Kinetic study of the aqueous Kolbe-Schmitt reaction enabled by automated reaction analysis

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1. Introduction

The Kolbe-Schmitt reaction is the standard industrial method for converting anhydrous salts of phenols into phenolic acids under pressurised CO_2 and elevated temperatures. Compared to monohydric phenol, resorcinol is more electron-rich and undergoes carboxylation in aqueous systems with bicarbonate salts at atmospheric pressure to afford 2,4-dihydroxybenzoic acid. The utilisation of CO_2 as a C1 building block offers excellent atom economy. Furthermore, process intensification strategies have been explored to enhance productivity. However, previous mechanistic and kinetic studies have yielded only empirical rate equations and have drawn contradictory conclusions regarding the rate-determining step and the order in CO_2.[1,2] A detailed microkinetic study of the aqueous Kolbe-Schmitt reaction is therefore needed.

2. Methodology

In this project, the kinetics of the aqueous Kolbe-Schmitt reaction were investigated using in-situ IR spectroscopy, HPLC with on-line sampling, gas evolution monitoring, and pH measurements. Unattended reagent addition and sampling were implemented in automated (pressurised) reactors to reduce human error. A custom Python package was developed to enable holistic analysis across all monitored parameters as well as global kinetic model fitting. For the first time, comprehensive reaction profiles revealed the importance of the complex equilibrium between multiple dissociated species during the reaction. A step-by-step experimental approach was employed to independently elucidate the kinetics of mass transfer of CO_2, dissociations, decarboxylation of products, and, finally, the overall aqueous Kolbe-Schmitt reaction.

Due to the complicated reaction network involving multiple equilibria of more than 10 different species, including the carbonate equilibria, common kinetic analysis tools such as RPKA and VTNA are less effective for the aqueous Kolbe-Schmitt reaction. In the present study, we adopted a hybrid data-driven approach for microkinetic modelling, combining previously reported kinetic model for the carbonate equilibria and computer-generated reaction network for the reversible carboxylation step. The most plausible reaction mechanism was selected based on Akaike information criterion of the candidate models.

3. Results and conclusions

This study has revealed the intrinsic kinetic parameters and mass transfer effects and elaborated mechanistic understanding of the aqueous Kolbe-Schmitt reaction of resorcinol. Based on these results, further developments in highly efficient flow reactors and sustainable large-scale production of high-value phenolic acids will be accelerated. Additionally, the automated experimental and data analysis workflow will support future data-rich kinetic studies.

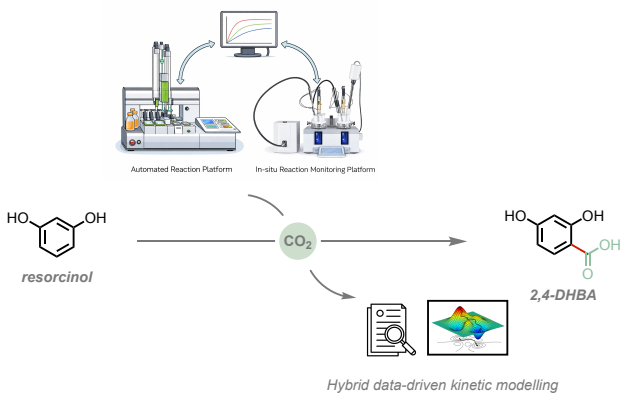

Fig. 1: Graphical abstract illustrating the aqueous Kolbe-Schmitt reaction and the automated kinetic analysis approach.

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References

1 V. Barbarossa, F. Barzagli, F. Mani, S. Lai and G. Vanga, *J. CO2 Util.*, 2015, **10**, 50–59.
2 A.-L. Dessimoz, C. Berguerand, A. Renken and L. Kiwi-Minsker, *Chem. Eng. J.*, 2012, **200–202**, 738–747.