

Charline Berguerand, Anne-Laure Dessimoz and Lioubov Kiwi-Minsker*

Intensification of slow reversible chemical transformation: carboxylation of resorcinol as a case study

Abstract: Conjugated kinetic and thermodynamic modeling is suggested as a suitable approach to identify a novel process window (NPW) for the intensification of slow reversible reactions. The aqueous Kolbe-Schmitt synthesis of β -resorcylic acid is taken as a model. The potential of operating at high pressure (P) and temperature (T) is evaluated in order to reduce the characteristic reaction time (t_r) and increase the specific productivity. For the first time, a reliable kinetic model for this reaction is derived from batch experiments. Based on this model, an NPW of P=10 bars, T=453 K is determined for a continuous reactor operated at a residence time of 28 s. It is predicted that the specific productivity can be increased by a factor of 100 with a 4.2 times less concentrated KHCO_3 solution, as compared to a conventional batch process, if the reaction is kinetically controlled. The model prediction is experimentally validated with a continuously operated milli-reactor equipped by SMXS mixer elements (Sulzer Chemtech, Switzerland) ensuring a fast mixing (characteristic mixing time $\sim 4.10^{-2}$ s). The milli-reactor renders exclusively β -resorcylic acid (selectivity 100%) and confirms process intensification (PI) of two orders of magnitude as compared to conventional batch operation.

Keywords: β -resorcylic acid; carbon dioxide fixation; kinetics; new operating window; process intensification.

*Corresponding author: Lioubov Kiwi-Minsker, Group of Catalytic Reaction Engineering, Ecole Polytechnique Fédérale de Lausanne (GGRC-ISIC-EPFL), Lausanne, Switzerland, e-mail: lioubov.kiwi-minsker@epfl.ch

Charline Berguerand and Anne-Laure Dessimoz: Group of Catalytic Reaction Engineering, Ecole Polytechnique Fédérale de Lausanne (GGRC-ISIC-EPFL), Lausanne, Switzerland

1 Introduction

In the context of green chemistry, process intensification (PI) has become a vibrating area of chemical engineering. PI is a general approach that aims at development of

substantially smaller, cleaner and more energy efficient processes [1–3]. As the PI approach is highly sensitive to the type of chemical transformations, it is helpful to classify them according to the characteristic reaction time (t_r) under standard industrial conditions (T<423 K; P<10 bar) [4–6].

$$t_r = \frac{C_{1,0}}{-R_{1,0}} \quad (1)$$

where $C_{1,0}$ =initial concentration, $R_{1,0}$ =initial transformation rate.

Based on this number, a general PI strategy can be proposed. Fast ($t_r < 1$ s) and exothermic reactions are often performed in conventional reactors at low temperatures (T) to avoid runaway and selectivity losses resulting in low specific productivities [6]. Continuously operated micro- and milli-reactors offer high mass and heat transfer performances (Figure 1) being suitable for intensification of these transformations [7]. Many examples of successful applications of microreactors with increased specific performance for fast and exothermic reactions have already been reported [8, 9].

In order to attain PI of slow chemical transformations ($t_r > 100$ s), the reactions are carried out under high pressures (P), high T and/or high concentrations (novel process windows, NPW) to drastically accelerate the intrinsic kinetics. Micro/milli-reactors are also suitable tools to study reactions under harsh conditions, due to excellent control of process parameters (T, P and residence time) and an inherent safety (Figure 1) [5, 10–14]. For irreversible reactions, the specific productivity will always increase at high P and T, a question of effective mass and heat transport, material stability and/or selectivity issues. However, in the case of reversible reactions, this trivial increase will not always lead to PI, since the equilibrium conversion may be affected. Therefore, operating conditions should be optimized in view of the reaction kinetics and thermodynamics.

The aqueous Kolbe-Schmitt synthesis of β -resorcylic acid (Figure 2) was chosen as a model of slow reversible transformation. The aromatic hydroxycarboxylic acids

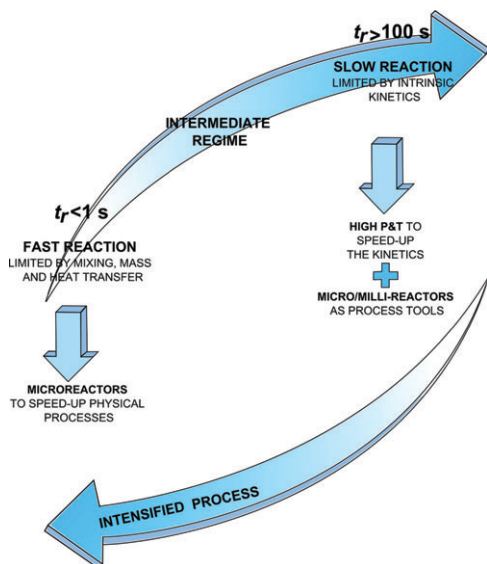


Figure 1 General strategy for process intensification (PI) of slow reactions.

are used in the preparation of pharmaceutical, cosmetic products and in the production of dyes and plastics [15]. β -resorcylic acid (**2**) is industrially produced by the reaction of resorcinol (**1**) with aqueous KHCO_3 in the presence of CO_2 . γ -resorcylic acid (**3**) is formed as an undesired by-product. In a batch reactor under reflux at 373 K and 1 bar, a reaction time of 2 h is needed to reach 60% equilibrium conversion with concentrated aqueous solutions ($C_{1,0}=1$ M and $C_{\text{KHCO}_3,0}=5$ M) [16, 17]. Taking into account a dead time of about 2 h needed for batch operation, the specific productivity is extremely low, being $0.0025 \text{ mol l}^{-1} \text{ min}^{-1}$.

Currently, there is an interest to develop a more efficient synthesis in terms of higher production rate of the acid (**2**), with reduced consumption of KHCO_3 to diminish an environmental impact. Therefore, an NPW (high P and T) was suggested in addition to the change from batch to continuous operation.

Hessel et al. [18] and Krtschil et al. [19] investigated the aqueous Kolbe-Schmitt synthesis using continuously operated capillary reactors (393–543 K and 35–40

bar with $C_{1,0}=0.8$ M and $C_{\text{KHCO}_3,0}=2.4$ M), but the specific performance was not optimized. In the present study, a general approach toward the optimal NPW is proposed and applied for the synthesis of β -resorcylic acid from resorcinol, as a model of slow reversible transformation. The feasibility of the proposed concept has been proved experimentally using a continuous milli-reactor equipped by SMXS mixer elements from Sulzer Chemtech (Switzerland) to ensure a fast mixing (characteristic mixing time $\sim 4 \cdot 10^{-2}$ s). This reactor type is suitable for industrial scale production and allows PI by a factor of 100.

2 Experimental

2.1 Materials

Resorcinol (Acros, Belgium, 98%) and KHCO_3 (Applichem, Germany, pure Ph. Eur. USP) were used, as supplied without further purification. The solutions were prepared as required with deionized water. Diluted solutions of resorcinol (Acros, Belgium, 98%), β -resorcylic acid (VWR, USA, for synthesis) and γ -resorcylic acid (VWR, USA, for synthesis) in hydrochloric acid 0.1 M [Titrisol or dilution of HCl 25% Merck (Switzerland), for analysis] were used for the calibration of the UV-Vis spectrophotometer.

2.2 Continuous milli-reactor

To demonstrate the feasibility of the concept, the reaction was carried out under high P and T in a milli-reactor containing static mixers (Figure 3). In the present study, the SMXS and SMXL mixer types were used, as they enable efficient mixing and heat transfer under laminar flow [20, 21].

The milli-plant is composed of two main parts. The first part was designed to achieve a rapid heating and mixing of the reaction mixture at the reactor inlet. It is made of 20 jacketed SMXS mixer elements (Sulzer

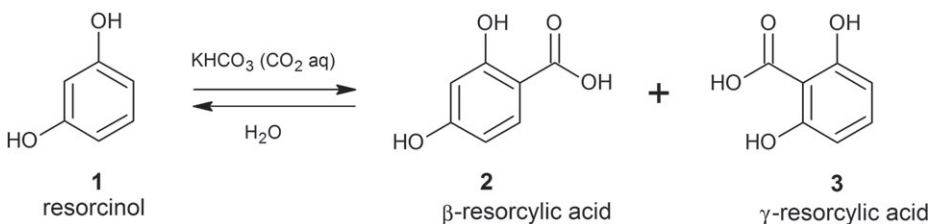


Figure 2 Reaction scheme for the synthesis of β -resorcylic acid (2,4-dihydroxybenzoic acid) from resorcinol.

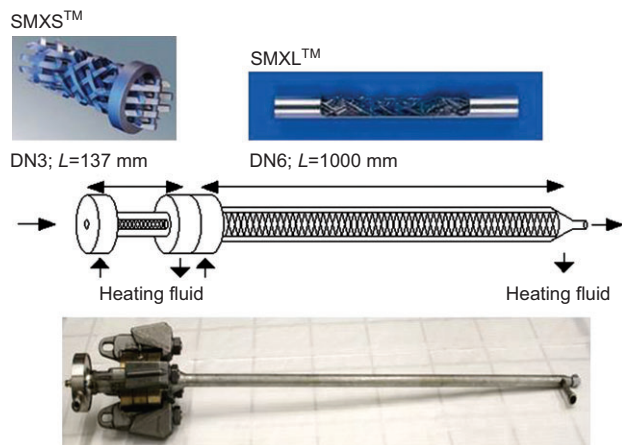


Figure 3 Milli-reactor containing static mixers.

Chemtech, Switzerland) within a tube of 3 mm diameter, for a total length of 137 mm. The second part consists of jacketed SMXL mixer elements (Sulzer Chemtech, Switzerland) within a tube of 6 mm diameter. This part has a length of 1000 mm and provides a good mixing under laminar flow (characteristic mixing time 0.3 s) and a sufficient residence time to complete the reaction. The connection of the different elements is insured by clamping flanges (Franco-Montan, France).

As the reaction is very slow under ambient conditions, premixed reactant solutions were pumped into the milli-reactor with an HPLC pump (Waters 510, USA). The inlet concentrations of resorcinol and KHCO_3 were fixed at 0.4 M and 1.2 M, respectively. Oil was circulating from an oil bath (Haake N3 digital, Germany) into the double mantel and maintained at a constant T of 433 K. After the reaction section, the mixture was cooled down to stop the reaction (quenching section). A P of 21 bar was maintained by a fine metering valve (Swagelok, USA), to avoid solvent and carbon dioxide evaporation from the reaction mixture, in both the reaction and quenching section. In the product separator, P was released and the reaction mixture was collected. The samples were diluted in HCl 0.1 M and analyzed by UV-Vis spectrophotometry.

2.3 Analysis

The quantification of resorcinol, β -resorcylic acid and γ -resorcylic was based on absorption measurements at three wavelengths: 275, 295 and 314 nm [22]. The absorbances were recorded with a UV-Vis spectrophotometer (Perkin Elmer Lambda 20, USA) against a blank solution made of HCl 0.1 M.

After analysis, the concentrations of the three compounds were calculated by solving the following linear equation system.

$$\begin{aligned} Abs_{275} &= 0.02 + 1662 \cdot C_1 + 3158 \cdot C_2 + 464 \cdot C_3 \\ Abs_{295} &= 0.02 + 5083 \cdot C_2 + 2018 \cdot C_3 \\ Abs_{314} &= 0.01 + 915 \cdot C_2 + 2830 \cdot C_3 \end{aligned} \quad (2)$$

The mean error of the method is less than $\pm 8\%$ [23]. The main advantage of this method is that the three compounds can be quantified quickly, simultaneously and quantitatively in the reaction mixture.

2.4 Data treatment

The concentrations of resorcinol obtained with the equation system [Eq. (2)] were used to calculate the conversion X (constant fluid density):

$$X = \frac{C_{1,0} - C_1}{C_{1,0}} \quad (3)$$

where $C_{1,0}$ is the initial concentration and C_1 the concentration at time t.

The methodology applied for PI is based on the optimization of the specific performance $L_{P,V}$ of a continuously operated reactor:

$$L_{P,V} = \frac{C_{1,0} \cdot X}{\tau} \quad (S=1) \quad (4)$$

where X=conversion, τ =residence time, S=selectivity

3 Results and discussion

3.1 Determination of the optimal new process window

Recently, we performed a detailed kinetic and thermodynamic study of the carboxylation of resorcinol in aqueous solutions using a micro-plant [23]. In this reaction, resorcinol (1) and carbon dioxide are the two reactants where carbon dioxide is formed in solution by dissociation of KHCO_3 . We established that the partial P of carbon dioxide has no effect on the reaction behavior for concentrated KHCO_3 solutions ($C_{\text{KHCO}_3,0}/C_{1,0} > 1$). It was also shown that the formation of γ -resorcylic acid (3) is negligible at short residence times, $\tau < 30$ s. Based on these experimental

results, for the first time a reliable kinetic and thermodynamic model has been proposed:



$$\begin{aligned} r_1 &= k_1 \cdot C_1 & k_1 &= f(C_{\text{KHCO}_3,0}, T) \\ r_2 &= k_2 \cdot C_2 & k_2 &= f(C_{\text{KHCO}_3,0}, T) \end{aligned} \quad (6)$$

where r is the reaction rate, k is the kinetic constant and T is the reaction temperature.

Using this model, the residence time τ needed to reach a given conversion which can be calculated. It is important to note that in this case, the maximum conversion is limited by the equilibrium. Moreover, as the reaction is exothermic, the equilibrium conversion decreases with an increase of the T while the reaction rate increases.

Figure 4 shows the evolution of the specific productivity as a function of T for a conversion of 30%. The star indicates the value obtained at conventional 373 K. As can be seen, the specific productivity goes through a maximum which corresponds to the optimal process window for the chosen diluted conditions. Under these optimal conditions ($T=450$ K, $P=10$ bar, $t_r=8$ s and $\tau=29$ s), the specific productivity increases 100-fold. At the same time, the consumption of KHCO_3 is decreased 4-fold, as compared to the industrial protocol that used at least 5 M of KHCO_3 .

The optimal conversion for a chemical process can only be determined, based on a detailed economic analysis being out of the scope of this study. Since the equilibrium conversion decreases with T , the same procedure of T optimization has been applied for lower equilibrium conversions as presented in Figure 5. As can be seen,

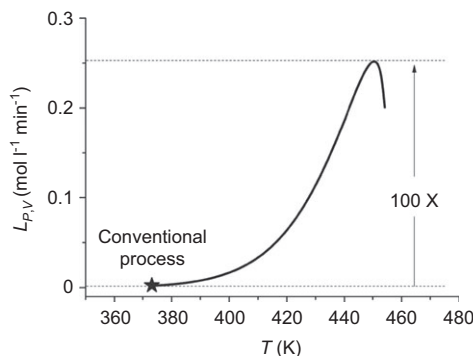


Figure 4 Specific performance $L_{p,v}$ as a function of the temperature (T) representative for the determination of the optimal novel process window at $P=10$ bar, $C_{1,0}=0.4$ M, $C_{\text{KHCO}_3,0}=1.2$ M and $X=30\%$. The conventional batch process is represented by the star.

the intensification factor reaches 100,000 for a conversion equal to 10%. Even more impressive PI factors can be attained (up to 10^7) keeping the concentrations as high as in the conventional industrial process. The prediction could be extended for concentrated solutions, which can be seen in Figure 6, showing the PI factor up to $9 \cdot 10^6$ at conversion of 10% with $C_{1,0}=1$ M and $C_{\text{KHCO}_3,0}=5$ M. It is worth noting that this prediction is based on increased intrinsic kinetics only. These fast reaction transformations could not be easily attained even using micro-reaction equipment, due to heat and mass transfer limitations. Thus, at

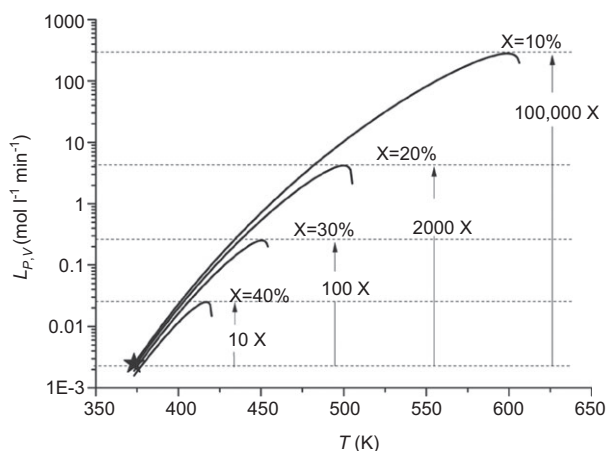


Figure 5 Specific performance $L_{p,v}$ as a function of the temperature representative for the determination of the optimal novel process window at $P=10$ bar, $C_{1,0}=0.4$ M, $C_{\text{KHCO}_3,0}=1.2$ M for different equilibrium conversions. The conventional batch process is represented by the star.

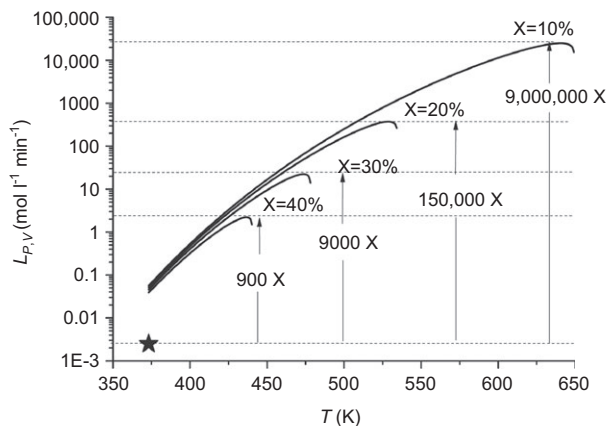


Figure 6 Specific performance $L_{p,v}$ as a function of the temperature representative for the determination of the optimal novel process window for different equilibrium conversions at $P=10$ bar, for concentrated solutions $C_{1,0}=1$ M and $C_{\text{KHCO}_3,0}=5$ M. The conventional batch process is represented by the star.

530 K, the characteristic reaction time becomes $t_r=0.16$ s, and at 630 K only $t_r=0.004$ s. In comparison, under standard industrial conditions $t_r=1000$ s.

3.2 Validation of the PI prediction in the milli-reactor with static mixers

In order to validate the predicted PI, a milli-reactor equipped with static mixer elements was used (for details see the experimental section). The experimental conditions were set at 433 K, P of 21 bar and the equilibrium conversion of 35%. Under these conditions, the characteristic reaction time of $t_r=8$ s is more than one order of magnitude higher of characteristic mixing time (0.04 s), ensuring efficient mixing in the first compartment of the reactor. The adiabatic T rise has been estimated as only a few degrees since a relatively low concentration of reactants was used. Therefore, no issue of heat removal has to be considered.

The simulations were performed applying mass and energy balances corresponding to a plug flow reactor. For static mixers, the assumption of an ideal plug flow reactor is justified by the presence of metal baffles, which produce an intense radial mixing.

The mass balance can be expressed as a function of the reactor length (z) as follows [24]:

$$\frac{dF_i}{dz} = S \cdot R_i \quad (7)$$

where F_i is the molar flow rate of compound i , S the reactor section and R_i represents the transformation rate of compound i .

Assuming a constant T over the section of the reactor, a heat balance on a differential volume element can be performed [24]:

$$\frac{dT}{dz} = \frac{S \cdot \sum_j r_j \cdot (-\Delta H_j)}{Q_0 \cdot \rho \cdot \bar{c}_p} + \frac{S \cdot U}{Q_0 \cdot \rho \cdot \bar{c}_p} \cdot \frac{4}{d_t} \cdot (T_f - T) \quad (8)$$

where r_j is the rate of reaction j , ΔH_j the enthalpy of reaction j , Q_0 the inlet volumetric flow rate, ρ the fluid density, \bar{c}_p the specific heat, d_t the tube diameter, T_f the T of the external heat exchange fluid, T the mean T of the reaction mixture and U corresponds to the overall heat transfer coefficient.

In the present study, the external heat transfer and the wall resistance were neglected. Moreover, the internal heat transfer coefficient (h) was estimated using

correlations based on the dimensionless Nusselt number (Nu) [25]:

$$U = h = \frac{Nu \cdot \lambda}{d_t} \quad (9)$$

$$Nu = 5A \cdot (Re_D \cdot Pr)^a \cdot \left(\frac{Pr}{Pr_w} \right)^b \approx A \cdot (Re_D \cdot Pr)^a \quad (10)$$

The corresponding definitions for the Reynolds number (Re) and Prandlt number (Pr) are the following:

$$Re_D = \frac{\rho \cdot u \cdot D}{\mu}, \quad Pr = \frac{\mu \cdot c_p}{\lambda} \quad (11)$$

Re is calculated based on the normalized diameter (D). The Pr_w is the Pr referred to the wall T. The parameters for the equation corresponding to each static mixer are recapitulated in Table 1.

The estimation of the kinetic constants was done based on the following empirical kinetic model [23]:

$$\ln(k_1) = 23.98 + 0.58 \cdot C_{\text{KHCO}_3,0} - 12'603.74 \cdot \frac{1}{T} \quad (12)$$

$$\ln(k_2) = 30.30 + 0.51 \cdot C_{\text{KHCO}_3,0} - 15'053.70 \cdot \frac{1}{T}$$

By applying this model, the results of the simulations were compared with a set of experimental data obtained at 433 K and 21 bar (Figure 7). Even if the optimal T is 450 K, the experiments at 433 K validate the idea where a residence time in the range of <1 min could be attained with a milli-reactor.

A threshold P (21 bar) has to be applied to avoid solvent and CO_2 evaporation from the reaction mixture. The deviation between the experimental results and the simulation is in the order of 15%. The agreement is satisfactory, considering the simplifications that were done in the simulation model. These experiments prove the feasibility of proposed concepts and shows that the milli-scale reactor is a suitable design for industrial scale production.

Table 1 Parameters for the heat transfer correlations [6].

| | A | a | b |
|------|------|------|------|
| SMX | 2.6 | 0.35 | 0.14 |
| SMXL | 0.98 | 0.38 | 0.14 |

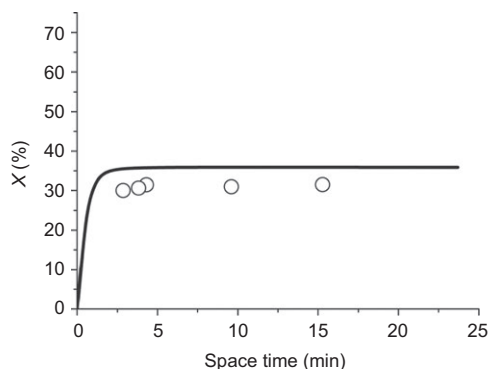


Figure 7 Conversion as a function of time for 21 bar at 433 K, $C_{1,0}=0.4$ M, $C_{\text{KHCO}_3,0}=1.2$ M for equilibrium conversion of 35%; the simulation (solid dark line) results are compared with the experimental data (symbols).

4 Conclusions

In summary, PI of slow ($t_r > 100$ s under standard industrial conditions) reversible chemical transformations can be

achieved by performing them at higher P and T in NPW. To reach the maximum specific productivity for the reversible reaction, a detailed kinetic and thermodynamic study, conjugated with modeling, has to be performed and the NPW has to be optimized.

This PI approach has a general nature and is validated using the carboxylation of resorcinol as a model reaction. PI factors up to 100 are experimentally demonstrated as compared to a conventional batch operation and the process was also more environmentally benign, due to a lower amount of KHCO_3 being required.

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Charline Berguerand obtained her MSc degree in Chemical and Biotechnological Engineering from the Swiss Federal Institute of Technology in Lausanne (EPFL) in 2010. She is currently a PhD student in the Group of Catalytic Reaction Engineering at EPFL. Her research activities are focused on the preparation, characterization and application of polymer stabilized metal nanoparticles as effective catalysts for liquid phase hydrogenation and the combination of these catalysts with the microreactors aiming at process intensification.



Dr. Lioubov Kiwi-Minsker is a Professor at the Swiss Federal Institute of Technology in Lausanne (EPFL) where she has been working since 1994. She is actually a head of the group of Catalytic Reaction Engineering at EPFL. Her research interests are in the field of novel catalytic materials and microreactor technology for process intensification. She is a co-author of more than 200 peer reviewed publications, six book contributions and seven patents (H-index=33).



Dr. Anne-Laure Dessimoz graduated from the Swiss Federal Institute of Technology in Lausanne (EPFL) with an MSc degree in Chemical Engineering and continued her PhD studies in the Group of Catalytic Reaction Engineering, obtaining her PhD degree in 2011. Her research work focused on the intensification of industrial chemical processes using microreactors and new operating windows. She is a LEAN process engineer at Syngenta Crop Protection AG, Monthey, Switzerland.