การเตรียม 1-เฮโล-2,3-โพรเพนไดออลและกลีเซอริลโมโนเอสเทอร์จากของเสียกลีเซอรอล

นางสาวลดาวัลย์ จันทรเดช

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
สาขาวิชาปิโตรเคมีและวิทยาศาสตร์พอลิเมอร์
คณะวิทยาศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
ปีการศึกษา 2551

PREPARATION OF 1-HALO-2,3-PROPANEDIOL AND GLYCERYL MONOESTER FROM GLYCEROL WASTE

Miss Ladawan Chantharadet

A Thesis Submitted in Partial Fulfillment of the Requirements
for the Degree of Master of Science Program in Petrochemistry and Polymer Science
Faculty of Science
Chulalongkorn University
Academic Year 2008

Thesis Title	PREPARATION OF 1-HALO-2,3-PROPANEDIOL AND GLYCERYL MONOESTER FROM GLYCEROL WASTE
By	Miss Ladawan Chantharadet
Field of Study	Petrochemistry and Polymer Science
Thesis Advisor	Assistant Professor Warinthorn Chavasiri, Ph.D.

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
(Professor Pattarapan Prasassarakich, Ph.D.)

Warinthorn Chavasiri
..... Thesis Advisor
(Assistant Professor Warinthorn Chavasiri, Ph.D.)

W. Trakarnpruk
..... Examiner
(Associate Professor Wimonrat Trakarnpruk, Ph.D.)

Kitti Nivatvongs
..... External Examiner
(Kitti Nivatvongs, Ph.D.)

ลดาวัลย์ จันทรเดช : การเตรียม 1-เฮโล-2,3-โพรเพนไดออลและกลีเซอริลโมโนเอสเทอร์จากของเสียกลีเซอรอล. (PREPARATION OF 1-HALO-2,3-PROPANEDIOL AND GLYCERYL MONOESTER FROM GLYCEROL WASTE) อ. ที่ปรึกษาวิทยานิพนธ์หลัก: ผศ.ดร.วรินทร ชวศิริ, 60 หน้า.

ได้แยกของเสียกลีเซอรอลจากกระบวนการผลิตไบโอดีเซลที่ได้จากโรงกลั่นบางจากและนำมาเตรียมโมโน-และไดกลีเซอไรด์เพื่อให้มีมูลค่ามากขึ้น การทำให้กลีเซอรอลบริสุทธิ์ทำได้อย่างมีประสิทธิผลโดยวิธีการสกัดด้วยกรด-เบส พบว่ากรดซัลฟูริก เป็นกรดที่เหมาะสมและสามารถแยกกลีเซอรอลได้ในช่วง 40-45 เปอร์เซ็นต์ ได้เตรียม 1,2-ออร์โทไอโซโพรพิลริดีนกลีเซอรอลจากกลีเซอรอลที่ทำให้บริสุทธิ์แล้วได้พัฒนากระบวนการที่มีประสิทธิภาพภายใต้ภาวะที่ไม่รุนแรงสำหรับเตรียม (2,2-ไดเมทิล-1,3-ไดออกโซแลน-4-อิล)เมทิลเอสเทอร์ จากปฏิกิริยาเอสเทอริฟิเคชันระหว่าง 1,2-ออร์โทไอโซโพรพิลริดีนกลีเซอรอลกับกรดไขมันหลายชนิดโดยใช้ Cl_3CCONH_2 และ PPh_3 ภายใต้ภาวะที่ไม่รุนแรงและให้ผลิตภัณฑ์เอสเทอร์สูง นอกจากนี้ ได้ค้นพบวิธีการใหม่ในการเปิดวงไอโซโพรพิลริดีนจาก (2,2-ไดเมทิล-1,3-ไดออกโซแลน-4-อิล)เมทิลเอสเทอร์เป็นกลีเซอริลมอนอเอสเทอร์ ได้เปอร์เซ็นต์ผลิตภัณฑ์ดีเยี่ยมโดยใช้ $Br_3CCOCBr_3$ ในเมทานอลภายใต้ภาวะแสงยูวี คลอรีเนชันของ 1,2-ออร์โทไอโซโพรพิลริดีนกลีเซอรอลด้วย Cl_3CCONH_2 และ PPh_3 ได้เป็นแอลคิลคลอไรด์ที่สอดคล้องกันในปริมาณปานกลาง ข้อดีของวิธีการเตรียมนี้คือเกิดภายใต้ภาวะที่ไม่รุนแรงเตรียมได้ง่ายและให้ผลที่ดีต่อการเข้ากันได้ของการเกิดแอลคิลคลอไรด์จากไซคลิกอีเทอร์ใน 1,2-ออร์โทไอโซโพรพิลริดีนกลีเซอรอล

สาขาวิชา.....ปิโตรเคมีและวิทยาศาสตร์พอลิเมอร์.....ลายมือชื่อนิสิต.....

ปีการศึกษา.....2551.....ลายมือชื่ออ.ที่ปรึกษาวิทยานิพนธ์หลัก .....

4972462023 : MAJOR PETROCHEMISTRY AND POLYMER SCIENCE
KEY WORD: GLYCERYL MONOESTER / GLYCEROL / ESTERIFICATION

LADAWAN CHANTHARADET: PREPARATION OF 1-HALO-2,3-PROPANEDIOL AND GLYCERYL MONOESTER FROM GLYCEROL WASTE. THESIS ADVISOR: ASST. PROF. WARINTHORN CHAVASIRI, Ph.D., 60 pp.

Glycerol waste from biodiesel production of Bangchak oil refinery plant was separated and utilized to prepare value-added products as mono- and diglycerides. The purification of glycerol waste was successfully carried out by acid-base extraction. The most appropriate acid was H_2SO_4 and the glycerol could be recovered in the range of 40-45%. 1,2-*O*-isopropylideneglycerol was next synthesized from the purified glycerol. The mild and efficient approach for (2,2-dimethyl-1,3-dioxolan-4-yl)methyl ester synthesis by esterification of various fatty acids with 1,2-*O*-isopropylideneglycerol is developed employing Cl_3CCONH_2 and PPh_3 under mild conditions providing the desired esters in high yield. The novel method for deprotecting isopropylidene group of (2,2-dimethyl-1,3-dioxolan-4-yl)methyl ester into the corresponding glyceryl monoester in excellent yield by $Br_3CCOCBr_3$–UV irradiation in methanol is also successfully performed. The chlorination of 1,2-*O*-isopropylidene glycerol to the corresponding alkyl chlorides in moderate yield can also be achieved by the combination of Cl_3CCONH_2 and PPh_3. The advantages of these methods were mild reaction conditions, operational simplicity and good compatibility to alkyl chlorides from cyclic ether of 1,2-*O*-isopropylidene glycerol.

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

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

ACKNOWLEDGEMENTS

The author wishes to express her highest appreciation to her advisor Assistant Professor Dr. Warinthorn Chavasiri for his generous assistance, benevolent guidance and encouragement throughout the course of this research. In addition, thanks are extended to Natural Products Research Unit, Department of Chemistry, Faculty of Science, Chulalongkorn University, Thailand and Program of Petrochemistry and Polymer Science.

The greatest thanks are also extended to Professor Dr. Pattarapan Prasassarakich, Associate Professor Dr. Wimonrat Trakarnpruk and Dr. Kitti Nivatvongs for their comments, corrections and helps as thesis examiners. Appreciations are likewise stretched to the Program of Petrochemistry and Polymer Science, the Graduate School, Chulalongkorn University and Thailand Research Fund (TRF-MAG) for the financial support.

A deep affectionate gratitude is acknowledged to her family for their understanding, encouragement and support throughout the education course and also to her friends, seniors for their friendship, advices and succors in the entire course of study. Without them, the author would never have been able to achieve this goal.

CONTENTS

Page

Page

Page

LIST OF TABLES

Tables **Page**

LIST OF FIGURES

Figures **Page**

LIST OF SCHEMES

Scheme **Page**

LIST OF ABBREVIATIONS

%	percent
°C	degree of Celsius
α	alpha
δ	chemical shift
anh	anhydrous
$Br_3CCOCBr_3$	hexabromoacetone
$Br_3CCOOEt$	tribromoethylacetate
$CDCl_3$	deuterated chloroform
CH_2Cl_2	dichloromethane
$CHCl_3$	chloroform
cm	centimeter
cm^{-1}	unit of wavelength
CBr_4	carbon tetrabromide
CCl_4	carbon tetrachloride
d	doublet (NMR)
dd	doublet of doublet (NMR)
DMSO-d_6	deuterated dimethyl sulfoxide
D_2O	deuterium oxide
EtOAc	ethyl acetate
EtOH	ethanol
equiv	equivalent
Fig	figure
FFA	free fatty acid
g	gram (s)
h	hour (s)
hν	photoirradiation
Hz	hertz
J	coupling constant
m	multiplet (NMR)
m.p.	melting point
mg	milligram (s)

min	minute (s)
mL	milliliter
mm	millimeter
mmol	millimole
mol%	percent by mole
MeOH	methanol
MeOD-d_4	deuterated methanol
nm	nanometer
NMR	nuclear magnetic resonance
p-TsOH	*p*-toluenesulfonic acid
ppm	part per million
q	quartet (NMR)
Quant	quantitative
RT	room temperature
s	singlet (NMR)
t	triplet (NMR)
TLC	thin layer chromatography
UV	ultra violet
w	watt

CHAPTER I

INTRODUCTION

Nowadays, biodiesel is commonly produced by the transesterification of the vegetable oil or animal fat feedstock. There are several methods for carrying out this transesterification including the common batch process, supercritical process, ultrasonic method, and even microwave method. Chemically, transesterified biodiesel comprises a mixture of mono-alkyl esters of long chain fatty acids. The most common form uses methanol to produce methyl esters as it is the cheapest alcohol available, though ethanol can be used to produce an ethyl ester biodiesel and higher alcohols such as isopropanol and butanol have also been used. Using alcohols of higher molecular weights improves the cold flow properties of the resulting ester, at the cost of a less efficient transesterification [1-2]. A lipid transesterification production process is used to convert the base oil to the desired esters. Any free fatty acids (FFAs) in the base oil are either converted to soap and removed from the process, or esterified to gain more biodiesel using an acidic catalyst [3-4]. After this processing, unlike straight vegetable oil, biodiesel has combustion properties very similar to those of petroleum diesel, and can replace in most current uses.

A by-product of the transesterification process is glycerol. For every ton of biodiesel manufactured, 100 kg of glycerol are produced. Originally, there was a valuable market for the glycerol, which assisted the economics of the process as a whole. However, with the increase in global biodiesel production, the market price for this crude glycerol (containing 20% water and catalyst residues) has crashed. Many researches are being conducted globally to use this glycerol [5-9].

1.1 Introduction of glycerol

The utilization of glycerol for the synthesis of value added chemicals is a theme of great industrial interest because glycerol is formed in large amounts during the production of biodiesel from natural triglycerides [10-15] and represents a waste that must be used or eliminated. Several conversion processes [16-25] are described in the literature to transform glycerol into useful materials as presented in Fig 1.1.

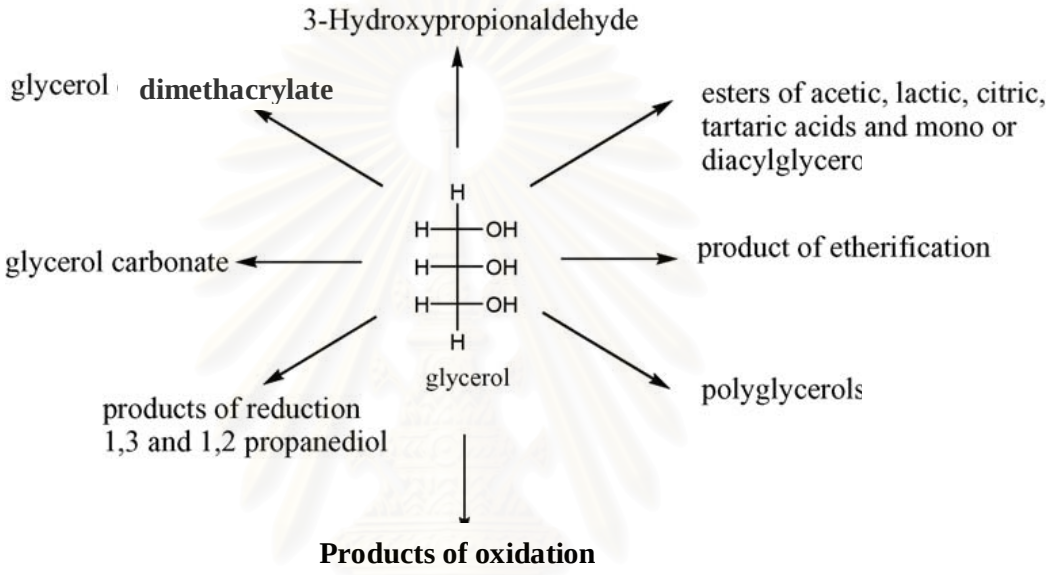


Figure 1.1. Processes of conversion of glycerol into useful chemicals

Among the transformation mentioned above, the conversion of glycerol to mono, diglyceride and 1-halo-2,3-propanediol could lead to many diverse applications, both as a material in their own right, for example as a food ingredient or a plasticizer, and as a chemical building block for other materials in industries [26].

1.2 Introduction of monoglyceride and diglyceride

Monoglycerides have become very important for a sustainable chemistry. More specifically, the fatty acid monoesters of glycerol are valuable compounds with wide applications [27-29] as presented in Table 1.1.

Table 1.1 Applications of monoglyceride and diglyceride

Applications of monoglyceride and diglyceride	
Food and drink	• Manufacture use as emulsifiers • Manufacture of polyglyceryl esters as an additive in margarine and butter. • Used as filler and sweetener in low-fat food products such as cookies • Used as humectant and sweetener in a wide range of products – keeps cakes moist
Pharmaceuticals	• Used as a lubricant and humectant in pharmaceutical preparations such as suppositories, cough syrups and expectorants
Personal care	• Used in a wide range of personal care products as an emollient, humectant, solvent and lubricant; including skin care, hair care, toothpastes, shaving creams and soaps
Polymers	• Producing polyether polyols for polyurethane foams and other flexible foams • As a plasticiser in cellophane • Production of alkyd resins for paints and coatings

Glycerolysis of fatty methyl esters is an interesting route for monoglyceride synthesis. There are two main synthetic routes for obtaining monoglycerides: direct esterification of glycerol with fatty acid and transesterification of glycerol with triglycerides or fatty acid methyl esters. The industrial processes generally use homogeneous acid or basic catalysts leading to a mixture of mono-, di- and triglycerides (40:50:10). Before their applications, a molecular distillation must be carried out to obtain a monoglyceride with a high purity (90%). In industry, mineral

acid (sulfuric acid) or organic acid (*p*-toluenesulfonic acid) are the most often use. But besides the environmental problems, these catalysts favor side-reactions from the degradation of the fatty acid (oxidation, dimerisation) or from the glycerol (polymerization, dehydration into acrolein and oxidation). Therefore, there is still a great need to look for new conversion processes to transform glycerol into monoglyceride and/or diglyceride selectively.

1.2.1 Literature reviews on monoglyceride and diglyceride synthesis

In 1969, Bentley and coworkers introduced dihydroxyacetone as an ideal starting material for the synthesis of long-chain 1,3-diglycerides, such as glyceryl dipalmitate and glyceryl dioleate since it was readily acylated with fatty acid chloride in the presence of pyridine in high yield. The synthesis of short chain diglycerides was also possible by this method, but the results were less satisfactory and gave only 10% 1,2-isomer of monoglycerides [30].

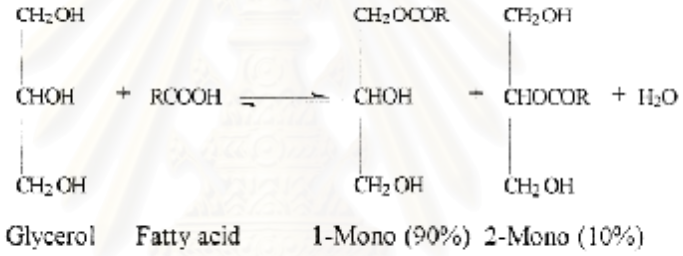
In 1988, Sonnet and coworkers reported the preparation of the acetonide of glycerol using lipase catalysis. In this process, the procedure for the preparation of 2-alkylglycerols was developed and could be applied for the synthesis of various substituted monoester diethers and monoether diesters of glycerol [31].

In 1996, Srisiri and coworkers introduced the syntheses of polymerizable monoacylglycerol and 1,2-diacylglycerol. The monodienoylglycerol was obtained in 80% yield from 1,2-*O*-isopropylideneglycerol and dienoyl fatty acid. The dienoic acid was accessible in 60% yield from the base-catalyzed hydrolysis of dienoyl ester which was synthesized from the Wittig-Horner reaction of aldehyde and trimethyl 4-phosphono-crotonate. The 1,2-diacylglycerol was synthesized by acylation of 3-(4-methoxybenzyl)-glycerol with dienoyl fatty acid in the presence of 4-(dimethylamino)pyridine (DMAP) and dicyclohexylcarbodiimide (DCC). The removal of the 4-methoxybenzyl group could be accomplished by dimethylboron bromide. The overall yield for the synthesis of the polymerizable 1,2-diacylglycerol from the dienoyl fatty acid was *ca* 50% [32].

In 1997, Fureby and coworkers addressed the preparation of 1,2-diglycerides by alcoholysis using lipase from *Penicillium roquefortii* immobilized on porous polypropylene particles. The screening results using commercially available lipases revealed that lipases from *Penicillium* species produced high amounts of 1,2-diglycerides from triglycerides. Reaction parameters such as solvent, type of alcohol

and fatty acid chain length were investigated. The positional selectivity of the lipase as well as the selectivity for type of glyceride species was studied [33].

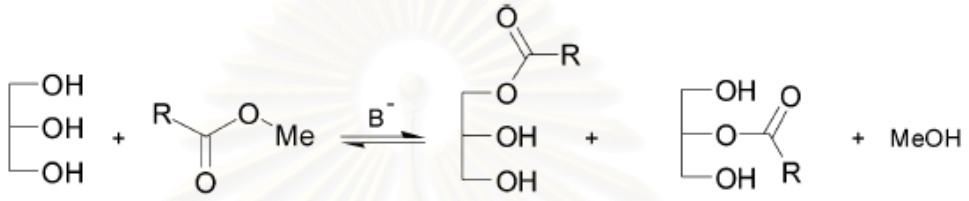
In 1999, Pouilloux and coworkers presented the selective esterification of glycerol with fatty acid for the production of monoglycerides in the presence of ion-exchange resins. The activity and selectivity to monoglycerides were influenced by the resin structure. The catalytic properties of these polymers were in addition strongly influenced by the nature of reagents. The catalyst activity was found to depend on the adsorption rate of glycerol and oleic acid on the catalyst surface. The strong adsorption of glycerol, the swelling of the resin in the oleic acid favored the elimination of water during the reaction by using a molecular sieve and the decrease of the hydrocarbon chain length of the fatty acid. Nevertheless, at the end of the reaction, there still was a mixture of 1- and 2-isomers [34].



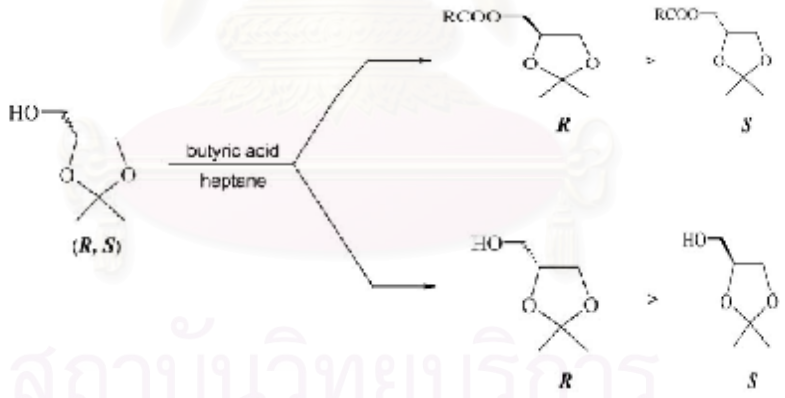
In 1999, Artamonov and coworkers investigated the synthesis of monoglycerides from aromatic acids such as phenolcarboxylic acids, hydroxycinnamic acids, and others. The protecting groups were required for this synthesis and the by-products were invariably formed when acid chlorides and anhydrides were used [35].

In 2004, Barrault and coworkers investigated the preparation of monoglycerides from fatty methyl esters and glycerol in the presence of acid or basic catalysts. The use of porous and basic solid catalysts could induce a shape selectivity modifying the monoglyceride selectivity. Fatty acid methyl esters (C12-C18) were used in the reaction with several MCM-41 magnesium-containing catalysts. Over an Mg-MCM-41 catalyst, glycerol monolaurate was obtained with selectivity and yield of about 80%. However, the monoglyceride selectivity was rather similar and a distribution of mono/di/triglycerides was observed [36].

In 2005, Corma and coworkers reported the use of solid Brönsted base with higher activity and much higher specific rate than the reported Lewis basic hydrotalcite catalyst for transesterification of oleic acid methyl ester with glycerol. The selectivity of the former for monoglycerides was higher. Calcined Li–Al hydrotalcites gave higher activity than MgO or Al–Mg hydrotalcites. On the contrary, the reaction of transesterification of diglycerides required longer reaction time to complete the reaction and however still produced 1,2-isomer approximately 82%[37].



In 2006, Romano and coworkers reported that the lyophilized mycelium of *Rhizopus oryzae* CBS 112.07 and *Aspergillus oryzae* MIM could be advantageously used as biocatalysts for the direct esterification or interesterification between 1,2-*O*-isopropylideneglycerol and butyric acid under optimized conditions yielding (*R*)-1,2-



O-isopropylideneglyceryl butyrate with 56%*ee* and a molar conversion of 52%. The enantiomerically enriched ester was recovered and then enantioselectively hydrolyzed of (*R*)-1,2-*O*-isopropylideneglycerol butyrate with thermally-treated cells of *Bacillus coagulans*. The (*S*)-1,2-*O*-isopropylideneglyceryl butyrate was obtained enantiomerically pure, while the (*S*)-alcohol was recovered with 90%*ee* [38].

In 2007, Cateni and coworkers investigated the preparation of monoglucosyl diglycerides with medium length fatty acid chains and examined the antimicrobial activity against Gram-positive, Gram-negative bacteria and fungi. 3-*O*-(β-*D*-2,3,4,6-tetra-*O*-levulinyl-glucopyranosyl)-*rac*-glycerol was directly submitted to

transesterification catalyzed by *Mucor miehei* lipase in the presence of the appropriate octanoate and caprate vinyl esters in CH_2Cl_2. The reactions were completely regioselective affording 1-*O*-acyl-3-*O*-(β-D-2,3,4,6-tetra-*O*-levulinylglucopyranosyl)-*rac*-glycerols in good yields (95–98%). However, the synthesis of monoglyceride required muti-step methods to prepare intermediate [39].

The processes for the preparation of monoglycerides are the glycerolysis, the hydrolysis of triglycerides and the direct esterification of glycerol with fatty acids. Nevertheless, at the end of the reaction, there is a mixture of glycerol, fatty acid, monoglycerides (35-40%), diglycerides (40-50%) and triglycerides (10-15%) [27] and secondary products: acrolein, polyethers or polyesters of glycerol. Before their use in industry, a separation step is necessary in order to obtain a pure product. Indeed, the esterification is generally catalyzed by homogeneous acid catalyst such as H_2SO_4 [34], but the selectivity to monoglycerides is low. Furthermore, the use of such catalysts creates environmental problems as corrosion or chemical problems as the difficulty of catalyst recycling. The reaction also required muti-step methods to synthesize monoglycerides and the workup presents some drawbacks, among which are the use of a biphasic system, dilute media, and large reactors.

1.2.2 Literature reviews on halogenated reagents for synthesis of esters

The preparation of esters from their corresponding carboxylic acids is an important and well–known transformation in organic synthesis [40]. Carboxylic acid activation can be achieved either by conversion into more reactive functional groups such as acyl halide, anhydride, acyl azide, active esters or by *in situ* activation by coupling reagents such as carbodiimides.

Acid chlorides are valuable intermediates in organic synthesis and are generally prepared by the reaction of carboxylic acids with reagents such as thionyl chloride ($SOCl_2$), PCl_3, PCl_5, and oxalyl chloride. The methodologies for the preparation of ester utilizing halogenated reagents have been extensively studied in many research groups.

In 1966, Lee and coworkers reported the treatment of carboxylic acids with CCl_4 and PPh_3 leading to the formation of the corresponding alkyl chlorides in good yield. However, this method required temperature above RT in order to proceed the reaction [41].

In 1999, Jang and coworkers developed an alternative method to prepare the respective acid chlorides from carboxylic acids by the combination use of PPh_3 and Cl_3CCN. Subsequent addition of primary amines resulted in the acquirement of secondary amides in high yield [42].

In 2002, Vago and coworkers reported a novel acylation using polymer support, with ***in situ*** generated acyl chlorides using Cl_3CCN and PPh_3 [43].

In 2003, Azumaya and colleagues addressed [44] the conversion of carboxylic acid to the corresponding acid halides by using dichlorotriphenylphosphorane in $CHCl_3$.

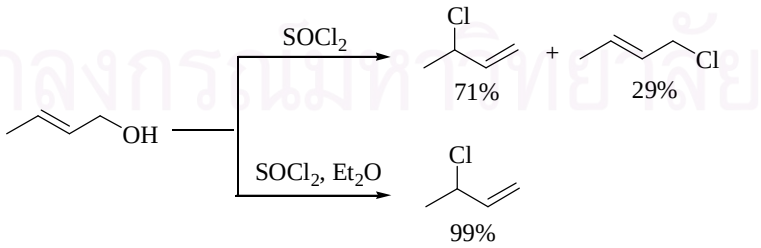
In 2003, Chaysripongkul introduced the novel methodology for the synthesis of amides and esters using Cl_3CCONH_2 and PPh_3 at reflux temperature of CH_2Cl_2. This method provided a viable procedure as a mild reaction with short reaction time. In addition, this reagent could also be applied to prepare bioactive ester compounds efficiently [45].

1.3 Literature reviews on alkyl chloride synthesis from alcohols

Conversion of alcohols into alkyl chlorides can be accomplished by several approaches. The reaction of an alcohol with common reagents such as HCl (g) and $SOCl_2$ to give alkyl chloride are among classical methods. Some newer methods have also appeared such as the use of PPh_3 in combination with CCl_4.

Alcohols react readily with HCl to yield alkyl chlorides and water. The reaction is carried out either by passing dry HCl (g) into alcohol, or by heating alcohol with concentrated aqueous acid.

In 1955 Caserio and coworkers reported the chlorination of allylic alcohols by using $SOCl_2$ in the presence of dilute ether solution [46].



However, alcohols could be converted to alkyl chlorides on treatment with two or three times of redistilled $SOCl_2$. In some cases, the reactions took place immediately but usually the mixture had to be refluxed with stirring at the boiling

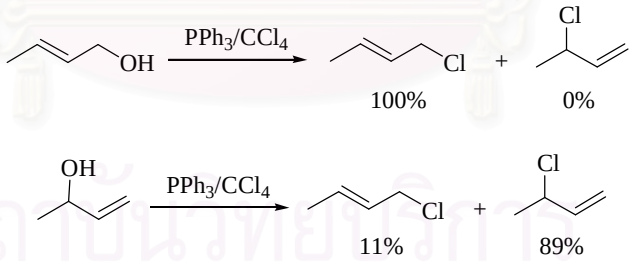
point of $SOCl_2$. Since the by-products of the reaction were gaseous, they were readily removed and any excess $SOCl_2$ was distilled off. These by-products are harmfully corrosive chemicals and invariably make the conditions become acidic.

1.3.1 Phosphorus compounds with halogenated reagents

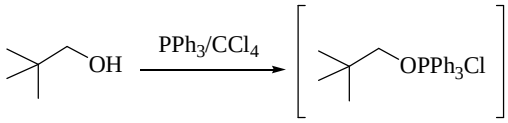
The convenient methodology for the preparation of alkyl chlorides using comparatively non-toxic reagents under mild conditions has been constantly studied such as a combination of organophosphorus reagent and halogenated reagent such as PPh_3/Cl_2, PPh_3/CCl_4, PPh_3/Cl_3CCCl_3, PPh_3/Cl_3COCCl_3 or PPh_3/Cl_3CCN systems. These reagents are attractive since the reaction could be performed under mild and acid-free conditions with good yield.

In 1964, Wiley and coworkers reported that an important characteristic of PPh_3/Cl_2 system was its tendency to induce substitution without elimination or rearrangement. Phenols could be converted at elevated temperatures without positional isomers being formed [47].

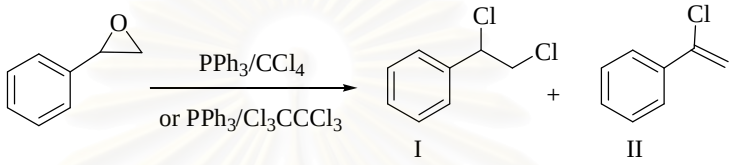
In 1972, Snyder introduced the conversion of alkyl alcohols to the corresponding chlorides without rearrangement [48].



In 1978, Jones and co-workers reported the rate of formation of phosphorylated intermediate formed by reacting PPh_3, CCl_4 and an alcohol. This combination was only slightly influenced by steric effects. The relative rates of intermediate formation were primary > secondary > neopentyl. The relative rates of intermediate decomposition followed the order of primary > secondary > neopentyl [49].



In 1979, Hashimoto and coworkers addressed the reaction of PPh_3-trichloromethyl compounds such as CCl_4 and CCl_3CCl_3 with styrene oxide to give I and II.



The reaction was accelerated in polar solvents such as CH_3CN. **I** was quantitative formed when excess PPh_3 was used. **II** was formed in high yield when phenols were added to the reaction mixture. The reactions using other Cl_3C-compounds (except Cl_3CCCl_3) gave products analogous to those of CCl_4. Cl_3C-compounds having more electron withdrawing groups other than Cl gave higher **I** and **II** ratios than did CCl_4. The reaction with Cl_3CCCl_3 gave **I** quantitatively at RT [50].

However, the conversion of alcohols to the desired alkyl chlorides using above combinations could not be proceeded within short reaction time at RT. Later, the combination of Ph_3P/Cl_3COCCl_3 or Ph_3P/Cl_3CCN systems has been addressed as another viable route for the preparation of alkyl chloride with high efficiency.

In 1979, Magid and coworkers reported a mild reagent for the regioselective and stereospecific chlorination. Allylic alcohols reacted with $PPh_3/Cl_3CCOCCl_3$ in less than 20 min at 10-15°C to produce excellent yields of the corresponding alkyl chlorides. Isolation was accomplished simply by flash distillation. The conversion occurred with total preservation of double bond geometry and with >99% inversion of configuration for optically active alcohol. All primary and secondary alcohols gave predominantly the unrearranged alkyl chlorides whereas tertiary alcohols furnished mostly rearranged product. With more highly substituted systems, elimination to diene became an important side reaction [51].

In 1983, Bringmann and coworkers converted alcohols to alkyl chlorides by using the combination of PPh_3/Cl_3CCCl_3 and $PPh_3/BrCl_2CCCl_2Br$ in high yield [52].

In 1991, Matveeva and coworkers reported the regiospecific conversion of alcohols into the corresponding alkyl chlorides with Cl_3CCN in the presence of PPh_3. If an external nucleophile such as iodide and rhodanide was introduced to the reaction, the alkyl chloride was still a predominant product [53].

In 1995, Matveeva and co-workers investigated continually a regio- and stereoselective substitution of halide for hydroxyl groups in allylic alcohols. Treating *cis*- and *trans*-$RCH=CHCH_2OH$ (R = Me, *n*-C_5H_{11}) with CCl_3R_1 (R_1 = CN, CO_2Et, $COCCl_3$) in CH_3CN and PPh_3 gave the corresponding alkyl chloride with ^{3} 95% regio- and stereoselectivity. The selectivity for analogous reactions of *cis*- and *trans*-$HOCHRCH=CH_2$ was 81-92%, while $CH_2=CHCHDOH$ gave 53% $CH_2=CHCHDCl$ [54].

In 1998, Drabowicz and co-workers reported that alkyl chlorides could be prepared from alcohols with the combination of PPh_3/CCl_4 under mild and neutral conditions. The reaction took place rapidly to produce the desired product, triphenylphosphine oxide and $CHCl_3$. This reaction did not generate any strong acidic material, thus it is suitable for the preparation of alkyl chloride containing acid sensitive functional group [55].

Recently, Cl_3CCONH_2, another alternative halogenating reagent for conversion of carboxylic acids to their analogous amides and esters upon the combination with PPh_3 has been introduced by Chaysripongkul. This reagent, even though a bit less reactive compared with CCl_3CN, its cost and the ease of work-up made this reagent far more conceivable to be employed.

1.4 The objectives of this research

The objectives of this research are to explore and develop the optimized conditions for the preparation of glyceryl monoester and 1-halo-2,3-propanediol from glycerol.

- To apply Cl_3CCONH_2 and PPh_3 for the synthesis of esters and alkyl chlorides.
- To search for the optimum conditions for the synthesis of glyceryl esters and 1-halo-2,3-propanediol.
- To explore the highly efficient deprotecting reagent under mild conditions and selective for deprotection of isopropylidene group.

CHAPTER II

EXPERIMENTAL

2.1 General procedures

Chromatography: thin layer chromatography (TLC) was carried out on aluminium sheets precoated with silica gel (Merck, Kieselgel 60 PF_{254}). Column chromatography was performed on silica gel (Merck, Kieselgel 60G Art 7734, 70-230 mesh; or Art 9385, 230-400 mesh) and aluminium oxide 90 active neutral (70-230 mesh). Spectrometer: ^{1}H and ^{13}C-NMR spectra were obtained in deuterated chloroform ($CDCl_3$), deuterated methanol (MeOD-d_4) and dimethylsulfoxide (DMSO-d_6), with Fourier transform nuclear magnetic resonance spectrometer of Varian model Mercury+400 spectrometer which was operated at 400 MHz for ^{1}H and 100 MHz for ^{13}C nuclei, or Bruker model AC-100F spectrometer which was operated at 100 MHz for ^{1}H.

2.2 Chemical reagents

All solvents used were purified, except for those being reagent grades, and dried prior to use by standard methodology. The substrates and reagents for synthesizing the precursors and products employed in this work were purchased from Merck, Fluka and Sigma-Aldrich Co., Ltd. and were used without further purification.

2.3 Preparation of substrates

2.3.1 Halogenating agents

2.3.1.1 General procedure for synthesis of $Br_3CCOOEt$ [56-57]

1 mL of conc. H_2SO_4 was cautiously added to a mixture of 40 mmol of Br_3CCOOH and 45 mmol of EtOH. The mixture in the rounded bottom flask fitted by a condenser was refluxed for 3-6 h and then poured into 100 mL of water in a separation funnel. The upper layer of crude ester was removed and washed with 50 mL of water, saturated aqueous $NaHCO_3$ and water, respectively, and dried over Na_2SO_4. The product is colorless oil (72%). IR (neat): 2981, 1750, 1469, 1361, 1233 and 1021 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.44 (3H, *t*, *J* = 7.2 Hz) and 4.46 (2H, *q*, *J* = 7.2 Hz).

2.3.1.2 General procedure for synthesis for $Br_3CCOCBr_3$ [57]

Anhydrous NaOAc 0.085 mol was mixed with 20 mL of glacial AcOH in the rounded bottom flask equipped with reflux condenser, thermometer and heater. The mixture was heated to 60°C, and 1 mL of acetone was added, followed by the dropwise addition of 7 mL of liquid Br_2 over a 10 min period with stirring. The liquid Br_2 reacted immediately, and the reaction was mildly exothermic such that no external cooling was needed to maintain a temperature of 60-70°C. The mixture was then heated to 95°C and held there for 6-8 h, after which it was cooled to RT and mixed with cool water to precipitate the desired product as white solid. Recrystallization from hexane to obtain white crystal (87%), m.p. 122-123°C. ^{13}C-NMR ($CDCl_3$) δ (ppm): 173.5 and 24.5.

2.4 General procedure for separation of glycerol waste [58-59]

The waste containing glycerol was obtained from Bangchak oil refined factory, Bangkok in September 2007. The pH of crude waste (100 g) was adjusted to pH 1 by acid, followed by heating at 40-50°C with gently stirring. The solution was separated into two layers. The resulting free fatty acid was separated as appeared in an upper layer and its composition was analyzed by HPLC utilizing method T-CM-005 based on compendium of methods for food analysis, Thailand (2003). The lower layer was separated and 10 M NaOH was added to adjust the pH close to 7. After the mixture was stirred and heated, the salt was filtered. The obtained solution was then extracted by MeOH and hexane. The extracts were dried over anhydrous Na_2SO_4 and

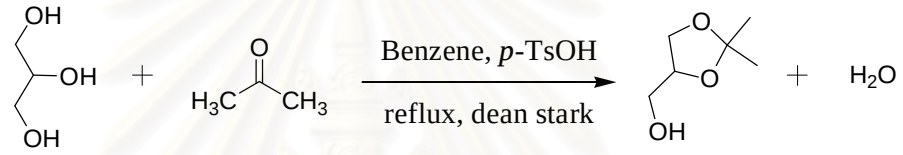
concentrated *in vacuo*. The residue was decolorized by activated charcoal. The yield of light brown oil identified as glycerol was 54%.

Glycerol: colorless oil ^{1}H-NMR (D_2O) δ (ppm): 3.54 (2H, *dd*, *J* = 11.7 and 6.5 Hz), 3.63 (2H, *dd*, *J* = 11.7 and 4.3 Hz), 3.76 (1H, *m*). ^{13}C-NMR (D_2O) δ (ppm): 74.8 and 65.2

2.4.1 Effect of acids on the purification of glycerol from waste

To purify the glycerol waste, the same manner as previously described was performed but different acids were used including HCl, H_2SO_4 and H_3PO_4.

2.5 General procedure for the synthesis of 1,2-*O*-isopropylideneglycerol [60]

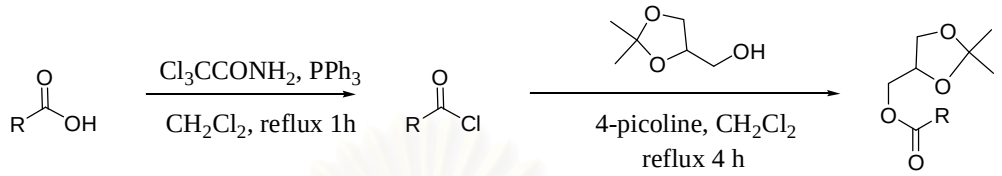


Glycerol 1 eq (3 mol) and acetone 3 eq (9 mol) were mixed with *p*-TsOH (0.5 mmol) in benzene 10 mL and refluxed using Dean stark apparatus until no more water was collected in the trap of the separating head. The mixture was cooled to RT and freshly saturated aqueous $NaHCO_3$ was added. The mixture was then filtered, and benzene and excess acetone were removed under reduced pressure. The fraction boiling at 80-82°C/11 mm was collected. The yield of colorless oil 1,2-*O*-isopropylideneglycerol was 82%.

1,2-O-isopropylideneglycerol: colorless oil (82%) ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.31 (3H, *s*), 1.38 (3H, *s*), 2.82 (2H, broad, *s*) 3.54 (1H, *dd*, *J* = 11.6 and 5.3 Hz), 3.65 (1H, *dd*, *J* = 11.6 and 3.9 Hz), 3.72 (1H, *t*, *J* = 6.6 Hz), 3.98 (1H, *t*, *J* = 6.6 Hz) and 4.14-4.20 (1H, *m*).

2.6 General procedure for the synthesis of glyceryl monoester from 1, 2-*O*-isopropylideneglycerol

2.6.1 General procedure for synthesis of (2,2-dimethyl-1,3-dioxolan-4-yl)methyl ester



Step I **Step II**

Step 1: PPh_3 2 eq (6 mmol) in CH_2Cl_2 6 mL was added to a mixture of carboxylic acid 1 eq (3 mmol) and Cl_3CCONH_2 2 eq (6 mmol) in CH_2Cl_2 6 mL at reflux temperature.

Step 2: A mixture of 1, 2-*O*-isopropylideneglycerol 1 eq (3 mmol) and 4-picoline 3 eq (9 mmol) was added to the above mixture. The reaction was refluxed and continued stirring or followed by TLC at selected temperature.

When the reaction was completed, the organic layer was extracted with 10% HCl and saturated aqueous $NaHCO_3$, respectively, dried over Na_2SO_4 and evaporated *in vacuo*. The mixture was separated with silica gel column eluting with hexane/EtOAc.

2.6.2 Study on the optimum conditions

2.6.2.1 Effect of temperature and reaction time

The general synthesis procedure of (2,2-dimethyl-1,3-dioxolan-4-yl)methyl benzoate using PPh_3 and Cl_3CCONH_2, 1,2-*O*-isopropylideneglycerol, 4-picoline and solvent, respectively was carried out at different reaction times: 0.5, 1, 2 and 4 h in steps I and II .

2.6.2.2 Effect of the amount of 1, 2-*O*-isopropylideneglycerol

The same general procedure as described above was performed for 1 h except for varying the amount of 1, 2-*O*-isopropylideneglycerol: 1, 2 and 3 mmol in step II.

2.6.2.3 Variation of carboxylic acids on the formation of ester

The same procedure was carried out at reflux temperature for 1 h using different carboxylic acids: α-naphthoic acid, nonanoic acid, lauric acid, stearic acid, palmitic acid and oleic acid instead of benzoic acid.

(2,2-dimethyl-1,3-dioxolan-4-yl)methyl-1-benzoate: colorless oil (92%), ^{1}H-NMR ($CDCl_3$) *d* (ppm): 1.38 (3H, *s*), 1.45 (3H, *s*), 3.87 (1H, *dd*, *J* = 14.4 and 5.9 Hz), 4.14 (1H, *dd*, *J* = 14.8 and 6.9 Hz), 4.36-4.39 (2H, *m*), 4.43-4.47 (1H, *m*), 7.44 (2H, *t*, *J* = 7.6 Hz), 7.55 (1H, *t*, *J* = 7.3 Hz) and 8.05 (2H, *d*, *J* = 7.3 Hz).

(2,2-dimethyl-1,3-dioxolan-4-yl)methyl-1-nonanoate: colorless oil (94%), ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.86 (3H, *t*, *J* = 6.7 Hz), 1.26 (10H, *d*, *J* = 6.7 Hz), 1.36 (3H, *s*), 1.42 (3H, *s*), 1.59-1.65 (2H, *m*), 2.35 (2H, *t*, *J* = 7.5 Hz), 3.72 (1H, *dd*, *J* = 14.6 and 6.0 Hz), 4.04-4.09 (2H, *m*), 4.15 (1H, *dd*, *J*= 11.4 and 4.6 Hz) and 4.27-4.33 (1H, *m*).

(2,2-dimethyl-1,3-dioxolan-4-yl)methyl-1-palmitate: white solid (96%), ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.86 (3H, *t*, *J* = 6.5 Hz), 1.24 (24H, *s*), 1.36 (3H, *s*), 1.42 (3H, *s*), 1.61 (2H, *s*), 2.33 (2H, *t*, *J* = 7.5 Hz), 3.72 (1H, *dd*, *J* = 14.6 and 6.3 Hz), 4.05-4.10 (2H, *m*), 4.15 (1H, *dd*, *J* = 11.5 and 4.6 Hz) and 4.28-4.33 (1H, *m*).

(2,2-dimethyl-1,3-dioxolan-4-yl)methyl-1-stearate: white solid (89%), ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.87 (3H, *t*, *J* = 5.5 Hz), 1.24 (28H, *s*), 1.36 (3H, *s*), 1.42 (3H, *s*), 1.58 (2H, *s*), 2.33 (2H, *t*, *J* = 7.4 Hz), 3.73 (1H, *t*, *J* = 7.3 Hz), 4.05-4.10 (2H, *m*), 4.16 (1H, *dd*, *J* = 11.5 and 4.6 Hz) and 4.28-4.33 (1H, *m*).

(2,2-dimethyl-1,3-dioxolan-4-yl)methyl-1-naphthoate: colorless oil (95%), ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.40 (3H, *s*), 1.48 (3H, *s*), 3.92 (1H, *dd*, *J* = 13.9 and 5.7 Hz), 4.17 (1H, *dd*, *J* = 14.5 and 6.3 Hz), 4.42-4.55 (3H, *m*), 7.48-7.55 (2H, *m*), 7.62 (1H, *t*, *J* = 7.2 Hz), 7.88 (1H, *d*, *J* = 8.0 Hz), 8.03 (1H, *d*, *J* = 8.1 Hz), 8.22 (1H, *d*, *J* = 7.2 Hz) and 8.92 (1H, *d*, *J* = 8.6 Hz).

(2,2-dimethyl-1,3-dioxolan-4-yl)methyl-1-oleate: colorless oil (92%), ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.84-0.88 (3H, *m*), 1.26 (20H, *d*, *J* = 14.2 Hz), 1.35 (3H, *s*), 1.42 (3H, *s*), 1.61 (2H, *t*, *J* = 6.5 Hz), 1.97-2.00 (4H, *m*), 2.32 (2H, *t*, *J* = 7.4 Hz), 3.72 (1H, *dd*, *J* = 14.6 and 6.2 Hz), 4.04-4.09 (2H, *m*), 4.15 (1H, *dd*, *J* = 11.5 and 4.6 Hz), 4.27-4.33 (1H, *m*) and 5.31-5.38 (2H, *m*).

(2,2-dimethyl-1,3-dioxolan-4-yl)methyl-1-laurate: colorless oil (85%), ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.86 (3H, *t*, *J* = 6.5 Hz), 1.24-1.27 (16H, *d*, *J* = 10.2 Hz), 1.36 (3H, *s*), 1.42 (3H, *s*), 1.60 (2H, *s*), 2.33 (2H, *t*, *J* = 7.4 Hz), 3.73 (1H, *dd*, *J* = 14.5 and 7.2 Hz), 4.04-4.10 (2H, *m*), 4.16 (1H, *dd*, *J* = 11.7 and 4.6 Hz) and 4.28-4.33 (1H, *m*).

2.6.3 Selective deprotection of isopropylidene using various catalysts and reagents

2.6.3.1 Variation of catalysts and reagents

A typical procedure for the selective cleavage of an isopropylidene protecting group using acid catalyst or deprotecting reagent: 2M HCl, 5% *p*-TsOH, CBr_4 $Br_3CCOOEt$, and $Br_3CCOCBr_3$ are as follows:

General deprotection of isopropylidene acetals without photoirradiation condition

A solution of isopropylidene acetals 1.0 equiv (0.25 mmol), deprotecting reagent 0.10 equiv (0.025 mmol) and anhydrous MeOH (10 mL) in a Pyrex round bottom flask was stirring without irradiation at RT. After the reaction was completed (by TLC), the organic solvent was removed under reduced pressure. The quantitative analysis was performed by ^{1}H-NMR based on a standard toluene 10 µL.

General deprotection of isopropylidene acetals with photoirradiation condition

A solution of acetals 1.0 equiv (0.25 mmol), CBr_4 or $Br_3CCOCBr_3$ 0.1 equiv (0.025 mmol) and anhydrous MeOH (10 mL) in a Pyrex round bottom flask was irradiated by a TLC-lamp [67] (Uvltec Limited, 245 nm, 6W) for 0.5 h, followed by stirring at RT without irradiation for 24 h. After the reaction was completed (by TLC), the organic solvent was removed under reduced pressure. The obtained crude was analyzed by ^{1}H-NMR and the yield was calculated based on a standard toluene 10 µL added.

2,3-dihydroxypropyl benzoate: colorless oil, ^{1}H-NMR (DMSO-d_6) δ (ppm): 3.71 (1H, *dd*, *J* = 11.5 and 5.7 Hz), 3.81 (1H, *dd*, *J* = 11.5 and 3.9 Hz), 4.09 (1H, *m*), 4.43 (1H, *dd*, *J* = 11.5 and 5.8 Hz), 4.49 (1H, *dd*, *J* = 11.5 and 5.0 Hz), 7.43 (2H, *d*, *J* = 7.6 Hz), 7.54 (1H, *t*, *J* = 7.3 Hz) and 8.02 (2H, *d*, *J* = 7.4 Hz).

2,3-dihydroxypropyl nonanoate: colorless oil, ^{1}H-NMR (DMSO-d_6): 0.88 (3H, *t*, *J* = 7.2 Hz), 1.30–1.28 (8H, *m*), 1.65–1.60 (2H, *m*), 2.13 (1H, broad, *s*), 2.36 (2H, *d*, *J* = 7.6 Hz), 2.57 (1H, broad, *s*), 3.58–3.63 (1H, *m*), 3.68–3.73 (1H, *m*), 3.90–3.97 (1H, *m*), 4.14 (1H, *dd*, *J* = 11.7 and 6.1 Hz) and 4.21 (1H, *dd*, *J* = 11.7 and 4.6 Hz).

2,3-dihydroxypropyl-1-napthoate: white solid, ^{1}H-NMR (MeOD-d_4): 3.74 (1H, *dd*, *J* = 11.5 and 5.7 Hz), 3.88 (1H, *dd*, *J* = 11.5 and 3.9 Hz), 4.14 (1H, *m*), 4.43 (1H, *dd*, *J* = 11.5 and 5.8 Hz), 4.53 (1H, *dd*, *J* = 11.5 and 5.0 Hz), 7.48-7.55 (2H, *m*),

7.60-7.63 (1H, *t*, *J* = 7.3 Hz), 7.88 (1H, *d*, *J* = 8.0 Hz), 8.03 (1H, *d*, *J* = 8.1 Hz), 8.22 (1H, *d*, *J* = 7.2 Hz) and 8.92 (1H, *d*, *J* = 8.6 Hz).

2,3-dihydroxypropyl laurate: white solid, ^{1}H-NMR (DMSO-d_6): 0.88 (3H, *t*, *J* = 6.6 Hz), 1.26 (16H, *s*), 1.59–1.68 (2H, *m*), 2.21 (1H, broad, *s*), 2.35 (2H, *t*, *J* = 7.8 Hz), 2.63 (1H, broad, *s*), 3.60 (1H, *dd*, *J* = 11.2 and 5.6 Hz), 3.63 (1H, *d*, *J* = 11.2 Hz), 3.90–3.97 (1H, *m*), 4.14 (1H, *dd*, *J* = 10.0 and 6.1 Hz) and 4.21 (1H, *dd*, *J* = 11.7 and 4.6 Hz).

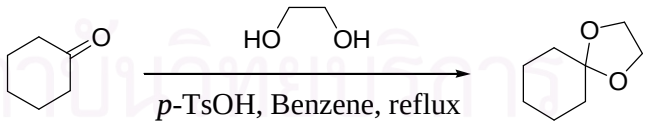
2,3-dihydroxypropyl stearate: white crystals, ^{1}H-NMR (DMSO-d_6): 0.88 (3H, *t*, *J* = 6.7 Hz), 1.26 (20H, *s*), 1.63 (2H, *d*, *J* = 7.3 Hz), 2.04 (1H, broad, *s*), 2.35 (2H, *t*, *J* = 7.7 Hz), 2.48 (1H, broad, *s*), 3.59–3.62 (1H, *m*), 3.68–3.71 (1H, *m*), 3.93–3.97 (1H, *m*), 4.15 (1H, *dd*, *J* = 11.7 and 6.1 Hz) and 4.21 (1H, *dd*, *J* = 11.7 and 4.6 Hz).

2,3-dihydroxypropyl palmitate: white crystals, ^{1}H-NMR (DMSO-d_6): 0.88 (3H, *J* = 6.7 Hz), 1.26 (20H, *s*), 1.63 (2H, *t*, *J* = 7.4 Hz), 2.04 (1H, broad, *s*), 2.35 (2H, *t*, *J* = 7.7 Hz), 2.48 (1H, broad, *s*), 3.59–3.61 (1H, *m*), 3.69–3.71 (1H, *m*), 3.93–3.96 (1H, *m*), 4.15 (1H, *dd*, *J* = 11.7 and 6.1 Hz) and 4.21 (1H, *dd*, *J* = 11.7 and 4.5 Hz),

2,3-dihydroxypropyl oleate: white crystals, ^{1}H-NMR (DMSO-d_6): 0.96 (3H, *s*), 1.30-1.24 (16H, *d*, *J* = 10.8 Hz), 1.38 (3H, *s*), 1.43 (3H, *s*), 1.61 (2H, *s*), 2.34-2.39 (2H, *m*), 3.78 (1H, *dd*, *J* = 14.2 and 7.0 Hz), 4.00-4.09 (2H, *m*), 4.14 (1H, *dd*, *J* = 11.5 and 4.4 Hz) and 4.29-4.35 (1H, *m*).

2.7 Application of developed procedures for the deprotection of acetals

2.7.1 General procedure for synthesis of 1,3-dioxolane [61]



A 100 mL round-bottomed flask was charged with 1.0 equiv (20 mmol) of cyclohexanone, 1.1 equiv (22 mmol) of 1,2-ethanediol, 250 mL of benzene, and 0.01 g of *p*-TsOH. The flask was attached to a water separator under a reflux condenser fitted with a drying tube. A heating mantle was placed under the flask, and the reaction mixture was refluxed until close to the theoretical amount of water (8-9.5 mL) had collected in the trap. The reaction mixture was cooled to RT, extracted

successively with 10% NaOH, portions of water, dried over anhydrous Na_2SO_4, and distilled.

This typical procedure for synthesis acetals is also applied for other substrates: 1,3-dioxolane-2-spirocyclohexane, 2-methyl-2-phenyl-1,3-dioxolane, 2-phenyl-1,3-dioxolane and 2,2-diphenyl-1,3-dioxolane.

1,3-dioxolane-2-spirocyclohexane: colorless oil, ^{1}H-NMR ($CDCl_3$) δ (ppm): 2.10 (2H, *s*), 1.57 (8H, *m*) and 3.91 (4H, *s*).

2-methyl-2-phenyl-1,3-dioxolane: colorless oil, ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.66 (3H, *s*), 3.75-3.79 (2H, *m*), 4.02-4.05 (2H, *m*), 7.25-7.35 (3H, *m*) and 7.48 (2H, *d*, *J* = 6.9 Hz).

2-phenyl-1,3-dioxolane: colorless oil, ^{1}H-NMR ($CDCl_3$) δ (ppm): 3.98-4.07 (2H, *m*), 4.08-4.18 (2H, *m*), 5.82 (1H, *s*), 7.35-7.41 (3H, *m*) and 7.45-7.51 (2H, *m*).

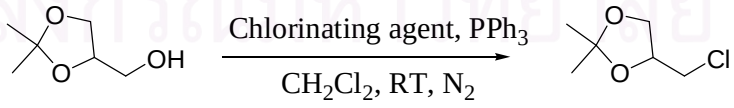
2,2-diphenyl-1,3-dioxolane: white solid, ^{1}H-NMR ($CDCl_3$) δ (ppm): 4.06 (4H, *s*), 7.25-7.61 (8H, *m*) and 7.82 (2H, *d*, *J* = 7.7 Hz).

2.7.2 General procedures for the deprotection of acetals

A solution of acetal 1.0 equiv (0.25 mmol), $Br_3CCOCBr_3$ 0.1 equiv (0.025 mmol) and anhydrous MeOH (5 mL) in a Pyrex round bottom flask was irradiated by a TLC-lamp (Uvltec Limited, 245 nm, 6W) for 0.5 h, followed by stirring at RT without irradiation. After the reaction was completed (by TLC), the organic solvent was removed directly under reduced pressure. The obtained crude was analyzed by ^{1}H-NMR and the yield was calculated based on a standard toluene 10 µL added.

2.8 Synthesis of 3-chloropropane-1,2-diol

2.8.1 General procedure for synthesis of 4-(chloromethyl)-2,2-dimethyl-1,3-dioxolane [62]



A typical procedure involves the reaction of 1,2-*O*-isopropylideneglycerol 1.0 equiv (0.5 mmol), halogenating reagent 1.5 equiv (0.75 mmol) and PPh_3 1.5 equiv (0.75 mmol) in CH_2Cl_2 10 mL at reflux temperature. The mixture was washed with saturated $Na_2S_2O_3$. The organic layer was extracted with Et_2O, dried over anhydrous

Na_2SO_4, and purified by alumina column eluting with hexane/EtOAc to give the corresponding alkyl chloride.

4-(chloromethyl)-2,2-dimethyl-1,3-dioxolane: colorless oil, ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.20 (3H, *s*), 1.32 (3H, *s*) and 4.34–3.12 (5H, *m*).

2.8.2 Study on the optimum conditions for synthesis of 4-(chloromethyl)-2,2-dimethyl-1,3-dioxolane

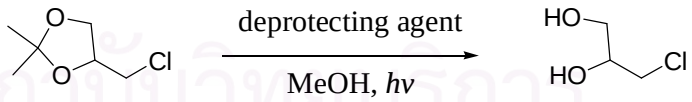
2.8.2.1 Effect of chlorinating agents

The reaction of 1,2-*O*-isopropylideneglycerol (1.0 equiv), PPh_3 (1.5 equiv) with various chlorinating agents: CCl_4, Cl_3CCCl_3, Cl_3CCO_2Et, $Cl_3CCOCCl_3$, Cl_3CCN and Cl_3CCONH_2 in CH_2Cl_2 (10 mL) was stirred under N_2 at reflux temperature at the reaction time for 48 h. The crude was concentrated and analyzed by ^{1}H-NMR based on a standard toluene 10 µL.

2.8.2.2 Effect of the amount of chlorinating agent, temperature and reaction time

The reaction of 1,2-*O*-isopropylideneglycerol (1.0 equiv), PPh_3 (1.5 equiv) with various amounts of chlorinating agent: 0.5, 1.0, 2.0 and 3.0 equiv in CH_2Cl_2 (10 mL) was stirred under N_2 at reflux temperature at the reaction time ranging from 1 to 48 h. The crude was concentrated and purified by alumina column eluting with hexane/EtOAc to give the corresponding alkyl chloride.

2.8.2.3 General deprotection of isopropylidene acetals under photoirradiation condition

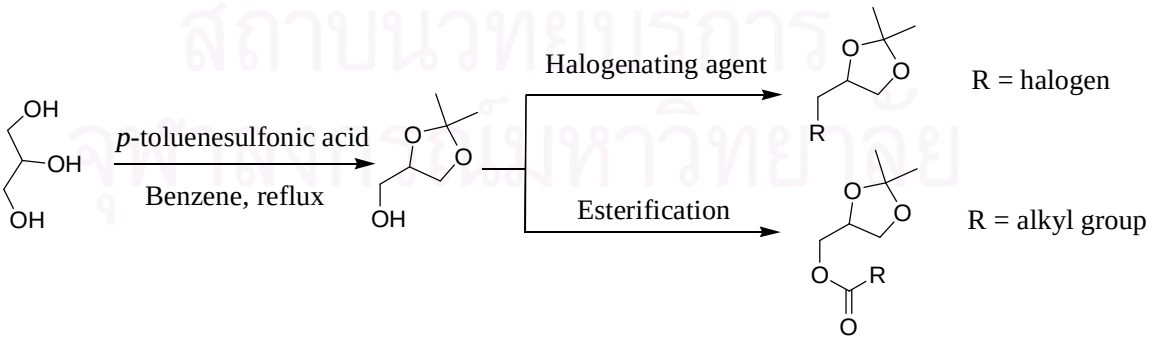


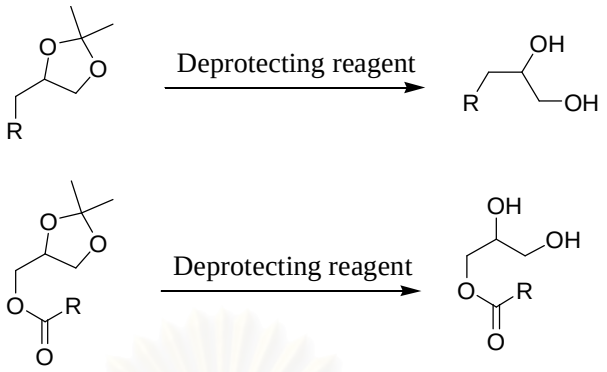
A solution of acetal 1.0 equiv (0.25 mmol), $Br_3CCOCBr_3$ 0.1 equiv (0.025 mmol) and anhydrous MeOH (5 mL) in a Pyrex round bottom was irradiated by a TLC-lamp (Uvltec Limited, 245 nm, 6W). Other steps were carried out according to the general procedure previously described.

CHAPTER III

RESULTS AND DISCUSSION

Biodiesel, which is defined as monoalkyl esters, mainly composes of methyl esters of long-chain fatty acids derived from renewable biological sources, such as vegetable oils or animal fats. The main reactions used first in oleochemistry are the hydrolysis or the methanolysis of triglycerides leading to glycerol and fatty acids or fatty methyl esters. However, these reactions invariably lead to the formation of glycerol by-product. To find the way to utilize this by-product will be valuable applications for the overall process of producing biodiesel. The main purposes of this research are to characterize and optimize a eutectic extraction system capable of purifying glycerol from the biodiesel product, and to synthesize 1-halo-2,3-propanediol and glyceryl monoester from glycerol waste. The transformation of glycerol to glyceryl monoesters and 1-halo-2,3-propanediol is of significant applications in food, pharmaceuticals, cosmetics or detergent industries [63]. The general equations for this research can be simplified as shown below.





3.1 Separation and characterization of glycerol waste

3.1.1 Separation of free fatty acid using acid extraction

The glycerol waste was obtained from Bangchak oil refined factory, Bangkok in September 2007. The waste (100 g) was then purified by acid extraction. Three selected acids including HCl, H_2SO_4 and H_3PO_4 were added to the glycerol waste to reach the pH of 1. The resulting free fatty acid was separated as appeared in an upper layer (Table 3.1).

Table 3.1 The amounts of free fatty acids from glycerol waste extracted by various acids

Acids	FFA (g)	Color
HCl	51.54	dark grey
H_2SO_4	54.00	dark grey
H_3PO_4	53.18	dark grey

All selected acids could assist the separation of FFA from glycerol waste. There was no significant difference in using diverse acids. Nonetheless, based on the practical sense, H_2SO_4 was found to be the best acid for separation the FFA from the glycerol waste. The composition of the obtained FFA was further analyzed by HPLC and the results are presented in Table 3.2.

Table 3.2 The analysis of the composition of FFA obtained from the extraction of glycerol waste with H_2SO_4

Saturated fatty acid (g/100g fatty acid)	
Lauric acid (C12:0)	2.36
Myristic acid (C14:0)	1.80
Palmitic acid (C16:0)	28.92
Stearic acid (C18:0)	5.41
Unsaturated fatty acid (g/100g fatty acid)	
Palmitoleic acid (C16:1)	1.94
Oleic acid (C18:1, *cis*)	42.10
Linoleic acid (C18:2, *cis*)	16.51
α-Linolenic acid (C18:3, *cis*)	0.96

Table 3.2 shows that the composition of fatty acid separated from glycerol waste of Bangchak oil refined factory contained both saturated and unsaturated fatty acids. For saturated fatty acid, the composition was lauric acid (C12:0), myristic acid (C14:0), palmitic acid (C16:0) and stearic acid (C18:0), whist the major constituent was palmitic acid 28.92 g per 100 g fatty acid. For unsaturated fatty acid, palmitoeic acid (C16:1), oleic acid (C18:1, *cis*), linoleic acid (C18:2, *cis*) and α-linolenic acid (C18:3, *cis*) were the main compositions. The major unsaturated fatty acid was oleic acid, 42.10 g per 100 g fatty acid.

Oils and fats were composed primarily of triglycerides. Triglycerides consisted of a glycerin backbone with fatty acid attached in place of the hydroxyls. The relative amount of different fatty acids determines the properties of the specific triglyceride. As FFA levels increased, this became undesirable because of the loss of feedstock as well as the deleterious effect of soap on glycerin separation. The soaps promoted the formation of stable emulsions that prevent separation of the biodiesel.

The acid extraction procedure from the outcome of this experiment appears to be quite effective for separation of FFA and is simple for the practical sense.

3.1.2 Separation of glycerol using acid-base extraction

The glycerol is an unwanted by-product and must be removed before the ester biodiesel can be used as fuel. As the viscosity of the glycerol present in the mixture impedes the high-pressure injection system of a modern diesel engine and may cause damage. Several methods have been used to remove glycerol from biodiesel and these include adsorption over silica, membrane reactors. There are numerous problems associated with the costs and complication of operating biodiesel synthesis on an industrial scale [64].

The purification step selected in this work was acid-base extraction of the glycerol waste which was inexpensive and simple process. Table 3.3 displays the amount of glycerol obtained from the acid-base extraction of glycerol waste.

Table 3.3 The purification of glycerol from glycerol waste by extraction with various acids

Glycerol waste (g)	Acids	% Recovery of glycerol	Color
100	HCl	40.66	Light brown
	H_2SO_4	40.12	Light brown
	H_3PO_4	45.07	Dark brown

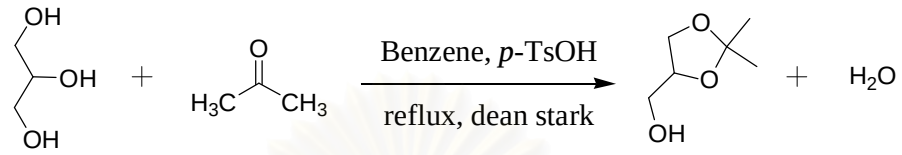
Upon acid extraction, two layers were formed. The upper layer contained mainly FFA as previously described. The lower layer was then separated, stirred and heated, 10 M NaOH was added to the liquid phase to adjust the pH close to 7. The resulting mixture was then extracted by MeOH. The extracts were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was decolorized by activated charcoal. Various acids could aid the separation of glycerol from glycerol waste. H_2SO_4 seemed to be the best acid choice for this regards concerning the yield of glycerol obtained.

From these outcomes, it clearly showed that glycerol could simply be purified from free fatty acid and other components in glycerol waste by acid-base extraction.

3.2 Synthesis of 1,2-*O*-isopropylideneglycerol from glycerol

3.2.1 Condition optimization for the synthesis of 1,2-*O*-isopropylideneglycerol

The synthesis of 1,2-*O*-isopropylideneglycerol using glycerol and acetone was demonstrated by the general equation shown below.



1,2-*O*-Isopropylideneglycerol could be prepared from acetone and glycerol in the presence of *p*-TsOH in benzene. The effect of the amounts of acid and reaction time were explored and the results are summarized in Table 3.4.

Table 3.4 Effect of the amounts of *p*-TsOH and reaction time in the synthesis of 1,2-*O*-isopropylideneglycerol

Entry	*p*-TsOH (mmol)	Time (h)	% Isolated yield
1	2	48	48
2	5	24	57
3	5	36	62
4	5	48	80
5	5	60	82
6	8	48	84

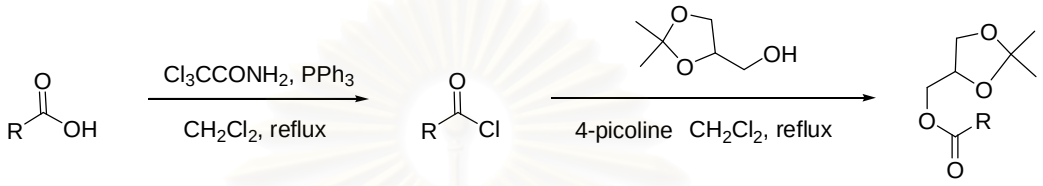
Reaction condition: glycerol (0.1 mol), acetone (0.4 mol), Benzene (10 mL).

As the result shown in Table 3.4, for the first entry the reaction employed 2 mmol of *p*-TsOH under reflux for 48 h, 48% of 1,2-*O*-isopropylideneglycerol was obtained. Increasing the amount of *p*-TsOH to 5 mmol, high yield of the desired product, 80% was attained (entry 4). The reactions employing *p*-TsOH 5 mmol with increasing reaction time from 48 to 60 h did not improve the yield of the desired product compared with the former case (entries 4 and 5). Increasing the amount of *p*-TsOH to 8 mmol and reaction time 48 h, the desired product was a bit altered. Therefore, the optimal conditions were the amount of *p*-TsOH 5 mmol under reflux for 48 h.

3.3 Synthesis of glyceryl monoester

3.3.1 Study on the optimized conditions for (2,2-dimethyl-1,3-dioxolan-4-yl) methyl ester

Optimum conditions for the preparation of acid chloride from carboxylic acid using a combination of Cl_3CCONH_2 and PPh_3 were examined. (2,2-Dimethyl-1,3-dioxolan-4-yl)methyl ester was accomplishly prepared by the acid chloride formed *in situ* and 1,2-*O*-isopropylideneglycerol.



Step I **Step II**

Benzoic acid, the first chosen substrate was transformed to benzoyl chloride and then converted to (2,2-dimethyl-1,3-dioxolan-4-yl)methyl benzoate. Variable parameters studied are reaction times, the amounts of 1,2-*O*-isopropylideneglycerol and the variety of carboxylic acids.

3.3.1.1 Effect of reaction time

Reaction times in steps I and II of the general procedure were altered in order to find out the optimal time for the reaction that could provide (2,2-dimethyl-1,3-dioxolan-4-yl)methyl benzoate in the highest yield. The results are displayed in Table 3.5.

Table 3.5 Effects of the reaction time on the yield of (2,2-dimethyl-1,3-dioxolan-4-yl) methyl ester

Entry	Reaction time of step I (h)	Reaction time of step II (h)	% Isolated yield
1	0.5	1	45
2	1	1	82
3	1	2	86
4	1	4	92

Reaction condition: Benzoic acid (3 mmol), CH_2Cl_2 (6 mL), Cl_3CCONH_2 (6 mmol), PPh_3 (6 mmol), 1,2-*O*-isopropylideneglycerol (3 mmol), 4-picoline (9 mmol) at reflux temperature.

At reflux temperature (38-40°C) when the reaction was treated for 1 h in step I, the maximum yield of acid chloride was obtained. The reflux time in step II was increased from 2 to 4 h with the expectation to lift up the yield of benzoate ester. As expected, the desired benzoate ester was highly increased. This result indicated that refluxing time affected on this reaction.

3.3.1.2 Effect of the amounts of 1,2-*O*-isopropylideneglycerol

To investigate the generality of this developed method, the amount of alcohol was investigated and the results are summarized in Table 3.6.

Table 3.6 Effect of the amounts of 1,2-*O*-isopropylideneglycerol for the synthesis of ester

Entry	Reaction time of step II (h)	Amount of 1,2-*O*-isopropylideneglycerol (mmol)	% Isolated yield
1	1	1	60
2	1	3	74
3	4	1	82
4	4	3	92
5	4	4	94

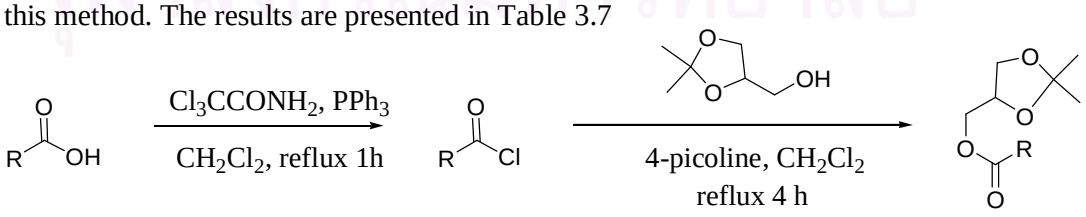
Reaction condition : Benzoic acid (3 mmol), CH_2Cl_2 (6 mL), Cl_3CCONH_2 (6 mmol), PPh_3 (6 mmol), 4-picoline (9 mmol), reflux (38-40°C)

Reaction time : Step I (1 h)

As clearly seen from Table 3.6, when the reaction time in step I was altered from 0.5 to 1 h, the high yield 82% (entry 3) was obtained. Table 3.6 demonstrates that when the reflux time in step II was increased from 1 to 4 h with the amount of alcohol 3 mmol, the reaction could produce the desired ester in excellent yield 92% (entry 4). Increasing the amount of 1,2-*O*-isopropylideneglycerol to 4 mmol, the desired product was a bit altered (entry 5).This result suggested that the procedure for the preparation of ester should be: 1 equiv of carboxylic acid, 2 equiv of Cl_3CCONH_2 and 2 equiv of PPh_3 in reflux CH_2Cl_2 for 1 h, followed by 1 equiv of 1,2-*O*-isopropylideneglycerol and 3 equiv of 4-picoline under reflux CH_2Cl_2 for 4 h.

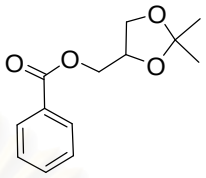
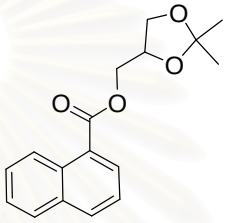
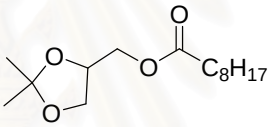
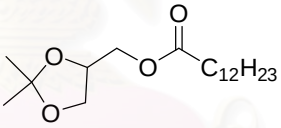
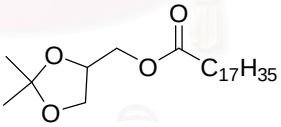
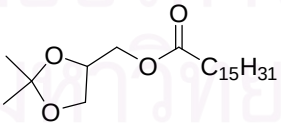
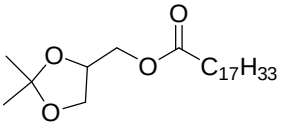
3.3.1.3 Effect of various carboxylic acids on the synthesis of ester

The variation of carboxylic acids was examined to observe the scope of this method. The results are presented in Table 3.7



Step I **Step II**

Table 3.7 Effect of various carboxylic acids on the formation of ester

Entry	Carboxylic acid	Ester	% Isolated yield	
1	Benzoic acid		74[a]	92
2	Alpha-naphthoic acid			95
3	Nonanic acid			94
4	Lauric acid			95
5	Stearic acid		46[a]	89
6	Palmitic acid		50[a]	96
7	Oleic acid			92

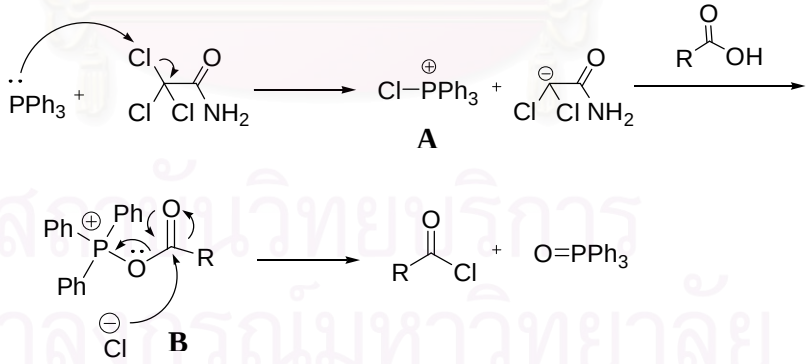
[a]reflux 1 h in step II

According to the results presented in Table 3.7, the use of PPh_3/Cl_3CCONH_2 with benzoic acid and 1,2-*O*-isopropylideneglycerol furnished the formation of (2,2-dimethyl-1,3-dioxolan-4-yl)methyl benzoate in moderate yield 74% (entry 1). To try to lift up the yield of the desired benzoate ester, time in step II was increased from 1 to 4 h resulting in the formation of the target product 92% (entry 1). In the case of α-naphthoic acid, the desired ester was attained in high yield 95% (entry 2). The reaction of aliphatic carboxylic acid such as nonanic acid could also proceed smoothly to gain the corresponding ester in high yield 94% (entry 3). Treatment of stearic acid and palmitic acid, a long chain aliphatic carboxylic acid, at refluxing CH_2Cl_2 for 1 h in step II, only 46 and 50% isolated yield of the corresponding products was obtained. Increasing the refluxing time to 4 h (step II), the corresponding ester could be afforded in high yield 89 and 96% (entries 5-6), respectively. The reaction of lauric acid, aliphatic carboxylic acid yielded the corresponding ester in high yield 95% (entry 4). The preparation of oleate ester, unsaturated aliphatic carboxylic acid, was also achieved in good yield 95% (entry 7).

3.3.2 The mechanism of the one-pot synthesis of ester

The mechanism in step I

The mechanism in step I, the formation of acid halide was believed to take place similar to that reported [65]. The proposed mechanism is shown in Scheme 3.1.



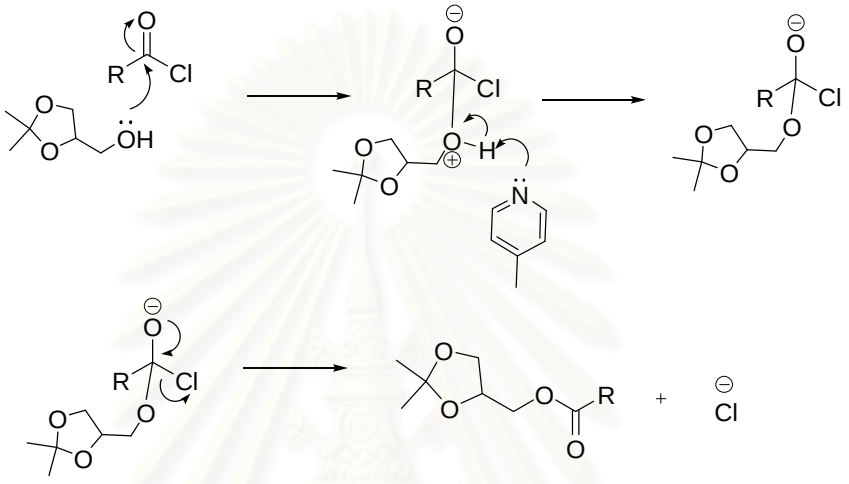
Scheme 3.1 The mechanism for the formation of acid halide

The conversion of carboxylic acid to acid chloride was obviously a multi-step process. The initial step involved the generation of intermediate **A** from PPh_3 and halogenated agent and then the substitution of **A** with carboxylic acid yielded an

alkoxyphosphonium salt **B** which then transformed to the corresponding halide by S_N2 displacement.

The mechanism in step II

The mechanism in step II occurred *via* nucleophilic substitution. The reaction pathway for the formation of ester is proposed as demonstrated in Scheme 3.2.



Scheme 3.2 The mechanism for the formation of ester

In the first step, the addition of a nucleophilic alcohol to an electrophilic carbonyl group was taken place. 4-Picoline was important to remove the proton from the alcohol as it attacked the carbonyl group. The alkoxide intermediate generated would collapse by elimination losing chloride ion. Finally, the ester was formed.

3.3.3 Deprotection of isopropylidene acetal

Although many reagent have been reported for effective cleavage of isopropylidene groups [66-67], lack of selectivity was encountered with these methods. Table 3.8 accumulates the present study on the selective isopropylidene deprotection of (2,2-dimethyl-1,3-dioxolan-4-yl)methyl benzoate carried out by various catalysts and reagents.

Table 3.8 Selective deprotection of isopropylidene group of (2,2-dimethyl-1,3-dioxolan-4-yl)methyl benzoate

Entry	Reagents	Conditions	Time (h)	%Yield[a]
1	2M HCl	reflux	5	80
2	5 mol% *p*-TsOH	reflux	5	58
3	15 mol% CBr_4	reflux	5	80
4	15 mol% $Br_3CCOOEt$	UV	1	83
5	15 mol% $Br_3CCOOEt$	UV	3	87
6	20 mol% $Br_3CCOOEt$	UV	3	Quant
7	15 mol% CBr_4	UV	3	85
8	20 mol% CBr_4	UV	3	Quant

Reaction condition: (2,2-dimethyl-1,3-dioxolan-4-yl)methyl benzoate 1 equiv in MeOH 10 mL, [a]analyzed by ^{1}H-NMR based on a standard toluene 10 μL

Table 3.8 demonstrates that several reagents could be utilized to deprotect an isopropylidene group, for example employing HCl and *p*-TsOH under reflux yielding the deprotected product in moderate yields (entries 1-2). However, it should be noted at this point that using acidic conditions may concomitantly produce an unsatisfied side reaction such as an ester hydrolysis.

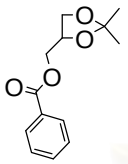
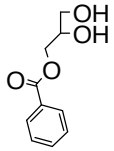
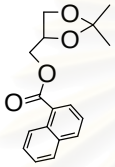
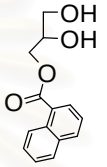
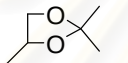
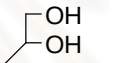
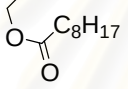
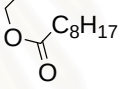
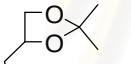
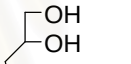
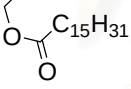
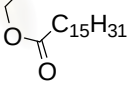
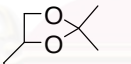
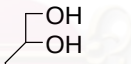
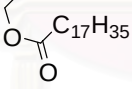
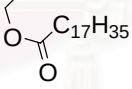
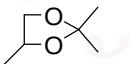
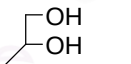
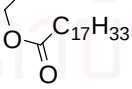
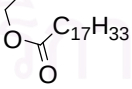
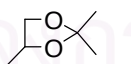
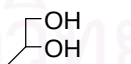
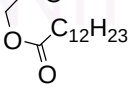
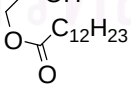
The photoirradiation conditions could also be applied for the selective deprotection of isopropylidene group. For instance, 15 mol% $Br_3CCOOEt$ could be used to deprotect the isopropylidene group under UV-irradiation for 3 h. Glyceryl monobenzoate was obtained in high yield 87% (entry 5). Increasing the amount of $Br_3CCOOEt$ up to 20 mol%, the amount of glyceryl monobenzoate was attained in almost quantitative yield (entry 6). However, $Br_3CCOOEt$ was not accounted as a good reagent for the deprotection of acetal because of its instability. In the presence of 15 mol% CBr_4, glyceryl monobenzoate could also obtain in high yield 85% (entry 7). When the amount of CBr_4 was increased to 20 mol%, glyceryl monobenzoate was successfully deprotected in quantitative yield (entry 8). Therefore, the most suitable

conditions for deprotection of isopropylidene group was 20 mol% CBr_4 under UV-irradiation for 3 h.

3.3.4 Deprotection of isopropylidene group with CBr_4/MeOH under photoirradiation conditions

CBr_4 has been addressed as a versatile reagent for various transformations including the efficient cleavage of acetals. The success deprotection depended on the *in situ* generation of HBr with MeOH; however, the conditions still required anhydrous and acidic conditions [67]. The selective deprotection of isopropylidene using CBr_4/MeOH under photoirradiation conditions was examined and presented in Table 3.9.

Table 3.9 Selective deprotection of isopropylidene with 20 mol% CBr_4/MeOH photoirradiation conditions

Entry	Substrate		Product		%Yield[a]
1		**1**		**2**	Quant[b,c]
2		**3**		**4**	Quant[b,c]
3		**5**		**6**	23[b,e]
4					56[d,e]
5		**7**		**8**	8[b,e]
6					17[d,e]
7		**9**		**10**	Trace[b,e]
8					13[d,e]
9		**11**		**12**	Trace[b,e]
10					12[d,e]
11		**13**		**14**	13[b,e]
12					33[d,e]

Reaction condition: (2,2-dimethyl-1,3-dioxolan-4-yl)methyl ester 1equiv, 20 mol% CBr_4 and MeOH 10 mL, irradiated by UV-lamp (245 nm, 6W) and stirred at RT for another 24 h.

[a]Analyzed by ^{1}H-NMR based on a standard toluene

[b]Irradiated by UV-irradiation for 1 h

[c] Isolated yield

[d] Analyzed by ^{1}H-NMR based on a standard tetrachloroethane

[e] Irradiated by UV-irradiation for 3 h

The selective cleavage of the isopropylidene group was tabulated in Table 3.9. The selective deprotection of isopropylidene group in esters **1** and **3** was carried out by using a catalytic amount of 20 mol% CBr_4 in MeOH under UV-irradiation for 1 h. The desired **2** and **4** were formed in quantitative yield (entries 1 and 2). Nonetheless, the cleavage of isopropylidene in alkyl ester derivatives **5**, **7**, **9**, **11** and **13** by the same method provided the corresponding glyceryl monoesters **6**, **8**, **10**, **12** and **14**, respectively with relatively low yield 5-23% (entries 3, 5, 7, 9 and 11). When the UV-irradiation time was prolonged from 1 to 3 h, the amount of glyceryl monoester produced was a little change (entries 4, 6, 8, 10 and 12).

The reason why the isopropylidene groups of **1** and **3** were more easily cleaved than the others might be explained from the difference in reactivity which was derived from electron withdrawing properties of the substituents on ester derivatives (-CH_2-O-CO-**R**). In the presence of an alkyl group such as aliphatic, long chain aliphatic or unsaturated hydrocarbon, the yield of glyceryl monoester was low. This may be because of a steric hindrance.

It should be concluded that this procedure is more suitable for aromatic substituents containing in ester derivatives than aliphatic ones, respectively.

3.3.5 A new and selective deprotection of isopropylidene group with $Br_3CCOCBr_3$ under photoirradiation conditions

In continuation of recent findings on $Br_3CCOCBr_3$, a versatile brominating agent for efficient transforming alcohols to alkyl bromides and carboxylic acids to acid bromides under mild conditions [68], this reagent was chosen to further explore as a selective deprotecting agent for an isopropylidene group. Optimum conditions for the selective deprotection of isopropylidene acetal with $Br_3CCOCBr_3$ were examined.

3.3.5.1 Condition optimizations of selective deprotection of isopropylidene group with $Br_3CCOCBr_3$ under photoirradiation conditions

Optimum conditions for the selective deprotection of isopropylidene group in the presence of $Br_3CCOCBr_3$ under photoirradiation conditions are presented in Table 3.10.

Table 3.10 Effect of $Br_3CCOCBr_3$ ratios for cleavage of isopropylidene group

Entry	Amount of $Br_3CCOCBr_3$	Conditions	Time (h)	%Yield[a]
1	10 mol%	-	24	N.R.
2	10 mol%	UV	0.25	63
3	10 mol%	UV	0.5	80
4	10 mol%	UV	1	Quant
5	10 mol%	reflux	1	15
6	10 mol%	UV	3	Quant
7	20 mol%	UV	0.5	Quant

Reaction condition: (2,2-dimethyl-1,3-dioxolan-4-yl)methyl benzoate 1 equiv, MeOH 10 mL

[a]Analyzed by ^{1}H-NMR based on a standard toluene 10 μL

Variable parameters studied included the amounts of reagent and photoirradiation time using (2,2-dimethyl-1,3-dioxolan-4-yl)methyl benzoate as a model compound. It was found that when the reaction was irradiated by UV for 0.5 h with amount of 10 mol% $Br_3CCOCBr_3$, glyceryl monobenzoate was obtained 80% (entry 3). When the reaction was treated for 1 h by UV, the maximum yield of glyceryl monobenzoate was obtained (entry 4). Comparing the reactions carried out at reflux temperature and irradiated by UV for 1 h, it was found that the reaction performed at reflux temperature gave a little amount of glyceryl monobenzoate 15% (entry 5) than that carried out and irradiated by UV for 1 h (entry 4). Increasing the reaction time for 1 to 3 h, the yield of product was obtained in excellent yield (entry 6). A typical procedure involves the reaction of acetal (1 equiv), $Br_3CCOCBr_3$ (0.1 equiv), anhydrous MeOH (10 mL) under UV-irradiation for 1 h and followed by stirring without irradiation at RT for another 24 h. These developed photoirradiation conditions were applied to the selective deprotection of various isopropylidene groups.

3.3.5.2 Deprotection of isopropylidene acetals with $Br_3CCOCBr_3$/MeOH under photoirradiation conditions

Variable parameters studied were the amounts of $Br_3CCOCBr_3$ and photoirradiation time were also applied to the selective deprotection of other isopropylidene acetals. The results are presented in Table 3.11.

Table 3.11 Selective deprotection of isopropylidene with $Br_3CCOCBr_3$/MeOH under photoirradiation conditions

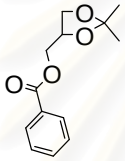
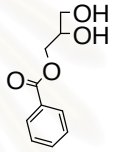
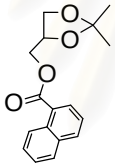
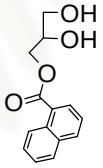
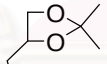
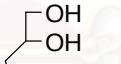
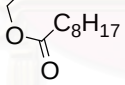
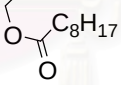
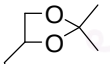
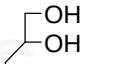
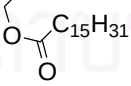
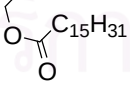
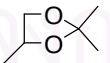
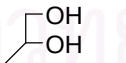
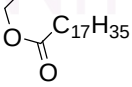
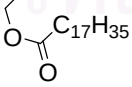
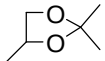
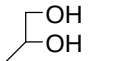
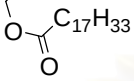
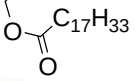
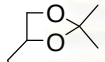
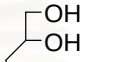
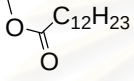
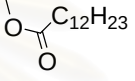
Entry	Substrate		Product		% Yield[a]
1		**1**		**2**	Quant[b,c]
2		**3**		**4**	Quant[b,c]
3		**5**		**6**	62[d]
4					Quant[e]
5		**7**		**8**	27[d]
6					Quant[e]
7		**9**		**10**	20[d]
8					Quant[c,e]

Table 3.11(Con.) Selective deprotection of isopropylidene with $Br_3CCOCBr_3$/MeOH under photoirradiation conditions

Entry	Substrate		Product		% Yield[a]
9		**11**		**12**	21[d]
10					Quant[e]
11		**13**		**14**	68[d]
12					Quant[e]

Reaction condition: (2,2-dimethyl-1,3-dioxolan-4-yl)methyl ester 1equiv, 10 mol% $Br_3CCOCBr_3$and MeOH 10 mL, under UV-irradiation for 1 h (245 nm, 6W) and stirred at RT for another 24 h.

[a]Analyzed by ^{1}H-NMR based on a standard tetrachloroethane

[b]Analyzed by ^{1}H-NMR based on a standard toluene

[c] Isolated yield

[d] 20 mol% $Br_3CCOCBr_3$/ MeOH 10mL/ under UV-irradiation for 1 h

[e] 20 mol% $Br_3CCOCBr_3$/ MeOH 10mL/ under UV-irradiation for 3 h

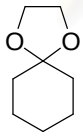
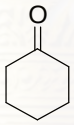
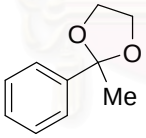
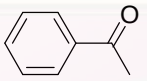
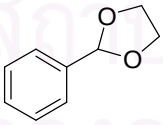
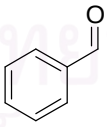
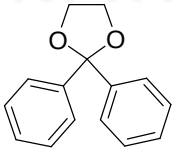
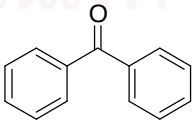
The terminal isopropylidene acetal of benzoate and naphthanoate esters **1** and **3** were successfully deprotected by 10 mol% $Br_3CCOCBr_3$ in MeOH under UV-irradiation for 1 h in quantitative yields (entries 1 and 2). After increasing the amount of $Br_3CCOCBr_3$ up to 20 mol% under UV-irradiation for 3 h, for a terminal isopropylidene acetal of chain aliphatic ester **5** and **13** only moderate yield was obtained 62 and 68 % yields (entries 3 and 11) whereas for long chain aliphatic esters **7**, **9,** and **11** only low yields were detected 27, 20 and 21 yields (entries 5, 7 and 9). When the reaction time was increased for 1 to 3 h, the corresponding aliphatic esters were achieved in excellent yields (entries 4, 6, 8, 10 and 12). The details of the mechanistic study of $Br_3CCOCBr_3$-photoirradiation deprotection would nonetheless require further investigation.

This part of the research work describes a new reagent and efficient method for removing isopropylidene acetal group using $Br_3CCOCBr_3$ in MeOH. The method provides several advantages including operational simplicity, mild reaction conditions, low cost and high yields of deprotecting products.

3.3.6 Applications of the developed procedure for deprotection of other acetals with $Br_3CCOCBr_3$

To explore whether the developed protocol could be effective in selectively cleaving of other types of acetals, a series of experiments were performed and the results are accumulated in Table 3.12.

Table 3.12 The cleavage of acetals using $Br_3CCOCBr_3$/MeOH under photoirradiation conditions

Entry	Acetal	Product	Amount of $Br_3CCOCBr_3$ (mol%)	%Yield[a]
1		 cyclohexanone	10	52
2			20	85
3	 Me	 acetophenone	10	62
4			20	96
5		 benzaldehyde	10	58
6			20	95
7		 benzophenone	10	94
8			20	Quant

Reaction condition: acetal 1equiv, several of $Br_3CCOCBr_3$ and MeOH 10 mL, under UV-irradiation for 3 h (245 nm, 6W) and stirred at RT for another 24 h.

[a]Analyzed by ^{1}H-NMR based on a standard toluene

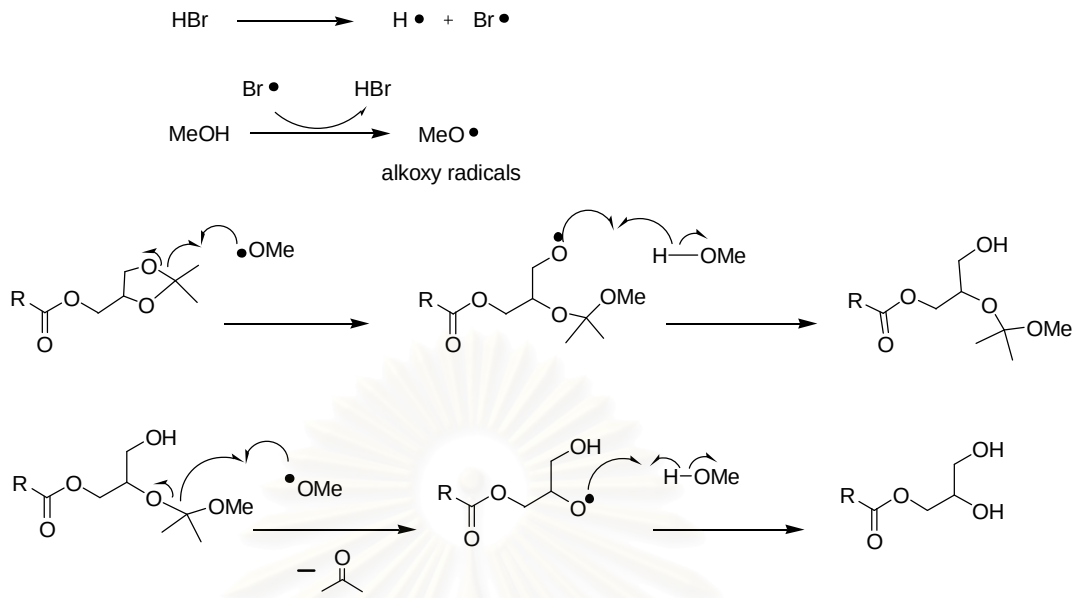
Treatment of cyclohexanone ketal with a catalytic amount of 10 mol% $Br_3CCOCBr_3$ in MeOH under irradiation with UV- lamp for 3 h furnished the formation of cyclohexanone in moderate yield 52% (entry 1). When the amount of $Br_3CCOCBr_3$ was increased up to 20 mol%, the corresponding product was achieved in high yield, 85% (entry 2). Under the same reaction conditions, acetophenone ketal, benzaldehyde ketal and benzophenone acetal could smoothly be transformed to the corresponding ketones and aldehydes in 62, 58 and 94% yield (entries 3, 5 and 7), respectively. Particularly under the conditions employing 20 mol% of $Br_3CCOCBr_3$, the quantitative yields of the target molecule could be achieved and provided the corresponding ketone and aldehydes 96, 95 and quantitative yields (entries 4, 6 and 8). These series of experiments disclosed the new and effective procedure for smooth deprotection of acetals at RT under photoirradiation conditions using $Br_3CCOCBr_3$.

3.5 Possible mechanism of the deprotection of isopropylidene acetal

3.5.1 The mechanism of deprotection of acetal

The mechanism of deprotection of acetal in this research was believed to take place similar to that reported by Yadav and Subba [69]. The proposed mechanism is described as shown in Scheme 3.3. MeOH was found to be the most effective solvent for the cleavage. The occurrence of this cleavage could be attributed to the *in situ* formation of HBr itself by the reaction of CBr_4 with MeOH. To confirm the effect of the solvent, the reaction was carried out in refluxing CH_3CN in the presence of CBr_4 resulting in low to moderate yield of the target product after a long reaction time. When the reactions were carried out using 10 mol% CBr_4, the cleavage required longer reaction time to achieve comparable yield with 20 mol% CBr_4. The outcome of these reactions was the formation of dioxolane by combination of the alkoxy radicals. Radicals of these types could be used for the oxidation of alcohol.

The fate of such radicals could be decomposed to acetone and a methyl radical or else abstraction of hydrogen from a solvent molecule and in these latter, the products were formed *via* dihydroxyl group.

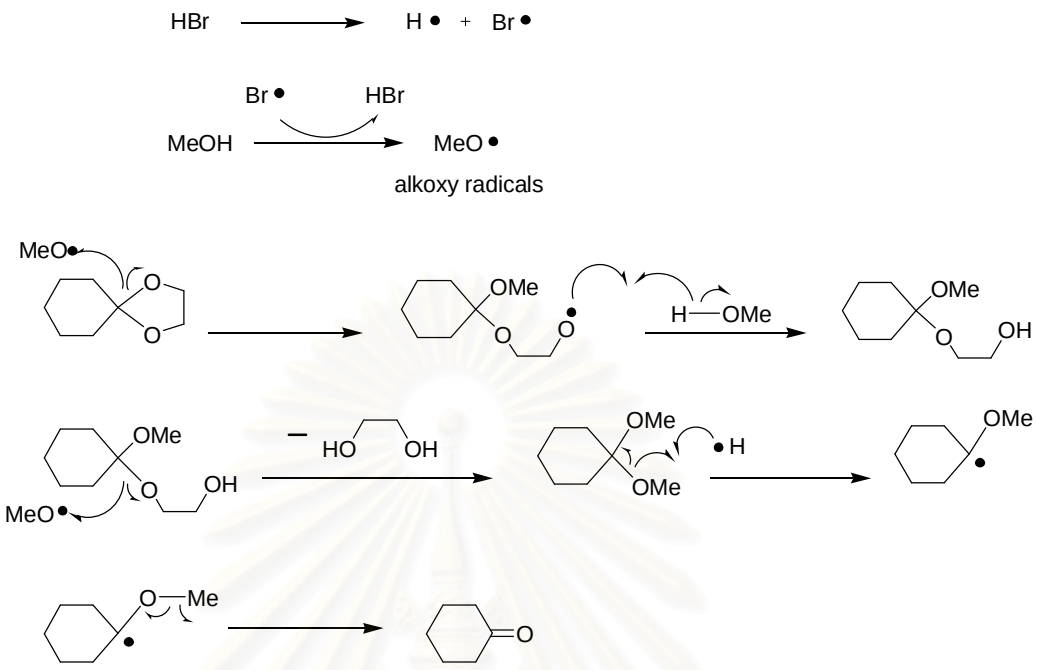


Scheme 3.3 The mechanism for selective cleavage of isopropylidene acetal for the conversion of (2,2-dimethyl-1,3-dioxolan-4-yl)methyl ester to glyceryl monoester

For deprotection of isopropylidene by $Br_3CCOCBr_3$, the mechanism was probably similar to the deprotection of isopropylidene previously described.

3.5.2 Applications of the deprotection of acetal by $Br_3CCOCBr_3$/MeOH under photoirradiation conditions

The mechanism for cyclic acetals (ketals) upon irradiation was believed to undergo the decomposition to afford alkoxy radicals as shown in Scheme 3.4, followed by the ring closure to give the epoxide and rearrangement to a ketone.



Scheme 3.4 The mechanism for selective cleavage of isopropylidene acetal for the conversion of 1,3-dioxolane-2-spirocyclohexane to cyclohexanone

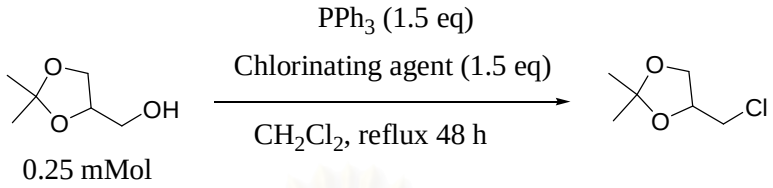
3.6 Synthesis of 3-chloropropane-1,2-diol

3.6.1 Study on the optimized conditions for the synthesis of 4-(chloromethyl)-2,2-dimethyl-1,3-dioxolane

3.6.1.1 Effect of chlorinating agents

Optimum conditions for the preparation of alkyl chlorides from 1,2-*O*-isopropylidene-glycerol utilizing various chlorinated reagents coupled with PPh_3 were examined in Table 3.13.

Table 3.13 Effects of chlorinating agents on the yield of 4-(chloromethyl)-2,2-dimethyl-1,3-dioxolane



0.25 mMol

Entry	Chlorinating agents	% yield[a]
1	none	0
2	CCl_4	83
3	Cl_3CCCl_3	86
4	Cl_3CCN	85
5	$Cl_3CCOCCl_3$	80
6	Cl_3CCO_2Et	80
7	Cl_3CCONH_2	78

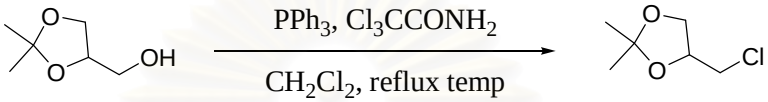
[a]Determined by ^{1}H-NMR based on standard toluene

The efficiency of the chlorinating agent greatly depended on the type of substituent on the chlorinating agents. The reagents in entries 2 and 3 have been previously utilized for conversion of alcohols into alkyl chlorides. Under the specified conditions, the desired product was obtained in high yield in the case of Cl_3CCCl_3. The trichloromethyl group (Cl_3C–), Cl_3CCN and $Cl_3CCOCCl_3$, reagents bearing electron-withdrawing groups, gave the desired products in high yields 85 and 80%, respectively (entries 4, 5). The electron withdrawing group-containing reagents were chosen to prove this assumption. For example, the weak electrophilicity of Cl_3CCO_2Et and Cl_3CCONH_2 (entries 6 and 7) furnished the target product in high yields. Based on the results obtained, Cl_3CCONH_2 was considered as the most suitable chlorinating agent for further investigation since it is commercially available, cheap and leads to a simple work-up procedure.

3.6.1.2 Effect of the amount of chlorinating agent, temperature and reaction time

The quantities of PPh_3 and Cl_3CCONH_2 were varied to find the suitable ratio to provide the maximum yield of 4-(chloromethyl)-2,2-dimethyl-1,3-dioxolane. The results are presented in Table 3.14.

Table 3.14 Effect of the amount of Cl_3CCONH_2, temperature and reaction time on the yield of 4-(chloromethyl)-2,2-dimethyl-1,3-dioxolane



0.25 mMol

Entry	PPh_3 (equiv)	Cl_3CCONH_2 (equiv)	Time (h)	% Isolated yield
1	0.5	0.5	1	Trace
2	1	1	7	10
3			9	13
4			24	25
5	2	2	9	42
6			24	51
7			48	66
8	3	3	9	44
9			24	63
10			48	78

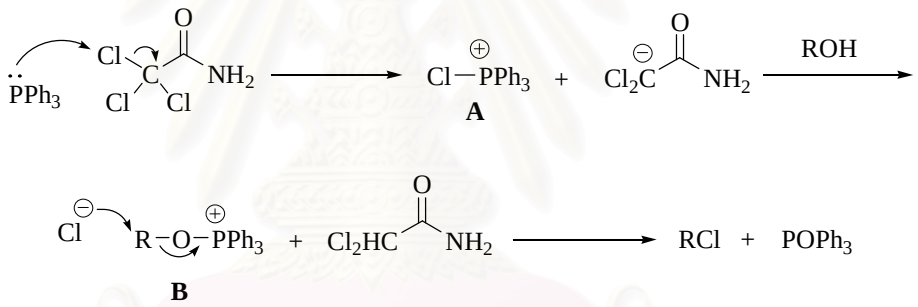
The use of PPh_3 and Cl_3CCONH_2 in 0.5:0.5 and 1:1 eq (based on alcohol) furnished alkyl chloride in low yields, respectively (entries 1-4). Increasing the amount of PPh_3 and Cl_3CCONH_2 to 2 equiv and reaction times from 9 to 24 h (entries 5-6), the reaction gave the moderate yield of 4-(chloromethyl)-2,2-dimethyl-1,3-dioxolane. The target product could be attained only in a little change when the amounts of PPh_3 and Cl_3CCONH_2 were increased to 2 and 3 equiv at reaction time of

48 h (entries 7 and 10). Nevertheless, the quantitative yield was gained when 3 equiv of PPh_3 and Cl_3CCONH_2 and reaction time 48 h were used. Thus, the most suitable radio of 1,2-*O*-isopropylideneglycerol : PPh_3 : Cl_3CCONH_2 was 1:3:3 (entry 10).

This method provides several advantages, including operational simplicity, mild reaction conditions, low cost of the reagents. However the reaction required prolonged reaction time to be quantitatively to preparation of alkyl chloride.

3.6.1.3 The mechanism of acid chloride formation

The mechanism of acid chloride formation in this research was believed to take place similar to that reported by Pluempanupat [62]. The proposed mechanism in Scheme 3.6 involved the formation and the decomposition of the alkoxyphosphonium intermediate. The use of combination of PPh_3/Cl_3CCONH_2 was also believed to proceed in a similar manner. The proposed mechanism is shown below.



Scheme 3.5 The mechanism for convertion of alcohols into alkyl chlorides

PPh_3 reacts with Cl_3CCONH_2 to give **A** which then reacts with alcohol to give alkoxyphosphonium salt (**B**), the formation of which is thermodynamic driving force for the reaction, which suffer nucleophilic attack by the chloride. In the last step, that intermediate eventually decomposes to give alkyl chloride and phosphine oxide *via* inversion of configuration by S_N2 displacement.

3.6.1.4 Deprotection of isopropylidene acetal under photoirradiation conditions

As aforementioned, many reports on the preparation of 1-chloro-2,3-propanediol have been documented. Those reports mainly involved the use of hazardous reagents such as CCl_4 and strong acids. To search for a novel and mild approach for the preparation of 1-chloro-2,3-propanediol, the chlorination of alcohols using new protocols was focused. The reactions using the combination of Cl_3CCONH_3 coupled with PPh_3 could provide chlorides. Unfortunately, the deprotecting of isopropylidene acetal from 4-(chloromethyl)-2,2-dimethyl-1,3-dioxolane was not fruitful. According to the unsuccessful results above, the cleavage of isopropylidene with MeOH in the presence of $Br_3CCOCBr_3$ under UV-irradiation was tried at 1 h; nevertheless, the reaction did not proceed at all. It was noteworthy that 4-(chloromethyl)-2,2-dimethyl-1,3-dioxolane could be instantly unstable for moisture and decomposed to Cl_2 even if it was kept and refrigerated in the dark at temperature around less then 4 °C. UV-sensitive might also cause of these inactive.

CHAPTER IV

CONCLUSION

The combination of Cl_3CCONH_2/PPh_3 was disclosed as an efficient coupling reagent for conversion of fatty acids to esters. The utilization of this reagent could also be fruitfully applied for the preparation of monoglyceride under mild conditions with high yields of the desired product.

From this research, the optimum conditions were disclosed: fatty acid 1equiv as a substrate, Cl_3CCONH_2 2 equiv and PPh_3 2 equiv as a combination reagent, CH_2Cl_2 6 mL as a solvent, *4*-picoline 3 equiv as a base and the reaction was recommended to carry out under reflux CH_2Cl_2 for 4 h or followed by TLC. This developed protocol was indeed disclosed to be an efficient system to convert fatty acid to its ester. Various fatty acids were examined to verify this developed procedure and it was manifested that this method was suitable for aromatic carboxylic acids and short chain aliphatic acids. The long chain aliphatic fatty acids rendered the yield of the desired product. The substituents on an ester at carbonyl position were explicitly uneffected the outcome of the reaction either being an electron-withdrawing or electron-donating group. From the variation of fatty acid, the yields of the desired product were insignificantly depended on the reactivity of alkyl group.

The synthesis of glyceryl monoester depends on the efficient deprotection of the isopropylidene group. Although many methods have been reported for the selective deprotection of protected hydroxyl groups, a catalytic amount of CBr_4/MeOH under photochemical reaction conditions was demonstrated to successfully deprotect isopropylidene acetals. Isopropylidene groups are selectively cleaved without causing any damage to ester group.

Nevertheless, the rate of the reaction was slower and gave low yield, the selectivity of the reaction was depended on the chain length of aliphatic fatty acids. The development of a new and catalytic method for deprotection of isopropylidene has been successful employing $Br_3CCOCBr_3$/MeOH under UV-irradiation conditions. The occurrence of this cleavage could be attributed to the formation of HBr in *situ*. The application of this developed method for the deprotection of 1,3-dioxolanes could be carried out under mild conditions, and provided the high yield of product.

In summary, a mild and efficient procedure for removal of the acetals by $Br_3CCOCBr_3$/MeOH under photoirradiation conditions. The method offers several advantages like mild reaction conditions, simple experimental: work-up procedure, high yields of deprotected products and compatibility with other acid-sensitive functional groups. This method could further examined on the applicability for deprotection of other protecting groups such as methoxyethoxymethyl (MEM) or methoxymethyl (MOM).

During the course of this research, the preparation of (2,2-dimethyl-1,3-dioxolane-4-yl)methyl ester from acid chlorides could be accomplished. The outcome under optimized conditions for the chlorination of alcohol was 1,2-*O*-isopropylidene-glycerol 1 equiv as a substrate and chlorinating agent 3 equiv with PPh_3 3 equiv were recommended to carry out under refluxing CH_2Cl_2 for 48 h. 1,2-*O*-isopropylidene-glycerol was transformed to the corresponding chloride in high yields.

Propose for the future work

This research distinctly reveals the development of successful methodology for the preparation of glyceryl monoester from glycerol waste. The outcome opened many possibilities to deal with future exploration. The applications of these newly methods for the preparation of some commercial compounds such as glyceryl diester, glyceryl triester with different fatty acids should be attempted. In addition, this research concerns with the development for the synthesis of 1-chloro-2,3-propanediol. Formation of 3-chloropropane-1,2-diol should be investigated in model mixtures consisting of 4-(chloromethyl)-2,2-dimethyl-1,3-dioxolane, followed by the deprotection of isopropylidene acetal group would yield 1-chloro-2,3-propanediol. This target product could be utilized in both organic and these compounds and was of growing interest for industrial syntheses.

REFERENCES

[1]. You, Y. D.; Shie, J. L.; Chang, C. Y.; Huang, C. P.; Yu, Y.; Chang, C. H. Economic Cost Analysis of Biodiesel Production: Case in Soybean Oil. *Energy Fuels*. 22(1)(2008) : 182-189.

[2]. Canakci, M.; Gerpen, J. V. Biodiesel Production From Oils and Fats With High Free Fatty Acids. *Transactions of the ASAE*. 4(6)(2001) : 1429-1436.

[3]. Einloft, S.; Magalhães, T. O.; Donato, A.; Dullius, J.; Ligabue, R. Biodiesel from Rice Bran Oil: Transesterification by Tin Compounds. *Energy Fuels*. 22(1)(2008) : 671-674.

[4]. Ngo, H. L.; Zafiropoulos, N. A.; Foglia, T. A.; Samulski, E. T.; Lin, W. Efficient Two-Step Synthesis of Biodiesel from Greases. *Energy Fuels*. 22(1)(2008) : 626-634.

[5]. Mu, Y.; Xiu, Z. L.; Zhang, D. J. A Combined Bioprocess of Biodiesel Production by Lipase with Microbial Production of 1,3-propanediol by *Klebsiella pneumoniae*. *Biochem. Eng. J.* 40(2008) : 537-541.

[6]. Liu, X.; Piao, X.; Wang, Y.; Zhu, S. Calcium Ethoxide as a Solid Base Catalyst for the Transesterification of Soybean Oil to Biodiesel. *Energy Fuels*. 22(2)(2008) : 1313-1317.

[7]. Sakai, T.; Kawashima, A.; Koshikawa, T. Economic Assessment of Batch Biodiesel Production Processes Using Homogeneous and Heterogeneous Alkali Catalysts. *Bioresource Technology*. 100(2009) : 3268-3276.

[8]. Silva, G. P.; Mack, M.; Contiero, J. Glycerol: A Promising and Abundant Carbon Source for Industrial Microbiology. *Biotechnol. Adv*. 27(2009) : 30-39.

[9]. Garcı´a, E.; Laca, M.; Pe´rez, E.; Garrido, A.; Peinado, J. New Class of Acetal Derived from Glycerin as a Biodiesel Fuel Component. *Energy Fuels*. 22(6)(2008) : 4274-4280.

[10]. Nagy, M.; Kerr, B. J.; Ziemer, C. J.; Ragauskas, A. J. Phosphitylation and Quantitative ^{31}P NMR Analysis of Partially Substituted Biodiesel Glycerols. *Article in press.* (2009).

[11]. Gutirrez, L. F.; Snchez, J.; Cardona, C. A. Process Integration Possibilities for Biodiesel Production from Palm Oil. *Bioresource Technology*. 100(2009) : 1227-1237.

[12]. Chin, L. H.; Hameed, B. H.; Ahmad, A. L. Process Optimization for Biodiesel Production from Waste Cooking Palm Oil (*Elaeis guineensis*) Using Response Surface Methodology. *Energy Fuels*. (2)(2009) : 1040-1044.

[13]. Sun, J.; Ju, J.; Ji, L.; Zhang, L.; Xu, N. Synthesis of Biodiesel in Capillary Microreactors. *Ind. Eng. Chem. Res.* 47(5)(2008) : 1398-1403.

[14]. Hamad, B.; Lopes de Souza, R. O.; Sapaly, G.; Carneiro Rocha, M. G.; Pries de Oliveira, P. G.; Gonzalez, W. A. Andrade Sales, E.; Essayem, N. Transesterification of Rapeseed Oil with Ethanol Over Heterogeneous Heteropolyacids. *Catal Comm*. 10(2008) : 92-97.

[15]. Bulent Koc, A. Ultrasonic Monitoring of Glycerol Settling During Transesterification of Soybean Oil. *Bioresource Technology*. 100(2009) : 19-24.

[16]. Dimitratos, N.; Messi, C.; Porta, F.; Prati, L.; Villa, A. Investigation on The Behaviour of Pt(0)/carbon and Pt(0), Au(0)/carbon Catalysts Employed in the Oxidation of Glycerol with Molecular Oxygen in Water. *J. Mol. Cata. A-Chem*. 256(2006) : 21-28.

[17]. Ford, W. C. L. The Oxidation of Glycerol 3-Phosphate By Testicular and Epididymal Spermatozoa. *Comp. Biochem. Physiol.* 68(1980) : 289-293.

[18]. Nippon Shokubai Co., Ltd. New biodiesel/glycerol process generates no waste. *Focus on Catalysts*. 7(2008) : 6.

[19]. Wilson, R.; Van Schie, B. J.; Howes, D. Overview of the Preparation, Use and Biological Studies on Polyglycerol Polyricinoleate (PGPR). *Food. Chem. Toxicol.* 36(1998) : 711-718.

[20]. Aresta, M.; Dibenedetto, A.; Nocito, F.; Pastore, C. A Study on The Carboxylation of Glycerol to Glycerol Carbonate with Carbon Dioxide: The Role of The Catalyst, Solvent and Reaction Conditions. *J. Mol. Cat. A-Chem.* 257(2006) : 149-153.

[21]. Garcia, R.; Besson, M.; Gallezot, P. Chemoselective catalytic oxidation of glycerol with air on platinum metals. *Appl. Catal. A-Gen*. 127(1995) : 165-176.

[22]. Silva, G. P.; Mack, M.; Contiero, J. Glycerol: A promising and abundant carbon source for industrial microbiology. *Biotechnol. Adv.* 27(2009) : 30-39.

[23]. Robles Medina, A.; Esteban Cerda´n, L.; Gime´nez Gime´nez, A.; Camacho Pa´ez, B.; Iba´n˜ez Gonza´lez, M. J.; Molina Grima, E. Lipase-Catalyzed Esterification of Glycerol and Polyunsaturated Fatty Acids from Fish and Microalgae Oils. *J. Biotechnol*. 70(1999) : 379-391.

[24]. Kimb, S. C.; Kima, Y. H.; Lee, H.; Yoon, D. Y.; Songb, B. K. Lipase-Catalyzed Synthesis of Glycerol Carbonate from Renewable Glycerol and Dimethyl Carbonate through Transesterification. *J. Mol. Catal B-Enzym*. 49(2007) : 75-78.

[25]. Tang, S.; Boehme, L.; Lam, H.; Zhang, Z. *Pichia pastoris* Fermentation For Phytase Production using Crude Glycerol from Biodiesel Production as The Sole Carbon Source. *Biochem. Eng. J.* 43(2009) : 157-162.

[26]. Johnson, W. Amended Final Report on the Safety Assessment of Glyceryl Dilaurate, Glyceryl Diarachidate, Glyceryl Dibehenate, Glyceryl Dierucate, Glyceryl Dihydroxystearate, Glyceryl Diisopalmitate, Glyceryl Diisostearate, Glyceryl Dilinoleate, Glyceryl Dimyristate, Glyceryl Dioleate, Glyceryl Diricinoleate, Glyceryl Dipalmitate, Glyceryl Dipalmitoleate, Glyceryl Distearate, Glyceryl Palmitate Lactate, Glyceryl Stearate Citrate, Glyceryl Stearate Lactate, and Glyceryl Stearate Succinate. *Int. J. Toxicol*. 26(3)(2007) : 1-30.

[27]. Pouilloux, Y.; Metayer, S.; Barrault, J. Synthesis of Glycerol Monooctadecanoate from Octadecanoic Acid and Glycerol. Influence of Solvent on The Catalytic Properties of Basic Oxides. *Chemistry*. 3(2000) : 589-594.

[28]. Eychenne, V.; Debrauwer, L.; Mouloungui, Z. O-Etherification Between Glycerol and Glycerol Monooleate, Demonstration of Formation of Diglycerol Monooleate and Triglycerol Monooleate by Fast Atom Bombardment Mass Spectroscopy and ^{13}C Nuclear Magnetic Resonance. *J. Surfactants. Deterg*. 3(2)(2000) : 173-177.

[29]. Burgos, C. E.; Ayer, D. E.; Johnson, R. A. A New, Asymmetric Synthesis of Lipids and Phospholipids. *J. Org. Chem.* 50(22)(1987) : 4973-4977.

[30]. Bentlev, P. H.; Mccrae, W. An Efficient Synthesis of Symmetrical 1,3-Diglycerides. *J. Org. Chem.* 36(6)(1970) : 2082.

[31]. Sonnet, P.; Antonian, E. Synthesis and Evaluation of Pseudolipids To Characterize Lipase Selectivities. *J. Agric. Food Chem.* 36(1988) : 856-862.

[32]. Srisiri, W.; Lamparski, H. G.; O'Brien, D. F. Syntheses of Polymerizable Monoacylglycerols and 1,2-Diacyl-*sn*-glycerols. *J. Org. Chem.* 61(1996) : 5911-5915.

[33]. Fureby, A. M.; Tian, L.; Adlercreutz, P.; Mattiasson, B. Preparation of diglycerides by lipase-catalyzed alcoholysis of triglycerides. *Enzyme Microb. Technot.* 20(1997) : 198-206.

[34]. Pouilloux, Y.; Abro, S.; Vanhove, C.; Barrault, J. Reaction of glycerol with fatty acids in the presence of ion-exchange resins Preparation of monoglycerides. *J. Mol. Cat. A-Chem.* 149(1999) : 243-254.

[35]. Artamonov, A. F.; Nigmatullina, F. S. Synthesis of α-Monoglycerides of Aromatic Acids. *Chem. Nat. Compd.* 35(4)(1999) : 404-408.

[36]. Barrault, J.; Bancquart, S.; Pouilloux, Y. Selective Glycerol Transesterification Over Mesoporous Basic Catalysts. *C. R. Chimie.* 7(2004) : 593-599.

[37]. Corma, A.; Abd Hamid, S. A.; Iborra, S.; Velty, A. Lewis and Brönsted basic active sites on solid catalysts and their role in the synthesis of monoglycerides. *J. Catal.* 234(2005) : 340-347.

[38]. Romanoa, D.; Ferrario, V.; Molinari, F.; Gardossi, L.; Montero, J. S.; Torre, P.; Converti, A. Kinetic resolution of (*R, S*)-1,2-*O*-isopropylideneglycerol by esterification with dry mycelia of moulds. *J. Mol. Catal B-Enzym.Catalysis.* 41(2006) : 71-74.

[39]. Cateni, F.; Bonivento, P.; Procida, G.; Zacchigna, M.; Favretto, L. G.; Scialino, G.; Banfi, E. Chemoenzymatic synthesis and antimicrobial activity evaluation of monoglucosyl diglycerides. *Bioorgan. Med. Chem.* 15(2007) : 815-826.

[40]. March, J. C. *Advanced Organic Chemistry*. New York: John Wiley & Sons:, (1992) : 416-425.

[41]. Lee, J. B. Preparation of Acyl Halides under Very Mild Conditions. *J. Am. Chem. Soc.* 88(14)(1966) : 3440-3441.

[42]. Jang, D. O.; Park, D. J.; Kim, J. A Mild and Efficient Procedure for the Preparation of Acid Chlorides from Carboxylic Acids. *Tetrahedron Lett.* 40(1999) : 5323-5326.

[43]. Vago, I.; Istvan, G. A useful acylation method using trichloroacetonitrile and triphenylphosphine for solid phase organic synthesis. *Tetrahedron Lett.* 43(2002) : 6039-6041.

[44]. Azumaya, I.; Okamoto, T.; Imabeppu, F.; and Takayanagi, H. Simple and convenient synthesis of tertiary benzanilides using dichlorotriphenylphosphorane. *Tetrahedron.* 59(2003) : 2325-2331.

[45]. Chaysripongkul, S. Reagent Development for the Preparation of Acid Chloride for Synthesis of Bioactive Compound, Master's Thesis, Department of Chemistry, Chulalongkorn University, (2003)

[46]. Caserio, F. C.; Dennis, G. E.; Dewolfe, R. H.; Young, W. G. The Reaction of Thionyl Chloride with Allylic Alcohols. *J. Am. Chem. Soc.* 77(1955) : 4182-4783.

[47]. Wiley, G. A.; Hershkowitz, R. L.; Rein, B. M.; Chung, B. C. Studies in Organophosphorus Chemistry. I. Conversion of Alcohols and Phenols to Halides by Tertiary Phosphine Dihalides. *J. Am. Chem. Soc.* 86(1964) : 964-965.

[48]. Snyder, E. I. Conversion of Allylic Alcohols to Chlorides by without Rearrangement. *J. Org. Chem.* 37(1972) : 1466.

[49]. Jones, L. A.; Sumner, C. E.; Franzus, Jr. B.; Huang, T. T.-S.; Snyder, E. I. The Intermediate from the Triphenylphosphine-Tetrachloromethane-Alcohol Reaction: Relative Rates of Intermediate Formation, Kinetics, and Mechanism of Intermediate Decomposition. *J. Org. Chem.* 43(1978) : 2821-2827.

[50]. Hashimoto, S.; Furukawa, I.; Goto, H. Reaction of Triphenylphosphine-Trichloromethyl Compounds with Styrene Oxide. *Nippon Kagaku Kaishi* 10(1979) : 1337-42.

[51]. Magid, R. M.; Fruchey, S.; Johnson, W. L.; Allen, T. G. Hexachloroacetone/ Triphenylphosphine: A Mild Reagent for the Regioselective and

Stereospecific Production of Allylic Chlorides from the Alcohols. *J. Org. Chem.* 44(1979) : 359-363.

[52]. Bringmann, G.; Schneider, S. Improved Methods for Dehydration and Hydroxy/Halogen Exchange Using Novel Combinations of Triphenylphosphine and Halogenated Ethanes. *Synthesis*. (1983) : 139-141.

[53]. Matveeva, E. D.; Yalovskaya, A. I.; Cherepanov, I. A.; Bundel, Yu. G.; Kurts, A. L. Regioselective Substitution of the Hydroxyl Group in Alcohols by Derivatives of Trihaloacetic Acids in the Presence of Triphenylphosphine. *Zhurnal Organicheskoi Khimii*. 27(1991) : 1611-1618.

[54]. Matveeva, E. D.; Erin, A. S.; Mitroshin, D. B.; Kurts, A. L. Regio- and Stereoselective Substitution of Halo for Hydroxyl Groups in Allylic Alcohols. *Zhurnal Organicheskoi Khimii*. 31(1995) : 1121-1125.

[55]. Drabowicz, J.; Luczak. J.; Mikolajczyk, M. Triphenylphosphine/ Dichloroselenurane: A New Reagent for a Selective Conversion of Alcohols into Alkyl Chlorides. *J. Org. Chem.* 63(1998) : 9565-9568.

[56]. Vogel, A. I. *A Text book of Practical Organic Chemistry*. London: Longman Group, (1989).

[57]. Tietze, L. F.; Eicher, T. H. *Reaction and Syntheses in the Organic Chemistry Laboratory*. Califonia: Unversity Science Book. (1988) : 110.

[58]. Buenemann, T. H.; Oudejans, J. C.; Gamba, P. V.; Rampi. A. V. Process for Purifying Crude Glycerol. *E.P. patent 0358255 A1*. March 14, (1990).

[59]. Gilbeau, P.; Gosselin, B.; Claessens, S. Process For Production Dichloropropanol from Glycerol, the Glycerol Coming Eventually from The Conversion of Animal Fats The Manufacture of Biodiesel. *PCT. patent WO 2005/054167*. June 16, (2005).

[60]. Renoll, M.; Newman, M. S. *dl*-Isopropylideneglycerol. *Organic Syntheses, Coll.* 3(1955) : 502.

[61]. Daignault, R. A.; Eliel, E. L. 2-Cyclohexyloxyethanol. *Organic Syntheses, Coll.* 5(1973) : 303.

[62]. Pluempanupat, W.; Chavasiri, W. An efficient method for chlorination of alcohols using PPh_3/Cl_3CCONH_2. *Tetrahedron Lett*. 47(2006) : 6821-6823.

[63]. Muniyappa, P. R.; Brammer, S. C.; Noureddini, H. Improved Conversion of Plant Oils and Animal Fats into Biodiesel and Co-product. *Bioresource Technology*. 56(1996) : 19-24.

[64]. Sato, K.; Kishimoto, T.; Morimoto, M.; Saimoto, H.; Shigemasa, Y. Hydrolysis of acetals in water under hydrothermal conditions. *Tetrahedron Lett*. 44(2003) : 8623-8625.

[65]. Procopio, A.; Gaspari, M.; Nardi, M.; Oliverio, M.; Tagarellib, A.; Sindonab, G. Simple and Efficient MW-Assisted Cleavage of Acetals and Ketals in Pure Water. *Tetrahedron Lett.* 48(2007) : 8623-8627.

[66]. Sabitha, G.; Kiran Kumar Reddy, G. S.; Bhaskar Reddy, K.; Mallikarjuna Reddy, N.; Yadav, J. S. Vanadium(III) Chloride: A mild and Efficient Catalyst for the Chemoselective Deprotection of Acetonides. *J. Mol. Cat. A-Chem.* 238(2005) : 229-232.

[67]. Chen, M. Y.; Patkar, L. N.; Jan, M. D.; Yuan Leec, A. S.; Linb, C. C. CBr_4-Photoirradiation Protocol for Chemoselective Deprotection of Acid Labile Primary Hydroxyl Protecting Groups. *Tetrahedron Lett*. 45(2004) : 635-639.

[68]. Tongkate, P.; Pluempanupat, W.; Chavasiri, W. Hexabromoacetone and Ethyl tribromoacetate: a Highly Efficient Reagent for Bromination of Alcohol. *Tetrahedron Lett*. 49(2008) : 1146-1148.

[69]. Yadav, J. S.; Subba Reddy, B. V. A mild and selective cleavage of p-Methoxybenzyl ethers by CBr_4-MeOH. *Chemistry Lett.* (2002) : 566-567.

APPENDICES

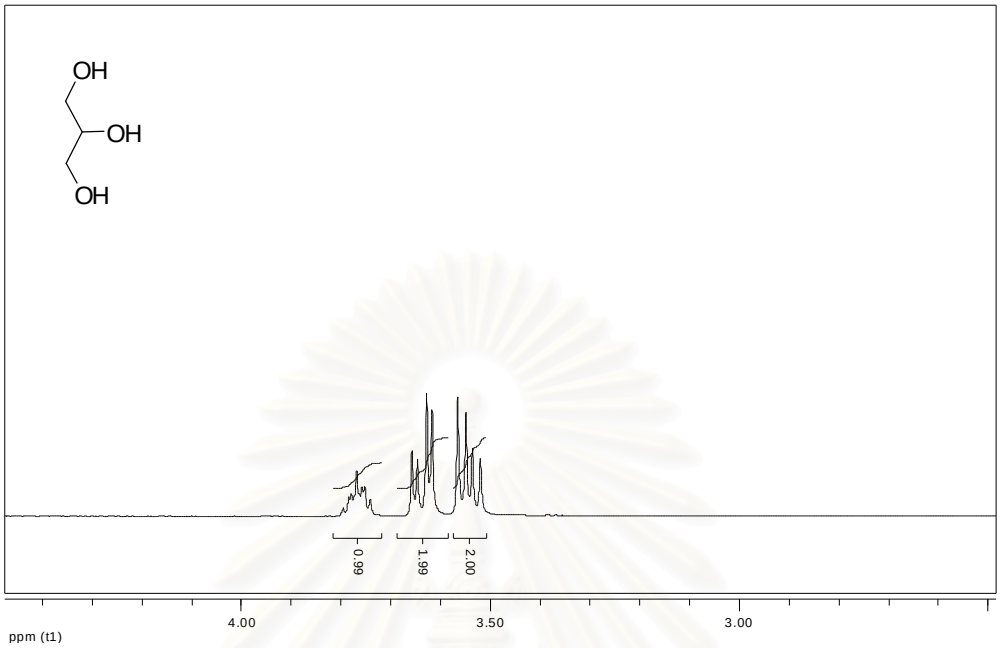


Figure A1 ^{1}H -NMR spectrum of glycerol

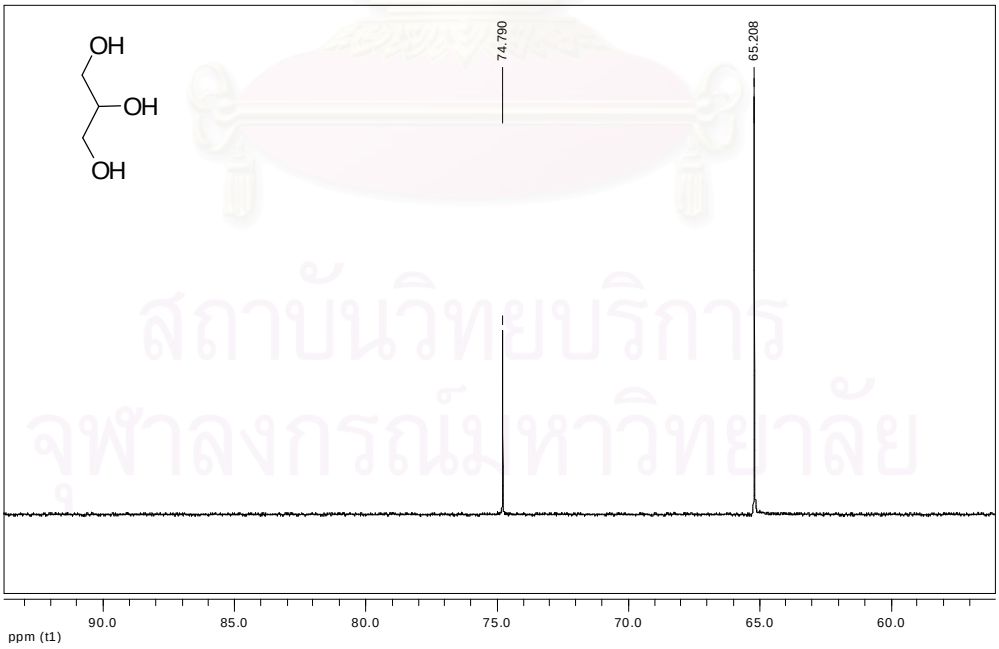


Figure A2 ^{13}C-NMR spectrum of glycerol

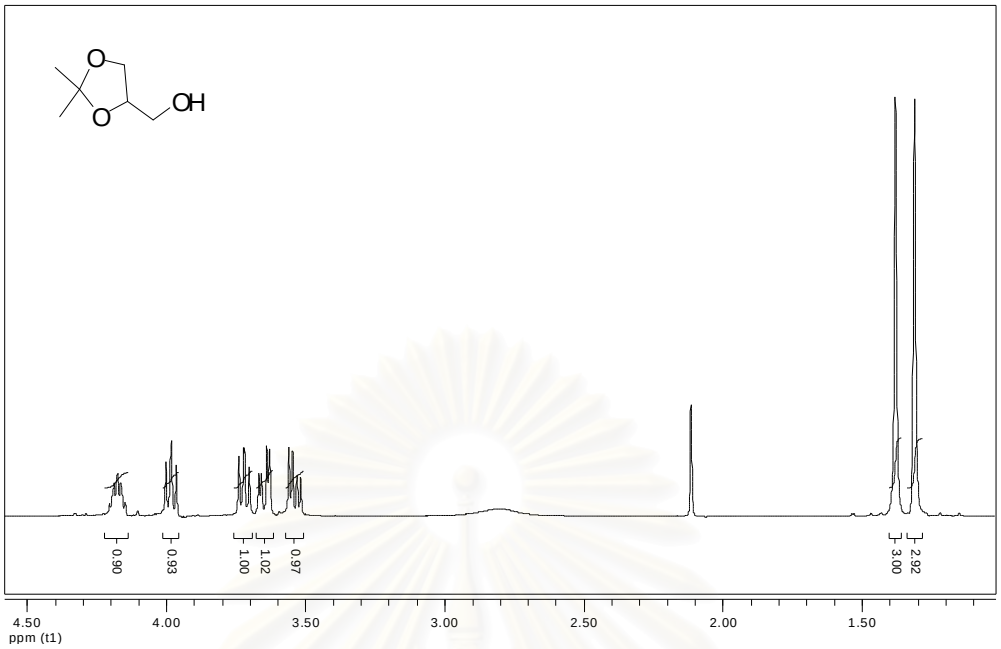


Figure A3 ^{1}H -NMR spectrum of 1, 2-*O*-isopropylideneglycerol

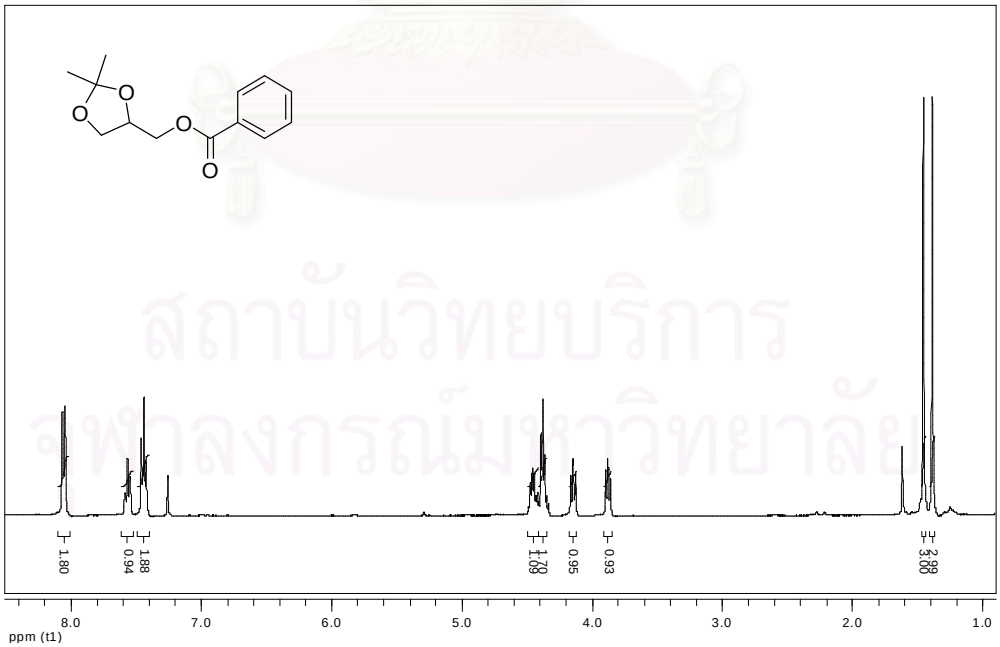


Figure A4 ^{1}H -NMR spectrum of (2,2-dimethyl-1,3-dioxolan-4-yl)methyl-1-benzoate

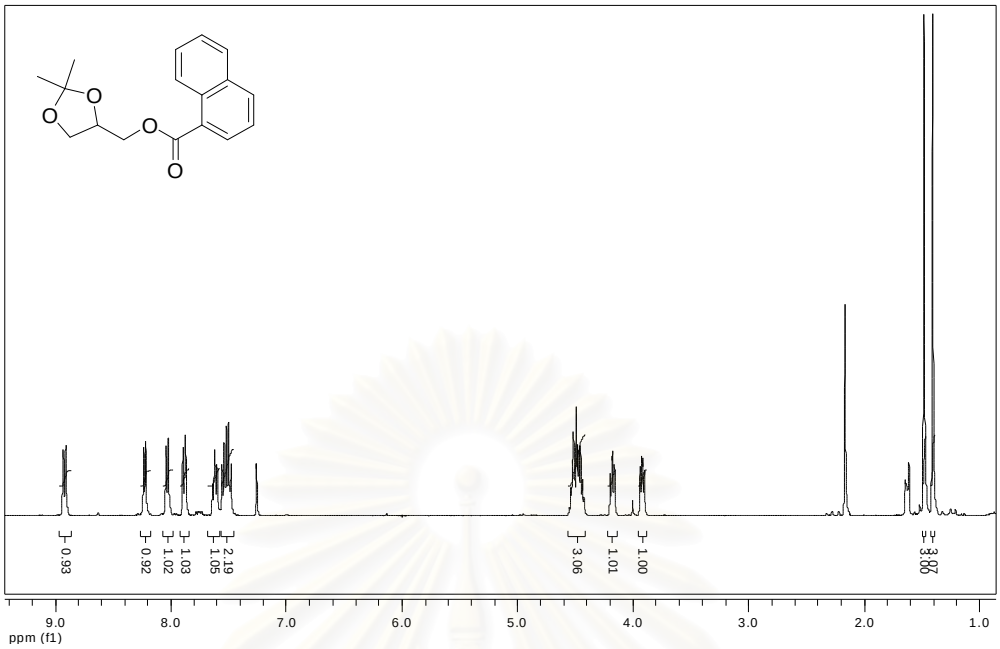


Figure A5 ^{1}H -NMR spectrum of (2,2-dimethyl-1,3-dioxolan-4-yl) methyl-1-naphthoate

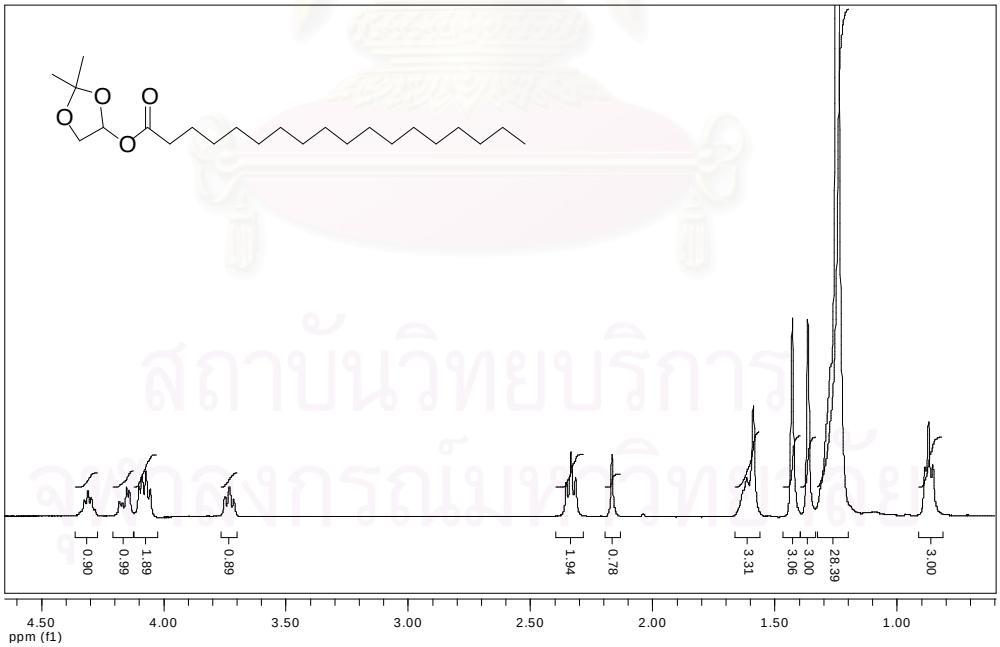


Figure A6 ^{1}H -NMR spectrum of (2,2-dimethyl-1,3-dioxolan-4-yl) methyl-1-stearate

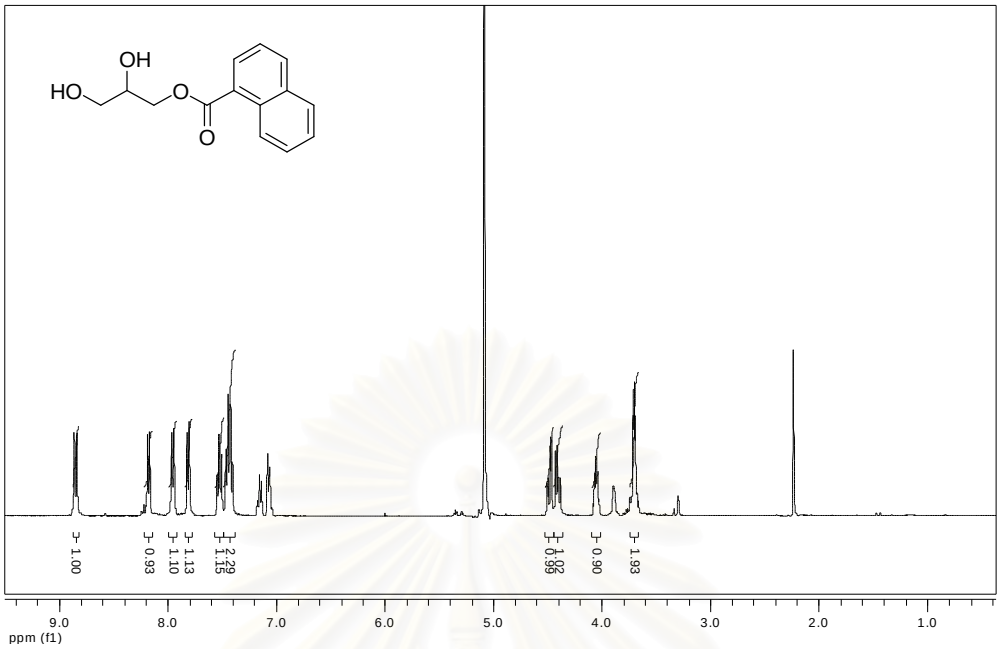


Figure A7 ^{1}H -NMR spectrum of 2,3-dihydroxypropyl-1-napthoate

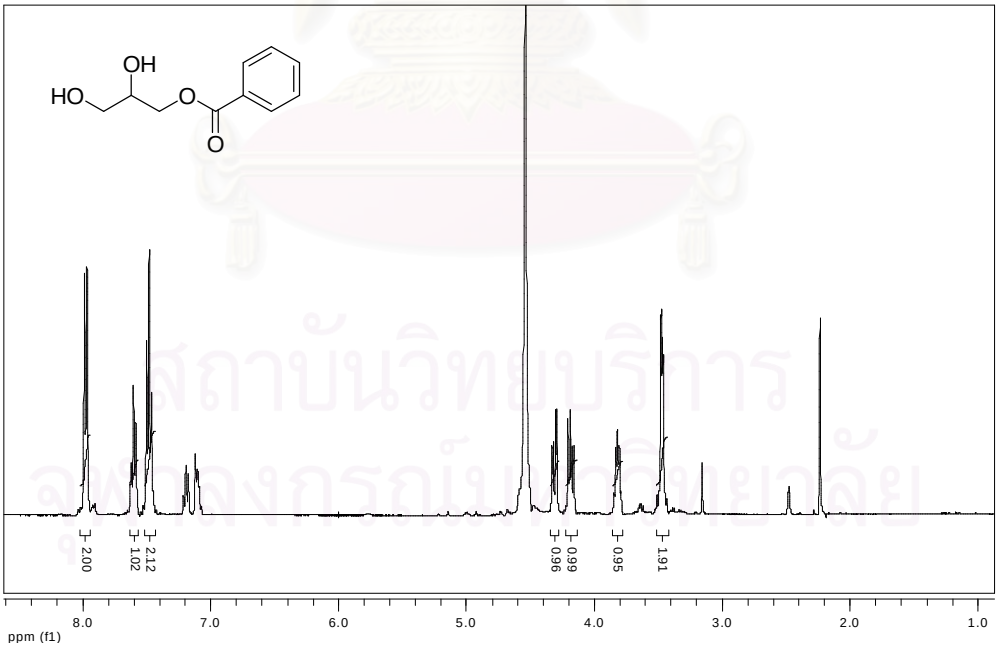


Figure A8 ^{1}H -NMR spectrum of 2,3-dihydroxypropyl-1-benzoate

VITA

Ms. Ladawan Chantharadet was born on January 5, 1983, in Bangkok, Thailand. She received a Bachelor Degree of Science, majoring in Chemistry from Chulalongkorn University in 2006. Since 2006, she has been a graduate student studying in the Program of Petrochemistry and Polymer Science, Faculty of Science, Chulalongkorn University.

Her present address is 39/12 Nonthaburi-Phathumthani Rd., Banchang, Meng, Phatumthani, Thailand 12000.

EXPERIENCES

2007 Poster-presented entitled "UTILIZATION OF GLYCEROL FROM THE PRODUCTION OF BIODIESEL", 3rd MPSGC International Graduates Congress 2007, University of Malaya, Malaysia, December 12-14, 2007.

2007 Oral presentation entitled "UTILIZATION OF GLYCEROL FROM THE PRODUCTION OF BIODIESEL**"**, International symposium on catalysis and fine chemicals 2007, Nanyang Technological University, Singapore, December 17-21, 2007.

2008 Poster-presented entitled "UTILIZATION OF PREPARATION OF GLYCERYL MONOESTER FROM WASTE GLYCEROL UTILIZING Cl_3CCONH_2/PPh_3", 17th International Conference on Organic Synthesis, Daejeon Convention Center, Daejeon, Korea, 22-27 June, 2008.

2009 Poster-presented entitled "HEXABROMOACETONE: A NEW AND SELECTIVE DEPROTECTING AGENT FOR ACETALS", Pure and Applied Chemistry International Conference, Naresuan University, Thailand, January 14 - 16, 2009.

2009 Oral presentation entitled "PREPARATION OF GLYCEROL MONOESTER FROM GLYCEROL WASTE", The Science Forum 2009, The 17th Annual Academic Meeting of the Faculty of Science, Chulalongkorn University, Thailand, March 12-13, 2009.