Gain insight into sodium benzoate synthesis using FTIR based in-line reaction analysis system

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The main objective of this study was to develop overall kinetic model of sodium benzoate synthesis, from ethyl benzoate and sodium hydroxide. For this purpose a series of experiments were performed in an automated RC1 reactor system (Mettler Toledo). The ethyl benzoate and sodium benzoate molar concentration profiles were indirectly real-time monitored using FTIR based ReactIR^{TM} iC10 analysis system, (Mettler Toledo). The heterogeneous reaction mixture was initially homogenized. The proposed second order kinetic model gives very good prediction of the experimental data. Obtained results are in agreement with previously published data.

Introduction

Meeting the global challenges in knowledge-based product engineering requires a step change towards sustainable design and development of real-time continuously controlled and fully flexible efficient processes that will ensure targeted and tailored products. Consequently, to fulfil the rigorous demands of process analytical technology (PAT), it is necessary to include intelligent in-line, on-line or at-line analyzing control methods in those processes. Among others, Fourier Transform Infrared Spectroscopy (FTIR) is nowadays perhaps one of the most powerful, proven and widely used PAT tools (Littler, 2008; Lin et al., 2006).

Benzoic acid and its salts are widely used as chemical additives, preservatives and flavouring agents especially in food, cosmetic and pharmaceutical industries (Dudley et al., 2008; Ankudovich et al., 2008). Furthermore, the sodium benzoate is also used as a corrosion inhibitor (e.g., in technical systems as an additive to automotive engine antifreeze coolants) (Bozzini et al., 2007). Because both chemicals are essential ingredients in many commercial products, it is expected that their global demand will be increased in the future. Therefore, the innovations in benzoic acid and sodium benzoate production are the key issue.

The synthesis pathways of sodium benzoate are well known and frequently described in the literature. One of them is a model reaction of ethyl benzoate saponification with aqueous sodium hydroxide solution (Mouhab et al., 2008). The kinetic parameters of above reaction have already been published (Moseley and Ohang, 1997; Dudley et al., 2008; Ankudovich et al., 2008). However, the analytic method (traditional titrimetric technique), which has been used for the dynamic monitoring of the concentration profiles so far, is time consuming, less accurate and does not allow real-time and *in-situ/operando* analysis of the reaction mixture. In order to improve the analytics

accuracy and to enable the dynamic in-line sodium benzoate synthesis monitoring, the novel analytic strategy should be used.

The main objective of the present study was to develop overall kinetic model of sodium benzoate synthesis using FTIR based in-line reaction analysis system. This exothermic reaction is normally carried out in a heterogeneous liquid-liquid reaction medium (Moseley and Ohang, 1997; Dudley et al., 2008; Ankudovich et al., 2008). However, the heterogeneous system prevents, especially at non-ideal mixing regime, optimal real-time and *in-situ* FTIR monitoring. Therefore, the two-phase reaction medium was initially homogenized by adding ethanol as a cosolvent. For kinetic study of sodium benzoate synthesis, a series of experiments were performed in RC1 reactor system.

Materials and methods

1.1 Kinetic model

In order to gain fundamental insight into sodium benzoate synthesis using FTIR based in-line analysis system, the hydrolysis of ethyl benzoate in homogeneous medium was used in our study. The reaction mechanism is described in Fig. 1.
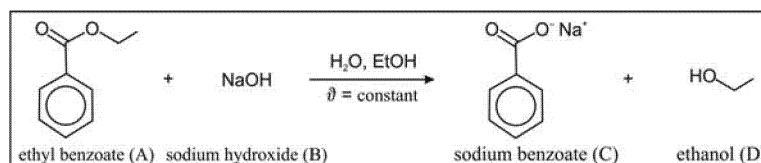

Fig. 1: Reaction mechanism of ethyl benzoate saponification with aqueous sodium hydroxide solution.

Considering equimolar mixture of ethyl benzoate (A) and sodium hydroxide (B), the consumption rate of A, $-r_A$ and production rate of sodium benzoate (C), r_C, in batch reactor can be described by a simple second order kinetics (Levenspiel, 1999):

$$-r_A = -\frac{dc_A}{dt} = kc_A c_B = kc_A^2 \qquad (1)$$

$$r_C = -\frac{dc_C}{dt} = kc_A c_B = kc_A^2 \qquad (2)$$

where k, reaction rate constant, t, reaction time, and c, molar concentration. According to the chemical reaction engineering principles, the k value among other process parameters depends only upon reaction media temperature, ϑ. The relationship between k and ϑ is mathematically usually expressed with Arrhenius equation:

$$k = k_0 \exp^{-\frac{E_a}{R(\vartheta + 273.15)}} \qquad (3)$$

where k_0, pre-exponential factor, E_a, activation energy and R, ideal gas constant.

1.2 Equipment and chemicals

All experiments were performed in an automated, computer controlled reactor (Mettler Toledo, model: RC1 classic). RC1 is a double walled glass-made laboratory batch reactor with active volume, $V = 2$ L. The reactor was equipped with FTIR based ReactIR™ iC10 analysis system coupled with a flexible Silver Halide (AgX) FiberConduit™ and 6.3 mm DiComp™ probe (Mettler Toledo, model: 910–7002), which was used for the real time monitoring of ethyl benzoate and sodium benzoate molar concentration profiles. The spectral range covered with the probe shifts from wavenumber, $v = 650$ cm^{-1} to $v = 2\,000$ cm^{-1}. Each spectrum represents 256 co-added

scans measured at resolution, $\Delta v = 8$ cm^{-1} with the Happ-Genzel apodization. In the treatment of absorbance data, the validity of the Beer-Lambert law is assumed.

All chemicals (ethyl benzoate (purity, $w \geq 99$ %; Fluka), ethanol ($w \approx 96$ %; Sigma-Aldrich), sodium benzoate ($w \geq 99.5$ %; Fluka) and sodium hydroxide ($w \geq 99$ %; Riedel-de-Haën) are commercially available and were used as received without further purification.

1.3 Regresion analysis

The parameters of the proposed overall kinetic model of sodium benzoate synthesis (k, k_0, E_a) were estimated by fitting differential equations (1), (2) and Arrhenius equation (Eq.(3)) to the experimental data. The goodness of regression was evaluated with standard errors of parameters, $S.E.$, coefficients of the variation, CV and adjusted coefficient of the determination, R_{adj}^2. Statistical indicators SE and R_{adj}^2 were directly obtained from the curve fitting software (Scientist®), meanwhile CV was calculated as quotient between $S.E.$ and parameter's estimation multiplied by 100.

Experimental

A set of eight experiments were carried out in RC1 reactor system at different rotational frequencies of the stirrer, f (50, 80 and 110 min^{-1}) and reaction media temperatures, ϑ (18, 22, 30, 34 and 38 °C). Individual experiment was started by charging the RC1 reactor by ethyl benzoate. It is almost impossible to perform the FTIR based analysis in heterogeneous system, therefore ethanol was added to ethyl benzoate as a cosolvent. Thereupon, the solution was stirred at defined f and heated up to the desired ϑ. After approximately 30 minutes, the aqueous sodium hydroxide solution was added. The initial molar concentration of ethyl benzoate and sodium hydroxide in the homogenous reaction mixture was, $c = 1.15$ mol L^{-1}. The progress of the sodium benzoate synthesis was monitored using the FTIR based ReactIR™ iC10 analysis system. The ReactIR iC software was used to control spectrometer and to collect the spectra every 2 minutes.

Results and discussion

The potential influence of rotational frequency of the stirrer on reaction rate constant was analyzed first. Three experiments were performed at different values of f and at constant temperature, $\vartheta = 30$ °C. The FTIR spectra collected during one selected experiment are presented in Fig. 2.
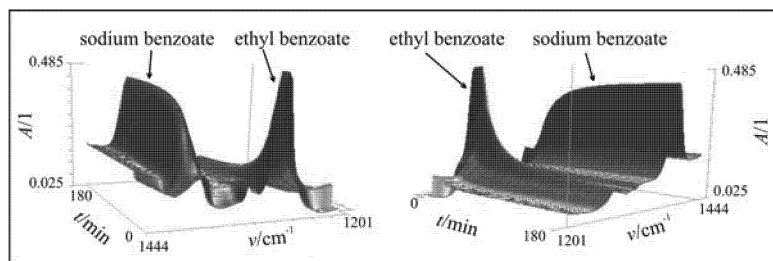

Fig. 2: Waterfall plots of FTIR spectra during the sodium benzoate synthesis at temperature, $\vartheta = 30$ °C and rotational frequency of stirrer, $f = 50$ min^{-1}.

The intensity of ethyl benzoate peak (absorbance, A) at wavenumber range, $v = (1268–1292)$ cm^{-1} decreases over reaction time, while the one of sodium benzoate at wavenumber range, $v = (1372–1396)$ cm^{-1} increases. Afterwards, the FTIR spectra were

transformed to the real-time molar concentration profiles of ethyl benzoate and sodium benzoate using simple peak areas treatment of the corresponding peaks. Furthermore, those profiles were simultaneously fitted by Eqs. (1) and (2). Graphic comparison of experimental and model-based values of ethyl and sodium benzoate molar concentrations in relation to reaction time at different rotational frequencies of the stirrer and at constant temperature is presented in Fig. 3. There is practically no difference in ethyl benzoate and sodium benzoate concentration profiles regarding the rotational frequency of the stirrer. The graphic analysis has shown very good agreement between experimental data and those estimated with the proposed kinetic model of sodium benzoate synthesis.
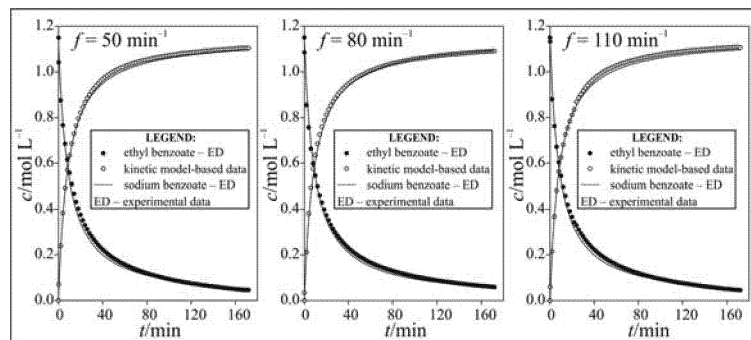

Fig. 3: Experimental and second order kinetic model-based values of ethyl benzoate and sodium benzoate molar concentrations in relation to reaction time.

In Table 1, the estimated reaction rate constants (k) with appurtenant statistical indicators, obtained from fitting the proposed second order kinetic model of sodium benzoate synthesis to the experimental data, are reported. A very significant feature of those parametric results is that all three k values, proposed by kinetic model, are almost the same, which is in accordance with the theory. Precisely, the variation of estimated k values at different rotational frequencies of the stirrer is within the range $\pm$ 4.1 % ($k = (0.10128 \pm 0.00411)$ L mol^{-1} min^{-1}). The predictive efficiency of proposed kinetic model of sodium benzoate synthesis was confirmed with relatively high values of R_{adj}^2.

Table 1: Parametric results from fitting the proposed kinetic model to experimental data (different f and constant ϑ).

ϑ/°C	f/min^{-1}	k/L mol^{-1} min^{-1}	$S.E.$/L mol^{-1} min^{-1}	CV/%	R_{adj}^2/1
	50	0.10314	0.00094	0.91	0.9986
30	80	0.09717	0.00072	0.74	0.9990
	110	0.10355	0.00081	0.78	0.9988

In the second part of the study, the influence of reaction media temperature on k value was analyzed and thereupon, the activation energy, E_a, and pre-exponential factor, k_0, for the reaction of ethyl benzoate saponification were estimated. Five experiments were performed at different reaction media temperatures (18, 22, 30, 34 and 38 °C) and constant rotational frequency of the stirrer, f = 80 min^{-1}. Changes in ethyl benzoate and sodium benzoate molar concentrations versus reaction time at different reaction media temperatures, are presented in Fig. 4. Moreover, the molar concentration profiles, obtained by simultaneous fitting the proposed second order kinetic model (Eqs. (1) and (2)) to the experimental data, are also shown.
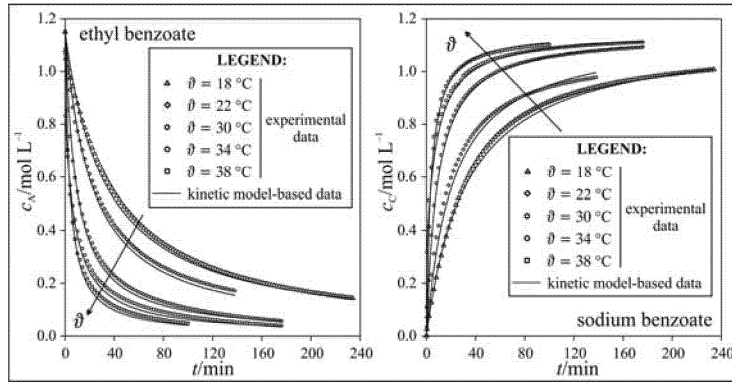
Fig. 4: Experimental and second order kinetic model-based values of ethyl and sodium benzoate molar concentrations in relation to reaction time.

From Fig. 4 it is evident that reaction media temperature, $\vartheta = 18$ °C is not high enough for reaching molar concentration of sodium benzoate as it was at $\vartheta = 38$ °C, although the reaction time was much longer. The synthesis is obviously faster at higher temperature. Proposed second order kinetic model of sodium benzoate synthesis gives very good predictions of experimental data. The estimated reaction rate constants, k, with appurtenant $S.E$, CV and R_{adj}^2 values are collected in Table 2. Exponential increase of k values with reaction media temperature is theoretically expected.

Table 2: Parametric results from fitting the proposed kinetic model to experimental data (different ϑ and constant f).

f/min^{-1}	ϑ/°C	k/L mol^{-1} min^{-1}	$S.E.$/L mol^{-1} min^{-1}	CV/%	R_{adj}^2/1
	18	0.02662	0.00014	0.52	0.9977
	22	0.04075	0.00040	0.98	0.9938
80	30	0.09717	0.00072	0,74	0,9990
	34	0.14793	0.00129	0,87	0.9992
	38	0.23450	0.00031	0.13	0.9988

The activation energy, E_a, and pre-exponential factor, k_0, of the reaction of ethyl benzoate saponification were estimated in continuation by fitting the Arrhenius equation (Eq. (3)) to the experimentally-based k values (Table 2). Graphic comparison between experimentally-based and Arrhenius model-based data is shown in Fig. 5.
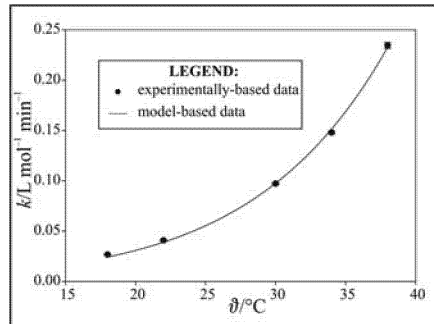

Fig. 5: Experimentally-based and kinetic (Arrhenius) model based-values of reaction rate constant, k, in relation to reaction media temperature, ϑ.

Briefly, it is clear from Fig. 5 that Arrhenius model gives excellent prediction of experimentally-based data, which is also confirmed with relatively high value of the adjusted coefficient of the determination, $R_{adj}^2 = 0.9991$. The activation energy was found to be $E_a = (85.25 \pm 2.18)$ kJ mol^{-1}, and pre-exponential factor $k_0 = (4.77 \pm 3.97)$ 10^{13} L mol^{-1} min^{-1}. Direct comparison with the literature data was impossible, because other authors conducted their reactions in heterogeneous systems. But on the other side, indirect comparison of both kinetic parameters was possible with the values reported by Moseley and Ohang, 1997. Most of the values are comparable after the extrapolation of the literature data.

Conclusion

The results obtained in this study are in agreement with previously published findings where traditional, less flexible and long-term more expensive titrimetric technique was used to develop overall kinetic model of sodium benzoate synthesis, from ethyl benzoate and sodium hydroxide. Moreover, the results definitely proved that FTIR based reaction analysis system is powerful PAT tool for the gain insight into sodium benzoate synthesis without grab sampling, sample preparation and material loss. Namely, the ReactIR^{TM} iC10 enables not only real-time and in-line monitoring of the ethyl benzoate saponification progression, but also efficiently helps understanding the reaction behaviour under different process conditions. Summarily, the application of intelligent FTIR system can significantly accelerate sodium benzoate production processes development and consequently presents one of the most efficient tools for solving the challenges in knowledge-based product engineering.

References

Ankudovich K., Chandra K., Gonzalez R., Martitz Z., Mulroe V., Powers S., API Synthesis in a batch reactor: Production of benzoic acid as a model system, http://www.osd.rutgers.edu/gs/07papers/batchreactor.pdf, June 2008.

Bozzini B., Mele C., Romanello V., 2007, An in situ FT-IR evaluation of candidate organic corrosion inhibitors for carbon steel in contact with alkaline aqueous solutions, Mat. Corr. 58, 362–368.

Dudley C., Bautista V., Blazer A., Yan H., Yu K., Biopharmaceutical production of benzoic acid in a batch reactor, http://www.osd.rutgers.edu/gs/06papers/benzoic.pdf, June 2008.

Levenspiel O., 1999, Chemical Reaction Engineering, John Wiley, New York.

Lin Z., Zhou L., Mahajan A., Song S., Wang T., Ge Z. Ellison D., 2006, Real-time endpoint monitoring and determination for a pharmaceutical salt formation with in-line FT-IR spectroscopy, J. Pharmaceut. Biomed. 41, 99–104.

Littler B.J., 2008, PAT tools in early chemical development, Chim. Oggi. 26, 20–22.

Moseley P.G.N., Ohag M., 1997, Thermodynamic functions of activation of the alkaline hydrolysis of ethyl benzoate and of ethyl p-nitrobenzoate in ethanol–water mixtures of various compositions at different temperatures, J. Chem. Soc., Perkin Trans. 2, 509–512.

Mouhab N., Balland, L., Ben Talouba I., Cosmao J.M., 2008, Study of a chemical reaction in heterogenous liquid-liquid medium producing a surfactant and cosolvent, Chem. Eng. Process. 47, 363–369.