รีดักชันของ 1,3-ไดไฮดรอกซีแอซีโทน

นางสาวศศิพิมพ์ คงสุจริต

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
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REDUCTION OF 1,3-DIHYDROXYACETONE

Miss Sasipim Kongsutjarit

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Thesis Title	REDUCTION OF 1,3-DIHYDROXYACETONE
By	Miss Sasipim Kongsutjarit
Field of Study	Petrochemistry and Polymer Science
Advisor	Associate Professor Amorn Petsom, Ph.D.
Co-Advisor	Assistant Professor Patchanita Thamyongkit, Dr.rer.nat.

Accepted by the Faculty of Science, Chulalongkorn University in Partial Fulfillment of the Requirements for the Master's Degree

S. Hannongbua ..... Dean of the Faculty of Science

(Professor Supot Hannongbua, Dr.rer.nat.)

THESIS COMMITTEE

..... Chairman

(Associate Professor Supawan Tantayanon, Ph.D.)

..... Advisor

(Associate Professor Amorn Petsom, Ph.D.)

Patchanita T. ..... Co-Advisor

(Assistant Professor Patchanita Thamyongkit, Dr.rer.nat)

Warinthorn Chavasiri ..... Examiner

(Assistant Professor Warinthorn Chavasiri, Ph.D.)

Nantanit Wanichacheva ..... External Examiner

(Nantanit Wanichacheva, Ph.D.)

ศศิพิมพ์ คงสุจริต : รีดักชันของ 1,3-ไดไฮดรอกซีแอซีโทน. (REDUCTION OF 1,3-DIHYDROXYACETONE) อ.ที่ปรึกษาวิทยานิพนธ์หลัก : รศ.ดร.อมร เพชรสม, อ.ที่ปรึกษาวิทยานิพนธ์ร่วม : ผศ.ดร.พัชณิตา ธรรมยงค์กิจ, 73 หน้า.

งานวิจัยนี้มีจุดประสงค์ในการศึกษาปฏิกิริยารีดักชันของ1,3-ไดไฮดรอกซีแอซีโทนด้วยปฏิกิริยาโวลฟ์-คิชเนอร์ และเคลมเมนเซน เพื่อทำการเปลี่ยนหมู่คาร์บอนิลไปเป็นหมู่เมทิลีน โดยปฏิกิริยาโวลฟ์คิชเนอร์ โดยนำไดไฮดรอกซีแอซีโทนมาทำปฏิกิริยาออกซิเมชัน และตามด้วยปฏิกิริยารีดักทีฟดีออกซิเมชันของสารประกอบออกซีมของไดไฮดรอกซีแอซีโทนในภาวะเบส พบว่า ไม่สามารถสังเคราะห์ 1,3-โพรเพนไดออล เนื่องจากเกิดสารมัธยันตร์ 3,3,6,6,-เททราไฮดรอกซีเมทิล-1,2,4,5-เททราซีเนน ซึ่งสลายตัวที่อุณหภูมิ 120 องศาเซลเซียส ส่วนปฏิกิริยาเคลมเมนเซนรีดักชันของ 1,3-ไดไฮดรอกซีแอซีโทน พบว่าเกิดกรดแลกติก 84 เปอร์เซนต์แทนที่จะได้ 1,3-โพรเพนไดออล โดยกลไกการเกิดปฏิกิริยาจาก 1,3-ไดไฮดรอกซีแอซีโทนไปเป็นกรดแลกติก คาดว่าเกิดผ่านคีโท-อีนอลทอโทเมอไรเซชัน และตามด้วยปฏิกิริยาโปรตอนทรานสเฟอร์ กลไกการเกิดปฏิกิริยายืนยันด้วยการทำปฏิกิริยาในดิวเทอเรียมออกไซด์ ซึ่งมีการรับอะตอมของดิวทิเรียมเข้าไปในหมู่เมทิลของกรดแลกติก

สาขาวิชา...ปิโตรเคมีและวิทยาศาสตร์พอลิเมอร์ ลายมือชื่อนิสิต....ศศิพิมพ์.....คงสุจริต.....
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SASIPIM KONGSUTJARIT : REDUCTION OF 1,3-DIHYDROXYACETONE. ADVISOR : ASSOC. PROF. AMORN PETSOM, Ph.D., CO-ADVISOR : ASST. PROF. PATCHANITA THAMYONGKIT, Dr.rer.nat., 73 pp.

The purpose of this study was to investigate the Wolff-Kishner and Clemmensen reduction of 1,3-dihydroxyacetone in order to convert carbonyl group to methylene group. Wolff-Kishner reduction was carried out on 1,3-dihydroxyacetone by oximation followed by reductive deoximation of 1,3-dihydroxyacetone oxime in the presence of base. It was observed that 1,3-propanediol was not obtained due to unexpected formation of an intermediate 3,3,6,6-tetrahydroxymethyl-1,2,4,5-tetrazinane which was decomposed at 120 °C. Clemmensen reduction of 1,3-dihydroxyacetone was carried out. Surprisingly, it gave lactic acid in 84 %yield instead of the expected 1,3-propanediol. The mechanism of transformation from 1,3-dihydroxyacetone to lactic acid took place via keto-enol tautomerization and followed by proton transfer from solvent. The mechanism was proposed and supported by the reaction in D_2O in which deuterium atom was incorporated into methyl group of lactic acid.

Field of Study...Petrochemistry and Polymer Science..Student's Signature: Sasipim Kongsutjarit

Academic Year.....2008..... Advisor's Signature:

Co-Advisor's Signature: Patchanita T.

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LIST OF ABBREVIATIONS

CH_3COOH	:	acetic acid
^{13}C-NMR	:	carbon-^{13}nuclear magnetic resonance spectroscopy
δ	:	chemical shift
^{1}H-NMR	:	proton nuclear magnetic resonance spectrospy
J	:	coupling constant
^{o}C	:	degree Celcius
equiv	:	equivalent
EtOH	:	ethanol
EtOAc	:	ethyl acetate
g	:	gram (s)
Hz	:	hertz (s)
h	:	hour (s)
$NH_2NH_2{\cdot}H_2O$	:	hydrazine hydrate
HCl	:	hydrochloric acid
$NH_2OH{\cdot}HCl$	:	hydroxylamine hydrochloride
IR	:	Infrared resonance spectroscopy
m/z	:	mass per charge ratio
MS	:	mass spectroscopy
m.p.	:	melting point
CH_3OH	:	methanol
Mg	:	milligram
µL	:	microlitre
mL	:	millilitre
mM	:	millimolar
mmol	:	millimole
min	:	minute
M	:	molar
nm	:	nanometer
NMR	:	nuclear magnetic resonance spectroscopy
ppm	:	part per million
H_3PO_4	:	phosphoric acid
^{1}H-NMR	:	proton nuclear magnetic resonance spectroscopy

rt	:	room tempterrature
s	:	singlet (NMR)
H_2SO_4	:	sulfuric acid
st	:	stretching vibration (IR)
t	:	triplet (NMR)
cm^{-1}	:	unit of wavenumber (IR)

CHAPTER I
INTRODUCTION

Consumption of diesel fuel has risen dramatically in worldwide. Diesel engines are a major source of particulate and smog-forming pollution because of the growing use of diesel engine to transport goods around the state, transporting 90% of all products and foodstuffs consumed in the country, and the vast majority of our imports and exports [1].

The above mentioned problems are related to environmental and economic concern especially when the price of the petroleum is increasing day by day. It is increasingly necessary to develop alternative clean and renewable energy sources substitute petroleum source.

Biodiesel is a renewable energy source to substitute the petroleum fuel as the monoalkyl ester of long chain fatty acids derived from a renewable source, such as vegetable oil or animal fat. The advantages of biodiesel are non-toxic, less or no environmental problem, biodegradable, lower CO content, no sulfur emission, essentially free of sulfur and aromatics, a cheaper product, and the better fuel properties [2,3]. World consumption of biodiesel is shown in Figure 1-1.

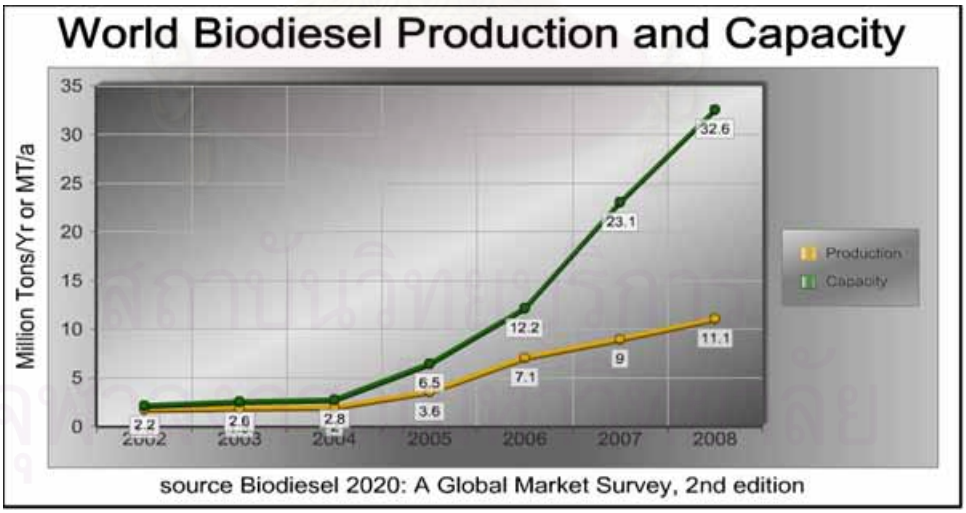


Figure 1-1 World consumption of biodiesel [4].

Nowadays, the biodiesel industry is rapidly expanding in worldwide, a glut of crude glycerol is therefore being increased as well. Approximately 10 kg of glycerol is produced for every 100 kg of production of biodiesel. Pure glycerol has many

applications in food, pharmaceutical, cosmetics, and many other industries. The usage of low-grade quality of glycerol obtained from biodiesel production is a big problem as this glycerol cannot be used for direct food and cosmetic uses and it is too expensive to refine the crude glycerol to a high purity, especially for medium and small biodiesel producer. An effective usage or conversion of crude glycerol to specific products will cut down the biodiesel production costs [5].

This research involves the synthesis of 1,3-propanediol and lactic acid from dihydroxyacetone which is one of products from glycerol oxidation for value-added utilization of crude glycerol from biodiesel production.

1.1 Objective of this research

Objective of this research is to reduce 1,3-dihydroxyacetone by using Wolff Kishner reduction and Clememsen reduction.

1.2 Scope of research

Scope of this research covers the redction of 1,3-dihydroxyacetone by using Wolff-Kishner reduction and Clemmensen reduction, optimization of the reaction condition and complete characterization of the products by spectroscopic techniques, i.e. FT-IR, ^{1}H-NMR and ^{13}C-NMR spectrometry, mass spectrometry, and X-ray crystallography, and study on the mechanism of transformation from 1,3-dihydroxyacetone into lactic acid by deuterium exchange.

CHAPTER II
THEORY AND LITERATURE REVIEWS

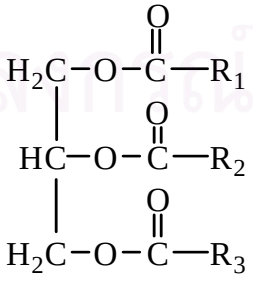
2.1 Biodiesel

2.1.1 Introduction

Over the past few years, worldwide demand for diesel fuel and other distillate fuel oils has been increasing steadily. Diesel fuel is widely used for transport of industrial, agricultural goods and dialy life. It is also used for many other applications. Pollution problems due to diesel engines of trucks and buses exhaust cause oxides of nitrogen (NOx) and fine particulate [6]. This has stimulated recent interest in alternative sources for petroleum-based fuel. An alternative fuel must be technically feasible, economically competitive, environmentally acceptable, and readily available. Biodiesel is an altetnative energy source. It is biodegradable, non-toxic and has low emission profiles as compared to petroleum diesel. Biodiesel is derived from vegetable oil or animal fats by transesterification. Thus, biodiesel refers to lower alkyl esters of long chain fatty acids, which are synthesized either by transesterification with lower alcohols or by esterification of fatty acids [7].

2.1.2 Transesterifcation and mechanism

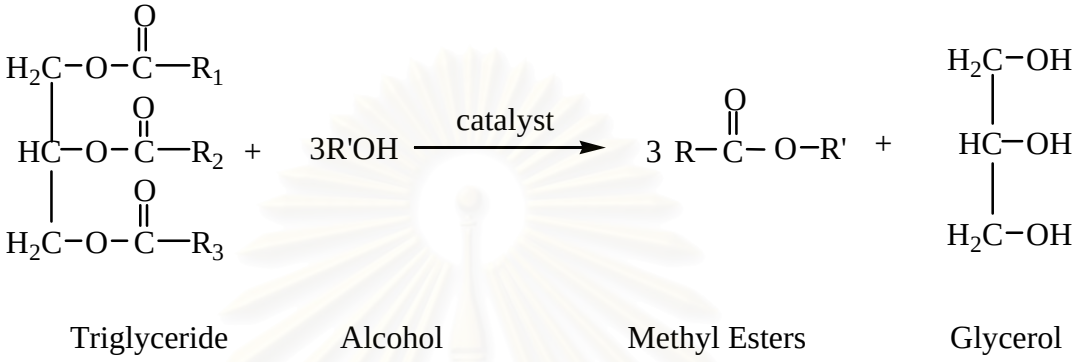
Transesterification is a reaction of vegetable oil or animal fat with an alcohol in the presence of a catalyst to produce fatty acid methyl ester and glycerol. Both oil and fat are triglycerides or fatty esters of glycerin. The triglyceride molecule has a chemical structure as shown in Figure 2-1.



Where R_1, R_2, and R_3 represent long chain fatty acids

Figure 2-1 Triglyceride chemical structure.

The stoichiometric of transesterification requires 3:1 molar ratio of alcohol to triglyceride. Transesterification reaction is shown in Scheme 2-1. The transesterification can be catalyzed by alkaline, acid or enzyme. Alcohol that can be used in this process are methanol, ethanol, propanol, butanol and amyl alcohol. The transesterification process is a useful method for reducing the high viscosity of triglyceride oils.

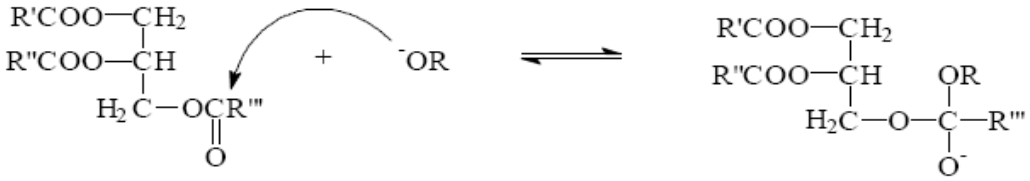


Scheme 2-1 Transesterification of triglyceride with alcohol.

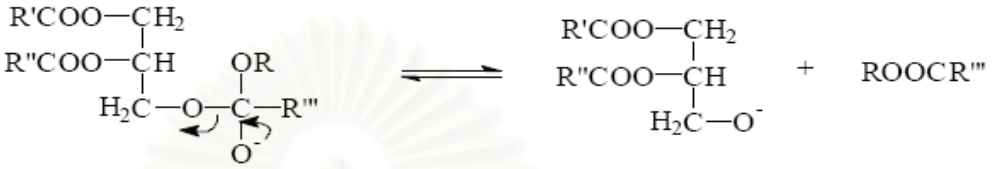
The alkaline-catalyzed transesterification is the most common, because this process is faster and the reaction conditions are moderated than acid-catalyzed [8]. Sodium hydroxide, sodium methoxide or potassium hydroxide are the common alkaline catalysts. The step-wise reactions are reversible and a little excess of alcohol is used to shift the equilibrium towards the formation of esters. The mechanism of transesterification for alkali-catalyzed has three step (Scheme 2-2). The first step is the reaction of the base with the alcohol, producing an alkoxide and the protonated catalyst. The nucleophilic attack of the alkoxide at the carbonyl group of the triglyceride generates a tetrahedral intermediate (Step 2) from which the alkyl ester and the corresponding anion of the diglyceride are formed (Step 3). The latter deprotonates the catalyst, thus regenerating the active species (Step 4), which is now able to react with a second molecule of the alcohol, starting another catalytic cycle. Diglycerides and monoglycerides are converted by the same mechanism to a mixture of alkyl esters and glycerol.

Step1

Step 2



Step 3



Step 4

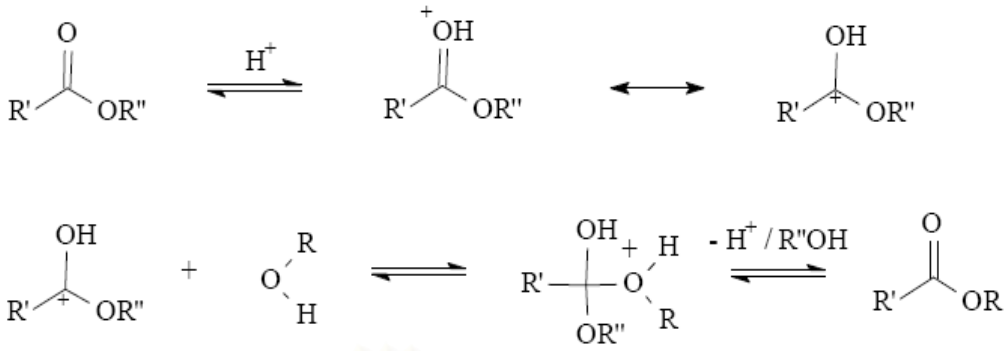
Where R" = CH_2- CH-OCOR' CH_2-OCOR'

R' = Carbon chain of fatty acid

R = Alkyl group of alcohol

Scheme 2-2 Mechanism of alkaline catalyzed transesterification.

Acid-catalyzed transesterification can produce biodiesel from low-cost triglyceride feedstocks, generally associated with high FFA concentration commonly have FFAs levels of ≥ 6%. Sulfuric acid is the most commonly used acid catalyst, but other acids, such as HCl, BF_3, $H3PO_4$, and organic sulfonic acids are used also as acid catalysts. The mechanism of acid catalyzed transesterification of vegetable oil (for a monoglyceride) is shown in Scheme 2-3. However, it can be extended to di- and tri-glycerides. The protonation of carbonyl group of the ester leads to the carbocation, which after a nucleophilic attack of the alcohol produces a tetrahedral intermediate. This intermediate eliminates glycerol to form a new ester and to regenerate the catalyst [9].



R" = O⁻ / O H / O H ; glycerides

R' = carbon chain of fatty acis, R = alkyl group of the alcohol

Scheme 2-3 Mechanism of acid-catalyzed transesterification.

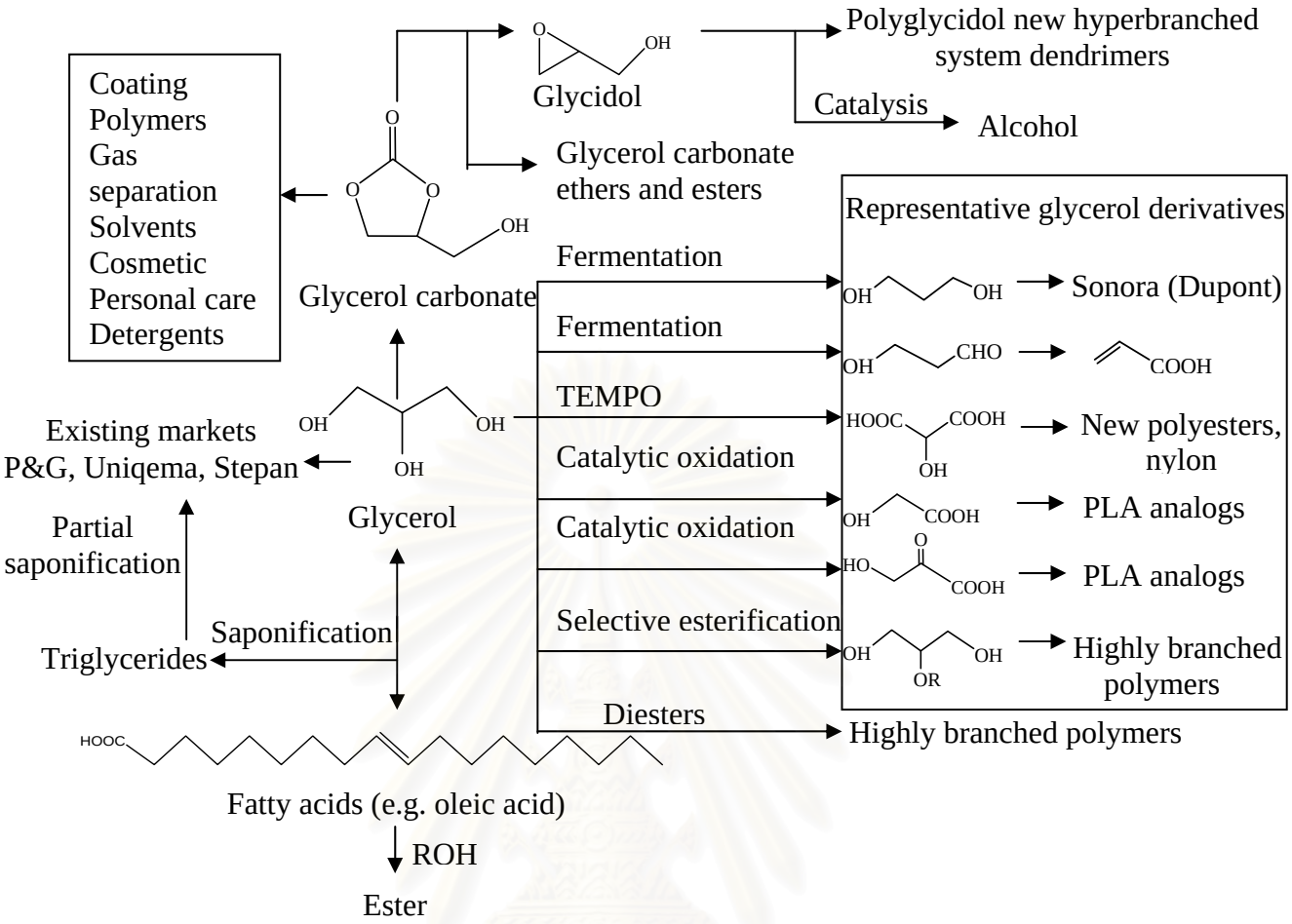
2.2 Glycerol

2.2.1 Chemical structure

Glycerol also well known as glycerin and less commonly as propane-1,2,3-triol, 1,2,3-propanetriol, 1,2,3-trihydroxypropane, glyceritol, and glycyl alcohol, is a colorless, odorless, hygroscopic, and sweet-tasting viscous liquid. It melts at 17 °C, boils with decomposition at 290°C, and is miscible with water and ethanol. The chemical formula for glycerol is OH-CH_2-CH(OH)-CH_2–OH. It is an important component of triglycerides (i.e. fats and oils) and of phospholipids. Glycerol is a three-carbon substance that forms the backbone of fatty acids in fats [10].

2.2.2 Application of glycerol

Glycerol has found many different applications. The process of refining crude glycerol involves removing residual organic nonglycerin matter, water, salt and odors. Refined glycerin is used by many industries, including the food, cosmetic and pharmaceutical industries. Glycerol derivatives from possible glycerol reactions is shown in Scheme 2-4.



Scheme 2-4 New glycerol platforms [11].

An effective usage or conversion of crude glycerol to specific products will cut down the biodiesel production costs. Glycerol conversion into useful products is shown in Table 2–1.

Table 2-1 Useful products from the conversion of glycerol [12] .

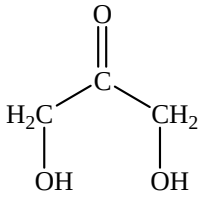
Product Name	Process Method/Nature	Researchers
1,3-propanediol	Continuous and Batch Microbial Fermentations mainly by the microorganisms *Clostridium butyricum* and *Klebsiella pneumoniae*. The cultures are specificied by nutrient, microbial and glycerol concentrations. The key parameters are temperature, pH, time, and agitation speed. The target is to maximize the yield and productivity of 1,3-propanediol.	Himmi et al.(1999) Papanikolaou and Aggelis (2003) Zeng (1997) Xiu et al.(2004) Menzel et al.(1997) Wang et al.(2001)
Succinic acid	Selective hydroxylation technique involving three stages of acetalization, tosylation, and detosylation.	Wang et al.(2003)
Hydrogen	Continuous microbial fermentation by *Enterobacter aerogenes* HU-101.	Ito et al. (2005)
	Catalytic reforming operating at moderate temperatures and pressures.	Wood (2002)
Hydrogen	Steam reforming of glycerol in the gas phase with group 8-10 metals catalysts.	Hirai et al.(2005)
	Aqueous-phase reforming over a tin-promoted Raneynickel catalysts.	Huber et al.(2003)
	Pyrolysis and steam gasification of glycerol.	Valliyappan (2001)
Dihydroxyacetone	Chemoselectve catalytic oxidation with platinum metals.	Garcia et al.(1994)
	Selective oxidation of glycerol with platinum-bismuth catalyst.	Kimura (2001)
	Microbial fermentations by *Gluconobacter oxydant* in a Batch/Semi-continuous process.	Bauer et al.(2005)

Product Name	Process Method/Nature	Researchers
Polyesters	Reacting glycerol and adipic acid in the presence of tin catalysts.	Stumbe and Bruchmann (2004)
	Reacting citric acid and glycerol at different mole ratios.	Pramanick et al. (1988)
	Polycondensation of oxalic acid and glycerol.	Alksnis et al.(1976)
	Reacting glycerol and aliphatic dicarboxylic acids.	Nagata et al.(1996)
Polyglycerols	Selective etherification of glycerol.	Clacens et al.(2002)
Polyhydroxy-alkanoates	Fermentation of hydrolyzed whey permeate and glycerol liquid phase by osmophilic organism.	Koller et al.(2005)
1,2-propanediol	Microbial fermentation by *Anaerobiospirillum succiniciproducens*.	Lee et al.(2001)
	Low-pressure hydrogenolysis in multi-clave reactor pressurized with hydrogen.	Dasari et al.(2005)
	Selective hydrogenolysis with Raney nickel catalyst in an autoclave with hydrogen.	Perosa and Tundo (2005)

2.3 1,3-Dihydroxyacetone

2.3.1 Chemical structure

Dihydroxyacetone (**1**) is a triose carbohydrate having chemical formula $C_3H_6O_3$ (Figure 2-2). It is a hygroscopic white crystalline powder. It has a sweet cooling taste and a characteristic odor. It is the simplest of all ketoses and, having no chiral center, is the only one that has no optical activity. The normal form is a dimer which is slowly soluble in 1 part water and 15 parts ethanol. When freshly prepared, it reverts rapidly to the monomer in solution. The monomer is very soluble in water, ethanol, diethyl ether and acetone [13].



1

Figure 2-2 Chemical structure of 1,3-dihydroxyacetone.

2.3.2 Application of 1,3-dihydroxyacetone [14]

1,3-Dihydroxyacetone is an important chemical used in the cosmetics industry as a tanning substance and also in fungicides. In particular, **1** is the main active ingredient in all sunless tanning skincare preparations, since it is the most effective sun free tanning additive. This skin browning effect is nontoxic, and similar to the Maillard reaction. **1** reacts with the amino acid groups, which are part of the protein containing keratin layer on the skin surface. Various amino acids react differently to **1**, producing different pigments (melanoidins) that are similar in coloration to melanin, the natural substance in the deeper skin layers which browns or 'tans' upon exposure to UV rays. Its commercial sales are rapidly increasing as concerns surrounding damage associated with UV tanning options spurred further popularity of sunless tanning products as an alternative to UV tanning. 1,3-dihydroxyacetone is used in the chemical industry as a versatile building block for the synthesis of a variety of fine chemicals.

2.3.3 Method for production of 1,3-dihydroxyacetone (**1**) [15]

2.3.3.1 Chemical process

The literature study reveals that **1** can be chemically produced via two different sources of substrate; formaldehyde and glycerol. Chemical production of dihydroxyacetone from formaldehyde is based on a condensation reaction called as "formoin reaction". Josep Castells and co-workers first described this reaction in 1980, according to which condensation of formaldehyde in the presence of conjugate bases of thiazolium ions (thiazolium ylides) yields a complex mixture of branched and unbranched aldehydes and ketones. A process based on this method obtained **1** in 82%. A problem associated with this method is difficulty in purifying **1**, which also adds to the cost.

The production of **1** from glycerol via chemical means can be done either catalytically or electrocatalytically. Glycerol is a highly functionalized molecule, which can yield different kinds of products in the presence of specific catalytic conditions. It has been found that by controlling the parameters like temperature, pH, and by the use of metals like Pt, Pd, etc as catalyst, the orientation of glycerol oxidation can be directed towards either primary alcohol functions or secondary alcohol functions. Orientation towards secondary alcohol functions, i.e., towards **1** production, can be directed in an efficient way by the use of Bi doped Pt catalyst. Around 50–70% conversion was obtained by this method. On the other hand, electrocatalytic oxidation of glycerol can be done by simply applying an electric potential (1.1 V vs. Ag/AgCl) to a glycerol solution in the presence of 15-mol% TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl) maintained at a pH of 9.1. The oxidation via this method can be done in a single pot itself and also this method is waste free. It was found that after 20 h of reaction, 25% yield of **1** was obtained during electrocatalytic oxidation of glycerol. Upon extension of the reaction time, overoxidation of the **1** occurs and hydroxypyruvic acid is formed [16].

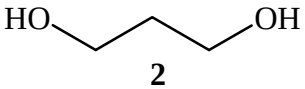
2.3.3.2. Microbial process

The production of **1** from glycerol by suitable microorganisms has long been generally known. **1** currently produced from glycerol by microbial fermentation over *Gluconobacter oxydans* is one of such valued oxygenate products [16].

2.4 1,3-Propanediol (PDO)

2.4.1 1,3-Propanediol structure [17]

1,3-propanediol (**2** in Figure 2–3) is a linear aliphatic glycol with the formula $CH_2(CH_2OH)_2$ **2** is a non-flammable, low toxicity liquid that is colorless and odourless. It is hygroscopic and is completely soluble in water. **2** is miscible in all proportions with low molecular weight aliphatic alcohols and ketones. It is slightly soluble in aromatic hydrocarbon solvents and has very low miscibility with aliphatic hydrocarbon solvents.



2

Figure 2-3 Chemical structure of 1,3-propanediol.

2.4.2 Application of 1,3-propanediol

The market situation for **2** has changed significantly since recent commercialization of a new polyester operation based on terephthalic acid and **2**. The odd number of carbon atoms of **2** imparts unique properties to polymeric products. Polytrimethylene terephthalate (PTT) is particularly appropriate for fiber and textile applications for excellent properties, such as good resilience, inherent stain resistance, and low static generation. **2** is expected to become a new commodity chemical. It is used to produced poltethers and polyurethane. The relatively high cost of the raw materials is one of the major limitations for industrial microbial production of **2** [18].

For a long time it only found niche applications such as as a solvent and for the production of dioxanes and specialty polymers that have small market volumes. This situation began to change in 1995–1996 when two leading chemical companies, Shell and Dupont, announced their commercialization of a new polyester, polytrimethylene terephthalate, termed PTT (Shell) or 3GT (Dupont) which is based on **2**. This copolyester is a condensation product of **2** and terephthalic acid. It has excellent properties such as good resilience, stain resistance, low static generation, etc., and is particularly suitable for fiber and textile applications. It is also a very promising engineering plastic that has the potential to replace the traditional polyethylene terephthalate (PET) and polybutylene terephthalate (PBT). PTT can be produced in an environmentally friendly way and at a price very competitive to that of PET and PBT. The production volume in the year 2000 was estimated to be around 70000–80000 t/a. According to a projection of the consulting company CONDUX (USA), the production volume of PTT will increase up to a level of 1 Mio. t/a in a few years. **2** also has a number of other interesting applications in addition to that of a polymer constituent. It can give improved properties for solvents (increased flexibility in blending ester quats and other additives), adhesives, laminates, resins (low intrinsic viscosity, less solvent for coating), detergents (preventing phase separation and loss of enzyme activity), and cosmetics (long-lasting but not sticky moisturizing effect). It can even be used to produce biocides for industrial disinfection and treatment of industrial circulation water, and freshness-keeping agents for cut flowers. In a recent patent it was also discussed as a component of animal feed [19].

2.4.3 Method for production of 1,3-propanediol [19]

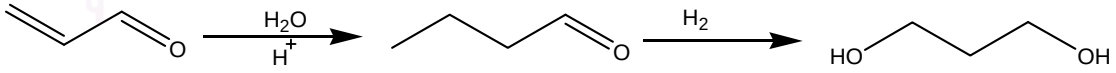
2.4.3.1 Chemical process

Until recently, **2** was regarded as not easily chemically amenable due to the relatively low selectivity in the existing processes. Increasing demand has now led to new patents that are both practiced on a considerable scale. The process of Degussa, now owned by Dupont, uses the conventional preparation method starting from acrolein which is obtained by catalytic oxidation of propylene. Acrolein is hydrated at moderate temperature and pressure to 3-hydroxypropionaldehyde which, in a second reaction, is hydrogenated to **2** over a rubidium catalyst under high pressure (90 bar).

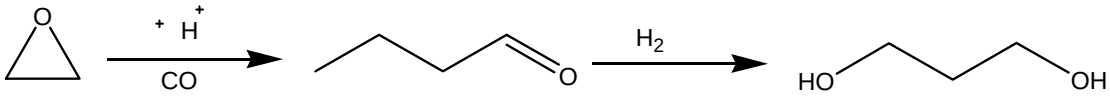
The process of Shell starts from ethylene oxide, which is prepared by oxidation of ethylene. Ethylene oxide is transformed with synthesis gas in a hydroformylation process to 3-hydroxypropanal as well, but for this reaction very high pressure (150 bar) is required. The aldehyde is extracted from the organic phase with water and subjected to hydrogenation using nickel as a catalyst, again under high pressure.

In the first process the yield does not exceed 65% of the starting compound due to simultaneous formation of 1,2-propanediol, while in the second, a yield of 80% is obtained. Adding the fact that the market price of ethylene oxide is lower than acrolein, the Shell process can be regarded as economically more favorable. This is reflected in the much higher production volume reported for the production of **2** from ethylene oxide, which amounted to 45,000 t/a in 1999 as opposed to 9000 t/a from acrolein. Chemical process of acrolein into **2** requires high temperature, high pressure and expensive catalysts. Chemical process shown in Scheme 2-5.

a. Acrolein based process.



b. Hydrocarbonylation of ethylene oxide.

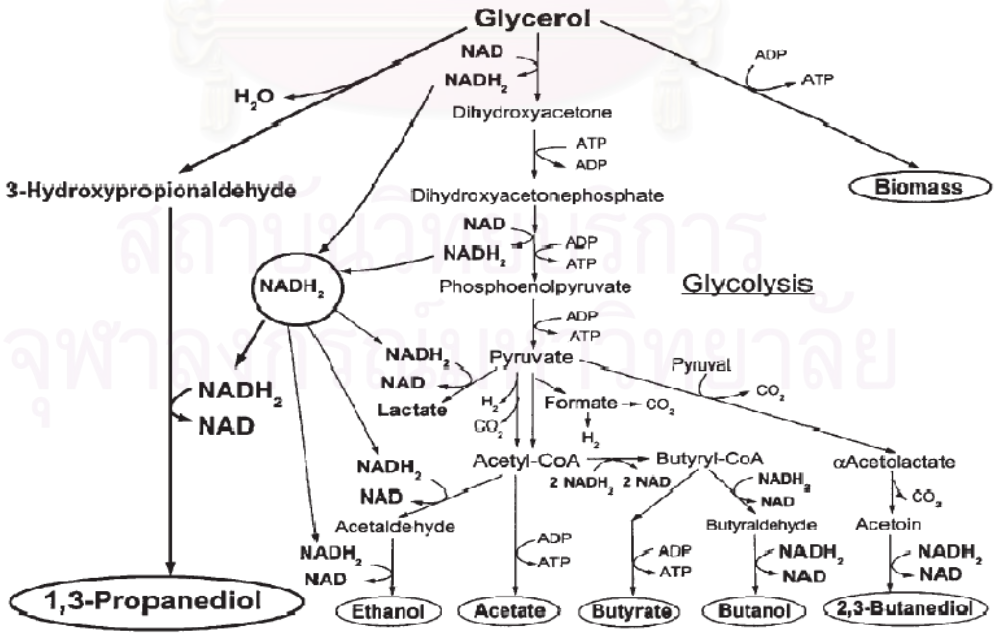


Scheme 2-5 Chemical processes of 1,3-propanediol [20].

2.4.3.2 Microbial formation

For almost 120 years a bacterial fermentation has been known as a method convert glycerol to **2**. However only very recently, since 1990, its biotechnological significance has been recognized, and it is more directly research initiated. There has been some economic interests in this reaction as glycerol has been a surplus product at times. It is released from fat cleavage to further manufacture the fatty acids and is also a by-product in biodiesel production from rape-seed oil. In addition, glycerol is also a minor by-product in ethanol fermentation and its recovery from this process has recently been discussed. Its concentration can be increased by cultural measures or strain development. Unpurified glycerol, in particular from biodiesel plants, has been shown to be an excellent fermentation substrate for **2** production.

The metabolic reactions involved in the glycerol fermentation are diverse shown in Scheme 2-6, but, in principle, the glycerol fermentation can be divided into two pathway branches. In the reductive branch, glycerol is first dehydrated to 3-hydroxypropionaldehyde that is then reduced to **2** under the consumption of reducing power ($NADH_2$). The reducing power is generated in the oxidative metabolism of glycerol that makes use of the major glycolysis reactions and results in the formation of by-products.



Scheme 2-6 Metabolic pathways of glucose metabolism [19].

The yield of **2** depends on the combination and stoichiometry of the reductive and oxidative pathways. It has been shown that the combination of **2** generation with acetic acid as the sole by-product of the oxidative pathway results in the maximum yield of **2**. The yield of **2** for this reaction is 67% (mol/mol). If biomass formation is considered the theoretical maximal yield reduces to 64%. In the actual fermentation a number of other by-products are formed, i.e., ethanol, lactic acid, succinic acid, and 2,3-butanediol, by the enterobacteria *Klebsiella pneumoniae*, *Citrobacter freundii and Enterobacter agglomerans*, butyric acid by *Clostridium butyricum*, and butanol by *Clostridium pasteurianum*. All these by-products are associated with a loss in **2** relative to acetic acid, in particular ethanol and butanol, which do not contribute to the $NADH_2$ pool at all.

2.5 Lactic acid

2.5.1 Lactic acid structure [21]

Lactic acid (2-hydroxypropanoic acid, **3** in Figure 2–4) is a three carbon organic acid; one terminal carbon atom is part of an acid or carboxyl group, the other terminal carbon atom is part of a methyl or hydrocarbon group, and the central carbon atom is part of an alcohol carbon group. **3** exists in two optically active isomeric forms and has many usages in beverages, foods, cosmetics, and pharmaceuticals as an acidifying agent and acidulant.

Figure 2-4 structure of lactic acid (**3**).

2.5.2 Lactic acid application

3 use wildely in many industrial applications. It used in food and beverages manufacturing. It is also used as preservation in the production of beer, jelly, cheese, dried egg white and other food products. It used an intermediate for polylactic acid production. Polylactic acid is a biodegradable polymer. It has become a significant commercial bioplastic. Its clarity makes it useful for recyclable and biodegradable packaging, such as bottles, yogurt cups, and candy wrappers.

Each year, world wide market for biodegradable plastics grows by more than 20 percent; thus, substantially increasing the demand for lactic acid. The worldwide consumption rates of lactic acid are approximately 130,000-150,000 tons per year in 1999. By the end of 2011, the global demand for lactic acid is expected to reach 200,000 tons [22].

2.5.3 Method for production of lactic acid [23]

2.5.3.1 Chemical process

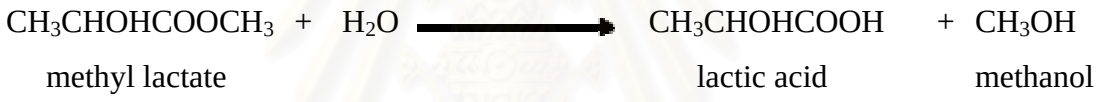
Commercial process for chemical synthesis is based on lactonitrile. Hydrogen cyanide is added to acetaldehyde in the presence of base to produce lactonitrile. This reaction occurs in liquid phase at high atmospheric pressures. The crude lactonitrile is recovered and purified by distillation. It is then hydrolyzed to **3**, either by concentrated HCl or by H_2SO_4 to produce the corresponding ammonium salt and **3**. **3** is then esterified with methanol to produce methyl lactate, which is removed and purified by distillation and hydrolyzed by water under acid catalyst to produce **3** and the methanol, which is recycled. This process is represented by the following reactions. Raw materials and processing costs do not lend support to this chemical synthesis approach for large-scale, low-cost manufacturing in the future. The chemical synthesis method produces a racemic mixture of **3**. Two companies Musashino, Japan and Sterling Chemicals Inc., USA are using this technology. The chemical process for **3** production shown in Scheme 2-7.

(a) Addition of hydrogen cyanide

(b) Hydrolysis by H_2SO_4

(d) Esterification

(e) Hydrolysis by H_2O



Scheme 2-7 Chemical process for lactic acid production.

Other possible routes are base catalyzed degradation of sugars, oxidation of propylene glycol, reaction of acetaldehyde, carbon monoxide and water at elevated temperature and pressures, hydrolysis of chloropropionic acid, carbohydrate fermentation and nitric acid oxidation of propylene.

2.5.3.2 Microbial formation

3 can be also produced by bacterial and fugal fermentation. Lactic bacteria, *Lactobacilli*, have been extensively used in lactic acid fermentation because they can synthesize the optical isomers of lactic acid at high production rate. Microbial process for **3** production is shown in Scheme 2-8.

(a) Fermentation and neutralization

$C_6H_{12}O_6$ + $Ca(OH)_2$ $\xrightarrow{\text{fermentation}}$ $2CH_3CHOHCOO^-)\ Ca^{2+} + 2H_2O$

Carbohydrate — Calcium hydroxide — Calcium lactate

(b) Hydrolysis by H_2SO_4

$2(CH_3CHOHCOO^-)\ Ca^{2+} + H_2SO_4 \longrightarrow 2CH_3CHOHCOOH + CaSO_4$

Calcium lactate — Sulphuric acid — Lactic acid — Calcium sulphate

(c) Esterification

$CH_3CHOHCOOH + CH_3OH \longrightarrow CH_3CHOHCOOCH_3 + H_2O$

Lactic acid — Methanol — Methyl lactate

(d) Hydrolysis by H_2O

$CH_3CHOHCOOCH_3 + H_2O \longrightarrow CH_3CHOHCOOH + CH_3OH$

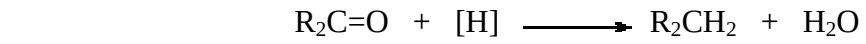
Methyl lactate — Lactic acid — Methanol

Scheme 2-8 Microbial process for lactic acid production.

Broth containing calcium lactate is filtered to remove cells, carbon treated, evaporated and acidified with sulphuric acid to get lactic acid and calcium sulphate. The insoluble calcium sulphate is removed by filtration; lactic acid is obtained by hydrolysis, esterification, distillation and hydrolysis.

2.6 Conversion of carbonyl group to methylene group [24-25]

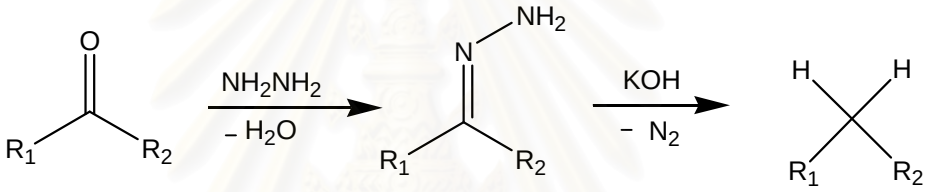
Reductive conversion of a carbonyl group of aldehyde or ketone to a methylene group such as Clemmensen reduction or Wolff kishner reaction. This process requires complete removal of the oxygen, and is called deoxygenation. In the shorthand equation shown here the [H] symbol refers to unspecified reduction conditions which effect the desired change. Three very different methods of accomplishing this transformation will be described in Scheme 2-9.



Scheme 2-9 General reaction of deoxygenation.

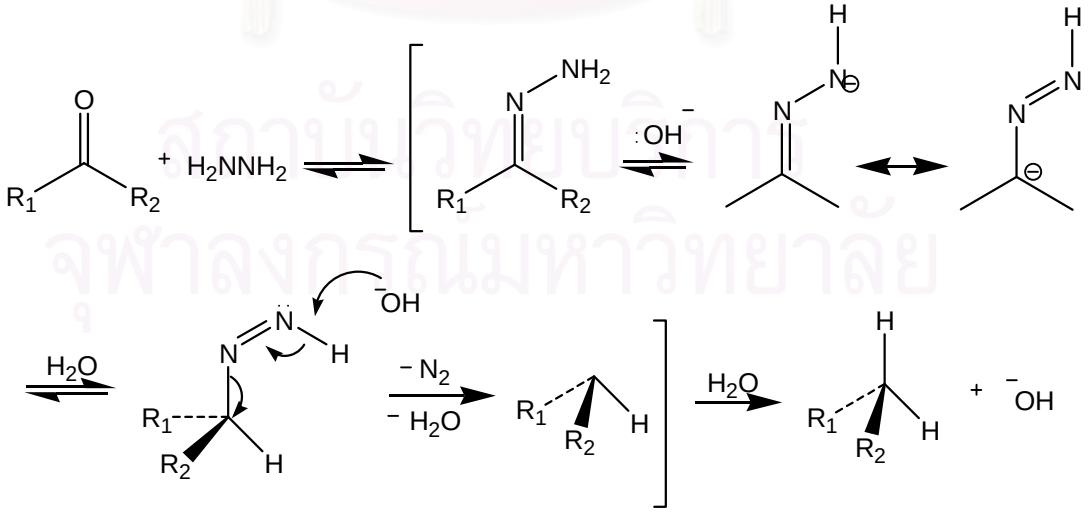
2.7 Wolff-kishner Reaction [26]

Reaction of an aldehyde or ketone with excess hydrazine generates a hydrazone derivative, which on heating with base gives the corresponding hydrocarbon. A high-boiling hydroxylic solvent, such as diethylene glycol, is commonly used to achieve the temperatures needed. The strongly basic conditions used in this reaction preclude its application to base sensitive compounds (Scheme 2-10).



Scheme 2-10 General reaction of Wolff-Kishner reduction.

The most probable mechanism involves the elimination of an alkyl anion as the final step shown in Scheme 2-11:

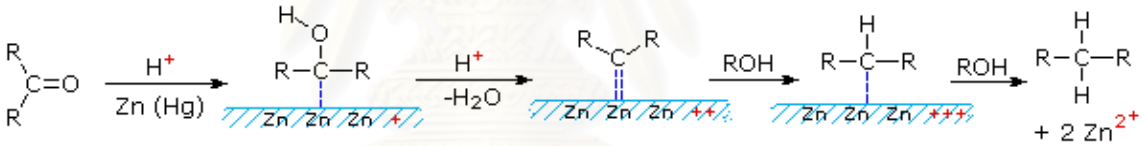


Scheme 2-11 Mechanism of Wolff-Kishner reaction.

The mechanism first involves the formation of the hydrazone in a mechanism that is probably analogous to the formation of an imine. Successive deprotonations eventually result in the evolution of nitrogen. The mechanism can be justified by the evolution of nitrogen as the thermodynamic driving force.

2.8 Clemmensen reaction [25]

This alternative reduction of carbonyl group to methylene group was Clemmensen reduction. It involves heating a carbonyl compound with finely divided, amalgamated zinc in a hydroxylic solvent (often an aqueous mixture) containing an acid such as HCl. Mercury alloyed with the zinc does not participate in the reaction but serves only to provide a clean active metal surface. Substituents such as hydroxyl, alkoxyl & halogens are reduced first, the resulting unsubstituted aldehyde or ketone is then reduced to the parent hydrocarbon. A possible mechanism for the Clemmensen reduction is shown in Scheme 2-12.



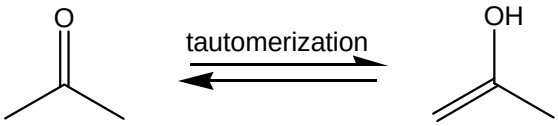
Scheme 2-12 Mechanism of Clemmensen reaction.

2.9 Tautomerization [27]

In organic chemistry, keto-enol tautomerism refers to a chemical equilibrium between a keto form (a ketone or an aldehyde) and an enol. The enol and keto forms are said to be tautomers of each other (Scheme 2-13). The interconversion of the two forms involves the movement of a proton and the shifting of bonding electrons; hence, the isomerism qualifies as tautomerism.

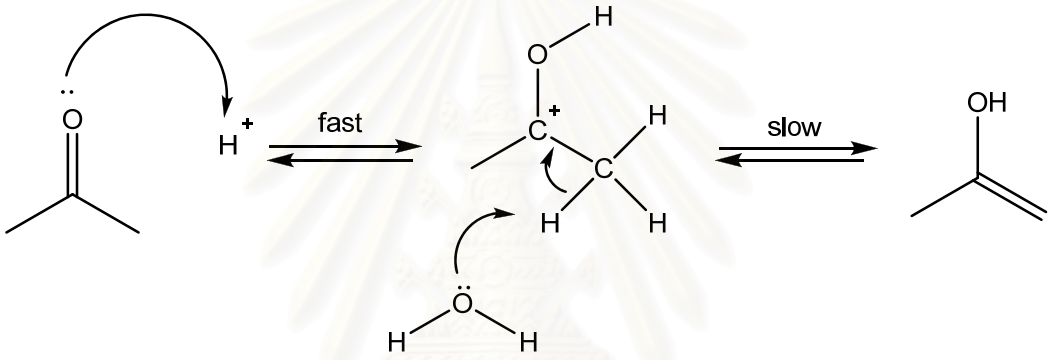
A compound containing a carbonyl group (C=O) is normally in rapid equilibrium with an enol tautomer, which contains a pair of doubly bonded carbon atoms adjacent to a hydroxyl (−OH) group, C=C-OH (Scheme 2-13). The keto form predominates at equilibrium for most ketones. Nonetheless, the enol form is important for some reactions. Furthermore, the deprotonated intermediate in the

interconversion of the two forms, referred to as an enolate anion, is important in carbonyl chemistry, in large part because it is a strong nucleophile [27].



Scheme 2-13 Keto-enol tautomerism.

Most ketones exist predominantly in the ketone form. In other words, the rate of the reverse reaction (enol ⟶ ketone) is much faster than (ketone ⟶ enol) transformation (Scheme 2-14).



Scheme 2-14 Mechanism of tautomerization.

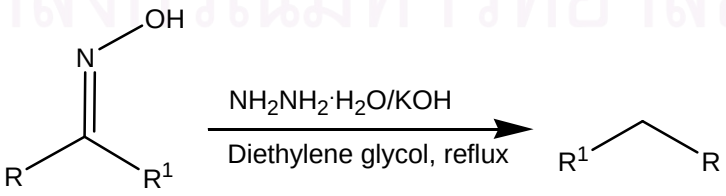
LITERATURE REVIEWS

Garcia et al. studied the liquid-phase oxidation of glycerol with air on platinum catalysts at different pH [28]. Oxidation of aqueous solutions of glycerol were carried out at atmospheric pressure in a (500 mL) thermostated glass reactor equipped with a stirrer, a gas supply system, an oxygen electrode and a pH electrode. The catalyst was suspended in 300 mL of water under nitrogen atmosphere and the suspension was heated to 333 K whilst stirring continuously at 1200 rpm. Glycerol was then added and, following a delay of 10 min, air was bubbled through the slurry at 0.75 mL/min. The initial concentration of the aqueous glycerol solution was 1 mol/L. The reaction medium was maintained at a constant pH by addition a 30% sodium hydroxide solution using a pump controlled by a pH meter. The selectivity to glyceric acid was 70% at 100% conversion on Pd/C at pH 11. On Pt/C catalyst, glyceric acid was the main product with 55% selectivity, but the deposition of

bismuth on platinum particles orientates the selectivity towards the oxidation of the secondary hydroxyl group to yield **1** with a selectivity of 50% at 70% conversion.

Kimura *et al.* studied the selective oxidation of glycerol using a fixed bed reactor packed with a Pt-Bi catalyst (weight ratio of Bi to Pt = 0.2) supported on granular charcoal was performed [29]. A new catalyst system to perform continuous oxidations was developed. Oxidation of a 50% aqueous solution of glycerol at 50° C, oxygen-to-glycerol mole ratio of 2 and a glycerol aq. solution based LHSV (h^{-1}) of 0.06 produced **1** with a selectivity of ca. 80% at a glycerol conversion of 80%. EPMA (electron probe micro analysis) line analysis of active BiPt catalysts showed the necessity of inner layer impregnation of both elements for selective oxidation of the secondary hydroxy group of glycerol. Wood based granular charcoal with a high BET surface area (>1200 m^2/g) and a low bulk density (<200 g/l) was the preferred catalyst support.

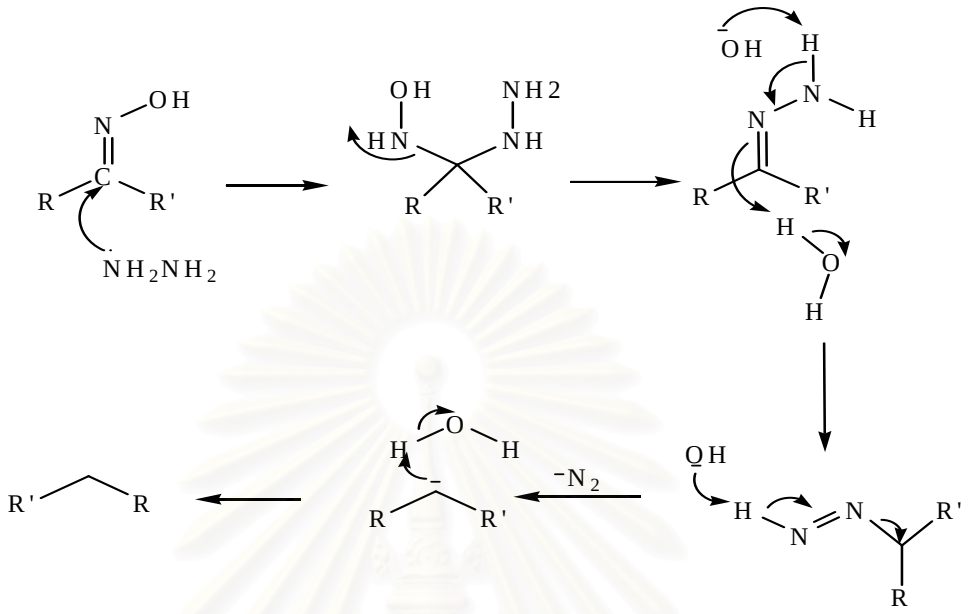
Nanjundaswamy *et al.* studied the direct conversion of oximes to hydrocarbons of aryloximes by reductive deoximation (Scheme 2-15) [30]. This research used aryloxime such as benzophenone oxime, carvone oxime, and cyclohexyl oxime as starting materials which were treated with hydrazine hydrate and diethylene glycol as a solvent. It was found that different substituted oximes can be readily converted into the respective hydrocarbons under these reaction conditions in high yields. Although diaryl and arylalkyloximes furnish the expected methyl or methylene derivatives, dialkyl oximes such as camphor oxime, carvone oxime, and cyclohexyl oxime give a complex mixture of products under these reaction conditions. Because oximes can be readily converted into hydrazones, the present reaction is expected to proceed by the formation of hydrazone intermediates.



R = phenyl or substituted phenyl groups; R' = alkyl or aryl group.

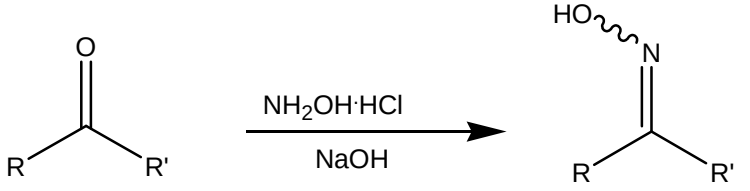
Scheme 2-15 Reaction of reductive deoximation.

A plausible mechanism for the formation of hydrocarbons from oximes via hydrazone intermediates is shown in Scheme 2-16.



Scheme 2-16 Proposed mechanism of reductive deoximtion.

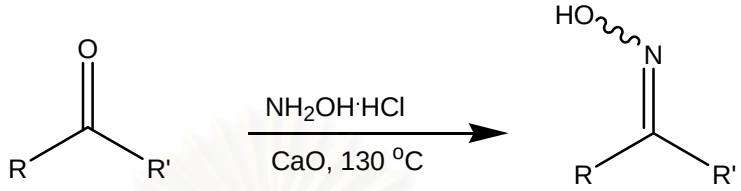
Damljanovic *et al.* reported the synthesis oxime of alicyclic and aliphatic carbonyl compounds as well as aromatic aldehydes into the corresponding oximes (up to quantitative yields) Scheme 2-17 [31]. These oxime was achieved by simply grinding these reactants, hydroxylamine hydrochloride and sodium hydroxide without solvent at room temperature. However, It was found that this procedure was unsuccessful in the case of aromatic ketones. In this case it was necessary to add silica gel as a catalyst. This procedure is a quick, simple, and extremely efficient method of oxime synthesis without a solvent, in most cases also without a catalyst, heating, or microwave irradiation.



R, R’ = cycloalkyl; R, R’ = alkyl; R = H, R = alkyl or aryl.

Scheme 2-17 Synthesis of oxime.

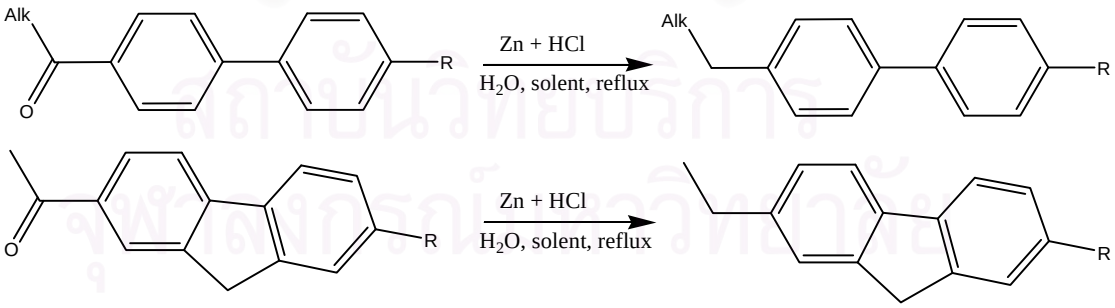
Sharghi, H. *et al.* reported the synthesis of oxime that was achieved effectively by CaO under mild condition [32]. The used of CaO for preparation of oximes was examined and it was found that CaO react with various types of ketones and aldehydes under mild condition to give the corresponding oximes in a quantitative yield (Scheme 2-18).



Scheme 2-18 Synthesis of oxime with CaO.

It was found that CaO was as an efficient reagent for the production of oximes from ketones and aldehydes in solid state. This procedure is also environmentally benign protocol because the oximation is achieved in solvent free condition and mild condition. The reagent (CaO) is inexpensive, and CaO can be used for several times. Other advantages include short reaction time, ease of work-up procedure and very satisfactory yield.

Bulavka, V. N. *et. al.* studied the reduction of carbonyl group to methylene group in Clemmensen reduction with non-amalgated zinc (zinc metal) instead zinc amalgam Scheme 2-19 [33].

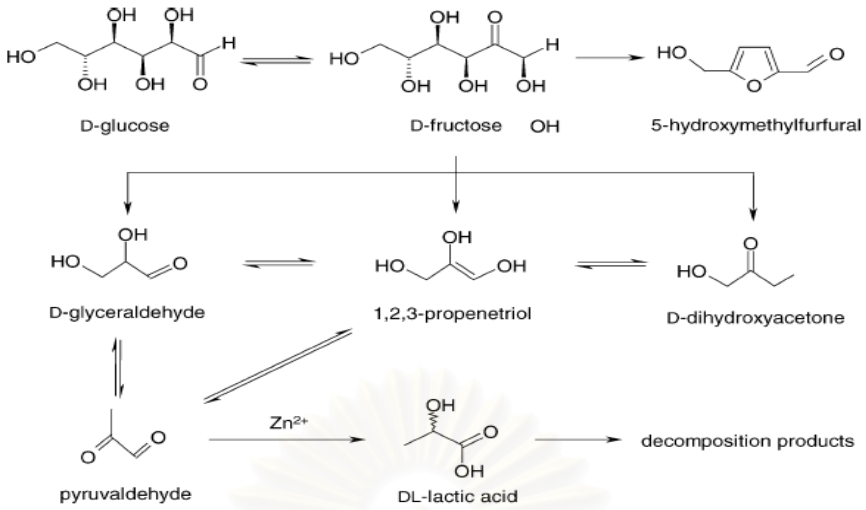


Scheme 2-19 Modified Clemmensen reduction.

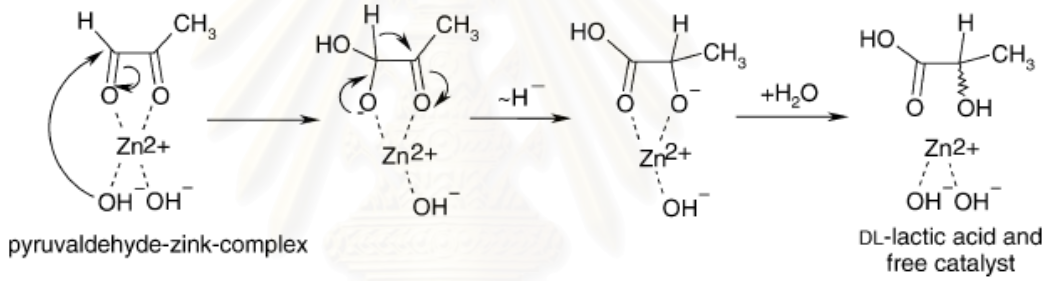
This research used some unsubstituted arylalkylketones and substituted arylalkylketones as starting materials. It was found that unsubstituted arylalkylketones were reduced to corresponding alkylarenes with moderate yields.

Reactions of arylakylketones proceed more slowly than those of alkylphenylketones, probably, due to more hydrophobic character of compounds used. Addition of solvent immiscible with water slightly increases yields, while addition of solvents miscible with water increases yields significantly. Yields of hydroxy-substituted compounds were higher than that of non-phenolic compounds. For comparison, granulated zinc and zinc dust were used for reduction and it was found that reduction with granulated zinc required longer time than that with zinc dust.

Bicker, M. *et. al*. studied the influence of metal ions on the reaction of biomass-relevent sugars such as sucrose, glucose and fructose in subcritical water (T = 200-360 °C) for lactic acid production [34]. The system contained a high pressure pump delivers the feed (1% (g g^{-1}) glucose or sucrose and 400 ppm ($g.g^{-1}$) $ZnSO_4$ in water) through a heat exchanger (pre-heater) into the reactor. The reactor discharge was simultaneously cooled down. The plugflow reactor was heated up to 300 °C, pressure was kept at 25MPa. For downstream processing pressure was relieved to ambient pressure and lactic acid purification was accomplished by reactive extraction with *n*-butanol/tri-*n*-hexylamine [12]. The reaction was performed by using six different metal ions such as Co(II), Ni(II), Cu(II) and Zn(II) to the reaction media. As a result, high lactic acid selectivities can be obtained by Co(II), Ni(II) and Zn(II) whereas zinc sulfate as the catalyst gave the best results. This is very favorable as it is very cheap and absolutely nontoxic. Because of their Lewis-acidity, transition metal cations polarize nucleophilic subtrates. As Cu(II) is even more lewis-acidic than Zn(II), the possibility that higher lewis-acidity of the metal cation leads to higher lactic acid selectivity is eliminated. The lactic acid yield is increased up to 42% (g g^{-1}) starting from sucrose and 86% (g g^{-1}) starting from 1,3-dihydroxyacetone is shown in Scheme 2-20. Possible mode of action of Zn(II) in the formation of lactic acid from pyruvaldehyde is shown in Scheme 2-21.



Scheme 2-20 Simplified reaction scheme for the zinc-catalyzed degradation of carbohydrates in subcritical water.



Scheme 2-21 Possible mode of action of Zn(II) in the formation of lactic acid from pyruvaldehyde.

CHAPTER III
EXPERIMENTAL

3.1 Chemicals

1. Acetic acid
   Analytical grade; MERCK, Darmstadt, Germany
2. Diethylene glycol
   Analytical grade; MERCK, Darmstadt, Germany
3. 1,3-Dihydroxyacetone
   Analytical grade; MERCK, Darmstadt, Germany
4. Distilled water
5. Ethanol
   Analytical grade; MERCK, Darmstadt, Germany
6. Ethyl acetate
   Distilled from commercial.
7. Hydrazine hydrate
   Analytical grade; Carlo Erba Reagent.
8. Hydrochloric acid
   Analytical grade; MERCK, Darmstadt, Germany
9. Hydroxylamine hydrochloride
   Analytical grade; Carlo Erba Reagent
10. Sodium hydroxide
    Analytical grade; MERCK, Darmstadt, Germany
11. Potassium hydroxide (pellets)
    Analytical grade, Carlo Erba Reagent.
12. Sulfuric acid
    Analytical grade; MERCK, Darmstadt, Germany
13. Zinc (dust)

3.2 Analytical instruments

Melting points were determined with a Stuart Scientific Melting Point SMP1 (Bibby Sterlin Ltd., Staffordshire, UK).

FT-IR spectra were recorded on a Nicolet Fourier Transform Infrared Spectrophotometer: Impact 410 (Nicolet Instruments Technologies, Inc. WI, USA). Infrared spectra were recorded between 400 cm^{-1} to 4,000 cm^{-1} in transmittance mode.

^{1}H-NMR and ^{13}C-NMR spectra were obtained in deuterated chloroform ($CDCl_3$) using Varian Mercury NMR spectrometer operated at 400.00 MHz for ^{1}H and 100.00 MHz for ^{13}C nuclei (Varian Company, CA, USA). Chemical shifts (δ) were reported in parts per million (ppm) relative to the residual $CHCl_3$ peak (7.26 ppm for ^{1}H-NMR and 77.0 ppm for ^{13}C-NMR). Coupling constants (*J*) were reported in Hertz (Hz).

Mass spectra were recorded on Mass Spectrometer: Waters Micromass Quatto micro API ESCi (Waters, MA, USA). Samples were dissolved in water and directly injected into Mass Spectrometer in 50 μL (Compound **4, 5** and **6**).

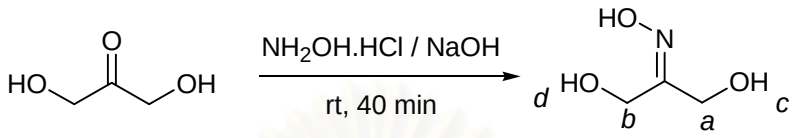
X-Ray diffraction data were collected on a Bruker SMART CCD diffractometer using graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). Intensity data were collected at 293 K to a maximum 2θ value of 60.08°. Of the 4712 reflections collected, 4083 were unique (R_{int} = 0.0102).

Crystal structure was solved by direct methods and using program SHELXS97 [36]. Refinements were made by full-matrix least squares on all F^2 data using SHELXS97 [37]. The all non-hydrogen atoms were anisotropically refined. All hydrogen atoms were located by a geometrical calculation at calculated and refined using a riding model. Refined atomic parameters and equivalent isotropic temperature factors for the non-hydrogen atoms.

3.3 Experimental procedure

Part 1: Wolff-Kishner reduction of 1,3-dihydroxyacetone

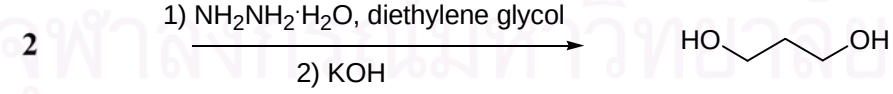
3.3.1 1,3-dihydroxyacetone oxime (4)



1 **4**

Following a reported procedure [31], a mixture of **1** (2.00 g, 22.0 mmol, 1.00 equiv), $NH_2OH{\cdot}HCl$ (1.84 g, 12.0 mmol, 1.20 equiv), and NaOH (1.06 g, 12.0 mmol, 1.20 equiv) was grinded in a mortar with a pestle at room temperature. After 40 min, the reaction mixture was washed with ethyl acetate and filtered to remove the insoluble materials. The resulting filtrate was concentrated to dryness to give compound **2** as a colorless solid (1.99 g, 82% yield). m.p. 80 °C. ^{1}H NMR: δ (ppm) 4.02 (d, *J* = 5.6 Hz, 2H,–C$\underline{H}_{2a}$OH), 4.24 (d, *J* = 5.6 Hz, 2H, C$\underline{H}_{2b}$OH), 4.63–4.66 (m, 1H, –C$\underline{H}_2$OH$_c$), 4.80–4.83 (m, 1H, –CH$_2$O$\underline{H}_d$), 10.60 (s, 1H, O$\underline{H}$) (**Figure A-1**); ^{13}C NMR: δ (ppm) 54.9 (C$_b$), 60.0 (C$_a$), 159.6 (C=N) (**Figure A-2**); ν_{max} (cm^{-1}) 3063 (O–H st), 1653 (C=N st) (**Figure A-3**); HRESI–MS obsd 106.0556 $[M+H]^+$cald for $[C_3H_7NO_3+H]^+$ 106.0504 (**Figure A-4**).

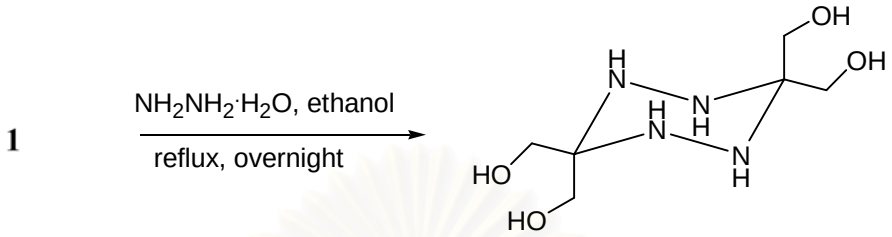
3.3.2 Reductive deoximation of 1,3-dihydroxyacetone oxime (4) using Wolff- Kishner reduction



Following a general procedure [30], a solution of oxime **1** (1.05 g, 10.0 mmol, 1.00 equiv), diethylene glycol (5.00 mL), and $NH_2NH_2{\cdot}H_2O$ (2.00 mL) was refluxed for 1 h. After the removal of the unreacted hydrazine hydrate and water by distillation between 100–120 °C, the reaction mixture was treated with KOH pellets (1.68 g, 30.0

mmol, 3.00 equiv.) under reflux for 3.5 h. Water (10 mL) was added. The crude product was then subjected to NMR measurement.

3.3.3 3,3,6,6-Tetrahydroxymethyl-1,2,4,5-tetrazinane (6)

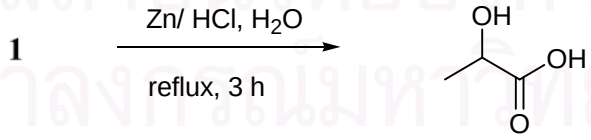


6

Following a general procedure [38], a solution of **1** (1.00 equiv, 10.0 mmol, 0.90 g, 0.20 mM), $NH_2NH_2{\cdot}H_2O$ (1.00 equiv, 0.49 mL, 0.20 mM), in ethanol was refluxed overnight. The resulting mixture was allowed to stand at room temperature until the volume of the mixture was reduced by half. The title compound was collected by filtration as a colorless crystal (1.64 g, 79% yield). m.p. ~120 ^{o}C (decomposition); ^{1}H NMR: δ (ppm) 3.87 (s, 4H), 4.08 (s, 4H), 4.00 (s, 2H), 5.01 (s, 2H), 6.05 (s, 1H) (**Figure A-5**); ^{13}C NMR: δ (ppm) 58.4 ($\underline{C}H_2OH$), 63.2 ($\underline{C}H_2OH$), 149.7 ($\underline{C}$–N) (**Figure A-6**); ν_{max} (cm^{-1}) 3277 (N–H, O–H st), 1062 (C=O st) (**Figure A-7**) HRESI–MS obsd 231.1078 $[M+Na]^+$ cald for $[C_6H_{16}N_4O_4+Na]^+$ 231.1070 (**Figure A-8**).

Part 2: Clemmensen reduction of 1,3-dihydroxyacetone

3.3.4 Clemmensen reduction of 1



3

Following a standard procedure [34], a solution of **1** (90.0 mg, 1.00 mmol, 1.00 equiv.), zinc dust (0.196 g, 30.0 mmol, 3.00 equiv.), in water (2.5 mL) and concentrated hydrochloric acid (2.5 mL) was refluxed for 1 h. The resulting mixture was cooled to room temperature and filtered to remove Zn dust. Then neutralized with a saturated aqueous solution of sodium hydroxide, filtered to remove salt and

concentrated to obtained a yellow liquid (68%). ^{1}H NMR: δ (ppm) 1.29 (d, *J* = 6.8 Hz, 3H, C<u>H</u>$_3$), 4.15(q, *J* = 6.8 Hz, 1H, C<u>H</u>–OH) (**Figure A-9**); ^{13}C NMR: δ (ppm) 19.9, 63.2, 181.8 (COOH) (**Figure A-10**); ν_{max} (cm^{-1}) 3277 (O–H st), 1062 (C=O st) (**Figure A-11**).

<u>Part 3: Study on the optimized conditions for lactic acid formation</u>

To optimize reaction condition for the lactic acid formation, effects of zinc dust and hydrochloric acid, the amount of acid, reaction time and temperature were investigated. In this optimizing condtion, the obtained product was characterized by ^{1}H-NMR based on a standard acetic acid (20 μL).

3.3.5 Effect of parameter on the lactic acid formation

The effect of type and amount of acid, time and temperature on Clemmensen reaction were determined as described below.

3.3.5.1 Lactic acid formation by Zn and hydrochloric acid

To investigate the effect of Zn dust, a solution of **1** (90.0 mg, 1.00 mmol, 1.00 equiv), zinc dust (0.196 g, 30.0 mmol, 3.00 equiv) in water (5 mL) was refluxed for 1 h. The resulting mixture was cooled to room temperature and and filtered to remove Zn dust. Then neutralized with a saturated aqueous solution of sodium hydroxide, filtered to remove salt and concentrated. The crude product was analyzed using ^{1}H-NMR.

To investigate the effect of hydrochloric, a solution of **1** (90.0 mg, 1.00 mmol, 1.00 equiv) in water (2.50 mL) and concentrated hydrochloric acid (2.50 mL) was refluxed for 1 h. The resulting mixture was cooled to room temperature and neutralized with a saturated aqueous solution of sodium hydroxide, filtered to remove salt and concentrated to obtain yellow liquid.

3.3.5.2 Effect of acid type

A solution of **1** (90.0 mg, 1.00 mmol, 1 equiv) in water (2.5 mL) and concentrated hydrochloric acid (2.5 mL) was refluxed for 1 h. The resulting mixture was cooled to room temperature and neutralized with a saturated aqueous solution of sodium hydroxide, filtered to remove salt and concentrated to obtain a yellow liquid.

In the similar manner as described for Zn/HCl condition, the uses of H_2SO_4, H_3PO_4 and CH_3COOH in the amount as shown in Table 3-1 for lactic acid formation were investigated.

Table 3-1 Type and amount of acid used in these experiments

Entry	Catalyst (% w/w)	Amount of acid (% v/v in H_2O)	Concentration of acid (M)
1	Hydrochloric acid (37%)	33.0	6
2	Sulfuric acid (96%)	50.0	6
3	Phosphoric acid (85%)	40.0	6
4	Acetic acid (99%)	35.0	6

3.3.5.3 Amount of hydrochloric acid

The use of HCl as a reagent was further studied by performing the same experiment as mentioned in 3.3.5.1 in the presence of HCl in various amounts as shown in Table 3–2.

Table 3-2 Amount of HCl used in these experiments

Entry	Amount of HCl (% v/v)
1	10.0
2	20.0
3	30.0
4	40.0
5	50.0
6	60.0
7	70.0
8	80.0

3.3.5.4 Effect of temperature

The use of 60% HCl as a reagent was further studied by performing the same experiment as mentioned in 3.3.5.1 at various temperature as shown in Table 3–3.

Table 3–3 Reaction temperature for these experiments

Entry	Temperature (°C)
1	30
2	50
3	100

3.3.5.5 Effect of time

The use of 60% HCl as a catalyst at 100 °C was further studied by performing the same experiment as mentioned in 3.3.5.1 at various time as shown in Table 3–4.

Table 3–4 Reaction time for these experiments

Entry	Time (h)
1	1
2	6
3	12
4	24

Part 4: Mechanistic study of lactic acid formation

3.3.6 NMR measurement

A solution of **1** (100 mg, 1.11 mmol) in D_2O (300 µL) was added to a clean, dry NMR tube by using a 1000 µL precision Gilson pipette. Then the tube was shaken and the sample was measured for a NMR spectrum. After that, HCl (200 µL) was added into the tube and the tube was shaken well to ensure the complete mixing and this sample was subjected to NMR measurement immediately. Immediately after the experiment, the tube was warmed up to 100 °C in an oil bath for 1 h. After that, the tube was put into an ice bath, and the NMR measurement was repeated.

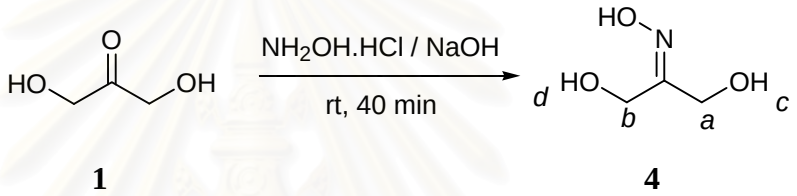
CHAPTER IV

RESULTS AND DISCUSSION

Part 1: Wolff-Kishner reduction of 1,3-dihydroxyacetone

4.1 1,3-Dihydroxyacetone oxime (4)

Compound **1** was successfully transformed into the corresponding oxime **4** in 82% yield by a simple grinding $NH_2OH{\cdot}HCl$ and NaOH in a mortar with a pestle at room temperature for 30–40 min without using any solvent (Scheme 4-1).



1 **4**

Scheme 4-1 Synthesis of 1,3-dihydroxyacetone oxime.

Compared with other previous synthesis [39,40], this procedure has many advantages, such as extremely simple reaction condition and short reaction time without using solvent and catalyst. Moreover, the purification step requires no column chromatography and was easily performed by washing and filtration. These results point to an efficient method for the conversion of **1** to the corresponding oximes in scalable synthesis.

Considering ^{1}H-NMR spectral analysis, a signal of hydroxyl proton of C=N–OH appeared as a singlet at δ 10.60 ppm (**Figure A-1**) indicating that the molecule bears intramolecular hydrogen bond between the H-bonded =N-OH group as shown in Figure 4-1.

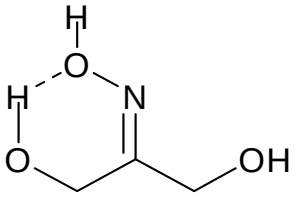
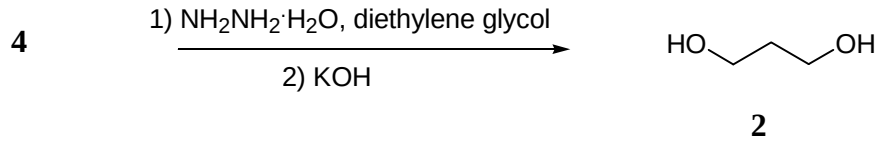


Figure 4-1 Intramolecular hydrogen bond in 1,3-dihydroxyacetone oxime.

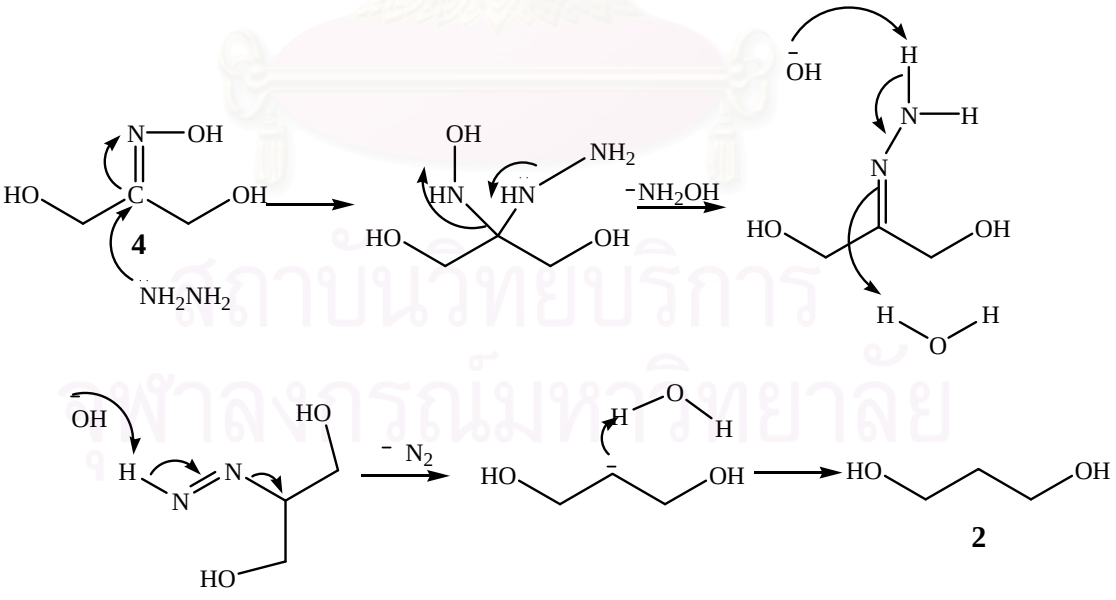
4.2 Reductive deoximation of 1,3-dihydroxyacetone oxime (4) using Wolff-Kishner reduction.



Scheme 4-2 The synthesis of 1,3-propanediol.

An attempt to synthesize 1,3-propanediol using the method in 3.3.2 was investigated (shown in 4-2). In this study, the NMR spectrum was measured after finished reaction without work up. The ^{13}C NMR spectrum of reaction product indicated that 1,3-propanediol was not obtained (no CH_3 group of 1,3-propanediol at δ 34 ppm).

. Reducive deoximation is an application of the Wolff–Kishner on the direct conversion of oximes to hydrocarbons. Since oximes can be readily converted into hydrazones, the present reaction is expected to proceed by the formation of hydrazone intermediates. Successive deprotonations eventually resulted in the evolution of nitrogen to yield the corresponding alkane. According to Nanjundaswamy *et al.* [30], the mechanism for the formation of **2** from **4** via dihydroxyacetone hydrazone intermediates should be as shown in Scheme 4-3.



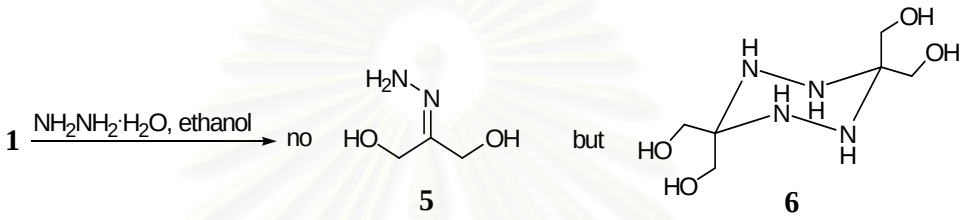
Scheme 4-3 Proposed mechanism of reductive deoximation of **1**.

If the reaction proceded as shown in Scheme 4-3, then the hydrazone intermediate should be synthesized and used directly.

4.3 3,3,6,6-Tetrahydroxymethyl-1,2,4,5-tetrazinane (6)

From the proposed mechanism in Scheme 4-3, hydrazone is an key intermediate from reaction [41]. Therefore, synthesis of a hydrazone (**5)** was persued by the reaction of **1** (1 equiv) with $NH_2NH_2{\cdot}H_2O$ (1 equiv) in ethanol under reflux overnight according to the conventional method [38].

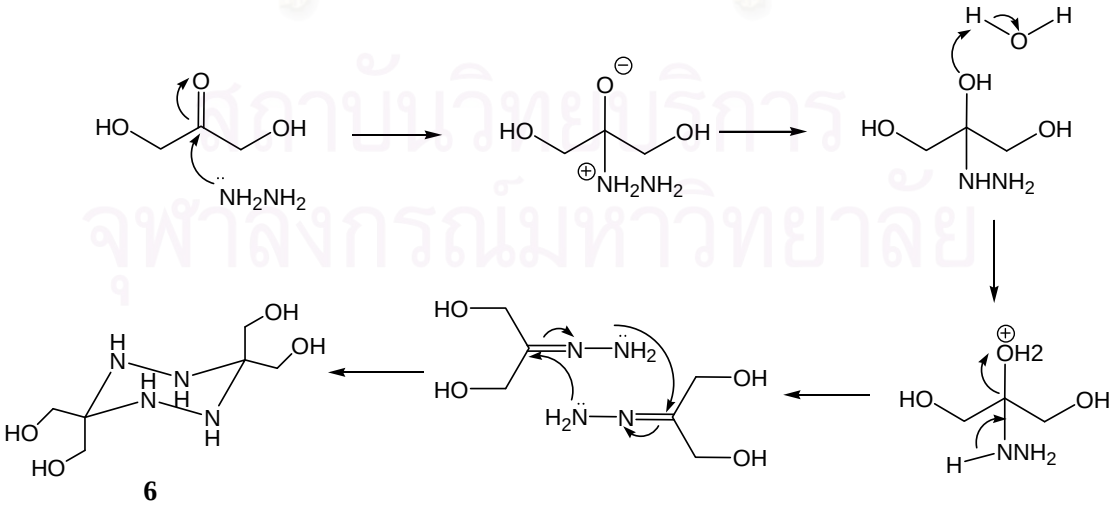
Surprisingly, tetrazinane (**6**) was obtained instead of the expected hydrazone (Scheme 4–4).



Scheme 4-4 Synthesis of 3,3,6,6-tetrahydroxymethyl-1,2,4,5-tetrazinane.

The tetrazinane **6** was a new compound and its decomposition point was observed at 120 °C which is significantly lower than the reaction temperature for Wolff-Kishner reduction (~180–200 °C) and thus explained why the desired compound **3** was not achieved.

A proposed mechanism for the formation of **6** is shown in scheme 4-5. Compound **1** was reacted with hydrazine hydrate to generate hydrazone which undergoes self-condensation to give **6**.



Scheme 4-5 Proposed mechanism for the formation 3,3,6,6-tetrahydroxymethyl-1,2,4,5-tetrazinane.

The formation of compound **6** was structurally confirmed by single crystal X-ray crystallographic analysis as shown in Figure 4-1. Crystal data (Appendix B) colorless crystal; $C_3H_{12}N_2O_4$, M_r=140.15, triclinic, $P1$, a = 6.3071(6)Å, b = 7.0326(7) Å, c = 8.4034(8)Å, α = 71.041(2)°, β = 74.459(2)°, γ = 85.082(2)°, Z = 2 and V = 339.63(6) Å^3, Mo Kα radiation, λ = 0.71073 Å. Intensity data were collected at 293 K to a maximum 2θ value of 50.92°. Of the 2478 reflections collected, 2091 were unique, 195 parameters (R_{int} = 0.0108). Crystal structure was solved by a direct method and using the SHELXS97 [36] program. Refinements were made by full-matrix least squares on all F^2 data using SHELXL97 [37] to final R values [$I>2\sigma(I)$] of $R1$ = 0.0347, $wR2$ = 0.0948 and Goodness of fit on F^2 = 1.050.

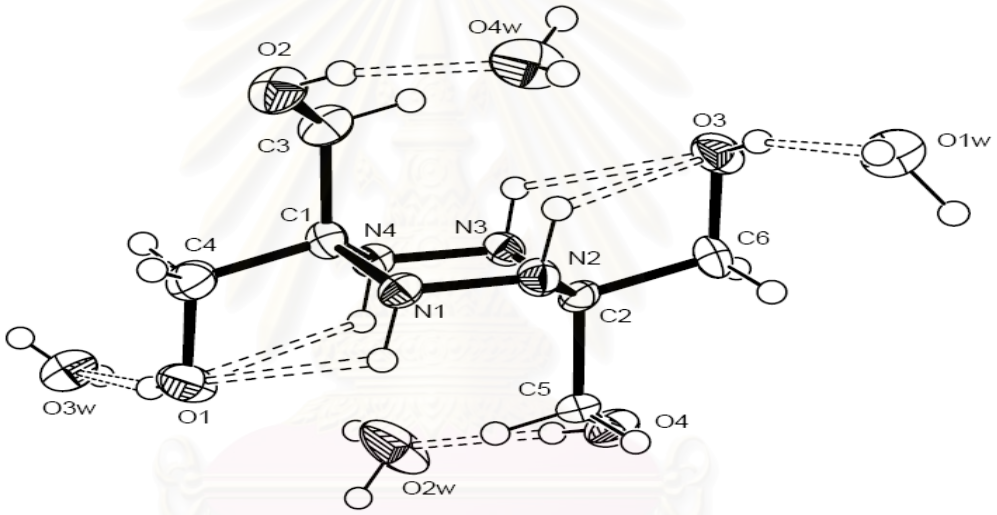


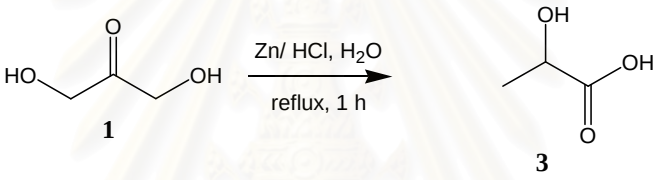
Figure 4-2 X-ray structure of tetrahydroxymethyl-1,2,4,5-tetrazinane.

It is very interesting to obtain **6** from this simple experiment since this group of compound is quite rare. Only a hardfull example of tetrazinane are reported in the literature. Therefore, chemistry and application of **6** will be investigated and reported elsewhere.

Part 2: Clemmensen reduction of 1,3-dihydroxyacetone

4.4 Clemmensen reduction of 1

Since the conversion of **1** to **3** by Wolff-Kishner reduction could not give the desired product due to the decomposition of intermediate **6**, therefore, the reduction of **1** by Clemensen reduction was carried out. In general, Clemmensen reduction has been used to reduce a great variety of ketones and aldehydes to the corresponding methylene derivatives [42–43]. In this study, investigation was directed to replace zinc amalgam by zinc dust in Clemmensen reduction of carbonyl group to methylene group [33, 44]. By refluxing **1** and 50% HCl (% v/v) in the presense of Zn, surprisingly this reduction gave lactic acid instead of the expected 1,3-propanediol as shown in Scheme 4-6.



1 **3**

Scheme 4-6 Clemmensen reduction of 1 with 50% HCl and Zn dust.

Lactic acid (**3**) was characterized by ^{1}H- and ^{13}C-NMR spectroscopy. ^{1}H-NMR spectrum (Figure A-9) showed doublet of CH_3 group and C<u>H</u>–OH at δ_H 1.26 and 4.15, respectively. ^{13}C-NMR spectrum of carboxylic group appeared at δ_C 181.8. Carbon signals of methyl and CH–OH were observed at δ_C 19.9 and 67.3 respectively (Figure A-10).

Moreover, it was found that the presence of Zn dust was not necessary in the formation of lactic acid. Thus, the reaction pointed out to the acid catalyze tautomerization.

Part 3: Study on the optimized conditions for lactic acid formation

4.5 Effect of parameter on the lactic acid formation

To investigate the optimized condition for the synthesis of lactic acid by acid catalyze tautomerization reaction, the effects of type of acids, the amount of acid, temperature, reaction time were investigated.

4.5.1 Lactic acid formation by Zn and hydrochloric acid

In this study, it was found that the reaction in the presence of 50% HCl (% v/v) afforded lactic acid in 68% yield. On the other hand, under the similar reaction in the presence of 3.0 equiv of zinc dust without the use of 50% HCl, the conversion of **1** to **3** was not achieved and based on ^{1}H-NMR analysis the starting material was still remained. This result showed that zinc dust alone had no effect on lactic acid production, but only 50% HCl can produced lactic acid. Therefore, HCl was used for further studies.

4.5.2 Effect of acid type

In this study, the effect of commencially available acids, *i.e.* HCl, H_2SO_4, H_3PO_4 and CH_3COOH on the formation of **3** as described in Table 4-1 was investigated.

Table 4-1 Type and amount of acid used in these experiments

Entry	Catalyst (% w/w)	Amount of acid (% v/v in H_2O)	Concentration of acid (M)	Yield (%)[a]
1	Hydrochloric acid (37%)	33.0	6	68
2	Sulfuric acid (96%)	50.0	6	59
3	Phosphoric acid (85%)	40.0	6	3
4	Acetic acid (99%)	35.0	6	0

[a]Analyzed by ^{1}H-NMR using 20 μL acetic acid as internal standard

The reaction in the presence of H_2SO_4 and HCl gave good yield compared to H_3PO_4. CH_3COOH was not an effective acid for this reaction. The % yield of **3** was in the order of HCl > H_2SO_4 > H_3PO_4 > CH_3COOH. Therefore, the 50% HCl (%v/v) was chosen for further studies.

4.5.3 Amount of hydrochloric acid

In this study, the amount of HCl was varied from 10 to 80% v/v. The results are summarized in Table 4-2.

Table 4-2 Amount of HCl used in these experiments

Entry	Amount of HCl (% v/v in H_2O)	Yield (%)[a]
1	10	53
2	20	57
3	30	60
4	40	64
5	50	68
6	60	79
7	70	74
8	80	73

[a]Analyzed by ^{1}H-NMR using 20 μL acetic acid as internal standard

The increase in the concentration of HCl from 10 to 80% (% v/v) led to a remarkable increase in the lactic acid yield. The yield of **3** started to increase from 10% HCl until it reached the maximum at 79%, when 60% HCl was employed. When the amount of HCl was higher than 60%, the yield remained relatively constant. Thus, 60% HCl was a suitable acid amount for this synthesis and was chosen for further studies.

4.5.4 Effect of temperature

In this study, the effect of reaction temperature was varied from 30 to 100 °C on formation of **3** as described in Table 4-3.

Table 4-3 Reaction temperature for these experiments

Entry	Temperature (°C)	Yield (%)[a]
1	30	0
2	50	35
3	100	79

[a]Analyzed by ^{1}H-NMR using 20 μL acetic acid as internal standard

In this study, the reaction temperature was varied from 25 to 100 °C (Table 4–3). It was shown that, no lactic acid formation was achieved at room temperature. When the temperature was increased to 50 °C, the yield of **3** was increased to 35% after 1 h with remaining starting material. Longer reaction time might be required at this temperature. At 100 °C, it was observed that 79% yield of **3** was obtained and was chosen for further studies.

4.4.5 Effect of time

In this study, the effect of reaction time was varied from 1 to 24 h on the formation of **3** as described in Table 4-4.

Table 4-4 Reaction time for these experiments

Entry	Time (h)	Yield (%)[a]
1	1	79
2	6	80
3	12	84
4	24	85

[a]Analyzed by ^{1}H-NMR using 20 μL acetic acid as internal standard.

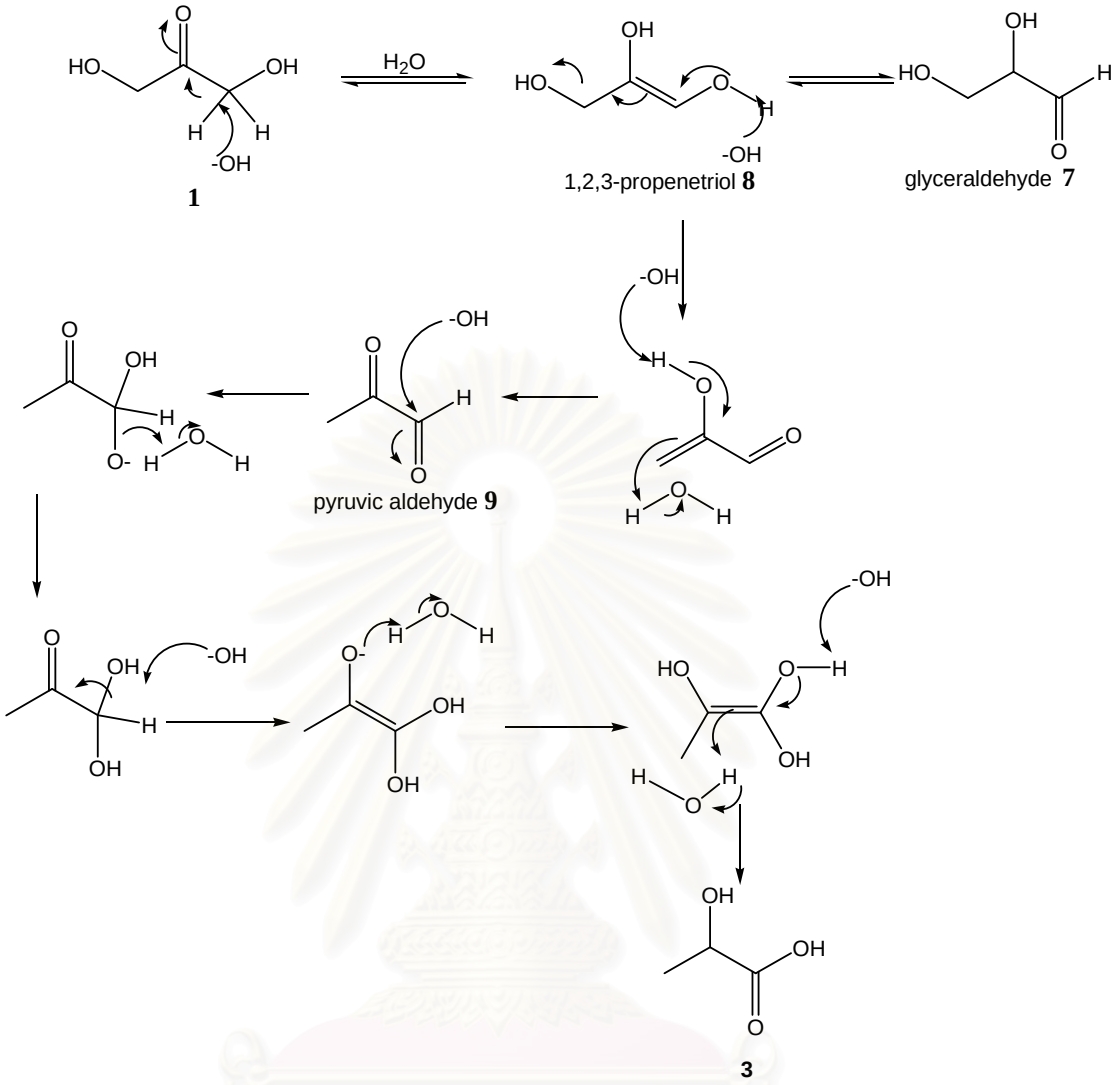
In this study, the effect of reaction time from 1 to 24 h (Table 4–4) were investigated. According to ^{1}H-NMR analysis, the reaction was completed within 1 h (entry 1 in Table 4-4). However when the reaction time was increased, the product yield was slightly increased. At 12 h, it was observed that 84% yield of **3** was obtained.

Therefore, the optimized condition for lactic acid formation was 1,3-dihydroxyacetone (1 equiv) in the presence of 60% HCl under refluxing for 12 h and gave 84% yield of lactic acid.

Part 4: Study of mechanism by deuterium exchange

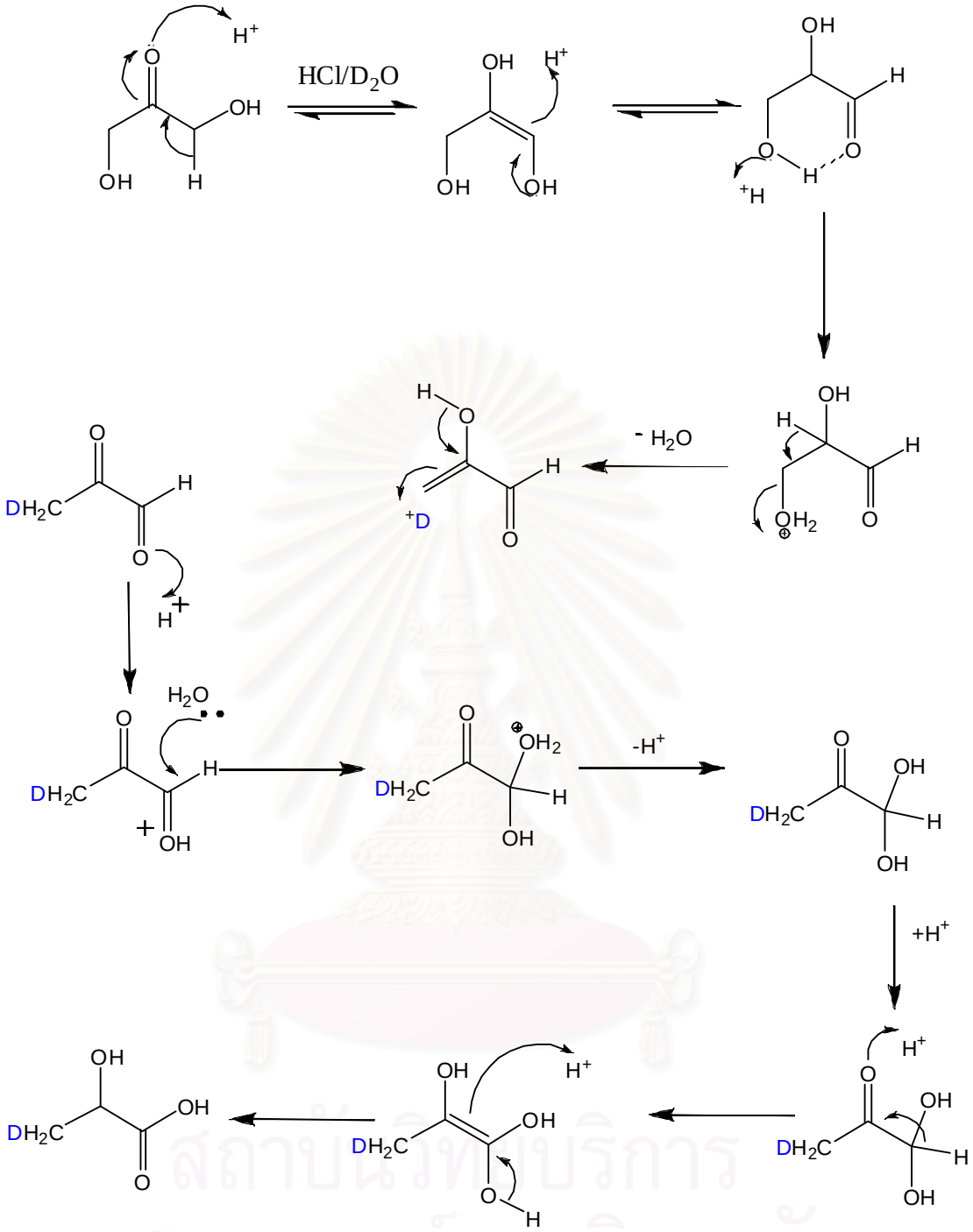
4.6 NMR measurement

Many reports on the mechanism of **3** formation have been documented [34, 44–46]. The mechanism of transformation of **1** to **3** with catalysis by base is shown in Scheme 4-7. In aqueous alkaline solution, **1** which is gradually keto-enol tautomerized into **7** [47] and transformed to **8** as an intermediate. The latter is converted to **9** and then tautomerize to **3**.



Scheme 4-7 Proposed mechanism of base-catalyzed conversion **1** to **3** [44].

From this study, the mechanism for the formation of lactic acid by tautomerization was proposed as shown in Scheme 4-8. In the first step, compound **1** was protonated by acid and tautomerized into enol **8** and then converted to compound **7**. After that, compound **7** lose water to convert to compound **9** and change into **6**. Mechanism of lactic acid production from compound **1** was investigated by the incorporation of deuterium atom from solvent into the product as shown in Scheme 4-8. The resulting product could be observed by ^{1}H and ^{13}CNMR spectroscopy.



Scheme 4-8 Proposed mechanism for the formation of **3** in HCl/D_2O.

In this study, mechanism of **3** formation under optimized condition obtained from above studies was investigated by ^{13}C NMR spectroscopy. Firstly, the solution of compound **1** without HCl in D_2O was run for ^{13}C NMR spectrum. Spectrum consisted of the signals at δ 211.7 of C=O and NMR spectrum indicated the presence of cyclic hemiacetal dimer as shown in Figure 4-3 [46,48].

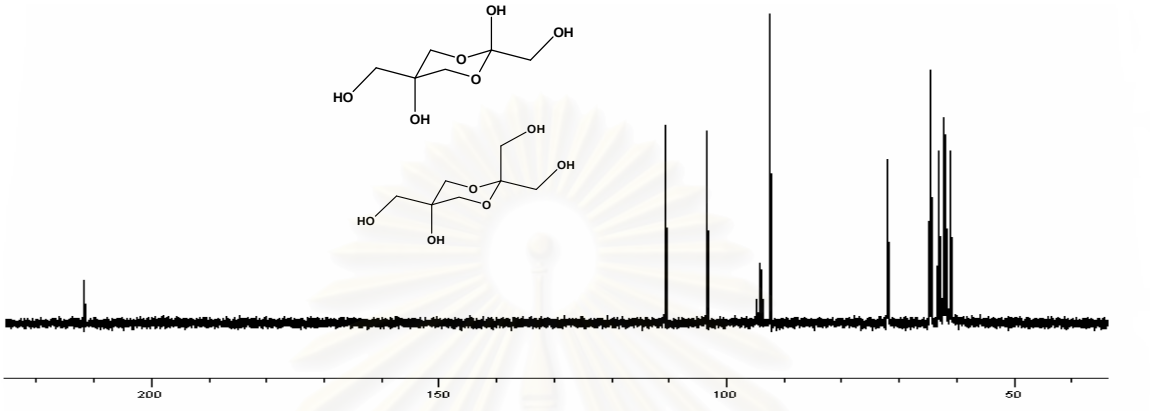


Figure 4-3 ^{13}C-NMR spectrum of dihydroxycetone in D_2O.

Then, the solution of **1** was treated with HCl and ^{13}C spectrum was recorded immediately. NMR spectrum contained signals at δ 63.9 of CH_2 and δ 209.6 of C=O and the cyclic hemiacetal dimer almost disappeared (Figure 4-4).

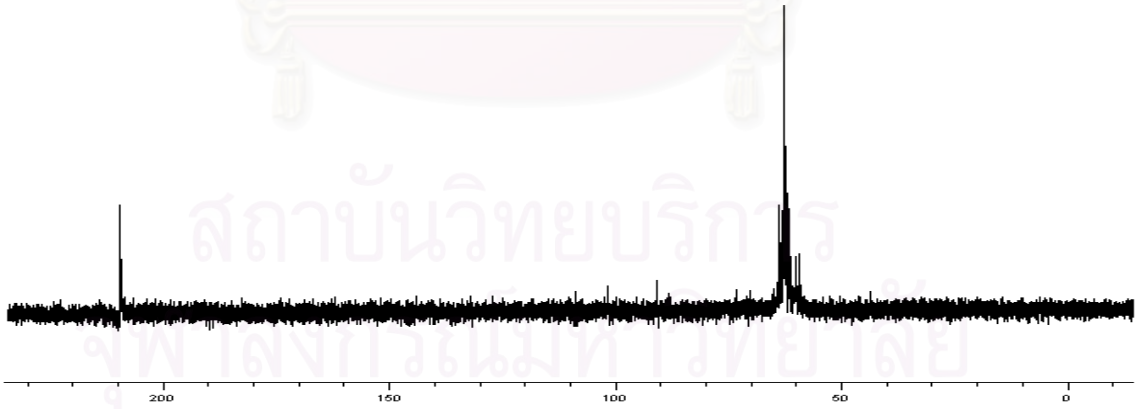


Figure 4-4 ^{13}C-NMR spectrum of dihydroxycetone with 60% HCl in D_2O at room temperature.

After that, the solution was heated at 100 °C for 1 h, the NMR tube was cooled to 0°C. As soon as possible the NMR spectrum was recorded. The ^{13}C NMR spectrum indicated peak of carboxylic acid at δ 181.7 and methyl group at δ 19.9 as shown in Figure 4-5.

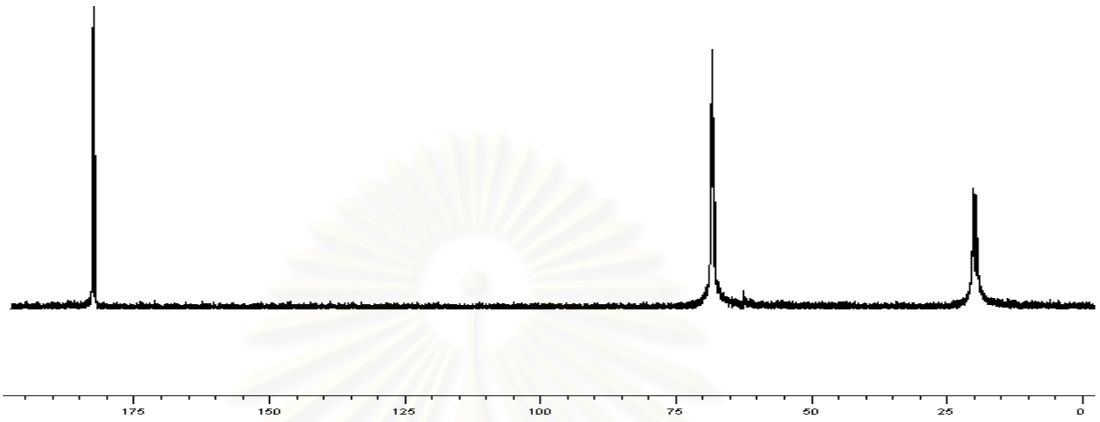


Figure 4-5 ^{13}C-NMR spectrum of dihydroxycetone with 60% HCl in D_2O under reflux at 100 °C for 1 h.

For comparison, it was found that the methyl group of commercial lactic acid appeared as singlet in NMR spectrum but for the methyl group of lactic acid obtained in this reaction the signal appeared as multiplet including a triplet in the ^{13}C NMR spectrum which indicated that solvent deuterium atom was incorporated into product. Since deuterium has spin quantum number I = 1, thus the carbon bearing one deuterium atom will split to three peaks. However, CH–OH both of compound **3** from standard and the one obtained from this reaction were not different as shown in Figure 4-6. Therefore, it supported that the mechanism involved the keto-enol tautomerization and proton transfer from solvent.

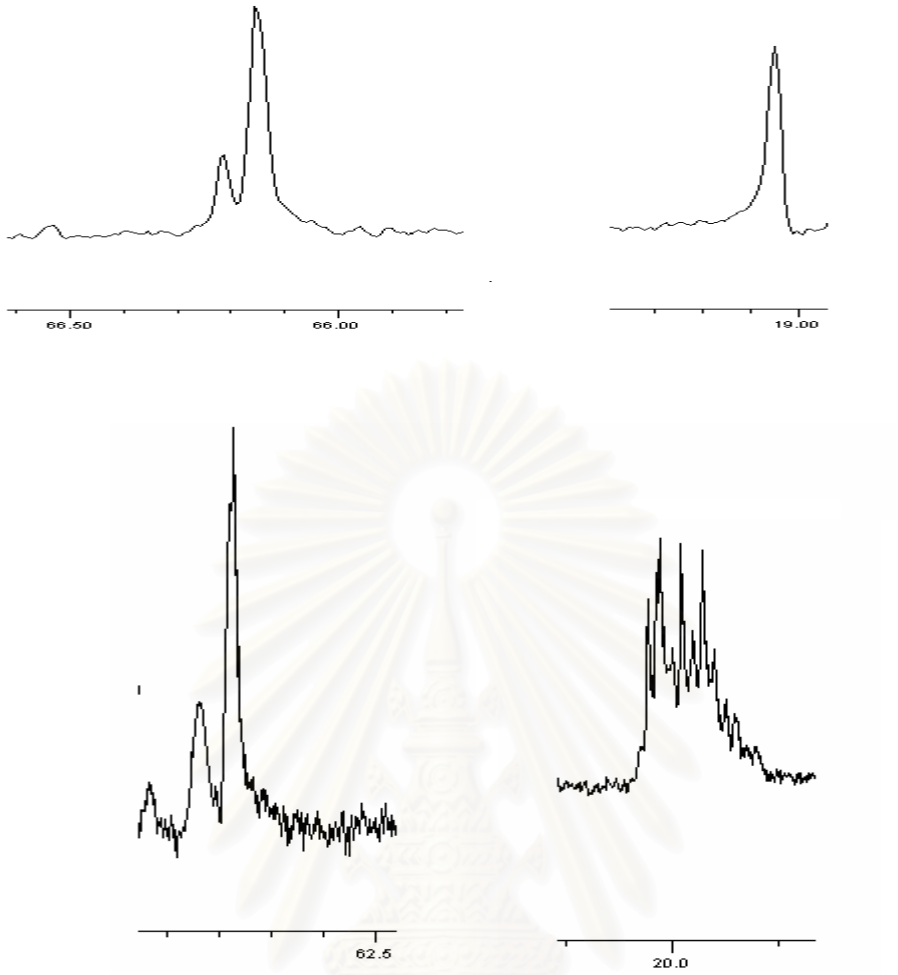


Figure 4-6 ^{13}C NMR of lactic acid by deuterium exchange. Upper part: commercial lactic acid. Lower part: lactic acid obtained from rearrangement dihydroxyacetone in D_2O+HCl.

CHAPTER V
CONCLUSION

5.1 Conclusion

The purpose of this study was to study the Wolff-Kishner and Clemmensen reduction of 1,3-dihydroxyacetone in order to convert carbonyl group to methylene group. Wolff-Kishner reduction was carried out on 1,3-dihydroxyacetone by oximation followed by reductive deoximation. However, 1,3-propanediol (**2**) was not successfully prepared from Wolff-Kisnner reaction due to the unexpected formation of 3,3,6,6-tetrahydroxymethyl-1,2,4,5-tetrazinane (**6**). The formation of this new compound was structurally confirmed by single crystal X-ray crystallographic analysis. Since the conversion of **1** to **3** by Wolff-Kishner reduction could not give the desired product due to the decomposition of intermediate **6**, therefore, the reduction of **1** by Clemmensen reduction was carried out. Surprisingly, this reaction gave lactic acid instead of the expected 1,3-propanediol. The optimized condition for lactic acid formation was 1 equiv of 1,3-dihydroxyacetone in the presence of 60% HCl under refluxing for 12 h. The yield of lactic acid was 84%. The mechanism of transformation from 1,3-dihydroxyacetone into lactic acid took place via keto-enol tautomerization and followed by proton transfer from solvent. The mechanism was proposed and proved by deuterium exchange.

5.2 Future study

- The chemistry and application of 3,3,6,6-tetrahydroxymethyl-1,2,4,5-tetrazinane should be studied.
- The kinetic of lactic acid formation from dihydroxyacetone in acid solution should be investigated.

REFERENCES

[1] Dalai, A. Value-added co-products can improve the economics of a climate friendly fuel. 2006 [online] Available from: http://www.biocap.ca [2008; August 7].

[2] Marchetti, J. M.; Miguel, V. U.; Errazu, A. F. Heterogeneous esterification of oil with high amount of free fatty acids. Fuel 86 (2006): 906–910.

[3] Leung, D.Y.C.; Transesterification of neat and used frying oil: optimization for biodiesel production. Fuel Process. Technol. 87 (2006): 883–890.

[4] 2020: A Global Market Survey, 2nd Edition [online] http://www.emerging-markets.com/biodiesel/ [2008; December 16]

[5] Glycerin to Propylene Glycol: An Introduction [online] Available from: http://www.renewablealternatives.com/glycerin_pg_intro.pdf [2008; Septempber 24].

[6] Air Pollution from Large Diesel Trucks and Buses [online] Available from: http://www.edf.org/article.cfm?contentID=1160 [2007, July 24].

[7] Vicente, G.; Martinez, M.; Aracil, J. Intergrated biodiesel production: a comparison of different homogeneous catalysts system. Bioresour. Technol. 92 (2004): 297–305.

[8] Ma, F.; Hanna M.A. Biodiesel production: A review. Bioresour. Technol. 70 (1999): 1–15.

[9] Jitputti, J.; Kitiyanan, B.; Rangsunvigit, P.; Bunyakiat, K.; Attanatho, L. Jenvanitpanjakul, P. Transesterification of crude palm kernel oil and crude coconut oil by different solid catalysts. Chem. Eng. J. 116 (2006): 61–66.

[10] Glycerol [online] Available from: http://en.wikipedia.org/wiki/Glycerol [2008; October 7]

[11] Bozell, J.J., Oleochemicals in the Biorefinery: Products and Opportunities 2006 Growing the Bioeconomy Conference Iowa State University Ames, IA August 28, 2006.

[12] Naresh, P., and Brian, H., Value-added Utilization of Crude Glycerol from biodiesel production: A Survey of Current Research Activities, J. American Society of Agricultural and Biological Engineers (ASABE), Paper Number: 066223, 2006.

[13] Dihydroxyacetone [online] Available from: http://en.wikipedia.org/wiki/Dihydroxyacetone [2008; December 12].

[14] Ciriminna, R.; Palmisano, G.; Pina, C.D.; Rossi, M.; Pagliaro, M. One-pot electrocatalytic oxidation of glycerol to DHA. Tetrahedron Lett. 47 (2006): 6993–6995.

[15] Mishra, R.; Rani, S.; Kumar, A. Microbial production of dihydroxyacetone. Biotechnol. Adv. 26 (2008): 293–303.

[16] Bauer, R.; Hekmat, D. Development of a transient segregated mathematical model of the semicontinuous microbial production process of Dihydroxyacetone. Biotechnol. Prog. 22 (2006): 278–284.

[17] 1,3-propanediol product overview [online] Available from: http://www.shell.com/home/content/chemicals/products_services/our_products/corterra_pdo/1_3_propanediol/product_overview/1_3_propanediol_overview.html [2007; November 3]

[18] Huang, H.; Gong, C.S.; Tsao, G.T. Production of 1,3-propanediol by Klebsiella pneumoniae. Appl. Biochem. Biotechnol. 98 (2002): 687–698.

[19] Zeng, A.P.; Biebl, H. Bulk chemicals from biotechnology: the case of 1,3-propanediol production and the new trends. Adv. Biochem. Eng. 74 (2002): 240–259.

[20] Haas, T.; Jaeger, B.; Weber, R; Mitchell, S.F.; King, C.F. New diol processes: 1,3-propanediol and 1,4-butanediol. Appl. Catal., A. 280 (2005): 83–85.

[21] Mchugh, J.; Dumont, S.N.; Paradis, J.; Nguyen, A.L.; Levesque, S.; Carrier, A. New and Simple HPLC Method for the determination of lactic acid content in ciprofloxacin injection. J. Liq. Chromatogr. Related Technol. 29 (2006): 1905–1916.

[22] Boonkong, W. Separation of lactic acid from fermentration broth by ion-exchange resin and electrodialysis. Master's Thesis. Program in Petrochemistry and Polymer Science, Faculty of Science, Chulalongkorn University, 2007.

[23] Narayanan, N.; Roychoudhury, K.P.; Srivastava, A. L (+) lactic acid fermentation and its product polymerization. Electron. J. Biotechnol. 7 (2004): 167–179.

[24] Choi, J.; Kang, Y. Direct deoxygenation of aryl ketones using gallium (III) chloride and chlorodimethylsilane. Bull. Korean. Chem. Soc. 26 (2005):343– 344.

[25] Aldehydes and Ketones: Clemmensen reaction [online] Available from: http://www.cem.msu.edu/~reusch/VirtualText/aldket1.htm [2007; September 14]

[26] Streitwieser, A; Heathcock, C.H., Kosower, M.E. Introduction to organic chemistry. 4rd ed. New York: Macmillan, (1992) 414–415.

[27] Keto-enol tautomerism [online] Available from: http://en.wikipedia.org/wiki/Keto-enol_tautomerism [2008; Novemver 24].

[28] Garcia, R.; Besson, M.; Gallezot, P. Chemoselective catalytic oxidation of glycerol with air on platinum metals. Appl. Catal., A 27 (1995): 165–176.

[29] Kimura , H. Selctive oxidation of glycerol on a platinum-bismuth catalyst by using a fixed bed reactor. Appl. catal., A Gen. 105 (1993): 147–158.

[30] Nanjundaswamy, H.M.; Pasha, M. H. Reductive deoximation of aryloximes into hydrocarbons by hydrazine/KOH: A novel application of the Wolff-Kishner reduction. Synth. Commun. 36 (2006) 2183–2187.

[31] Damljanovic, I.; Vukicevic, M.; Vukicevic, R. D. A simple synthesis of oximes. Monatsh. Chem. 137 (2006): 301–305.

[32] Sharghi, H.; Sarvari, M. H. A mild and versatile method for the preparation of oximes by use of calcium oxide. J. Chem. Research (S). (2000): 24–25.

[33] Bulavka, N.V. Modified Clemmensen reduction of some polycyclic alkylarylketones. Comparison of zinc dust and granulated zinc action 9th International Electronic Conference on Synthetic Organic Chemistry, 2006[online], Available from: http://www.lugo.usc.es/~qoseijas/ecsoc-9.htm [2008; September 3]

[34] Bicker, M.; Endres, S.; Ott, L.; Vogel, H. Catalytic conversion of carbohydrate in subcritical water: A new chemical process for lactic acid production. J. Mol. Catal. A: Chem. (2005): 151–157.

[35] Yan, X.; Jin, F.; Tohji, K.; Moriya, T.; Enomoto, H. Production of lactic acid from glucose by alkaline hydrothermal reaction. J. Mater. Sci. (2007): 9995–9999.

[36] Sheldrick, G. M., SHELXS-97, Program for Crystal Structure Refinement, University of Göttinggen, Germany 1997.

[37] Sheldrick, G. M., SHELXL-97, Program for Crystal Structure Refinement, University of Göttinggen, Germany 1997.

[38] Kuznetsov, A.I.; Vladimirova, I.A.; Serova, T.M.; Moskovkin, A.S. Heteroadamantanes and their derivatives. 17.*wolff-kishner reduction of 3,6- diazahomoadamantan-9-ones. Chem. Heterocycl. Compd. 28 (1992): 551–555.

[39] Toshihiko, M.; Masahiro, Y.; Shohei, I. Selective synthesis of DL-dendroketose from Formaldehyde. Chem. Lett. (1984): 1819–1822.

[40] Boggs, R.A.; Hasan F.B.; Mahoney, J.B.; Mehta, A.C.; Palumbo, C.M.K.; Puttick, A.J.; Taylor, L.D. Kinetics and mechanism of the alkaline release of phenyl(mercapto)tetrazoles from a-oximes. J. Chem. Soc., Perkin Trans. 2: Physical Organic Chemistry (1992): 1271–1277.

[41] Huang, M. Simple modification of the Wolff-Kishner reduction. J. Am. Chem. Soc. 68 (1946): 2487–2488.

[42] Elmore, L.; Martin, L. A modification of the Clemmensen method of reduction. J. Am. Chem. Soc. 58 (1936): 1438–1442.

[43] Dey, A.N.; Linsted, R.P. The Supposed isolation of a second form of ββ-dimethylcyclohexanone. Ring rearrangement during Clemmensen reaction reduction J. Chem. Soc. (1935): 1063.

[44] Evans, W.L., Cornthwaite, R. The mechanism of carbohydrate oxidation. VII. The action of potassium hydroxide on dihydroxyacetone. J. Am. Chem. Soc. 50 (1928): 486–492.

[45] Degani, C.; Halmann, M. Alkaline ractins of D-glucose 6- phosphate. J. Am. Chem. Soc 90 (1968): 1313–1317.

[46] Eriksen, J.; Monsted, O.; Monsted, L. Mechanism of lactic acid formation catalyzed by tetraamine rhodium (III) complexes. Transition Met. Chem. 23 (1998): 783–787.

[47] Rona - Dihydroxyacetone Product Information [online] Avaliable from: www.synergyscents.com/supplies/Dihydroxyacetone.pdf [2008; September 4]

[48] Glushonok, G. K.; Glushonok T. G.; Maslovskaya L. A.; Shadyro O. I. A ^{1}H and ^{13}C NMR and UV Study of the State of Hydroxyacetone in Aqueous solutions. Russ. J. Gen. Chem. 73 (2003): 1027–1031.

APPENDICES

APPENDIX A

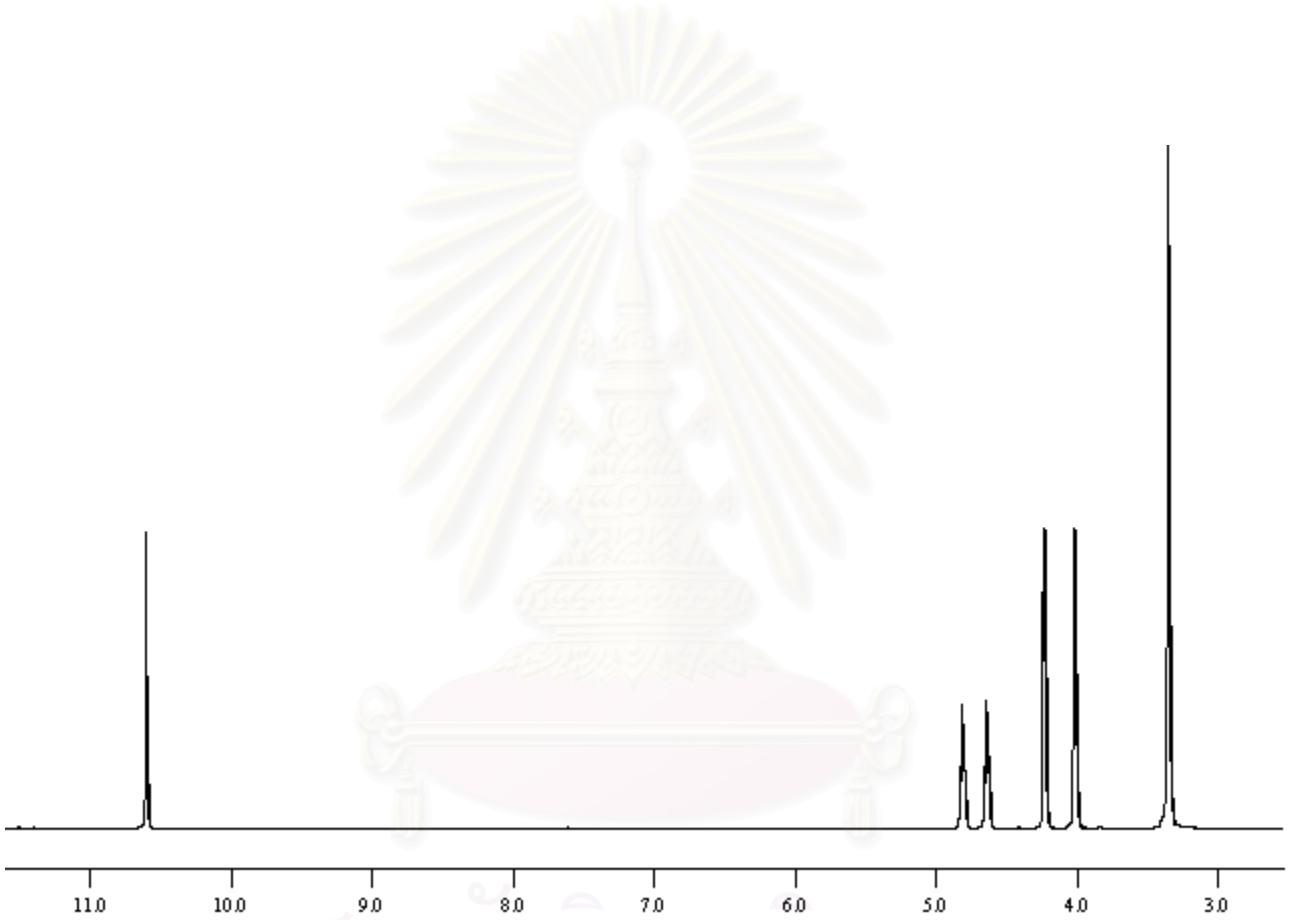


Figure A-1 ^{1}H-NMR spectrum of dihydroxyacetone oxime (**4**).

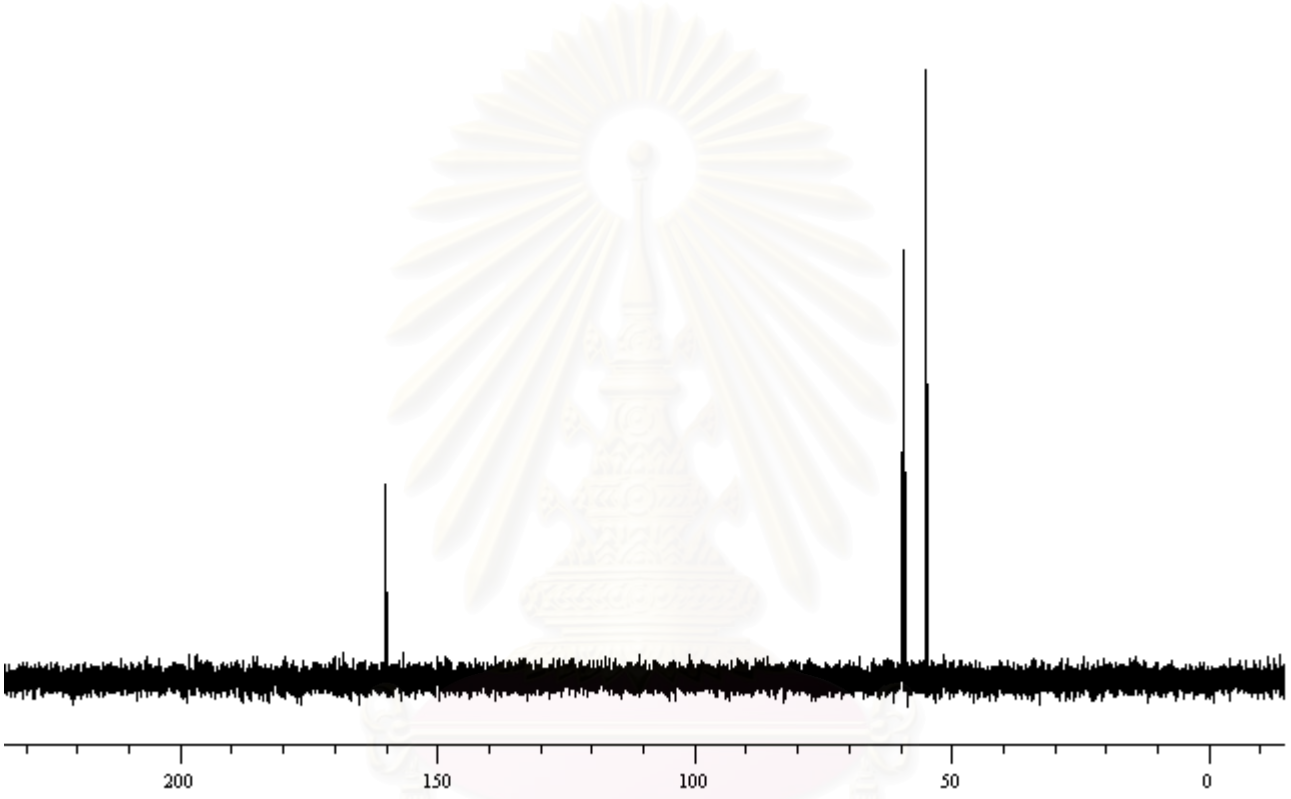


Figure A-2 ^{13}C-NMR spectrum of dihydroxyacetone oxime (**4**).

58

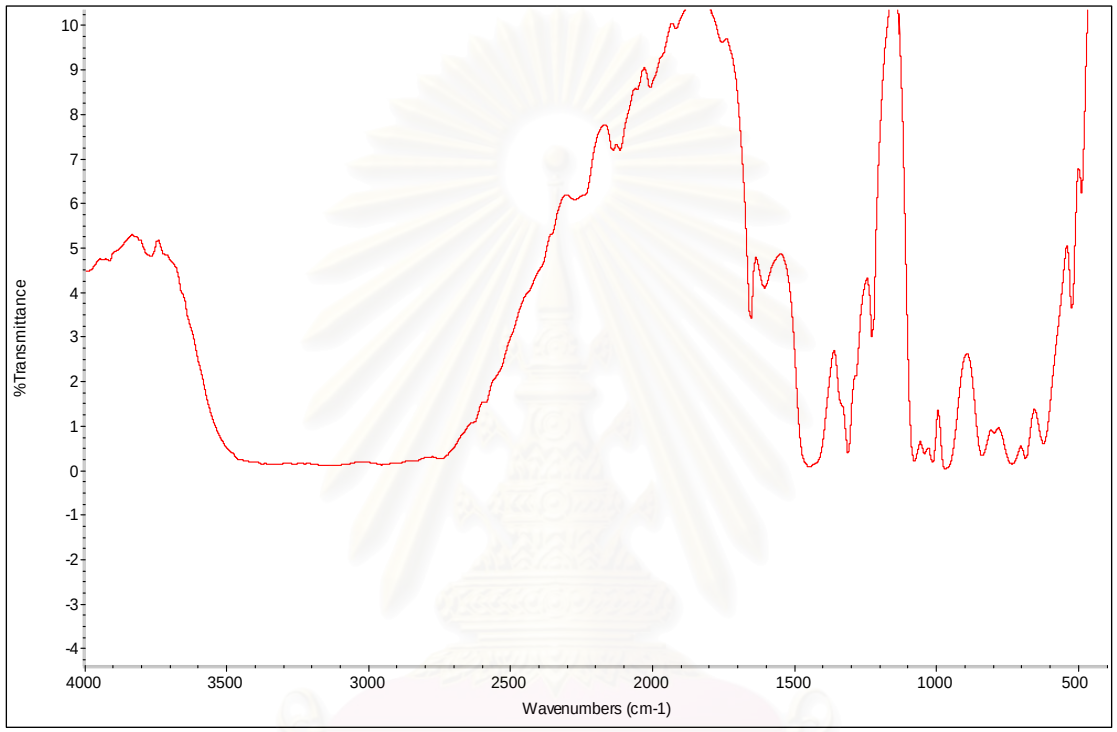


Figure A-3 IR of dihydroxyacetone oxime (**4**).

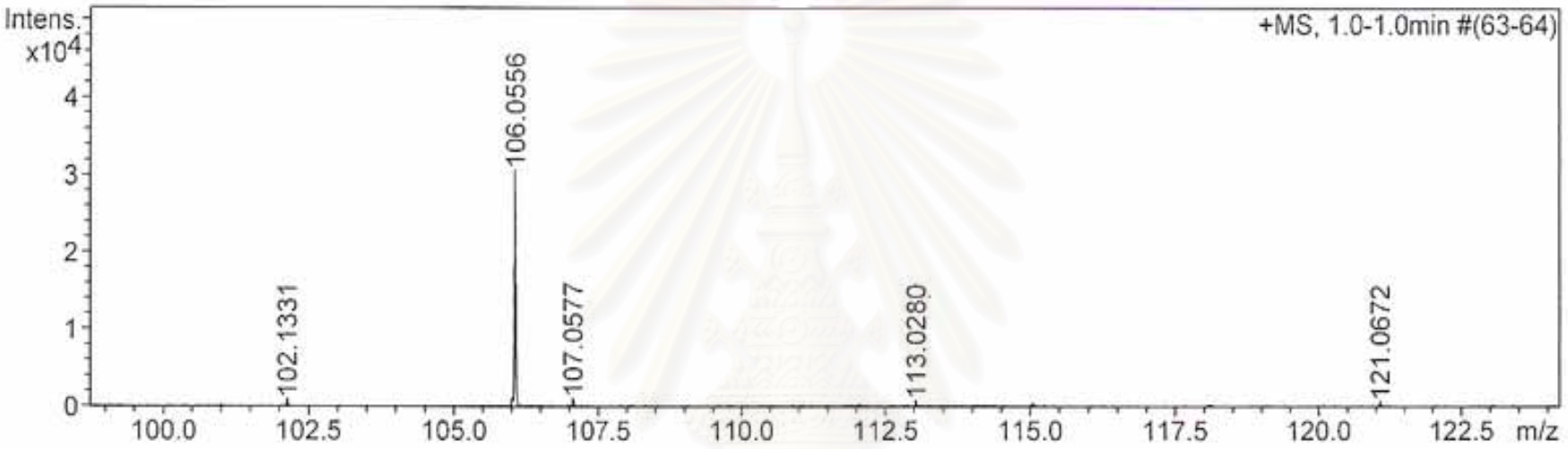


Figure A-4 Mass spectrum of dihydroxyacetone oxime (**4**).

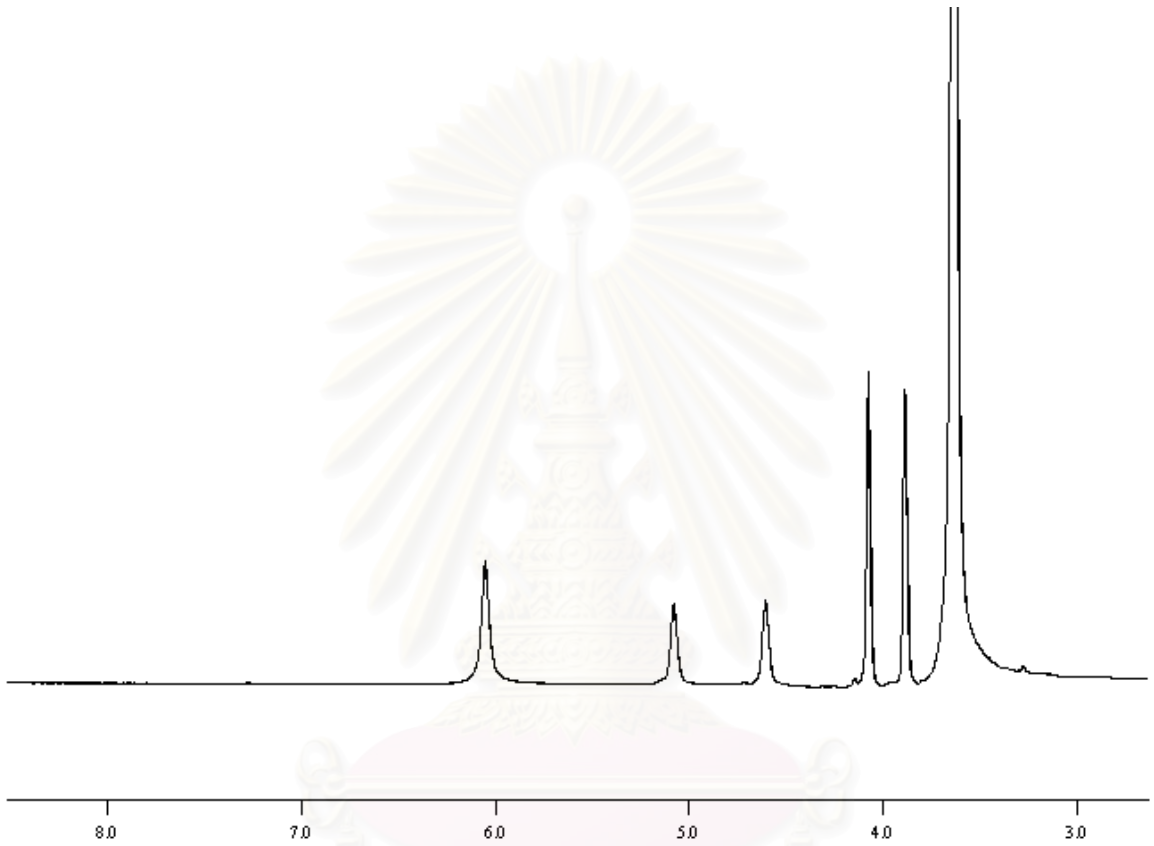


Figure A-5 ^{1}H-NMR spectrum of 3,3,6,6-tetrahydroxymethyl-1,2,4,5-tetrazinane (**6**).

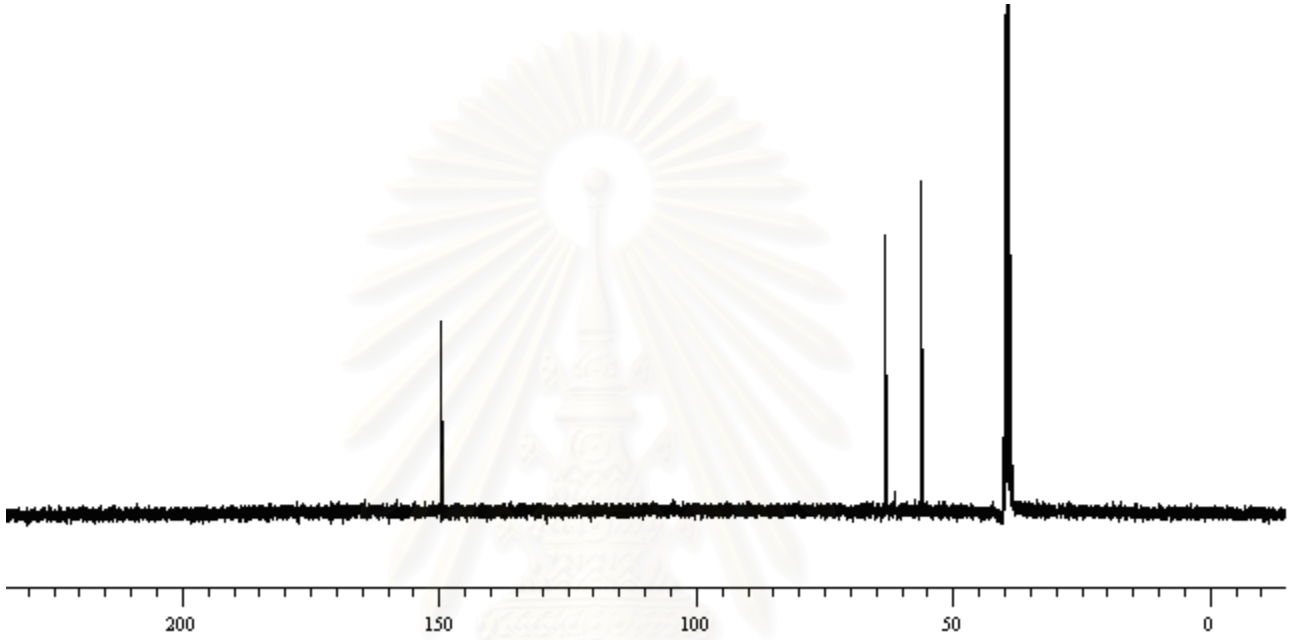


Figure A-6 ^{13}C-NMR spectrum of 3,3,6,6-tetrahydroxymethyl-1,2,4,5-tetrazinane (**6**).

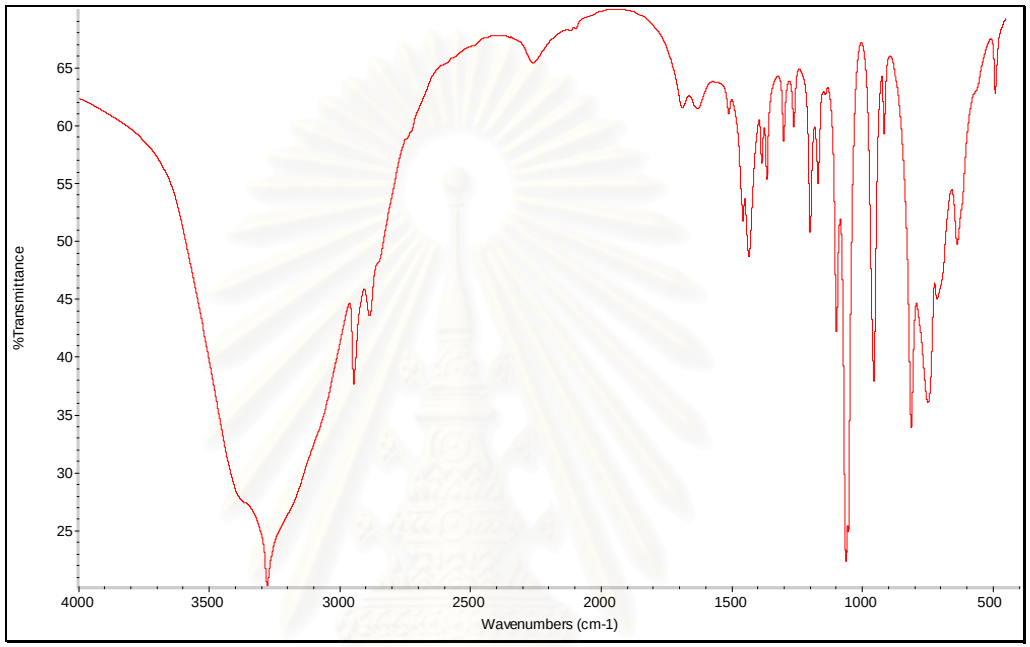


Figure A-7 IR spectrum of 3,3,6,6-tetrahydroxymethyl-1,2,4,5-tetrazinane (**6**).

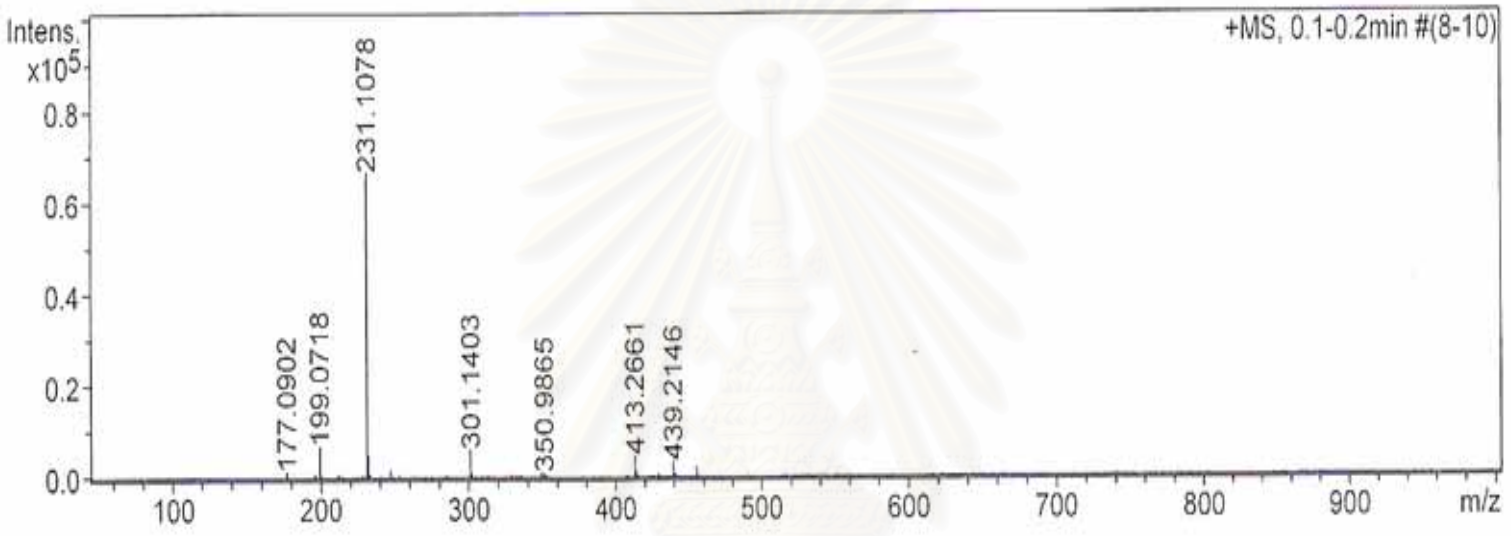


Figure A-8 Mass spectrum of 3,3,6,6-tetrahydroxymethyl-1,2,4,5-tetrazinane (**6**).

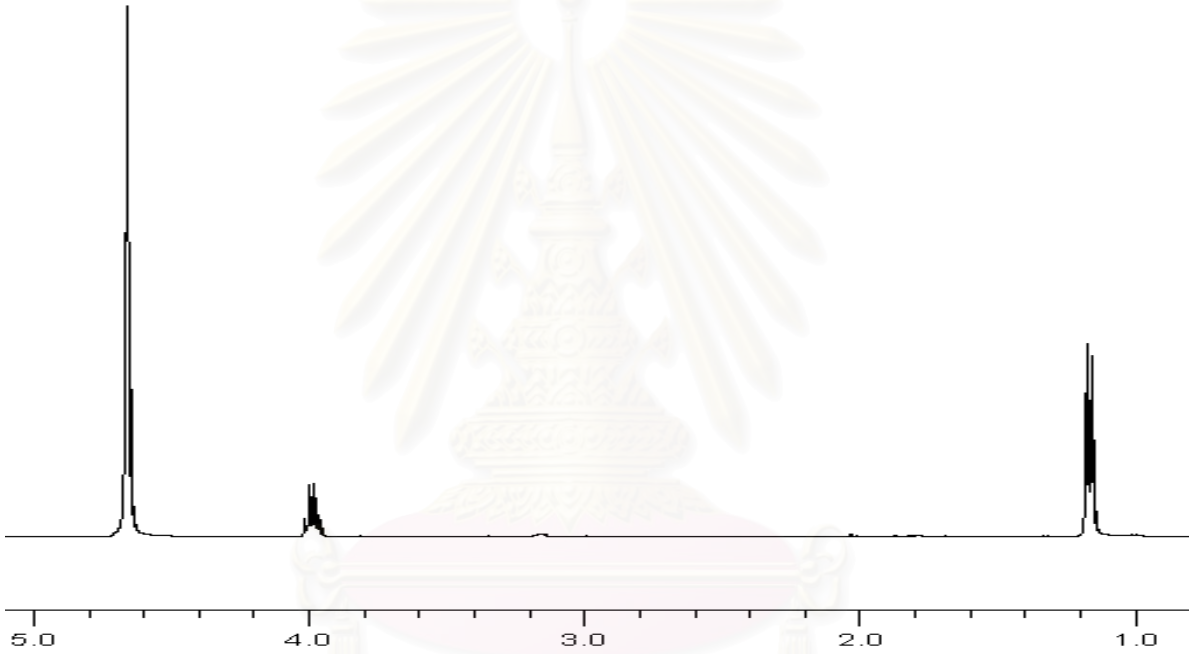


Figure A-9 ^{1}H-NMR spectrum of Lactic acid (**3**).

65

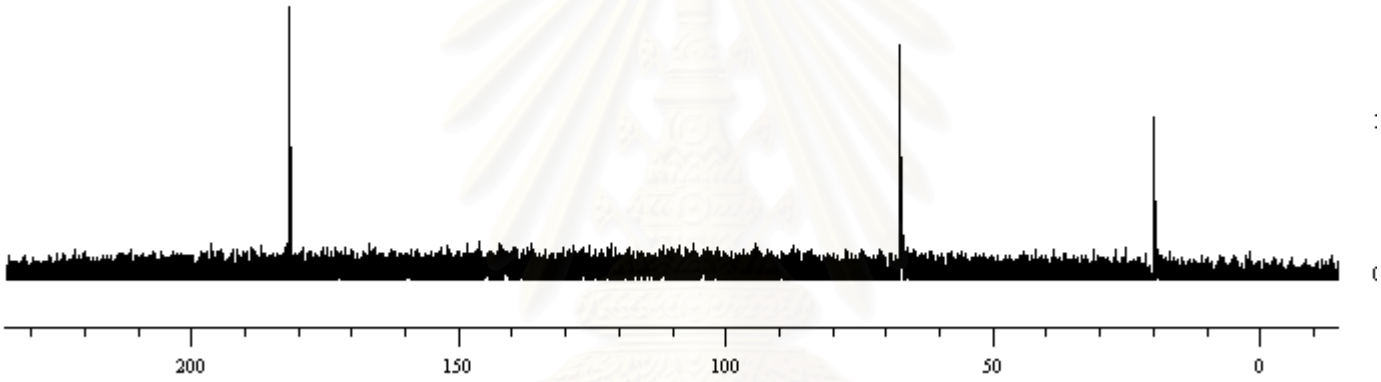


Figure A-10 ^{13}C-NMR spectrum of Lactic acid (**3**).

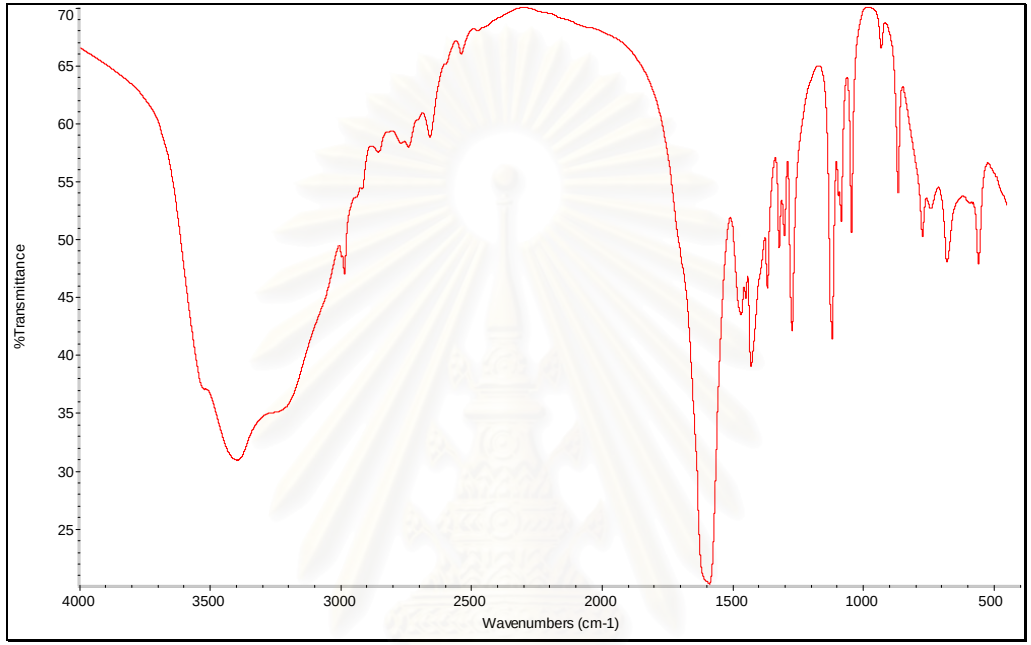


Figure A-11 IR spectrum of lactic acid (**3**).

APPENDIX B

Table B-1 Crystal and experiment data.

Chemical formula: $C_3H_{12}N_2O_4$

Formula weight: 140.15

T = 293.2 K

Crystal system: Triclinic

Space group: $P1$ $Z = 2$

a = 6.3071(6)Å α = 71.041(2)°

b = 7.0326(7)Å β = 74.459(2)°

c = 8.4034(8)Å γ = 85.082(2)°

V = 339.63(6) Å^3

D_x = 1.50 g/cm^3

Radiation: Mo Kα (λ = 0.71073Å)

μ (Mo Kα) = 0.124 mm^{-1}

F(000) = 152.0

Crystal size = 0.25 x 0.25 x 0.25 mm

No. of reflections collected = 4712

No. of independent reflections = 4083

θ range for data collection: 2.65° to 30.42°

Data/Restraints/Parameters = 2091/3/195

Goodness-of-fit on F^2 = 1.050

R indices [I>2σ(I)]: $R1$ = 0.0347 , $wR2$ = 0.0948

R indices (all data): $R1$ = 0.0439 , $wR2$ = 0.1006

$(\Delta\rho)_{max}$ = 0.289eÅ^{-3}

$(\Delta\rho)_{min}$ = -0.203eÅ^{-3}

Measurement: Bruker SMART CCD diffractometer

Program system: X

Structure determination: Direct methods

Refinement: Full-matrix least-squares on F^2 (*SHELXL-97*)

CCDC deposition number: X

Table B-2 Final atomic coordinates (x 10^4) and equivalent isotropic thermal parameter (U_{ij}) (Å^2 x 10^3).

Atom	***x***	***y***	***z***	U_{ij}
O(1W)	7053(6)	7712(4)	8891(4)	36(1)
O(2W)	1506(6)	-2358(6)	8795(6)	67(1)
O(3W)	831(6)	-1580(4)	4116(4)	35(1)
O(4W)	-3640(6)	-1670(5)	4355(5)	45(1)
C(4)	3647(7)	3376(5)	4828(5)	22(1)
C(2)	4266(6)	2818(5)	8174(5)	21(1)
C(3)	5727(7)	4397(6)	3502(5)	30(1)
C(4)	2054(8)	2980(7)	3891(6)	32(1)
C(5)	2196(6)	1721(6)	9514(5)	23(1)
C(6)	5860(7)	3213(6)	9136(6)	27(1)
O(1)	210(5)	1820(5)	5056(4)	37(1)
O(2)	5258(5)	6355(4)	2434(4)	35(1)
O(3)	7717(5)	4324(4)	7919(4)	34(1)
O(4)	2663(5)	-175(4)	10565(4)	34(1)
N(2)	3591(5)	4760(5)	7136(4)	23(1)
N(1)	2497(5)	4640(4)	5875(4)	21(1)
N(4)	4322(5)	1381(4)	5858(9)	21(1)
N(3)	5415(5)	1509(4)	7151(4)	22(1)

Table B-3 Bond lengths (Å) and bond angles (°).

Compound 5

Bond lengths (Å)	
C(1)-N(2)	1.466(5)
C(1)-N(4)	1.485(5)
C(1)-C(4)	1.522(5)
C(1)-C(3)	1.529(5)
C(2)-N(2)	1.460(5)
C(2)-N(3)	1.476(5)
C(2)-O(6)	1.539(5)
C(2)-C(5)	1.546(4)
C(3)-O(2)	1.434(5)
C(4)-O(1)	1.418(5)
C(5)-O(4)	1.397(5)
C(6)-O(3)	1.423(5)
N(2)-N(1)	1.437(5)
N(4)-N(3)	1.463(5)

Bond angles (°)	
N(1)-C(1)-N(4)	114.2(3)
N(1)-C(1)-C(4)	107.2(3)
N(4)-C(1)-C(4)	106.7(3)
N(1)-C(1)-C(03)	111.7(3)
N(4)-C(1)-C(3)	106.9(3)
C(4)-C(1)-C(3)	109.9(3)
N(2)-C(2)-N(3)	114.4(3)
N(2)-C(2)-C(6)	108.0(3)
N(3)-C(2)-C(6)	107.4(3)
N(2)-C(2)-C(5)	108.3(3)
N(3)-C(2)-C(5)	109.2(3)
C(6)-C(2)-C(5)	109.5(3)
O(2)-C(3)-C(1)	111.5(3)

O(1)-C(4)-C(1)	112.5(4)
O(4)-C(5)-C(2)	112.9(3)
O(3)-C(6)-C(2)	110.2(3)
N(1)-N(2)-C(2)	114.2(3)
N(2)-N(1)-C(1)	113.5(3)
N(3)-N(4)-C(1)	112.8(3)
C(4)-N(3)-C(2)	113.6(3)

Table B-4 Anisotropic displacement parameters ($A^{\wedge 2}$ x $10^{\wedge 3}$)

U12	**U11**	**U22**	**U33**	**U23**	**U13**	**U12**
O(1W)	37(2)	31(2)	37(2)	-10(1)	-7(1)	7(1)
O(2W)	35(2)	74(2)	126(4)	-80(3)	-20(2)	7(2)
O(3W)	41(2)	27(2)	31(2)	-5(1)	-5(1)	6(1)
O(4W)	37(2)	35(1)	60(2)	-21(1)	-4(1)	-1(1)
C(1)	24(2)	18(2)	22(2)	-3(1)	-11(1)	2(1)
C(2)	23(2)	23(2)	18(2)	-9(1)	-1(1)	-2(2)
C(3)	38(3)	21(2)	25(2)	-3(2)	-6(2)	2(2)
C(4)	36(3)	33(2)	25(2)	-7(2)	-5(2)	6(2)
C(5)	20(2)	28(2)	18(2)	-6(1)	0(1)	-4(1)
C(6)	28(2)	29(2)	30(2)	-10(2)	-16(2)	0(2)
O(1)	25(2)	41(2)	47(2)	-21(2)	-4(1)	-4(1)
O(2)	46(2)	25(1)	27(2)	2(1)	-11(1)	-1(1)
O(3)	27(2)	33(2)	46(2)	-22(2)	-6(1)	-2(1)
O(4)	40(2)	29(1)	25(2)	-3(1)	-1(1)	-5(1)
N(2)	25(2)	23(1)	22(2)	-6(1)	-9(1)	-1(1)
N(1)	23(2)	20(2)	19(2)	-7(1)	-3(1)	1(1)
N(4)	25(2)	16(1)	22(2)	-7(1)	-4(1)	0(1)
N(3)	19(2)	23(2)	25(2)	-6(1)	-9(1)	2(1)

VITA

Miss Sasipim Kongsutjarit was born on October 7, 1982 in Chonburi province, Thailand. She got a Bachelor's Degree in Chemistry from the faculty of Science, Chulalongkorn University in 2006. After that, she continued her Master Degree program in Petrochemistry and Polymer Science, Faculty of Science, Chulalongkorn University and completed the program in 2008.