



Efficiency in CO₂-utilization strategies: The case of styrene carbonate synthesis in microdroplets conditions

Daniele Urbani^{a,b,1}, Caterina Rovegno^{a,b,1}, Alessandro Massi^b, Mumin Enis Leblebici^c, Emine Kayahan^c, Eleonora Polo^d, Paolo Dambruso^{a,*}

^a Institute for Organic Synthesis and Photoreactivity of the Italian National Research Council, Area della Ricerca di Bologna, via P. Gobetti 101, 40129 Bologna, Italy

^b Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, via L. Borsari 46, 44121 Ferrara, Italy

^c Center for Industrial Process Technology, Department of Chemical Engineering, KU Leuven, Agoralaan Building B, 3590 Diepenbeek, Belgium

^d Institute for Organic Synthesis and Photoreactivity of the Italian National Research Council, UOS Ferrara, via L. Borsari 46, 44121 Ferrara, Italy

ARTICLE INFO

Keywords:

CO₂ utilization
Cyclic carbonates
Aerosol reactions
Microdroplets
Nebulization

ABSTRACT

The styrene oxide to styrene carbonate conversion performed in CO₂ atmosphere, herein selected as a case study, was implemented in microdroplets (aerosol) reactions at the preparative scale (3.5 mmol of the starting material) and mild conditions (1 atm CO₂ pressure), within a custom-made ultrasonic nebulization reactor. Upon optimization of the promoter stoichiometry (1 eq of 4.3 TEG/KI ratio) and methanol (MeOH) dilution (7.5 mL of 2.5 v/v MeOH/TEG), performances under mass transfer-limited conditions of this novel methodological paradigm have been compared at 25 °C and 50 °C with those implemented as: a) no-stirred, b) stirred, and c) sonicated bulk reactions. Complete selectivity and an apparent acceleration factor (AAF) of 1.9 was registered at both temperature for microdroplets reactions in respect with the sonicated counterparts, these latter performing better than the other bulk reactions. These significative efficiency improvements, candidate aerosol reactions as a preferred process intensification approach in the realm of effective CO₂-utilization strategies and, in general, in the development and exploitation of gas-liquid two-phase reactions.

1. Introduction

The emission of CO₂ in the atmosphere has dramatically increased over the last two decades, causing global warming and consequent environmental damages. [1] In this scenario, net-zero CO₂ emissions are actively pursued through the balance between anthropogenic emissions and removals from the atmosphere ('sinks'). [2] Accordingly, carbon capture and storage (CCS) strategies are being developed using different types of solid and liquid adsorbents. [3] An attractive complementary approach to the storage of CO₂ is its re-use, that means the valorization of CO₂ as renewable C1-building block to produce added-value chemicals and fuels, thus compensating the energy consumption and costs associated with its capture and transport ('carbon dioxide refinery' concept). [4] Indeed, carbon capture and utilization (CCU) methodologies are currently attracting a lot of interest from academia and process industry, [5] with some important challenges to be faced due to the high chemical stability of CO₂ and the need to develop innovative processes competitive with those already established by the petrochemical

industry. Hence, in order to overcome energetic-environmental-economic issues, [6] utilization of CO₂ as a chemical feedstock should be designed under mild conditions (ambient or moderate temperature and pressure) using low-cost sustainable catalysts (non-noble metals, [7] organocatalysts [8]), eventually with the support of enabling technologies such as flow chemistry [9] to improve the chemical efficiency of the whole process.

In recent years, microdroplet-based technologies have also emerged as valuable synthetic tools at the preparative scale in virtue of the remarkable acceleration of reactions in microdroplets compared to the conventional bulk-phase counterparts. [10] Microdroplets generated in microfluidic channels, [11] microemulsions, [12] and aerosols [13] behave, in fact, as confined and high-surface-area units (microreactors) with unique features at the droplet interface (pH alteration, accumulation of reagents, effective diffusion, concentration effect by fast solvent evaporation, etc.). [10] In particular, various homogeneous liquid phase and liquid-liquid two-phase reactions have been reported to occur on the millisecond timescale in aerosols, representing successful milestones in

* Corresponding author.

E-mail address: paolo.dambruso@isof.cnr.it (P. Dambruso).

¹ Daniele Urbani and Caterina Rovegno equally contributed to this research.

this field. [13] Although much less explored, gas-liquid two-phase reactions have been also demonstrated to be accelerated by applying different nebulization technologies. [14–16] Case studies, including work of our groups, [15a] have been focused on aerobic oxidations, [14] singlet oxygen photooxidations [15] and, very recently, on the formation of carbamic acids from amines using CO₂ as nebulization gas. [16] Notably, although this latter study was conducted at the analytical scale with an electrosonic spray ionization (ESSI) source, it allowed to elucidate the mechanism of CO₂ activation at the gas-liquid interface and the origin of the much faster kinetics in aerosol than in the bulk, thus paving the way for the development of innovative and highly effective CCS strategies. In general, microdroplets chemistry appears particularly promising in the realm of biphasic gas-liquid transformations, since the mass transfer across the interface, which is often the rate-controlling step in this type of reactions, is inherently favored by the increased surface-area-to-volume (SA/V) ratio in microdroplets. [10].

The synthesis of cyclic carbonates from epoxides and CO₂ is a fundamental pillar of the carbon dioxide refinery as it has been estimated that, together with the dry reforming of methane, it could consume up to 25% of waste CO₂ produced annually. [8a] A previous work performed in conventional stirred batch reactors suggested that the synthesis of cyclic carbonates with CO₂ is a mass-transfer limited reaction. [17] This literature data encouraged us to conduct a comparative study of the reaction of styrene oxide (SO) with CO₂ promoted by a practical and sustainable catalytic system at ambient pressure under bulk and microdroplet conditions, with the final aim to detect any eventual appreciable enhancement in the production rate of the styrene carbonate (SC) product (Fig. 1).

In this proof-of-concept study, ultrasonic nebulization (UN), which produces micrometer-sized droplets from an acoustically excited membrane, [18] was chosen for aerosol generation due to the preparative value of this technique, as already reported for the synthesis of a diverse range of materials [19] and discrete molecules. [20] Additionally, in the present design, UN offered the opportunity to build a closed reacting system to avoid the consumption of large amounts of CO₂ as it would happen, instead, with pneumatic nebulization using CO₂ as sheath gas. The effect of temperature variation on product selectivity in bulk and aerosol experiments has been also considered in this study, along with the resulting mechanistic implications to ultimately evaluate opportunities and limitations of the presented CO₂-utilization methodology.

2. Experimental section

2.1. Materials

Styrene oxide (>98%) was purchased from TCI Europe N.V.; Methanol (HPLC grade, ≥99,9%), Triethylene glycol (≥99,0%) and Potassium Iodide (≥99,0%) were purchased from Merck; CDCl₃ (99.8%) was purchased from CortecNet. All chemicals were used without any further purification.

2.2. Optimized reaction mixtures preparation and reaction procedures

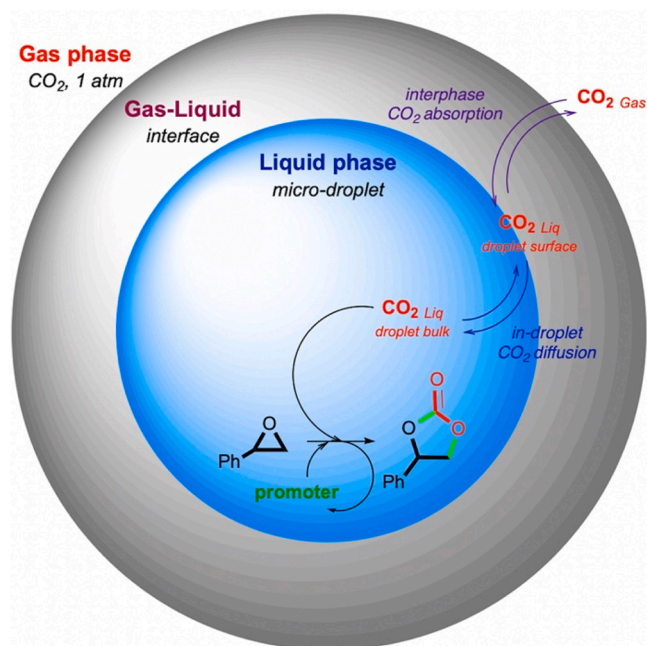
Only optimized procedures thoroughly assessed by careful experimentation are reported herein.

2.2.1. Reaction mixtures preparation

In a 10 mL vial, the homogeneous reaction mixtures were prepared by stirring at RT (90 min, 950 rpm) a mixture of styrene oxide (SO, 0.4 mL, 3.5 mmol, 1 eq), potassium iodide (KI, 0.581 mg, 3.5 mmol, 1 eq), triethylene glycol (TEG, 2 mL, 15 mmol, 4.3 eq), and methanol (MeOH, 5 mL).

2.2.2. Reaction, work-up and purification procedures

The freshly prepared homogeneous mixtures were allowed to react with CO₂ following 4 different procedures:



Ultrasonic Nebulization (UN) for CO₂-Utilization

Process conditions

- closed reacting system
- ambient pressure
- ambient/mild temperature
- low-cost/practical/sustainable reaction promoter

Opportunities and limitations

- possible rate acceleration
- custom-made reactor assembled with readily available components

Fig. 1. Synthesis of styrene carbonate in microdroplets generated by ultrasonic nebulization (UN).

- no-stirred bulk reaction
- stirred bulk reaction
- sonicated bulk reaction
- microdroplets (aerosol) reaction.

All data were acquired in triplicates, and averaged values have been reported.

Accordingly, the homogeneous reaction mixtures were, case by case, transferred into the proper reactor and, upon three vacuum/CO₂ cycles, the gas-liquid reactions were performed at ambient CO₂ pressure and at the specified temperature (RT or 50 °C), following the highlighted specific conditions (Table 1).

After 3 h, the solvent was evaporated under reduced pressure. The crude was then partitioned between ethyl acetate/water (1:1 mixture, 20 mL overall volume), and the residual organics were extracted with ethyl acetate (3 × 10 mL) from the aqueous phase. The collected organic phases were evaporated at reduced pressure. Products were then isolated by medium pressure preparative chromatography, eluting the obtained residue with a cyclohexane (Cy) / ethyl acetate (EtOAc) gradient on silica gel. (Chromatographic method: CombiFlash RF 200 LC system; stationary phase: silica 120, CV = 192 mL; flow rate: 85 mL/min; elution method: 1 CV isocratic 100% Cy, 1 CV gradient to 10% EtOAc, 3 CV isocratic 10% EtOAc, 1 CV gradient to 20% EtOAc, 3 CV isocratic 20% EtOAc, 5 CV gradient to 100% EtOAc, 2 CV isocratic 100%

Table 1
Procedure's specific reactors and conditions.

Procedure	Reactor	Specific conditions
a)	25 mL single-neck round-bottom flask, connected to a 1 L chromatography reservoir equipped with a gas connector.	Without stirring.
b)		Stirring at 600 rpm.
c)		The single-neck round-bottom flask was dipped into the water bath of a Yuwell 402B ultrasonic nebulizer, therein centering the flask to avoid the reaction mixture nebulization. The reaction mixture was sonicated at the specified temperature, in turn regulated by an external circulation water bath.
d)	The homogeneous reaction mixture was transferred into the custom-made aerosol reactor (detailed description in Section 2.4).	The reaction mixture was nebulized and maintained at the specified temperature (see Section 2.4 for temperature regulation procedures of both the ultrasonic nebulizer water bath and the nebulized reaction mixture).

EtOAc).

2.3. Products characterization

With an Agilent DD2 NMR system, equipped with a 11.7 T (500 MHz) PremiumCompact+ superconducting magnet and an Agilent OneNMR probe, all isolated products were fully characterized by NMR spectroscopy through ¹H NMR, ¹³C NMR, ¹H-¹H COSY, ¹H-¹³C HSQC and ¹H-¹³C HMBC experiments performed on CDCl₃-dissolved samples.

Kinetic data were acquired by NMR spectroscopy, sampling all reaction mixtures at pre-defined reaction times, and performing pre-saturated quantitative ¹H NMR experiments.

2.3.1. Styrene oxide

¹H NMR (500 MHz, CDCl₃), δ (ppm): 7.39–7.30 (m, 5 H, AR), 3.88 (dd, 1 H, CH, $J_{\text{CH-CH}_2} = 3.96$ Hz, $J_{\text{CH-CH}_2'} = 2.67$ Hz), 3.16 (dd, 1 H, CH₂, $J_{\text{CH}_2\text{-CH}_2'} = 5.46$ Hz, $J_{\text{CH}_2\text{-CH}} = 4.16$ Hz), 2.82 (dd, 1 H, CH₂', $J_{\text{CH}_2'\text{-CH}_2} = 5.50$ Hz, $J_{\text{CH}_2'\text{-CH}} = 2.58$ Hz).

¹³C NMR (500 MHz, CDCl₃), δ (ppm): 137.55 (AR_{ipso}), 128.42 (AR_{meta}), 128.10 (AR_{para}), 125.42 (AR_{ortho}), 52.27 (CH), 51.11 (CH₂).

2.3.2. Styrene carbonate

¹H NMR (500 MHz, CDCl₃), δ (ppm): 7.46–7.36 (m, 5 H, AR), 5.68 (t, 1 H, CH, $J_{\text{CH-CH}_2} = J_{\text{CH-CH}_2'} = 8.01$ Hz), 4.81 (t, 1 H, CH₂, $J_{\text{CH}_2\text{-CH}_2'} = J_{\text{CH}_2\text{-CH}} = 8.40$ Hz), 4.35 (t, 1 H, CH₂', $J_{\text{CH}_2'\text{-CH}_2} = J_{\text{CH}_2'\text{-CH}} = 8.29$ Hz).

¹³C NMR (500 MHz, CDCl₃), δ (ppm): 154.77 (OCOO), 135.76 (AR_{ipso}), 129.68 (AR_{meta}), 129.18 (AR_{para}), 125.82 (AR_{ortho}), 77.94 (CH), 71.11 (CH₂).

2.4. Aerosol reactor

The homemade ultrasonic nebulizer ([Fig. 2](#)), adapted from the Heated Ultrasonic Nebulization (HUN) system reported by Zare and co-workers, [\[20\]](#) consisted of a 25 mL bottom-threaded cylindrical nebulization chamber ($\phi = 25$ mm) that was bottom-capped with 0.20 mm thick aluminum foil, and thereupon sealed with a plastic screw cap. On the upper end, the nebulization chamber was connected to the aerosol reaction chamber (adapted from 1 L dry solvents reservoir), in turn equipped with a three-way valve for vacuum/CO₂ cycles, CO₂ feed, and crude collection. The nebulization chamber was dipped into the water bath of a Yuwell 402B ultrasonic nebulizer, and centered on the piezoelectric transducer allowing a vigorous nebulization of the reaction mixture. The temperature of the ultrasonic nebulizer water bath was

regulated at the specified temperature (RT or 50 °C) with an external circulation water bath, while, in the case of 50 °C reactions, the nebulized reaction mixture was maintained at that temperature using two 100 W IR lamps to warm the nebulized mixture. The apparatus was reverted upside-down at the end of the reaction time, and the crude was recovered in the collection round-bottom flask, in turn cooled at 0 °C.

2.5. Monitoring of reactions temperature

Temperature of all reactions were monitored and measured using a Testo thermal imaging camera model: Testo 890 Thermal Imager, allowing a 0.04 °C (40 mK) thermal sensitivity in the temperature measuring range of 0 to + 650 °C, and featuring a SuperResolution option 960 pixels accounting for overall 1228800 pixels). Thermographic analyses were performed with Testo IRSoft software (version 4.8).

3. Results and discussion

As anticipated, the direct carbonation of **SO** (**1**) with CO₂ to produce **SC** (**2**) was selected as the model reaction for our study on CO₂-utilization in microdroplet conditions. Many different homogeneous and heterogeneous catalytic systems have been developed for this transformation performed with ordinary methodologies often requiring, however, harsh reaction conditions to reach satisfactory levels of conversion efficiency (pressure >10 atm, temperature >100 °C). [\[21\]](#) Guided by the previously mentioned criteria of chemical efficiency, the study of an effective CO₂-utilization strategy [\[6a\]](#) based on the microdroplet synthesis of **SC** has been approached with a catalytic system belonging to the more restricted class of soluble promoters capable to activate the target carbonation under mild reaction conditions (atmospheric pressure, temperature ≤50 °C). [\[6c\]](#) The triethylene glycol-potassium iodide (TEG/KI, **3**) complex reported by Kaneko and Shirakawa [\[22\]](#) ([Scheme 1](#)) appeared well-suited to the objectives of our research due to its low-cost, practicality, recyclability, sustainability, and good catalytic activity through a bifunctional activation mechanism. [\[23\]](#) Furthermore, this catalytic complex can be easily prepared without any synthetic effort from cheap and readily available commercial chemicals.

Our first modification to the reported in-bulk procedure (1:1 TEG/KI [10 mol%], CO₂ atmospheric pressure, neat **SO**, 25 °C, 24 h: 67% **SC** yield) [\[22\]](#) entailed the variation of the TEG/KI ratio to obtain a fully homogeneous reaction mixture and, consequently, an efficient ultrasonic nebulization. Unfortunately, the 1:1 TEG/KI complex initially obtained as a homogeneous solution, resulted in a heterogeneous slurry upon **SO** addition. Further stepwise additions of TEG favourably reduced the amount of precipitate, thus resulting in a clear and homogeneous solution at the optimized 4.3 TEG/KI ratio.

From this point forward, a three-hour reaction time was arbitrarily considered in our kinetic study, matching the need for both fast screening and reliable data acquisition. Next, the achievement of mass-transfer limited conditions was explored by gradually increasing the amount of the TEG/KI complex vs **SO** ([Table 2](#)). Actually, when the CO₂ transfer across the gas-liquid interface becomes the rate limiting step, the rate of **SC** formation is no longer controlled by chemical mechanisms and/or variation of extrinsic reaction parameters such as the catalyst loading.

After some experimentation (entries 1–4), it resulted that the yield of **SC** (52%) remained almost unchanged with the optimized 4.3 TEG/KI complex at KI loadings higher than 50 mol%; nonetheless, equimolar KI/**SO** was utilized in the continuation of the study to definitively ensure the operation under a mass transfer limited regime (entry 4). Disappointingly, any attempt to nebulize the identified reaction mixture failed with our homemade ultrasonic nebulizer ([Section 2.4](#)), thus making necessary dilution with a suitable solvent to obtain an appropriate viscosity of the nebulizing solution. Methanol was selected to this purpose,

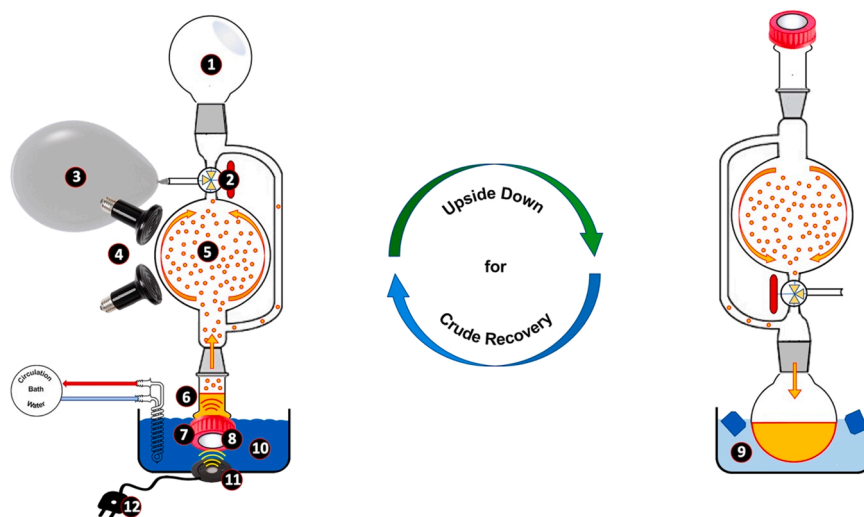
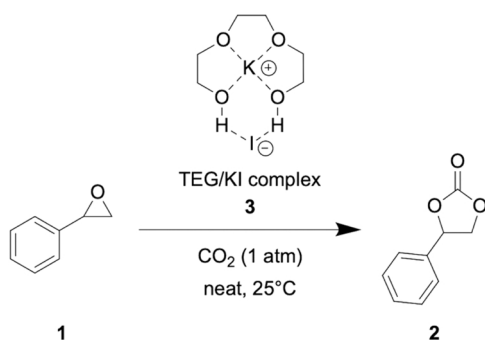


Fig. 2. Ultrasonic nebulization apparatus for the microdroplet synthesis of styrene carbonate. In details: 1) collection flask; 2) three-way valve; 3) CO₂ balloon; 4) IR lamps; 5) aerosol reaction chamber; 6) bottom-threaded nebulization chamber; 7) plastic screw cap; 8) aluminum foil; 9) melting ice bath; Yuwell 402B ultrasonic nebulizer consisting of the following key elements: 10) water bath; 11) piezoelectric transducer, and 12) plug for power supply.



Scheme 1. The model reaction and the selected catalyst, as reported by Kaneko and Shirakawa [22].

Table 2

Propaedeutic bulk experiments for subsequent microdroplet synthesis of styrene carbonate (SC) under mass transfer limited conditions.^a

Entry	KI (mol%)	MeOH/TEG (v/v)	SC yield (%) ^b	UN ^c
1	25	–	36	–
2	50	–	52	–
3	75	–	51	–
4	100	–	49	–
5	100	1.25	26	no
6	100	2.50	23	yes
7	100	5.00	15	yes
8	100	7.00	9	yes

^a SO (3.50 mmol), 4.3 TEG/KI optimized ratio, MeOH/TEG ratio as reported.

^b Detected by pre-saturated quantitative ¹H NMR experiments on the crude reaction mixture.

^c Effective ultrasonic nebulization (UN) in the homemade aerosol reactor.

because of its good environmental acceptability, [24] easy recyclability (distillation), and high CO₂ absorption capability. [25] The optimal compromise between effective nebulization and SO conversion was

found with the 2.5:1 MeOH/TEG volumetric ratio, being the yield of SC unavoidably reduced to 9% (at 7.0:1 MeOH/TEG volumetric ratio) due to dilution effects (entries 5–8). The comparative study on styrene oxide carbonation in bulk and microdroplet conditions was performed utilizing the prototype reactor described in Section 2.4., and sketched in Fig. 2. Inspired by the design of Zare and co-workers, [20] our homemade aerosol apparatus was fabricated from readily available commercial components ensuring an easy experimental reproducibility. Our reactor setup can also be integrated with one (or two) infrared (IR) lamps placed perpendicularly to the nebulization chamber for microdroplet heating and with a thermographic camera for the real-time monitoring of the reaction temperature (Fig. 3).

As planned, the effect of the specific surface area of reactant solution on SC yield was examined in bulk and microdroplet experiments under

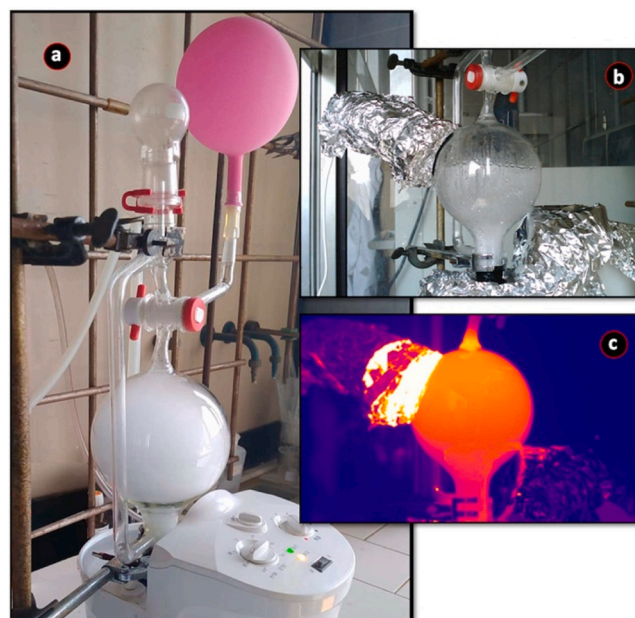


Fig. 3. Ultrasonic nebulization apparatus for the microdroplet synthesis of styrene carbonate. In detail: a) the apparatus nebulizing the crude at 25 °C; b) the nebulized mixture warmed at 50 °C with one 100 W IR lamp; c) real-time monitoring of the reaction temperature with a thermographic camera.

mass transfer limited conditions. Accordingly, the ratio between the CO₂-liquid surface area and the liquid volume (SA/V ratio) was progressively increased conducting the carbonation reaction in a conventional batch reactor with and without magnetic stirring and in the homemade UN apparatus. While the SA/V value of 130 m²/m³ can be easily calculated for the non-stirred batch reactor used herein,² previous reports indicate SA/V data of ca. 10³ m²/m³ and 10⁴-10⁶ m²/m³ for biphasic gas-liquid reactions run under stirred batch [26] and UN conditions, [15b,20] respectively. For a better comparison with the microdroplet synthesis of SC, sonication was also investigated in bulk experiments to normalize the effect on reaction efficiency of the complex physico-chemical phenomena that may occur in the liquid phase when applying this technique. The kinetic plots of the planned four experiments were readily acquired by monitoring (pre-saturated quantitative ¹H NMR analysis) the yield of SC with time (Fig. 4). Of note, in the case of microdroplet reaction the kinetic profile was obtained by performing different UN experiments with the same feed composition but with different reaction times.

As expected, without magnetic stirring, the reaction yield after 180 min slightly decreased from 23% to 18% (blue-dotted and orange-dashdotted lines), whereas sonication (water bath regulated at 25 °C) produced a small increase to 29% yield (grey-dashed line). Quite satisfyingly, the product yield of the microdroplet reaction was 54% (red-solid line), corresponding to an apparent acceleration factor (AAF) of 1.9 in respect with the bulk reaction under sonication. The AAF was calculated by the ratio between the values of product yield in microdroplet and bulk reactions carried out for the same period of time (180 min; AAF = [SC]_{droplet}/[SC]_{bulk}). It is important to emphasize that the determined AAF should not be intended as a quantitative measure because of the many kinetic variables involved moving from bulk to microdroplet experiments; however, this simple method of approximating the AF clearly shows that the synthesis of styrene carbonate is significantly accelerated in microdroplet conditions. The productivity of the UN setup was also investigated after 6 h detecting an increased SC yield to 73%. On the other hand, not all reactions undergo dramatic

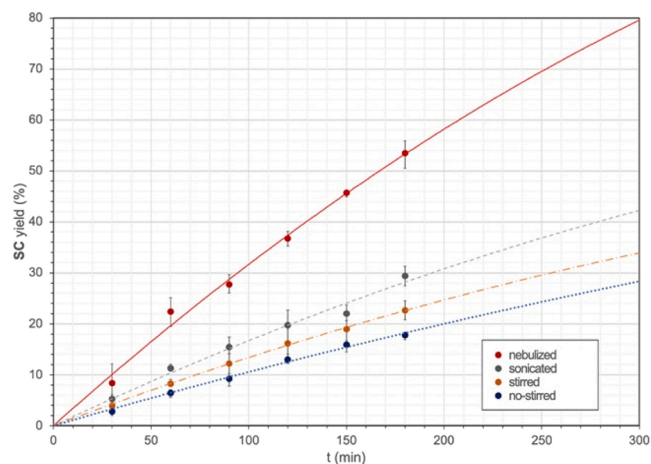


Fig. 4. Kinetic profiles of styrene carbonate synthesis at 25 °C in non-stirred (blue-dotted line), stirred (orange-dashdotted line), sonicated (grey-dashed line) bulk experiments and microdroplet conditions (red-solid line) using the homemade aerosol reactor. All reactions were performed in triplicates. Error bars were represented as min-max range of measured values. Averaged experimental data were fitted with a 2nd grade polynomial curve embedded in Microsoft Excel for MAC (version 16.16.27 (201012)).

² calculated considering the 3.5 cm diameter circular surface of a 7.4 mL reaction solution in a 25 mL round-bottomed flask

acceleration in microdroplets, [20a,27] being the mechanism behind this phenomenon strictly dependent on the intrinsic features of the reaction under investigation. In the case of carbonation of styrene oxide, it can be speculated that the enhanced mass transfer of CO₂ in microdroplets can improve the catalyst turnover and so increase the reaction efficiency.

It is well known that the reaction of epoxides with CO₂ to give the corresponding cyclic carbonates is deeply affected by temperature. [5] Therefore, the synthesis of styrene carbonate was next investigated at 50 °C in the bulk with sonication and in microdroplet conditions (Fig. 5).

This thermal study was greatly facilitated by our experimental setup integrated with one IR lamps and the thermographic camera for a precise determination of the operating temperature (Fig. 6).

Satisfyingly, the bulk experiment proceeded smoothly at 50 °C affording SC with an increased 40% yield and complete reaction selectivity (reaction time: 180 min). To our delight, also the UN reaction selectively produced SC in higher yield (78%), compared to the experiment at ambient temperature. In light of this outcome, the corresponding AAF resulted 1.95, thus confirming also at 50 °C, a twofold acceleration of the UN reaction vs the bulk counterpart performed under sonication.

All results obtained in this study were in full agreement with the mechanistic hypothesis proposed by the groups of Shirakawa and Butera, [22,23] herein sketched in Scheme 2, in which is clearly highlighted the CO₂ insertion step.

4. Conclusions

Herein we demonstrated for the first time the beneficial effect of an innovative enabling technology on the styrene oxide to styrene carbonate conversion, selected as a case study in the realm of CO₂-utilization strategies. The ultrasonic nebulization herein implemented at the preparative scale caused a twofold acceleration of the identified model reaction in very mild conditions, offering an innovative and powerful tool in the continuous efforts toward the efficient exploitation of CCU approaches. The learned lesson is also of great general value, being straightforwardly extendible to all gas-liquid two-phase reactions plagued by mass-transfer limitation phenomena. A batch approach has been adopted in this study, allowing the minimal CO₂ consumption, in sharp contrast with continuous flow operations that, in the case of pneumatic nebulization using CO₂ as sheath gas, would have required unacceptable amounts of CO₂ and apparatus size.

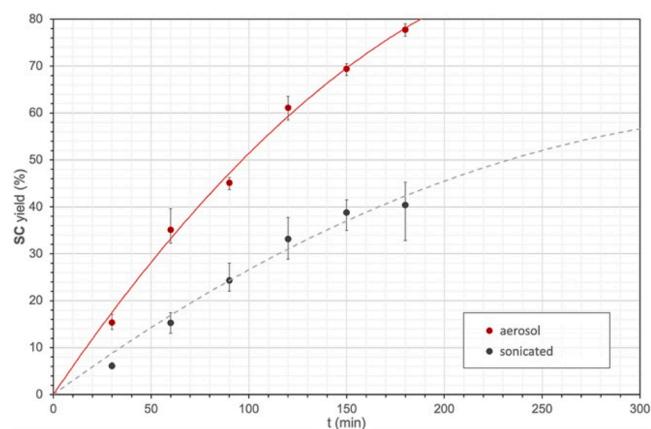


Fig. 5. Kinetic profiles of styrene carbonate synthesis at 50 °C in sonicated (grey-dashed line) bulk experiment and microdroplet conditions (red-solid line) using the heated aerosol reactor. All reactions were performed in triplicates. Error bars were represented as min-max range of measured values. Averaged experimental data were fitted with a 2nd grade polynomial curve embedded in Microsoft Excel for MAC (version 16.16.27 (201012)).

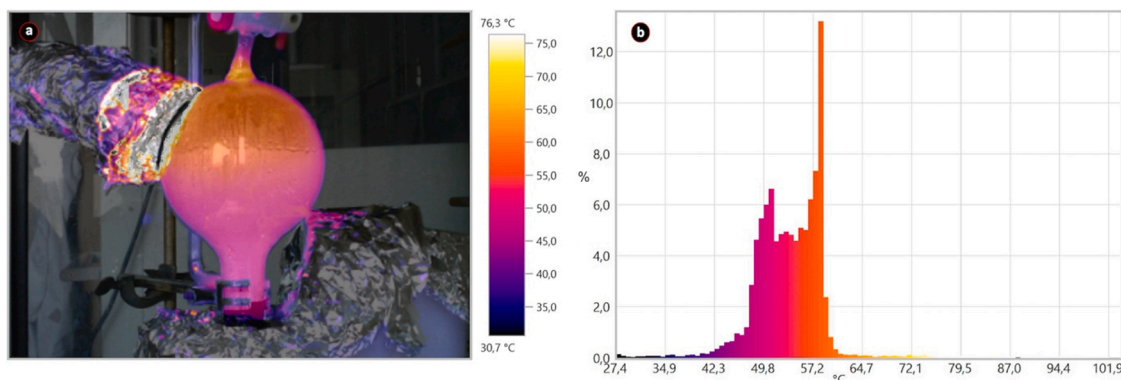
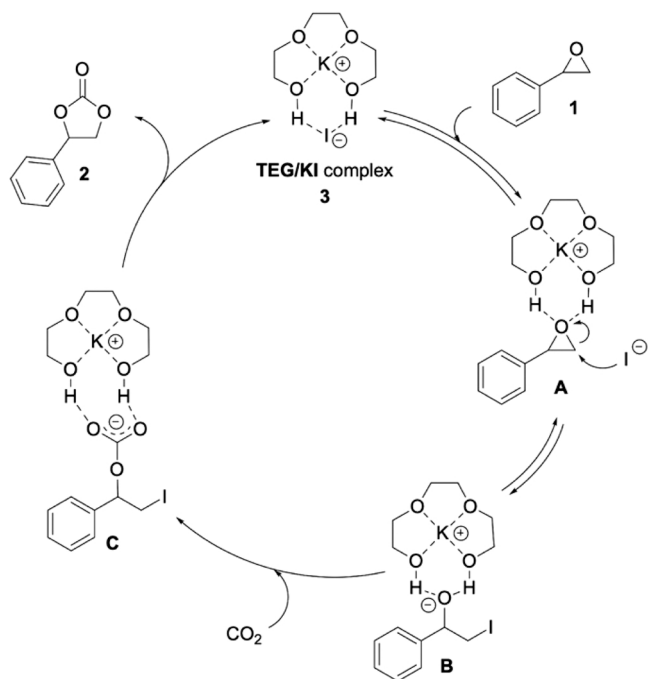


Fig. 6. Real-time monitoring of reaction temperature in the nebulization chamber by thermographic camera. In detail: a) thermo-image of the aerosol warmed at 50 °C (averaged temperature); b) temperature profile within the nebulization chamber.



Scheme 2. The proposed reaction mechanism, in accordance with those proposed by Kaneko/Shirakawa [22] and Butera. [23].

These results pave the way for further studies in this field, and we are currently exploring additional exploitation opportunities of the ultrasonic nebulization. At the same time, new challenges need new solutions, and we are constantly involved in the improvement of the ultrasonic nebulization apparatus setup. The novel methodological paradigm herein introduced deserves further studies aimed at identifying key physico-chemical and aerosol-phase composition parameters causing the reported acceleration. [28] Although literature speculations largely assign the temperature-dependent kinetic performances to the reduced droplets size registered at higher temperatures, [20a] the effect on the reaction kinetic of aerosol phase molar composition and catalyst/reactant molar ratio, CO₂ solubility and solvent evaporation should be taken into account to deeply clarify ongoing phenomena. Results of these investigations will be reported in due course.

Credit authorship contribution statement

Daniele Urbani and **Caterina Rovegno** equally contributed to this research. **Daniele Urbani**: Aerosol reactor manufacturing, Aerosol and

bulk reactions experiments, Data curation. **Caterina Rovegno**: Bulk reactions experiments, Data curation. **Alessandro Massi**: Conceptualization, Methodology, Writing. **Mumin Enis Leblebici**: Methodology, Supervision. **Emine Kayahan**: Data analysis, Writing – review & editing. **Eleonora Polo**: Writing – review & editing. **Paolo Dambruoso**: Project coordination, Conceptualization, Methodology, Supervision, Writing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

Data will be made available on request.

Acknowledgements

The present work was supported by the NATO Science for Peace and Security Programme (NATO SPS, Grant No. MYP G5885, project acronym: TANGO). The authors are grateful to the funding agency.

References

- [1] J. Rogelj, G. Luderer, R.C. Pietzcker, E. Kriegler, M. Schaeffer, V. Krey, K. Riahi, Energy system transformations for limiting end-of-century warming to below 1.5 °C, *Nat. Clim. Chang.* 5 (2015) 519–527, <https://doi.org/10.1038/nclimate2572>.
- [2] J. Rogelj, M. Schaeffer, M. Meinshausen, R. Knutti, J. Alcamo, K. Riahi, W. Hare, Zero emission targets as long-term global goals for climate protection, *Environ. Res. Lett.* 10 (2015), 105007, <https://doi.org/10.1088/1748-9326/10/10/105007>.
- [3] M. Bui, C.S. Adjiman, A. Bardow, E.J. Anthony, A. Boston, S. Brown, P.S. Fennell, S. Fuss, A. Galindo, L.A. Hackett, J.P. Hallett, H.J. Herzog, G. Jackson, J. Kemper, S. Krevor, G.C. Maitland, M. Matuszewski, I.S. Metcalfe, C. Petit, G. Puxty, J. Reimer, D.M. Reiner, E.S. Rubin, S.A. Scott, N. Shah, B. Smit, J.P.M. Trusler, P. Webley, J. Wilcox, N. Mac Dowell, Carbon capture and storage (CCS): the way forward, *Energy Environ. Sci.* 11 (2018) 1062–1176, <https://doi.org/10.1039/C7EE02342A>.
- [4] W. Guo, J.E. Gómez, À. Cristòfol, J. Xie, A.W. Kleij, Catalytic transformations of functionalized cyclic organic carbonates, *Angew. Chem. Int. Ed.* 57 (2018) 13735–13747, <https://doi.org/10.1002/anie.201805009>.
- [5] W. Gao, S. Liang, R. Wang, Q. Jiang, Y. Zhang, Q. Zheng, B. Xie, C.Y. Toe, X. Zhu, J. Wang, L. Huang, Y. Gao, Z. Wang, C. Jo, Q. Wang, L. Wang, Y. Liu, B. Louis, J. Scott, A.-C. Roger, R. Amal, H. He, S.-E. Park, Industrial carbon dioxide capture and utilization: state of the art and future challenges, *Chem. Soc. Rev.* 49 (2020) 8584–8686, <https://doi.org/10.1039/D0CS00025F>.
- [6] a) Y. Yang, J.-W. Lee, Toward ideal carbon dioxide functionalization, *Chem. Sci.* 10 (2019) 3905–3926, <https://doi.org/10.1039/C8SC05539D>; b) R.R. Shaikh, S. Pornpraprom, V. D'Elia, Catalytic strategies for the cycloaddition of pure, diluted, and waste CO₂ to epoxides under ambient conditions, *ACS Catal.* 8 (2018) 419–450, <https://doi.org/10.1021/acscatal.7b03580>.
- [7] a) S.-S. Yan, Q. Fu, L.-L. Liao, G.-Q. Sun, J.-H. Ye, L. Gong, Y.-Z. Bo-Xue, D.-G. Yu, Transition metal-catalyzed carboxylation of unsaturated substrates with CO₂,

- Chem. Rev. 374 (2018) 439–463, <https://doi.org/10.1016/j.ccr.2018.07.011>;
- b) S. Dabral, T. Schaub, The use of carbon dioxide (CO₂) as a building block in organic synthesis from an industrial perspective, *Adv. Synth. Catal.* 361 (2019) 223–246, <https://doi.org/10.1002/adsc.201801215>.
- [8] a) L. Guo, K.J. Lamb, M. North, Recent developments in organocatalysed transformations of epoxides and carbon dioxide into cyclic carbonates, *Green Chem.* 23 (2021) 77–118, <https://doi.org/10.1039/D0GC03465G>;
- b) P. Sreejyothi, K.M. Swadhin, From CO₂ activation to catalytic reduction: a metal-free approach, *Chem. Sci.* 11 (2020) 10571–10593, <https://doi.org/10.1039/D0SC03528A>;
- c) M. Liu, P. Zhao, W. Zhang, X. Cheng, H. Fei, J. Ma, F. Liu, Rational self-assembly of triazine- and urea-functionalized periodic mesoporous organosilicas for efficient CO₂ adsorption and conversion into cyclic carbonates, *Fuel* 315 (2022), 123230, <https://doi.org/10.1016/j.fuel.2022.123230>;
- d) F. Liu, S. Du, W. Zhang, J. Ma, S. Wang, M. Liu, F. Liu, Construction of zwitterionic porous organic frameworks with multiple active sites for highly efficient CO₂ adsorption and synergistic conversion, *Chem. Eng. J.* 435 (2022), 134921, <https://doi.org/10.1016/j.cej.2022.134921>;
- e) L. He, W. Zhang, Y. Yang, J. Ma, F. Liu, M. Liu, Novel biomass-derived deep eutectic solvents promoted cycloaddition of CO₂ with epoxides under mild and additive-free conditions, *J. CO₂ Util.* 54 (2021), 101750, <https://doi.org/10.1016/j.jcou.2021.101750>;
- f) X. Cheng, P. Zhao, M. Zhang, S. Wang, M. Liu, F. Liu, Fabrication of robust and bifunctional cyclotriphosphazene-based periodic mesoporous organosilicas for efficient CO₂ adsorption and catalytic conversion, *Chem. Eng. J.* 418 (2021), 129360, <https://doi.org/10.1016/j.cej.2021.129360>.
- [9] a) T.Q. Bui, L.J. Konwar, A. Samikannu, D. Nikjoo, J.-P. Mikkola, Mesoporous melamine-formaldehyde resins as efficient heterogeneous catalysts for continuous synthesis of cyclic carbonates from epoxides and gaseous CO₂, *ACS Sustain. Chem. Eng.* 8 (2020) 12852–12869, <https://doi.org/10.1021/acsschemeng.0c03123>;
- b) A.S. Martinez, C. Hauenberger, A.R. Sahoo, Z. Csendes, H. Hoffmann, K. Bica, Continuous conversion of carbon dioxide to propylene carbonate with supported ionic liquids, *ACS Sustain. Chem. Eng.* 6 (2018) 13131–13139, <https://doi.org/10.1021/acsschemeng.8b02627>;
- c) T. Wang, W. Wang, Y. Lyu, X. Chen, C. Li, Y. Zhang, X. Songa, Y. Ding, Highly recyclable polymer supported ionic liquids as efficient heterogeneous catalysts for batch and flow conversion of CO₂ to cyclic carbonates, *RSC Adv.* 7 (2017) 2836–2841, <https://doi.org/10.1039/C6RA26780G>;
- d) X. Zhang, D. Su, L. Xiao, W. Wu, Immobilized protic ionic liquids: efficient catalysts for CO₂ fixation with epoxides, *J. CO₂ Util.* 17 (2017) 37–42, <https://doi.org/10.1016/j.jcou.2016.11.005>;
- e) A. Rehman, F. Saleem, F. Javed, A. Ikhtlaq, S.W. Ahmad, A. Harvey, Recent advances in the synthesis of cyclic carbonates via CO₂ cycloaddition to epoxides, *J. Environ. Chem. Eng.* 9 (2021), 105113, <https://doi.org/10.1016/j.jece.2021.105113>.
- [10] a) X. Yan, R.M. Bain, R.G. Cooks, Organic Reactions in Microdroplets: Reaction Acceleration Revealed by Mass Spectrometry, *Angew. Chem. Int. Ed.* 55 (42) (2016) 12960–12972, <https://doi.org/10.1002/anie.201602270>;
- b) Z. Wei, Y. Li, R.G. Cooks, X. Yan, Accelerated reaction kinetics in microdroplets: overview and recent developments, *Annu. Rev. Phys. Chem.* 71 (2020) 31–51, <https://doi.org/10.1146/annurev-physchem-121319-110654>.
- [11] a) A. Fallah-Araghi, K. Meguellati, J.C. Baret, A. El Harrak, T. Mangeat, M. Karplus, S. Ladame, C.M. Marques, A.D. Griffiths, Enhanced chemical synthesis at soft interfaces: a universal reaction-adsorption mechanism in microcompartments, *Phys. Rev. Lett.* 112 (2014), 028301, <https://doi.org/10.1103/PhysRevLett.112.028301>;
- b) M. Guardingo, F. Busqu, D. Ruiz-Molina, Reactions in ultra-small droplets by tip-assisted chemistry, *Chem. Commun.* 52 (2016) 11617–11626, <https://doi.org/10.1039/C6CC03504C>.
- [12] a) K. Holmberg, Organic reactions in microemulsions, *Eur. J. Org. Chem.* 5 (2007) 731–742, <https://doi.org/10.1002/ejoc.200600741>;
- b) M.A. López-Quintela, C. Tojo, M.C. Blanco, L. García Rio, J.R. Leis, Microemulsion dynamics and reactions in microemulsions, *Curr. Opin. Colloid Interface Sci.* 9 (2004) 264–278, <https://doi.org/10.1016/j.cocis.2004.05.029>.
- [13] a) X. Yan, R.M. Bain, R.G. Cooks, Organic reactions in microdroplets: reaction acceleration revealed by mass spectrometry, *Angew. Chem. Int. Ed.* 55 (2016) 12960–12972, <https://doi.org/10.1002/anie.201602270>;
- b) S. Banerjee, E. Gnanamani, X. Yan, R.N. Zare, Can all bulk-phase reactions be accelerated in microdroplets? *Analyst* 142 (2017) 1399–1402, <https://doi.org/10.1039/C6AN02225A>;
- c) R.G. Cooks, X. Yan, Mass spectrometry for synthesis and analysis, *Annu. Rev. Anal. Chem.* 11 (2018) 1–28, <https://doi.org/10.1146/annurev-anchem-061417-125820>;
- d) X. Yan, Emerging microdroplet chemistry for synthesis and analysis, *Int. J. Mass Spectrom.* 468 (2021), 116639, <https://doi.org/10.1016/j.ijms.2021.116639>.
- [14] X. Yan, Y.-H. Lai, R.N. Zare, Preparative microdroplet synthesis of carboxylic acids from aerobic oxidation of aldehydes, *Chem. Sci.* 9 (2018) 5207–5211, <https://doi.org/10.1039/C8SC01580E>.
- [15] a) E. Kayahan, D. Urbani, P. Dambruoso, A. Massi, L. Braeken, T. Van Gerven, M. E. Leblebici, Overcoming mass and photon transfer limitations in a scalable reactor: Oxidation in an aerosol photoreactor, *Chem. Eng. J.* 408 (2021), 127357, <https://doi.org/10.1016/j.cej.2020.127357>;
- b) G.I. Ioannou, T. Montagnon, D. Kalaitzakis, S.A. Pergantis, G. Vassilikogiannakis, A novel nebulizer-based continuous flow reactor: introducing the use of pneumatically generated aerosols for highly productive photooxidations, *ChemPhotoChem* 1 (2017) 173–177, <https://doi.org/10.1002/cptc.201600054>;
- c) G.I. Ioannou, T. Montagnon, D. Kalaitzakis, S.A. Pergantis, G. Vassilikogiannakis, One-pot synthesis of diverse γ -lactam scaffolds facilitated by a nebulizer-based continuous flow photoreactor, *ChemPhotoChem* 2 (2018) 860–864, <https://doi.org/10.1002/cptc.201800068>;
- d) G.I. Ioannou, T. Montagnon, D. Kalaitzakis, S.A. Pergantis, G. Vassilikogiannakis, Synthesis of cycloprop-2-enones from furans using a nebulizer-based continuous flow photoreactor, *Org. Biomol. Chem.* 15 (2017) 10151–10155, <https://doi.org/10.1039/C7OB02557B>.
- [16] K.-H. Huang, Z. Wei, R.G. Cooks, Accelerated reactions of amines with carbon dioxide driven by superacid at the microdroplet interface, *Chem. Sci.* 12 (2021) 2242–2250, <https://doi.org/10.1039/D0SC05625A>.
- [17] I.S. Metcalfe, M. North, P. Villuendas, Influence of reactor design on cyclic carbonate synthesis catalysed by a bimetallic aluminum(salen) complex, *J. CO₂ Util.* 2 (2013) 24–28, <https://doi.org/10.1016/j.jcou.2013.07.001>.
- [18] R.W. Wood, A.L. Loomis, XXXVIII. The physical and biological effects of high-frequency sound-waves of great intensity, *Philos. Mag.* 4 (1927) 417–436, <https://doi.org/10.1080/14786440908564348>.
- [19] a) J.H. Bang, K.S. Suslick, Applications of ultrasound to the synthesis of nanostructured materials, *Adv. Mater.* 22 (2010) 1039–1059, <https://doi.org/10.1002/adma.200904093>;
- b) Y. Zhang, K.S. Suslick, Synthesis of Poly(3,4-ethylenedioxythiophene) microspheres by ultrasonic spray polymerization (USPO), *Chem. Mater.* 27 (2015) 7559–7563, <https://doi.org/10.1021/acs.chemmater.5b03423>.
- [20] a) C. Liu, J. Li, H. Chen, R.N. Zare, Scale-up of microdroplet reactions by heated ultrasonic nebulization, *Chem. Sci.* 10 (2019) 9367–9373, <https://doi.org/10.1039/C9SC03701B>;
- b) K. Luo, J. Li, Y. Cao, C. Liu, J. Ge, H. Chenc, R.N. Zare, Reaction of chloroauric acid with histidine in microdroplets yields a catalytic Au–(His)₂ complex, *Chem. Sci.* 11 (2020) 2558–2565, <https://doi.org/10.1039/C9SC06221A>.
- [21] a) H. Büttner, L. Longwitz, J. Steinbauer, C. Wulf, T. Werner, Recent developments in the synthesis of cyclic carbonates from epoxides and CO₂, *Top. Curr. Chem. (Z.)* 375 (2017) 50, <https://doi.org/10.1007/s41061-017-0136-5>;
- b) M. Kokoja, M.E. Wilhelm, M.H. Anthofer, W.A. Herrmann, F.E. Kühn, Synthesis of cyclic carbonates from epoxides and carbon dioxide by using organocatalysts, *ChemSusChem* 8 (2015) 2436–2454, <https://doi.org/10.1002/cssc.201500161>;
- c) C. Martín, G. Fiorani, A.W. Kleij, Recent advances in the catalytic preparation of cyclic organic carbonates, *ACS Catal.* 5 (2015) 1353–1370, <https://doi.org/10.1021/cs5018997>;
- d) J.W. Comerford, I.D.V. Ingram, M. North, X. Wu, Sustainable metal-based catalysts for the synthesis of cyclic carbonates containing five-membered rings, *Green Chem.* 17 (2015) 1966–1987, <https://doi.org/10.1039/C4GC01719F>;
- e) M. Alves, B. Grignard, R. Mereau, C. Jerome, T. Tassaing, C. Detrembleur, Organocatalyzed coupling of carbon dioxide with epoxides for the synthesis of cyclic carbonates: catalyst design and mechanistic studies, *Catal. Sci. Technol.* 7 (2017) 2651–2684, <https://doi.org/10.1039/C7CY00438A>.
- [22] S. Kaneko, S. Shirakawa, Potassium iodide–tetraethylene glycol complex as a practical catalyst for CO₂ fixation reactions with epoxides under mild conditions, *ACS Sustain. Chem. Eng.* 5 (2017) 2836–2840, <https://doi.org/10.1021/acsschemeng.7b00324>.
- [23] V. Butera, H. Detz, Cyclic carbonate formation from epoxides and CO₂ catalyzed by sustainable alkali halide–glycol complexes: a DFT study to elucidate reaction mechanism and catalytic activity, *ACS Omega* 5 (2020) 18064–18072, <https://doi.org/10.1021/acsomega.0c01572>.
- [24] a) R.A. Sheldon, Fundamentals of green chemistry: efficiency in reaction design, *Chem. Soc. Rev.* 41 (2012) 1437–1451, <https://doi.org/10.1039/C1CS15219J>;
- b) F.M. Kerton, *Alternative Solvents for Green Chemistry*, RSC Publishing, Cambridge, 2009, <https://doi.org/10.1039/9781847559524>.
- [25] a) D.R. Lide, *Handbook of Chemistry and Physics*, 85th ed., CRC Press, Boca Raton (FL), 2004, pp. 8–87;
- b) G. Hochgesand, Rectisol and purisol, *Ind. Eng. Chem.* 62 (1970) 37–43, <https://doi.org/10.1021/ie50727a007>.
- [26] F. Lévesque, P.H. Seeberger, Highly efficient continuous flow reactions using singlet oxygen as a “green” reagent, *Org. Lett.* 13 (2011) 5008–5011, <https://doi.org/10.1021/ol2017643>.
- [27] Z.W. Wei, M. Wlekinski, C. Ferreira, R.G. Cooks, Reaction acceleration in thin films with continuous product deposition for organic synthesis, *Angew. Chem. Int. Ed.* 56 (2017) 9386–9390, <https://doi.org/10.1002/anie.201704520>.
- [28] a) Z. Zhou, X. Yan, Y.-H. Lai, R.N. Zare, Fluorescence polarization anisotropy in microdroplets, *J. Phys. Chem. Lett.* 9 (2018) 2928–2932, <https://doi.org/10.1021/acs.jpclett.8b01129>;
- b) S.E. Skrabalak, K.S. Suslick, Porous carbon powders prepared by ultrasonic spray pyrolysis, *J. Am. Chem. Soc.* 128 (2006) 12642–12643, <https://doi.org/10.1021/ja064899h>.