

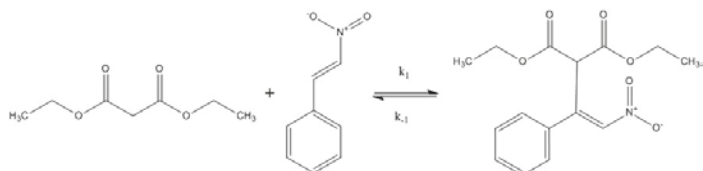
## Influence of High Pressure and of Solvent on a Michael Addition

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The thermodynamic variable pressure is an important influencing factor for chemical reactions. Even though liquid phases are generally assumed to be incompressible, pressure can have a strong influence on reaction kinetics and could therefore be used to optimize production processes. In this work, the pressure effects on reaction kinetics and reaction equilibrium of a Michael addition were investigated. An activity-based kinetic modeling was used to predict the effect of pressure and of solvent on reaction kinetics and reaction equilibrium using PC-SAFT, which allows predicting molecular interactions as function of pressure and of reaction solvent. Prediction results were in good agreement with experimental data for different reaction solvents for the first time even at pressures in the kilo bar range.

Different properties can be varied (temperature, concentration, pressure, solvent) to optimize a chemical reaction. Even in liquid-phase reactions, pressure influences both, kinetics and equilibrium of a reaction. Pressure effects on kinetics are characterized by the activation volume  $\Delta v^\ddagger$ . A negative activation volume  $\Delta v^\ddagger$  indicates that the reaction rate will increase with increasing pressure. The class of Michael additions is known to have negative activation volumes of  $-40 \text{ cm}^3 \text{ mol}^{-1} < \Delta v^\ddagger < -5 \text{ cm}^3 \text{ mol}^{-1}$ . Hence, strong dependence of the reaction rate on pressure is expected for reactions of this class.

In this work, the Michael addition of diethyl malonate and nitrostyrene to diethyl nitro-phenylethyl malonate (DENPEM) was investigated.



This reaction was analyzed experimentally in toluene, n-hexane and dichloromethane (DCM) at 25 °C at 1 bar and at 4400 bar. Experimental results are shown in Figure 1. It can be seen that an increase in pressure drastically increases the reaction rate. Additionally, the reaction was found to be faster in n-hexane and slower in DCM.

The kinetics of this reaction was described by an activity-based kinetic model. The experimental concentration-over-time plots for the reaction in toluene at 1 bar as well as 4400 bar were used to fit the pressure-dependent kinetic parameters  $k_1$  and  $k_{(-1)}$  that are used in the kinetic model. Further, PC-SAFT predicted activities of each reacting agent in the reaction system were required.

PC-SAFT parameters for the reacting agents were fitted to vapor-pressure data and to new experimental density data up to 500 bar. These parameters allowed predicting the pressure and solvent influence on the Michael addition.

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The PC-SAFT prediction results are also shown in Figure 1. It can be seen that PC-SAFT correctly predicts an accelerated reaction rate in n-hexane and a slower reaction rate in DCM. These predictions are validated at 1 bar as well as at 4400 bar. The activation volume was calculated to be  $\Delta v^\ddagger = -24 \text{ cm}^3 \text{ mol}^{-1}$ , which is in the expected range for Michael additions.

A solvent screening was performed to predict product yield in different solvents. PC-SAFT predictions suggested highest yield in n-hexane and lowest yield in DCM. These predictions were also validated by the experimental data.

PC-SAFT is a thermodynamic model that accounts for pressure effects. In this work PC-SAFT predictions were for the first time performed in the kilo bar range resulting in an almost quantitative agreement with experimental data.

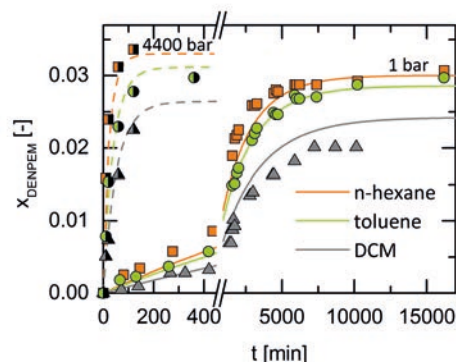


Figure 1: Concentration-over-time plot for the addition of nitrostyrene and diethyl malonate to DENPEM at 25°C. Symbols: experimental data, full lines: PC-SAFT modeling results at 1 bar, dashed lines: PC-SAFT modeling results at 4400 bar.

### Publications:

M. Knierbein, L. Bittorf, T. Weinbender, O. Reiser, R. Siewert, S.P. Verevkin, C. Held, G. Sadowski; High-Pressure Influence on an Organocatalytic Reaction, Presentation at 30th ESAT 2018, 11 June 2018, Prague.

M. Knierbein, L. Bittorf, T. Weinbender, O. Reiser, C. Held, G. Sadowski; Vorhersage des Hochdruck- und Lösungsmiteleinflusses auf das Reaktionsgleichgewicht einer organokatalytischen Reaktion, Presentation at, Thermodynamik-Kolloquium 2018, 27 September 2018, Kassel.