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Lab-Scale Microreactor Plant for the Study of Methylations with Liquid Chloromethane

Chloromethane is an important reagent for methylations in the process industry. However, as a gas suspected of causing cancer, it is rarely used at laboratory scale. Therefore, a setup is presented here for studies in a laboratory under safe and reproducible conditions. The use of a microreactor guarantees high heat transfer rates and a low holdup of the reagent. As a proof-of-concept, the reaction of chloromethane with the secondary amine morpholine in aqueous solution is investigated. By applying elevated pressures, a liquid-liquid system with enhanced solubility of chloromethane in the aqueous phase is accessible.

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Supporting Information available online

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1 Introduction

Chloromethane (methyl chloride, CH_3Cl) is a methylating agent widely used in industrial chemistry. Since the installation of the first commercial plant for its synthesis via chlorination of methane in 1923 by Farbwerke Hoechst, Germany, the worldwide production capacities have risen to about 10^6 tons per year [1]. The main applications of chloromethane are the manufacturing of silicones and methyl cellulose, which jointly account for roughly two-thirds of the demand. The remainder is used for other alkylation reactions in the synthesis of specialty chemicals such as pharmaceuticals, surfactants, and agricultural chemicals [2].

Alternative broadly applicable reagents for methylations are dimethyl sulfate and iodomethane. In comparison with these, the use of chloromethane is linked with a higher atom economy as a larger proportion of the molecular weight is incorporated in the product. However, in all three cases, a base such as sodium hydroxide is consumed in stoichiometric amounts and contributes to the overall waste balance. In some cases, the traditional methylating agents mentioned above may be replaced by the less toxic and non-carcinogenic dimethyl carbonate or methanol. These are regarded as more environmentally friendly options as the only waste products formed are carbon dioxide and methanol or water, respectively, but they lack general applicability [3]. Therefore, many industrial processes still rely on the use of chloromethane for methylations. This is in strong contrast with the low number of studies of its reactions found in literature. However, one of the major obstacles when working with chloromethane is the need for special equipment. Chloromethane is a toxic, flammable gas (physical properties are listed in Tab. 1), which may cause cancer, and hence has to be handled in a closed system under pressure. Therefore, dimethyl sulfate and iodomethane are the preferred reagents in synthetic chemistry at laboratory scale.

Continuous-flow microreactors offer several advantages over conventional equipment for tackling the challenges related to the study of reactions with chloromethane. High pressures are easily achieved and tolerated by the material due to the small dimensions of channel cross sections. A low holdup of hazardous reagents leads to a higher process safety. Furthermore, microreactors can be operated under conditions which guarantee a narrow residence time distribution, excellent control of temperature, and enhanced mass transfer [4, 5]. Under these conditions, reliable and reproducible kinetic data of reactions can be obtained.

Gaseous chloromethane can be employed in combination with water or various organic solvents in a two-phase system. In general, a base has to be added in order to remove acidic protons from the substrate or to take up the hydrogen chloride formed in the course of the reaction. In aqueous medium, inexpensive sodium hydroxide is often used. Chloromethane is slightly soluble in water with a solubility of $6.52\,g\,kg^{-1}$ at 30 °C and 1 bar [2]. The concentration in the aqueous phase can be increased by applying pressure to the system until the saturation vapor pressure (Fig. 1) is reached, resulting in a biphasic liquid-liquid system, which is discussed in the following in more detail.

This system can particularly benefit from microreaction technology as the effective interfacial mass transfer area between the two immiscible liquids is enlarged compared to conventional agitated reactors [7]. For the system studied, slug or Taylor flow may be assumed to be present in a capillary microreactor, in which one phase forms periodic elongated

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Table 1. Physical properties of chloromethane [2].

Property	Value
Boiling point at 1 bar [°C]	−23.9
Vapor pressure at 20 °C [bar]	4.89
Density of liquid at 20 °C and 5 bar [$kg\,m^{-3}$]	920
Viscosity of liquid at 20 °C and 5 bar [Pa s]	2.7×10^{-4}
Critical temperature [K]	416.3
Critical pressure [bar]	66.8
Solubility in water at 30 °C and 1 bar [$g\,kg^{-1}$]	6.52

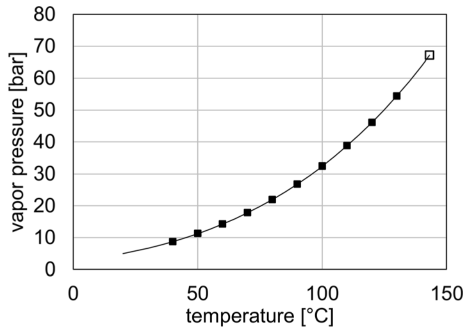

Figure 1. Vapor pressure curve of chloromethane (■ experimental data; □ critical point; data from [6]).

droplets called slugs within the continuous carrier phase (Fig. 2). Mass transfer can occur both at the front and end caps of the slugs and in the film layer between the droplet and the capillary wall, depending on the capillary material and the wetting properties of the fluids [7]. Taylor flow and its applications are described in-depth in the literature, e.g.. see [8–14]. However, the interplay between mass transfer and intrinsic reaction kinetics in the context of the flow pattern has to be investigated.

As described above, chloromethane is widely used in bulk chemical manufacturing processes but there is also potential for extension of fine chemistry applications. The aim of this work is to create a better understanding of the reactions involved and bridge the gap between the low use in organic chemistry laboratories and potential industrial processes. Therefore, a lab-scale microreactor plant for the methylation with chloromethane has been developed to employ the scope of this important reagent in organic synthesis and also to facilitate studies of reaction kinetics for scale-up purposes in a safe environment. Herein, the complex experimental setup and preliminary investigations of the methylation of morpholine are presented and discussed.

2 Microreactor Plant

The microreactor plant has been designed to enable experiments under a wide range of conditions. In particular, the target involves working with chloromethane in the liquid state at temperatures of up to 120 °C, which requires pressures of up to 50 bar (see Fig. 1). The focus was on setting up an easy-to-use system which guarantees a high process safety. Therefore, a lab automation system is employed for instrument control and also for safety monitoring. This makes it possible to move the system to safe operating conditions when a problem such as pressure buildup or a leakage is detected via pressure transmitters or a gas detector. In this case, the pumps will stop and a normally closed solenoid valve will shut down the chloromethane supply at the gas cylinder without manual intervention. In addition, pressure relief valves are installed to prevent burst of equipment. The process flow diagram is illustrated in Fig. 3, together with the complete setup, which is arranged within a fume hood.

Pressure in the reactor is built up using dual syringe pumps for continuous liquid dosing in conjunction with a back pressure regulator (BPR). Chloromethane is taken from a gas cylinder, which is heated to 35 °C by a heating tape and installed with the valve pointing downwards. In this way, liquid chloromethane can be withdrawn constantly with a sufficiently high supply pressure. A three-way valve on the suction side of the pump allows for purging with water using a steel cylinder pressurized by argon. A second syringe pump delivers the aqueous reactant solution. The streams are contacted in a Swagelok 1/16" T-piece before entering the reactor. The reactor (Tab. 2) is a helically coiled 1/16" stainless-steel capillary, in which the direction of curvature is inversed after every second turn, affording a compact design. Due to the repeated inversion, radial mixing is enhanced like in a coiled flow inverter [15–17] (Fig. 3c).

The reactor temperature is controlled by immersion into a bath thermostat. The process stream is quickly cooled down in a double-pipe heat exchanger operated with cold water after passing the reactor to stop the reaction after the desired residence time. Following the BPR, the chloromethane evaporates and the liquid phase is collected in a vessel. The gaseous chloromethane is guided to a scrubber. Problems in the form of blockage of the BPR may

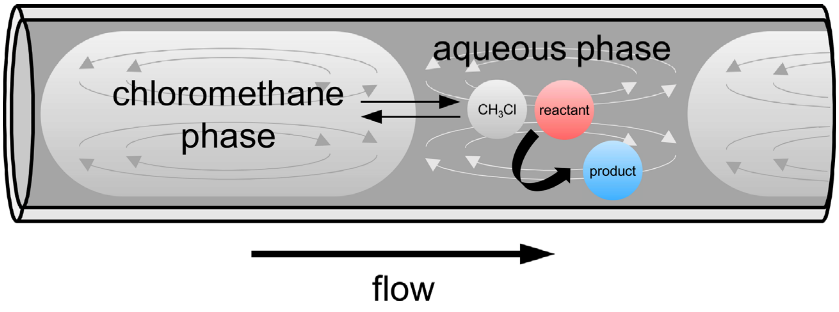

Figure 2. Potential liquid-liquid slug flow of chloromethane and aqueous phase in a stainless-steel capillary. Mass transfer between the two immiscible liquid phases in equilibrium can take place in the slug interfaces and the wall film. The methylation reaction between chloromethane and a reactant presumably occurs in the aqueous phase.

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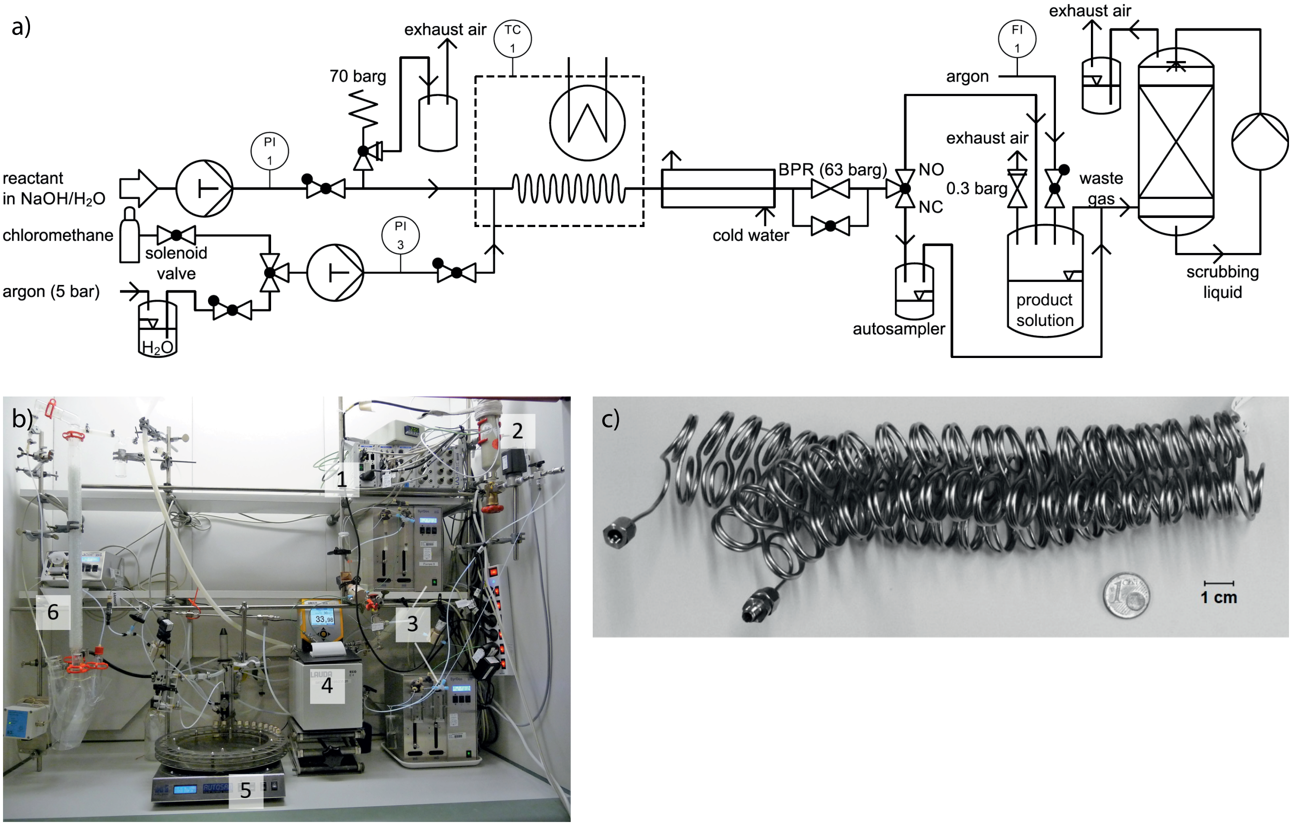

Figure 3. (a) Process flow diagram. (b) Setup of the lab-scale microreactor plant for the study of methylation reactions using chloromethane. (1) Lab automation system; (2) chloromethane gas cylinder with solenoid valve attached; (3) dual syringe pumps for continuous dosing of reactant solution and chloromethane; (4) bath thermostat with immersed capillary reactor; (5) autosampler; (6) scrubber). (c) Coiled stainless-steel capillary reactor with inner diameter of 0.5 mm and inner volume of 1 mL.

Table 2. Reactor properties.

Material	Stainless steel 1.4401	Stainless steel 1.4401
Internal volume [mL]	2.5	1
Internal diameter [mm]	0.5	0.5
Radius of curvature [mm]	6.5	6.5
Length [m]	12.73	5.09
Flow rate [mL $\min^{-1}$]	0.5–1.7	0.7–2.0
Residence time [min]	1.5–5	0.5–1.5

arise because of formation of solid chloromethane hydrate when the stream temperature falls below 7.5 °C [18] due to evaporation cooling. To avoid clogging, the flow rate of the reactant solution should be at least seven times the flow rate of liquid chloromethane (for details see Supporting Information).

Safety aspects play an important role in the design process of the plant. Thus, the entire plant is realized as a closed system from the dosing of reactants to sampling and treatment of residual chloromethane. Sampling from the closed system without the need for operator contact with medium is enabled using an automated sampling instrument. The sample is fed into a vial with septum cap via a double needle (see Supporting Information). Through the second needle remaining chloromethane gas can leave towards the scrubber where unreacted chloromethane is destroyed by the reaction with sodium dimethyldithiocarbamate (Fig. 4) [19].

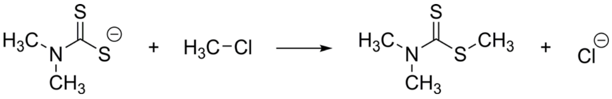

Figure 4. Destructive scrubbing of chloromethane using sodium dimethyldithiocarbamate.

Dithiocarbamate is a very strong nucleophile, which rapidly reacts with chloromethane to give methyl dithiocarbamate. The latter is very sparingly soluble in water, therefore tetrahydrofuran (THF) is added to the 40 % aqueous sodium dimethyldithiocarbamate solution, which is recirculated through a packed glass column using a peristaltic pump. A bubbler is connected to the top gas outlet of the scrubber in order to demonstrate the complete uptake of chloromethane and protect the system from incoming oxygen. As the presence of air in the

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system poses an explosion risk due to the flammability of chloromethane and the tendency of THF to form peroxides, those parts of the plant not filled with liquid, i.e., the collecting vessel, the scrubber, and the connecting tubes, are purged with argon prior to the experiments. The size of the gas cylinder is chosen such that, even in the case of complete release of the entire content within a minute, the lower explosive limit of chloromethane is not exceeded due to ventilation in the fume hood. Under normal operating conditions, a leak would not lead to concentrations in the fume hood above the MAK value of 50 ppm [20] because of the low feed rate.

The microreactor setup presented has been used for initial studies of the kinetics of the *N*-methylation of morpholine. *N*-Methylmorpholine is used in the production of polyurethane foams [21] and as a precursor for the industrially important *N*-methylmorpholine *N*-oxide, which is employed as a solvent in the manufacturing process of cellulose fibers [22].

3 Materials and Methods

3.1 Chemicals

The chemicals were purchased as follows: morpholine from Merck KGaA, Germany (purity $\geq$ 99 %), sodium hydroxide from Carl Roth GmbH & Co. KG, Germany ($\geq$ 99 %), anhydrous sodium acetate from Sigma-Aldrich Chemie GmbH, Germany ($\geq$ 99.0 %), and THF from Grüssing GmbH, Germany (99 %). Chloromethane 2.8 was supplied by Linde AG, Germany, in a small steel cylinder (380 mL, 270 g content). Sodium dimethyldithiocarbamate was purchased as a 40 % aqueous solution from Sigma-Aldrich Chemie GmbH, Germany. Deuterium oxide ($\geq$ 99.9 atom % D) with 0.03 % TMSP-d_4 was obtained from Deutero GmbH, Germany.

3.2 Equipment

Reactants are dosed using high-pressure continuous tandem syringe pumps (SyrDos 2, 90 bar version, Hitec Zang GmbH, Germany) with glass syringes (H-KP, Innovative Labor Systeme GmbH, Germany). The reactant feeds are mixed in a stainless-steel T-piece (SS-100-3, Swagelok Company, USA) and pumped through 1/16" stainless-steel capillaries (Chromatographie Handel Müller GmbH, Germany) used as residence time modules immersed in a bath thermostat (ECO E4G, Lauda Dr. R. Wobser GmbH & Co. KG, Germany) filled with silicone oil. A back pressure regulator (P-465 and P-795, IDEX Health & Science LLC, USA) is employed to keep up the pressure in the reactor. The scrubber for uptake of unreacted chloromethane consists of a glass column (0.5 m length, 30 mm inner diameter, Lenz Laborglas GmbH, Germany) filled with Raschig rings (3 mm).

The scrubbing liquid is circulated using a peristaltic pump (LabDos P100, Hitec Zang GmbH, Germany). A pressure relief valve (SS-4R3A, Swagelok Company, USA) is installed and set to 70 bar. Flow rates, temperature, the solenoid valve (Type 6027, number 308851, Bürkert GmbH & Co. KG, Germany) as well as the autosampler (AutoSam, Hitec Zang GmbH, Germany) are controlled by means of a laboratory automation system (LabBox and LabVision software, Hitec Zang GmbH, Germany). This system also enables safety monitoring in combination with in-line pressure transmitters (Type S-11, WIKA Alexander Wiegand SE 6 Co. KG, Germany) and an infrared gas transmitter for detection of chloromethane (CH4 MECCOS iTR, Leopold Siegrist GmbH, Germany) placed in the lower part of the fume hood.

Special care was taken in the selection of suitable materials that withstand contact with chloromethane and aqueous sodium hydroxide at elevated temperature and pressure. Stainless steel was the material of choice for all wetted parts in heated regions of the plant. Standard stainless-steel tube fittings (Swagelok Company, USA) were used to guarantee leak tightness at elevated pressure. For unheated high-pressure connections, polyether ether ketone (PEEK) was also employed in combination with fingertight polyoxymethylene (POM) fittings and ethylene tetrafluoroethylene (ETFE) ferrules (IDEX Health & Science LLC, USA). Additionally, polytetrafluoroethylene (PTFE) tubing (Chromatographie Handel Müller GmbH, Germany) and standard glassware were taken for the ambient-pressure part. Seals were made of fluoroelastomers (FKM) or perfluoroelastomers (FFKM) [23–25].

3.3 Experimental Procedure

Prior to the experiments, the liquids paths are flushed with water, whereas all parts that are flown through by gas are purged with argon. The scrubber is charged with equal volumes of a 40 % aqueous sodium dimethyldithiocarbamate solution and THF. Recirculation of the mixture is set to 40 mL min^{-1} with the suction hose being placed in the bottom of the vessel in order to draw from the aqueous layer that forms when chloromethane is absorbed. During start-up the intake of one pump is switched to liquid chloromethane via the three-way valve whilst the water flow of the other pump is maintained on a high level to prevent blockages due to formation of gas hydrates. When the first droplets of chloromethane reach the outlet of the reactor, dosing of the substrate solution, i.e., an aqueous solution of morpholine and sodium hydroxide with the desired concentrations, is started. The temperature and the flow rates of substrate solution and chloromethane are set to the desired values. After waiting for at least three times the mean residence time, three samples are taken using the autosampler.

3.4 Analytical Methods

Samples are analyzed by quantitative nuclear magnetic resonance (NMR) spectroscopy on an Oxford NMR 300 instrument with Mercury Plus console (Varian Inc., USA). The sample preparations are done by charging a 5-mm NMR tube with 300 µL sample, 250 µL sodium acetate solution (30 mg mL^{-1}) as an internal standard. and 138 µL D_2O with 0.03 % 3-(trimethylsilyl)propionic acid sodium salt (TMSP) for referencing. Spectra are recorded using a standard proton NMR experiment. Data is analyzed by a TopSpin 4.0 (Bruker Corporation,

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USA). Integrals are determined relative to the CH_3 signal of the standard sodium acetate at $\delta = 1.92$ ppm (s, 3 H) after applying phase and baseline corrections. Concentrations of the substrate morpholine and methylated reaction products are determined from the corresponding peak integrals: morpholine – $\delta = 2.82$ ppm (t, 4 H, $N(CH_2)_2$), *N*-methylmorpholine – $\delta = 2.25$ ppm (s, 3 H, NCH_3), *N*,*N*-dimethylmorpholinium – $\delta = 3.26$ ppm (s, 6 H, $N(CH_3)_2$). An exemplary spectrum is given in the Supporting Information.

4 Results and Discussion

4.1 Reliability of Measured Data

The microreactor measurement system was designed to enable reliable and reproducible measurements for the determination of the microkinetics of a reaction. To achieve this, it was aimed at approximately isothermal conditions and a reactor with a narrow residence time distribution close to ideal plug flow behavior. In this way, collection of kinetic data is facilitated as backmixing effects and the acceleration of the reaction rates due to formation of local hot spots become negligible and do not have to be considered. A key to achieve this is a small width of the microreactor channels. Therefore, capillaries with an inner diameter of 0.5 mm were chosen. The aspects of residence time distribution and heat transfer are discussed below together with mass transfer.

Residence time distribution. Bodenstein numbers as a measure for the degree of backmixing can be calculated for the reactors and parameters listed in Tab. 2, assuming a single-phase system with the properties of water for simplification. On the basis of the work by Daskopoulos and Lenhoff on dispersion of laminar flow in curved tubes [26], values of 100 and higher were obtained. This indicates a narrow residence time distribution and a behavior close to ideal plug flow [27–29]. Hence, effects on conversion due to backmixing can be neglected in good approximation.

Heat transfer. The heat transfer characteristics of the reactor system play an important role when measuring kinetic data. An elevation of temperature as a consequence of insufficient heat removal from exothermic reaction processes can cause an increase of the reaction rate coefficients and, hence, influences product and side product formation [30]. Therefore, nearly isothermal conditions and thus a high removal potential are desirable. Westermann and Mleczko [31] discussed the heat management in microreactors in detail and developed a short-cut approach to estimate the temperature increase in a capillary reactor, which is used here. For the exothermic methylation of morpholine, the standard reaction enthalpy is $-128.65\,\mathrm{kJ\,mol^{-1}}$ [32–34]. At 70 °C, the initial rate is approximately $10^{-2}\,\mathrm{mol\,L^{-1}s^{-1}}$ for an initial concentration of $1\,\mathrm{mol\,L^{-1}}$ of starting materials. In a reactor with an inner diameter of 500 µm the temperature increase is as low as 0.07 K and thus negligible. The process can be regarded as nearly isothermal. More details are given in the Supporting Information.

Mass transfer. Mass transfer can become limiting if it proceeds on the same or a slower time scale as the chemical reactions considered [35]. The apparent reaction rates may be lower compared to the actual values in a system without these limitations. Therefore, yield and selectivity may be influenced by poor mass transfer. When the same experiment was performed in two reactors with the same total volume but different internal diameter, i.e., 0.5 mm and 0.75 mm, which results in a change of the interfacial area, no significant deviations were observed (see Supporting Information). This underlines that there is no evidence for mass transfer limitations.

4.2 Chloromethane-Water System

For the discussion of the kinetics of the methylation with chloromethane in a biphasic system containing water, it is important to have insight into the phase equilibrium. The reaction rate of the reaction step involving chloromethane depends on its concentration in the aqueous phase, which is equal to the equilibrium solubility concentration, provided no mass transfer limitations exist. To our knowledge, experimental data available on the mutual solubilities in the liquid chloromethane-water system is limited to the range of about 10–50 °C. Holldorff and Knapp [18] reported that the extrapolation of gas solubility data in terms of Henry coefficients to the vapor pressure of the vapor-liquid-liquid equilibrium (VLLE) system according to Henry's law affords solubilities that match the data they measured.

In order to get information on the solubility over a broader temperature interval, data from various sources was used for extrapolation purposes. VLLE vapor pressure data from Holldorff and Knapp was fitted ($R^2 = 0.9999$) and extrapolated in accordance with the Clausius-Clapeyron equation. The values reported are consistent with the correlation given by Mansoorian et al. for the vapor pressure of chloromethane [6], which is stated above. Temperature-dependent Henry coefficients were taken from Horvath [36] (range 0–80 °C) and extrapolated after van't Hoff ($R^2 = 0.994$). Again, good agreement was observed with other published data [37, 38]. The resulting solubility curve based on this data is given in the Supporting Information for the temperature range from 20 °C to the critical temperature.

4.3 Methylation of Morpholine

In this work, the methylation of morpholine is examined as a proof-of-concept. In general, methylation of secondary amines gives a mixture of products. As the tertiary amine, which exists in equilibrium with the protonated species, generated in the first reaction step still has a nucleophilic lone electron pair, it reacts with another molecule of chloromethane, yielding a quaternary ammonium compound (Fig. 5).

In the initial studies, the reaction of morpholine was conducted in alkaline aqueous solution with liquid chloromethane at about 50 bar and 70 °C. Under these conditions, chloromethane is a liquid and its saturation concentration in aqueous solution is about $0.67\,\mathrm{mol\,L^{-1}}$ (see Supporting Information). Fig. 6 indicates the measured concentrations of the reactant morpholine, the products *N*-methylmorpholine and *N*,*N*-dimethylmorpholinium, and the side-product methanol, which

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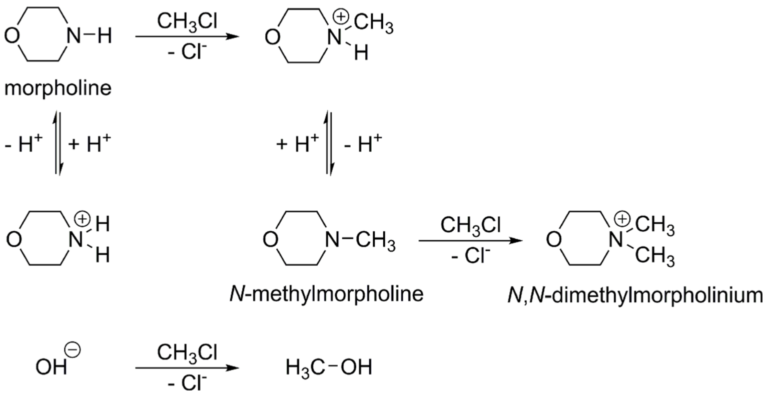

Figure 5. Reaction scheme of methylation of morpholine, including hydrolysis of chloromethane to methanol.

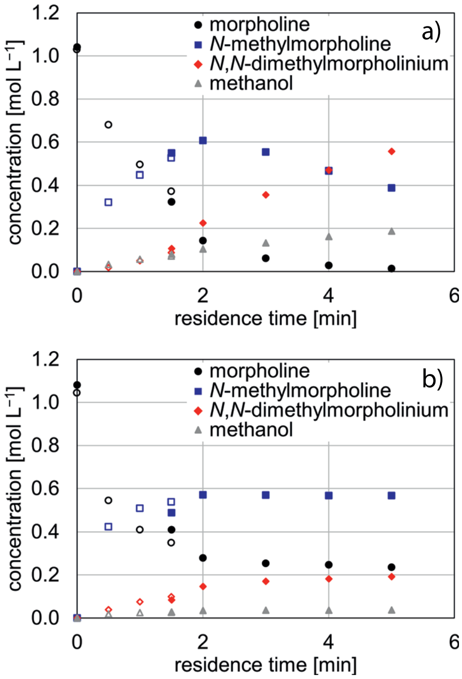

Figure 6. Concentration profiles of morpholine and methylated species *N*-methylmorpholine and *N*,*N*-dimethylmorpholinium as well as side-product methanol versus residence time at 70 °C with an initial concentration of morpholine of approximately 1 mol L^{-1} and (a) two equivalents or (b) one equivalent of CH_3Cl and NaOH each. Unfilled markers represent data points that were determined in the 1-mL reactor, filled markers correspond to data points obtained using the 2.5-mL reactor.

results from hydrolysis of chloromethane in base. The residence time was adjusted by changing the volumetric flow rates of both liquid chloromethane and the aqueous reactant solution as well as the length of the capillary reactor. For residence times between 0.5 and 1.5 min, a reactor with 1.0 mL inner volume was used, whereas residence times up to 5 min were achieved in a 2.5-mL capillary. Both had an inner diameter of 0.5 mm.

Values for a residence time of 1.5 min were determined in both reactors. Two scenarios with different stoichiometry were investigated: 2 eq. of each CH_3Cl and NaOH (Fig. 6a) and 1 eq. of each (Fig. 6 b). The initial concentration of morpholine was approximately 1 mol L^{-1} but varied slightly between the experiments. All values were determined by quantitative NMR spectroscopy as the average of three samples. The standard deviations are on the order of 0.01 mol L^{-1}. In the beginning of the reaction, the system consists of two separate liquid phases, whereas it becomes a single phase as soon as sufficient chloromethane is consumed for the remainder being soluble in water. Concentrations given in the graph refer to the aqueous solution, which was collected after the BPR. Following the change to atmospheric pressure, the solubility of chloromethane decreases and evaporation follows.

With two equivalents of both chloromethane and NaOH (Fig. 6a), the reaction shows nearly complete conversion of morpholine within 5 min. After this period of time, more double- than single-methylated product is formed. The maximum amount of *N*-methylmorpholine, about 0.6 mol L^{-1}, is obtained at a residence time of 2 min. A significant amount of methanol is formed, with the hydrolysis being considerably slower than the methylation of the amines. When only one equivalent of base and chloromethane are used (Fig. 6b), the reactions cease at residence times of 3 min and longer, as the reagent chloromethane is almost completely consumed. A ratio of *N*-methylmorpholine to *N*,*N*-dimethylmorpholinium of approximately 3:1 is reached.

In the current work, a detailed kinetic model is derived based on an extended experimental data set. This can be used for the optimization of reaction conditions and will provide a basis for a scale-up towards an industrial-scale continuous process. A model-based scale-up with simultaneous solution of mass and energy balances presents a scientifically sound approach to cover the subject of heat transfer [13]. In addition, sufficient residence time and moderate mixing have to be provided since the reaction kinetics indicate a reaction time in the range of several minutes. Continuous dispersion of the two-phase flow in a helical tube reactor or coiled flow inverter (CFI) [39] will guarantee sufficient mass transfer on larger scale.

5 Summary and Outlook

A complete microreactor setup for the study of methylations using liquid chloromethane is presented. Many industrial processes exist using chloromethane, which may benefit from insights into the reaction kinetics. Safety aspects played an important role in the development process. The setup is a closed system and automatized to a great extent, including monitoring of internal pressure and automatic sampling for reproducible experiments. It is demonstrated that the reactor system is suitable for the measurement of reliable kinetic data as deviations from an ideal isothermal plug-flow reactor are negligible.

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First results of kinetic studies are discussed for the methylation of morpholine in an alkaline aqueous system with chloromethane. Within 5 min, full conversion of morpholine is achieved but leads to a mixture of the single- and double-methylated products as expected. More research is needed to build a detailed kinetic model based on the mechanism of the reactions. This will be a helpful tool for optimization towards a process with high yield of the desired product at minimum level of expenses and a scale-up to pilot or full commercial scale.

Supporting Information

Supporting Information for this article can be found under DOI: 10.1002/ceat.202000011. This section includes additional references to primary literature relevant for this research [40–42].

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Symbols used

Nu	[–]	Nusselt number
R^2	[–]	coefficient of determination

Greek letter

δ	[ppm]	chemical shift (NMR)

Abbreviations

BPR	back pressure regulator
CFI	coiled flow inverter
eq.	equivalent(s)
NC	normally closed
NMR	nuclear magnetic resonance
NO	normally open
s	singlet (NMR)
t	triplet (NMR)
THF	tetrahydrofuran
TMSP	3-(trimethylsilyl)propionic acid sodium salt

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