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Kinetic study of the homogeneous acid-catalyzed esterification of malic acid with methanol to form dimethyl malate

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**Kinetic study of the homogeneous acid-catalyzed esterification of malic acid with methanol
to form dimethyl malate**

by

Chukwuemeka Mba

A thesis submitted to the graduate faculty
in partial fulfillment of the requirements for the degree of

MASTER OF SCIENCE,

Major: Chemical & Biological Engineering

Program of Study Committee:
Brent Shanks, Major Professor
George Kraus
Jean-Philippe Tessonier

The student author, whose presentation of the scholarship herein was approved by the program of study committee, is solely responsible for the content of this thesis. The Graduate College will ensure this thesis is globally accessible and will not permit alterations after a degree is conferred.

Iowa State University

Ames, Iowa

2019

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DEDICATION

This thesis is dedicated to my Lord and savior, Jesus Christ, who I constantly prayed to in the course of undertaking this work. There were just too many failed ideas, road blocks and reasons to lose motivation but my inspiration was revived through prayers and typing this, I surmise, is my evidence that it worked.

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NOMENCLATURE

DMF	Dimethyl Fumarate
DMM	Dimethyl Malate
HPLC	High Performance Liquid Chromatography
MA	Malic Acid
MeOH	Methanol
MMM	Monomethyl Malate
MS	Mass Spectrometry
NIST	National Institute of Standards and Technology
PDA	Photo Diode Array
RI	Refractive Index

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I would like to thank my committee chair, Dr. Brent Shanks, and my committee members, Dr. George Kraus, and Dr. Jean-Philippe Tessonier, for their guidance and support throughout the course of this research.

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ABSTRACT

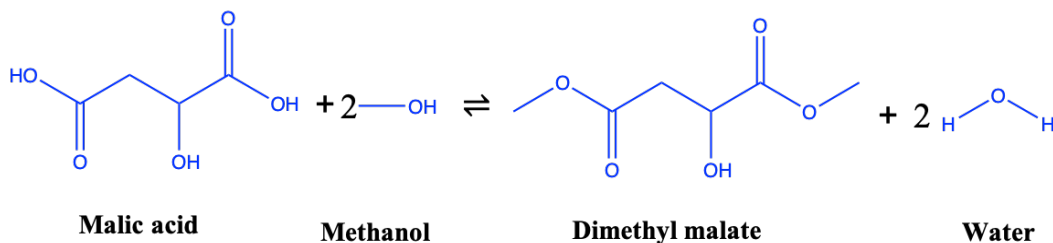
The dearth of literature on the esterification of dicarboxylic acids containing a hydroxyl group attached to the chain was the lodestar behind this project. Since Malic acid typifies molecules belonging to this sect of hydroxydicarboxylic acids, a synthesis and kinetic study of the liquid-phase Sulfuric acid-catalyzed Fischer esterification reaction of Malic acid with Methanol to form Dimethyl Malate are presented. The preliminary synthesis study involved adjustments of operating conditions in isothermal reactions staggered in temperatures between (80-100) °C, at a milder catalyst concentration, and at distended reaction times to obtain a yield of the desired ester (87-91) % which was comparable to the figures obtained from previous synthesis studies. Then, using these conditions at their dialed-back states for conducting similar reactions, a kinetic study was conducted and experimental data were extracted. Afterwards, the effect of temperature, catalyst concentration and reactant molar ratio (in an uncatalyzed regime) were investigated and the findings discussed. A kinetic model was subsequently proposed based on certain assumptions and tested for fitness through computation and regression analysis of the kinetic data. They were revealed to be good fits in most conditions under investigation and an explanation was given for the circumstance in which the model seemingly-failed. A rationalization for the failure of the model, with a basis upon which another model can be developed, were adduced therein and can be used for the design and simulation of processes such as the reactive distillation for Dimethyl Malate formation.

CHAPTER 1 INTRODUCTION

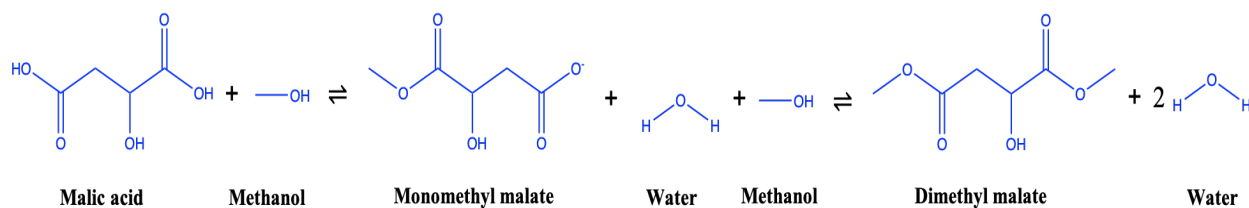
1.1 Introduction to Organic Acid Esters

Organic acid esters are polarizing in the way we contemplate them in terms of their conception and usage. On the one hand, their importance to us cannot be gainsaid or over-emphasized. They find application as intermediates in the synthesis of acidulants, fine chemicals, cosmetics, detergents, drugs, dispersants, emulsifiers, fragrances, herbicides, insecticides, plasticizers, pharmaceuticals, precursors for biorenewables, softeners, solvents, surfactants and biofuels etc.¹⁻⁸ On the other hand, we can acquire them almost readily, biologically, so it begs the question why chemical engineers and chemists alike, are still intrigued by how they are synthesized.

A subset of these organic acid esters is even more fascinating. The esters of the dicarboxylic kind in particular. For years on end, the Fischer esterification method has been employed in reactions involving carboxylic acids and alcohols to produce these esters as past literature has shown, but there is a virtual taciturnity with respect to the ones that pertain to dibasic esters. The reason behind this is not far-fetched. Similarly-weak carboxylic acids like, the monocarboxylic variants esterify to engender monoesters due to the protonation of the carbonyl oxygen on the carboxylic group, thereby activating a nucleophilic attack by the alcohol to form the tetrahedral intermediate which, on disproportionation, yields the ester.⁵ This is regarded as the rate initiating or determining step. The constructed intermediate, now a monocarboxylic ester, is further nucleophilated by the excess alcohol into the dicarboxylic ester which is industrially pertinent when not unavailable. Schematic representations of these phenomena are displayed below in (Schemes 1 and 2).



Scheme 1 Overall Esterification Reaction of Malic Acid with Methanol to form Dimethyl Malate



Scheme 2 Esterification Reaction of Malic Acid with Methanol showing Intermediate Step

1.2 Inevitability of Catalysts

Since, this process is agonizingly slow, catalysts can be deployed to essentially foster this protonation and subsequently augment the reaction rate. Principally, they achieve this by lowering the activation energy and permitting an alternate mechanism enroute to fast-tracking the reaction's equilibration. In other words, without catalysts, this di-esterification process will be subjected to enduring a very long reaction time to reach equilibrium. The type and nature of catalysts deployed will, to a large degree, dictate the effectiveness of the procedure. Albeit, heterogeneous catalysts circumvent the drawbacks associated with the highly-acidic homogeneous type, namely; corrosive nature, difficulty in separation after use, possible damage to other sensitive functional groups, implausibility for re-usage and lastly, how they generate acid wastes which cause severe environmental problems, the latter type of catalysts, it is reported, still ultimately precipitate higher yields of the carboxylate in a shorter time due to its greater density of acid sites per gram and ability to prevent side reactions.⁹ Even though, the

second motive adduced is controversial, it is for the foremost reason that a homogenous catalyst was selected for use in this present study.

1.3 Introduction to Hydroxycarboxylic Acids

These naturally-occurring and synthetic carboxylic acids containing at least one hydroxyl group, are of the α -alpha, β -beta and γ -gamma type depending on the position of the hydroxyl group on the carbon chain. They could be relatively short-chained (Tartronic acid, Mesoxalic acid and Malic acid) or longer-chained (Tartaric and Oxaloacetic acids) and are primarily used in the cosmetics and food industries due to their dermal and epidermal effects^{10,11} even as some of them are cleaved oxidatively to form aldehydes which are themselves multifaceted in application.¹²

The hydroxydicarboxylic acid of interest in this study - Malic acid - has gained traction coincidentally with the advent of bioprivileged molecules.¹³ In 2004, the Department of Energy cited it as one of the twelve most promising bio-based platform molecules.¹⁴ Malic acid plays an instrumental role in the carbohydrate metabolism and production of energy for cellular processes. In the Krebs's cycle, it is the predecessor of both the Tartaric and Oxaloacetic acids which are applied in confectioneries to initiate tartness in food. Its delegation as a precursor for these other acids is contingent upon its four-carbon dicarboxylic structure which surely determines the further molecules that can be derivatized from reactions involving it. One of such derivatives currently being venerated is Methyl Coumalate. Even though several procedures have been proposed for the synthesis of this molecule, the method conspired by Kraus et al is at present, the most feasibly scalable and is additionally being applied to the production of biorenewable chemicals and thermoformed parts.¹⁷ The (Figure 1)⁴¹ depicts some of the other less-celebrated Malic acid derivatives below.

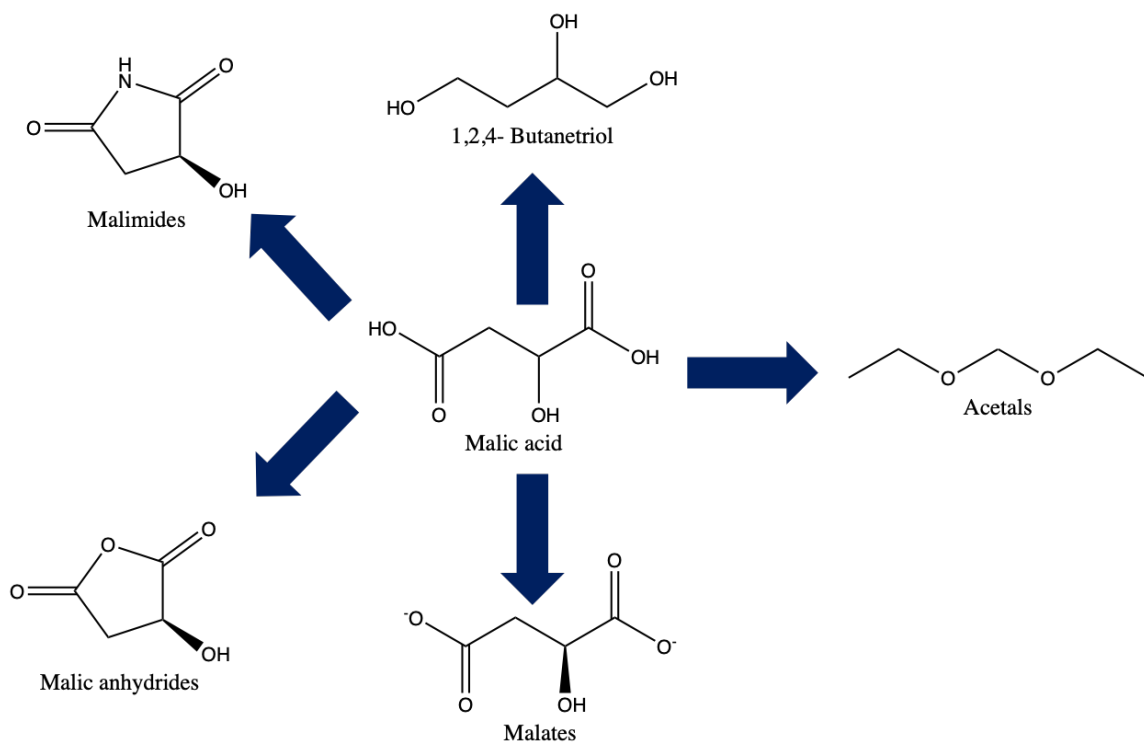


Figure 1 Derivatives of Malic acid

Industrially, it is produced through the double-hydration of the Maleic Anhydride and appears in L and D stereoisomers although the L-enantiomer is more naturally occurring.^{15, 16} Its diprotic acid nature and relative short-chain amongst the other hydroxycarboxylic acids necessitates its inclusion in this investigation on the di-esterification of dicarboxylic acids with basic alcohols as the reaction solvents.

1.4 Aim of the Project

This study aims to investigate the kinetics behind the esterification reaction of Malic acid (herein, MA) and Methanol (MeOH) to produce the dimethyl ester – Dimethyl Malate (DMM), which is a precursor in the synthesis of Methyl Coumalate¹⁷ and Tulipalin-B which in-turn are engaged in the production of antimicrobial products, biorenewable chemicals, biopesticides, biofungicides and plastic beverage containers.¹⁸⁻²¹ The derivative molecules (see Figure 2)⁴¹ like; 1, 2, 4-Butanetriol, Malamides and 3, 4-Dihydroxybutanoic acid, via which, these end-products

are generated, are of accreting importance to industrial scientists and engineers, thus strengthening the motivation for this project. In addition to the kinetic study, the project targets to propose a synthesis study which will delineate a more efficient reaction process by modifying the stipulated parameters to a less exerting version. Parameters such as temperature, mole ratio of reactant and solvent, volume and concentration of catalyst as well as residence time for the batch process.

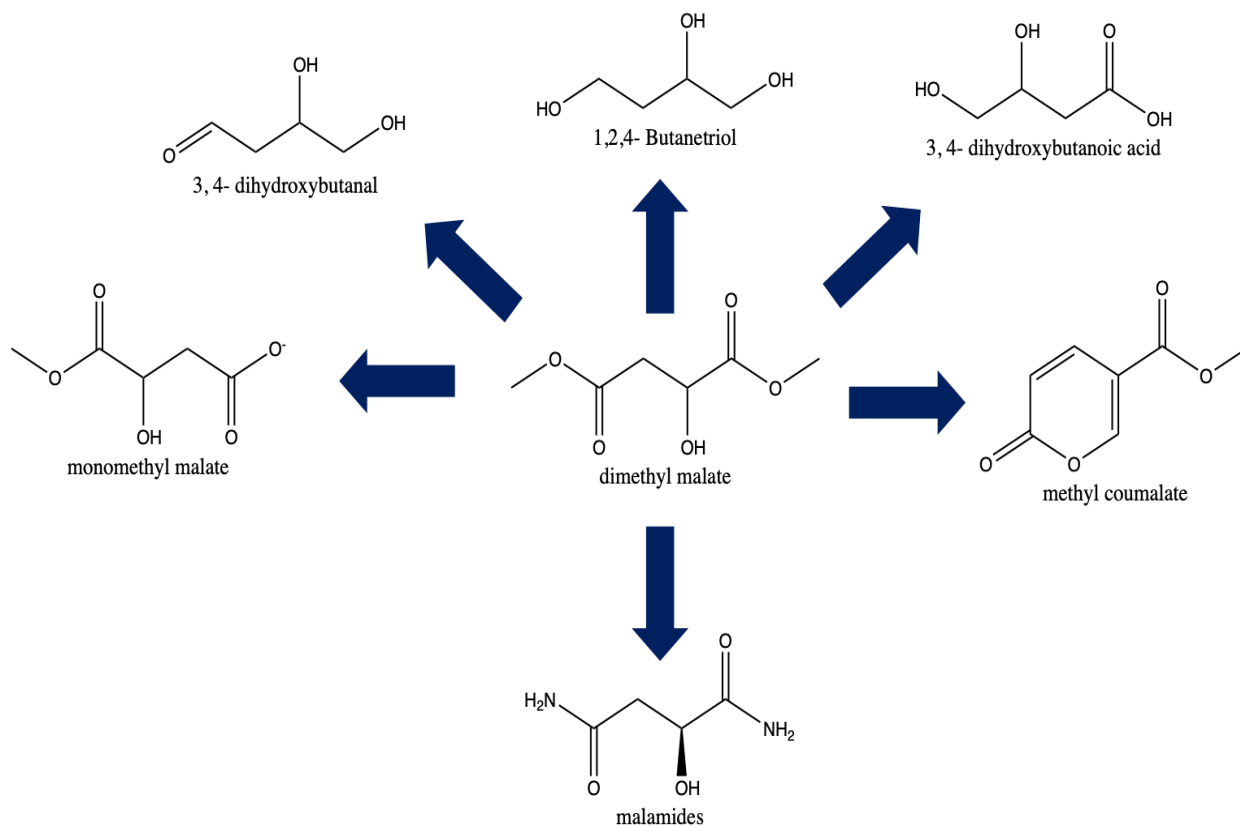


Figure 2 Derivatives of Dimethyl Malate

Presently, there is no information available in the open literature describing the kinetics of esterification of MA with MeOH in the presence of a mineral acid. Consequently, we have conducted isothermal experimental batch studies on the liquid-phase esterification of MA with MeOH in the presence of Sulfuric acid as the homogeneous catalyst. A simplified pseudo first-order kinetic model is proposed for the correlation of the experimental data acquired with a simple power law representing the first esterification stage, while another slightly more complicated rate law derived from the consecutive network of reactions (in the second stage) leading to the desired product is also implemented and their validity in explicating the reaction kinetics is argued. In addition, a preliminary synthesis study is presented discussing a plausible adjustment of reaction parameters that could potentially optimize the formation of the DMM synthesized based on the reaction species and conditions specified in this study.

CHAPTER 2 EXPERIMENTAL

2.1 Reactant Materials

The following were used at some point during the reaction and separation phase(s). They were used without purification. They are: DL- Malic acid (99%) which was in a powdery-crystal form as well as powdery white solid Monomethyl Malate (98%) were both purchased from Sigma-Aldrich (USA). HPLC grade Methanol (99.9%), Silicon oil and Sulfuric acid (Certified ACS) (98.08%) were procured from Fischer Scientific (USA). Dimethyl Fumarate (98%) and Dimethyl Malate (98%) were obtained from TCI (Japan). Amberlyst 45™ Resin acquired from Dow chemicals (USA) was also used sparingly.

2.2 Fischer Esterification Set-up and Procedure

Fischer esterification is utilized here as a result of its capacity to thermodynamically control the extent of the reaction and consequently favor the forward step of the process which subliminally favors the more stable species (the desired ester). The reaction was carried out in a 50 mL round-bottom flask placed in a silicon oil bath mounted on an Isotemp™ stirring hot plate with a knob to adjust the temperature and another to set the stirring speed. A glass-thermometer was placed in the oil bath to regulate and maintain the temperature whilst the stirring speed was sustained at 400 rpm for uniform mixing of catalyst and to curtail mass transfer limitations in the reaction mixture. A spiral condenser, filled with circulated water from an affixed chiller, was connected vertically to the reaction flask to uphold reflux i.e. Reduce vapor losses of the volatile solvent from the reactor. The reaction was timed, starting from the moment the agitating speed and temperature reached their pre-set values. After the reaction, the solution formed was collected in a vial and confirmed by HPLC.

Procedurally, 1.34 g (0.01 mol) of the powdery-crystalline MA was weighed using a Mettler Toledo ML204 Newclassic mL Analytical Balance with a 220 g x 0.1 mg (maximum and minimum) capacity. It was couched on a weighting paper and masterfully charged into the round-bottom flask already accommodating a magnetic stirring bar to aid uniformity of mixing in the sealed chamber. 8 mL of MeOH (~6.09 g, 0.19 mol), carefully poured into a 10 mL KIMAX® graduated cylinder till the lower meniscus of the solvent was on the cusp of the 8 mL mark, was also added into the flask now containing the MA and stirring bar. A collection of 100-1000 μ L measuring pipettes were used to measure and transfer the varying concentrations of Sulfuric acid as the reaction procedure dictated. The round-bottom flask was afterward fastened (via the orifice) to the end of the spiral cooling column (acting as the reflux unit) and was secured by means of a plastic clamp to prevent vapor leaks as well as the unlikelihood of the reactor vessel dropping due to gravity.

The reaction was only considered as commenced when the pre-set agitation speed and temperature were met prior to placing the reaction-apparatus in the oil bath that was positioned on the hot plate. The conclusion of the reaction was initiated after the condenser was lifted from the oil bath and the hot stirring plate was turned completely off. The solution was allowed to cool only briefly, to preclude further reaction. It was relocated to a 50 mL volumetric flask where HPLC-grade MeOH was used to dilute the sample. The now diluted solution was robustly agitated in the ultrasonic water bath for 5 minutes in readiness for the quantitative analysis by the High-Pressure Liquid Chromatography (HPLC). In the course of this procedure, different temperatures of the reaction ranging from 40-100°C, acid-to-alcohol molar ratio (1:9.5-38) and time(s), from 0.5-20 hours were spent even as this batch process was isothermal. (Figure 3) is a schematic diagram of the simple batch system constituted for this kinetic study.

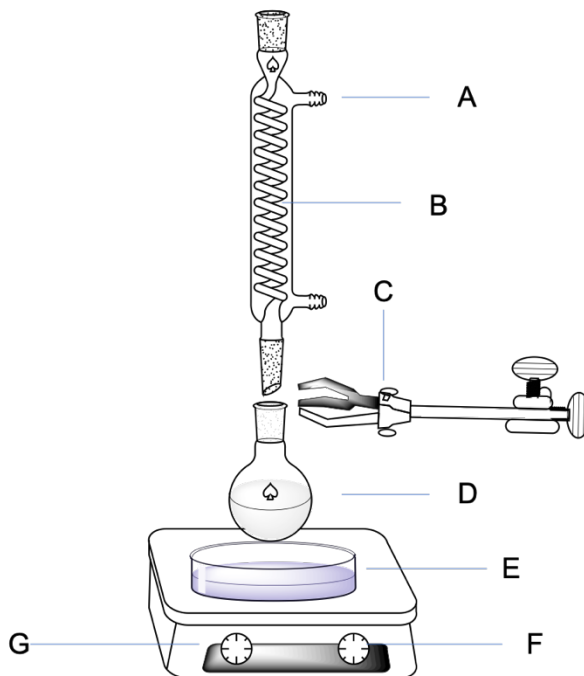


Figure 3 Simple Esterification Experiment Set-up

A- Coolant-out Orifice; B- Graham Spiral Condenser; C- Fastening Clamp; D- Round-Bottom Flask; E- Silicon Oil Bath; F- Stirring Speed Knob; G- Temperature Knob

2.3 HPLC Analysis

On completion of the reaction, the formed sample was extracted and inserted in a 50mL volumetric flask where it was diluted by Methanol to the pre-designated mark on the flask. The constituents of the flask were then vigorously mixed by a sonicator in low heat to maintain uniformity. The well-distributed solution was then extracted by a syringe which was subsequently muzzled with a non-pyrogenic filter before being deposited in the 1.5 mL vial that was placed on the carousel of the HPLC.

HPLC separation and quantitative analysis were carried out by the Waters e2695 High Performance Liquid Chromatographer – Separations Module – equipped with a 2998 Photodiode (PDA) Detector, 2414 Refractive Index (RI) Detector and an Acquity QDa™ Mass Spectrometer (MS) Detector. The HPLC chromatogram was developed to aid the characterization and

quantification of the sample while the QDa™-MS was used to confirm the identity of the compounds formed. A calibration curve for the dimethyl Malate, Malic acid, monomethyl Malate and dimethyl fumarate were constructed using the purchased standards of the chemicals as well as the HPLC chromatogram.

The actual separation in the system was executed by a Phenomenex-branded reverse-phase HPLC/UPLC C-18 column designated as the Gemini 3-micron C18 110A with a size 250×4.60 mm (diameter). The externals of this column were conserved at 40°C with the internals at 25°C while the sample itself was stored at 10°C in the 1.5 mL vial now resident in the carousel of the cooling unit of the HPLC. The mobile phase; 5 mM of Sulfuric acid/deionized water mix (A, 55%) and HPLC-grade Methanol (B, 45%) were isocratically pumped at a flow rate of 0.45 mLmin⁻¹ through the reverse column with high- and low-pressure limits of 4000 and 0 psi respectively. Typically, this culminated at approximately 2650-2850 psi.

The conspired method set for the samples began with an equilibration step that ran before the injectors and detectors were purged prior to the column being re-equilibrated. The total run time for these functions were 40 minutes with each step accounting for 10 minutes. The injected blank sample was erstwhile processed ahead of the produced sample which was set at 15 minutes of run-time since all the expected peaks had eluted signifying that virtually all the constituent molecules of the sample had been separated. Each injector volume of blank and sample was consistently 10 µL.

The PDA detector monitored the effluents at wavelengths (λ) of 190 to 250 nm within a 1.2 nm resolution but was fine-tuned to an absorbance data mode where the λ of 210 nm was set, having been identified as the closest channel strength to the analytes.

On the other side, the RI detector was configured with a sampling rate of unity mV. The filter time and sensitivity were set at 1 and 4 correspondingly and the polarity was kept at positive (+) all through.

The QDa™ detector operated at a range in the region of 65-180 Da with both capillary and cone voltages set at ±0.8 kV and ±15 V individually. Due to the disruptive and corrosive nature of Sulfuric acid used in the solvent for the PDA detector, another solvent, 0.1% Acetic acid/deionized water mix was introduced as part A under a 55% volume schedule whilst MeOH was retained as the part B- 45% volume. The esterification at this juncture was also set-up using Amberlyst 45™ as the reaction catalyst.

As an interesting side note, apart from the yield, conversion and selectivity played a pivotal role in the analysis of the diester formed. Using the intensity/peak obtained from the chromatogram, in the line of regression constructed to calibrate the products, by-products and unreacted reactant, the conversion of MA and its selectivity in yielding the desired ester was calculated as follows:

$$Y_{DMM} = \frac{C_{DMM} \text{ (Actual)}}{C_{DMM} \text{ (Theoretical)}} \times 100 \quad (1)$$

$$Y_{MMM} = \frac{C_{MMM} \text{ (Actual)}}{C_{MMM} \text{ (Theoretical)}} \times 100 \quad (2)$$

$$X_{MA} = 1 - \frac{C_{MA} \text{ (Unreacted)}}{C_{MA0} \text{ (before reaction)}} \times 100 \quad (3)$$

Where Y_{DMM} , Y_{MMM} , and X_{MA} represent, the yield of Dimethyl Malate, yield of Monomethyl Malate, and conversion of Malic acid respectively.

The material balance was correct up to (0.95-1.05) since the calibration curve developed could only account for (95%) of the DMM when (100%) of it was expected or the mass balance summed up to (105%) when (100%) was expected. This $\pm 5\%$ error is attributed to three reasons namely: problem of leverage in the curve due to uneven spacing of data points, error as a result of sample preparation i.e. standard stock/mother-solution use and error of having non-zero intercepts on the linear curve. A study has shown that it is practically impossible to get any less than a 0.5% error in using HPLC for quantitative analysis but for the purpose of this particular project, the error did not impair the data significantly.

2.4 HPLC Identification

Deploying the purchased standard of Dimethyl Malate (DMM), Monomethyl Malate (MMM), Dimethyl Fumarate (DMF) and Malic acid (MA) at specific volumes and weights in a 50 mL volumetric flask where they had their concentration(s) attenuated by MeOH to the calibrated mark of the flask. Each sample (now deposited in a small vial) was then introduced to the separation column of the HPLC for analysis. The RI and PDA detectors (both simultaneously configured into the sample set method for the procedure) –using the peaks on the chromatogram- identified the following retention time(s) for each of the samples (see Figure 4) and was corroborated by the spectrum developed by the mass spectrometer which presented tentative molecular weight fragments that mirrored values extracted from the NIST data base. This validated the quality of the purchased sample standards and acted as a reference to verify that the same molecules were present following the esterification reaction. The retention times in minutes were: MA – (6.5 \pm 0.05), MMM – (7.1 \pm 0.09), DMM – (7.88 \pm 0.04), XXX – (10.3 \pm 0.05), DMF – (14.6 \pm 0.06). To substantiate this, QDa™ detection was also implemented by comparing the spectrum and mass/charge for the standard(s) to that derived by experimentation. The values obtained for the mass/charge for each section was compared with the same from the NIST

database. The values with the corresponding retention times are: DMM standard (~7.875 minutes, 102.95 m/z), DMM synthesized (~7.869 minutes, 103.09 m/z), DMM NIST (~103 m/z). DMF standard (~14.515 minutes, 112.97 m/z), DMF synthesized (~14.583 minutes, 112.94 m/z), DMF NIST (~113 m/z). .MA standard (~6.431 minutes,) MA NIST (~71 m/z)

Using these times and MS spectrums detected for the standards and juxtaposing it with those observed in the experiment proper, the rationale for running this study via HPLC was established.

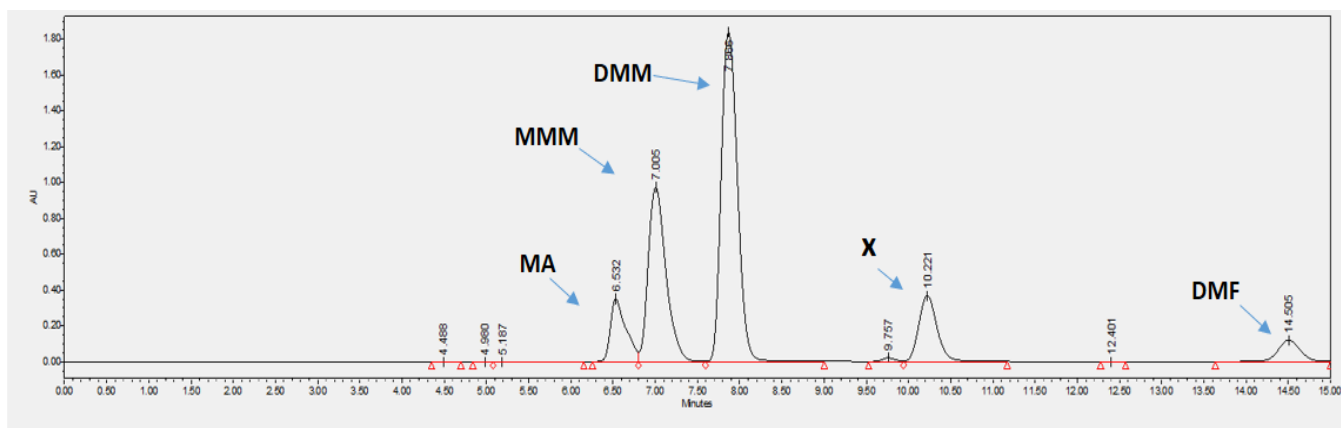


Figure 4 Typical Chromatogram Depicting Peaks of Studied Diester, Unreacted MA and Side Products

CHAPTER 3 RESULTS AND DISCUSSION

3.1 Introduction

The glaring paucity of literature on the kinetic study of the acid-catalyzed esterification of dicarboxylic acids was the motivation behind this work. Since hydroxycarboxylic acid-esters (when not being useful to chemists and chemical engineers likewise) are even more problematic to synthesize, Malic acid (herein, MA) which represents dicarboxylic acids with a hydroxyl group, became an interesting prospect for this kinetic study. MeOH was proposed as the reaction solvent owing to Malic acid's almost-excellent solubility in it, and on the predicted potential of the dimethyl ester formed during the Fischer esterification reaction.

The underlying objective was to optimize the subsistent reaction conditions from a chemical engineering standpoint and to illuminate the mechanism and kinetics that somewhat validates this so-called optimization. Consequently, the results and discussions in this chapter are demarcated into a synthesis and kinetic studies. Whilst the former, delineates certain adjustments in the reaction parameter that will improve the yield of the DMM produced viz-a-viz reducing reaction time and concentration of acid-catalyst and so on, the latter expounds the reaction mechanism using a devised kinetic model to fit the data points and corroborate the suppositions of the synthesis study. This was accomplished by; throwing light on the effect of temperature, absence or presence of the acid-catalyst, reaction rate constant(s), activation energy and pre-exponential constant as they influence the yield of the desired product and the conversion of the reactant species. The formation of the intermediate as well as other side-products were also reported as they were discovered and a snippet on the impact of selectivity on the production of the diester.

Every product and by-products of all the reactions in this study were analyzed primarily via HPLC which helped confirm the analytes and calibrate the concentration of the species.

3.2 Synthesis Study of the Acid-Catalyzed Fischer esterification of Malic acid and Methanol

A study of the past works on the esterification of MA with Methanol was carried out. It was readily noticed however, that there was virtually nothing done on the kinetic study or how most efficiently this carboxylate could be synthesized. Most of the patents and literature were more focused on synthesizing the molecule as a precursor for a subsequent step.

3.2.1 Review of Past Synthesis Studies

According to the scarce literature and patents, the typical operating conditions for the homogenous acid-catalyzed esterification of MA with MeOH had a duration of 16-19 hours, 10 mg MA (7.463×10^{-5} mol) / (33g, 0.25 mol), 10 mL MeOH / (150 mL), and (5%) / (2%) Sulfuric acid with reaction temperature at 25°C. This yielded (83-84%) of the DMM.^{38, 39} The reaction parameters for the patent had 20 g MA (0.149 mol), 300 g MeOH at 100°C which ran for 5 hours. The yield of the DMM was (79%).³⁷ Predictably, DMM yield varied depending on the reaction conditions many of which were less efficient. For instance, Xiang et al produced (85-87) % of DMM esterifying MA with MeOH in the presence of Sulfuric acid catalyst. The runtime for the reaction was 5 hours and the isothermal conditions meant that the reactor was sustained at between (80-120) °C.³⁶ Using somewhat similar parameters but with a heterogeneous catalyst, Dowex 50W-X8 resin and a 24-hour residence time, only (76%) of the DMM was synthesized.³³ This not only signified the germane role that acid-catalyst-strength plays in the formation of the desired ester but also demonstrated the importance of homogenous catalysts in the esterification of aliphatic hydroxyl acids in general. As was detected, the extension of the reaction time did not meaningfully improve the synthesis of the desired product in the same potency as the catalytic-

enclave did. When Thionyl Chloride (SOCl_2) was introduced as the catalyst for the same process (having adjusted some of the other reaction settings) (88%) of the ester was produced albeit the reaction ran overnight and was limited to absolute temperature or 0°C .³⁵

Table 1 Excerpts of Diester Yields and Reaction Conditions Obtained from Literature

Temperature ($^\circ\text{C}$)	Molar ratio	Catalyst	Time (hour)	Dimethyl Malate (%)	Reference
25	1:95	Dowex	24	76	[33]
100	1:3182	H_2SO_4	5	79	[37]
25	1:14	H_2SO_4	16	83	[39]
25	1:63	H_2SO_4	16	84	[38]
90	-	H_2SO_4	5	85-87	[36]
0	-	SOCl_2	24	88	[35]
75	-	H_2SO_4	2	92	[31]
-15-0	-	H_2SO_4	-	93	[34]
100	1:29	$\text{H}_5[\text{PMo}_{10}\text{V}_2\text{O}_{40}]$	1.5	98	[32]

A summary of a few of the various yields of the DMM and some of the varying operating conditions are displayed in (Table 1). The greatest amount of DMM was obtained when a very strong acid, Phosphovanadomolybdates ($\text{H}_5[\text{PMoV}_2\text{O}_{40}]$) was used as the catalyst in the esterification of MeOH enroute to decarboxylating MA into Dimethyl Malonate. Owing to the relative swiftness in which this synthesis occurred, together with the almost-complete conversion of the reactant species in the same time, carrying out a kinetic study of the product was most certainly improbable. The unlikelihood of this fairly necessitated the current investigative study depicted via (Table 2).

3.2.2 Initial Synthesis Study

Batch-esterification experiments were carried out to investigate and optimize the synthesis of the dimethyl malate in the process. In each experiment, the operating conditions were adjusted based on the overarching objective of the project and the established understanding of chemical reaction engineering.

Agitation speed and the temperature of the cooling unit were maintained as constant as possible to facilitate comparison among different operating conditions. In doing this, it was observed, for instance, that the speed of the stirrer (and likewise in the case of the set temperature of the condenser) at values close to or above 200 rpm, did not significantly alter the conversion rates of the reactions owing to the near-perfect solubility of MA in MeOH at virtually every temperature above room-temperature. As a result, all experiments were conducted at 400 rpm to avoid external mass transfer limitations. Internal diffusion was negligible under the employed esterification reaction conditions. In like manner, the temperature of the cooling column was preserved at 7.5°C and only altered upwards to 15°C to preclude condenser-sweating which could negatively impact the oil bath and in-turn, could have affected the reaction rate.

Table 2 Excerpts of the Maximum Yields of the Diester Obtained from Conducted Experiments

Temperature (°C)	Molar ratio	Time (hour)	Catalyst/Volume (M/vol %)	Yield (%)	Conversion (%)
80	1:19	3	1/6	87.1	99.2
80	1:19	6	14/6	91.1	100
80	1:19	19	Amberlyst45™	80.5	96.7
100	1:19	2.5	1/6	86.6	99.2
100	1:38	3	1/6	88.2	99.2
100	1:19	3	14/6	89.2	99.8
100	1:19	3	14/12.5	89.5	99.9
100	1:19	3	14/25	89.8	99.9
100	1:38	3	1/6	90.1	99.6
100	1:19	20	14/6	90.5	99.8

From the Table, the slender variations in the concentrations of the Sulfuric acid that was used to catalyze the reaction, saw at least (99%) of the MA converted. This was irrespective of whether concentrated or 1 M Sulfuric acid was used. It also showed how slightly inconsequential, what volume percent of this acid catalyst was administered. The implication was, a lower concentration of the Sulfuric acid could be installed in the operating condition instead of the undesirable concentrated variant since there was negligible compromise in the reactant conversion within the same time span. In addition, doubling the volume of the catalyst had little impact. In a 3-hour duration, the product yield for the same reaction parameters save the catalyst volume increasing from (12.5%) to (25%) advanced from (89.2 to 89.5) %.

Reaction time itself played less of a key role than past literature suggested. Although, there was a shift in the DMM yield to (90.5%) in a reaction that ran for 20 hours, the 17-hour gap appeared pleonastic and unjustified seeing that the reaction equilibrated in a time considerably less than that. This indicated that a similar yield of the Malate could be obtained in a shorter time and the data extracted from the so-designed experiment validated this hypothesis.

The ideal reaction temperature from the data showed that 80°C was sufficient to produce the best diester yield. Although, this realization should be cushioned by the fact that (6%) catalyst volume of concentrated Sulfuric acid was utilized in this particular reaction that yielded over (91%) of the product in 6 hours. Higher temperature-designed reactions gave closer percent yields to the 6-hour run one but not any greater. Temperature played less of a dynamic function beyond 64.5°C which represents the boiling point of the solvent but it definitely quickened the reaction rate. Consequently, we observed that a runtime of 3 hours for the same catalyst concentration and volume at 80°C generated (87%) of the diester and about the same quantity was achieved in 30 minutes less of the residence time when the reactor was conditioned at 100°C.

When excess Methanol was charged into the operation, the third closest value yield-wise was obtained which was also the most optimum. In this, slightly over (90%) of the DMM was realized when the acid-alcohol mole ratio was adjusted from 1:19 to 1:38. In only 3 hours and at 100°C, 1 M concentration of the catalyst helped catalyze the esterification reaction into the over (90%) yield in this excess solvent ambiance. When this temperature was adjusted to 80°C, the yield was slightly lower at the same time but ebbed to over (90%) at 6 hours. This specified that the ideal reaction time without overburdening the reactant materials was 6 hours at the concentration of the catalyst. This was particularly desirable as eliminating the use of the very corrosive concentrated Sulfuric acid was pertinent to this study.

This same acid-alcohol mole ratio could be preserved with a reduction in the MA used. When the MA was halved with the MeOH maintained at the original volume, the DMM synthesized was close to (90%). The insinuation, obviously, is that excess alcohol is essential to the high-yield of the ester -even more than the amount of reactant charged into the system.

Summarily, the general trend in the investigation evinced that excess alcohol was essential to the optimization of the Malate. It preceded the reaction duration which seemed to be insignificant after the system had both thermo- and chemo- dynamically reached its equilibrium.

Next, temperature dictated how quickly the reaction progressed into equilibration but could not demonstrably differentiate what the yield of the desired product would be between close temperature values. The concentration of the homogenous catalyst functioned rather similarly in the sense that the DMM realized was close in magnitude even when all other reaction parameters were held constant save the catalyst concentration. Although, Liu et al have demonstrated that, using a very strong oxidative acid, way over (90%) of the DMM can be obtained during this esterification process in less than 2 hours.³² The potency of the acid catalyst, more than its concentration was responsible for this. In contrast, Amberlyst45™ resin was also used under similar reaction conditions (but at 19 hours) and albeit (97%) of the MA was converted, only roughly (81%) of the dimethyl ester was formed. This validated the assumption that the runtime and catalyst-use have weaker influence(s) on the esterification of MA in MeOH than the acid-alcohol mole ratio.

3.2.3 Preliminary Results Screening

From the tabulated data, a screening of the results was conducted upon which base conditions for the actual kinetic study would be determined. These base conditions were established contingent upon the maximum yield of the diester formed, that were comparable to those obtained during the review of the past synthesis study and were less-dependent on the relatively harsh reaction conditions that were fixtures of the reviewed synthesis studies. The (Table 3) below illustrates this.

Table 3 Tabulated Synopsis of Preliminary Results

Temperature (°C)	Molar ratio	Time (hour)	Catalyst (M)	Yield (%)	Conversion (%)
80	1:19	6	14	91.1	100
100	1:19	3	14	89.2	99.9
80	1:19	3	1	87.1	99.2
100	1:19	2.5	1	86.6	99.2

Dialing back from the previous conditions used in the trial runs, a molar ratio of 1:19, at 6 hours of reaction time, under an 80°C temperature reaction and with concentrated Sulfuric acid as the homogeneous catalyst, it was lucid that complete conversion of the MA was actualized which yielded over (91%) of the desired ester. Subsequently, it was pertinent for the reaction time to be curtailed by the increase of kinetic energy through a temperature increase. As a result, 100°C of temperature was introduced into the same reaction conditions as described afore save for the reaction time being whittled to 3 hours. In this, we observe that comparably similar conversions are realized with approximately similar diester yields as procured from the 6-hour run experiments. This therefore indicated that the additional 3 hours of reaction duration was surplus to requirements and was unnecessary to the efficient synthesis and kinetic study of the DMM.

Considering the unfeasibility of using concentrated Sulfuric acids for industrial scale-up, it was also important to test-run these same experiments at lower Sulfuric acid concentrations. 1 M Sulfuric acid was therefore deployed into the same operating conditions but at the same reaction time of 3 hours. Interestingly, over (99%) of the reactant MA was converted and (87%) yield of the ester was formed and even more interestingly, about the same estimations were calculated when the temperature was increased to 100°C and reaction time cut down to 2.5 hours. These data set were then isolated as the base conditions for the kinetic study and are depicted below in the (Table 4).

Table 4 Base Operating Conditions

Parameter	Base condition	Unit
Catalyst	1	M
Substrate Molar Ratio	1:19	-
Temperature	100	°C
Time	2.5	hour
Agitation Speed	400	rpm

3.3 Kinetic Study of Acid-Catalyzed Esterification of Malic Acid with Methanol

The acid-catalyzed esterification reaction of MA and MeOH was investigated in a batch kinetic system. The substrate molar ratio used for all reactions in this part of the study was 1:19. The concentration of Sulfuric acid used was 0.1 M and 1 M when stated and the reaction durations span from (0.5-2) hour(s). The temperature range was constrained to (40-70) °C with a 10°C difference between each mark. The agitation speed was maintained at 400 rpm and the previously described experimental set-up and procedure were adhered to.

These operating conditions were followed judiciously to accommodate for lower conversions which was crucial to the kinetic study. A kinetic model was constructed and the kinetic data extracted by the HPLC was fitted into this model to test for fitness. From the results, the reaction rate constant(s), activation energies and pre-exponential factors for the first esterification step to produce the monoester and those in the second phase to produce the diester were calculated and printed in this study. The effect of different reaction factors was also analyzed. A table illustrating the selected conditions for the kinetic table is presented in (Table 5).

Table 5 Conditions used for Kinetic Study

Parameter	Kinetic condition	Unit
Catalyst	0.1-1	M
Substrate Molar Ratio	(1:9.5-19-38)	-
Temperature	40-70	°C
Time	0.5-2	hour
Agitation Speed	400	rpm

3.3.1 Effect of Temperature

The (Figures 5 and 6) represent the effect of temperature on conversion and yield(s) of the MA, MMM and DMM respectively as acquired from the investigation which was carried out in differing reaction catalyst concentrations.

It is observed that the pseudo first-order rate constants under both reaction conditions in the initial esterification stage increased with increasing temperature. This was theorized to be as a result of the augmentation of the inter-molecular collisions between reactant particles as a consequence of an influx of kinetic energy through the temperature change. This also indicated a temperature-dependence on the pre-exponential factor -although subtle- seeing that there were palpably more collisions leading to reactions per second as the temperature was increased in the reaction scheme. Additionally, there were significantly more conversions detected for both sparingly-catalyzed reactions as the temperature gradient rose from high to low which then led to the reactions approaching equilibrium. For instance, in the same reaction duration of 2 hours and 1 M of the H_2SO_4 , there was a (97%) conversion of MA at 70°C compared to a (76.2%) conversion at 40°C. In the same vein, there was a (73.2%) yield of the DMM contrasted with a (56.4%) yield when the temperatures were set at 70°C and 40°C and 1 M of H_2SO_4 was used in the operating condition. The synopsis of this being, an increase in temperature more often than not, equated to an increase in the desired product but also provoked the reaction towards equilibrium faster than it would have been without the influx of temperature. At 70°C, the

equilibrium time was reached at 2 hours and \sim (97%) conversion. At that time, the yield as we determined was \sim (73%). At the lowest temperature under investigation however, the equilibrium was not reached till beyond 3.5 hours showing the very strong influence of temperature on the reaction reaching equilibrium.

The same trend was undeniably observed in the formation of the intermediate across the temperature profile. An increase in temperature coincided with an increase in the MMM formed regardless of the batch-reaction duration adhered to. This observation was more evident at lower catalyzed reactions – concentration wise – than it was in the condition of higher catalyst concentration. Nevertheless, the overarching influence of temperature was fully imprinted in the extracted data and kinetic study.

However, the second step of the esterification process was non-Arrheniuc in its behavior. The second pseudo first order rate constant decreased with increasing temperature which is contrary to Arrhenius' hypothesis and was indicative of a negative activation energy estimated at ($-3.954 \text{ KJmol}^{-1}$) for the 1 M Sulfuric acid reaction and ($-25.48 \text{ KJmol}^{-1}$) for the 0.1 M sulfurized esterification reaction. This phenomenon, although almost counter-intuitive, was not unusual as many papers have cited. The rationale given has vacillated from the understanding that negative activation energies are sometimes artifacts of the experimental techniques employed in the kinetic analysis;²² that reactions which epitomize this occurrence also possess verifiable features such as the presence of 2 or more reaction paths in which the first step is the formation of a loosely bound or unstable complex/intermediate²²⁻²⁹ and that the elementary steps exhibiting this peculiar occurrence are usually “barrier-less” in operation.²³ Consequently, the elementary steps are assumed to transpire in scenarios where the molecules are conceptualized to be in a potential Well in which the other reacting molecules will be less probable to collide with those within that

Well as the temperature increases in the system.²³ In other words, if the positive activation energy indicates the minimum energy barrier a system needs to overcome for a reaction to occur, then a negative activation energy will imply the amount of energy the system will need to receive to forestall the reaction or deter it from occurring. Therefore, the kinetic data extracted from this study showed that the intermediate (monomethyl ester) was inclined towards reversing to the reactant or endothermic side of the reaction and an increase in temperature was boosting this reversion while the contrary was precluding it. These dynamics resulted in our observance of the gradual decrease in the rate constant as the temperature increased and the concomitant negative activation energy that was experimentally calculated.

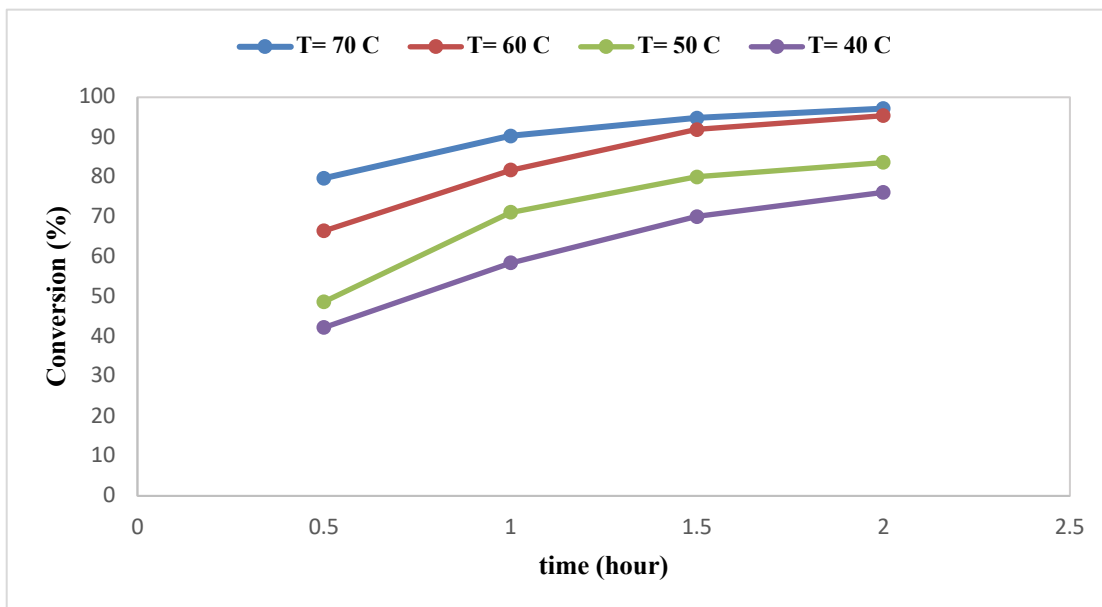


Figure 5 Influence of Temperature on Conversion of Malic Acid at 1% Volume of 1 M Sulfuric Acid

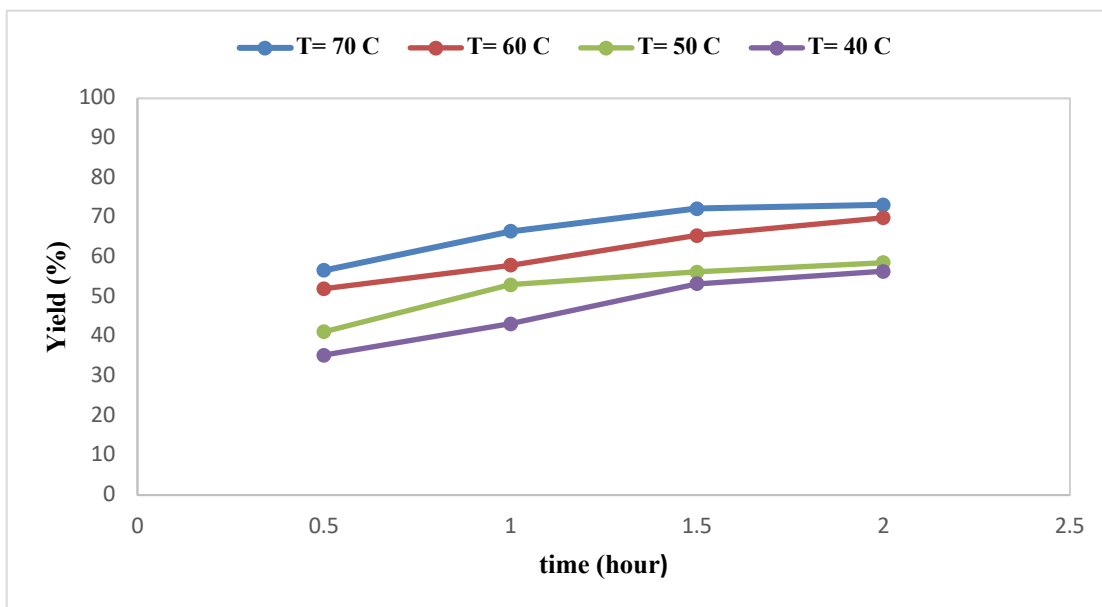


Figure 6 Influence of Temperature on the Yield of Dimethyl Malate at 1% Volume Of 1 M Sulfuric Acid

3.3.2 Effect of Catalyst Concentration

The (Figure 7) depicts the relationship between a catalyzed/non-catalyzed reaction and the conversion of the MA at a fixed reaction temperature. From this figure, we can analyze that the presence of the homogeneous catalyst aided the establishment of the reaction's equilibrium more swiftly than it occurred in its absence. This trend was evident even as the concentration profile of the Sulfuric acid progressed from being non-existent i.e. having no catalyst, when the concentration was at 0.1 M, to finally when it was at 1 molarity.

The estimated activation energies were also investigated in the different concentration regimens adduced in the study. The close-proximity in the value(s) of the activation energies at the opening esterification stage suggested that the catalyst concentration played no role in the energy barrier of the reaction. This was expected since our understanding of catalysts inform us to the reality that they customarily only affect the reaction rates without necessarily impairing the

activation energy at certain operating conditions. In contrast to this however, the pre-exponential factor and consequently, the entropy of the activation, could be altered by the presence or absence of the catalyst. In the study, the pre-exponential factor of the catalyzed reaction at 0.1 M to 1 M improved by a factor of roughly 1.7. This insinuated that the kinetics at this phase, appeared to be faster at a higher concentration of the catalyst and became slower up to when no catalyst was used.

Moreso, the rate constant - which encompasses the frequency factor - showed that catalytic regions influenced the magnitude of the rate constant which indirectly implied that the rate itself was affected significantly. At a constant temperature, it was observed that the rate constants for the reactions between the investigated catalyst concentrations showed the lower concentration to be approximately 3.4 times less than the experiments done at the higher concentration. This inferred that the concentration of the catalyst appreciably affected the rate constant similar to the way temperature did by increasing it in favor of the MMM synthesis. However, the concentration of the catalyst was crucial to the formation of the desired product-DMM as was also detected. Lower concentrations of the catalyst at varying temperatures under examination did show lower yields of the diester when juxtaposed with those obtained in higher concentration milieus (See Figure 8).

In like manner, the study also evinced the effect of the absence or presence of the catalyst on the conversion of the reactant species. Isolating a 30-minute reaction run and scrutinizing it, we notice the flagrant nature of this catalytic effect. In a 70°C-batch system, the conversion of the MA was at (21.7%) in a non-catalytic system, (33.1%) when 0.1 molarity of the Sulfuric acid was charged and (79.7%) when the Sulfuric acid was 10 times more in terms of its molar potency. The approach to equilibrium was also as observed in the effect of temperature, in that

stronger catalyst concentrations also caused the overall reaction to reach equilibrium faster than in lower catalyst regimes. For example, in the reaction conditions being discussed, equilibrium was reached at 2 hours when 1 M concentration of the Sulfuric acid was used as the reaction catalyst. This equilibrium time was then increased to beyond 3 hours when the reaction was catalyzed by 0.1 M Sulfuric acid and also to further-beyond 3 hours when no catalyst was used.

From a side-reactions point of view, the presence of catalysts did facilitate more undesirable by-products. Trace amounts of the dimethyl fumarate were observed especially in shorter reaction durations (0.5-1.5) hour when 1 M of the acid catalyst was used but was insubstantial when 0.1 M Sulfuric acid catalyzed the system. DMF was also quantifiably trifling when the catalyst was nonexistent in the reaction. This finding did not negate or challenge any pre-established knowledge of the catalytic effect of mineral acids in esterification reactions as one of the more accepted drawbacks is the formation of undesirable side reactions due to the dehydrating nature of the Sulfuric acid which could protonate the Methanol instead of the Malic acid or worse still, react with the formed ester itself thereby dehydrating it into side-products.

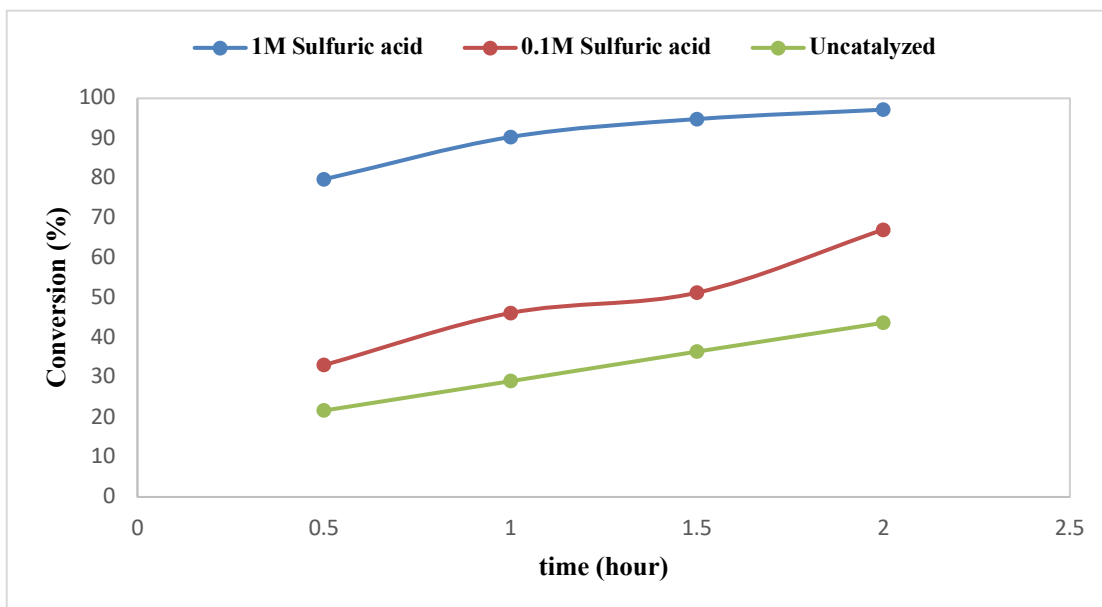


Figure 7 A Comparison of the Conversion of the Malic Acid versus the Time for Catalyzed and Uncatalyzed Reactions Under Consideration

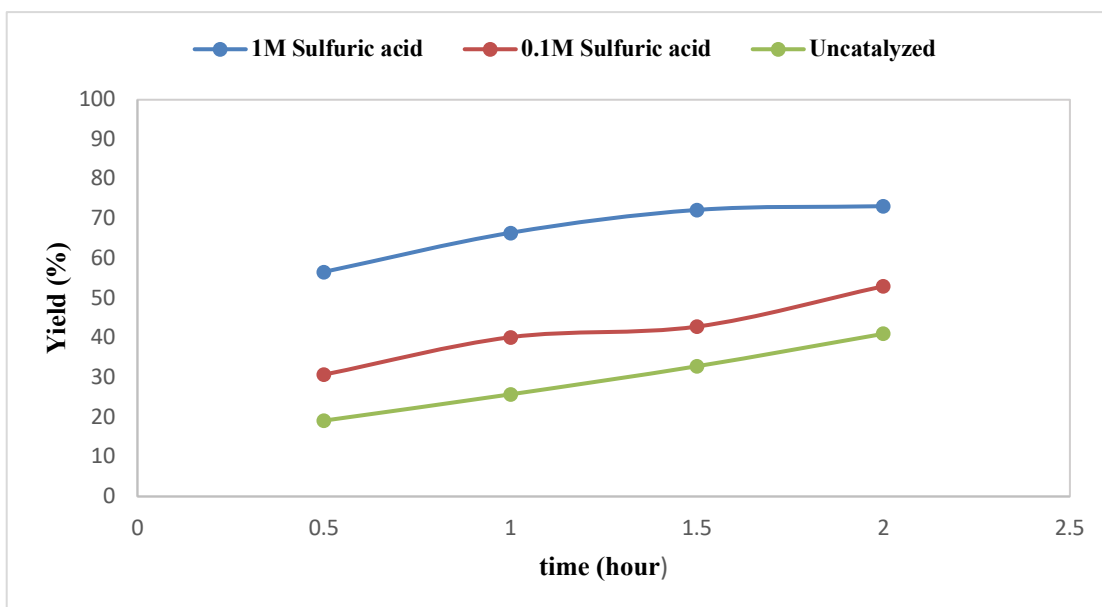


Figure 8 A Chart of the Yield of the Dimethyl Malate versus the Reaction Duration Comparing the Effect of Catalyzed and Uncatalyzed Reactions

3.3.3 Effect of the Acid/Alcohol Mole Ratio

The role of the substrate molar ratio was investigated in the study in non-catalytic environments following the redundancy of reproducing the same experiments in a catalyzed milieu having investigated the effect of catalyst concentration on the reaction and formation of the carboxylate of Malic acid. A 70°C-isothermal batch system as previously discussed was preserved, but in this case, a reactant molar ratio of 1:38 and 1:9.5 were employed and juxtaposed with the same system where 1:19 of the substrate molar ratio was originally used. In this scheme, it was pleonastic to investigate catalyzed regions since they were already investigated in the previous sub-chapter. It was apparent from that study that the catalyzed regions not only dictated the terms of equilibration more quickly depending on their molar potency, but that they also influenced higher conversions and yields of the reactant species and desired product.

However, the uncatalyzed region was studied based on the operating conditions described afore and (Figure 9) demonstrates the effect of the molar ratio of reactants with respect to the conversion of the MA progressively. It is seen that the conversion of the MA is most-significantly represented in lower reactant molar ratios than higher. For instance, in the regime being studied and at 0.5 hour, the conversion of MA at (1:9.5) is 29.75% which then diminishes to 21.68% at (1:19) and 17.14% at (1:38).

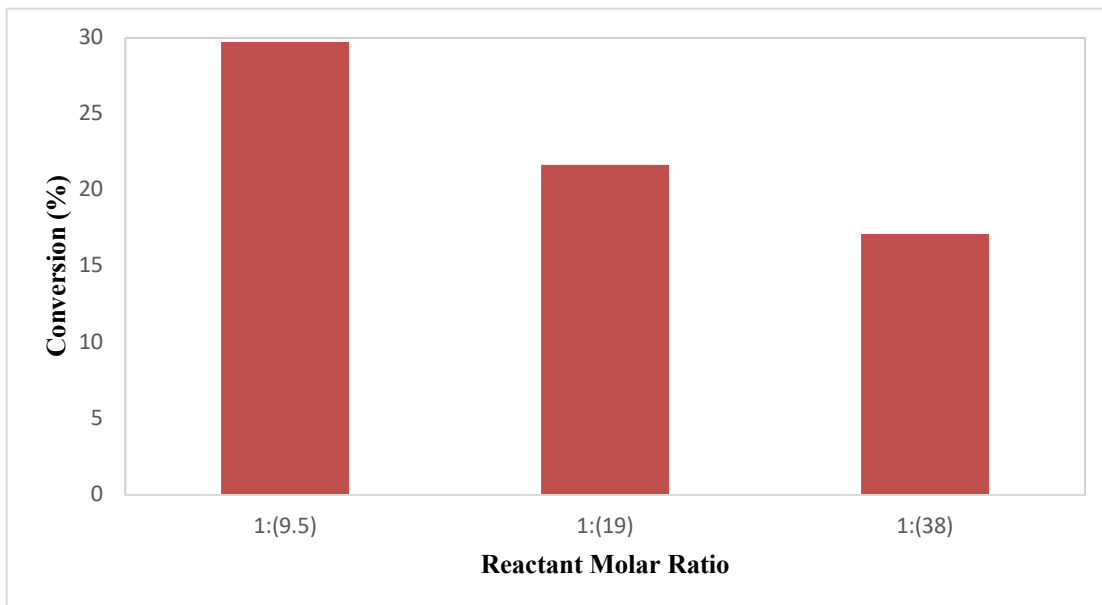


Figure 9 A Chart Depicting the Conversion of MA to the Reactant Molar Ratio for the Reaction Operated at 70°C, 0.5 h for an Uncatalyzed System

The rationale for this is related to the comparative difference in dissociation constants of MA in a solution of MeOH. The presence of the two alkanolic moieties each representing their own pKa values (3.51 and 5.03) compared to (14.5 for MeOH) played a more crucial role than the catalyzed environment had allowed us to understand. This goes in line with our knowledge of how particles dissociate in a solution when the volume of the solution increases. It is conventional that an excess of the solvent will instigate more solvation of the reactant solute species and direct it to disintegrate in the solution which will ultimately lead to lower conversions of the active sites. This will invariably project lower yields of the DMM due to this solvent excess. In our study (Figure 10), in all 3 cases, around (25%, 19% and 16%) of the DMM were produced respectively. As expected, the lowest fractionally-trivial value was at 1:38 and it is lucid that even in micro and macro scales, the molar ratio of the acid and alcohol was still influential to the whole chemical kinetic framework.

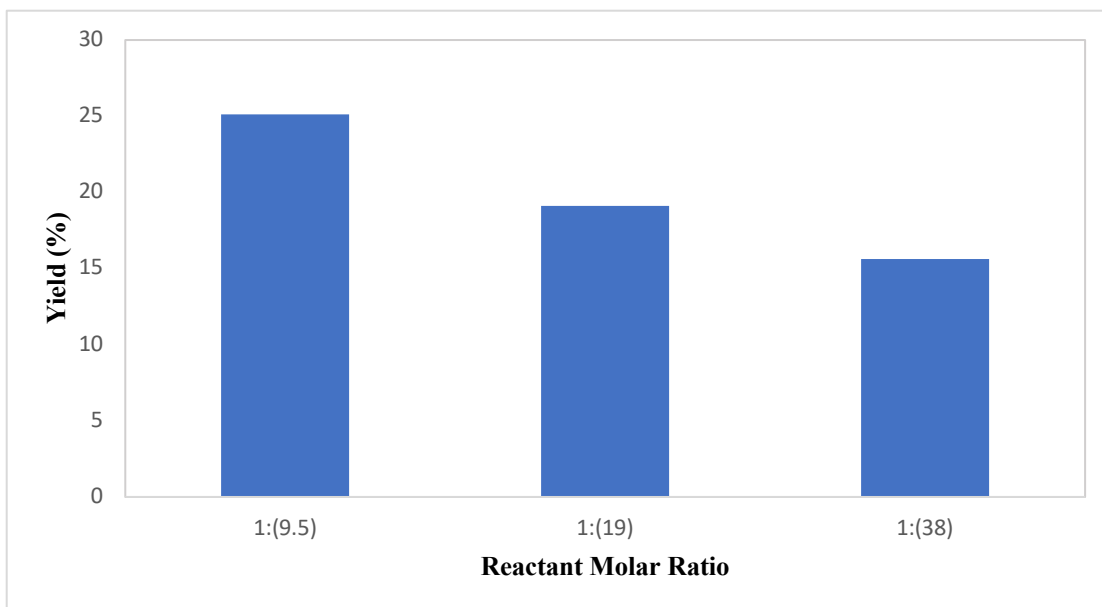


Figure 10 A Chart Displaying the Yield of DMM with the Reactant Molar Ratio for an Uncatalyzed System Operating at 70°C and 0.5 h

In contrast to the DMM, the substrate molar ratio affected the synthesis of the intermediate in a different fashion as it pertained to whether the system was uncatalyzed. For the uncatalyzed system, the trend followed the same consistency as there was more yield of the MMM at the smallest acid/solvent ratio than there was at the highest or middling substrate ratios.

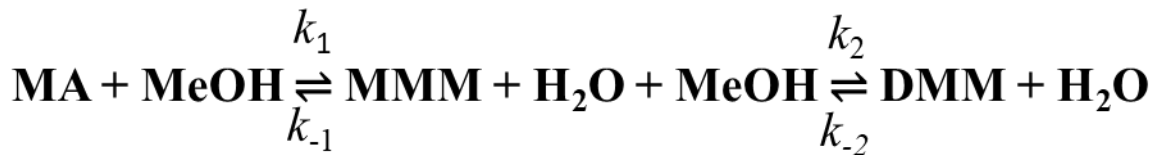
The rationale behind this was not fully understood except that kinetically, a solvent could react with a desired product thereby protecting it against further production and this phenomenon was more prone when the solvent was in great excess (i.e. when the acid/molar ratio was very high) which was the case for (1:38).³⁰

3.4 Kinetic Model

The following assumptions were made in arriving at the model used in this investigation:

- I. Although the esterification reaction is reversible, the rate constant for the hydrolysis reaction(s) is/are assumed negligible since the backward reaction is very slow and previous extracted data displayed (100%) conversion of the MA.
- II. In lieu of the hydrolysis reaction, the second-rate constant represents the second esterification reaction involving the esterification of the monomethyl ester by the excess Methanol.
- III. The Methanol used was in excess so its concentration was trivial or constant throughout the whole process. Experiments confirmed it to be zero-order in Methanol.
- IV. The order of the concentration of the MA was to be the same as the order of the formation of MMM.
- V. The reaction rate was calculated from the rate of disappearance of the reactant (MA) which was assumed to be similar to the rate of formation of the intermediate which in itself was related to the product (DMM) through its disappearance. This rate model was explicitly concentration-based.

Prior to postulations, we can propose that the overall stoichiometric reaction mechanism for this Fischer esterification involving Malic acid and Methanol which should have been reversible, and thus epitomized as:



Scheme 3 Typical Chemical Reaction Equation for MA Reversible Esterification by MeOH to form DMM & H₂O

Due to postulation (I), (Scheme 3) can then be illustrated as:



Scheme 4 Reconfigured Chemical Reaction Equation for MA Esterification by MeOH to form DMM & H₂O taking the Model Assumptions into Consideration

Which forms the basis upon which the concentration-based kinetic model was proven and built.

The rate of disappearance of MA:

$$-r_{MA} = k_1 C_{MA}^a C_{MeOH}^b - k_2 C_{MMM}^x C_W^y \quad (4)$$

Where r_{MA} represents the rate of Malic acid disappearance, C_{MA} represents concentration of Malic acid, C_{MeOH} , concentration of Methanol, C_{MMM} , concentration of Monomethyl Malate and C_W , concentration of water (which was simply conceptual knowing that esterification reactions release water).

The orders of the concentration of the reactant and product species can then be experimentally determined to simplify the model.

3.4.1 Order of the Concentration of the Reactant Species

To effectively propose a reliable kinetic model, it was necessary to experimentally determine the order of the active reactant species which will play conspicuous roles in the kinetic

model. The Integral method of determining the reaction order is utilized here because of its propensity to readily predict the reaction orders by smoothening the data points and minimizing the possible errors of the experimentally-derived data sets.

The integral method commences by assuming a power law for the rate of disappearance of the MA with relation to the formation of the MMM. The rate law should be thus:

$$-r_{MA} = k_1 C_{MA}^a C_{MeOH}^b - k_{-1} C_{MMM}^x C_W^y \quad (5)$$

This was proposed based on (Scheme 3) as the rate law depicting the disappearance of MA with respect to the formation of MMM. Since the excess technique of the integral method is being used, the order of the concentration of the solvent becomes 0 (i.e. $b \approx 0$) and the rate constant of the backward step is assumed negligible with the rate law then reducing to:

$$-r_{MA} = k_1 C_{MA}^a \quad (6)$$

To solve this reduced rate law by method of integration, the order, a , has to be guessed and then integrally-solved to find a rate equation of the form of a linear curve $y = mx + c$ so that inputting values from experiments can verify if the assumed or guessed order is right. That is, the order becomes confirmed when the curve generated is a straight line with very good regression value.

Guessing a as 1, the rate of disappearance of MA becomes:

$$-r_{MA} = k_1 C_{MA} \quad (7)$$

$$\frac{-dC_{MA}}{dt} = k_1 C_{MA} \quad (8)$$

Which by separation and integration resolves to:

$$\int_{C_{MA0}}^{C_{MA}} \frac{-dC_{MA}}{C_{MA}} = \int_0^t k_1 dt \quad (9)$$

$$\ln[C_{MA}]_{C_{MA0}}^{C_{MA}} = -k_1 t \quad (10)$$

And becomes:

$$\ln C_{MA} = \ln C_{MA}^0 - kt \quad (11)$$

That is similar to $y = mx + c$ where y is the natural log of the concentration of MA and x is the time (t) of reaction in seconds. The slope will represent the pseudo first-order rate constant while the intercept will represent the natural log of the concentration of MA at initial time. Using experimental data collected at 70°C and 1 M of Sulfuric acid with the time in seconds, (Figures 11 & 12) are obtained and used to ascertain that the guess was in order.

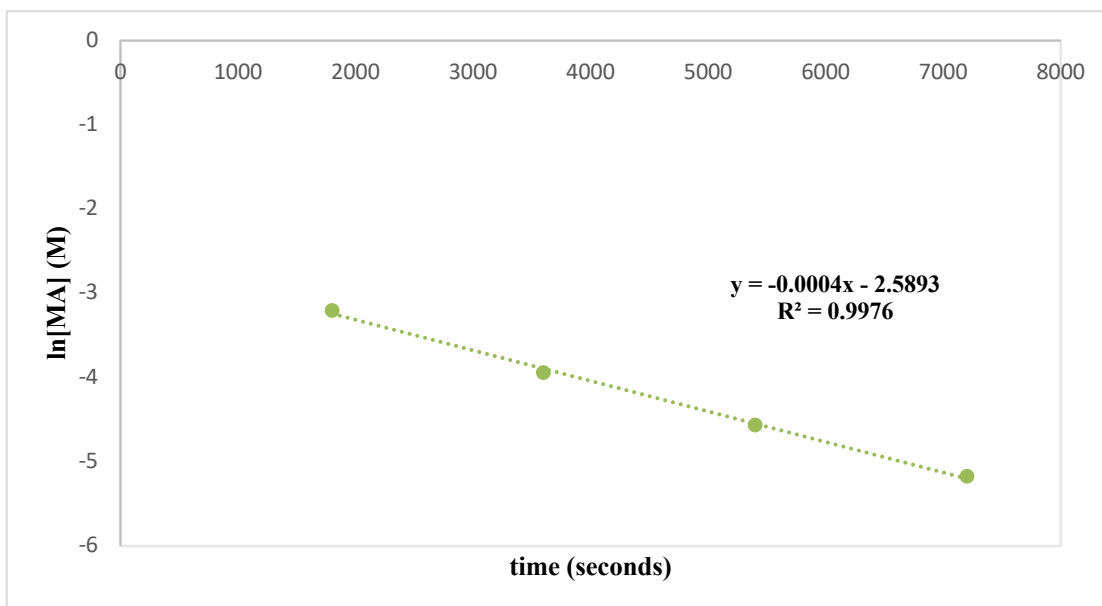


Figure 11 Plot of Natural Log of MA to Time in Seconds to Estimate the Reaction Order

Alternately, the order can also be confirmed if the plot of the concentration of MA is plotted against time and a declining curve is obtained. (Figure 12) illustrates this:

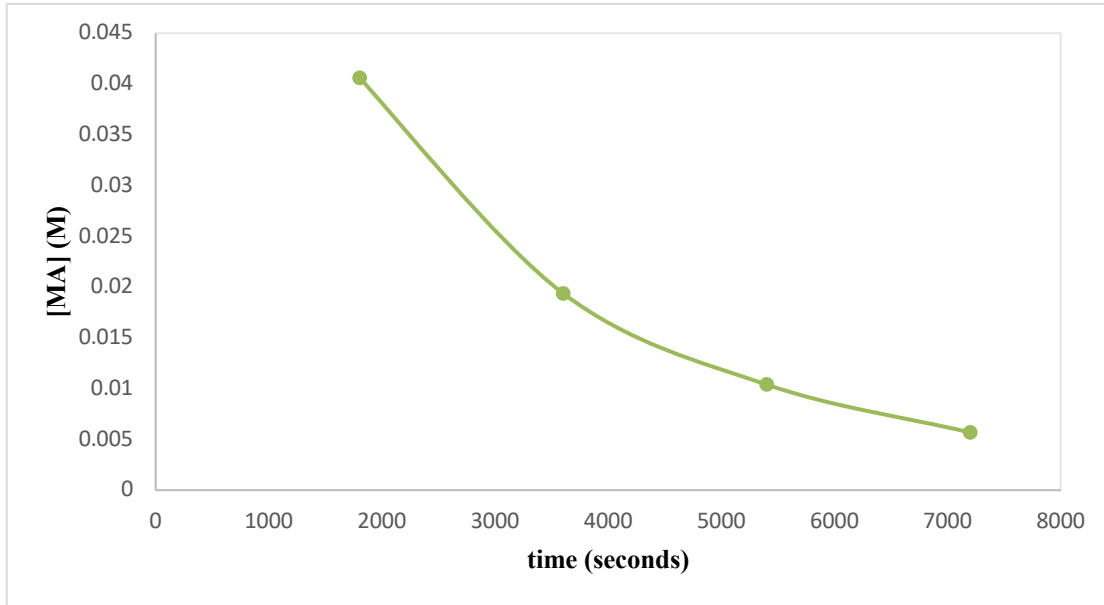


Figure 12 Declining Curve of MA Concentration against Time

3.4.2 Determination of Pseudo First-order Rate Constant k_1

Since concentration of MeOH was assumed and also experimentally determined to be zero-order, MA first-order, DMM and W unknown, and consequently, the hydrolysis-induced rate constant is deemed negligible, the rate equation for MA disappearance reduces to:

$$-r_{MA} = k_1 C_{MA} \quad (12)$$

$$\frac{-dC_{MA}}{dt} = k_1 C_{MA} \quad (13)$$

Which by separation and integration leads to:

$$\int_{C_{MA0}}^{C_{MA}} \frac{-dC_{MA}}{C_{MA}} = \int_0^t k_1 dt \quad (14)$$

$$\ln[C_{MA}]_{C_{MA0}}^{C_{MA}} = -k_1 t \quad (15)$$

Which finally resolves to:

$$\ln \left[\frac{C_{MA}}{C_{MA0}} \right] = -k_1 t \quad (16)$$

When data points extracted from the batch experiments are fitted into $\ln \left[\frac{C_{MA}}{C_{MA0}} \right]$ in (Equation 17) as the ordinate or Y-axis, and time (t) for each experiment corresponding with the concentrations, as the abscissa or X-axis, a linear curve is derived whose line passes through the origin and the slope of the graph, will represent the pseudo-first order rate constant k_1 .

3.4.3 Determination of Pseudo First-order Second Rate Constant k_2

The second rate constant k_2 becomes the pseudo first-order rate constant for the second esterification phase i.e. the esterification of the monoester to generate the diester. The rate law demonstrating this is represented as (Equation 17) where the order of the monoester is assumed to be unity:

$$r_{MMM} = k_1 C_{MA} - k_2 C_{MMM} \quad (17)$$

$$\frac{dC_{MMM}}{dt} + k_2 C_{MMM} - k_1 C_{MA} = 0 \quad (18)$$

Which has the form of an ordinary differential equation (ODE) which can be solved by method of integrating factor (I.F), where C_{MA} becomes:

$$C_{MA} = C_{MAo} e^{-k_1 t} \quad (19)$$

Substituting (Equation 19) into (Equation 18) the ODE then becomes (Equation 20) which takes the form needed to be solved by I.F method.

$$\frac{dC_{MMM}}{dt} + k_2 C_{MMM} = k_1 C_{MAo} e^{-k_1 t} \quad (20)$$

Compared to the linear first order differential equation of the Bernoulli form where $P(t)$ and $g(t)$ are continuous functions:

$$\frac{dy}{dt} + P(t)y = g(t) \quad (21)$$

We can see that on comparing both equations, $y = C_{MMM}$; $P(t) = k_2$ and $g(t) = k_1 C_{MAo} e^{-k_1 t}$ and r_{MMM} is the rate of disappearance of the monoester. Therefore,

$$I.F = \exp \left[\int P(t) dt \right] \quad (22)$$

and,

$$\int d(I.F(y)) = \int (I.F(g(t)dt)) \quad (23)$$

Using this idea in (Equation 24) to evaluate (Equation 21), we have:

$$\int d(C_{MMM} e^{k_2 t}) = \int k_1 C_{MAo} e^{(k_2 - k_1)t} dt \quad (24)$$

Which can then be resolved to:

$$C_{MMM} = \frac{k_1 C_{MA0}}{k_2 - k_1} (e^{-k_1 t} - e^{-k_2 t}) \quad (25)$$

Exercising the data extracted for the concentration of MMM (C_{MMM}) formed at time (t), concentration of MA charged into the reaction initially, value for k_1 for each temperature as estimated from the (Equation 16), and the (Equation 25), values for the second rate constant k_2 can also be estimated and used in an Arrhenius plot to calculate the value(s) for the activation energies and frequency factor(s) for both reaction conditions in the study. Due to the complexities involved in extracting k_2 from (Equation 25) through regression analysis, computational analysis was introduced via MATLAB and the values for k_2 were straightforwardly-obtained.

Interestingly, the data points were reasonably good fits into the first model at each temperature with a constant volume and concentration of the catalyst, and the rate constant k_1 , for each was determined from the plot (Figure 13). These rate constant(s) were used subsequently in the Arrhenius plot to define the activation energies and pre-exponential factors of the chemical reaction. Similarly, the data fit very adequately into the second model for the kinetic study carried out in higher concentration of the catalyst than it did in the experiments where a lower concentration of the catalyst was used.

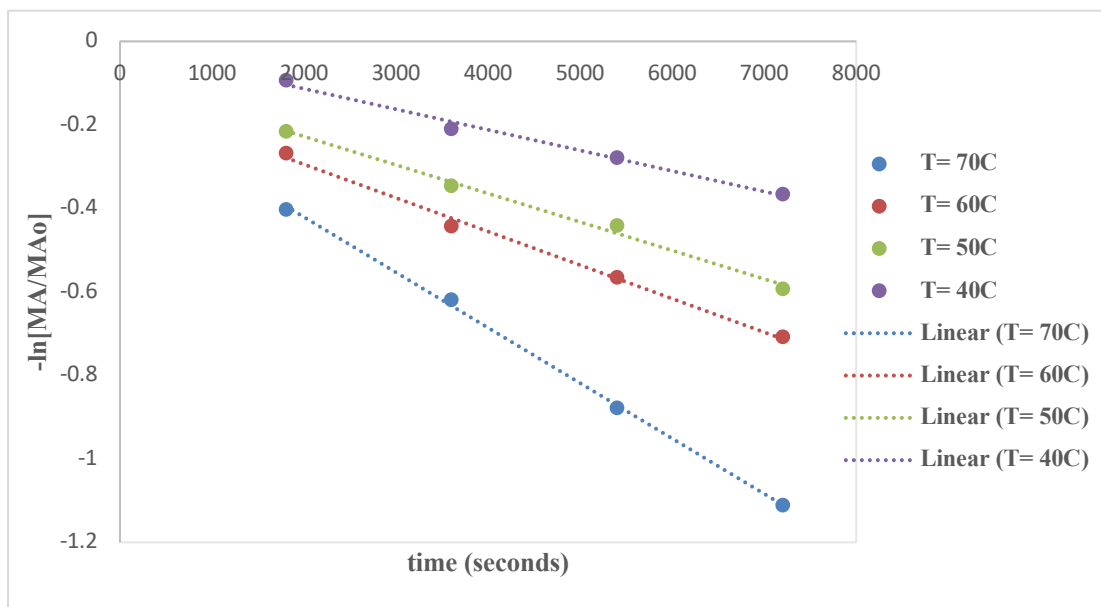


Figure 13 Kinetic Plot used to Estimate the Pseudo First-Order Rate Constant k_1 for Varying Reaction Temperatures and (1%) 0.1 M Sulfuric Acid

In this research, two different concentrations of the Sulfuric acid used were 0.1 M and 1 M respectively. The reaction temperatures were staggered from (40-70) °C whilst each reaction was preserved for 30 minutes up to 2 hours with the natural log of each rate constant calculated was plotted against the inverse of each temperature in Kelvin-scale corresponding values. The gradient of this plot was determined to be the ratio of the activation energy (E_a) to the universal gas constant (R) and the intercept symbolized the natural log of the frequency factor. A justification for this in both discretized steps of the reaction is demonstrated in (Equations 26 & 27) thus:

$$\ln k_1 = \ln A - \frac{E_{a1}}{R} \left(\frac{1}{T} \right) \quad (26)$$

$$\ln k_2 = \ln A - \frac{E_{a2}}{R} \left(\frac{1}{T} \right) \quad (27)$$

The value for the activation energy E_a and pre-exponential factor A for catalyst concentration of the chemical reaction kinetics were then tabulated in (Table 6) even as the Arrhenius plots that were deployed in their determination are presented in (Figures 14 & 15) and were used to explain how each kinetic parameter had an effect on the chemical kinetics of the reaction.

From the Arrhenius plot for the second pseudo first order rate constant(s) obtained for each temperature under experimentation, it is apparent that the kinetic model proposed was an almost-excellent fit to the data procured from the 1 M Sulfuric acid-catalyzed reaction and was recognizably better in comparison with those acquired from the 0.1 M Sulfuric acid catalyzed reaction. The reason tendered for this sizeable disparity in model-fitness was attributed to the presence of water in the Sulfuric acid of lower concentration which is known to strongly inhibit catalytic activity of the acid.⁴⁰ In fact, one paper suggested that this catalytic activity of the Sulfuric acid diminished by (90%) as the amount of water increased, and this deactivating effect of the water exhibited itself by altering the activation energy and the pre-exponential factor.⁴⁰ This dwindled influence of the catalytic protons extant in the Sulfuric acid is attributed to its tendency to solvate preferentially to the water instead of the Methanol during the esterification process.⁴⁰

Table 6 Activation Energies and Frequency Factors for both Catalyzed Systems in the Study

	Sulfuric acid (1 M)	Sulfuric acid (0.1 M)	Unit
E_{a1}	25.98	27.87	KJmol^{-1}
E_{a2}	-3.954	-25.48	KJmol^{-1}
A1	3.599	2.148	S^{-1}
A2	2.715×10^{-5}	5.367×10^{-9}	S^{-1}

Table 7 First and Second Reaction Rate Constants for 1% Volume 1 M H₂SO₄ Catalyzed Reactions

Temperature (°C)	k_1 (S ⁻¹)	k_2 (S ⁻¹)
70	3.624×10^{-4}	1.027×10^{-4}
60	3.607×10^{-4}	1.054×10^{-4}
50	2.080×10^{-4}	1.118×10^{-4}
40	1.656×10^{-4}	1.167×10^{-4}

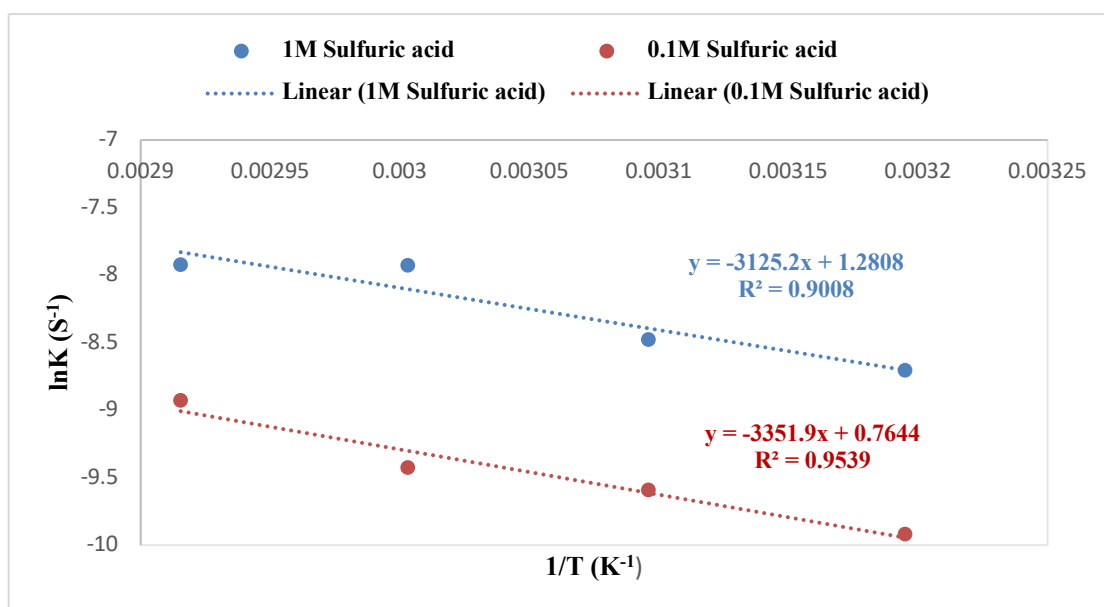


Figure 14 Relationship between Temperature and Pseudo First-order Rate Constant k_1 for 1 M and 0.1 M Sulfuric Acid Regimes

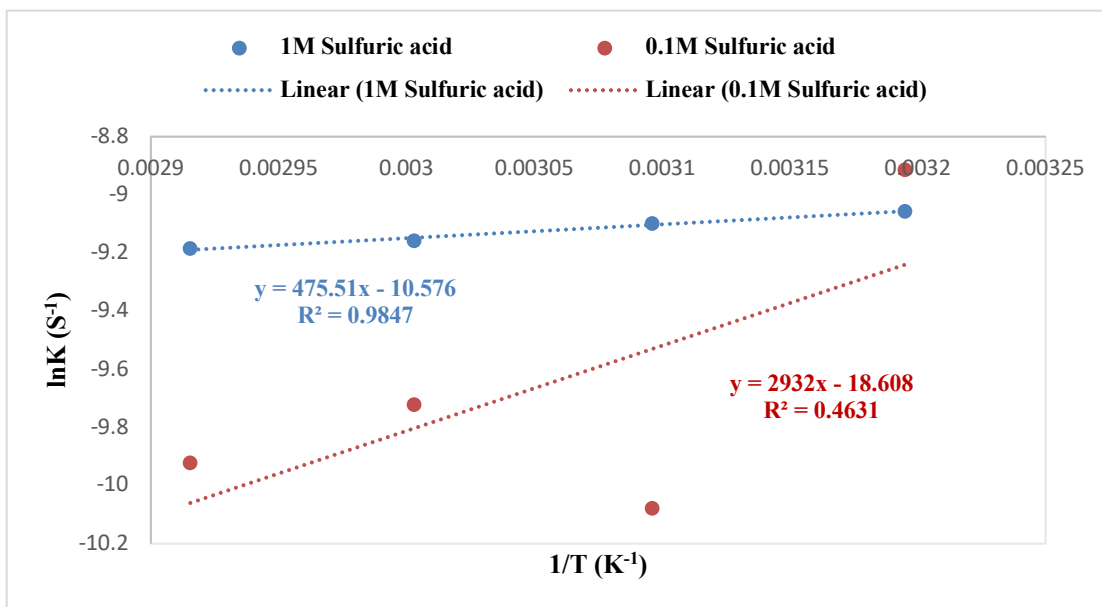


Figure 15 Relationship between Temperature and Pseudo First-order Second Rate Constant k_2 for 1 M and 0.1 M Sulfuric Acid Regimes

3.5 Rationalization for Failure of Proposed Model

Regardless of the justifications provided by all the cited papers on the estimated negative activation energies as well as the good regression values obtained from the Arrhenius plots constructed based on the equations derived from the overall model, it was ultimately apparent that the model failed. The reasons put forward for this are exhaustive but the major pointers are thus:

- I. The unstable nature of the monoester was not significantly considered in proposing the model: It was suspected that the side reactions observed could have been consequences of the dehydration or hydrolysis of the formed monoester with either Sulfuric acid or produced water respectively. As the data explicated, an increase in reaction temperature was suspectedly decomposing the MMM even as it was increasing the yield of the DMM simultaneously. The resultant of this implied that the MMM was predominantly reverting

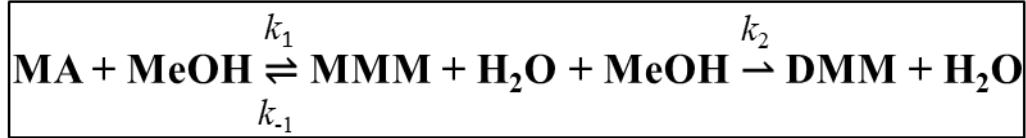
to the backward reaction at higher temperatures and this unpredictability, unfortunately, was not accounted for in the earlier proposed model.

- II. As a result of (I) it was also apparent that k_{-1} representing the rate constant of the backward reaction was more impactful than the forward rate constant k_2 in the formation of the diester in reactions conducted at higher temperatures. In coming to this reflection, we observed the decrease in k_2 with an increase in temperature which is evidently contrary to our understanding of rate constants and exposed the flaw in the second rate-law arising from the proposed model.

To correct the issues that were created by the oversights in the previously proposed model, the following were put forward to represent the reaction mechanism for the di-esterification of MA with MeOH. To come to this overall reaction scheme, some new assumptions were still projected to predict our present understanding of the overall scheme.

- a. DMM produced is more readily non-hydrolysable and therefore stable in water following hydrolysis post-esterification. The reversible rate constant k_{-2} can therefore still be assumed negligible or non-trivial. However, the reverse rate constant for the first esterification stage k_{-1} is essentially non-trivial and must be incorporated into the reaction scheme.
- b. As a consequence of the foregoing, the concentration of the water formed should be included into the power law and the order of the water determined for the first esterification stage. This is to accommodate the water's potential to induce the MMM in a different kinetic direction than the previous model had made room for.
- c. The concentration of the MeOH can still be considered as trivial and its order assumed same for model simplification.

Following this, the overall reaction equation for the formation of DMM via esterification with MA is predicted thus:



Scheme 5 Newly Proposed Overall Reaction Scheme for Esterification of MA by MeOH to form DMM

Taking the new reaction scheme in (Scheme 5) into cognizance, the rate law for the disappearance for MA becomes:

$$-r_{MA} = k_1 C_{MA}^y - k_{-1} C_{MMM}^a C_W^b \quad (28)$$

While the rate of formation of MMM is:

$$r_{MMM} = k_1 C_{MA}^y - (k_{-1} C_W^b + k_2) C_{MMM}^a \quad (29)$$

And the rate of formation of DMM used simultaneously with (Equation 29) to ferret out k_{-1} and k_2 by first solving C_{MMM} is:

$$r_{DMM} = k_2 C_{MMM}^a \quad (30)$$

It is expected, that by employing all 3 rate laws in the derivation for the model proposed for the formation of the DMM, a reasonable and industrially-scalable model capable of predicting the shifts and erratic nature of the kinetic data extracted from the experiments can be proposed.

CHAPTER 4 CONCLUSIONS

The kinetics of the esterification of Malic acid by Methanol in the presence of a homogeneous acid-catalyst carried out in a batch reactor, was investigated in this study. To ensure the comprehensiveness of the investigation, various operating conditions were proffered and analogized with those considered *ab initio*. Some of the various conditions included the use of a heterogeneous acid catalyst, the non-use of catalysts in its entirety, a variation of temperature regimes, and an adjustment of the reactant molar ratios.

The first aim of the project was to efficiently synthesize the diester: to optimize the production of the desired product – Dimethyl Malate – by tweaking the extant parameters or operating conditions of the given constituents obtained from previous synthesis studies to actualize milder settings via which the DMM can not only be synthesized and compared to those extracted from such literature, but upon which kinetic studies can be carried out. The second objective, a kinetic study, was to attempt to elucidate the kinetics behind this reaction and to offer a justification for the results that were obtained in the synthesis study.

It was garnered that, by using 1 M Sulfuric acid (6% by volume), a substrate molar ratio of (1:19), reaction temperature of 100°C and a 2.5-hour reaction duration, over (87%) of the diester was produced even as over (99%) of the Malic acid was converted. This was a far-cry from the operating conditions that were used in the previous study and showed that those conditions were not only less-efficient, but an overkill with respect to the formation of the Malic acid dimethyl ester.

Furthermore, to explicate these findings through a kinetic study, the operating conditions used above were dialed-back to lower acid concentrations of lower volumes (1% volume of 1 M

and 0.1 M Sulfuric acid) to simulate an environment of lower Malic acid conversions which were pertinent to the kinetic study.

Subsequently, the effect of temperature, acid/solvent ratio and catalyst concentration were investigated using data extracted from the experiments conducted by the conditions described afore.

The temperature and time range for the experiments used in the kinetic study were (40-70) °C and (0.5-2) hours respectively. Similarly, the acid/Methanol ratios were (1:9.5, 1:19 and 1:38). From the study, it was apparent that temperature had an effect on the overall reaction rate. It demonstrated this effect by increasing the rate constant of the first esterification stage favoring the mono ester formation and alluding to its endothermicity. It also provoked the reaction closer to equilibrium faster at higher temperatures. This provocation led to the estimation of the kinetic parameters like activation energy and pre-exponential factor. The activation energies estimated for both catalyzed conditions at this stage were fairly similar and roughly (27 ± 0.7) KJmol⁻¹ in value. The temperature effect in the second esterification stage however was puzzling. The rate constant increased as the temperature decreased leading to a negative activation energy. This suggested that whilst the formation of the monomethyl ester was endothermic, the formation of the dimethyl ester showed exothermic tendencies that may need to be further investigated. Nevertheless, this uncanny relationship between temperature and the second esterification stage implied that the intermediate (MMM) formed is unstable and requires less temperature to prevent its reversion to the reactant acid. That is, the negative activation energy signified that the di-esterification stage of the process was losing energy being used for activation or better still, that there existed a minimum energy that the system needed to overcome for the reaction to stop occurring in the backward direction.

Likewise, the effect of catalyst concentration was investigated and there is sufficient data to conclude that there was more conversion of the reactant and yield of the desired product at higher catalyst concentrations than when the concentrations were lower. In fact, there were significantly lower conversions and yields when the reaction conditions were devoid of catalyst use. In addition, catalytic effect was also detected to be influential in the valuation of the activation energies and pre-exponential factors. Albeit, not very glaring in the first esterification stage, the strength of the catalyst did show that there was greater conformance to the proposed kinetic model with more activation energy and pre-exponential factor in the second esterification stage for the reactions in higher catalyst concentration than there was in those done with lower catalyst concentration. Finally, the presence of by-products caused by side-reactions was shown to be a fixture of higher catalyst concentrations than lower. For example, a plethora of the kinetic data showed that 1 M Sulfuric acid concentration catalyzed reactions invoked more yield of the dimethyl fumarate which was non-existent in many of the 0.1 M and “zero-catalyst” catalyzed/non-catalyzed systems.

Greater acid/solvent ratios displayed less conversions and yield of the MA and DMM than the lower ratios. It was not exactly unexpected due to the understanding of the fact that an excess solvent could preclude the formation of the desired product and result in lower yields of the product but it also indicated the impact of the dissociation constant of the MA in the solution of MeOH in terms of DMM synthesis. It was glaring that the reaction could proceed without the effect of the Sulfuric acid catalyst due to the difference in pKa values of the MA when compared to the MeOH and this disparity was shown in the uncatalyzed region under which this effect of reactant molar ratio investigations was carried out.

A facile kinetic model was proposed for the esterification reaction under certain assumptions that were made to aid with the simplification of this kinetic model. One of such assumptions led to the equation illustrating the first esterification stage. Additionally, another slightly more complicated equation, derived from a rate law for the formation of MMM was proposed for the second esterification reaction and used to estimate the second esterification reaction rate constant. This model via its concomitant equations was tested for fitness. The first equation was discovered to be a very good fit for the first phase whilst the second equation was near-perfect for the second phase under the higher acid concentrations, although, it failed relatively for the lower acid-concentration system. A reason for this obvious failure was offered in the study.

Lastly, a rationalization for the failure of the model was explained in detail and other assumptions were proffered that should be considered in the proposal of a model that could capture the dynamics involved in the formation of the dimethyl malate in an industrially scalable way.

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