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ESTERIFICATION OF CARBOXYLIC ACIDS USING IRON COMPLEXES

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ศึกษาเอสเทอริฟิเคชันของกรดคาร์บอกซิลิกกับแอลกอฮอล์ โดยใช้เหล็กรีเอเจนต์ พบว่าสามารถสังเคราะห์สารต้นแบบเอทิลเบนโซเอตได้ในปริมาณสูง ได้ศึกษาปัจจัยต่างๆ ที่มีผลต่อการสังเคราะห์ผลิตภัณฑ์ที่ต้องการ ปริมาณเหล็กรีเอเจนต์ ปริมาณเอทานอล เวลาที่ใช้ในการทำปฏิกิริยา นอกจากนี้ยังได้ศึกษาเพื่อเปรียบเทียบชนิดของเหล็กรีเอเจนต์ ชนิดของกรดคาร์บอกซิลิกและชนิดของแอลกอฮอล์ที่เหมาะสม ได้ประยุกต์ภาวะที่เหมาะสมเหล่านี้เพื่อสังเคราะห์กลิ่นที่ต้องการได้อย่างมีประสิทธิภาพ ในกรณีแอลกอฮอล์ที่มีตำแหน่งเบนซิลิกจะเกิดปฏิกิริยาอีเทอริฟิเคชันแข่งขันได้ นอกจากนี้เหล็กคลอไรด์เฮกซะไฮเดรตยังเป็นรีเอเจนต์ที่ดีสำหรับปฏิกิริยาทรานส์เอสเทอริฟิเคชัน ได้ประยุกต์นำภาวะที่เหมาะสมดังกล่าวเพื่อสังเคราะห์ไบโอดีเซลจากน้ำมันพืชและเมทานอล พบว่าได้ผลิตภัณฑ์ในปริมาณสูง

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CHUTHARAT KHUMNOON: ESTERIFICATION OF CARBOXYLIC ACID USING IRON COMPLEXES. THESIS ADVISOR: ASST. PROF. WARINTHORN CHAVASIRI, Ph.D., 61 pp.

Esterification of carboxylic acids with alcohols using iron reagent was studied. Ethyl benzoate as a model was obtained in good yields. The effect of the main variables involved in the process, the amount of iron reagent, the amount of ethanol and reaction time has been investigated. For comparison, type of iron reagent, type of carboxylic acids and type of alcohols were also studied. The optimal conditions could be applied for the synthesis of selected fragrances which were obtained in excellent yields. Furthermore, in the case of using alcohols containing benzylic site, the etherification was also competitive. In addition, it was found that $FeCl_3{\cdot}6H_2O$ was suitable to perform not only the esterification but also transesterification. This iron reagent also indicated good results for transesterification of vegetable oil with methanol to biodiesel.

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LIST OF ABBREVIATIONS

δ	chemical shift
AA	atomic adsorption spectrometry
^oC	degree Celsius
^{13}C-NMR	carbon nuclear magnetic resonance
cm^{-1}	unit of wavenumber
CH_2Cl_2	dichloromethane
CH_3CN	acetonitrile
d	doublet (NMR)
dd	doublet of doublet (NMR)
$Fe(TCA)_3$	iron(III) trichloroacetate
$Fe(TFA)_3$	iron(III) trifluoroacetate
$FeCl_3\cdot 6H_2O$	iron(III) chloride hexahydrate
$FeCl_2\cdot 4H_2O$	iron(II) chloride tetrahydrate
$FeSO_4\cdot 7H_2O$	iron(III) sulfate heptahydrate
$Fe(acac)_3$	iron(III) acetyl acetonate
$Fe(NO_3)_3\cdot 9H_2O$	iron(III) nitrate nonahydrate
FID	flame ionization detector
FTIR	fourier transform infrared spectrometry
G	gram(s)
GC	gas chromatography
^1H-NMR	proton nuclear magnetic resonance
H	hour(s)
Hz	hertz
J	coupling constant (NMR)
M	multiplet (NMR)
Min	minute(s)
mL	milliliter
mmol	millimole(s)
q	quartet (NMR)
qui	quintet (NMR)
R_f	retardation factor
s	singlet (NMR)

sex	sextet (NMR)
t	triplet (NMR)
TCA	trichloroacetic acid
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	Thin layer chromatography

CHAPTER I

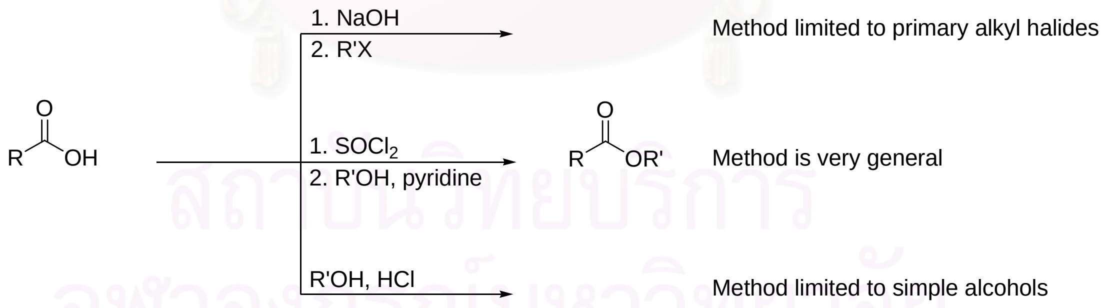
INTRODUCTION

Esters are among the most widespread of all naturally occurring compounds. Many simple esters are pleasant-smelling liquids which are responsible for the fragrant odors of fruits and flowers. For example, methyl butanoate is found in pineapple oil, and isopentyl acetate is a constituent of banana oil. The ester linkage is also present in animal fats and in many biologically important molecules [1].

The chemical industry uses esters for a varity of purposes. Ethyl acetate, for instance, is a commonly used solvent, and dialkyl phthalates are used as so-called plasticizers to keep polymers from becoming brittle.

1.1 Preparation of esters [2]

Esters are usually prepared from carboxylic acids by esterification. Thus, carboxylic acids are converted directly into esters by the reaction of a carboxylate ion with a primary alkyl halide or by Fischer esterification of a carboxylic acid with an alcohol in the presence of a mineral acid catalyst. In addition, acid chlorides are converted into esters by treatment with an alcohol in the presence of base.



1.2. Lewis acid catalysts [3]

The use of Lewis-acid catalysts in modern organic synthesis has grown by leaps and bounds in the past few decades. The commercial availability of many of these Lewis-acid reagents should encourage further development of new chemistry in this area [4].

The reagent function index listed metal widely used as Lewis-acid reagents: aluminum, hafnium, iron, lanthanum, lithium, magnesium, molybdenum, nickel, palladium, phosphorus, silicon, silver, sulfur, thallium, tin, titanium, vanadium, ytterbium, zinc, and zirconium. A wide variety of elements can thus be used as Lewis-acid reagents and each metal has its own characteristic features.

Lewis acid-mediated reactions can be classified into two groups as shown in Fig 1.1. In type 1 the complexes between substrate and Lewis-acid reagent produce the product. Claisen rearrangement promoted by a Lewis-acid catalyst was a typical example of this type. Some complexes from between Lewis acids and substrates were, however, stable enough to react with a variety of reagents from outside the system to generate the product (type 2). The esterification between carboxylic acid and alcohol was an example of type 2 reactions.

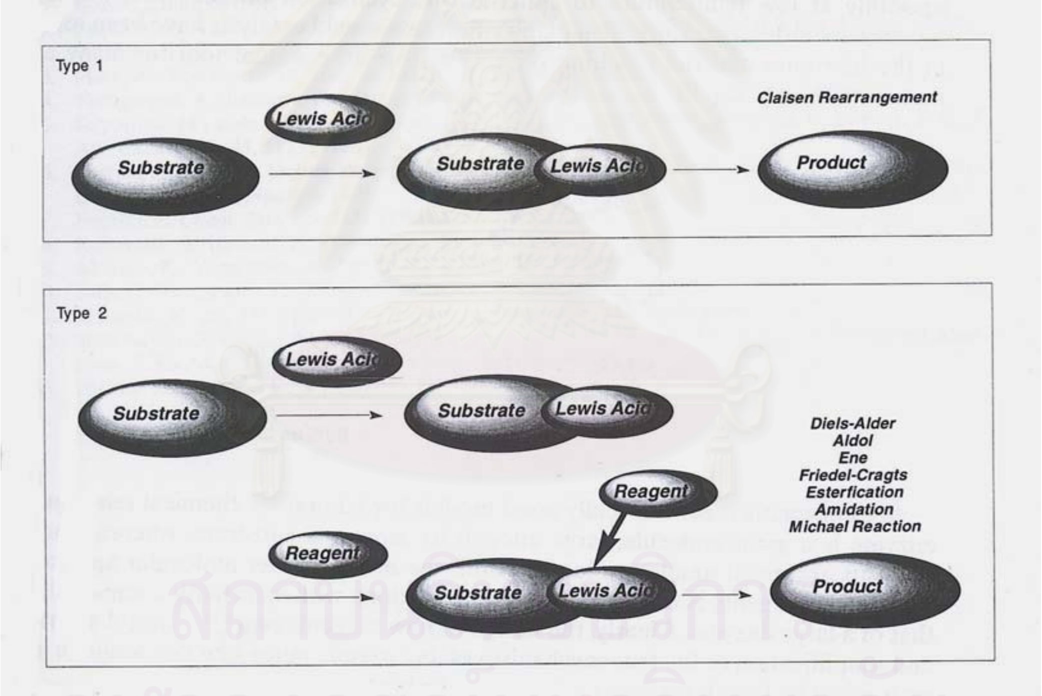


Figure 1.1 Type 1 and type 2 of Lewis acid-mediated reactions.

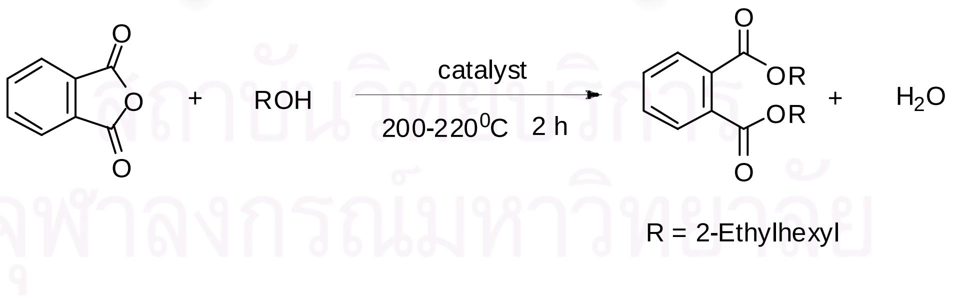
Lewis acid is an excellent candidate as a proton substitute. Thus, an organometallic compound have several ligands around the metal, the structural design of such a catalyst could be quite flexible.

1.3 Literature reviews on the esterification of carboxylic acids

The ester group is an important functional group that can be synthesized in a number of different ways. Recent reports on chemical literatures found that numerous catalytic systems have received intensive interest and have been developed.

In 1998, Gui-Sheng [5] presented the esterification of aliphatic carboxylic acid with alcohols using $Fe_2(SO_4)_3 \cdot xH_2O$. The reaction was simply performed by refluxing a mixture of alcohols, acids and solvent with a catalytic amount of $Fe_2(SO_4)_3 \cdot xH_2O$ for several hours. It was observed that $Fe_2(SO_4)_3 \cdot xH_2O$ showed a higher performance catalyst. In addition, the presence of long chain aliphatic acid such as palmitic acid and dicarboxylic acid such as adipic acid have also been esterified to corresponding product in high yield (84%-95%).

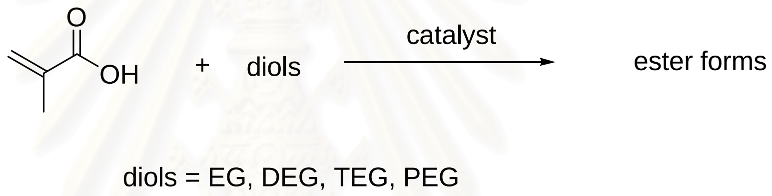
In 2000, Zhao [6] investigated the esterification of phthalic anhydride with 2-ethylhexanol over aluminophosphate and silicoaluminophosphate molecular sieves. The effect of some factors such as temperature, the molar ratio of 2-ethyl hexanol/phthalic anhydride, the amount of catalyst used, the amount of cyclohexane used and reaction time on the reaction were investigated. The yield of di-(2-ethylhexyl)phthalate obtained was over 95% when the reaction conditions used were as follows: the molar ratio of 2-ethylhexanol/phthalic anhydride = 2.8:1; the amount of cyclohexane used = 25 mL/mol phthalic anhydride; H-CHSAPO-1 also possesses high selectivity and good activity for the reaction. The H-CHSAPO-1 catalyst prepared by ion exchange from silicoaluminophosphate molecular sieve possessed the highest activity.



In 2002, Pipus *et al.* [7] reported the esterification of benzoic acid with 2-ethylhexanol in a microwave stirred-tank reactor. Esterification of benzoic acid with 2-ethylhexanol was homogeneously catalyzed with sulfuric acid and *p*-toluene sulfonic acid. As heterogeneous catalysts, $Cs_{2.5}H_{0.5}$-$PW_{12}O_{40}$, sulfated ZrO_2, $Fe_2(SO_4)_3$ and montmorillonite KSF were used. The results showed that homogeneous catalysts were more effective than heterogeneous catalysts. $Fe_2(SO_4)_3$ was the most effective catalyst among the solid catalysts tested. The operating conditions: high-pressure and high-temperature allowed the reaction rate of esterification to be greatly increased.

In 2002, Ramalinga *et al.* [8] presented a mild and efficient method for esterification and transesterification catalyzed by iodine. The high catalytic activity of iodine can be used for transesterification of esters by different alcohols including tertiary alcohols and sterically hindered primary and secondary alcohols. The method presented is especially effective for esterification and transesterification.

In 2004, Shanmugam *et al.* [9] reported the use of solid acid to catalyze esterification of methacrylic acid (MAA) with triethylene glycol (TEG) in the presence of various acid catalysts. The result clearly demonstrated that phosphortungstic acid is a better catalytic system compared to amberlyst-15, *p*-toluenesulfonic acid and sulfuric acid.

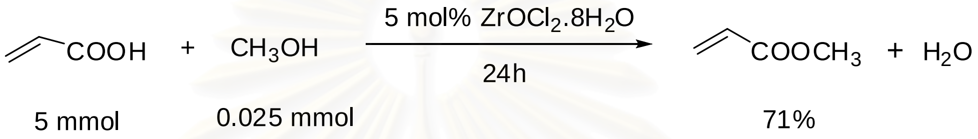


In 2004, Kirumakki *et al.* [10] further reported the esterification of benzyl alcohol with acetic acid over zeolites Hβ, HY and HZSM5. The main product was found to be benzyl acetate. The formation of dibenzyl ether was also observed depending on the zeolites Hβ and HY used. Dibenzyl ether being a bulky molecule was not formed within the pore of ZSM5 whereas the formation was facilitated by large pores zeolites like Y, β. This study suggested that the ether formation occurs within the pores of the zeolites.

In 2005, Salavati-Niasari *et al.* [11] reported the esterification of *tert*-butanol with acetic anhydride over $InCl_3$, $GaCl_3$, $FeCl_3$, $ZnCl_2$, $CuCl_2$, $NiCl_2$, $CoCl_2$ and $MnCl_2$ supported on alumina catalysts. The activity of *tert*-butanol upon the esterification with acetic anhydride decreased in the series of $InCl_3/Al_2O_3$ > $GaCl_3/Al_2O_3$ > $FeCl_3/Al_2O_3$ > $ZnCl_2/Al_2O_3$ > $CuCl_2/Al_2O_3$ > $NiCl_2/Al_2O_3$ > $CoCl_2/Al_2O_3$ > $MnCl_2/Al_2O_3$ > Al_2O_3.

In 2005, Sejidov*et al.* [12] reported the esterification of phthalic anhydride with 2-ethylhexanol using solid heterogeneous acid catalysts under solvent-less conditions. In this work, various acidic catalysts and zeolite were used for preparation of dioctylphthalate. The observed reactivity order of the investigated catalysts was as follows: sulfated ZrO_2 ~ *p*-toluenesulfonic acid > natural zeolite > ASHNCH$_3$- > ZEOKAR-2. Sulfated zirconia showed the best reactivity and efficiency among the investigated heterogeneous catalysts.

In 2006, Hong-Bin *et al.* [13] investigated the esterification of carboxylic acids with equimolar amount of alcohols catalyzed by $ZrOCl_2.8H_2O$. Acrylate esters were obtained in good yields under solvent-free conditions at ambient temperature after 24 h.



According to the literatures cited, the esterification can be accomplished by the reaction of carboxylic acid with alcohols catalyzed by H_2SO_4, solid catalyst and other catalysts. However, only a few literatures that reported on the esterification of carboxylic acid with alcohol using iron reagent. Due to its inexpensiveness and ease of preparation, this research is therefore focused on the esterification of carboxylic acid and alcohol to furnish esters using iron reagent.

1.5 The goal of this research

The goal of this research can be summarized as follows:

1. To study the optimum conditions for the esterification of carboxylic acid using iron salts and its complexes.
2. To search for effective iron salts and its complexes for the esterification of carboxylic acid.
3. To apply the optimum conditions and effective iron reagent for the synthesis of selected fragrances.

CHAPTER II

EXPERIMENTAL

2.1 Instruments and equipments

Spectrometers: Fourier transform-infrared spectra (FT-IR) were performed on Nicolet Impact 410 FT-IR spectrometer. Solid samples were incorporated to KBr to form pellet. The ^{1}H- and ^{13}C-NMR spectra were obtained in $CDCl_3$ or otherwise stated, with Fourier transform nuclear magnetic resonance spectrometer of Varian model Mercury+400 spectrometer which operated at 399.84 MHz for ^{1}H and 100.54 MHz for ^{13}C nuclei. The chemical shifts (δ) are assigned by comparison with residue solvent protons.

Chromatography: Thin layer chromatography (TLC) was carried out on aluminium sheets precoated with silica gel (Merck's, Kieselgel 60 PF_{254}). Column chromatography was performed on silica gel (Merck's, Kieselgel 60G Art 7734 (70-230 mesh)) and aluminium oxide 90 (70-230 mesh ASTM). Gas chromatographic analysis was carried out on Varian gas chromatograph CP-3800 instrument equipped with flame ionization detector (FID) using nitrogen as a carrier gas, the column used was a capillary column type CP-SIL8 (30m x 0.25mm) from VARIAN Inc.

2.2 Chemicals

All solvents used in this research were purified prior to use by standard methodology except for those which were reagent grades. The reagents utilized for synthesizing metal carboxylate complexes and all organic substrates were purchased from Fluka Chemical Company or otherwises stated were used without further purification.

2.3 Synthesis and characterization of iron complexes

2.3.1 Iron(III) trichloroacetate complex [14]

An excess of trichloroacetic acid (13 g, 79 mmol) was added to anhydrous iron (III) chloride (1 g, 6.15 mmol) in a round-bottomed flask under nitrogen atmosphere and the resulting mixture was stirred magnetically and refluxed for 48 h. The products were washed with *n*-hexane and filtered to obtain brown solid, 85% yield, m.p. 193-195°C.

IR (KBr): 1661 (s), 1392 (s) and 851 (m) cm^{-1}.

2.3.2 Iron(III) trifluoroacetate complex [15]

This complex was prepared employing the similar method to that described for metal trichloroacetate by using trifluoroacetic acid (5 mL, 44 mmol) and anhydrous iron(III) chloride (1 g, 6.15 mmol). The resulting red cake was collected and dried at 70°C for 3 h. Iron (III) trifluoroacetate was gained as red powder 2.39 g, 92% yield, m.p. 111-114°C.

IR (KBr): 1689 (s), 1211 (s), 1157 (s) and 725 (m) cm^{-1}.

2.4 General procedure for the esterification of carboxylic acids with alcohols using iron reagents

Carboxylic acid (25 mmol) was dissolved in alcohol (25 mmol) then benzene (25 mmol) and iron reagent (1 mmol) were added into a round bottom flask fitted with dean stark. The mixture was turned to orange suspension. The reaction mixture was heated at reflux temperature with stirring for 24 h. The mixture was then extracted three times with Et_2O and water (3:2). The combined extracts were washed twice with H_2O, dried over anhydrous Na_2SO_4, filtered and the solvent was removed under reduced pressure. The residue was purified by silica gel column eluting with EtOAc and hexane to give the desired product. The product yield was determined by GC with the addition of an exact amount of appropriate internal standard or ^{1}H-NMR.

Ethyl benzoate: colorless liquid (94%), R_f 0.60 (10% EtOAc/hexane). ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.37 (3H, t, J = 7.2 Hz), 4.35 (2H, q, J = 7.1 Hz), 7.41 (2H, t, J = 7.8 Hz), 7.52 (1H, t, J = 7.4 Hz) and 8.04 (2H, d, J = 7.1 Hz).

Ethyl-3-nitro benzoate: colorless liquid (68%), R_f 0.65 (10% EtOAc/hexane). ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.41 (3H, t, J = 7.1 Hz), 4.41 (2H, q, J = 7.2 Hz), 7.63 (1H, t, J = 8.0 Hz), 8.36 (2H, t, J = 8.2 Hz) and 8.86 (1H, s).

Ethyl-3-methoxy benzoate: colorless liquid (55%), R_f 0.68 (10% EtOAc/hexane). ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.39 (3H, t, J = 7.2 Hz), 3.85 (3H, s), 4.38 (2H, q, J = 7.2 Hz), 7.10 (3H, dd, J = 1.6, 8.0 Hz), 7.34 (1H, t, J = 8.0 Hz), 7.56 (1H, s) and 7.64 (1H, d, J = 7.6 Hz).

Ethyl cinnamate: yellow liquid (69%), R_f 0.71 (10% EtOAc/hexane). ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.32 (3H, t, J= 7.1 Hz), 4.24 (2H, q, J= 7.1 Hz), 6.42 (1H, d, J = 16.0 Hz), 7.37-7.71 (5H, m).

Ethyl laurate: yellow liquid (79%), R_f 0.76 (10% EtOAc/hexane). ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.87 (3H, t, J = 6.8 Hz), 1.25 (19H, s), 1.61 (2H, t, J = 6.8 Hz), 2.27 (2H, t, J = 7.2 Hz) and 4.11 (2H, q, J = 7.2 Hz).

Ethyl stearate: yellow liquid (64%), R_f 0.74 (10% EtOAc/hexane). ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.80 (3H, t, J = 6.8 Hz), 1.17 (31H, s), 1.54 (2H, t, J = 7.2 Hz), 2.20 (2H, t, J = 7.2 Hz) and 4.04 (2H, q, J = 7.2 Hz).

Diethyl itaconate: yellow liquid (83%), R_f 0.78 (10% EtOAc/hexane) ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.19 (6H, q, J = 7.12, 7.22 Hz), 3.28 (2H, s), 4.10 (2H, s), 4.08 (2H, q, J = 7.12, 7.16 Hz), 5.65 (1H, s), and 6.27 (1H, s).

Ethyl sorbate: yellow liquid (88%), R_f 0.74 (10% EtOAc/hexane) ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.23 (3H, t, J = 7.07 Hz) , 1.80 (3H, d, J = 5.84 Hz). 4.12 (2H, q, J = 7.10 Hz), 5.71 (1H, d, J = 15.29 Hz), 6.04 (2H, m) and 7.17 (1H, dd, J = 10.11, 15.28 Hz)

Butyl benzoate: colorless liquid (86%), R_f 0.77 (10% EtOAc/hexane). ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.98 (3H, t, J = 7.2 Hz), 1.48 (2H, q, J = 7.2 Hz), 1.75 (2H, q, J = 6.8 Hz), 4.32 (2H, t, J = 6.8 Hz), 7.43 (2H, t, J = 7.6 Hz), 7.54 (1H, t, J = 7.6 Hz), and 8.05 (2H, d, J = 7.2 Hz).

2-Butyl benzoate: colorless liquid (85%), R_f 0.71 (10% EtOAc/hexane). ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.97 (3H, t, J = 7.6 Hz), 1.34 (3H, d, J = 6.0 Hz), 1.63-1.79 (2H, m), 5.10 (1H, sex, J = 6.0 Hz), 7.43 (2H, t, J = 7.6 Hz), 7.54 (1H, t, J = 7.2 Hz), and 8.05 (2H, d, J = 7.2 Hz).

1-Octyl benzoate: colorless liquid (84%), R_f 0.67 (10% EtOAc/hexane). ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.87-1.80 (15H, m), 4.31 (2H, t, J = 6.8 Hz), 7.41 (2H, t, J = 7.2 Hz), 7.57 (1H, t, J = 7.2 Hz) and 8.02 (2H, d, J = 7.2 Hz).

2-Octyl benzoate: colorless liquid (78%), R_f 0.57 (10% EtOAc/hexane). ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.85-1.78 (15H, m), 5.16 (1H, sex, J = 6.4 Hz), 7.42 (2H, t, J = 7.6 Hz), 7.57 (1H, t, J = 7.3 Hz) and 8.05 (2H, d, J = 7.6 Hz).

1-Dodecanyl benzoate: yellow liquid (99%), R_f 0.67 (10% EtOAc/hexane). ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.86 (3H, t, J = 6.0 Hz), 1.26 (17H, m), 1.73 (2H, t, J = 6.5 Hz), 4.30 (2H, t, J = 6.4 Hz), 7.41 (2H, t, J = 7.4 Hz), 7.53 (1H, t, J = 7.5 Hz) and 8.04 (2H, d, J = 7.9 Hz).

Benzyl benzoate: colorless liquid (72%), R_f 0.77 (10% EtOAc/hexane). ^{1}H-NMR ($CDCl_3$) δ (ppm): 5.41 (2H, s), 7.36-7.50 (7H, m), 7.56 (1H, t, J = 7.8 Hz), 8.12 (2H, d, J = 7.7 Hz)

2-Phenethyl benzoate: colorless liquid (82%), R_f 0.57 (10% EtOAc/hexane). ^{1}H-NMR ($CDCl_3$) δ (ppm): 3.12 (2H, t, J = 7.0 Hz), 4.58 (2H, t, J = 7.0 Hz), 7.29 (5H,m), 7.45 (2H, t, J = 7.6 Hz), 7.56 (1H, t, J = 7.7 Hz) and 8.10 (2H, d, J = 8.1 Hz).

2.5 Study on the optimum conditions for the esterification of carboxylic acids

2.5.1 Effect of amount of catalysts

The esterification was carried out as described in the general procedure, but the amount of catalyst was varied: 0, 0.25, 0.50, 0.75, 1.0 and 1.50 mmol.

2.5.2 Effect of amount of alcohols

The esterification was carried out in the same manner as described above but the different amount of alcohol was varied: 5, 20, 25, 30, 50 and 100 mmol.

2.5.3 Effect of reaction time and amount of reagents

The esterification was carried out in the same manner aforementioned at various reaction times was as 1, 6, 12, 18 and 24 h using 1 mmol of iron reagents and switching iron reagents from 1 mmol to 3 mmol. At different reaction time proceed: 0.5, 1, 3 and 6 h.

2.5.4 Effect of type of iron reagents

The esterification was carried out in the same manner as previously described employing various iron reagents: $FeCl_3.6H_2O$, $FeCl_2.4H_2O$, $FeSO_4.7H_2O$, $Fe(TCA)_3$, $Fe(TFA)_3$, $Fe(acac)_3$, $Fe(NO_3)_3.9H_2O$ as a catalyst.

2.5.5 Effect of type of carboxylic acids

The esterification was performed according to the general procedure mentioned earlier with diverse type of carboxylic acids: acetic acid, benzoic acid, 3-nitrobenzoic acid, 3-methoxybenzoic acid, trans-cinnamic acid, lauric acid, stearic acid, itaconic acid and sorbic acid.

2.5.7 Effect of type of alcohols

The esterification was carried out in the same manner as described above using different type of alcohols: 1-butanol, 2-butanol, *tert*-butanol, 1-octanol, 2-octanol, 1-dodecanol, benzyl alcohol and 2-phenethyl alcohol.

2.6 Application of developed procedures for the synthesis of selected fragrances and target molecules

Developed procedures for the synthesis of selected fragrances and target molecules were performed according to the general procedures under the optimum conditions.

1-Octyl acetate: colorless liquid (quant), R_f 0.72 (10% EtOAc/hexane). ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.87 (3H, t, J = 7.0 Hz), 1.27 (10H, s), 1.59 (2H, quin, J = 6.8 Hz), 4.04 (3H, t, J = 6.8 Hz) and 2.03 (3H, s)

Nopyl benzoate: colorless liquid (87.96%), R_f 0.76 (10% EtOAc/hexane). ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.84 (3H, s,CCH_3), 1.27 (3H, s, CCH_3), 2.08-2.44 (8H, m, alkyl group), 4.33 (2H, m, OCH_2), 5.36 (1H, t, J = 1.60 Hz, CH=C), 7.43 (2H, t, J = 7.55 Hz, *m*-ArH), 7.55 (1H, t, J = 7.20 Hz, *p*-ArH) and 8.02 (2H, d, J = 7.2 Hz, *o*-ArH).

Dioctyl phthalate: colorless liquid (quant), R_f 0.72 (10% EtOAc/hexane). ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.85 (6H, s), 1.27 (20H, s), 1.69 (4H, m), 4.27 (3H, t, J = 6.8 Hz), and 7.51-7.72 (4H, m)

2.7 General procedure for the transesterification using iron reagents

Ester (5 mmol) was dissolved in alcohol 3 mL then dry benzene (co-solvent) 1 mL and iron reagent (3 mmol) were added in to a round bottom flask fitted with dean stark. The mixture was turned to an orange suspension. The reaction mixture was heated at reflux temperature with stirring for 24 h. The reaction mixture was then extracted twice with Et_2O and water (3:2). The combined extracts were washed twice with H_2O, dried over anhydrous Na_2SO_4, filtered and the solvent was removed under reduced pressure. The residue was purified by silica gel eluting with EtOAc and hexane to give the desired product. The product yield was determined by GC with the addition of an exact amount of appropriate internal standard or ^{1}H-NMR spectroscopy.

Methyl-3-nitro benzoate: colorless liquid (86%), R_f 0.60 (10% EtOAc/hexane). ^{1}H-NMR ($CDCl_3$) δ (ppm): 3.98 (3H, s,), 7.64 (1H, t, J = 8.0 Hz), 8.36 (2H, dd, J = 8.0, 19.1 Hz), and 8.87 (1H, s).

Methyl-3-nitro benzoate: colorless liquid (86%), R_f 0.60 (10% EtOAc/hexane). ^{1}H-NMR ($CDCl_3$) δ (ppm): 3.98 (3H, s,), 7.64 (1H, t, J = 8.0 Hz), 8.36 (2H, dd, J = 8.0, 19.1 Hz), and 8.87 (1H, s).

Methyl-3-methoxy benzoate: colorless liquid (77%), R_f 0.63 (10% EtOAc/hexane). ^{1}H-NMR ($CDCl_3$) δ (ppm): 3.84 (3H, s), 3.90 (3H, s), 7.08 (1H, dd, J = 2.3, 8.2 Hz), 7.26 (1H, t, J = 8.0 Hz), 7.35 (1H,s) and 7.55 (1H, d, J = 7.5 Hz).

Methyl cinnamate: yellow liquid (88%), R_f 0.62 (10% EtOAc/hexane). ^{1}H-NMR ($CDCl_3$) δ (ppm): 3.80 (3H, s), 6.42 (1H, d, J = 16.0 Hz), 7.37-7.51 (4H, m), and 7.68 (1H, d, J = 16.0 Hz).

Methyl 2-phenylacetate: yellow liquid (91%), R_f 0.68 (10% EtOAc/hexane). ^{1}H-NMR ($CDCl_3$) δ (ppm): 3.64 (2H, s), 3.70 (3H, s) and 7.26 (5H, m).

Methyl stearate: yellow liquid (76%), R_f 0.78 (10% EtOAc/hexane). ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.87 (3H, t, J = 6.5 Hz), 1.26 (28H, s), 1.61 (5H, m), 2.29 (2H, t, J = 7.4 Hz) and 3.67 (3H, s).

2.8 Study on the optimum conditions for the transesterification

2.8.1 Effect of type of esters

The transesterification was carried out as described in the general procedure, using various types of esters: ethyl 3-nitrobenzoate, ethyl 3-methoxybenzoate, ethyl cinnamate, ethyl benzoate, ethylphenyl acetate and ethyl stearate.

2.8.2 Effect of amount of methanol

The transesterification of ethylphenyl acetate was carried out as described in the general procedure, but the amount of methanol was varied: 1, 2, 3, 4, 5 and 6 mL.

2.8.3 Effect of amount of iron reagents

The transesterification was carried out as described in the general procedure, but the amount of iron reagents were varied: 1, 2 and 3 mmol.

2.8.4 Effect of reaction time

The transesterification was carried out as described in the general procedure, at different reaction times: 6, 12, 18, 24 and 48 h.

2.9 Application of developed procedures for the synthesis of biodiesel from vegetable oil

Developed procedures for the synthesis of biodiesel from vegetable oil were performed according to the general procedures using the optimum conditions. The product yield was determined by GC with the addition of an exact amount of appropriate internal standard or ^{1}H-NMR spectroscopy.

Methyl oleate: yellow liquid, R_f 0.68 (10% EtOAc/hexane). ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.87 (3H, t, J = 6.0 Hz), 1.26 (20H, m), 1.63 (2H, m), 1.98 (4H, m), 2.29 (2H, m), 3.67 (3H, s) and 5.39 (2H, m).

Methyl palmitate: yellow liquid, R_f 0.78 (10% EtOAc/hexane). ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.87 (3H, t, J = 6.0 Hz), 1.26 (24H, m), 1.61 (2H, s), 2.29 (2H, t, J = 7.4 Hz) and 3.67 (3H, s).

Methyl stearate: yellow liquid, R_f 0.78 (10% EtOAc/hexane). ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.87 (3H, t, J = 6.5 Hz), 1.26 (28H, m), 1.61 (5H, m), 2.29 (2H, t, J = 7.4 Hz) and 3.67 (3H, s).

Methyl linoleate: yellow liquid, R_f 0.70 (10% EtOAc/hexane). ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.82 (7H, m), 1.25 (22H, m), 1.61 (4H, m), 1.96 (2H, m), 2.01 (2H, m), 2.74 (2H, t, J = 7.3 Hz), 1.62(1H, m), 3.66 (3H, s) and 5.37 (2H, m).

2.10 General procedure for the etherification of alcohols using iron reagents

Alcohol (8 mmol) and THF 2 mL (solvent) were added in a round bottom flask fitted with dean stark. Iron reagent 3 mmol was added to giving an orange suspension. The reaction mixture was heated at reflux temperature with stirring for 24 h. The mixture was extracted two times with Et_2O and water (3:2). The combined extracts were washed twice with H_2O, dried over anhydrous Na_2SO_4, filtered and the solvent was removed under reduced pressure. The residue was purified by silica gel column eluting with EtOAc and hexane to give the desired product. The product yield was determined by GC with the addition of an exact amount of appropriate internal standard or ^{1}H-NMR spectroscopy.

Benzyl ether: yellow liquid (76%), R_f 0.68 (10% EtOAc/hexane). ^{1}H-NMR ($CDCl_3$) δ (ppm): 4.59 (4H, s) and 7.37 (2H, m).

2.11 Study on the optimum conditions for the etherification of alcohols

2.11.1 Effect of type of solvents

The etherification was carried out in the same manner as described above except for THF, CH_2Cl_2, benzene, hexane and CH_3CN were used as a reaction medium.

2.11.2 Effect of amount of solvents

The etherification was carried out in the same manner as described above with different amount of solvents: 1, 2, 3, 4 and 5 mL.

2.11.3 Effect of reaction time and amount of iron reagents

The etherification was carried out as described previously employing various amount of $FeCl_3.6H_2O$: 1, 2 and 3 mmol and the reaction time was varied from 6, 12, 18, 24 and 48 h.

CHAPTER III

RESULTS AND DISCUSSION

Esterification reactions are conventionally carried out homogeneously in batch processes using mineral acids such as sulfuric acid or *para*-toluene sulfonic acid (PTSA) as catalysts. Nevertheless, the applications of these mineral acids cause some problems such as corrosion, difficulty in separation and environmental problems [16].

This research focuses on the development of an efficient catalytic procedure for the direct esterification of carboxylic acids with alcohols employing iron reagents with the following requirements: (1) esters should be obtained in high yields; (2) esterification should proceed at ambient temperature and (3) the separation procedure should be simple. After screening a number of iron reagents, $FeCl_3.6H_2O$ worked efficiently and possessed the necessary properties to meet the requirements as described above.

3.1 The esterification of carboxylic acids with alcohols using iron reagents

3.1.1 Effect of amount of iron reagents

The amount of $FeCl_3$ was first investigated with a model reaction of benzoic acid and ethanol. The desired product, ethyl benzoate was quantified by GC compared with the prepared authentic specimen.

The ^{1}H-NMR spectrum of ethyl benzoate (Fig 3.1) reveals the proton signals of ethyl group at δ_H 1.36 (3H, t, J = 7.6 Hz) and δ_H 4.34 (2H, q, J = 7.2 Hz). The signals around δ_H 7.37-8.04 (5H, m) were assigned for aromatic protons. The ^{13}C-NMR spectrum (Fig 3.2) displays an sp^3 carbon signal of methyl group and an sp^3 carbon signal connecting with oxygen at δ_C 14.3 and 60.9, respectively. The signals around δ_C 128.3-132.8 with six sp^2 carbons were assigned to aromatic carbons. The signal at δ_C 166.5 was belonged to a carbonyl carbon of ester.

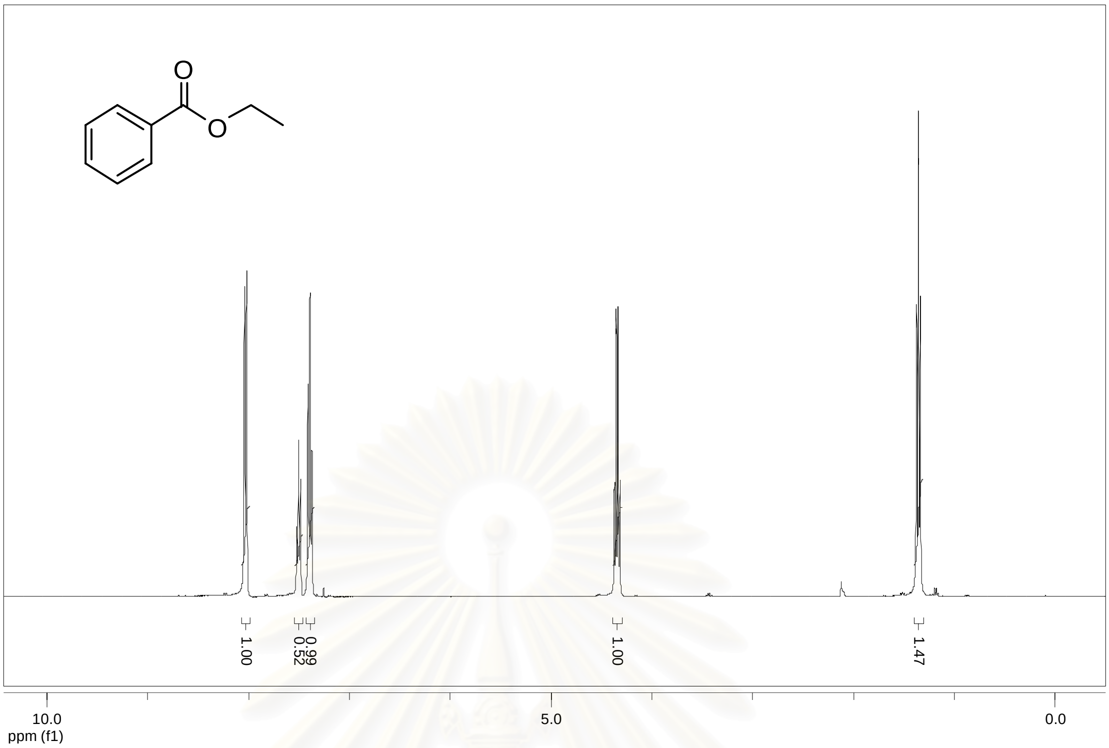


Figure 3.1 The ^{1}H-NMR spectrum of ethyl benzoate

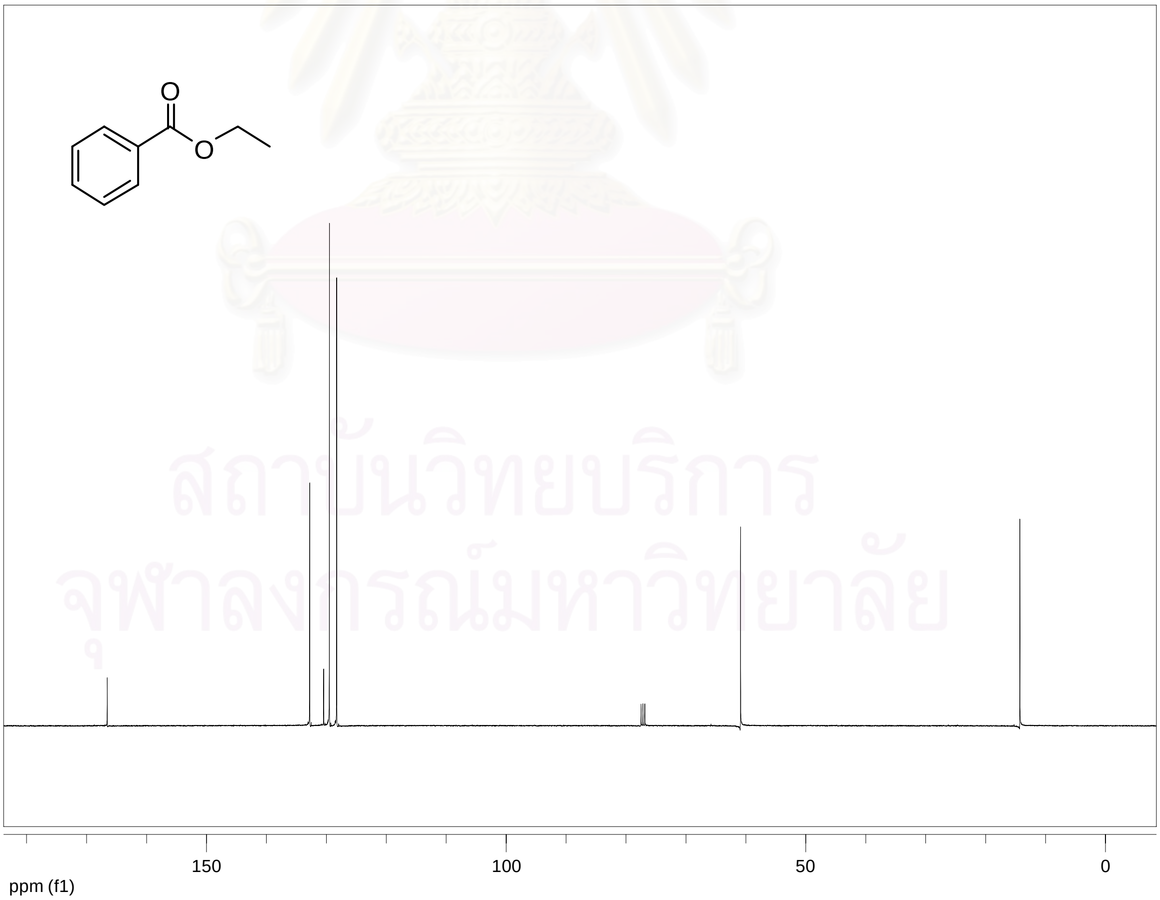


Figure 3.2 The ^{13}C-NMR spectrum of ethyl benzoate

The results of the effect of the amount of $FeCl_3$ on the esterification of benzoic acid with ethanol are shown in Table 3.1.

Table 3.1 Effect of amount of $FeCl_3$ on the esterification of benzoic acid with ethanol

Entry	**$FeCl_3$ (mmol)**	**%Yield**
1	0	0
2	0.25	22.42
3	0.50	34.84
4	0.75	62.89
5	1.00	70.48
6	1.50	71.19

Reaction conditions: benzoic acid (5 mmol), ethanol (1.17 mL), dried benzene (2.0 mL) and $FeCl_3$ (vary) at reflux temperature for 18 h.

The observations obtained from Table 3.1 provided an interesting result. A blank experiment clearly revealed that in the absence of $FeCl_3$, no reaction occurred. The results from other entries lucidly showed that the amount of iron reagent was directly influenced on the esterification of benzoic acid. Since the amount of obtained product derived from the use of $FeCl_3$ 1.0 mmol was not different from that using $FeCl_3$ 1.5 mmol, further investigation was thus carried on using $FeCl_3$ 1.0 mmol.

3.1.2 Effect of amount of alcohols

With the fixed amount of $FeCl_3$, the amount of ethanol was the next parameter to examine. The amount of ethanol in the reaction was varied from 0.30-5.90 mL and the results are summarized in Table 3.2.

Table 3.2 Effect of amount of alcohols on the esterification of benzoic acid with ethanol

Entry	Alcohol (mL)	%Yield
1	0.30	12.98
2	1.20	78.42
3	1.50	89.84
4	2.00	76.87
5	3.00	69.45
6	6.00	43.29

Reaction conditions: Benzoic acid (5 mmol), ethanol (vary), dried benzene (2.0 mL) and $FeCl_3$ at reflux temperature for 18 h.

From the above results, ethanol 1.50 mL provided the best result for the esterification of benzoic acid. Since the esterification under acidic conditions is well known to be reversible, less amount of ethanol than 1.50 mL may not enough to make the reaction straightforward proceed. The excess of ethanol will however possibly make the reaction somewhat too dilute to reach the maximized yield.

3.1.3 Effect of reaction time and amount of iron reagents

Time course study gives an insight into the performance of the reaction progress. Thus, various diverse reaction times were needed to be explored to observe the reactivity of iron reagents in such kind of reaction. Two conditions employing $FeCl_3$ 1 and 3 mmol upon the esterification of benzoic acid were compared and the results are presented in Fig 3.3.

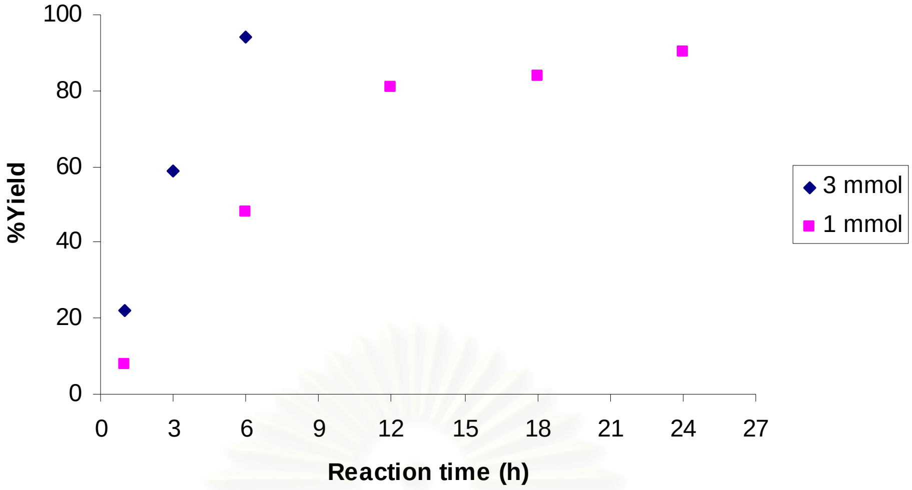


Figure 3.3 Effect of reaction time and amount of iron reagents on the esterification of benzoic acid and ethanol.

The esterification of benzoic acid and ethanol using $FeCl_3{\cdot}6H_2O$ 3 mmol afforded ethyl benzoate in 93% within 6 h and the half-life was approximately 2.5 h, while that using $FeCl_3{\cdot}6H_2O$ 1 mmol provided the expected ester in 90.1% within 24 h and the half-life was approximately 4.5 h. It could therefore be summarized that the amount of $FeCl_3{\cdot}6H_2O$ employed was markedly influenced on the yield of ethyl benzoate.

3.1.4 Synthesis and characterization of iron complexes

Iron(III) trichloroacetate ($Fe(TCA)_3$) and iron(III) trifluoroacetate ($Fe(TFA)_3$) were synthesized according to those previously reported protocols [17, 18]. The identities of both synthesized complexes were confirmed by IR. The general vibration bands of carboxylate ligands "asymmetric stretching of C=O at 1661 cm^{-1}, and symmetric stretching of C-O bond at 1392 cm^{-1}" were resembled to that of carboxylate ligands of iron(III) carboxylate. The illustration of IR spectra of $Fe(TCA)_3$ and $Fe(TFA)_3$ are exhibited in Figs 3.4 and 3.5.

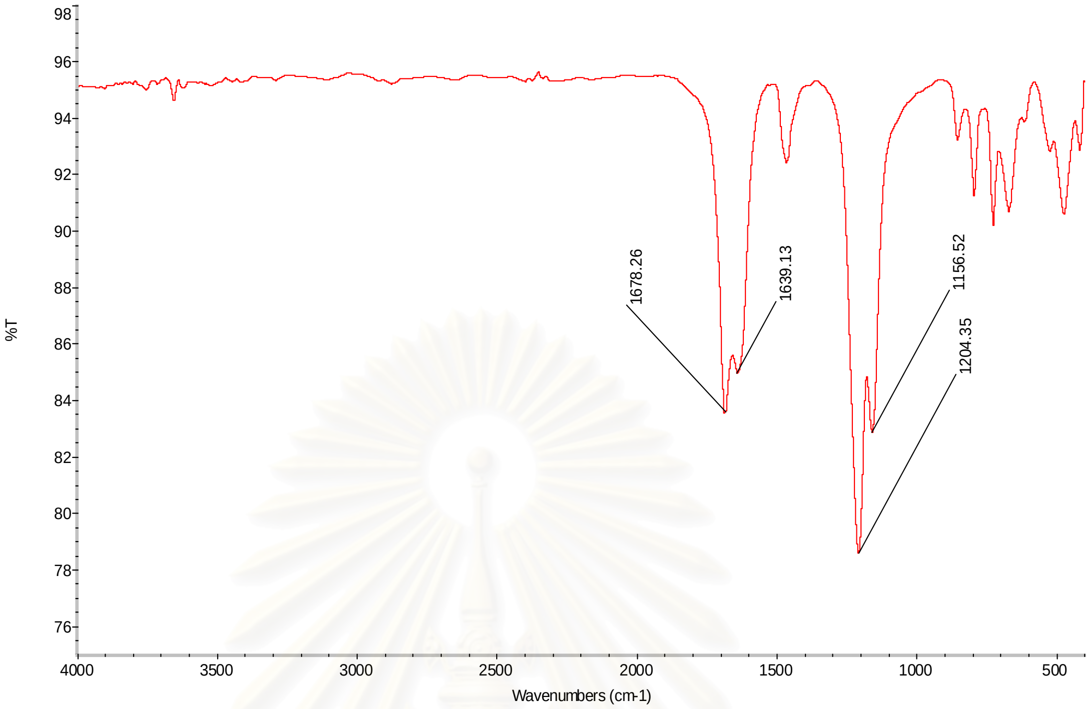


Figure 3.4 The IR spectrum of Fe(TCA)$_3$

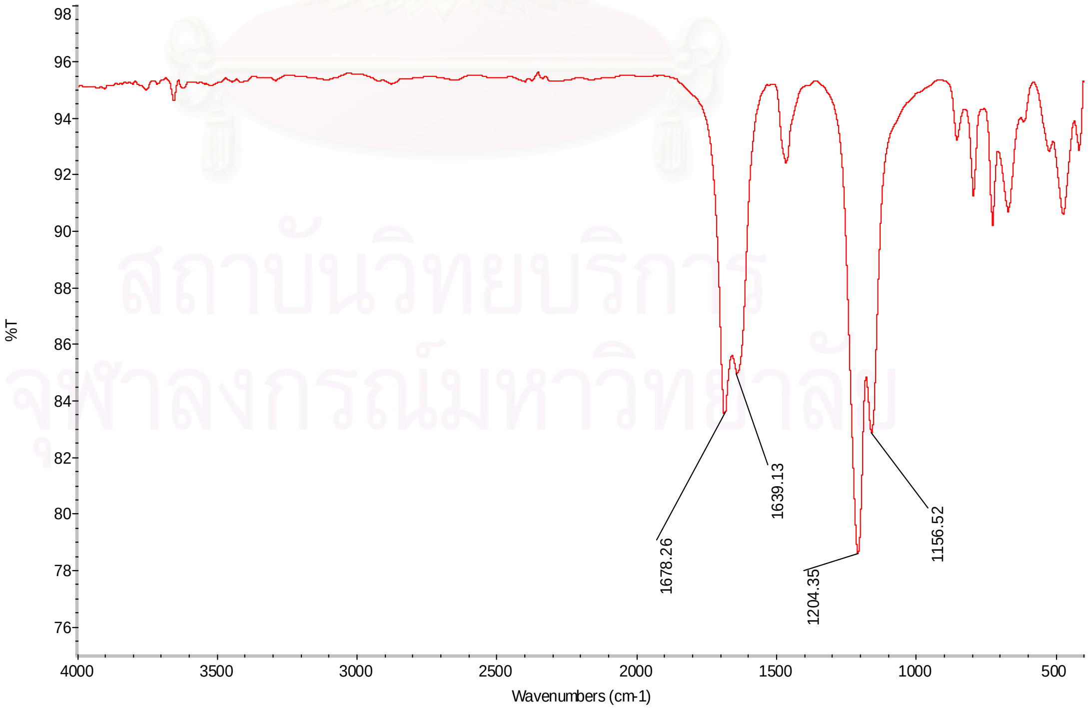


Figure 3.5 The IR spectrum of Fe(TFA)$_3$

Both prepared iron carboxylate complexes were employed to examine their reactivity on the esterification reaction.

3.1.5 Effect of type of iron reagents

Seven iron reagents, namely $FeCl_3{\cdot}6H_2O$, $FeCl_2{\cdot}4H_2O$, $FeSO_4{\cdot}7H_2O$, $Fe(TCA)_3$, $Fe(TFA)_3$, $Fe(acac)_3$ and $Fe(NO_3)_3{\cdot}9H_2O$ were selected for conducting the esterification of benzoic acid with ethanol. Dried benzene was used as solvent. The results are presented in Table 3.3.

Table 3.3 The esterification of benzoic acid with ethanol using iron reagents

Entry	**Iron reagents**	**%Yield**	
		12 h	24 h
1	$FeCl_2{\cdot}4H_2O$	63.09	85.11
2	$FeCl_3{\cdot}6H_2O$	87.89	94.17
3	$Fe(NO_3)_3{\cdot}9H_2O$	50.59	65.29
4	$FeSO_4{\cdot}7H_2O$	4.46	17.64
5	$Fe(acac)_3$	6.68	12.96
6	$Fe(TCA)_3$	21.94	35.61
7	$Fe(TFA)_3$	12.23	27.79

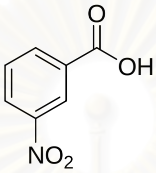
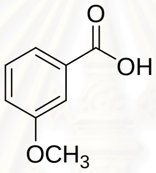
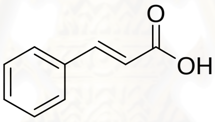
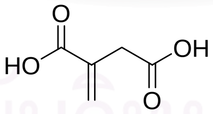
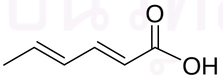
Reaction conditions: benzoic acid (5 mmol), ethanol (1.5 mL), dried benzene (2 mL) and iron complex (1 mmol) at reflux temperature

The iron reagents employed in entries 1-5 are commercially available whereas those in entries 6-7 were synthesized. From Table 3.3, it was revealed that different iron reagents provided different amount of the desired products. It is interesting to note that iron salts: $FeCl_3{\cdot}6H_2O$ and $FeCl_2{\cdot}4H_2O$ gave better results than other iron reagents. In the case of $FeCl_3{\cdot}6H_2O$, the yields of the target product obtained are much greater than $FeCl_2{\cdot}4H_2O$ and $Fe(NO_3)_3{\cdot}9H_2O$. This may be explained that Fe^{3+} exhibited hard acid more than Fe^{2+} [19]. While iron carboxylate complexes: $Fe(TCA)_3$ and $Fe(TFA)_3$ (entries 6-7) and $Fe(acac)_3$ (entry 8) provided poor yield of the desired product possibly because these iron complexes had steric effect with substrate [20]. According to the results shown above, $FeCl_3{\cdot}6H_2O$ was thus selected to use as a reagent for further examination.

3.1.6 Effect of type of carboxylic acids

To explore the scope of the esterification utilizing this developed protocol, the relationship between the structures of carboxylic acid with ethanol was examined. The results of the effect of carboxylic acids on the esterification are presented in Table 3.4.

Table 3.4 Effect of type of carboxylic acids

Entry	Carboxylic acid	%Isolated yield	
		24 h	48 h
1		68.72	89.95
2		55.56	80.93
3		69.51	95.54
4		79.02	Quant
5		64.82	90.15
6		82.64	Quant
7		65.58	87.66

Reaction conditions: Carboxylic acid (5 mmol), ethanol (1.5 mL), dried benzene (1 mL) and $FeCl_3{\cdot}6H_2O$ (1 mmol) at reflux temperature

Victor *et al.* studied the esterification of benzoic acids with phenols and reported that the yield of ester depending on benzoic acid substituents [21]. In the present work, aromatic carboxylic acids containing electron withdrawing substituent such as 3-NO_2 yielded the corresponding ester in higher yield than that derived from those bearing electron donating group as 3-OCH_3 (entries 1-2). This was probably due to the fact that a nitro group at *meta* position of benzoic acid made a carbonyl carbon being highly electrophilic. On the other hand, a methoxy group rendered the electrophilic property of the carbonyl site. Ethyl cinnamate containing C=C in the molecule could be accomplishly obtained in moderate yield (69.51%, entry 3). It was observed that the desired ester manipulated using short chain aliphatic carboxylic acids could be achieved in higher yield than that derived from the long chain ones (entries 4-5). This may be because of the solubility of the longer carbon chain aliphatic acids. To illustrate this, the long chain aliphatic acid had low capability to dissolve in medium and it was likely hindering the progress of the esterification. Xinzhong *et al.* addressed that with the increasing of carbon chain of aliphatic acids the yields of esters were decreased [22]. This present method in addition could apply for the preparation of diethyl ester of itaconic acid which contained an unsaturation conjugated with a carbonyl group. The corresponding ester was obtained in good yield (82.64%, entry 6). In the case of sorbic acid bearing two conjugated double bonds, the corresponding ester was afforded in moderate yield (65.58 %, entry 7). The yield of the desired ester could possibly lift up by a bit modification of the reaction conditions such as prolonging the reaction time (entry 7) [23]. When the reaction time was prolonged from 24 to 48 h, the yield of ethyl 3-nitrobenzoate increased from 68.72 % to 89.95 % (entry 1). Even better results could be observed with long chain aliphatic compound such as stearic acid (90.15 %, entry 5) and sorbic acid (87.66%, entry 7).

Selected ^{1}H-NMR spectra of the desired esters are shown in Figs 3.6-3.12.

The ^{1}H-NMR spectrum of ethyl 3-nitrobenzoate (Fig 3.6) demonstrates the proton signals of ethyl group at δ_H 1.44 (3H, t, J= 7.2 Hz) and δ_H 4.45 (2H, q, J= 7.2 Hz). Aromatic protons can be detected at δ_H 7.65 (1H, t, J = 8.0 Hz), 8.38 (1H, d, J = 7.6 Hz), 8.42 (1H, d, J = 8.4 Hz) and 8.87 (1H, s).

The ^{1}H-NMR spectrum of ethyl 3-methoxybenzoate (Fig 3.7) visualizes the proton signals of ethyl group at δ_H 1.39 (3H, t, J = 7.2 Hz) and δ_H 4.38 (2H, q, J = 7.2 Hz), while the proton signal of methoxy group observed at δ_H 3.85 (3H, s). The aromatic protons can be detected at δ_H 7.10 (3H, dd, J = 1.6, 8.0 Hz), 7.34 (1H, t, J = 8.0 Hz), 7.56 (1H, s) and 7.64 (1H, d, J = 7.6 Hz).

The ^{1}H-NMR spectrum of ethyl cinnamate (Fig 3.8) visualizes the proton signals of ethyl proton at δ_H 1.34 (3H, t, J= 7.2 Hz) and δ_H 4.26 (2H, q, J= 7.2 Hz). The two olefinic proton signals are observed at δ_H 6.46 (1H, d, J= 16.0 Hz) and 7.77

(1H, d, *J*= 16.4 Hz). The signals between δ_H 7.36-7.53 (5H, m) are assigned for aromatic protons.

The ^{1}H-NMR spectrum of ethyl laurate (Fig 3.9) shows the proton signals of ethyl group at δ_H 0.87 (3H, t, *J* = 6.8 Hz) and δ_H 4.11 (2H, q, *J* = 7.2 Hz), while the proton signals of C_3-C_{11}, C_2 and C_1 of laurate group can be observed at δ_H 1.25 (19H, s), 1.61 (2H, t, *J* = 6.8 Hz) and 2.27 (2H, t, *J* = 7.2 Hz), respectively.

The ^{1}H-NMR spectrum of ethyl stearate (Fig 3.10) exhibits the proton signals of ethyl group at δ_H 0.80 (3H, t, *J* = 6.8 Hz) and δ_H 4.04 (2H, q, *J* = 7.2 Hz). The proton signals at C_3-C_{17} of stearate group expose at δ_H 1.17 (31H, s) while those of C_2 and C_1 can be observed at δ_H 1.54 (2H, t, *J* = 7.2 Hz) and 2.20 (2H, t, *J* = 7.2 Hz), respectively.

The ^{1}H-NMR spectrum of diethyl itaconate (Fig 3.11) exhibits the proton signals at δ_H 1.21 (3H, t, *J* = 7.16 Hz) and δ_H 1.25 (3H, t, *J* = 7.12 Hz) for methyl groups at $C_{a'}$ and C_a positions, respectively. The methylene protons at C_3 position observed at δ_H 4.10 (2H, m). The methylene protons at $C_{b'}$ and C_b positions could be observed at δ_H 4.12 (2H, q, *J* = 7.15 Hz) and δ_H 4.17 (2H, q, *J* = 7.11 Hz), respectively. For vinylic protons, the proton signals at δ_H 5.65 (1H, s) and δ_H 6.27 (1H, s) were detected.

The ^{1}H-NMR spectrum of ethyl sorbate (Fig 3.12) shows the proton signals of ethyl group at δ_H 1.24 (3H, t, *J* = 7.07 Hz) and δ_H 4.14 (2H, q, *J* = 7.10 Hz), while the methyl group on sorbate side exhibits the signal at δ_H 1.80 (3H, d, *J* = 5.84 Hz). The proton signal at δ_H 5.72 (1H, d, *J* = 15.29 Hz) exposes for the protons at α-position, while that at δ_H 6.12 (2H, m) exhibits for overlapping of two proton signals of two protons at γ- and δ-positions (C_4, C_5). The last proton signal belonging to the proton at β-position (C_3) demonstrates at δ_H 7.20 (1H, dd, *J* = 11.15, 29.00 Hz).

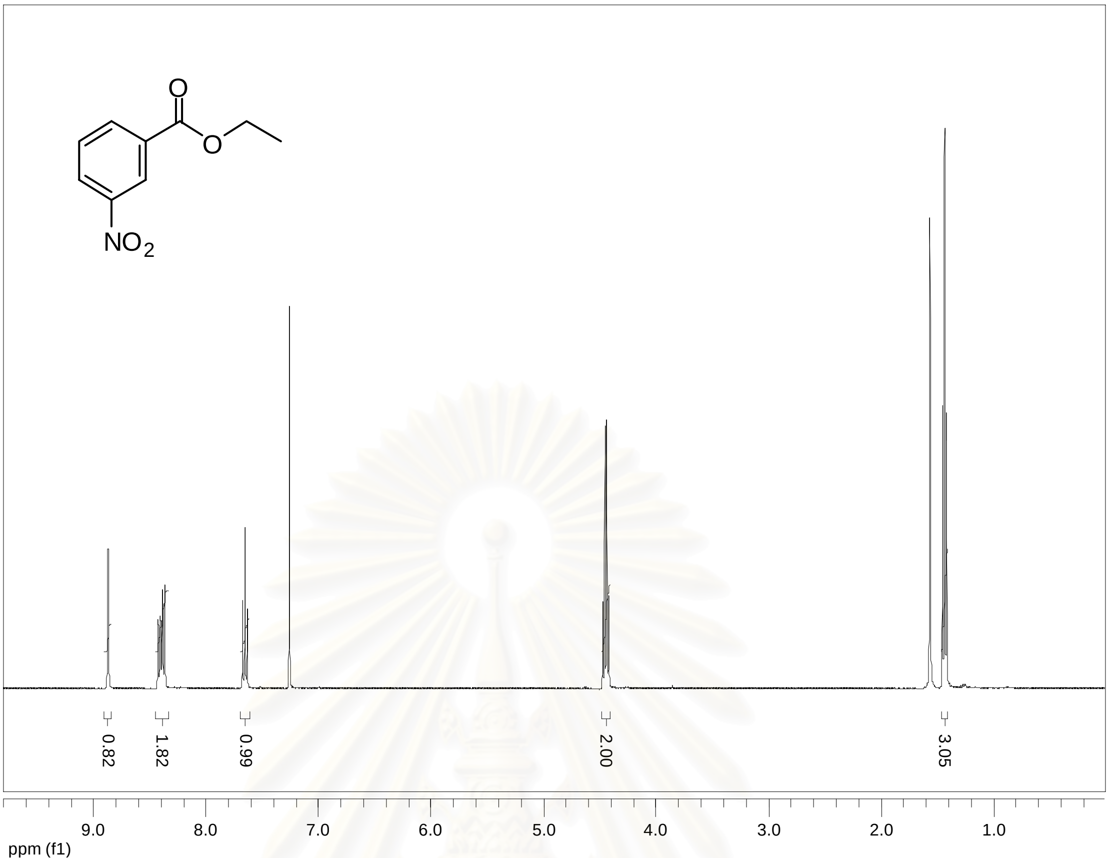


Figure 3.6 The ^{1}H-NMR spectrum of ethyl-3-nitrobenzoate

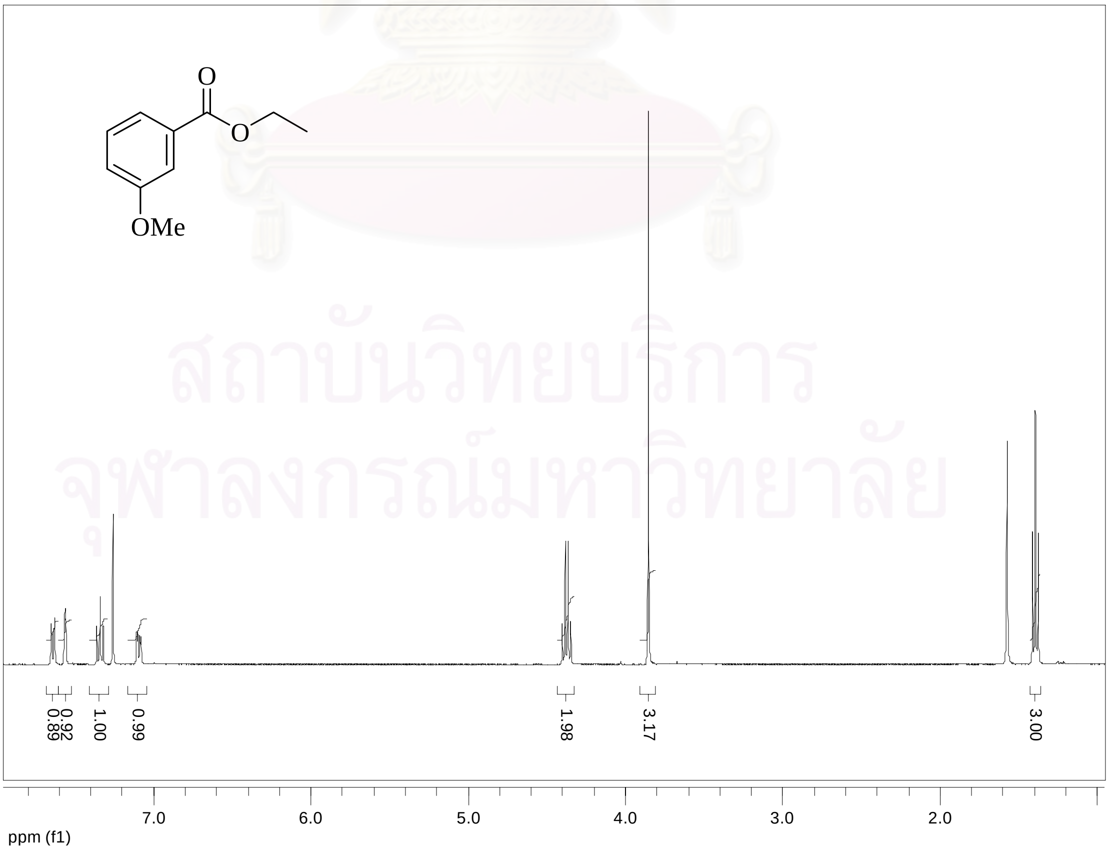


Figure 3.7 The ^{1}H-NMR spectrum of ethyl 3-methoxybenzoate

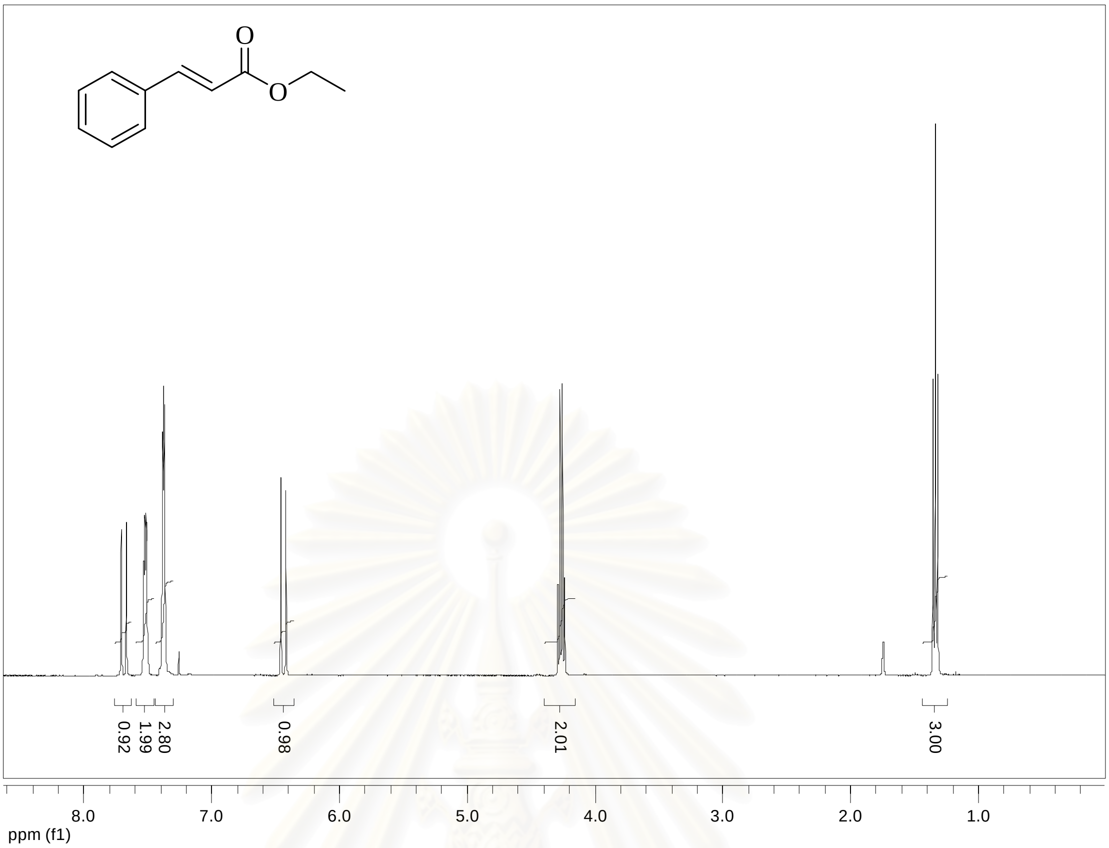


Figure 3.8 The ^{1}H-NMR spectrum of ethyl cinnamate

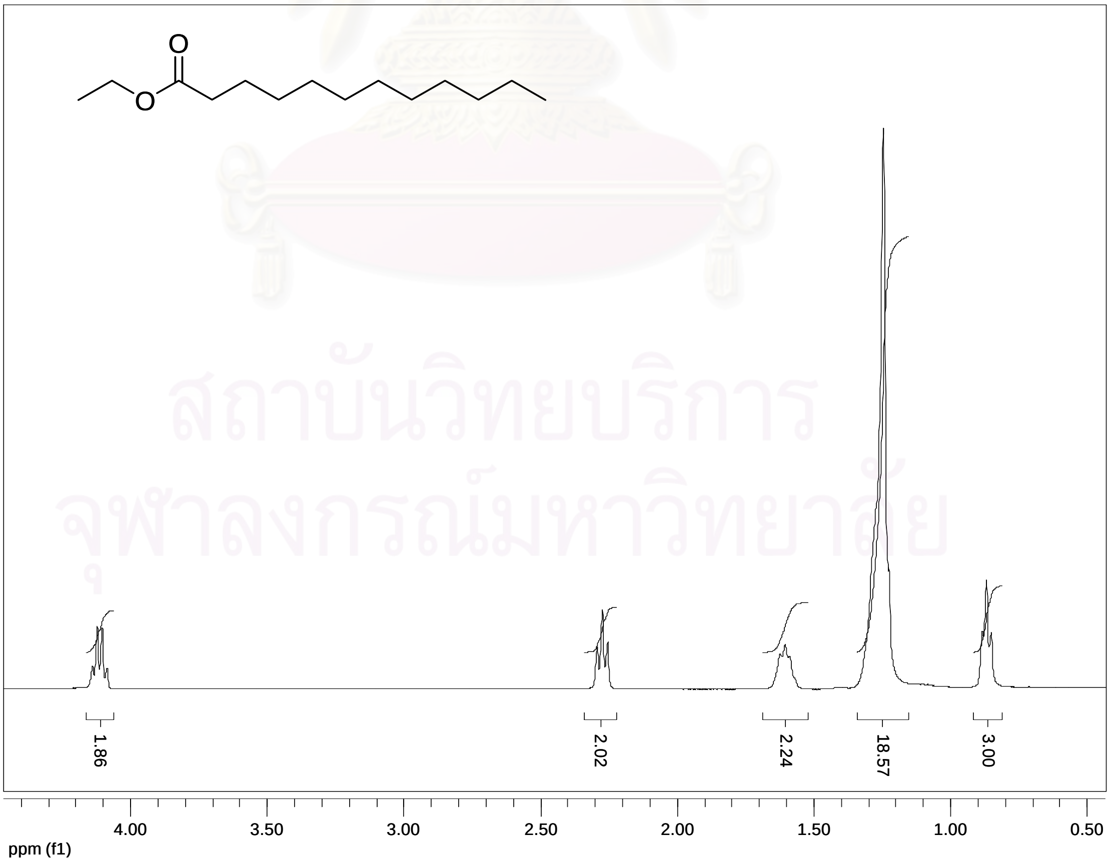


Figure 3.9 The ^{1}H-NMR spectrum of ethyl laurate

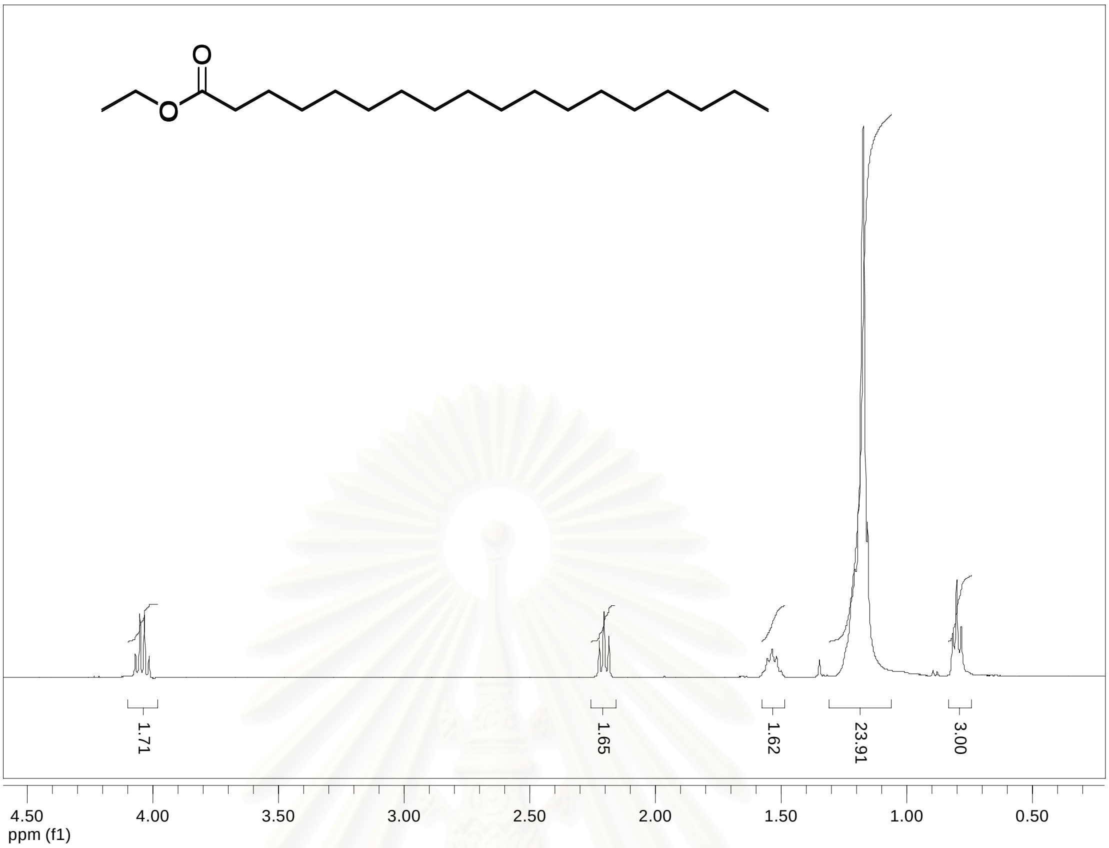


Figure 3.10 The ^{1}H-NMR spectrum of ethyl stearate

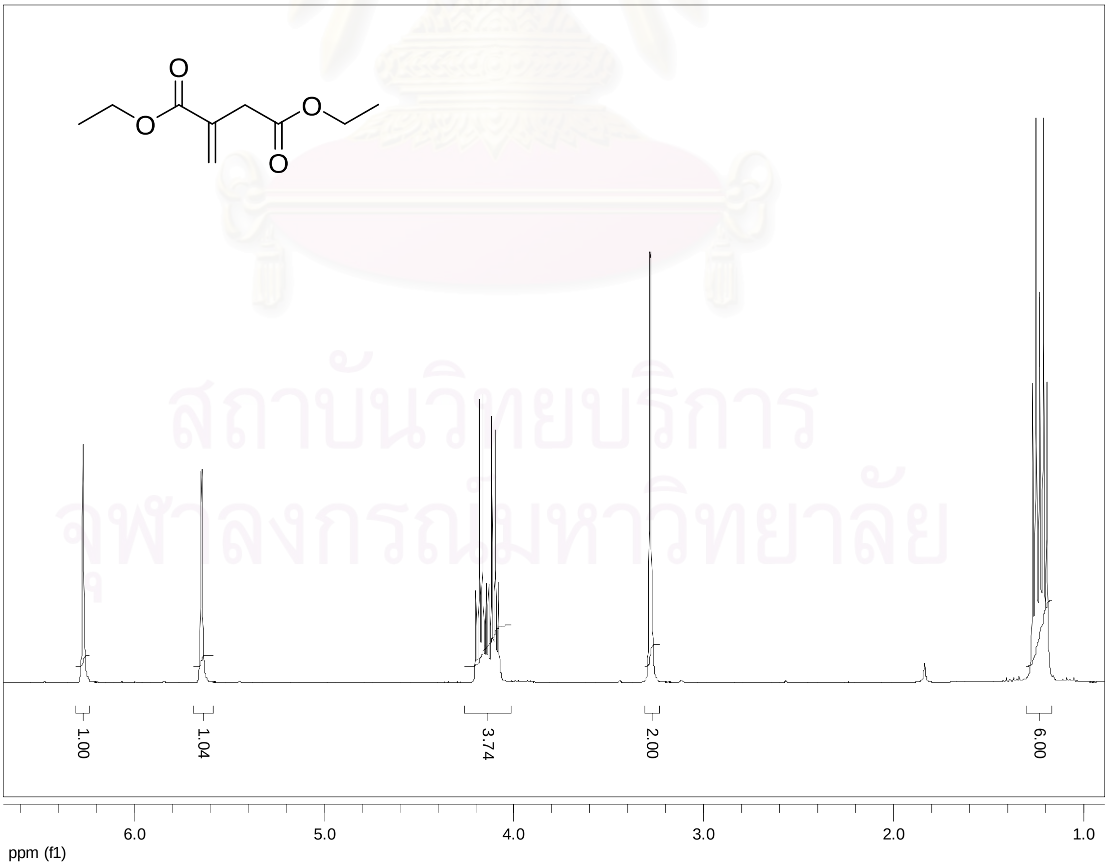


Figure 3.11 The ^{1}H-NMR spectrum of diethyl itaconate

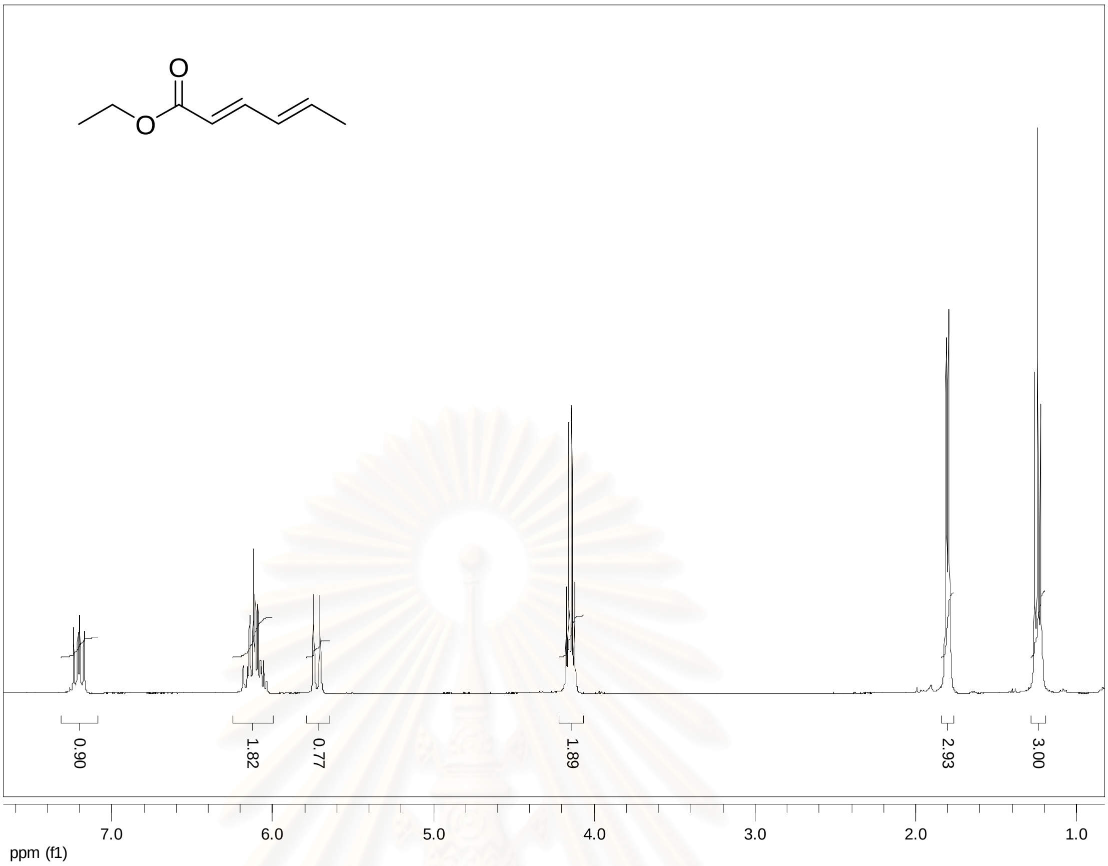
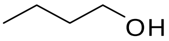
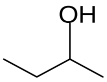
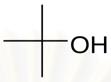
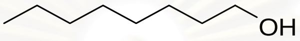
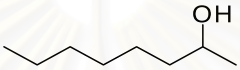
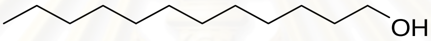
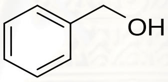
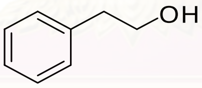


Figure 3.12 The ^{1}H-NMR spectrum of ethyl sorbate

3.1.7 Effect of type of alcohols

To examine the effects of type of alcohols, the esterifications of benzoic acid with a variety of alcohols including 1-butanol, 2-butanol, *t*-butanol, 1-octanol, 2-octanol, 1-dodecanol, benzyl alcohol and 2-phenethyl alcohol were investigated and the results are tabulated in Table 3.5.

Table 3.5 Effects of types of alcohol

Entry	**Alcohol**	**Isolated yield**	
		6 h	**24 h**
1		86.20	Quant
2		65.87	85.02
3		0	0
4		84.53	Quant
5		50.93	78.26
6		52.06	Quant
7		40.78	72.26
8		68.96	82.36

Reaction condition: Benzoic acid (5 mmol), alcohol (25 mmol), dried benzene (1 mL) and FeCl$_3$·6H$_2$O 3 mmol at reflux temperature

The above results indicated that the order of the reactivity upon the ester formation relied greatly on types of alcohols. With short carbon chain, the reactivity towards the esterification under this optimized conditions was much more than the longer ones. The ester yield decreased with the increment of a carbon chain. Mercs *et al.* employed 1-octanol to esterify benzoic acid using diphenylammonium triflates (DPAT) as a catalyst. The high yield (89 %) and albeit relatively long reaction times (48 h) were required [24]. Under this studied condition, 1-octyl benzoate was attained in high yield (84.53%, entry 4) after 6 h. The primary alcohol such as 1-butanol also gave the desired product in high yield (86.20 %) (entry 1), while with the secondary alcohol such as 2-butanol, the corresponding product was afforded a little bit lower in 65.87% (entry 2). Nevertheless, in the case of *t*-butanol, a sterically hindered alcohol, the reaction did not proceed, no desired product was obtained. Almost benzoic acid was recovered. The steric properties of alcohols were thus suggested to play an important role in the esterification. Jermy *et al.* investigated the esterification of acetic acid with various alcohols using Al-MCM-41 catalyst. The effect of different feed alcohols: *n*-butanol, 2-butanol and *t*-butanol conversion were studied. *n*-Butanol conversion was found to be higher than that of 2-butanol and to fail completely in the case of *t*-butanol, mainly according to the steric hindrance of the substrate [25]. The reactivity of alcohols towards the esterification under this particular condition can be ordered as: primary > secondary > tertiary alcohols (entries 1, 2 and 3). Following the effect of types of carboxylic acids, when increasing the reaction time, the yields of the desired products were also increased. Therefore, the reactions may need to perform using longer reaction time from 6 to 24 h under the same conditions. This assumption still worked well, 2-butyl benzoate was accomplishly attained in 85.02%.

Selected ^{1}H-NMR spectra of the desired esters are depicted in Figs 3.13 – 3.22.

The ^{1}H-NMR spectrum of *n*-butyl benzoate (Fig 3.13) shows the proton signals of butyl group at δ_H 0.98 (3H, t, *J*= 7.2 Hz) for the proton signal at C_4, 1.48 (2H, sex, *J*= 7.2 Hz) for C_3, 1.75 (2H, quin, *J* = 6.8 Hz) for C_2 and 4.32 (2H, t, *J*= 6.8 Hz) for the proton signal on carbon connecting with oxygen of an ester group. The aromatic proton signals can be visualized at δ_H 7.43 (2H, t, *J* = 7.6 Hz), 7.54 (1H, t, *J* = 7.6 Hz), and 8.05 (2H, d, *J* = 7.2 Hz).

The ^{1}H-NMR spectrum of 2-butyl benzoate (Fig 3.14) exhibits the proton signals of butyl group at δ_H 0.97 (3H, t, *J* = 7.6 Hz) for C_4, 1.34 (3H, d, *J* = 6.0 Hz) for C_1, 1.63-1.79 (2H, m) for C_3 and 5.10 (1H, sex, *J* = 6.0 Hz) for the proton signal on carbon connecting with oxygen of an ester group. The aromatic proton signals can be observed at δ_H 7.43 (2H, t, *J* = 7.6 Hz), 7.54 (1H, t, *J* = 7.2 Hz), and 8.05 (2H, d, *J* = 7.2 Hz).

The ^{1}H-NMR of 1-octyl benzoate (Fig 3.15) shows the protons of methyl group at δ_H 0.88 (3H, t, *J* = 7.0 Hz), while the protons at C_3-C_7 display at δ_H 1.28 (8H, s). The protons at C_2 can be observed at δ_H 1.76 (2H, quin, *J* = 6.7 Hz) while those at C_1 can be detected at δ_H 4.31 (2H, t, *J* = 6.7 Hz). The aromatic protons can be detected at δ_H 7.44 (2H, t, J = 7.5 Hz), 7.55 (1H, t, J = 7.4 Hz) and 8.05 (2H, d, J = 7.2 Hz).

The ^{1}H-NMR spectrum of 2-octyl benzoate (Fig 3.16) indicates the proton signals of 2-octyl group at δ_H 0.87 (3H, t, J = 6.9 Hz), 1.34 (11H, m), 1.61 (1H, m), 1.73 (1H, m) and 5.15 (1H, m), while the protons of aromatic ring exposed the signals between δ_H 7.42-8.05 (5H, m).

The ^{1}H-NMR spectrum of 1-dodecanyl benzoate (Fig 3.17) visualizes the proton signals of dodecanyl group at δ_H 0.88 (3H, t, J = 7.0 Hz), for the proton signals at C_4-C_{11} of stearate group shown at δ_H 1.26 (16H, s), the proton signal at C_3 observed at δ_H 1.40-14.7 (2H, m), the proton signal at C_2 obtained at δ_H 1.76 (2H, quin, J = 6.8 Hz) and the protons signal at C_1 indicated at δ_H 4.31 (2H, t, J = 6.6 Hz). For aromatic proton signals could be achieved at δ_H 7.43 (2H, t, J = 7.4Hz), 7.55 (1H, t, J = 7.5 Hz), and 8.04 (2H, d, J = 7.9 Hz).

The ^{1}H-NMR spectrum of benzyl benzoate (Figure 3.18) presents the signal of two protons of methylene group at δ_H 5.41 (2H, s) and the proton signals of two aromatic rings approximately δ_H 7.36-8.14 (10H, m).

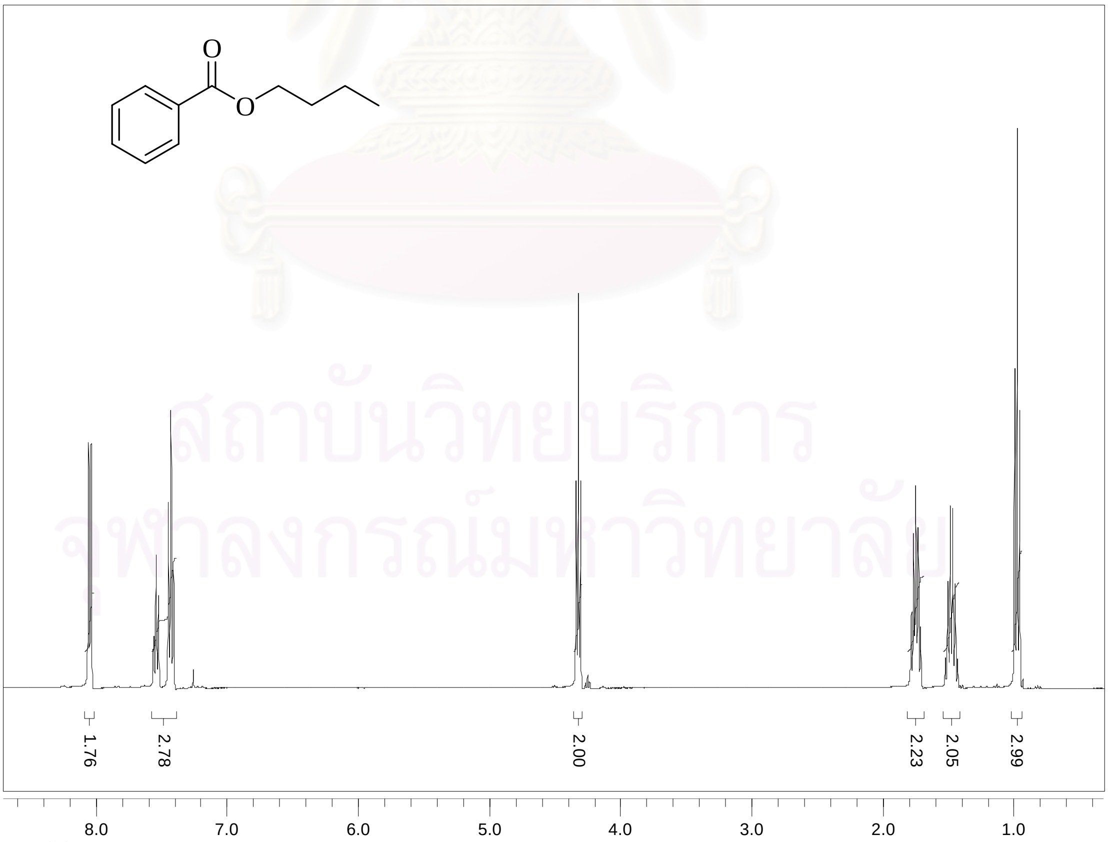


Figure 3.13 The ^{1}H-NMR spectrum of *n*-butyl benzoate

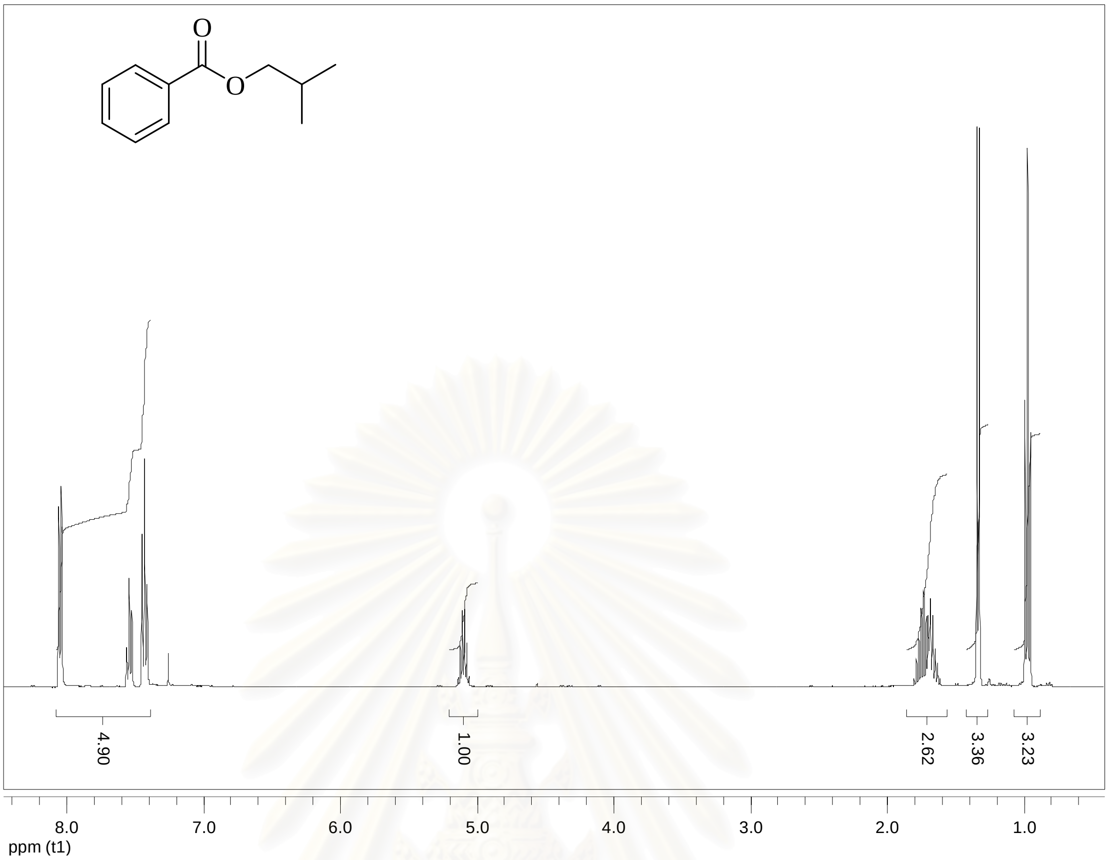


Figure 3.14 The ^{1}H-NMR spectrum of 2-butyl benzoate

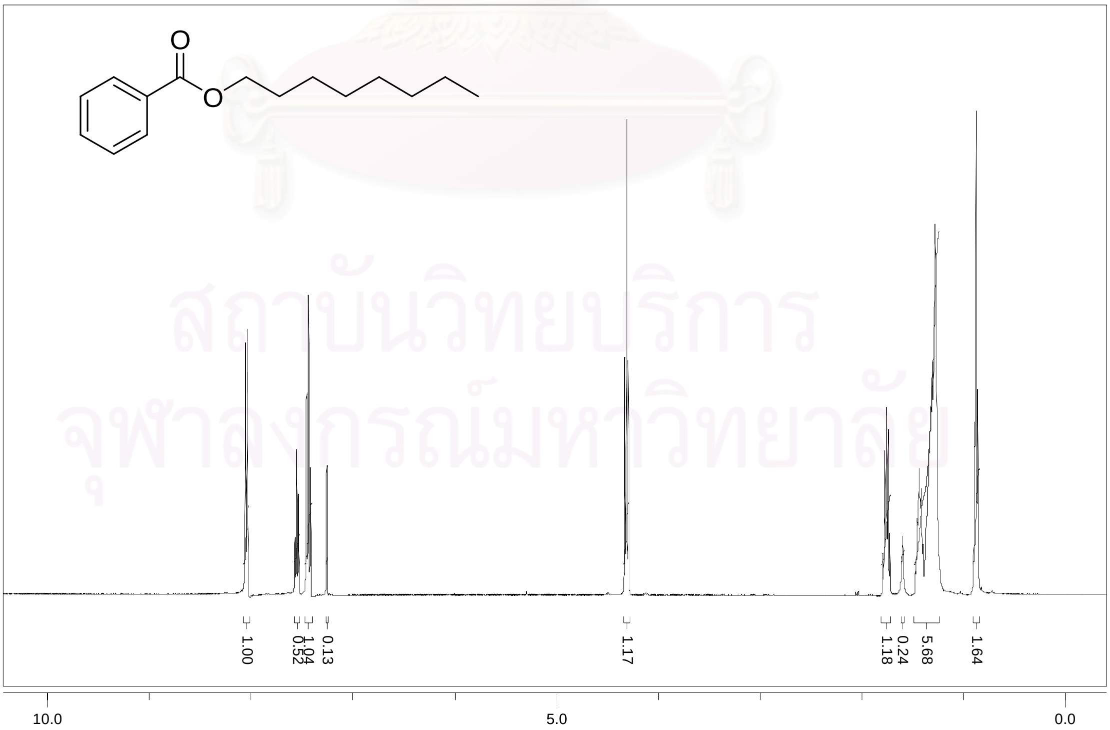


Figure 3.15 The ^{1}H-NMR spectrum of 1-octyl benzoate

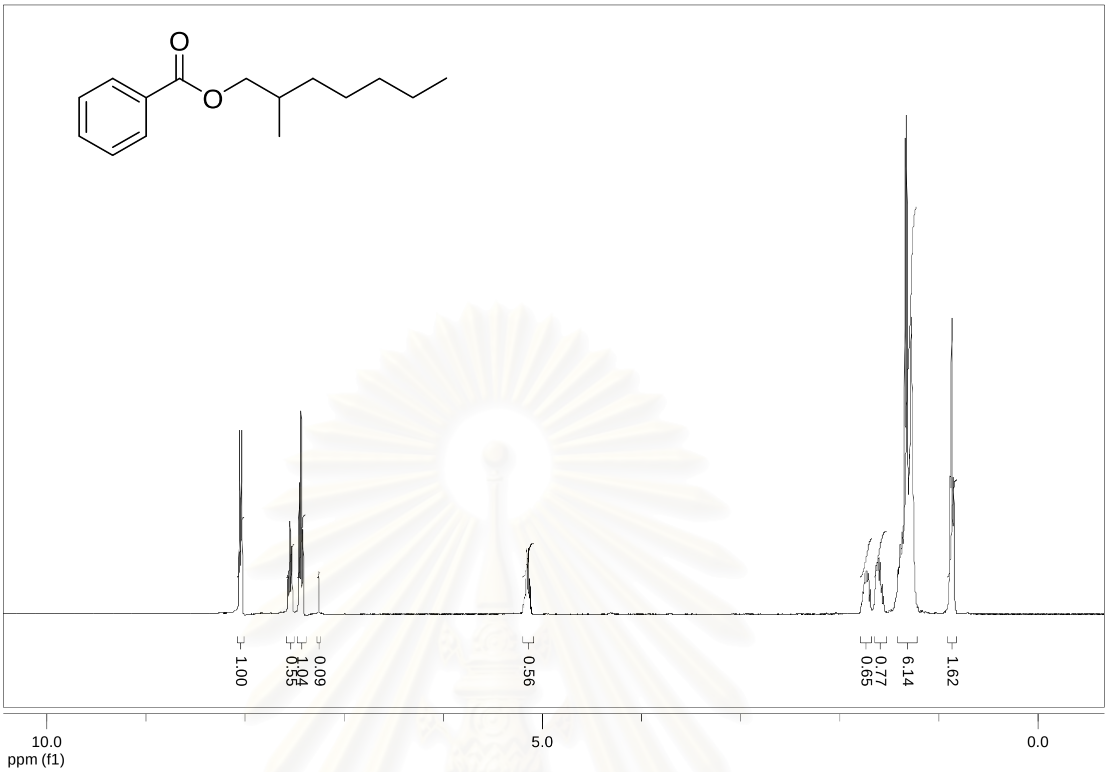


Figure 3.16 The ^{1}H-NMR spectrum of 2-octyl benzoate

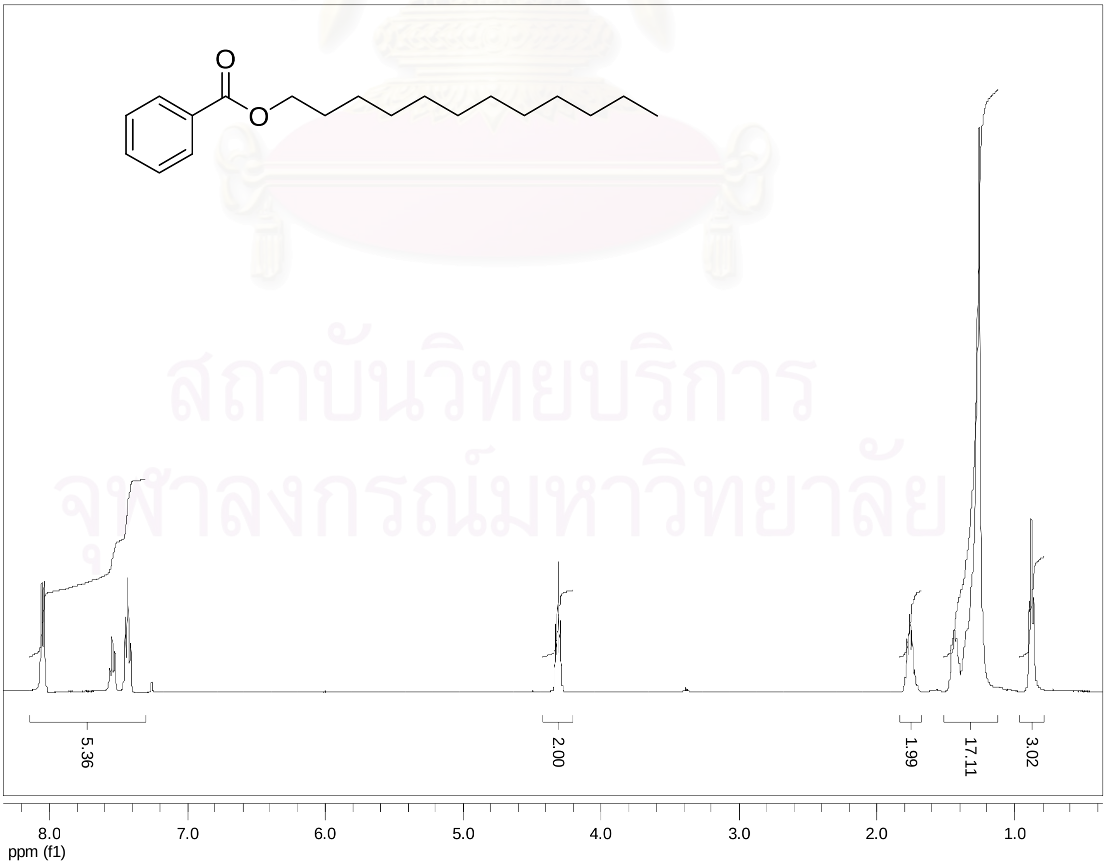


Figure 3.17 The ^{1}H-NMR spectrum of 1-dodecanyl benzoate

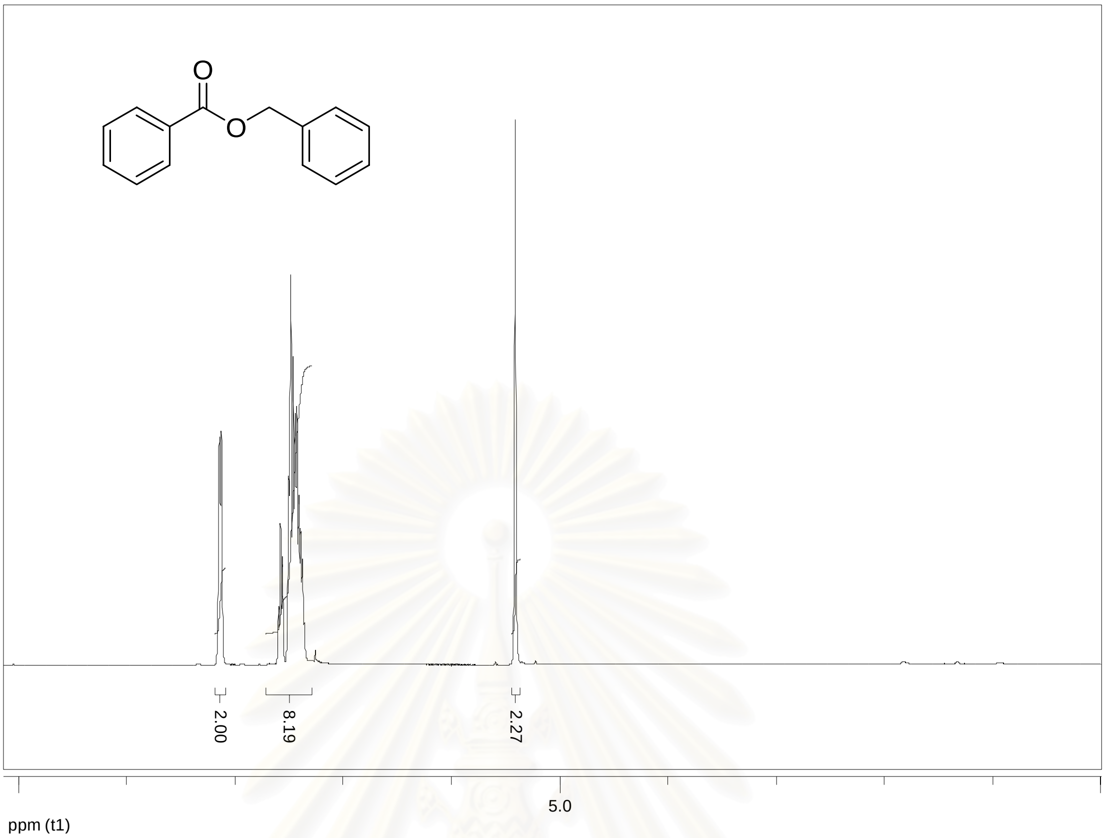


Figure 3.18 The ^{1}H-NMR spectrum of benzyl benzoate

According to the attained results, the esterification of benzoic acid with 1-butanol, 2-butanol, 1-octanol, 2-octanol, 1-dodecanol and cinnamyl alcohol gave high yield of the desired products. The esterification of benzoic acid with benzyl alcohol however gave two distinct products upon the detection with GC. To verify this observation, the whole reaction mixture was thus worked-up, subjected to silica gel column to furnish two pure products. Based on ^{1}H NMR, the first product was clearly identified as the desired ester, benzyl benzoate, 41% yield. The other was attained as a clear liquid (27%). The ^{1}H-NMR spectrum of the latter (Fig 3.20) reveals the benzylic protons at δ_H 4.65 (2H, s) and the aromatic protons at δ_H 7.36-7.48 (10H, m). The ^{13}C-NMR spectrum (Fig 3.21) displays two sp^3 carbon signals of methylene group at δ_C 72.2. The carbon signals between δ_C 127.7-138.4 with twelve sp^2 carbons can be assigned for aromatic carbons. According to the spectral data, this compound was identified as dibenzyl ether.

Another model, 2-phenethyl alcohol was selected to affirm this observation. This alcohol was allowed to react with benzoic acid under the standard conditions.

The corresponding ester was obtained in 68.96 % together with the other product, finally characterized as 2-phenethyl ether.

The ^{1}H-NMR spectrum of 2-phenylethyl benzoate (Fig 3.19) confirmed the proton signals of ethylene group at δ_H 3.11 (2H, t, J = 7.0 Hz) and δ_H 4.56 (2H, t, J = 7.0 Hz), while the proton signals of two benzene ring expressed around δ_H 7.23-8.87 (10H, m).

The ^{1}H-NMR spectrum of 2-phenylethyl ether (Fig 3.20) manifested the proton signals of two ethylene groups at δ_H 2.86 (4H, t, J = 6.7 Hz) and δ_H 3.82 (4H, t, J = 6.6 Hz), while the proton signals of two aromatic rings exhibited between δ_H 7.24-7.36 (10H, m).

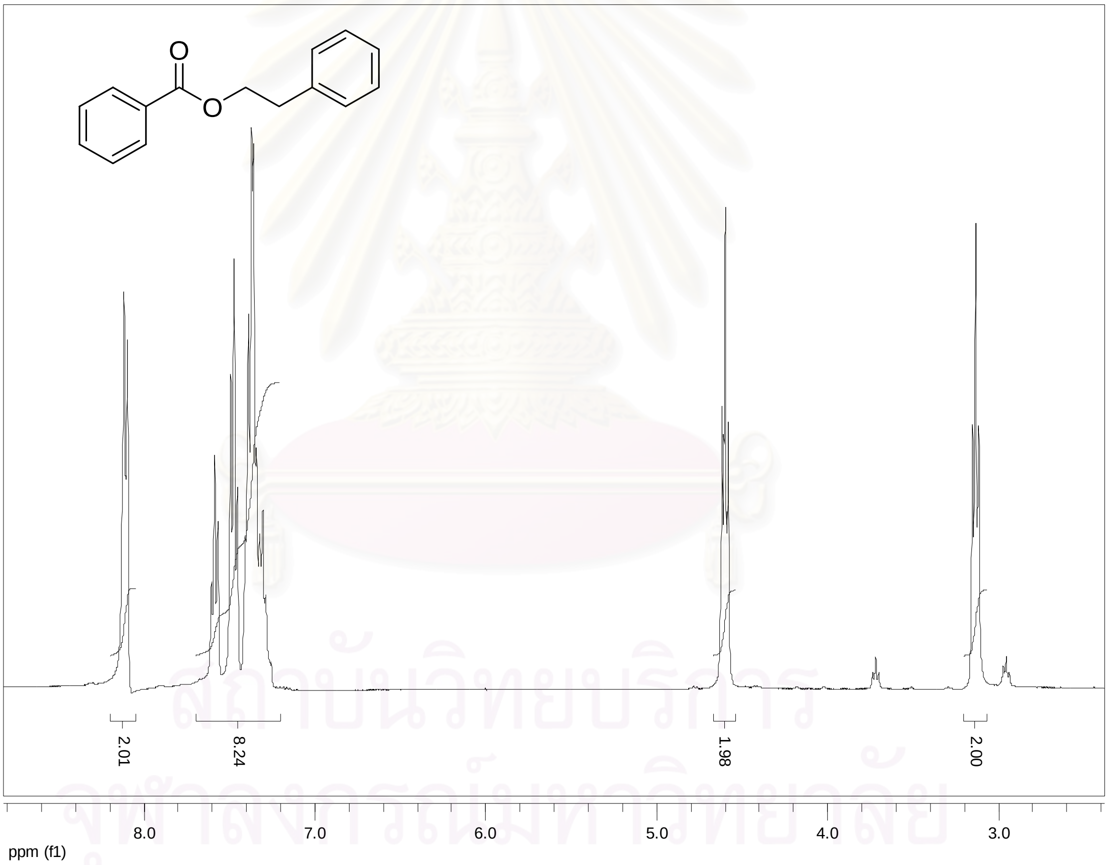


Figure 3.19 The ^{1}H-NMR spectrum of 2-phenethyl benzoate

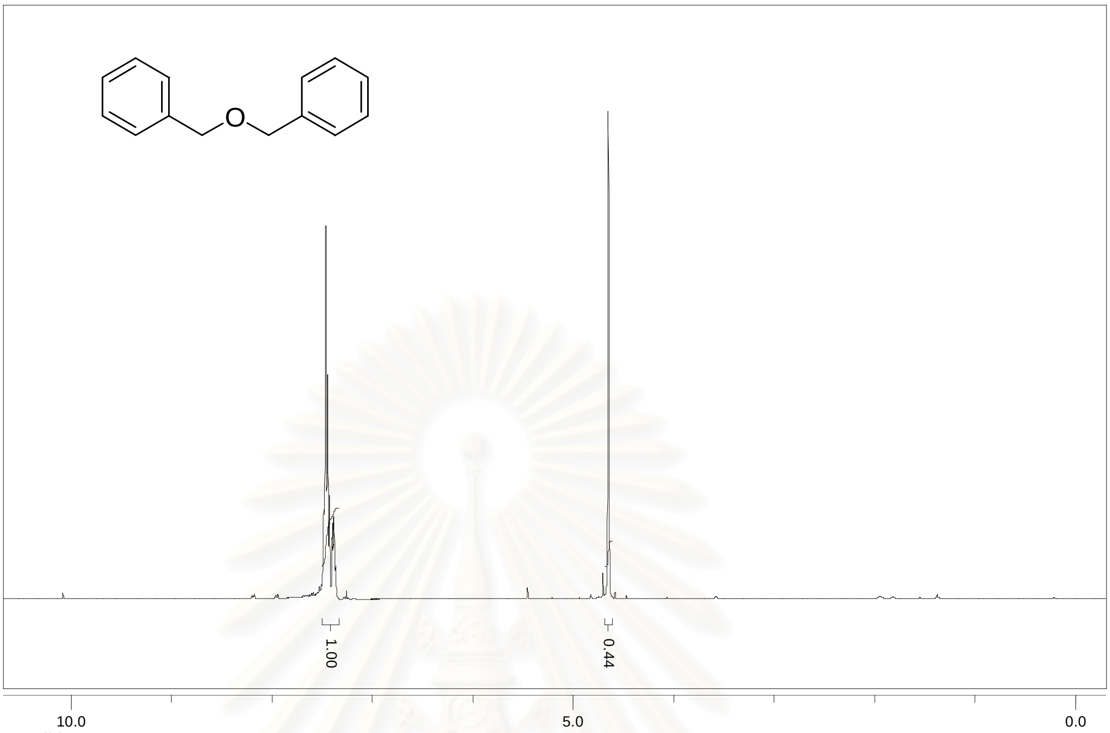


Figure 3.20 The ^{1}H-NMR spectrum of dibenzyl ether

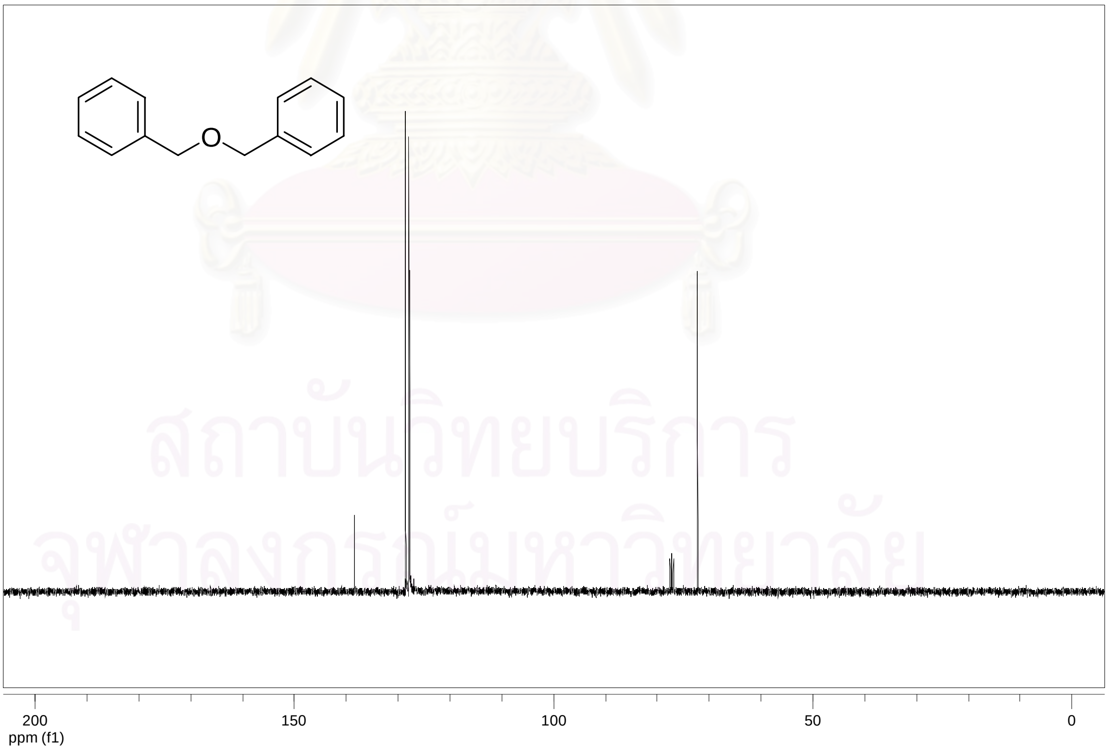


Figure 3.21 The ^{13}C-NMR spectrum of dibenzyl ether

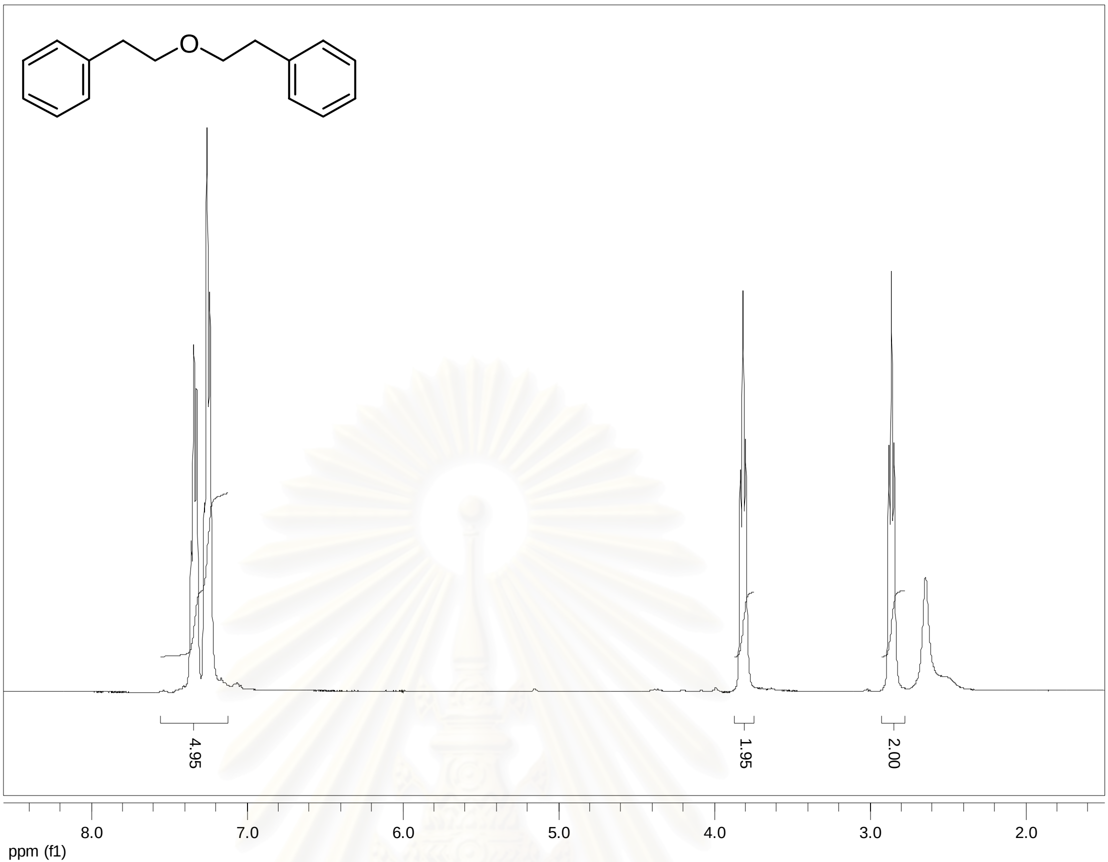


Figure 3.22 The ^{13}H-NMR spectrum of 2-phenethyl ether

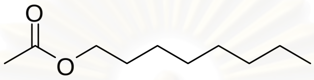
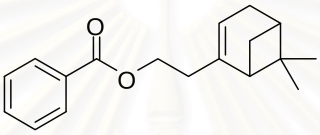
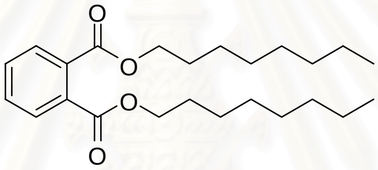
It should thus be noted that the reaction with benzylic alcohols may take place with two competitive reactions. To illustrate this, the first route was the esterification of benzoic acid with alcohol while the second one involved the etherification of alcohol itself. More details on the etherification study will be discussed in topic 3.3.

3.1.8 Application of the developed procedures for the synthesis of selected fragrances and target molecules

The ester group is an important functional group. The low-molecular weight esters have very pleasant odors and indeed are the major components of the flavor and odor aspects of a number of fruits. Although natural flavors may contain nearly a hundred different compounds, single esters approximate natural odors and often used in food industry for artificial flavors and fragrances. For example, octyl acetate of orange, nopyl acetate of gardenia [26]. Apart from that, a series of ester of long chain carboxylic acid could be used as surfactant [27]. Dioctyl phthalate is a kind of widely used plasticizer.

To extend the utilization of this developed methodology for the synthesis of esters, octyl acetate, nopyl acetate and dioctyl phthalate were selected as three examples. The results are presented as shown in Table 3.6.

Table 3.6 Synthesis of selected fragrances and target molecules

Entry	Product	%Isolated yield
1		Quant
2		87.96
3		88.98

Reaction conditions: Carboxylic acid (5 mmol), alcohol (25 mmol), dried benzene (1.5 mL) and $FeCl_3 \cdot 6H_2O$ (3 mmol) at reflux temperature for 24 h.

From the above result, it was observed that the modification of the reaction condition could improve the yield of desired product. Joseph and co-workers studied a green, efficient and reusable catalyst system for Fischer esterification. Their results showed the esterification of 1-octanol with acetic acid using 1-methylimidazolium tetrafluoroborate $[MIM]^+$ BF_4^-] as catalyst and solvent at 110 ^{0}C for 4 h. The yield of 1-octyl acetate was 70.8 % [28]. In this study, under the developed conditions 1-octyl acetate could be synthesized in quantitative yield (entry 1). In addition, benzoic acid and nopol can also proceed smoothly to gain the corresponding ester in 87.96% when $FeCl_3 \cdot 6H_2O$ 3 mmol was employed at reflux temperature for 24 h. Li *et al.* [29] addressed that dioctyl phthalate was synthesized using acid functionalized ionic liquid as catalyst. The results indicated that HSO_3^- functionalized Bronsted acidic ionic liquids showed good catalytic and reusable performance. Under the optimum condition, the reaction time 1.5 h, at 115-125 ^{0} C, ionic liquids dosage 30%w, the yield of dioctyl phthalate was 98%. In this work, the esterification of phthalic anhydride with 1-octanol was typically carried out at reflux temperature for 24 h using inexpensive $FeCl_3 \cdot 6H_2O$ 3 mmol as reagent. The yield of dioctyl phthalate was 88.98 %. It was clearly seen that this method was convenient and efficient to prepare the ester.

The ^{1}H-NMR of 1-octyl acetate (Fig 3.23) demonstrates the protons of methyl group at δ_H 0.87 (3H, t, J = 7.0 Hz), seven methylene protons at δ_H 1.27 (10H, s), 1.59 (2H, quin, J = 6.8 Hz) and 4.04 (3H, t, J = 6.8 Hz). The protons of acetate group expose at δ_H 2.03 (3H, s).

The ^{1}H-NMR spectrum of nopyl benzoate (Fig 3.24) displays two signals of two methyl groups at δ_H 0.84 and 1.27 (6H, s). The doublet signal of methine proton was observed at δ_H 1.17 (1H, d, J = 8.8 Hz). The signals around δ_H 2.08-2.44 (8H, m) were ascribed to eight protons of alkyl group. The presence of a multiplet signal at δ_H 4.33 (2H, m) indicated the presence of two protons on the carbon connecting with oxygen atom. The olefinic proton was inferred from the presence of triplet signal at δ_H 5.36 (1H, t, J = 1.6 Hz). The signals around δ_H 7.43-8.02 were assigned for five aromatic protons.

The ^{1}H-NMR spectrum of dioctyl phthalate (Fig 3.25) exhibits the proton signals of octyl group at δ_H 0.85 (6H, t, J = 6.0 Hz) for two methyl groups, δ_H 1.20-1.45 (20H, m) for ten methylene groups (C_3-C_7), δ_H 1.65-1.75 (4H, m) for two methylene groups (C_2) and δ_H 4.29 (4H, t, J = 6.8 Hz) for two methylene groups connecting to oxygen atoms. The proton signals belonging to aromatic moiety can be visualized around δ_H 7.48-7.78 (4H, m).

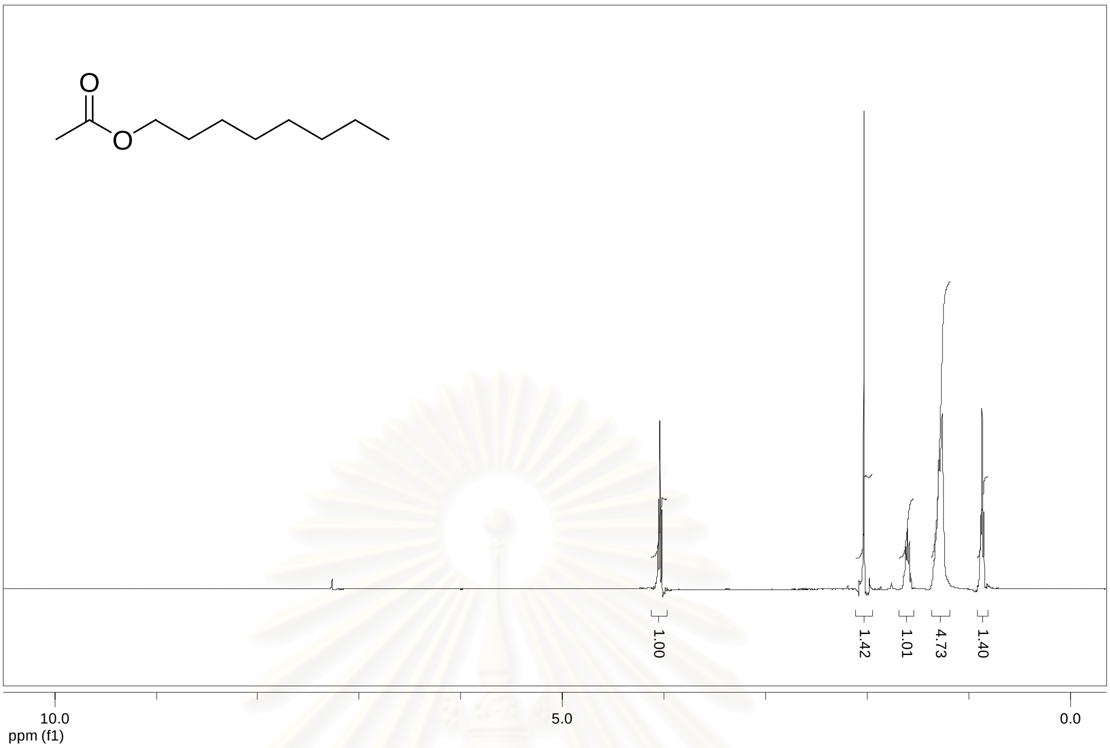


Figure 3.23 The ^{1}H-NMR spectrum of 1-octyl acetate

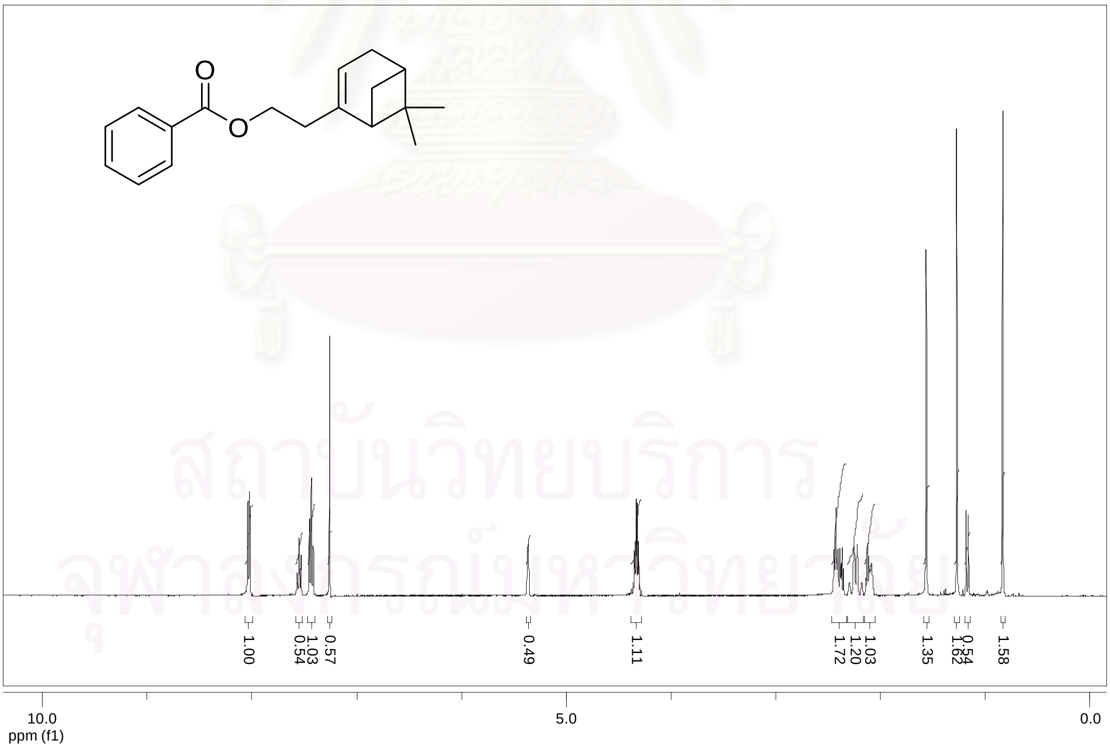


Figure 3.24 The ^{1}H-NMR spectrum of noply benzoate

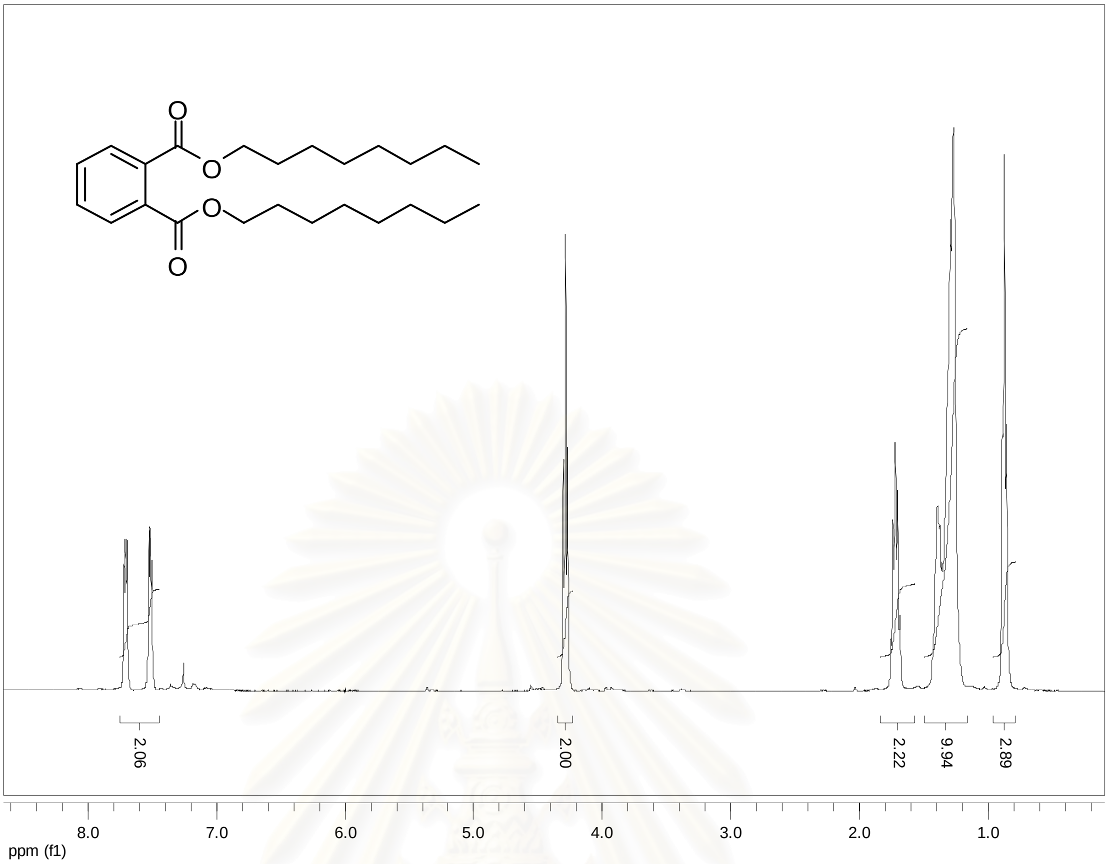
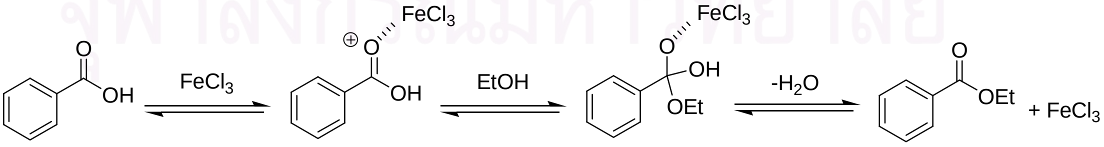


Figure 3.25 The ^{1}H-NMR spectrum of dioctyl phthalate

3.1.9 The mechanistic pathway for the esterification of carboxylic acid with alcohol by iron reagent

Understanding the mode of esterification of carboxylic acid with alcohol catalyzed by iron reagent was important for predicting the formation of products. Besides the activity, the selectivity and the competitive study on the esterification of various substrates mentioned above, the mechanistic pathway was proposed as depicted in Scheme 3.1.



(1) (2) (3) (4)

Scheme 3.1 The proposed mechanism for the esterification of carboxylic acid with alcohol using iron (III) reagent

Generally, the carbonyl group of carboxylic acid is not sufficiently electrophilic to be attacked by alcohols. Thus, the activated carbonyl is necessary for the proceeding of the esterification. In the first step, iron reagent accepts an electron pair from lone pairs on the oxygen to generate the activated carbonyl, which then reacts with the hydroxy group of the alcohol to form the new carbon-oxygen bond. In the last step, a molecule of water is lost from that intermediate to afford the ester and the iron reagent has been regenerated**.**

3.2 The transesterification of esters with alcohols using iron reagents

Transesterificion or alcoholysis is the displacement of alcohol from an ester by another process similar to hydrolysis, except that alcohol is used instead of water [30]. Transesterification is one of the reversible reactions and proceeds essentially by mixing the reactants. However, the presence of a catalyst (a strong acid or base) accelerates the conversion [31].

3.2.1 Literature reviews on other approaches for transesterification

Kim *et al.* [32] in 2004 reported transesterification of vegetable oil to biodiesel using heterogeneous base catalyst. The Na/NaOH/γ-Al_2O_3 heterogeneous base catalyst was firstly used for the production of biodiesel from soybean oil. The maximum biodiesel production yield reached to 94%, which was almost the same value compared to the conventional homogeneous NaOH catalyst system.

Azcan and Danisman [33] in 2007 addressed the microwave assisted transesterification of rapeseed oil. Experiments were carried out in the presence of two different alkali catalysts: NaOH and KOH. About 95% yield of biodiesel was achieved in the presence of 1.0% KOH at 338K after 2 h by conventional heating.

Barakos, Pasias and Papayannakos [34] in 2007 studied transesterification of triglycerides in high and low quality oil feeds over an HT2 hydrotalcite catalyst. The use of a heterogeneous catalyst, the basic Mg-Al-CO_3 hydrotalcite catalyst used showed a high activity for methanolysis in a refined and an high acidic cottonseed oil as well as in a representative high water content animal fat feed. The experiments were performed at 200 ^{o}C within 3 h, a 99% conversion of triglycerides to biodiesel was achieved while the free fatty acids content decreased considerably to 1 wt% when HACO or AFF used.

Sinha and Garg [35] in 2007 developed biodiesel from rice bran oil. The optimum conditions for transesterification of rice bran oil with methanol were found to be 55^{o}C for 1 h, 9:1 molar ratio of oil to methanol and 0.75% NaOH as catalyst. These conditions gave an ester yield of 90%.

Fernandes *et al.* [36] in 2007 reported for the first time both the production of the lipase of *Burkholderia cepacia* in solid-state fermentation and biocatalysis of esterification and transesterification through the direct addition of the lyophilized fermented solids to organic reaction media. The transesterification of corn oil with ethanol was possible, although longer reaction time was necessary (94% in 18 h).

Demirbas [37] in 2007 reported the comparison of transesterification methods for the production of biodiesel from vegetable oils and fats. The reaction converted esters from long chain fatty acids into mono alkyl esters. Vegetable oils can be transesterified by heating them with a large excess of anhydrous methanol and an acidic or basic reagent (alkaline, acid or enzyme). The base catalyzed (CH_3ONa) transesterification of vegetable oils proceeded faster than the acid (BF_3) and enzyme (Novozym 435) with high yields (98%) in 30 min.

Encinar and co-workers [38] in 2007 investigated ethanolysis of used frying oil. The transesterification of used frying oil by means of ethanol using NaOH, KOH, NaO and KO as catalysts was studied. The results showed that 1 wt% KO gave the highest ester yield 95% at 78^{o}C. The best ethanol/oil molar ratio was 12:1.

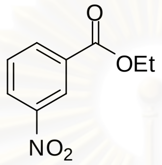
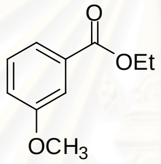
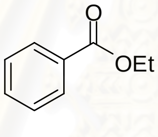
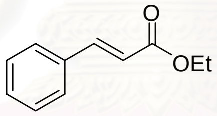
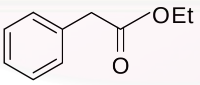
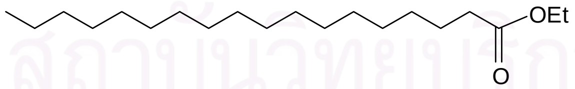
Demirbas [39] in 2008 studied on cottonseed oil biodiesel prepared in non-catalytic supercritical fluid conditions. The transesterification of linseed oil in SCF such as methanol and ethanol has proved to be the most promising process. A simple autoclave for supercritical alcohol transesterification was used. In the supercritical methanol transesterification, the yield of ester raised 88-98% for first 8 min at 250 ^{o}C and 8.1 MPa.

Previous results clearly revealed that an iron reagent as $FeCl_3 \cdot 6H_2O$ provided high yield of the desired ester. Particularly $FeCl_3 \cdot 6H_2O$ has never been reported in chemical literature for transesterification. Thus, $FeCl_3 \cdot 6H_2O$ was chosen to further explore for the transesterification.

3.2.2 Effect of type of esters on the transesterification with methanol

To investigate the generality and scope of this method, the reaction was carried out with various structural esters, the range of esters are tested using this developed procedure. The results are outlined in Table 3.7.

Table 3.7 Effect of type of esters on the transesterification with methanol

Entry	Ester	%Isolated yield
1		54.98^a 86.03^b
2		40.54^a 76.68^b
3		46.57^a 82.24^b
4		88.28^b
5		90.83^b
6		77.56^b

Reaction conditions: Ester (5 mmol), dried benzene (1.0 mL). ^{a} MeOH (1.0 mL), $FeCl_3{\cdot}6H_2O$ (1 mmol) reflux temperature 24 h. ^{b} MeOH (3.0 mL), $FeCl_3{\cdot}6H_2O$ (3 mmol), reflux temperature 48 h.

As presented in Table 3.7, the reaction of ethyl 3-nitrobenzoate with methanol furnished methyl 3-nitrobenzoate in moderate yield (54.98 %, entry 1). To lift up the yield of the desired ester, the amount of methanol, the amount of catalyst and the reaction time were increased. The desired ester could be isolated in higher yield (86.03%) similar to the other cases presented. In addition, a type of the substituent on benzoic acid also revealed the significant effect on the reactivity of the reaction, ethyl 3-methoxybenzoate with methanol furnished the formation of the corresponding ester in moderate yield (76.68% entry 2) compared with ethyl 3-nitrobenzoate (86.03% entry 1). This also implied that the active site of the catalyst used should be of electrophilic in character [40]. In the case of ethyl benzoate, the desired ester was attained in high yield (82.24%, entry 3). Moreover, this method was applicable to prepare methyl cinnamate which contained C=C in the molecule. The reaction proceeded smoothly, C=C was intact (88.28%, entry 4). In the case of ethyl 2-phenyl acetate with methanol, the corresponding methyl ester was obtained in good yield (90.83%), whereas in the case of ethyl stearate, a sterically hindered ester, the reaction still proceeded, the corresponding methyl ester was obtained in moderate yield (77.56%).

3.2.3 Effect of amount of methanol on the transesterification of ethyl 2-phenylacetate

The purpose of this study is to explore the effect of amount of nucleophile on the transesterification of ethyl 2-phenylacetate with the aim to minimize the amount of nucleophile while maintaining the efficiency of the reaction. The results are exhibited in Table 3.8.

Table 3.8 Effect of amount of methanol on the transesterification on ethyl 2-phenylacetate

Entry	methanol (mL)	%Yield
1	1	65.86
2	2	70.43
3	3	84.06
4	4	86.54
5	5	88.59

Reaction conditions: Ethyl 2-phenylacetate (5 mmol), methanol (vary), dried benzene (1.0 mL) and $FeCl_3{\cdot}6H_2O$ (3 mmol) at reflux temperature for 24 h.

Most researchers found that excess alcohol was required to drive the reaction close to completion [41]. In the present study, the amount of methanol has a significant impact on the yield of the desired product. The product yield lifted up as the amount of methanol increased. Transesterification of ethyl 2-phenylacetate with methanol 3 mL gave high yield (84.06%, entry 3) of the desired product at lower methanol using. From this result, only 3 mL of methanol was enough to alter the reaction pathway and exclusively produced the desired ester in good yield. In the case of increasing amount of methanol, the yield of product was increased. This effect may be because the probability of collision between substrate and methanol took place.

3.2.4 Effect of amount of iron reagents on the transesterification of ethyl 2-phenylacetate with methanol

One of the most important parameters affecting the yield of ester is the amount of reagent. The effect of amount of $FeCl_3 \cdot 6H_2O$ on the transesterification of ethyl 2-phenylacetate with methanol was examined and the results are shown in Fig 3.25.

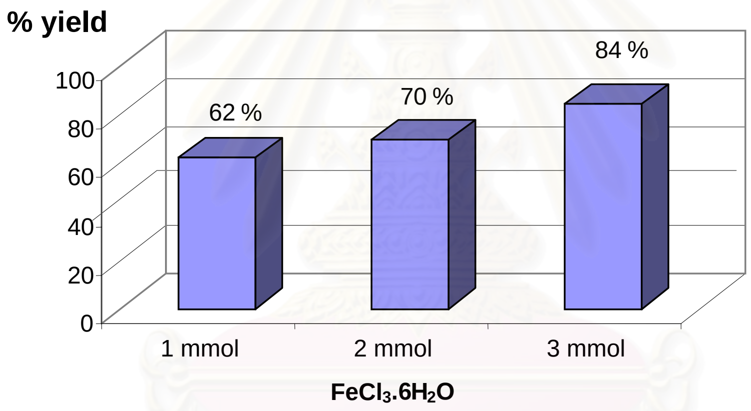


Figure 3.26 The amount of iron reagent on transesterification of ethyl 2- phenylacetate with methanol

Fig. 3.26 shows the effects of the amount of $FeCl_3 \cdot 6H_2O$ on transesterification of ethyl 2-phenylacetate with methanol. Crabbe *et al.* [42] and Marchetti and co-workers [43] found that the amount of catalysts had a strong influence on the yield of methyl ester. The reaction profile presented in Fig 3.25 also indicated that the transesterification was strongly dependent upon the catalyst applied. The yield of product was significantly improved with the increment of $FeCl_3 \cdot 6H_2O$. The product reached 84.06% after 24 h when the amount of reagent was 3 mmol.

3.2.5 Effect of reaction time on the transesterification of ethyl 2-phenylacetate with methanol

With the aim to maximize the yield of the desired product, the reaction time was varied. The results are collected in Fig 3.27.

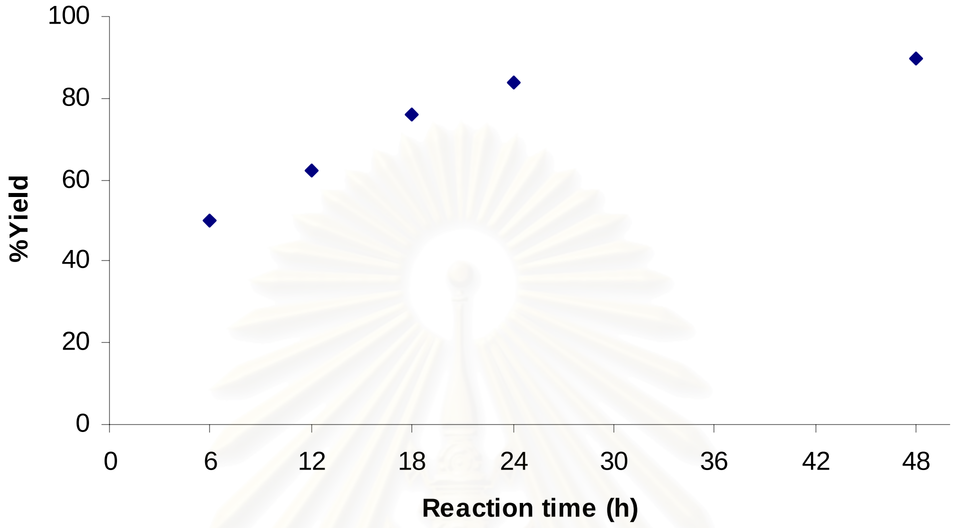


Figure 3.27 Effect of reaction time on the transesterification of ethyl 2-phenylacetate with methanol

The optimum reaction time for the production of methyl ester was determined by performing reaction at varying reaction time in the range of 6-48 h. The experimental results indicated that the conversion increased steadily in the reaction time range between 6-24 h, and thereafter remained almost constant as a result of a nearly equilibrium conversion. It could be obviously seen that when the reaction time was a bit modified, the yield of the desired product was more satisfied. % Yield was increased when the reaction time was prolonged. The production of methyl ester reached the maximum at about 48 h.

3.2.6 Application of the developed procedures for the synthesis of biodiesel from vegetable oil

According to previous results, the experiments on transesterification for the production of biodiesel from vegetable oil was investigated. The possibility of using vegetable oils as fuel has been recognized since the beginning of diesel engines. Vegetable oil has too high viscosity for direct use in most existing diesel engines as a straight replacement fuel oil. There are a number of ways to reduce the viscosity of vegetable oil. Dilution, micro-emulsification, pyrolysis and transesterification are four techniques applied to solve the problems encountered with high fuel viscosity. Transesterification is one of the most common methods used to reduce oil viscosity in biodiesel industries [44]. The transesterification proceeds well in the presence of some homogeneous catalysts such as potassium hydroxide/sodium hydroxide and sulfuric acid, or heterogeneous catalysts such as metal oxides or carbonates. $FeCl_3{\cdot}6H_2O$ has however never been reported in chemical literature for transesterification. In this study, the transesterification of vegetable oil to produce methyl ester as biodiesel using $FeCl_3{\cdot}6H_2O$ as reagent was investigated. The results are displayed in Fig 3.28.

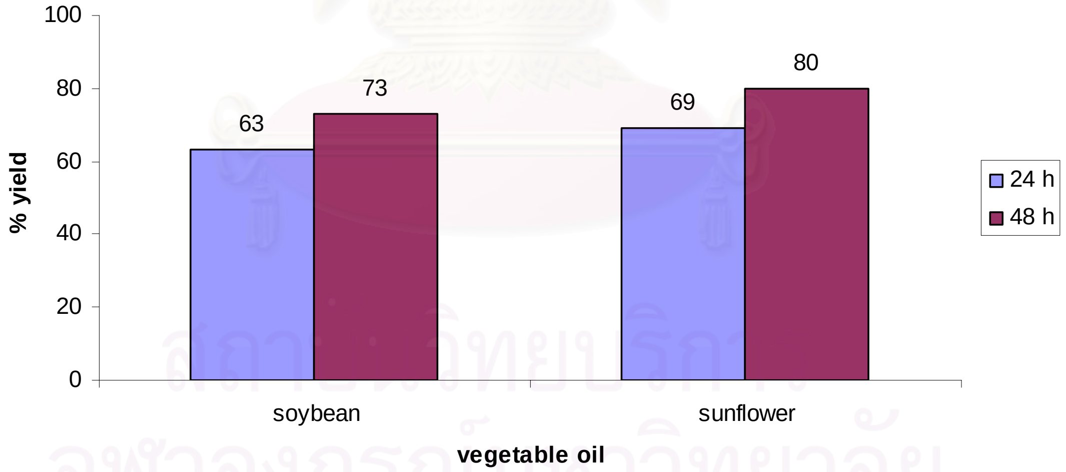


Figure 3.28 Application of the developed procedures for the synthesis of biodiesel from vegetable oil

When the reaction time was prolonged to 48 h, soybean oil and sunflower oil could be converted to their corresponding methyl esters in high yield (73%, 80%, respectively). Hau *et al.* [45] reported that the transesterification of soybean oil to biodiesel *via* Lewis acid catalysts such as $Pb(OOCCH_3)_2$, $Cd(OOCCH_3)_2$ and

$Zn(OOCCH_3)_2$ were carried out in the subcritical methanol phase (2 MPa, 180 ^{0}C, reaction time 30 min). The results showed that the transesterification of soybean oil with $Pb(OOCCH_3)_2$ conversion reached 73%. That system could provide similar yield of methyl ester to this work, but the procedure of this work was simple and could carry out under milder conditions. Arzamendi *et al.* [46] investigated transesterification of soybean oil to biodiesel using Na/NaOH/γ-Al_2O_3 heterogeneous base catalyst. The maximum biodiesel production yield reached to 94%, which was higher yield compared with the system employing homogeneous Lewis acid as $FeCl_3{\cdot}6H_2O$ system. However, that reported system required complicated and difficult method to prepare heterogeneous base catalyst.

3.3 The etherification of alcohols using iron reagents

Based on preliminary studies, the esterification of benzoic acid with benzyl alcohol and 2-phenethyl alcohol showed unexpected results. The reaction afforded two products as ester and ether which were well-confirmed by ^{1}H-NMR. Following previous results that iron reagents can be used to accomplish esterification in a high efficient manner. The goal of this study was to screen for suitable conditions for the etherification of benzyl alcohol using $FeCl_3{\cdot}6H_2O$ as reagent. Two reasons for the selection of benzyl alcohols as a model substrate are 1) it is relatively bulky molecule and 2) its interest in some fine chemistry applications for the production of fragrances and flavorings [47].

Basudeb [48] in 1998 studied ion-exchange resin catalyzed etherification of dicyclopentadiene (DCPD) with methanol. The maximum conversion (99%) of DCPD using macroporous cation-exchange resins was obtained at 110 ^{o}C after 7 h. Kinetics of this reaction was studied in a $1.0\text{x}10^{-4}$ m^3 capacity autoclave in the temperature range of 80-110 ^{o}C.

Linnekoski *et al.* [49] in 1998 reported the etherification of isobutene with 1-propanol and 2-propanol. A macroreticular, strong cation exchange resin was used as a catalyst. A plug flow reactor was used for differential experiments and a batch reactor at temperature of 40-80^{o}C for the equilibrium experiments. The etherification reaction with 1-propanol was found to be faster than that with 2-propanol. This could be due to the different steric hindrance of the reacting alcohols or forming intermediates.

Liu and co-workers [50] in 2001 studied the etherification of dimethylbutenes in excess methanol. The production of the C_7 ether, 2,3-dimethyl-2-methoxybutane (DM2MB) was investigated in a batch reactor from 50-70 ^{o}C at high methanol concentrations. A macroporous cation exchange resin, Amberlyst 15, was employed as catalyst for the etherification of 2,3-dimethyl-1-butene (DM1B) and 2,3-dimethyl-2-butene (DM2B) with methanol. The results showed that DM1B was much more reactive than DM2B. The maximum yield of ether occurred in 75% at 50^{o}C 1500 min.

Kim *et al.* [51] in 2003 reported the preparation and characterization of zeolite catalysts for etherification. The catalytic etherification of 2-naphthol with ethanol has been studied over zeolite catalysts such as H-Beta, H-MOR and H-ZSM-5. H-Beta zeolite showed higher conversion than other catalysts for 2-naphthyl ethyl ether. The reaction was carried out at 180 ^{o}C and 75% yield of product was collected after 2 h.

Sow [52] in 2004 reported the etherification of 1-butanol over sulfonated mesostructured silica and organo-silica. The reaction was carried out in liquid phase inside a batch reactor equipped with a diamond FTIR probe for continuous concentration monitoring of 1-butanol and reaction products namely dibutyl ether (DBE) and water. ArSAF-MES showed the highest 1-butanol conversion (80%) at 200 ^{o}C compared to all other catalysts tested.

Uozumi and Kimura [53] in 2005 presented the asymmetric π-allylic etherification of cycloalkenyl esters with phenols in water using a resin-supported chiral palladium complex. The heterogeneous aquacatalytic asymmetric etherification of cycloalkenyl esters with phenolic nucleophiles was catalyzed by PS-PEG resin-supported palladium-imidazoindolephosphine complex to give optically active aryl (cycloalkenyl) ethers in up to 94%.

3.3.1 Effect of type of solvents on the etherification of benzyl alcohol

Following previous results, benzene was selected as a solvent for the esterification of benzoic acid with benzyl alcohol. However, it is necessary to search for types of solvent that are suitable for etherification of benzyl alcohol. The main criteria for the solvents selected included those that could dissolve both benzyl alcohol and reagent. The results are demonstrated in Table 3.9.

Table 3.9 Effect of type of solvents on the etherification of benzyl alcohol

Entry	**Solvent**	**%Yield**
1	THF	55.22
2	THF(dry)	66.82
3	CH_2Cl_2	31.50
4	CH_3CN	50.96
5	Hexane	38.56
6	Benzene	45.78

Reaction conditions: Benzyl alcohol (10 mmol), solvent (2.0 mL) and $FeCl_3\cdot 6H_2O$ (3 mmol) at reflux temperature for 24 h.

Five common solvents including THF, CH_2Cl_2, CH_3CN, hexane and benzene were examined. Dried THF was the most suitable solvent for etherification because it could dissolve both $FeCl_3\cdot 6H_2O$ and substrate. It gave the highest yield compared with other solvents. Comparison with THF, % yield of product from the reaction performed in dry THF was higher than that obtained from commercial THF and benzene (45.78 %, entry 6). It was thus clearly seen that water content in solvent did affect on etherification. CH_2Cl_2 gave lower yield of benzyl ether (31.50 %, entry 3). In the case of CH_3CN, the reaction produced the product in moderate yield (50.96%, entry 4). From this study it was clearly seen that CH_3CN could be used instead of THF in this reaction. Whereas non-polar solvents such as hexane (38.56%, entry 5) and benzene (45.78 %, entry 6) were not appropriate solvents because of the insolubility of substrate in the solvent.

3.3.2 Effect of amount of solvents on the etherification of benzyl alcohol

An amount of solvent is one of important parameters for conditions optimization. The amount of THF in the reaction was varied from 1-5 mL. The results are pointed out in Table 3.10.

Table 3.10 Effect of amount of solvents on the etherification of benzyl alcohol

Entry	THF (mL)	%Yield
1	1	48.92
2	2	66.82
3	3	58.96
4	4	44.56
5	5	30.77

Reaction condition: Benzyl alcohol (10 mmol), dired THF (vary), $FeCl_3{\cdot}6H_2O$ (3 mmol) at reflux temperature for 24 h

When THF 2 mL was used, the reaction provided the highest yield of the desired product (66.82%, entry 2). The amount of the desired ether was lessened when THF used was more than 2 mL. This effect may be because the probability of collision between benzyl alcohol and itself was decreased when the amount of THF was increased. Only 1 mL of THF was not enough to alter the reaction pathway. Therefore, THF 2 mL was selected for etherification of benzyl alcohol in the future experiments.

3.3.3 Effect of reaction time and amount of iron reagent on the etherification of benzyl alcohol

The aim of this study was to search for appropriate reaction time and amount of iron reagent. The results are summarized in Fig 3.29.

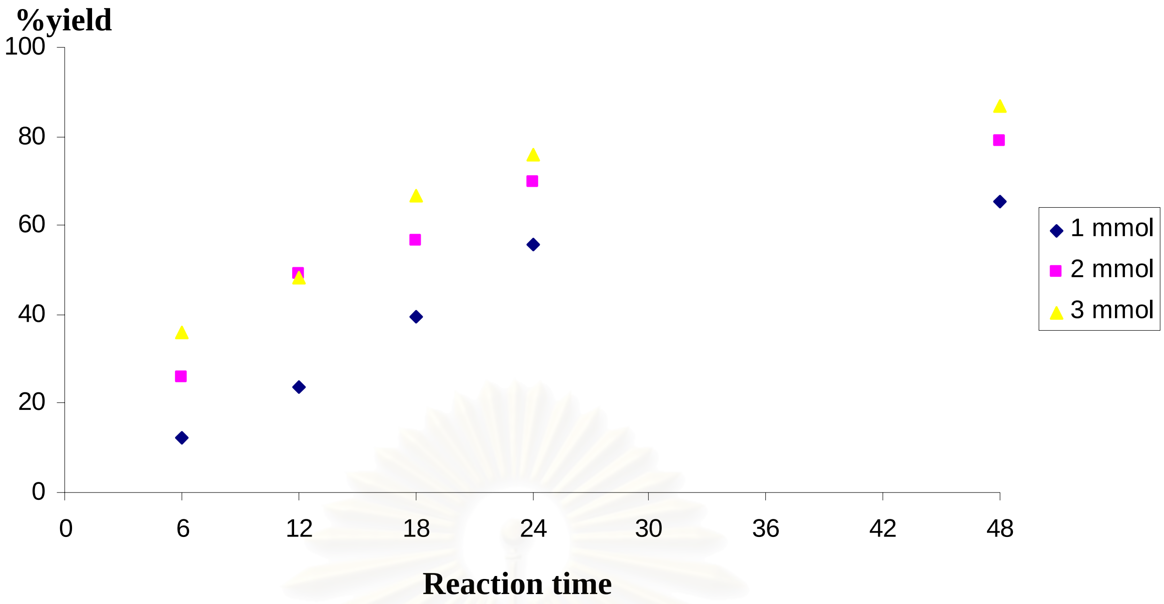
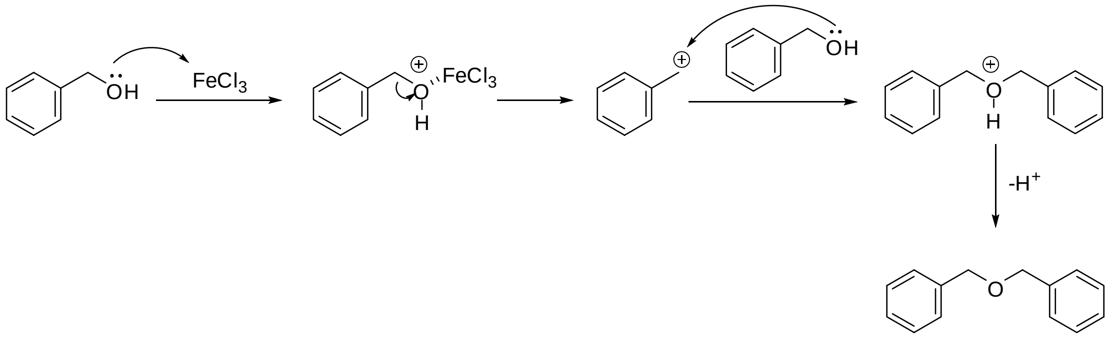


Figure 3.29 Effect of reaction time and amount of iron reagents on the etherification of benzyl alcohol

Fig 3.29 displays the productivity of the desired dibenzyl ether derived from the variation of the amount of $FeCl_3{\cdot}6H_2O$: 1, 2 and 3 mmol. Benzyl alcohol was converted to dibenzyl ether in few to high yield. As proceeding, 48 h was taken as the most favorable reaction time at which the maximum yield of the etherification was occurred. The maximum yield was about 65.24%, 78.94% and 86.64% using $FeCl_3{\cdot}6H_2O$ 1, 2, and 3 mmol, respectively. The half-life of the etherification of benzyl alcohol using $FeCl_3{\cdot}6H_2O$ in each case was approximately 24 h. It could be summarized that the amount of $FeCl_3{\cdot}6H_2O$ employed was markedly influenced on the yield of dibenzyl ether. Watanabe *et al.* [54] reported the etherification of secondary alcohols using *p*-toluenesulfonic acid as a homogeneous catalyst. The results showed that the yield of ether was directly related to the reaction time and the amount of catalyst.

3.3.4 The mechanistic pathway for the etherification of alcohols by iron reagents

A widely accepted mechanism of etherification catalyzed by acids involves protonation of the hydroxyl group of an alcohol to give the corresponding oxonium ion as a better leaving group. The reaction then can proceed through substitution by another molecule of the alcohol. The mechanistic pathway is demonstrated in Scheme 3.2.



Scheme 3.2 The proposed mechanism for the etherification of benzyl alcohol

In the first step, the lone pair of electron on the oxygen atom of a hydroxyl group donates to an empty orbital of $FeCl_3 \cdot 6H_2O$ to generate the benzyl oxonium ion. Next, the carbon-oxygen bond of this oxonium ion is broken to furnish the formation of benzylic carbocation, which then reacts with the hydroxy group of the other benzyl alcohol to give dibenzyl ether. It should also be noted that ethers with a benzylic position may cleave by an S_N1 or E_1 mechanism because these substrates can produce stable intermediate carbocations [55].

CHAPTER IV

CONCLUSION

From the proceeding results and discussion, the main focus of this research was to search for another appropriate catalyst for esterification of carboxylic acid and apply the optimum conditions for synthesis selected fragrance and target molecules. Moreover, $FeCl_3.6H_2O$ have been also used as reagent for transesterification and etherification. The optimum conditions of transesterification could be applied for synthesis biodiesel from vegetable oil. The products could be easily separated by extraction. The cost of the reagent used was found to be cheap to other related methods cited in the literatures.

On the basis of the results of esterification, the outcome from the study on the effect of strating manifested that this method was suitable for aliphatic carboxylic acid and short chain aliphatic acids more than aromatic carboxylic acid and long chain aliphatic carboxylic acid. A comparison of each type of alcohol for the esterification reaction shows that the activity in alcohol decreases in the series: primary alcohol > secondary alcohol > tertiary alcohol. In the esterification of benzyl alcohol with benzoic acid in stoichiometric amounts was formed benzyl ether as a by-product. However, it has a commercial value; thus, the optimal condition for etherification was a field of continuing interest.

In case of the transesterification, $FeCl_3.6H_2O$ was successful reagent and gave high yield of product. Fortunately, The optimum conditions of transesterification: ester 5 mmol, methanol 5 mL, $FeCl_3.6H_2O$ 3 mmol, dried benzene 1 mL at reflux temperature for 48 h. From the etherification research, $FeCl_3.6H_2O$ was an efficient reagent provided the high yield of benzyl ether (86.64%). From the condition optimization, it was found that the reaction carried out with 8 mmol of substrate, 3 mmol of reagent, 2 mL of THF as solvent, at reflux temperature for 48 h was the optimal condition.

Suggestion for the future work

This research relates to the application of $FeCl_3.6H_2O$ for the synthesis of ester. The outcome opened many possibilities to deal with future exploration. The development of $FeCl_3.6H_2O$ for other catalyst systems are imperative to investigate. Esterification of carboxylic acid using $FeCl_3.6H_2O$ should be attempted to apply for the industrial chemistry.

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