Intricate kinetics: *in-situ* FTIR-spectroscopy discloses a phase change during ionic liquid synthesis

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The kinetics of the methylation of triethylamine (NEt₃) with dimethyl carbonate (DMC) in methanol have been investigated by means of *in-situ* ATR-IR-spectroscopy. The data shows an autocatalytic influence of the ionic product on reaction kinetics. A bend in the reaction rate progress indicates a sudden change from solvated ions to a microstructured biphasic system, which is reflected in the dependence of the reaction rate constant from the product concentration and the Hildebrand parameter.

Introduction

The syntheses of ionic liquids (ILs) are often Menshutkin reactions¹ from tertiary amines and alkyl halogenides to quaternary ammonium salts via an S_N2 mechanism. In general, an autocatalytic behaviour² of the reaction can be assumed, because the ionic product increases the polarity of the solvent and thereby the conversion of further substrate is favoured following the Hughes-Ingold-rules³. This work deals with a reaction similar to the Menshutkin reaction² starting from NEt₃ and DMC to the IL triethylmethylammonium monomethyl carbonate (MeNEt₃⁺ MeOCOO⁻) (Scheme 1).

Scheme 1: General formulation of the Menshutkin reaction and methylation of triethylamine with dimethyl carbonate[†] in the temperature range used for this work. The solvent methanol is necessary because in neat experiments a phase separation takes place⁷ which complicates the IR measurements.

Only few examples of autocatalytic Menshutkin reactions are mentioned in literature, while the majority of researchers do not seem to observe an autocatalytic effect. Grant and Hinshelwood⁴ have reported an autocatalytic effect in the reaction of benzoyl chloride and aniline in hexane. Matsui and Tokura⁵ have investigated 96 different reactions of N,N-

dimethylbenzylamine derivatives with methyl iodide in 14 solvents and reported an autocatalytic effect for two chloro-substituted derivatives in cyclohexane only. Furthermore, Pocker⁶ described a weak positive kinetic salt effect of the product for the reaction of pyridine with methyl bromide in benzene. Jess and Große Böwing⁷ observed autocatalysis in the reaction between N-methylimidazole and butyl chloride in ethanol and correlated that effect over the exponential relation between ionic strength and rate constant as a kinetic salt effect. Most recently Firaha and Paulechka⁸ investigated the kinetics for the synthesis of 1-alkyl-3-methylimidazolium halogenide ILs. They described the autocatalytic effect of the product by variation of the activity coefficients of substrates and transition state with increasing product concentration. None of the studies used *in-situ* process analytics as they have become readily available.

We report the first *in-situ*-IR-spectroscopic investigation of the reaction between DMC and the NEt₃ performed in methanol between 90–140 °C (Scheme 1). The thermodynamics of this reaction have been investigated by Kalb *et al.*⁹ According to their work, the methylation of triethylamine by DMC is proceeding towards the products with an equilibrium constant K_x of $5.7 \cdot 10^2$.⁵ The kinetics of the reaction analysed by off-line HPLC have been reported by Weisshaar *et al.*¹⁰ They observed that the reaction follows a second-order rate law with a first order dependence in both substrates.

The advantage of the *in-situ* method is that real-time data can be obtained with a resolution up to one minute for high quality IR spectra and distortions due to sampling can be avoided. Moreover, the concentrations of participating components are determined under reaction conditions. Thereby, effects due to thermal expansion resulting in decreased concentrations and phase equilibria between liquid and gas phase can also be observed. In contrast to a second-order rate law, our results point towards a more complex rate law, as an autocatalytic influence of the product has to be considered. Concentration

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profiles are derived from time-resolved IR spectra by Peak Integration. Subsequently, three kinetic models are presented and evaluated to describe the autocatalytic behaviour of the reaction system.

Methods

Calibration Procedure

To enable the prediction of concentrations, spectra of binary mixtures of methanol and either DMC, NEt_3 or $\text{MeNEt}_3\text{MeOCOO}$ have been measured with the Bruker Matrix-MF spectrometer^{§§} used for reaction monitoring. Quaternary mixtures of all species present have been used to validate the calibration with respect to interactions between substrates and product. Characteristic, isolated absorption bands have been calibrated by Peak Integration with PEAXACT 4 from S-PACT (ESI). Due to overlap between the methanol signal and the spectra of other reaction components, the concentration of the solvent can only be estimated by integration of the central area of the $\nu(\text{C-O})$ band. The root mean square errors of cross-validation (RMSECVs) of the calibrated model are sufficient to derive concentration profiles of all present species from the time-resolved spectra.

Reaction Monitoring

All experiments have been performed in an autoclave optimized to monitor biphasic reaction systems, as described by Hardy *et al.*¹¹ Two ATR-IR fiber probes have been applied, one for the lower liquid phase, one for the upper gaseous phase. Triethylamine (>99 %, Sigma Aldrich) and DMC (>99 %, Sigma Aldrich) and methanol (>99 %, Fisher Scientific) have been used without further purification. After recording a reference spectrum against air, the solvent methanol and the substrates triethylamine and dimethyl carbonate are inserted and the autoclave is sealed. While continuously recording spectra of upper and lower phase in an alternating manner, the autoclave is heated up and held at reaction temperature for several hours.

Kinetic Modelling

The reaction rate is assumed to be first order in both dimethyl carbonate and triethylamine (Eq. 1), if the reaction proceeds via an $\text{S}_{\text{N}}2$ mechanism. The apparent rate coefficient k_{app} is obtained from the fraction of reaction rate and the product of substrate concentrations (Eq. 2).

$$r = \frac{dc_{\text{IL}}}{dt} = k_{\text{app}} c_{\text{DMC}} c_{\text{NEt}_3} \quad (1)$$

$$k_{\text{app}} = \frac{r}{c_{\text{DMC}} c_{\text{NEt}_3}} \quad (2)$$

Based on k_{app} , three different approaches are pursued to find out the origin of autocatalysis.

1. Parallel Reaction

A new reaction pathway can be assumed that proceeds via a ternary complex of the substrates and the product. This would lead to a parallel reaction with an uncatalysed pathway of second order and a catalysed pathway of third order. A linear dependence between k_{app} and c_{IL} reflects this behaviour (Eq. 3).

$$k_{\text{app}} = k_0 + k_{\text{w}} c_{\text{IL}} \quad (3)$$

The other approaches are based on the transition state theory¹² which states that the reaction rate coefficient is dependent on the activities and hence on the activity coefficients of the substrates and the transition state (Eq. 4-5). Increased activity coefficients of the substrates are thereby favourable for an increased reaction rate coefficient.

$$k_{\text{app}} = k_0 \frac{\gamma(\text{DMC}) \cdot \gamma(\text{NEt}_3)}{\gamma(\text{transition state})} \quad (4)$$

$$\ln(k_{\text{app}}) = \ln(k_0) + \sum_i \ln(\gamma_i^{v_i}) \quad (5)$$

2. Salting-out Effect

The activity coefficients of neutrally charged substances are affected by the ionic strength I of the surrounding medium.¹³ This has an impact on the solubility and is known as salting-out or salting-in effect. The activity coefficient grows or falls exponentially with increasing I . In this case, I is equal to c_{IL} , so the logarithmic activity coefficient and thereby $\ln(k_{\text{app}})$ would depend linearly on c_{IL} (Eq. 4). The fit parameter b can be interpreted as a combination of the exponential fit parameters of the substrates and the transition state, the so called Setschenow constants.

$$\ln(k_{\text{app}}) = \ln(k'_0) + b \cdot c_{\text{IL}} \quad (6)$$

3. Regular Solution Theory

According to the regular solution theory¹⁴ the activity coefficients substances in mixtures can be predicted via the Hildebrand solubility parameter δ . The parameter δ is also called cohesive energy density and can be derived merely from the enthalpy of vaporization and the molar volume (Eq. 7). An average over the volume fractions of the components leads to δ_{mean} . The activity coefficient of a component in a mixture depends quadratically on δ_{mean} (Eq. 8). Thereby, $\ln(k_{\text{app}})$ depends on δ_{mean} under the assumption that specific interactions between different substances can be neglected (Eq. 9).

$$\delta_i = \sqrt{\frac{\Delta_{\text{vap}} H_i - RT}{V_{\text{m},i}}} \approx \sqrt{\frac{\Delta_{\text{vap}} H_i}{V_{\text{m},i}}} \quad (7)$$

$$RT \ln(\gamma_i) = V_{\text{m},i} (\delta_i - \delta_{\text{mean}})^2 \quad (8)$$

$$\ln(k_{\text{app}}) = \ln(k''_0) + a_1 \delta_{\text{mean}}^2 + a_2 \cdot \delta_{\text{mean}} + a_3 \quad (9)$$

Results and Discussion

From IR-Spectra to Reaction Rate Progress

The time-resolved spectra (Fig. 1, ESI) as well as the derived concentrations (Fig. 2, ESI) give a qualitative insight into the reaction progress. As expected, the substrate concentrations decrease and the product concentration increases, while the methanol concentration increases surprisingly after a period on a more or less constant level. Throughout all experiments, the sudden increase in solvent concentration can be correlated with a critical product concentration c_{crit} .

The numerical differentiation of product concentration with respect to time forms the progress of reaction rate r (Fig. 3). As the vapour pressure of DMC depends strongly on the concentration of organic salts,¹⁵ and as the NEt_3 concentration is computed less accurately from the raw measurement data, these concentration profiles are not regarded to derive the reaction rate. The progress of r is split into an increasing section and a decreasing section which are separated by a non-differentiable point as the maximal rate is reached. The point of maximal reaction rate matches to c_{crit} . The increasing reaction rate in the beginning clearly depicts that the product has a catalytic influence on the reaction. At longer reaction times or low reaction rates present, r tends to scatter and fluctuate. For low reaction rates (ESI Fig. 23) this behaviour is obvious as the signal-to-noise ratio is decreased by numerical differentiation. At longer reaction times, the concentrations of the reaction mixture possibly fluctuate (Fig. 2) for another reason: the reaction mixture now contains a significant amount of ionic liquid which has virtually no vapour pressure. The other components partition into the gas phase and condense in the headspace. From there, they flow back into the liquid phase in an intermittent manner. The instantaneous dilution of the ionic liquid by the backflowing drops of the volatile components leads to a fluctuation of r after numerical differentiation.

Validation of the Kinetic Models

The three approaches to describe the autocatalytic behaviour of the reaction system provide dependencies of k_{app} and c_{IL} , $\ln(k_{\text{app}})$ and c_{IL} or $\ln(k_{\text{app}})$ and δ_{mean} . The validity of the underlying assumptions is checked by comparison of the respective plots with the expected dependencies of Eq. 3, Eq. 6 and Eq. 9, resp.

1. Parallel Reaction

The autocatalytic influence of the product is illustrated in the plot of k_{app} versus c_{IL} , because k_{app} increases monotonically with increasing product concentration (Fig. 4). The sections of increasing and decreasing reaction rate (Fig. 3) can be distinguished better the higher the temperature is (ESI). The underlying concept of a parallel reaction with a catalysed pathway is proven wrong, because the sections of k_{app} before and after the bend develop a positive curvature and differ systematically from a linear shape. The positive curvature gets more significant at elevated temperatures (ESI).

2. Salting-out Effect

The plot of $\ln(k_{\text{app}})$ versus c_{IL} can be matched with a steeper linear fit function from low c_{IL} up to the bend and a flatter linear fit function at higher c_{IL} (Fig. 5). This depicts that the IL has a high catalytic activity at low concentrations which is damped above a critical concentration c_{crit} . Since a linear function is a valid fit, the idea of the autocatalytic influence by a salting-out effect of the IL is valid.

Nevertheless, the origin of c_{crit} remains unclear if only the kinetic data is considered.

3. Regular Solution Theory

An insight into the phase behaviour of the reaction mixture is gained considering the plot of $\ln(k_{\text{app}})$ versus δ_{mean} (Fig. 6). This plot can only be evaluated qualitatively, because the enthalpy of vaporisation of MeNEt_3 MeOCOO as well as its density at reaction temperature is not known and approximations have been performed (ESI). δ_{mean} is expected to increase with increasing product concentration, but for c_{IL} smaller than c_{crit} the averaged Hildebrand parameter remains approximately constant. Thus, $\ln(k_{\text{app}})$ does not depend on δ_{mean} for small product concentrations which lets the model of a regular solution collapse in this concentration range.

The basic assumption in the regular solution theory is that the mixture components have no strong specific interactions with each other. At small c_{IL} , the IL does not behave as a pure substance but interacts with the solvent. This points towards the formation of solvated ions or small clusters¹⁶. At concentrations above c_{crit} the model of a regular solution fits better, because here δ_{mean} correlates with increasing rate coefficients. It is plausible that the ion clusters aggregate at higher concentrations. So, the IL behaves as a bulk phase in this concentration range which is separated from the organic phase on a microscopic scale.

If separated phases are assumed, the increase of methanol concentration can be clarified. The partial molar volume of methanol is higher in the organic phase than in the IL phase, because methanol and the IL form attractive interactions which results in an exothermic heat of mixing. So, the concentration of methanol in the IL phase is greater than in the organic phase and the IL phase is denser. The amount of IL phase increases with reaction progress, leading to a volume decrement of the reaction mixture (ESI). Thereby, the methanol concentration raises although the methanol amount remains constant.

Comparison to Literature

A view into literature helps to understand what happens as c_{crit} is exceeded. Molecular dynamics (MD) simulations from Bernardes *et al.*¹⁷ show that the IL 1-ethyl-3-methylimidazolium ethylsulfate forms ion clusters in water at low concentrations. At molar fractions between $x_{\text{IL}} = 0.05$ to 0.20, the IL forms a continuous phase that is entwined with a continuous water phase. MD simulations from Gupta *et al.*¹⁸ have demonstrated that solutions of trihexyl(tetradecyl)phosphonium chloride in methanol are

more structured regarding the ion-ion distances at higher concentrations. This can be also explained by the formation of a biphasic mixture. The determination of molar excess enthalpies by the measurement of vapour pressures in IL-water mixtures¹⁹ shows that the ions arrange themselves at a critical molar fraction of 0.015. Adapting these results, c_{crit} is the concentration at which the IL MeNEt₃ MeOCOO forms a microstructured biphasic system with methanol and has thereby a weaker catalytic activity than isolated ion clusters.

Conclusions

In conclusion, we demonstrated that the ionogenic S_N2 reaction between dimethyl carbonate and triethylamine is autocatalytic due to the increasing solvent polarity with the ongoing reaction. Furthermore, a critical concentration can be observed below which ion clusters are solvated and above which a microstructured biphasic system is formed. In the microstructured biphasic system, the solvent concentration increases with higher IL concentration. The autocatalytic activity of the product is high in the diluted concentration range and damped at higher concentrations. The distinctness of this effect arises out of the high concentration range of the substrates, the relatively slow reaction progress and the fast acquisition of *in-situ* data. Especially the high scanning frequency enabled to observe a phase change in the reaction mixture. Previous kinetic investigations of Menshutkin reactions or IL syntheses may not have found this effect or observed the presence of a phase change due to high substrate dilutions, faster reaction progress or slow data acquisition rates.

Outlook

The autocatalytic behaviour of the reaction system is a feature that can be used for further investigations. Ionogenic S_N2 reactions should be performed under addition of product to increase reaction rates which is advantageous over the use of other salts by means of product separation to increase solvent polarity. Furthermore, kinetic investigations on IL syntheses should consider the concentration range of the substrates as the phase behaviour influences the catalytic activity of the product.

To verify the results of this work, further investigations with other techniques are desirable. For instance, *in-situ*-Raman spectroscopy is a complementary spectroscopic method to determine concentrations, but a high fluorescence background prohibited the usage in this study. Therefore, fluorescence suppression techniques²⁰ such as stimulated Raman spectroscopy (SRS) are necessary to gain evaluable Raman spectra. Furthermore, the structure of the ionic clusters and of the separated IL phase remains unclear. A powerful tool to investigate the interactions in ionic clusters would be dielectric relaxation spectroscopy²¹ (DRS), as it probes intermolecular oscillations. Finally, the size of the IL domains in the biphasic system could be probed by small-angle X-ray scattering (SAXS).

For *in-situ* measurements, the use of a high-pressure cell in combination with synchrotron radiation²² would be feasible.

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Notes and references

‡ Dimethyl carbonate²³ (DMC) is mostly used as an electrolyte in lithium ion batteries. Furthermore, it can be used as a substrate in methylation reactions as a green substitute for methyl halogenides or dimethyl sulfate, because it is non-toxic and can be synthesized directly from methanol in an oxidative carbonylation via the EniChem²⁴-process. The quaternization reaction of tertiary amines with DMC is used to obtain halogen-free ILs, in which the anion is exchanged by strong acids to produce a wide range of ILs. This type of reaction has been patented as the Carbonate Based Ionic Liquids process²⁵ (CBILS®) by the Austrian proionic GmbH.

§ The equilibrium constant K_x is derived from a theoretically calculated K_p and the vapour pressures of substrates and product. As the vapour pressure of the produced ionic liquid MeNEt₃ MeOCOO is not measured yet, the vapour pressure of [emim][NTf₂] has been used which may introduce a great error in the K_x value.

§§ The spectrometer has a liquid nitrogen cooled MCT-detector which has been cooled down for at least one hour before measurements were started.

- 1 N. Menshutkin, *Z. Physik. Chem.*, 1890, **5**, 589; N. Menshutkin, *Z. Physik. Chem.*, 1890, **6**, 41; J.-L. M. Abboud, R. Notario, J. Bertrán and M. Solà, *Progress in Physical Organic Chemistry*, 1993, **19**; M. Solà, A. Lledós, M. Duran, J. Bertrán and J.-L. M. Abboud, *J. Am. Chem. Soc.*, 1991, **113**, 2873.
- 2 R. Plasson, A. Brandenburg, L. Jullien and H. Bersini, *J. Phys. Chem. A*, 2011, **115**, 8073.
- 3 E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, 1935, 244.
- 4 G. H. Grant and C. N. Hinshelwood, *J. Chem. Soc.*, 1933, 1351.
- 5 T. Matsui and N. Tokura, *Bull. Chem. Soc. Jpn.*, 1971, **44**, 756.
- 6 Y. Pocker, *J. Chem. Soc.*, 1957, 1279.
- 7 A. Große Böwing and A. Jess, *Green Chem.*, 2005, **7**, 230.
- 8 D. S. Firaha and Y. U. Paulechka, *Int. J. Chem. Kinet.*, 2013, **45**, 771.
- 9 R. S. Kalb, E. N. Stepurko, V. N. Emelyanenko and S. P. Verevkin, *Phys. Chem. Chem. Phys.*, 2016, **18**, 31904.
- 10 D. E. Weisshaar, G. W. Earl, E. M. Villa, J. L. Zierke, C. J. Fry, K. L. Becvar, S. K. Li and M. C. Schaefer, *Int. J. Chem. Kinet.*, 2010, **42**, 4, 221.
- 11 S. Hardy, I. M. de Wispelaere, W. Leitner and M. A. Liauw, *Analyst*, 2013, **138**, 819.
- 12 S. R. Logan, *Grundlagen der Chemischen Kinetik*, Wiley-VCH, Weinheim, 1997, 75.

- 13 B. E. Poling, J. M. Prausnitz and J. P. O'Connell, *The Properties of Gases and Liquids*, 5th ed., Mc Graw-Hill, Singapore, 2007, 8.44.
- 14 W. F. McDevit and F. A. Long, *J. Am. Chem. Soc.*, 1952, **74**, 7, 1773.
- 15 C. Yang, X. Yin and S. Ma, *J. Chem. Eng. Data*, 2012, **57**, 1, 66.
- 16 S. Chen, S. Zhang, X. Liu, J. Wang, J. Wang, K. Dong, J. Sun and B. Xu, *Phys. Chem. Chem. Phys.*, 2014, **16**, 5893.
- 17 C. E. S. Bernardes, M. E. Minas de Piedade and J. N. Canongia Lopes, *J. Phys. Chem. B*, 2011, **115**, 9, 2067
- 18 A. Gupta, S. Sharma and H. K. Kashyap, *J. Chem. Phys*, 2015, **142**, 134503.
- 19 H. Katayanagi, K. Nishikawa, H. Shimozaaki, K. Miki, P. Westh and Y. Koga, *J. Phys. Chem. B*, 2004, **108**, 19451.
- 20 D. Wei, S. Chen and Q. Liu, *Appl. Spectrosc. Rev.*, 2015, **50**, 5, 387.
- 21 A. Stoppa, J. Hunger, G. Hefter, R. Buchner, *J. Phys. Chem. B*, 2012, **116**, 25, 7509.
- 22 D. Hermida-Merino, G. Portale, P. Field, R. Wilson, S. P. Bassett, J. Jennings, M. Dellar, C. Gommès, S. M. Howdle, B. C. M. Vrolijk and W. Bras, *Rev. Sci. Instr.*, 2014, **85**, 093905.
- 23 P. Tundo and M. Selva, *Acc. Chem. Res.*, 2002, **35**, 706.
- 24 G. Paret, G. Donati and M. Giardini, EP0460735, 1991.
- 25 R. S. Kalb, W. Wesner, R. Hermann, M. Kotschan, M. Schelch and W. Staber, EP1658262B1, 2005.

Figure 1: IR spectra of the reaction mixture at 125 °C in 2D-view (left) and 3D-view (right). The colour gradient extends from blue (start of the reaction) to red (end of the reaction). An increase of the $\nu(\text{C}=\text{O})$ stretching vibration band at 1650 cm^{-1} permits the monitoring of the product formation, while the decrease of the $\nu(\text{C}=\text{O})$ band at 1750 cm^{-1} as well as the $\delta(\text{NC}_3)$ deformation vibration band at 750 cm^{-1} visualize the consumption of the substrates. Surprisingly, the methanol $\nu(\text{C}-\text{O})$ band at 1030 cm^{-1} increases after one hour reaction time.

Figure 2: Concentration time profiles of the reaction mixture at 125 °C. For NET_3 (dotted line), DMC (empty line), $\text{MeNEt}_3\text{ MeOCOO}$ (full line) and MeOH (circles, right axis). The vertical line marks the point at which the reaction rate reaches its maximum (Fig. 3).

Figure 3: Reaction rate profile of the experiment with 125 °C temperature. An increasing and a decreasing section can be observed, separated by a bend (vertical line).

Figure 4: Reaction rate constant versus product concentration with linear fits for the sections before and after the bend. The vertical line marks the critical concentration c_{crit} . A positive curvature can be recognized especially in the section after the bend.

Figure 5: Logarithm of reaction rate constant versus product concentration with linear fits for the sections before and after the bend. The vertical line marks the critical concentration c_{crit} .

Figure 6: Logarithm of reaction rate constant versus averaged Hildebrand parameter. The beginning of the reaction corresponds to the points bottom left, the end of the reaction corresponds to the points top right. The vertical line marks the phase change from solvated ion clusters to a biphasic system.