Parameters study on the production of isoamyl acetate via milli-reactor in a solvent-free system

Nuraini Mansor, Rajaviknesswaran Singaravelan, Syamsul Rizal Abd Shukor*
School of Chemical Engineering, Engineering Campus, Universiti Sains Malaysia, 14300, Nibong Tebal, Penang. Malaysia

*chsyamrizal@usm.my

Abstract. Isoamyl acetate is an aromatic ester that has a similar smell to banana. This ester is high in demand for various industries application, especially in the flavour and fragrance sectors. This research aims to investigate the effects of synthesis parameters on the production of isoamyl acetate in a milli-reactor. Non-catalyzed reaction was performed by reacting isoamyl alcohol with acetic anhydride without further dilution. The flow rate of 40 to 80µL/min, reaction temperature of 20 to 50°C, and acid-alcohol molar ratio of 0.5 to 2.0 were chosen as the reaction parameters. All samples were analyzed through gas chromatography with flame-ionization detection (GC-FID). The results revealed that the highest production of isoamyl acetate was obtained at the flow rate of 60µL/min and temperature of 50°C with the acid-molar ratio of 0.5. In conclusion, these synthesis parameters significantly influence the non-catalyzed esterification reaction of isoamyl acetate production in a milli-reactor.

Keywords: Esterification; Milli-reactor; Solvent-free; Isoamyl acetate

1.0 Introduction

Esters are organic compounds that commonly created in nature. Normally, short-chain esters, which contained two to eight carbon atoms have pleasant smell and were always used in flavour and fragrance industries [1]. Isoamyl acetate, also known as isopentyl acetate is an ester of colourless liquid. This ester has naturally exists in fruits like bananas, apples, pears, peaches, and others [2]. Isoamyl acetate is commercially used in food and beverage fields such as ice cream, candy, soft drink, etc. Due to low toxicity properties, isoamyl acetate was used in making nail polish, perfumes, soap, lotion and shampoo. Isoamyl acetate has been produced in various kinds of methods. Previously, isoamyl acetate was extracted from natural sources through the extraction process, but it is impractical for commercial exploitation due to high cost and inefficient processes [1]. Various reports have been found on the synthesis of isoamyl acetate through fisher esterification where carboxylic acid and alcohol were involved in the reaction with the presence of a catalyst. Usually, sulphuric acid has been used to catalyse the reaction. This method consumed many chemicals and solvents, which is unfavourable in industries and required additional downstream treatment. Then, biocatalyst was introduced instead of the chemicals catalyst. This method is classified as a green method as it is environmentally safe [3]. However, biocatalyst, in the form of enzyme is very expensive resulting in high production cost. This has prompt researchers to put interests towards ionic liquid as a replacement of chemicals solvents for esterification reaction. Ionic liquid is an organic compound that is tagged with high market price making it unsuitable for large-scale industry and requires to be separated from the product before being marketed.
Solvent-free esterification was then introduced to improve the drawbacks of the esterification process. Many published studies mentioned the significant impact of the solvent-free method because of the reduction in chemical consumption and high yield production [4–11].

To date, process intensification is broadly recognized among researchers. This is because of the advantages gained from this system such as very efficient in heat and mass transfer, provide fast mixing, high surface area to volume ratio, safely and selectively compared to traditional batch system [2,3,6,7,12–15]. Commonly, the esterification studies were carried out with present of solvents and ionic liquid [2,3,16,17]. The study on solvent-free esterification in milli-reactor is not widely being explored.

This work aimed to determine the effect of reaction parameters on esterification between acetic anhydride and isoaamyl alcohol for the production of isoamyl acetate using microreactor. Due to This study was done in a solvent-free and non-catalyzed reaction to minimize chemical usage and economic purpose. The experiments were conducted by manipulating the acid-alcohol molar ratio, volumetric flow rate, and reaction temperature.

2.0 Materials Methodologies

2.1. Chemicals
Isoamyl alcohol (98.5%), acetic acid (100 %), isoamyl acetate (≥99%) and n-hexane used were purchased from Merck Co., Malaysia. Meanwhile, acetic anhydride (98+ %) was purchased from Sigma Aldrich, Malaysia. All chemicals used in this research are analytical grades and were consumed directly without further purification and dilution.

2.2. Milli-reactor set-up
This research was conducted in a custom-made glass milli-reactor attached to automated syringe pumps as depicted in Figure 1. The glass tubing with an inner diameter of 1mm and a total length of 1490 mm were placed inside the tubing jacket. Two syringe pumps were used to manipulate the volumetric flow rates of reactants injected into the milli-reactor through Y-shape mixer. The reaction temperature was controlled by using a water bath that is integrated to the milli-reactor. Sample collector was attached at the outlet of the glass tubing.

Figure 1. Milli-reactor used for the effects of the parameters on the synthesis of isoamyl acetate.
2.3. Procedures of esterification in milli-reactor
Isoamyl acetate was synthesized experimentally through direct esterification reaction between acetic anhydride and isoamyl alcohol in a solvent-free system. The synthesis procedures were started by the injection of acid anhydride and isoamyl alcohol at a desired volume flow rate. The esterification process between acetic anhydride and isoamyl alcohol were performed inside the milli-reactor tubing glass. The residence time of every reaction is 16 to 28 minutes, depending on the flow rates used. The output was then aliquot in triplicate from the milli-reactor for analysis using gas chromatography.

2.4. Sample analysis
Analysis of the sample was carried out through gas chromatography (Agilent GC-7820A) equipped with a hydrogen flame ionization detector (FID) and an SGE B21 (FFAP) column (60m x 0.32mm x 0.25µm). Helium was used as the carrier gas at a flow rate of 5ml/min. The initial oven temperature was kept constant at 100°C and increased to 60°C/min until it reached 140°C. The temperature was maintained at 140°C until the analysis is done. The retention time for each compound was appeared as follow; isoamyl acetate, 3.662 min; isoamyl alcohol, 3.749min; acetic anhydride, 3.940min and acetic acid, 4.717min.

3.0 Results
Two reactions occurred in the esterification of acetic anhydride and isoamyl alcohol, as shown in Scheme 1. The first reaction occurs between acetic anhydride and isoamyl alcohol, producing isoamyl acetate and acetic acid as intermediate. Meanwhile, the second reaction involves the reaction between acetic acid and the excess of isoamyl alcohol, producing isoamyl acetate and water as a by-product [18,19]. The esterification reaction is reversible, thus the reaction must be shifted to the forward reaction. According to Le Chatelier's principle, the excess of one of the reactants or removing one product might elevate the ester production. These reactions are influenced by several factors, and three of them are discussed in this work, which are the effect of the acid-alcohol molar ratio, volumetric flow rate, and temperature.

First reaction:
\[ \text{C}_4\text{H}_6\text{O}_3 + \text{C}_5\text{H}_{12}\text{O}_1 \leftrightarrow \text{C}_2\text{H}_4\text{O}_2 + \text{C}_7\text{H}_{14}\text{O}_2 \]
Acetic anhydride     Isoamyl alcohol     Acetic acid     Isoamyl acetate

Second reaction:
\[ \text{C}_2\text{H}_4\text{O}_2 + \text{C}_5\text{H}_{12}\text{O}_1 \leftrightarrow \text{C}_7\text{H}_{14}\text{O}_2 + \text{H}_2\text{O} \]
Acetic acid     Isoamyl alcohol     Isoamyl acetate     Water

Overall reaction:
\[ \text{C}_4\text{H}_6\text{O}_3 + 2\text{C}_5\text{H}_{12}\text{O}_1 \leftrightarrow 2\text{C}_7\text{H}_{14}\text{O}_2 + \text{H}_2\text{O} \]
Acetic anhydride     Isoamyl alcohol     Isoamyl acetate     Water

Scheme 1. Reactions involve in esterification for production of isoamyl acetate

3.1. Effect of acid-alcohol molar ratio
Determination of acid-alcohol molar ratio effect on esterification was conducted at constant temperature and volumetric flow rate, which were set at 30°C and 60µL/min, respectively. The acid-alcohol molar ratio was varied between 0.5 and 2.0. The increases in the ratios mean the decrease of alcohol in the reaction.

Figure 2 showed the concentration of compounds in samples analyzed from acid-alcohol molar ratio study. The results obtained reveal that isoamyl acetate was produced the most when the ratio is 0.5, and the lowest was at a ratio of 2.0. This shows that the excess of alcohol is essential to gain high ester
production. The overall reaction equation in Scheme 1 shown that two moles of isoamyl alcohol are required to react with one mole of acetic anhydride and the excess of nucleophile (alcohol) concentration pushes the equilibrium of the reaction in a forward reaction [6]. The excess alcohol was then reacted with the produced acetic acid to form ester [20,21].

High molar ratio of acid-alcohol means the amount of alcohol is lower than acetic anhydride. At this condition, alcohol was very limited to react with the excess acetic anhydride. Due to this, the production of ester was also reduced. It can be seen from the figure that the unreacted acetic anhydride increases as the ratio of acid-alcohol is increase especially at ratio 1.5 and 2.0.

![Figure 2](image_url)

**Figure 2.** Effect of acid-alcohol molar ratio on the esterification process.

### 3.2. Effect of the volumetric flow rate of reactants

This study was conducted by manipulating the volumetric flow rate of acetic acid anhydride at 40, 50, 60, 70 and 80 µL/min. Temperature and acid-alcohol molar ratio were kept constant at 30°C and 1.0, respectively.

According to Figure 3, it was observed that the concentration of isoamyl alcohol and acetic anhydride is high, and the production of acetic acid is low at the volume flow rate of 40 and 50µL/min. This indicated that the poor performance of the reaction was due to poor mixing of the reactants inside the milli-reactor. The degree of mixing was influenced by the diffusion force between both reactants. Thus, poor mixing means the diffusion is inefficient. The residence time for these flow rate were higher compared to others, but because of inefficient of mixing and diffusion of the fluids, the reaction cannot performed well.

At a volumetric flow rate of 60µL/min, the concentration of isoamyl acetate was the highest meanwhile the reactants consumed the most at other flow rates. It can be deduced that the reaction occurred more efficient compared to the volume flow rate of 40 and 50µL/min.

As the flow rate of reactant increases up to 70 and 80µL/min, the concentration of isoamyl acetate dropped, meanwhile the concentration of acetic acid was high. This was due to the lack of time for the reaction to complete. This situation indicates that the main reaction is still ongoing as the mixtures exiting the milli-reactor. The acetic anhydride and isoamyl alcohol reacted to produce an ester and acetic acid, but the reaction between acetic acid and isoamyl alcohol was uncompleted due to time constraint. This can be seen from Figure 2 that the concentration of acetic acid is high beyond 60µL/min as compared to flow rate lower than 60µL/min. This has proven the hypothesis of flow rate is inversely proportional to residence time; thus, as the flow rate increases resulting in the shortening of residence time and cause reduction of ester at the outlet [3].
3.3. Effect of reaction temperature

Temperature has been known to be a significant parameter as higher temperature increases the reaction rate for any given chemical reaction. This can be explained based on the collision frequency of the reactant particles. Supplied heat encouraged the particles with higher kinetic energy to collide rapidly, consequently provide enough energy to trigger the reaction to occur. Additionally, the increase in temperature resulted in the acceleration of the forward reaction [22]. In this study, the effect of temperatures was conducted at several temperatures (30, 35, 40, 45 and 50°C) at a constant volumetric flow rate (60µL/min) and equal molar acid-alcohol molar ratio.

The results in Figure 4 depicted the concentration of compounds in the sample at various reaction temperatures. The bar graph showed that isoamyl acetate increases as the temperature increases from 30 to 50°C. It can be seen that at a temperature of 50°C, the concentration of acetic anhydride and isoamyl alcohol was the lowest compared to at other temperatures. This indicates that the acid and alcohol reacted at a higher reaction rate with higher consumption producing a higher yield of ester. This can be elucidated based on Arrhenius equation theory, whereby an increase in reaction temperature would increase the kinetics of the reaction which related to the collision of the particle as stated above.
4.0 Conclusion
The performance of solvent-free esterification between acetic anhydride and isoamyl alcohol in milli-reactor has been investigated in this study. Three main reaction parameters were manipulated to determine their effects on the production of isoamyl acetate. The optimal flow rate obtained was 60µL/min which gave the highest yield where the reactant was consumed the most. Lower flow rate showed much lesser yield due to lower driving force for the diffusive mixing meanwhile higher flow rate translated into a much shorter residence time resulting in lower yield due to incomplete mixing. Higher reaction temperature has been shown to significantly influence the reaction. Also, excess of alcohol in reaction provides the high tendency for forward path reaction, enhancing ester yield where the maximum yield was achieved at the acid-alcohol molar ratio of 0.5.

5.0 References
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