“Process Intensification of Selected Chemical Reactions by Continuous Flow Microstructured Reactors”

A thesis submitted in the partial fulfillment of the requirement for
the award of the degree of

DOCTOR OF PHILOSOPHY
IN
CHEMICAL ENGINEERING

By

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Dedicated

To

My Beloved Parents & Family

All My Teachers Who Taught,
Motivated and Made Me Directly or
Indirectly with Positive or Negative
Thoughts What I am Today.

DECLARATION

This is to certify that the work presented in the thesis entitled **“Process Intensification of Selected Chemical Reactions by Continuous Flow Microstructured Reactors”**, is an authentic work done by me under the supervision of Dr. Shirish Hari Sonawane was not submitted elsewhere for the award of any degree.

I declare that this written submission represents my idea in my own words and where other’s ideas or words have not been included. I have adequately cited and referenced the original sources. I also declare that i have adhered to all principles of academic honesty and integrity and have not misinterpreted or fabricated or falsified any idea/data/fact/source in my submission. I understand that any violation of the above will be a cause for disciplinary action by the Institute and can also evoke penal action from the sources which have thus not been properly cited or from whom proper permission has not taken when needed.

Date: 12 – 03 – 2020.
Place: Warangal

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CERTIFICATE

This is to certify that the thesis entitled **“Process Intensification of Selected Chemical Reactions by Continuous Flow Microstructured Reactors”** that is being submitted by **Mr. Maralla Yadagiri** in a partial fulfillment for the award of Doctor of Philosophy (**Ph. D)** in the Department of Chemical Engineering, National Institute of Technology, Warangal, Telangana State, India, is a record of authentic work carried out by him under my guidance and supervision. The results incorporated in this thesis have not been submitted to any other Universities or Institutes for the award of any other degree or diploma.

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Mr. Maralla Yadagiri

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ABSTRACT

This research work mainly deals with process intensification by a continuous flow Microstructured reactor for the synthesis of different organic products. The main aim of the research work is to study the performance of a Microstructured reactor for a selected chemical reaction. In this work, stainless steel capillary microreactor, Teflon capillary microreactor and Corning® Advanced Flow^{TM} – Reactor (AFR) were used. Recently, microreactor technique was explored as a one of the emerging advanced technology for synthesis of various chemical, pharmaceutical and fine chemical products in a shorter period with increased yield and selectivity. In the present work, four different case studies are reported.

Case Study – I: This chapter briefly reported on the synthesis of 5-(4'-methyl-[1, 1'-biphenyl]-2-yl)-1-trityl-1H-tetrazole (MBPTT) by stainless steel capillary microreactors (SSCR) and Corning® Advanced Flow Reactor (AFR). A continuous flow process has been successfully developed for the synthesis of MBPTT. The reaction was carried out in three different configurations of microreactors at room temperature. The SSCR-2 mm and 1 mm (stainless steel capillary coil microreactors) gave a yield of 92.87 and 93.72% for the residence time of 324 s and 71 s respectively. Among the three microreactors, Corning® AFR gave effectively higher yield (95.18 %) at the residence time of 27 s. The product formation was confirmed by TLC and Melting point. Further, the product was characterized by FTIR and NMR. Overall, AFR could be recommended for the synthesis of MBPTT. Furthermore, hydrodynamic studies were also reported for the microreactors. Thus, the 5-(4'-methyl-[1, 1'-biphenyl]-2-yl)-1-trityl-1H-tetrazole is a useful intermediate material for some of the pharmaceutical products that could be produced industrially using a microreactor.

Case Study – II: This chapter deals with the continuous flow synthesis of performic acid which has versatile oxidizing properties. In this work, an attempt has been made for the synthesis of performic acid in a continuous flow microreactor of Teflon helical capillary microreactor (HCMR) with a homogeneous catalyst. The effect of catalyst concentration, hydrogen peroxide concentration, temperature and radius of curvature on the formation of performic acid was studied. The maximum conversion of FA was obtained within 6 minutes at 30 °C and 4 mol % catalyst. The maximum conversion of FA was obtained (X_{FA} = 72.78%) when the reaction was performed in helical capillary microreactor having 13.25 mm radius of curvature (number of turns = 21). However, in the radius of curvature of 18.25 mm (Number of turns 15) and 23.25 mm (Number of turns 12) of the HCMR gave 3.393 mol/L and 3.105 mol/L of PFA respectively at a residence time of 9 min. Based on the kinetic equations and experimental data, the kinetic constants were determined. Based on the kinetic data, it was found that the activation energies of PFA synthesis and hydrolysis were 45.746 and 51.692 kJ/mol respectively.

Case Study – III: This chapter demonstrates synthesis of peroxypropionic acid by HCMR. In this study, an attempt was made for the synthesis of peroxypropionic acid in a helical capillary microreactor with homogeneous catalyst. The chapter reports the perhydrolysis of peroxypropionic acid with effect of various parameters like concentration of hydrogen peroxide, molar ratio of reactants, radius of curvature of the microreactor, concentration of catalyst and temperature. The reaction is slow, as the peroxypropionic acid equilibrium was reached within 10 minute at temperature of 50 °C and at 10 mol % catalyst loading based on propionic acid. The reaction was carried out in 13.25 and 23.25 mm radius of curvature of the microreactor in which 4.0375 and 3.488 mol/L concentrations of peroxypropionic acid respectively was obtained at 50 °C and 10 mol % catalyst. It indicates that as radius of curvature decreases, better mixing was provided among the reactants for the reaction to give enhanced yield and selectivity. From the experimental data, the activation energies and reaction rate constants were determined. For peroxypropionic acid synthesis and hydrolysis, the activation energies for both the cases were 45.26 and 50.04 kJ/mol respectively with catalyst of 10 mol % based on propionic acid.

Case Study – IV: This chapter deals about the continuous flow synthesis of peracetic acid. It has been recently increasing its importance due to its oxidative property. A continuous flow Microstructured reactor technique has been efficiently employed for the synthesis of peracetic acid using sulfuric acid as catalyst. The experiments were carried out at different molar ratios, three different configurations of microreactors, catalyst concentration and temperature. The reaction looks to be mildly slow because the equilibrium was reached in 9 minute at 60 ℃ at 12 mol % catalyst in 13.25 mm radius of curvature of microreactor with maximum concentration of peracetic acid was 3.751 mol/L (X_{AA} = 62.21%). The kinetic expressions of peracetic acid formation and hydrolysis were developed and the constants of kinetic model were determined from the experimental records. The activation energies of peracetic acid formation and hydrolysis were 45.850 & 49.550 kJ/mol and 45.536 & 49.235 kJ/mol for AFR and HCMR respectively. The equilibrium constant (Ke) was determined at different temperatures as 2.971, 2.838, 2.711, 2.590 and 2.475 at 20, 30, 40, 50 and 60 ℃ respectively.

The results obtained through these studies explored the contribution and importance of the microreactor technology as a synthesis technique for obtaining better yield of the organic products in shorter time with enhanced yield and selectivity when compared with conventional methods. From these studies it was observed that the microreactor technology can also be useful for bulk production by numbering up the units through incorporation of number of microreactors and increasing the size of the pump.

CHAPTER – 1

INTRODUCTION

1.0. Introduction and background

The ethics of sustainability or green chemistry takes account of avoiding waste generation. Planning of the safer chemicals processing with maximum yield and zero generation of toxic waste and low energy consumption. New pharmaceutical products are emerging into the market, which are valuable for a progressive and future society. To meet the specific needs, the society and nature at the same time, these industries are looking for sustainable manufacturing processes [1].

Microscale (different geometries or channel) reactors have offers advantages over conventional batch methods due to miniaturization, rapid mixing, improved mass transfer as well as heat transfer. The higher aspect ratio of a microchannel improves heat dissipation for highly exothermic processes, consequently minimizing the generation of toxic chemicals. It permits the reaction control that requires shorter residence time, quick mixing, facilitates greener, economical and safer route of synthesis. Further, microreactors (MR) and microreactor technology (MT) deals with the opportunity to carry out the chemical processes in a feasible and safer method because of miniaturization of geometry, low volume or hold up and enhanced safety. The microreactor technology shows increasing in a chemical, pharmaceutical, biochemical and biobased process industries [1]

1.1. Process intensification (PI)

A simple definition of PI is “a chemical engineering progress that contributes to a significantly smaller, cleaner and advanced efficient energy technology is known as “**Process Intensification**”, [2, 3] or “the physical miniaturization of a process tools while retaining output and performance”. The another definition of PI is “the development of advanced device/equipment and procedures that offer radical progress in the chemical production and processing, considerably reducing plant size, reducing energy consumption, reducing waste generation, and finally resulting to safer, inexpensive, justifiable technologies (sustainable technologies) [4, 5].

Process intensification is one of the advanced cutting edge technologies in the field of chemical engineering. The concept is hardly a couple of decades from the past. The process intensification is an extremely new idea in the design of chemical industries. The PI comprises the development of innovative equipment and procedures associated in the direction of the current state – of – art. The main aim of process intensification is to bring remarkable progresses in the manufacturing process more safely, substantially reducing a plant size, capital cost, energy consumption. The PI technique reduces the pollution, waste generation, and better yield as well as selectivity. Therefore, the idea of PI is closely associated with reducing the physical size of the industry [5 – 10].

1.2. Micro structured reactors and microreactor technology

Manufacturing of bulk chemicals is generally accomplished in a large conventional reactor or vessel (e.g., Batch Reactors (BR) and Continuous Stirred Tank Reactors (CSTR)) [11, 12]. The required quantity of reactants are fed into the reactor and reaction is allowed to take place. After the reaction completion, the reactor is allowed for further post – processing. The process is a well industrialized and common procedure followed for any type of chemical reaction at large scale, however, yield and selectivity are major issues with the conventional batch reactors.

The chemical processes are classified into bulk chemical, intermediate chemical and fine chemical. The bulk chemicals are manufactured in huge amounts in manufacturing plants. The intermediates, fine chemicals, and pharmaceutical products are manufactured in kilograms mostly by the conventional batch processes. The batch vessels (or reactors) are most flexible and can be simply used for numerous products. Thus, the batch vessels are considered to be suitable for a chemical process from many years. There was no significant and drastic alteration in the technology of batch manufacturing processes. Nevertheless, if one considers exothermic and fast reactions, these procedures are restricted by their inertia and the drawbacks such as limitations of a small aspect ratio. [13].

There are two approaches for designing a reactor which are based on chemistry and chemical engineering. The first one, the improvement of different synthesis and processing methods, e.g., the selection of catalyst, employing specific reaction conditions and environment. This process is known as a characteristic chemical methodology. In the second approach, the heat transfer and mass transfer rates are enhanced by improving a specific interfacial area, hence, thereby reducing the length of the diffusion paths. This leads to increase the safety by advantage of the smaller volume (holdup) and better thermal control for highly exothermic processes. [12]. The development of a process is often stated as "Intensification of a Process" or "Process Intensification", this is defined in several ways subjecting to the presentation (application) involved. The micro structured technology is one of the most influential tools to obtain the target of the PI [4]. To overcome the above problem, micro structured reactors (MSR) are best possible solution.

The idea of miniaturizing of plants (equipment) was introduced by Prof. Ramshaw and his team at Imperial Chemical Industries, UK, in the 1970s. He reported that by keeping the same production rate, one could decrease the equipment volume (size) by numerous orders of magnitude. A micro reactor is generally defined as “a miniaturized reactor with characteristic dimensions in micrometers and reaction holdups in the nanoliter to microliter range” [14]. The miniaturized methods are the chemical treating systems in three dimensional structured with internal measurement in the submillimeter range which is referred as micro reactors, microchannels, and/or micro structured reactors, it is also called as “microreaction” or “micro reactor” technology [15].

From the last few years, the use of a miniatured system in process industries is one of growing area. Miniaturization was shown significant development in many areas and as a result, micro structured reactors have gained a lot of acceptance. A micro structured reactor is a device consisting of several interconnecting microchannels fabricated by methods of microtechnology and precision methodologies [16 – 18]. The word ‘micro’ usually refers to the inner dimensions of the reactor and hence, it becomes more appropriate to use the term ‘micro structured reactor’ than using ‘micro reactor’ which is usually preferred for the outer dimensions [19, 20]. Different figures of microreactors are shown in **Figure (1.1)** and **Figure (1.2)**.

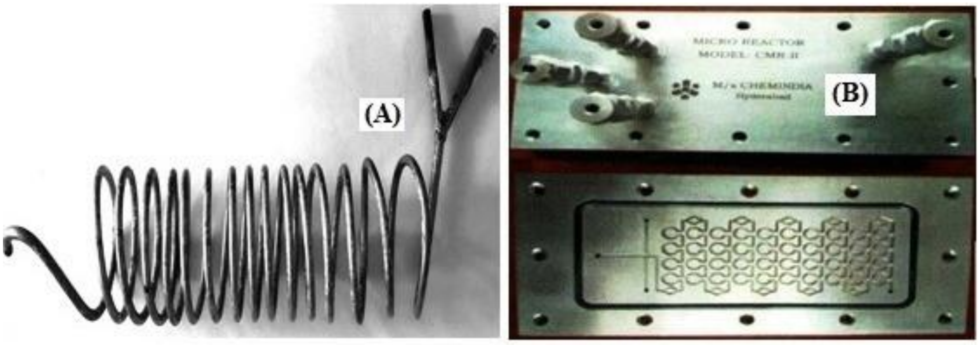


Figure (1.1). Microreactors (A) Helical (B) Plate with Omega structure.

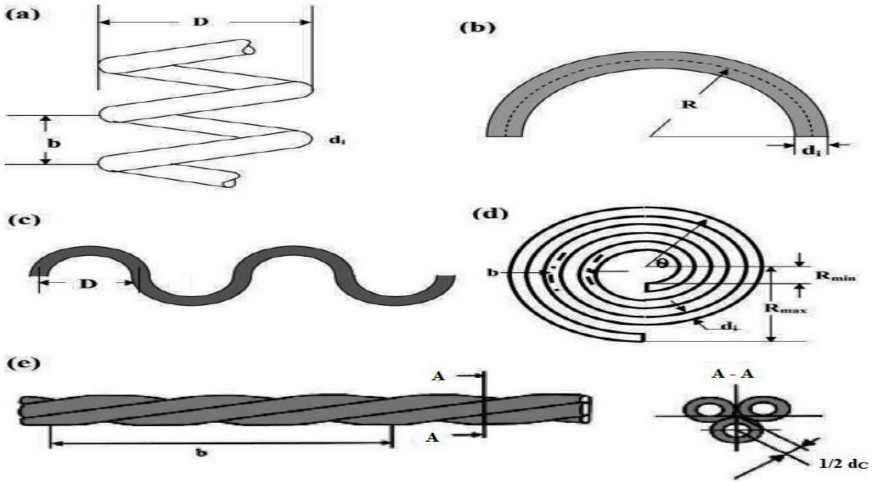


Figure (1.2). Different types of curved tube micro reactors (a) helical coil, (b) bend tube, (c) serpentine rube, (d) spiral, and (e) twisted tubes.

Micro reactor technology or micro reaction technology is a moderately new area. The initial micro reactor methods was reported in a German patent. Micro reactor technology has been taking as a tool in nanomaterial production, wastewater treatment, chemical synthesis, pharmaceutical products synthesis (Active Pharma Ingredients (APIs)) and also used to liquid – liquid (L – L), gas – liquid (G – L), liquid – solid (L – S), gas – solid (G – S) and gas – liquid – solid (G – L – S) phase methods. The micro reactor technology is a branch of PI to reduce equipment volume (size) which leads to occupy less space, low energy consumption, and minute waste production [17, 21 – 23].

Micro reactors fulfill the principles of sustainability by decreasing the generation of polluting components and allows to carry hazardouns reactions safely. Micro structured reactors are miniaturized reactors having dimensions from sub – millimeter to sub – micro meter internally. Micro structured reactors are commonly operated in a continuous flow mode having small hold up. The quantity of some kgs per day can be produced with a small volume. The smaller sizes of micro channels enhance the surface – to – volume ratio, which enhances the heat transfer as well as mass transfer. The micro reactors allow better control over chemical reactions. The micro structured reactors are suitable for exothermic as well as hazardous chemical reactions and reactions conducted at high pressure and temperature. The small diffusion space of micro structured reactors offers improved mixing which increases the conversion, quality, selectivity and yield of the chemical products [19 – 22].

Safe processing of dangerous, rapid, and strong exothermic reactions in microchannels is often the driving force to use the micro structured reactors [26, 27]. Since such reactors make use of small volumes, it permits the safe use of toxic and explosive reactants [7, 28, 29]. These reactions can be been performed in micro structured reactors that otherwise would to auto acceleration if performance at a large scale. For example, sodium nitrotetrazolate, a key reactant for the formulation of explosives and propellants, was produced by using a micro structured reactor [30]. Fluorination reactions which require F_2 charging and produces HF as a undesired product are particularly well suited to micro structured reactors due to their toxicity [31, 32]. Ebrahimi et al., [33] carried out continuous flow production of peroxyacetic acid and peroxyformic acid, both of which are highly unstable chemicals, in a micro structured reactor. They used sulfuric acid as a homogenous catalyst and the reactants were corresponding carboxylic acids and hydrogen peroxide. The benefit of the small length scale of these micro channel reactor systems from a safety point of view has made them most suitable for high pressure applications [34 – 36]. The use of micro reactor technology provides key to the manufacturers to attain the goals of green chemistry of chemical products by controlled operations [29, 37 – 39]. Liebner et al., [40] suggested a method for determining maximum safe diameters for micro structured reactors regarding detonative blast spread. They had studied the ethane oxide process and found that the $\lambda/3$ rule applied to microscale channels or tubes for stoichiometric combinations of ethane – nitrous oxide and ethane – oxygen, where λ

stands for report cell diameter. According to λ/3 rule, the explosion can spread if the internal diameter of a tube is greater than λ/3.

Another noteworthy feature of the micro reactors is the considerable reduction in operation time. This was demonstrated by Lomel et al., [41] who took the investigational works of Krummradt et al., [42] as basis, and showed how micro reactor is capable of conducting the chemical reactions in small time. The decrease in significant operation time from a semi – batch stirred tank reactor as compare to a continuous flow micro structured reactor in which mixing, heat transfer and mass transfer rates are high. Similarly, Liu et al., [43] effectively produced polyamide dendrons and dendrimers by a continuous flow micro structured reactor. These reactor shows numerous advantages as compared to a conventional flask (batch) reactor method. The advantage was that pure dendrons and dendrimers could be produced within a few seconds of residence time as compared to hours of time in a conventional batch mode reactor.

The above characteristics of micro structured reactors have made them efficient tools for improving the productivity fast exothermic reactions which were carried out in a conventional batch reactor. For instance, Wang et al., [44] performed a kinetics study on a fast exothermic reaction between oleum and cyclohexane carboxylic acid. They observed that the whole reaction method was accomplished in less than 1 second and the rate of reaction was controlled by the mixing of reactants efficiently. Besides, they also claimed that the improved mixing performance and detailed control of reaction time give high selectivity about 97 % at finishing temperatures ranging from 40 to 90 ℃. Thus, to use a continuous flow micro structured reactor for extremely exothermic reactions assists uniform temperature control during the reaction in the reactor owing to the higher surface area [45].

1.2.1. Micro reactors: material of construction, advantages and limitations

Material of construction: The selection of material for micro reactors is based on which type of reaction has to be carried out. Most of the micro reactors were made up of borosilicate glass, Corning glass, stainless steel (SS304, SS309, SS316, etc.), copper, PFE, PTFE, etc [21, 46 – 52].

Advantages: The advantages of the micro structured reactors are quicker process development and scaleup from lab to the industrial production scale by avoiding bench scale to pilot scale, it is simply possible by numbering up of micro reactors. The numbering up means increasing the number of micro channels or micro structured reactors when the operational developments keep on the same in all the single units. A serious disadvantage of micro reactor technology is the handling of solid/catalyst particles or slurry solution during a reaction. The solid particles can choke the micro reactor channels and halt a fluid flow. On the other hand, in spite of the risks, well ordered MRT is believed to be beneficial for various applications, particularly in the pharmaceutical industry and the fine chemical industry [21, 46].

Following are significances of micro structured reactors

1). Reliable scale – up.
2). Enhanced reaction rate, reaction selectivity, and reproducibility.
3). Fast mixing.
4). Fast heat exchange.
5). It is possible to conduct multiphase chemistry.
6). Multistep reaction in sequences can be conducted.
7). Immobilized catalysts can be used.
8).Improved safety of operation.
9). The reduction in overall cost of the plant. (to reduce overall cost) (e.g., due to smaller plant size, reduced and compact piping, lower energy, higher reaction rate, and product selectivity, increased purity (assay) and yields, negligible byproduct or a smaller amount of waste, etc.).
10). It improves the safety of reactions (e.g., controlled reaction conditions and small hold – up).
11). It can be accommodated in small space. Considerably high production quantity and several products per unit area of manufacturing).
12). It will decrease plant erection, operation and start up time (i.e., time to market).
13). Precise control over the process can be achieved.

Limitations: A micro structured reactor is a micro scale tool. Generally, a micro structured reactor has length 1cm to 5 m, breadth in the micro meter to the milli meter and perhaps thickness is in less than one – sixteenth of an inch (1.56 mm), although dimensions vary in the micro meter range [21, 53]. A micro structured reactor has normally input(s) and output tubes, with minute channels or chambers inside where a reaction takes place. Generally, the reactants and the product are fluids (liquids/gases or a combination of them). The reactants may be feed by syringe/HPLC pumps [21]. Micro reactors are used only for experimental and prototyping purposes, however, there is a real view for large scale production of useful chemicals.

The micro structured reactor is generally fabricated by etching small channels onto an appropriate material in a similar method used for the fabrication of integrated circuits. They can be prepared from silicon wafers, glass, metal or ceramic materials [46, 47]. The micro reactor of capillary size may not be bigger than a human hair. The etching may be done by laser, electrical discharge or by chemical methods. Frequently, the micro reactor is prepared from two different etched plates sandwiched together [50, 51]. While preparing the micro structured reactor very important care has to be taken otherwise there is a chance to get damaged to the microreactor. The main drawback of a micro structured reactor is clogging by tiny solid particle or suspension solid particle. Another problem is that it is difficult to carry out a chemical reaction having solids, either reactants/catalyst or products, in a micro reactor as they tend to block the micro structured reactor.

1.2.2. Flow behaviour in a micro structured reactor

When two immiscible fluids (liquid – liquid or gas – liquid) are fed into a micro channel at laminar flow through a mixing device, there is a chance for generation of four different flow patterns can exist. Those flow patterns are (1) parallel flow, (2) slug flow (3) regular droplet flow and (4) irregular dispersed flow. The flow patterns of straight and serpentine micro reactors are shown in **Figure (1.3)**. The flow patterns can be managed by the effect of various parameters such as velocity of the fluids, flow ratio of the fluids, physical properties of the fluids, geometry of the micro structured reactor and wall coating materials [238, 235 – 238]. There are many reports on the flow pattern in the literature that describes the formation of the flow pattern by employing Y – shaped as well as T – shaped mixing devices with various inlet arrangements [178, 228, 239 – 240]. The flow patterns are characterized by dimensionless numbers such Reynolds number, Capillary number, Weber number and etc. the dimensionless numbers formulas and their physical significances are reported in **Table (1.1)**. When a liquid – liquid flow patterns are formed, based on mass transfer rate, sufficient residence time for mass transfer has to be set in the micro reactors. The residence time for mass transfer in a micro reactor is the time that is spent from the first contact point at mixing device (element) up to the complete isolation of the phases at the phase splitter.

Table (1.1). Dimensionless numbers to characterize flow behaviour in a micro reactor.

Reynolds number (Re)	$\mathrm{Re} = \frac{\text{Inertial forces}}{\text{Viscous forces}}$	$\mathrm{Re} = \frac{\rho\, u\, d_h}{\mu}$
Capillary number (Ca)	$\mathrm{Ca} = \frac{\text{Viscous forces}}{\text{Liquid−liquid surface tension}}$	$\mathrm{Ca} = \frac{\mu u}{\sigma}$
Weber number (We)	$\mathrm{We} = \frac{\text{Inertial forces}}{\text{Liquid−liquid surface tension}}$	$\mathrm{We} = \frac{u^2\, \rho\, d_h}{\sigma}$

Where ρ is fluid density, u is velocity of the fluid in a microreactor, d_h is hydraulic diameter of the microreactor, μ is viscosity of the fluid and σ is surface tension between the fluids.

In the laminar flow regime, agitation of a parabolic velocity contour inside a straight capillary micro reactor can simply be obtained by coiling the capillary around a rod. The agitation is caused by the centrifugal forces that acts normal to the flow direction of the fluid along the helical capillary tube. Consequently, secondary flow pattern can be retained on the circular cross – section of the capillary micro reactor that is so called as Dean vortices. The Dean vortices can be denoted by Dean number, which relates the curvature ratio and Reynolds number (Re). The Dean number is determined by using Eq (1.1).

$$\mathrm{De} = \mathrm{Re} * \sqrt{\frac{\mathrm{d_t}}{\mathrm{d_c}}} \tag{1.1}$$

Where ρ is fluid density, υ is velocity of the fluid flow, $\mathrm{d_t}$ is diameter of tube inlet, μ is the viscosity of the fluid, $\mathrm{d_c}$ is the curvature diameter of the path of the tube and Re is the Reynolds number.

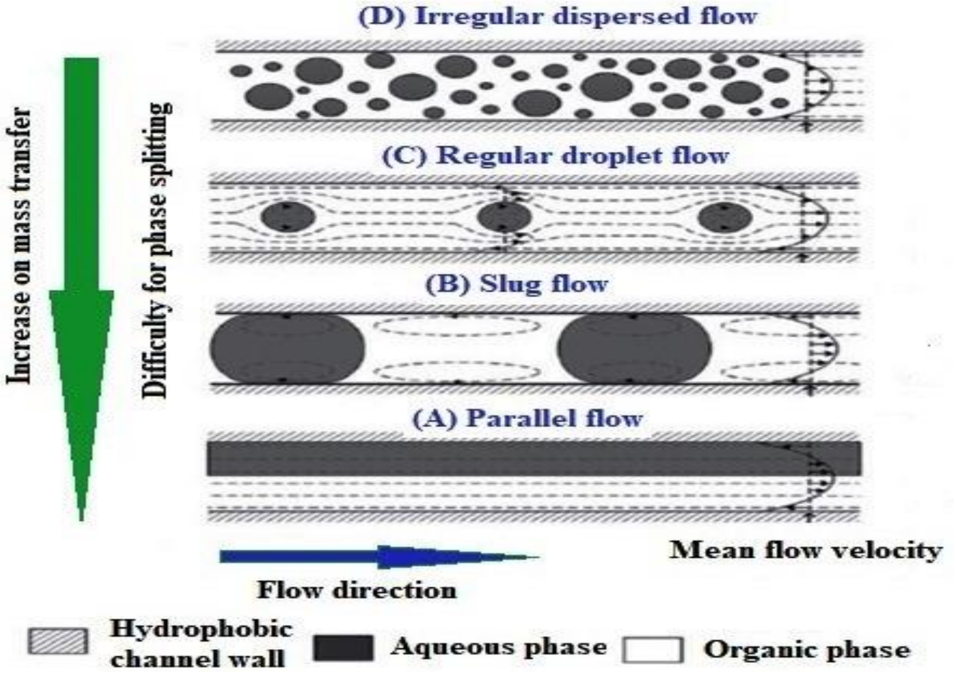


Figure (1.3). Flow pattern in micro structured reactor (a) parallel (b) slug (c) regular droplet and (d) irregular dispersed. [241].

1.2.3. Applications of the micro structured reactors

The application of a micro structured reactor in organic synthesis is a promising area. A micro structured reactor provides good mixing of raw materials, reduces reaction times, improved yields, enhanced selectivity and safe control of toxic and explosive materials. The development from laboratory to industrial production does not include any alteration to the techniques to reach optimum outputs. It is simply a matter of adding several micro reactor units or simply numbering up of micro reactor units. However, several issues that must get over to get efficient large scale manufacturing of chemicals by a micro structured reactor. One of them is the wall effect: reactants and products may tend to adhere to the walls of the reaction chamber. It is normally, insignificant for conventional chemical production using big reaction vessels but on the micro scale, a significant proportion of the possible yield may be increased [25, 54 – 56].

Micro structured reactors have heat exchange coefficient in the range of 1 – 500 MW/(m·K) but in a conventional batch reactor (10 kW/(m·K). Therefore, micro structured reactors could take away considerably and efficiently more heat than conventional batch reactor and even critical exothermic reactions such as nitration can be performed at higher temperatures. Hot spot condition may exist because of higher heat release rate in conventional reactor. Thus, micro structured reactors can permit improved kinetic studies, for the reason that local temperature gradients disturbing reaction rates are considerably lesser than in a batch reactor. Cooling and heating a micro structured reactor is also considerably faster and operating temperatures are as low as −100 ℃. Consequently, the higher heat transfer, reaction temperatures may be far higher, when compared to conventional batch reactors. A lower temperature process as metal – organic chemistry can be carried out in a micro structured reactor at − 10 ℃ rather than – 50 to – 78 ℃ as in laboratory glass equipment [21, 53].

Micro structured reactors are generally performed continuously. Continuous flow micro structured process allows the consequent treating of unstable intermediates. Particularly, at a lower temperature, chemical reactions with time in the range of millisecond to second. This quick work up avoids decrease the intermediates and frequently permits enhanced selectivity [57, 58]. Continuous flow process and mixing makes a different concentration profile over a batch method. In a conventional method, reagent A is fed in and reagent B is slowly fed. As a result, B finds initially a large excess of A. In a micro structured reactor, A and B are mixed virtually instantaneously and B would not be revealed to a high excess of A. This may be a disadvantage based on a reaction mechanism. It is essential to be attentive to such diverse concentration graphs. Though a benchtop micro structured reactor can produce chemicals only in lesser quantities, scaleup to industrial size is simply a procedure of increasing the number of micro structured reactors [59, 60].

Pressurization of ingredients within micro structured reactors is usually easier than with conventional batch methods (reactors). It permits reactions to be enhanced in rate by increasing the temperature at a boiling point of a solvent. This distinctive Arrhenius performance is more easily assisted in micro structured reactors and should be taken as an important advantage. The pressurization can also permit dissolving of reactant gasses inside the flow stream. Currently, researches are reviewing how to improve micro reactors's performance. Moreover, the surface to volume ratio is higher in micro reactors than in normal reactors. This characteristic brings about large wall effects in micro structured reactors. The chemicals in solution adsorb on the micro structured reactor walls which cause in a loss of concentration of a chemical [1].

Developments of micro structured reactors are guessed to rise their use in the formation of chemicals. In chemical engineering, there are some fields where the features of micro – process may be adpated especially process engineering. Micro structured reactors have been employed, e.g. in various harmful reactions (fluorination, chlorination, oxidation, sulfonation, nitration, and bromination) because of their safety features. Occasionally, the reactions have been carried out at higher pressure and temperature in the absence of safety issues. Peroxyformic and peroxyacetic acid are peracids having lower molecular weight, which were carried out by microstructured reactors. Hence, safety characteristics in the manufacture have to be stressed.

In the micro structured reactor, rapid mixing and quick heating are anticipated to form a small nucleation time, avoiding further nucleation and resulting in a fine particle size distribution. Instead, in the batch reactor elongated heating periods and a lesser mixing is expected in the formation of particle nuclei over a longer time, giving nanoparticles having bigger particle size distributions.

From last more than two decades, MSRs are used for the synthesis of various compounds of inorganic and organic materials which are most economically useful in the preparation of other compounds. It is also used to develop a new process and new technology. The MSRs are suitable for carrying out a numerous of chemical reactions in the field of chemical manufacturing industries, bulk drug industries, pharmaceutical industries, fine chemical industries, and some other specialty chemical industries in a continuous flow method.

1.3. Corning® Advanced – Flow™ Reactor (AFR)

Corning was found in 1851. Corning® Incorporated is familiar in specialty ceramics and glasses. It creates and makes basis materials that support high – technology methods. They followed through their continuous investment in R & D (Research and Development) over 160 years for materials science, process engineering information and distinctive, combined culture. They prepared a specialty glass. The Corning® micro structured reactors are well – matched with a wide diversity of chemicals making most of the chemistries possible to occur in it.

Corning had made continuous flow micro structured reactors over 160 years of their innovation. It was introduced in the year 2002. The technology provided for bigger gen sizes of advanced materials (glass and/or ceramics) to increase throughput. They extended broad capacity from possibility to bulk production scale and change from batch method to continuous mode. A single plate volume (about 0.45 mL) is low internal volume and also used for minimal number of reactants [61]. The innovative capacity is now making for noteworthy performance benefits to industrial chemical manufacturing in the formula of Corning® Advanced – Flow™ Reactor (AFR) (glass microreactor). The AFR gives a huge output and is simple scalable microstructured reactor that may be tailored to customers' precise need supporting a cost-effective result for a single reaction or multiple reactions [61, 62]

Advanced – Flow™ Reactor (AFR), is patented technology of Corning® industry, the name itself suggests the continuous flow process. It is invented by a Corning® industry. The AFR is one of the continuous flow micro structured reactor in which numerous conventional batch reactions can be successfully performed and significantly optimized.

The number of AFR plate units are assembled to form a continuous flow operation unit. It assists handling of tons of quantity product per year with small volumes, usually a few liters. The AFR can be employed for optimizing a chemical reaction or group of chemical reactions, some of which have not earlier been possible. The modules of Corning micro structured reactors are well suited to treat a wide range of chemicals and solvents from – 60 up to 230 ℃ and pressures up to 18 bar. Different designs can be made to put up multi – phase systems that can be sequentially assembled into an engineered reactor, allowing mixing of various reactants with suitable residence times. The AFR can be employed for continuous flow manufacturing of a variety of chemical products like pharmaceutical, biodiesel, dyes, etc.

Corning® Advanced – Flow™ Reactors are five types. They are Low flow, G1, G2, G3, and G4 reactors. In brief, the low flow has the volume of 0.5 mL, G1 has the volume of 5 – 9 mL, G2 has the volume of 20 – 25 mL, G3 has the volume of 50 – 70 mL and G4 has the volume of 250 mL of a single plate. Low flow holds low internal volume and uses the minimum number of reactants. G1 holds small holdup, it can be used from lab test to production scale and it can be used as a optimization tool. G2 and G3 can be used for continuous flow production of a large number of chemicals. Finally, G4 holds large volumes, small footprint, manufacturing more than 300 kg/h [63, 64].

A key element of an AFR is a specialty glass module of fluidic of hydraulic diameters from 0.3 mm to upto few millimeters. The AFR has small channels (heart – shaped) offers advantages over conventional batch method and some other micro structured reactors as a result of faster and vigorous mixing, improved heat transfer and mass transfer. The higher aspect ratio of the micro channels increases heat transfer for exothermic reactions, therefore avoiding thermal degradation of the product form. It tolerates the control of reactions that need very shorter residence time, good as well as quick mixing and assists in carrying out greener, cheaper to run and safer procedures. It is combined of series of like modules (cells) with variable area and internal elements whose presence governs the formation of a jet as well as forces the liquid to split and then rejoin. The mechanism is shown in **Figure (1.4)**. It results in an efficient and continuous good mixing along the live time path, even at low flow rates, without the need for catalyst, additives and so on.

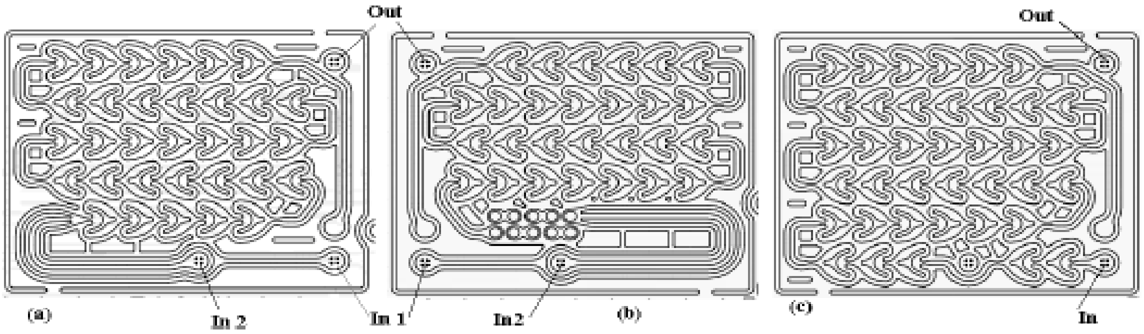


Figure (1.4). Mixing and dwell time fluidic module [65].

1.3.1. Mass transfer and heat transfer in AFR

The fluidic module which has shown in **Figure (1.5)**, consist of four glass plates, these are some standard size of plates designed by the corning as per the scale – up requirements. The modules are specially designed to increase the mixing, turbulence in the reaction so that they increase the mass and heat transfer rates. So, it reported that there is a tremendous increase in heat transfer and mass transfer, it contributes to an increase in conversion of reactants [62, 66].

From **Figure (1.5)**, it is noticed that there are four plates which are fixed in the manner such that a chemical process (chemical reaction) is carried out inside the reaction layer. The reactants are allowed into continuous flow reactor (AFR) at the same time. The outside layer named as a heat exchange layer, which is the pathway for utility. The layers are used to manage the temperature of a chemical reaction by allowing circulation of the fluid, cold or hot fluid, as per the process requirement. It is found that there are negligible heat losses in AFR because of their special fluidic module designed. This reactor is best effective for liquid – liquid reaction, liquid – gas reaction, and non – miscible liquids and a slurry reaction having a particle size less than 200 µm [66].

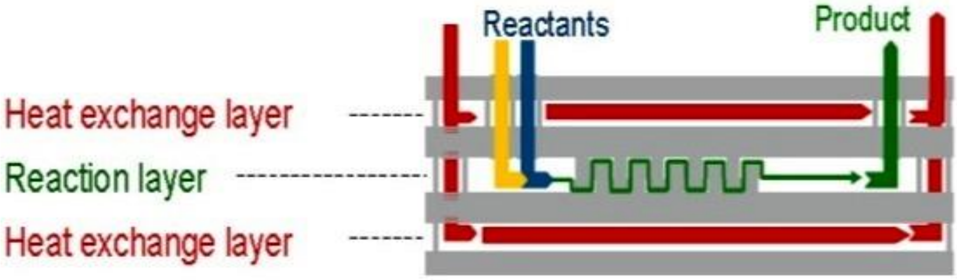


Figure (1.5). Heat exchange and mixing integrated with a fluidic module [66].

The AFR has the potentiality to carry out various reactions simultaneously without batch work out delays. Furthermore, the AFRs require a lesser amount of energy, less space, and small amount of raw materials per volume of finished material which results in reducing the cost of manufacturing with enhancing the quantity, quality, and safety of chemical processing of a chemical reaction. The reactors are also aimed to avoid cross – contamination of finished products. The AFR supports to increase product assay, selectivity and finally production yield. Advanced flow reactor is scalable, reliable, customized, and cost – effective, apart from this many pharmaceutical industries are applying this technology to improve their product quality and production quantity in a very short time.

1.3.2. Applications of AFR

The AFR was used for many reaction processing, which is as follows

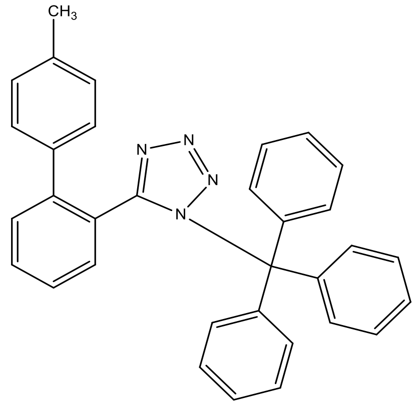
1. Chemistry of chloroformate: improved yield easily monitored by online Raman spectroscopy as a process analytical technology (PAT).
2. Ritter reaction of diastero – selective – Increased productivity with safe and easy to deal with the operation.
3. Reactions of nitration in Advanced Flow Reactor: decreased solvent usage, increased yield of the safe operation, Feasibility → pilot → successful production → cGMP, mixing quality versus conversion and selectivity.
4. Hydrogenation with a selective slurry catalyst: 98% plus conversion and selectivity
5. Reduced temperature applications: energy saving and/ or higher yield
6. Green process technology: Glycerol conversion to fuel additives: extensively decreased the usage of raw materials.
7. Application of sulphonation reactions – full conversion reached with high assay (purity).
8. Application of Beckmann rearrangement – stable and enhanced results conforming to performance targets.
9. Application of photochemical reaction – high productivity with ease of controls
10. Enhancing the reaction rates in the AFR – substitution to microwave reactors
11. The reaction of schotten – Baumann amidation: higher yield through better mixing.
12. Application of dipeptides production – no formation of precipitates in biphasic solvents for amine attachment.
13. Preparation of Grignard reagent – specific control results in the improved assay (purity) of finished products.
14. Continuous flow synthesis of alkyl nitrite – higher production capacity.

1.4. Tritylation reaction and uses of tritylated compounds

The trityl group (triphenylmethyl) is a protecting group for biphenyl tetrazole and hydroxyl benzyl tetrazole. The trityl group can be easy detached and attached by slight acid process [67 – 74]. It is extensively known that the reaction of tritylation involves the addition of the triphenylmethyl carbonium ion on the nucleophilic compound through an S_N1/S_N2 mechanism. The substitution rate is influenced by the capability of its components to privilege the heterolytic breaking of the Tr – Y bond. The triphenylmethyl bromides and triphenyl methyl chlorides (Y = Cl, Br) are employed in the presence of bases of organic (pyridine or triethylamine or 2, 4, 6 – collidine or 1, 8 – diazabicyclo [5.4.0] undec – 7 – ene (DBU) or N, N – dimethylamino pyridine (DMAP) or 2, 4, 6 – tertbutyl pyridine, etc.) or bases of inorganic (potassium carbonate or sodium carbonate and so on) [74, 75].

5 – (4' – methyl – [1, 1' – biphenyl] – 2 – yl) – 1 – trityl – 1H – tetrazole chemical structure was shown in chemical structure 1.1, which is a significant used material for the synthesis of numerous angiotensin – II antagonists, they fall under the Sartan’s family drugs [76 – 83] such as trityl Irbesartan, trityl olmesartan, losartan potassium, candesartan, valsartan, trityl candesartan cilexetil, etc., [83 – 88].

Till date, researchers are attracted to alter conventional procedures to continuous flow micro structured reactor methods to decrease the time of a reaction as well as the cost of production. The main benefits of the continuous flow micro structured reactors compared to the conventional batch reactors are continuous output and better micromixing and enhanced selectivity and yield in a shorter time. Researchers are attracted by the process intensification by the continuous flow micro structured reactors to be used for the complex pharacutical reactions. Pharmaceutical drugs preporation reactions and extremely exothermic reaction processes are intensified through a continuous flow micro structured reactors. Micro structure reactors can be engaged for the continuous flow manufacture of pharmaceuticals chemical products as well as fine chemicals. Helical coiled tubular devices in micro scale can additional enhance the performance of momentum and mass transport due to the secondary flow generation (Dean Vortices) [89]. The secondary flow increases the radial mixing along the tube and it causes to decrease the axial mixing [90 – 94]. Because of the narrow geometric constructions of a channel, micro structured reactors offer increased selectivity and yield. Consequently, they can be applied as the intensification of a process tool [7].



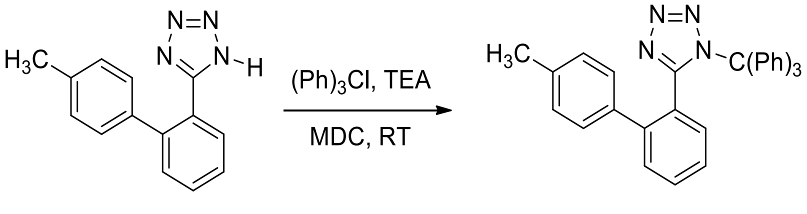
5-(4'-methyl-[1,1'-biphenyl]-2-yl)-1-trityl-
1*H*-tetrazole

Chemical Structure: 1.1. Structure of MBPTT.

One of the significant limitations of the tritylation reaction carried out the process by a conventional batch is nonhomogeneous mixing of the raw materials which results in lower yield. Moreover, the reaction is completed within 2 h by the conventional batch method. Although, continuous flow tritylation procedure has the benefit of efficient mixing, the increased conversion in a very shorter time (i.e. approximately 27 s to 324 s). Therefore, there is a huge amount of energy – saving and operating cost. The reaction performed in micro structured reactors is safe to treat compared to the batch method.

Many researchers were carried out the tritylation reaction using a conventional batch mode at various operational conditions. Pineshkumar et al., [95], Wang et al., [96], and Ana et al., [97], were studied formation of 5 – (4' – methyl – [1, 1' – biphenyl] – 2 – yl) – 1 – trityl – 1H – tetrazole (MBPTT) in a traditional batch procedures at different temperature (from room temperature to upto 80 °C) and using the different type of solvents (monochlorobenzene, toluene etc) and obtained yield in the range of 83 % – 92.6 %. Although, in this thesis, it has been planned to perform the continuous flow tritylation reaction at room temperature using dichloromethane as solvent. So, it was found that better yield is obtain in small time compared to conventional batch reactor, which is the key advantage over the conventional mode (batch) procedure.

The balanced chemical reaction is shown in **Scheme – (**1.I).



(1.I)

Scheme – (1.I). Synthesis of 5 – (4' – methyl – [1, 1' – biphenyl] – 2 – yl) – 1 – trityl – 1H – tetrazole.

There is no report found on the formation of 5 – (4' – methyl – [1, 1' – biphenyl] – 2 – yl) – 1 – trityl – 1H – tetrazole by continuous flow micro structured reactors. So, it encouraged and motivated us to carry out this work by using different continuous flow micro structured reactors configurations. Furthermore, comparison of the stainless steel capillary coil reactor (SSCR – 2 mm and SSCR – 1 mm internal diameter) and AFR is made in terms of yield for synthesis of MBPTT in a homogeneous liquid phase.

1.5. Peroxycarboxylic acids and their uses/applications

Performic acid (PFA), Peracetic acid (PAA), Perpropinic acid (PPA) belongs to Peroxycarboxylic acids (PCA, RCOOOH, where R = H, CH_3, C_2H_5 and so on) family. The PCA also some times called as Peracids (PA).

Performic acid: the PFA is an organic solvent having low molecular weight. The performic acid is ecofriendly and generally employed in many industries such as textile, paper, medical, food and chemical for bleaching, disinfectant agent and chemical processing owing to its high oxidative property [98 – 103]. The performic acid is very active oxidizer and decomposes at a temperature of 40 ℃ and above [101].

The PFA is a strong oxidizer compared to PAA (peroxyacetic acid) and HP (hydrogen peroxide) which makes the PFA a more familiar oxidizing agent. The PFA is a very multipurpose epoxidation agent for unsaturated oil [104 – 107]. Generally, epoxidation of vegetable oil is catalyzed by mineral acids for example sulfuric acid (H_2SO_4) along with the performic acid. The peroxyformic acid is employed in the epoxidation of soybean and any other vegetable oils in the presence of a catalytic quantity of a mineral acid such as sulfuric acid [107 – 114]. The PFA is mainly prepared using the reaction between formic acid and hydrogen peroxide in the absence or presence of a catalyst such as a homogeneous catalyst of a mineral acid (H_3PO_4 or H_2SO_4) [33, 115, 116] or the presence of a heterogeneous catalyst (Amberlyst and Amberlyte and so on) [117, 118]. The chemical reaction is as reported below as shown in **Scheme – (**1.II).

$$\mathrm{HCOOH\ (A)} + \mathrm{H_2O_2\ (B)} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \mathrm{HCOOOH\ (C)} + \mathrm{H_2O\ (W)} \qquad (1.II)$$

Scheme – (1.II). Synthesis of performic acid.

The synthesis of performic acid is mild exothermic reaction. The forward reaction is called as “perhydrolysis” and the backward reaction is called as “hydrolysis”. Some of the reports have shown that hydrogen peroxide is stable below 100 ℃ in an acid environment, while performic acid is subject to break down at room temperature in contact with impurities like metal [105, 117, 119, 120].

A micro structured reactor has taken a place for numerous hazardous as well as exothermic reactions such as fluorination, bromination, chlorination, nitration, oxidation, etc., as there is improved control over the reaction rate as compared to traditional batch reactors

[16, 53, 121, 122]. Many researchers reported planar geometries of micro structured reactors to study the advantages of better mixing, mass and heat transfer in a continuous flow production. Mixing, mass as well as heat transfer in a micro structured reactor, is taken by the laminar flow. The perturbation of a laminar flow supports to increase the diffusion in the micro structured reactor. The perturbation is influenced by curved geometries which cause to produce vortices in the micro structured reactors [123 – 125]. Formation of vortices influences the mixing by convection. Hence, the axial dispersion within the capillary micro structured reactor can be reduced [126, 127].

As compared to the planar geometries of micro reactors, the helical coiled capillary micro structured reactors compete in terms of residence time distribution (RTD). The planar micro structured reactors have the residence time in minutes, while the reaction in a helical coiled capillary micro reactor completes the reaction within few seconds. The extended residence time in planer geometries largely affects the selectivity of compounds [125, 127 – 131]. It is a well – known fact that as the Dean vortices increases [89], the mixing along with the radial direction increases, eventually it will affect the rate of reaction. The RTD profile is narrow in case of helical coiled capillary micro structured reactors as compared to straight capillary micro structured reactors [131 – 134]. Recent reports discovered that the helical coiled capillary micro structured reactor consistently gives enhanced mass transfer and heat transfer coefficients over straight capillary micro structured reactors due to the generation of secondary flow pattern, i. e., Dean vortices [89, 134]. Therefore, looking to the number of advantages of the helical coiled capillary micro structured reactor mentioned above. So an attempt was made for the synthesis of organic compounds.

However, several studies described the formation of the PFA in a traditional batch method. Although, some researchers studied the formation of the PFA in a planar micro structured reactor system [33, 117, 135 – 137].

Peroxypropionic acid: Peroxypropionic acid is an organic solvent having a molecular formula of C_2H_5COOOH (RCOOOH, R = C_2H_5). The peroxypropionic acid classified under the family of peracids [138 – 141]. The percarboxylic acids are usually used due to their effective oxidation properties. The peroxycarboxylic acids are extensively employed for the decomposition of pollutants, pesticides, and as bleaching agents in the paper industry as well as in the manufacturing processes of the fine chemical products [103, 137, 142 – 146]. The peroxypropionic acid is produced by the reaction between propionic acid and hydrogen peroxide using a catalyst [118]. It can also synthesized without catalyst however, the yield obtain is very small. So, a catalyst is used to produce peroxypropionic acid. The catalyst may be homogeneous catalyst such as mineral acids like sulfuric acid, phosphoric acid, etc., [114, 146] or heterogeneous catalyst such as Amberlite IR – 120, Amberlyst 15, Smopex – 101, Dowex, etc) [118, 147]. The chemical reaction was as shown in **Scheme** – (1.III).

$$\mathrm{C_2H_5COOH\ (A)\ +\ H_2O_2\ (B)} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \mathrm{C_2H_5COOOH\ (C)\ +\ H_2O\ (W)} \qquad (1.III)$$

Scheme – (1.III). Synthesis of peroxypropionic acid.

Presently, micro reactor technology is one of the most beneficial current technologies in chemical manufacturing, pharmaceutical chemical production, process technology and so on. The micro structured reactors afford numerous benefits in the chemical process engineering [147 – 150]. As a result, hazardous or exothermic reactions can safely be performed using the micro structured reactors because of the small amount of volume used in the micro structured reactors [21, 33, 122]. There is energy – saving and safe operation can be conducted compared to conventional batch methods. The improvements are essentially important in multiphase reaction processes (gas – liquid or liquid – liquid processes) and in other categories of mixing processes. Furthermore, micro reactor technology extends entry to an innovative process methodology and formation of a product. Nowadays, micro reactor technology has efficiently utilized as a tool for optimization and process intensification in the R and D labs of chemical processes plants and research organizations.

A helical capillary micro structured reactor (HCMR) provides improved mass transfer and heat transfer as well as better mixing of the reactants as compared to the planar micro structured reactors (PMR). The RTD (residence time distribution) is narrow in the HCMR whereas the RTD is significantly broad in the PMR. It could occur because of secondary flow generation by Dean vortices [89, 133, 135] in the HCMR. Mixing occurs along the length of the PMR whereas the mixing takes place along the length of the micro structured reactor as well as in the radial direction in the helical capillary micro structured reactor. So, the secondary flow, in the helical capillary micro structured reactor, affects the reaction rate is reduced residence time. Therefore, due to an enormous of advantages of the helical capillary micro structured reactor, an attempt was made to use the helical capillary micro structured reactor for the synthesis of perpropionic acid [126, 127, 129, 134, 135, 151].

Peracetic acid: the Peracetic acid is an organic solvent and has the chemical formula of CH_3COOOH. Peracetic acid is a colorless liquid. It has pungent fragrance indicative of acetic acid [152]. The PAA comes under the family of the peracids (RCOOOH) and also called as an organic peroxide. The PAA is ecofriendly oxidizing chemical (solvent) and usually used as a solvent in many industries (e.g., chemical, paper, textile, medical, food, etc) [103, 143, 144, 152 – 155]. The PAA is very active oxidizer and weaker acid than acetic acid and it has a pK_a of 8.2 [152]. Furthermore, the peracetic acid is unstable solvent (compound) which can be decomposed at the higher heat (at the higher temperature, i.e. above 80 °C) and contact with impurities like metals even in mild conditions [33].

The PAA is more active than peroxypropionic acid and less active than peroxyformic acid. So, peracetic acid is also one of the popular oxidizing chemicals like hydrogen peroxide. The peracetic acid is normally produced from the reaction of hydrogen peroxide and acetic acid in the absence or the presence of a catalyst (H_2SO_4 or H_3PO_4 (mineral acids)) [33, 121, 154, 155]. The reaction is represented in **Scheme** – (1.IV).

$$\mathrm{CH_3COOH\ (A)\ +\ H_2O_2\ (B)} \xrightleftharpoons[k_2]{k_1} \mathrm{CH_3COOOH\ (C)\ +\ H_2O\ (W).} \qquad (1.IV)$$

Scheme – (1.IV). Synthesis of peracetic acid.

The reaction is reversible as well as mildly exothermic in nature. The conversion of the constituents at the equilibrium state are comparable. The forward reaction is termed as "perhydrolysis" and the reverse reaction is termed as "hydrolysis". The forward reaction and reverse reactions are very slow at room temperature. It is further found that the peracetic acid and hydrogen peroxide are not stable and decomposes when the temperature rises (i.e for specific compound) above a certain threshold value [53, 117, 121, 122].

Micro structured reactors have been employed for numerous types of reactions such as hazardous reactions (such as chlorination, bromination, fluorinations, nitration, and oxidation) and nonhazardous reactions etc., due to their safety aspect [121, 123, 156, 157].

There are some studies on planar microreactors, to classify their mixing, mass transfer and heat transfer performance over the helical capillary micro reactors which were introduced. In a micro reactor, the flow is laminar due to the smaller size (few mm) in a channel or tube, which governs the mixing, mass transfer and heat transfer within a micro structured reactor [126, 129, 158, 159]. So, the perturbation of the laminar flow is preferred to increase the transport developments. The perturbation can be influenced by changing planar structure to curved geometries to form vortices in the micro structured reactors [125, 126, 129, 159 – 164]. The generation of vortices can associate in the convective mixing. Henceforward, the axial diffusion along the micro structured reactor can be reduced. Consequently, a reasonably narrow RTD can be attained for the residence times from few minutes to few seconds. On the other hand, a narrow RTD with high residence time of a few minutes can be important for the methods, where complex chemical process arise to enhance a desired product selectivity [126, 128 – 131, 135, 165 – 169]. It is reported that Dean Vortices increases the agitation or mixing in the radial direction along with axial direction for the single or multiple phase flow. Hence, it affects narrow residence time distribution compared to straight capillary micro structured reactors. Consequently, recent literature studies reported that helical capillary micro reactor offers increased heat transfer as well as mass transfer rates as compared to planar capillary micro structured reactors by the generation of secondary flow (Dean vortices) [89, 135].

There are a very few reports found on the synthesis of peracetic acid in both batch and planar continuous flow micro structured reactor system [33, 121, 155, 170 – 173]. In this thesis, a comparison of the serpentine capillary micro reactor, Corning® Advanced – Flow™ Reactor and helical capillary micro reactor were employed to study the formation of the peracetic acid and performance of micro reactors.

Uses of peroxycarboxylic acid:

Performic acid: the performic acid is employed for splitting disulfide links in protein mapping, besides for hydroxylation, epoxidation, and reactions of oxidation in the organic chemistry. The performic acid used as a disinfectant agent to clean the equipment in the medical as well as food industries. The performic acid is active agent against some mycobacteria, microscopic fungi, algae, viruses, bacterial spores, and zooplankton. The most important disadvantage is handling of PFA. Due to its instability and high reactivity, at above 50 ℃, PFA should be employed within 12 h of it being synthesized. [102].

Peracetic acid: the peracetic acid is used as an antimicrobial for indoor cleaning and as well as it is used in the agricultural sector, washrooms, and hospitals. The PAA also employed in the dairy processing plants and cleaning of processing equipment of the food preparation industry, such as pasteurizers, breweries, wineries plants, etc. The peracetic acid also employed for the disinfection of hospitals, to inhibit the biofilm formation in the industries such as pulp making, as a disinfectant as well as a water purifier. The PAA furthermore employed as water disinfectant for cooling tower industrially, where it stops biofilm formation and to effectively control legionella bacteria. The peracetic acid applied for an epoxidation of various types of alkenes [154, 172]

Peroxypropionic acid: the peroxypropionic acid may be used for epoxidation, hydroxylation, for the production of a lactone, production of quinone, ring – opening reactions of aromatic compounds, production of phenols, ketone oxidation.

1.6. Aim and objectives of the research work

Aim: the aim of this research work is to study the performance of a micro structured reactor for a continuous flow synthesis/production for selected chemical reactions which are industrially important.

Objectives: The objectives of the research work are as follows

1. Synthesize of 5 – (4' – methyl – [1, 1' – biphenyl] – 2 – yl) – 1 – trityl – 1H – tetrazole through a micro structured reactor and its characterization by Melting Point, FTIR, and NMR.

2. Synthesis of percarboxylic acids and their kinetic studies through a micro structured reactor.
3. To study the effect of different parameters for instance temperature, molar ratio, the radius of curvature, concentration of catalyst on the production of percarboxylic acids and comparison of different micro reactors for the production of MBPTT and PAA, etc.

1.7. Scope of the thesis work

The present study mainly focused on the development of an efficient tool for the production of organic chemicals using micro reactor technology.

Thesis reports about the performance of micro structured reactors for selected organic chemical reactions such as tritylation reaction and percarboxylic acids reaction. In this work, the synthesis of 5 – (4' – methyl – [1, 1' – biphenyl] – 2 – yl) – 1 – trityl – 1H – tetrazole was carried out by using stainless steel capillary micro reactors and Corning® Advanced – Flow™ Reactor, the MBPTT was characterized by FTIR and NMR. Similarly, synthesis of different peroxycarboxylic acids (peroxyformic acid, peroxyacetic acid, and peroxypropionic acid) was carried out by using Teflon helical capillary micro structured reactor and AFR (for peracetic acid). The concentration of peracids were determined by titration method.

Chapter – 1 reveals the introduction and background of micro structured reactors, process intensifications and its application. This chapter describes the fundamentals of micro structured reactors, advantages, and disadvantages of micro structured reactors and its applications for various types of reactions, etc. This chapter also describes the flow pattern in a micro reactor. This chapter also describes Corning® Advanced – Flow™ Reactor and its working principle as well as its application for various types of reactions.

Chapter – 2 represents the comprehensive review of the literature on micro structured reactors. This chapter also describes the literature on the tritylation reaction and percarboxylic acid synthesis and its kinetic studies. A brief literature review was carried out on process intensification, micro reactors or micro structured reactors. This chapter also reports the motivation, problem definition and gaps identified from the literature.

Chapter – 3 This chapter reports about the experimental setup which is used to carry out the experiments on tritylation reaction as well as peracids reactions. Different types of micro reactors were used to carry out chemical reactions. In this chapter, the experimental condtions were explained briefly and the images of different micro reactors are reported. To carry out the experiments, stainless steel capillary micro structured reactor, Advanced – Flow™ Reactor and Teflon capillary micro structured reactor were used.

Chapter – 4 is divided based on different types of reactions carried out in micro reactors. The first reaction is the tritylation reaction, in which synthesis of 5 – (4' – methyl –

[1, 1' – biphenyl] – 2 – yl) – 1 – trityl – 1H – tetrazole is carried out. The second reaction is the synthesis of performic acid. The third reaction is the synthesis of perpropionic acid. Finally, the fourth reaction is the synthesis of peracetic acid.

4.1. Case Study – I gives the detail information about materials used in the preparation of 5 – (4' – methyl – [1, 1' – biphenyl] – 2 – yl) – 1 – trityl – 1H – tetrazole. This chapter provides the production of the MBPTT by using different micro structured reactors. This chapter also provides the information of characterization of the MBPTT. This chapter also provides the details of hydrodynamics of fluid flow through SSCR – 2 mm, SSCR – 1 mm and AFR and there flow regimes.

4.2. Case Study – II demonstrates the synthesis of performic acid by using a Teflon capillary micro reactor. This chapter also gives the information on the effect of various parameters like concentration of catalyst, the concentration of hydrogen peroxide, temperature and radius of curvature on the synthesis of PFA. The best operating parameters were developed for the formation of performic acid and also kinetic studies are reported.

4.3. Case Study – III describes the continuous flow production of peroxypropionic acid by using the helical capillary micro structured reactor. This chapter describes the perhydrolysis of peroxypropionic acid and the effect of various parameters like concentration of hydrogen peroxide, the molar ratio of reactants, radius of curvature of the micro reactor, concentration of catalyst and temperature. This chapter gives information about the kinetic study, the expressions of reaction rate constants and activation energies.

4.4. Case Study – IV reveals the production of the PAA using different micro structured reactors. This chapter gives information on the production of peracetic acid at different molar ratios, three different configurations of micro reactors, the concentration of catalyst and temperature. This chapter also provides the information on the kinetic study for the formation of the PAA by AFR and Teflon capillary micro structured reactor.

Finally, the **chapter – 5** reveals information about the overall conclusions as well as the future scope of the present work.

CHAPTER – 2

REVIEW OF LITERATURE

From the last few years, the use of micro structured reactors is rapidly growing technology in the pharmaceutical as well as in the bulk chemical manufacturing industries to fulfill the demand in industries. Many researchers are working on mico structured reactors and their applications in wide areas in order to investigate their applicability in a chemical industry.

The present chapter consists of brief literature survey on a micro structured reactor, Corning® Advanced – Flow™ Reactor, tritylation reaction by conventional batch method, and synthesis of peracids (for example peroxyformic acid, peroxyacetic acid and peroxypropionic acid) by batch as well as using micro reactors.

2.1. Review on micro structured reactors

Wolfgang et al., [53], reported that the word “micro reactor” generally represented to the small scale tubular reactor employed in chemical processing and research areas of catalysis. So, developments of micro reaction technology, which had developed synonymous to micro fabricated methods involving numerous sub – millimeter channels where fluid flows continuously and a chemical reaction takes place in channels. The micro structured reactors gives higher throughput over the conventional batch method. The miniaturized systems were fabricated by micro technology methods as well as precision engineering methods. The characteristic measurements of the inner structures of micro structured reactors normally in the range from submicrometer to submillimeter.

Burns and Ramshaw, [174], described the process intensification of a fast reaction in multiphase methods using slug flow in capillaries. They carried out all experiments in micro device made up of glass. They used micro reactor of dimensions such as W = 0.38 mm, H = 0.38 mm and L = 70 mm for the system of acid – base reaction. They used T – joint to introduce the reactants to the micro structured reactor setup. The reaction of (acetic acid (AA) and NaOH or KOH) scheme as shown in **Scheme – (2.I)**. The ratio of flow was set at 1: 1 for all the experiments. The generation of internal circulation within the slugs during the flow of slug was shown in **Figure (2.1).** They noticed that 62 % AA had been moved in 1.6 s at high speed of 28 mm/s as compared to a time of 3 s at slow speed of 5 mm/s. Moreover, they identified that the acetic acid – NaOH (62 % in 2 s) consumption had shown better mass transfer than the acetic acid – KOH (50 % in 3 s). The reason for the variance in slug sizes is due to the effect of chemical concentration (composition) on the surface wetting as well as contact angles for the different methods. Nevertheless, it could not seem to disturb the relationship between slug length and mass transfer or velocity and mass transfer. They also studied the time and distance requirement for acetic acid transfer, slug lengths produced, mass transfer during slug generation. They also used an empirical model for acetic acid transfer and estimation of mass transfer coefficients for the systems.

$$CH_3COOH + NaOH \text{ or } KOH \longrightarrow CH_3COONa \text{ or } CH3COOK + H_2O \qquad (2.I)$$

Scheme – (2.I). The reaction of acetic acid with base.

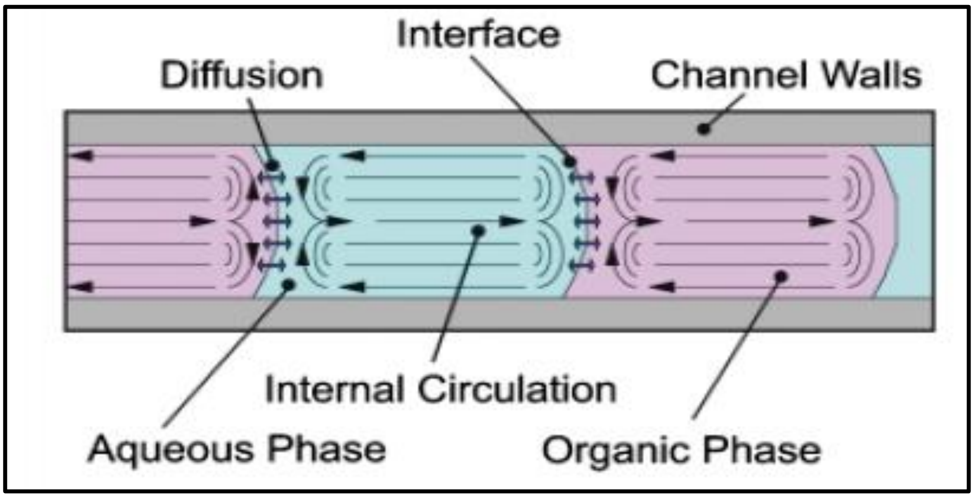


Figure (2.1). Image of the internal circulation generated within immiscible slug flow [174].

Burns and Ramshaw, [175] studied benzene nitration and toluene nitration using a stainless steel micro reactor (internal diameter = 127, 178, 254 µm bores and length = 50 cm) and toluene using a polytetraflouroethylene tube (PTFE, internal diameter = 150 µm bore tube and length = 135 cm) reactor using nitrating agent as nitric acid (HNO_3) in presence of homogeneous catalyst (for example sulfuric acid (H_2SO_4)). The experimental setup was shown in **Figure (2.2)**. They performed mixed acid nitration reaction over benzene or toluene in a capillary micro reactor using different mixtures of acid, flow rates, temperatures, and aqueous phase – organic phase flow ratios. The product was collected from micro reactor in the sample bottle, it contains organic and aqueous components: those were water and toluene for benzene nitration and dichloromethane for toluene nitration. The benzene nitration was performed at different parameters like sulfuric acid (70 to 85 %), acid mixture (sulfuric acid: nitric acid = 72: 4.5, 78: 4.9 and 73: 2.6, the ratios are in percentage), temperature (60 to 90 ℃) and flow velocity (2.0, 7.7 and 18.5 cm/s). Similarly, nitration of toluene was performed at different parameters like temperature (25, 60 ℃), acid mixture (sulfuric acid: nitric acid = 80: 12, 78: 7, 63: 25 and 49: 35, the ratios are in percentage) and acid and organic flow ratios varied from 2 to 7. Therefore, they concluded that flow of slug in the capillary micro reactor gives an efficient mass transfer among the two immiscible reacting liquids in seconds. The flow behaviors were shown in **Figure (2.3)**. Finally, nitration of toluene and benzene outcomes revealed that higher flow rates could be employed to increase rates of the reaction with sufficient residence time, at the cost enhanced pressure drops, because of the enhanced convective transport inside the slugs. Both toluene and benzene had stated that the rates of the reaction from 0.5 min^{-1} to 20 min^{-1} could be produced from a capillary micro reactor.

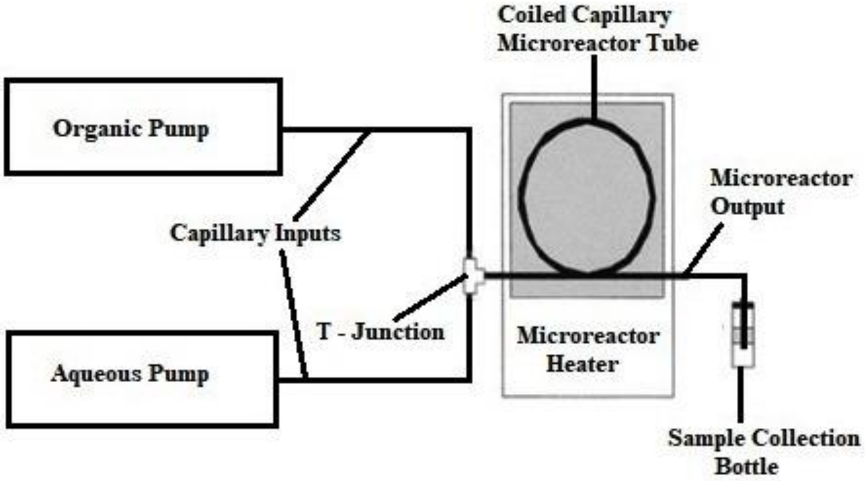


Figure (2.2). Schematic representation of capillary microreactor used for organic nitration. [175].

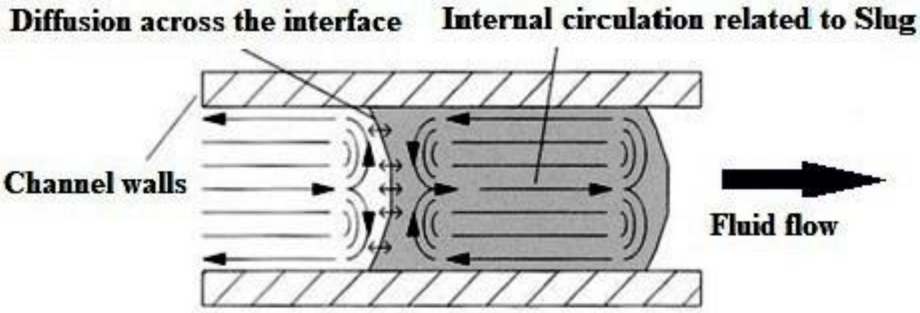


Figure (2.3). The schematic illustration of circular motion generated within each liquid slug [175].

Yoshikuni et al, [176], reported the fabrication technique and pile – up a process for the preparation of glass micro reactor and the glass micro reactor was used for the amide formation reaction. To fabricate the glass micro reactor, they used conventional photography method, wet etching, and thermal bonding. The glass micro reactor had the dimensions of W = 360 µm, H = 120 µm and L = 47 cm. The micro reactor was made from glass plates by inserting it between alumina plates. Glass plates were refined to certain surface roughness and loads were employed on them. The sandwiched plates were heated at 650 °C for 5 h. after the fabrication, the reactor was used for the amide formation reaction. The procedure behind the reaction is that the two micro syringes (10 mL each) were filled with 0.01 mol solution of DL – 1 – phenyl amine in 0.1 mol NaOH and 3, 5 – dinitrobenzoyl chloride in EA (ethyl acetate) respectively. The solution was passed through the glass micro reactor at different flow rates. The reaction product (R – (–) – N – (3, 5 – dinitrobenzoyl) – α – phenyl – ethylamine) was isolated from the solution mixture and analyzed by chromatography. The yield of the amide reaction by using the single – layered and pile – up glass micro reactor is shown in **Table (2.1)**.

Table (2.1). Details of flow rates and output of phase transfer amide reaction in glass micro reactor.

Reactor	Pile up (10 layers) glass micro reactor			Single layered glass micro reactor		
Flow rate (mL/min) for each syringe	15.00	10.00	5.00	1.25	1.00	0.50
Yield (%)	70.00	77.00	83.00	82.00	83.00	82.00
Throughput (mg/min)	33.00	24.00	13.00	3.20	2.60	1.30

Dummann et al, [177], reported the use of capillary micro reactor for enhancement of heat transfer as well as mass transfer of a liquid – liquid phase reaction. The experimental setup was shown in **Figure (2.4).** The capillary micro reactor was a PTFE capillary with internal diameter was in the range of 0.50 – 1.00 mm. The nitration of the aromatic was carried out under the isothermal conditions despite of the high negative enthalpy. The heat was removed effectively as a result of the smaller diameter of the capillary and the micro reactor was covered using insulation jacket. They maintained the same residence time (2.95 min) for all experiments by varying the capillary length (1– 4 m) and volumetric flow rate (9 – 36 mL/h). They obtained 50 % conversion of an aromatic compound at residence time of 2.95 min at 60 and 120 °C with 4 and 1m long capillary micro reactor respectively. The product was analyzed by chromatographic technique. The reaction scheme is shown in the **Scheme – (2.II).**

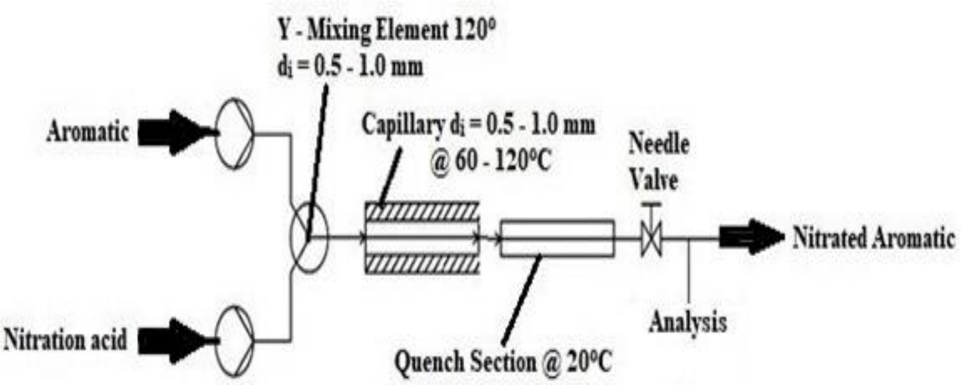
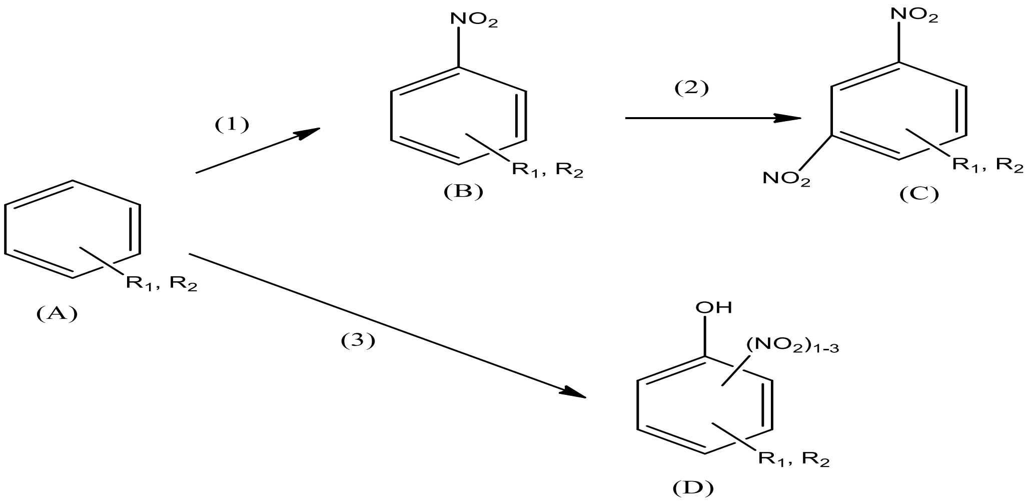


Figure (2.4). Schematic diagram of experimental setup of capillary micro reactor for nitration of a single ring aromatic compound. [177].



Scheme – (2.II). Nitration of a single aromatic ring (A) to the mononitro product (B), dinitrated byproduct (C) and phenolic byproducts (D). [177].

Kashid et al., [178] reported the review on micro structured reactors (MSR) for multiphase reactions. They noticed that production of chemicals in the micro structured reactors is an innovative branch of chemical engineering and technology mostly focusing on the intensification of a process as well as safety. Micro structured reactors have the equivalent hydraulic diameter of few micro meters and so offer enhanced mass and heat transfer efficiently enhancing the reactor performance significantly over conventional batch reactors. Moreover, they described different types of micro structured reactors and their advantages over conventional batch reactors. They identified the parameters which regulate the flow profile generated in micro capillaries concerning to efficiency of the mass transfer. They also reported in details of various case studies of different multiphase reactions which were performed in a micro structured reactor.

Calabrese et al., [13] reported that continuous flow micro reactor represents an emerging technology of manufacturing. They predicted that micro reactor possess important benefits interms costs, quantity, quality besides safety intended for huge areas of chemical production. The use of advanced flow reactors and its commercial development is growing exponetially. However, the replace the convetional batch reactors in existing systems is current difficulty. Many benefits including lower production, accomodating in smaller space, enhanced quality, yield, and selectivity still makes the micro reactors attractive.

2. 2. Review on Corning® Advanced – Flow^{TM} Reactor (AFR)

Lavric and Woehl, [64] studied the performance of a Corning® Advanced – Flow^{TM} reactors of GEN 1 and GEN 2 for seamless scale – up for the systems of immiscible fluid – fluid flow (water – heptane and gas-liquid dispersion). In this case, they used GEN 1 and GEN 2 for the system of water – heptane and gas – liquid system. The GEN 2 has 1.8 times more internal volume of GEN 1. For these systems, they studied the parameters of mixing effect, emulsion effect and residence time distribution. They reported that in case of formation of emulsion, the higher liquid flow rate resulted into the finer the emulsion. Furthermore, they also reported that there is no impact of pressure drop on the chemical performance but flow rate changes. The thermal performance study proved that a lower thermal resistance of the wall and 40 % better a volumetric heat transfer coefficient are offered by GEN 2 than GEN 1 at low residence times. Finally, they concluded that (1) complementary to numbering up, an efficient scale – up, was achieved by enhancing channel height or/and the footprint and internally separating the flow, (2) using GEN 1 and GEN 2, mixing quality, pressure drop, heat transfer performance and emulsion quality is same in both GEN 1 and GEN 2, for the family of advanced flow glass reactor. Therefore, while employing chemical flow reactors with millimetric internal dimensions, the output could be enhanced by scaling up without altering the performance of chemical processes.

Chivilikhin et al., [179] described the CFD analysis of thermal and hydrodynamic behavior of AFRs. The CFD study comprises the decomposition of a structure into a mesh of elements or cells, carrying out the fluid flow computations at the nodes of each cell. They studied the CFD on the AFR by considering the composed of chains of the same cells with variable cross – sectional elements which push the liquid to divide and rejoin arrangement. For this case they recommended operating flow rate was in the range of 30 to 120 g/min for water – like fluids. They also reported the study of velocity profile which is skewed profile, pressure drop up to 1.5×10^5 Pa at 150 g/min can be sustained and volumetric heat transfer coefficient was 10.4×10^5 W/ $(m^2 \cdot K)$ at 120 – 150 g/min was achieved.

Chamrai, [66] reviewed about the process intensification by the application of Corning® Advanced – Flow™ Reactor technology over conventional batch methods. All the issues and benefits of AFR technology for the intensification of the processes are reported. They concluded that for a chemical process, AFR technology offers an intensification of reaction rates as well as yields, allows a new reaction process development and make a downstream process simpler. The corning technology induces an important contribution towards any chemical process safety development, reducing the undesired intermediate formation and making in sometimes high energy chemistry. So, it was clear that the corning AFR technology, likely to increase the efficiency of a chemical manufacturing process, lower operational costs due to low energy consumption, enhance safety and helps to decrease risks associated with scale – up of a process. Furthermore, it was found that the corning technology confirms for the intensification of a chemical process while minimizing environmental issues.

Zhang et al., [65] studied the intensification of mixing of immiscible liquids and mass transfer by using the Advanced – Flow™ Reactors which was supplied by corning technology. The AFR was employed for continuous flow production of various chemicals and it had the hydraulic diameter of 0.3 mm to few millimeters. The AFR allows the chemical reactions from conventional batch method to continuous flow manufacturing with higher efficient, more economical and enhanced safer processes. They used the system of the extraction was n – heptane and water with iodine to intensify liquid – liquid mass transfer to extract the iodine from the system. They first studied the extraction of iodine from the system by using the conventional method at different rpms (500 – 2020 rpm) and the mass ratio of organic phase to water was in the range of 0.25 to 4.0. So, in the conventional method, at 1530 rpm and 30 seconds, they observed and reported the efficiency of the extraction in the range of 0.79 to 0.90. The same parameters of the batch method were applied for the heart cell based AFR fluidic module using the ratio of the organic phase to the aqueous phase of 0.25. In this case, they reported the efficiency of the extraction in the range of 0.79 to 0.90 at the flow rate of 2.5 – 10 g/min. Finally, concluded that the good extraction efficiency was achieved without adding any emulsifiers and the high extraction efficiency showed that the AFR was an efficient tool offers good characteristics for the multiphase applications.

Rossi et al., [180] described the process for the generation of diazomethane in conventional as well as a continuous flow reactor (low flow (0.9 – 1.35 mL) and GEN1 (15 – 25 mL)). In the study, they compared the yield of the diazomethane and residence time for the low flow and GEN1 reactors. They maintained residence time in the range of 24 – 50.8 s for low flow reactor and obtained yield in the range of 6 – 75 %. GEN1, the residence time in the range of 21.5 – 34.8 s and obtained yield in the range of 29.3 – 97 %. Finally, reported that the flow reactors were effectively used for the generation of harmful diazomethane through a base induced disintegration of N – methyl – N – Nitro – sourea. The procedure scale – up was quick and efficient. They produced the diazomethane about 19 mol/day at feed flow rate of 53 mL/min.

Jorda and Vizza, [181] reported a review study on Corning seamless glass micro reactors of different types. They compared the volumetric mass transfer for water, acetone and toluene for corning reactors as well as conventional liquid – liquid contactors. The comparison of the volumetric mass transfer data is presented in **Table (2.2)**. They reported some key parameters like numbering up and internal scale – up, mixing quality, mass transfer and heat transfer, residence time, and pressure drop. Furthermore, concluded that transferring a chemical process from a conventional method to a continuous flow method could bring down cost, risks, and difficulty associated with the process scale – up.

Table (2.2). Comparison of the volumetric mass transfer for water acetone and toluene for corning reactors with flow reactors of liquid – liquid contactors [181].

Type	**V, mm^3**	**$k_L \cdot a$ @ 5 s residence time**	**Output (mL/min)**
T square	48.23	0.070	0.6
Y rectangular	82.95	0.050	1.0
Caterpillar	23.67	0.035	0.3
Low Flow	633	0.113	7.5
GEN1	7320	0.149	90
GEN2	18400	0.120	230

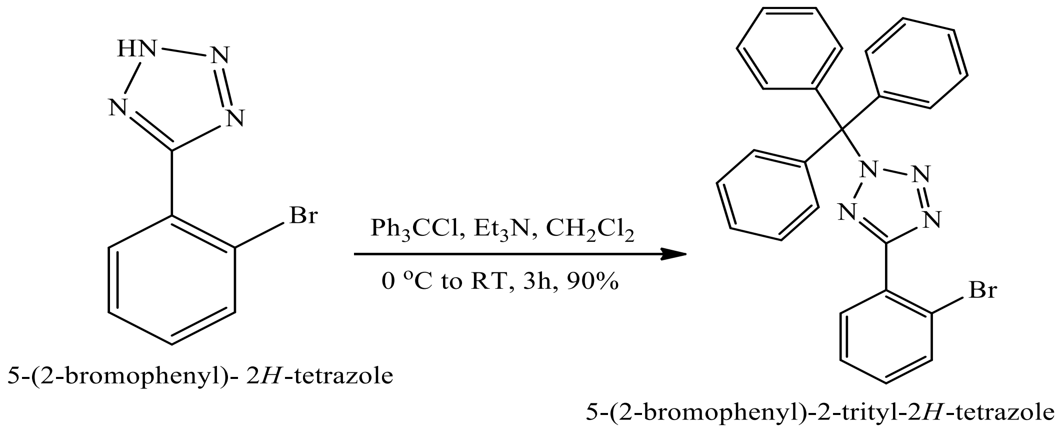
Remacha et al., [61] described hydrodynamic study of liquid – liquid dispersion by using an Advanced – Flow^{TM} Reactor. For this case, they have chosen hexane – water system. They evaluated the Reynolds number, Weber number, Capillary number and Morton number. The above numbers were determined for the flow rate from 10 – 80 mL/min. The determined values of the numbers were shown in **Table (2.3)**. They concluded that AFR is one of commercially available microreactor for scale – up of multiphase reactions from the micro scale to milli scale to bulk (mass) scale). Due to the complex geometry of AFR, there is change in flow within the heart cells which results in change in pressure. It causes to droplets formation and breakup leading to enhance mass transfer among the particles. They obtained the drop sizes of 0.33 mm, and coefficient of mass transfer about 10 s^{-1} for flow rate of 10 – 80 mL/min each phase.

Table (2.3). The dimensionless numbers for Hexane – Water system in AFR at the flow rate at 10 – 80 mL/min [61].

Phase	**Reynolds number**	**Weber number**	**Capillary number**	**Morton number**
Hexane	180 – 1400	0.30 – 19	0.003 – 0.024	2.5×10^{-11}
Water	390 – 3200	0.45 – 29		
Hexane – Water	460 – 3700			

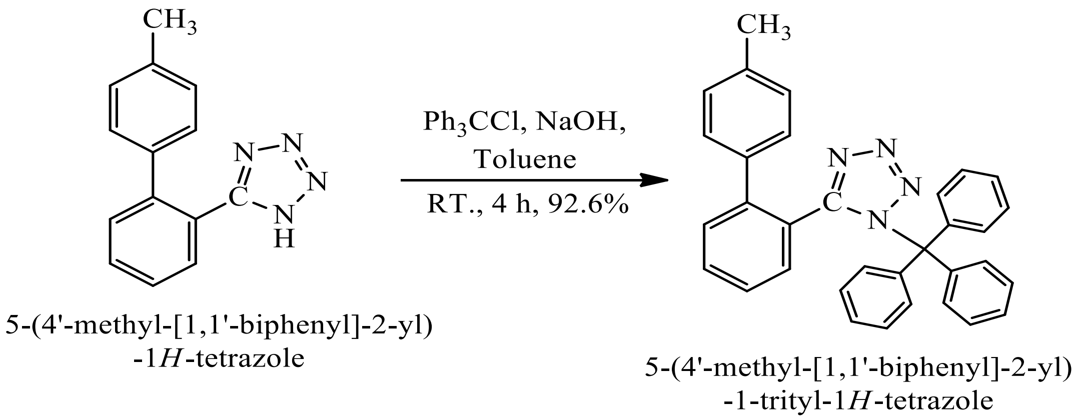
2.3. Review on tritylation reaction by conventional batch method

Myznikov et al., [74] reported the production of 5 – substituted 2 – triphenyl methyl tetrazoles in a conventional batch method. A mixture of 2.5 mmol of 5 – phenyl tetrazole, 0.2 mmol of tetra butyl ammonium bromide and 10 mL of 10% aqueous NaOH (sodium hydroxide), chloroform of 10 mL added and the mass was stirred for 15 min at 20 °C. A solution of 3 mmol of trityl chloride (TTC) in 20 mL of chloroform was charged and the whole mass was stirred for 4 h at 20 °C. The yield obtained was about 93 % and with melting point of 158 – 160 °C. Further, it was characterized by FTIR and ^1H NMR. The trityl group was one of the protecting groups for the tetrazole rings. It was revealed that alkylation of tetrazoles by TTC gives only the N_2 products (**Scheme – (2.III)**). The reaction is normally performed in the presence of a base.



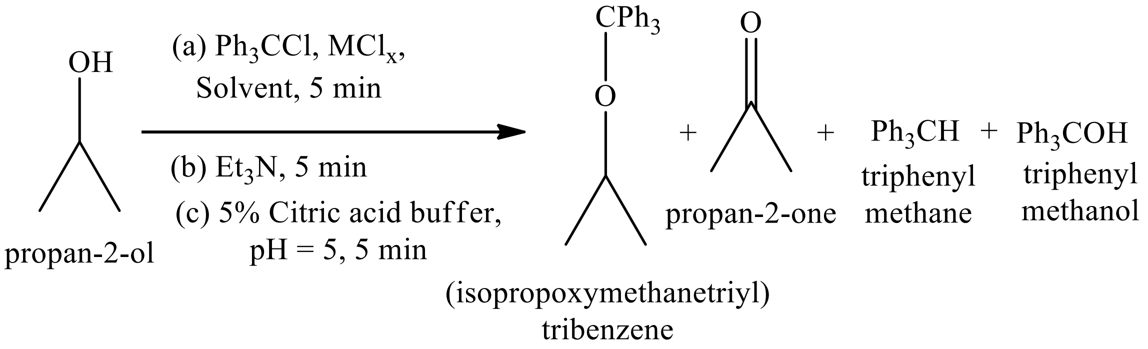
Scheme – (2.III). Preparation of 5 – (2 – bromophenyl) – 2 – trityl – 2H – tetrazole.

Wang et al., [96] reported synthesis of 5 – (4' – methyl – [1, 1' – biphenyl] – 2 – yl) – 1H – trtrazole with slight modification as reported by Chao et al 2005 [233]. At ambient temperature, under stirring 4' – methyl – 2 – (1H – tetrazol – 5 – yl) biphenyl (18.9 g, 0.080 mol) and 30 % NaOH (10.7 g, aqueous) were added to toluene (100 mL). The mass was agitated for 10 min, and then trityl chloride (0.08 mol, 22.3 g) was fed to reactor. The entire mass was vigorously agitated and maintained for 4 h at room temperature. Finally, the mass bring down to temperature of 0 °C. Further, 40 mL of water and 120 mL of petroleum ether were charged to the mass. Recrystallization of the product was carried out by using ethyl acetate, it gave as a white crystalline product (35.5 g) with yield of 92.6 % based on 4' – methyl – 2 – (1H – tetrazol – 5 – yl) biphenyl. The melting point was in the range of 165 – 167 °C. further, the product was analyzed by FTIR and NMR. The reaction was shown in **Scheme – (2.IV)**.



Scheme – (2.IV). Preparation of 5 – (4' – methyl – [1, 1' – biphenyl] – 2 – yl) – 1 – trityl – 1H – tetrazole.

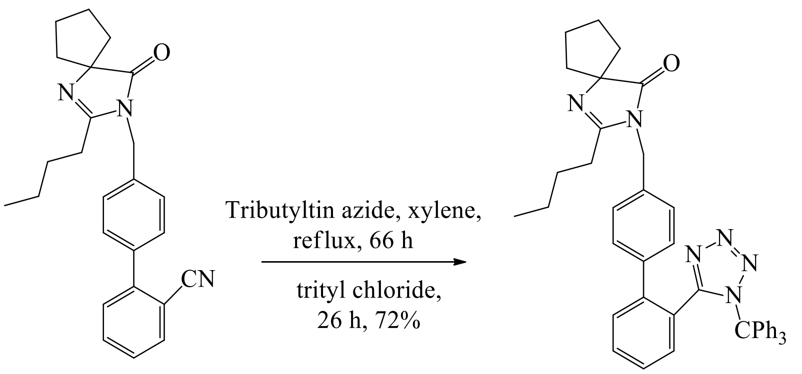
Bernini and Maltese, [75] described the general method of tritylation of less reactive hydroxyls. The substrate, hydroxyls, (1.0 mmol) was charged to trityl chloride solution (TrCl or Ph_3CCl) (1.0 mmol) and chloride metal (1.0 mmol) in the selected solvent (acetonitrile or dichloromethane) of 6.0 mL and the solution was maintained at room temperature for 5 min and then, triethylamine solvent (TEA, 1.0 mmol, 2.0 mL) was added in the same solvent over 5 min. The yield of (isopropoxymethanetriyl) tribenzene was in the range of 23 – 66 % based on propan – 2 – ol for $AlCl_3$ + CH_2Cl_2 and $HgCl_2$ + CH_3CN respectively. Similarly, the yield of triphenylmethane was in the range of 6 – 77 % based on propan – 2 – ol for $FeCl_3$ + CH_2Cl_2 and $FeCl_3$ + CH_3CN respectively. Finally, the product was analyzed by GCMS analysis. The reaction was shown in **Scheme – (2.V)**.



$MClx = ZnCl_2, HgCl_2, FeCl_3$ and $AlCl_3$
Solvent = CH_3CN and CH_2Cl_2

Scheme – (2.V). Process of tritylation of 2 – propanol.

Narender Rao and Sudhakar Babu, [182] described the procedure for the production of 2 – butyl – 3 – ((2' – (1 – trityl – 1H – tetrazol – 5 – yl) – [1, 1' – biphenyl] – 4 – yl) methyl) – 1, 3 – diazaspiro [4.4] non – 1 – en – 4 – one from 4' – ((2 – butyl – 4 – oxo – 1, 3 – diazaspiro[4.4] non – 1 – en – 3 – yl) methyl) – [1, 1' – biphenyl] – 2 – carbonitrile. They adapted the above method from Bernhart et al 1993 [234]. Further, the product was analyzed by TLC, MP, FTIR, NMR, and LC – MS. In this process they got 72 % of 2 – butyl – 3 – ((2' –(1 – trityl – 1H – tetrazol – 5 – yl) – [1, 1' – biphenyl] – 4 – yl) methyl) – 1, 3 – diazaspiro [4.4] non – 1 – en – 4 – one based on 4' – ((2 – butyl – 4 – oxo – 1, 3 – diazaspiro [4.4] non – 1 – en – 3 – yl) methyl) – [1, 1' – biphenyl] – 2 – carbonitrile.



4'-((2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl)-[1,1'-biphenyl]-2-carbonitrile

2-butyl-3-((2'-(1-trityl-1*H*-tetrazol-5-yl)-[1,1'-biphenyl]-4-yl)methyl)-1,3-diazaspiro[4.4]non-1-en-4-one

Scheme – (2.VI). Procedure for preparation of 2 – butyl – 3 – ((2' – (1 – trityl – 1H – tetrazol – 5 – yl) – [1, 1' – biphenyl] – 4 – yl) methyl) – 1, 3 – diazaspiro [4.4] non – 1en – 4 – one.

Maltese et al., [183] described the general method of tritylation of less reactive hydroxyls. The substrate, hydroxyls, (1.0 mmol) was charged to a solution of trityl chloride (TrCl or Ph_3CCl) (1.0 mmol) and $ZnCl_2$ (1.0 mmol) in the acetonitrile of 6.0 mL and the mass solution was maintained at room temperature for 5 min and then, triethylamine solution (TEA, 1.0 mmol) (2.0 mL) was fed in the solution in the period of 5 min. The organic phase was isolated under vaccum and the final mass mixture was separated by diethyl ether. The yield of $ROCPh_3$ was in the range of 50 – 87 % based on ROH for $ZnCl_2$ + CH_3CN in acetonitrile + triethylamine. The product was analyzed by using melting point method and NMR. The reaction is shown in **Scheme – (2.VII)**.

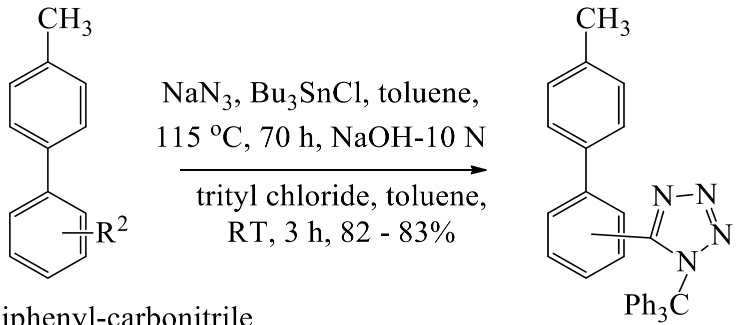
$$\mathrm{ROH} \xrightarrow[\substack{\text{(b) Et}_3\text{N, 5 min} \\ \text{(c) 5\% Citric acid buffer,} \\ \text{pH = 5 - 6, 5 min}}]{\substack{\text{(a) Ph}_3\text{CCl, MCl}_x\text{,} \\ \text{CH}_3\text{CN or CH}_2\text{Cl}_2}} \mathrm{ROCPh_3}$$

R = Alkyl, aryl, acyl

MClx = $ZnCl_2$, $HgCl_2$, $FeCl_3$ and $AlCl_3$

Scheme – (2.VII). Process for tritylation of ROH.

Sánchez et al, [97] reported the formation process of 5 – (4' – Methyl – biphenyl – 3 or 4 – yl) – 1 – trityl – 1H – tetrazole. 4 – methyl – biphenyl – carbonitrile (23.5 mmol, 4.5 g,), NaN_3 (sodium azide, 23.5 mmol, 1.5 g) and Bu_3SnCl (tri – n – butyltin chloride, 25 mmol, 8.4 g) were added in toluene, then heated up to 115 °C and stirred about 70 h. The mass solution diluted by adding 35 mL toluene and cooled downed to RT. For this solution mass, NaOH 10 N (sodium hydroxide, 27 mmol, 2.7 mL) and Ph_3CCl (24 mmol, 6.7 g, triphenylmethyl chloride) were charged and the mass was maintained at room temperature about 3 h. The toluene separated by applying vacuum. The recrystallization of the compound was done by ethyl acetate and dichloromethane. The final compounds were analyzed by melting point, NMR and MS.



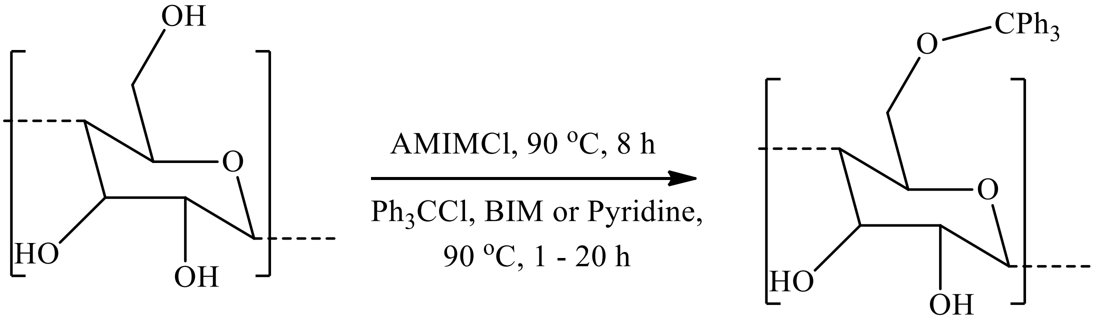
4-methyl-biphenyl-carbonitrile

5-(4'-Methyl-biphenyl-3 or 4 -yl)-1-trityl-1H-tetrazole

R^2 = m-CN, p-CN

Scheme – (2.VIII). Synthesis process of 5 – (4' – methyl – biphenyl – 3 or 4 – yl) – 1 – trityl – 1H – tetrazole.

Lv al., [184] reported the formation procedure for the cellulose tritylation in 1 – Allyl – 3 – methylimidazolium chloride (AMIMCl). Dry cellulose (12.3 mmol, 2.0 g) was charged in AMIMCl (113.6 mmol, 18.0 g) in a flask having three necks and the mass was heated up to 90 °C for 8 h with agitation. A viscous and clear mass was observed, for this trityl chloride (36.9 – 73.8 mmol, 10.3 – 20.6 g) and 1-butylimidazole (BIM) (73.8 – 246.0 mmol, 9.7 – 32.3 mL) (or dried pyridine (73.8 – 172.2 mmol, 5.9 – 13.9 mL)) were charged at 90 °C. The whole mass was maintained for 1 – 20 h. After completion of the reaction, the mass was precipitated by 200 mL methanol and then mass was filtered. The filtrate trityl cellulose washed many times by methanol and finally dried in vacuum at 60 °C . The yield of trityl cellulose about 90 – 93 % and analysed by FTIR as well as NMR.

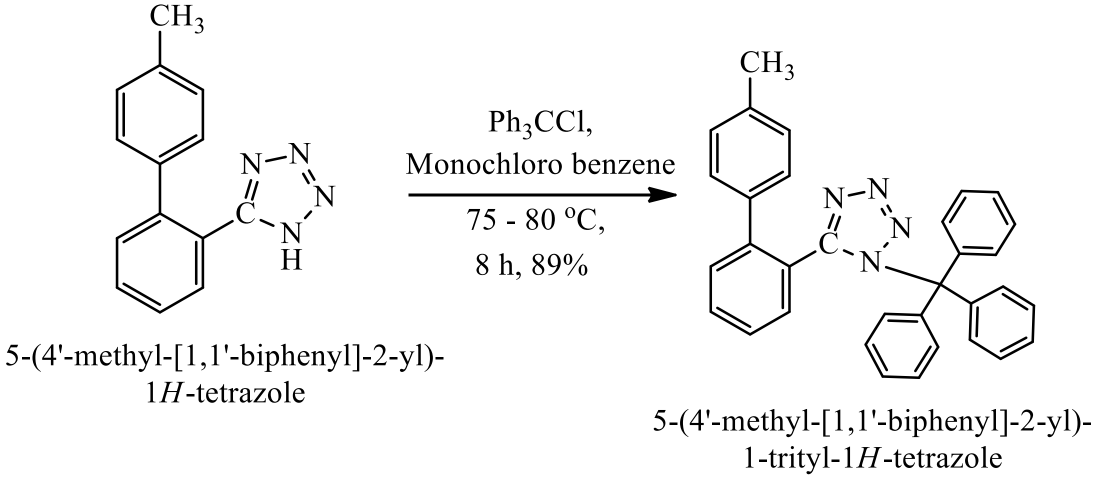


Cellulose

Trityl Cellulose

Scheme – (2.IX). Synthesis of trityl cellulose from cellulose.

Patel and Karia, [95] reported method for the formation of 5 – (4' – methylbiphenyl – 2 – yl) – 1 – trityl – 1H – tetrazole. 5 – (4' – methylbiphenyl – 2 – yl) – 1H – tetrazole (10 g, 0.040 mol), trityl chloride (13.6 g, 0.049 mol), and triethyl amine (5.8g, 0.057 mol) were fed to monochloro benzene solvent. The reaction mixture was maintained at 75 – 80 °C for 8 h. The movement of the reaction was observed by thin layer chromatography. The mobile phase used was toluene: ethyl acetate. The yield of the product was about 89 % based on the 5 – (4' – methylbiphenyl – 2 – yl) – 1H – tetrazole. The product was analyzed by melting point (167 – 169 °C), FTIR and NMR.



Scheme – (2.X). Preparation of 5 – (4' – methyl – [1, 1' – biphenyl] – 2 – yl) – 2 – trityl – 2H – tetrazole.

2.4. Percarboxylic Acids/Peroxycarboxylic Acids

Percarboxylic acids also known as peroxycarboxylic acids or per acids which were efficient and ecofriendly oxidizing reagents. The acids can be used in many industries like chemical processing industries as disinfection agent and bleaching agent. The market capacity can be estimated to be more than 10 kilotonnes worldwide. The general chemical formula of a percarboxylic acid is R – COOOH, where R was functional group such as H, CH_3, C_2H_5, C_3H_7 etc., and – OOOH is oxidative functional group. Small chain peroxycarboxylic acids are miscible with water and have a nasty odour. They have explosive nature when expose in the pure form or with high concentration. Peracids show more prospective as antimicrobial reagents compared to hydrogen peroxide. The peracids are quickly active at low concentrations by a wide spectrum of microorganism.

2.4.1. Review on synthesis of performic acid

Synthesis of performic acid in batch as well as in a micro reactor for continuous mode was reported by few researchers [33, 115, 116]. Performic acid is an unstable colorless liquid. It could be prepared from the reaction between hydrogen peroxide and formic acid in the presence or absence of a catalyst which is either homogeneous or heterogeneous. The PFA is an oxidizing agent employed in chemical processing, bleaching, synthesis etc. The PFA is also well – known as disinfectant, and food preservative in the medical as well as food industry respectively. The performic acid is a very useful epoxidizing reagent for the processes of the epoxidation of the unsaturated oil to produce epoxy plasticizer with higher yield. The individual researchers’ reported details are given as follows.

Gehr e al., [110] prepared performic acid (PFA) in a batch method by using formic acid (50 mL, 85 wt %) and hydrogen peroxide (50 mL, 35 wt %) in presence of sulphuric acid (4.7 mL, 95 – 98 wt %). The reaction was carried out below 20 °C up to 90 min to get the performic acid. The obtained PFA has concentration of 9 wt % and has a density about 1.18 g/mL. The prepared PFA solution was used for the wastewater treatment. The performic acid concentration and hydrogen peroxide concentration were determined by 0.1 N sodium thiosulfate solution and 0.1 N ammonium cerium sulphate solution respectively.

Filippis et al., [119] had been studied the synthesis of peroxyformic acid (PFA) in conventional batch reactor. They used 16.0 mL of hydrogen peroxide (HP, 50 % w/w) and 8.0 mL of formic acid (FA, 98% w/w) as reactants for the reaction. The experiments were carried out without a catalyst. The experiments were carried out at 30 – 60 ℃. All the experiments were performed with the same initial molar ratio of HP: FA. In this case, they achieved higher concentration of the PFA of about 3.0 mol/L, the PFA decomposes to CO_2 and H_2O. The reaction is reversible in nature, so both the reactions were catalyzed by hydrogen ions and there is no decomposition of hydrogen peroxide. They also developed rate equations and from the experimental data, they determined rate constants expressions as follows

$$\mathrm{k_1} = 13.065 * 10^3 * \exp\left(\frac{-5234.8}{\mathrm{T}}\right) \tag{2.1}$$

$$\mathrm{k_2} = 06.513 * 10^9 * \exp\left(\frac{-8735.2}{\mathrm{T}}\right) \tag{2.2}$$

$$\mathrm{k_1} = 13.065 * 10^3 * \exp\left(\frac{-43524.74}{\mathrm{RT}}\right) \tag{2.3}$$

$$\mathrm{k_2} = 06.513 * 10^9 * \exp\left(\frac{-72628.82}{\mathrm{RT}}\right) \tag{2.4}$$

From the above expressions, the PFA formation reaction, pre exponential factor was 13.0651*103 L^6 mol^{-2} s^{-1} and activation energy was 43.524 KJ mol^{-1} and similarly for the reversible decomposition of PFA, pre exponential factor was 6.513*10^9 L^6 mol^{-2} s^{-1} and activation energy was 72.628 KJ mol^{-1}.

Ebrahimi et al., [33] reported the continuous flow production of performic acid (PFA) in a micro reactor. Performic acid and hydrogen peroxide were employed as reactants. Sulfuric acid was used as homogeneous catalyst. The production rates of the PFA were studied at different concentrations of the catalyst (0 – 12 wt % based on the reaction mixture) and temperatures (5 – 40 ℃). The experiments were carried out in a micro reactor system. The micro reactor setup was made up of the PTFE (polytetra fluoroethelene) tube and the slit interdigital micro mixer. Height of the single micro channel was 200 µm and breadth 45 µm. The internal diameter of the tube was 1.0 or 1.6 mm and length was in the range of 0.75 to 5.0 m. The reaction was observed to be fast as the PFA equilibrium was achieved within 4 min at 40 °C and at catalyst concentration of 6 wt % based on the reaction mixture. The concept is adaptable in terms of manufacturing capacity of 1 – 12 kg/h (maximum of 100 tonnes per annum).

Xiaoying et al., [115] reported synthesis of performic acid by taking 5.5 mL formic acid and 34.5 mL hydrogen peroxide. The reaction was autocatalysed. In this case, they used formic acid concentration of 3.16 mol/L, hydrogen peroxide concentration of 8.42 mol/L and water concentration of 37.56 mol/L and maitained stirring speed was 600 rpm. The reaction was carried out at different temperatures (20, 30, 45, 55 and 65 ℃). The maximum concentration of PFA of 0.46 mol/L was obtained at temperature 55 ℃ and reaction time of 33 min. They reported an overview of performic acid synthesis, hydrolysis, decomposistion and reaction mechanism carried out by various researchers. The macro – kinetic models of formation, hydrolysis and decomposition of performic acid were examined by formic acid as an auto catalyzed reaction. The intrinsic (k_1 and k_2) and observed reaction (k_{1obs}, k_{2obs} and k_{3obs}) rate constant expression were given below. The experimental outcomes showed that decomposition of the performic acid was likely to occur even at the ambient temperature.

$$k_1 = 3.99 * 10^{10} * \exp\left(\frac{-75200}{RT}\right) \tag{2.5}$$

$$k_2 = 1.10 * 10^{5} * \exp\left(\frac{-40400}{RT}\right) \tag{2.6}$$

$$k_{1obs} = [H^+] * 3.99 * 10^{10} * \exp\left(\frac{-75200}{RT}\right) \tag{2.7}$$

$$k_{2obs} = [H^+] * 1.10 * 10^{5} * \exp\left(\frac{-40400}{RT}\right) \tag{2.8}$$

$$k_{3obs} = 2.68 * 10^{13} * \exp\left(\frac{-95400}{RT}\right) \tag{2.9}$$

Ebrahimi et al., [121] described the kinetics of the performic acid formation in a tubular micro reactor from the formic acid (90 wt %) and hydrogen peroxide (50 wt %) as reactants and sulfuric acid (96 wt %) as a catalyst. The experiments were carried out continuously in the micro reactor. The specifications of the micro reactor were same as reported by **Ebrahimi et al., 2011**. They carried out the experiments at different parameters such as residence times, different catalyst concentrations (sulfuric acid: 0 – 12 wt %), temperatures (20 – 70 ℃) and different residence times (0.6 – 31 min (average velocity was 0.1 – 4 cm/s). Three different models were studied to detemine the kinetic parameters for instance the reaction rate constants and activation energies. The three models were assumed as plug flow model and laminar flow model. They determined reaction parameters for instance reaction rate constants and activation energies for forward as well as reverse reactions. The reaction rate constants and activation energies were determined by taking as plug flow model and laminar flow model and the values were shown in **Table (2.4)**. They reported equilibrium constant for the reaction of the performic acid formation and it was shown in Eq (2.10). The determined equilibrium constants for the performic acid synthesis were 2.7, 2.28, 1.95, 1.67 and 1.25 at 5, 10, 15, 20 and 30 ℃ respectively.

Table (2.4). Estimated parameters values for laminar flow model and plug flow model.

Performic acid	Plug flow model $R^2 = 97.90$	Laminar flow model $R^2 = 97.98$
$k_{1,\,mean}$ [$L^2/(mol \cdot s)$]	6.27×10^{-6}	5.43×10^{-6}
$k_{2,\,mean}$ [$L^2/(mol \cdot s)$]	4.68×10^{-6}	3.77×10^{-6}
E_1 [J/mol]	60.4×10^{3}	75.7×10^{3}
E_2 [J/mol]	63.6×10^{3}	97.3×10^{3}

$$K_{eq} = \frac{k_1}{k_2} = 1.44 \text{ x } \exp\left(\frac{21600}{R}\left(\frac{1}{T} - \frac{1}{298}\right)\right) \quad (2.10)$$

Santacesaria et al., [116] reported the kinetics of performic acid formation and its decomposition by a technology of a gas volumetric system in which they detemined the gas volume generated during the reaction time. The performic acid was synthesized from formic acid (1.524 – 6.399 g) and hydrogen peroxide (9.858 – 24.647 g) in the presence of catalytic quantity of sulfuric acid (0.192 – 0.726 g) or orthophosphoric acid (0.184 – 0.644 g). The experimental work was carried out at 30 – 70 ℃. They reported that there was decomposirion of perfomic acid above 50 ℃ and no decomposition of hydrogen peroxide in the reported temperature range. They reported that perfomic acid was decomposing into CO_2 and H_2O. Both (forward and reverse reaction) were catalysed by hydrogenium ions. They deretmined a rate constant expresions for performic acid synthesis and its decomposition in the presence of orthophosphoric acid and sulfuric acid as catalyst separately. The proposed rate constant expresions were given below for orthophosphoric acid and sulfuric acid separetely.

For orthophosphoric acid catalyst

$$k_{1T} = (1.16 \pm 0.13) * 10^{-3} * \exp\left[\left(\frac{-83816 \pm 2905}{8.314}\right)\left(\frac{1}{T} - \frac{1}{323}\right)\right] \quad (2.11)$$

$$k_{2T} = (1.36 \pm 0.32) * 10^{-4} * \exp\left[\left(\frac{-98989 \pm 3014}{8.314}\right)\left(\frac{1}{T} - \frac{1}{323}\right)\right] \quad (2.12)$$

For sulfuric acid catalyst

$$k_{1T} = (1.03 \pm 0.05) * 10^{-3} * \exp\left[\left(\frac{-47518 \pm 3061}{8.314}\right)\left(\frac{1}{T} - \frac{1}{323}\right)\right] \quad (2.13)$$

$$k_{2T} = (9.61 \pm 1.56) * 10^{-5} * \exp\left[\left(\frac{-87497 \pm 2374}{8.314}\right)\left(\frac{1}{T} - \frac{1}{323}\right)\right] \quad (2.14)$$

For Absence of catalyst

$$k_{1T} = (1.20 \pm 0.16) * 10^{-3} * \exp\left[\left(\frac{-55304 \pm 1288}{8.314}\right)\left(\frac{1}{T} - \frac{1}{323}\right)\right] \quad (2.15)$$

$$k_{2T} = (1.60 \pm 0.32) * 10^{-4} * \exp\left[\left(\frac{-105073 \pm 8419}{8.314}\right)\left(\frac{1}{T} - \frac{1}{323}\right)\right] \quad (2.16)$$

Gaikwad et al., [185] reported process intensification for a continuous flow formation of performic acid by Corning® Advanced – Flow^{TM} Reactor (AFR). In which they maintained equimolar ratio of formic acid (FA) to hydrogen peroxide (HP) i.e., FA : HP = 1:1 (C_{FA} = C_{HP} = 8.658 mol/L) for all experiments. They studied the effect of the different parameters such as residence time, temperature, hydrogen peroxide concentration, feed flow rate, concentration of the catalyst on the performic acid formation. Therefore, they achieved maximum concentration of performic acid of 6.25 mol/L at 30 °C, a residence time of 41 s, catalyst concentration about 1 wt % of total moles and hydrogen peroxide concentration of 30 w/w %.

2.4.2. Review on peroxyacetic acid synthesis

Dul'neva and Moskvin, [172] described the synthesis process and studied kinetics for the synthesis of peroxyacetic acid (PAA) in the conventional method. The peroxyacetic acid was prepared from hydrogen peroxide and acetic acid using a catalyst. They studied the effect of hydrogen peroxide and acetic acid molar ratio, catalyst (sulfuric acid) concentrtion and temperature for the formation of peroxyacetic acid. They carried out all the experiments in the aquesous solution to avoid explosion. They maintained the reaction parameters were acetic acid : hydrogen peroxide from 6: 1 to 1: 6, concentration of sulfuric acid from 0 to 9 wt % and the tmperature at 20, 40 and 60 ℃. They reported the concentration of the peracetic acid was 2.3 mol/L. They suggested the best operational parameters for attaining the equilibrium conversion of acetic acid were molar ratio of acetic acid to hydrogen peroxide was 2.5 : 1, sulfuric acid concentration (catalyst) of 0.057 mol/L and temperature of 20 ℃. They determined the equilibrium constant as K = 2.10 (20 ℃), 1.46 (40 ℃), 1.07 (60 ℃) and also determined $\Delta H_r^0 = -13.7\,\mathrm{kJ/mol}$. Besides the rate of reaction for both forward reaction and reverse reaction increase with the increase in concentration of sulfuric acid from 0 to 5 wt % and further increasing catalyst concentration does not show any effect on the reaction rate. Moreover, they reported the average value of the rate constant of forward and reverse reaction as k_1 and k_2 were $6.81\text{x}10^{-5}$ and $3.25\text{x}10^{-5}$ L/(mol·s) respectively.

Xiaobing et al., [141] reported the method for the formation of peroxyacetic acid in an autoclave. The peroxyacetic acid is produced from the reaction between acetic acid with hydrogen peroxide using sulfuric acid (98 % strength) as homogeneous catalyst. They used the reaction parameters such as the molar ratio of acetic acid (27 %) and hydrogen peroxide was 1: 1, catalyst concentration of 2 to 5 wt % on the reaction volume and temperature of 25 to 35 ℃. They maintained the reaction mass up to 3 h. They obtained the product of 50 % peracetic acid, 11 % acetic acid and 39 % water.

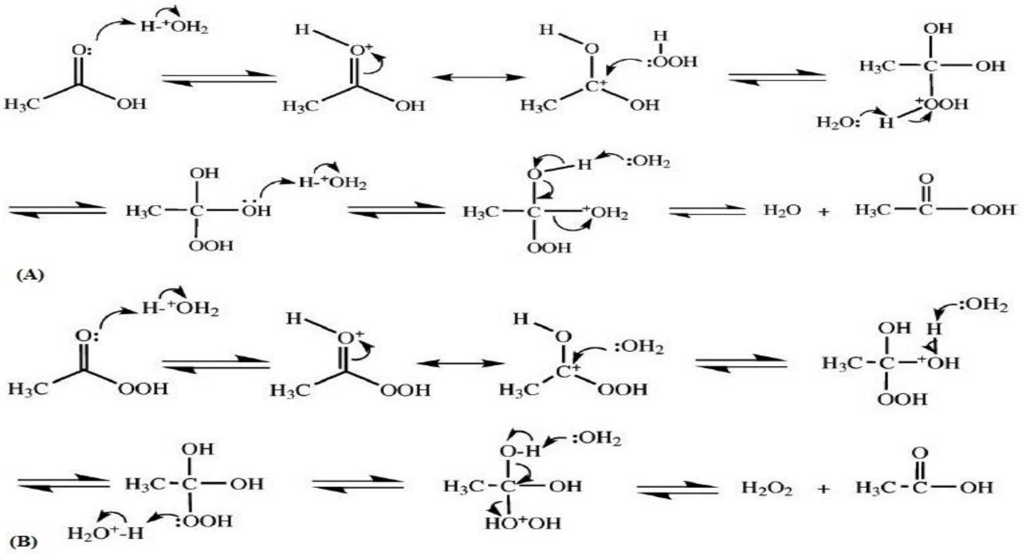
Zhao et al., 2007, [170] developed a homogeneous kinetic model for the production of peracetic acid (PAA) by the reaction between acetic acid and hydrogen peroxide using catalyst such as sulphuric acid in the aqueous phase by the conventional method. They also proposed reaction mechanism for the formation of peracetic acid and hydrolysis of peracetic acid, which is shown in **Scheme – (2.XI)**.

The kinetic model equations of PAA formation and hydrolysis were shown in the equations (2.17) and (2.18) and the kinetic constants were determined from the experimental data by employing a simplex optimization method.

$$\frac{dC_{PAA}}{dt} =$$
$$6.83x10^{8}\exp\left(\frac{-57846.15}{RT}\right)x[H^{+}](C_{AA0} - C_{PAA})C_{HP} -$$
$$6.73x10^{8}\exp\left(\frac{-60407.78}{RT}\right)x[H^{+}](C_{H_2O0} + C_{PAA})C_{PAA} \tag{2.17}$$

$$\frac{dC_{HP}}{dt} =$$
$$6.73x10^{8}\exp\left(\frac{-6040.78}{RT}\right)x[H^{+}]\,(C_{H_2O0} + C_{PAA})C_{PAA} -$$
$$6.83x10^{8}\exp\left(\frac{-57846.15}{RT}\right)x[H^{+}](C_{AA0} - C_{PAA})C_{HP} \tag{2.18}$$

Where C_{PAA} and C_{HP} are concentration of peracetic acid and hydrogen peroxide and C_{AA0} and C_{H_2O0} are initial concentrations of acetic acid and water respectively.



Scheme – (2.XI). Reaction mechanism of peracetic acid formation and hydrolysis in the presence of acid catalysis: (A) peracetic acid synthesis; (B) peracetic acid hydrolysis. [170].

Zhao et al., [186] reported the formation of peroxyacetic acid from the reaction of acetic acid by hydrogen peroxide by using sulfuric acid as homogeneous catalyst in a conventional batch method. They studied different parameters such as effect of temperature (20 – 50 ℃), sulfuric acid effect, hydrogen peroxide concentration (27 – 90 wt %, 0.2 – 1.2 g/mL) and volumetric ratio of acetic acid to hydrogen peroxide (1.2 – 1.5) for formation of peracetic acid. They found higher concentration of the peracetic acid was 3.27 mol/L experimentally and 3.56 mol/L from model calculation at 50 wt % hydrogen peroxide, the molar ratio of acetic acid to hydrogen peroxide of 2.0 and 30 ℃. They reported equilibrium constant (K_C) 2.91, 2.81, 2.72, and 2.63 at 20, 30, 40 and 50 ℃ respectively. They also reported that the study of thermodynamic on the peracetic acid formation and determine the equilibrium constant and Gibbs free energy of peracetic acid from the equilibrium constant as – 276 kJ/mol. The reaction attained an equilibrium within 24 h when the reaction was carried out at 30 ℃, sulfuric acid at 1 – 1.5 wt %, the volumetric ratio of anhydrous acetic acid and 30 wt % hydrogen peroxide in the range of 1.2 – 1.5.

Leveneur et al., [147] described the process for the synthesis of peracetic acid from hydrogen peroxide and acetic acid using a heterogeneous catalyst, the process comes under green process technology, in a continuous flow fixed bed reactor. The Amberlite IR – 120 was used as a heterogeneous catalyst for formation of peracetic acid in a continuous flow fixed bed reactor. The experiments were carried out at various parameters such as different wet catalyst loadings (2.5 to 4.9 g), mean residence times (10 to 55 min) and reactor temperature (30 to 60 ℃). They reported RTD to study performance of continuous flow pattern at various flow rates and catalyst loading by applying impulse and unit step procedures with a tracer input. They observed that the catalyst distribution in the packed reactor did not disturb the flow configuration. They reported the HCl tracer study by the impulse method presented a better explanation of the flow configuration. They determined the pressure drop as well as mass transfer parameters like mass flux, Sherwood number, Schmidt number, j – factor and so on. They also developed a model one was absence of axial dispersion – plug flow model and another one was the presence of axial dispersion model.

Ebrahimi et al., [121] reported the synthesis method for the peracetic acid formation in a tubular microreactor from hydrogen peroxide (50 wt %), acetic acid (100 wt %), and sulfuric acid (96 wt %). The experiments were carried out continuously in the micro structured reactor. The specifications of the micro reactor were same as reported by **Ebrahimi et al., 2011**. They carried out the experiments at different parameters such as different catalyst concentration (sulfuric acid: 0 – 12 wt %) different temperature (20 – 70 ℃) and different residence time (0.6 – 31 min (average velocity was 0.1 – 4 cm/s). They determined reaction rate constants and activation energies for forward reaction and reverse reaction. The reaction rate constants and activation energies were found by considering the plug flow model and laminar flow model and the values were shown in **Table (2.5)**. They determined the equilibrium constant for the reaction of the peracetic acid formation and shown in Eq (2.19). The determined equilibrium constant for peracetic acid synthesis were 6.45, 5.77, 5.20, 4.72, 4.31, 3.95 and 3.64 at 20, 30, 40, 50, 60, 70 and 80 ℃ respectively.

Table (2.5). Estimated parameters values for plug flow and laminar flow model.

Peracetic acid	Plug flow model R^2 = 97.90	Laminar flow model R^2 = 97.98
$k_{1,\text{ mean}}$ [L^2/(mol · s)]	1.22 x 10^{-6}	0.816 x 10 – 6
$k_{2,\text{ mean}}$ [L^2/(mol · s)]	2.98 x 10^{-7}	0.134 x 10 – 6
E_1 [J/mol]	34.9 x 10^{3}	36.6 x 10^{3}
E_2 [J/mol]	35.1 x 10^{3}	44.8 x 10^{3}

$$K_{eq} = \frac{k_1}{k_2} = 6.1 \text{ x } \exp\left(\frac{8200}{R}\left(\frac{1}{T} - \frac{1}{298}\right)\right) \qquad (2.19)$$

Jolhe et al., [136] described the synthesis process for peroxyacetic acid from hydrogen peroxide (30 wt %) and anhydrous acetic acid by using a heterogeneous catalyst for example Amberlite IR – 120H. The schematic experimental setup was shown in **Figure (2.5)**. They studied different operational parameters like effect of molar ratio of hydrogen peroxide to acetic acid (0.45: 1, 1: 1 and 2.5: 1), flow rate (20, 30 and 40 mL/h), catalyst loading (340 – 707 mg/mL), temperature (20 – 60 °C), catalyst activity, and effect of ultrasound for the synthesis of peracetic acid. They proposed the better operating parameter such as molar ratio of hydrogen peroxide to acetic acid was 1: 1, flow rate of feed was 30 mL/h, temperature of 40 °C and catalyst loading was 471 mg/mL, with these parameters, the equilibrium of the reaction was achieved within 10 min as compared to conventional method. They compared the conventional method and ultrasonic bath based micro reactor for the peracetic acid formation. They obtained the peracetic acid concentration of 3.375 mol/L in the conventional method and 5.125 mol/L in the micro reactor.

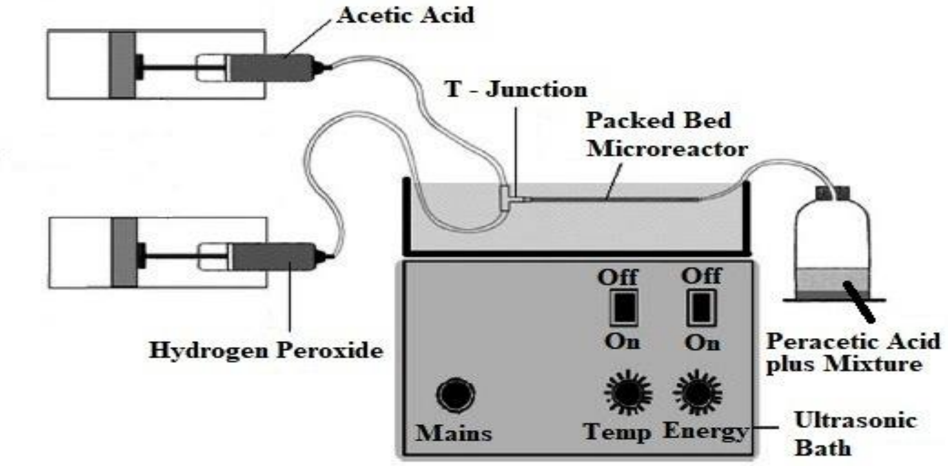


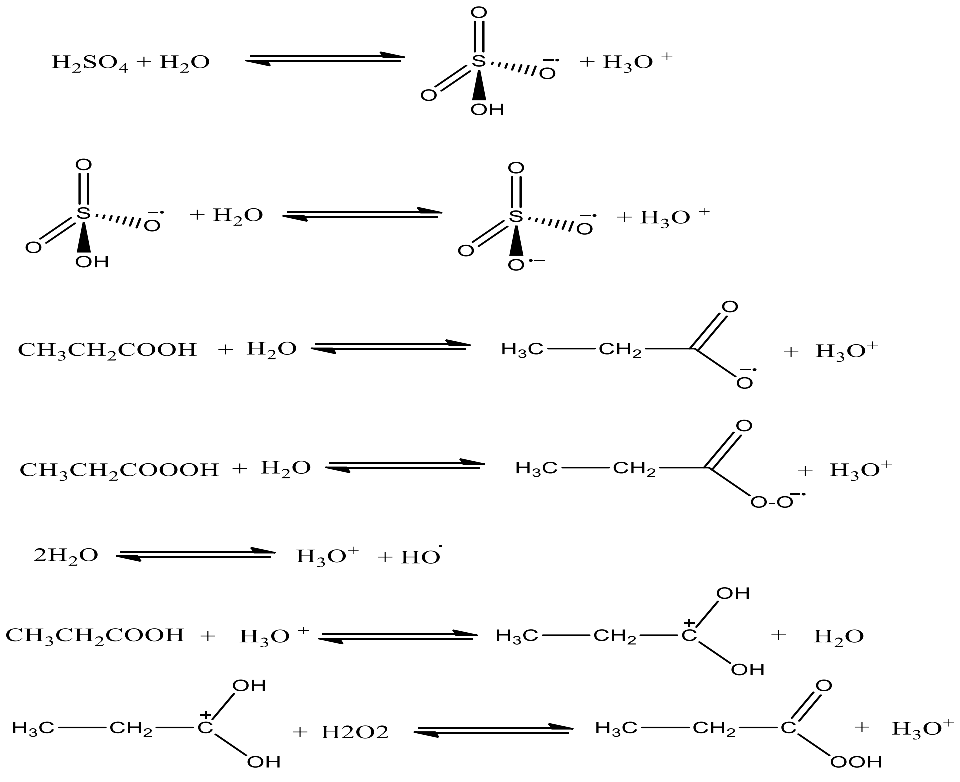
Figure (2.5). Schematic depiction of experimental setup for the synthesis of peracetic acid in ultrasound-assisted microreactor. [136].

2.4.3. Review on synthesis of perpropionic acid

Inaba et al., (US5206425A, 1993), [139] described that the process for formation of perpropionic acid from the reaction of hydrogen peroxide by propionic acid by employing a homogeneous catalyst such as boric acid and adding suitable stabilizing agents such as picolinnic acid, dipicolinic acid, rutidine, 2 – Picoline and n – oxide and the reaction solvent is ethyl propionate. They carried out the reaction at 50 to 80 ℃, molar ratio of propionic acid to hydrogen peroxide was 1.5 to 6.0, catalyst loading is 0.001 to 1.0 mol per 1 mol of hydrogen peroxide, reaction pressure is 10 to 300 Hg.

Leveneuret et al., [146] described the peroxypropionic acid (PPA) synthesis from propionic acid (PA) by hydrogen peroxide (HP, 30 wt %) employing sulfuric acid as a homogeneous catalyst. They performed experiments in a conventional batch reactor keeping it in an isothermal water bath to maintain the reaction temperature. They developed a kinetic model for the batch reactor for the reaction at 30 – 60 ℃. The experimentally operational conditions for the reaction in the batch reactor were shown in **Table (2.6)**. Even if the experiments at higher concentration of sulfuric acid seems to like to be impossible on an industrial bulk scale due to the nonideality of the mixtures should be considered into account at lower concentrations.

The proposed reaction mechanism and kinetic equation were as follows



Scheme – (2.XII). Reaction mechanism for the peroxypropionic acid formation catalyzed by sulfuric acid in the aqueous media. [146].

Table (2.6). The experimental conditions for the reaction in the batch reactor. [146].

Parameters	**Limit/range**
Reaction temperature	30 – 60 ℃
Stirrer speed	200 rpm

$[H_2O_2]_o/[PA]_o$	0.4 – 2.05
$[H_2O]_o$	16.77 – 40.66 mol/L
Concentration of sulfuric acid	0 – 1.41 mol/L

Leveneura et al, [118] reported the production of peroxypropionic acid (PPA) from propionic acid (PA) and hydrogen peroxide (HP) by using different cation exchange resins as a catalysts (heterogeneous catalysts). The experiments were performed at 40 ℃, equimolar ratio of reactants and an apparent Brønsted concentration of 0.2 M. They used various cation exchange resins The experimental conditions for catalyst comparison in the batch reactor were shown in **Table (2.7)**.

Table (2.7). The experimental conditions for catalyst comparison in the batch reactor. [118].

Pamameters	**Limit/range**
Reaction temperature	40 ℃
Stirrer speed	250 – 600 rpm
$[H_2O_2]_o/[PA]_o$	0.9 – 1.0
$[H_2O]_o$	21.8 – 26.3 mol/L
$[PA]_o$	5.5 – 6.4 mol/L
Apparent $[H^+]$	0.18 – 0.22 mol/L

They studied the different parameters like sulfuric acid effect at low concentration on the conversion of PA, effects of mass transfer (external mass transfer and internal mass transfer effect), comparison among the pretreated and the native catalyst, cross – linking effect, comparison of the solid catalyst with sulfuric acid and deactivation of the catalyst. Hence, they concluded that the productivity of the cation exchange resins was compromise among their catalytic efficiency and their deactivation. So, cross – linking with higher degree caused by a slower rate of reaction. The catalytic activities of the cation exchange resins were on the same concentration as sulfuric acid at comparable and decrease in the order of Dowex – 50 Wx2 > Smopex – 101 > Dowex – 50 Wx8 ≈ Amberlite IR – 120 > Amberlyst – 15. However, there are benefits upon the use of heterogeneous catalysts over homogeneous catalyst like easy separation of product.

Leveneur et al., [147] described the process for the perpropionic acid synthesis from the reaction of propionic acid by the reaction of hydrogen peroxide in the presence of a heterogeneous catalyst, the process comes under green process technology, in a continuous flow fixed bed reactor. The Amberlite IR – 120 was employed as a heterogeneous catalyst for the peracetic acid formation in a continuous flow fixed bed reactor. The experiment was carried out at different parameters such as different wet catalyst loadings (2.5 to 4.9 g), mean residence times (10 to 55 min) and temperatures (30 to 60 °C). They reported the residence time distribution to study the performance of the flow configuration at different total flow rates and different catalyst loading by applying impulse and unit step procedures with various tracer inputs. They observed that the catalyst scattering in the packed reactor did not disturb flow configuration. They reported the HCl tracer study by the impulse method gave explanation of the flow configuration. They also determined the pressure drop as well as some mass transfer parameters like mass flux, Sherwood number, Schmidt number, j – factor and so on. They also developed a model one was Absence of axial dispersion – plug flow model and another one was the presence of axial dispersion model.

2.5. Gap identifications based on the literature review

From the literature survey, it was observed that there was no reported data on the formation of 5 – (4' – methyl – [1, 1' – biphenyl] – 2 – yl) – 1 – trityl – 1H – tetrazole by micro structured reactor. Therefore, an attempt was made for the tritylation reaction for the synthesis of MBPTT. The MBPTT is industrially important intermediate product and it is used for seven to eleven sartan drug preparation. Similarly, synthesis of performic acid (PFA), peroxypropionic acid (PPA) and peracetic acid (PAA) were reported in planar structured micro reactor but there is no report on PPA using a helical capillary micro reactor. Hence, an attempt was made for the synthesis of PFA, PPA and PAA and their kinetic studies.

2.6. Problem statement and motivation

The numbers of chemical reactions are performed by a conventional batch reactor by adding the required reactants. In the conventional method, a reaction needs more time to complete based on the reaction type and operational parameters. The convention batch reactors give less yield due to some dead zones of the reactor and there is a chance to occur side reactions which form an undesired product. The formation of undesired product which leads to give a lesser yield of the desired product with poor quality and selectivity. In order to overcome the problem, a micro structured reactor found a place in chemical industries. It can be able to resolve the problem in a lesser time with improved yield and selectivity of the higher quality desired product.

A micro structured reactor has the dimensions below one millimeter. The grouping of small dimensioned reactors and high pressure deals new visions into chemical reaction engineering as well as technology. The decrease in the characteristic length and diameter, leads to increase of the surface – volume ratio. This is the main advantage for the significant application of the micro structured reactor in chemical engineering. Major advantages are mechanical stability and improved heat and mass transfer. The micro structured reactors also give improved yield, conversion, and selectivity in lesser time with a better quality product. This is the motivation for this thesis. The gaps identified from the literature is the main motivation to carry out research work on the process intensification by a continuous flow micro structured reactor method for selected chemical reactions of organic chemistry.

CHAPTER – 3

MATERIALS AND METHODS

In the present chapter, the details of materials, from where they are procured and which are required to carry out the experiments, are given. The detailed experimental setup description as well as detailed experimental procedure are reported for the four different case studies. Similarly, the detailed analytical procedure for each case study is reported.

3.0. Experimental setup

The experiments were carried out by using a micro structured reactor (MSR). The schematic picture of the experimental structure was shown in **Figure (3.1)**. The experimental setup consists of micro structured reactor, syringe pumps, syringes and water bath for maintaining the reaction temperature. The volume of micro reactors were from 0.45 to 6.28 mL. To carry out the experiments, two syringe pumps were employed in order to feed the reactants through the micro structured reactor system. Different total flow rates of feed were keep up at different operating conditions based on a chemical reaction. The reactant – A (with catalyst or with catalyst) and reactant – B were fed to the micro structured reactor by using syringe pumps. Both reactant were added at equimolar or different molar ratios. The experiments carried out with a homogeneous catalyst at different operating specifies. The number of experiments carried out to find the most favorable operating conditions for a reaction by the micro structured reactor system. The experimental runs were conducted at different temperatures by maintaining constant temperature using a water bath. The maximum operating temperature was maintained for different reactions. The samples collected from the micro structure reactor and were analyzed immediately. The detailed analysis procedure is reported in analytical section for corresponding reactions.

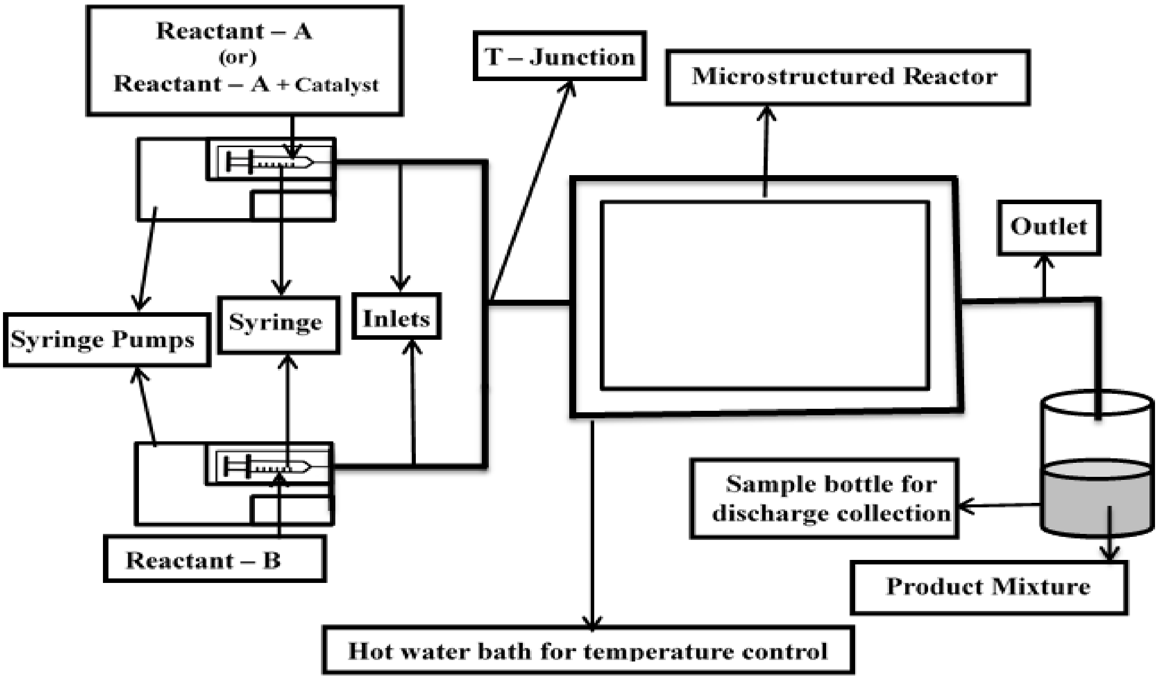


Figure (3.1). Schematic depiction of experimental system.

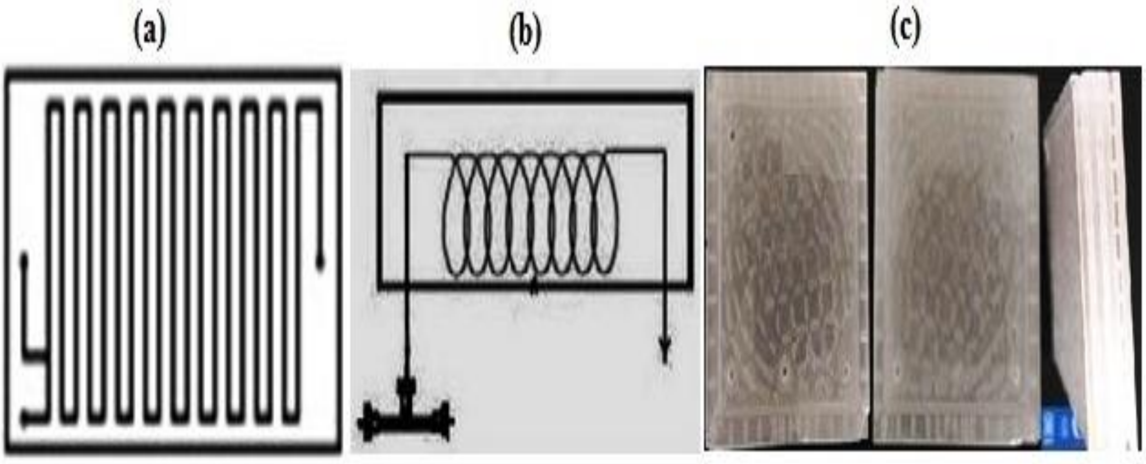


Figure (3.2). Schematic representation of (a) Serpentine MR (b) Helical MR (c) Advance – Flow™ Reactor.

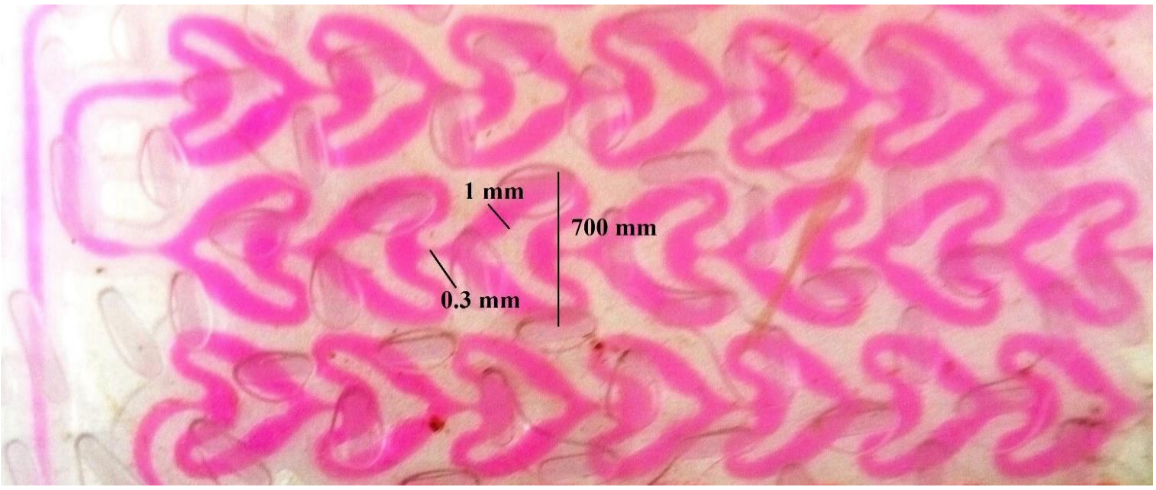
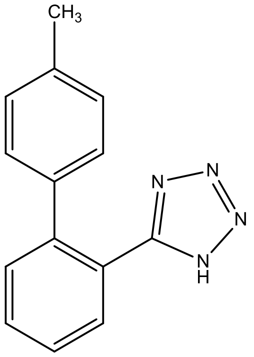


Figure (3.3). Photograph of AFR (side view).

3.1. Case Study – I: Continuous flow synthesis of 5 – (4' – m ethyl – [1, 1' – biphenyl] – 2 – yl) – 1 – trityl – 1H – tetrazole by a micro structured reactor and its characterizations

3.1.1. Materials

For the synthesis of 5 – (4' – methyl – [1, 1' – biphenyl] – 2 – yl) – 1 – trityl – 1H – tetrazole (MBPTT), all the analytical reagents and solvents were procured from the Hi Theme Chemicals, India and used without further any purification. The reagents were 5 – (4' – methyl – [1, 1' – biphenyl] – 2 – yl) – 1H – tetrazole (MBPT), structure was shown in chemical structure 3.1, triphenylmethyl chloride (TPMC, trityl chloride (TTC)), triethylamine (TEA). The solvents were dichloromethane (DCM), methanol (MeOH), ethyl acetate (EA), and n – hexane (NHA). The reaction carried out at atmospheric pressure and room temperature (27 ± 2 ℃). The completion of the reaction was observed and confirmed by the thin layer chromatography (TLC) by using ethyl acetate – hexane system as mobile phase. Solvents were distilled off from the reaction mixture at atmospheric pressure. At the end of distillation, the reduced pressure was applied to remove the solvent (DCM) completely. The solvent removed by using a vacuum pump.



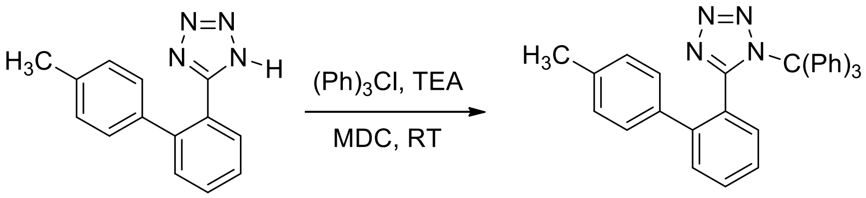
5-(4'-methyl-[1,1'-biphenyl]-2-yl)-1*H*-tetrazole

Chemical Structure 3.1: Structure of MBPT.

3.1.2. Experimental procedure for the synthesis of 5 – (4' – methyl – [1, 1' – biphenyl] – 2 – yl) – 1 – trityl – 1H – tetrazole

Starting material 5 – (4' – methyl – [1, 1' – biphenyl] – 2 – yl) – 1H – tetrazole (MBPT) (1 g, 4.2323 mmol), Triethylamine (TEA) (1equivalent, 0.63 mL, 4.2323 mmol) were dissolved in dichloromethane (DCM) taken into a syringe. Trityl chloride (1.025equiv, 1.209 g, 4.3368 mmol) was dissolved in dichloromethane (DCM) taken into another syringe. The filled syringes were attached to the syringe pumps and predetermined flow rate was set to feed into the micro structured reactor. The same procedure was employed for a different flow rate for different micro structured reactors. The output was collected and quenched in a vessel which already contains water in it. The organic phase was washed using distilled water twice. First water washing was carried out in 5 mL of dichloromethane (DCM). During the water washing. stirring was maintained for 5 to 10 min and the organic layer was separated after settling. The separated organic layer was washed by water two times and the organic phase was separated. The separated organic phase was taken into a threenecked flask. The solvent was removed under atmospheric pressure at 40 – 45 ℃. Finally, reduced pressure (vacuum) was applied to remove the solvent (DCM) completely. The crude product was recrystallized by adding methanol. The crystals of the pure product were isolated from the mother solution by filtration at 25 ℃. The wet sample was taken into a petri dish and dried below 50 ℃ for 1 – 2 h. The dry product was weighed on a balance for knowing quantity.

The balanced chemical reaction was as shown in **Scheme – (1.I).**



(1.I)

Three different micro reactors were used as shown in **Figure (3.1)**, **Figure (3.2)** and **Figure (3.3)** those were the stainless steel capillary coiled reactors (SSCR – 2 mm and SSCR – 1 mm) with internal diameters 2 mm and 1 mm respectively and the Corning® Advanced – Flow™ Reactor (AFR). The different configurations of micro reactors and Corning® AFR are reported for various types of reactions [97, 187 – 190]. The details of the three different configurations of micro reactors were given in **Table (3.1).**

Table (3.1). Specification of helical micro reactors and Corning® AFR.

Specification	**SSCR – 2 mm**	**SSCR – 1 mm**	**Corning® AFR**	**Teflon HCMR**
Internal diameter	2.00 mm	1.00 mm	0.30 mm	0.80 mm
Length	2.00 m	2.00 m	-	2.0 m
Diameter of curvature	45.00 mm	45.00 mm	-	13.25, 18.25 & 23.25
Number of turns	14	15	-	21, 15 & 12
Internal volume	6.28 mL	1.57 mL	0.45 mL	1.0 mL
MOC	SS – 316L	SS – 316L	Corning glass	Teflon

3.1.3. Analytical method

The formations of the products were confirmed by thin layer chromatography. The analytical thin layer chromatography has accomplished on Merck Precoated Silica gel 60 F_{254} plates. The mobile phase was hexane and ethyl acetate and the ratio was 1: 4 (v/v).

Furthermore, The thin layer chromatography was carried out under UV light (λ = 254 nm) as well as in an iodine vapor. The melting points were observed in an open capillaries on Stuart melting point (SMP30) instrument. The FTIR spectra were noted down in the solid state as KBr pellets by using an FTIR spectrophotometer (Perkin – Elmer Spectrum 100) (s, m, and w indicate strong, medium and weak respectively). The NMR (^{1}H (proton) and ^{13}C (carbon)) were recorded in deuterated chloroform ($CDCl_3$) as a solvent, at 400 MHz on an NMR spectrometer (Bruker AscendTH 400). The chemical shifts values were stated in δ ppm relative to tetramethylsilane (TMS) (s, d, and m indicate singlet, doublet and multiplet respectively).

3.2. Case Study – II: Continuous flow synthesis of performic acid using a helical capillary micro reactor and its kinetic study

3.2.1. Materials

Formic acid (FA, HCOOH) (98 – 100 %), hydrogen peroxide (HP, H_2O_2) (30 % w/v), sulfuric acid (SA, H_2SO_4) (98 %), potassium iodide (PI, KI), ferroin indicator solution (FI, 1, 10 – phenanthroline ferrous sulfate $[Fe(C_{12}H_8N_2)_3]SO_4$) and sodium thiosulphate (STS, $Na_2S_2O_3{\cdot}5H_2O$) were obtained from S D fine – chem Limited, Mumbai, India and ammonium cerium sulphate (ACS, $(NH_4)_4Ce(SO_4)_4{\cdot}2H_2O$) (98 %) was procured from Loba Chemie Pvt Ltd, Mumbai, India, starch maize powder (corn, $(C_6H_{10}O_5)n$) procured from Molychem, Mumbai, India. Formic acid and hydrogen peroxide were used as reactants and sulfuric acid was used as a catalyst to carry out the experiments. Ammonium cerium sulphate, ferroin indicator, sodium thiosulphate, potassium iodide and starch maize solution (as an indicator) were used for the analysis of performic acid samples. Distilled water was employed for preparing the stock solutions. The formation rates of performic acid were studied. The synthesis reaction of the PFA was shown in **Scheme – (1.II)**. The reaction was carried out in the presence and absence of a homogeneous catalyst such as sulfuric acid.

3.2.2. Experimental setup and procedure for the synthesis of performic acid

The experiments were performed in polytetrafluoroethylene (Teflon) helical capillary micro reactor (HCMR). The schematic picture of the experimental setup for the synthesis of peroxyformic acid was shown in **Figure (3.4).** Experimental setup contains Teflon helical capillary micro reactor, syringe pumps, syringes, and water bath for maintaining the reaction temperature. The volume of helical capillary micro reactor was 1.0 mL (ID = 0.80 mm, OD = 1.0 mm and Length = 2 m). To carry out the experiments, two syringe pumps were used to charge the reactants through the HCMR system. Flow rates of feed were kept in the range of 5 to 72 mL/h. The reactants of formic acid (with a catalyst) and hydrogen peroxide were added to the helical capillary micro reactor using syringe pumps. Both reactants were added in equimolar ratio. The experiments were carried out with sulfuric acid as a homogeneous catalyst. The numbers of experiments were carried out to find out the optimum operating conditions for the synthesis of the performic acid by the HCMR system. The experimental runs were conducted at different temperatures (10, 20, 30 and 40 ℃) which were maintained at constant temperature using the water bath. The maximum operating temperature was maintained at 40 ℃ beyond this temperature, the product starts to decompose. The samples were collected from the helical capillary micro reactor and analyzed immediately. The detailed analysis procedure is reported in the analytical section 3.2.3.

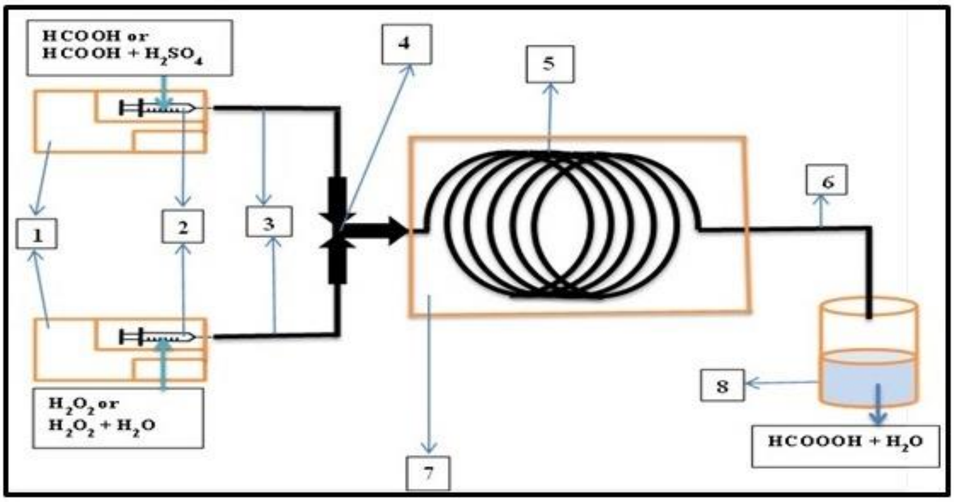


Figure (3.4). The schematic picture of experimental setup for the synthesis of PFA.

Where 1. Syringe pumps (Model: Caddo 15B), 2. Disposable syringes, 3. Inlets, 4. T – Mixer (ID = 0.8 mm), 5. Teflon Helical Capillary Micro reactor (HCMR) for reaction (ID = 0.80 mm, OD = 1.5 mm and Length = 2 m), 6. Outlet, 7. Water bath for maintaining temperature, 8. Beaker for output collection.

3.2.3. Analytical method

The product performic acid was collected and immediately titration was carried out to determine the conversion of formic acid as well as concentration of the performic acid. From the collected sample, pipetted out 0.1 to 0.2 mL performic acid mixture (sample) (or weighed accurately ~ 0.115 to 0.23 g) and added into a 500 mL flask which already having 100 to 200 mL of ice cold 1N sulfuric acid to permit the titration at 0 – 10 ℃. Then, 1 – 2 drops ferroin indicator solution were added and titrated against 0.1N ammonium cerium sulphate solution till the vanishing of the salmon color of the indicator and appearance of a light bluish color, which was the end point. The titre value was recorded to calculate the concentration of hydrogen peroxide (HP). Further, for that solution, 5 to 10 mL of 10 % KI solution (or 0.5 to 1 g of dry KI) and 1 – 2 mL starch indicator were added and titrated against with 0.1N sodium thiosulphate solution to liberate iodine until the solution turns from blackish to salmon color back (salmon color stable for 2 – 5 minute) which was the required endpoint. The titration value was also recorded to calculate the concentration of PFA [101, 191–193].

3.3. Case Study – III: Continuous flow synthesis of peroxypropionic acid by using a helical capillary micro reactor and its kinetic study

3.3.1. Materials

Propionic acid (PA, C_2H_5COOH, 99.5 %) and ammonium cerium sulphate (ACS, $(NH_4)_4Ce(SO_4)_4{\cdot}2H_2O$, 98 %) were procured from Sisco Research Laboratories Pvt. Ltd., Mumbai, India, hydrogen peroxide (HP, H_2O_2, 30 % w/w) and sulfuric acid (SA, H_2SO_4, 97 %) were obtained from Fisher Scientific, Mumbai, India, potassium iodide (KI), ferroin solution (as an indicator) and sodium thiosulphate (STS, $Na_2S_2O_3{\cdot}5H_2O$) were procured from S D fine – chem Limited, Mumbai, India and starch maize powder (SMP, corn, $(C_6H_{10}O_5)n$) was obtained from Molychem, Mumbai, India. PA and HP were reactants and SA employed as catalyst to perform the experiments. ACS, FI (as an indicator), STS, KI and SMP solution (as an indicator) were employed for the analysis of peroxypropionic acid product. The required stock solutions were prepared using distilled water. The rate of formation of peroxypropionic acid was studied. The synthesis reaction of the peroxypropionic acid was shown in **Scheme – (III)**. The reaction was carried out in the presence of a homogeneous catalyst such as sulfuric acid.

3.3.2. Experimental setup and experimental procedure for the synthesis of peroxypropionic acid

All experiments were carried out in Teflon helical capillary microreactor (HCMR). The graphical depiction of the experimental system for the production of peroxypropionic acid was shown in **Figure (3.5)**. The experimental system contains the Teflon helical capillary micro reactor, syringe pumps, syringes and water bath to maintain temperature of the reaction. The volume of Teflon helical capillary micro reactor was 1.0 mL (ID = 0.80, OD = 1.0 mm, radius of curvature = 13.25 mm / 23.25 mm and Length = 2 m). In order to perform the experiments, syringe pumps were employed to charge reactants into the HCMR system. The feed flow rates were kept in the range of 5 to 72 mL/h. The reactants PA (with a catalyst) and HP were fed into the micro reactor by employing syringe pumps. The reactants were added at different molar ratios. The experiments were carried out with a homogeneous catalyst for instance sulfuric acid. It was observed that the presence of a catalyst in a reaction mixture, which increases the rate of reaction as well as increases yield within shorter time as compared to reaction without a catalyst. The experiments were carried out by varying parameters like concentration of hydrogen peroxide, molar ratio of reactants, radius of the curvature of the micro reactor and temperature to find best operating parameters for the production of the propionic acid by the HCMR. The experimental runs were carried out at various temperatures (30, 40, 50 and 60 ℃) by maintaining constant temperature of the water bath. The highest operating temperature was kept at 60 ℃ and above this temperature the PPA generated vapor phase. The product samples collected from the HCMR and analyzed immediately. The analytical method was given in analytical section 3.3.3.

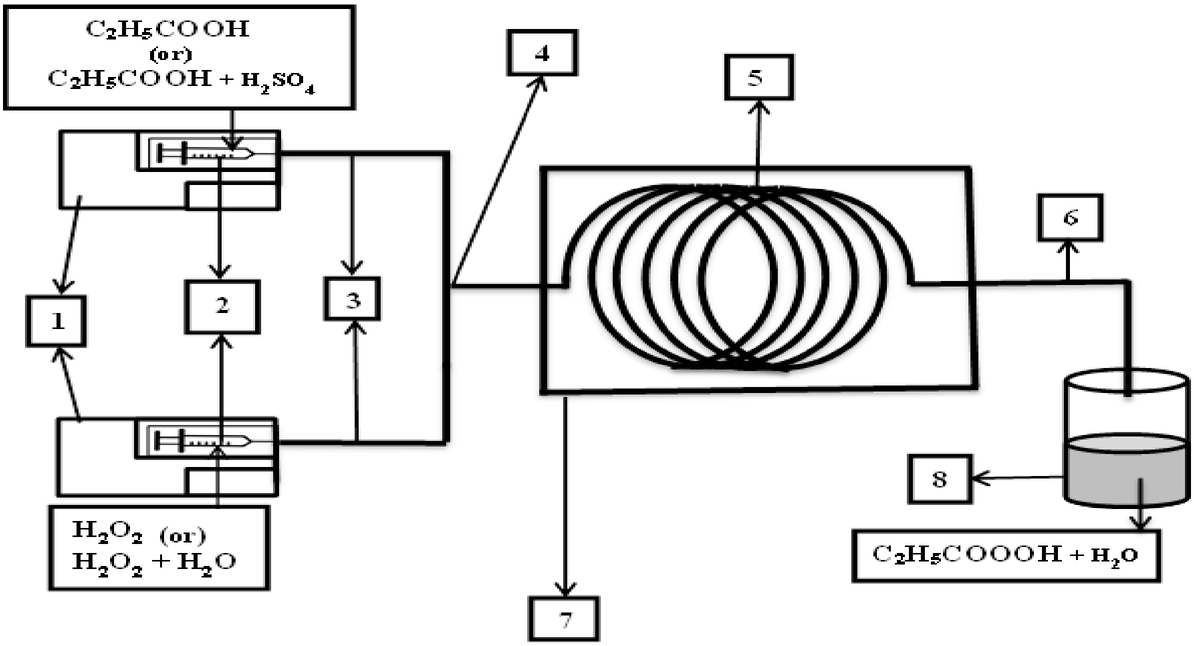


Figure (3.5). The schematic depiction of the experimental setup for the synthesis of PPA. where 1. Syringe pumps (Model: Caddo 15B), 2. Plastic syringes, 3. Inlets, 4. T – Mixer (ID = 0.8 mm), 5. Teflon helical capillary micro structured reactor (HCMR) for reaction (ID = 0.80 mm, OD = 1.5 mm, radius of curvature = 13.25 mm / 23.25 mm and Length = 2 m), 6. Outlet, 7. Water bath to maintain the temperature of the system and 8. Glass beaker for collecting the product.

3.3.3. Analytical method

The liquid phase of the sample (product) was examined offline by titration procedures using Greenspan and Mackellar method [98, 101, 105, 118, 146, 191]. The concentration of hydrogen peroxide was found by titration against a prepared standard solution of ACS and the concentration of the perpropionic acid was found out by titration against prepared standard solution of sodium thiosulphate. The titeration values were recorded and estimated the percentage conversion of PA as well as concentration of PPA.

3.4. Case Study – IV: Comparative study for continuous flow synthesis of peracetic acid using a micro structured reactor and its kinetic study

3.4.1. Materials

Acetic acid (CH_3COOH, AA, 98 – 100 %), hydrogen peroxide (H_2O_2, HP, 30 % w/v), sulfuric acid (H_2SO_4, SA, 98 %), potassium permanganate (PPM, $KMnO_4$, 99 %), potassium iodide (PI, KI, 99%), sodium thiosulphate (STS, $Na_2S_2O_3{\cdot}5H_2O$, 99%), ferroin indicator (FI, $Fe(C_{12}H_8N_2)_3]SO_4)$) and starch maize powder (SM, $(C_6H_{10}O_5)n$) were procured from local chemical supplier. AA, HP, SA, FI, STS are procured from SD Fine – chem Limited, Mumbai, India. PPM is procured from Finar, Ahmedabad, India. KI is procured from SRL, Mumbai, India. Starch maize powder is procured from Molychem, Mumbai, India. HP, AA and SA (catalyst) chemicals were used to carry out the experiments. PPM, STS, PI, FI (indicator) and solution of SM (indicator) chemicals were used for the analysis of product mixture sample. Required stock solutions were prepared by distilled water. The formation rates of peracetic acid were studied. The peracetic acid formation reaction was reported in **Scheme – (IV)**. The experiments were carried out using sulfuric acid which is a homogeneous catalyst in three different microstructured reactors.

3.4.2. Experimental setup and experimental procedure for the synthesis of peracetic acid

Experiments were carried out in Teflon serpentine capillary micro reactor (SCMR), Corning® Advanced – Flow™ Reactor and Teflon helical capillary micro reactor (HCMR). The experimental setup for the formation of peracetic acid was shown in **Figure (3.6)**. The experimental setup consists of syringe pumps, micro structured reactor, syringes, and hot water bath to keep reaction temperature constant. The holdup of capillary micro reactors was 1.0 mL (ID = 0.80 mm, OD = 1.0 mm and Length = 2 m). The volume of AFR is 0.45 mL of single module with opening of 0.3 mm. To perform the experimental runs, two syringe pumps were used to feed the reactants into the micro reactor system. The total feed flow was kept at 5 to 60 mL/h (residence time was 12 – 1 min).

The experiments were carried out in a micro structured reactor. The different configurations of micro reactors were shown in **Figure (3.2)**. One feed was acetic acid with catalyst and second feed was hydrogen peroxide. The two feeds were allowed into the micro reactors system at different molar ratios. All the experiments were carried out using sulfuric acid as catalyst at different loadings and temperature. It was observed that a catalyst for a reaction, enhances rate of the reaction as well as yield and conversion rate in reduced time as compared to a reaction without a catalyst. Numerous experiments were carried out by the micro reactor system to intensify the reaction and to find suitable operating parameters for formation of peracetic acid. All experiments were carried out at atmospheric pressure and various temperatures (20, 30, 40, 50 and 60 °C). The reaction temperature was kept constant by keeping water bath temperatures constant. The maximum temperature was kept at 60 °C. However, at high temperature and higher catalyst loading the reaction get backward or product get starts to decompose. The product mixture was obtained from the micro reactor and immediately analyzed. The concentration of hydrogen peroxide was found by titration against standard potassium permanganate solution, similarly, the concentration of peracetic acid was checked by titration with standard sodium thiosulphate solution [154, 171, 191, 194].

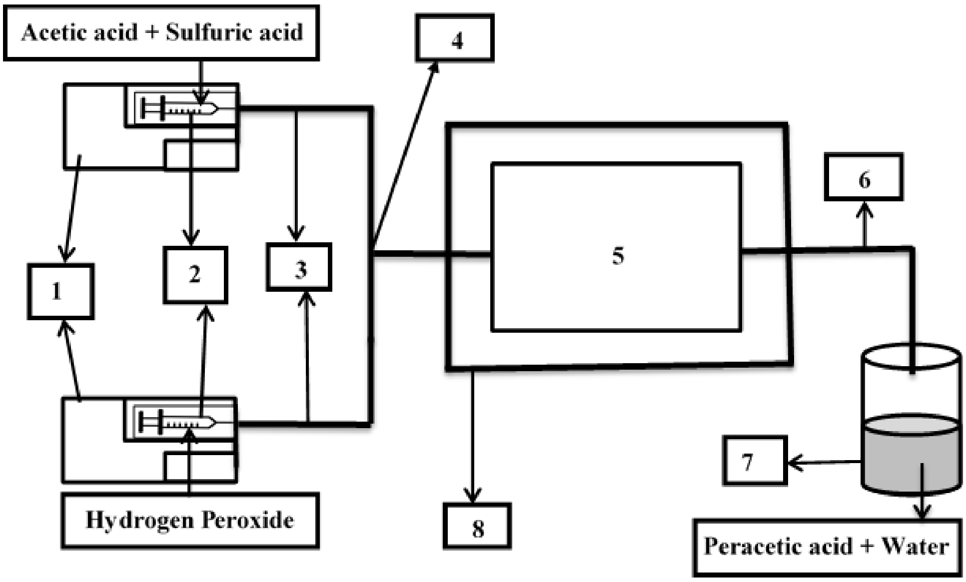


Figure (3.6). The schematic depiction of the experimental setup for the synthesis of PAA.. Where 1. Syringe pumps, 2. Plastic Syringes, 3. Inlets, 4. T – Joint (0.8 mm ID), 5. Serpentine capillary micro reactor (SCMR) or helical capillary micro reactor (HCMR) with ID is 0.80, OD is 1.5 and Length is 200 mm or Corning$^{®}$ Advanced – Flow^{TM} Reactor (0.30 mm opening, 1.0 mL volume of two modules) 6. Outlet, 7. Sample bottle to collect product sample from the microreactor system and 8. Water bath to maintain temperature

3.4.3. Analytical method

The product mixture was collected from the micro reactor. The sample might contains peracetic acid, water, unreacted acetic acid, unreacted hydrogen peroxide and sulfuric acid. The product mixture was immediately titrated to find the concentration of acetic acid and peracetic acid. From the collected sample 0.1 to 0.2 mL of sample was pipetted out and transfer into a 500 mL conical flask which already contains 100 to 200 mL ice cold 1N sulfuric acid solution. The titration need to be carried out at 0 to 10 °C. Few drops of ferroin indicator was added and the mixture was titrated against standard potassium permanganate solution still the vanishing of salmon color of the indicator and appearance of light pink color. The run down value of the burette was tabulated to find the concentration of hydrogen peroxide. Further, for the same solution mixture, 5 to 10 % potassium iodide solution and 1 to 2 mL starch indicator solution were added and titrated against standard sodium thiosulphate solution to liberate iodine until the solution turns from blackish to salmon color back (salmon color should be stable up 10 to 15 min). The run down value was tabulated to find the concentration of acetic acid and concentration of peracetic acid [154, 172].

CHAPTER – 4

RESULTS AND DISCUSSIONS

4.1. Case Study – I: Continuous flow synthesis of 5 – (4' – methyl – [1, 1' – biphenyl] – 2 – yl) – 1 – trityl – 1H – tetrazole by a micro structured reactor and its characterizations

In this case study, it is reported that the flow behaviour in the helical and AFR micro reactors and also the characterization details of the synthesized product. The complete details are as follows.

4.1.1. Hydrodynamic of fluid flow through SSCR – 2 mm, SSCR – 1 mm and Corning® AFR: Flow regimes

The experiments were carried out at room temperature and atmospheric pressure, total flow rates of 50 to 120 mL/h. The observed flow behavior in all the micro reactors is laminar flow and it was confirmed by Reynolds number. The Reynolds number (Re), for SSCR – 2 mm, SSCR – 1 mm and Corning® AFR, was determined based on velocity at the inlet of the circular shape of SSCR – 2 mm and SSCR – 1 mm and the heart shape of Corning® AFR.

$$\mathrm{Re} = \frac{d v \rho}{\mu} \tag{4.1}$$

Where d is internal diameter of the channel, v is velocity, ρ is fluid density, and μ is viscosity of the solution mixture. Here the density of the dichloromethane was considered as the fluid density (1326 kg/ m^3) and the viscosity of solution mixture (6.47×10^{-4} Pa. s) was estimated by using Rheometer (Rheolab instrument, Model No. QC SN80156956-FW1.20). The estimated Re at the inlet of different micro structured reactors were found to be 18.12 – 43.49, 36.24 – 86.98 and 94.88 – 227.72 for SSCR – 2 mm, SSCR – 1mm and AFR respectively. Therefore, the flow behaviour is a laminar flow in all three micro reactors. The comparison of flow rates, residence times and Reynolds numbers of SSCR – 2mm, SSCR – 1mm, and AFR respectively were given in **Table (4.1)**.

Nevertheless, the total feed flow rates in AFR are 50 – 120 mL/h, and in the laminar regime, the hydrodynamic features of advanced flow reactor could be different as compared to simple micro structured reactors. Therefore, in the advanced flow reactor (AFR), for a reactive system, while the surface tension and the viscosity could remain same, the superficial velocity changes considerably based the cross – sectional area. [61, 62, 195].

The Dean number (De) is a dimensionless group and provides information about flow behaviour through the curved pipes/capillaries in fluid mechanics [196] [89, 197 – 203].

According to Reynolds number, it can interpret physical understanding of the Dean number in terms of the force balances among the forces because of centripetal acceleration, forces of inertia and the forces of viscous by rearranging the terms. Hence, which is the product of the Reynolds number and the square root of the curvature ratio.The Dean number is given as follows

Table (4.1). Comparison of Re of SSCR – 2 mm, SSCR – 1mm, and Corning® AFR.

Flow Rate, mL/h.	**SSRC – 2 mm**		**SSRC – 1 mm**		**Corning® AFR**	
	t_r, min	**Re**	**t_r, min**	**Re**	**t_r, sec**	**Re**
50	07.54	18.12	01.88	36.24	32.40	94.88
60	06.28	21.75	01.57	43.49	27.00	113.86
70	05.39	25.37	01.35	50.74	23.14	132.84
80	04.71	28.99	01.18	57.99	20.25	151.81
90	04.19	32.62	01.05	65.24	18.00	170.79
100	03.77	36.24	00.94	72.48	16.20	189.76
110	03.43	39.87	00.86	79.73	14.73	208.74
120	03.14	43.49	00.79	86.98	13.50	227.72

$$\mathrm{De} = \frac{\sqrt{(\text{Centripetal forces}) * (\text{Inertial forces})}}{\text{Viscous forces}} = \frac{\rho \upsilon d_t}{\mu} * \sqrt{\frac{d_t}{d_c}} = \mathrm{Re} * \sqrt{\frac{d_t}{d_c}} \qquad (4.2)$$

Where ρ is fluid density, υ is velocity of the fluid flow, d_t is diameter of tube inlet, μ is the viscosity of the fluid, d_c is the curvature diameter of the path of the tube and Re is the Reynolds number. For the experiments, it was observed that Dean number in the range of 3.82 – 9.17 for SSCR – 2mm and 5.40 – 12.97 for SSCR – 1mm.

The application of dimensional study revealed that a fully developed laminar flow of a fluid in a cylindrical tube can be described by a single dimensionless group that is equivalent to the product f*Re. In case of the flow in curved tubes, the pressure drop is higher than that of straight tube at the same flow rate and length of the tube. Some researches carried out experiments concerning fluid flow in helical coiled tubes with circular crosssections [197–202]. In the experiment, helical micro reactors used as mentioned above. The theoretical curve tube friction factor, f_c, in a helical coil micro reactor, was evaluated. The correlation of friction factor for the fully developed laminar flow is given as follows

$$f_c = f_s\left(1.03058 * \left(\frac{De^2}{288}\right)^2 + 0.01195 * \left(\frac{De^2}{288}\right)^4\right) \qquad (4.3)$$

Where De is Dean number, and f_s is friction factor of straight tube. Using the correlation, given equation (4.3), the curve tube friction factor (f_c) for helical micro reactor was estimated by using the Reynolds numbers and the friction factor of the straight tube (f_s =

16/ Re). The estimated f_s values were in the range of 0.88 – 0.37 and 0.44 – 0.18 for SSCR – 2 mm and SSCR – 1 mm respectively. The estimated f_c are in the range of $2.34x10^{-3}$ – $3.23x10^{-2}$ and $4.67x10^{-3}$ – $6.49x10^{-2}$ for SSCR – 2 mm and SSCR – 1 mm respectively. The comparison of flow rate (Q), residence time (t_r), Dean Numbers, f_s and f_c of SSCR – 2 mm and SSCR – 1 mm were given in **Table (4.2).** From the above study, it could be decided that as the residence time increases, the Dean Number decreases due to the decrease in the velocity by decreasing the flow rate. By increasig the flow rate which leads to decrease in f_s and f_c. It was observed that their effects were high in SSCR – 1 mm when it was compared to SSCR – 2 mm.

Table (4.2). Comparison of Q, t_r, De, f_s, and f_c of SSCR – 2 mm, and SSCR – 1 mm.

Flow Rate, mL/h.	**SSRC – 2 mm**				**SSRC – 1 mm**			
	t_r, min	**De**	**f_s**	**f_c x 10^3**	**t_r, min**	**De**	**f_s**	**f_c x 10^3**
50	07.54	3.82	0.88	2.34	01.88	5.40	0.44	4.67
60	06.28	4.58	0.74	4.04	01.57	6.48	0.37	8.08
70	05.39	5.35	0.63	6.41	01.35	7.56	0.32	0.128
80	04.71	6.11	0.55	9.57	01.18	8.64	0.28	0.192
90	04.19	6.88	0.49	0.136	01.05	9.72	0.25	0.273
100	03.77	7.64	0.44	0.187	00.94	10.81	0.22	0.375
110	03.43	8.40	0.40	0.249	00.86	11.89	0.20	0.499
120	03.14	9.17	0.37	0.323	00.79	12.97	0.18	0.649

Reynolds numbers were in the range from 18.12 – 43.49 and 36.24 – 86.98 for SSCR – 2 mm and SSCR – 1 mm respectively. The pressure drop shows essential role in the design of the micro reactors like helical coiled capillaries and Corning® AFR [16, 19, 162, 163, 204 – 210]. In the experiments, a horizontal helical coiled capillary and vertical Corning® AFR with homogeneous liquid flow of the laminar regime was considered. The pressure drop (△ P) due tothe frictional effects of the fluid flow. For a laminar flow, the pressure drop is given by the Hagen – Poiseuille equation as follows

$$\frac{\Delta P}{L} = \frac{32\mu v}{d_t^2} \qquad (4.4)$$

Where L is length of the capillary or reaction path length, μ is viscosity of the fluid, v is velocity of the fluid flow in the capillary helical coiled tubes and Corning® AFR, d_t is the internal diameter of SSCRs and opening diameter for heart shape of Corning® AFR (assumed for pressure drop estimation). C. M. White [211] studied that the Dean number associatedwith pressure drop in a curved tube by the function of the Dean number, defined as below [198, 205, 212 – 215]

$$f(De) = 0.37xDe^{0.36} \tag{4.5}$$

Hence, the resistance of laminar flow in a straight tube (equation (4.4)) can be multiplied with equation (4.5) and implies the following equation as below.[209, 216].

$$\frac{\Delta P}{L} = \frac{32\mu v}{d_t^2} x0.37xDe^{0.36} \tag{4.6}$$

By using equation (4.6), the pressure drop was estimated for SSCR – 2mm and SSCR – 1mm in the range of 13.72 – 45.12 and 248.64 – 817.83 Pa/m respectively and by using equation (4.4) the pressure drop was estimated for Corning® AFR in the range of 35500.69 – 85201.65 Pa/m. The comparison of the flow rate, residence time, and pressure drop of SSCR – 2 mm, SSCR – 1 mm and were given in **Table (4.3).** The pressure drop calculation is helpfull for the determination of the power consumption. It directly dictates the specific interfacial area. In the Corning® AFR, only the pumping of the fluids into the device is required and no additional power to provide agitation as in the case of stirred vessels is needed.

Table (4.3). Comparison of Q, t_r, △ P of SSCR – 2 mm and SSCR – 1 mm and Corning® AFR.

Flow Rate, mL/h.	**SSRC – 2 mm**		**SSRC – 1 mm**		**AFR**	
	t_r, min	**△ P, Pa/m**	**t_r, min**	**△ P, Pa/m**	**t_r, sec**	**△ P, Pa/m**
50	07.54	13.72	01.88	248.64	32.40	35500.69
60	06.28	17.58	01.57	318.61	27.00	42600.82
70	05.39	21.68	01.35	392.92	23.14	49700.96
80	04.71	25.99	01.18	471.17	20.25	56801.10
90	04.19	30.51	01.05	553.02	18.00	63901.23
100	03.77	35.21	00.94	638.23	16.20	71001.37
110	03.43	40.08	00.86	726.56	14.73	78101.51
120	03.14	45.12	00.79	817.83	13.50	85201.65

4.1.2. Continuous flow process for the tritylation reaction of 5 – (4' – methyl – [1, 1' – biphenyl] – 2 – yl) – 1H – tetrazole.

In comparison of SSCR – 2mm and SSCR – 1mm with Corning® AFR, the AFR is one of the commercially existing choices to scale – up single phase and multiphase reactions from the laboratory scale to industrial bulk production scale. The complex geometry of Corning® AFR with continuously varying cross – section along the path of the flow and obstacles inside the heart cells produces pressure variations and flow direction fluctuations that lead to enhance mass transfer as well as heat transfer. The performance of the AFR against other continuous flow SSCR in terms of overall yield and residence time has been shown. Synthesis of 5 – (4' – methyl – [1, 1' – biphenyl] – 2 – yl) – 1 – trityl – 1H – tetrazolewas carried out by three different micro reactors of different internal diameters as said above procedure [83, 84, 217]. The details of the micro reactors were given in **Table (3.1).**

The obtained yield of the productat different flow rates in SSCR – 2mm, SSCR – 1mm and Corning® AFR were shown in **Table (4.4)**.The comparison of residence times and yield obtained by the three micro reactors were shown in **Table (4.4)**. The change in percentage of yield at different flow rate in SSCR – 2 mm, SSCR – 1 mm and Corning® AFR were shown in **Figure (4.1)**. The melting points were found using melting point instrument (Model was SMP30) for all the compounds, the melting points were in the range of 165 – 168 ℃ [95, 96]. The obtained yield varies from the reactor to reactor based on the flow rates and the residence time. The highest yield was obtained in Corning® AFR at the residence time of 27s is 95.18 %. In other reactors, the obtained yield is 93.72 % at a residence time of 71 s (1.18 min) and 92.87 % at a residence time of 324 s (5.39 min) in SSCR – 1mm and SSCR – 2 mm respectively. The variation in the percentage of yield was observed due to different mixing patterns in the different micro reactors and different geometries. Further, as the flow rate increases, the residence time for reaction decreases, which leads to less reaction conversion results decrease in the percentage of yield. The process was demonstrated and confirmed for continuous flow production of MBPTT within 27 s (residence time) and gave yield about 95.18 % (comparable literature batch mode yield was about 92.6 %) [96].

Table (4.4). Comparison of t_r and yield of SSCR – 2 mm, SSCR – 1 mm, and Corning® AFR.

Sr. No.	**Flow Rate, mL/h.**	**SSCR – 2 mm**		**SSCR – 1 mm**		**Corning® AFR**	
		t_r, min	**Yield, %**	**t_r, min**	**Yield, %**	**t_r, s**	**Yield, %**
1	50	07.54	92.87	01.88	93.72	32.40	95.18
2	**60**	06.28	92.87	01.57	93.72	**27.00**	**95.18**
3	**70**	**05.39**	**92.87**	01.35	93.72	23.14	92.71
4	**80**	04.71	88.89	**01.18**	**93.72**	20.25	89.41
5	90	04.19	85.31	01.05	89.68	18.00	87.24
6	100	03.77	82.01	00.94	86.82	16.20	84.31
7	110	03.43	79.00	00.86	83.56	14.73	80.67
8	120	03.14	74.54	00.79	80.88	13.50	75.69

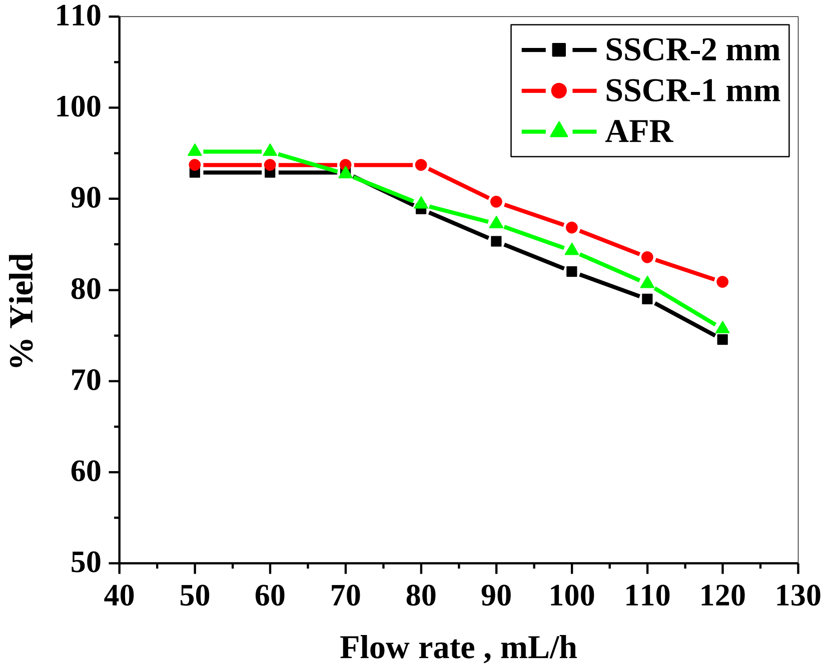


Figure (4.1). Flow rate versus the percentage of yield.

The FTIR spectra of a standard material and synthesized material by the above mentioned micro reactors was shown in **Figure (4.2)**. The details of functional groups of the synthesized material by the three different micro reactors were given as follows

Peak at 3056 cm^{-1} (m) indicates the presence of the alkenes (= C – H stretch), 1603 – 1604 cm^{-1} (s), peak arise due to the amines (N – Hbend), 1488 cm^{-1} (w) is a weak peak of the aromatics (C – C stretch in ring), 1468 cm^{-1} (m) is observed due to the alkanes (C – H bend), 1446 cm^{-1} (m) and 1429 cm^{-1} (m) are present due to the aromatics (C – C stretch in ring), 1357 cm^{-1} (s) peak is observed due to the alkanes (C – H rock), 1288 cm^{-1} (w) is observed due to the aromatic ring (C – N stretch), 1000 cm^{-1} (w) and 940 cm^{-1} (w) are noticed due to the alkenes (= C – H bend), 828 cm^{-1} (m) and 782 cm^{-1} (m) are due to the aromatics (C – H “oop”), 731 cm^{-1} (m) is due to the aromatic (C – H bend), 699 cm^{-1} (m) and 635 cm^{-1} (m) are due to the alkynes, (– C ≡ C – H; C – H bend). The FTIR spectra of standard material of MBPTT and synthesized material of MBPTT by the above mentioned microreactors, were same and the spectra values were given below

FTIR (KBr, cm^{-1}): [96] 3056(m), 1604 (s), 1488 (w), 1468 (m), 1446 (m), 1429 (m), 1357 (s),1288 (w), 1000 (w), 940 (w), 828 (m), 782 (m), 731 (m), 699 (m), 635 (m).

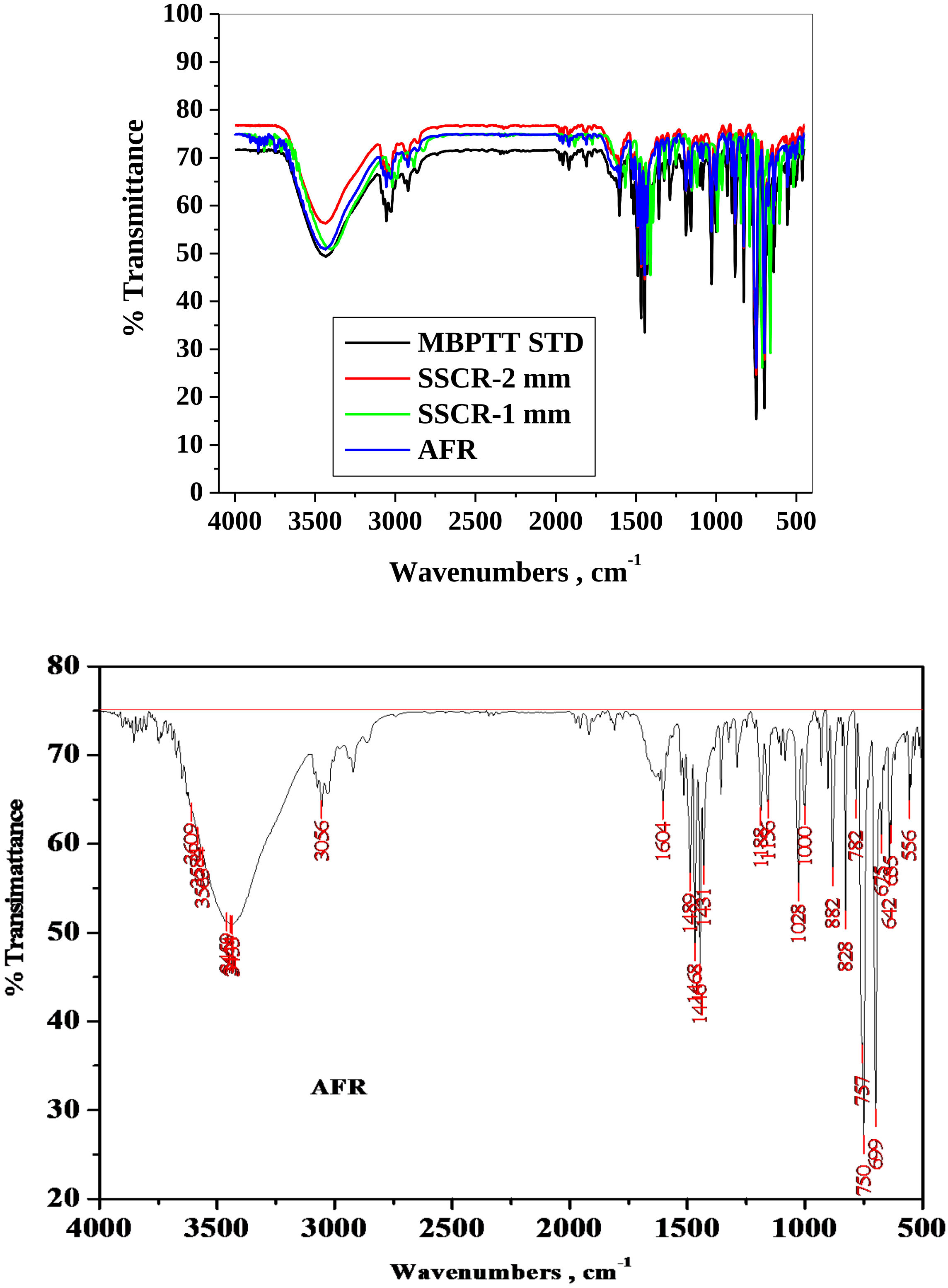
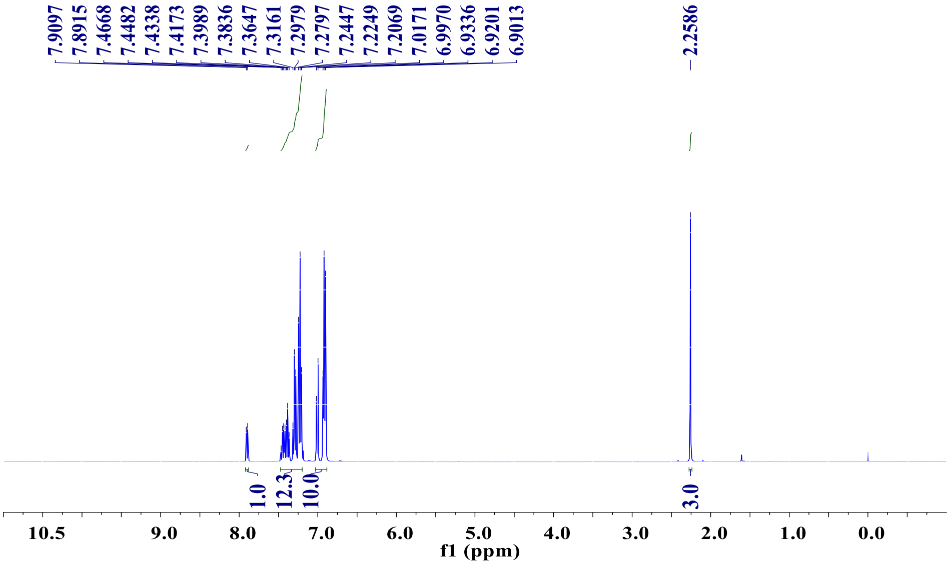


Figure (4.2). The FTIR spectra graph of (a) MBPTT standard material and synthesized material of MBPTT by (b) SSCR – 2 mm (c) SSCR – 1 mm and (d) Corning® AFR microreactors.

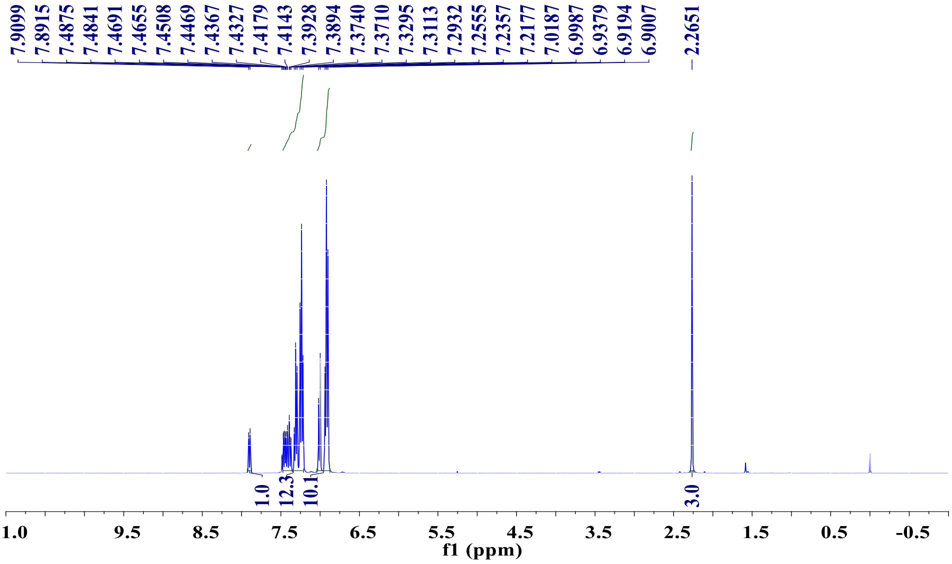
The ^{1}H NMR spectra recorded by $CDCl_3$ as a solvent and the chemical shifts stated in δ ppm corresponding to tetramethylsilane (TMS). The NMR spectra of a standard material and synthesized material by the above mentioned micro reactors shown in **Figure (4.3)**. The

^{1}H NMR spectra of standard material and synthesized material, by the above mentioned micro reactors, were obtained same and the spectra values were given below

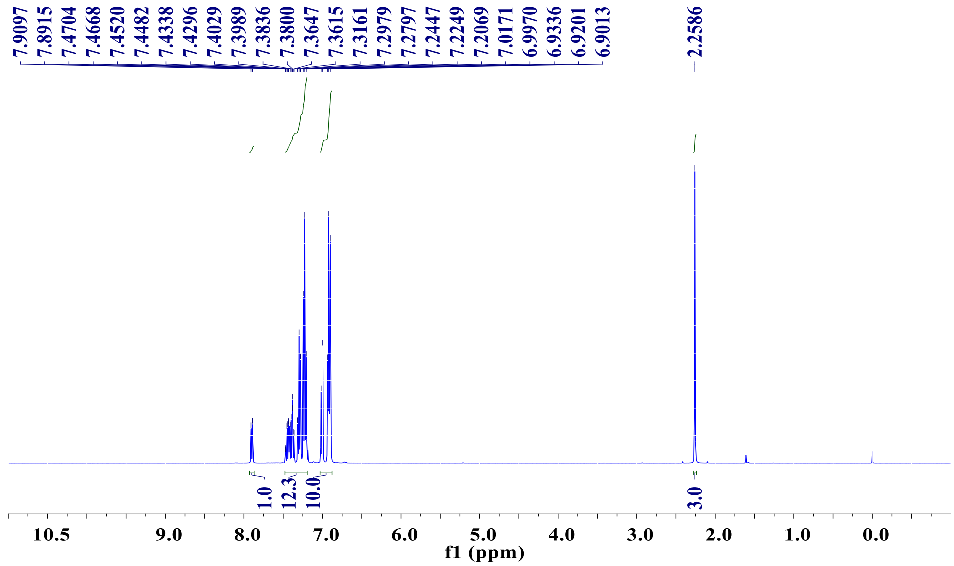
^{1}H NMR (400 MHz, $CDCl_3$) δ: [96,218,219] 2.27 (s, 3H, CH_3), 6.88-7.03 (m, 10H, ArH), 7.19-7.48(m, 12H, ArH), 7.89-7.91 (d, J = 7.30 Hz; 1H, ArH). **Total = 26H**



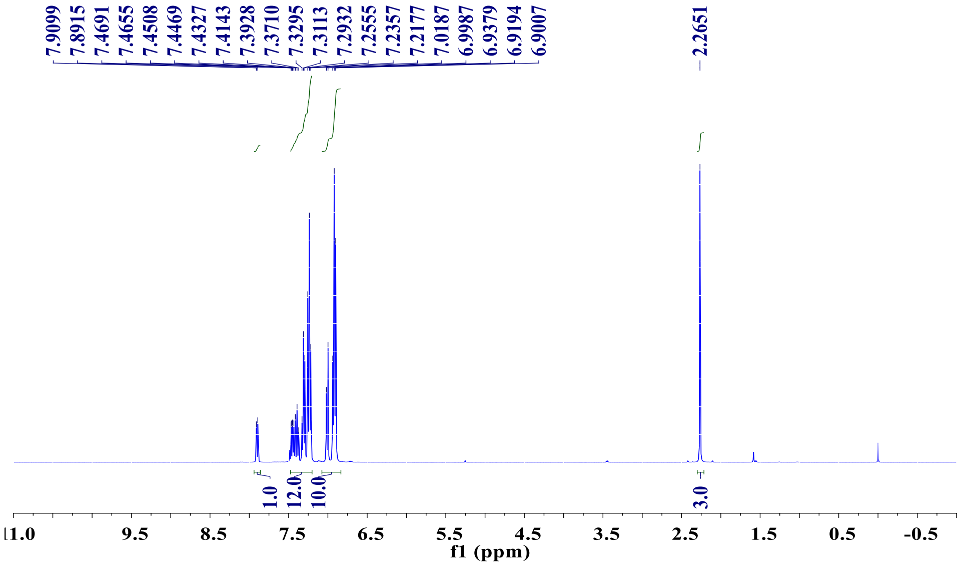
(a). MBPTT – Standard Material.



(b). MBPTT – SSCR – 2 mm.



(c). MBPTT – SSCR – 1 mm.

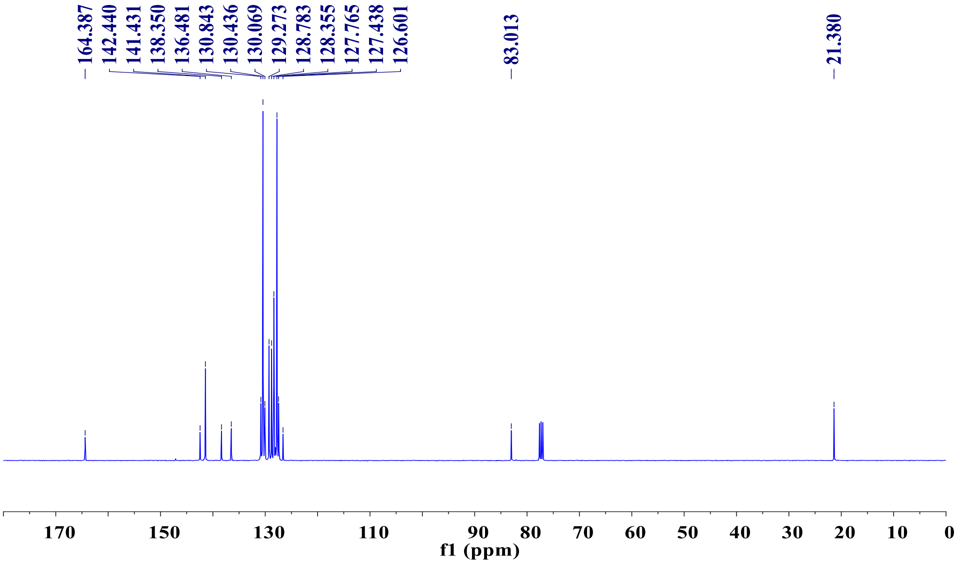


(d). MBPTT – Corning® AFR.

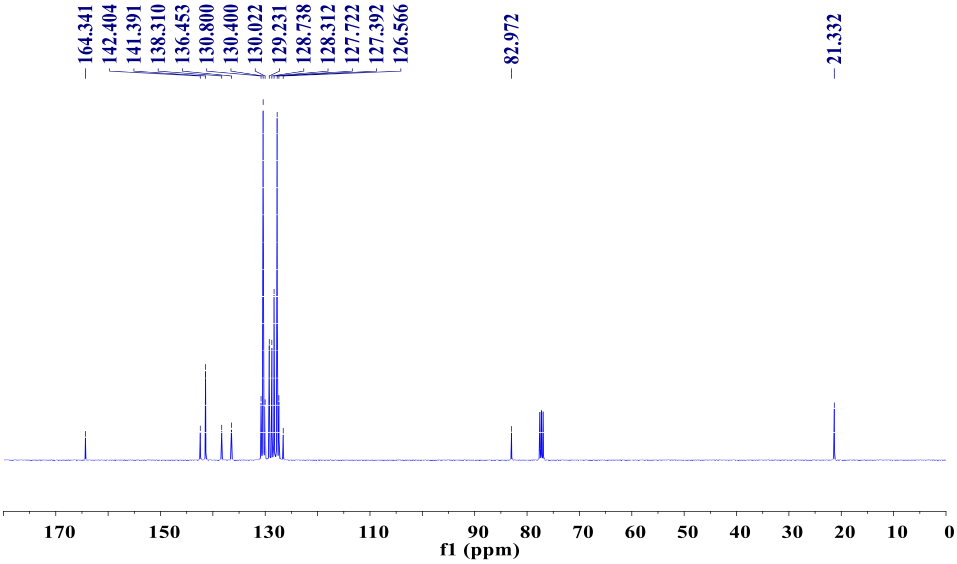
Figure. (4.3). The ^{1}HNMR spectra graph of (a) standard material and synthesized material by (b) SSCR – 2 mm (c) SSCR – 1 mm and (d) Corning® AFR microreactors.

The ^{13}C NMR spectra recorded by $CDCl_3$ as a solvent and the chemical shifts stated in δ ppm relative to tetramethylsilane (TMS). The NMR spectra graphs of a standard material and synthesized material by the above mentioned micro reactors shown in **Figure (4.4)**. The ^{13}C NMR spectra of standard material and synthesized materials, by the above mentioned micro reactors, were obtained same and the spectra values were given below

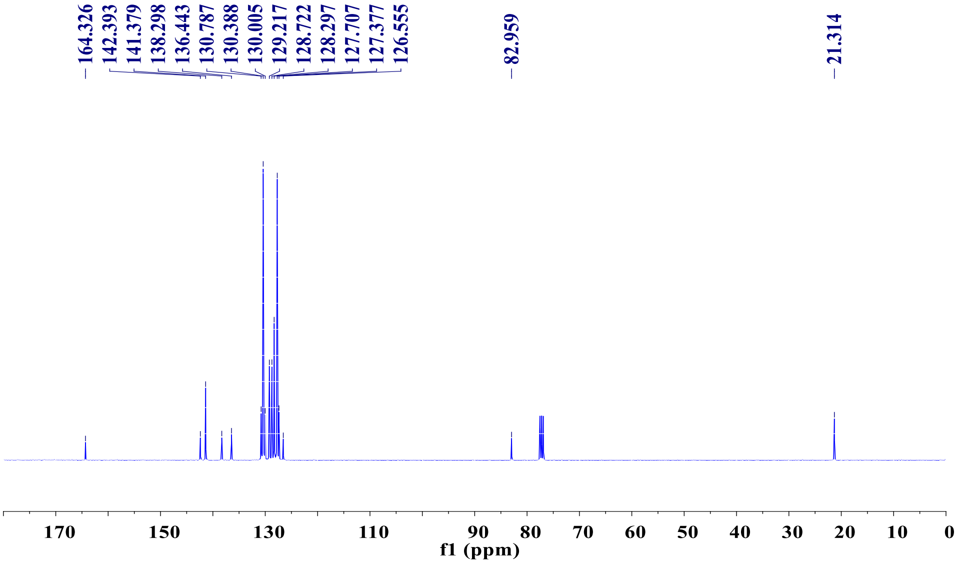
^{13}C NMR (101 MHz, $CDCl_3$) δ: [96, 218, 219] 21.38 (CH_3), 83.01(C), 126.60 (C), 127.44 (3C), 127.77 (2C), 128.36 (1C), 128.78 (1C), 129.27 (6C), 130.07 (7C), 130.44 (2C), 130.84 (1C), 136.48 1C), 138.35 1C), 141.43 (1C), 142.44 (3C), 164.39 (C). **Total = 33C.**



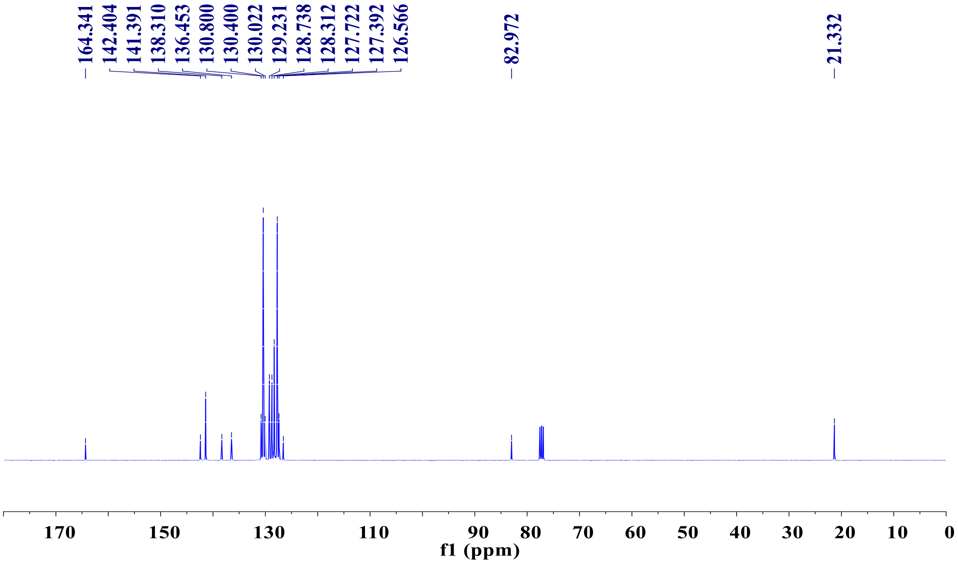
(a). MBPTT - Standard Material



(b). MBPTT – SSCR – 2 mm.



(c). MBPTT – SSCR – 1 mm.



(d). MBPTT – Corning® AFR.

Figure (4.4). The ^{13}C NMR spectra graph of (a) standard material and synthesized material by (b) SSCR – 2 mm (c) SSCR – 1 mm and (d) Corning® AFR micro reactors.

4.2. Case Study – II: Continuous flow synthesis of performic acid using a helical capillary micro reactor and its kinetic study

Different parameters for instance temperature, flow rate, concentration of catalyst and concentration of hydrogen peroxide were intensified by carrying out the reaction in the HCMR. As the concentration of reactants increases, it results in increase in the reaction rate and leads to achieve maximum conversion in a shorter period. However, it can be said that the hydrogen peroxide plays avital role in equilibrium shift in the reaction. At the end of the reaction, the product contains the performic acid, hydrogen peroxide, water, and unreacted FA. All titrations performed immediately in order to bring consistency in the results of the sample and to avoid abnormality in the data.

4.2.1. The effect of concentration of HP on the formation of PFA

Selection of concentrations of reactants plays vital role in a chemical reaction. When the concentration of reactants increases, there is increse in the reaction rate. Nevertheless, the yield is being affected by certain parameters like temperature, catalyst loading (concentration of catalyst), reaction time, reaction pressure, etc. In all experiments, the concentration of FA was maintained 7.11 mol/L which is based on the 1: 1 molar ratio. **Figure (4.5)** describes the effect of different concentrations of hydrogen peroxide such as 10, 20 and 30 % w/v at 0 mol % and 4 mol % catalyst (sulfuric acid) on the concentration of performic acid at different residence time. From **Figure (4.5)**, it can be concluded that 30 % w/v HP and 4 mol % catalyst at 30 °C with 6 minute residence time gave a high concentration of PFA (5.175 mol/L, X_A = 72.80 %).

The residence time of the reaction depends upon the internal holdup of the HCMR and the total feed flow rate. The internal volume of the micro reactor was 1 mL. It is observed that at the flow rate of 10 mL/h and 4 % catalyst maximum conversion obtained was 5.175 mol/L of PFA. It was observed that above 10 mL/h there is no significant change in the PFA concentration was noticed. The plausible reason behind was sufficient residence time required to complete the chemical reaction. So, the residence time 6 min (10 mL/h) was a sufficient flow rate to get the maximum conversion. Increasing above 10 mL/h flow rate would reduce the overall conversion as the residence time will not sufficient. The effect of catalyst concentration was studied (see section 3.1.3) from 2 to 6 mol % based of FA, it was noticed that 4 mol % catalyst (i.e., H_2SO_4) produces sufficient quantity of H^+ ions which aids in getting a maximum concentration of PFA.

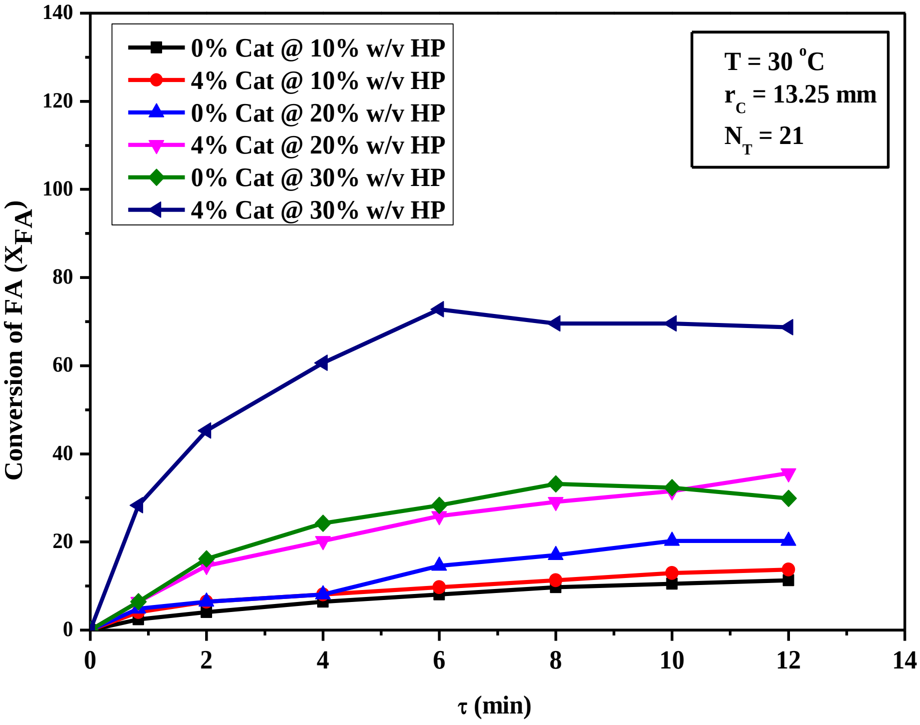


Figure (4.5). Effect of concentration of HP at 30 ℃ on the conversion of formic acid.

4.2.2. The effect of radius of curvature on the formation of PFA

Helical capillary micro reactors with alternating curvatures have been studied for continuous flow applications. It provides very narrow residence time distributions, improved mass transfer and heat transfer in the flow of laminar regions for a residence time up to few minutes [91, 135, 220, 221].

In the laminar flow region, a velocity profile of parabolic form within a simple straight capillary micro structured reactor can certainly be developed by means of looping the straight capillary around the cylindrical pipe or bar. The perturbation affected by the centrifugal forces that act vertical direction to the fliud flow direction in the helical coiled micro structured reactors. Consequently, the secondary flow pattern may be maintained in the circular cross – section of the capillary micro structured reactor that is so called as “Dean vortices”. The idea of the Dean vortices could be well defined by Dean Number that takes into consideration of the ratio of curvature and Reynolds number [89].

Here three different radius of curvature were applied to study the performance of the HCMR for the performic acid synthesis at 30 ℃ temperature and 4 mol % catalyst at different flow rates. In this study, the radius of curvature used were 13.25, 18.25 and 23.25 mm with a number of turns of 21, 15 and 12 respectively. As the radius of curvature decrease, the number of turns increases resulted in higher mixing, enhanced heat transfer and mass transfer. A lower radius of curvature of the HCMR resulted in a higher concentration of PFA.

From **Figure(4.6)**, it observed that at temperature of 30 ℃ and 4 mol % catalyst, radius of curvature of 13.25 mm (number of turns were 21) of HCMR afforded maximum concentration of PFA (5.175 mol/L) whereas the radius of curvature of 18.25 mm (number of turns were 15) and 23.25 mm (number of turns were 12) of the HCMR gave 3.393 mol/L and 3.105 mol/L of PFA respectively at residence time of 9 min. Hence, based on the above observation it could be concluded that 13.25 mm radius of curvature of the HCMR is best helical capillary micro reactor configuration for the synthesis of PFA.

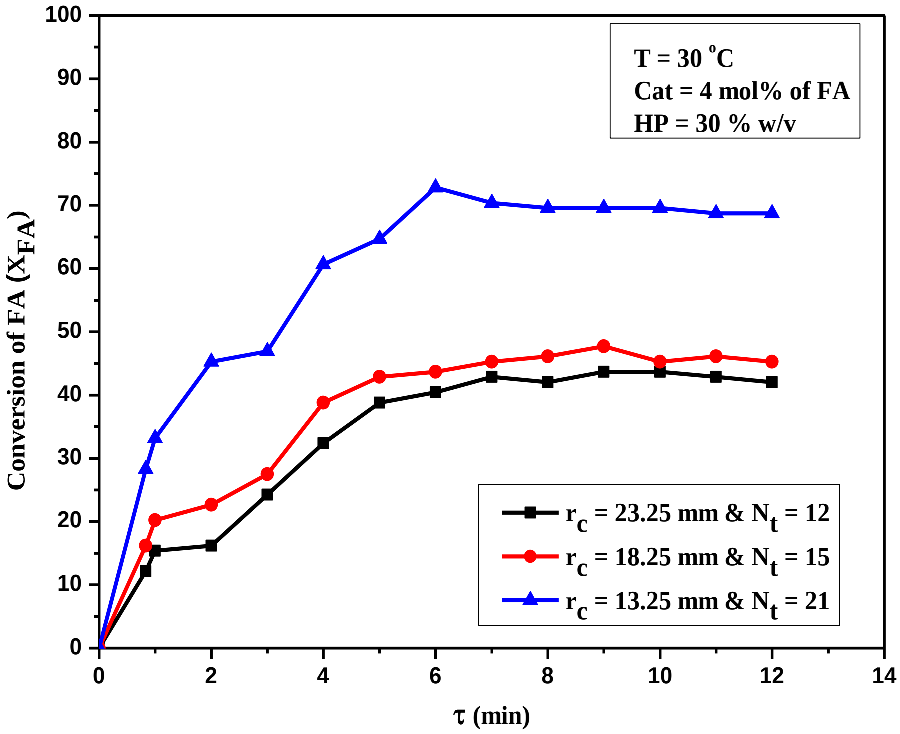


Figure (4.6). Effect of radius of curvature at the temperature of 30 ℃ and 4% mol catalyst on the conversion of formic acid.

4.2.3. The effect of concentration of catalyst on formation of PFA

Catalyst loading is one of the most significant parameters that would take into consideration for the design of reactors. In case of synthesis of PFA, a homogenous or heterogeneous catalyst can be used, however, heterogeneous catalyst loading may cause the problems of clogging in narrow capillary micro reactors. Hence, a homogenous catalyst is preferred for the synthesis of PFA in narrow capillary micro reactors. As reported in the literature, for the formation of PFA, homogenous catalysts such as sulfuric acid (H_2SO_4) or phosphoric acid (H_3PO_4) was employed [116, 119, 120, 173]. In present work, sulfuric acid was used as a homogenous catalyst for the synthesis of performic acid at different percentages such as 0, 2, 4 and 6 mol % based on FA.

Figure (4.7) depicts the conversion of formic acid with respect to residence time at various catalyst concentration at 30 ℃ temperature. Performic acid also formed without catalyst but it has been observed that with the addition of the catalyst, there is increasing in rate of formation of the product. Further, the addition above 4 mol % of H_2SO_4 does not improve the conversion of formic acid. Moreover, the addition of a higher percentage of catalyst at higher temperatures resulted in the vaporization of PFA. It will leads to the formation of vapor (gas) results in formation of slug flow in the capillary micro structured reactor, which causes decomposition reactants and PFA. It has been reported that PFA may decompose to CO_2 and H_2O [33]. From **Figure (4.7)**, it could be concluded that at 30 ℃ and 4 mol % catalyst yields the higher conversion of formic acid in the HCMR at residence time of 6 min.

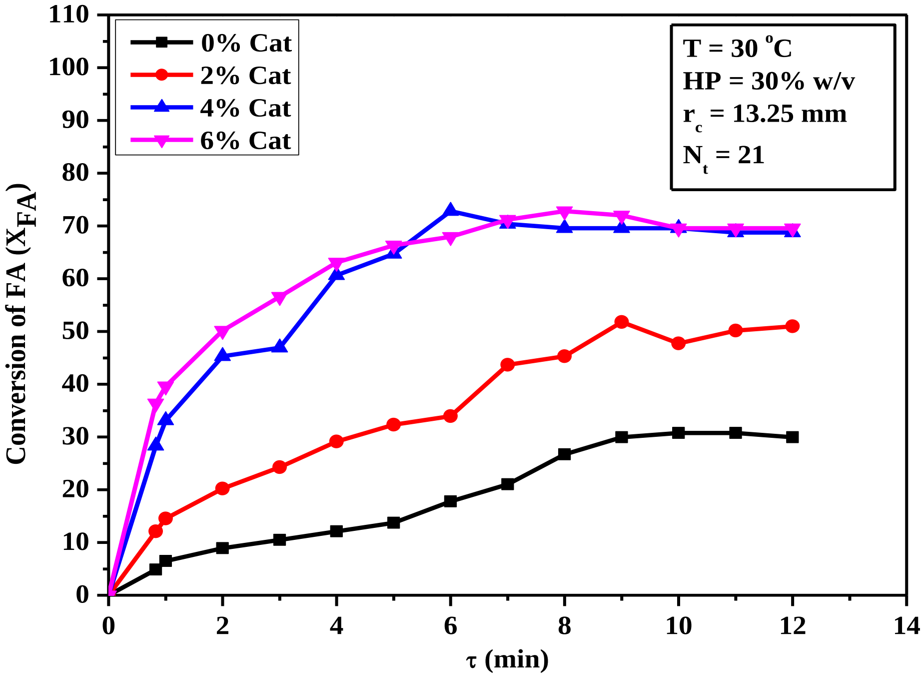


Figure (4.7). Effect of concentration of catalyst at the temperature of 30 ℃ on the conversion of formic acid.

4.2.4. The effect of temperature on the formation of PFA

The experiments were accomplished at different temperatures from 10 to 40 ℃ to observe its effect on the reaction rate. The reaction was carried out at 0 and 4 mol % of catalyst with 30 % w/v hydrogen peroxide concentration. The flow rates were kept in the range of 5 – 72 mL/h at different operating temperatures (10, 20, 30 and 40 ℃) at 13.25 mm radius of curvature of the HCMR. **Figure (4.8)** shows the variant in the conversion of formic acid with respect to the residence time at different temperatures without the catalyst. It was noticed that the maximum concentration of PFA was 2.415 mol/L (X_A = 33.97 %) at 40 °C without catalyst at a residence time of 7 minutes. Further, it was observed that the above 7 minutes, there was a backward reaction. Further, PFA decomposes at a higher temperature and a higher concentration of catalyst. Hence, above 7 minutes of residence time, it was observed a lesser concentration of PFA.

From **Figure (4.9),** it was observed that performic acid concentration decreases with increase in temperature from 30 to 40 ℃ and above 4 mol % catalyst. The maximum conversion of formic acid was X_A = 72.80 % (concentration of PFA was 5.175 mol/L) at a residence time of 6 minutes and 4 mol % catalyst at 30 ℃. It was observed that the reaction equilibrium shifts towards backward reaction when the temperature was increased. This happens because the reaction is exothermic and reversible in nature. Therefore, 30 ℃ is most suitable temperature to carry out the continuous flow synthesis of performic acid in HCMR [33, 136, 137].

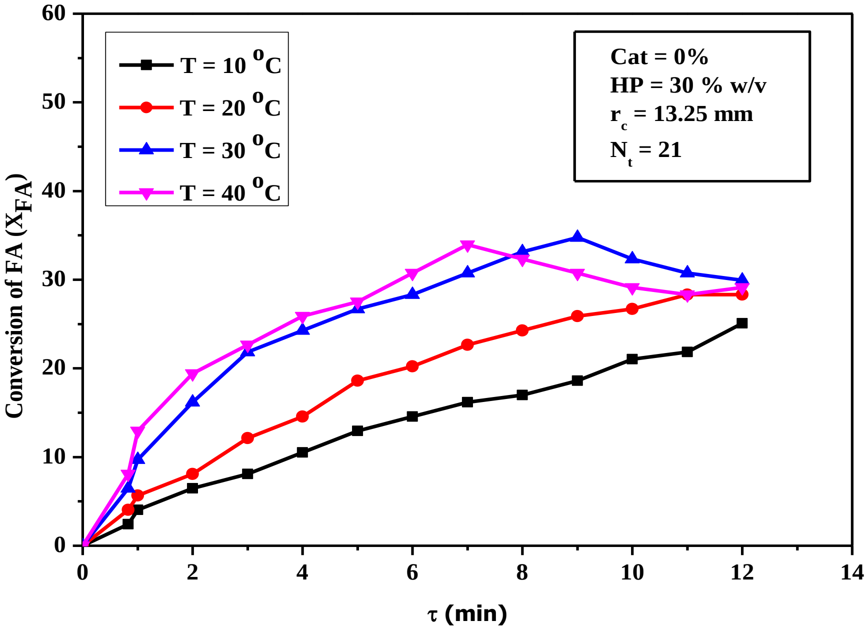


Figure (4.8). Effect of temperature at 0 mol % catalyst on the conversion of formic acid.

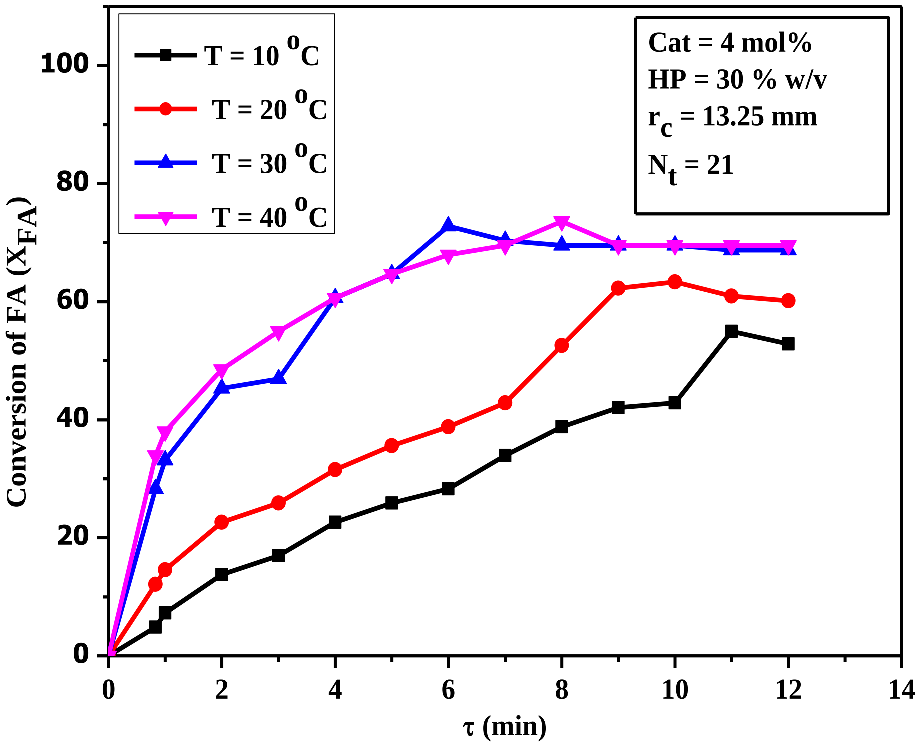


Figure (4.9). Effect of temperature at 4 mol % catalyst on the conversion of formic acid.

4.2.5. Development of kinetic model and determination of kinetic constants

4.2.5.1. Assumptions of the kinetic model

Before developing the kinetic model, the following assumptions were made.

- There is no change in reaction volume during the reaction at any particular temperature
- Hydrogen peroxide is very stable when no catalyst used in the system, even at an elevated temperature. Moreover, the thermal decomposition of performic acid is obvious only at a higher temperature above 40 °C [33, 173].
- Besides, there is a certain amount of water generated in the reaction and it has a stronger nucleophilic group than HP and PFA. Hence, the consumption of PFA is essentially due to its hydrolysis.

Therefore, the chemical reactions in this system consist of two reactions, synthesis PFA and hydrolysis of PFA.

$$\text{HCOOH (A)} + \text{H}_2\text{O}_2\text{ (B)} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \text{HCOOOH (C)} + \text{H}_2\text{O (W)} \qquad (1.\text{II})$$

4.2.5.2. Determination of kinetic constants

The present system mainly emphasizes on the PFA synthesis and hydrolysis with a catalyst to determine the reaction rate constants. **Figure (4.10)** stated the effect of the residence time on the synthesis of performic acid at different temperatures. The data reported in **Figure (4.9)** was employed to find the reaction rate constants and the activation energies of the reaction **Scheme – (1.II)**. Most of the researchers reported that at higher temperatures (i.e.

> 40 °C), PFA decomposes into CO_2 and H_2O [33, 101]. Several researchers reported the kinetic model for the synthesis of PFA and decomposition of PFA at various conditions in conventional batch method. A very few authors reported the kinetic model for the synthesis of PFA in planar micro structured reactor system [33][120]. The kinetic model was developed for the synthesis of PFA with a catalyst by assuming HCMR as plug flow model.

The kinetic model for reaction **Scheme – (1.II)** of PFA is reported in appendix, model equations are reported on page no. 99 – 100 [222 – 224]. **Figure (4.10)** and **Figure (4.11)** were employed to find the rate constants and activation energies for the performic acid synthesis and hydrolysis. From **Figure (4.11)**, the activation energies of performic acid synthesis and hydrolysis were 45.746 and 51.692 kJ/mol respectively. The forward reaction has a lesser activation energy than the reverse reaction. Therefore, it can be observed that the decomposition of performic acid is affected by the temperature significantly than the performic acid synthesis and hydrolysis. The rate constants k_1 and k_2 [$L^2/(mol^2 \cdot min)$] for formic acid catalyzed reaction can be determined from the following expressions.

$$k_1 = 15.03 * 10^6 * \exp\left(\frac{-45746.38}{RT}\right) \quad L^2/(mol^2 \cdot min) \tag{4.7}$$

$$k_2 = 24.20 * 10^6 * \exp\left(\frac{-51692.91}{RT}\right) \quad L^2/(mol^2 \cdot min) \tag{4.8}$$

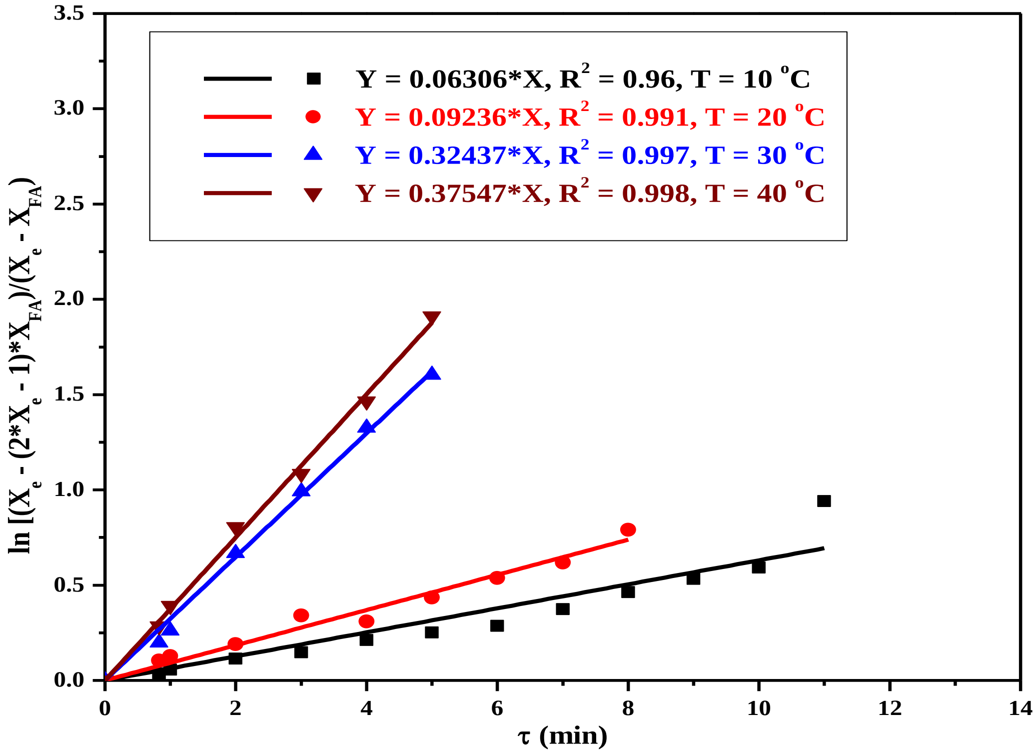


Figure (4.10). The graph of residence time versus ln (conversion ratio) to find rate constants at different temperatures.

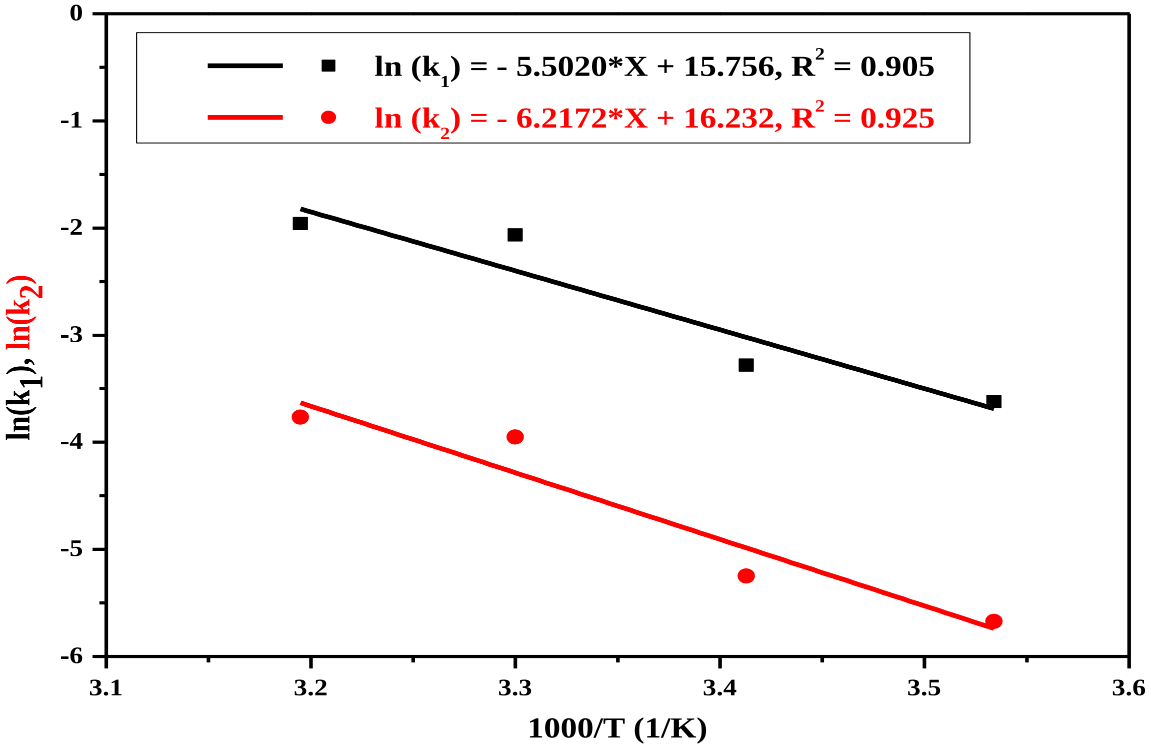


Figure (4.11). Arrhenius plot to find the activation energy for the synthesis of PFA.

4.3. Case Study – III: Continuous flow synthesis of peroxypropionic acid using a helical capillary micro reactor and its kinetic study

For the synthesis of peroxypropionic acid and to find the best operational parameters in a micro reactor, the following parameters were studied such as hydrogen peroxide concentration, molar ratio of reactants, radius curvature, catalyst concentration and temperature. The detailed study of the parameters for the synthesis of peroxypropionic acid were as follows.

4.3.1. Effect of hydrogen peroxide concentration on PPA synthesis

In a chemical process, the selection of concentration of reactants is one of the most significant parameters, which plays a significant role in conversion of reactants into desired products. As the concentration of one of the reactant increases, it shows the effect on the conversion of the other reactant.This will also alters reaction time as well as the yield of the product and selectivity. So, in this section, three different concentrations of hydrogen peroxide such as 20, 25 and 30 % w/w were studied for the synthesis of peroxypropionic acid at 50 ℃ and 10 mol % catalyst based on the propionic acid. The hydrogen peroxide of concentration 30 % w/w is used as it was received. The hydrogen peroxide concentrations of 20 and 25 % w/w were prepared from 30 % w/w hydrogen peroxide concentrations in the laboratory by adding double distilled water. From **Figure (4.12)**, it was observed that the concentration of hydrogen peroxide at 30 % w/w was shown high conversion of propionic acid as compared to 20 and 25 % w/w hydrogen peroxide. From the **Figure (4.12),** it was noticed that maximum conversion of propionic acid was noticed at higher concentration of hydrogen peroxide (i. e., 30 % w/w). Therefore, from **Figure (4.12),** it could be concluded that 30 % w/w hydrogen peroxide is preferable for the synthesis of peroxypropionic acid for better selectivity and yield. Furthermore, it could be concluded that 30 % w/v hydrogen peroxide and 10 mol % catalyst at 50 °C with 10 minute residence time gives higher conversion of propionic acid (X_A = 72.36 %) [105, 185].

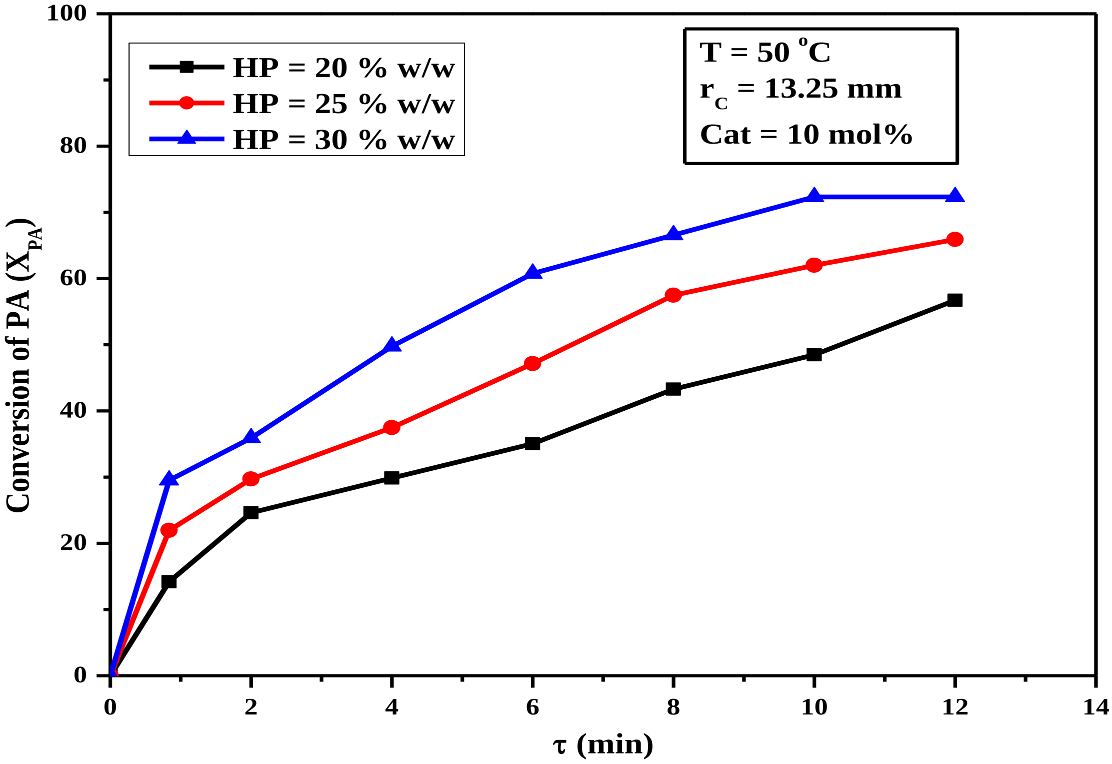


Figure. (4.12). Effect of hydrogen peroxide concentration on the conversion of propionic acid.

4.3.2. Molar ratio of hydrogen peroxide and propionic acid

Figure (4.13) describes the effect of hydrogen peroxide to propionic acid molar ratio from 0.75: 1.00 to 1.25 : 1.00 [136, 137] for the formation of peroxypropionic acid. The experiment was carried out at temperature of 50 ℃, 10 mol % catalyst loading based on propionic acid and total flow rate at 5 to 72 mL/h (residence time of 12 min to 50 s). According to the reaction **Scheme – (1.III)** reported, it has been observed that 1 mole of propionic acid reacts with 1 mole hydrogen peroxide to give 1 mole of peroxypropionic acid. From **Figure (4.13)**, it has been noticed that the conversion of propionic acid enhances from 49.62 to 73.46 % with increase of the molar ratio of hydrogen peroxide to propionic acid from 0.75 : 1.00 to 1.25 : 1.00 respectively. Further, when compared to molar ratio of 1: 1 and 1.25:

1.00, it was noticed that by increasing beyond the molar ratio of 1.25: 1.00, there was no significant change of molar ratio on the conversion of propionic acid. Furthermore, when compared to molar ratio of hydrogen peroxide to propionic acid of 1: 1 and 1.25: 1.00, it gave almost same conversion of propionic acid. Thus, from **Figure (4.13)**, it could be concluded that molar ratio of 1: 1 of hydrogen peroxide to propionic acid is preferred for the formation of peroxypropionic acid. Nevertheless, using excess hydrogen peroxide does not lead to higher conversion.

Micro structured reactor with very large surface area for a chemical reaction [33, 53, 124, 177, 225]. Which enhances the reaction rate for the formation of peroxypropionic acid fast and offers less time in capillary micro structured reactor. Moreover, the concentration of peroxypropionic acid was observed to be constant, it was reduced after residence time of 10 min. This is because of the backward hydrolysis reaction among peroxypropionic acid and water take place to form propionic acid and hydrogen peroxide because of decomposition of peroxypropionic acid.

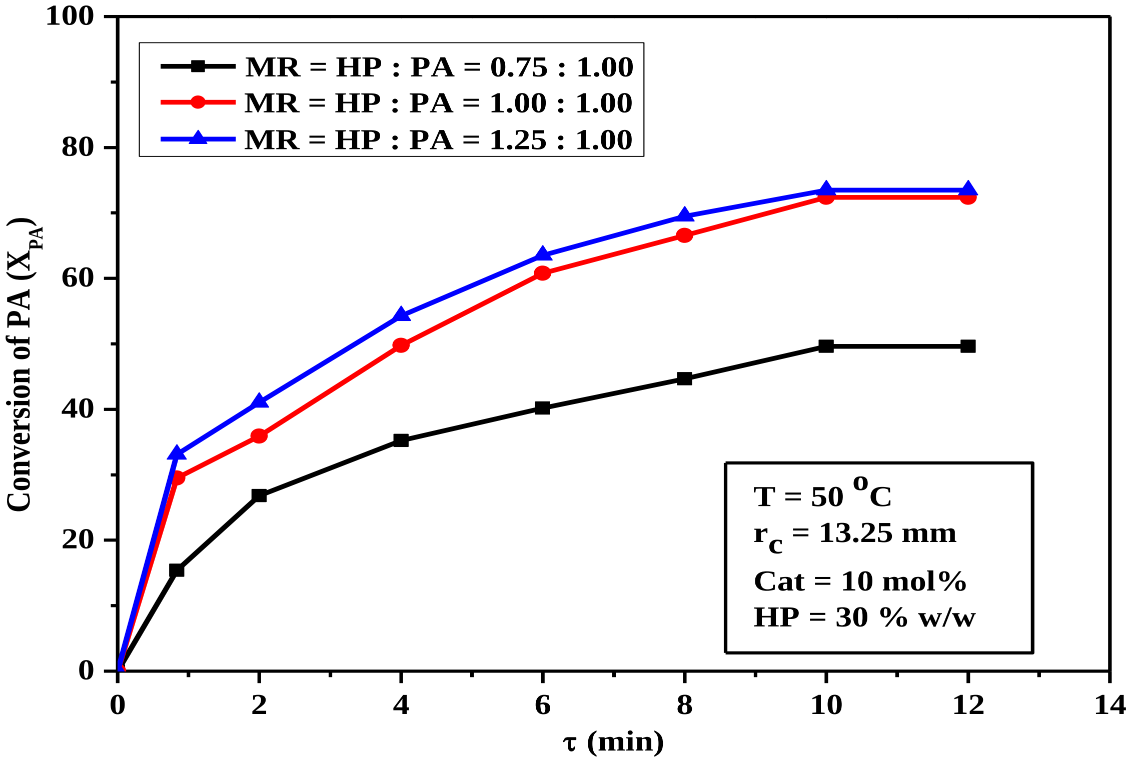


Figure (4.13). Effect of molar ratio of HP to PA on conversion of propionic acid.

4.3.3. Effect of radius of curvature of the helical capillary micro structured reactor

Helical capillary micro structured reactor (HCMR) with alternative curves have been planned for continuous flow applications as it provide better residence time distributions (RTD), enhanced heat transfer as well as mass transfer in laminar stream (regimes) for a residence time up to few minutes/ seconds based on the reaction type [53, 220, 221, 225, 226].

In this work, two different radiuses (radii) of curvatures were applied to study the performance of the HCMR for the production of peroxypropionic acid at 50 °C temperature and 10 % catalyst loading based on propionic acid at various total feed flow rates. Here, the radius of curvatures employed were 23.25 mm and 13.25 mm having number of turns of 12 and 21 respectively. However, when the radius of curvature reduces, the number of turns extends which results into enhanced mixing, improved mass transfer as well as heat transfer, vice versa. A lesser radius of curvature of HCMR leads to give higher conversion of propionic acid. From **Figure(4.14)**, it was found that at 50 °C temperature and 10 mol % catalyst loading based on propionic acid, radius of curvatures of 13.25 mm HCMR, gave optimum conversion of propionic acid, X_{PA} = 72.36 %, whereas 23.25 mm HCMR gave maximum conversion of propionic acid, X_{PA} = 62.52 %. Furthermore, it could be concluded that 13.25 mm HCMR is best continuous flow capillary micro reactor for the formation of PPA.

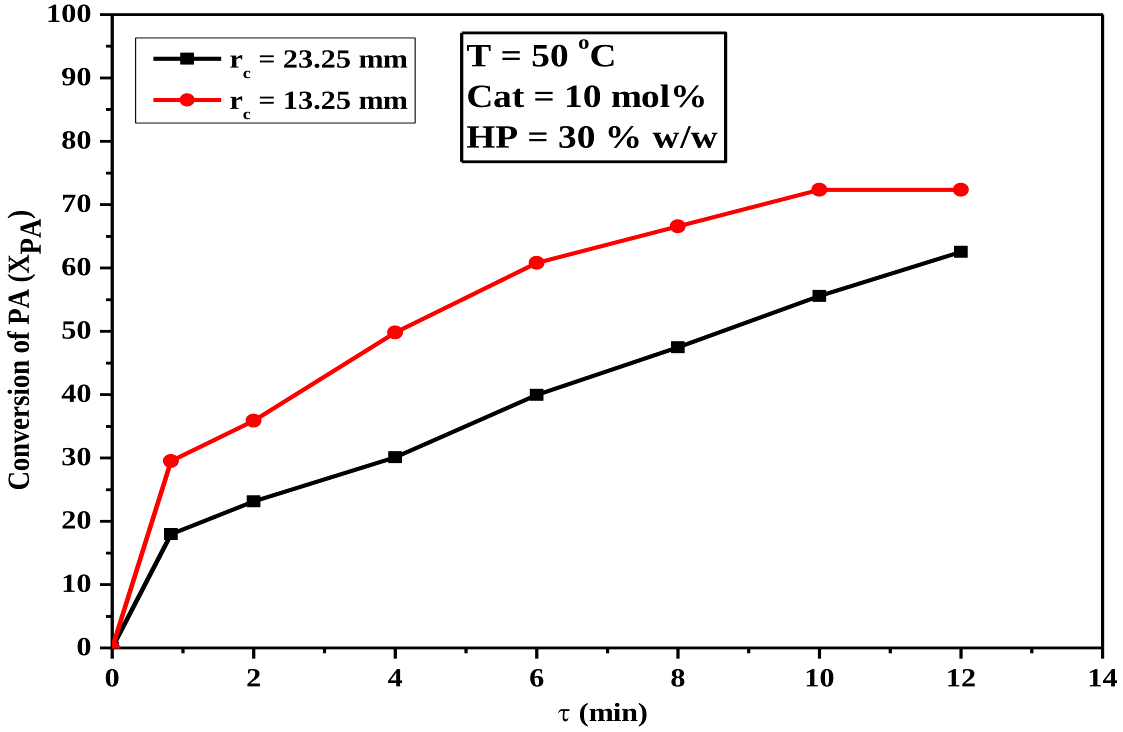


Figure (4.14). Effect of radius of curvature on the conversion of propionic acid.

4.3.4. Effect of concentration of catalyst on PPA synthesis

Figure (4.15) describes the effect of concentration of catalyst on the peroxypropionic acid formation by maintaining constant molar ratio of hydrogen peroxide to propionic acid at 1: 1 and temperature 50 °C [33, 116, 120, 137, 155, 227]. The conversion of PA at 4 mol % of catalyst loading was observed to be X_{PA} = 60.20 %. The conversion of propionic acid was observed to be increased from 60.20 to 73.51 % at the catalyst loading from 4 to 12 mol % at 50 °C. This is due to the presence of higher number of H^+ ions at high catalyst concentration. On the other hand, higher concentration of catalyst i.e., above 12 mol % at 50 °C, the conversion of propionic acid was observed to be closer to X_{PA} = 73.51 %, which is almost near to 10 mol % catalyst concentration. It is because of adequate numbers of H^+ ions being delivered by the catalyst concentration of 10 mol %. Moreover, even though a larger number of H^+ ions were prevailing at catalyst concentration of 12 mol %, the presence of insufficient quantities of propionic acid confines the peroxypropionic acid formation in the HCMR. Therefore, the conversion of propionic acid remains unaltered. In present work, the equilibrium is reached at the end of 10 min. Hence, from **Figure (4.15),** it could be concluded that 10 mol % catalyst concentration is best one at 50 °C and 30 % w/w hydrogen peroxide to produce peroxypropionic acid by using a helical capillary micro reactor with radius of curvature of 13.25 mm.

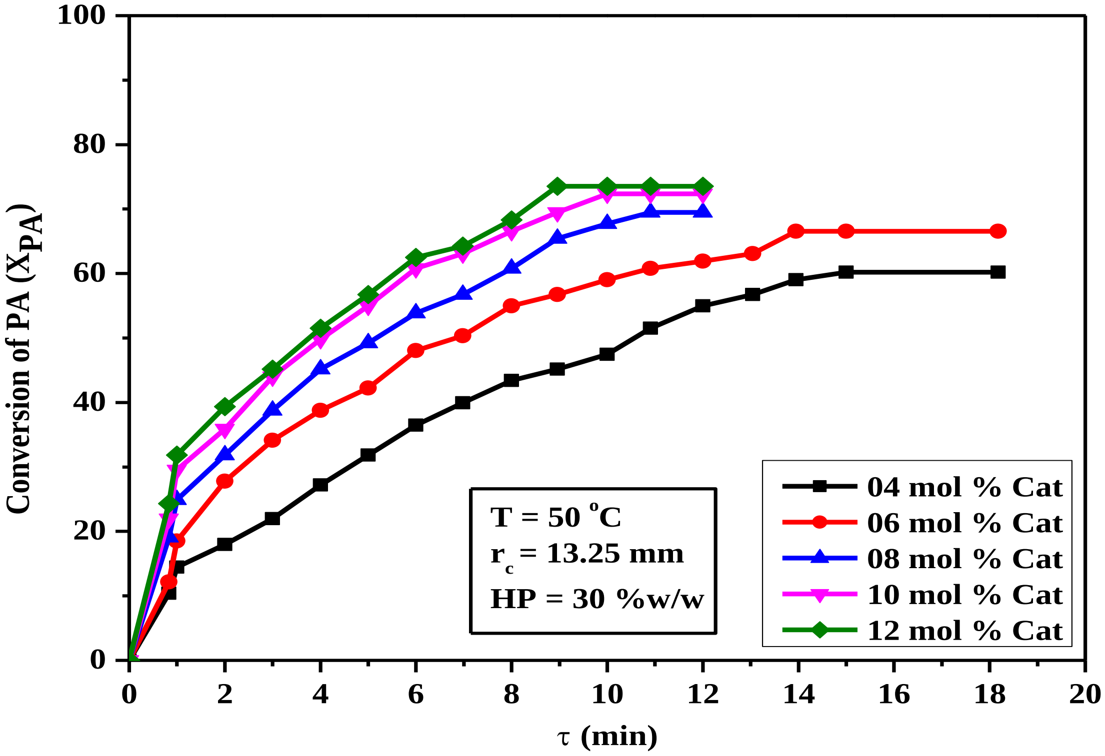


Figure (4.15). Effect of concentration of catalyst on the conversion of propionic acid.

4.3.5. Effect of the temperature on PPA synthesis

Experiments were performed at various temperatures from 30 to 60 °C to study the temperature effect on the production of peroxypropionic acid. The temperature effect for the production of peroxypropionic acid was shown in **Figure (4.16)**.The total feed flow rate of reactants were kept at 5 – 72 mL/h, molar ratio of hydrogen peroxide to propionic acid is 1: 1 and catalyst concentration of 10 mol % based on propionic acid in the temperature from 30 to 60 °C. The concentration of peroxypropionic acid was noticed to be 3.4884 mol/L (X_{PA} = 62.52 %) at residence time 12 min, 30 °C and was noticed to be enhanced to 4.0375 mol/L (X_{PA} = 72.36 %) at residence time 10 min, at temperature of 50 °C in the presence of homogeneous catalyst loading at 10 mol % catalyst based on propionic acid. So, it was noticed that as the temperature increases, the rate of reaction increases, which results in increase of the reactants conversion and further which leads to obtain better product with improved yield and selectivity. Then, it was also observed that decrease in formation of peroxypropionic acid at temperature above 60 °C due to the decomposition of the peroxypropionic acid [139].

The decomposition of PPA at higher temperature (above 60 °C) and higher catalyst concentration causes the reduction in concentration of peroxypropionic acid compared to 50 °C. In addition, at higher temperature and higher concentration of catalyst, vapours of reaction mixture gets formed in the micro reactor which reduces the conversion of propionic acid. On the contrary, at lower temperature (50 °C), the vapour pressure of the reaction mixture is low.

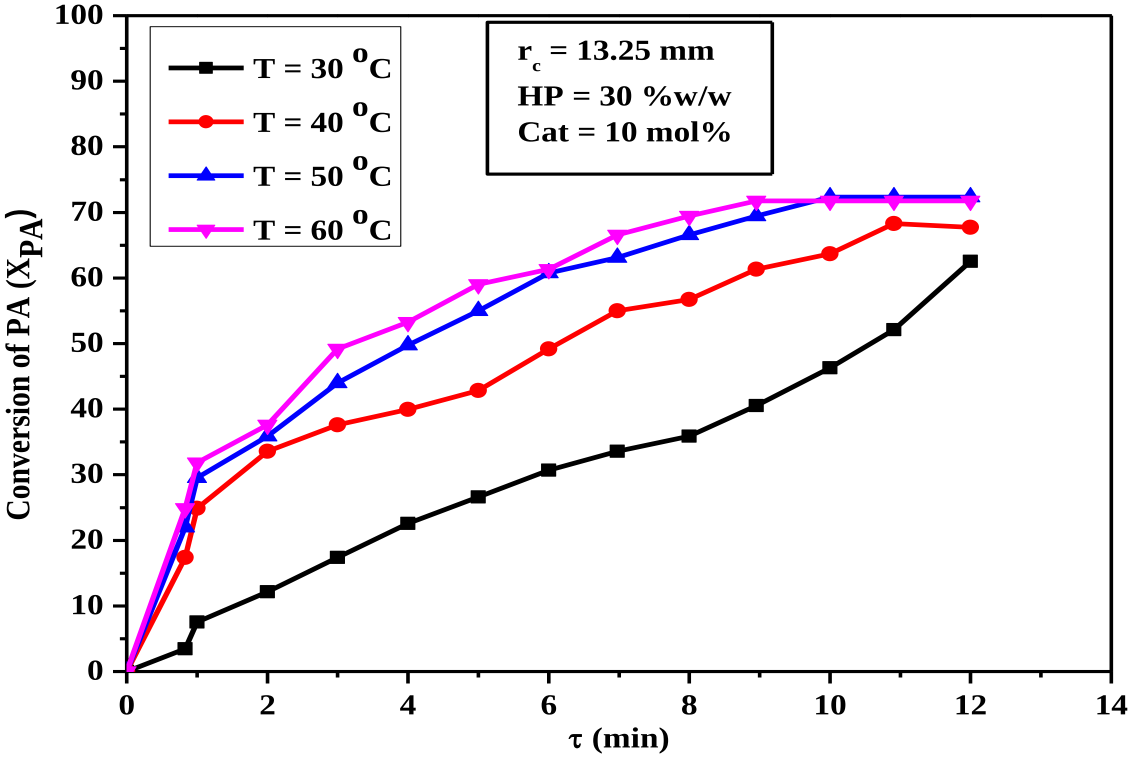


Figure (4.16). Effect of temperature on conversion of propionic acid with catalyst.

4.3.6. Formation of kinetic model and finding of kinetic constants

Assumptions: Before developing a kinetic model, following assumptions were made. (1) The reaction volume is constant during the reaction at a temperature, (2) HP is unchanging when no catalyst was used in the reaction, even at higher temperature up to some extent. Furthermore, thermal decomposition of peroxypropionic acid is apparent only at temperature above 80 °C [139 – 142] and (3) Furthermore, there is small quantity of water would be produced in the synthesis of peroxypropionic acid. It is a robust group of nucleophilic than hydrogen peroxide and peroxypropionic acid. Hence, the consumption of peroxypropionic acid is mostly owing to its hydrolysis. Hence, the reaction **Scheme – (1.III)** consist of the two main reactions, synthesis PPA and hydrolysis of PPA.

$$C_2H_5COOH\ (A) + H_2O_2\ (B) \xrightleftharpoons[k_2]{k_1} C_2H_5COOOH\ (C) + H_2O\ (W) \qquad (1.III)$$

Determination of kinetic constants: The peroxypropionic acid synthesis and hydrolysis in presence of homogeneous catalyst were used to estimate reaction rate constants. **Figure (4.17)** shows the residence time effect on the production of peroxypropionic acid in the presence of the catalyst at different temperatures. The data stated in **Figure (4.18)** was used to find the activation energies and the reaction rate constants of the **Scheme – (1.III)**. A very few researchers stated that at higher temperatures (above 80 ℃) [139], percarboxylic acids decomposes [33]. A very few researchers reported the kinetic model for the synthesis of peroxypropionic acid and decomposition of peroxypropionic acid in a conventional batch method [118,146]. In this thesis, the kinetic model was developed for synthesis of peroxypropionic acid with catalyst by treating HCMR as model of plug flow reactor (PFR). The kinetic model for the **Scheme – (1.III)** of peroxypropionic acid is described in appendix, model equations were reported on page no. 99 – 100 [222–224]. From Eq. (19) and (20) of appendix and **Figure (4.17)** and **Figure (4.18)** were used to find the activation energies and the reaction rate constants for the peroxypropionic acid production and hydrolysis with catalyst. From **Figure (4.18)** the activation energies of peroxypropionic acid synthesis and hydrolysis were determined as 45.257 and 50.044 kJ/mol with catalyst loading of 10 mol % based on propionic acid respectively. The forward reaction has lesser activation energy than the backward reaction. As a result, it could be noticed that the breakdown of peroxypropionic acid is predominant by the temperature considerably over the peroxypropionic acid synthesis and hydrolysis. The reaction rate constants k_1 and k_2 ($L^2/(mol^2 \cdot min)$) for propionic acid with catalytic reaction could be estimated from the following equations respectively.

$$k_1 = 18.06 * 10^5 * \exp\left(\frac{-45257.49}{RT}\right),\ L^2/(mol^2 \cdot min) \qquad (4.9)$$

$$k_2 = 17.59 * 10^5 * \exp\left(\frac{-50044.14}{RT}\right),\ L^2/(mol^2 \cdot min) \qquad (4.10)$$

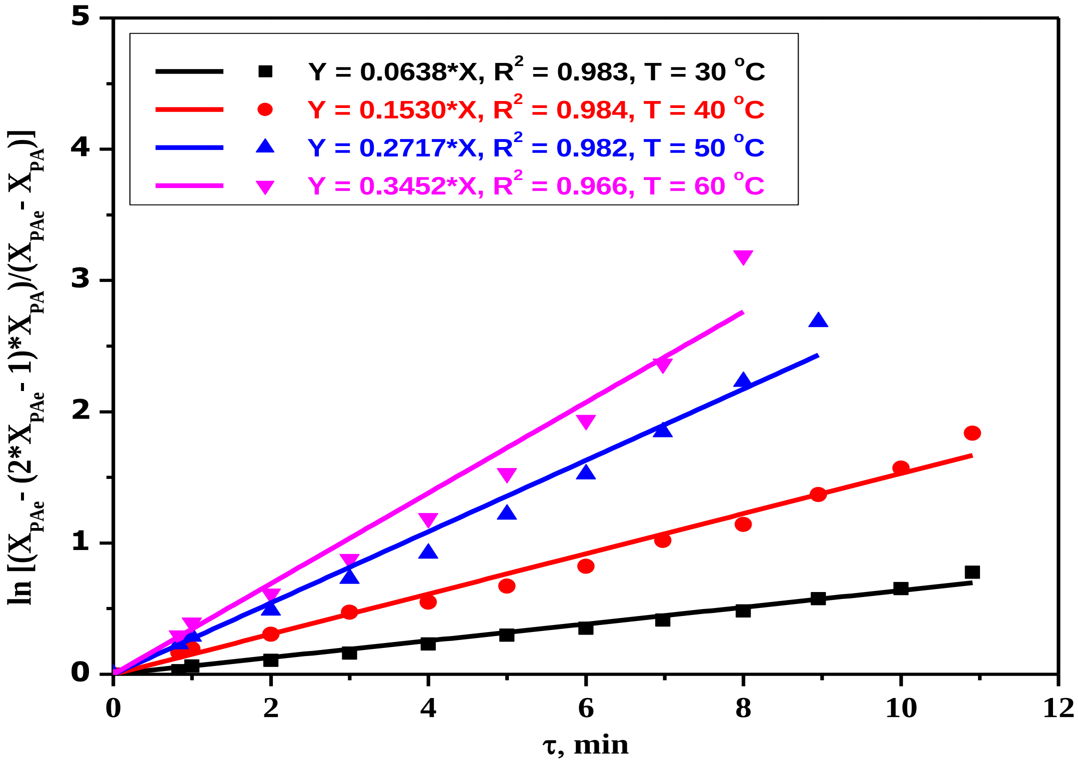


Figure (4.17). The plot of residence time verses ln (conversion ratio) for conversion of propionic acid to determine the rate constants at different temperatures with catalyst.

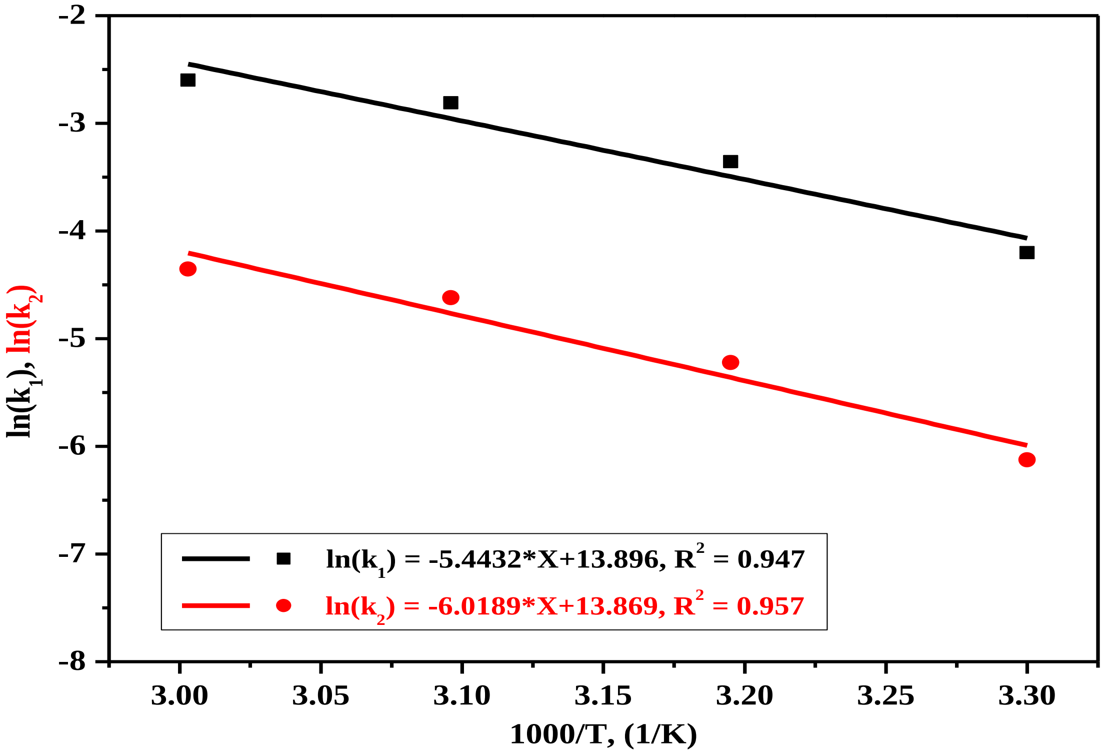


Figure (4.18). Arrhenius plots on conversion of propionic acid with catalyst.

4.4. Case Study – IV: Comparative study for the synthesis of peracetic acid using a micro structured reactor and its kinetic study

The experiments were carried out by the HCMR, two reactants were fed to the micro reactor by using syringe pumps. The reaction was carried out using sulfuric acid (catalyst) at total feed flow rates are 5 to 60 mL/h (residence time = 12 to 1 min). The residence time is inversely proportional to the total flow rate. Hence, feed flow rates were varied and carried out the experiments at different temperature and catalyst loading by keeping the equimolar ratio of hydrogen peroxide to acetic acid (1: 1). The acetic acid reacts with hydrogen peroxide from T – junction and continues through the length of the micro reactor to form the peracetic acid. In all the experiments, hydrogen peroxide used in equimolar amount of acetic acid, with the aim of acetic acid get consumed to give high conversion (equilibrium). When the reaction reaches its equilibrium, the product mixture may contain the peracetic acid, water and unreacted acetic acid and hydrogen peroxide. The unreacted hydrogen peroxide concentration was determined by the titration against to standard potassium permanganate solution. The unreacted hydrogen peroxide existing in the product mixture, it decomposes at certain period of time. The peracetic acid concentration was determined by the titration against standard sodium thiosulfate solution. The product mixture was analyzed immediately so as to make accuracy in the results and to avoid deviation in the data.

4.4.1. Effect of molar ratio for the formation of peracetic acid

Selection of reactants concentration is one of the most important parameter to carry out any chemical reaction. When the reactants concentration increases, which result in enhancing rate of reaction to give increased conversion of reactant and enhanced yield at certain parameters such as catalyst loading, reaction time, temperature etc. Furthermore, according to the reaction S**cheme – (1.IV)**, it was noticed that for the synthesis of one mole of peracetic acid, equal moles of acetic acid and hydrogen peroxide are needed. However, in this present study, it is expected that there is a lower or higher molar ratio of reactants might give lower or higher conversion of acetic acid respectively. So, the experiments were carried out at three molar ratios. **Figure (4.19)** describes the change in the peracetic acid concentration at different molar ratio of hydrogen peroxide to acetic acid such as 0.75: 1.00, 1.00: 1.00 and 1.25: 1.00 at 10 mol % catalyst concentration (sulfuric acid) and 50 °C in helical capillary micro reactor. Hence, from **Figure (4.19)**, it was observed that equimolar ratio of the reactant was showing higher conversion of acetic acid at residence time of 12 min, 10 mol % catalyst concentration and 50 °C in helical capillary micro reactor. The residence time of the chemical reaction can be determined by the internal holdup of the micro structured reactor and the flow rate of the feed. As the internal hold up of the micro reactor was 1 mL, at 5 mL/h, 10 % catalyst concentration and 50 °C, conversion of acetic acid obtained was X_{AA} = 59.90 % (peracetic concentration was 3.558 mol/L). So, further experiments were carried out at equimolar ratio of hydrogen peroxide and acetic acid to find the best operating parameters for the formation of peracetic acid [136, 155, 170, 172].

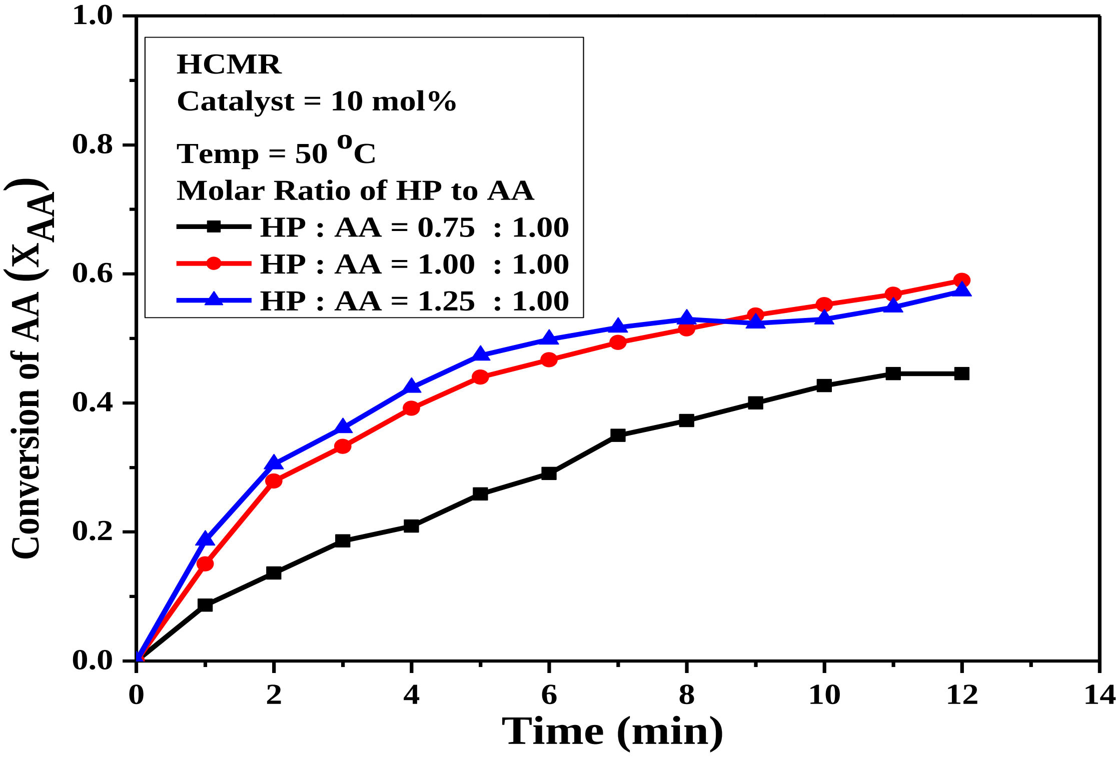


Figure (4.19). Effect of reactant molar ratio on the conversion of acetic acid.

4.4.2. Comparison of SCMR, AFR and HCMR for formation of peracetic acid

In this work, three different configurations of micro structured reactors, having equal volume for each, were employed for the synthesis of peracetic acid. The three different configurations were shown in **Figure (3.2)**, those are serpentine capillary micro reactor, helical capillary micro reactor and Corning® Advanced – Flow™ Reactor respectively. In the serpentine capillary micro reactor, the major concentration changes occurs along the length and hence, the working principle of serpentine capillary micror eactor is almost as same as ideal plug flow reactor. In the Corning® Advanced – Flow™ Reactor, the mixing occurs within the individual heart cell. The working principle is split and rejoin, during period of the split and rejoin mixing of reactants, chemical reaction takes place. Moreover, the geometry is not uniform along the reaction path length. Hence, due to the non – uniformity of the geometry, pressure is not constant i.e, pressure variation was there along the reaction path length. The working principle of single cell of the module is as same as continuous flow stirred tank reactor or mixed flow reactor but overall the working principle of AFR is analogous to the ideal plug flow reactor model since all heart shape cells are connected in series [61, 62, 185, 228, 229].

Helical capillary micro reactors having numerous turns have been reported for the application of continuous flow processes in chemical, pharmaceutical and other industries. The HCMR offers sharp narrow RTD (residence time distributions), increased heat transfer and mass transfer in the laminar regime for the residence times from few minutes to few seconds [90 – 92, 94, 159, 200, 220, 230 – 232]. Generally, laminar flow has the parabolic velocity profile for straight capillary micro structured reactor whereas skewed velocity profile exists in a helical capillary micro reactor which can be made by twisting the capillary tubes on a cylindrical bar or pipe. The agitation caused by the centrifugal forces which plays normal direction to the fluid flow along the helical capillary micro reactor. Therefore, secondary flow profile exists in the cross section of the helical capillary micro reactor, it is defined as “Dean Vortices”. The main intension of Dean Vortices is extensively stated by Dean Number which is the product of Reynolds number and ratio of the helical capillary micro reactor diameter to radius of curvature of the helical capillary micro reactor [89].

So, the three different micro structured reactors were employed to study the performance of them for the formation of peracetic acid at 10 mol % catalyst loading, 50 ℃ and different total feed flow rates. Among these micro reactors, it was observed that the helical capillary micro reactor offered the best performance. The performance of the micro reactor shown in **Figure (4.20)**. In the next sections, helical capillary micro reactor was used to study effect of catalyst loading and temperature for the formation of peracetic acid. From **Figure (4.20)**, it was noticed that at 10 mol % catalyst loading and 50 ℃, helical capillary micro reactor gave the concentration of peracetic acid of 3.557 mol/L at residence time of 12 min whereas serpentine capillary micro reactor and AFR gave the concentration of peracetic acid of 2.652 and 3.428 mol/L respectively. Therefore, from the **Figure (4.20)**, it could be concluded that helical capillary micro reactor is the best one to synthesis the peracetic acid and similar type reactions.

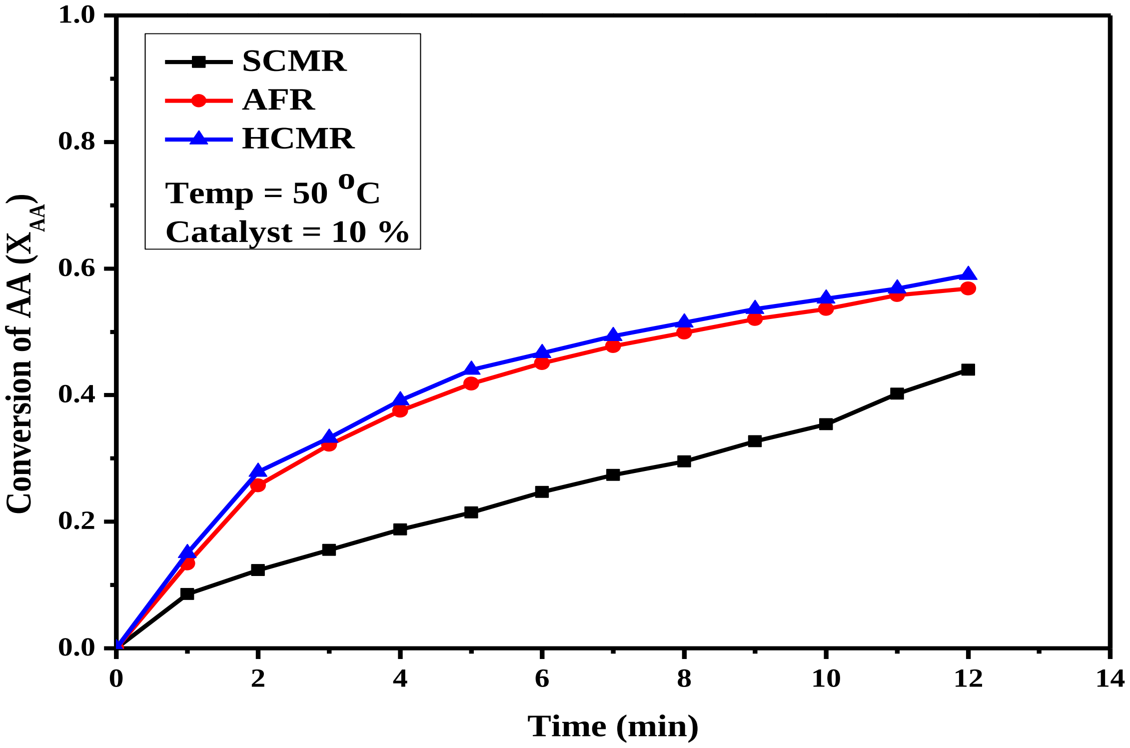


Figure (4.20). Comparison of different microstructured reactors for the conversion of acetic acid.

4.4.3. Effect of catalyst concentration on formation of peracetic acid

Catalyst plays the most important role in a reactions. A chemical reaction can take place without a catalyst but the reaction rate is slow and conversion also very less. Moreover, the selection of a catalyst for a reaction is very important parameter. Furthermore, heterogeneous catalyst give less conversion over the homogeneous catalyst. The usage of heterogeneous catalyst causes clogging of the micro reactor. Furthermore, Homogenous catalyst is miscible with reactant phase. It will not cause for clogging of the micro reactor and is the most suitable one depends on a reaction. So, here a homogeneous catalyst was chosen for formation of peracetic acid. For formation of peracetic acid, homogenous catalysts for example sulfuric acid or phosphoric acid can be used. In the present report, sulfuric acid is applied as a catalyst for the formation of peracetic acid at different concentrations from 4 - 14 mol % based on acetic acid [121, 172].

Here the different catalyst loading (4 – 14 mol %) were studied by using the AFR at 50 ℃ and equimolar ratio of HP – AA for the synthesis of peroxyacetic acid. **Figure (4.21) (A)** describes the catalyst loading effect for the synthesis of peroxyacetic acid at 50 ℃ for the AFR. From **Figure (4.21) (A)** at 5 mL/h (residence time = 12 min), at 4 mol % and 14 mol % catalyst concentration, the conversion of acetic acid was observed to be X_{AA} = 30.57 % and X_{AA} = 60.60 %. Moreover, it was noticed that at 12 mol %, the conversion of acetic acid was X_{AA} = 61.14 % at flow rate of 5.5 mL/h (residence time = 11 min). Thus, at 50 ℃, the conversion of AA was increased from 30.57 to 61.14 % for the catalyst concentration in the range of 4 to 12 mol % respectively. Furthermore, it was observed that conversation of acetic acid was almost same at catalyst loading of 12 and 14 mol %. Which was due to sufficient number of active H^+ ions were generated from the catalyst (sulfuric acid). Therefore, even though supply of more amount of catalyst, shows the almost same conversion of acetic acid as at the catalyst loading of 12 mol %. However, from **Figure (4.21) (A)**, it could be concluded that 12 mol % catalyst loading is the sufficient for the reaction to reach the equilibrium conversion at 50 ℃ and residence time of 11 min.

Figure (4.21) (B) describes the conversion of acetic acid at different catalyst loading from 4 – 14 mol % at 50 ℃ in the helical capillary micro reactor. From the **Figure (4.21)**, it could be noticed that as the catalyst concentration increases, the conversion of acetic acid also increases. At the catalyst concentration of 12 and 14 mol %, the conversion trends looks almost similar. As concentration of catalyst increases at higher residence time, the decrease trend of conversion of acetic acid is observed which is due to the reversibility of the reaction or the dissociation of peracetic acid [33]. The addition of catalyst beyond 14 mol%, it does not show variation in the conversion of acetic acid. Therefore, the catalyst concentration of 12 mol % is sufficient for the conversion of acetic acid [33, 136, 155, 170]. Form **Figure (4.21) (B)**, it can be observed that high acetic acid conversion (higher concentration of peracetic acid) occurred at 12 mol % catalyst and 50 ℃ in the helical capillary micro reactor at residence time of 9 min.

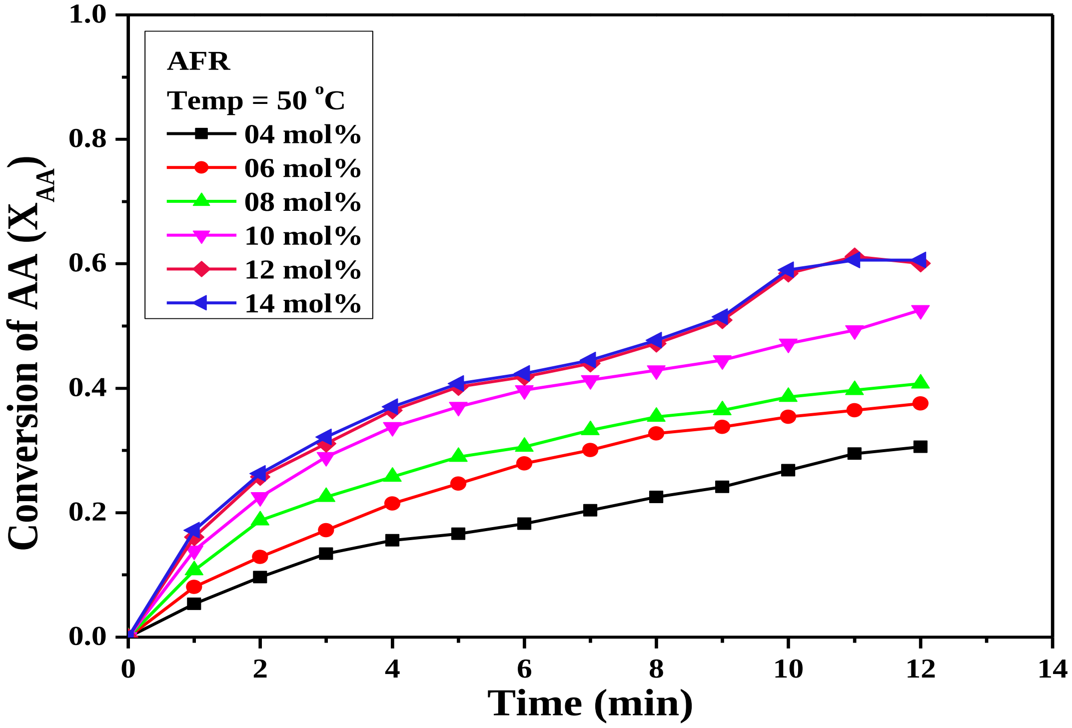


Figure (4.21) (A). Effect of concentration of catalyst on conversion of acetic acid at 50 ℃ in AFR.

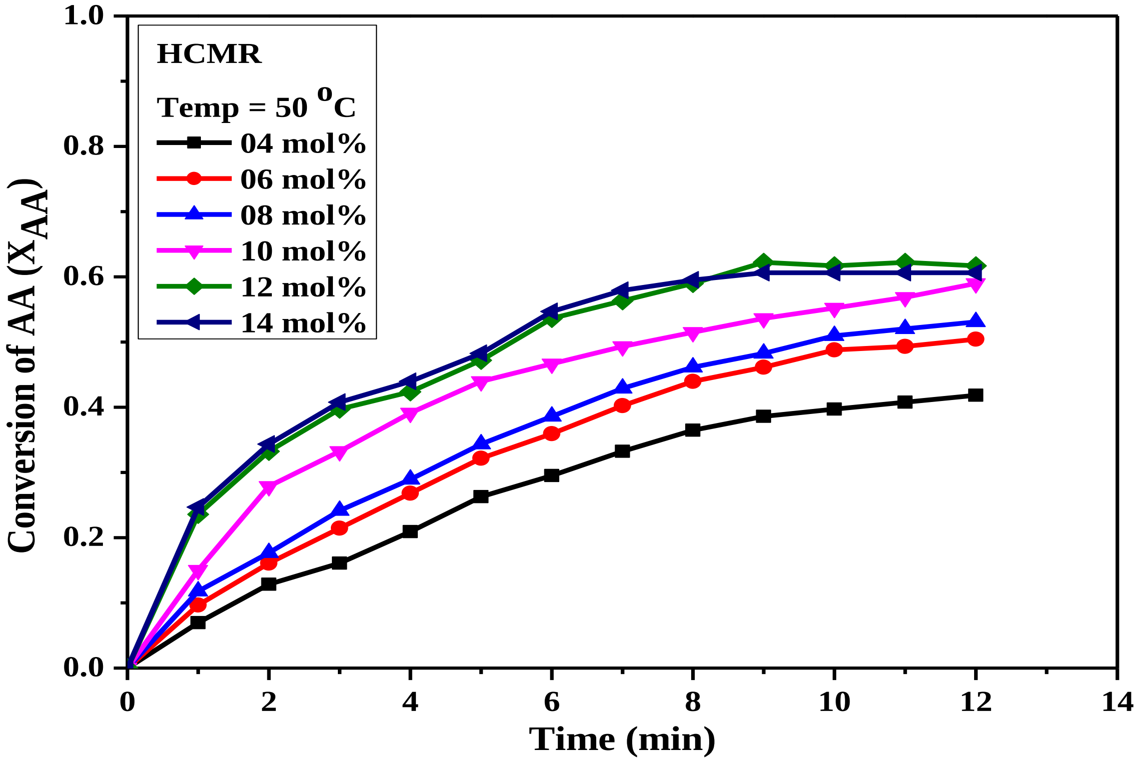


Figure (4.21) (B). Effect of concentration of catalyst on conversion of acetic acid at 50 °C in HCMR.

4.4.4. Effect of temperature on formation of peracetic acid

All experiments were performed at atmospheric pressure and various temperatures. The temperature effect is also depends on the geometry where the chemical reaction take place. The temperature effect was studied for the formation of peracetic acid. Here the temperature was maintained in the range of 20 – 60 °C at catalyst loading of 10 mol % in the AFR as well as the helical capillary micro reactor for formation of peracetic acid. During the study of temperature effect on the acetic acid conversion, the total feed flow rates were maintained at 5 – 60 mL/h (residence time is 12 – 1 min). Generally, as the temperature rises, the conversion of a reactant increases by increasing the residence time. Here it was observed that the reaction was moving backward direction due to the reaction is mildly exothermic in nature at higher temperature. Furthermore, at higher temperature and catalyst concentration, the peracetic acid might decomposes into acetic acid and hydrogen peroxide. So, the equilibrium of the reaction shifts towards left when higher temperature and higher catalyst loading maintained. Moreover, at lower temperature and catalyst concentration, the reaction reaches its equilibrium during longer time. From **Figure (4.22) (A)**, it could be concluded that 60 °C, 12 mol % catalyst loading and residence time of 11 min (5.5 ml/h) were best operating parameters for the synthesis of peroxyacetic acid in the AFR.

Figure (4.22) (B) describe that the conversion of acetic acid at 10 mol% and different total feed flow rates in the temperature range of 20 – 60 °C in the helical capillary micro reactor. Consequently, from **Figure (4.21) (B)** and **Figure (4.22) (B)**, It could be concluded that for the maximum conversion of acetic acid at 50 ℃ and 12 mol % at residence time of 9 min are best suitable operational parameters in the helical capillary micro reactor. Therefore, the helical capillary micro reactor is suitable for the similar type reactions [33, 136].

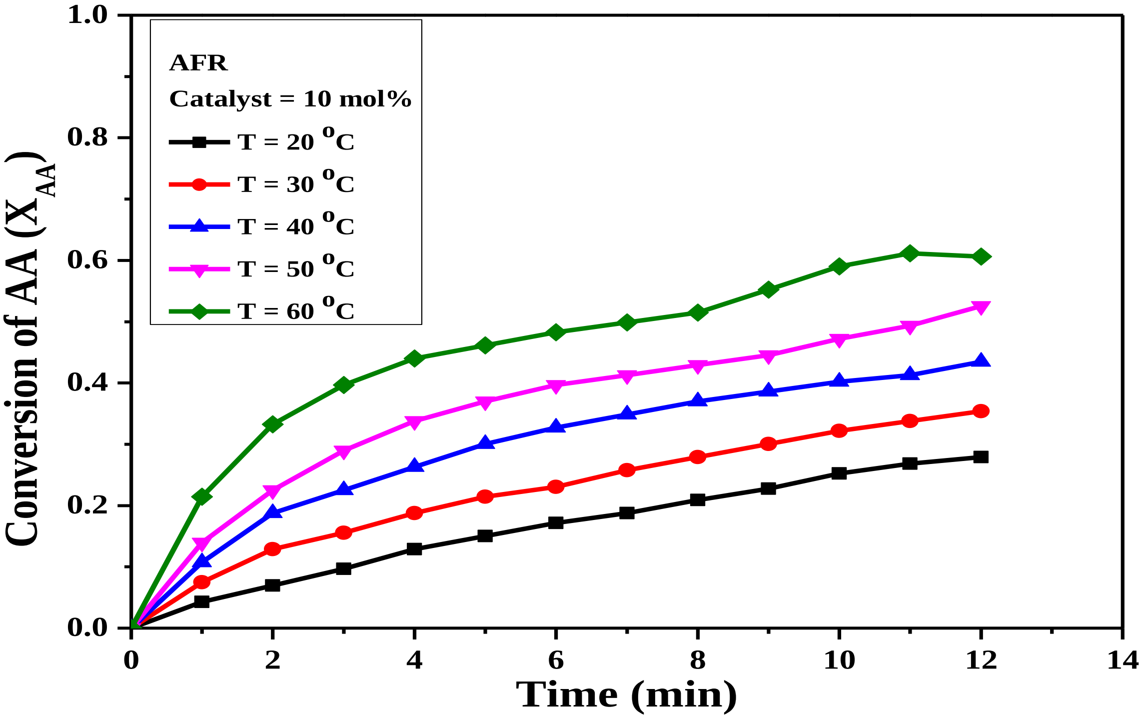


Figure (4.22) (A). Effect of temperature at 10 mol % catalyst loading in AFR on the conversion of acetic acid.

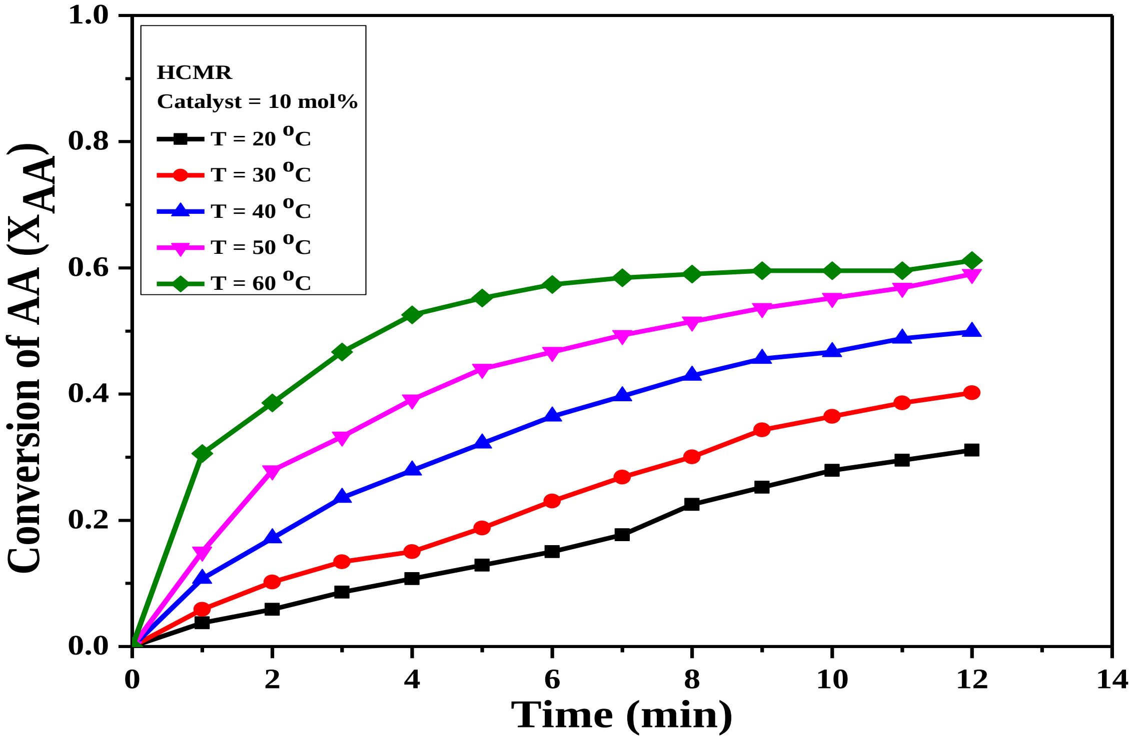


Figure (4.22) (B). Effect of temperature at 10 mol % catalyst loading in HCMR on the conversion of acetic acid.

4.4.5. Development of kinetic model and finding of kinetic constants

For developing the kinetic expression, some basic postulates were made to make the system simple and easier. The assumptions were as follows (1) the reaction volume of the liquid phase is constant for the period of the reaction at a temperature, (2) In the pK_a value of acetic acid and peracetic acid, changes takes place with temperature however, it neglected in this study, (3) the thermal decomposition of hydrogen peroxide as well as peracetic acid in the temperature range of 20 – 60 ℃ was negligible, (4) Moreover, there is a generation of some amount of water in the formation of peracetic acid and it possesses strong nucleophilic group than peracetic acid and hydrogen peroxide. Thus, the consumption of peracetic acid is because of its hydrolysis reaction [33, 173].

Hence, the chemical reaction **Scheme** – (1.IV) possesses two chemical reactions that is the forward reaction (synthesis) and the backward reaction (hydrolysis) of peracetic acid. In this case study, mainly focused on the formation of peracetic acid by sulfuric acid (catalyst) at different temperatures. **Figure (4.23)** describes temperature effect on the formation of peracetic acid at different residence times and the data presented in the **Figures (4.23) – (4.24)** was used to find out the rate constants of the reaction. **Figure (4.23)** and **Figure (4.24)** are drawn by assuming the AFR and the helical capillary micro reactor as plug flow reactor (PFR) model. **Figure (4.24**) data was used to estimate the activation energies of the forward and backward reactions.

The kinetic equations for the **Scheme – (1.IV)** of peracetic acid are reported in appendix, so for model equations please refer appendix page no. 99 – 100 [222 – 224]. From appendix Eq. (13) and (20) and **Figure (4.23)** and **Figure (4.24)**, the rate constants were determined and the activation energies (E_a) were determined for the peracetic acid formation and hydrolysis. From **Figure (4.24)**, the activation energies (E_{a1}, E_{a2}) for the forward reaction and reverse reaction are 45.850 & 49.550 kJ/mol and 45.536 & 49.235 kJ/mol for AFR and HCMR respectively. The forward reaction has lower E_a than the backward reaction. Hence, it could be concluded that formation of peracetic acid is mild exothermic reaction in nature. The rate constants k_1 and k_2 for peracetic acid synthesis can be estimated from the expressions (4.11) & (4.12) and (4.13) & (4.14) for AFR and HCMR respectively.

$$k_1 = 12.37 * 10^5 \exp\left(\frac{-45850.31}{RT}\right) \text{ For AFR} \tag{4.11}$$

$$k_2 = 18.99 * 10^5 \exp\left(\frac{-49550.26}{RT}\right) \text{ For AFR} \tag{4.12}$$

$$k_1 = 12.67 * 10^5 \exp\left(\frac{-45536.02}{RT}\right) \text{ For HCMR} \tag{4.13}$$

$$k_2 = 19.43 * 10^5 \exp\left(\frac{-49235.97}{RT}\right) \quad \text{For HCMR} \qquad (4.14)$$

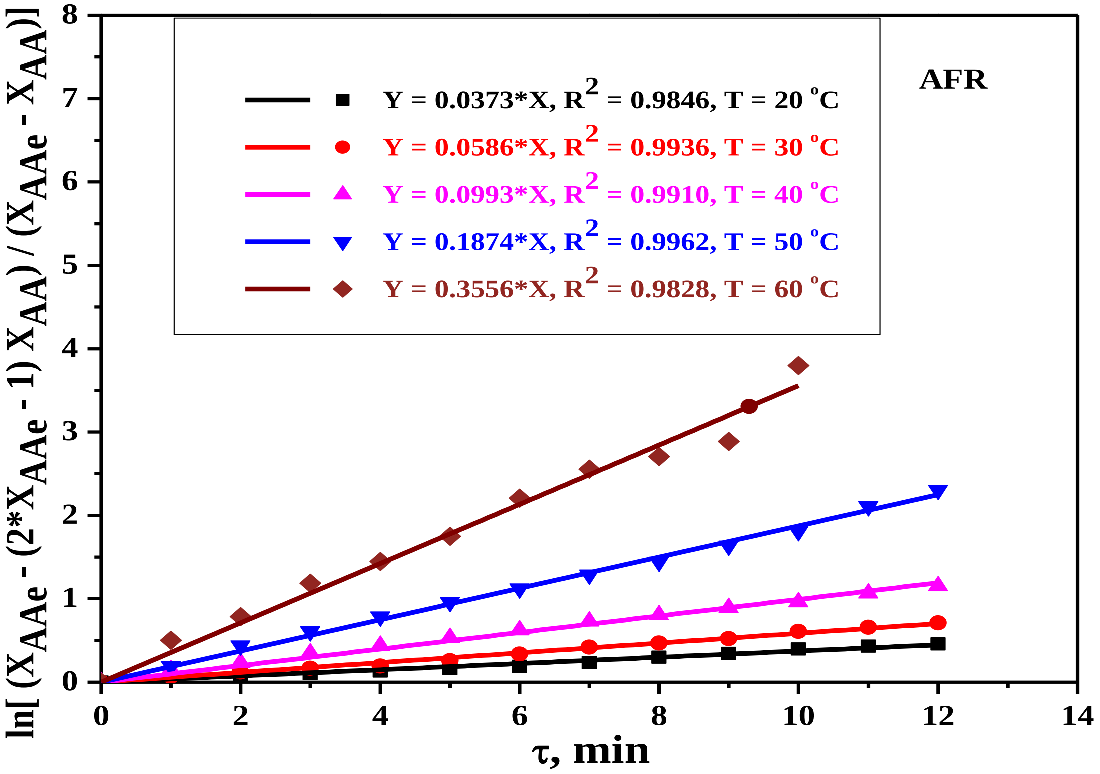


Figure (4.23) (A). The plot of residence time verses ln (conversion fraction) to determine rate constants of the reaction at different temperatures for AFR.

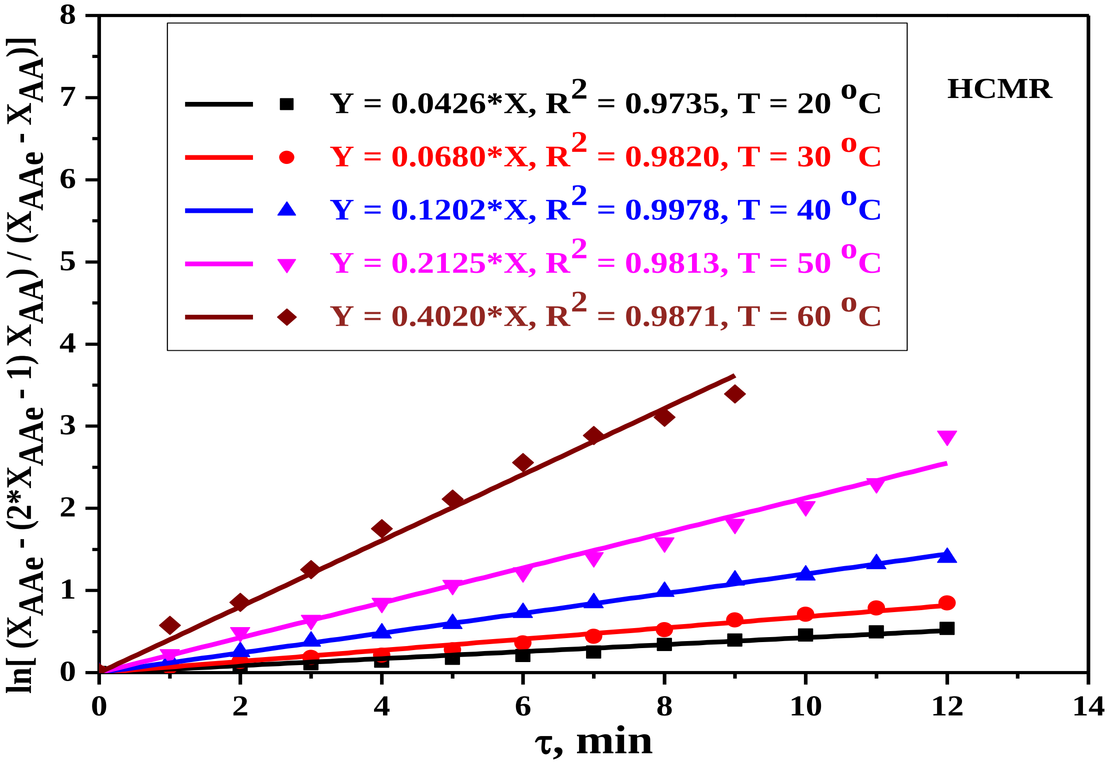


Figure (4.23) (B). The plot of residence time verses ln conversion fraction to determine rate constants of the reaction at different temperatures for HCMR.

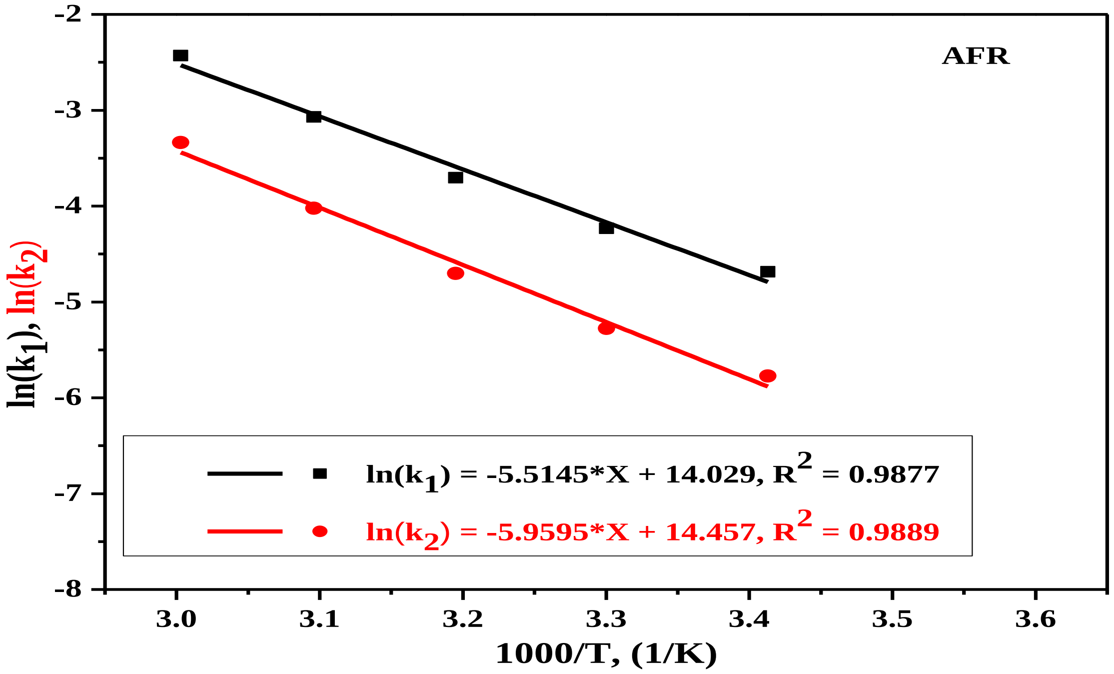


Figure (4.24) (A). Arrhenius plot of the temperatures and the rate constants of the formation of peracetic acid for AFR.

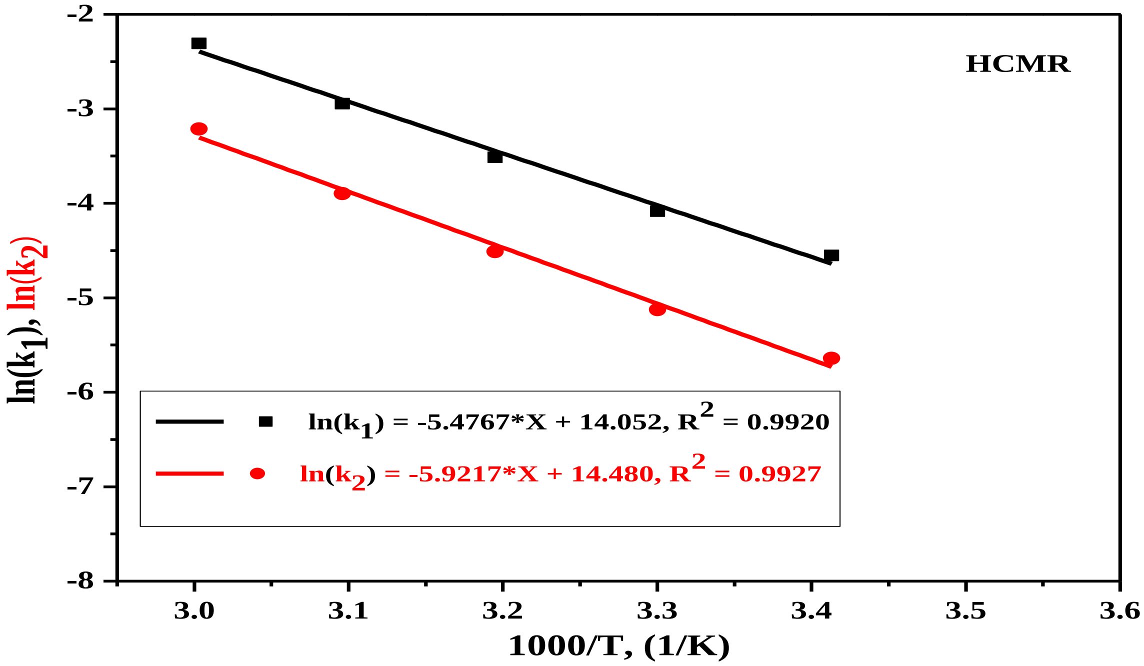


Figure (4.24) (B). Arrhenius plot of the temperatures and the rate constants for of formation of peracetic acid for HCMR.

From **Figure (4.24)**, the equilibrium constant (K_e) was derived and shown in Eq. (4.15). From the Eq. (4.15) the equilibrium constants were determined and K_e values were 2.971, 2.838, 2.711, 2.590 and 2.475 at different temperatures of 20, 30, 40, 50 and 60 ℃ respectively. Finally, it can be concluded from the Eq. (4.15) that formation of peracetic acid is mild exothermic reaction in nature.

$$K_e = 0.6518 \exp\left(\frac{3699.9525}{RT}\right) \tag{4.15}$$

Chapter – 5

CONCLUSIONS AND FUTURE SCOPE OF THE WORK

5.1. Overall conclusions

From the eperimental studies of four different case studies as mentioned in the previous chapters, the conclusions for each case study are mentioned as follows.

Case study – I: A continuous flow method for the synthesis of 5 – (4' – methyl – [1, 1' – biphenyl] – 2 – yl) – 1 – trityl – 1H – tetrazole in a micro reactor was successfully developed. This protocol allows the use of trityl chloride as the tritylating reagent in a safer, more efficient and convenient way. The Corning® AFR effectively gives higher yield of 95.18 % in a residence time of 27 s comparing with SSCR – 2 mm & SSCR – 1 mm micro reactors. The product was confirmed by TLC and melting point. The structures of synthesized MBPTT was confirmed by FTIR, ^{1}H NMRand ^{13}C NMR. Therefore, the Corning® AFR is scalable micro reactor to carry out the similar type of tritylation reactions at industrial level. The flow behavior in all three micro reactors was noticed as a laminar flow, which was confirmed by Reynolds number (Re). The Dean Number was estimated which was high in SSCR – 1 mm due to small diameter than SSCR – 2 mm. The estimated f_c was high in SSCR – 2 mm than SSCR – 1 mm because of internal diameter and variable flow rate. The Corning® AFR was shown the higher pressure drop compared to SSCR – 2 mm and SSCR – 1 mm, this could be due to the very narrow flow channel. The pressure drop analysis could be used to estimate power consumption. The micro reactor technology might be a useful tool for a similar type of reactions of other organic compounds and industrial drugs.

Case study – II: The synthesis of performic acid in the presence of a catalyst (sulfuric acid) was successfully performed in a continuously operated polytetrafluoroethylene helical capillary micro structured reactor system. In this work, the effect of various parameters for instance feed flow rates, the concentration of hydrogen peroxide, concentration of catalyst, temperature and radius of curvature of the helical capillary micro structured reactor for the synthesis of peroxyformic acid were studied. The results indicate that HCMR is suitable for continuous flow production of peroxyformic acid in a micro reactor system. The catalyst enhanced the rate of the reaction and reduced the time required for obtaining the equilibrium (maximum) conversion. The experimental results and kinetic studies shown that HCMR is an efficient technology for converting formic acid into peroxyformic acid.The observed best parameters were found to be 30 ℃, feed flow rate 10 mL/h (residence time = 6 minutes), catalyst concentration of 4 mol % based of formic acid, hydrogen peroxide concentration of 30 % w/v and radius of curvature of the helical capillary micro reactor was 13.25 mm (number of turns = 21) to afford maximum peroxyformic acid concentration about 5.175 mol/L (X_A = 72.78 %). A kinetic model for the peroxyformic acid formation was developed and rate constants were determined. The activation energies of performic acid synthesis and hydrolysis from Arrhenius graphs were 45.746 and 51.692 kJ/mol respectively.

Case study – III: The synthesis of peroxypropionic acid in continuous Teflon helical capillary micro reactor was efficiently performed by employing a homogeneous catalyst. The most favorable reaction conditions for the synthesis of peroxypropionic acid were total feed flow rate of 6 mL/h (residence time of 10 min), molar ratio of hydrogen peroxide to propionic acid is 1: 1, temperature of 50 ℃ and 10 mol % catalyst concentration based propionic acid. Hence, the maximum conversion of the propionic acid at these parameter was X_{PA} = 72.36 %. Furthermore, the reaction time was considerably decreased and reaction rate was significantly enhanced in the presence of catalyst in Teflon helical capillary micro reactor with radius of curvature of 13.25 mm. Hence, reaction gets completed within 10 min in a helical capillary micro reactor as compared to conventional batch processes. The continuous flow micro reactor procedure for the production of peroxypropionic acid was efficiently demonstrated.

Case study – IV: The synthesis of peracetic acid from acetic acid, hydrogen peroxide and sufuric acid as homogeneous catalyst was successfully carried out in the continuously operated micro reactors. In this study, for the synthesis of peracetic acid, the effect of molar ratio of reactants, different configurations of micro reactors, catalyst concentration and temperature was studied. Among the three micro reactors, the helical capillary micro reactor has afforded best performance for formation of peracetic acid. In the helical capillary micro reactor, the equilibrium was reached within 9 min at 12 mol % catalyst concentration & 50 ℃. So, the best operational parameter for the synthesis of peracetic acid in the capillary micro reactor are 12 mol % catalyst loading (sulfuric acid), 50 ℃ and total feed flow rate at 6.7 ml/h. For the reaction, kinetic model was developed and equilibrium constant (K_e) was determined at different temperatures. It was found that the reaction is mild exothermic reaction. Hence, the helical capillary micro reactor could be efficient tool for similar type reactions and also for other type of reactions.

The micro reactor technology could be a advantageous technique and promising tool for similar type of percarboxylic acid reactions which can be scaled up for an industrial processes.The micro reactor technology proved as an efficient tool for production of unfeasible batch process into a continuous flow mode with enhanced improvement of sustainability and process intensification. Thus, it is clear that micro reactor technology is getting acceptance in numerous areas of chemical manufacturing industries because of their characteristic features like short molecular diffusion length, high specific interfacial area, better mixing and excellent mass transfer as well as heat transfer characteristics.

5.2. Future scope of the work

To study the performance of a micro structured reactor on the system of gas – liquid system, on the system of liquid – liquid immiscible system. To carry out the experiments on multistage reactions which are industrially unfeasible and it is difficult for pharmaceutical reactions with single stage or multistage. Conducting the experiments on multistage reactions which are industrially unfeasible. Process intensification of pharmaceutical reactions of single stage or multistage reactions by micro structured reactors. Process intensification of heterogeneous reactions by micro structured reactors could be one of the future research area. Add examples (for exmple: (1) synthesis of propionic acid using solid catalyst, (2) synthesis of valeric acid (pentanoic acid) using solid catalyst and etc.). The HCMR is recommended for the similar type of acid – based reactins of irreversible as well as reversible processes. The monolithic reactors and photocatalytic reactions using micro reactors is also one of the promising area in petrochemical and pharmacutical area respectively.

Appendix - I

The general representation of a chemical reaction was shown in equation (AI)

$$A + B \leftrightarrow C + W \tag{AI}$$

Case – I: Assume reaction Scheme (AI) is without a catalyst [222 – 224].

$$-r_A = -r_B = -\frac{dC_A}{dt} = -\frac{dC_B}{dt} = (k_1 C_A C_B - k_2 C_C C_W) \tag{A1}$$

$$r_C = r_W = \frac{dC_C}{dt} = \frac{dC_W}{dt} = (k_1 C_A C_B - k_2 C_C C_W) \tag{A2}$$

Equation (A1) and (A2) represents the kinetic model for the reaction Scheme – (AI) without a catalyst. After the components balance, the reactant A and product D concentrations were as follows

$$C_A = C_{A0} - (C_{B0} - C_B) \tag{A3}$$

$$C_A = C_{A0} - C_C \tag{A4}$$

$$C_W = C_{W0} + (C_{B0} - C_B) \tag{A5}$$

Where C_{Z0} is the concentration at time t = 0 and C_Z is the concentration at time t of component Z. Therefore, the kinetic models could be written as follows

$$-r_A = -r_B = -\frac{dC_A}{dt} = -\frac{dC_B}{dt} = k_1(C_{A0} - C_C)C_B - k_2 C_C(C_{W0} + (C_{B0} - C_B)) \tag{A6}$$

$$r_A = r_B = \frac{dC_A}{dt} = \frac{dC_B}{dt} = k_1(C_{A0} - C_C)C_B - k_2 C_C(C_{W0} + (C_{B0} - C_B)) \tag{A7}$$

For a PFR model (by assuming), the performance equation was as follows

Input = output + disappearance by the reaction (A8)

$$F_A = (F_A + dF_A) + (-r_A)dV \tag{A9}$$

$$F_{A0} dX_A = (-r_A)dV \tag{A10}$$

Eq. (A8) – (A10) represents the interpretation for reactant A in the degree of difference portions of reactor volume dV. F_{PA0}, feed flow rate, is maintained constant. On the other hand, –r_A is a function of the reactants concentration, and the reaction temperature. Rearranging the expression of Eq. (A10), as a result, attained the resulting equation as follows

$$\tau = \frac{V}{v_0} = \frac{VC_{A0}}{F_{A0}} = C_{A0} \int_0^{X_{Ae}} \frac{dX_A}{-r_A} \tag{A11}$$

For equimolar concentration $C_{A0} = C_{B0}$ and $C_{C0} = C_{W0} = 0$ at time t = 0, at equilibrium

$$-\frac{dC_{PA}}{dt} = 0 \tag{A12}$$

Consequently, the equilibrium constant (K_e) is determined as follows

$$K_e = \frac{k_1}{k_2} = \frac{C_{Ce} C_{We}}{C_{Ae}\, C_{Be}} = \frac{X_{Ae}^2}{(1 - X_{Ae})^2} \tag{A13}$$

From the Equations (A1), and (A11) and after integration, attained the following expression

$$\ln\left[\frac{(X_{Ae} - (2X_{Ae} - 1)X_A)}{(X_{Ae} - X_A)}\right] = 2k_1\left(\frac{1}{X_{Ae}} - 1\right)C_{A0}\tau \tag{A14}$$

Case – II: Assume reaction Scheme (AI) is with a catalyst [222 – 224].

$$-r_A = -r_B = -\frac{dC_A}{dt} = -\frac{dC_B}{dt} = (k_1C_AC_B - k_2C_CC_W)C_{SA} \quad (A15)$$

$$r_C = r_W = \frac{dC_C}{dt} = \frac{dC_W}{dt} = (k_1C_AC_B - k_2C_CC_W)C_{SA} \quad (A16)$$

Equation (A15) and (A16) represents the kinetic model for the reaction Scheme – (AI) with a catalyst. After the components balance, the reactant A concentration and product D concentration were as follows

$$C_A = C_{A0} - (C_{B0} - C_B) \quad (A3)$$

$$C_A = C_{A0} - C_C \quad (A4)$$

$$C_W = C_{W0} + (C_{B0} - C_B) \quad (A5)$$

Where C_{Z0} is the concentration at time t = 0 and C_Z is the concentration at time t of species Z. Therefore, the kinetic models could be written as follows

$$-r_A = -r_B = -\frac{dC_A}{dt} = -\frac{dC_B}{dt} = \Big(k_1(C_{A0} - C_C)C_B - k_2C_C\big(C_{W0} + (C_{B0} - C_B)\big)\Big)C_{SA} \quad (A17)$$

$$r_C = r_W = \frac{dC_C}{dt} = \frac{dC_W}{dt} = \Big(k_1(C_{A0} - C_C)C_B - k_2C_C\big(C_{W0} + (C_{B0} - C_B)\big)\Big)C_{SA} \quad (A18)$$

For a Plug Flow Reactor model (by assuming), the performance equation was as follows

Input = output + disappearance by the reaction (A8)

$$F_A = (F_A + dF_A) + (-r_A)dV \quad (A9)$$

$$F_{A0}dX_A = (-r_A)dV \quad (A10)$$

Eq. (A8) – (A10) represents the interpretation for reactant A in the degree of difference portions of reactor volume dV. F_{PA0}, feed flow rate, is maintained constant. On the other hand, –r_A is a function of the reactants concentration, catalyst concentration and the reaction temperature. Rearranging the expression of Eq. (A10), as a result, attained the resulting equation as follows

$$\tau = \frac{V}{v_0} = \frac{VC_{A0}}{F_{A0}} = C_{SA}C_{A0}\int_0^{X_{Ae}} \frac{dX_A}{-r_A} \quad (A19)$$

For equimolar concentration $C_{A0} = C_{B0}$ and $C_{C0} = C_{W0} = 0$ at time t = 0, at equilibrium

$$-\frac{dC_{PA}}{dt} = 0 \quad (A12)$$

Consequently, the equilibrium constant (K_e) is determined as follows

$$K_e = \frac{k_1}{k_2} = \frac{C_{Ce}C_{We}}{C_{Ae}\,C_{Be}} = \frac{X_{Ae}^2}{(1-X_{Ae})^2} \quad (A13)$$

From the Equations (A11), and (A15) and after integration, attained the following expression

$$\ln\left[\frac{(X_{Ae}-(2X_{Ae}-1)X_A)}{(X_{Ae}-X_A)}\right] = 2k_1\left(\frac{1}{X_{Ae}} - 1\right)C_{SA}C_{A0}\tau \quad (A20)$$

Appendix – II

Sample calculations

For tritylation reaction (Case Study – I)

$$\text{Theotical yield} = \frac{\text{output moles}}{\text{input moles}}$$

$$\text{Percentage of yield} = \frac{\text{Actual yield}*100}{\text{Theoritical yield}}$$

For MBPTT product

$$\text{Theotical yield} = \frac{\text{output moles}}{\text{input moles}} = \frac{478.59}{236.28} = 2.026$$

Where 478.59 g/mol is the molecular weight of MBPTT and 236.28 g/mol is the molecular weight of MBPT

Actual yield we obtained was given in the following table the yield percentage was done based on the MBPT

Micro reactor	Output wt, g (actual yield)	Yield, %	Residence time (τ)
SSCR – 1	1.8815	$= \frac{1.8815}{2.026} = 92.87\ \%$	5.39 min
SSCR – 2	1.8988	$= \frac{1.8815}{2.026} = 93.72\ \%$	1.18 min
AFR	1.9283	$= \frac{1.9283}{2.026} = 95.18\ \%$	27.00 sec

For percarboxylic acid (Case Study – IV) Synthesis of PAA (only Sample calculation).

Molarity: Potassium permanganate (PPM) (1.6 g in 1 L)

Molecular wt = 158.032 g/mol

$$\text{Molarity (M2)} = \frac{1.6}{158.032*1} = 0.01013\ \text{M}$$

Volume of sample = 0.1 m

$$\text{PPA Concentration} = \frac{\text{Vol of STS}*\text{M2}}{\text{Vol of sample}}$$

For the reaction conditions at 50 ℃, concentration of catalyst = 10 mol %, concentration of propionic acid C_{PA0} = 6.03 mol/L and residence time 9 min in AFR.

$$\text{PAA Concentration } (C_{PAA}) = \frac{\text{Vol of STS}*\text{M2}}{\text{Vol of sample}} = \frac{9.7*0.0322}{0.1} = 3.13698\ \text{M}$$

Concentration of $C_{AA} = C_{AA0} – C_{PAA}$ = 6.03 – 3.13698 = 2.89302 M

$X_{AA} = 1 – C_{AA}/C_{AA0}$ = 1 – 2.89302/6.03 = 0.52023

% X_{AA} = 0.52023 * 100 = 52.023%

For this case X_{AAe} = 0.63286, C_{SA} = 0.67 mol/L (Catalyst concentration)

For equimolar and second order reversible reactions, the following can be used for evaluating k_1. From this k_1, Ke can be evaluated as follows

$$\ln\left[\frac{(\mathrm{X_{AAe}}-(2\mathrm{X_{AAe}}-1)\mathrm{X_{AA}})}{(\mathrm{X_{AAe}}-\mathrm{X_{AA}})}\right] = 2 * \mathrm{k_1}(\frac{1}{\mathrm{X_{AAe}}} - 1)\mathrm{C_{AA0}C_{SA}}\tau$$

$$\ln\left[\frac{(0.52023-(2*0.63286-1)*0.52023)}{(0.63286-0.52023)}\right] = 2 * \mathrm{k_1}\left(\frac{1}{0.63286} - 1\right)0.52023 * 0.67 * 9$$

k_1 = 0.3040 (L^2/ (mol^2·min))

$$\mathrm{K_e} = \frac{\mathrm{k_1}}{\mathrm{k_2}} = \frac{\mathrm{C_{Ce}C_{We}}}{\mathrm{C_{Ae}\,C_{Be}}} = \frac{\mathrm{X_{AAe}^2}}{(1-\mathrm{X_{AAe}})^2} = \frac{0.63286^2}{(1-0.63286)^2} = 2.971$$

For Case Study –II

$$\mathrm{k_1} = 15.03 * 10^6 * \exp\left(\frac{-45746.38}{\mathrm{RT}}\right); \qquad \mathrm{k_2} = 24.20 * 10^6 * \exp\left(\frac{-51692.91}{\mathrm{RT}}\right)$$

$$-\mathrm{r_A} = \ -$$

$$\frac{\mathrm{dC_A}}{\mathrm{dt}} = \ \left(15.03 * 10^6 * \exp\left(\frac{-45746.38}{\mathrm{RT}}\right)\mathrm{C_A C_B} \ - 24.20 * 10^6 * \exp\left(\frac{-51692.91}{\mathrm{RT}}\right)\mathrm{C_C C_W}\right)\mathrm{C_{SA}}$$

E_{af} = 45.746 kJ/mol ; E_{bf} = 51.692 kJ/mol

For Case Study –III

$$\mathrm{k_1} = 18.06 * 10^5 * \exp\left(\frac{-45257.49}{\mathrm{RT}}\right); \mathrm{k_2} = 17.59 * 10^5 * \exp\left(\frac{-50044.14}{\mathrm{RT}}\right)$$

$$-\mathrm{r_A} = \ -$$

$$\frac{\mathrm{dC_A}}{\mathrm{dt}} = \ \left(18.06 * 10^5 * \exp\left(\frac{-45257.49}{\mathrm{RT}}\right)\mathrm{C_A C_B} \ - 17.59 * 10^5 * \exp\left(\frac{-50044.14}{\mathrm{RT}}\right)\mathrm{C_C C_W}\right)\mathrm{C_{SA}}$$

E_{af} = 45.257 kJ/mol ; E_{bf} = 50.044 kJ/mol

For Case Study –IV

For AFR

$$k_1 = 12.37x10^5 exp\left(\frac{-45850.31}{RT}\right) \ ; \ k_2 = 18.99x10^5 exp\left(\frac{-49550.26}{RT}\right)$$

$$-\mathrm{r_A} = \ -$$

$$\frac{\mathrm{dC_A}}{\mathrm{dt}} = \ \left(12.37x10^5 ex\,p\left(\frac{-45850.31}{RT}\right)C_A C_B \ - 18.99x10^5 ex\,p\left(\frac{-49550.26}{RT}\right)C_C C_W\right)C_{SA}$$

E_{af} = 45.850 kJ/mol ; E_{bf} = 49.550 kJ/mol

For HCMR

$$\mathrm{k_1} = 12.67 * 10^5 \exp\left(\frac{-45536.02}{\mathrm{RT}}\right) \ ; \mathrm{k_2} = 19.43 * 10^5 \exp\left(\frac{-49235.97}{\mathrm{RT}}\right)$$

$$-\mathrm{r_A} = \ -$$

$$\frac{\mathrm{dC_A}}{\mathrm{dt}} = \ \left(12.67 * 10^5 \exp\left(\frac{-45536.02}{\mathrm{RT}}\right)\mathrm{C_A C_B} \ - 19.43 * 10^5 \exp\left(\frac{-49235.97}{\mathrm{RT}}\right)\mathrm{C_C C_W}\right)\mathrm{C_{SA}}$$

E_{af} = 45.536 kJ/mol ; E_{bf} = 49.235 kJ/mol and $\mathrm{K_e} = 0.6518\ \exp\left(\frac{3699.95}{\mathrm{RT}}\right)$

Appendix – III

Mass and Heat Transfer for multiphase system [178, 210, 228, 232]

For Heat transfer

In micro structured tubular reactors, the heat is usually removed or supplied by keeping constant temperature of the cooling (T_c) or the heating media (T_h) respectively. The heat transfer production of a system is the function of the heat exchange surface (A) and the overall heat transfer coefficient (U).

$$\dot{Q} = U * A * (T_c - T) \qquad \text{(AIII.1)}$$

Where T is the temperature of a reacting fluid.

Due to the small channel widths of the micro channels, laminar flow could be considered. The radial velocity profile in the channels progresses from the entrance to the position where a complete Poiseuille profile is recognised. The length of the entrance zone is a function of Re (Reynolds Number) and channel width. Similarly, radial temperature profiles grow. This is shown in **Figure AIII.1**.

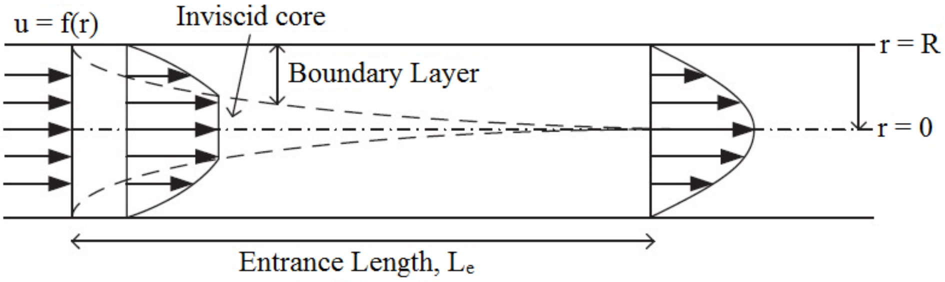


Figure AIII.1. Schematic image of develop of laminar flow (velocity profile). [210].

Inside the entry region the heat transfer coefficient reduces, reaching a limiting value. The constant wall temperature can be described in terms of the Nusselt numbers

$$Nu = \frac{h * d_h}{\lambda} \qquad \text{(AIII.2)}$$

Where λ is the thermal conductivity of a fluid and $d_h$is a hydraulic diameter of a channel.

For a laminar flow and completely established radial velocity and temperature profiles, the local heat transfer is constant and the mean Nu approaches an asymptotic value, given by Nu_∞. The same value is obtained for the asymptotic Sherwood number, Sh_∞ describing the mean mass transfer between the fluid and the channel wall. The asymptotic Nu and Sh are function of the channel geometry. For parallel emerging radial velocity and temperature profiles, the thickness of the boundary layers increase with increasing distance from entrance of a channel. As a result, the local heat transfer reduces until the profile is completely established. The mean Nu over the channel length depends on the ratio of d_h/L_t, the Reynolds number, Re, and the Prandtl number, Pr.

$$\mathrm{Nu_m} = \mathrm{f}[\mathrm{Re} \cdot \mathrm{Pr} \cdot \mathrm{d_h}/\mathrm{L_t}];\ \mathrm{Re} = \frac{\mathrm{u} \cdot \mathrm{d_h}}{\upsilon};\ \mathrm{Pr} = \frac{\upsilon}{\alpha} \qquad \text{(AIII.3)}$$

Where α is the thermal diffusivity. The following relation describes the mean Nu for all lengths, L_t of the tubular reactor at constant wall temperature.

$$\mathrm{Nu_m} = [\mathrm{Nu}_\infty^3 + 0.7^3 + (\mathrm{Nu}_2 - 0.7)^3 +\cdot \mathrm{Nu}_3^3]^{1/3} \qquad \text{(AIII.4)}$$

$$\text{Where}\mathrm{Nu}_2 = 1.615 * [\mathrm{Re} * \mathrm{Pr} * (\mathrm{d_h}/\mathrm{L_t})]^{1/3};\mathrm{Nu}_3 = \left[\frac{2}{1+22\mathrm{Pr}}\right]^{1/6} [\mathrm{Re} * \mathrm{Pr} * (\mathrm{d_h}/\mathrm{L_t})]^{1/2}$$

(AIII.5)

For Mass Transfer: Estimation of Mass transfer coefficient

B. Urvashi et al, [242], reported that hydrodynamic, mass transfer and RTD Studies of fluid flow in a spiral micro reactor for the system of n – butyl acetate and NaOH solution, the details are as follows C^*_{aq} is the concentration of n – butyl acetate, which is transferred from organic to aqueous phase. To study the performance of the spiral microreactor, volumetric mass transfer coefficient was used which was derived from mass transfer rate relations as:

$$\mathbf{K_L a} = \frac{\mathbf{1}}{\boldsymbol{\tau}} \mathbf{ln}\ \left(\frac{\mathbf{C^*_{aq} - C_{aqi}}}{\mathbf{C^*_{aq} - C_{aqo}}}\right) \qquad \text{(AIII.6)}$$

C_{aqi} and C_{aqo} represent the amount of n – butyl acetate at the inlet and at the outlet respectively for aqueous phase. The τ is the residence time of micro reactor.

The volumetric mass transfer coefficient ($k_L a$) obtained using above equation varies in the range of 0.02 to 0.37 s^{-1}. The aqueous phase outlet concentration of n – butyl acetate was measured. It indicated that the outlet concentration of n – butyl acetate was directly proportional to the flow rate due to decrease in the residence time inside microreactor. From the equation (AIII.6) it was clear that volumetric mass transfer coefficient was inversely proportional to the residence time, therefore directly affected by the variation in the volumetric flow rate. As the volumetric flow rate was increasing, the interfacial mass transfer area was also increasing due to presence of internal circulations within slug. [243]

Correlation of mass transfer data for physical mass transfer

There was no empirical model available to estimate the volumetric mass transfer coefficient in spiral microreactor. The assumption was density and viscosity of system fluids was constant throughout the micro reactor. Reynolds number and Capillary number were employed to estimate the volumetric mass transfer coefficient in spiral microreactor. It was considered that the following variables were affecting the mass transfer coefficient in the mass transfer extraction [244].

$$k_L a = f(\mathrm{Re, Ca, d, L})\ ;\ k_L a = a\ (\mathrm{Re}*\mathrm{Ca})^b (d/L)^c \qquad \text{(AIII.7)}$$

Using a least square regression analysis of the experimental data, the correlation was developed for volumetric mass transfer coefficient in spiral microreactor. By evaluating the values of a, b and c in order to correlate Re, Ca, diameter and length of spiral microreactor with good fitting curve. Hence the following correlation was reported.

$$\mathbf{k_L a = 0.4617(Re * Ca)^{0.657}\left(\frac{d}{L}\right)^{-0.1}} \qquad \text{(AIII.8)}$$

Mass Transfer in Catalytic Micro Structured Reactors

Prior to catalytic heterogeneous reaction, which takes place on the surface of a solid catalyst, the reactant molecules have to first reach the catalyst surface and, therefore, the rate of mass transfer is an important functioning parameter. Two types of mass transfer need to be considered in fluid–solid reactions: external and internal mass transfer. Mass transfer influences should be avoided, as they diminish the performance of the reactor and strongly affect product yield and selectivity. The reactions occur on the outer surface of the catalyst particle or of the wall catalytic layer. The observable effective reaction rate is determined by the ratio of the characteristic mass transfer time, t_m, and the characteristic reaction time, t_r, commonly known as second Damköhler number DaII.

$$\mathrm{DaII} = \frac{t_m}{t_r} = \frac{k_r c_{1,b}^{n-1}}{k_m a} \qquad \text{(AIII.9)}$$

The characteristic mass transfer time is given by the mass transfer coefficient in the fluid, k_m, and the specific outer surface area of the catalyst, a.

$$t_m = \frac{1}{k_m a} = \frac{V}{k_m A} \qquad \text{(AIII.10)}$$

Where A is the active surface of the catalyst and V is the reaction volume. To eliminate mass transfer effect in practice, the characteristic transfer time should be approximately 1 order of magnitude smaller than the characteristic reaction time. Low values of DaII ($t_m \ll t_r$) correspond to a situation where the effect of mass transfer can be neglected and the observed reaction rate is close to the intrinsic rate.

$$-R_{1,eff} \cong k_r c_{1,b}^{n} \qquad \text{(AIII.11)}$$

At high values of DaII ($t_m \gg t_r$) the rate of the transformation is completely controlled by mass transfer from the bulk of the fluid phase to the catalyst surface, with the surface concentration being nearly zero ($c_{1,s} \cong 0$).

$$-R_{1,eff} \cong k_{mr} a \cdot c_{1,b} \qquad \text{(AIII.12)}$$

Characterization of Mass Transfer in Fluid – Fluid Systems

Different approaches have been used to model mass transfer performance of reactors. They comprise two main parts: the micro model, describing the mass transfer between two phases, and the macro model, describing the mixing pattern within the individual phase. The micro models assume two types of interfacial behavior: stagnant films or dynamic absorption in small elements at the contact surface.

For example, the gas – liquid mass transfers. In the stagnant film model, it is postulated that mass transfer proceeds via steady – state molecular diffusion in a hypothetical stagnant film at the interface with thickness δ while the bulk of the liquid is well mixed [245]. Though this model incorporates the important features of the real system and is simple to use, the prediction of hydrodynamic parameter δ is difficult as it depends on the contactor geometry, liquid agitation, and physical properties.

The penetration model, reported by Higbie [246], assumes that an element of surface is exposed to gas for the same time (t) before being replaced by a liquid of bulk composition. The exposure time (t) is investigated using hydrodynamic properties such as interface velocity and its length. Film and penetration models are most commonly used defining the liquid – side mass transfer coefficients (k_L) as follows.

Penetration model: $k_L = 2\sqrt{\frac{D_m}{\pi t}}$ (AIII.13)

Film model: $k_L = \frac{D_m}{\delta}$ (AIII.14)

Where D_m is molecular diffusivity of solute in liquid phase and δ is imaginary interfacial film thickness in the liquid phase.

A micro structured reactor is generally compared to ideal plug flow or backmixed flow reactor with narrow residence time distribution. In the case of slug or Taylor flow, both fluids flowing through micro channels interchange mass among the same compartments (e.g., among same gas and liquid slugs). Therefore, one driving force is required to define the mass transfer rate.

In conclusion, the gas – liquid mass transfer in Taylor flow has two contributions (see Figure A2): (i) the caps (treated as hemispherical) at both ends of the bubble and (ii) the liquid film surrounding the lateral sides of the bubble. Considering these two contributions and assuming resistance in the liquid phase, the relationship for the overall mass transfer coefficient ($k_{ov}a \cong k_La$) is given in the following.

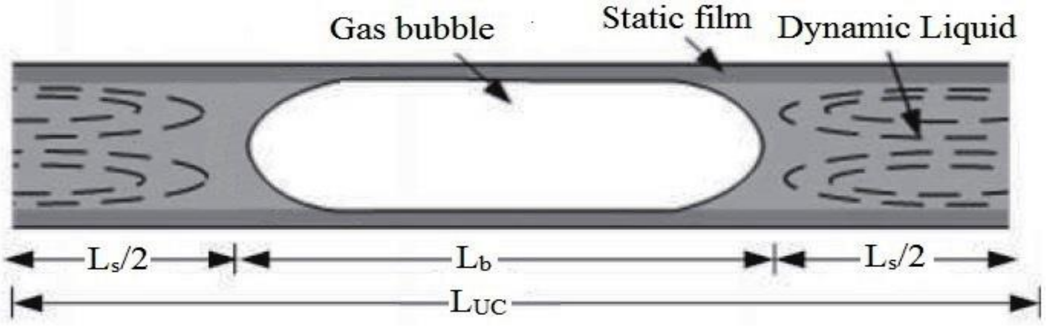


Figure A2. Schematic image of Taylor flow in a horizontal capillary (L_b – length of bubble and L_{UC} – unit slug length). [247]

$k_L a = k_{L,c} a_c + k_{L,f} a_f$ (AIII.15)

$$k_L a = 2\sqrt{\frac{2D_m u_b}{\pi^2 d_t}}\frac{4}{L_{UC}} + \sqrt{\frac{D_m}{\pi\theta_{c,f}}}\frac{4\varepsilon_G}{d_t} \tag{AIII.16}$$

$$k_L a \cong 4.5\sqrt{\frac{D_m u_G}{\varepsilon_G^2 L_{UC}}}\frac{\varepsilon_G}{d_t} = 4.5\sqrt{\frac{D_m u_G}{L_{UC}}}\frac{1}{d_t} \tag{AIII.17}$$

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1) **Yadagiri Maralla**, Shirish Sonawane, Dhurke Kashinath, Makarand Pimplapure, Banoth Paplal, "Process Intensification of Tetrazole reaction through tritylation of 5-[4'-(Methyl) Biphenyl-2-Yl] using microreactors", Chemical Engineering and Processing: Process Intensification, 112 (2017) 9 – 17. **Impact Factor: 3.031.**

2) **Yadagiri Maralla**, Shirish Sonawane, "Process intensification using a spiral capillary microreactor for continuous flow synthesis of performic acid and its kinetic study", Chemical Engineering and Processing: Process Intensification, 125 (2018) 67 – 73. **Impact Factor: 3.031.**

3) **Yadagiri Maralla** and Shirish Sonawane, "Process intensification by using a helical capillary microreactor for a continuous production of Peroxypropionic acid and kinetic study", Periodica Polytechnica Chemical Engineering, 64 (1) (2020) 9 – 19. **Impact Factor: 1.382.**

4) **Yadagiri Maralla** and Shirish Sonawane, "Comparative study for production of unstable peracetic acid using microstructured reactors and its kinetic study", Journal of Flow Chemistry, 9 (2) (2019) 145 – 154. **Impact Factor: 2.277.**

As Co – Author

1) Srinath Suranani, **Yadagiri Maralla**, Shekhar M. Gaikwad, Shirish Sonawane, "Process intensification using Corning® Advanced – Flow™ reactor for continuous flow synthesis of biodiesel from fresh oil and used cooking oil", Chemical Engineering and Processing: Process Intensification, 126 (2018) 62 – 73. **Impact Factor: 3.031.**

2) Urvashi Bhivgade, **Yadagiri Maralla**, Bharat A. Bhanvase and Shirish Sonawane, "Hydrodynamic, Mass Transfer and RTD Studies of Fluid Flow in a Spiral Microreactor", Journal of the Institution of Engineers (India): Series E., 100 (2) (2019) 139 – 146.

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1) **Yadagiri Maralla** and Shirish Sonawane, "Synthesis of unstable performic acid in a continuous flow microreactor", 2nd International Conference on Emerging Trends in Engineering, Science and Technologies (ICETEST-18), February 16th – 17th, 2018, Warangal, Telangana. **Oral Presentation.**

2) **Yadagiri Maralla** and Shirish Sonawane, "Hydrodynamic Flow Behavior of Immiscible Liquids in an Advanced – Flow Reactor", Two Day National Conference on "Dynamics of Interfaces In Multiphase Systems – DIMS 2018" 15th – 16th , 2018, at department of chemical engineering, NIT, Warangal, Telangana. **Oral Presentation.**

Patent

1) Shirish H. Sonawane, **Yadagiri Maralla**, G. Uday Bhaskar Babu, Komel Ansari and Aditya Deshmukh, "Particle Size Reduction of Pharmaceutical Material/Drugs using Innovative Crystallization Process", Date of filing of Application: 04/09/2018, Publication Date: 14/09/2018. Application No.201841033163 A. **Under FIR.**