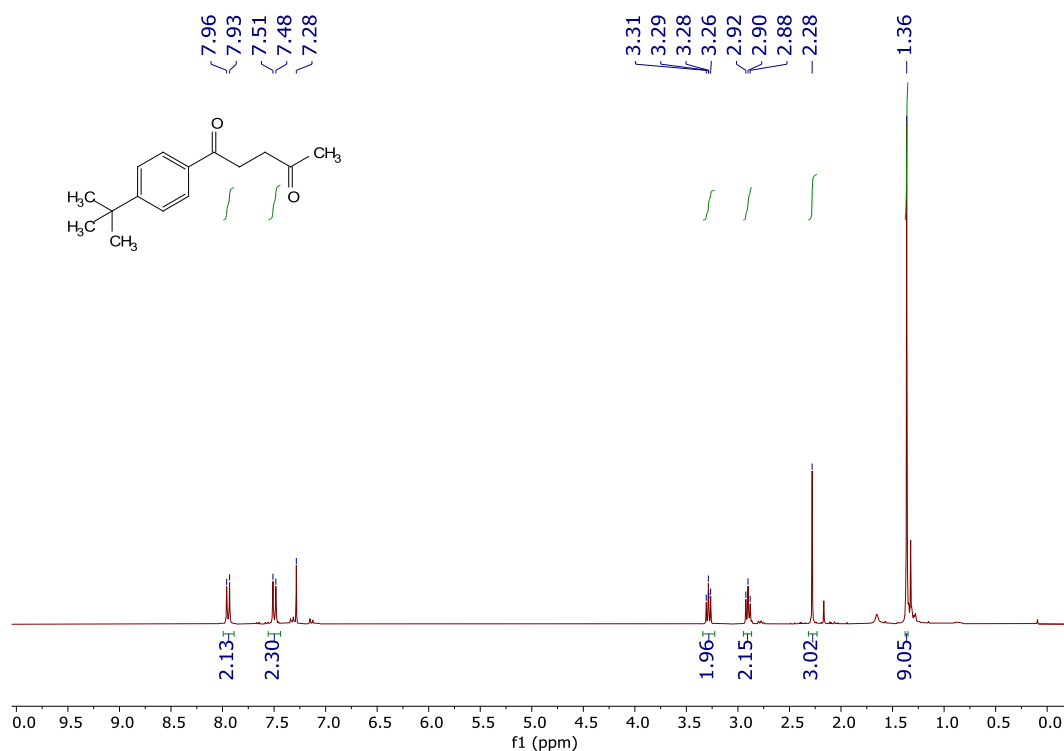


Figure S 136: ¹H NMR (300 MHz, CDCl₃) δ 7.95 (d, J = 8.5 Hz, 2H), 7.50 (d, J = 8.5 Hz, 2H), 3.29 (dd, J = 6.9, 5.8 Hz, 2H), 2.90 (t, J = 6.3 Hz, 2H), 2.28 (s, 3H), 1.36 (s, 9H).

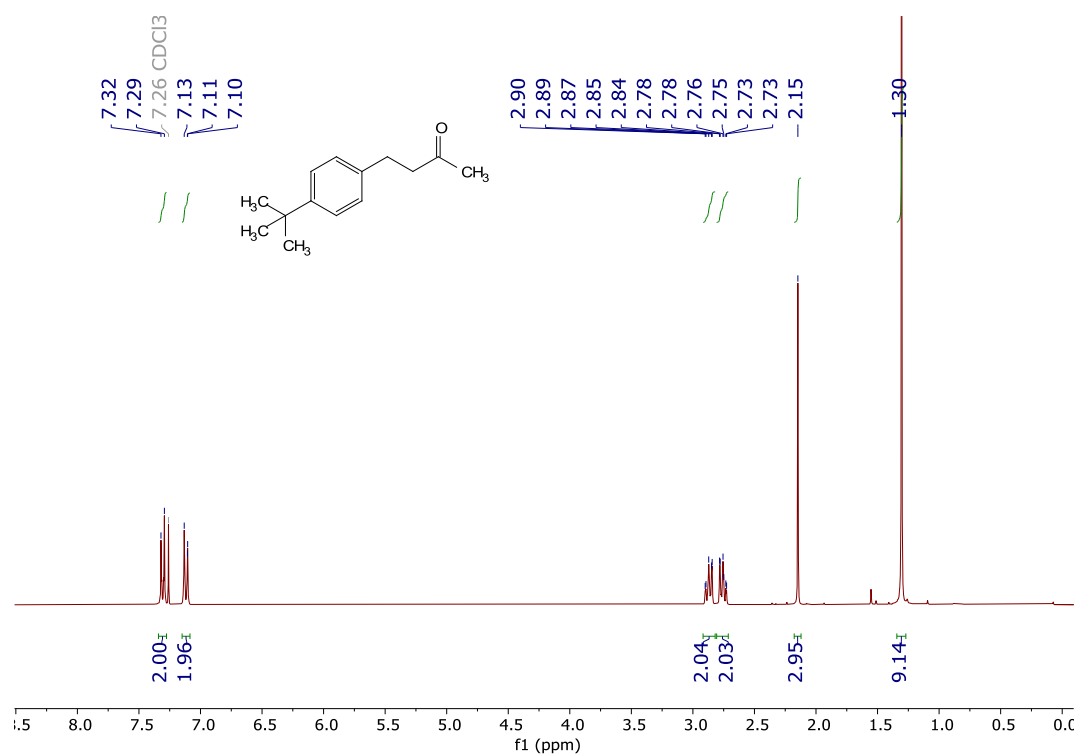


Figure S 137: ¹H NMR (300 MHz, CDCl₃) δ 7.31 (d, J = 8.3 Hz, 2H), 7.12 (d, J = 8.4 Hz, 2H), 2.92 – 2.82 (m, 2H), 2.81 – 2.71 (m, 2H), 2.15 (s, 3H), 1.30 (s, 9H).