EXPERIMENTAL STUDY ON THE SOLVENT-FREE, NON-CATALYTIC SYNTHESIS OF ETHYL ACETATE BY THE ESTERIFICATION OF ETHANOL WITH ACETIC ANHYDRIDE IN A COILED FLOW INVERTER

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by

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF SYMBOLS

Symbol	**Description**	**Unit**
μ	Average Dynamic viscosity of Fluid	kg/m.s
U	Average Flow Velocity of Reactants	m/s
[C]	Concentration of Acetic Acid	M
[A]	Concentration of Acetic Anhydride	M
[B]	Concentration of Ethanol	M
[D]	Concentration of Ethyl Acetate	M
$[H_2O]$	Concentration of Water	M
T_C	Critical temperature	K
A	Cross-sectional Area of Tubing	m^2
ρ	Density	kg/m^3
R_A	Design Parameter	-
d	Diameter of the Pipe	m
N	Number of Bends	-
T	Operating Temperature	K
RT	Residence Time	min
Re	Reynold's Number	-
Q_T	Total Volume of Reactor	µL
V	Total Volumetric Flow Rate of reactants	µL/min
μ_{gas}	Viscosity of Gas	kg/m.s
μ_{liquid}	Viscosity of Liquid	kg/m.s

LIST OF ABBREVIATIONS

Symbol	**Description**
ADH	Alcohol Dehydrogenase
ANOVA	Analysis of Variance
ARHCR	Advanced Rotational Hydrodynamic Cavitation Reactor
CFI	Coiled Flow Inverter
CHC	Continuous Hydrodynamic Cavitation
CPVC	Chlorinated Polyvinyl Chloride
FAME	Fatty Acid Methyl Ester
FID	Flame Ionisation Detector
GC	Gas Chromatography
HCTD	Helically Coiled Tubular Device
HTST	High-Temperature Short Time
LTLT	Long-Time Low Temperature
NADH	Nicotinamide Adenine Dinucleotide (NAD) + hydrogen (H)
PDI	Polydispersity Indexes
PTFE	Polytetrafluoroethylene
PVC	Polyvinyl Chloride
RSM	Response Surface Methodology
RTD	Residence Time Distribution
UHT	Ultra-High Temperature
UPVC	Unplasticised Polyvinyl Chloride

KAJIAN EKSPERIMEN TENTANG SINTESIS ETIL ASETAT BEBAS PELARUT DAN TANPA PEMANGKIN MELALUI PENGESTERAN ETANOL DENGAN ANHIDRIDA ASETIK DALAM PENYONGSANG ALIRAN BERGELUNG

ABSTRAK

Penghapusan pelarut dan mangkin menimbulkan beberapa cabaran utama, seperti kadar tindak balas yang perlahan, hasil produk utama yang rendah, dan pengeluaran produk sampingan yang berlebihan. Oleh sebab itu, eksperimen ini tertumpu pada pengesteran bukan pemangkin, bebas pelarut antara anhidrida asetik dengan etanol dalam penyongsang aliran bergelung (CFI). Penggunaan CFI yang merangkumi prinsip intensifikasi proses telah menunjukkan potensi besar dalam mengecilkan taburan masa kediaman kerana kehebatan sifat pemindahan haba dan jisim dan sifat pencampuran. Pengesteran dalam kajian ini ialah tindak balas tidak boleh balik antara anhidrida asetik dan etanol untuk mengelakkan produk daripada membentuk bahan tindak balas. Dua parameter telah dipilih untuk dikaji, iaitu suhu operasi (dimanipulasi antara 40 hingga 80 ° C) dan bilangan selekoh CFI (3, 7, 11). Interaksi antara kedua-dua parameter juga dianalisis melalui Design Expert V.13 untuk mencari keadaan operasi yang optimum. Berdasarkan pendapatan kajian, keadaan operasi optimum ialah pada 60℃ dalam CFI 3-bengkok kerana dalam keadaan operasi tersebut, kepekatan etil asetat adalah paling tinggi (1.7592 mol/dm^3) dan kepekatan anhidrida asetik adalah rendah (0.8511 mol/dm^3). Hal ini menunjukkan bahawa kebanyakan bahan tindak balas pengehad, iaitu anhidrida asetik, dibelanjakan untuk membentuk produk utama, etil asetat.

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ABSTRACT

The elimination of solvents and catalysts pose several major challenges, such as a slow rate of reaction, low yield of main product, and an excessive production of side products. Thus, this experimental study focuses on the non-catalytic, solvent-free esterification using ethanol and acetic anhydride in a coiled flow inverter (CFI). The application of CFI, which embodies the principles of process intensification, has demonstrated great potential in narrowing the residence time distribution due to superb heat and mass transfer properties and mixing properties. Besides, the non-reversible esterification reaction between acetic anhydride and ethanol to prevent the products from shifting back to the left-hand side of the equilibrium to form the reactants. Two parameters were selected in this study, which were operating temperature (manipulated between 40 to 80 °C) and the number of bends of the CFI (3,7, 11). The interaction between the two parameters were also analysed using Design Expert V.13 to find the optimum operating conditions. Based on the findings obtained, the optimum operating condition is at 60 °C using a 3-bend CFI, because under the operating conditions mentioned, the concentration of ethyl acetate, which is the main product, is the highest (1.7592 mol/ dm^3), and the concentrations of acetic anhydride is low (0.8511 mol/dm^3) , implying that most of the limiting reactant, which is acetic anhydride, is spent on forming the main product, ethyl acetate.

CHAPTER 1

INTRODUCTION

This chapter covers the research background, which encompasses the nature of the esterification process and the challenges that follow, and also the advantages of the coiled flow inverter that makes it stand out from other choices of microreactors and reactors. The problem statement and research objectives are included in this section as well.

1.1 Industrial Application of Esters

Esters are naturally and synthetic organic compounds widely applied in different sorts of processes, such as industrial and domestic processes. The reaction to synthesise esters is among the most crucial reactions in the synthesis of organic chemicals. It produces ester products which are frequently found in biofuels, solvents, paints, varnishes, pharmaceuticals, plastics, and coatings (Khan et al., 2021).

Ethyl acetate, which is the product of the esterification reaction proposed, has 4 main applications. First, it acts as a coatings solvent for liquids including paint, lacquer, and varnish. It also functions as an extraction solvent for different processes such as the decaffeination of coffee and tea. Besides, in the pharmaceutical industry, it also plays the role of process solvent. Moreover, ethyl acetate is also commonly applied in the production of synthetic leather and perfumes, household products such as airplane glue, paint, and nail polish removers. Due to its fruity taste upon dilution, ethyl acetate is also a flavour enhancer found in food and pharmaceuticals. It also finds particular use as an indirect food additive in some packaging materials (Marino and Ch, 1998). In general, ethyl acetate is a valuable chemical with various applications in the chemical processing and food industry.

1.2 The Nature of Fischer Esterification Process, Challenges in Terms of Process Efficiency, and Suggested Solutions to Tackle the Issues

To produce esters such as ethyl acetate, Fischer esterification is the most-practised process in the industry, despite its severe constraints due to its low conversion and long reaction time, which is mainly caused by the presence of a thermodynamic equilibrium. In a typical Fischer esterification process, carboxylic acid and an excess amount of alcohol is heated in the presence of a catalyst to produce its corresponding ester. This reaction eventually reaches equilibrium after some time, and not only does it require an excess amount of one of its reactants, which is usually alcohol, it also requires the continuous removal of water to shift its reaction to the product side. The chemical equation for the typical Fischer esterification process is shown below (Khan et al., 2021).

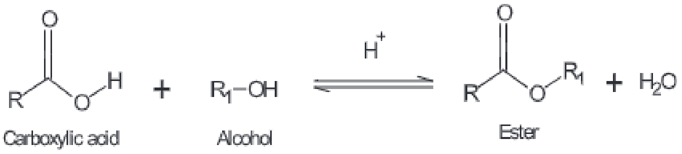

Figure 1. 1 Chemical Equation of Esterification Reaction

In addition to the limitations arising from the nature of the reaction itself, the use of catalysts and solvents in esterification also pose numerous issues. In catalysed esterification reactions, the catalysts may be in various forms, such as homogeneous and heterogeneous catalysts. Homogeneous acid catalysts such as $AlCl_3$, HF, and H_2SO_4 are commonly used in the industry, but the disadvantages that come with their application are significant as well. The large volumes of toxic waste produced which could potentially harm the environment, difficult separation process, corrosiveness, and the cost inefficiency are among the many drawbacks of using a homogeneous acid catalyst. Long-term and short-term exposure to the toxic waste and chemicals could lead to severe health problems among workers and the public. Heterogeneous solid acid catalysts could be used instead of homogeneous catalysts due to the advantages they offer, such as their simplified recovery, reusability, excellent accessibility of reactive centres, large surface area, chemical and thermal stability (Sirsam et al., 2016). However, the cost of the heterogeneous catalyst also has to be taken into consideration.

Although enzyme catalysts have been suggested to tackle this issue, the high cost of enzymes, inhibitory effect of alcohols on enzymes, and mass transfer limitations which result in low conversions are among the disadvantages of this type of catalyst. Enzymes are also highly sensitive to the operating temperature and may denature at excessively high temperatures. Moreover, the need for the continuous removal of water and the maintenance of the mechanical stability of the enzymes hinder the scale up of this method for industrial applications (Khan et al., 2021).

Furthermore, solvents occupy around 80-90% of the total mass used in any organic reaction, and 80-85% of the waste it produces. The pharmaceuticals and fine chemicals industry rely on solvent-based organic synthesis but the safe disposal of the vast amount of solvent waste is difficult and costly (Sansom, 2018). In enzymatic catalysis, the use of organic solvents to support the formation of enzymes and purification are challenges in designing a green and environmentally friendly process (Khan et al., 2021).

Therefore, based on 2 of the principles of green chemistry, which are waste prevention and use of safer solvent and reaction conditions, a solvent-free, non-catalytic esterification via the reaction between alcohols and acid anhydrides in a coiled-flow inverter is investigated ("12 Principles of Green Chemistry," n.d.). By avoiding the use of solvents and catalysts, not only can the costs of operation, separation, and disposal be reduced, the use of certain hazardous chemicals and the generation of toxic wastes can also be avoided.

1.3 Esterification Reaction between Ethanol and Acetic Anhydride

In this study, ethanol and acetic anhydride are the reactants. This esterification process consists of 1 main reaction and 2 side reactions. In the main reaction, which is a forward reaction, acetic anhydride (A) reacts with ethanol (B) to produce acetic acid (C) and ethyl acetate (D). Acetic acid (C) reacts with ethanol to produce ethyl acetate (D) and water, but the process is reversible and its reaction rate should be negligible without the presence of a strong acid catalyst. In the second side reaction, acetic anhydride (A) reacts with water to produce acetic acid (C). The process demonstrates an autocatalytic behaviour in which the acetic acid (C) produced in the main reaction reacts with alcohol to form water, which in turn causes the hydrolysis of acetic anhydride (Lee et al., 2021). However, another autocatalytic behaviour, which is the significant catalytic effect of the carboxylic acid formed on the acetic anhydride has not been frequently reported. Based on a research conducted by Widell and Karlsson, the reaction rate in the acetic anhydride-methanol system increased as the initial acetic acid concentration was increased, which strongly indicated the possibility of autocatalysis (Widell and Karlsson, 2006). The 3 chemical reactions are shown below(Lee et al., 2021).

$$A + B \rightarrow C + D \tag{1}$$

$$B + C \leftrightarrow D + H_2O \tag{2}$$

$$A + H_2O \rightarrow 2C \tag{3}$$

Although the main reaction is a forward reaction instead of a reversible reaction such as in Fischer esterification, in order to increase the rate of the acylation reaction, the reaction is sluggish without an activator (Bartoli et al., 2003). Common methods include the application of catalysts such as pyridine and metal triflates in the reaction (Bartoli et al., 2003), (Lugemwa et al., 2013). Pyridine is commonly used as a catalyst in the acetylation reaction of alcohols with acetic anhydride, but it is toxic and smells bad. Moreover, it has a high boiling point, which complicates the process of removing the catalyst after the reaction. Since pyridine is usually used in excess, the process of isolating the product is also difficult if the amount of ester produced is extremely small (Lugemwa et al., 2013). Metal triflate catalysis presents several disadvantages such as rigorously anhydrous reaction conditions (for example, during the use of $Sc(OTf)_3$ and Me_3SiOTf) and low reaction temperatures to prevent the occurrence of side reactions (Bartoli et al., 2003). Due to the drawbacks mentioned above, more eco-friendly and cost-saving methods such as the use of a coiled flow inverter (CFI) as a reactor for the esterification process is suggested.

1.4 A Coiled Flow Inverter (CFI) as an Innovation

The use of a CFI is innovative because it improves mixing characteristics, increase heat transfer and mass transfer because of the increased surface-to-volume ratio, decreased holdup of chemicals, as well as improved management of toxic chemicals in comparison with a conventional reactor for batch processes (Lee et al., 2021). The advantages mentioned lead to greater yields and conversions in a shorter time compared with traditional batch reactors.

A CFI is a type of helically coiled tubular device (HCTD) which has several 90° bends inverting secondary flow patterns produced by centrifugal forces in the inverter (Dean vortices). There are several benefits of implementing a CFI in the esterification reaction.

First of all, the stagnant mixing zones in the cross-sections of the tube along the inverter are eliminated, thus improving mixing characteristics and heat transfer. Besides, the residence time distribution (RTD) is also narrowed and axial dispersion in single-phase flow processes are also reduced. The benefits lead to improved reaction rates and yield compared with those obtained using conventional equipment (Kurt et al., 2017).

In this research, by manipulating factors such as the operation temperature, the molar ratio between the reactants and the number of bends of the coiled flow inverter, the efficiency of the coiled flow inverter in the production of esters and the optimisation of the process is investigated.

1.5 Problem Statement

Based on literature, the use of solvents and catalysts have resulted in negative effects such as large amounts of toxic chemical discharge, exhaustion of non-renewable sources, difficult separation processes, as well as cost inefficiency. To eliminate the adverse impacts caused by the application of solvents and catalysts, a greener, non-catalytic, solvent-free process with an improved reactor design is required. However, by removing the solvent and catalyst, which are vital components of the reaction from the process, several issues arise, and they include a possible decrease in reactant solubility, high or extreme operating conditions, longer reaction time, increased formation of by-products, and low yield. Besides that, conventional esterification reactions, for instance, Fischer esterification, are also known to be restricted by a thermodynamic equilibrium, low product yield, low conversion, long reaction time, and slow rate of reaction. In order to address the issues, process intensification may be implemented in the design of the reactor and the esterification. Moreover, conventional reactors require a long reaction time as well as catalysts and solvents to carry out esterification besides producing a large amount of side products, thus rendering the esterification process inefficient. Miniaturisation of the reactor is required for enhanced heat and mass transfer characteristics to obtain a higher product yield. Despite the lack of a solvent and a catalyst, the application of a coiled flow inverter (CFI) resulted in greater yields of ester products compared with conventional batch reactors. However, the effect of factors such as the number of bends of the coiled flow inverter (CFI) and the operating temperature on the conversion of reactants and the yield of the ester product require further investigation to obtain the optimum ester yield. Therefore, in this research, the non-catalytic, solvent-free esterification of ethanol and acetic anhydride in a coiled flow inverter to produce ethyl ethanoate has been proposed to resolve the issues. A sample of the final product will be collected and analysed using gas chromatography (GC) to analyse its components and concentrations. Additionally, factors such the number of bends of the inverter and reaction temperature are manipulated to find out the optimum reaction conditions at which the ester yield is the highest, the consumption of acetic anhydride is the highest, and the production of acetic acid is the lowest, by using Response Surface Methodology (RSM).

1.6 Research Objectives

The objectives of this research are:

i. To investigate the effect of the operating temperature on the conversion of the reactants and yield of ethyl acetate in a CFI.

ii. To study the effect of the number of bends of the coiled flow inverter on the reactant conversion and the ethyl acetate yield.

iii. To optimise the esterification process by identifying the critical parameters and optimum reaction conditions to increase the concentration of ethyl acetate at the CFI outlet through response surface methodology (RSM).

CHAPTER 2

LITERATURE REVIEW

2.1 Advantages and Limitations of Solvent-Free, Non-Catalytic Processes

The adverse effects brought upon by the use of solvents and catalysts have sparked the idea of green synthesis processes. The concept of "no solvent is the best solvent" has led to the design of greener, solvent-free processes, which have been proven to be possible. In some reactions, the use of catalysts has even been avoided as well. These changes have resulted in several advantages such as (Sarkar et al., 2016):

i) Cost savings due to the removal of the cost of purchasing large volumes of solvents and catalysts.

ii) Cost reduction because the collection, purification, recycling, and removal of solvents and catalysts are no longer required, leading to less equipment costs and simpler process designs.

iii) An increase in reaction rate and a decrease in reaction time, because reactants are more available. Some of the reactions can be carried out under ambient conditions such as at room temperature. For instance, microwave irradiation and ball milling.

iv) Environmental benefits because there is no toxic discharge of catalysts and solvents. Many organic solvents including chlorinated hydrocarbons are poisonous and volatile in nature but are widely used in large amounts for organic reactions. The continuous disposal of such toxic solvents not only threaten the environment, but also human safety and health. Hence, the removal of organic solvents from a process is a huge step towards greener chemical synthesis.

v) Increased energy savings due to less handling of chemicals.
vi) A great reduction in reactor size and capital investment.
vii) Stages related to the handling of solvent is no longer required, such as the storage, loading, removal, and recycling of solvents (Balland et al., 2002).

However, despite the great many advantages solvent-free and catalyst-free chemical reactions bring, there are still numerous existing limitations that such reactions have yet overcome. The limitations include (Gawande et al., 2014):

i) Issues on the solubility of reactants or reagents.
ii) High operating conditions such as temperature and pressure.
iii) Determination of active starting raw materials.
iv) Increased reaction time and more formation of by-products.
v) Excess addition of reactants or reagents.
vi) Issues on product selectivity.
vii) Restricted feasibility of implementation in solid-phase reactions. Significant amounts of solvents are still required to enable the adsorption of reactants and extraction of products before and after the reaction.
viii) Low product yield.
ix) Increased constraints in terms of technical and safety, such as a greater risk of thermal runaway in exothermic reactions due to the lack of solvent as a thermal buffer (Balland et al., 2002).

Solvents play an important role in creating the reaction environment for liquid-phase reactions. Hence, solvents have a strong impact on the reaction kinetics, yield, and the purification steps that follow the process (Riechert et al., 2015). The changes in the solvent could impact the rate and reaction path, which in turn affects the yields and product ratios. Thus, solvents play a crucial role in each reaction step, including the solvation of reactants, transition state and products, and lastly the reduction of activation energy to the product formation (Kumar and Nigam, 2012). Additionally, solvent mixtures are also used in order to facilitate catalyst recycling or to provide certain properties to the reaction media (Riechert et al., 2015). A catalyst speeds up the rate of reaction, thus enabling higher product yields within shorter time frames. By removing the solvent and catalyst, including biological catalysts such as enzymes, which are crucial in the esterification process, changes such as the selection of an alternative chemical reaction and an improvement in the design of the reaction equipment are required to ensure that the performance of the developed process is comparable or even greater than that of the conventional process. A chemical reaction which is not restricted by chemical equilibrium may be selected to increase product yield.

2.2 Working Principle of a Coiled Flow Inverter (CFI)

Improvements in reaction equipment by adhering to the principles of process intensification has led to the miniaturisation of the reactor and optimisation of the reaction conditions, resulting in the invention of a coiled flow inverter (CFI). In helically coiled tubes, heat and mass transfer are enhanced due to the unbalanced centrifugal forces in the system which result in the development of Dean flow. Helical pipes are among the most commonly applied curved tubes due to the presence of Dean flow, which results in highly efficient mixing even during laminar flow, causing a low pressure drop in comparison with that in the turbulent regime. In contrast with the application of stirrers or static mixers, helically coiled tubes also hardly need maintenance due to the lack of moving parts or obstacles in the reactor design (Mansour et al., 2020a). Dean flow refers to the formation of symmetrical vortices on the cross-sectional plane of the tube. Dean number quantifies the effect of centrifugal forces on viscous forces in a fluidic system. An increment in the Dean number results in the transition of the primary transport mechanism from molecular diffusion to chaotic advection (López-Guajardo et al., 2017). By inducing chaotic advection, the mixing of reactive phases which are in the laminar flow regime can be improved. A perturbation in the flow of a helical coiled tube has to be introduced for chaotic advection to be induced, and the solution to this is the invention of the coiled flow inverter (CFI), which is a form of microreactor.

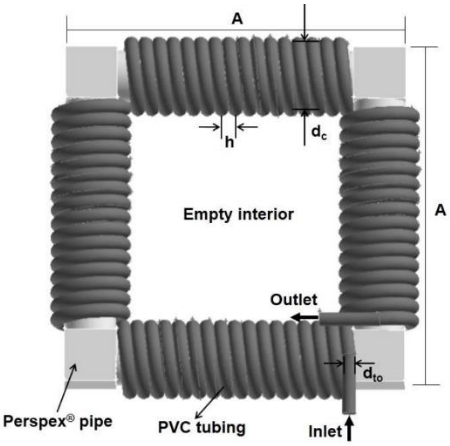

Figure 2. 1 Structure of a Standard CFI

A standard CFI has the appearance of a square duct and has helically coiled arms as each side. There is also plenty of empty space in the middle (Figure 2.1) (Soni et al., 2019). According to David et al. (2020), the structure of the CFI used in the simulation study on continuous low pH viral inactivation consisted of 10 frames with either 5 or 10 turns each