

Continuous Flow Synthesis of 1,3-Dimethylimidazolium-4-carboxylate - a Precursor for Unusual Ionic Liquids

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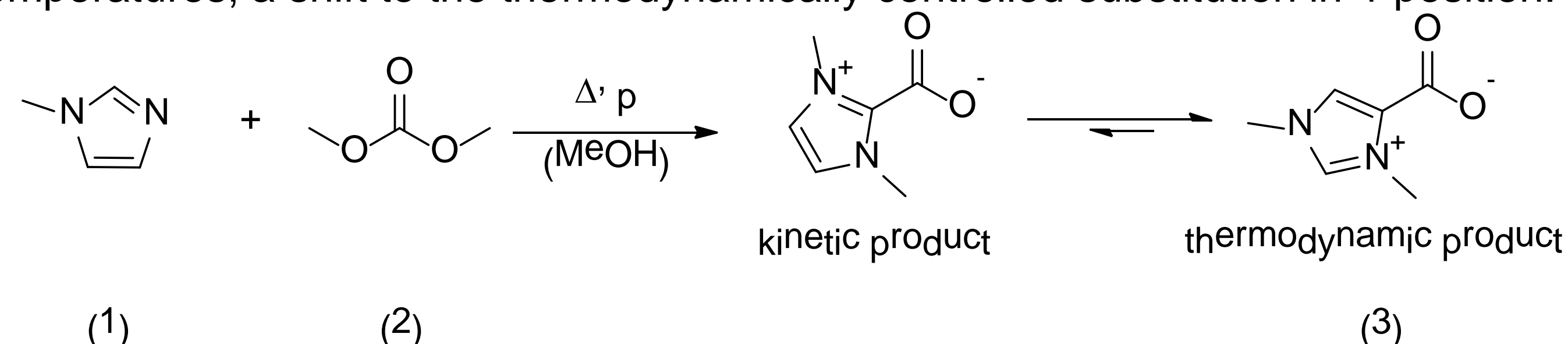
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Introduction

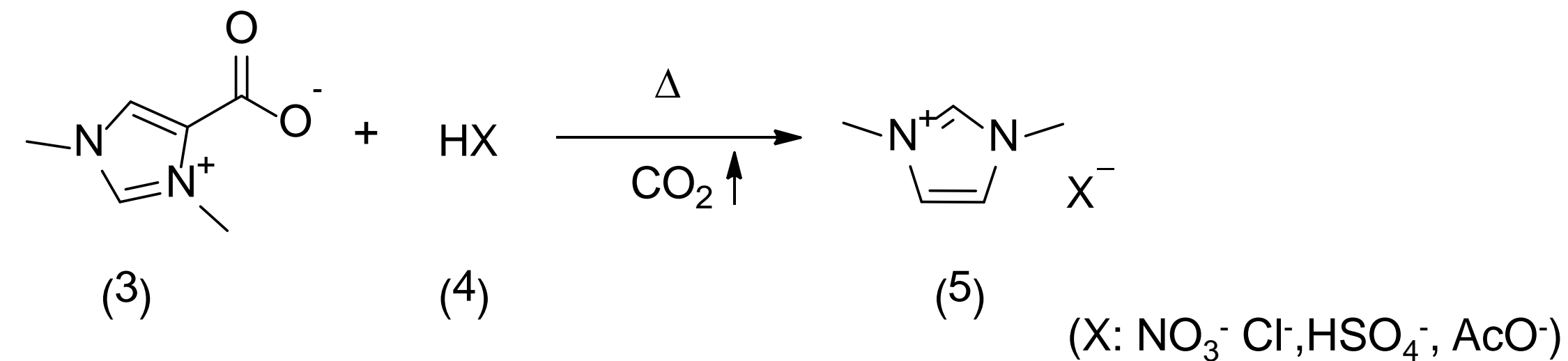
The synthesis of ionic liquids (IL) suffers from several problems, such as multi-step processing, the use of hazardous alkylation reagents, high heat release, complicated purification procedures and, in many cases, the formation of undesirable halide containing by-products.^[1] ILs are named as “designer solvents” due to the fact that their physical and chemical properties can be adjusted with a variety of substituents at the imidazolium cation and the respective anion. However not all desirable anion-cation combinations can be obtained by simple chemical syntheses. A common way is to use metathesis reactions for the anion exchange. Since this procedure has some major disadvantages, e.g. the use of large amounts of solvents, expensive reagents and long reaction times, an economical, worthwhile scale up is difficult.^[2]

State of the Art

The solid zwitterion 1,3-dimethylimidazolium-4-carboxylate ([DMIM]CO₂) is a versatile precursor for imidazolium based ionic liquids.^[3] The formation of the precursor ([DMIM]CO₂) requires autoclave conditions and long reaction times. Commonly, a yield of 81% [DMIM]CO₂ was achieved at 140°C and an elevated pressure of about 0.5 MPa within 20 hours.^[4-5] As a result, two products are formed depending on the reaction conditions: a kinetically controlled H-substitution in 2-position and, at higher temperatures, a shift to the thermodynamically controlled substitution in 4-position.

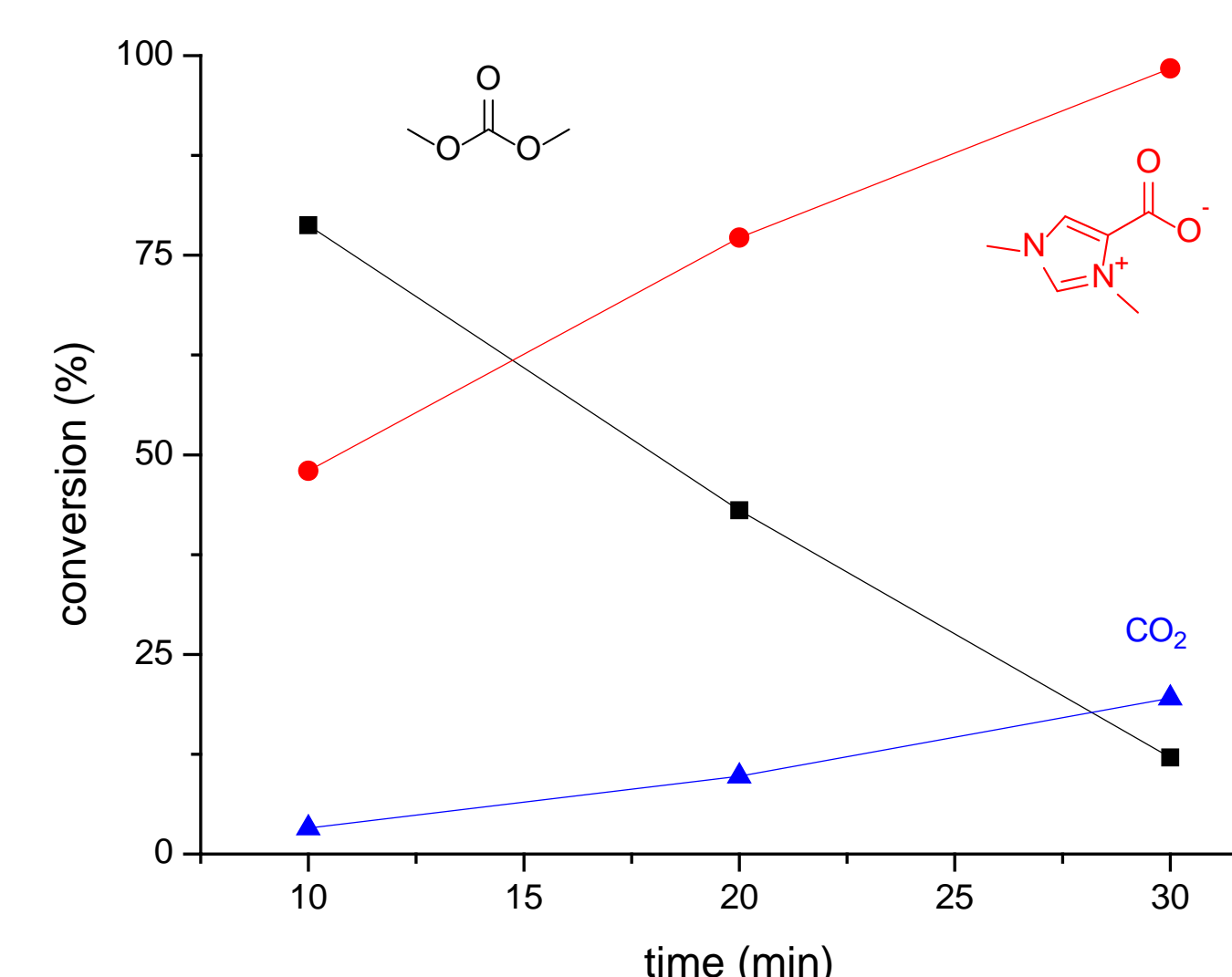


Treatment of ([DMIM]CO₂) with protic acids under mild conditions leads to the decarboxylation and concurrently to the incorporation of the acid anion to form the respective IL.



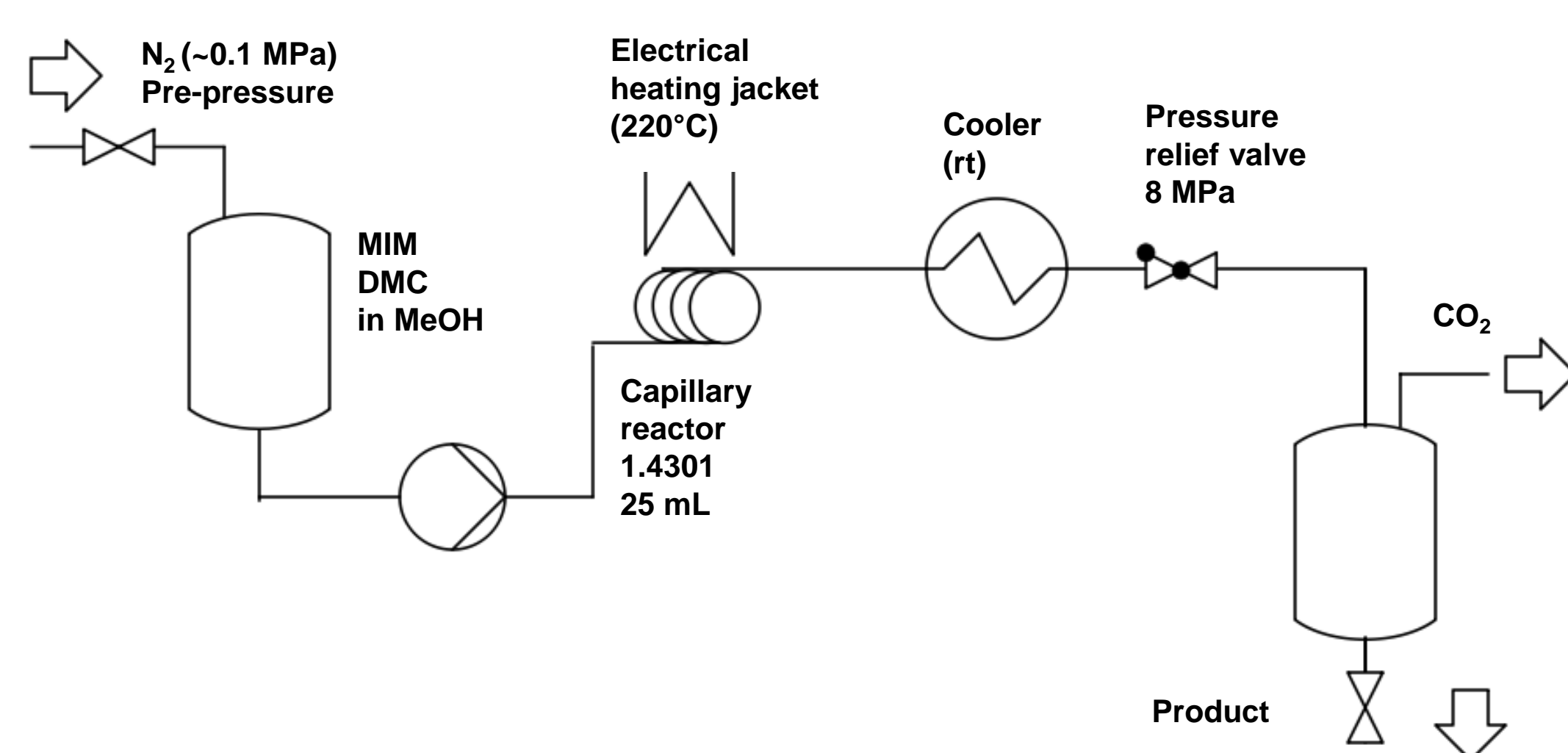
Heterogeneous Catalysis

The use of a capillary reactor filled with a heterogeneous catalyst, e.g. alkaline Al₂O₃ particles (50-200 μm diameter) enhances the reaction speed and yield significantly. A nearly quantitative conversion of MIM to [DMIM]CO₂ was achieved at 200°C and 0.8 MPa pressure (space-time yield of 700 g·h⁻¹·l⁻¹). The catalyst turnover frequency is in the range of about 3.1 mmol·m⁻²·h⁻¹ (56 g [DMIM]CO₂ per 1 g Al₂O₃, hour and one liter reactor volume).



The product was precipitated from ethyl acetate as white crystalline fine particles. The formation and yield of [DMIM]CO₂ was monitored with an IR-ATR spectrometer and gravimetrically validated. [DMIM]CO₂ was further characterized by ¹H-NMR spectroscopy (300 Hz).

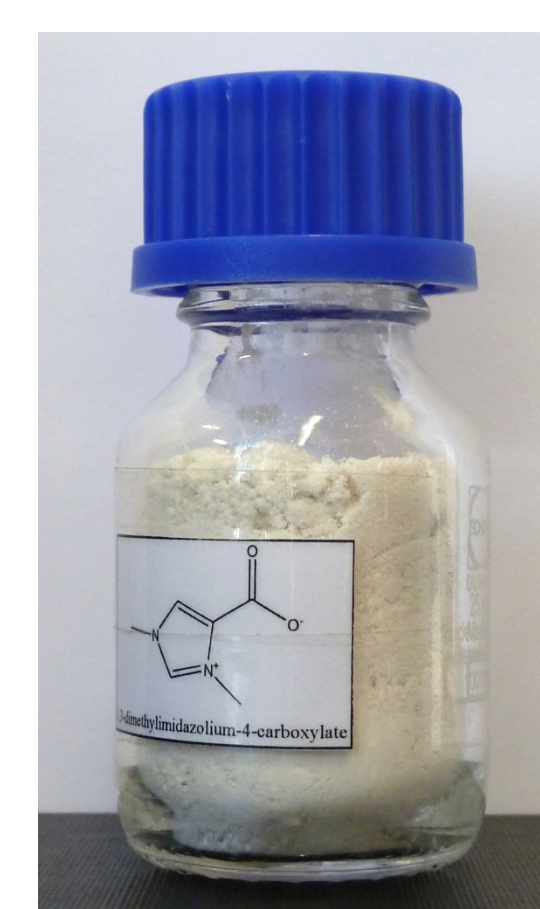
Continuous Flow Setup



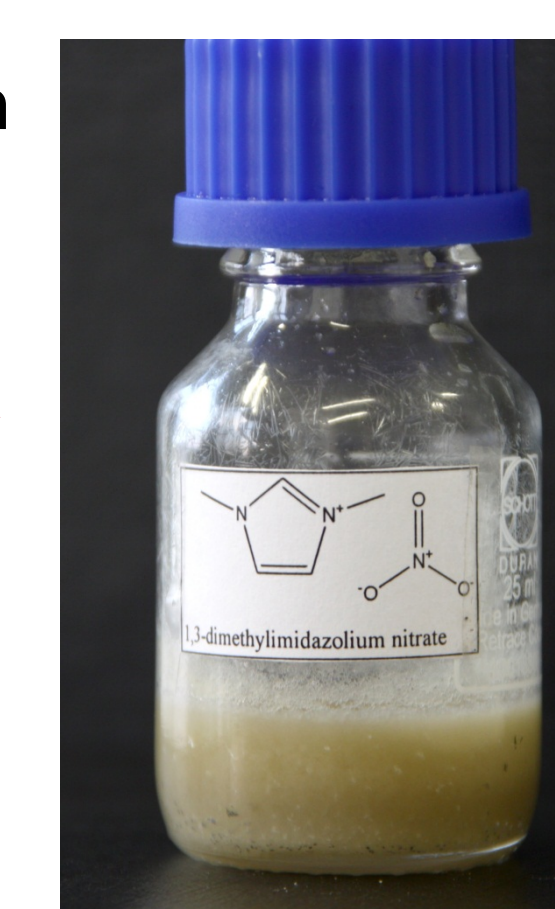
Since the reaction rate of MIM (1) with DMC (2) at room temperature is negligible, the reactants are premixed and diluted with methanol to avoid the precipitation of the product. Operation pressure and temperatures ranging from 6.0 to 8.0 MPa, and 180°C, to 220°C respectively. Reaction times varying between 12.5 min and 100 min.

Precursor Conversion

A continuous flow synthesis/purification of the carboxylate containing precursor and subsequent formation of a desired Ionic Liquid, e.g. [DMIM]NO₂, by simply treating the precursor [DMIM]CO₂ (8,3 g; 0,06 mol) with diluted nitric acid (20mL H₂O and 65% HNO₃; 0,06 mol) under reflux.

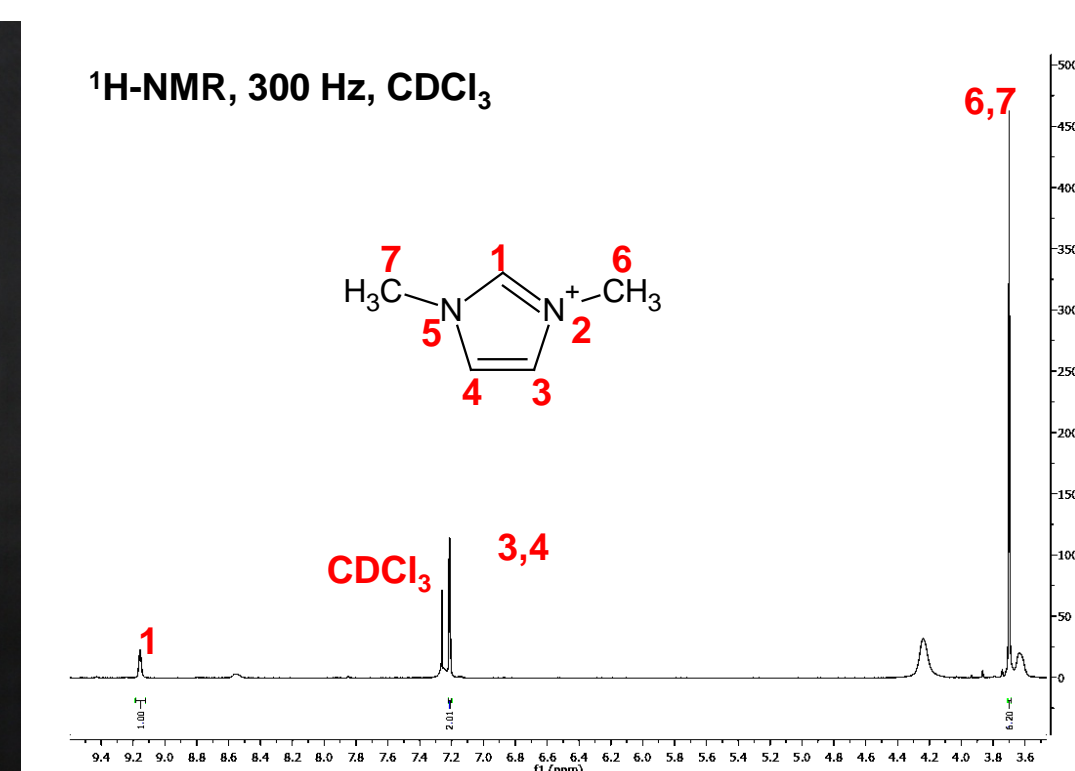


Conversion with diluted HNO₃ reflux, 180 min
- CO₂



Decomposition >240°C

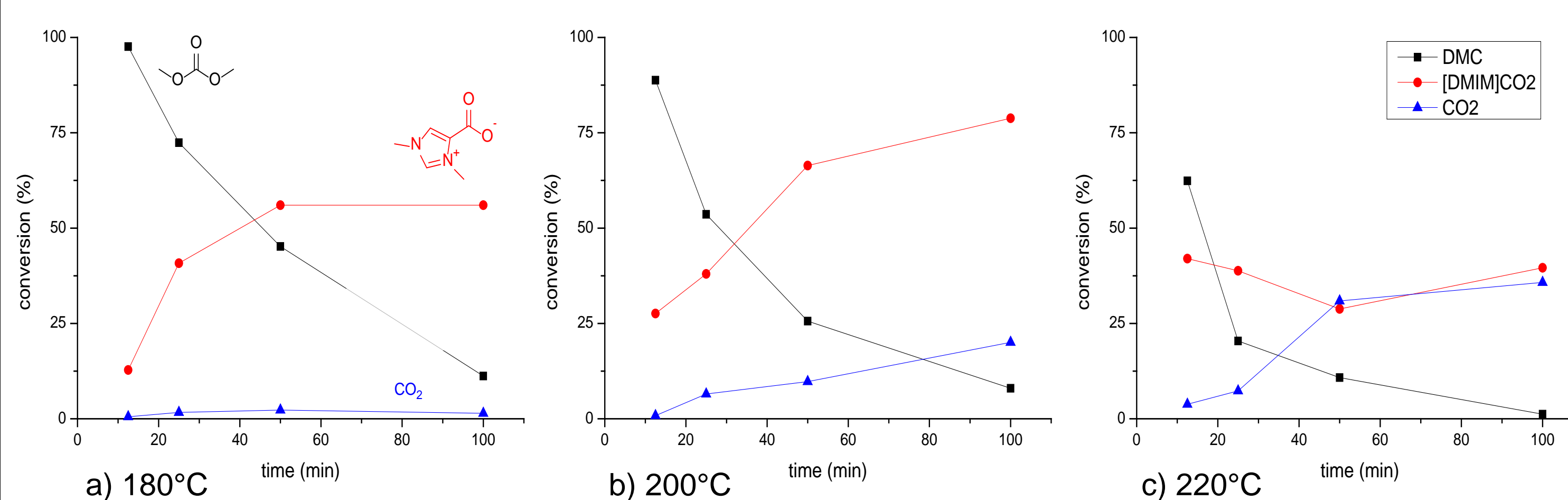
Mp. 59-61°C



Complete conversion

Experimental Results

Adapting the process described above to micro flow conditions is challenging due to the formation of a non-soluble solid product. Decomposition of DMC takes place depending on the reaction temperature. Therefore, a moderate excess of DMC (10 to 30 mol%) is used. Also, the flow conditions are changed from simple single-phase laminar to a gas/liquid plug flow.

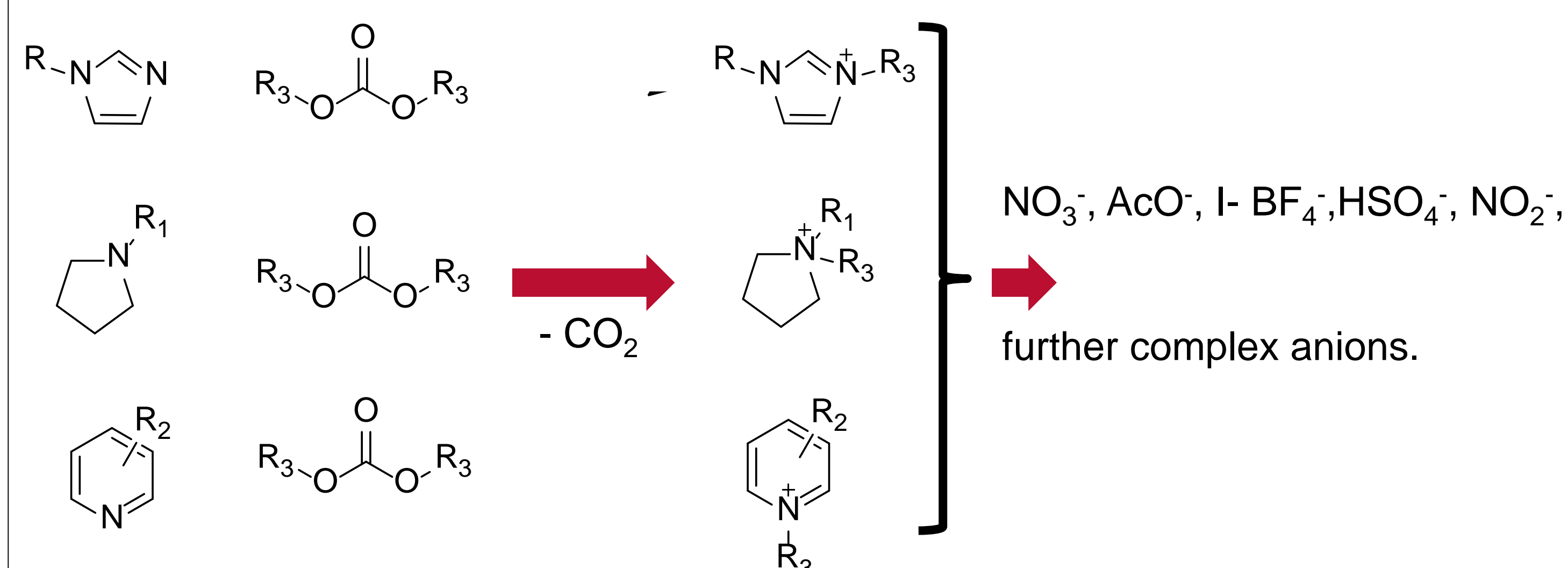


At a reaction temperature of 200°C and 100 min residence time, a yield of 80% [DMIM]CO₂ was achieved, corresponding to a space-time-yield of about 105 g·h⁻¹·L⁻¹. At 180°C, the yield decreases down to 54%. When the temperature was increased to 220°C, the decomposition of DMC became dominant and the yield decreased to 40% only.

After the removal of volatile components in vacuum, a yellow colored crude product was obtained. Further purification by precipitation from ethyl acetate was necessary in order to obtain a white crystalline product.

Outlook

Extension of the present carboxylation results to different substrates, e.g. alkylimidazoles, pyrrolidine and pyridine derivatives as well as different carbonate based alkylation agents. Easy access to special Ionic Liquids which cannot be synthesized by direct alkylation using common protocols.



References

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- [5] Schmidt, A., Beutler, A., Albrecht, M., Snovydyovych, B. & Ramirez, F.J. Imidazol-2-and-4-ylidene by decarboxylation. Studies on the cross-conjugated mesomeric betaine-alkaloid norzoanemonine and its pseudo-cross-conjugated isomer. Org. Biomol. Chem. 6, 287-295 (2008).